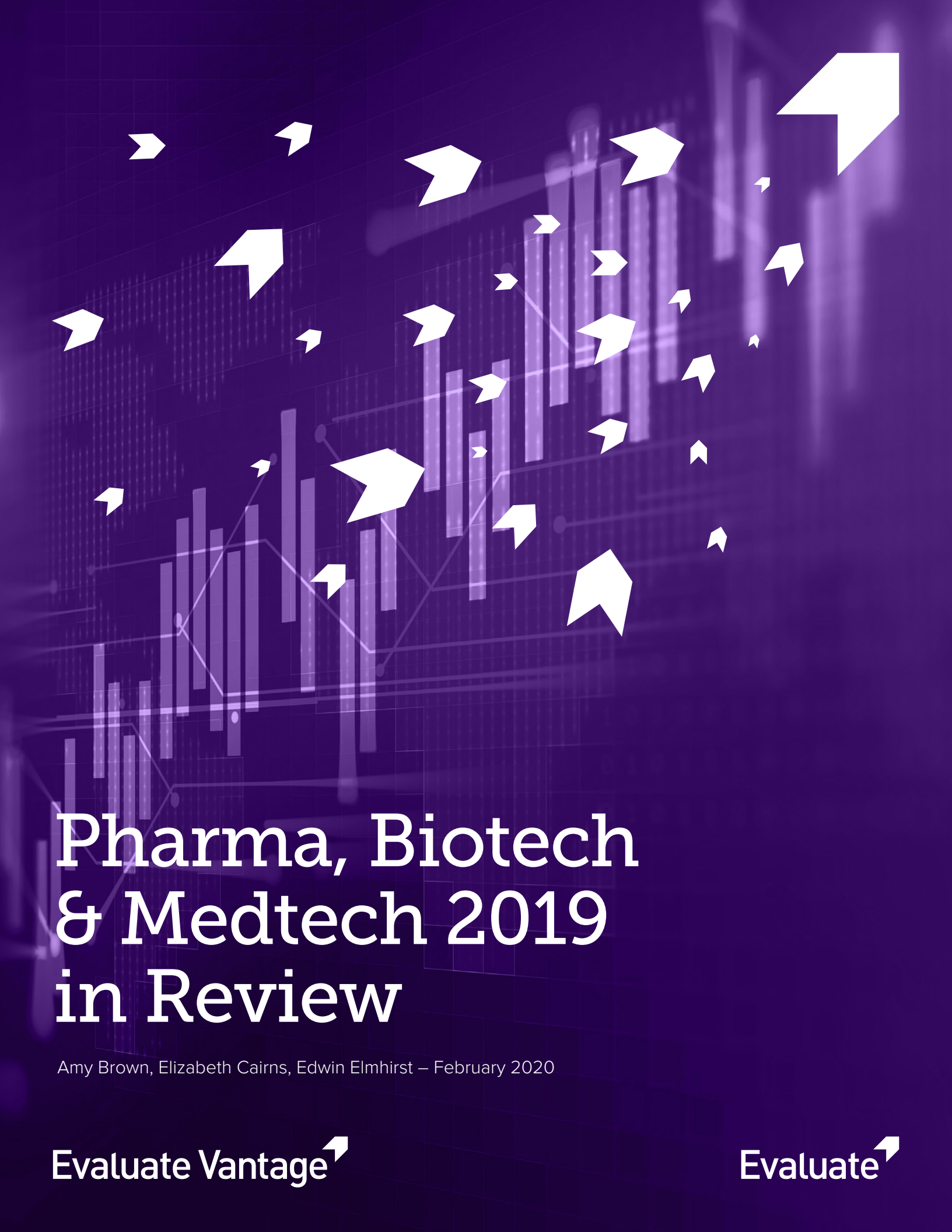


Pharma, Biotech & Medtech 2019 in Review

Amy Brown, Elizabeth Cairns, Edwin Elmhirst – February 2020

Evaluate Vantage

Evaluate

Evaluate Vantage Pharma, Biotech and Medtech 2019 in review

On almost all measures the pharma and biotech sectors had a very successful 2019.

A fourth-quarter surge on the stock markets meant that many publicly listed companies ended the year on a high note, as investors flocked to drug developers both big and small. This was in no small part driven by a late flurry of deal making, capping off a year that was already heading for the record books.

Medtech arguably did even better, justifying its reputation as a safe haven for investors' cash, particularly judging by the big-cap groups' stock performance. Moreover, the rises seen in big- and mid-cap medtechs' share prices outpaced anything biopharma could muster.

EvaluatePharma calculates that global drug makers spent $217bn on M&A deals, a touch below 2014's record-breaking levels. Medtech business development activity, by contrast, regressed to the mean after a bonanza in 2017 and tumbleweeds last year.

The late market rally also kept the IPO window open at the end of the year, a period that many were expecting to be marked by investor caution as the US headed into a presidential election year. In the end 2019 was actually a pretty respectable period for biotech flotations, with 55 new issues arriving on Western exchanges.

Almost the opposite pattern was seen in medtech, market optimism contributing to a very welcoming atmosphere for fledgling public companies. 2019's medtech IPOs were larger, on average, than the sums raised by floating biotechs. That is, until the fourth quarter, when things seemed to go awry, despite the stock markets being in rude health.

The degree to which drug makers and device companies compete for shareholder enthusiasm is debatable, but it seems likely that at least some investors switched allegiance from medtech to biotech in the dying month of 2019.

In the biopharma IPO and the venture financing worlds, 2019 also saw an increasing concentration of capital into the hands of fewer developers. The average amounts raised per IPO and per venture round were close to record highs, as investors sought to fully finance their portfolio companies.

This came alongside a dip in the total venture capital invested in start-ups on 2018; that was a record year for the sector, however, and a cooling was probably inevitable. A retrenchment was also seen in medtech, with both the number of deals and the total cash raised dwindling from the prior year.

Elsewhere, the FDA confirmed that it remained one of biopharma's best friends, approving another bumper crop of medicines, including several speedy approvals. This is another way in which the fates of biopharma and medtech seemed to diverge; the US FDA's rate of approving novel medical devices dropped starkly in the second half.

Report authors | **Amy Brown, Elizabeth Cairns, Edwin Elmhirst** – February 2020

Unless stated, all data are sourced to Evaluate and were accessed in January 2020

Contents

Late surge sees biopharma end the year on a high note

The biopharma sector managed to largely shake off fears about a tightening of drug pricing legislation in the US last year, and most big cap stocks celebrated healthy, double-digit share increases. Perhaps most extraordinary of all was the turnaround effected by Lilly, which at the end of the third quarter had stood off 3% year to date, but in the following three months managed to climb sufficiently to finish the year up 14%.

In fact, most US groups enjoyed a fourth-quarter comeback. Thus indices such as the Nasdaq biotech, S&P pharma and Dow Jones pharma and biotech, which were either flat or up in anaemic single digits at the end of the summer, roared back to end 2019 with double-digit gains.

Indices

Stock index	12-mth % change
Nasdaq Biotechnology (US)	24%
S&P Pharmaceuticals (US)	12%
Dow Jones Pharma and Biotech (US)	14%
S&P 500 (US)	29%
DJIA (US)	22%
Dow Jones Stoxx 600 Healthcare (EU)	29%
Thomson Reuters Europe Healthcare (EU)	26%
Euro Stoxx 50 (EU)	20%
FTSE-100 (UK)	12%
Topix Pharmaceutical Index (Japan)	21%

Overall, however, the year belonged to a trio of EU-based big cap stocks: Astrazeneca, driven by the oncology drugs Tagrisso and Lynparza, Roche, propelled by Ocrevus and Hemlibra, and Novartis. The last has remained an aggressive asset buyer, and in Zolgensma looks to have a marketed product that could, after several false starts, mark gene therapy's coming of age.

On the debit side, Pfizer remained big pharma's worst-performing stock, driven down by concerns over its corporate strategy. Abbvie, like Lilly, saw a major fourth-quarter recovery, finishing down 4% after standing off 18% at the end of the third quarter.

Big pharma: top risers and fallers in 12 months

Source: Evaluate® January 2020

	Share price	Market capitalisation ($bn)	
Top 3 risers	**12-mth change**	**31 December 2019**	**12-mth change ($bn)**
Astrazeneca	31%	130.82	34.60
Roche	29%	271.67	61.11
Novartis	27%	214.44	18.62
Top 3 worst performers			
Pfizer	(10%)	216.83	(35.49)
Abbvie	(4%)	130.94	(7.74)
Johnson & Johnson	13%	383.91	37.80

Among large biopharma companies just outside the big cap sphere, those not based in the west continued to dominate. Jiangsu Hengrui is emerging as one of China's most popular healthcare picks thanks to its strength in oncology, while Chugai – majority-owned by Roche – is reaping the rewards of the Swiss group's Hemlibra success.

At the bottom of the table Regeneron continued to suffer from the imminent erosion of its Eylea franchise, and Gilead was unable to shake off questions over its lack of business development nous.

Still, the worst performer in this stock category was actually Biogen, a somewhat surprising result given that some now think that the company's Alzheimer's project aducanumab is headed for US approval this year. Before the biotech's shock claim that the amyloid-beta MAb actually works the stock had been trading off 30% on the year.

Other big drugmakers ($25bn+): top risers and fallers in 12 months

Source: Evaluate® January 2020

	Share price	Market capitalisation ($bn)	
Top 3 risers	**12-mth change**	**31 December 2019**	**12-mth change ($bn)**
Jiangsu Hengrui Medicine	100%	54.5	26.5
Chugai Pharmaceutical	58%	52.2	20.5
CSL	49%	85.1	25.4
Top 3 worst performers			
Biogen	(1%)	53.5	(7.1)
Regeneron Pharmaceuticals	1%	40.5	0.8
Gilead	4%	82.2	0.3

A spectacular end to the year for biotech stocks helped generate several clear winners among the world's small drug makers across 2019. The broad geographical spread of the best-performing companies really stands out, with most major regions represented in the top five gainers.

The same goes for the sector laggards, where failures and disappointments brought down companies from Japan's Sumitomo Dainippon, to Nektar in the US and Irlab in Sweden. It is notable however that even the worst performers among the mid-caps avoided all-out calamity – previous years have seen much more severe declines in this category.

Nektar, which has been hurt by flagging confidence in its lead cytokine asset, stands out as the sole US faller. US biotechs have benefited the most from the market rally, and companies based in America dominate the list of small-cap risers.

