Last year, biopharma won its share of new drug approvals, though not as many as we’re used to in the U.S., as research spending came to fruition. But drugmakers also suffered a number of R&D setbacks, cut research staff, rejigged their operations and refocused their pipelines.

Drug R&D also found itself in the spotlight as one of the biggest political issues to arise last year—drug pricing—became inextricably linked to the cost of biomedical research and development. U.S. industry groups PhRMA and BIO, as well as Europe’s EFPIA and the U.K.’s ABPI, have all said, and will continue to say, that the inherent reason drug prices are what they are is because of the huge R&D investment most (though not all) companies funnel into their scientists and labs.

It’s a risky business: The majority of drugs that begin phase 1 won’t be approved, and over the years, failures in phase 3 have cost individual companies hundreds of millions of dollars each time. Sometimes failures stem from problems with the studies themselves, sometimes a company simply refuses to give up on a dead asset, but often, a failure in the lab is simply part and parcel of the trial-and-error approach inherent to pharmaceutical and biotech research.

Based on figures from their 2016 annual reports, the top 10 pharma R&D budgets (all using their GAAP figures) combined totted up to $70.5 billion, with full-year revenue coming in at $404.8 billion.

On average last year, the top 10 Big Pharmas spent just over 17% of their top line on research, with GlaxoSmithKline spending the second least in percentage terms at 12.9%, and the least in absolute numbers at £3.62 billion ($4.49 billion).

AstraZeneca and Bristol-Myers Squibb shelled out the most on R&D in percentage terms, both spending just over 25% of their revenue.

Both of those companies have, however, sales at the lower end of the Big Pharma list: AZ brought in $23 billion last year, while BMS took in just $19.4 billion. Their respective R&D budgets of $5.89 billion and $4.94 billion, while topping the ranking percentage-wise, came in near the bottom in absolute numbers.
There is a bit more to the BMS story as well: In 2015, the company spent $5.9 billion on research, but last year, that dropped by $1 billion, or 16%. In percentage terms in 2015, BMS put 42% of its revenue toward R&D. This was by far the largest drop in an R&D budget for the top 10 last year.

Most of the others upped their spend slightly, a few significantly, although AZ also spent less in 2016, with a decline of 1.7% off its total 2015 budget.

Eli Lilly was a close third to AZ and BMS, with 24.7% of its total $21.2 billion in sales last year going into R&D. That spending represented a 9% increase on its 2015 figures.

The lowest in percentage terms was Johnson & Johnson, which laid out just 12.6% of its sales on research in 2016. J&J’s spending was comparatively large at $9 billion (though that figure included research on medical devices and other areas outside pharmaceuticals), but so was its revenue at $71.9 billion, more than any of its top 10 peers. To match BMS and AstraZeneca in percentage terms, it would have had to spend $18 billion.

Swiss oncology major Roche was tops in total terms, spending a massive CHF11.53 billion ($11.42 billion) last year, nearly 23% of its CHF50.57 billion in revenue. It also recorded a 20% jump in R&D spending compared with 2015, the biggest increase among the top 10, with most of this increase going into its pharmaceuticals divisions, the rest into diagnostics.

Generally, research budgets moved up with sales in percentage terms, although some may feel that an average 17% of its total revenue going into R&D seems a little small. And the $70 billion R&D figure for the top 10 together is, in fact, the same as it was back in 2012 and 2011, so total spend has remained stagnant for some time.

1. Roche

R&D budget (pharmaceuticals and diagnostics):
CHF 11.53 billion ($11.42 billion)
Change from 2015: Up 20%
Total 2016 revenue: CHF 50.57 billion
R&D budget as percentage of revenue: 22.8%

Roche is a big R&D spender, forking out CHF 11.53 billion ($11.42 billion) last year. Although at 22.8% of its total revenue, it’s not quite top in terms of percentages.

But it did have the largest jump in R&D funding, up 20% from CHF 9.58 billion in 2015, counting both pharmaceuticals and its diagnostics division.
The biggest boost was in its pharmaceuticals R&D, up from CHF 8.3 billion two years ago to CHF 10.1 billion last year. Diagnostics saw a much smaller increase, from CHF 1.2 billion in 2015 to CHF 1.3 billion in 2016.

