Biopharma and Medtech Review 2021

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Evaluate Vantage

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Foreword

Welcome to *Evaluate Vantage's* 2021 review. This report provides a roundup of our end of year data stories, which dig into the trends driving business development decisions and financing deals across the pharmaceutical, biotechnology and medtech sectors.

These industries certainly generated mixed signals last year. Biotech indices deteriorated markedly in the US and IPOs slowed, but the venture industry continued to deploy substantial amounts of capital. Developers that capitalised on the pandemic reaped huge rewards and solid investor support, but many others had to work extra hard to attract attention.

Contradictions were on show in the medtech arena too. The markets here were more buoyant than for pharma though, unusually, among the bigger groups those listed in the US had a harder time than those in Europe. Huge amounts were raised by device makers going public, almost entirely in the US – but these companies too had a tricky time once on the market.

Indeed it was perhaps a good year to stay private, with venture investors disbursing more cash than ever before.

On the M&A front the pharma sector failed to provide the sort of deals that set the sector alight. Drug developers were still active dealmakers, or course, but seemed to prefer smaller transactions when it came to buyouts.

The opposite was true in medtech, with big acquisitions ticking over nicely but a conspicuous drop in the number of smaller deals. In fact, the average price paid for M&A in 2021 was higher than ever, at $1.12bn.

At least the FDA remained friendly, with 58 novel therapeutics approved in 2021. Seven of last year's new arrivals are forecast to become blockbusters within the next five years, *Evaluate Pharma's* consensus data show.

But the pandemic is still being felt in the regulatory world. Several high-profile drugs were delayed due to travel restrictions, while diagnostic device approvals dipped because the agency had to prioritise Covid-related products.

Evaluate Vantage will keep monitoring these trends in 2022, but for a closer look at what investors and others are thinking about the coming year, **download our free preview here**.

For the original articles that make up this Review of 2021 report, check out the **data section on our website**.

Key Takeaways

- **58 novel therapeutics approved** (three-year high) but Covid delayed more
- **$14.2bn raised over 98 IPOs** but biotech indices deteriorated significantly in the US
- **Private companies hauled in $28.5bn** in 2021
- M&A in biopharma didn't set the world alight – but **medtech did well, with an average price at a record $1.12bn**

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Big beasts drive biopharma valuations higher in 2021

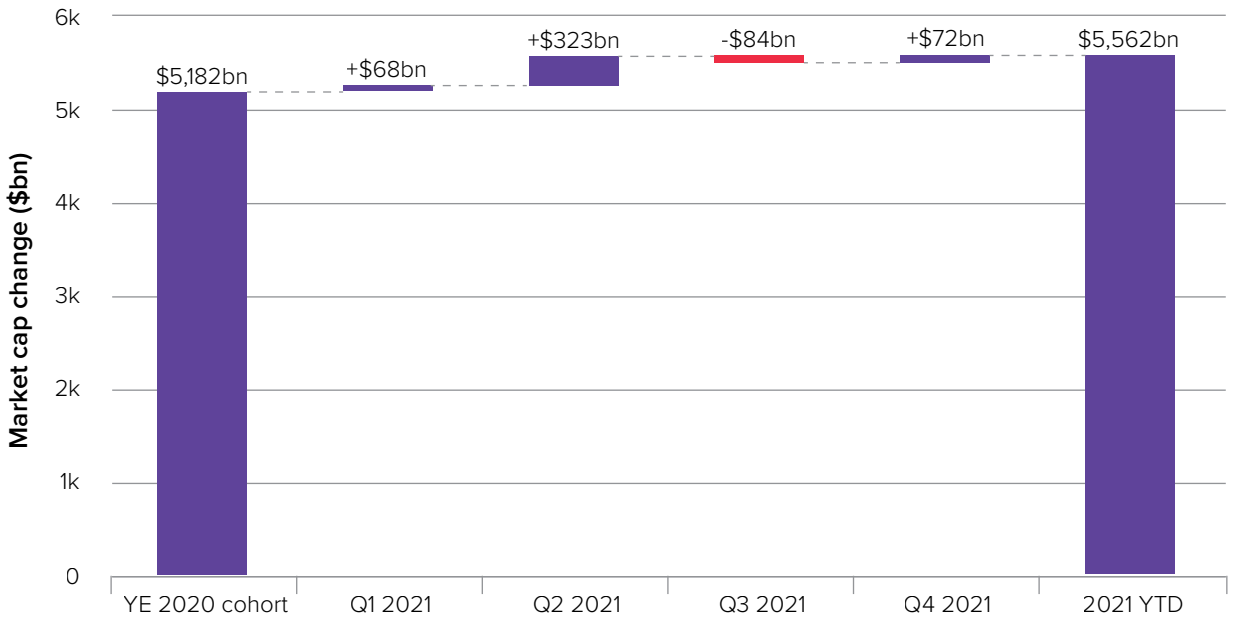
The biopharma industry saw dramatic divergences in fortunes on the stock market last year. A handful of larger developers, many propelled by Covid-19 windfalls, enjoyed huge valuation bumps, while the smaller end of the sector witnessed a painful desertion of investor support.

Overall, pharma and biotech stocks did manage to gain in value in 2021, according to *Evaluate Vantage's* global overview of share price performances. But advances were much harder won as the year progressed, while the final quarter's last gasp had a lot to do with Pfizer's massive $90bn market cap bounce.

> Pharma and biotech stocks did gain value in 2021 – but those advances were hard won.

At the start of 2021 *Evaluate Vantage* started tracking 701 globally-listed, pure-play drug developers, information on which are collected by *Evaluate Pharma*. These groups added $380bn in market cap over the year, the chart below shows, thanks to a very strong second quarter; third quarter losses were not recovered in the final months of the year.

The shifting valuation of global drugmakers



Source: Evaluate.

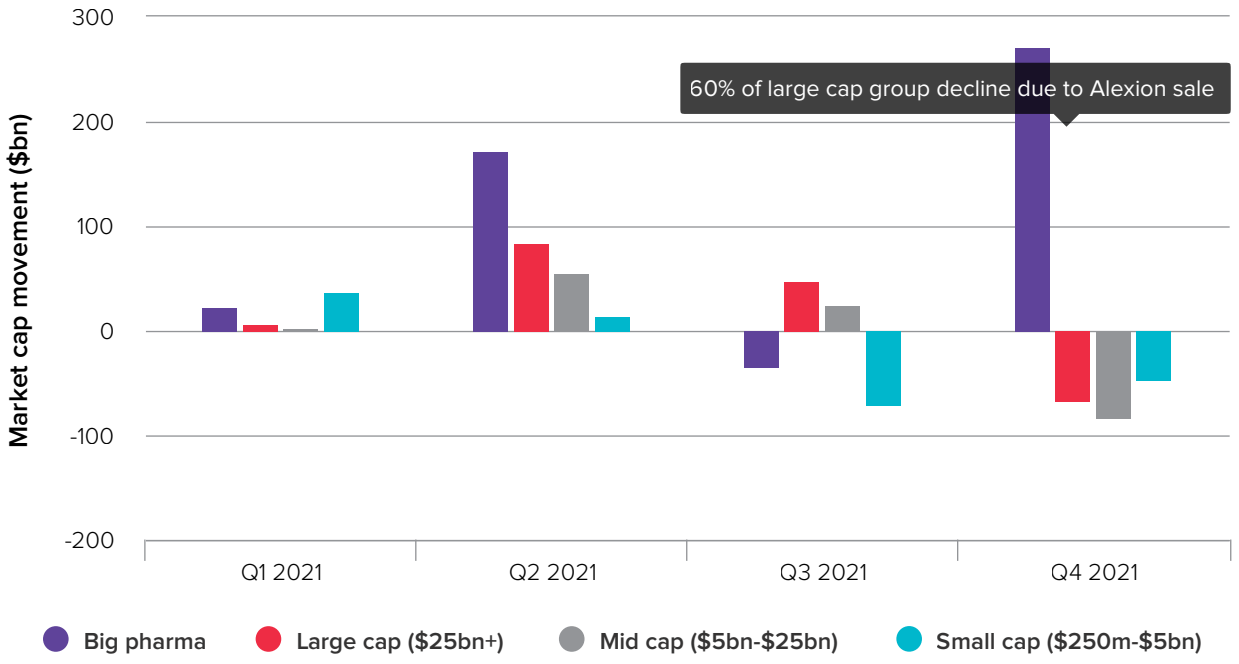
Any analysis based on market capitalisation will be heavily influenced by the big beasts of the sector, of course, so the trend above is largely driven by big pharma companies, as the more detailed charts below show. These were constructed by splitting the 701-strong universe into four cohorts based on market capitalisation at the start of the year; companies remained in the same group throughout the year.

The world's 11 big pharma firms had a very strong end to the year. Only Astrazeneca dipped in value in the fourth quarter, although it should be remembered that this stock hit a record high in November after an incredibly strong run.

Pandemic success stories produced gainers elsewhere, with Moderna a stand-out example. A serious pullback in the fourth quarter knocked more than $50bn from the RNA researcher's market cap, but the company still managed to end the year worth more than $100bn. For context, only 16 drug developers were trading above that threshold at the end of 2021.

Moderna's deflation had a lot to do with the large cap group's fourth-quarter decline. So too did the loss of Alexion, whose takeover by Astrazeneca erased $40bn in market cap from the cohort, making the year-end reverse appear more severe than it really was.

