EP Vantage 2017 Preview

Amy Brown – December 2016

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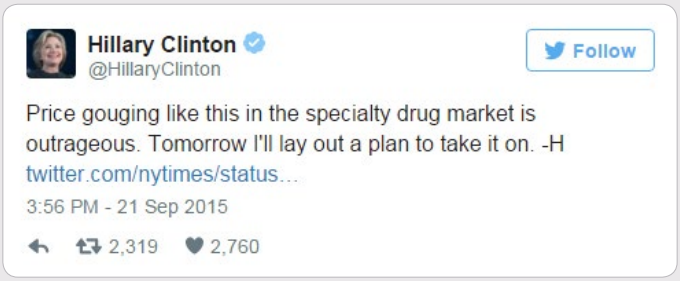
Foreword

Meditating on what 2017 might have in store for the pharma and biotech sector would have been pointless before the big event of the year. Investment decisions and strategic moves were in many cases on pause, awaiting the outcome of the US election to gauge the approaching political climate.

On November 9 the weather forecast turned extremely sunny, according to investors at least, who dramatically bid up drug stocks in reaction to the Trump victory and the new Republican dominance. The bounce was based on expectations of a slew of business-friendly initiatives and the likely lessening of aggressive political rhetoric towards drug pricing; this last issue has been a huge drag on sentiment towards the sector for the past 18 months.

"Really, since Hillary Clinton put thumb to Blackberry, pharma and biotech was being viewed as the wrong place to be, with real fears over future profitability and growth prospects. Now the threat has been removed, people can start contemplating fundamentals again," says David Pinniger, a healthcare fund manager for Polar Capital Partners in London.



The question for investors is whether the euphoria can be maintained. Drug price scrutiny is not going away, and the pressure from payers across the globe is unlikely to abate. On a wider level, economic uncertainty abounds in many regions of the world which, together with hotspots of regional instability, continues to worry investors.

However many believe that the political wind in the world's biggest drug market is, for the time being, blowing in the right direction.

> The premium on innovation has just been re-established, says Mr Pinniger.

For a sector flush with new confidence about the future – and possibly cash if the US tax repatriation holiday happens – this could mean a new push on the M&A front after a quiet 2016. The IPO markets are unlikely to recover to the biotech boom days, but there are few obvious reasons why a serious contraction would happen in 2017; the same goes for the venture financing market, with funds still well stocked.

R&D productivity, another big barometer for the sector, is arguably pointing to less clement times. Approvals of novel drugs in the US – a closely watched yardstick – are heading for a drop this year, while the blow-up of Lilly's Alzheimer's disease project solanezumab in late November was a massive setback. The data represented the most hotly awaited R&D readout for the sector for a number of years and the unequivocal failure serves as a reminder of the inherent risk in drug development – and the dangers of overblown expectations.

As such, the loss of one of pharma's biggest pipeline hopes does not set an encouraging tone for the clinical milestones that are approaching in 2017. Important products that will be closely watched as the year unfolds include the numerous immuno-oncology assets, many of which are expected to generate impressive leaps forward for the cancer space, while a couple of big cardiovascular trials also hold the potential to steer sentiment around the industry's late-stage R&D work.

Progress will also be expected from early-stage investigations of cutting edge scientific techniques – CAR-T, Crispr gene editing and gene therapies, for example. These areas are among the most highly valued in drug development but represent huge risk, so any serious setbacks could easily undermine confidence in R&D efforts more widely.

On the commercial front, many expect that the industry's cautious stance adopted in 2016 amid wider political uncertainties will become more aggressive heading into 2017. That ought to translate into more corporate activity and bring investor cash into the sector. With many companies remaining well capitalised after the boom of 2014 and 2015, and financing easy to come by for the larger players, there is certainly the potential for pharma and biotech to experience something of a bounce next year.

That said, as the US presidential election and the UK's vote to leave the EU amply demonstrate, surprises and shocks to the system can emerge from anywhere.

Report author | Amy Brown

2017 in numbers

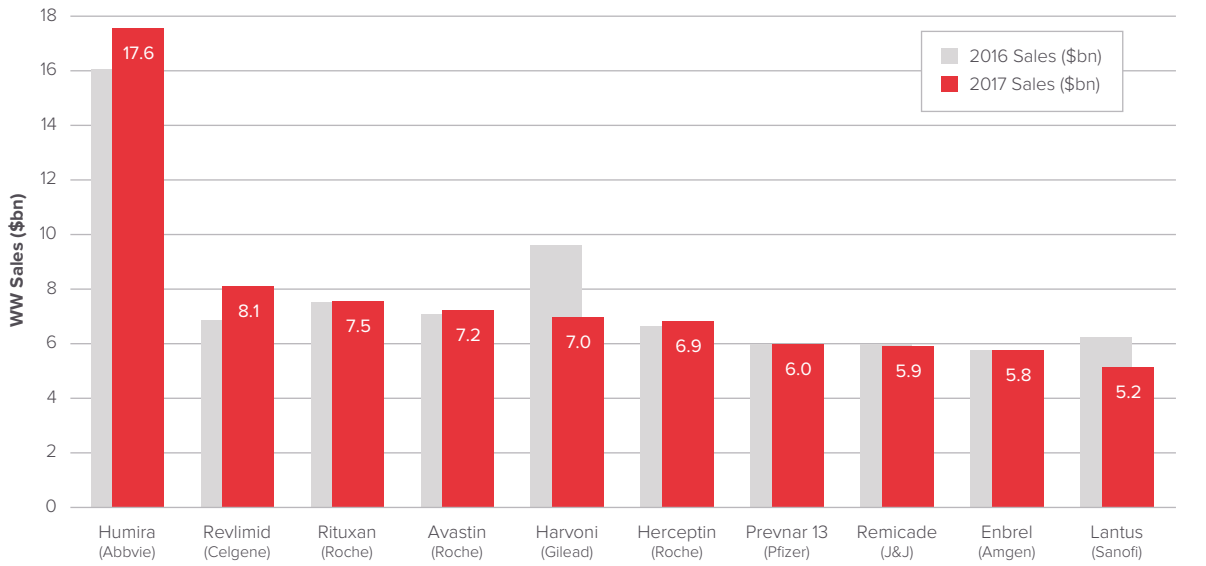
Making qualitative predictions about the coming year is indisputably difficult; some quantitative forecasts, however, are easier to come by. The following analyses have been drawn from EvaluatePharma's consensus forecasts.

For example, the graph below shows that next year's biggest-selling drug brand will once again be Humira, leading by a long way.

The strength and breadth of this franchise is one of the success stories of the pharmaceutical industry, and the debate about its longevity one of the most keenly followed. With biosimilar players desperately trying to break the final couple of patents that remain in place, and Abbvie even more desperately defending them, the ongoing legal battles will continue to feed one of the sector's most closely watched issues in 2017.

