

KymaNEWS

BIOPHARMA



A Publication for Professionals in the Biopharma/Biotech Manufacturing Industry

2005:Retrospective | 2006:Outlook

This is Kymanox's first newsletter. The timing of this issue is significant. Each year companies and individuals alike take time to review the previous year and make plans and resolutions for the next year. Some "Year-in-Review" articles are written *before* the end of year and fail to capture all the data which provide proper perspective that comes only with the passage of time.

Please use the information herein to organize and archive your 2005 thoughts as

well as inspire you to reinvigorate the 2006 plans you've already set in motion. It's no secret that at this time of year most New Years initiatives lose steam — evidence of this trend abounds at your local health club!

The focus of this initial issue is on news and data that each of us *should* be familiar with, but may not have had the time to follow and review due to heavy workloads and hectic schedules. Hopefully you'll find some



The way things look is a function of your vantage point.

of the tables useful enough to keep near your desk for the entire year.

Best wishes for a successful 2006!

Regards,

Stephen M. Perry, PMP

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Did You Know?

- 2 of the 13 newly FDA-approved drugs in 2005 were mammalian cell culture products.
- The lines between Biotech and Pharma are blurring: small molecules are getting bigger, protein-like products are getting smaller, CDER has a Biotech office and some Pharma companies are buying Biotech companies outright.
- BIO 2006 is coming to Chicago this April.
- Personalized medicine is here now! BiDil was approved in 2005 for black heart patients and Tysabri is making a likely comeback with new patient screening measures.

Financially Speaking

Last year was a good year financially for Biopharma/Biotech, especially for the new market capitalization leader, Genentech.

Pharma, on the other hand, was mostly flat. A look at the largest companies in these sectors, shown in the two adjacent tables, supports this assertion.

2005 BIG BIOTECH

Co. (Ticker)	2005 Δ	Market Cap. (\$B)
Genentech (DNA)	+72%	98
Amgen (AMGN)	+24%	97
Gilead S. (GILD)	+49%	24
Serono (SRA)	+25%	21
Genzyme (GENZ)	+21%	18

2005 BIG PHARMA

Co. (Ticker)	2005 Δ	Market Cap. (\$B)
Johnson & J. (JNJ)	(-4%)	179
Pfizer (PFE)	(-13%)	172
Glaxo S. (GSK)	+7%	143
Novartis (NVS)	+5%	123
Sanofi-A. (SNY)	+13%	117

Sources: Yahoo! Finance (30DEC05, 29JAN06) and Michael Rosen on www.wistechology.com (04JAN06)

Inside this issue:

Great Gains!	2
M&A Transactions	2
FDA Personnel Changes	3
FDA Product Approvals	3
Trend Watch	3
Ideal Knowledge Transfer	4
2006 Industry Events	4

Notable Gainers in 2005

According to Burrill and Company, "The Burrill Biotech Select Index widely outperformed the NASDAQ and Dow Jones Industrial on a year-to-date basis — an incredible testimony to the industry's successful year (up 22% versus +1.3% for NASDAQ and -0.61% for the Dow)."

Abgenix (ABGX) shareholders got a nice ~50% valuation boost this past December when Amgen announced its buy offer of \$2.2B. Some other companies had notable gains in 2005 as shown on the right.

Co. (Ticker)	2005 Gain	Primary Industry
Viropharma (VPHM)	+444%	Biotech
Myogen (MYOG)	+272%	Drug Mfg.
Adventrix P. (ANX)	+185%	Biotech
Biocryst P. (BCRX)	+182%	Biotech
Interleukin G. (ILI)	+58%	Diagnostic Substances

Companies that are following Genzyme's core business model, which is focused on rare diseases and genetic screening, also made some splashes in 2005 and may continue to do well in 2006.



The real winners: future patients with new treatments or alternatives.

Sources: Yahoo! Finance (29JAN06) and G. Steven Burrill on www.burrillandco.com (29JAN06)

Urge to Merge

Another key story of 2005 was the size, number and quality of merger and acquisition transactions. Bigger Pharma companies with cash on hand (e.g., Pfizer, GSK and Novartis) bought entire biotech companies or parts of those companies to ensure their long-term

Biotechs are merging to gain efficiency; Pharmas are buying Biotechs to gain diversity.

pipeline and overall growth. Collaborations were also hot in 2005 and will continue to be popular because of gained efficiencies and risk minimization. Below is a table of selected transactions that were announced in 2005:

Acquirer	Acquired	~Value (\$B)	Acquirer	Acquired	~Value (\$B)
Novartis	Chiron	5.1	Cephalon	Zeneus Pharma	0.36
Allergan	Inamed	3.2	GlaxoSmithKline	Corixa	0.30
Amgen	Abgenix	2.2	Johnson & Johnson	Peninsula Pharmaceuticals	0.25
Pfizer	Vicuron Pharmaceuticals	1.9	Sosei	Arakis	0.19
Shire	Transkaryotic Therapies	1.6	Roche	Glycart Biotechnology AG	0.18
GlaxoSmithKline	ID Biomedical	1.4	Beckman Coulter	Agencourt Bioscience	0.14
OSI Pharmaceuticals	Eyetech Pharm.	0.94	EpiCept	Maxim Pharmaceuticals	0.14
Quest Diagnostics	LabOne	0.93	Invitrogen	BioSource International	0.13
Meda AB	Viatrix GmbH	0.93	Jazz Pharmaceuticals	Orphan Medical	0.12
Genzyme	Bone Care International	0.72	Affymetix	ParAllele Bioscience	0.12
Crucell	Berna Biotech	0.45	TABLE TOTAL		21.3

Sources: Yahoo! Finance (29JAN06) and G. Steven Burrill on www.burrillandco.com (29JAN06)

FDA: Personnel Δ 's + Drug Approvals in 2005

Although Biopharma had a good year in terms of its financials, the regulatory environment and its governing body, the FDA, had a difficult year. Big Pharma's high-profile recalls (e.g., Vioxx and Celebrex) pushed the always-moving pendulum back to "ultra-cautious." Biopharma was not spared. The recall of Tysabri, which is now seeking reinstatement, also played a part in FDA's woes. A selection of the numerous and significant personnel changes within FDA in 2005 are highlighted in the adjacent table.

Person (Date)	Position	Person (Date)	Position
Kathy Heuer (JAN)	CFO and Associate Commissioner for Management	Murray Lumpkin (JUL)	Deputy Commissioner for International and Special Programs
Randall Lutter (MAR)	Associate Commissioner for Policy and Planning	Patrick Ronan (JUL)	Chief Staff Officer to Commissioner
Richard Pazdur (APR)	Director of Office of Oncology Drug Products	Linda Tollefson (AUG)	Assistant Commissioner for Science
Margaret O'K. Glavin (APR)	Associate Commissioner for Regulatory Affairs	Douglas Throckmorton (SEP)	Deputy Director of CDER
Steven Galson (JUL)	Director of CDER	Andrew von Eschenbach (SEP)	Commissioner
Scott Gottlieb (JUL)	Deputy Commissioner for Medical and Scientific Affairs	Gerald Dal Pan (OCT)	Director, Office of Drug Safety in CDER
Janet Woodcock (JUL)	Deputy Commissioner for Operations and Chief Operating Officer	Kathleen Uhl (NOV)	Director of FDA's Office of Women's Health (OWH)



The FDA's core mission — protecting public health — is a difficult job.

Source: FDA on www.fda.gov (29JAN06)

A total of 13 drug products were approved in 2005. Three of these compounds, denoted with an *, utilize rDNA biosynthesis (e.g., CHO cell, *E.Coli*) for production. It is possible approvals will be harder to obtain this year. Hopefully, FDA's own initiatives will help offset some of the expected regulatory slowdown. The "fast-tracked, personalized medicine" initiative was announced this past March. "Process Analytical Technology (PAT)" for manufacturing has been gaining momentum recently; PAT is an outflow of the FDA's "21st Century cGMPs: A Risk-Based Approach" initiative.

Name (Generic)	Date	Description (MW)	Treatment Area (Indication)	Company
Symlin (pramlintide)	MAR	Synthetic analog of human amylin (3949 Da)	Endocrinology (diabetes)	Amylin P.
Baraclude (entecavir)	MAR	Guanosine nucleoside analogue (295 g/mol)	Immunology (hepatitis B)	Bristol-Myers Squibb
Byetta (exenatide)	APR	Amino acid peptide amide (4187 Da)	Endocrinology (diabetes)	Amylin P. / Eli Lilly
Naglazyme* (galsulfase)	MAY	Glycoprotein (56 kDa)	Musculoskeletal (Maroteaux-Lamy syndrome)	BioMarin P.
Aptivus (tipranavir)	JUN	Non-peptidic protease inhibitor (603 g/mol)	Immunology (HIV)	Boehringer Ingelheim
BiDil (isosorbide dinitrate / hydralazine HCl)	JUN	Drug mixture (236 g/mol)	Cardiology/Vascular Diseases (heart failure)	NitroMed
Rozerem (ramelteon)	JUL	Propion-type amide (259 g/mol)	Neurology (insomnia)	Takeda
Increlex* (mecasermin)	AUG	Insulin-like growth factor (7649 Da)	Endocrinology (growth failure)	Tercica
Arranon (nelarabine)	OCT	Cytotoxic deoxyguanosine analogue (297 g/mol)	Oncology (leukemia/lymphoma)	GlaxoSmith-Kline
Revlimid (lenalidomide)	DEC	Thalidomide analogue (259 g/mol)	Hematology (myelodysplastic syndromes)	Celgene
Vaprisol (conivaptan)	DEC	Non-peptidic vasopressin receptor antagonist (499 g/mol)	Nephrology (euvoletic hyponatremia)	Astellas P.
Nexavar (sorafenib)	DEC	Multikinase inhibitor (637 g/mol)	Oncology (renal cell carcinoma)	Bayer / Onyx
Orencia* (abatacept)	DEC	Fusion protein (92 kDa)	Rheumatology (rheumatoid arthritis)	Bristol-Myers Squibb

