



*What's that image fading from view? Pharma just sped through an unprecedented period of patent expiries, during which some \$30 billion in brand revenue went over the cliff. But stay focused on the road. Another patent peak, equally scary, lies ahead. **Mare Iskowitz** reports*

**2013  
PHARMA  
REPORT**

# **DON'T LOOK BACK!**

The sluggish economy, combined with what Michael Kleinrock, director, research development for the IMS Institute, calls “an unprecedented period of patent expiries,” led to a drop in overall drug spend of 1% last year to \$325.8 billion — the first time IMS had ever recorded a decrease in US drug sales.

The period from 2008-2012 was the biggest-ever for expiries, says Kleinrock. Following Lipitor’s 2011 patent implosion, last year saw the demise of mega-blockbusters like Bristol-Myers Squibb’s blood thinner Plavix. The impact is evident on the following list; only half the companies grew US sales.

Kleinrock expects the same minus-one growth in 2013, due to “the carryover of 2012 expiries,” before spending rebounds in 2014 and then another patent peak hits. The two peaks — 2011-12 and 2014-15 — are relatively similar in size, with about \$30 billion of lost sales per year for brands.

Milder impact from expiries, breakthrough drug approvals, and healthcare reform will drive spend on prescription drugs to rise by 3-4% in 2014, IMS predicts. Growth will then fall to just over 2% in 2015 and climb again in 2016 to almost 4%.

Why not a return to double-digit growth? Many new drugs target smaller patient populations. Also, generic meds accounted for 84% of prescriptions dispensed in 2012 and, in another five years or so, will probably reach 87%.

“We’re at sort of a saturation point,” Kleinrock says, where “newer brands with better efficacy will be used, and that will slow down all of these gains that generics are making.”

That, and specialty drug prices, spending for which boomed 18.4% last year, according to Express Scripts. “The specialty drugs are less price-sensitive, and we will continue to see the portion of specialty medications grow in the total drug bill,” says Jeffrey Russell, North American managing director for Accenture’s life sciences practice.

Revenue losses notwithstanding, pharmas have helped shore up profitability and shareholder value by slimming down, doing mega-mergers and in-licensing products. Going forward, what capabilities will help them?

“New products are the key to survival,” says fund manager Les Funtleyder, now with Poliwogg. Some on the list are spending 17-20% of revenues on R&D. Yet, while pipelines have been looking more attractive, R&D attrition rates have risen. And due to major pressures in the pricing and reimbursement area, “The industry can no longer continue to emphasize clinical efficacy and safety requirements to determine which therapies to develop,” Russell says.

Commanding higher prices, even for personalized medicines, will take total product value and real-world evidence. If not, pricing levels will not be sustainable.

“We have to do a better job when we bring new products to market,” agrees Robert Bazemore, president, Janssen Biotech. “The burden’s going to fall much more on us to demonstrate the value these products really add.”

Janssen biologics like Remicade helped parent Johnson & Johnson keep US losses in check and to grow global revenue. But with Remicade due to hit the patent wall in 2018, the company exemplifies the pressure the industry faces.

“Many expected industry growth to decline much more than it actually has ended up doing,” concludes Kleinrock. “To keep it at only -1% is a pretty big success in a number of ways.”







*With additional reporting by Matthew Arnold, Deborah Weinstein and Kevin McCaffrey*

# THE TOP 20

AbbVie	
Actavis	44
Amgen	45
AstraZeneca	43
Boehringer Ingelheim	41
Bristol-Myers Squibb	45
Eli Lilly	44
Gilead	43
GlaxoSmithKline	46
Johnson & Johnson	42
Merck	44
Mylan	40
Novartis	45
Novo Nordisk	40
Otsuka	46
Pfizer	46
Roche	40
Sanofi	42
Takeda	44
Teva	46
	41









**1 Novartis** \$20.0B ▼1.2%

-  **Global revenue:** \$56.7B (3rd); **down 3.2%**
-  **Top brands:** Diovan (\$2.1B), Gleevec (\$1.7B), Diovan HCT (\$1.4B), Gilenya (\$852M)
-  **Promotional spend:** \$852M (6th); 4.3% of rev.
-  **R&D spend:** \$9.1B (1st); down 1.1%; 16.1% of rev.
-  **Planned launches:** SOM230 (onc.), Relaxin (HF), QVA149 (resp.), NVA237 (resp.)
-  **Patent expirations:** Myfortic (2013), Zometa (2013), Sandostatin (2014)

Although a weak cold and flu season didn't help matters, fewer sneezes weren't the only reason for falling 2012 sales. The OTC division continued to stumble, paralyzed by the shuttered Lincoln, Neb., site over manufacturing problems that kept medicines off shelves. Pharmaceuticals, which powers the other five divisions, saw sales slide 1% to \$32.2 billion due to generics. Despite the onslaught of negatives, the company has a strong rep as a powerhouse, particularly in niche categories, and the company predicted in November 2012 that sales will rebound from the Diovan patent loss (2012). Analysts are split on how, and if, Biogen Idec's new MS drug, Tecfidera, will threaten Gilenya's sales, but the company told investors in November that the future includes 138 potential therapies and around 10 regulatory filings with seven approvals this year. Novartis expects this to be a foundational year with single-digit sales growth in 2014 and 2015.

