



The National Institute for Innovation in Manufacturing Biopharmaceuticals

AMERICAN INNOVATION AT WORK

Developing Next Generation Technologies in the Context of a Public-Private Partnership

10 April 2019

Our Mission

The NIIMBL mission is to accelerate biopharmaceutical manufacturing innovation, support the development of standards that enable more efficient and rapid manufacturing capabilities, and educate and train a world-leading biopharmaceutical manufacturing workforce, fundamentally advancing U.S. competitiveness in this industry.



A place where industry, academic, state, and U.S. federal resources synergize to

- meet industry's needs
- de-risk and streamline process development & manufacturing
- train a growing workforce

Enhanced process robustness is obtained

Major manufacturers work with suppliers to develop new technologies

Standardization of interfaces, assays, parts, and certifications is achieved

New methods, technologies, and best practices are demonstrated collaboratively with health authorities

Workforce creation matches industry needs



Funding

\$70,000,000
National Institute of Standards
and Technology

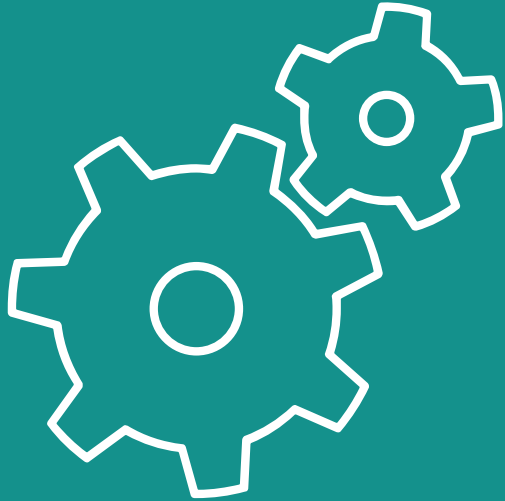


\$180,000,000
Other Commitments



NIIMBL is funded by a \$70,000,000 cooperative agreement from the National Institute of Standards and Technology and leverages >\$180,000,000 in other commitments.

NIST is a non-regulatory federal agency within the U.S. Department of Commerce. NIST's mission is to promote U.S. innovation and industrial competitiveness by advancing measurement science, standards, and technology in ways that enhance economic security and improve our quality of life.



