

EvaluatePharma®

# World Preview 2016, Outlook to 2022



# Welcome to the EvaluatePharma® World Preview 2016, Outlook to 2022

The ninth edition of EvaluatePharma's World Preview brings together many of our analyses to provide a top level insight, from the world's financial markets, into the expected performance of the industry between now and 2022. Based on EvaluatePharma's coverage of the world's leading 5,000 pharmaceutical and biotech companies, the World Preview highlights trends in prescription drug sales, patent risk, R&D spend, global brand sales and market performance by therapy area. Also included this year are new analysis on Worldwide Pharma Innovation 2008-2022 with insights into the companies with most valuable pipelines based on NPV analysis, best performing products and the most successful launches since 2010. Complimentary copies of the full report can be downloaded at:

www.evaluate.com/PharmaWorldPreview2016

### **Foreword**

Recent events in the world of health care could give cause to think that the good times might be at an end for the pharma industry, following a spectacular four-year bull run.

Increasingly vocal politicians railing against US drug pricing, a weak global recovery, the uncertainties thrown up by Brexit, and the outcome of US presidential race have all combined to make investors jittery. The situation has led to a sharp re-rating of stock prices in 2016 and the IPO and venture financing markets being hit heavily.

But for those willing to take a longer term view the outlook is a bit more nuanced.

This year's World Preview shows worldwide prescription sales are forecast to show annual compound growth of 6.3% between 2016 and 2022.

Most of this growth is being driven by the prospects for a raft of new products that will come onto the market in the next seven years – treatments that will hopefully take the torch from industry's superstars, like Harvoni, whose light is now fading.

Roche's Tecentriq was approved in bladder cancer this year and the anti-PD-L1 MAb is set to be one of the best selling drugs in 2022, its stable mate Ocrevus is set to be approved this year and along with other R&D stars such as dupilumab should help the industry to keep moving in the right trajectory.

Meanwhile, recent R&D productivity gains have resulted in ever more treatments moving swiftly through the pipeline, with 56 products approved in 2015, a number that broke what seemed like the unassailable record of 50 in 2014.

However, at the current run rate 2016 might only see 47 drugs approved, raising the following question: rather than being a new normal, was 2015 the peak? If this is the case then the forecast 2.8% increases in compounded annual R&D spend to 2022 might now only yield diminishing returns.

The potential for falling drug approvals is not the only possible change in the industry. For the first time in years Novartis has had its crown snatched as the number one pharma company by prescription sales. Roche is now top of the heap, albeit by the most slender of margins, thanks in part to some of the more untraditional areas of its pipeline. Multiple sclerosis drug Ocrevus and haemophilia treatment emicizumab are both among the top 20 most valuable R&D projects and have helped Roche eclipse its fellow countryman as well as claim the title of the company with the most valuable pipeline.

But with only a cigarette paper between Novartis and Roche, the current rankings could be quickly reversed, especially given the Roche's higher exposure to biosimilar competition.

#### **Foreword**

What perhaps is more interesting in the battle of giants is the rapid advancement made by big biotech Celgene, and surprisingly Shire, both of whom have significantly improved their positions in the table – Celgene can thank the continued strength of Revlimid and newer products Otezla and Pomalyst, while Shire has achieved its advancement by the acquisition of Baxalta.

Certain therapy areas are also set to continue to increase rapidly, adding to the strong overall growth forecasts for the industry. Oncology remains the sector's powerhouse, clocking up compound annual sales growth of almost 13% over the next seven years, driven by recent advances in immunotherapy that have facilitated the launch of drugs such as Keytruda, Imbruvica and Tecentriq.

Expanding waistlines across the globe are helping to prop up sales of anti-diabetic drugs. The therapy area is set to grow 7% annually by 2022.

The aging population and the concomitant need to treat macular degeneration are driving the expansion of sales in the sensory organs sector.

Indeed, there is no therapy area forecast to see a decline in sales. The worst performing, anti-virals, only recorded flat growth due mainly to the rapid slowdown in hepatitis C sales following a spectacular peak in 2015.

There are, however, several issues that could spoil this rosy picture of uninterrupted growth.

Few could have predicted the savage reversal of fortune suffered by speciality pharma groups and particularly Valeant. These were the companies that drove much of the M&A activity and sector share price gains in 2014-2015. During that time they were rewarded for their business models of aggressive debtfuelled expansion, and price increases for elderly products.

It was the eventual political scrutiny over pricing of some of these older drugs that started the wheels in motion, first bringing Turing Pharmaceuticals to its knees and then Valeant. The recent outcry over Mylan's price increases for EpiPen –followed by the company's repeated capitulations – show just how sensitive pricing models can be to political pressure.

What this could result in is companies having to spend more time in pricing drugs according to real world benefits and proven efficacy, rather than what they believe the market can bear.

And with the US presidential elections around the corner, the political pressure on pricing is unlikely to ease. While any rhetoric is unlikely to make it into legislation anytime soon, the uncertainty could impact the industry. What all of this will almost certainly do is make market access one of the most important deciding factors in a drug's success or failure, as shown by the slow uptake of the PCSK9 class and heart failure drug Entresto.

The other seismic impact on the industry could be the widespread adoption of biosimilars. Last month Sandoz's biosimilar version of Enbrel was approved in America, in the next five years some of the industry's biggest beasts will succumb to lookalike competition in the US. The likes of Humira, Rituxan and Avastin are all forecast to fall by 2020.

#### **Foreword**

The big question is if sell side analysts have properly estimated the threat. If the uptake of Remsima in Europe, which has forced Merck to discount its list price for Remicade by 25% in the UK and seen biosimilars capture over 90% of the Norwegian market, are anything to go by then the sales of biosimilars in the US could be much higher than currently forecast.

However, the biosimilar threat will be held at bay, for now, until biosimilar developers can finally end the patent dance, a process that is currently keeping approved US products off the market.

But strong support for biosimilars is coming both from politicians and payers, with the likes of Express Scripts weighing into the debate about how much of the healthcare budget could be saved by using biosimilar products.

Drug failure also remains a risk to the industry. Opdivo's recent disappointment in non-small cell lung cancer should serve as a warning, not only for the perils involved in clinical trials, but also the over exuberance of sell-side forecasts.

So while currently the industry does have plenty to celebrate, there are numerous potential brakes on progress that could make the outlook much more mixed.

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## **Analysis Highlights**



- Worldwide prescription drug sales forecasted to grow at 6.3% (CAGR) 2016-2022
- 50% of the 2022 increase in sales to come from R&D projects (+\$169bn)
- Novartis and Roche to compete head to head for the crown of worldwide prescription sales in 2022. Pfizer to challenge them following Medivation acquisition.
- Celgene (+16%) and Shire (+19%) expected to record the fastest sales growth (CAGR) by 2022.

### **Analysis Highlights**

- Biologics to contribute 50% of the Top 100 product sales by 2022;
   Roche leads market.
- Roche has the highest valued pipeline (NPV) at \$43bn in 2022.
- Gilead is the top value creator based on 2015 sales from recently launched products.
- Tecfidera best commercial launch after hepatitis C's success stories Harvoni and Sovaldi.
- Roche's ocrevus and Sanofi's dupilumab projected to be the most valuable R&D projects.
- Worldwide pharmaceutical R&D spend expected to grow by 2.8% (CAGR) to \$182bn in 2022.
- Roche overtakes Novartis with biggest spend on pharmacuetical R&D in 2022.
- New drug approvals in 2015 reach a record 56 NMEs.
- Oncology is still the largest therapy area by sales (+12.5% CAGR) 2016-22.
- Roche remains the leader of the oncology field but its growth is set to fade due to biosimilars.
- Abbvie still dominates anti-rheumatics market in 2022; high expectations on Lilly's baricitinib.
- GlaxoSmithKline gains vaccines market leadership following oncology portfolio deal swap with Novartis.
- Pfizer's pneumococcal vaccine Prevnar-13 remains the top selling vaccines product.
- Gilead's lead continues in anti-viral market in 2022 largely due to its HIV portfolio.
- Opdivo and Revlimid to compete for the top selling products in the world in 2022.
- Roche products make up 10% of top 50 selling products in the world in 2022.
- AbbVie's Humira will continue to be the leading product in the USA in 2022, with sales of \$10.7bn.
- Xarelto to emerge as the top selling brand in Europe with €2.5bn sales in 2022.

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# Worldwide Prescription Drug Sales (2008-2022)



### Worldwide prescription drug sales forecasted to grow at 6.3% (CAGR) through to 2022.

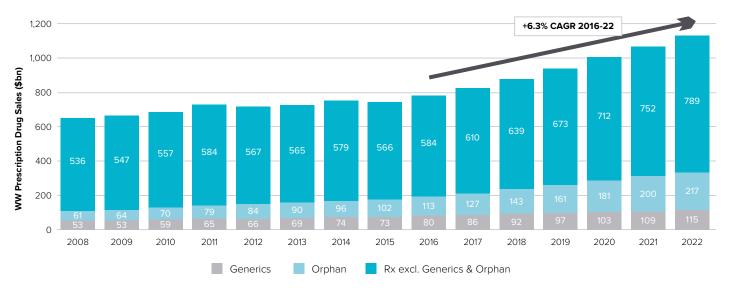
According to EvaluatePharma® consensus forecasts, the pharmaceutical industry is set to grow at 6.3% per year (CAGR) reaching \$1.12tr by 2022. The new wave of innovative therapies (Opdivo, Keytruda and Ibrance among others) approved by regulators in the last three years will be the core engine behind this trend and it also seems to prove that the transformation of the pharmaceutical R&D model is moving into the right direction. The orphan drug market is expected to almost double between 2016-22, peaking at \$217bn in 2022 and further demonstrates that R&D programmes are increasingly oriented towards more narrow patient populations

characterised by larger unmet need and easier market access.

There are two dynamics at play that could affect this optimistic outlook. Firstly, the \$249bn of sales at risk between 2016 and 2022 signals that the pharma industry has just entered a second patent cliff era where top biologic blockbusters will be challenged by biosimilars. And the current scenario modelled by brokers tends to forecast a very conservative impact for upcoming biosimilars. Secondly, the US market access landscape is rapidly transforming and the criteria set by payers, once looser, are much more stringent. The slow uptake of Entresto and the PCSK9 inhibitors (Praluent and Repatha), as well as the recent increase in the number of drug exclusions announced by both CVS and Express Scripts are points in case.

#### Worldwide Total Prescription Drug Sales (2008-2022)

Source: EvaluatePharma® August 2016



#### Worldwide Sales At Risk from Patent Expiration (2008-2022)

Source: EvaluatePharma® August 2016



**Patent Analysis:** 'Total Sales at Risk' represents the worldwide product sales in the year prior to patent expiry but allocated to the year of expiry. E.g. Plavix had sales of \$7.1bn in 2011, this is shown above as 'At Risk' in 2012.



#### **Worldwide Prescription Drug Sales (2008-2022)**

Source: EvaluatePharma® August 2016

	WW Prescription Sales (\$bn)														
Year	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022
Prescription	650	663	687	729	717	724	749	742	778	822	873	931	996	1,060	1,121
Growth per Year		+2.0%	+3.5%	+6.1%	-1.6%	+0.9%	+3.5%	-1.0%	+4.8%	+5.7%	+6.2%	+6.6%	+7.0%	+6.5%	+5.7%
Change vs. June 2015 (\$bn)									6	6	2	5	9		
Generics	53	53	59	65	66	69	74	73	80	86	92	97	103	109	115
Generics as % of Prescription	8.2%	8.0%	8.6%	9.0%	9.2%	9.5%	9.9%	9.9%	10.3%	10.5%	10.5%	10.4%	10.4%	10.3%	10.2%
Prescription excl. Generics	596	610	627	663	651	655	675	669	698	736	781	834	893	952	1,006
Growth per Year		+2.3%	+2.8%	+5.8%	-1.9%	+0.6%	+3.1%	-1.0%	+4.4%	+5.5%	+6.2%	+6.7%	+7.1%	+6.6%	+5.7%
Orphan	61	64	70	79	84	90	96	102	113	127	143	161	181	200	217
Prescription excl. Generics & Orphan	536	547	557	584	567	565	579	566	584	610	639	673	712	752	789

Prescription incl. Generics CAGR 16-22 +6.3%

Note: Industry sales based on Top 500 pharmaceutical and biotech companies.

Sales to 2015 based on company reported sales data. Sales forecasts to 2022 based on a consensus of leading equity analysts' estimates for company product sales and segmental sales.

# Regional Prescription Drug Sales: USA, Europe & Japan (2013-2015)



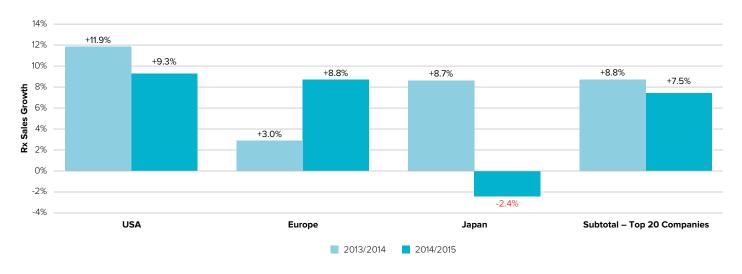
Key prescription drug sales jump 7.5% in 2015, driven by the sustained growth in both US and Europe. Japan slumps 2.4% in yen.

According to sales reported by the Top 20 companies, the market across US, Europe and Japan has accelerated by 7.5% in 2015, primarily driven by the growth of new innovative therapies in US

(+9.3% vs. 2014) and Europe (+8.8% vs. 2014). While questions remain on the sustainability of this trend in the long run, we are not expecting any major change in 2016. The growth in the western regions is counterbalanced by the slow down in the Japanese market where the Top 20 companies' sales declined by 2.4% in local currency vs. the previous year.

# 2014 & 2015 Regional Local Currency Prescription Drug Sales Growth: Top 20 Companies in each Region

Source: EvaluatePharma® August 2016



#### Regional Prescription Drug Sales (2013-2015): Observed Top 20 Companies in each Market

Source: EvaluatePharma® August 2016

					Growth					
	Sales (\$bn)			(US\$	)	(Local Currency)				
Region	2013	2014	2015	2013/14	2014/15	2013/14	2014/15			
USA	204.2	228.6	250.0	+11.9%	+9.3%	+11.9%	+9.3%			
Europe	118.3	121.9	110.7	+3.0%	-9.1%	+3.0%	+8.8%			
Japan	65.2	58.4	52.3	-10.5%	-10.5%	+8.7%	-2.4%			
Subtotal - Top 20 Companies	387.8	408.9	413.0	+5.4%	+1.0%	+8.8%	+7.5%			
Unallocated	335.5	339.8	328.5							
Total Worldwide Prescription Sales	723.3	748.7	741.5	+3.5%	-1.0%					

#### **Currency Sensitivity Analysis**

Source: EvaluatePharma® August 2016

Currency (ending December)	2012	2013	2014	2015	2012/13	2013/14	2014/15
<b>Euro</b> (1€ = US \$)	1.33	1.33	1.11	1.12	+0.0%	-16.5%	+0.5%
<b>Japan</b> (100 ¥ = US \$)	1.25	1.03	0.95	0.84	-18.1%	-7.7%	-11.6%
China (1 RMB = US \$)	0.16	0.16	0.16	0.16	+2.6%	-0.2%	-1.0%

Analysis is based on observing the reported geographic sales from US, Europe and Japan for the top 20 companies in each market in 2015. In addition, available reported government data on pharmaceutical purchases was reviewed.

