

A sunny day — in — Pharmaland

THE 2015 PHARMA REPORT

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ILLUSTRATION: BEN KIRCHNER



Fueled by breakthrough drugs that actually broke through, spending on pharma products surged an incredible 13.1% in 2014, a figure that stunned even the sunniest of optimists. But with some of the contributing factors looking like one-time-only events, pundits wonder if perhaps the gains have been overstated—and don’t get them started on the threat posed by payers pushing back against drug prices. **Larry Dobrow attempts to place the number in its proper context**

For those not inclined to delve deeper than the contents of a headline, US pharma sales data released last month by the IMS Institute for Healthcare Informatics must have delivered a jolt. After a few years of minimal growth and/or declines, spending on prescription medicines surged 13.1% in 2014, to \$373.9 billion. The jump of \$43 billion in spending over 2013 levels represented the largest single-year growth total since the dawn of pharma sales record-keeping (the previous high was \$26.4 billion, in 2001).

A 13% increase in sales? Happy days are here again!—you could almost hear the shallow-minded among us thinking. *First I’m gonna tell the patent-cliff pessimists to go find an actual cliff! Then I’ll liberate the R&D folks from the lab and let ’em play Ultimate Frisbee on the quad! Heck to Betsy, perhaps I’ll even hire a sales rep or three!*

Which puts Michael Kleinrock, the IMS Institute’s director, research development, in the unusual role of wet blanket. At this time last year, after reporting that total US drug spend jumped to \$329.2 billion in 2013 (which represented a 3.2% gain over 2012), Kleinrock expressed surprise about the sales bump and genuine enthusiasm about the state of the industry union. So how is it that he characterizes 2014—and, to repeat, its 13.1% sales cloudburst—as merely “a reasonably good year”?

It’s because skepticism is ingrained in Kleinrock’s line of work. Also, he’s had a chance to dissect the data. “While [the 13% growth figure] is astonishingly high—again, it’s a big number—what’s interesting is that it stems from a series of very narrow, very specific happenings. It’s not a broad-based ‘everything’s up 13%.’ A few events, what you might call outliers, are driving it,” Kleinrock says.

To that end, he does some quick net-basis math. Remove the borderline unprecedented spending on hep.-C products from the equation, and the 13% figure drops to 10%. Factor in the significantly diminished impact of patent expiries—\$11.9 billion, versus the 2012 high of \$30.7 billion—and we’re down even further, to 7%. Then add to the mix the relative illusion of list-price growth—up 13.5% on an invoice basis, but really just 7% or 8% once rebates and concessions are taken into account—and we’re down roughly another 4.8%.

“One way to look at it is that, without those outlier events, we’re at 2.3% [growth],” Kleinrock concludes.

Which means that 2014 was a solid year for the business, but perhaps not the world-beater that 13.1% would imply. Indeed, that seems to be the opinion of most people in and around the industry.

“In general, drugs did pretty well,” shrugs Les Funtleyder, healthcare portfolio manager at E Squared Asset Management.

Ipsen chairman and CEO Marc de Garidel agrees: “We saw some things that were very encouraging.” De Garidel points in particular to what he views as a golden era of innovation. “After 2010 there was barely anything. Now you see major breakthroughs finally reaching the patient.”

Of course, any mention of breakthrough products (hi, Sovaldi) prompts immediate discussion of what may well be big pharma’s biggest concern right now: pricing and the related payer pressure that emerged as a huge headache in 2014. “If you go back five years, what pharma companies were hearing was, ‘Develop breakthrough medicines. We’re not going to pay for the other [less effective] ones.’ For all the rhetoric and screaming about prices, pharma is delivering the goods,” says Rick Edmunds, a senior partner at PwC network firm Strategy& and leader of its global healthcare practice.

To a person, industry experts believe that Gilead didn’t overreach with its pricing of Sovaldi and Harvoni; “reasonable” is the most common adjective used to describe the company’s approach. The problem, as Kleinrock sees it, “is that we don’t have a mechanism for accepting breakthrough medicines into the healthcare system that takes pricing into account. It shouldn’t be the innovators’ problem alone.” With advances in immuno-oncology and gene therapy imminent, this could get worse before it gets better.

In the wake of L’Affaire Hep.-C, the big industry worry is that the episode may have emboldened payers to push back more aggressively against drugmakers hoping to secure premium pricing for products that only offer incremental benefits over older, cheaper ones. As Adam Scott Roberts, SVP, media of CMI/Compas, notes, “You didn’t see anyone protesting in the streets ... People still don’t understand why drugs cost what they do.”

The pricing contretemps didn’t entirely overshadow the rest of the year’s industry intrigue, which included 41 FDA approvals (versus 27 in 2013), continued erosion in the collective size of pharma sales forces (to 62,000, down 4%, per ZS Associates) and near paralysis in R&D budgets (a 1% decrease among the top 20 companies by US sales). Still, the surge in M&A activity—\$212 billion worth of deals, up 170% from 2013, according to EvaluatePharma—prompted more than a few gasps. “Large transactions indicate that even the biggest companies recognize that the velocity they get from them is a good thing,” de Garidel notes.

Funtleyder believes much of the M&A activity was a no-brainer from a financial perspective: “With interest rates basically zero and the cost of capital so low, many of the deals make better sense than they would’ve otherwise.” What interests him more is the possibility that the biggest pharma companies might invest directly in smaller ones, as Merck recently did with NGM Biopharmaceuticals and Bristol-Myers Squibb with uniQure.

Looking to the rest of 2015, Funtleyder believes the IPO market will remain strong through at least the middle of the year. Kleinrock is slightly less optimistic, at least when it comes to the potential for another cluster of outlier events. “We could see a continuous stream of breakthrough drugs like [Gilead’s] Sovaldi and [Biogen’s] Tecfidera, but historically it usually doesn’t work that way,” he says. “Slowing to mid-single-digit [sales] growth is the expectation.”

With additional reporting by Frank Celia, Kevin McCaffrey and Deborah Weinstein.

I. ASTRAZENECA \$19.5B ▲7.2%

Global revenue: \$33.3B (7th); up 4.9%

Top brands: Nexium (\$5.9B); Crestor (\$5.8B); Symbicort (\$2.2B); Seroquel (\$1.3B)

Promotional spend: \$1.6B (2nd); 8.2% of rev.

