CLINICAL

CIRM
CALIFORNIA INSTITUTE FOR REGENERATIVE MEDICINE

CLIN2: Funding Opportunity for Clinical Trials



Program Announcement

May 14, 2025

CLIN2 Awards: Funding Opportunity for Clinical Trials

Summary

<table>
<tr><th colspan="4">OVERVIEW</th></tr>
<tr><td colspan="2">Objective</td><td colspan="2">To accelerate clinical development of stem cell-based and genetic therapies to late-stage trials by encouraging innovative clinical trial designs, and incentivizing stage-appropriate market access strategies and pre-commercialization activities.</td></tr>
<tr><td colspan="2">Scope</td><td colspan="2">All activities necessary for the completion of an interventional phase 1, 2, or 3 trial, plus studies to understand mechanism of action and potency assay development, patient support activities, and data sharing activities. May support manufacturing for the next phase trial.</td></tr>
<tr><td colspan="2">Program Recurrence</td><td colspan="2">Four times per year</td></tr>
<tr><th colspan="4">AWARD DETAILS</th></tr>
<tr><td rowspan="2">Funds</td><td>Stage</td><td>First in Human*</td><td>Phase 2 or Subsequent**</td><td>Phase 3 or Pivotal</td></tr>
<tr><td>Max Award Amount</td><td>$8,000,000 (for-profit)
$12,000,000 (non-profit)</td><td>$15,000,000</td><td>$15,000,000</td></tr>
<tr><td colspan="2">Max Duration</td><td colspan="2">Up to 4 years</td></tr>
<tr><th colspan="4">ELIGIBILITY REQUIREMENTS</th></tr>
<tr><td colspan="2">Applicant Organization</td><td colspan="2">California or non-California-based for-profit or non-profit organizations may apply
Specific allowable costs apply, see “What should one know before preparing the budget?” for further information.</td></tr>
<tr><td colspan="2">Applicant PI</td><td colspan="2">Must commit at least 15% effort and adhere to CIRM’s requirements*</td></tr>
<tr><td colspan="2">Critical Role</td><td colspan="2">The project team must include an experienced project manager who commits a minimum 50% effort.</td></tr>
<tr><td colspan="2">Co-funding</td><td colspan="2"><table><tr><th>First in Human**</th><th>Phase 2 or Subsequent***</th><th>Phase 3 or Pivotal</th></tr><tr><td>30% (for-profit****)
None (non-profit)</td><td>50% (for-profit)
None (non-profit)</td><td>50%</td></tr></table>The minimum co-funding requirement may be fulfilled by cash-based or warrant-based co-funding.</td></tr>
<tr><th colspan="4">SCHEDULES AND DEADLINES</th></tr>
<tr><td colspan="2">Application Due Dates</td><td colspan="2">Four times per year</td></tr>
<tr><td colspan="2">GWG Review</td><td colspan="2">Approximately 90 days after application deadline</td></tr>
<tr><td colspan="2">Award Approval</td><td colspan="2">Approximately 60 days after GWG review</td></tr>
<tr><td colspan="2">Start Date</td><td colspan="2">Must be ready to start award activities within 60 days of award approval</td></tr>
</table>

CONTACT AND ADDITIONAL RESOURCES
https://www.cirm.ca.gov/researchers/funding-opportunities-clinical-trial-stage-research/ For additional information on the program or applications, contact clinical@cirm.ca.gov. For questions related to the review and approval of applications, contact review@cirm.ca.gov. ***Additional requirements and definitions may be found in CIRM Funding Opportunities: Common Requirements and Definitions, and are incorporated herein by reference.** **For this program announcement, a trial is considered First-in-Human if it is the first clinical trial using this therapeutic candidate in the proposed disease indication and using a given route of administration. *** For this program announcement, "Subsequent" trials are any phase 1 trials following a First-In-Human trial in the proposed disease indication and using a given route of administration. This definition excludes phase 3 or pivotal phase 2 trials. ****Co-funding requirement also applies to for-profit partners of non-profit applicants.

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Background

The mission of the California Institute for Regenerative Medicine (CIRM) is to accelerate world class science to deliver transformative regenerative medicine treatments in an equitable manner to a diverse California and world.

