

SPECIAL REPORT

Pharm Exec

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**Our Sixth Annual Report
of the World's Top 50
Pharma Companies»**

Untying the Gordian Knot

BY NICOLE GRAY

In 2004, global prescription sales crossed the \$500 billion threshold, as the industry underwent profound transformation. Change was evident, but some things stayed the same. Pfizer retained its number one status and reported full-year pharma earnings of \$46 billion (including full-year revenues from acquired Pharmacia). The cardiovascular therapeutics market remained strong. Cholesterol and triglyceride reducers continued to lead the pack, racking up combined sales of more than \$30 billion. Sales of Lipitor alone surpassed \$10 billion. In spite of Merck's voluntary withdrawal of Vioxx in September, the company stayed in the top 10, moving down in rank from three to five. Merck also

benefited from the successful launch of Vytarin, co-developed and marketed with Schering Plough, number 16.

Total revenues grew by 7 percent to \$550 billion (according to IMS Health), and PhRMA members' combined R&D investment increased 12.6 percent to \$38.8 billion. The demand for innovative pharmacotherapy continued unabated in 2004: A total of 31 new chemical entities and five biological therapeutics were launched, including four oncology products. Though cancer drugs were not a leading therapeutic class in the analysis of 2003, the size of the global oncology market grew 16.9 percent in constant dollars (allows for currency fluctuations) in 2004, making oncology the third leading therapy based on sales.

The merger of Sanofi and Aventis in August resulted in a company with more than \$31 billion in revenues, making Sanofi-Aventis the largest pharma company in Europe and third largest in the world. The spate of merger announcements continued. In April 2004, Fujisawa and Yamanouchi announced their merger, which became effective last month, when the joint company became Astellas. The trend continues: Look for the Daiichi-Sankyo merger in 2005 to impact next year's rankings.

There were formidable challenges to growth. This year, like last, earnings momentum was tempered by generic erosion worldwide. Sales of former blockbusters Celexa and Diflucan slipped under \$1 billion due to generic competition. Japan maintained its position as the second largest market, but grew an anemic 1.5 percent due to governmental cost containment efforts that cut overall sales by 4.2 percent. A state-mandated clawback tax of 16 percent in

- 1 Pfizer
- 2 GlaxoSmithKline
- 3 Sanofi-Aventis
- 4 Johnson & Johnson
- 5 Merck
- 6 AstraZeneca
- 7 Novartis
- 8 Bristol-Myers Squibb
- 9 Wyeth
- 10 Abbott Labs
- 11 Eli Lilly
- 12 Roche
- 13 Amgen
- 14 Boehringer-Ingelheim
- 15 Takeda
- 16 Schering Plough
- 17 Schering AG
- 18 Bayer
- 19 Eisai
- 20 Teva
- 21 Merck KGaA
- 22 Genentech
- 23 Yamanouchi
- 24 Otsuka
- 25 Novo Nordisk
- 26 Baxter International
- 27 Fujisawa
- 28 Sankyo
- 29 Forest Labs
- 30 Chugai
- 31 Akzo Nobel
- 32 Altana
- 33 Serono
- 34 Solvay
- 35 UCB
- 36 Genzyme
- 37 Allergan
- 38 Mitsubishi Pharmaceuticals
- 39 Shionogi Seiyaku
- 40 Watson
- 41 Ivax Corporation
- 42 Alcon Labs
- 43 Lundbeck
- 44 Biogen Idec
- 45 Mylan Labs
- 46 Shire
- 47 Ono
- 48 King Pharmaceuticals
- 49 Tanabe Seiyaku
- 50 Purdue

Germany put pressure on that market and also slowed growth to less than 2 percent. The dollar remained weak, and companies with substantial earnings in euros and yen benefited from favorable exchange rates.

Some notes on the list:

Figures listed in this ranking do not represent total revenues; they represent only human prescription products. Diagnostics, devices, and animal health are excluded.

When sales were not reported in dollars, they have been converted to dollars based on the average monthly conversion rate for the fiscal year. In some cases this will give a different dollar figure than is included in the company's own material.

Because of Roche's unusual structure, with two large majority-held subsidiaries, Genentech and Chugai, it is difficult to accurately represent that company's position. We have chosen to report each of the three companies separately. If Roche's share of Genentech and Chugai sales were folded into its numbers, it would rank as number eight on the list.

