Biopharma Market Update

April 21, 2025

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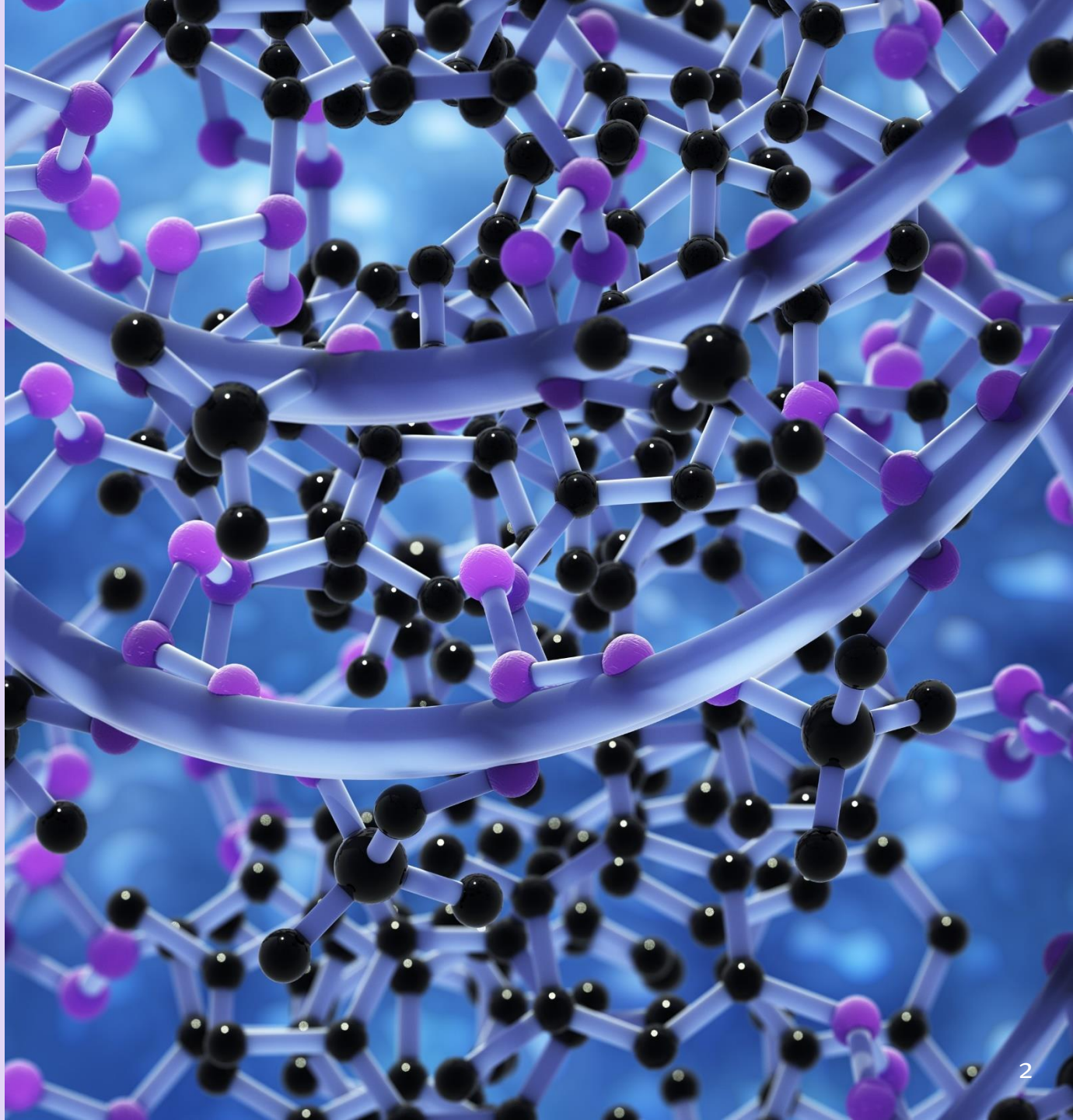

Past Issues

To get on the mailing list for this publication feel free to contact Jenna Hill (hillje@stifel.com). Past issues of this publication can be read online at:

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Apr 7, 2025 (Biotech Market Break)
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Links to Stifel Biopharma Special Topic Publications

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[Mar 26, 2025]

2025 Biotech Outlook

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2024 Biotech Mid-Year Outlook

[July 15, 2024]

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2024 Biotech Outlook

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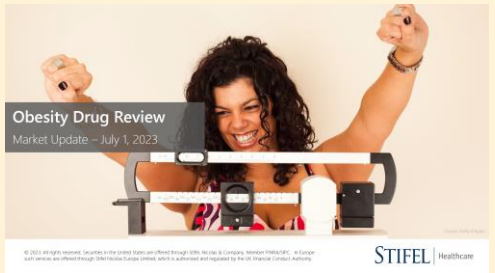
Why Invest in Biotech?

[November 22, 2023]

Obesity Drug Review



[July 1, 2023]

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To Learn More
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Macro Update

With Inflation Progress Slow, Fed's Daly Says Rate Cuts to Wait

***Reuters*, April 18, 2025 (excerpt)**

San Francisco Federal Reserve President Mary Daly said on Friday that while she is still comfortable with a couple of interest rate cuts this year, rising risks of inflation mean the central bank may need to do less, especially given that uncertainty over President Donald Trump's trade policy has so far done little to disrupt still-solid U.S. economic growth.

"Continuing to gradually reduce the policy rate with no urgency to react fast is the right thing to do," she said at an event held by the University of California, Berkeley's Fisher Center for Real Estate & Urban Economics. "Ultimately, we made a single promise to the American people - I think you all remember what it was - we are going to restore price stability. That is the critical foundation of all other things we do."

The Fed has held the policy rate steady in the 4.25%-4.50% range since December. Policymakers have generally said tariffs are likely to increase inflation and slow the economy. Many, including Fed Chair Jerome Powell, say they want to wait and see what actually happens on trade and other policies before making any adjustments, a view that Daly also embraced.

The Fed's wait-and-see approach on interest rates has angered Trump, and on Friday a Trump adviser said the administration is studying options for firing Powell.

Daly said it is possible the Fed could deliver more than two rate cuts this year if inflation drops faster than expected or the labor market falters. But it was clear she sees more danger on the other side of the coin.

Mary Daly
President
Federal Reserve Bank of San Francisco

Source: https://www.reuters.com/markets/rates-bonds/with-inflation-progress-slow-feds-daly-says-rate-cuts-may-need-wait-2025-04-18/

Risk of Financial Panic Tempers Trump on Firing Powell

Colby Smith, Jonathan Swan and Maggie Haberman, *New York Times*, April 18, 2025 (excerpt)

President Trump this week revived a **longstanding threat** against Jerome H. Powell when he accused the Federal Reserve chair of "playing politics" and moving too slowly to lower interest rates. But privately, according to people close to Mr. Trump, the president has for months been aware that trying to **oust Mr. Powell could inject more volatility into jittery financial markets**.

Investors are already uneasy after a period of tumult due to a blitz of tariffs announced by the administration this month. Undermining the political independence of the Fed, which is seen as critical across Wall Street, could risk a much more significant financial panic.

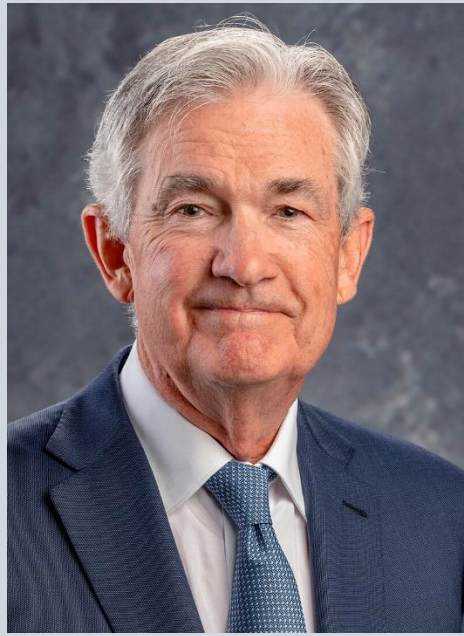
"If I want him out, he'll be out of there real fast, believe me," Mr. Trump told reporters in the Oval Office of the White House on Thursday when asked about Mr. Powell. The warning came on the heels of an early morning social media post in which Mr. Trump said, "Powell's termination cannot come fast enough!"

Mr. Trump's advisers have repeatedly told him that firing Mr. Powell is both legally and financially fraught — and that the uncertainty could cause a significant downturn in financial markets. Mr. Trump, at least for the moment, has seemed persuaded, the people said.

At an event at the Economic Club of Chicago on Wednesday, Mr. Powell made clear that it was the Fed's "obligation" to ensure that "a one-time increase in the price level does not become an ongoing inflation problem" even as he reiterated his warnings about the prospects of slower growth. He also stressed that the Fed could afford to be patient on taking further action on interest rates until it had more clarity about the outlook.

Those comments, coupled with the fact that the European Central Bank was readying to lower interest rates on Thursday, appeared to set off Mr. Trump's tirade against Mr. Powell.

Mr. Powell has been emphatic that the law does not permit a president to remove the chair of the central bank nor meddle directly with the institution. The Federal Reserve Act says members of the Fed's seven-strong Board of Governors can be removed only "for cause," which is interpreted as serious misconduct and other violations.



Jerome Powell
Chair
Board of Governors of the Federal Reserve

Source: https://www.nytimes.com/2025/04/18/business/trump-powell-fed-markets.html

Unusual Sell-off in the Dollar Raises Specter of Investors Losing Trust in the U.S. Under Trump

Bernard Condon, *PBS News*, April 18, 2025 (excerpt)

Among the threats tariffs pose to the U.S. economy, none may be as strange as the sell-off in the dollar. Currencies rise and fall all the time because of inflation fears, central bank moves and other factors. But economists worry that the recent drop in the dollar is so dramatic that it reflects something more ominous as President Donald Trump tries to reshape global trade: a loss of confidence in the U.S.

The dollar's dominance in cross-border trade and as a safe haven has been nurtured by administrations of both parties for decades because it helps keep U.S. borrowing costs down and allows Washington to project power abroad — enormous advantages that could possibly disappear if faith in the U.S. was damaged.

"Global trust and reliance on the dollar was built up over a half century or more," says University of California, Berkeley, economist Barry Eichengreen. "But it can be lost in the blink of an eye."

Since mid-January, the dollar has fallen 9 percent against a basket of currencies, a rare and steep decline, to its lowest level in three years. Many investors spooked by Trump don't think the dollar will be pushed quickly from its position as the world's reserve currency, instead expecting more of a slow decline. But even that is scary enough, given the benefits that would be lost.

Source: https://www.pbs.org/newshour/economy/unusual-sell-off-in-the-dollar-raises-specter-of-investors-losing-trust-in-the-u-s-under-trump

Trump Wants his Tariffs to Reset the World. He Might Get his Wish

Luciana Lopez, *CNN*, April 18, 2025 (excerpt)

President Donald Trump has repeatedly touted what he calls the return of manufacturing to the United States, hailing companies that have vowed to pour large amounts of money into making everything from computer chips to cars in America.

But announcements are easy to make. In the long term, why would companies and other countries decide to invest in the US, which has upended the global economic order in just weeks? The United States moved from a stable economy, a trusted partner in trade agreements and global security, to a source of confusion and doubt in mere weeks after Trump assumed office on January 20.

Perhaps no one has put it more bluntly than Ursula von der Leyen, the president of the European Commission, on Wednesday, when she said to a news outlet in Germany: “The West as we knew it no longer exists.”

In other words: **The United States isn’t the only trade game in town.**

Sure, the US is the world’s biggest economy, with a gross domestic product of almost $30 trillion. But China, the world’s No. 2 economy, is at about $18 trillion, according to the World Bank. And the total value of the European Union’s economy is around 17 trillion euros, or about $19 trillion.

“We have 166 members in the organization. US trade is 13% of world trade. That means that there’s 87% of world trade happening between the other members of the WTO,” Ngozi Okonjo-Iweala, director-general of the World Trade Organization, told CNN’s Richard Quest on Wednesday.

The changes have been not only swift but also deep. “These are very fundamental policy changes,” Federal Reserve Chair Jerome Powell said at an event hosted by the Economic Club of Chicago on Wednesday. “There isn’t a modern experience of how to think about this.”

His comments sent US stock markets slumping, with investors clearly uneasy about what it means when a usually staid central banker suggests the world economic order is being turned topsy-turvy. (Trump ripped Powell on social media the next day, ostensibly for not lowering interest rates quickly enough, writing: “Powell’s termination cannot come fast enough!”)

Source: https://edition.cnn.com/2025/04/18/economy/global-trade-relationships-trump-tariffs/index.html

Treasuries Pare Weekly Advance as Yield Curves Steepen Globally

Michael Mackenzie and Elizabeth Stanton, *Bloomberg*, April 17, 2025 (excerpt)

US Treasuries pared their weekly advance in a low-volume, holiday-shortened session Thursday, with long-maturity yields rising most amid a rise in oil prices that boosted inflation expectations.

The yield curve steepened notably, with the 30-year exceeding the five-year by nearly 90 basis points, aided by a large trade in Treasury futures. Curve-steepening in European bond markets after the European Central Bank's rate decision, and US President Donald Trump's broadside against Fed Chair Jerome Powell contributed as well.

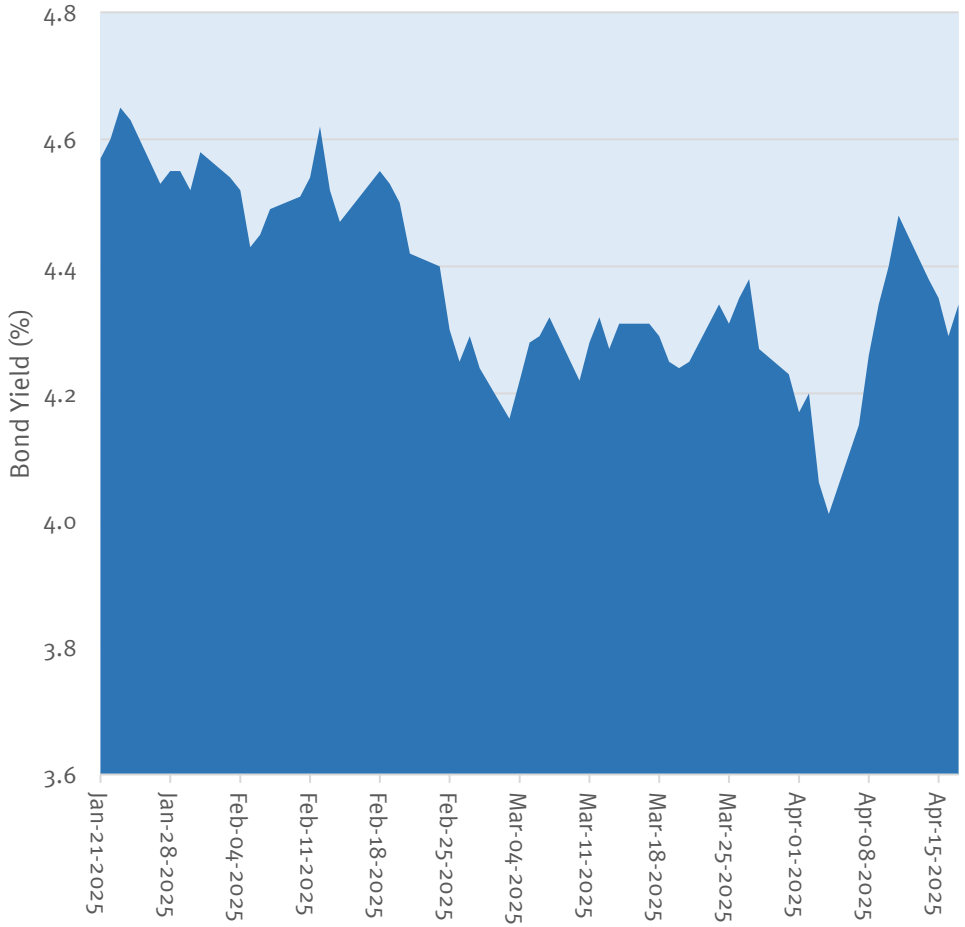
The 30-year yield rose as much as seven basis points, exceeding Wednesday's high, and remained near session highs. A large futures block trading during US morning appeared to ignite the move. Later, crude oil futures rose to the highest level in more than a week, supporting inflation expectations even as an auction of Treasury inflation-protected securities drew middling demand.

While euro-zone government bonds rallied after the European Central Bank cut interest rates as expected and said global trade tensions threatened the region's economic recovery, those yields curve also steepened, reinforcing the trend in Treasuries, said Tom di Galoma, managing director at Mischler Financial Group.

Thursday's highs in yields were reached earlier amid gains for US equity index futures after signs of progress in trade talks between the US and Japan. The benchmark 10-year note's yield rose as much as five basis points to 4.32%. It dipped back below 4.28% amid steeper declines for most euro-zone 10-year yields. Traders almost fully priced in another rate cut in June after ECB President Christine Lagarde said downside risks to economic growth had increased.

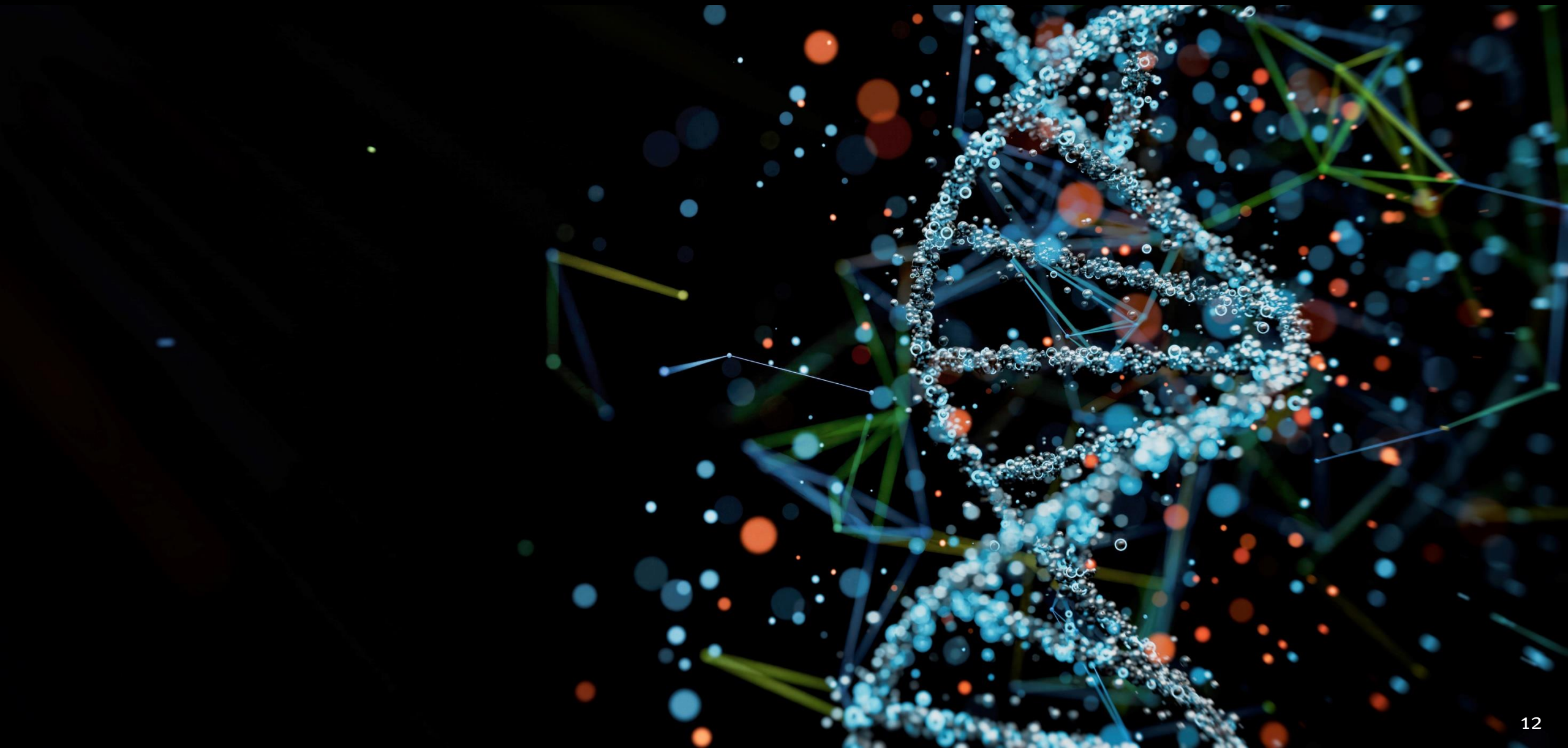
United States Treasury 10 Year Yield

Jan 21, 2025 to April 17, 2025



Source: https://www.bloomberg.com/news/articles/2025-04-17/us-treasuries-decline-as-powell-s-hawkish-message-sinks-in

Biopharma Market Update



The XBI Closed at 75.9 Last Friday (Apr 17), Up 2.2% for the Week

The Stifel Global Biotech Value Tracker rose by 6% last week, substantially more than the XBI (+2.2). Treasury yields came down but remain high. The XBI is down 15.7% for the year while the Stifel Global Biotech Value Tracker is down 15.9% for the year.