Mid cap ($5-25bn): top risers and fallers in 12 months

Source: Evaluate® January 2020

	Share price	Market capitalisation ($bn)	
Top 5 risers	**12-mth change**	**31 December 2019**	**12-mth change ($bn)**
Galapagos	125%	13.3	8.3
Sino Biopharmaceutical	111%	17.5	9.2
Daiichi Sankyo	106%	47.4	25.3
Seattle Genetics	102%	19.6	10.5
Vifor Pharma Group	65%	11.6	4.6
Top 5 worst performers			
Sumitomo Dainippon Pharma	(39%)	7.8	(4.5)
Aurobindo Pharma	(37%)	3.8	(2.1)
Teva Pharmaceutical Industries	(36%)	10.7	(6.1)
Piramal Enterprises	(36%)	4.3	(1.7)
Nektar Therapeutics	(34%)	3.8	(1.9)

It is among the small caps that the more frothy aspects of the market can really be seen: Kodiak and Arrowhead, for example, have a long way to go to prove the worth of their respective projects, though the latter has been boosted by deal making in the RNAi space.

The Medicines Company's takeout by Novartis is an example here – the deal has not gone through but the stock is sitting on a 344% gain this year. The target group has been removed from this ranking, as have Arqule and Synthorx, whose takeouts by Merck & Co and Sanofi represented gains of 621% and 302% on the beginning of 2019.

The fallers are as usual populated by companies blighted by clinical failure; in a sign of the competitive nature of the Duchenne muscular dystrophy space, both Solid and Wave are in the doldrums after setbacks with their respective contenders for the muscle wasting condition.

Small cap ($250m-$5bn): top risers and fallers in 12 months

Source: Evaluate® January 2020

	Share price	Market capitalisation ($m)	
Top 5 risers	**12-mth change**	**31 December 2019**	**12-mth change ($m)**
Kodiak Sciences	913%	2,666	2,405
Arrowhead Pharmaceuticals	411%	6,064	4,919
Eidos Therapeutics	317%	2,152	1,646
Epizyme	299%	2,240	1,752
Reata Pharmaceuticals	264%	5,063	3,717
Top 5 worst performers			
Novavax	(89%)	106	(598)
Irlab Therapeutics	(88%)	152	(128)
Solid Biosciences	(83%)	205	(745)
Wave Life Sciences	(81%)	275	(964)
Aptinyx	(79%)	115	(439)

More in-depth analyses of biopharma share price movements over 2019 can be found here:

The big cap empire strikes back

A handful of huge gains stand out among mid and small-cap biotechs

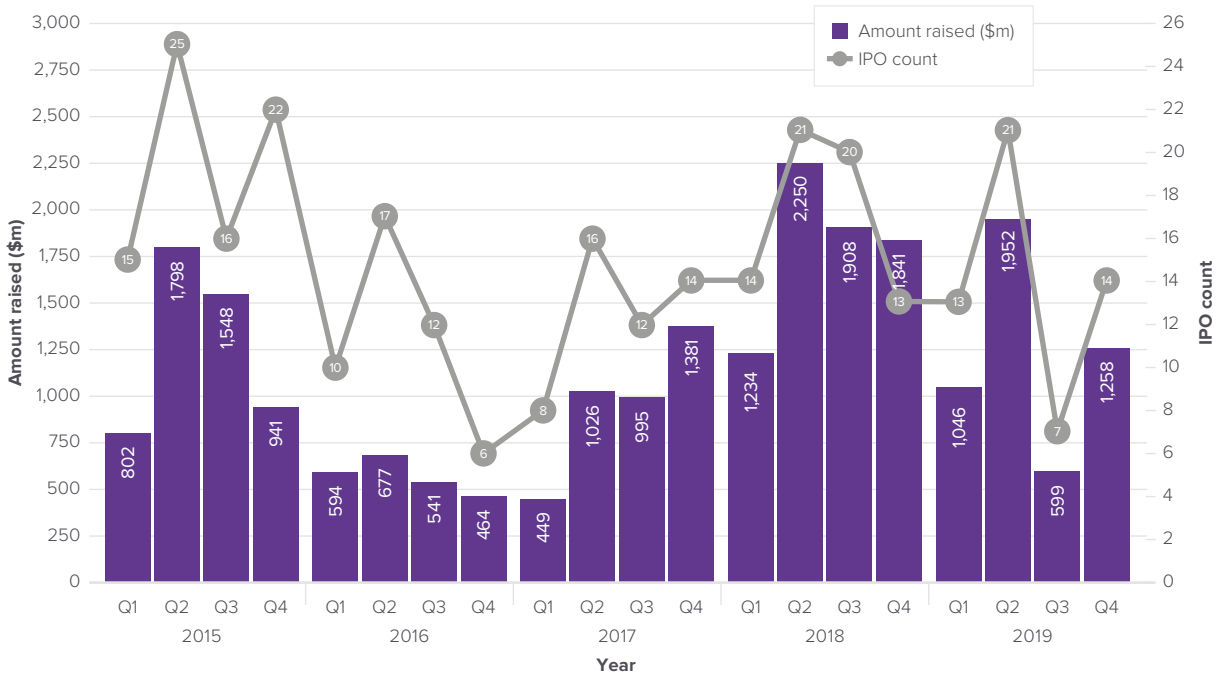
Last-ditch rally saves 2019 float tally

Until October it had looked as if the IPO window for young drug makers might be shutting as western stock markets contracted. Instead 14 listings, including four $100m-plus floats, helped 2019 finish with a flourish as the markets bounced back to health.

As with all the data in the pharma and biotech section of this report, this analysis looks only at drug developers, excluding sectors like medtech and genomics.

Biotech initial public offerings by quarter on Western exchanges

Source: Evaluate® January 2020



The strong fourth quarter means that, looking back over the decade, 2019 was far from a disappointing period for drug maker flotations. The average amount raised, at $88m, was the second highest over the decade; this suggests that the concentration of capital into the hands of fewer companies is not limited to the venture financing field.

A decade of biopharma flotations

Source: Evaluate® January 2020

Date	No. of IPOs	Amount raised ($bn)	Avg. amount raised ($m)	No. raising >$100m
2019	**55**	**4.9**	**88**	**17**
2018	68	7.2	106	31
2017	50	3.9	77	15
2016	45	2.3	51	3

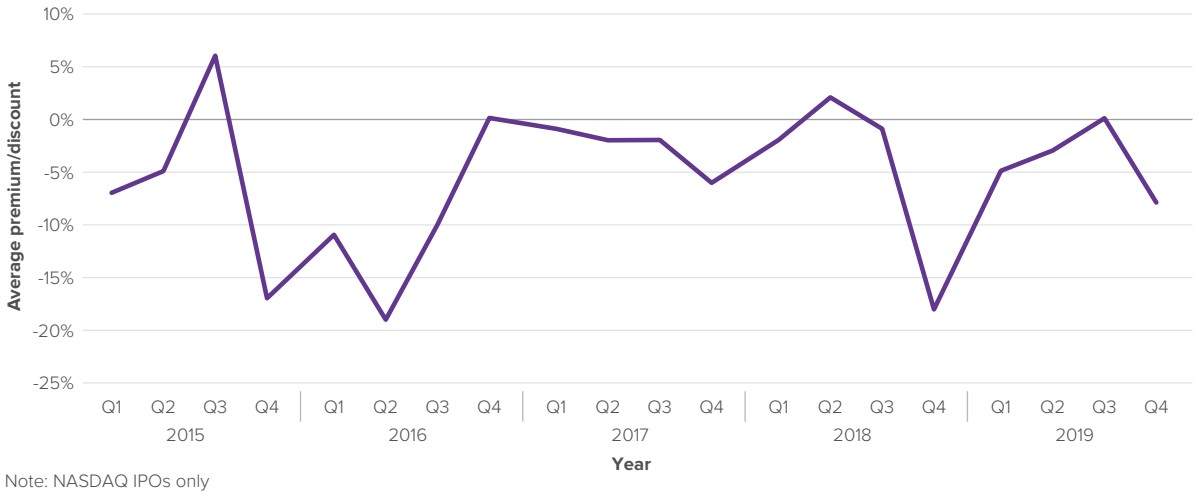
Date	No. of IPOs	Amount raised ($bn)	Avg. amount raised ($m)	No. raising >$100m
2015	78	5.1	65	17
2014	97	6.5	67	18
2013	54	3.3	60	7
2012	19	1.0	51	2

A look at trends in investor sentiment shows that the final quarter of the year is traditionally a tough period to float, and last year was no exception. However, the average discount to initially proposed price ranges was at least less severe than in the final quarter of 2018.

The second chart below looks at the difference between the average share price achieved while a company was private – a figure supplied in most US registration documents – and the price at float. Early investors are apparently not able to achieve the valuation uplifts at IPO they once could.

Average Nasdaq premium/(discount) to IPO price range

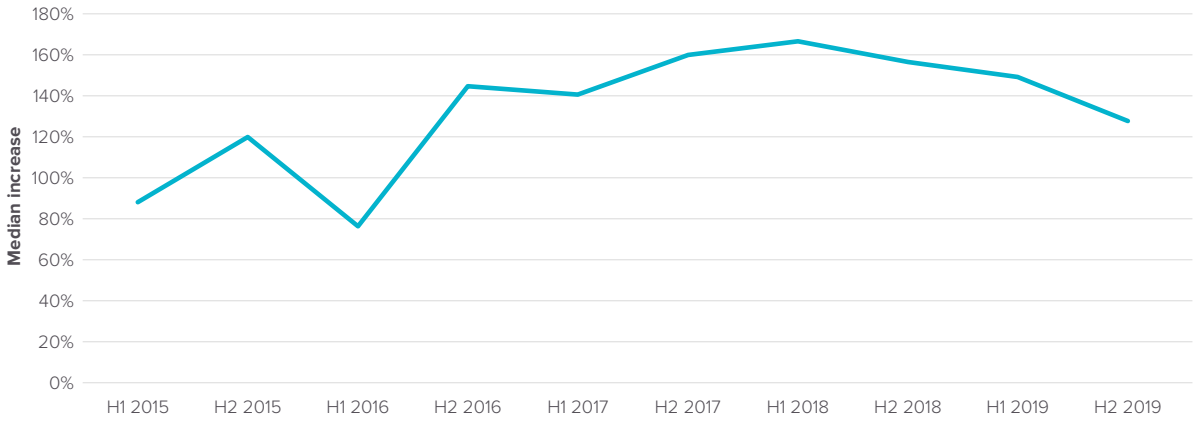
Source: Evaluate® January 2020



Note: NASDAQ IPOs only

Median increase in pro-IPO average share price to float

Source: Evaluate® January 2020



A more in-depth analysis of the biotech IPO market can be found here:

Last-ditch rally saves 2019 float tally

Biopharma venture financing retreats, but not by much

The financing climate for young drug makers cooled last year, but cash was far from scarce. If anything, the major concern heard from private investors is the long-term implications of an excess of capital.

There were few signs of restraint in 2019, however. The average financing size dipped on 2018's peak but remained at record levels; the frequency of mega rounds, those that amassed $100m or more, barely slowed.