Despite our efforts, there are a number of companies, most of them privately held, for which we have never been able to obtain reliable figures for prescription sales. They include Servier, Procter & Gamble, Mundi International, Merckle, Menarini, and Hexal Group. It is possible that some or all of these companies deserve to be ranked in the Top 50.

Finally, in the pages that follow, sales figures in the company ranking table come from the company's reported figures. In some of the additional charts, sales figures are taken from IMS, which are calculated a different way. Some discrepancies will be noticeable.

The Top 10

The top 10 companies each had sales in excess of \$13.7 billion. Together they grossed \$235 billion in prescription drug sales and marketed more than products that generated in excess of \$1 billion in sales (not all products are listed here). Another company to keep in mind in the context of the top 10 is Roche, which generates approximately a third of its revenues through its majority-owned subsidiaries, Genentech and Chugai. If the appropriate share of their sales were added to Roche, it would have ranked in tenth place with prescription drug revenues of 17.322 billion.

Rank [03 Rank]	Company & Headquarters [website]	2004 Global Pharma Sales [change from 2003]	R&D Spend	2004 Top Selling Drugs
1 [1]	Pfizer New York, NY [pfizer.com]	\$46.133 B [+16%]	\$7.52 B	Lipitor \$10.862 B Norvasc \$4.463 B Zoloft \$3.361 B
	Key Developments » Product launches include Caduet, Inspra, and Spiriva in the US; Lyrica in the US and UK; Prodif in Japan; Macugen co-launched in the US » Bextra achieves blockbuster status	What Analysts Say “Pfizer miscalculated the complexity for physicians using Caduet, which has become one of the bigger disappointments for this company within the last year and a half. We’re in a top-line-constrained environment because of the consolidation of purchasing power among the payer base. So Pfizer needs to leverage its ability to become more efficient.” MARA GOLDSTEIN, CIBC WORLD MARKETS		
2 [2]	GlaxoSmithKline London, England [gsk.com]	\$31.377 B [+5%]	\$5.195 B	Seretide/Advair \$4.503 B Avandia \$2.042 B Seroxat/Paxil \$1.945 B
	Key Developments » Seretide/Advair approved for use in children ages 4 to 11 with asthma » In Phase II trials, Cervarix shows 100% efficacy against human papilloma virus » Sales of Lamictal grew 38% to \$338 million	What Analysts Say “This company’s pipeline has breadth and depth, with an inordinate number of shots on goal. The size of their pipeline relative to the R&D investment is impressive.” CHRIS SHIBUTANI, MD, J.P. MORGAN		
3 [17/5]	Sanofi-Aventis Paris, France [sanofi-aventis.com]	\$30.919 B [+12%]	\$9.31 B	Lovenox \$2.38 B Plavix \$2.17 B Allegra \$1.87 B
	Key Developments » Sanofi-Aventis merger completed in August » Apidra launched in the US and Germany » Exanta injection and tablet formulations filing rejected in the US, but launched in Finland » Taxotere approved by FDA and EMEA for adjuvant post-surgical treatment of patients with operable node-positive breast cancer	What Analysts Say “The key question is ‘Is Accomplia the next big thing?’ I like what I see in the data. Accomplia has a lot of potential.” JOHN T. BORIS, HARRIS NESBITT		
4 [4]	Johnson & Johnson New Brunswick, NJ [jnj.com]	\$22.128 B [+13%]	\$5.203 B	Procrit/Eporex \$3.589 B Risperdal \$3.050 B Remicade \$2.145 B
	Key Developments » Procrit sales declined 12% » Sales of Duragesic grew 28% to \$2.083 billion » Received approvals in the US for Topamax for migraine prevention in adults, Levaquin tablets/injection to treat multi-drug resistant strains of <i>Streptococcus pneumoniae</i> in community-acquired pneumonia, and Procrit for once-weekly dosing	What Analysts Say “The acquisition strategy works for Johnson & Johnson. You can’t argue with the fact that they are a well-run company.” THOMAS MOTTER, CHILTON CAPITAL OF HOUSTON		
5 [3]	Merck Whitehouse Station, NJ [merck.com]	\$21.493 B [-4%]	\$4.01 B	Zocor \$5.2 B Fosamax \$3.2 B Cozaar/Hyzaar \$2.8 B
	Key Developments » Merck voluntarily withdraws Vioxx from market in September » Launches cardiovascular combination product Vytorin, the only dual mechanism-of-action cholesterol inhibitor, with Schering Plough; Head-to-head trial versus Lipitor shows Vytorin more effectively reduces cholesterol » Global sales of Fosamax increase 18% to \$3.2 billion	What Analysts Say “As much as Vioxx yielded a nice profit, this company is large and diversified. The issue is whether the pipeline can replenish lost revenues. It has three novel vaccines in Phase III development that have potential.” MARA GOLDSTEIN, CIBC WORLD MARKETS		

