NIIMBL | Viral Vector Manufacturing & Analytics Program

Building a Shared AAV Manufacturing Resource: A Public Workshop

NIIMBL Public Workshop
February 2026

Announcements:

Webinar Details

- You will be muted during the presentations, but microphones will open during the Q&A sessions.
  - You can also type your question into the Q&A at any time.
- There will be a 10 min break at ~12:50

Confidentiality

- This webinar is open to NIIMBL members and non-members.
- Please do not post NIIMBL confidential or proprietary information in the chat.

Questions:

- During discussion periods, please raise your hand and unmute when invited to speak.
- You may also type your question in the Q&A.
- We will capture additional questions in a “parking lot” and return to them during the final discussion.

Agenda

- Welcome / housekeeping (5 min)
- Intro to NIIMBL and Viral Vector Program (25min)
- Theme 1: Defining the Platform + Dialogue (45min)
- Theme 2: Deploying the Platform + Dialogue (40min)
- BREAK (10min)
- Theme 3: Supporting the Platform + Dialogue (40min)
- Questions / Wrap-up (15min)

Presenters

Eric Hacherl
NIIMBL Senior Fellow and Viral Vector Program Lead

Chris Williams
Viral Vector Program Co-lead

Angie Snell Bennett
Scientific Project Manager

Tim Charlebois
NIIMBL Senior Fellow
National Institute for Innovation of Manufacturing Biopharmaceutica...

Introduction to NIIMBL

Tim Charlebois
NIIMBL Senior Fellow
Viral Vector Program Advisor

Manufacturing USA Network

ELECTRONICS

- AIM Photonics — Integrated Photonics — *Albany, NY*, *Rochester, NY*
- NextFlex — Flexible Hybrid Electronics — *San Jose, CA*
- PowerAmerica — Wide Bandgap Semiconductors — *Raleigh, NC*

MATERIALS

- AFFOA — Advanced Fibers and Textiles — *Cambridge, MA*
- IACMI — The Composites Institute — Advanced Composites — *Knoxville, TN*, *Detroit, MI*
- LIFT — Advanced Materials — *Detroit, MI*

ENERGY/ ENVIRONMENT

- RAPID — Transforming Process Industries — Modular Chemical Process Intensification — *New York, NY*
- REMADE — Sustainable Manufacturing — *Rochester, NY*
- CESMII — The Smart Manufacturing Institute — Smart Manufacturing — *Los Angeles, CA*
- EPIXC — Industrial Process Decarbonization — *Phoenix, AZ*

DIGITAL/ AUTOMATION

- America Makes — Additive Manufacturing — *Youngstown, OH*, *El Paso, TX*
- ARM Institute — Advanced Robotics & AI — *Pittsburgh, PA*
- MxD — The Digital Manufacturing & Cybersecurity Institute — Digital Manufacturing & Cybersecurity — *Chicago, IL*
- CYMANII — the cybersecurity manufacturing innovation institute — Cybersecurity in Manufacturing — *San Antonio, TX*

BIO-MANUFACTURING

- biofabusa — Regenerative Manufacturing — *Manchester, NH*
- NIIMBL — Biopharmaceutical Manufacturing — *Newark, DE*
- BioMADE — Bioindustrial Manufacturing — *St. Paul, MN*

NIIMBL's Mission and Vision

Mission

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.

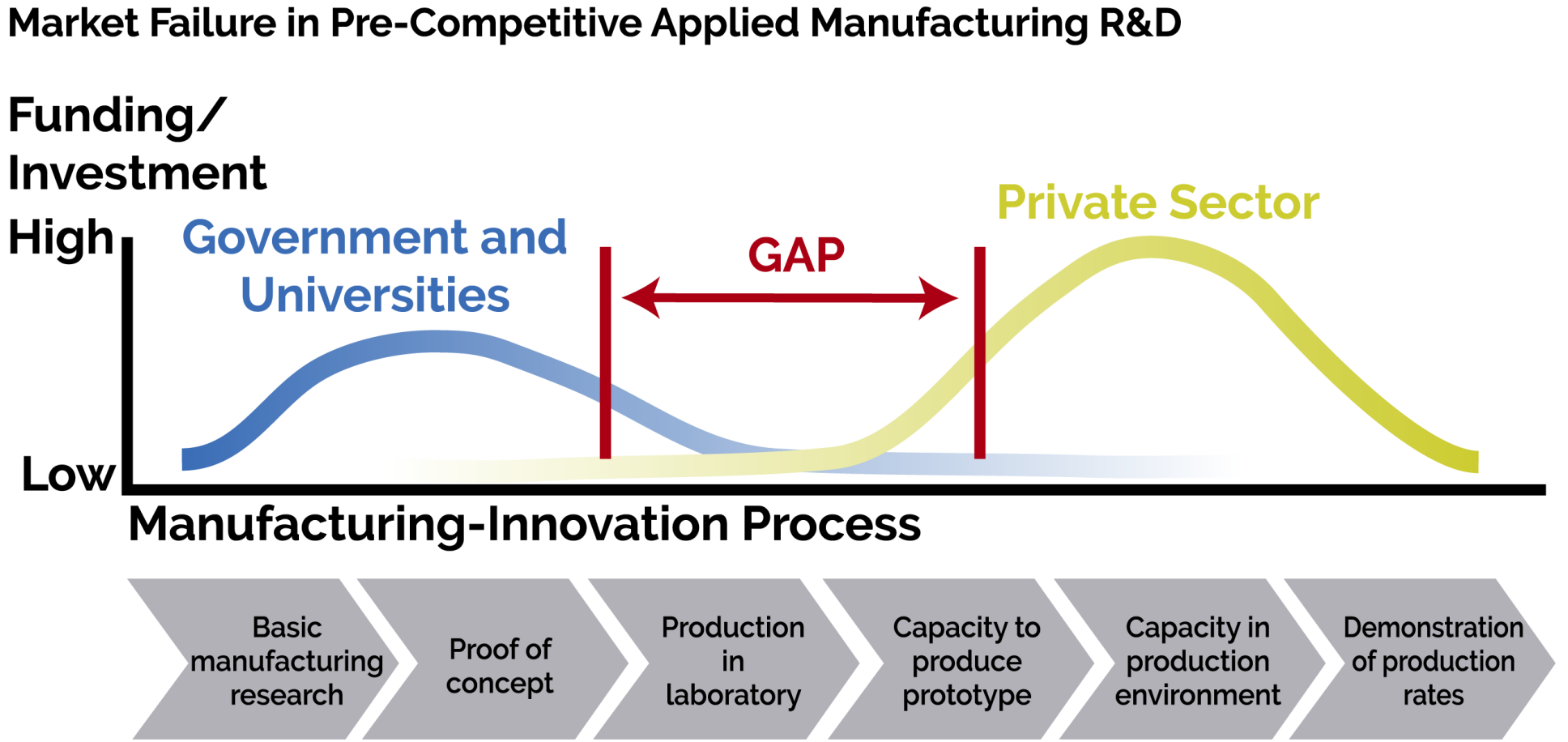
Vision

NIIMBL will lead and transform the **development and adoption of next-generation biopharmaceutical manufacturing technologies that contribute to patient well-being**. As a public-private partnership, NIIMBL will forge and catalyze advancements that are vital to the acceleration of innovative technologies and a skilled workforce, and these strategic efforts and investments will be undertaken to secure U.S. biopharmaceutical manufacturing leadership.

