Q1 2023 Round Up: And so it continues...

BY AMY BROWN, EDWIN ELMHIRST, ELIZABETH CAIRNS AND MADELEINE ARMSTRONG
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eBOOK

Evaluate Vantage

Foreword

Anyone hoping that a new year would bring an immediate change of fortunes for battered biotech will have been less than impressed with the first quarter of 2023. Given the state of the global economy and the stock markets, a recovery was perhaps too much of an ask.

Regardless, we must dig into the data to understand where we are and if – at last – we might be hitting the much anticipated bottom. As always, the *Evaluate Vantage* team has investigated the share price performance, IPO action, M&A activity and venture financing situation across the biopharma sector. In this eBook, we've pulled it all together to provide a single, if not uplifting, view.

There are, if you squint, some signs of promise on the IPO front. There were a third more IPOs in the first quarter than in the preceding three months, though that's less impressive when you recall there were only three flotations at the end of last year. Still, for the first time since early 2021 the cohort on average priced at a premium to their preannounced ranges, rather than a discount and, so far, their prices have risen since flotation.

Venture financing took another downturn, however, which does not point to any immediate uplift in the IPO market.

The M&A situation is all about one name – Pfizer. The not-very-shocking announcement of the big pharma's planned acquisition of Seagen made up the bulk of the dealmaking spend for the quarter and gives the industry its first megadeal since 2020. It was by no means the only deal in town, with Sanofi and Astrazeneca also splashing some cash, but it was by far the biggest.

The share price picture remains pretty bleak for all but a handful of players, and we share two articles which analyse around 500 listed, global biopharma companies and compare their performance to their peers. Spoiler alert – Pfizer tops a table here too. Read on to see which.

There is plenty of food for thought and with some exciting catalysts coming up in the remainder of the year, particularly in some hotly contested indications, there are plenty of events on the horizon that might drive further big share price swings in 2023. For now, though, let's get on with it.

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Biopharma stocks go back to bleak

BY EDWIN ELMHIRST AND MADELEINE ARMSTRONG
APRIL 05, 2023

Hopes for a better 2023 look optimistic as markets take another turn for the worse.

At the end of last year it seemed like things might be looking up for biopharma stocks, with big pharma riding high. The first quarter of 2023, however, has fallen back into an all-too-familiar pattern, with large losses for many of companies in the *Evaluate Vantage* universe.

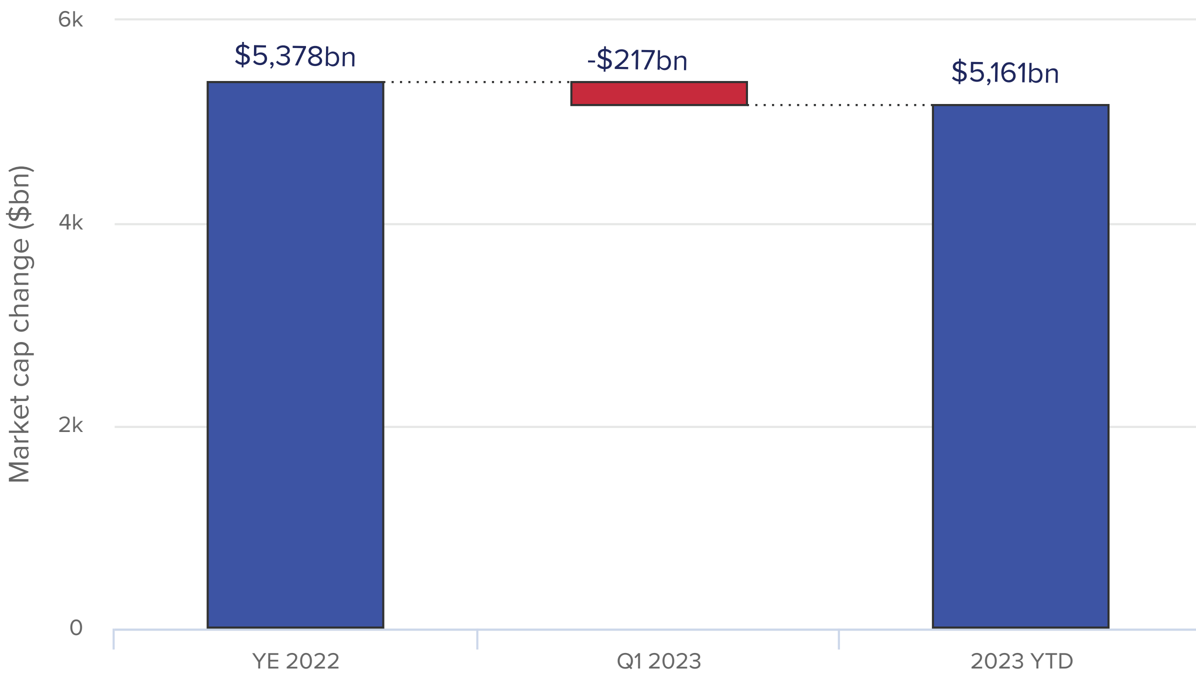
Big pharma crashed, losing $199bn in value overall. And a boost in the large-cap group was flattered by the rocketing share price of Seagen on the news that the group was being acquired by Pfizer. Hopes that the bottom of the market had been reached now look premature.