Overall, however, the company had a mixed bag in 2016: A key success saw the FDA approval of its I-O med Tecentriq (atezolizumab) in bladder cancer, coming third in the new PD-L1/PD-1 world after Merck and Bristol-Myers, but becoming the first PD-L1 checkpoint inhibitor to market and beating out rivals AstraZeneca and Pfizer/Merck KGaA.

The med is expected to go on and do big things, especially after it scored an FDA nod in lung cancer, despite being third to market. And the company is, like many others in this space, looking to combine its new med with other experimental drugs (such as Kite’s cutting-edge CAR-T candidate) to see if it can boost efficacy and immune responses across a range of cancers.

But the Swiss major is coming under the looming threat of biosimilars to its aging batch of superstar oncology products, and some of its attempts to offset these future sales declines saw major setbacks last year.

One of the biggest problems came out of its hemophilia test, the study of which is centered around the “game-changing” emicizumab (ACE910) that saw two thromboembolic events and two cases of thrombotic microangiopathy in patients.

But in February of this year, Roche revealed that a patient died in a phase 3 hemophilia trial of its bispecific antibody.

The trial investigator ruled the death was unrelated to emicizumab, but with the event following other reports of serious adverse reactions, it has added to questions about the safety of the experimental regimen.

The Swiss major also failed a late-stage trial pitting one of its newer drugs against an aging stalwart as it failed to help patients with an aggressive form of blood cancer live longer.

Specifically, the phase 3 GOYA study of Gazyva (obinutuzumab) used with a cocktail of chemo agents missed its primary endpoint in improving progression-free survival in patients with diffuse large B-cell lymphoma when compared to Roche’s own blockbuster cancer and autoimmune drug Rituxan (rituximab), also with a chemo regimen.

The company also dropped vanucizumab, which was intended as a follow-on to blockbuster cancer drug Avastin (bevacizumab), as a cancer monotherapy on a phase 2 trial failure.

Development of vanucizumab on its own was discontinued given that it failed to meet its primary endpoint in a key test, but it continues life in several ongoing combo trials.
2. Johnson & Johnson

R&D budget (also includes device and consumer healthcare work): $9.09 billion ($7 billion for pharmaceuticals)
Change from 2015: Up 0.5%
Total 2016 revenue: $71.9 billion
R&D budget as percentage of revenue:
12.6% (10% for pharmaceuticals)

Johnson & Johnson, a major friend, investor and incubator in early-stage biotechs with big ideas, had one of the highest research budgets in dollar terms again last year, although the lowest in percentage terms among its Big Pharma peers, partly because it also has one of the highest revenues.

In recent years, Johnson & Johnson and its biopharma unit Janssen have won plaudits for innovation and won admiration in biotech circles with its JLABS project, which has created lab space, some investor funding and promises of potential future grants and licensing deals for early-stage companies looking to test out a wide range of innovative ideas.

Last year it expanded its JLABS empire, launching its first site outside the U.S. in Toronto, joining San Diego, San Francisco, Boston, Houston and early this year, New York.

At the start of the new year Johnson & Johnson added 15 new deals to its list, now totaling over 300, as it looked to get its teeth into the lucrative NASH R&D race, with a pact and a potential buyout of Bird Rock Bio and its fatty liver candidate namacizumab.

It also set up a new collaboration with Medicines for Malaria Ventures, building on its vaccine work with GlaxoSmithKline, as well as a deal with Synthetic Genomics to develop a ribonucleic acid (RNA) technology that enables a tuneable, multigenic approach to elicit desired antigen expression and immune response for a variety of applications.

Also at the start of the year, J&J, after walking away once and seemingly set to lose out to Sanofi, came in and swooped up Actelion for $30 billion. The biotech spun out its R&D unit into a standalone company, basing and listing the new drugmaker in Switzerland and handing J&J a hefty minority stake.

In 2015, Johnson & Johnson said it wanted to submit to the FDA applications for 10 potential blockbusters by the end of 2019, with some of these centered around the hot new area of I-O (immuno-oncology). Last year, in a conference call around its financials in October, the company’s global head of pharmaceutical R&D, William Hait, said the pharma has 15 immuno-oncology assets in development, including eight that are already in the clinic.
He said that last year, J&J had been investing in “four critical areas including vaccines, T cell checkpoint inhibitors, T cell redirection and myeloid mechanisms of action.”