This opportunity is in support of CIRM's Strategic Allocation Framework (SAF) goals as approved by the Independent Citizens' Oversight Committee (ICOC) in September 2024, including the goal to propel 15-20 therapies targeting diseases affecting Californians to late-stage trials and the goal to advance 4-7 rare disease programs to the stage of filing a Biologics License Application (BLA) with the U.S. Food and Drug Administration (FDA).

Through the CLIN2 program, CIRM continues to create funding opportunities for the types and stages of clinical research that otherwise do not exist or are of limited scope and focus to advance the field of regenerative medicine. The CLIN2 program is a part of CIRM's core product development programs that unlike other funding sources, provide reliable and predictable funding throughout the award period.

Objective

The objective of this funding opportunity is to support the completion of an interventional phase 1, 2, or 3 trial (including pivotal trials) as defined by a single FDA-cleared clinical protocol, for an innovative stem cell-based or genetic therapy addressing a serious unmet need and with the potential for transformative benefits to patients, families and the health care system. In addition to the interventional trial, the program may also support a lead-in normal healthy volunteer study or natural history study that is needed for baseline or control data for the interventional trial. The trial should be part of a clinical development program aiming for marketing approval and which proposes stage-appropriate pre-commercialization activities, including development of an access and affordability strategy. The clinical development program for the supported trial should demonstrate a commitment to enrolling a patient population reflective of the demographics of the disease population. Further, the clinical development program should leverage CIRM-funded and externally funded infrastructure for data, resource or knowledge sharing to drive rigor, efficiency, and transparency of clinical trial results.

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.

Scope and Structure

The CLIN2 award supports completion of an interventional phase 1, 2 or 3 clinical trial for a stem-cell based or genetic therapeutic candidate and may also fund an associated natural-history comparator or lead-in normal healthy volunteer study. Applicants are encouraged to use accelerating trial designs where appropriate, such as basket trials or adaptive design dose-escalation protocols.

Program funding areas

The CLIN2 Program aims to advance clinical candidates that have the potential for transformative patient impact and that address barriers to access and affordability. To support this goal, align with Proposition 14's mandate, and remain responsive to an evolving scientific and regulatory landscape, funding preferences will be set on an annual basis. These preferences will be guided by portfolio analyses and other strategic considerations in a cyclical manner. These preferences will be implemented through the CLIN2 Qualification process (see "Qualification Process", page 13) and via programmatic considerations by the Application Review Subcommittee of the ICOC.

Preference areas

For fiscal year 2025-2026 CLIN2 cycles, the following modalities and project features will be prioritized:

PREFERENCE
Pluripotent stem cell-derived therapies
In vivo genetic therapies
Therapies using non-viral nucleic acid delivery
Projects addressing diseases of the brain and CNS
Applications from California organizations
Projects progressing from CIRM-funded IND-enabling or earlier phase clinical trial awards
Projects with Fast Track, RMAT or Breakthrough designations
Projects proposing pivotal clinical trials (as agreed-to by the FDA)

Program activities

CIRM **will fund** the following activities under this opportunity:

	REQUIRED ACTIVITIES
✓	All clinical operations activities needed to complete the trial according to the proposed timeline
✓	Outreach, enrollment, and retention activities to achieve trial enrollment demographics reflecting the target patient population
✓	Treatment of patients with the therapeutic candidate (or control) and follow-up visits per the clinical protocol
✓	Sharing of any non-clinical as well as clinical data per the CIRM data sharing requirements
✓	Establishment and regular convening of a Strategic Planning Committee (SPC) with clinical development expertise to provide forward-looking strategic advice
✓	Activities associated with managing, preserving, and sharing data and knowledge from the study
✓	Activities associated with access and affordability planning for the therapeutic candidate in the proposed indication
	ALLOWABLE ACTIVITIES
✓	Natural history studies needed for baseline or control data for the interventional trial
✓	Lead-in studies in normal healthy volunteers for the interventional trial
✓	Studies to develop biomarkers, understand mechanisms of action and develop a potency assay
✓	Regulatory activities including FDA interactions and requests for designations
✓	Non-clinical studies required by the FDA (FDA documentation required)
✓	Strategic planning activities
✓	Manufacturing activities to supply the current clinical trial, including technology transfer and FDA-approved comparability studies, if needed
	CONDITIONALLY ALLOWABLE ACTIVITY

✓	Manufacturing for the next phase trial. Funding of that activity will be conditioned on 1) an interim evaluation by CIRM and a panel of independent experts of the clinical trial data to date, and 2) provision of 50% co-funding for this activity, if co-funding is required as specified in "Award Amount and Duration" below

