



# GLOBAL PHARMACEUTICALS

## 2018 industry statistics

Over the last few weeks, most of the multi-national pharmaceutical companies have reported results for 2018, which has given us the opportunity to update our industry statistics and drug database. This report provides the first publication of global and US rankings of the top 15 drug companies for 2018. Comparisons are made with historical data to show how different company strategies have evolved. In addition, analysis has been provided for the evolution of therapeutic biopharmaceutical drugs, which saw sales rise 7.5% to \$219bn, representing 25% of the market, and driven by growth in antibody-derived drugs.

- ▶ **Global market:** Hardman & Co estimates that the worldwide prescription drug market had underlying growth of 4.3%, boosted to 4.8% in USD terms, in 2018 to \$865bn, up from \$825bn in 2017. This is consistent with the 5% growth rate that was reported in the annual reports of several drug companies.
- ▶ **US market:** The US market was an important driver of growth, rising 4.3% to \$337bn in 2018, from \$323bn in 2017, representing 39% of the global market. The FDA approved a new record number of drugs in 2018, with 59 approvals, reflecting the Commissioner's stated goal to improve the agency's efficiency.
- ▶ **Biopharmaceuticals:** The spend on drugs classified as biopharmaceuticals grew 7.5% to \$219bn in 2018; these drugs now represent just over 25% of the entire market. Within this category, drugs using antibody technology grew 16.7% to ca.\$116bn.
- ▶ **Best-selling drugs:** Humira (AbbVie) remains the biggest drug, with ex-factory sales approaching \$20bn (+8.2%). The top 10 drugs in the world had reported sales of \$82.1bn in 2018, and represented 9.5% of the entire market. On a cumulative basis, there remain six drugs in the \$100bn club.
- ▶ **R&D investment:** The top 15 drug companies by sales re-invested 20.8% of Rx drug sales into new drug development, spending \$90.7bn out of the total spend of \$122bn by the 40 largest companies. The average R&D spend was \$7.0bn, ranging from \$9.9bn (Roche) to \$3.4bn (Bayer).

### Pharmaceutical sector performance – UK vs. global



Source: Eikon Thomson Reuters

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## 2018 drug industry statistics

*Updating our industry database and generating first cut of global 2018 rankings...*

Although the focus of Hardman & Co is predominantly on companies in the small- to mid-sized market capitalisation range, when writing research reports, it is important to position them relative to the industry in which they operate. Apart from Japanese companies, all the major global pharmaceutical companies have reported full-year results for 2018 over the past few weeks; therefore, we have taken the opportunity to update our industry database and generate the first cut of global rankings for 2018. For an industry that requires a long investment cycle – it still takes, on average, 10 years from discovery to launch of a new drug – decisions made many years ago have important consequences on current financial results. Therefore, looking back at operational performance over 20 years reveals how different company strategies have panned out.

*...basing our analysis on annual accounts of ca.40 multi-national companies*

### Our pharmaceutical database

Whatever the size of a company, it is imperative to outline the commercial market opportunity that the company's (often disruptive) technology is targeting. While such work requires significant research, it often constitutes only a very small part of the overall report. It does, however, have the advantage of providing us with a global commercial dataset that is reliable and independent of third-party input.

Pharmaceutical sales are defined as anything that requires a prescription (Rx), and specifically excludes Over-The-Counter (OTC) and consumer products. It is important to note that this does include generic drugs and biosimilars, both of which require a prescription.

Our database of pharmaceutical companies and drugs goes back to 1985. All the data are based on net ex-factory sales reported by companies, and exclude all discounts and allowances, returns, chargebacks and government rebates, such as Medicaid and Medicare. All reported numbers are converted into USD at daily average exchange rates – available from the Bank of England website. These data have, therefore, been compiled consistently and with great care, so that direct comparisons among companies can be made.

We have based our analysis on the annual accounts of ca.40 multi-national companies, which cover ca.75% of the global pharmaceutical market and ca.90% of the US drug market. Market share statistics have been calculated from our provisional estimate for the global prescription drug market, which cannot be finalised until after the Japanese drug companies and Boehringer Ingelheim report in May 2019.

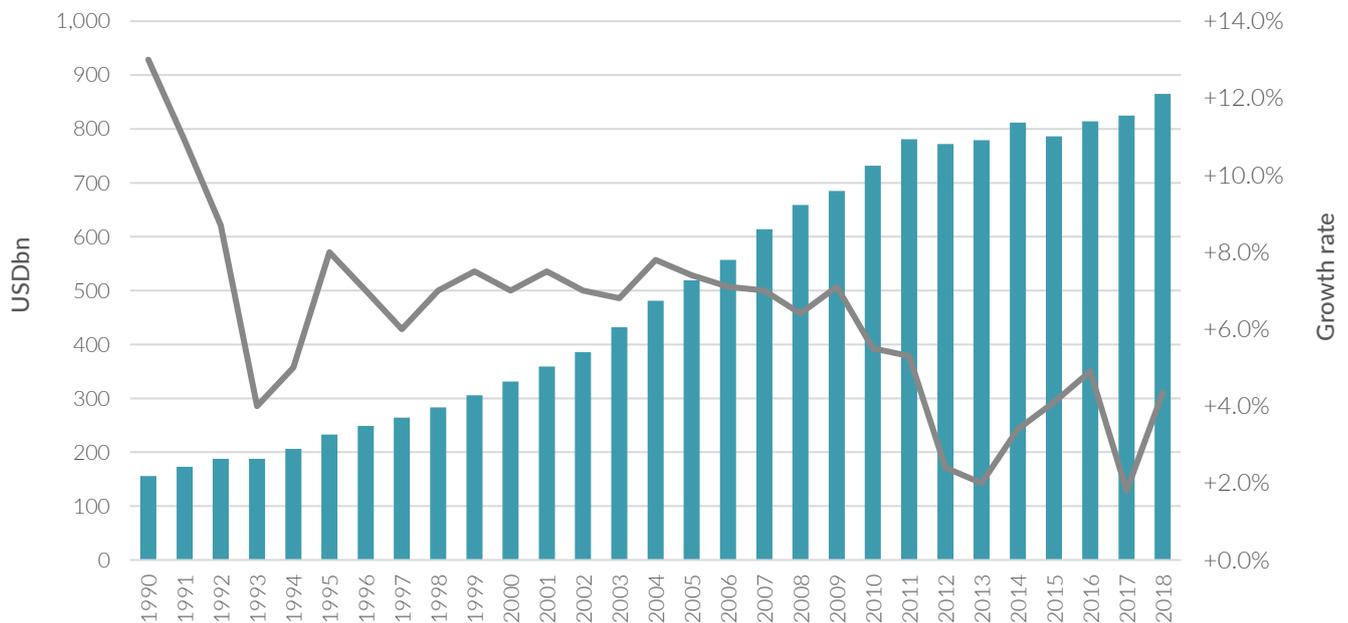
*We estimate 4.3% underlying growth for worldwide prescription drug market in 2018...*

