

GET BACK IN SHAPE

When big pharma looks in the mirror, what does it see? A body beset by old, expiring brands and not enough energetic, youthful ones to replace them. **Marc Iskowitz** has industry's regimen for regaining form

Once bloated and winded, the drug industry has made strides at shaping up its US operations, shedding excess pounds and taking steps to shore up long-term health. That's a start. Getting back into real shape will take a package of exercises that build muscle in more ways than one, analysts say.

Industry had a positive 2011, with spending on branded products in the US up by 2.2% in actual dollars to \$258 billion from \$252 billion, according to IMS Health. It bettered 2010, when spending on protected medicines shrunk 0.7% to \$229 billion, and it helped boost overall drug outlay by 3.7% to \$320 billion for the year.

New product launches, many of them for innovative medicines and indications to treat rare diseases, helped fuel the increase. But patent losses continue to bite. The glut of expiries is set to reduce global brand revenues by \$120 billion through 2015.

Those losses will be felt the most this year and next, predicts Michael Kleinrock, director of research development for the IMS Institute. "Brand growth will be historically low," in the 0-1% range.

Perhaps the most important trend to watch in terms of the industry's comeback lies in new drug pipelines. These may be slowly improving, yet no company has more upcoming launches than expiries, Sanford Bernstein analyst Tim Anderson tells *MM&M*: "GlaxoSmithKline starts to get into positive territory because their patent expiries lapse. Pfizer—any drug that they launch, or that launched, [when] netted against expiry is a flat line." Even Bristol-Myers Squibb—widely hailed as the most productive biopharma company—winds up being a flat-liner.

In the following profiles of the top 20 companies as ranked by 2011

US sales, you can judge the performance for yourself. In addition to revenues, US and global; top brands and their US sales (courtesy of IMS); and promotional spend (as per Cegedim Strategic Data; ranking encompasses US sales top 20 vs. ranking on pp. 44-45 based purely on promo spend), we include a list of each firm's planned launches—late-stage compounds that analysts believe stand a strong chance of making it to the US market—and upcoming patent expirations.

Pfizer's oral RA drug tofacitinib and Eliquis (apixaban), the blood-thinning drug Pfizer is co-developing with BMS, are the high-profile agents coming due in 2012. There will also be pivotal data sets this year, the most dramatic being in Alzheimer's disease, although the category lacks a launchable drug in 2012.

"If these Alzheimer's drugs work [Lilly's solanezumab and J&J/Pfizer's bapineuzumab]," says Anderson, "they would put the industry back on the map, but scientists put the odds at less than 50%. These drugs could help resurrect the image of the industry."

Putting money into R&D

Among other steps companies are taking to get back into shape, most plowed more money into R&D last year, despite the fact that it's hard to scale innovation. Our company profiles rank firms on their actual R&D spend, indicating the change vs. 2010, and calculate spend as a percentage of revenue.

Pfizer, for one, did not follow the pack in this department. "Pfizer could theoretically spend less and get the same output, which is why they are ratcheting down their R&D spend," says Anderson.

Profiles also show what's emerging from pipelines, as does the

approvals table on page 50. Drilling down into last year's newbies, Healogix CEO Harris Kaplan notes that only 23% of 2011 approvals were for drugs with new mechanisms of action vs. almost 60% in 2002. And orphan drug approvals—which were up last year—aren't a replacement for better chronic therapy treatment.

“While orphan drugs with their associated high prices are helping to fill the gap caused by generic expirations,” says Kaplan, “they do not substitute for an ongoing patient and industry need for new advances in large, chronic disease categories where there is still significant unmet need such as hypertension, depression, GI disorders, etc.”

Industry can pat itself on the back for a productive 2011 both in terms of drugs approved (30, vs. 23 in 2010) and the therapeutic advances they represent, but one year is not a trend, cautions Wayne Pines, a former FDA associate commissioner who is now president, regulatory services and healthcare for APCO Worldwide.

“I don't think the approval numbers indicate anything significant about FDA,” says Pines. “The agency can approve new drugs only when the data meet its standard for safety and effectiveness.”

Pines and Kaplan say they're more concerned that these innovative drugs get reimbursed. Kaplan says payers are beginning to push back on reimbursing drugs costing patients well into six figures per year.

Another strategy companies continue to employ to fill revenue gaps is M&A, like Sanofi's acquisition of consumer health firm Chattam last year. The easiest way to replace lost sales, these are likely to continue, says Anderson.

Of course, many firms continue to trim their bottom line through wave after wave of job cuts and corporate reorganizations. “In terms of cost-cutting, these companies have a long way to go before they've cut to the bone,” says Anderson. He expects more of the same operationally in all buckets—including sales force and R&D.

“Orphan drugs... do not substitute for an ongoing patient and industry need for advances in large disease categories.”

— Harris Kaplan, Healogix

But the most significant predictors of financial health include more than just a company's willingness to diet. A big one is the firm's degree of diversification into areas like consumer and animal health—businesses that are not subject to the pushes and pulls of the pharma business. “If you broadened it out,” says Anderson, “Abbott and J&J are most diversified and have had the best stock performance.”

Another leading indicator is the durability of companies' product lines, i.e., how high is the line's barrier to entry. “Animal health and vaccines—they are oligopolies,” says Anderson, in that competition is less and they don't have generics issues.

Exposure to emerging markets is a third important variable, as everyone agrees that their future growth is likely to outpace US and Europe. European companies like Sanofi, GSK and Novartis have the most exposure, while for domestics like BMS and Eli Lilly, it's 10% or less.







Again, don't look for this to be industry's magic pill. “Those that are reaching out to new geographies are making 50 cents on the dollar,” says Anderson, “but that is better than making no cents on the dollar. It is almost like the industry is pulling out the couch cushions to look for spare change.”

