Opening Thoughts
Manufacturing and Football

“There’s always something to be said for doing multiple things and giving different looks, [but] in the end, it comes down to execution. If you can do them, great.

If you can’t, then you’re probably better off doing fewer things and doing them well.”

Bill Belichick
Head Coach, New England Patriots

US Biomedical Industry: Economic Impact

Size of Biomedical Industry, 2009

<table>
<thead>
<tr>
<th>Industry</th>
<th>Employment</th>
<th>Wages, US$B</th>
<th>Outputs, US$B</th>
</tr>
</thead>
<tbody>
<tr>
<td>Biopharmaceuticals</td>
<td>283,700</td>
<td>$29.0</td>
<td>$82.4</td>
</tr>
<tr>
<td>Medical devices and equipment</td>
<td>409,200</td>
<td>$26.5</td>
<td>$66.2</td>
</tr>
<tr>
<td>Research, testing and medical labs</td>
<td>526,300</td>
<td>$40.3</td>
<td>$64.5</td>
</tr>
<tr>
<td>Total biomedical</td>
<td>1,219,200</td>
<td>$95.9</td>
<td>$213.2</td>
</tr>
</tbody>
</table>

Total Economic Impact of Biomedical Industry, 2009

<table>
<thead>
<tr>
<th>Industry</th>
<th>Employment</th>
<th>Wages, US$B</th>
<th>Outputs, US$B</th>
</tr>
</thead>
<tbody>
<tr>
<td>Biopharmaceuticals</td>
<td>2,127,983</td>
<td>$110.3</td>
<td>$206.1</td>
</tr>
<tr>
<td>Medical devices and equipment</td>
<td>1,554,952</td>
<td>$98.1</td>
<td>$152.3</td>
</tr>
<tr>
<td>Research, testing and medical labs</td>
<td>1,578,915</td>
<td>$80.6</td>
<td>$161.3</td>
</tr>
<tr>
<td>Total biomedical</td>
<td>5,261,850</td>
<td>$289.1</td>
<td>$519.7</td>
</tr>
</tbody>
</table>

Source: Bureau of Labor Statistics, Moody’s Analytics, Milken Institute
Pharma Industry Revenue and Profit

INFLATION ADJUSTED

Pharma industry revenues, 1989 – 2009

$ billions

Revenue +278%
Profit +131%

Source: S&P Capital IQ Unit; McKinsey

Pharmaceutical Industry Trends

R&D Productivity
Healthcare Cost Pressure
Demand Drivers

Regulatory Environment
Mergers & Acquisition
Evolving Portfolios
Emerging Markets
**BioPharma R&D Statistics**

- $1.3$ Billion cost of research and development for an approved product.
- 5 out of 5000 compounds will reach clinical trials.
- 1 out of 5 compounds that reach clinical trials obtain a Marketing Authorization.
- 2 out of 10 approved products recoup their investment in R&D.

**Unprecedented Period of Loss of Exclusivity**

<table>
<thead>
<tr>
<th>Company</th>
<th>2009 sales at risk because of U.S. patent expiries between 2010-17, ($Bn)</th>
<th>Share of 2009 Pharma sales at risk because of U.S. patent expiries 2010-17, (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pfizer</td>
<td>25</td>
<td>54</td>
</tr>
<tr>
<td>sanofi aventis</td>
<td>19</td>
<td>45</td>
</tr>
<tr>
<td>gsk</td>
<td>16</td>
<td>39</td>
</tr>
<tr>
<td>Roche</td>
<td>11</td>
<td>30</td>
</tr>
<tr>
<td>johnson &amp; johnson</td>
<td>8</td>
<td>34</td>
</tr>
<tr>
<td>novartis</td>
<td>17</td>
<td>42</td>
</tr>
<tr>
<td>MERCK</td>
<td>12</td>
<td>43</td>
</tr>
<tr>
<td>AstraZeneca</td>
<td>23</td>
<td>72</td>
</tr>
<tr>
<td>Lilly</td>
<td>16</td>
<td>79</td>
</tr>
<tr>
<td>Bristol-Myers Squib</td>
<td>10</td>
<td>52</td>
</tr>
<tr>
<td>Wyeth</td>
<td>6</td>
<td>40</td>
</tr>
</tbody>
</table>

Source: Evaluate 2010

Figures represent pre-Wyeth acquisition by Pfizer.
### Major Cost Reduction Programs Announced