### 2018 global pharmaceutical market

Annual reports published by several drug companies over the last two months have cited 5% growth for the global pharmaceutical industry in 2018 (source usually market research organisation IQVIA). This includes a modest currency gain (ca.0.5%) when figures are translated into USD. Based on the reported sales outcomes from most of the top 40 companies in the world, Hardman & Co estimates that the global Rx drug market had underlying growth of 4.3% in 2018, which translates into USD reported growth of 4.8% to \$865bn, from \$825bn, in 2017. This is consistent with the IQVIA market research estimate which is for the MAT to September 2018.

*...boosted to 4.8% as reported in USD terms*

Following a 10-year (2003-13) period in which the rate of growth of the drug industry was trending downwards, the last five years have been more volatile. The CAGR of the global pharmaceutical market was 2.12% (from 2013 to 2018) and 2.76% (from 2009 to 2018), lower than many industry commentators had predicted given the introduction of some high-profile, and high-priced, new drugs.

**Global prescription drug market – 1990-2018**


Source: Hardman & Co Life Sciences Research

*The US market is an important driver of global growth...*

*...rising 4.3% to \$337bn in 2018...*

*...equating 39.0% of the global market*

*Difficult year in 2018, with positive demographics and advances in science and technology being offset by political uncertainty, as well as pressure on drug prices*

Our data suggest that the top 15 ranked drug companies had 52.7% of the world market in 2018, compared with 53.0% in 2017. Historically, the US market has been an important contributor of growth to the global outcome. Hardman & Co estimates that the rate of growth for the US prescription drug market in 2018 was similar to the underlying rate for the global market, increasing 4.3% to \$337bn, up from \$323bn in 2017, and representing 39.0% of the global market. Validation of this estimate is derived from the fact that US sales reported by the top 20 companies grew by a weighted average of 4.2% in 2018.

2018 was, once again, a difficult year for the industry, due largely to a background of considerable political uncertainty, and government and media attention on drug pricing – particularly in relation to older drugs – as well as a rapidly rising number of generic and biosimilar approvals. However, we continue to believe that innovation will win out in the long term, as evidenced by strong sales growth in biopharmaceuticals (+7.5%), which, in turn, was led by antibody-derived drugs (+16.7%), and explains the continued heavy investment in R&D.

### Investment in R&D remains strong

- ▶ In 2018, the top 15 companies reinvested 20.8% of pharmaceutical sales into new drug development, compared with 20.3% in 2017.
- ▶ The average R&D spend of the top 15 companies was \$7.0bn in 2018 (\$5.7bn in 2017) – ranging from \$9.9bn (Roche) to \$3.4bn (Bayer).
- ▶ R&D spend of the top 15 companies was \$90.7bn (\$86.6bn) out of a total estimated spend of \$122bn by 40 companies.

Companies are continuing to invest heavily in their futures, as all managements can see that successful innovation pays off with handsome returns (see pages 10-12). Over the last 10 years, the top 15 ranked companies have increased investment in R&D at a CAGR of 2.3%, from \$72.3bn (19.3% of pharma sales) to \$90.7bn (20.0%). In 2018, the highest relative spenders were Celgene (37.2% of sales), AZN (25.5%) and Bristol-Myers Squibb (24.1%), while the lowest spenders were GlaxoSmithKline (15.4%) and Amgen and Gilead (both 16.2%). It should be noted that the 15 constituent companies that comprise the top 15 are different each year.

## Company highlights

### Overview

No dramatic changes in rankings in the last 12 months...

There were no dramatic changes in ranking of pharmaceutical companies by Rx drug sales in 2018 compared with 2017. Pfizer remained the world #1 company, although it did see its market share eroded from 5.50% in 2017 to 5.25% in 2018.