Top 10 Drugs by 2017 Sales ($bn)

Source: EvaluatePharma® 20 November 2016



It is notable that only Humira and Revlimid are showing anything like growth among the top 10. The world's biggest blockbusters are obviously not going to be in explosive growth stage, but this analysis suggests that the next few years will see a change in guard at the top. With biosimilars biting at the heels of a number of these franchises, this is not surprising.

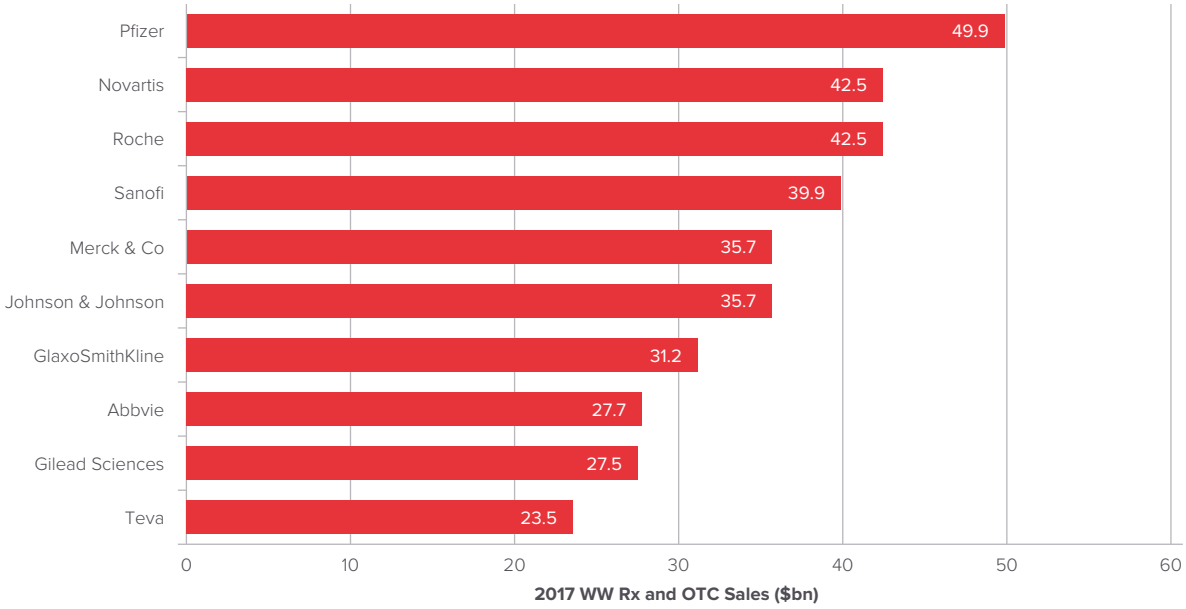
It is worth pointing out that this graphic understates the dominance of Gilead in terms of ownership of the biggest drug franchises next year. Its three marketed hepatitis C products, all of which contain sofosbuvir, are forecast to generate sales of $11.7bn next year. However this is an empire in decline: in 2016 these products brought in $14.9bn. Gilead's efforts to replace these revenues, – failed efforts, some might say – again hold the potential to generate many headlines in 2017.

These products and its huge HIV franchise will mean that the California company remains one of the world's biggest sellers of pharmaceuticals next year, as the graph below shows.

Gilead's inclusion in this ranking, and Teva taking 10th place, shows just how the industry has shifted in the past few years. Big pharma names like Astrazeneca, Bristol-Myers Squibb and Lilly, big casualties of patent expiries over the past five years, are now to be found at 13th, 14th and 15th place respectively.

Top 10 Companies by 2017 Rx and OTC Sales ($bn)

Source: EvaluatePharma® 20 November 2016



Gilead will have to buy some big near-term revenues to stay in the top 10 in 2018 – its top line is projected to shrink 6% over the course of next year. This cannot be ruled out, and many investors are pushing for a big corporate move – the prospect of a large US acquisition has increased with Donald Trump's pledge to push through a repatriation tax holiday, many believe. Gilead is estimated to have one of the biggest ex-US cash piles of the industry, with an estimated $16bn, equivalent to 60% of its net cash, held off shore.

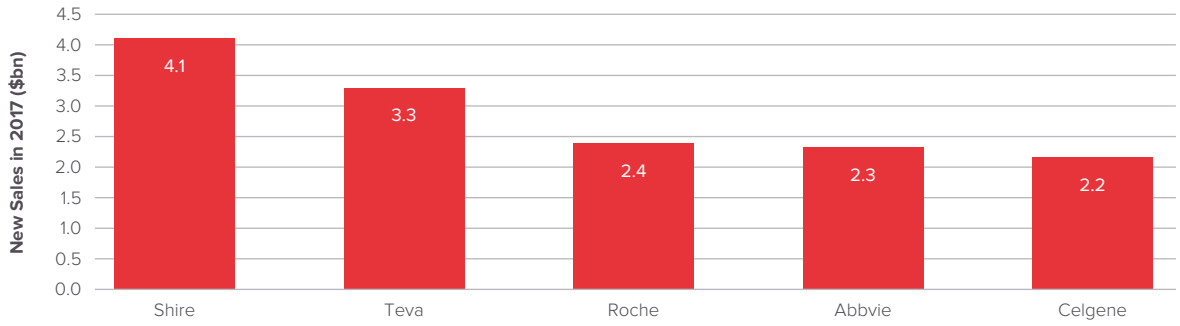
Pfizer, meanwhile, has maintained its pole position through acquisitions, seemingly unhindered by a similarly large ex-US cash position. Its last big buys were Hospira for $17bn and Medivation for $14bn, and further substantial moves by the profligate pharma giant cannot be ruled out next year.

Sanofi is also thought to have acquisitive ambitions, having missed out on Medivation which fell to Pfizer in September 2016. And in late 2016 Johnson & Johnson confirmed its interest in Switzerland's Actelion – this target would provide immediate growth for any buyer, although it would come with a huge price tag.

Looking at the companies forecast to add the most new sales next year, over the page, an entirely different ranking emerges.

Top 5 Companies by New Sales in 2017 ($bn)

Source: EvaluatePharma® 20 November 2016



Again, the two leaders are here largely by dint of acquisition – Shire's buy of Baxalta and Teva's consolidation of Allergan's generics business.

Abbvie and Celgene can thank their still-expanding cash cows, Humira and Revlimid, which astonishingly also rank as two of the biggest-growing products next year, as the following analysis shows. Having been launched in 2003 and 2006 respectively these brands are still adding more than $1bn in sales a year, helped by the broad approval settings that have been won over the years.

