PRECLINICAL

CIRM
CALIFORNIA INSTITUTE FOR REGENERATIVE MEDICINE

RAPID: Funding Opportunity for Rare Disease Platform Projects

Request for Applications

May 20, 2026

Rare Disease Acceleration Through Platform Innovation and Delivery (RAPID) Funding Opportunity for Preclinical Stage Projects

Summary

OVERVIEW			
Objective		To create a scalable model that rapidly delivers transformative, platform-based genetic therapies to patients with rare diseases	
Scope		CIRM will support activities in the IND-enabling and clinical stages for RAPID Validation and in the pre-IND and IND-enabling stages for RAPID Innovation	
Recurrence		Annual (until RAPID program funds exhausted)	
AWARD DETAILS			
Stage-specific Amount and Duration	**Stage**	**RAPID Validation**	**RAPID Innovation**
	Amount	No maximum amount	No maximum amount
	Duration	6 years	3.5 years
ELIGIBILITY			
Applicant Organization		Only non-profit or for-profit organizations that meet CIRM's definition of a California Organization are eligible to apply	
Critical Roles		• A Principal Investigator, who must commit a minimum 15% effort • An experienced project manager at a minimum 50% effort	
Stage Readiness		**RAPID Validation:** pre-IND completed **RAPID Innovation:** INTERACT completed or requested at time of application submission	
SCHEDULES AND DEADLINES			
GWG Selection		Approximately 60 days after application submission deadline	
GWG Discussion		Approximately 30 days after GWG Selection	
Award Approval		Next available Application Review Subcommittee meeting	
Start Date		Must be ready to start award activities within 90 days of award approval (see Eligibility section 7 for more details)	
CONTACT AND ADDITIONAL RESOURCES			
https://www.cirm.ca.gov/researchers/funding-opportunities-preclinical-research/ For additional information on the program or applications, contact preclinical@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 here by reference.**			

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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. In September 2024, CIRM's Governing Board, the Independent Citizens' Oversight Committee (ICOC), approved a Strategic Allocation Framework (SAF) to guide and optimize the impact of CIRM's current and future investments. A recommendation of the SAF was to implement a platform-based approach to accelerate therapy development for rare diseases.

Advances in platform-based genetic technologies, increasing regulatory receptiveness to master protocols and basket trial designs, and the persistent unmet needs of patients with rare disease together create a timely opportunity to accelerate development through a coordinated, platform-driven approach. By reducing per-indication development costs and enabling the efficient advancement of therapies for patients with rare diseases that are often not commercially viable under traditional models, platform-based approaches support broader access to transformative treatments.

To accelerate the development of genetic therapies for rare diseases[1], CIRM has launched the Rare Disease Acceleration Through Platform Innovation and Delivery (RAPID) program. This initiative is designed to harness the power of platform-based development to enable the efficient advancement of multiple related therapies through shared technologies and infrastructure. CIRM defines platforms as a common set of technologies that are leveraged for accelerated and resource-efficient development, manufacture, clinical delivery, and regulatory review of multiple related therapies. By supporting platforms that integrate common components across therapeutic candidates, RAPID facilitates faster development timelines, more efficient use of resources, and a scalable model where each new candidate strengthens the overall platform. This approach allows for the parallel progression of multiple therapies with streamlined testing requirements, reduces capital and operational costs through shared development pathways, and builds a cumulative evidence base that enhances regulatory confidence and accelerates future approvals.

Through the RAPID program, CIRM is accelerating the preclinical and clinical development of platform-based genetic therapies for rare diseases by supporting innovative baskets of therapies through to clinical proof of concept in first-in-human (FIH) trials. This initiative directly contributes to the SAF goal of advancing 4–7 rare disease programs toward BLA. By investing in scalable, sustainable therapeutic platforms, RAPID not only drives scientific and regulatory innovation but also reduces key barriers to patient access—helping to expand the reach of transformative treatments to patients with rare diseases.

Objective

The objective of the RAPID program is to create a scalable model that rapidly delivers transformative, platform-based genetic therapies to patients with rare diseases.

