Biopharma Market Update

Feb 10, 2025

STIFEL | Healthcare

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Petri dishes are named after German physician Julius Petri (assistant to Robert Koch). In the late 1880's Petri developed a set of nesting glass plates that created an ideal environment for growing microorganisms. The deep, flat dish filled with a nutrient-rich gelatin provided a place for growth.

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September 11, 2023 (US Health System)
September 5, 2023 (FTC, IRA, Depression)
August 21, 2023 (Covid, China)
July 7, 2023 (Biotech market review – H1 '23)
July 1, 2023 (Obesity drugs)
June 19, 2023 (Generative AI)
June 12, 2023 (IRA, State of Industry)

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Macro Update

Inflation Fears Spike in February as Tariff Worries Hit Consumer Sentiment

***Jeff Cox*, CNBC, Feb 7, 2025 (excerpt)**

Consumers grew **dramatically more worried about near-term inflation** as President Donald Trump pushed aggressive tariffs against major U.S. trading partners, a closely watched survey showed Friday.

The University of Michigan consumer survey for February showed that respondents expect the inflation rate a year from now to be 4.3%, a 1 percentage point jump from January and the highest level since November 2023.

Though Trump postponed tariffs against Canada and Mexico, the looming threat of price pass-throughs to consumers shook sentiment. China has levied retaliatory tariffs following Trump's move. The survey window ran from Jan. 21, the day after Trump took office, to Feb. 3.

"Many consumers appear worried that high inflation will return within the next year," said Joanne Hsu, the survey's director. "This is only the fifth time in 14 years we have seen such a large one-month rise (one percentage point or more) in year-ahead inflation expectations."

Longer-run expectations weren't hit as much, with the five-year outlook drifting up to 3.3%, a 0.1 percentage point gain.

Worries over inflation dovetailed with lower optimism overall, as the headline index fell to 67.8, a one-month drop of 4.6% and an 11.8% move lower from the same month a year ago. Economists surveyed by Dow Jones had been looking for a reading of 71.3.

The survey sometimes is influenced by shifting political winds. However, Hsu noted that declining sentiment was "pervasive, with Republicans, Independents, and Democrats all posting sentiment declines from January, along with consumers across age and wealth groups."

Stocks turned lower after the report, with the Dow Jones Industrial Average initially off nearly 300 points.

We are now entering the fourth week of the Trump presidency.

We have seen visible theatrics regarding tariffs.

It's not at all clear how severe tariffs will end up being.

However, consumer expectations in the economy have dramatically shifted.

In general, this is not a *good* thing. Inflationary expectations can become self-sustaining.

Source: https://www.cnbc.com/2025/02/07/consumer-inflation-fears-spike-in-february-as-tariff-worries-hit-sentiment.html

US Job Growth, Rising Inflation Views Leave Room for Fed to Hold Rates Steady

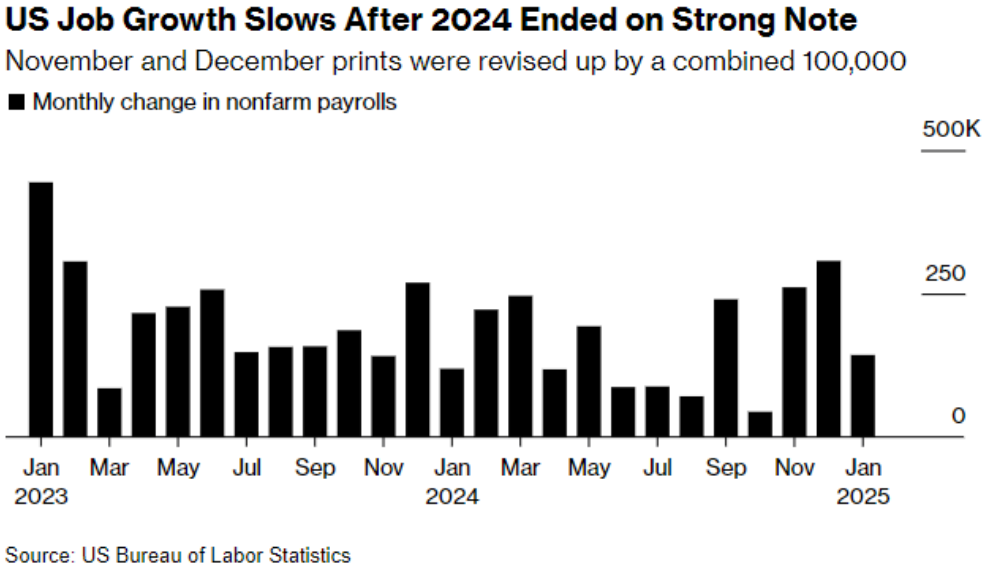
Augusta Saraiva, *Bloomberg*, Feb 7, 2025 (excerpt)

Slowing but healthy US job growth, combined with rising inflation expectations, supports the Federal Reserve's inclination to keep interest rates on hold for the foreseeable future.

Nonfarm payrolls moderated last month, unemployment fell, and annual government revisions now show job gains were softer but still solid in 2024, according to a Bureau of Labor Statistics report out Friday. Separate data from the University of Michigan showed consumers expect prices to rise much faster in the year ahead as President Donald Trump pushes forward with tariffs.

The reports illustrate a moderating yet still-strong labor market that continues to fuel the economy, while proposed policies from the Trump administration risk reigniting inflationary pressures. That helps explain why Fed officials have signaled they aren't in a hurry to lower borrowing costs further after a full percentage point of interest-rate cuts last year.

"What we're seeing in the data is they don't have to do anything right now," said Sarah House, a senior economist at Wells Fargo & Co. "Why would the Fed move at this point, especially when you have a lot of potential policy changes that you don't know exactly know what the direction or what the magnitude is going to be?"



Payrolls increased by 143,000 last month after upward revisions to the prior two months, according to BLS. Other revisions only carried out once a year weren't as severe as once thought — job gains averaged 166,000 a month last year, a slowdown from the initially reported 186,000 pace.

Source: https://www.bloomberg.com/news/articles/2025-02-07/us-added-143-000-jobs-in-january-after-2024-downward-revision

They Still Want ‘One Big, Beautiful Bill.’ They’re Nowhere Close

Benjamin Guggenheim and Meredith Lee Hill, *Politico*, Feb 7, 2025 (excerpt)

House Republicans are still far from finalizing several key details of a budget blueprint that Speaker Mike Johnson is pledging to advance in the House next week, with negotiations expected to continue through the weekend as the Senate races ahead with its own plans.

While House GOP leaders trumpeted tremendous progress coming out of a White House meeting with President Donald Trump on Thursday, key holdouts on Trump’s sweeping agenda of tax cuts, border security and energy initiatives indicated Friday that they remained unconvinced about the level of spending cuts in the bill.

Separately, Republican tax writers continue to struggle with the ballooning costs of Trump’s wishlist, which includes not only an extension of his 2017 tax cut package, but also new income tax exemptions for tips, overtime earnings and Social Security benefits. Meanwhile, Senate Budget Chair Lindsey Graham released a plan Friday that would get border and energy policies out the door first and save the thorny tax questions for later. That is directly at odds with House leadership plans to roll everything into a single bill.

House Republican hard-liners continued to push for deeper spending cuts. One prominent budget hawk complained that several key lawmakers were cut out of the White House meeting.

Leadership “failed to talk to us,” said Rep. Tim Burchett (R-Tenn).

“They go to the White House and they take all the people that are going to be for it, and there’s four of us that are pretty consistent, and we’ve let our views be known,” said Burchett, naming Reps. Andy Biggs (R-Ariz.), Victoria Spartz (R-Ind.) and Thomas Massie (R-K.y.) as the other critical holdouts.

Johnson, who had previously said Republicans would release a plan Friday, will now work through the weekend with other leaders to try to finalize an agreement. Senior Republicans aren’t expecting any final details until Monday — adding another delay to the speaker’s ambitious timeline.

Source: https://www.politico.com/news/2025/02/07/house-gop-leaders-scramble-to-extinguish-tax-cut-fires-00203092

U.S. Treasury Secretary Bessent Focused on Lowering Long Bond Yields

By Davide Barbuscia and Saeed Azhar, *Reuters*, Feb 6, 2025 (excerpt)

NEW YORK, Feb 6 (Reuters) - U.S. Treasury Secretary Scott Bessent's pledge to contain yields on 10-year Treasury notes met some skepticism in the bond market on Thursday, as inflationary pressures and expectations of a widening federal deficit threaten to outweigh efforts to curb borrowing costs.

Bessent said in an interview with Fox Business on Wednesday that while President Donald Trump wants lower interest rates, he will not ask the Federal Reserve to cut rates, and that he and the president were intently focused on the 10-year Treasury yield. He added that lower energy prices will help contain price pressures, while spending cuts will improve the fiscal outlook.

Benchmark 10-year Treasury yields have a direct impact on mortgage and credit card rates as well as consumer loans, while the Fed's short-term interest rate impacts money markets and, only indirectly, borrowing costs.

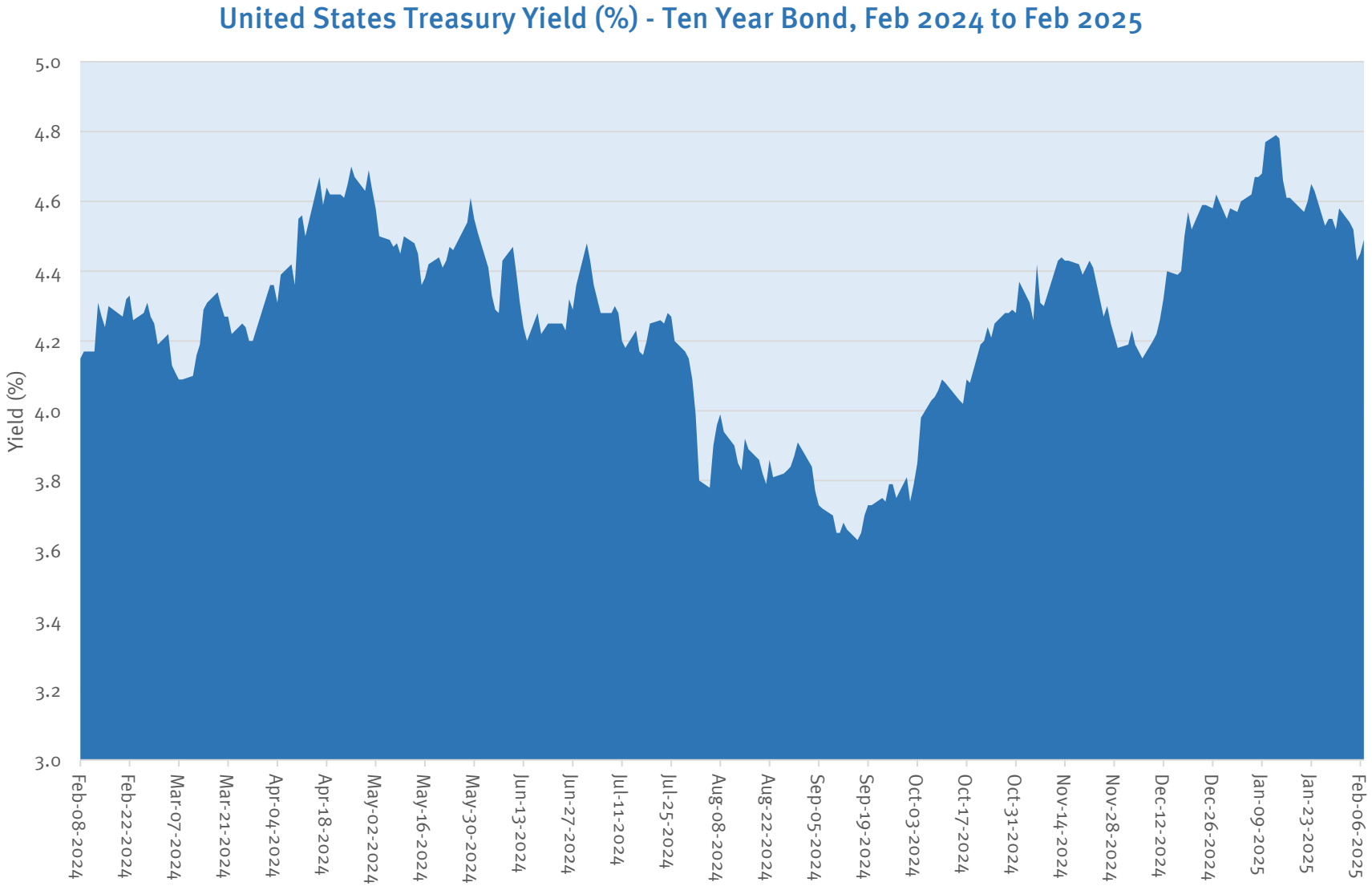
But bond investors and analysts remained somewhat unconvinced by Bessent's comments, as Trump's trade and fiscal policies are expected to push long-term Treasury yields higher, despite lower energy prices and government spending cuts.

"The bigger issue in the inflation complex is service-sector inflation, and the stickiness of inflation generally in the past number of months," said Padhraic Garvey, regional head of research for the Americas at ING. "The tariff agenda can only place upward pressure on prices, and, in fact, (is) likely to prove more impactful than the energy price containment plan," he added.

The yield on 10-year Treasury notes, last at 4.43%, hit a seven-week low on Wednesday due to factors including signs of a slowing economy, as well as some safe-haven buying due to geopolitical uncertainty and guidance from the Treasury Department this week that assuaged market concerns, opens new tab about imminent increases in long-term government debt issuance.

Source: https://www.reuters.com/markets/us/us-bond-market-lukewarm-bessents-10-year-yield-pledge-2025-02-06/

U.S. Treasury Bond Yields Starting to Creep Down



10-year US Treasury yields started to come down last two weeks as it becomes clear that the Trump Administration is serious about control of fiscal deficits.

In total the yield has fallen by 30 basis points since Jan 12th. Not a minor move as these things go. We see this as a definite positive for biotech.

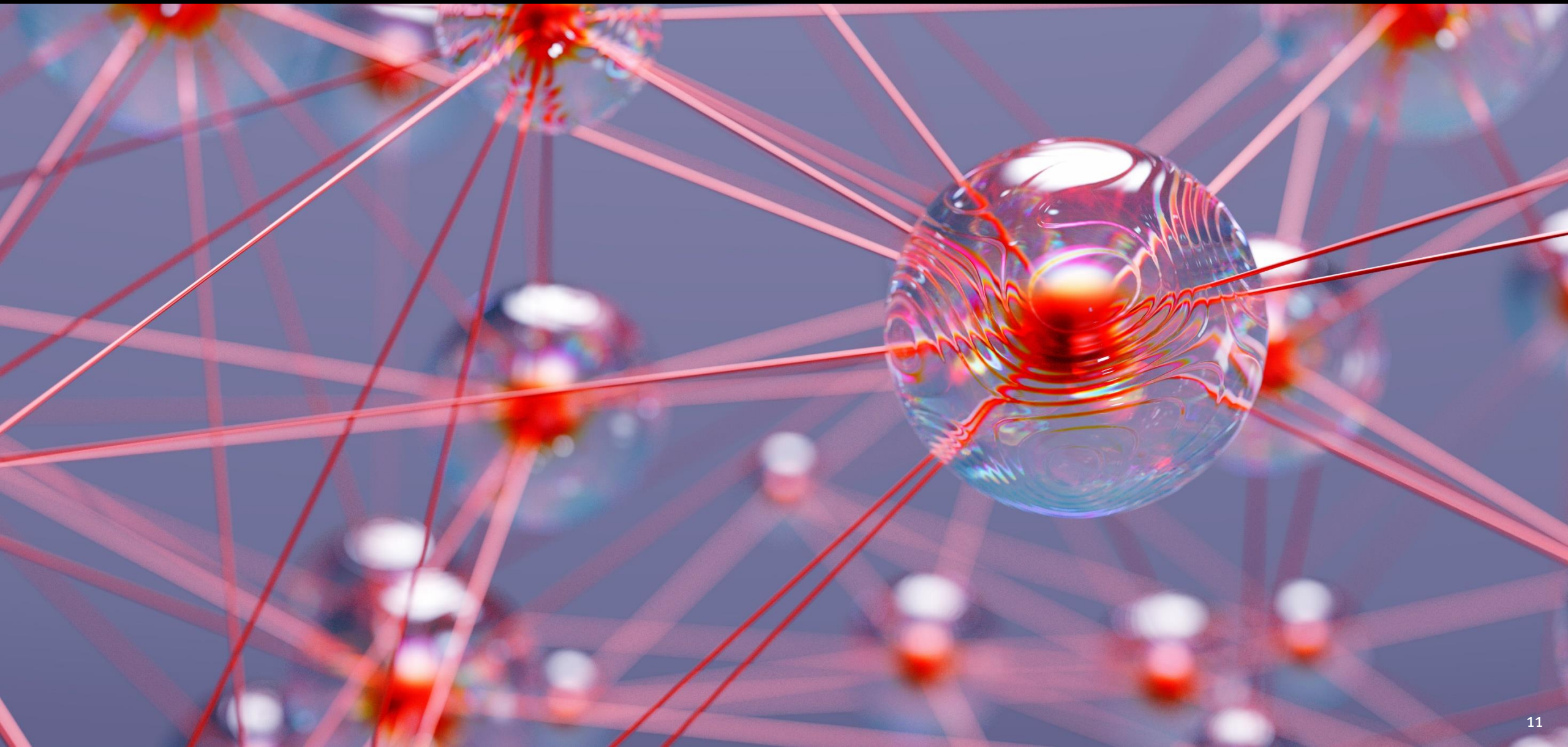
While tariffs have potential to be inflationary, they also directly deposit cash into government coffers with attendant benefits on the deficit.

Nonetheless, rates remain high by recent standards. The Fed continues to be slow in lowering rates.

This week's CPI readout will be an important one as it will help to influence Fed direction in the coming months.

Source: S&P Capital IQ

Biopharma Market Update



Biotech Gloom is Starting to Lift

The overall gloom in public biotech market sentiment has improved since mid-January.

While we continue to hear concerns about inflation and Treasury rates as a headwind on biotech market performance, investors increasingly acknowledge the abundance of bargains in the market.

If there are changes in mood emerging, it is from an increasing understanding that differentiation of assets is important. Just having a good late-stage dataset may not be enough.

There is also increasing understanding that we might not necessarily be in an environment where M&A takeouts alone will drive performance.

Rather, investors understand that another way to perform well is to invest in a company that performs well commercially. As we will discuss later, there is increasing recognition that product differentiation and commercial organization structure has a lot to do with how well biotech's perform when they transition to the commercial stage.

There are several great recent examples of excellence in launch performance. The adage that one should "short the launch" of any biotech is starting to come under pressure as we are seeing launches do well.

While we are nowhere near a biotech boom, we are seeing dark biotech skies lighten up a bit in recent weeks.

Investors Mixed on Market Direction

We had the occasion to attend Stifel's Winter biotech conference last week in Park City Utah. The event was well attended by leading buysiders and we had the chance to speak with a couple of dozen groups on their thoughts on the market.

What was striking to us is that investors are very mixed right now. While sentiment was uniformly negative a month ago– we heard quite a bit of positive chatter from investors and a view that the market might be heading up from here. Rather than try to synthesize all of this, we can simply share some of the comments made.

Negative comments: "There's no way I would put my PA into the XBI right now. Would you?"

"The China thing is a big problem. I see more downside and less upside than last year."

"The generalists are gone from our market and are clearly not coming back anytime soon. I don't see how the market performs well in 2025 without them."

More Bullish Thoughts

Others were more **positive** saying things like:

“This time last year – everyone said the market would go up. It didn’t. Now, everyone is saying the market isn’t going up. We’ll play contrarian. We are going long the market because conditions for a bull rally are quite strong.”

“We’ve done well in recent years but tend to avoid the stocks that everyone else is piling in to. We’re avoiding privates. We’re avoiding the stocks that our fellow specialists love. Instead, we are investing heavily in ex-US biopharma stories and are combing through smaller cap names for bargains and finding them.”

“There are so many great stories right now where the price is right. I see this as a market where stock picking is going to make money. That’s what we’re doing.”

“This is clearly a bigger year for M&A. This is going to be good for us.”

“After last week, the chances that RFK becomes head of HHS is over 90%. I wasn’t so sure what he’d mean for the market but after watching his confirmation testimony, we are a lot more bullish on what the Trump Administration is going to mean for biotech. We like the set up for biotech in 2025.”

