Biopharma Market Update

Mar 24, 2025

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Table of Contents

Medici owned table with rich marquetry decoration of hard stones (lapis lazuli, chalcedony, jasper, etc.) with scrolls, floral foliage, and animals. Photo from Pallazo de Pitti, Florence, March 2025. Taken by author while attending Bio-Europe.

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:

Feb 24, 2025 (Retail Pharma Trends)
Feb 10, 2025 (Pharma Earnings)
Jan 27, 2025 (Women's Health, Obesity)
Dec 17, 2024 (Biotech Blues)
Nov 25, 2024 (Biotech Balance Sheets)
Nov 18, 2024 (New Administration)
Nov 4, 2024 (Election, Obesity)
Oct 21, 2024 (China, Pfizer)
Oct 7, 2024 (VC update)
Sep 23, 2024 (The Fed Rate Cut)
Sep 9, 2024 (Sector Outlook)
Aug 12, 2024 (Biotech Market)
July 8, 2024 (Obesity Market Update)
June 17, 2024 (Lab Market)
June 8, 2024 (Oncology Review)
May 27, 2024 (GLP-1's)
May 20, 2024 (Returning Capital)
May 13, 2024 (Brain, AlphaFold 3)
May 6, 2024 (Earnings, Obesity)
April 29, 2024 (M&A, Japan)
April 22, 2024 (Pharma Pricing)
April 15, 2024 (AI in Pharma)
April 8, 2024 (The Buyside)
April 1, 2024 (Biotech Balance Sheets)
March 25, 2024 (Women's Health)
March 18, 2024 (Inflammasome)
March 11, 2024 (IRA, Immunology)
March 4, 2024 (Biotech Employment)
Feb 26, 2024 (Biotech Strategy)
Feb 19, 2024 (Big Drugs, Autoantibodies)
Feb 12, 2024 (Fibrosis, Endometriosis)
Feb 5, 2024 (Severe Disease in Women)
Jan 29, 2024 (Pharma R&D Productivity)
Dec 18, 2023 (Expectations for Future)
Dec 11, 2023 (ASH, R&D Days)
Dec 4, 2023 (Big Pharma, CEA)
November 20, 2023 (M&A)
November 13, 2023 (AHA, Bear Market)
November 7, 2023 (Unmet Needs)
October 30, 2023 (ADCs)
October 23, 2023 (ESMO Review)
October 16, 2023 (Cancer Screening)
October 9, 2023 (Biosimilars, M&A)
October 2, 2023 (FcRn, Antibiotics)
September 25, 2023 (Target ID)
September 18, 2023 (Pharma Strategy)
September 11, 2023 (US Health System)
September 5, 2023 (FTC, IRA, Depression)
August 21, 2023 (Covid, China)
June 19, 2023 (Generative AI)
June 12, 2023 (IRA, State of Industry)

Comprehensive and highly influential early Renaissance book on practical medicine. Author, Michele Savonarola (1384 to 1466), was a professor at Padua and Ferrara. Illuminated page shown from his 1486 book *Practica medicinae, sive De aegritudinibus* (The Practice of Medicine, or On diseases).

Links to Stifel Biopharma Special Topic Publications

2025 Biotech Outlook

[Jan 8, 2025]

2024 Biotech Mid-Year Outlook

[July 15, 2024]

Obesity Drug Update

[July 8, 2024]

AI in medicine

[Jan 22, 2024]

2024 Biotech Outlook

[Jan 8, 2024]

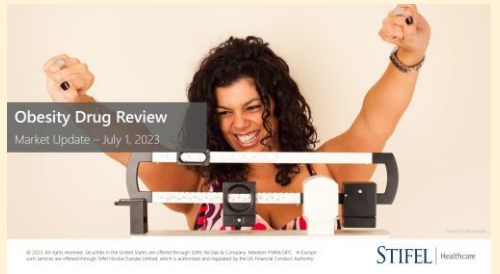
Why Invest in Biotech?

[November 22, 2023]

2023 Biotech Mid-Year Outlook

[July 7, 2023]

Obesity Drug Review



[July 1, 2023]

Feel Free to Join Us at Biotech Hangout

Please join us this Friday at noon EST for the latest episode.

To Learn More
https://www.biotechhangout.com/

Macro Update

Group of office workers relaxing during lunch break, Osaka Japan, March 2025. Taken by author while visiting Japan.

Fed Projections See an Economy Dramatically Reset by Trump's Election

Not long ago, Federal Reserve officials presumed that 2025 would simply be about getting to the soft landing.

Nick Timiraos, *Wall Street Journal*, March 19, 2025 (excerpt)

The Federal Reserve's first set of projections since Donald Trump's inauguration underscored—in the central bank's understated and technocratic fashion—just how much the president's plans to press ahead with widespread tariffs have turned the economic outlook on its head.

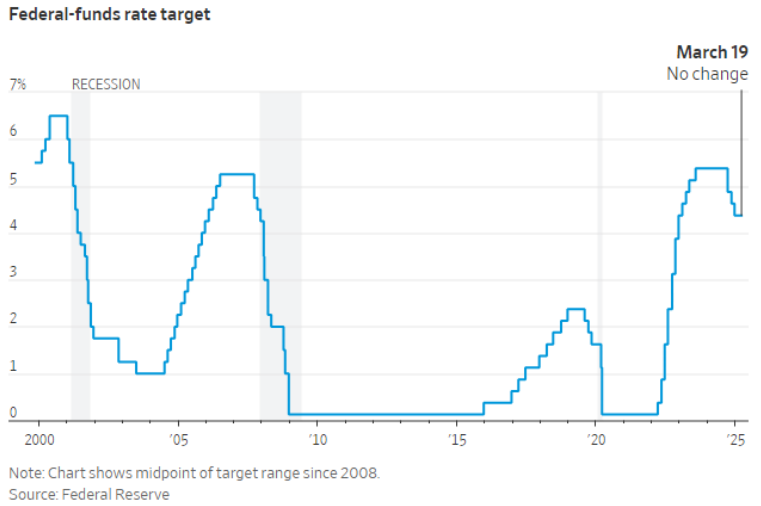
Months ago, policymakers presumed they would spend 2025 gradually cutting rates to keep inflation heading down without a big rise in joblessness to achieve the so-called soft landing. The latest projections point to the prospect that tariffs covering a swath of goods and materials will send up prices while sapping investment, sentiment and growth, at least in the short run.

"We now have inflation coming in from an exogenous source, but the underlying inflationary picture before that was basically 2½% inflation, 2% growth and 4% unemployment," said Fed Chair Jerome Powell on Wednesday.

Officials projected weaker growth, higher unemployment and higher inflation than they had anticipated in December. Moreover, nearly all officials judged that if their forecasts were to be proven wrong, it would be in the direction of even softer growth, more joblessness and firmer price growth.

A combination of stagnant growth and higher prices, sometimes called stagflation, could make it harder for the Fed to cut interest rates this year to pre-empt any slowdown.

Stocks rallied because a majority of officials penciled in two rate cuts for this year, the same as in December. Powell held out, with low conviction, the prospect that "tariff inflation" might not demand any meaningful change in the Fed's interest-rate posture.



Sunday Comment from Stifel Cap Mkts Desk

…a market that was in correction territory earlier in the month posted the first weekly gain in 4 weeks. It wasn't much but it's progress. It wasn't just M&A in Big Tech, we also saw a late surge in the underlying equities (ex TSLA). The Fed – kept rates unchanged and the markets didn't take it personally. A strong finish to the week was positive given Fed commentary that highlighted, economic uncertainty, slowing GDP growth and lingering inflation. The hard part here is the change in governmental spending and the impending tariff news on April 2nd. The result of all of this is the expectation of two 25bps rate cuts between here and the end of the year. Gold hit a record high above $3,000 per ounce last week, reflecting a flight to safety as investors hedged against tariff risks and a choppy equity outlook. But in the same week, Big Tech helped lead the markets higher…

Source: https://www.wsj.com/economy/central-banking/fed-forecast-inflation-tariffs-trump-economy-5a5098a1

Powell Revives a Debate on ‘Transitory’ Inflation

By Andrew Ross Sorkin and colleagues, *New York Times*, March 20, 2025 (excerpt)

“Transitory” is back

Jay Powell wants businesses and investors to know: The Fed chair shares their concerns about President Trump’s tariff skirmishes as the economic outlook dims.

But there is a silver lining, he said Wednesday at a news conference. Tariff-driven inflation is likely to be “transitory” and just for this year. That’s the “base case,” he added, words that seemed to lift stocks. S&P 500 futures were climbing on Thursday as traders price in roughly two to three interest rate cuts this year.

But the “transitory” label — one that Treasury Secretary Scott Bessent has embraced — has set off alarm bells elsewhere.

It remains a loaded term, especially for critics of the Fed’s handling of pandemic-era inflation. Some worry that Powell may be mistakenly playing down the risks of Trump’s trade war, as he did in 2022 when he wrongly called inflation “transitory.”

Several economists see tariffs disrupting global supply chains, raising prices and denting growth. And Trump has reiterated that more tariffs are coming. “April 2nd is Liberation Day in America!!!,” he wrote on Wednesday on Truth Social, presumably referring to the date when reciprocal tariffs on major trading partners are expected to go into effect.

It’s too early to say if “the inflationary effects will be transitory, especially given that companies and households still have fresh in their minds the recent history of high unanticipated inflation,” Mohamed El-Erian, the economist who called the Fed too cautious in handling the last inflation surge, wrote on X.

Surveys show business sentiment weakening and consumers’ inflation fears growing. Such downbeat vibes were around during the Biden administration. But add trade war uncertainty, and some economists and Wall Street analysts have begun to raise the odds of a recession.

Source: https://www.nytimes.com/2025/03/20/business/dealbook/powell-tariff-transitory-inflation.html

Trump's Self-Inflicted Economic Wounds

Josh Bivens, *Time*, March 20, 2025 (excerpt)

The U.S. economy is often compared to a cruise ship—it takes a lot of time and force to change its direction. This is why so many economists looked at the strong economy that was inherited by the Trump Administration and projected fast growth, low unemployment, declining inflation, and healthy stock market appreciation continuing for the next couple of years. But President Donald Trump's impact on the economy so far has been less a matter of turning the ship's rudder and more similar to a ship firing torpedoes at itself.

The reversal in economic data since the Trump Administration took over has been historically rapid—and bad. The stock market is in near free fall. Interest rates are also falling, but for an undesirable reason: investors are assuming the Federal Reserve will need to swoop in soon to try to aggressively rescue a falling economy with future interest rate cuts. Unemployment insurance claims for federal workers have noticeably jumped even before the full force of the Department of Government Efficiency (DOGE) layoffs have been recorded.

Of course, economic data is reported retrospectively. But "nowcasts," short-term predictions which allow us to estimate the current and future states of the economy, indicate that growth in gross domestic product for the first quarter of 2025 is collapsing, with some prominent projections showing outright economic contraction. Of note: A recession is often defined as two consecutive quarters of economic contraction. Plus, measures of economic policy uncertainty are rivaling, or exceeding, what prevailed during the worst phases of the COVID-19 pandemic.

Source: https://time.com/7269516/trumps-self-inflicted-economic-wounds/

Stock Market Return Since Trump's Jan 20, 2025 Inauguration

(1/20 to 3/21, 2025)

Source: S&P Capital IQ

Hold the Obituary: Europe Comes to Life as U.S. Stumbles

Greg Ip, *Wall Street Journal*, March 20, 2025 (excerpt)

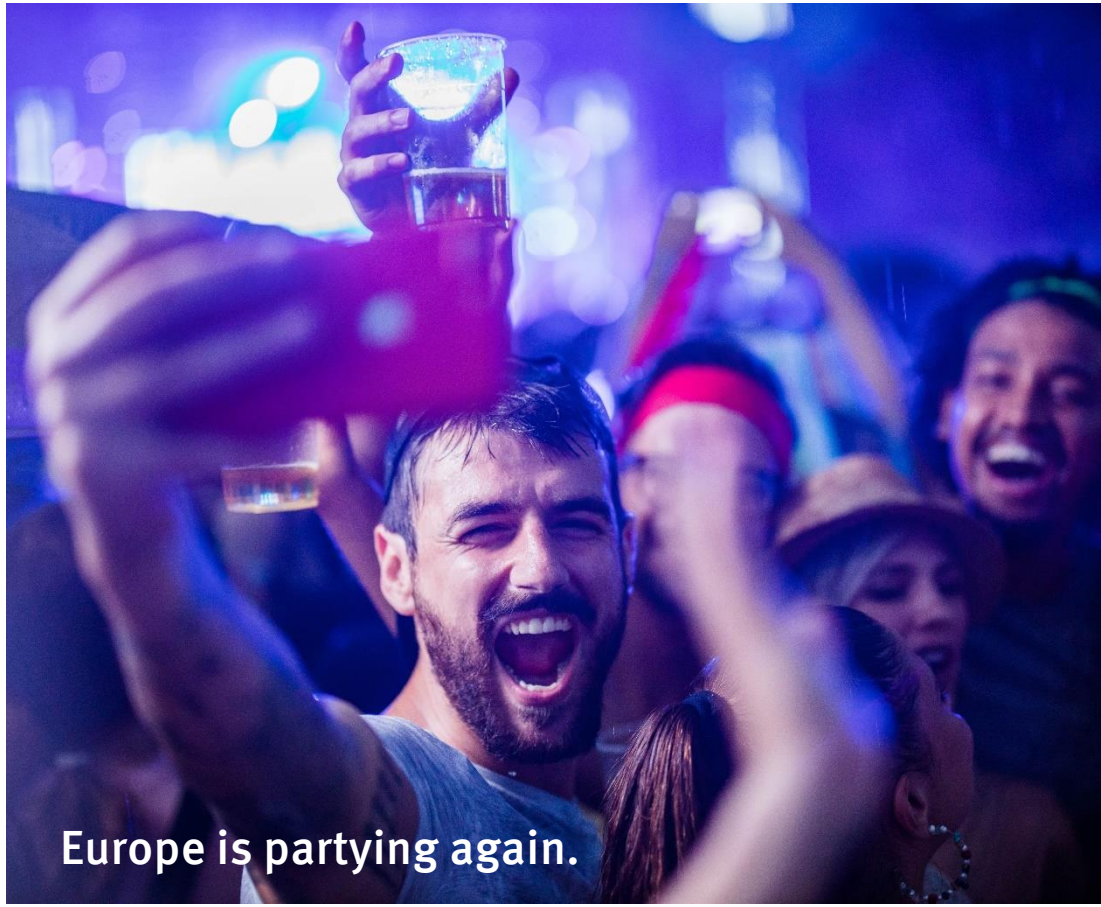
At the World Economic Forum in Davos two months ago, the mood around Europe was funereal. Its economy and markets had underperformed the U.S. for years. Now a newly inaugurated President Trump promised to sledgehammer Europe with tariffs while juicing U.S. growth with lower taxes, less regulation and cheaper energy.

As usual, the Davos consensus got it wrong. Since then, the moods across the Atlantic have switched places. European stocks are up nicely, while the American market has had a correction (a 10% drop). On Wednesday, Federal Reserve officials revised their outlook for inflation up and for growth down. The dollar, which shot up after Trump was elected, has sunk.

Some perspective is in order. A market reversal was overdue; the valuation gap between European and American stocks was becoming absurd. Even with revisions, the U.S. is still likely to grow faster than the European Union and Britain this year. Business activity indicators in Europe remain weak.

Yet a more fundamental reappraisal of the two regions' prospects might be in order, and it has a lot to do with Trump—though not the way most expected.

U.S. growth prospects have actually slipped since Trump's arrival. In January, economists expected growth of 2.2% annualized in the current quarter. Now, estimates are around 1% to 1.5%.



Source: https://www.wsj.com/economy/global/hold-the-obituary-europe-comes-to-life-as-u-s-stumbles-2e7fc916

Investors Who Were All In on U.S. Stocks Are Starting to Look Elsewhere

Owen Tucker-Smith, *Wall Street Journal*, March 22, 2025 (excerpt)

Keith Moffat was born in Canada, lives in the Netherlands and has an Irish passport. But until recently, his stock portfolio was (almost) all-American.

At one point, around 90% of Moffat's investments were in U.S. stocks. He sold all of his American holdings in the past few weeks and piled into exchange-traded funds that hold shares of European and other international companies, alongside European defense stocks. Moffat said the U.S. market is overpriced. But President Trump's rhetoric referring to Canada as the 51st state has also stung.

"It was the dagger in the heart," he said. "There are a lot of Europeans with money who are upset over what's happening in the U.S. Why would we put our money there?"

Just two months after JPMorgan Chase declared American exceptionalism "the broad and dominant" investing theme of 2025, ordinary investors across the world are looking elsewhere. Instead of riding the wave of U.S. outperformance, they are parsing the potential implications of tariff wars and major shifts in U.S. foreign policy. And for much of this volatile stretch, markets in China and Europe outpaced expectations.

The case for European stocks got a jolt Friday when the German government green-lit a plan to inject up to €1 trillion, equivalent to $1.09 trillion, into the nation's economy, with much of the funds supporting the country's defense efforts. Germany's DAX index has shot up almost 15% this year, and some investors hope that heavy spending will pull the country out of its slump. Countries across Europe are ramping up domestic military spending as the U.S. signals an increasingly isolationist foreign-policy position. As a result, shares of the region's defense companies are booming.

Source: https://www.wsj.com/finance/stocks/investors-who-were-all-in-on-u-s-stocks-are-starting-to-look-elsewhere-ddacd1e8

European Countries Implement Initiatives to Attract US Researchers Amid ‘Brutal Funding Cuts’

Gabrielle Masson, *Fierce Biotech*, March 21, 2025 (excerpt)

As the U.S. cuts federal research funding and infrastructure, European countries are strategizing ways to attract top scientific talent, with the Netherlands government setting up a fund designed to do just that.

The country wants to launch financing for the efforts as soon as possible, according to a March 20 letter penned by Netherlands’ Education Minister Eppo Bruins and obtained by Fierce Biotech.

"There is currently a great global demand for international top scientific talent,” Bruins wrote in the letter. “At the same time, the geopolitical climate is changing, which is currently increasing the international mobility of scientists.”

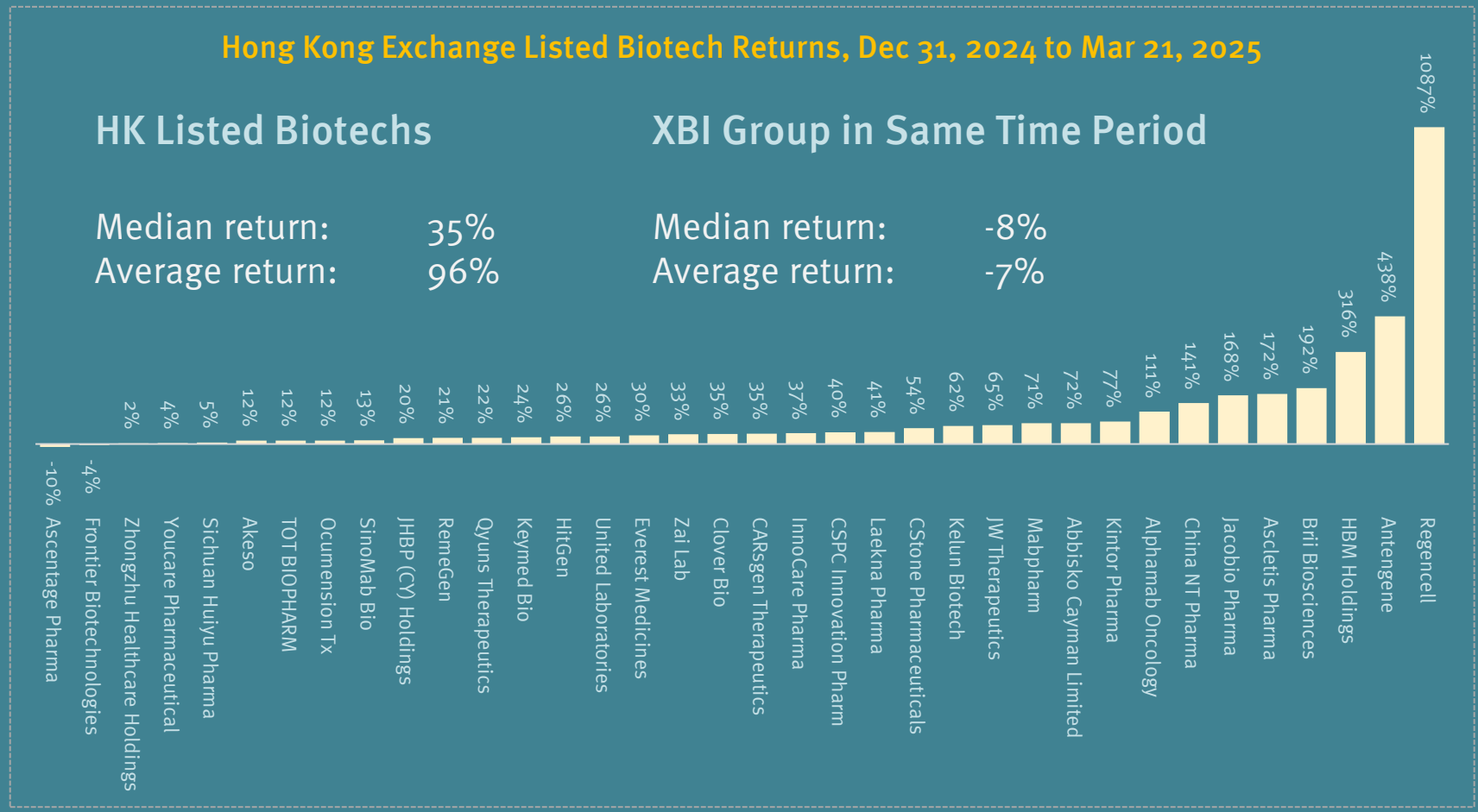
Separately, 12 European countries came together to brainstorm ways in which they could appeal to researchers in the U.S.

The countries want to attract talent from abroad "who might suffer from research interference and ill-motivated and brutal funding cuts," according to a letter to the European Commission and viewed by *Politico*.

Source: https://www.fiercebiotech.com/biotech/several-european-countries-universities-implement-initiatives-attract-us-researchers-amid

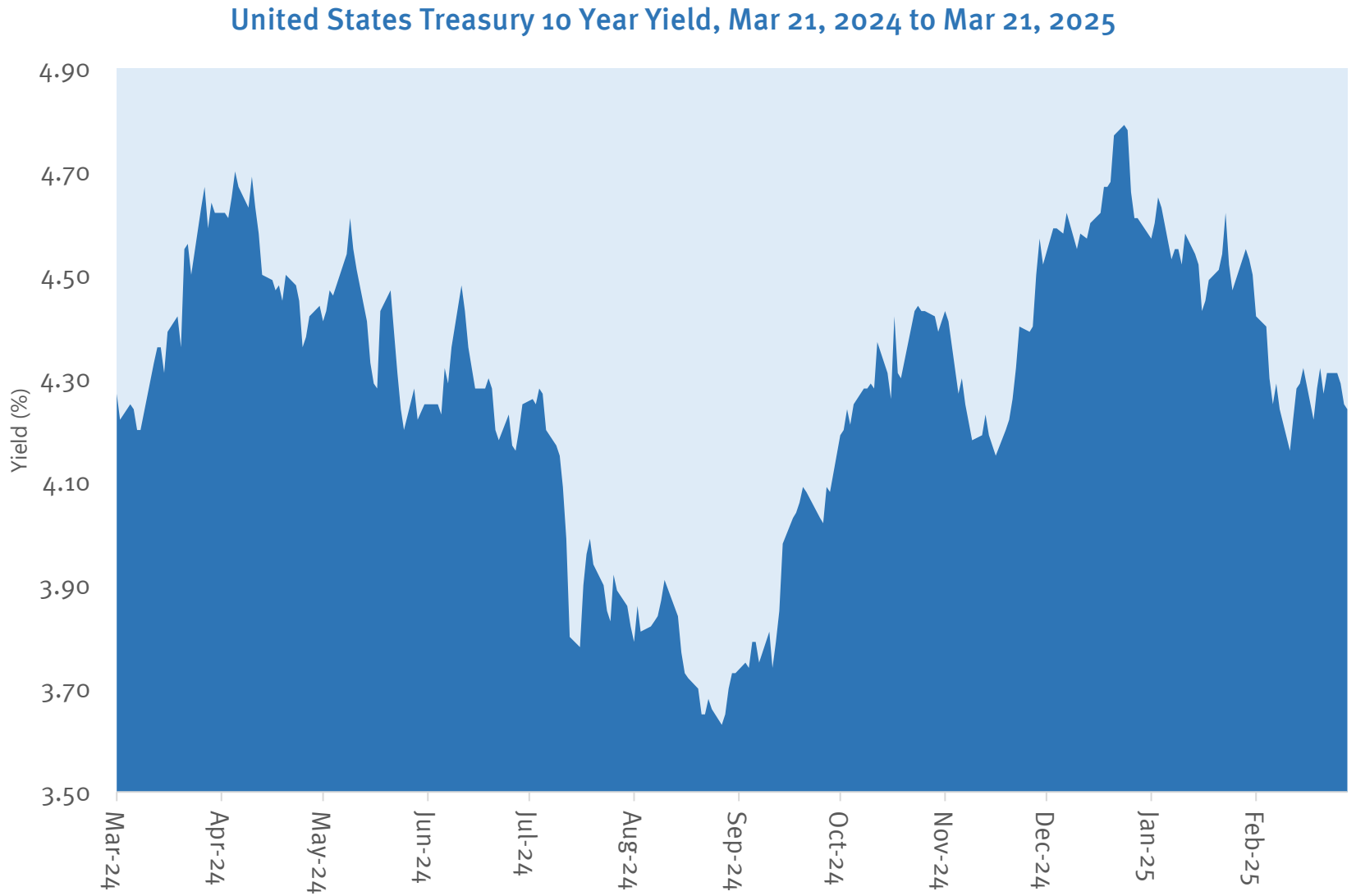
A Similar Phenomenon is Playing Out in Biotech

The much-anticipated recovery in biotech stocks occurred in 2025. Just in a different market. At this point, the median return of a Hong-Kong listed biotech in 2025 is 35%. Compare this to a median return of an XBI member of -8%. China biotech is highly energized at present. On our recent March trip to China, we heard again and again how pleased Chinese biotechs are to have Western players show up in Hong Kong market. It is rumored that a number of U.S. and Europe hedge funds are participating in the HK market.