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Rank [03 Rank]	Company & Headquarters [Web site]	2004 Global Pharma Sales [change from 2003]	R&D Spend	2004 Top Selling Drugs
6 [6]	AstraZeneca London, England [astrazeneca.com]	\$21.426 B [+13.5%]	3.803 B	Nexium \$3.8 B Seroquel \$2.02 B Losec/Prilosec \$1.94 B
	Key Developments » FDA rejects Exanta approval for all filings » Crestor sales fall to \$908 million after allegations of safety risk » Seroquel receives indication for the treatment of acute mania in bipolar disorder » Seroquel sales up 33% to over \$2 billion			What Analysts Say “The launch of Crestor shows that this company misjudged the amount of pent-up demand for high-potency statins. On the positive side, they have been able to successfully turn around the Seroquel franchise and make it a meaningful player.” MARA GOLDSTEIN, CIBC WORLD MARKETS
7 [7]	Novartis Basel, Switzerland [novartis.com]	\$18.497 B [+2.5%]	\$3.480 B	Diovan \$3.09 B Gleevec/Glivec \$1.634 B Zometa \$1.07 B
	Key Developments » Launches Certican in Germany and Ketek in the US » Gleevec achieves blockbuster status			What Analysts Say “This company doesn’t have any meaningful patent expirations until 2015 and Gleevec could be an even bigger product years out. Dan Vasella has done a good job of rationalizing costs. Their belief that it’s important to do a lot of their own drug development works to their advantage, because in the process they develop in-house experience and knowledge to nurture their pipeline.” THOMAS MOTTER, CHILTON CAPITAL OF HOUSTON
8 [8]	Bristol-Myers Squibb New York, NY [bms.com]	\$15.482 B [+4%]	\$2.5 B	Plavix \$3.3 B Pravachol \$2.6 B Taxol \$991 M
	Key Developments » Sales of Reyatez increase approximately 370% to \$414 million » Sales from alliance revenues of Abilify more than double to \$593 million up from \$283 million in 2003 and \$25 million in 2002 when the product was launched » Glucophage franchise sales decrease 65% to \$336 million			What Analysts Say “BMS has faced continual patent expirations on products that collectively represent a lot of revenue. This company has had a hard couple of years, but company strategists have been able to execute to regain a solid operating platform. Their future lies in the ability to execute on their pipeline. Pravachol is going off patent and Plavix’s exclusivity is at risk, but muriglitazone, on the other hand, is a promising first-in-class treatment.” MARA GOLDSTEIN, CIBC WORLD MARKETS
9 [9]	Wyeth Madison, NJ [wyeth.com]	\$13.964 B [+10.5%]	\$2.46 B	Effexor \$3.34 B Protonix \$1.59 B Prevnar \$1.05 B
	Key Developments » Premarin sales slip below \$1 billion » Plevnar becomes first blockbuster vaccine			What Analysts Say “With respect to generic exposure, Wyeth is relatively clean. There is not a major drug or franchise going off patent in the near future, and they are well-positioned to retain their status. Wyeth’s pipeline is well matched, evenly balanced, and aligned with their existing in-line franchises. Regarding the Premarin controversy, the damage is done although subsequent analyses of WHI data lessened the potential severity of the data implications.” CHRIS SHIBUTANI, MD, J.P. MORGAN
10 [11]	Abbott Labs Abbott Park, IL [abbott.com]	\$13.756 B [+11.6%]	\$1.69 B	Prevacid \$1.3 B [TAP] Biaxin \$1.18 B