Manufacturing USA Technology Projects

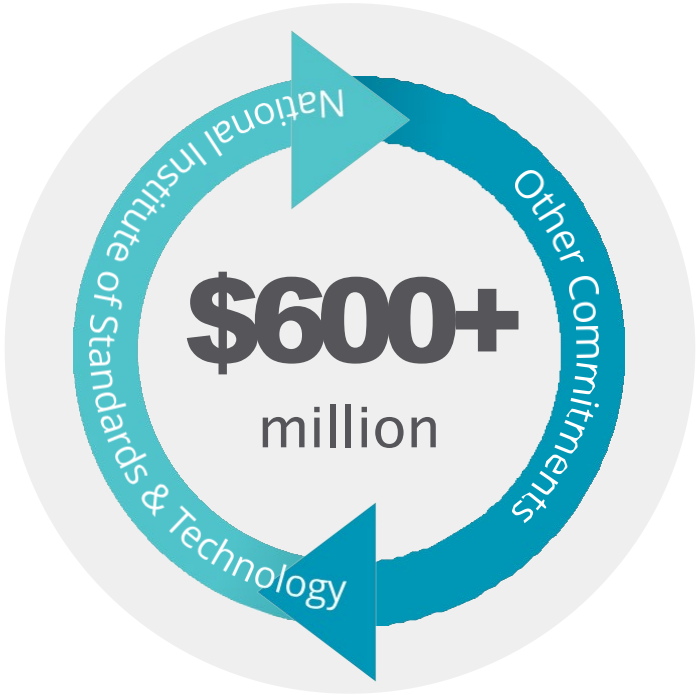
Bridge Gaps

Manufacturing Readiness Levels (1-10)



Slide Credits: NIST AMNPO

Strategic Goals



NIIMBL is funded by cooperative agreements from the National Institute of Standards and Technology and leverages other non-Federal commitments.

NIST

- **Increase** the competitiveness of U.S. manufacturing
- Facilitate the transition of **innovative technologies** into scalable, cost-effective, and high-performing domestic manufacturing capabilities
- **Accelerate** the development of an advanced manufacturing workforce
- Promote a network of institutes that build **long-term support** for and from their communities

The NIIMBL Success Framework

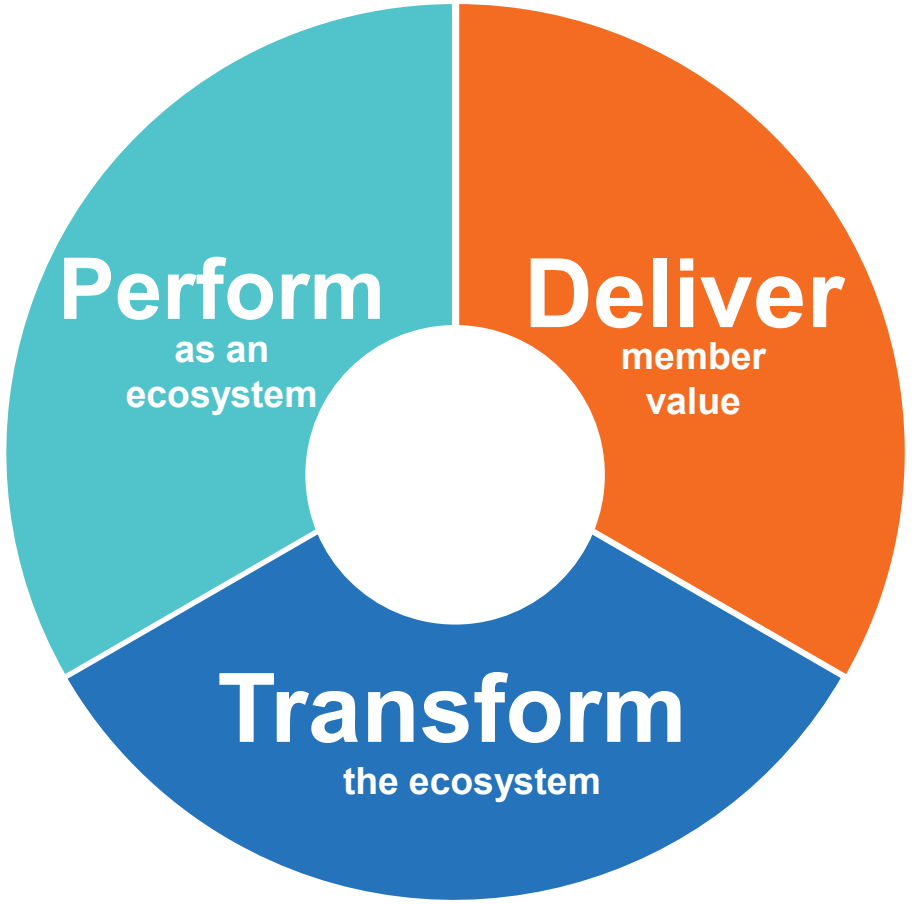
As a consortium of companies, universities, colleges, non-profits, and federal stakeholders,

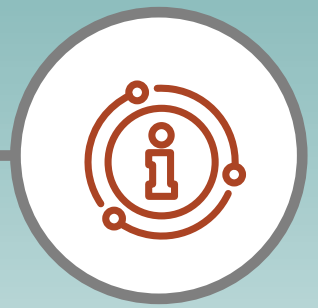
<u>we</u> will be successful when....

1) **We perform effectively.** We must operate effectively within our defined parameters as a federally-funded public private partnership.

2) **We deliver value.** We must generate value for the entire member community that can be captured as ROI in their organizations.

3) **We transform the industry.** We must drive systems change that fundamentally advances the biopharmaceutical manufacturing industry at large.





Q&A:
NIIMBL Background

Viral Vector Manufacturing & Analytics

One of Four 'NIIMBL-Led' Programs

Background: Development of Program Focus & Objectives

- Initial Public Workshops: focused on AAV Process & Analytical Needs
- Decision to focus on AAV-based vectors for *in vivo* gene therapy
- Team recruitment: Steering Committee; Process & Analytical Workstreams
- Decisions & focus
  - Shared-access process platform for vector development & manufacture
  - Supporting, enabling analytical toolkit
  - HEK 293-based, transient transfection suspension-based upstream
  - Chromatography-based downstream
  - Compatible with US industrial investments
- Key principles
  - Assemble & leverage expertise
  - Disseminate learnings & experience
  - Support community uptake & value proposition

Viral Vector Manufacturing & Analytics: Mission and Vision

Mission

Develop and make broadly available a **robust, economically viable, shared-access platform** for the technical development, manufacturing, and characterization of **AAV-based gene therapy vectors**. Support **workforce awareness & training** for this platform.

Vision

A gene-based therapeutics industry capable of serving patients across the full spectrum of unmet needs—from prevalent indications to ultra-rare diseases—that has **access to high-quality viral vectors without cost or speed limitations**

NIIMBL Viral Vector Manufacturing & Analytics Program (HIGH LEVEL)

Achieving The Viral Vector Program's
MISSION

Through The Viral Vector Program's
WORKSTREAMS

PROCESS

Develop AAV manufacturing processes and demonstrate process capabilities enabling broad expansion of AAV gene therapy applications

ANALYTICS

Develop and disseminate AAV analytical capabilities and support standards availability for process & product characterization, batch release, and stability monitoring

Realizing The Viral Vector
INDUSTRY'S VISION

Enabling these
BENEFITS

- **Reduce individual investment and resources**
- **Accelerate R&D timelines & patient access**
- **Improve therapy yield of manufacturing platforms**
- **More consistently analyze viral vectors and resulting clinical outcomes**
- **Increase confidence in viral vector quality attributes**
- **Streamline regulatory reviews through more standardized and integrated evidence of product quality, safety, and efficacy**

Open Access Enhances Every Stage of the Therapeutic Pathway

Open access viral vector platforms reshape how therapies move from the lab to the patient. By removing barriers to essential tools and data, open platforms speed up access to promising treatments without compromising quality or safety.