Source: S&P Capital IQ. Returns are calculated as the percentage change in price per share in USD from Dec 31, 2024 to Mar 31, 2025.

U.S. Treasury Bond Yields Dropping Slightly



10-year US Treasury yields have dropped by 26 basis points in the last month and 34 basis points since the year began.

This reflects an improving situation and the possibility of an improving U.S. fiscal budget deficit.

Treasury rates remain high by recent standards and the Fed continues to be slow in lowering rates.

Source: S&P Capital IQ

Biopharma Market Update

The XBI Closed at 87.12 Last Friday (Mar 21), Unchanged for the Week

The Stifel Global Biotech Value Tracker fell by 0.4%, a little less than the XBI (no change). Treasury yields fell. The XBI is down 3.3% for the year. Last week saw big pharma substantially outperform the S&P 500 amidst broad market uncertainty – visible in the rise in the VIX.

Biotech Stocks Flat Last Week

Return: Mar 13 to Mar 20, 2025

Nasdaq Biotech Index: +0.0%
Arca XBI ETF: 0.0%
Stifel Global Biotech EV (adjusted): -0.4%*
S&P 500: +0.5%

Return: Dec 31, 2024 to Mar 20, 2025 (YTD)

Nasdaq Biotech Index: +3.1%
Arca XBI ETF: -3.3%
Stifel Global Biotech EV (adjusted): -4.8%*
S&P 500: -3.7%

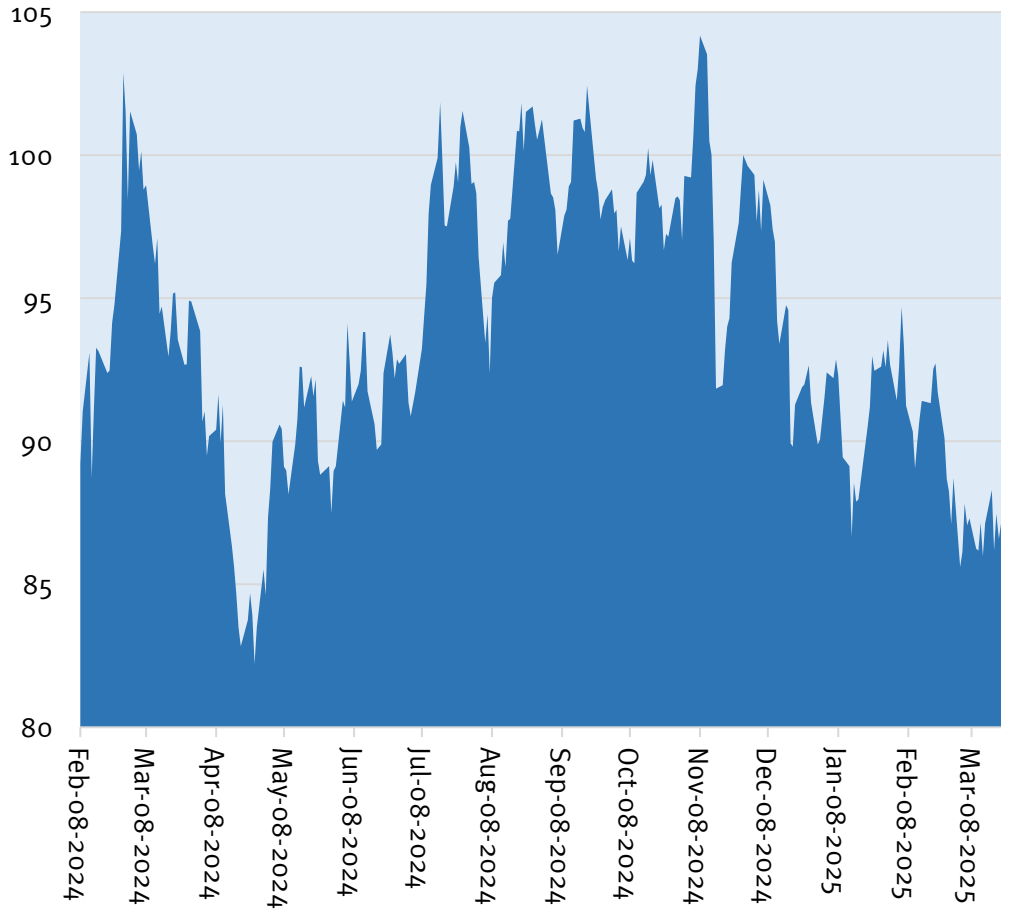
VIX Up

Dec 29, 2023: 12.45%
Mar 29, 2024: 13.0%
Aug 2, 2024: 23.4%
Oct 19, 2024: 18.0%
Dec 13, 2024: 13.8%
Jan 24, 2025: 14.2%
Feb 21, 2025: 18.2%
Mar 21, 2025: 19.2%

10-Year Treasury Yield Down

Dec 29, 2023: 3.88%
Aug 2, 2024: 3.80%
Oct 19, 2024: 4.08%
Dec 13, 2024: 4.4%
Jan 24, 2025: 4.6%
Feb 21, 2025: 4.4%
Mar 21, 2025: 4.25%

XBI, Feb 8. 2024 to Mar 21, 2025

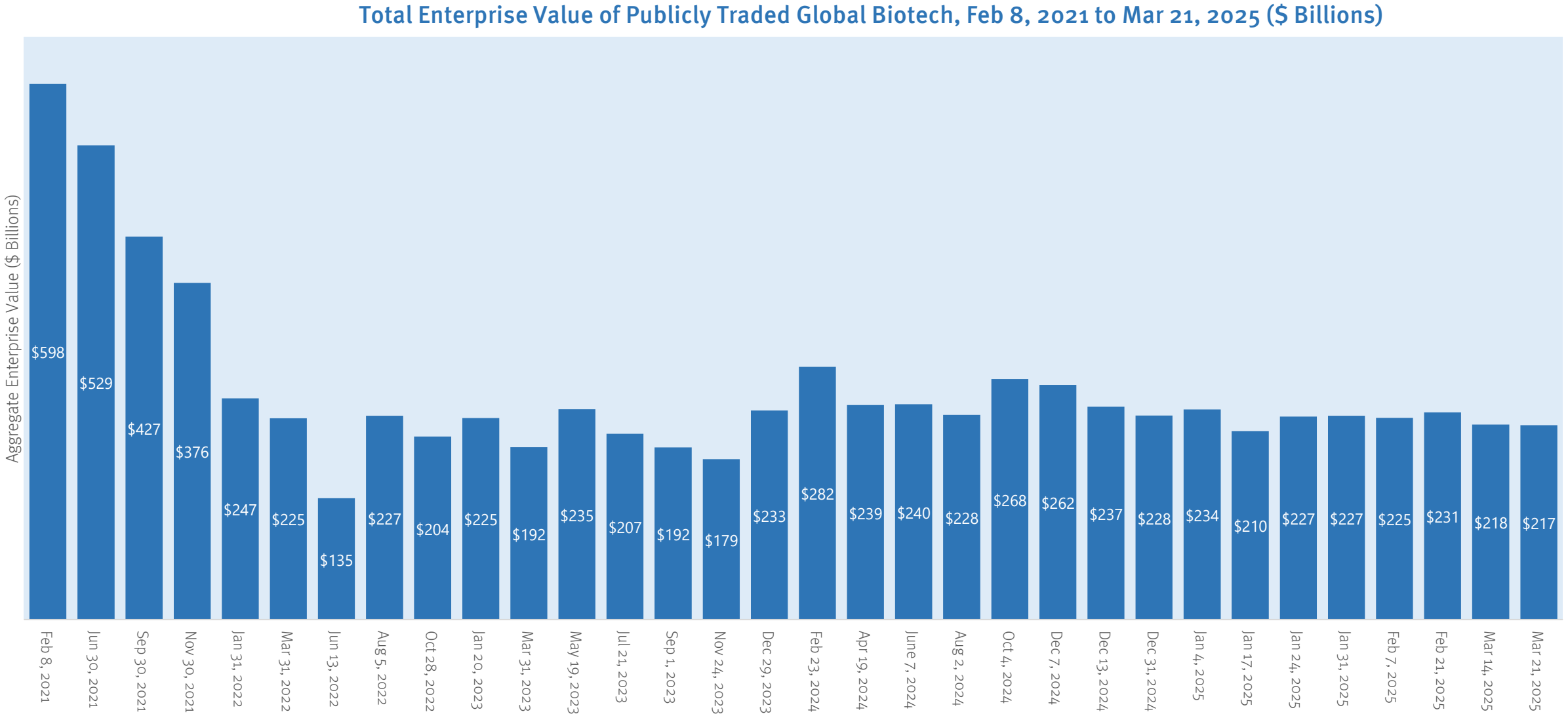


* Change by enterprise value. The adjusted number accounts for the effect of exits and additions via M&A, bankruptcies and IPOs. The annual change by market cap is even higher.

Source: S&P Capital IQ and Stifel analysis

Total Global Biotech Sector Fell 0.4% Last Week

Biotech stocks fell 0.4% in the last week – more than the XBI. By our math, the total global biotech sector is down 4.8% for the year.

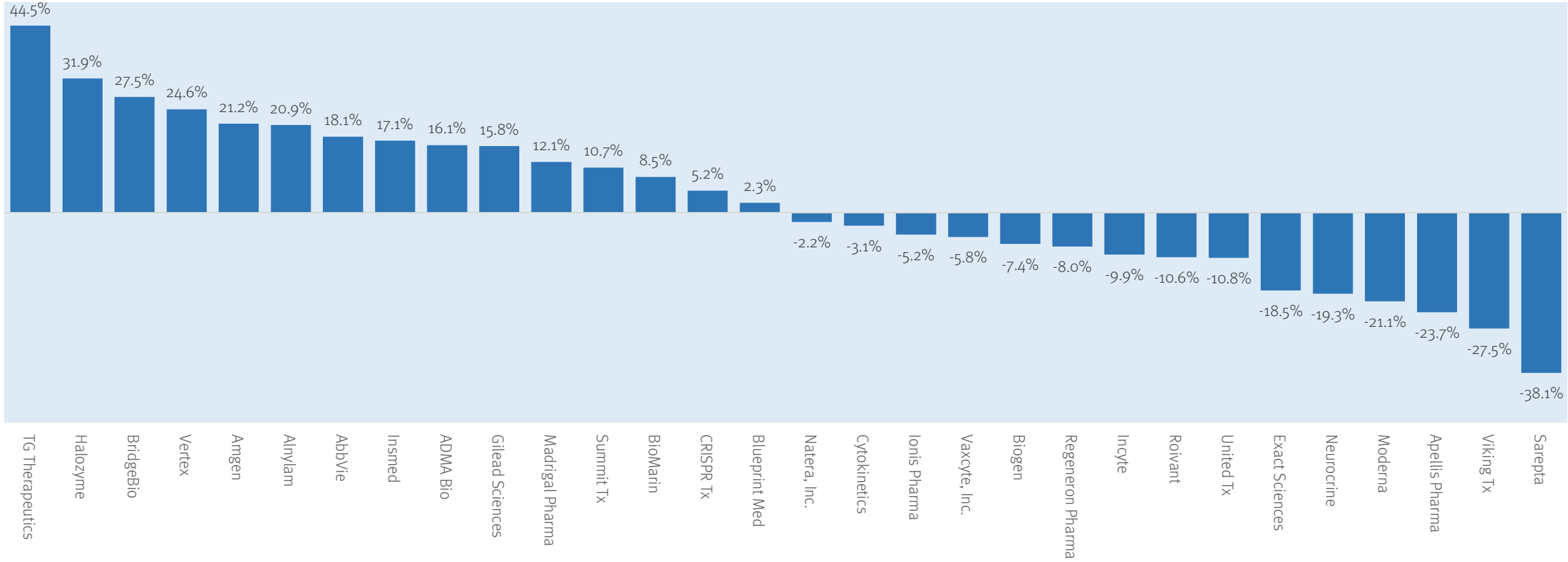


Source: CapitalIQ. Biotechs are defined as any therapeutics company without an approved product on any global stock exchange.

XBI 30 Performance Solid 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 in value this year is up 2.2%. TG Therapeutics, Halozyme, BridgeBio, Vertex, Alnyam and Amgen have been the best performers for the year to date. Sarepta, Viking, Moderna, Neurocrine and Apellis have all been down.

Top 30 XBI Influencers, Percent Change in Market Cap, YTD (Dec 31, 2024 to Mar 21, 2025)

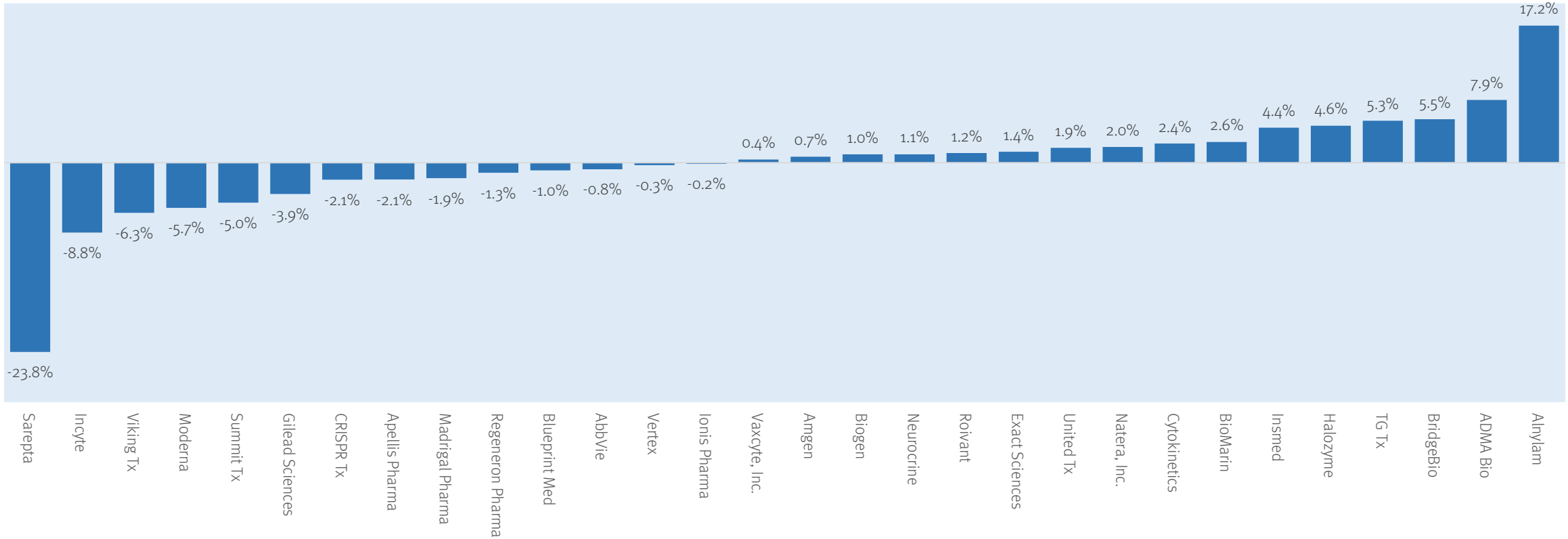


Source: CapitalIQ. Biotechs are defined as any therapeutics company without an approved product on any global stock exchange.

XBI 30 Performance Mixed Last Week

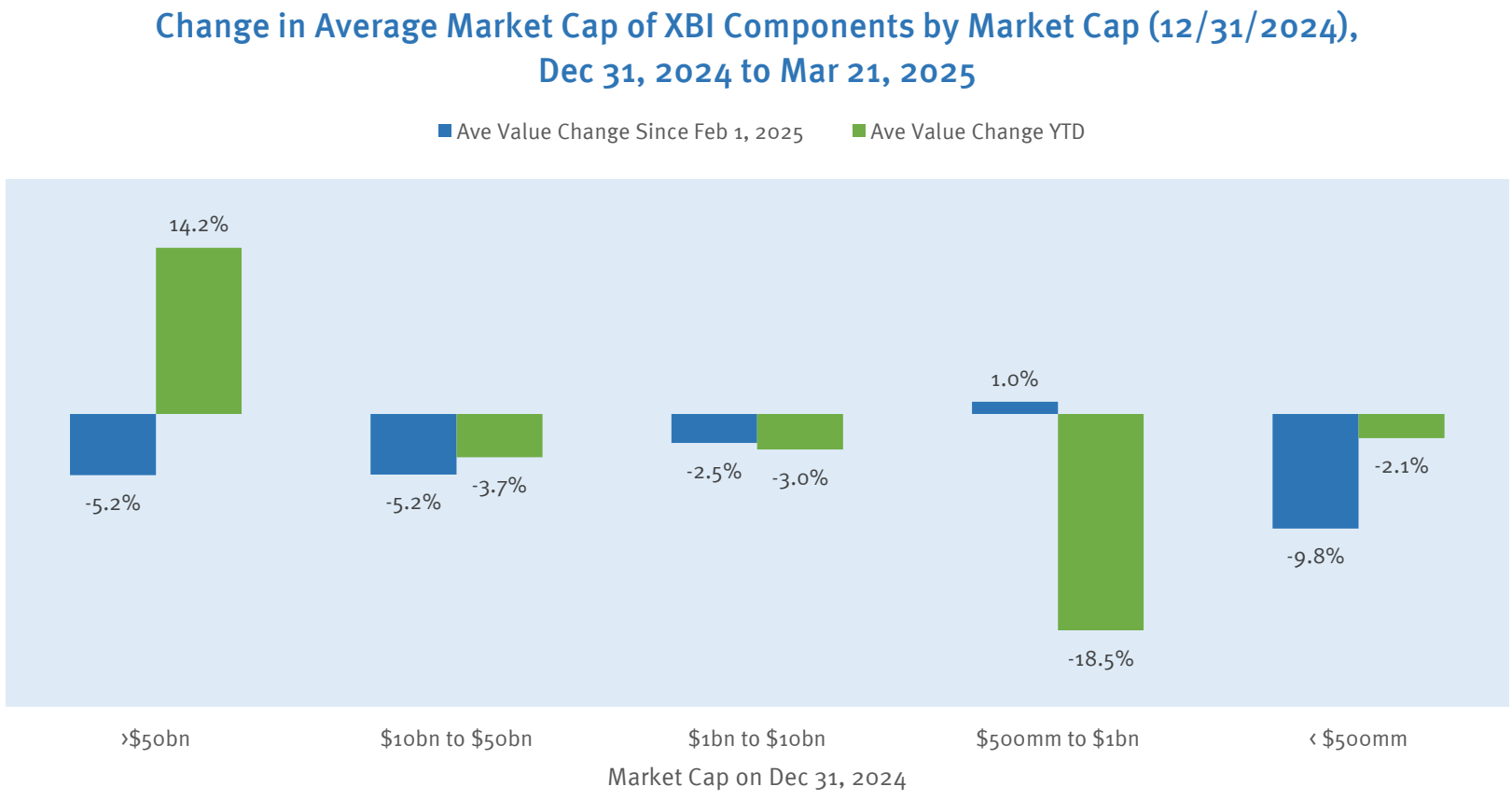
This chart shows the change in market cap this year for the 30 most influential stocks in the XBI. These 30 stocks comprise 60% of the weight of the XBI (out of 138 stocks total). The mean percentage change in value last week was -0.1%. The median change was 0.6%. Sarepta fell on a patient death. Alnylam did well on an FDA approval and strong label. Incyte's Povorcitinib, an oral JAK1, passed the marks in a hidradenitis suppurativa Phase 3 study but the profile did not appear to be competitive. Hence the 8.8% drop in Incyte shares last week.

Top 30 XBI Influencers, Pecent Change in Market Cap, Week of Mar 14 to Mar 21, 2025



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

This Year Has Been Good for Large Pharmas in the XBI



We are seeing large caps ($50bn+ cap) do substantially better than other stocks in the XBI.

Big caps in the XBI are up 14% YTD.

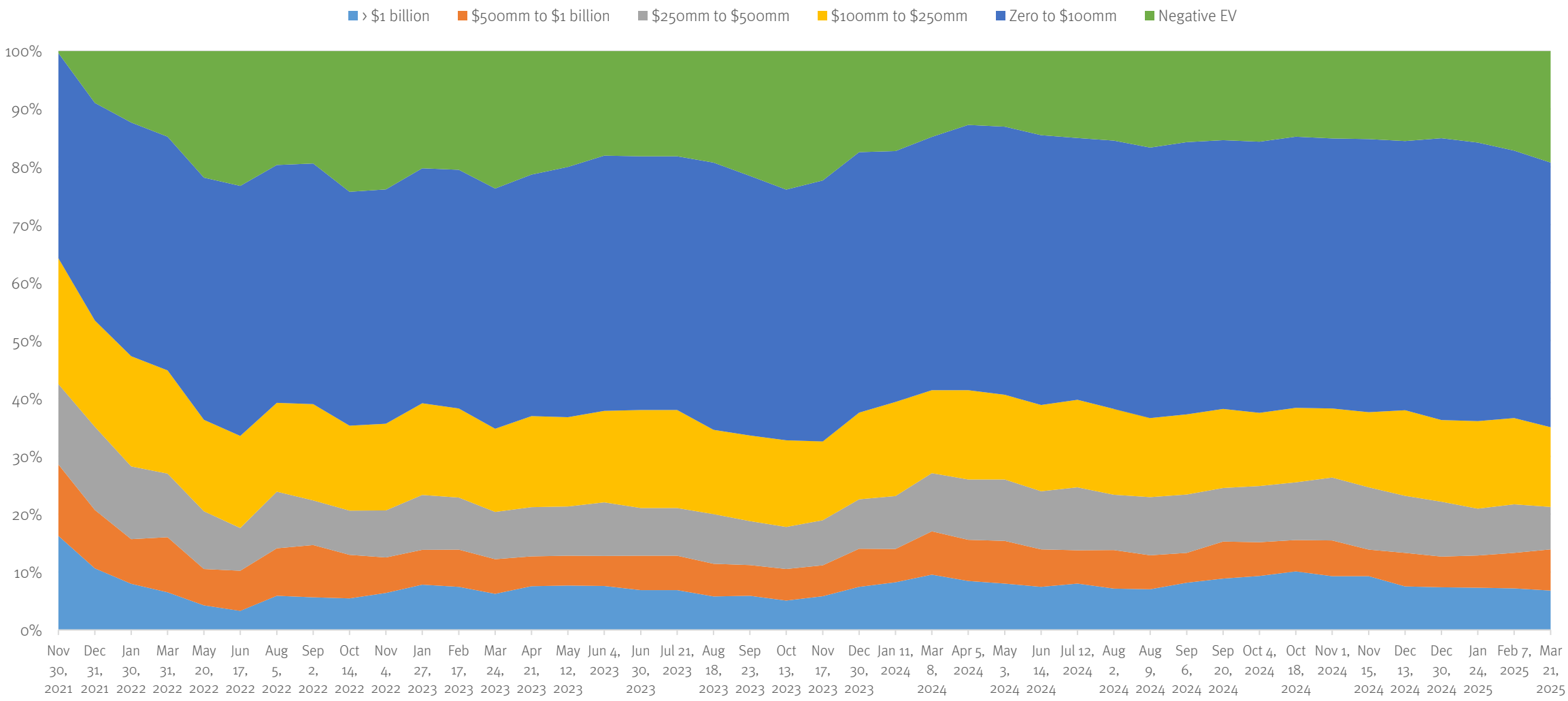
Sub-$1bn stocks are not doing as well.

