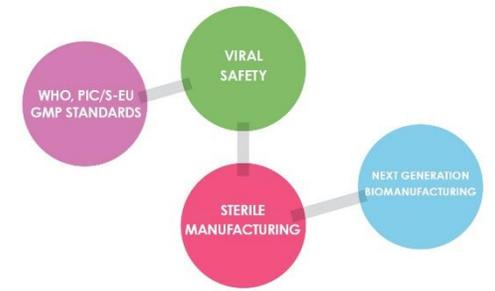


Wallace I Torres, BS, MBA, PhD, Singapore

- Executive Director – Site Quality Head, Amgen Singapore Manufacturing
- President-Elect of the Parenteral Drug Association Singapore Chapter



Transforming operations with next generation biomanufacturing

Wallace I Torres, BS, MBA, PhD
18 December 2019

Transforming Operations with Next Generation BioManufacturing

Wallace Torres

Executive Director – Quality Site Head
Amgen Singapore Manufacturing

Amgen's Development Strategy Uses a Multi-Modality Approach



- **Biologic medicines diverse and highly engineered**
- **Target Product Profile drives development activities**
- **Heterogeneity requires need for flexibility and adaptability**

Source:
<https://www.amgenscience.com/the-shape-of-drugs-to-come/>

Amgen is Evolving Operations Capabilities to Enable Delivery of Progressive/Multi-Modality Medicines

Amgen Strategy

Innovative Medicines

Branded Biosimilars

Global Geographic Reach

Next-Generation Biomanufacturing

Improved Drug Delivery Systems

Capital Allocation and Investing for Long-Term Growth

- Improve **patient experience** and **differentiate products** with innovative delivery devices
- More **targeted** products
- Maintain **modality independence**
- Pursue **strategic acquisitions**
- Consider **Biosimilars** opportunities
- Establish operations in **new markets**
- Manage **demand uncertainty**
- Meet **local SKU profile/requirements**

Outcome

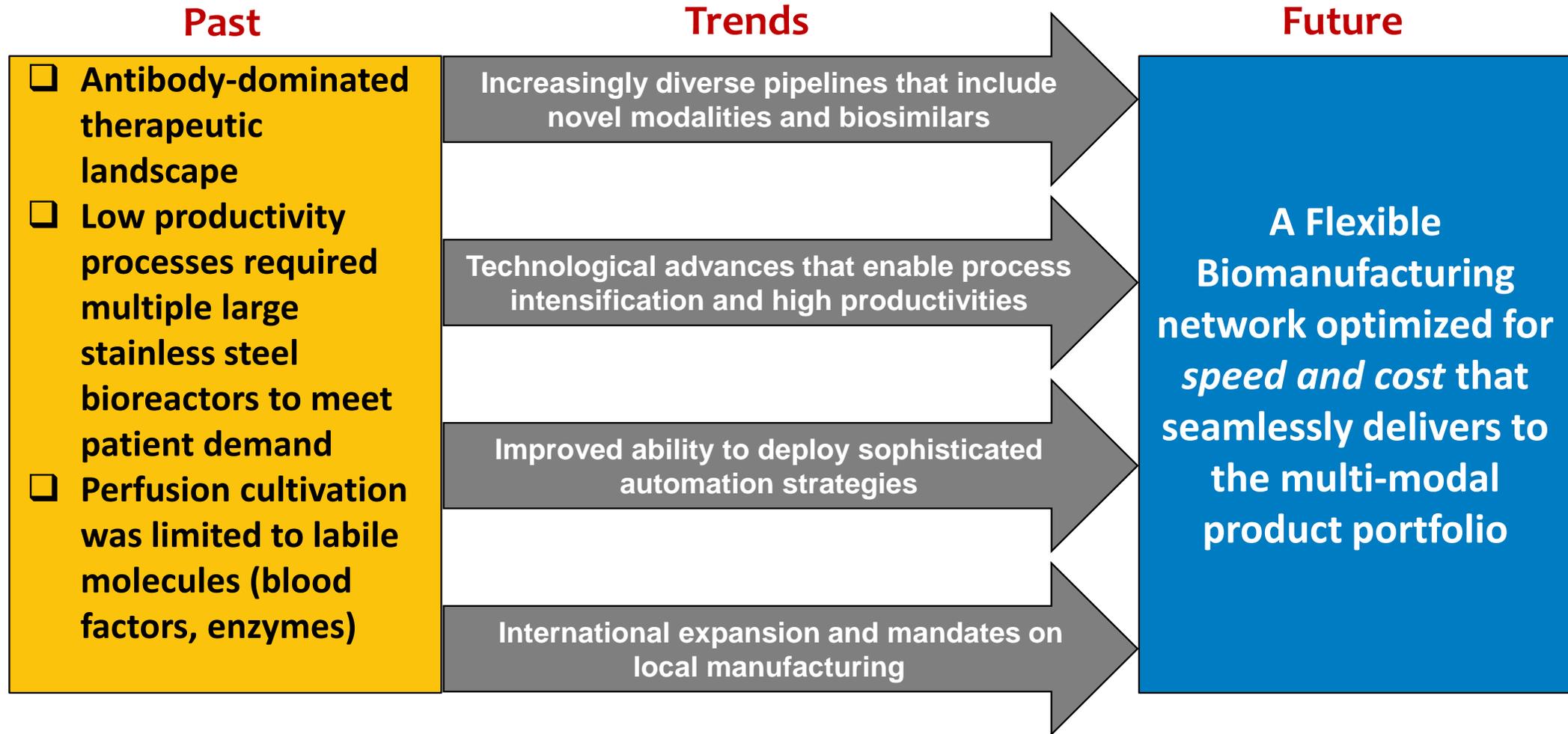
Product Heterogeneity

Greater Demand Uncertainty

Lower Per Product Volume

Balance use of existing footprint with addition of new capabilities to lower costs, and increase flexibility and speed