**Announced annual cost saving targets, USD billion**

<table>
<thead>
<tr>
<th></th>
<th>2007</th>
<th>2008</th>
<th>2009</th>
<th>2010</th>
</tr>
</thead>
<tbody>
<tr>
<td>AstraZeneca</td>
<td>0.9</td>
<td>2.4</td>
<td>+1.9</td>
<td></td>
</tr>
<tr>
<td>Johnson &amp; Johnson</td>
<td>1.3-1.6</td>
<td>1.4-1.7</td>
<td></td>
<td></td>
</tr>
<tr>
<td>GSK</td>
<td>1.4</td>
<td>2.7</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pfizer</td>
<td>1.5-2.0</td>
<td>3.0</td>
<td>4.5-5.0</td>
<td></td>
</tr>
<tr>
<td>Merck</td>
<td>3.8-4.2</td>
<td></td>
<td>+3.5</td>
<td></td>
</tr>
<tr>
<td>Bristol-Myers Squibb</td>
<td></td>
<td>2.5</td>
<td></td>
<td>1.9</td>
</tr>
<tr>
<td>Roche</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Source: Companies' Annual Reports and websites, press releases*

### Performance Significantly Lags Other Industries

<table>
<thead>
<tr>
<th>Measure</th>
<th>Pharma/Med. Products</th>
<th>Automotive</th>
<th>Aerospace</th>
<th>Computer</th>
<th>CPG</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall equipment effectiveness, percent</td>
<td>10-60</td>
<td>70-85</td>
<td>50-70</td>
<td>80-90</td>
<td>70-90</td>
</tr>
<tr>
<td>Annual productivity improvement, percent</td>
<td>1-3</td>
<td>5-15</td>
<td>5-10</td>
<td>1-3</td>
<td>5-15</td>
</tr>
<tr>
<td>First-pass yield – zero defects, percent</td>
<td>60-80</td>
<td>90-99</td>
<td>70-90</td>
<td>90-99</td>
<td>90-99</td>
</tr>
<tr>
<td>Lead time, days</td>
<td>120-180</td>
<td>1-7</td>
<td>7-120</td>
<td>5-10</td>
<td>3-7</td>
</tr>
<tr>
<td>Inventory of finished goods, days</td>
<td>60-90</td>
<td>3-30</td>
<td>3-30</td>
<td>5-50</td>
<td>10-40</td>
</tr>
<tr>
<td>Labor value-add time, percent</td>
<td>10-30</td>
<td>60-70</td>
<td>60-70</td>
<td>60-70</td>
<td>60-90</td>
</tr>
<tr>
<td>Direct/indirect labor ratio</td>
<td>1:1</td>
<td>10:1</td>
<td>10:1</td>
<td>10:1</td>
<td>10:1</td>
</tr>
</tbody>
</table>

*Source: McKinsey Operations practice*
**Biologics Manufacturing: Developing Trends**

- **Blockbusters**
- **Niche products**
- **Biosimilars**
- **Yields**
- **Capacity utilization**
- **Regulatory harmonization**
- **Emerging market regulations**
- **Emerging market mfg**
- **Asian suppliers**
- **US Manufacturing**

**Global Mammalian Capacity – New Commercial Expansion Driven by Asia**

- Global mammalian capacity is stabilizing ~3mio L
- Additional idle capacity is estimated about half a million L (referring to inactive suites / facility only, NOT utilization).

Source: Evaluate Pharma, Thomson Pharma, PharmaProjects, ‘Cell culture manufacturing capacity’ by Bio Process Technology Consultants
Market studies suggest available capacity will continue to exceed demand.

Industrial wide utilization projected to increase from 40% to 60% in 3-5 years.

<table>
<thead>
<tr>
<th>Volume required (KL/Yr)</th>
</tr>
</thead>
<tbody>
<tr>
<td>500</td>
</tr>
</tbody>
</table>

- High case demand
- Base case demand
- Low case demand
- Available capacity
- Clin & comm

Source: The Changing Landscape of Mammalian Cell Culture Manufacturing Capacity, BPTC presentation at Eighth Annual bioProcessUK Conference, Dec 2011; Global Trends in Mammalian Cell Culture Capacity and Biomanufacturing, BPTC presentation at Swiss Biotech Program at BioPharm America, Sep 2011