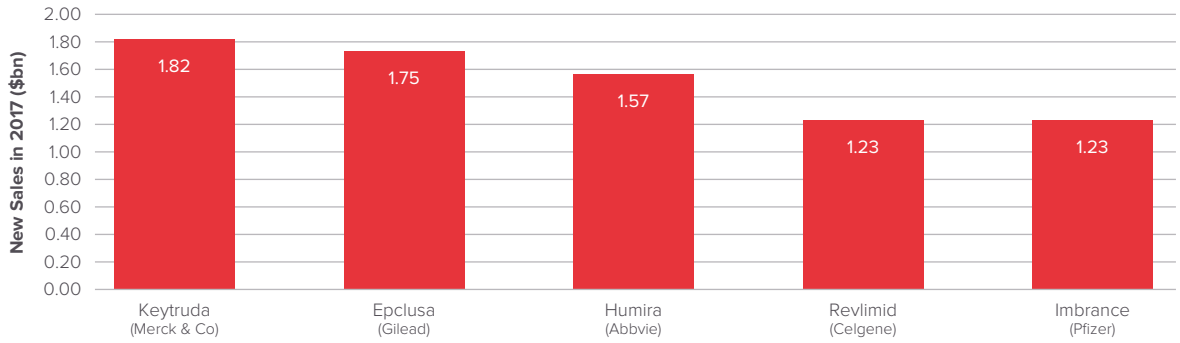
Roche's top line is growing largely thanks to Tecentriq, its contender in the immuno-oncology race, while Merck & Co's rival Keytruda ranks as one of the fastest-growing drugs, below.

Considering that the first wave of immuno-oncology drugs have only been available for a few years – Keytruda was launched in late 2014 – the fact that they are already making a noticeable impact on the industry's top line is a sign of just how big these products could become.

In fact Keytruda's impact has probably been boosted by Bristol-Myers Squibb's disastrous attempt to win approval in a broad first-line lung cancer setting for its rival Opdivo. The unequivocal failure of a phase III trial has since given a huge boost to its competitor.

Top 5 Drugs by New Sales in 2017 ($bn)

Source: EvaluatePharma® 20 November 2016



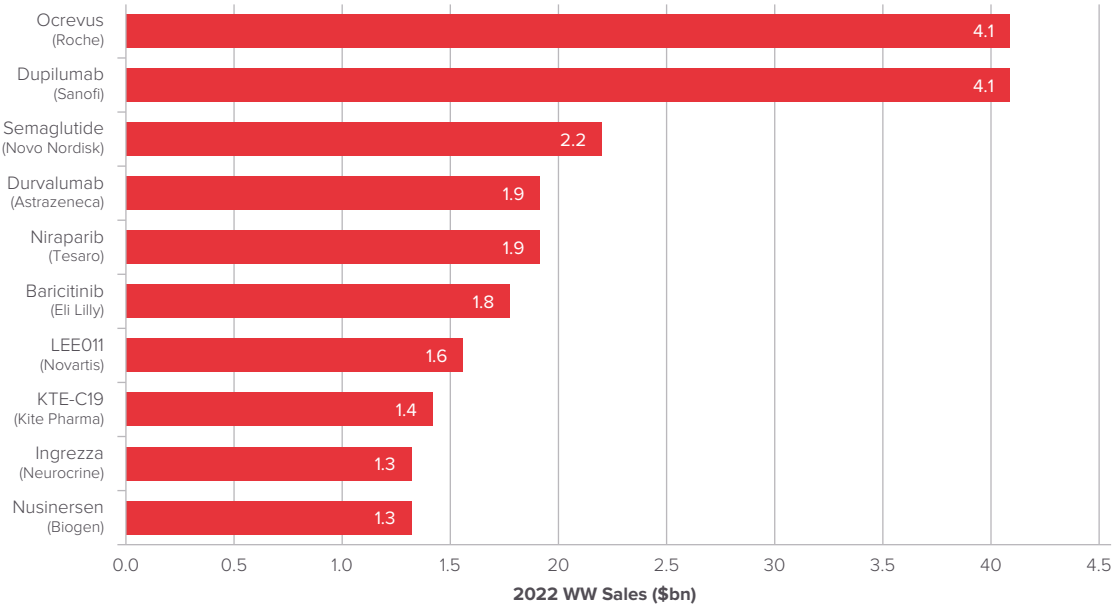
A look at which companies are expected to be enjoying growth further down the line can be gleaned from an analysis of next year's biggest launches. This analysis is ranked on sales further out, in 2022.

Two products stand out here: Roche's new MS contender Ocrevus and Sanofi's novel dermatology therapy dupilumab. Both are awaiting regulatory judgement – the former should know by the end of 2016 and the latter by next spring – and represent two of the most keenly awaited approvals for the sector.

Although small in comparison, the other eight future blockbusters on this list are also going to be hot topics for 2017. Of particular note is KTE-C19, the CAR-T therapy being advanced by Kite – the recent setback of Juno's JCAR015 makes its rival's early approval ambitions look ever more optimistic.

Top Launches in 2017 by 2022 Sales ($bn)

Source: EvaluatePharma® 20 November 2016

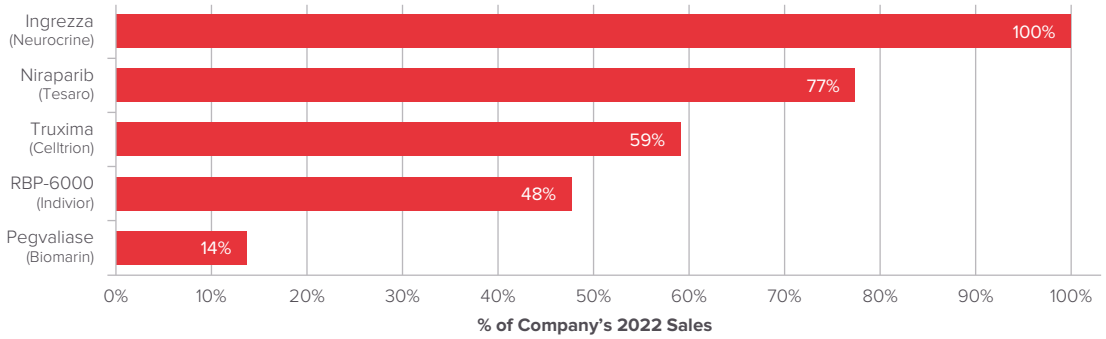


While these potential blockbusters naturally attract much attention, smaller product launches matter to smaller players. Over the page, the same analysis ranked by the importance of the new product to the company's total sales highlights some big decisions pending for the other end of the sector.

The inclusion of Tesaro's breast cancer pill niraparib in both cuts of the data emphasises what a huge event the arrival of this product represents, for the company and for the oncology space. If any company were a target for big pharma desperate to buy in new growth, Tesaro is surely it – and its $7bn market value reflects this.

Top Launches in 2017 by % of Company's 2022 Sales

Source: EvaluatePharma® 20 November 2016



The flip side to these stories of new growth is frequently patent expiry. The table below shows the five biggest products with key US patents that expire next year.