# Regional Prescription Drug Sales: USA (2013-2015)



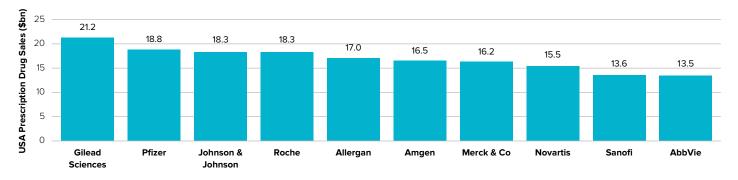
## US prescription drug market continues to grow at a sustained pace, +9.3% vs. 2014. Gilead mantains number one spot.

Despite the growing challenges posed by US payers and large pharmacy benefit managers, the US market continues to perform strongly with 9.3% growth vs. the previous year. Gilead mantains its leadership position fuelled by the growth

of its hepatitis C franchise, notable performance are also shown by Abbvie, Celgene and Valeant. Negative performances have been observed for AstraZeneca, Sanofi and GSK where their key products have suffered from increasing branded and generic competition, although the near term outlook is expected to show improvement.

#### **USA Prescription Drug Sales in 2015: Top 10 Companies**

Source: EvaluatePharma® August 2016



## USA Prescription Drug Sales (2013-2015): Top 20 Companies (Pro-forma adjusted for M&A)

		U	S Prescription Sa	les (\$bn)	Growth (US\$)		
Rank	Company	2013	2014	2015	2013/14	2014/15	
1.	Gilead Sciences	6.7	18.2	21.2	+171.6%	+16.8%	
2.	Pfizer	16.3	16.5	18.8	+1.0%	+14.1%	
3.	Johnson & Johnson	13.9	17.4	18.3	+25.0%	+5.2%	
4.	Roche	16.3	17.3	18.3	+6.2%	+5.8%	
5.	Allergan	11.1	15.9	17.0	+42.5%	+7.3%	
6.	Amgen	14.0	14.7	16.5	+4.9%	+12.2%	
7.	Merck & Co	14.9	14.2	16.2	-4.3%	+14.2%	
8.	Novartis	15.2	15.2	15.5	-0.3%	+2.0%	
9.	Sanofi	12.9	13.9	13.6	+8.4%	-2.6%	
10.	AbbVie	10.2	10.8	13.5	+6.5%	+24.7%	
11.	Teva Pharmaceutical Industries	10.5	10.6	11.2	+1.7%	+5.8%	
12.	GlaxoSmithKline	9.1	10.7	10.4	+17.7%	-3.1%	
13.	AstraZeneca	9.7	10.1	9.5	+4.4%	-6.4%	
14.	Eli Lilly	11.7	7.9	8.6	-32.6%	+8.9%	
15.	Novo Nordisk	7.0	7.7	8.5	+10.6%	+10.1%	
16.	Bristol-Myers Squibb	8.3	7.7	8.2	-7.2%	+6.1%	
17.	Valeant Pharmaceuticals International	3.2	4.5	7.1	+39.8%	+59.2%	
18.	Biogen	3.6	5.6	6.5	+55.5%	+17.6%	
19.	Celgene	3.9	4.5	5.6	+16.1%	+25.0%	
20.	Boehringer Ingelheim	5.9	5.2	5.4	-11.7%	+3.4%	
	Total	204.2	228.6	250.0	+11.9%	+9.3%	

#### **Country Level Retail Expenditure on Prescription Drug Sales**

Source: EvaluatePharma® August 2016

		Sales (\$bn)			US\$)
Country	2013	2014	2015	2013/14	2014/15
USA <sup>1</sup>	271.1	305.1	328.4	+12.5%	+7.6%

1: Source: USA CMS. 2015 is a CMS forecast.

Analysis is based on observing the reported geographical prescription drug sales in the US for the top 20 companies in 2015. In addition, available government data (CMS) on pharmaceutical purchases of drugs was reviewed.

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# Regional Prescription Drug Sales: Europe (2013-2015)



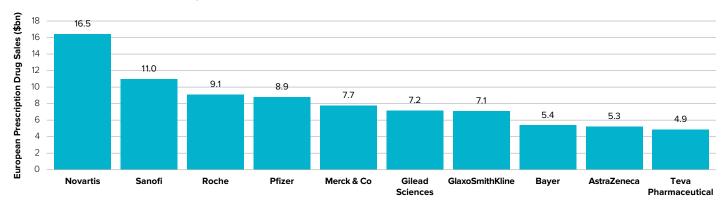
## Europe surprises with a 8.8% growth rate vs. 2014. Novartis still market leader, but Gilead is the largest growth driver.

The European trend follows the same growth trajectory observed in the US with 8.8% growth in local currency vs. 2014 (Top 20 companies). While Novartis and Sanofi are still at the top of the rankings (respectively, number one and two), Roche overtakes Pfizer on the podium. Among the growth drivers Gilead deserves a special mention with 58.4% growth vs. previous year thanks to the uptake of its hepatitis C franchise in Europe. Celgene and GSK have

also shown strong growth, +36% and +28.4% respectively.Negative performances were evident for Pfizer, AstraZeneca and Merck & Co, although the anticipated uptake of novel therapies is expected to reverse this trend in the 2016-17 period.If we look at the market as a whole based on government reported data sources (Evaluate European Drug Forecast\*), Europe is expected to show a 3% CAGR 2016-22, mainly driven by the launch of new products currently in development. Xarelto to emerge as the top selling brand with €2.5bn of sales in 2022.

#### **European Prescription Drug Sales in 2015: Top 10 Companies**

Source: EvaluatePharma® August 2016



#### **Europe Prescription Drug Sales (2013-2015): Top 20 Companies**

Source: EvaluatePharma® August 2016

		EU Pre	scription Sa	les (\$bn)	Growth	(US\$)	EU Preso	ription Sale	s (€bn)	Growt	h (€)
Rank	Company	2013	2014	2015	2013/14	2014/15	2013	2014	2015	2013/14	2014/15
1.	Novartis	17.2	17.5	16.5	+1.8%	-5.8%	12.9	13.2	14.8	+1.8%	+12.8%
2.	Sanofi	13.3	13.1	11.0	-1.1%	-16.2%	10.0	9.9	9.9	-1.1%	+0.3%
3.	Roche	10.0	10.3	9.1	+3.2%	-11.9%	7.5	7.8	8.2	+3.2%	+5.5%
4.	Pfizer	11.0	10.9	8.9	-0.9%	-18.9%	8.3	8.2	8.0	-0.9%	-2.9%
5.	Merck & Co	9.6	9.6	7.7	-0.4%	-19.5%	7.2	7.2	7.0	-0.4%	-3.6%
6.	Gilead Sciences	3.6	5.4	7.2	+50.6%	+32.3%	2.7	4.1	6.5	+50.6%	+58.4%
7.	GlaxoSmithKline	6.6	6.6	7.1	+0.5%	+7.2%	5.0	5.0	6.4	+0.5%	+28.4%
8.	Bayer	5.2	5.8	5.4	+12.2%	-7.5%	3.9	4.4	4.9	+12.2%	+10.8%
9.	AstraZeneca	6.7	6.6	5.3	-0.3%	-19.8%	5.0	5.0	4.8	-0.3%	-4.0%
10.	Teva Pharmaceutical Industries	6.0	5.8	4.9	-2.8%	-16.0%	4.5	4.4	4.4	-2.8%	+0.6%
11.	Eli Lilly	4.3	4.5	3.9	+3.9%	-12.5%	3.3	3.4	3.6	+3.9%	+4.8%
12.	Bristol-Myers Squibb	3.9	3.6	3.5	-8.6%	-2.8%	3.0	2.7	3.1	-8.6%	+16.4%
13.	Novo Nordisk	3.6	3.6	3.1	+0.5%	-13.8%	2.7	2.7	2.8	+0.5%	+3.2%
14.	Merck KGaA	3.3	3.2	3.0	-2.3%	-6.0%	2.5	2.4	2.7	-2.3%	+12.6%
15.	Boehringer Ingelheim	3.9	3.6	3.0	-6.4%	-16.6%	2.9	2.7	2.7	-6.4%	-0.1%
16.	Astellas Pharma	2.6	2.9	2.8	+8.5%	-2.6%	2.0	2.2	2.5	+8.5%	+16.6%
17.	Celgene	1.9	2.3	2.6	+23.9%	+13.6%	1.4	1.7	2.4	+23.9%	+36.0%
18.	Biogen	1.6	2.2	2.2	+38.3%	-1.4%	1.2	1.7	2.0	+38.3%	+18.1%
19.	STADA Arzneimittel	2.6	2.6	2.2	+1.8%	-16.9%	1.9	2.0	1.9	+1.8%	-0.5%
20.	UCB	1.5	1.5	1.3	+3.3%	-12.3%	1.1	1.1	1.2	+3.3%	+5.0%
	Total	118.3	121.9	110.7	+3.0%	-9.1%	89.1	91.7	99.8	+3.0%	+8.8%
	Currency Impact (\$bn) at 2012 rates:		0.0	-21.9							

Note: Johnson & Johnson does disclose European pharmaceutical sales. Novartis's sales based on actual and estimated segment sales.

Source: EvaluatePharma® August 2016

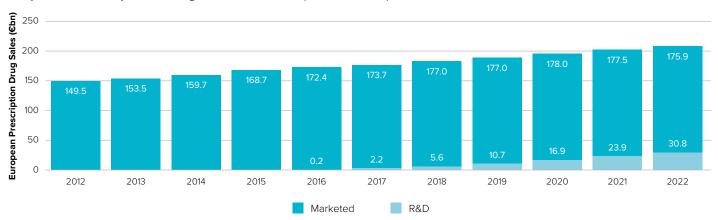
Currency Rate	2013	2014	2015	2013/14	2014/15
1€ = US \$	1.33	1.33	1.11	+0%	-16%

Analysis is based on observing the reported geographic sales for the top 20 companies in Europe in 2015.

### Europe Total Market Growth (2015-2022)

#### **European Prescription Drug Sales Growth (2012-2022)**

Source: EvaluatePharma® August 2016



#### **Europe Top 5 Selling Products 2015 & 2022**

Source: EvaluatePharma® August 2016

Rank	Product	EU Prescription Sales (€m) 2015	Product	EU Prescription Sales (€m) 2022
1.	Humira	3,292.9	Xarelto	2,531.5
2.	Enbrel	2,127.9	Opdivo	2,375.8
3.	Herceptin	2,116.8	Revlimid	2,085.1
4.	Harvoni	2,000.1	Eylea	1,782.7
5.	Rituxan	1,914.6	Soliris	1,575.3

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# Regional Prescription Drug Sales: Japan (2013-2015)



## Japan market contracts -2.4% in local currency. Takeda, Daiichi-Sankyo and Astellas still leading the market.

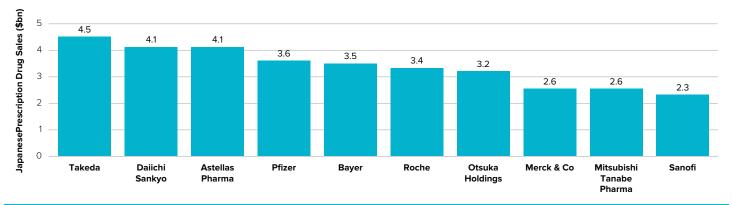
The Japanese market sales showed a -2.4% decline during the 2014-15 period, with more than half of the Top 20 companies reporting negative performances. Eli Lilly and Bayer are the only non-Japanese companies increasing sales, while among the local players Ono Pharmaceuticals has recorded the highest growth

(+18.1%), driven by the uptake of Opdivo.

The performance of the PD-1 inhibitor and its high price tag have drawn further attention to the high cost of some of the novel pharmaceuticals in Japan and more action is expected from the government to control pharmaceutical expenditure. Daiichi-Sankyo has now taken over Astellas as the second largest player in the Japanese market.

#### Japanese Prescription Drug Sales in 2015: Top 10 Companies

Source: EvaluatePharma® August 2016



#### Japanese Prescription Drug Sales (2013-2015): Top 20 Companies

		Japan Pres	scription Sa	les (\$bn)	Growt	h (\$)	Japan Pres	cription Sal	es (¥bn)	Growth (¥)	
Rank	Company	2013	2014	2015	2013/14	2014/15	2013	2014	2015	2013/14	2014/15
1.	Takeda	5.8	5.1	4.5	-11.7%	-12.0%	483	514	496	+6.5%	-3.5%
2.	Daiichi Sankyo	4.9	4.4	4.1	-9.6%	-6.1%	403	440	453	+9.1%	+3.0%
3.	Astellas Pharma	5.3	4.6	4.1	-14.0%	-10.4%	440	457	449	+3.8%	-1.7%
4.	Pfizer	5.1	4.4	3.6	-13.6%	-18.7%	409	431	380	+5.5%	-11.9%
5.	Bayer	3.3	3.6	3.5	+8.7%	-1.5%	261	347	371	+32.8%	+6.8%
6.	Roche	3.7	3.6	3.4	-1.8%	-7.2%	293	352	354	+20.0%	+0.5%
7.	Otsuka Holdings	3.7	3.3	3.2	-11.2%	-2.7%	309	331	354	+7.1%	+6.8%
8.	Merck & Co	3.9	3.4	2.6	-14.2%	-23.1%	315	330	275	+4.8%	-16.7%
9.	Mitsubishi Tanabe Pharma	3.4	3.0	2.6	-13.2%	-13.3%	283	297	282	+4.7%	-4.8%
10.	Sanofi	3.3	2.8	2.3	-15.5%	-17.9%	266	274	244	+3.3%	-11.1%
11.	Kyowa Hakko Kirin	2.7	2.4	2.3	-11.0%	-3.5%	214	232	243	+8.8%	+4.5%
12.	Eisai	3.1	2.5	2.2	-18.1%	-12.6%	258	255	244	-1.2%	-4.1%
13.	Novartis	3.3	2.7	2.2	-18.2%	-18.5%	263	263	232	-0.0%	-11.7%
14.	Eli Lilly	2.1	2.0	2.0	-1.8%	+0.3%	165	198	215	+20.0%	+8.7%
15.	AstraZeneca	2.5	2.2	2.0	-10.4%	-9.3%	198	217	213	+9.5%	-1.7%
16.	GlaxoSmithKline	2.6	2.4	1.9	-8.3%	-22.1%	207	232	196	+12.1%	-15.6%
17.	Boehringer Ingelheim	2.0	1.9	1.7	-5.3%	-11.9%	163	188	179	+15.6%	-4.6%
18.	Meiji Holdings	1.4	1.3	1.4	-3.5%	+1.6%	115	134	149	+16.5%	+11.5%
19.	Shionogi	1.7	1.5	1.4	-12.2%	-8.4%	140	148	149	+5.9%	+0.5%
20.	Ono Pharmaceutical	1.4	1.2	1.3	-13.2%	+7.7%	119	124	147	+4.7%	+18.1%
	Total	65.2	58.4	52.3	-10.5%	-10.5%	5,304	5,765	5,625	+8.7%	-2.4%
	Currency Impact (\$bn) at 2012 rates:		-11.0	-15.5							

Source: EvaluatePharma® August 2016

Currency Rate (Ending 31 March)	2012	2013	2014	2015	May				
Fiscal year	2011	2012	2013	2014	2015	2011/12	2012/13	2013/14	2014/15
1 ¥ = \$	0.0127	0.0120	0.0100	0.0091	0.0083	-5%	-17%	-9%	-9%
1 \$ = ¥	79.0	83.0	100.2	109.9	120.4				

NOV 2012: Yen depreciation due to change in monetary policy after Shinzo Abe elected Prime Minister.

Analysis is based on observing the reported geographical prescription drug sales in the US for the top 20 companies in 2015.

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# Worldwide Prescription Drug Sales in 2022: Top 20 Companies



Novartis and Roche to compete for the crown in 2022. Celgene (+16%) and Shire (+19%) expected to record fastest sales growth by 2022.