Flexible Manufacturing is One Lever to Optimally Deliver a Multi-Modal Product Portfolio to Patients



Amgen Singapore Manufacturing: Amgen's Newest Operation and First in Asia

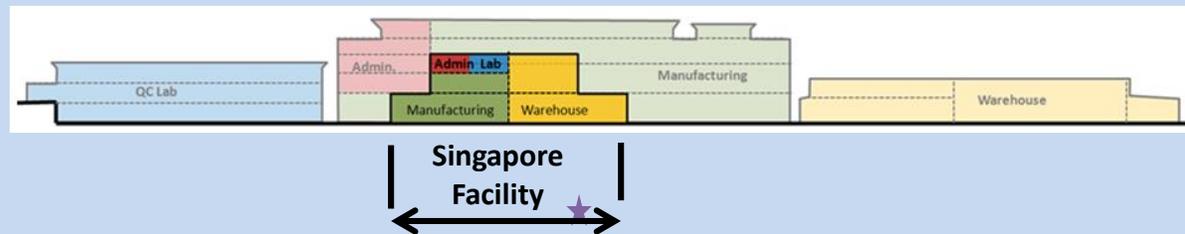


Conventional Facility—750k sq ft

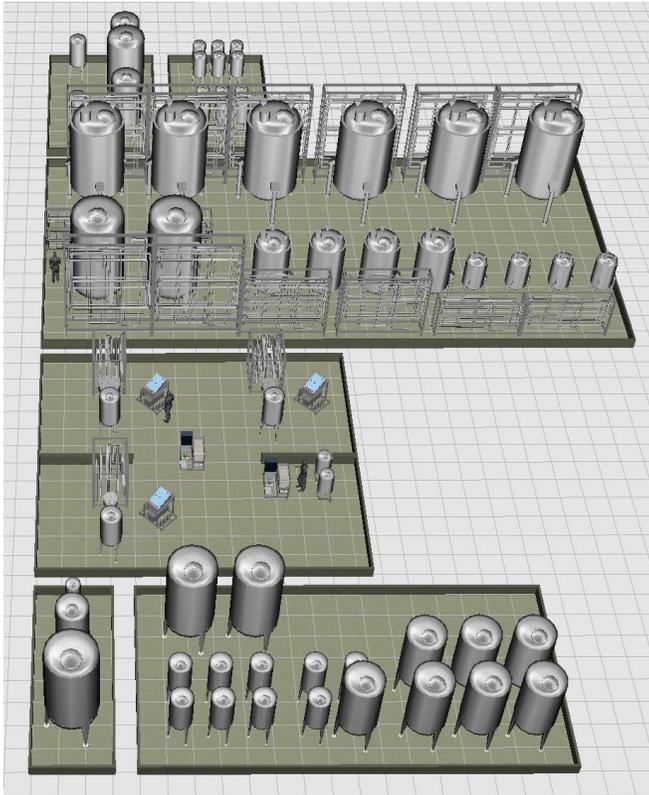
QC Lab	Utilities
Mechanical Support	Warehouse
Manufacturing	Admin and Amenities

Next-Generation Facility
120k sq ft

~ 80% Size Reduction With
the Same Throughput



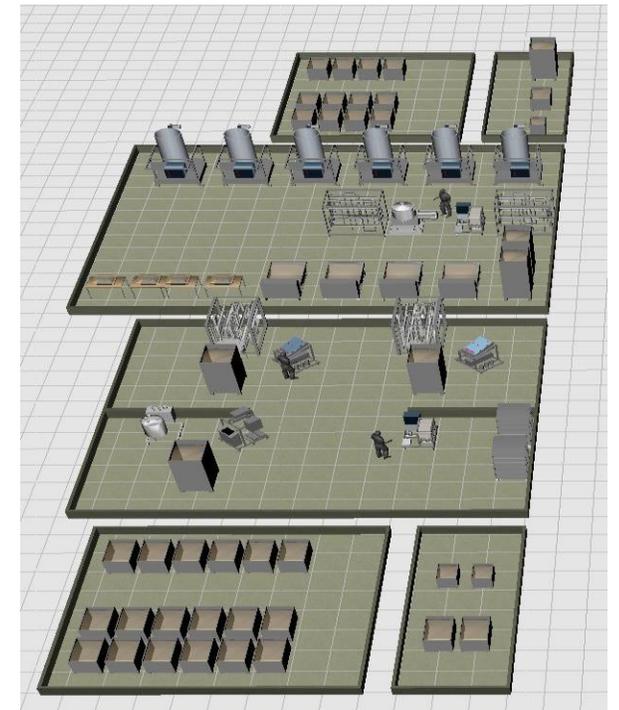
Conventional



Key Enabling Technologies

- High titer processes
- Single-use systems
- Modular design and construction
- Connected processing
- Online / At-line analytics
- Real-time remote monitoring
- Raw material variation control

