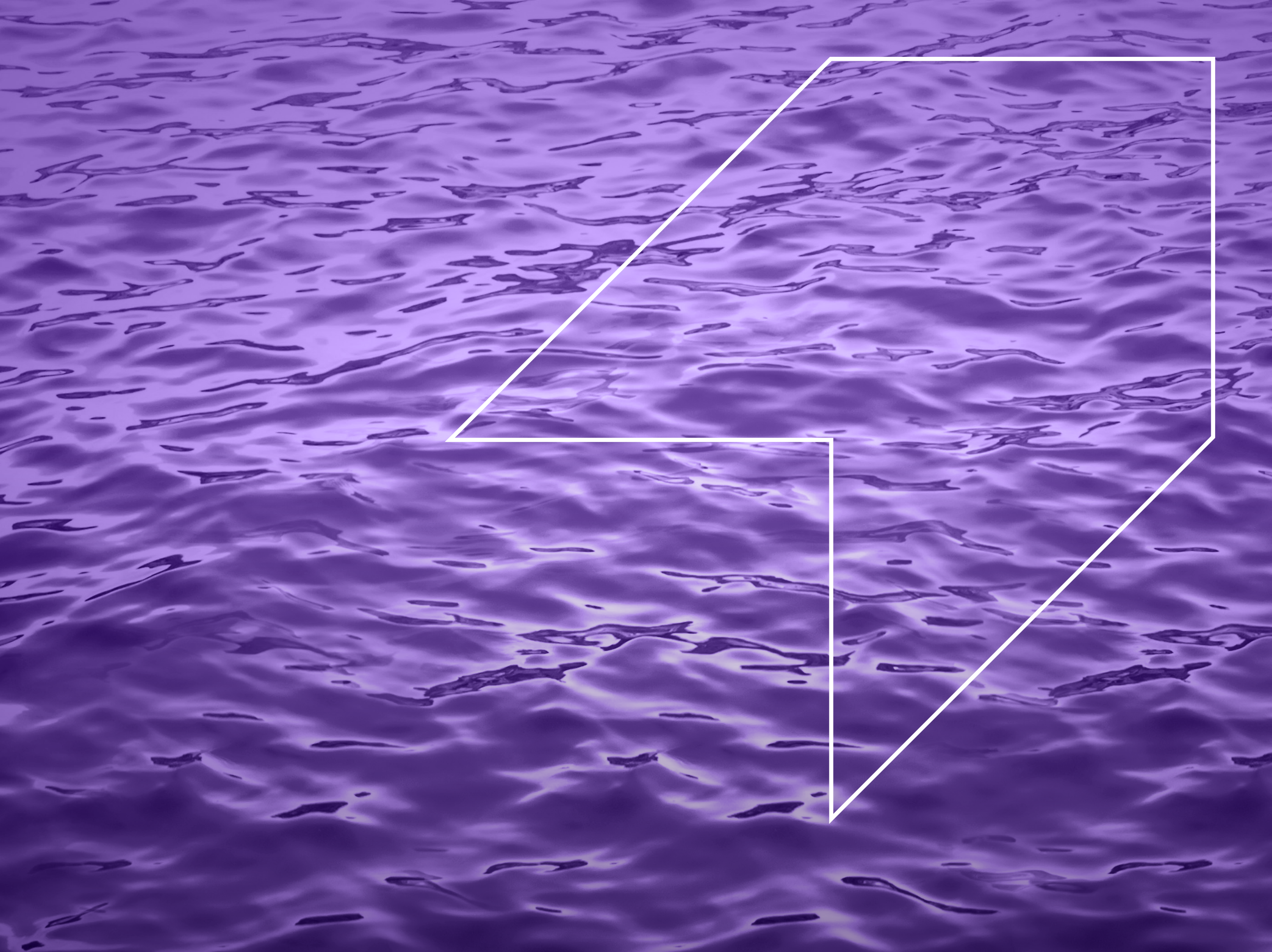

Q1 2022: In choppy waters, where are the safe havens?

By Edwin Elmhirst, Madeleine Armstrong & Amy Brown | MAY 2022

Introduction

If the first quarter of 2022 was a bellwether for the rest of year, many in the drug development market might want to don wet weather gear and hunker down for a blustery time. The Evaluate Vantage team has produced its round up of the investment and financial side of the industry and the results make for interesting – if sobering – reading.

Big pharma was the big winner – if winner is the right term in the current market – with all but two of these large developers trading up at the end of the first quarter. Across the Evaluate Pharma universe, however, 75% of biotech stocks were trading down for a $200bn decline in combined market cap.

Those big pharma companies might have plenty of capital to play with but there's little to show for that on the M&A side which hit a rather depressing five year low. Whatever it is that will get people shopping again, low valuations are clearly not it. So what is?

Meanwhile over on IPO corner, that loud bang you just heard was the IPO window slamming shut – or pretty close to it. Sentiment around biopharma - driven in part by wider geo-political and economic uncertainty – is distressingly low at the moment. And while a reset might be the answer to some of the recent concerns around the quality of businesses coming to the market, a complete closure of that window would be disastrous.

A break in the clouds comes from venture funding which is in fine fettle. Q1 outperformed almost every previous quarter with areas like gene therapy and "cellular rejuvenation programming" raking in the cash. But these VCs have a habit of wanting their money back at some stage, so the clock is ticking.

