November 2015

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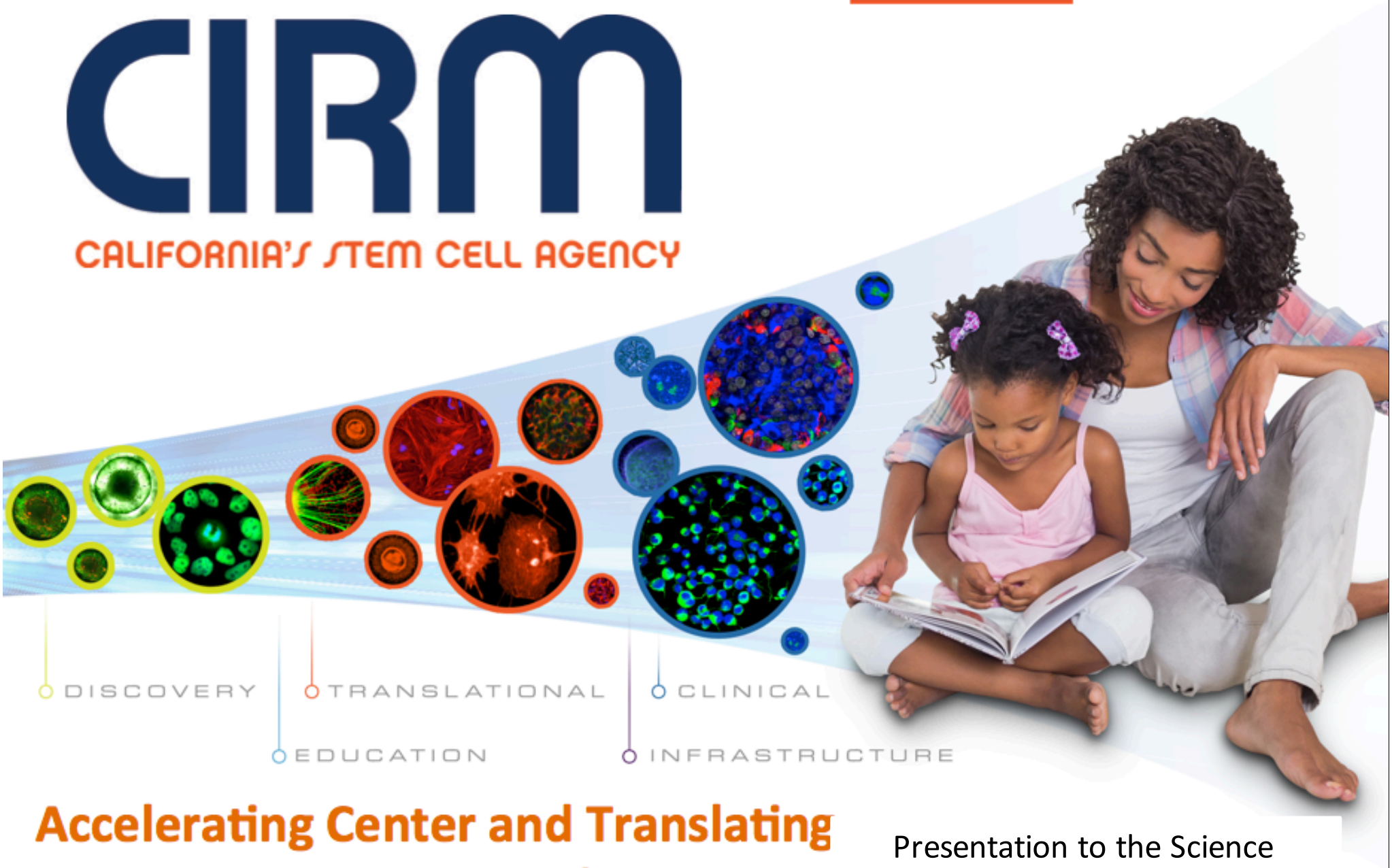

