

Alpha Stem Cell Clinics Network Expansion Award

INFR 4



REQUEST FOR APPLICATIONS

03.02.17 (copy edit revision 03.14.17)



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Alpha Stem Cell Clinics Network Expansion Award

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Objective

The mission of the California Institute for Regenerative Medicine (CIRM) is to accelerate stem cell treatments to patients with unmet medical needs. To support this mission, CIRM created the Alpha Stem Cell Clinic Network (the "Network") to deliver high-quality stem cell clinical trials to patients. The Network currently includes sites at University of California San Diego, City of Hope, University of California Los Angeles, and University of California Irvine. Twenty-nine clinical trials are being conducted at these sites and 186 patients have been enrolled¹. These trials emanate from CIRM's funding pipeline as well as non-CIRM funded investigator and industry sponsored projects.

The objective of the Network Expansion Award is to support additional Alpha Clinic sites that will (1) deliver core services necessary to deliver high-quality stem cell clinical trials², (2) support the career development of physicians seeking to perform clinical trials and (3) enhance the value of the Network, as a whole. Proposed sites could enhance the value by, for example, broadening the Network's geographic reach, providing expertise in new disease areas, providing new/unique technical capability, or other elements that accelerate/support stem cell clinical trials.

This award provides infrastructure funding to California-based medical centers to operate an Alpha Stem Cell Clinic. The clinics will provide a platform (personnel, facilities and operations) specifically dedicated to supporting the unique needs of clinical trials for investigational stem cell treatments. Funds from this award shall be used to leverage existing assets within the medical center to support these clinical trials. The award does not directly fund the clinical trials or the construction of new facilities.

Organizations funded under the CIRM Infrastructure Programs must participate in a coordinated effort to develop systems and capacities to accelerate the efficient delivery of stem cell treatments to patients. This effort will be facilitated by the Alpha Stem Cell Clinics Network Steering Committee. The Committee comprises the Program Directors from each Alpha Clinic, a CIRM representative and a designee from the CIRM Stem Cell Center, which provides translational and clinical services to CIRM awardees.

The Network is one of multiple coordinated Infrastructure Programs designed to overcome obstacles and accelerate the progression of stem cell treatments through translational, preclinical, and clinical research to demonstrate clinical proof of

¹ As of October 2016.

² *Stem cell clinical trials* are defined as those trials that are eligible under the CIRM Partnering Opportunity for Clinical Trial Stage Projects (CLIN2) program.
https://www.cirm.ca.gov/sites/default/files/files/about_stemcells/CLIN2_rev_03.21.16.pdf

concept.³ Other Infrastructure Programs include the CIRM Stem Cell Center. Together, these CIRM Infrastructure Programs will support CIRM-funded translational, preclinical, and clinical projects to develop stem cell treatments for patients with unmet medical needs.



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³ See Beyond CIRM 2.0: 2016 Strategic Plan p. 26 -30.
https://www.cirm.ca.gov/sites/default/files/files/agenda/151217_Agenda_7_CIRM_StratPlan_final_120815.pdf



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Award Information

What is the CIRM funding allocation and project term?

Under this RFA, up to two organizations will be supported to develop and operate the Alpha Stem Cell Clinics within California. Each award will provide up to \$8.0 million in total funding over a four-year period.

What activities must be performed under the CIRM award?

The Alpha Stem Cell Clinic will contract with sponsors to conduct CIRM-funded and non CIRM-funded clinical trials. The clinic must provide the following Core Services for stem cell clinical trials and contribute to the development of the Network:

- ✓ **Patient access, recruitment, education and consent.** Enable patients in California to access the Network. Maintain systems designed to identify and recruit patients. Provide education services to support robust informed consent. These systems should include the capacity to effectively recruit and educate among California's diverse population.
- ✓ **Clinical trial operations and management services.** Work with sponsors to facilitate clinical trial agreements/contracts and required assurances. Provide coordinated care for patients enrolled in a clinical trial. Develop operations and management systems to address the unique technical needs of stem cell clinical trials – including but not limited to specialized platforms for cell processing, manufacturing and delivery – with the aim of achieving optimal outcomes.
- ✓ **Physician training and career development.** Develop a CIRM Alpha Clinic Fellows Program to support the career development of physicians seeking to perform stem cell stem cell clinical trials. This program should orient physicians to clinical and regulatory considerations unique to stem cell therapies. Training may include (1) regulatory strategy, (2) protocol design, and (3) data collection, management and reporting methods to support successful trials and product commercialization.
- ✓ **Network participation and development.** Contribute to the development of a Network designed to expand and accelerate stem cell treatments to patients with unmet medical needs. Provide a proportional contribution to the development of Network wide assets deemed to be a priority by the Alpha Stem Cell Clinics Network Steering Committee.