This analysis includes around 500 globally listed biophama stocks tracked by *Evaluate Pharma*; only pure-play developers, and only those that started 2023 with a market cap of at least $250m, are considered. Companies are assigned to their cohort at the start of the year, and will remain there throughout 2023. The changes to these groups versus 2022 make a direct comparison with last year's analyses difficult.

In addition the large-cap cohort this year comprises players with a market cap of $20bn or above; previously, this bracket included $25bn-plus groups.

Notwithstanding these caveats, the charts below show a reverse in fortunes for big pharma, often considered a relatively safe haven during turbulent times.

The shifting valuation of global drug makers

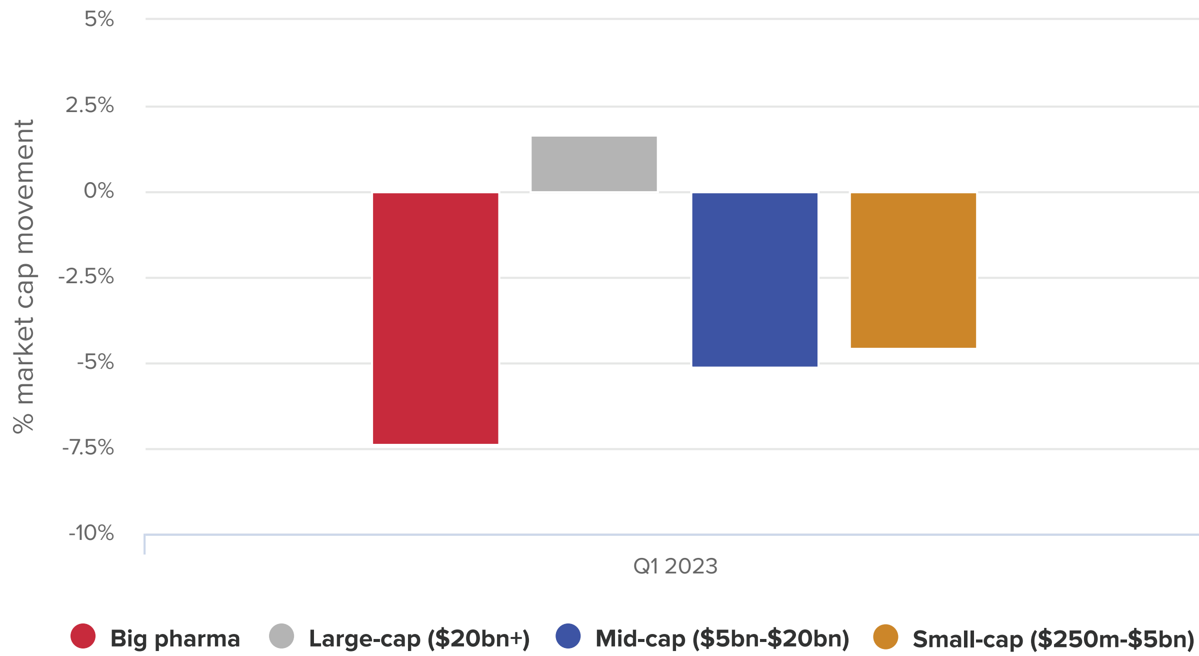


Source: Evaluate

Pfizer had a particularly rough ride, losing 21% of its market cap in the first quarter. The group's Covid franchise is waning and patent expiries are looming, while there are doubts about its R&D pipeline. Pfizer is buying furiously to fill this hole, spending $43bn on Seagen last month, following last year's bolt-ons of Biohaven and Global Blood.

Other big pharma groups also suffered, with falls almost across the board. Only Astrazeneca and Sanofi escaped the bloodbath, with the latter's 12% rise due to success with its own big seller, the Regeneron-partnered Dupixent, in COPD.

Percentage market cap gains and losses, by size bracket



Source: Evaluate

Aside from Seagen – which is included in this analysis as the deal has yet to close – there were other gainers in the large-cap cohort. This included Regeneron, also boosted by the Dupixent COPD data, and Novo Nordisk, which is seeing strong demand for its obesity drug Wegovy.