R&D spend: \$4.9B (7th); up 2%; 14.7% of rev.

Planned launches: MEDI-4736 (onc.); tremelimumab (onc.); lesinurad (gout); brodalumab (psoriasis)

Patent expirations: Symbicort (2015); Synagis (2015); Crestor (2016)

In the heat of Pfizer’s failed \$100 billion takeover bid last year, AZ’s CEO Pascal Soriot made a promise to shareholders: If the company remained independent, he would lead it to sales of \$45 billion by 2023—a 75% increase. When the smoke cleared, he walked back those bold words a little, but they are not completely outlandish. The UK-based drugmaker ranks among the “big four” of immuno-oncology companies (the others being Bristol-Myers Squibb, Roche and Merck) at the forefront of what many researchers believe might soon be one of medicine’s most rewarding fields. In the coming months, interest in data from AZ’s rich oncology pipeline will be high, especially the combo-drug MEDI-4736 and tremelimumab, with its unique CTLA-4 mechanism of action. However, even in best-case scenarios, the company likely faces lean times before new therapies pay off. Profits were down last year and might have been worse had a generic competitor to Nexium emerged sooner. Top-earner Crestor’s patent expires in 2016. And the FDA’s investigation of Onglyza for possible cardiovascular side effects jeopardizes AZ’s diabetes-heavy portfolio.

2. NOVARTIS \$19.4B ▲3.0%

Global revenue: \$51.3B (1st); up 3.7%

Top brands: Gleevec (\$2.3B); Diovan/Co-Diovan (\$1.4B); Gilenya (\$1.3B)

Promotional spend: \$577M (11th); 3% of rev.

R&D spend: \$9.6B (1st); 0% change; 18.7% of rev.

Planned launches: LCZ696 (CV); secukinumab (auto.); LEE011 (onc.); Zaxzio (onc.)

Patent Expirations: Gleevec (2016); Ritalin/Focalin (2018)

Faced with aggressive generic competition, the Swiss-based company spent much of last year overhauling its portfolio. In a three-way asset swap, Novartis bought GlaxoSmithKline’s cancer franchise for a reported \$16 billion and sold its vaccine unit to GSK for \$7 billion; the two companies agreed to pool their OTC products. Novartis also sold its animal health assets to Eli Lilly for \$5.4 billion and its blood diagnostics unit to the Spanish company Grifols for \$1.7 billion. A successful lawsuit delayed generic competition to blockbuster leukemia drug Gleevec until 2016, but patent expirations remain problematic, with an estimated \$10 billion at risk over the next year alone. On the bright side, Gleevec’s replacement, Tasigna, tallied sales of \$1.5 billion in 2014, and oncology drug Zaxzio recently became the first-ever biosimilar approved by the FDA. The company also has high hopes for LCZ696, a heart-failure drug expected to receive FDA approval this year. However, the first-in-its-class agent will face an uphill battle against time-tested, safe, inexpensive ACE inhibitors.

3. JOHNSON & JOHNSON \$19.1B ▲37.4%

Global revenue: \$36.4B (6th); up 20.9%

Top brands: Remicade (\$4.5B); Xarelto (\$2.1B); Olysio (\$2.0B); Stelara (\$1.5B); Zytiga (\$971M)

Promotional spend: \$1.0B (5th); 5.2% of rev.

R&D spend: \$8.5B (3rd); up 0.6%; 23.4% of rev.

Planned launches: guselkumab (imm.); daratumumab (onc.)

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

Behemoth Johnson & Johnson has a presence in just about every category that has the market’s attention, including cancer drugs (Imbruvica, which has garnered four indications since its 2013 approval for mantle cell lymphoma), hepatitis-C treatments (Olysio) and blood drugs (Xarelto). J&J sat out 2014’s wave of tax-inversion efforts and M&A activity, but it was scooped by AbbVie’s \$21-billion bid to buy Imbruvica partner Pharmacyclics. In its wake, J&J has pursued a lower-key purchase of XO1 Limited, which is developing anti-anticoagulants that can counter offerings like the aforementioned Xarelto, which are shadowed by bleeding concerns. Of course, given its presence in just about every category, J&J is sensitive to industry tremors and could soon find itself in a turf war between branded biologics, like Remicade, and the biosimilars that are expected to chip away at the branded market. While CEO Alex Gorsky said he expects Europe’s Remicade biosimilar will have an impact on 2015 sales, at least one industry watcher expects US sales of the drug to notch single-digit yearly growth until its expected 2018 patent expiration.

TOP 20 PHARMACEUTICAL COMPANIES BY US SALES, 2014

Rank	Company	2014 Total (Billions)	2013 Total (Billions)
1	AstraZeneca	\$19.5	\$18.2
2	Novartis	\$19.4	\$18.8
3	Johnson & Johnson	\$19.1	\$13.9
4	Gilead Sciences	\$18.4	\$7.6
5	Pfizer	\$18.0	\$16.9
6	Roche	\$17.7	\$16.6
7	Merck	\$17.6	\$16.2
8	Teva	\$17.5	\$15.3
9	Amgen	\$16.4	\$14.8
10	Sanofi	\$14.6	\$12.2
11	Actavis	\$13.8	\$14.1
12	AbbVie	\$12.6	\$12.1
13	GlaxoSmithKline	\$12.2	\$12.7
14	Eli Lilly	\$11.8	\$15.3
15	Novo Nordisk	\$10.4	\$8.2
16	Mylan	\$8.7	\$7.9
17	Boehringer Ingelheim	\$8.3	\$7.7
18	Otsuka	\$8.2	\$6.8
19	Biogen	\$6.1	\$3.9
20	Shire	\$5.0	\$4.2
	Total others	\$98.6	\$87.1
	Total market	\$373.9	\$330.5

Source: IMS Health, National Sales Perspectives

4. GILEAD SCIENCES \$18.4B ▲140.9%

Global revenue:
\$23.7B (10th), up 115%

Top brands: Sovaldi (\$7.9B); Atripla (\$3.0B); Truvada (\$2.5B); Harvoni (\$1.5B); Stribild (\$1.3B)

Promotional spend:
\$224.4M (25th); 1.2% of rev.