Within the RAPID program, CIRM will serve not only as a funding agency but as an active partner, providing internal resources and leveraging a network of expert advisors to support awardees throughout development. A central feature of the program is the CIRM Awardee Knowledge Network, which will facilitate real-time sharing of technical, scientific, and regulatory insights across CIRM-funded teams. In addition, CIRM will promote external data sharing beyond its portfolio, with a focus on disseminating regulatory learnings to benefit the broader field.

This collaborative model emphasizes scaling platform innovations, advancing regulatory science, expanding the safety and efficacy evidence base, and reducing the cost and time of development—ultimately creating a sustainable and knowledge-driven pathway for rare disease therapeutic development.

Program Guiding Principles

[1] CIRM defines rare disease as a disease with a prevalence of <200,000 patients in the US

Guiding Principles are how CIRM translates the SAF recommendations into portfolio outcomes. Guiding Principles shape program objectives, inform the criteria by which projects are selected by the Grants Working Group (GWG) for discussion and recommendations, and inform the recommendations that CIRM teams bring to the Application Review Subcommittee (ARS) to support funding decisions.

The RAPID Program is designed to expand access to life-changing genetic therapies for rare disease patients by accelerating development through scalable platform approaches, regulatory efficiency and shared learnings across multiple candidates and indications. To achieve these objectives, the RAPID portfolio will:

- Advance safe and effective *in vivo* genetic therapies for rare disease patients with limited or no treatment options
- Demonstrate platform scalability across additional candidates and indications by delivering meaningful reductions in time and cost
- Contribute to a shared regulatory and technical foundation to accelerate therapy development across diversified platform approaches and rare disease areas

Scope and Structure

The RAPID program supports platform-based genetic therapy development via two complementary award types: RAPID Validation and RAPID Innovation. For both types of awards, platforms are expected to deliver accelerated and cost-effective development efficiencies through shared preclinical data and models, shared CMC processes and analytics, and streamlined clinical development approaches that support rapid expansion to additional candidates with reduced incremental burden. Within this shared platform framework, the RAPID program distinguishes between two award types based on stage of development, regulatory readiness and expected outcomes:

- **RAPID Validation** is intended for projects that have already engaged with the FDA and received preliminary regulatory alignment on their platform approach for at least three in vivo genetic therapy candidates via a pre-IND meeting. RAPID Validation awards will support all activities required to initiate and complete a FIH master protocol[2] clinical trial of at least three in vivo genetic therapy candidates. Applicants may propose a development plan that includes IND-enabling studies, submission and clearance of a master protocol IND, and execution of the FIH clinical trial. The expected outcome for RAPID Validation awards is the completion of the FIH clinical trial of at least three in vivo genetic therapy candidates that demonstrates clinical proof of concept for the platform.
- **RAPID Innovation** focuses on earlier-stage projects that are exploring novel or emerging platform technologies. These projects are expected to push the boundaries of what constitutes a platform, including innovations that could reduce testing requirements or expand applicability across multiple rare diseases. Applicants must have either completed an INTERACT meeting with the FDA or have submitted the INTERACT meeting request to the FDA at the time of application. Applicants may propose activities ranging from platform optimization, IND-enabling studies and submission of a master protocol IND. The expected outcome for RAPID Innovation awards is master protocol IND clearance for an FIH trial of at least three in vivo genetic therapy candidates.

Program activities

Applicants may request funds to cover costs for research activities conducted wholly in California and may also request costs for research activities conducted outside of California, provided that the California

[2] A master protocol is a clinical trial protocol designed with multiple coordinated sub-studies to evaluate one or more investigational drugs for one or more diseases within the overall trial structure. For purposes of RAPID, “Master Protocol IND” may include one or more INDs as required by FDA for the proposed FIH trial.

Organization exercises direction and control over the activities.

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

	ALLOWABLE ACTIVITIES	EXPECTED OUTCOMES
RAPID Validation	• All activities required to achieve Master Protocol IND clearance • All activities required to conduct a Master Protocol clinical trial • Activities associated with managing, preserving, and sharing data and knowledge from the project • Activities associated with access planning for the platform	Completion of the FIH clinical trial of at least three in vivo genetic therapy candidates that demonstrates clinical proof of concept for the platform.
RAPID Innovation	• All activities required to achieve Master Protocol IND clearance • Activities associated with managing, preserving, and sharing data and knowledge from the project • Activities associated with access planning for the platform	Master Protocol IND clearance for an FIH trial of at least three in vivo genetic therapy candidates

CIRM **will not fund** the following activities under this opportunity:

UNALLOWABLE ACTIVITIES ACROSS ALL STAGES	
✘	RAPID Innovation: The conduct of a clinical trial beyond start-up activities (patient recruitment, screening, or enrollment are not allowed)
✘	Activities already budgeted or paid for under a prior, existing or pending CIRM award, or which are already supported by another funder
✘	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
✘	Costs incurred on or before the date of ICOC approval

See Appendix A for examples of allowable activities under the RAPID award.

