



Q3 Round Up: Alive but not kicking

BY AMY BROWN, EDWIN ELMHIRST AND MADELEINE ARMSTRONG | OCTOBER 2022



Introduction

In our last quarterly eBook, after a rather grim first half, we asked: is the only way up? Q3 answered that question with a resounding “no”. The global economy is being buffeted by complex geopolitical events, and biopharma is finding new depths to plumb.

M&A activity is still alive if not kicking. But its blood is mostly flowing as a result of Pfizer releasing some of its Covid cash. Barring a mega-deal emerging in the closing months of the year, it looks like 2022 will be slow on the buyout front.

The IPO window remains all but closed with another exceptionally quiet quarter. July to September saw just three companies get away, matching the record low we saw in Q2. Short of giftwrapping some companies for the upcoming festive season, 2022 looks set to be a particularly weak for flotations. Biotechs can take some solace in knowing that’s true across all sectors.

Venture funding is also retreating, as these private investors pull the purse strings tight. Again, this is being seen across all industries, but the high-risk drug development sector always feels the pain particularly fiercely.

Then of course, there are share prices. Big pharma, previously a safe haven in choppy waters, took a big hit in Q3 with a number of challenges including pending US drug legislation and potential litigation.

All in all, 2022 feels like a year that most in the industry will be happy to have firmly behind them. Still, it’s not over yet. In this eBook, we bring you up to speed on all the big issues – whether you like them or not.

Brace yourself.



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The biopharma flotation remains a rare beast

BY EDWIN ELMHIRST AND AMY BROWN
OCTOBER 04, 2022

Few developers are feeling bold enough to brave the markets, though the bigger deals are finding some support.

For the second quarter running only three drug developers floated on Western stock exchanges, as the biotech bear market continued to squash demand for new offerings. And the stats get worse: the total sum raised plunged once again, with only \$153m banked in the third quarter, Evaluate Vantage finds.

Most of that was raised by one company, Third Harmonic, [which managed to upsize its offering](#), raising more than originally intended. The group has also just about managed to keep its head above water, with its share price only briefly breaking issue and slipping below its offer price.



Third Harmonic's reception might help persuade some groups to test demand, though a look at the IPO queue suggests that many remain to be convinced. Only one biotech, Prime Medicine, is eyeing a sizeable deal, having filed to raise \$100m. The others readying registration documents are preparing tiny, sub-\$25m offerings.

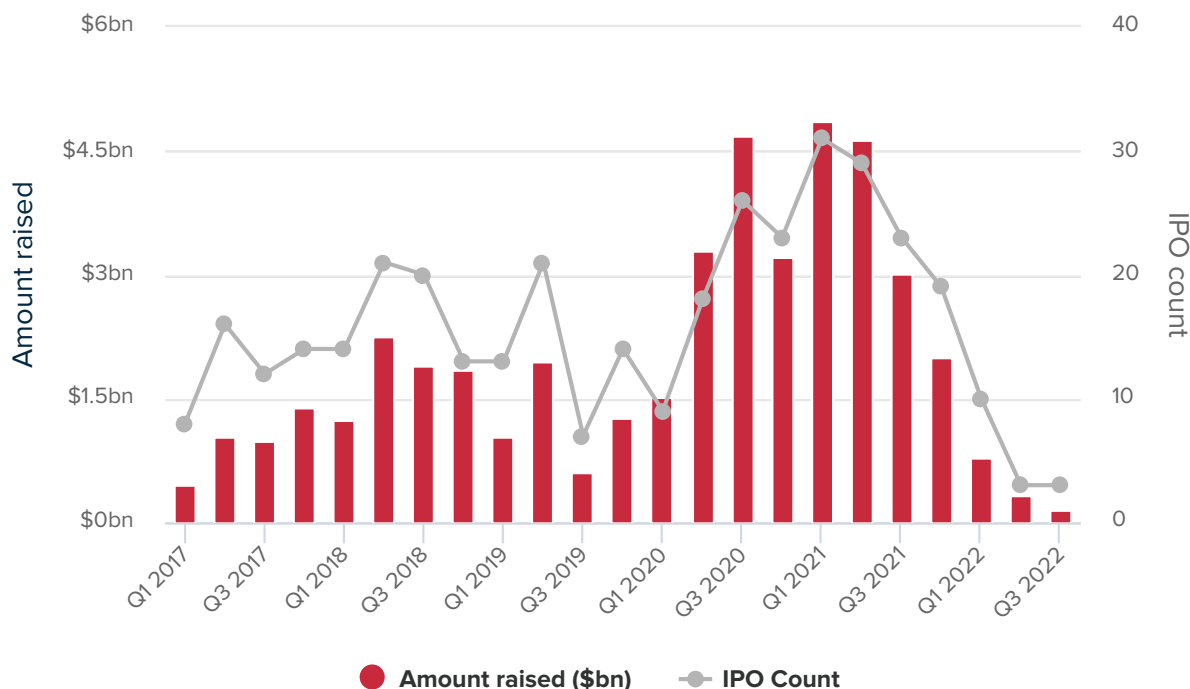
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Biotech IPOs by quarter on Western exchanges



Source: Evaluate

Small deals have been a feature of this year's IPO scene, which has seen the average amount raised plunge to \$79m. Last year this average reached \$142m, having hit \$167m in 2020.

