DISCOVERY

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DISC2: Discovery Stage Research Funding Opportunity for Quest Awards

PROGRAM ANNOUNCEMENT

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DISC2: Discovery Stage Research Funding Opportunity for Quest Awards

Objective

The mission of 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 Quest Awards Program will promote the discovery of promising new stem cell-based and genetic therapy technologies that could be translated to enable broad use and ultimately, improve patient care. Projects funded through the Quest Awards should propose technology that is uniquely enabled by human stem/progenitor cells or directly reprogrammed cells, or uniquely enabling for the advancement of stem cell-based therapies or aimed at developing a genetic therapy approach.

Award Information

The Expected Outcome of a Quest Award is to produce, within 3 years, a project deliverable that is a novel candidate therapeutic; or within 2 years, a novel candidate device, diagnostic test or tool that can immediately progress to translation to enable broad use.

What is the award amount and duration?

CIRM will fund direct project costs of up to

- $500,000 per award to achieve a candidate that is a diagnostic test, a device or a tool; Award duration is up to two years.
- $1,500,000 per award to achieve a candidate that is a therapeutic; Award duration is up to three years.

  Up to an additional $200,000 per award may be requested for activities related to obtaining and/or sharing clinically compatible pluripotent stem cell lines; testing multiple lines for selecting the final candidate to be translated; or for addressing scientific diversity. Budget request must be strongly justified on a per line basis.

The amount of direct project costs requested must be adequately justified and is subject to adjustments prior to issuance of an award based upon assessments of the Grants Working Group (GWG), the CIRM team, or by the Application Review Subcommittee of CIRM's Governing Board. The proposed project period must not

exceed the maximum period from the award start date (approximately 90 days after the date of ICOC approval) indicated above.

How will funds be awarded?

Awards will be made in the form of a grant. Funds will be disbursed pursuant to a CIRM Notice of Award. The first payment will be issued upon initiation of an award and subsequent payments will be disbursed on a regular interval at CIRM's option. Continued funding is contingent upon timely progress, as outlined in the project milestones and timeline established under the Notice of Award, and, when applicable, the ongoing ability of the applicant to fund its operations and to satisfy its co-funding commitment.

What activities will CIRM fund?

CIRM funds will support the following activities under this opportunity:

- ✓ Activities that will lead to selection of a novel candidate therapeutic, diagnostic, medical device, or tool ready for translation to enable broad use and ultimately, improve patient care including:
  - ✓ Developing and implementing assays to identify/test/characterize candidate (or prototype) therapeutic, device, diagnostic test, tool/technology
  - ✓ Feasibility and initial reproducibility assessment
  - ✓ Characterization/optimization of candidate(s)
  - ✓ Proof of concept studies with candidate; for non-stem cell-based candidates (e.g., certain devices, diagnostic tests, tools), proof of concept testing with human stem, progenitor, directly reprogrammed cells, or relevant human somatic cells targeted by a genetic therapy)
  - ✓ Developing Target Product Profile (Product Concept Document) for candidate therapeutic, device, diagnostic test or tool
  - ✓ Preparation for and conduct of stage appropriate regulatory meetings (e.g., for stem cell-based cell therapeutic candidates – an INTERACT meeting)

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

- For stem cell projects, research lacking a strong rationale for the unique necessity of human stem/progenitor cells or directly reprogrammed cells to achieve the project deliverable OR research uniquely enabling for the advancement of stem cell-based therapies that does not include testing with human stem/progenitor cells or directly reprogrammed cells to achieve the project deliverable
- Translational activities to develop either a Good Manufacturing Process (GMP) - compliant process, or a Clinical Laboratory Improvement Amendments (CLIA) - compliant process

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- Translational activities to implement Design Control including initiation and maintenance of Design History File
- Translational activities to develop a process for commercialization for a tool or technology
- Translational activities necessary for the filing of a well-supported IND, 510(k) or IDE with the FDA, for validation testing under CLIA or for commercialization
- Preparation for and conduct of clinical trials

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What is the expected outcome of a Quest Award?