R&D spend: \$2.8B (13th); up 25.7%; 11.8% of rev.

Planned launches: darunavir/cobicistat/emtricitabine/GS-7340 (HIV); idelalisib (hem/onc.); ranolazine (CV)

Patent expirations:
Viread (2017); Atripla (2021); Truvada (2021)

Gilead almost had too good a year in 2014: The company reaped such huge sales that it drew sticker-shock backlash from payers and senators—even the Philadelphia Transportation Authority. This was largely due to the pricing of its hep.-C cures—Sovaldi and Harvoni, which collectively raked in more than \$10 billion in 2014. Their success even scuttled the competition, with the FDA rescinding Merck’s Breakthrough Therapy designation for another HCV contender. In 2015 and beyond, Gilead will use its bolstered coffers to fund a new focus in oncology. The company saw its first cancer drug, Zydelig, approved in the EU and US in 2014 for blood cancers; it also plans to evaluate Zydelig in other stages of lymphoma. Gilead also licensed a BTK inhibitor, GS-4059, from Ono Pharmaceuticals, which will be jointly developed for use in malignant B-cells. To help lead the oncology charge, the drugmaker snared well-respected industry veteran Phillippe Bishop to serve as SVP.

5. PFIZER \$18B ▲UP 6.7%

Global revenue:
\$44.9B (2nd); up 3.6%

Top brands: Lyrica (\$3.1B); Celebrex (\$2.4B); Viagra (\$1.3B)

Promotional spend:
\$2.1B (1st); 11.7% of rev.

R&D spend: \$7.2B (4th); up 9.1%; 16% of rev.

Planned launches: bococizumab (CV); ertugliflozin (diab.)

Patent expirations: Premarin (2015); Zyxov (2015); Lyrica (2018); Bosulif (2019); Chantix (2020)

Pfizer’s frustrated attempt to take over AstraZeneca was the company’s most visible moment in 2014, but the company got off to a fast start in 2015 when the FDA approved its first-in-class CDK 4/6 inhibitor Ibrance for breast cancer. The approval was notable not only for the breakneck speed with which it happened but also because it handed the company a potential cornerstone medication for what could become an independent company—that is, if Pfizer decides to break itself into smaller pieces after it delivers financials for each of its three divisions in 2017. In 2014 the impact of patent expirations—for blockbusters Lipitor and Celebrex—was felt, but not enough to push the company’s sales numbers into the red. And Pfizer’s purchase of Hospira for \$17 billion filled out the firm’s biosimilar pipeline, including one product that could compete with Johnson & Johnson’s Remicade autoimmune biologic. Up next, per one industry pundit: more acquisitions that could “materially change [the company’s] outlook.”

6. ROCHE \$17.7B ▲6.9%

Global revenue:
\$37.6B (4th); up 4.9%

Top brands: Rituxan (\$3.5B); Avastin (\$2.9B); Herceptin (\$2.2B); Lucentis (\$1.9B)

Promotional spend: \$279.0M (21st); 1.6% of rev.

R&D spend:
\$9.5B (2nd); up 2%; 25.3% of rev.

Planned launches: PD-L1 (onc.); cobimetinib (onc.); ocrelizumab (MS); lomalizumab (ophthal.); crenezumab (Alzheimer’s)

Patent expirations:
Tamiflu (2017); Xolair (2018)

For those who limit their analysis to a glimpse at the bottom line, Roche had a rough 2014. Its net income after taxes dipped 10% below 2013’s number and annual profits sank 16%—the first time in three years earnings failed to rise. But Roche management claims those figures resulted mainly from unfavorable foreign-exchange rates and a debt-restructuring deal. Despite some notable setbacks—poor Phase-III results on pipeline drugs gantenerumab (Alzheimer’s), bitopertin (schizophrenia) and MetMab (lung cancer)—the company’s short-term fundamentals appear strong. In 2014 HER2-positive breast-cancer medicine sales rose 20%, Avastin sales jumped 5% and Tamiflu sales soared 54%. Additionally, Roche’s promising anti-PD-L1 oncology drug recently received Breakthrough Therapy status, which could lead to a filing for FDA approval before yearend. Long term, the company has bet heavily against biosimilars, choosing instead to improve existing products (the “bio-better” strategy). If the bio-generics take off, Roche’s sales will take a hit. Nevertheless, Roche continues to outwardly exhibit confidence.

7. MERCK \$17.6 ▲8.4%

Global revenue:
\$36.5B (5th); up 3.9%

Top brands: Januvia (\$3.5B); Zetia (\$2B); Janumet (\$1.2B); Nasonex (\$1.2B)

Promotional spend:
\$1.2B (4th); 6% of rev.

R&D spend: \$7.1B (5th); down 4.3%; 19.4% of rev.

Planned launches: MK-3102 (diabetes); odanacatib (osteoporosis); grazoprevir/elbasvir (HCV)

Patent expirations: Cubicin (2016); Zetia/Vytorin (2017); Nuvaring (2018); Nasonex (2018); Januvia/Janumet (2022)

Merck renewed its commitment to infectious diseases and oncology in 2014. It launched Keytruda in September 2014, the first of a new and highly touted class of cancer immunotherapies known as PD-1s to reach US shores. While the drug was initially approved for use only as a second-line treatment in melanoma, GlobalData analyst Fenix Leung wrote in January that it’s likely to receive a first-line indication soon. And as of press time, Merck filed the drug for treatment of non-small cell lung cancer. Keytruda will face stiff competition from BMS’s PD-1 Opdivo, but Bernstein analyst Tim Anderson believes it will still reach \$900 million in sales for 2015. Elsewhere, Merck attempted to gain some ground in hep.-C by acquiring Idenix Pharmaceuticals in June for \$3.9 billion. It gained a nucleotide inhibitor, an NS5A and a protease inhibitor. Shortly thereafter, however, the FDA rescinded Merck’s Breakthrough Therapy designation for its HCV doublet therapy after rival competitors (AbbVie’s Viekira Pak and Gilead’s Harvoni) beat it to market in the fall of 2014.

