CALIFORNIA'S STEM CELL AGENCY

TO: Members of the ICOC

FROM: Patricia Olson, Ph.D. Executive Director, Discovery & Translation

DATE: May 9, 2016

RE: Proposed Updates to the Translation Program Concept Plan

Executive Summary

In July of 2015, the ICOC approved concept plans for the Translation Program (PA 15-10 (TRAN 1), -11 (TRAN 2), -12 (TRAN 3) and -13 (TRAN 4)) and a budget of $40 million over two cycles in 2016. The ICOC recently approved awards to 8 applicants in the first cycle of the year, which comprise almost the entire $40 million budget for the year. CIRM proposes allocating up to $15 million for one additional Translation cycle this year (2016) as planned.

CIRM also proposes to reduce the direct cost allocation for TRAN 1 (Therapeutic) projects by 20%.

In addition, the team proposes clarifying the "Translation – Tool" (TRAN 4) program announcement to emphasize the goal of development for commercialization for that stage of translation.

Proposed Changes

1. Additional Allocation for 2016:

Currently, the partnering opportunities for translational research projects are offered on a biannual basis. With approval of the concept plan last year, the Board allocated $40 million to cover two cycles of awards. Recently, CIRM completed its first cycle, with 8 projects awarded nearly $40 million, indicating both the quality of the applications and the pent- up demand for translational funding. Because CIRM had planned to offer two funding opportunities in 2016, we propose that Board approve up to an additional $15 million for the second Translational cycle in 2016. For 2017 and thereafter, CIRM will present a proposed budget for the program, including the number of cycles proposed for that year, to the Board as part of the Board's consideration of the annual research funding budget. CIRM intends to present the annual research funding budget to the Board in December.

2. TRANS-Tool Clarification

CIRM provides four opportunities for translational research projects. The "Tool" program is aimed at projects that address a critical bottleneck to the discovery or development of a stem cell-based therapy that is not subject to regulation by the FDA. Ideally, successful projects are those that develop a novel tool for commercialization and broad use and not simply a mechanism to conduct research on a tool where broad use is construed as distributing from the lab, a common misconception seen in numerous cycle 1 proposals. The proposed amendment to the concept plan eliminates such confusion by describing a successful project as one that develops a novel tool "for commercialization." Such clarification should assist applicants prepare better proposals and CIRM to fund better-targeted research.

3. Adjustment of Direct Project Cost Caps for TRAN 1:

Applicants to the first cycle of TRAN 1 (Therapeutic) were eligible for up to $5 million per award in direct project costs for projects where the therapeutic candidate included a cell therapy or a biologic, or up to $2.5 million where the therapeutic candidate was a small molecule. Based on the first round of applications received this year, however, CIRM believes these caps could be reduced to $4 million and $2 million respectively. Reducing the caps will better align the program to the realistic project costs and will maximize the overall number of projects that may be funded.

Recommendation 1: Approve proposed amendments to TRAN concept plan.

Recommendation 2: Approve allocation of up to $15 million for a second TRAN cycle in 2016.

Recommendation 3: Approve the adjustment of TRAN 1 (Therapeutic) direct project costs to up to $4 million per award for projects where the therapeutic candidate includes a cell therapy or a biologic, and up to $2 million for projects where the therapeutic candidate is a small molecule.

Attachment – Concept Plan

Accelerating and Advancing the Translation of Novel Stem Cell Treatments and Applications

The mission of CIRM is to accelerate the development of stem cell treatments to patients with unmet medical needs. To better serve this mission, CIRM is proposing a new paradigm for driving the rapid translation of promising new stem cell technologies towards improving patient care. Through this program, CIRM will provide funding opportunities that:

- Are predictable and recur regularly.
- Provide multiple translational pathways for advancement of stem cell discoveries
- Link to downstream CIRM clinical funding opportunities

To accomplish these goals, CIRM will establish calls for proposals and will accept applications twice a year. This concept plan further describes the four proposed Translation Stage Program Announcements listed below.

