

THE PHARMA REPORT 2014

**NEW
CYCLE
OF LIFE**



The damage inflicted by pharma's longtime nemesis—the patent cliff—wasn't painless. But it did come to a mercifully quick end last year, helping nudge growth in prescription drug spend back into positive territory. Now, with a host of breakthrough medicines launching, **Marc Iskovitz** finds, enthusiasm is tempered as the sector—led by the 20 companies on the following pages—grapples with how to make them a commercial success

For spending on prescription medicines, 2013 was a surprisingly good year. And, contrary to popular belief, it's not due to the Affordable Care Act. Total drug spend swung to a 3.2% gain, reaching \$329.2 billion, from a 1% decline (its largest ever) in 2012, according to data from the IMS Institute for Healthcare Informatics.

The spending increase was a big improvement—and a surprise, explained Michael Kleinrock, director, research development for the IMS Institute. Key reasons for the recovery were timing-related, Kleinrock told *MM&M*. “A number of the big patent expiries kind of happened real quick and wore off.” The result was a second-half comeback, as the biggest historic period ever of patent expiries—\$19 billion of brand revenue in 2013, following \$29 billion in 2012—ended.

It coincided with a very strong year for innovative medicines—36 NME launches vs. 27 in 2012, including 17 orphan drug launches, the most since passage of the 1983 Orphan Drug Act, says IMS.

The third factor was the start of the next wave of products set for generic oblivion, as these so-called pre-patent expiries exerted a “growth bump,” Kleinrock said. “What you're seeing,” he adds, “is the passing of an era.” So a standard pharma bogeyman—the patent cliff—was less of a nemesis. Eli Lilly depression med Cymbalta, one of the last top-10 blockbusters, lost exclusivity in December.

For pharma, “things are looking better, especially compared to the middle-to-late part of the last decade,” says Les Funtleyder, a fund manager with Bluecloud Healthcare, an investing firm.

Turning the page has been good for the sector. “The patent cliff annualized for more companies,” says Bernstein Research senior pharma analyst Tim Anderson, “so more firms are returning to growth.”

The increase broke down as follows: specialty therapy areas grew by 11% to \$73 billion. Primary care therapy areas grew by 11% to \$37 billion. The largest amount of spending—\$128 billion in 2013—came in areas with limited innovation or patent expiries but still grew 7%.

Another driver of growth was price hikes on protected brands, which added \$20 billion to growth in 2013, up from \$15.6 billion in 2012. That's even as generic medicines now represent 86% of prescriptions.

And it occurred prior to implementation of Obamacare. Whereas IMS had forecast some points of growth associated with the ACA and from fewer expiries, now due to patent settlements and changes in some product expiry dates, it means the ACA and the patent cliff will offset each other, Kleinrock says. He expects spending growth in the same 3.5% range in 2014, even with big products like AstraZeneca heartburn pill Nexium, a \$6-billion drug, set to go generic this month.

While two-thirds of the companies on the following pages grew sales last year, others still grapple with expiries. Essentially, every company needs to make sure they're the right size for their portfolio. Many continue to do so by jettisoning smaller businesses, and by narrowing product lineups and re-focusing.

Firms have also cut the number of sales reps, from 107,000 to about 55,000-58,000—a reduction of close to half over the last few years, says Pratap Khedkar, managing principal at ZS Associates, the consultancy. “Pharma sizing decisions are closer to being optimal,” he says.

Pipeline traction will characterize the next 12 months, especially with a lot of excitement in the oncology area. R&D budgets for the 11 big pharma firms Anderson covers rose a collective 1% last year, and he expects the same plus-one growth in '14.

But while the IMS data might suggest that industry watchers proved overly concerned with the negatives of the patent cliff, any exuberance should be tempered by the reality of a tougher environment for new drugs. Two-thirds of launches don't meet sales expectations, according to a 2014 report from McKinsey & Co.

Market access is a big hurdle in primary care. “When there are several DPP-4 [diabetes pills] that look the same, payers are starting to pit manufacturers against each other,” says Anderson.

Yet they're limited in the hepatitis C space, despite the arrival of pricey drugs, like Gilead's Sovaldi last December. “Ultimately, when there's such a huge leap in terms of efficacy, it would be a challenge for payers not to afford that treatment,” says Pamela Morris, director, syndicated research at Zitter Group, a managed markets think tank.

Morris says research suggests that payers are more aggressively managing specialty categories like oncology, RA and MS through tools like prior authorization and preferred formulary status.

“For HCV, it's a little bit of a different dynamic,” she says. “The first two or three launches of these new revolutionary products are in a really good position. They're priced at a high price point, presumably because they offer greater value over current therapy, and that's different from the majority of other [specialty] categories.”

That hasn't stopped a flood of yellow flags over Sovaldi's price, which comes to \$1,000 a pill. And, as more specialty agents come to market with high price tags, the pricing ire is not going to disappear.

None of that bothers Funtleyder. “The barbarians are still a long way from the gates,” the fund manager says. “But industry has the potential to at least forestall or mitigate what could happen if they are willing to engage both the payers and regulators.” He says the first warning shot on Sovaldi was fired by Express Scripts last fall when the PBM knocked many newer brands off formulary, like Pfizer RA drug Xeljanz, J&J psoriasis treatment Stelara, and GlaxoSmithKline respiratory drug Breo Ellipta. “Prior to that, biotech investors, in part, took it as a *fait accompli* that no matter what biotech charged, if it was an important enough disease, payers would pay.” Says Funtleyder, “I think that that preconceived notion is going to be tested.”

With additional reporting by Deborah Weinstein, Kevin McCaffrey, Joe Dysart and Noah Pines.