**2 Merck** \$19.8B ▼0.3%

-  **Global revenue:** \$47.3B (5th); **down 1.5%**
-  **Top brands:** Januvia (\$4B); Singulair (\$3.8B); Zetia (\$2.5B); Remicade (\$2B); Vytorin (\$1.7B)
-  **Promotional spend:** \$1.39B (3rd), 7.0% of rev.
-  **R&D spend:** \$7.8B (4th), down 1.3%; 16.5% of rev.
-  **Planned launches:** Bridion (neuromusc. block); V503 (HPV); Atozet (lipid)
-  **Patent expirations:** Remicade (2014), Zetia (2016), Vytorin (2017)







It's been a difficult time for Merck. Niacin-statin combo Tredaptive was pulled in Europe, and the Singulair allergy blockbuster came off-patent last year. First-quarter 2013 brought news that osteoporosis candidate odanacatib is delayed. Moreover, IMPROVE-IT, the trial of combo cholesterol med Vytorin, was allowed to run its course but may not matter much in the end due to the patent window and availability of generic statins, and a possible link to pancreatitis may affect prescribers' enthusiasm for top seller Januvia. Analysts have high hopes for new R&D chief Roger Perlmutter, who comes with a proven track record from Amgen. Merck's bet on the future lies in part with anacetrapib, an HDL-lowering treatment that the industry is skeptical of—Phase III trial data will not come until 2017. Merck is likely to receive approval for sleep therapy suvorexant in late June/early July, but Bernstein Research analyst Tim Anderson wrote in an investor note, "It is very difficult to get excited about this opportunity, (given the crowded nature of the sleep market)."

**Fig. 1: Top 20 Pharmaceutical Companies by US Sales '12**

Rank	Company	2012 Total (Billions)	2011 Total (Billions)
1	Novartis	\$20.0	\$20.2
2	Merck	\$19.8	\$19.8
3	Pfizer	\$18.2	\$26.1
4	AstraZeneca	\$17.3	\$20.4
5	Teva	\$16.3	\$15.6
6	Roche	\$15.4	\$14.6
7	GlaxoSmithKline	\$14.1	\$14.7
8	Lilly	\$14.0	\$15.3
9	Amgen	\$13.9	\$13.4
10	Abbott*	\$12.5	\$12.0
11	Sanofi	\$12.1	\$12.4
12	Johnson & Johnson	\$12.0	\$12.1
13	Bristol-Myers Squibb	\$8.3	\$12.0
14	Boehringer Ingelheim	\$7.9	\$7.2
15	Actavis	\$7.7	\$6.0
16	Mylan	\$7.3	\$5.8
17	Gilead	\$6.7	\$5.6
18	Novo Nordisk	\$6.6	\$5.4
19	Otsuka	\$6.0	\$5.3
20	Takeda	\$5.5	\$7.1
<b>Total others</b>		<b>\$84.4</b>	<b>\$78.0</b>
<b>Total market</b>		<b>\$325.8</b>	<b>\$329.2</b>

Source: IMS Health, National Sales Perspectives \*On January 2, 2013, Abbott's research-based pharma business, AbbVie, became a separate entity


**3 Pfizer** \$18.2B ▼30.2%

-  **Global revenue:** \$59.0B (2nd); **down 9.6%**
-  **Top brands:** Lipitor (\$2.0B), Celebrex (\$2.0B), Lyrica (\$2.0B), Viagra (\$1.1B), Zyxos (\$721M)
-  **Promotional spend:** \$1.6B (2nd); 8.8% of rev.
-  **R&D spend:** \$7.9B (3rd) down 13.2%; 13.4% of rev.
-  **Planned launches:** Celebrex (pain, 2014), Premarin (2015), Zyxos (2015)
-  **Patent expirations:** Celebrex (pain, 2014), Premarin (2015), Zyxos (2015)

Having sold its infant nutrition unit to Nestle and spun off its animal health business, Pfizer brass is now turning to fixing its core pharma business and taking tentative steps toward a possible breakup into "innovative (new drugs)" and "value (mature and off-patent meds)" companies through separate management and reporting structures. Pfizer has several years to go before it's fully over the patent cliff, and there are several big shoes left to drop in the next couple of years. Analysts and investors are bullish on Ian Read's stewardship of the company, in good measure because of increased dividends. More importantly, Pfizer's pipeline is producing, particularly in oncology, where the firm has seen a string of approvals including Bosulif, Inlyta, Sutent and Xalkori—not to mention recent FDA approvals of RA drug Xeljanz and clot-buster Eliquis, a co-market with BMS. Wild cards could include early decisions on breast cancer candidate palbociclib or its meningitis B vaccine.


## 4 AstraZeneca


\$17.3B ▼15.2%

 **Global revenue:** \$28.0B (8th); **down 16.7%**

 **R&D spend:** \$4.5B (9th); down 10.0%; 16.1% of rev.

 **Top brands:** Crestor (\$3.1B); Nexium (\$2.2B); Symbicort (\$1B); Onglyza (\$237M); Brilinta (\$19M)

 **Planned launches:** Brodalumab (RA/psoriasis), fostamatinib (arthritis), lesinurad (gout)

 **Promotional spend:** \$1.1B (4th); 6.4% of rev.


 **Patent expirations:** Symbicort (2014); Nexium (2015); Synagis (2015)


It's been a wild year at AstraZeneca. CEO Pascal Soriot, who came from Roche last August, has wasted little time putting his mark on the company. In January, he fired the firm's heads of commercial operations and R&D. Soriot forecasted a 2013 revenue decline in the "mid-to-high single digits" and vowed to jolt the company's "consensus-driven" and "conservative" culture. In March, the company announced another sweeping round of layoffs and office closings, moving much of its US sales and marketing functions in with MedImmune and its global headquarters from London to Cambridge, UK (which is kind of the Cambridge, MA, of England). It's all part of Soriot's efforts to shed the firm's small molecule-focused and inward-facing past in favor of a more collaborative and biotech-driven future. The company's diabetes partnership with Bristol-Myers Squibb is the lynchpin of its near-term commercial plan, and about half its Phase I and II pipeline is comprised of biologics.