Biopharma and venture capital – a look at the topline numbers

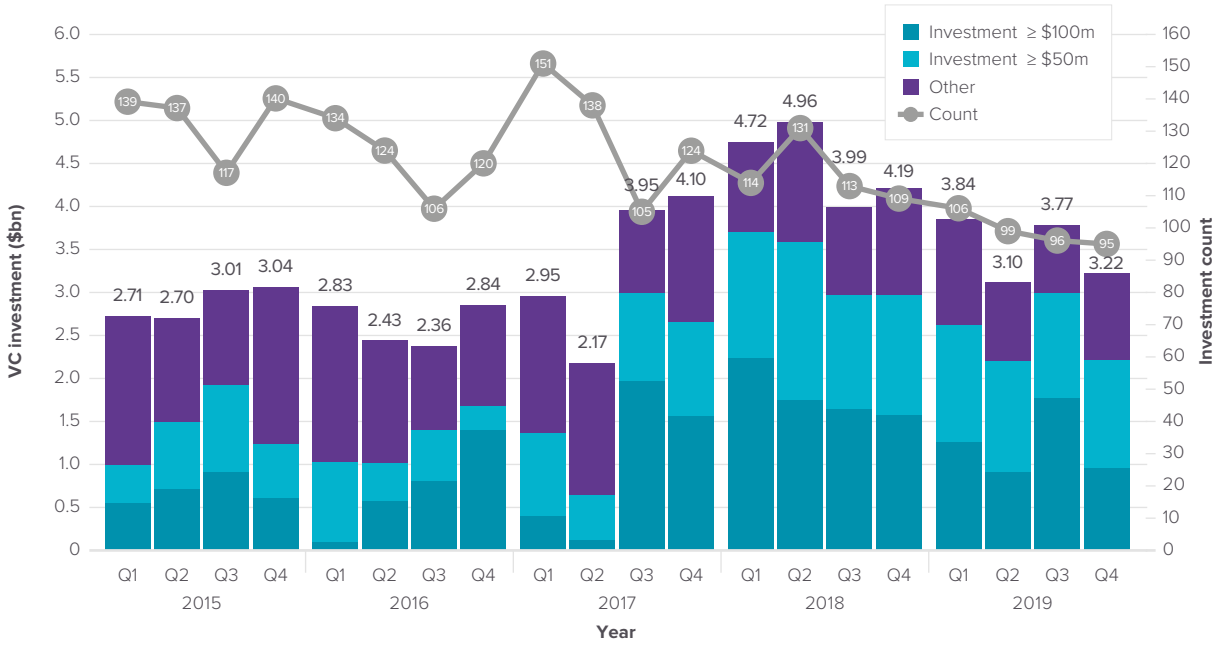
Source: Evaluate® January 2020

Year	Total investment ($bn)	Financing count	Avg per financing ($m)	No. of rounds ≥$50m	No. of rounds ≥$100m
2019	13.9	396	36.7	110	32
2018	17.9	467	40.2	130	39
2017	13.2	518	37.8	76	19
2016	10.5	484	23.0	52	15
2015	11.5	533	22.4	59	15

All of which points to an even more pronounced concentration of capital into the hands of a shrinking number start-ups – the count of rounds raised fell to below 400 last year for the first time since at least 2010, according to *EvaluatePharma*.

Global quarterly biopharma venture investments

Source: Evaluate® January 2020

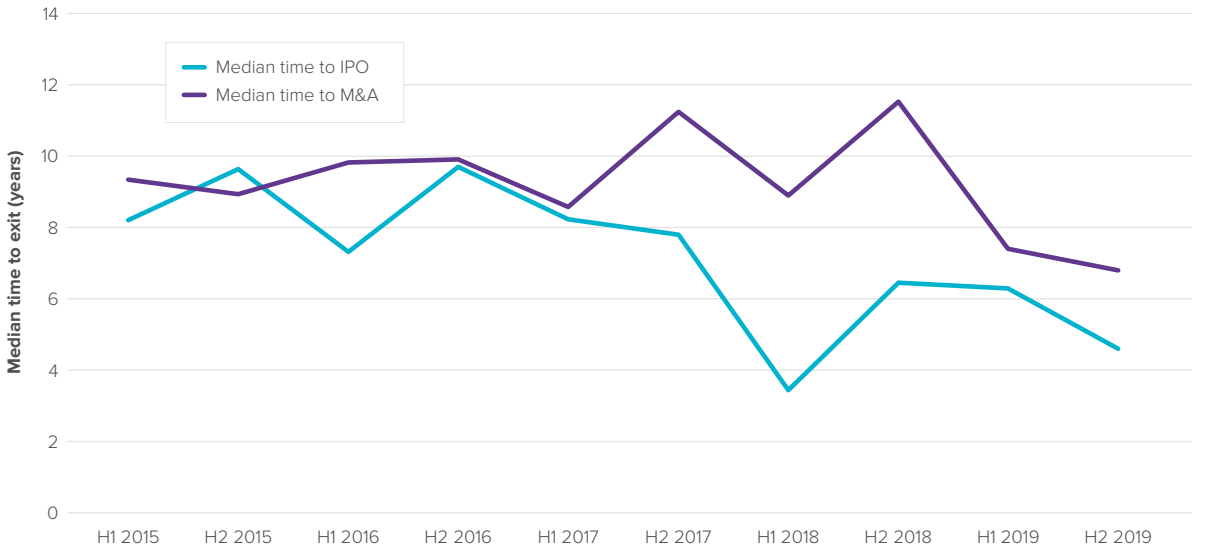


The focusing of capital reflects a shift in investment strategy that has been widely embraced by these company builders and which, as they describe it, allows start-ups to be properly funded and given the best chance of success.

There is some evidence that this strategy is working. The median time to exit via M&A, measured from date of company foundation to buyout, dipped noticeably in 2019, while time to IPO is also historically swift.

Time to exit (from established) for venture backed companies

Source: Evaluate® January 2020



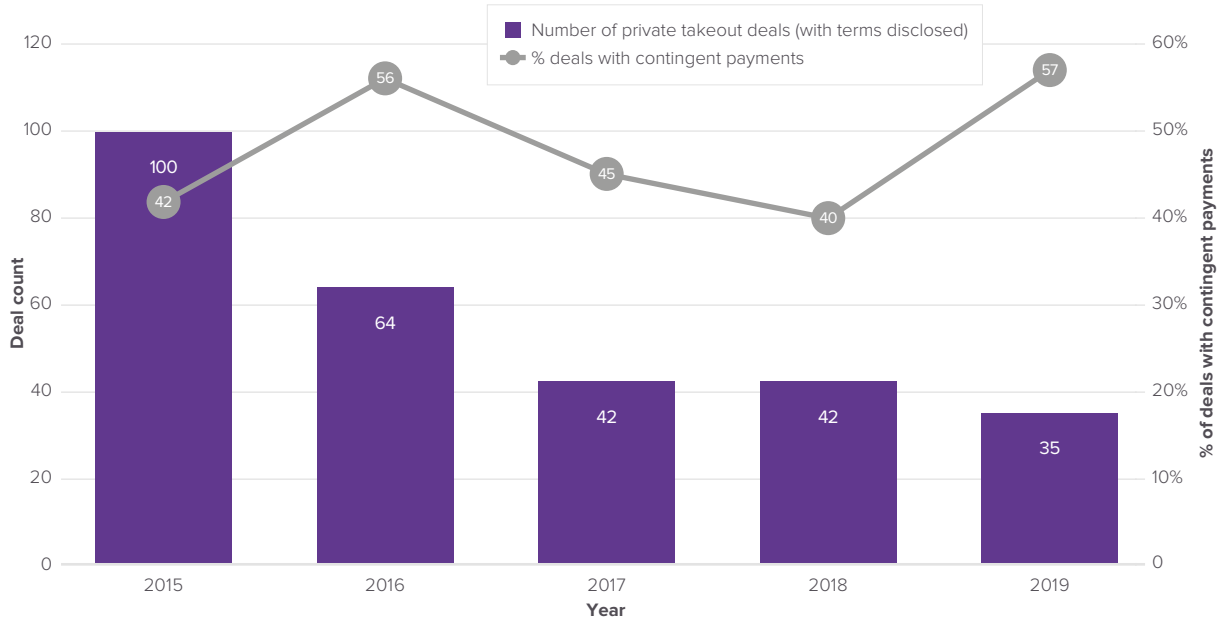
Time to IPO is largely a reflection of the relative receptiveness of stock markets, of course. In terms of takeouts, in the private sphere the M&A wheels are increasingly being greased by deal structures that contain future payments, contingent on future successes.

The chart below finds that the proportion of private company takeouts that involved some sort of contingent value jumped to almost 60% in 2019, substantially higher than in the previous two years.

This analysis also shows that the number of private takeouts has declined substantially over the past five years, both in absolute terms and as a proportion of all deals. True, the venture-backed world is substantially better funded now, making selling out less of a necessity. But viewed alongside a declining number of venture financings, the drop in private transactions is a trend to keep an eye on.

Private takeout deals

Source: Evaluate® January 2020



A more in-depth analysis of the venture financing climate for biopharma can be found here:

Biopharma venture financing retreats, but not by much

As takeouts of private companies dip, investors grease the deal wheels

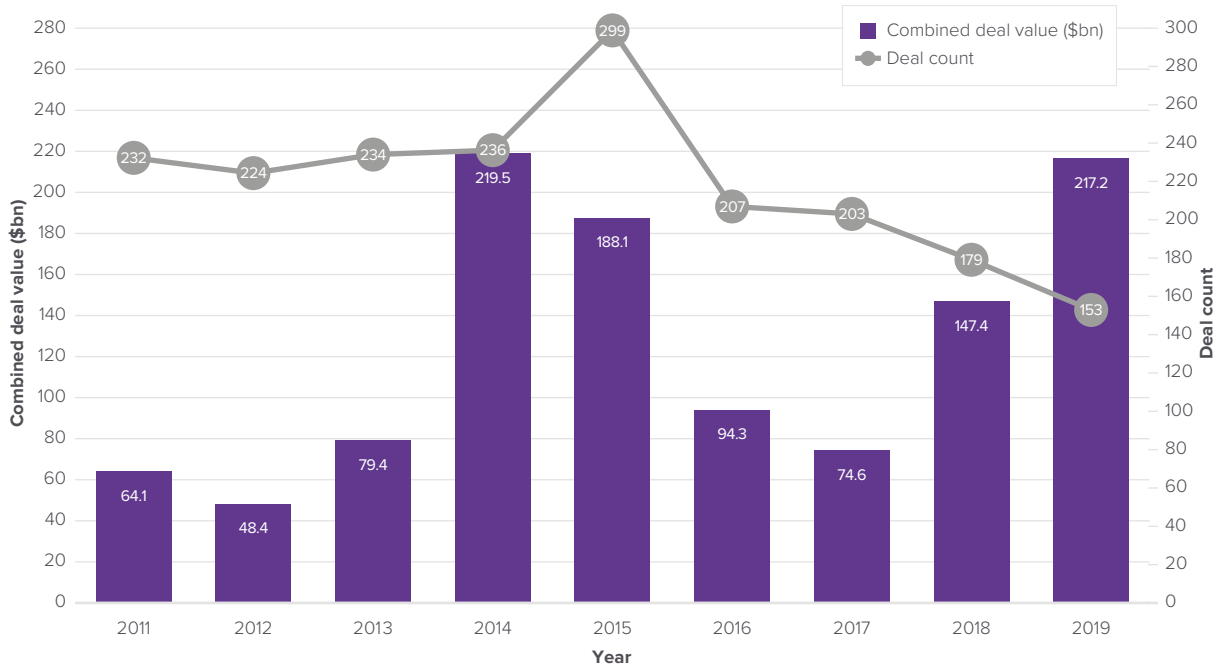
A big finish confirms 2019 as a takeover year to remember

A long wished-for pick-up in company takeouts at the end of last year confirmed 2019 as a bumper period for biopharma deal-making. *EvaluatePharma* calculates that global drug makers spent $217.2bn on M&A deals, a touch below 2014's record-breaking levels.