Navigating Amidst Uncertainty

Overall, sentiment is **split** in this market. The topic of sentiment came up on last Friday's (Feb 7) Biotech Hangout. We argued that sentiment has shifted from a "2" out of ten to a "4". Another commentator said, ok, "how about from a 1 to a 3". Yet another said, "more like a "2 to a 3". Whatever the case, while sentiment is starting to improve it clearly has a long way to go. There is no "FOMO" driving the market presently.*

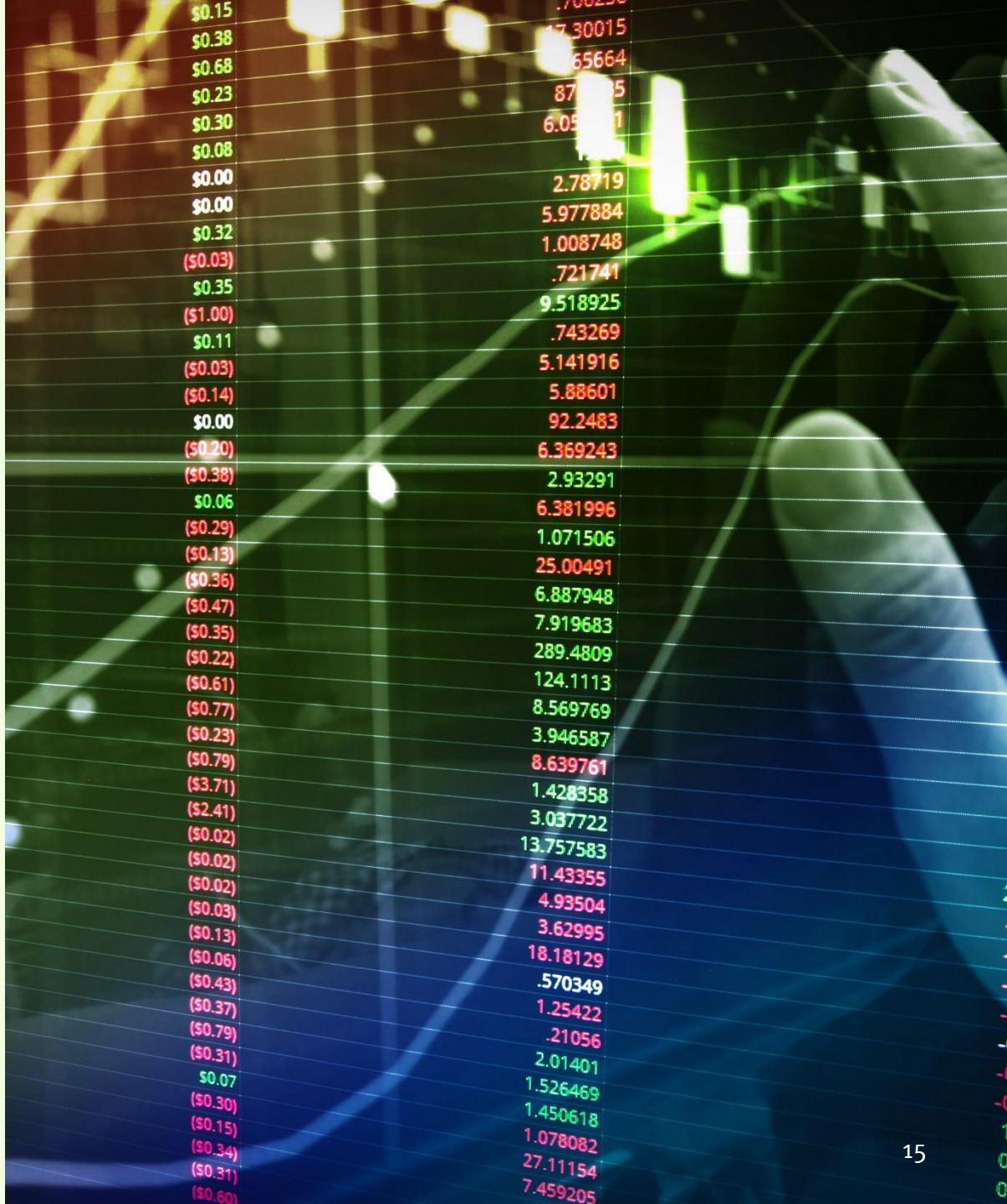
The political backdrop for the pharma sector is not terribly clear right now. How we get greater generalist participation also isn't particularly clear. Many LP's are discouraged which has been driving outflows.

However, there are positives – including growing need for medicines amidst long-term economic expansion, the prospect of a restructure of the IRA, a slowdown in AI market dynamics, an improving rate environment and an improving M&A environment.

What we heard on the ski slopes is that most investors are jumping into the market right now and playing their picks as well as they can. We agree that it is times like this that are likely to be the ones where optimism wins.

Obviously, time will tell.

* Fear of Missing Out



The XBI Closed at 91.2 Last Friday (Feb 7), Down 1.5% for the Week

The XBI lost ground last week as Neurocrine guided to soft INGREZZA® growth. Neurocrine is the single most influential member of the XBI. The XBI is up 1.3% so far this year.

Biotech Stocks Fell Last Week

Return: Feb 1 to Feb 7, 2025

Nasdaq Biotech Index: -0.8%
Arca XBI ETF: -1.5%
Stifel Global Biotech EV (adjusted): -1%*
S&P 500: -0.2%

Return: Dec 31, 2024 to Feb 7, 2025 (YTD)

Nasdaq Biotech Index: +4.3%
Arca XBI ETF: +1.3%
Stifel Global Biotech EV (adjusted): -1.1%*
S&P 500: +2.5%

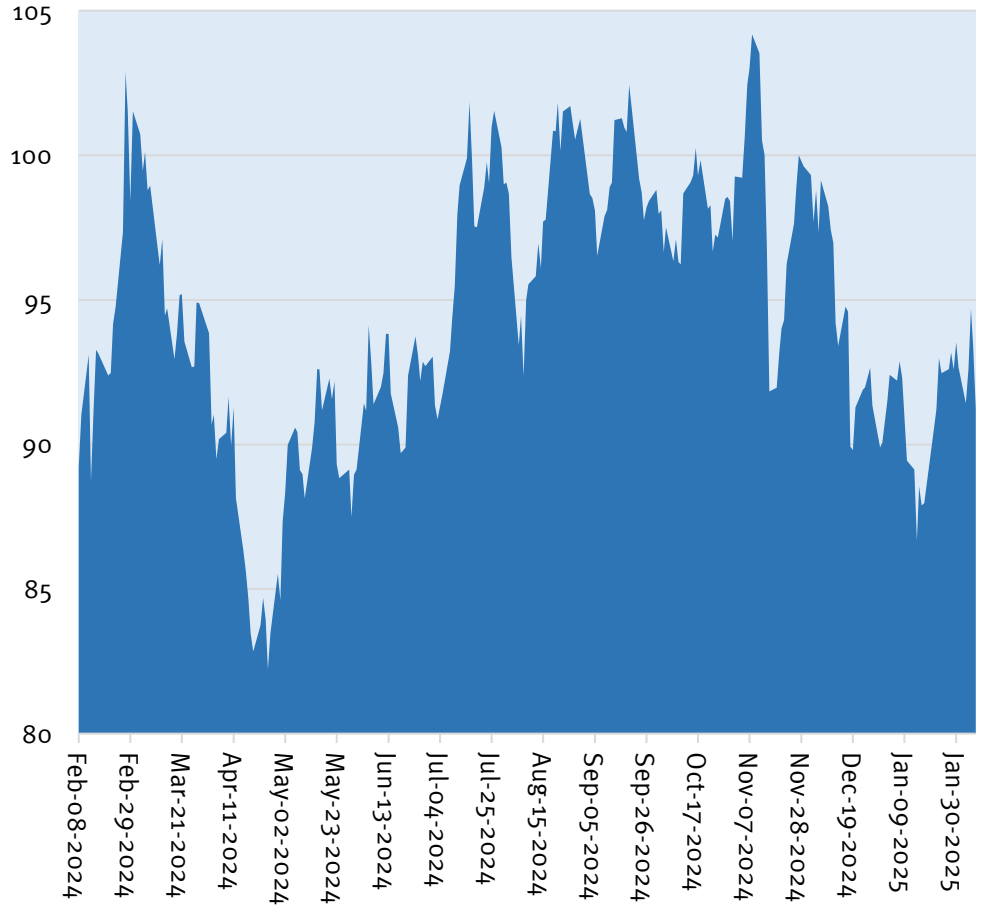
VIX Up

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 7, 2025: 16.5%

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 7, 2025: 4.4%

XBI, Feb 8. 2024 to Feb 7, 2025

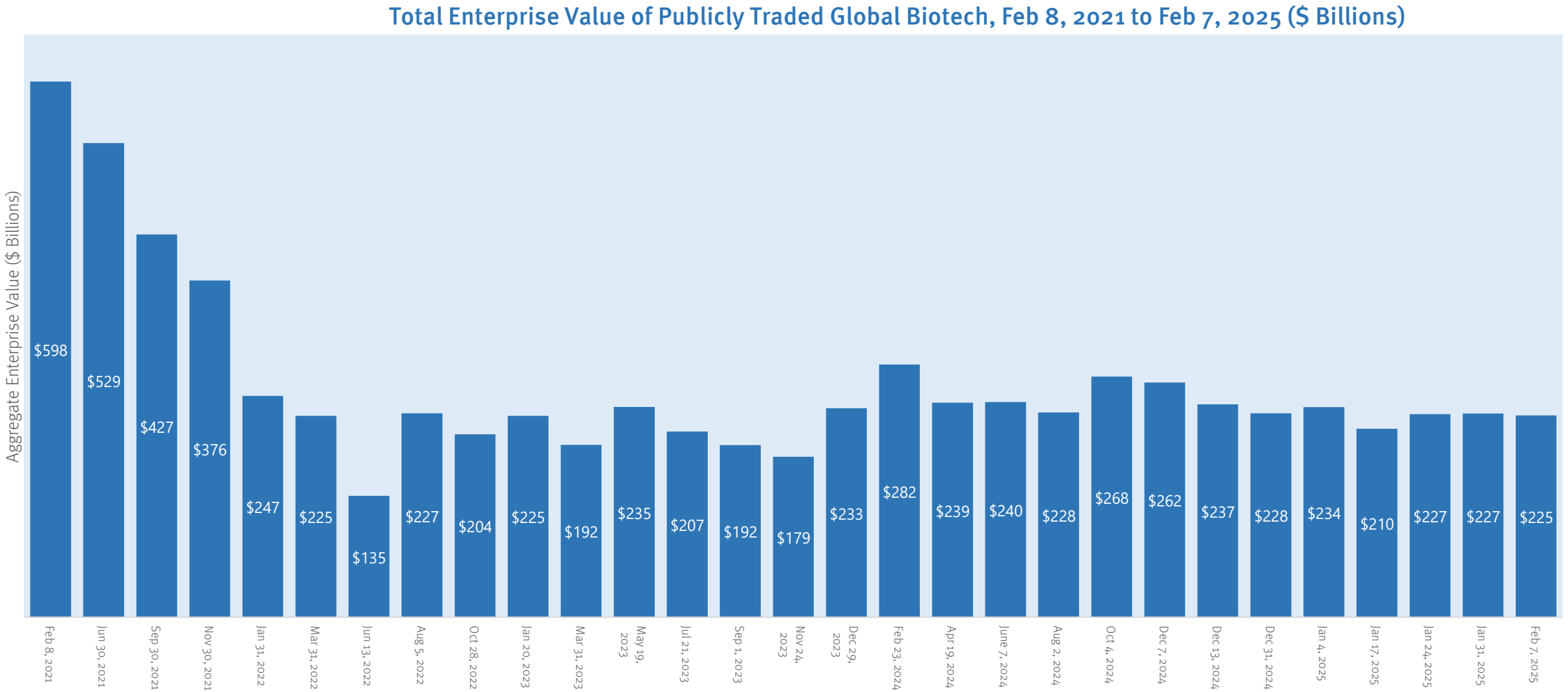


* Change by enterprise value. The adjusted number accounts for the effect of exits and additions via M&A, bankruptcies and IPOs. The annual change by market cap is even higher.

Source: S&P Capital IQ and Stifel analysis

Total Global Biotech Sector Fell 1% Last Week

Biotech stocks fell 1% in the last week – less than the XBI. However, biotech has been weak all year. By our math, the total global biotech sector is down 1.1% for the year. This has not been a strong start to the year.

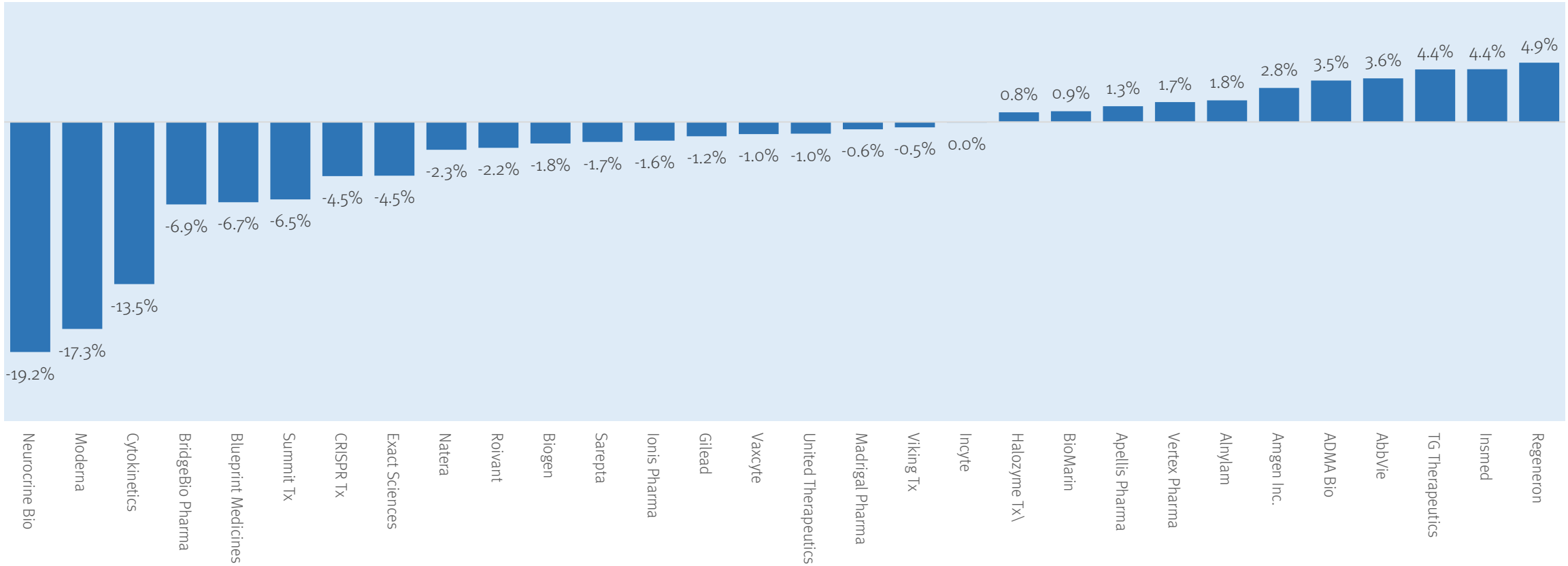


Source: CapitalIQ. Biotechs are defined as any therapeutics company without an approved product on any global stock exchange.

Not a Great Year Thus Far for XBI Component Stocks

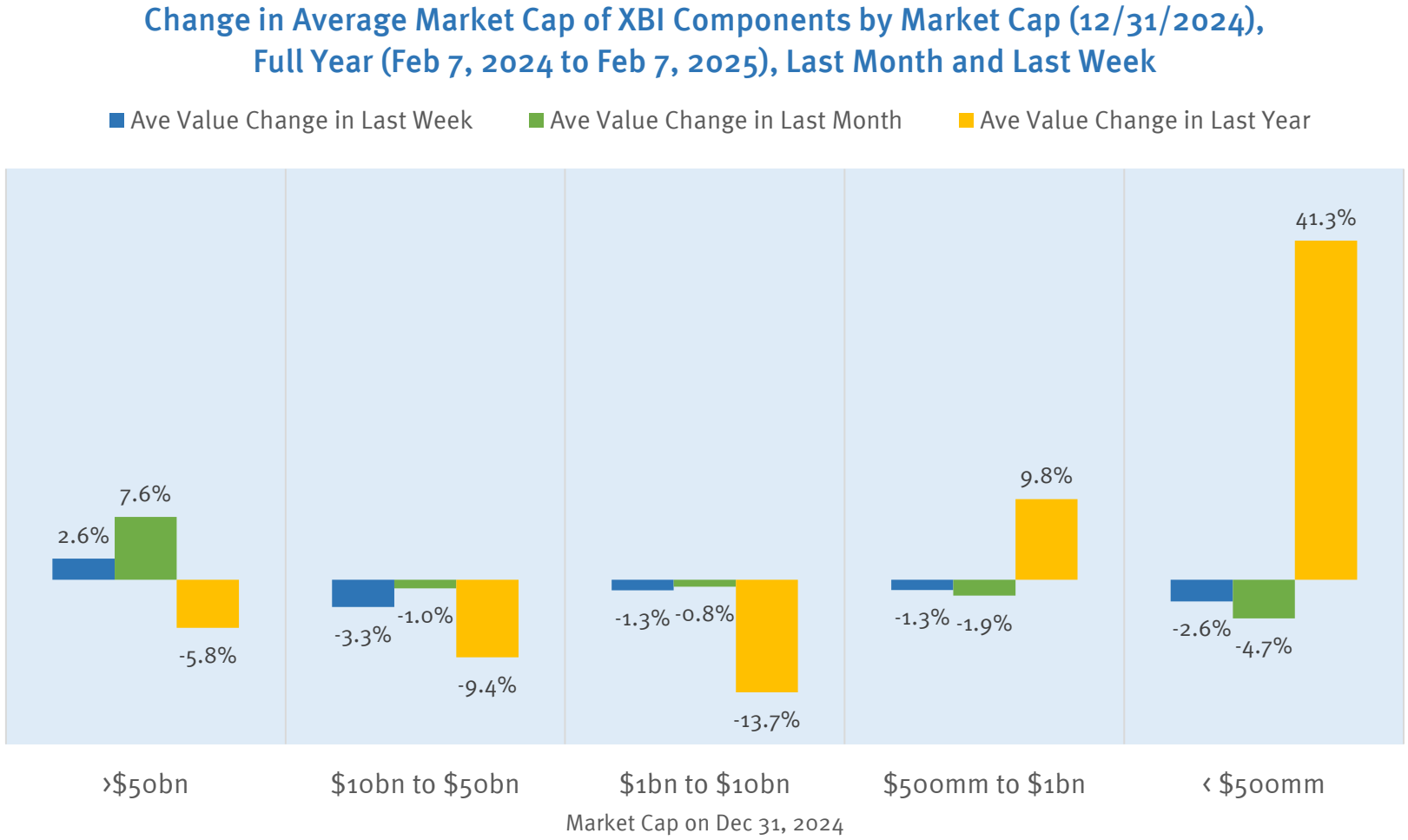
This chart shows the change in market cap this year for the 30 most influential stocks in the XBI. These 30 stocks comprise 60% of the weight of the XBI (out of 138 stocks total). The mean percentage change in value this year so far has been -2% (median -1%). Neurocrine, Moderna, Cytokinetics and BridgeBio have dragged the XBI down. In contrast, good performance of Regeneron, Insmed, TG, AbbVie, ADMA and Amgen has positively impacted the group.

Top 30 XBI Influencers, Percent Change in Market Cap, Week of Dec 31, 2024 to Feb 7, 2025



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

Last Month Has Been Good for Large Pharma and Not Great for all Other Market Cap Groups in the XBI

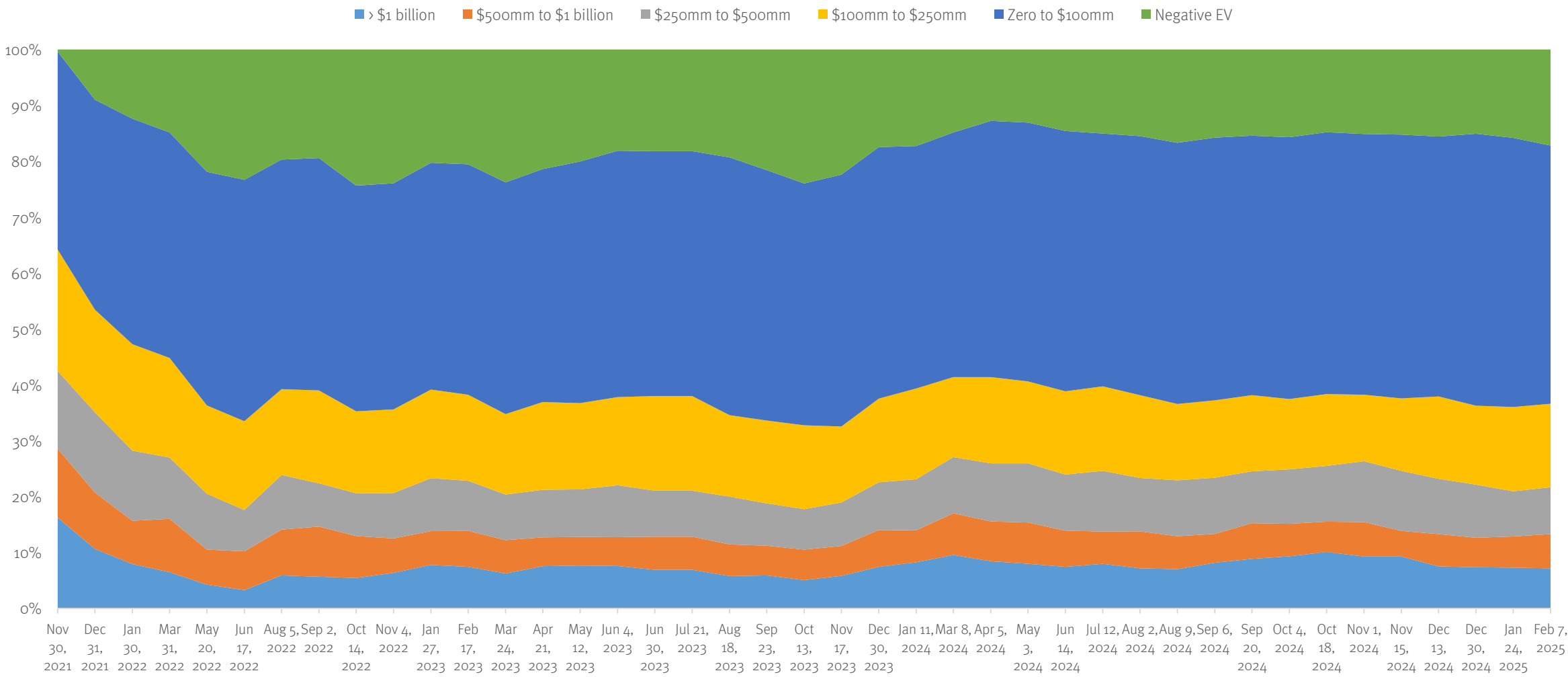


Last year saw small cap company underperformance and negative results for those with caps over $1bn (the opposite of what is normally seen in a recovery). This has been reversed in 2025. We are seeing large caps ($50bn+ cap) do substantially better than other stocks.