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Outside big pharma, life remains tough for listed developers

BY EDWIN ELMHIRST & AMY BROWN

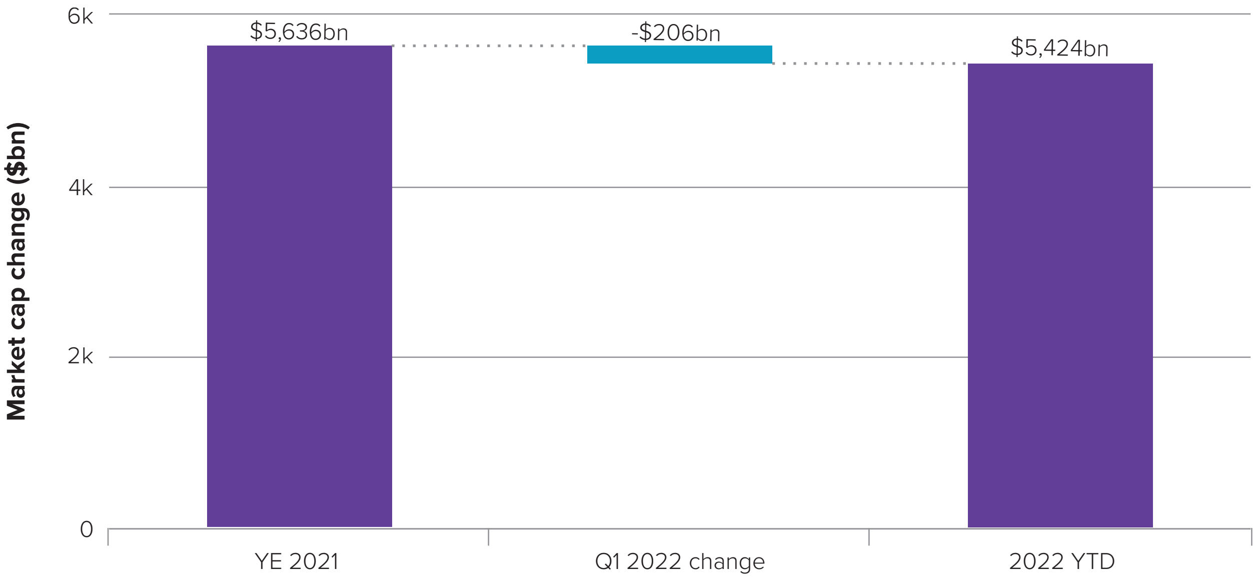
A look at stock performances over the first quarter of 2022 shows the extent to which investors have backed away from high-risk drug development.

Followers of the biotech market will be well aware of just how tough conditions for young developers are right now. That pain is not restricted to the small cap end of the market, Evaluate Vantage's quarterly look at global drug stocks shows.

With the exception of big pharma all market cap brackets suffered serious declines over the first quarter, in both absolute terms and percentage-wise. And while it was the big names in Covid vaccines that suffered the steepest drops, investors walked away from plenty of other non-pandemic stories.

This analysis is constructed from the almost 700 globally listed drug makers covered by Evaluate Pharma, sorted into four cohorts based on year-end 2021 valuations. Nano-caps worth less than $250m are not considered; companies will remain in their assigned bucket for the whole of 2022.

Figure 1: The shifting valuation of global drug makers



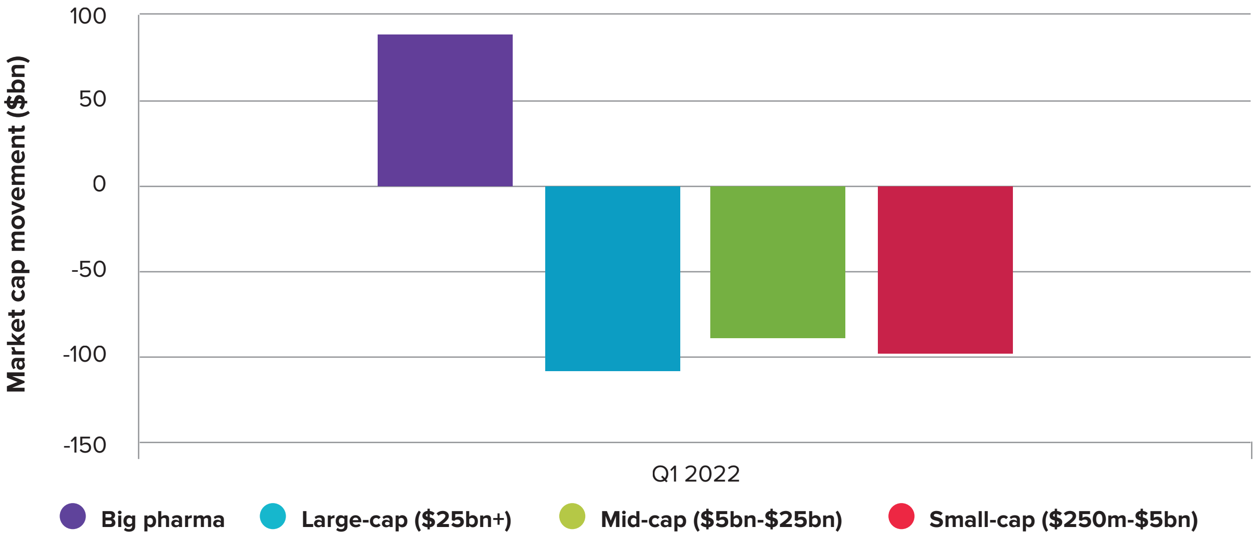
Source: EvaluatePharma®

The first chart, above, shows that this universe collectively lost more than $200bn in market cap over the first three months of the year. To put that in perspective, last year the biggest quarterly decline registered was $84bn, while the market crash of 2020, when the pandemic was declared, amounted to a $448bn plunge in the second quarter.

