CIRM
Strategic Roadmap for Continued Innovation
WHITE PAPER

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DISCOVER · DEVELOP · DEPLOY

CIRM Strategic Roadmap for Continued Innovation: Strategic Roadmap

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CIRM Strategic Roadmap for Continued Innovation: Strategic Roadmap

I. STRATEGIC ROADMAP OVERVIEW

1. Goal

This 'Strategic Roadmap for Continued Innovation' White Paper provides recommendations that, if approved and implemented, will enable continued and expanded funding and development of CIRM-sponsored projects to increase formation of new therapeutic products as envisioned by Proposition 71.

2. Strategy Framework

Framework: To guide the CIRM 'Strategic Roadmap for Continued Innovation' an analytic framework was prepared. That framework focuses on how to build the pipeline from research to the bedside or marketplace and the requirements at each stage. This framework has been used to examine CIRM's continuum of regenerative medicine activities, to identify key 'gaps' in funding and organization, and specify potential bridges across those key points or gaps. The project goal is to define appropriate bridges along the pipeline that CIRM can consider building.

Objective: The objective of this effort is to enhance and accelerate the quantity of CIRM-sponsored research projects that become approved therapies and the number of therapies reaching the clinic. The means to that end is to (1) expand funding for CIRM's translational research portfolio, enabling more projects to reach clinical trials phase 1 and 2a,b; (2) in doing so, concurrently enhance commercial readiness of each research project, and (3) set the stage for commercialization by overcoming major technical and financial constraints to the delivery of regenerative medicine therapies to patients.

Approach: A three-step process was carried out with review by a steering committee comprised of CIRM staff and ICOC members at each step:

- **SWOT**: Review of CIRM structure and activities identified an overview of challenges and pipeline gaps that could be addressed.
- **Model Analysis**: A range of approaches to bridging challenges and gaps facing CIRM was screened, focusing on potential models that could help CIRM achieve its mission, leading to therapeutic candidates for further clinical assessment.
- **Stakeholder Assessment**: Decision-makers from the biopharmaceutical industry, patient advocacy foundations (i.e., disease foundations), and investors were asked to review proposed recommendations in terms of their importance to the reviewer, their feasibility,

and the readiness of each organization to participate in planning and implementing new initiatives.

- **Recommendations**: This White Paper integrates the information developed and presents key recommendations for CIRM and ICOC consideration.

3. Summary of Recommendations

Three Recommendations Developed: Three proposals were developed and examined in terms of their capacity to address CIRM needs:

1. Public-Private Funding Partnership for Regenerative Medicine

Goal: Maximize the volume of regenerative medicine research projects that successfully complete clinical trials phase 1 and 2 and are commercially ready for adoption.

Approach: Leverage a portion of CIRM's balance of uncommitted funds through partnering with foundations, pharmaceutical firms, early stage venture interests and individual donors, to select and fund individual and/or groups of projects in specific disease areas, such as, neurodegenerative disease, spinal-cord injury, heart disease, diabetes, blindness, HIV, genetic disease and cancer. Partnership funding will focus on CIRM's over 90 funded early translational and later stage translational research projects reaching IND and clinical trials, as well as new projects.

Pilot: CIRM will engage a range of potential co-funders to explore co-funding of CIRM projects. These projects will be presented for co-funding by CIRM, with agreement from the research teams, from its portfolio of projects by disease-theme or themes agreed upon by co-funders. Co-funders will screen and select one or more projects from those presented by CIRM to co-fund, leveraging CIRM funds, expertise and experience.

Scale-up: Within a year or more of pilot operations CIRM may be able to expand co-funding of projects informally working with partners, or, if appropriate, establish donor advised accounts into which funders can place funds targeted to specific projects or types of projects. Over time, if appropriate, CIRM could also help launch a legally approved 501(c)(3) foundation as intermediary to actively convene co-funding partners and mediate screening and commitment to funding regenerative medicine projects from CIRM and new sources, with the possibility of growing an evergreen fund achieved by the foundation participating in downstream revenue from projects. This entity would maintain minimal operational size and concentrate on

managing the partnership and project funding from across co-funders. CIRM would maintain possession and control of its funds in such a scenario and operation of such a fund would be in compliance with all laws and CIRM policies.

Outcome: This partnership would expand funds committed to CIRM's existing project portfolio, and enable funding of a larger number of regenerative medicine projects through phase 1 and 2a,b clinical trials and be a natural conduit to Phase 3 trials.

2. **CIRM Regenerative Medicine Accelerator**

Goal: Maximize market readiness of all projects funded by CIRM.

Approach: Provide commercial readiness services to *each* project funded by CIRM—whether university projects or early-stage enterprise. Acceleration services will encompass three sets of resources: (1) Direct Guidance: Hands-on-advisory services delivered by teams of CIRM personnel and selected world-class professionals, organized by disease theme and domain expertise, who will meet with projects quarterly and provide direct guidance on a continuous basis, tracking projects against specific research and commercial development milestones. (2) Provision of centralized CIRM support services for regulatory, process development, production and clinical trials management. This will include alignment of projects with CIRM's five-year Alpha Clinics Program to ensure efficiency of clinical trials across California. (3) Screening and referral of each project to campus or community-based self-funded non-profit as well as for-profit accelerators and early-stage venture firms with their own seed funds.

Pilot: Build on past CDAP model and existing centralized CIRM services and deliver services to a set of to-be-agreed upon priority CIRM projects. Work with a set of these priority projects to ensure that they meet key preparatory stages of commercial readiness and introduce these projects to biopharmaceutical industry partners and investors, where appropriate.

Scale-up: Based on lessons learned from the structure and operations in the pilot formalize the CIRM Accelerator. This will include CIRM's organizing five to ten Accelerator teams will which each guide and advise three to five CIRM projects in a *related* theme area, whether Early Translational or Disease Team projects. Accelerator services to early translational research projects will be less intensive than later stage.

Outcome: This program will enhance investment readiness of each CIRM sponsored project. This will ensure that research is carried out in a manner that is consistent and replicable, that clinical trials structure meets pharmaceutical industry expectations. Outcomes will increase the number of successful introductions and formation of development partnerships with

pharmaceutical firms and early-stage investment by venture firms.

3. **Pre-Competitive Regenerative Medicine R&D Program**

Goal: Overcome technical and economic obstacles to development, production and delivery of regenerative medicine to the healthcare marketplace.

Approach: Build on CIRM's prior award of grants to identify and fund technical solutions to developmental 'bottlenecks' facing regenerative medicine research. Focus now on organizing collaborative R&D projects with industry and government to generate further breakthroughs that will enable development, production and delivery of therapies to the patient. This may concentrate on specific issues already raised pertaining to production and product characterization defined with ARM and industry stakeholders. This will also include collaborative funding research and development to define and test new models for reimbursement and regulatory pathways.

Pilot: CIRM will work with organizations such as ARM to bring together pharmaceutical industry companies and donors to jointly fund research into technical issues currently hampering production and scale-up of regenerative medicine therapies. CIRM will serve as the organizer, manager and co-funder of the pilot project. CIRM's goal should target funding perhaps 25% of the total cost, though this can be open. An RFP will be issued to secure appropriate R&D services with co-funders also actively participating in the R&D process to enhance utility diffusion of results.

Scale-up: Based on CIRM's leadership role, knowledge and expertise in regenerative medicine a pre-competitive R&D program will be formalized and expanded from the test project. Collaborators from associations, industry and agencies will participate in defining a strategic roadmap on pre-competitive issues in technical areas as well as finance/reimbursement and regulatory procedure. CIRM will continue to organize and manage a program of pre-competitive translational and technology solving projects in key theme areas, coordinating agreements of participant roles, and diffusion/transfer of results. The CIRM Pre-Competitive R&D Program operations will be supported internally at the start but will become primarily self-sustaining as more collaborative projects are funded. Moreover, if the Public-Private Pre-Clinical & Clinical Trials Fund is scaled-up, it is very likely that some of those sponsors will join in pre-competitive R&D projects on a case-by-case basis. Over time, if deemed appropriate by CIRM and the ICOC, this program could also shift to the foundation 501(c)(3) formed to house the Public-Private Pre-Clinical & Clinical Trials Fund.

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Outcome: Development, transfer and application of specific technical, financial and regulatory breakthroughs (tools, processes, policies) that will minimize barriers and enable regenerative medicine therapies to progress to the clinic and patient.

White Paper Structure

The core of this White Paper presents each of these three recommendations as follows with stakeholder comments within key sections:

- **Objectives**: The intention of the proposed action.
- **Organization**: The proposed structure of the recommended action.
- **Need**: The CIRM challenge that the recommendation addresses.
- **Operations**: How CIRM will manage the proposed action and its functions.
- **Source of Funding**: Anticipated sources of financing for the action.
- **Sequence for Development/Timing**: The steps and stages for implementing the action from planning through pilot to full scale-up.
- **Examples of Models**: Brief reference of illustrative programs and partnerships that are similar to or have informed the recommendations.

This White Paper concludes with a review of important steps CIRM will need to take to implement these recommendations.

II. REC. 1. PUBLIC-PRIVATE FUNDING PARTNERSHIP FOR RM PRE CLINICAL & CLINICAL TRIALS

1. Objectives

CIRM has funded 90 projects from early stage to later stage translational research and is committed to ensuring that as many of those projects as possible continue to progress and to reach and complete phase 1 and 2 clinical trials.

Given that CIRM's funding is limited, how can CIRM achieve this objective? The answer is by leveraging its balance of funds, its portfolio of projects, its expertise in regenerative medicine and its experience in managing research grant awards. CIRM has and can continue to serve as a convergence point for regenerative medicine interests of patient advocacy foundations, biopharmaceutical companies and individual and corporate donors prepared to co-fund already rigorously screened CIRM projects.

By playing this catalytic role in concentrating its own funds with those of third-parties on a carefully screened portfolio of regenerative medicine research projects—both pre-clinical and clinical trials phases—CIRM can achieve and expand its primary mission.

Moreover, this role should grow over time, with CIRM continuing to serve as the anchor and organizer of regenerative medicine projects. In fulfilling this role, CIRM will not only achieve leverage of its Proposition 71 funding (with a high ROI for California taxpayers), it will play a crucial role in meeting the need to bridge the financial gap between laboratory research and market-ready projects.

Focus: ***The overall objective of Recommendation 1 is to enhance the quality and quantity of Regenerative Medicine (RM) therapies made possible through CIRM support. To accomplish this the Strategic Roadmap recommends forming a Public-Private Funding Partnership (PPFP) for RM Pre-Clinical & Clinical Trials.***

The PPFP would raise substantial non-taxpayer funds that would be used in several ways to fund pre-clinical and clinical trials:

- **Existing Projects**: To partly fund the CIRM portfolio of 90+ early translational and later stage translational research projects.
- **Other Projects**: To partly fund RM projects, as recommended by the Grants Working Group (GWG) and approved by the Independent Citizens' Oversight Committee (ICOC).
- **Priority Projects**: To fund projects from CIRM's current portfolio that have the highest potential and readiness to move to market.

A Broad Base of External Funding: Greater leverage for CIRM's current funding will be sought by raising additional funding from outside sources, including:

- **Foundations**: Disease-focused foundations where RM is expected to be of benefit as well as major family foundations concerned with public health and health costs.
- **Philanthropists**: Traditional and venture philanthropists (including business angels) concerned with fostering innovation, health and longevity.
- **Investors**: Early-stage venture capital and seed funds seeking medical innovations.
- **Biopharmaceutical industry**: Research units as well as corporate venture funds.
- **Health insurance industry**: Providers concerned with health care and health care finance.
- **Government**: The National Institutes of Health (NIH), National Institute for Standards and Technology (NIST) and Centers for Medicare & Medicaid Services (CMS).

Building on Existing CIRM Programs: CIRM has already added funding programs for later stages of the development process through phases 1 and 2 of clinical trials, an accepted transition point from research to commercial uptake. These programs include, but are not limited to, the Strategic Partnership Program. The Strategic Roadmap recommendation to establish a PPFP is intended to build on this experience to provide an additional funding vehicle attractive to a broader array of funders.

2. Needs

Existing Projects: With a portfolio of 90+ early translational and later stage translational research projects, CIRM already has more projects than it can continue to fund through to phase 2 clinical trials. To date, many of these recipients are funded only through the candidate selection stage. Only a small number are currently in clinical trials. In order to advance these projects, as well as CIRM's funded Disease Team projects, to IND and phases 1 and 2 of clinical trials, significant additional funding will be required. This gap does not have any traditional resource that is easily accessed. In fact, the difficulty in raising capital for early-stage biopharmaceuticals research and development in regenerative medicine was one of the key reasons CIRM was founded.

Given the large number of projects already in CIRM's development pipeline, the magnitude of the capital needs to move them forward through the next phases of development are substantial, even assuming typical attrition rates for the CIRM projects. Clearly, a systematic and scalable solution is needed to raise the requisite capital.

New Projects: In addition to its current portfolio, it is highly likely that CIRM will want to make additional, new grants for selected projects that are promising, and/or supplement the support

it is already providing to existing projects. The longer CIRM continues as an operating entity, the greater the need will be for additional project funds.

The Funding Gap: The early stages of biomedical research have traditionally been funded by public agencies, such as the National Institutes of Health (NIH), and foundations and carried out by academic and research institutions. It is not until successful completion of phase 1 clinical trials and sometimes phase 2a/b, early-stage discoveries have evolved into promising new therapies. At this point research typically qualifies for and attracts funding by pharmaceutical companies and/or venture capital investors.

Between the earliest development and completion of phase 1 clinical trials and sometimes phase 2a/b there is often a multi-year period during which funding for continued development is difficult to obtain. This period straddles the milestone of the NDA filing, and that is why this period is often referred to as the 'gap' or "Valley of Death" period.

An Opportunity in the Gap: The gap period, already a structural weakness in the therapy development pipeline, is being worsened by current economic and institutional trends:

- **Federal Funding**: The first of these trends is the decline in availability of federal funding for early stage translational research, but the rise in stem cell support. Since 2002 human stem cell research support by the federal government has risen from $10.1 million to $146.5 million for embryonic stem cell research and from $170.9 million in non-embryonic human stem cell research to $504 million. In non-human stem cells research support has risen from $71.5 million in embryonic research to $163.9 million and in non-embryonic research from $134.1 million to $653.0 million.[1] There has been growth in funding of basic and applied research, but not in support for the gap, with the exception of certain orphan drug cases.
- **Pharmaceutical Industry Shifts & Limits**: A second trend, however, is the rise in pharmaceutical company outsourcing early-stage research, although, to date, with relatively limited expenditures on regenerative medicine. The pharmaceutical industry spends extensively on R&D. Worldwide, the total annual spend on R&D by the pharmaceutical industry is about $135 B, with the top ten pharmaceutical companies accounting for roughly one-half of the total, at $67.3 B.[2] Of this spending, only a small portion currently goes towards Regenerative Medicine. In 2012, the RM sector obtained about $300 M from grant sources, and an additional $900 M in funding from private sources and public markets.[3]
- **Disease Foundations, General Foundations & Donor-Driven Action**: The third trend is the increasingly catalytic role of disease foundations, general or family foundations, as

[1] *http://stemcells.nih.gov/research/funding/pages/Funding*

[2] *Source:* International Federation of Pharmaceutical Manufacturers & Associations, Individual company annual reports, as quoted by Motley Fool, Sept. 23, 2013

[3] *Source:* ARM 2013 Annual Report

well as high net worth individuals in funding research along the developmental path, seeking to leverage the resources of agencies and corporations. Foundations focused on key diseases, such as diabetes, leukemia, breast cancer, Parkinson's, heart disease, HIV-AIDS, spinal and neurological injuries, among others, expend roughly $1 B a year and continue to actively raise funds not only for research but also for later stages of development. Moreover, general and family foundations expend another $4 B (not including the Gates Foundation), much of it on healthcare matters. And, the new generation of high net worth individuals and venture philanthropists from the high tech industry are also are establishing substantial funds for launching advanced research on biomedical technologies, therapies and devices. These major new donations by individuals, such as the recent Denny Sanford donation to UCSD of $100 M for Sanford Stem Cell Clinical Center, create new possibilities for assembling funding around research and development. This growing wave of focused interest creates a strong window of opportunity for regenerative medicine research. Further, as more projects move into human trials, it can be expected that private sector sources of funding for early developmental stage research will increase. These include angel funders, early-stage venture capital funds, and (as discussed later) venture-backed accelerators. Collectively, these sources can provide substantial funding for development during the "gap" period. The key is to create a structure and set of operating policies that are attractive to these participants.

Need for an Anchor Organization: These three trends increase the need as well opportunity for structural innovation in development pipeline funding. They point to the importance of new types of public-private partnerships. Current conditions and trends create an important value-added role for CIRM. More than ever, there is a need for entities that can create partnerships between diverse sources of funding, while adhering to high scientific and economic standards. In a sense, there is a convergence of interests between all parties (public, private and patients), and ***an important role to be played by an intermediary***.

The costs of developing new therapies are high, despite efforts to try and lower them. In traditional therapies, phase 1 clinical trials can cost in the ~$20 million range, phase II clinical trials in the ~$25-40 million range and phase III ~$90+ million, although there can be substantial variation case to case. Moreover, the time required for completion of the development process is similarly challenging, easily running up to 6-8 years for clinical trials alone, starting with the IND.

Given the magnitude of the resources required to develop new therapies, the need to aggregate financial resources through new partnerships is compelling, if not essential, to the future of regenerative medicine progress to market.