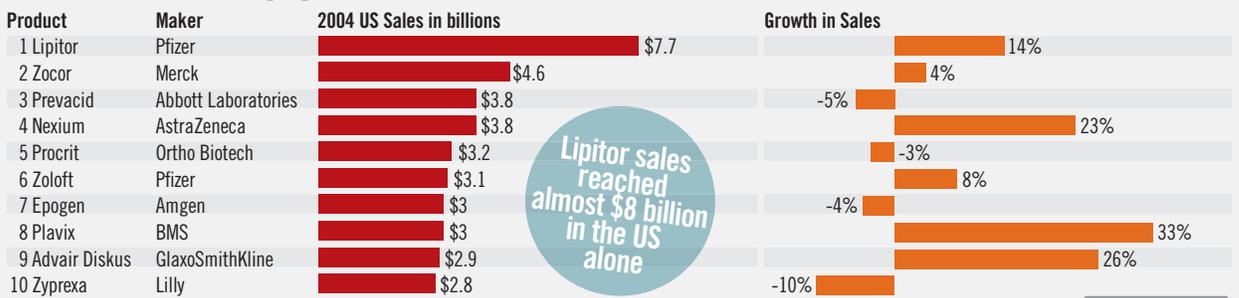
Rank [03 Rank]	Company & Headquarters [Web site]	2004 Global Pharma Sales [change from 2003]	R&D Spend	2004 Top Selling Drugs
11 [10]	Eli Lilly Indianapolis, IN [lilly.com]	\$13.059 B [+4%]	\$2.69 B	Zyprexa \$4.4 B
12 [12]	Roche Basel, Switzerland [roche.com]	\$17.322 B [+41.5%]	\$5.40 B	MabThera/Rituxan \$4.18 B
13 [15]	Amgen Thousand Oaks, CA [amgen.com]	\$10.6 B [+35%]	\$1.996 B	Epogen \$2.6 B
14 [14]	Boehringer-Ingelheim Ingelheim, Germany [boehringer-ingelheim.com]	\$8.698 B [+8%]	\$1.527 B	Flomax \$912.6 M
15 [16]	Takeda ¹ Osaka, Japan [takeda.com]	\$8.274 B [+12%]	\$1.223 B	Actos \$1.676 B

TOP 10 PRODUCTS 2004 [GLOBAL]



SOURCE: IMS Health, IMS MIDAS®, MAT Dec 2004 *biopharmaceutical division of Janssen-Cilag

TOP 10 PRODUCTS 2004 [US]



SOURCE: IMS Health

A PharmExec Graphic

16 [17]	Schering Plough Madison, NJ [sch-plough.com]	\$6.417 B [+4%]	\$1.607 B	Remicade \$746 M
17 [18]	Schering AG Berlin, Germany [schering.de]	\$6.085 B [+11%]	\$745 M	Betaferon \$969 M
18 [19]	Bayer Leverkusen, Germany [bayer.de]	\$5.44 B [+1%]	\$1.527 B	Cipro \$1.04 B
19 [21]	Eisai ¹ Tokyo, Japan [eisai.co.jp]	\$5.006 B [+32%]	\$724 M	Aricept \$1.335 B
20 [25]	Teva Petach Tikva, Israel [tevapharm.com]	\$4.276 B [+30.5%]	\$338 M	Copaxone \$936 M



Rank [03 Rank]	Company & Headquarters [Web site]	2004 Global Pharma Sales [change from 2003]	R&D Spend	2004 Top Selling Drugs
21 [24]	Merck KGaA Darmstadt, Germany [merck.de]	\$3.845 B [+14%]	\$597 M	Glucophage \$339 M
22 [xx]	Genentech South San Francisco, CA [gene.com]	\$3.749 B [43%]	\$948 M	Rituxan \$1.7 B
23 [22]	Yamanouchi ¹ Tokyo, Japan [yamanouchi.co.jp]	3.73 B [+5%]	\$661 M	Harnal \$1.15 B
24 [40]	Otsuka ² Tokyo, Japan [otsuka.co.jp]	3.719 B [+20%]	\$500 M	Abilify \$ 895 M
25 [23]	Novo Nordisk Bagsvaerd, Denmark [novonordisk.com]	\$3.51 B [+2%]	\$664 M	Anti-diabetic therapies \$3.076 B
26 [26]	Baxter International Deerfield, IL [baxter.com]	\$3.504 B [+7%]	\$517 M	R/antihemophilic factor \$1.329 B
27 [28]	Fujisawa ¹ Osaka, Japan [fujisawa.co.jp]	\$3.201 B [+9%]	\$695 M	Progral \$985 M
28 [20]	Sankyo ¹ Tokyo, Japan [sankyo.co.jp]	\$2.908 B [-24%]	\$661 M	Pravastatin \$1.817 B
29 [32]	Forest Labs ¹ New York, NY [frx.com]	\$2.65 B [+20%]	\$246 M	Lexapro \$1.089 B
30 [xx]	Chugai Tokyo, Japan [chugai-pharm.co.jp]	\$2.62 B [28%]	\$454 M	Epogin \$651 M