Absolute market cap gains and losses, by size bracket



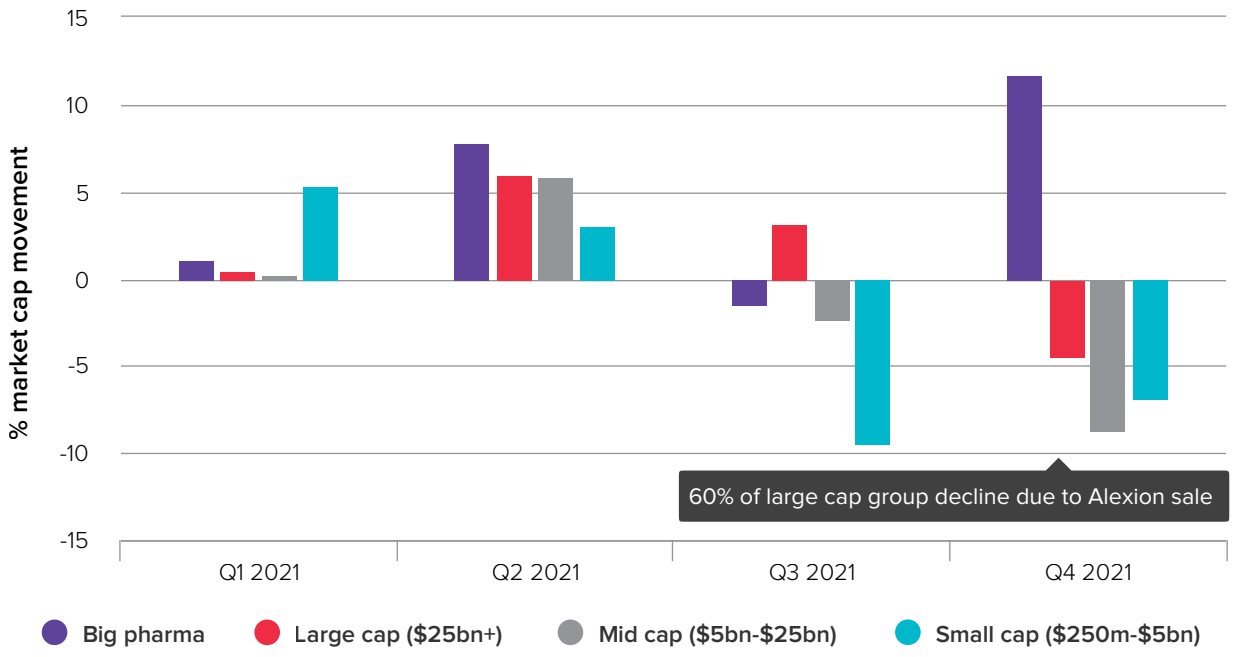
Source: Evaluate.

Asian pharma groups also dealt the large caps a hit. Big decliners over the fourth quarter and the year included Chugai, whose questionable ability to replace some of its big sales generators is causing concern.

Finally, among the mid and small caps, the real pain began in the second half of 2021, when losses really start to rack up in both absolute and percentage terms. Two-thirds of the stocks in these two groups ended 2021 in negative territory.

As always, clinical setbacks were responsible for big individual drops, but sentiment towards US biotech stocks deteriorated rapidly as 2021 progressed, causing broader declines.

Percentage market cap gains and losses, by size bracket



Source: Evaluate.

Biopharma's stock market winners of 2021 revealed

Covid's ability to infect share prices remained intact last year: the pandemic spurred some of the best individual performances among biopharma stocks, and was also responsible for several fallers. Indeed, a few names appeared on the other side of **the leader boards compared with this time last year**.

For example, the bubble burst for Shin Poong, the South Korean developer that had soared in 2020 on hopes that its repurposed malaria drug might play a big role in the pandemic. On the other hand, the big names in Covid vaccines were the clear 2021 winners, while Lilly deserves a mention for becoming the best-performing big pharma stock for the second year in the row.

Huge expectations for tirzepatide, a novel diabetes and obesity project, and the Alzheimer's contender donanemab drove Lilly's valuation to a record high. The group's market cap has doubled in the past two years, a remarkable advance for a company of this size.

Novo Nordisk has also had a spectacular run. Its stock also recently hit record highs after doubling in two years, thanks to the very successful launch of its new obesity drug, Wegovy. Elsewhere, Biohaven and Horizon's successful transitions to commercial-stage developers continue to attract investors.

Biopharma's biggest stock market winners in 2021

Company	2021 share price change	2021 market cap change ($bn)	Market cap at Dec 30. 2021 ($bn)
Big pharma			
Lilly	64%	103	264
Pfizer	60%	127	331
Abbvie	26%	50	239
Large cap ($25bn+ market cap)			
Moderna	149%	62	103
Merck KGaA	59%	42	113
Novo Nordisk	57%	92	255
Mid cap ($5-25bn market cap)			
Biontech	216%	42.9	62.5
Biohaven	61%	3.9	9.0
Horizon	51%	8.3	24.4
Small cap ($250m-5bn market cap)			
Prothena	311%	1.8	2.3
Bicycle Therapeutics	239%	1.4	1.8
Anavex Life Sciences	221%	1.0	1.3
Arising from the nano caps (sub $250m market cap)			
Bellus Health	180%	0.2	0.8
Bonus Biogroup	160%	0.1	0.5
Evolus	94%	0.1	0.4

Source: Evaluate Pharma. Note: companies were assigned these groupings based on year-end 2020 market cap.

Among the small caps, Prothena was a beneficiary of progress in Alzheimer's disease, although it has other irons in the fire; Anavex also probably benefited from rising expectations of progress in the neurological field. Bicycle operates in the red-hot targeted oncology space, where its work has shown early promise.

Finally, nano caps that saw big advances, sufficient for them to join the small caps in 2022's analysis, included Bellus Health. The company's stock more than doubled towards the end of 2021 after a successful phase 2b trial revived hopes for the company's chronic cough project, BLU-5937.

As for the fallers, among the big pharma names these single-digit retreats are unlikely to cause long-term investors too much concern; however, it is certainly true that all three companies are under pressure to replenish their late-stage pipelines.

The large-cap cohort is dominated by Asian developers, many of which struggled in 2021, outside this top three. Celltrion was one of 2020's biggest risers, having also received something of a Covid boost after developing an antibody therapy, but sentiment turned last year with investors unconvinced about demand for that product and its wider biosimilar portfolio.

Among the smaller developers it is, as always, clinical blow-ups behind the catastrophic declines. Both **Allakos** and **Bridgebio** crashed out in the final days of 2021, providing investors with salient reminders of the risks of drug development.

Biopharma's biggest stock market losers in 2021

Company	2021 share price change	2021 market cap change ($bn)	Market cap at Dec 30. 2021 ($bn)
Big pharma			
Novartis	-7%	-19	196
Merck & Co	-6%	-13	194
Bristol Myers Squibb	1%	-2	138
Large cap ($25bn+ market cap)			
Jiangsu Hengrui	-49%	-31	57
Celltrion	-45%	-19	23
Chugai	-32%	-33	55
Mid cap ($5-25bn market cap)			
Allakos	-93%	-6.8	0.5
Bridgebio	-77%	-6.3	2.5
Shin Poong	-74%	-4.3	1.4
Small cap ($250m-5bn market cap)			
Oncopeptides	-95%	-1.2	0.1
Sigilon Therapeutics	-94%	-1.3	0.1
Forte Biosciences	-94%	-0.4	0.0

Source: Evaluate Pharma. Note: companies were assigned these groupings based on year-end 2020 market cap.

This analysis was constructed by tracking pure-play drug developers, listed globally, with a market cap in excess of $250m at the start of 2021. Companies were split into four cohorts and remained in the same group throughout the year. The 11 companies that comprise the big pharma group are: Johnson & Johnson, Roche, Pfizer, Eli Lilly, Abbvie, Novartis, Merck & Co, Astrazeneca, Bristol Myers Squibb, Sanofi and Glaxosmithkline.

More detailed analyses of these data and Evaluate Vantage's wider coverage of share price performances can be found on our website here.

After a record year, where next for biopharma flotations?

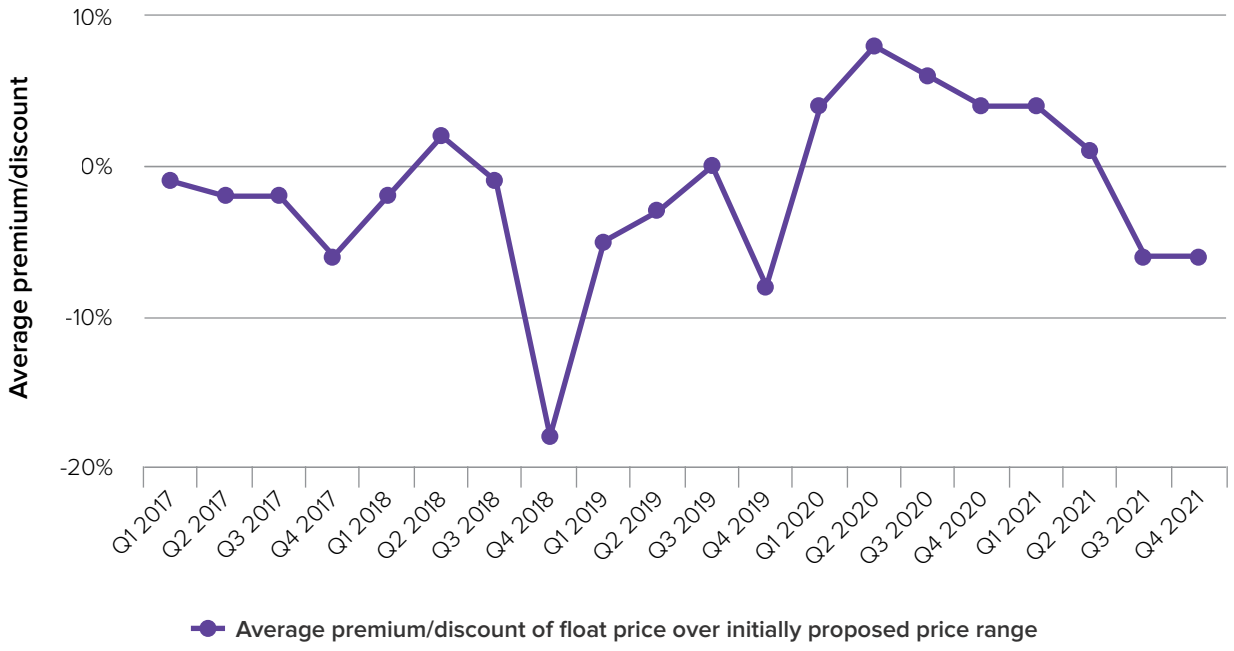
The pace of biopharma IPOs might have slowed over the course of 2021 but on many measures the year was unprecedented. Those record-setting days are over, however, with many predicting further retrenchment in 2022.