1 Novartis

\$18.9B ▼3.7%



Global revenue: \$57.9B (2nd); up 2.1%



R&D spend: \$9.6B (1st); 16.6% of rev.; up 5.3%



Top brands: Diovan (\$2.2B), Gleevec (\$1.9B); Gilenya (\$1.1B), Afinitor (\$720M), Sandostatin (\$700M)



Planned launches: LCZ696 (CV), LDK378 (onc.), buparlisib (onc.), LEE011 (onc.), secukinumab (auto.)



Promotional spend: \$810.4M (6th); 4.3% of rev.



Patent expirations: Gleevec (2014), Myfortic (2017)

The drugmaker enjoyed another year of branded profits from off-patent Diovan. This year it could finally see competition as Ranbaxy's generic version of the BP drug seems set to reach US shores. The Swiss-based company is also slated to witness blockbuster oncology drug Gleevec go generic. Novartis hopes replacement therapy Tasigna will lessen the blow. A bright spot is LCZ696, a therapy for chronic heart failure which analysts say could help fill the void left by Diovan. A Phase-I trial was closed after an independent committee recommended stopping it because the agent was working well. That news broke a week after an FDA advisory panel recommended against approving acute heart failure drug Serelaxin, citing insufficient evidence to back up its indication. For 2013 overall, Novartis saw a 1% jump in pharma sales, a figure so small CEO Joe Jimenez said that pharma SG&A costs will come under scrutiny, as well as "reducing what has historically been a relatively unconstrained budget in pharma R&D." Also rumored is a consumer-for-animal health unit swap with Merck.

2 Pfizer

\$17.0B ▼4.8%



Global revenue: \$52.6B (4th); down 12.5%



R&D spend: \$6.6B (5th); down 16.5%; 12.8% of rev.



Top brands: Lyrica (\$2.5B), Celebrex (\$2.3B), Viagra (\$1.2B), Prevnar 13 (\$809M)



Planned launches: Palbociclib (onc.), dacomitinib (onc.), bococizumab (CV)



Promotional spend: \$1.9B (1st); 11.2% of rev.



Patent expirations: Celebrex (2014), Lyrica (2014), Premarin (2015)

Pfizer's big 2013 news was, it was indeed contemplating a breakup, but that analysts were going to have to hold on for four years before the drugmaker will get serious about dividing into three companies. The company's experimental cancer drug palbociclib is the lynchpin for one of the possible spin-offs, and Pfizer has hinted it may be ready to approach the FDA with the breast cancer drug earlier than expected. Meanwhile, RA drug Xeljanz and blood thinner Eliquis have failed to make significant dents in prescribing trends. The New York drugmaker also has its hand in the PCSK9 race. Bernstein's Tim Anderson notes the field is getting crowded, but Pfizer says its effort—the Phase-III agent bococizumab—addresses a broader population, which will give it an edge. Celebrex and Viagra continue to be important, and Pfizer is at work in the courts reviving the recently lost Celebrex patent and fending off Viagra interlopers.

Fig. 1: Top 20 Pharmaceutical Companies by US Sales '13

Rank	Company	2013 Total (Billions)	2012 Total (Billions)
1	Novartis	\$18.9	\$19.6
2	Pfizer	\$17.0	\$17.8
3	AstraZeneca	\$16.7	\$16.7
4	Merck	\$16.5	\$19.4
5	Roche	\$15.8	\$14.8
6	Teva	\$15.3	\$16.1
7	Eli Lilly	\$15.3	\$13.7
8	Amgen	\$14.8	\$13.7
9	Johnson & Johnson	\$13.9	\$11.7
10	GlaxoSmithKline	\$12.8	\$12.5
11	Sanofi	\$12.3	\$12.0
12	AbbVie	\$12.1	\$12.2
13	Actavis	\$10.3	\$10.2
14	Novo Nordisk	\$7.9	\$6.4
15	Mylan	\$7.8	\$7.1
16	Boehringer Ingelheim	\$7.7	\$7.5
17	Gilead	\$7.6	\$6.5
18	Otsuka	\$6.8	\$5.8
19	Bristol-Myers Squibb	\$5.6	\$7.7
20	Shire	\$4.2	\$3.9
Total others		\$89.9	\$83.8
Total market		\$329.2	\$319.1

Source: IMS Health, National Sales Perspectives

3 AstraZeneca

\$16.7B ▼0.4%



Global revenue: \$25.7B (8th); down 8.2%



R&D spend: \$4.3B (9th); down 4.4%; 16.7% of rev.



Top brands: Nexium (\$6.2B), Crestor (\$5.4B), Symbicort (\$1.6B), Seroquel XR (\$1.2B), Synagis (\$769M)



Planned launches: Naloxegol (constip.), olaparib (onc.), Epanova (CV), lesinurad (gout), brodalumab (psoriasis)



Promotional spend: \$1.1B (3rd); 6.6% of rev.









Patent expirations: Nexium (2014), Symbicort (2015), Synagis (2015), Crestor (2016)

For sophomore CEO Pascal Soriot, it's all going to plan—although it hasn't been pretty. Last year the CEO predicted "mid-to-high single digit" revenue decline and was on the mark as sales tumbled by 8% in 2013 to \$25.7 billion. In March of this year, the drugmaker further reined in costs by eliminating 5,050 jobs and saving \$800 million in the process. After analysts said the BMS-AZ diabetes joint-venture wasn't operating smoothly, AZ bought out the franchise for \$2.7 billion up front. While that move gives it full control of Byetta, Bydueron and Onglyza, Jefferies analyst Jeffrey Holford wrote at the time that AZ may have bought itself into a corner. Novo Nordisk's Victoza holds 70% of the GLP-1 market, and that figure has grown nearly 7% from the year prior. Eli Lilly's dulaglutide—another GLP-1 shown to be comparable to Victoza, and which is slated to make it debut this year—could further dice up the market

and lead AZ's new diabetes franchise to the margins. The drugmaker did see a win with another diabetes product, SGLT2 inhibitor Farxiga (hamstrung in the approval process due to cancer concerns), but it was the second drug to market behind J&J's Invokana. Morningstar analyst Damien Conover says the AZ drug could see annual sales of \$1.5 billion.