And in a bear market it tends to be the small fry that get eaten. Of the eight developers that raised less than \$50m at IPO this year, six have broken issue.

The larger deals are finding some support. Of the six developers that raised more than \$100m at IPO

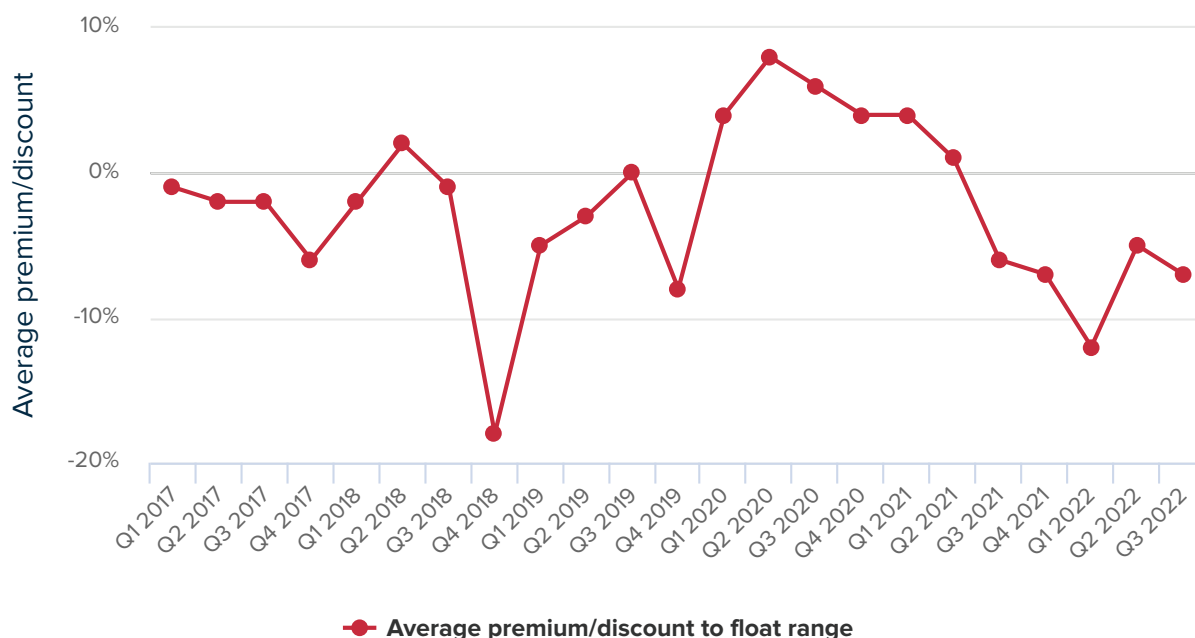
this year, only one is trading below its float price. So perhaps there are glimmers of hope to be found.

For this analysis *Evaluate Vantage* considers IPOs of pure-play drug developers only; secondary listings or unit offerings are not included. For now, this paints a picture of the US market. No European flotations have happened since Aelis Farma arrived on Euronext in February, and the situation on that continent is even more dire than in the US.



Bumps and haircuts

(Nasdaq IPOs only; offer price to middle of initially proposed range)



Source: Evaluate

It is also encouraging to see that all three of the third-quarter's flotations got away without a haircut – so within the initially proposed price range – albeit right at the bottom for Maia. This is presumably a result of bankers approaching investors with a realistic valuation in the first place, rather than signalling a supportive environment.

Overall, it is hard to see this picture changing much this year. The IPO market is dead across all sectors, largely thanks to the spectre of rising interest rates, which haunts the cash-burning biotech space particularly fiercely.

Three's a crowd? Third-quarter IPOs				
Company	Primary focus	Amount raised	Premium/(discount); float price to initial offer	Share price change since float to end Q3
Telomere-targeting immuno-oncology	Telomere-targeting immuno-oncology	\$10m	-10%	-34%
Paxmedica	Neurodevelopmental disorders	\$8m	-17%	-54%
Third Harmonic Bio	Allergy and inflammation	\$135m	0%	12%

Note: amount raised does not include over-allotments.

Source: Evaluate Pharma.



No big bang for biopharma buyouts

BY EDWIN ELMHIRST AND AMY BROWN
OCTOBER 05, 2022

Pfizer's Covid cash keeps the M&A scene alive, but few other developers dug deep in a quiet third quarter.

Deep-pocketed buyers held their fire in the third quarter, with a relatively pedestrian \$14bn deployed on biopharma M&A over the period. Pfizer's Covid cash continues to keep the scene alive, with the drug maker's \$5.4bn takeout of Global Blood the period's biggest deal.

The volume of transactions dipped slightly on the previous quarters but largely held up, so the buyout scene is far from dead. But the prospect of a [\\$30bn move on Seagen](#) was dangled in front of investors earlier this year, a deal that would transform 2022 into a year to remember.