According to EvaluatePharma® consensus forecasts, Novartis and Roche are competing for the number one spot in 2022. Roche has a small edge based on the figures available as of August 2016, but many factors will be at play. Entresto, Cosentyx and ribociclib (LEE001) are expected to drive Novartis' growth, while Roche's performance will be dependent on continuous growth of Perjeta and Gazyva, the launch of the PD-1 inhibitor Tecentriq and the success of Ocrevus in the highly competitive multiple sclerosis market. The higher exposure of Roche's portfolio to biosimilars and Pfizer's recent acquisition of Medivation

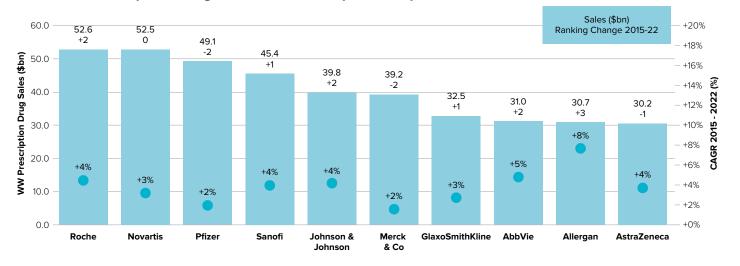
(and its leading asset Xtandi) could change the ranking.

Shire and Celgene are expected to achieve the highest CAGR in the 2016-22 timeframe (+19% and +16% respectively). The acquisition of Baxalta is the main engine driving Shire's expected performance, while Celgene's growth is expected to come from the sustained performance of Revlimid along with novel therapies Otezla and Pomalyst.

Gilead Sciences is the only company expected to decline through 2022 due to the largely anticipated slow down of its hepatitis C franchise which will only be partly compensated by new launches in the HIV space. However, the outlook does not take into account potential acquisitions that Gilead may undertake to fill the portfolio gap.

#### Worldwide Prescription Drug Sales in 2022: Top 10 Companies





# Worldwide Prescription Drug Sales (2015 - 2022): Top 20 Companies & Total Market

Source: EvaluatePharma® August 2016

		ww F	Prescription Sale	s (\$bn)	ww	Market Share		Rank
Rank	Company	2015	2022	CAGR	2015	2022	Chg. (+/-)	Chg. (+/-)
1.	Roche	38.7	52.6	+4%	5.2%	4.7%	-0.5pp	+2
2.	Novartis	42.5	52.5	+3%	5.7%	4.7%	-1.0pp	+0
3.	Pfizer	43.1	49.1	+2%	5.8%	4.4%	-1.4pp	-2
4.	Sanofi	34.8	45.4	+4%	4.7%	4.0%	-0.7pp	+1
5.	Johnson & Johnson	29.9	39.8	+4%	4.0%	3.6%	-0.5pp	+2
6.	Merck & Co	35.2	39.2	+2%	4.8%	3.5%	-1.3pp	-2
7.	GlaxoSmithKline	27.1	32.5	+3%	3.6%	2.9%	-0.7pp	+1
8.	AbbVie	22.7	31.0	+5%	3.1%	2.8%	-0.3pp	+2
9.	Allergan	18.4	30.7	+8%	2.5%	2.7%	+0.2pp	+3
10.	AstraZeneca	23.3	30.2	+4%	3.1%	2.7%	-0.4pp	-1

Top 11-20 continued over...



Source: EvaluatePharma® August 2016

		ww	Prescription Sale	es (\$bn)	ww	Market Share		Rank
Rank	Company	2015	2022	CAGR	2015	2022	Chg. (+/-)	Chg. (+/-)
11.	Gilead Sciences	32.2	29.0	-1%	4.3%	2.6%	-1.7pp	-5
12.	Bristol-Myers Squibb	14.5	27.6	+10%	2.0%	2.5%	+0.5pp	+5
13.	Novo Nordisk	16.1	27.3	+8%	2.2%	2.4%	+0.3pp	+1
14.	Amgen	20.9	27.0	+4%	2.8%	2.4%	-0.4pp	-3
15.	Celgene	9.1	25.6	+16%	1.2%	2.3%	+1.1pp	+8
16.	Eli Lilly	15.9	22.0	+5%	2.1%	2.0%	-0.2pp	-1
17.	Shire	6.1	20.5	+19%	0.8%	1.8%	+1.0pp	+12
18.	Bayer	15.6	19.6	+3%	2.1%	1.7%	-0.4pp	-2
19.	Boehringer Ingelheim	12.4	18.3	+6%	1.7%	1.6%	-0.0pp	-1
20.	Teva Pharmaceutical Industries	17.0	17.5	+0%	2.3%	1.6%	-0.7pp	-7
	Total Top 20	475.4	637.4	+4%	64.1%	56.9%	-7.2pp	
	Other	266.1	483.4	+9%	35.9%	43.1%		
	Total	741.5	1,120.9	+6%	100.0%	100.0%		

Note: Prescription drug sales include generic drug sales. Excludes alliance revenue and royalties where possible.

# Worldwide Prescription Drug & OTC Sales by Technology (2008-2022)



Use of biotech technology continue to rise, contributing to 50% of the Top 100 product sales by 2022. Roche still market leader.

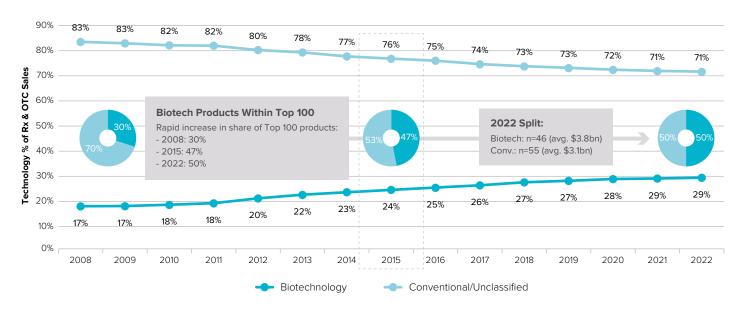
The uptake of biologics is expected to continue as novel biologic blockbusters keep entering the pharmaceutical market. The penetration of biotech products is set to increase from a 24% market share in 2015 to 29% in 2022. According to the latest EvaluatePharma® consensus forecast, in 2022 50% of the value of the top 100 products will come from biologics as established chemical products drop off the patent cliff and new breakthrough biologics get approved.

Within this outlook, Roche will continue to be the undisputed market leader and is expected to further consolidate its position with the launch of novel biologic therapies (Tecentriq and Ocrevus, but also emicizumab and lampalizumab). Bristol Myers Squibb is expected to climb the ranking provided Opdivo mantains the current expectations.

Amgen is set to fall down the rankings due to a number of its biologics going off patent, but new launches are expected to still ensure a positive CAGR (+3%) through 2022.

## Worldwide Prescription Drug & OTC Pharmaceutical Sales: Biotech vs. Conventional Technology

Source: EvaluatePharma® August 2016



#### Worldwide Prescription Drug & OTC Sales by Technology (2008-2022)

Technology	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022
Biotechnology	17%	17%	18%	18%	20%	22%	23%	24%	25%	26%	27%	27%	28%	29%	29%
Conventional/Unclassified	83%	83%	82%	82%	80%	78%	77%	76%	75%	74%	73%	73%	72%	71%	71%
Total Prescription & OTC Sales	100%	100%	100%	100%	100%	100%	100%	100%	100%	100%	100%	100%	100%	100%	100%

	WW Sales (\$bn)														
Technology	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022
Biotechnology	117	119	128	141	152	165	178	184	200	220	242	266	290	315	337
Conventional	423	433	442	463	440	431	442	433	440	453	473	497	526	556	582
Other Unclassified Sales	151	145	151	162	161	166	168	159	171	185	196	207	220	232	245
Total Prescription & OTC Sales	691	697	720	766	754	762	788	776	812	858	911	970	1037	1102	1164



## Worldwide Prescription Drug Sales from Biotechnology in 2022: Top 10 Companies

Source: EvaluatePharma® August 2016

			WW Sales (\$bn)			WW Market Share			
Rank	Company	2015	2022	% CAGR 15-22	2015	2022	Chg. (+/-)	Rank Chg.	
1.	Roche	31.1	43.6	+5%	16.9%	12.9%	-4.0pp	+0	
2.	Sanofi	14.9	25.3	+8%	8.1%	7.5%	-0.6рр	+2	
3.	Novo Nordisk	15.1	24.4	+7%	8.2%	7.2%	-1.0pp	+0	
4.	Amgen	18.8	23.2	+3%	10.2%	6.9%	-3.3pp	-2	
5.	Bristol-Myers Squibb	4.5	18.2	+22%	2.5%	5.4%	+2.9pp	+6	
6.	Johnson & Johnson	10.9	17.7	+7%	5.9%	5.2%	-0.7pp	+1	
7.	AbbVie	14.8	15.5	+1%	8.0%	4.6%	-3.4pp	-2	
8.	Eli Lilly	6.6	15.4	+13%	3.6%	4.6%	+1.0pp	+1	
9.	Pfizer	11.9	14.8	+3%	6.5%	4.4%	-2.1pp	-3	
10.	Merck & Co	7.9	13.0	+7%	4.3%	3.9%	-0.4pp	-2	

Note: Company drug sales from undisclosed products are presumed to be from conventional (small molecule) technology.

### Worldwide Pharma Innovation (2008-2022)



Roche has the highest value pipeline but its portfolio strategy carries risks. BMS portfolio strategy stands out. Tecfidera commercial best practice behind Harvoni and Sovaldi success stories in hepatitis C.

Roche continues to lead the rankings by showcasing the most valuable pharmaceutical pipeline in the industry. Most of the value is driven by Roche's efforts outside its core portfolio, oncology, notably Ocrevus and crenezumab (multiple sclerosis and Alzheimer's disease, respectively), emicizumab in haemophilia and lampalizumab for the treatment of an advanced form of agerelated macular degeneration.

The podium is completed by Novartis and AstraZeneca whose

pipeline is charged with a lot of expectations (including durvalumab and acalabrutinib).

However, if we place the lens on the best companies at capitalizing on recent launches (according to EvaluatePharma sales for product introduced in the market after December 2012), the top spot goes to Gilead which recorded an unprecedented performance following the launch of its hepatitis C blockbusters, Sovaldi and Harvoni. Biogen follows second with the success of Tecfidera, while GSK is third with the performance of its HIV franchise (developed by ViiV Healthcare). This trend does confirm that specialisation at therapy area level and a focused strategy are likely to pay off in terms of commercial success.

#### Value Creators: Top 10 Pipelines NPV, \$m

Rank	Company	Pipeline NPV, \$m
1.	Roche	43,171
2.	Novartis	24,091
3.	AstraZeneca	23,160
4.	Eli Lilly	19,677
5.	AbbVie	19,364
6.	Pfizer	18,214
7.	Sanofi	17,699
8.	Celgene	16,246
9.	Biogen	13,621
10.	Johnson & Johnson	13,157

#### Value Creators: Best companies at capturing value from recent launches (Dec 2012+)

Top companies based on 2015 WW sales from recently launched products (Dec 2012+)

Top companies based on 2022 WW sales from recently launched products (Dec 2012+)

Rank	Company	2015 WW Sales, \$bn	Primary Value Drivers
1.	Gilead Sciences	21,142	Harvoni, Sovaldi, Stribild
2.	Biogen	4,532	Tecfidera
3.	GlaxoSmithKline	3,853	Triumeq, Tivicay, Otrivin
4.	Roche	2,611	Perjeta, Kadcyla
5.	Bristol-Myers Squibb	2,548	Daklinza, Opdivo
6.	AbbVie	2,298	Viekira Pak, Imbruvica
7.	Johnson & Johnson	2,252	Invokana, Olysio, Imbruvica
8.	Astellas Pharma	2,240	Xtandi
9.	Sanofi	1,985	Aubagio, Lemtrada, Toujeo
10.	Pfizer	1,959	Ibrance, Xeljanz, Inlyta

Rank	Company	2022 WW Sales, \$bn	Primary Value Drivers
1.	Gilead Sciences	17,720	Harvoni, Genvoya, Descovy
2.	Roche	17,215	Tecentriq, Perjeta, Gazyva
3.	GlaxoSmithKline	14,625	Triumeq, Tivicay, Nucala
4.	Novartis	14,502	Entresto, Cosentyx, Reaslanz
5.	Bristol-Myers Squibb	14,297	Opdivo, Empliciti, Daklinza
6.	Sanofi	13,016	Praluent, Toujeo, Aubagio
7.	Johnson & Johnson	12,346	Imbruvica, Darzalex, Invokana
8.	Merck & Co	10,747	Keytruda, Zepatier
9.	Pfizer	10,038	Ibrance, Xeljanz, Inflectra
10.	AstraZeneca	8,154	Farxiga, Tagrisso, Eklira Genuair



When comparing portfolio strategies, interesting differences emerge between the top pharma companies. Bristol Myers Squibb has emerged from the post-patent cliff crisis with a virtuous portfolio strategy. GSK and Novartis seem also to fall into the same cluster. Despite a highly valued pipeline, there are two major risks looming on Roche's portfolio: biosimilars and potential clinical setbacks with

products outside its core specialty area. Similar considerations apply to Eli Lilly where the long term success of its portfolio is dependent on several pipeline projects (between abemaciclib, solanezumab and baricitinib only the latter seems to hold high promises based on the latest clinical development updates).

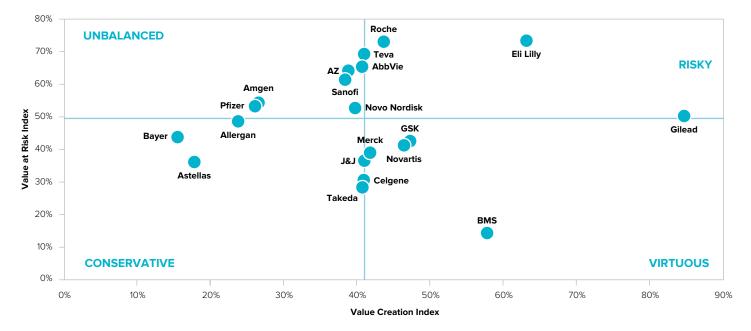
Top 20 Pharma: Value Creation vs. Value at Risk

Rank	Company	Value Creation Index	Value at Risk Index
1.	AbbVie	41%	65%
2.	Allergan	24%	49%
3.	Amgen	27%	55%
4.	Astellas Pharma	18%	36%
5.	AstraZeneca	39%	64%
6.	Bayer	16%	44%
7.	Bristol-Myers Squibb	58%	14%
8.	Celgene	41%	31%
9.	Eli Lilly	63%	73%
10.	Gilead Sciences	85%	50%

Rank	Company	Value Creation Index	Value at Risk Index
11.	GlaxoSmithKline	47%	42%
12.	Johnson & Johnson	41%	37%
13.	Merck & Co	42%	39%
14.	Novartis	46%	41%
15.	Novo Nordisk	40%	53%
16.	Pfizer	26%	53%
17.	Roche	44%	73%
18.	Sanofi	38%	61%
19.	Takeda	41%	28%
20.	Teva Pharmaceutical Industries	41%	69%
	Average	41%	49%

Value creation index: % 2022 WW sales coming from pipeline and recently launched products (Dec 2012+) Value at risk index: % of 2022 WW sales at risk either because of generics or technical failure (pipeline products)

#### Portfolio Strategy: Value Creation vs. Value at Risk





In terms of commercial innovation, EvaluatePharma® has looked at the performance two years after launch of all the products launched globally from 2010 onward. If we exclude the exceptional

performance of Harvoni and Sovaldi, a special mention goes to Tecifdera which stood out in the highly competitive multiple sclerosis market with \$3bn in sales after two years.