## 5 Teva


\$16.3B ▲4.2%

 **Global revenue:** \$20.3B (10th); **up 11.0%**

 **R&D spend:** \$1.4B (18th); up 27.3%; 6.9% of rev.

 **Top brands:** Copaxone (\$3.6B); Proair HFA (\$1.1B); Budesonide (\$944M); Treanda (\$606M)

 **Planned launches:** Tevagrastim (onc.), laquinimod (MS), SA GCSF (onc.)

 **Promotional spend:** \$289M (15th); 1.8% of rev.

 **Patent expirations:** Azilect (2013), Treanda (2013), Copaxone (2014)

Teva progressed toward its 2011 goal to be known for brands more than generics: generics contributed 51% of revenues while specialty, like the blockbuster Copaxone, brought in 40%. That's a reversal from 2011, when generics were the heavier-lifters at 56% with specialty drugs the relative lightweights at 35%. Yet the turnaround is still largely dependent on branded drugs that came over with the 2011 Cephalon purchase, and those have a short patent window ahead: Oncology drug Treanda goes generic next year, with sleep med Nuvigil following in 2016. Despite its increased emphasis on non-generics, the company remains invested in the business and expects to grind out 23 new ones in 2013, as it did in 2012. Future plans include upping its focus on CNS, respiratory drugs and new therapeutic entities, while at the same time pursuing a program that could slash \$2 billion in costs over the span of three to five years.

**Fig. 2: Top 20 Prescription Drugs by US Sales '12**

Rank	Product	Company	2012 Total (Billions)	2011 Total (Billions)
1	Nexium	AstraZeneca	\$6.0	\$6.4
2	Abilify	Otsuka/BMS	\$5.9	\$5.3
3	Crestor	AstraZeneca	\$5.1	\$4.6
4	Advair Diskus	GlaxoSmithKline	\$4.9	\$4.8
5	Cymbalta	Eli Lilly	\$4.7	\$3.8
6	Humira	Abbott*	\$4.6	\$3.7
7	Enbrel	Amgen	\$4.3	\$3.8
8	Remicade	Johnson & Johnson	\$3.9	\$3.5
9	Copaxone	Teva	\$3.6	\$3.2
10	Neulasta	Amgen	\$3.5	\$3.3
11	Singulair	Merck	\$3.3	\$4.8
12	Rituxan	Genentech/Roche	\$3.2	\$3.0
13	Plavix	Bristol-Myers Squibb	\$3.0	\$7.1
14	Atripla	BMS/Gilead	\$2.9	\$2.6
15	Spiriva Handihaler	Boehringer Ingelheim	\$2.8	\$2.5
16	Oxycontin	Purdue	\$2.8	\$2.9
17	Januvia	Merck	\$2.7	\$2.2
18	Avastin	Genentech/Roche	\$2.7	\$2.7
19	Lantus	Sanofi	\$2.3	\$2.1
20	Truvada	Gilead	\$2.3	\$2.0
<b>Total others</b>			<b>\$240.8</b>	<b>\$246.4</b>
<b>Total market</b>			<b>\$325.8</b>	<b>\$329.2</b>

Source: IMS Health, National Sales Perspectives

\*On January 2, 2013, Abbott's research-based pharma business, AbbVie, became a separate entity

**Fig. 3: Top 20 Therapeutic Classes by US Sales '12**

Rank	Categories	2012 Total (Billions)	2011 Total (Billions)
1	Oncologics	\$25.9	\$24.0
2	Mental Health	\$23.5	\$29.7
3	Respiratory Agents	\$22.1	\$21.7
4	Antidiabetics	\$22.0	\$20.5
5	Pain	\$18.2	\$17.9
6	Lipid Regulators	\$16.9	\$21.3
7	Autoimmune Diseases	\$14.8	\$12.5
8	Antihypertensives	\$13.6	\$14.0
9	HIV Antivirals	\$11.7	\$10.4
10	ADHD	\$10.4	\$9.2
11	Anti-Ulcerants	\$10.0	\$10.5
12	Multiple Sclerosis	\$8.9	\$7.6
13	Antibacterials	\$7.9	\$9.3
14	Nervous System Disorders	\$7.2	\$6.9
15	Vaccines	\$6.8	\$6.4
16	Hormonal Contraception	\$5.5	\$5.2
17	Other CNS	\$5.0	\$4.8
18	Immunostimulants	\$4.7	\$4.6
19	Antivirals, excl. Anti-HIV	\$4.5	\$3.8
20	Platelet Aggregation Inhibitors	\$4.4	\$8.2
<b>Total others</b>		<b>\$82.0</b>	<b>\$80.9</b>
<b>Total market</b>		<b>\$325.8</b>	<b>\$329.2</b>

Source: IMS Health, National Sales Perspectives

\*On January 2, 2013, Abbott's research-based pharma business, AbbVie, became a separate entity

Fig 4: US Spend for Total Promo, DTC, eDetailing, Professional Detailing, Professional Meetings, Journal Ads