Merck & Co's interest in Seagen has never been officially confirmed, of course, even after the way was cleared by [the conclusion of an arbitration process](#). The biotech's stock is now trading lower than before the Wall Street Journal triggered the



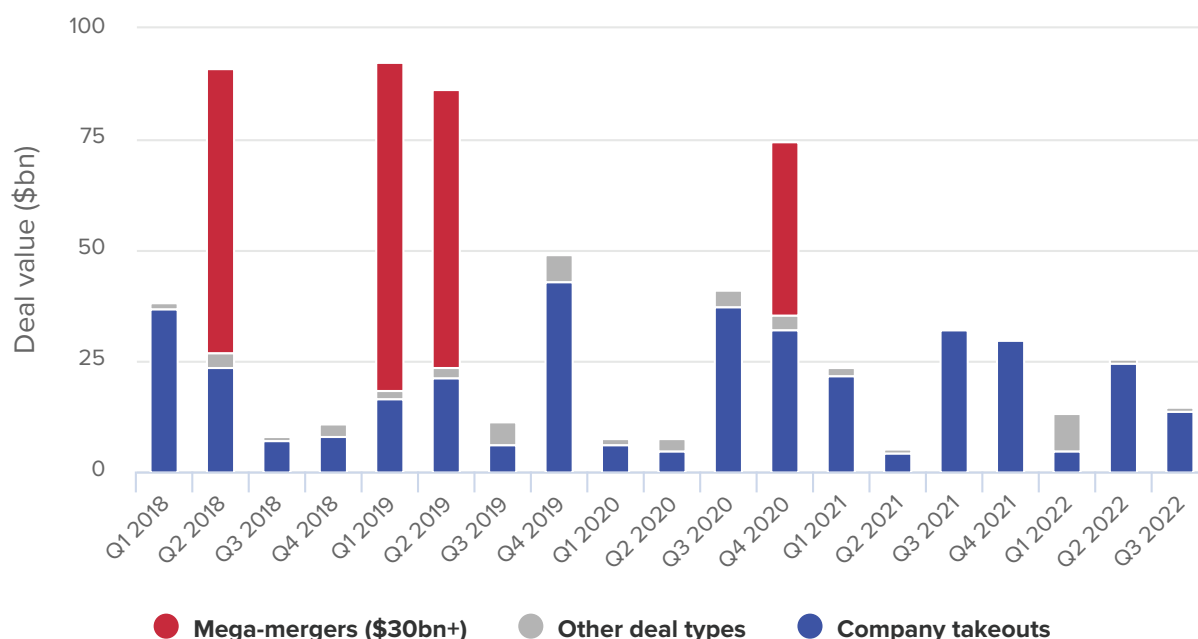
speculation, meaning that the market considers the prospect of any approach to be low.

Perhaps Merck is playing hardball on valuation, a strategy that could pay dividends in the current market. A number of small developers have had to accept the new reality this year, with [the likes of Epizyme, F-Star and Radius](#) agreeing to lowball takeouts.



Quarterly biopharma M&A

(combined deal value)



Source: Evaluate

As things stand, 2022 is shaping up to be a slow year for M&A spend, with just \$53bn committed in the first three quarters. Excluding the megamergers highlighted in the chart above, 2018 is the low bar to beat, when \$84bn was pledged on buyouts.

One sobering statistic is that Pfizer is responsible for a third of the M&A cash deployed this year, via its acquisitions of Biohaven, Global Blood, Reviral and a

stake in Valneva.

For this analysis, which is based on data collected by *Evaluate Pharma*, *Evaluate Vantage* includes only M&A deals struck by pure-play drug developers, with sectors like medtech or diagnostics excluded. Other deal types refers to majority and minority stake purchases and business unit buys; licensing deals are not counted.

Biggest biopharma M&A deals announced in Q3 2022

Acquirer	Target	Status	Deal value (\$m)
Pfizer	Global Blood	Open	5,400
Amgen	Chemocentryx	Open	3,700
Novo Nordisk	Forma	Open	1,100
Alcon	Aerie	Open	770
Gilead	Mirobio	Closed	405

Source: Evaluate Pharma.