In its marketed cancer meds, Johnson & Johnson also posted “standout” data in myeloma for Darzalex (daratumumab) as it looked to gain stronger sales from its big med. This also comes as it fights biosimilars to its blockbuster immunology drug Remicade (infliximab), which is already under pressure from cheaper versions of the biologic.

3. Novartis

R&D budget: $9 billion
Change from 2015: Up 0.8%
Total 2016 revenue: $48.5 billion
R&D budget as percentage of revenue: 18.5%

Novartis has in recent years remained a big hitter in the R&D stakes, and it continued its run with an impressive $9 billion spent on R&D last year—although this was only slightly up on the $8.93 billion it had spent the year before.

One of the biggest R&D stories to come out from Novartis in 2016 was in fact a negative one: In August, the Switzerland-based big pharma said that it was planning to redeploy most of those 400 employees from its cutting-edge cell and gene therapy unit. Around 120 employees were set for the ax, according to reports, and that came only two years after the unit was formally created.

That unit is responsible for one of Novartis’ biggest future launches—its CAR-T med CTL019 in certain blood cancers. The drug could hit the market this year, setting up a battle with rival biotech Kite and its CAR-T offering KTE-C19.

The unit still appears to have a large focus on this area, but its downsizing (along with a small exodus of senior R&D heads in 2016) raised eyebrows.

Novartis also announced another research revamp last year when announcing that it was moving its Singapore research base for dengue fever and malaria over to California. In turn, that reduced the headcount at its Zurich facility and its China biologics group.

The company said that it would be closing down the Shanghai biologics group and shift its Institute for Tropical Diseases in Singapore to the San Francisco area to “centralize its scientists.” It has just under 100 staffers there, but it kept mum on how many it may cut in the process.

Still, it did bulk out its pipeline with some bolt-on buys, including its $665 million for sickle cell player Selexys, its deal to obtain U.K. biotech Ziarco and its midstage leading eczema candidate ZPL-389.
4. Pfizer

R&D budget: $7.87 billion  
Change from 2015: Up 3%  
Total 2016 revenue: $52.82 billion  
R&D budget as percentage of revenue: 14.8%

For many years before the loss of its Lipitor (atorvastatin) patents, Pfizer was hit by waves of criticism for its failure to develop new blockbusters to replace the big drugs that had bulked up its revenue. Those critics wanted to see more outsourcing, more partnerships and smaller in-house research empires. Pfizer has in many ways steered toward that course, and 2016 saw more evidence of this. 

The Big Pharma is still one of the biggest players in the world when it comes to medical R&D spend. Although it no longer tops the list, it still spent big on buying up other companies’ research last year with its $14 billion buyout of cancer biotech Medivation and its blockbuster prostate cancer med Xtandi (enzalutamide).

Its newly expanded pipeline includes the late-stage PARP candidate talazoparib, as well as blood cancer drug pidilizumab, which is in midstage testing. A candidate for bladder cancer and a multiple myeloma therapy are also now in its early-stage pipeline.

This deal came, however, after it failed to buy Allergan in a $160 billion-plus megamerger that was dropped a year ago, after new tax rules made a pact less appealing, and likely prompted Pfizer’s desire to steal the in-demand company away from the likes of Sanofi.

Pfizer did in fact spend much time and money in 2016 on R&D outside of its pipeline, with a big focus on its near-$1 billion checkpoint inhibitor deal with German Merck for avelumab (Bavencio), homing in on assessing its efficacy when combined with a host of other drugs from across a series of classes.

The two are testing the drug in many different cancers, including lung cancers, renal cell carcinoma and ovarian, gastric and bladder cancer, and Merkel cell carcinoma, which in March this year became its first approval.

Pfizer is playing catch-up in this new cancer class space and is some years behind leaders Bristol-Myers Squibb, Merck & Co. and Roche, but still managed to beat out AstraZeneca to be the fourth to market.