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

UNALLOWABLE ACTIVITIES	
✘	Costs incurred on or before the date of ICOC approval
✘	Discovery or translational research
✘	Activities already budgeted or paid for under a prior, existing or future CIRM award
✘	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

Award amount and duration

	FIRST IN HUMAN	PHASE 2 OR SUBSEQUENT	PHASE 3 OR PIVOTAL
Max Award (total cost)	$8,000,000 (for-profit) $12,000,000 (non-profit)	$15,000,000	$15,000,000
Max Duration	Up to 4 years (48 months)		

The amount of total project costs requested must be adequately justified and is subject to adjustments prior to the issuance of an award based on assessments of the Grants Working Group (GWG), the CIRM team, or by the Application Review Subcommittee of the ICOC.

Funding allocation

CIRM anticipates funding between 9-16 CLIN2 awards in FY25-26, contingent on the number of applications at each funding level that are recommended.

Provisional timetable

CLIN2 funding opportunities will recur four times per year. The anticipated timeline of each funding cycle is as follows:

PROVISIONAL TIMETABLE	
Applications Open	Four times per year
Applications Due	Please visit Funding Opportunities on the CIRM website for current application deadlines
Grants Working Group (GWG) Review	Approximately 90 days after application deadline
Application Review Subcommittee (ARS) Award Approval	Approximately 60 days after GWG Review
Award Start	60 days after award approval

Eligibility

All the following requirements must be fully satisfied for an application to be accepted and considered for funding by CIRM.

(1) The applicant must propose an interventional phase 1, 2, or 3 clinical trial for a stem cell-based or genetic therapy.

Refer to CIRM Funding Opportunities: Common Requirements and Definitions for definitions of stem cell-based or genetic therapies in scope for the CLIN2 program. The overall project and proposed activities must fall within the defined scope of this opportunity.

(2) The applicant must meet readiness criteria at the time of application.

For projects not progressing from a CIRM preclinical stage award, the IND application and clinical protocol must be cleared by FDA at the time the CIRM application is submitted. For projects progressing from a CIRM preclinical stage or earlier phase clinical trial award, the IND application must have been submitted to FDA by the time of the CLIN2 application and must be cleared to proceed within 30 days of the CLIN2 application submission.

(3) The Principal Investigator (PI) must commit a minimum of 15% effort and adhere to CIRM's requirements.

The PI must commit a level of effort on the project consistent with achieving the CLIN2 program objective and not less than 15% on average over the project period. The PI must adhere to general eligibility requirements described in CIRM Funding Opportunities: Common Requirements and Definitions.

(4) The project team must include an experienced project manager who commits at least 50% effort.

The project team must include a Project Manager with experience in managing relevant clinical development projects. The PM should be familiar with and utilize a variety of processes and tools to manage team communication, team dynamics, project budget, project schedule, project resources and project risks to help their team achieve the project objective in a timely manner. The Project Manager must commit at least 50% effort on average over the project period.

(5) The project team must include an experienced Data Project Manager.

To ensure effective and collaborative sharing and management of data, a Data Project Manager must be part of the team. This individual must have demonstrated experience in data handling and is responsible for interfacing with a data management team(s), interfacing with CIRM's planned data infrastructure, reporting progress on data management and sharing as well as maintaining the integrity of data during

ingestion. The Data Project Manager role can be distributed among multiple people and may be fulfilled by Key Personnel with other Critical Roles.

(6) The CIRM applicant must be the IND sponsor.

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

(7) The applicant must have at least one trial site located in California.

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

California applicant organizations must have at least one clinical trial site in California and must provide justification for inclusion of any sites located outside the State. Applicants are strongly encouraged to use CIRM Alpha Clinic sites when feasible.

(8) The applicant must be ready to initiate work on the funded project within 60 days of approval.

Given the urgency of CIRM's mission, all approved awardees must initiate work on the funded project within 60 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.**

(9) The application must be accurate and complete.

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

(10) The applicant must propose appropriate co-funding and demonstrate availability of funds.