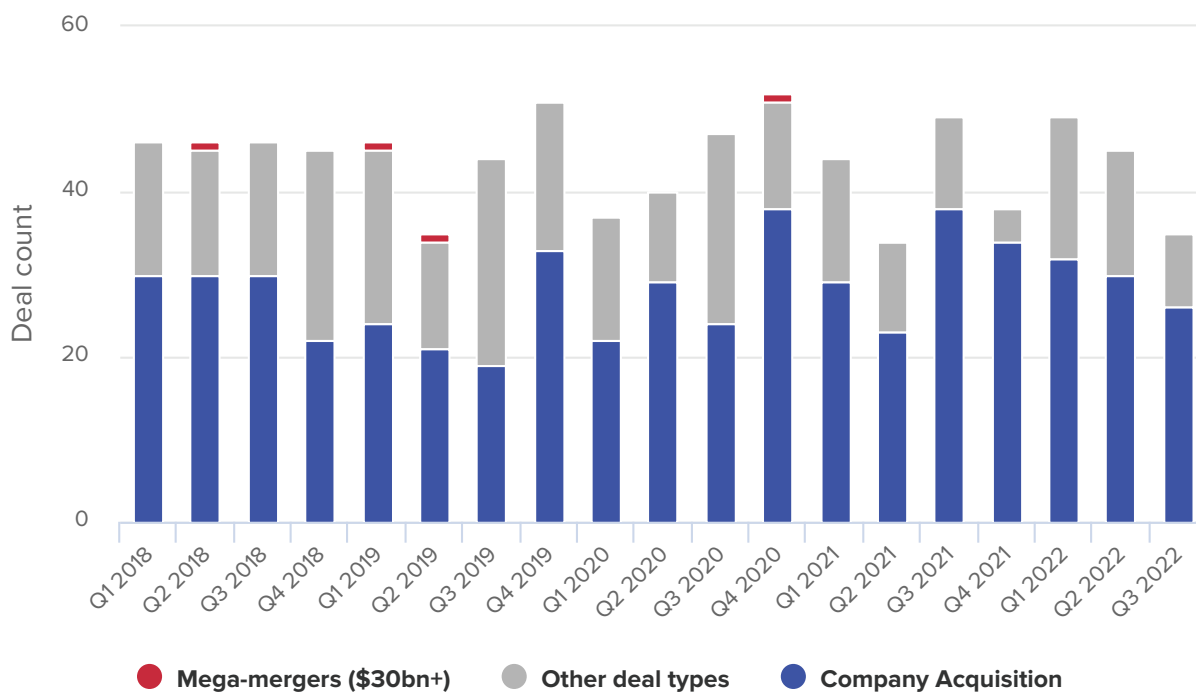
A look at the biggest deals of the quarter finds only three that breached the \$1bn mark. In some ways 2022 is shaping up a bit like last year, when small takeouts dominated (The year of the small buyout, January 28, 2022).

In 2021, however, the quiet M&A scene was blamed

on stretched valuations, which were apparently deterring buyers. That cannot be said this year.

True, desirable assets in biopharma will always attract a big premium, whatever the market cycle. But it is increasingly feeling like buyers are biding their time.

Quarterly M&A deal counts



Source: Evaluate



Venture investors keep the purse strings tight

BY EDWIN ELMHIRST AND AMY BROWN | OCTOBER 06, 2022

Third-quarter numbers show that biopharma venture investments are firmly back in 2018 territory.

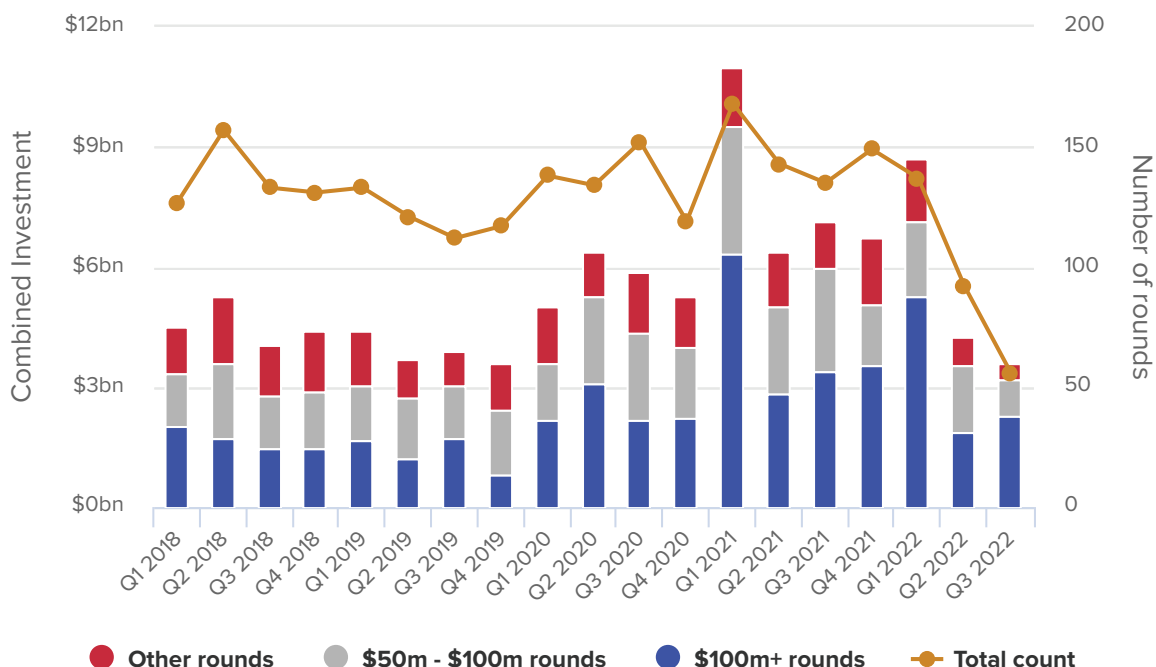
The IPO window is all but shut, equity markets are jumpy and global interest rates are climbing. Little wonder that venture investors are treading carefully when it comes to biotech, surely the highest-risk sector out there.