Splitting the universe by market cap, in the two charts below, further details the damage. Among the large caps Moderna and Biontech lost a combined $55bn in value, while concerns about the potential delisting of Chinese biotechs sent several big dual-listed developers down.

Twelve of the 21 stocks that make up the big cap group fell over the quarter, which sounds pretty bad until the smaller cap brackets are considered. 75% of the 88 mid-cap stocks and 80% of the 550-odd small cap companies in this universe traded down in the opening months of the year.

Figure 2: Absolute market cap gains and losses, by size bracket

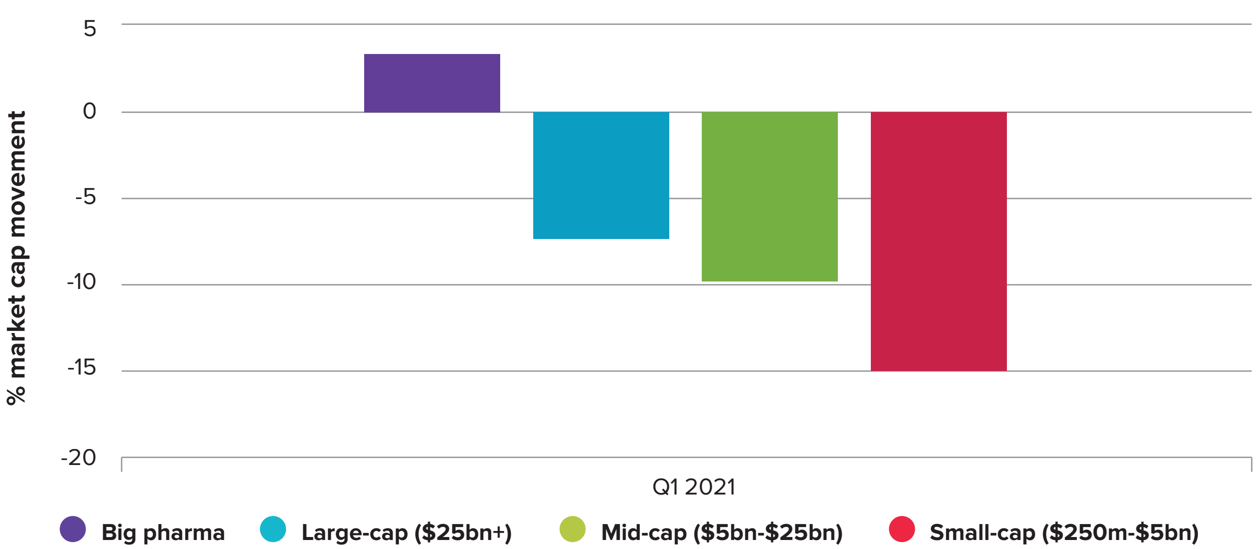


Source: EvaluatePharma®

Big pharma, which is considered something of a safe haven in more risk-averse times, was the only bright spot. Only two stocks ended March down on the year – Pfizer and Roche – with the former being this group's most notable decliner, shedding $34bn in market cap.

It seems that Covid is over, for investors at least, many of whom continue to flee biotech for industries that are returning to post-pandemic growth. With inflation fears mounting and global instability seemingly worsening, life could remain tough for this high-risk sector for many months to come.

Figure 3: Percentage market cap gains and losses, by size bracket



Source: EvaluatePharma®

First-quarter biotech risers work hard for the win

BY AMY BROWN

Amid a difficult start to the year for the drug development sector, Abbvie, Bayer, Ipsen and Lantheus stand out as stock market gainers.

Outside the safe haven world of big pharma the opening months of 2022 proved a torrid time for biopharma stocks. The declines of last year deepened as investors remained disinclined to back high-risk drug development, leaving the vast majority of the sector in the red.

All of which makes the gains that were achieved in the first quarter all the more notable. Top marks go to Lantheus in the small caps and Ipsen in the mid caps, both of which put on impressive valuation gains. Meanwhile, among the long list of decliners the exit from Covid stocks gathered pace.

This analysis was constructed from the almost 700 listed, global biopharma companies covered by Evaluate Pharma that were worth at least $250m at the start of 2022. These stocks will be tracked by Evaluate Vantage over the year.

A look at the biggest winners of the quarter reveals moderate moves, with none of the flashy market caps gains of previous years. In a stark statistic, by the end of March almost three-quarters of the stocks in this universe were trading down.

Big pharma benefitted from the market's flight from risk, with only two groups falling over the three months. Abbvie's gain is still notable, however – the stock went on to hit a record high in April, driven in part by hopes for Rinvoq after the drug's approval in ulcerative colitis.