What activities will CIRM not fund?

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

- ✗ Activities already paid for by CIRM under a prior or existing award, i.e., double billing
- ✗ Construction or renovation of physical facilities
- ✗ Subsidizing direct costs of core services provided to non-CIRM funded projects



What are the expected outcomes of the CIRM Alpha Clinics Network?

The CIRM Alpha Clinics Network must demonstrate substantial progress toward improving the efficiency of stem cell clinical trials as measured by performance metrics. These performance metrics are compiled by CIRM through semi-annual Network progress reporting.

Integration with CIRM Infrastructure Programs. The Expansion Sites will coordinate with the existing Network to bring new stem cell clinical trials to the network and leverage, improve upon, and scale up the services and unique resources provided by the Network, so called AVARs (Accelerating and Value Added Resources). Existing Network AVARs and those under development are described in Appendix A. Expansion sites should propose new AVARs and/or facilitate the development of existing AVARs to support stem cell clinical trials throughout the state. The Alpha Clinics Network Steering Committee, which will include representatives from the Expansion Sites, will coordinate AVAR development.

Sustainability. The Expansion Sites are expected to develop a sustainability plan designed to leverage these assets in the context of CIRM's Infrastructure Programs. The aim of this leveraging strategy is to create a sustainable platform for delivery of stem cell clinical trials and treatments to patients.

The Business and Sustainability plan must be designed to (i) maximize broad access to sponsors who are developing stem cell treatments, (ii) increase the probability of creating a sustainable business enterprise and (iii) minimize competing interests to support business development.

How will funds be awarded?

CIRM will disburse funds pursuant to a Notice of Award (NOA) and based on operational milestones. **Costs resulting from a delay or failure to meet an operational milestone will be the sole responsibility of the recipient.** Successful applicants will have thoughtfully accounted for foreseeable project risks and developed contingency plans that **do not** require additional funding from CIRM.



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Eligibility

What are the eligibility requirements for partnering with CIRM?

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

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

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

(2) Must have a California operating location

Both non-profit and for-profit organizations are eligible to apply. At the time of the application deadline, the applicant organization must be located in California. At the time of application, the applicant organization must have the appropriate hospital/clinics and facilities accreditations and operational medical facilities in California. If these requirements are not met, CIRM may terminate all further action on the application.

(3) Must have demonstrated ability to perform stem cell clinical trials

The applicant organization must currently be conducting at least one clinical trial that meets the eligibility criteria for a CIRM [Clinical Trial Stage Projects](#). Applicants must identify two lead clinical trials that are active or would be initiated in 2017. The lead clinical trials must conform to the eligibility criteria for CIRM [Clinical Trial Stage Projects](#). Applicants must also provide a Pipeline Development Plan for attracting additional eligible clinical trials.

(4) Must reside in an existing academic medical center with demonstrated capacity to conduct clinical trials

Applicants must be located within an academic medical center⁴, licensed by the California Department of Public Health, that is currently performing regulated clinical trials registered on ClinicalTrials.gov. The medical center should consist of the necessary facilities and infrastructure to successfully implement stem cell clinical trials that meet the eligibility criteria for a CIRM [Clinical Trial Stage Projects](#).

(5) For-Profit applicants must demonstrate solvency

For-profit applicants must provide documentation indicating the entity is a going concern with a minimum of 180 days cash on-hand from the date of application submission to fund operations and the financial ability to meet the contingency requirements for the term of the project.

⁴ Defined as a medical center that has an accredited medical school and/or accredited medical residency or fellowship programs and that conducts regulated clinical trials.



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(6) Must not currently have an onsite CIRM Alpha Clinic program.

(7) Application must be accurate and complete

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

(8) Applicant must be in “good standing”

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

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

- The applicant's Chief Executive Officer, Chief Financial Officer, and Center Director must not have been convicted of, or currently under investigation for, crimes involving fraud/misappropriation; and
- The applicant must have accounting systems in place that are capable of tracking CIRM funds.