This looks like a classic recovery where generalists buy into larger companies first.

Global Biotech Neighborhood Analysis

The population of biotechs trading for less than cash has grown precipitously in the last month.

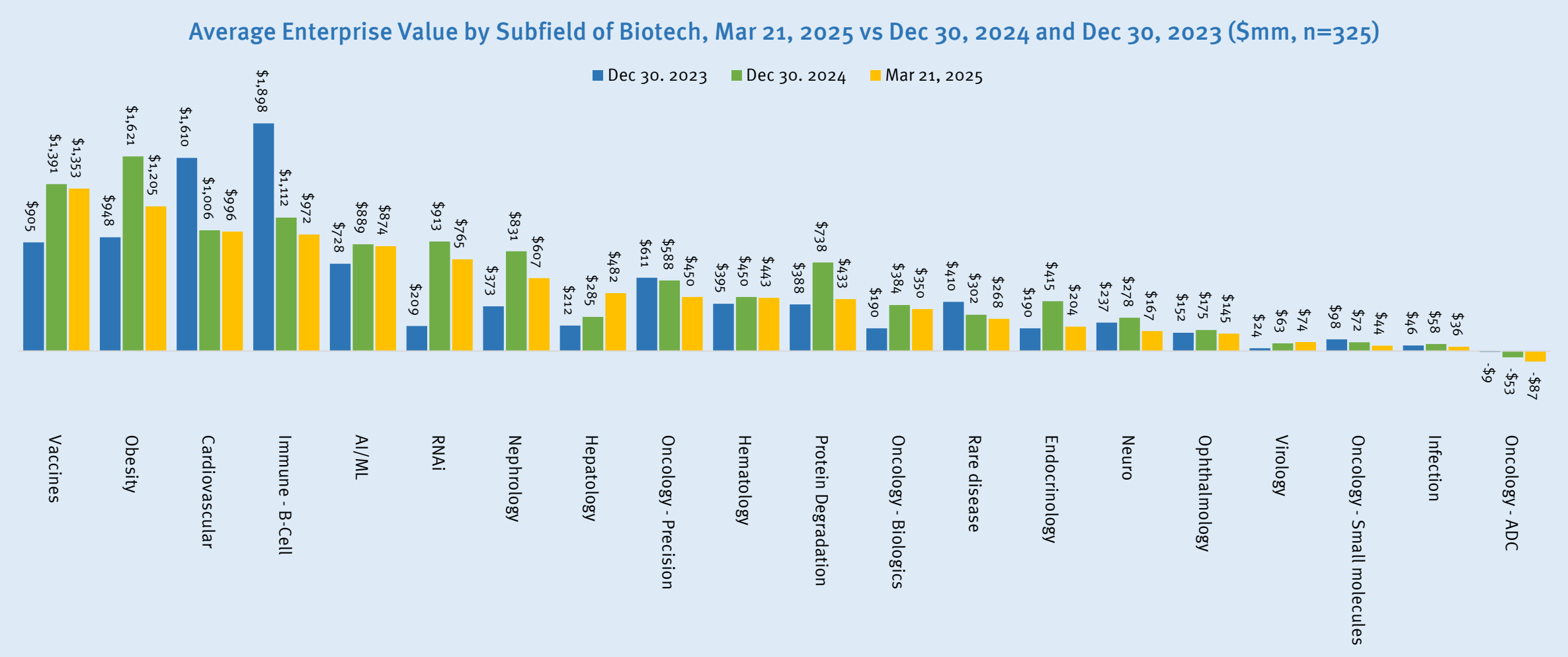
Global Biotech Universe by Enterprise Value Category, Nov 30, 2021 to Mar 21, 2025



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

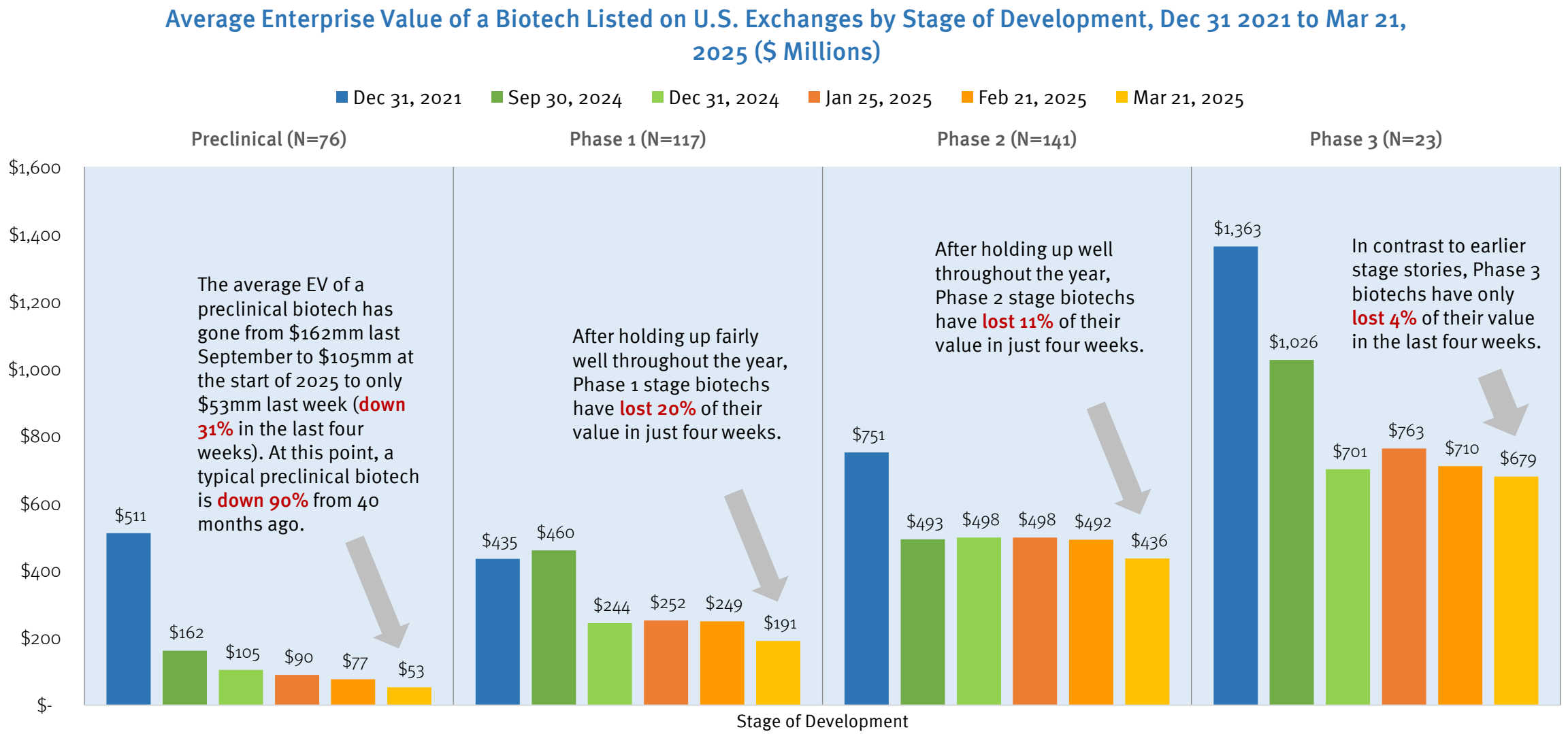
U.S. Biotech Values Today Highest in Obesity, Vaccines and AI

The most valued sectors in biotech today are (in order) vaccines, obesity and AI. At the start of the year, B-cell immunology was in the third position. Fields that have lost substantial value in the last year include ADC's, precision oncology, protein degraders and rare disease. Hepatology stocks are gaining in value.



Source: S&P CapitalIQ and Stifel analysis.

Biotech Market is Penalizing Early-Stage Stories



Source: CapitalIQ and Stifel analysis. Phase of development is defined by release of at least some efficacy data from a given stage of clinical development.

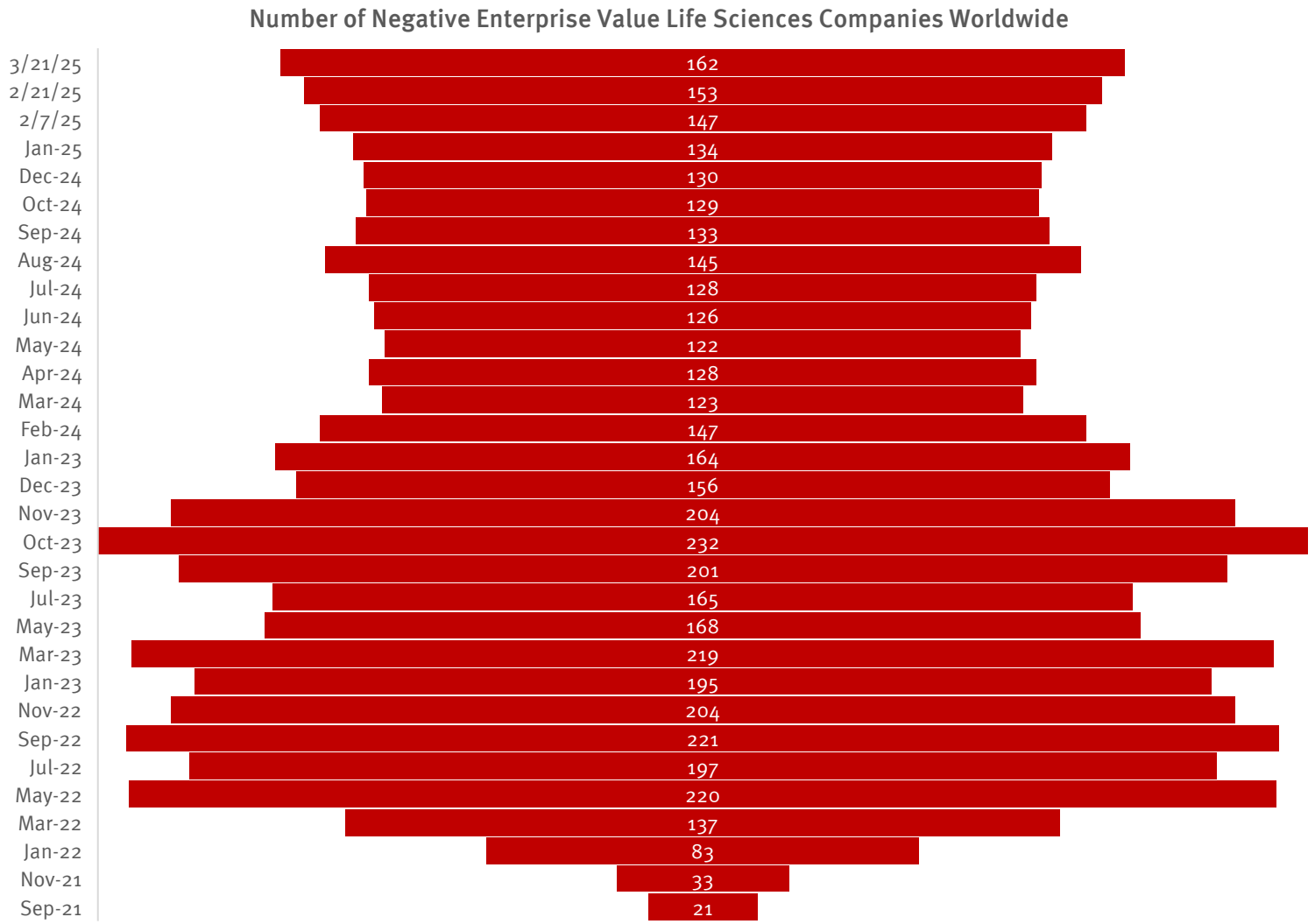
Life Sciences Sector Gained $40 Billion in Value Last Week (0.4%)

Last week saw strength in the API, CDMO and OTC areas. HCIT, Life Science Tools and biotech all lost value. The total value of the life sciences sector is flat for the year and stands at $9.6 trillion.

Sector	Firm Count	Enterprise Value (Mar 21, 2025, $millions)	Change in Last Week (percent)	Change in Last Month (percent)	Change in Last Year (percent)
API	79	$87,411	3.1%	-0.5%	11.5%
Biotech	731	$217,651	-0.4%	-8.6%	-5.1%
CDMO	37	$153,791	2.1%	-2.3%	11.5%
Diagnostics	76	$252,111	0.7%	-5.6%	-10.3%
OTC	29	$24,167	1.3%	-0.3%	-13.0%
Commercial Pharma	697	$6,296,693	0.6%	0.7%	1.2%
Services	38	$163,716	0.1%	-1.4%	-17.6%
Tools	50	$606,472	-0.7%	-3.6%	-17.1%
Devices	174	$1,774,183	0.3%	-5.4%	5.1%
HCIT	7	$25,968	-2.7%	-15.6%	32.7%
Total	**1918**	**$9,605,364**	**0.4%**	**-1.3%**	**-0.3%**

Source: CapitalIQ and Stifel analysis

Number of Negative Enterprise Value Life Sciences Companies Jumped in Last Month



The count of negative EV life sciences companies worldwide rose from 153 four weeks ago to 162 last Friday.

This measure of sector distress continues to go in the wrong direction.

We believe that issues with funds that invest in microcaps may be part of the explanation for the recent growth in negative EV companies.

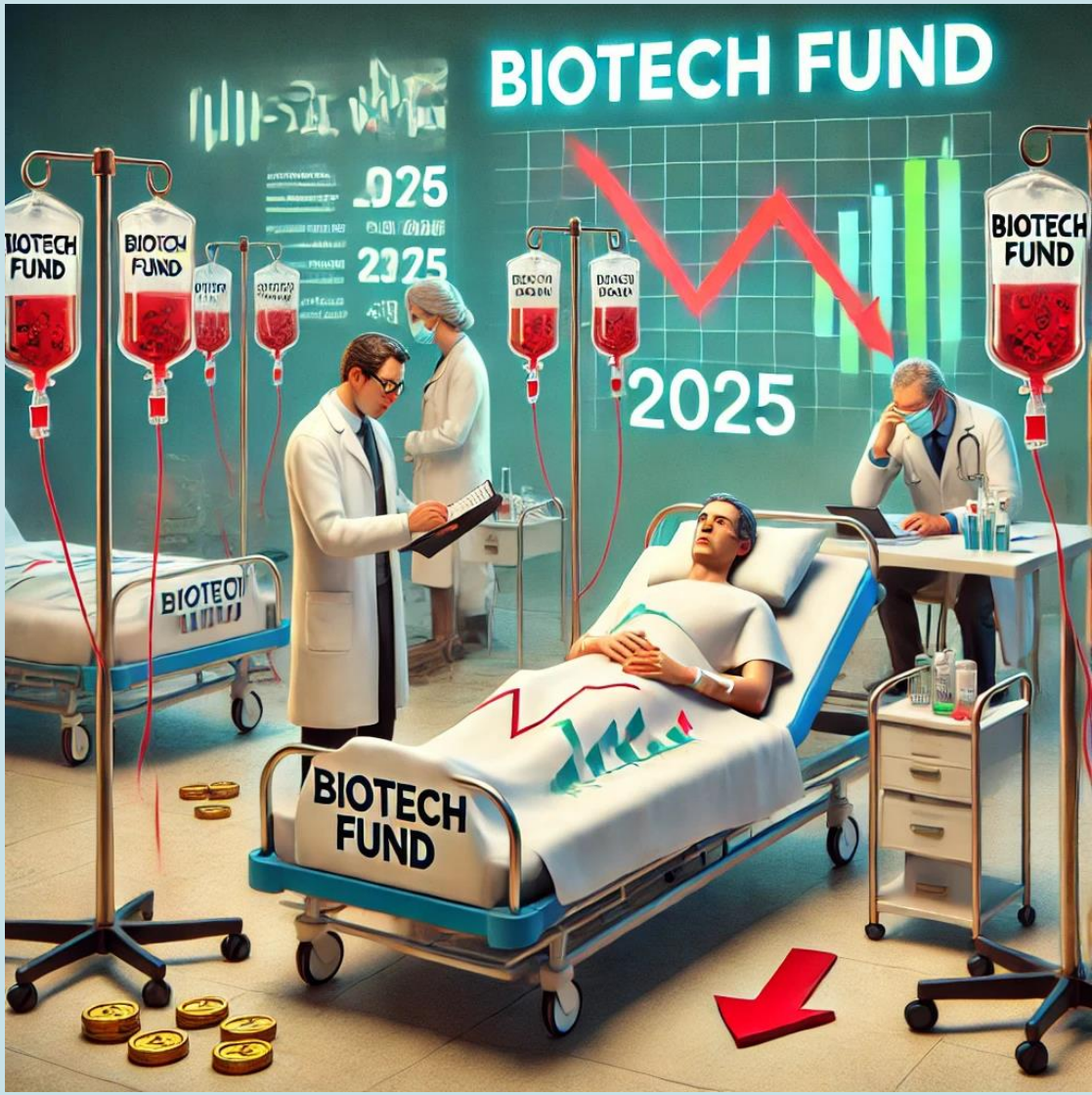
Source: CapitalIQ

Biopharma Funds Are in Sick Bay

Stephen Taub, *Institutional Investor*, March 12, 2025 (excerpt)

"February was a disaster for many biopharma, life sciences, and other health care hedge funds. Most lost money, several by double-digit rates, and as a result were in the red heading into March.

As *Institutional Investor* previously reported, investors are jittery about the sector over concerns the new U.S. administration may slow down or pause the approval process for drugs currently in development. In addition, the stock market's general volatility and sell-off have been especially rough on fledgling companies with little or no revenue and earnings — including this sector — exacerbating investor concerns."



Source: https://www.institutionalinvestor.com/article/2ej1odwnbkz58mdfdgpvk/biopharma-funds-are-in-sick-bay

Unleased Lab Space. Plunging Valuations. Layoffs. In Massachusetts, the Biotech Slump is Taking its Toll

Robert Weisman, *Boston Globe*, March 13, 2025 (excerpt)

This was supposed to be the year of biotech's comeback.

At least that was the hope of many in the sector who started 2025 pointing to scientific advances and falling interest rates. Some foresaw a pickup in buyouts and initial public offerings, rewarding investors in the highly risky and cyclical business of bringing drugs to market. But three months into the new year, the mood has soured and the outlook has clouded as a cyclone of threats and unknowns gathers speed. Despite some notable successes, including US approval in January of a nonopioid painkiller by Boston biotech Vertex, there are few signs the industry — responsible for more than 115,000 Massachusetts jobs — is pulling out of its four-year slump.

The biotech index fund XBI is down nearly 5 percent since the start of the year. The biotech cluster based in Cambridge and Boston, the nation's largest, grapples with a record 16.1 million square feet of unleased lab space. And hiring remains soft, with many biopharma companies continuing to lay off workers — though at a slower pace than last year — and tap part-time "fractional" executives to save money.

While the building blocks of science and company creation are strong, said life sciences entrepreneur and investor Alexis Borisy, the decade-or-longer marathon of developing breakthrough therapies requires stability and predictability in the business and regulatory arenas. There's been no shortage of either in recent weeks. Plunging valuations across the biotech sector were thrust into the spotlight last month when Bluebird Bio, a Somerville gene therapy company that once topped $10 billion in market value, nearly stumbled into bankruptcy before selling to a pair of investment firms for less than $30 million.

In many ways, biotech is stuck in postpandemic doldrums. Investors and real estate developers pumped billions into the sector in the run-up to COVID and through the pandemic's first year, then were caught flat-footed when demand for drugs slowed and the broader economy stalled.

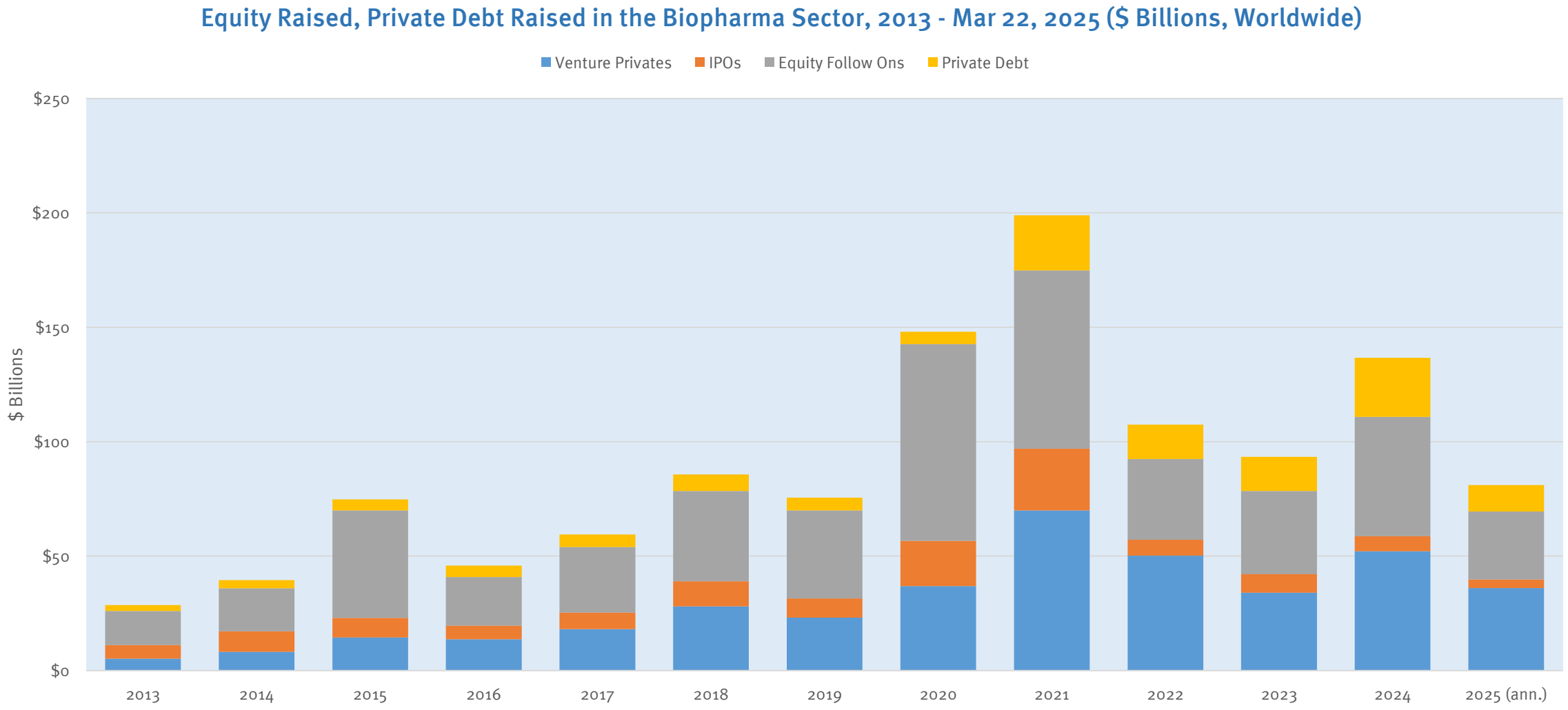
In the short term, the biggest obstacle to recovery may be the growing number of uncertainties hanging over the sector, many stemming from Trump administration's changes in policies and personnel.

Source: https://www.bostonglobe.com/2025/03/13/business/moderna-vertex-biogen-massachusetts-biotech/

Capital Markets Update

Financing Activity Thus Far in 2025 Well Below 2024 Levels

A slow public equity market is putting us on pace for a $75 billion financing year. Compare this to $140bn in 2024.