1

PATIENTS & PATIENT ORGANIZATIONS

Streamlined activities contribute to faster access to experimental therapeutics

2

ACADEMIC RESEARCH INTO DRUG DISCOVERY

Fewer work packages required to develop new investigational therapeutics

CDMOS & TESTING LABS

Lowers risk when working with clients with limited technical expertise and minimal production demand

3

REGULATORS

Time and effort savings when reviewing standard packages with higher quality analytics and more supporting data.

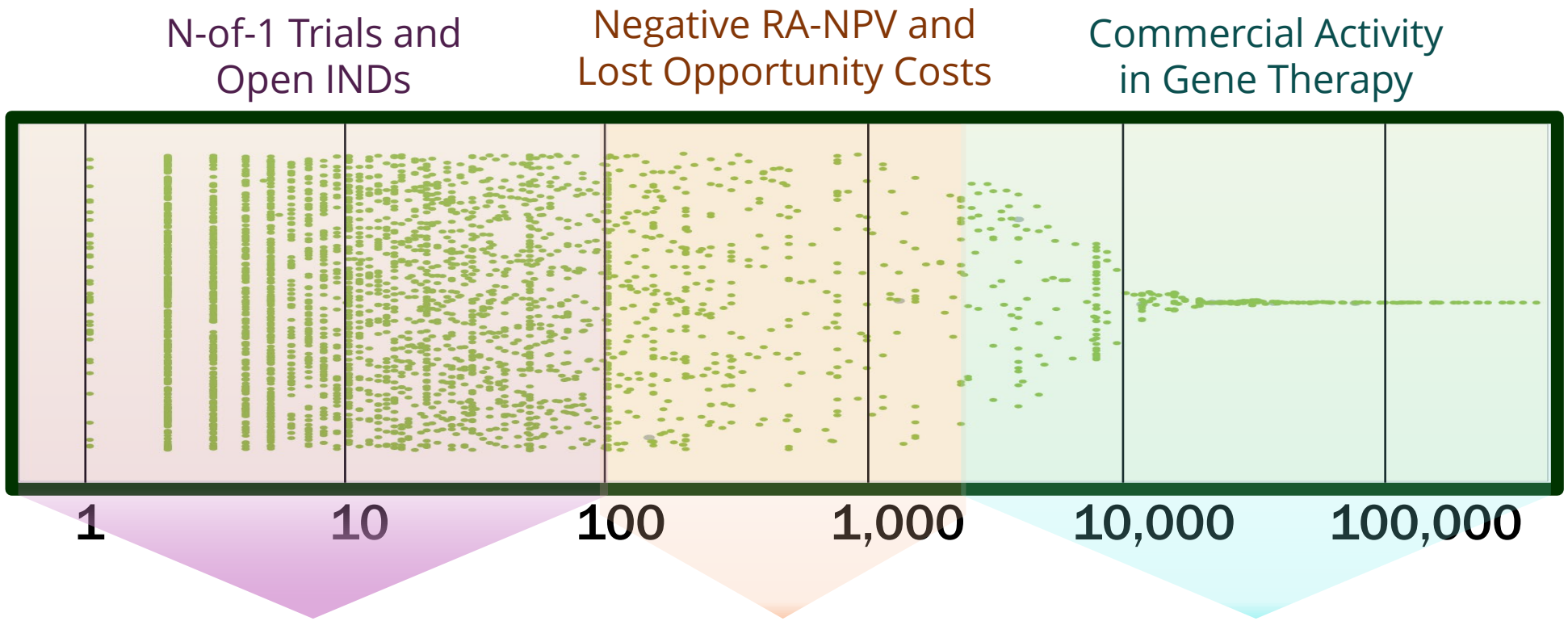
4

5

INVESTORS & DRUG DEVELOPERS

More products demonstrating clinical evidence and with fewer technical risks to commercializations

Underserved Market Segment | Upside Potential



Cheaper, faster, safer options for philanthropic Gene Therapies

Sustainable economic opportunity by reducing up-front cost and lowering barriers to commercialization

Fill gaps left by industry divestments from Gene Therapies and Rare Indications

NIIMBL Platform Process

Manufacturing and Analytics

Eric Hacherl
Viral Vector Program Co-Lead

Theme 1: Defining the Platform

THE GAP

Academic labs and small biotechs developing rare disease AAV therapies have breakthrough science — but lack the manufacturing knowledge, analytical benchmarks, and regulatory documentation to file Phase 1 INDs.

NIIMBL's AAV Platform bridges this gap by providing

✓ Demonstrated manufacturing process

✓ Comprehensive analytical framework

✓ IND-supporting documentation and data

IN THIS SESSION

What we've built (process + analytics)

What we've proven (50L batch data)

What we need from you (strategic input on v1.0 scope)

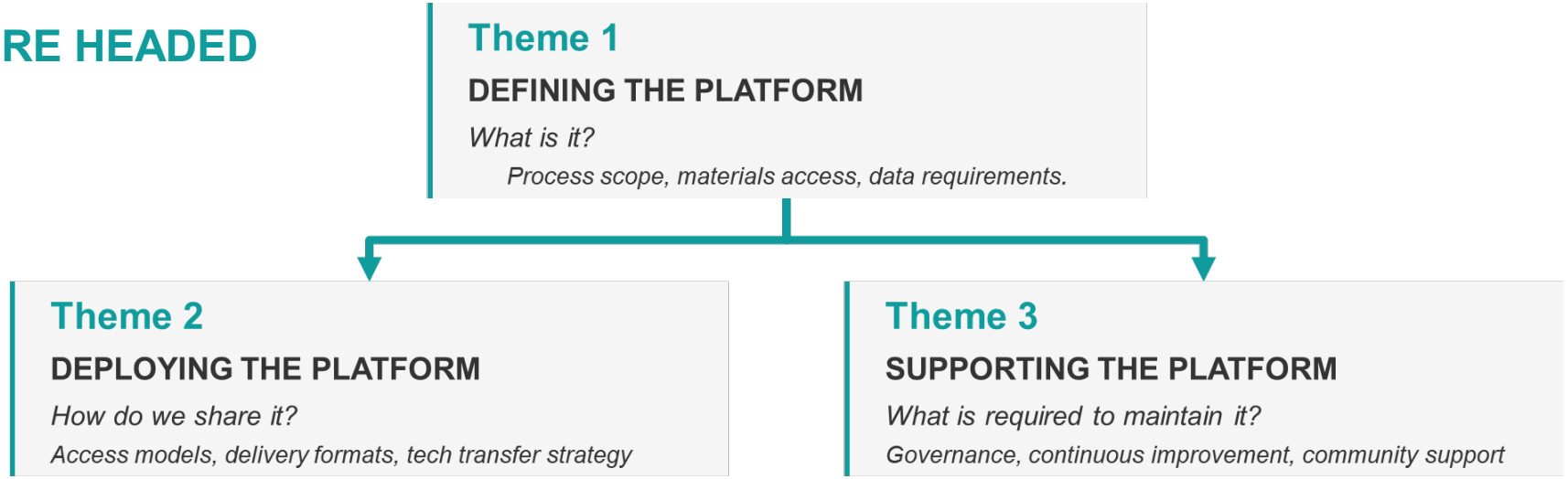
Strategic Prioritization Framework

WHAT WE'VE ACCOMPLISHED:

Over the past 18 months, NIIMBL has developed and demonstrated a complete AAV manufacturing platform:

- Process development: 2L → 10L → 50L scale progression with successful tech transfer to Landmark Bio
- Quality confirmation: Comprehensive CQA panel tested against Phase 1 IND standards (71% full capsids, <2 ng/mL HCP)
- Analytical advancement: 4 industry-leading studies addressing critical measurement gaps (NGS, aggregation, capsid titer, AUC)

WHERE WE'RE HEADED



Theme 1: What We've Built: 18 Months of Progress

Process Development

Starting point: Caring Cross collaboration — 25L rocker bag, no polishing step.

What NIIMBL added: Stirred tank bioreactor at 50L + AEX chromatography polishing.

What the Landmark Bio batch taught us:

- Process transferred successfully to an outside CDMO
- Scale-up from 10L → 50L required no major redesign
- AEX polishing delivered meaningful purity improvement

Analytical Development

The gap: Inconsistent AAV measurements create regulatory risk for every IND filer.

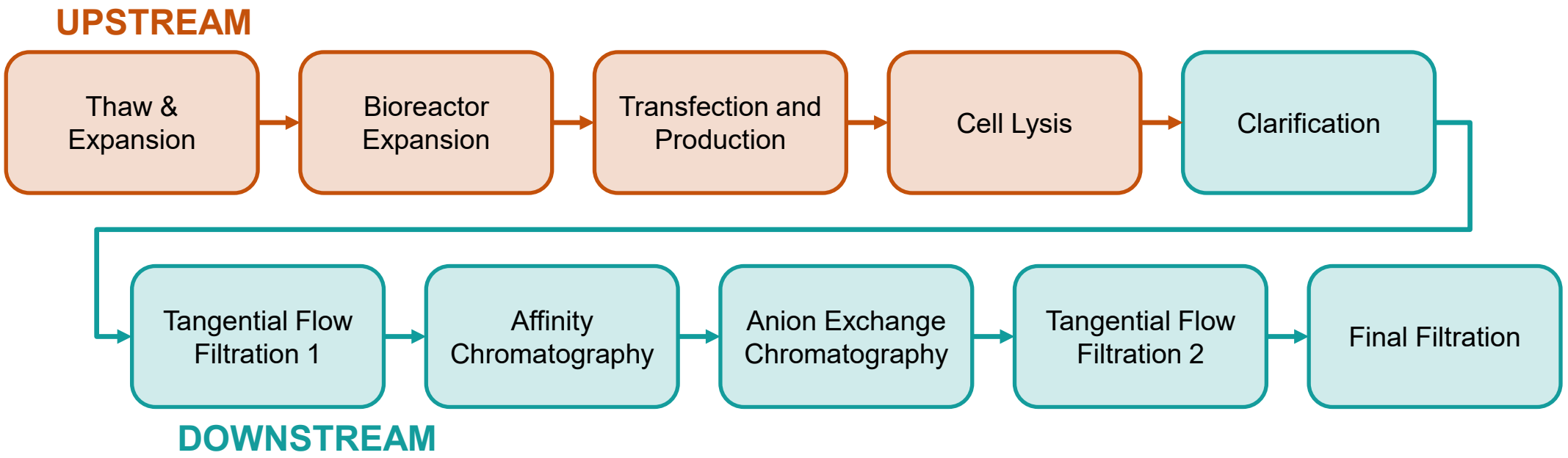
What NIIMBL launched: 4 studies targeting the industry's biggest analytical weaknesses:

- NGS-based QC — earlier defect detection
- Aggregation testing — standardizing a poorly characterized CQA
- Capsid titer interlab — addressing FDA-flagged measurement variability
- AUC interlab — standardizing full/empty capsid characterization

We have a transferable process and an advancing analytical framework.
Today, we want your input on where to take it next.

Theme 1: The Baseline Process: Architecture

The BASELINE Process:



Theme 1: The Baseline Process: Key Design Decisions

Key Attributes of the BASELINE Process:

- **Cell line**: HEK293F (WXATUS0028 cell line)
- Serotype: AAV9 (plasmids donated by Pfizer, Inc.)
- Medium: BalanCD HEK293 with 4 mM GlutaMAX
- Transgene: expressing tdTomato and Luc2 (transgene donated by UF)
- **Transfection**: Mirus Bio AAViator + RevIT transfection system
- **Plasmid Ratio**: 2:3:1 (rep/cap: Ad helper: GOI)
- Lysis buffer: Deviron® C16
- Endonuclease: Denarase® High Salt
- **Affinity resin**: POROS™ CaptureSelect™ AAVX
- **Anion exchange resin**: POROS™ 50 HQ
- Final formulation: 20 mM Tris, 200 mM NaCl, 2 mM MgCl2, 0.005% Poloxamer 188, pH 7.5

All components selected for commercial availability, regulatory precedent, and CDMO transferability.

Theme 1: The Baseline Process: What We Measured

We developed our CQA panel in alignment with input from industry, FDA, NIH, and academic institutions, representing the current industry and regulatory consensus on what matters for Phase 1 AAV.

The 50L demonstration batch was tested against every applicable measure.

All critical quality attributes met Phase 1 expectations for safety, purity, and potency.

PRELIMINARY

Test Description	Method	Unit of Measure	Results
VP Titer	ELISA	VP/mL	6.3×10^{13}
VG Titer	qPCR	VG/mL	2.8×10^{13}
Capsid Content	Mass Photometry	% full capsid	71.4
Capsid Content	AUC	% full capsid	75.0
TU Titer	Flow Cytometry	TU/mL	1.6×10^{7}
Vector Genome Identity	NGS	n/a	Confirmed
Capsid Size	MADLS	nm	28.7
Capsid Aggregation	MADLS	% monomer	100 / no aggregation
Residual HCP	ELISA	ng/mL	< 2.1 (BLOQ)
Residual dsDNA	Picogreen	ng/mL	< 40.0 (BLOQ)
Residual Nuclease	ELISA	pg/mL	< 31.3 (BLOQ)
Residual Plasmid DNA	qPCR	copies/mL	1.3×10^{11}
Residual DNA Fragments >200bp	Agarose Gel	n/a	Not observed
Appearance	Visual Appearance	n/a	Colorless (Clear), Not Turbid (Clear), Particulates Not Detected
Subvisible Particle Analysis	FIM	Particles/sample (1.3mL)	35 (>10µm)
			3 (>25µm)
pH	pH probe	n/a	7.45
Osmolality	Osmometer	mOsm/kg	420
Sterility	BacT/ALERT	n/a	No growth
Mycoplasma	ddPCR	n/a	Not detected
Bioburden	Microbial enumeration	CFU/mL	0
Endotoxin	Spectrophotometry	EU/mL	< 0.100

Theme 1: The Baseline Process: What We Learned

- **The process is transferable**

  Landmark Bio executed it successfully without process modifications

- **Scale-up is straightforward**

  10L to 50L required no major redesign—**same unit operations, similar yields**—supporting future flexibility

- **The analytical package is defensible**

  Results are consistent with Phase 1 expectations across **key CMC attributes**: titer, purity, and safety categories

This is a platform you can build your Phase 1 IND CMC section around.