This does not necessarily mean that generics will enter, of course, and a number are still fighting to protect their intellectual property. Lilly is still battling to keep its exclusive position with the cancer drug Alimta, for example.

This list also does not show any biologicals, a number of which lose patent protection in the coming few years. The threat of biosimilars is looming for many drug makers – Roche in particular – although exactly how much of a danger these represent remains to be quantified, particularly in the US market.

Top 5 Products with US Patents at Threat in 2017

Source: EvaluatePharma® 20 November 2016

Product	Company	2016 US Sales ($m)	% of 2016 Company WW Rx and OTC Sales	% of 2016 Company US Sales
Cialis	Eli Lilly	1,467	14%	16%
Viagra	Pfizer	1,200	3%	6%
Velcade	Takeda	1,171	8%	24%
Alimta	Eli Lilly	1,105	13%	12%
Prezista	Johnson & Johnson	1,087	5%	6%

Launches of biosimilars in Europe have in some markets come at a significant discount – a biosimilar of Remicade was launched in Scandinavia at a third of the cost of the original, for example. It is far from clear whether this will be true for the world's biggest drugs market.

The response of the originator companies has also yet to be assessed – it would be folly to underestimate the effectiveness of what are bound to be huge efforts to protect these massive brands. The emergence of these strategies over the course of 2017 will be closely watched, as will the ongoing legal battles of the biosimilar makers.

Of course it is not just patent fights that alter a drug's prospects. In the past few years the increasing power of payers, particularly in the US, has placed substantial pressure on certain therapy areas. Diabetes and respiratory have been particularly hard hit, with older franchises unable to raise prices as freely as in the past, and new launches unable to command any sort of premium.

The power of the payers

Eyes will be peeled for evidence that this pressure is spreading into other therapy areas in 2017 – the anti-TNFs are already a new area of scrutiny. Amgen warned at its third-quarter results that Enbrel would not see any net price rises next year in the US owing to increased rebates to pharmacy benefit managers, to help maintain its formulary positions.

For many years, companies and investors took price growth for granted in the US, and the harsh reality of the need to drive volumes for topline expansion has come as a bit of a shock.

"If you look at the four large cap biotech stocks – Amgen, Gilead, Celgene and Biogen – the only one that's really growing on volume is Celgene," says the Mizuho Securities analyst Salim Syed, who cites this as one reason why biotech shares remained depressed in 2016.

"Investors have been saying, if Celgene is the only growth story, why should I invest in the sector?"

Companies will have to work hard next year to fight this concern as payers are expected to flex their muscles in other highly competitive areas; MS and rheumatoid arthritis are ones to watch.

Interestingly, it seems that the sellside has been slow on the uptake in some of these categories. The table below shows the individual products that have received some of the biggest upgrades and downgrades to 2017 consensus sales forecasts over the course of 2016.

The Biggest Swingers: Shifts in 2017 Consensus Over Previous 12 Months

Source: EvaluatePharma® 20 November 2016

BIGGEST UPGRADES	Product	Company	Change in WW 2017 Sales ($m)
	Ibrance	Pfizer	1,188.32
	Enbrel	Pfizer/Amgen	810.05
	Revlimid	Celgene	769.00
	Eliquis	Bristol Myers-Squibb	720.91
	Xtandi	Astellas	632.31
BIGGEST DOWNGRADES			
	Lantus	Sanofi	-802.24
	Entresto	Novartis	-720.80
	Xifaxan 550	Valeant	-573.12
	Epogen	Amgen	-496.05
	Tecfidera	Biogen	-425.57

This year Sanofi's insulin Lantus was removed from a number of formularies in favour of Lilly's approaching biosimilar Basaglar; as a result almost a billion dollars was erased from Sanofi's 2017 sales forecast over the course of 2016. The French pharma giant's inadequate response to this contributed to the toppling of its then chief executive, Chris Viehbacher; the other big diabetes player, Novo Nordisk, has also felt the pain of squeezes in this space.

On the flip side, Enbrel has seen substantial upgrades. This analysis was conducted before Amgen's third-quarter warning, serving to demonstrate that many analysts are still underestimating the extent of the on-going price battle in the US.

> You've got dynamics unleashed now that will continue to mean those offering undifferentiated products in big therapeutic categories that are a big cost burden will continue to face headwinds with respect to pricing, says Mr Pinniger of Polar Capital.

This definition could arguably apply to Enbrel, Epogen and Tecfidera in this analysis on the previous page; the former two agents are also facing biosimilar competition.

Elsewhere, the novel cholesterol-lowering agents Praluent and Repatha, despite offering significantly stronger efficacy than statins, have been strictly limited by payers. Their ongoing cardiovascular outcome studies will have to yield extremely positively data to change the stance on these costly medicines – these readouts and the payers' responses represent another big story for 2017.

This is because it is widely expected that those offering real advances or innovation will be more shielded from price pressure. Ibrance, Pfizer's new breast cancer pill, and Xtandi, the Medivation prostate cancer drug fought over by Pfizer and Sanofi, fall into this category, and have as a result seen their prospects improve.

Little evidence of payer pressure has emerged in cancer; if it does, this could easily trigger another flight for the exit for many investors.

Sentiment vs consensus

Of course other factors are always in play, and pricing prospects are far from the only influence on drug forecasts. And in a fluid and ever-shifting industry like pharmaceuticals, even near-term predictions can change, sometimes dramatically.

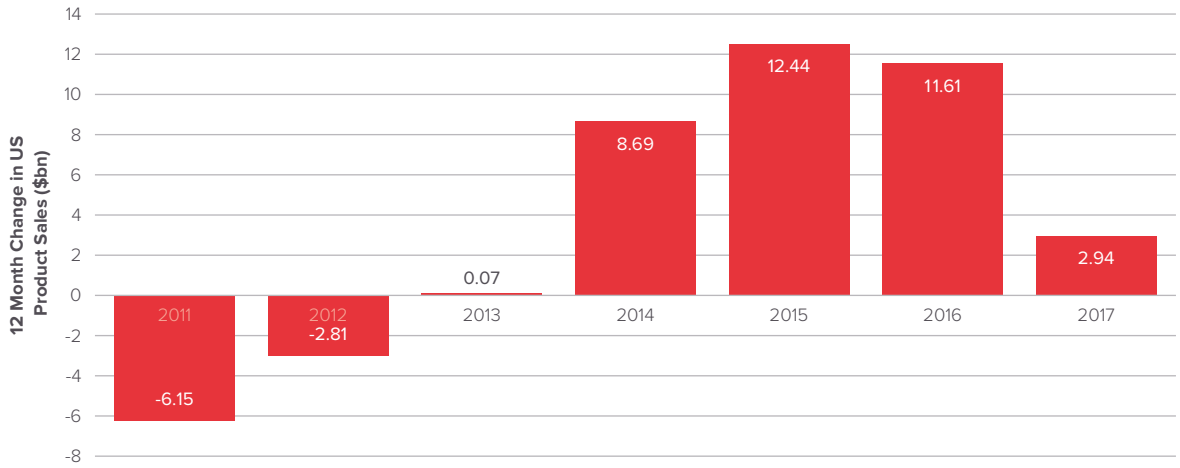
Over the course of 2016, for example, the consensus forecast for total US drug sales in 2017 grew by $6.2bn. On the surface this figure looks encouraging, until compared with the substantially bigger upgrades the previous four years received, in their preceding 12-month run-ups.