US SPEND FOR TOTAL PROMO, DTC, E-DETAILING, TRADITIONAL DETAILING, MEETINGS, JOURNAL ADS

Rank	Company	TOTAL PROMO SPEND		DTC		E-DETAILING		TRADITIONAL DETAILING		JOURNAL ADVERTISING		MEETINGS		Company	Rank
		2014 (Millions USD)*	% change vs 2013	2014 (Millions USD)*	% change vs 2013	2014 (Millions USD)*	% change vs 2013	2014 (Millions USD)*	% change vs 2013	2014 (Millions USD)*	% change vs 2013	2014 (Millions USD)*	% change vs 2013		
1	Pfizer	\$2,130.22	12.1%	\$1,107.84	28.0%	\$46.26	39.1%	\$874.92	-1.0%	\$3.82	36.3%	\$97.38	-15.4%	Pfizer	1
2	AstraZeneca	\$1,584.03	37.4%	\$335.35	17.1%	\$26.31	92.3%	\$1,084.59	40.9%	\$4.70	307.3%	\$133.07	62.3%	AstraZeneca	2
3	Actavis	\$1,358.70	-5.4%	\$103.68	6267.4%	\$23.23	7.8%	\$1,126.34	-10.7%	\$2.01	-68.2%	\$103.44	-28.9%	Actavis	3
4	Merck	\$1,244.59	-14.5%	\$211.64	-20.6%	\$39.01	102.7%	\$903.11	-15.2%	\$1.85	49.5%	\$88.98	-14.8%	Merck	4
5	Johnson & Johnson	\$1,040.31	38.0%	\$257.51	118.9%	\$32.29	54.5%	\$629.78	23.7%	\$5.27	-10.9%	\$115.46	14.8%	Johnson & Johnson	5
6	Boehringer Ingelheim	\$858.88	2.7%	\$124.10	71.8%	\$13.65	37.4%	\$662.20	-2.9%	\$2.40	-3.1%	\$56.52	-18.8%	Boehringer Ingelheim	6
7	GlaxoSmithKline	\$824.71	2.7%	\$112.55	-26.6%	\$21.36	50.5%	\$623.85	6.6%	\$3.80	47.5%	\$63.16	32.6%	GlaxoSmithKline	7
8	Eli Lilly	\$823.95	-23.9%	\$337.01	-25.9%	\$12.39	15.8%	\$437.75	-22.0%	\$2.14	-2.5%	\$34.65	-35.0%	Eli Lilly	8
9	Bristol-Myers Squibb	\$668.58	-16.1%	\$222.40	43.6%	\$7.70	5.4%	\$377.66	-29.2%	\$2.27	-1.6%	\$58.56	-40.9%	Bristol-Myers Squibb	9
10	AbbVie	\$636.36	36.1%	\$363.19	13.9%	\$5.04	286.6%	\$230.53	81.9%	\$1.38	63.8%	\$36.23	82.5%	AbbVie	10
11	Novartis	\$576.50	-25.9%	\$12.95	-76.1%	\$44.96	104.1%	\$431.06	-28.3%	\$1.63	28.9%	\$85.90	-12.8%	Novartis	11
12	Takeda	\$570.02	20.1%	\$0.13	-95.3%	\$9.57	-1.8%	\$498.90	20.6%	\$2.43	782.5%	\$59.00	23.2%	Takeda	12
13	Novo Nordisk	\$564.37	-2.4%	\$60.95	-50.7%	\$7.88	-2.2%	\$433.62	13.0%	\$0.68	-39.7%	\$61.23	-1.1%	Novo Nordisk	13
14	Daiichi Sankyo	\$458.57	-8.0%	\$0.02	20.3%	\$3.61	33.0%	\$431.12	-8.5%	\$0.86	180.0%	\$22.96	-6.6%	Daiichi Sankyo	14
15	Sanofi	\$456.61	-3.6%	\$20.54	-29.8%	\$11.09	23.7%	\$373.73	3.3%	\$2.61	193.1%	\$48.64	-32.9%	Sanofi	15
16	Allergan	\$429.75	18.3%	\$247.82	24.1%	\$2.45	14.5%	\$149.49	7.7%	\$0.62	-10.1%	\$29.37	34.2%	Allergan	16
17	Dainippon Sumitomo	\$415.41	48.8%	\$191.70	555.9%	\$4.85	17.2%	\$183.60	-11.6%	\$1.13	-14.0%	\$34.12	-7.1%	Dainippon Sumitomo	17
18	Otsuka	\$361.38	0.0%	\$108.14	-11.2%	\$12.59	335.7%	\$194.21	2.6%	\$1.01	14.7%	\$45.42	-2.6%	Otsuka	18
19	Amgen	\$334.08	-19.2%	\$135.87	-29.1%	\$4.53	15.0%	\$143.38	-12.0%	\$2.04	56.7%	\$48.27	-9.8%	Amgen	19
20	Teva	\$327.94	9.5%	\$7.56	-53.7%	\$9.42	-1.0%	\$265.73	11.5%	\$1.91	95.4%	\$43.31	26.7%	Teva	20

*Total promotional spend does not include spending towards samples, clinical trials or direct mail; Source: IMS Health, Strategic Data—Promotion Audits

8. TEVA \$17.5B ▲14.0%

Global revenue: \$26.0B (9th); up 8.6%

Top brands: Copaxone (\$3.9B); Proair HFA (\$1.2B); Qvar (\$695M)

Promotional spend: \$328M (20th); 1.9% of rev.

R&D spend: \$1.5B (17th); up 4.3%; 5.8% of rev.

Planned launches: CEP-33237 ER hydrocortisone (CNS); Laquinimod (CNS); reslizumab (resp.)