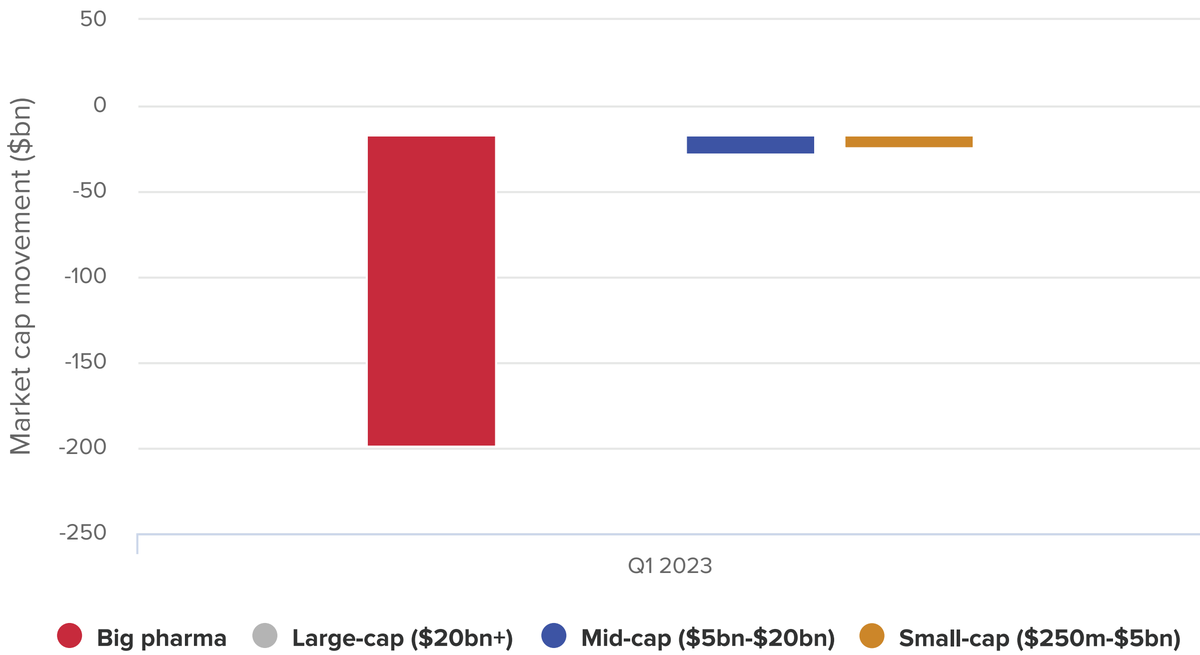
There has been some discussion about whether Novo, among others, should be included in the big pharma cohort, but for now the group's relatively narrow therapeutic focus means that it has stayed in the large cap bracket.

Even excluding Seagen the large-cap cohort added $21bn in market cap, an increase of 1% – representing a win, albeit a small one.

Mid and small-cap players were not so lucky. On a relative basis these did just as badly as the big pharma group. There were some success stories here, driven by the usual mix of clinical and regulatory wins – see Apellis, Bridgebio, Protagonist and Reata – and takeouts such as those of Albireo, Amryt and Provention Bio.

But only around a third of the mid and small-cap groups ended the first quarter in positive territory. The longer the current market gloom continues, the tougher it will get for those at this end of the spectrum – but this latest analysis shows that big groups are not immune either.

Absolute market cap gains and losses, by size bracket



Source: Evaluate

Note: Evaluate Vantage's universe is constructed from pure-play drug developers listed globally, with the majority sited in the US, Europe or Japan. Chinese developers must have a dual ex-China listing for inclusion. The big pharma cohort consists of 11 companies: Pfizer, J&J, Merck & Co, Lilly, Abbvie, Roche, Astrazeneca, Novartis, Bristol Myers Squibb, Sanofi, GSK.

The Covid crash continues

BY MADELEINE ARMSTRONG AND EDWIN ELMHIRST
APRIL 06, 2023

Pfizer keeps declining, but it is not the only pandemic player to suffer.

Covid made Moderna and Biontech household names and propelled Pfizer to the top spot in the big pharma league. But with the pandemic a distant memory the good times are over for these players, *Evaluate Vantage's* quarterly analysis of the stock markets has found. In the coming months and years these groups' pipelines look set to come into sharper focus.

Winners were rarer, but some companies are still being rewarded for unexpected clinical and regulatory success – just ask the likes of Apellis, Reata and Bridgebio. Sanofi's shares were also bolstered by a surprise win with Dupixent in COPD; that group's stock is now almost back to year-ago levels, before the threat of Zantac litigation appeared. This will be a relief to its under-fire boss, Paul Hudson.

This analysis was constructed from the around 500 listed, global biopharma companies covered by *Evaluate Pharma* that were worth at least $250m at the start of 2023. These stocks will be tracked by *Evaluate Vantage* over the year – an analysis of the performance of four cohorts, grouped by market cap, was published yesterday (*Biopharma stocks go back to bleak*, April 5, 2023).

Big pharma is not looking like much of a safe haven, with all but two of these groups – Sanofi and Astrazeneca – falling. In addition to Pfizer, big losers included Roche, which is facing questions about its pipeline following recent failures, and Johnson & Johnson, whose baby powder controversy continues. Yesterday shares climbed after J&J, which is in the midst of separating its consumer business, proposed a $9bn settlement.