Now we need YOUR input to shape Platform v1.0. Let's discuss four critical decisions...

Theme 1 Discussion Section: Process Scope

Your Input Will Shape Platform v1.0

FOUR QUESTIONS FOR DISCUSSION:

1. Where are you in your development timeline — and what's your BIGGEST CMC bottleneck right now?
2. Which ONE serotype beyond AAV9 would unblock the most rare disease programs?
    - AAV8 (liver/metabolic)
    - AAVrh10 (CNS/patent workaround)
    - AAV5 (lung/airway)
    - Other
3. Is one 50L demonstration batch sufficient to support your IND CMC section, or do you need N=3 reproducibility data? Do 50L batches add value or would a scale-down model be more useful?
4. If NIIMBL could do ONE thing in the next 12 months to make this platform more useful to you, what should it be?

Theme 1: IND-Enabling Data and Documentation

What do you need to build a credible IND CMC section?

FDA Expectations for Phase 1 AAV Gene Therapy:

- Process description (flow diagram, unit operations)
- Starting materials characterization (cell line, plasmids, reagents)
- Manufacturing controls and in-process testing (process parameters, acceptance criteria)
- Analytical results against defined CQAs (identity, purity, potency, safety)

What NIIMBL Could Provide to Accelerate YOUR IND Preparation:

- **Detailed process description** and batch record templates
- **Platform performance data:** titer, recovery, purity from 50L demonstration batch
- **Complete CQA dataset:** you can reference our analytical results as feasibility data
- **Comparability framework:** guidance for when you change serotype, scale, or transgene

> **DISCUSSION:**
> - Which of these is most valuable for your program?
> - What's missing that would make this MORE useful for IND filing?

Theme 1: Enabling Materials and Access

What's blocking you today from adopting a platform process?

We think the THREE BIGGEST barriers are:

1. **Cell line access**—research-grade vs. GMP-banked options
   → GMP-banked cells: $50-100K cost, 6-12 month lead time
2. **Plasmid access**—no standard reference configurations
   → Every group negotiates separate licenses, delays program start by months
3. **Vendor-neutral BOM**—no curated bill of materials for IND filing
   → Forces you to validate vendor equivalency without a reference standard

> ❓ **FEEDBACK NEEDED:**
> - Are these YOUR biggest blockers, or are we missing something?
> - Which ONE should NIIMBL tackle first?
> - What would "minimum viable access" look like for your Phase 1 program?

Theme 1 Summary: Platform v1.0 Decisions

YOUR INPUT Will Shape These Trade-offs:

1. SEROTYPE PRIORITY

Beyond AAV9, which serotypes should we validate next?

- AAV8 (liver/metabolic)
- AAV5 (lung/airway)
- AAVrh10 (CNS/patent workaround)
- Other

2. PERFORMANCE BENCHMARKS

What platform performance metrics matter most for YOUR adoption decision?

- Productivity (vg/L yield)
- Robustness (process consistency)
- Tech transfer ease
- Material costs ($/dose)
- Analytical rigor (measurement precision)
- Scale flexibility

3. DEEPER UNDERSTANDING

Where should we invest in deeper understanding?

- Critical Process Parameters
- Filtration throughput
- Failure modes
- In-process stability
- Worst case conditions
- Other

Which priorities would accelerate YOUR path to IND filing?

Deploying the NIIMBL Platform

Chris Williams
Viral Vector Program Co-Lead

Have you heard the fable of a Eierlegende Wollmilchsau ?

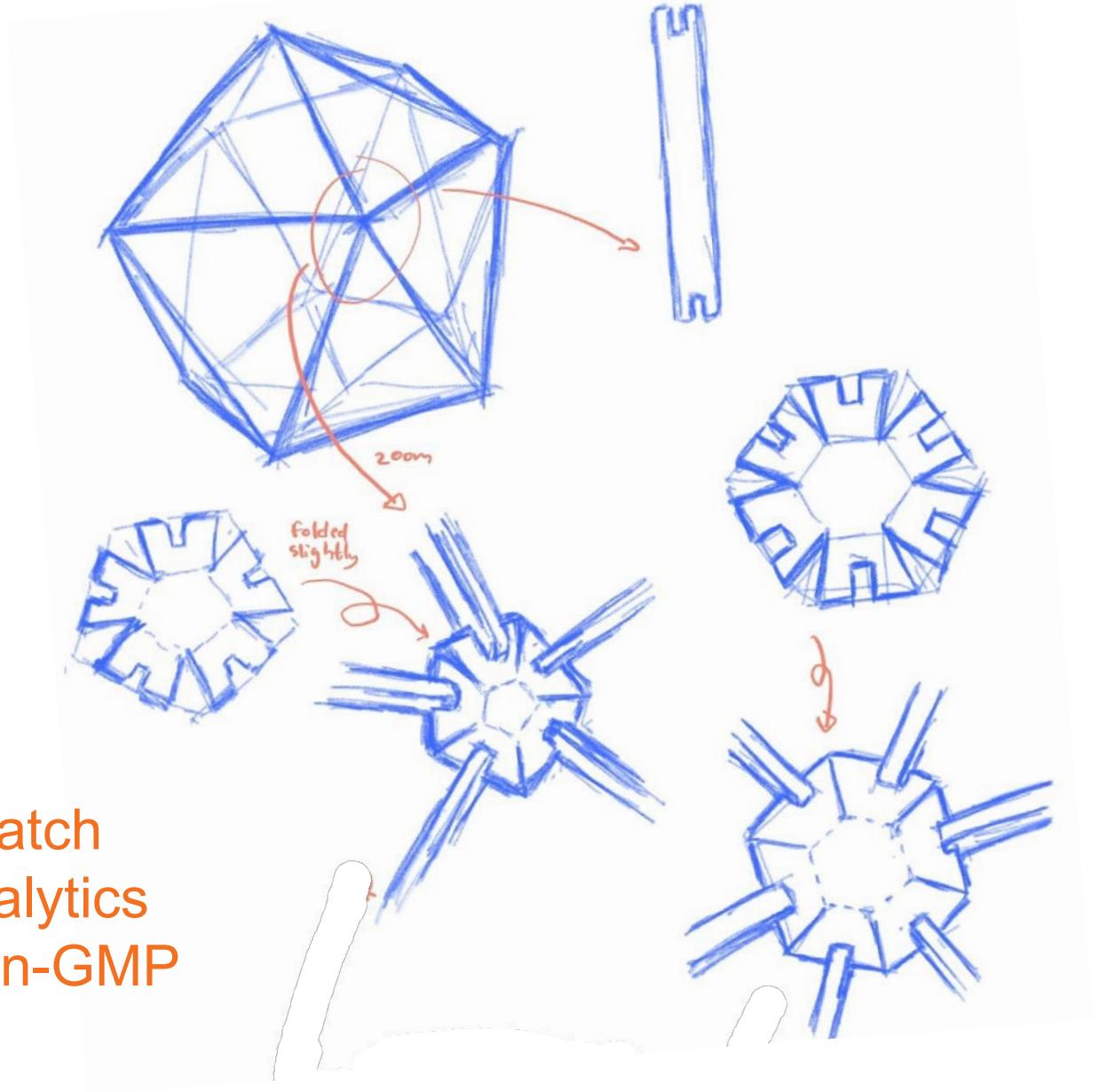
The mythical Egg-laying Wool-milk Sow !