The table below illustrates just how much firepower was unleashed last year, relative to spending throughout the decade, though the vast majority of the cash deployed in 2019 went on buying Celgene for $74bn and Allergan for $63bn.

A decade of biopharma M&A

Source: Evaluate® January 2020

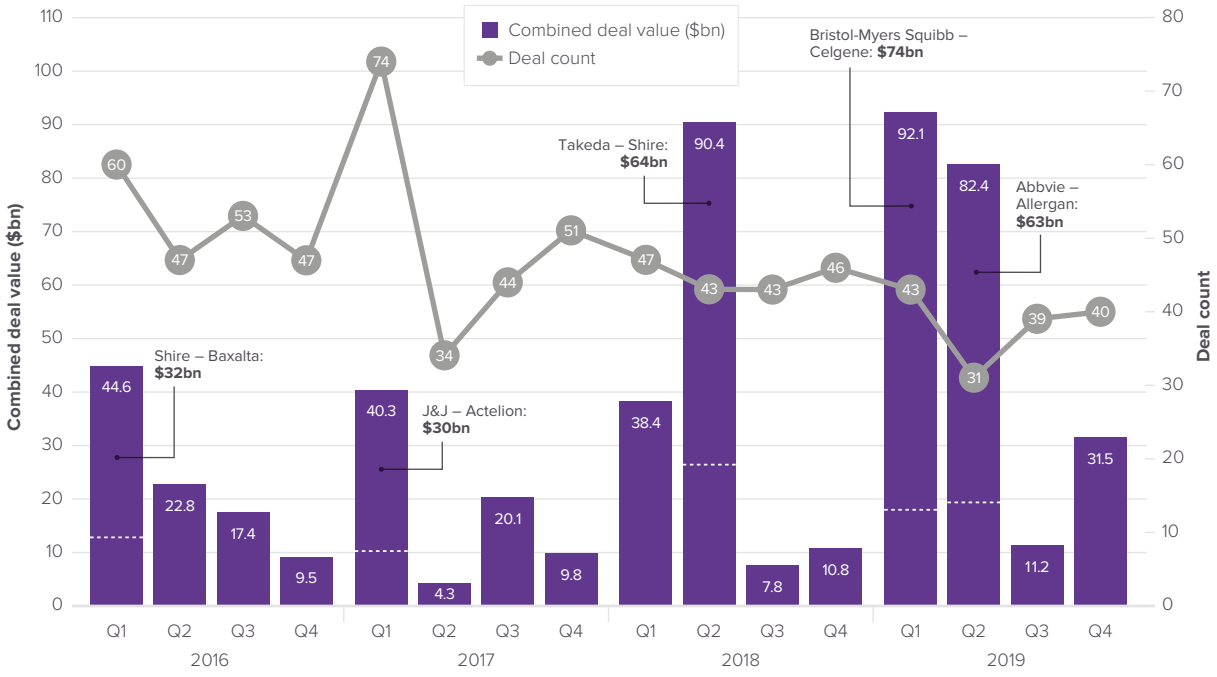


An important point here is that this analysis incorporates various types of M&A deal. As well as company takeouts – which accounted for around half of the transactions last year – minority and majority stake purchases, acquisitions of business units, reverse mergers and option deals are also counted.

This should be remembered when looking at the total transaction volume, which has been declining since hitting a peak in 2015, and currently sits at a low for the decade. This has been driven by a slump in these other types of M&A deals – straight company takeouts have remained largely flat over the past couple of years.

Pharma and biotech M&A transactions announced each quarter

Source: Evaluate® January 2020



When looking specifically at straight company takeouts, below, the data reveal a rebound in mid-size deals in 2019, to the highest level since 2015. Big pharma's "sweet spot" will fall somewhere into here, although the ideal bolt-on price will differ between companies.

Biopharma company takeouts, by size bracket

Source: Evaluate® January 2020

	2015	2016	2017	2018	2019
$0-500m	87	54	45	47	33
$500m-1bn	10	15	9	9	12
$1-15bn	20	14	8	13	17
$15-30bn	2	0	0	0	0
$30bn+	0	1	1	1	2
All	119	84	63	70	64

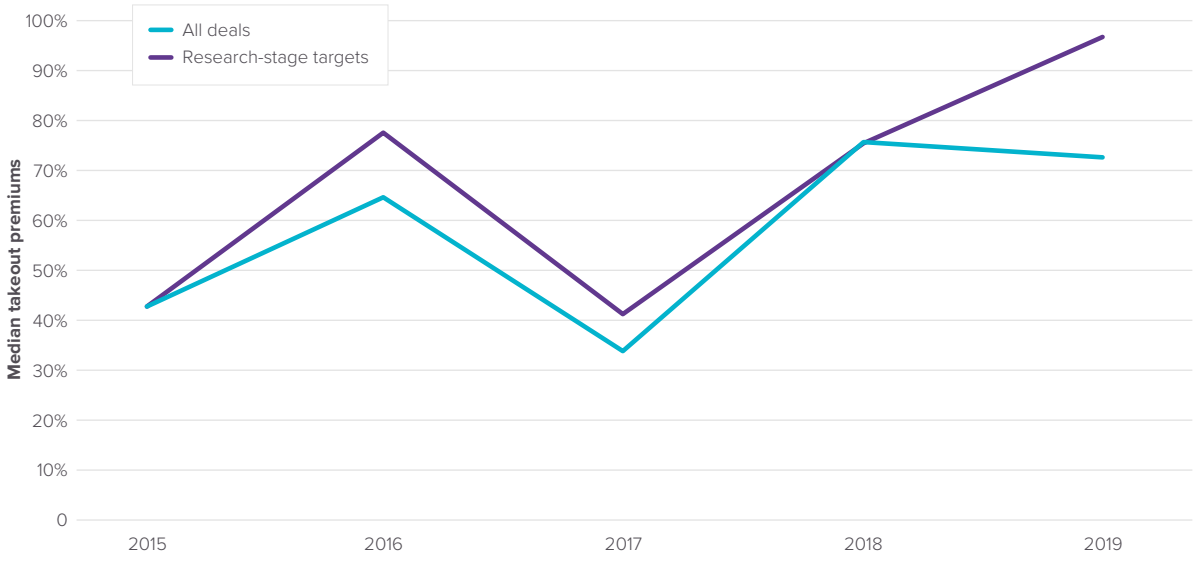
Meanwhile, last year premiums climbed to the highest point since at least 2015, with research-stage companies commanding particularly high prices.

Premiums can be considered as a proxy for the level of competition for assets, and a look at the following analyses suggests that last year acquirers were fighting over some of these deals. The median takeout premium for a research-stage drug developer reached 97% in 2019, the highest level for at least five years.

That 97% median premium was derived from 28 transactions, almost double the number of research-stage buyouts that happened in 2015.

Median takeout premiums

Source: Evaluate® January 2020



A more detailed analysis of this M&A data can be found here:

A big finish confirms 2019 as a takeover year to remember

What makes a great year for takeovers?

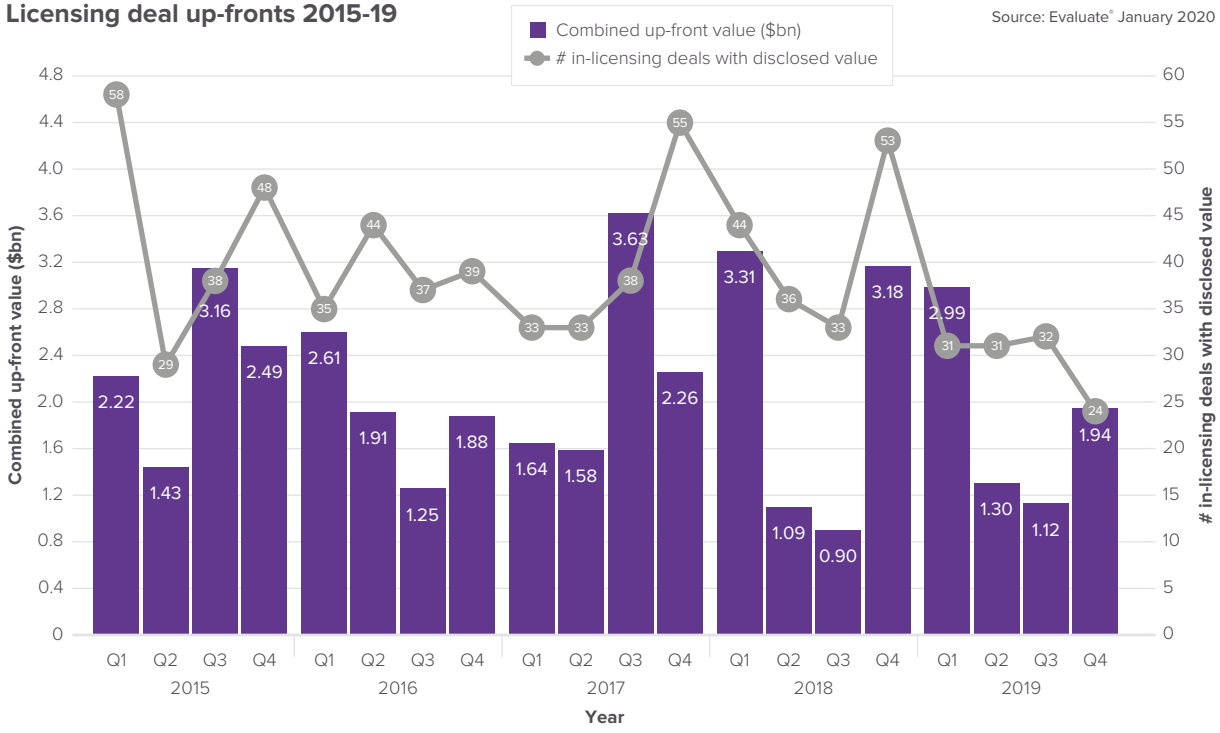
Cash-rich biotechs turn down the licensing deal volume

Another big area of deal making for biopharma is the licensing deal market and, echoing the decline being seen in straight company takeouts, activity has been fading over the past couple of years.