The expected outcome (project deliverable) of a Quest Award is a new candidate therapeutic, medical device, diagnostic or tool that is ready for translational stage activities. Criteria defining readiness for translation for each type of candidate include the following:

Therapeutic:

- A candidate therapeutic identified
- A draft Target Product Profile (see Appendix) developed
- Measures of identity, activity and purity developed
- Demonstration of reproducible disease/injury modifying activity:
    - For candidates composed of or manufactured from stem cells, reproducible disease/injury modifying activity is demonstrated with the candidate in preclinical model(s) relevant to the target indication(s).
        - Autologous candidates, or those derived from an allogeneic source where donor might change, should demonstrate proof of concept with candidate from >1 donor to establish reproducibility
    - For a genetic therapy candidate that is not a stem cell therapy: disease/injury modifying activity must be demonstrated using a clinically relevant model; and evidence that the genetic therapy candidate will target or have activity on a clinically relevant human cell population must be established.

      CIRM recognizes that for certain types of genetic therapy candidate, it may not be technologically possible to establish evidence of activity in human cell models with the intended candidate. For these rare exceptions, and with justification provided, applicants may propose an alternative set of experiments to generate data supporting the ability of the surrogate candidate to target and/or impact the function of the relevant human cell population.

    - For all other biologic or small molecule candidates (not manufactured from stem cells), disease/injury modifying activity must be demonstrated on or with a clinically relevant human stem/progenitor or cancer stem cell population
- Initial studies performed assessing mechanism of action, pharmacokinetics (PK) (bio-distribution) and early safety
- For any therapeutic candidate containing allogeneic (donor derived) cells[1]:
    - Cells meet the Good Tissue Practices (GTP) requirements for donor eligibility, or there is plan in place to address GTP (donor eligibility requirements are described here https://www.fda.gov/media/73072/download)
    - Cell source (tissue or cell line) has been appropriately consented by donor for intended use and for clinical development and sale

[1] If you are unable to provide this verification, CIRM may require changing from the proposed cell line(s) to one that complies with these requirements. CIRM is working with organizations to provide researchers the opportunity to obtain such lines. See Appendix for more details.

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Diagnostic:

- A candidate diagnostic identified
- A draft Target Product Profile (or Product Concept Document, see Appendix) developed
- Demonstration of technical feasibility: tests with diagnostic candidate (research prototype, component prototype) show that it will be feasible to meet product design requirements
- Demonstration of scientific proof of concept:
    - Testing with the diagnostic candidate (research prototype, including technology, biomarkers) demonstrates that analyte can be reproducibly measured at biologically relevant levels for the intended use in sufficient samples to distinguish relevant differences within the target population
    - If the diagnostic is not stem cell based, then testing with a clinically relevant human stem/progenitor or directly reprogrammed cells demonstrates its utility to address a critical bottleneck to the discovery, development or use of stem cell-based therapies
    - If the diagnostic is intended for use with gene therapy, then testing with a clinically relevant human cell population demonstrates its utility to address a critical bottleneck to the discovery, development or use of gene therapies
- If diagnostic candidate includes an allogeneic cell, to be competitive for the next stage of CIRM funding (TRAN), the cell source (tissue or cell line) will need to be appropriately consented by donor for intended use, product development and sale

Medical Device:

- A candidate medical device identified
- A draft Target Product Profile (or Product Concept Document, see Appendix) developed
- Demonstration of technical feasibility: Tests with device candidate (research prototype) show that it will be feasible to meet product design requirements
- Demonstration of scientific proof of concept:
    - In test model(s) relevant to the intended use, the medical device candidate (research prototype) meets initial performance criteria
    - If the device technology is not stem cell based, then testing with human stem/progenitor or directly reprogrammed cells demonstrates its utility to address a critical bottleneck to the discovery, development or use of stem cell-based therapies
    - If the device technology is intended for use with gene therapy, then testing with a clinically relevant model and, if possible, with a human cell population, demonstrates its utility to address a critical bottleneck to the discovery, development or use of gene therapies
- If device candidate includes an allogeneic cell, to be competitive for the next stage of CIRM funding (TRAN), the cell source (tissue or cell line) will need to be

appropriately consented by donor for intended use, product development and sale

Tool

- A candidate tool identified
- A draft Target Product Profile (or Product Concept Document, see Appendix) developed
- Demonstration of technical feasibility: Tests with tool candidate (research prototype) show that it will be feasible to meet product design requirements
- Demonstration of scientific proof of concept:
    - In test model(s) relevant to the intended use, the tool candidate (research prototype) meets initial performance criteria
    - If the tool/technology is not stem cell based, then
        - Testing with human stem/progenitor or directly reprogrammed cells demonstrates its utility to address a critical bottleneck to the discovery, development or use of stem cell-based therapies OR
        - Testing with relevant human cells demonstrates its utility to address a critical bottleneck to the discovery, development or use of gene therapies
- If the tool/technology candidate includes an allogeneic cell, to be competitive for the next stage of CIRM funding (TRAN), the cell source (tissue or cell line) will need to be appropriately consented by donor for intended use, product development and sale

Eligibility

What types of projects are eligible for partnering?

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

(1) 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 Application Review Subcommittee of CIRM's governing board, the Independent Citizens' Oversight Committee ("ICOC").

(2) The applicant must propose studies for a new technology that will achieve the expected outcome, and that is uniquely enabled by human stem cells or uniquely enabling for the advancement of human stem cell-based or genetic therapies as follows:

Eligible Therapeutic Candidates

- Discovery research for a novel therapeutic candidate

- That is a cell therapy where human stem or progenitor cells[2] (collectively, "stem cells") either compose the therapy or are used to manufacture the cell therapy.
- That is a genetic therapy[3] approach (**i**) that targets a human somatic cell for its therapeutic effect, AND (**ii**) is intended to replace, regenerate, or repair the function of aged, diseased, damaged, or defective cells, tissues, and/or organs.
- That acts on or is dependent on endogenous human stem cells for its therapeutic effect, that is dependent on targeting human cancer stem cells for its therapeutic effect, that modifies a stem cell therapy, OR where a human stem cell is necessary to manufacture the therapy (e.g., extracellular vesicles).
- Where human stem cells are uniquely required for candidate identification and testing.

Eligible Technology Candidates (Device, Diagnostic, Tool)

- Discovery research for a novel human stem/progenitor cell-based diagnostic, assay or tool candidate that can be used to discover, advance, monitor, or evaluate new therapies, OR
- Discovery research for a novel technology candidate (a medical device, diagnostic test, tool) that addresses a critical bottleneck to the discovery, development or use of stem cell-based or genetic therapies where the proposed activities include proof of concept testing with human stem cells or relevant human somatic cells targeted by a genetic therapy

(3) Co-funding is not required.

If the project requires funding over and above that which CIRM provides to achieve the expected outcome, documentation demonstrating the commitment of funds to cover the required additional amount must be provided by the application deadline (e.g., copy of executed term sheet showing amount of co-funding, conditions and source).

(4) For-profit organizations must demonstrate solvency.

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

(5) Application must be accurate and complete

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

[2] Under Proposition 14, progenitor cells are "multipotent or precursor cells that are partially differentiated, but retain the ability to divide and give rise to differentiated cells." Progenitor cells may include directly reprogrammed cells if they meet the criteria in the above definition.