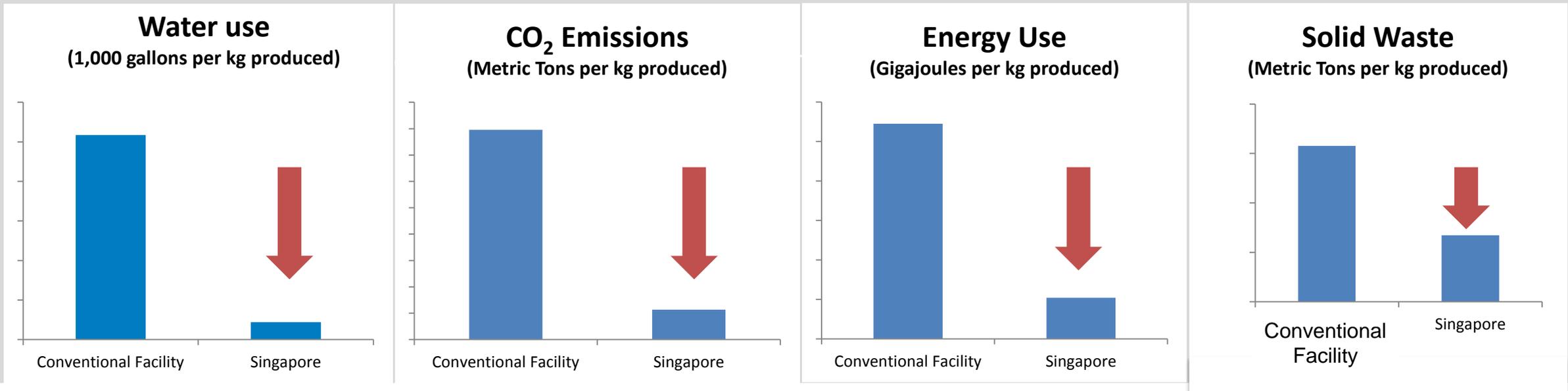
Flexible



Source of illustrations: Next-Generation Facilities for Monoclonal Antibody Production, N. Guldager, Pharmaceutical Technology (July 2009)

Next Generation Biomanufacturing Technologies Provides Key Benefits

- Enables us to dramatically increase our “bulk” production capabilities vs conventional alternatives
 - 1/4 of the capital cost; 1/2 of the construction time; 1/3 of the operating expense
- Manufacturing site flexibility, significant cost savings, estimated cost reduction per gram of protein
- Reduce environmental impact: Less water for heating, cooling, and cleaning of equipment; Smaller facility and lower air quality classifications



Amgen's Reconfigurable Manufacturing System is Central to Basis of Design

Cell Culture

High cell culture productivity in small bioreactors

- Significantly reduces facility footprint

High utilization of single-use equipment

- 95% of product contact surface is single-use
- Closed operations; pre-sterilized systems; aseptic connections

Connected/continuous purification processing

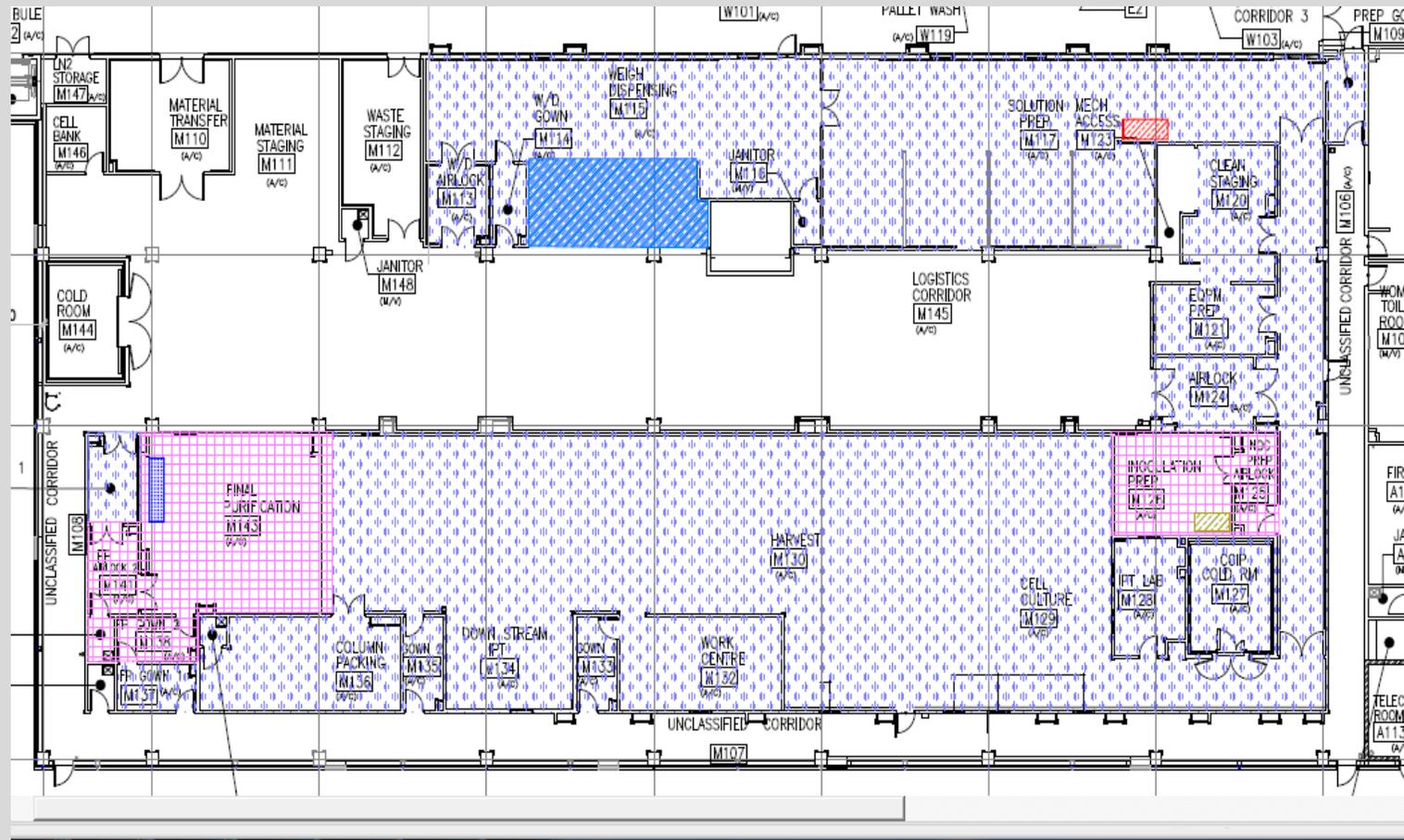
- Eliminates product pools between unit operations