Biopharma's biggest stock market losers in Q1 2023			
Company	**Q1 share price chg**	**Q1 market cap chg ($bn)**	**Market cap at 31 Mar 2023 ($bn)**
Big pharma			
Pfizer	-21%	-60.4	227.2
Johnson & Johnson	-13%	-58.2	403.7
Roche	-11%	-28.5	228.0
Large cap ($20bn+ market cap)			
Biontech	-19%	-6.8	29.6
Alnylam	-17%	-4.9	24.3
Moderna	-17%	-11.6	57.4
Mid cap ($5-20bn market cap)			
Halozyme Therapeutics	-33%	-2.5	5.2
United Therapeutics	-22%	-2.6	10.1
Neurocrine Biosciences	-19%	-2.1	9.4
Small cap ($250m-5bn market cap)			
Oramed Pharmaceuticals	-82%	-0.4	0.1
Veru	-75%	-0.3	0.1
Altimmune	-73%	-0.6	0.2

Source: Evaluate Pharma. Companies are assigned these groups based on year-end 2022 market caps, and remain in the same group for the rest of the year.

Investors are jittery about Alnylam's chances in amyloidosis cardiomyopathy, while Halozyme and Neurocrine are facing questions about the impact of the Inflation Reduction Act. United Therapeutics, meanwhile, dropped after strong results from Merck & Co's sotatercept, a rival to United's pulmonary arterial hypertension projects.

Oramed and Altimmune were hit by old-fashioned clinical failures, while Veru got an FDA knockback for its Covid contender sabizabulin.

ACTIVIST AGITATION

Among the winners, investors hope that the incoming Bayer chief executive, Bill Anderson, could be planning to separate its healthcare and agricultural businesses. He said this week that he was keeping an "open mind" about a potential break-up.

Shareholders are also agitating for change at Exelixis, where the fund Farallon Capital has been building a stake, a fact that explains that group's share price rise in the wake of a recent clinical failure.

More traditional reasons were behind other rises. Apellis and Reata got surprising approvals for the geographic atrophy drug Syfovre and Friedreich's ataxia therapy Skyclarys respectively, while Bridgebio rocketed on promising achrondroplasia data in 10 patients. And Aurinia, once mooted as a takeover target, is seeing sales of its lupus drug Lupkynis pick up after initially disappointing.

Biopharma's biggest stock market winners in Q1 2023			
Company	**Q1 share price chg**	**Q1 market cap chg ($bn)**	**Market cap at 31 Mar 2023 ($bn)**
Big pharma			
Sanofi	12%	14.2	135.9
Astrazeneca	1%	2.6	212.8
Large cap ($20bn+ market cap)			
Seagen	57%	13.9	37.8
Bayer	18%	9.1	60.6
Novo Nordisk	17%	53.5	358.0
Mid cap ($5-20bn market cap)			
Apellis Pharmaceuticals	28%	1.6	7.4
Exelixis	20%	1.0	6.2
Shanghai Pharmaceuticals Holding	15%	2.2	9.9
Small cap ($250m-5bn market cap)			
Aurinia Pharmaceuticals	161%	1.0	1.6
Reata Pharmaceuticals	137%	1.7	2.9
Bridgebio Pharma	130%	1.5	2.7

Source: Evaluate Pharma. Companies are assigned these groups based on year-end 2022 market caps, and remain in the same group for the rest of the year.

Note: Evaluate Vantage's universe is constructed from pure-play drug developers listed globally, with the majority sited in the US, Europe or Japan. Chinese developers must have a dual ex-China listing for inclusion. The big pharma cohort consists of 11 companies: Pfizer, J&J, Merck & Co, Lilly, Abbvie, Roche, Astrazeneca, Novartis, Bristol Myers Squibb, Sanofi, GSK.