[3] For the scope of this solicitation, CIRM considers genetic therapy to mean a human therapeutic intervention that: 1) alters the genomic sequence of cells or 2) introduces or directly manipulates nucleic acids (such as mRNAs, antisense oligonucleotides) in cells. The intervention may include strategies to repair a disease-causing gene sequence, remove or inactivate a disease-causing gene, or introduce new or modified nucleic acids that augment the therapeutic potential of the target cells.

(6) Applicant must be in "good standing"

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

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

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

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

Who can apply?

Only California Organizations are eligible to apply for this opportunity.

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

For a California Organization, Allowable Project Costs include:

- Costs for research activities conducted wholly in California; and
- Costs for research activities conducted outside of California, provided that the California Organization exercises direction and control over the activities.

Unallowable Costs

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

Who can serve as the Principal Investigator (PI)?

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

- Must be an employee of the applicant organization or be accountable for the conduct of the proposed project to the applicant organization through a formal contract
- Must commit at least 20 percent effort to working on the project. Any effort for which salary from CIRM is claimed must be expended in California.
- Must be authorized by the applicant organization to conduct the research and assume the responsibilities of the PI
- Must not currently have another application pending review or approval under this funding opportunity.
- Must not currently have another application that is substantially similar or has overlapping activities pending review or approval under any CIRM opportunity.

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Schedule and Deadlines

Applications Due	There are generally two cycles per year.
Grants Working Group (GWG) Review	Approximately 60-90 days post submission
ICOC Review and Approval	Approximately 90-120 days post submission
Award Start	Must start within 90 days of award approval

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Application Review Information

What is the process for evaluating an application?

Pre-submission Consultation

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

Eligibility Review

CIRM will assess whether the proposed project meets eligibility requirements sought under this program. If CIRM determines, in its sole discretion, that an application does not meet the eligibility requirements of the program 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.

Scientific Review

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

The fifteen participating scientists on the GWG will evaluate the applications and score them according to scientific and technical merit, applying the review criteria described below.

CIRM anticipates that the number of applications submitted will be very high for this competition. When the number of applications received in a cycle is significantly in excess of the number that can be reviewed by the GWG panel, the GWG members conduct the review in two stages. In the first stage, GWG members (including scientific members and patient advocate and nurse members of the Governing Board) will conduct a pre-review of applications (called "Positive Selection") to identify applications that the panel believes are most responsive to the funding opportunity and hold the most potential for impact. Applications that are not selected are examined by the CIRM scientific team and CIRM President to determine whether any additional applications merit a full GWG review. The remaining non-selected applications are deemed to be denied. Since the selection process is focused on quickly identifying promising proposals rather than identifying deficiencies in applications, no reviewer comments are collected at this stage. Positively selected applications advance to the second stage of review, which involves assignment to specific reviewers on the panel, a full discussion at review meeting, and scoring by the GWG.

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

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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 may be disclosed to government agencies under confidentiality agreements.)

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How will the scientific merit of an application be evaluated?

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

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

Is the proposed technology likely to result in a candidate that could impact an unmet medical need? Would the expected candidate accelerate or increase the likelihood of successfully developing a stem cell technology or genetic therapy that significantly improves patient care or that address a critical bottleneck to the discovery, development or use of stem cell-based or genetic therapies? Has the applicant presented thoughtful options for progression from successful candidate discovery to translation?

2. Is the rationale sound?

Is the proposed project based on sound scientific rationale? Is the preliminary data compelling and supportive of the proposed project? Is the proposed project uniquely enabled by human stem/progenitor cells or directly reprogrammed cells, or uniquely enabling for the advancement of stem cell-based or genetic therapies?

3. Is the project well planned and designed?

Is the project appropriately planned and designed to achieve the expected outcome, including proof-of-concept data for a product candidate that is ready to advance to translational studies? For candidates that include allogeneic cell components, is the cell source likely to meet donor eligibility requirements and has it been appropriately consented for intended use? Is this a well-constructed, quality project? Are potential pitfalls identified and alternative approaches presented? Do the project plan and timeline demonstrate an urgency that is commensurate with CIRM's mission?