Third-quarter numbers collated by *Evaluate Pharma* show that the retrenchment that started earlier this year is continuing. Biopharma groups raised \$3.6bn from July to September, around a three-year low. Big rounds are still happening, however, suggesting that the gulf between the haves and the have-nots is widening.



These data refer to pure-play drug developers only, with sectors like digital health and medtech excluded.

Quarterly biopharma VC rounds



Source: Evaluate



The absence of crossover rounds – substantial fundraisings intended to shore up a company's balance sheet before an IPO – will be a big reason for the topline drop-off here. But the make-up of some of these larger rounds suggests that venture and other investors intend to start flipping developers on the market as soon as they can.

Acelyrin, for example, feels like prime IPO material. The group banked the quarter's largest round, with a broad syndicate of big-name investors behind it. This deal followed a large \$250m series B in 2021. The funds are ostensibly intended to pay for pivotal programmes of the group's IL-17A inhibitor izokibep, in psoriatic arthritis and axial spondyloarthritis, and submission with the FDA.

Top five rounds of Q3 2022			
Company	Investment (\$m)	Financing round	Description
Acelyrin	300	Series C	Immunology
Orna Therapeutics	221	Series B	Circular RNA therapeutics
Arsenalbio	220	Series B	Car-T therapies for solid tumours
Retro Biosciences	180	Seed capital	Age-related diseases
Carmot Therapeutics	160	Series D	Oncology and metabolic diseases

Source: Evaluate Pharma.

Carmot is another interesting name in the top table. The developer has been around for a lot longer than the others in the top five, having been founded in 2008; none of the other four existed before 2019.

Carmot's claim to fame is that it helped Amgen discover Lumakras, under a collaboration that started back in 2014. The small biotech is owed royalties on sales of the drug, a Kras G12C inhibitor. Carmot's primary focus is metabolic disease, however; a big chunk of the new funds will be used to complete mid-stage trials of CT-388, a dual GLP-1/GIP inhibitor.

This is the same mechanism as that of Lilly's newly approved Mounjaro, which is forecast to become a huge blockbuster in obesity and type 2 diabetes. Carmot says CT-388 has been optimised for

improved tolerability and once-weekly dosing; the group's new investors apparently believe that this profile has big potential.

For companies that do not tick enough boxes for venture investors, however, the situation is likely to be very different right now. Financiers are well aware that their existing portfolio companies are going to need support for longer in the current market, so the bar to sending money down new roads is going to be extremely high.

Venture players point out that the money flowing into early-stage biopharma remains historically high, and this might be true. But a flight to safety is surely under way.



The gloom deepens for biopharma stocks

BY EDWIN ELMHIRST AND MADELEINE ARMSTRONG
OCTOBER 10, 2022

With most glimmers of hope extinguished in the third quarter, 2022 is shaping up to be an annus horribilis for sector share prices.

A few months ago, it looked like there might be [some reasons to be cheerful about the state of biopharma](#). But the sector's stock market performance in the third quarter has had even the most optimistic of investors [feeling down](#).

Evaluate Vantage's quarterly look at sector-wide share price movements shows that there is always further to fall. The plight of big pharma, usually a popular safe haven in times of strife, is particularly alarming: the world's 11 largest drug makers collectively lost a staggering \$294bn in market cap in the period.

"WINNERS" AND LOSERS

Of this group, only Roche and Lilly did not see a quarter-on-quarter decline, buoyed by the [surprise success of Biogen and Eisai's Alzheimer's project lecanemab](#); both big pharma companies have amyloid-beta antibodies of their own. Still Lilly was merely flat, despite the hopes pinned on its Alzheimer's asset donanemab and its potential diabetes and obesity mega-blockbuster Mounjaro, illustrating just how tough the climate has been.