#### Global pharmaceutical industry – 2018 ranking vs. 2008

---- Rank ----		Company	Ticker	Rx sales	----- Market share -----		
2018	2008			CAGR	2018	2008	Δ
1	1	Pfizer	PFE	+0.8%	5.25%	6.36%	-1.11%
2	5	Roche	ROG	+3.1%	5.19%	5.04%	+0.15%
3	4	Novartis	NOVN	+2.6%	5.17%	5.28%	-0.10%
4	7	Johnson & Johnson	JNJ	+5.2%	4.71%	3.73%	+0.98%
5	8	Merck & Co	MRK	+5.4%	4.32%	3.35%	+0.97%
6	2	Sanofi	SAN	-0.9%	4.06%	5.85%	-1.79%
7	11	AbbVie	ABBV	+6.5%	3.71%	2.60%	+1.11%
8	3	GlaxoSmithKline	GSK	-2.2%	3.51%	5.74%	-2.22%
9	14	Amgen	AMGN	+4.4%	2.60%	2.23%	+0.38%
10	25	Gilead Sciences	GILD	+15.6%	2.51%	0.77%	+1.73%
11	10	Bristol-Myers Squibb	BMY	+2.0%	2.49%	2.69%	-0.19%
12	9	Eli Lilly	LLY	+1.3%	2.48%	2.86%	-0.38%
13	6	AstraZeneca	AZN	-3.7%	2.43%	4.66%	-2.22%
14	15	Bayer	BAYGN	+2.7%	2.21%	2.23%	-0.01%
15	20	Novo Nordisk	NOVN	+7.1%	2.05%	1.36%	+0.69%
<b>Global Rx market</b>				<b>+2.8%</b>	<b>52.7%</b>	<b>54.7%</b>	<b>-2.0%</b>

Source: Hardman & Co Life Sciences Research

### Risers in 2018 – increased market share

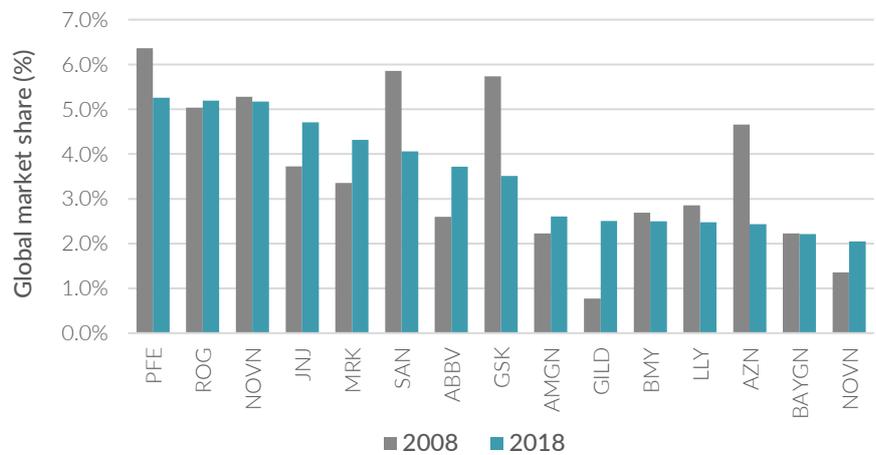
- ▶ **Roche:** The company is benefiting from being at the forefront of drugs derived from antibodies, with three drugs in the top 10, all of which play an important role in the combination approach to treating many forms of cancer. Overall sales growth of 7% was above the industry average, driving market share to 5.19% in 2018. Pressure is mounting from the introduction of biosimilars.
- ▶ **AbbVie:** The company can do no wrong at present, the enormous contribution from Humira (rheumatoid arthritis) being supported by successful recent launches of Mavyret (hepatitis C) and Imbruvica (lymphoma/leukaemia). These drove sales growth of 15% in 2018, and an increase in market share to 3.71% from 3.42%. The introduction of three Humira biosimilars could temper short-term prospects.
- ▶ **Bristol-Myers Squibb (BMY):** The recovery of BMY continues. Strong growth in Opdivo (lung cancer) and Eliquis (stroke/blood clots) led to further market share gains in 2018, from 2.33% to 2.49%. BMY has benefited from its early investment into antibody therapeutics. In the event that the company closes its proposed acquisition of Celgene, BMY would be propelled into the top five globally and the top three in the US market.

### Fallers in 2018 – decreased market share

- ▶ **Pfizer (PFE):** There was no obvious reason for PFE's loss of share in 2018, apart from the lack of growth in Lyrica (Alzheimer's) and the loss of US patent protection on Viagra. Another observation is PFE's lack of participation in the fast-growing antibody market.

- ▶ **Gilead Sciences (GILD):** GILD's leading position in anti-viral therapies for hepatitis C and HIV/AIDS was short-lived, with sales being eroded by increased competition. The market share of GILD fell back from 3.11% in 2017 to 2.51% in 2018, and it is now ranked #10 globally.
- ▶ **Teva:** The troubles at Teva continue, necessitating a significant restructuring of the business. Loss of sales and market share (from 2.30% to 1.76%) has seen the company fall out of the top 15 in 2018. This demonstrates how difficult it is for a company dominated by sales of generic drugs to overcome the loss of patent on one of its few branded products (Copaxone).

**Global ranking and market share, 2008-18 – winners and losers**



Source: Hardman & Co Life Sciences Research

**Upcoming changes**

*Takeda/Shire Pharmaceuticals*

...but consolidation will cause changes in the ranking in 2019

Completion of Takeda's (4502) acquisition of Shire Pharmaceuticals (SHP) in January 2019 will bring about a change in the rankings. Sales of these two companies were broadly similar in 2018 at ca.\$15.0bn, which ranked them #19 and #18, respectively. The combined entity is forecast to have sales in excess of \$30bn in 2019, which would rank it in the top 10.