When cash is easy to come by, young drug makers can keep their options open, and this is one likely reason for the downward trends seen in both M&A and licensing.

Licensing deal up-fronts 2015-19

Source: Evaluate® January 2020



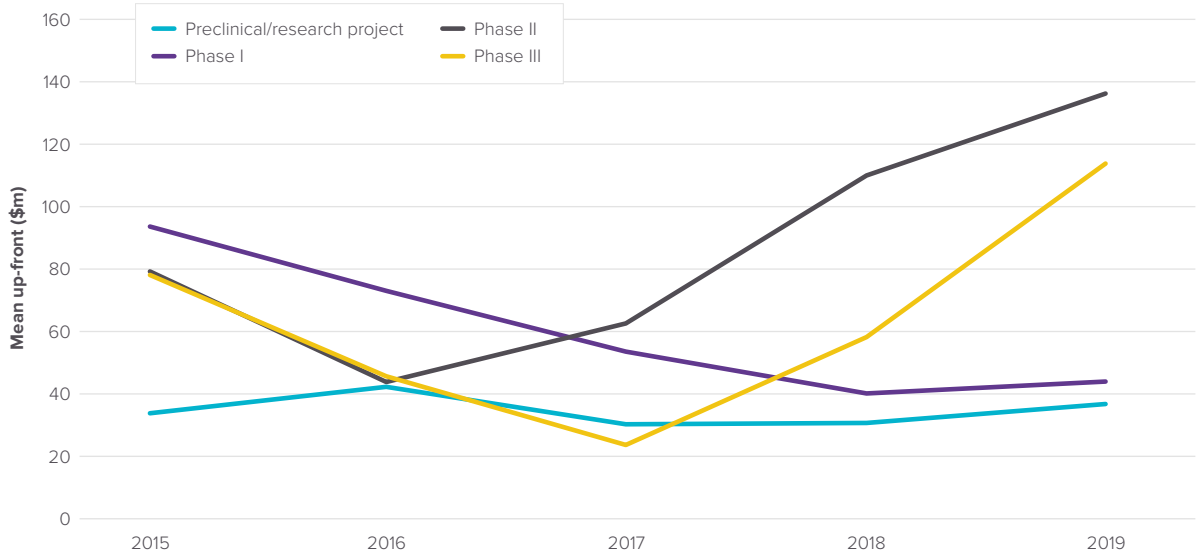
The chart above looks at long-term trends in licensing deals between drug makers – it excludes medtech or diagnostic collaborations – and counts only those transactions with a disclosed up-front fee. This analysis therefore understates the real volume of licensing deals happening, though it should still reflect overall trends.

Using only deals with up-fronts allows a more rigorous look at trends – the "biobuck" total deal values cited are rarely useful beyond headline fodder for press releases, and in most cases will go largely unpaid.

Up-front fees represent a real chunk of cash changing hands, and this analysis of *EvaluatePharma* data show that the sector paid out $7.4bn in these initial payments over 118 deals last year. Both of these figures are five-year lows.

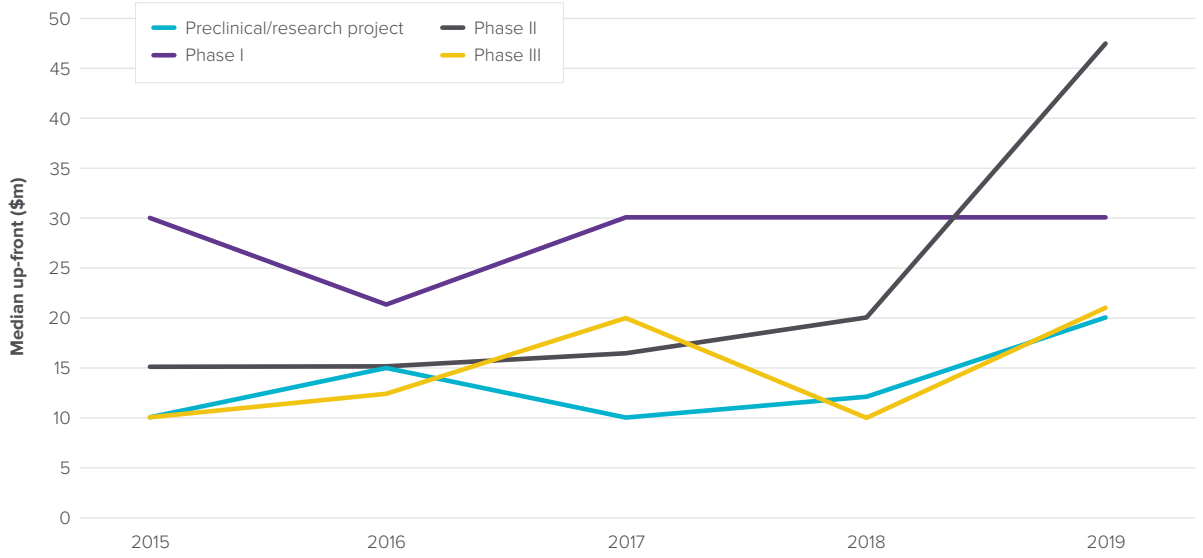
Mean in-licensing deal up-front

Source: Evaluate® January 2020



Median in-licensing deal up-front

Source: Evaluate® January 2020



A further analysis of these data shows that asset prices held up last year, however. Most notably, the average up-front fee paid for a phase II asset surged to almost $140m, a more than five-year high.

Averages can, however, be skewed by outliers, though this jump at phase II can also be seen in the median values. It is also revealing that phase III assets tend to attract lower prices than those at earlier clinical stages – hope and hype are apparently much more effective tools to drive up price tags than later-stage data, which might inconveniently reveal the true value of an asset.

Biggest research-stage licensing deals of 2019

Source: Evaluate® January 2020

Product (status on deal)	Company	Deal partner	Up-front fee ($m)	Total deal value ($bn)
Enhertu (phase III)	Astrazeneca	Daiichi Sankyo	1,350	6.9
SRP-9001 (phase II)	Roche	Sarepta	750	2.9
Bintrafusp Alfa/M7824 (phase II)	Glaxosmithkline	Merck KGaA	339	4.2
AKCEA-ANGPTL3-LRx (phase II)	Pfizer	Akcea	250	1.6
DCR-HBVS (phase I)	Roche	Dicerna	200	1.7

A more in-depth analysis of licensing deal data can be found here:

Cash-rich biotechs turn down the licensing deal volume

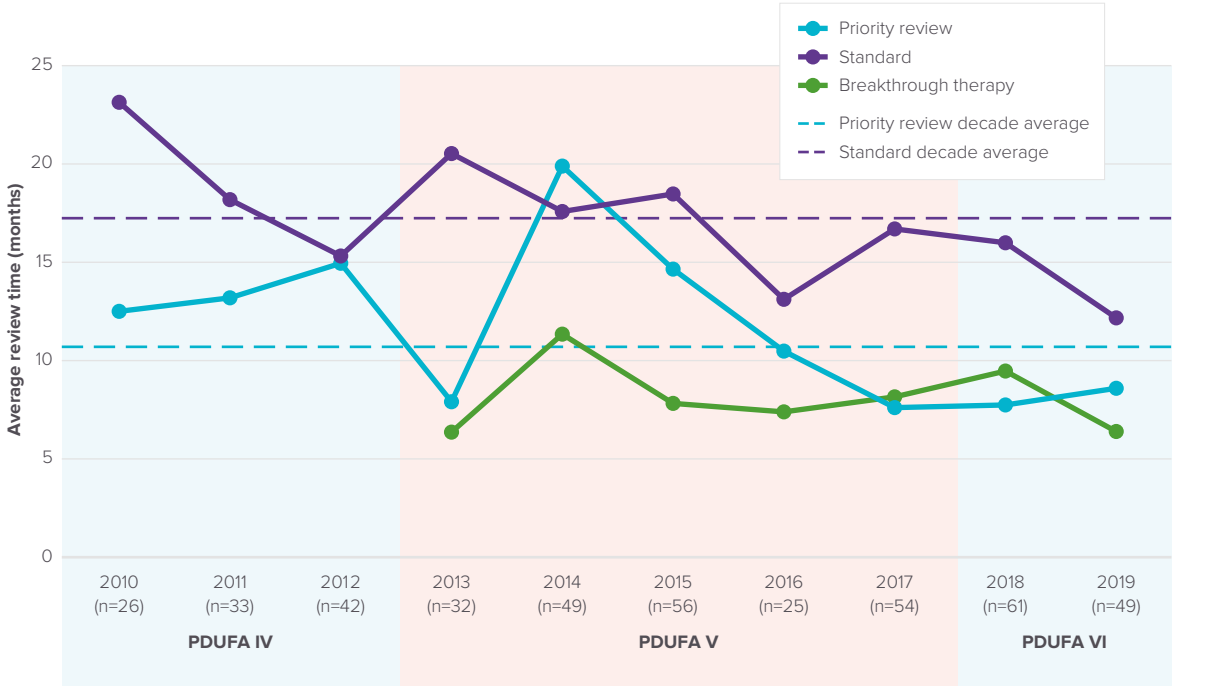
Rare diseases top another strong year for novel drug approvals

It was not only a takeover spree that put the wind in biopharma's sails towards the end of last year – the FDA contributed with several surprisingly speedy approvals.

Average approval times in the breakthrough designation category improved markedly in 2019, to give the regulator its best score since 2013; the 6.3-month mean is even more remarkable considering that in that year, when BTD was first introduced, only three projects used this pathway. In 2019 the average was derived from the review of 15 projects.

CBER+CDER average approval times

Source: Evaluate® January 2020



Two of the class of 2019 – Trikafta and Enhertu – made it into the 10 fastest approval decisions since 2010. Behind these agents there were plenty of other quick reviews last year, however: almost a quarter of 2019's submissions were approved in less than six months.