The depth of any slowdown is the big unknown, and the signs so far are mixed. Impressively, four developers floated in the opening days of the year, three of which managed to upsize their deals, while a couple more groups are sitting in the queue. The other side to this story is weak demand for newly floated biotech stocks, and a couple of recently pulled IPOs.

This suggests that while the window of opportunity is narrowing, it has not completely shut. Considering the parlous state of US biotech stocks, which have endured a 10-month bear market that shows no sign of bottoming out, this is in many ways remarkable.

An explanation can be found in **well-stocked venture and crossover funds**, which are able support portfolio companies throughout, and after, the IPO process. But with conditions getting tougher, private groups that manage to get away successfully this year will surely represent the cream of the venture-backed crop.

Tracking demand via bumps and haircuts



Source: Evaluate.

The prospects will be much dimmer for developers that do not fit into that category, and indeed there is much evidence to suggest this is already the case. Signs of weakening of demand started to emerge in mid-2021 when, as the graph above suggests, it became harder for bankers to extract any uplift to an initially proposed valuation.

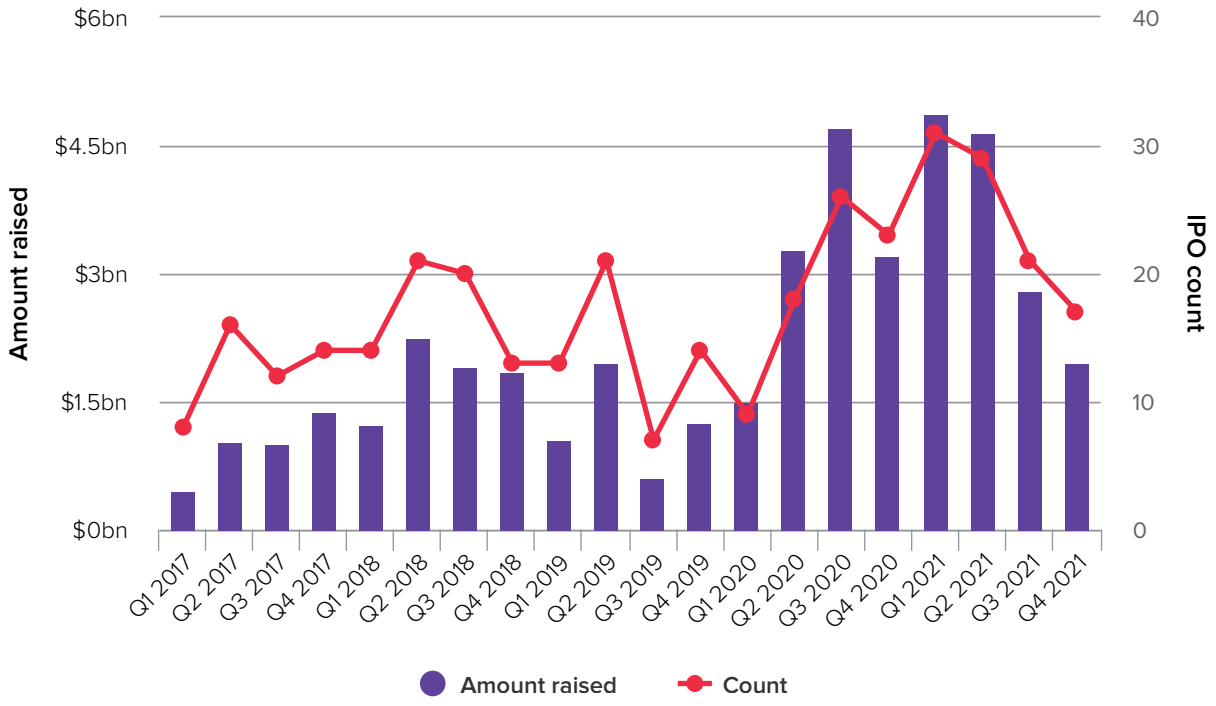
> Did the flood of early stage and, in some cases, low-quality new issues take the steam out of the biotech market?

It is also worth noting that almost 80% of last year's new issues were trading below their float price by the end of 2021. Some have already seen huge declines, with 35% losing more than half of their value. It is also true, however, that broader market conditions have been terrible and small caps have borne the brunt of this, as the previous section discussed.

None of this will make for comforting reading for those companies still hoping to test the public market waters. But it is also true that the final quarter of 2021 was far from a disaster, generating respectable stats when looking over the past five years.

This chart below illustrates the sheer size of 2021. On almost every metric the year set a new record, from the $14.2bn raised over 98 IPOs, to the number of deals that banked more than $100m: 62, according to *Evaluate Pharma*.

Biotech IPOs by quarter on Western exchanges



Source: Evaluate.

This is a performance unlikely to be matched in 2022, though that might not be a bad thing. Many blame the flood of early-stage and, in some cases, low-quality new issues for taking the steam out of the biotech market more generally. Even some venture capitalists will concede that a slowdown would not be all bad.

Biopharma watchers will be keen to find out whether this year's early rush continues at pace, or quickly fizzles out.

More detailed analyses of these data and Evaluate Vantage's wider coverage of IPO trends can be found on our website here.

In 2021 it paid to stay private when the chips were down

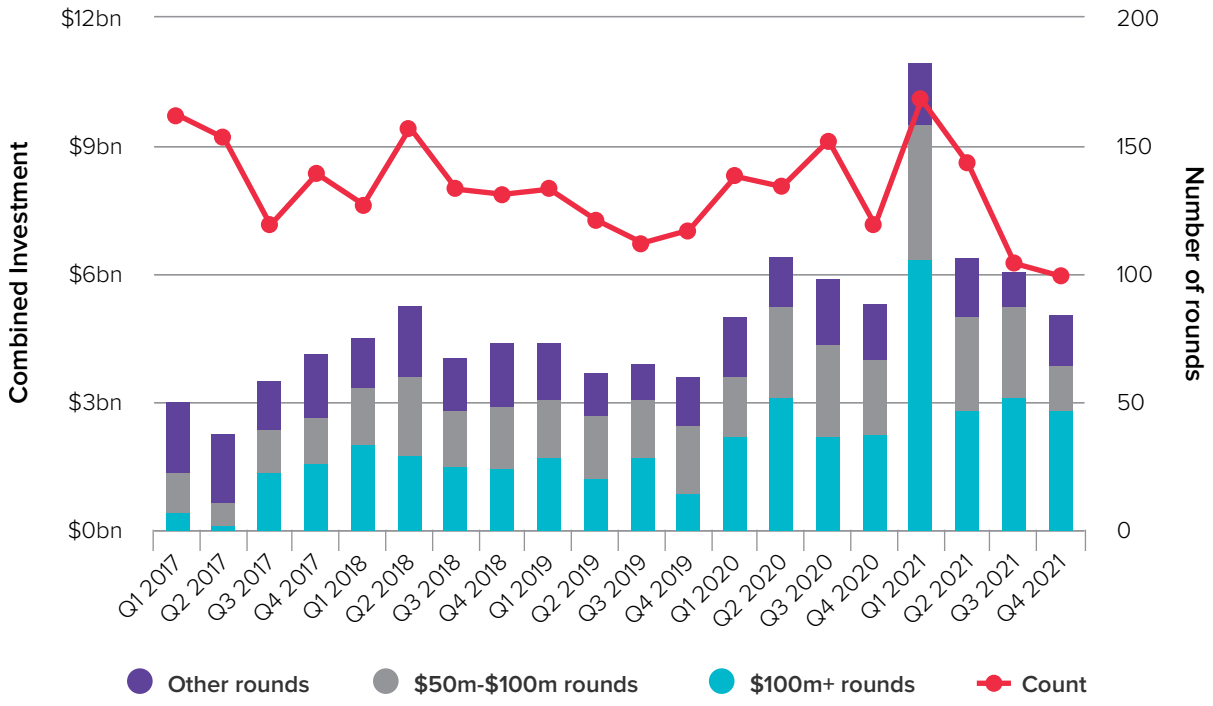
For biotech in 2021 it paid to be private. While waning public investor sentiment made the year a minor disaster for listed companies, closely held groups enjoyed their most successful 12 months ever, with secured venture capital eclipsing 2020's then record-breaking total by 26%.