A little more quietly than its Medivation deal, Pfizer also bought up gene therapy player Bamboo Therapeutics, adding advanced recombinant adeno-associated virus-based gene therapies, which it expects will complement its existing rare disease and gene therapy portfolios.
These include a preclinical neuromuscular candidate for Duchenne muscular dystrophy, a rare disease that has seen a number of recent clinical disappointments (but also two recent FDA approvals), as well as preclinical candidates to treat Friedreich’s ataxia and Canavan disease and a phase 1 candidate for giant axonal neuropathy.

But Pfizer was also hit last year when its 13-year veteran senior principal scientist Min-Jean Yin appeared to be cut from the company, coming after the U.S. Big Pharma giant initiated a series of research article retractions after allegations of data manipulation.

It also saw a major pipeline failure, saying in November that it was to dump all work on its proprotein convertase subtilisin/kexin type 9 inhibitor (PCSK9i) bococizumab due to weak data and an “evolving treatment and market landscape for lipid-lowering agents.”

The shock announcement came as the Big Pharma found that bococizumab was “not likely to provide value to patients, physicians, or shareholders” after its ability to lower LDL-C weakened over time and increased the risk of some adverse events. In short, it didn’t really work, and it caused side effects.

This was a big knock for the company, coming as Amgen and the Medicines Company/Alnylam look to carve out a new, and potentially lucrative, market in the PCSK9i space.

5. Merck

R&D budget: $7.19 billion
Change from 2015: Up 7.3%
Total 2016 revenue: $39.8 billion
R&D budget as percentage of revenue: 18%

Merck had a major trial win last fall when its marketed checkpoint inhibitor Keytruda (pembrolizumab) scored in first-line lung cancer patients. Just a few weeks later, it was given the nod from the FDA in this key, lucrative setting.

This also came after aggressive rival Bristol-Myers Squibb saw its checkpoint inhibitor Opdivo (nivolumab) fail its key test in the same setting, handing a major win to its rival.

Things got better when, at the start of 2017, Keytruda took another step closer to eclipsing its competitors in lung cancer after the FDA accepted its application for a new Keytruda-plus-chemo combo that could expand its market considerably. The billions spent on research Keytruda have certainly paid off.

But not everything came up roses last year for Merck, which had a high-end budget in dollar terms but was middling when it came to the budget as a percentage of revenue. As a result, the ax fell on several programs and staffers.
In September, the U.S. big pharma said it was giving up on its delayed and long-troubled bone drug odanacatib after it became apparent the safety risk from using the experimental med was just too high.

This came several years after phase 3 results had shown that while the drug could reduce fractures, it also increased the risk of atrial fibrillation and stroke. This was a blockbuster contender for the company, so its official loss in 2016 was a blow for the company and a drain on its R&D coffers.

And in the summer, Merck announced that it would be giving with one hand and taking away with the other as it confirmed cuts across its discovery and early-stage R&D businesses, but said it will also be boosting investment in two research sites.

The pharma said it would be increasing its investment in exploratory biology in Cambridge, Massachusetts, and the San Francisco Bay area. It also said, however, that there will be cuts and shifts, namely at its Kenilworth and Rahway, New Jersey, sites and the North Wales, Pennsylvania, screening facility.

This all comes around three years after Merck, in a $2.5 billion restructuring plan, axed 8,500 staffers, with much of the money saved up for use on research spending and deals. This went hand-in-hand with a rethink on its R&D strategy.

On the positives, Merck’s FDA fast-tracked antiviral etermovir hit its primary endpoint in a phase 3 test. That came as the partners looked to capitalize on Chimerix’s blowup after its late-stage antiviral brincidofovir flopped in 2015.

At the start of the year, Merck, which has been focusing a little more on academic and charity deals in recent years, bought into a cancer research U.K. program that targets an enzyme key to the development of cancer and blood disease. It wagered as much as $515 million on the effort, its first public partnership into epigenetics.

Quartet Medicine, at work on first-in-class treatments for pain and inflammation, also partnered up with Merck in January last year, signing a deal that could lead to a $575 million buyout agreement.

And Merck also teamed up with Moderna, the biotech of much intrigue (and funding), with $200 million upfront to help develop mRNA-based personalized cancer vaccines, as well as Keytruda combos.