Rank	Company	Total Promo Spend		DTC		eDetailing	
		2012 (Millions)*	% change vs 2011	2012 (Millions)	% change vs 2011	2012 (Millions)	% change vs 2011
1	Eli Lilly	\$1,669.00	-10.0%	\$453.00	-8.0%	\$10.00	87.0%
2	Pfizer	\$1,610.00	-24.0%	\$597.00	-31.0%	\$26.00	40.0%
3	Merck	\$1,394.00	3.0%	\$288.00	25.0%	\$14.00	0.0%
4	AstraZeneca	\$1,111.00	-12.0%	\$207.00	-38.0%	\$10.00	-2.0%
5	Boehringer Ingelheim	\$986.00	15.0%	\$175.00	-8.0%	\$5.00	47.0%
6	Forest Laboratories	\$863.00	8.0%	<\$1.0	N/A	\$8.00	22.0%
7	Novartis	\$852.00	-31.0%	\$73.00	-27.0%	\$18.00	76.0%
8	GlaxoSmithKline	\$844.00	-18.0%	\$175.00	-15.0%	\$11.00	114.0%
9	Abbott	\$828.00	20.0%	\$290.00	79.0%	\$6.00	105.0%
10	Bristol-Myers Squibb	\$811.00	-8.0%	\$178.00	-34.0%	\$7.00	79.0%
11	Johnson & Johnson	\$541.00	19.0%	\$68.00	15.0%	\$17.00	137.0%
12	Takeda	\$507.00	-26.0%	\$14.00	-85.0%	\$6.00	5.0%
13	Daiichi Sankyo	\$496.00	10.0%	<\$1.0	N/A	\$1.00	-1.0%
14	Amgen	\$432.00	28.0%	\$231.00	62.0%	\$5.00	61.0%
15	Sanofi	\$430.00	-8.0%	\$39.00	10.0%	\$9.00	75.0%
16	Novo Nordisk	\$426.00	9.0%	\$85.00	18.0%	\$5.00	100.0%
17	Allergan	\$340.00	10.0%	\$193.00	24.0%	\$3.00	201.0%
18	Sunovion	\$296.00	-12.0%	\$49.00	-37.0%	\$5.00	163.0%
19	Teva	\$289.00	-16.0%	\$38.00	-27.0%	\$6.00	112.0%
20	Roche	\$239.00	-13.0%	\$47.00	-27.0%	\$6.00	64.0%

\* Total promotional spend figure does not include amount spent on samples, clinical trials or direct mail. Source: CSD—CegeDim Strategic Data Note: Due to resampling of Journals in the CSD audit, 2011 and 2012 data may not be comparable for all publications and manufacturers.

**6 Roche** \$15.4B ▲5.6%

- Global revenue:** \$48.9B (4th); up 5.4%
- R&D spend:** \$9.1B (2nd), up 5.0%, 18.6% of rev.
- Top brands:** Rituxan (\$3.2B); Avastin (\$2.7B), Herceptin (\$1.9B), Lucentis (\$1.6B), Xeloda (\$724M)
- Planned launches:** GA101 (onc.), RG1678 (CNS)
- Promotional spend:** \$239M (16th), 1.6% of rev.
- Patent expirations:** Xeloda (2013), Rituxan (2014), Herceptin (2019), Avastin (2019)

Roche continues to corner the oncology market with blockbusters Rituxan, Herceptin and Avastin. Future success hinges on whether it can keep the hits coming, as biosimilars will begin to cut into Herceptin's and Rituxan's profits starting in 2015, Bernstein Research analyst Tim Anderson predicts. The analyst notes that he's "willing to make the bet" that Roche's pipeline delivers some meaningful new entries the next few years, perhaps offsetting any loss of branded biologics revenue. The past few months have seen approval for oncology drugs Perjeta and Kadcyla, and these have been well-received. Analysts are particularly excited about two cancer pipeline candidates: GA101 for CLL and MetMAB for NSCL. Both have shown positive top-line results with more data scheduled to be released in 2013 and 2014.

**7 GlaxoSmithKline** \$14.1B ▼4.1%

- Global revenue:** \$40.1B (7th); down 6.9%
- R&D spend:** \$6.1B (7th); up 3.4%; 15.1% of rev.
- Top brands:** Advair (\$3.9B), Flovent (\$687M), Pediarix (\$576M), Avodart (\$349M)
- Planned launches:** Anoro, Relvar (resp.); dolutegravir (HIV); dabrafenib, trametinib (onc.)
- Promotional spend:** \$844M (7th); 6.0% of rev.
- Patent expirations:** Avodart (2015), Lovaza (2015)

Slim down, diversify and get that sluggish pipeline moving again. That's the game plan at GSK, which has weathered a particularly brutal patent cliff. CEO Andrew Witty says GSK could launch up to 15 products over the next three years globally. The company's late-stage pipeline includes products for COPD, cancer, HIV/AIDS and diabetes, and includes a few potential breakthrough treatments, like anti-cancer immunotherapy MAGE-A3, HGS heart drug darapladib and HIV drug dolutegravir, part of GSK's ViiV JV with Pfizer and Shionogi. GSK was an early and aggressive entrant in the scramble for emerging markets, and that bet seems to be bearing fruit. Like Pfizer, GSK sees two tracks: a premium, innovative drug business in the US and Japan, and a volume consumer and OTC business in emerging markets.





Detailing		Meetings		Journal		Company	Rank
2012 (Millions)	% change vs. 2011	2012 (Millions)	% change vs. 2011	2012 (Millions)	% change vs. 2011		
\$640.00	-10.0%	\$61.00	-19.0%	\$1.98	-74.0%	Eli Lilly	1
\$888.00	-19.0%	\$90.00	-23.0%	\$3.60	-35.0%	Pfizer	2
\$975.00	-1.0%	\$114.00	-2.0%	\$0.67	-42.0%	Merck & Co.	3
\$791.00	-1.0%	\$100.00	7.0%	\$0.67	-5.0%	AstraZeneca	4
\$704.00	21.0%	\$96.00	25.0%	\$3.34	-20.0%	Boehringer Ingelheim	5
\$743.00	7.0%	\$96.00	33.0%	\$7.35	-34.0%	Forest Laboratories	6
\$663.00	-33.0%	\$94.00	-22.0%	\$1.72	-61.0%	Novartis	7
\$607.00	-16.0%	\$48.00	-43.0%	\$1.45	0.0%	GlaxoSmithKline	8
\$457.00	1.0%	\$71.00	4.0%	\$2.17	-14.0%	Abbott	9
\$522.00	0.0%	\$97.00	32.0%	\$4.52	22.0%	Bristol-Myers Squibb	10
\$352.00	15.0%	\$95.00	27.0%	\$4.32	20.0%	Johnson & Johnson	11
\$434.00	-16.0%	\$50.00	-22.0%	\$0.87	-64.0%	Takeda	12
\$459.00	11.0%	\$34.00	0.0%	\$0.27	-61.0%	Daiichi Sankyo	13
\$135.00	-3.0%	\$59.00	22.0%	\$0.97	-31.0%	Amgen	14
\$320.00	-9.0%	\$57.00	-12.0%	\$0.84	-80.0%	Sanofi	15
\$282.00	6.0%	\$51.00	6.0%	\$2.27	-33.0%	Novo Nordisk	16
\$129.00	-1.0%	\$14.00	-27.0%	\$0.77	-45.0%	Allergan	17
\$201.00	-10.0%	\$39.00	27.0%	\$0.67	49.0%	Sunovion	18
\$198.00	-22.0%	\$46.00	30.0%	\$0.23	-21.0%	Teva	19
\$123.00	-17.0%	\$59.00	14.0%	\$2.84	-11.0%	Roche	20

