

# Trends in the Global Biopharmaceutical Industry

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# About BioCentury

Value-added business information & analysis for life science companies, investors, academia and government on the strategic issues essential to the formation, development & sustainability of life science ventures.

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# The State of the Global Biopharmaceutical Industry

# The Challenges to Big Pharma

Growth and Innovation

Pricing and reimbursement

Safety

Rising efficacy hurdles

# P/Es & Growth

Company	P/E	Annual EPS growth rate (next 5 yrs)
Abbott	17.1	12%
AstraZeneca	8.6	3%
Bayer	13.9	NA
Bristol-Myers	12.6	11%
Eli Lilly	13.1	7%
GlaxoSmithKline	10.9	3%
Johnson & Johnson	14.6	8%
Merck	11.4	10%
Novartis	14.5	12%
Pfizer	8.8	4%
sanofi-aventis	9.4	3%
Schering-Plough	9.5	18%
Wyeth	12.2	5%
<b>RX median</b>	<b>12.0</b>	<b>8%</b>
<b>RX average</b>	<b>12.2</b>	

\*Data as of the end of 1Q08; 2008 EPS used to calculate P/E

# Wave of Genericization

# Big Pharma M&A

Big pharma	Year	Merger between
AstraZeneca	1999	Astra & Zeneca
Bristol-Myers Squibb	1989	Bristol-Myers & Squibb
GlaxoSmithKline	1989	Beecham & SmithKline Beckman
	1995	Glaxo & Wellcome
	2000	GlaxoWellcome & SmithKline Beecham
Novartis	1996	Ciba-Geigy & Sandoz
Pfizer	1995	Pharmacia & Upjohn
	2000	Pfizer & Warner-Lambert
	2003	Pfizer & Pharmacia
sanofi-aventis	1990	Rhone-Poulenc & Rorer
	1999	Rhone-Poulenc Rorer & Hoechst Marion Roussel
	1999	Sanofi & Synthelabo
	2004	Aventis (formed from Rhone-Poulenc & Hoechst merger) & Sanofi-Synthelabo

# Big R&D

Big pharma tries to create industrial-scale R&D building on the genomics revolution

# Research & Return

Company	5-yr annualized return (A)	R&D/ Rev (5 yrs)	R&D (5 yrs)(B)	Company	5-yr annualized return (A)	R&D/ Rev (5 yrs)	R&D (5 yrs)(B)
<b>Big pharma</b>				<b>Biotech</b>			
Pfizer	-3%	16%	\$38.3	Amgen	-1%	21%	\$12.6
Johnson & Johnson	7%	12%	\$31.3	Genentech	32%	20%	\$7.2
GlaxoSmithKline	10%	14%	\$29.3	Biogen Idec	11%	29%	\$3.6
sanofi-aventis	11%	16%	\$27.1	Genzyme	20%	19%	\$2.6
Roche	15%	16%	\$25.8	Shire	30%	22%	\$1.9
Novartis	10%	15%	\$24.5	Cephalon	8%	24%	\$1.6
Merck	6%	18%	\$20.8	Gilead	40%	14%	\$1.7
AstraZeneca	7%	16%	\$19.7	Celgene	54%	32%	\$1.1
Eli Lilly	-1%	19%	\$14.7	Sepracor	22%	24%	\$0.9
Bristol-Myers	7%	15%	\$13.9				
Wyeth	6%	14%	\$13.7				
Schering-Plough	5%	20%	\$10.1				
Abbott	11%	9%	\$9.9				

(A) Annualized return = Avg annual stock price performance from 12/31/02 to 12/31/07; (B) R&D = Total R&D spend 2003-07; \$B

