Ensuring the Supply of Quality Biopharmaceuticals: *Integrated Manufacturing Network* & *Continual Improvement of Manufacturing Process*

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Presentation Overview

Our Biologics Network

Complex and Evolving Operating Environment

Strategies and Tactics to Address Environment

Closing Thoughts
Biologics is made up of 11 internal and 37 external sites...

Our Biologics Network

...we manufacture over 20 products that serve our patients globally
There are many complexities to get to the final product.
Supply Reliability

*Ability to continuously & reliably supply medicines to patients*

- Dual / Multiple Sourcing
- Agility Capacity
- Risk Mitigation Inventory

Business Continuity Management

Risk Assessment & Management – focus on prevention

Process Robustness – basis for resilient supply

Manufacturing Network: Combination of internal and external partners to achieve pillars of supply chain resiliency
Ensure the Network Can Respond to Demand Volatility

1. Agile capacity – target 80% internal utilization
2. Ability to dual source and maintain inventory targets

Maintain a Reliable Asset Base at Defined Utilization

1. Optimize the size, shape and expertise of each site to ensure fit-for-purpose
2. Base Load - external manufacturing network

Implement Sourcing Solutions Applicable to Product Life Cycle

1. Launch products internally where capability & capacity exist
2. Outsource mature products, to create available capacity
Biologics Manufacturing Plan

Multi-year plan for creating an Agile and Robust Manufacturing Network

Near Term (<12 months)

- Increased run rates in Basel, Singapore and Oceanside facilities
- Debottlenecking efforts in South San Francisco, Penzberg, Basel and Singapore
- Continue to transfer existing products into new Drug Product plants in Hillsboro Oregon and Kaiseraugst Switzerland

Mid Term (1-3 years)

- Strategic Investments in Internal Drug Substance Manufacturing
- Strategic Investments in External Drug Substance and Drug Product Manufacturing

Long Term (4+ years)

- Internal Antibody Drug Conjugation Manufacturing
- Additional investment in internal Drug Product Manufacturing
Biologics Manufacturing Plan

**Contract Manufacturing Operations (CMO) Partnership and Oversight**

- **Organization & Governance**
  - Establish one Biologics network approach
  - Joint management teams at senior and operational levels.
  - Lifecycle management: Select-Implement-Manage-Decommission

- **Qualification of new CMOs**
  - Contract Quality Requirements (CQR’s) including Quality Risk Management (QRM), Quality Agreements, Tech Transfers
  - CMO selection and filing readiness requires approval by Head of OU Quality
  - GMP audits by Corporate Inspection Management

- **Establish Key Strategic Relationships**
  - Co-investment; Long term supply commitment (base-load CMO’s); Alignment of Contract Quality Requirements; Quality Improvement Plans

- **Ongoing oversight**
  - Dedicated team, Person in Plant, as appropriate
  - Key changes, deviations, and final batch disposition managed by Genentech/Roche
  - Issues escalated to Quality Review Board (QRB) and regular QSMR
Technical Product Management (TPM)

Cross-functional product management teams created to provide strategic leadership for all commercial products

Benefits

- Proactive and strategic view
- Integrated product portfolio visibility and oversight
- Product and process capability
- Supply chain and product quality health
- Quality inputs assessed throughout the product lifecycle
Manufacturing Process - Use of QbD in Development

Advantage for Overall Product Quality Life Cycle Risk Management

- Quality by Design (QbD) can be a highly effective global driver of change in the industry providing:
  - Enhanced level of assurance of product quality and process robustness
  - More rapid resolution of manufacturing discrepancies
  - The foundation for continued improvement and risk-based regulatory action

- Ultimate goal is a process that sustains quality supply

- High incentive for regulators and the industry to work together to realize the overall benefits and objectives of QbD, and to enable the vision of risk-based, lifecycle management
Leveraging Engrained Quality

*Increasing compliance sustainability and reliable quality supply*

**Optimize PQS and IT Systems / Business Process Integration** *(PQS Realization/Monitoring, IT Roadmap)*

**Track & Trend and improve process capability** *(Quality by Design, Six Sigma, Post Approval Lifecycle Management)*

**Continue to develop leadership & technical competencies and depth** *(Quality Certification Program (QCP), Investigator Certification Program (ICP))*

**Advance compliance sustainability and proactive risk management** *(Technical Product Management (TPM), Quality Risk Management (QRM))*

**Continue to enhance quality ownership, and assess and advance quality culture** *(Mindset training & tools, Senior Management Engagement)*
The ability to meet global supply demand requires....

Key Take-Aways

- Robust Quality Systems
- Network of internal and external sites
- Multi-Year plan to build agility and flexibility
- Dual sourced, reliable Supply Chain strategy

It’s a journey that takes focus and resilience...
Doing now what patients need next