Green light ahead: the fastest FDA decisions since 2010

Source: Evaluate® January 2020

Product	Year approved	Status	Months to approval
Blincyto	2014	Breakthrough therapy	2.5
Iclusig	2012	Priority review	2.6
Jevtana	2010	Priority review	2.6
Spinraza	2016	Priority review	3.0
Alecensa	2015	Priority review	3.1
Trikafta	2019	Breakthrough therapy	3.1
Xtandi	2012	Priority review	3.3
Kalydeco	2012	Priority review	3.5
Zelboraf	2011	Priority review	3.6
Enhertu	2019	Breakthrough therapy	3.7

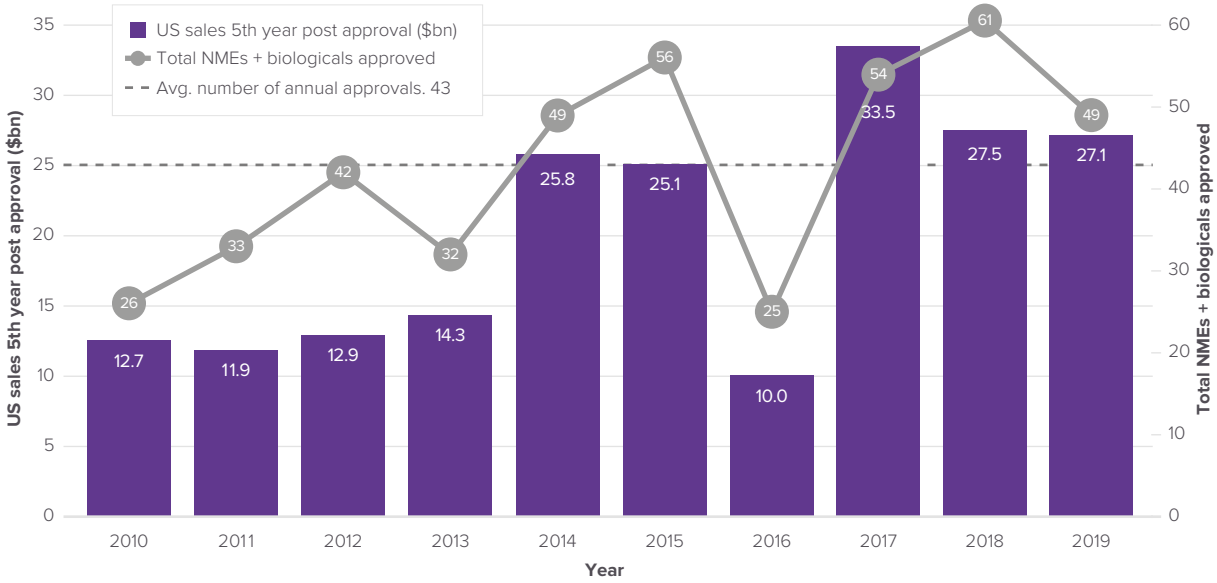
A look at the picture across the whole of 2019 confirms that the US drugs regulator remains one of the sector's best friends. Over the year the agency approved 49 novel medicines with a fifth-year sales potential of $27.1bn, according to an *Evaluate Vantage* analysis of *EvaluatePharma* data.

Nine drugs predicted to become future blockbusters launched last year, four of which are predicted to be bringing in more $2bn in the US by 2024. As well as Trikafta, this includes two new arrivals for Abbvie: the psoriasis antibody Skyrizi and the Jak inhibitor Rinvoq for RA.

Pfizer's amyloidosis treatment Vyndaqel is also seen as having a hugely successful future, with 2024 sales of $2.5bn pencilled in. This therapy and Trikafta both treat rare diseases and are prime examples of the sort of products that biopharma is chasing right now: small, definable patient populations in which big price tags are accepted.

FDA approval count vs. 5th year US sales

Source: Evaluate® January 2020



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)
2017 – Ocrevus (Roche), Dupixent (Sanofi)
2018 – Biktarvy (Gilead), Epidiolex (GW Pharmaceuticals)
2019 – Vyndaqel (Pfizer), Skyrizi (AbbVie)

A more in-depth analysis of FDA approval data can be found here:

Rare diseases top another strong year for novel drug approvals

Big cap medtechs see out the decade in style

The good times continued to roll for big cap device makers last year. No group in this cohort – those with a market cap of $10bn or more – endured a share price fall over the year.

These businesses have been aided by the general market atmosphere. The indices covering US-listed medtech companies are up around 30% and, highly unusually, EU-listed healthcare groups seem to be equalling this performance.

Indices

Stock index	% change in 2019
Thomson Reuters Europe Healthcare (EU)	26%
Dow Jones U.S. Medical Equipment Index	31%
S&P Composite 1500 HealthCare Equipment & Supplies	27%

The big-cap medtech cohort includes only companies that obtain more than 40% of their revenues from the sale of diagnostic or therapeutic medical technology.

A sign of just how good 2019 was for the larger-scale device makers is that the worst-performing company still saw a share price rise of 12%. The last time this analysis showed across-the-board stock rises was two years ago. But the lowest rise that year was 7%, suggesting that 2019 was better still.

Large cap ($10bn+) medtech companies: top risers and fallers in 2019

Source: Evaluate® January 2020

	Share price 12-mth change	Market cap at Dec 31 ($bn)	Market cap 12-mth change ($bn)
Top 5 risers			
Insulet ($)	116%	10.6	5.9
Olympus (¥)*	100%	21.4	5.9
Dexcom ($)	83%	20.0	9.4
Straumann (SFr)	54%	15.2	5.3
Edwards Lifesciences ($)	52%	48.7	16.6
Top 3 worst performers			
Becton Dickinson ($)	12%	73.6	8.6
Varian Medical Systems ($)	15%	12.9	1.7
Siemens Healthineers (€)	17%	42.4	0.5

* Olympus carried out a 4:1 stock split in April.

Lower down the size scale, new products and strategic execution buoyed mid and small-cap medtechs, and no fewer than five mid-size medtech groups more than doubled in. But the mid-size cohort seems to be doing better than the smaller groups, perhaps pointing to the inherent volatility at this end of the market.

Other significant risers and fallers in 2019 (ranked on market cap)

Source: Evaluate® January 2020

	Share price 12-mth change	Market cap at Dec 31 ($bn)	Market cap 12-mth change ($bn)
Top 5 risers			
Novocure ($)	152%	7.8	4.7
Nevro ($)	202%	3.6	2.5
Natera ($)	141%	2.6	1.7
Sectra (SKr)	107%	1.5	0.8
EI En (€)	161%	0.7	0.4
Top 5 fallers			
Abiomed ($)	(48%)	7.7	(6.9)
ICU Medical ($)	(19%)	3.9	(0.8)
Merit Medical Systems ($)	(44%)	1.7	(1.3)
Inogen ($)	(45%)	1.5	(1.2)
Meridian Bioscience ($)	(50%)	0.4	(0.4)

While the mid-cap device companies tended to sink or swim owing to technological successes or failures, the smaller groups' shareholders appear motivated for the most part by financial performance. For those wishing to invest in device developers the big caps are still the safest bet – but the mid-cap range is where the greatest gains may be seen.

More in-depth analyses of medtech share price movements over 2019 can be found here:

Big cap medtechs see out the decade in style

2019 was all about execution for smaller device makers

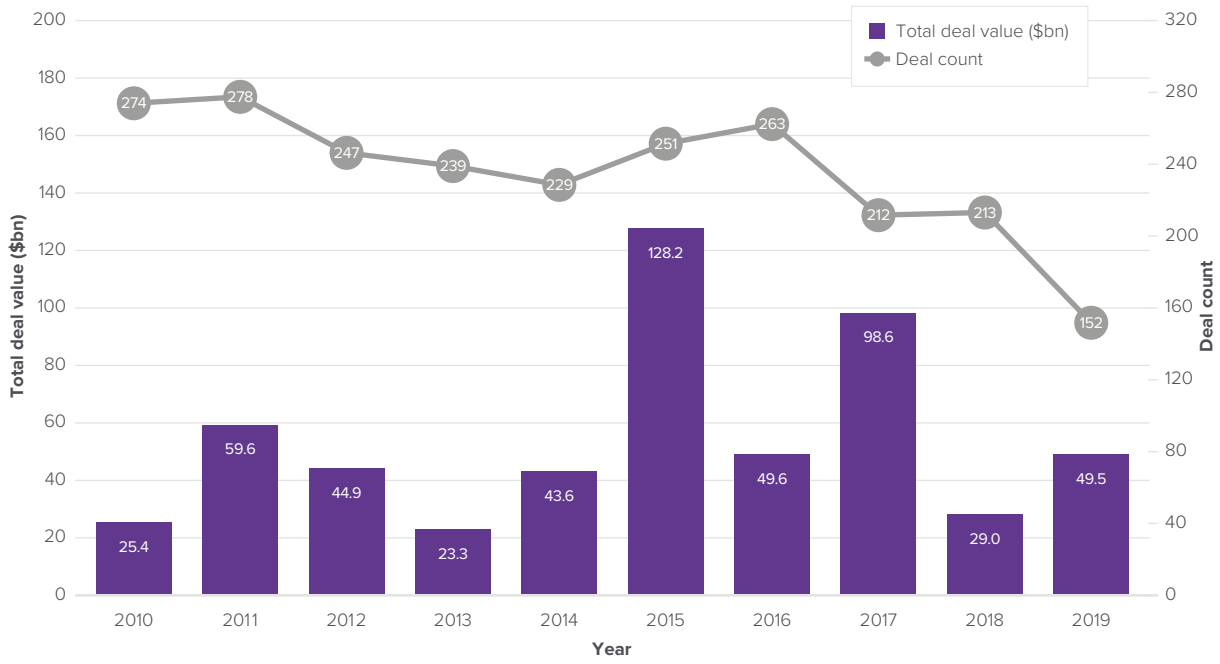
A thoroughly average year for medtech mergers

Despite last year seeing the completion of no fewer than 13 transactions worth more than $1bn, the medtech M&A landscape came nowhere near the heights reached in 2015 and 2017. Still, at $49.5bn, the total value of all the deals closed at least showed an increase from the previous year's low total.

The number of deals also shrunk – to the lowest annual figure for more than a decade. With just 152 mergers and acquisitions having closed last year the situation might soon become dire for small companies seeking a buyer. And the M&A climate has clouded over recently, with the FTC forcing Illumina and PacBio to call off their megadeal. 2020 could be quieter still.