# Handcrafted R&D

Company	R&D breakdown
AstraZeneca	Aligned its discovery research along therapeutic units of 600-800 people each.
GlaxoSmithKline	Divided the company's discovery component from lead molecule selection to Phase I trials into Centers of Excellence for Drug Discovery (CEDDs). Each CEDD is therapeutically aligned or devoted to a technology platform, with 240-400 people per therapeutically defined CEDD and 60-150 people per technology defined CEDD. Also has Center of Excellence for External Drug Discovery (CEEDD) for managing discovery alliances.
J&J	Split pharma activities into three business units: biologics group focused on hematology, oncology and immunology; virology group focused on HIV and HCV; and CNS IM, which focuses on CNS, infection and metabolic diseases and cardiology.
Roche	Created research units focused on specific disease biology areas (DBAs), which are virtual clusters of related molecular mechanisms or biological systems. Each DBA has 300-500 people.

# Biotech Takeouts by Big Pharma

Year	Acquired	Acquirer	Value (A)
2007	MedImmune	AstraZeneca	\$15.6
2001	Alza	J & J	\$14.7
2007	Serono	Merck KGaA	\$13.2
2006	Chiron (B)	Novartis	\$5.2
1999	Centocor	J & J	\$5.0
2006	Kos	Abbott	\$3.7
2003	Scios	J & J	\$2.4
2007	Icos	Eli Lilly	\$2.3
2005	Vicuron	Pfizer	\$1.9
2004	Esperion	Pfizer	\$1.3
2006	Sirna	Merck	\$1.1
2006	Cambridge Antibody	AstraZeneca	\$1.0

(A) Value at time of completion; (B) Paid about \$5.2B for the 56% it didn't already own; price in \$B

# Mid-Tier Takeouts

Year	Acquired	Acquirer	Value (A)
2007	Tanox	Genentech	\$919.0
2000	Medeva	Celltech	\$912.0
2003	Powderject	Chiron	\$878.0
2005	Eyeteq	OSI	\$829.7
2005	Bone Care	Genzyme	\$719.0
2000	PathoGenesis	Chiron	\$700.0
2000	Liposome Co.	Elan	\$699.2
2004	Atrix	QLT	\$642.2
2006	Connetics	Stiefel Labs	\$640.0
2001	Aurora Bio	Vertex	\$616.0
2006	NeuTec	Novartis	\$605.0
2003	Sangstat	Genzyme	\$600.0
2006	AnorMed	Genzyme	\$584.0
2005	Angiosyn	Pfizer	\$527.0
2003	Cima	Cephalon	\$515.0

Biotech takeouts for \$500M-\$1B since 2000. (A) Value at time of completion

# Next-Generation Takeouts

Year	Acquired	Acquirer	Value (A)
2007	Adnexus (B)	Bristol-Myers	\$505.0
2007	Domantis	GlaxoSmithKline	\$450.0
2006	Avidia	Amgen	\$290.0
2007	BioRexis	Pfizer	ND

(A) Value at time of completion, includes milestone payments; (B) Proposed

# Big Biotech Becomes Big Pharma

As biotech companies grow,  
they will face the same problems as big pharma

# P/Es & Growth

Company	P/E	Annual EPS growth rate (next 5 yrs)
Amgen	10.0	10%
Biogen Idec	18.7	13%
Celgene	40.3	43%
Genentech	23.7	23%
Genzyme	18.6	20%
Gilead	27.3	18%
ImClone	33.7	8%
Shire	18.3	NA
UCB	19.0	NA
<b>BT median</b>	<b>19.0</b>	<b>19%</b>
<b>BT AVG</b>	<b>23.3</b>	
*Data as of the end of 1Q08; 2008 EPS used to calculate P/E		