THE TOP 20

| | |
|----------------------|----|
| Abbott | 46 |
| Amgen | 45 |
| AstraZeneca | 40 |
| Boehringer Ingelheim | 46 |
| Bristol-Myers Squibb | 46 |
| Eli Lilly | 44 |
| Forest Laboratories | 50 |
| Gilead Sciences | 48 |
| GlaxoSmithKline | 45 |
| Johnson & Johnson | 46 |
| Merck | 42 |
| Mylan | 48 |
| Novartis | 42 |
| Novo Nordisk | 50 |
| Otsuka America | 50 |
| Pfizer | 40 |
| Roche | 44 |
| Sanofi | 46 |
| Takeda | 48 |
| Teva | 42 |









1 Pfizer \$25.1B ▼7.7%

| | | | |
|---|---|---|---|
|  | Global revenue: \$67.4B (1st); up 0.4% |  | R&D spend: \$8.4B (3rd) down 9.7%; 12.5% of rev. |
|  | Top brands: Lipitor (\$7.7B), Lyrica (\$1.8B), Celebrex (\$1.8B), Geodon (\$1.4B), Viagra (\$1.0B) |  | Planned launches: Eliquis (SPAF), tofacitinib (RA) |
|  | Promotional spend: \$2.2B (1st); 8.6% of rev. |  | Patent expirations: Lipitor (2011), Celebrex (2014), Zyxon (2015) |

Pfizer has pretty much made it past a chasm of a patent cliff with relatively minor adjustments, and now boasts one of the best late-stage pipelines. It recently won approval for cancer drugs Xalkori (crizotinib) and Inlyta (axitinib) along with a label expansion for vaccine Prevnar 13. Waiting in the wings are rheumatoid arthritis drug tofacitinib and anticoagulant Eliquis (apixaban)—a JV with BMS for stroke prevention that analysts have high hopes for, despite an FDA delay. The biggest of pharmas acquired Wyeth in 2009 and King in 2010, and last year lost exclusivity for \$10-billion mega-blockbuster Lipitor—along with two-thirds of the statin's market share, despite an aggressive defense. CEO Ian Read floated plans for a big shakeup, but ended up placing only Pfizer's animal health and nutrition units on the block. Pipeline wins haven't quieted calls for more aggressive action—most recently Goldman analyst Jami Rubin's call for a full-scale Abbott-style spin-off.

2 AstraZeneca \$19.9B ▲2.1%

| | | | |
|---|--|---|---|
|  | Global revenue: \$33.6B (9th); up 0.9% |  | R&D spend: \$5.0B (8th) up 19%; 14.9% of rev. |
|  | Top brands: Seroquel IR (\$3.3B); Crestor (\$3.1B); Nexium (\$2.4B); Symbicort (\$846M) |  | Planned launches: Fostamatinib (arth.): NKTR-118 (constipation) |
|  | Promotional spend: \$1.3B (4th); 6.9% of rev. |  | Patent expirations: Seroquel IR (2012); Nexium (2014); Symbicort (2015); Crestor (2016) |

AstraZeneca faces one of the steepest revenue declines of the pharma majors. Combined with a pipeline analysts consider anemic at best, analysts talk about an acquisition as being a necessary lifeboat for the firm. Most recently, AZ abandoned its depression medication known as TC-5214 after the compound missed its Phase III primary endpoint. A back-and-forth patent drama over anti-psychotic Seroquel, whose IR form goes off patent later this year, yielded a bit of good news: a US judge asserted that the extended-release version would remain covered until 2017 (although the UK High Court declared that Seroquel XR no longer had protection). The company's present outlook is one of hunkering down: besides multiple waves of job cuts, the firm shuttered at least one R&D location. Its fourth-quarter 2011 earnings call was an unvarnished one: CEO David Brennan acknowledged the pipeline is underperforming, while CFO Simon Lowth said significant revenue declines are in store.

Fig 1: Top 20 Pharmaceutical Companies by US Sales '11

| Rank | Company | 2011 Total (Billions) | 2010 Total (Billions) |
|--------------|----------------------|-----------------------|-----------------------|
| 1 | Pfizer | \$25.1 | \$27.2 |
| 2 | AstraZeneca | \$19.9 | \$19.5 |
| 3 | Merck & Co. | \$19.3 | \$18.6 |
| 4 | Novartis | \$19.2 | \$18.0 |
| 5 | Teva | \$15.1 | \$15.9 |
| 6 | Eli Lilly & Co. | \$14.9 | \$14.3 |
| 7 | Roche | \$14.5 | \$13.8 |
| 8 | GlaxoSmithKline | \$14.2 | \$15.2 |
| 9 | Amgen | \$13.1 | \$12.7 |
| 10 | Johnson & Johnson | \$12.1 | \$12.9 |
| 11 | Sanofi | \$11.8 | \$12.2 |
| 12 | Abbott | \$11.5 | \$10.9 |
| 13 | Bristol-Myers Squibb | \$10.9 | \$9.8 |
| 14 | Boehringer Ingelheim | \$7.0 | \$6.4 |
| 15 | Takeda | \$6.6 | \$6.7 |
| 16 | Mylan | \$5.6 | \$4.8 |
| 17 | Gilead Sciences | \$5.5 | \$4.7 |
| 18 | Novo Nordisk | \$5.3 | \$4.5 |
| 19 | Otsuka | \$5.2 | \$4.6 |
| 20 | Forest Laboratories | \$5.2 | \$4.7 |
| Total others | | \$77.9 | \$70.0 |
| Total market | | \$319.9 | \$307.4 |