**Pharmaceutical industry – evolution of global ranking 2003-2018**

#	2003		2008		2013		2018	
	Company	Share	Company	Share	Company	Share	Company	Share
1	Pfizer	8.95%	Pfizer	6.36%	Novartis	6.02%	Pfizer	5.25%
2	GlaxoSmithKline	6.88%	Sanofi	5.85%	Pfizer	5.81%	Roche	5.19%
3	Merck & Co	4.76%	GlaxoSmithKline	5.74%	Roche	5.03%	Novartis	5.17%
4	Johnson & Johnson	4.52%	Novartis	5.28%	Merck & Co	4.81%	Johnson & Johnson	4.71%
5	Aventis	4.39%	Roche	5.04%	Sanofi	4.77%	Merck & Co	4.32%
6	Novartis	4.38%	AstraZeneca	4.66%	GlaxoSmithKline	4.28%	Sanofi	4.06%
7	AstraZeneca	4.24%	Johnson & Johnson	3.73%	Johnson & Johnson	3.61%	AbbVie	3.71%
8	Roche	3.41%	Merck & Co	3.35%	AstraZeneca	3.30%	GlaxoSmithKline	3.51%
9	Bristol-Myers Squibb	3.23%	Eli Lilly	2.86%	Eli Lilly	2.64%	Amgen	2.60%
10	Eli Lilly	2.77%	Bristol-Myers Squibb	2.69%	AbbVie	2.41%	Gilead Sciences	2.51%
11	Wyeth	2.77%	Abbott Labs	2.60%	Teva	2.35%	Bristol-Myers Squibb	2.49%
12	Abbott Labs	2.45%	Schering-Plough	2.50%	Amgen	2.34%	Eli Lilly	2.48%
13	Takeda	2.21%	Wyeth	2.46%	Novo Nordisk	1.91%	AstraZeneca	2.43%
14	Sanofi	2.04%	Amgen	2.23%	Bayer	1.91%	Bayer	2.21%
15	Amgen	1.82%	Bayer	2.23%	Takeda	1.90%	Novo Nordisk	2.05%
		<b>58.8%</b>		<b>57.6%</b>		<b>53.1%</b>		<b>52.7%</b>

Source: Hardman & Co Life Sciences Research

## The US market in 2018

*We estimate the US pharmaceutical market grew 4.3% in 2018 and represented 39% of the global market*

Hardman & Co estimates that the US pharmaceutical market grew 4.3% in 2018 to \$337bn (\$323bn) and represented 39% of the global market. The US rate of growth was consistent with the global rate of growth, driven by the record number of new drugs approved by the FDA, positive demographics and technology advances. These are offsetting the declines in market share experienced by some large players, notably Pfizer and Teva, and pricing pressure led by the Trump administration. As a cross-check for the accuracy of our market estimate, the weighted average rate of growth for the top 20 companies in the US in 2018 (with only Boehringer Ingelheim still to report) was 4.2%. Our data are derived from monitoring companies with sales in the US of more than \$1.5bn, which represents an estimated 91% of the market.

In 2018, Rx drug sales for the top 15 ranked companies grew above average, at 5.2%, and represented 69.1% of the US market, as shown in the following table. Taking a longer-term view and interrogating the data over a 10-year period, these companies have seen their market share increase by 8.2 percentage points (ppts) over this period, with the likes of Gilead, Celgene and Novo Nordisk entering the ranking. However, compared with the market share of the top 15 companies in 2008, at 71.1%, which comprised a different company composition, the market share in 2018 fell 2.0ppts to 69.1%.

### US pharmaceutical industry – 2018 ranking vs. 2008

---- Rank ----					Rx sales	----- Market share -----		
2018	2008	Company	Ticker	10y CAGR	2018	2008	Δ	
1	5	Roche	ROG	+6.1%	7.04%	5.35%	+1.69%	
2	3	Johnson & Johnson	JNJ	+4.6%	6.91%	6.05%	+0.86%	
3	12	AbbVie	ABBV	+9.2%	6.39%	3.64%	+2.74%	
4	1	Pfizer	PFE	+1.6%	6.07%	7.15%	-1.08%	
5	8	Amgen	AMGN	+4.3%	5.17%	4.68%	+0.49%	
6	4	Merck & Co	MRK	+2.1%	4.86%	5.46%	-0.60%	
7	41	Gilead Sciences	GILD	+18.9%	4.81%	1.17%	+3.64%	
8	9	Novartis	NOVN	+3.1%	4.34%	4.39%	-0.06%	
9	2	GlaxoSmithKline	GSK	-2.1%	3.95%	6.73%	-2.78%	
10	10	Bristol-Myers Squibb	BMJ	+1.8%	3.73%	4.31%	-0.58%	
11	11	Eli Lilly	LLY	+2.2%	3.67%	4.07%	-0.41%	
12	7	Sanofi	SAN	-0.2%	3.67%	5.14%	-1.48%	
13	32	Celgene	CELG	+20.3%	2.97%	0.65%	+2.33%	
14	27	Shire Pharma	SHP	+17.0%	2.92%	0.84%	+2.08%	
15	22	Novo Nordisk	NOVO	+11.2%	2.56%	1.21%	+1.35%	
<b>US Rx market</b>				<b>+2.9%</b>	<b>69.1%</b>	<b>60.9%</b>	<b>+8.2ppts</b>	

Source: Hardman & Co Life Sciences Research

## Company highlights

### Risers

- ▶ **Roche** became the top-ranked drug company in the US in 2018, with a 7.04% market share, on the back of 14% sales growth, led by its mAb therapies. The company's CAGR over the last 10 years has been double that of the market.
- ▶ **AbbVie's** sales grew 18% in 2018, moving the company up to #3 (#5 in 2017), with a 6.39% market share. The reasons are the same as those driving its global presence.
- ▶ **Celgene's** global performance is being driven by that from the US, where the company derives two-thirds of its sales.