If this measure can be considered a barometer for the sector, then maybe confidence in the coming year is not running as high as in the recent past.

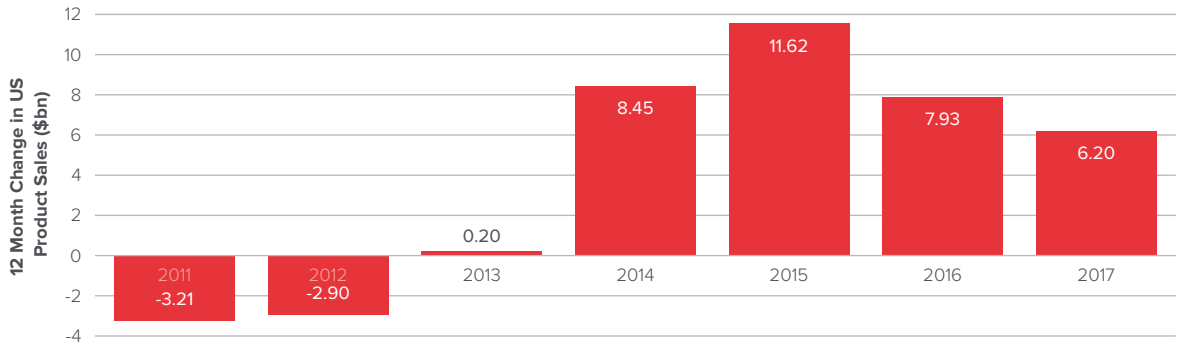
The Shifting Outlook for US Drug Sales: Change in Consensus Over the Previous Year

Source: EvaluatePharma® 20 November 2016

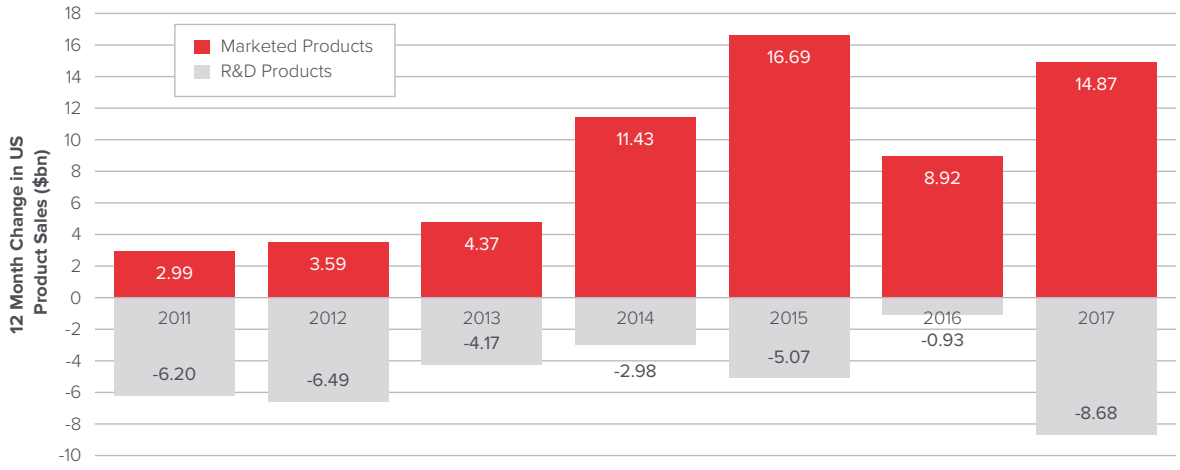
US Sales NMEs ($bn)



US Sales All Drugs Excluding Generics ($bn)



US Sales for Marketed and R&D Drugs Excluding Generics ($bn)



This analysis was constructed from EvaluatePharma's consensus of sell-side analysts' drug forecasts. The change in consensus over a 12 months period running October to October for the following calendar year was calculated, and the net change, positive or negative, is reflected here. It excludes generics.

This would seem to be a reasonable conclusion when looking at US drug indices, such as the Nasdaq Biotechnology Index and S&P Pharmaceuticals. As the previous graphs show, the acceleration in stock prices that really kicked off in 2013 is reflected in a period of ever-improving previous-year consensus drug forecasts. Pre-biotech boom, the sellside was adopting a more cautious stance on the approaching 12-month periods.

Whether consensus follows sentiment or the other way around is an open question, and to a certain extent they probably exist as a feedback loop. However it is clear that, going into 2017, equity analysts and many investors are adopting an optimistic stance for the US drugs market, albeit one of less exuberance than in previous years.

A major caveat is that this analysis was conducted before the surprise outcome of the US election. With investors and companies now factoring in a much more friendly business environment in the world's biggest drugs market, the outlook for 2017 could already have shifted.

From a healthcare generalist point of view we are expecting to see more dollars moving into the sector in 2017, says Mr Syed of Mizuho.

He expects biotechnology stocks in particular to benefit, although pharmaceuticals should also find more favour, he says.

Mr Pinniger of Polar Capital agrees.

"The threat of aggressive and/or draconian government action on how drugs are priced is really off the table as the Republicans are not into that kind of intervention. For the more innovative and smaller companies, the premium on innovation will be allowed to express itself once again," he says.

Is an uptick in M&A on the way?

When analysts and investors talk about more money being put to work in the sector, the topic naturally turns to mergers and acquisitions. After a relatively quiet 2016, many are hoping for a rebound next year.

Through the end of November 2016 M&A transactions reached $96bn, half the amount spent in 2015, with a concomitant drop in the number of deals. Many have attributed this lull to a watch-and-wait phase, amid concern about what a Clinton administration would have meant for the sector.

"With a pro-business administration in place, C-suite execs will start to feel a lot more comfortable about the operating and pricing environment. Combine that with some sort of tax reform effort and a repatriation holiday, and the environment is improving for big-ticket M&A," says Mr Pinniger of Polar Capital.

Add to this the retraction of equity valuations since the peak of the market in mid-2015, and the premiums that many companies could reasonably expect to command start to look more realistic.

Still, this rebasing of valuations cannot really be seen in the M&A data. As the table over the page shows, average deal values fell on one cut of the data, though on another they climbed.