Global Biotech Neighborhood Analysis

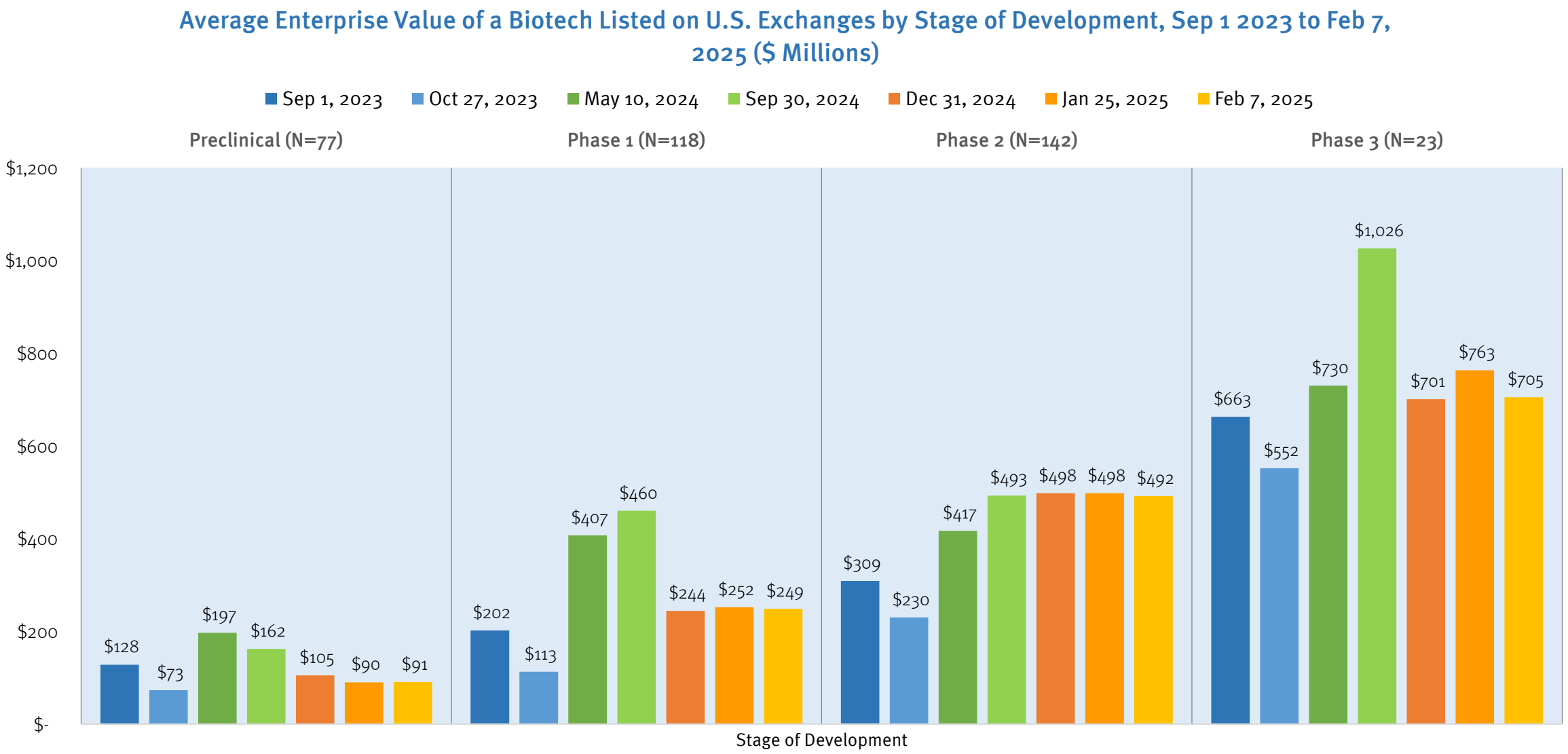
The population of companies trading for less than $250mm has grown the most in the relatively tough biotech tape of 2025.

Global Biotech Universe by Enterprise Value Category, Nov 30, 2021 to Feb 7, 2025



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

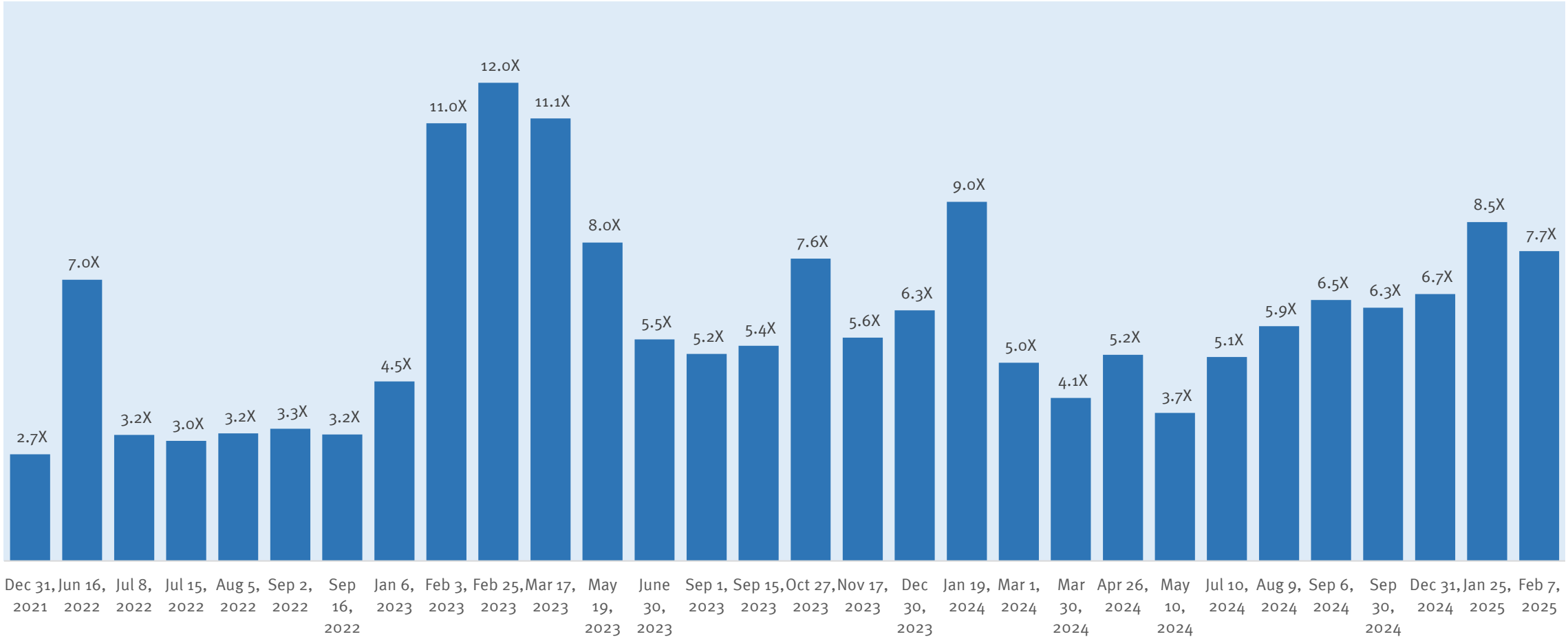
Phase 3 Stocks Dropping Value in Recent Weeks



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.

Recent Interest Rate Decline Reflected in Slight Drop in Phase 3 to Pre-Clinical Biotech Value Premium

Ratio of Average Value of a U.S. Phase 3 to a Preclinical Stage Biotech, 2021 to 2025



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.

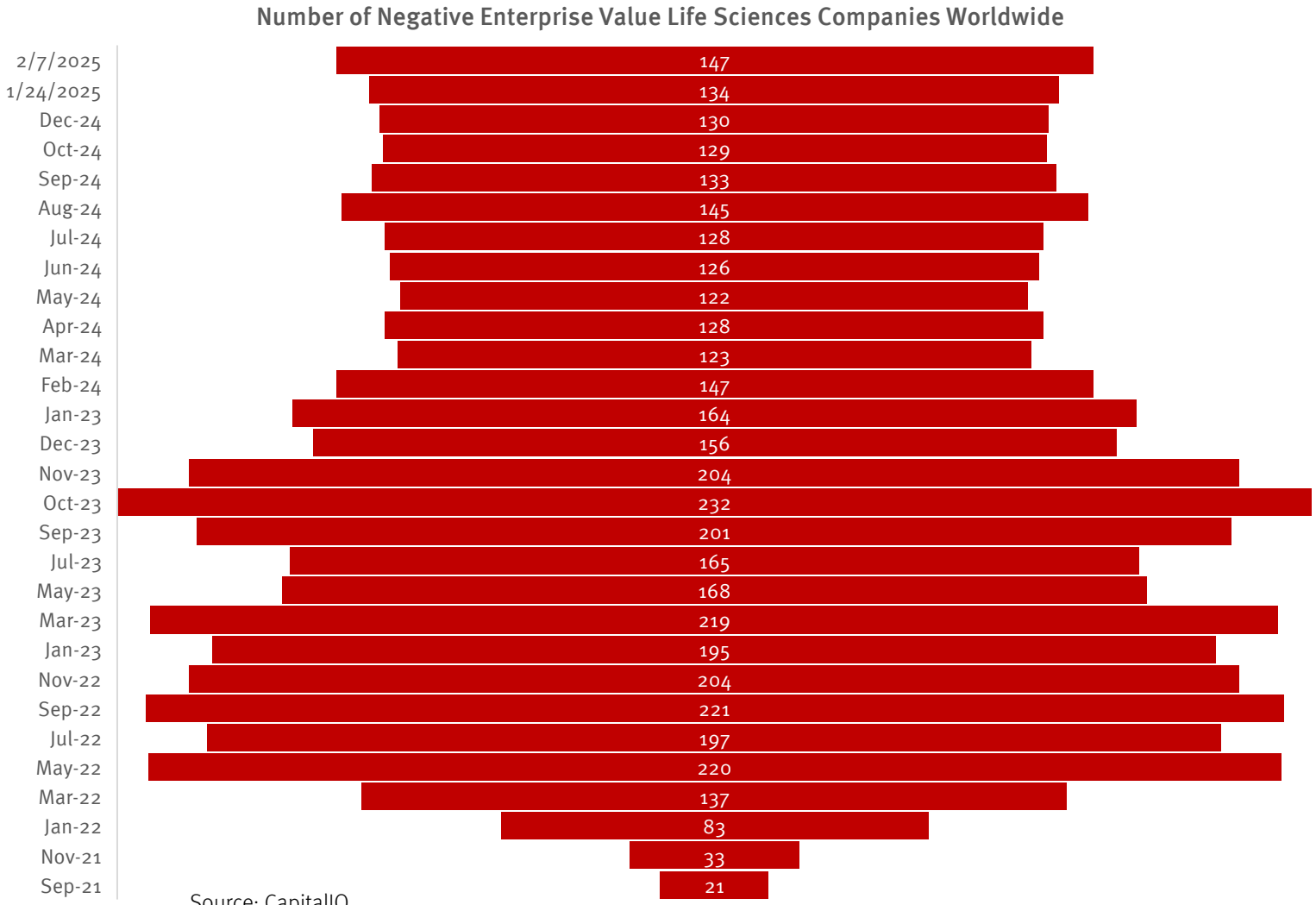
Life Sciences Sector Gained $30 Billion in Value Last Week (0.3%)

Last week was solid for the life sciences sector with big gains in HCIT, diagnostics and solid performance in CDMO's. In contrast, the life science tools sector was weak.

Sector	Firm Count	Enterprise Value (Feb 7, 2025, $millions)	Change in Last Week (percent)	Change in Last Month (percent)	Change in Last Year (percent)
API	79	$90,027	2.6%	-0.9%	14.2%
Biotech	733	$233,613	-1.0%	-0.5%	-5.1%
CDMO	37	$155,900	5.2%	10.9%	19.1%
Diagnostics	77	$262,424	0.6%	3.8%	-2.6%
OTC	29	$24,366	1.9%	2.4%	-10.4%
Commercial Pharma	700	$6,202,706	1.1%	3.2%	2.0%
Pharma Services	38	$172,094	0.4%	0.9%	-9.0%
Life Science Tools	50	$653,833	-4.9%	-2.9%	-5.1%
Medical Devices	174	$1,864,470	-0.9%	4.6%	11.5%
HCIT	7	$27,374	20.7%	29.5%	35.5%
Total	**1924**	**$9,686,808**	**0.3%**	**3.1%**	**3.2%**

Source: CapitalIQ and Stifel analysis

Number of Negative Enterprise Value Life Sciences Companies Jumped in Last Two Weeks



Source: CapitalIQ

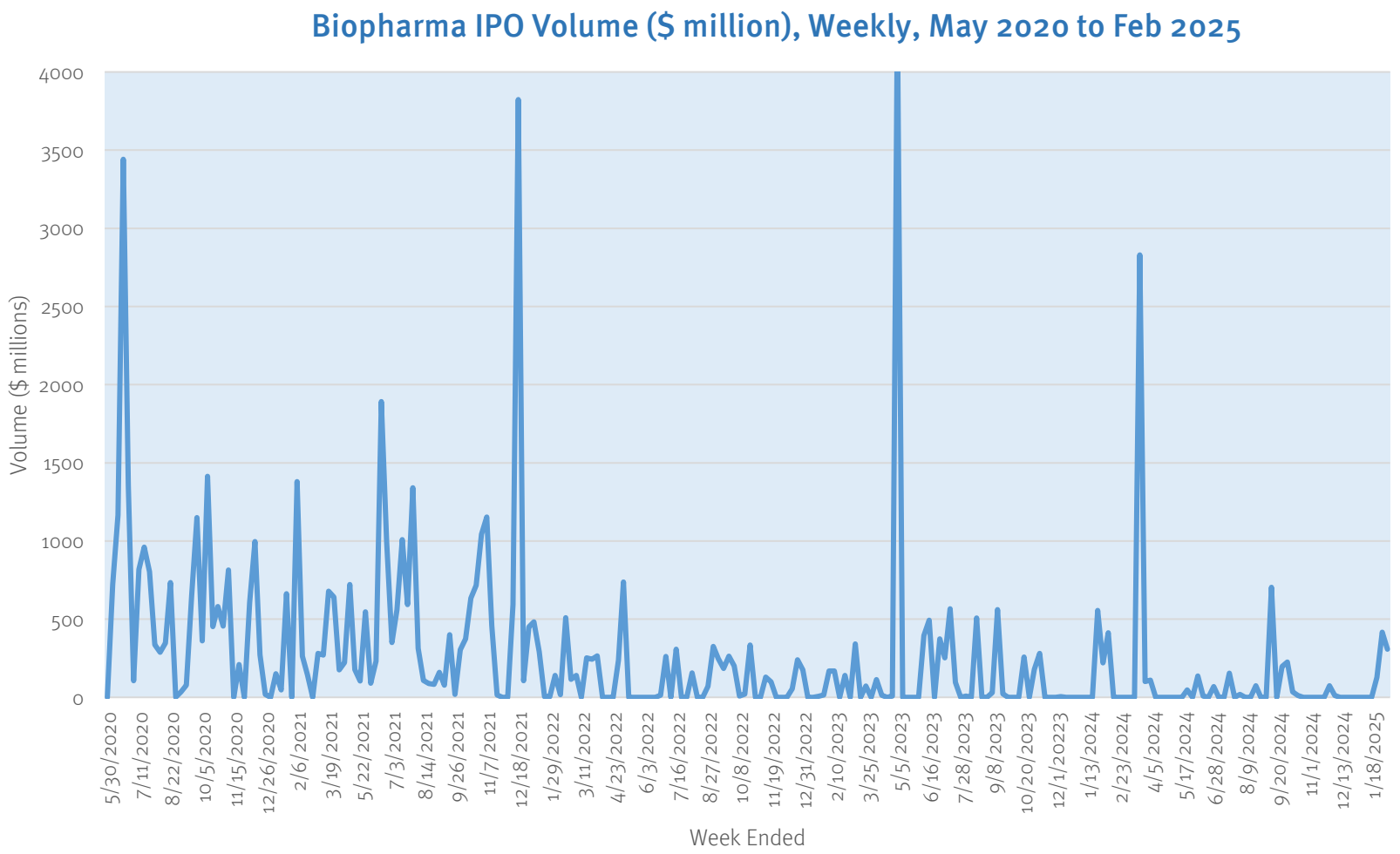
The count of negative EV life sciences companies worldwide rose from 134 two weeks ago to 147 last Friday.

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

We only expect to see a big improvement once the Fed starts to more meaningfully reduce the discount rate.

Capital Markets Update

IPO Market Perking Up



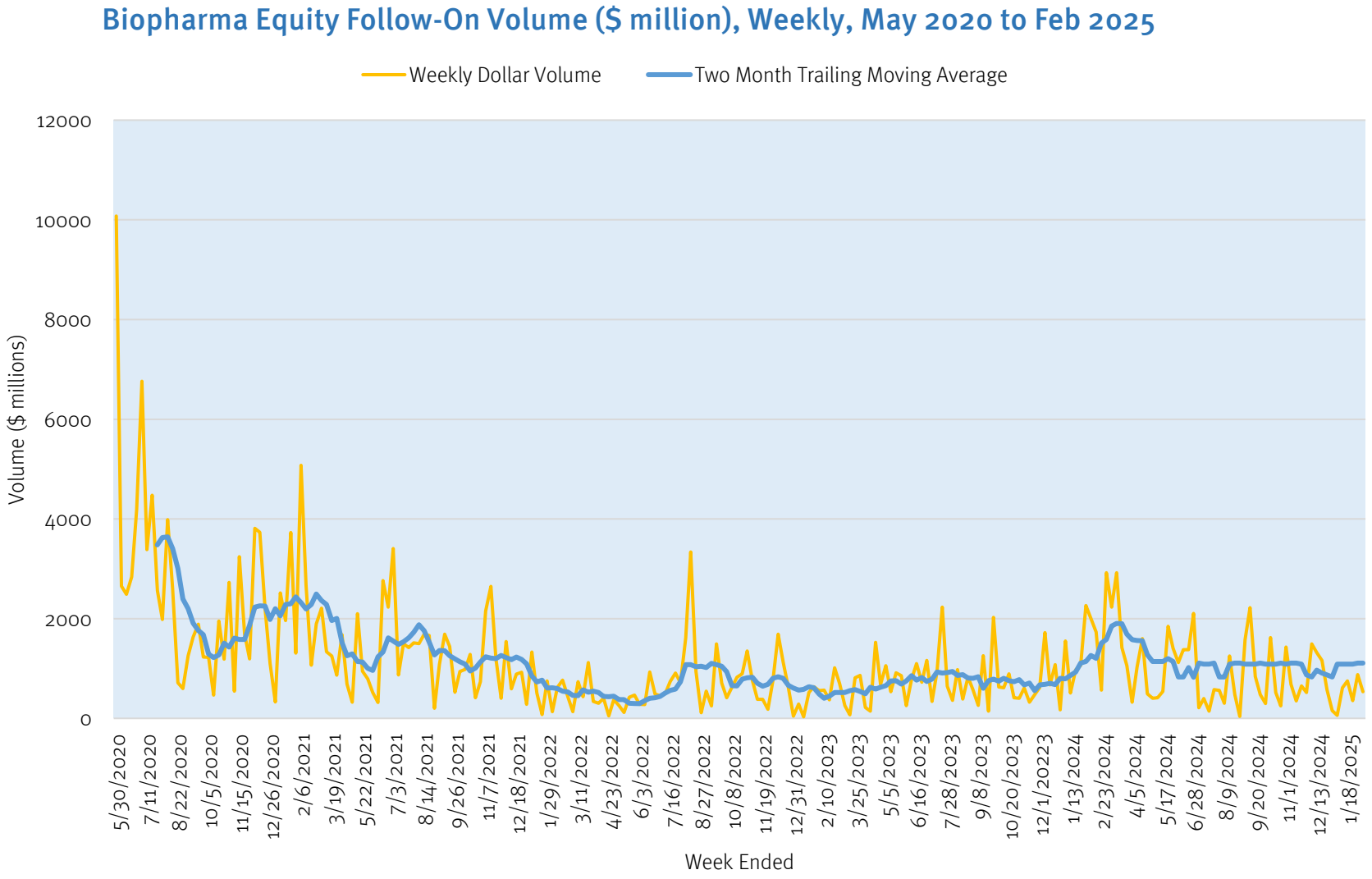
We have seen four companies raise $50mm or more in the IPO market in the last two weeks. Total volume raised has been $750mm in two weeks.