Award amount and duration

CIRM expects RAPID projects to advance quickly from preclinical development to master protocol IND clearance (RAPID Innovation) and FIH clinical trial completion (RAPID Validation) and will not accept applications with timelines exceeding program limits. RAPID Validation applicants must request support for activities spanning IND-enabling and Phase 1 clinical trial stages, while RAPID Innovation applicants may request support for preclinical activities spanning pre-IND and IND-enabling stages.

There is no maximum award amount specified for this program. The amount of total project costs requested must be adequately justified and is subject to adjustments prior to issuance of an award based upon assessments of the GWG, the CIRM team, or by the ARS of CIRM's governing board.

Upon achievement of distinct project milestones (e.g., RAPID Validation awards at the clinical trial stage

or RAPID Innovation awards following a pre-IND meeting), awardees may request supplemental funding to accelerate the project, subject to availability of RAPID program funds and CIRM approval. Supplements are not guaranteed and may only be requested at designated points in the award. Award supplements may be used for - but are not limited to - the addition of new candidates for RAPID Validation, and activities in response to FDA feedback received for RAPID Innovation or RAPID Validation.

AWARD TYPE	MAX AMOUNT	MAX DURATION
RAPID Validation	None	6 years
RAPID Innovation	None	3.5 years

Funding allocation

CIRM expects to fund 2-3 awards in the FY 26-27 application cycle.

Provisional timetable

The RAPID funding opportunity will recur once per year. The anticipated timeline of each funding cycle is as follows:

PROVISIONAL TIMETABLE	
GWG Selection	Approximately 60 days after application submission deadline
GWG Discussion	Approximately 30 days after GWG Selection
ARS Award Approval	Next available Application Review Subcommittee meeting
Start Date	Must be ready to start award activities within 90 days of award approval (see Eligibility section 7 for more details)

Eligibility

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

(1) The application must propose a platform comprising at least three *in vivo* genetic therapy candidates targeting rare diseases.

The platform candidates must share preclinical, CMC and clinical development elements in a manner that reduces testing and supports scalable addition of new candidates. The shared development elements and the minimum number of candidates (three) must be maintained throughout the project period.

Refer to CIRM Funding Opportunities: Common Requirements and Definitions for the definition of genetic therapies in scope for the RAPID program. Note that for RAPID, genetic therapies must be designed to treat diseases by delivering the genetic therapy *in vivo* directly to cells in the body.

The overall project and proposed activities must fall within the defined scope of this opportunity.

(2) The application must demonstrate that the project is at an appropriate stage of readiness at the time of application.

The application must provide data demonstrating reproducible disease-modifying activity for least one of the proposed in vivo genetic therapy candidates. Demonstration of readiness must include the following:

- Disease-modifying activity must be demonstrated in preclinical model(s) relevant to the target clinical indication(s).
- Model justification and alternative evidence must be provided where no relevant preclinical model exists for the proposed in vivo genetic therapy, including justification for the absence of such models and alternative data demonstrating biological or translational relevance to the target clinical indication.
- Additional proposed candidates within the platform must be supported by a plausible biological mechanism of action.

The application must also demonstrate regulatory readiness for the platform through regulatory interactions addressing the platform and covering all proposed candidates as described below. Documentation supporting these interactions must be provided at the time of application.

- **RAPID Validation:** Completion of an FDA Pre-IND meeting covering the platform and all proposed candidates. The application must include documentation demonstrating that FDA feedback addressed the proposed platform approach and informed the planned development strategy.
- **RAPID Innovation:** Submission of an FDA INTERACT meeting request covering the platform and all proposed candidates.