CIRM will require co-funding as specified in the table below, based on the total "Allowable Project Costs". Non-profit applicants applying for funding for trials that are not phase 3 or pivotal may provide co-funding but it is only required when project costs are more than the maximum CIRM award amount. The requirements for a for-profit applicant also apply to non-profit applicants with for-profit Partners. Visit CIRM Funding Opportunities: Common Requirements and Definitions for CIRM's definition of a "Partner." Co-funding requirements will be based on trial stage and partnership status at the time of application. Applicants must also 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. Allowable Project Costs for research funded by CIRM are detailed in the CIRM Grants Administration Policy for Clinical Stage Projects and include 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. Only funds that will be spent concurrently with CIRM funds (i.e., no sooner than board approval and no later than completion of the final Operational Milestone) will qualify toward this co-funding requirement.

Description and documentation demonstrating the commitment of funds to cover the proposed co-funding amount must be provided as part of the application and by the application deadline. The co-funding may come from any funding source arranged by the applicant but may not include "in-kind" or similar types of support. The applicant may propose to use cash-on-hand, committed funding and/or planned fundraising as sources of funds for the co-funding commitment but must demonstrate that it will have cash-on-hand at project start date to co-fund at least the first operational milestone disbursement. Applicants are advised to refer to the Solvency and Co-Funding Template in the Document Uploads Section of the Application for additional instructions and guidance on co-funding requirements.

Alternatively, for-profit applicants and for-profit Partners of non-profit applicants may elect to fulfill all or a portion of the minimum co-funding requirement by agreeing to issue equity warrants to CIRM. Applicants electing the warrant-based co-funding requirement may request CIRM funding to cover the co-funding commitment up to the award limit. Applicants who elect the warrant-based co-funding requirement must sign the Warrant Term Sheet at application submission and must issue equity warrants at the award start

date. Applicants are advised to contact legal@cirm.ca.gov for additional guidance and information on warrant-based co-funding.

CLIN2 Co-funding Requirements

	First in Human	Phase 2 or Subsequent	Phase 3 or Pivotal	Manufacturing for Next Trial
Co-funding Requirement	30% (for-profit*) None (non-profit)	50% (for-profit) None (non-profit)	50% (for-profit or non-profit)	50%, if overall award has a co-funding requirement

(11) For-profit organizations must demonstrate solvency.

Solvency requirements are defined in CIRM Funding Opportunities: Common Requirements and Definitions.

(12) The applicant must be in "good standing."

Applicants and their affiliates must represent and certify that they are in good standing, as described in CIRM Funding Opportunities: Common Requirements and Definitions.

Application Preparation

Consultations and Webinars

CIRM staff aims to conduct public webinar(s) and Q&A sessions after posting of this program announcement. Prospective applicants are encouraged to sign up for email alerts and register for these sessions on our website. In addition, prospective applicants may request a consultation with a member of the Clinical Development team, to address questions about their project's eligibility or other project-specific questions. To request a consultation please email *clinical@cirm.ca.gov*.

How does one submit an Application?

Applications must be completed and submitted online using the CIRM Grants Management Portal at https://grants.cirm.ca.gov. A prospective PI must create a login in the system to access and submit application materials. Applications are available in the system only to the PI. **A PI may submit only one CLIN2 application per review cycle.**

What components does an Application include?

CIRM's online application is designed to collect information for CIRM staff to assess eligibility, for Grants Working Group reviewers to evaluate the project, and for CIRM rapidly to initiate an award if the project is approved for funding.

In the online portal, applicants must fill out an eligibility form, indicate Key Personnel involved in the project, provide a list of consultants and subcontracts, provide an overview of proposed activities, and prepare and justify an appropriate budget. In addition, applicants must certify that appropriate institutional approvals (e.g. SCRO, IACUC or IRB) will be in place during the award.

The application uploads page provides templates for the Scientific Proposal, Access and Affordability Proposal, candidate eligibility information, biosketches, financial solvency and co-funding information, and other funding support information. Applicants **must** use the provided templates. In addition, the uploads page provides links for uploading the clinical protocol, FDA correspondence, the manufacturing plan, investigator brochure, intellectual property plan and quotes to support the budget.

What are the contents of the Scientific Proposal?

The Scientific Proposal comprises the bulk of detailed information on the project, organized within the following sections. Page limits and formatting information will be provided on the Proposal template.

Project Summary: A high-level summary of the project.

Target Product Profile: Template-based product label containing base case and optimal specifications for the proposed product.

Value Proposition: Description of the unmet need, standard of care, affected patient population, competitive landscape, and the therapy's potential value (health and financial) for patients, families, caregivers and the healthcare system.

