Pharma & Biotech 2016 in Review

Amy Brown – February 2017

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2016 – the new normal?

For the world's drug makers 2016 was a year of two halves. Activity like deal-making and venture funding held up over the first two quarters, still buoyed by the retreating bull market. However, as the US presidential election loomed ever closer on the horizon, companies went into lockdown.

Not that 2016 ever had the exuberance of the preceding two years – the sector tumbled into January with a stock market selloff that firmly put the excesses of the biotech boom to bed. Investor sentiment never recovered over the year, with every uptick slapped down by the recurring nightmares of a Clinton administration and the threat of action on US drug prices.

In the end, the former never became reality, although it seems that the latter might still come to pass; with President Trump continuing to prove that he is nothing if not unpredictable, very little can be ruled out in terms of his proposals. Whether they will ever be turned into actions is another question entirely.

However, in 2016 this was all still supposition, and with the outcome of the US election and the policies of a new administration unknowable, few were willing to make big strategic gambles. This certainly explains the virtual absence of M&A activity in the last quarter of the year – a big question for 2017 is the extent to which this will pick up.

The IPO market also dimmed, as many investors took money out of the sector – a huge amount of cash was withdrawn from biopharmaceutical investments across the year, amid mounting uncertainty. Still, fledgling companies were able to raise a respectable amount of money, and the IPO window can by no means be considered closed – again this is a metric that will be closely watched in the opening months of the year.

Venture funding did hold up well over 2016, however. Many of the funds that back private enterprise remain well stocked and keen to invest in start-up drug developers. Big pharma continues to prove that it is an enthusiastic buyer of innovation, and this situation is unlikely to change, a guarantee that is not lost on investors in this segment of the sector.

In terms of share prices, the volatility of 2016 has not improved much even with the identity of the US president confirmed. Investors and companies, therefore, must perhaps brace themselves for these stormy waters to become the new normal in 2017. Despite an arguably too-little-too-late fightback from industry in an attempt to justify high drug prices, this issue will remain the sector's gremlin in 2017.

Unless stated, all data are sourced to EvaluatePharma and were compiled in January 2017.

Investors head for the exit

Last year the Nasdaq Biotechnology Index ended in the red for the first time since 2008 – a disappointing fact to frame 2016. With all major pharma and biotech indices registering declines even as broader markets climbed, the desertion of investor support last year was clear.

Investors are notorious in their dislike of risk – even those prepared to invest in biotech, surely the highest-risk equity gamble – and the sector's fall from grace in 2016 was a worrying stumble. Another year of volatility might not be considered too terrible, as long as money stops exiting the sector in such volumes.

Investment banks have widely reported that billions of dollars were withdrawn from biotech funds last year, reversing the huge flows of cash that poured into the sector with the biotech boom. The Trump win prompted inflows to resume, but this was short-lived, and this year banks are reporting outflows once again. This metric provides an accurate gauge of investor sentiment, and it will be closely watched as the year progresses, particularly by companies hoping to tap the markets for cash.

Indicies

Source: EvaluatePharma® January 2017

Stock Index	% Change in 12M
NASDAQ Biotechnology (US)	(22%)
S&P Pharmaceuticals (US)	(4%)
Dow Jones Pharma and Biotech (US)	(9%)
S&P 500	10%
DJIA	13%
Dow Jones STOXX Healthcare (EU)	(11%)
Thomson Reuters Europe Healthcare (EU)	(12%)
Euro STOXX 50	0%
FTSE-100	14%
TOPIX Pharmaceutical Index (Japan)	(11%)

As a group big pharma is arguably less exposed to the temperature of the specialist biotech investor market that fared so badly last year. Even so, losers outweighed the winners in 2016. Of the 11 big cap names in the *EvaluatePharma* universe only five managed to advance over the year, and as a group around $100bn in market value was lost.

As such, the advances of Glaxo, J&J and Merck are all the more impressive; it should be noted, however, that the UK pharma giant's gains were propelled by the steep plunge in sterling against the dollar.

Merck can thank its wins in the anti-PD-1 antibody race for its share price rise, with the company emerging a clear immuno-oncology leader. Arch rival Bristol-Myers Squibb was down 15% over the year, while Astrazeneca and Roche were also punished for failing to keep up.

J&J meanwhile was rewarded for its success in backing a couple of big future blockbusters – the myeloma therapy Darzalex, for example. However, its warning at the start of 2017 that its drug sales would slow, and the company's willingness to pay top dollar for Actelion, suggests that maybe this advance has run its course.

Big Pharma Companies: Top Risers and Fallers in 12 Months

Source: EvaluatePharma® January 2017

		Market Capitalisation ($bn)	
Top 3 Risers	**Share Price % Change**	**YE 2016**	**12M Change**
Glaxosmithkline (£)	14%	94.5	(-5.6*)
Johnson & Johnson ($)	12%	313.4	30.4
Merck & Co ($)	11%	162.3	15.4
Top 3 Fallers			
Allergan ($)	(33%)	78.8	(44.4)
Astrazeneca ($)	(20%)	69.1	(16.7)
Roche (SFr)	(16%)	204.0	(35.5)

*Decline due to dollar conversion; in native currency the market cap grew £10bn ($12bn).

A stock market rout was clearly visible in the world's largest drug makers outside the big pharma stable, classified by *EP Vantage* as those with a market cap above $25bn. Of the 18 companies in this peer group none advanced over the year, with Celgene's 3% decline representing the "best" performance.

Many of these companies – Amgen and Biogen, for example – have come to rely on price hikes to drive revenue growth in the US. So it was inevitable that these stocks would be hurt by mounting fears of action to bring an end to the sector's almost free rein in this regard.

Of course there were also unique issues hitting certain stocks. The collapse of Valeant – which has been demoted to the mid-caps for 2017 – has been well documented. Teva has failed to convince investors that it did not overpay for the huge $43bn Allergan generics deal. And sales of Vertex's new cystic fibrosis drug, Orkambi, have disappointed.

Other Big Pharma Companies ($25bn+): Top Fallers in 12 Months

Source: EvaluatePharma® January 2017

		Market Capitalisation ($bn)	
Top 3 Performers	**Share Price % Change**	**YE 2016**	**12M Change**
Celgene ($)	(3%)	89.7	(4.4)
Astellas Pharma (¥)	(6%)	33.7	1.1
Biogen ($)	(7%)	61.7	(6.6)
Top 3 Fallers			
Valeant Pharmaceuticals International ($)	(86%)	5.0	(29.7)
Teva Pharmaceutical Industries ($)	(45%)	36.8	(29.9)
Vertex Pharmaceuticals ($)	(41%)	18.3	(12.6)

Smaller cap drug developers were certainly not immune to the collapse in investor support last year, but at least this section of the industry managed to generate some returns for shareholders.

Actelion, Genmab, Exelixis and Tesaro can count themselves as some of the standout success stories on the stock market in 2016.

Of course there are always blow-ups in biotech – step forward Ophthotech, Juno and Alnylam. With the speciality space also a complete mess – Valeant, Endo and Perrigo combined haemorrhaged $50bn of market capitalisation over the year – there were plenty of stories of value destruction around.