Accelerating Center and Translating Center Concept Proposals

Presentation to the Science Subcommittee of CIRM's ICOC

Background:

- CIRM's pipeline is maturing, with growing numbers of late preclinical- and clinical stage projects
- Challenge Areas:
  - ✓ Process development of cGMP compliant manufacturing processes
  - ✓ Efficient assembly of preclinical datasets
  - ✓ Regulatory path uncertainty
  - ✓ Efficiencies in clinical trials with stem cell therapeutics
- Advantages of Core Infrastructure to address these challenges:
  - Aggregated experience and datasets
  - "one stop shop" for stakeholders in stem cell therapies:
    - ✓ Patients
    - ✓ Regulators
    - ✓ Developers/sponsors

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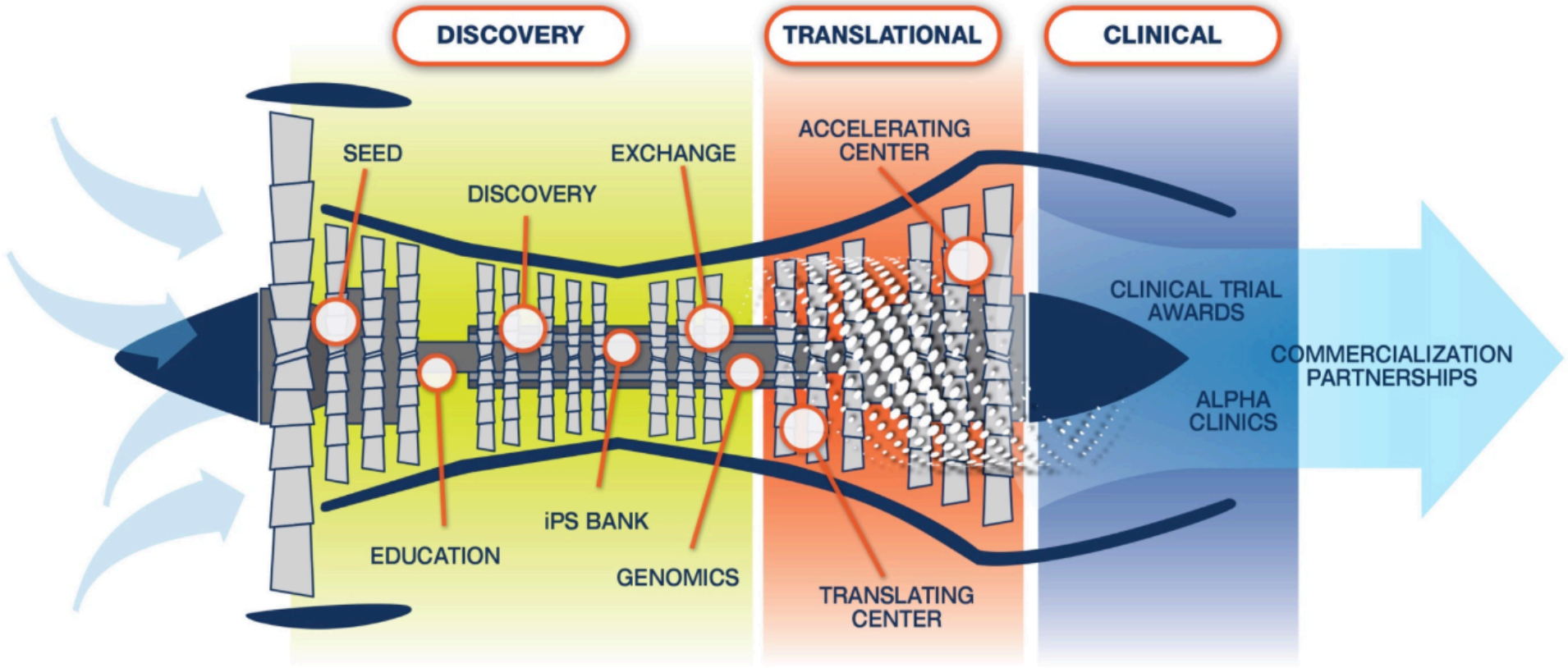
Translational & Clinical Infrastructure Push Operational Excellence