IMAGING A UNIVERSAL PLATFORM

Any
Serotype
Transgene
Cell Line
Media
Resin

Any
Volume
Scale
Site
Use Case

Minimal Viable Process



How AAV was made – Demonstration Batch
How AAV was measured – Available Analytics
What was observed – 10 L and 50 L, non-GMP

What will make this baseline process viable for you on day 1?

How does open-access evolve from a feature to a catalyst?

Collaborative Product Development

Voice of Customer Survey for Early Adopter Use Cases

1 Purpose

Propose an Open-Access AAV Platform

Identify User Requirements & Desirable Features

2 Adopters

Patient/Parent Led Foundations/Initiatives

Academic Research & Medical Centers

Vector Cores, Testing Centers & Contract Manufacturers

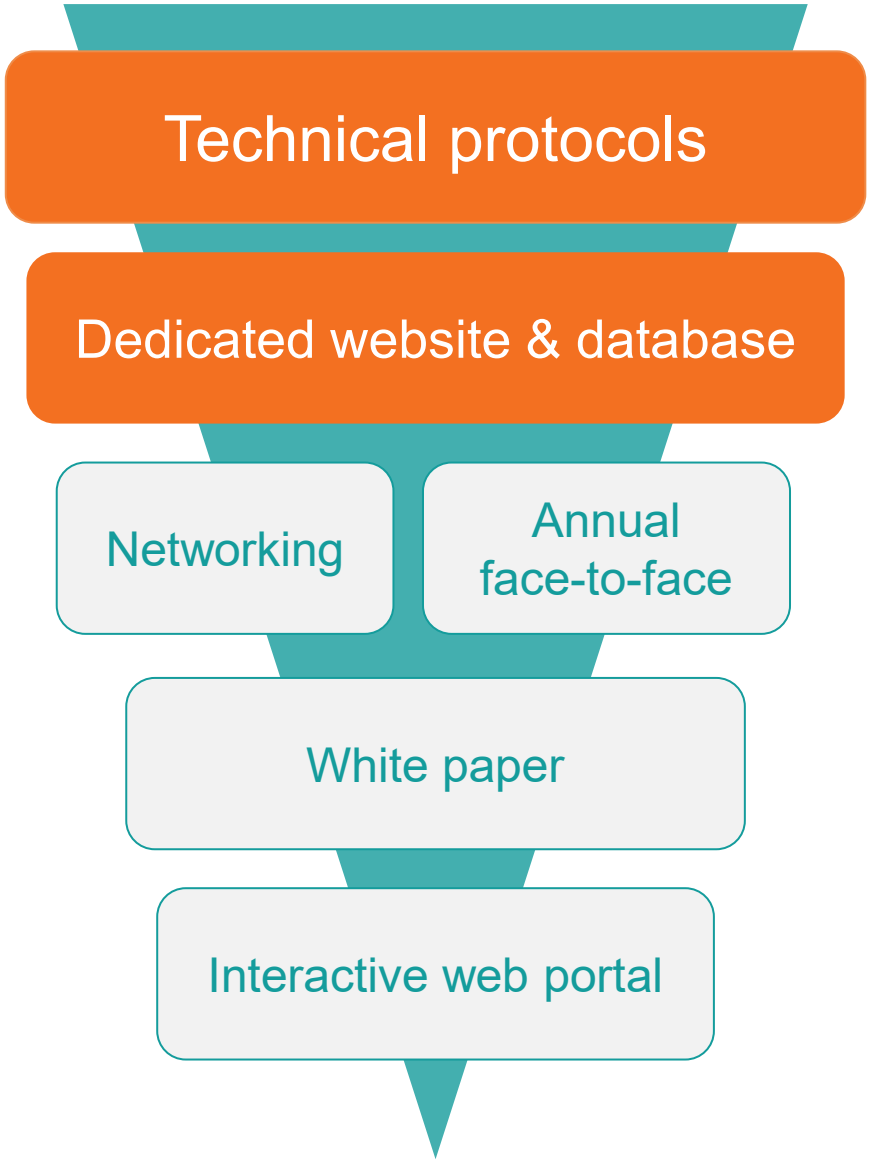
3 Method

Qualitative Market Research & Concept Testing

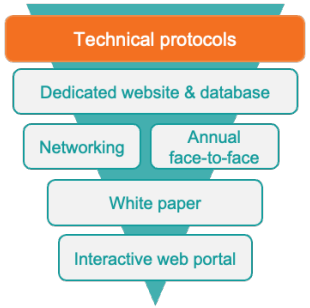
Facilitated Virtual Interviews

Results

A presentation of
"Service Levels"
signaled the most desirable
References and Tools