Biopharma's biggest stock market winners in Q1 2022			
Company	Q1 share price change	Q1 market cap change ($bn)	Market cap at March 30, 2022 ($bn)
Big pharma			
Abbvie	20%	47.1	286.5
Bristol Myers Squibb	17%	18.3	156.7
Astrazeneca	14%	23.5	203.9
Large cap ($25bn+ market cap)			
Bayer	31%	14.5	67.4
Vertex	19%	9.8	65.7
Takeda	12%	1.4	44.9
Mid cap ($5-25bn market cap)			
Ipsen	41%	3.0	10.8
Exelixis	24%	1.5	7.2
Jazz Pharmaceuticals	22%	1.8	9.6
Small cap ($250m-5bn market cap)			
Lantheus Holdings	91%	1.81	3.77
Biodelivery Sciences	80%	0.27	0.58
Ascletis Pharma	58%	0.26	0.73

Companies were assigned these groups based on year end 2021 market caps, and will remain in the same group for the remainder of the year.

Source: Evaluate Pharma.

Other larger, profitable biopharma groups like Bayer, Vertex and Ipsen will also have benefitted from offering something of a safe haven. And for investors that want to maintain a lower-risk exposure to biotech, companies like Exelixis and Jazz, which have successfully ushered products on to the market, will have been more appealing than earlier-stage developers.

Among the small caps, Lantheus's impressive gains stem from a hugely improved financial performance, partly thanks to its acquisition of Progenics. Biodelivery Sciences is being taken private by speciality pharma group Collegium, while hopes for a novel Covid antiviral boosted Chinese biotech Ascletis.

On the way down

Several Chinese companies also feature in the fallers, knocked by fears of tightening audit rules proposed by the US regulator. Beigene and Hutchmed are both on the SEC's non-compliance list, although the situation looks likely to be resolved.

Fellow Chinese biotech Innovent fell after its Lilly-partnered anti-PD-1 checkpoint inhibitor, Tyvyt, was turned down by the FDA.

One pattern that looks likely to persist this year is pressure on the big Covid vaccine suppliers; these groups could see further declines on growing doubts about future demand. And of course the ever-present biotech trend – clinical failure – will always be on show.

Kodiak is trading well below cash in the wake of its macular degeneration disaster; Proqr is looking similarly doomed after its failure with a gene therapy for a rare cause of blindness; and finally MEI is being punished for pushing on with PI3K inhibition, a cancer mechanism associated with toxicity and weak efficacy and on which the FDA has clearly heard enough.

Biopharma's biggest stock market losers in Q1 2022

Company	Q1 share price change	Q1 market cap change ($bn)	Market cap at March 30, 2022 ($bn)
Big pharma			
Pfizer	-12%	-33.6	297.9
Roche	-3%	-9.2	350.9
Novartis	0%	0.3	195.9
Large cap ($25bn+ market cap)			
Biontech	-34%	-21.2	41.4
Moderna	-32%	-33.6	69.4
Beigene	-30%	-8.4	19.3
Mid cap ($5-25bn market cap)			
Novavax	-49%	-5.2	5.6
Hutchmed	-46%	-2.8	3.3
Innovent Biologics	-44%	-4.0	5.1
Small cap ($250m-5bn market cap)			
Kodiak Sciences	-91%	-3.98	0.40
Proqr Therapeutics	-88%	-0.33	0.06
MEI Pharma	-77%	-0.22	0.08

Companies were assigned these groups based on year end 2021 market caps, and will remain in the same group for the remainder of the year.

Source: Evaluate Pharma.

Takeover-driven resurgence fails to materialise for biotech

BY AMY BROWN & EDWIN ELMHIRST

Deal making in biosimilars dominates a slow start to the year for biopharma M&A.

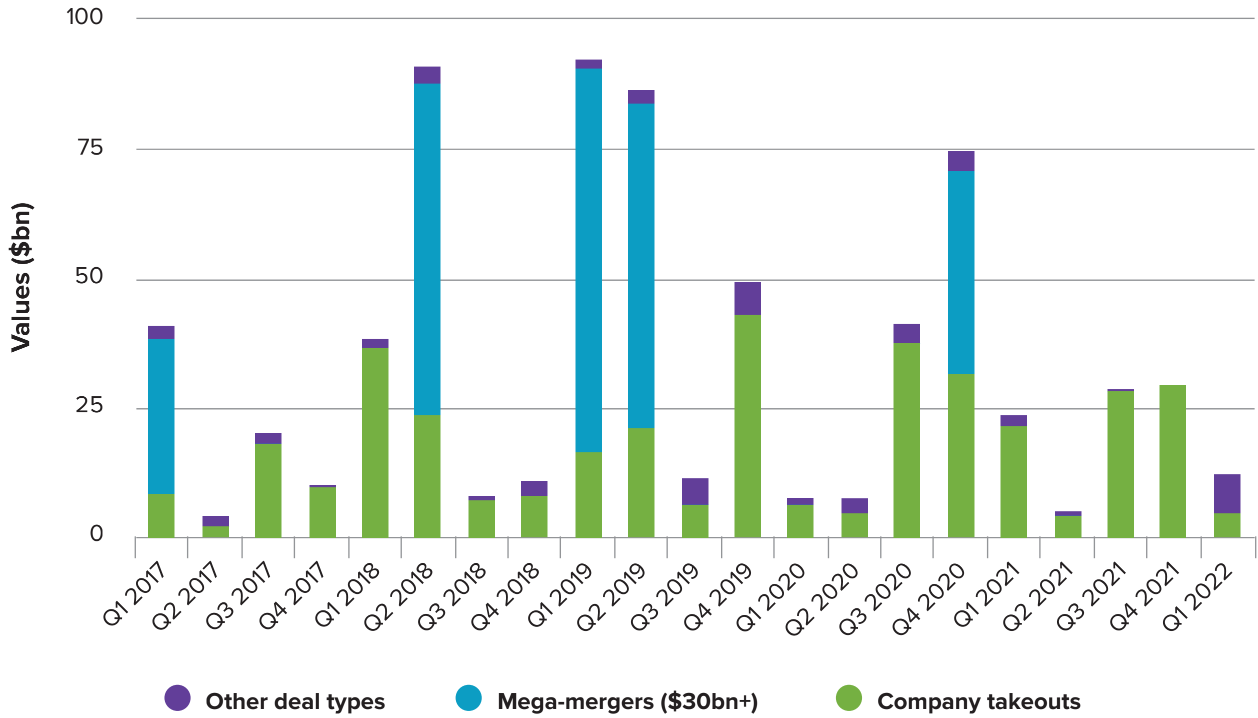
Those hoping for a string of buyouts to tempt investors back into biotech will be disappointed by the opening months of 2022. Transaction volume fell to a five-year low in the first quarter, while the sums involved were only rescued by two big joint-venture deals in the biosimilars space.