Mid Cap ($25-5bn): Top Risers and Fallers in 12 Months

Source: EvaluatePharma® January 2017

		Market Capitalisation ($m)	
Top 5 Risers	**Share Price % Change**	**YE 2016**	**12M Change**
Actelion (SFr)	58%	24.6	8.1
Genmab (DKr)	28%	10.5	2.5
Celltrion (KRW)	27%	11.1	3.0
Lundbeck (DKr)	22%	8.4	1.6
Otsuka Holdings (¥)	18%	27.3	7.0
Top 5 Fallers			
Endo International ($)	(73%)	3.7	(10.2)
Juno Therapeutics ($)	(67%)	2.0	(3.5)
Alnylam Pharmaceuticals ($)	(60%)	3.2	(4.8)
Hanmi Pharmaceutical (KRW)	(53%)	3.2	(3.1)
Perrigo Company ($)	(42%)	11.9	-9.3

Related EP Vantage Comment and Analysis

Top 5 Risers	
Actelion (SFr)	Why J&J shouldn't buy Actelion
Genmab (DKr)	Darzalex inherits mantle as the Harvoni of 2016
Celltrion (KRW)	US biosimilar space reaches its Inflectra point
Lundbeck (DKr)	Weekly Market Movers: Global Majors & Industry (to 4 Nov 2016)
Otsuka Holdings (¥)	-
Top 5 Fallers	
Endo International ($)	Daily Market Movers: Global Majors & Industry (6 May 2016)
Juno Therapeutics ($)	Ash – Relapses spell more CAR-T uncertainty for Juno
Alnylam Pharmaceuticals ($)	Alnylam failure puts RNAi under the spotlight again
Hanmi Pharmaceutical (KRW)	Boehringer makes olmutinib a Hanmi-back
Perrigo Company ($)	What Papa might preach to Valeant

The biggest riser in our mid-cap space – those companies valued from $5bn to $25bn at the beginning of the year – was the bid target Actelion. Having succumbed to a staggering $30bn bid from J&J in January, it seems that investors were substantially undervaluing the company.

Genmab has benefited from growing hopes for the J&J-partnered Darzalex, while Exelixis and Tesaro, below in the small caps, are riding high on clinical successes for Cabometyx in renal cell carcinoma and niraparib in ovarian cancer respectively.

These firms are also considered prime takeout targets – case in point is Ariad, our fourth-biggest small cap riser in 2016, which was acquired in the opening days of 2017 by Takeda for $5.2bn.

Notably, no US company claimed a space among the top five mid-cap risers in 2016, although Seattle Genetics just missed out with an 18% rise, adding $1.2bn in market cap over the year. Using this as a measure of value creation, the cancer specialist stands out as the only US mid-cap company to rise in value last year.

On the flip side, its domestic cousins dominate the mid-cap fallers. While Juno and Alnylam were laid low by fears of the side effects of their therapies, Endo and Perrigo continued to struggle to justify their debt-fuelled takeover sprees of the past few years.

Small Cap ($5bn-250m): Top Risers and Fallers in 12 Months

Source: EvaluatePharma® January 2017

		Market Capitalisation ($m)	
Top 5 Risers	**Share Price % Change**	**YE 2016**	**12M Change**
Exelixis ($)	164%	4,271	2,989
Tesaro ($)	157%	7,182	5,084
Array BioPharma ($)	108%	1,482	880
ARIAD Pharmaceuticals ($)	99%	2,416	1,233
Theravance Biopharma ($)	95%	1,656	1,036
Top 5 Fallers			
Ophthotech ($)	(94%)	172	(2,573)
Proteon Therapeutics ($)	(88%)	54	(253)
Northwest Biotherapeutics ($)	(89%)	32	(224)
ProNAi Therapeutics (C$)	(87%)	45	(285)
KemPharm ($)	(85%)	43	(244)

Related EP Vantage Comment and Analysis

Top 5 Risers	
Exelixis ($)	Therapy focus – New kidney cancer data emerge in time for Asco
Tesaro ($)	Esmo – Tesaro enjoys a ta-dah moment
Array BioPharma ($)	Array plays catch-up in Braf-Mek derby
ARIAD Pharmaceuticals ($)	-
Theravance Biopharma ($)	-
Top 5 Fallers	
Ophthotech ($)	Ophthotech flop opens up Novartis nightmare scenario
Proteon Therapeutics ($)	Weekly Market Movers: Global Majors & Industry (to 16 Dec 2016)
Northwest Biotherapeutics ($)	Vantage Snippet – Northwest heads for the bulletin boards $NWBO
ProNAi Therapeutics (C$)	Asco event analyser – 2016's winners and losers
KemPharm ($)	Daily Market Movers: Global Majors & Industry (6 May 2016)

Among the fallers in the small caps, Ophthotech stands out as one of the biggest catastrophes of the year, with the unequivocal failure of its macular degeneration asset Fovista. The loss of $2.6bn of market cap illustrates the hopes that were attached to this project.

Phase III failure also crushed Proteon, this time in kidney disease, while Pronai lost its lead lymphoma candidate in phase II. Kempharm, meanwhile, made it all the way to the finish line with its opioid-based pain project Apadaz, but regulators' refusal to grant an abuse-deterrent claim scuppered its commercial ambitions.

The sorts of setbacks that triggered these falls are not unusual in drug development, and similar stories will undoubtedly emerge this year. What investors will not want to see is large numbers of stocks ending the year in negative territory.

Overall, publicly traded pharma and biotech companies failed to paint a picture of investor support in 2016. Many are pinning hopes on an M&A spree and a relatively calmer US political climate to encourage cash back into the sector this year.

January has certainly provided the deals, and at huge premiums. The question is whether the threat of punitive action from the Trump White House cancels out this positive trend, which in normal circumstances would be fuelling substantial investor interest.