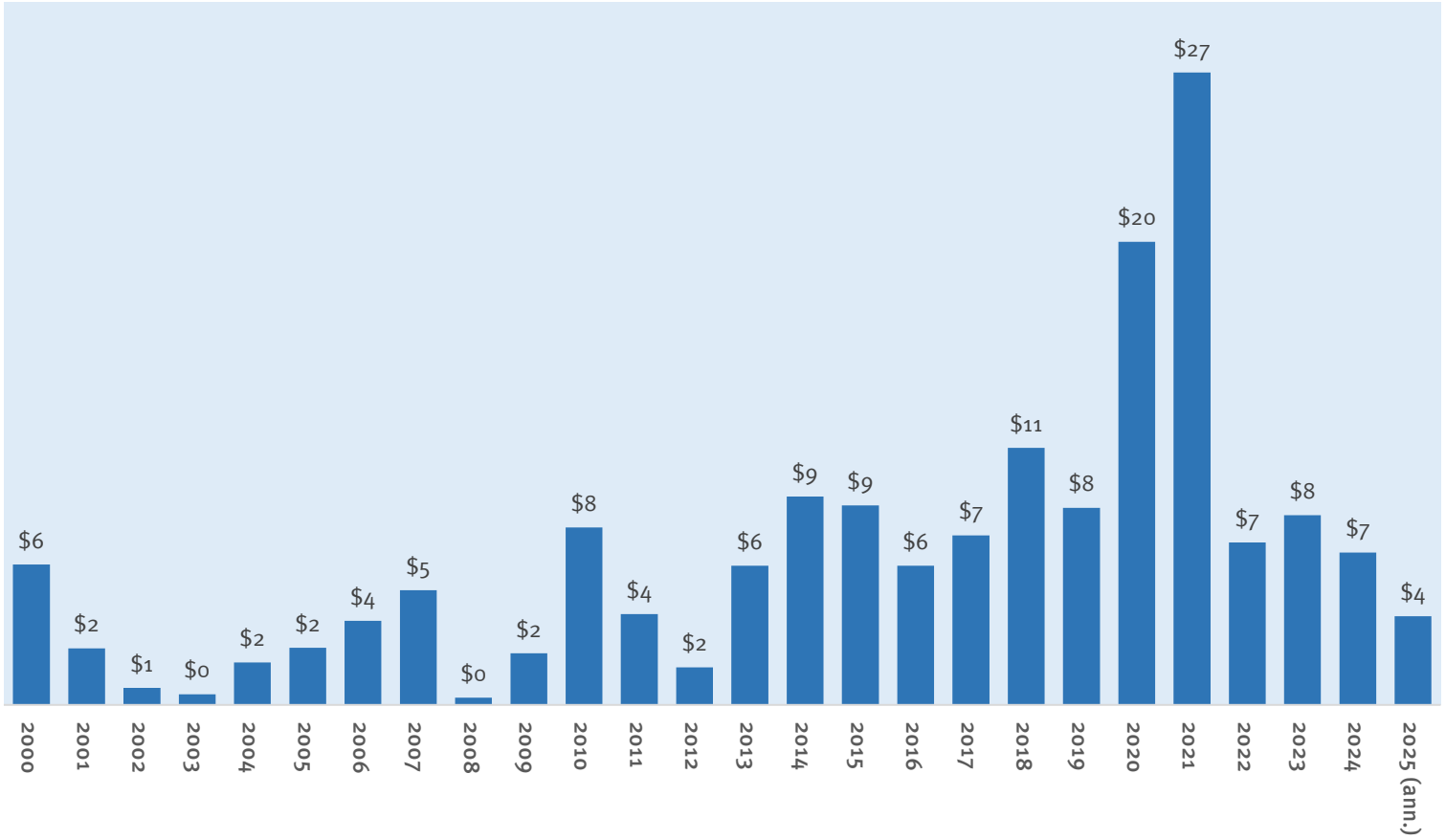


Source: Data from CapitalIQ and Stifel research.

NASDAQ IPO Market Has Quieted Down

IPO Volume in the Biopharma Sector, 2000 - 2025 (annualized)

($ Billions, Worldwide)



We have not seen any IPO's brave the U.S. capital market since Aardvark priced their deal more than a month ago.

Thus far, we have seen five IPOs go out in the Nasdaq with more than $50mm raised.

At this point two of this year's five IPO's are trading above deal price.

Only two of last year's 18 Nasdaq IPO's are trading above deal price.

We saw Visen Pharma price an $86mm HK IPO on Friday.

We expect to see very substantial IPO activity in the Hong Kong market later this year given the strength in that market.

Source: Data from CapitalIQ and Stifel research.

Visen Pharmaceuticals, Prices $101M Hong Kong IPO

Kyle LaHucik, *Endpoints News*, Mar 20, 2025 (excerpt)

"Visen Pharmaceuticals, a biotech developing much of Ascendis Pharma's endocrine-related disease pipeline for the China market, will go public on the Hong Kong Stock Exchange on Friday.

The company expects net proceeds of about 672 million HKD ($86.5 million) from the initial public offering, which will take place Friday local time or Thursday afternoon New York time, according to a regulatory filing.

Investors in the IPO include AnkeBio, Suzhou Harvest, Vivo Capital and WuXi Biologics HealthCare Venture, among others, according to the filing.

There have been few HKEX biopharma IPOs in recent quarters. A couple listing hopefuls have let their filings lapse after six months of no action, including Insilico Medicine, which went with a $110 million Series E instead.

Duality Biologics, an ADC biotech partnered with multiple big-name drugmakers, let its HKEX IPO ambitions stall last month, but the Shanghai-based startup quickly refiled days later.

Visen was approaching its own six-month deadline, having filed for the IPO last September."

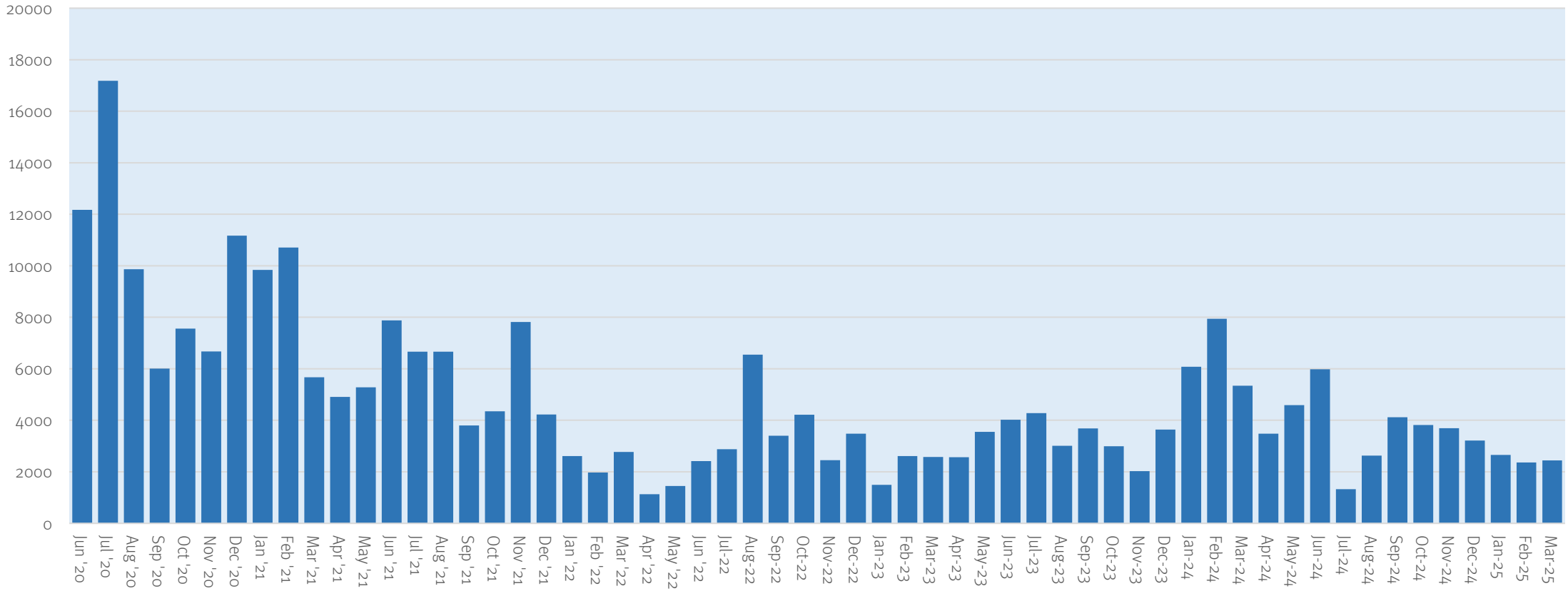
Visen shares have traded flat in HK and the company closed Friday with a $996 million market cap. The company is poised to achieve China approvals for several Ascendis drugs.

Source: https://endpts.com/visen-pharmaceuticals-prices-86m-hong-kong-ipo/

Monthly Follow-On Equity Offerings Have Slowed Down

The follow-on equity market has been running at $2.5bn global volume for the last two months. Compare this to volume in the $3bn to $4bn area just six months ago. This reflects the tough biotech tape of 2025. Average aftermarket performance has been weak for companies with market caps under $500mm. While average aftermarket performance for larger issuers has been better it has also been negative through February and March. This reflects underlying equity market dynamics and will likely turn around when inflows into the biotech sector improve.

Equity Follow-On ($volume, $mm), Jun 2020 to Mar 2025

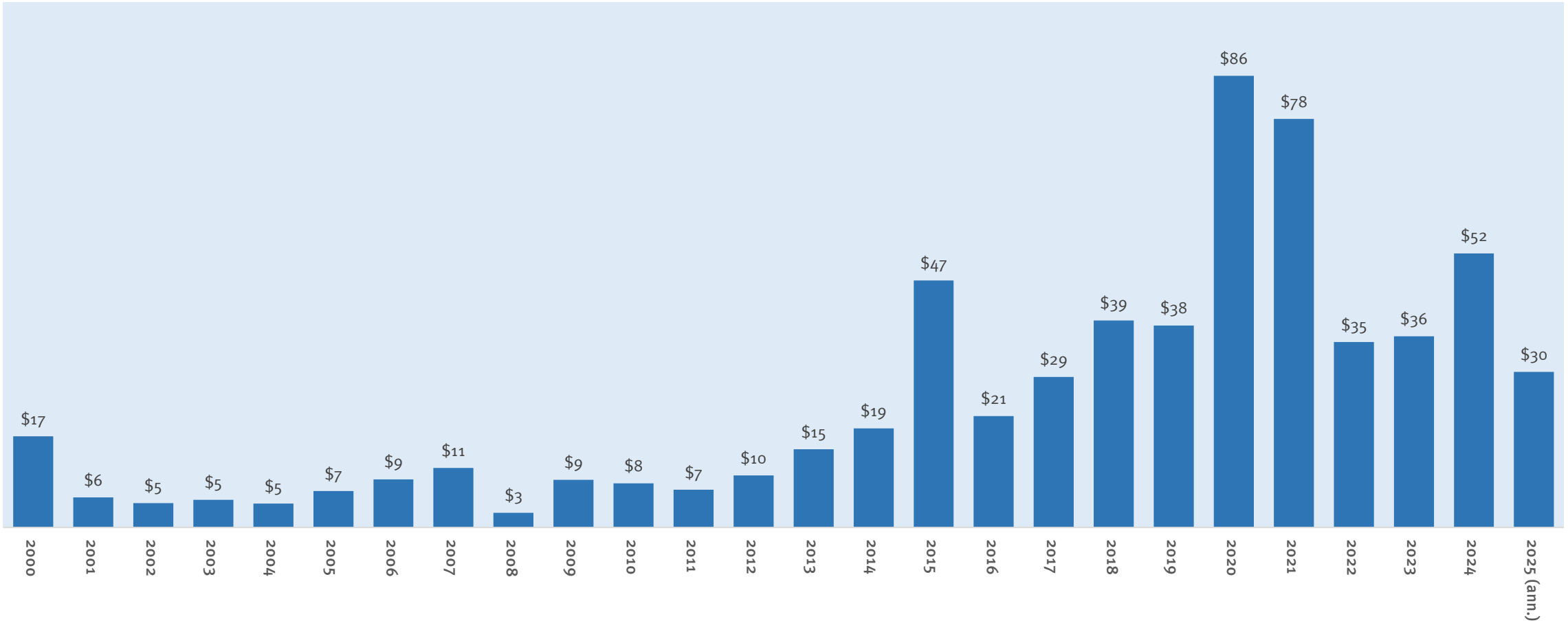


Source: Data from CapitalIQ, Crunchbase. The first three weeks of March data are extrapolated to quarter end.

At This Point, Follow-On Equity Market Volume is the Lowest Since 2017

Follow-On Equity Issuance in the Biopharma Sector, 2000 - 2025 (annualized)

($ Billions, Worldwide)

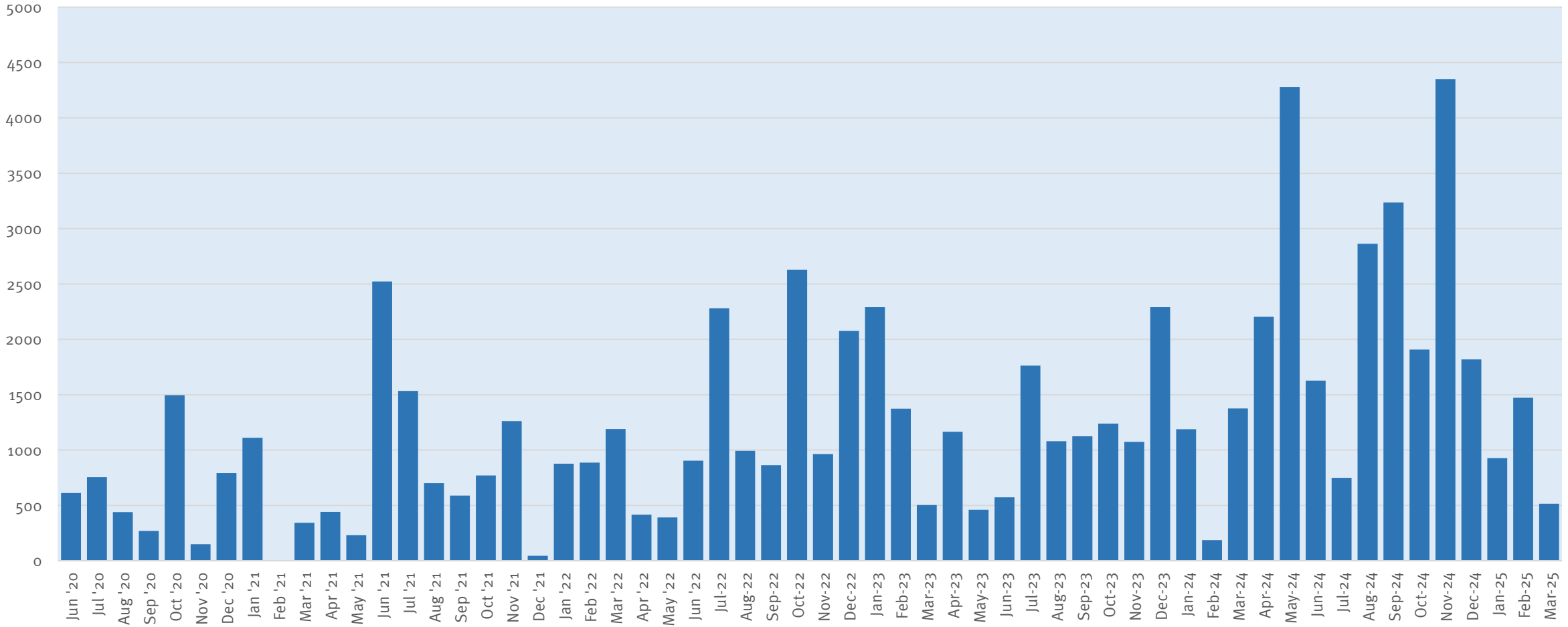


Source: Data from CapitalIQ and Stifel research. Data for 2025 is annualized as of Mar 21, 2025.

Global Biopharma Private Debt Placement Market Cooling in 2025

The pace of private debt issuance has been quite slow thus far in March 2025 and we are seeing the effect of overall market uncertainty feed back into the credit markets after a very strong 2024.

Private Debt Issuance ($volume, $mm), June 2020 to Mar 2025



Source: Data from CapitalIQ, Crunchbase. The first three weeks of March data are extrapolated to quarter end.

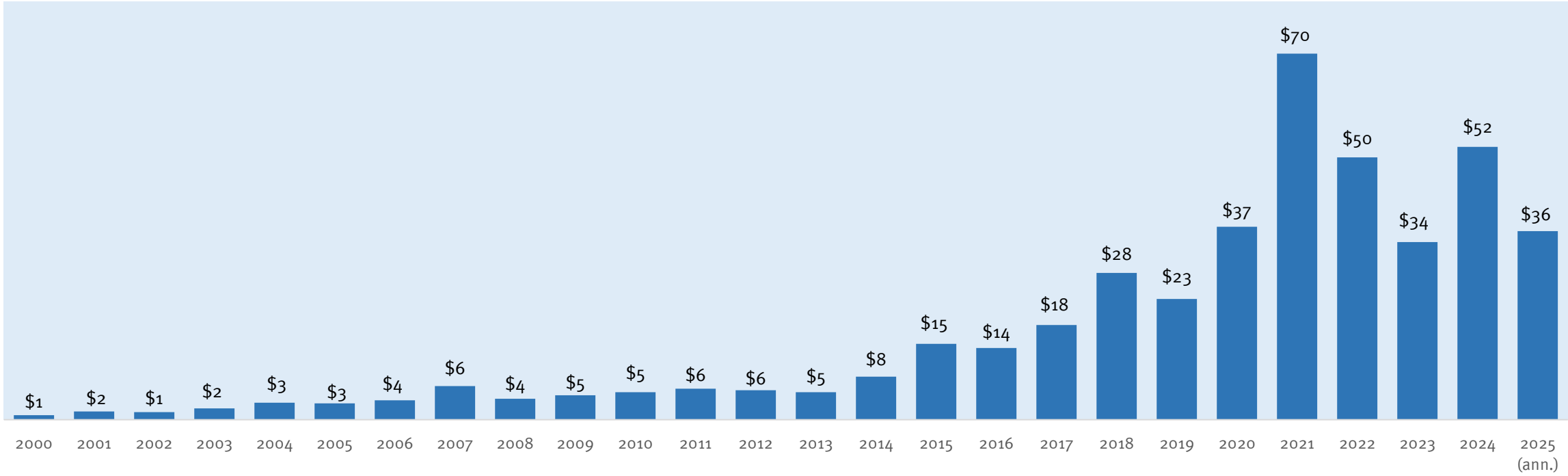
Biopharma Venture Equity Market Trends – Mar 21, 2025

Biopharma Sector Venture Equity Deals Total Volume in 2025 Down Versus 2024 Levels

Looking back, 2024 turned out to be the second most active in history for venture investments in biopharma companies. This year (2025) is slower but, nonetheless, would be the fifth most active year since 2000 given the current pace of activity.

Dollar Volume of Venture Private Equity Financings in the Biopharma Sector, 2000 - 2025

($ Billions, Worldwide)

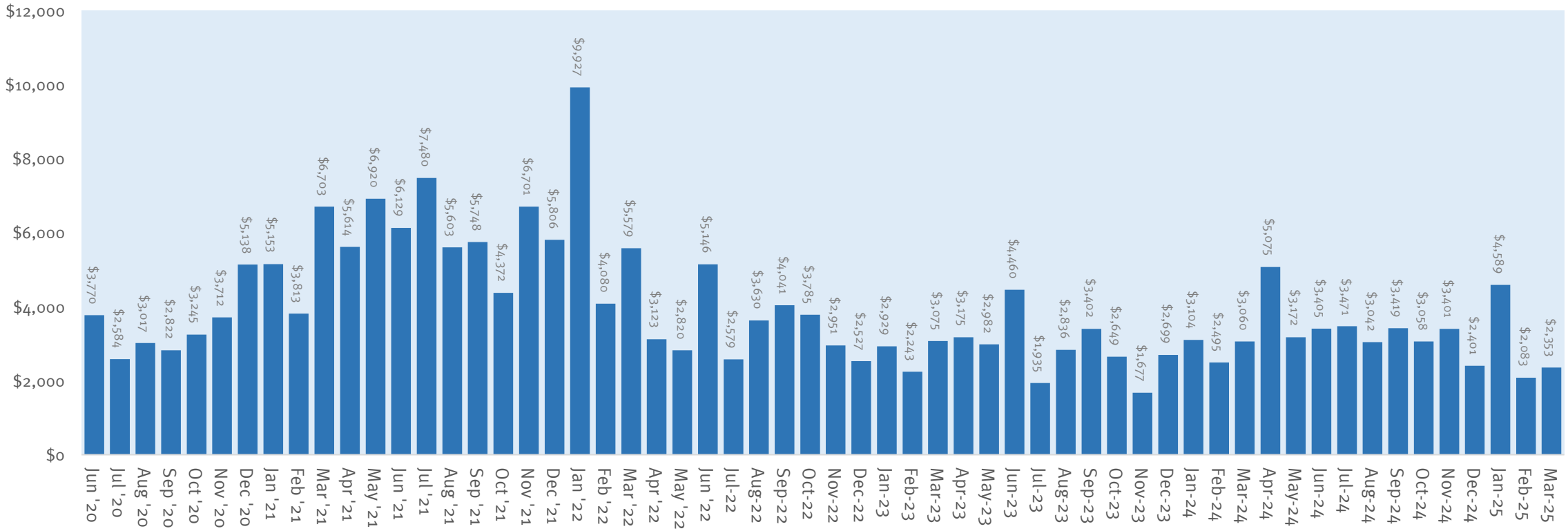


Source: Stifel internal database, CapIQ, Crunchbase. Data for 2025 is annualized as of Mar 21, 2025.

Venture Privates Market is Slowing Down in Last Two Months

After a strong January we have seen the venture private market slow down, clocking $2.5bn in monthly volume in the last two months. Compare this to average issuance volume of approximately $3bn in the previous year. The relatively weak public equity market is clearly starting to impact the privates market.

Monthly Private Equity Placement ($volume, $mm), Jun 2020 to Mar 2024



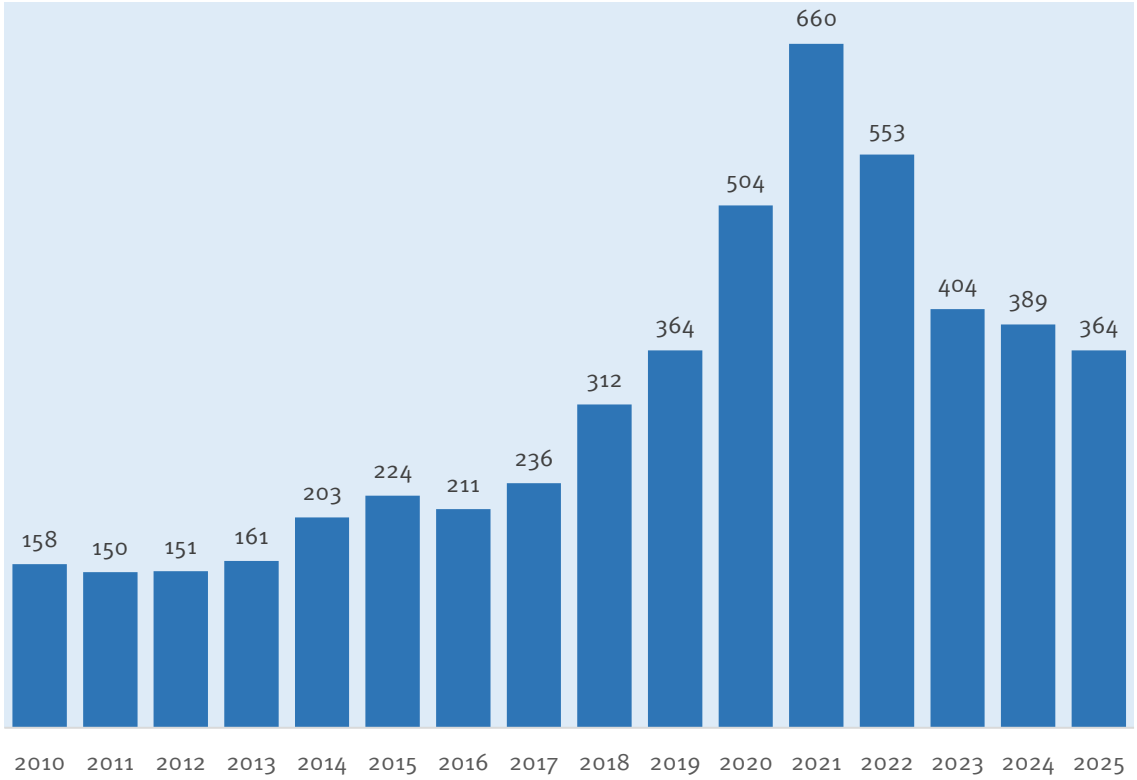
Source: Data from CapitalIQ, Crunchbase. The first three weeks of March data are extrapolated to quarter end.

While the Number of Venture Deals in Biopharma, the Average Amount Raised is Hitting a New Record in 2025

While not shown we ran an exercise where we removed the 12 most influential funds that favor large rounds (e.g., Arch) to see if a minority of funds are driving the trend to larger rounds, using the data shown on the next several pages. The answer is that they are not. The ratio of the average round size in 2025 to the average size in 2015 was about the same for the rest of the funds. Across the board, since 2021 venture funds are choosing to do fewer total rounds but put more money to work in each round.