Integrated manufacturing layout

- Smaller facility impact to process and equipment changes



Facility Layout is Efficient and Well-Controlled to Protect Product



Central manufacturing suite

- Cell culture through viral filtration
- Closed processing via aseptic connections
- Reduced personnel and maintenance

Area classification

- Closed processing allow most operations to occur in ISO 9

In-line and at-line testing

- Enhanced process control, detection and response

Workflow



Analytical cycle time limits information availability for real-time decisions

New Analytical Technology Leads to Timely and Impactful Quality Decision Making

Immediate water quality feedback



Microbe ID in 2 days for faster root cause identification



Immediate verification of titer on the floor



Immediate ID of raw materials, Fingerprint for attribute trending



Immediate endotoxin results stops the process

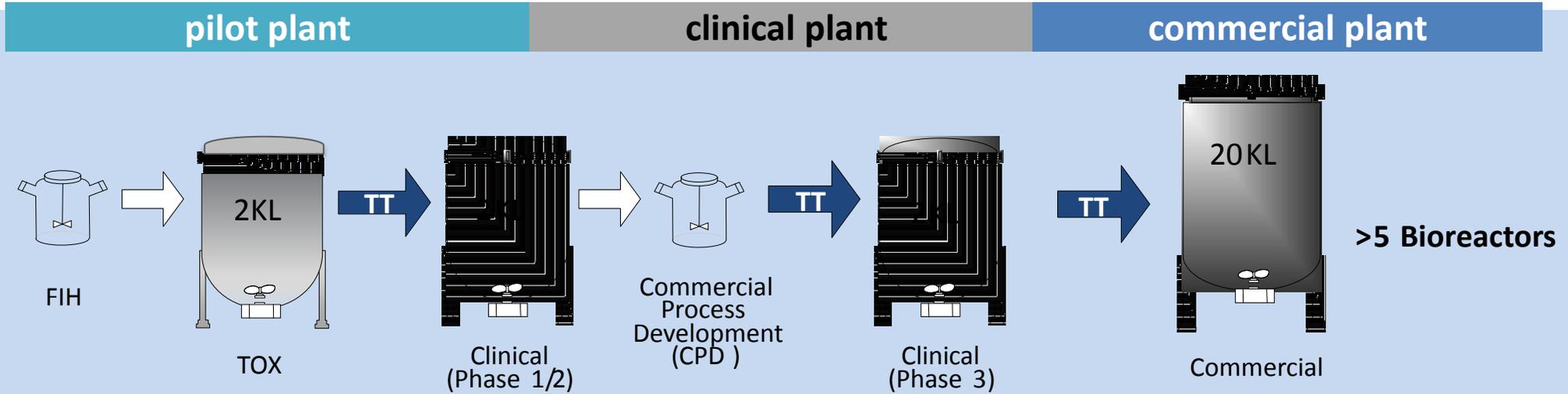


Determine step protein concentration yield real time on the floor without sample dilution



Next Generation Biomanufacturing Accelerates Commercialization Timeline

Traditional



Next-Gen Mfg



Process Performance Qualification Completed 29 Months After Land Acquisition



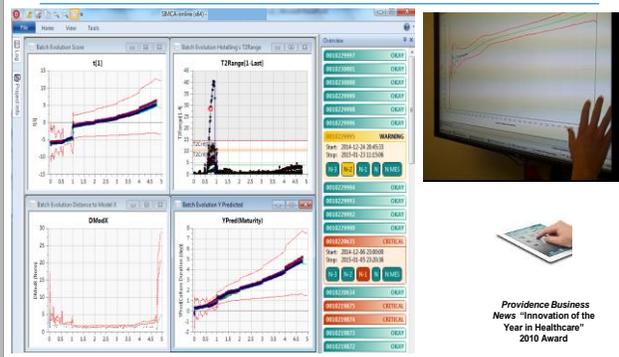
Regulatory inspections conducted; Licensure achieved

