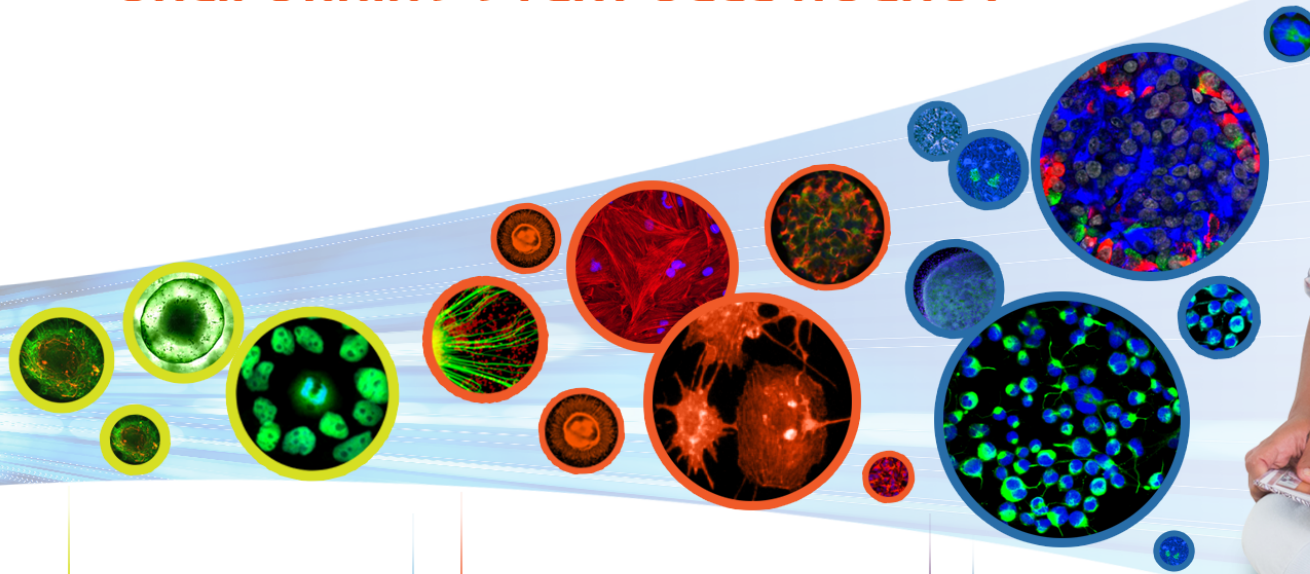


Dec. 17, 2015

CIRM

CALIFORNIA'S STEM CELL AGENCY



DISCOVERY

TRANSLATIONAL

CLINICAL

EDUCATION

INFRASTRUCTURE

Accelerating Center and Translating Center Concept Proposals

Maria T. Millan, M.D.
Presentation to CIRM's ICOC

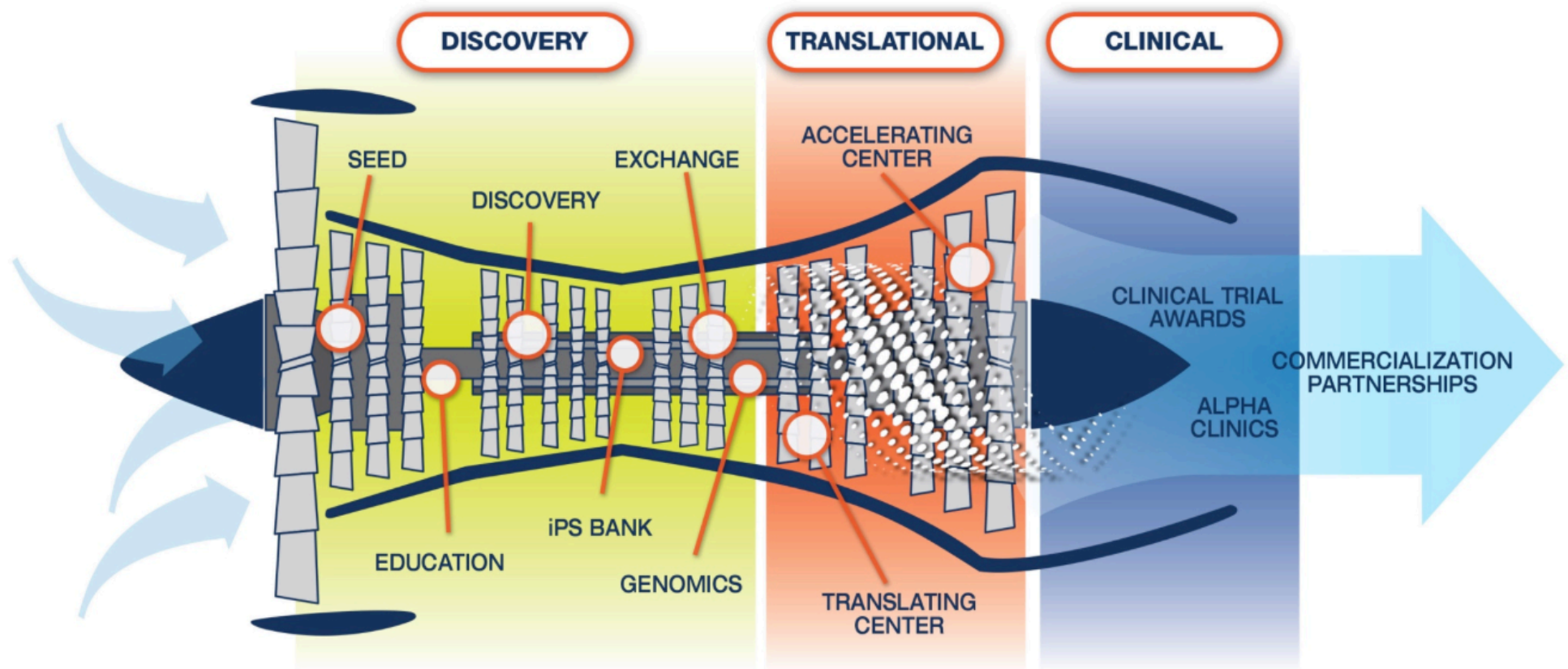
Background:

- **The Need:** CIRM's pipeline is maturing, with growing numbers of late translational and clinical stage projects, but many investigators don't have extensive experience initiating FDA regulated clinical trials
- **The Opportunity:** To significantly decrease the time it takes to bring stem cell therapy development projects from the translational to the clinical stage
- **The Solution:** CIRM's Infrastructure Programs to strategically address the unique challenges associated with the translational- and early clinical stages of stem cell research

CIRM's Infrastructure Programs: Address Challenges & Create Opportunity

- **Challenges:**
 - Process development of cGMP compliant manufacturing processes
 - Efficient assembly of preclinical datasets
 - Regulatory path uncertainty
 - Efficiencies in clinical trials with stem cell products
- **Opportunities with Infrastructure Programs:**
 - Focused expertise to address the above challenges
 - Aggregated experience will allow continual improvements and efficiencies
 - “One stop shop” for stakeholders- patients, regulators, researchers and trial sponsors

CIRM Infrastructure Programs: To Accelerate Translational and Clinical Research



The Alpha Clinic Network: CIRM's clinical trial infrastructure program



Goal: To accelerate the development and delivery of stem cell therapies to patients by leveraging existing assets to form an efficient, scalable and sustainable clinical network well positioned to attract and conduct high quality stem cell trials

Alpha Clinics Network: Year 1 Update

- Approved for \$24M of CIRM funds in October 2014
- Launched February-April 2015
- Steering committee & working groups formed
- Currently supports 14 active clinical trials - cancer, diabetes, heart disease, HIV, pediatric disease, CNS, eye disease

<https://www.cirm.ca.gov/patients/alpha-clinics-network/alpha-clinics-trials>

- Building a robust pipeline of new trials
- Developing Accelerating and Value Add Resources (AVARs)

Accelerating and Value Add Resources (AVARs)