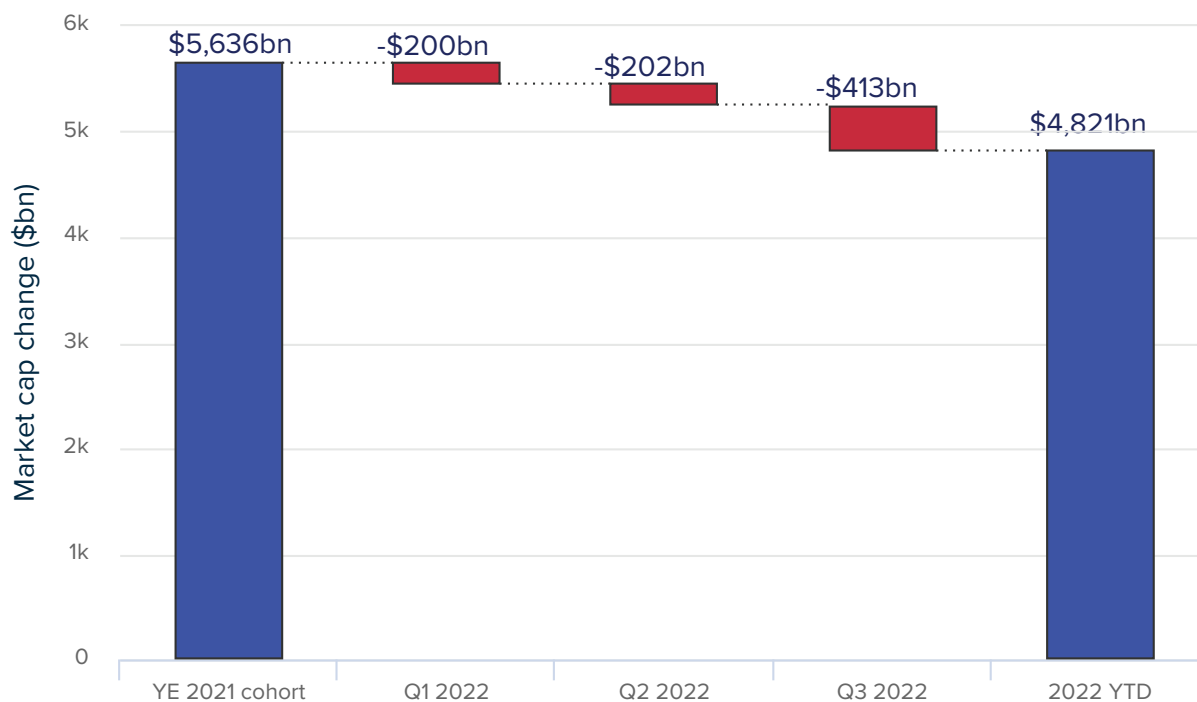
The biggest losers were GSK and Sanofi, which were hit by [worries about Zantac litigation](#), a concern that was a big contributor to this cohort's collapse in valuation last quarter. The spin off of GSK's consumer arm, Haleon, also caused a readjustment in that developer's market cap.

Still, previously feted names like Abbvie also did badly, against the backdrop of the [threat of US drug pricing reform](#). This has caused some serious investor disquiet, largely because the potential long-term impacts are unclear.

This all came on top of the wider market downturn, amid continuing fears about inflation and the war in Ukraine.



The shifting valuation of global drugmakers



Source: Evaluate

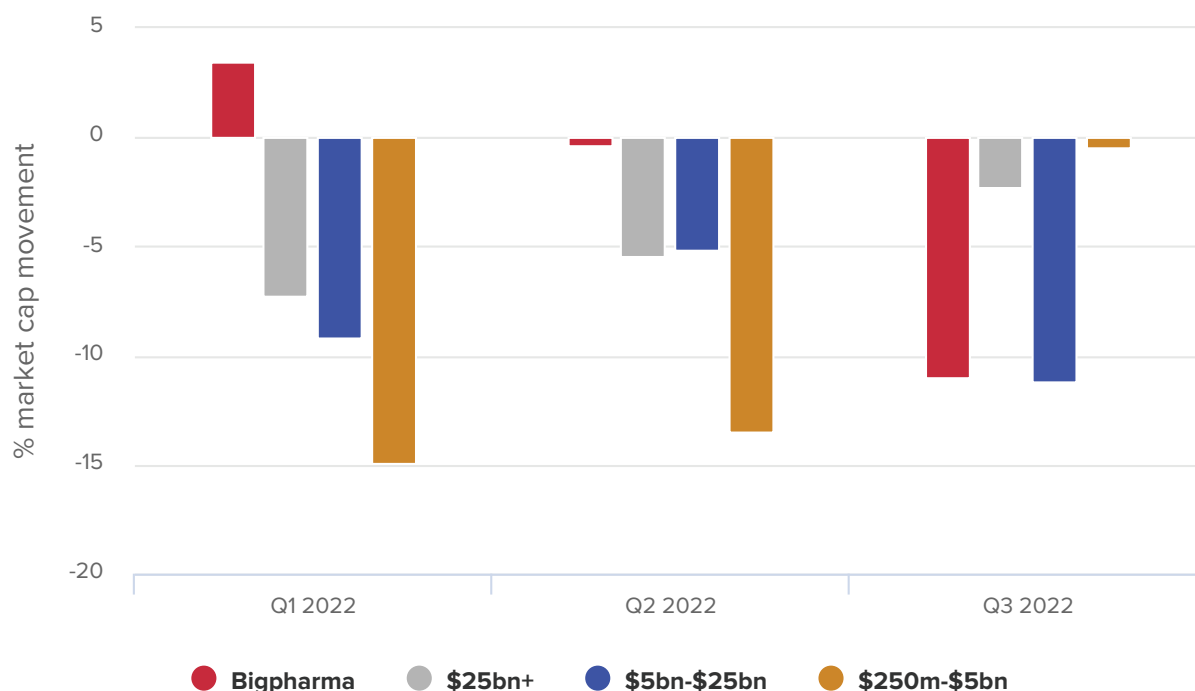
This analysis is constructed from the almost 700 globally-listed drug makers covered by Evaluate Pharma, sorted by Evaluate Vantage into four cohorts based on year-end 2021 valuations. Companies remain in their grouping throughout the year; nano-caps worth less than \$250m are not considered.

Aside from big pharma's disastrous showing, things were not great for the rest of the sector either, with mid-cap developers faring particularly poorly.