1. FISCAL YEAR 2003 ENDS 3-31-04 2. JAN-DEC 2004 EARNINGS FROM IMS

TOP 10 COMPANIES BY US MARKET SHARE

Company	Total Sales US billions [Market Share]
1 Pfizer	\$30.720 [13.1%]
2 GlaxoSmithKline	\$18.793 [8.0 %]
3 Johnson & Johnson	\$16.239 [6.9 %]
4 Merck & Co	\$15.004 [6.4 %]
5 AstraZeneca	\$11.338 [4.8 %]
6 Novartis	\$10.226 [4.3 %]
7 Sanofi-Aventis	\$10.022 [4.3 %]
8 Amgen	\$9.534 [4.1 %]
9 Bristol-Myers Squibb	\$9.207 [3.9 %]
10 Wyeth	\$8.214 [3.5 %]

SOURCE: IMS Health, IMS MIDAS®, MAT Dec 2004

Pfizer captured 13% of the market in 2004

Companies that rose in ranking this year include: Otsuka, Forest Labs, Altana, Serono, Genzyme, Watson, Mylan Labs, Shire and Ono. Hovering just below the Top 50 were Daiichi (\$1.246 B), Barr Pharmaceuticals (\$1.231 B), and Gilead Sciences (\$1.2 B).

[7]
PERCENT THAT REVENUES FOR PHARMA COMPANIES GREW IN 2004, TO A TOTAL \$550 BILLION

PhRMA MEMBERS' COMBINED R&D INVESTMENT IN 2004 WAS \$38.8 BILLION. A PERCENTAGE INCREASE OF

[12.6]

TOP 10 MOVERS 2003-2004

Company	Growth
1 Amgen	35%
2 Genzyme	34%
3 Eisai	32%
4 Teva	30.5%
5 Ivax	29%
6 Chugai	28%
7 Alcon Labs	18%
8 Pfizer	16%
9 UCB	15%
10 Merck KGaA and Altana	14%

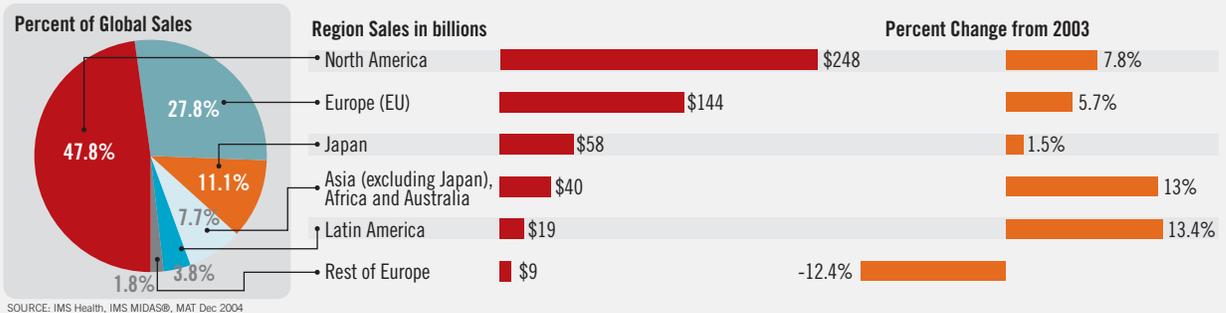
SOURCE: Pharmaceutical Executive

A PharmExec Graphic



Rank [03 Rank]	Company & Headquarters [Web site]	2004 Global Pharma Sales [change from 2003]	R&D Spend	2004 Top Selling Drugs
31 ^[27]	Akzo Nobel Arnhem, Netherlands [akzonobel.com]	\$2.37 B [-23%]	\$642 M	Remeron \$450 M
32 ^[36]	Altana Bad Homburg, Germany [altana.de]	\$2.23 B [+14%]	\$504 M	Pantoprazole \$1.488 B
33 ^[35]	Serono Geneva, Switzerland [serono.com]	\$2.177 B [+7%]	\$595 M	Rebif \$1.1B
34 ^[34]	Solvay Brussels, Belgium [solvay.com]	\$2.163 B [+4%]	\$358 M	Androgel \$286 M