True, the data are not wholly positive: 2021 was driven by a massive first quarter, after which VC financing fell, and the absolute number of deals continued the broad downward trend of the past few years. As such it was a handful of gigantic rounds, including a $700m series C by a Chinese group, that secured 2021's place in the record books.

But it says something that this round, raised by Abogen Biosciences largely to finance development of a thermostable mRNA Covid-19 vaccine, came in an otherwise lacklustre third quarter. This period overall was on a par with 2020's third quarter, and its $6.0bn of VC financing was barely half that seen in the first three months of 2021.

> Private companies hauled in a whopping $28.5bn of cash.

Quarterly biopharma VC rounds



Source: Evaluate.

Over the year private companies hauled in $28.5bn of cash, with Abogen accounting for $1bn of this annual total. Its $700m series C, led by seven investors including Singapore's state investment firm Temasek Holdings, was the biggest single VC raise of the year; it was followed in the fourth quarter by a series "C+", which amounted to another $300m.

Other notable fourth-quarter VC rounds included a $500m series A by Neumora, a US biotech focusing on neuroscience, whose raise was the joint third-biggest of 2021.

That said, 2021's VC total will most likely be remembered for a record-breaking first quarter, which included raises by the cell therapy group Elevatebio and by EQRX, a company seeking to shake up oncology drug pricing.

Annual biopharma venture investments

Year	Investment ($bn)	Financing count	Avg per financing ($m)	No of rounds ≥$50m	No of rounds ≥$100m
2021	28.45	514	55.56	216	93
2020	22.56	543	42.41	173	63
2019	15.65	483	33.58	125	37
2018	18.18	548	34.83	127	36
2017	12.89	573	24.5	73	16

Source: Evaluate Pharma.

However much the public markets struggled in 2021, the hope emerging from the year's VC data is that many financiers see a turnaround sooner rather than later. The possibility of public listing remains key to underpinning a company's valuation when it is seeking private funds.

EQRX is a case in point. Though it is by no means clear whether competing on price in oncology is a realistic strategy, the group is now going public, albeit by means of a Spac, in a $1.8bn deal.

2021's biggest biotech venture rounds

Company	Country	Investment ($m)	Financing round
The top five of Q4 2021...			
Neumora	US	500	Series A
Sotio	Czech Republic	315.9	Series undisclosed
Abogen Biosciences	China	300	Series C+
Acelyrin	US	250	Series B
Cardurion Pharma	US	219.7	Series undisclosed
...and the best of 2021 overall			
Abogen Biosciences	China	700	Series C
Elevatebio	US	525	Series C
EQRX	US	500	Series B
Neumora	US	500	Series A
Biosplice	US	438	Series A

Source: Evaluate Pharma.

More detailed analyses of these data and Evaluate Vantage's wider coverage of venture financing trends can be found on our website here.

Biotech investors pray for a M&A miracle

Last year failed to deliver much fizz on the M&A front, though the final months of the year raised hopes for a pick-up in activity. Unfortunately, the week of the JP Morgan Healthcare conference, a favourite time for biopharma companies to unveil their latest moves, was bereft of big-ticket buyouts.

True, a string of smaller transactions did emerge, and few would dispute that the sector remains an active deal-making space. But with US biotech stocks languishing investors are desperate for sentiment to improve. A clear signal that the large end of the sector is putting serous money to work could help trigger an upturn.

The problem is that large developers seem to prefer small bolt-ons and licensing deals, a trend that EY also highlighted in its annual review of biopharma spending. According to *Evaluate Pharma* the two biggest company takeouts in 2021 barely breached $10bn. In this analysis, *Evaluate Vantage* considers only deals between pure-play drugmakers, and sorts the data by announcement data, rather than when transactions officially close.

Biggest biopharma M&A deals announced in 2021

Acquirer	Target	Status	Value
CSL	Vifor Pharma Group	Open	$11.7bn
Merck & Co	Acceleron Pharma	Closed	$11.5bn
Jazz	GW Pharmaceuticals	Closed	$7.2bn
Pfizer	Arena Pharmaceuticals	Open	$6.7bn
Novo Nordisk	Dicerna Pharmaceuticals	Closed	$3.3bn

Source: Evaluate Pharma.

The sector's last mega-buyout was Astrazeneca's $39bn swoop on Alexion, which was announced in December 2020. Deals of that size are infrequent, of course, but based on timing alone biopharma is probably due another big one.

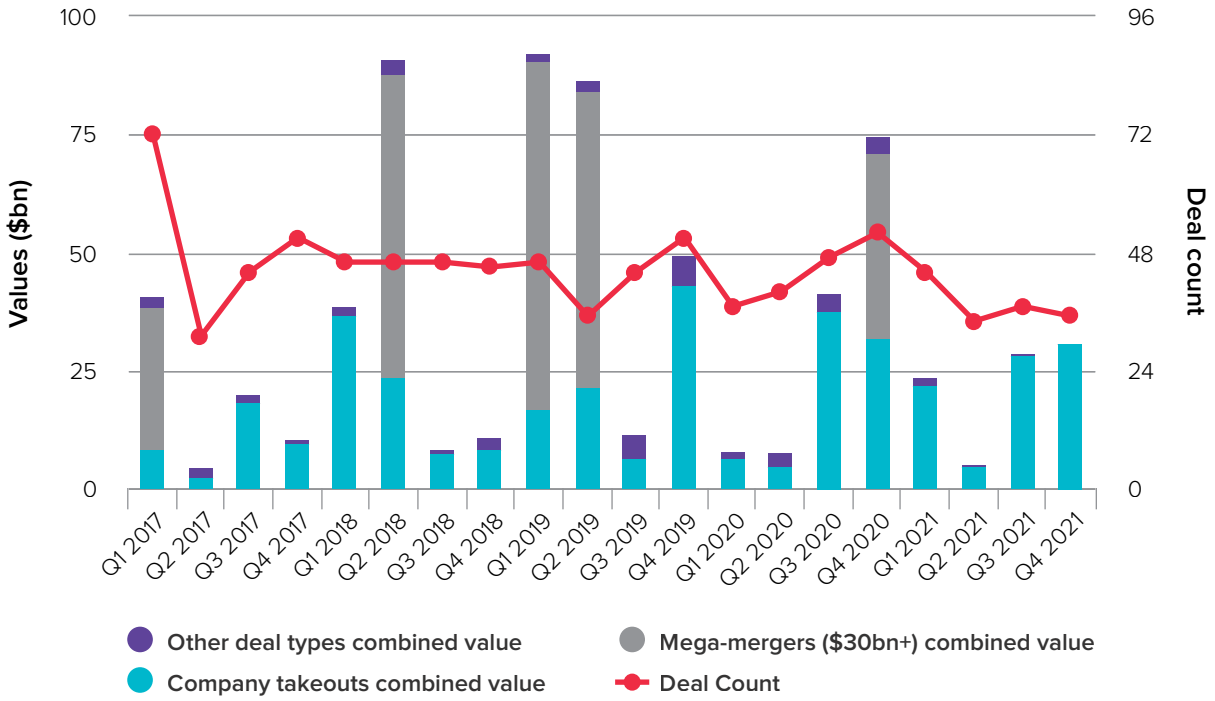
What this might be is the burning question. Biogen was recently added to the list of motivated buyers, after comments made by the company's chief executive. Shares in Aurinia, Biohaven and Amylyx all rose after being named as potential targets by Stat.

Aurinia has long been considered a target, with both Bristol Myers Squibb and Glaxosmithkline reported to be interested, though no buyout has appeared. And, with a market cap of $2.4bn, its acquisition would hardly set the sector on fire.

With Novartis sitting on a windfall from the sale of its Roche stake, Pfizer rich on Covid cash and plenty of others well stocked, biopharma is not bereft of firepower. Going by the state of the markets it might soon not be short of sellers.

The closely watched exchange-traded fund the XBI fell below $100 in the opening days of 2022 for the first time in 18 months. Demand for US biotech stocks is as poor as many can remember for some time. It might take a string of Aurinia-type deals, and possible a couple of Alexion's size, before this tanker is turned around.

Quarterly M&A deals



Source: Evaluate.

More detailed analyses of these data and Evaluate Vantage's wider coverage of M&A trends can be found on our website here.