Investors in these groups are often gunning for a takeout, so the fact that a hoped-for pick-up in [M&A](#) [has so far failed to materialise](#) probably hit sentiment here.



Percentage market cap gains and losses, by size bracket



Source: Evaluate

There were some winners in the third quarter. This includes Alnylam, which had [positive data with Onpattro in amyloidosis cardiomyopathy](#), and the aforementioned Eisai.

Sarepta, meanwhile, rose 48% quarter-on-quarter on the mere promise of accelerated approval for its DMD gene therapy candidate, SRP-9001, bucking the current trend for caution around gene therapy names.

As for large players outside big pharma, there were almost as many losers as winners. Those that kept the faith with Biogen will be celebrating a Lazarus-

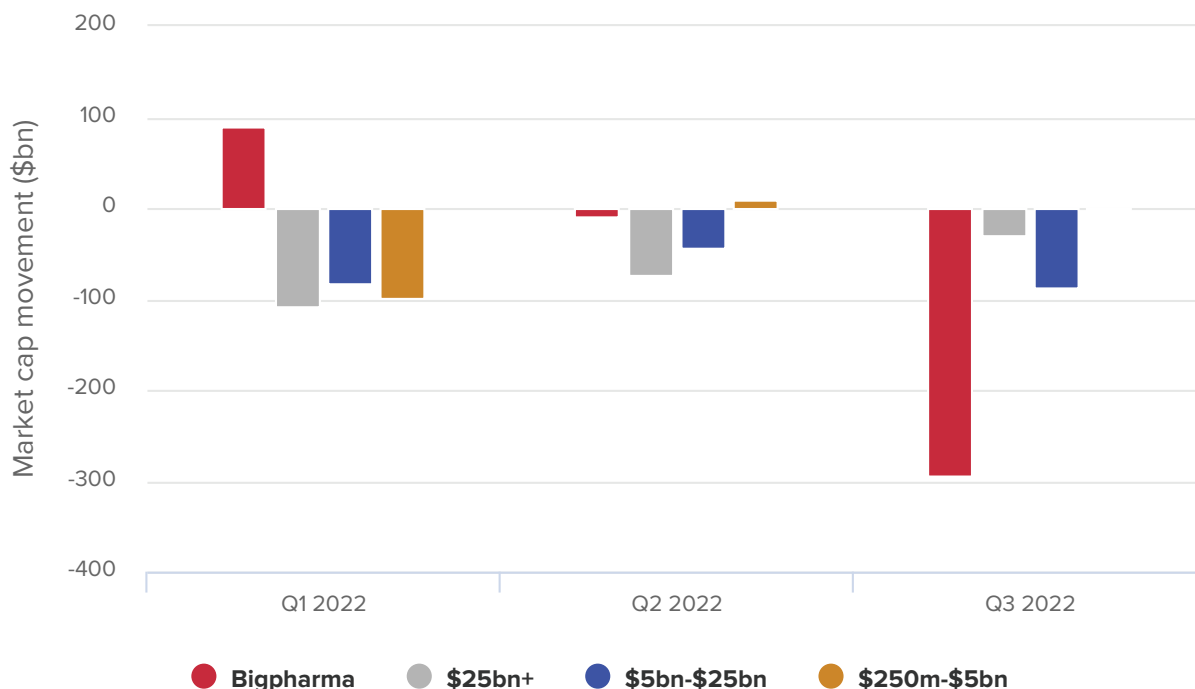
like resurrection, while Daiichi Sankyo continued to ride the Enhertu wave, and Regeneron got a boost from a [win with its long-acting version of Eylea](#).

Overall, though, this analysis shows that success stories have been few and far between, both in the third quarter and in 2022 so far. It is always dangerous to call the bottom, but the sector has to hope that there is not too much further to fall.

13/10/22 note: For this analysis the ADRs of Novartis and AstraZeneca are used, rather than main listings, and text in this article has been amended to reflect this.



Absolute market cap gains and losses, by size bracket



Source: Evaluate

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Few safe havens surface in another down quarter for biopharma

BY AMY BROWN AND EDWIN ELMHIRST
OCTOBER 13, 2022

Lilly, Daiichi and Vertex are on track to be 2022's best performing stocks, as the Covid crash continues.

Three quarters of the trading year are done, and many biopharma stocks are in a perilous state. With big pharma now feeling the pressure alongside small and mid-cap groups, safe havens are proving hard to find.

The unwinding of the Covid trade is readily apparent in Evaluate Vantage's latest quarterly look at the sector's biggest winners and losers. And on the up are developers that have delivered pipeline progress, like Lilly, Daiichi and Sarepta.

This analysis was constructed from the almost 700 listed biopharma companies covered by Evaluate Pharma, and that were worth at least \$250m at the start of 2022. These stocks, sorted into four cohorts based on year-end 2021 valuations, are being tracked by Evaluate Vantage over the year.

An analysis looking at the combined performance of these four groups was published earlier this week ([The gloom deepens for biopharma stocks](#), October 10, 2022). This found another huge drop in this universe's combined market cap, mainly owing to the painful tumbling of the world's largest drug developers.