Stakeholder Comments on

Importance of Public-Private Funding Partnership for Pre-Clinical & Clinical Trials

"This is an important direction for CIRM to take and expand in and important to this foundation." – Patient Advocacy Foundation

"Very important need. CIRM is an '800 pound gorilla' with reach and influence. The question from our disease specific perspective is, can CIRM help bring resources to focus on the key issues with which we are working? — Patient Advocacy Foundation

"CIRM should focus on big and strategic RM science—but CIRM needs to vet the science more aggressively against market potential." – Industry

"If you think of CIRM as a government body, the best focus are the bigger problems, because of risk profiles, to put an infusion into specific areas, big, bold with clear milestones and deliverables over a number of years." – Industry

"…all research universities are hustling to create enterprise, since they own the technology. But universities are uneven in their efforts to build enterprise". – Investor

"This foundation has funded clinical trials phase 1 and 2 as well as investments in companies running the trials, with the goal of enhancing outcome measures." Patient Advocate Foundation

"CIRM's direction is of considerable interest and the foundation is delighted to hear about this. The directions laid out make sense with regards to where this foundation is going in its own activities." – General Foundation

"Funding for phase 1 and 2 is crucial and is absolutely the key to advancing RM. There is a dearth of data on human settings that is robust." – Investor

"I believe that regenerative medicine is moving into prime time. However, the mix of real and questionable RM therapies will make advancing the field challenging. Getting science closer to clinical trials? That is key and CIRM should do this." – Investor

3. Organization

Developing the PPFP: CIRM needs to formally commit to building public-private partnerships as a means of leveraging its current Proposition 71 funding. As a collaborative mechanism for the joint funding of RM projects that have been approved by CIRM, a new public-private funding partnership represents a logical extension of CIRM's current Strategic Partnership program.

However, here projects will initially come from CIRM's portfolio and be presented to partners for co-funding.

Pilot Will Focus on Projects: The PPFP pilot will focus on specific projects with partners that have been invited or who have sought participation. Pilot projects will not necessarily be limited to a single disease category, and multiple projects within a particular disease category could be funded. CIRM will initiate the partnering process on a case-by-case basis, by selecting projects from its portfolio to present to the organizations that are participating in the pilot. Negotiations will take place with each case, depending on the characteristics of the case and the objectives of the pilot partners. For example, a disease foundation may want certain milestones in return for funding, while a pharmaceutical firm may want the right of first negotiation on the intellectual property (IP). In a way, the pilot itself is a "discovery" initiative – to enable CIRM to learn what projects and terms are appealing to outside funders.

Managing the Pilot: A typical partnership funding cycle will consist of these steps:

1. **Select**: CIRM selects a particular project from its portfolio, to present to other PPFP funders.
2. **Convene**: CIRM will reach out to, brief and invite prospective partners to participate in considering the selected of projects.
3. **Due Diligence**: The co-funders will perform their own due diligence and review with CIRM and other partners project characteristics, milestones and funding terms.
4. **Partnering Terms**: CIRM will negotiate co-funding terms with the set of PPFP funders. As mentioned above, these could vary widely by type of funder.
5. **Award and Track**: CIRM will monitor the performance of the recipient, report on milestones and other salient performance to the funders.
6. **Strategic Roadmap**: As the pilot progresses CIRM may find that convening groups of co-funders to collaboratively shape a strategic roadmap for development in specific theme areas of regenerative medicine can be used to retain engagement of current co-funders and communicate to and expand participation of new partners.

No Major Changes to CIRM: The Pilot of the PPFP requires no major changes to CIRM's current organization or structure. In fact, the current Disease Team structure, under GWG and ICOC control, with CDAP oversight, is a precursor to the managerial processes that would be followed by the pilot PPFP. The primary difference is that there will be a negotiation process that will probably require more resources than the negotiation done already for the Strategic Partnership program.

Incentives to Partnership Co-Funders: A key value for co-funders will be in having "a seat at the table" to see early-stage research, discoveries and clinical performance. Beyond this, different

funders will probably have different objectives. CIRM's portfolio of carefully screened and funded projects, reflecting CIRM's own due-diligence, as well as its experience in tracking projects, will reinforce the value of participating as a partner in the pilot, with the early rounds of partnership activity serving to guide steps to expanding and possibly institutionalizing operations.

Co-Funder Terms: As noted earlier, CIRM will need to be prepared to mediate differences in priorities and terms among and across co-funding partners. For example, a disease foundation may want certain required milestones in return for funding from a future royalty stream. In contrast, a major pharmaceutical firm may want right of first negotiation on the intellectual property (IP). Certain funders, such as venture philanthropists, angels and early-stage seed funders might want "payback" in the form of a predetermined multiple of their initial funding if and when the grantee generates royalties or revenues.

Options for Scaling Up: If the pilot is successful, and CIRM wants to increase the pace of partnership funding and/or fund new projects, CIRM can consider scaling up the Pilot to a more formal mechanism. There are two key options for scaling up operations following the pilot:

1. **Donor-Advised Funds**: To permit efficient aggregation and allocation of funds for pre-clinical and clinical trials, donor funds could be 'contributed' to by various funders, and managed by CIRM through a specific 'account'. CIRM policies and process still apply, but the donors 'advise' CIRM on the type of funding use they prefer, so that their interests are accommodated to the extent possible. If appropriate and legally permitted CIRM could take a modest management fee for administering the fund (analogous to other donor-advised funds). This model may be particularly attractive to smaller philanthropists and family foundations, but could be applied to cases where a third party—whether a foundation or corporation is prepared to allocate specific funds for regenerative medicine initiatives and wishes to obtain tax benefits (which could be available depending on the terms negotiated for the donation). A variation on this model would be to have a true commingled fund, in which CIRM's funds are combined with those of other funders.

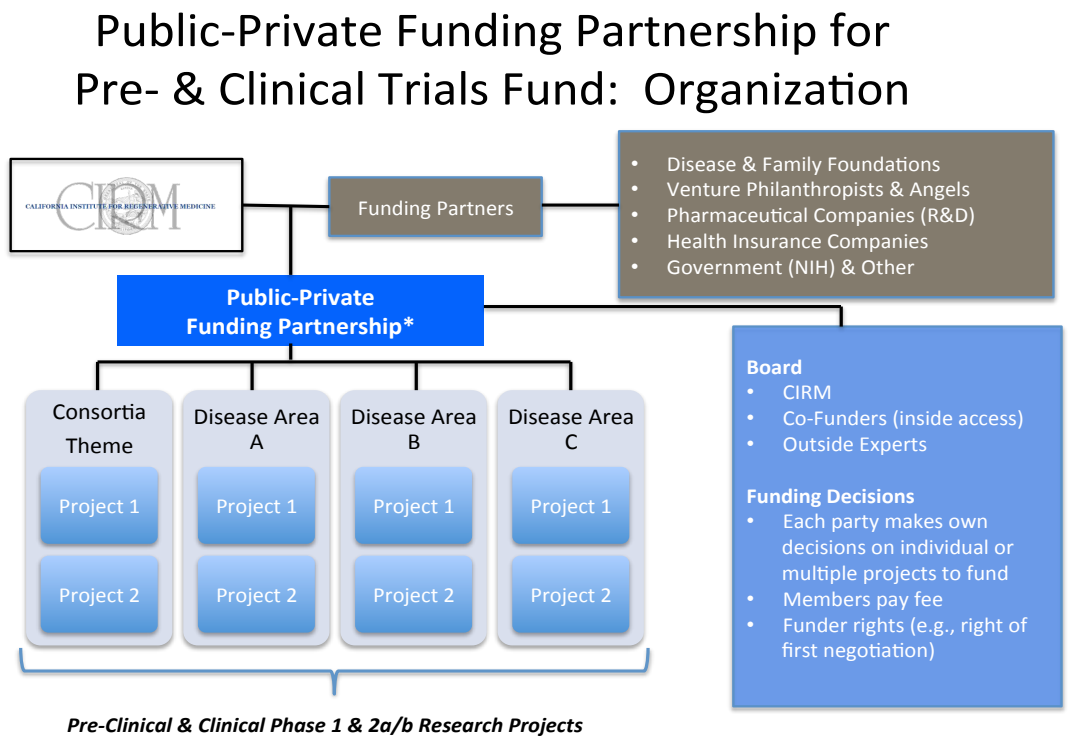
2. **CIRM Foundation:** A separate entity, such as a 501(c)(3) foundation, could be launched to serve as the conduit for funds from outside sources to the CIRM grantee portfolio. A foundation might scale up relatively fast and, as a distinct entity, would also probably provide the greatest continuity for CIRM's mission if CIRM's original funding is not renewed. Board members would probably be sought from a variety of backgrounds, much like the current CIRM board, to ensure continuity of CIRM mission and operations.

   The foundation will also be appropriate if CIRM wants to move to an "evergreen" model that is self-funded from periodic liquidity events within its portfolio. The pilot PPFP is not envisioned as being evergreen. However, if CIRM wants to move to an evergreen

model, a foundation would be the logical vehicle. Unlike CIRM, the foundation would be able to own equity (or equity-like securities) or other assets. From time to time, the foundation may choose to sell these holdings. As a separate entity, the returns from sales would go back to the foundation, thus helping to replenish the grant funds available to other recipients.

3. **Role of the Accelerator:** PPFP funded projects should be eligible for accelerator services, from CIRM or outside accelerators, under arrangement with CIRM. In fact, agreeing to utilize accelerator services could be required as a condition of funding. The built-in connection to an accelerator will enhance the value proposition of the PPFP to prospective funders. Initially, these accelerator services would most likely be paid directly by CIRM, as an extension of services it currently provides to its grant recipients. However, if the PPFP scales up as a separate entity, the cost of the accelerator services could probably be borne by the new entity, and in some cases, by the recipient itself.

Figure II.1



*__Administration__: ***Pilot***, separate concurrent funding of projects. ***Scale-Up,*** options from donor advised accounts managed by CIRM to launch of CIRM Foundation to convene co-funding partners, allocate and manage awards.

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Stakeholder Comments on
Feasibility of a Public-Private Partnership for
Pre-Clinical & Clinical Trials

"A multi-pharmaceutical pool with disease-focused foundations focusing on CIRM projects within specific disease themes makes sense." – Industry

"Recommends co-funding five projects, incrementally (tranches) with the expectation that two make it through to phase 2. You would need $100 M to $200 M to that point, after that another $200 M to $300 M would be provided by pharmaceutical firms from registration to commercialization." – Industry

"CIRM might be able to take this new technology challenge (RM) and keep the momentum of development going. In fact, CIRM might be the only chance for RM." – Industry

"Achieving expanded funding of clinical trials is crucial. CIRM should do this. With $100 M CIRM can fund many translational research projects. With the same money could fund six projects through phase 2. So, CIRM presumably needs tight criteria to apply to screen deals and funds to support them." – Industry

"Building a new mechanism for funding CIRM related work can be informed by foundations that are very structured in the continuum of their research, development work. A CIRM entity can and should attract funders who are concerned with a simple disease, around that theme, building up pools of funds in disease themed RM initiatives. The challenge is finding foundations of sufficient size and able to contribute to building a critical mass of funds." – Industry

"Most foundations will be interested in how CIRM funds can leverage foundation dollars." – General Foundation

"Projects need to fit/match foundation directions. Once funded, how each project gets managed is an important feature of any collaborative agreement. Foundations will want to play a role in project management, in some way." – General Foundation

"Believe in collaborative funding of research. Our foundation has run a research consortium since 1995, and while complex, the effort works towards achieving synergies across investigators who are not solely specialists in our problem, but also with basic research and molecular work that can address key issues." – Patient Advocacy Foundation

"Aggregating resources could be very helpful. RM might be a good test bed for this. There is no good transition capacity in this field right now—the chasm—lab to clinical trials to clinic and use. That is where help is needed." – Patient Advocacy Foundation

"To move ahead triage is needed on CIRM projects. CIRM faces gaps as well as overlap across the ET and DT portfolio. The overlaps need review and screening, independent of the GWG. Awards of large amounts of funding need further rigorous screening or face wasting expenditures." – Investor

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"The idea of raising funds around a disease theme makes good sense. Donors often have a disease interest. The idea of creating a consortium of disease foundations, such as diabetes, heart, or cancer may make sense. Perhaps one or more might partner with CIRM to build a pool of funds for later stage translational development and phase 3 or other pre-venture stage development." – Investor

"CIRM should continue to fund later stage translational research IF they apply tough criteria on the decisions to put projects into phase 1 or 2. CIRM criteria must be comparable to pharmaceutical firms. Must be grounded in tough-minded thinking. To do otherwise is a 'crazy' notion." – Investor

"Matching, non-dilutive capital, is a major incentive for early-stage investors. If CIRM puts up non-dilutive money, they would be interested in investing. They and other VCs are interested in this. VC is starving for projects that are moving to or at the clinic. But need to carefully screen each project/asset." – Investor

4. Operations

Outreach and Engagement: The core and largest single activity of the pilot PPFP will be bringing together partners for co-funding regenerative medicine projects. This will include these individual tasks:

- **Identify Potential Co-Funding Partners:** CIRM will identify and group prospective co-funders by their interest and commitment to regenerative medicine, including interests in specific disease themes, stage of RM development, therapeutic modality, as well as geographic or institutional interests (e.g., California or specific universities). Through this targeting CIRM will conduct outreach to invite participation in the PPFP at planned meetings.
- **Present Projects to Prospective Partners:** Having identified the interests and readiness of prospective partners to explore co-funding regenerative medicine projects, CIRM will select projects from its portfolio to present. CIRM will then convene prospective co-funders for face-to-face presentation and review of projects selecting candidates for co-funding.
- **Negotiate Terms of Co-Funding**: CIRM will need to help co-funders determine terms and conditions of their participation, depending on the needs of each co-funder. In the Pilot stage funding agreements will be between co-funders and recipient institutions (e.g., universities or firms), mediated by CIRM. In a future scale-up stage co-funders may directly give funds to CIRM to manage (via donor advisory accounts) or to the CIRM Foundation (with thematic funding programs). There are numerous precedents that can be used to reach agreement, including agreements previously used by each type of funder, from foundation or biopharmaceutical companies to venture philanthropists and private seed funds.

- **Complete Funding Awards, Launch and Track**: Co-funding commitments from each co-funder will be achieved, grant award transactions will be completed with the recipient university or firm, and project work will be launched and monitored against clear milestones.

Building the Partnership: Although the pilot phase can be open and flexible, CIRM could designate $50 M of its existing grant recipient funding for PPFP projects. That is, CIRM would seek to match this amount with a minimum of $50 M to $100 M from co-funders, within the first 6 to 12 months. The combined funding of $100 M (or more) could be used to support five translational projects (at an average estimated funding of $20M each). This is an ambitious target and will necessitate a creative and energetic "campaign". The fact that this is a new activity for CIRM will of course offer the potential for generating greater visibility. The value proposition to prospective co-funders will be CIRM's:

- **Funding**: Ability to provide a substantial pool of funds for co-funding.
- **Portfolio**: CIRM's existing range of 90 regenerative medicine projects across 15 disease themes and different stages of progress to market.
- **Knowledge**: Record of strong science oversight over projects in regenerative medicine.
- **Support**: The ability to offer a full-range of services to fund recipients through CIRM's centralized services and through its expanded accelerator services (see Recommendation 2 in this White Paper).

Staffing for Co-Funder Outreach: The identification, outreach, convening and management of the co-funders for the pilot stage PPFP can be performed by the CIRM staff, as well as ICOC members and the broader CIRM community. Assuming CIRM brings in a new president during the next 12 months, championing outreach to engage co-funders in the Public-Private Funding Partnership should be a designated high priority.

Administrative/Legal: The Pilot of the PPFP requires minimal changes to CIRM's current operations, and should not engender any legal issues beyond those specific to a co-funding case. In the Pilot PPFP, as the initiative will be a voluntary collaboration, the CIRM staff will handle most, if not all the coordinative functions (as noted above). There will be tasks involved in dealing with funders and prospective co-funders. This will include maintaining regular communications to grow participants into a CIRM community (including bringing CIRM into the co-funders community). Activities, such as bookkeeping for funds and generating records for tax filings should be minimal for the pilot stage, but will be added accordingly if the PPFP is scaled-up to a formal program within CIRM or a CIRM foundation.

Managing the Partnership: The pilot PPFP will have oversight by CIRM senior management. Once the pilot stage has proven effective CIRM may want to grow its outreach to co-funders through a formalized fundraising/solicitation program. Strong infrastructure and management will be need for co-funder relationship building, positioning of projects, and confirmation of agreements. CIRM should also have a contingency plan in place to manage cases where co-funders rescind funding commitments.

Feedback to CIRM: Some developments from the PPFP activities will impact CIRM. In particular, in cases where the PPFP brings in project funding that may substitute for funds that CIRM has earmarked for that project, this information needs to be communicated so that CIRM's portfolio funding plans can be modified accordingly.

Going Forward: After the PPFP pilot has been operating for a year or longer CIRM can evaluate its effectiveness in raising co-funding and the challenges of operations related to engaging co-funding partners, and make a decision on how to continue. If the pilot transitions to a scaled-up PPFP, and additional staffing are believed to be required, those expenses can be borne by the larger program. Those requirements will determine whether the future PPFP can be sustained within existing CIRM operations, or whether use of donor-advised funds in addition to current CIRM operations, or launch of a formal Foundation is needed.

Communications: CIRM should plan and manage a communications plan to support the PPFP as it scales up. As noted earlier, to retain and build participation in the PPFP, CIRM can work with PPFP members and outside experts to prepare one or more strategic roadmaps for development in specific fields of regenerative medicine. These can be used to guide partnership funding directions and to communicate with the co-funding community, patient advocates, and industry on achievements and directions in regenerative medicine.

5. Sources of Funding

Sources of Non-Taxpayer Funds for PPFP: The PPFP will attract co-funders from multiple sources. Each source of co-funding will have its own priorities by disease, stage and perhaps modality/technology, and even geography. Given the size of CIRM's portfolio of grant recipients, there is a good chance that most of CIRM's portfolio can be presented to one or more potential funders for co-funding. Ideally, CIRM will have already organized groups of prospective co-funders around themes matched to their interests. When meeting and presenting candidate projects CIRM should further prioritize projects based on factors most likely to interest specific co-funding organizations. The PPFP for regenerative medicine could collaborate in shaping a strategic roadmap that would guide and encourage the concentration of co-funding around key therapeutic directions in RM.