Scientific Rationale: Description of the proposed product and scientific data supporting use of that product as a therapy for the target indication.

Preclinical Studies: Template-based tabular summary of key preclinical studies, including IND-enabling study results.

Clinical studies: Template-based tabular summary of completed or ongoing clinical studies with the proposed or a related product.

Gantt-Like Timeline: Timeline with monthly granularity for all major activities, including activities described in the Access and Affordability Proposal.

Project Plan: Description of all proposed activities detailing how the objective of the Program Announcement will be met.

FDA Correspondence: Template-based tabular high-level summary of regulatory requests and proposed action plans.

Manufacturing Plan Synopsis: Template-based synopsis describing key aspects of the manufacturing plan for the proposed trial.

Clinical Protocol Synopsis: Template-based synopsis describing key aspects of the protocol for the proposed trial.

Clinical Operations Plan:

- Template-based synopsis describing key aspects of the planned clinical operations for the proposed trial with emphasis on how this plan supports the feasibility of meeting the patient enrollment timelines.
- Description of the population impacted by the indication. Description of proposed study sites for the trial and plans to leverage study site and other resources for outreach to and enrollment of affected patient populations. Description of plans to address barriers to participation faced by affected patient populations.
- Target Enrollment Table listing the planned number of trial participants and a rationale for enrollment targets.

Clinical Development and Commercialization Plan: A detailed description of the overall clinical development strategy for the proposed therapy in the target indication. Option to include descriptions of recommended stage-appropriate commercial planning, market access planning, health economics and outcomes research and medical affairs planning activities as described in CIRM's Access and Affordability Planning Requirements resource document and further described below.

Data Sharing Overview: A detailed description of how raw data, processed data and metadata produced from the project will be made available to the research community consistent with FAIR (Findability, Accessibility, Interoperability, and Reusability) data sharing principles. Refer to CIRM Data Sharing and Management) for additional information on how applicants should address data sharing and how the data sharing overview will be evaluated. The requirements described in CIRM Data Sharing and Management are incorporated here by reference.

Team Organization: Qualifications of the Principal Investigator and key personnel representing all critical functions of the project.

Plans for Risk Mitigation and Financial Contingency: Project risks, mitigation strategies, contingency plans, associated costs, and non-CIRM sources of contingency funding.

Resources and Project Environment: Institutional offerings that will benefit the project.

References: Sources cited in the proposal.

What should one know about CIRM's requirements for Access and Affordability Strategic Planning?

Successful and rapid access to approved stem cell-based and genetic therapies requires stage-appropriate strategic planning throughout preclinical and clinical stages of development to ensure that the therapy is accessible and affordable for the affected patient populations. To help ensure that projects are adequately preparing for access and affordability, CIRM has developed a roadmap and associated requirements for stage-appropriate strategic planning activities in preclinical and clinical development funding programs. Applicants must review the Access and Affordability Planning Requirements resource document for CLIN2 access and affordability activities required for each trial stage. These include both prerequisite activities (which must be completed by the time of application submission) and activities which must be proposed during the award period. Applicants must adequately describe progress to date and propose a plan for conducting relevant stage-appropriate activities in the Access and Affordability Proposal. The Proposal is organized in the following sections:

1. Summary of patient needs and approach to access and affordability for the proposed therapeutic
2. Activities table describing status, completion date (if applicable), and description of stage-required activities
3. An option to append supporting materials, including completed reports or work plans related to the listed activities.

Additional activities identified as supporting commercialization and market access activities may be included in the "Clinical Development and Commercialization Plan" section of the Scientific Proposal Template as described above.

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. The total CIRM Award is subject to a total Award cost cap of Allowable Project Costs. Allowable Project Costs are detailed in the CIRM Grants Administration Policy for Clinical Stage Projects and include Direct Facilities and Indirect Costs. Generally, project costs for personnel, supplies, travel, equipment, and subcontracts may be claimed. Limits for specific cost categories must be observed.

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, contingent on 1) an interim evaluation by CIRM and a panel of independent experts of the clinical trial data to date, and 2) provision of 50% co-funding for this activity, if co-funding is required for the overall award (see CLIN2 Co-funding Requirements table above).

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

- 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 contingent on 1) an interim evaluation by CIRM and a panel of independent experts of the clinical trial data to date, and 2) provision of 50% co-funding for this activity, if co-funding is required for the overall award (see CLIN2 Co-funding Requirements table above).