Manufacturing USA network

Manufacturing USA Technology Projects Bridge Gaps

Manufacturing Readiness Levels (1-10) →

Market Failure in Pre-Competitive Applied Manufacturing R&D

Funding/
Investment

High

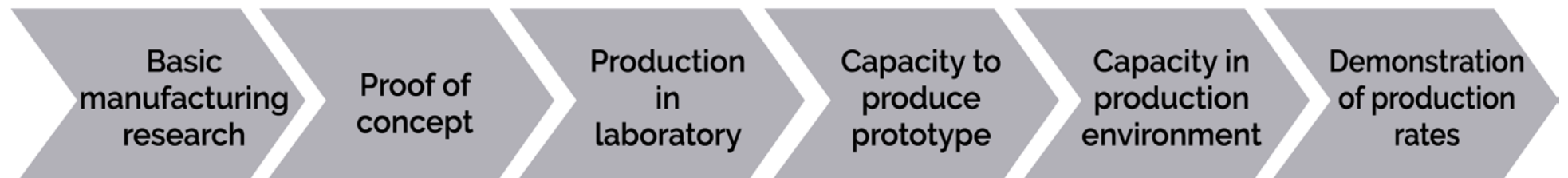
Government and
Universities

GAP

Private Sector

Low

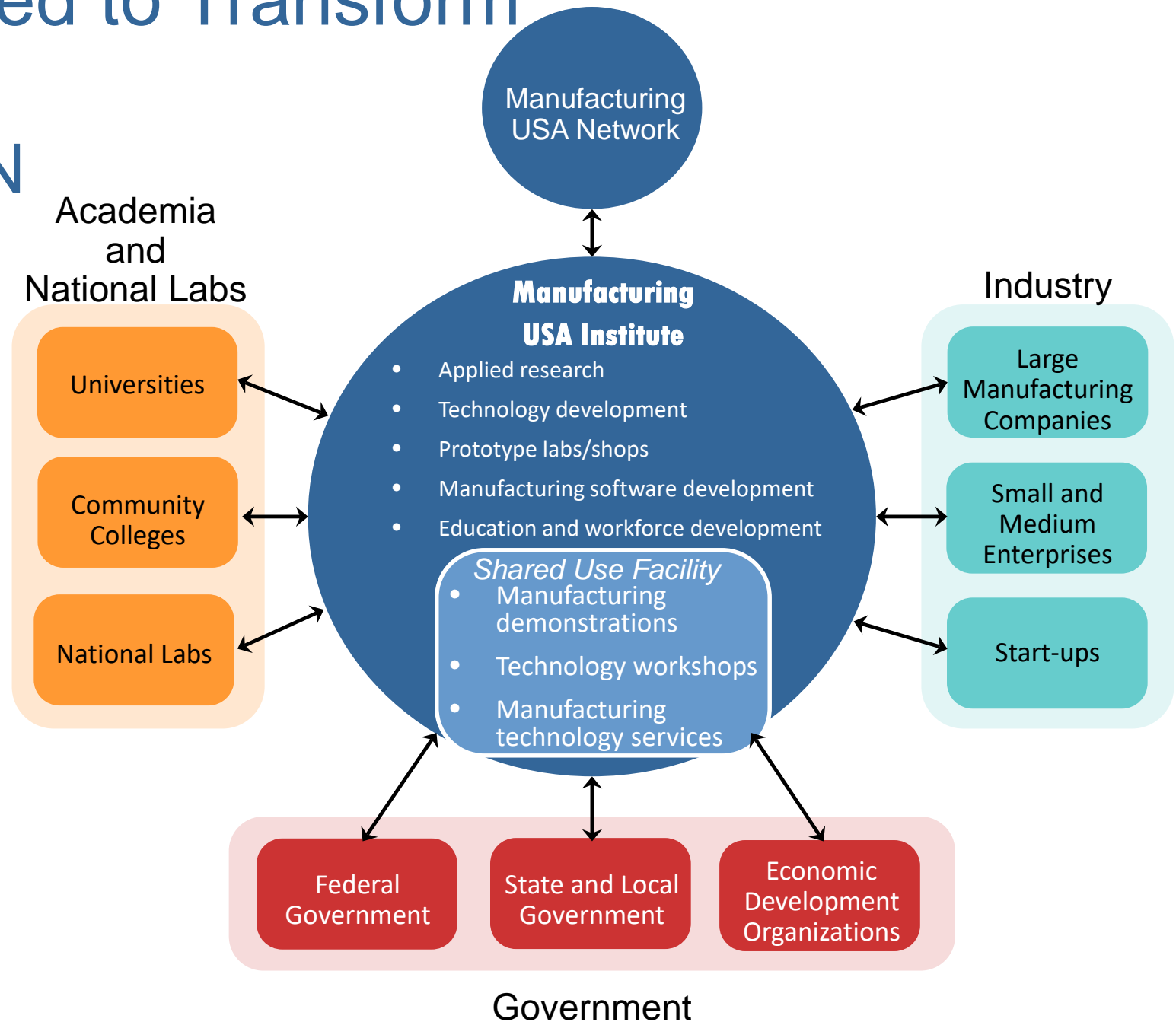
Manufacturing-Innovation Process



Slide credit: NIST AMNPO

Institutes Designed to Transform

TECHNOLOGY COLLABORATION



Manufacturing USA INSTITUTES



NEXT FLEX

Flexible Hybrid Electronics

San Jose, CA

CLEAN ENERGY SMART MANUFACTURING INNOVATION INSTITUTE

Smart Sensors and Digital Process Control

Los Angeles, CA

DMDII
a UI LABS Collaborator

Digital Manufacturing & Design

Chicago, IL

REMADE INSTITUTE

Sustainable Manufacturing

Rochester, NY

AIM photonics

Integrated Photonics

Albany, NY
Rochester, NY

biofabusa

Regenerative Manufacturing

Manchester, NH

affova

Advanced Fibers and Textiles

Cambridge, MA

RAPID
Transforming Process Industries

Modular Chemical Process Intensification

New York, NY

NIIMBL
The National Institute for Innovation in Manufacturing Biopharmaceuticals

Bio-pharmaceutical Manufacturing

Newark, DE

lift

Lightweight Metals

Detroit, MI

America Makes

Additive Manufacturing

Youngstown, OH
El Paso, TX

THE COMPOSITES iacmi INSTITUTE

Advanced Composites

Knoxville, TN
Detroit, MI

ARM

Advanced Robotics

Pittsburgh, PA

POWER AMERICA









Wide Bandgap Semiconductors

Raleigh, NC



Slide credit: NIST AM

NEEDS

-  Global competitiveness
-  Reduced offshoring and outsourcing
-  Workforce training and education
-  Domestic biomanufacturing
-  Reduced medical costs
-  Precision medicines
-  Standardization
-  Secure supply of medicines/pandemic readiness