# Lightning Rods on Pricing

Avastin: \$46,000 for 5 added months of life

Avastin vs. Lucentis in AMD

ESAs: Medicare's largest line item

# NICE & Velcade: Pay for Performance

	No rebate	Scenario I [low end](A)	Scenario II [Velcade+dex](A)	Scenario III [high end](B)
No. of pts in U.K. potentially taking Velcade	5,000	5,000	5,000	5,000
% pts reaching $\geq 25\%$ reduction in M-protein at 4 cycles [Janssen-Cilag proposal]	NA	45%	55%	70%
% pts reaching $\geq 50\%$ reduction in M-protein at 4 cycles [NICE proposal]	NA	30%	40%	50%
Pts who could be covered under Janssen-Cilag's program	NA	2,250	2,750	3,500
Pts who could be covered under NICE's program	NA	1,500	2,000	2,500
<b>NHS spending [no rebates](C)</b>	<b>£125.0M</b>	<b>NA</b>	<b>NA</b>	<b>NA</b>
<b>NHS spending [Janssen-Cilag proposal](C)(D)</b>	<b>NA</b>	<b>£56.3M</b>	<b>£68.8M</b>	<b>£87.5M</b>
<b>NHS spending [NICE proposal](C)(D)</b>	<b>NA</b>	<b>£37.5M</b>	<b>£50.0M</b>	<b>£62.5M</b>

(A) Estimates of % of patients reaching the 25% and 50% thresholds in reduction of M-protein at 4 cycles from Paul Richardson, lead investigator of the APEX trial; (B) Estimates of % of patients reaching the 25% and 50% thresholds from Myeloma U.K.; (C) Assumes cost of eight cycles of treatment of about £25,000 per patient; (D) Accounts for rebates; NA=Not applicable

# Comparative Efficacy & Effectiveness

# Biosimilars

Biosimilar EPOs hit Europe

# The New Regulatory Environment

Drug	Indication	Issue	Outcome
Vioxx	Osteoarthritis	CV risks	Withdrawn from the market
Other COX-2 inhibitors	Osteoarthritis	CV risks	Bextra withdrawn from the market; Arcoxia received a not approvable letter from FDA
Avandia	Diabetes	CV risks	FDA panel voted 22-1 to keep on the market; boxed warning added to the label
Pargluva	Diabetes	CV risks	FDA panel recommended approval; received approvable letter requesting additional data; Bristol-Myers dropped compound
Zimulti	Obesity	Seizures and suicidality	FDA panel voted 14-0 against approval; Sanofi withdrew NDA

# The Issues

Safety only vs. risk/benefit

% risk vs. absolute risk

Patient choice

Politics

# The New Safety Regime

Active postmarket risk identification system  
Risk Evaluation and Management Strategies (REMS)  
Postmarket study requirements  
Mandate label changes  
Joint meetings of drug and drug safety offices

# The New System in Action

Safety & efficacy hurdles

# The New System in Action

Superiority: NSAIDs, antibiotics

# The New System in Action

Larger and longer trials

Diabetes drugs, cholesterol drugs

# The New System in Action

On the other hand...

FDA bends over for Avastin

# The U.S. Presidential Campaign

## *Obama vs. McCain*

### Where they agree

- ❖ Make health insurance portable
- ❖ Lower drug prices by allowing importation and faster introduction of generics
- ❖ Cost effectiveness studies
- ❖ Provide assistance to Americans who need subsidies for their premiums
- ❖ Put reasonable limits on insurance premiums
- ❖ Guarantee access to insurance
- ❖ Use IT to reduce costs

# The U.S. Presidential Campaign

## *Obama vs. McCain*

Where they may differ

### **McCain**

- ❖ Tax credit
- ❖ Tort reform
- ❖ Expand HSAs

### **Obama**

- ❖ Insurance program comparable to existing federal program
- ❖ Limit cost of malpractice insurance
- ❖ Require all employers to contribute to health coverage
- ❖ Require all children be covered
- ❖ Repeal ban on Medicare negotiations with drug companies