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Alpha Stem Cell Clinic Network Update

Alpha Stem Cell Clinic 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

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Network Sites Operational in Year 1

City of Hope

ACT-I Alpha Clinic for Cell Therapy and Innovation

UC San Diego Health System

CIRM Alpha Stem Cell Clinics Network

UCLA UCI Alpha Stem Cell Clinic

CIRM California's Stem Cell Agency

Alpha Clinics Network Activities (Year 1)

- ICOC approved $24M funding in October 2014
- 3 Alpha Clinics launched February-April 2015
- Currently supporting 14 clinical trials
  cancer, diabetes, heart disease, HIV, pediatric disease, CNS, eye
  https://www.cirm.ca.gov/patients/alpha-clinics-network/alpha-clinics-trials
- Robust pipeline of new trials
- Steering Committee & Working Groups
- Accelerating and Value Add Resources (AVARs)

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Accelerating and Value Add Resources (AVARs)

- Accelerate IRB process (IRB Reliance)
- Improve patient informed consent process and trial recruitment (UCRex) and enrollment
- Utilize and refine data management tools (RedCaP) to enable data capture and cost/performance metrics across the Network
- Share operational knowledge to improve clinical trial operations and to enhance patient experience (nursing competencies and best practices)

The formation of the Accelerating Center would enable the Network to most efficiently operationalize the AVARs across the Alpha Clinics Network and would enable other stem cell clinical sites throughout California.

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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 rigor and quality

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Accelerating Center Major Activities

- Support stem cell clinical trials by providing customized support in:
  - ✓ Regulatory affairs
  - ✓ Clinical trial support
  - ✓ Data management
- Work with the Translating Center to accelerate the regulatory path for stem cell therapeutics to the clinics
- Coordinate with the Alpha Clinics Network to scale up/scale out accelerating and value add resources (AVARs) to more broadly 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

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Accelerating Center-Regulatory Affairs

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

  - ✓ Planning and consultative services for activities necessary to obtain regulatory approval for a clinical trial
  - ✓ Compilation and submission of regulatory applications (IND)
  - ✓ Management of regulatory requirements for clinical trials

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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

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Accelerating Center-Data Management

- Data management systems, biostatistics and analytics:
  - ✓ Provide the efficient and robust systems to support clinical trial data capture and analysis
  - ✓ Enable researchers and the stem cell community to optimally leverage the cumulative and aggregated knowledge to inform the best path forward for delivering cell therapeutics to patients

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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

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Science Subcommittee Motion

CIRM requests that the Science Subcommittee recommend Board approval of 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.

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ALPHA STEM CELL CLINICS NETWORK

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 accelerate the efficient conduct of preclinical activities that will result in successful assembly of regulatory packages to enter clinical testing

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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 Development and Manufacturing
- IND-enabling safety/toxicity studies
- IND filings in coordination with the Accelerating Center

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Translating Center-
Process Development and Manufacturing

- Planning and consultative services for assembling the necessary Chemistry, Manufacturing and Controls (CMC) requirements for cell therapy products
- Process optimization and development for the production of the cell therapy product that ensure compliance with FDA cGMP requirements
- Quality systems and Assay Development
- Technology transfer and scale-up/scale out plans

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Translating Center – Preclinical Studies and IND Support

- Management of preclinical datasets that are required for submission of an IND, in coordination with:
  - ✓ Sponsor/investigator who will conduct the unique preclinical work
  - ✓ Contract research organizations who conduct standard safety/toxicity, bio-distribution and other animal studies
  - ✓ Internal translating center personnel to compile in vitro process development datasets
- Coordination with the Accelerating Center to support IND compilation and submission.

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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

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Science Subcommittee Motion

CIRM requests that the Science Subcommittee recommend approval of the concept plan for the CIRM Translating Center, with budget authorization of up to $15 million to fund a single award over 5 years.