NIIMBL

MEMBERS

- Industry
- Academia
- States
- NIST
- FDA
- MEPs
- MIIIs
- NGOs
- NIH
- DOD
- BARDA
- Trade organizations

FOCUS AREAS

   Existing products
mAbs, proteins, vaccines









   Emerging products
ADCs, bispecifics, virus-like particles

  Emerging products
gene and cell therapies

MANUFACTURING PROCESS THEMES



OUTCOMES

-  Skilled workforce
-  Novel real-time analytical technologies
-  Integrated continuous processing
-  Automation
-  Reference standards and protocols
-  Advanced process modeling and control
-  Process integration and intensification
-  Energy/water savings

IMPACT

NATIONAL

-  Growth of globally-competitive domestic industry
-  Regional economic development
-  Secure, integrated supply chain
-  Access to new and improved medicines

INDUSTRY

-  Flexible, adaptive manufacturing
-  De-risked manufacturing innovation
-  Lower costs
-  Accelerated development and approval

What we wrote

The industry saves, sustains, and improves lives.

It is one of the most valuable and important business sectors in the US and growing rapidly.

The success of US biomanufacturing over the last 30 years is, in part, the result of industry-academic partnerships that supported the early development of the industry.

Today, the industry finds itself at a crossroads.

What we wrote II

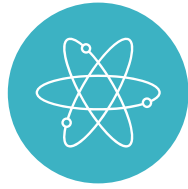
To enable industry to meet variable market needs for lot size and demand, as well as to address speed to market and improved flexibility, the industry requires further industrialization in manufacturing technology.

To enable patient access to emerging therapies, there is a need for new small-scale manufacturing platforms, integrated with robust product and process measurement capabilities, and automated for consistency.

There is a need to ensure standards and robust measurement technologies are available to support the consistent, high quality manufacture of all biotherapeutic product types and to enable advanced process control.



A Community-Wide Need for Manufacturing Innovation



For existing products, companies increasingly compete on the molecule, not the process.



For emerging products, there are no well-established commercial manufacturing methods and the challenges are numerous.



A science-based regulatory environment. Highly regulated nature of the industry compounds perceived challenges associated with rapid technology adoption.

A Role For Public-Private Partnerships

01

Sharing of appropriate knowledge / experience.

02

De-risk technology adoption.

03

Leveraged investments for technology advancement.





Stakeholders

We are mobilizing as a community !