Source: FDA on www.fda.gov (29JAN06)

Trends to Watch in 2006

According to data presented by Doug Braunstein at JP Morgan's 24th Annual Healthcare Conference, healthcare expenditures for 2006 are expected to be \$2 trillion; this represents a 5-fold increase from 1983 spending levels. As the US population ages, along with other countries like Japan, the growth in healthcare spending will continue at a more accelerated pace. Take the Baby Boomer effect into account and the numbers start to really explode!

Although the US is still the clear leader and epicenter of Biopharma, India and China will

start making significant moves in 2006. With their labor advantages, India and China will take on in earnest a large number of less-complex projects, like generics. Down-the-road, pricing pressures will intensify and US companies will have to make plans to compete on a head-to-head basis. There will then exist a large economic driving force for efficiency and waste reduction, replacing the "first-to-market-at-any-cost" strategies of the past. To achieve this, companies will need to maximize employee output. Tools and techniques from the field of project management will be especially important.

Networking will be critical for collaborative efforts within companies, partnerships and the entire industry.

Lastly, outsourcing to 3rd-party manufacturers (CMOs) will become increasingly common. Companies with excess capacity will suddenly find themselves acting as a CMO while, perhaps, simultaneously using CMOs on other select projects. The management and organization of these outsourced arrangements will be critical to control timelines, quality and costs.



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Kymanox, with its partner KMB Innovations, has announced the development of a new web networking tool for Biopharma professionals who work on or support manufacturing activities. **WorkForceDB|Biopharma** launches Spring 2006. Founding members are currently being sought to support the initial roll out; long-term perks and recognition will be provided in return. For more information on this project or to enroll as a founding member, please send your confidential information requests to info@workforcedb.com.

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Mark Your Calendars!

Kymanox has made note of these selected events for informational purposes only. People new to the industry may find this sprinkling of conferences and meetings helpful. Old timers may appreciate the reminder; these meetings come up on you fast!

Bio 2006 is coming to **Chicago** this April for the first time. This is an important event for the Midwest region. It demonstrates that Biopharma has a strong presence in Chicagoland and that area manufacturing and related service companies have been recognized by their (coastal) peers.

Hopefully you will be able to attend of one of these — or similar — events this year.

Event (Meeting / Conference)	Dates	Location
IBC's Outsourcing of Biopharmaceuticals, Technology Transfer, Process Validation and International Antibody Conferences	27FEB06-03MAR06	Carlsbad, CA
IQPC's Annual Technology Transfer Summit for Pharmaceutical and Biotech Industries	27FEB06-01MAR06	Philadelphia, PA
BioSquare 2006	08-10MAR06	Geneva, Switzerland
Horizons 2006—RAPS Conference and Exhibition: Innovation to Regulation	29-31MAR06	San Diego, CA
Bio 2006	08-12APR06	Chicago, IL
Bangalore Bio 2006	27-30APR06	Karnataka, India
WilBio's Waterside Conference and Transgenic BioProcessing Annual Meeting	01-03MAY06	Chicago, IL
AAPS / FDA Bioanalytical Workshop	01-03MAY06	Arlington, VA
IBC's BioPharma Opportunities China	13-15JUN06	Shanghai, China
WilBio's Facilities for Mammalian Cell Products Annual Meeting	16-18OCT06	Raleigh, NC
SPI USA BioManufacturing Technology Training Seminar	05-06OCT06	San Francisco, CA
Burrill's Annual CEO Biotech Meeting	08-10OCT06	Dana Point, CA
ISPE's Annual Meeting	05-09NOV06	Orlando, FL
IBC's BioProcess International Conference & Exhibition	06-09NOV06	San Francisco, CA

Sources: www.ibclifesciences.com, www.iqpc.com, www.ebdgroup.com, www.raps.org, www.bio.org, www.bangalorebio.com, www.wilbio.com, www.fda.gov, www.usaspi.com, www.burrillandco.com and www.ispe.org (31JAN06)