Source: IMS Health, National Sales Perspectives

Fig 2: Top 20 Prescription Drugs by US Sales '11

| Rank | Product | Company | 2011 Total (Billions) | 2010 Total (Billions) |
|--------------|---------------|----------------------|-----------------------|-----------------------|
| 1 | Lipitor | Pfizer | \$7.7 | \$7.3 |
| 2 | Plavix | BMS/Sanofi | \$6.8 | \$6.1 |
| 3 | Nexium | AstraZeneca | \$6.2 | \$6.3 |
| 4 | Abilify | Bristol-Myers Squibb | \$5.2 | \$4.6 |
| 5 | Advair Diskus | GlaxoSmithKline | \$4.6 | \$4.7 |
| 6 | Seroquel | AstraZeneca | \$4.6 | \$4.4 |
| 7 | Singulair | Merck & Co. | \$4.6 | \$4.1 |
| 8 | Crestor | AstraZeneca | \$4.4 | \$3.8 |
| 9 | Cymbalta | Eli Lilly & Co. | \$3.7 | \$3.2 |
| 10 | Humira | Abbott | \$3.5 | \$2.9 |
| 11 | Enbrel | Pfizer/Amgen | \$3.5 | \$3.3 |
| 12 | Remicade | Merck & Co. | \$3.5 | \$3.3 |
| 13 | Actos | Takeda | \$3.4 | \$3.5 |
| 14 | Neulasta | Amgen | \$3.3 | \$3.0 |
| 15 | Rituxan | Roche | \$3.0 | \$2.8 |
| 16 | Zyprexa | Eli Lilly & Co. | \$3.0 | \$3.0 |
| 17 | Copaxone | Teva | \$3.0 | \$2.3 |
| 18 | Lexapro | Forest Laboratories | \$2.9 | \$2.8 |
| 19 | Oxycontin | Purdue | \$2.9 | \$3.1 |
| 20 | Epogen | Amgen | \$2.8 | \$3.3 |
| Total others | | | \$237.3 | \$229.6 |
| Total market | | | \$319.9 | \$307.4 |







Source: IMS Health, National Sales Perspectives

3 Merck \$19.3B ▲3.8%

| | |
|---|--|
|  Global revenue: \$48.0B (4th); up 4.3% |  R&D spend: \$7.7B (4th) down 4.9%; 16% of rev. |
|  Top brands: Singulair (\$4.5B); Januvia (\$2.1B); Zetia (\$1.3B); Vytorin (\$1.1B) |  Planned launches: Vorapaxar (TRA); Tredaptive & MK-0524B (athero.); odanacatib (osteo.) |
|  Promotional spend: \$1.3B (3rd); 7.0% of rev. |  Patent expirations: Singulair (2012); Avelox (2014); Nasonex (2014) |







Merck performed well domestically and globally, thanks in large part to the Januvia diabetes franchise, which now accounts for 76% of the global DPP-IV market. This franchise will keep growing from almost \$5.9B (globally) to \$9.4B by 2016, Bernstein's Tim Anderson predicts, helping offset top seller Singulair's loss of exclusivity this year and plugging shortfalls in other franchises, like Isentress, which is at risk due to HIV/AIDS competition from Gilead and GSK/Shionogi; Remicade, whose revenues are declining after some control was ceded to partner J&J in 2010; and cholesterol meds Vytorin and Zetia, down about 45% in US sales since the 2008 Enhance study, and which face a renewed threat from generic Lipitor. Whether the ezetimibe franchise gets vindicated by the IMPROVE-IT trial won't impact P&L too much. What matters more is whether late-stage pipeline drugs suvorexant (sleep), odanacatib (osteo.), vorapaxar (TRA) and Tredaptive stay on track.

4 Novartis \$19.2B ▲6.7%

| | |
|---|---|
|  Global revenue: \$58.5B (3rd); up 15.6% |  R&D spend: \$9.2B (1st) up 13.6%; 15.7% of rev. |
|  Top brands: Diovan/Co-Diovan (\$2.3B); Gleevec (\$1.5B); Zometa (\$642M); Sandostatin (\$574M) |  Planned launches: Bexsero (men. B vacc.); Seebri Breezhaler (NVA237)/QVA149 (COPD) |
|  Promotional spend: \$973M (6th); 5.1% of rev. |  Patent expirations: Diovan (2012); Zometa (2013); Gleevec (2015) |

Novartis is bracing for some ugly patent exclusivity losses, with blockbuster Femara having gone off patent and \$2.3-billion Diovan, the company's top seller, facing generic competition in September. Next year, \$642-million Zometa goes over the patent cliff, and in 2015, \$1.5-billion Gleevec loses exclusivity. But the Swiss giant has cobbled together an Alpine portfolio from steadily-performing smaller brands while diversifying its business into generics (Sandoz), vaccines and diagnostics and, most recently, vision care with its acquisition of Alcon in 2010. The company boasts a muscular R&D operation, as evidenced by MS drug Gilenya, a likely blockbuster approved in 2010, and Arcapta Neohaler for COPD, approved in July, along with a robust late-stage pipeline. However, Novartis has been plagued by manufacturing issues at plants in Quebec and Nebraska. Other potential pitfalls include safety concerns about Gilenya that could hamper that key product's potential, and FDA delays on approvals of the Menveo vaccine and Seebri Breezhaler (NVA237).

5 Teva \$15.1B ▼5%

| | |
|---|--|
|  Global revenue: \$18.3B (12th); up 13.7% |  R&D spend: \$1.1B (18th) up 18.3%; 6% of rev. |
|  Top brands: Copaxone (\$3.0B); Provigil (\$1.1B), ProAir HFA (\$953M), budesonide (\$856M) |  Planned launches: Custirsen (onc.); neugranin (onc.); Revascor (CV) |
|  Promotional spend: \$257M (16th); 1.7% of rev. |  Patent expirations: Copaxone (2014), Treanda (2015) |

This multi-billion dollar company is proof that generics can be big business. Although Teva saw its North America earnings power shrink to 48% of its sales in 2011 from 62% in 2010, the Israeli company balanced things out, increasing sales to 31% in Europe, up from 24% in 2010, and hauled in 21% of its take from international sales, compared with 14% the year before. Although the company remains solidly in the unbranded drug space, its \$6.8-billion purchase last year of Cephalon and its CNS portfolio means more exposure to the brand side of the patent-protection wars, as CNS drugs Provigil, Copaxone and Treanda burn through their exclusivity periods. Teva dealt Par the right to sell an authorized generic of Provigil, meaning Teva earns from both ends of the patent spectrum. The company says it has 177 product registrations awaiting FDA approval—120 of these are patent challenges for first-to-market generic rights.