<table>
<thead>
<tr>
<th>MFG Employment</th>
<th>Growth/Decline Since 2002</th>
</tr>
</thead>
<tbody>
<tr>
<td>2011</td>
<td>2007</td>
</tr>
<tr>
<td>CA</td>
<td>42,903</td>
</tr>
<tr>
<td>NJ</td>
<td>30,032</td>
</tr>
<tr>
<td>NC</td>
<td>20,395</td>
</tr>
<tr>
<td>PA</td>
<td>20,291</td>
</tr>
<tr>
<td>NY</td>
<td>19,587</td>
</tr>
<tr>
<td>IL</td>
<td>17,959</td>
</tr>
<tr>
<td>PR</td>
<td>15,239</td>
</tr>
<tr>
<td>IN</td>
<td>14,848</td>
</tr>
<tr>
<td>TX</td>
<td>9,595</td>
</tr>
<tr>
<td>MA</td>
<td>8,654</td>
</tr>
<tr>
<td>MI</td>
<td>7,643</td>
</tr>
<tr>
<td>CT</td>
<td>7,003</td>
</tr>
<tr>
<td>MD</td>
<td>6,874</td>
</tr>
<tr>
<td>MO</td>
<td>4,637</td>
</tr>
</tbody>
</table>

Source: U.S. Bureau of Labor Statistics, Quarterly Census of Employment and Wages (QCEW)
To turn ideas into medicine – you need to understand the marketplace – and have a clear strategy that sets the course for the future.
BMS Strategic Foundation

Best of Biotech

Best of Pharma

Helping more patients prevail in their fight against serious disease

Next Generation BioPharma

Innovation

Selective Integration

Continuous Improvement

Agile, Entrepreneurial & Accountable Culture

BMS Diversified Portfolio

Currently Marketed Products

**ABILIFY** (aripiprazole)

**REYATAZ** (atazanavir sulfate)

**ATRILTA** (doravirine 800 mg capsules, tenofovir disoproxil fumarate 300 mg tablets)

**Baraclude** (entecavir)

Life-Cycle Products

**ORENCIA** (abatacept)

**SPRYCEL** dasatinib

**ERBITUX** cetuximab

New Product Launches

**YERVION** (ipilimumab)

**ONGLYZA** (saxagliptin)

**KOMBIGLYZE XR** (saxagliptin and metformin HCl extended-release tablets)

**BYDUREON** extended-release for injectable suspension

**ELIQUIS** apixaban
Pearl Strategy allows BMS to achieve desired pipeline output in face of high attrition in development.

**Intersection of Innovative Portfolio and Selective Integration**

- Strategic set of select transactions in targeted disease areas
- Provides access to innovation that enhances or complements our pipeline and capabilities
- Each transaction uniquely structured to leverage best of BMS and best of biotech

---

**Our Biologics Pipeline**

- **Exploratory Development**: >20 early development projects
  - Anti-PD1
  - Anti-IL6

- **Full Development**: Eliotuzumab (Anti-CS1)
  - Necitumumab
  - Metreleptin
  - PEG Interferon α

- **Marketed Product Development**
  - ERBITUX®
  - YERVYO™
  - ORENCIA®
  - NULOJIX®
  - RECOTHROM®

* Discovery through Phase II
^ Registrational program
† Approved in at least one major market
Our Manufacturing Network

- United States
  - Devens, MA
  - Mt. Vernon, IN
  - Syracuse, NY (R&D)
- Mexico
  - Tlalpan
- Puerto Rico
  - Humacao
  - Manati
- France
  - UPSA
- Ireland
  - Swords
  - Cruiserath
- Italy
  - Anagni
- Japan
  - Aichi
- China
  - SASS-Shanghai
- Mexico
  - Tlalpan

Pharmaceutical (9) Biological (3) ✓ API Plant • Finishing Plant

BMS Biologics Process Development & Manufacturing

Supply Chain Excellence
Scientific & Technical Excellence
Operational Excellence

PARTNERSHIP & COLLABORATION
PEOPLE & CULTURE
We Aim to Become the Benchmark Biologics Development and Manufacturing Organization

Unique Challenges:

- Pearl strategy has led to a collection of widely different manufacturing processes
  - E. coli inclusion bodies and periplasmatic expression
  - Expression of antibodies in yeast
  - A range of mammalian cell based processes using CHO and NS0 cells, DHFR and GS expression systems
  - No platform processes or analytics

- Acquired sites bring their own capabilities and cultures into the organization

- How to build a top tier, benchmark organization?

Current Biologics Network

- Hopewell, NJ
  Process Development

- Bloomsbury, NJ
  Process Development

- Seattle
  Process Development

- Syracuse
  Process Development & DS Manufacturing

- Devens
  Large Scale DS Manufacturing

- Manati
  DP Manufacturing
Biologics Manufacturing 2013 and Beyond

“By failing to prepare, you prepare to fail.”