Collaborative Product Development



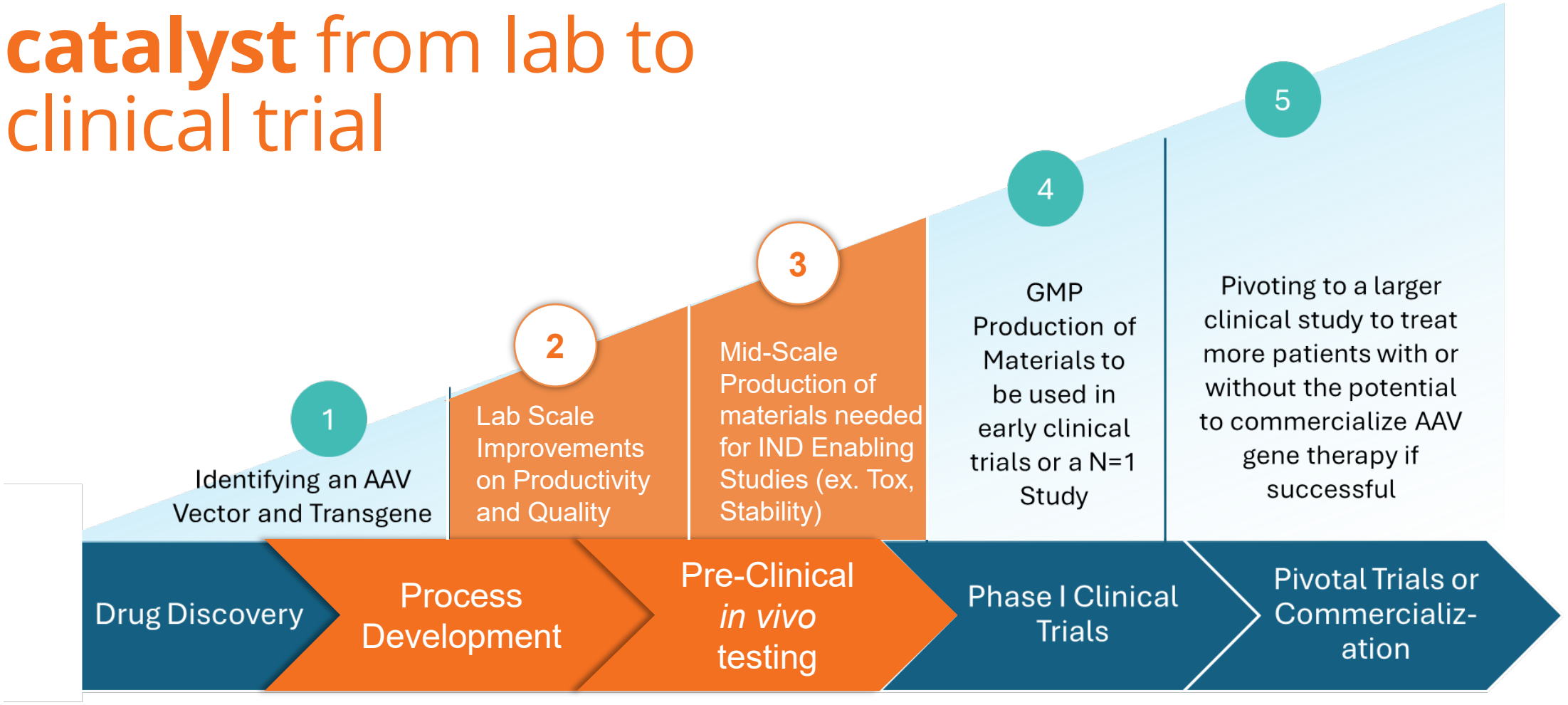
Complexity Scale

Conceptual → **Operational** → **Transferable**

Conceptual	Operational	Transferable
Materials & Methods	Technical Protocols	Batch Records, Test Sheets, Standard Operating Procedures
Results & Discussion	Method Procedures	
	Data Sets	

What other **references and tools** would be useful?

NIIMBL MVP as a **catalyst** from lab to clinical trial



BEFORE

What risks are there with selecting an open platform, and how can we mitigate them?

AFTER

What role would the open-platform manager fill in the preparation for an IND?

INTERACT Meeting | Pre-IND Meeting | IND Submission

NIIMBL | Viral Vector Manufacturing & Analytics Program

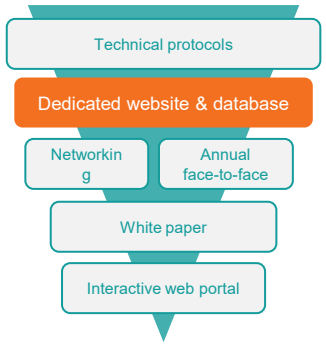
Coffee Break Time!

Stretch, sip, breathe...
we'll be back shortly!

NIIMBL Public Workshop
February 2026

Supporting the NIIMBL Platform

Chris Williams
Viral Vector Program Co-Lead



Online Resources

UNDER DEVELOPMENT

NIIMBL Platform Beta Version

Technical Elements in Development

Process

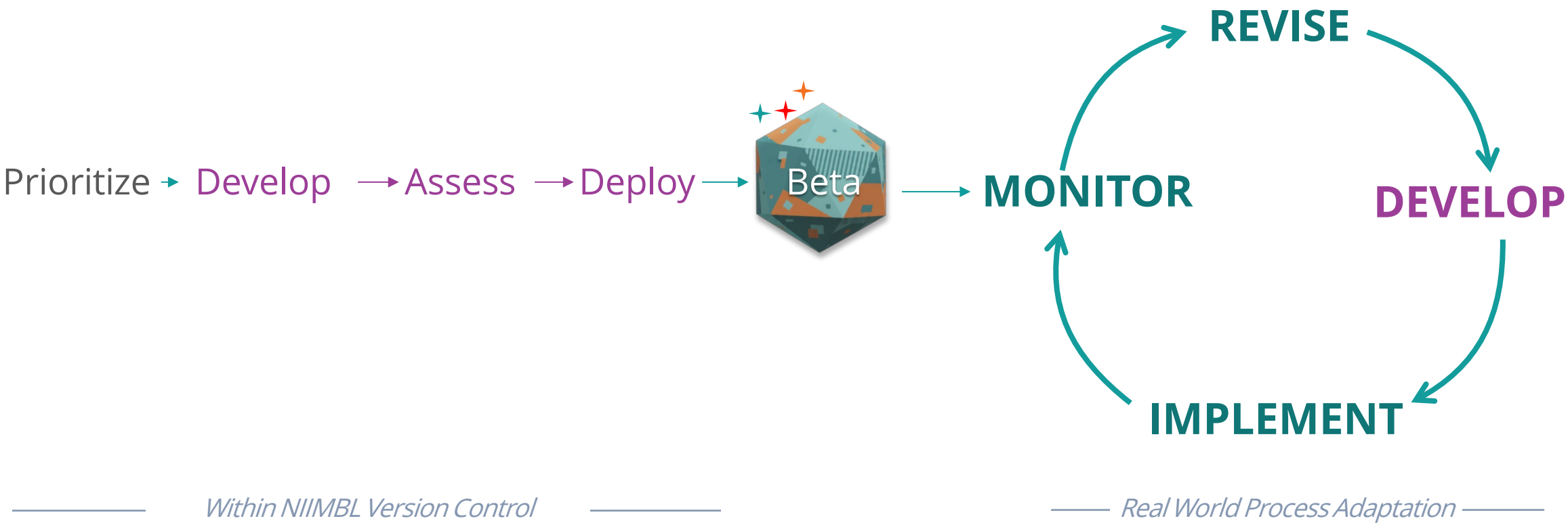
Bill of Materials
Cell Expansion
Transfection
Harvest
Capture
Full Enrichment

Analytics

Genome Titer
Capsid Titer
Full : Partial : Empty
Aggregation
Sequencing

Continuous Improvement

What assessment criteria is considered sufficient for Technical Element deployment?



What development packages would be **most valuable** to your processes?

Process

Bill of Materials
Cell Expansion
Transfection
Harvest
Capture
Full Enrichment

Analytics

Genome Titer
Capsid Titer
Full : Partial : Empty
Aggregation
Sequencing

Evolution of the Web

Web 1.0

The era of the static internet

Web 2.0

Interactive, user participation, social networking

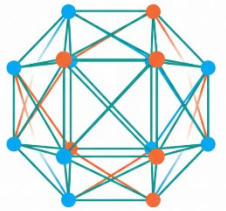
Web 3.0

Algorithms, AI, extensive networking of data

What is the **desired level of interactivity** for within the NIIMBL Platform?