## Commercial innovation – Best selling products after 2 years from launch

Analysis based on products launched after January 2010

Rank	ww	Year 2 WW Sales, \$m
1.	Harvoni (Gilead)	6,362
2.	Sovaldi (Gilead)	5,461
3.	Tecfidera (Biogen)	3,228
4.	Eylea (Bayer, Regeneron)	1,692
5.	Opdivo (BMS)	1,654
6.	Incivek (Vertex)	1,545
7.	Triumeq (GSK)	1,234
8.	Daklinza (BMS)	1,173
9.	Zytiga (J&J)	1,105
10.	Imbruvica (J&J, Abbvie)	1,104
11.	Viekira Pak (Abbvie)	968
12.	Xgeva (Amgen)	931
13.	Olysio (J&J)	918
14.	Gilenya (Novartis)	888
15.	Stribild (Gilead)	848
16.	Yervoy (BMS)	781
17.	Entyvio (Takeda)	721
18.	Tivicay (GSK)	694
19.	Xtandi (Astellas)	686
20.	Pomalyst (Celgene)	680

## Commercial innovation – Best selling products after 1 year from launch

Analysis based on products launched after January 2010

Rank	ww	Year 1 WW Sales, \$m
1.	Harvoni (Gilead)	12,626
2.	Sovaldi (Gilead)	8,690
3.	Olysio (J&J)	2,016
4.	Incivek (Vertex)	1,541
5.	Tecfidera (Biogen)	1,382
6.	Viekira Pak (Abbvie)	1,133
7.	Daklinza (BMS)	763
8.	Ibrance (Pfizer)	723
9.	Eylea (Bayer, Regeneron)	587
10.	Orkambi (Vertex)	574
11.	Yervoy (BMS)	514
12.	Zytiga (J&J)	496
13.	Triumeq (GSK)	442
14.	Imbruvica (J&J, Abbvie)	348
15.	Jublia (Valeant)	325
16.	Pomalyst (Celgene)	305
17.	Xgeva (Amgen)	285
18.	Cosentyx (Novartis)	261
19.	Kadcyla (Roche)	253
20.	Stribild (Gilead)	250

# Top 20 Most Valuable R&D Projects (Ranked by Net Present Value)



### Roche's Ocrevus and Sanofi's dupilumab anticipated to be the most valuable projects in the pharmaceutical pipeline.

If it is not surprising to see Roche topping the ranking of the most valuable R&D projects, what is news is the fact that the innovation is not coming from its established oncology pipeline. Ocrevus (ocrelizumab), an anti-CD20 MAb, is expected to reach close to \$4bn in the challenging multiple sclerosis market by 2022. Dupilumab, Sanofi/Regeneron's novel therapy for atopic dermatitis, is likely to face a less competitive environment in the first two years following launch (at least in terms of novel therapies), hence allowing enough time to navigate the market access landscape and consolidate a leading position within the clinical community.

In the oncology market, Pfizer's CDK inhibitor Ibrance, will be challenged by two novel therapies with simlar mechanisms of action, Novartis' ribociclib and Eli Lilly's abemaciclib. The sellside forecast of the latter product does not take into account the recent setback emerged from the interim read-out of the Monarch-2 study. High hopes are also placed on Alzheimer's therapies, Eli Lilly's solanezumab and Biogen's aducanumab.

It is also worth mentioning two products appearing in the top 20: Amgen's ABP501, a biosimilar of the Abbvie's megablockbuster Humira, and the first CAR-T cell therapy, Juno's JCAR017. Overall, EvaluatePharma® consensus forecast estimates the additional sales expected from R&D projects to reach \$169bn in 2022, about 50% of the total incremental sales during the 2016-2022 period.

#### Top 20 Most Valuable R&D Projects (Ranked by Net Present Value)

Source: EvaluatePharma® August 2016

Rank	Product	Company	Phase (current)	Pharmacological Class	WW Product Sales (\$m) 2022		Today's NPV (\$m)	
1.	Ocrevus	Roche	Filed	Anti-CD20 MAb	3,962	New entry	16,965	
2.	Dupilumab	Sanofi	Phase III	Anti-interleukin-4 (IL-4) & interleukin-13 (IL-13) MAb	3,725		12,884	
3.	Ozanimod	Celgene	Phase III	Sphingosine-1-phosphate (S1P) 1 & 5 receptor modulator	2,112		9,458	
4.	Durvalumab	AstraZeneca	Phase III	Anti-programmed death-1 ligand-1 (PD-L1) MAb	1,673		8,276	
5.	Abemaciclib	Eli Lilly	Phase III	Cyclin-dependent kinase (CDK) 4 & 6 inhibitor	1,619	New entry	7,919**	
6.	Veliparib	AbbVie	Phase III	Poly (ADP-ribose) polymerase (PARP) inhibitor	1,714	New entry	7,502	
7.	Semaglutide	Novo Nordisk	Phase III	Glucagon-like peptide 1 (GLP-1) agonist	2,356	New entry	6,889	
8.	Aducanumab	Biogen	Phase III	Anti-beta-amyloid (Abeta) MAb	939	New entry	6,889	
9.	LEE011	Novartis	Phase III	Cyclin-dependent kinase (CDK) 4 & 6 inhibitor	1,410	New entry	6,370	
10.	Emicizumab	Roche	Phase III	Anti-factor IXa/X bispecific MAb	1,765	New entry	6,336	
11.	ABP 501	Amgen	Filed	Anti-tumour necrosis factor alpha (TNFa) MAb	810	New entry	6,273	
12.	Lanadelumab	Shire	Phase III	Anti-plasma kallikrein MAb	1,064	New entry	5,915	
13.	Solanezumab	Eli Lilly	Phase III	Anti-beta-amyloid (Abeta) MAb	1,556		5,577	
14.	Fovista	Ophthotech	Phase III	Anti-platelet derived growth factor (PDGF)-B aptamer	1,973		5,514*	
15.	Apalutamide	Johnson & Johnson	Phase III	Anti-androgen	1,160	New entry	5,366	
16.	Bictegravir/F/TAF	Gilead Sciences	Phase III	Nucleoside reverse transcriptase inhibitor (NRTI) & HIV integrase inhibitor	3,489	New entry	5,276	
17.	Verubecestat	Merck & Co	Phase III	Beta secretase cleaving enzyme (BACE) 1 inhibitor	1,480	New entry	5,219	
18.	JCAR017	Juno Therapeutics	Phase II	Anti-CD19 chimeric antigen receptor (CAR) T cell therapy	1,086	New entry	4,836	
19.	Mongersen	Celgene	Phase III	Smad7 mRNA antisense	1,205	New entry	4,719	
20.	Sirukumab	Johnson & Johnson	Phase III	Anti-interleukin-6 (IL-6) MAb	1,134	New entry	4,708	
	Top 20				36,232		142,893	
	Other				133,225		394,980	
	Total				169,457		537,873	9%
	NPV of R&D Pipeline MAY 2015:							

Note: Abemaciclib's forecast may have been adjusted downward by equity research analysts after this analysis went to press. The adjustment is due to the recent announcement that Abemaciclib failed to meet the criteria for an early Phase III halt, which suggests an early filing will not be possible.

 $<sup>^{\</sup>ast}$  Fovista assumed to be forecast on "best-case" basis and not fully adjusted for development risk

<sup>\*\*</sup> NPV as of 19 Aug 2016



# Most Valuable R&D Projects (Ranked by NPV) in May 2015 Which Have Since Been Approved or Suffered Setbacks

Source: EvaluatePharma® August2016

Change vs. May '15	Product	Company	Status (May 2015)	Status Change Since May 2015	May 2015 NPV (\$m)	Today's NPV (\$m)	Change vs. May 15 (%)
Approved	Tecentriq	Roche	Phase III	Marketed	9,619	26,464	175%
	Repatha	Amgen	Filed	Marketed	8,213	22,027	168%
	Entresto	Novartis	Filed	Marketed	16,246	16,297	0%
	Praluent	Sanofi	Filed	Marketed	4,967	11,530	132%
	Orkambi	Vertex Pharmaceuticals	Filed	Marketed	16,037	9,979	-38%
	Ocaliva	Intercept Pharmaceuticals	Phase III	Marketed	7,755	3,306	-57%
	Tagrisso	AstraZeneca	Phase III	Marketed	5,376	9,234	72%
	Ninlaro	Takeda	Phase III	Marketed	3,534	8,658	145%
	Venclexta	AbbVie	Phase III	Marketed	4,386	8,768	100%
				Sub-Total	76,133	116,263	53%
Setback <sup>1</sup>					0	0	n/m
				Sub-Total	0	0	n/m
Total					76,133	116,263	53%

Note: <sup>1</sup> None of the top 20 R&D projects listed in May 2015 have suffered a clinical setback over the past twelve months.

# Worldwide R&D Spend by Pharma & Biotech Companies (2008-2022)



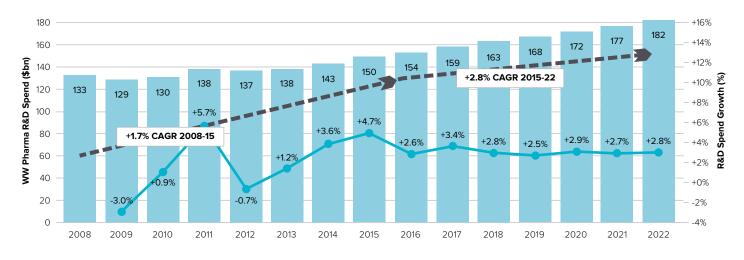
Worldwide pharmaceutical R&D spend to grow by 2.8% (CAGR) to \$182bn in 2022. Increase in productivity signalled by decrease in spend per NME.

EvaluatePharma\* finds that worldwide pharmaceutical R&D totalled \$149.8bn in 2015 representing an increase of 4.7% on the previous year. Looking forward, R&D spend is forecast to grow at a rate of 2.8% per year, compared with the compound annual growth

rate of 1.7% between 2008 and 2015. The spend per NME, based on a three-year lag period between R&D expenditure and NME approval\*, was \$2.4bn per NME, the lowest for at least the past eight years. Such a trend signals a boost in R&D productivity as a result of more focused clinical development programmes and a growing collaboration between manufacturers and regulatory authorities to align on clinical trial design.

#### Worldwide Total Pharmaceutical R&D Spend in 2008-2022

Source: EvaluatePharma® August 2016



#### Worldwide R&D Spend by Pharma & Biotech Companies (2008-2022)

Source: EvaluatePharma® August 2016

						V	VW Presc	ription Sa	iles (\$bn)						
Year	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022
Pharma R&D Spend	132.9	129.0	130.1	137.5	136.5	138.2	143.1	149.8	153.8	159.0	163.4	167.5	172.3	177.0	182.0
Growth per Year		-3.0%	+0.9%	+5.7%	-0.7%	+1.2%	+3.6%	+4.7%	+2.6%	+3.4%	+2.8%	+2.5%	+2.9%	+2.7%	+2.8%
WW Prescription (Rx) Sales	659	665	687	729	717	724	749	742	778	822	873	931	996	1,061	1,121
R&D as % of WW Rx Sales	20.2%	19.4%	19.0%	18.9%	19.0%	19.1%	19.1%	20.2%	19.8%	19.3%	18.7%	18.0%	17.3%	16.7%	16.2%
Generics	53	53	59	65	66	69	74	73	80	86	92	97	103	109	115
Rx excl. Generics	606	613	627	663	651	655	675	669	698	736	782	834	893	952	1,006
R&D as % of Rx excl. Generics	21.9%	21.1%	20.7%	20.7%	21.0%	21.1%	21.2%	22.4%	22.0%	21.6%	20.9%	20.1%	19.3%	18.6%	18.1%

CAGR 15-22 on Pharma R&D Spend +2.8%. Cumulative 10 year R&D Spend (2006-15) \$1,333bn.

Year	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015
Number of NMEs	38	28	29	26	31	34	26	35	43	35	50	56
Spend per NME (\$bn)	2.4	3.6	3.9	4.8	4.3	3.8	5.0	3.9	3.2	3.9	2.9	2.7
Spend per NME (\$bn) (3 year lag)*				3.4	3.2	3.3	4.8	3.8	3.0	3.7	2.8	2.4

Note: Industry sales based on Top 500 pharmaceutical and biotech companies.

Forecast pharmaceutical research and development spend based on a consensus of leading equity analysts' estimates for company level R&D spend, extrapolated to pharmaceutical R&D when a company has non-pharmaceutical R&D activity.

<sup>\*</sup>Spend per NME (\$bn) (3 year lag) uses the R&D expense for 3 years prior to the NME approval instead of the same year. e.g. the 2015 figure of \$2.4bn is the R&D expense in 2012 divided by the number of NMEs in 2015.

# Pharmaceutical R&D Spend in 2022: Top 20 Companies

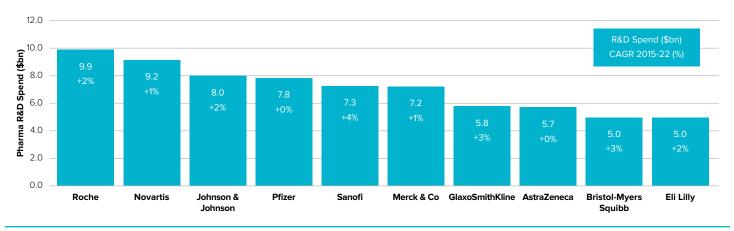


### Roche forecast to be the biggest spender on pharmaceutical R&D in 2022.

EvaluatePharma® finds that Roche will have overtaken Novartis to spend the most on research and development in 2022, with a spend of \$9.9bn. Novartis is forecast to reduce its R&D spending, from \$10.5bn in 2020 to only \$9.2bn in 2022. Of the top 20, Celgene and Regeneron are forecast to grow their R&D expenses most rapidly, with R&D spend forecast to increase 11% per year until 2022. Overall, total R&D spend is expected to increase by 2.8% each year, reaching \$182bn in 2022.

#### Pharmaceutical R&D in 2022: Top 10 Companies

Source: EvaluatePharma® August 2016



#### Pharmaceutical R&D Spend (2015 & 2022): Top 20 Companies & Total Market

Source: EvaluatePharma® August 2016

		Phar	ma R&D (\$bn)		R&D As a % of Pro	escription Sales	
Rank	Company	2015	2022	CAGR 15-22	2015	2022	Chg. (+/-)
1.	Roche	8.5	9.9	+2%	21.8%	18.9%	-2.9pp
2.	Novartis	8.5	9.2	+1%	19.9%	17.4%	-2.5pp
3.	Johnson & Johnson	6.8	8.0	+2%	22.8%	20.0%	-2.9pp
4.	Pfizer	7.7	7.8	+0%	17.8%	15.9%	-1.9pp
5.	Sanofi	5.6	7.3	+4%	16.2%	16.0%	-0.2pp
6.	Merck & Co	6.6	7.2	+1%	18.8%	18.5%	-0.3pp
7.	GlaxoSmithKline	4.7	5.8	+3%	17.5%	17.9%	+0.4pp
8.	AstraZeneca	5.6	5.7	+0%	24.1%	18.9%	-5.2pp
9.	Bristol-Myers Squibb	4.0	5.0	+3%	27.9%	18.1%	-9.8pp
10.	Eli Lilly	4.5	5.0	+2%	28.2%	22.7%	-5.5pp
11.	Celgene	2.3	4.9	+11%	25.3%	19.2%	-6.1pp
12.	Boehringer Ingelheim	3.1	4.5	+6%	24.8%	24.7%	-0.1pp
13.	Amgen	3.9	4.5	+2%	18.7%	16.5%	-2.2pp
14.	AbbVie	3.6	4.4	+3%	15.9%	14.0%	-1.9pp
15.	Gilead Sciences	3.0	4.3	+5%	9.4%	14.8%	+5.4pp
16.	Novo Nordisk	2.0	3.5	+8%	12.6%	12.9%	+0.3pp
17.	Regeneron Pharmaceuticals	1.6	3.4	+11%	60.3%	65.7%	+5.4pp
18.	Takeda	2.9	3.3	+2%	24.1%	20.3%	-3.8pp
19.	Bayer	2.6	3.1	+3%	16.6%	15.8%	-0.8pp
20.	Biogen	2.0	2.7	+4%	21.9%	21.2%	-0.7pp
	Total Top 20	89.6	109.4	+2.9%	20.2%	18.8%	-1.4pp
	Other	60.2	72.6	+2.7%			
	Total	149.8	182.0	+2.8%	13.4%	16.3%	+2.9pp

Note: Forecast pharmaceutical R&D spend based on a consensus of leading equity analysts' estimates for company-level R&D spend.