4 Merck

\$16.5B ▼15.0%







 Global revenue: \$44.0B (6th); down 7.0%	 R&D spend: \$7.1B (4th); down 9.0%; 16.1% of rev.
 Top brands: Januvia (\$2.9B), Zetia (\$1.7B), Nasonex (\$1.2B), Isentress (\$1.0B)	 Planned launches: MK-3475 (onc.), omarigliptin (diab.), anacetrapib (CV)
 Promotional spend: \$1.5B (2nd); 9.1% of rev	 Patent expirations: Nasonex (2014), Emend (2015), Zostavax (2016)

Merck sales were down last year, and the long-term financial outlook for the firm looks reasonable but not great, says Bernstein's Tim Anderson. Key factors dragging on its performance include a number of pending patent expirations, along with ongoing or new pressures on its franchises, including Januvia/Janumet (diabetes), Remicade (RA), Vytorin (cholesterol), Isentress (HIV), and hepatitis C drugs PEG-Intron and Victrelis. Merck's performance in 2014 will most likely be flat, with a bump-up to modest growth thereafter, Anderson says. Merck's long-term, reliable

track record is popular with many investors, the analyst says. And its most interesting, late-stage product is MK-3475 (anti-PD-1), a treatment for various cancers. Near-term, Merck's most interesting move will likely be the launch of MK-3475 in late 2014/early 2015, he predicts.

5 Roche

\$15.8B ▲7.2%

 Global revenue: \$53.1B (3rd); up 8.6%	 R&D spend: \$9.3B (2nd); down 2.2%; 17.5% of rev.
 Top brands: Rituxan (\$3.3B), Avastin (\$2.7B); Herceptin (\$1.9B), Lucentis (\$1.9B)	 Planned launches: MetMab (onc.), PD-L1 (onc.); bitopertin (CNS), gantenerumab (CNS)
 Promotional spend: \$248M (16th); 1.6% of rev.	 Patent expirations: Valcyte (2014), Rituxan (2014), Tamiflu (2017)

Roche is synonymous with oncology. The cancer segment makes up 62% of the company's \$41 billion in pharmaceutical sales, and the company has safeguarded its hold on the cancer market through what some would consider a strategic succession plan that included the 2013 approvals of Gazyva (to replace Rituxan), Kadcyla (to replace Herceptin) and Perjeta, which did not so much replace a drug, as jump the line and get greenlighted for presurgical use among breast cancer patients. Additional performers include eye medication Lucentis, which racked up a 15% increase in sales despite market creep by Regeneron's Eylea. The company

Fig. 2: Top 20 Prescription Drugs by US Sales '13

Rank	Product	Company	2013 Total (Billions)	2012 Total (Billions)
1	Abilify	Otsuka/BMS	\$6.6	\$5.7
2	Nexium	AstraZeneca	\$6.2	\$5.9
3	Humira	AbbVie	\$5.6	\$4.5
4	Crestor	AstraZeneca	\$5.4	\$5.0
5	Cymbalta	Eli Lilly	\$5.3	\$4.6
6	Advair Diskus	GlaxoSmithKline	\$5.2	\$4.8
7	Enbrel	Amgen	\$4.7	\$4.2
8	Remicade	Johnson & Johnson	\$4.1	\$3.8
9	Copaxone	Teva	\$3.7	\$3.5
10	Neulasta	Amgen	\$3.6	\$3.4
11	Rituxan	Genentech/Roche	\$3.3	\$3.1
12	Lantus SoloStar	Sanofi	\$3.0	\$2.2
13	Spiriva Handihaler	Boehringer Ingelheim	\$3.0	\$2.7
14	Atripla	BMS/Gilead	\$2.9	\$2.8
15	Januvia	Merck	\$2.9	\$2.6
16	Avastin	Genentech/Roche	\$2.7	\$2.6
17	Lantus	Sanofi	\$2.6	\$2.2
18	Oxycontin	Purdue	\$2.5	\$2.8
19	Lyrica	Pfizer	\$2.4	\$2.0
20	Epogen	Amgen	\$2.3	\$2.2
Total others			\$251.3	\$248.5
Total market			\$329.2	\$319.1

Source: IMS Health, National Sales Perspectives

Fig. 3: Top 20 Therapeutic Classes by US Sales '13

Rank	Categories	2013 Total (Billions)	2012 Total (Billions)
1	Oncologics	\$27.9	\$25.5
2	Antidiabetes	\$24.3	\$21.7
3	Mental Health	\$23.7	\$25.0
4	Respiratory	\$20.4	\$21.6
5	Pain	\$18.7	\$18.0
6	Autoimmune	\$17.9	\$15.1
7	Lipid Regulators	\$13.6	\$16.5
8	Antihypertensives	\$12.5	\$13.2
9	HIV Antivirals	\$12.5	\$11.3
10	Multiple Sclerosis	\$10.6	\$8.8
11	Anti-Ulcerants	\$10.0	\$9.8
12	ADHD	\$9.9	\$10.3
13	Dermatologicals	\$8.9	\$7.7
14	Antibacterials	\$8.6	\$7.8
15	Nervous System Disorders	\$8.1	\$7.0
16	Anticoagulants	\$7.4	\$9.6
17	Vaccines, excl. flu	\$6.0	\$6.0
18	Sex Hormones	\$5.8	\$5.3
19	Ophthalmology	\$5.6	\$5.0
20	Hormonal contraceptives	\$5.6	\$5.5
Total others		\$71.2	\$68.4
Total market		\$329.2	\$319.1