We Continue to Evolve Our Operations With Next Generation Biomanufacturing



Modular with Connected Processing

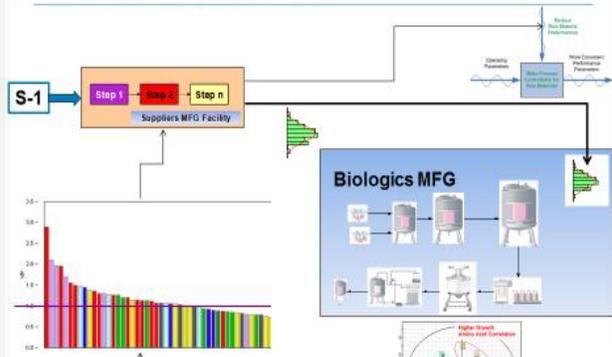
RT-MSPM technology is improving our process understanding and enabling holistic proactive monitoring



Providence Business News "Innovation of the Year in Healthcare" 2010 Award

Real-time Remote Monitoring

Manufacturing Data Analysis Indicate Raw Material Variation Contribution to Process Variance

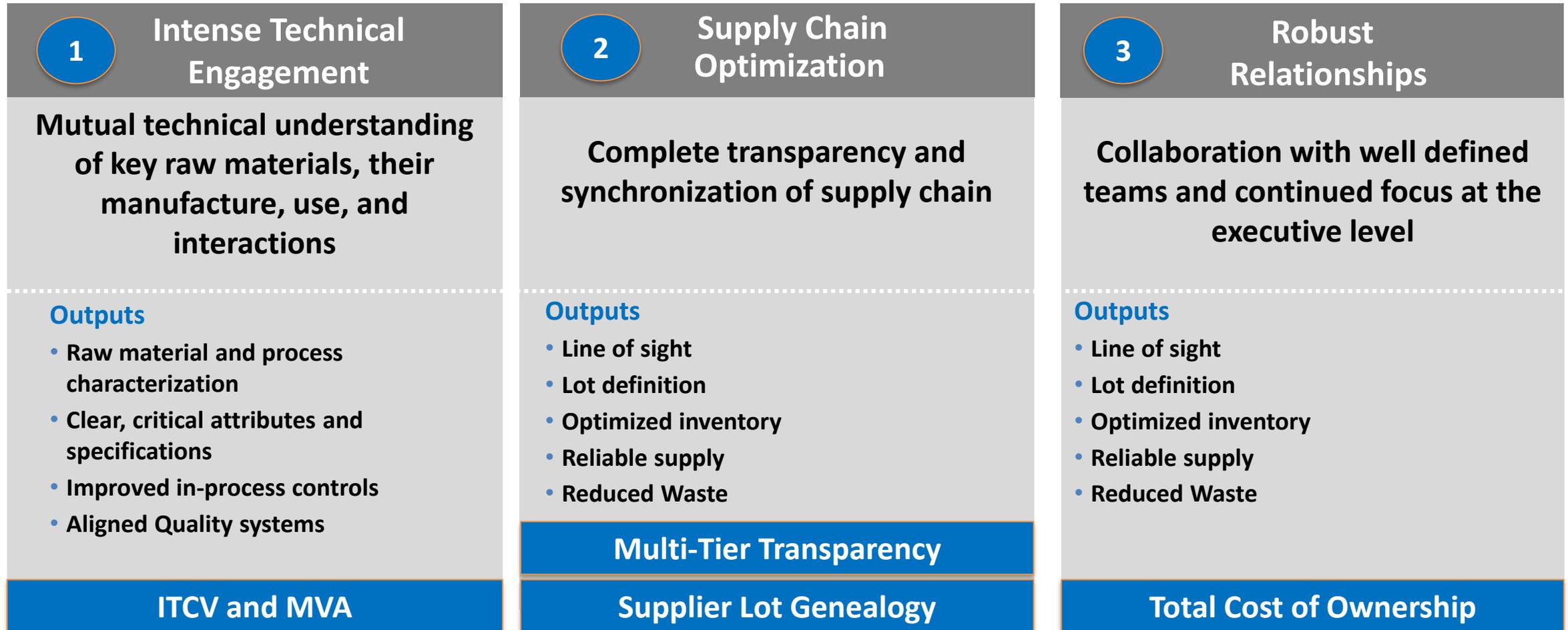


Raw Material Variation Control

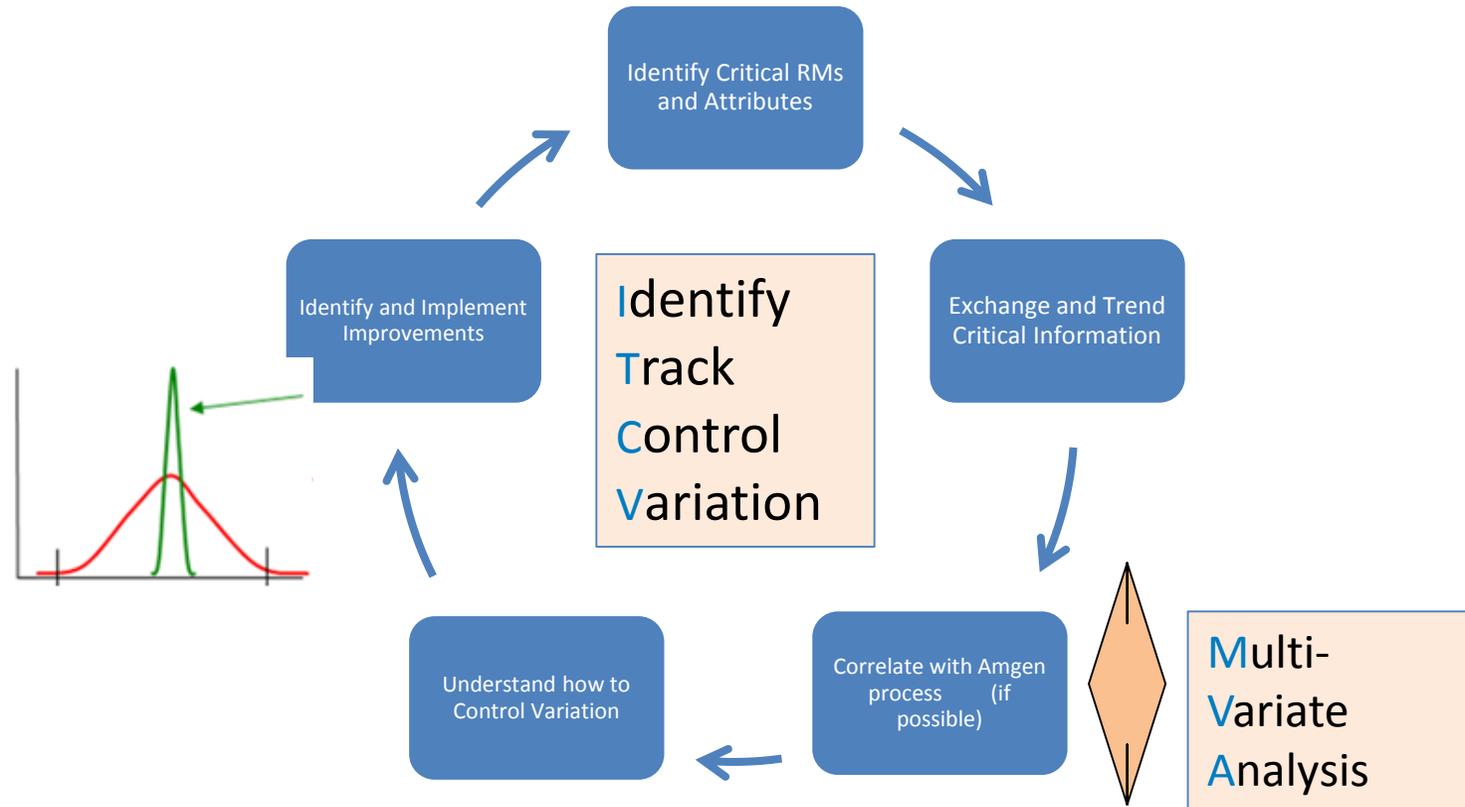


Single-use technologies

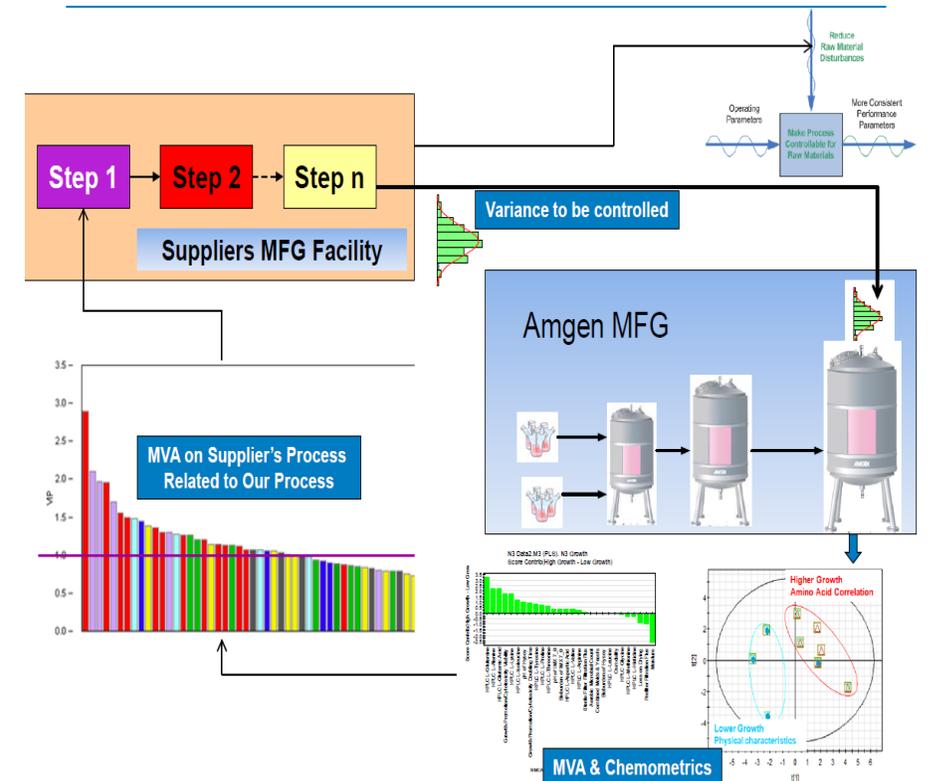
Amgen's Supplier Relationship Is Designed to Improve Quality, Increase Reliability, and Decrease Variability