Importantly, investors are not losing money on these IPO's as a group. Both first day and pricing to current are up on three of four of these deals.

The current price of Metsera is now up 64% from its offer level, in particular.

Source: Data from CapitalIQ and Stifel research.

Follow-On Equity Financing Market Continues to be Soft



The first five and a half weeks of 2025 have seen $3.2 billion in follow-on ("FO") biopharma offerings. This is well below the $1bn a week pace that was seen in Q4 2024. While deals are getting done, less than salubrious investor sentiment has restrained volume.

Discounts to last trade have averaged 8% (in line with historic averages). The average after-market performance of follow-on's has been slightly negative so far in 2025.

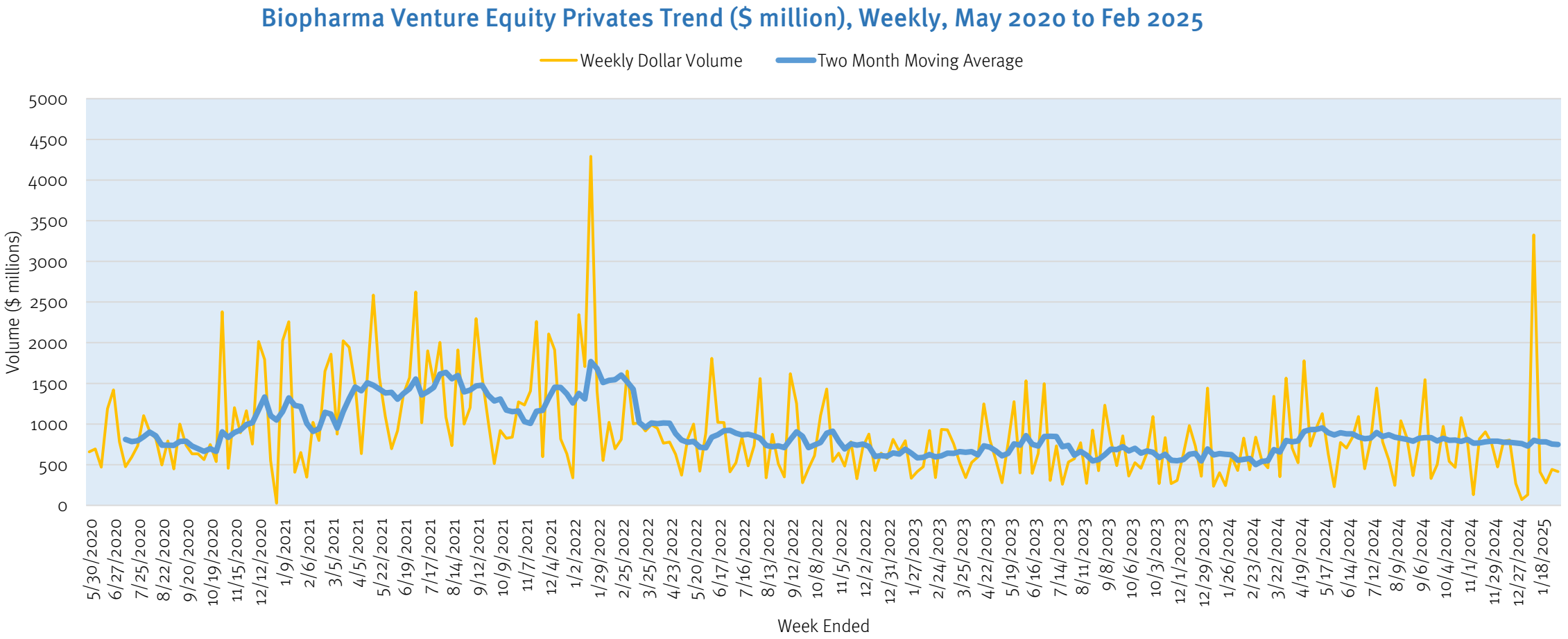
However, for deals from companies with market caps under $2.5 billion, the average after-market performance has been even to slightly positive.

The majority of deals have a confidential component. However, 21.4% of deals this year have been in the PIPE format. Compare this to 30% in 2024 and 28.6% in 2025. This is because the market has been more dominated by larger issuers in 2025, who tend not to use the PIPE format.

Source: Data from CapitalIQ and Stifel research.

This Year Has Been Running Hot in the Privates Market

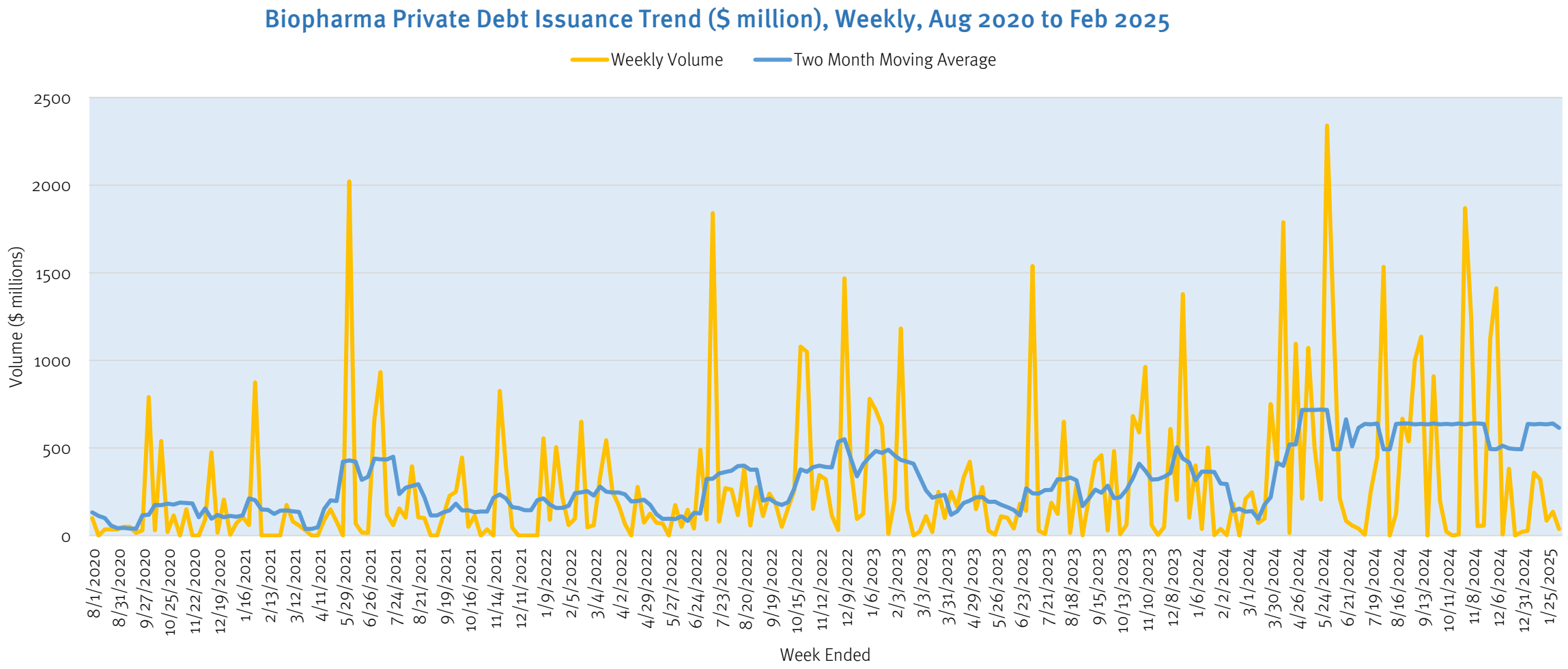
The market for venture privates has seen $5 billion in issuance in the first five and a half weeks of the year. This pace is well up from last year. Nonetheless, the last weeks have been more restrained than earlier in January.



Source: Data from CapitalIQ, Crunchbase.

Global Biopharma Private Debt Placement Market Cooling in 2025

We have seen $960 million in private debt deals get done so far this year. This is well below the blistering pace seen in Q4 2024.

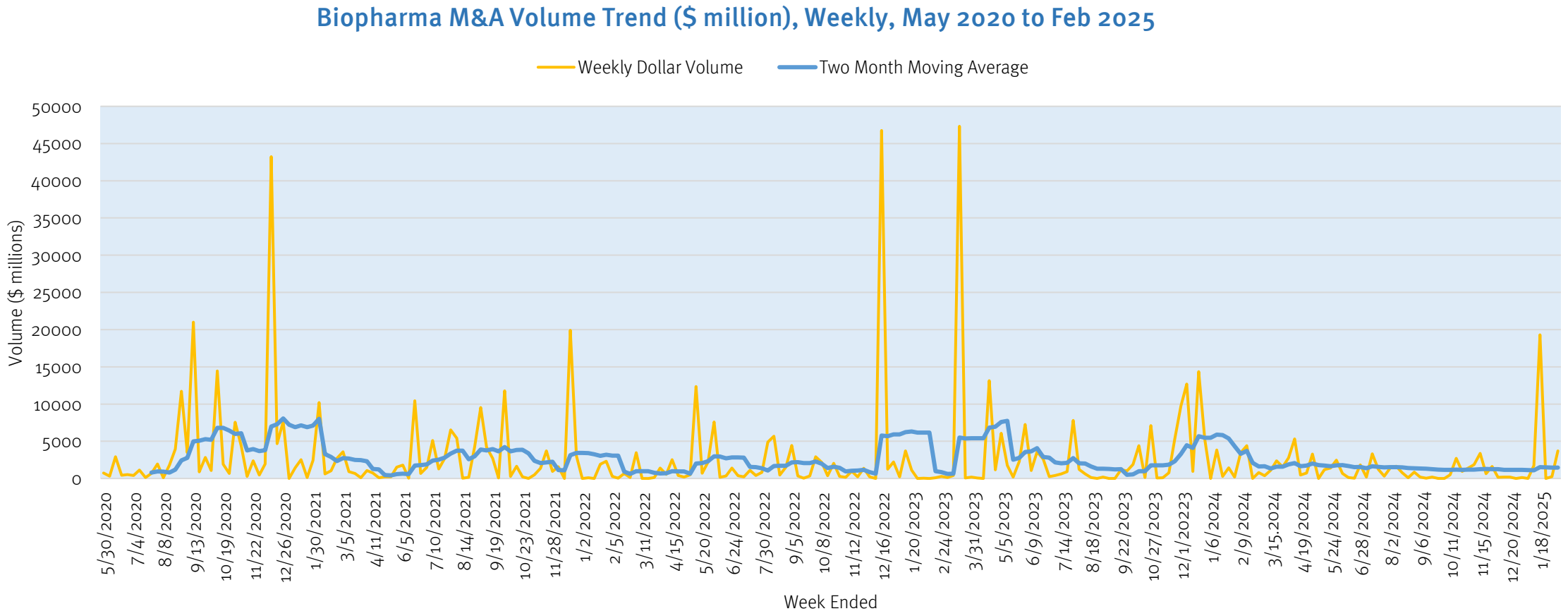


Source: Data from CapitalIQ, Crunchbase.

Deals Update

M&A Market Well Ahead of 2024 Pace

We have seen $25 billion in M&A volume in the first five and a half weeks of 2025. This is one of the strongest starts to the year seen in a long time. If this pace were sustained, this would be the second strongest year for biopharma M&A in history ($250bn pace).* One comparison metric is the number of $1bn+ deals announced. So far this year, we have seen five such deals (including last week's buyout of Mitsubishi Tanabe by Bain Capital) – and the year is one tenth done. Compare this to a total of fifteen $1bn+ M&A deals in all of last year.



Source: S&P, CapitalIQ

*Previous volume high water marks were 2019 ($328bn) and 2014 ($227bn).

Bain Buys 340-year-old Pharma Company to Fast-track Japan's Drug Development

David Keohane and Leo Lewis, *Financial Times*, Feb 7, 2025 (excerpt)

Bain Capital has placed a $3.3bn bet on a historic shift in Japan's conservative drugs approval regime by buying a pharmaceutical company founded more than three centuries ago. The US firm on Friday agreed a deal for Tanabe Pharma with longtime owner, Mitsubishi Chemical Group, in the largest-ever private equity deal in Japan's healthcare sector.

The carve-out puts Bain in control of a drugs company that was founded in Osaka in 1678, when Japan was still ruled by a shogun military commander. It is part of a wider trend of global private equity firms competing fiercely to deploy capital as governance changes push large Japanese conglomerates to sell non-core businesses.

Bain has bought Tanabe in the hope that it can tap into its own connections to other global pharmaceutical groups to find and license new or promising drugs to bring to Japan, particularly new drugs treating rare diseases. For years, Japan has suffered from what is known as the "drug loss" phenomenon. Its highly conservative regulatory stance, including a requirement that drugs be tested on Japanese subjects in addition to original clinical trials, means products approved by overseas regulators often do not receive approval in Japan.The expense of running such trials has often been considered too high for foreign drugmakers to bother filing applications in the country. The result is that Japanese patients suffer from a historically large gap between the number of drugs and treatments available to them compared with their counterparts in the US and elsewhere.

As of March 2023, 86 drugs approved in Europe and the US have yet to be developed in Japan, according to the Pharmaceuticals and Medical Devices Agency.

However, in a belated attempt to address the issue last year, the Ministry of Health, Labour and Welfare took steps to ease the requirements for approval applications, especially for drugs viewed as potentially very beneficial to patients in Japan. That change represented an opportunity, said senior executives at Bain.

Bain's buyout of Mitsubishi-Tanabe is the second largest M&A deal announced so far this year.

It's also a rare takeout of a major Japanese pharma company.

It's interesting to see a PE firm emerge as victor in what was likely a well-run auction process for Mitsubishi-Tanabe.

Bain gets access to Radicava®, a soon-to-be blockbuster for ALS in the U.S. for what seems like a low price on the surface but also takes on a Japan business and large R&D organization that has substantial overhead expense.

Source: https://www.ft.com/content/6fd756af-c63f-4587-ba67-189009102e5f

Immune Drugmakers Alumis and Acelyrin to Merge

Gwendolyn Wu, *Biopharma Dive*, Feb 7, 2025 (excerpt)

Alumis and Acelyrin are merging, the biotechnology companies said Thursday afternoon, in an all-stock deal that leaves the combined company with a bigger cash balance and three drugs in clinical testing.

Per deal terms, Acelryin stockholders will receive 0.4274 shares of Alumis stock for each share they own, leaving them with about 45% of the combined company and Alumis equity holders with 55%. The new company, which will keep the Alumis name and be run by its executive team, would have $737 million in cash, enough to keep operating into 2027.

The merged entity will continue to develop Alumis' two so-called TYK2 inhibitors, one of which is being developed for plaque psoriasis and lupus while the other is targeting neuroinflammatory conditions like multiple sclerosis. Acelyrin's top prospect, a thyroid eye disease drug called lonigutamab, is part of the deal, too, but the program will be re-evaluated to "confirm its differentiation in a capital efficient manner," the companies said.

Source: https://www.biopharmadive.com/news/alumis-acelyrin-merger-deal-tyk2-lonigutamab/739505/

Legacy Pharma Inc. Announces the Acquisition of InterMune, Inc. and the U.S. Rights to Esbriet®

LEGACY PHARMA

Press Release, Feb 6, 2025 (excerpt)

George Town, Cayman Islands, February 06, 2025 --(PR.com)-- Legacy Pharma Inc. SEZC (“Legacy Pharma” or the “Company”), a specialty pharmaceutical company, announced the completion of the acquisition of InterMune, Inc. (“InterMune”) and the intellectual property rights to Esbriet® (pirfenidone) in the United States from Genentech, a member of the Roche Group. This strategic acquisition underscores Legacy Pharma's commitment to expanding its portfolio of high-quality pharmaceutical products and enhancing patient access to innovative treatments.

Esbriet®, a medication used to treat idiopathic pulmonary fibrosis (IPF), has shown significant promise in improving the lives of patients with this chronic and life-threatening lung disease. With this acquisition, Legacy Pharma aims to ensure the continued availability and distribution of Esbriet® to patients across the United States. Genentech will continue to provide access to Esbriet® in the United States until the completion of the business transfer. Furthermore, Roche will retain commercial rights in all other territories.

"We are excited to acquire InterMune and add Esbriet® to our portfolio of essential medications," said Mark Thompson, CEO of Legacy Pharma. "This acquisition aligns with our mission to provide patients with access to innovative and life-changing treatments."

Source: https://www.pr.com/press-release/930210

Pfizer Says it has at Least $10B Available for Deals in 2025, With a Focus on Pipeline

May Bayer, *Endpoints News*, Feb 4, 2025 (excerpt)

Pfizer's next deals are likely to be longer-term efforts to reload its R&D work rather than big-ticket, late-stage assets, the company's top executives said Tuesday.

"Looking forward, we are looking at more strategic opportunities right now, which will enhance the pipeline in areas that we would like to play, rather than near-term revenues," CEO Albert Bourla told investors Tuesday.

The company has about $10 billion to $15 billion it could put toward M&A this year, according to CFO Dave Denton. He previously guided that while there's always "a little flexibility to do BD," large transactions would likely be kicked to 2026 or beyond. Pfizer has made de-levering a priority, with billions in cost cuts initiated and executed, and billions more raised by selling off stakes in Haleon, a consumer health wing co-run with GSK.

Like many other drugmakers, New York-based Pfizer is looking at the explosion of assets coming out of China. The number of deals being made there "has not escaped our attention," chief strategy and innovation officer Andrew Baum said Tuesday.

"They're mostly fast followers, but I expect that will change as well," Baum said. "It's an area that we are very, very active in."

Albert Bourla
CEO, Pfizer

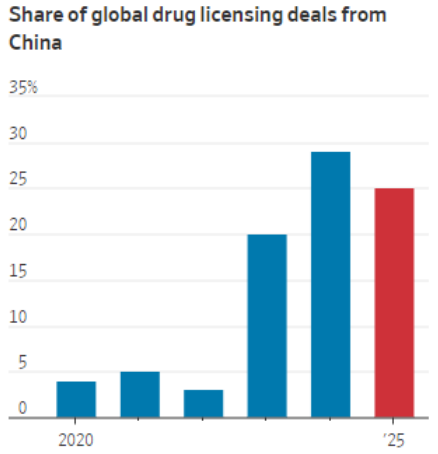
Source: https://endpts.com/pfizer-says-it-has-at-least-10b-available-for-deals-in-2025/

The Drug Industry Is Having Its Own DeepSeek Moment

David Wainer, *Wall Street Journal*, Feb 7, 2025 (excerpt)

The biotech industry's DeepSeek moment came last fall. That is when Summit Therapeutics, backed by billionaire Bob Duggan, announced that its drug had outperformed Merck's blockbuster therapy Keytruda in a head-to-head lung-cancer trial. Keytruda, a $30 billion-a-year immunotherapy juggernaut, is the bestselling drug in the pharma industry and has long dominated the market. So the prospect of a superior competitor was seismic. Even more remarkable: Summit had licensed the drug just two years earlier from a little known Chinese biotech called Akeso.

The news added billions of dollars to Summit's market capitalization, catapulting it into biotech's upper ranks despite having no approved drugs. While Summit's drug still hasn't received U.S. regulatory approval, the results were a watershed moment for the industry, underscoring the competitive threat emanating from China. China's rise in biotech has been years in the making, but it is now impossible to ignore. In 2020, less than 5% of large pharmaceutical transactions worth $50 million or more upfront involved China. By 2024, that number had surged to nearly 30%, according to DealForma. A decade from now, many drugs hitting the U.S. market will have originated in Chinese labs.



Note: Percentage of $50 million+ upfront Big Pharma licensing deals originating from China. 2025 is through 1/21
Source: DealForma Database

China's biotech boom mirrors its rise in tech. In both cases, China has moved up the value chain, from manufacturing goods to becoming a more sophisticated hub for innovation, competing in industries once dominated by the U.S. There are several reasons for the industry's growth. For one, many top scientists trained in the U.S. have returned to China over the past decade, fueling the emergence of biotech hubs around Shanghai. And just as DeepSeek built a formidable chatbot—allegedly on a lean budget with limited access to semiconductors—Chinese biotech companies are also scrappier, capitalizing on a highly skilled, lower-cost workforce that can move faster.

For now, much of China's biotech innovation is incremental rather than groundbreaking. Many companies focus on improving existing drugs—tweaking the chemistry, enhancing efficacy or differentiating them in key ways.

But Chinese innovation is steadily improving and is already starting to disrupt the U.S. drug-development ecosystem. For decades, the U.S. biotech industry has thrived in hubs such as Boston-Cambridge and the San Francisco Bay Area, fueled by talent streaming from top academic centers like Massachusetts Institute of Technology and Stanford University. Those biotech companies have an insatiable client in Big Pharma, which is willing to pay top dollar for new drugs to replace those going off-patent.