Only three of the 11 big pharma companies in our grouping were above water at the nine-month mark. [Zantac litigation fears](#) and concern about US drug price controls are adding to pipeline doubts at several of these majors.

GSK's market cap was also affected by the spin-out of Haleon, and its valuation is now so diminished that its membership of the "big pharma" group could be questioned. It ended the third quarter ranked 19th on market cap in our universe, behind several large but less diversified developers like Regeneron and Vertex.



Biopharma's biggest stock market winners at 9 months			
Company	9-mth share price chg	9-mth market cap chg (\$bn)	Market cap at Sep 30, 2022 (\$bn)
Big pharma			
Lilly	17%	43.0	307
Bristol Myers Squibb	14%	13.4	152
Merck & Co	12%	24.6	218
Large cap (\$25bn+ market cap)			
Daiichi Sankyo	38%	12.3	62.3
Vertex	32%	18.4	74.3
Takeda	20%	3.64	47.2
Mid cap (\$5-25bn market cap)			
Neurocrine	25%	2.08	10.2
Sarepta	23%	1.84	9.68
Orion	20%	0.70	6.58
Small cap (\$250m-5bn market cap)			
Rhythm	145%	0.86	1.37
Lantheus	143%	2.88	4.84
Bioarctic	128%	1.09	2.09

Source: Evaluate Pharma. Companies were assigned these groups based on year-end 2021 market caps, and will remain in the same group for the rest of the year.

It should be noted that because AstraZeneca and Novartis report in US dollars rather than their native currencies, pounds Sterling and Swiss franc, Evaluate Pharma tracks these firms' ADRs, not their main share listings. This has unfairly disadvantaged Astra in this analysis because the drop in the value of Sterling has hit the company's US-listed ADRs.

Its London-listed stock was up 15% at the end of the third quarter, so in reality Astra should also be considered one of the better performing big pharma names this year.

ON THE UP...

Alzheimer's disease has been a big mover of share prices this year, with hopes for success buoying Lilly and Bioarctic, the former thanks to its phase 3 asset donanemab and [the latter as the originator of Eisai's lecanemab](#). Roche's year-to-date performance would be a lot worse had lecanemab not hit in its

pivotal trial, though pending data on the Swiss firm's gantenerumab will determine which way its stock moves in the coming months.

Among the large caps, Daiichi has benefited from Enhertu's successes in breast cancer. Takeda and Vertex are recovery stories, with both stocks having been laid low on pipeline concerns last year. Among the mid-caps Neurocrine continues to find fans for its CNS focus; Sarepta has seen expectations for [its DMD gene therapy rekindled](#); and Finland's Orion is riding high on a mid-stage [prostate cancer candidate that Merck & Co paid handsomely to license](#).

Rhythm is up on approval of Imcrivee for the rare genetic condition Bardet-Biedl syndrome. And finally Lantheus has led the minnows all year thanks to the hugely successful launch of a novel prostate cancer diagnostic, Pylarify, and its presence in radiopharmaceuticals.



Biopharma's biggest stock market losers at 9 months			
Company	9-mth share price chg	9-mth market cap chg (\$bn)	Market cap at Sep 30, 2022 (\$bn)
Big pharma			
Pfizer	-26%	-85.8	246
GSK	-19%	-49.2	59.9
Roche	-15%	-75.8	284
Large cap (\$25bn+ market cap)			
Moderna	-53%	-55.9	47.0
Beigene	-50%	-13.8	14.0
Biontech	-48%	-29.8	32.7
Mid cap (\$5-25bn market cap)			
Novavax	-87%	-9.40	1.42
Curevac	-77%	-4.94	1.48
Bausch Health	-75%	-7.43	2.49
Small cap (\$250m-5bn market cap)			
Endo	-97%	-0.86	0.02
Rubius	-96%	-0.83	0.04
Nordic Nanovector	-95%	-0.24	0.01

Source: Evaluate Pharma. Companies were assigned these groups based on year-end 2021 market caps, and will remain in the same groups for the rest of the year.

The first table above, highlighting the bright spots, masks the fact that few developers have seen substantial value gains this year. Four fifths of our universe was sitting on share price losses at the nine-month mark, with the low tide of investor support lying behind a lot of the declines.

Certain groups have been particularly punished, like the former pandemic plays, which are now coming back to earth. Pfizer, Moderna, Biontech, Novavax and Curevac all fall into this camp.

Another big group of losers is China-based developers, several of which have failed to recover from fears of tightening audit rules proposed by the US financial regulator. Ongoing concerns about the [the FDA's reluctance to use China-only data](#) in

approvals, as well as the broader malaise around high-risk biotechs, will also be weighing.

Elsewhere, Bausch Health became a smaller company after [floating its large eyecare division](#), Bausch + Lomb, in May. And Endo filed for bankruptcy protection in the face of mounting opioid litigation.

Finally, good old-fashioned clinical failure took down [Rubius](#) and [Nordic Nanovector](#).

Note: the 11 big pharma companies in this analysis are: Pfizer, Lilly, J&J, Roche, GSK, Abbvie, Bristol Myers Squibb, AstraZeneca, Sanofi, Merck & Co and Novartis.

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