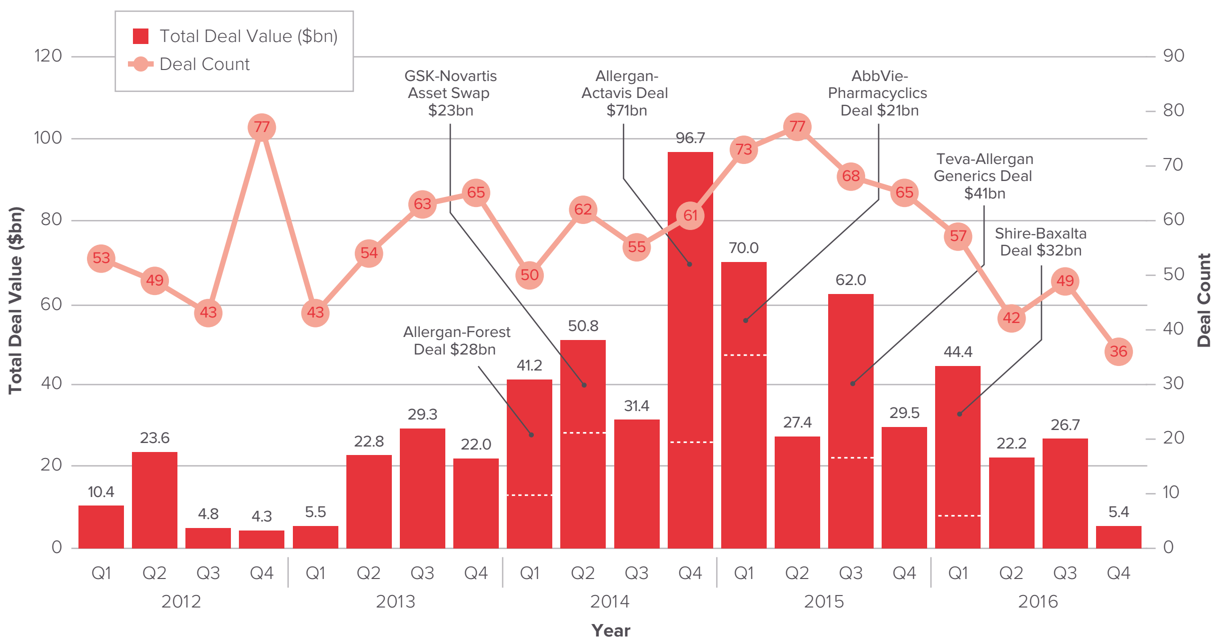
An industry on pause?

A look at the quarterly flow of acquisitions shows just how steeply the appetite for takeovers diminished in the last quarter of 2016. Pharma groups were biding their time and exercising caution, causing M&A deal volumes to fall back substantially from the free-spending days of 2014 and 2015.

Activity in the fourth quarter was deeply suppressed by the run-up to the US presidential election, especially as key issues – drug pricing, health insurance coverage and corporate tax reform – hung on the outcome. It could be no coincidence that to find a three-month period with less activity you have to go back to the last US presidential election at the end of 2012.

Pharma and Biotech M&A Transactions Announced Each Quarter

Source: EvaluatePharma® January 2017



The $98.7bn spent on acquisitions in 2016 was less than half that of the biotech boom's peak in 2014 even though many biotech targets became more affordable as their valuations tumbled through the course of the year. However, business development teams chose to practise restraint, paused by expectations of further falls for biotech and hopes that US big pharma could soon be awash with overseas cash thanks to a repatriation tax holiday.

Some perspective is in order, however. Before the boom, $98.7bn would have been seen as a good year, particularly as 2016 only featured one megamerger, the acquisition of Baxter's Baxalta spinoff by Shire. The boom years were marked by multiple megamergers each year, three in 2014 and two in 2015.

This analysis only includes acquisitions by pharma and biotech companies – it excludes medtech and diagnostic players, for example.

10 Biggest Pharma and Biotech M&A Deals Announced in 2016

Source: EvaluatePharma® January 2017

Date Announced	Acquirer	Target	Value ($bn)
Jan 2016	Shire	Baxalta	32.0
Aug 2016	Pfizer	Medivation	14.0
Apr 2016	AbbVie	Stemcentrx	9.8
Feb 2016	Mylan	Meda	7.2
May 2016	Pfizer	Anacor Pharmaceuticals	5.2
Dec 2016	Lonza	Capsugel	3.5
Sep 2016	Allergan	Tobira Therapeutics	1.7
Aug 2016	Pfizer	AstraZeneca's ex-US anti-Infectives	1.6
Jul 2016	Galenica	Relypsa	1.5
May 2016	Jazz Pharmaceuticals	Celator Pharmaceuticals	1.5

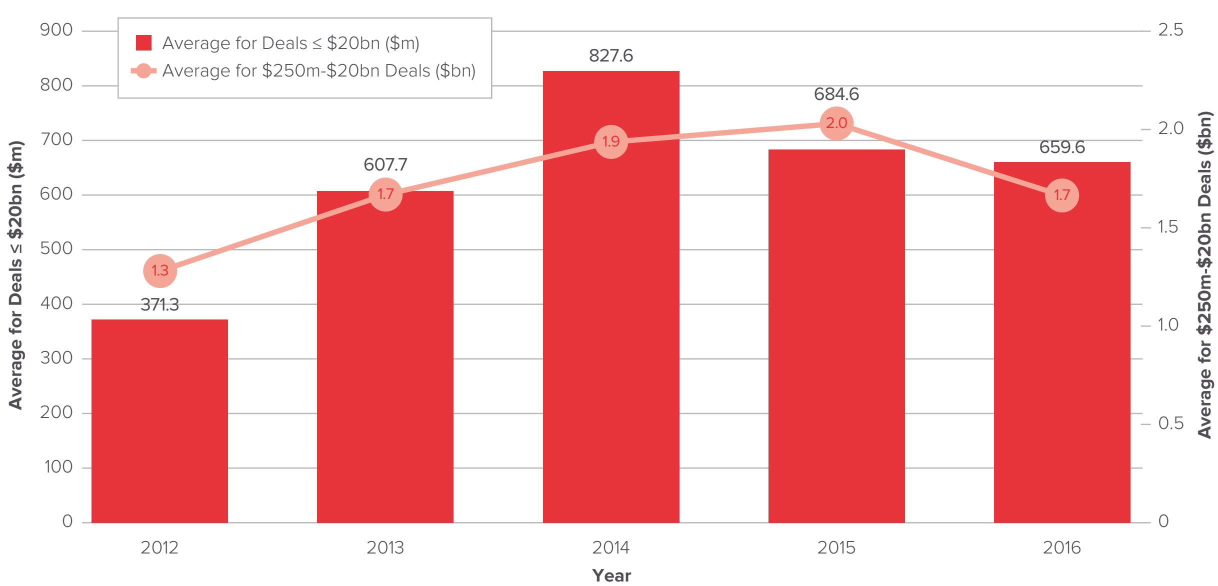
Moreover, the table above highlights how the big deals of the year were tilted towards lower risk. Six of the top 10 acquisitions were of companies with established products; a seventh was of Celator, a company that had already passed a phase III milestone; and an eighth, Anacor, had already submitted Eucrisa to the FDA when Pfizer made its play.

That leaves only Abbvie's acquisition of Stemcentrx and Allergan's of Tobira as truly risky transactions.

A look at average deal values, sliced a couple of ways, also shows a pullback in 2016. This could well be a result of the general avoidance of more risky moves, as well as lower valuations overall.

Average M&A Deal Values Per Year

Source: EvaluatePharma® January 2017



What makes for encouraging viewing, however, is the state of private company takeouts, which remain in rude health.