CIRM Strategic Roadmap for Continued Innovation: Strategic Roadmap

As noted earlier, sources for co-funding the CIRM project portfolio and future projects include:

- **Patient Advocacy Foundations:** Disease-specific foundations grant over $1 B annually, primarily for research and development. Although at present, only a small portion of these funds currently go for RM R&D, CIRM can target specific disease categories and/or foundation for co-funding. There are several precedents for this already, e.g. CIRM's co-funding ViaCyte with the Juvenile Diabetes Research Foundation.
- **General Foundations:** Life science-oriented charities grant about four times as much, over $4 B annually, as patient advocacy foundations. (The $3+ B in annual grants made by the Gates Foundation is not included in this figure.) Given the rapid evolution of RM, there should be interest in funding regenerative medicine by some of these more broadly themed foundations as well.
- **Philanthropists and family offices:** Individual philanthropists, along with family offices, which frequently act as extensions of individual philanthropists, on behalf of their family, may also be good candidates for co-funding. These funders are typically interested in disease categories with which they've had personal experience (e.g. an afflicted family member), and matching them with CIRM portfolio projects should not be overly difficult.
- **Venture Philanthropists:** This relatively new class of funders, a hybrid of a philanthropic and venture capital models, may be particularly interested in RM R&D. Currently, these organizations make roughly $600 M in grants annually (using the Milken Institute's TRAIN program members as a proxy for this class). As this model gains popularity, this amount should grow steadily. These funders typically seek a payback of their contributed capital, with imputed earnings in some cases.
- **Early-Stage Venture Capital Seed Funds and Angel Investors:** Although most of the funding for pre-clinical and clinical trials is expected to come from outside the private sector, it is possible that some funding will come from early-stage venture capital seed funds and/or angel investors. These sources should be approached as well, in the interest of casting the funding net as widely as possible.
- **Biopharmaceutical industry:** As collaborations and partnerships with the biopharmaceutical industry become more common, additional opportunities to co-fund RM projects directly with CIRM should become available. CIRM's Strategic Partnership Program is already a step in this direction, and can probably be modified and expanded to seek funding for existing grant recipients in CIRM's portfolio. The counterparty for projects co-funded with industry could be either an operating group within a company, or the venture capital arm of the company (given that many large biopharmaceutical companies now have venture or venture-like groups in-house).
- **Government**: Co-funding of projects with the US, Canadian and EU governments can be important to the PPFP. CIRM can co-fund with the NIH in earlier stage projects. CIRM has had a collaborative relationship in which CIRM supports California-based scientists working on NIH projects based elsewhere. The Cardiovascular Cell Therapy Research Network, one of the 27 NIH-funded institutes/centers, has already expressed interest in working with CIRM. CIRM might also co-fund small research/development companies via the federal Small Business Innovation Research/Small Business Technology Transfer

(SBIR/STTR) programs. In addition, CIRM has executed MOUs with about 20 different governments or government agencies outside the US via CIRM's Collaborative Funding Partners program.

- **Alliance for Regenerative Medicine (ARM):** There may also be potential in collaborating with ARM to jointly seek sources of co-funding for regenerative medicine R&D and commercialization (see below).

Relationships with industry organizations: It would be useful to explore a "tandem investment" fund approach that would provide seed funding for early-stage research, including clinical trials. A core tenet to this model is that different classes of funders (including NFPs) have different risk/return requirements. A tandem entity attempts to parse the total funding for a project into tranches, each with a risk/reward profile designed to appeal to a particular class of funder (e.g. venture philanthropists, venture capital seed funds, etc.). In fact, ARM's capital formation committee has begun looking at various fund concepts that could be useful, if executed properly, in addressing some of the national requirements for financing early clinical development. One structure they have been researching is that of a "tandem investment".

Figure II.2

Potential Not-for Profit Funding Sources

Funding Source	Annual Amount (~2011 $M)	Source & Comments
Disease-Specific Foundations	$1,080	"Top 20 Grant-Giving Disease Foundations". Source: *Genetic Engineering & Biotechnology News*, May 28, 2013. Note: The criterion for inclusion in this list was not size (of assets or contributions), but percentage of income distributed for research. However, this is still a very representative list of disease-specific foundations.
Life Science Oriented Charities and Foundations	$4,110	"10 Life Science-Loving Charitable Funds and Foundations". Source: *Genetic Engineering & Biotechnology News*, June 4, 2013.Note: Gates Foundation is 44% of the total; excluding Gates, the amount is $4,110 M.
FasterCures TRAIN (Proxy for venture philanthropy)	$600	Approx. total of annual medical research grants by 55 NFP organizations profiled in TRAIN project (Milken Institute). Non-Profit Disease Research Foundations. (Only modest overlap with "Top 20" Foundations above.) About half of TRAIN profilees have supported at least one clinical trial. About 90% partner with biotechnology and pharmaceutical companies. Source: FasterCures, 2013.
Sub-Total (without Gates Foundation)	$5,790	Gate Foundation adds an additional $3,208 M to the sub-total, for a grand total of $8,998 M.

* About half of TRAIN profilees have supported at least one clinical trial. About 90% partner with biotechnology and pharmaceutical firms.

Not included above:
- Venture capital, seed funds, angel investors, or other private-sector funding sources that may fund early-stage research.
- Institutions that care for patients as well as carry out research (e.g. Dana-Farber, Mayo Clinic).
- Research Institutes.

CIRM Strategic Roadmap for Continued Innovation: Strategic Roadmap

CIRM's Window of Opportunity: CIRM should be well positioned to assume a leadership role in aggregating and allocating financing for regenerative medicine development. CIRM has the scale, reputation and network, including a wide range of industry and investor contacts, to succeed in building up co-funding, while remaining in compliance with Proposition 71.

Legal/Administrative: As discussed in Operations, CIRM should be able to manage fundraising for the Pilot PPFP with current staffing, and minimal organizational changes. However, as CIRM builds out and expands its fundraising activities, there may be a need for a robust, dedicated fundraising group within CIRM. The size of this initiative would be scaled to the level of activity and fundraising/partnering potential, of course.

Membership Model Option: As an optional model for engaging prospective co-funders CIRM might be able to charge an annual fee for a "seat at the table" to industry and foundations so that they could be first to be presented with co-funding opportunities. In addition to this "first look" privilege, participation might provide a robust and broad view of research in the early stages of the developmental pipeline. These benefits might be of value to a number of organizations. The annual membership fee, and the number of organizations paying this fee, might create sufficient cash flow to support some portion of the outreach and engagement process to achieve co-funding objectives. This model is not envisioned for the Pilot PPFP, since it would need to be built on a proven value proposition. As CIRM's fundraising activities grow, however, this model should be considered and could be integrated into a scaled-up PPFP.

Stakeholder Comments
Readiness to Participate

"Ready to explore a private fund with other firms leveraging CIRM dollars. But projects will need to be prioritized by CIRM, first by disease theme and the match to pharmaceutical industry interest." – Industry

"Have invested in similar initiatives in the past. A new public-private program or organization focused on research, pre-competitive studies and commercial makes good sense, but needs accountability to sponsors." – Industry

"We are open to projects, within and outside California, to bring complementary funds together on regenerative medicine projects." – Patient Advocacy Foundation

"The outsourcing of early stage research by pharmaceutical firms is growing. Pharmaceuticals and foundations fund projects with translational potential. That is a trend that CIRM can and is serving." – Patient Advocacy Foundation

"Ready to explore a public-private partnership with CIRM. …Willing to participate with other foundations and pharmaceutical firms on the possibility of leveraging CIRM funds with private funding. I like the idea of this convergence." – General Foundation

"CRIM has the advantage of bringing money to the table. CIRM should be able to attract a range of partners to specific projects or a pool." – Patient Advocacy Foundation

"There is a need for what CIRM is proposing to do and this foundation could be interested in participating. The foundation is certainly willing to explore doing so." – Patient Advocacy Foundation

"The idea of leveraging funding streams is timely. Foundations cannot afford to work alone in today's environment. For this reason, there is a real need for aggregation around disease themes that might bring together shared needs and interest in a cost-effective way." – Patient Advocacy Foundation

"Absolutely agrees that CIRM can serve as a 'bundler' of public-private funds that will support RM research at California institutions. That is an appropriate and exciting potential. We are ready to join a collaborative process to talk each of the elements through from pre-clinical and clinical trials to commercialization to pre-competitive R&D." – General Foundation

"Disease focused-foundations should be partners in the future of regenerative medicine and should co-fund future collaborative initiatives". – Investor

"If CIRM is able to produce a flow of phase 2b clinical trials projects, this fund and many others will be prepared to partner in building a specialized venture fund." – Investor

6. Sequence for Development/Timing

PPFP Pilot Phase: Planning for the pilot can be launched immediately. Other tasks can be started in sequence (see Figure II.3). The pilot should be provided with a year to implement and meet its initial target. The initial co-fund target is $50 million from non-taxpayer sources to fund projects already in CIRM's portfolio. However, it may not be necessary to set aside any specific funding as the likely piloted programs will have already received a CIRM award which will be disbursed over the coming years. Private funding would then be either dedicated to future development or would otherwise supplement the current funding. This milestone will provide "proof of concept" for the PPFP, and will lay the groundwork for expanding the Pilot into a larger more permanent operation, as described previously. The key Pilot steps are to:

1. **Complete Plan**: Specify objectives, structure and collaborative operations. Complete an internal plan for the PPFP Pilot based on dialog with CIRM Research and Development to identify co-funding candidates and prioritize as needed. This plan should define program

objectives and set in place a clear work plan, with team assignments and key milestones. (Months 2-3)

2. **Target Partners and Terms:** Identify and screen foundations, pharmaceuticals, venture philanthropists, seed funders. Associate potential funders with specific diseases/therapies. Develop "templates" of terms appropriate for different types of funders. (Months 2-5)

3. **Prepare Package**: Prepare the co-funding solicitation materials. These could draw heavily on the original application to CIRM for funding, publications as well as new materials representing CIRM as the 'anchor' and experienced portfolio manager in regenerative medicine. These materials should also address topics around time to market, private sector interest level, competing therapies and their stage of development. (Months 2-4)

4. **Conduct Group Briefings**: Having identified targets and conducted initial invitational and communications outreach, now plan and convene collaborative work sessions during which CIRM will present its implementation plan and explore interests and concerns of co-funders, and shape a collaborative agenda for the PPFP that will give co-funders a strong sense of membership. Then, working with co-funding candidates, conduct one or more rounds of review of candidate CIRM projects, with invited principal investigators, and then next prioritize projects that are of interest—recognizing that there will be different configurations of interest. Follow-up with participants with both the organizational plan for the PPFP as well as the first round of agreed upon candidates for co-funding. (Months 4-9)

5. **Commit & Negotiate:** CIRM will confirm commitments made by co-funder participants and then facilitate negotiation of co-funding participation and terms with recipient universities or firms**.** (Months 6-12). As with most negotiations, this may be an iterative process of several rounds per project. Note: there may be much earlier contact, on an informal basis, particularly with organizations CIRM has worked with previously. (Months 6-12, then on-going as needed)

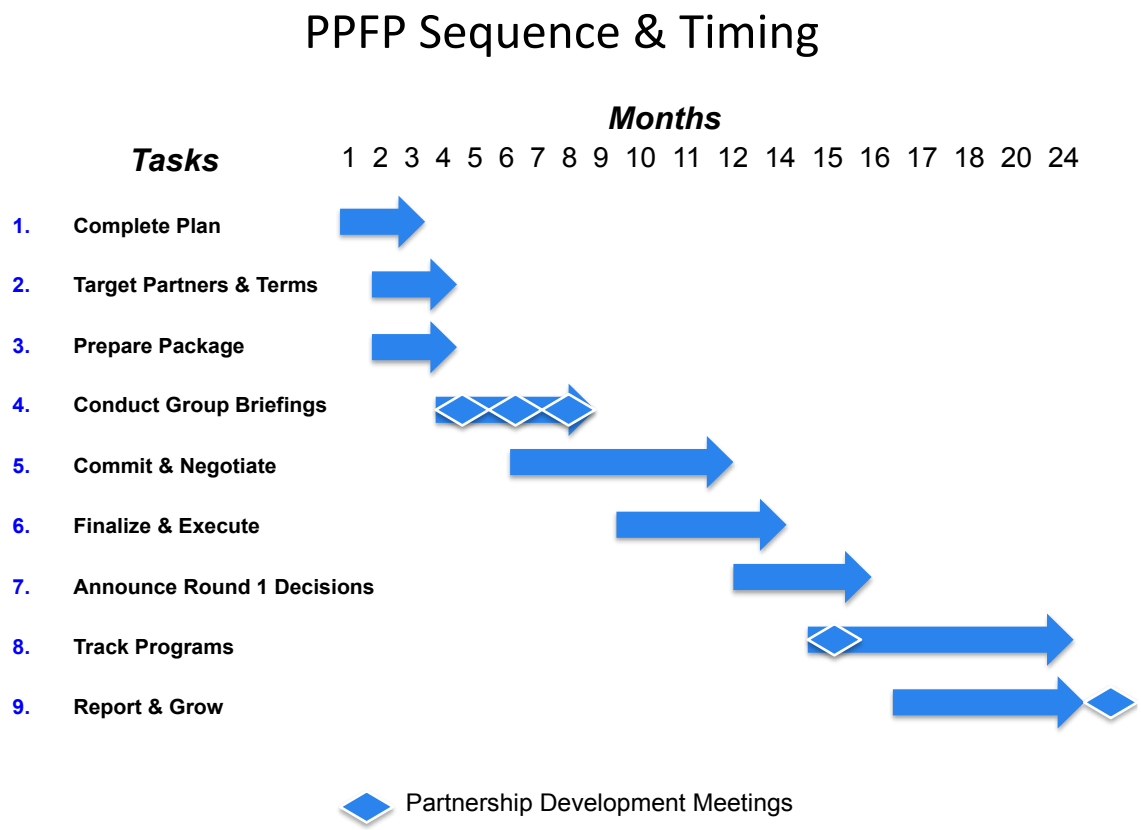
6. **Finalize & Execute:** Finalize the terms of co-funding with various funders**.** Draw up and execute necessary legal documents with recipient institutions. Ensure grant awards are in place and that, in a timely manner, funds are dispersed from co-funder. (Months 9-14)

7. **Announce PPFP Round 1 Decisions:** Announce the first set of co-funding (co-funders and projects) agreements. (Months 12-16). Note: There may also be earlier decisions, particularly with organizations CIRM has worked with previously.

8. **Track Programs: Using agreed upon milestones** CIRM team will oversee funding, and continue oversight over project (as it does already). CIRM will coordinate with accelerator as needed. (Months 14-24)

9. **Report & Grow:** Create public communications deliverables about the PPFP co-funding initiative. Prepare annual event to showcase recipients and plan next steps (Month 16+)

Figure II.3



7. **Examples: Public-Private Funding Partnerships**

Purpose and Types: Partnerships are a proven, well-established structure for advancing shared goals. The specific roles, responsibilities and rights (including ownership rights, if applicable) are determined by negotiation. There is a broad continuum of types of partnerships, from informal affiliations at one end all the way to highly-structured consortia that sometimes act like a single,

unified entity at the other end. In general, the key purposes of partnerships are to: aggregate resources; share costs; avoid duplication of effort; bring different competencies to the initiative; and focus activities on clear objectives.

Partnerships can be opportunistic and short-lived, or highly strategic with great longevity. The partnership itself may be as simple as a set of agreements, all the way up to a separate operating entity of significant scale and authority. The key to a partnership is to tailor the structure and terms to the needs of the individual participants, and to be willing to make changes as conditions change.

To provide context to the PPFP being recommended in the Strategic Roadmap, several types of R&D partnerships, with examples, are identified below:

Private-Private Partnerships

- Roche and Inception Science and Versant: To "hunt" new therapeutic discoveries for treating hearing loss.
- Atlas and Novartis and Amgen: $265 M fund to invest in pharmaceutical start-ups.

University-Private Partnerships

- Harvard and Evotec: CureBeta (for diabetes research)
- UCLA and Newco: The structure of Newco is unique; Newco is a NFP entity that sits in between a UC campus and the private sector – although it is expected to operate in a manner that's supportive of the private sector). (Newco is temporary name. Also it will eventually be established on all UC campuses.)
- California Institute for Quantitative Biosciences (QB3). University of California and Roche and Mission Bay Capital.

Multi-Party Cluster Partnerships

- TransCelerate Biopharma, a collaboration of 10 large pharmaceutical companies for research aimed at accelerating drug development, starting with streamlining clinical trials
- Personalized Medicine Partnership of Florida: A collaboration of the Moffitt Cancer Center, Sanford-Burnham Medical Research Institute and Florida Hospital for research on cancer and metabolic diseases.

Government-Private Partnerships

- Massachusetts Life Science Center. $467 state funding (to date). Total state contribution will be $1 B over 10 years, for Life Sciences Initiative. Funding partners include private sector investors, NFP foundations, research institutes, academic institutions, the NIH, and other private sector funders. Objective is to "grow" life sciences companies, not to fund clinical trials directly.

- Maryland Stem Cell Research Fund. $100 M+ disbursed to date, as grants and loans to public and private entities. Focus is on both basic and translational research on human stem cells.
- Connecticut: $100 M over 10 years. Although this program is primarily designed to support academic institutions and research hospitals, grants are available for "any entity that conducts biomedical research or embryonic or human adult stem cell research".
- Ohio Development Services Agency (Third Frontier program). $2.3 B initiative to "foster the formation and attraction of new companies in emerging industry sectors". A variety of support and services for the private sector (although not specific to biopharmaceuticals).
- Israel Life Sciences Fund. $222 M total capitalization; up to $80 M from the government. Other funders include venture capital investors.

Foundation-Private Partnerships

- Fast Forward: "Venture philanthropy" organization, funded with $19 M (to date), owned by the National MS Society. Funders include pharmaceuticals, NFPs, and EMD Serono (Merck).

The CIRM PPFP: In its pilot phase, the CIRM PPFP would be at the "less complex" end of the partnership continuum. The PPFP would consist of CIRM bringing together potential co-funders, showing them specific projects, and obtaining separate agreements from each partner to directly co-fund a specific project. CIRM will be playing the role of intermediary by bringing parties together and facilitating agreements and commitments. There would be no formal operating entity, although there could be a formal agreement by co-funders via a memoranda of understanding (MOU) to participate in the PPFP or agree to serve as members of an a network or association of mutual interest focused on regenerative medicine development.