Unallowable Costs

- 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
- For a non-California applicant, the per subject share of the costs of clinical and non-clinical research activities, whether conducted in California or outside of California, that are **NOT** directly attributable to the treatment of California subjects enrolled in the proposed clinical trial

For any proposed subcontracts over $500,000, a tabulated summary of at least three proposals must be provided, and the selection of the subcontractor must be justified in detail. If any such subcontracts are sole sourced, detailed justification must be provided. The "Resources" section of this PA describes available resources for CIRM-funded projects including the CIRM Alpha Clinic Network, the CIRM academic GMP Manufacturing Network and the CIRM Industry Resource Partners composed of reagent, equipment and service providers (i.e. CDMOs, CROs, etc.)

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

Direct Facilities Costs are the general operating costs of the grantee'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 costs for for-profit Awardees or any non-profit Awardees without a federally negotiated Facilities and Administrative Rate agreement are limited to 35% of direct project costs and must be consistent with facilities rates applied to similar research awards at the organization. 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.

What are Indirect Costs and how much can an applicant claim?

Indirect Costs are administrative costs of the awardee incurred for common or joint objectives, which cannot be readily and specifically identified with a particular project. For-profit organizations cannot claim indirect costs. For non-profit organizations, indirect costs will be limited to 20% of allowable direct research funding costs awarded by CIRM (i.e., 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.

Change in Status

Applicants are required to notify CIRM of any material change in status while the application is pending review (e.g., a change in PI, the applicant no longer qualifies as a California Organization, etc.).

Application Review Information

What is the process for evaluating an application?

Eligibility and Completeness 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 or that the submitted application is incomplete or contains false or inaccurate information, CIRM

will notify the applicant of its decision and, if CIRM deems it appropriate, allow an opportunity for the applicant to remedy the deficiencies. If CIRM deems it inappropriate, or if the applicant does not remedy the error in a timely manner, CIRM will terminate all further action on the application.

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

Qualification process

When the number of applications submitted for a given application deadline exceeds the number that can be reviewed by the GWG panel, CIRM staff will prioritize applications that best align with CIRM's goals and the objective program preference areas defined for the current fiscal year (See "Preference Areas" on page 5 above).

The highest scoring applications that do not exceed the GWG capacity will proceed to GWG review. If multiple applications receive the same objective score and additional prioritization is necessary, the following Subjective Qualification process will apply:

1. The GWG will score tied applications based on their potential value proposition.
2. If ties remain after GWG scoring, CIRM staff will make final selections based on the representation of the disease area in CIRM's clinical portfolio and the degree of innovation of the approach.

All applicants will be notified of the outcome of this qualification process.

Scientific Review

The scientific merit of each application that is selected for full review will be assessed by the GWG, which is composed of fifteen subject matter experts from outside California, seven patient advocate or nurse members of the ICOC (called "GWG Board Members"), and the Chair of the ICOC. Information about the bylaws of the GWG and a list of scientific members who may participate in the GWG review can be found at https://www.cirm.ca.gov/about-cirm/working-groups/. The composition of the ICOC can be viewed on the CIRM website https://www.cirm.ca.gov/about-cirm/governing-board/

The fifteen participating scientists on the GWG will evaluate the applications and score them on a scale of 1-100 according to scientific and technical merit, applying the review criteria described below. For purposes of making funding recommendations to CIRM's board, each application will be assigned to one of two categories based on the median score as follows:
Median score 85 or above: The application has exceptional merit and warrants funding, if funds are available; or

Median score below 85: The application is not recommended for funding.

The Application Review Subcommittee of the ICOC will make final funding decisions.

Budget Review

CIRM will review the proposed budget to ensure all costs are reasonable, allocable, consistently treated and allowable. When CIRM determines that a proposed budget differs significantly from market rates, 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, CIRM will adjust the budget prior to issuance of an award based upon assessments of the GWG, the CIRM team, or by the Application Review Subcommittee of the ICOC.

Consideration of Past 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.

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, experts providing input to 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?

1. Value Proposition- *Evaluate the extent to which the therapy offers a compelling value proposition based on holistic consideration of the following:*

- Assess the therapy's potential to provide a meaningful and substantial improvement in clinical outcomes for the intended population as compared to therapies currently available or in trials (e.g., efficacy, safety, patient burden).
- Assess the expected impact of addressing the unmet medical need on patients, caregivers, and healthcare system.
- Evaluate the feasibility and practicality of the therapy's uptake by patients, healthcare providers and payors.