Source: IMS Health, National Sales Perspectives

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

Rank	Company	Total Promo Spend		DTC		eDetailing	
		2013 (Millions)*	% change vs 2012	2013 (Millions)	% change vs 2012	2013 (Millions)	% change vs 2012
1	Pfizer	\$1,858.85	-12.0%	\$801.64	34.2%	\$33.26	8.2%
2	Merck & Co.	\$1,489.41	-2.6%	\$246.85	-14.2%	\$18.99	12.1%
3	Forest Laboratories	\$1,139.22	23.0%	\$0.58	44.1%	\$13.89	23.3%
4	AstraZeneca	\$1,137.77	-8.9%	\$247.62	19.9%	\$13.77	-6.2%
5	Eli Lilly	\$1,063.02	-22.6%	\$415.97	-8.2%	\$10.70	-18.8%
6	Boehringer Ingelheim	\$833.41	-9.1%	\$65.49	-62.7%	\$9.94	-9.3%
7	Novartis	\$810.38	-22.8%	\$46.04	-36.9%	\$22.42	3.7%
8	GlaxoSmithKline	\$802.99	-10.4%	\$144.03	-17.7%	\$14.33	2.4%
9	Bristol-Myers Squibb	\$787.86	-6.1%	\$134.05	-23.6%	\$7.28	-31.2%
10	Johnson & Johnson	\$755.92	16.2%	\$97.87	43.4%	\$20.90	2.0%
11	Novo Nordisk	\$572.06	15.0%	\$109.97	29.1%	\$8.06	23.4%
12	Daiichi Sankyo	\$502.52	-2.8%	\$0.02	-95.8%	\$2.71	79.9%
13	Sanofi	\$486.99	0.3%	\$29.27	-25.7%	\$8.96	-29.7%
14	Takeda	\$479.98	-8.0%	\$2.68	-81.2%	\$9.74	6.9%
15	Amgen	\$398.08	-7.5%	\$184.35	-20.1%	\$3.36	-43.2%
16	AbbVie	\$369.24	56.1%	\$286.79	44.4%	\$1.01	-10.6%
17	Allergan	\$360.60	-0.2%	\$185.79	-7.8%	\$2.14	-46.9%
18	Otsuka Pharmaceutical Group	\$353.22	678.5%	\$112.73	3,731.9%	\$2.89	268.8%
19	Teva	\$300.59	11.9%	\$14.85	-60.5%	\$9.18	4.7%
20	Sunovion	\$281.65	-14.4%	\$28.17	-42.4%	\$4.14	-35.3%

* 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, 2012 and 2013 data may not be comparable for all publications

is sinking more money into R&D. The market has been accepting so far, but cost concerns have swirled around some products, such as Lucentis, when cheaper Avastin is available. Bernstein's Anderson asked in his January summary if Kadcyla—priced around \$94K—is effective enough to sway doctors to bypass Herceptin-plus-chemotherapy treatment.

6 Teva \$15.3B ▼4.9%

- Global revenue:** \$20.3B (10th); flat
- Top brands:** Copaxone (\$3.7B), Proair HFA (\$1.2B), Budesonide (\$1.0B), Treanda (\$681M)
- Promotional spend:** \$301M (15th); 2.0% of rev.
- R&D spend:** \$1.4B (17th); flat; 6.9% of rev.
- Planned launches:** Laquinimod (CNS), XR hydrocodone (CNS), Albuterol MDPI (resp.)
- Patent expirations:** Copaxone (2014), Nuvigil (2016), Azilect (2017)

Teva's 2013 was eventful. Talk of board friction, layoffs, a new CEO—plus a 4.9% US sales skid—painted a bleak picture for the Israeli drugmaker. Following a rumored rift between then-CEO Jeremy Levin and chairman Phillip Frost over cost-saving measures, Teva found a new CEO in Erez Vigodman this January. That news followed the October 2013 announcement that Teva would lay off 5,000 employees—10% of its staff—citing Copaxone's expiry. Patients from the older MS drug may not all be lost to Teva, as the company is trying to convert them to its newest formulation, which offers less-frequent dosing and could buoy sales.

7 Eli Lilly \$15.3B ▲11.7%

- Global revenue:** \$23.1B (9th); up 2.2%
- Top brands:** Cymbalta (\$5.3B), Humalog (\$1.2B), Alimta (\$1.2B); Cialis (\$1.1B), Humalog KwikPen (\$902M)
- Promotional spend:** \$1.1B (4th); 7.2% of rev.
- R&D spend:** \$5.5B (7th); up 4.2%; 23.8% of rev.
- Planned launches:** Ramucirumab (onc.), necitumumab (onc.), dulaglutide (diab.), empagliflozin (diab.)
- Patent expirations:** Evista (2014), Alimta (2022), Cialis (2017)

Eli Lilly enjoyed a bump in revenues last year mostly from mature brands, but it needs to replenish its portfolio as it battles the patent cliff. A win in April 2014—cancer drug Alimta's patent extension into the next decade—could help offset another major expiry, that of CNS brand Cymbalta this year. The drugmaker froze salaries for 2014 and reduced all cash-bonus targets for most workers. A biosimilar version of Sanofi insulin blockbuster Lantus won't hit shelves soon, either. Sanofi sued Lilly for patent infringement, which could keep the drug off the US market until mid-2016. It saw another hiccup with its SGLT2 medication empagliflozin, as FDA delayed the medication citing deficiencies in a Boehringer Ingelheim facility where the drug is to be made. GLP-1 candidate dulaglutide, though, stands to capture a third of the \$3-billion GLP-1 market, according to ISI Group analyst Mark Schoenebaum. The drug's main advantage over Novo Nordisk's Victoza is that it only requires once-weekly dosing, compared to Victoza's once-daily frequency.