Source: https://www.wsj.com/health/pharma/the-drug-industry-is-having-its-own-deepseek-moment-68589d70

Rapid Trials Prompt Deals Rush for Chinese ‘Super Me-too’ Drugs

Hannah Kuchler in London and Wang Xueqiao in Shanghai, *Financial Times*, Feb 6, 2025 (excerpt)

Western drugmakers are striking more deals in China to access “bio-better” treatments for diseases from obesity to cancer, taking advantage of the early data on offer from the country’s faster and more lightly regulated trials.

Large pharmaceutical groups including GSK, Merck and AstraZeneca have each signed $1bn-plus agreements in the past two years to buy the rights to develop and sell Chinese drugs outside the country.

Meanwhile, investors including Forbion, Bain Life Sciences and General Atlantic have ploughed hundreds of millions of dollars into new biotechs that will develop Chinese assets for western markets, hoping to be bought by major drugmakers.A third of all the compounds that large pharmaceutical companies bought the rights to last year came from China, a dramatic jump from just 12 per cent two years ago, according to investment bank Stifel.

“Shanghai has become the centre for search and evaluation for all global pharma,” said one life sciences investor.

The rapid rise has been fuelled partly by early data from a soaring number of trials, which some analysts say do not have the same ethical oversight or tight regulations as they would have in the west.Investment in China presents a possible challenge to US and European biotechs, which often seek to sell to big pharma groups. Chinese biotechs may be willing to sell rights to their drugs at lower valuations because funding has dried up in their home market.

Their drugs are often called “biobetters” because they are designed to tackle known biological targets rather than starting with a new discovery about how a disease works. These “super me-too” drugs are then engineered to work better than currently available ones.

Brad Loncar, a US-based investor and founder of interview site BiotechTV, said western companies were licensing Chinese drugs because rapidly conducted trials allowed data to be assessed at an early stage to see if an asset was worth buying.

“China has a huge competitive advantage over the US,” he said. “You can start a trial in months and find out if something works, whereas here it can sometimes take years.” He warned that the biotech industry could be disrupted by China, as the semiconductor sector was. “If you start outsourcing innovation and science as a nation, you risk declining in those areas over the long term,” he said.

Source: https://www.ft.com/content/f76c2e6b-dcc4-4e2c-a007-b53330226a5f

Pharma Earnings Update

AbbVie Moves into #2 Spot in Life Sciences Public Company Value Rankings in Last Two Weeks

Value Rank (Feb 7 , 2025)	Company	Feb 7, 2025	Value Rank (Feb 7, 2025)	Dec 31, 2024	Value Rank (Dec 31, 2024)	Dec 30, 2023	Value Rank (June 17, 2022)	Jun 17, 2022	Value Rank (Feb 8, 2021)	Feb 8, 2021
1	Lilly	$818,099	1	$722,374	1	$541,487	4	$275,160	9	$199,050
2	abbvie	$400,894	2	$378.10	3	$321,532	2	$310,463	3	$267,777
3	novo nordisk	$397,371	3	$382,368	2	$458,427	6	$239,281	11	$163,171
4	Johnson&Johnson	$384,109	4	$363,364	4	$383.73	1	$446,793	1	$441,136
5	Roche	$280,840	5	$260,970	6	$261,190	3	$278,801	2	$301,332
6	AstraZeneca	$247,721	6	$228,175	7	$234,801	8	$226,761	8	$207,897
7	ThermoFisher SCIENTIFIC	$244,412	7	$227,963	8	$234,504	9	$212,736	12	$150,063
8	MERCK	$244,383	8	$275,044	5	$302,407	7	$236,919	7	$211,317
9	Abbott	$231,356	11	$203,674	10	$199,953	11	$281,482	6	$227,339
10	NOVARTIS	$228,400	10	$212,877	9	$220,692	10	$188,764	5	$231,398

Source: CapitalIQ

Lilly has the highest enterprise value of any life sciences company in the world by far (up from a ranking of #9 on Feb 8, 2021). While not an all-time high, LLY has performed quite well in 2025 (up 13%).

In contrast, with recent data on cagrilintide, Novo Nordisk has lost its #2 spot and is now #3.

Remarkably, AbbVie has now taken the #2 spot (up 6% YTD). Its strength is very much a testament to the power of I&I in a market that has been dominated by obesity stories.

J&J, the historical long-time industry value leader now sits in the #4 spot. Interestingly, J&J is not that far off from taking the #2 or #3 spot (up 6% YTD).

Other strong performers this year have been AZ, Roche and Thermo.

AbbVie Reaffirmed Long-Term Growth on Jan 31, 2025

AbbVie Reports Full-Year and Fourth-Quarter 2024 Financial Results

- *Reports Full-Year Diluted EPS of $2.39 on a GAAP Basis, a Decrease of 12.1 Percent; Adjusted Diluted EPS of $10.12, a Decrease of 8.9 Percent; These Results Include an Unfavorable Impact of $1.52 Per Share Related to 2024 Acquired IPR&D and Milestones Expense*
- *Delivers Full-Year Net Revenues of $56.334 Billion, an Increase of 3.7 Percent on a Reported Basis and 4.6 Percent on an Operational Basis*
- *Full-Year Global Net Revenues from the Immunology Portfolio Were $26.682 Billion, an Increase of 2.1 Percent on a Reported Basis, or 2.9 Percent on an Operational Basis; Global Humira Net Revenues Were $8.993 Billion; Global Skyrizi Net Revenues Were $11.718 Billion; Global Rinvoq Net Revenues Were $5.971 Billion*
- *Full-Year Global Net Revenues from the Oncology Portfolio Were $6.555 Billion, an Increase of 10.8 Percent on a Reported Basis, or 12.0 Percent on an Operational Basis; Global Imbruvica Net Revenues Were $3.347 Billion; Global Venclexta Net Revenues Were $2.583 Billion*
- *Delivers Fourth-Quarter Net Revenues of $15.102 Billion, an Increase of 5.6 Percent on a Reported Basis and 6.1 Percent on an Operational Basis*
- *Provides 2025 Adjusted Diluted EPS Guidance Range of $12.12 to $12.32; Excludes Any Unfavorable Impact Related to Acquired IPR&D and Milestones Expense*
- *Reaffirms Expectations for High Single-Digit Compound Annual Revenue Growth Rate through 2029; Raises 2027 Combined Sales Outlook for Skyrizi and Rinvoq to More Than $31 Billion; Updates Outlook for Aesthetics to Deliver High Single-Digit Compound Annual Revenue Growth Rate from 2025 through 2029*

Source: https://investors.abbvie.com/events-and-presentations/upcoming-events

Lilly Showed Very Strong 2024 Growth with Tirzepatide

Q4 2024 Summary

- **Revenue grew 45%,** driven by Mounjaro and Zepbound, while non-incretins grew 20%[1]
- Continued to **speed life-changing medicines** to patients:
  - **Zepbound** approved in the U.S. as the first and only prescription medicine for moderate-to-severe obstructive sleep apnea in adults with obesity
  - Submitted **imlunestrant** for ER+ HER2- metastatic breast cancer globally
  - Disclosed positive topline results in Phase 3b **SURMOUNT-5** study
  - Announced agreement to acquire Scorpion Therapeutics' mutant-selective PI3Kα inhibitor program
- Q4 **investment growth** largely driven by early and late-stage R&D activities and promotional efforts to support launches
  - Announced a **$3 billion manufacturing expansion** of recently acquired facility in Wisconsin
- Returned to shareholders over **$1 billion via the dividend** and approximately **$2 billion via share repurchases**

Invest in Current Portfolio

Invest in Future Innovation

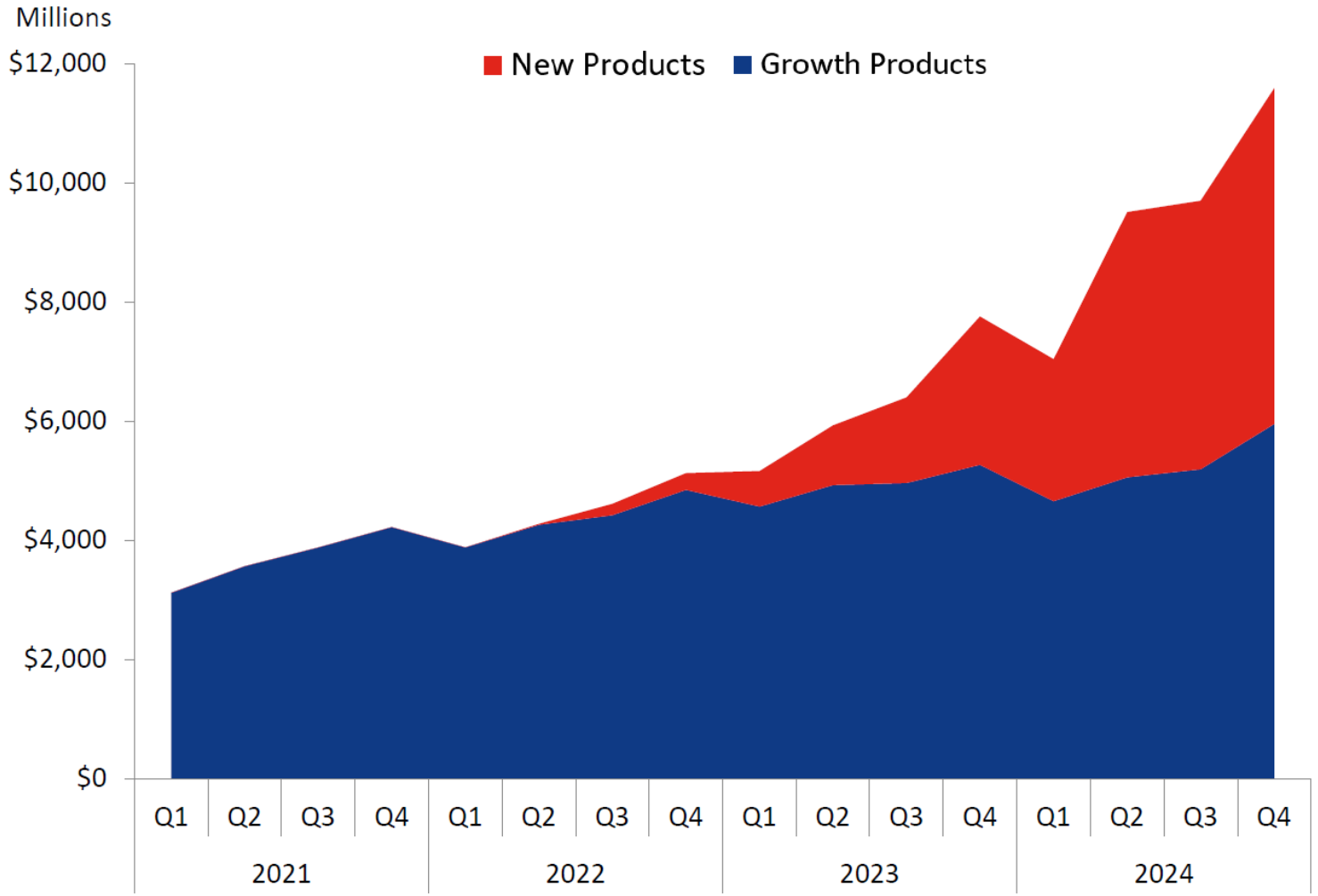
Deliver Revenue Growth

Speed Life-Changing Medicines

Return Capital to Shareholders

Source: https://investor.lilly.com/webcasts-and-presentations

Mounjaro Up 44% in 2024 and Zepbound Up 48%



New Products: Ebglyss, Jaypirca, Kisunla, Mounjaro, Omvoh, and Zepbound
Growth Products: Cyramza, Emgality, Jardiance[1], Olumiant, Retevmo, Taltz, Trulicity, Tyvyt, and Verzenio

[1] Jardiance is part of the company's alliance with Boehringer Ingelheim. Lilly reports as revenue royalties received on net sales of Jardiance

NEW PRODUCTS

MOUNJARO
- U.S. T2D injectable incretins TRx SOM nearly 37% and NBRx SOM nearly 44% at end of Q4 2024
- Lilly T2D injectable incretins TRx SOM over 50% at end of Q4 2024

ZEPBOUND
- U.S. branded anti-obesity TRx SOM over 48% and NBRx SOM nearly 56% at end of Q4 2024

JAYPIRCA
- Q4 2024 sales increased to $114 million

OMVOH
- Q4 2024 sales increased to $57 million with launches in the U.S. and international markets

EBGLYSS
- Q4 2024 sales of $20 million with launches in the U.S. and international markets

KISUNLA
- Q4 2024 sales increased to $8 million

GROWTH PRODUCTS

JARDIANCE[1]
- U.S. TRx SOM over 65% at end of Q4 2024
- U.S. TRx grew nearly 24% vs. Q4 2023

TALTZ
- U.S. TRx grew over 5% vs. Q4 2023

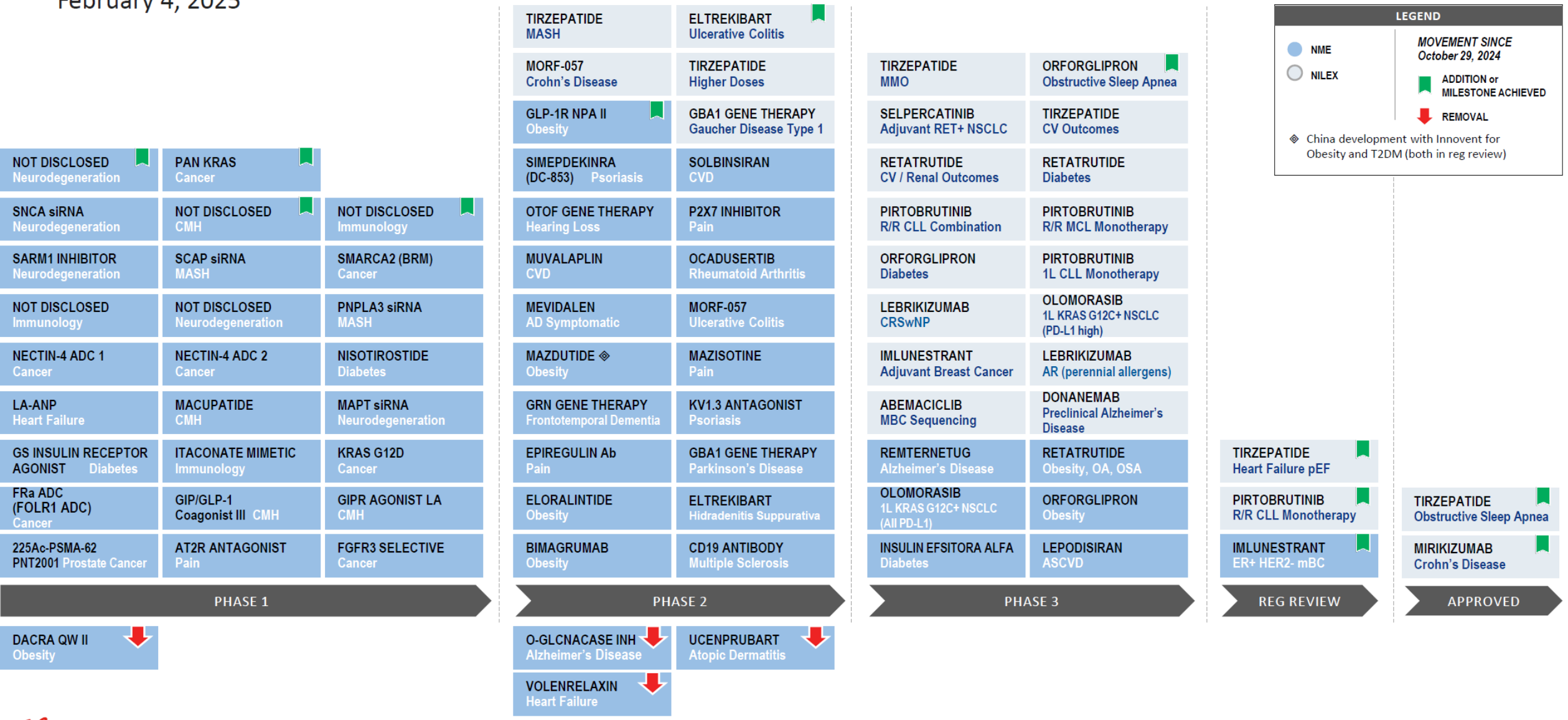
TRULICITY
- U.S. T2D injectable incretins TRx SOM over 14% at end of Q4 2024

VERZENIO
- U.S. TRx grew over 15% vs. Q4 2023

Source: https://investor.lilly.com/webcasts-and-presentations

Lilly Select NME and NILEX Pipeline

February 4, 2025



Source: https://investor.lilly.com/webcasts-and-presentations

Eli Lilly to Release Late-Stage Data on Next-generation Weight Loss Drug Retatrutide in 2025

Annika Kim Constantino, *CNBC*, Feb 6, 2025 (excerpt)

Eli Lilly on Thursday said it expects to release data from a late-stage trial on its next-generation weight loss drug retatrutide later this year, a few months earlier than anticipated.

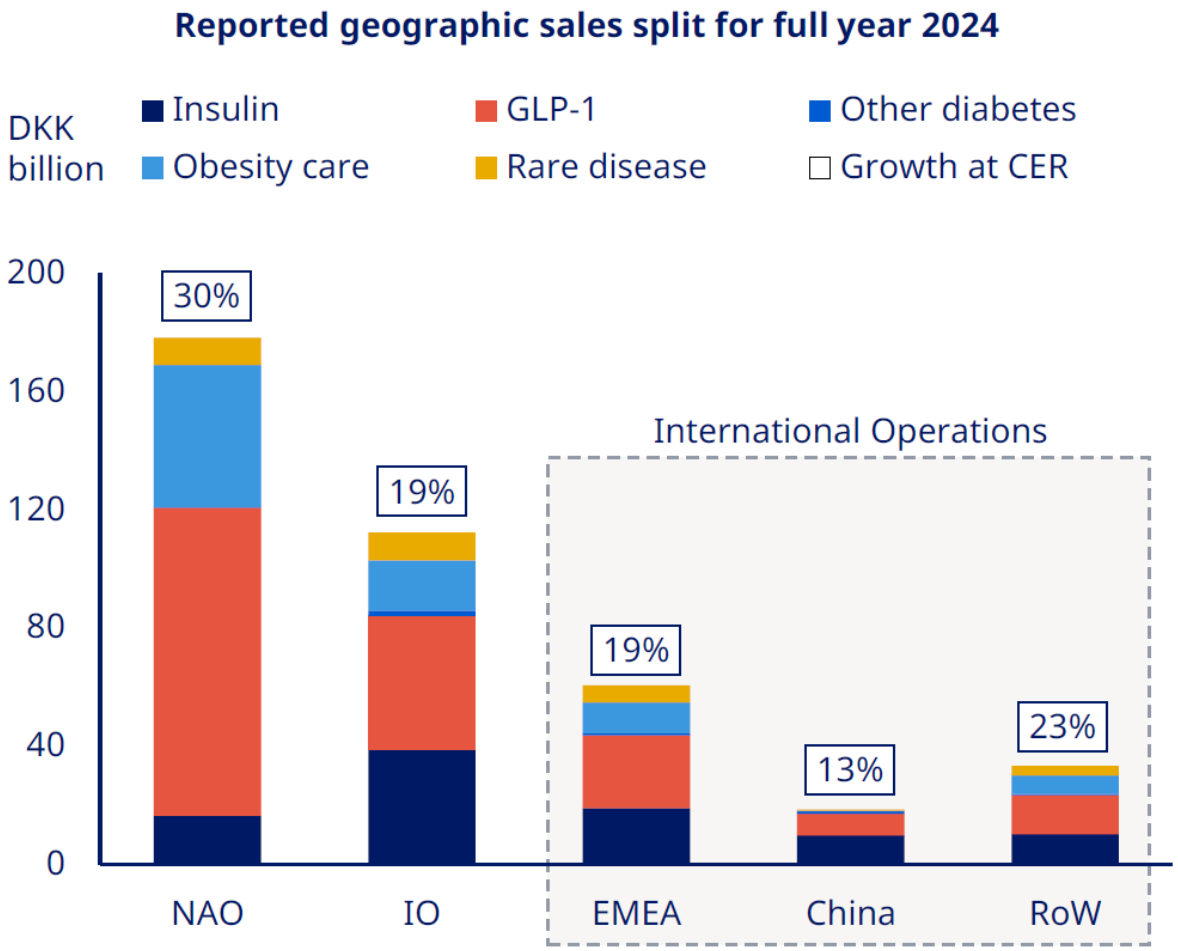
The company expects to provide results from a 68-week study in people with obesity and osteoarthritis of the knee in 2025, according to fourth-quarter earnings slides on its website. Eli Lilly previously said that phase three study was expected to finish in February 2026.