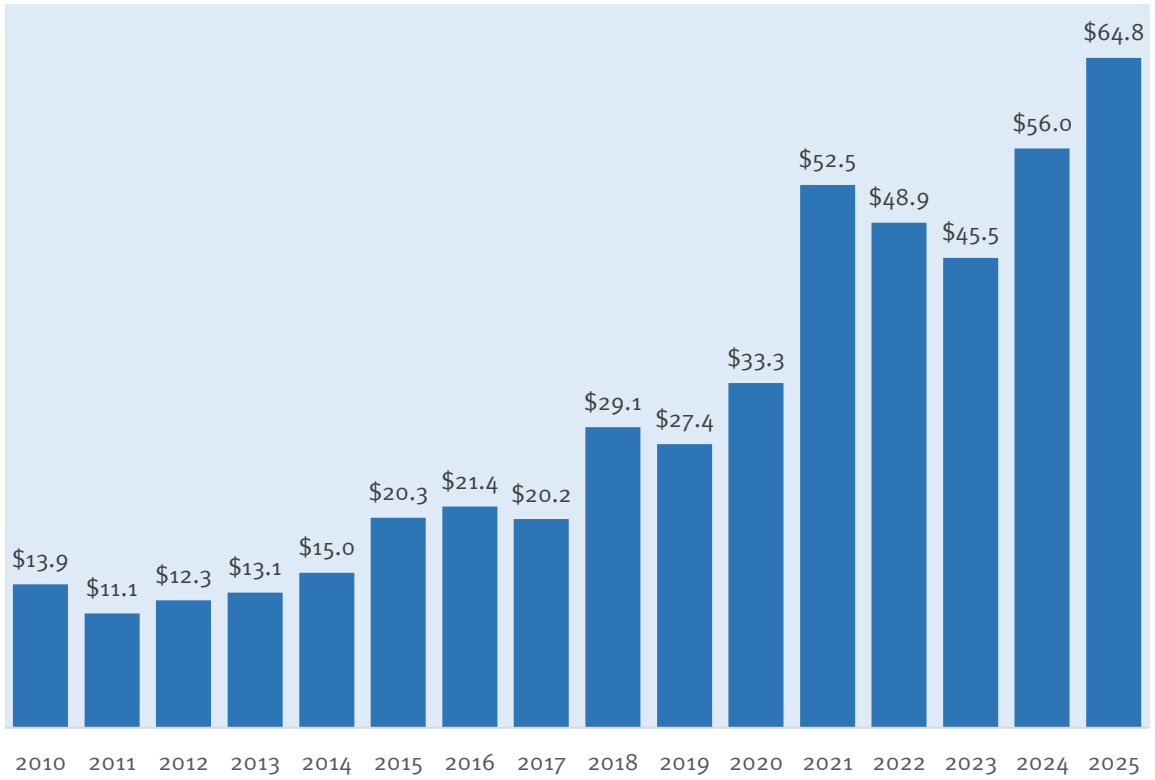
Number of Venture Rounds in the DealForma Database

By year, 2010 to 2025 ($ millions)



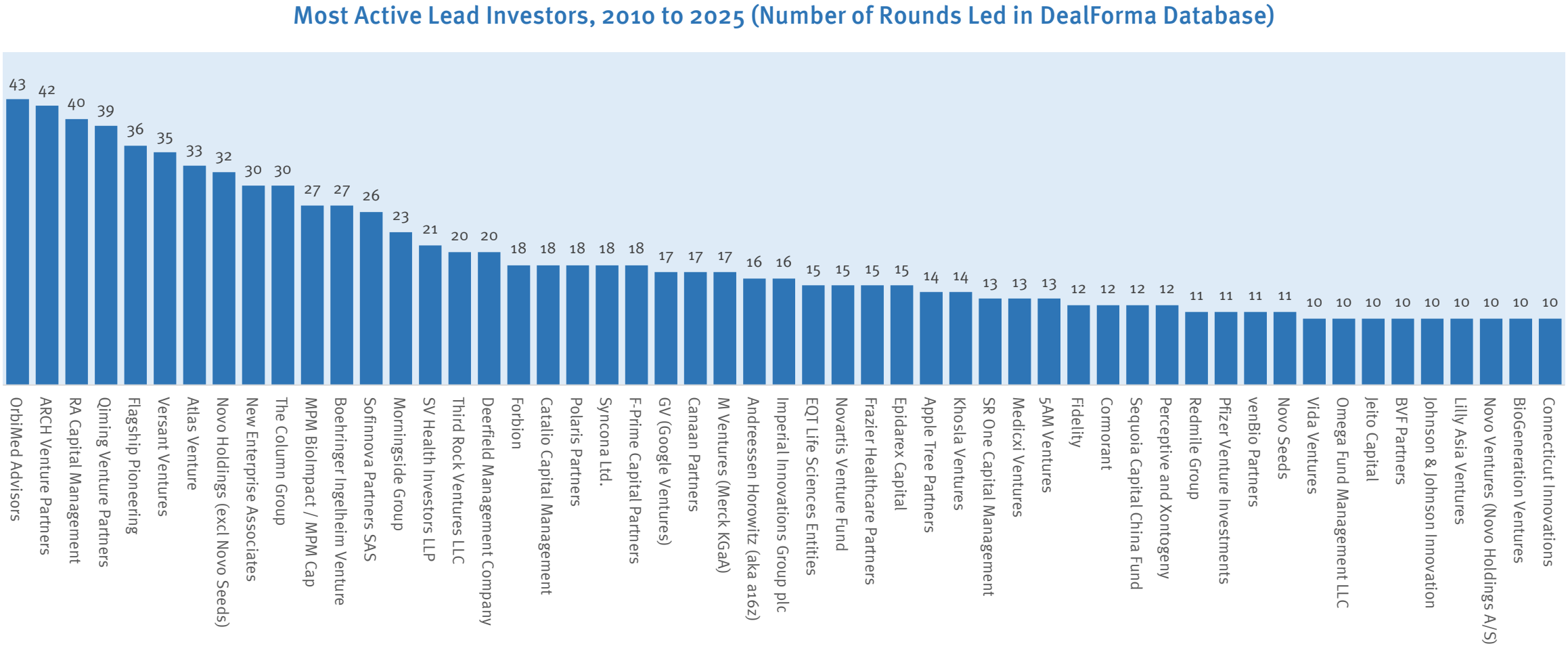
Average Amount Raised Per Venture Round

By year, 2010 to 2025 ($ millions, DealForma Database)



Source: DealForma. Venture investments into the biopharma sector. Data for 2025 through Feb 23rd.

OrbiMed, ARCH and RA Capital Have Been the Most Active Venture Investors in Biopharma in the Last 16 years



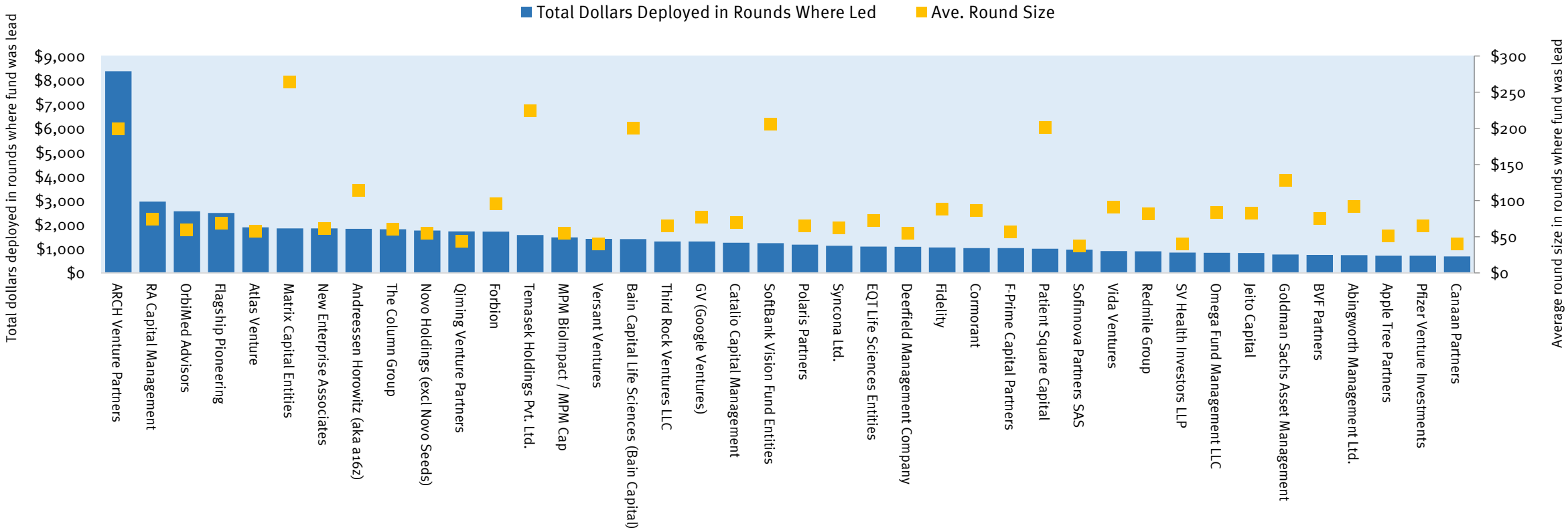
Source: DealForma. Venture investments into the biopharma sector. Data for 2025 through Feb 23rd.

Sum of Total Round Sizes by Lead Investor in the 2010 to 2025 Period

The amounts deployed in rounds that ARCH has led in the last sixteen years have been the largest by far of all funds. RA and OrbiMed are next. Average round size depends on the style of each lead investors. The average round size, for example, in an ARCH-led deal has been around $200mm while average round size for RA Capital led deals is $74mm and $60mm when OrbiMed leads.

Most Active Lead Investors, 2010 to 2025

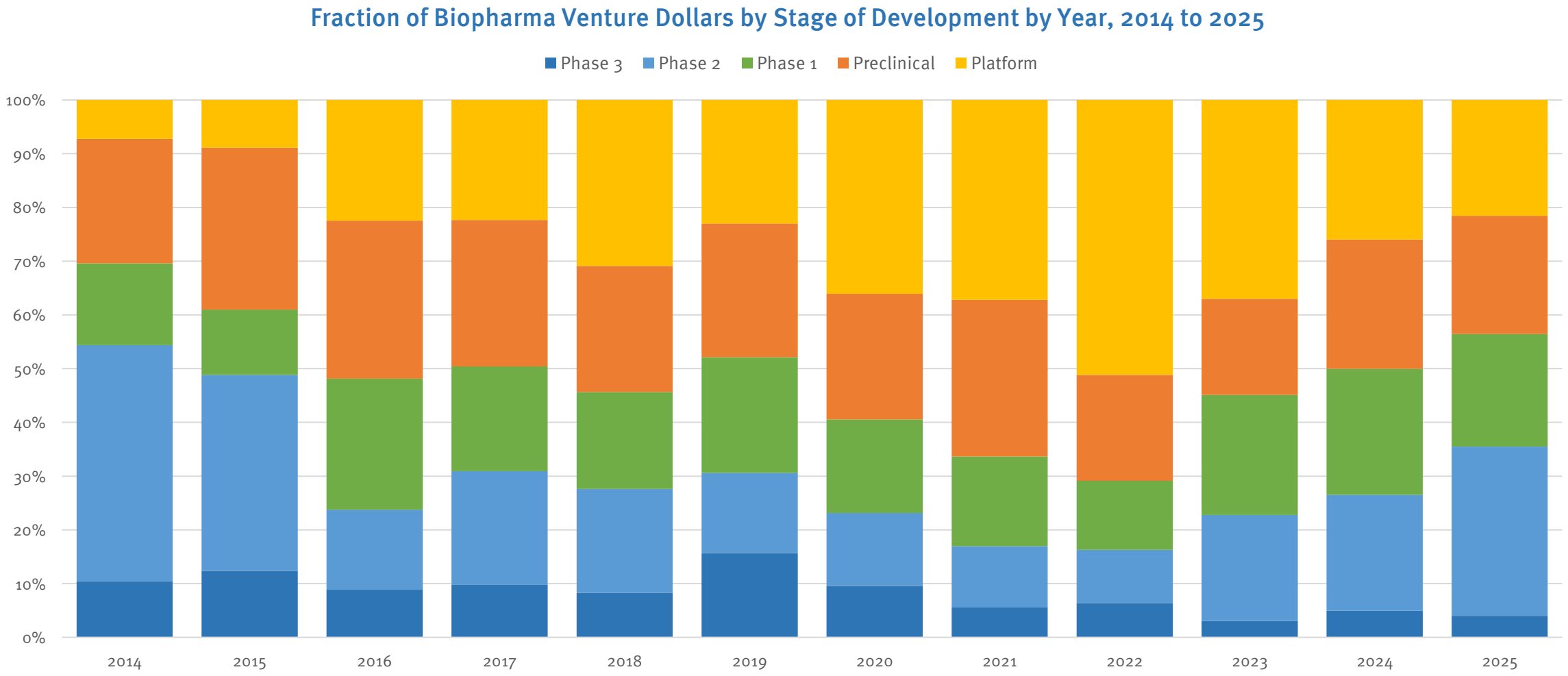
(Total Dollars Deployed in Rounds Where the Lead Fund Led and Average Round Size of Fund)



Source: DealForma. Venture investments into the biopharma sector. Data for 2025 through Mar 21st.

Trend to Later Stage Venture Deals Continuing in 2024/2025

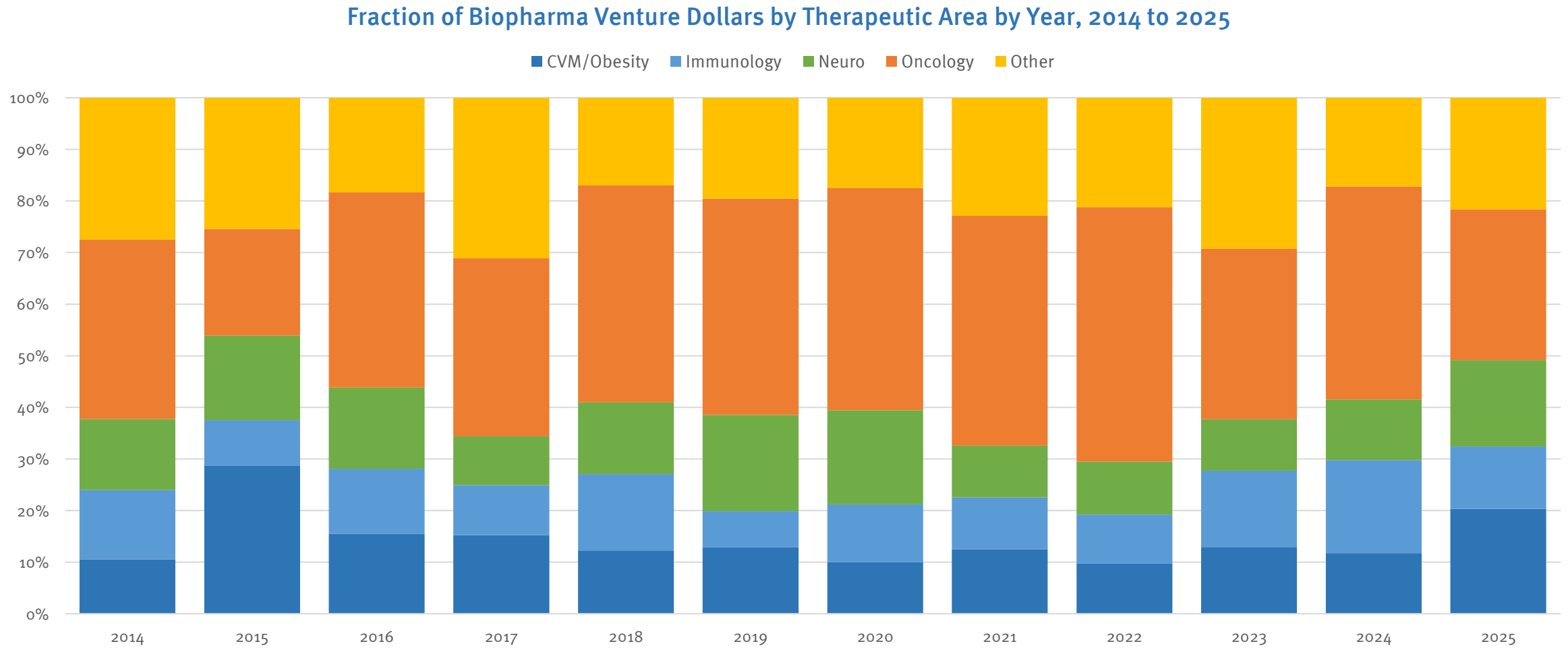
The share of venture dollars invested in later stage molecules has gone up in 2024 and 2025. The only time historically when late-stage investment was more prevalent was 2014 and 2015. Platform investment levels peaked in 2022 and have fallen off substantially since then. However, over the long-term, the popularity of investing in platform companies is a relatively new thing, taking off in a meaningful way only in 2016.



Source: DealForma. Venture investments into the biopharma sector. Data for 2025 through Feb 23rd.

Cardiology/Obesity and Neuro Investment Areas Up in 2025

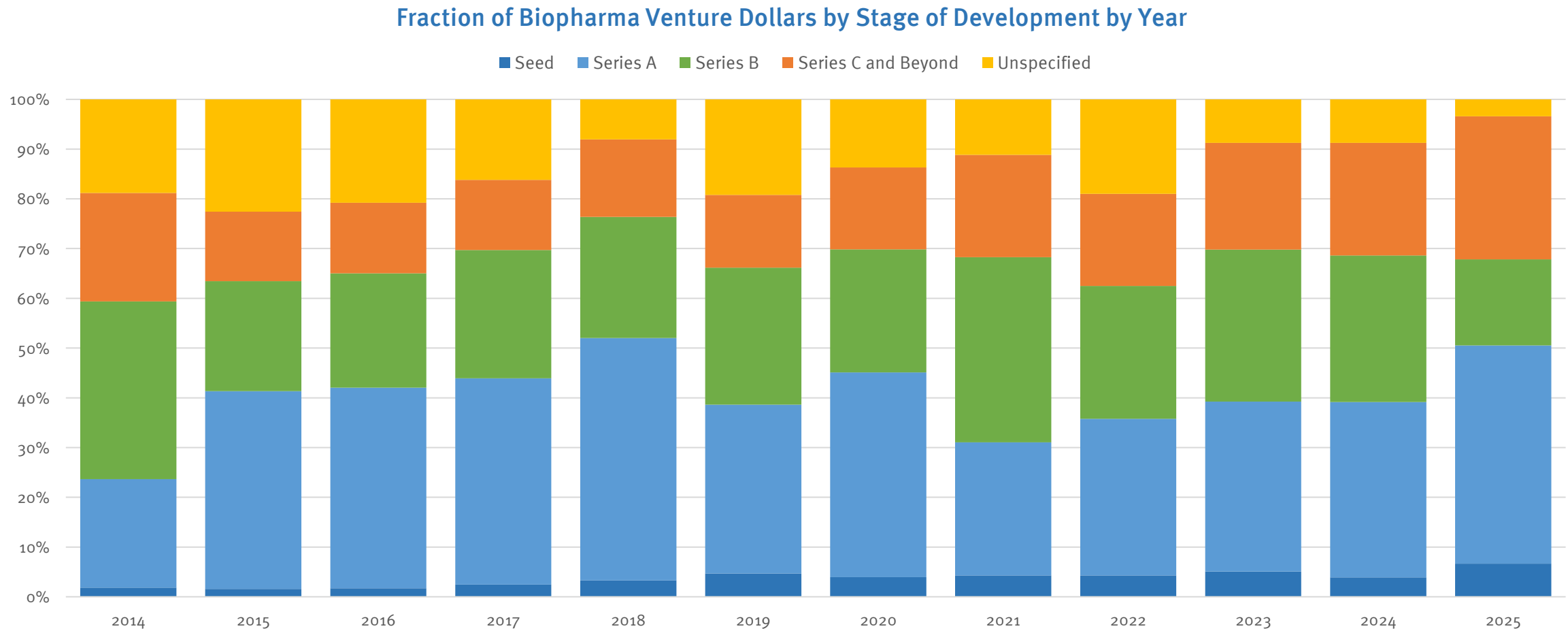
We have seen venture investments into oncology and immunology companies fall in 2025. We are seeing a surge in investment into the CVM/obesity area and neuro areas relative to recent years.



Source: DealForma. Venture investments into the biopharma sector. Data for 2025 through Mar 21st. Immunology encompasses investments in autoimmune and inflammation. CVM/obesity includes hepatology, obesity, diabetes, cardiology and endocrinology.

We are Seeing a Big Drop Off in Series B Deals in 2025

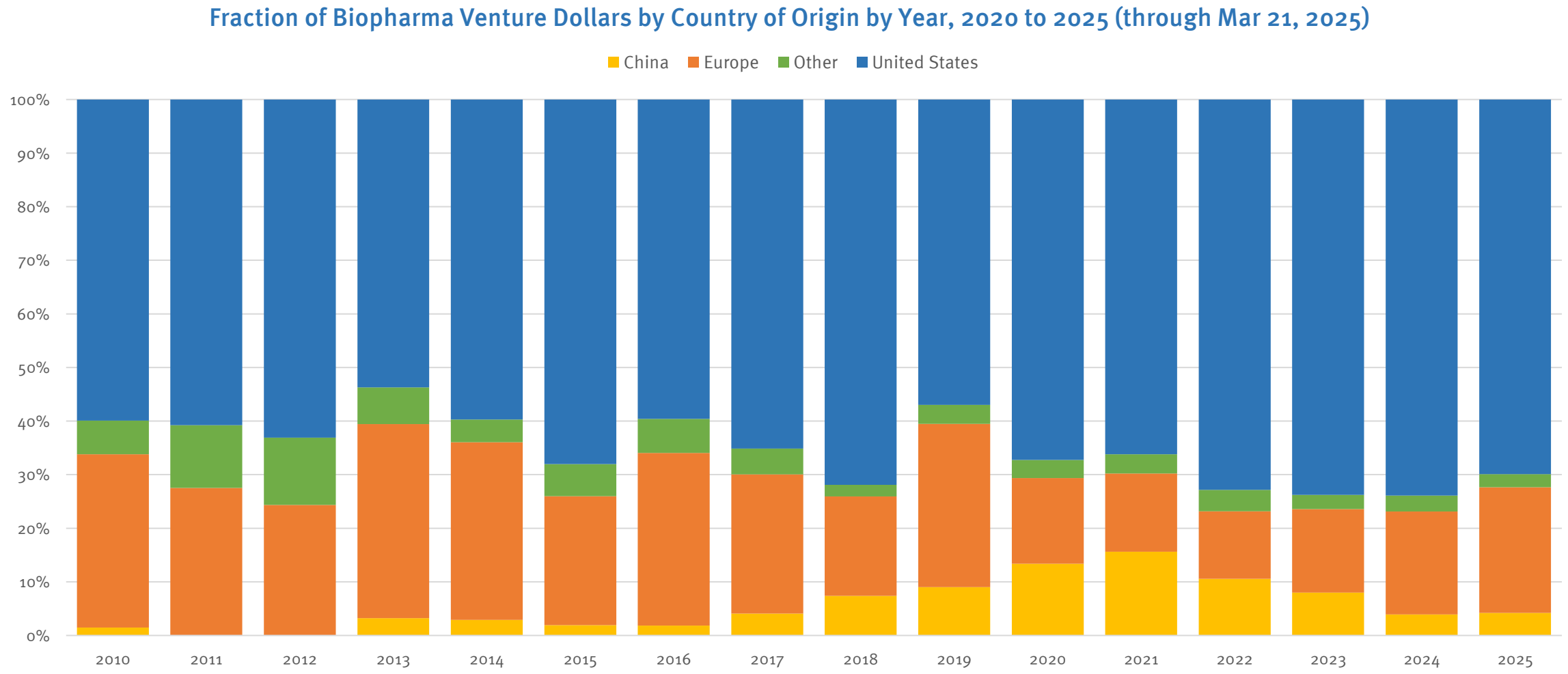
The share of money going into Series B deals has fallen substantially in 2025. In contrast, we are seeing more money go into Series A, Series Seed and later stage deals (Series C and beyond).



Source: DealForma. Venture investments into the biopharma sector. Data for 2025 through Mar 21st.