If the pilot scales up the informal organization or network could become a formal operating entity. As described earlier, the most likely forms being an affiliation of co-founders around one or more Donor-Advised Funds or a semi-autonomous foundation (see Organization). As seen above, there are many precedents and many options for structuring a public-private funding partnership.

II. REC 2. CIRM ACCELERATOR

1. Objectives

CIRM funded projects at both the early translational and later translational stage need to be guided through fulfillment of their research milestones along a development path to market readiness. Providing this guidance and technical assistance is essential to ensuring that CIRM funds are well used. This means that as CIRM sponsored projects progress they have a higher probability of producing viable candidate INDs and successfully reaching and completing clinical trials that attract pharmaceutical firms to license or venture investors. Systematically providing this guidance, given the title 'acceleration' here, has a preceding history at CIRM and builds on existing capabilities, but can and should be substantially expanded.

The priorities set by CIRM for its first five years were designed to establish a strong a foundation for leadership in stem cell research and seeding the entire field with discoveries using a variety of stem cell based platforms.[4] CIRM has, with strong peer review through its Grants Working Group (GWG), Clinical Development Advisory Panel (CDAP) and oversight by the Independent Citizens Oversight Committee (ICOC), maintained a rigorous overall process for inviting, screening and managing projects and has undertaken efforts to introduce CIRM-funded Disease Team projects to pharmaceutical companies and private investors.[5]

CIRM's effort has resulted in a stem cell diversified portfolio that includes; cellular therapy, bioengineering, small molecule, and antibodies, as well as multiple disease categories, and has led to the funding in 2009 of 8 early translation projects with a goal of achieving a therapeutic development candidate ready for IND enabling development in 2012/13); 42 early translation projects funded in 20911/2012 with a goal of achieving a development candidate or proof of concept for a development candidate by 2014/15); and 14 Disease Team projects funded in 2010 with a goal of filing an approvable IND in 2014 (2 are already in clinical trials as of 2913, and several are under review for the next round of disease team funding for the completion of an early phase clinical trial, to be awarded by the ICOC in December 2013), and 12 disease team/strategic partnership projects funded in 2012/13, with a goal of filing an IND and/or completing an early phase clinical trial by 2016/17). Of the 90+ translational programs funded

[4] *CIRM Scientific Advisory Board Information Document, August 23rd, 2013, p.9*
[5] *CIRM Strategic Roadmap for Continued Innovation: SWOT, p.3*

by CIRM, it is expected that by the end of 2017 CIRM will have funded at least 10 therapeutic candidates that will be in phase 1 or 2 clinical trials, representing 5 different therapeutic areas.[6]

In its next five years, CIRM's focus will be to drive more promising therapeutics in its diverse portfolio to clinical trials in order to develop evidence of therapeutic benefits of Regenerative Medicine innovations in human health.[7] CIRM pursues this focus while recognizing that it may take more than a decade for regulatory approval for a therapeutic to be achieved. CIRM is approaching the latter period of its Proposition 71 funding and needs to optimize its funding priorities and market readiness of funded projects in order to accomplish its stated primary mission to benefit patients through stem cell research.

There remain challenges that must be overcome in order for CIRM to advance regenerative medicine therapeutics through clinical development and to the market. While diversity in its portfolio has enabled advancements across the pipeline and into new developmental areas, this diversity arguably diffuses funding, rather than concentrating it on screened priorities.[8] Further, while CIRM has in place a scientific and administrative infrastructure for fulfilling its objectives to advance the field with discoveries using a variety of stem cell based platforms, it does not have a formal transition to drug approval program to assist the development and acceleration of potential products for license of start-ups for commercial launch.[9] These challenges fall into three basic themes:

1. **Prioritization of Projects**: How should projects be screened and prioritized to focus funding on the development of therapeutic targets that are of importance to industry?
2. **Investment Readiness of Projects**: What services are needed to assist in the development and acceleration of projects for investment readiness—whether with universities or early-stage enterprise?
3. **Leveraging Resources:** How should CIRM leverage its internal resources to reduce the costs of clinical trials?

Addressing these challenges is of fundamental importance if CIRM is to accomplish its primary mission to benefit patients through stem cell research. To that end, CIRM should (1) provide an integrated set of centralized services in production (process and manufacturing) management and clinical regulatory management; (2) expand the 'CDAP model' to add additional external industry experts with deep commercial expertise and network connections to extend the product development and partnering capabilities of CIRM. This newly expanded 'Accelerator Team' will comprise teams of selected external industry experts and be organized by disease

[6] *CIRM Research Funding Report by Patricia Olson, July 12, 2013*
[7] *CIRM Scientific Advisory Board Information Document, August 23rd, 2013, p.10*
[8] *CIRM Strategic Roadmap for Continued Innovation: SWOT, p.3*
[9] *CIRM Strategic Roadmap for Continued Innovation: SWOT, p.14*

themes to guide each CIRM project step-by-step to achieve commercial readiness and accelerate their market entry; and (3) link CIRM funded projects to accessible external business, technical and laboratory services. (See examples in Section 7).

By implementing these recommendations, CIRM will better leverage its internal resources and maximize market readiness of Regenerative Medicine innovations – whether with universities or early-stage enterprise. Acceleration services will be delivered by teams of world class professionals from biopharmaceutical, investment, legal, marketing, and academic fields (complying with conflict of interest terms). These professionals will assist in the development and acceleration of projects for investment-readiness based on benchmarked industry expectations and needs. Through their networking linkages these professionals will enhance CIRM's industry engagement and partnering potential with industry and investors.

In addition, CIRM, through its centralized support services will develop a full complement of services necessary in the areas of regulatory, process development, production and clinical trials management to enable CIRM to focus on projects having the greatest chance of development progress and clinical success. Finally, CIRM has just solicited proposals for its five-year Alpha Clinic Program that will help ensure a high quality, efficient infrastructure for conducting stem cell clinical trials across California.

2. Needs

The needs leading to this recommendation to provide an integrated set of centralized services to include production (process and manufacturing) management and clinical regulatory management, and to develop Accelerator Teams of external industry experts by disease themes, were identified in the SWOT analysis and confirmed in stakeholder interviews. Similar needs were also raised by the External Advisory Panel (EAP) and Science Advisory Board (SAB) in their prior observations on CIRM projects. Those needs are to:

Proactively Ready CIRM-sponsored Projects for Commercialization: CIRM's peer review system brings stringent evaluation capabilities to the appraisal of candidate projects, where the focus is on progress from scientific, pre-clinical and early clinical stages of development. In 2011, more focused evaluations of market potential and intellectual property protection began to be included in the assessment of a project. The EAP recommendation raised the question whether CIRM Disease Team projects can be even more systematically reviewed by outside interdisciplinary experts against objective benchmarks pertaining to development progress and

clinical success.[10] The SWOT analysis revealed an opportunity for CIRM in targeting markets and building support for commercialization around innovations actively screened, prioritized and matched to the target markets. Having CIRM create Accelerator Teams by disease themes to guide each CIRM project step-by-step will assist CIRM in identifying and focusing on projects with the strongest development outlook, permitting allocation of greater funding for clinical trials phase 1 and 2 and thereby enhancing commercial readiness and the likelihood that biopharmaceutical firms or investors will readily pick up the next steps.

Leverage Internal Resources and Funding: CIRM's current Centralized Services include Early Translation project management, Disease Team project management and Clinical Research Management. Adding to these core services production (process and manufacturing) will provide CIRM with the expertise needed to guide funding and selection priorities and to improve the investment readiness of its projects. Focusing advancement of projects with a greater likelihood of development and clinical success will ultimately decrease costs for pre-clinical and clinical research and through reducing risk and increasing readiness attract a greater pool of funds to be available from external sources for advancing more projects to market.

Bridge the Gap from Phase 2 Clinical Trials to Market: Among CIRM's strengths is its strong innovation feedstock. CIRM continues to fill the pipeline for regenerative medicine cures and innovations, advancing the number of projects to phases 1 and 2 clinical trials. The EAP, in its review of CIRM, recommended that it evaluate various healthcare delivery models and become proactively focused on clinical translation, product development and healthcare delivery.[11] The SWOT analysis revealed a CIRM weakness is the lack of a current structure to bring additional resources of funding to enable development to bridge the gap from Phase 2 to market. While the private sector may select specific innovations arising from CIRM-sponsored efforts, this leaves a gap for the balance.[12] Creating a bridge to market will go far to sustain and enable CIRM's ability to fulfill its mission. This bridge to market is the Accelerator Program recommended herein.

Internally, the Accelerator Program will enable CIRM to prepare and de-risk candidate therapies for investment readiness and transfer to industry through its core centralized services, an expanded Accelerator Team and clinical research coordination through the future Alpha Clinic Program. Locally the Accelerator Program will have the capability to link CIRM-funded projects to accessible business, technical and laboratory services (See Section 7 for examples), through collaborations with non-profit accelerators across universities in California. Nationally, the Accelerator Program will engage expertise and services to develop market-readiness of projects,

[10] *CIRM Report of the External Advisory Panel, Recommendation 3; p.10*
[11] *CIRM Strategic Roadmap for Continued Innovation: SWOT, p.34*
[12] *CIRM Report of the External Advisory Panel, Recommendation 4; p.1*

arrange license and collaboration arrangements with biopharmaceutical companies and/or partner with venture backed accelerators and early-stage venture firms.

Stakeholder Comments on
Importance of a CIRM Accelerator Program

"This is a fundamental need" – Industry

"There is a need to jump over the valley of death." – Industry

" Great Idea. CIRM needs to pick and focus on successes to sustain operations" – Patient Advocacy Foundation

" Acceleration is an important activity where foundations are increasingly focusing" – Patient Advocacy Foundation

"A pre-venture stage acceleration service is very valuable as it helps prepare the path for firms, such as ours, and makes it more attractive for them sponsor or co-sponsor ongoing research." – Industry

" Absolutely a desirable activity and needed outcome" – Investor

"The entity can and should play a role from the pre-clinical stage up through the phase I and II stage, reducing risk and increasing readiness."— Investor

"Someone needs to build a prototype to try these ideas out—to explore how RM can flow to patients, not just develop the science."— Industry

"RM should be a strength of CA." – Industry Advocacy Foundation

"This is an important and needed activity that foundations are doing more and more"— Patient Advocacy Foundation

"Likes the concept of acceleration of commercial readiness, but it must be autonomous to ensure that politics and competition don't create complications. An acceleration process makes everyone smarter, enables building a clearing house of information, helps scientists to see what is important, almost a design of experiment question—how to get to next step—whether tangible financial milestones or performance parameters—a great resource." – Industry

"This is absolutely a desirable activity and needed outcome, but needs to be handled correctly. An intermediary that can play an active role from the pre-clinical stage up through completion of phase 1 and 2 would be very valuable, if sufficiently well financed and objective." – Investor

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"Each project needs more oversight through CDAP, boards of directors and advisory boards, who meet on a quarterly basis to track issues and progress and provide guidance. Even if this shifts the development time line, an enhanced overview body with authority, like a board, should have the flexibility to address needs and reschedule accordingly." – Investor

"At a minimum, reducing the costs of clinical trials makes sense, streamlining the process without violating regulatory oversight, sharing costs or reducing them, all is important." – Industry

"CIRM should have an intensive business development program structure that systematically screens projects in terms of science first, then markets second, provides hands on management, brings them to a next level of development with very systematic outreach and partnership development with the biopharmaceutical industry." – Investor

"With venture capital 'gone' (at a low ebb), the challenge of regenerative medicine investment attract is higher. Mitigating risk is key and that the Accelerator could actively do this, but under what terms? If CIRM provides the acceleration services without charge or equity, CIRM would only get one result—a higher portion of successful projects reaching market.

"Building a qualified source of deal flow that has human data on efficacy to merit focus could attract capital and possibly a specialized venture fund." – Investor

3. Organization

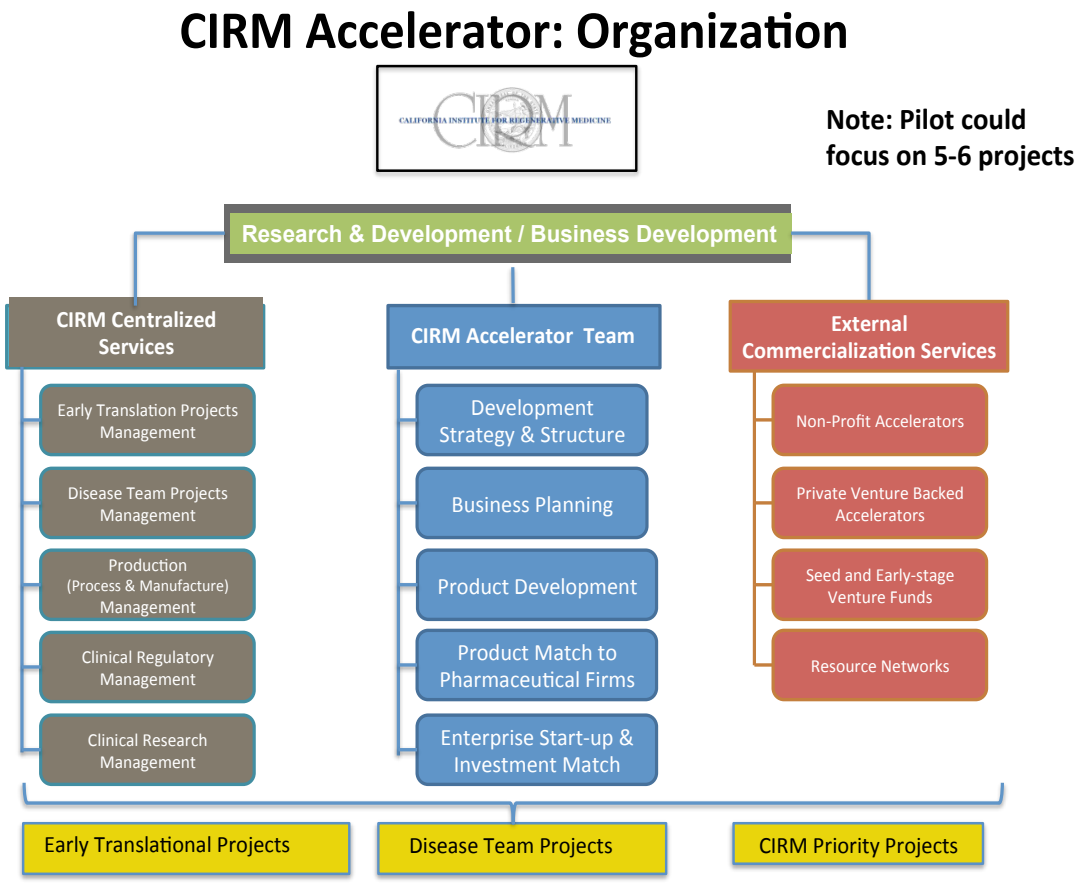
There is no need for a new organization to implement this recommendation to establish a CIRM Accelerator. CIRM is already well positioned to implement accelerator services by providing an integrated set of centralized services (rather than the current practice of funding such services within funded projects) and developing Accelerator Teams to guide each CIRM project step-by-step to achieve commercial readiness. To formalize and strengthen CIRM's role in accelerating the research and development of projects and enhance market readiness, the following steps are recommended:

- **Provide Integrated Set of Centralized Services:** Currently, regulatory, process and production expertise is delivered to individual projects and paid for out of grant funds. Integrating and centralizing these services at CIRM enhances its project management capabilities. Such services enhance pre-commercial readiness of CIRM projects.
- **Develop Disease-Specific Accelerator Teams**: CIRM should build on its current CDAP model with specially configured external professional teams of industry experts organized by disease themes and other domain knowledge to ensure each CIRM funded project achieves quality pre-clinical and clinical trials results and pre-commercial readiness. One Accelerator Team might work with multiple projects within a given disease theme.