Fig 3: Top 20 Therapeutic Classes by US Sales '11

| Rank | Categories | 2011 Total (Billions) | 2010 Total (Billions) |
|---------------------|---------------------------------|-----------------------|-----------------------|
| 1 | Oncologics | \$23.2 | \$22.3 |
| 2 | Respiratory Agents | \$21.0 | \$19.3 |
| 3 | Lipid Regulators | \$20.1 | \$18.8 |
| 4 | Antidiabetes | \$19.6 | \$17.7 |
| 5 | Antipsychotics | \$18.2 | \$16.2 |
| 6 | Autoimmune Diseases | \$12.0 | \$10.6 |
| 7 | Antidepressants | \$11.0 | \$11.6 |
| 8 | HIV Antivirals | \$10.3 | \$9.3 |
| 9 | Anti-Ulcerants | \$10.1 | \$11.9 |
| 10 | Narcotic Analgesics | \$8.3 | \$8.4 |
| 11 | ADHD | \$7.9 | \$6.7 |
| 12 | Platelet Aggregation Inhibitors | \$7.8 | \$7.1 |
| 13 | Angiotensin II | \$7.6 | \$8.7 |
| 14 | Multiple Sclerosis | \$7.1 | \$5.8 |
| 15 | Vaccines (Pure, Comb, Other) | \$6.3 | \$5.7 |
| 16 | Anti-Epileptics | \$5.9 | \$5.6 |
| 17 | Hormonal Contraceptives | \$5.2 | \$4.8 |
| 18 | Erythropoietins | \$5.1 | \$6.1 |
| 19 | Immunostimulating Agents | \$4.5 | \$4.2 |
| 20 | Antivirals, excl. Anti-HIV | \$3.7 | \$3.2 |
| Total others | | \$105.0 | \$103.4 |
| Total market | | \$319.9 | \$307.4 |

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 | |
|------|----------------------|---------------------|---------------------|--------------------|---------------------|--------------------|---------------------|
| | | 2011 (Millions)* | % change vs 2010 | 2011 (Millions) | % change vs 2010 | 2011 (Millions) | % change vs 2010 |
| 1 | Pfizer | \$2,153.00 | -10.7% | \$781.00 | -11.3% | \$20.00 | -4.8% |
| 2 | Eli Lilly | \$1,374.00 | -5.4% | \$460.00 | 9.3% | \$7.00 | 75.0% |
| 3 | Merck & Co. | \$1,348.00 | -7.7% | \$203.00 | -17.5% | \$15.00 | 7.1% |
| 4 | AstraZeneca | \$1,326.00 | 5.6% | \$323.00 | -12.9% | \$13.00 | 160.0% |
| 5 | GlaxoSmithKline | \$1,035.00 | -24.1% | \$200.00 | -36.9% | \$7.00 | 16.7% |
| 6 | Novartis | \$973.00 | -17.5% | \$92.00 | 41.5% | \$11.00 | 22.2% |
| 7 | Bristol-Myers Squibb | \$906.00 | -18.1% | \$253.00 | -34.1% | \$4.00 | 0.0% |
| 8 | Boehringer Ingelheim | \$906.00 | 41.3% | \$175.00 | 124.4% | \$5.00 | 150.0% |
| 9 | Forest Laboratories | \$866.00 | 1.4% | \$0.00 | N/A | \$8.00 | 166.7% |
| 10 | Abbott | \$699.00 | -11.2% | \$157.00 | 45.4% | \$4.00 | 33.3% |
| 11 | Takeda | \$668.00 | 6.0% | \$96.00 | 52.4% | \$6.00 | 200.0% |
| 12 | Sanofi | \$477.00 | -26.0% | \$32.00 | -25.6% | \$7.00 | 16.7% |
| 13 | Daiichi Sankyo | \$469.00 | -6.8% | \$0.00 | N/A | \$2.00 | 100.0% |
| 14 | Johnson & Johnson | \$438.00 | 9.8% | \$16.00 | -36.0% | \$7.00 | 133.3% |
| 15 | Bayer Healthcare | \$434.00 | 17.0% | \$175.00 | 116.0% | \$5.00 | 150.0% |
| 16 | Novo Nordisk | \$433.00 | 29.6% | \$71.00 | 373.3% | \$4.00 | 33.3% |
| 17 | Sunovion | \$353.00 | 8.0% | \$65.00 | -22.6% | \$2.00 | 100.0% |
| 18 | Amgen | \$346.00 | 46.0% | \$128.00 | 91.0% | \$4.00 | 100.0% |
| 19 | Warner Chilcott Labs | \$315.00 | 14.4% | \$21.00 | -4.5% | \$1.00 | 0.0% |
| 20 | Allergan | \$305.00 | -13.0% | \$145.00 | -12.7% | \$2.00 | 100.0% |

* Total promotional spend figure does not include amount spent on samples, clinical trials, direct mail (physical) or web advertising.

Source: CSD—Cegedim Strategic Data

6 Eli Lilly

\$14.9B ▲4.2%



Global revenue:
\$24.3B (10th); **up 5.2%**



Top brands: Cymbalta (\$3.2B), Zyprexa (\$2.2B), Humalog (\$1.4B), Alimta (\$995M), Evista (\$707M)



Promotional spend:
\$1.4B (2nd); 9.2% of rev.



R&D spend: \$5.0B (9th)
up 2.0%; 20.6% of rev.



Planned launches:
BI 10773 (diab.), dulaglutide (diab.)



Patent expirations:
Humalog (2013), Cymbalta (2014), Evista (2014)

Eli Lilly spends the most of the top 20 drugmakers, as a percentage of revenue, on R&D. Unfortunately, R&D output is not necessarily correlated with what you spend, showed a study funded by the Midwest company which was cited by the Sanford Bernstein analyst Tim Anderson. Anderson predicts a bolt-on acquisition. But Lilly's pipeline is slowly improving. After its GLP-1 partnership with Amylin dissolved late last year, dulaglutide moved to the forefront as its lead GLP-1 candidate, and Lilly is aiming for a 2013 filing. Somewhat of a longshot is Alzheimer's candidate solanezumab, which passed an interim safety analysis in January. Recent launch Tradjenta was the third DPP-IV to market and has diabetes giant Januvia to contend with. Patent expirations loom on two megablockbusters—CNS drug Cymbalta and diabetes med Humalog.