# FDA New Drug Approval Analysis NMEs & Biologicals: (2001-2015)



### New drug approvals in 2015 reach a new record with 56 NMEs, topping 2014 high.

The approval of 56 NMEs by the FDA in 2015 beats the previous record registered in 2014 (50 NMEs) and confirms the increasing productivity of the pharmaceutical pipeline. Besides the number of products approved, a key indicator is represented by the value (calculated as USA sales expected five years after launch) of the

new approvals. In 2015 the top NMEs include Pfizer's Ibrance, J&J's Darzalex and Gilead's Genvoya with a cumulative value of \$32bn of sales expected in 2020. The increasing number of breakthrough therapy approvals also prove the ability of the pharmaceutical R&D to offer incremental benefits to targeted patient segments with larger unmet needs.

#### FDA Approval Count vs. Total USA Product Sales 5 Years After Launch

Source: EvaluatePharma® August 2016



#### Key Approvals in Top 6 Years

**2002** — Neulasta (AMGN), Abilify (Otsuka/BMS), Zetia (MRK/SGP), Humira (ABT)

**2004** – Avastin (Roche), Cymbalta (LLY), Spiriva (BI/PFE), Lyrica (PFE)

2012 – Eliquis (BMY/PFE), Xtandi (Astellas), Perjeta (Roche), Strilbid (GILD)

2013 – Tecfidera (BIIB), Imbruvica (ABBV), Invokana (JNJ)

2014 – Opdivo (BMY), Harvoni (GILD), Keytruda (MRK)

2015 – Ibrance (PFE), Genvoya (GILD), Entresto (NVS)

## FDA Approval Count (NMEs & Biologicals) vs. 5th Year after Launch USA Product Sales

Source: EvaluatePharma® August 2016

Year	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015
No. of NMEs Approved	24	17	21	31	18	18	16	21	19	15	24	33	25	30	32
No. of Biologicals Approved	8	9	14	7	10	11	10	10	15	11	11	10	10	20	24
Total NMEs + Biologicals	32	26	35	38	28	29	26	31	34	26	35	43	35	50	56
% Chg.		-19%	+35%	+9%	-26%	+4%	-10%	+19%	+10%	-24%	+35%	+23%	-19%	+43%	+12%
USA Sales 5yrs Post Launch \$bn	8.5	12.7	8.3	14.1	6.4	9.2	4.3	5.6	5.4	13.5	11.4	13.6	16.0	27.1	32.4
% Chg.		+50%	-34%	+69%	-55%	+44%	-53%	+28%	-3%	+148%	-16%	+20%	+17%	+69%	+19%
5yr USA Sales per Approval \$m	264	487	238	371	228	316	167	180	160	519	325	317	458	542	578
% Chg.		+84%	-51%	+56%	-39%	+39%	-47%	+8%	-11%	+225%	-37%	-2%	+44%	+19%	+ <b>7</b> %

Note: The number of biologicals approved include biologicals from both CDER and CBER. In 2015 there were 13 CDER biologicals approved and EvaluatePharma estimates that there were 11 CBER biologicals approved: Vonvendi, Fluad, Adynovate, Imlygic, Nuwiq, Anavip, Raplixa, Ixinity, Quadracel, Anthrasil, Bexsero.



## Top 10 New Molecular Entities in 2015: Ranked on USA Consensus Sales in 2020

Source: EvaluatePharma® August 2016

					USA Sa	ales (\$m)
Rank	Product	Company	Approved	Review Status	2015	2020
1.	Ibrance	Pfizer	Feb 2015	Breakthrough therapy	718	3,297
2.	Genvoya	Gilead Sciences	Nov 2015	Standard	44	2,512
3.	Entresto	Novartis	Jul 2015	Priority review	21	2,104
4.	Orkambi	Vertex Pharmaceuticals	Jul 2015	Breakthrough therapy	351	1,992
5.	Repatha	Amgen	Aug 2015	Standard	7	1,838
6.	Cosentyx	Novartis	Jan 2015	Standard	220	1,809
7.	Darzalex	Johnson & Johnson	Nov 2015	Breakthrough therapy	9	1,802
8.	Tresiba	Novo Nordisk	Sep 2015	Standard	-	1,542
9.	Praluent	Sanofi	Jul 2015	Priority review	10	1,331
10.	Rexulti	Otsuka Holdings	Jul 2015	Standard	38	1,219
	Other				684	12,934
	Total				2,102	32,381

Note: Sales forecasts based on a consensus of leading equity analysts' estimates.

5th year USA sales for products approved up to the end of 2010 are based on actual company reported sales.

Darzalex, Cosentyx, Repatha USA sales figures for 2015 are estimated.

# Worldwide Prescription Drug & OTC Sales by Therapy Area in 2022



## Oncology still the fastest growing therapy area with a +12.5% CAGR during the 2016-22 period.

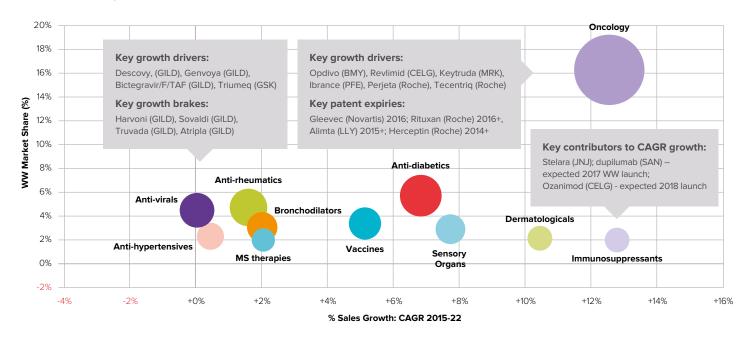
EvaluatePharma® finds that oncology will remain the largest segment in 2022 with an expected annual growth of 12.5% per year, reaching \$190.0bn in sales in 2022. Oncology growth through to 2022 is driven by Opdivo and Revlimid with contributions from the expected launches of durvalumab and Tecentriq to compensate for a number of key patent expires between 2015 and 2022. The stagnant growth of anti-virals is the result of a balance between

growth drivers and brakes in the HIV and hepatitis C markets. Anti-diabetics is forecast to be the second biggest therapy area with sales of \$66.1bn in 2022, less than half that of oncology.

The upcoming launches of dupilumab and onazimod are expected to fuel the growth of the immunosuppressants segment which is expected to grow at a 12.8% CAGR during the 2016-22 period. Sustained growth is also expected in the anti-cogulants market driven by the performance of Xarelto (Bayer/J&J), Eliquis (BMS) and Savaysa (Daiichi-Sankyo).

#### Top 10 Therapy Areas in 2022, Market Share & Sales Growth

Source: EvaluatePharma® August 2016



## Worldwide Prescription Drug & OTC Sales by EvaluatePharma® Therapy Area (2015 & 2022): Top 15 Categories & Total Market

Source: EvaluatePharma® August 2016

		WW Sa	iles (\$bn)	CAGR	ww	Market Share		Rank
Rank	Therapy Area	2015	2022	% Growth	2015	2022	Chg. (+/-)	Chg. (+/-)
1.	Oncology	83.2	190.0	+12.5%	10.7%	16.3%	+5.6pp	+0
2.	Anti-diabetics	41.7	66.1	+6.8%	5.4%	5.7%	+0.3pp	+2
3.	Anti-rheumatics	48.8	54.5	+1.6%	6.3%	4.7%	-1.6pp	+0
4.	Anti-virals	50.7	50.9	+0.0%	6.5%	4.4%	-2.2pp	-2
5.	Vaccines	27.6	39.0	+5.1%	3.5%	3.4%	-0.2pp	+1
6.	Bronchodilators	30.2	34.7	+2.0%	3.9%	3.0%	-0.9pp	-1
7.	Sensory Organs	19.8	33.3	+7.7%	2.6%	2.9%	+0.3pp	+2
8.	Anti-hypertensives	25.7	26.5	+0.4%	3.3%	2.3%	-1.0pp	-1
9.	Dermatologicals	12.1	24.3	+10.4%	1.6%	2.1%	+0.5pp	+3
10.	MS therapies	20.2	23.2	+2.0%	2.6%	2.0%	-0.6pp	-2

Top 11-15 continued over...

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Source: EvaluatePharma® August 2016

		WW Sa	ales (\$bn)	CAGR	ww	/ Market Share		Rank
Rank	Therapy Area	2015	2022	% Growth	2015	2022	Chg. (+/-)	Chg. (+/-)
11.	Immunosuppressants	9.5	22.1	+12.8%	1.2%	1.9%	+0.7pp	+6
12.	Anti-coagulants	11.9	20.3	+8.0%	1.5%	1.7%	+0.2pp	+1
13.	Anti-hyperlipidaemics	15.4	18.2	+2.4%	2.0%	1.6%	-0.4pp	-3
14.	Anti-bacterials	12.4	16.9	+4.5%	1.6%	1.4%	-0.2pp	-3
15.	Anti-fibrinolytics	11.1	15.8	+5.2%	1.4%	1.4%	-0.1pp	+0
	Тор 15	420	636	+6.1%	54.1%	54.6%	+0.5pp	
	Other	356	529	+5.8%	45.9%	45.4%	-0.5pp	
	Total WW Prescription & OTC Sales	776	1,164	+6.0%	100.0%	100.0%		
	Total 'Prescription & OTC Sales' includes:							
	WW Generic Sales	73.1	114.8	+6.7%	9.4%	9.9%	+0.4%	
	OTC Pharmaceuticals	34.7	43.5	+3.3%	4.5%	3.7%	-0.7%	

Note: Industry sales based on Top 500 pharmaceutical and biotech companies. Sales in 2015 based on company reported data. Sales forecasts to 2022 based on a consensus of leading equity analysts' estimates for product sales and segmental sales.

### Oncology Market to 2022



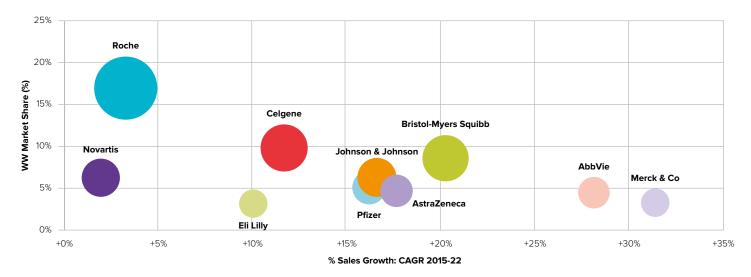
### Roche remains ahead of the field but its growth set to fade following the launch of biosimilars.

Roche's pre-eminence is expected to diminish with an estimated 14% decline in market share through 2022. The market-leader struggles with a compound annual growth rate of 3% as opposed to an average of 17% amongst the rest of its peers within the top ten. This lackluster growth rate is likely due to the impact of biosimilars cannibalising sales of its core products, including Avastin, Herceptin and Rituxan. If forecasts hold, Keytruda, an anti-programmed cell death protein 1 (PD-1) drug will catapult Merck & Co into the top 10 with worldwide

sales forecasted to reach approximately \$6bn in 2022. Additionally, Keytruda may be primed for even more growth after Bristol-Myers Squibb's Opdivo failed to hit first-line treatment goals in a recent lung cancer study. Not to be left behind, Abbvie is acquiring its way into the marketplace with a big bet on Pharmacyclics and their key drug Imbruvica and most recently, Stemcentrx and their candidate Rova-T. Overall, the foundation of the market of established drugs launched prior to 2013 is expected to only slightly increase with recent and newly launched drugs driving growth by an estimated 13% (CAGR) to \$190bn.

#### Worldwide Sales, Market Share & Sales Growth (2015-2022)

Source: EvaluatePharma® August 2016



Note: Bubble = WW Sales in 2022

#### Top 10 Companies & Total Worldwide Oncology Sales (2015-2022)

Source: EvaluatePharma® August 2016

		ww	/ Sales (\$m)	CAGR	WW Marke	t Share	Rank Chg.
Rank	Company	2015	2022	2015-22	2015	2022	2015-22
1.	Roche	25,707	32,206	+3%	30.9%	17.0%	-
2.	Celgene	8,597	18,680	+12%	10.3%	9.8%	+1
3.	Bristol-Myers Squibb	4,499	16,397	+20%	5.4%	8.6%	+1
4.	Novartis	10,357	11,889	+2%	12.5%	6.3%	-3
5.	Pfizer	3,392	9,723	+16%	4.1%	5.1%	-
6.	Johnson & Johnson	4,068	11,918	+17%	4.9%	6.3%	+1
7.	AstraZeneca	2,825	8,807	+18%	3.4%	4.6%	+1
8.	AbbVie	1,485	8,406	+28%	1.8%	4.4%	+4
9.	Eli Lilly	2,989	5,806	+10%	3.6%	3.1%	-3
10.	Merck & Co	920	6,195	+31%	1.1%	3.3%	+8
	Top 10	64,839	130,026	+10%	77.9%	68.4%	
	Other	18,342	59,959	+18%	22.1%	31.6%	
	Total Industry	83,181	189,985	+13%	100.0%	100.0%	

Note: Opdivo's forecast may have been adjusted downward by equity research analyst while this paper went to press. The adjustment is due to the recent failure of Opdivo in a Phase III study for use in first line in advanced NSCLC.

#### **Top 5 Oncology Products Worldwide in 2022**

Source: EvaluatePharma® August 2016

					WW Sales (\$m)		CAGR	WW Market Share		Current
Rank	Product	Generic Name	Company	Pharma Class	2015	2022	2015-22	2015	2022	Status
1.	Opdivo	nivolumab	Bristol-Myers Squibb + Ono Pharmaceutical	Anti-programmed death-1 (PD-1) MAb	1,119	14,634*	+44%	1.3%	7.7%	Marketed
2.	Revlimid	lenalidomide	Celgene	Immunomodulator	5,801	13,024	+12%	7.0%	6.9%	Marketed
3.	Imbruvica	ibrutinib	AbbVie + Johnson & Johnson + Pharmacyclics	Bruton's tyrosine kinase (BTK) inhibitor	1,299	7,287	+28%	1.6%	3.8%	Marketed
4.	Keytruda	pembrolizumab	Merck & Co	Anti-programmed death-1 (PD-1) MAb	566	5,959	+40%	0.7%	3.1%	Marketed
5.	Ibrance	palbociclib	Pfizer	Cyclin-dependent kinase (CDK) 4 & 6 inhibitor	723	5,709	+34%	0.9%	3.0%	Marketed

Note: \*Opdivo's forecast may have been adjusted downward by equity research analysts after this analysis went to press. The adjustment is due to the recent failure of Opdivo in a key Phase III study for use in first line in advanced NSCLC.