CIRM Strategic Roadmap for Continued Innovation: Strategic Roadmap

- **Establish Pilot Accelerator Program:** CIRM organizes and internally funds first demonstration of the CIRM Accelerator focusing on six-to-eight agreed upon priority projects, also leveraging external campus associated accelerator services.
- **Scale-up CIRM Accelerator**: CIRM formalizes its Accelerator Program to encompass multiple teams with possible financing from the public-private funding partnership, syndicates of pharmaceutical corporate venture funds and/or early-stage venture investors to deliver quality and readiness of projects.
- See Operations for description of the proposed steps for the program's operation

Figure III.1



CIRM Strategic Roadmap for Continued Innovation: Strategic Roadmap

Stakeholder Comments on
Feasibility of a CIRM Accelerator Program

"Creating a pool of funds for de-risked RM projects will then make sense." – Industry

"Our foundation does this now, providing readiness services, there are steps."— Patient Advocacy Foundation

"Scale-up the CDAP structure to enable generating documentation and interaction." — Investor

"The foundation believes that there are pre-competitive developments that could be done around very core issues, such as quality assurance, standards and manufacturing." – Patient Advocacy Foundation

"…enhancing the deal quality of projects that are 'investigator-driven' and *not yet* partnered with big pharma or investors makes sense."-- Patient Advocacy Foundation

"The science quality is good through CIRM, but managing to a clinical hypothesis is needed"—Industry

"…. public-private partnerships to foster support for RM therapies that will have visibility is highly plausible"-- Accelerator Program

"Absolutely agrees that CIRM could serve as a 'bundler' of funds that will support RM research at California institutions. That is an appropriate and exciting potential."— General Foundation

"CIRM should work with industry on development, pay attention to regulatory side requirements. Deal with the issue of reimbursement in this era of prosperity, given likely constraints." – Patient Advocacy Foundation

"While CIRM has specified milestones it does not have the authority or 'infrastructure' to manage projects so they hit milestones." – Investor

"CIRM needs to think carefully about how to move projects forward to clinical trials. Academics cannot or will not usually take projects through phase 2. CIRM needs to carefully manage who receives support once clinical trials are started and carefully manage and control of clinical trials data, if any business is to flow out of this." – Industry

"To provide good next steps in moving research to market, CIRM needs to get more aggressive in managing development. CIRM needs to focus on absolute progress in programs, showing that the whole field is advancing. They need to be more clinically selective, pick winners and losers. Focus on what will serve a market, what is most cost effective and what will attract companies and investment." – Industry

CIRM Strategic Roadmap for Continued Innovation: Strategic Roadmap

"An accelerator would not necessarily focus on motivating faculty entrepreneurs but would mine the research findings and IP to explore and organize prospects for a product or a new enterprise." – Industry

"CIRM should set the stage for future investment deals. Making sure getting the horse in front of the cart is key. So, CIRM in some way needs to create deal flow with more selectivity up front in their process." – Industry

"There needs to be CIRM staff (or an intermediary) actively engaged in each of the disease teams or the companies receiving the grant (e.g., strategic partnerships). In doing so they will gain knowledge in terms of new ideas, new concepts, cross-fertilization of ideas. So, if progress is good, well monitored, a new proposal is not required, development continues. – Industry

"Put all projects on the table, with project timelines, make a total portfolio analysis, leading to choices, 20% of projects will give 80% of results." – Industry

"To better attract mainstream venture capital CIRM or an intermediary needs to advance the science, clinical efficacy, reduce regulatory risk information and improve how it is presented to industry. Package deals for pre-series A from output of staged projects managed either by CIRM or an accelerator program. Having the CIRM non-diluting funding will also enhance readiness to consider often expensive and risky A round investments. That risk reduced deal flow should induce greater interest in RM projects." – Industry

"CIRM needs to delineate the key steps that need to be carried out to move innovation to commercialization and prepare the management, documentation and solutions to get there." – Investor

"Getting projects to, and through, clinical trials phase 1 or phase 2 is vital. Yet, for this to work you need the right team in place with the right focus. For that the applicant team and partners need to think about and understand: (1) what the commercial product should look like, (2) its clinical path, (3) its clinical development, (4) the regulatory hurdles, (4) IP management, (5) market structure and size, (6) reimbursement, (7) cost of goods sold, and (7) competitive environment, and so forth. This would lead to being able to offer a true package for the investor that investors will understand. There is definitely a need for a managed structure." – Investor

"Foundations can actually provide models for how CIRM could structure its market preparation of projects. They have thought through downstream issues—including end points, such as how to get VCs, pharmaceutical industry to accelerate development, despite dead ends in certain areas." – Investor

"Accelerators, unlike incubators, have one management team with many ideas that they leverage and for which they build companies step by step. This is needed to aggressively move development forward." – Investor

CIRM Strategic Roadmap for Continued Innovation: Strategic Roadmap

4. Operation

The CIRM Accelerator Program can and should operate as an enhancement of its current operations. The *formalization* of an Accelerator Program as a strategic focus for CIRM is important. The reason is that having this program formalized is a way to reinforce its leadership position in the US and worldwide through its ability to accelerate the research and development pathway for regenerative medicine innovations from laboratory to market. A formal CIRM Accelerator Program offers a means to further contact and engage major biopharmaceutical firms, disease foundations, insurance firms, public and private accelerators, as well as federal and state healthcare finance, health and safety, and technology agencies.

The operations of the CIRM Accelerator Program uses existing capabilities to accomplish the following pilot—with project volume growing over time:

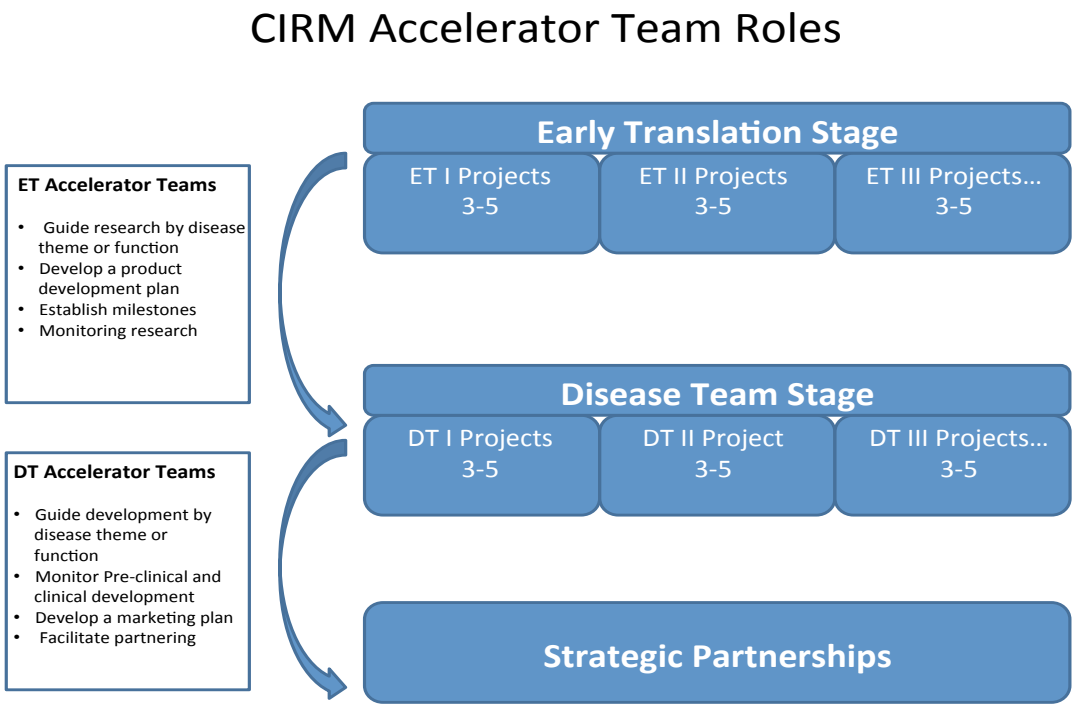
- **Add Integrated Set of Centralized Services:** Add manufacturing, process development and associated expertise to the core of CIRM Centralized Services. Integrate these services at CIRM to enhance its project management capabilities. Although CIRM will maintain a centralized core of support services to support research programs it funds, CIRM may partner with external acceleration programs, such as university associated non-profits with accelerator services (such as QB3 and Catalyst at UC campuses in the San Francisco Bay Area or SPARK at Stanford) and venture backed accelerators such (such as Accelerator Corporation), and early venture funds (such as Versant and 5AM) for funding to leverage its internal resources. (See Section 7 for those external services.) Such external services provide a range of services, including access to facilities, educational programs, internships, mentoring, management teams, incubators resources (for a fee) and funding.
- **Develop Accelerator Pilot**: Identify and recruit additional external experts with a range of industry product development and networking expertise matching CIRM projects to form a real commercialization services team to guide each CIRM project step-by-step to achieve market readiness for partnering with industry and/or investors.
- **Arrange Compensation**: Offer compensation for additional commercialization services in some form (such as a limited retainer) to those experts for their services. For the pilot this would need to come from CIRM, but over time would come from private sources.
- **Complete Structure**: Organize the Accelerator Team around a specific disease theme (with the possibility of future teams by theme) with a team reflecting the continuum of development needs (perhaps flexibly or staged over time by a core team).
- **Early Translation Screen**: Accelerator Team and CIRM staff will meet quarterly and review existing Early Translation (ET) (or pre-IND) projects and guide research by disease

theme or function, and begin to develop a product development plan, establishing and monitoring research milestones that must be met for continued funding. The selected ET projects must have 'high relevance' for Disease Theme (DT) consideration from the commercial vantage point. (One Accelerator Team might work with several projects aligned with a disease theme.)

- **Disease Team Screen**: Accelerator Team and CIRM staff will meet quarterly and will review existing DT (or IND) projects and prioritizes those projects having the best development and clinical potential. They will monitor the pre-clinical development milestones and provide guidance for meeting the milestones. The Team and CIRM together will develop a strategic roadmap for marketing and pre-market readiness of DT projects, assembling the pre-clinical and clinical packages, identify potential target partners in the marketplace and build those relationships leading to commercial licenses. One Accelerator Team might work with several projects aligned with a disease theme.
- **Direct Assistance**: Accelerator Team and CIRM staff work with each set of selected projects and apply a set of consistent pre-commercialization criteria and advisory service beginning with the first quarterly meeting (each of those meetings could last several days per project), and continuing with projects doing their own response between quarterly meetings with ongoing virtual communications.
- **External Support**: Accelerator Team and CIRM staff work from findings of early project reviews to prepare and match DT projects to financially accessible outside resources near each project university--whether QB3 and Catalyst, Spark, Connect--or, will introduce projects to possible accelerator firms who agree to consider candidates from CIRM.
- **Matching**: Accelerator Team and any outside partners conduct limited research and use their own networks to advance the selected DT projects within the pilot disease team to form appropriate partnerships with pharmaceutical firms or venture capital firms. This would go beyond meet and greet to more market-driven linkages.
- **Review**: The Teams will review their progress with each project at the ET and particularly the DT level quarterly, concluding the year with a major review and group meeting to compare and explore the outcomes of the year.
- **Scale-up**: Consider continuing pilot or expanding into a multi-team structure, anchored by a core team (perhaps) with strong external resources.

CIRM Strategic Roadmap for Continued Innovation: Strategic Roadmap

Figure III.2



5. Source of Funding

The development of the CIRM Accelerator Program can be carried out now as follows:

Centralized Services: This continuum of services is already provided through CIRM research support services. Whether they can be expanded or not needs to be determined.

CIRM Accelerator Team: CIRM can build its Pilot stage Accelerator team of five to ten professionals through hiring these advisors as consultants without issuing an RFP/RFA. These professionals can be recruited or appointed and placed on a limited retainer. In that role these advisors would have a direct report relationship to CIRM, providing services to the research investigators on behalf of CIRM and ensuring compliance with agreed upon milestones by research teams.

Organizationally, the provision of these services may be funded by research dollars. As these services are intended to guide and enhance project performance whether early or later stage translational research, and as they will ensure compliance with milestones that could lead to decisions regarding project continuity or termination.

CIRM may have flexibility as to whether the provision of accelerator services is done as a separate program initiative over time. For the Pilot stage these "CDAP 2.0" services will be provided on a project-by-project basis. There are precedents for this proposal as CIRM has funded several initiatives aimed at funding research infrastructure/support, as opposed to primary research.

CIRM research dollars should, in fact, be available to pay for this advice in the context of specific projects where such advice and support is critically important to development and commercialization of a CIRM-funded innovation. This would be, for example, analogous to the CIRM Patent Assistance Fund that covers certain patent prosecution costs for non-profit grantees, paid for with research dollars.

An alternative approach that CIRM might consider in due course would be to include external 'project management' costs associated with accelerations services as part of a grant award, but withhold those funds from the actual disbursement to the grantee on the grounds that CIRM is providing the research services on an in-kind basis. This would be akin to a charge-back arrangement for CIRM funded programs using centralized services.

The Accelerator should also be proposed as part of the Public-Private Funding Partnership (PPFP) as it scales up. This would ensure that every co-funded project has a professional advisory team separate from the research team working on advancing the project to successful pre-market outcomes.

University-Associated Accelerator Services: CIRM can and should contact and negotiate appropriate agreements with university-associated accelerators to ensure that CIRM projects are welcome and can be served as may be necessary. As described earlier, as the CIRM Accelerator advances the product and market-readiness of each project they will link each project when appropriate to external, complementary, accelerator services. For university projects or university-affiliated start-ups the CIRM Accelerator will introduce projects to campus associated non-profit accelerators that provide access to laboratory and office space, legal, financial and marketing advisory services at no or low-fees. Many of these accelerators now also offer access to pre-seed funds and introductions, when appropriate, to early-stage venture capitalists.

Corporate Accelerators: There are an increasing number of technology development firms that provide hands-on advisory services and seed capital to very early stage projects, also known as accelerators. CIRM can and should provide access to these firms to help secure further preparation of regenerative medicine candidate therapies. These corporate accelerators may be venture-backed development corporations or early-stage venture firms, including corporate venture firms (particularly in the biopharmaceutical field). In exchange for their services and pre-seed or seed capital these companies seek early access to innovation that they believe can be grown into venture ready enterprises or corporate acquisitions. CIRM already has contacts with several of these corporations (see Examples) and should systematically learn about and

discuss with other accelerators how the CIRM Accelerator program can and will prepare a growing number of lower-risk, pre-venture stage candidates for their consideration and funding. These private accelerators will seek an early equity position or rights in exchange for their intensive services and pre-venture stage seed funding. For this type of relationship to work, CIRM-funded candidates need to have successfully completed key development milestones. CIRM core services and the Accelerator team can then help each project and their university to reach suitable agreements for a given project to transition to private accelerator services. Not all projects will require or be ready for these services. However, CIRM's enhancement of the readiness of projects will provide the option of transitioning projects to these corporate development services as may be deemed appropriate by the project principals and the CIRM Accelerator team.

Stakeholder Comments on
Readiness to Participate in a CIRM Accelerator Program

"Company and corporate venture funds may consider participating." – Industry

"Ready to explore this with CIRM."—Patient Advocacy Foundation

"We do this now and are ready to explore this with CIRM."— Patient Advocacy Foundation

"If corporate venture fund participates they would expect conventional terms."—Industry

"Open to many agreements. May seek royalties to offset funds placed." --Patient Advocacy Foundation

"Access to non-dilutive funds for projects can attract participation." – Investor

"Have partnerships with [other organizations] and other foundations. They would be open [to working with CIRM]." Patient Advocacy Foundation

"…willing to participate with other foundations and pharma on the possibility of leveraging CIRM funds with private funding. Likes the idea of this convergence."—Patient Advocacy Foundation

6. Sequence for Development/Timing

The development of timing of the CIRM Accelerator Program can be implemented in straightforward steps, corresponding with Organization and Operations features described above and described in the figure below:

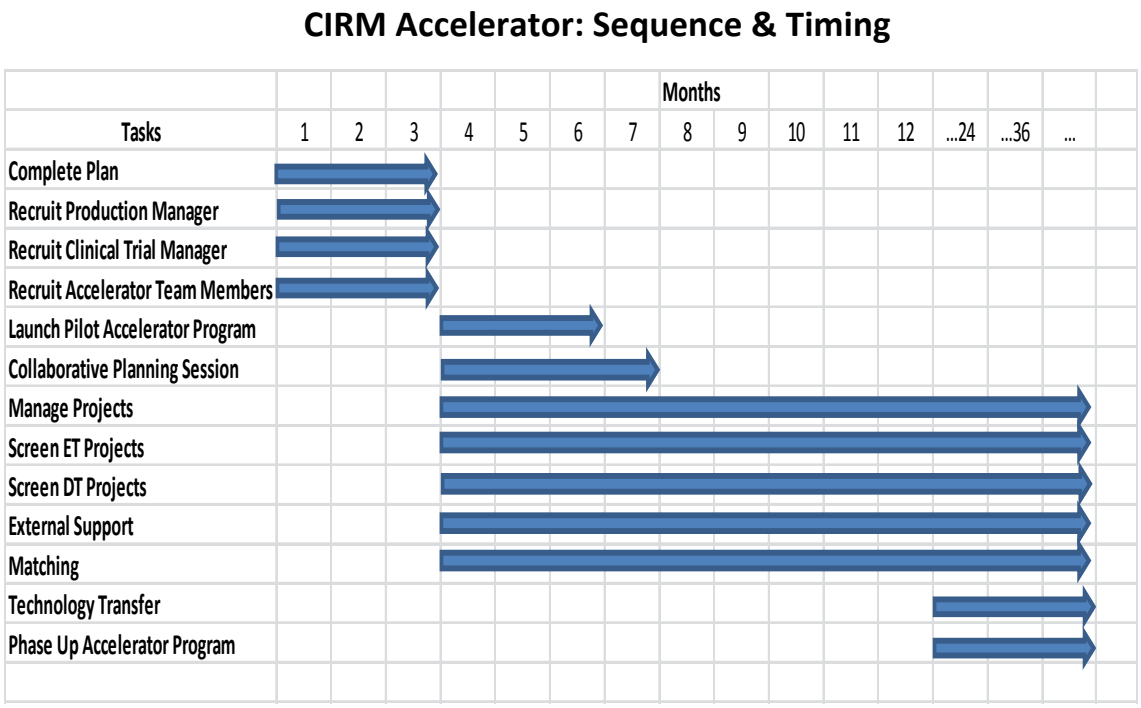
CIRM Strategic Roadmap for Continued Innovation: Strategic Roadmap

- **Complete Plan**: Complete an internal plan for adding internal Accelerator services in Production (process and manufacturing) Management and Clinical Trial Management; and for Pilot Accelerator Program (1-3 months)
- **Recruit Production Manager and Clinical Trial Manager:** Select and hire regulatory, process and production expertise and organize under CIRM Centralized Services. (1-3 months)
- **Recruit Accelerator Team Members:** Retain a range external of experts matching CIRM projects to form a commercialization services team to guide each CIRM project step-by-step to achieve investment readiness. (1-3 months)
- **Launch Pilot Accelerator Program**: Organize the Accelerator teams around a specific disease theme, with the possibility of future teams also being organized by theme, with composition of members reflecting the continuum of development needs, perhaps flexibly or staged over time by a core team. (4 -6 months)
- **Collaborative Planning Session**: Invite, confirm and facilitate one or more collaborative work sessions with Accelerator Teams and CIRM staff to establish work groups with each set of selected projects and develop and apply a set of consistent pre-commercialization criteria and advisory services beginning with the first quarterly meeting (each of those meetings could last several days per project), continuing with projects completing their response between quarterly meetings with ongoing virtual communications. After the initial meeting continue on a quarterly schedule.
- **Manage Projects:** Accelerator Teams and CIRM staff will oversee project execution, including coordinating collaborative roles of Accelerator Team members and CIRM staff. (4 months and beyond)
- **Screen Early Translation Projects**: Accelerator Teams and CIRM staff reviews existing Early Translation (ET) or pre-IND projects and tracks all by disease theme or function, but recommends those that have 'high relevance' for Disease Theme (DT) consideration from the commercial vantage point. (4 months and beyond)
- **Screen Disease Team Projects**: Accelerator Teams and CIRM staff reviews existing DT (or IND) projects and prioritizes those on which they will concentrate hands-on oversight and assistance, based on a minimum of intensive quarterly meetings. (4 months and beyond)
- **External Support**: Accelerator Teams and CIRM staff work from findings of early project reviews to prepare and match DT projects to 'free' outside resources near each project university--whether QB3 and Catalyst, Spark, Connect--or, will introduce projects to possible accelerator firms who agree to consider candidates from CIRM. (4 months and beyond)
- **Matching**: Accelerator Teams members and any outside partners conduct limited research and use their own networks to advance the selected DT projects within the pilot disease team to form appropriate partnerships with pharmaceutical firms or

venture capital firms. This would go beyond meet and greet to more market-driven linkages. (4 months and beyond)