### Fallers

- ▶ For the third year running, **PFE** has seen an erosion of its market share, such that the company has dropped from #1 to #4 in the ranking. Although PFE has had three small molecule new chemical entities (NCEs) approved by the FDA, two of these are orphan drugs and too small to offset the lack of momentum from established drugs.
- ▶ **GILD** is struggling with increased competition and lack of exclusivity in its core anti-viral franchises, and with seven of its top 15 drugs experiencing sales declines in 2018, most notably Harvoni and Epclusa (both hepatitis C), and Atripla (AIDS/HIV). Overall US sales declined 13%, with GILD falling from #4 in 2017 to #7 in 2018 in the US ranking.

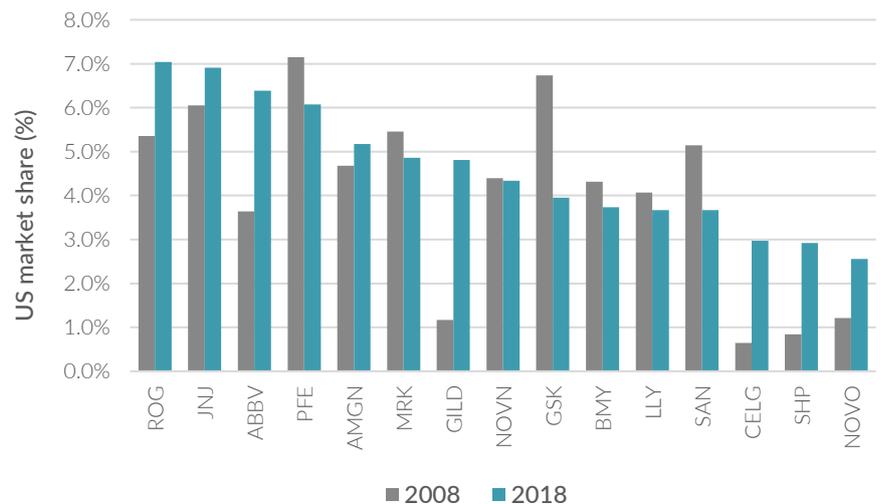
### Different strategies

*Last decade ideal for highlighting different strategies employed by management teams*

The table above and the chart below highlight the ranking of the top 15 companies by US Rx drug sales in 2018 compared with 2008, emphasising the change in market share over this period. The last decade accentuates how the different strategies employed by company management teams have panned out:

- ▶ **Organic growth:** Success is being generated largely by the launch of new drugs from in-house development and by embracing new technologies, e.g. Roche, AbbVie, GILD, Celgene and Novo Nordisk.
- ▶ **Buy-and-build:** Sales growth, and entry into the leading group of companies, has been through acquisitions, e.g. SHP and Teva. However, sometimes this is a step too far, as evidenced by Teva falling out of the top 15 US companies in 2018. All eyes are now focused on whether Takeda’s acquisition of SHP will be successful.
- ▶ **Defensive:** Market share has been retained by acquiring smaller competitors, often to offset the loss of patent expiry on major drugs, e.g. Pfizer, Merck & Co and Sanofi.

**US ranking and market share, 2008-18 – winners and losers**



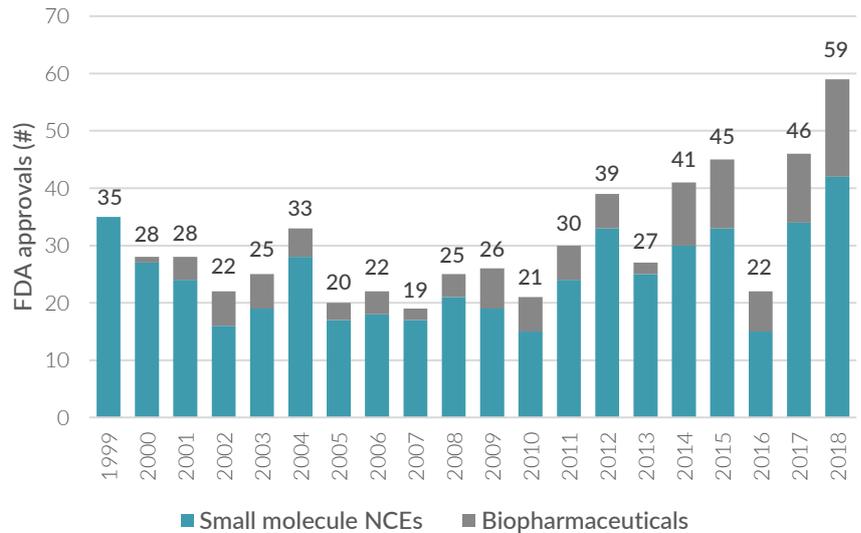
Source: Hardman & Co Life Sciences Research

## FDA approvals in 2018

A new record year for FDA activity

2018 proved to be another exceptional year for FDA activity, with the approval of 59 NCEs, easily surpassing the previous record set in 2017, when 46 new drugs were approved. The composition of this was 42 small molecule NCEs and 17 biopharmaceuticals/biologicals. The 20-year track record for new drug approvals by the FDA can be seen in the following chart.