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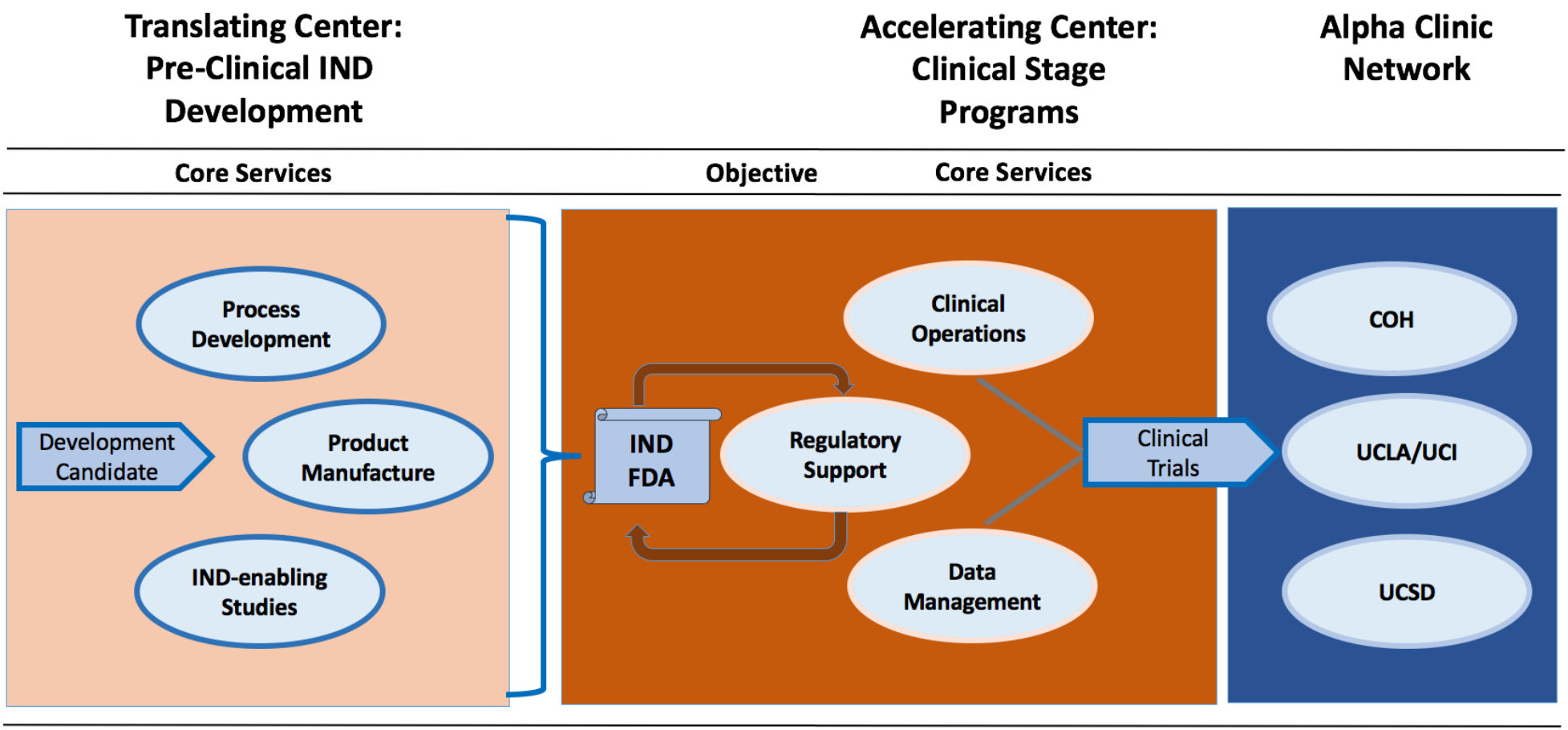
Infrastructure Coordination



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MISSION

Our Mission

Accelerating stem cell treatments to patients with unmet medical needs.