NIIMBL Membership - 115 members

42 Companies

36 Universities

33 Community colleges / non-profits

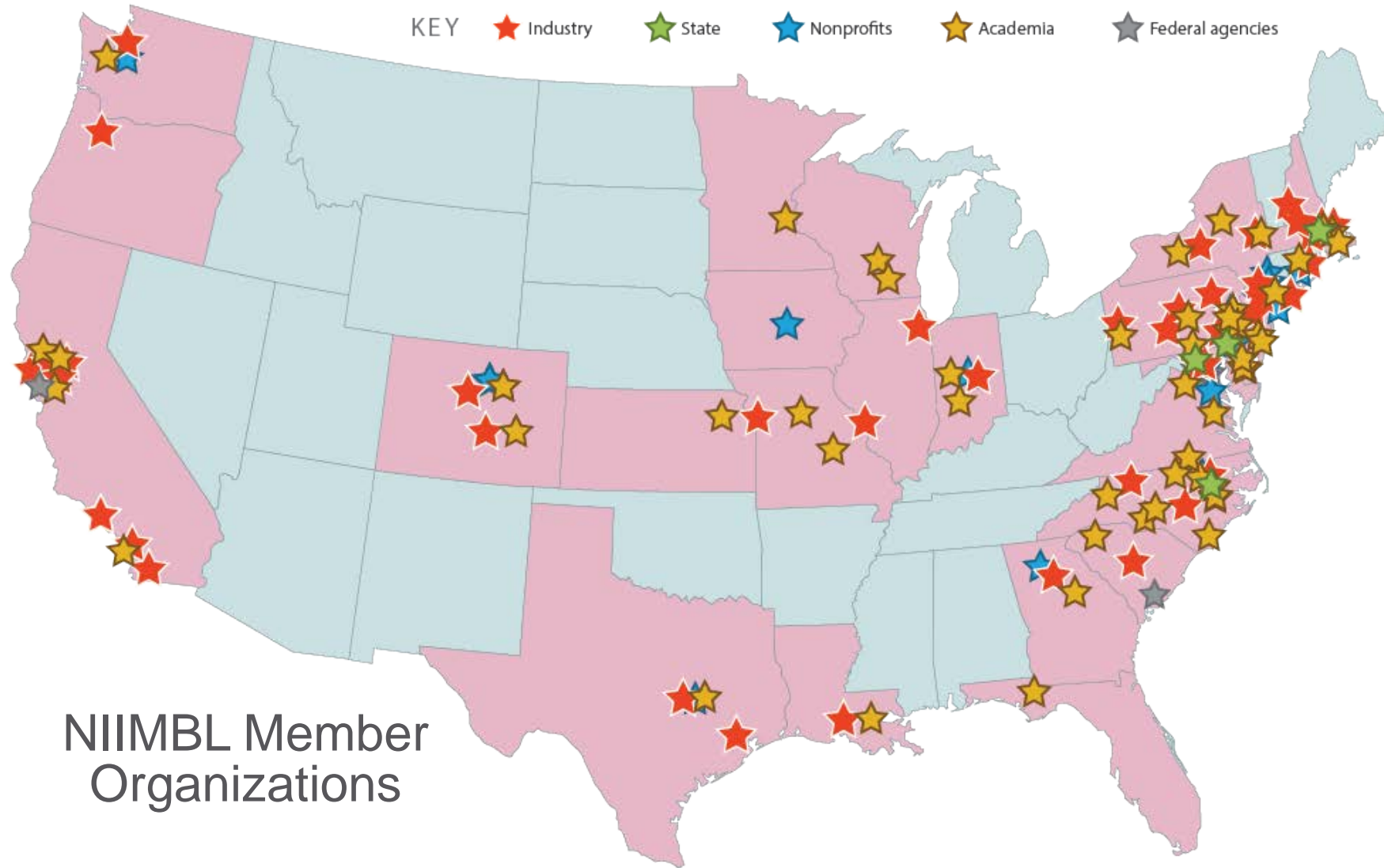
4 States are engaged (DE, MA, NC, MD)

Federal engagement: NIST, FDA, NSF, NIH, BARDA

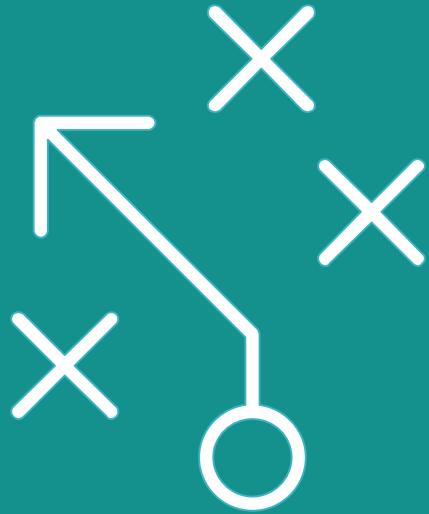
BILL & MELINDA
GATES foundation



Graphic includes a sample of NIIMBL members. For a full list, visit NIIMBL.org.



