Transforming Biotechnology Manufacturing: Adapting Technology to a Changing Environment

Robert A. Bradway
President and COO
Amgen’s Mission…

...to serve patients

Manufacturing excellence is critical to achieving this mission and a source of competitive advantage.
About Amgen

- Founded in 1980 in California, the “birthplace” of biotechnology
- One of the first companies to be successful with biotech medicines
- Now the world’s largest independent biotech company, with 17,000 staff in 50+ countries
- Our medicines have reached more than 22 million patients

**Marketed Products**

<table>
<thead>
<tr>
<th>EpoGen (Epoetin Alfa)</th>
<th>Neupogen (Filgrastim)</th>
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</thead>
<tbody>
<tr>
<td>Aranesp (darbepoetin alfa)</td>
<td>Neulasta (pegfilgrastim)</td>
</tr>
<tr>
<td>Enbrel (etanercept)</td>
<td>Sensipar (cinacalcet) Tablets 30mg, 60mg, 90mg</td>
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<tr>
<td>Mimpara (cinacalcet)</td>
<td>Nplate (romiplostim)</td>
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<tr>
<td>Prolia (denosumab)</td>
<td>Xgeva (denosumab)</td>
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For additional information about Amgen products, including important safety information, visit www.amgen.com
About Biotechnology Medicines: Manufacturing in Living Cells

<table>
<thead>
<tr>
<th>Traditional Pharmaceuticals</th>
<th>Biotechnology Medicines</th>
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</thead>
<tbody>
<tr>
<td>Chemical ingredients in simple structures</td>
<td>Proteins produced by living systems</td>
</tr>
<tr>
<td>Relatively stable</td>
<td>Variable; sensitive to conditions</td>
</tr>
<tr>
<td>Defined structure and easy to characterize</td>
<td>Heterogeneous structures and difficult to characterize</td>
</tr>
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Developing and Producing Biotechnology Medicines Is Difficult and Risky…

Long and costly process

High risk of failure

Understanding of biology evolving

…but important and worthwhile for society
Manufacturing Really Matters for Biotechnology Medicines

- Product quality is affected by how a medicine is made
- Even small variations can alter efficacy, safety, or product availability
- Knowing which variations matter requires extensive biotechnology manufacturing experience

Reasons for Sterile Injectable Drug Shortages 2010

- Due to product quality issues*: 54%
- Due to delays/not enough manufacturing capacity: 21%
- Due to discontinuations: 11%
- Due to raw material issues: 5%
- Increase in demand due to another shortage: 4%
- Due to loss of manufacturing site: 3%
- Due to component problems/shortage: 2%

*Includes particulate, microbial contamination, newly identified impurities, stability changes

Source: FDA
Amgen Is a Leader in the Manufacturing of Biotechnology Medicines
Evolving Landscape Makes Manufacturing More Challenging for the Industry

- More patients globally
- Complex supply chains
- Market shifts
- Competition
- Cost pressures
- Changing regulatory environment
Amgen’s Approach to Operational Excellence Helps Us Meet the Challenges

- High Reliability Performance
- Defense in Depth
- Knowledge Management
- Lean

Driving quality through continuous improvement
We Are Continuing to Lead the Way With Manufacturing of the Future

Yesterday

Today

Tomorrow

Achieving additional improvements in yield and reductions in cost per gram
The Next Generation of Biotech Manufacturing Won’t Be Easy

- Investment
- Regulation
- Integration
But Continuous Improvement Is Vital to Our Long-Term Performance

<table>
<thead>
<tr>
<th>Directional State</th>
<th>Quality</th>
<th>Economics</th>
<th>Culture</th>
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<tbody>
<tr>
<td>Intervention and correction</td>
<td>Prevention, zero-defect thinking</td>
<td>Cost-competitive</td>
<td>Cross-functional collaboration and staff ownership</td>
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<tr>
<td>Build to stock, high inventory</td>
<td>Demand-driven, risk-based</td>
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<tr>
<td>Reactive, long cycle times</td>
<td>Fast and responsive</td>
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<td>High fixed-cost burden</td>
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<td>Organizational silos</td>
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Patients Around the World Depend on Our Success

And we aim to deliver... to every patient, every time