- **Technology Transfer**: CIRM will help facilitate license agreements with prospective licensees and CIRM grantees (Month 24-36)
- **Phase Up and Formalize Accelerator Program—Year 2**: CIRM will expand the Pilot Accelerator Program and formalize the Accelerator Program to encompass multiple teams with possible financing from the public-private partnership, syndicates of pharmaceutical corporate venture funds and/or early-stage venture investors to deliver quality and readiness of projects. (Month 24-On)

Figure III.3



7. Examples

There are a number of external acceleration programs from which CIRM can learn as well as partners for commercialization services to leverage its internal programs. These programs fall into three general categories:

CIRM Strategic Roadmap for Continued Innovation: Strategic Roadmap

- **University/Non-profit Accelerators:** In recent years public and private universities have increasingly encouraged and co-supported the formation of (typically) non-profit services to assist faculty in forming new enterprises. These programs provide a continuum of low cost services, which include education and training on enterprise development, business planning and management services (including mentoring and entrepreneurs in residence), linkages to pre-seed, angel/seed and venture capital funds, as well as access to facilities (an incubator facility with labs). The following are examples of potential non-profit accelerator partners and entrepreneur support networks and the services they provide:
    - **QB3** (USCF, UCB, UCSC): The University of California created QB3 in 2000 to help grow the state's economy and improve the quality of life for its residents. QB3 reaches out to faculty and graduate students prepared to explore becoming entrepreneurs and provides key educational programs, internships, mentoring and facilities through its adjacent-to-campus incubators/innovation centers. They have a small affiliated seed fund and an associated venture fund (Mission Bay Capital). QB3 has been extremely successful in responding to faculty readiness to form new enterprise, helping these to grow and progress to market.
    - **CTSI Accelerator & Catalyst** (UCSF): UCSF's Clinical and Translational Science Institute (CTSI) is an extensive integrated program to help support early translational research progress to application. The Accelerator service brokers key resources needed to move innovation from pre-clinical trials to clinic. The Catalyst award that combines customized expert advice with funding to help drive promising early-stage research. Also offered is 'Launchpad,' an on-line resource to assist entrepreneurial faculty to identify unmet needs, target product profile, collaboration, development plan and organizational support—as well as other resources for researchers.
    - **SPARK** (Stanford): Program was created at Stanford to provide access to technical expertise, core laboratory facilities, and funding to support translational efforts. SPARK provides a cost-effective model to generate proof-of-concept, using industry standards.
    - **LARTA** (Los Angeles Regional Technology Alliance): LARTA Institute was founded to identify, nurture, and promote promising early-stage high-tech and life science companies in the Los Angeles area. LARTA's services assist in the design and implement commercialization programs, provide policy advice; bridge market gap and elevate market-readiness. LARTA also offers support services directly to SBIR and STTR awardees to accelerate their commercial outcomes.
    - **CONNECT** (UCSD): CONNECT was created to catalyze the creation of innovative technology and life sciences products in San Diego County. CONNECT focuses its efforts on accelerating the commercialization of new technology and life

sciences products by linking inventors and entrepreneurs with coaching and networking resources.

- **MaRS Innovation** (Ontario, Canada): MaRS Innovation collaborates with its 16 Toronto-based member institutions and their technology transfer offices to commercialize market-disruptive intellectual property. MaRS provide management teams and market and business development intelligence to prime early-stage technologies for potential investors.

- **Private Venture Backed Accelerators**: Corporations specializing in early-stage technology development have been increasingly formed with venture capital backing to improve identification and formation of new enterprises. These development companies mine intellectual property, form new firms, provide seed capital, build their teams, manage the testing and preparation of their product, including leveraging of non-dilutive capital (e.g., grants) and then, having completed pre-venture stage readiness, participate in full venture funding or an exit via acquisition. Two examples include:

  - **Accelerator Corporation:** This organization is a privately–held, multiple venture capital fund-backed, biotechnology investment and development company. Accelerator screens intellectual property and research projects to identify and screen prospects for development from universities and research institutes. They then evaluate, start, finance, and manage emerging technologies, including provision of management, technical expertise and laboratory facilities. They are associated non-exclusively with a research institute in Seattle, WA (the Institute for Systems Biology).

  - **Community of Innovation Pharma:** COI Pharma is a venture-pharmaceutical entity established as a collaboration between Avalon Ventures and Glaxo SmithKline. The aim of this company is to provide intellectual capital and operational support for entrepreneurs through access to facilities, industry mentors and leadership.

- **Early Stage Venture Funds**: There are a number of venture funds that invest in early stage development in the life sciences. As an example, a typical initial investment for Atlas Ventures ranges from $500K to $5M. Examples of early-stage venture funds are:

  - **Versant Ventures**: Versant Ventures is a venture capital firm that specializes in investments in game changing medical devices, biopharmaceuticals, and other life science opportunities. It is currently investing a $500 million fund raised in July 2008; focus is medical devices, biopharmaceuticals, and other life sciences.

  - **5AM Ventures:** 5AM is focused on building next-generation life science companies and is often directly involved in setting company strategy, management recruiting, business development and fundraising, they also frequently take on a short-term operating role.

CIRM Strategic Roadmap for Continued Innovation: Strategic Roadmap

- **Atlas Ventures**: Atlas Ventures is a venture capital firm that invests in earliest stages; typical initial investment ranges from $500K to $5M; raised 9 funds with most recent for $265M in April 2013
- **Third Rock**: Third Rock has raised more than $1.3 billion and invested in more than 31 companies; invests in projects 3-5 years from Series A; provides leadership. Its focus is on launching and growing companies.

IV. REC 3. PRE-COMPETITIVE RM R&D PROGRAM

1. Objectives

CIRM has played a catalytic role in enabling the science of regenerative medicine to take shape and grow. Not only has CIRM funded basic research and a continuum of early and later stage translational research, CIRM has funded training of scientists and new laboratories, as well as development of new tools needed by researchers. CIRM support has helped set the stage for the growth in regenerative medicine research and development now underway in California and globally.

There remain challenges that must be overcome in order for regenerative medicine therapies to be developed and reach the clinic and patient. These challenges are not strictly about science discoveries, early translational research or advancing disease team development to FDA approval. These challenges fall into three basic themes:

- **Production**: How can regenerative medicine therapies be developed and produced on a consistent and cost-effective scale for the patient marketplace?
- **Reimbursement**: Given how regenerative medicine therapies may be produced and delivered (autologous and allogeneic) how will they be reimbursed by the healthcare system?
- **Regulation**: As an emerging field that applies new modes of delivery to achieve therapeutic results what range of standards and regulations need to be in place to protect all parties?

Addressing these challenges is fundamental to the transformation in medicine that has been made possible in large measure through CIRM support. However, these important technical, financial and regulatory hurdles are not specific to any one project, therapy or firm. These are shared problems that need to be addressed if the progress of regenerative medicine to market is to continue. These issues are 'pre-competitive' and merit collaborative actions that will benefit producers and users alike.

For this reason, defining the core challenges to enabling production, financing and regulation of therapies and collaboratively ensuring that the answers are explored and then applied makes sense as a continuing role for CIRM.

To that end, CIRM should play an active role in defining and co-sponsoring research and development focused on strategic pre-competitive challenges facing regenerative medicine.

By anchoring the development of these pre-competitive initiatives CIRM will not only accelerate progress towards answering key questions or needs that will smooth the path of regenerative medicine to market, but in doing so will also preserve and strengthen the visibility of CIRM as a core resource nationally, if not globally.

2. Needs

The needs leading to this recommendation to expand conduct of pre-competitive R&D projects were briefly identified in the SWOT Analysis and confirmed in stakeholder interviews, but have also been raised in by CIRM in the course of managing its ongoing portfolio of projects. Those needs are:

Research 'Bottleneck' Challenges: CIRM has long had among its priorities in early translational research addressing 'bottlenecks' to advancement to the clinic of effective and novel cell therapies, particularly cell therapies derived from human pluripotent stem cells. Moreover, 23 invention disclosures have come from that work. The eight CIRM Bottleneck awards focused on better models for developing and testing candidate therapies and on characterizing and mitigating risks of PSC-derived cell therapies (teratoma, tumorgenicity, genetic instability and immunogenicity). These initiatives have been pursued directly through CIRM projects. There also remain many laboratory challenges that need to be resolved for regenerative medicine development to move ahead. Many of these past projects have successfully leveraged non-CIRM collaborative funding. Future projects may be pursued through CIRM RFAs and perhaps through the future public-private pre-clinical and clinical trials partnership.

Technical Challenges: Focusing on challenges that regenerative medicine development will face in producing therapies for the commercial marketplace, CIRM has recently led a workshop with co-sponsors including ARM and the UK Catapult to prepare a White Paper on "Key Tools and Technology Hurdles in Advancing Stem-Cell Therapies" (September, 2013). That White Paper identified, with input from industry and scientists, 28 technology opportunities in product manufacturing, product characterization and imaging that could serve as the basis for cross-cutting, collaborative, pre-competitive projects. Illustrative examples of opportunities include the need for breakthroughs in methods and tools to enable:

- Expanding pluripotent and differentiated cells to large numbers.
- Making the growth microenvironment more hospitable to cells.

- Enclosed volume reduction without centrifugation.
- Small molecules to replace growth factors and cytokines.
- Synthetic matrices to replace biological ones.
- Sensitive assays to analyze cell heterogeneity and detect contaminating cells.
- Guidance systems to deliver cells *in vivo* and control homing.
- Sensitive methods for understanding immune response to allogeneic cells and tolerance induction strategies.
- Monitoring clinical efficacy and outcomes.
- Screening teratoma formation.

Economic and Financial Challenges: While CIRM research has concentrated on breakthroughs that will lead to new therapies based on regenerative medicine, the downstream issues that might stimulate or impede progress to the marketplace have not yet been tackled. While this is understandable given the time new therapies take to reach approval for market entry, the reality is that unless the economics of applying new forms of regenerative medicine in health care are understood in advance, adoption of new therapies could be slowed if not actually blocked or ignored in favor of conventional treatments in the future.

Pre-competitive examination of models and eventual testing and demonstration of the effectiveness of regenerative medicine cures and financial models for enabling delivery of care are needed. Exploring and testing financial models in advance could, in fact, clear the way for greater investment in regenerative medicine development, as the risks and value associated with downstream introduction of new therapies would become clearer.

The national healthcare insurance industry is facing pressures to adapt to new national policies as well as continual cost containment pressures. For that reason there has been less expression of direct interest in the potentially profound impacts that regenerative medicine therapies might deliver to patients in the healthcare system within the next five to ten years. Nonetheless, regenerative medicine may be a major means for addressing many healthcare cost issues. Getting that message across in a timely way and inducing insurance and public healthcare finance participation in examining the potential of regenerative medicine will make increasing sense.

There may even be new financial advocates for future regenerative medicine therapies. Reinsurers are now just beginning to explore new approaches to managing health cost factors and risks in a way that benefits multiple parties. Reinsurers are now at the earliest stages of considering how to assume financial risk for innovative drug therapies; providing a clinical, evidence-based, capacity for medical management; pre-certification and quality control for the

continuum of health care; collective purchasing of products, including from manufacturer; networked management with centers of excellence in care by disease; and patient disease management for selected patients. While still very early, CIRM can play a catalytic role in informing and engaging insurers and reinsurance and major healthcare finance stakeholders in considering the importance and requirements for enabling autologous and allogeneic therapies to reach healthcare markets.

Regulatory Environment: Among topics where collaboration can yield constructive results for new innovations in health care is regulatory process. Here, CIRM has been active independently and through ARM, in providing input to the FDA pertaining to the regenerative medicine research now reaching INDs and soon clinical trials. The key challenges have been ensuring compliance while managing costs—whether allogeneic (using cells from another source) or autologous therapies (where an individual's cells are removed, processed, and reintroduced). Advancing the dialogue on evolving regulatory issues may require collaborative analysis and strategy between FDA as well as research institutes, the biopharmaceutical industry and healthcare system. CIRM can play an important role here as a focal point.

Given these needs, CIRM has the opportunity to define an important leadership role for itself and California, building on past efforts to achieve greater national if not international focus and visibility on key cross-cutting challenges facing regenerative medicine.

Stakeholder Comments on
Importance of a CIRM Pre-Competitive R&D Program

"CIRM can and should initiative pre-competitive R&D projects as a credible third party. CIRM has credibility with academia and an improving image with industry. CIRM can be the convener. The timing is right." – Academic

"We embrace the need for pre-competitive R&D. There is a need for standardized methods. A key example is the issue of the replication of laboratory work. Need to be able to replicate science findings in independent laboratories." – Patient Advocacy Foundation

"Very important. We are very concerned with improving stem cell development tools, standards and production processes, and management of research and clinical trials so that the right data is ready for the pharmaceutical industry early on." – Industry

"Our foundation believes that there are pre-competitive developments that could be done around very core issues, such as quality assurance, standards and manufacturing." – Patient Advocacy Foundation

CIRM Strategic Roadmap for Continued Innovation: Strategic Roadmap

"Yes, pre-competitive R&D is important and [our company] believes in collaborative process and in thinking about the broader process from start to patient and its implications." – Industry

"Pre-competitive research on technical but particularly business model/delivery issues is an excellent focus." – Industry

"There are significant needs in resolving issues in cellular processes. In autologous therapies you are dealing with a process that moves from the patient and goes back in. In allogeneic processes the issues are tougher, as you take one cellular element, differentiate and control it, produce it and give it to patients. The complexity here is new and techniques need to become reliably consistent." – Industry

"We have actively supported forming a pre-clinical tools model to enable better development process focusing on the big issue of standardization around iPS cells, emphasizing standardizing and distributing starting materials in a manner that works for companies." – Patient Advocacy Foundation

"This field still needs consistent protocols and procedures. For example, there are clearly questions about the level of undifferentiated cells that are acceptable in any RM therapy development. What percent should be acceptable as a final ratio? There is therefore a need for a process that will get standards and benchmarks in place so that firms don't have to plow the same expensive ground for each development. Pre-competitive sharing is key. " – Industry

"Unearthing shared insights is good. We just had a three-day consortium meeting. Investigators spoke about the type of tools and expertise they need. Imaging is key. Imaging tools is one of many pre-competitive issues that could be winnowed down and focused on collaboratively." Patient Advocacy Foundation

"Finding ways to provide manufacturing of cells is an abiding issue. Manufacturing undifferentiated cell lines for others following agreed upon quality standards, and then producing differentiated cell lines is important." – Industry

"Researching regulatory solutions and reimbursement models is a key theme for pre-competitive R&D, working with FDA, healthcare agencies, insurance and pharmaceutical industry. Pursuing this would be very important and possible for CIRM, given its size and leadership." – Patient Advocacy Foundation

"Today the pharmaceutical industry depends on chronic revenue stream from treatment. What reimbursement models will work with stem cells? CIRM should explore demonstrations of contingent performance compensation programs. – Patient Advocacy Foundation

"We believe that pre-competitive research on technical but particularly business model/delivery issues is an excellent focus for CIRM. This is so important that there should be a way for CIRM to manage or assist projects between clinical trials and hospitals and their health care systems—to test reimbursement models." – Industry

"A collaborative around a regional health center focusing on RM is needed. Need to build a prototype to try RM ideas out—to explore how RM can flow to patients; not just development of the science. The idea is to show how a cell therapy could reach patients--through the pharmacy, specialized clinic, through the hospital?" – Industry

3. Organization

There is no need for a new organization to implement this recommendation. CIRM is already well positioned to implement a formal pre-competitive R&D program. CIRM has previously selected and funded workshops and white papers as well as projects through the RFA process on regenerative medicine 'bottlenecks'.

To formalize and strengthen CIRM's role in addressing pre-competitive R&D challenges facing the field of regenerative medicine, the following internal organizational steps can be taken:

Confirm CIRM Pre-Competitive R&D Program: With the approval of the ICOC CIRM should make clear internally and globally that CIRM is committed to serving as the anchor and catalytic agent for addressing pre-competitive issues facing regenerative medicine.