Biotech Stocks Up Last Week

Return: Apr 12 to Apr 19, 2025

Nasdaq Biotech Index: +1.5%
Arca XBI ETF: +2.2%
Stifel Global Biotech EV (adjusted): +6.0%*
S&P 500: -1.5%

Return: Dec 31, 2024 to Apr 19, 2025 (YTD)

Nasdaq Biotech Index: -7.9%
Arca XBI ETF: -15.7%
Stifel Global Biotech EV (adjusted): -15.9%*
S&P 500: -10.2%

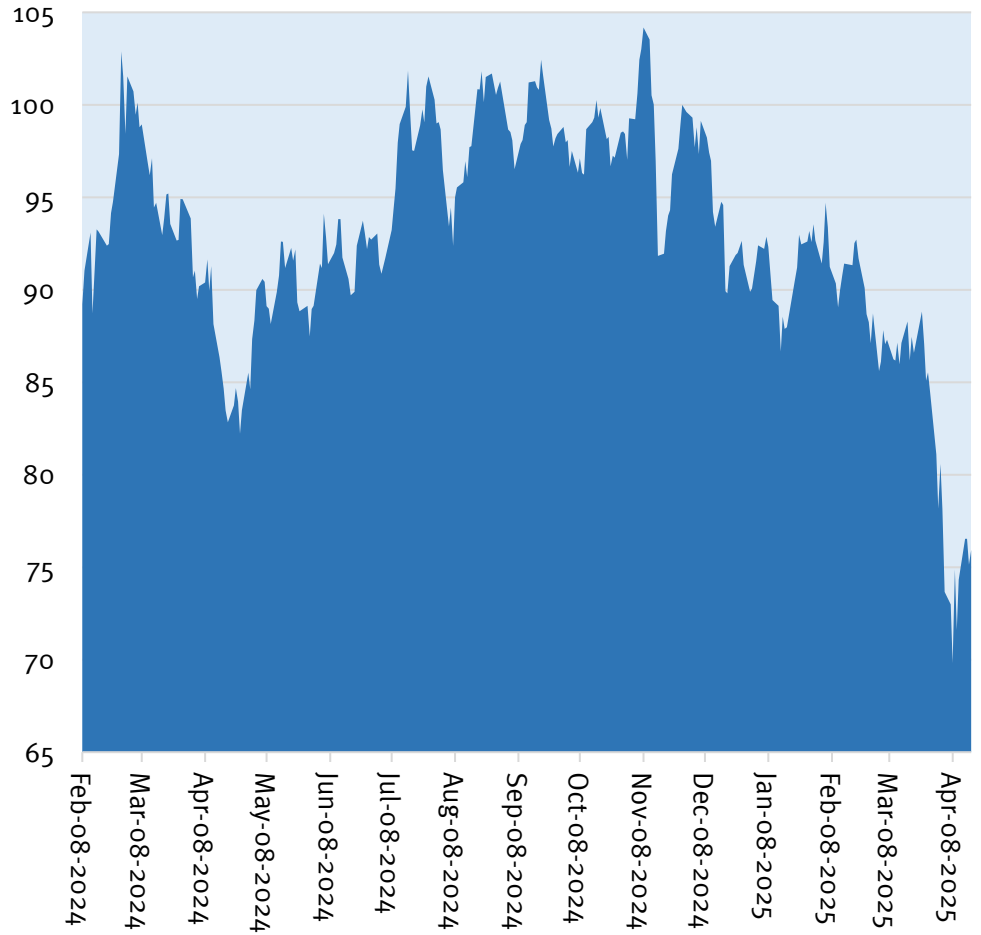
VIX Down

Mar 29, 2024: 13.0%
Aug 2, 2024: 23.4%
Dec 13, 2024: 13.8%
Jan 24, 2025: 14.2%
Feb 21, 2025: 18.2%
Mar 28, 2025: 21.7%
Apr 11, 2025: 37.6%
Apr 18, 2025: 29.7%

10-Year Treasury Yield Down

Dec 29, 2023: 3.88%
Aug 2, 2024: 3.80%
Dec 13, 2024: 4.4%
Jan 24, 2025: 4.6%
Feb 21, 2025: 4.4%
Mar 28, 2025: 4.27%
Apr 11, 2025: 4.48%
Apr 18, 2025: 4.34%

XBI, Feb 8. 2024 to Apr 17, 2025

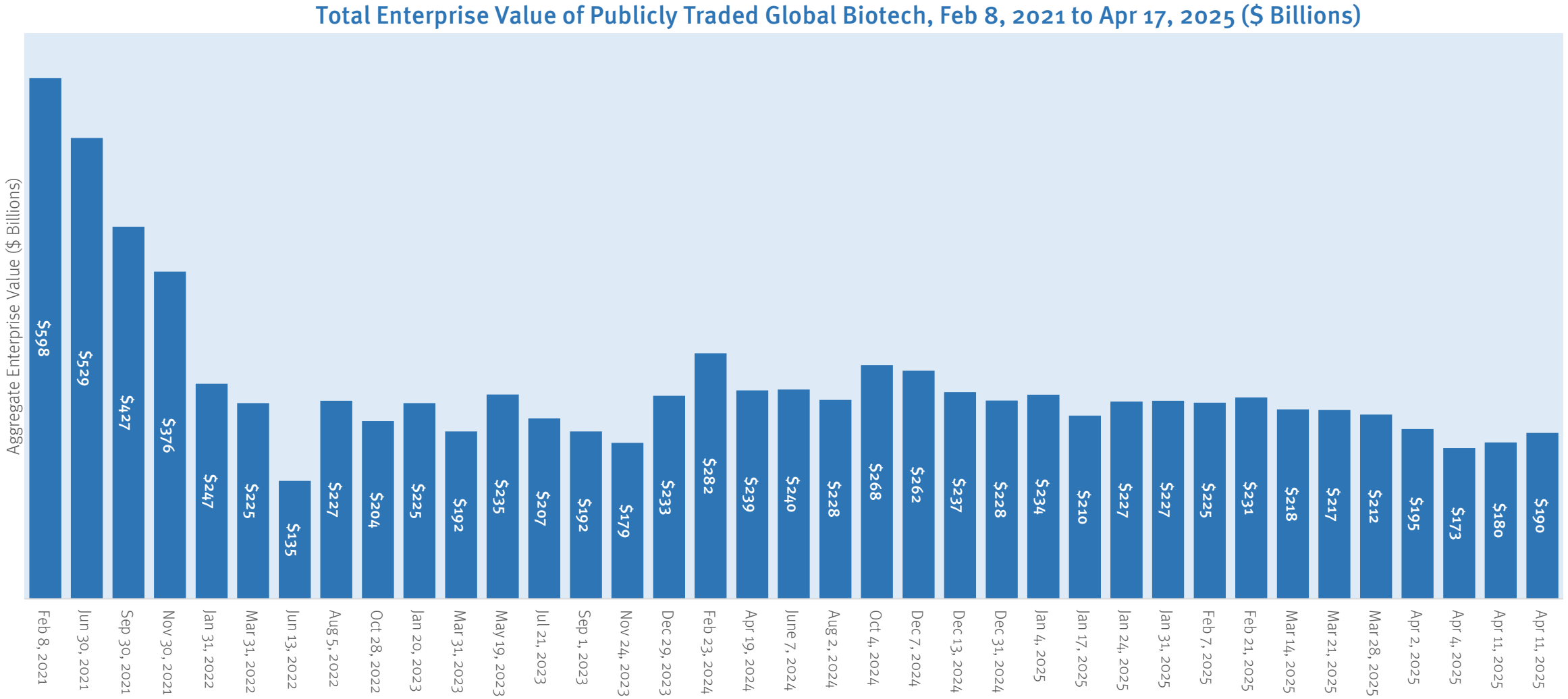


* Change by enterprise value. The adjusted number accounts for the effect of exits and additions via M&A, bankruptcies and IPOs. The annual change by market cap is even higher.

Source: S&P Capital IQ and Stifel analysis

Total Global Biotech Sector Rose 6% Last Week

Biotech stocks rose 6% in the last week, much more than the XBI. The biggest contributors to the rise were Summit (+5.9%), Structure Therapeutics (+37%), SanBio (+34%), ABL Bio (+15.3%) and Xenon (+11%).

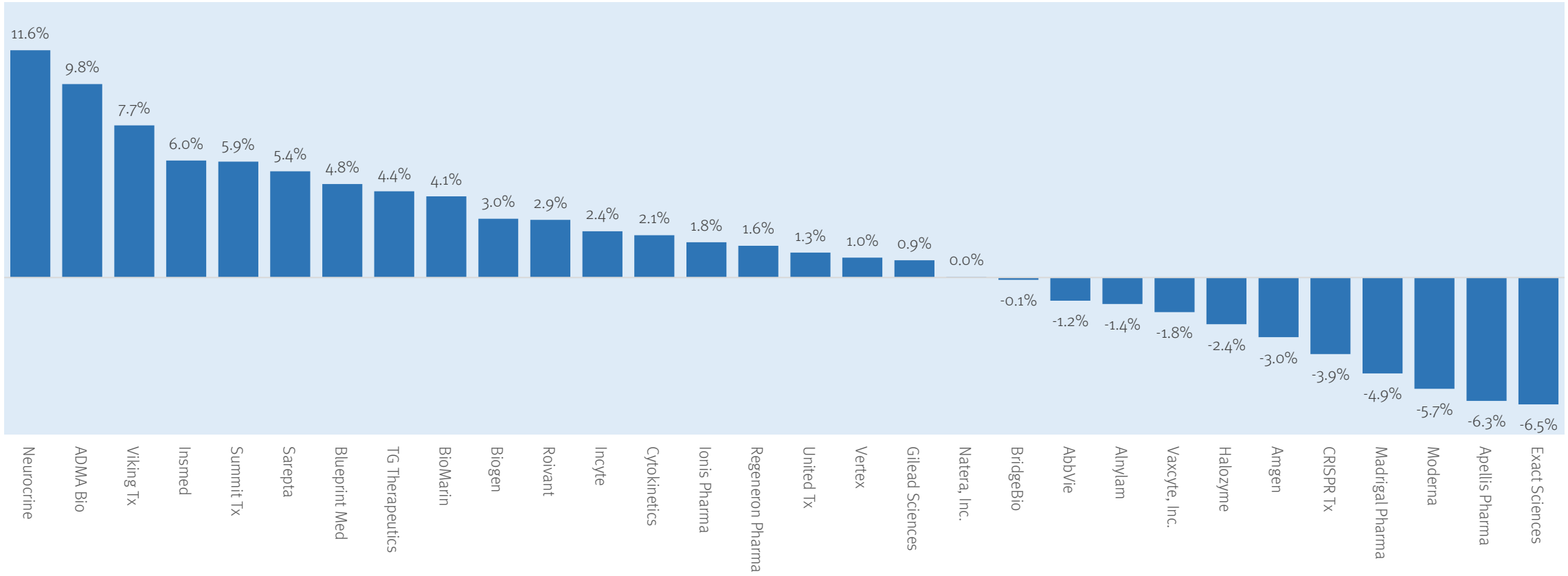


Source: CapitalIQ. Biotechs are defined as any therapeutics company without an approved product on any global stock exchange.

XBI 30 Performance Up Last Week

This chart shows the change in market cap this year for the 30 most influential stocks in the XBI. These 30 stocks comprise 60% of the weight of the XBI (out of 138 stocks total). The mean percentage change in value last week was +1.3%. The median change was +1.4%. Neurocrine, ADMA and Viking did the best (up 7% or more) while Exact Sciences, Apellis and Moderna all fell more than 5%.

Top 30 XBI Influencers, Pecent Change in Market Cap, Week of Apr 11 to Apr 17, 2025

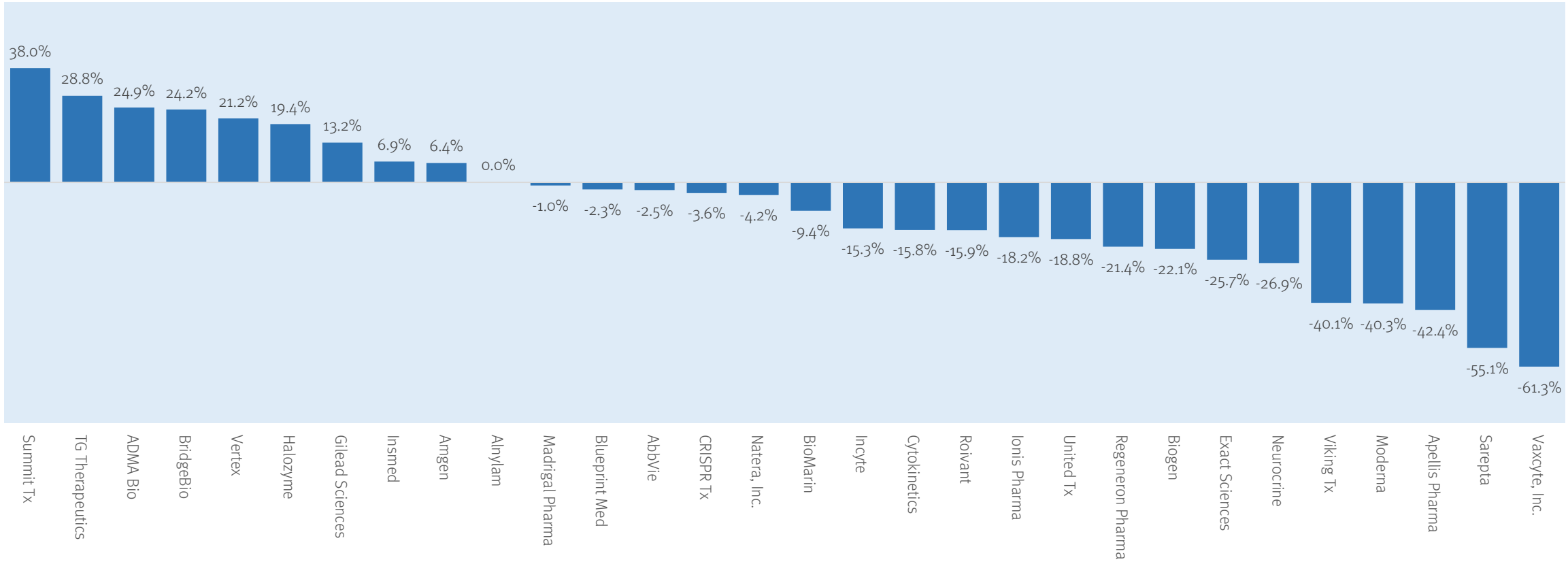


Source: CapitalIQ. Biotechs are defined as any therapeutics company without an approved product on any global stock exchange.

XBI 30 Performance Year to Date

This chart shows the change in market cap this year for the 30 most influential stocks in the XBI. These 30 stocks comprise 60% of the weight of the XBI (out of 138 stocks total). The mean percentage change this year has been -8.6%. The median change was -6.8%. Summit, TG Therapeutics and ADMA, BridgeBio and Vertex have all had returns in the 20%+ category while Viking, Moderna, Apellis, Sarepta and Vaxcyte are all down 40% or more since the year began.

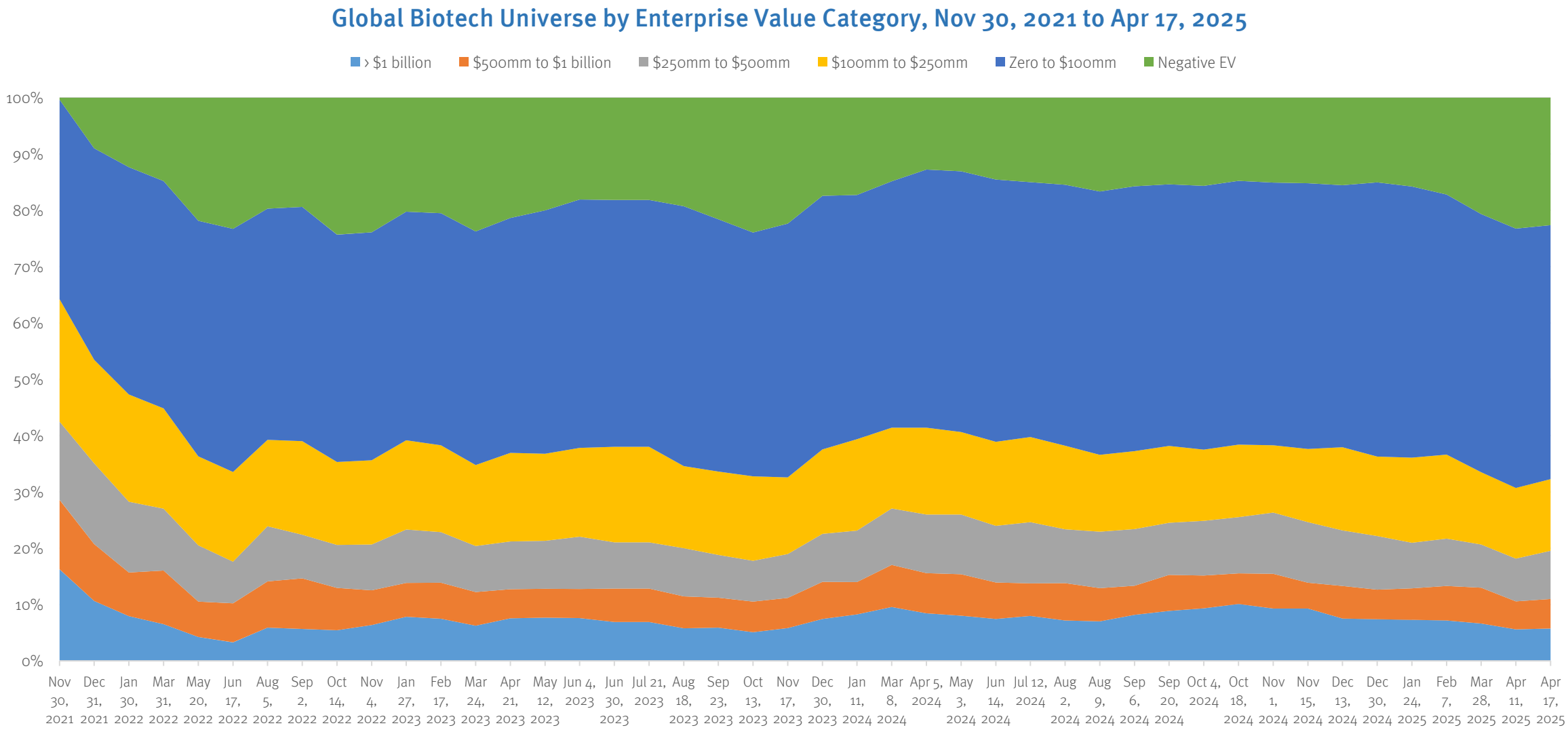
Top 30 XBI Influencers, Pecent Change in Market Cap, Week of Dec 31, 2024 to Apr 17, 2025



Source: CapitalIQ.