Patent expirations: Nuvigil (2016); Azilect (2017)

The Israeli drugmaker's future looks a lot brighter than it did just a year ago. In CEO Erez Vigodman's first months on the job, Teva overhauled its management structure and shuttered several manufacturing plants, eventually trimming \$600 million in net costs. Refocusing on its core strengths of generics and specialty medications, the leaner Teva launched four new products—including Adasuve, an inhalation powder to treat schizophrenia—that generated \$200 million. A favorable Supreme Court ruling delayed generic competition to profit-center MS drug Copaxone, giving patients more time to switch to its longer-lasting successor. Finally, the FDA pushed back the launch date of Mylan's generic version of Nexium, making Teva the sole US generic Nexium producer for the next several months. House back in order, the company opted to join the M&A craze gripping the pharmaceutical industry. In April it announced plans to strengthen its position in neurological R&D with a \$3.2-billion purchase of California biotech firm Auspex Pharmaceuticals, whose new treatment for Huntington's chorea, SD-908, recently passed Phase-III trials.

9. AMGEN \$16.4B ▲10.9%

Global revenue: \$20.5B (11th); up 10.4%

Top brands: Enbrel (\$5.5B); Neulasta (\$3.8B); Epogen (\$2.4B); Xgeva (\$857M); Sensipar (\$796M)

Promotional spend: \$334M (19th); 2.0% of rev.

R&D spend: \$4.3B (10th); up 5.2%; 21.0% of rev.

Planned launches: Corlanor (CV); Repatha (CV); Talimogene laherparepvec (onc.)

Patent expirations: Epogen (2015); Neulasta (2015); Sensi-

Amgen pushed past \$20 billion in sales for the first time in 2014—and is already making waves in 2015, courtesy of its involvement in two of this year's most-watched developments. First, Amgen finds itself in a heated race with Sanofi and Regeneron in the nascent PCSK9 anti-cholesterol space. Should the company establish a beachhead within the category, it would also acquire valuable reach in the sub-category of rare-disease drugs that have mass-application appeal. Second, the FDA's approval of Sandoz's Neupogen biosimilar, Zarxio, made Amgen the first company to have a biologic that will face off against a lookalike drug; Amgen's branded biologic Neupogen will compete with a biosimilar that shares all five indications. Additionally, Amgen's biosimilar pipeline includes lookalikes for Roche's Avastin and AbbVie's Humira; it expects to launch its first biosimilar in 2017.

10. SANOFI \$14.6B ▲19.9%

Global revenue: \$40B (3rd); up 8.1%

Top brands: Lantus Solostar (\$4.5B); Lantus (\$3.4B); Renagel/Renvela (\$491M); Aubagio (\$345M); Synvisc/Synvisc-One (\$290M)

Promotional spend: \$456M (15th); 3.1% of rev.

R&D spend: \$5B (6th); up 2%; 12.5% of rev.

Planned launches: alirocumab (CV); sarilumab (RA); lixisenatide (diabetes)

Patent expirations: Aubagio (2017); Multaq (2018); Toujeo (2018)

Sanofi's new CEO Olivier Brandicourt, who replaced ousted CEO Chris Viehbacher, faces a number of challenges, none of which are more important than finding a revenue replacement for blockbuster insulin Lantus, which came off patent in February 2015. Making matters more challenging, Lantus's heir-apparent, Toujeo, has already faced a serious setback: When it was approved in February, it received what some analysts considered a "limiting" label. "All the label shows is non-inferiority of Toujeo to Lantus and the trends in blood-sugar reduction are not uniformly in favor of Toujeo," wrote Bernstein's Tim Anderson. Sanofi execs said at a November pipeline presentation that current Lantus patients would be prime targets for Toujeo, leaving questions about potential new markets for the new drug. It's not all doom and gloom for the Paris-based drugmaker, however. Sanofi's PCSK9 Praluent (alirocumab), one of a new highly touted class of cholesterol-lowering treatments, has shown in testing that it can reduce bad cholesterol levels by 60%. It could also be the first PCSK9 to market: Sanofi redeemed a purchased priority review voucher, which places it ahead of Amgen's Repatha (evolocumab) in the FDA queue.

11. ACTAVIS \$13.8B ▼2.4%

Global revenue: \$16.0B (17th); down 0.8%

Top brands: Namenda; Linzess; Teflaro (US sales revenue N/A)

Promotional spend: \$1.4B (3rd); 10.1% of rev.

R&D spend: \$1.1B (18th); up 78.2%; 6.9% of rev.

Planned launches: DARPIn (ophthal.); Semprana (CNS); aripiprazole (CNS); dalbavancin (infect.)

Patent expirations: Namenda (2015)

According to Actavis CEO Brent Saunders, the days of reaping easy profits from "me-too" branded products are over. The future, he believes, belongs to pharmaceutical companies that can either innovate to meet unmet medical needs or supply low-cost medications (i.e., generics) to large global markets—or do both, like his company. Actavis enjoyed a strong reputation in generics before outbidding Valeant Pharmaceuticals last year to acquire Allergan, paying \$66 billion for the company and its blockbuster franchises in ophthalmology, neuroscience and aesthetics. The merger, the fourth largest in pharmaceutical history, gives Actavis newfound cachet in R&D culture plus a robust pipeline that will be a key to future success. In fact, the company plans to change its name to Allergan sometime this year. Saunders hopes to launch seven to ten new products in 2016 and maintain a similarly rigorous output moving forward, he says. Launches to watch include: DARPIn, an age-related macular-degeneration drug with easier dosing; Levadex, an inhaled migraine abortive; caripiprazole, to prevent schizophrenia relapse; and Natrelle Inspira, a breast implant.

12. ABBVIE \$12.6B ▲4.7%

Global revenue:
\$19B (13th); up 5.5%

Top brands: Humira (\$7.2B); Synthroid (\$998M); Androgel (\$934M); Lupron (\$580M); Creon (\$516M)

Promotional spend:
\$636M (10th); 5% of rev.

R&D spend: \$3.2B (12th); up 15%; 16.8% of rev.

Planned launches: elotuzumab (onc.); adalimumab [humira] (pediatric crohn's); elagolix (endometriosis pain)

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

AbbVie’s proposed \$54-billion acquisition of Shire never made it to the finish line, felled by US tax rules that deter inversions. So attention turned back to Humira—whose patent clock is ticking, with generic competition set to arrive by December 2016. Still, while the Humira patent and the Shire negotiations kept AbbVie in the headlines, the company made news in other ways. It acquired Pharmacyclics for \$21 billion. It also sealed a forward-minded \$1.5-billion agreement to become the marketing and commercialization partner for Google’s independent biotech, Calico. And AbbVie made inroads in oncology, announcing positive Phase-II results for leukemia drug venetoclax, with one patient going into full remission. The results were so impressive, in fact, that they prompted always-skeptical Evercore ISI analyst Mark Schoenebaum to ask, in one of his famed e-blasts, “Is this a cure?” Another drug that should soften the imminent Humira blow is HCV triplet therapy Viekira Pak, expected to reach annual sales of \$2 to \$3 billion in 2015.