FDA new drug approvals, 1999-2018



Source: FDA, Washington Analysis Group, Hardman & Co Life Sciences Research

- ▶ The approval of 59 NCEs represented a rise of 28% in 2018, continuing the positive trend since the low point in 2016.
- ▶ 42 (71%) were traditional small molecule NCEs and 17 (29%) were novel biopharmaceuticals.
- ▶ In contrast, there were 808 approvals of generic drugs, down 5% from the record 847 approved in 2017. As a reminder, ‘user fees’ for generic drugs (GDUFA) were introduced in 2013, and revised in 2017.
- ▶ Exiting FDA Commissioner, Scott Gottlieb, has a stated goal to improve efficiency at the agency, particularly with respect to oncology drugs and generics, and the rate of approvals seen over the last two years reflects this approach.
- ▶ Interestingly, there have been 356 NCEs approved by the FDA over the last 10 years. This averages out at just 0.91 new drug approvals per company p.a.
- ▶ According to Washington Analysis Group, at the end of 2018, there were 27 (37 at 31 December 2017) NCEs pending approval, and it cautions that, unless there are a considerable number of priority review applications and/or resubmitted NCEs early in the year, the total approvals for 2019 will be lower. This situation has been exacerbated by the public shutdown encountered in the early part of the year.
- ▶ From all the new drugs approved by the FDA in 2018, none made a significant/meaningful contribution to the IP owners’ sales.

## Top-selling drugs in 2018

- ▶ The biggest-selling drug in 2018 was, once again, Humira (AbbVie), with sales approaching \$20bn (+8%).
- ▶ The top 10 drugs in 2018 accounted for 9.5% of the world market – the same as in 2017.
- ▶ Biopharmaceuticals represented ca.25% of the world market in 2018, with sales of \$219bn, and growth of 7.5%.
- ▶ Within biopharmaceuticals, drugs derived from monoclonal antibodies (mAb) were the growth drivers, with 2018 sales of \$116bn, up 16%.
- ▶ The biggest-ever drug in history is still Lipitor, with cumulative ex-factory sales since launch of \$156bn.

## Top 10 best sellers

*Humira remains well out in front*

In 2018, the top 10 best-selling drugs recorded ex-factory sales of \$82.1bn and represented 9.5% of the global pharmaceutical market. Way out in front was Humira (adalimumab, AbbVie), with reported sales of \$19.9bn and growth of 8.2%. Since it was launched 16 years ago, this drug has generated cumulative sales of \$133.0bn. Humira was the first 'humanised' mAb to be approved by the FDA, and is indicated for the treatment of autoimmune diseases such as rheumatoid arthritis, Crohn's disease and psoriasis.

### Global top 10 best-selling drugs in 2018

Rank	Drug	Primary indication	Marketer	Sales (\$m)	Growth
1	Humira	Arthritis	ABBV	19,936	8.2%
2	Revlimid	Multiple myeloma	CELG	9,685	18.3%
3	Keytruda	Advanced melanoma	MRK	7,171	88.3%
4	Herceptin	Cancer	ROG	7,132	0.1%
5	Avastin	Cancer	ROG	6,996	2.9%
6	Rituxan/MabThera	Cancer	ROG	6,897	-8.1%
7	Opdivo	NSCLC	BMV	6,735	36.1%
8	Eliquis	Stroke/blood clots	BMV	6,438	32.1%
9	Pevnar	pneumococcal vaccine	PFE	5,802	3.6%
10	Remicade	Arthritis	JNJ	5,326	-15.7%

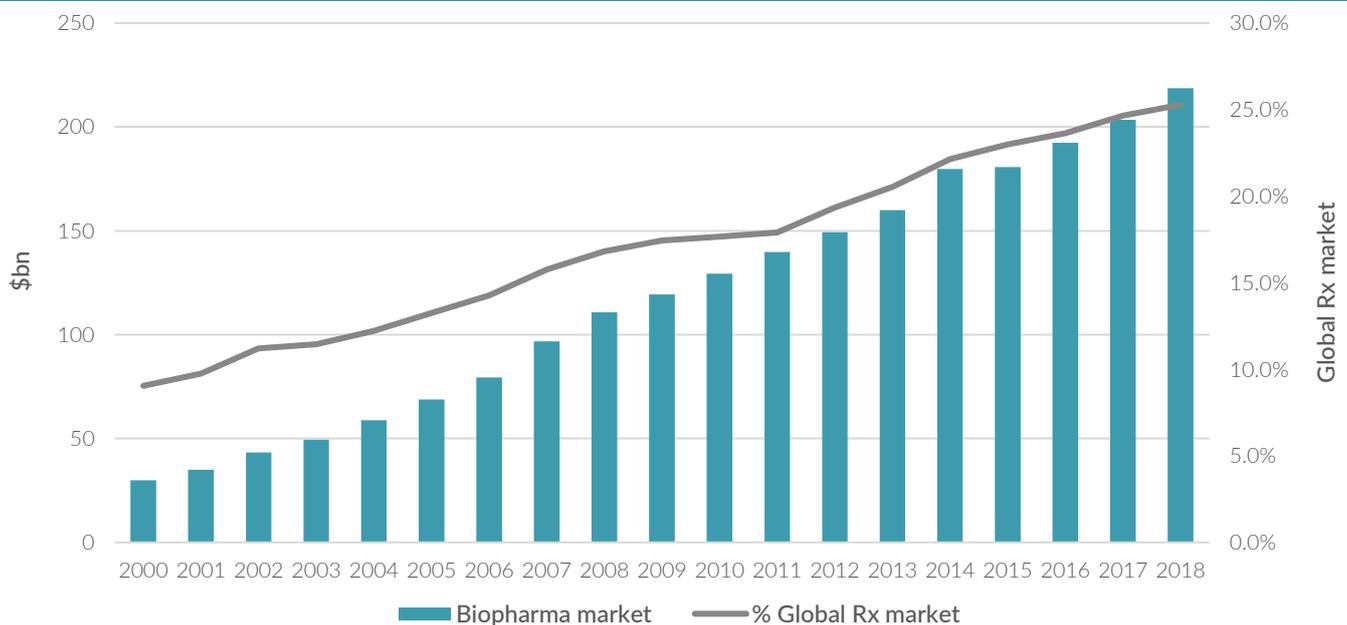
Source: Hardman & Co Life Sciences Research