Pharma and Biotech M&A: Average Deal Values and Totals

Source: EvaluatePharma® 20 November 2016

Year Announced	Avg for $250m-$20bn Deals ($bn)	Avg for Deals ≤ $20bn ($m)	Value All Deals ($bn)	Deal Count
2016*	1.73	803	96	160
2015	2.03	649	189	275
2014	1.95	785	220	217
2013	1.67	614	80	206
2012	1.28	371	44	204
2011	1.36	349	57	216
2010	1.39	485	110	206

*To end of November

This year has been skewed by the fact that very few deals have been struck, allowing one very large transaction, Pfizer's $14bn move on Medivation, to shift the needle northwards. This deal notwithstanding, it is clear that valuations in many cases remain high. This means that no matter how keen the acquirer, many targets are likely to remain looking very expensive in 2017.

This is particularly true in hot technology or therapy areas: CAR-T, for example, NASH, gene therapy and of course immuno-oncology, where expectations of huge leaps forward for the treatment of various cancers are driving asset valuations sky high.

The big potential deal in the offing as 2017 commences looks likely to involve Actelion, which in many ways provides a perfect example of just how stretched valuations have become. The Swiss company had a market cap of $17bn before news of the J&J approach emerged, while the combined net present value of its products stood at $7.3bn, according to EvaluatePharma's consensus NPV.

According to reports, J&J pitched a takeover bid worth $26bn, and is prepared to raise that.

There are therefore huge divergences in value according to the sellside, the market and the industry. If Actelion is acquired at anything close to what these reports have claimed then 2017 starts to look like a year in which anything can happen in the M&A world.

IPO activity

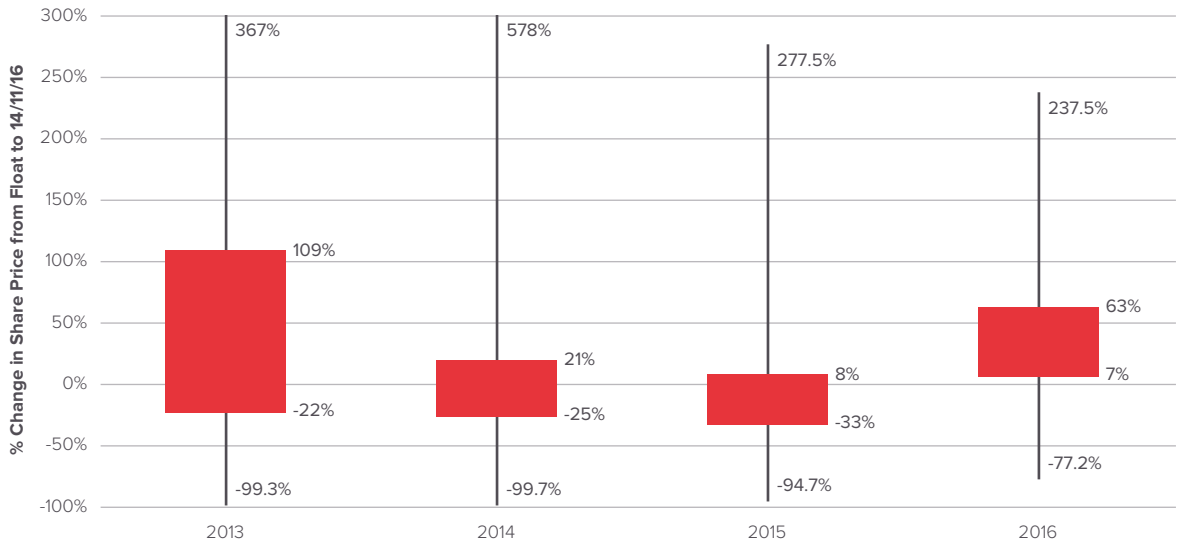
One area that greatly benefited from the surging valuations of the past few years was the IPO market. This experienced something of a retraction in 2016 as investors turned away from the sector, though many are hoping for an uptick in 2017.

This would be driven by the return of investor interest in the sector generally; many companies blamed "poor market conditions" for shelving IPO plans this year.

Still, while it seemed like in 2015 anyone with a balance sheet and half a molecule could find an underwriter, this opening of the floodgates could in the long term prove a hindrance. A look at the performance of Nasdaq IPOs suggests a gradual decline in returns, with 2015 looking to have been a poor year for investors who backed new issues.

Share Price Performance of Recent Nasdaq-listed Drug Developers

Source: EvaluatePharma® 20 November 2016



This analysis calculates the share price change from flotation to November 14, for all drug development companies coming to the Nasdaq market since 2013. The analysis has been restricted to those involved in human therapeutics, excluding medtech companies and CROs, for example. It also excludes those no longer listed, whatever the reason.

Of course 2015 saw the biotech rally come to an end, hitting fledgling stocks hard, while those newly listed this year have had less time to reach important events. But investors will always look at past returns when making a decision, and this analysis will not make for comforting reading.

The box on the graph above shows the performance range of the middle two quartiles of companies. Over the past three years both the upper and lower limit has dropped, a worrying trend if this suggests a gradual decline in the average return from these IPOs.

Of course this analysis is always a moveable feast – in November the 2014 floater Juno demonstrated the fragility of these valuations, with news of further deaths in its clinical programme. From registering a 37% advance on its IPO price the high-profile CAR-T player is now trading in negative territory.

For those considering whether to brave these investments in 2017, this analysis highlights the importance of careful stock selection.

Venture funding

Another big beneficiary of the IPO boom was the venture sector, which was finally able to pass portfolio companies into the hands of public investors. While a takeover remains the dream exit scenario for these funds, the ability to float companies presented an alternative option and also brought a lot of new money into the private sphere, in the form of crossover funds.

These types of investor, with deep pockets that can help beef up a balance sheet ahead of any float, largely exited the biotech space in 2016 as IPOs dried up. This largely explains the dip in venture financing this year, as the analysis below shows.

As such, 2016 is on track to be a respectable year for venture investments; new funds are still being raised at a decent rate so many see this continuing in 2017.

"The funding environment for biotech focused VCs is really strong at the moment," says Tom Woiwode, a manager director at the US firm Versant Ventures. "First, 2013, 14, 15 were banner years for biotech IPOs and there was a lot of liquidity generated for companies going public. But what is really driving interest in the sector is the acquisition of biotech by pharma, and that trend is here to stay."

Big drug developers have been downsizing their early-stage R&D operations for many years and they recognise that the biotech environment is better at moving forward quickly and nimbly with innovative projects, Mr Woiwode argues.

Although the previous top-line M&A data do not fully illustrate the interest shown in the private sphere by big pharma, deal activity in this space – both takeouts and licensing – remains strong. Plus, for a sector that defines success on multiples, the fact that valuations remain high also bodes well.