Global Biotech Neighborhood Analysis

We saw a significant positive turn in the number of negative EV companies last week. Valuations of microcaps improved substantially.

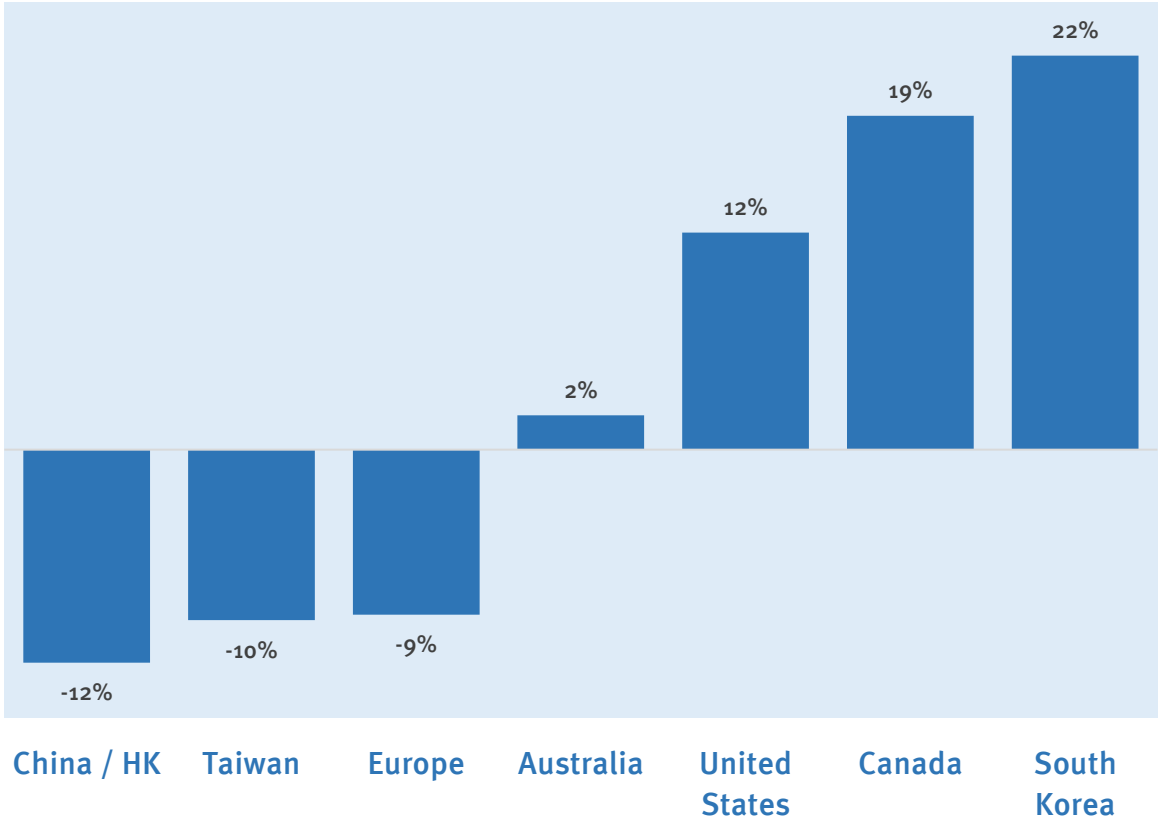


Source: CapitalIQ and Stifel analysis. Biotechs are defined as any therapeutics company without an approved product on any global stock exchange.

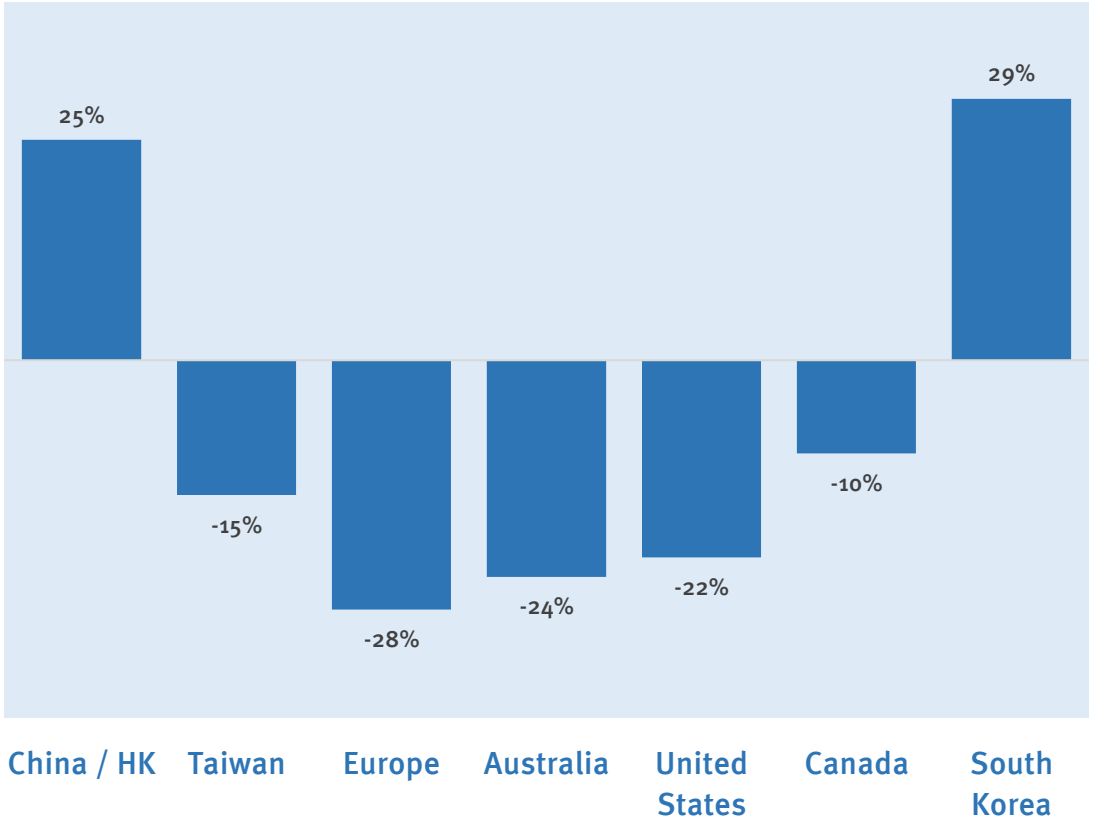
Biotech Performance by Region

Last week saw a strong recovery take place in U.S. biotech (up 12%, change in total market cap) while Canada and South Korea did even better. Europe, China and Taiwan were all down substantially last week. For the year to date, the U.S., Australia and Europe have all seen relatively weak performance of their biotech sectors while China and South Korea have seen very positive performance (up 25% and 29%, respectively).

Percent Change in Total Market Cap of Public Biotech by Country/Region, Apr 11, 2024 to Apr 17, 2025



Percent Change in Total Market Cap of Public Biotech by Country/Region, Dec 31, 2024 to Apr 17, 2025



Source: CapitalIQ and Stifel analysis. Biotechs are defined as any therapeutics company without an approved product on any global stock exchange.

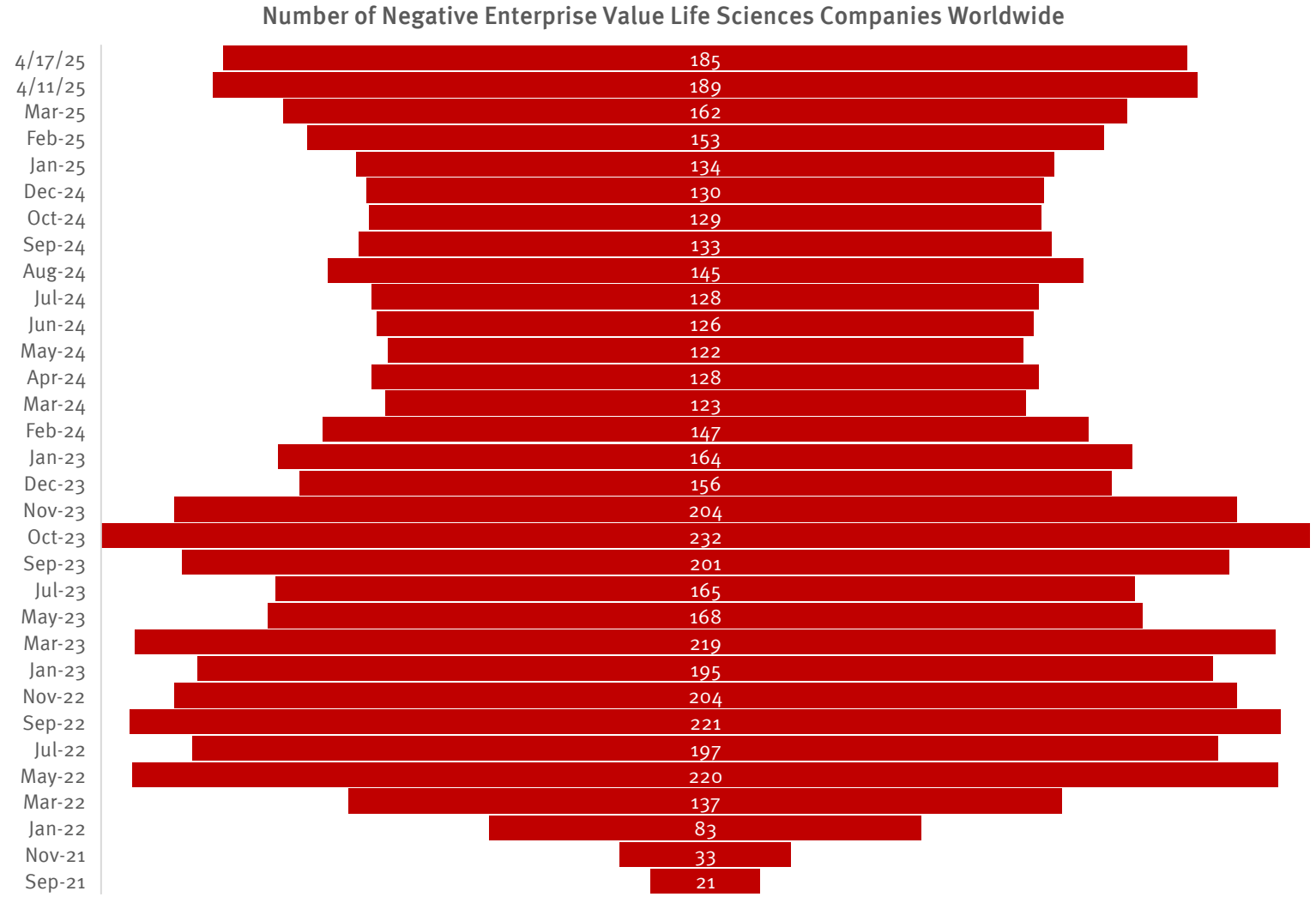
Life Sciences Sector Gained $223 Billion in Value Last Week (+2.5%)

Last week saw strength in biotech, commercial pharma and API. HCIT, Pharma Services and Life Science Tools declined in aggregate.

Sector	Firm Count	Enterprise Value (Mar 28, 2025, $millions)	Change in Last Week (percent)	Change in Last Month (percent)	Change in Last Year (percent)
API	79	$85,271	2.5%	-2.5%	11.2%
Biotech	728	$189,861	6.0%	-13.0%	-5.1%
CDMO	37	$149,028	1.4%	-3.1%	18.6%
Diagnostics	75	$239,255	1.5%	-5.1%	-8.0%
OTC	29	$23,480	0.7%	-3.0%	-9.5%
Commercial Pharma	696	$5,874,854	3.5%	-6.3%	-1.1%
Pharma Services	38	$140,300	-0.5%	-14.2%	-23.4%
Life Science Tools	50	$527,832	-0.9%	-13.0%	-20.5%
Devices	174	$1,711,112	0.8%	-3.5%	7.1%
HCIT	7	$22,688	-1.3%	-12.6%	35.6%
Total	**1913**	**$8,968,682**	**2.5%**	**-6.4%**	**-1.5%**

Source: CapitalIQ and Stifel analysis

Number of Negative Enterprise Value Life Sciences Companies Fell in Last Week



The count of negative EV life sciences companies worldwide fell from 189 a week ago to 185 last Friday.

This was the first week in over a month where this metric of sector health improved.

Source: CapitalIQ

‘Chaos’ in the Biotech Market has Dampened Hopes of a Rebound. What Does that Mean for Dealmaking and IPOs?

Amy Baxter, *PharmaVoice*, April 15, 2025 (excerpt)

Stock market whiplash is dampening hopes for a comeback year in the biotech arena. Roughly 25% of biotech stock values sank below their cash holdings last week amid sudden changes to U.S. trade policy, Bloomberg reported.

In an economic situation that’s shifting by the day, “the only thing that’s certain is uncertainty,” said David Crean, managing partner at M&A consulting firm Cardiff Advisory. At the beginning of the year, pharma M&A was expected to rise and the biotech IPO market appeared steady. Now, the biotech space has been roiled by several abrupt changes stemming from new Trump administration policies.

When the FDA’s Peter Marks was forced out of the agency last month, biotech stocks sunk. The former director of the agency’s Center for Biologics Evaluation and Research played a key role in the development of the COVID-19 vaccines and was seen as an ally among vaccine makers that are now up against potential changes from HHS’s new Secretary, Robert F. Kennedy Jr. — a known vaccine skeptic.

Amid the whirlwind and the market’s loss of value, biotech IPOs are likely to slow.

M&A kicked off 2025 on a high note with a handful of major deals announced at the J.P. Morgan Healthcare Conference in San Francisco, including J&J’s $14.6 billion acquisition of psychiatric drug developer Intra-Cellular Therapies. The conference is often seen as a barometer of M&A activity for the coming year, and the smattering of deals announced in January had investors “pumped,” according to Crean.

But by March, it became clear that drugmakers were still holding out. “[M&A] started off as gangbusters in January, but it’s been relatively quiet and muted up through April,” Crean said. Big Pharma faces pressures that may force its hand this year. Looming patent cliffs are creating revenue gaps companies need to fill, and acquisition or licensing deals with biotechs that bolster their pipelines are still the go-to strategy. Some large pharmas are also sitting on cash in their balance sheets that “needs to be put to good use,” according to Crean.

“They’re going to have to be very aggressive and dip into their balance sheet to buy assets, and particularly late-stage assets, to fill that portfolio gap. There’s no other way of doing it,” Crean said. Crean also expects to see bigger deals, or “transformative M&A,” later in the year, due to the size of the revenue losses ahead for some companies. Smaller deals won’t be enough.

Source: https://www.pharmavoice.com/news/biotech-market-ipos-manda-stocks-pharma/745288/

China Advantage in Biotech Continues to Grow

Business Korea, April 21, 2025 (excerpt)

In a remarkable display of growth, China's biotechnology sector has surged ahead in the global market, leaving South Korea trailing significantly. In the first quarter of 2025, China's biotech exports reached an impressive $36.929 billion, a figure 20 times greater than South Korea's $1.98 billion. This development underscores China's rapid ascent as a dominant force in the biotech industry, driven by strategic government support, flexible regulations, and an influx of skilled professionals.

Since 2021, China has consistently ranked first in global clinical trial numbers, surpassing even the United States. This leadership position is attributed to China's ability to secure human subject data swiftly and extensively, making it an attractive destination for conducting trials. An industry insider from the Korea Pharmaceutical and Bio-Pharma Association noted, "China can secure proof of concept (POC) data faster and more extensively than any other country." This capability has been further bolstered by the Chinese government's full support.

The regulatory environment in China has also played a crucial role in this growth. The National Medical Products Administration (NMPA) has set up four accelerated pathways to expedite drug approvals, including a priority review program. In 2024 alone, the NMPA approved 48 first-in-class innovative drugs, marking the highest number in the past five years. Lee Seung-kyu, vice chairman of the Korea Bio Association, commented on this progress, stating, "China's bio industry is far ahead of South Korea in all areas, including regulations, capital, and workforce."

China's biotech sector has not only excelled domestically but also made significant strides internationally. In 2022, Chinese pharmaceutical and biotech companies accounted for 12% of big pharma's technology introduction contracts; this share rose to 29% in 2023 and 31% in 2024. This trend highlights China's growing influence and attractiveness as a partner for global pharmaceutical companies.

The return of Chinese scientists from big pharma to their home country has further fueled this growth. Lee remarked on this phenomenon: "The era has opened where China directly deals with global companies based on manpower." The presence of experienced professionals returning to China has enhanced research and development capabilities and facilitated collaborations with international partners.

As China continues to solidify its position as a leader in biotechnology exports and innovation, experts anticipate the emergence of drugs with annual sales exceeding $1 billion originating from Chinese technology. Lee said that the emergence of such drugs is only a matter of time. With ongoing government support and strategic international partnerships, China is poised to remain at the forefront of biotechnological innovation and exportation for years to come.

Source: https://www.businesskorea.co.kr/news/articleView.html?idxno=240319

Cause for Optimism at the FDA?