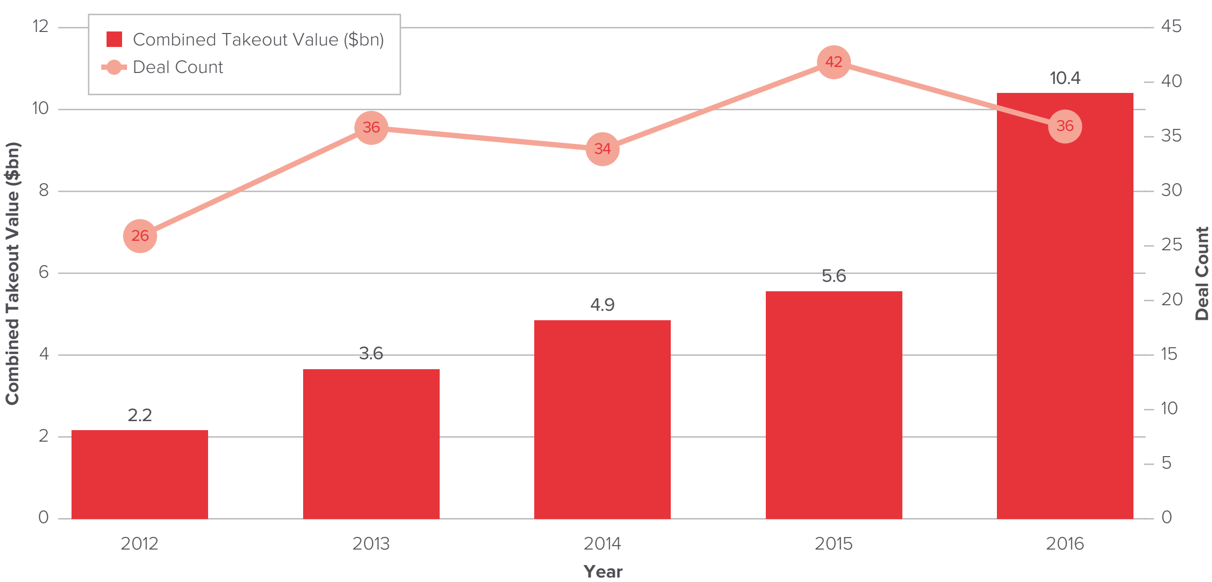
Over the past five years the absolute number of venture-backed businesses sold has held steady, while their combined value soared from $2.2bn in 2012 to $10.4bn last year. It seems that, whatever turmoil the markets are experiencing, bigger groups still see private biotech as a key source of R&D assets.

At its extreme this appetite was demonstrated last year by Abbvie's takeover of Stemcentrx, a group that had barely emerged from stealth mode, for $5.8bn up front. Subsequent underwhelming data on the private company's key asset, the antibody-drug conjugate Rova-T, might have left Abbvie with a feeling of buyer's remorse.

Even if Stemcentrx is excluded 2016 showed a healthy number of private company take outs, with 35 transactions bringing in a total $4.6bn. The figures, where possible, comprise just the up-front deal amount, though by and large private takeovers tend to disclose only the total deal amount.

Five Years of Private Takeouts – Values and Volumes

Source: EvaluatePharma® January 2017



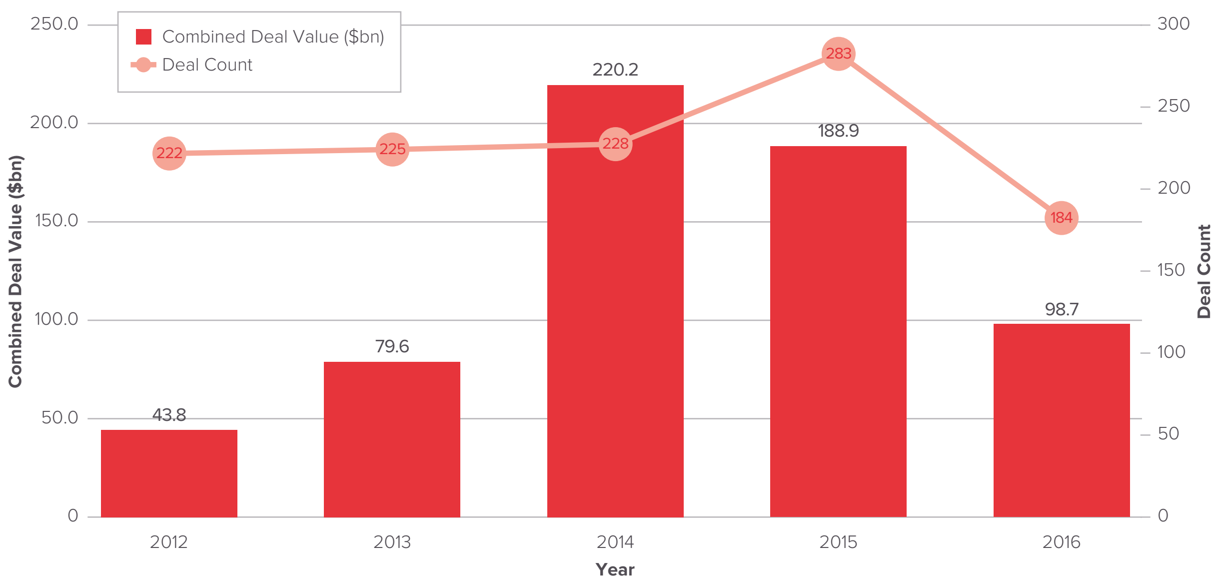
As of the end of January 2017 almost $40bn in takeover deals, public and private, have been announced, with Actelion making up three quarters of this amount. The year is clearly off to a good start. It is perhaps worth remembering, however, that 2016 also opened with the biggest transaction of the year, Shire's move on Baxalta.

Many are pinning hopes on a surge in M&A to help encourage investors back into the sector. But with President Trump's policies on tax and regulatory reforms still largely unformed, it will be a difficult year for anybody trying to estimate valuations accurately. This uncertainty has the potential to suppress M&A through 2017.

However, if it was true that big players kept their powder dry last year, waiting for valuations to fall, maybe the time is now right – biotech has broadly fallen around a third from its mid-2015 peak. The question is whether valuations have fallen far enough – or enough time elapsed since the top of the market – for enthusiastic buyers to jump back in.