Total Professional Detailing 2013 (Millions)	% change vs. 2012	Journal Advertising 2013 (Millions)	% change vs. 2012	Total Professional Meetings 2013 (Millions)	% change vs. 2012	Company	Rank
\$916.88	-12.0%	\$1.99	-69.5%	\$115.07	27.3%	Pfizer	1
\$1,113.37	-2.2%	\$0.80	-52.1%	\$101.92	-10.5%	Merck & Co.	2
\$1,020.54	21.6%	\$3.74	-76.9%	\$112.02	13.7%	Forest Laboratories	3
\$798.77	-12.1%	\$0.84	-21.7%	\$112.02	-18.0%	AstraZeneca	4
\$571.91	-23.5%	\$1.49	-62.0%	\$82.15	-12.8%	Eli Lilly	5
\$691.57	-14.6%	\$1.09	-57.1%	\$53.34	-27.3%	Boehringer Ingelheim	6
\$652.45	-15.7%	\$1.89	-20.6%	\$69.65	4.1%	Novartis	7
\$602.77	-12.2%	\$1.89	-20.6%	\$99.35	1.7%	GlaxoSmithKline	8
\$540.20	-12.2%	\$1.53	-76.8%	\$47.63	2.7%	Bristol-Myers Squibb	9
\$529.39	10.8%	\$4.37	-39.6%	\$98.81	5.3%	Johnson & Johnson	10
\$391.71	16.2%	\$1.05	-66.2%	\$100.56	22.4%	Novo Nordisk	11
\$473.69	-11.4%	\$0.20	-53.1%	\$61.90	-28.2%	Daiichi Sankyo	12
\$371.09	-2.6%	\$0.74	-68.6%	\$24.59	26.4%	Sanofi	13
\$423.70	-12.3%	\$0.13	-91.7%	\$72.50	-0.8%	Takeda	14
\$155.95	-5.1%	\$1.01	-29.9%	\$49.98	-17.0%	Amgen	15
\$63.02	43.5%	\$0.75	-28.6%	\$49.28	10.1%	AbbVie	16
\$140.89	2.5%	\$0.66	-26.8%	\$17.27	51.3%	Allergan	17
\$191.84	620.7%	\$0.71	-35.0%	\$46.61	234.7%	Otsuka Pharmaceutical Group	18
\$247.09	8.5%	\$0.77	28.3%	\$34.18	-26.2%	Teva	19
\$211.93	-13.9%	\$0.85	-40.4%	\$36.73	-6.2%	Sunovion	20

8 Amgen

\$14.8B ▲8.1%



Global revenue:
\$18.7B (13th); up 8.1%



Top brands: Enbrel (\$4.7B), Neulasta (\$3.6B), Epogen (\$2.3B), Neupogen (\$963M), Aranesp (\$816M)



Promotional spend:
\$398M (12th); 2.7% of rev.



R&D spend: \$4.1B (10th); up 7.9%; 21.9% of rev.



Planned launches: Evolocumab/AMG 145 (CV), ivabradine (CV), talimogene laherparepvec (onc.)



Patent expirations: Aranesp (2014), Sensipar (2015), Neulasta (2015)

Amgen global revenues jumped 8% in 2013 to \$18.7 billion. Product sales grew 10% in the US and 8% in the rest of the world, with oncology treatments Neulasta bringing in more than 75% of its filgrastim business. Powerhouse RA drug Enbrel continued to yield attractive returns, and is projected to bring in \$800 million in incremental operating income in 2014, according to Amgen's annual report. Other heavyweight performers in 2013 were Sensipar/Mimpara for CKD, racking up more than \$1 billion in sales, and bone drug Prolia, which brought in \$1.8 billion in sales and became available in all major European markets. Xgeva, a higher dose of Prolia for cancer, also brought in impressive results—the seventh product in Amgen's portfolio to exceed \$1 billion in sales in a single year. The company also made some strategic buys in 2013, including its acquisition of Onyx Pharmaceuticals and the US rights to ivabradine, purchased from Servier. Amgen also reacquired rights to filgrastim and pegfilgrastim in eastern Europe, Latin America, Asia, the Middle East and Africa.

9 Johnson & Johnson

\$13.9B ▲18.6%



Global revenue:
\$71.3B (1st); up 6.1%



Top brands: Remicade (\$4.1B), Procrit (\$1.0B), Xarelto (\$1.0B), Prezista (\$1.0B), Stelara (\$966M)



Promotional spend:
\$756M (9th); 5.4% of rev.



R&D spend: \$8.2B (3rd); up 7.0%; 11.5% of rev.



Planned launches: Sirukumab (RA), mepolizumab (resp.), Yondelis (onc.)



Patent expirations: Prezista (2016), Zytiga (2016), Remicade (2018)

Amidst a medicine cabinet force, Johnson & Johnson has challenges, despite notable approvals that include diabetes medication Invokana, hepatitis C medication Olysio and cancer medication Imbruvica. Its problems include lawsuits over some of its marketing practices and device businesses, and quality control issues in its OTC businesses. As of December, J&J and its subsidiaries managed to put 75% back in stores, and paired this effort with a multi-platform consumer push. While court time continues to mount, the company still grows, seeing worldwide pharmaceutical sales jump almost 11% in 2013, with new drugs such as Zytiga (cancer) adding to the performance curve. The company also marked the year with a unique industry footprint—being considered a major social media force, by IMS Healthcare. The informatics company said in January that this achievement is not just because J&J is a household presence, noting that other companies have consumer businesses as well. “J&J...has, more than other companies, embraced the notion that patients are increasingly gathering at social-media channels and sites,” IMS said.

