## Turning Ideas into Medicines – Biologics Manufacturing in 2013 and Beyond

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#### **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

Bristol-Myers Squibb

#### **US Biomedical Industry: Economic Impact**

Size of Biomedical Industry, 2009				
Industry	Employment	Wages, US\$B	Outputs, US\$B	
Biopharmaceuticals	283,700	\$29.0	\$82.4	
Medical devices and equipment	409,200	\$26.5	\$66.2	
Research, testing and medical labs	526,300	\$40.3	\$64.5	
Total biomedical	1,219,200	\$95.9	\$213.2	

#### **Total Economic Impact of Biomedical Industry, 2009**

Industry	Employment	Wages, US\$B	Outputs, US\$B
Biopharmaceuticals	2,127,983	\$110.3	\$206.1
Medical devices and equipment	1,554,952	\$98.1	\$152.3
Research, testing and medical labs	1,578,915	\$80.6	\$161.3
Total biomedical	5,261,850	\$289.1	\$519.7

#### Pharma Industry Revenue and Profit

INFLATION ADJUSTED



#### **Pharmaceutical Industry Trends**



**R&D Productivity** 



Healthcare Cost Pressure



**Demand Drivers** 



Regulatory Environment



Mergers & Acquisition



Evolving Portfolios



Emerging Markets

## **BioPharma R&D Statistics**



### **Unprecedented Period of Loss of Exclusivity**





### Performance Significantly Lags Other Industries

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

### **Biologics Manufacturing: Developing Trends**



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



Source: Evaluate Pharma, Thomson Pharma, PharmaProjects, 'Cell culture manufacturing capacity' by Bio Process Technology Consultants



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

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#### Biotechnology R&D Employment

	2007	2011
СА	19,134	22,592
MD	10,154	8,933
MA	24,656	28,177
MO	4,262	3,659
NJ	8,567	9,338
NY	2,679	3,677
NC	7,042	6,785
ОН	2,696	3,098
PA	16,902	11,234
ТХ	4,229	4,299
WA	2,499	3,832

#### **BioPharma Manufacturing**

MFG Employment 2011		Growth/Decline Since 2002		
1	CA	42,903	CA	7.5%
2	NJ	30,032	MD	36.5%
3	NC	20,395	ОН	22.0%
4	PA	20,291	ТΧ	7.8%
5	NY	19,587	MA	4.3%
6	IL	17,959	NC	-1.5%
7	PR	15,239	MO	-6.5%
8	IN	14,848	NY	-8/6%
9	ΤХ	9,595	IL	-14.4%
10	MA	8,654	СТ	-33.8%
11	MI	7,643	МІ	-35.9%
12	СТ	7,003	IN	<b>-24</b> .1%
13	MD	6,874	PA	-25.2%
14	OH	5,220	NJ	-23.7%
15	MO	4,637	PR	-42.3%
			US	-7.90 <u>%</u>

#### What does it all mean?

To turn ideas into medicine – you need to understand the marketplace – and have a clear strategy that sets the course for the future.







# Pearl Strategy allows BMS to achieve desired pipeline output in face of high attrition in development







#### **BMS Biologics Process Development & Manufacturing**



#### 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



*Syracuse* Process Development & DS Manufacturing



*Bloomsbury, NJ* Process Development



Devens Large Scale DS Manufacturing



*Seattle* Process Development



*Manati* DP Manufacturing



#### **Biologics Manufacturing 2013 and Beyond**





#### Make vs. Buy Decision Process

Capability	Strategy	Rationale
Process Development	Keep internal	<ul> <li>Key enabler for development</li> <li>Create IP, know how</li> </ul>
Clinical Manufacturing	Keep internal where possible	<ul> <li>Key enabler for development</li> </ul>
Commercial Manufacturing	Outsource as needed to meet demand	<ul> <li>Utilize existing capacity in industry</li> <li>Avoid capital investments at risk</li> </ul>







# What Kind Of Manufacturing Capability Do We Want To Build?

Key Criteria	Stainless Steel	Hybrid disposable	Fully disposable	Notes
Both hybrid and	l fully dispos	sable systems	enable strateg	ic imperatives
DS production in Emerging Markets	$\bigcirc$			<ul> <li>Disposable systems allow smaller footprint, faster modular construction, and less utility requirements.</li> </ul>
Streamlined tech transfer (Clin > Comm)	•	•	•	<ul> <li>Disposable trains typically designed as identical integrated systems to allow smooth tech transfer.</li> <li>Need to be aware of regulatory requirements for switching between disposable and SSL</li> </ul>
Operational flexibility	O	•		<ul> <li>Fully disposable system requires little to no cleaning/sanitization &amp; reduced change over time between products, while hybrid system requires partial cleaning &amp; sanitization</li> </ul>
Fully disposable system carries a higher technological risk at the current stage				
Technology maturity			•	<ul> <li>Fully disposable system currently has very limited downstream disposable options; hybrid disposable only uses relatively mature technology</li> </ul>
least favorable most favorable Bristol-Myers Squibb				



#### Summary

- Massachusetts has been very successful over the past years to build and expand it's 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

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#### **Closing Thought**

"Every crisis is an opportunity, if managed properly."



Robert Kraft Owner, New England Patriots