4. Is the project feasible?

Are the proposed milestones and expected project outcome logical and likely to be achieved within the proposed timeline? Is the proposed team appropriately qualified and staffed? Does the team have access to all the necessary resources to conduct the proposed activities? Is the budget appropriate for the research proposed? If a special budget supplement was requested for acquiring and/or evaluating clinically compatible PSC lines for candidate selection, have these additional activities and costs been adequately considered and justified?

5. Does the project uphold principles of Diversity, Equity, and Inclusion (DEI)?

Does the project plan and design adequately address and account for the influence of race, ethnicity, sex and gender diversity? Would the project outcomes inform the development of a product or tool that serves the unmet medical needs of the diverse California population, including underserved racial/ethnic communities? Does or will the applicant incorporate perspectives and experience from the population that will benefit from the proposed product in the implementation of the research project?

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Application Components and Submission

How does one apply?

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

What components does an application include?

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

The main components of the application include the following key sections:

Application Preview Page: This section will be utilized by reviewers to prescreen applications and select a subset to move forward to the second and final stage of review.

- Project Summary
- Area of Impact
- Vision for Progression
- Diversity, Equity and Inclusion

Resubmission Statement: If this application is a resubmission then the applicant will provide a brief statement on how this application addresses the reviewers' critiques.

Candidate Product Profile: Table summary describing proposed candidate and usage attributes (template provided).

Statement of Significance and Impact: Description of how the proposed candidate, if successful, could impact an unmet medical need, and/or accelerate or increase likelihood of successfully developing a stem cell technology or genetic therapy that significantly improves patient care, or how it could address a critical bottleneck to the discovery, development, or use of stem cell-based therapies.

Diversity, Equity and Inclusion (DEI): A statement describing how the overall study plan and design has considered the influence of race, ethnicity, sex, gender and age diversity. Include an explanation of how the project outcomes might extend or validate the applicability of regenerative medicine discoveries to underserved populations, including underserved racial/ethnic communities. The statement should also include a description of the research team's prior efforts or proposed plans for outreach, partnership, or educational activities to inform the development of DEI within the research project.

Objective and Milestones: A concise description of the project objective and project milestones (template provided), and criteria for success.

Rationale: Description of the scientific rationale for the proposed research and the preliminary data.

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Research Plan: A concise but detailed description of methods and techniques to be employed to achieve milestones, and potential pitfalls and alternative approaches.

Summary of Deliverables: Provide a brief summary of how the research plan will address the Expected Outcomes for the type of candidate to be developed.

Timeline: Activities-based timeline for achieving project milestones.

Principal Investigator and Team: A description of the PI and team's expertise and experience.

Resources and Environment: A brief description of the resources available to the project and environment.

References

Data Sharing and Management Plan (DSMP): A description of the proposed plan to share and manage data generated from the project. Guidelines to complete this section will be provided in the application. The description must include:

a. Data types (i.e., the type(s) and quantity of data expected to be produced, what data will be preserved and shared, a justification for not sharing certain data, and what metadata and other relevant data will be made accessible),

b. Related tools, software and/or code needed to access or manipulate shared scientific data,

c. The standards that will be applied to the data and associated metadata,

d. Data preservation (i.e., repository(ies) where shared data and metadata will be archived), access (how will shared data be findable and identifiable) and associated timelines,

e. Considerations of factors affecting access, distribution, or reuse of shared data by others,

f. The approach and personnel for oversight of data management and sharing, and

g. Expected costs and budget justification.

How does one address Diversity, Equity and Inclusion (DEI)?