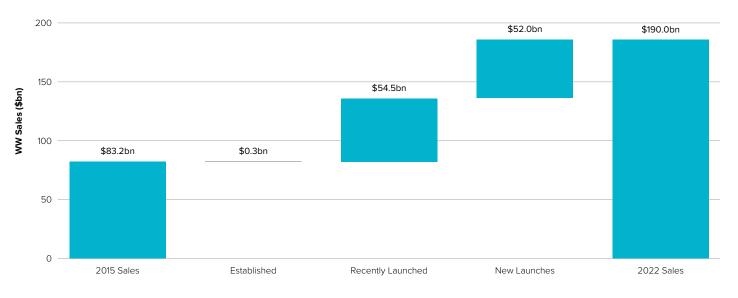
Oncology includes: Alkaloids, Alkylating agents, Anti-metabolites, Anti-neoplastic MAbs, Cytotoxic antibiotics, Hormone therapies, Platinum compounds and other anti-cancer. Excludes anti-emetics and anti-anaemics used in chemotherapy-induced anaemia. Also excludes: Interferons, Immunostimulants & Immunosuppressants.

#### Top 5 Oncology R&D Products Worldwide in 2022

Source: EvaluatePharma® August 2016

Rank	Product	Generic Name	Company	Pharma Class	WW Sales (\$m) 2022	WW Market Share 2022	Status
1.	Durvalumab	durvalumab	AstraZeneca + Celgene	Anti-programmed death-1 ligand-1 (PD-L1) MAb	1,911	1.0%	Phase II & III
2.	Veliparib	veliparib	AbbVie	Poly (ADP-ribose) polymerase (PARP) inhibitor	1,714	0.9%	Phase III
3.	Abemaciclib	abemaciclib	Eli Lilly	Cyclin-dependent kinase (CDK) 4 & 6 inhibitor	1,619	0.9%	Phase III
4.	LEE011	ribociclib	Novartis	Cyclin-dependent kinase (CDK) 4 & 6 inhibitor	1,410	0.7%	Phase III
5.	PB272	neratinib	Puma Biotechnology	Pan-HER (ErbB) inhibitor	1,363	0.7%	Filed

#### **Product Segment Contribution to Sales in 2022**





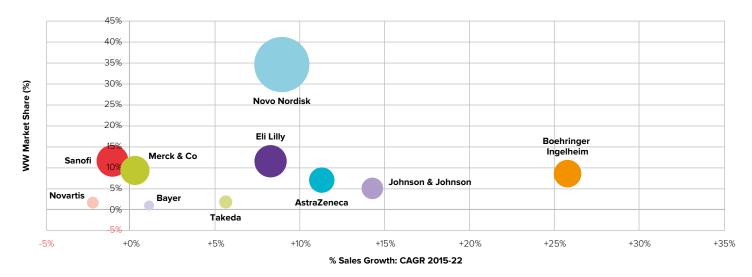
Novo Nordisk expected to remain the major player in 2022; Sanofi to lose market share; Boehringer Ingelheim climbs the charts.

EvaluatePharma\* finds that Novo Nordisk is expected to maintain its dominance in the anti-diabetic market through 2022. Novo's sales are forecast to grow by 9% per annum to \$22.9bn in 2022, representing a 34.7% share of the market. Sanofi, with anti-diabetic sales of \$7.70bn in 2022, is a long way behind in second place

as biosimilar competition to its long-acting insulin Lantus and the entry of new competitors into the space is expected to reduce its market share from 20.0% in 2015 to 11.7% in 2022. Jardiance, launched in 2014, proves a game changer for Boehringer Ingelheim; market share rockets from 2.8% in 2015 to 8.6% in 2022 with an unparalleled 26% CAGR.

#### Worldwide Sales, Market Share & Sales Growth (2015-2022)

Source: EvaluatePharma® August 2016



Note: Bubble = WW Sales in 2022

#### Top 10 Companies & Total Worldwide Anti-Diabetic Sales (2015-2022)

		ww	/ Sales (\$m)	CAGR	WW Marke	et Share	Rank Chg.
Rank	Company	2015	2022	2015-22	2015	2022	2015-22
1.	Novo Nordisk	12,662	22,909	+9%	30.4%	34.7%	+0
2.	Sanofi	8,331	7,698	-1%	20.0%	11.7%	+0
3.	Merck & Co	6,044	6,120	+0%	14.5%	9.3%	-1
4.	Eli Lilly	4,418	7,669	+8%	10.6%	11.6%	+1
5.	AstraZeneca	2,219	4,663	+11%	5.3%	7.1%	-1
6.	Johnson & Johnson	1,308	3,314	+14%	3.1%	5.0%	-1
7.	Novartis	1,220	1,036	-2%	2.9%	1.6%	-2
8.	Boehringer Ingelheim	1,147	5,688	+26%	2.8%	8.6%	+3
9.	Takeda	796	1,160	+6%	1.9%	1.8%	+1
10.	Bayer	597	641	+1%	1.4%	1.0%	-1
	Top 10	38,742	60,899	+7%	93.0%	92.2%	
	Other	2,935	5,151	+8%	7.0%	7.8%	
	Total Industry	41,677	66,050	+7%	100.0%	100.0%	

#### **Top 5 Anti-Diabetic Products Worldwide in 2022**

Source: EvaluatePharma® August 2016

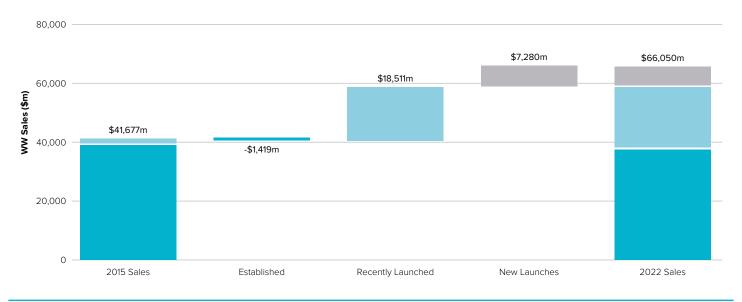
					WW Sales (\$m)		CAGR	WW Market	Share	Current
Rank	Product	Generic Name	Company	Pharma Class	2015	2022	2015-22	2015	2022	Status
1.	Januvia/ Janumet	sitagliptin phosphate	Merck & Co, Ono, Daewoong, Sigma-Tau, Almirall	Dipeptidyl peptidase IV inhibitor	6,333	5,913	-1.0%	15.2%	9.0%	Marketed
2.	Victoza	liraglutide [rDNA origin]	Novo Nordisk	Glucagon-like peptide 1 (GLP-1) agonist	2,682	4,133	+6.4%	6.4%	6.3%	Marketed
3.	Jardiance	empagliflozin	Boehringer Ingelheim	Sodium-glucose cotransporter-2 (SGLT2) inhibitor	118	3,932	+65.0%	0.3%	6.0%	Marketed
4.	Invokana	canagliflozin	Johnson & Johnson	Sodium-glucose cotransporter-2 (SGLT2) inhibitor	1,308	3,314	+14.2%	3.1%	5.0%	Marketed
5.	NovoRapid	insulin aspart	Novo Nordisk	Insulin analogue	3,082	2,976	-0.5%	7.4%	4.5%	Marketed

#### Top 5 Anti-Diabetic R&D Products Worldwide in 2022

Source: EvaluatePharma® August 2016

Rank	Product	Generic Name	Company	Pharma Class	WW Sales (\$m) 2022	WW Market Share 2022	Current Status
1.	Semaglutide	semaglutide	Novo Nordisk	Glucagon-like peptide 1 (GLP-1) agonist	2,356	3.6%	Phase III
2.	Faster-acting Insulin Aspart	insulin aspart	Novo Nordisk	Insulin analogue	1,054	1.6%	Filed
3.	LixiLan	insulin glargine; lixisenatide	Sanofi	Glucagon-like peptide 1 (GLP-1) agonist & insulin analogue	966	1.5%	Filed
4.	Saxadapa FDC	dapagliflozin propanediol; saxagliptin hydrochloride	AstraZeneca	Dipeptidyl peptidase IV (DPP-IV) inhibitor & sodium-glucose co-transporter 2 (SGLT2) inhibitor	476	0.7%	Filed
5.	MK-1293	insulin glargine	Merck & Co	Insulin analogue	309	0.5%	Filed

#### **Product Segment Contribution to Sales in 2022**



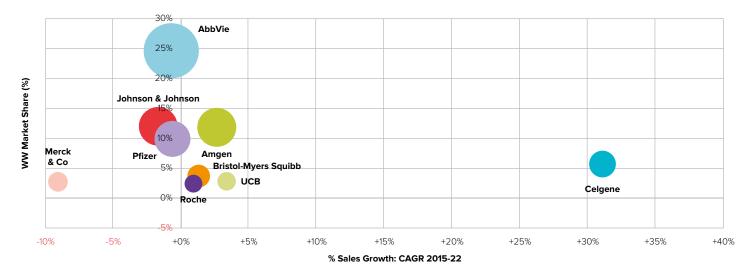
# Abbvie continues to dominate anti-rheumatics market in 2022; J&J's Remicade is forecast to lose market share.

AbbVie retained its number one position as the top anti-rheumatic company in 2015 and is forecast to remain market leader in 2022, with an expected market share of 24.4%. Humira is still forecast to be the best-selling anti-rheumatic product, despite the imminent threat of biosimilar competition. Recent clinical trial results have demonstrated barcitinib's superiority to Humira in treating the signs and symptoms of rheumatoid arthritis, which may be why baricitinib

is projected to be the most successful R&D product in 2022. ABP 501 is also likely to erode Humira sales in the future, with Amgen expecting FDA approval for the biosimilar in late September. Another product facing competitive pressure is J&J's Remicade — whose market share is expected to reduce dramatically, from 16.7% in 2015 to just 6.7% in 2022. The anti-rheumatics market continues to be a low growth market at just 2% per year (CAGR) to \$54.5bn in 2022. The low growth rate is due to the price erosion caused by the anticipated entry of biosimilars.

### Worldwide Sales, Market Share & Sales Growth (2015-2022)

Source: EvaluatePharma® August 2016



Note: Bubble = WW Sales in 2022

### Top 10 Companies & Total Worldwide Anti-Rheumatic Sales 2015-22

Source: EvaluatePharma® August 2016

		wv	V Sales (\$m)	CAGR	WW Mark	et Share	Rank Chg.
Rank	Company	2015	2022	2015-22	2015	2022	2015-22
1.	AbbVie	14,012	13,303	-1%	28.7%	24.4%	+0
2.	Johnson & Johnson	7,307	6,486	-2%	15.0%	11.9%	+0
3.	Amgen	5,364	6,431	+3%	11.0%	11.8%	+1
4.	Pfizer	5,667	5,408	-1%	11.6%	9.9%	-1
5.	Celgene	472	3,128	+31%	1.0%	5.7%	+10
6.	Bristol-Myers Squibb	1,885	2,065	+1%	3.9%	3.8%	+0
7.	Eli Lilly*		1,807		0.0%	3.3%	
8.	Merck & Co	2,955	1,520	-9%	6.0%	2.8%	-3
9.	UCB	1,202	1,517	+3%	2.5%	2.8%	-1
10.	Roche	1,258	1,345	+1%	2.6%	2.5%	-3
	Top 10	40,122	43,010	+1%	82.1%	78.9%	
	Other	8,727	11,510	+4%	17.9%	21.1%	
	Total Industry	48,849	54,519	+2%	100.0%	100.0%	

Note: \*Eli Lilly had no marketed anti-rheumatics in 2015

### **Top 5 Anti-Rheumatic Products Worldwide in 2022**

Source: EvaluatePharma® August 2016

					WW Sales (\$m)		CAGR	WW Marke	t Share	Current
Rank	Product	Generic Name	Company	Pharma Class	2015	2022	2015-22	2015	2022	Status
1.	Humira	adalimumab	AbbVie + Eisai	Anti-tumour necrosis factor alpha (TNFa) MAb	14,359	13,645	-1%	29.4%	25.0%	Marketed
2.	Enbrel	etanercept	Amgen + Pfizer + Takeda	Tumour necrosis factor alpha (TNFa) inhibitor	9,037	7,177	-3%	18.5%	13.2%	Marketed
3.	Remicade	infliximab	Johnson & Johnson + Merck & Co + Mitsubishi Tanabe Pharma	Anti-tumour necrosis factor alpha (TNFa) MAb	8,151	3,635	-11%	16.7%	6.7%	Marketed
4.	Simponi	golimumab	Johnson & Johnson + Merck & Co	Anti-tumour necrosis factor alpha (TNFa) MAb	2,018	3,139	+7%	4.1%	5.8%	Marketed
5.	Otezla	apremilast	Celgene	Phosphodiesterase IV (PDE4) inhibitor	472	3,128	+31%	1.0%	5.7%	Marketed

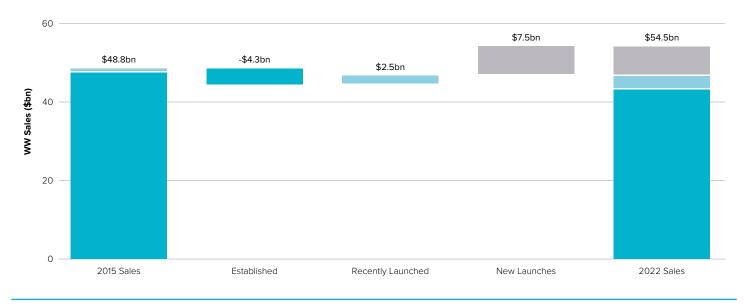
Note: Anti-tumour necrosis factor alpha (TNFa) inhibitor sales include RA, Crohn's and Psoriasis.

## **Top 5 R&D Anti-Rheumatic Products Worldwide in 2022**

Source: EvaluatePharma® August 2016

Rank	Product	Generic Name	Company	Pharma Class	WW Sales (\$m) 2022	WW Market Share 2022	Current Status
1.	Baricitinib	baricitinib	Eli Lilly	Janus kinase (JAK)-1/2 inhibitor	1,807	3.3%	Filed
2.	Sirukumab	sirukumab	Johnson & Johnson	Anti-interleukin-6 (IL-6) MAb	1,134	2.1%	Phase III
3.	ABP 501	adalimumab	Amgen	Anti-tumour necrosis factor alpha (TNFa) MAb	810	1.5%	Filed
4.	Sarilumab	sarilumab	Sanofi	Anti-interleukin-6 receptor (IL-6R) MAb	799	1.5%	Filed
5.	Mavrilimumab	mavrilimumab	AstraZeneca	Anti-granulocyte macrophage colony-stimulating factor receptor (GM-CSFR) MAb	235	0.4%	Phase II

# **Product Segment Contribution to Sales in 2022**



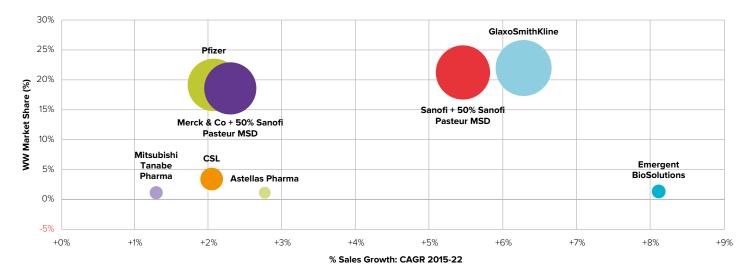
# GSK gains market leadership following deal with Novartis. Pfizer's Prevnar-13 remains top selling product.

GlaxoSmithKline has emerged as the market leader in the vaccines market following the completion of its transaction with Novartis to swap its oncology assets to gain Novartis' vaccines portfolio. Behind GSK, Sanofi, Pfizer and Merck are expected to maintain a

moderate growth rate through 2022. Novavax enters the top 10 and is expected to be one of the largest growth contributors with the launch of two new vaccines, and reach over \$2bn in worldwide sales by 2022. Following the acquisition of Novartis' flu vaccines, CSL's share of the global vaccine market is expected to be 3.4% in 2022.