2. Rationale - *Evaluate the scientific rationale for the proposed therapy and the strength of the supporting data*

- Assess the fundamental robustness of the scientific rationale including justification for the indication, therapeutic approach, regimen and route of administration.
- Assess the extent to which the rationale for clinical development of the proposed therapy is supported by the body of available data, including compelling evidence of disease modifying activity in relevant disease models and any available clinical trial data generated using the proposed therapeutic approach.
- Consider the strengths and limitations of the data presented and/or the models utilized in completed studies.

3. Project Plan and Design - *Evaluate the project's plan and design.*

- Evaluate the extent to which the proposed activities are necessary and appropriate to efficiently and effectively drive clinical development of the proposed therapy. For example, the applicant should consider:
    - whether the project will generate data to enable stage appropriate go/no-go decision making for further investment in the approach;
    - the feasibility of achieving timely full enrollment of the trial; and
    - the appropriateness of the manufacturing process, plan and analytical development plans.
- Consider the whether the project's objective is likely to be achieved within the proposed budget and timeline.
- Assess the validity of the potential project risks identified and contingency plans presented.

4. Project Team and Resources - *Evaluate the expertise and resources that will be deployed to achieve the project deliverables.*

- Evaluate the appropriateness of the team's leadership, expertise and staffing to successfully complete all aspects of the project.
- Consider whether a robust plan for coordination and execution of the project has been clearly outlined.
- Assess the extent to which the team has access to all the necessary resources and facilities, including manufacturing facilities, to successfully conduct the proposed activities.

- Consider whether the collective team, including consultants and subcontractors, have a demonstrated track record of supporting stem cell-based and genetic therapy projects through clinical trials and/or towards licensure, as stage-appropriate.

5. Population Impact – *Evaluate the extent to which the project considers the potential impact of the proposed therapy across affected populations*

- Evaluate the applicant's understanding and consideration of the affected population for the target indication, including any differences in detection/diagnosis, disease burden, care, and health outcomes across the affected population.
- Assess the appropriateness of the proposed trial study population in the context of current knowledge of demographic groups at risk for the target indication.
- Consider the applicant's goals to achieve a comprehensive distribution of subjects appropriate to the proposed indication and whether key criteria to disqualify any at-risk groups are justified.
- Evaluate the extent to which the applicant's plan for participant outreach, engagement, enrollment and retention addresses key barriers to trial participation by all affected population groups, is well-matched to the proposed study population and is feasible in the proposed time frame.

How will the Access and Affordability Proposal be evaluated?

CLIN2 Access and Affordability Proposals will be evaluated by subject matter experts using the rubric described in the Access and Affordability Planning Requirements. Evaluations from these experts will inform applicant feedback, programmatic funding recommendations, and award management.

Award Administration

Issuance of Award

CIRM issues awards through a Notice of Award (NOA), which serves as the official contract defining terms, conditions, and funding commitments. Before finalizing the NOA, CIRM reserves the right to modify project activities and budgets, including improving data sharing plans submitted during pre-funding administrative review. After consulting with project teams, CIRM establishes milestones, success criteria, and timelines based on application information and data sharing plans and may consult external advisors when developing operational milestones for research, data sharing, and access and affordability planning activities. CIRM will also review key agreements critical to project success to ensure compliance with applicable policies and regulations.

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 Award based upon information provided in the Application. CIRM may consult with external advisors to inform development of operational milestones for the proposed research and/or Access and Affordability strategic planning activities. 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. If a Suspension Event is not resolved to CIRM's sole satisfaction, CIRM has the right to terminate the award. CIRM establishes Suspension Events for inclusion in the NOA based on information provided in the Application.

Strategic Planning Committee

Upon approval of an award, CIRM will require that the awardee assemble an independent Strategic Planning Committee (SPC) to provide expertise in clinical development, including manufacturing, regulatory and commercialization strategies. It is expected that this SPC will meet within the first quarter after award launch and thereafter at least twice a year. All SPC meetings must be attended by the CIRM program officer and may include other CIRM staff. To ensure appropriate expertise is represented on the SPC, membership is subject to CIRM approval. Remuneration of SPC members will be considered an allowable expense from CIRM project funds. Minutes of SPC meetings must be agreed to by all SPC members and supplied to CIRM within 30 days.