Five Years of M&A – Deal Values and Volumes

Source: EvaluatePharma® January 2017



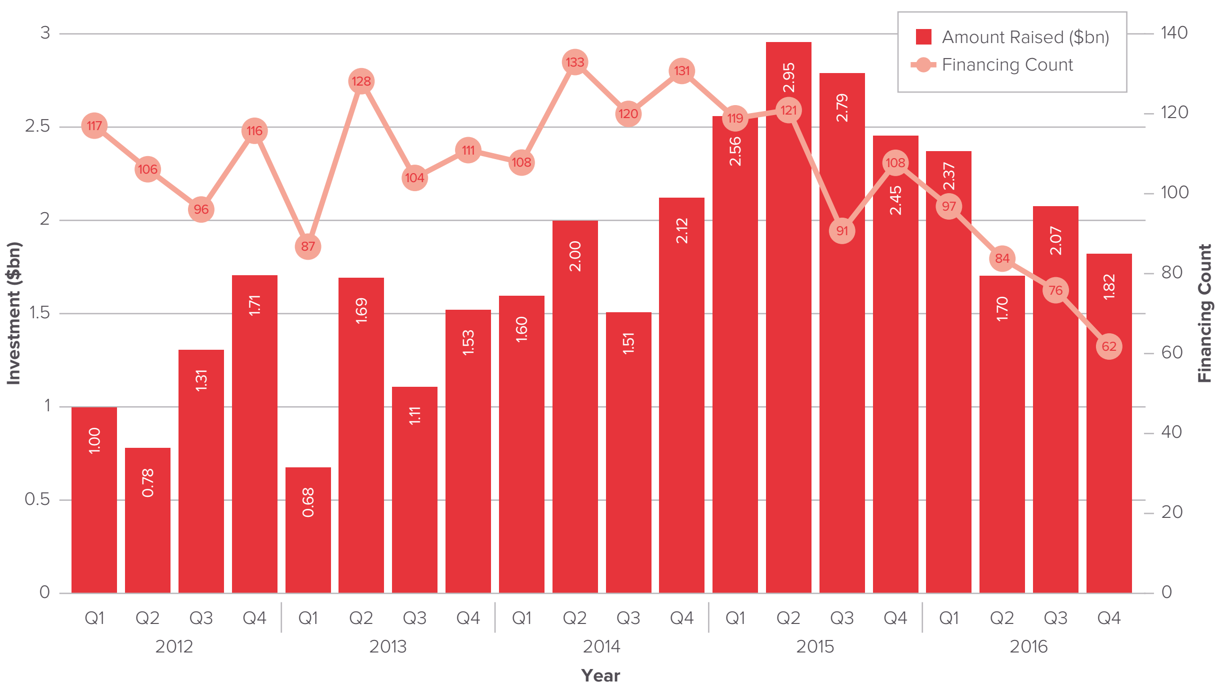
Venture riches

Some of the biggest beneficiaries of the takeovers that did happen last year were venture firms, which have pumped huge amounts of cash into private start-ups in the past few years. These firms wasted no time raising new funds while the biotech bull run charged ahead, and many remain well stocked and willing to make new investments.

This much is clear from the quarterly analysis below, which shows that 2016 was an active year for fund-raisings. While the totals might have dropped off from 2015, this was largely down to the exit of crossover funds from the sector. These investors, who help fund large pre-IPO rounds, were in less demand as the rate of new issues also declined last year.

Quarterly VC Investments

Source: EvaluatePharma® January 2017



A remarkable fourth quarter saw three rounds breaking the $200m barrier, and included four of the 10 biggest of the year. The big prize of 2016 went to Moderna Therapeutics, which has been a master showman in exceeding the mythical $1bn mark before revealing more of itself to the world at the JP Morgan conference this year.

The downside to this analysis is perhaps the continuing slide in the number of fund-raisings, particularly for groups trying to raise their first round of investment. The fourth quarter of 2016 saw the fewest rounds, 62, of any three-month period since 2008. This broke the previous low of 76 in the third quarter of 2016. The annual number, 319, is also the lowest recorded in this time period.

Venture firms put this down to a growing desire for young firms to be sufficiently capitalised to reach important milestones, rather than having to keep coming back for more money. This means bigger syndicates raising bigger pots, which naturally limits the number of fund-raisings that can be done.

Annual VC Investments

Source: EvaluatePharma® January 2017

Date	Investment ($bn)	Financing Count	Avg per Financing ($m)	No. of Rounds ≥$50m	No. of Rounds ≥$100m
2016	8.0	319	25	43	11
2015	10.7	439	24	57	14
2014	7.2	492	15	35	4
2013	5.0	433	12	12	3
2012	4.8	437	11	16	2
2011	4.4	408	11	11	3
2010	5.0	452	11	13	3

Still, the $8bn that came in in 2016 is second only to 2015 in terms of amount raised, showing that there are substantial funds to be tapped. The lesson here is that private biotechs need to have a more compelling story than ever to earn venture backing. And, if they succeed, the rewards will be rich.

This thesis is confirmed by the $25m average raise last year, the highest since at least 2010 and likely to be a record. And the number of companies raising bumper $50m+ and $100m+ rounds remains high, even with the exit of crossover funds.

Few expect 2017 to witness any notable slowing in the venture capital environment. With well-stocked investors and plenty of enthusiastic acquirers, this section of the drug development world should remain a bright spot this year.

Top 10 Rounds of 2016

Source: EvaluatePharma® January 2017

Company	Investment ($m)	Round	Date
Moderna Therapeutics	451	Series Undisclosed	Aug
Innovent Biologics	260	Series D	Nov
BlueRock Therapeutics	225	Series A	Dec
Intarcia Therapeutics	206	Series Undisclosed	Dec
Intarcia Therapeutics	215	Series I	Sep
Denali Therapeutics	130	Series B	Aug
UNITY Biotechnology	116	Series B	Oct
Zai Lab	100	Series B	Jan
DalCor Pharmaceuticals	100	Series B	Apr
Hengrui Therapeutics	100	Series Undisclosed	Jun

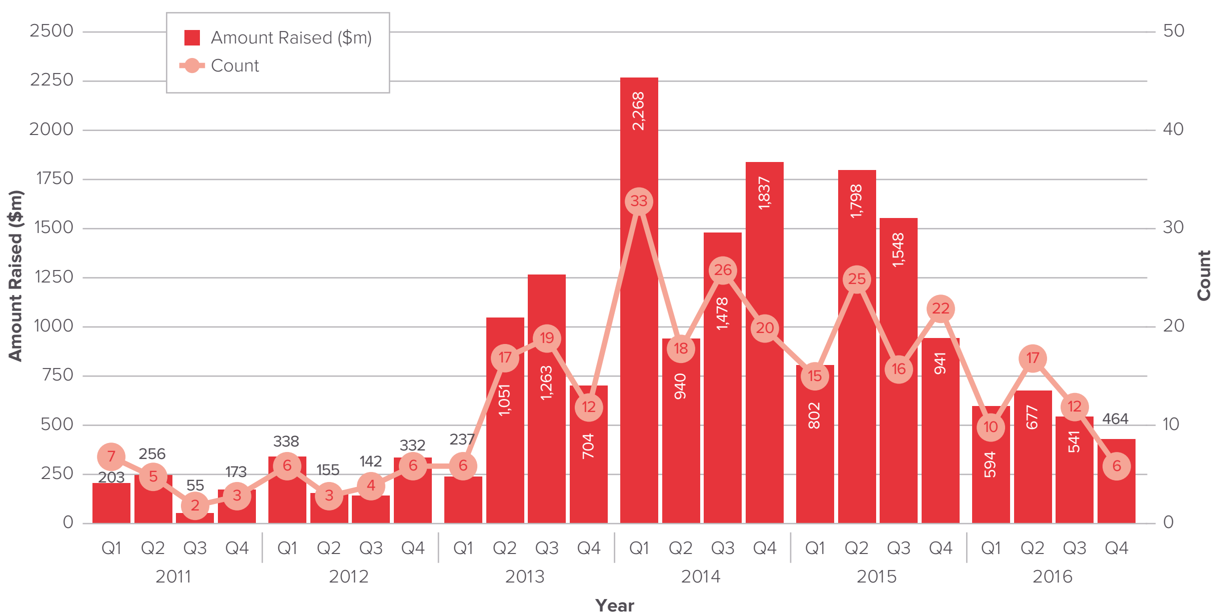
New issues tumble

A look at the statistics on biotech flotations last year makes it clear just how important big buyers remain to the venture capital world. Not a single key metric makes last year's figures on IPOs looks impressive.