NIIMBL Member Organizations



Activities

- Roadmapping

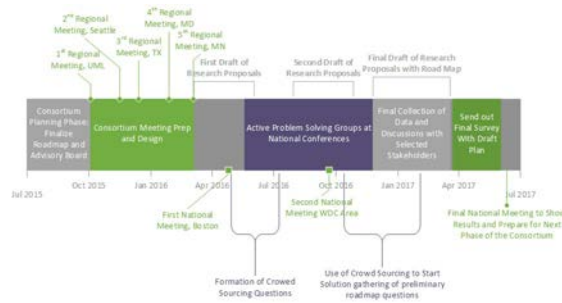
Technology Roadmapping For Industry Growth



Lyophilization Roadmapping
(Purdue led)



Cell Therapy Roadmapping
(Georgia Tech led)



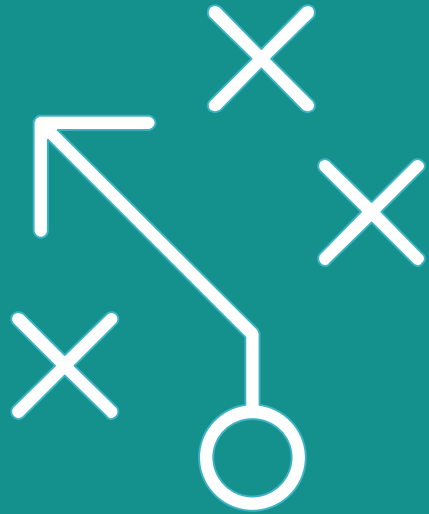
Biologics DS
(UML led)

NIIMBL Roadmapping is an Open Process and complementary to other roadmaps.

NIIMBL Roadmaps

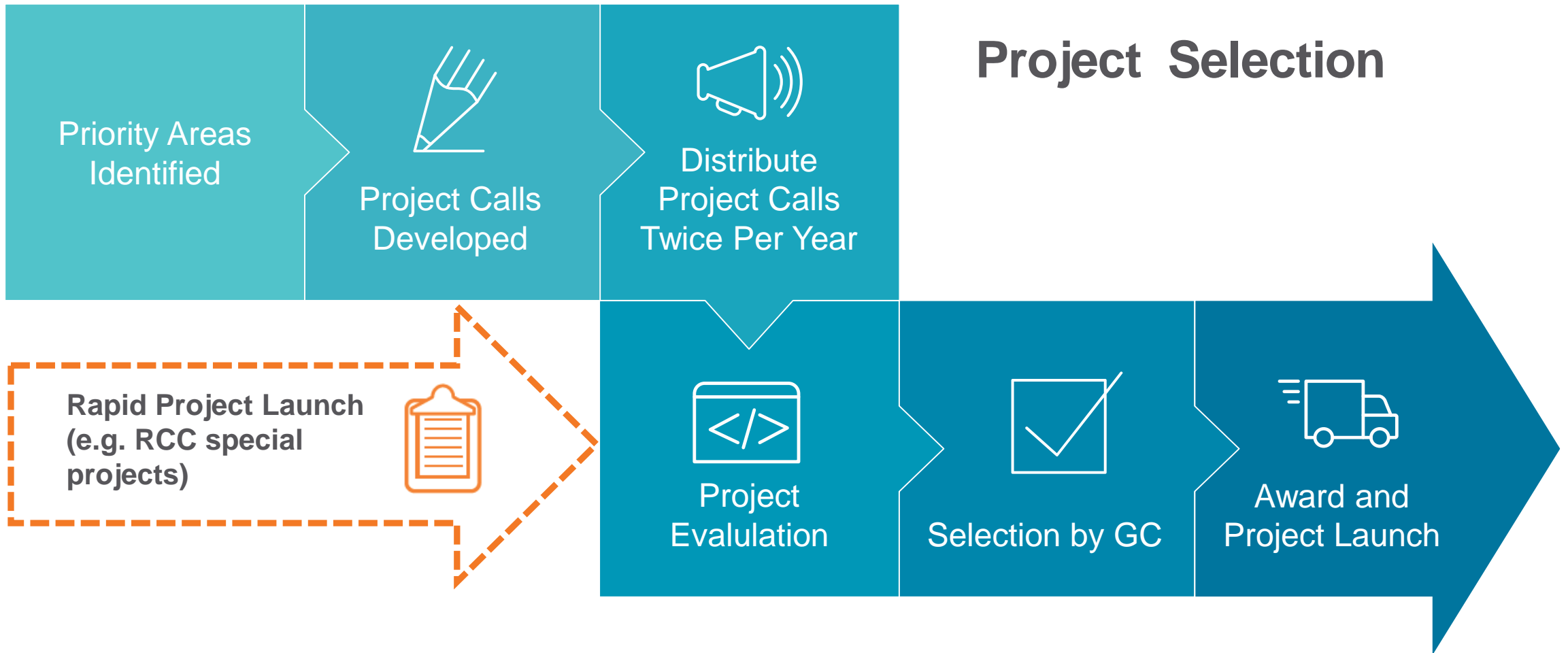
- Published roadmaps for Gene Therapy, ADCs / Bispecifics, and Vaccines
- Contributions by more than 40 organizations
- Available to the biopharmaceutical community by visiting <http://www.niimbl.org>





Activities

- Projects



A typical Project Call commits ~\$7.5M NIIMBL funds (\$16M total) over 18 months for 12 projects.