The FDA brushes off the pandemic with a pick-up in novel drug approvals

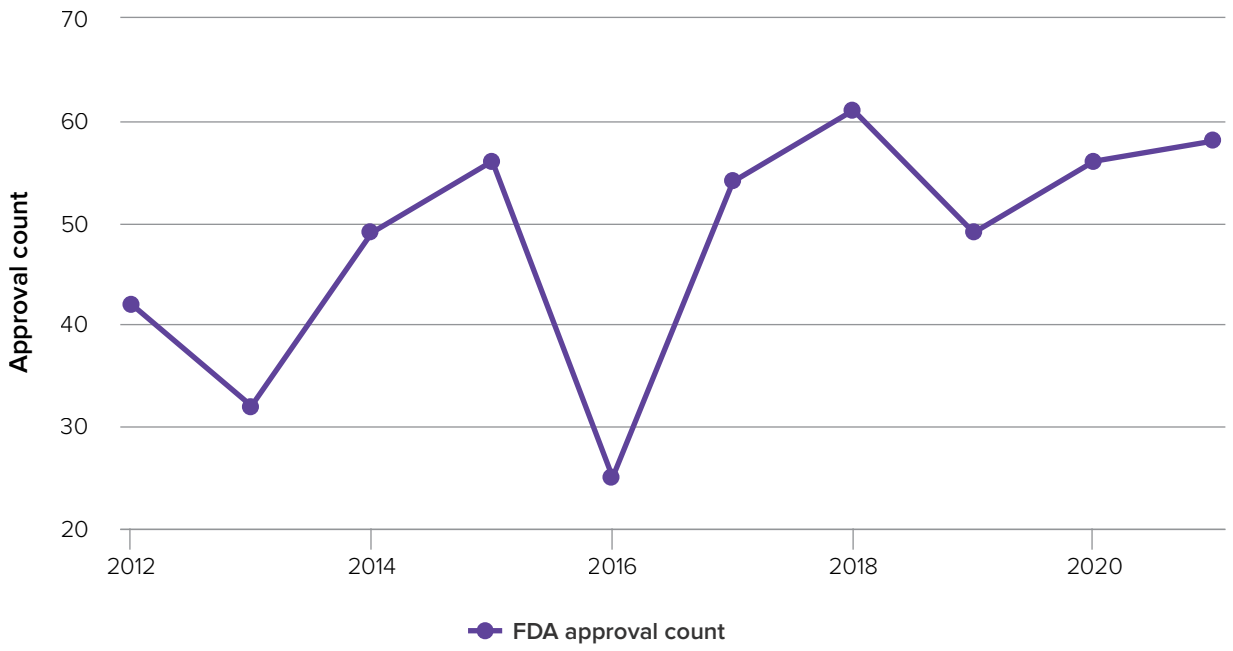
The US drugs regulator approved 58 novel drugs last year, the highest number for three years and well above the 10-year average of 48. With travel limitations blamed for decision delays in a number of cases, Novartis's Leqvio and UCB's Bimzelx included, this uptick could presumably have been steeper under more normal conditions.

The only Covid product included in this count is Biontech and Pfizer's Comirnaty; all the other pandemic-related projects are on the market under emergency use authorisations, rather than full approvals.

> The US drugs regulator approved 58 novel drugs last year – well above the 10-year average of 48.

Comirnaty is almost certainly going to become last year's biggest approval commercially speaking, though by 2026 annual sales are forecast to have dipped substantially.

Ten years of FDA approvals



Source: FDA.

This time last year Biogen's Aduhelm was **predicted to be the class of 2021's biggest seller**, according to fifth year sales as predicted by sellside analysts. But **should January's punitive US coverage decision hold** consensus is likely to drop to close to zero.

That still leaves plenty of potential future blockbusters that arrived on the market in 2021, according to *Evaluate Pharma's* consensus in the table below. It is worth remembering that several of these projects need to win expanded labels, or carve out share in highly competitive therapy areas, to reach these lofty levels.

Potential blockbuster table

Product	Company	Description	2026e US sales
Leqvio	Novartis	siRNA-based anti-PCSK9 for high cholesterol; approved in heterozygous familial hypercholesterolaemia and atherosclerotic cardiovascular disease.	$1.7bn
Abecma	Bristol Myers Squibb/Bluebird	Anti-BCMA Car-T cell therapy; approved for B-cell and follicular lymphomas	$1.4bn
Comirnaty	Pfizer	Covid-19 vaccine	$1.4bn
Tezspire	Amgen	Anti-TSLP MAb; approved in severe asthma	$1.2bn
Vyvgart	Argenx	Anti-FcRn MAb for IgG-mediated autoimmune diseases; approved in myasthenia gravis	$1.2bn
Lumakras	Amgen	Kras G12C inhibitor; approved in non-small cell lung cancer	$1.2bn
Lupkynis	Aurinia	Calcineurin inhibitor; approved in lupus nephritis	$1.1bn

Source: Evaluate Pharma.

More detailed analyses of these data and Evaluate Vantage's wider coverage of regulatory trends can be found on our website here.

Medtech Review 2021

A bad year to be an American medtech

With better availability of rapid Covid tests, often free of charge, and more centralised healthcare systems overseeing vaccination efforts, European countries have arguably been better able to manage the effects of the pandemic than the US. Perhaps this is why nearly all the big-cap groups that enjoyed the biggest increases in valuation last year were listed in Europe, and nearly all the fallers listed in New York.

Better investor confidence in Europe seems the likeliest explanation for the Swedish group Getinge having more than doubled in value while Teleflex, a US company that plays in similar hospital supply and cardiology areas, experienced a 20% share price fall.

The medical device indices back this interpretation, the Stoxx Europe 600 health care index having outpaced the Dow Jones US medical equipment basket. That said, these do not track precisely with big-cap companies; the Dow Jones index, for example, tracks 65 US-listed groups with a median market cap of $4.3bn.

Indices

Stock index	% change in 2021
Stoxx Europe 600 health care	23%
Dow Jones US medical equipment index	21%
S&P composite 1500 healthcare equipment & supplies	18%

Source: Evaluate Medtech.

As the Omicron variant threatens to overwhelm hospitals despite its apparently milder symptoms, a hospital equipment manufacturer rules the roost. Sweden's Getinge, which sells acute care products used in the ICU, as well as cardiac, vascular and pulmonary devices, more than doubled in value across last year.

The remaining risers are in disparate sectors – dental, cardiovascular, diagnostics and hearing – but all but Penumbra are hosted on European exchanges.

The converse is seen with the fallers. Only one, Philips, has a European berth. This group **had a disastrous year**, and arguably did well to get away with a loss of just a quarter of its value.

Large cap ($10bn+) medtech companies: top risers and fallers in 2021

	Share price 12-mth change	Market cap at Dec 31 ($bn)	Market cap 12-mth change ($bn)
Top 5 risers			
Getinge (SKr)	106%	11.5	5.9
Straumann (SFr)	88%	33.5	15.5
Penumbra ($)	64%	10.7	4.4
Siemens Healthineers (€)	59%	85.3	30.3
Sonova (SFr)	56%	24.2	8.3
Top 5 fallers			
Teladoc Health ($)	(54%)	14.7	(14.3)
Exact Sciences ($)	(41%)	13.4	(6.5)
Philips (€)	(25%)	32.9	(13.9)
Guardant Health ($)	(22%)	10.2	(2.7)
Teleflex ($)	(20%)	15.4	(3.8)

Source: Evaluate Medtech.

Other fallers are US-based and have perhaps suffered excessively harsh punishment. The digital health behemoth Teladoc led the risers at the end of 2020 as locked-down users flocked to its virtual healthcare tech. As restrictions eased in 2021 it has been unable to maintain the same growth, and skittish investors deserted.

The mid-caps – those whose market cap sits beneath $10bn but above $2.5bn – were led by diagnostics group Fulgent Genetics, which nearly doubled in value. Fulgent's 93% growth came partly as a result of its Covid tests; its **PCR assay was authorised in the US in May 2020** and the cash this generated enabled the company to **triple in size across 2020**.

Other significant risers and fallers in 2021 (ranked on market cap)

	Share price 12-mth change	Market cap at Dec 31 ($bn)	Market cap 12-mth change ($bn)
Top 5 risers			
Tandem Diabetes Care ($)	57%	9.6	3.7
Fulgent Genetics ($)	93%	3.0	1.7
Ypsomed (SFr)	28%	2.6	0.5
Senseonics ($)	207%	1.2	1.0
Iradimed ($)	103%	0.6	0.3
Top 5 fallers			
Novocure ($)	(57%)	7.8	(9.8)
Invitae ($)	(63%)	3.5	(3.9)
Haemonetics ($)	(55%)	2.7	(3.3)
Cardiovascular Systems ($)	(57%)	0.8	(1.0)
Tactile Systems Technology ($)	(58%)	0.4	(0.5)

Source: Evaluate Medtech.

Insulin pump developers did well, with Tandem and Ypsomed among the five biggest mid-cap risers. The former rose steadily across the year as sales of its insulin pumps picked up as lockdowns were lifted. It also benefited late in the year from the **ongoing quality control nightmare** at Medtronic's diabetes pump manufacturing site.

Another diabetes player, Senseonics, also rose significantly. The company makes Eversense, a tiny blood glucose monitor that is implanted in a patient's upper arm and works for either three or six months. Senseonics had a rotten 2019 and a lacklustre 2020, but came roaring back in early 2021 as a distribution agreement with Ascensia began to bear fruit.

Overall 2021 was a relatively staid year for small and mid-cap device makers, with the huge gains of 2020 nowhere to be seen. Perhaps sentiment will pick up in 2022.

More detailed analyses of these data and Evaluate Vantage's wider coverage of share price performances can be found on our website here.