Fig. 5: Estimated US Patent Expirations through 2018

Brand	Company	Indication	Expiry
Aranesp	Amgen	Anemia	2014
Celebrex	Pfizer	Pain	2014
Copaxone	Teva	Multiple sclerosis	2014
Evista	Eli Lilly	Osteoporosis	2014
Gleevec	Novartis	Oncology	2014
Intuniv	Shire	ADHD	2014
Lunesta	Sunovion	Insomnia	2014
Nasonex	Merck	Allergies	2014
Nexium	AstraZeneca	Heartburn	2014
Rituxan	Roche	Oncology/RA	2014
Abilify	BMS/Otsuka	Depression/bipolar	2015
Avodart	GlaxoSmithKline	BPH	2015
Lantus	Sanofi	Diabetes	2015
Namenda	Forest	Alzheimer's disease	2015
Neulasta	Amgen	Neutropenia	2015
Premarin	Pfizer	Menopausal symp.	2015
Symbicort	AstraZeneca	Asthma/COPD	2015
Zyvox	Pfizer	Infection	2015
Benicar	Daiichi Sankyo	Hypertension	2016
Crestor	AstraZeneca	Atherosclerosis	2016
Humira	AbbVie	RA/Crohn's/psoriasis	2016
Prezista	J&J	HIV	2016
Zytiga	Janssen	Cancer	2016
Alimta	Eli Lilly	Cancer	2017
Cialis	Eli Lilly	Erectile dysfunction	2017
Reyataz	Bristol-Myers Squibb	HIV	2017
Seroquel - all	AstraZeneca	Schizophrenia	2017
Vytorin	Merck	Cholesterol	2017
Zetia	Merck	Cholesterol	2017
Nuvaring	Merck	Contraception	2018
Pulmicort	AstraZeneca	Asthma	2018
Ritalin/Focalin	Novartis	ADHD	2018
Tarceva	Roche	Oncology	2018
Vesicare	Astellas	OAB	2018
Xolair	Novartis/Roche	Asthma	2018

Source: Barclays Research

billion last year. Despite the windfall, the company and investors are wary of Act II, when generics threaten Advair. Replacement drugs, like the Breo and Anoro Ellipta are in place, but Advair's rep has been its own undoing in terms of converting patients. The company accounted for 19% of FDA's 2013 approvals, including Breo Ellipta and HIV medication Tivicay. But the company has also been wading through public scrutiny, over allegations of improper behavior in China, which damaged regional sales, and efforts at transparency that have been perceived as merely sleights of hand.

11 Sanofi

\$12.3B ▲2.8%



Global revenue: \$45.6B (5th); flat



R&D spend: \$6.3B (6th); flat; 13.8% of rev.



Top brands: Lantus SoloStar (\$3.0B), Lantus (\$2.6 B)



Planned launches: SAR236553 (CV), Lemtrada (CNS), sarilumab (RA)



Promotional spend: \$487M (11th); 4.0% of rev.



Patent expirations: Allegra (2014); Lantus (2015); Nasacort (2016)

Sanofi posted modest growth in 2013, and its long-term outlook looks promising, with Bernstein analytics showing uninterrupted revenue and EPS growth through the close of the decade, says Tim Anderson. Much of that anticipated growth is rooted in Sanofi's presence in various natural oligopoly-like areas. "All the company really has to do is execute on the current business to grow," Anderson says. The analyst is expecting growth in animal health, insulin-based diabetes therapies, vaccines, and orphan drugs. The piece still missing from the story is quality R&D, Anderson says. While Sanofi has the option to source new pipeline products from its agreement with Regeneron, its pipeline seems quite thin, he notes.

12 AbbVie

\$12.1B ▼1.5%



Global revenue: \$18.8B (12th); up 2.2%



R&D spend: \$2.8B (13th); up 7.9%; 14.9% of rev.



Top brands: Humira (\$5.6B), AndroGel (\$1.4B), Niaspan (\$897M)



Planned launches: Elotuzumab (onc.); ABT-267/333/450 (HCV); dactilizumab (MS)



Promotional spend: \$369M (13th); 3.1% of rev.



Patent expirations: AndroGel (2015); Kaletra (2016); Humira (2016)

AbbVie's first year as an independent company felt similar to 2012. The Abbott spinoff's sales were largely driven by blockbuster autoimmune biologic Humira. Its next-best-selling drug in the US, testosterone drug AndroGel, received scrutiny after FDA announced it's giving the drug class a second look due to safety worries. A bigger concern: Humira's impending patent loss, as it accounts for half of sales. With payers fretting over the price of rival HCV drug Sovaldi, AbbVie's HCV combo may be the answer—if approved and priced competitively. Goldman Sachs analyst Jami Rubin says AbbVie's collaboration with Roche for CLL treatment ABT-199 could provide stability. She also highlighted the drugmaker's endometriosis agent Elagolix, for which it expects to file for approval in 2016.

10 GlaxoSmithKline

\$12.8B ▲2.9%



Global revenue: \$42.9B (7th); up 6.2%



R&D spend: \$5.3B (8th); down 3.6%; 12.4% of rev.



Top brands: Advair (\$5.2B), Lovaza (\$1.1 B), Flovent (\$1.1B)



Planned launches: Sirukumab (RA), umeclidinium (resp.)



Promotional spend: \$803M (7th); 6.2% of rev.



