Viral Vector Manufacturing: Meeting Escalating GMP Demand for Gene Therapies

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Agenda

01 The Challenge – Fast Growth Across Different Vectors
02 Flexible Facilities – Efficient Asset Utilization
03 Robust & Scalable Platforms – Speedy & Reliable Delivery
Demand for Viral Gene Therapy Manufacturing Growing Across Multiple Types of Vectors

**AAV**
- Numerous promising and diverse clinical results from Hemophilia to genetic blindness to spinal muscular atrophy - driving increased demand
- Added demand from gene editing applications

**Lenti**
- Large demand driven by CAR-T and other ex vivo HSC applications in rare diseases
- In vivo candidates hold additional promise

**Adeno**
- Encouraging therapies advancing towards market (oncology, infectious disease)
- Several later phase candidates progressing in pivotal trials

**Oncolytic**
- Amgen’s TVEC approval was a major catalyst. Several astonishing early clinical trials results
- Attracting substantial new investments (VC, BMS, Pfizer, Celgene, etc.)
Manufacturing Process Diversity and Immaturity Makes the Challenge Complicated

- AAV
  - Triple Transfection HEK293 (adherent or suspension)
  - Baculovirus / sf9 (suspension)
  - HeLa producer cell line (suspension)
  - HSV (adherent or suspension)

- Lenti
  - HEK293T (adherent or suspension)

- Adeno
  - HEK293 (suspension or adherent)
  - PER.C6 (suspension)
  - Others (generally adherent)

- Oncolytic
  - HEK293 (adherent or suspension)
  - Vero (adherent)
  - Others (adherent & suspension)
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01 The Challenge – Fast Growth Across Different Vectors

02 Flexible Facilities – Efficient Asset Utilization

03 Robust & Scalable Platforms – Speedy & Reliable Delivery
Adoption of Modular Cleanroom Construction and Single-Use Technologies Are Critical

- Capital efficient
- Fast construction / installation
- Flexible to accommodate variety of unit operations (cell factories, wave, roller bottle, SUBs, etc)
Lonza Is Building World’s Largest (Anticipated) Viral Vector Facility in a Suburb of Houston, TX*

**Significant up-front investment** in infrastructure / support areas

**Oversized “ballroom” manufacturing areas** allow for quick modular clean room expansion

Initial rooms on track to be **GMP-ready late 2017**

*NOTE: Relocating from existing smaller Houston facility which will continue to operate as needed until new facility is operational*
Concept for Commercial Capacity Expansion

Initially oversized support areas
- Warehouse, buffer prep, material staging, QC, utilities, autoclave admin, etc.

Initial cleanrooms to supply initial demands

Expansion “ballroom” space
- Additional modules can be installed quickly with relatively little incremental CAPEX to meet growing demand
On Track – Initial Late 2017 Capacity Already Sold; Taking Orders for H1 2018
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03 Robust & Scalable Platforms – Speedy & Reliable Delivery
Platforms Make Operations Simpler, More Reliable and Efficient

Investment in novel process technology & innovation

- Standardize on minimal number of essential cell lines
- Standardize on suspension culture in single-use bioreactors
- Standardize on versatile single-use unit operations that can be reliably scaled and developed quickly and predictively

Cell lines:
- AAV
  - Triple Transfection HEK293 (adherent or suspension)
  - Baculovirus / sf9 (suspension)
  - HeLa producer cell line (suspension)
  - HSV (suspension)
- Lenti
  - HEK293T (adherent)
- Adeno
  - HEK293 (suspension and adherent)
  - PER.C6 (suspension)
  - Others (adherent)
- Oncolytic
  - HEK293 (adherent)
  - Vero (adherent)
  - Others (adherent & suspension)

Image Credits: University of Louisville; Sartorius
Example: Baculovirus Platform Is a Commercially-Viable Platform for AAV Today

**Upstream**

- Baculovirus Generation
  - Baculovirus-RepCap
  - Baculovirus-GOI
  - SF9
  - Co-infect
  - SF9
  - AAV-GOI

**Downstream**

- Capture Column
- Polishing Column
Key Takeaways

**Demand for vector manufacturing** growing across several types

**Flexible facility designs** can quickly and efficiently add capacity in line with demand

**Manufacturing platforms** are key to operational excellence