The fastest-growing drug within the top 10 was Keytruda (pembrolizumab, Merck & Co), rising 88% to \$7.2bn, as it becomes included in more combination cancer schedules. Revlimid (lenalidomide, Celgene) for multiple myeloma should also be highlighted for its growth rate of 18.3% to \$9.7bn, and demonstrating how innovation can transform a company's fortunes, and attract the attention of a predator (BMV).

## Biopharmaceuticals

*Above-average rate of growth for biopharmaceuticals in 2018*

Within the overall global prescription market, drugs classified as biopharmaceuticals (ca.130 + vaccines) had reported sales of \$218.7bn in 2018, and now represent 25.3% of the entire market. The growth rate in 2018 was again above average, at 7.5%. Every year since 2000, biopharmaceuticals have represented a greater proportion of the global pharmaceutical market. The steady growth in the annual sales of biopharmaceutical drugs, together with their rising proportion of the global Rx drugs market, is demonstrated in the following graphic.

**Evolution of biopharmaceutical sales – 2000-2018**


Source: Hardman & Co Life Sciences Research

For clarification, we classify a biopharmaceutical as a drug derived from biological sources, which may be through extraction or semi-synthesised, and would include the likes of monoclonal antibodies (mAb), vaccines and blood products.

Over the last 10 years, the biopharmaceutical market has grown at a compound rate of 7.0%, compared with 2.8% for the entire Rx drug market.

**Evolution of global biopharmaceuticals market – 2003 to 2018**

2018 rank	Drug	2003 (\$m)	2008 (\$m)	2013 (\$m)	2018 (\$m)	CAGR 2008-18
1	Vaccines	7,318	17,088	21,946	28,731	5.3%
2	Insulin/analogues	6,282	13,732	24,877	26,894	7.0%
3	Humira	280	4,521	10,659	19,936	16.0%
4	Enbrel	1,599	6,445	8,790	9,034	3.4%
5	Keytruda	0	0	0	7,171	-
6	Herceptin	876	4,680	6,558	7,132	4.3%
7	Avastin	0	4,785	6,746	6,996	3.9%
8	Rituxan/MabThera	2,065	5,443	7,498	6,897	2.4%
9	Obdivo	0	0	0	6,735	-
10	Human Growth Hormone	2,431	4,658	5,646	5,562	1.8%
<b>Total biopharmaceuticals</b>		<b>49,472</b>	<b>110,757</b>	<b>159,977</b>	<b>218,687</b>	<b>+7.0%</b>
% global Rx market		9.0%	16.8%	20.5%	25.3%	+2.8%

Source: Hardman & Co Life Sciences Research

**Antibody-derived therapeutics**

There are now 80 approved drugs on the market derived from mAb. Seven of the top 10 drugs in 2018 were based on mAb. In 2018, drugs derived from mAb were the fastest-growing sub-segment of the Rx market, with growth of 16.7% to ca.\$115.8bn, and representing 13% of the entire market. There are currently 80 (71 in 2017) regulatory-approved mAb drugs. The following table shows the ranking of the top 10 drugs by ex-factory sales. The table highlights also that drugs derived from mAb have generated cumulative sales approaching a staggering \$787bn since the first one was launched in 1995. These figures are expected to rise further in coming years, given the large numbers currently in late-stage clinical trials.

There are 80 approved drugs derived from antibodies...

...which had sales of ca.\$115.8bn in 2018, with growth of 16.7%

## Top 10 antibody drugs – 2018

2018 rank	Drug	Generic name	Company	2017 (\$m)	2018 (\$m)	Growth	Cumulative (\$m)
1	Humira	adalimumab	AbbVie	18,427	19,936	+8.2%	133,050
2	Keytruda	pembrolizumab	Merck & Co	3,809	7,171	+88.3%	13,003
3	Herceptin	trastizumab	Roche	7,128	7,132	+0.1%	80,901
4	Avastin	bevacizumab	Roche	6,797	6,996	+2.9%	77,884
5	Rituxan/MabThera	rituximab	Roche	7,508	6,897	-8.1%	95,355
6	Opdivo	nivolumab	Bristol-Myers Squibb	4,948	6,735	+36.1%	15,938
7	Remicade	infliximab	Johnson & Johnson	6,315	5,326	-15.7%	78,139
8	Stelara	ustekinumab	Johnson & Johnson	4,011	5,156	+28.5%	20,605
9	Soliris	eculizumab	Alexion Pharma	3,144	3,563	+13.3%	19,096
10	Cosentyx	secukinumab	Novartis	2,071	2,837	+37.0%	6,297
<b>Total mAb sales</b>				<b>99,237</b>	<b>115,767</b>	<b>+16.7%</b>	<b>786,518</b>

Source: Hardman & Co Life Sciences Research

It is clear that certain companies embraced this technology early on and are reaping the benefits. Roche was one of the first to buy in to biotechnology through its innovative deal with Genentech. The rewards from these investments are considerable. The question for companies and investors alike is, therefore, 'what is the next technology on which companies should be focusing?'