- TRAN 1: Partnering Opportunity for Translational Research Projects: Therapeutic
- TRAN 2: Partnering Opportunity for Translational Research Projects: Diagnostic
- TRAN 3: Partnering Opportunity for Translational Research Projects: Medical Device
- TRAN 4: Partnering Opportunity for Translational Research Projects: Tool

TRAN 1: TRANSLATION STAGE PARTNERING OPPORTUNITY for THERAPEUTICS

OBJECTIVE

The objective of this funding opportunity is to enable completion of early preclinical development stage activities for a stem cell based therapeutic candidate. Completion of these activities will position the therapeutic candidate for initiation of pivotal IND-enabling preclinical studies for an IND filing with the FDA. CIRM expects projects under this program to advance rapidly and to be accomplished within 30 months and must be adequately justified.

For projects that are developing a cell-based therapy, a combination product including a cell therapy component, or an eligible biologic, the **objective** is to conduct a well prepared pre-IND meeting resulting in correspondence from the FDA confirming agreement with the IND-enabling preclinical plan.

For projects that are developing an eligible small molecule candidate, the **objective** is to complete, with the lead candidate, activities that will enable initiation of pivotal IND-enabling preclinical studies for an IND filing with the FDA.

AWARD INFORMATION

What is the CIRM project funding and project term?

- CIRM will fund direct project costs of up to $4M per award for projects where the therapeutic candidate includes a cell therapy, or direct project costs up to $2M where the therapeutic candidate is a small molecule. Project costs must be well justified.
- The project period is up to 30 months and must be adequately justified.

Deleted: 5

Deleted: .5

What activities will CIRM support?

CIRM funds will support the following activities under this opportunity:

- All activities necessary to ready a single therapeutic candidate for pivotal IND-enabling preclinical studies including:
  - Preparation of cGMP-compliant Master and Working cell banks
  - Assay development and qualification (e.g. in-process and release assays, stability, activity, tumorigenicity and immunogenicity assays)
  - Stability studies
  - Process development and transfer to manufacturing
  - Candidate production to support translational studies

- Biomarker development
- Conduct of non-clinical studies including pharmacodynamic, pharmacokinetic (cell biodistribution/fate), immunogenicity and mechanism of action (MOA) studies
- Studies to select dose, determine regimen and route of administration
- Selection of indication, development of a clinical plan, including a clinical protocol synopsis and draft protocol, for a Phase 1 trial
- Preparation for and conduct of a Pre-IND meeting with the FDA

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

- Generally, cGMP manufacturing to supply the intended Phase 1 clinical trial
- Clinical trial activities including start-up activities
- Studies for therapeutic candidate discovery including lead optimization

How will applications be reviewed?

Should the demand for Early Development Awards exceed the capacity of a Grants Working Group (GWG) review session, members of the GWG will review applications in two stages. In the first stage, GWG members will conduct a pre-review of applications (called "Positive Selection", see Appendix) to advance a subset of applications to the second stage, which will involve a full review by the GWG.

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.

How will funds be awarded?

CIRM will disburse funds pursuant to a Notice of Award. Under the Grants Administration Policy for Discovery and Translation Projects "D&T GAP"), Translation Research Therapeutic awardees (TRAN 1) may elect to treat their award as a loan pursuant to the Loan Election Option in the Grants Administration Policy for Clinical Stage Projects. If an awardee does not make this election, the award will be treated as a grant. Except for the first payment issued upon initiation of an award, payments will be disbursed semi-annually or 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 (see below).

ELIGIBILITY

What types of projects are eligible for funding?

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 the Independent Citizens' Oversight Committee.

Therefore, investigators should only apply when their program has reached the stage where all eligibility criteria are met.

(2) The applicant must propose studies with an eligible therapeutic candidate.

CIRM will support preclinical studies that enable readiness to execute on the IND-enabling preclinical plan for a single IND filing with the FDA for a therapeutic candidate that is either:

- A cell therapy where human stem, progenitor cells or directly reprogrammed cells either compose the therapy or are used to manufacture the therapy. (Minimally manipulated bone marrow cells, minimally manipulated cord blood or unmodified hematopoietic stem cells (HSCs), are **not** eligible under this call.)
- A small molecule or biologic that (**i**) stimulates/recruits endogenous stem cells as the primary MOA for repair/regeneration OR specifically targets cancer stem cells as the primary MOA, and (**ii**) is being developed for a rare or unmet need unlikely to receive funding from other sources.