TOP 20 THERAPEUTIC CLASSES BY US SALES, 2014				
Rank	Company	2014 Total (Billions)	2013 Total (Billions)	
1	Oncology	\$32.6	\$27.9	
2	Antidiabetes	\$32.2	\$24.7	
3	Mental health	\$23.1	\$23.8	
4	Autoimmune	\$22.2	\$17.9	
5	Respiratory	\$22.0	\$20.4	
6	Pain	\$20.4	\$18.8	
7	HIV antivirals	\$14.3	\$12.5	
8	Multiple sclerosis	\$13.8	\$11.1	
9	Lipid regulators	\$13.7	\$13.6	
10	Viral hepatitis	\$12.3	\$1.9	
11	Antihypertensives	\$12.0	\$12.5	
12	ADHD	\$10.1	\$9.9	
13	Nervous system disorders	\$9.5	\$8.1	
14	Dermatologicals	\$9.5	\$8.9	
15	Anti-ulcerants	\$9.3	\$10.1	
16	Anticoagulants	\$8.5	\$7.4	
17	Antibacterials	\$8.0	\$8.6	
18	Vaccines (excluding flu)	\$6.8	\$6.1	
19	Other cardiovasculars	\$6.3	\$5.2	
20	Ophthalmology	\$6.3	\$5.6	
	Total others	\$81.0	\$75.5	
	Total market	\$373.9	\$330.5	

Source: IMS Health, National Sales Perspectives

13. GLAXOSMITHKLINE \$12.2B ▼4.5%

Global revenue:
\$31.5B (8th); down 0.3%

Top brands: Advair Diskus (\$4.8B); Flovent HFA (\$1.1B); Ventolin (\$811M)

Promotional spend:
\$825M (7th); 6.8% of rev.

R&D spend: \$4.6B (9th); down 13%; 14.6% of rev.

Planned launches: Sirukumab (RA); mepolizumab (resp.); HZ/su (zoster vaccine)

Patent expirations:
Avodart (2015)

Britain’s No. 2 drug manufacturer must have been glad to bid 2014 farewell. The company saw an 18% decline in sales of its prized respiratory drugs, mostly driven by aging superstar Advair’s 25% dive. Would-be lung drug blockbusters Breo and Anoro turned out to be anything but, bringing in only \$44 million and \$21 million respectively. On top of all that, a bribery scandal in China resulted in a fine of nearly half a billion dollars. Incoming chairman-designate Philip Hampton, whose last job was seeing the Royal Bank of Scotland through the financial crisis, is expected to make some changes. Two board members have already resigned and others will likely soon follow; word is that CEO Andrew Witty’s job is on the line as well. On the plus side, a \$20-billion-plus asset swap with Novartis made GSK a major player in consumer health products and the global leader in vaccines. Vaccines don’t receive a lot of media attention, but the market is growing 10% a year, Witty has noted.

TOP 20 PRESCRIPTION DRUGS BY US SALES, 2014				
Rank	Product	Company	2014 Total (Billions)	2013 Total (Billions)
1	Sovaldi	Gilead Sciences	\$7.9	\$0.1
2	Abilify	Otsuka	\$7.8	\$6.5
3	Humira	AbbVie	\$7.2	\$5.6
4	Nexium	AstraZeneca	\$5.9	\$6.2
5	Crestor	AstraZeneca	\$5.8	\$5.4
6	Enbrel	Amgen	\$5.5	\$4.7
7	Advair Diskus	GlaxoSmithKline	\$4.8	\$5.2
8	Remicade	Johnson & Johnson	\$4.5	\$4.1
9	Lantus SoloSTAR	Sanofi	\$4.5	\$3.1
10	Copaxone	Teva	\$3.9	\$3.7
11	Neulasta	Amgen	\$3.8	\$3.6
12	Rituxan	Genentech/Biogen	\$3.5	\$3.3
13	Januvia	Merck	\$3.5	\$2.9
14	Lantus	Sanofi	\$3.4	\$2.6
15	Spiriva Handihaler	Boehringer Ingelheim	\$3.3	\$3.0
16	Lyrica	Pfizer	\$3.1	\$2.5
17	Atripla	BMS/Gilead	\$3.0	\$2.9
18	Avastin	Genentech/Roche	\$2.9	\$2.7
19	Tecfidera	Biogen	\$2.6	\$0.9
20	Truvada	Gilead Sciences	\$2.5	\$2.3
	Total others	\$284.5	\$259.2	
	Total market	\$373.9	\$330.5	

Source: IMS Health, National Sales Perspectives

14. ELI LILLY \$11.8B ▼22.8%

Global revenue:
\$19.9B (12th); down 13.5%

Top brands: Humalog (\$1.7B); Humalog KwikPen (\$1.4B); Cialis (\$1.4B); Humulin (\$713M); Forteo (\$539M)

Promotional spend:
\$824M (8th); 7.0% of rev.

R&D spend: \$4.7B (8th); down 14.4%; 23.6% of rev.

Planned launches: ixekizumab (RA); Lantus biosimilar (diab.); Peglispro (diab.)

Patent expirations:
Cialis (2017); Effient (2017); Strattera (2017); Forteo (2018)

Eli Lilly had a rough 2014. But while the Indiana drugmaker lowered expectations for 2015, market sentiment is that it is poised for some potential long-term payoffs. This includes pitting its Lantus biosimilar against Sanofi’s branded diabetes biologic and carving out a distinct spot in the PCSK9 cardiovascular space with products that work differently from those offered by competitors Amgen and Sanofi. And Lilly is primed to take advantage of renewed interest in its experimental CTEP inhibitor evacetrapib, which one market watcher says may have an advantage over Merck’s anacetrapib. The company has maintained its focus on Alzheimer’s and continues to stand by its experimental treatment solanezumab. While questions about liver toxicity may eventually push aside diabetes drug Peglispro, analysts actually seem to be rooting for its disappearance. Lilly would then be free to focus its energy on its Lantus biosimilar.