True, a couple of deals emerged, with Glaxosmithkline's move on Sierra Oncology showing that big pharma is still shopping. But large public buyouts have been notable by their absence in 2022 so far, with only three of the 21 company acquisitions recorded by Evaluate Pharma in the first quarter concerning a listed developer.

One of those, Eagle's buy of the distressed group Acacia, was struck at a 30% discount – hardly the transaction to get investors' pulses racing.

The dearth of takeouts shows that depressed valuations should not be considered a driver of M&A. Such theories are wishful thinking and, as the Acacia situation shows, the outcome of deals struck in more difficult times can be disappointing, particularly for those left holding the bag.

Figure 1: Combined M&A deal values



Source: EvaluatePharma®

As the chart above shows, M&A deals other than full company takeouts dominated in the first quarter; this "other deal type" category incorporates majority and minority stake purchases and business unit buys.

This analysis does not concern licensing deals, or transactions not involving therapeutics; companies involved in medtech or digital health are not considered, for example.

It was two biosimilars joint-venture deals that moved the needle in the first quarter: Biogen's sale of its 49.9% stake in Samsung Bioepis to the other party in the joint venture, Samsung Biologics, and Biocon's buyout of certain biosimilar assets from Viatris.

UCB's move on the US biotech Zogenix, for its rare epilepsy drug, was the most notable full company takeover of the quarter.

Biggest biopharma M&A deals announced in Q1 2022			
Acquirer	**Target**	**Status**	**Deal terms**
Biocon	Viatris biosimilar venture	Open	Total value $3.3bn (includes $1bn of shares in Biocon Biologics)
Samsung Bioepis	Biogen stake in biosimilar JV	Open	Total value $2.3bn (includes $1bn cash up front)
UCB	Zogenix	Closed	$1.9bn in cash up front (plus $2 per share CVR)
Biohaven	Knopp's Channel Biosciences unit	Open	Total value $1.2bn ($100m up front)
Abbvie	Syndesi Therapeutics	Closed	Total value $1.0bn ($130m up front)

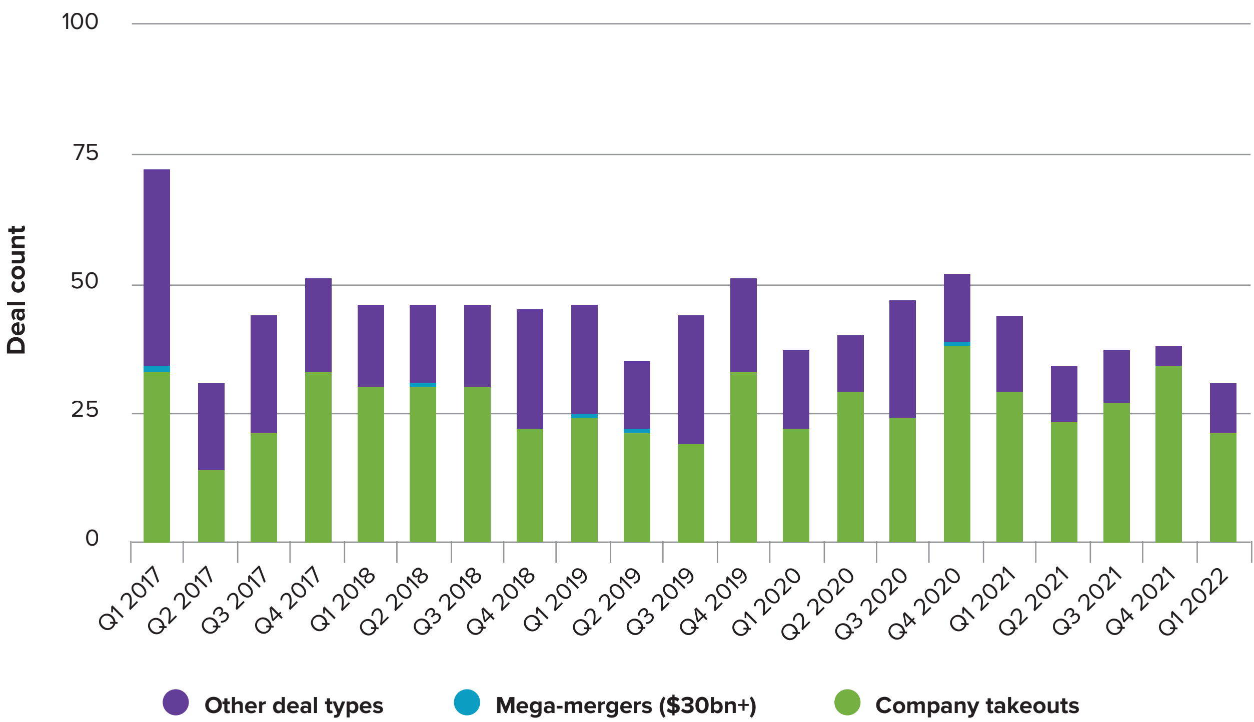
Source: Evaluate Pharma.