FDA is Looking to Significantly Accelerate Approvals in 2025

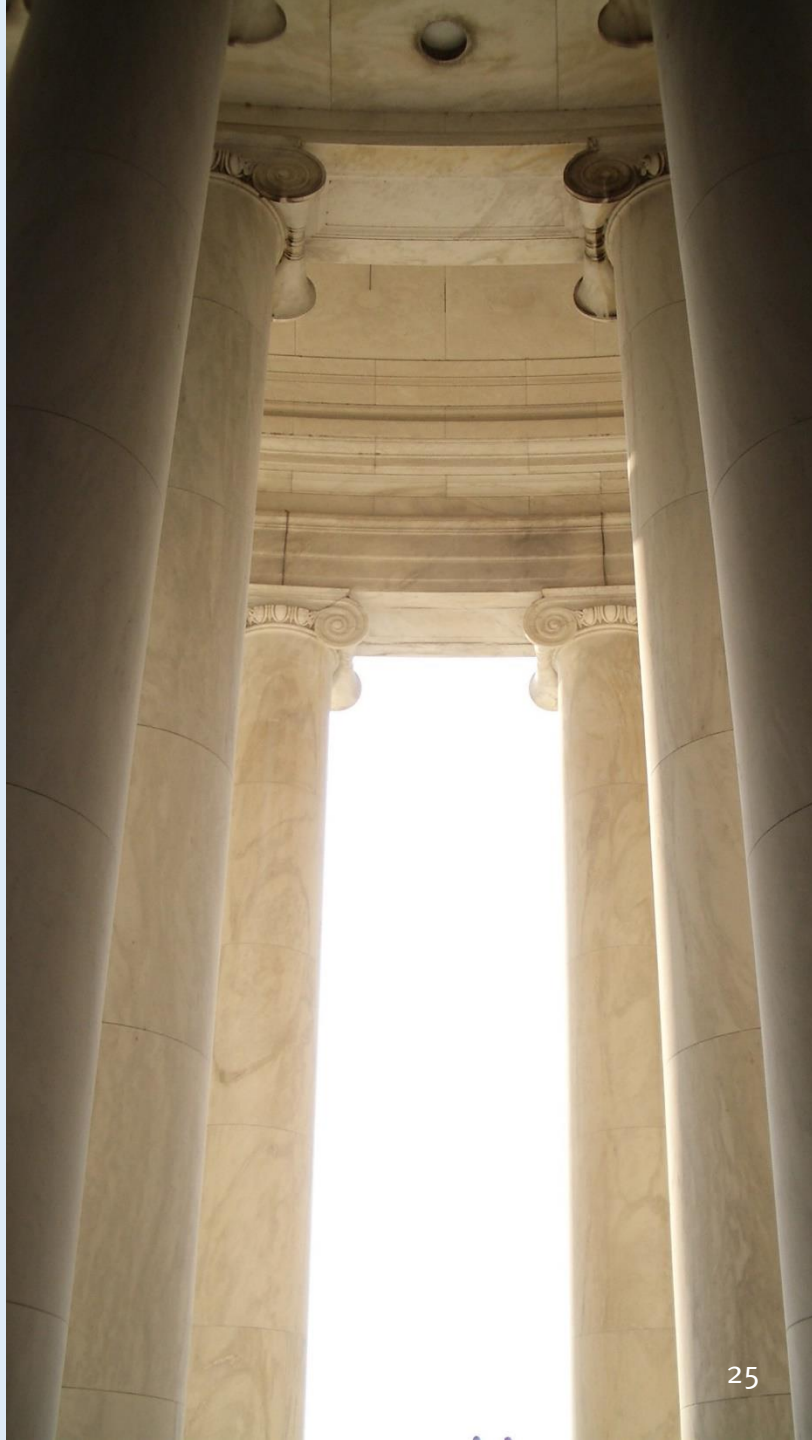
In our biopharma update report a week ago we indicated that we are hearing rumors that FDA is looking to significantly accelerate the pace of approvals in the remainder of 2025.

This week we can confirm that:

1. FDA Commissioner Marty Makary indicated last week in an interview that he would like the agency to accelerate drug approvals.
2. He noted that the case for doing this with drugs for rare disease is particularly strong.
3. We have heard quite strong confirmation from knowledgeable sources that senior staff at CDER and CBER are looking to “put the afterburners on” for drugs that meet significant unmet needs and can save lives:
    a. Highest priority is rare disease
    b. But a real sense that the FDA can do more to speed up approvals for drugs that will make a big difference for patients
    c. A desire to get away from bureaucratic designations that certain drugs are “breakthrough” etc. and just get to work on getting files through
4. An acknowledgement from inside sources that some files may be complex and that with personnel cuts there could be delays and higher probabilities of a CRL but a commitment to work very hard so that this does not happen.

Washington DC Chatter on FDA

5. Other knowledgeable sources indicate that Trump was put off that his “right to try” idea from the first Administration went no where.
6. For Trump 2.0, the idea is that FDA itself will take more of a “right to try” attitude. If there is a drug that could really work for a difficult cancer, rare disease or the like, perhaps the FDA could work to get the file approved quickly. Obviously, reviewers and division directors have to work within the law.
7. The whispers on this major shift at FDA got a lot louder last week and were shared with us by more than a few connected individuals. In addition, sponsors are having surprisingly permissive conversations since Makary has joined FDA.
8. To illustrate, we spoke to one sponsor this month who had a recent meeting at FDA regarding the approval of a drug that would serve something like a thousand children with a likely fatal disease:
    a. The sponsor had data that the drug was making a clear difference in a small group of patients and that the efficacy signal was strong.
    b. The sponsor was going through its plans for a Phase 3 study to confirm the signal relative to historical controls.
    c. The FDA attendees asked why the sponsor was going to do a Phase 3 at all. Why not just file?
    d. The conversation quickly shifted to what it would take to file this drug – mainly CMC work.
9. We have spoken to another sponsor who has been told that they may be able to file for approval this year using Phase 2 drug for a severe autoimmune disease where options are not good today.
10. There was a sense of easing barriers for approval for rare disease drugs in the last year of the Biden Administration. We are hearing an even more libertarian approach ahead with Makary describing approval pathways based on a single Phase 3 or even no Phase 3 if there is plausible biology at work and a disease is rare enough.



Cognitive Dissonance and the Buyside

11. We have spoken to a number of investors about these developments in recent days. We see this as *highly bullish* for biotech in 2025.

12. Sentiment is so bad right now that many on the buyside appear to be experiencing **cognitive dissonance** regarding this new information coming out of the Trump Administration.

13. Almost everyone we spoke to jumped to explain why this new approach might somehow be a bad thing. The general belief is that drug development is going to slow down under Trump 2.0 because of cuts at the FDA.

14. Many observers are attached to the narrative from two weeks ago that the FDA is going downhill and that Trump is degrading a much-cherished regulatory institution.

15. Maybe true, but the implications of changing regulatory winds have clearly not been picked up in the stock market.

16. The XBI movement last week was absolutely tepid and there were net outflows from the market.

17. As we went to the Easter Break on Thursday afternoon, we were mainly hearing talk about which hedge funds were in trouble, why the tariff thing was going to end badly and the like.

18. Investors are largely coalescing around a position that this is going to be a terrible year to invest in biotech. The combination of an unfriendly Administration, an unpredictable President, higher than desired interest rates have caused many investors and LP's to move to the sidelines or go outright net short.

19. These concerns are not without justification and the current situation for biotech stocks is highly fluid.

20. Arguably, this is the most uncertain situation we have seen regarding fundamentals in a long time in biotech.

Cognitive dissonance takes place when new data arrives that is in complete contradiction to a person's prior beliefs. In such a case it is not uncommon for the person receiving this information to deny it completely. There are numerous examples of military defeats linked to cognitive dissonance regarding rapidly changing battlefield conditions.

Marty Makary Comments in Megyn Kelly Interview (4/17/25)

"Now we have giant big data from electronic health records nationally. Now we can have our researchers and universities go in there and look at everyone who's taken a new medication match to somebody who's similar who is not taking that medication and look at the adverse event rate and ask is it working? Is there a safety signal? You don't have great rates about certain complications when you have self-reported data. Self-reported data is terrible data."

See: https://www.youtube.com/watch?v=R4mojSYOTnQ

"In the void of good scientific data every opinion fills that void. So, we can do a better job. And if we have good post-approval monitoring of drugs and devices then we can also tell companies instead of doing two randomized controlled trials to get your drug on the market, how about one and we'll take a close look in the post-approval monitoring on how the drug is doing in real time immediately after it's approved.

And if we have good post-approval monitoring of drugs and devices then we can also tell companies instead of doing two randomized controlled trials to get your drug on the market, how about one and we'll take a close look in the post-approval monitoring on how the drug is doing in real time immediately after it's approved.

And that's particularly important when you're talking about rare diseases.

When you talk about a genetic deformity issue that affects 52 kids in the world and that's a real thing. You've got to say "Hey, this is a very difficult condition. It's incurable. It's fatal. It's a permanent disability. We're going to customize the approval process to the condition. **And, so we're going to be rolling out a new pathway for drugs which is a pathway based on a plausible mechanism. If there's a rare condition or a condition that's incurable that affects a small number of people we may be approving drugs based on a plausible mechanism on sort of a conditional basis."**

Marty Makary Interview with Megyn Kelly Last Week

"Let's say there's a condition that affects 75 people in the world and there's a new treatment that makes sense physiologically. The mechanism is scientifically plausible that this treatment would help these individuals. No one's forcing these medications on these individuals. If they want to try these new medications even though we don't have a randomized controlled trial because it's not feasible we will allow that and at the same time monitory everybody who gets it so that we can we make inferences as soon as the data speaks with a signal in the data."

See: https://www.youtube.com/watch?v=R4mojSYOTnQ

"We're speeding up the approval process. We made an announcement last week that we are reducing the requirements for some perfunctory things like animal testing. Why are we testing every single drug in chimpanzees and dogs, usually beagles because they're obedient. It's sad and it's unnecessary. So, we are taking steps to reduced animal testing requirements. And we live in a modern world where we have computational modeling using AI that can evaluate a molecule and predict its toxicity in humans better than the animal testing. We also have something called organ-on-a-chip technology.

We're bringing in a team that is really exciting. They're going to introduce AI into the review process to help the reviewing make the workstream much more streamlined and summarize things. There are parts of the drug application that are so perfunctory, that are outdated that could be streamlined and abstracted with AI to help the reviewer.

Why does it take ten years to bring a drug to market in the United States? It's because of the regulatory steps. I mean people are dying. People need cures and meaningful treatments. Our number goal is delivering cures and meaningful treatments and healthier foods for Americans.

And so you've heard about changes or consolidations at the FDA. Those were not cuts to scientists or reviewers or inspectors. Absolutely none. They were cuts to communication staff, FDA's lobbyists to Congress and to the IT systems here where there's a lot of opportunity for efficiencies. There was a massive growth of FDA employees under the Biden Administration."

Summary of Makary Interview Comments (Apr 17, 2025)

In his interview with Megyn Kelly, Marty Makary outlines a vision for a more agile and technologically integrated FDA, emphasizing **faster drug approvals**, especially for **rare diseases** where traditional large-scale trials are impractical. In such cases, approval may be granted based on **mechanism of action**, with **post-market surveillance** and **patient tracking** used to confirm effectiveness. A key theme in his approach is leveraging **Electronic Health Records (EHRs)** and **modern data systems**—including **federated learning**—to enhance adverse event detection and drug monitoring, potentially catching problems like **Vioxx®** much earlier. He also strongly advocates for reducing reliance on animal testing, particularly through the adoption of **organoids** and **organs-on-chips** to modernize preclinical research.

As FDA Commissioner, Dr. Makary stresses his desire to support pharmaceutical innovation but with **appropriate guardrails**. He aims to **return the agency to its lean, science-focused structure** reminiscent of 2006, noting that recent staff reductions primarily impacted non-scientific functions like communications and lobbying. Dr. Makary contrasts this with the previous commissioner's focus on "misinformation," instead prioritizing **scientific review** and **regulatory modernization**. He is also deeply committed to the **"Food" mission of the FDA**, pushing for stricter oversight of **food dyes, seed oils, carcinogens, and microplastics**. Under his leadership, the agency is exploring ways to integrate **AI tools** to help its most effective reviewers accelerate decision-making and overcome bureaucratic delays that can keep life-saving treatments from patients for years.

Martin Makary
Head
U.S. Food and Drug Administration

RTW Investments: Summary of Makary Interview

Makary's first interview. Given all the swirl, I'm glad he did this, putting himself out there and making his views known. the ideas are perfectly reasonable, if he is also an effective leader, FDA has a shot at not only retaining its strengths, but by adding modern technology, cutting red tape, and promoting teamwork help us innovate faster (and take the lead back on speed from china, the uk, and australia).

Summary:

- reiterates RFK interest in tackling chronic disease.
- wants to change culture from silos to teamwork. fair criticism of fda shortcoming in my view. ability to change, like all cultural shifts devil is in the execution.
- reiterates RFK interest on the 'F' in fda.
- opioid crisis: talks about the fda reviewer that determined oxycontin label going to work for purdue.
- talks about protecting innovation. example: 1 instead of 2 RCTs, then leverage real world data. affirmation of existing trend.
- new pathway for rare diseases based on mechanism without an RCT. leverage real world data. affirmation of existing trend.
- health information exchange (EMR data) can help show real world adverse event rates. aers is self reported, limited ability to discern real rates. i agree with this, a good idea.
- need fda independence from drug companies. eg on adcoms will replace pharma rep with patient advocate. i think in practice hard to find anyone in the trenches that would say anything other than fda is super tough (in fact in some cases too bureaucratic and rigid and don't consider patient desires and risk benefit enough). that said, ideas like this, are absolutely good hygiene to improve trust.
- want to make things faster by reducing red tape. examples: will reduce animal testing (by using computational models and organoids), use AI to make review more efficient. drug development shouldn't take 10yrs. YES, these are new ideas that are good.
- gave context to cuts. 100% increase in fda employees since 2006. reiterated no cuts to reviewers, wants them to have resources to do their jobs. whether there is disruption is THE debate. lots of negativity especially on wallstreet. ceo's don't seem to agree.... yet. i remain cautiously optimistic.
- defended RFK leadership. said open to listening.

Rod Wong, M.D.
Managing Partner
RTW Investments

Source: https://x.com/docrodwong

Biotech Buyside Update

Update of the Stifel Buyside Study

We previously published reports on the biotech buyside in our November 21, 2022, April 17, 2023 and Apr 7, 2024 issues.

Today, we are updating this using data on fund holdings as of December 31, 2024.

We have accessed Form ADV's which are filed with the SEC by Registered Investment Advisors (RIA's) in the U.S. Any fund holding more than $110mm and managing money for at least two persons needs to file a Form ADV. This captures most groups but would miss institutions that manage their own money or small funds.

These include Novo Holdings and family office type investors such as Tang Capital or Ridgeback Capital.

We also collected fund level data as of the start of April on biotech holdings from S&P CapIQ. These would draw off of Form 13G, 13F and 13D reports filed by investors earlier. These data will largely reflect holdings of the buyside on Dec 31, 2024.

A particularly thorny issue that we wish to be upfront about is that our definition of biotech (R&D stage therapeutics) and that of CapitalIQ is not the same. CapitalIQ's definition of biotech is hard to fathom and encompasses about 75% of R&D stage therapeutics companies but also includes AbbVie, Gilead, Moderna and many other commercial stage companies. Take these data for what they are.

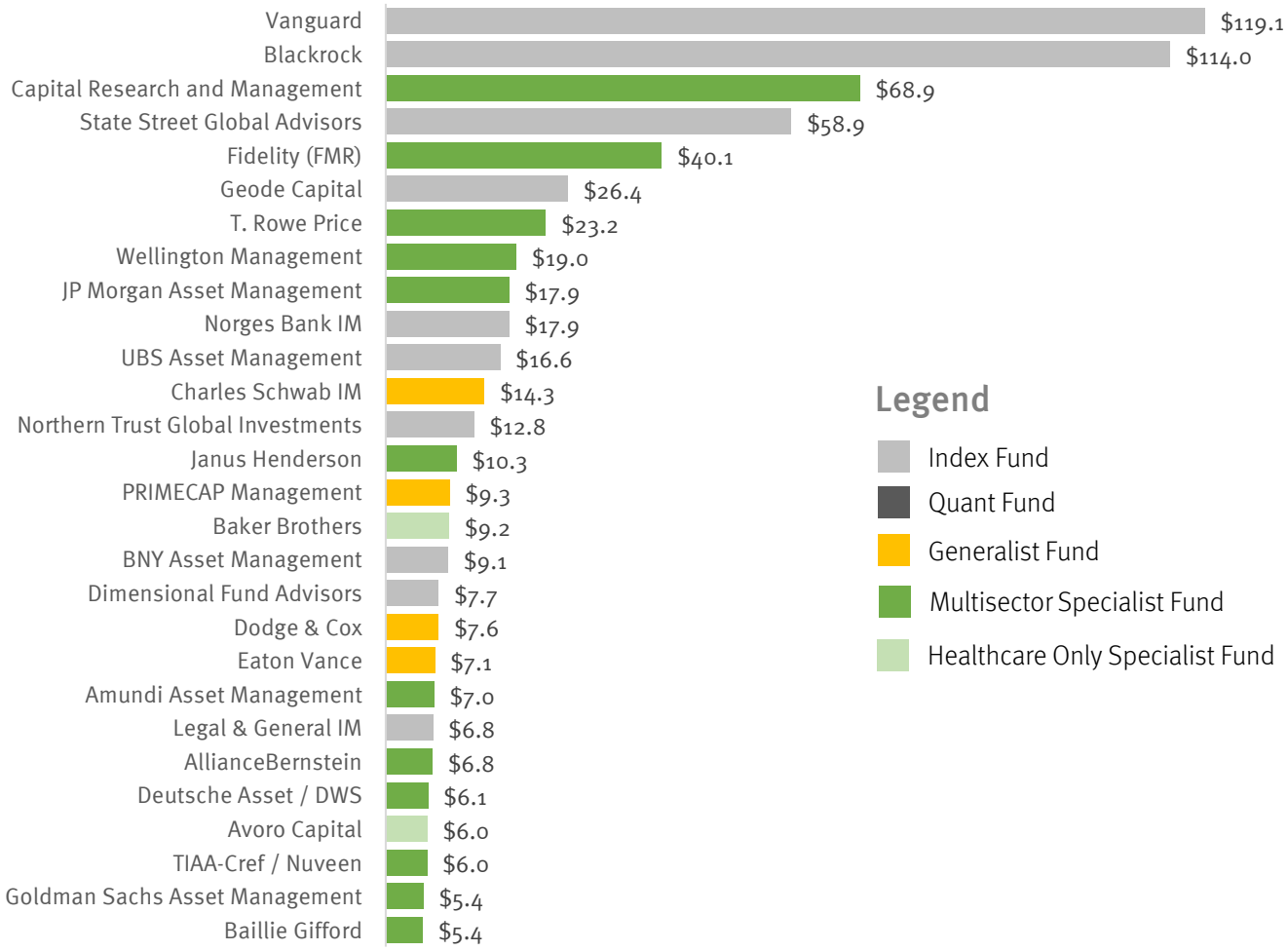
Nonetheless, we have found that there is a lot to be learned from the available data and are happy to share our latest findings with you.

Today's analysis is designed to coincide with the release of Form ADV's which provide total AUM data for RIA's as of Dec 31, 2024. these were due at the SEC on March 31, 2025.

Who Are the Largest Owners of Biotech Stocks?

Largest Disclosed Holders of Biotechnology Stocks on April 17, 2025

($ Billions, CapitalIQ Definition of Biotechnology, Shows holdings as of Dec 30, 2024)



Source: CapitalIQ Holdings data and Stifel analysis of data.

These data are from S&P CapitalIQ and show the level of biotech holdings as of Dec 30, 2024 and are ranked by amount of biotech owned by fund. Recall that these data reflect some holdings of large pharmas such as AbbVie given that the data on biotechnology holdings are sourced from CapitalIQ.