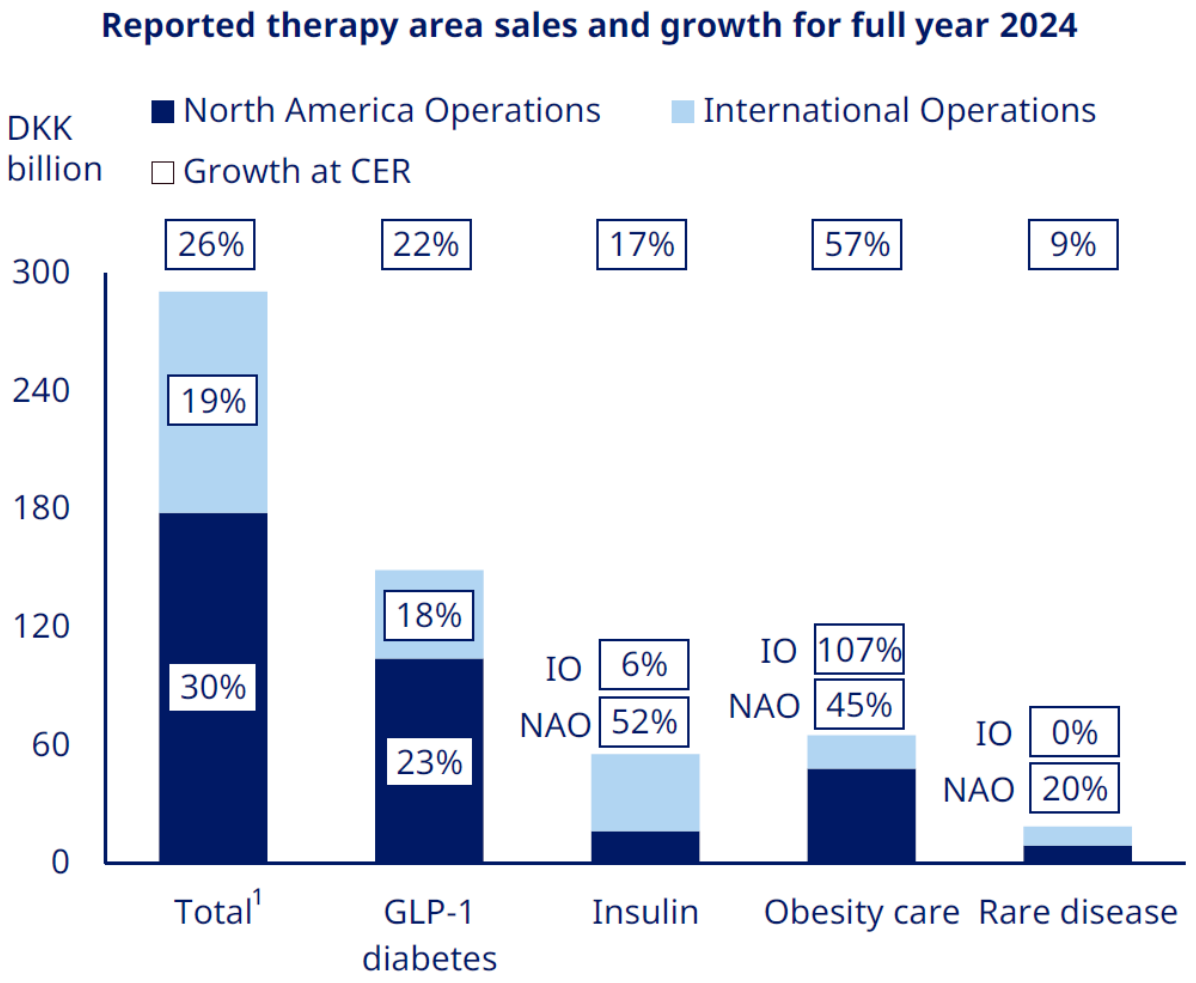
It is among at least nine closely watched clinical trials on retatrutide, which works differently from the obesity and diabetes treatments on the market and appears to be even more effective at weight loss.

“We believe this potential new medicine can deliver even more weight loss than tirzepatide and it could potentially provide additional health benefits,” Daniel Skovronsky, Lilly’s chief scientific and medical officer, said during an earnings call on Thursday.

Source: https://www.cnbc.com/2025/02/06/eli-lilly-to-release-weight-loss-drug-retatrutide-data-in-2025.hTML

Novo Nordisk Saw 26% Sales Growth in 2024



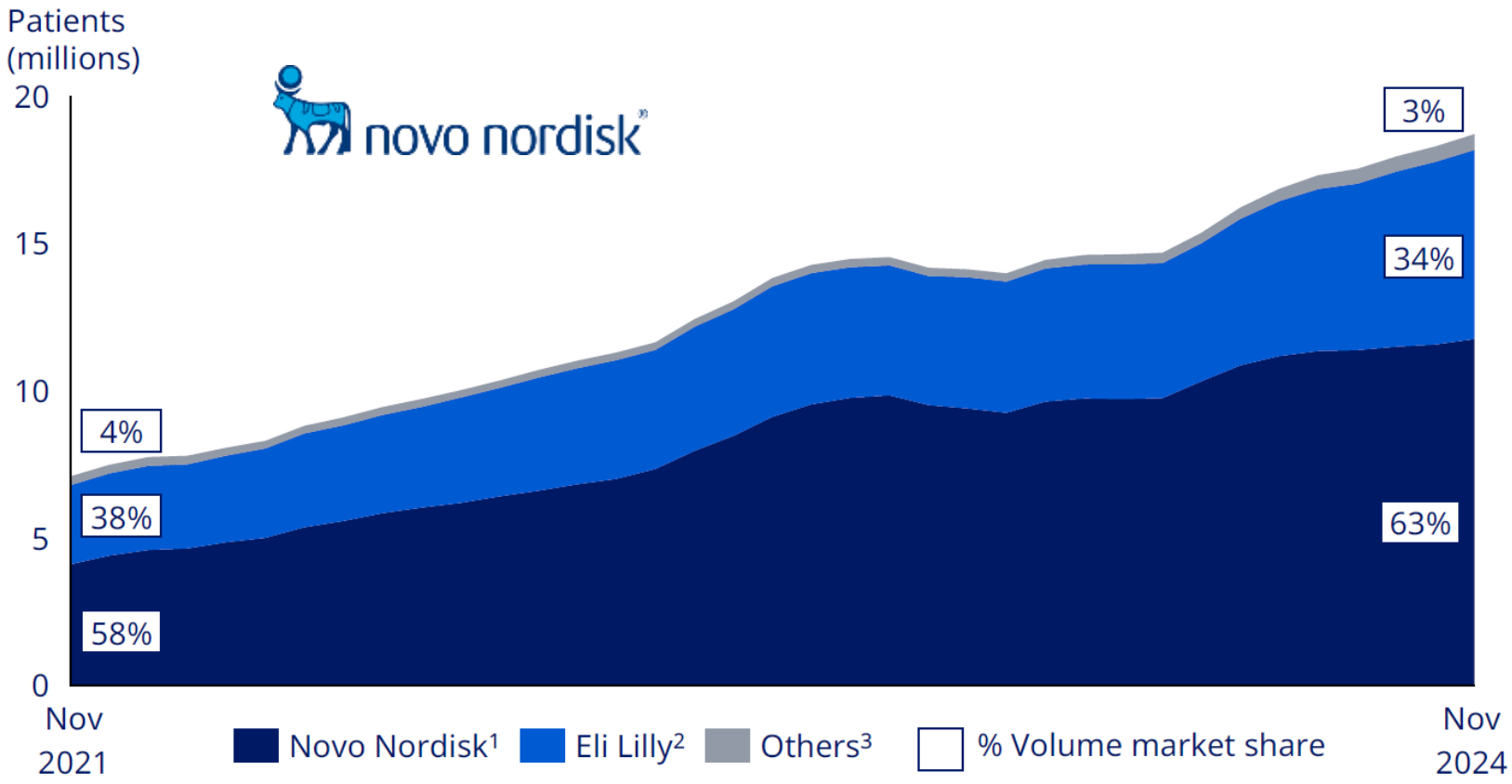


[1]'Other diabetes' is included in total in RHS graph
CER: Constant exchange rates; China: Mainland China, Hong Kong and Taiwan; EMEA: Europe, Middle East and Africa; IO: International Operations; NAO: North America Operations; RoW: Rest of World
Note: Unless otherwise specified, sales growth rates are at CER

Source: https://www.novonordisk.com/content/dam/nncorp/global/en/investors/irmaterial/annual_report/2025/q4-2024-investor-presentation.pdf

Novo Nordisk Has Tripled GLP-1 Patient Reach in 3 Years

Global number of patients on GLP-1s across diabetes and obesity



Novo Nordisk GLP-1 patient reach

- Ongoing scaling efforts has supported almost a tripling of GLP-1 patient reach from ~4m to ~12m over the past 3 years
- Novo Nordisk is the global market leader with a GLP-1 volume market share of 63%

Scaling of capacity

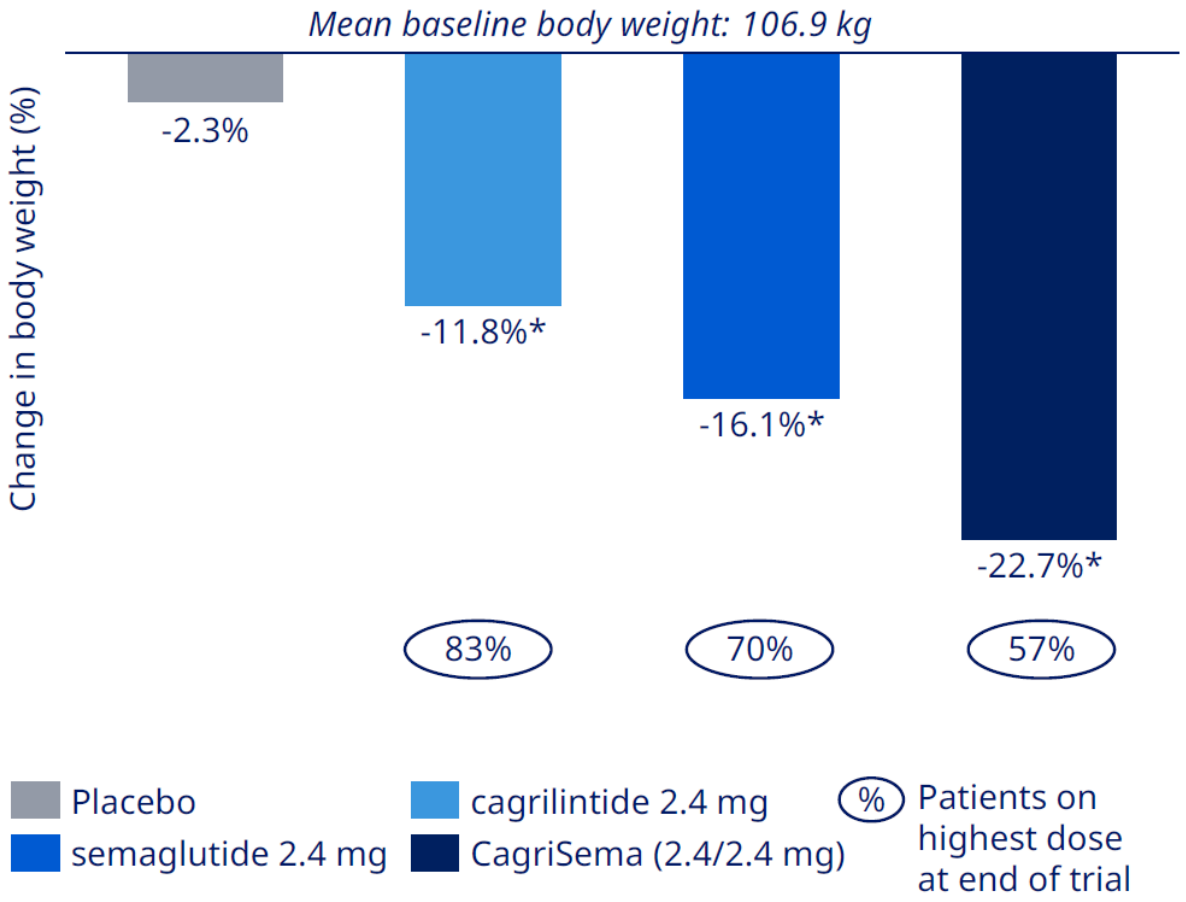
- Several large investment announcements since 2021, totalling more than 130 bDKK
- In December 2024, the Catalent transaction was completed, expanding the Novo Nordisk global fill-finish footprint from 11 to 14 sites

¹Includes liraglutide and semaglutide ²Includes dulaglutide and tirzepatide ³Includes e.g. exenatide
Source: Based on information licensed from IQVIA: IQVIA MIDAS® monthly volume sales data for the period 01.11.2021 to 01.11.2024 (R3M) reflecting estimates of real-world activity.

Source: https://www.novonordisk.com/content/dam/nncorp/global/en/investors/irmaterial/annual_report/2025/q4-2024-investor-presentation.pdf

Novo's CagriSema Demonstrated 22.7% Weight Loss in REDEFINE 1

CagriSema demonstrated superior weight loss at week 68[1]



CagriSema appeared to have a safe and well-tolerated profile

Observed gastrointestinal adverse events per patient per year

CagriSema 2.4 mg/2.4 mg	Cagrillintide 2.4 mg	Semaglutide 2.4 mg
2.8	1.2	2.6

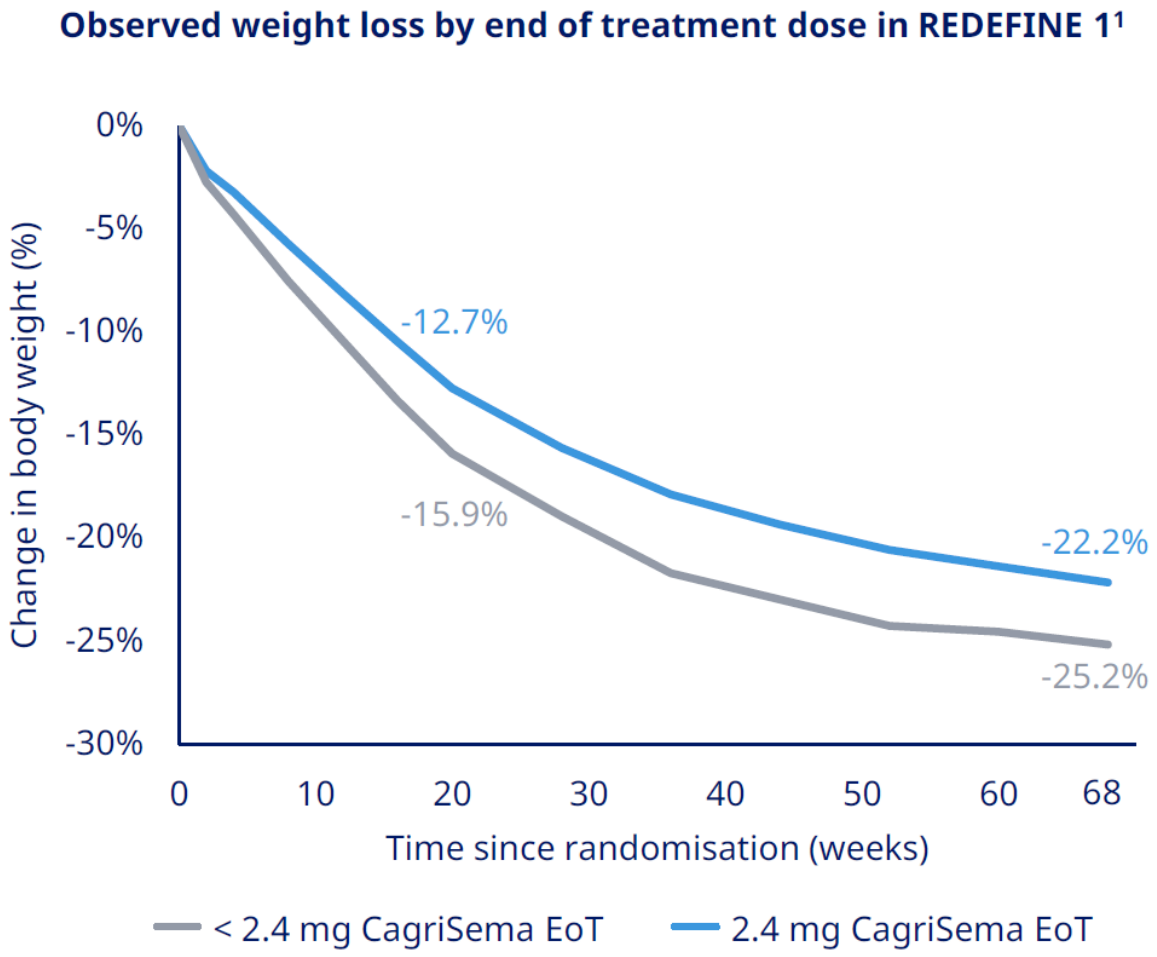
Discontinuation percentage due to GI adverse events

CagriSema 2.4 mg/2.4 mg	Cagrillintide 2.4 mg	Semaglutide 2.4 mg
3.6%	1.3%	1.3%

*Statistically significant [1]Based on the trial product estimand
AE: Adverse Events; CagriSema; cagrilintide 2.4 mg and semaglutide 2.4 mg; GI: gastrointestinal
Note: Weight loss based on the treatment policy estimand in REDEFINE 1: CagriSema: 20.4%, cagrilintide 2.4 mg: 11.5%, semaglutide 2.4 mg: 14.9% and placebo: 3.0%

Source: https://www.novonordisk.com/content/dam/nncorp/global/en/investors/irmaterial/annual_report/2025/q4-2024-investor-presentation.pdf

Further CagriSema Weight Loss Potential to be Investigated by Exploring a Longer Trial Duration and Dose Re-escalation



Patients treated with the highest dose[2] at end of treatment

- Weight loss: 12.7% at week 20, 22.2% at week 68
- Tolerability: Average GI AEs per year of 1.9
  - Mean BMI of 30.4 with average dose of 2.4 mg at EoT
- Investigate further weight potential e.g. by longer study duration

Patients treated with lower doses[3] at end of treatment

- Weight loss: 15.9% at week 20, 25.2% at week 68
- Tolerability: Average GI AEs per year of 4.0
  - Mean BMI of 26.5 with average dose of 1.1 mg at EoT
- Dose reductions due to: e.g. GI AEs and BMI of lower normal range
- Investigate further weight loss potential e.g. by dose re-escalation

Correction to the footnote: "[1]Based on the trial product estimand according to the trial protocol, regardless of dose strength…"
Should have been: "[1]Patients are included while on treatment defined until first treatment pause (no trial product for 14 days)…"

[1]Based on the trial product estimand according to the trial protocol, regardless of dose strength. A post-hoc analysis of REDEFINE 1. [2]Highest dose: 2.4 mg/2.4 mg CagriSema. [3]Lower doses: <2.4mg/2.4mg CagriSema.
AE: Adverse events; BMI: Body mass index; CagriSema 2.4mg/2.4mg: cagrilintide 2.4 mg and semaglutide 2.4 mg; GI: Gastrointestinal; EoT: End of treatment.

Source: https://www.novonordisk.com/content/dam/nncorp/global/en/investors/irmaterial/annual_report/2025/q4-2024-investor-presentation.pdf

Ziltivekimab phase 3 development programme targets high unmet need populations within CVD

novo nordisk

ZEUS
ziltivekimab cardiovascular outcomes trial

Atherosclerosis and chronic kidney disease

n = 6,200

R (1:1)
- Ziltivekimab 15 mg sc + SoC
- Placebo sc + SoC

2021 – ~2026

Event driven
~ 4 years

Primary Endpoint:
Time to the first occurrence of 3-point MACE
- Cardiovascular death
- Non-fatal myocardial infarction
- Non-fatal stroke

HERMES
ziltivekimab

HFmrEF and HFpEF

n = 5,600

R (1:1)
- Ziltivekimab 15 mg sc + SoC
- Placebo sc + SoC

2023 – ~2027

Event driven
~ 4 years

Primary Endpoint:
Time to the first occurrence of
- Cardiovascular death
- Hospitalisation for heart failure
- Urgent heart failure visit

ARTEMIS
ziltivekimab in patients with acute myocardial infarction

Acute myocardial infarction

n = 10,000

R (1:1)
- Ziltivekimab 15 mg sc + SoC
- Placebo sc + SoC

2024 – ~2027

Event driven
~ 2.5 years

Primary Endpoint:
Time to the first occurrence of 3-point MACE
- Cardiovascular death
- Non-fatal myocardial infarction
- Non-fatal stroke

Source: https://www.novonordisk.com/content/dam/nncorp/global/en/investors/irmaterial/annual_report/2025/q4-2024-investor-presentation.pdf

We are Poised to Deliver Strong Long-Term Growth

AMGEN

- Revenues increased 19% YoY in 2024, with 10 products delivering at least double-digit sales growth
- Rapidly advancing innovative pipeline with multiple potentially first-in-class and/or best-in-class medicines across our therapeutic areas
- Invested $5.9B* in research and development in 2024, up 25% YoY
- Increased dividend 6% YoY in 2024

Non-GAAP financial measure—if this slide is in hard copy, see reconciliations accompanying the presentation, or if this slide is delivered electronically, see reconciliations available at: www.amgen.com within the Investors section.