7 Roche

\$14.5B ▲5.1%



Global revenue:
\$46.4B (5th); **down 10.4%**



Top brands*: Xeloda (\$648M), Boniva (\$582M), Pegasys (\$519M), Valcyte (\$325M), Cellcept (\$269M)



Promotional spend:
\$182M (17th); 1.3% of rev.



R&D spend: \$9.1B (2nd)
down 5.2%; 19.6% of rev.



Planned launches:
Pertuzumab (onc.), TDM-1 (onc.)



Patent expirations:
Xeloda (2013)

Roche continues to boast a muscular pipeline and a high-performing portfolio of high-science (and high margin) drugs, biologics and diagnostics with negligible exposure to patent expirations (apart from Xeloda, a \$648 million drug that loses exclusivity next year). The company recently won approval for Erivedge (vismodegib), for basal cell carcinoma, and just filed pertuzumab for breast cancer. Several other products for various cancers, asthma and atherosclerosis (like CETP inhibitor dalcetrapib) are in late-stage development. The Swiss firm solidified its standing in biologics with its acquisitions of Genentech (2009) and a majority stake in Chugai Pharma (2002), and is now pursuing a hostile takeover of San Diego gene sequencing specialist Illumina.

*Does not include Genentech brands

| Detailing | | Meetings | | Journal | | Company | Rank |
|--------------------|----------------------|--------------------|------------------------|--------------------|----------------------|----------------------|------|
| 2011 (Millions) | % change vs. 2010 | 2010 (Millions) | % change (vs. 2010) | 2010 (Millions) | % change vs. 2010 | | |
| \$1,260.00 | -10.0% | \$83.00 | -4.6% | \$9.00 | -59.1% | Pfizer | 1 |
| \$834.00 | -9.1% | \$58.00 | -40.8% | \$15.00 | 15.4% | Eli Lilly | 2 |
| \$1,038.00 | -3.6% | \$89.00 | -25.2% | \$3.00 | -25.0% | Merck & Co. | 3 |
| \$920.00 | 12.7% | \$69.00 | 9.5% | \$1.00 | 0.0% | AstraZeneca | 4 |
| \$763.00 | -21.1% | \$63.00 | -11.3% | \$2.00 | -33.3% | GlaxoSmithKline | 5 |
| \$799.00 | -20.5% | \$66.00 | -29.8% | \$5.00 | -16.7% | Novartis | 6 |
| \$591.00 | -8.9% | \$52.00 | -18.8% | \$6.00 | 20.0% | Bristol-Myers Squibb | 7 |
| \$657.00 | 24.4% | \$63.00 | 103.2% | \$6.00 | 200.0% | Boehringer Ingelheim | 8 |
| \$775.00 | 2.0% | \$60.00 | -11.8% | \$23.00 | 0.0% | Forest Laboratories | 9 |
| \$486.00 | -21.7% | \$48.00 | -9.4% | \$4.00 | 100.0% | Abbott | 10 |
| \$525.00 | -0.9% | \$37.00 | 15.6% | \$4.00 | 33.3% | Takeda | 11 |
| \$390.00 | -25.3% | \$42.00 | -31.1% | \$6.00 | -53.8% | Sanofi | 12 |
| \$447.00 | -5.5% | \$19.00 | -32.1% | \$1.00 | 0.0% | Daiichi Sankyo | 13 |
| \$345.00 | 1.5% | \$67.00 | 131.0% | \$3.00 | 50.0% | Johnson & Johnson | 14 |
| \$234.00 | -13.3% | \$17.00 | 13.3% | \$3.00 | 0.0% | Bayer Healthcare | 15 |
| \$312.00 | 15.1% | \$42.00 | 10.5% | \$4.00 | -42.9% | Novo Nordisk | 16 |
| \$258.00 | 14.7% | \$25.00 | 47.1% | \$3.00 | N/A | Sunovion | 17 |
| \$171.00 | 33.6% | \$40.00 | 11.1% | \$3.00 | -25.0% | Amgen | 18 |
| \$262.00 | 12.0% | \$32.00 | -20.0% | \$1.00 | N/A | Warner Chilcott Labs | 19 |
| \$140.00 | -14.6% | \$16.00 | -20.0% | \$2.00 | 0.0% | Allergan | 20 |

8 GlaxoSmithKline \$14.2B ▼6.6%



Global revenue:
\$43.4B (7th); **down 3.6%**



Top brands: Advair (\$4.6B), Lovaza (\$899M), Flovent (\$709M), Avodart (\$525M), Vesicare (\$199M)



Promotional spend:
\$1.0B (5th); 7.3% of rev.



R&D spend: \$5.9B (7th)
down 3.3%; 13.6% of rev.



Planned launches:
Relovair (asthma); 444+719 (COPD); GSK1349572 (HIV/AIDS)



Patent expirations:
Diskus device (2013-25); Avodart (2015), Lovaza (2017)

Despite three new vaccine approvals and a 12% return on R&D investment, GlaxoSmithKline continues to tread rough waters. The number eight pharmaceutical company has seen vaccine and pharmaceutical sales shrink 31% between 2009 and 2011, partly due to patent expirations. The company exhibits a dogged commitment to plan: despite a US government push to vaccinate boys against HPV, the company said girls and women will remain the target group for vaccine Cervarix, yielding the field to Merck's Gardasil; a generic of top seller Advair could launch soon; and the company has also given ground in the OTC market, including selling 17 brands to Prestige Brand Holdings, although it's having trouble unloading weight-loss drug Alli.

9 Amgen \$13.1B ▲3.1%



Global revenue:
\$15.6B (15th); **up 3.3%**



Top brands: Enbrel (\$3.5B), Neulasta (\$3.0B), Epogen (\$2.0B), Sensipar (\$518M), Xgeva (\$343M)



Promotional spend:
\$346M (15th); 2.6% of rev.



R&D spend: \$3.2B (14th)
up 10.3%; 20.5% of rev.



Planned launches:
AMG386 (onc.); ganitumab (onc.)