Money raised, both in total and on average, is down, as are absolute numbers of companies going public. This record strongly demonstrates that the IPO market has followed the broader biotech equity indices in retrenching to pre-boom levels.

Biotech Initial Public Offerings by Quarter on Western Exchanges (Excludes Medtech)

Source: EvaluatePharma® January 2017



There are a few individual success stories to be found, including some biotechs that neither had to cut offer prices nor have suffered in the market post-float. These include Beigene, a China-based cancer researcher, and the gene therapy plays Avexis and Audentes Therapeutics.

Still, these are few and far between, and since their market debut the class of 2016 has broadly performed disappointingly.

As such it is hard to escape the conclusion that the times of plenty are over. The $464m raised in biotech IPOs in last year's fourth quarter was the lowest seen in a three-month period since the first quarter of 2013, and marked the worst fourth quarter since 2012 – periods when the biotech bull market was just starting to get under way.

Full-year totals are no better, with 2016 seeing the lowest total number of floats since 2013; the total amount raised and average IPO size were the lowest since 2012 and 2011 respectively.

Biotech IPO Market by Year

Source: EvaluatePharma® January 2017

Year	No. of IPOs	Amount raised ($bn)	Avg. amount raised ($m)	No. raising >$100m
2016	45	2.3	51	3
2015	61	4.7	77	17
2014	87	6.3	72	18
2013	44	3.0	67	7
2012	16	0.9	58	2
2011	17	0.7	40	2

Again, however, there is a silver lining. The fourth quarter saw the impressive $218m flotation of Myovant Sciences, which, though it has performed poorly in the market, was priced at a premium to its range. For investors who like this sort of thing it bodes well for floats of other majority-owned subsidiaries of Vivek Ramaswamy's Roivant stable, of which Axovant and Myovant are the first two.

Myovant ended up the biggest float of 2016, and raised the most since Axovant's $315m a year before. Only two other 2016 IPOs raised over $100m: Beigene with $158m and Intellia with $113m.

However, Intellia and its genome editing rivals Editas and Crispr Therapeutics show how last year it became increasingly difficult to get nebulous, early-stage biotechs away. The last of the trio was the last to float and had to take a cut to its proposed price range to get away. Of the three, however, its stock is alone in currently trading above its eventual listing price – albeit marginally – perhaps reflecting a more realistic valuation from the beginning.

Biggest IPOs in 2016

Source: EvaluatePharma® January 2017

Company	Date	Amount Raised ($m)	Discount/ Premium	2016 Chg Since Float
Myovant Sciences	Oct	218	11%	(17%)
Beigene	Feb	158	4%	27%
Intellia Therapeutics	May	113	6%	(27%)
AveXis	Feb	95	0%	139%
Editas Medicine	Feb	94	(6%)	1%
Ra Pharmaceuticals	Oct	92	0%	17%
Protagonist Therapeutics	Aug	90	0%	83%
Audentes Therapeutics	Jul	75	0%	22%
Kadmon	Jul	75	(33%)	(55%)
Corvus Pharmaceuticals	Mar	71	(6%)	(5%)

However, it is important to stress that price haircuts have by no means become an essential means of getting biotechs onto the public markets. Only two of the six fourth-quarter floats were priced at a discount and 2016 overall saw no discernible difference in pricing trends versus previous years; were it not for one disastrous outlier, Kadmon, 2016 would have looked a lot better.

If nothing else this shows that bankers and investors are acutely aware of the new reality, and are prepared to shift their expectations to match. With further market volatility expected this year, the performance of those in the IPO queue will be watched closely to see whether the window of opportunity is getting any smaller.

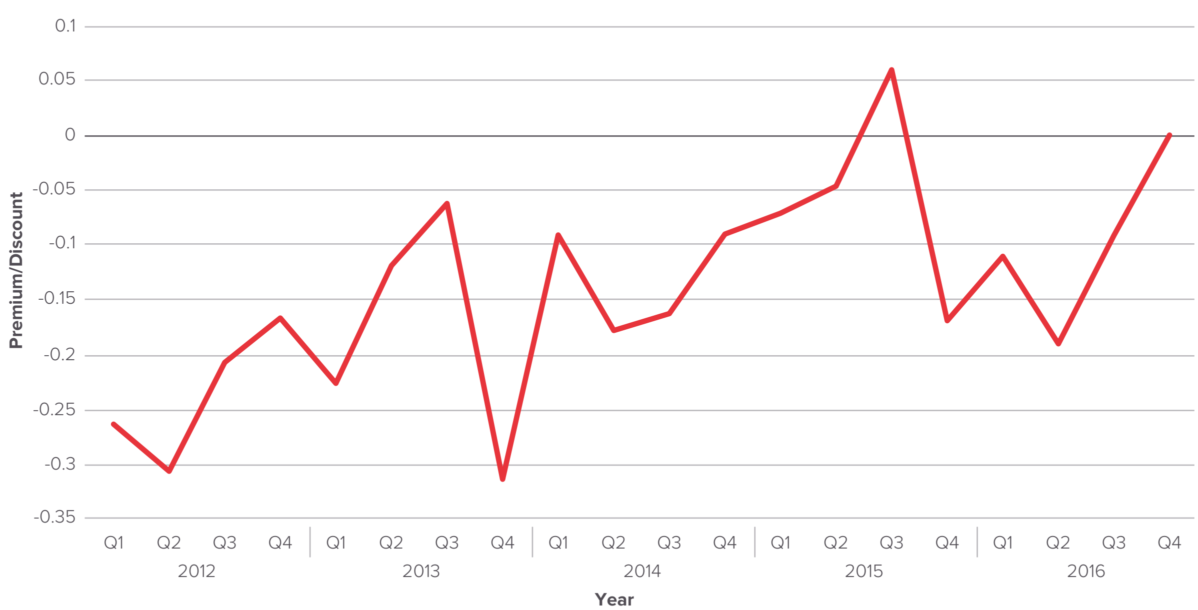
January saw both encouraging and warning signals. By the end of the month three Nasdaq IPOs had taken place, most notably of Jounce Therapeutics, which raised $102m in an upsized offering. Admittedly Jounce is operating in the red-hot immuno-oncology space and already boasts a deal with Celgene, factors that no doubt allowed it to sell more shares and at a higher price than it originally intended.

On the flipside, two companies have already scrapped flotation plans in 2017: the vaccines specialist Visterra and Braeburn Pharmaceuticals, which sells products to treat opioid addiction. Both cited market conditions, which no doubt deteriorated in the wake of President Trump's Twitter attack on drug makers in the second week of January.