All applicants for the DISC2 program will be required to provide a statement describing how their overall study plan and design has considered the influence of race, ethnicity, sex, gender and age diversity. Applicants should discuss the limitations, advantages and/or challenges of their research proposal in developing a product or tool that addresses the unmet medical needs of the diverse California population, including underserved racial/ethnic communities. Examples include use of models and tools that account for population diversity (e.g., HLA types, gender, genomics data, cell models **– see Appendix: Other Resources**). Applicants should also address how the research team has or will incorporate diverse perspectives and experience in the implementation of the research project, including, for example, developing partnerships with patient organizations, acquiring training in cultural competence and/or DEI, utilizing institutional resources for DEI, and allocating funds and/or personnel to address DEI.

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

What is required in a Data Sharing and Management Plan?

The sharing of data and knowledge produced from CIRM-funded projects is key to advancing the field of regenerative medicine and accelerating treatments to patients. CIRM requires applicants to develop and execute a Data Sharing and Management Plan that includes management and preservation of data and making applicable data 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. CIRM requires sharing of data in accordance with FAIR data principles (Findability, Accessibility, Interoperability, and Reusability) through established repositories including, but not limited to, specialized repositories, generalist repositories, cloud platforms and institutional repositories.

The Data Sharing and Management Plan must be included in the application and the plan is subject to evaluation (not scored) by the Grants Working Group. Reviewers will be asked to comment on the quality of the Data Sharing and Management Plan and advise CIRM on any improvements they recommend.

Who are Key Personnel?

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

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

What should one know before preparing the budget?

Budgets must be justified in detail, including all subcontracts and consulting fees, including, if applicable, any additional costs that would be funded from another source. Allowable Project Costs for research funded by CIRM are detailed in the CIRM Grants Administration Policy for Discovery and Translation Stage Programs. Generally, project costs for personnel, supplies, travel, equipment, data sharing and subcontracts may be claimed. Limits for specific cost categories must be observed.

What are Direct Facilities Costs?

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 rates for for-Profit applicant organizations are limited to 35% of the direct project costs. Facilities rates are applied to direct project costs exclusive of the costs of equipment, tuition and fees, research patient care costs, as well as the costs of each individual subcontract, consultant, and service agreement in excess of $25,000. The facilities cost rates approved and in place at the time of the application are to be applied to the entire award project period.

How much can an applicant claim for indirect costs?

For-profit organizations cannot claim indirect 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.

Award Administration

Issuance of Award

A CIRM award is issued via a Notice of Award (NOA), which is the formal contract that defines the terms and conditions of an award and documents the commitment of funds from CIRM. CIRM reserves the right to modify or establish funded project activities and the associated budget prior to issuance of the Notice of Grant Award. CIRM also establishes project milestones, success criteria and timelines for milestone achievement at its sole discretion after consultation with the PI and based on information provided in the application. CIRM may also review key contracts/agreements that are critical to the success of the project for compliance with CIRM's policies and regulations.

Payments and Reporting

Upon execution of the NOA, CIRM will issue an initial payment; subsequent disbursements will be made as outlined in the NOA. Continued CIRM funding is contingent upon timely scientific progress against milestones as outlined in the project milestones and timelines established under the NOA. Where project milestones are not timely met, CIRM reserves the right to either redirect resources to maximize the project outcome or, at its sole discretion, to suspend payment and/or terminate the project.

Grantees will be required to provide periodic written progress and financial reports to CIRM. CIRM will partner with the grantee to foster the success of the project. Grantees will have ongoing communication with the CIRM Program Officer throughout the duration of the award, typically meeting by teleconference and periodically in person.

Upon approval of an award, CIRM may appoint a Data Advisory Panel (DAP) to partner with the awardee for optimal sharing and managing of data. In such cases, awardees will have ongoing communication with the DAP throughout the duration of the award.

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No-Cost Extensions

Timely progress on funded projects is of critical importance to CIRM. Therefore, CIRM will consider a one-time, No-Cost Extension (NCE) request of no more than 6 months, submitted at least 30 days before the project end date. Such requests should properly justify how such an extension will advance the project towards its expected outcome, but Grantees should not assume CIRM will approve a NCE request.