Floating biotechs prompt tiny sparks of hope

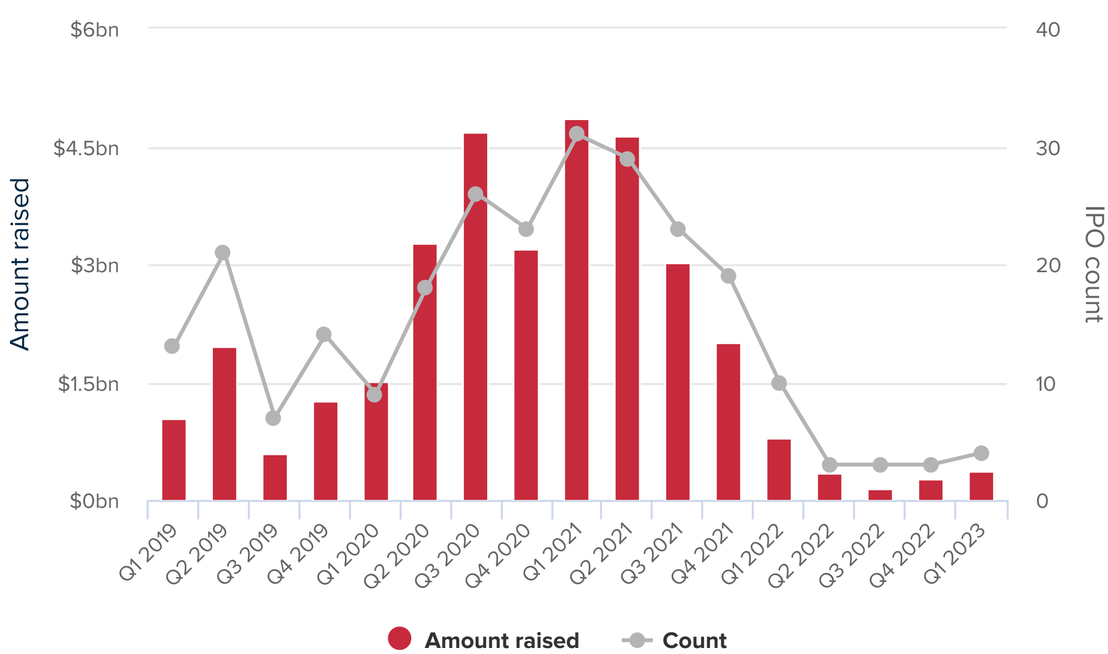
BY ELIZABETH CAIRNS AND EDWIN ELMHIRST
APRIL 06, 2023

But with only four IPOs so far this year, there is no disguising a moribund market.

The best that can be said for the biotech IPO scene in the first quarter of this year is that, with a grand total of four flotations collectively raising $375m, it is at least better than the previous three months.

There are other green shoots of hope: for the first time since the second quarter of 2021 the cohort on average priced at a premium to their preannounced ranges, rather than a discount. And they have, again on average, seen their shares rise since floating, no mean feat in the current environment. Even so, the possibility of recapturing the glory days that began three years ago seem as dim as ever.

Biotech IPOs by quarter on Western exchanges



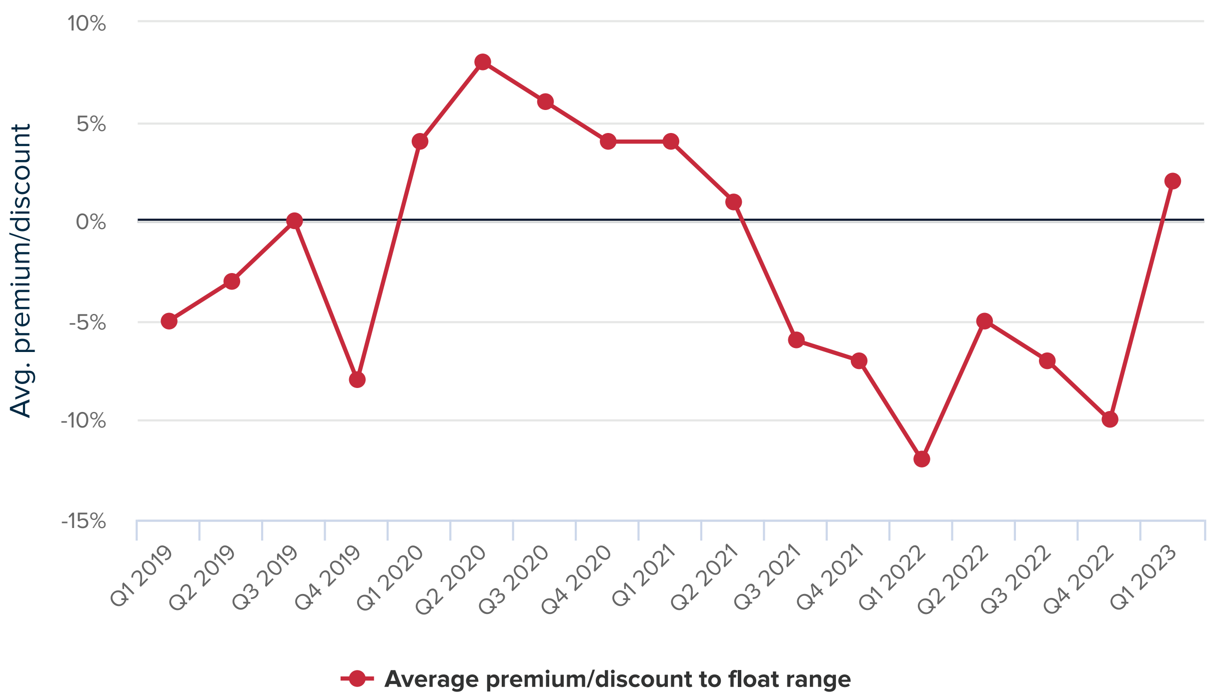
Source: Evaluate

The outstanding success of this quarter is Genelux, whose lead project has two major aspects that appeal to investors: it is a cancer therapy, and it is already in late-stage trials. The company kicked off the pivotal study of Olvi-Vec, which is based on a modified oncolytic vaccinia virus, in September, and data could come next summer.