2004 GLOBAL PHARMACEUTICAL SALES BY REGION



THE NUMBER OF BIOLOGICAL THERAPEUTICS LAUNCHED IN 2004
[5]

[12 TO 15%]
THE RATE AT WHICH CHINA'S PHARMACEUTICAL MARKET IS GROWING

Almost half of 2004 pharma sales came from the US, with Europe coming in second with close to 28 percent of global sales. Latin America experienced the most growth—over 13 percent—with \$19 billion in global sales.

A PharmExec Graphic

35 ^[N/A]	UCB Brussels, Belgium [ucb-group.com]	\$2.08 B [+15%]	N/A	Keppra \$517 M
36 ^[41]	Genzyme Cambridge, MA [genzyme.com]	\$1.976 B [+34%]	\$391 M	Renagel \$364 M
37 ^[37]	Allergan Irvine, CA [allergan.com]	\$1.842 B [+5%]	\$350 M	Botox \$705 M
38 ^[N/A]	Mitsubishi Pharmaceuticals¹ Osaka, Japan [www.m-pharma.co.jp]	\$1.812 B [N/A]	\$476 M	Radicut \$258 M
39 ^[31]	Shionogi Seiyaku¹ Osaka, Japan [shionogi.co.jp]	\$1.641 B [-29%]	\$281 M	Flomox \$325 M
40 ^[42]	Watson Corona, CA [watsonpharm.com]	\$1.6405 B [+12%]	\$134.2 M	Bupropion hydrochloride \$162 M

1. FISCAL YEAR 2003 ENDS 3-31-04



Rank [03 Rank]	Company & Headquarters [Web site]	2004 Global Pharma Sales [change from 2003]	R&D Spend	2004 Top Selling Drugs
41 [N/A]	Ivax Corporation Miami, FL [ivax.com]	\$1.557 B [est +29%]	\$162 M	Respiratory products \$371.5 M
42 [45]	Alcon Labs Hünenberg, Switzerland [alconinc.com]	\$1.542 B [+18%]	\$400 M	Pantanol \$307 M
43 [N/A]	Lundbeck Copenhagen, Denmark [lundbeck.com]	\$1.518 B [-8%]	\$295 M	Cipramil \$485 M
44 [44]	Biogen Idec Cambridge, MA [biogen.com]	\$1.486 B [+9.5%]	\$686 M	Avonex \$1.42 B
45 [46]	Mylan Labs Canonsburg, PA [mylan.com]	\$1.374 B [+8%]	\$101 M	Omeprazole \$212 M

LEADING THERAPY CLASSES IN 2004 GLOBAL PHARMACEUTICAL SALES

Therapeutic Class	2004 Sales in billions [% Share of Global Market]	Growth in Sales
Cholesterol and triglyceride reducers	\$30.2 [5.8%]	11.7%
Antiulcerants	\$25.5 [4.9%]	1.4%
Cytostatics	\$23.8 [4.6%]	16.9%
Antidepressants	\$20.3 [3.9%]	1.3%
Antipsychotics	\$14.1 [2.7%]	12.1%
Antirheumatic Non-Steroidals	\$13.1 [2.5%]	3.3%
Angiotensin-II Inhibitors	\$12.0 [2.3%]	22.1%
Calcium Antagonists Plain	\$11.6 [2.2%]	1.6%
Erythropoietin Products	\$11.4 [2.2%]	8.9%
Anti-Epileptics	\$11.3 [2.2%]	17.7%

SOURCE: IMS Health, IMS MIDAS®, MAT Dec 2004

The cardiovascular therapeutics market remained strong. Cholesterol and triglyceride reducers led the pack with combined sales of more than \$30 billion.