## 8 Eli Lilly


\$14.0B ▼8.5%

 **Global revenue:** \$22.6B (9th); down 7.0%

 **Top brands:** Cymbalta (\$3.9B), Humalog (\$1.4B), Alimta (\$1.1B), Cialis (\$782M), Evista (\$700M)

 **Promotional spend:** \$1.7B (1st); 11.9% of rev.

 **R&D spend:** \$5.3B (8th); up 5.1%; 23.4% of rev.

 **Planned launches:** Enzastaurin (onc), ramucirumab (onc), dulaglutide (diab), empagliflozin (diab.)

 **Patent expirations:** Humalog (2013), Cymbalta (2014), Evista (2014), Alimta (2017)


Indiana drug maker Eli Lilly is having a time of it. Despite being among the top R&D spenders in Bernstein analyst Tim Anderson's portfolio, the company has experienced a series of disappointments. Among them: tossing experimental drug tabalumab on the RA dust heap in 2012, weakened diabetes medication sales, and being pinched by generic Zyprexa (schizophrenia). Plus, the company's 2013 launch slate is a goose egg. Yet Anderson is intrigued by the pipeline's potential upside. Among the treatments getting his attention is Ph.III oncology drug ramucirumab, data for which is expected this year. He also wrote in March that the company is "historically a good R&D company," and has the chance to transform itself. As ISI's Mark Schoenebaum told investors, "If they execute... Lilly is the only company that in two or three years will have one of every branded diabetes drug... That's going to be very powerful when you go to payers and governments."

## 9 Amgen


\$13.9B ▲3.5%

 **Global revenue:** \$17.3B (13th); up 10.9%

 **Top brands:** Enbrel (\$4.0B), Neulasta (\$3.2B), Epogen (\$1.9B), Neupogen (\$1.0B), Aranesp (\$782M)

 **Promotional spend:** \$432M (12th); 3.1% of rev.

 **R&D spend:** \$3.8B (11th); up 18.8%; 22.0% of rev.

 **Planned launches:** AMG145 (lipids), brodalumab (infla.), AMG-386 (onc.)

 **Patent expirations:** Neupogen (2013), Neulasta (2013), Vectibix (2017), Xgeva (2017), Prolia (2017)

Biologics thrust it into biotech's big leagues but, while Amgen locked up exclusivity for mega-blockbuster Enbrel until 2028 (and took over US field sales from Pfizer last year), a chunk of its biologics portfolio is staring down the patent cliff. New CEO Robert Bradway wants to stand his ground against the threat of biosimilars while joining the fray as a biosimilars participant. So, he's building the business globally while packing the pipeline with six biosimilars, due to be launched starting in 2017. The rest of Amgen's late-stage pipeline ranges from a PCSK9 agent for hard-to-treat cholesterol (AMG-145), to T-VEC, which could be an attractive option for melanoma patients. One setback was the FDA's refusal last year to allow Amgen to expand the approval for its Xgeva bone drug into pre-metastases bone cancer. But Xgeva, and its denosumab-based cousin Prolia, saw combined global sales of \$1.2 billion for 2012, and officials said they expect the pair to exceed \$3 billion.

**Fig. 5: Estimated US Patent Expirations through 2014**

Brand	Company	Indication	Expiry
Aciphex	Eisai/Janssen	Heartburn	2013
Humalog	Eli Lilly	Diabetes	2013
Neupogen	Amgen	Low neutrophil count	2013
Oxycontin	Purdue	Pain	2013
Xeloda	Roche	Cancer	2013
Zometa	Novartis	Osteoporosis	2013
Actonel	Sanofi	Osteoporosis	2014
Celebrex	Pfizer	Pain	2014
Copaxone	Teva	Multiple sclerosis	2014
Cymbalta	Eli Lilly	Depression	2014
Evista	Eli Lilly	Osteoporosis	2014
Nexium	AstraZeneca	Heartburn	2014

Source: Barclays Research

the world's biggest pharma, boasts a packed late-stage pipeline, thanks in good measure to its acquisition of Genzyme two years ago—and with top-selling Lantus (diabetes) nearing the end of its patent life in the US, they'd better hope some of those candidates pan out. The company has won some recent FDA approvals—for MS drug Aubagio and Kynamro, for an inherited cholesterol disorder—and has several more, including Lyxumia, for type 2 diabetes, and Lemtrada, for MS, filed with FDA.