The Venture Capital World, Sliced and Diced

Source: EvaluatePharma® 20 November 2016

Financing Round	Total Investment ($m)					Total Finance Deals					% Investment per Financing Round				
	2016*	2015	2014	2013	2012	2016*	2015	2014	2013	2012	2016*	2015	2014	2013	2012
Seed Capital	141	178	132	146	216	18	35	30	55	50	2%	2%	2%	3%	4%
Series A	1,793	2,149	1,503	1,384	1,185	80	117	130	138	134	27%	21%	21%	28%	25%
Series B	1,701	2,875	2,489	1,034	1,117	48	95	129	74	96	26%	28%	35%	21%	23%
Series C	583	1,587	960	900	794	19	57	62	52	53	9%	15%	13%	18%	17%
Series D	270	1,192	722	447	673	10	30	29	29	29	4%	12%	10%	9%	14%
Series E	136	467	233	489	195	3	13	16	17	11	2%	5%	3%	10%	4%
Series F	30	148	67	205	140	1	5	7	5	10	0%	1%	1%	4%	3%
Series G-I	-	51	430	62	210	-	4	6	3	2	-	0%	6%	1%	4%
Series Undisclosed	1,948	1,625	669	351	281	89	67	77	58	51	30%	16%	9%	7%	6%
Total	**6,601**	**10,273**	**7,204**	**5,020**	**4,811**	**268**	**423**	**486**	**431**	**436**					

*Up to 23/11/16

What could perhaps be interpreted as a worrying trend in the analysis above is the drop in the number of financing deals. This would seem to point to a polarisation of venture capital into the hands of fewer companies.

Over the past few years venture funds have been increasingly keen that companies have enough cash to reach key milestones and control their own destiny, which means forging bigger syndicates and larger rounds, says Rafaèle Tordjman, a managing partner at Paris-based Sofinnova Partners. But this trend also reflects a much more selective stance taken throughout the industry, in an attempt to improve returns, she says.

> Hurdles are much higher. They are higher for us to raise money, and higher for the entrepreneurs. So maybe there are fewer companies, but they are better quality.

Ms Tordjman also accepts that valuations in the private sphere have been rising, in Europe as well as the US, to the extent that Sofinnova has walked away from some proposals.

“Even in Europe we are seeing a lot more competition than in the past. For Sofinnova we invest very early where it is less competitive, but even with this type of philosophy of investment there are more investors and more cash available.”

In Europe, US investors are increasingly shopping around, she says, partly because of competition in their domestic market but also drawn by local success stories, like the allergy player DBV Technologies.

“There is a lot more sophisticated money around,” she says.

Measuring output – the true barometer?

Ms Tordjman, like Mr Woiwode, does not foresee a change in this clement climate. An optimistic stance from the start-up end of the sector is an encouraging portent for the coming year.

“We all know about the pricing pressure, and that’s not going away just because Trump won the election,” says Mr Woiwode. “But pharma recognises that and they are going after these highly innovative approaches – the types of drug that biotech do the best job of innovating.

“So the real capital coming into this sector is from the pharma commitment, the acquisitions and the partnerships. IPO windows come and go. But in the meantime we are still going to be doing deals with pharma.”

The view from the sellside is perhaps less optimistic on the deal front, after a slow 2016.

“Companies have been waiting for valuations to reset themselves to the new reality, so they can go back into the market and start negotiating,” says Mr Syed. “But frankly I haven’t seen much of that.”

Next year, he hopes for at least a small pick-up in the small and mid-cap space, although he sees little action among the large players unless a tax repatriation holiday happens in the US.

Predicting what a President Trump will actually do is hard, of course, as his policies were never clearly articulated. The FDA is said to be in his crosshairs, in terms of efforts to speed drug approvals, and of course the Affordable Care Act could be replaced or even repealed. And while these acts would create the sort of short-term uncertainty that investors dislike, on the other hand his business-friendly initiatives are being cheered.

What he is unlikely to do anything about is drug pricing, something that will undoubtedly rear its head again and again.

> We will continue to see discussions on drug pricing in 2017 but I don't think it's going to go up in intensity. It will be an iterative process – in the US market there are so many players involved, says Mr Syed.

The sustainability of a system where prices can be ramped year after year without justification is clearly questionable – both commercially and morally – and the sector will continue to be called out on this if examples abound. Efforts to address the issue more honestly must be made next year.

"Industry needs to do a better job at vocalising its value proposition – it has been very quiet defending itself," says Polar Capital's Mr Pinniger. "A lot of people are taking risks here – investors, patients – and at the end of the day there need to be rewards for everyone engaged in that process. Sure, spread the risk around, but people need to understand that medicine is expensive, and industry needs to get better at communicating that."

For many years industry has relied on the often-quoted and often-disputed statistic of a billion dollars to develop a drug. Given the sophisticated analysis of drug pricing that many are now accustomed to, this statistic is too simplistic to keep returning to. And it certainly does not justify the sorts of aggressive price hikes that have tarnished the whole sector.

Of course that billion-dollar number was also supposed to include drug failures, further examples of which 2017 will no doubt provide. It also encompassed regulatory setbacks, which seemed fairly common in 2016.

So while those whose businesses involve striking deals are perhaps predictably positive for the prospects of 2017, this preview of the coming year will end on a statistic on R&D productivity. At the end of the day there is really only one way to judge the performance of the drug development sector: by looking at its output.

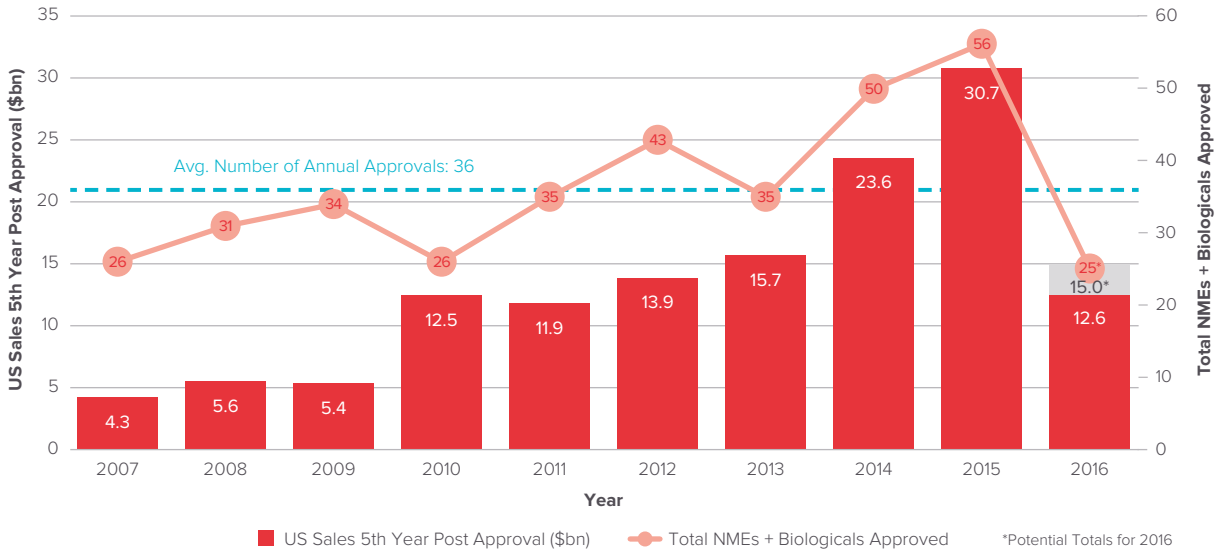
Of course this is in itself a controversial and complex aspect to measure and the analysis below, looking at FDA approvals of novel molecules, is far from perfect. For example, it does not capture the breadth of a drug that has utility in many settings – although the inclusion of fifth-year sales forecasts attempts to signal this – and it provides no indication of input, in either time or money, to generate these drugs.