The OnPrime trial, testing Olvi-Vec on top of platinum-doublet chemo and Avastin against those therapies alone, is in the tricky setting of platinum-resistant ovarian cancer. A hit will repay investors – but clinical data so far, while promising, come from small patient numbers, with the phase 2 Viro-15 trial enrolling just 27 subjects. And the history of oncolytic viruses has been patchy, though Replimune scored a notable success late last year.

The IPO was priced at the bottom of the proposed range and subsequently the group saw its share price soar 362%. Management might well be reproaching themselves, in retrospect, for only seeking $15m.

Tracking demand for IPOs



Source: Evaluate

The other newly public group that has enjoyed a share price rise since its debut is Structure Therapeutics. This company, too, is active in a hot area: its frontrunner is a GLP-1 agonist for diabetes and obesity, and a GIP/GLP-1 is also in the works. None of its programmes is past phase 1, however.

The worst-performing stock market debutante so far this year is Cadrenal Therapeutics, which is focused on a single asset: tecarfarin, a vitamin K antagonist anticoagulant for thrombosis and atrial fibrillation. The asset has been passed from pillar to post: Cadrenal got it from Horizon Technology

Finance, a company that provides loans to venture-backed groups including biotechs. Horizon had acquired the rights from Espero, which had merged with Armetheon in 2017; Armetheon had obtained tecarfarin from Aryx after that group was wound up in 2011.

As long ago as 2009, when Aryx held the asset, tecarfarin disappointed clinically. Cadrenal must think it can do better, though investors clearly hold out little hope. Bearing in mind its sole project's chequered pedigree it is perhaps surprising that Cadrenal managed to attract any interest.

Compared with the fourth quarter of 2022, last quarter does represent an improvement. But young developers needs the IPO window to open more than a crack, and for that to happen the wider biotech market will have to tick up. Sadly, there is little sign of that happening for now.

First-quarter 2023 IPOs

Company	Primary focus	Amount raised	Premium/(discount), float price to initial offer	Share price change since float to end Q1
Mineralys Therapeutics	Therapies for diseases driven by elevated aldosterone levels	$192m	7%	-2%
Structure Therapeutics	Oral therapies for chronic diseases including obesity	$161m	7%	59%
Genelux	Oncolytic virus-based immunotherapies	$15m	-8%	362%
Cadrenal Therapeutics	Oral anticoagulant for thrombosis and atrial fibrillation	$7m	0%	-72%

Source: Evaluate Pharma.

A lean first quarter for venture-backed developers

BY EDWIN ELMHIRST AND AMY BROWN
APRIL 04, 2023

While venture investors keep the purse strings tight, they themselves continue to enjoy fundraising success.

Biopharma venture financings fell over each consecutive quarter last year, and that theme continued in the opening three months of 2023. The $3.3bn raised by private drug developers suggests that the sector could be heading back to 2017, when quarterly funding levels last dipped below $3bn.

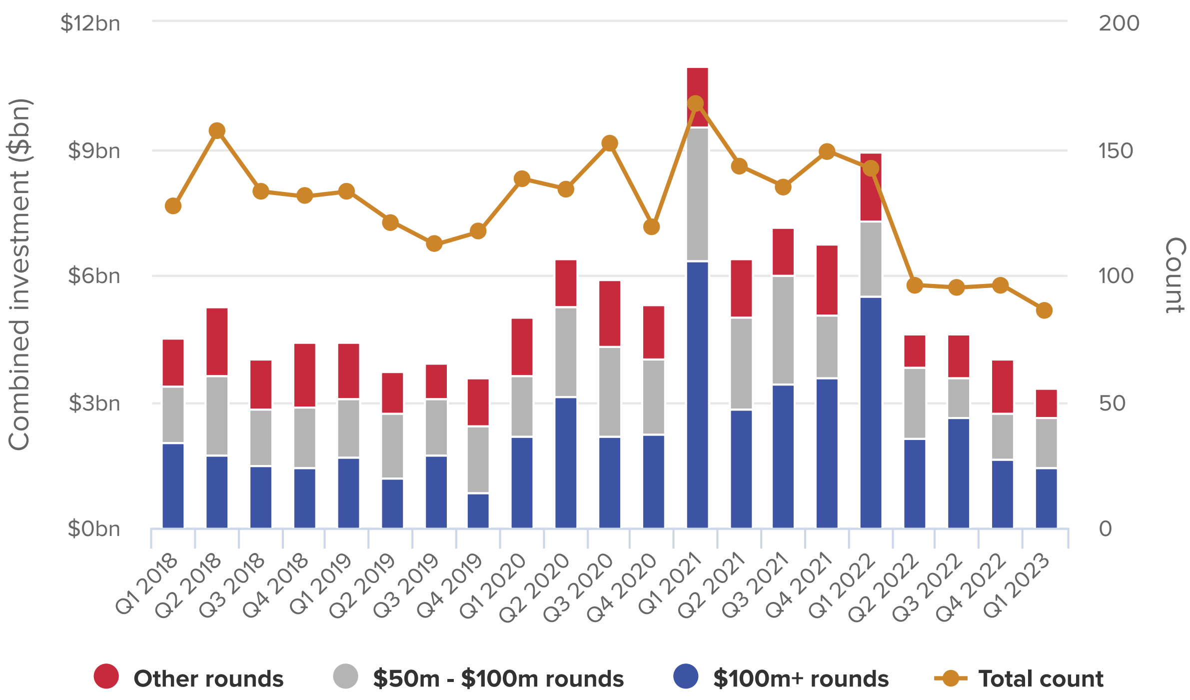
There are reasons to hope that these numbers might not drop too much further, however. Biopharma venture firms had a strong open to the year in terms of the new funds they raised, according to the investment bank Torreya. Few expect a dramatic turnaround in the financing climate this year, particularly on the public markets, but private money is at least still showing interest in the sector.