(3) The therapeutic candidate must be at an appropriate stage of readiness.

- Reproducible disease modifying activity must have been demonstrated with the lead candidate in preclinical model(s) relevant to the target indication(s)
- All projects developing an allogeneic cell therapy:
    - Cells meet the donor eligibility requirements as described in "Guidance for Industry: Eligibility Determination for Donors of Human Cells, Tissues, and Cellular and Tissue-Based Products (August 2007)" http://www.fda.gov/downloads/BiologicsBloodVaccines/GuidanceComplianceRegulatoryInformation/Guidances/Tissue/ucm091345.pdf OR, IF NOT:
    - A plan is proposed to address the donor eligibility requirements

(4) The project team must include an experienced Project Manager

The project team must include a Project Manager who has experience in managing development programs and who is able to devote at least 50 percent effort to the project.

(5) The applicant must demonstrate appropriate levels of co-funding.

CIRM will require for-profit applicants to co-fund at least 20% of the total "Allowable Project Costs". Allowable Project Costs are those costs permitted under CIRM policies and regulations and include both direct and indirect costs. The sum of CIRM funds requested plus the co-funding contribution by the applicant make up the total Allowable Project Cost. Non-profit applicants may provide co-funding but it is only required when project costs are in excess of allowable CIRM award funding. The co-funding may come from any funding source arranged by the applicant but may not include "in-kind" or similar types of support. Documentation demonstrating the commitment of funds to cover the proposed co-funding amount must be provided at the time of application submission (e.g., copy of executed term sheet showing amount of co-funding, conditions, and source).

(6) 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.

(7) Application must be accurate and complete

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

Who can apply and on what activities can funds be spent?

California Organizations

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

For a California Organization, Allowable Project Costs include:

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

Non-California Organizations

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

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

- Cost of research activities conducted wholly in California; and
- Share of costs for research activities conducted outside of California that are directly required to support research conducted in California.

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 30 percent effort to working on the project (note: "project" includes both the CIRM-funded and applicant co-funded components). Any effort for which salary from CIRM is claimed must be expended in California
- Must be authorized by the applicant organization to conduct the research and assume the responsibilities of the PI
- Must not currently have another application pending review or approval under this funding opportunity

SCHEDULE AND DEADLINES

Applications Due	Specific dates and times will be posted on the CIRM website
Grants Working Group (GWG) Review	Approximately 3 months post submission
ICOC Review and Approval	Approximately 5-6 months post submission
Award Start	Must start within 3 months of award approval

Deleted: March and September of each yearIt is anticipated that applications under this program announcement will be accepted at approximately month intervals.

Formatted: Font color: R,G,B (237,125,49)

Deleted: Page Break

TRAN 2: TRANSLATION STAGE PARTNERING OPPORTUNITY for DIAGNOSTICS

OBJECTIVE

The objective of this funding opportunity is to enable completion of early stage development activities for diagnostics for patient screening, risk stratification, diagnosis, treatment selection or monitoring that are based on stem cells or critical for stem cell based therapy development or use. CIRM expects projects under this program to advance rapidly and to be accomplished within 24 months and must be adequately justified.

For projects that are developing a diagnostic (including medical imaging agents) for multi-site use,

the **expected outcome** is to conduct a well-prepared Pre-Investigational Device Exemption (Pre-IDE) or comparable Pre- Submission meeting* or a Pre-IND meeting resulting in correspondence from the FDA indicating agreement with completed/proposed activities to allow rapid advancement toward clinical studies and subsequent filing for clearance/approval to market..

For projects that are developing a diagnostic for a single commercial reference lab use, the **expected outcome** is to complete activities to achieve acceptance of a well-prepared analytical validation/verification report and clinical validation plan that meets requirements under CLIA (Clinical Laboratory Improvement Amendments) to enable diagnostic test launch.

*(http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/UCM311176.pdf)

AWARD INFORMATION

What is the CIRM project funding and project term?

- CIRM will fund direct project costs of up to $1.2M per award. Project costs must be well justified.
- The project period is up to 24 months and must be adequately justified.

What activities will CIRM support?