All Applicants

The Center Director 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 serve as the Center Director (CD)?

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

Must be authorized by the Institution's Authorized Organizational Officer to apply for this RFA.

- Must have an active California medical license and hospital privileges at the applicant institution's medical center.
- The CD must commit a level of effort on the project consistent with achieving the center's objectives and not less than 30% effort.



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Schedule and Deadlines

Applications Due	2:00 PM PT, May 15, 2017
Grants Working Group (GWG) Review	July 2017
ICOC Review and Approval	August 2017
Award Start	Must start within 45 days of award approval

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 ensure the submission of high quality applications. Therefore, prospective applicants are encouraged to contact CIRM before applying with questions or to discuss their project's eligibility, scientific, or budget considerations.

Eligibility Review

CIRM will assess whether the proposed project meets eligibility requirements. If CIRM determines, in its sole discretion, that an application does not meet the eligibility requirements of the program, CIRM will notify the applicant of its decision, and if CIRM deems it appropriate, allow an opportunity to remedy. If CIRM deems it inappropriate, or if the applicant does not timely remedy the deficiency, CIRM will terminate all further action on the application.

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

Budget Review

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



Scientific Review

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

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

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

Consideration of Related CIRM Award Information (If Applicable)

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

A "related CIRM award" includes: (1) an award for which the applicant Center Director 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. Will the proposed Alpha Clinic accelerate completion of stem cell therapy clinical trials, enhance the value of the Alpha Stem Cell Clinic Network, and be positioned to be sustainable?

Would the proposed clinic accelerate and/or expand patient access to stem cell clinical trials? Would the proposed clinic expand the value of the Network, for example, broadening the Network's geographic reach, providing expertise in new disease areas, providing new/unique technical capability, or other elements that accelerate/support stem cell clinical trials. Does the proposed center offer a sufficient, impactful, and practical value proposition for patients, trial sponsors and/or health care providers? Is the proposed clinic positioned to be sustainable beyond four years?

2. Has the applicant developed a plan designed to successfully establish and operationalize the Alpha Clinic?

Does the project plan and timeline for establishing the center, conducting clinical trials, and implementing the pipeline development plan demonstrate an urgency that is commensurate with CIRM's mission? Does the application propose all required core activities (including the Fellows Program, see page 4 for all core activities) and are they appropriately designed to meaningfully enhance the value of the Network? Is the operation of the clinic appropriately planned and designed to provide meaningful, accelerating, and impactful resources dedicated to stem cell clinical trials?

3. Is the proposal feasible?

Is the proposed plan, including the fellows program and pipeline development plan, feasible and likely to be implemented within the proposed timeline? Is the proposed team appropriately qualified and staffed and have access to all the necessary resources to establish, operate, and maintain the clinic? Will the clinic have the capability and resources to provide the required core services to support stem cell clinical trials? Does the team have a viable contingency plan to manage risks and delays?



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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 <https://grants.cirm.ca.gov>. Any prospective CD must create a login in the system to access application materials and apply. Applications are available in the system only to the CD. A CD may submit only a single application.

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 objectives of the partnering opportunity, provide a detailed plan of proposed activities, complete a detailed budget, and provide reference materials that confirms the status of the project. Applicants will also be required to provide a financial contingency plan that addresses how the applicant will cover possible funding shortfalls.

The main body of the proposal contains the following sections:

1. **Program Summary:** A brief description of the overall structure and objectives of the proposed Alpha Clinic.
2. **Add value for Stem Cell Clinical Trials.**
 - a. Describe how the proposed Alpha Clinic will accelerate the completion of stem cell therapy clinical trials.
 - b. Describe how the proposed Alpha Clinic will expand patient access to clinical trials.
3. **Add value for the Alpha Clinic Stem Cell Network.**
 - a. Describe how the proposed Alpha Clinic would expand the value of the existing Network.
 - b. Describe how the clinic will coordinate with the existing Network to bring new stem cell clinical trials to the network and leverage, improve upon, and scale up the services and unique resources provided by the Network, so called AVARs (Accelerating and Value Added Resources).
4. **Value Proposition:** Describe the value proposition for trial sponsors, patients, and/or health care providers above that already provided by the organization's clinical trial offerings that will lead to preferential utilization of the Alpha Stem Cell Clinic and positively affect the delivery of stem cell treatments to patients.
5. **Sustainability.** Describe how the Alpha Clinic will build a business sustainable beyond the four-year award period. The Business and Sustainability plan must be designed to (i) maximize broad access to sponsors who are developing stem cell treatments, (ii) increase the probability of creating a sustainable business enterprise and (iii) minimize competing interests to support business development.
6. **Timeline:** Provide an activities-based timeline for clinic set-up, establishment of all proposed and required operations, and pipeline development in Gantt chart-like format