Patent expirations:
Neupogen (2013), Neulasta (2015), Epogen (2015), Sensipar (2015)

Amgen has enjoyed a stable of top-earning biologic products. Over the next several years, many of the patents on these products will expire, and the company expects to face competition, including from biosimilars. Teva has already filed a BLA for a Neupogen-like biosimilar. Amgen's ESA drugs Aranesp and Epogen have also been buffeted by new CMS bundling rules and by warnings on their labels. Launches of denosumab drugs Prolia and Xgeva haven't met projections. Luckily for Amgen, top seller Enbrel shouldn't see biosimilar competition for some time—Amgen and ex-US marketing partner Pfizer just locked up protection for another 17 years. Moreover, the Enbrel co-promote expires in late 2013, after which Amgen will pocket overseas revenues for the biologic, as well.

10 Johnson & Johnson

\$12.1B ▼6.2%



Global revenue:
\$65.0B (2nd); up 5.5%



R&D spend: \$7.5B (5th)
up 10.3%; 11.5% of rev



Top brands: Remicade (\$3.5B), Procrit (\$1.2B), Concerta (\$856M), Levaquin (\$778), Prezista (\$630M)



Planned launches: Canagliflozin (diab.), TMC-435 (HCV), bapineuzumab (Alz.)



Promotional spend:
\$438M (13th); 3.6% of rev.



Patent expirations: Remicade (2014), Prezista (2016), Zytiga (2016)

J&J's past year can be summed up in one word: recalls. The healthcare products giant had a lot of them, fueling discussions of a company that has lost its luster. This came in addition to lawsuits alleging fraudulent marketing of its antipsychotic Risperdal. The impact of these missteps shows: the government shutdown of a McNeil plant hurt inventory levels, and OTC sales fell 3% in the US last year. But a recent poll showed consumers are still attached to J&J. CEO William Weldon, who was in place during much of the product recalls, was replaced by Alex Gorsky.

11 Sanofi

\$11.8 ▼3.3%



Global revenue:
\$43.8B (6th); up 3.3%



R&D spend: \$6.7B (6th)
up 11.7%; 15.3% of rev.



Top brands: Lantus (\$2.3B); Eloxatin (\$806M); Lovenox (\$633M); Taxotere (\$243M); Plavix (\$196M)



Planned launches: Teriflunomide (MS), visamerein (VTE), Lemtrada (MS), lixisenatide (diab.)



Promotional spend:
\$477M (12th); 4.0% of rev.



Patent expirations: Plavix (2012), Multaq (2014), Actonel (2014)

The diabetes medication merchant said in February that it expects business to fall off between 12% and 15% this year, as it weathers the aftershocks of patent losses on Lovenox, Ambien CR, Taxotere and Plavix. But it hopes to add diabetes treatment lixisenatide, a GLP-1 agonist scheduled to be filed this year. The GLP-1 field is a crowded one; Sanofi could bump up against Amylin's newcomer, Bydureon. Despite the uncertainty, Sanford Bernstein analyst Tim Anderson praised the company, in part because its patent cliff levels off next year.

12 Abbott

\$11.5B ▲5.5%



Global revenue:
\$38.9B (8th); up 10.5%



R&D spend: \$3.8B (10th)
up 8.6%; 9.8% of rev.



Top brands: Humira (\$3.5B), Tricor (\$1.3B), Niaspan (\$1.2B), AndroGel (\$1.1B), Synthroid (\$657M)



Planned launches: Bardoxolone (renal), elotuzumab (onc.), daclizumab (MS)



Promotional spend:
\$699M (10th); 6.1% of rev.



Patent expirations: Trilipix/Tricor (2013), Niaspan (2013), Humira (2016)

With mega-earner Humira in its back pocket and a dearth of major patent expirations, Abbott seems well-positioned. Sales rose in 2011, and the company saw out-of-US sales take the lead in its revenue portfolio. In an April research note, Jefferies analyst Jeffery Holford called the company a top pick, citing "impressive top-line results" for its all-oral hepatitis C therapy (in Phase IIb) and positive earnings momentum. Abbott also managed to expand its Humira empire when the EU approved the drug to treat ulcerative colitis. Company plans also include dividing into two this year. The changeover will result in a diagnostics/devices firm called Abbott and a research-based pharma company named AbbVie, now up for sale.

13 Bristol-Myers Squibb

\$10.9B ▲11.2%



Global revenue:
\$21.2B (11th); up 8.7%



R&D spend: \$3.6B (11th)
up 5.9%; 17.0% of rev.



Top brands: Plavix (\$6.8B), Abilify (\$5.2B), Avapro (\$952M), Sustiva (\$940M)



Planned launches: Eliquis (SPAF); brivanib (onc.); necitumab (onc.)



Promotional spend:
\$906M (7th); 8.3% of rev.



Patent expirations: Plavix (2012), Avapro (2012), Abilify (2015)

Bernstein analyst Tim Anderson foresees eight years of flattish growth for BMS. Among the reasons: losing exclusivity of blockbuster drug Plavix this month and pushback from the FDA, which wants more information about its diabetes contender dapagliflozin, which, if approved, would join a crowded market. On tap is the blood thinner Eliquis—the FDA delayed review for this drug, as well, by three months. The firm's recent strategy has included buying biotech Inhibitex in February 2012 and Amira in September 2011, as well as jettisoning non-pharmaceutical brands. Anderson says the sell-offs have made BMS the most "pure play" pharmaceutical company he covers in the US and Europe.

14 Boehringer Ingelheim

\$7.0B ▲9.4%



Global revenue*:
\$16.5B (14th); down 1.2%



R&D spend*: \$3.3B (13th)
up 2.0%; 19.8% of rev.



Top brands: Spiriva (\$2.4B), Combivent (\$1.1B), Pradaxa (\$559M), Aggrenox (\$471M), Fluticasone (\$352M)



Planned launches: Afatinib (onc.), Vargatef (onc.), volasertib (onc.), BI 10773 (diab.)



Promotional spend:
\$906M (8th); 12.9% of rev.