Medtech M&As over the last decade – number and value of deals closed

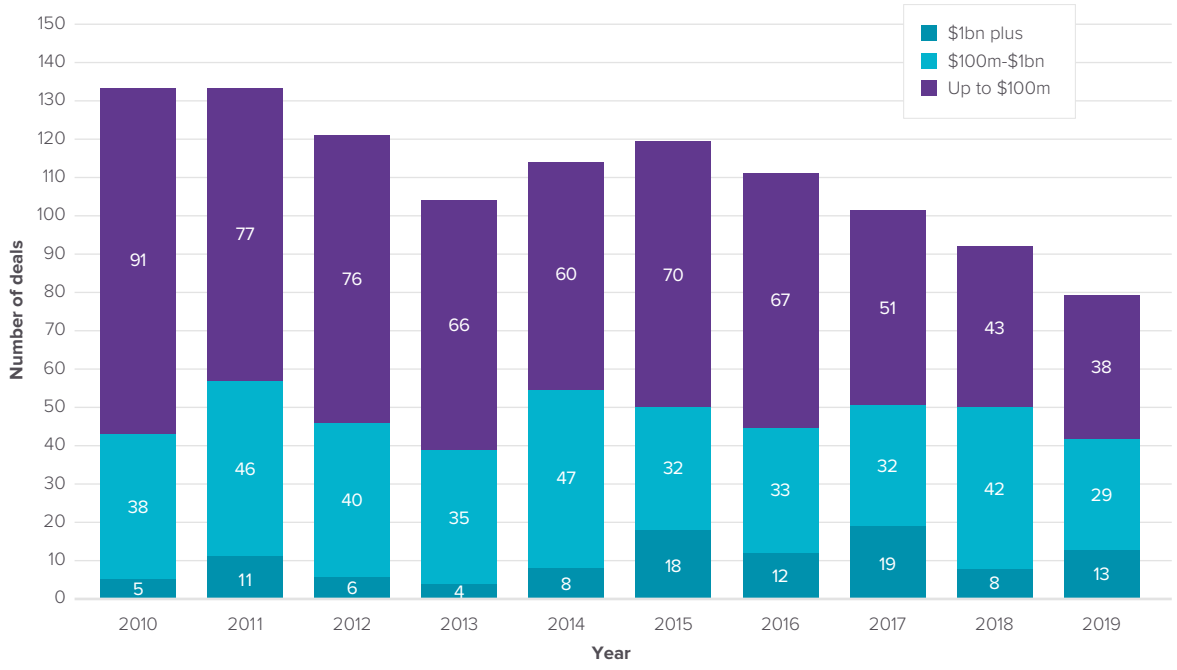
Source: Evaluate® January 2020



The strong stock market performance of medtech players over 2019 will have played its part here. Valuations are soaring, and many groups will now be prohibitively expensive to potential buyers. The consolidation of years past will also have had consequences for 2019's M&A scene. There are fewer exit opportunities simply because there are fewer companies around to buy.

Medtech M&As by size – number of deals closed over the last decade

Source: Evaluate® January 2020



Note: only includes deals with known value.

Deal-making activity is white-hot in a few areas, however. Robotic surgery companies are finally gearing up to compete with Intuitive Surgical, and many larger groups, eager to avoid being left behind, have bought in similar technologies.

Many of the very largest deals were focused on hospital-based technologies, with makers of orthopaedic implants, sterilisation products and IT systems being taken over. Perhaps the buyers here feel that there are efficiencies to be had that will allow them to make a success of this low-margin segment.

Top 10 deals closed in 2019

Source: Evaluate® January 2020

Completion date	Acquirer	Target	Value ($bn)	M&A focus
Oct 11	3M	Acelity	6.7	Wound management
Apr 1	Johnson & Johnson	Auris Health	5.8	Endoscopy; general & plastic surgery
Feb 11	Veritas Capital and Elliott Management	Athenahealth	5.7	General hospital & healthcare supply; healthcare IT
Aug 19	Boston Scientific	BTG	4.2	Cardiology; general & plastic surgery; neurology; radiology
Feb 22	Colfax	DJO Global	3.2	Orthopaedics; physical medicine
Apr 1	Fortive	Advanced Sterilization Products business of J&J	2.8	Endoscopy; general hospital & healthcare supply
Nov 8	Exact Sciences	Genomic Health	2.8	In vitro diagnostics
Feb 21	Fresenius Medical Care	Nxstage Medical	2.0	Blood; nephrology
Aug 26	Agilent Technologies	Biotek	1.2	In vitro diagnostics
Mar 31	Montagu Private Equity and Astorg	Nemera	1.2	Drug delivery

There is an argument to be made that 2020 could see an upswing in M&A. The markets might well be more skittish in the run-up to the US presidential election, depressing valuations and making acquisitions of listed groups likelier, though it should be remembered that medtech is generally less prey to wider market volatility than biopharma.

A more in-depth analysis of medtech M&A activity over 2019 can be found here:

A thoroughly average year for medtech mergers

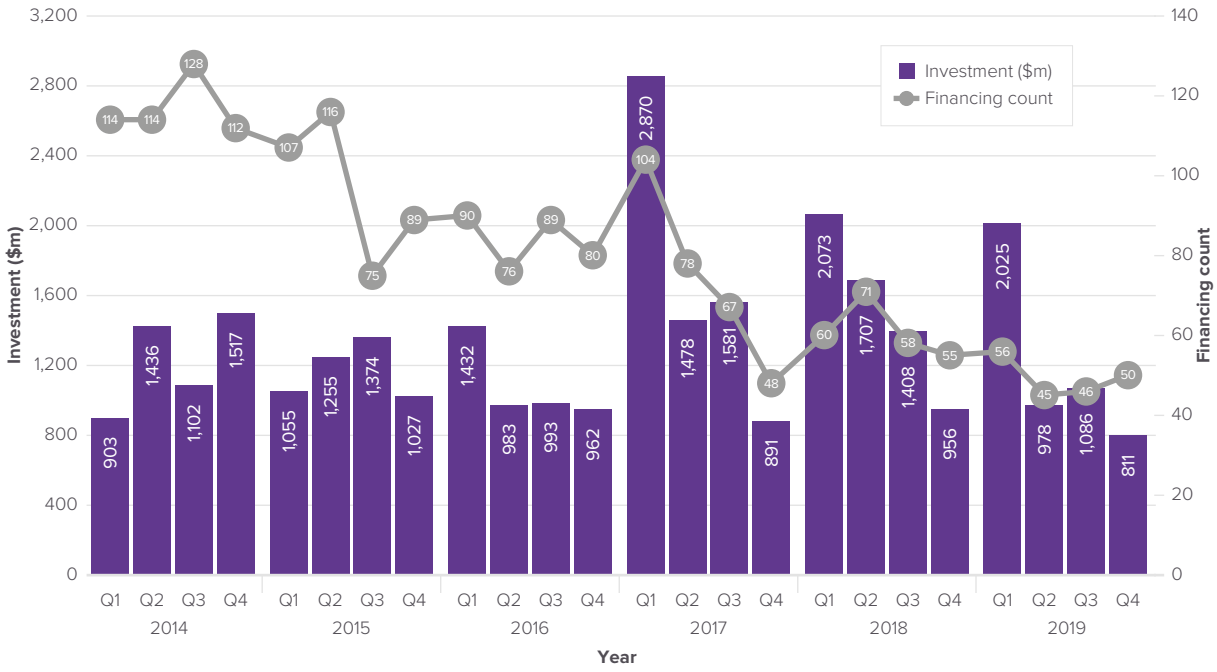
How low can medtech venture investment go?

Private medical device companies raised a respectable amount of venture cash in 2019 – just shy of $5bn – but an analysis of trends over the past decade shows a steady decline in the number of deals done each year.

That said, the top 10 deals of 2019 comprise only 40% of the cash that flowed into the sector; last year's leaderboard made up more than half of the total raised. Perhaps the climate for smaller, younger companies seeking growth capital might be improving, if only slowly.

Medtech VC investment, 2014-2019

Source: Evaluate® January 2020



Excluding Verily's monster $1bn round, the other $4bn raised in 2019 was doled out to just 195 companies, meaning that the average size of these rounds, $24.9m, has barely decreased from last year's bloated figure.

VCs still prefer to minimise their risk, and there are several ways of doing this. One is to build huge syndicates. Another is to wait until a target company has gained not only approval for its technology but reimbursement too.

Top 10 VC rounds of 2019

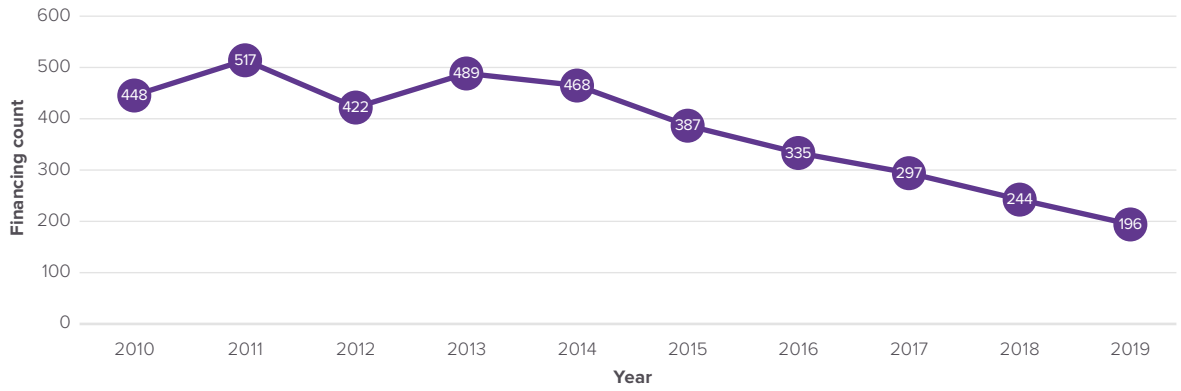
Source: Evaluate® January 2020

Date	Round	Company	Investment ($m)	Focus
Jan 3	Undisclosed	Verily Life Sciences	1,000	Diabetic care; ophthalmics; patient monitoring
Sep 17	Series C	CMR Surgical	240	General & plastic surgery
Jul 24	Series B	Freenome	160	In vitro diagnostics
May 19	Series A	Thrive Earlier Detection	110	In vitro diagnostics
Jun 20	Series D	Acutus Medical	100	Cardiology
Dec 3	Series D	Impulse Dynamics	80	Cardiology
Feb 11	Series E	Nuvaira	79	Anaesthesia & respiratory
Jan 3	Series D	Ablative Solutions	77	Cardiology
Jan 4	Undisclosed	Sophia Genetics	77	Healthcare IT
Jun 28	Undisclosed	Saluda Medical	75	Neurology

The top 10 may be sucking up a smaller proportion of the total funding than in years past, but there is no denying the declining number of deals done each year. A look at this trend over the 2010s shows a peak in 2013, with 489 VC rounds raised by device makers. This number has shrunk every year since.

A decade of decline – annual medtech VC deals

Source: Evaluate® January 2020



If this trend continues at the same rate of decline the situation will become extremely parlous by 2022 or 2023.

A more in-depth analysis of medtech VC activity over 2019 can be found here:

How low can medtech venture investment go?