Europe is Picking Up Share in the Venture Market in 2025

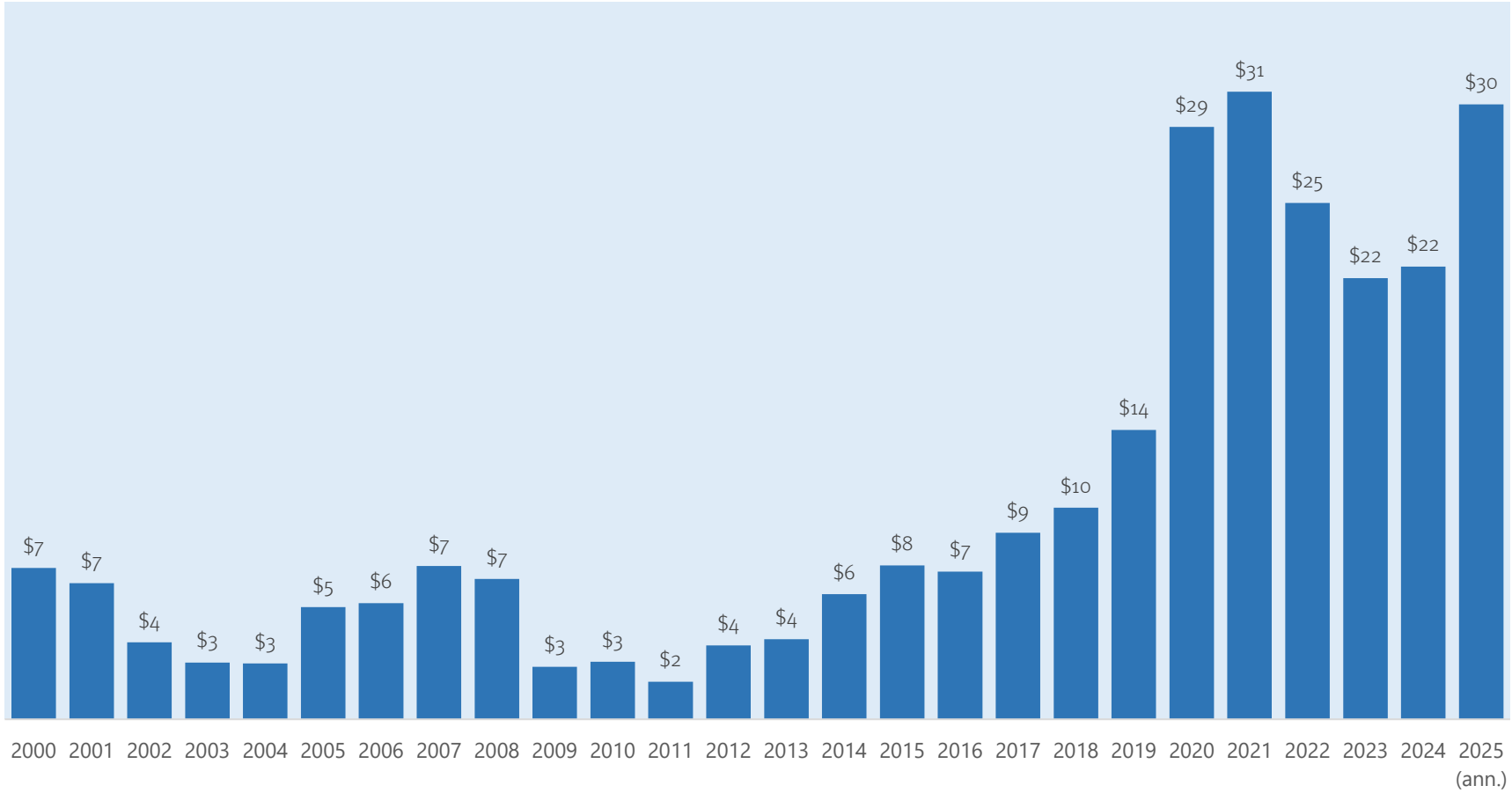
The share of venture dollars invested US is dropping in 2025 versus other regions, particularly Europe. China volume is way off in 2025. However, on a recent trip to China we learned that most financing rounds are never announced so we can only say that announced venture financing in China is down. Informally, we heard that venture financings have been returning in China due to the strong biotech market in Hong Kong.



Source: DealForma. Venture investments into the biopharma sector. Data for 2025 through Mar 21st.

New Capital Flows into Life Sciences Venture Funds Up in 2024 vs 2023

Biopharma Venture Capital Funds, Amounts Raised $billions, 2000 to 2025



On the back of a robust quarter (Blackstone raising $1.6bn and Bain raising $3bn) we are seeing a very strong market for inflows into venture funds in the life sciences.

The current annualized pace ($30bn raised) is at the record levels set in 2020 and 2021.

However, one strong quarter does not necessarily make the year so let's see how the rest of the year plays out.

Source: Data from CapitalIQ, Crunchbase.

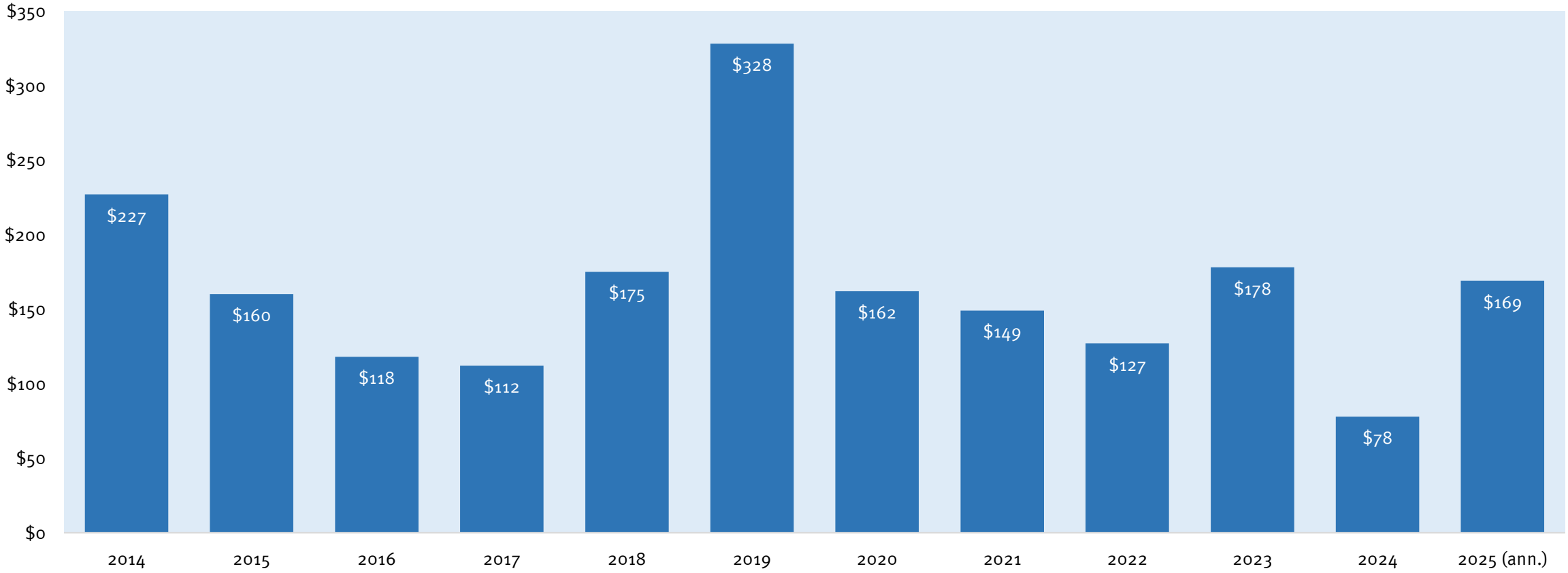
M&A Update

We are on Track for the Second Strongest M&A Year Since 2019

Based on M&A volumes through Mar 21, 2025 we are tracking to a $169bn year for M&A volume. This would be the second strongest year since 2019 and above the annual average for the 2014 to 2024 period.

M&A Volume in the Biopharma Sector, 2014 – 2025 (annualized)

($ Billions, Worldwide)

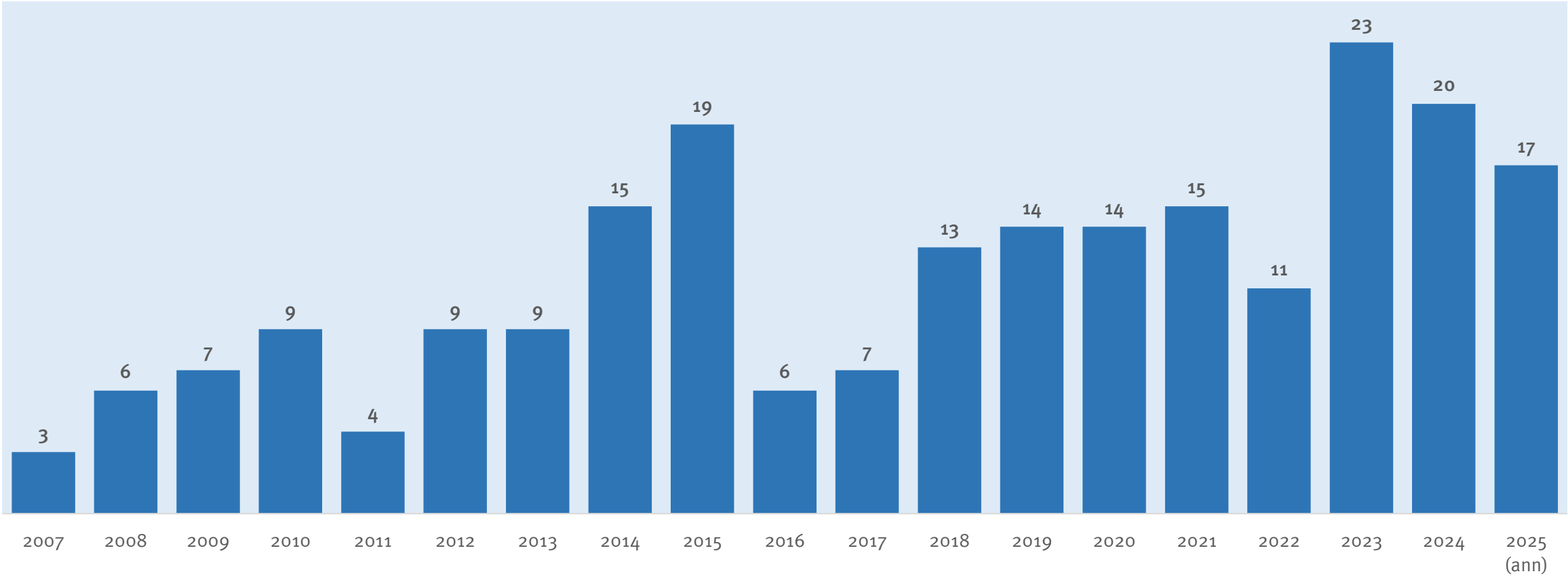


Source: Data from CapitalIQ and Stifel research. Data for 2025 is annualized as of Mar 21, 2025.

We are Tracking for 17 Billion Plus Deals in 2025

So far in 2025 we have seen four transactions for $1bn or more. On an annualized basis, we are tracking for a 17 $1bn+ upfront M&A deals. While not a record, this is a good number.

Count of Biopharma M&A Deals with $1bn or More Upfront, 2007 to 2025

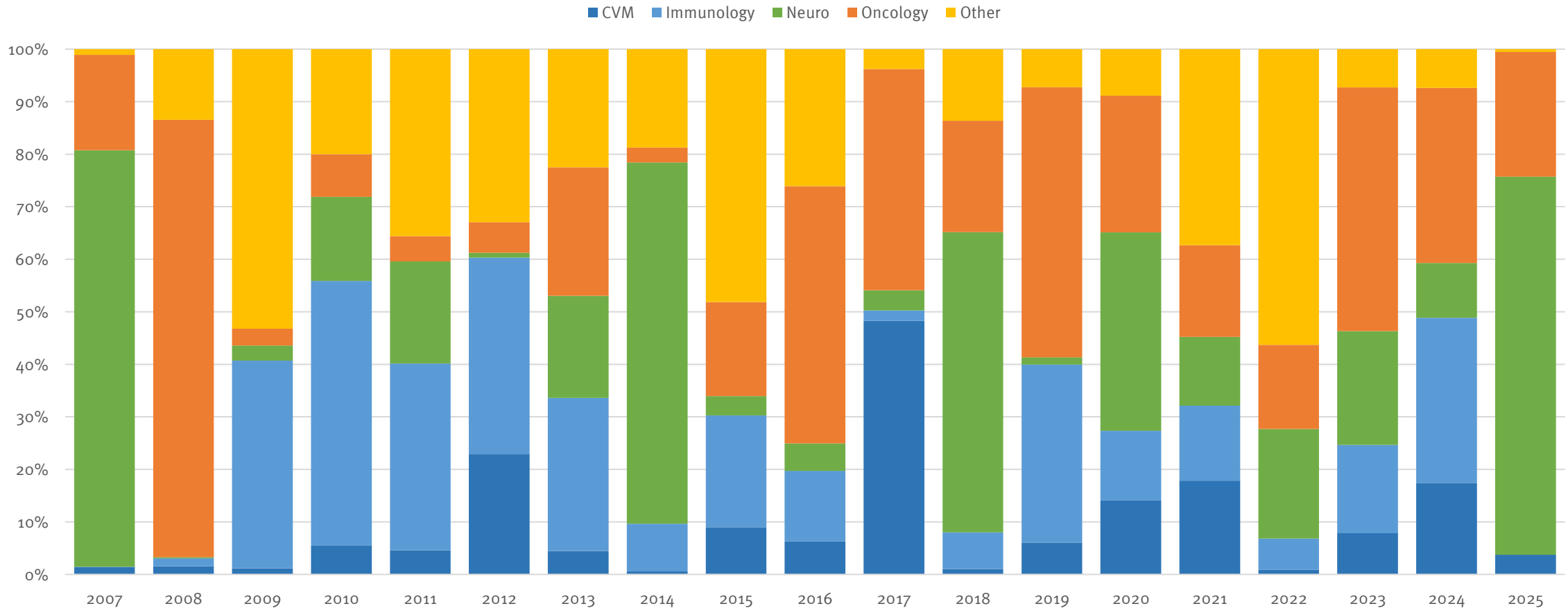


Source: DealForma. Data for 2025 is annualized as of Mar 21, 2025.

M&A Activity in 2025 Has Been Heavily Neuro Oriented

Two of the larger deals in 2025 have been for IntraCellular (psychiatry) and Tanabe Pharma (neurology). We have not seen a large immunology M&A deal this year as buyers have been opting for licensing deals instead (the Acelyrin deal is the only immunology deal so far). Oncology continues to have significant M&A share with takeouts this year of Scorpion, IDRx and Chimerix.

Biopharma M&A Activity (Dollar Volume) by Therapeutic Area, 2007 to 2025



Source: DealForma. M&A deals for the biopharma sector. Data on dollar volume for 2025 through Mar 21st.

Two Early-Stage Private Oncology Takeouts Announced Last Week

AstraZeneca Buying EsoBiotec

Announcement Date:	Mar 17, 2025
Upfront Cash:	$425mm
Total Milestones:	$575mm

AstraZeneca is acquiring EsoBiotec. EsoBiotec's lead assets were phase I ESO-T01 for multiple myeloma and other assets in discovery phase including ESO-TX101, ESO-TX102, and ESO-TX103 for the treatment of solid tumors. The company's other asset was the ENaBL vector platform, which enables direct genetic programming of immune cells within the patient's body, potentially transforming cell therapy by eliminating the need for complex manufacturing and long treatment timelines. The acquisition will expand AstraZeneca's cell therapy capabilities, accelerating the development of more accessible and scalable cancer and immune disease treatments. EsoBiotec will become a wholly owned subsidiary of AstraZeneca, with operations in Belgium. The deal is expected to close in Q2 2025, pending regulatory approvals. EsoBiotec will receive $425M up front and is eligible for up to $575M in development and regulatory milestones.

TAIHO 大鵬薬品 Buying araris

Announcement Date:	Mar 17, 2025
Upfront Cash:	$400mm
Total Milestones:	$740mm

Taiho is acquiring Araris Biotech, a portfolio company of 4BIO Capital. Araris' lead assets were preclinical ARC-01, targeting CD79B for the treatment of B-cell malignancies, along with Anti-HER2 ADC and Anti-Nectin-4 ADC, both in preclinical development for solid tumors, all developed using AraLinQ technology.

The therapies are expected to enter clinical trials between 2025 and 2026, with help from Taiho Pharmaceutical's clinical development expertise. Araris will receive $400M up front and is eligible for up to $740M in milestone payments. The acquisition is expected to be completed in H1'2025, after which Araris will become a wholly owned Taiho subsidiary, continuing its R&D in Zurich, Switzerland.

Source: DealForma.

Paratek Buying OptiNose for $100mm Upfront

Paratek Pharmaceuticals to Acquire Optinose, Creating Significant Commercial Expansion Opportunities for XHANCE® in Chronic Rhinosinusitis (CRS)

BOSTON and YARDLEY, Pa., March 19, 2025 (GLOBE NEWSWIRE) -- Paratek Pharmaceuticals and Optinose, Inc. (NASDAQ:OPTN) today announced they have entered into a definitive merger agreement under which Paratek will acquire Optinose, including its approved product XHANCE® (fluticasone propionate). The transaction value is up to $330 million, with consideration payable to shareholders of up to $14 per share, including the payment of contingent value rights (CVRs) tied to future commercial milestones. This acquisition expands Paratek's commercial portfolio beyond its flagship antibiotic, NUZYRA® (omadacycline), and strengthens its position as a multi-product company focused on innovative specialty therapies for primary care providers and specialists, addressing important medical health threats.

XHANCE is an innovative, drug-device combination product approved for the treatment of CRS with or without nasal polyps. By optimally targeting the site of inflammation with a proven corticosteroid using its proprietary Exhalation Delivery System™ (EDS®), XHANCE addresses a significant unmet clinical need, improving CRS symptoms with the potential to avoid and/or delay more invasive or expensive treatment options. Originally approved in 2017 for CRS with nasal polyps with a commercial focus on ear, nose, and throat (ENT) and allergy specialists, the XHANCE label was broadened in 2024 to include an additional indication for CRS without nasal polyps. This approval expanded the potential addressable market ~10-fold, the majority of which is treated by primary care providers.

Over the past 15 months, Paratek has significantly expanded its primary care field force to have a national footprint. Paratek will leverage its expanded commercial infrastructure along with existing Optinose specialist sales expertise to accelerate awareness and adoption of XHANCE among both ENT and allergy specialists and primary care providers.

Under the terms of the agreement, Paratek will acquire all of Optinose's outstanding shares for $9 per share in cash, plus up to $5 per share in CVRs payable in the event that certain net revenue milestones are achieved by XHANCE. Pursuant to the CVRs, Paratek would pay $1 per share if XHANCE achieves $150M in net sales in any calendar year prior to December 31, 2028, and $4 per share if XHANCE achieves $225M in net sales in any calendar year prior to December 31, 2029. The upfront consideration of $9 per share represents a 50% premium to Optinose's closing trading price on March 19, 2025.

Source: https://ir.optinose.com/news-releases/news-release-details/paratek-pharmaceuticals-acquire-optinose-creating-significant

Sanofi Buys Dren Bio's T-Cell Engager for $600MM Upfront

Phil Taylor, *Pharmaphorum*, Mar 20, 2025 (excerpt)

Sanofi says it has reached an agreement with Dren Bio that would see it take control of autoimmune disease treatment DR-0201, a bispecific antibody-based myeloid cell engager with the potential to "reset the immune system."

Under the terms of the deal, Sanofi will pay $600 million upfront to buy an affiliate of the California-based biotech, called Dren-0201, which was set up to develop the therapy. Dren Bio could also make another $1.3 billion tied to future development and launch objectives for DR-0201.

The potentially first-in-class drug, which targets CD20, is able to achieve "deep B-cell depletion" by stimulating cells of the immune system to engulf and destroy B-cells in the presence of a specific antigen.

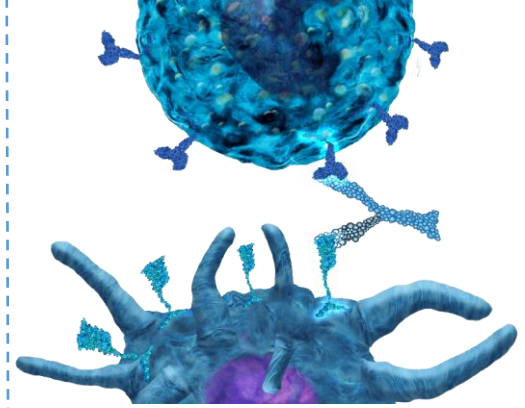
According to Sanofi and Dren Bio, DR-0201 treatment could be used to sustain treatment-free remission in patients with hard-to-treat diseases such as lupus.
"Deep B-cell depletion is at the frontier of treating autoimmune diseases and using the myeloid cell engager DR-0201 has the potential to elevate the treatment effect for patients, in particular patients refractory to existing treatments," commented Sanofi's head of R&D Houman Ashrafian.

The deal builds on Sanofi's already formidable presence in immunological diseases currently spearheaded by Dupixent (dupilumab), its $14 billion blockbuster that targets diseases associated with type 2 inflammation like atopic dermatitis and asthma.

DR-0201 is currently being evaluated in two phase 1 studies, one in the blood cancer non-Hodgkin lymphoma (NHL) and another in a range of autoimmune diseases including SLE, cutaneous lupus erythematosus (CLE), Sjögren's syndrome, dermatomyositis/polymositis, scleroderma, and diffuse cutaneous systemic sclerosis (dcSSc).

"It has been a privilege to advance our lead platform programme, DR-0201, into clinical development and evaluate its potential to achieve potent B-cell depletion," said Dren Bio's co-founder and chief executive, Nenad Tomasevic.

Source: https://pharmaphorum.com/news/sanofi-signs-19bn-deal-buy-dren-bio-autoimmune-drug



dren bio

Dren Bio's Targeted Myeloid Engager and Phagocytosis Platform is a bispecific antibody-based technology that induces potent depletion of pathogenic cells, protein aggregates, and other disease-causing agents by engaging a novel phagocytic receptor that is selectively expressed on myeloid cells. Bispecific antibodies generated from the platform are specifically engineered to enable controlled myeloid cell activation only in the presence of the target antigen, which may result in greater therapeutic indexes and offer superior safety profiles compared to other therapeutic modalities such as T-cell engagers and Antibody Drug Conjugates (ADCs).

Chimerix Engaged With 7 Other Biopharmas Before Choosing Jazz's $935M Deal—Here's Why it Won

Gabrielle Masson, *Fierce Biotech*, Mar 21, 2025 (excerpt)

Before Jazz Pharmaceuticals inked a $935 million deal for Chimerix earlier this month, the biotech had been in talks with six other pharmas and one biotech about several different potential offers. Ultimately, Chimerix's board went with Jazz's offer due to its cash payable nature and the recent downward trend in biopharma financial markets, plus a general volatility tied to escalating political and global trade tensions, according to Securities and Exchange Commission documents filed Friday.

Buying Chimerix gives Jazz control of the brain cancer drug candidate dordaviprone, also known as ONC201, a small molecule designed to treat recurrent H3 K27M-mutant diffuse glioma. But Jazz wasn't first on site. Since August of 2023, Chimerix had been in discussions about potential licensing deals for ONC201 with a "global pharmaceutical company," known as "party A" in the filings.

Chimerix steadily entered discussions with more companies—termed parties B through G—about potential strategic transactions related to the oncology candidate, per the docs. Jazz was one of the last contenders to enter the scene, reaching out after Chimerix publicly announced on Dec. 9, 2024, its plan to submit a new drug application seeking accelerated approval for ONC201 before the year ended.

On Dec. 18 and Dec. 19, Chimerix's board reviewed its offers from several different companies, including a potential equity financing, a possible ex-U.S. licensing transaction for ONC201 and a potential acquisition. The board ultimately decided to move forward with multiple options at the same time. On Jan. 26, party A came back again with a revised proposal to acquire Chimerix on the same terms as before, but with the deadlines to hit the payment-triggering milestones removed. Chimerix management told party A on Jan. 30 that the revised offer was still not good enough. On Feb. 6, Jazz outlined an acquisition offer for an upfront payment of $5.50 per share and one CVR per share representing the right to receive one-time payments of $1 upon FDA approval, 25 cents upon receipt of pricing approval in at least three major European markets and $1.50 once global net sales of ONC201 were above $500 million in a calendar year. Chimerix told Jazz the offer was insufficient, but that Chimerix would provide additional due diligence materials so Jazz could increase its offer.

Ten days later, Chimerix publicly announced that the FDA had accepted its new drug application seeking accelerated approval, with the application receiving priority review and a decision expected by Aug. 18 of this year. On March 3, Jazz submitted its final proposal: $8.55 per share in all cash.

Source: https://www.fiercebiotech.com/biotech/chimerix-engaged-7-other-biopharmas-choosing-jazzs-935m-deal-heres-why-jazz-won

Recent Think Tank Conversations on U.S. Healthcare

US Urged to ‘Think Bigger’ on Healthcare Amid Trump Onslaught on Sector

Jessica Glenza, *The Guardian*, Mar 22, 2025 (excerpt)

An academic journal may inject some optimism into US health policy – a scarce commodity amid the Trump administration’s mass layoffs, funding freezes and the ideological research reviews. A new issue of *Health Affairs Scholar* argues the conversation around healthcare can change – and radically – if academics think “bigger” and policymakers invest in their communities. “We saw what happened in the public outcry of the murder of the United HealthCare CEO,” said Dr Victor Roy, a family physician and director of the health and political economy project at the New School in New York City.

“There is a sense people are fed up and people are looking for bigger alternatives. People have really visceral feelings around these issues and we have a way to tackle them if people come up with ideas on the scale of the challenges people are experiencing.” Health policy has quickly become a major touchstone of the Maga (“Make America great again”) right, as the Trump administration undertakes a shock and awe campaign that has dramatically altered public health institutions.