The question for investors is what might be holding buyers back. Access to capital is never a problem for the world's largest developers, a group that will buy desired assets pretty much regardless of wider market conditions. Indeed, an influx of Covid cash has driven expectations for an uptick in buyouts.

And the closing of Pfizer's acquisition of Arena without any apparent antitrust interference might have calmed the worst fears of a tightening stance from anti-competition regulators.

Perhaps the answer lies more on the other side of the negotiating table. Targets will be disinclined to sell up while valuations are so low, and for now much of the sector remains cashed up and able to resist low-ball approaches. But the funds raised while the going was good will not last for ever.

Figure 2: Quarterly M&A deal counts



Source: EvaluatePharma®

Flotations tank in the first quarter

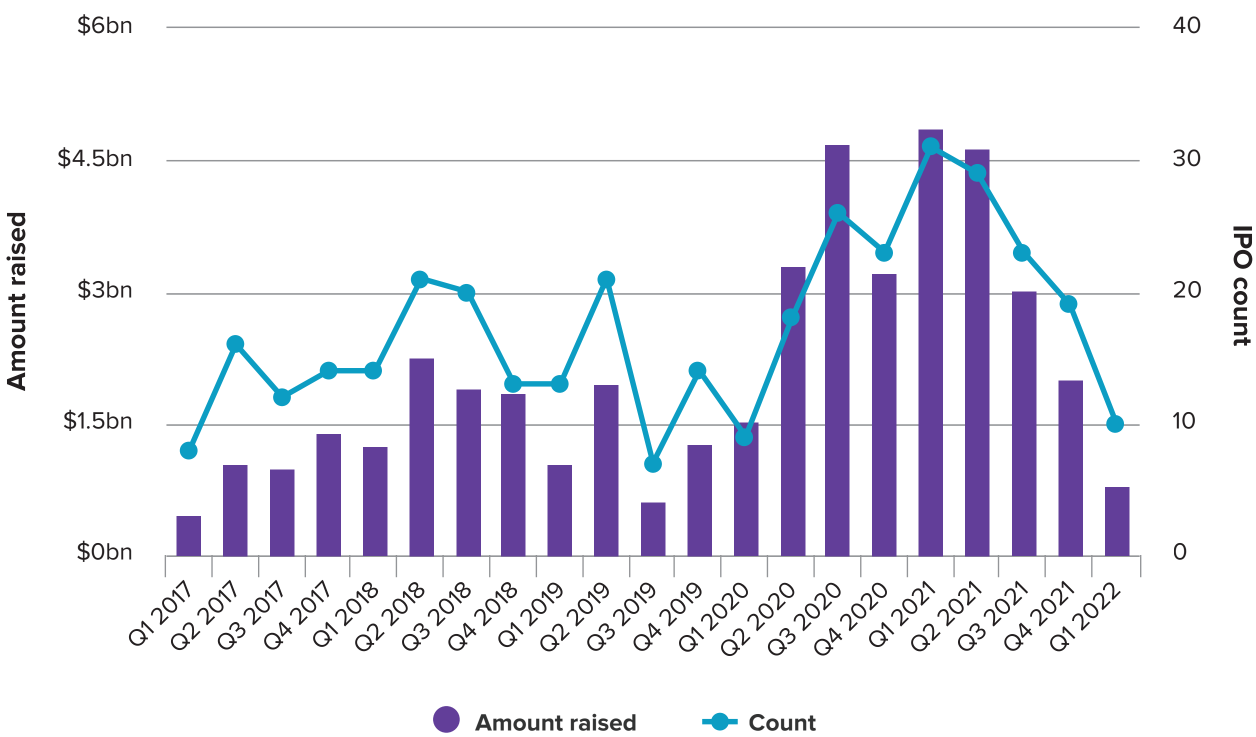
BY EDWIN ELMHIRST & MADELEINE ARMSTRONG

A correction – as long as it is not too severe – might not be a bad thing for the sector.

After a couple of years in which biotechs had seemingly unfettered access to the public markets it's official: the IPO window is closing. The latest analysis of Evaluate Pharma data shows a marked drop in public offerings in the first quarter, with the fewest flotations since early 2020, when the pandemic hit.

However, unlike in 2020, this does not look like a blip. Sentiment around biopharma is dismal, and there are broader fears about the impact of war and inflation. Things look set to get worse before they get better; the question now is how low IPOs can go.