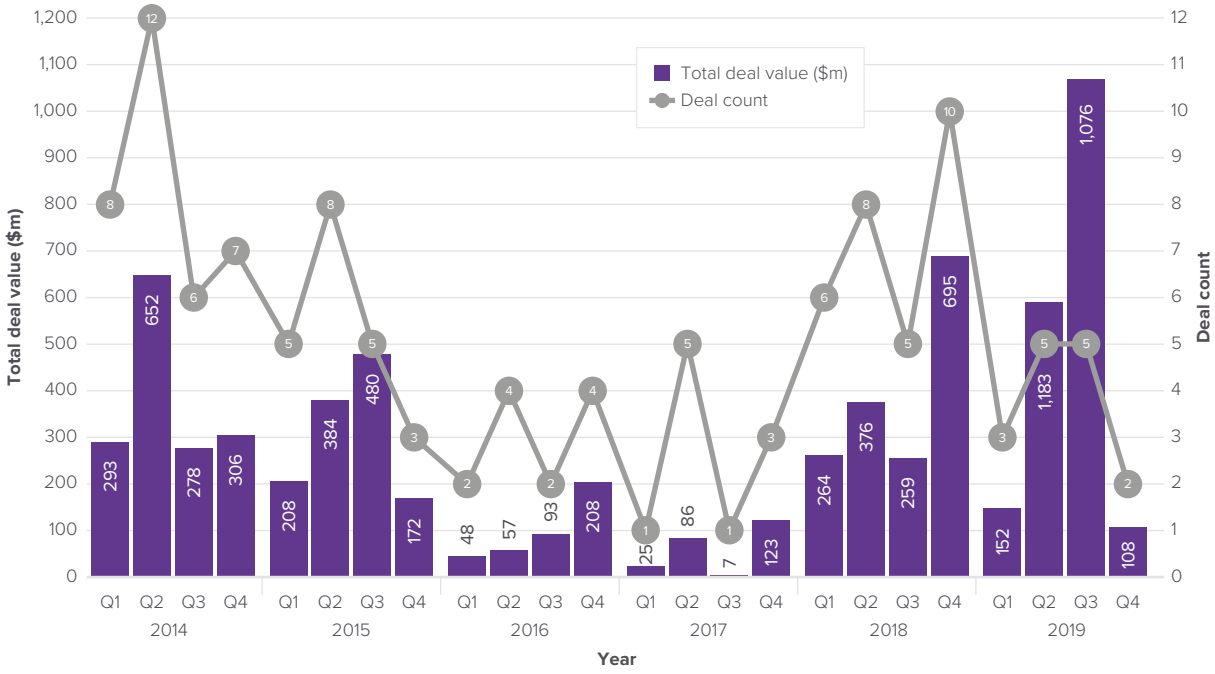
Poor fourth quarter mars strong year for medtech floats

The device sector enjoyed a mid-year IPO bonanza, and the amount raised by the 15 groups that went public in 2019 is impressive, at $2.5bn. After floating, however, the class of 2019 had a torrid time. Seven of the 13 listing companies have seen their valuations wither, and the dental group Smiledirectclub, which conducted 2019's largest flotation, has been the worst performer of all.

The middle of 2019 was astonishingly strong when it comes to the sheer amount of money raised on the public markets by medical device companies. The graph below excludes the multibillion-dollar IPOs of Convatec and Siemens Healthineers in 2016 and 2018 respectively, as well as Smiledirectclub's $1.3bn offering in September, so as to give a fairer picture of underlying trends.

Medtech IPOs, 2014-2019

Source: Evaluate® January 2020



Broadly those companies that went out on US exchanges did better than those in the rest of the world, and only three of the 10 US-based offerings lost money.

Top 10 medtech IPOs of 2019

Source: Evaluate® January 2020

Date	Company	Focus	Amount raised ($m)	Discount/ premium	Share price change to year end
Sep 12	Smiledirectclub	Dental	1,300	12%	(62%)
Sep 18	Envista*	Dental	589	(2%)	35%
Apr 4	Medacta Group**	Neurology; orthopaedics	588	8%	(30%)
Jul 26	Livongo	Diabetic care; patient monitoring	355	30%	(11%)
Jun 27	Adaptive Biotechnologies	In vitro diagnostics	345	25%	50%
Apr 4	Silk Road Medical	Cardiology; neurology	120	25%	25%
Mar 7	Shockwave Medical	Cardiology	111	13%	158%
May 2	Transmedics	Surgery	105	0%	19%
Jul 26	Castle Biosciences	In vitro diagnostics	74	7%	115%
Sep 20	Exagen	In vitro diagnostics	58	(7%)	81%

* IPO on the NYSE. ** IPO on Six Swiss exchange. All others are Nasdaq.

Overall, the 2019 data show an obvious, and potentially worrying, pattern. Both the top 10 table and the quarterly analysis show a definite shrinking of investor appetite going into the third quarter. The fourth quarter's two offerings were small – less than $60m – but still had to be priced below their initially proposed ranges to get away, and both fell again once trading commenced. Almost all the groups that listed in spring and summer were able to charge a premium.

If the window of opportunity is swinging shut, 2020 could be a difficult year for medtechs in search of capital.

A more in-depth analysis of medtech IPO activity over 2019 can be found here:

Poor fourth quarter mars strong year for medtech floats

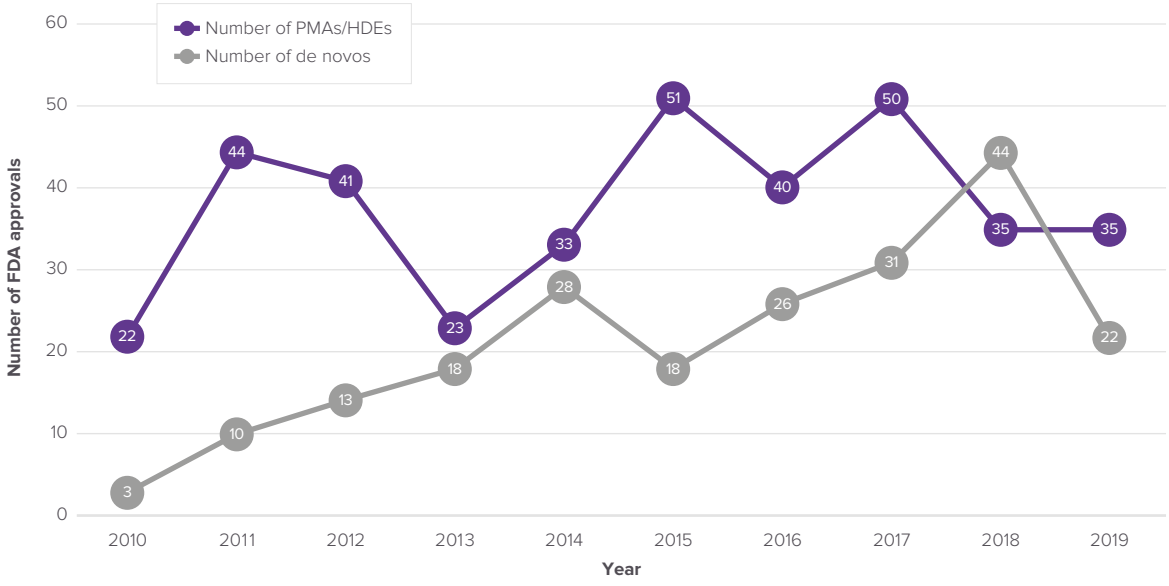
A quiet six months for device approvals

Increased scrutiny of high risk devices following several well-publicised cases of patient harm could be one possible reason behind the sharp drop in the rate of FDA approvals of these types of product in the second half of 2019, as opposed to the first. But this does not explain the equally precipitous fall in low-risk device clearances, a marked contrast to the figures in 2018.

At the half-year point, 23 innovative high-risk devices had been approved, but the second half of last year saw only 12 premarket approvals and humanitarian device exemptions – the regulatory paths taken by high-risk medical technologies. At 35, across all of 2019 the total approvals for this class of device was the same as in 2018.

Medtech approvals over the last decade

Source: Evaluate® January 2020



The most obvious factor that might have acted as a brake on the agency's activity was the furore surrounding the Implant Files investigation in November 2018. This highlighted several cases of neglectfully designed and manufactured medical devices, including pacemakers, contraceptive implants and surgical meshes.

This might have prompted the agency to be more circumspect when considering whether to approve high-risk products or companies more cautious in submitting approval requests.

2019's PMAs and HDEs by therapy area

Source: Evaluate® January 2020

EvaluateMedTech classification	No of PMAs & HDEs	Average approval time (mths)
Cardiology	12	13.0
In vitro diagnostics	7	7.2
Orthopaedics	7	18.2
Neurology	3	10.8
Urology	2	8.7
Ear, nose & throat	1	5.9
Obstetrics & gynaecology	1	7.5
Gastroenterology	1	9.2
Anaesthesia & respiratory	1	11.5
Overall	**35**	**12.0**

The big drop in de novo clearances is harder to explain. Most implanted devices cannot use this pathway so the Implant Files could only have had a minimal effect.

2019's de novos by therapy area

Source: Evaluate® January 2020

EvaluateMedTech classification	Number of de novos	Average approval time (mths)
In vitro diagnostics	7	9.8
Neurology	5	10.5
Gastroenterology	2	8.4
Diabetic care	2	4.3
Anaesthesia & Respiratory	1	18.8
Wound Management	1	13.2
Orthopaedics	1	12.5
Endoscopy	1	12.0
Blood	1	11.3
Cardiology	1	10.3
Overall	**22**	**10.2**

A silver lining to this data is that though there are fewer approvals, those that have been granted came through relatively swiftly. Last year the FDA took an average of 15 months to approve high-risk novel products and 13 months for low-risk; both of these figures have fallen.

A more in-depth analysis of medtech approval trends over 2019 can be found here:

A quiet six months for device approvals

Outlook for 2020

The main driver of caution heading into 2020 was the potential fallout from US presidential election campaigns, and while the biopharma sector has avoided too much scrutiny so far, this could easily change. The identity of the final Democratic candidate, and their chance of beating the incumbent, represent important unknowns for drug developers and their investors.

Outside of this, many of the trends that buoyed pharma and biotech companies in 2019 look set to continue. The FDA in particular shows no sign of deviating from its lenient ways, and a major test of this stance, the review of Biogen's Alzheimer's disease project aducanumab, is one of the biggest events facing the sector in the coming months. The outcome of this review will help set sentiment for the remainder of the year.

The drop in device approvals in the second half of 2019 is a worry for that sector. With a rubber-stamp for regulators increasingly regarded as a validation of a company's technology, the shortfall could mean fewer VC rounds, acquisitions and IPOs in the coming year.

Fortunately there is reason to suspect FDA activity might ramp up in 2020. A number of larger medtechs, Medtronic among them, are aiming to bring a suite of new products to market in 2020, so next year's device approval figures could be very different.

For signs of how 2020 might go, investors will also be watching how the M&A markets develop. With several larger pharma groups under pressure to restock pipelines, there should be no shortage of active deal makers out there.

But the first quarter has been remarkably quiet – perhaps understandable after a busy end to 2019 – and nervousness will increase should deal-making activity not start to pick up soon. With only one medtech megamerger yet to close there is no indication that we are heading into bumper year for medtech M&A, either.

These factors could weigh against the medtech VC climate staying strong. That said, there are early signs that then venture financing landscape in 2020 might ape that of 2019. Certainly the first quarter is off to a strong start, with four VC rounds topping $80m in the first five weeks of the year. At least one of these might well make the top 10 of 2020; with luck, there will be smaller sums for start-up companies, too.

An important question for both medtech and biopharma is whether the well-funded smaller ends of these sectors can be persuaded to sell up at acceptable levels.

Unless stated, all data are sourced to Evaluate and were accessed in January 2020

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