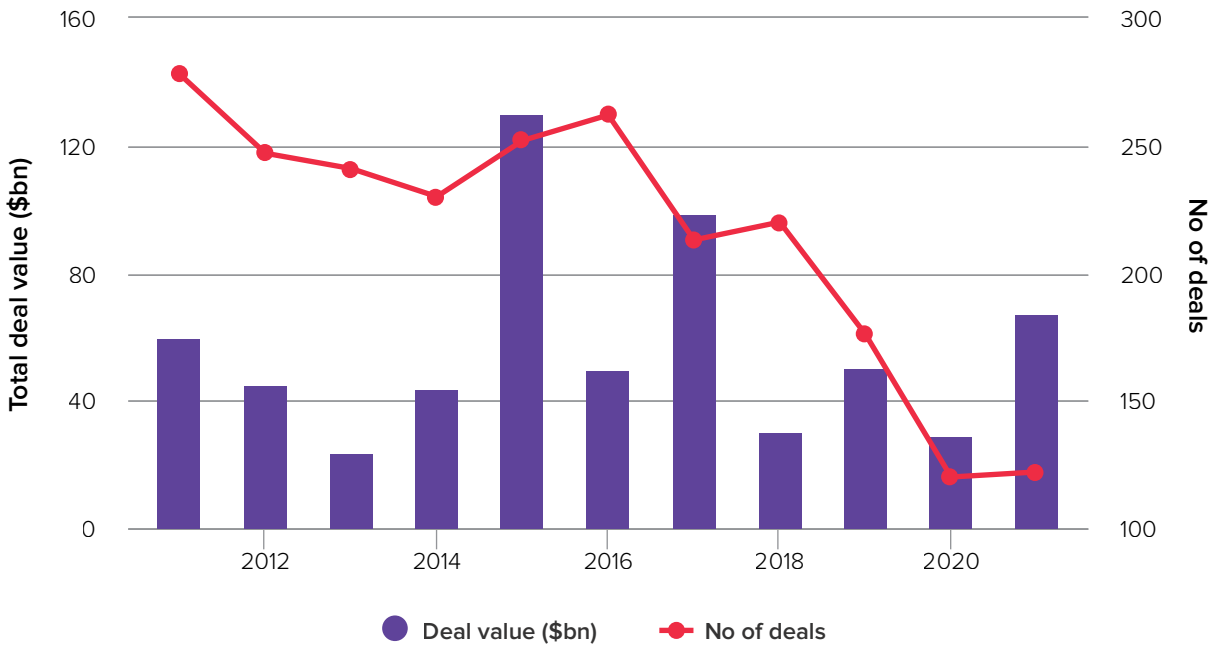
Device makers buy big

After a pause device makers are buying again, mostly thanks to either stockpiles of Covid cash or, among the less fortunate, a pressing need to build scale during a difficult time. Acquisitions of medtech companies worth a total of $67.2bn were closed in the medical device sector last year, the highest figure since 2017.

And while the sector saw only 10 acquisitions worth more than $1bn – three fewer than in pre-pandemic 2019 – the relatively low number of deals closed last year means the average price paid is higher than ever, at $1.12bn.

Since this analysis tracks the closing of deals rather than their announcement, many date from 2020 and the height of the first wave of the pandemic, underlining the remarkable nature of this resurgence.

M&A over the past decade – number and value of deals closed



Source: Evaluate Medtech.

Siemens Healthineers, which closed the biggest deal of 2021, is these days in the Covid cash category, having done extraordinarily well thanks to its pioneering tests for the coronavirus. But its $16bn bid for the imaging company Varian predates this success; when the deal was announced in the summer of 2020 the German group was hurting from the cancellation and postponement of non-urgent imaging procedures.

Acquisitions of medtech companies worth a total of $67.2bn were closed in the medical device sector last year, the highest figure since 2017.

Another strong trend across 2020 and 2021 was a clear shift into digital and remote technologies. Baxter spent $11bn on Hillrom largely for the latter's "connected care" systems, which include electronic health records, communication systems and wireless patient monitors, as well as the software to link them.

Top 5 M&A deals closed in 2021

Completion date	Acquirer	Target	Value ($bn)	M&A focus
Apr 15	Siemens Healthineers	Varian Medical Systems	16.4	Radiotherapy
Dec 13	Baxter International	Hillrom	10.5	General hospital & healthcare supply, in vitro diagnostics, patient monitoring
Aug 18	Illumina	Grail	8.0	In vitro diagnostics
Jun 2	Steris	Cantel Medical	4.6	Endoscopy, general & plastic surgery, nephrology
Feb 9	Philips	Biotelemetry	2.8	Patient monitoring

Source: Evaluate Medtech.

Another major issue, and possibly a worrying one, was the dearth of smaller deals. Just 18 acquisitions worth less than $100m were closed last year, fewer even than in sluggish 2020. Start-ups rely on the prospect of takeovers to lure venture investors; if medtechs in this size bracket are not being bought, the knock-on effects for younger groups in need of growth capital could be severe.

M&A by size – number of deals closed over the past decade

Note: Only includes deals with known value. Source: Evaluate Medtech.

For deals that exemplify the spending of Covid testing revenues look no further than Hologic. The diagnostics group made around $2.4bn from its Covid assays, instruments and collection kits across its fiscal 2021, which ended on September 25. It was able to use this windfall to close five acquisitions in 2021, the largest being that of Mobidiag for $795m.

> 2020 and 2021 saw a clear shift into digital and remote technologies

Plenty of other groups whose coffers have been swollen with coronavirus-related revenues have signed deals, but those deals simply have not closed yet, and so will feature in future analyses. Roche's $1.8bn acquisition of Genmark Diagnostics is one, as is Quidel's recently announced $6bn takeover of Ortho Clinical Diagnostics. This trend is not even close to finished.

And the wave of spin-outs sweeping the industry will also free up capital and create smaller, more adroit groups capable of more focused deal making. Expect to see purchases by the newly independent GE Healthcare and Zimvie, the spine and dental company soon to emerge from Zimmer Biomet, in the coming year.

More detailed analyses of these data and Evaluate Vantage's wider coverage of M&A trends can be found on our website here.

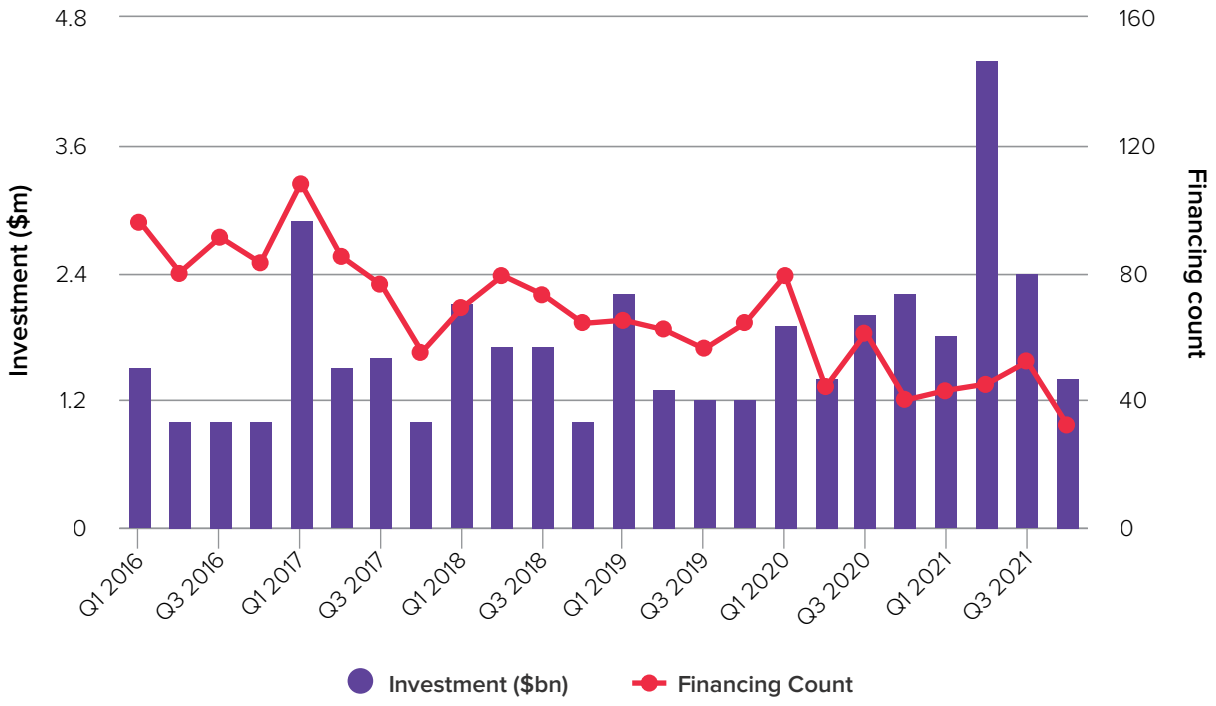
Medtech scores its biggest-ever venture haul

Medical device companies have just concluded a storming year for both acquisitions and flotations, and that means venture backers felt justified in ploughing their cash into the sector. They have done so in a big way – medtech has had its strongest ever year for venture financing, with a total haul of $9.9bn.

Diagnostics developers have done best over the year, with liquid biopsy and Covid test makers represented in the top 10. The cancer testing company Caris Life Sciences, which employs the investor catnip of artificial intelligence in its technology, raised the greatest single deal of the year with an $830m infusion in May.

Unusually, the second spot is taken by a UK company. The robotic surgery group CMR Surgical closed a $600m series D round in June, and this in combination with Caris's deal helped the second quarter of 2021 to a new record.

VC quarterly investment



Source: Evaluate Medtech.

The second quarter of 2021 was the largest since Evaluate Medtech's records began, its $4.4bn total smashing the $2.9bn taken in the first period of 2017. The above below incorporates VC rounds from developers of medical devices, telehealth products and diagnostics, excluding biotech and pharma groups.

Diagnostics companies are also strongly represented among the top 10 – and many are liquid biopsy developers, with Caris, Freenome and Intervenn all working in this area. The others offer Covid tests or testing services.