(3) The application must propose studies designed to achieve the expected outcome of the applicable RAPID award type.

- **RAPID Validation:** The expected outcome is completion of the FIH clinical trial of at least three in vivo genetic therapy candidates that demonstrates clinical proof of concept for the platform. Proposed activities should be designed to generate data capable of informing clinical proof of concept for the platform and future advancement of additional therapeutic candidates. Activities must support IND-enabling studies, submission and clearance of a master protocol IND, conduct of the clinical trial of at least three in vivo genetic therapies.
- **RAPID Innovation:** The expected outcome is clearance of a master protocol IND, supported by early regulatory engagement to enable advancement of the platform toward clinical development and reduce regulatory and development risk. Proposed activities must support platform development, IND-enabling studies and regulatory submission activities required for IND clearance.

(4) 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 RAPID 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.

(5) The project team must include an experienced Project Manager at a minimum 50% effort.

The project team must include a Project Manager with experience in managing relevant preclinical therapeutic development projects. The Project Manager 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.

(6) 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.

(7) The applicant must be ready to initiate work on the funded project within 90 days of approval.

Given the urgency of CIRM's mission, all approved awardees must initiate work on the funded project within 90 days of approval and authorization for funding by the ARS of CIRM's governing board, the ICOC. Upon the effective date of the Award Management Policy, this timeframe will remain at 90 days from award approval.

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.**

(8) The application must be accurate and complete.

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

(9) The applicant organization must meet CIRM's definition of a California Organization.

The applicant organization must be a California organization per CIRM's definition described in CIRM Funding Opportunities: Common Requirements and Definitions at the time of application.

An institution or organization may submit more than one application per funding cycle under this opportunity.

(10) For-profit organizations must demonstrate solvency.

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

(11) 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 Video Guide

CIRM staff aims to publish a video guide of the program after posting of this Request for Applications (RFA).

In addition, prospective applicants are required to complete a consultation with the CIRM Preclinical Development team prior to submission of a RAPID application. This mandatory step must be completed to apply. The consultation is intended to confirm preliminary eligibility, assess alignment with RAPID scope and objectives, and provide guidance on program requirements and expectations. Completion of this step supports preparation of applications responsive to the program criteria as outlined in this RFA. To initiate a consultation, applicants must email preclinical@cirm.ca.gov with the subject line "RAPID Consultation Request" to complete and submit an online Consultation Form, which will request key information about the proposed project including:

- Information on core team members, project title and award type (Validation or Innovation).
- Basic project information: platform description, therapeutic candidates, mechanism of action, indication, major activities, prior regulatory interactions, prior CIRM funding.
- Eligibility Upload Document (must use provided template): Data and information in support of candidate eligibility and readiness eligibility as described in CIRM Funding Opportunities: Common Requirements and Definitions and Eligibility criteria #1-2, respectively.

Following review of the Consultation Form, applicants may schedule a consultation with CIRM staff to discuss eligibility and program fit.

All post-consultation inquiries will be addressed with written responses.

How does one submit an Application?

All 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 RAPID application per review cycle**.

What components does an Application include?

The RAPID online application will only be open to applicants who have completed a pre-application consultation and is designed to collect information for CIRM staff to assess eligibility, for GWG reviewers to evaluate the project, and for CIRM to rapidly 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, describe how the proposal addresses the objective of the funding opportunity, provide an overview of proposed activities, and prepare and justify an appropriate budget.

The application uploads page provides templates and guidelines for writing the Application Proposal, Biosketches, Project milestones and timelines, and other key components of the application. Applicants must use the provided templates. Applicants must describe all necessary activities to achieve the expected outcome of the award.

What are the contents of the Application Proposal?

The Application 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 actual Proposal template.

Project Summary: High-level summary of the project.

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

Value Proposition: Description of the platform's potential to enable time and cost efficiencies across multiple aspects and stages of development and its ability to scale across multiple candidates and/or indications. Description of the potential clinical benefit of the proposed platform-based therapies relative to available treatments and candidates in development for the affected patient population including impacts on caregivers, healthcare providers, and payors. Description of the platform's potential to advance therapies that enable broader patient access and that are ultimately adopted by patients and the healthcare system.