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7. **Project Plan:** Describe the project plan, including the description of how required Core Service will be provided to achieve the objectives of the RFA and to add value to the existing Network.
 - a. **Patient access, recruitment, education and consent.** Describe how the proposed clinic will enable patients in California to access the Alpha Stem Cell Clinics Network, maintain systems designed to identify and recruit patients, provide education services to support robust informed consent, including the capacity to effectively recruit and educate among California's diverse population.
 - b. **Clinical trial operations and management services.** Describe how the proposed clinic will work with sponsors to facilitate clinical trial agreements/contracts and required assurances, provide coordinated care for patients enrolled in a clinical trial, develop operations and management systems to address the unique technical needs of stem cell clinical trials – including but not limited to specialized platforms for cell processing, manufacturing and delivery – with the aim of achieving optimal outcomes.
 - c. **Physician training and career development.** Describe how the proposed clinic will develop a CIRM Alpha Clinic Fellows Program to support the career development of physicians seeking to perform stem cell stem cell clinical trials.
 - d. **Network participation and development.** Describe how the proposed clinic will contribute to the development of a Network designed to expand and accelerate stem cell treatments to patients with unmet medical needs.
 - a. **Marketing.** Describe the marketing plan to attract sponsors and lead to successful pipeline development of stem cell clinical trials.
 - e. **Pipeline Development.** Describe the pipeline development plan. Forecast and align capacity with demand for services for clients across the state. Describe how the Center will optimally support the CIRM pipeline of projects while building a business that includes non-CIRM funded projects.
8. **Alpha Clinic Operations:** Describe the plan to operationalize the Alpha Clinic and Fellows Program. The operational plan should support establishment of the clinic within proposed timelines and result in sustainability.
9. **Team.**
 - a. Describe the qualifications and staffing of the team that support its ability to establish, operate, and maintain the clinic according to the proposed project plan and timelines.
 - b. Describe the team structure, leadership, and communications plan.
10. **Organizational Capacity, Assets, and Resources.** Describe organizational capacity, assets, and resources that will enable the proposed clinic to provide the required core services, implement the proposed plan, and enhance the value of the Network as a whole including AVAR development.
 - a. Describe the capacity of the proposed clinic and support that the organization and team has the appropriate experience in cellular therapy and resources to support the described capacity.



- b. Describe available assets and resources that will enable the organization and team to successfully implement the proposed project plan.

11. Contingency Plan: Summary of potential risks, costs associated with those risks, and mitigation strategies, together with a financial contingency plan outlining viable funding sources in the event that costs exceed the amount of funding disbursement.

12. References: List all references used in the body of the proposal.

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 center 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.

Other Personnel Requirements

In addition, the applicant will either identify existing personnel or commit to a plan to hire, at a minimum, the following personnel upon initiation of the award: a 1.0 FTE Alpha Stem Cell Clinics Study Coordinator and a 1.0 FTE Alpha Stem Cell Clinics Patient Care Coordinator.

What should one know before preparing the budget?

A specific and well-justified 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 Programs](#). Generally, project costs for personnel, supplies, travel, equipment, and subcontracts may be claimed. Limits for specific cost categories must be observed.

What are the rules for spending CIRM funds outside of California?

Awardees may use CIRM funds for Allowable Project Activities conducted both in California and outside of California. “Allowable Project Activities” means those activities that are conducted in California and those activities conducted outside of California, provided that: (a) the Awardee exercises direction and control over the activities and (b) a separate out-of-state organization that performs project activities does not retain intellectual property or independent publication rights in any intellectual property (e.g., invention, technology, data) arising out of the CIRM funded project.



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What are Direct Facilities Costs?

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

How much can an applicant claim for indirect costs?

Indirect Costs will not be funded by this RFA.