Top 10 VC rounds of 2021

Date	Company	Investment ($m)	Round	Focus
May 11	Caris Life Sciences	830	Undisclosed	In vitro diagnostics
Jun 27	CMR Surgical	600	Series D	Robotic surgery
Apr 27	Livi/Kry	316	Series D	Telehealth
Dec 7	Freenome	300	Series D	In vitro diagnostics
Jun 29	Element Biosciences	276	Series C	In vitro diagnostics
Jul 15	Imperative Care	260	Series D	Cardiovascular
Jun 23	Quanta	245	Series D	Home dialysis
May 13	Cue Health	235	Series D	In vitro diagnostics
Jul 29	Exo	220	Series C	Diagnostic imaging
Aug 2	Intervenn Biosciences	201	Series C	In vitro diagnostics
Jan 4	Color	167	Series D	In vitro diagnostics

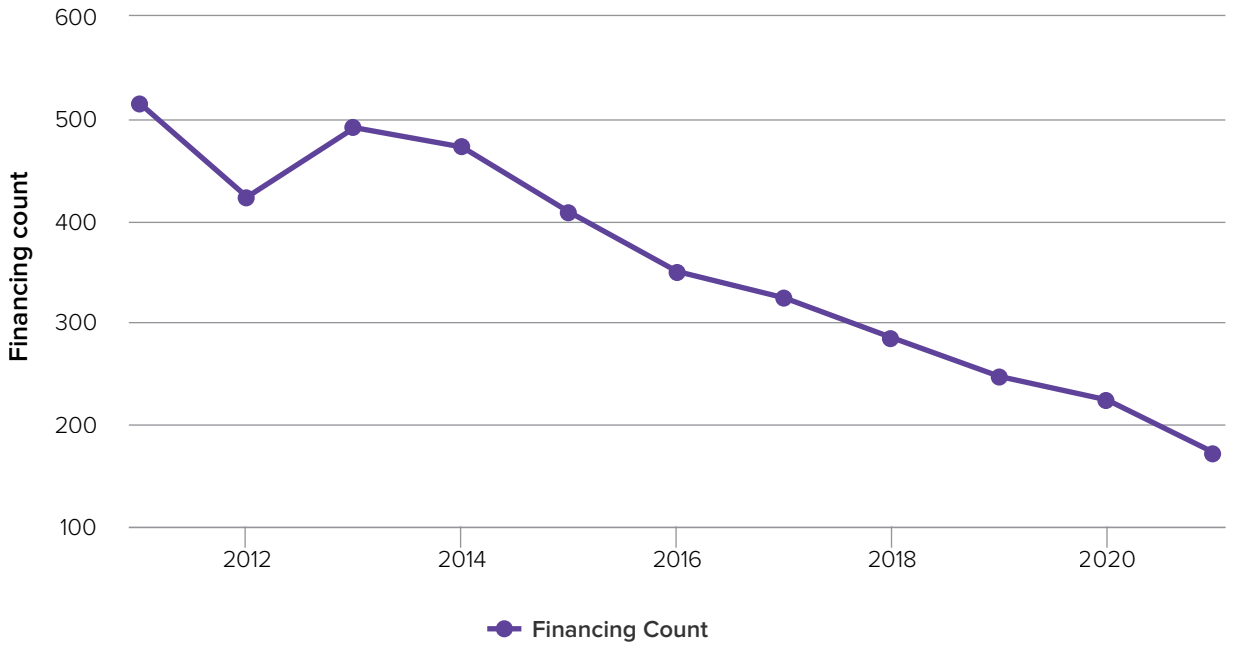
Source: Evaluate Medtech.

It seems that nearly two years after the coronavirus emerged VCs still see test makers as promising investment prospects. Those that backed Cue Health were arguably correct – the group went public in September, though its stock has done poorly since.

The pandemic is also a likely driver of the funding rounds closed by Kry and Quanta. Kry, which operates in the UK and France under the name of Livi, provides video consultation technology to connect patients with healthcare professionals, and Quanta makes home-based dialysis machines.

> Medtech has had its strongest ever year for venture financing, with a total haul of $9.9bn.

A new low – annual VC deals



Source: Evaluate Medtech.

In some ways there are encouraging signs that the cash is being spread around to a greater degree than in prior years. The top 10 rounds made up just 31% of the total VC haul, a relatively low proportion, and the year's largest round is smaller than in either 2019 or 2020.

That said, the number of rounds closed has fallen once again. This number has been shrinking year-on-year since 2013, a downward trend that shows no signs of reversing.

More detailed analyses of these data and Evaluate Vantage's wider coverage of venture financing trends can be found on our website here.

Medical device groups float – then sink

Last year was a tricky one on the public markets, but this did nothing to discourage private medical device developers from venturing into the choppy waters. In 2021 over $5.5bn was raised across 28 deals, as companies sought capital from investors still eager to back healthcare – and particularly diagnostics – groups.

But there were limits to shareholders' ardour. Many of the companies that went public last year had to accept lower valuations to get away, while more than two thirds of them had seen their share price decline by the end of the year.

Despite these risks, this strategy paid off in spades for some groups. The most remarkable case was that of Ortho Clinical Diagnostics, whose listing by its private equity owners in January was 2021's biggest at $1.5bn. Ortho Clinical was public for less than a year, however, before being **snapped up by Quidel for a startling $6bn**.

The 10 biggest medtech IPOs of 2021

Date	Company	Focus	Amount raised ($m)	Premium/ discount	Share price change to Dec 31
Jan 28	Ortho Clinical Diagnostics	In vitro diagnostics	1,486	(21%)	26%
Feb 11	Signify Health	Healthcare IT	649	17%	(41%)
Sep 30	Oxford Nanopore Technologies	In vitro diagnostics	442	3%	64%
May 27	Singular Genomics Systems	In vitro diagnostics	258	5%	(47%)
Feb 11	Talis Biomedical	In vitro diagnostics	254	7%	(9%)
Jul 15	Sight Sciences	Ophthalmics	240	2%	(27%)
Jul 23	Sophia Genetics	Healthcare IT	235	0%	(22%)
Sep 25	Cue Health	In vitro diagnostics	200	0%	(16%)
Feb 5	Lucira Health	In vitro diagnostics	176	6%	10%
Sep 15	Procept Biorobotics	Urology	164	9%	0%
Jul 15	Rapid Micro Biosystems	In vitro diagnostics	158	5%	(47%)

All listings on Nasdaq, except Signify on the NYSE and Oxford Nanopore on the LSE. Source: Evaluate Medtech & company websites.

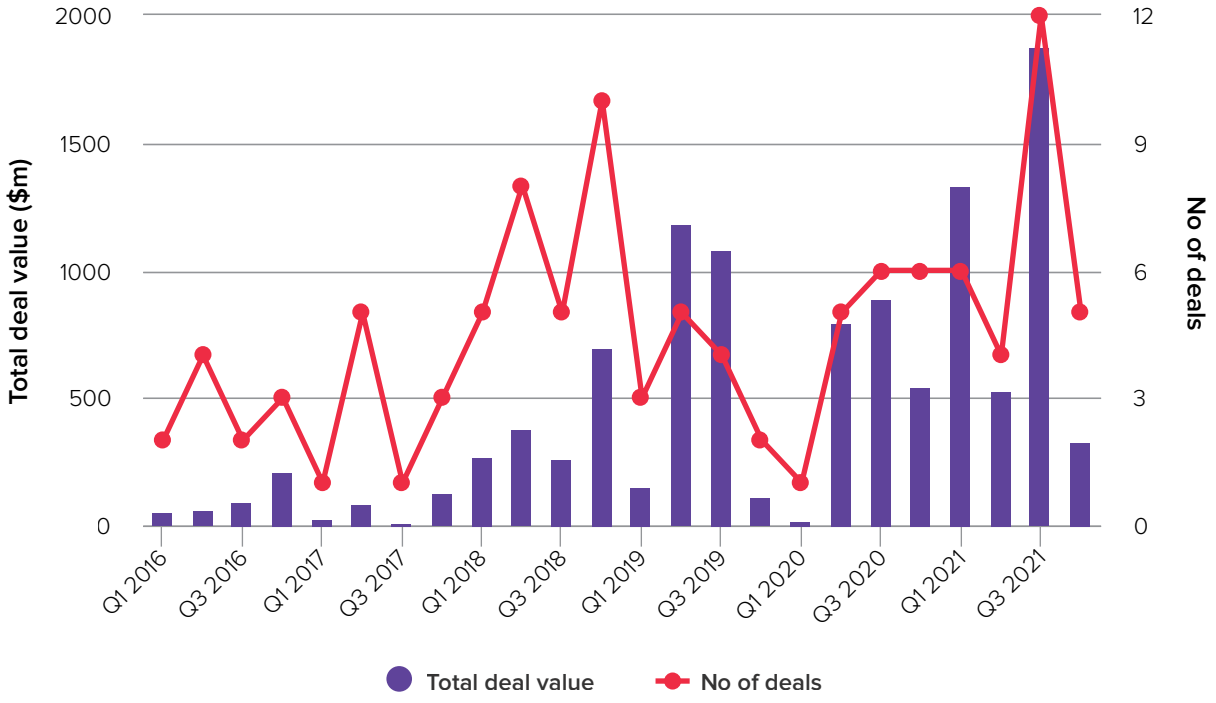
Apria, too, was bought less than a year after its IPO, by the hospital equipment supplier Owens & Minor for $1.5bn. Its flotation in February raised $150m, putting it just outside the top 10, and by the end of 2021 its stock was up 63%, the second highest rise of 2021.

The deal also shows that the vogue for buying developers of remote internet-enabled technologies is continuing into this year.

The preponderance of diagnostics companies in the top 10 is a reflection of the broad popularity of this subsegment with investors of all kinds. Six of the top 10 venture rounds last year went to test companies, for instance.

The other clear message to come out of 2021's data is that the US is still seen as the land of opportunity. With two exceptions – Oxford Nanopore's flotation in London and Affluent Medical's €33m ($30m) listing on the Euronext Paris – all last year's IPOs occurred in New York.