In just a few weeks in office, the administration has scrubbed government health websites of information on women and racial minorities, reviewed billions in scientific grant applications for conformity to the president’s agenda, and confirmed the nation’s foremost vaccine critic, Robert F Kennedy Jr, as the nation’s top health leader at the Department of Health and Human Services. The administration has also said it will pull the US out of the World Health Organization (WHO), which it helped found in 1948. How to fix it? Don’t tinker around the edges, Roy argues. Instead, look upstream for solutions to health problems. Abandon narratives about “deserving-ness”. Examine what is working in cities and states.

In an interview, Roy cited the example of the Philadelphia Joy Bank – a small program that provides pregnant and postpartum women with a $1,000 basic income. This money comes with no questions asked, which is a world of difference from traditional “welfare”, or temporary assistance for needy families (TANF).

TANF once provided temporary cash assistance to the poor. Since Clinton-era welfare reforms, the program has been drained of resources; its scant payments have lost venue with inflation and work requirements have saddled many with insurmountable bureaucratic barriers.

In Connecticut, lawmakers established first-in-the-nation “baby bonds”, a small investing account for each low-income child born in the state. The program provides $3,200 per child that is invested in the market, and can be used to buy a house, start a business, or pay for higher education or retirement.

“Prevailing approaches to health policy are leaving people in America behind, including rural and low-income residents and people from historically marginalized communities,” Kathryn A Phillips, the editor-in-chief of *Health Affairs Scholar*, said in a statement about the issue.

Source: https://www.theguardian.com/us-news/2025/mar/22/us-healthcare-trump

General Catalyst Advocates Greater Transparency and Use of AI in Healthcare Delivery

CATALYZING CARE: A FRAMEWORK FOR A HEALTHIER AMERICA

GOAL

Transform U.S. healthcare delivery through market-driven health assurance approaches to include healthier outcomes for all, technological innovation, patient-first care, data, and accessibility, prudent fiscal practices that reduce fraud and waste, as well as U.S. talent to deliver healthcare that works.

SHORT-TERM ACTIONS	LONGER-TERM ACTIONS
1. Foster Healthier Outcomes for All	
Launch Regional Healthcare Innovation Sandboxes	Upgrade Rural Health Clinics for Greater Access and AI-Augmented Care
2. Refine Needed Innovations Without Red Tape	
Establish a Fast-Track AI Approval Process	Implement AI-Driven Measurements To Eliminate Red Tape and Waste
3. Advance Patient-First Care, Data, and Accessibility	
Create Patient-Controlled Health Data Infrastructure	Launch an Interoperable, State-Based Health Data Infrastructure
4. Maximize Fiscal Responsibility for U.S. Healthcare	
Implement Next-Gen AI-Powered Fraud Detection Systems	Advance Comprehensive Cost-Saving Preventive Care Programs
5. Enhance U.S. Medical Talent for Today and Tomorrow	
Advance U.S. Healthcare Provider Mobility	Accelerate Training for AI-Empowered Healthcare Workers

Figure 1: Catalyzing Care: A Framework for a Healthier America - Goal, Pillars, & Actions

The moment for transformative action to advance U.S. healthcare that works is now. Through dynamic market-driven approaches, we can and will harness innovative technology while championing value-based healthcare outcomes and ensuring patient safety through 'radical transparency' in healthcare delivery systems.

By embracing patient-first care, data, and accessibility, implementing prudent fiscal practices, and mobilizing U.S. talent, we can achieve transformation through market-driven innovation.

This bold transformation will be achieved through the five pillars for Catalyzing Care: A Framework for a Healthier America that rally market-driven approaches – collectively with startups, educational institutions and other partners working alongside federal and state governments – to deliver U.S. healthcare that works for all Americans.

Source: https://files.elfsightcdn.com/eafe4a4d-3436-495d-b748-5bdce62d911d/a430b75e-8613-4c40-996f-e31cbb418c87/US-Healthcare-That-Works-Whitepaper.pdf

Trump Think Tank Resurrects International Drug Pricing Model to go After ‘Global Freeloading'

Zachary Brennan, *Endpoints News*, Mar 21, 2025 (excerpt)

President Donald Trump appears poised to bring back one of the drug pricing policies from his first term, as part of efforts to go after other countries “freeloading” on US pharma innovation.

A new report published Friday from a nonprofit think tank designed to promote Trump’s policy agenda, known as the America First Policy Institute, offers one of the first looks at the president’s wider plans around drug pricing.

While stressing what HHS Secretary Robert F. Kennedy Jr. has called an epidemic of chronic diseases, the report notes the need to accelerate the development of drugs to treat these diseases while ending “global freeloading.” It describes that as other countries paying significantly less than the US for prescription drugs, even as the US funds the vast majority of the world’s R&D.

This status quo “allows other wealthy countries to have their cake and eat it too — to get lifesaving drugs for their citizens without paying the necessary costs to develop them,” the report says.

Source: https://endpts.com/trump-think-tank-resurrects-international-drug-pricing-policy/

AFPI
AMERICA FIRST POLICY INSTITUTE

March 21, 2025

ISSUE BRIEF | Center for a Healthy America

Put Americans First by Ending Global Freeloading

Charlie Katebi

Patients in every country benefit when drug manufacturers develop new medications to treat and cure diseases. However, many wealthy countries enforce price-setting policies that undercompensate drug manufacturers that sell products to their citizens. These countries are potentially withholding billions of dollars from drug manufacturers, which could invest those dollars to develop lifesaving treatments or lower prices for American patients.

Policymakers should put patients first and end global freeloading off American drug innovation. They could use the regulatory authority available to CMS and USTR to encourage other countries to pay higher prices for prescription drugs. This would provide drug manufacturers with billions of dollars to develop new medications. In turn, patients in the United States and abroad would live longer and healthier lives due to these newly available drugs. Reducing freeloading abroad would also allow U.S. policymakers to lower American drug prices while ensuring sustained investment in pharmaceutical innovation and the development of lifesaving therapies.

No Patient Left Behind Response

https://www.nopatientleftbehind.org/protect-american-innovation

NPLB No Patient Left Behind

March 11, 2025

Catherine Gibson
Deputy Assistant US Trade Representative for Monitoring and Enforcement
600 17th Street NW
Washington, DC 20508

RE: *Request for Comments on Unfair Trade Practices and Reciprocal Trade Arrangements*
Docket Number: USTR-2025-0001

Dear Deputy Assistant USTR Gibson,

Thank you for the opportunity to provide comments regarding the US Trade Representative's (USTR) review of unfair trade practices and potential remedies in response to the America First Trade Policy Presidential Memorandum and the Reciprocal Trade and Tariffs Memorandum.

I am writing on behalf of *No Patient Left Behind* (NPLB), a coalition of biotech investors, innovators, researchers, physicians, and patient advocates committed to lowering patient out-of-pocket costs while preserving incentives for US biomedical innovation.

The Free-Riding Problem

We urge USTR to use its tariff and market access negotiating tools to ensure high-income OECD countries (e.g., the UK, France, Canada, and Australia) contribute equitably to biomedical innovation costs. These nations do not maintain true markets for medicines, as their governments impose price controls that undervalue the life-saving benefits of new treatments. USTR should use trade negotiations to ensure these countries pay their fair share, just as the Trump Administration successfully encouraged European nations to increase their defense spending to support global security.

Furthermore, wealthy foreign trade competitors use faulty and outdated cost-effectiveness analysis (CEA) formulas that fail to consider quantifiable patient and societal benefits of medicines, including increased workforce participation, reduced caregiver burdens, disease severity, and changes in patient population numbers over time. Unlike hospitals, which remain expensive, medicines eventually become affordable generics, yet these countries continue to undervalue them, resulting in a greater burden for US innovators and American consumers.[1]

Wealthy nations systematically undervalue novel American therapeutic innovations leading to reduced investment and delayed patient access to groundbreaking treatments. For example, because Australia's government health technology assessment (HTA) entity relies in part on outdated CEA formulas, Cystic Fibrosis (CF) patients there had to wait more than two years after regulatory approval to gain access to and coverage for Vertex's Trikafta.[2] This not only weakens global innovation but ultimately harms patients worldwide who rely on US biomedical leadership for new treatments and cures.

As highlighted by Bobby Jindal and Charlie Ketabi from the America First Policy Institute's Center for a Healthy America in *STAT News*, price controls in other wealthy countries "reduced drug sales by 77% in 2018 alone, amounting to a $254 billion shortfall. This practice allows these nations to benefit from American drug innovation while shirking the necessary investment required to develop new treatments."[3]

Ensuring Continued US Biomedical Innovation Leadership

It is important for USTR to recognize the critical role that the US market plays in sustaining global biomedical innovation. American investors fund new treatments because they rely on a fair valuation of medicines in the US market. If foreign price controls were imposed domestically, investment in biomedical R&D would plummet, endangering the nation's leadership in innovation.

The impact on US biomedical innovation leadership is not hypothetical. Please take a moment to watch this video from leading US biopharma specialist investors.[4] Some investors would lose interest in funding biomedical innovation and the US would develop fewer products if Canadian, European or Australian price controlled prices were imposed in the US. Private funders of biomedical R&D know those are far too low to justify their investments. Americans would lose out. And when there are fewer products, there's less therapeutic and generic price competition, which means US prices may go up.

Yet, other wealthy countries would still get the benefit of whatever innovation the American market supported on its own. That's because biopharma medicines will eventually go generic and be available at low cost and benefit anyone in the world who needs them. Americans would end up paying more and getting fewer medicines. Patients, which is to say, all of us, would lose. And that's not what anyone wants.

Rather than forcing US prices to align with artificially suppressed foreign prices, a more effective approach would be to require other wealthy nations to contribute more equitably to global biomedical advancements.

Recommendations

To address these disparities, we hope that USTR will pursue trade negotiations that leverage its market access and tariff negotiating authority to require high-income nations to:

- Encourage market pricing so our trade competitors more proportionally contribute to global R&D costs based on their economic capacity.
- Reform and update their health technology assessment methodologies to better reflect the value of new medicines by incorporating quantifiable patient and societal benefits.
- Ensure timely patient access to newly approved therapies.

These measures would promote more equitable contributions to biomedical innovation while preserving America's leadership in the biopharma sector.

We appreciate USTR's dedication to advancing fair trade policies that benefit American innovators and patients worldwide. We urge USTR to take strong action to address these unfair trade practices and ensure that all wealthy nations share in the cost of biomedical progress.

Please feel free to contact me should you require further information.

Thank you for your consideration.

Sincerely,

Peter Rubin
No Patient Left Behind

[1] The value of medicines https://www.nopatientleftbehind.org/value-of-medicines

[2] For Two Years, Australia Failed People With Cystic Fibrosis; It Can't Happen Again. https://www.realclearhealth.com/articles/2022/02/18/for_two_years_australia_failed_people_with_cystic_fibrosis_it_cant_happen_again_111317.html

[3] "Global freeloading: Americans shouldn't bear the brunt of drug development costs When other countries systematically underpay for drugs, everyone suffers" https://www.statnews.com/2025/03/05/global-freeloading-drug-manufacturers-pharmaceuticals-america-innovation/

[4] Protech American Innovation. www.nopatientleftbehind.org/protect-american-innovation

Key Counterpoints to AFPI Arguments

A very similar argument to that in the AFPI was made in early 2024 by Senator Bernie Sanders. Here is revision of the some of the points we made then.

1. The AFPI proposal would ask partner countries to voluntarily increase the prices that they pay for drugs.
2. This is completely unrealistic given that these countries have policies and budgets in place built around prices negotiated over time.
3. Further, these countries, in general, use a flawed cost-effectiveness framework to justify lower prices than those paid in the U.S. Ultimately, they may "free load" to some degree.
4. But the reality is that many drugs available in the U.S. are simply not available in those countries. Ultimately, patients are the loser. Over 100 approved drugs in the U.S., for example, are not available in Japan.
5. The U.S. has long made a choice to pay more for pharmaceutical products than other countries. Roughly 40% of total global pharma spend is made by the U.S. even though it has approximately 4% of the world's population.
6. This has been with full support of the government and the Congress. It's well recognized that the U.S. is subsidizing pharma spend – which has numerous positive externalities, including those for residents of other countries such as Canada and France who benefit from its largesse.
7. This is what it means to be a global leader. Similarly, the U.S. spends far more of its resources on national defense than other countries. The share of pharma spend between the U.S., France and Canada is nearly identical to that spent on national defense between the same countries.
8. There is a huge global dividend to pharma spending and R&D. Specifically, pharma innovation over the last three decades explains roughly a third of the total gain in life expectancy.[1]
9. Given that we have added roughly eleven years to the average human's life expectancy in the last thirty years, pharma spend can explain roughly four years of that.[2] That is about 30 billion person-years of life given current population levels. Far from being "outrageously expensive" to society, the pharma industry is providing great positive externalities to the world.

1 See Buxbaum JD, Chernew ME, Fendrick AM, Cutler DM. Contributions Of Public Health, Pharmaceuticals, And Other Medical Care To US Life Expectancy Changes, 1990-2015. Health Affairs 2020 Sep;39(9):1546-1556.
2 See https://ourworldindata.org/life-expectancy

Counterpoints to AFPI Arguments (continued)

10. Drug spend also has direct cost saving effects by reducing the need for other medical care and further creates other indirect benefits to society.[3]

11. Were the U.S. to magically reduce its spending per capita on pharma products to say that of Canada, there would be an immediate reduction in pharma sales of approximately $450 billion.

12. While pharma companies appear quite profitable, the reality is that the industry is marginal from an economic profit perspective if R&D spend is capitalized. The ratio of free cash flow (with R&D added back) divided by the sum of ten year lagged spend on R&D, CapEx and acquisitions is 13.5% for the top 1,050 public companies in pharma.

13. If one applies a capital charge of 10% (low given the rate environment), this industry is marginally profitable in an economic sense. Others also find that the pharma industry is only marginally economically profitable and big pharma has dramatically underperformed the S&P 500 in recent years.[4]

14. This is particularly true in the area of R&D spend. The ROI from pharma R&D spend (as highlighted later in this issue) is close to zero.[5] Large pharma is now spending over $6 billion for every NCE introduced to market.

15. There is nothing hypothetical about the effects of changing ROI on R&D spend. The last two years have seen long rates rise and capital formation in biopharma drop precipitously.

16. The consequences of reduced spend on pharma R&D would be profound for human life expectancy, system spend and human welfare.

17. Price controls in the pharma industry have had profound negative effects on medication access in other countries.[6]

3. See, for example, https://www.nopatientleftbehind.org/about/presentations and https://www.wsj.com/articles/the-folly-of-targeting-big-pharma-1449792625
4. See, for example, Manning and Subramaniam, Economics Profits in the Biopharmaceutical Industry," Intensity Research, 2022. (link)
5. See IQVIA Institute, Lifetime Trends in Biopharmaceutical Innovation, 2017 and Standish Fleming, "Why Pharma Risk Is Inherently Unpredictable And Why It Matters," *Forbes* Nov 6, 2018.
6. See, for example, https://www.forbes.com/sites/waynewinegarden/2019/10/18/price-controls-are-not-the-answer-to-expensive-drugs

In Praise of Big Pharma

Tevi Troy, *Commentary*, April 2025 (excerpt)

Watch a movie or a TV show these days and there is a good chance that you'll see a scheming pharmaceutical executive among the ranks of the villains. These white-collar masterminds dominate the category of America's pop-culture bad guys, often resorting to the most nefarious of means—hiring assassins, employing hit squads, destroying evidence, and subverting justice—all in the pursuit of profit. The biggest TV hit of the year is Matlock, in which Kathy Bates infiltrates a law firm to get the inside story on a pharma firm whose product killed her addict daughter.

The anti-pharma plot resonates because the plotline intersects so visibly with the real world. From the bully pulpit, Big Pharma is routinely denounced by politicians on both the left and the right. In the courts, pharma has become a lucrative target for trial lawyers. In the media, journalists and popular podcasters portray pharmaceutical companies as greedy capitalists looking to squeeze dollars out of patients desperate for meds that can make the difference between life and death. In state legislatures and in the halls of Congress, Big Pharma has become what Big Tobacco was in the 1980s and 1990s—a rapacious industry that works in its own interest and harms the general public.

The difference, however, is that tobacco kills people while pharma transforms lives—and people know it. Most of the advertising on television is for lifesaving, life-enhancing, and life-extending medications created by Big Pharma. From antibiotics to antidepressants to antihistamines to gastric-acid reducers, modern pharmaceutical products have been extending and improving lives for nearly a century.

There are a variety of sources for all this hostility, ranging from the organic to the nefarious. One problem for the pharmaceutical companies is that drugs have indeed gotten more expensive. As we reached the limits of discovery in the realm of small-molecule biochemical products—in other words, pills—we have entered a new realm of more complicated biologics. These are sophisticated, non-chemically synthesized products.

Biologics are harder to produce, harder to get approved, and harder to administer, since they have to be infused rather than swallowed—but they also have far more potential to create transformative therapies in the areas of cancer and autoimmune diseases. All these factors make the new products more costly. In addition, the Biden administration's Inflation Reduction Act imposed a new penalty that incentivizes companies to make more-expensive biologics rather than pills.

The industry even has trouble finding defenders. Most people I spoke to for this article took pains to clarify that they were not on the record. Web searches on this subject uncover reams of material assaulting the industry, denunciations that vastly outnumber any defenses that the companies or their allies can muster. And the attacks against defenders can get ugly. A friend of mine suffered a host of negative media attacks simply for asking a pharma executive to look at a draft of an article to check for factual errors. You had better believe that the atmosphere around the industry limits the number of industry defenders and makes those brave enough to try it exceedingly nervous.

Yet the constant assault against the pharmaceutical companies for trying to create new cures has got to be discouraging. At some point, we need to wonder whether these business are just going to say enough is enough and either go elsewhere or close down their operations in this country. Perhaps Americans would rethink things were that to happen, but by then it would be far too late to make up for the loss. As Tauzin, himself a cancer survivor because of pharmaceutical intervention, told me, "If we allow the hatred of the industry to continue, we are going to lose investment, and people are going to die."

Source: https://www.commentary.org/articles/tevi-troy/in-praise-of-big-pharma/

Zero-Toll Medicine

D.A. Wallach, Head of Time BioVentures, *Commentary*, April 2025 (excerpt)

The U.S. health insurance system is stupid, immoral, and infuriating. It is time to get rid of it altogether and replace it with an intelligent, modern, and efficient infrastructure befitting the American people and the 21st century. Incrementalism is not the answer, and solutions that amount to adding further fragmentation and complexity (including Medicare Advantage, ACOs, delegated managed care, and integrated managed care) ultimately obscure the need to burn it down and start afresh. I propose in this essay a novel model, "Zero-Toll Medicine," which leverages advances in AI and blockchain technology to deliver health insurance free of toll-taking intermediaries like private insurance companies and PBMs. This scheme aims to put patients in control of their own healthcare spending, eliminate vast amounts of administrative cost and complexity, and drive far more efficient market-based competitive pricing. It is rooted in libertarian and socialist idealism alike, exploiting the virtues of decentralized decision making and markets while realizing the civilized goal of healthcare as a fundamental right of American citizenship.

Why Do We Have Health Insurance?

Insurance exists primarily to pool risk. We do not know at birth who will require substantial medical care over his or her lifetime, but we can be certain that many of us will. And as the philosopher John Rawls argued, we should design our society such that we would be ok being born into any particular lot in life, since none of us chooses his or her circumstances at birth. Pooling our resources to guarantee basic medical care to everyone no matter where we're born or how our lives unfold should be uncontroversial given our enormous societal wealth.

Limits on this commitment must arise from the fact that medical care can be very costly, and so we are unlikely to agree as a nation to cover unlimited care for every individual without regard to how much longevity or happiness it might buy. Therefore, rationing or "managing" the amount of care is inevitable. Furthermore, we cannot be held hostage to medical care at any price, and so should desire that medicine exist within the market economy, subject to competitive forces that optimize supply via price signals.

These three goals: 1) risk pooling 2) rationing care and 3) competitive pricing, are in theory the functions of our existing insurance system. But it fails at all three.

1. It fails to pool risk efficiently because, unlike in other insurance markets, we (rightly) prohibit insurers from discriminating on the basis of pre-existing conditions, or pricing policies on the basis of individual risk (apart from generic characteristics of a patient like geographic location and age). In principle, if carriers had the ability to discriminate, they could generate profits from careful underwriting and risk prediction. But in our system, they effectively must cover any patient who subscribes. Furthermore, if we seek to maximally spread out costs, we should have the largest risk pool possible, one that includes everyone. Our current system, by contrast, splits the population into thousands of smaller risk pools, among them: employees of individual companies (self-insured employer plans), poor people in each state (Medicaid plans), retirees (Medicare), and so forth.

2. It fails to ration care ethically because this rationing is largely done at the insurance plan level. Pre-authorizations, claim denials, and benefit design are managed by plans, which amounts to their "playing doctor." This is not a job that insurers are qualified to do, and they do not do it well. Moreover, evidence-based medicine demands that a "standard of care" dictate what care is appropriate and medically necessary, and this standard should be universal vs. varying arbitrarily across different insurers.

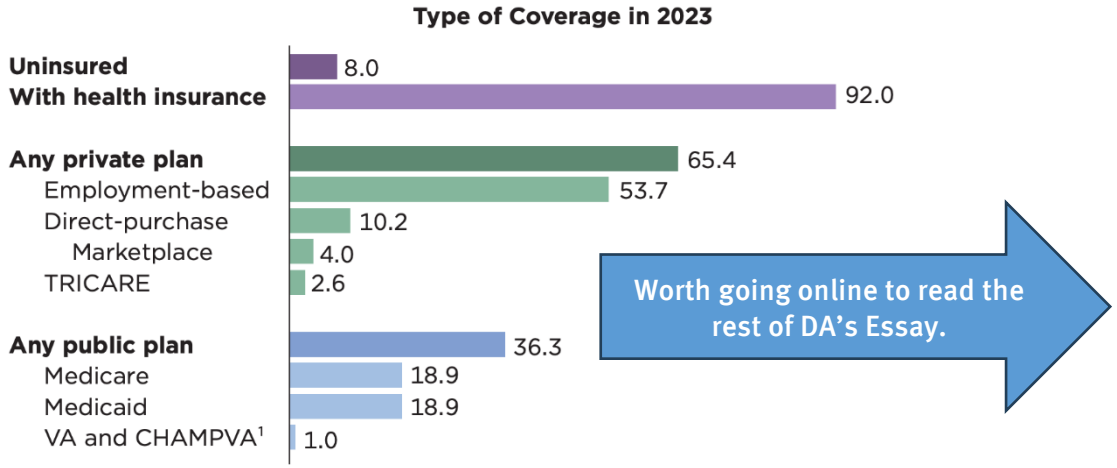
3. It fails to drive optimal competitive market pricing and supply because it aggregates both supply and demand into oligopolistic blocs and removes decision making power from the actual providers and users of care. On the demand side, each insurer effectively becomes a representative of tens of thousands of patients (and their employers, who hire plans and bear costs). On the supply side, large health systems and private-equity-financed provider roll ups are increasingly the counterparties in price negotiations. In other words, large insurance companies negotiate against large providers to set prices.

Source: https://dawallach.substack.com/p/zero-toll-medicine

Wallach Essay (Continued)

Subsidizing Subsidies

What I have described so far are failures of our employer-based private insurance system, which covers just over half of Americans. The other side of our system is public insurance, which covers 36% of the population in total. Among those publicly insured are 93% of those 65 and older (Medicare), 36% of children (Medicaid), and 16% of working-age adults (Medicaid). The public system is itself a patchwork of government and private entities. For example, Medicaid is run by the states, but outsources substantially to private insurance companies in what are known as MCO arrangements (managed care organizations). Similarly, Medicare is run by the federal government, but a majority of beneficiaries now choose Medicare Advantage plans, which are also outsourced plans run by private insurers. Even Traditional Medicare (the original plan that is managed by CMS and not outsourced) outsources its claims processing and assorted functions to 12 "MAC"s (Medicare Administrative Contractors), privately-owned and somewhat mysterious vendors that also engage in care rationing across Medicare patients (for advanced diagnostics, as one example).



Worth going online to read the rest of DA's Essay.

% of US Population Insured by Insurance Type. Source: U.S. Census Bureau, Current Population Survey, 2023 and 2024 Annual Social and Economic Supplements (CPS ASEC).

Radical Simplification

A smart and modern healthcare system would achieve the following goals:

1. Enable every American citizen to afford a satisfactory level of medical care
2. Ensure that medical care is evidence-based and transparent
3. Create robust competition among healthcare providers and pharmaceutical companies to win the business of patients, driving efficiency, patient experience, and innovation

Decentralized ledgers and smart contracts, technologies originated in the cryptocurrency industry, enable a new model of American healthcare capable of meeting these goals with a radical new open insurance and payments system, "Zero Toll Medicine" (ZTM). Here are the building blocks of this system:

1. A new, open blockchain protocol, ZTM, on which every US citizen and healthcare provider would have a wallet. This wallet would function as a bank account specifically for government-funded healthcare spending and receipts.
2. A minimal federal government health insurance agency, which could replace CMS. This "agency" would primarily comprise a computer codebase governing its interactions with the ZTM protocol and participants, but would inevitably require some number of staffers to manage activities in which human judgment is unavoidable.
3. A ZTM stablecoin pegged to the US Dollar.
4. A library of composable smart contracts enabling programmable payments in the stablecoin.
5. A computer-readable standard of care.