#### Worldwide Sales, Market Share & Sales Growth (2015-2022)

Source: EvaluatePharma® August 2016



Note: Bubble = WW Sales in 2022

## **Top 10 Companies & Total Worldwide Vaccine Sales 2015-2022**

		wv	WW Sales (\$m)		WW Marke	et Share	Rank Chg.
Rank	Company	2015	2022	2015-22	2015	2022	2015-22
1.	GlaxoSmithKline	5,588	8,553	+6%	20.3%	21.9%	+3
2.	Sanofi + 50% Sanofi Pasteur MSD	5,724	8,295	+5%	20.8%	21.2%	+1
3.	Pfizer	6,439	7,430	+2%	23.4%	19.0%	-2
4.	Merck & Co + 50% Sanofi Pasteur MSD	6,177	7,238	+2%	22.4%	18.5%	-2
5.	Novavax	-	2,107			5.4%	
6.	CSL	1,150	1,323	+2%	4.2%	3.4%	-1
7.	Emergent BioSolutions	294	507	+8%	1.1%	1.3%	+1
8.	Mitsubishi Tanabe Pharma	389	426	+1%	1.4%	1.1%	-2
9.	Astellas Pharma	338	409	+3%	1.2%	1.0%	-2
10.	Dynavax Technologies	-	406			1.0%	
	Top 10	26,099	36,694	+5%	94.7%	94.0%	
	Other	1,454	2,343	+7%	5.3%	6.0%	
	Total Industry	27,553	39,037	+5%	100.0%	100.0%	

## **Top 5 Vaccine Products Worldwide in 2022**

Source: EvaluatePharma® August 2016

				WW Sales (\$m)		CAGR	WW Market Share		Current
Rank	Product	Generic Name	Company	2015	2022	2015-22	2015	2022	Status
1.	Prevnar 13	pneumococcal vaccine	Pfizer + Daewoong Pharmaceutical	6,328	6,069	-1%	23.0%	15.5%	Marketed
2.	Gardasil	human papillomavirus (HPV) vaccine	Merck + Sanofi Pasteur MSD + CSL	2,157	2,476	+2%	7.8%	6.3%	Marketed
3.	Fluzone	influenza vaccine	Sanofi + Sanofi Pasteur MSD	1,595	2,015	+3%	5.8%	5.2%	Marketed
4.	Pentacel	DTPa, Hib & polio vaccine	Sanofi	1,496	1,754	+2%	5.4%	4.5%	Marketed
5.	Pediarix	DTP, hepatitis B & polio vaccine	GlaxoSmithKline	1,120	1,322	+2%	4.1%	3.4%	Marketed

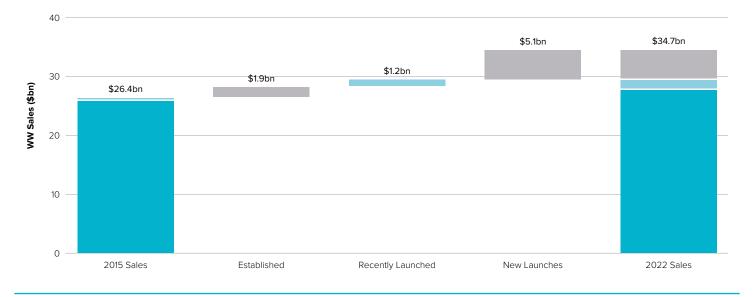
Note: Sanofi Pasteur MSD is a European joint venture between Merck & Co and Sanofi.

## **Top 5 Vaccine R&D Products Worldwide in 2022**

Source: EvaluatePharma® August 2016

Rank	Product	Generic Name	Company	WW Sales (\$m) 2022	WW Market Share 2022	Status
1.	Combination Respiratory Vaccine	influenza vaccine & respiratory syncytial virus (RSV) vaccine	Novavax	1,066	2.7%	Pre-clinical
2.	Shingrix	herpes zoster vaccine	GlaxoSmithKline	970	2.5%	Phase III
3.	RSV F Vaccine	respiratory syncytial virus (RSV) vaccine	Novavax	845	2.2%	Phase III
4.	PF-06290510	staphylococcus aureus vaccine	Pfizer	489	1.3%	Phase II
5.	Heplisav-B	hepatitis B vaccine	Dynavax Technologies	419	1.1%	Filed

# **Product Segment Contribution to Sales in 2022**





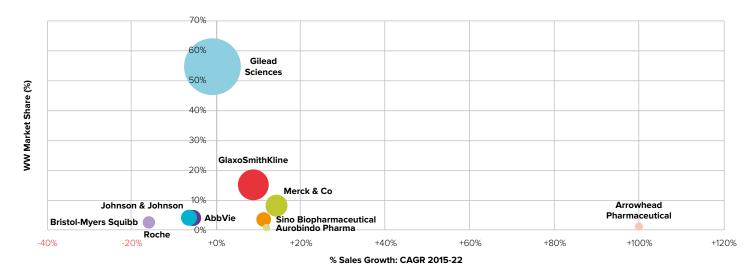
#### Gilead continues to dominate anti-viral market in 2022.

EvaluatePharma\* finds that Gilead will continue to command over 50% of the anti-virals market in 2022. Gilead's success in this area is largely due to its hepatitis C and HIV franchise, which are collectively forecast to contribute over \$27bn to 2022 worldwide anti-viral sales, with Harvoni being the top seller. Gilead also

appears to dominate the R&D sector contributing over \$7bn in 2022, with Bictegravir/F/TAF as the leading product. Roche sales are forecast to drop by approximately 70% in 2022, primarily due to declining Tamiflu and Valcyte sales hit by increased competition from GSK's Relenza and Valcyte generics.

#### Worldwide Sales, Market Share & Sales Growth (2015-2022)

Source: EvaluatePharma® August 2016



Note: Bubble = WW Sales in 2022

### Top 10 Companies & Total Worldwide Anti-viral Sales 2015-22

		wv	/ Sales (\$m)	CAGR	WW Marke	et Share	Rank Chg.
Rank	Company	2015	2022	2015-22	2015	2022	2015-22
1.	Gilead Sciences	30,190	27,924	-1%	59.5%	54.9%	+0
2.	GlaxoSmithKline	4,365	7,762	+9%	8.6%	15.3%	+0
3.	Merck & Co	1,665	4,193	+14%	3.3%	8.2%	+3
4.	Johnson & Johnson	3,166	2,091	-6%	6.2%	4.1%	+1
5.	AbbVie	3,334	2,088	-6%	6.6%	4.1%	-1
6.	Sino Biopharmaceutical	863	1,802	+11%	1.7%	3.5%	+2
7.	Bristol-Myers Squibb	4,214	1,233	-16%	8.3%	2.4%	-4
8.	Arrowhead Pharmaceuticals	-	480	n/m	-	0.9%	New
9.	Aurobindo Pharma	183	400	+12%	0.4%	0.8%	+2
10.	Roche	1,187	318	-17%	2.3%	0.6%	-3
	Top 10	49,167	48,291	-0%	96.9%	94.9%	
	Other	1,547	2,573	+8%	3.1%	5.1%	
	Total Industry	50,714	50,864	+0%	100.0%	100.0%	

## **Top 5 Anti-viral Products Worldwide in 2022**

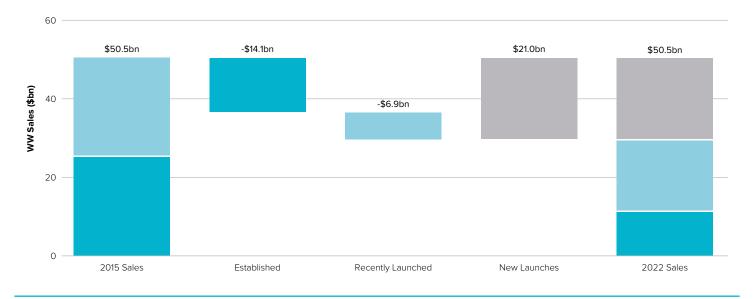
Source: EvaluatePharma® August 2016

						WW Sales (\$m) CAGR		WW Market Share		Current
Rank	Product	Generic Name	Company	Pharma Class	2015	2022	2015-22	2015	2022	Status
1.	Harvoni	ledipasvir; sofosbuvir	Gilead Sciences	Hepatitis C nucleoside NS5A & NS5B polymerase inhibitor	13,864	4,531	-15%	27.3%	8.9%	Marketed
2.	Triumeq	abacavir sulfate; dolutegravir sodium; lamivudine	GlaxoSmithKline	Nucleoside reverse transcriptase inhibitor (NRTI) & HIV integrase inhibitor	1,116	4,449	+22%	2.2%	8.7%	Marketed
3.	Descovy	emtricitabine; tenofovir alafenamide	Gilead Sciences	Nucleoside reverse transcriptase inhibitor (NRTI), CYP3A inhibitor & protease inhibitor	-	4,343	n/m	-	8.5%	Marketed
4.	Genvoya	cobicistat; elvitegravir; emtricitabine; tenofovir alafenamide fumarate	Gilead Sciences	Nucleoside reverse transcriptase inhibitor (NRTI), HIV integrase inhibitor & CYP3A inhibitor	45	3,731	+88%	0.1%	7.3%	Marketed
5.	Bictegravir/ F/TAF	bictegravir sodium; emtricitabine; tenofovir alafenamide fumarate	Gilead Sciences	Nucleoside reverse transcriptase inhibitor (NRTI) & HIV integrase inhibitor	-	3,489	n/m	-	6.9%	Phase III

# Top 5 R&D Anti-viral Products Worldwide in 2022

Rank	Product	Generic Name	Company	Pharma Class	WW Sale 2015	s (\$m) 2022	CAGR 2015-22	WW Market 2015	Share 2022	Current Status
1.	Bictegravir/ F/TAF	bictegravir sodium; emtricitabine; tenofovir alafenamide fumarate	Gilead Sciences	Nucleoside reverse transcriptase inhibitor (NRTI) & HIV integrase inhibitor	-	3,489	n/m	-	6.9%	Phase III
2.	Cobicistat/ Emtriva/ GS 7340/ Prezista STR	cobicistat; darunavir; emtricitabine; tenofovir alafenamide fumarate	Gilead Sciences	Nucleoside reverse transcriptase inhibitor (NRTI), CYP3A inhibitor & protease inhibitor	-	1,612	n/m	-	3.2%	Phase III
3.	Tenofovir Alafenamide	tenofovir alafenamide fumarate	Gilead Sciences	Nucleoside reverse transcriptase inhibitor (NRTI)	-	1,014	n/m	-	2.0%	Phase III
4.	Sofosbuvir, Velpatasvir & Voxilaprevir	sofosbuvir; velpatasvir; voxilaprevir	Gilead Sciences	Hepatitis C NS3 protease, Hepatitis C nucleoside NS5A & NS5B polymerase inhibitor	-	897	n/m	-	1.8%	Phase III
5.	ARC-520	-	Arrowhead Pharmaceuticals	Hepatitis B RNAi therapeutic	-	480	n/m	-	0.9%	Phase II

# **Product Segment Contribution to Sales in 2022**



# 2022: Top 50 Selling Products in the World



# Opdivo and Revlimid to compete for the top spot in 2022, while Humira is expected to step down following biosimilar launch.

EvaluatePharma\* sellside consensus forecast finds that Opdivo, Bristol-Myers Squibb's anti-PD-1 monoclonal antibody, will be the number one selling product worldwide in 2022, with sales of \$14.6bn. However, following the recent setback in NSCLC, Revlimid could take the crown with expected sales of \$13bn in 2022 provided that Humira loses ground following the potential launch of biosimilars (current forecast still positions Humira at number 2 with

\$13.6bn in 2022). In the PD-1 gold rush, Merck's Keytruda - currently anticipated to reach close to \$6bn in 2022 - is expected to take advantage of Opdivo's reccent setback in NSCLC, while Roche's Tecentrig is expected to reach \$5.3bn in 2022.

Only three products currently in R&D are present in the top 50, the biggest of which is Roche's Ocrevus, a phase III anti-CD20 MAb for the treatment of multiple sclerosis, it is expected to launch worldwide in December 2017.

Source: EvaluatePharma® August 2016

						duct Sales		Market
Rank	Product	Generic Name	Company	Pharmacological Class	2015	2022	CAGR	Status
1.	Opdivo	nivolumab	Bristol-Myers Squibb + Ono Pharmaceutical	Anti-programmed death-1 (PD-1) MAb	1,119	14,634	+44%	Marketed
2.	Humira	adalimumab	AbbVie + Eisai	Anti-tumour necrosis factor alpha (TNFa) MAb	14,359	13,645	-1%	Marketed
3.	Revlimid	lenalidomide	Celgene	Immunomodulator	5,801	13,024	+12%	Marketed
4.	Xarelto	rivaroxaban	Bayer + Johnson & Johnson	Factor Xa inhibitor	3,930	7,827	+10%	Marketed
5.	Eylea	aflibercept	Regeneron Pharmaceuticals + Bayer + Santen Pharmaceutical	Vascular endothelial growth factor receptor (VEGFr) kinase inhibitor	4,372	7,702	+8%	Marketed
6.	Imbruvica	ibrutinib	AbbVie + Johnson & Johnson	Bruton's tyrosine kinase (BTK) inhibitor	1,299	7,287	+28%	Marketed
7.	Enbrel	etanercept	Amgen + Pfizer + Takeda	Tumour necrosis factor alpha (TNFa) inhibitor	9,037	7,177	-3%	Marketed
8.	Prevnar 13	pneumococcal vaccine	Pfizer + Daewoong Pharmaceutical	Pneumococcal vaccine	6,328	6,069	-1%	Marketed
9.	Keytruda	pembrolizumab	Merck & Co	Anti-programmed death-1 (PD-1) MAb	566	5,959	+40%	Marketed
10.	Januvia/ Janumet	sitagliptin phosphate	Merck & Co + Ono Pharmaceutical + Almirall + Daewoong Pharmaceutical	Dipeptidyl peptidase IV (DPP-IV) inhibitor	6,333	5,913	-1%	Marketed
11.	Ibrance	palbociclib	Pfizer	Cyclin-dependent kinase (CDK) 4 & 6 inhibitor	723	5,709	+34%	Marketed
12.	Soliris	eculizumab	Alexion Pharmaceuticals	Anti-complement factor C5 MAb	2,590	5,657	+12%	Marketed
13.	Eliquis	apixaban	Bristol-Myers Squibb	Factor Xa inhibitor	1,860	5,422	+17%	Marketed
14.	Tecentriq	atezolizumab	Roche	Anti-programmed death-1 ligand-1 (PD-L1) MAb	-	5,331		Marketed
15.	Avastin	bevacizumab	Roche	Anti-vascular endothelial growth factor receptor (VEGFr) MAb	6,945	5,178	-4%	Marketed
16.	Prolia/Xgeva	denosumab	Amgen + Daiichi Sankyo	Anti-RANKL MAb	2,925	5,148	+8%	Marketed
17.	Victoza/Saxenda	liraglutide [rDNA origin]	Novo Nordisk	Glucagon-like peptide 1 (GLP-1) agonist	2,701	4,918	+9%	Marketed
18.	Darzalex	daratumumab	Johnson & Johnson	Anti-CD38 MAb	9	4,909	+146%	Marketed
19.	Botox	onabotulinumtoxinA	Allergan + GlaxoSmithKline	Botulinum toxin	2,808	4,823	+8%	Marketed
20.	Perjeta	pertuzumab	Roche	Anti-HER2 (ErbB-2) MAb	1,502	4,775	+18%	Marketed
21.	Entresto	sacubitril; valsartan	Novartis	Angiotensin II receptor (AT1) antagonist & neprilysin inhibitor (ARNI)	21	4,698	+117%	Marketed
22.	Tecfidera	dimethyl fumarate	Biogen	Fumarate	3,638	4,677	+4%	Marketed
23.	Xtandi	enzalutamide	Astellas Pharma	Androgen receptor antagonist	2,101	4,658	+12%	Marketed
24.	Harvoni	ledipasvir; sofosbuvir	Gilead Sciences	Hepatitis C nucleoside NS5A & NS5B polymerase inhibitor	13,864	4,531	-15%	Marketed
25.	Stelara	ustekinumab	Johnson & Johnson	Anti-interleukin-12 (IL-12) & interleukin-23 (IL-23) MAb	2,474	4,527	+9%	Marketed

Top 26-50 continued over...