Figure 1: Biotech IPOs by quarter on Western exchanges



Source: EvaluatePharma®

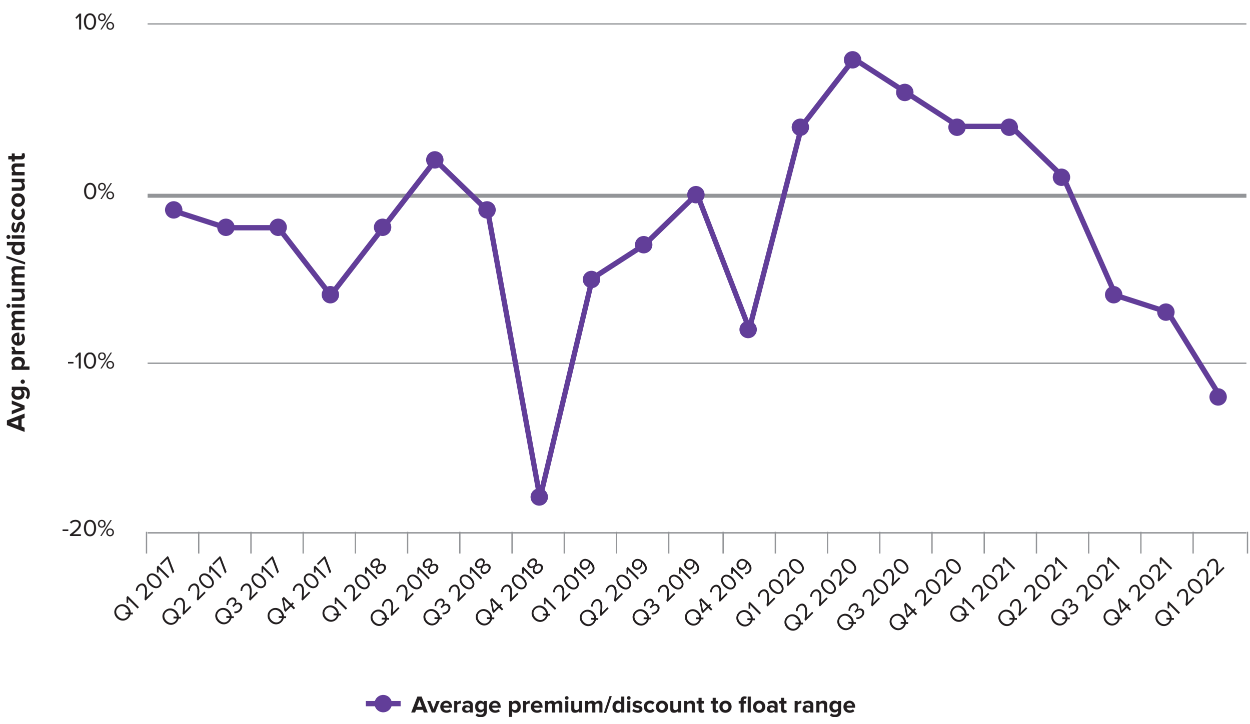
Still, for the biotech sector at least, a slowdown in public offerings might not be all bad. Some investors have long bemoaned a flood of low-quality companies onto the public markets, blaming this, at least in part, for dragging down biotech stocks in general (for more on this, see **Evaluate Vantage's 2022 Preview**).

Some groups did manage to get away in the first quarter, but the chart below shows that many of these have had to accept the harsh new reality: the average discount to a planned IPO price reached lows not seen since late 2018, another period marked by stock market turmoil.

And many of the big floaters have not done well on the markets since their public debuts. A case in point is Amylyx, whose shares plunged after an FDA adcom raised doubts about the chance of its amyotrophic lateral sclerosis project AMX0035 gaining early approval.

Amylyx is an uncommon example of a late-stage company going public, but all of the first quarter's top five groups at least have projects in the clinic – unlike some recent periods that have been marked by preclinical IPOs, a trend that has attracted a lot of flak.

Figure 2: Tracking demand for IPOs



Source: EvaluatePharma®

The other big IPO last quarter involved the phase 2 player Cincor, which is in the somewhat unfashionable area of hypertension. Cincor and Amylyx have each pinned their hopes on one asset, so it should quickly become apparent whether either group has a future.

The CNS player Vigil, meanwhile, is tied not to one project but to a single target, Trem2. There are questions about this approach: the FDA has stopped the group dosing over 20mg/kg with its lead asset, VGL101, while Denali's similarly acting DNL919 is on clinical hold, and Alector/Abbvie's Trem2-targeting project AL002 has been linked with amyloid-related imaging abnormalities (Aria).

Of course, investing in biotech is always risky, and the current crop will be no exception. Ultimately, though, if an IPO reset leads to an improvement in the quality of companies reaching the public markets this would be a good thing. On the flipside, a complete closing of the IPO window would be a disaster for the sector, which relies on a pool of early innovation to feed the bigger companies.

Biggest IPOs by amount raised in the first quarter of 2022				
Company	**Primary focus**	**Amount raised ($m)**	**Premium/(discount); float price to initial offer**	**Share price change since float to end Q4**
Cincor Pharma	Cardio-renal diseases	194	0%	10%
Amylyx Pharmaceuticals	Neurodegenerative diseases	190	0%	-32%
Arcellx	T-cell therapies	142	-6%	-7%
Vigil Neuroscience	Neurodegenerative diseases	98	-13%	-50%
AN2 Therapeutics	Infectious diseases	69	0%	0%

Source: Evaluate Pharma & SEC filings.