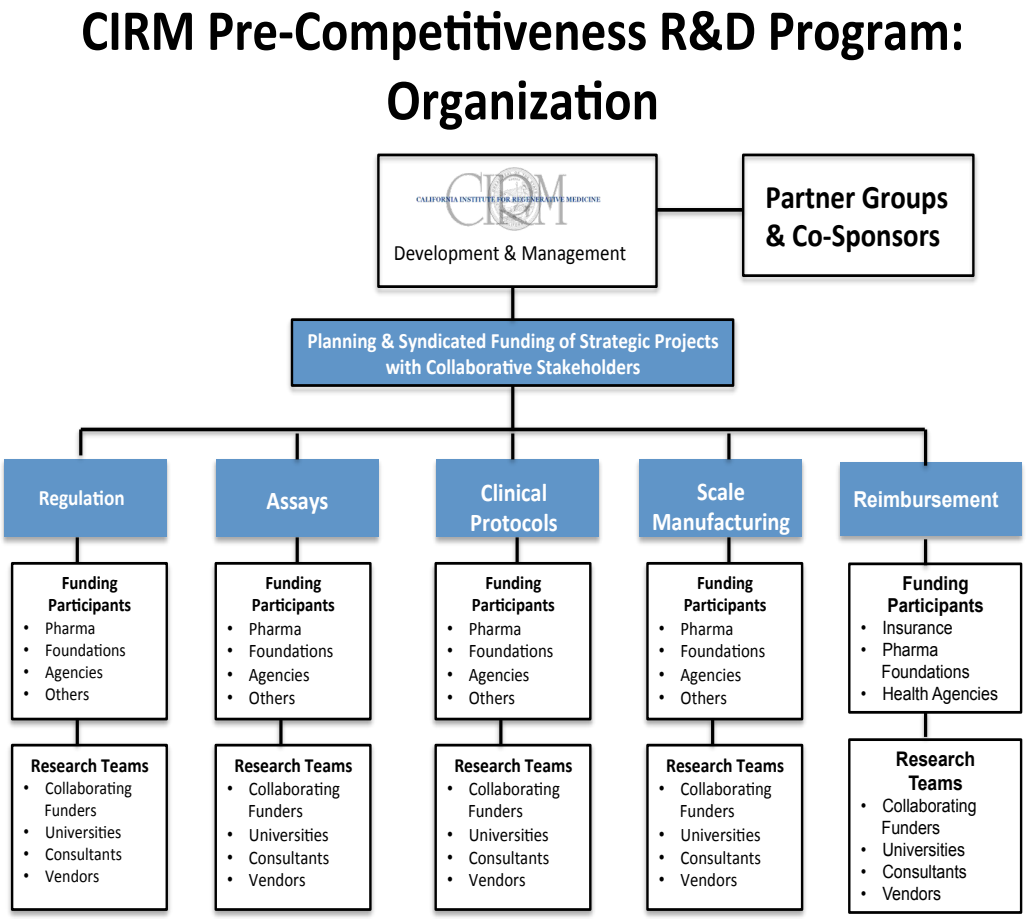
Form Internal Team: Building on past project experience, the internal CIRM science, R&D management, and business development teams within CIRM should organize a 'virtual' team structure for the purpose of developing and managing pre-competitive R&D projects. This virtual team should work towards mutually agreed upon targets for developing and launching pre-competitive projects. Partnering with ARM should be integrated into these early organizational steps.

Prepare Pre-Competitive Program Package: Following internal planning CIRM can develop and launch projects on an incremental, project-by-project basis. While this could begin with one project, multiple projects can be developed over time. However, the key is to show that CIRM has formalized an internal pre-competitive R&D program for use in outreach to potential collaborators and co-funders. See Figure 4.1 Organization below that illustrates how the internal structure of this program might look. While the program might start with one topic, over a two- to three-year period CIRM could launch a portfolio of strategic pre-competitive initiatives.

Coordinate with Public-Private Pre-Clinical & Clinical Trials Fund: The development of the first pre-competitive R&D project can and should be started at the earliest opportunity. That effort and the continuing efforts of the Pre-Competitive R&D Program can be coordinate with the development of the Public-Private Pre-Clinical & Clinical Trials Fund. Specifically, outreach to biopharmaceutical corporations, foundations and agencies focusing on securing co-funding of

pre-clinical and clinical trials projects can also be used to raise interest in broader, cross-cutting pre-competitive projects. There should be a natural synergy. If, after the pilot programs the Public-Private Fund is scaled-up and managed through a new foundation, that same shell organization could be used to house funds for pre-competitive R&D programs, if helpful to sustaining program activities.

Figure IV.1



Stakeholder Comments on

Feasibility of CIRM Pre-Competitive R&D Program

"There is a need for "stewardship" that CIRM can formally play. CIRM could lead collaborative initiatives to examine and resolve challenges facing the complexity of cellular therapies from the academic to the corporate lab and production facility." – Industry

"The foundation believes that there are pre-competitive developments that could be done around very core issues, such as quality assurance, standards and manufacturing." – Patient Advocacy Foundation

"Pre-competitive R&D is very feasible and appropriate. Our firm participates in a variety of these." – Industry

"Securing support for collaborative projects requires reaching the right people in potential sponsor companies in pharmaceuticals. For CIRM, having matching funds to bring to the table will induce openness and attention by the pharmaceutical industry." – Patient Advocacy Foundation

"Pre-competitive projects might be useful, there just needs careful definition so that they really do address shared challenges facing industry." – Industry

"To have a pre-competitive project you need to have specificity of a problem that will impact everyone who will be in the field. That needs to be made visible by CIRM." – Finance

"Get the message out. The President's Council of Science Advisors completed a report on bioscience and recommended consortia to address specific challenges—but among the 10 heads of pharmaceutical and biotech firms there was no mention of stem cells." – Finance

4. Operations

The CIRM Pre-Competitive R&D Program can and should operate as an enhancement of current operations. The *formalization* of pre-competitiveness as a strategic focus for CIRM is important. The reason is that having this program formalized is a way to build national and global visibility among those who may also concurrently become co-funders of the proposed Public-Private Pre-Clinical & Clinical Trials Fund, though not necessarily. Having a formal pre-competitive R&D program offers a means to further contact and engage major biopharmaceutical firms, disease foundations, health insurance and re-insurance firms, healthcare providers as well as federal and state healthcare finance, health and safety, and technology agencies.

CIRM Strategic Roadmap for Continued Innovation: Strategic Roadmap

The operations of the CIRM Pre-Competitive R&D Program use existing capabilities to accomplish the following pilot—with project volume growing over time:

Plan: CIRM should use its excellent base knowledge of issues facing the field of regenerative medicine to define theme areas to which it is committed to advancing collaborative solutions and engaging prospective collaborators. This activity can include these steps:

- **Poll**: Conducting limited research of stakeholders concerns and readiness to explore collaboration in the three areas described earlier.
- **Convene**: Convening invitees to discuss and prioritize pre-competitive issues. For example, as CIRM recently did with ARM on production, but can also do on reimbursement and finance, as well as regulation.
- **Communicate**: Preparing and disseminating the outcome of findings on pre-competitive R&D challenges on which CIRM and partners will be seeking collaborators for action.

Organize: CIRM will manage development of co-funded pre-competitive collaborative R&D projects on a case-by-case basis with external partners. This will involve steps to:

- **Prepare**: CIRM will use the materials generated in the planning process to prepare a statement of the problem and outline of research plan on specific pre-competitive challenges.
- **Position**: CIRM and key partners (e.g., ARM) will then communicate these to a roster of target collaborators identified through previous polling and meetings and announce the development of a specific collaborative project. This may range from a simple multi-client project, to a syndicated program or broader consortium.
- **Confirm**: CIRM will contact and engage companies and/or agencies to confirm a given pre-competitive research issue, secure their input into the research plan as a collaborator, and obtain their commitment to participate as a co-funder with CIRM and key terms (such as how intellectual property will be shared)..

Manage: CIRM will serve as the overall manager of the pre-competitive projects, with an advisory board of co-funders, as follows:

- **Grant/Contract Awards**: Once funding has been obtained CIRM will serve as the manager of collaborative projects and will issue an RFA or RFP once co-funding of the project has been agreed upon and formally announced. CIRM will manage compliance with milestones by those receiving grants or contracts (approved through the ICOC).

- **Collaborators**: CIRM will coordinate the hands-on participation of the collaborating companies or agencies, with the input and feedback of the co-funder advisory board. This active engagement is key to ensuring that the pre-competitive research is focused on agreed upon challenges and will produce results that can be utilized.
- **Progress**: CIRM will work with the advisory board to report on project progress and convene quarterly briefings leading to a concluding event on project completion.
- **Dissemination**: CIRM and its project advisory board will determine how best to disseminate the findings of the pre-competitive R&D project. This will vary depending on the nature of the project and any intellectual property. However, CIRM will ensure that communication of developments is made public through academic, industry and public policy channels, including partner associations, such as ARM.

5. Sources of Funding

The development of the CIRM Pre-competitive R&D Program can be carried out now using existing internal CIRM professional staff time and effort.

All CIRM Pre-competitive R&D Program project execution will be co-funded by CIRM and its range of collaborators.

Funding for pre-competitive R&D will vary by project topic. However, there is interest in co-funding of specific pre-competitive topics from multiple sources. Moreover, securing financial commitments for these projects will be less difficult than for pre-clinical and clinical trials projects. Illustrative sources of funding include:

- **Biopharmaceutical Corporations**: Development as well as production units have expressed interest and are likely co-funders for issues where the outcomes ease or resolve market entry challenges. There is a preference for breakthroughs on technical challenges and production, including characterization and quality assurance.
- **Foundations**: Disease-focused foundations are concerned with issues that might impede or constrain how therapies affecting their patient population are developed (technical) and how delivery may be structured and financed (reimbursement). Family foundations may have broader interests in collaborative research on new approaches to healthcare finance.
- **Health Insurance & Reinsurance Corporations**: There is direct interest on the part of healthcare insurance in breakthroughs that minimize the costs of therapy development and delivery as well as in reimbursement. As noted earlier, the reinsurance industry may

soon be ready to explore multiple ways of reducing financial risks and managing costs while fostering investment in regenerative medicine.

- **Federal Agencies**: Government agencies have often matched funds when the private sector or other state governments raise a fair share. In the case of regenerative medicine federal agencies, such as NIH and NIST (technical) and HHS/AHRQ (financial) may find pre-competitive projects worthy of co-support.

CIRM share of expenditures for a given project are recommended to be large enough to attract co-funders, perhaps up to 25% of a given project's budget. Levels of co-funding may vary across projects. The objective here is convergence and leverage—creating a focal point for collaborative actions that will enhance progress of regenerative medicine to market.

To run this program CIRM can charge projects for CIRM's internal program management services. This can enable the program operations to become at least partially if not fully self-funding over time. However, operational costs should be limited at the start of this program.

The costs of anticipated pre-competitive projects will vary, but can range from $250,000 for analytic or 'white paper studies' on regulatory or finance issues to much larger amounts for collaborative projects in which a new technology is developed or a reimbursement model is tested in the field.

Stakeholder Comments on
Readiness to Participate in A CIRM Pre-Competitive R&D Program

"Ready to join in collaborative projects with a host, universities, contract manufacturers and other biotech and pharmaceutical firms." – Industry

"No specific terms needed for us to participate. Usually, as part of a collaborative, we would like first right of negotiation and freedom to use intellectual property arising from a pre-competitive project." – Industry

"Ready to explore pre-competitive projects with CIRM, foundations and pharmaceuticals." – Patient Advocacy Foundation

"Very ready to explore specific areas for collaboration on pre-competitive R&D with CIRM, foundations and pharmaceutical industry as well as FDA, and other agencies." – Patient Advocacy Foundation

"Open to exploring this, where there is relevance to our broader needs." – Patient Advocacy Foundation

"This foundation has been active in this area [biomarkers] and participates in a collaborative project with 14 partners, primarily pharmaceutical companies." – Patient Advocacy Foundation

CIRM Strategic Roadmap for Continued Innovation: Strategic Roadmap

"We care about collaboration. This foundation just had a three-day consortium meeting on spinal chord issues." – Patient Advocacy Foundation

6. Sequence for Development/Timing

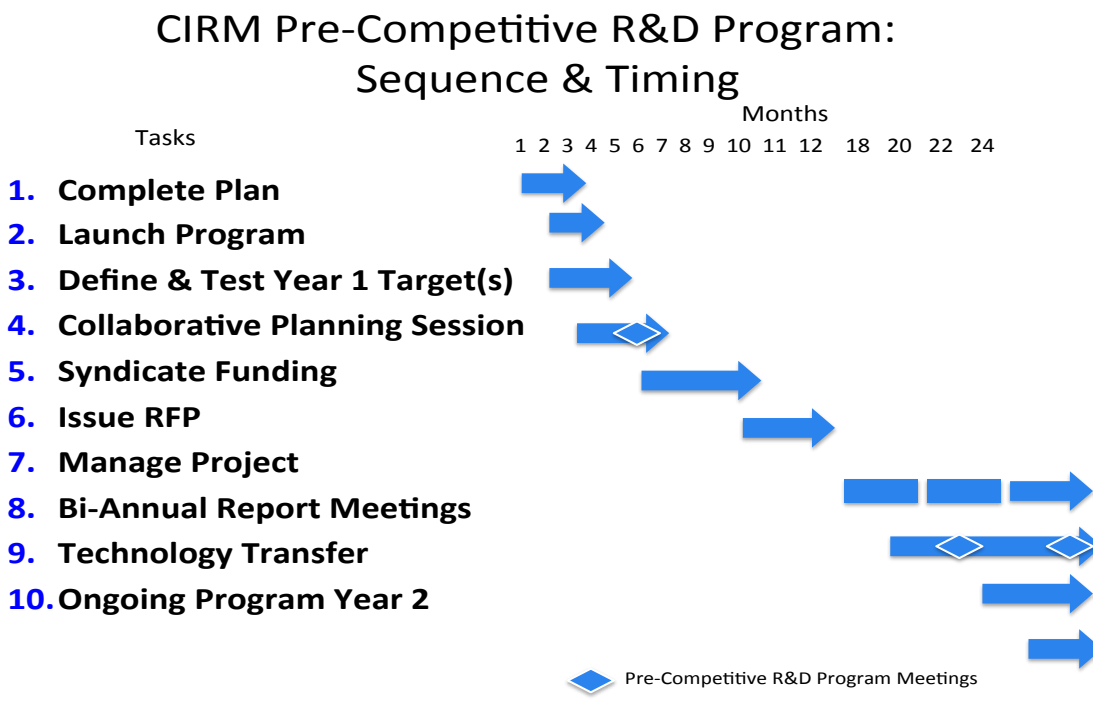
The development and timing of the CIRM Pre-Competitive R&D Program can be implemented in straightforward steps, corresponding with the Organization and Operations features described above and described in figure IV.2 below:

1. **Complete Plan**: Complete an internal plan for this program based on existing materials and further polling and meetings with biopharmaceutical industry and/or health insurance and healthcare finance industry. This plan should define program objectives, structure and collaborative operations and strategic relationships, such as with ARM as well as other associations. (Months 1-3)
2. **Launch Program**: Announce the new CIRM Pre-Competitive R&D Program via CIRM website, newsletters and generally invite target industries and agencies to participate, with CIRM as the coordinating anchor. (Months 2-4)
3. **Define & Test Year 1 Targets**: CIRM will survey/poll industry on strategic pre-competitive RM issues and then invite biopharmaceutical companies, foundations, health insurance and reinsurance firms to participate in planning next steps, with CIRM acting as anchor and coordinator. (Months 2-5)
4. **Collaborative Planning Session**: Invite, confirm and facilitate one or more collaborative work sessions with biopharmaceutical firms, foundations, health insurance, and reinsurance as well as federal and state government to prioritize themes for co-funded projects, including specifying collaborative roles for participants. (Months 3-6)
5. **Syndicate Funding**: Guided by the priorities set in the collaborative planning sessions follow-up with the prospective co-funders associated with key themes to secure commitments to one or more collaborative projects with CIRM match and ongoing management. (Months 5-9)
6. **Announce First Project/Issue RFP**: On securing commitments to fund the first, pilot Pre-Competitive R&D Project, prepare an RFP with input from co-funders that defines objectives and key roles, then issue the RFP for bids from universities, institutes, laboratories and private firms, that will then be screened and selected. (Month 9-12)
7. **Manage Project**: CIRM team members, working with a co-sponsor and external expert advisory board for that first project, will oversee project execution, including

coordinating collaborative roles of participating firms along with contracted providers. The typical project will be carried out between six months and a year. (Months 12-24)

8. **Bi-Annual Report Meetings**: CIRM will manage this first project and coordinate participant roles against agreed upon milestones. CIRM will provide quarterly updates and host bi-annual meetings to review findings and implications. The year-end completion can be timed to correspond with a variety of industry or policy conferences and forums, where appropriate. (Months 18-24)
9. **Technology Transfer**: CIRM will work with co-funders and association partners to define and disseminate the first pre-competitive R&D project findings according to agreements formed at program launch. Content will be presented to and shared with industry and policy forums or made available via licensing agreements. (Months 24-30)
10. **Ongoing Program—Year 2**: CIRM will work with existing and new co-funders to prioritize and syndicate funding for one or more strategic pre-competitive projects, in cases continuing work in a given challenge area or other priority themes. (Months 24+)

Figure IV.2



7. **Examples: Pre-Competitive R&D**

CIRM Strategic Roadmap for Continued Innovation: Strategic Roadmap

Pre-Competitive R&D has been permitted and encouraged under federal law since the early-1980s. Initiation of pre-competitive R&D can come from the public or private sector. There are many forms of pre-competitive R&D, but the core driver usually is a shared need that cannot be cost-effectively addressed by any single company or institution. Pre-competitive R&D initiatives have been carried out by industries together and with government for many years. Examples range from microelectronics (SEMATECH) to automobiles (USCAR) to pharmaceuticals. The range of pre-competitive initiatives in pharmaceuticals has included: genomic mapping and matching of similarities among humans, tropical disease diagnostics and treatment, genetic markers for drug safety, biomarkers for disease and drug development, pre-clinical and translational markers, protein structure to enable drug design, prediction of safety and efficiency).

The private sector recognizes that pre-competitive R&D consortia are key to breaking down barriers to drug discovery and development. They view consortia as a means for leveraging capabilities beyond what one company can do through pooling of resources. This can be strictly financial, but can also include pooling of samples and data collected from clinical trials across pharmaceutical companies and academic institutions, enhanced access to diverse intellectual capacities, all leading to new enabling processes.

Consortium: As the pharmaceutical industry faces challenges in building its product pipeline they have become more active in seeking and participating in pre-competitive R&D programs. The 10 largest pharmaceutical companies spend approximately $67.3 B a year on research. To enhance their productivity they have become more active in outsourcing R&D to universities. This has led to more multi-pharmaceutical company (as well as foundation) funding of early translational as well as later stage translational research across multiple centers of excellence in areas of interest. Among these consortia are the SNP Consortium, WIPO Re:Search, Adverse Event Consortium, the Biomarkers Consortium, the Predictive Safety Testing Consortium, the Structure Genomics Consortium, the Coalition Against Major Diseases, the Innovative Medicines Initiative and the Human Blood Plasma Consortium.