CIRM funds will support the following activities under this opportunity:

- Evaluation and verification of unmet medical and user needs
- Implementation of Design Control including initiation and maintenance of Design History File
- Implementation of risk analysis and risk management
- Diagnostic product design development including assay, software development and optimization
- Development of design verification and validation protocols
- Initial verification and validation testing
- Demonstration of sensitivity, specificity, reproducibility and accuracy adequate for intended use
- Testing with optimized assay of sufficient well characterized clinical samples to confirm performance adequate for intended use
- Activities necessary to ready a single medical imaging agent for pivotal IND-enabling preclinical studies (see Appendix A for representative activities)
- Determination/evaluation of intended use, regulatory path and clinical plan
- Development of clinical (validation/verification) protocols
- Development of a full validation report of test performance characteristics

- Development of manufacturing plan
- Preparation for and conduct of Pre-IDE (or other Pre-Submission) or a Pre-IND meeting(s) with the FDA (http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/UCM311176.pdf)

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

- Implementation of manufacturing of final diagnostic product design to meet applicable regulatory requirements
- Conduct of final verification, validation testing
- Clinical studies required for marketing approval
- Biomarker, technology discovery, candidate test discovery

How will applications be reviewed?

Should the demand for Early Development Awards exceed the capacity of a Grants Working Group (GWG) review session, members of the GWG will review applications in two stages. In the first stage, GWG members will conduct a pre-review of applications (called "Positive Selection", see Appendix) to advance a subset of applications to the second stage, which will involve a full review by the GWG.

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.

How will funds be awarded?

CIRM will disburse funds pursuant to a Notice of Award. Except for the first payment issued upon initiation of an award, payments will be disbursed semi-annually or 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 on-going ability of the applicant to fund its operations and to satisfy its co-funding commitment (see below).

ELIGIBILITY

What types of projects are eligible for funding?

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 the Independent Citizens' Oversight Committee.

Therefore, investigators should only apply when their program has reached the stage where all eligibility criteria are met.

(2) The applicant must propose studies with an eligible candidate.

CIRM will support studies on a candidate diagnostic test for patient screening, risk stratification, diagnosis, treatment selection or monitoring that will be regulated by the FDA or or by the CMS (Centers for Medicare & Medicaid Services) under CLIA:

- Where stem, progenitor or directly reprogrammed cells either comprise the test or are used to manufacture the test OR
- Where the diagnostic test is being developed for an intended use with human stem, progenitor or directly reprogrammed cells OR
- Where the intended use of the diagnostic addresses a critical bottleneck to translation, clinical development or use of stem cell therapies AND where testing with human stem, progenitor or directly reprogrammed cells confirms the utility of the diagnostic for stem cell based therapy development or use.

(3) The candidate must be at an appropriate stage of readiness.

Proof of concept studies with a prototype test (technology, biomarker(s)) must have demonstrated that the analyte(s) can be measured at biologically relevant levels for the intended clinical use in sufficient samples to distinguish relevant differences within the target population.

(4) The project team must include an experienced Project Manager

The project team must include a Project Manager who has experience in managing development programs and who is able to devote at least 50 percent effort to the project.

(5) The applicant must demonstrate appropriate levels of co-funding.

CIRM will require for-profit applicants to co-fund at least 20% of the total "Allowable Project Costs". Allowable Project Costs are those costs permitted under CIRM policies and regulations and include both direct and indirect costs. The sum of CIRM funds requested plus the co-funding contribution by the applicant make up the total Allowable Project Cost. Non-profit applicants may provide co-funding but it is only required when project costs are in excess of allowable CIRM award funding. The co-funding may come from any funding source arranged by the applicant but may not include "in-kind" or similar types of support. Documentation demonstrating the commitment of funds to cover the proposed co-funding amount must be

provided at the time of application submission (e.g., copy of executed term sheet showing amount of co-funding, conditions, and source).

(6) 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.

(7) Application must be accurate and complete

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

Who can apply and on what activities can funds be spent?

California Organizations

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

For a California Organization, Allowable Project Costs include:

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

Non-California Organizations

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

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

- Cost of research activities conducted wholly in California; and
- Share of costs for research activities conducted outside of California that are directly required to support research conducted in California.