SR One, for example, closed its second fund at $600m last month, beating a $500m target. Its chief executive, Simeon George, tells *Evaluate Vantage* that the prospects for new technologies like Crispr and gene therapy continue to be a strong draw for investors. Having a couple of successful portfolio companies helps with the fundraising process, he admits.

Nimbus's deal with Takeda, for example, was a "massive return for us", SR One having been an investor in the small developer since 2011. It has been a long-term investor in Arcellx, one of the few successful 2022 IPO candidates, which went on to sign a huge deal with Gilead. SR One also backed Turning Point, which was bought by Bristol Myers Squibb last year for $4.1bn.

SR One was formerly GSK's venture arm until the two separated in 2020. The pharma giant remains an anchor investor, albeit with no special rights over other limited partners, and its exposure has decreased to less than 10% in Fund II, George says.

Quarterly biopharma VC rounds



Source: Evaluate

In a further encouraging sign, it is not only venture firms with a track record raising funds this year. Cure Ventures raised its first fund, closing at $350m, today. True, its partners are not new to the sector, but this suggests that there are limited partners willing to inject new capital into biopharma – and not just to protect existing investments.

Despite all this, there are unfortunately more points of gloom than glimmers of hope in biopharma financing data right now. The chart above is based on financing news collected by *Evaluate Pharma*; the data concern only pure-play drug developers, with medtech and digital health groups excluded.

With the IPO window barely open any wider than last year, and the equity markets leery of high-risk propositions, the picture for cash-hungry small developers is bleak.

The current situation presents "an existential crisis for every startup. It's how do you survive over the next one, two, however many years," SR One's George says.

Companies should be considering all tools to help cash last longer, including opening up previous financing rounds, raising capital through partnerships, or focusing on fewer programmes, he says. "The reality is, no round is worse than a down round."

The table below shows that, when the story is right, young developers are still amassing substantial sums of money. The Car-T player Cargo Therapeutics, which raised $200m, albeit from a very broad syndicate with three co-leads – Third Rock, RTW and Perceptive Xontogeny – is one example.

But investors and executives alike are under no illusions about how tough the coming months will be, and the daily press releases detailing layoffs and project curtailments confirm this to be true.

"We have to brace ourselves for the fact that things aren't going to dramatically turn back to where they were a year or two ago," George says. "We're all going to have to focus on the fundamentals of our businesses."

Top five biopharma VC rounds of Q1 2023			
Company	**Investment ($m)**	**Financing round**	**Description**
Cargo Therapeutics	200	Series A	Car-T cell therapies
Arrivent Biopharma	155	Series B	Developing phase 3 EGFR kinase inhibitor
Amolyt Pharma	138	Series C	Rare endocrine and metabolic disorders
Hemab	135	Series B	Rare bleeding and clotting disorders
Flare Therapeutics	123	Series B	Targeted small molecules for cancer

Source: Evaluate Pharma.