**12 Johnson & Johnson** \$12.0B ▼0.7%

- Global revenue:** \$67.2B (1st); up 3.4%
- R&D spend:** \$7.7B (5th); up 1.6%; 11.4% of rev.
- Top brands:** Remicade (\$3.6B), Procrit (\$805M), Prezista (\$672M), Stelara (\$627M), Concerta (\$609M)
- Planned launches:** Simeprevir (HCV), ibrutinib (onc.)
- Promotional spend:** \$541M (10th); 4.5% of rev.
- Patent expirations:** Doxil (2014), Prezista (2016), Remicade (2018)

Alex Gorsky's J&J is looking a lot like that of former CEO Bill Weldon. In short: recalls and bad press over items as diverse as faulty glucose meters, bad hips and marketing prescription drugs for off-label uses. This is in addition to notice from the FDA in March that it's repeating some bad manufacturing practices from 2009. Despite this, the company's 2012 balance sheets showed that most of the major declines—i.e., the 88% sales drop in Levaquin sales—are more in line with typical patent issues than reputational ones, but failures like that of bapineuzumab (Alzheimer's), have forced the company to slim down, in this case, by 130 employees.

**13 Bristol-Myers Squibb** \$8.3B ▼31.1%

- Global revenue:** \$17.6B (12th); down 17.0%
- R&D spend:** \$3.9B (10th); up 2.6%; 22.2% of rev.
- Top brands:** Plavix (\$2.4B), Abilify (\$2.1B), Reyataz (\$783M), Sustiva (\$1.0B), Orencia (\$797M)
- Planned launches:** Daclatasvir (HCV), nivolumab (onc.), elotuzumab (onc.), Forxiga (diab.)
- Promotional spend:** \$811M (9th); 9.8% of rev.
- Patent expirations:** Abilify (2015), Baraclude (2015), Sustiva (2015)

Patent losses last year on mega-brand Plavix, as well as on Avapro and Avalide, left a revenue crater. After downsizing, BMS is vying to return to growth. The FDA rejected SGLT2 drug dapagliflozin, but Amylin—bought last year for \$5.3 billion—brings Bydureon and Byetta (co-promoted with AstraZeneca) into the diabetes fold. Blood thinner Eliquis, which BMS co-markets with Pfizer, is off to a slow-but-steady launch—the Street predicts \$400 million in global sales this year—and analysts maintain it will eventually take the market. On the oncology front, a combo trial of melanoma drug Yervoy with Roche's Zelboraf was stopped due to toxicity, yet potential exists to layer Yervoy with Bristol's own anti-PD-1 agent, nivolumab, an immunotherapy. And don't ignore BMS when it comes to hep. C—“It's possible that BMS and Vertex could

**10 AbbVie** \$12.5B ▲4.1%

- Global revenue:** \$18.4B (11th); up 5.7%
- R&D spend:** \$2.8B (14th); up 6.1%; 15.1% of rev.
- Top brands:** Humira (\$4.4B), AndroGel (\$1.2B), Tricor/Trilipia (\$1.1B)
- Planned launches:** ABT-267/333/450 (HCV), GLP-G0634 (infl.), BT-061/Tregalizumb (infl.)
- Promotional spend:** \$828M (8th); 6.6% of rev.
- Patent expirations:** Niaspan (2013), Triplix (2013)

Spin-off AbbVie entered 2013 with a Humira-centric focus. The RA blockbuster is the company cornerstone as it looks for traction in specialty care. Projects include treatments for MS and multiple myeloma as well as an experimental interferon-free hepatitis C treatment. While this could be big for hep. C, Bernstein analyst Tim Anderson notes that AbbVie has more pills than rival Gilead and Bristol Myers Squibb treatments. Meanwhile, Humira accounts for about half of AbbVie's sales, and the company still pours money into expanding its indication reach. While this dependency has some on edge, the FDA and states are wrangling over biosimilars, possibly cushioning the impact of its 2017 patent expiration.







**11 Sanofi** \$12.1B ▼2.3%

- Global revenue:** \$45.6B (6th); up 4.1%
- R&D spend:** \$6.4B (6th); down 4.0%; 14.1% of rev.
- Top brands:** Lantus (\$3.9B), Eloxatin (\$920M), Renegel/Renvela (\$577M)
- Planned launches:** Lemtrada (MS), Lyxumia (diab.)
- Promotional spend:** \$430M (13th); 3.5% of rev.
- Patent expirations:** Actonel (2013), Eloxatin (2013)

Sanofi not only survived a nasty plunge off a particularly steep patent cliff in 2012 but managed to grow a respectable 4.7%, despite the loss of clot-buster Plavix. The French giant, which last year overtook Pfizer as

launch a Gilead look-alike regimen [NS5A+nuc] some time in the 2016 timeframe,” ISI Group’s Mark Schoenebaum recently told investors.







## 14 Boehringer Ingelheim \$7.9B ▲9.8%

 <b>Global revenue*:</b> \$17.2B (14th); up 4.2%	 <b>R&amp;D spend*:</b> \$3.3B (12th); up 2.6%; 19.1% of rev.
 <b>Top brands:</b> Spiriva Handihaler (\$2.8B); Combivent (\$1.1B); Pradaxa (\$871M)	 <b>Planned launches:</b> Afatinib (onc.), empagliflozin (diab.)
 <b>Promotional spend:</b> \$986M (5th); 12.5% of rev.	 <b>Patent expirations:</b> Micardis (2014), Spiriva Handihaler (2018)

Boehringer’s first-to-market warfarin replacement Pradaxa is losing some of its luster as newer rivals Eliquis (Pfizer/BMS) and Xarelto (J&J/Bayer) start to siphon off share. But FDA has the anticoagulant’s back on safety worries, and that’s sure to, well, stem some of the bleeding. That’s good news for Boehringer, as its Tradjenta DPP-IV co-market with Lilly faces tough competition, and its best seller, Spiriva Handihaler, a co-market with Pfizer worth \$2.8 billion in the US, is starting to get a bit long in the teeth, despite a patent extension to 2018, while BP drug Micardis starts to lose exclusivity next year. The closely held company’s pipeline appears flush with promising candidates for COPD, asthma and pulmonary fibrosis as well as an array of oncology products.