There was a total of $840 billion of biotech stocks held by funds that we track in our database. This is based on holdings as of Dec 30, 2024. This is down from $845bn a year earlier.

The data reveal that index and quant funds account for $423.3 billion of the holdings of top biotech funds (almost exactly half).

These funds are not proactive and simply follow indices like the Russell 3000 and buy whatever companies are included to mimic the market return at a low cost.

Specialist multisector funds investors such as Janus Henderson account for another $260bn+ or so of holdings. Generalist funds (think Charles Schwab Investment Management) are not as important in the market (holding only $32bn of biotech assets). Increasingly, we think that holdings at generalist funds and multisector specialists may be partly indexed as well.

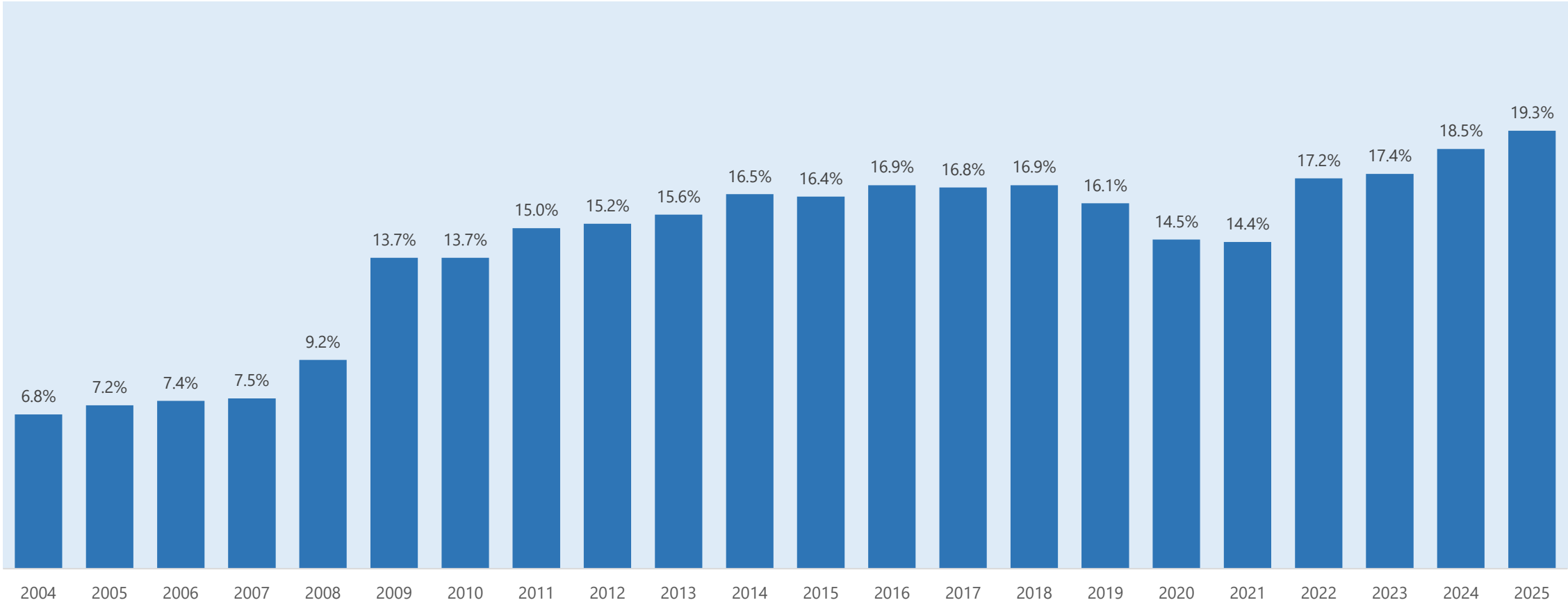
This analysis does not include retail investors at all and so may overstate the relative importance of indexers and specialists but certainly gives a sense of the ownership structure of the biotech market.

An important observation is that index funds today, overall, have substantially more ownership of biotech stocks than do specialist funds.

Index Fund Ownership of Biotech Up Last Year

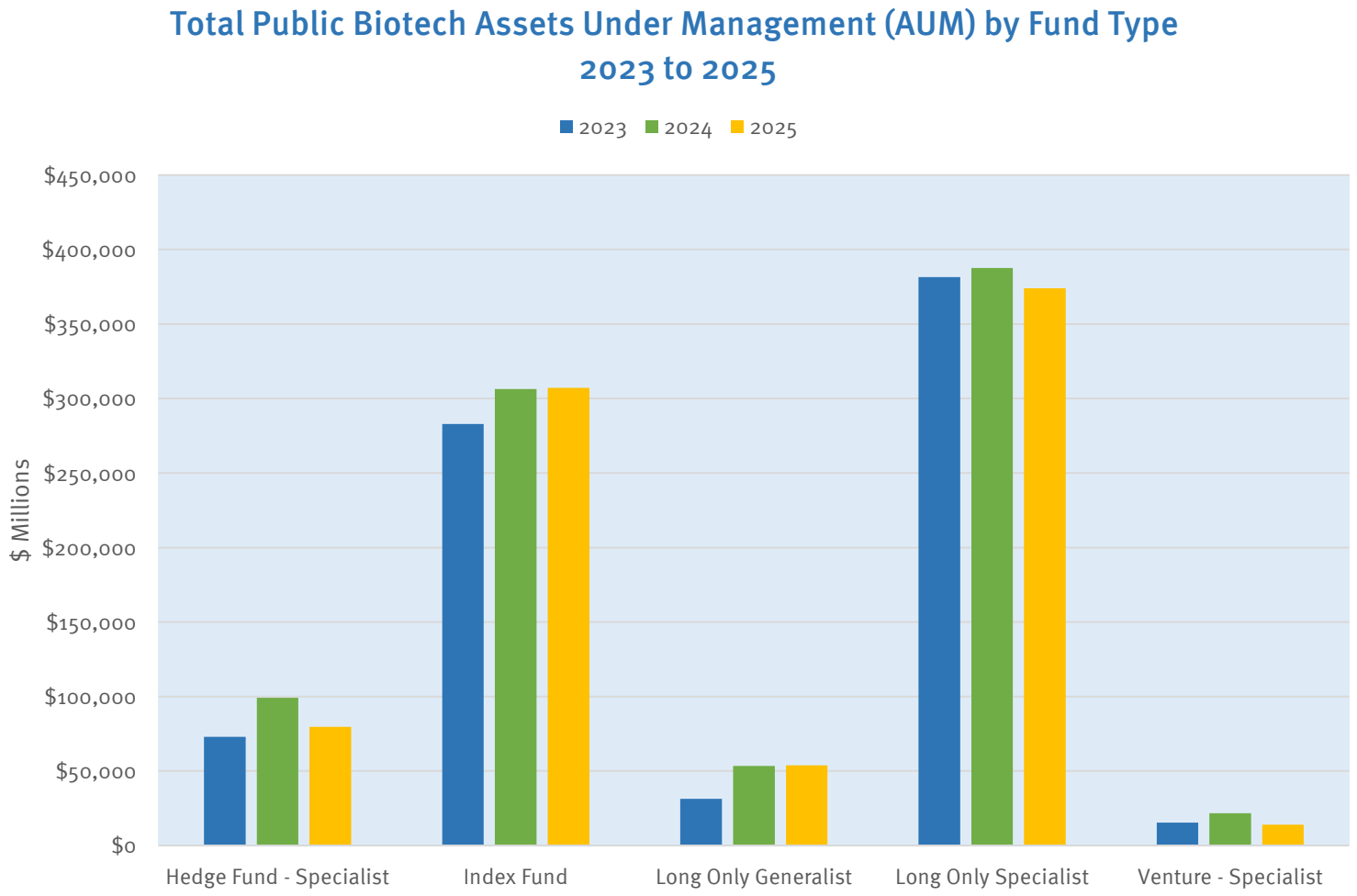
The ownership of the biotech market by indexers has nearly tripled over the last twenty years. Biotech ownership by top index funds is at an all time high. More than half of the biotech market today is owned by passive asset managers (index funds or quant funds).

Percent of CapIQ Biotech Stocks Owned by Top 5 Index Funds, December 2004 to April 2025



Source: CapitalIQ Holdings data and Stifel analysis of data. This chart shows the market value of shares owned by Blackrock, Geode Capital, Norges Bank, State Street and Vanguard divided by the total value of biotech stocks. For each year, the shares are valued on Dec 30th. For 2023 and 2024 shares are valued as of the start of April.

Index Fund and Generalist Long Funds Gained Relative Share of Biotech Holdings in 2024 as Specialists Pulled Back



The chart at left looks at total public biotech stock ownership by fund type. Long-short specialist funds decreased their biotech ownership in the last year (but did not lose AUM). This means that they went more heavily short (or to cash) in 2024.

Long-short funds were obviously able to shield themselves from losses in this time interval by shorting the market.

Index funds grew slightly and gained total share. Long specialist funds reduced biotech holdings the most, but we think this was mainly by allocating away from biotech. Venture specialist funds with public holdings saw the value of their holdings drop. Overall, 2024 was a year where the importance of specialist shrunk somewhat.

Source: CapitalIQ Holdings data and Stifel analysis of data. Data shown are for the first day of the calendar year.

Largest Biotech Investors by Median Holding Size

Most biotechs have market caps under $5bn and the majority are now under $250mm in size. Importantly, the most important investors in this sub-$250mm company group are index funds and quants. Citadel (a fundamental analysis investor) is the 8th ranked owner by size of groups that have a median biotech portfolio cap under $250mm. All larger players do not invest based on fundamentals. Fidelity, T. Rowe, Baker, JP Morgan, and AllianceBernstein are important players in the small cap space and are all fundamentalists. Leading fundamental medium Cap managers include CapRe, Wellington, JP Morgan AM, Janus Henderson and PRIMECAP. Bear in mind that this analysis is based upon S&P's definition of biotech.

Large Cap (Median Holding $5bn+)	**Medium Cap** (Median Holding $1bn-$5bn)	**Small Cap** (Med Holding $250mm-$1bn)	**Micro Cap** (Median Holding < $250mm)
Dodge & Cox	Capital Research and Management	State Street Global Advisors	Vanguard
Boston Partners	Wellington Management	Fidelity (FMR)	Blackrock
ClearBridge Investments	JP Morgan Asset Management	T. Rowe Price	Geode Capital
Neuberger Berman	Norges Bank IM	Charles Schwab IM	UBS Asset Management
Chevy Chase Trust	Janus Henderson	Baker Brothers	Northern Trust Global Investments
Nomura Asset Management	PRIMECAP Management	BNY Asset Management	RA Capital
Paulson & Co.	Amundi Asset Management	Dimensional Fund Advisors	Renaissance Technologies
Eagle Asset Management	Avoro Capital	Eaton Vance	Citadel Advisors LLC
Gilder Gagnon & Howe	Baillie Gifford	Legal & General IM	Millennium Management LLC
Frontier Capital Management	PGIM / Jennison	AllianceBernstein	Biotechnology Value Fund / BVF
Columbia Threadneedle	Franklin Resources	TIAA-CREF	Point72
Calamos Advisors	Artisan Partners	DWS / Deutsche AM	Armistice Capital

Source: CapitalIQ

The Specialist Biopharma Fund Universe

We often speak of specialist fund managers in biotech in a broad sense. But specifically, how many are there? How much do they manage? And, how many, like Perceptive, are “healthcare only”?

The data at right show rapid growth in AUM and the number of funds that are healthcare only.

Most dedicated healthcare funds are small. For example, a year ago we counted 53 HC-only specialist funds with $1 billion or more in assets. Today, we count 52 such funds. Most HC-only funds are managing less than a billion in assets.

* There are some specialist funds that do not need to file as an investment advisor. SEC Rule 203A-1 permits an investor to avoid registering if they do not provide investment advice to others (in other words, if they are solo, this is not required) or if they manage less than $110 million. Many groups that manage less than $110 million still file Form ADV due to state securities rules. Examples of well-known funds that do not file an ADV include Pivotal, Quogue, Ridgeback and Tang. These are effectively family office investors.

Here is our accounting of the specialist biopharma fund universe:

$322 billion

of biotech assets as of Apr 17, 2025 are held by specialist funds.* This is down from $388bn at the same time in 2023 and $315bn on June 30, 2022.

201 funds

We count 201 funds that invest in Biopharma with at least one MD or Ph.D. on staff. Compare to 149 funds in 2022 and 198 funds a year ago.

35 stocks

The average healthcare only specialist fund has 35 biotech positions.* This is down from 43 funds two years ago.

93 funds

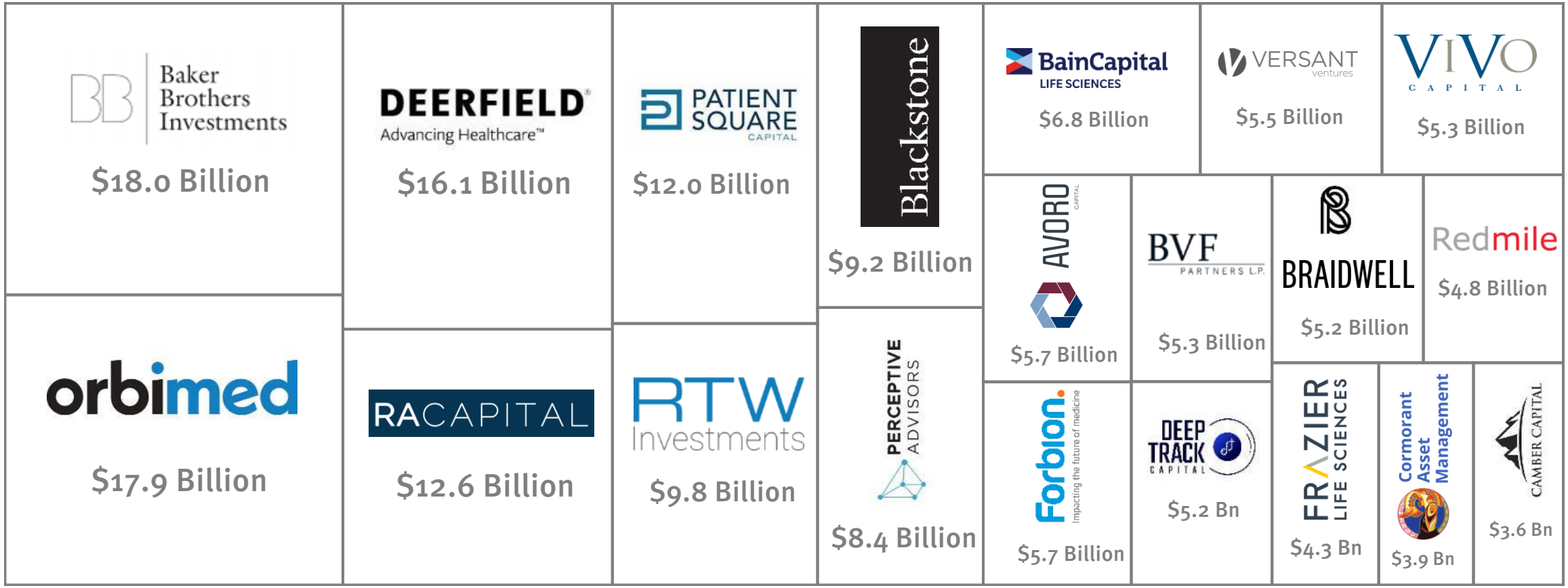
We count 93 healthcare only specialist funds (compared to 94 in 2024). These funds have $251bn in AUM. But only $71bn of this was in long positions.

* Using S&P’s definition of biotech.

Top 20 Healthcare Only Investment Managers by AUM

This chart lists AUM of top healthcare only investment managers with exposure to the public markets. Baker Brothers regained the #1 spot from OrbiMed at the end of 2024. However, because OrbiMed also gained AUM in 2024, they are neck and neck with Baker. OrbiMed is very likely to gain AUM in 2025 as they were not in a big fund-raising mode last year, so next year's rankings are going to be interesting to watch. Also, notable, in a very tough year RA Capital was able to gain AUM (mainly through positive returns). Patient Square is only in its third year on this list and is now in the #5 position. Due to a difficult market, last year was a tough year, in general, for specialist hedge fund models. While groups pursuing this model like Perceptive and RTW held on to their assets quite well, we saw major advancement in relative AUM of funds with heavy private holdings like Blackstone, Bain, Versant, Vivo and Forbion in 2024. If we get a strong up year (one of these days) we would expect to see funds with a more public market orientation do well on a relative basis. Frazier and Camber appear on this list for the first time in 2025.

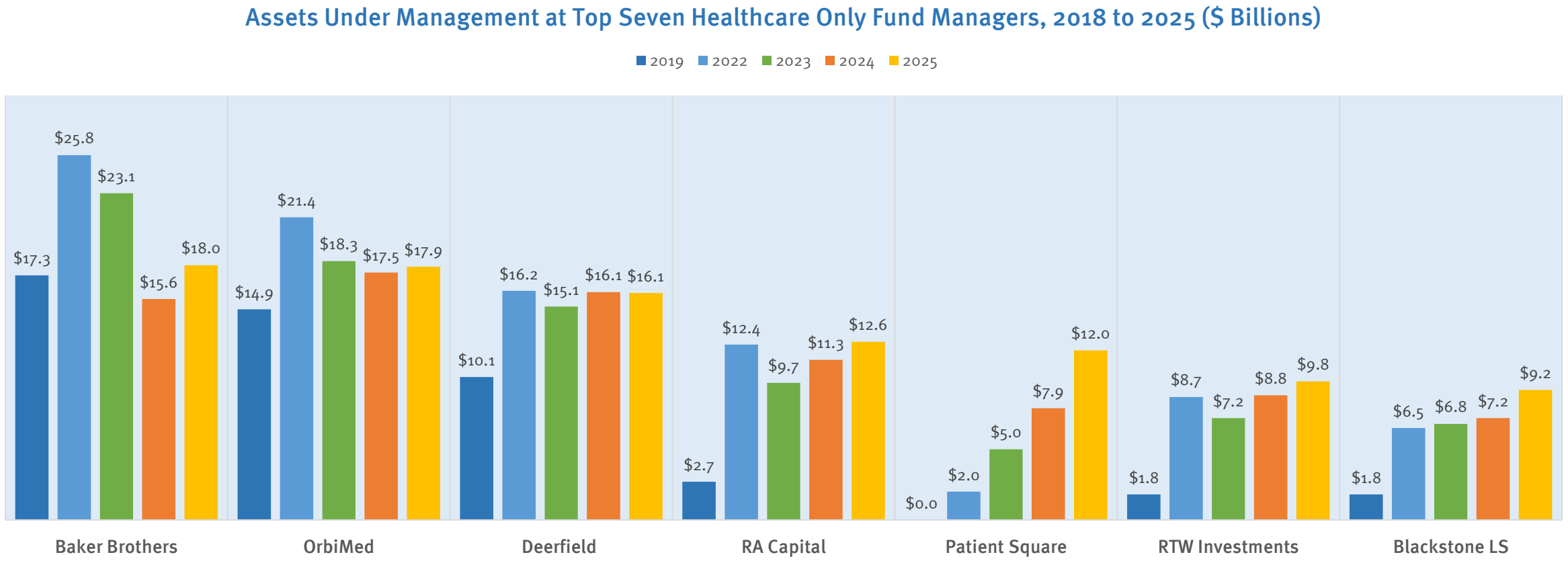
Assets Under Management (Q1 2025 / End of 2024, $ Billions, From Form-ADV Filings made in late Q1 2025)



Source: U.S. Securities and Exchange Commission Filings.