ESTIMATED US PATENT EXPIRATIONS THROUGH 2019			
Brand	Company	Indication	Expiry
Abilify	BMS/Otsuka	Depression/bipolar	2015
Androgel	AbbVie	Low testosterone	2015
Avodart	GlaxoSmithKline	BPH	2015
Epogen	Amgen	Anemia	2015
Intuniv	Shire	ADHD	2015
Namenda	Actavis	Alzheimer’s disease	2015
Neulasta	Amgen	Neutropenia	2015
Symbicort	AstraZeneca	Asthma/COPD	2015
Zyvox	Pfizer	Infection	2015
Benicar	Daiichi Sankyo	Hypertension	2016
Crestor	AstraZeneca	Atherosclerosis	2016
Gleevec	Novartis	Leukemia	2016
Humira	AbbVie	RA/Crohn’s/psoriasis	2016
Prezista	Johnson & Johnson	HIV	2016
Zytiga	Johnson & Johnson	Cancer	2016
Alimta	Eli Lilly	Cancer	2017
Cialis	Eli Lilly	Erectile dysfunction	2017
Levemir	Novo Nordisk	Diabetes	2017
NovoLog	Novo Nordisk	Diabetes	2017
Seroquel	AstraZeneca	Schizophrenia	2017
Tamiflu	Roche	Influenza	2017
Tysabri	Biogen	MS	2017
Vytorin	Merck	Cholesterol	2017
Forteo	Eli Lilly	Osteoporosis	2018
Lyrica	Pfizer	Fibromyalgia	2018
Mirapex	Boehringer Ingelheim	Parkinson’s disease	2018
Nasonex	Merck	Allergies	2018
Remicade	Johnson & Johnson	Crohn’s/ulcerative colitis	2018
Spiriva	Boehringer Ingelheim	COPD	2018
Toujeo	Sanofi	Diabetes	2018
Xolair	Novartis/Roche	Asthma	2018
Cymbalta	Eli Lilly	Depression/fibromyalgia	2019
Gonal-F	EMD Serono	Infertility	2019

Source: Barclays Research, company reports and DrugPatentWatch

15. NOVO NORDISK \$10.4B ▲26.4%

Global revenue:
\$16.8B (16th); up 17.0%

Top brands: NovoLog FlexPen (\$1.9B); NovoLog (\$1.6B); Victoza 3-Pak (\$1.4B); Levemir FlexPen (\$1.3B)

Promotional spend:
\$564M (13th); 5.4% of rev.

R&D spend: \$2.0B (15th); down 9.1%; 11.9% of rev.

Planned launches: Tresiba (diab.); IDegLira (diab.); Saxenda (obesity); semaglutide (diab.)

Patent expirations: Norditropin (2015); Levemir (2017); NovoLog (2017)

Novo has again changed its schedule for resubmitting Tresiba to the FDA, now saying it could happen as early as this spring. If approved, the long-acting insulin, currently undergoing additional study for possible cardiovascular side effects, would compete against Sanofi’s Toujeo, approved in February. Novo plans to put more R&D muscle behind its diabetes franchise in the coming months, having exited the inflammation market last year when its anti-IL-20 rheumatoid arthritis drug failed a Phase-II trial. It also has high hopes for new weight-loss drug Saxenda.

NEW DRUG APPROVALS, 2014 *			
Brand	Company	Indication	Approval month
Farxiga	AstraZeneca	Type 2 diabetes	January
Hetlioz	Vanda	Non-24-hour sleep/wake disorder	January
Vimizim	BioMarin	Mucopolysaccharidosis type IVA	February
Northera	Lundbeck	Neurogenic orthostatic hypotension	February
Myalept	Amylin	Congenital/acquired lipodystrophy	February
Neuraceq	Piramal Imaging	Neuritic amyloid- plaques	March
Impavido	Knight	Leishmaniasis	March
Otezla	Celgene	Psoriatic arthritis, plaque psoriasis	March
Tanzeum	GlaxoSmithKline	Type 2 diabetes	April
Cyramza	Eli Lilly	Gastric cancer	April
Sylvant	Janssen Biotech	Multicentric Castleman’s disease	April
Zykadia	Novartis	ALK-positive metastatic NSCLC	April
Zontivity	Merck	Thrombotic cardiovascular events	May
Entyvio	Takeda	Ulcerative colitis, Crohn’s disease	May
Dalvance	Durata	ABSSSI	May
Jublia	Dow	Onychomycosis of the toenails	June
Sivextro	Cubist	ABSSSI	June
Beleodaq	Spectrum	Peripheral T-cell lymphoma	July
Kerydin	Anacor	Onychomycosis of the toenails	July
Zydelig	Gilead Sciences	CLL, B-cell non-Hodgkin lymphoma	July
Striverdi Respirmat	Boehringer Ingelheim	COPD	July
Jardiance	Boehringer Ingelheim	Type 2 diabetes	August
Orbactiv	The Medicines Co.	ABSSSI	August
Belsomra	Merck	Insomnia	August
Plegridy	Biogen	Multiple sclerosis	August
Cerdelga	Genzyme	Gaucher’s disease	August
Keytruda	Merck	Metastatic melanoma	September
Movantik	AstraZeneca	Opioid-induced constipation	September
Trulicity	Eli Lilly	Type 2 diabetes	September
Lumason	Bracco	Cardiovascular imaging	October
Akynzeo	Helsinn	Chemotherapy-related nausea	October
Harvoni	Gilead Sciences	Genotype 1 HCV	October
Esbriet	InterMune	IPF	October
Ofev	Boehringer Ingelheim	IPF	October
Blincyto	Amgen	B-ALL	December
Xtoro	Alcon	Swimmer’s ear	December
Lynparza	AstraZeneca	BRCA-mutated ovarian cancer	December
Viekera Pak	AbbVie	Chronic HCV genotype 1 infection	December
Zerbaxa	Cubist	Intra-abdominal and UTIs	December
Rapivab	BioCryst	Influenza infection	December
Opdivo	Bristol-Myers Squibb	Melanoma	December