*\*Global revenue and R&D spend are based on the fiscal year ending December 31, 2011, the latest data available at press time.*

## 15 Actavis \$7.7B ▲27.5%

 <b>Global revenue:</b> \$5.9B (20th); up 29.0%	 <b>R&amp;D spend:</b> \$401.8M (19th), up 36.0%, 6.8% of rev.
 <b>Top brands:</b> Methylphenidate ER (\$1.5B), atorvastatin ca (\$738M), HYCD/APAP (\$451M), Metoprolol succin (\$253M)	 <b>Planned launches:</b> Generic versions of Lidoderm (post-herpetic neuralgia), Crestor (hyperlipidemia)
 <b>Promotional spend:</b> \$103M (17th); 1.3% of rev.	 <b>Patent expirations:</b> N/A







The generics giant previously known as Watson has, in one year, shot up the ranks from the 5th to the 3rd largest generics player in the space—behind Teva and Sandoz. Watson acquired Actavis this year to further build on their international visibility and even went a step further by assuming the acquiree’s name. It’s looking to sales of products like generic Lipitor and its authorized version of ADHD med Concerta to keep the ship afloat while execs work to deliver generic Crestor in 2016. But with the firm’s performance tied to these anchor products, analysts warn that increased risk—including another generic version of Concerta expected later this year—could drag down 2013. There could be upside for Actavis if its generic Pulmicort, pegged for Q2 launch, actually materializes. Longer term, it has a collaboration with Amgen for biosimilar versions of Herceptin, Avastin and Rituxan/Mabthera—three of the biggest treatments in oncology.

**Fig. 6: New Drug Approvals 2012\***

Brand	Company	Indication	Approval
Voraxaze	BTG International	Methotrexate toxicity	Jan. 17
Picato	Leo Pharma	Actinic keratosis	Jan. 23
Inlyta	Pfizer	Renal cancer	Jan. 27
Erivedge	Genentech	B-cell carcinoma	Jan. 30
Kalydeco	Vertex	Cystic fibrosis	Jan. 31
Zioptan	Merck	Glaucoma	Feb. 10
Surfaxin	Discovery Labs	Resp. distress synd.	Mar. 6
Omontys	Affymax	Anemia	Mar. 27
Amyvid	Avid Radiopharma	Alzheimer’s diagnosis	Apr. 6
Stendra	Vivus	Erectile dysfunction	Apr. 27
Elelyso	Pfizer	Gaucher’s disease	May. 1
Perjeta	Genentech	Breast cancer	Jun. 8
Belviq	Eisai	Obesity	Jun. 27
Myrbetriq	Astellas	Overactive bladder	Jun. 28
Prepopik	Ferring	Colon cleansing	Jul. 16
Kyprolis	Onyx	Multiple myeloma	Jul. 20
Tudorza Pressair	Forest	COPD	Jul. 23
Zaltrap	Sanofi	Colorectal cancer	Aug. 3
Stribild	Gilead	HIV-1 infection	Aug. 27
Neutroval	Sicor Biotech	Neutropenia	Aug. 29
Linzess	Forest	IBS	Aug. 30
Xtandi	Astellas	Prostate cancer	Aug. 31
Bosulif	Pfizer	Leukemia	Sep. 4
Aubagio	Sanofi	Multiple sclerosis	Sep. 12
Choline C-11	MCPRF	Prostate canc. diagn.	Sep. 12
Stivarga	Bayer	Colorectal cancer	Sep. 27
Jetrea	Thrombogenics	SVA	Oct. 17
Fycompa	Eisai	Seizures	Oct. 22
Synribo	Ivax	Leukemia	Oct. 26
Xeljanz	Pfizer	Rheumatoid arthritis	Nov. 6
Cometriq	Exelixis	Thyroid cancer	Nov. 29
Iclusig	Ariad	Leukemia	Dec. 14
Signifor	Novartis	Cushing’s disease	Dec. 14
Raxibacumab	HGS	Anthrax	Dec. 14
Gattex	NPS	Short bowel syndrome	Dec. 21
Juxtapid	Aegerion	HoFH	Dec. 21
Eliquis	Bristol-Myers Squibb	SPAF	Dec. 28
Sirturo	Janssen	Tuberculosis	Dec. 28
Fulyzaq	Salix	HIV-assoc. diarrhea	Dec. 31

\* NMEs and new biologics approved by FDA’s Center for Drug Evaluation and Research (CDER)







## 16 Mylan \$7.3B ▲25.8%

 <b>Global revenue:</b> \$6.8B (19th); up 11.5%	 <b>R&amp;D spend:</b> \$401M (20th); up 33.3%; 5.9% of rev.
 <b>Top brands:</b> EpiPen (\$508M), Fentanyl (\$433M), omeprazole Rx (\$278M)	 <b>Planned launches:</b> Generic versions of Lidoderm, Advair, Generess Fe
 <b>Promotional spend:</b> \$66M (19th); 1.0% of rev.	 <b>Patent expirations:</b> EpiPen (2017)









Analysts had seen M&A in the cards for Mylan, and the generics maker didn't disappoint. It scooped up sterile injectable manufacturer Agila this year for \$1.6 billion. The deal, after closing, is expected to make Mylan/Agila the third-biggest global player in the specialty injectable business and provide Mylan with a bigger pipeline of ANDAs. New revenue channels are important. Mylan's top-selling EpiPen brand is facing a new threat from the launch of Sanofi's Auvi-Q in the emergency anaphylaxis market. "Physicians forecast Auvi-Q capturing 50% share by 2016," wrote Leerink Swann's Jason Gerberry in an investor note. Although EpiPen volumes were down in Q1, the recent approval of Mylan's generic Zovirax (a \$230-million brand) should provide durable upside—at press time there were no competitor approvals.