Patent expirations: Spiriva Handihaler (2018)

Boehringer Ingelheim is firing on all cylinders, with six products planned to launch over the next two years, the global roll-out of Pradaxa under way and scarcely a patent expiration in sight. The company has a host of oncology and hepatitis C virus treatments in late-stage clinical trials (BI201335/BI207127), and its partnership with Lilly is already bearing fruit on the diabetes front, with Jentadueto having followed Tradjenta to market. The firm has just completed a \$350-million expansion in the US, which accounts for 45% of sales. Blood thinner Pradaxa now must fend off competition from J&J/Bayer

Xarelto, and maybe soon Pfizer/BMS drug Eliquis (apixaban).

**Global revenue and R&D spend are based on the 2010 financial year, the latest data available at press time.*

15 Takeda

\$6.6B ▼1.5%



Global revenue**:

\$17.5B (13th); down 3.3%



Top brands:

Actos (\$3.4B); Velcade (\$693M), Dexamet (\$555M); ActoPlusMet (\$472); Amitiza (\$264M)



Promotional spend:

\$668M (11th); 10.1% of rev.



R&D spend**:

\$3.5B (12th) down 5.4%; 20% of rev.



Planned launches:

Alogliptin (diab.), TAK-700 (onc.), Contrave (obesity), peginesatide (anemia)



Patent expirations:

Actos (2012)

Takeda is in the teeth of a steep patent cliff, with Prevacid bleeding share and Actos, which accounts for half of US sales, set to lose exclusivity in August. The Japanese firm hopes to overcome these headwinds via its “Transformation into a New Takeda” plan, which includes a new R&D hub in Shonan, streamlining the US sales force (by 1,400 US jobs in 2010 and another 700, announced in January) and acquisitions like last year’s \$13.7-billion deal for European pharma Nycomed and this year’s \$800-million deal for URL Pharma, while reaching beyond its heritage in metabolic, oncology (Millennium) and CNS to immunology and inflammation. And the company hopes to grow US sales of Prevacid follow-on Dexamet, Daliresp for COPD, Uloric for gout, cancer drug Velcade and antihypertensive Edarbi. Two late-stage candidates, obesity drug Contrave and DPP-4 inhibitor alogliptin, have run into FDA roadblocks.

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

16 Mylan

\$5.6B ▲16.7%



Global revenue:

\$6.1B (19th); up 10.9%



Top brands:

Fentanyl (\$472M), bupropion XL (\$336M), omeprazole Rx (\$242M), EpiPen (\$226M)



Promotional spend:

\$2M (20th); 0.04% of rev.



R&D spend:

\$282M (20th) up 4.6%; 4.8% of rev.



Planned launches:

Generic versions of Advair Diskus (resp.)



Patent expirations:

N/A

Five years ago, the Pittsburgh generics giant cobbled together an empire through its acquisitions of Dey Pharma, Matrix Laboratories and the Merck KGaA generics business, going from being the No. 3 player in US generics to No. 3 worldwide. Now Mylan is looking to expand in markets where generics are underutilized, including much of Europe, the Middle East and Asia (half the company’s revenues come from generics-happy North America), while increasing the number of products it markets from 4,700 to 6,700 by 2015 and pushing into generic biologics. The firm faces some generic erosion of its own, though, as Sanofi and Intelliject will launch a competitor to its lucrative EpiPen Auto-Injector franchise in November.

Fig. 5: Estimated US Patent Expirations through 2016

| Brand | Company | Indication | Expiry |
|-------------|-----------------|----------------------|--------|
| Plavix | BMS/Sanofi | Stroke | 2012 |
| Seroquel IR | AstraZeneca | Depression | 2012 |
| Singulair | Merck | Asthma | 2012 |
| Actos | Takeda | Diabetes | 2012 |
| Lexapro | Forest Labs | Depression | 2012 |
| Diovan | Novartis | Hypertension | 2012 |
| Provigil | Teva | Sleep | 2012 |
| Oxycontin | Purdue | Pain | 2013 |
| Aciphex | Eisai/Janssen | Heartburn | 2013 |
| Humalog | Eli Lilly | Diabetes | 2013 |
| Neupogen | Amgen | Low neutrophil count | 2013 |
| Zometa | Novartis | Osteoporosis | 2013 |
| Xeloda | Roche | Cancer | 2013 |
| Actonel | Sanofi | Osteoporosis | 2014 |
| Nexium | AstraZeneca | Heartburn | 2014 |
| Cymbalta | Eli Lilly | Depression | 2014 |
| Copaxone | Teva | Multiple sclerosis | 2014 |
| Celebrex | Pfizer | Pain | 2014 |
| Evista | Eli Lilly | Osteoporosis | 2014 |
| Abilify | BMS/Otsuka | Depression/bipolar | 2015 |
| Avodart | GlaxoSmithKline | BPH | 2015 |
| Gleevec | Novartis | Cancer | 2015 |
| Namenda | Forest Labs | Alzheimer’s disease | 2015 |
| Treanda | Teva | Cancer | 2015 |
| Zyvox | Pfizer | Infection | 2015 |
| Premarin | Pfizer | Menopausal symp. | 2015 |
| Symbicort | AstraZeneca | Asthma/COPD | 2015 |
| Crestor | AstraZeneca | Atherosclerosis | 2016 |
| Alimta | Eli Lilly | Cancer | 2016 |

Source: IMS Health, MM&M research

17 Gilead Sciences

\$5.5B ▲17.0%



Global revenue:

\$8.4B (18th); up 6.3%



Top brands:

Atripla (\$2.6B), Truvada (\$2.0B); Viread (\$466M), Ranexa (\$320M), Hepsera (\$69M)



Promotional spend:

\$32M (18th); 0.6% of rev.



R&D spend:

\$1.2B (17th) up 14.5%; 14.6% of rev.