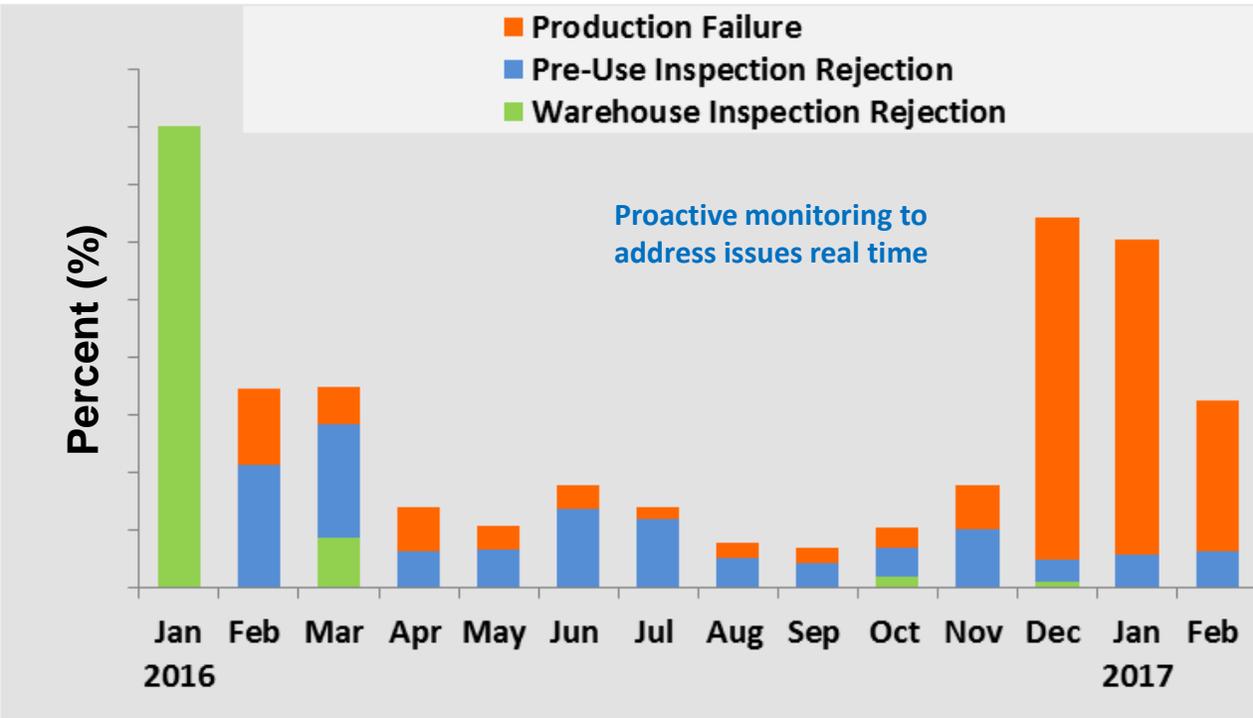
Technical Engagement Involves ITCV (Identify, Track and Control Variation) and Multivariate Analysis (MVA)



Variance in Suppliers Manufacturing Process is Transmitted to Our Processes

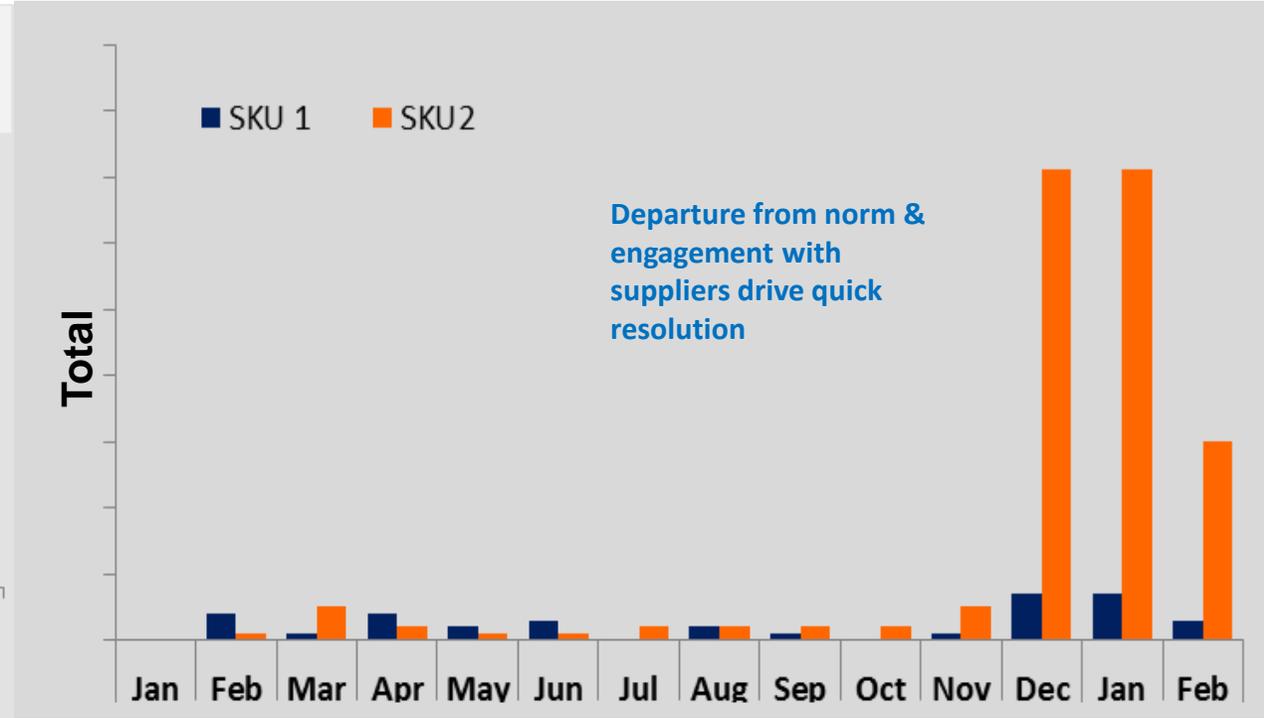


Single Use System Monitoring Focused on Understanding Failure Modes and applying Corrective Actions