These caveats aside, it is clear that 2016 was a pretty woeful year for new drug approvals. With only one month of the year left, it looks like only 25 novel biologics or small molecules will have passed regulatory muster in the US. After a couple of years of scorching drug approval rates and huge fifth-year sales estimates this is a disappointing dip in productivity.

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

Source: EvaluatePharma® 20 November 2016

2010 – Prevnar 13 (Pfizer), Victoza (Novo Nordisk), Prolia/Xgeva (Amgen)
2011 – Xarelto (J&J/Bayer), Eylea (Regeneron/Bayer)
2012 – Eliquis (Bristol-Myers Squibb/Pfizer), Stribild (Gilead)
2013 – Sovaldi (Gilead), Tecfidera (Biogen)
2014 – Opdivo (Bristol-Myers Squibb), Harvoni (Gilead)
2015 – Orkambi (Vertex), Ibrance (Pfizer)
2016 – Tecentriq (Roche), Epclusa (Gilead), Venclexta (Abbvie)



Still, many believe that 2016 was a comparatively quiet year for product development news, something that also contributed to the dip in investor interest.

“There wasn’t much data around in 2016 for investors to get excited about, which didn’t help valuations in the sector,” says Mr Syed.

All will be watching to see how this metric develops in 2017 – there are certainly plenty of events building. After several years of seemingly improved output and the arrival of a string of substantial new products, this year’s disappointing record on drug approvals will be closely watched for signs of repeating itself – particularly after a number of big late-stage disappointments towards the end of 2016, like solanezumab’s failure and Pfizer’s decision to scrap its PSCK-9 inhibitor bococizumab.

In the past few years, industry managed to mount a convincing argument that its productivity problems were behind it, and pricing is the new bogeyman. Signs that the output of new drugs is flagging once again could quickly give investors something else to worry about.

Appendix

Big events for the big drug makers 2017

	Product	Company	Event	Date
Q1	Crisaborole	Pfizer	US approval (psoriasis)	6 January
	Keytruda	Merck & Co	KEYNOTE-040 data (2nd line HNSCC)	January
	Opdivo	Bristol-Myers Squibb	Checkmate 568 data (1st line lung cancer)	January
	Inflectra/Remicade	Pfizer/J&J	Hearing on production patent ('083) - biosimilar	Mid-February
	Revlimid	Celgene	US approval (maintenance, post ASCT)	24 February
	Dupilumab	Sanofi/Regeneron	US approval (atopic dermatitis)	29 March
	Esketamine	J&J	Transform 2 data (treatment resistant depression)	March
	Durvalumab	AstraZeneca	Mystic (1st line lung cancer)	Q1
	Xeljanz	Pfizer	EU approval (RA)	Q1
	Repatha	Amgen	Fourier outcomes data (dyslipidemia)	Q1
	Perjeta	Roche	Aphinity data (Adjuvant breast cancer)	Q1
	Tecfidera	Biogen	Potential ANDA filings/IPR decisions	Q1
	CTL019	Novartis	US filing in paediatric ALL/ DLBCL	Q1/Q2
	Baricitinib	Eli Lilly (Incyte)	US/EU approvals (RA)	Q1/Q2
	Pegvaliase	Biomarin	US filing and approval (PKU)	Q1/Q4
Q2	Ingrezza	Neurocrine	US approval (tardive dyskinesia)	11 April
	ZS-9	AstraZeneca	US/EU approvals (hyperkalaemia)	18 April/H1
	Nusinersen	Biogen (Ionis)	US/EU approvals (SMA)	26 May/Q2
	Avelumab	Pfizer/Merck KGaA	US approval (MCC)	May
	Darzalex	J&J	US approval (3rd-line multiple myeloma)	16 June
	LEE011	Novartis	US/EU approvals (breast cancer)	30 June/Q3
	Opdivo	Bristol-Myers Squibb	Checkmate 143 data (Glioblastoma)	Q2
	RTH258	Novartis	Phase III data (wet AMD)	Q2
	Rexulti	Otsuka/Lundbeck	Phase III data (Alzheimer's agitation)	Q2
H1	Durvalumab	AstraZeneca	Arctic and Condor data (2nd and 3rd line lung cancer)	H1
	Nusinersen	Biogen (Ionis)	Cherish data (SMA)	H1
	Ozanimod	Celgene	Radiance and Sunbeam data (MS)	H1
	Abemaciclib	Eli Lilly	Monarch 2 data (2nd line HR- breast cancer)	H1
	Advair	Glaxo	Progress of Mylan and Hikma's US generic Advair filings	H1
	Serelaxin	Novartis	RELAX-AHF-2 data (heart failure)	H1
	Niraparib	Tesaro	US/EU approvals (ovarian cancer)	H1/H2

	Product	Company	Event	Date
Q3	Romosozumab	Amgen	US approval (osteoporosis)	19 July
	Verubecestat	Merck & Co	Epoch data (Alzheimer's)	July
	Avelumab	Pfizer/Merck KGaA	JavelinLung100 data (1st line lung cancer)	August
	Sirukumab	J&J/Glaxo	US approval (RA)	22 September
	Keytruda	Merck & Co	Keynote-189 data (1st line lung cancer)	September
	Opdivo	Bristol-Myers Squibb	Checkmate 459 data (liver cancer)	Q3
Q4	Shingrix	Glaxo	US approval (shingles prevention)	24 October
	Darzalex	J&J	Phase III data (1st line MM)	November
	Dupilumab	Sanofi/Regeneron	Phase III data (persistent asthma)	Q4
	Praluent	Sanofi/Regeneron	Odyssey outcomes data (hypercholesterolemia)	Q4
H2	Lynparza	AstraZeneca	US filing (ovarian cancer)	H2
	Tagrisso	Astrazeneca	Flaura data (1st line lung cancer)	H2
	Tecentriq	Roche	IMpower150 data (1st line lung cancer)	H2
TBC	Semaglutide	Novo Nordisk	US/EU approvals (type 2 diabetes)	TBC
	KTE-C19	Kite Pharma	US approval (NHL)	TBC
	Glecaprevir & Pibrentasvir	AbbVie	Filing/approval in hepatitis C	TBC
	FF/UMEC/VI	Glaxo	US approval (COPD)	TBC

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