[31]
THE NUMBER OF
NEW CHEMICAL
ENTITIES
LAUNCHED IN 2004

This year's Sanofi-Aventis merger made the combined entity the third largest pharma company in the world, and the largest in Europe. Last month, Fujisawa and Yamanouchi joined forces to become Astellas. The merger trend is likely to continue.

A PharmExec Graphic

46 [47]	Shire Hampshire, England [shire.com]	\$1.363 B [+8%]	\$196 M	Adderall \$607 M
47 [33]	Purdue Pharma Stamford, CT [pharma.com]	\$1.34 B [-39%]	\$294 M	Oxycontin \$1.29 B
48 [50]	Ono¹ Osaka, Japan [ono.co.jp]	\$1.31 B [+13%]	\$250 M [est]	Opalmon \$220 M
49 [39]	King Pharmaceuticals Bristol, TN [kingpharm.com]	\$1.304 B [-14%]	\$679 M	Altace \$347.3 M
50 [43]	Tanabe Seiyaku Osaka, Japan [tanabe.co.jp]	\$1.296 B [-6%]	\$232 M	Herbaser \$158 M



1. FISCAL YEAR 2003 ENDS 10-31-04 2. FISCAL YEAR 2003 ENDS 6-30-04

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Harbingers of Change

Murray Aitken shares his insights on government-led activism, generic erosion, biologics, and the China factor.

BY NICOLE GRAY

MURRAY L. AITKEN, SENIOR VICE PRESIDENT, CORPORATE STRATEGY, FOR IMS, is a widely respected industry analyst whose views are frequently published by *Pharm Exec* because of his profound ability to look beyond immediate circumstances and recognize how various factors will affect the industry over the long term. His penchant for spotting trends and looking at micro and macro data points feeds an industry with a huge appetite for systematically analyzed information.

Recently, IMS tapped Aitken's ability to take the broad view and compiled an analytical compendium of the top 10 harbingers of change for the pharmaceutical industry. These trends are outlined in detail in *Intelligence.3601*, a new IMS publication. Aitken spoke with *Pharm Exec* about these harbingers of change.

Pharm Exec: IMS estimates that delays in the approval process could reduce the value of companies' pipelines globally by approximately 20 percent. What factors are most challenging?

Aitken: The safety issues raised in connection with Cox-2 inhibitors and other products, and the attendant media attention, surrounding these events has led to increased scrutiny all around. The approval process could slow down as the FDA starts to require more evidence prior to approval. As a result, companies will need to establish a larger base of evidence, especially for chronic care drugs.

There's also the impact on physicians. Every day, physicians make tradeoffs between risks and benefits when it comes to prescription drugs. Changes in the regulatory process could change doctors' ability to make those tradeoffs, effectively taking the decision-making authority out of their hands. If the medications are not approved, physicians will not have access to them.

What can companies do to counter the negative impact of a longer approval process?

The Clinical Trials Registry is part of the trend of making data more transparent. There are numerous medications out there that tend to be underutilized, and there is already a great deal of data available about these products. We can do more with the information that already exists.

There's another important dimension to the drug safety issue. Manufacturers need to develop much more robust information about the benefits of drugs. That way, we can have an appropriately balanced conversation. As a result, there can be a balanced review of drugs. For the industry, that means stepping up the level of investment it makes, including more post-marketing surveillance and outcomes studies in general that document health benefits.

You refer to Mark McClellan, Administrator of CMS since March 2004, as a leader with an activist agenda. Which aspects of his policy qualify him as an activist?

Medicare reform is clearly a transformative event in US healthcare. The fact that large numbers of patients have access to drug benefits is important. The implementation of the Medicare Modernization Act (MMA) will ultimately impact



the quality of drug therapy and the movement toward a more rational approach to medication reimbursement.

McClellan is focused on evidence-based medicine. Aside from his goal of lowering drug prices for the more than 40 million people treated under Medicare, Dr. McClellan is focused on developing better evidence about the comparative risks and benefits of drugs. This approach calls for more head-to-head trials. Eventually, pay-for-performance metrics will be

applied throughout the delivery chain.

I predict that McClellan's zeal for reform vis-à-vis MMA implementation will bring a much greater premium to innovative products that have demonstrable benefits over existing alternatives. For the industry, willingness to engage in more hard-nosed clinical trials that demonstrate products' superiority will be competitively advantageous.