Source: https://www.commentary.org/articles/tevi-troy/in-praise-of-big-pharma/

Industry Update

NIH Budget Preserved in Most Recent Budget Bill

Jocelyn Kaiser and Sara Reardon, *Science*, Mar 21, 2025 (excerpt)

Biomedical research was mostly spared in the spending bill enacted on 15 March that keeps federal agencies funded for the rest of this fiscal year at the same levels as 2024. But the bill will mean major cuts for high-profile neuroscience and genomic medicine initiatives at the National Institutes of Health (NIH) and a massive research grants program at the Department of Defense (DOD).

The legislation, called a continuing resolution (CR), extends a current spending freeze through the fiscal year's end on 30 September. The law does not cut NIH's $47.4 billion base budget.

But it fails to make up for a drop in this year's funding from a separate pot of federal money, provided under the 2016 21st Century Cures Act, for two efforts: the Brain Research Through Advancing Innovative Neurotechnologies (BRAIN) Initiative and the All of Us genomic medicine project. Their total funding, which fell last year by more than one-third, shrinks further from $759 million to $479 million.

The bigger hit is to All of Us, an ambitious plan to recruit 1 million volunteers in the United States who agree to share their DNA and health records for precision medicine studies. Its budget this year is $158 million, a 71% drop compared with 2023.

The program, which is up to about 850,000 participants, is making what CEO Josh Denny called "difficult decisions" in December that will slow recruitment. That includes scrapping three buses that made recruiting trips to inner city communities and rural areas, said an NIH source familiar with the situation. Scores of enrollment centers run by health care providers will close and recruitment will be online only. In addition, in-person clinical assessments of participants could move to a digital format.

Most disappointing to some researchers is that a plan to recruit at least 100,000 children, which is so far up to just 350 participants, will slow to a crawl for now. "Part of what saddens me is that children will be left behind once again," says medical geneticist Wendy Chung of Boston Children's Hospital, who studies rare childhood genetic diseases.

Source: https://www.science.org/content/article/biomedical-research-takes-hits-u-s-budget-deal

J&J Joins Pharma Peers With $55B US Manufacturing Boost Following Trump's Tariff Threats

Annalee Armstrong, *Biospace*, Mar 21, 2025 (excerpt)

Johnson & Johnson follows Eli Lilly in spending billions on U.S. manufacturing after President Donald Trump threatened major tariffs on pharmaceutical products. Pfizer has also promised a similar commitment.

President Donald Trump's demand for U.S. manufacturing has brought around another Big Pharma. Johnson & Johnson followed in the footsteps of Eli Lilly Friday, announcing a massive $55 billion manufacturing and R&D investment over the next four years.

The healthcare giant will boost its U.S. investment by 25% compared to the previous four years, according to a its news release. The announcement coincides with the groundbreaking of a manufacturing site in North Carolina, CEO Joaquin Duato said in a statement.

The investment will also include three new manufacturing facilities and the expansion of existing sites for J&J's medicines and medtech business. No additional information was provided on the sites. J&J vowed to boost R&D infrastructure to find treatments for indications in oncology, neuroscience, immunology, cardiovascular disease, along with robotic surgery.

All in all, J&J's economic impact in the U.S. will now be an estimated $100 billion.

At the new Wilson, N.C., site, J&J will be building a 500,000-square-foot biologics manufacturing facility, which will provide additional capacity for treatments to tackle cancer and immune-mediated and neurological diseases, according to the release. The construction will support about 5,000 jobs, while 500 positions will be created to run the facility itself.

The massive investment follows a similar, albeit smaller, commitment from Lilly in the wake of political pressures from Trump to bring more manufacturing to the U.S. In February, Lilly announced an investment of $27 billion in U.S. manufacturing capacity at an event in Washington, D.C. that was attended by U.S. officials. The announcement was made days after Trump threatened a 25% tariff on pharmaceutical products if companies did not bring more manufacturing stateside.

Source: https://www.biospace.com/business/j-j-joins-pharma-peers-with-55b-us-manufacturing-boost-following-trumps-tariff-threats

Alnylam Jumps As A New Approval Sets Up Its Next Battle With Pfizer, BridgeBio

Allison Gatlin, *Investors Business Daily*, Mar 21, 2025 (excerpt)

Alnylam stock jumped Friday after the drugmaker won a second Food and Drug Administration approval for its drug, Amvuttra.

Amvuttra was already approved to treat patients with transthyretin amyloid polyneuropathy, a rare disease in which abnormal protein builds up on the nerves, causing systemic damage. Now, the FDA has signed off on it in patients with cardiomyopathy, a significantly bigger market.

Alnylam Pharmaceuticals (ALNY) will take on Pfizer's (PFE) Vyndaqel and BridgeBio Pharma's (BBIO) new Attruby. But, while Vyndaqel and Attruby are daily pills, Amvuttra is a shot given every six months.

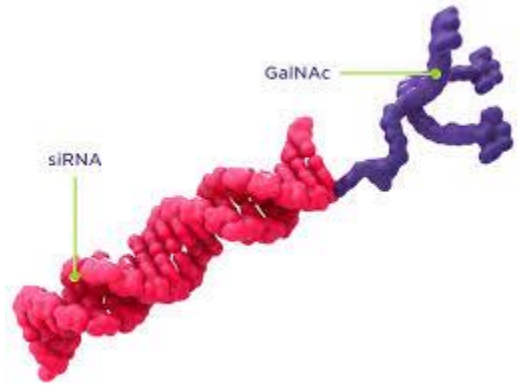
Amvuttra is the first in its class to enter the ATTR cardiomyopathy market. Vyndaqel and Attruby work by stabilizing the errant amyloid protein. Amvuttra, instead, works by silencing the gene that makes amyloid.

Analysts largely expected Amvuttra's approval, though had split view on the price. Alnylam said it would retain the $477,000 per year Amvuttra price for the cardiomyopathy launch.

Pfizer's Vyndaqel earned $5.5 billion in sales last year and only captured about 20% of the market. In 2030, analysts expect Vyndaqel to do $1.9 billion in sales — falling after a patent cliff — with Attruby bringing in $1.7 billion and Amvuttra in the lead at $5.1 billion.

Further, diagnosis rates are on the rise and Amvuttra appears favorable for younger and healthier cardiomyopathy patients, William Blair's Minter said. He rates Alnylam stock an outperform.

This "positions Amvuttra well for first-line usage in the milder and younger disease population that is reflective of the current disease population," he said.



Source: https://www.investors.com/news/technology/alnylam-stock-amvuttra-approval-cardiomyopathy-pfizer-bridgebio/

Bausch + Lomb CEO Brent Saunders on Innovation

Torben Danger Interview with Brent Saunders, *BCG*, Mar 19, 2025 (excerpt)

When you began your stint as CEO of Bausch + Lomb, what were the first areas you wanted to focus on?

I wanted to focus on top-line sales growth, operational excellence , and innovation. Top-line growth was about valuing those frontline salespeople, reestablishing that trusted relationship with our customers, and giving the salespeople all the tools necessary to do their job. Once you get that top line going, it's a lot easier to invest in other areas. Second, operational excellence. Can we make our products with the quality and efficiency that they deserve and the margins we expect? Lastly, can we invest in innovation with confidence, supplementing our R&D team to drive innovation and feel comfortable? Most innovation in our industry is a long-term bet and high risk. You need to de-risk with talented scientists. I feel really good about the progress we've made, although we still have a lot of work to do.

You've held many senior management positions in the biopharmaceutical industry. What are the leadership rules that you most consistently follow when facing today's challenges?

What distinguishes any successful biopharmaceutical or medtech company is products solving for real medical need, really helping patients. You do that through meaningful innovation. So the value of your R&D and all the processes that support innovation, whether it be business development and licensing or just internal processes around how to source and find great innovation, is paramount. The second is a focus on customers. It tunes your culture in to the real needs of the population you're trying to solve problems for. In addition, you look for ways to solve things like affordable medicine or reimbursement. You look for ways to help your physicians interact with you around medical education or scientific discovery in ways that are perhaps better, therefore giving your products a better chance to shine in that environment.

Your pharma strategy focuses on dry eye and retinal diseases. How does that fit into the overall growth story, and what are some of the early successes?

We have three different businesses: pharma, vision care, and surgical. While all three have slightly different strategies, they all focus on being the best eye health company. For example, in our pharma business, we wanted to be a leader in dry eye. So one of the first things I did was acquire the drug XIIDRA® from Novartis. That way, when our own dry eye drug was approved and launched, we would have the two best assets in that class. We've also invested in R&D talent to expand our retina capabilities, and we've focused early business development and licensing around retina opportunities. The goal is, in three to five years, to start really talking about solving some unmet needs for patients.

Brent Saunders
CEO, Bausch + Lomb

Source: https://www.bcg.com/publications/2025/leading-eye-health-company-explores-innovation-and-customer-centricity

Anti-Amyloid Drug Shows Potential to Delay Alzheimer's

***Inside Precision Medicine*, Mar 21, 2025 (excerpt)**

A new clinical trial led by Washington University School of Medicine suggests that early intervention with an anti-amyloid drug could delay or even prevent Alzheimer's-related dementia. The study, published in The Lancet Neurology, focused on individuals with rare genetic mutations that cause early-onset Alzheimer's disease, providing compelling evidence that removing amyloid plaques from the brain well before symptoms appear may significantly delay cognitive decline.

The study followed 73 participants who inherited genetic mutations that virtually guarantee the development of Alzheimer's disease in their 30s, 40s, or 50s. Among a subgroup of 22 participants who had no cognitive symptoms at the start and received the experimental drug for an average of eight years, the risk of developing symptoms was cut from nearly 100% to about 50%.

"Everyone in this study was destined to develop Alzheimer's disease, and some of them haven't yet," said senior author Randall J. Bateman, MD, study director and Knight Distinguished Professor of Neurology at WashU Medicine. "We don't yet know how long they will remain symptom-free—maybe a few years or maybe decades."

This finding reinforces the amyloid hypothesis, which suggests that the accumulation of amyloid plaques in the brain is the first step toward the condition. By targeting amyloid years before symptoms emerge, researchers hope to slow or halt the progression of the disease.

Participants were originally part of DIAN-TU-001, the world's first Alzheimer's prevention trial. When the trial ended in 2020, researchers reported that gantenerumab, an anti-amyloid drug developed by Roche/Genentech, effectively lowered amyloid levels but had unclear cognitive benefits. To gather more data, trial leaders extended the study, treating all participants with gantenerumab regardless of their previous treatment status.

Although Roche/Genentech halted gantenerumab's development in 2022 due to disappointing results in a broader trial, the extended study showed that long-term early treatment had a meaningful impact on cognitive decline. "This study provides the strongest evidence to date that removing amyloid plaques years before symptoms arise can delay the onset of Alzheimer's," Bateman explained. "While we still need confirmation from larger studies, these results suggest early intervention could change the course of the disease."

While this trial focused on genetic early-onset Alzheimer's, its findings may have broader implications. Both early-onset and late-onset Alzheimer's follow similar amyloid-driven pathways, meaning future trials could determine whether the same preventive approach could benefit millions at risk for late-onset Alzheimer's. "I'm highly optimistic," Bateman said. "One day soon, we may be able to delay or even prevent Alzheimer's disease for millions of people."

Source: https://www.insideprecisionmedicine.com/topics/precision-medicine/anti-amyloid-drug-shows-potential-to-delay-alzheimers-symptoms/

Fibrosis: Cross-organ Biology and Pathways to Development of Innovative Drugs

Rieder, F., Nagy, L.E., Maher, T.M. et al., *Nat Rev Drug Discovery*, Mar 18, 2025 (excerpt).

Fibrosis is a pathophysiological mechanism involved in chronic and progressive diseases that results in excessive tissue scarring. Diseases associated with fibrosis include metabolic dysfunction-associated steatohepatitis (MASH), inflammatory bowel diseases (IBDs), chronic kidney disease (CKD), idiopathic pulmonary fibrosis (IPF) and systemic sclerosis (SSc), which are collectively responsible for substantial morbidity and mortality. Although a few drugs with direct antifibrotic activity are approved for pulmonary fibrosis and considerable progress has been made in the understanding of mechanisms of fibrosis, translation of this knowledge into effective therapies continues to be limited and challenging. With the aim of assisting developers of novel antifibrotic drugs, this Review integrates viewpoints of biologists and physician-scientists on core pathways involved in fibrosis across organs, as well as on specific characteristics and approaches to assess therapeutic interventions for fibrotic diseases of the lung, gut, kidney, skin and liver. This discussion is used as a basis to propose strategies to improve the translation of potential antifibrotic therapies.

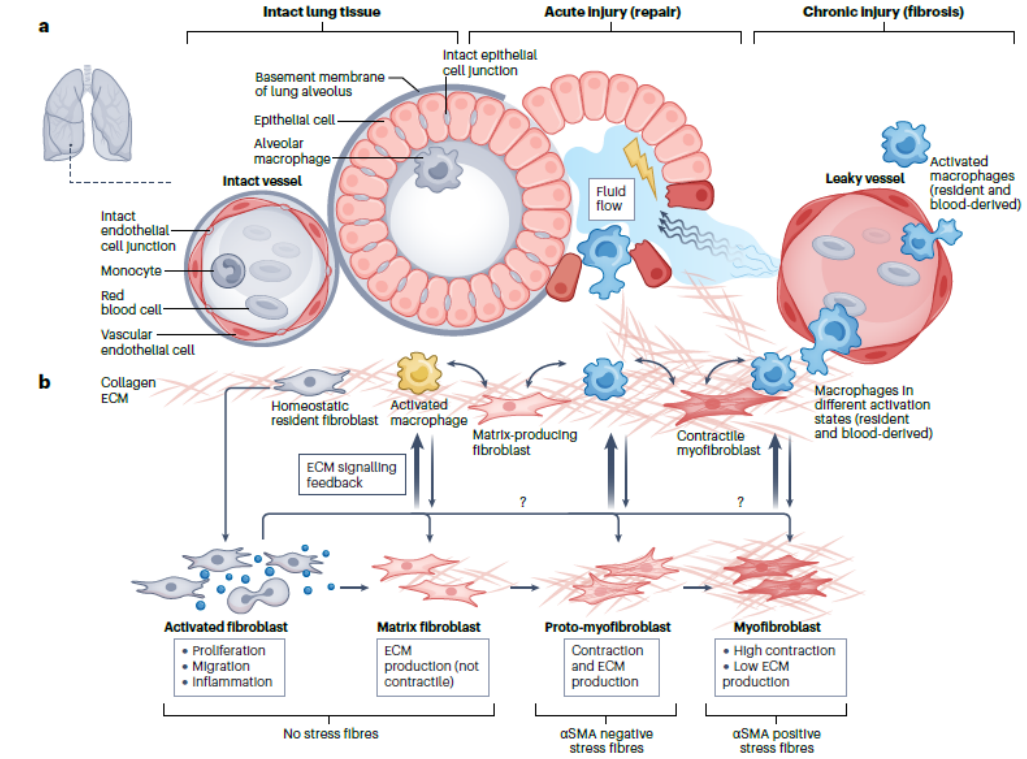


Fig. 1 | Initiation of fibrosis. a, Onset of fibrosis upon epithelial injury. Both normal and fibrotic tissue repair typically start with an injury to the epithelial lining of organs, here exemplified by lung alveolar epithelium. Injury to epithelial cells (indicated by the lightning symbol) – for example, owing to genetic polymorphisms, autoimmune disease or exposure to environmental toxins – compromises tissue architecture and barrier function, which results in local mechanical stresses that arise from enhanced fluid flow and cell strain. Epithelial cell-derived injury signals activate local and circulating monocytes and/or macrophages (centre of the figure) and fibroblasts (left) into various repair phenotypes. Persistent crosstalk between such activated cells (curved arrows) can result in the formation of profibrotic niches that drive the fibrotic process. **b**, Fibroblastic cell activation states and functions. Mesenchymal cells with various homeostatic functions and locations in normal tissue are activated by tissue injury to contribute to acute repair by proliferating, migrating into the injury site and performing basic inflammatory functions. Either directly or by passing over these initial activation states (it is not currently clear which), activated matrix fibroblasts produce collagen extracellular matrix (ECM) to restore lost tissue architecture. The low traction forces of migrating fibroblasts lead to collagen fibre alignment and enhanced mechanical resistance of the scar ECM, resulting in the formation of actomyosin bundles. Initially, these so-called stress fibres are composed of cytoplasmic β- and γ-actins in contractile proto-myofibroblasts that further contribute to ECM remodelling and stiffening. With increasing ECM stiffness, proto-myofibroblast stress fibres progressively incorporate neoexpressed α-smooth muscle actin (αSMA), which confers even higher contractile activity to overcome higher ECM stiffness.

Source: https://www.nature.com/articles/s41573-025-01158-9

Matrix-Producing Neutrophils Populate and Shield the Skin

Vicanolo T, et al., *Nature*, March 19, 2025

Defence from environmental threats is provided by physical barriers that confer mechanical protection and prevent the entry of microorganisms.

If microorganisms overcome those barriers, however, innate immune cells use toxic chemicals to kill the invading cells.

Here we examine immune diversity across tissues and identify a population of neutrophils in the skin that expresses a broad repertoire of proteins and enzymes needed to build the extracellular matrix. In the naive skin, these matrix-producing neutrophils contribute to the composition and structure of the extracellular matrix, reinforce its mechanical properties and promote barrier function. After injury, these neutrophils build ‘rings’ of matrix around wounds, which shield against foreign molecules and bacteria. This structural program relies on TGFβ signalling; disabling the TGFβ receptor in neutrophils impaired ring formation around wounds and facilitated bacterial invasion.

We infer that the innate immune system has evolved diverse strategies for defence, including one that physically shields the host from the outside world.

Source: https://www.nature.com/articles/s41586-025-08741-5

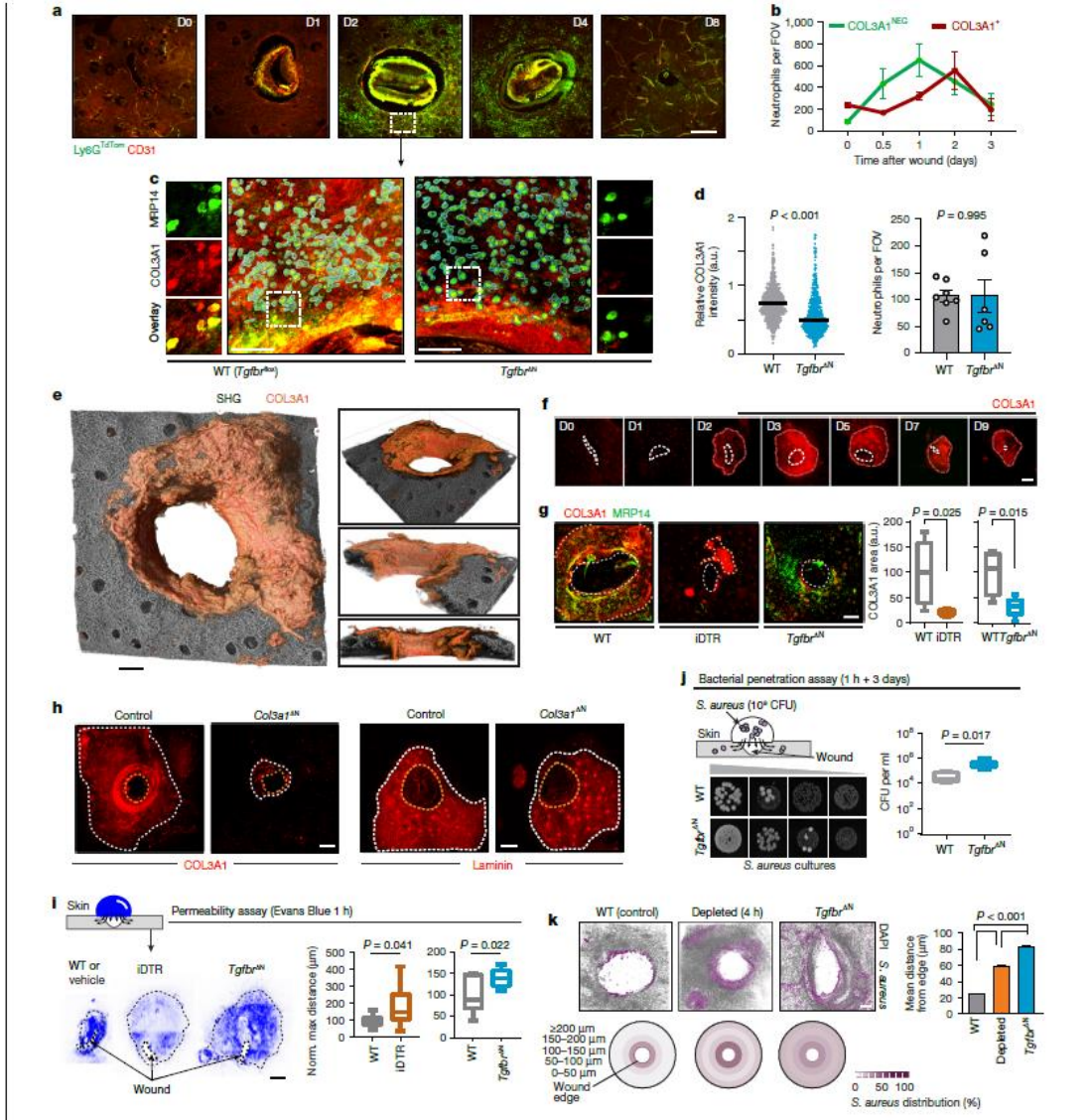


Fig. 4 | Neutrophils shield skin wounds by building matrix-rich rings. **a**, Kinetics of neutrophil recruitment to wounds in Ly6G^{Tomato} mice. Scale bar, 150 µm. **b**, Quantification of COL3A1^{NEG} and COL3A1^{+} neutrophils at day (D) 0 ($n = 9$), D0.5 ($n = 4$), D1 ($n = 3$), D2 ($n = 3$) and D3 ($n = 3$). Data are mean ± s.e.m. FOV, field of view. **c**, Multiphoton imaging of neutrophils around D2 wounds in *Tgfbr*^{flox} mice ($n = 6$) and *Tgfbr*$^{\Delta N}$ littermates ($n = 4$). Scale bars, 50 µm. **d**, COL3A1 signal intensity (748 cells from six mice for *Tgfbr*^{flox}; 640 cells from four mice for *Tgfbr*$^{\Delta N}$) and number of neutrophils (7 images for *Tgfbr*^{flox} and 6 for *Tgfbr*$^{\Delta N}$ mice). Bars show mean ± s.e.m.; a.u, arbitrary units. **e**, Three-dimensional reconstruction of a collagen ring in a D3 wound (Supplementary Video 3). Scale bar, 50 µm. **f**, Kinetics of COL3A1^{+} rings. Scale bar, 200 µm. **g**, Ring areas in neutropenic iDTR ($n = 5$ wounds, 3 mice) and *Tgfbr*$^{\Delta N}$ ($n = 5$ wounds, 3 mice) mice at D3, and their respective Cre^{NEG} ($n = 6$ wounds, 3 mice) and floxed ($n = 4$ wounds, 3 mice) littermates. Scale bar, 200 µm. **h**, COL3A1 and laminin deposits in D3 rings (dashed lines) from *Col3a1*$^{\Delta N}$ ($n = 5$) and Cre^{NEG} littermates ($n = 3$). Areas are quantified in Extended Data Fig. 10d. Scale bars, 200 µm. **I**, Permeability assay and images showing dye diffusion (dotted lines) in wounds from floxed littermate controls ($n = 10$), iDTR neutropenic mice ($n = 10$) and *Tgfbr*$^{\Delta N}$ mice ($n = 10$). Scale bar, 200 µm. **J**, Penetration of bacteria (*Staphylococcus aureus*) into wounded skin of *Tgfbr*$^{flox/flox}$ littermate controls ($n = 7$) and *Tgfbr*$^{\Delta N}$ mice ($n = 6$), scored as colony-forming units (CFU) three days after exposure (images at bottom). **k**, Top, spatial distribution of *S. aureus* 4 h after exposure to the wound. Scale bar, 100 µm. Bottom, distance distribution of individual bacteria to the wound edge. Right, mean distance values ± s.e.m. Data are from three wild-type, three neutropenic (anti-Ly6G) and seven *Tgfbr*$^{\Delta N}$ mice. Data were compared using two-sided unpaired Student’s *t*-test (**d**,**g**,**I**,**J**) or one-way ANOVA with Tukey’s multiple comparison test (**k**). All box plots show median ± interquartile range; whiskers show the range from minimum to maximum.

Disclosure

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