Venture funding stays strong despite the gloom

BY EDWIN ELMHIRST & MADELEINE ARMSTRONG

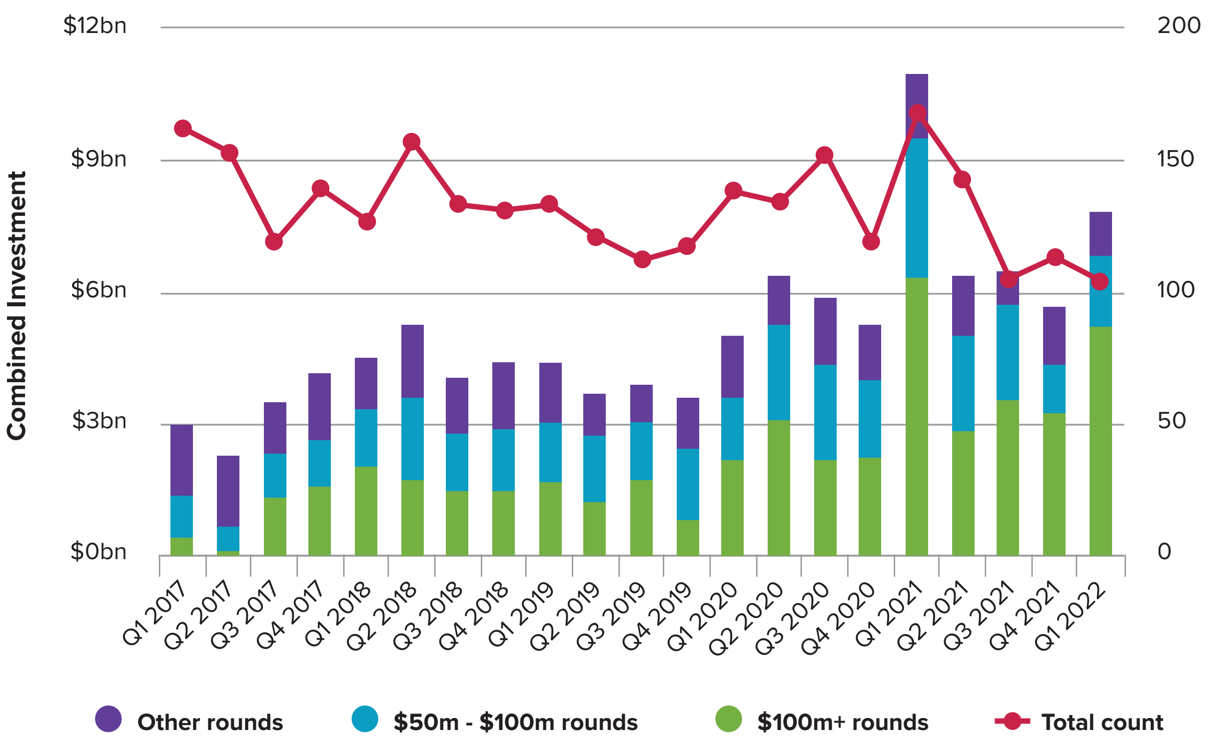
But how long can the money keep rolling in?

Biotech companies are struggling on the public markets, the IPO window is all but closed, and big pharma is not buying. Despite all this, venture financing for young biotech groups remains in rude health.

In fact, the first quarter of this year outperformed every other barring 2021's monster first quarter, the latest analysis of Evaluate Pharma data shows. The big question now is how long this source of funding can hold up given the broader issues the sector is facing.

Ultimately, venture backers want their exits, and if these are not available it will become harder for private companies to attract cash.

Figure 1: Quarterly biopharma VC rounds



Source: EvaluatePharma®

At least one VC, Bruce Booth of Atlas Venture, believes that the money will not dry up, at least in the near future. He noted that various funds had recently “reloaded”, with this cash earmarked for biotech.

However, he sounded a note of caution: the formation of new US biotech groups appears to have fallen off a cliff, based on the number of first financings, which might be an early sign of souring sentiment.

Live forever

For now, though, early-stage groups still have the opportunity to rake in huge amounts of cash. The first quarter demonstrated this neatly with a $3bn round for the newest anti-ageing specialist on the block, Altos Labs.

Altos will be headed by Glaxosmithkline’s Hal Barron, and is said to count Jeff Bezos among its investors; with a focus on “cellular rejuvenation programming” it is perhaps on the fringes of what can be classed as biotech. Removing this fund raising from the analysis makes the first quarter look more ordinary, but only in the context of the past two years, which set records for VC investment.

This analysis concerns pure-play drug developers only, and excludes sectors like medtech and digital health.

A look at the other big rounds shows that gene therapy and editing remain popular, despite the fact that this sector has largely failed to live up to the hype, and genetic medicine specialists have seen their stocks languish as a result. **For more on the next generation of genetic medicine, take a look at our new report.**

Still, Maze Therapeutics has not put all its eggs in the gene therapy basket, and is also developing large and small molecules against genetically defined targets. And Metagenomi gained validation via a partnership last year with Moderna.

For now, these young private groups – and others like them – appear to have little reason to worry. But if the current downturn persists then this picture is likely to change.

Top five rounds of Q1 2022			
Company	**Investment ($m)**	**Financing round**	**Description**
Altos Labs	3,000	Undisclosed	Cellular rejuvenation programming
Kallyope	236	Series D	Gut-brain axis therapies
Maze Therapeutics	190	Undisclosed	Rare and common genetically defined diseases
Affini-T Therapeutics	175	Undisclosed	T cell therapies
Metagenomi	175	Series B	Gene editing

Source: Evaluate Pharma.

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