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 30 percent effort to working on the project (note: "project" includes both the CIRM-funded and applicant co-funded components). Any effort for which salary from CIRM is claimed must be expended in California
- Must be authorized by the applicant organization to conduct the research and assume the responsibilities of the PI
- Must not currently have another application pending review or approval under this funding opportunity

SCHEDULE AND DEADLINES

Applications Due	Specific dates and times will be posted on the CIRM website
Grants Working Group (GWG) Review	Approximately 3 months post submission
ICOC Review and Approval	Approximately 5-6 months post submission
Award Start	Must start within 3 months of award approval

Deleted: It is anticipated that applications under this program announcement will be accepted at approximately month intervalsMarch and September of each year

Deleted: .

TRAN 3: TRANSLATION STAGE PARTNERING OPPORTUNITY for MEDICAL DEVICES

OBJECTIVE

The objective of this funding opportunity is to enable completion of development activities for a non-diagnostic medical device that is critical for stem cell based therapy development or use and that is subject to FDA regulation and approval for marketing either under a Premarket Notification 510(k), a Premarket Approval (PMA) or within a Biologics License Application (BLA). CIRM expects projects under this program to advance rapidly and to be accomplished within 24 months and must be adequately justified.

For projects that are developing a significant risk medical device that is new or not approved for a given use where clinical trials are required, the **expected outcome** is the conduct a well-prepared Pre-Investigational Device Exemption (Pre-IDE) meeting with the FDA resulting in correspondence from the FDA confirming agreement with the IDE-enabling preclinical plan.

For projects that are developing a non-significant risk or Class II medical device that is new or not approved for a given use, the **expected outcome** is the conduct a well-prepared Pre-Submission* meeting with the FDA resulting in correspondence from the FDA indicating agreement on the Clinical Plan and Intended Use to enable filing for clearance/approval to market under a 510(k) or a PMA.

*(http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/UCM311176.pdf)

AWARD INFORMATION

What is the CIRM project funding and project term?

- CIRM will fund direct project costs of up to $2M per award. Project costs must be well justified.
- The project period is up to 24 months and must be adequately justified.

What activities will CIRM support?

CIRM funds will support the following activities under this opportunity:

- Evaluation and verification of unmet medical and user needs
- Implementation of Design Control including initiation and maintenance of Design History File
- Implementation of risk analysis and risk management

- Device product design development including prototype optimization, and testing to demonstrate technical feasibility
- Development of design verification and validation protocols
- Initial verification and validation testing
- Determination/evaluation of intended use, regulatory path and clinical plan
- Development of clinical (validation/verification) protocols
- Development of a full validation report of test performance characteristics
- Development of manufacturing plan
- Preparation for and conduct of Pre-IDE (or other Pre-Submission) meeting(s) with the FDA (http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/UCM311176.pdf)

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

- Implementation of manufacturing process of locked device design that meets applicable regulatory requirements
- Conduct of final verification, validation testing
- Manufacturing to supply clinical studies and product launch
- Clinical studies required for marketing approval
- Technology discovery, device discovery

How will applications be reviewed?

Should the demand for Early Development Awards exceed the capacity of a Grants Working Group (GWG) review session, members of the GWG will review applications in two stages. In the first stage, GWG members will conduct a pre-review of applications (called "Positive Selection", see Appendix) to advance a subset of applications to the second stage, which will involve a full review by the GWG.

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.

How will funds be awarded?

CIRM will disburse funds pursuant to a Notice of Award. Except for the first payment issued upon initiation of an award, payments will be disbursed semi-annually or 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 on-going ability of the applicant to fund its operations and to satisfy its co-funding commitment (see below).

ELIGIBILITY

What types of projects are eligible for funding?

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 the Independent Citizens' Oversight Committee.

Therefore, investigators should only apply when their program has reached the stage where all eligibility criteria are met.

(2) The applicant must propose studies with an eligible candidate.

CIRM will support studies on a candidate device intended for use in the cure, mitigation, treatment or prevention of disease that will be regulated by the FDA:

- Where the device is being developed for an intended use with human stem, progenitor or directly reprogrammed cells OR
- Where the device is being developed for an intended use that addresses a critical bottleneck to translation, clinical development or use of stem cell therapies AND where testing with human stem, progenitor or directly reprogrammed cells confirms the utility of the device for stem cell based therapy development or use.

(3) The candidate must be at an appropriate stage of readiness.