According to IMS, the biologics market topped \$42 billion in 2004, and you noted that with a growth rate of 17 percent, it is the fastest growing segment of the pharmaceutical industry. Do you see that trend continuing, and are there any other dynamics that the industry should be aware of?

Right now, companies that do not have access to a robust pipeline of biologics are finding it hard to maintain their position in the marketplace. Investments from the last 20 years are paying off for

Companies are applying Western marketing techniques in Japan—and taking market share from the domestic companies.

companies that made them. Some companies now are in the position where they have nothing in their therapeutic pipeline that could be categorized as a biologic. Some might argue that it's a deliberate strategy, or it may simply be a function of the fact that they failed to invest 15 years ago.

In your opinion, which large companies have strong biologics pipelines?

Lilly, Johnson & Johnson, and Roche.

Regarding the Australian regulatory approval of Omnitrope, Sandoz's biogeneric form of somatropin, do you think this is the beginning of a larger trend? Is that market subject to generic erosion similar to that of small molecule products?

Generic competition is going to be a reality in this segment. Before, there were two major obstacles to developing and manufacturing biogenics. The first was that it was difficult to produce equivalent biologics. The second was an opaque regulatory pathway. The first barrier is no longer there, thanks to advances in biopharmaceutical manufacturing. The

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TOP 20 PHARMA COMPANIES BY SALES IN JAPAN

Company	Total Sales US billions [Market Share]
1 Takeda	\$3.6 [6.3%]
2 Pfizer	\$3.4 [5.8%]
3 Roche	\$2.4 [4.2%]
4 Otsuka	\$2.4 [4.1%]
5 Sankyo	\$2.2 [3.8%]
6 Novartis	\$2.1 [3.7%]
7 Eisai	\$2.0 [3.4%]
8 Daiichi	\$1.9 [3.3%]
9 Yamanouchi Seiyaku	\$1.6 [2.8%]
10 Merck & Co.	\$1.6 [2.7%]
11 Mitsubishi Pharma	\$1.5 [2.7%]
12 Shionogi Seiyaku	\$1.4 [2.5%]
13 AstraZeneca	\$1.3 [2.3%]
14 GlaxoSmithKline	\$1.3 [2.3%]
15 Fujisawa	\$1.2 [2.2%]
16 Tanabe Seiyaku	\$1.2 [2.1%]
17 Sanofi-Aventis	\$1.2 [2.1%]
18 Ono	\$1.2 [2.1%]
19 Sumitomo	\$1.1 [1.9%]
20 Kowa Shinyaku	\$1.0 [1.7%]

SOURCE: IMS Health, IMS MIDAS™, MAT Dec 2004; Corporation Level

A PharmExec Graphic

Takeda has
OVER 6%
market share
in Japan

Australian approval of Omnitrope essentially demonstrated a pathway for approval. So it's not if biologics arrive, it's when. The playing field is level now. The prospect of generic biologics coming into the US and European markets will cause innovative biotech companies to step up their efforts.

The Japanese market is ranked as having the second largest pharmaceutical market in the world, yet it only grew 1.5 percent last year. Is it going to lose its number two status?

Japan is a market that has seen very low levels of growth because of effective restraints on growth. Average growth within the last five years has averaged one percent to four percent, because of what I call "blunt instruments"—broad, across-the-board, price reductions. But, despite the fact that the market is only growing at that rate, some innovative companies doing business there are seeing double-digit increases. Over the last couple of years, companies such as Pfizer have applied Western marketing techniques and taken market share from domestic companies.

What about other Asian markets?

China is now the eighth largest pharmaceutical market in the world and has been growing at a rate of 12 to 15 percent with respect to hospital pharmaceutical sales. The pharmaceutical industry is an industry that can be truly global. For one thing, intellectual property [IP] is entirely transferable around the world, especially as China and India come into the fold through WTO implementation. In the longer-term view, the direction is clear. IP can flow, and the active pharmaceutical ingredient [API] market in China is now more than \$1 billion.

Plus, there are other factors at play: There is a growing middle class and the government wants to provide healthcare for its citizens. China is a good situation for companies that want to gain access to low-cost manufacturing and low-cost APIs along with IP. It is still a long-term situation. I'd suggest a 20- to 50-year time frame. As China implements WTO laws this mitigates risk, and the impact of the WTO legislation is attended by cultural shifts that occur over time. Companies with vision understand that China is the future. ☉