Scientific Rationale: Explanation of how published and preliminary research findings support use of the proposed therapeutic candidates as a therapy for the target indication(s). Description of how the study designs were informed by an understanding of the impact of genetic, environmental and other external factors on the affected patient population.

Preclinical Studies: Template-based tabular summary of completed preclinical studies that support achievement of the Program objective.

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

Project Plan: Detailed description of all proposed activities that will support achievement of the program objective organized by preclinical studies, chemistry manufacturing and controls (CMC) and clinical development as described below. Applicants will be required to describe plans for all activities in sufficient detail to facilitate GWG review, and to clearly indicate what study designs will be pending FDA feedback. See Appendix A for examples of allowable activities under RAPID awards.

Preclinical Studies: Description of proposed preclinical studies to achieve Program objective. Template-based tabular summary of planned preclinical studies. Description of how relevant study designs are informed by an understanding of the impact of genetic, environmental and other external factors on the affected patient population.

CMC Development Plan: Brief description of the overall CMC development strategy for the proposed therapies including any completed manufacturing and analytical process development and GMP technology transfer activities. Description of all proposed CMC activities to achieve Program objective. Template-based description of proposed or current manufacturing and analytical process plan. Template-based draft quality target product profile and draft risk assessment (separate uploads).

Clinical Plans: Description of all proposed clinical development activities to achieve Program objective. Description of how the clinical development strategy will be informed by an understanding of the impact of genetic, environmental and other external factors on the affected patient population. Description of completed and planned patient engagement strategies to inform clinical development activities. Template-based description of progress in the development and execution of the protocol, clinical operations plans and trial enrollment goals for the FIH clinical trial for the proposed therapies.

Milestones: Tabular description of proposed project milestones and success criteria to achieve Program objective. Applicants will be required to provide a Gantt-format timeline of all proposed activities in a separate application upload.

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

Patient Access and Commercialization Plans: Detailed description of strategic planning for patient access, market access and commercialization for the proposed therapies for the intended patient populations. Description of how patient access priorities inform the design, development and delivery of the proposed therapies. Description of completed and planned stage-appropriate patient access, market access and commercialization activities as described in CIRM Patient Access Planning Requirements.

Team Organization: Qualifications of the proposed team (including future stage-appropriate staffing needs) and plans for communication, decision-making and cross-functional team collaboration.

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

Resources & Project Environment: Description of dedicated facilities, equipment and resources that will support execution of the project.

Data Sharing Overview: A 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. Confirmation of participation in the CIRM Awardee Knowledge Network and description of potential knowledge sharing activities (described below).

References: Sources cited in the proposal.

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

Successful and rapid access to approved CIRM-funded therapies requires stage-appropriate strategic planning throughout preclinical and clinical stages of development to ensure that the therapy is accessible for the affected patient populations. To help ensure that projects are adequately preparing for access, CIRM has developed a toolkit with a roadmap and associated requirements for stage-appropriate strategic planning activities in preclinical and clinical development funding programs. Applicants must review the CIRM Patient Access Planning Requirements resource document for stage-appropriate access planning activities for RAPID projects. Applicants must adequately describe progress to date and

propose a plan for conducting stage-appropriate access planning activities as part of the RAPID application. Proposed access planning activities will be incorporated into RAPID award operational milestones.

Applicants will also be required to report progress on commercialization and market access strategic planning activities over the course of the RAPID award.

What should one know about CIRM's data sharing and knowledge sharing requirements for the RAPID program?

CIRM requires RAPID awardees to manage and preserve raw data, processed data and metadata, and share Applicable Data (see Data Terminology in CIRM Data Sharing and Management). Applicants must also allocate funds in their proposed budget for personnel and/or activities related to managing and sharing data produced from the funded project.

CIRM recognizes the balance between protecting intellectual property prior to commercialization and CIRM's commitment to open science and innovation, and as such there may be aspects of Applicable Data generated as part of RAPID awards which could be treated as confidential until filing for patent protection, as trade secrets with requisite enhanced company protection, or in advance of regulatory approval. Data and knowledge sharing will be maximized to the extent that is possible. Refer to CIRM Data Sharing and Management for additional information on how RAPID applicants should address data sharing and how the data sharing overview will be evaluated.