Top Seven Healthcare Only Specialist Funds Evolution Over the Last Six years

Last year had the potential to be quite toxic for the top managers on the buyside. The market was volatile and experienced several very rough periods. Despite all of this, there is not a single fund listed here that had January 1, 2025 AUM below where it was at the start of 2019. Healthcare specialist style investment grew massively after the Pandemic and has held up well despite extreme market conditions. Funds who were able to use specialist knowledge, short strategies and private investment strategies to hold onto assets in a challenging market.



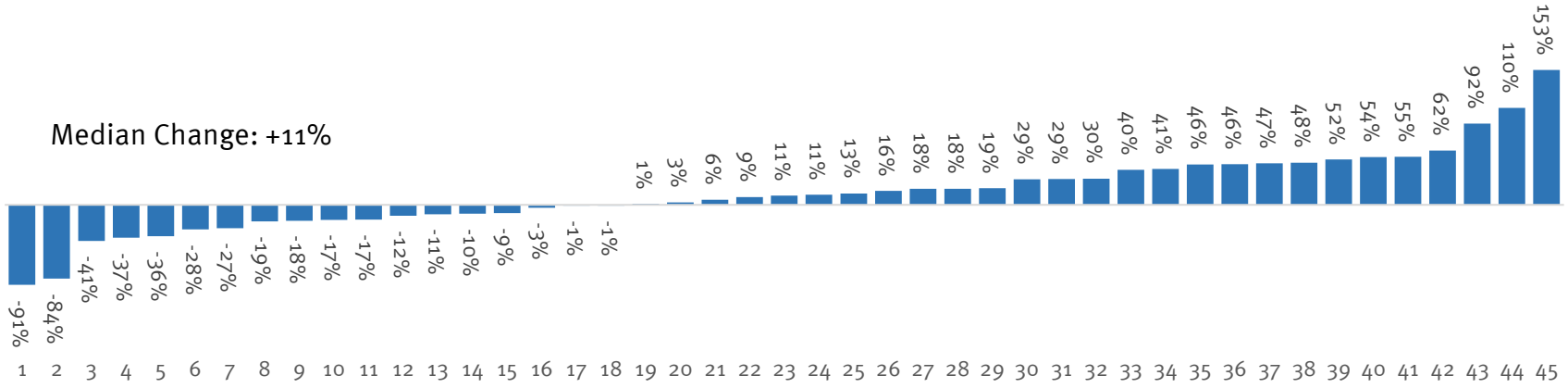
Source: U.S. Securities and Exchange Commission Form ADV Filings. Numbers are on the first day of each year.

Fund Type Mattered for AUM Gain in 2024 in HC Only Group

Long-only specialist funds, on average, lost AUM in the tough market of 2024. In contrast venture funds with public arms, multi-strategy funds and long-short hedge funds were all able to grow AUM, on average in 2024. Being able to short stocks or to participate in strategies away from long equities was an important survival trait in 2024.

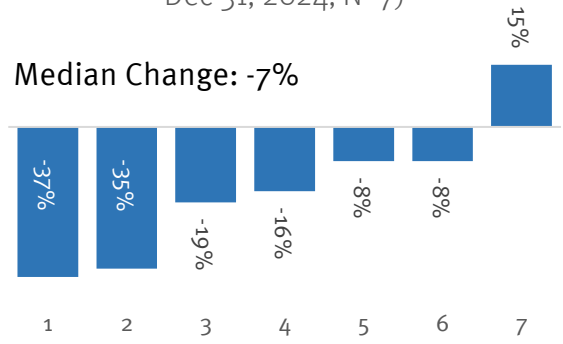
Long-Short Healthcare Only Hedge Funds Percent Change in AUM

(Change in AUM, Dec 31, 2023 to Dec 31, 2024, N=45)



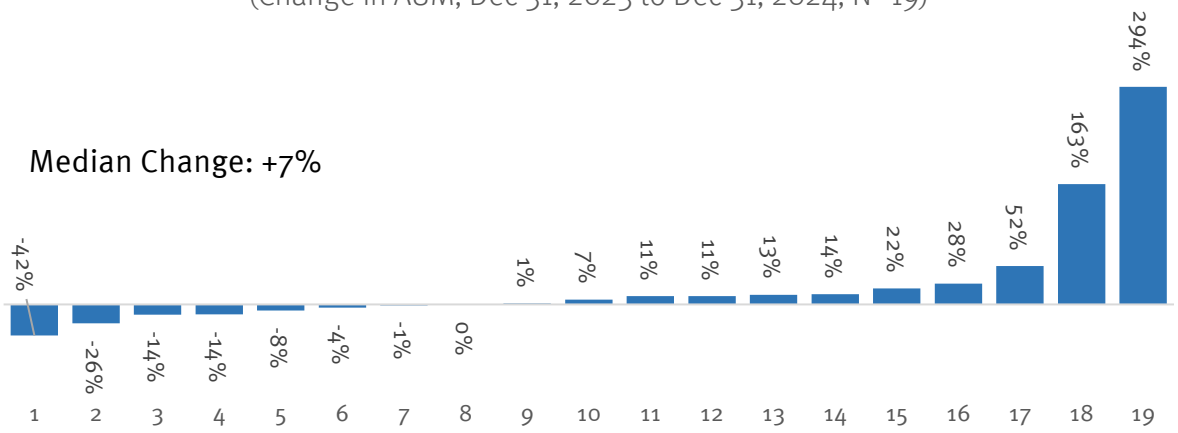
Long Only Specialist Funds, Percent Change in AUM

(Change in AUM, Dec 31, 2023 to Dec 31, 2024, N=7)



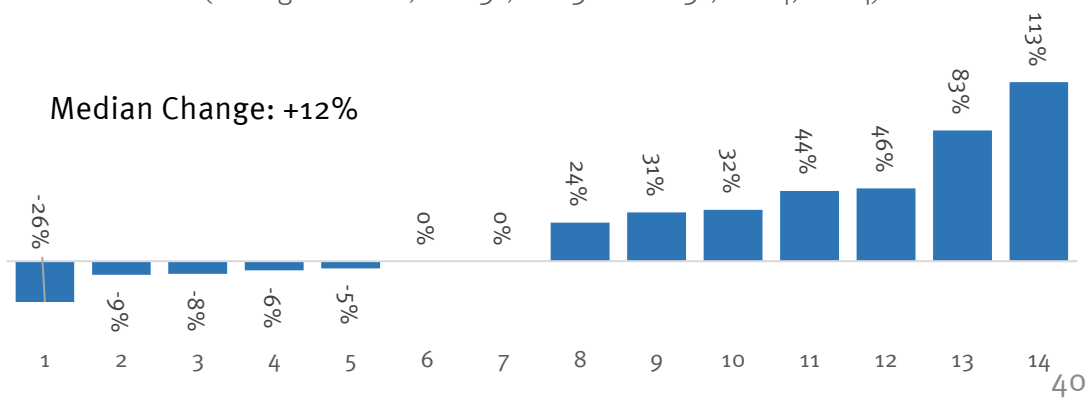
Multi-Strategy Funds, Change in AUM

(Change in AUM, Dec 31, 2023 to Dec 31, 2024, N=19)



Venture Funds with Public Funds, Percent Change in AUM

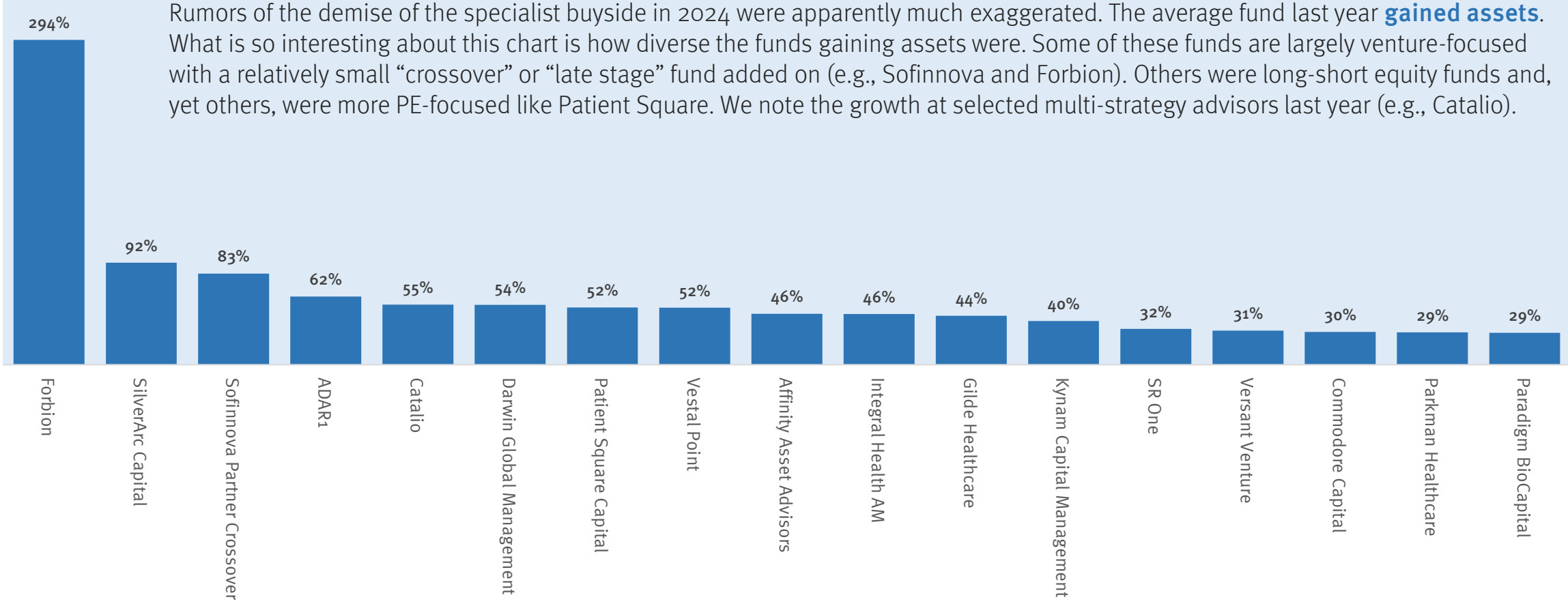
(Change in AUM, Dec 31, 2023 to Dec 31, 2024, N=14)



Top 15 Healthcare Only Specialist Funds by Gain in Percent Change in AUM During 2024

Change in AUM During 2024 (Dec 31, 2023 to Dec 31 2024)

Rumors of the demise of the specialist buyside in 2024 were apparently much exaggerated. The average fund last year **gained assets**. What is so interesting about this chart is how diverse the funds gaining assets were. Some of these funds are largely venture-focused with a relatively small "crossover" or "late stage" fund added on (e.g., Sofinnova and Forbion). Others were long-short equity funds and, yet others, were more PE-focused like Patient Square. We note the growth at selected multi-strategy advisors last year (e.g., Catalio).

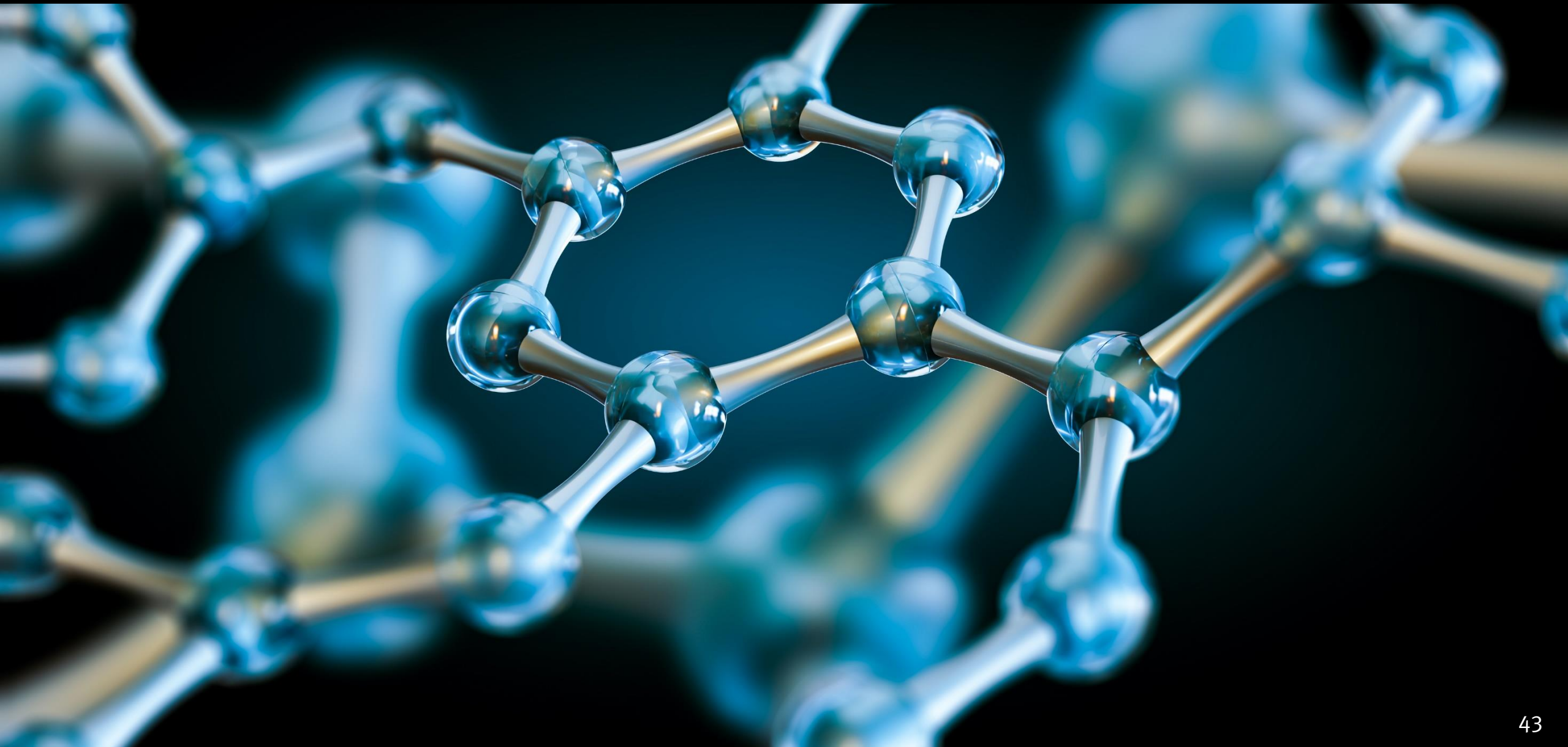


* only included funds with $500mm+ in AUM at end of 2024. Source: U.S. Securities and Exchange Commission Form ADV Filings.

Summary: The Evolving Healthcare Investor

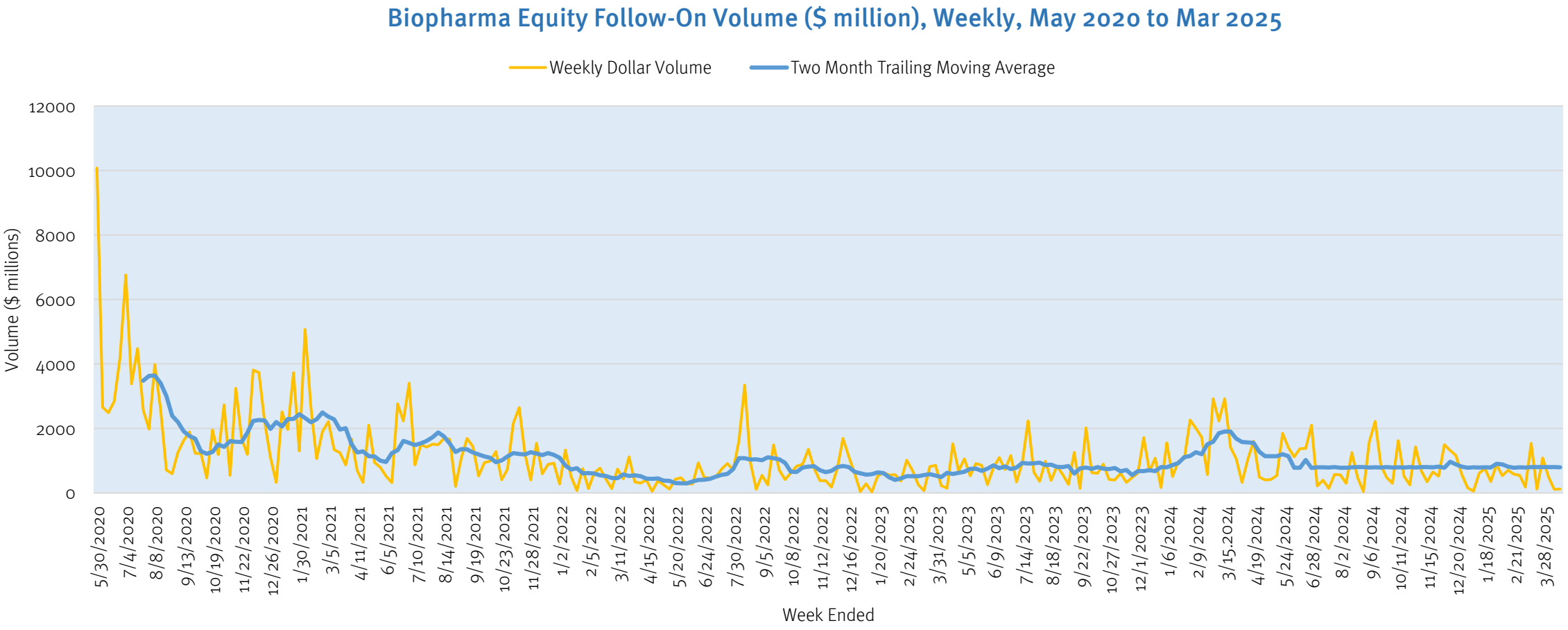
- The specialist life science buyside is **quite large.**
  - Nearly $322 billion of assets are held by biotech specialist funds.
  - The AUM of these funds has more than **doubled** since 2018
  - We count 201 specialist life sciences funds and 94 healthcare only specialist funds today.
- Despite rumors to the contrary, the specialist healthcare investor entered 2025 in good shape.
- **More specialist funds gained assets last year than lost assets**. This would be contrary to the "gloom and doom" perspective and poor sentiment we were hearing at year-end 2024 from several fund managers and their LP's.
- Nonetheless, 2024 was a year where funds that were unable to short the market took their lumps. Long-only specialist funds lost assets in 2024 while funds that could short, or affiliated with VC's or pursuing multi-strategy approaches did much better.
- Other facts of note include the ongoing growth of index funds. Their share of the total market is rising. **Passive investors own more than 50% of biotech in 2024 and gained substantial ground last year.**
- While we have yet to see data, a recent report in *Institutional Investor* indicated that many well-known specialist hedge funds had a tough Q1 2025. This is not surprising given the deep swoon that has taken place in the biotech market under President Trump.
- There is no doubt that this is a tough moment for the buyside as several well-known funds have been facing LP withdrawals.
- But, if there is a takeaway, from our analysis this year and that of recent years, it is that the U.S. biotech institutional investment community comprises a resilient, smart and significant group of fund managers who know how to manage risk through good and bad markets.
- We are hopeful that the current moment will, in retrospect, be near the market bottom. It is our belief that the deep fundamental analysis used by biopharma investors today will allow the quality of biotech companies to continue to improve and deliver medicines that will benefit patients for decades to come.