Proof of concept studies with a prototype device (candidate) must have demonstrated feasibility to meet initial performance criteria in test model(s) relevant to the intended use.

(4) The project team must include an experienced Project Manager

The project team must include a Project Manager who has experience in managing development programs and who is able to devote at least 50 percent effort to the project.

(5) The applicant must demonstrate appropriate levels of co-funding.

CIRM will require for-profit applicants to co-fund at least 20% of the total "Allowable Project Costs". Allowable Project Costs are those costs permitted under CIRM policies and regulations and include both direct and indirect costs. The sum of CIRM funds requested plus the co-funding contribution by the applicant make up the total Allowable Project Cost. Non-profit

applicants may provide co-funding but it is only required when project costs are in excess of allowable CIRM award funding. The co-funding may come from any funding source arranged by the applicant but may not include "in-kind" or similar types of support. Documentation demonstrating the commitment of funds to cover the proposed co-funding amount must be provided at the time of application submission (e.g., copy of executed term sheet showing amount of co-funding, conditions, and source).

(6) 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.

(7) Application must be accurate and complete

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

Who can apply and on what activities can funds be spent?

California Organizations

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

For a California Organization, Allowable Project Costs include:

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

Non-California Organizations

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

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

- Cost of research activities conducted wholly in California; and
- Share of costs for research activities conducted outside of California that are directly required to support research conducted in California.

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 30 percent effort to working on the project (note: "project" includes both the CIRM-funded and applicant co-funded components). Any effort for which salary from CIRM is claimed must be expended in California
- Must be authorized by the applicant organization to conduct the research and assume the responsibilities of the PI
- Must not currently have another application pending review or approval under this funding opportunity

SCHEDULE AND DEADLINES

Applications Due	Specific dates and times will be posted on the CIRM website.
Grants Working Group (GWG) Review	Approximately 3 months post submission
ICOC Review and Approval	Approximately 5-6 months post submission
Award Start	Must start within 3 months of award approval

Deleted: It is anticipated that applications under this program announcement will be accepted at approximately month intervalsMarch and September of each year.

TRAN 4: TRANSLATION STAGE FUNDING OPPORTUNITY for TOOL EARLY DEVELOPMENT AWARDS

Deleted: PA 15-13

OBJECTIVE

The objective of this funding opportunity is to drive the rapid translation of novel tools for broad use that address critical bottlenecks to the discovery or development of stem cell based therapies and that are not subject to regulation by the FDA (Food and Drug Administration) or by the CMS (Centers for Medicare & Medicaid Services (CMS) under CLIA (Clinical Laboratory Improvement Amendments). CIRM expects projects under this program to advance rapidly and to be accomplished within 24 months and must be adequately justified.

For projects that are developing a novel tool for commercialization, the **expected outcome** is to achieve a tool that consistently, robustly and effectively meets performance characteristics required to address the bottleneck and that is ready to be transferred to manufacturing.

Deleted: broad use

Deleted: **objective**

Deleted: For projects that are developing a novel tool for commercialization, the **objective** is to achieve a tool that consistently, robustly and effectively meets performance characteristics required to address the bottleneck AND that is ready to be transferred to manufacturing.

AWARD INFORMATION

What is the CIRM project funding and project term?

- CIRM will fund direct project costs of up to $1M per award. Project costs must be well justified.
- The project period is up to 24 months and must be adequately justified.

What activities will CIRM support?

CIRM funds will support the following activities under this opportunity:

- Evaluation and verification of unmet need (bottleneck) to be addressed by this tool
- Continued evaluation and refinement of criteria that tool must meet to adequately address the unmet need
- Tool prototype optimization and testing to address criteria
- Determination of "final" tool and testing to show consistent, robust and effective performance against criteria

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

- Development and implementation of manufacturing of "final" tool
- Conduct of final verification, validation testing
- Manufacturing to supply product launch
- Preparation for and conduct of clinical studies

- Technology discovery, tool discovery

How will applications be reviewed?

Should the demand for Early Development Awards exceed the capacity of a Grants Working Group (GWG) review session, members of the GWG will review applications in two stages. In the first stage, GWG members will conduct a pre-review of applications (called "Positive Selection", see Appendix) to advance a subset of applications to the second stage, which will involve a full review by the GWG.