NIIMBL Technology Project Landscape

Drug Substance



Drug Product



Process Control & Analytics



Existing Products

Emerging Products

Improved Lentiviral Vector Biomanufacturing for Cell & Gene Therapy Applications

Johns Hopkins, Repligen, RPI, Univ Massachusetts System, Unum Therapeutics, Artemis Biosystems

1. **Scalable perfusion cell culture process** – Efficient DNA production, Serum free suspension, HEK293T cell line, high cell density
2. **Single-day, closed lentiviral vector purification – 2 step purification**
Continuous from harvest to final UF – Digital PCR for vector copy number (VCN)
3. **Optimized growth profiles in HEK293** – Serum and nutrient formulations
4. **Optimized transfection parameters** - Optimized cell density and media
5. **Optimizing downstream processes** – Chromatographic approaches
6. **Integration of upstream and downstream** – Productivity, yield, purity, potency



New Modality Relevant Projects

- **Preparing for the future: a gene therapy vector production platform (AAV)**
- **A Lentiviral Vector Production Platform Process (LVV)**
- **Use of Carbon Thin Films to Reduce Leachable Contamination**
- **At-Bioreactor Trace Metal Quantification and Statistical Process Control in CHO Cell-Culture Production**
- **A Novel Perfusion-based 3D Bioreactor for Effective Selection, Activation, and Transduction of T-cells for Immuno-Gene Therapy**
- **Quantitative Trilineage Differentiation Assays for cGMP Cell Manufacturing of Human Mesenchymal Stem Cells**
- **Label-free Critical Quality Attributes of CAR T-Cell Products**
- **Next Generation Sequencing (NGS) Internal Controls for Adventitious Agent Testing to Ensure Sensitivity for All Targets in Every Sample**
- **Rapid Adventitious Agent Testing for Fail-Fast Process Decision-Making**
- **At-line Detection of Viral and Bacterial Contaminants in Mammalian Cell Culture Using High Affinity Probes and Label-free Single-cell Analysis**
- **Cell Therapy Manufacturing Courses and Certifications (2)**



Some of NIIMBL's Proposed Goals for Cell & Gene Therapy Products

Manufacturing Platforms for Emerging Products



- Massively parallel, small-scale, automated closed manufacturing platforms
- Optimized unit operations
- Improved gene vector manufacturing (titer, filled capsids, harvest, purification)
- Cell therapy product formulation for improved maintenance of CQA during storage, transportation, thawing
- Gene therapy formulations for improved activity and reduced aggregation
- Supply chain management

Standards & Measurement Technologies



- Reference standards and tools for product comparability
- Real-time, in-line, analytics for process parameters and product quality attributes
- Closed loop control of manufacturing process
- Rapid adventitious agent testing
- Standardizing raw materials
- Regulatory science, including standardized protocols

Education and Workforce Training Program



NIIMBL Workforce Project Landscape





New NIIMBL HQ Opening Q1 2020

Planned Next Steps (v 4.2019)

- >\$50M of activity launched through projects
- Project call 2.2 finishing
- NIIMBL – FDA CDER active listening workshop
- Launch of Global Health Fund

We are a community.

We are mobilizing as a community.

We have a structure to work together and we have the engagement with relevant Federal agencies –
to share the costs
to lower the risks
to leverage each other

We invite organizations to join with us and shape the future of the industry



Celebrate the network
Expand the network
Strengthen the network



NIXMBL

The logo features the acronym 'NIXMBL' in a bold, white, sans-serif font. The letter 'X' is replaced by a stylized DNA double helix. The two strands of the helix are colored blue and orange, with a red section at the bottom. The base pairs are represented by white horizontal bars.

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