Speaking of Keytruda combos, nearly every type of cancer class has been paired with the I-O drug last year, with a “throw everything at it and see what sticks” approach. That tactic is also used by its PD-1 and PD-L1 rivals BMS, Roche, AstraZeneca and Pfizer/Merck KGaA.
6. **AstraZeneca**

**R&D budget:** $5.89 billion  
**Change from 2015:** Down 1.7%  
**Total 2016 revenue:** $23 billion  
**Percentage of revenue:** 25.6%

AstraZeneca had a pretty rough few years of R&D setbacks and failures up until 2012, when its former chief, David Brennan, was all but pushed out as a result.

Things seem to have steadied somewhat since Pascal Soriot took the helm, though, and he has been bullish on its future. Relatively speaking, the U.K.-headquartered Big Pharma still spends big on research, a meaty 25.6% of its total revenue (of just under $23 billion), making it one of the largest in percentage terms.

But the company still saw some setbacks in 2016, the biggest of which was the unexpected FDA complete response letter to its $2.7 billion hyperkalemia candidate ZS-9, coming after manufacturing issues at its newly acquired biotech pushed back its approval and gave rival Relypsa time to consolidate its position on the market.

In fact, in early 2017, it did manage to get the drug recommended for use in Europe, only to be hit by a second CRL in March.

AstraZeneca also had continuing issues with its PD-L1 candidate durvalumab, with rival Roche beating it to market with Tecentriq (atezolizumab) last year and Pfizer and Merck KGaA getting an FDA nod for their checkpoint inhibitor Bavencio this year; AZ will now be fifth to market overall in the PD-1/PD-L1 market.

It also saw the agency place a partial clinical hold on a phase 3 trial of durvalumab, which restricted the pharma from adding new patients to clinical trials, as monotherapy and in combination, in head and neck squamous cell carcinoma, while adverse bleeding events were also observed in several late-stage tests.

Its MEK 1/2 inhibitor selumetinib also hit trouble after failing to improve either progression-free or overall survival in patients with KRAS mutation-positive non-small cell lung cancer last fall in another phase 3 setback.

And there was a familiar story back in February when its CTLA-4 drug tremelimumab flunked a solo challenge for mesothelioma, a form of lung cancer associated with asbestos and notoriously tough to treat.
It also lost talent when its head of research, Yong-Jun Liu at MedImmune, AZ’s biologic arm, left the company. Liu, one of the world’s most prolific researchers in immunology, was poached by European Big Pharma rival Sanofi.

But not all are seeing doom and gloom in AstraZeneca’s pipeline: Analysts at Leerink came out to bat for the Big Pharma last year, seeing a trial that puts tremelimunab and durvalumab together as a first-line treatment in lung cancer as being a potential major therapy (worth $4 billion at peak) for the company, especially after Bristol-Myers Squibb’s shock phase 3 lung cancer flop with Opdivo (nivolumab) last year.

And despite a littered pipeline of biopharma failures, including Lilly’s solanezumab, the U.S. pharma and AZ signed a new R&D pact on amyloid drug MEDI1814, which is currently in phase 1 trials and touted as “a potential disease-modifying treatment for Alzheimer’s disease.”

7. Sanofi

R&D budget: €5.17 billion ($5.45 billion)
Change from 2015: Up 1.8%
Total revenue in 2016: €33.82 billion ($35.64 billion)
R&D budget as percentage of revenue: 15.2%

Sanofi had a bit of a year to forget when it came to buying up biotechs and expanding its pipeline—it failed to beat out Pfizer in its winning $14 billion bid for cancer biotech Medivation, losing out on some increasingly hot cancer candidates (and blockbuster prostate cancer med Xtandi).

It got worse at the end of the year when it also appeared to fluff its lines in its failed attempt to buy Actelion.

It all seemed to be going the French pharma’s way when bidder Johnson & Johnson walked away from talks, allowing Sanofi to swoop in and take the deal with little resistance.

But in the end, J&J itself came back as a white knight and snapped up the biotech for $30 billion after Sanofi’s execs came in with a lowball offer (Medivation will see some similarities here), a list of “extensive due diligence requests,” and issues around the “tenor and content” of the meeting itself. Investors are not happy, and want Sanofi to get its M&A act together.