Capital Markets Update



Public Market Equity Financings Very Slow this Month

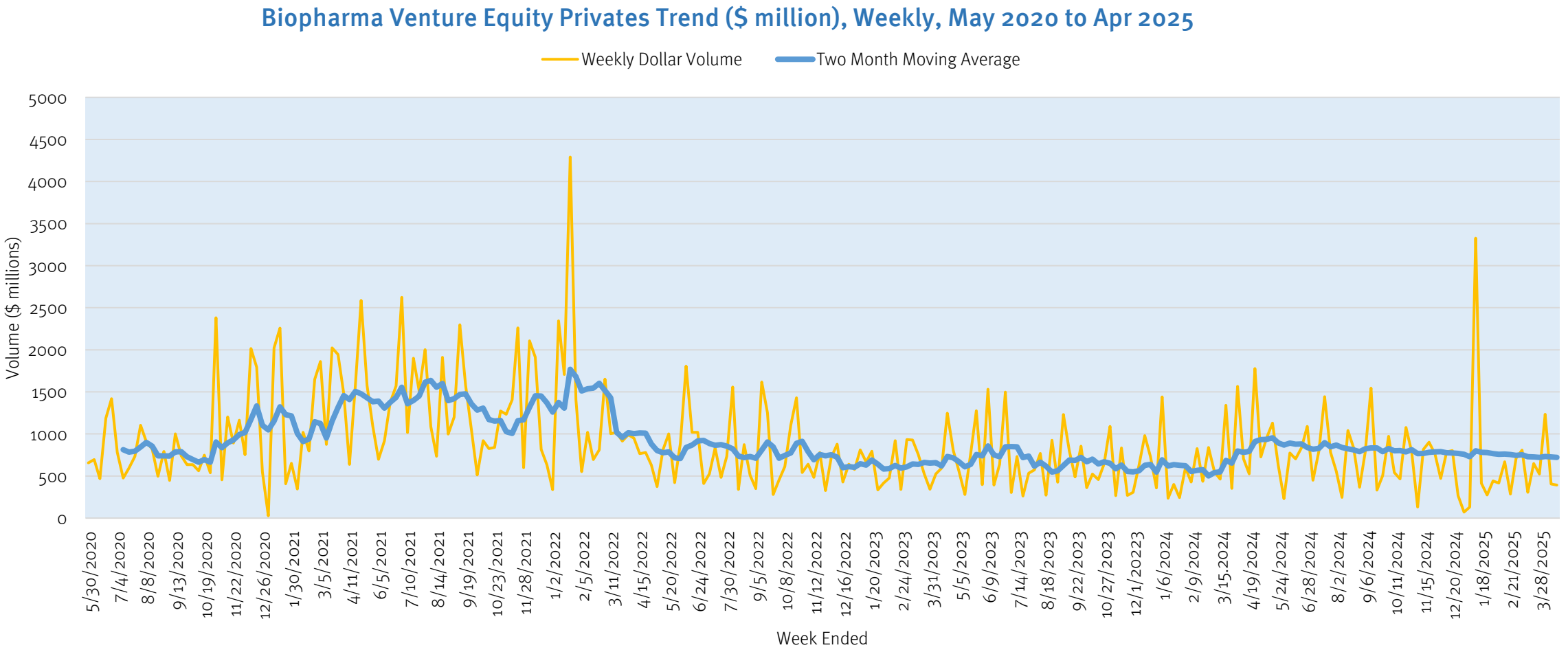
There were no IPO's last week. Follow-on volume for the first quarter of 2025 has average $600mm a week. In contrast, in April 2025, follow-on volume has averaged $245mm a week. Last week was a holiday-shortened week that saw only $123mm issued in the market. The week before saw $115mm issued. This is the slowest two week period since we started tracking volume statistics in May 2020.



Source: Data from CapitalIQ and Stifel research.

Venture Privates Market Slowing

Recent weeks have seen modest activity in the venture privates market. Last week saw $393 million in deals. Compare this to an average volume of $900mm in the first two months of 2025.

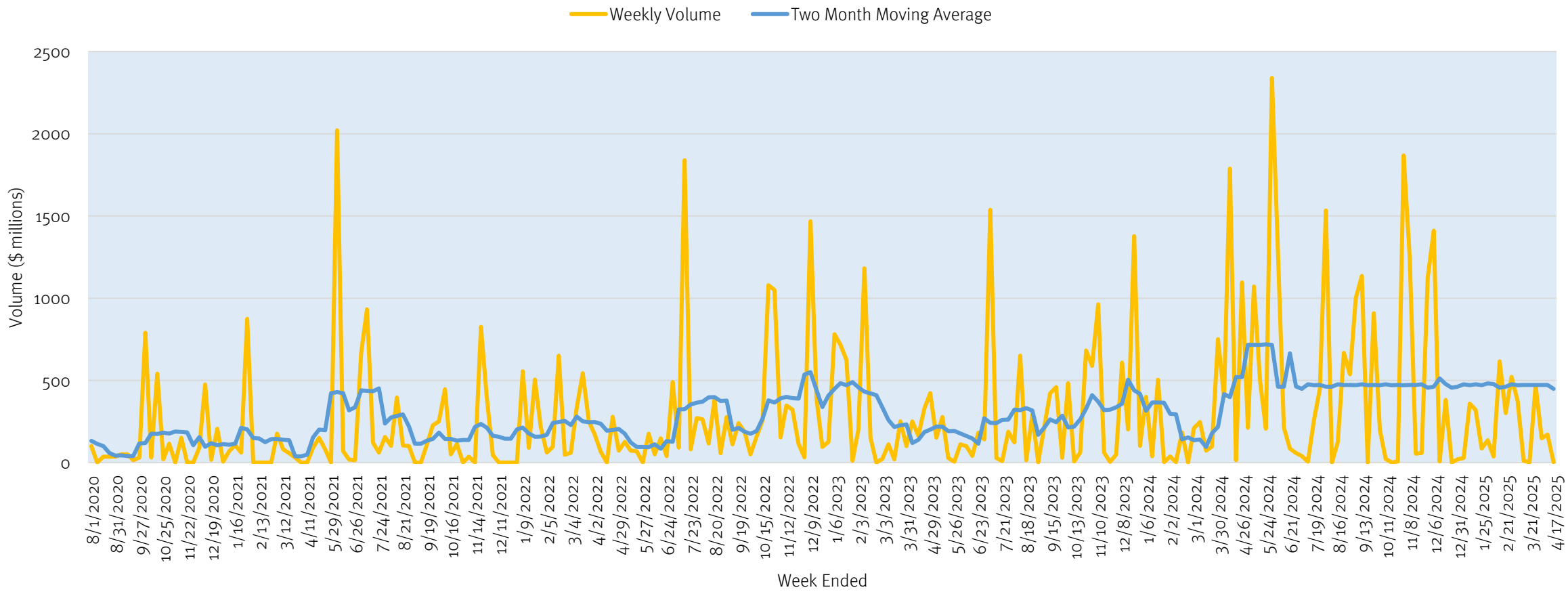


Source: Data from CapitalIQ, Crunchbase.

Global Biopharma Private Debt Placement Volume Has Fallen

Private debt issuance last week was slow. The volumes in this market appear to have been dropping in recent weeks due to high uncertainty in credit markets linked to Trump's tariff actions.

Biopharma Private Debt Issuance Trend ($ million), Weekly, Aug 2020 to Apr 2025

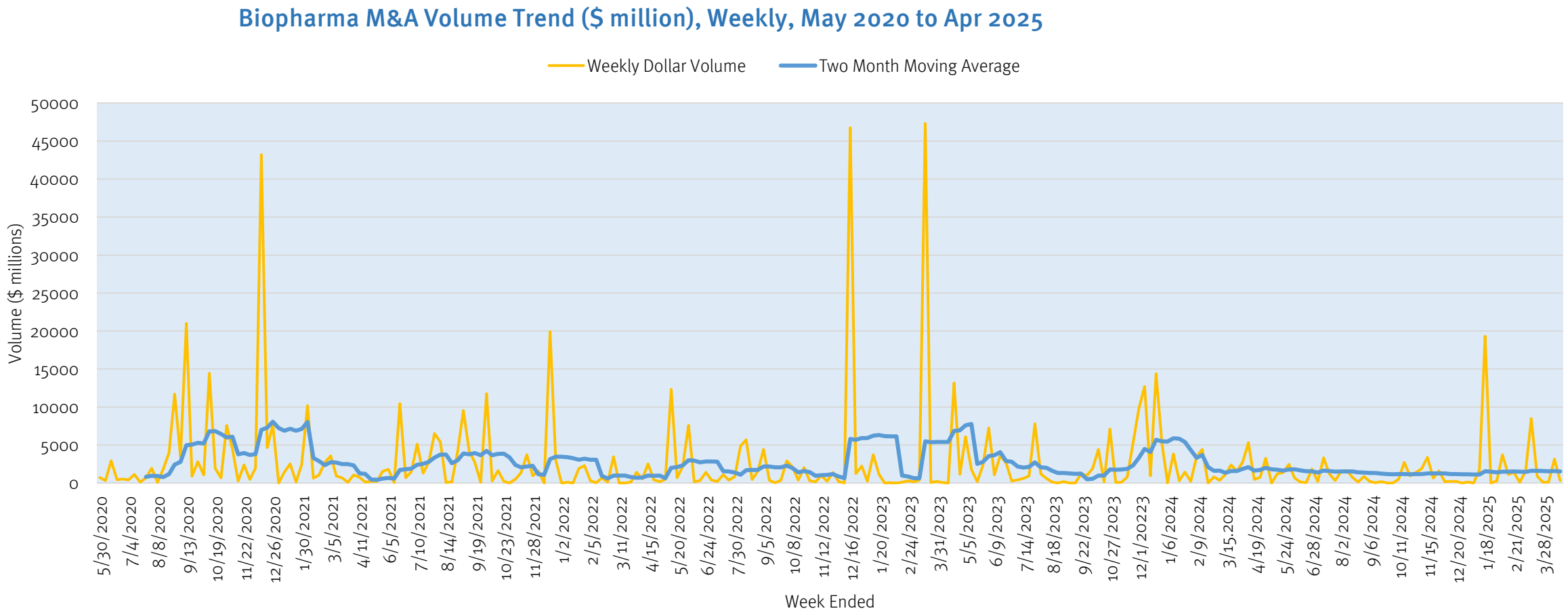


Source: Data from CapitalIQ, Crunchbase.

Deals Update

M&A Market Lightening Up in April

The M&A market was quite active in March 2025 with two large deals announcing (ENDO/Mallinckrodt and Bain/Tanabe). With the acquisition of Karo Bio by KKR two weeks ago and last week's Norgine, volume remains on an $8bn a month track in April. We continue to see very strong levels of commercial-stage M&A and much less public pre-commercial biotech M&A. At least so far. We continue to believe that this is likely to change.



Source: S&P, CapitalIQ

Norgine on a Growth Charge Again with Theravia Takeover Deal

Phil Taylor, *PharmaPhorum*, April 15, 2025 (excerpt)

Neuilly-Sur-Seine company Theravia – formed through the merger of Addmedica and CTRS in 2023 – has five product ranges on the market and has an R&D pipeline covering fertility, allergy, and skin disorders.

Theravia made more than €50 million in revenues in 2024 and has seen its sales rise by an annual rate of around 10% in recent years. For comparison, Norgine has annual revenues of more than €550 million a year.

The takeover deal comes amid a period of product portfolio-building at Norgine and follows licensing deals giving regional commercial rights to X4 Pharma's WHIM syndrome therapy Xolremdi (mavorixafor) and Fennec Pharma's Pedmarqsi (anhydrous sodium thiosulfate injection), used to prevent hearing loss in children treated with cancer chemotherapy cisplatin.

Taking control of Theravia from its current owners – which include private equity firm Mérieux Equity Partners, its majority shareholder – will add products including Siklos (hydroxycarbamide) for adults and children with sickle cell disease (SCD), Orphacol (cholic acid) for adults and children who have a genetic disorder that affects bile production by the liver, and wound care range Liquiband.

This acquisition is a unique opportunity for Norgine to bolster our growth trajectory, as well as our rare disease portfolio," said Norgine chief executive Janneke van der Kamp, a former head of pharma at Grünenthal, who replaced Chris Bath at the helm of the Dutch company at the start of this year.

"With our strong legacy and proven track record of successfully bringing innovative treatments to patients, we believe we are well placed to ensure the Theravia medicines reach their full potential," she added.

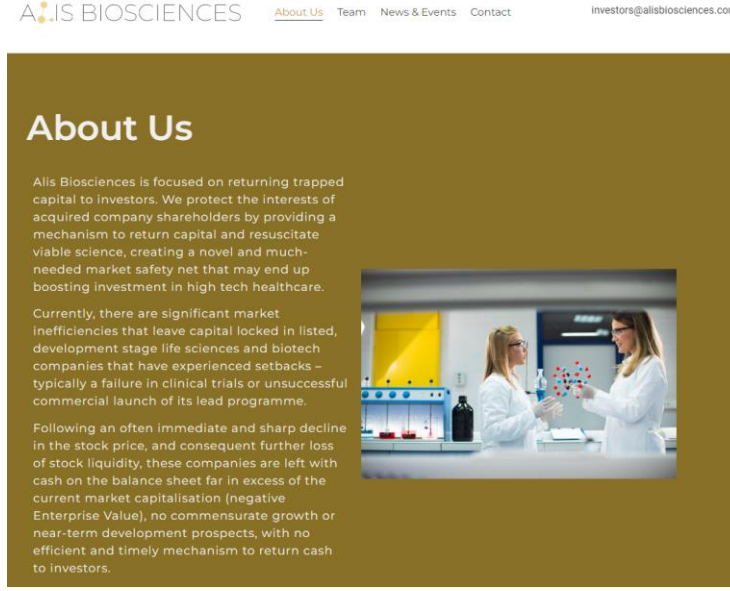
Van der Kamp also reiterated her plan for Norgine to continue its acquisitive spree and is looking for other acquisitions and in-licensing opportunities to drive growth.

Source: https://pharmaphorum.com/news/norgine-growth-charge-again-theravia-takeover-deal

Janneke van der Kamp
Chief Executive Officer
Norgine

Unusual New Fund Launches to Unlock Some $30B of Capital 'Trapped' in Public Biotechs

Annalee Armstrong, *Biospace*, April 18, 2025 (excerpt)



Taking a page out of the private equity playbook, a new fund has emerged to recycle over $30 billion of capital "trapped" in failed public biotechs.

London-based Alis Biosciences launched on Friday with a pledge to return to shareholders capital that's invested in publicly listed companies that have suffered a clinical failure or other stumbling block, with nowhere to turn.

The plan—which is carefully laid out in three different structures—is a familiar tactic in the private equity world. But Alis will instead be listed on the public markets "in due course," according to the Friday release.

"We founded Alis Biosciences to alter the status quo, where tens of billions of dollars of investors' funds are trapped in moribund listed life sciences and biotech companies," said Alis founder and board member Nicholas Johnston in a statement. "Our highly experienced team work collaboratively with shareholders, management, and boards, to provide the optimum mechanism to return capital to shareholders, while also allowing stakeholders the option to further develop residual science and IP where there is potential to do so."

Alis is targeting 300 listed, development stage biotechs or life sciences companies that have "experienced clinical, regulatory or commercial setbacks." The firm estimates these companies have a combined $30 billion on their balance sheets. But individually they have small market caps and low cash reserves. After a clinical failure, companies face a tough decision. Among the options available, they can advance another candidate, sell or liquidate.

Alis explained that if they opt to go after another target in their pipeline or merge with another company, shareholders' equity is heavily diluted. Plus, shareholders are forced into something very different from what they originally signed up for and "are left with no option but to follow the direction of management or the board, while tens of millions of dollars of investor capital remains on the balance sheet." Bankruptcies can be time-consuming and expensive, further draining cash reserves. The IP is also typically left untapped.

Source: https://www.biospace.com/business/unusual-new-fund-launches-to-unlock-some-30b-of-capital-trapped-in-public-biotechs

Theratechnologies Provides Update on Sale Process

Press Release, April 15, 2025 (excerpt)

Theratechnologies Inc. (“Theratechnologies” or the “Company”) (TSX: TH) (NASDAQ: THTX), a commercial-stage biopharmaceutical company, today announced that following careful consideration of the current circumstances, including the publicly announced proposal from Future Pak, the Board of Directors of the Company (the “Board”) has decided to further evaluate the potential sale of the Company through an open and non-exclusive process.

In connection with this determination, the Board has authorized the special committee, consisting of independent and disinterested directors (the “Special Committee”), to oversee the process and make a recommendation to the full Board. To support this process, in addition to Barclays as financial advisor and Fasken as legal advisor, the Special Committee has also engaged Raymond James as independent financial advisor and Norton Rose Fulbright as independent legal advisor.

There is no assurance that discussions with Future Pak or any other interested party will result in a transaction. The Company would like to reassure its clients, employees and partners that while these discussions may be ongoing, operations continue in the normal course.

The Company does not intend to provide further updates or comments with respect to the foregoing, other than as required pursuant to applicable securities laws.

Source: https://www.globenewswire.com/news-release/2025/04/15/3062186/0/en/Theratechnologies-Provides-Update-on-Sale-Process.html

Third Harmonic Outlines Plans for Dissolution

Gwendolyn Wu, *Biopharma Dive*, April 14, 2025 (excerpt)

Third Harmonic Bio plans to wind down operations and sell its assets, including its lead drug candidate, in a liquidation plan the company announced Monday.

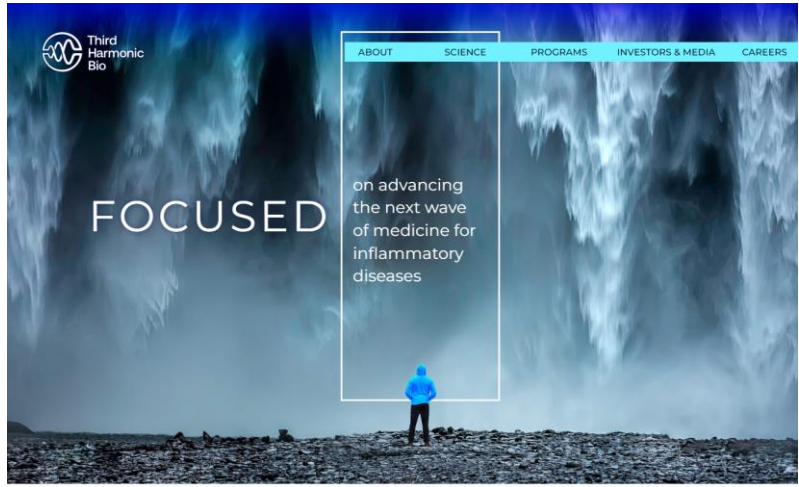
If approved by stockholders at an annual meeting in early June, the immune drug developer will dissolve in the third quarter of 2025.