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Contacts

For information and assistance with this program announcement:

Send email correspondence to Discovery@cirm.ca.gov

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Definitions

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

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

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

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

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

Appendix

CIRM Regulations

Grant awards made through this PA will be subject to all applicable CIRM regulations. These regulations can be found at http://www.cirm.ca.gov/reg/default.asp.

Target Product Profile

A Target Product Profile (TPP) is a strategic product development tool for therapeutic development that is the subject of a guidance document released by the FDA (https://wayback.archive-it.org/7993/20190918100706/https://www.fda.gov/media/72566/download).

Diagnostic, medical device and tool product development more typically employs a development tool often designated as the Product Concept Document (typically includes e.g. an assessment of unmet medical, technical and user needs, competitive and IP assessment, intended use, regulatory path to use, design input). For consistency in our Translation Program we request a TPP, specifically tailored to each candidate type (therapeutic, diagnostic, medical device or tool), which in the case of diagnostic, medical device or tool incorporates elements of the Product Concept Document. A draft TPP template for a candidate that is a therapeutic, a diagnostic, a medical device or a tool may be found within the respective proposal templates for the CIRM Translational Program applications.

Other Resources

CIRM iPSC Repository

As a resource to the regenerative medicine community, CIRM has funded the creation of an Induced Pluripotent Stem Cell Repository, a large, genetically diverse collection of stem cells produced from thousands of individuals representing various diseases of interest and healthy controls. The 2600+ lines were uniformly derived, have undergone rigorous quality control, and include demographic and clinical data. The CIRM Repository is managed by Fujifilm Cellular Dynamics, Inc., who have made the lines available for purchase at https://www.fujifilmcdi.com/cirm-ipsc-products/. SNP data for 2166 CIRM lines and whole genome sequence data for 299 of the CIRM iPSC donors is available at dbGaP. A list of CIRM lines with WGS data can be found here.

Applicants who are interested in using iPSCs to investigate mechanisms of disease, develop novel tools, discover therapeutic targets, or increase diversity in their experimental design are encouraged to explore the CIRM iPSC Repository or request additional information from CIRM program officers at discovery@cirm.ca.gov using the subject line “DISC2 application - iPSC Repository”.

Please note, cells in the CIRM iPSC Repository are for research use only and are not eligible nor consented for clinical use.

Donor Eligible PSC Lines

CIRM is working with organizations to potentially provide researchers the opportunity to obtain cell lines that a) comply with the FDA’s donor eligibility requirements; and b) are appropriately consented by the donor for intended use and for clinical development and sale. If you are interested in such lines, please visit CIRM’s Information for Applicants website or contact discovery@cirm.ca.gov with subject line “DISC2 application - clinically compatible PSC source” for current information on any available opportunities.

CIRM

CALIFORNIA'S STEM CELL AGENCY

Revisions

Revision Date	List of Changes
07/27/21	• Revised candidate eligibility: ○ Gene therapy-related devices, tools, and diagnostics are eligible • Updated expected outcomes for gene therapy projects • Added additional clarification language to requirement for diversity, equity and inclusion in research • Minor edits in gene therapy definition
12/07/21	• Revised expectation for allogeneic (donor-derived) cell therapeutic candidates

06/28/2022	• Updated CIRM's Mission
	• Updated the Objective of the Program Announcement
	• Adjusted maximum award amount and duration for therapeutic applications:
	  ○ Maximum direct project costs were increased to 1,500,000 for a therapeutic; Award duration is 36 months.
	  ○ Additional 200k budget available for specific product types and activities.
	• Replaced the requirement for (i) a statement on addressing underserved needs and (ii) a statement on promoting and upholding principles of DEI with a unified application section on DEI; updated review criterion 5 accordingly
	• Added the Data Sharing and Management Plan as an updated and separate application component
	• Updated names and descriptions of Proposal sections