Pfizer's fortunes overshadow first-quarter dealmaking

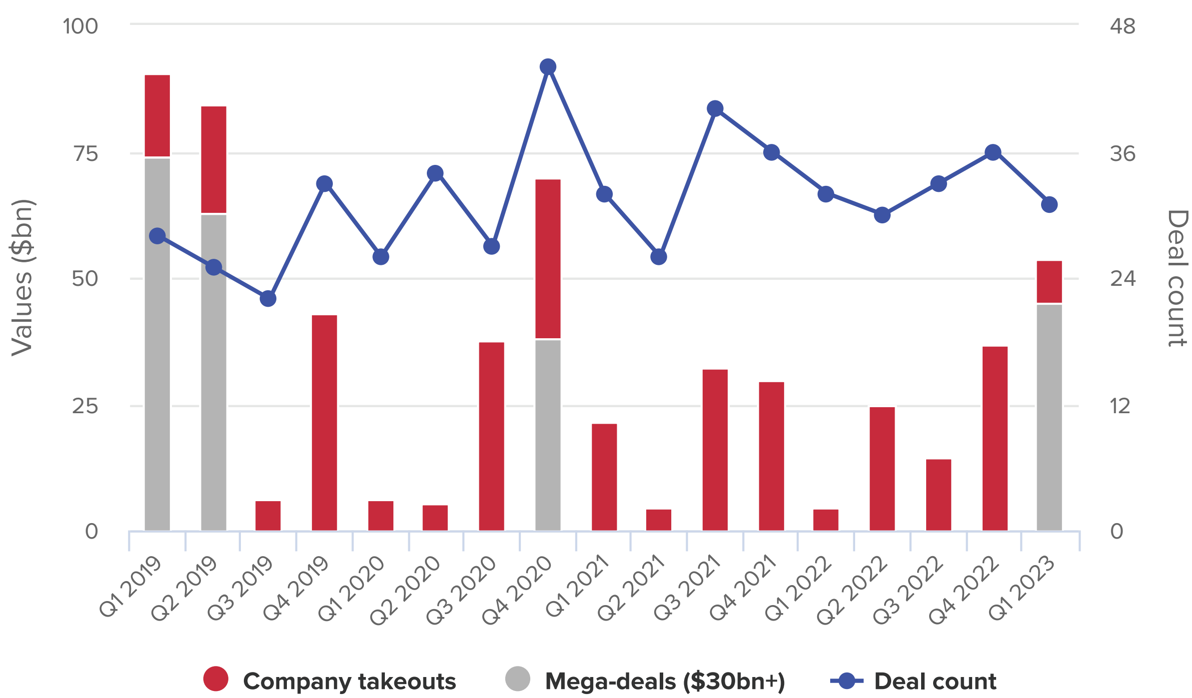
BY EDWIN ELMHIRST AND AMY BROWN
APRIL 11, 2023

Aside from Seagen, small takeouts dominate the first quarter.

Pfizer accounted for almost a quarter of biopharma's buyout spend last year, a contribution that looks set to grow considerably in 2023. This is thanks to the $45bn it has pledged to spend on Seagen – antitrust approval pending – in the sector's biggest buyout since the Abbvie-Allergan deal in 2019.

Excluding this huge transaction, however, drug developers spent a mere $8.8bn on buyouts in the first quarter, according to *Evaluate Pharma*. The volume of dealmaking remains in line with activity levels seen last year but, with the exception of Pfizer, the sector seems reluctant to spend big.

Quarterly biopharma takeouts



Source: Evaluate

The analysis above concerns only full company acquisitions where the target was a pure-play drug developer. Other types of M&A deals, like business unit buys, product acquisitions or licensing deals, are not considered; also excluded are takeovers of device makers or diagnostics groups, for example.

It is worth noting that the figures above include deals that have yet to close. Heightened FTC scrutiny of pharma deals is causing antitrust clearance to take much longer than in the past – Pfizer has said the Seagen acquisition might not clear until early 2024, and Sanofi yesterday delayed close of its Provention buy to give more time for FTC scrutiny.

Last year's biggest move, Amgen's $28bn bid for Horizon, is also stuck in regulatory limbo, although the big biotech says it hopes that this will close in the first half. Few expect these deals to be turned down in totality, although disposals might have to be made, news on which will be a big focus.

Some believe that the newly onerous antitrust process is making buyers think carefully before making a move. This is possibly increasing the appeal of smaller deals, which are more easily cleared; the sector has been favouring so-called bolt-on deals for some time now, for various reasons including the perception that huge mega-mergers are valuing destroying.

Apart from Seagen the first-quarter deals were small, with a huge valuation gap between that transaction and all others. Valuations are depressed, of course, and this lies at the root of another theme for 2023: the string of opportunistic moves that emerged.

Tough economic circumstances are forcing many developers to consider their options, and buyers are further flexing their muscles by insisting on contingent payments. Of the 10 first-quarter company takeouts with disclosed deal terms, eight employed either CVRs or downstream payments, dependent on predetermined future successes.

The equity markets remain tough, the IPO window is barely open and venture firms are keeping the purse strings tight. For sellers at the smaller ender of the sector these factors will make for difficult times at the negotiation table in the coming months.

Biggest biopharma buyouts announced in Q1 2023			
Acquirer	**Target**	**Status**	**Deal terms**
Pfizer	Seagen	Open	Total value $43bn
Sanofi	Provention Bio	Open	Total value $2.9bn
Astrazeneca	Cincor	Closed	$1.3bn up front (plus CVR worth a further $500m)
Chiesi	Amryt	Open	$1.25bn up front (plus CVR worth a further $225m)
Ipsen	Albireo	Closed	$952m up front (plus CVR worth a further $227m)

Source: Evaluate Pharma.

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