Benjamin Franklin

Network Design Principles

1. What capabilities do we need, how much and when?
2. What do we make versus buy?
3. What technology platforms do we choose for what we make?
4. Where do we build?

What is our pipeline and commercial portfolio?
What is our desired tech transfer model?
What is our business continuity model?

Source: BCG
### Example: Demand Projection using Monte Carlo Simulation

**Total mammalian cell based mfg production demand (kL of bioreactor capacity)**

- **Current Capacity**
- **Addl. capacity**

**Source:** BCG analysis – Figure is Illustrative

### Key takeaways
- Mfg demand increases quickly
- Investments in new assets potentially needed

### Key assumptions
- 80% target utilization
- 90% success rate

### Key sensitivities
- Pearl activities could cause fluctuations in demand
- PCO reduction could improve throughput

---

### Make vs. Buy Decision Process

<table>
<thead>
<tr>
<th>Capability</th>
<th>Strategy</th>
<th>Rationale</th>
</tr>
</thead>
<tbody>
<tr>
<td>Process Development</td>
<td>Keep internal</td>
<td>• Key enabler for development</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Create IP, know how</td>
</tr>
<tr>
<td>Clinical Manufacturing</td>
<td>Keep internal where possible</td>
<td>• Key enabler for development</td>
</tr>
<tr>
<td>Commercial Manufacturing</td>
<td>Outsource as needed to meet demand</td>
<td>• Utilize existing capacity in industry</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Avoid capital investments at risk</td>
</tr>
</tbody>
</table>
Bencharking of 46 major biotech facilities suggests PD critical to co-locate with Clinical (and to a lesser extent, Commercial)

21 Commercial Mfg (43 facilities)

5 Process Development (25 facilities)
17 Clinical & Launch (20 facilities)
3

Clinical facilities always co-located with Process Development
Many facilities have co-located all three activities
Commercial production is often a stand-alone facility

Note: Co-location assumed for facilities that are within 10 miles of each other
Source: BCG interviews / surveys, public research

Desired Organizational Design

R&D Interface Co-located with R&D
Cell Line Development
Development candidate selection
Advanced Analytics

Center of Excellence Microbial Expression
Process Development & Clinical Mfg co-located

Center of Excellence Mammalian Cell Culture
Process Development & Clinical Mfg co-located

BMS Commercial Manufacturing Plants
CMO Commercial Manufacturing Plants
**What Kind Of Manufacturing Capability Do We Want To Build?**

<table>
<thead>
<tr>
<th>Key Criteria</th>
<th>Stainless Steel</th>
<th>Hybrid disposable</th>
<th>Fully disposable</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Both hybrid and fully disposable systems enable strategic imperatives</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>DS production in Emerging Markets</td>
<td>○</td>
<td>●</td>
<td>●</td>
<td>• Disposable systems allow smaller footprint, faster modular construction, and less utility requirements.</td>
</tr>
</tbody>
</table>
| Streamlined tech transfer (Clin > Comm) | ●               | ●                 | ●               | • Disposable trains typically designed as identical integrated systems to allow smooth tech transfer.  
• Need to be aware of regulatory requirements for switching between disposable and SSL |
| Operational flexibility           | ●               | ●                 | ●               | • Fully disposable system requires little to no cleaning/sanitization & reduced change over time between products, while hybrid system requires partial cleaning & sanitization |

**Fully disposable system carries a higher technological risk at the current stage**

<table>
<thead>
<tr>
<th>Technology maturity</th>
<th>Stainless Steel</th>
<th>Hybrid disposable</th>
<th>Fully disposable</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>●</td>
<td>●</td>
<td>●</td>
<td>• Fully disposable system currently has very limited downstream disposable options; hybrid disposable only uses relatively mature technology</td>
</tr>
</tbody>
</table>

---

**Our Journey**

**Becoming the Best**

- **Become the Benchmark**
- **Build Capabilities**
- **Set the Foundation**

- 2012
- 2013
- 2014
- 2015+
Summary

- Massachusetts has been very successful over the past years to build and expand its share of the biopharmaceutical industry.

- The industry is facing a number of serious challenges that will require us all to change the way we operate.

- BMS is fully committed to develop, launch and market innovative therapies for unmet clinical needs.

- Biologics Manufacturing in BMS is rapidly repositioning itself to address a rapidly expanding portfolio in a changing business environment.

Closing Thought

“Every crisis is an opportunity, if managed properly.”

Robert Kraft
Owner, New England Patriots
Q & A

Thank You