As such, unless a company has a strong story to tell, it seems likely that the IPO market will remain a much more hostile environment this year

Offer Price Premium/Discount to Original IPO Price Range

Source: EvaluatePharma® January 2017



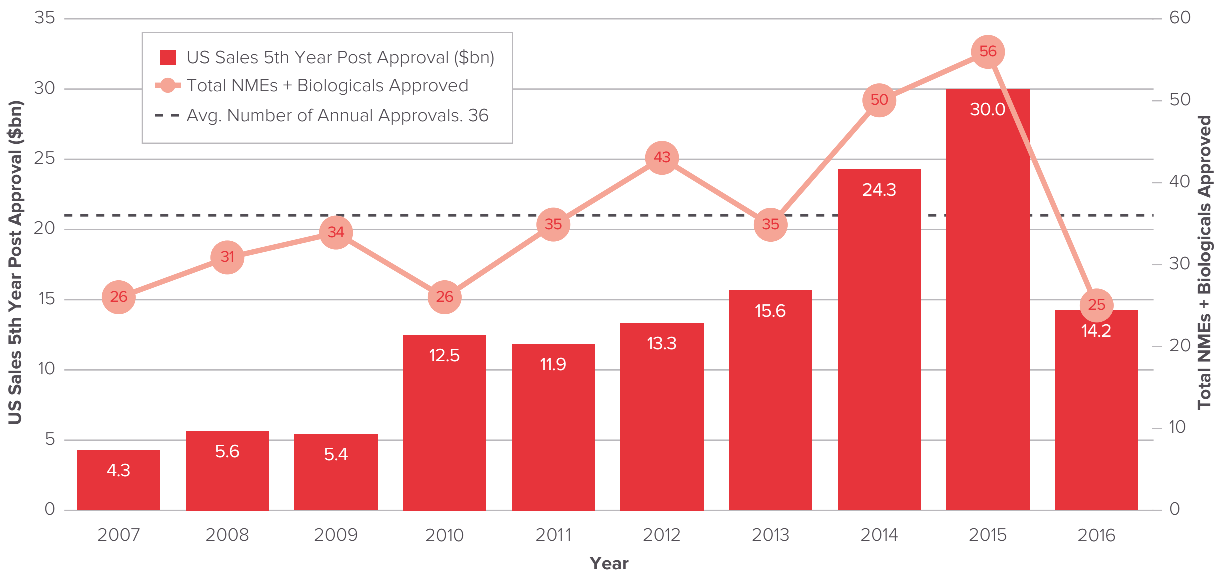
FDA approvals plummet

If last year framed a new reality for the corporate world, industry will be hoping that the FDA's performance on new drug approvals in 2016 was just a blip.

The 25 novel therapeutics approved last year by the US regulator's two drug review units, CDER and CBER, amounted to a decade low. And the combined fifth-year US sales estimate for the group, $14.2bn, is half the potential value of 2015's cohort.

FDA Approval Count vs. Total USA Product Sales

Source: EvaluatePharma® January 2017



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)

The agency itself put this apparent slump down to a natural phasing effect, whereby five 2016 PDUFA actions were approved in 2015 and fewer action dates fell into the calendar year, as well as a noticeable uptick in the number of complete response letters issued.

There is certainly no evidence of a lull in regulatory activity: CDER, the department responsible for reviewing small molecules and certain biologicals, received 36 NME applications, slightly higher than the decade average of 35, according to the FDA.

As such, fears that the last two years of astonishing R&D productivity were mere outliers are probably unfounded.

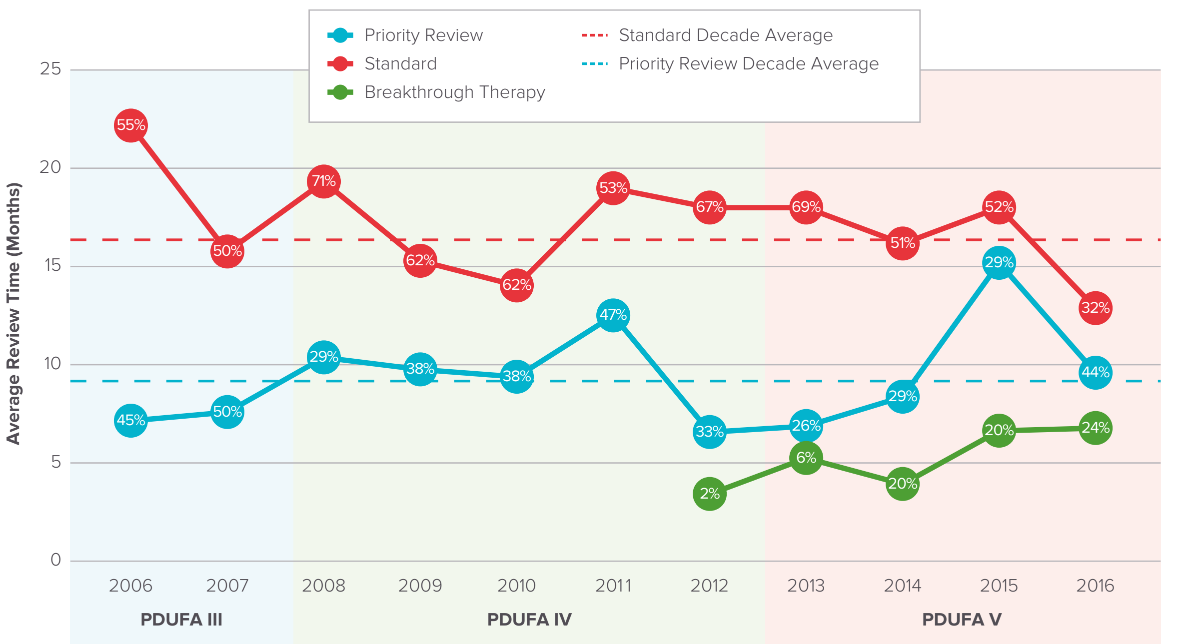
Realistically, something of a return to more sustainable levels was likely to happen. However no one will want to see another contraction this year, particularly as the sector struggles to calm fears around pricing. Even if 2014 and 2015 were extreme exceptions, the overall improvements in productivity witnessed from 2010 must be maintained to prevent even deeper investor doubts about the sector.

There is one silver lining to the FDA's record last year, however. Approval times got noticeably quicker than those in 2015.

Any assumption that this was a direct result of a lighter workload is disproved by the agency's own statistics mentioned earlier, so it seems that efforts over recent years to speed up the US regulatory process are having the desired effect. Industry will be keen for this record of improvement to continue, given that potential candidates to run the FDA under the Trump administration have called for shakeups to the drug approval process.

NME Approval Numbers and Time Over the Last Decade

Source: EvaluatePharma® January 2017



Notable new arrivals last year included Tecentriq, Roche's entry in checkpoint inhibition, Roche/Abbvie's novel leukaemia drug Venclexta and Biogen and Ionis's antisense therapy Spinraza, for the rare childhood wasting disease spinal muscular atrophy. All have blockbuster potential, analysts believe.

The top five, however, is dominated by Gilead, which saw three novel antiviral combinations approved in HIV and hepatitis C. The company's grip on both of these therapy areas cannot be doubted, although the real commercial potential of these particular agents is dimmed by the fact that sales forecast to a large extent reflect a cannibalisation of its earlier products.