Quarterly IPOs



Note: Graph does not include IPOs that raised more than $1bn. Source: Evaluate Medtech.

Cutting the data by quarter shows the action reaching fever pitch in the third period, with 12 deals raising $1.9bn. The graph above does not include IPOs worth more than $1bn, since they tend to distort the picture of underlying market trends. Without these megadeals, 2021 was the strongest year for total dollars raised since Vantage began tracking medtech IPOs in 2013.

Huge IPOs are still coming, however. In mid-January this year eye care group Bausch & Lomb filed with the SEC for an offering to raise $100m – but this is surely a placeholder amount for a deal some industry experts estimate could raise up to $3bn. The company is being spun out by its owner, Bausch Health, and if a buyer does not emerge in the meantime this seems likely to be the biggest IPO of 2022.

More detailed analyses of these data and Evaluate Vantage's wider coverage of IPO trends can be found on our website here.

Device approval times lengthen

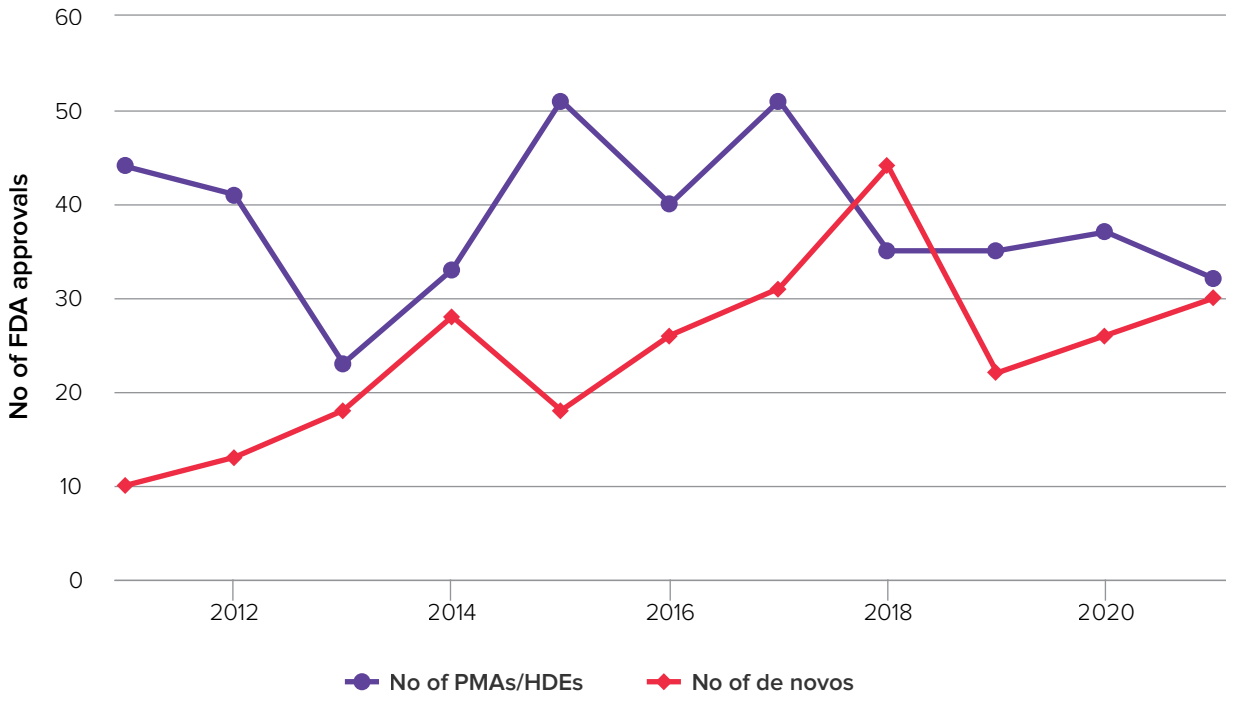
With 32 high-risk innovative medical devices approved in 2021, the picture for companies trying to bring new products to the US market is acceptable: by the end of the year, the overall number of approvals was only one shy of 2020's total.

In terms of review times, however, the agency has slowed down. Compared with 2020, it took around a month longer, on average, to examine the submissions for the approved devices. This is perhaps understandable: in a blog post towards the end of December, Jeff Shuren and William Maisel of the FDA's devices section said that a sustained high volume of filings was straining the centre's resources.

While the number of premarket approvals – the regulatory path that must be taken by high risk devices – fell slightly from 2020's total, this was balanced by a year-on-year increase in the number of low-risk products cleared for sale via the de novo clearance route.

This analysis considers first-time premarket approvals, humanitarian device exemptions and de novo 510(k) clearances. Standard 510(k)s and supplemental approvals are not covered.

US device approvals over the past decade



Source: Evaluate Medtech.

According to the FDA Voices blog post, the FDA's Center for Devices and Radiological Health has issued emergency use authorisation to over 1,900 medical devices for Covid, and continues to receive more than 100 EUA requests per month. On top of this the number of conventional submissions – PMAs and 510(k)s, including de novos, supplemental approvals, and pre-submissions – increased for the second consecutive year, reaching almost 18,000
last year.

With all this going on it is hardly surprising that the agency's timelines have slipped slightly. It should be stressed that the timings listed below are based solely on successful filings; the FDA does not make available the review times for rejected submissions.

> Last year saw a dearth of diagnostics approvals as the FDA prioritised Covid tests, companion diagnostics, breakthrough devices or assays with a significant public health impact.

2021's approvals by therapy area

Evaluate Medtech classification	Number of PMAs & HDEs	Avg approval time (mths)	Number of de novos	Avg approval time (mths)
Cardiology	13	14.0	6	12.5
Ear. nose & throat	1	15.0	2	17.2
Gastroenterology	3	20.5	1	7.0
In vitro diagnostics	8	15.1	3	11.5
Neurology	1	5.9	5	7.3
Ophthalmics	1	11.1	2	8.9
Orthopaedics	1	7.6	3	9.3
Radiology	2	10.1	1	17.6
Total	**32**		**30**	
Average		**13.9**		**11.2**

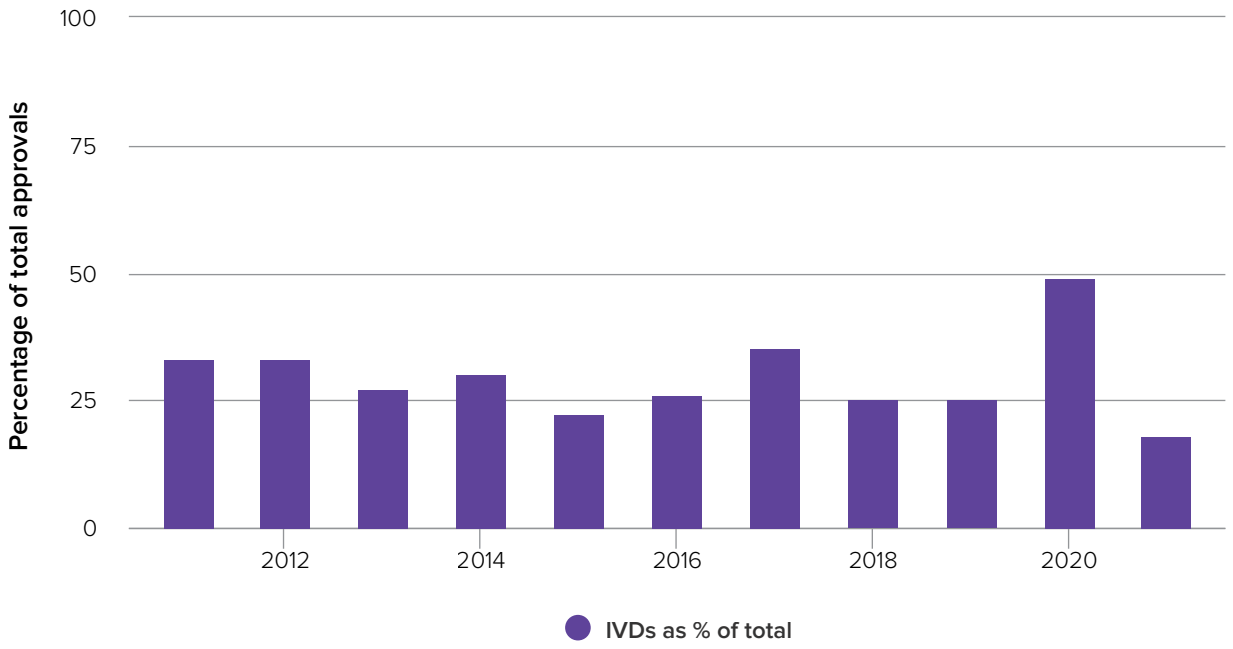
Note: Table only shows areas with at least three approvals. Source: Evaluate Medtech, FDA.

One notable feature of last year's approvals is the dearth of diagnostics, the result of a deliberate strategy by the agency to prioritise Covid tests, companion diagnostics, breakthrough devices or assays with a significant public health impact.

From 2011 to 2019, an average of 28% of device approvals awarded by the FDA were for in vitro tests of one kind or another. In 2020, this ballooned to 49%, as tests for cancer and infectious disease were prioritised. This figure did not include Covid tests, since all those that reached the US in 2020 did so under emergency authorisation.

Last year, however, saw a sharp pullback, with just 11 assays approved or cleared – 18% of the total. Non-covid IVD approval times also extended, to an average of more than 15 months last year, versus an average of 10.5 months for the prior decade.

IVDs as % of total approvals – includes PMAs, HDEs and de novo 510(k)s



Source: Evaluate Medtech.

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