Last year also saw the Big Pharma attempt to get back into oncology after steadily externalizing drug development over the past few years, downsizing its internal oncology R&D operations significantly in 2015.

But last January, it signed a deal with France’s Innate Pharma to get involved in the immuno-oncology space, where it is currently far behind its rivals, while recently retooling its deal with Massachusetts-based upstart Warp Drive Bio, under the eye of Sanofi’s Sunrise Initiative.
Sanofi currently has a small group of cancer drugs on the market but is far behind its Big Pharma rivals in the latest classes of oncology R&D, prompting its about-face last year with a mini deal spree with cancer biotechs.

And while failing in the deal department, Sanofi had a notable win when it poached Yong-Jun Liu as its new head of research from AstraZeneca's biologic arms MedImmune, while it looked to beef up its early-stage pipeline and senior R&D leadership team.

Liu, one of the world’s most prolific researchers in immunology, has seen his work lead to the development of several key drug targets in the areas of allergy, immunology and oncology. Under the French drugmaker’s direction, he’s now responsible for leading all of Sanofi’s research and will work alongside its leadership team to “build a competitive R&D organization,” according to a statement from the company.

But this all came amid some major cuts to Sanofi’s R&D ops, announcing in February last year that it was starting its latest round of job cuts, with more than 500 in its home country. This was said to include almost 300 open R&D jobs not being filled, with another 250-plus cuts hitting Sanofi’s commercial operations and corporate offices.

The company has been looking to save money since new CEO Olivier Brandicourt took over, given some major patent losses over the years combined with pricing pressures for its diabetes franchise.

8. Eli Lilly

R&D budget: $5.24 billion
Change from 2015: Up 9.3%
Total 2016 revenue: $21.2 billion
R&D budget as percentage of revenue: 24.7%

Eli Lilly spent nearly a quarter of its income on R&D last year, putting it near the top of its peers in percentage terms, and in 2016 saw some of that spend pay off—overall, however, last year was a mixed bag for the company’s research.

Let’s look at some of the positives first: In March, it got the FDA green light for blockbuster psoriasis contender Taltz (ixekizumab), an IL-17A anti-inflammatory, and followed in the footsteps of Novartis’ rival Cosentyx (secukinumab), the first IL-17A drug to hit the market.

Later on, in October, it also gained a U.S. approval for Lartruvo (olaratumab), in combination with doxorubicin, as a front-line therapy for patients with soft tissue sarcoma (STS).
But it was not all good news, and there were flops and setbacks in the clinic, the largest being what was the inevitable demise of its amyloid drug solanezumab, prompted by a series of failures and adding to the depressingly high pile of failed amyloid drugs.

There was also the announcement, made early last year, that the Big Pharma was to ax around 200 R&D positions, although this was dressed up as a “voluntary reallocation program” that saw it reduce its global R&D headcount by nearly 3%, although it did up its investment in other areas.

Later in the year, it also lost Richard Gaynor, M.D., one of the top execs out of its oncology division, to be succeeded by Levi Garraway, M.D., Ph.D., who joined the company from his former role as associate professor of medicine in the Department of Medical Oncology at the Dana-Farber Cancer Institute and Harvard Medical School.

Gaynor had been SVP of clinical development and medical affairs for Lilly Oncology since 2013 and at the division across several roles for nearly 15 years, with his retirement a big loss in terms of experience and talent.

The company is still pushing on with its cancer R&D, working on combo trials with Merck and its PD-1 drug Keytruda, as well as with AstraZeneca on its experimental PD-L1 durvalumab and Bristol-Myers with its Opdivo, while also signing up to work with Immunocore’s lead T-cell receptor-based candidate IMCgp100, in combination with its kinase inhibitors galunisertib (LY2157299) and merestinib (LY2801653) in melanoma.

One of its biggest new cancer hopes lies with its CDK4/6 inhibitor abemaciclib, but again is some way behind rival Pfizer, which has already seen its competing med Ibrance (palbociclib) approved by the FDA. And Novartis recently became the second, bagging a recent FDA approval for Kisqali (ribociclib), ahead of Lilly.

9. Bristol-Myers Squibb

R&D budget: $4.94 billion
Change from 2015: Down 16%
Total 2016 revenue: $19.42 billion
R&D budget as percentage of revenue: 25.4%

Bristol-Myers Squibb has long been highly regarded when it comes to its R&D—a small Big Pharma with a biotech bent, it has always funneled much money into its research budget.