In addition, RAPID includes enhanced knowledge-sharing requirements to accelerate platform-based genetic therapy development, including participation in the CIRM Awardee Knowledge Network (described below) and timely public sharing of regulatory interactions. The Project Teams will be responsible for any relevant intellectual property and confidentiality protections for pre-competitive sharing of proprietary and confidential information with other CIRM awardees as part of the CIRM Awardee Knowledge Network. CIRM will also require public sharing of regulatory interactions in a timely manner during the RAPID award period. For example, CIRM will require that FDA feedback from pre-IND meetings be publicly shared to support broader regulatory learning. At application submission, the applicant agrees to these requirements.

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 are detailed in the CIRM Grants Administration Policy for Clinical Stage Projects and includes Direct Facilities and Indirect Costs. Generally, project costs for personnel, supplies, travel, equipment, and subcontracts may be claimed.

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 RFA describes optional available resources for CIRM-funded projects including the CIRM academic GMP Manufacturing Network and the CIRM Industry Resource Partners composed of reagent, equipment and service providers (i.e. contract development and manufacturing organizations (CDMOs), contract research organizations (CROs) etc.).

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 Uniform Guidance (2 CFR 200). Facilities costs for for-profit awardees or any non-profit awardees without a federally negotiated Facilities & 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., change in PI, the applicant no longer qualifies as a California Organization, etc.).

Application Review Information

What is the process for evaluating a full 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 to remedy. 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.

GWG Application Selection

If the number of applications submitted exceeds the volume that can reasonably be discussed by the GWG panel, the GWG will conduct an initial screening to identify those applications that best align with the RAPID program objectives based on the criteria listed below. Applications will receive a composite score, which combines two measurements from the GWG reviewers, selection and rank. The two measurements are weighted 60% and 40% respectively. A composite score cut-off will be established at the closest numerical break to the target number of applications which will proceed to GWG discussion.

Reviewers may provide brief comments or categorical assessments at this stage; however, detailed feedback to applicants is not guaranteed.

The selection criteria for RAPID applications are:

- The extent to which the platform enables time and cost efficiencies across multiple aspects and stages of development and can scale across multiple candidates and/or indications.
- The feasibility and practicality of the therapies' uptake by patients, caregivers, and the healthcare system.

- The platform therapies' 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).

The CIRM President and CEO, upon recommendation from CIRM scientific staff, may advance a limited number of additional applications not selected by the GWG if there is a compelling programmatic justification.

GWG Discussion and Recommendations

The scientific merit of each application that is selected for discussion and recommendations 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. The list of scientific members who may participate in the GWG review, as well as GWG bylaws and policies, 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/about-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 shall 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 ARS of the ICOC will make final funding decisions.

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 and members of the ICOC. Per Gov. Code §6254.5(e), non-public records disclosed to government agencies under confidentiality agreements are not public records subject to disclosure to the public.

How will the scientific merit of an application be evaluated?

Applications will be scored based on the following review criteria.

1. **Value Proposition -** *Evaluate the extent to which the therapies offer a compelling value proposition based on holistic consideration of the following.*
   - Assess the extent to which the platform enables time and cost efficiencies across multiple aspects and stages of development and can scale across multiple candidates and/or indications.
   - Evaluate the feasibility and practicality of the therapies' uptake by patients, caregivers, and the healthcare system.
   - Assess the platform therapies' 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).

2. **Rationale -** *Evaluate the scientific rationale for the proposed therapies and the strength of the supporting data.*
   - Assess the fundamental robustness of the scientific rationale, including justification for the indication(s), therapeutic approach, and route of administration.
   - Assess the extent to which the rationale is supported by the body of available data. For example, consider whether there is compelling evidence of disease modifying activity in a relevant model and whether there is supported plausible mechanism of action extending to the additional candidates or indications.
   - Consider the strengths & limitations of the data presented and/or the models utilized in completed studies.

3. **Project Plan & 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 platform therapies (RAPID Validation) or progress the platform therapies to IND clearance (RAPID Innovation). For example, consider whether the proposed activities and development plan will leverage platform efficiencies and generate data sufficient to support regulatory milestones and go/no-go decisions for gating further investment in the platform.
   - Consider whether the RAPID Validation or Innovation objective can be achieved within the proposed budget and timeline.
   - Assess the validity of the potential project risks identified along with the mitigation and contingency plans presented.
   - Assess how well the project incorporates stage-appropriate patient access planning activities to support future market access.