## Entry of biosimilars

### Increase in FDA-approved biosimilars

However, a combination of patent expiry and increased activity at the FDA with respect to the approval of biosimilars is likely to influence the future growth rate of biopharmaceuticals and, in particular, mAbs. The following table indicates that there have been 14 biosimilars approved, up from six in 2017, by the FDA for a number of the current top-selling drugs.

### FDA-approved biosimilars

Generic	Original brand	Marketer	Biosimilar	Company
<b>2016</b>				
infliximab	Remicade	Johnson & Johnson	Inflectra	Celltrion
adalimumab	Humira	AbbVie	Amjevita	Amgen
<b>2017</b>				
infliximab	Remicade	Johnson & Johnson	Renflexis	Samsung Bioepis
adalimumab	Humira	AbbVie	Cyltezo	Boehringer Ingelheim
bevacizumab	Avastin	Roche	Mvasi	Amgen
trastizumab	Herceptin	Roche	Ogivri	Mylan/Biocon
infliximab	Remicade	Johnson & Johnson	Ixifi	Pfizer
<b>2018</b>				
erythropoetin	Epogen/Procrit	Amgen	Retacrit	Pfizer
pegfilgastrim	Neulasta	Amgen	Fulphilia	Mylan/Biocon
filgastrim	Neupogen	Amgen	Nivistym	Pfizer
adalimumab	Humira	AbbVie	Hyrmoz	Novartis
pegfilgastrim	Neulasta	Amgen	Udenyca	Coherus
rituximab	Rituxan	Roche	Truxima	Celltrion/Teva
trastizumab	Herceptin	Roche	Herzuma	Celltrion/Teva

Source: Washington Analysis Group, Hardman & Co Life Sciences Research

## The \$100bn club

### Six drugs have generated cumulative ex-factory sales of >\$100bn since launch

Although most analysis is done on sales made in an individual year and the growth that has been generated, the strength of our database allows us to look at the ex-factory sales in a slightly different way – cumulative sales since launch – which also provides an idea of return on R&D investment. In the entire history of pharmaceuticals, the number of drugs that have achieved ex-factory sales in excess of \$100bn since launch remains at six. Lipitor remains the biggest-ever-selling drug, with cumulative sales of \$156.1bn since its launch in 1997.

## About the authors

### *Dr Martin Hall*



Martin's career in the City started as a healthcare analyst in 1987, working at Morgan Grenfell and then UBS. He joined HSBC in 1992, where he was Head of Global Pharmaceutical/Healthcare Equity Research. In 2005, he set up as an independent Life Sciences Analyst and Corporate Broker under the umbrella of Eden Financial Limited. Martin is acknowledged for his thought-provoking and opinionated research. He joined Hardman & Co in June 2013.

Martin qualified as a pharmacist (B.Pharm.Hons) at the School of Pharmacy, University of London, and has a PhD in Neuropharmacology, also from the University of London. After two years of post-doctoral research under a Royal Society Fellowship at the Collège de France, Paris, he became leader in Biochemical Pharmacology at the Parke-Davis Research Centre in Cambridge. Martin is a member of Royal Pharmaceutical Society of Great Britain.

### *Dr Dorothea Hill*



Dorothea joined the Life Sciences team as an Equity Research Analyst in August 2016. She began her career researching vaccines as part of an international Gates Foundation/Wellcome Trust collaboration, following which she undertook a PhD in genetics and vaccines for meningococcal disease at the University of Oxford. She has broad experience in the field of vaccines research and development, having worked on the molecular biology of bacterial pathogens, antigen discovery, molecular diagnostics, and next-generation sequencing technologies. Dorothea has authored 13 papers, including first author publications in the Lancet Infectious Diseases and in Nature's Scientific Reports. She is passionate about drug development and the commercialisation of medical innovation.

### *Dr Grégoire Pavé*



Greg is an analyst in the Life Sciences team at Hardman & Co, and has considerable experience in the field of drug discovery and development. In 2003, he enrolled in a team-leader post-doctoral position at Imperial College London, working on natural product synthesis. In 2005, he joined Cancer Research Technology, the development and commercial arm of Cancer Research UK, where he was involved in multiple oncology projects. Greg has broad experience in drug discovery and development projects, from target identification and validation through to clinical trials. He has also gained valuable experience in evaluating life science projects and their commercial opportunities. In addition, he has played a role of reviewer in peer-review journals from the American Chemical Society. He is also an author of 14 scientific papers and owner of four patents. Greg joined Hardman & Co in March 2016. He has a PhD in Medicinal Chemistry from the University of Orléans in France, and holds the IMC and PRINCE2 qualifications.

## Glossary

FDA	US Food & Drug Administration
mAb	Monoclonal Antibody
GDUFA	Generic Drug User Fee Amendments
NCE	New Chemical Entity
NME	New Molecular Entity
OTC	Over-The-Counter
Rx	Prescription

### Companies (Ticker ISIN) mentioned in this report

AbbVie (ABBV US00287Y1091), Amgen (AMGN US0311621009), AstraZeneca (AZN GB0009895292), Bayer (BAYGN DE000BAY0017), Bristol-Myers Squibb (BMY US1101221083), Celgene (CELG US1510201049), Gilead Sciences (GILD US3755581036), GlaxoSmithKline (GSK GB0009252882), Johnson & Johnson (JNJ US4781601046), Eli Lilly (LLY US5324571083), Merck & Co (MRK US589333Y1055), Novartis (NOVN CH0012005267), Novo Nordisk (NOVO DK0060534915), Pfizer (PFE US7170811035), Roche (ROG CH0012032113), Sanofi (SAN FR0000120578), Takeda (4502 JP3463000004), Teva (TEVA US8816242098).

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