In 2015, it spent $5.9 billion on research, but last year the amount fell substantially by $1 billion dollars. BMS still has one of the highest budgets in percentage of revenue terms, at just over a quarter, but this is a big drop from the 42% it was hitting in 2015.
Sure, its revenue jumped 17% between 2015 and 2016, but the company has still had to tighten its belt in the research department.

BMS had a tough year all in all when its Opdivo (nivolumab) franchise lost out big time to Merck and its rival I-O med Keytruda (pembrolizumab) when the pair released late-stage results for their respective meds in first-line lung cancer.

Merck hit the heights, but BMS hit the skids when its drug flopped in this lucrative disease setting back in the fall. Analysts then pinned BMS as a new M&A target, after its shares were hit after the Opdivo setback.

A few months later, the company announced a major reworking of its R&D and manufacturing sites across the U.S. as it plans to shut down a host of centers while integrating others, forming part of its new research strategy announced earlier this year.

In a phased multiyear deal, the company said it would shut down its site in Hopewell, New Jersey, in a decade’s time. Bristol-Myers Squibb acquired the site for use as a research, data and administrative center nearly 20 years ago.

It will also not be renewing its lease at the Lake Union Steam Plant site in Seattle in 2019. The site is run by ZymoGenetics, which BMS bought in 2010 for nearly $900 million, and since 1993 has been predominately focused on the discovery and early manufacture of therapeutic proteins.

In December, BMS also confirmed previously announced plans that it will indeed close its Wallingford, Connecticut, site by the end of 2018. It will also no longer build a Connecticut development site as it had once planned.

Where there are cuts, however, there are also other investments and changes. Bristol-Myers said it will be making investments in the construction of a new R&D building at its Lawrenceville, New Jersey, campus as it closes down its Hopewell location.

Bristol-Myers has not sat quietly on its deal-making and did go on something of an R&D spending spree last year, signing a pact in July for Sweden’s Cormorant Pharmaceuticals in an acquisition worth just north of $500 million, just four months after BMS paid $600 million to buy out biotech startup Padlock Therapeutics and its autoimmune R&D platform.

BMS also beefed up its fast-growing fibrosis portfolio after paying $100 million upfront to Japanese biopharma Nitto in November to develop and sell its early-stage liver-scarring candidate, as well as an option to buy into other antifibrotic meds.

There were other trials and setbacks, however, and after already taking several steps back from diabetes in recent years, Bristol-Myers in May last year pulled out of its deal with Biocon to develop oral insulin, the next big thing in diabetes.
India’s biggest biotech Biocon struck a deal with BMS in 2012 to take an option on the worldwide rights to the potential next-gen product, but BMS pulled out of the pact.

Also this year, BMS’ Francis Cuss left as CSO, replaced by Thomas Lynch, the former CEO of Massachusetts General Physicians Organization.

10. **GlaxoSmithKline**

**R&D budget:** £3.62 billion ($4.49 billion)  
**Change from 2015:** Up 1.7%  
**Total 2016 revenue:** £27.88 billion ($34.6 billion)  
**R&D budget as percentage of revenue:** 12.9%

GlaxoSmithKline has one of the lowest R&D budgets in terms of percentage of revenue among its peers; although its research budget was slightly up on 2015, this is still markedly down from the around £4 billion it was spending in 2012-13.

Some investors want to see change at GSK: Its financials were for many years pretty dull (it has picked up in recent times, however), and its R&D not as exciting as that of some of its Big Pharma rivals; this may have prompted the company to bid farewell to long-serving CEO Sir Andrew Witty this year.

But his replacement, insider Emma Walmsley, has raised more questions over whether she can enact change (insider CEOs tend not to be that radical), and whether Walmsley, who will be paid less than Sir Andrew, has the experience in R&D required to run the company, given that her tenure before taking the chief reins was in the consumer biz.

What will Walmsley inherit? Its R&D is predominately focused on vaccines and respiratory, and with much of its late-stage and marketed cancer assets given to Novartis a few years back, its oncology pipeline is now mainly phase 1.