Alliances: There are also many new lateral pre-competitive initiatives where corporations create specific structure to share certain types of data or tools, such as information systems, to enhance identifying of potentially valuable molecules. Pfizer has shared software and standards for managing data on complex molecules on a pre-competitive basis with GSK, Roche and Bristol-Myers Squibb. The TranSMART Foundation, for example, was started by Johnson & Johnson to provide a platform warehouse of molecular, phenotypic and related data that scientists can search and study correlations between genetic data and information from clinical trials—and is actively used by pharmaceutical companies such as Roche and Sangamo. This

collaborative has also worked with another collaborative group, the Pistoia Alliance of multiple pharmaceutical firms focusing on data that permits uses to carry out more efficient drug discovery.

Downstream Collaborations: Precompetitive efforts like TransCelerate BioPharma tries and make the clinical trial process more efficient, for example, standardizing various aspects of the process. They have 10 initial members whose research heads are on the TransCelerate Board and they included the FDA in their formative stage. They have carried out five initial projects, all on enhancing clinical trials (e.g. recording of data).

Natural Step to Resolving Barriers: Pre-competitive initiatives today are growing in number and are organized around specific challenges shared by industry, government and foundations. Pre-competitive initiatives are becoming a logical way to address challenges facing emerging markets in an era of often distributed or decentralized capabilities. Further examples of ongoing pre-competitive initiatives include:

- Regenerative Medicine Consortium (RMC)
- Biomarkers Consortium (launched by NIH)
- Diabetes Genetics Initiative
- Electronic Patient-Reported Outcome Consortium
- Translation of Nanotechnology in Cancer (National Cancer Institute)
- Accelerating Innovation Research (National Science Foundation)
- Coalition for Accelerating Standards and Therapies
- Critical Path Institute
- Clinical Data Interchange Standards Consortium

IV. CONCLUSIONS & NEXT STEPS

1. CIRM Implementation: Integrated Action Path

CIRM has achieved an important goal. That goal is advancing regenerative medicine from basic science research to clinical trials. CIRM now has a portfolio of over 90 projects in perhaps the largest concentration of cohesively managed regenerative medicine research and development in the US. CIRM has constructively grown a pipeline of research that should yield an array of candidates for therapies across over 15 diseases. CIRM has funding commitments in place for ongoing projects and has a balance of approximately $650 million in unallocated funds with which to finance the continued progress of ongoing and new projects and ensure that these projects are not only completed, but achieve investment readiness. For this to take place three needs must be addressed:

1. **Raising New Non-Taxpayer Funds**: First, there is need for funding to continue and expand support of early translational stage projects through pre-clinical trials and to ensure that as many as possible later stage translational projects successfully complete at least phases 1 and ideally up to phase 2 of clinical trials. As CIRM has current limits on funds available through Proposition 71, new means of securing funds are required. To that end, given the rising interest in regenerative medicine's potential for specific diseases there is a strong argument for CIRM to leverage its funds through public private partnerships with foundations, pharmaceutical firms, and donors.
2. **Ensuring Projects Reach Product Readiness**: Second, there is a need to ensure that all of these projects successfully manage the transition from scientific laboratory to clinical and investment readiness. Every project needs 'hands-on' guidance and technical assistance to move towards a target outcome, beyond the laboratory. Formalized 'accelerator' support is necessary so that expenditures made to CIRM funded projects lead to strong IND candidates, successful completion of clinical trials phase 1 and 2, leading to valid candidate therapies that may be licensed by pharmaceutical firms or invested in as new regenerative medicine ventures.
3. **Solving Shared Needs to Enable Market Growth**: Third, given that the field of regenerative medicine is just emerging there are not as yet formally established tools, processes and standards for product development and production, nor established financial models for therapy delivery and reimbursement. For this reason there is a need for collaboration to prepare enabling solutions. Pre-competitive R&D projects focused on shared 'platform' needs will play a strategic role in generating breakthroughs in tools

and processes and their delivery that will help regenerative medicine move forward as a transformative field of medicine.

Importance of an Integrated Approach: There is an argument for individually taking action on each of these challenges through the recommendations that have been presented in this White Paper. However, there is an even stronger case for these recommended actions to be viewed as an integrated, concerted, CIRM strategy.

Raising new sources of funds for the current and future pipeline of CIRM projects through partnering is vital to optimizing CIRM's mission to bring regenerative medicine to the clinic and patients. However, ensuring that university and private sector projects funded by CIRM are able to prepare their scientific results in a manner that is replicable and focused on tangible product outcomes is essential to paving the way out of the laboratory to production and delivery in the clinic for patients. This continuity of due diligence and management is key to achieving the end value for consumers for which CIRM was founded. Finally, if the cross-cutting challenges constraining progress of regenerative medicine innovations to product readiness and market acceptance and use are not resolved in a timely way, breakthrough therapies may never reach the clinic and patients. Patient advocacy foundations, pharmaceutical firms and the healthcare finance industry all recognize that opening new doors means building key infrastructure first.

For these connected reasons, CIRM should consider pursuing the three recommended new directions as an integrated package that has shared understanding and interest across all likely participants and co-sponsors. An integrated approach to partnership funding, acceleration of project readiness, and pre-competitive problem solving will be viewed by the majority of collaborators as logical and attractive to achieving CIRM's goals and those of the future of regenerative medicine.

2. Pilots: Proposed Planning and Launch

The good news is that CIRM has already been active to a limited degree in each of the three areas for recommended action. While more systematic effort and management is required, the executive team within CIRM understands the objectives of the three recommended actions and can launch pilot initiatives to take them to the next stage of implementation and operation.

CIRM Public-Private Funding Partnership for Pre-Clinical & Clinical Trials: CIRM's current Strategic Partnership Program has provided matching funds to grantees that secure private sector funding for their projects. CIRM has just made commitments to its second round of these projects.

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To grow funding partnerships to a larger number of projects and greater amount of funding CIRM should announce the development of a pilot CIRM Public-Private Funding Partnership. This announcement should be followed by CIRM's identifying prospective partners and inviting them to participate in planning the partnership and subsequently launching its first round of activity. Participants would review, select and agree to fund a set of CIRM approved projects. The strategic and systematic outreach to disease foundations, family foundations, pharmaceutical firms, and possibly healthcare finance companies is key. Presenting well-prepared projects that have had suitable due diligence is essential (see CIRM Accelerator below). Organizing discussions with potential partners by disease theme interest is fundamental to obtaining commitments.

The preparation and execution of the partnership program should result in several multi-sponsor co-funding agreements that CIRM coordinates. This pilot phase of outreach, convening partners, and collaborative screening and selection of CIRM approved projects can be continued on this coordinative basis or scaled up to a more formal partnership structure based on interest expressed and the efficiency of CIRM management of this activity.

CIRM Accelerator: CIRM has had a well-managed process for its RFA process that has been enhanced over time. The Grants Working Group (GWG) and CDAP have ensured the scientific merit and progress of funded projects. An increased emphasis on the downstream therapeutic outcome, product readiness and match to potential partners has been introduced in the past two years.

CIRM management, the External Advisory Panel (EAP) and the Scientific Advisory Board (SAB) and professionals associated with CDAP have agreed that providing more intensive, continuous guidance and advisory services to each CIRM project is needed. While the emphasis on the need for hands on management for projects at the early translational stage are different, their needs form a continuous set of requirements that CIRM is able to address in two ways that can be organized and delivered more systematically.

A pilot program that will deliver acceleration services to early translational and later translational (disease team) projects can be launched by CIRM by taking three steps. First, by defining and setting in place formal centralized services for management of regulatory, process and production needs of projects, as is already done on an as-needed basis. Second, by building from the single CDAP model to structure a formal Accelerator team of professionals (on retainer) who will now meet quarterly with a select set of three to four projects and maintain continuity of advice and technical guidance on projects. Third, build relationships with the newly launched Alpha Clinics (five centers), as well as existing accelerators associated with universities

and/or where appropriate, private venture-backed accelerators and early-stage venture firms to work with the CIRM Accelerator and their projects.

The pilot phase will best focus on one CIRM Accelerator team working with three to five projects that will benefit most from guidance and technical support. These projects can be later stage projects that have been prioritized. However, having one or more earlier stage projects that can be assisted to follow the 'right path' for downstream readiness.

Evaluation of the progress of projects receiving acceleration services as well as the experience of the first full-scale CIRM Accelerator team working in conjunction with centralized CIRM staff and their services will determine the value and challenges of scaling up acceleration to serve all CIRM projects.

Pre-Competitive R&D Program: CIRM was formed because there was an absence of support for stem cell research and California citizens believe that this new form of developing cures for health care problems has value to those in need. CIRM was launched recognizing that cross-cutting needs needed to be addressed to enable this field to advance. CIRM then funded preparation of a science workforce to work in regenerative medicine. They funded the establishment of new R&D facilities at 12 universities across California to serve as a focal point for innovation in this field. And, CIRM funded research and development projects leading to the formation of new tools and processes needed to enable research in this new area of science. These efforts have paid off with new talent, new tools, and new start-ups. CIRM recently led a workshop co-sponsored with ARM and the UK Catapult and the biopharmaceutical industry to identify shared technical issues in production, product characterization and imaging.

Bringing regenerative medicine therapies to market is still at its earliest stage. There are still many unresolved technical as well as economic challenges facing development. Because these challenges are shared across those who will either bring regenerative medicine therapies to market or those financing the care from regenerative medicine, there is a strong reason for crafting solutions collaboratively. To that end, CIRM should build on its clear historic leadership in the field and use that platform to define a broad pre-competitive R&D program that it will anchor, organize, manage and jointly fund with partners.

With this broader mission CIRM can then reach out to the biopharmaceutical industry with ARM and organize a pilot pre-competitive project that could be the first of a continuing series. Concurrently, or following this first project, a similar effort could be made with family foundations concerned with healthcare, the healthcare insurance industry and healthcare finance agencies to organize first collaborative steps in examining downstream financial

business models for regenerative medicine therapies. These collaborative funded (multi-client or syndicated alliances or consortia) efforts anchored by CIRM should become self-supporting, with a small core management team internally and research and development outsourced to universities and private entities using an RFP process.

Ideally, CIRM should consistently raise awareness of pre-competitive challenges and share the outcomes of initial projects at major industry and public private forums. Further, by highlighting the role of co-funders, many of whom may also be participants in the Public-Private Funding Partnership, CIRM will be able to grow and sustain strong public visibility as the continuing national leader on the regenerative medicine front.

3. Scale-up: Progress to Full Operations

As individual programs or part of a strategic integrated set of actions CIRM should be prepared to learn from, adjust and grow each of the three recommended actions over time continuing to full-scale operations. As the pilot phase of these initiatives will not require new organizational structures or require any new CIRM funding, the progress of these programs will depend primarily on commitment of CIRM management and staff and response of collaborating partners. This commitment by CIRM will best be guided by having well-crafted business plans for each of these new activities in hand.

Of the three recommended actions, the eventual scale-up Public-Private Funding Partnership might require further organizational development steps by CIRM and possibly others. For instance, CIRM may need to manage internal donor advisory accounts for accepting contributions for specific collaboratively funded projects under terms acceptable to co-funding partners—such as disease foundations, pharmaceutical firms or individual donors.

Alternatively, if greater autonomy and self-sufficiency by the Public-Private Funding Partnership is sought, launching a foundation might be appropriate. That step, whose merits would be determined in the course of evaluating the pilot, could lead to the foundation being launched with a lean team that would convene co-funders, place their grants in agreed upon projects through disease-theme program accounts, and negotiate terms for any returns to sponsors from projects. As noted earlier, these returns could include capped royalties to offset funding by foundation, right of first negotiation for pharmaceutical firm co-funders, or even equity positions for the foundation itself. This could enable possible ‘evergreen’ funding of regenerative medicine pre-clinical and clinical trials by the foundation.

4. **Monitor: Progress in Implementation and Performance**

Milestones and metrics for the development as well as the operation of each of the three recommendations can be set in place to ensure CIRM and ICOC can track progress and performance. The milestones and metrics will be specific to each new activity. While these milestones should be developed during the planning of the three pilots, there are key metrics to consider:

- **Public-Private Funding Partnership Metrics**
    - **Input—Engaged Stakeholders**: This is a key measure of the probability of funding success. Interviews conducted with stakeholders showed that potential funding partners want to play an active role in shaping the public-private funding partnership directions and to collaborate in making funding decisions. The majority of possible co-funders do not want to simply be asked for funds for a specific project.
    - **Output—Aggregate Funding by Theme**: Levels of funding raised per project or by theme area, or by stage of development are important, emphasizing attainment of goals of funding target pre-clinical stages or, perhaps more clearly, phases 1 and 2 of clinical trials.
- **CIRM Accelerator Metrics**
    - **Input—Service Package for Projects**: Confirmation of core CIRM services and committed members to a given Accelerator Team and for a specific set of projects are key inputs, including agreements with the Alpha Clinics and with specific campus associated acceleration services to work with specific projects, as requested.
    - **Output—Fulfillment of Development Milestones**: CIRM sponsored project completion of milestones agreed to in their grant and their agreement with the CIRM Accelerator based on a core set of step-wise building blocks, from replicable laboratory procedures to completion of a development plan, followed by specific pre-commercialization outcomes fulfilling market readiness.
- **Pre-Competitive R&D Program Metrics**
    - **Input—Engagement of Impacted Providers**: Engagement of prospective partners by theme area in defining target pre-competitive challenges on which participants are willing to collaborate and co-fund. In contrast to raising funds for pre-clinical and clinical trials, where interest is likely to be by theme or disease, the focus here is on shared problems or uncertainties. Therefore,

success of this program will depend on building a constituency of partners—a group, syndicate, alliance or consortia—around each crosscutting technical or economic theme. That is why CIRM's recent work with ARM is a good start and why continued outreach around healthcare finance to insurers and healthcare finance agencies will be important to building future pre-competitive projects.

- **Output—Delivery of Enabling Solutions**: For each CIRM organized and managed pre-competitive project there will be a set of 'outcomes' agreed upon by co-funders. Results sought after will be defined on a project-by-project basis. Deliverables—such as publications on new technical process or financial models, intellectual property for new technology—will be intermediate outcomes with the longer-term target being the diffusion and adoption of these breakthroughs by the biopharmaceutical industry, healthcare services, healthcare finance industry, agencies or federal regulators being the ultimate outcome.

4. Outcome: Continued & Expanded CIRM Project Flow to Clinic and Patient

Where do these recommendations leave CIRM?

CIRM was established to develop regenerative medicine therapies that cure health problems. CIRM has achieved important steps along that path, having funded a portfolio of projects that have progressed from basic research to early translational research to later stage translational research.

Now, to maximize the number of projects that develop INDs, complete phase 1 and 2 clinical trials and are investment ready CIRM has the opportunity to leverage funding under Proposition 71. The good news is that this can be achieved using its existing CIRM resources, expertise and experience in new ways.

CIRM can harness its scale of activity as a funding source, its knowledge of this emerging field, and applying its objectivity and integrity as a catalyst and organizer. In doing so CIRM can bring new non-taxpayer funding to projects, ensure that projects are accelerated to market readiness, and enable the marketplace into which new solutions are introduced is ready to produce and deliver new therapies. The recommendations proposed here are a natural extension of the intuitive and empirical needs for bringing regenerative medicine to California's citizens and the world.

APPENDIX A: STAKEHOLDER INTERVIEWS

INVESTMENT

1.	Nessan Bermingham, PhD	Partner	Atlas Ventures
2.	George Bickerstaff	MD	M.M. Dillon
3.	Steve Burrill	CEO	Burrill & Company
4.	Jill Carroll	Partner	SR One (GSK funded VC)
5.	Allan Emkin	Mging Dir.	Pension Consulting Alliance
6.	Corey Goodman, PhD	Partner	VenBio
7.	Regis Kelly, PhD	Director	QB3 & Mission Bay Capital
8.	Bob Klein	President	Robert Klein Financial Corp.
9.	Ed Penhout, PhD	Partner	Alta Ventures
10.	Bill Rutter, PhD	CEO	Synergenics
11.	Steve Westly	CEO/Partner	The Westly Group

INDUSTRY

1.	Sean Bohen, MD, Phd	VP	Genentech
2.	Paul Cleveland, JD	Director	Sangamo BioSciences (Scheduled)
3.	Jason Gardener, PhD	VP, R&D	GSK VP & HD-RM Discovery
4.	Kieran Murphy& Ger Brophy	President/VP	GE Healthcare Life Science Div.
5.	Marcus Schindler, PhD	VP	Astra-Zeneca, CVMD
6.	John Walker, PhD	CEO	Neuraltis Pharmaceuticals
7.	Tachi Yamada, PhD	CSO/R&D	Takeda Corporation
8.	Phil Vanek, PhD	GM	GE Healthcare Cell BioProcessing

PATIENT ADVOCACY FOUNDATIONS

1.	Tim Bateman	Dir./CEO.	American Heart Association
2.	Jacqueline Bresnahan, PhD	Fmr. Chair Sci.	C&D Reeve Foundation
3.	Susan Howley, PhD	EVP	C&D Reeve Foundation
4.	Richard Insel, MD	Chief Sci. Off	JDR Foundation
5.	Thomas Peters, PhD	CEO	Marin Community Foundation
6.	Dr. Todd Sherer, PhD	CEO	Michael J. Fox Foundation

ASSOCIATIONS/ACADEMICS

1.	Naomi Aronson, PhD	Sr. VP	Tech Eval, BCBS, IL
2.	Raphael Hofstein, PhD	CEO	MaRS (Ontario, Canada)
3.	Gail Maderas	CEO	BayBio
4.	Philip Pizzo, MD	Former Dean	Stanford Medical School
5.	Cathy Prescott, PhD	Partner	BioLatris (re-insurance UK)
6.	Regina Rabinovich, MD	Professor	Harvard School of Public Health
7.	Morrie Ruffin	CEO	ARM