# Summing It All Up, I

More emphasis on comparative efficacy and safety

Resulting in larger and longer trials and  
more head-to-head trials

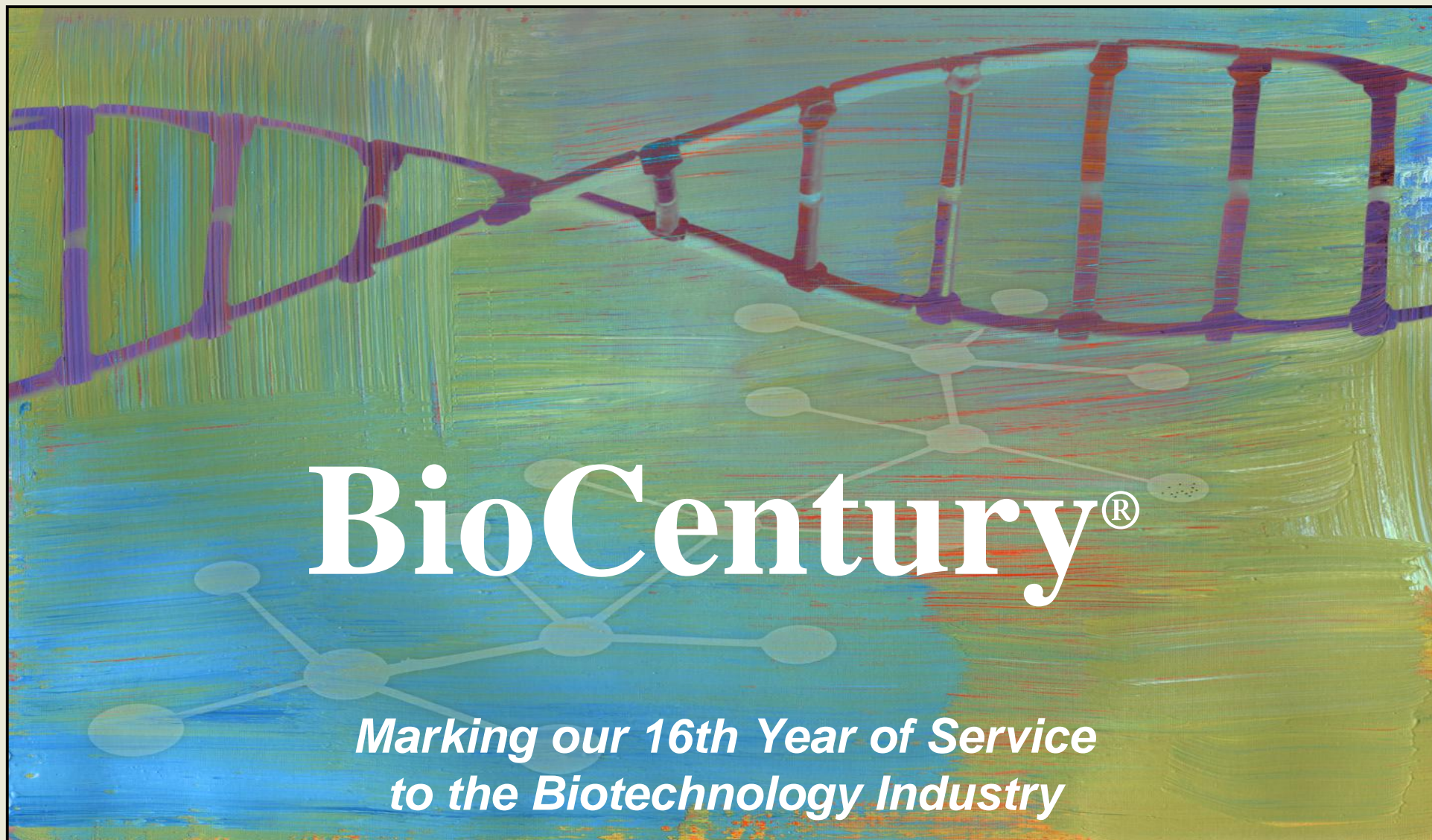
Leading to higher costs of drug development

Even as pricing pressures increase

# Summing It All Up, II

Pharma still needs products, platforms

Short-term safety valve as many products go generic



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