One of its more advanced cancer candidates, the phase 2 NY-ESO-1, is partnered with Adaptimmune and works as a T-cell therapy that targets the NY-ESO peptide which is present across multiple cancer types. In the U.S., the pair are conducting several phase 1/2 studies for the med in patients with synovial sarcoma, multiple myeloma, melanoma, NSCLC and ovarian cancer.

The company is also seeking deeper inroads into rare diseases, with a number of assets in late-stage development, and last year it scored a major regulatory win when Europe approved its “bubble boy syndrome” gene therapy Strimvelis.

The drug is an ex vivo gene therapy for severe combined immunodeficiency due to adenosine deaminase deficiency (ADA-SCID), a condition that only affects around a dozen patients in Europe, and 350 patients worldwide.
The drug came as a result of partnership between GSK and Italy’s San Raffaele Telethon Institute for Gene Therapy and the Milanese biotech MolMed, which is based at the Institute. A deal between the groups was struck back in 2010. It has not yet sought FDA approval however.

But there have been some issues here: At the beginning of this year, Carlo Russo joined a growing list of ex-GSK staffers moving into biotech after working on and helping launch Strimvelis, as he went over to Milan, Italy-based Genenta Science, a biotech focused on hematopoietic stem cell gene therapy in cancer, as its new CMO.

Russo, who was head of R&D rare disease unit, joined other GSK/Strimvelis vets, namely Andrea Spezzi and Nicolas Koebel, who left the company seeking a biotech role.

They in fact both now work at Fierce 15 winner Orchard Therapeutics, Spezzi as CMO and Koebel as SVP of business operations, and are working on a rival drug to Strimvelis using a lentivirus approach that they believe will be better, safer and easier to use for patients.

GSK did make some relatively big external bets last year, notably its $715 million joint venture with Alphabet’s Verily to create a new R&D company focused on bioelectronics, as well as a £175 million ($230 million) pay-out to gain global, exclusive rights to a phase 1 monoclonal antibody to treat severe asthma from Janssen.

The company is also in a development race to develop a more “natural" way to boost red blood cells in anemia after starting pivotal late-stage trials of its daprodustat candidate last year.

Daprodustat is a hypoxia-inducible factor prolyl hydroxylase inhibitor (HIF-PHI), an emerging class of drugs that are being pitched as a more convenient oral alternative to injectable erythropoiesis-stimulating agents like Amgen’s Epogen and Aranesp and Johnson & Johnson’s Procrit.

GSK is however playing catch-up in the development of the class with FibroGen—whose roxadustat started phase 3 testing since 2014 and has been licensed to Astellas and AstraZeneca—as well as Akebia Pharma/Mitsubishi Tanabe which has vadadustat in late-stage testing a little bit behind roxadustat.

But if GSK can serve up the goods, its drug could tap into a market estimated by Datamonitor to be worth around $5 billion a year. Sir Andrew, however, did say in his final results meeting in February: “The next 24 months will be significant for GSK’s pipeline and it marks the start of another intense period of R&D activity for the company, as we expect important data read-outs on around 20-30 assets in HIV, respiratory, immuno-inflammation, oncology and vaccines.”

But analysts at Leerink said ahead of its Q1 2017 results that its potentially “impactful pipeline" assets “still lack visibility.”

The firm said: “GSK’s early stage pipeline portfolio harbors some intriguing programs, but most of these assets are a few years away from real value realization. The company has a broad immuno-oncology, epigenetics, and cell therapy portfolio, mostly in phase1/2 studies.
“In HIV, the full potential of the cabotegravir long-acting treatment regimens and the new agents acquired from Bristol-Myers Squibb (e.g., attachment inhibitors and maturation inhibitors) remain to be seen. The Immunology portfolios with multiple ‘first-in-class’ agents and the daprodustat for treatment of anemia of chronic kidney disease could also be high impact assets, but all have expected filing dates in 2019 and beyond.”

At least there’s also good news for the Walmsley-led GSK. A (temporary) relief came when the FDA sent a CRL to Mylan in late March, turning away a generic to GSK’s respiratory revenue driver Advair. If no copycat is seen in 2017, GSK expects core earnings to expand by between 5% and 7% at constant exchange rates.