Patent expirations: Lovaza (2014), Avodart (2015)

GlaxoSmithKline appears to be working toward a singular persona, but one that's tending to separate public and pharmaceutical faces. Respiratory products remain its pharmaceutical foothold, bringing in \$12

Fig. 6: New Drug Approvals 2013*

Brand	Company	Indication	Approval
Nesina	Takeda	Type 2 diabetes	Jan. 25
Kynamro	Genzyme	HoFH	Jan. 29
Pomalyst	Celgene	Multiple myeloma	Feb. 8
Kadcyla	Genentech	Breast cancer	Feb. 22
Osphena	Shionogi	Dyspareunia	Feb. 26
Lymphoseek	Navidea	Breast cancer, melanoma	Mar. 13
Dotarem	Guerbet	MRI	Mar. 20
Tecfidera	Biogen Idec	Multiple sclerosis	Mar. 27
Invokana	Janssen	Type 2 diabetes	Mar. 29
Breo Ellipta	GSK	COPD	May 10
Xofigo	Bayer	Prostate cancer	May 15
Tafinlar	GSK	Melanoma	May 29
Mekinist	GSK	Melanoma	May 29
Gilotrif	Boehringer Ingelheim	Lung cancer (NSCLC)	Jul. 12
Tivicay	ViiV	HIV-1 infection	Aug. 12
Beintellix	Takeda	Depressive disorder	Sep. 30
Duavee	Pfizer	Hot flashes, osteoporosis	Oct. 3
Adempas	Bayer	Pulmonary hypertension	Oct. 8
Opsumit	Actelion	PAH	Oct. 18
Vizamyl	GE Healthcare	Alzheimer's disease	Oct. 25
Gazyva	Genentech	Leukemia (CLL)	Nov. 1
Aptiom	Sunovion	Epilepsy	Nov. 8
Imbruvica	Pharmacyclics	Mantle cell lymphoma	Nov. 13
Luzu	Medicis	Antifungal	Nov. 14
Olysio	Janssen	Hepatitis C	Nov. 22
Sovaldi	Gilead	Hepatitis C	Dec. 6
Anoro Ellipta	GSK	COPD	Dec. 18

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

13 Actavis

\$10.3B ▲1.0%

Global revenue: \$8.7B (18th); up 47.5%

R&D spend: \$617M (19th); up 5.4%; 7.1% of rev.

Top brands: Methylphenidate (\$1.1B), doxycycline (\$503M)

Planned launches: Cariprazine (CNS), Esmya (women's)

Promotional spend: \$113M (19th); 1.1% of rev.

Patent expirations: Namenda (2015)

Generic giant Actavis bolstered its portfolio in early 2014 with the purchase of specialty pharma and New York-based Forest Laboratories in a deal valued at \$25 billion. The deal spawned a specialty company with annual sales of about \$15 billion. With Forest under its belt, Actavis estimates that 50% of its revenue will be generated by its specialty brands business. The firm, formerly known as Watson Pharmaceuticals, doubled its specialty brand portfolio last year (along with doubling its revenue) with the \$8.5-billion purchase of Warner-Chilcott, which brought a pipeline of more than 25 products in various stages of development. Actavis says it will also harness Forest's sales and marketing force to propel growth in its specialty care arm, although Forest gives it a presence in primary care areas, as well.

14 Novo Nordisk

\$7.9B ▲23.7%

Global revenue: \$15.5B (14th); up 13.4%

R&D spend: \$2.2B (14th); up 15.2%; 14.2% of rev..

Top brands: Levemir (\$1.6B), NovoLog FlexPen (\$1.4B), NovoLog (\$1.4B)

Planned launches: Tresiba (diab.), IDegLira (diab.)

Promotional spend: \$572.1M (10th); 7.2% of rev.

Patent expirations: NovoLog (2014)

Despite double-digit growth in US sales, Novo had some bad luck in 2013: a warning letter from the FDA about one of its insulin-filling plants in Denmark, a US delay on diabetes agent Tresiba, a safety scare with GLP-1 blockbuster Victoza, and a product recall. Some researchers worry that Victoza—along with others in its class—could pose side-effect risks to the pancreas. The recall in some European countries was with its NovoMix insulin. Even with the setbacks, Novo's Tresiba claimed 8.6% of the Japanese market in 2013 after its initial launch there last February.

15 Mylan

\$7.8B ▲10.1%

Global revenue: \$6.9B (19th); up 1.5%

R&D spend: \$508M (20th); up 27.0%; 7.4% of rev.

Top brands: EpiPen 2-Pak (\$631M), Fentanyl (\$413M)

Planned launches: Generic Advair Diskus (resp.)

Promotional spend: \$96.2M (20th); 1.2% of rev.

Patent expirations: N/A

Mylan has become a leader in generic and specialty pharmaceuticals. Its \$1.4-billion acquisition of the Agila Specialties business from Strides Arcolab in 2014 expanded a diversified portfolio, which included acquisitions of Matrix Labs and Merck KGaA's generics and specialty pharmaceuticals business. With Agila, Mylan brings an even broader portfolio to the injectables market. The acquisition doubled its injectables portfolio to 120 products, and will up its production capacity from about 350 million units in 2013 to a projected 650 million units by 2016.

16 Boehringer Ingelheim

\$7.7B ▲2.7%

Global revenue: \$19.5B (11th); down 3.9%

R&D spend: \$3.8B (11th); up 15.8%; 19.5% of rev.

Top brands: Spiriva HandiHaler (\$3.0B), Pradaxa (\$843M)

Planned launches: Nintedanib (onc.), empagliflozin (diab.)







Promotional spend: \$833M (5th); 10.8% of rev.