## 17 Gilead \$6.7B ▲19.8%

 <b>Global revenue:</b> \$9.7B (18th); <b>up 15.5%</b>	 <b>R&amp;D spend:</b> \$1.8B (17th); up 43.4%; 18.0% of rev.
 <b>Top brands:</b> Atripla (\$2.9B), Truvada (\$2.3B), Viread (\$542M)	 <b>Planned launches:</b> Sofosbuvir (HCV), GS7340/combos (HIV), GS-1101 (onc.)
 <b>Promotional spend:</b> \$73M (18th); 1.1% of rev.	 <b>Patent expirations:</b> Viread (2017), Atripla (2021), Truvada (2021)

Gilead took flack for its expensive, \$11-billion pick-up of Pharmasset and hep. C "nuc" sofosbuvir. Now, vindication is at hand. At press time, Gilead—which last year saw its "Quad" HIV pill approved—had filed a sofosbuvir-based combo pill with the FDA (an EU filing is expected in Q2). Analysts say the biotech may be first-to-market, by early 2014, with a once-a-day oral drug. Street estimates stand at a billion dollars. "The real number is probably \$2 billion plus," ISI Group's Mark Schoenebaum told investors, adding, "Fifteen thousand patients, only, treated for hep. C equals a billion dollars in sales... There are 350,000 patients under the active care of a hep. C specialist right now that have been warehoused, that need therapy in the US." AbbVie and/or BMS could follow with their own interferon-sparing pills. In trials, all have offered cure rates of over 90% for patients with a variety of HCV types.







## 18 Novo Nordisk \$6.6B ▲21.1%

 <b>Global revenue:</b> \$13.7B (17th); <b>up 16.7%</b>	 <b>R&amp;D spend:</b> \$1.9B (16th) up 6.1%; 14.0% of rev.
 <b>Top brands:</b> NovoLog (\$1.2B), Levemir (\$1.1B), NovoLog Flexpen (\$1.1B), Victoza (\$808M)	 <b>Planned launches:</b> Liraglutide (obesity), turoctocog alfa (hem.), Tresiba (diab.)
 <b>Promotional spend:</b> \$426M (14th); 6.5% of rev.	 <b>Patent expirations:</b> Novolog (2014), Levemir (2014), Victoza (2017)

Novo Nordisk enjoyed positive returns from its diabetes franchise in 2012, but recent setbacks could dampen things. Novo's long-acting insulin Tresiba was denied by the FDA due to cardiovascular risks. And a group of researchers in March suggested a possible link between incretin

mimetics (like Victoza) and pancreatitis. That said, the Danish drug maker still holds 26% of worldwide diabetes market share, and analysts predict the US delay on Tresiba will only shave 6% off earnings in the coming years (the product is launching in the EU and Japan). Novo should watch its back, though. Insulin and GLP-1 biosimilars are already in the works, and its three best-selling products—NovoLog, Levemir and Victoza—are all scheduled to be off-patent by 2017.







## 19 Otsuka \$6.0B ▲11.8%

 <b>Global revenue*:</b> \$14.0B (16th); <b>up 6.9%</b>	 <b>R&amp;D spend*:</b> \$1.9B (15th); down 3.2%; 13.8% of rev.
 <b>Top brands:</b> Abilify (\$5.8B), Samsca (\$91M), Busulfex (\$11M), Pletal (\$2M)	 <b>Planned launches:</b> TAS-102 (onc.), OPC-34712 (psych.)
 <b>Promotional spend:</b> \$27M (20th); 0.5% of rev.	 <b>Patent expirations:</b> Abilify (2015)

Otsuka has been driving growth of schizophrenia drug Abilify, and while new products aren't exactly towing the line, CNS sales are holding steady. The patent on its top-seller dries up in 2015 in the US, though, where BMS handles marketing. Meanwhile, Otsuka and Lundbeck won FDA approval for a once-monthly injectable form of Abilify that will compete with J&J's Invega Sustenna. The Tokyo-based pharma also deepened its longtime CNS alliance with Lundbeck, agreeing to co-develop an Alzheimer's agent with the Danish drug maker, and to expand their existing Abilify (ex-US) co-promote to 14 countries. Otsuka is also hoping to wring more out of its nutraceuticals division.

\* Global revenue and R&D spend are based on the fiscal year ending March 31, 2012, the latest data available at press time.

## 20 Takeda \$5.5B ▼22.6%

 <b>Global revenue*:</b> \$15.6B (15th); <b>down 10.9%</b>	 <b>R&amp;D spend*:</b> \$2.9B (13th); down 11.4%; 18.6% of rev.
 <b>Top brands:</b> Actos (\$1.7B), Dexilant (\$798M), Velcade (\$715M), Colcrys (\$605M), Amitiza (\$311M)	 <b>Planned launches:</b> Vortioxetine (dep.), vedolizumab (inflam.), TAK-700 (onc.)
 <b>Promotional spend:</b> \$507M (11th); 9.2% of rev.	 <b>Patent expirations:</b> Velcade (2018)

Generic Actos took a \$1.8-billion bite out of Takeda's US sales last year. To fill in the gap, management is looking toward the pipeline. Its Millennium unit boasts three late-stage prospects—TAK-700 for prostate cancer, MLN9708 for multiple myeloma, and Vedolizumab for ulcerative colitis—and GPR40 agonist TAK875 could give the Japanese firm another run in diabetes. But there have been setbacks. Takeda and partner Affymax pulled anemia biologic Omontys due to a life-threatening adverse event, and Takeda faces a lawsuit over Actos' alleged link to bladder cancer. The company is exploring more early-stage compounds to offset its front-loaded pipeline.

\* Global revenue and R&D spend are based on the fiscal year ending March 31, 2012, the latest data available at press time.