Access information

Collaborate with users



Collaborate with users' information

Hypothetical Use Case #1

Risk Assessment and Gap Analysis for Process Adaptation

Sponsor and Manufacturer perform assessment against reference documents

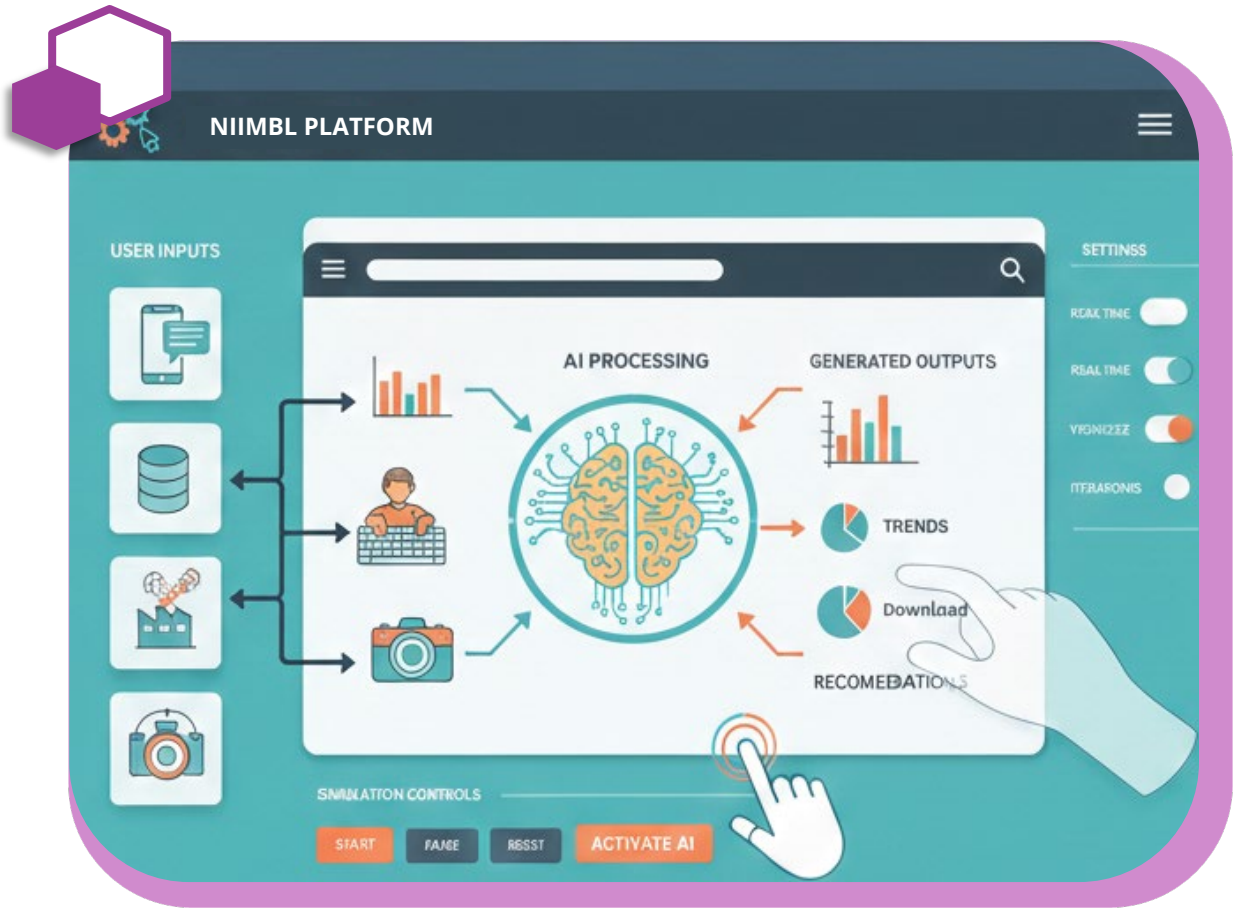
Web 1.0

Collaborative Assessment with reference documents in addition to context and supportive data

Web 2.0

Hypothetical Use Case #2

Risk Assessment for process adaptation within a community of users

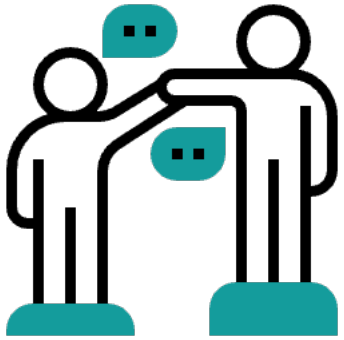


- Relevant user process and product data is collected
- Platform knowledge is built on patterns in performance
- Efficiencies gained in future users' process and analytical development

Web 3.0

NIIMBL Platform Training

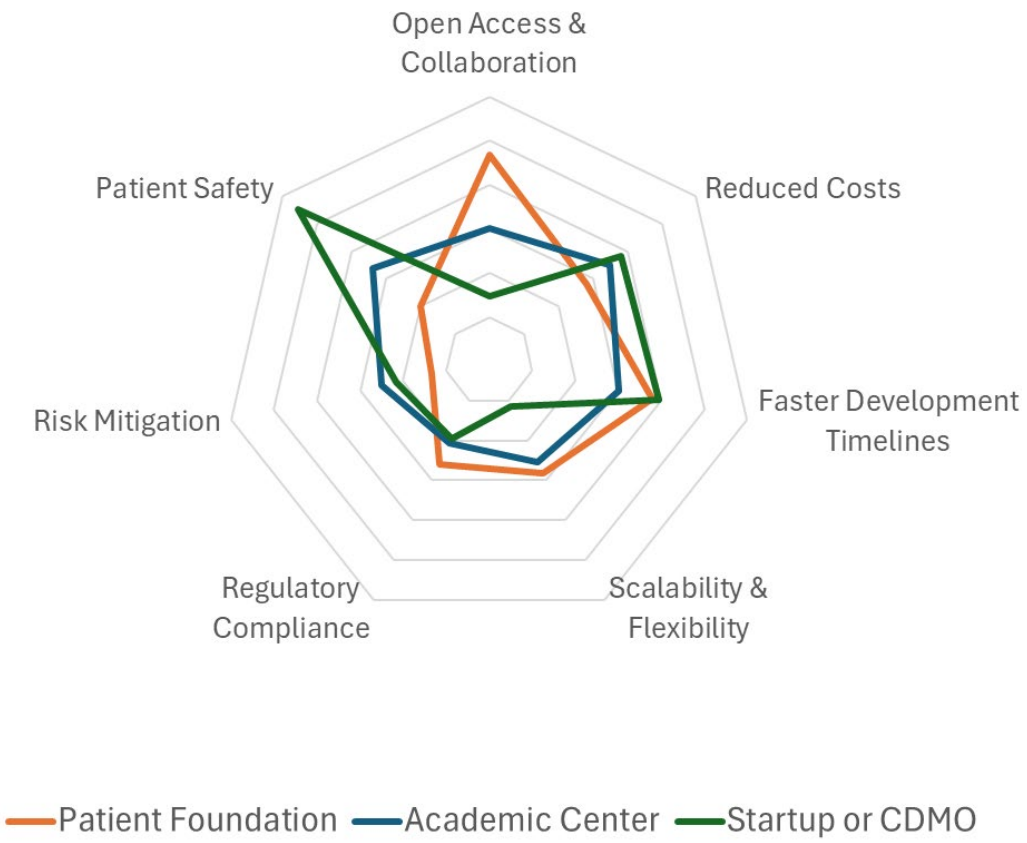
Self-Paced Training



Mentorship

Networking

How would you **integrate a platform expert** into your development team?



Measuring Success

1. Speed
2. Cost

Discussion & Next Steps

Thank you for your strategic input today.

Let's begin our discussion.

Workshop High-level Summary

Your Input Will Shape Platform v1.0

Feedback:

1. Data sharing would be helpful
2. Documentation on unit operations and levers or ways to customize.
3. Documentation of analytical methods including IND-ready justification of specifications support.
4. Vector cores can run the processes without using CDMOs, thereby reducing cost
5. Cost is key. Provide COGS information. Focus on reducing analytical and materials costs.
6. Regulatory document templates would be helpful.
7. Materials should include cell bank, plasmids, and reference standards with upfront details on licensing costs.
8. Process should be somewhere between Operational and Transferrable
9. Desire to be able to collaborate with individuals and with the data.

Closing

CONTACT US @

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- Chris Williams: chrisrw-ctr@niimbl.org

Program Manager:

- Angie Snell Bennett: asbenn@niimbl.org

NIIMBL National Meeting | Summary - 2026 NIIMBL National Meeting