“Our management team and board of directors together have completed an efficient review of our strategic alternatives for maximizing the value of our assets and have determined that returning cash to shareholders and selling our assets, including THB335, is the best path forward,” Natalie Holles, Third Harmonic’s CEO, said in a statement.

In February, Third Harmonic publicized its plans to weigh strategic alternatives as it reported Phase 1 results for THB335 in healthy volunteers. It laid off half its staff and stopped all R&D work outside of THB335, which is being evaluated in a different form of chronic hives.

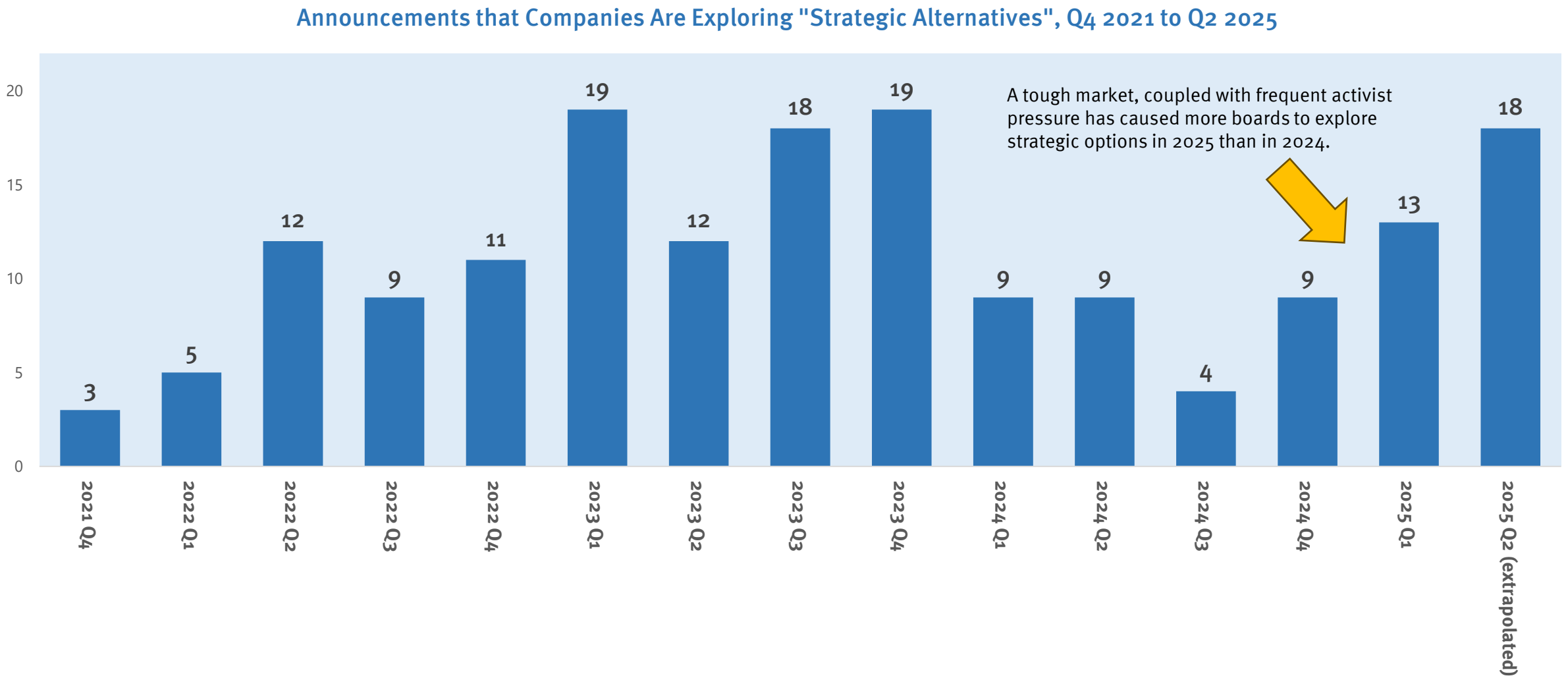
The company still intends to complete the work necessary to prepare THB335 for advancement into Phase 2 testing, so as to maximize the value the program might obtain in a sale.

Third Harmonic had $285 million in cash and cash equivalents as of Dec. 31. It expects to distribute between $246.6 million and $255.4 million to shareholders later this year if its dissolution plan is approved.



Source: https://www.biopharmadive.com/news/third-harmonic-bio-dissolution-strategic-alternatives/745263/

After a Lull, The Pace of Fresh “White Flag” Strategic Alternatives Announcements Has Risen Rapidly in 2025



Source: Stifel tracker built from company press releases.

Sixty Companies Have Active Process Underway to Explore Strategic Options as of Apr 17, 2025

Compare this to a count of 47 companies exploring strategic alternatives in July 2024.

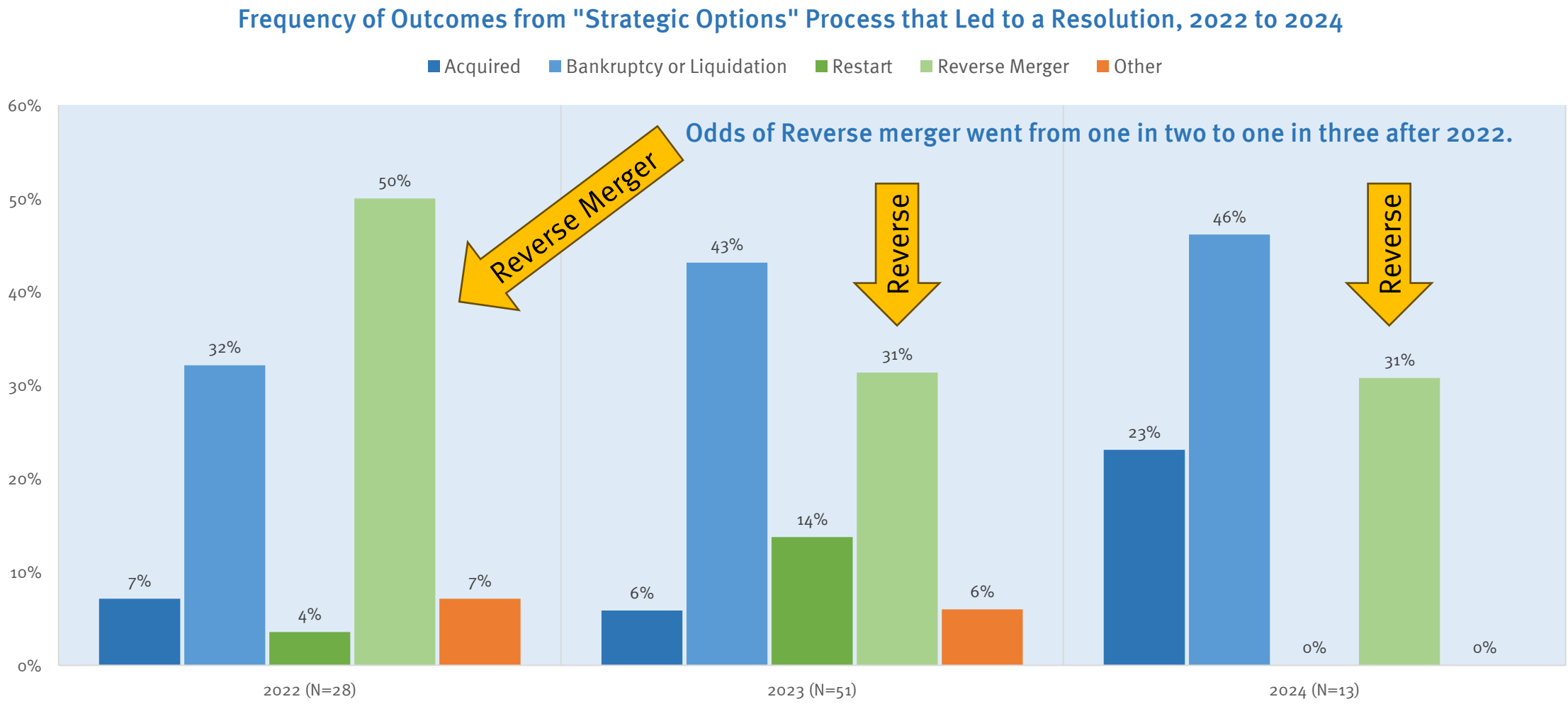
Announcement Date	Company Name	Cash on Hand, Last Reporting Period ($mm)	Enterprise Value ($mm), Apr 17, 2025
4/15/2025	Mural Oncology	$144	-$90
4/14/2025	Ironwood Pharmaceuticals	$89	$629
4/10/2025	Keros Therapeutics	$560	$30
4/10/2025	Tempest Therapeutics	$30	$11
3/31/2025	Carisma Therapeutics	$19	-$8
3/20/2025	Adaptimmune	$152	-$16
3/20/2025	Elevation Oncology	$93	-$39
3/18/2025	Cargo Therapeutics	$340	-$125
3/5/2025	Vincerx	$5	$0
2/20/2025	HOOKIPA Pharma Inc.	$40	-$29
2/13/2025	Matinas BioPharma	$7	-$1
2/4/2025	Turnstone Biologics	$29	-$20
2/3/2025	LAVA Therapeutics N.V.	$77	-$37
1/27/2025	Allakos Inc.	$81	-$51
1/27/2025	Sage Therapeutics	$504	-$36
1/16/2025	Atara Biotherapeutics, Inc.	$42	$39
12/26/2024	Viracta Therapeutics	$21	-$4
12/20/2024	Synaptogenix, Inc.	$18	-$14
12/9/2024	Relmada Therapeutics	$45	-$35
11/18/2024	Helius Medical	$1	$1

Announcement Date	Company Name	Cash on Hand, Last Reporting Period ($mm)	Enterprise Value ($mm), July 12, 2024
11/13/2024	Kronos Bio, Inc.	$112	-$33
11/8/2024	Athira Pharma	$51	-$41
11/7/2024	Trevena, Inc.	$13	$25
10/31/2024	ESSA Pharma Inc.	$121	-$41
8/12/2024	MEI Pharma, Inc.	$24	-$11
6/28/2024	GeNeuro	$2	$16
5/21/2024	Lyra Therapeutics	$41	$0
3/20/2024	Cyclacel	$3	$44
2/8/2024	Synlogic	$19	-$6
1/24/2024	Venus Concept	$4	$42
1/9/2024	Pulmatrix	$10	$14
1/4/2024	Portage Bio	$2	$10
12/22/2023	Allovir	$6	$0
12/7/2023	Hepion Pharmaceuticals	$0	$8
12/6/2023	Comera Life Sciences	$2	$3
11/28/2023	Kane Biotech	$0	$11
11/15/2023	Pharmacyte	$17	-$9
11/14/2023	Talis Biomedical Corporation	$60	-$38
10/30/2023	Zynex	$40	$100
10/16/2023	Athersys	$1	$18

Announcement Date	Company Name	Cash on Hand, Last Reporting Period ($mm)	Enterprise Value ($mm), July 12, 2024
10/4/2023	Brainstorm Cell Tx	$0	$7
9/26/2023	Galecto	$14	-$10
8/29/2023	IRIDEX	$2	$19
8/14/2023	Alaunos Therapeutics	$1	$3
8/8/2023	Salarius Pharmaceuticals	$2	-$1
8/2/2023	Vaxil Bio	$0	$0
7/20/2023	Arcadia Biosciences	$4	$0
7/18/2023	Pieris Pharma	$19	$0
6/30/2023	Spexis	$4	$0
6/29/2023	Aurinia Pharmaceuticals	$358	$785
6/24/2023	Bellorophon Therapeutics	$4	$0
5/23/2023	T2 Biosystems	$2	$20
3/14/2023	Bellicum Therapeutics	$6	$0
2/8/2023	Genetether	$1	$2
1/10/2023	Motus GI	$5	-$3
12/16/2022	OncoCyte	$9	$76
11/10/2022	Soligenix	$8	$0
10/31/2022	Humanigen	$2	$33
9/26/2022	Exicure	$12	$47
6/15/2022	Galmed	$22	-$12

Source: Stifel tracker built from company press releases.

Strategic Options Processes in 2023/2024 More Likely to Result in a Liquidation than a Reverse Merger Versus 2022 Cohort



Source: Stifel analysis of strategic options events built from company press releases.

Oral Obesity Drugs Update

Pfizer Provides Update on Oral GLP-1 Receptor Agonist Danuglipron

Pfizer, *Press Release*, April 14, 2025 (excerpt)

NEW YORK--(BUSINESS WIRE)-- Pfizer Inc. (NYSE: PFE) today announced the decision to discontinue development of danuglipron (PF-06882961), an oral glucagon-like peptide-1 (GLP-1) receptor agonist, which was being investigated for chronic weight management.

Pfizer's dose-optimization studies of once-daily formulations of danuglipron (NCT06567327 and NCT06568731) met key pharmacokinetic objectives and confirmed a formulation and dose with the potential to deliver a competitive efficacy and tolerability profile in Phase 3 testing, based on earlier studies of twice-daily danuglipron. While the overall frequency of liver enzyme elevations across the over 1,400 participant safety database of danuglipron is in-line with approved agents in the class, a single asymptomatic participant in one of the dose-optimization studies experienced potential drug-induced liver injury which resolved after discontinuation of danuglipron. After a review of the totality of information, including all clinical data generated to date for danuglipron and recent input from regulators, **Pfizer has decided to discontinue development of the molecule.**

"Cardiovascular and metabolic diseases including obesity remain important areas of unmet medical need, and we plan to continue applying our global capabilities to advance a pipeline of investigational treatments that have the potential to fill critical gaps in patient care, including continued development of our oral GIPR antagonist candidate and other earlier obesity programs," said Chris Boshoff, MD, PhD, Chief Scientific Officer and President, Research and Development at Pfizer. "While we are disappointed to discontinue the development of danuglipron, we remain committed to evaluating and advancing promising programs in an effort to bring innovative new medicines to patients."

Data from the danuglipron clinical development program will be presented at a scientific forum or submitted for publication in a peer-reviewed journal in the future.

Source: https://www.pfizer.com/news/press-release/press-release-detail/pfizer-provides-update-oral-glp-1-receptor-agonist

Lilly's Oral GLP-1, Orforglipron, Demonstrated Statistically Significant Efficacy Results and Safety Consistent with Injectable GLP-1 Medicines

Eli Lilly, *Press Release*, April 17, 2025 (excerpt)

Eli Lilly and Company (NYSE: LLY) today announced positive topline Phase 3 results from ACHIEVE-1, evaluating the safety and efficacy of orforglipron compared to placebo in adults with type 2 diabetes and inadequate glycemic control with diet and exercise alone. Orforglipron is the first oral small molecule glucagon-like peptide-1 (GLP-1) receptor agonist, taken without food and water restrictions, to successfully complete a Phase 3 trial. If approved, the company is confident in its ability to launch orforglipron worldwide without supply constraints. This would further Lilly's mission to reduce chronic diseases like type 2 diabetes, which is expected to impact an estimated 760 million adults by 2050.1

"ACHIEVE-1 is the first of seven Phase 3 studies examining the safety and efficacy of orforglipron across people with diabetes and obesity. We are pleased to see that our latest incretin medicine meets our expectations for safety and tolerability, glucose control and weight loss, and we look forward to additional data readouts later this year," said David A. Ricks, Lilly chair and CEO. "As a convenient once-daily pill, orforglipron may provide a new option and, if approved, could be readily manufactured and launched at scale for use by people around the world."

In the first Phase 3 trial of the ACHIEVE program, orforglipron met the primary endpoint of superior A1C reduction compared to placebo at 40 weeks, lowering A1C by an average of 1.3% to 1.6% from a baseline of 8.0%, using the efficacy estimand. In an additional key secondary endpoint, participants taking orforglipron lost an average of 16.0 lbs (7.9%) at the highest dose. Given that participants had not yet reached a weight plateau at the time the study ended, it appears that full weight reduction was not yet attained.

Efficacy Estimand Results				
	Orforglipron 3 mg	**Orforglipron 12 mg**	**Orforglipron 36 mg**	**Placebo**
Primary Endpoint				
A1C reduction from baseline of 8.0%	1.3 %	1.6 %	1.5 %	0.1 %
Key Secondary Endpoints				
Percent weight reduction from baseline of 90.2 kg (198.9 lbs)[i,ii]	4.7 %	6.1 %	7.9 %	1.6 %
Weight reduction from baseline of 90.2 kg (198.9 lbs)[i,ii]	4.4 kg (9.7 lbs)	5.5 kg (12.2 lbs)	7.3 kg (16.0 lbs)	1.3 kg (2.9 lbs)

Source: https://investor.lilly.com/news-releases/news-release-details/lillys-oral-glp-1-orforglipron-demonstrated-statistically

Interpreting the Lilly Data: Efficacy

The typical differential in weight loss between overweight individuals without diabetes and those with type 2 diabetes (T2D) treated with the same obesity drug is generally around 25% less weight loss. This is due to higher baseline insulin (which promotes fat storage).

Weight Loss Comparison Benchmarks

Drug	Population	Duration	Placebo-Adjusted Weight Loss
Semaglutide 2.4 mg (injectable)	Non-diabetics (STEP 1)	68 wks	~12.4%
	Type 2 Diabetes (STEP 2)	68 wks	~6.2%
Tirzepatide 15 mg	Non-diabetics (SURMOUNT-1)	72 wks	~18%
	Type 2 Diabetes (SURPASS-2)	40 wks	~11.2%
Orforglipron 36 mg (oral)	Non-diabetics (Phase 2)	36 wks	~8.6%
	Type 2 Diabetes (TRIUMPH-1)	40 wks	~6.3%

Based on last week's data, it's reasonable to expect something like 9 to 12% weight loss in a year on oral orforglipron.

One can obviously do better with emerging injectable therapies and tirzepatide.

A large portion of consumers won't use an injectable but would take a daily oral obesity pill. This looks like it could be the first drug of the type and, if approvable, should be quite popular in the market.

Interpreting the Lilly Data: Safety

Eli Lilly Press Release: The overall safety profile of orforglipron in ACHIEVE-1 was consistent with the established GLP-1 class. The most commonly reported adverse events were gastrointestinal-related and generally mild to moderate in severity. The most common adverse events for participants treated with orforglipron (3 mg, 12 mg and 36 mg, respectively) were diarrhea (19%, 21% and 26%) vs. 9% with placebo, nausea (13%, 18% and 16%) vs. 2% with placebo, dyspepsia (10%, 20% and 15%) vs. 7% with placebo, constipation (8%, 17% and 14%) vs. 4% with placebo, and vomiting (5%, 7% and 14%) vs. 1% with placebo. Overall treatment discontinuation rates due to adverse events were 6% (3 mg), 4% (12 mg) and 8% (36 mg) for orforglipron vs. 1% with placebo. No hepatic safety signal was observed.

The tolerability of the drug seemed in line or better than injectable.

There was no liver signal.

There has been concern in the market about cardio safety with orforglipron and this is not addressed except that Lilly says that the "overall safety profile of orforglipron in ACHIEVE-1 was consistent with the established GLP-1 class."

It would seem unlikely that Lilly would say this if they saw a worrisome cardiac signal in the data.

Source: https://investor.lilly.com/news-releases/news-release-details/lillys-oral-glp-1-orforglipron-demonstrated-statistically

Disclosure

STIFEL | Healthcare

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