- Accelerate IRB process (IRB Reliance)
- Improve patient informed consent process and trial recruitment and enrollment (UCRex)
- Capture and analyze data and cost/performance metrics across the Network (RedCaP)
- Share operational knowledge to improve clinical trial operations and to enhance patient experience (nursing competencies and best practices)
- Optimize the utilization and value of AVARs across the Network and throughout California (via the Accelerating Center)

CIRM Accelerating Center Concept Proposal

Accelerating Center Goal:

- To speed the progression of therapeutic candidates from the translational stage, through pre-clinical development and to clinical trials
- To accelerate the efficient conduct of clinical trials while maintaining the highest degree of rigor and quality

Accelerating Center Major Activities

- Customized support for stem cell clinical trials:
 - Regulatory affairs
 - Clinical trial management
 - Data management
- Actively work with the FDA to efficiently move stem cell products through the regulatory path to the clinics
- Coordinate with the Alpha Clinics Network to scale up/scale out AVARs to support stem cell clinical trials throughout the state and beyond
- Create a sustainable resource for the growing pipeline of stem cell translational and clinical programs

Accelerating Center – Regulatory Affairs

Play a central role for FDA interactions and ongoing sponsor and site regulatory support:

- Planning and consultative services for regulatory strategy
- Compilation and submission of regulatory applications (IND)
- Management of regulatory requirements for clinical trials

Accelerating Center-Clinical Trial Support

Clinical trial planning, operations and management for the efficient conduct of high quality clinical trials:

- Site selection, training and qualification
- Support site patient recruitment and enrollment
- Management and logistical support across multiple clinical sites, in coordination with vendors and third party organizations

Accelerating Center-Data Management

Data management systems, biostatistics and analytics:

- Provide efficient and robust systems to support clinical trial data capture and analysis
- Enable researchers and the stem cell community to apply aggregated knowledge to inform regulatory and cost considerations for delivering cell therapeutics to patients

Accelerating Center Timeline & Budget

Proposed budget \$15 million

| | |
|-----------------------------------|---|
| Applications Due | 1H2016 |
| Grants Working Group (GWG) Review | 1H2016 |
| ICOC Review and Approval | 2H2016 |
| Award Start | Must start within 45 days of award approval |

ICOC Motion

CIRM requests that the ICOC approve the concept plan for the CIRM Accelerating Center, with a budget authorization of up to \$15 million to fund a single award over 5 years.

CIRM Translating Center Concept

Translating Center Goal:

- To speed the progression of therapeutic candidates from the translational stage, through pre-clinical development and to clinical trials
- To efficiently conduct and manage preclinical activities that support regulatory filings

Translating Center Major Activities

The Translating Center will provide core services to enable the issuance of an FDA Investigational New Drug (IND) application by supporting:

- Cell Process- and Manufacturing Plan Development
- IND-enabling safety/toxicity studies
- IND preparation and submission (in coordination with the Accelerating Center)

Translating Center- Process Development and Manufacturing

- Optimize and develop cGMP compliant manufacturing processes
- Assist the Sponsor in addressing the Chemistry, Manufacturing and Controls (CMC) IND requirements
- Quality systems and Assay Development
- Technology transfer and scale-up/scale out plans

Translating Center – Preclinical Studies and IND Support

- Assemble preclinical datasets for IND submission, in coordination with:
 - Sponsor/investigator for preclinical datasets
 - External contract research organizations for safety/toxicity, bio-distribution and other outsourced animal studies
 - Internal team for process development and product characterization datasets
- Coordinate with the Accelerating Center to support IND compilation and submission

Translating Center Timeline & Budget

Proposed budget of up to \$15 million

| | |
|-----------------------------------|---|
| Applications Due | 2016 |
| Grants Working Group (GWG) Review | 2016 |
| ICOC Review and Approval | 2016 |
| Award Start | Must start within 45 days of award approval |

ICOC Motion

CIRM requests that the ICOC approve the concept plan for the CIRM Translating Center, with budget authorization of up to \$15 million to fund a single award over 5 years.