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Award Administration

Issuance of Award

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

Operational Milestones and Payment

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

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

Suspension Events

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

Reporting

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



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Contacts

For information about this RFA or the review process:

Send email correspondence to Infrastructure@cirm.ca.gov

or

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



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Definitions

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

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

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

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

“Subcontractor” means an organization (other than the applicant organization) that is expected to: (a) contribute to the scientific development or execution of the project in a substantive, measurable way *and* (b) receive \$50,000 or more through the proposed project. “Subcontractor” does not include suppliers of widely available goods.

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



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Appendix A

Description of Current Accelerating and Value Added Resources (AVARs) for the Alpha Stem Cell Clinic Network

The following is a description and list of accelerating and value added resources being developed by the Alpha Stem Cell Clinic Network. These AVARs may be developed or scaled to support the goal of accelerating stem cell clinical trials.

AVAR Definition

An AVAR is a discrete and time limited project that improves the operations and capabilities of the CIRM Alpha Clinic Network and/or related CIRM clinical trials.

An AVAR is:

- Actionable
- Impactful
- Measurable
- Beneficial to multiple members of the Alpha Stem Cell Clinic Network
- Feasible given the resources of the CIRM Alpha Stem Cell Clinic Network

Sample ASCC Network AVARs

1. IRB Reliance Agreement: An Agreement to Speed IRB Approval

The Network has put in place an MOU to facilitate IRB approval. The agreement is a reciprocal IRB authorization agreement where an institution may accept or “rely” on the determination of a lead IRB within the Alpha Clinics Network. The IRB reliance agreement is designed to reduce the time required for trial approval. Individual Network sites still retain the ability to perform their own review.

2. UC ReX and LADR: A Patient Registry to Speed Cohort Identification

<http://www.ucrex.org/#!data-explorer/c1c32>

UC ReX and LADR include 20 million+ de-identified patient records from the five UC biomedical centers and other participating centers. With the assistance of a Research Navigator, (staff position with the University of California Research eXchange) and a collaborating investigator. The system may be utilized for patient cohort identification without IRB approval. Once a cohort is identified, IRB approval can be obtained to request additional patient screening data. In some cases, patients may have already consented for record review. Otherwise patients may be contacted through their provider, an honest broker or the investigator.

3. Alpha Stem Cell Clinics Performance Metrics Registry

The ASCC Network is developing a system to capture performance metrics across trials. The metrics include but are not limited to variable to measure the speed of trial initiation, types of clinical indications, and patient recruitment. The metrics are



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intended to be utilized to evaluate Network performance in accelerating clinical trials and serve as a resource for illustrating the Network value proposition to potential sponsors. The ASCC Network Shared Resources Working Group has developed a draft data dictionary and data use agreement. A proposal for database design is currently under development.

4. Alpha Stem Cell Clinics Interested Persons Registry

The ASCC Network sites receive routine inquiries from patients interested in the availability of clinical trials. In some cases, trails may not be available at the time of inquiry. The Network is developing an Interested Persons Registry. This registry will capture relevant Research-related Health Information (http://ora.research.ucla.edu/OHRPP/Pages/HIPAA.aspx#rhi_and_phi) from all ASCC sites in the event a future trial becomes available. ASCC sites could query the registry and notify potential patients of new trial opportunities.

5. Accelerated Clinical Trial Agreement

The ASCC Network sites are developing an Accelerated Clinical Trial Agreement. This agreement is designed to work in conjunction with other AVARs (e.g. IRB Reliance) to enable contracting of studies at multiple ASCC Network sites.

6. Early Engagement with Clinical Trial Sponsors

The Network works in coordination with the Stem Cell Center (a CIRM funded CRO) and CIRM to support the initiation of clinical trials at ASCC sites. The ASCC Network has developed a set of standard operating procedures designed to engage sponsors that are both seeking to obtain CIRM funded and utilize the ASCC Network. Through this early engagement process with the Network and the Stem Cell Center sponsors can evaluate trial sites, identify collaborating investigators, perform cohort identification, and develop budget estimates. This information can serve to strengthen CIRM applications for clinical trial funding.



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Appendix B

CIRM Regulations

The award made pursuant to this RFA will be subject to all applicable CIRM regulations. These regulations can be found on CIRM's website at <http://www.cirm.ca.gov/reg/default.asp>. The CIRM Grants Administration Policy for Clinical Stage Programs will govern this award.