Patent expirations: Micardis (2014),

Boehringer Ingelheim's global sales fell about 4% in 2013, and the German company is bracing for more red ink. The last 12 months were "a transition year," management conceded, due to losses of exclusivity on products like Micardis, Sifrol and Viramune. Anticoagulant Pradaxa,







which added indications for deep vein thrombosis and pulmonary embolism, enjoyed higher sales, as did diabetes drug Tradjenta, but overall pharma revenues sank 4.5% vs. 2012. The next 12 months are not expected to bring a significant upswing: “2014 is certain to be another challenging year,” BI’s chairman wrote in the family-owned firm’s annual report.

17 Gilead \$7.6B ▲17.6%

 Global revenue: \$11.2B (17th); up 15.5%	 R&D spend: \$2.1B (15th); up 20.0%; 18.8% of rev.
 Top brands: Atripla (\$2.9B), Truvada (\$2.3B), Complera (\$630M), Stribild (\$605M)	 Planned launches: LDV+SOF (HCV), TAF+elvit egravir+cobicistat+emtrici tabine (HIV)
 Promotional spend: \$119M (18th); 1.6% of rev.	 Patent expirations: Viread (2017), Atripla (2018), Truvada (2018)

Gilead’s vaunted antiviral engine generated record global revenues of \$11.2 billion for 2013, and it’s poised to continue that trajectory. Its greatest score for the year was the December approval and introduction of Sovaldi, a treatment for chronic hepatitis C virus that’s already on track to reach several billion in sales this year. It also added new HIV treatments, and expanded its therapeutic focus to include oncology. Specifically, its HIV-treatment Stribild became a leading regimen for treatment-naïve HIV sufferers in the US. It also received approval to launch the treatment in Europe from the European Commission last May. Meanwhile, Gilead’s second single-tablet regimen for HIV, Complera, got a prescribing label expansion in the US to include suppressed patients switching from a stable, antiretroviral treatment regimen.







18 Otsuka \$6.8B ▲33.3%

 Global revenue*: \$13.0B (15th); up 15.0%	 R&D spend*: \$2.0B (16th); up 28.5%; 15.4% of rev.
 Top brands: Abilify (\$6.5B), Samsca (\$107M), Busulfex (\$78M), Abilify Maintena (\$45M)	 Planned launches: TAS-102 (onc.), OPC-34712 (CNS), S-1 (onc.), Sativex (CNS), OPC-67683 (I.D.)
 Promotional spend: \$353M (14th); 5.2% of rev.	 Patent expirations: Abilify (2015)

Otsuka focuses on four market sectors: pharmaceuticals, nutraceuticals, consumer products and “other business.” Last March, it launched Abilify Maintena, a central nervous system treatment, in the US with global partner Lundbeck. The treatment, an extended-release, once-monthly injection, is now sold in more than 60 countries. Otsuka also signed a global agreement with Lundbeck to co-develop and co-promote Lu AE58054, a treatment for Alzheimer’s. With Lundbeck’s track record in treatments for anxiety and depression and Otsuka’s results with antipsychotics, the two are planning to work together to penetrate the CNS sector further. In oncology, Otsuka is currently pursuing testing anti-cancer agent TAS-102 and has filed it in Japan.







**Global revenue and R&D spend are based on the fiscal year ending March 31, 2013, the latest data available at press time.*

19 Bristol-Myers Squibb \$5.6B ▼27.3%

 Global revenue: \$12.3B (16th); down 10.2%	 R&D spend: \$3.7B (12th); down 5.1%; 30.1% of rev.
 Top brands: Oncia (\$960M), Reyataz (\$941M), Sprycel (\$560M), Yervoy (\$559M)	 Planned launches: Nivolumab (onc.), asun aprevir+daclatasvir+B MS-791325 (HCV)
 Promotional spend: \$788M (8th); 14.0% of rev.	 Patent expirations: Baraclude (2014), Sustiva (2015), Abilify (2015), Erbitux (2016)

Like Merck, BMS went through retrenchment in 2013. The firm announced it was scuttling several categories, including diabetes, hepatitis and neuroscience. Unlike Merck, the general reaction was not “it’s about time,” but rather, “interesting.” As noted by Bernstein’s Tim Anderson, the company’s backlog of successes has created a foundation of goodwill. At the same time, he and other industry watchers have their limits, as both they and BMS are leaning heavily on immuno-oncology (I/O) to carry the company forward. Key products include the anti-PD-1 antibody nivolumab, and how it pairs with already-approved Yervoy. Anderson noted in January that Yervoy could become a “backbone agent to be combined with PD1/L1’s across multiple platforms,” which adds to its importance. A March announcement that BMS was pursuing a Phase-III nivolumab-Yervoy combo study has fanned expectations for the segment.

20 Shire \$4.2B ▲8.3%

 Global revenue: \$4.9B (20th); up 8.9%	 R&D spend: \$933M (18th); down 2.1%; 19.0% of rev.
 Top brands: Vyvanse (\$1.8B), Adderall XR (\$755M), Intuniv (\$588M), Lialda (\$561M), Pentasa (\$317M)	 Planned launches: SHP606 (dry eye), SHP555 (GI)
 Promotional spend: \$132M (17th); 3.1% of rev.	 Patent expirations: Intuniv (2014)

Shire reset in 2013 to focus entirely on developing and marketing specialty medicines. It expanded commercialization of its rare-diseases treatments to markets in 50 countries. And it established a subsidiary office in Japan in an effort to expand more aggressively into Asia. Its drug Elvanse, a treatment for ADHD in children and adolescents, received marketing authorization in the UK. And it sold its Dermagraft assets to Organogenesis. The company acquired four companies last year in order to further strengthen its specialty market focus: Lotus Tissue Repair, Premacure AB, SARcode Bioscience and ViroPharma. Drugs currently in development at Shire include a treatment for binge eating disorder. ■