Source: https://investors.amgen.com/

IMPORTANT 2025 PIPELINE MILESTONES

GENERAL MEDICINE

MariTide

- MARITIME Phase 3 study initiation(s) H1 2025 to H2 2025
- Phase 2 study data readout in Type 2 diabetes H2 2025
- Phase 2 Part 2 data readout H2 2025

Repatha®

- VESALIUS-CV Phase 3 study data readout H2 2025

Olpasiran

- Phase 3 primary prevention study initiation H2 2025 / H1 2026

RARE DISEASE

TEPEZZA®

- ✓ Japan launch in TED H1 2025
- EU regulatory approval in TED H2 2025

UPLIZNA®

- PDUFA date in IgG4-related disease Apr 3 2025
- Regulatory filing in generalized myasthenia gravis H1 2025

BKEMV™ (SOLIRIS® biosimilar)

- U.S. Launch Q2 2025

INFLAMMATION

TEZSPIRE®

- Regulatory submission in CRSwNP H1 2025
- Phase 3 study initiation in COPD H1 2025

Rocatinlimab

- ROCKET Phase 3 program milestones in atopic dermatitis
  - SHUTTLE H1 2025
  - IGNITE H1 2025
  - ASCEND H2 2025
  - ASTRO H2 2025

WEZLANA™ (STELARA® biosimilar)

- ✓ U.S. Launch Q1 2025

ONCOLOGY

IMDELLTRA™

- Phase 3 study data readout in 2L small cell lung cancer H1 2025

Bemarituzumab

- FORTITUDE-101 Doublet Phase 3 study data readout in 1L gastric cancer H1 2025
- FORTITUDE-102 Triplet Phase 3 study data readout in 1L gastric cancer H2 2025

BLINCYTO®

- Phase 2 study initiation in subcutaneous administration H2 2025

LUMAKRAS® (+ Vectibix®)

- ✓ PDUFA date in KRAS G12c mutated metastatic colorectal cancer 17 Jan 2025

ABP 206 (OPDIVO® biosimilar)

- Phase 3 study data readout H2 2025

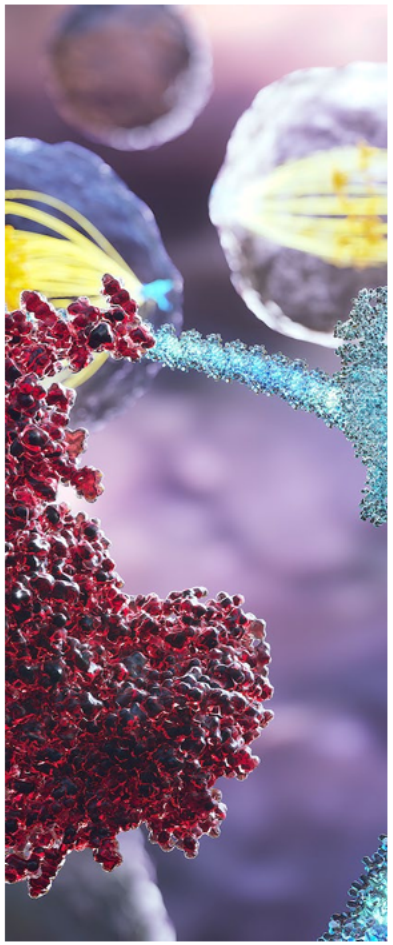
TED = thyroid eye disease; PDUFA = Prescription Drug User Fee Act; IgG4 = Immunoglobulin G4; CRSwNP = chronic rhinosinusitis with nasal polyps; COPD = chronic obstructive pulmonary disease; 2L = second-line; 1L = first-line; KRAS = Kirsten Rat Sarcoma.
Xaluritamig, formerly AMG 509, is being developed pursuant to a research collaboration with Xencor, Inc. TEZSPIRE® is being developed in collaboration with AstraZeneca. Rocatinlimab, formerly AMG 451/KHK4083, is being developed in collaboration with Kyowa Kirin. OPDIVO is a registered trademark of Bristol-Myers Squibb Company. STELARA is a registered trademark of Johnson & Johnson. SOLIRIS is a registered trademark of Alexion Pharmaceuticals, Inc.

Provided February 4, 2025, as part of an oral presentation and is qualified by such, contains forward-looking statements, actual results may vary materially; Amgen disclaims any duty to update.

Source: https://investors.amgen.com/

Remarkable execution across key fundamentals in FY 2024

AstraZeneca



Delivered on upgraded FY 2024 financial guidance

+21% Total Revenue (vs FY 2023)

+19% Core EPS (vs FY 2023)

+14% Core OpEx (vs FY 2023)

9 positive high-value Phase III trial readouts in 2024[1]

Multiple blockbuster opportunities with **combined PYR >$5bn**

8 NME approvals towards ambition of 20 by 2030[2]

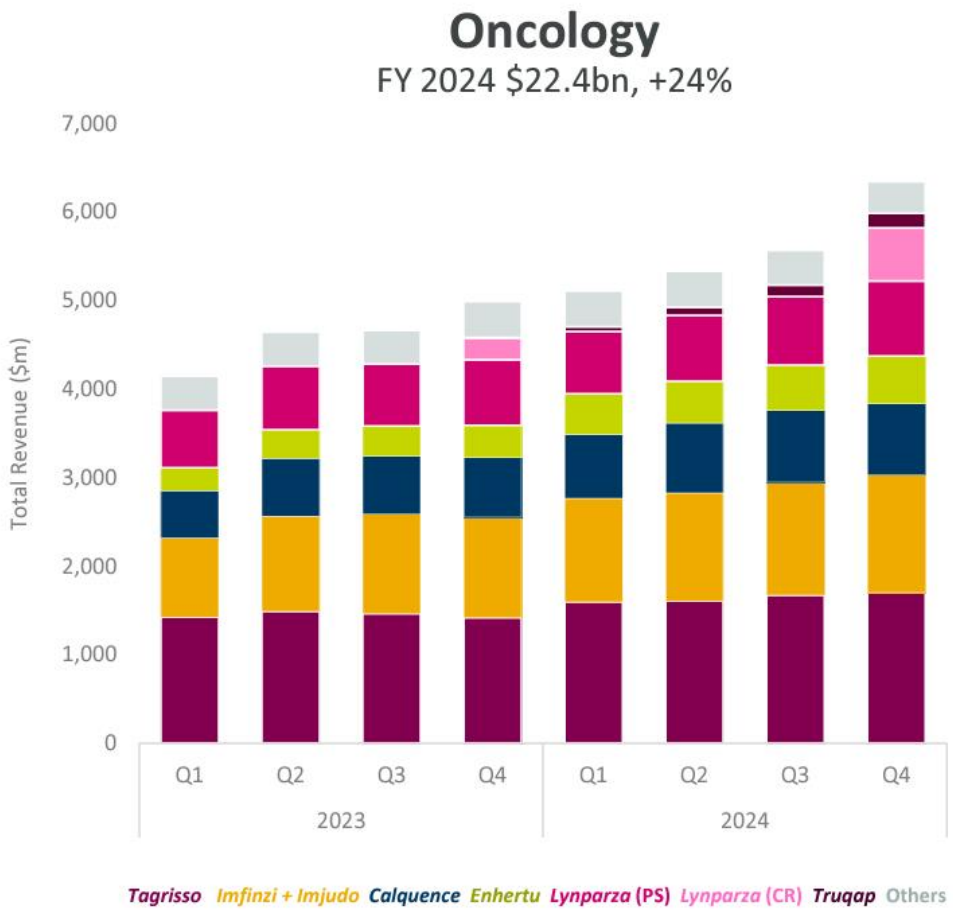
Kavigale DATROWAY

2 NME approvals since Q3 2024

All growth rates at CER. OpEx = Operating Expenses.
1. Full list of 2024 positive high-value Phase III readouts can be found in Appendix. 2. NME ambition tracking from date of first regulatory approval, dated from November 2022. Collaboration partner: Daiichi Sankyo (*Datroway*).
Appendix: Glossary.

Source: https://www.astrazeneca.com/investor-relations/results-and-presentations.html

AZ: Delivering in Oncology



Q4 2024: key dynamics

- ***Tagrisso*** +21%, strong demand across indications, partly offset by hospital ordering dynamic in CN
- ***Calquence*** +20%, sustained BTKi leadership in CLL in US and major markets
- ***Imfinzi*** +18%, strong demand growth in US, EU; continued JP repricing impact
- ***Imjudo*** +28%, durable demand across indications
- ***Lynparza* PS** +15%, sustained global PARPi leadership
- ***Enhertu*** +54%, continued demand across HER2+ and HER2-low breast, partly offset by post-NRDL inventory drawdown in CN
- ***Truqap*** $163m, market leader in 2L biomarker-altered population

- **Significant regulatory progress**: US (*Enhertu* DESTINY-Breast06, *Datroway* TROPION-Breast01, *Calquence* ECHO, *Imfinzi* ADRIATIC), EU (*Tagrisso* LAURA), JP (*Datroway* TROPION-Breast01, *Imfinzi* ± *Lynparza* DUO-E), CN (*Lynparza* OlympiA, *Tagrisso* LAURA, *Orpathys*)
- US Priority Review (*Datroway* TROPION-Lung05, *Imfinzi* NIAGARA)

All growth rates at CER. PS = Product Sales. CR = Collaboration Revenue.
Collaboration partners: Daiichi Sankyo (*Enhertu*, *Datroway*), Merck & Co., Inc. (*Lynparza*).
Appendix: Glossary.

Source: https://www.astrazeneca.com/investor-relations/results-and-presentations.html

Significant progress with transformative technologies to drive 2030+ growth

Weight management and risk factors	ADCs and Radioconjugates	Next-gen IO bispecifics	Cell therapy and T-cell engagers	Gene therapy and gene editing
Establish and lead in new weight management paradigm	Replace systemic chemotherapy and radiotherapy	Replace existing PD-1/ PD-L1 inhibitors	Develop scalable cell therapies and T-cell engagers across therapy areas	Make cure possible for a range of rare diseases
Multiple Phase II dose optimisation trials ongoing **AZD5004 (oGLP-1)** **AZD6234 (LAA)**	*Six ADCs in clinical development, including:* **AZD0901 (CLDN18.2) in Phase III** **FPI-2265 Phase II initiated in pre-treated PSMA-positive mCRPC**	**9 Phase III trials with rilvegostomig and volrustomig initiated** **First ADC combination data be shared this year**	**AZD0120 (BCMA/CD19) CAR-T Phase III planned in multiple myeloma** **AZD0486 (CD19/CD3) Phase III initiated in 1L FL**	*Preclinical and Phase I development ongoing across multiple platforms* **sAAVy and AAV capsid** **TALEN technology**

ADCs/RCs, next-gen IO and cell therapy/TCE progressed to Phase III

Source: https://www.astrazeneca.com/investor-relations/results-and-presentations.html

AZ: Making Two Clinical Bets to Win in the Obesity Market

AZD6234 (long-acting amylin)

AstraZeneca

Approved medicines
Late-stage development
Early development

Obesity with related co-morbidities

Trial	Population	Patients	Design	Endpoints	Status
Phase II APRICUS NCT06595238	Participants living with obesity or overweight with co-morbidity	231	• Randomised, double-blind, placebo-controlled trial	• Primary endpoints: percent change in body weight from baseline to Week 26 and weight loss ≥5% from baseline weight to Week 26	• FPCD: Q4 2024 • Data anticipated: H2 2025
Phase I NCT05511025	Healthy participants who are overweight or obese	64	• SAD trial	• Primary endpoint: safety	• FPCD: Q4 2022 • Data readout: Q1 2024
Phase I NCT06132841	Overweight or obese participants	142	• Randomised, single-blind, placebo-controlled trial with repeated doses of AZD6234 or placebo via s.c. injection	• Primary endpoints: safety and tolerability of repeat doses	• FPCD: Q4 2023 • Data anticipated: 2026

AZD5004 (oral GLP-1 RA)

Late-stage development
Early development

Type 2 diabetes, obesity

Trial	Population	Patients	Design	Endpoints	Status
Phase I NCT06555822	Healthy volunteers	31	• Part A – Arm 1: AZD5004 oral tablet • Part A – Arm 2: placebo oral tablet • Part B: single dose, open label crossover	• Primary endpoints (Part A): safety and tolerability • Secondary endpoints (Part A): PK and PD parameters • Primary endpoint (Part B): PK parameters • Secondary endpoints (Part B): safety and tolerability	• FPCD: Q3 2024 • Data anticipated: H2 2025
Phase I NCT06703658	Healthy volunteers or participants with type 2 diabetes mellitus	36	• SAD: 3 cohorts to receive AZD5004 or placebo tablet • MAD: 1 cohort to receive AZD5004 or placebo tablet • Japan only	• Primary endpoints: safety and tolerability • Secondary endpoints: PK and PD parameters	• FPCD: Q4 2024 • Data anticipated: H2 2025
Phase I NCT06742762	Healthy volunteers or participants with renal impairment	21	• Multi-centre, single-dose, non-randomised, open-label, parallel-group trial	• Primary endpoints: PK parameters • Secondary endpoints: safety and tolerability	• FPCD: Q1 2025 • Data anticipated: H2 2025

Source: https://www.astrazeneca.com/investor-relations/results-and-presentations.html

Pfizer Delivered Nice Topline Earnings Beat for 2024

FY 2024 Revenues and Adjusted[1] Diluted EPS

Revenues

$63.6B

Adjusted[1] Diluted EPS

$3.11

Ex-COVID Products, FY 2024 Revenues Grew 12% Op, Higher than Our Expectations of 9 to 11%

Source: https://s28.q4cdn.com/781576035/files/doc_financials/2024/q4/Q4-2024-Earnings-Charts-FINAL.pdf

2024: Strong Execution in Year of Transformative Changes

Leader in Oncology

- Successful integration of Seagen
- One of largest investments we have made in last decade

Refined commercial model

- Increased focus with split of U.S. & Int'l divisions
- New data-driven deployment of commercial, medical field forces
- Pfizer ranked #1 in 2024 IQVIA U.S. Field Force Ranking report

Transformed our R&D engine

- Created 4 end-to-end units focused on Oncology, Vaccines, Internal Medicine and I&I
- New leadership: Chief Scientific Officer and Chief Strategy and Innovation Officer

Disciplined financial execution

- Progress with expanded margins
- Strategically deployed capital to enhance shareholder value

Reinforced governance

- 2 new Board members with significant experience in financial markets, investment management, and capital allocation

Int'l=International; I&I=Inflammation & Immunology

Source: https://s28.q4cdn.com/781576035/files/doc_financials/2024/q4/Q4-2024-Earnings-Charts-FINAL.pdf

Strong track record of performance since demerger

- Attractive portfolio and pipeline of Specialty Medicines and Vaccines
- Outlooks consistently improving
- Quality of pipeline (FIC/BIC[1]) increased
- Year-on-year delivery sustained
- Profitability improvements made and remain key focus
- Transformed balance sheet and stronger cash generation now evident
- Delivering performance whilst investing for growth

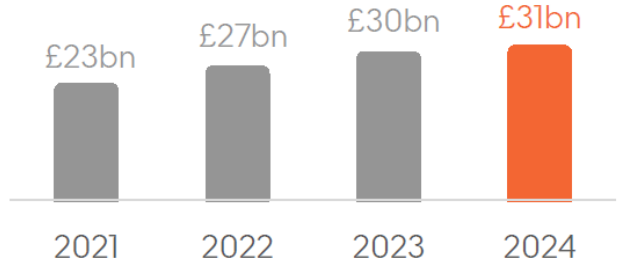
Sales mix shifting

Portion of sales in Specialty and Vaccines[2]

58%
2021

67%
2024

Consistent strong sales growth[6]



Improving Outlooks[3]

2031 sales ambition[2]

>£33bn
2021[4]

>£40bn
2024

Operating margin[6] up 360bps

On track to deliver >31% (2026)

25.6%
2021

29.2%
2024

Late-stage pipeline delivery

17 FDA approvals and filings since 2021[5]

19 assets currently in Ph III

Balance sheet transformation

Net debt

£20bn
2021

£13bn
2024

Source: https://www.gsk.com/en-gb/investors/

1. First-in-class/Best-in-class 2. Excluding COVID-19 solutions 3. All outlook statements are given on a CER basis and use 2024 average exchange rates as a base. 4. Per Investor Update June 2021 5. Includes first US FDA approvals, new indications and submitted filings. Excludes COVID-19 solutions. 6. GSK continuing basis only (Pharma and Vaccines) excluding COVID-19 solutions. 2021 Sales Excluding Covid: £23,291 million (£24,696 million, less £958 million Xevudy and £447 million Pandemic Vaccines)

2025 INGREZZA Net Sales and Expense Guidance

Item ($ Millions)	2024 Actuals	2025 Guidance Range
INGREZZA Net Product Sales[1]	$2,314	$2,500 - $2,600
GAAP R&D Expense[2]	$731	$960 - $1,010
Non-GAAP R&D Expense[2, 3]	$662	$890 - $940
GAAP SG&A Expense[4]	$1,007	$1,110 - $1,130
Non-GAAP SG&A Expense[3, 4]	$863	$955 - $975

1. INGREZZA sales guidance reflects expected net product sales of INGREZZA in tardive dyskinesia and chorea associated with Huntington's disease.
2. R&D guidance reflects the continued advancement of our pre-clinical and clinical portfolio including the initiation of our Phase 3 programs for osavampator in MDD and NBI-568 in schizophrenia. R&D guidance includes $60 million of expense for development milestones primarily in connection with our collaborations with Takeda and Nxera achieved or deemed probable to achieve. Acquired in-process research and development expense is included in guidance once significant collaboration and licensing arrangements have been completed.
3. Non-GAAP guidance adjusted to exclude estimated non-cash stock-based compensation expense of $70 million in R&D and $130 million in SG&A and vacated legacy campus facility costs.
4. SG&A guidance range reflects expense for ongoing commercial initiatives supporting INGREZZA growth and the launch of CRENESSITY.

NEUROCRINE® BIOSCIENCES

Source: https://www.neurocrine.com/investors/webcasts-presentations/

Industry Update

NIH Announces New Funding Policy that Rattles Medical Researchers

NPR, Feb 8, 2025

The National Institutes of Health is capping an important kind of funding for medical research at universities, medical schools, research hospitals and other scientific institutions.

In the latest step by the Trump administration affecting scientific research, the NIH says the agency is limiting funding for "indirect costs" to 15% of grants. That's far below what many institutions have been getting to maintain buildings and equipment and pay support staff and other overhead expenses. For example, Harvard receives 68% and Yale gets 67%, according to the NIH.

The NIH says the new policy, which marks a major change in how the agency funds research, is more in line what private foundations pay.

"Most private foundations that fund research provide substantially lower indirect costs than the federal government, and universities readily accept grants from these foundations," the NIH says in a notification released Friday announcing the change.

"Although cognizant that grant recipients, particularly 'new or inexperienced organizations,' use grant funds to cover indirect costs like overhead...NIH is obligated to carefully steward grant awards to ensure taxpayer dollars are used in ways that benefit the American people and improve their quality of life," the announcement says.

The NIH says the change will apply to both current and future grants, and even suggests the new policy would apply retroactively. But in response to questions Saturday, the Health and Human Services Department, which oversees NIH, told NPR that while HHS does "have the authority to make these changes retrospective for current grants and require grantees to return the excess overhead they have previously received," officials have "currently chosen not to do so to ease the implementation of the new rate." But "we will continue to assess this policy choice and whether it is in the best interest of the American taxpayer."

NIH spent more than $35 billion in 2023 fiscal year on nearly 50,000 grants to more than 300,000 researchers at more than 2,500 universities, medical schools, and other research institutions in the U.S., the agency says. This includes $9 billion for indirect costs.

"This is a surefire way to cripple lifesaving research and innovation," Matt Owens, president of the Council on Government Relations, an association of research universities and academic medical centers, said in a statement. "Reimbursement of facilities and administrative expenditures are part and parcel of the total costs of conducting world class research."

Owens says his organization is "carefully reviewing this policy change as it contradicts current law and policy."

"America's competitors will relish this self-inflicted wound," Owens says. "We urge NIH leaders to rescind this dangerous policy before its harms are felt by Americans."

Those sentiments were echoed by other medical researchers.

"We're all reeling," Dr. George Daley, the dean of the Harvard Medical School, wrote NPR in an email. "This would decimate medical research."

Source: https://www.npr.org/sections/shots-health-news/2025/02/08/g-s1-47383/nih-announces-new-funding-policy-that-rattles-medical-researchers

Katie Britt vows to work with RFK Jr. after NIH funding cuts cause concern in Alabama

Al.com, Feb 9, 2025

Alabama's junior U.S. senator said she will work with President Donald Trump's health secretary nominee Robert F. Kennedy, Jr. to "ensure our nation remains at the forefront" of innovation, research and care after funding cuts announced Friday night by the National Institutes of Health.

"Every cent of hard-earned taxpayer money should be spent efficiently, judiciously, and accountably — without exception," U.S. Sen. Katie Britt said on Saturday. "While the administration works to achieve this goal at NIH, a smart, targeted approach is needed in order to not hinder life-saving, groundbreaking research at high-achieving institutions like those in Alabama," Britt told AL.com.

On Friday night, the NIH announced it was cutting payments toward overhead costs for research institutions that receive its grants, a policy that could leave universities with major budget gaps, The Associated Press reported.

Currently, some universities receive 50% or more of the amount of a grant to put toward support staff and other needs, but that would be capped at 15%, according to AP. The University of Alabama at Birmingham and the University of Alabama in Huntsville are examples of the state institutions that could be affected by the cuts.