Planned launches:

Cobicistat (HIV/AIDS), “Quad” pill (HIV/AIDS), GS-7977 (HCV)



Patent expirations:

Hepsera (2014), Letairis (2015), Viread (2017)

This specialty biopharma firm remains highly competitive, most notably in antivirals. The leader in the field, Gilead launched HIV/AIDS drug Complera last year and filed the “Quad pill” for approval (set for FDA review in August). Complera and Quad represent important advances, and analysts expect both to get approved and to snag the bulk of new patient starts in coming years, although Gilead’s top seller, HIV/AIDS med Atripla, is not scheduled to lose exclusivity until 2021 and despite a generic version of Combivir. The firm also leaped ahead in

the hotly contested race to market an all-oral/interferon-free hepatitis C therapy, buying biotech Pharmasset for \$11 billion and access to that firm's Phase III pipeline asset GS-7977. The company also plays in the cardiovascular arena, where angina drug Ranexa is selling well, and the FDA's removal of a warning from the label of PAH product Letairis could mean higher sales of that drug. Despite a manufacturing shortage, the drug Cayston also plays an important role in treating pseudomonas aeruginosa in cystic fibrosis patients.

18 Novo Nordisk

\$5.3B ▲17.8%



Global revenue: \$11.7B (17th); **up 9.3%**



R&D spend: \$1.8B (16th) **up 5.9%**; 15.4% of rev.



Top brands: Novolog (\$1.0B), Levemir (\$843M), Novolog Flexpen (\$779M), Victoza 3-pack (\$457M), NovoSeven (\$385M)



Planned launches: Degludec/DegludecPlus (diab.), rFXIII (bleeding), liraglutide (obesity), Turoctocog alfa (haem. A)



Promotional spend: \$433M (14th); **8.2%** of rev.



Patent expirations: N/A

The Danish diabetes giant continues to soar on North American sales of its modern insulins, in particular. As of November, the company had captured half of the total global insulin market and almost that much of the modern insulin market. Victoza, launched in 2010 for type 2 diabetes, saw meteoric growth in 2011 and became a blockbuster, but faces competition from Amylin's Bydureon and is weighing the development of a once-weekly version to fend off the challenge. The firm has high hopes for its thrice-weekly Degludec, a basal insulin that would take on Sanofi's \$5-billion Lantus, and is exploring an obesity indication for Victoza, a possible gold mine. Now if only they could do something about Victoza spoke and bad press magnet Paula Deen.

19 Otsuka

\$5.2B ▲13.0%



Global revenue*: \$13.1B (16th); **down 2.2%**



R&D spend*: \$2.0B (15th) **up 11.7%**; 14.5% of rev



Top brands: Abilify (\$5.2B), Samsca (\$48M), Busulfex (\$12M), Pletal (\$2M)



Planned launches: Sativex (pain)



Promotional spend: \$15M (19th); **0.3%** of rev.



Patent expirations: Abilify (2015)

The Japanese holding company remains dependent upon its blockbuster antipsychotic drug Abilify, which it co-promotes with Bristol-Myers Squibb. In the fiscal year ending March 31, 2011, the drug provided half of the company's income. Otsuka says its goal is to continue to focus on teaming up with companies for research, with an emphasis on CNS and oncology. The company also noted that the earthquake that rocked Japan and toppled several warehouses did not significantly affect business.

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

Fig. 6: New Drug Approvals 2011 *

| Brand | Company | Indication | Approval |
|------------------|----------------------|---------------------|----------|
| Datscan | GE Healthcare | Imaging agent | Jan. 14 |
| Natroba | ParaPRO | Head lice | Jan. 18 |
| Viibryd | Forest Labs | Depression | Jan. 21 |
| Edarbi | Takeda | Hypertension | Feb. 25 |
| Daliresp | Forest Labs | COPD | Feb. 28 |
| Benlysta | HGS/GSK | Lupus | Mar. 10 |
| Gadavist | Bayer | Contrast agent | Mar. 14 |
| Yervoy | Bristol-Myers Squibb | Cancer | Mar. 25 |
| Horizant | GlaxoSmithKline | Restless legs synd. | Apr. 6 |
| Caprelsa | AstraZeneca | Cancer | Apr. 6 |
| Zytiga | Centocor | Cancer | Apr. 28 |
| Tradjenta | Boehringer Ingelheim | Diabetes | May 2 |
| Victrelis | Merck | Hepatitis C virus | May 13 |
| Edurant | Tibotec | HIV infection | May 20 |
| Incivek | Vertex | Hepatitis C virus | May 23 |
| Difcid | Optimer | Infection | May 27 |
| Potiga | Valeant | Seizures | Jun. 10 |
| Nulojix | Bristol-Myers Squibb | Organ rejection | Jun. 15 |
| Arcapta neohaler | Novartis | COPD | Jul. 1 |
| Xarelto | J&J | DVT | Jul. 20 |
| Brilinta | AstraZeneca | Thrombosis | Jul. 20 |
| Zelboraf | Roche | Cancer | Aug. 17 |
| Adcetris | Seattle Genetics | Cancer | Aug. 19 |
| Firazyr | Shire | HAE | Aug. 25 |
| Xalkori | Pfizer | Cancer | Aug. 26 |
| Ferriprox | ApoPharma | Iron chelator | Oct. 14 |
| Onfi | Lundbeck | Seizures | Oct. 21 |
| Jakafi | Incyte | Myelofibrosis | Nov. 16 |
| Eylea | Regeneron | Wet AMD | Nov. 18 |
| Erwinaze | EUSA Pharma | Cancer | Nov. 18 |

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

20 Forest Laboratories

\$5.2B ▲10.6%



Global revenue*: \$4.2B (20th); **up 7.7%**



R&D spend*: \$716M (19th) **down 34.9%**; 17.0% of rev.



Top brands: Lexapro (\$2.9B), Namenda (\$1.5B), Bystolic (\$383M)



Planned launches: Acridinium (COPD), linacotide (IBS)



Promotional spend: \$866M (9th); **17.5%** of rev.



Patent expirations: Lexapro (2012), Namenda (2015)

Forest's top-selling drug, \$2.9-billion SSRI Lexapro, just lost patent protection, and number two drug Namenda's next in 2015. On the other other hand, there's the boffo sideshow that is longtime chief Howard Solomon's ongoing battles with (some would say persecution by) HHS and activist investor Carl Icahn. The upside is the company launched Teflaro in March, following Daliresp and Viibryd, and plans to file NDAs for acridinium (COPD) and linacotide (IBS) this year.

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