Top approvals of 2016

Source: EvaluatePharma® January 2017

Product	Company	2022e sales ($bn)
Tecentriq	Roche	2.40
Taltz	Eli Lilly	1.43
Zepatier	Merck	1.38
Epclusa	Gilead	1.31
Ocaliva	Intercept	1.28

Encouragingly, 2017 is expected to herald the arrival of a number of substantial new products.

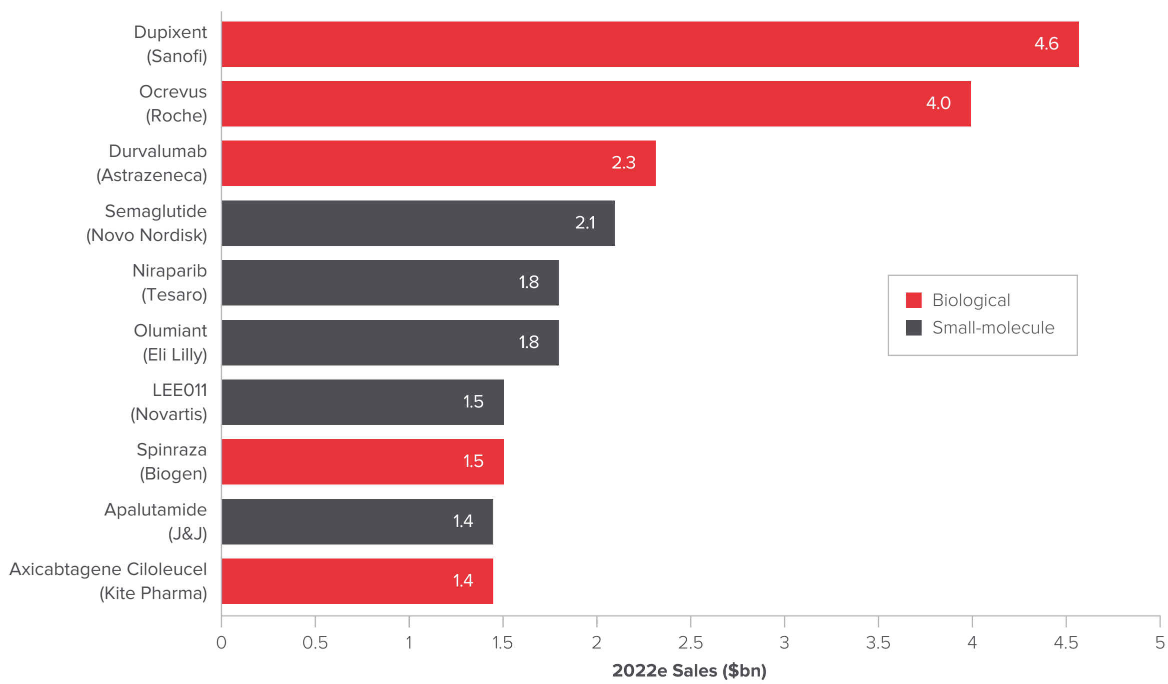
Given the stunning multiple sclerosis data seen with Roche's Ocrevus it could come as a surprise that this agent is not the biggest on the horizon – that honour belongs to Sanofi/Regeneron's dermatitis hopeful Dupixent.

With Novo Nordisk's once-weekly diabetes treatment semaglutide also waiting regulatory judgement, it seems that autoimmune diseases will join cancer to dominate this year's big launches.

Overall this year's expected tally of launches comprises no fewer than 15 blockbusters, plus another three drugs that are seen almost hitting $1bn of sales in 2022.

Biggest Expected Launches of 2017

Source: EvaluatePharma® January 2017



Other autoimmune disease-targeting biologicals that could be launched this year include Johnson & Johnson's RA antibody sirukumab, as well as its psoriasis asset guselkumab. Among the small molecules, Lilly's RA pill Olumiant and Pfizer's psoriasis treatment Eucrisa should reach the market in 2017.

Oncology stands out among conventional drug launches. Most important among these is Tesaro's niraparib, which could seriously challenge Astrazeneca's Lynparza and Clovis's Rubraca if it gets a favourable FDA decision by June 30. Astrazeneca is looking to join Bristol-Myers, Merck and Roche at the high altar of immuno-oncology with durvalumab, while 2017 could also see the approval of the first two CAR-T therapies.

These are undoubtedly two of the year's riskier launches and setbacks cannot be ruled out, here or elsewhere among the new contenders for 2017. However, forecast sales give investors bemoaning the state of the markets something positive to look forward to. The combined 2022 sales forecast of the top 2017 launches surpasses $30bn, which immediately makes this year look more bountiful than the lacklustre 2016.

Forecast: choppy with bright spots

The stats on biopharma's 2016 make it clear that heading into 2017 there are many reasons for optimism, as well as challenges new and old for the sector.

President Trump is perhaps the most important and yet the most unquantifiable. He was initially viewed as heralding the arrival of a business friendly administration, but the seemingly interventionist approach he quickly revealed has startled the industry and its investors.

With few firm proposals to emerge yet it is impossible to judge whether his impact will be positive or negative. And it should be remembered that it will take time and significant effort to shift the complex US healthcare pricing and reimbursement systems, for better or worse, and whatever the tweets may pledge.

However his stance towards the sector, and particularly his rhetoric around drug pricing, will be a big influence on investor sentiment. A key concern is that the pressure on drug prices – either real or perceived – will build further. It is almost impossible to imagine it lessening.

Clarity could be some time coming. In the meantime calls for pharma and biotech companies to take action, or at least do more to make their case, grow louder. Commitments to restrict price rises have only emerged from a handful of companies to date, which seems a weak response from a sector facing such an onslaught of bad publicity. The sector's lead lobby group, PhRMA, is also open to criticisms of complacency. Three years after the launch of the hepatitis C drug Sovaldi put drug pricing in the spotlight it finally launched a defence – in the shape of a new ad campaign.

Investors will look beyond these efforts to fundamentals, of course, and without quantifiable reasons to jump back into the sector pricing concern is likely to prove a big deterrent. What could tempt them back in is an upswing in M&A, and on this front January has delivered.

Hopes are high for further deals, big and small. Throughout the fourth-quarter results season chief executives from Lilly to Takeda made no attempts to hide their appetite for business development. Political uncertainties are unlikely to put companies of this size off smaller transactions. They might be enough to scupper bolder moves, however; for example an attempt by Pfizer to acquire Bristol-Myers Squibb seems likely to remain in investor fantasy land for now.

And woe betide any foreign invader that might try to buy a US drug maker – the wrath of the President's Twitter account would surely be felt.

M&A action aside, clinical success will also be a big swing factor for the sector this year. Numerous big clinical readouts are building, most notably in the immuno-oncology field. Real progress here, and in front of the regulator, will be rewarded. And for those working in hot therapy areas, the prospects of raising private or public money are strong.

As 2016 demonstrated, paths can very quickly change course. But the pharma and biotech sector has very recently enjoyed years of plenty, and the regulatory environment is arguably at its most amenable for years. The outlook for 2017 might be decidedly choppy, but there are plenty of bright spots on the horizon.

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