*NMEs and new biologics approved by FDA’s Center for Drug Evaluation and Research

16. MYLAN \$8.7B ▲10.3%

Global revenue: \$12.0B (20th); up 7.0%	R&D spend: \$582M (19th); up 14.6%; 4.9% of rev.
Top brands: EpiPen 2-Pak; Fentanyl (US sales revenue N/A)	Planned launches: Lidoderm generic (CNS); Copaxone generic (MS)
Promotional spend: \$111.4M (31st); 1.3% of rev.	Patent expirations: N/A

Mylan could serve as a case study for the M&A frenzy currently sweeping the industry. For mid-size companies, it's either buy or be bought. In April, just months after paying \$5.3 billion for a share of Abbott Laboratories' overseas generic business, Mylan made an offer for Ireland-based Perrigo. Rumors have circulated that the tender, which at press time was still pending, was either a defense against an imminent takeover bid from rival Teva or a way to drive up Mylan's price if that takeover bid ever occurs. In any case, the Abbott deal allowed Mylan to shift its tax headquarters from Pittsburgh to the Netherlands, for a projected savings of 20%.

17. BOEHRINGER INGELHEIM \$8.3B ▲UP 6.9%

Global revenue: \$17.7B (15th); up 4.5%	R&D spend: * \$3.8B (11th); up 15.8%; 21.5% of rev.
Top brands: Spiriva HandiHaler (\$3.3B); Combivent Respimat (\$892M); Tradjenta (\$571M)	Planned launches: Synjardy (diab.); nintedanib (onc.)
Promotional spend: \$859M (6th); 10.3% of rev.	Patent expirations: Aggrenox (2017); Mirapex (2018); Spiriva (2018)

It was a rough year for Boehringer. After the company lost patent protection on its blockbuster hypertension drug Micardis, overall drug sales slumped in the first half of 2014, prompting the family-owned firm to implement company-wide cost cutting and layoffs. Additionally, Spiriva lost its patent in India. Still, bright spots remain—like Synjardy, a combination diabetes drug it is developing with Lilly. Synjardy combines empagliflozin, an SGLT-2 inhibitor, with metformin, a time-tested generic often used in combination with insulin. The drug gained a recommendation from European regulators in March and is expected to earn FDA approval later this year. * Global R&D spend is based on the year ending December 31, 2013, the latest data available at press time.

18. OTSUKA \$8.2B ▲21.0%

Global revenue: \$12.3B (19th); up 14.1%	R&D spend: \$2.4B (14th); up 20.0%; 19.5% of rev.
Top brands: Abilify (\$7.8B)	Planned launches: TAS-102 (onc.); OPC-34712 (CNS); Sativex (CNS); OPC-67683 (I.D.)
Promotional spend: \$361M (18th); 4.4% of rev.	Patent expirations: Abilify (2015); Samsca (2015)

Otsuka faces the industry's steepest patent cliff this year when it loses exclusivity to Abilify. Second only to Gilead's Sovaldi in earnings, the antidepressant generated \$7.8 billion in 2014, accounting for more than

half of Otsuka's revenue. Softening the blow a little, Abilify received orphan-drug approval for treating pediatric Tourette syndrome in December. However, when the FDA expanded that indication to include adult Tourette's patients, Otsuka cried foul, arguing it would invalidate the seven-year exclusivity for pediatric use. The matter is pending in federal court. In other news, the FDA granted fast-track designation to the company's oral cancer therapy, TAS-100, which launched in Japan last year.

19. BIOGEN \$6.1B ▲UP 59%

Global revenue: \$9.7B (22nd); up 40.0%	R&D spend: \$1.9B (16th); up 31%; 19.6% of rev.
Top brands: Tecfidera (\$2.6B); Avonex (\$1.9B); Tysabri (\$1.4B); Alprolix (\$72M); Elocate (\$58M)	Planned launches: ocrelizumab (CNS.); zimbryta (CNS)
Promotional spend: \$41.6M (52nd); 0.7% of rev.	Patent expirations: Tysabri (2017); Tecfidera (2020); Elocate (2024); Plegridy (2025)

Biogen enters the second half of 2015 with a shorter name—it dropped Idex in March—and with high hopes for its Phase-III Alzheimer's compound aducanumab, which a small study showed can slow cognitive impairment in mild-case patients. This success is part of a bigger goal, which CEO George Scangos says is to push beyond Alzheimer's and into other neurodegenerative diseases. MS will remain a Biogen mainstay; the firm found that even with the FDA's new notice that Tecfidera is associated with the PML brain infection, patients have not stopped taking it. New-to-treatment patients, however, seem to be gravitating toward the company's newer MS drug Plegridy.

20. SHIRE \$5B ▲UP 18.6%

Global revenue: \$6B (24th); up 22%	39.3%; 9.4% of rev.
Top brands: Vyvanse (\$2.1B)	Planned launches: SHP555 (constipation); Lofitegrast (dry eyes); SHP 465 (ADHD)
Promotional spend: \$139.7M (29th); 2.8% of rev.	Patent expirations: Intuniv (2015); Firazyr (2015); Carbatrol (2016); Fosrenol (2018)
R&D spend: \$566M (20th); down	

After Shire fended off an AbbVie takeover, analysts said it would ultimately strengthen the company—and, perhaps, free the drugmaker to make acquisitions of its own. Those predictions proved accurate: In January Shire bolstered its presence in rare diseases by acquiring NPS Pharmaceuticals for \$5.2 billion. As part of the deal, it gained access to Natpara, a treatment associated with hypoparathyroidism. Jefferies analyst David Steinberg noted that he expects the drug to bring in \$35 million in second-quarter sales and \$243 million in the third quarter. Shire was also able to hold off five drugmakers looking to market generic versions of its most lucrative product, Vyvanse. A US District Court Judge in New Jersey blocked Mylan, Actavis, Amneal, Roxane and Sandoz from filing abbreviated new drug applications for the blockbuster ADHD medication, eliminating generic competition until 2023. Vyvanse also scored a label expansion into severe binge-eating disorder in February.