Month

Failure Rate



Month

Failure by SKU

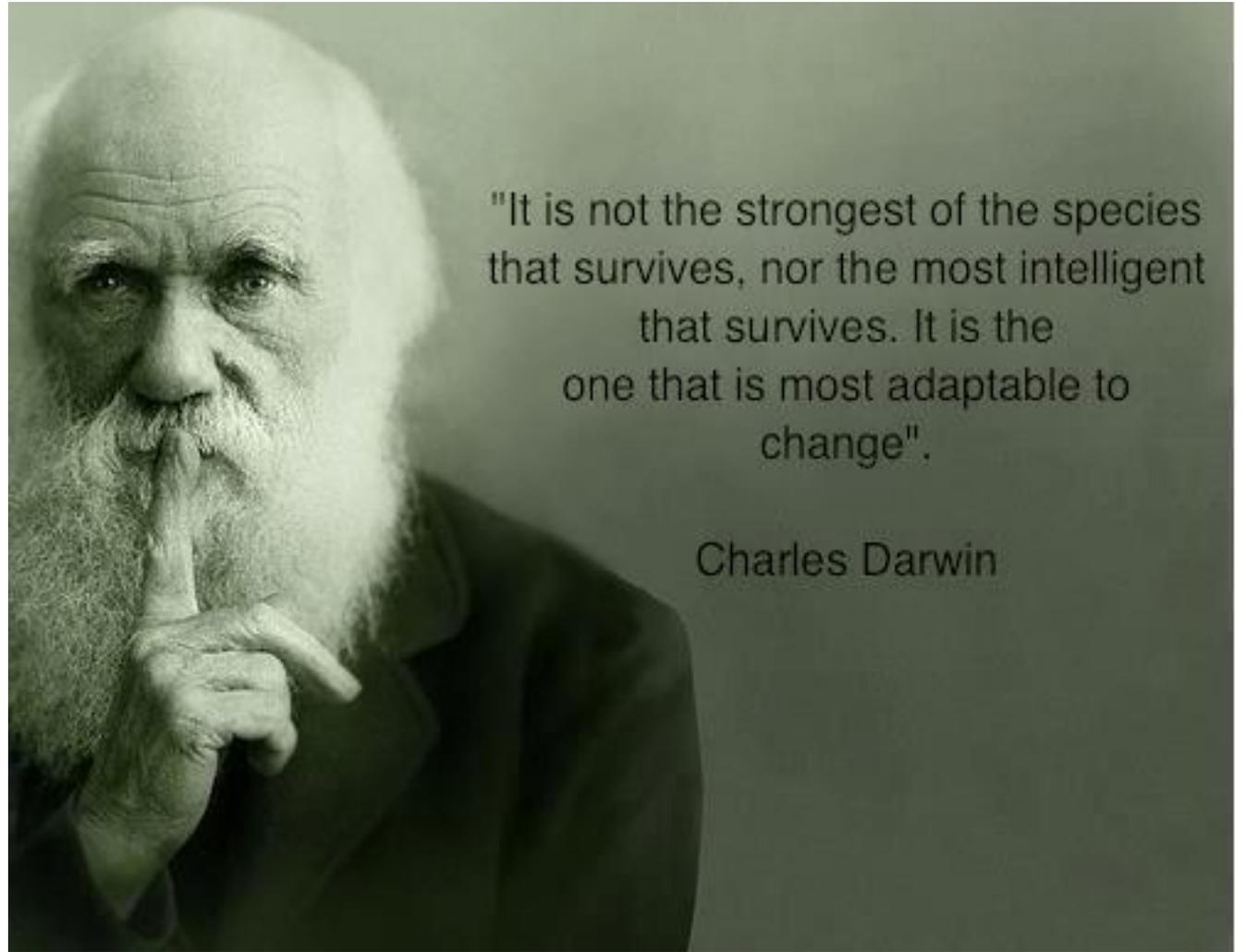
External and internal factors are driving changes in biologics production which demand new operational capabilities

Differentiating with efficiency, flexibility and reliability

Flexible drug substance manufacturing is now a viable option for commercial operations

We will continue to advance progressive manufacturing technologies into our Flexible Manufacturing operations

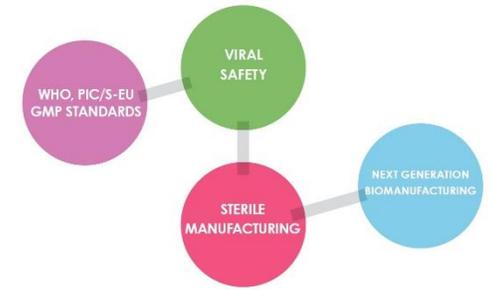
Partnership with suppliers is critical for mutual success



GaBI Educational Workshops

18 December 2019, Hotel Gran Mahakam, Jakarta, Indonesia

2nd ASEAN Educational Workshop on GMP FOR BIOLOGICALS/BIOSIMILARS



GaBi

GENERICS AND BIOSIMILARS INITIATIVE

Building trust in cost-effective treatments