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 plan to successfully complete all aspects of the project. For example, consider team leadership, expertise and staffing in relevant functional areas such as nonclinical, GMP manufacturing, analytical, regulatory and clinical.
   - 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 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 in vivo genetic therapy projects to clinical trials.

5. **Population Impact -** *Evaluate the extent to which the project considers the potential impact of the proposed therapies across affected populations.*
   - Evaluate the applicant's understanding and consideration of genetic, environmental and other external factors that may impact on the adoption, effectiveness or safety of the proposed therapies.
   - Assess the appropriateness of the intended clinical study population in the context of the project stage and current knowledge of demographic groups at risk for the target indication(s).
   - Evaluate the extent to which the applicant's prior or proposed activities incorporate perspectives and experience from patients and individuals affected by the target indication(s).

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 ARS of the ICOC.

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 patient access 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 patient access 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 any 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 adjust 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.

Awards progressing across key RAPID development stages (e.g. IND clearance for Validation, or pre-IND meeting for Innovation) will be reviewed by CIRM. Milestones and associated budgets may be amended, re-budgeted or refined in consultation with the project team and PDEV Expert Network as needed to ensure alignment with program objectives and regulatory feedback.

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.

Product Development Expert Network

To facilitate effective management of RAPID awards and collaborative partnership with RAPID project teams, CIRM will utilize a network of contracted external subject matter experts in relevant domains such as: CMC, clinical, nonclinical, and regulatory strategy (termed the "PDEV Expert Network"). At its discretion, CIRM will leverage the PDEV Expert Network to provide guidance on individual RAPID projects to help achieve the program objective. For example, experts may be called upon to advise on milestone achievement, to provide guidance on regulatory interactions, and to provide guidance on addressing FDA feedback. CIRM may enlist additional expertise on an ad-hoc basis depending on the needs of an award. RAPID awardees must review all regulatory strategies and submission packages with CIRM and PDEV Expert Network advisors prior to FDA submission. Failure to participate in the PDEV Expert Network may result in termination of the award.

Reporting

Awardees will be required to provide periodic written progress and financial reports to CIRM. RAPID Validation awardees will be required to provide clinical trial enrollee demographic data in the trial population as specified in the application as well as other reporting requests. CIRM will partner with the awardee to foster the success of the project. Awardees will have ongoing communication with the CIRM Science Officer throughout the duration of the award, typically meeting by teleconference and periodically in person. Key personnel responsible for critical process development and manufacturing activities may be required to submit progress reports to CIRM.

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. Refer to CIRM Data Sharing and Management for additional information on how awardees are required to develop and execute a Data Sharing and Management Plan (DSMP) and provide periodic written progress reports to CIRM. The requirements described in CIRM Data Sharing and Management are incorporated here by reference.

For RAPID awards, additional knowledge-sharing requirements apply, including participation in the CIRM Awardee Knowledge Network and timely public sharing of regulatory interactions (e.g. FDA pre-IND meeting feedback may be required to be shared within 90 days of receipt). Failure to comply may result in termination of the award.

Knowledge Network

CIRM intends to build a knowledge network of RAPID and PDEV awardees to help all CIRM-funded projects accelerate therapies to FIH clinical trials. The CIRM Awardee Knowledge Network will also support RAPID's enhanced knowledge-sharing framework, facilitating pre-competitive sharing of knowledge and resources between CIRM awardees to help advance best practices for preclinical and clinical development in areas such as, but not limited to, regulatory interactions, preclinical study designs, assay development, clinical trial design, clinical trial operations, patient engagement, and patient access planning. CIRM Awardee Knowledge Network activities may consist of thematic workshops, direct knowledge exchange between awardees, collaboration between awardees on project activities, sharing of relevant resources, etc. CIRM recognizes the balance between protecting intellectual property prior to commercialization and CIRM's commitment to advancing best practices for preclinical development across its program portfolio and thus will encourage pre-competitive knowledge sharing between awardees to the best extent possible.

CIRM Regulations

Grant awards made through this RFA will be subject to all applicable CIRM regulations. These regulations can be found at https://www.cirm.ca.gov/our-funding/cirm-stem-cell-grant-regulations.