Reporting

Awardees will be required to provide periodic written progress and financial reports to CIRM. CIRM requires awardees to provide clinical trial enrollee demographic data in the trial population as specified in the application as well as other reporting requests. Awardees developing a therapeutic will be required to submit a Quality Target Product Profile annually and at the conclusion of the award.

Data Sharing and Management

The sharing of data and knowledge produced from CIRM-funded projects is key to advancing the field of regenerative medicine and accelerating the discovery, validation and development of treatments for patients. CIRM requires awardees to manage and preserve raw data, processed data, and metadata, and make applicable data and metadata available to the broader scientific community. CIRM also requires applicants to allocate funds in their proposed budget for personnel and/or activities related to managing and sharing data produced from the funded project. See the CIRM Data Sharing and Management document for additional information on how applicants should address data sharing and how the data sharing overview will be evaluated. The requirements described in CIRM Data Sharing and Management are incorporated here by reference.

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
https://www.cirm.ca.gov/our-funding/cirm-stem-cell-grant-regulations/

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. See the Managing Your Grant webpage for answers to frequently asked questions regarding managing a CIRM award.

Resources

CIRM-Funded Infrastructure

CIRM has established a set of Infrastructure Programs to help CIRM applicants and awardees prepare competitive applications and to accelerate development of stem cell-based and genetic therapies.

The CIRM Alpha Clinics are a statewide network composed of nine leading California Medical Centers with a common goal of streamlining and accelerating the delivery of cell and gene therapies to patients who need them. The Network supports stem cell-based and genetic therapy clinical trials for academic and commercial partners. Applicants and awardees can partner with the CIRM Alpha Stem Cell Clinics Network to identify California trial sites, evaluate patient cohorts, and accelerate trial initiation and completion.

The CIRM Cell and Gene Therapy Manufacturing Network is composed of nine non-profit GMP manufacturing facilities that are co-located with the Alpha Clinics. Applicants and awardees can utilize the Network GMP facilities for process development, manufacturing, quality control testing and other related services.

CIRM Industry Resource Partner Program

The CIRM Industry Resource Partner Program is composed of select contract development and manufacturing organizations (CDMOs), contract research organizations (CROs) and other vendors and service providers that are committed to making their consultations, services, and resources more accessible to CIRM-funded projects.

Applicant Resources

- For more information about the CLIN2 program, please visit our Current Funding Opportunities page to access the current program announcement, webinar materials and FAQs.
- For scientific questions that are not addressed in the above resources, send email correspondence to clinical@cirm.ca.gov.
- For questions related to application review, send email correspondence to review@cirm.ca.gov.
- For questions related to budgets or allowable project costs, please consult the Managing Your Grant page on CIRM's website.
- Terms used in this document are defined in CIRM Common Requirements and Definitions.
- Information about CIRM's data sharing requirements is found in CIRM Data Sharing and Management.
- Requirements and guidelines to address access and affordability planning are available in Access and Affordability Planning Requirements

Recent Document Revisions

DATE	LIST OF CHANGES
05/14/2025	• Added list of program preferences that may be applied during qualification process • Revised qualification process • Added Access and Affordability Planning upload to the application requirements and provided applicant resources • Changed frequency of application deadlines to quarterly from monthly • Changed budget and co-funding requirements • Provided data sharing and Common Requirements and Definitions resource
07/03/2024	• Added qualification process • Added reference to CIRM Cell and Gene Therapy Manufacturing Network. • Revised candidate eligibility to be the same for all clinical trial phases • Clarified trial enrollment demographic data requirement • Updated PA contact information • Removed medical device track • Clarified fundable activities • Introduced co-funding for not-for-profit applicants with a for-profit Partner • Removed co-funding for unpartnered not-for-profit applicants • Introduced warrant co-funding option • Updated solvency language • Updated good standing requirements • Clarified definition of California organization • Removed references to CIRM/NHLBI Cure Sickle Cell Joint Initiative • Updated unallowable costs description • Updated budget review process • Updated eligibility review language • Referenced FDA's guidance "Enhancing the Diversity of Clinical Trial Populations - Eligibility Criteria, Enrollment Practices, and Trial Designs Guidance for Industry" • Added QTPP reporting requirement