Source: EvaluatePharma® 1 August 2016

					WW Pr	oduct Sales	(\$m)	Market
Rank	Product	Generic Name	Company	Pharmacological Class	2015	2022	CAGR	Status
26.	Herceptin	trastuzumab	Roche	Anti-HER2 (ErbB-2) MAb	6,794	4,467	-6%	Marketed
27.	Triumeq	abacavir sulfate; dolutegravir sodium; lamivudine	GlaxoSmithKline	Nucleoside reverse transcriptase inhibitor (NRTI) & HIV integrase inhibitor	1,116	4,449	+22%	Marketed
28.	Spiriva	tiotropium bromide	Boehringer Ingelheim + Pfizer	Long-acting muscarinic antagonist (LAMA)	3,942	4,390	+2%	Marketed
29.	Descovy	emtricitabine; tenofovir alafenamide	Gilead Sciences  Nucleoside reverse transcriptase inhibitor (NRTI), CYP3A inhibitor & protease inhibitor		-	4,343		Marketed
30.	Repatha	evolocumab	Amgen + Astellas Pharma	Anti-proprotein convertase subtilisin-like kexin type 9 (PCSK9) MAb	9	4,280	+141%	Marketed
31.	Ocrevus	ocrelizumab	Roche	Anti-CD20 MAb	-	3,962		R&D
32.	Jardiance	empagliflozin	Boehringer Ingelheim + Eli Lilly	Sodium-glucose cotransporter-2 (SGLT2) inhibitor	118	3,932	+65%	Marketed
33.	Cosentyx	secukinumab	Novartis	Anti-interleukin-17A (IL-17A) MAb	261	3,856	+47%	Marketed
34.	Genvoya	cobicistat; elvitegravir; emtricitabine; tenofovir alafenamide fumarate	Gilead Sciences	Nucleoside reverse transcriptase inhibitor (NRTI), HIV integrase inhibitor & CYP3A inhibitor	45	3,731	+88%	Marketed
35.	Dupilumab	dupilumab	Sanofi	Anti-interleukin-4 (IL-4) & interleukin-13 (IL-13) MAb	-	3,725		R&D
36.	Privigen <sup>1</sup>	immune globulin (human)	CSL	Immunoglobulin	2,467	3,701	+6%	Marketed
37.	Gazyva	obinutuzumab	Roche	Anti-CD20 MAb	133	3,643	+60%	Marketed
38.	Remicade	infliximab	Johnson & Johnson + Merck & Co + Mitsubishi Tanabe Pharma	Anti-tumour necrosis factor alpha (TNFa) MAb	8,151	3,635	-11%	Marketed
39.	Bictegravir/F/ TAF	bictegravir sodium; emtricitabine; tenofovir alafenamide fumarate	Gilead Sciences	Nucleoside reverse transcriptase inhibitor (NRTI) & HIV integrase inhibitor	-	3,489		R&D
40.	Orkambi	ivacaftor; lumacaftor	Vertex Pharmaceuticals	Cystic fibrosis transmembrane conductance regulator (CFTR) corrector	351	3,485	+39%	Marketed
41.	Invokana	canagliflozin	Johnson & Johnson + Mitsubishi Tanabe Pharma	Sodium-glucose cotransporter-2 (SGLT2) inhibitor	1,333	3,429	+14%	Marketed
42.	Vyvanse	lisdexamfetamine dimesylate	Shire + Shionogi	Psychostimulant	1,722	3,338	+10%	Marketed
43.	Simponi	golimumab	Johnson & Johnson + Merck & Co	Anti-tumour necrosis factor alpha (TNFa) MAb	2,018	3,139	+7%	Marketed
44.	Otezla	apremilast	Celgene	Phosphodiesterase IV (PDE4) inhibitor	472	3,128	+31%	Marketed
45.	Ocaliva	obeticholic acid	Intercept Pharmaceuticals + Sumitomo Dainippon Pharma	Farnesoid X receptor (FXR) agonist	-	3,076		Marketed
46.	Praluent	alirocumab	Sanofi	Anti-proprotein convertase subtilisin-like kexin type 9 (PCSK9) MAb	10	3,063	+127%	Marketed
47.	Rituxan	rituximab	Roche + Pharmstandard	Anti-CD20 MAb	7,393	3,036	-12%	Marketed
48.	NovoRapid	insulin aspart	Novo Nordisk	Insulin analogue	3,082	2,976	-1%	Marketed
49.	Lantus	insulin glargine	Sanofi	Insulin analogue	7,089	2,953	-12%	Marketed
50.	Tresiba	insulin degludec	Novo Nordisk	Insulin analogue	214	2,922	+45%	Marketed
	Total				144,025	254,346	+8%	
	Total WW Individ	lual Products Forecast in Ev	valuatePharma*		617,246	919,310	+6%	

Note: Sales represent company reported sales where available, otherwise based on an average of equity analyst estimates.

 $<sup>^{\</sup>mbox{\tiny 1}}$  Includes entire Immunoglobulin/VIg sales for company.

# 2022: Top 50 Selling Products in the USA



# Humira still the leading product in USA in 2022; Roche products make up 10% of Top 50 in 2022.

EvaluatePharma\* finds that AbbVie's Humira will continue to be the leading product in the USA in 2022, with sales of \$10.7bn This is a clear sign that sellside analysts are still very skeptical about the potential launch of a biosimilar version. Celgene's Revlimid will be in second place with sales growing on average 13% per year to \$8.1bn

in 2022, and with a CAGR of 36%, it won't be long before Opdivo is hot on their heels. Roche is set to have five products in the USA Top 50 by 2022, including their phase III anti-CD20 MAb, Ocrevus, for the treatment of multiple sclerosis, and recently approved Tecentriq, the third PD-1 product to launch in the market following Opdivo and Keytruda.

Source: EvaluatePharma® 1 August 2016

					USA Pro	duct Sales	(\$m)	
Rank	Product	Generic Name	Company	Pharmacological Class	2015	2022	CAGR	US Market Status
1.	Humira	adalimumab	AbbVie	Anti-tumour necrosis factor alpha (TNFa) MAb	8,405	10,729	+4%	Marketed
2.	Revlimid	lenalidomide	Celgene	Celgene Immunomodulator		8,145	+13%	Marketed
3.	Opdivo	nivolumab	Bristol-Myers Squibb	Anti-programmed death-1 (PD-1) MAb	823	7,222	+36%	Marketed
4.	Enbrel	etanercept	Amgen	Tumour necrosis factor alpha (TNFa) inhibitor	5,099	5,065	-0%	Marketed
5.	Eylea	aflibercept	Regeneron Pharmaceuticals	Vascular endothelial growth factor receptor (VEGFr) kinase inhibitor	2,676	5,014	+9%	Marketed
6.	Tecentriq	atezolizumab	Roche	Anti-programmed death-1 ligand-1 (PD-L1) MAb	-	3,810		Marketed
7.	Eliquis	apixaban	Bristol-Myers Squibb	Factor Xa inhibitor	1,023	3,731	+20%	Marketed
8.	Imbruvica	ibrutinib	AbbVie	Bruton's tyrosine kinase (BTK) inhibitor	985	3,683	+21%	Marketed
9.	Xarelto	rivaroxaban	Johnson & Johnson	Factor Xa inhibitor	1,868	3,606	+10%	Marketed
10.	Ibrance	palbociclib	Pfizer	Cyclin-dependent kinase (CDK) 4 & 6 inhibitor	718	3,462	+25%	Marketed
11.	Tecfidera	dimethyl fumarate	Biogen	Fumarate	2,908	3,310	+2%	Marketed
12.	Entresto	sacubitril; valsartan	Novartis	Angiotensin II receptor (AT1) antagonist & neprilysin inhibitor (ARNI)	21	3,279	+106%	Marketed
13.	Prevnar 13	pneumococcal vaccine	Pfizer	Pneumococcal vaccine	4,026	3,217	-3%	Marketed
14.	Stelara	ustekinumab	Johnson & Johnson	Anti-interleukin-12 (IL-12) & interleukin-23 (IL-23) MAb	1,677	3,172	+10%	Marketed
15.	Victoza/Saxenda	liraglutide [rDNA origin]	Novo Nordisk	Glucagon-like peptide 1 (GLP-1) agonist	1,936	3,079	+7%	Marketed
16.	Prolia/Xgeva	denosumab	Amgen	Anti-RANKL MAb	1,843	3,042	+7%	Marketed
17.	Vyvanse	lisdexamfetamine dimesylate	Shire	Psychostimulant	1,599	3,029	+10%	Marketed
18.	Ocrevus	ocrelizumab	Roche	Anti-CD20 MAb	-	3,025		R&D
19.	Descovy	emtricitabine; tenofovir alafenamide	Gilead Sciences	Nucleoside reverse transcriptase inhibitor (NRTI), CYP3A inhibitor & protease inhibitor	-	2,936		Marketed
20.	Jardiance	empagliflozin	Boehringer Ingelheim + Eli Lilly	Sodium-glucose cotransporter-2 (SGLT2) inhibitor	99	2,804	+61%	Marketed
21.	Keytruda	pembrolizumab	Merck & Co	Anti-programmed death-1 (PD-1) MAb	393	2,801	+32%	Marketed
22.	Triumeq	abacavir sulfate; dolutegravir sodium; lamivudine	GlaxoSmithKline	Nucleoside reverse transcriptase inhibitor (NRTI) & HIV integrase inhibitor	779	2,673	+19%	Marketed
23.	Xtandi	enzalutamide	Astellas Pharma	Androgen receptor antagonist	1,237	2,608	+11%	Marketed
24.	Avastin	bevacizumab	Roche	Anti-vascular endothelial growth factor receptor (VEGFr) MAb	3,178	2,591	-3%	Marketed
25.	Harvoni	ledipasvir; sofosbuvir	Valeant Pharmaceuticals International	Hepatitis C nucleoside NS5A & NS5B polymerase inhibitor	10,090	2,586	-18%	Marketed

Top 26-50 continued over...



Source: EvaluatePharma® 1 August 2016

Rank	Product	Generic Name	Company	Pharmacological Class	USA Product Sales (\$m)			
					2015	2022	CAGR	US Market Status
26.	Botox	onabotulinumtoxinA	Allergan	Botulinum toxin	1,715	2,486	+5%	Marketed
27.	Genvoya	cobicistat; elvitegravir; emtricitabine; tenofovir alafenamide fumarate	Gilead Sciences	Nucleoside reverse transcriptase inhibitor (NRTI), HIV integrase inhibitor & CYP3A inhibitor	44	2,471	+78%	Marketed
28.	Darzalex	daratumumab	Allergan	Anti-CD38 MAb	9	2,466	+123%	Marketed
29.	Invokana	canagliflozin	Johnson & Johnson	Sodium-glucose cotransporter-2 (SGLT2) inhibitor	1,238	2,454	+10%	Marketed
30.	Perjeta	pertuzumab	Roche	Anti-HER2 (ErbB-2) MAb	835	2,359	+16%	Marketed
31.	Repatha	evolocumab	Amgen	Anti-proprotein convertase subtilisin-like kexin type 9 (PCSK9) MAb	7	2,348	+128%	Marketed
32.	Cosentyx	secukinumab	Novartis	Anti-interleukin-17A (IL-17A) MAb	220	2,253	+39%	Marketed
33.	Otezla	apremilast	Celgene	Phosphodiesterase IV (PDE4) inhibitor	440	2,251	+26%	Marketed
34.	Tresiba	insulin degludec	Novo Nordisk	Insulin analogue	-	2,202		Marketed
35.	Soliris	eculizumab	Alexion Pharmaceuticals	Anti-complement factor C5 MAb	951	2,183	+13%	Marketed
36.	Neulasta	pegfilgrastim	Amgen	Granulocyte colony-stimulating factor (G-CSF)	3,891	2,158	-8%	Marketed
37.	Orkambi	ivacaftor; lumacaftor	Vertex Pharmaceuticals	Cystic fibrosis transmembrane conductance regulator (CFTR) corrector	351	2,152	+30%	Marketed
38.	Remicade	infliximab	Johnson & Johnson	Anti-tumour necrosis factor alpha (TNFa) MAb	4,453	2,148	-10%	Marketed
39.	Dupilumab	dupilumab	Sanofi	Anti-interleukin-4 (IL-4) & interleukin-13 (IL-13) MAb	-	2,087		R&D
40.	Venclexta	venetoclax	Roche + AbbVie	B-cell lymphoma 2 (Bcl-2) inhibitor	-	2,044		Marketed
41.	Xifaxan 200	rifaximin	Valeant Pharmaceuticals International	Ansamycin	716	2,005	+16%	Marketed
42.	Bictegravir/F/TAF	bictegravir sodium; emtricitabine; tenofovir alafenamide fumarate	Gilead Sciences	Nucleoside reverse transcriptase inhibitor (NRTI) & HIV integrase inhibitor	-	1,992		R&D
43.	Fovista	pegpleranib sodium	Ophthotech	Anti-platelet derived growth factor (PDGF)-B aptamer	-	1,973		R&D
44.	Trulicity	dulaglutide	Eli Lilly	Glucagon-like peptide 1 (GLP-1) agonist	208	1,785	+36%	Marketed
45.	Gardasil	human papillomavirus (HPV) vaccine	Merck & Co	Human papillomavirus (HPV) vaccine	1,521	1,783	+2%	Marketed
46.	Ocaliva	obeticholic acid	Intercept Pharmaceuticals	Farnesoid X receptor (FXR) agonist	-	1,767		Marketed
47.	Jakafi	ruxolitinib phosphate	Incyte	Janus kinase (JAK)-1/2 inhibitor	601	1,759	+17%	Marketed
48.	Xyrem	sodium oxybate	Jazz Pharmaceuticals	CNS depressant	955	1,737	+9%	Marketed
49.	Semaglutide	semaglutide	Novo Nordisk	Glucagon-like peptide 1 (GLP-1) agonist	-	1,710		R&D
50.	Rexulti	brexpiprazole	Otsuka Holdings	5-HT1A (serotonin) & D2 partial agonist & 5-HT2 (serotonin) receptor antagonist	38	1,665	+72%	Marketed
	Total				73,111	150,855	+11%	
	Total USA Individual Products Forecast in EvaluatePharma®				292,688	468,886	+ <b>7</b> %	

Note: Sales represent company reported sales where available, otherwise based on an average of equity analyst estimates.

# About EvaluatePharma®

Since 1996 EvaluatePharma has been providing senior decision makers within the pharmaceutical industry with an essential service that models the sector from the viewpoint of the world's financial markets.

EvaluatePharma's forward looking view of the market is hugely influential as it displays the consensus of expectations, which influence company stock market valuations. The forecasts of equity analysts reveal their perspectives on individual company performance, industry trends and the macro economic environment.

EvaluatePharma has captured the consensus forecasts of equity analysts and seamlessly integrated them with the historic results, as reported by companies. From this comprehensive view of the industry, its past and expected future performance emerges and can be analysed using EvaluatePharma. Analyses range from total market trends and therapeutic overviews to individual company performance and product progress.

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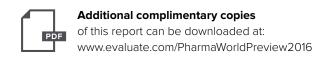
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