Resources

CIRM-Funded Infrastructure

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

The CIRM Alpha Clinics are a statewide network composed of nine leading California Medical Centers. The Network supports stem cell-based and genetic therapy clinical trials for academic and commercial partners. Applicants and awardees can choose to 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 choose to 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 CDMOs, CROs and other vendors and service providers that are committed to making their consultations, services, and resources more accessible to CIRM-funded projects.

CIRM does not require that applicants and awardees utilize Alpha Clinics, Manufacturing Network, or Industry Resource Partners; applicants and awardees are expected to conduct their own evaluation of the suitability of these resources for their proposed project.

Applicant Resources

- For scientific questions that are not addressed in the above resources, send email correspondence to preclinical@cirm.ca.gov.
- For questions related to application review, send email correspondence to review@cirm.ca.gov.
- For questions related to budgeting your application send email correspondence to grantsmanagement@cirm.ca.gov.
- For questions related to budgets or allowable project costs, please consult the Grants Management FAQ on CIRM's website under "For Researchers > Grants > Managing your Grant".
- Terms used here are defined in CIRM Common Requirements and Definitions.
- Information about CIRM's data sharing requirements, data sharing and management guidelines, and applicant resources are found in CIRM Data Sharing and Management.
- Requirements and guidelines to address patient access planning are available in Patient Access Planning Requirements.

Appendix A

Examples of allowable activities by category and RAPID award type include, but are not limited to, the following:

CATEGORY	RAPID VALIDATION	RAPID INNOVATION
Nonclinical	• Conduct of IND-enabling nonclinical GLP studies including pharmacodynamic and pharmacokinetic studies, safety and toxicology studies, MOA and efficacy confirmation • Conduct of any nonclinical activities required for platform expansion as required by the FDA to add additional new candidates to the ongoing / proposed FIH clinical trial or to expand to additional indications	• Conduct of nonclinical pilot studies including pharmacodynamic, pharmacokinetic studies, immunogenicity, pilot safety and MOA studies • Studies to select dose, treatment regimen and route of administration • Optimization of delivery mechanisms for platform therapeutic candidates • Conduct of IND-enabling nonclinical GLP studies including pharmacodynamic and pharmacokinetic studies, safety and toxicology studies, MOA and efficacy confirmation • Conduct of any nonclinical activities required for platform expansion as required by the FDA to add additional new candidates and/or to expand to additional indications
CMC	• GMP manufacturing of the therapeutic candidates to support IND-enabling studies or to supply the intended FIH clinical trial • Process development and transfer to GMP manufacturing • Analytical assay development and qualification (i.e. in-process and release assays, stability, activity, potency) • Development of Quality Target Product Profile (QTPP), critical quality attributes/critical process parameters (CQA/CPP) and performance of manufacturing risk assessment	• GMP-compatible process scale-up/development and transfer to GMP manufacturing • Analytical assay development and qualification (i.e. in-process and release assays, stability, activity, potency) • Manufacturing of therapeutic candidate(s) to support project activities • Development of QTPP, CQA/CPP and performance of manufacturing risk assessment • Process development and transfer to GMP manufacturing • GMP manufacturing of the therapeutic candidate to support IND-enabling studies or to supply the intended clinical trial

Clinical	• Clinical protocol development, informed by patient perspectives, for the FIH trial • Development of a clinical operations plan including patient outreach, engagement, recruitment and retention strategies to meet trial enrollment goals • Patient advocate and community engagement to inform clinical development and trial planning • All clinical operational activities needed to complete the FIH trial	• Development of a comprehensive clinical plan that incorporates patient perspectives • Clinical protocol development for the planned FIH trial • Development of a clinical operations plan including patient outreach, engagement, recruitment and retention strategies to meet trial enrollment goals • Patient advocate and community engagement to inform clinical development and trial planning
Regulatory	• Preparation and submission of the master protocol IND package to the FDA	• Preparation for and conduct of a pre-IND meeting with the FDA • Preparation and submission of the master protocol IND package to the FDA
Patient Access Planning	• Reimbursement and market access strategy planning • Market landscape research • Early revenue and market forecast	• Reimbursement and market access strategy planning • Market landscape research