Steve Ammons, president of the Birmingham Business Alliance, said he was unsure of the specifics of the cuts, "but certainly any reduction in funding would be a hit to UAB since they were in the top 30 for 2024 for NIH funding. Certainly something we need to watch and make sure we advocate for the state's largest employer."

"People need to be reminded that UAB is not just the largest employer in the city, it's the largest employer in the state," he said. "So as it relates to our state's GDP, as it relates to our economic growth, as it relates to our future around genomics, personalized medicine, and where health care is going, NIH research dollars play a massive, significant role. And without a doubt, without knowing numbers yet, I can tell you this early, just receiving the information, those in the UAB family have a right to be concerned."

Katie Britt
U.S. Senator, Alabama

Source: https://www.al.com/news/2025/02/katie-britt-vows-to-work-with-rfk-jr-after-nih-funding-cuts-cause-concern-in-alabama.html

Major FDA Staff Cuts Would Slow Drug Reviews, Experts Say

Zachary Brennan, *Endpoints News*, Feb 7, 2025 (excerpt)

The Trump administration's reported plans to potentially lay off thousands of FDA employees could slow the agency's reviews of new drugs, experts say, in addition to impacting other core agency functions.

Unlike most federal agencies that are funded entirely with taxpayer dollars, about half of the FDA's current budget is paid for by the biopharma industry and authorized under a law known as the Prescription Drug User Fee Act.

While staff cuts or other significant workforce disruptions via an executive order could ensnare thousands of FDA employees, according to a report by the Wall Street Journal, experts told Endpoints News they don't expect cuts to hit those who are paid by industry user fees. But even a reduction in other FDA staff could still create problems with drug reviews."

If we do see layoffs to this extent, it will cause a massive loss of institutional knowledge and definitely would have an impact on slowing down the work that FDA does," Chad Landmon, chair of Polsinelli's Hatch-Waxman and biologics practice, told Endpoints."

If the government chooses to fire [full-time employees] that were hired per PDUFA, where does the authority reside? I don't know the answer to that," said Peter Pitts, former FDA associate commissioner and current president of the Center for Medicine in the Public Interest.

Source: https://endpts.com/major-fda-staff-cuts-would-slow-drug-reviews-experts-say/

Comments From Amgen's Jay Bradner Last Week

Amgen's Jay Bradner Spoke to investors at Stifel's ski conference last week. Here are some of his comments based on notes we took (no transcript was used).

Q: Any view on the new FDA Commissioner?

No negative view on the new commissioner. I am molecule focused. Not expert enough to have an opinion on matters in Washington. I will say that there are natural limits on what the FDA commissioner can do. There is room for themes. For example, there is room for HHS in preventive health.

Q: To what degree has lower M&A been driven by FTC or has it been driven by other things such as China. How does this unfold over 2025/2026?

There are nuclear winters that have impact. There is a lot of free cash flow and firepower in the top 15 pharmas. If there is a dynamic, it's on the supply side for good fresh ideas. I see a lot of redundancy. After the first CD19 CAR therapy, there was another 200. Best in class is a euphemism for not first in class. A new drug has to be really convincing.

Q: If you look across companies in the gene therapy space, there has been a break from established precedent in accepting new biomarkers and natural history data. Views?

I think it's really exciting, especially in CNS diseases where tissue biomarkers are limited. New biomarkers have to be linked to underlying biology. I am hopeful that this trendline of being open to disease associated biomarkers continues.

Q: Is FDA going to be a predictable institution under the Trump Administration?

Our engagement with regulators has been pretty normal. We have every expectation that we will interact with new leaders in a business as usual and normal way.

Jay Bradner
EVP R&D, Amgen

More Thoughts from Amgen's Jay Bradner

Q: How much does the IRA impact your decisions?

We don't invoke the IRA at the time of portfolio decisions. It is, for sure, antagonistic to innovation. It is hopefully not the last act of our government in its effort to achieve price control. We like that we at Amgen have less exposure to the IRA because we are the world's leading biotherapeutic company. I think it's really sad we have an overhang on value capture on small molecule therapeutics. I do think the IRA reads through to how molecules are evaluated in partnering discussions.

Q: There is investor concern about crowding in obesity? Is this a zero sum game? What's your philosophy?

There is a huge residual unmet need in the obesity market. When you address an unmet need with a new medicine there is value created. People want to be shown succinctly why any particular medicine is so much better. How stock markets react to a dataset is not of interest to physicians. Physicians want to see patients still on medicine, still losing weight – over time. That's what we are focused on with MariTide. Racing to get some massive weight loss number that the markets react to is not our goal. We want steady predictable weight loss – over an extended time. In our second MariTide P3 we are looking at how patients do in year 2 and are using a design to tease out the ability to avoid weight rebound.

Q: How do you think about B cell depletion in autoimmunity?

It's a big opportunity for us. CD19 is on mature and immature B cells. You can imagine that a CD19 should be better than a CD20 – which is mainly on mature cells. The CAR-t data on CD19 in autoimmunity was breathtaking. There is a big opportunity to reposition two Amgen drugs – BLINCYTO and Uplinza for autoimmunity.

Q: What other trends in I&I space interest you?

There are two things I am looking at with high interest. The first is antigen-specific immune tolerance. Then we are at the root cause of autoimmunity. I would focus there. The second is targeting core transcription factors that drive the inflammatory state. The more we can get to state-defining transcription the more precise we can get in treating autoimmune disease. I am following STAT and IRF. There is an important opportunity, for example, to target molecular glues and related means to hit these type of transcription factors.

Novo Nordisk is Feeling the Competition From Compounded GLP-1s, Exec Says

Shelby Livingston, *Endpoints News*, Feb 5, 2025 (excerpt)

Many Americans have flocked to cheaper, compounded versions of GLP-1 weight loss drugs in lieu of brand-name treatments. That competition is cutting into demand for Novo Nordisk's prescriptions, a company exec said Wednesday.

"Our latest market intelligence does tell us and show us that it is having an impact and it is growing faster than we had anticipated," David Moore, Novo's head of US operations, said during the drugmaker's fourth-quarter earnings call.

He was responding to a question about compounded drugs' effects on demand for the company's products. Compounded drugs are copies of brand-name treatments mixed up by pharmacies, and they're typically permitted only when there's a drug shortage.

Over the last couple of years, these pharmacies have seized the opportunity to make alternative versions of semaglutide, the main ingredient in Novo blockbusters Ozempic and Wegovy, as well as tirzepatide, sold by Eli Lilly as Mounjaro and Zepbound, while they've been in shortage.

Novo's acknowledgment of the competition it faces contrasts sharply with Eli Lilly's comments on the subject. During an earnings call in October, Lilly CEO Dave Ricks said the company hadn't seen a financial impact from compounded GLP-1s.

David Moore
Head U.S. Operations, Novo Nordisk

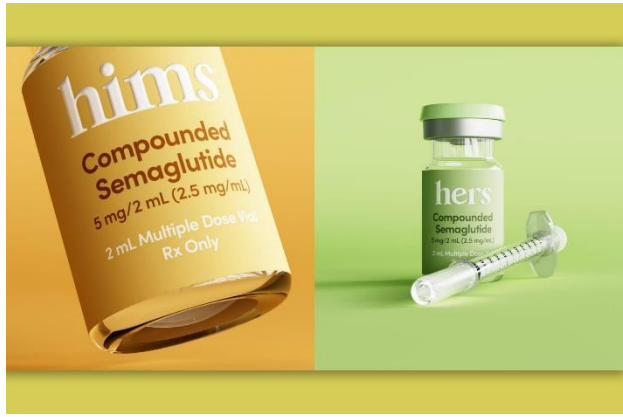
Source: https://endpts.com/novo-nordisk-is-feeling-the-competition-from-compounded-glp-1s-exec-says/

What is Compounded Semaglutide and is it Safe? The Weight Loss Drugs Hims & Hers is Selling, Explained

Nathalie Rahhal, *Yahoo! Life*, Feb 9, 2025 (excerpt)

"They're priced for profits, not patients." That's the critique from Hims & Hers Health's buzzy — and controversial — Super Bowl ad, leveling the accusation against brand-name weight loss drugs. Set to the tune of Childish Gambino's "This Is America," the 60-second spot, which reportedly cost between $14 million and $16 million to air during the big game, is plugging "affordable" versions of these medications, known as compounded GLP-1s (short for "glucagon-like peptide-1").

GLP-1s like Ozempic and Wegovy are expensive, with a month's supply of Ozempic costing around $1,000 without insurance, on average, according to Drugs.com. Hims & Hers' ad takes the issue head-on, but the more affordable solution the company offers falls under murky territory. Cheaper, compounded GLP-1s, often sold by online providers including, in addition to Hims & Hers, Ro, Eden and Weight Watchers, are legal and contain the same active ingredients as their pricier counterparts. But what makes them different is that they aren't regulated by the Food and Drug Administration in the same way as noncompounded medications. Some call these medications "generic Ozempic" (they're not); others, "fake Ozempic" (nope, except when the ads are for illegal or nonexistent drugs). And last year, the FDA issued warnings about the drugs, but they haven't been recalled and remain readily available.



Compounded semaglutide is priced at a discount of 70% to 80% of the branded price and has been tried by as many as 2 million Americans. One way of seeing how big this trend has become is the market cap of Hims & Hers itself: $9.3 billion.

First, what exactly is compounded semaglutide?
Compounded semaglutide is a legal copycat of the active ingredient in Ozempic and Wegovy. Normally, it would be illegal to make generic versions or copies of these medications until the patents for the drugs expire. But in special circumstances, including shortages, compounding pharmacies are permitted to manufacture otherwise protected drugs in order to meet demand.

Compounding pharmacies are required by law to follow the exact recipes provided by brand-name drugmakers when producing copies of their medications. So if all goes well, compounded medications should be identical to the brand-name ones. However, compounded medications aren't regulated with the same FDA testing as others, although these pharmacies are required to use ingredients manufactured by FDA-registered facilities. The second, more obvious distinction between noncompounded semaglutide (the active ingredient in Wegovy and Ozempic) and compounded semaglutide is how the drugs are administered. So compounded semaglutide is sold in a vial with a separate syringe.

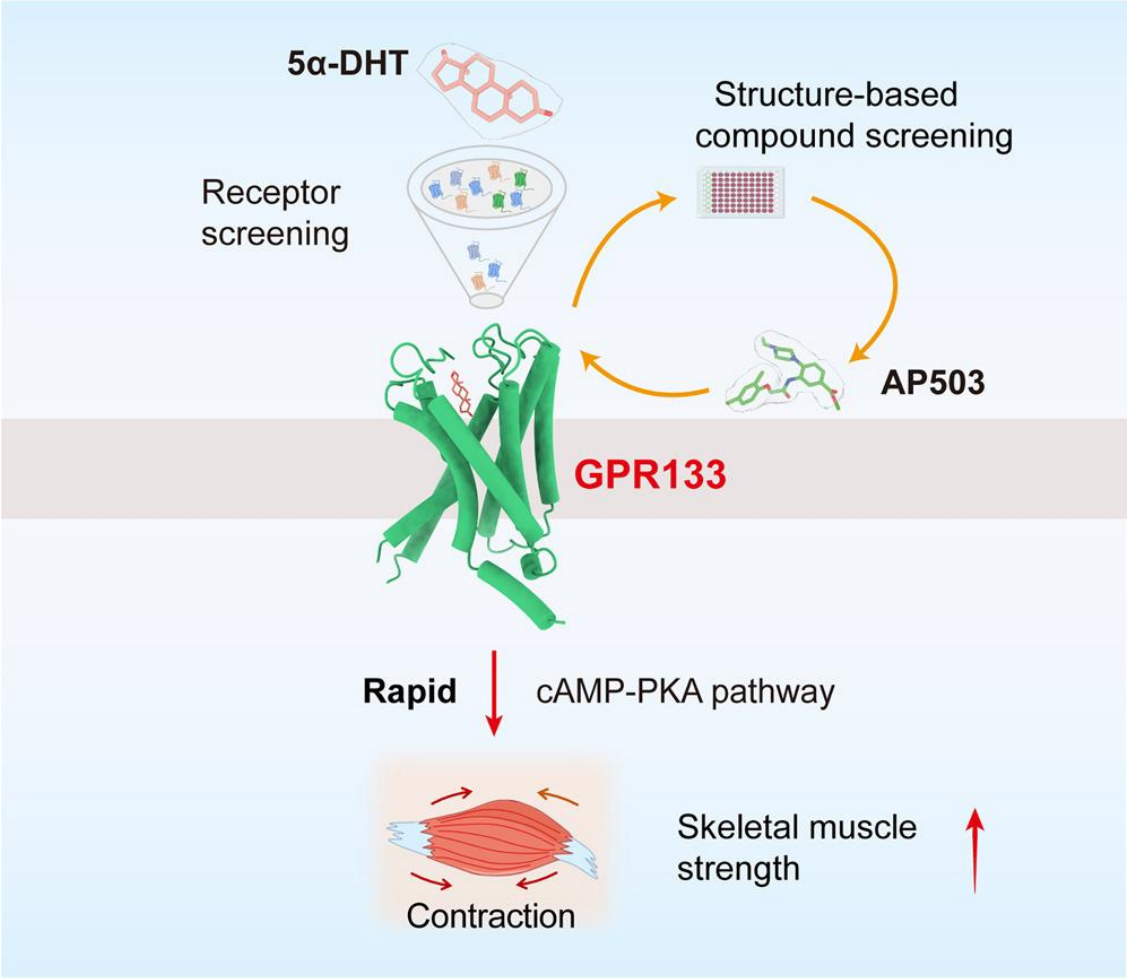
Many people are taking compounded semaglutide. How many is unclear.
It's hard to pin down exactly how many Americans are taking compounded versions of Ozempic and similar drugs because companies prescribing them keep data close to the chest. A poll last year estimated that as many as 1 in 8 Americans had taken some form of these blockbuster drugs, but didn't differentiate between FDA-approved and compounded medications. The CEO of one large compounding company, Olympia Pharmaceuticals, told CBS News that some 2 million Americans are taking drugs made by firms like his.

Source: https://www.yahoo.com/lifestyle/what-is-compounded-semaglutide-and-is-it-safe-the-weight-loss-drugs-hims--hers-is-selling-explained-221410889.html

Identification, Structure, and Agonist Design of an Androgen Membrane Receptor

Yang et.al., *Cell*, Jan 29, 2025 (excerpt)

Androgens, such as 5α-dihydrotestosterone (5α-DHT), regulate numerous functions by binding to nuclear androgen receptors (ARs) and potential unknown membrane receptors. Here, we report that the androgen 5α-DHT activates membrane receptor GPR133 in muscle cells, thereby increasing intracellular cyclic AMP (cAMP) levels and enhancing muscle strength. Further cryoelectron microscopy (cryo-EM) structural analysis of GPR133-Gs in complex with 5α-DHT or its derivative methenolone (MET) reveals the structural basis for androgen recognition. Notably, the presence of the "Φ(F/L)2.64-F3.40-W6.53" and the "F7.42××N/D7.46" motifs, which recognize the hydrophobic steroid core and polar groups, respectively, are common in adhesion GPCRs (aGPCRs), suggesting that many aGPCRs may recognize different steroid hormones. Finally, we exploited in silico screening methods to identify a small molecule, AP503, which activates GPR133 and separates the beneficial muscle-strengthening effects from side effects mediated by AR. Thus, GPR133 represents an androgen membrane receptor that contributes to normal androgen physiology and has important therapeutic potentials.

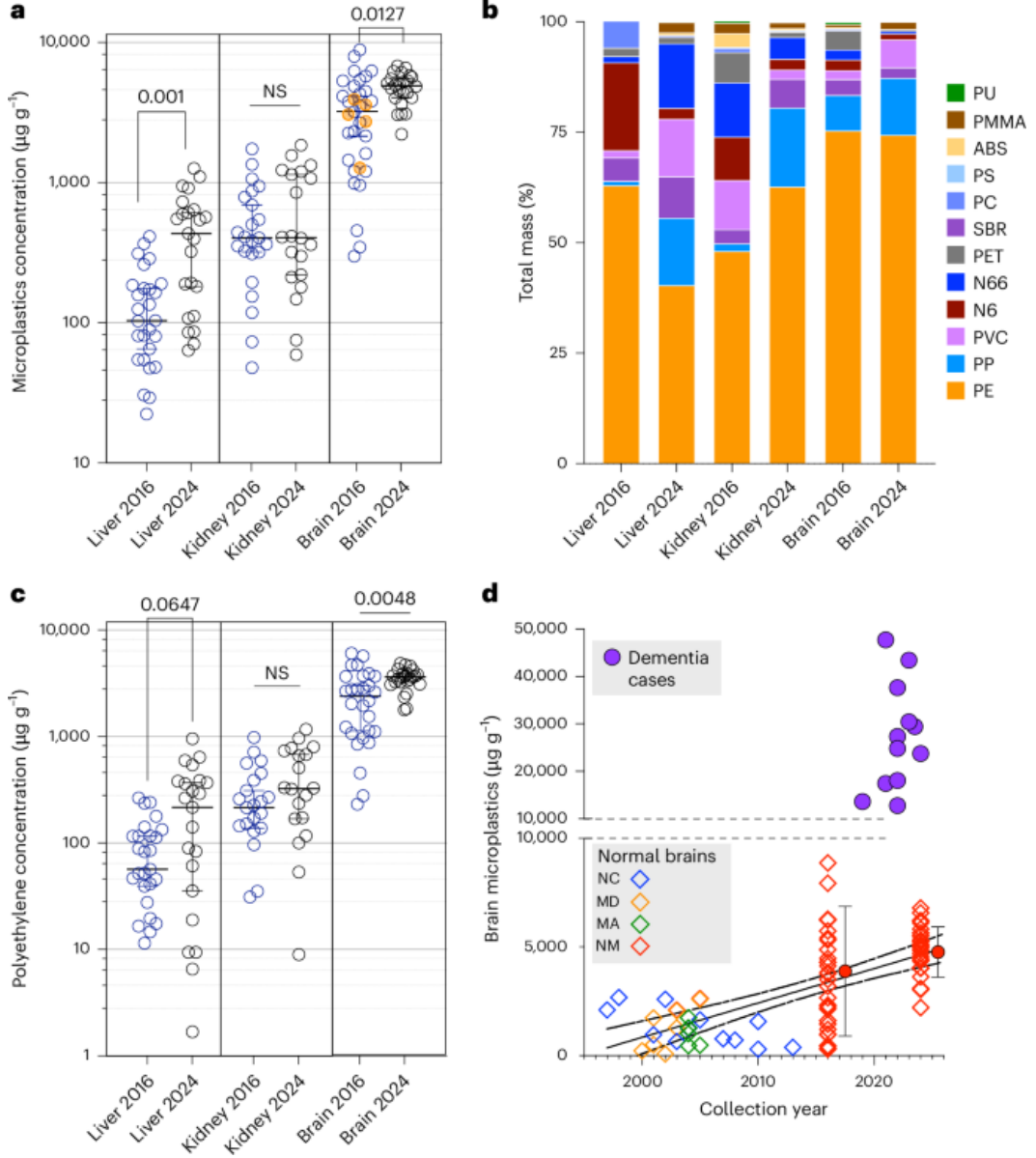


Source: https://www.cell.com/cell/abstract/S0092-8674(25)00035-2

Bioaccumulation of Microplastics in Decedent Human Brains

Nihart et.al., *Nature Medicine*, Feb 3, 2025 (excerpt)

Rising global concentrations of environmental microplastics and nanoplastics (MNPs) drive concerns for human exposure and health outcomes. Complementary methods for the robust detection of tissue MNPs, including pyrolysis gas chromatography-mass spectrometry, attenuated total reflectance-Fourier transform infrared spectroscopy and electron microscopy with energy-dispersive spectroscopy, confirm the presence of MNPs in human kidney, liver and brain. MNPs in these organs primarily consist of polyethylene, with lesser but significant concentrations of other polymers. Brain tissues harbor higher proportions of polyethylene compared to the composition of the plastics in liver or kidney, and electron microscopy verified the nature of the isolated brain MNPs, which present largely as nanoscale shard-like fragments. Plastic concentrations in these decedent tissues were not influenced by age, sex, race/ethnicity or cause of death; the time of death (2016 versus 2024) was a significant factor, with increasing MNP concentrations over time in both liver and brain samples (P = 0.01). Finally, even greater accumulation of MNPs was observed in a cohort of decedent brains with documented dementia diagnosis, with notable deposition in cerebrovascular walls and immune cells. These results highlight a critical need to better understand the routes of exposure, uptake and clearance pathways and potential health consequences of plastics in human tissues, particularly in the brain.



a, Microplastic concentrations in liver, kidney and brain decedent human samples (n = 20–28 separate participants for each timepoint; Supplementary Table 1) from the UNM OMI. Data are shown on a log10 scale, with the bar representing the group median value and 95% confidence interval. Orange-colored symbols in the 2016 brain samples were analyzed independently at Oklahoma State University. P values from Mann–Whitney tests (two-sided) indicate significant differences in samples from the same organ between 2016 and 2024 (with more comprehensive statistical treatments in Supplementary

Source: https://www.nature.com/articles/s41591-024-03453-1

Disclosure

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