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.

How will funds be awarded?

CIRM will disburse funds pursuant to a Notice of Award. Except for the first payment issued upon initiation of an award, payments will be disbursed semi-annually or 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 on-going ability of the applicant to fund its operations and to satisfy its co-funding commitment (see below).

ELIGIBILITY

What types of projects are eligible for funding?

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 the Independent Citizens' Oversight Committee.

Therefore, investigators should only apply when their program has reached the stage where all eligibility criteria are met.

(2) The applicant must propose studies with an eligible candidate.

CIRM will support studies on a candidate novel tool for commercialization that addresses a critical bottleneck to the discovery, development or use of stem cell based therapies and that will NOT be regulated by the FDA or under CLIA:

Deleted: broad use

- Where stem, progenitor or directly reprogrammed cells either comprise the tool or are used to manufacture the tool OR

- Where testing with human stem, progenitor or directly reprogrammed cells confirms the utility of the tool to address a critical bottleneck to the discovery, development or use of stem cell based therapies.

(3) The candidate must be at an appropriate stage of readiness.

Proof of concept studies with a prototype tool (candidate) must have demonstrated feasibility to meet initial performance criteria in test system(s) relevant to addressing the bottleneck.

(4) The project team must include an experienced Project Manager

The project team must include a Project Manager who has experience in managing development programs and who is able to devote at least 50 percent effort to the project.

(5) The applicant must demonstrate appropriate levels of co-funding.

CIRM will require for-profit applicants to co-fund at least 20% of the total "Allowable Project Costs". Allowable Project Costs are those costs permitted under CIRM policies and regulations and include both direct and indirect costs. The sum of CIRM funds requested plus the co-funding contribution by the applicant make up the total Allowable Project Cost. Non-profit applicants may provide co-funding but it is only required when project costs are in excess of allowable CIRM award funding. The co-funding may come from any funding source arranged by the applicant but may not include "in-kind" or similar types of support. Documentation demonstrating the commitment of funds to cover the proposed co-funding amount must be provided at the time of application submission (e.g., copy of executed term sheet showing amount of co-funding, conditions, and source).

(6) 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.

(7) Application must be accurate and complete

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

Who can apply and on what activities can funds be spent?

California Organizations

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

For a California Organization, Allowable Project Costs include:

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

Non-California Organizations

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

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

- Cost of research activities conducted wholly in California; and
- Share of costs for research activities conducted outside of California that are directly required to support research conducted in California.

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 30 percent effort to working on the project (note: "project" includes both the CIRM-funded and applicant co-funded components). Any effort for which salary from CIRM is claimed must be expended in California
- Must be authorized by the applicant organization to conduct the research and assume the responsibilities of the PI
- Must not currently have another application pending review or approval under this funding opportunity

SCHEDULE AND DEADLINES

Applications Due	Specific dates and times will be posted on the CIRM website.
Grants Working Group (GWG) Review	Approximately 3 months post submission
ICOC Review and Approval	Approximately 5-6 months post submission

Deleted: It is anticipated that applications under this program announcement will be accepted at approximately month intervalsMarch and September of each year.

Award Start	Must start within 3 months of award approval

Deleted: Page Break

REQUESTED FUNDING ALLOCATION

CIRM will request funding for this program from the Board on an annual basis as part of the Board's consideration of CIRM's annual research budget.

The indirect cost rate will be set at 20% for non-profit applicant organizations. CIRM will not fund indirect costs for for-profit applicant organizations.

Deleted: CIRM requests up to $40.0M to cover issuance of awards across these four Program Announcements for Therapeutic, Diagnostic Test, Device or Tool Early Development Awards programs over one annualized award cycle (two application calls).

REQUESTED DELEGATION OF BOARD AUTHORITY

CIRM does not expect the application volume for Translation Stage Awards to exceed the capacity of a Grants Working Group review session, however, when it does, CIRM proposes making use of the two stage streamlined process for high volume application review proposed for Discovery Stage Awards programs (see Appendix). This process requires delegation of Board Authority.

CIRM requests the Governing Board delegate to the President or his designee the authority to examine those applications that are not selected for a full review and to make the final determination whether to submit such applications to the GWG for a full review or to deny funding.