Biopharma Market Update

Feb 24, 2025

STIFEL | Healthcare

Table of Contents

STIFEL | Healthcare

Past Issues

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Feb 10, 2025 (Pharma Earnings)
Jan 27, 2025 (Women's Health, Obesity)
Jan 8, 2025 (Biotech Outlook)
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 15, 2024 (Halftime Report)
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)
Jan 22, 2024 (AI in medicine)
Jan 5, 2024 (Sector Outlook for 2024)
Dec 18, 2023 (Expectations for Future)
Dec 11, 2023 (ASH, R&D Days)
Dec 4, 2023 (Big Pharma, CEA)
November 22, 2023 (Bullish on Biotech)
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)
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

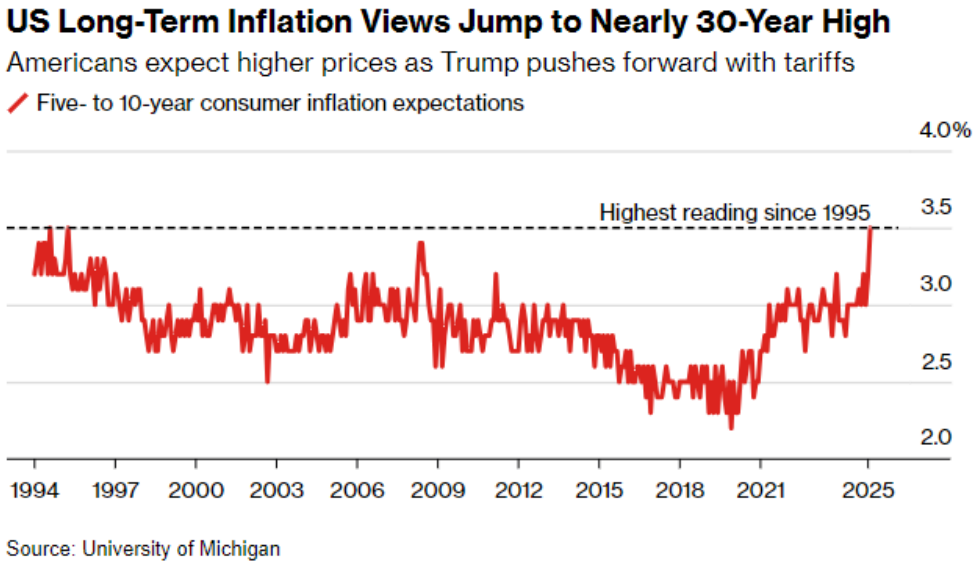
US Consumers Long-Run Inflation Views Rise to Highest Since 1995

Jarrell Dillard and Augusta Saraiva, *Bloomberg*, Feb 21, 2025 (excerpt)

US consumers' long-term inflation expectations rose to the highest level in almost three decades on concerns President Donald Trump's tariffs will translate into higher prices.

Consumers expect prices will climb at an annual rate of 3.5% over the next five to 10 years, according to the final February reading from the University of Michigan. The rate is the highest since 1995, based on data compiled by Bloomberg, and was almost entirely driven by views among survey respondents who are Democrats.

Partly as a result, the consumer sentiment index dropped to 64.7 from 71.7 in January — lower than analysts anticipated.



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

There is increasing evidence that there will be some increases in tariffs. Consumers view this as inflationary.

As a result, consumer expectations of inflation in the economy have dramatically shifted.

This is not a *good* thing for biotech because inflationary expectations can become self-sustaining.

Source: https://www.bloomberg.com/news/articles/2025-02-21/us-consumer-sentiment-drops-as-long-run-inflation-views-rise

Dow Tumbles More than 700 Points as Inflation and Tariff Fears Mount

David Goldman, *CNN*, Feb 21, 2025 (excerpt)

US stock markets fell sharply Friday after an economic report showed American consumers are growing increasingly fearful of price increases and how President Donald Trump's tariffs could reignite the inflation crisis.

The Dow Jones Industrial Average fell 748 points, or 1.7%. The broader S&P 500 also sank 1.7% and the Nasdaq was 2.2% lower. The Dow tumbled for the second consecutive day, falling about 1,200 points over the course of Thursday and Friday.

The University of Michigan's latest survey, released Friday, showed that US consumer sentiment declined in February for the second consecutive month, according to a final reading, down by a steep 10% from January. That was double the decline initially reported earlier this month.

A new CNN poll released Thursday similarly showed pessimism on the rise because of prices: Nearly two thirds of US adults nationwide, 62%, said they feel Trump isn't doing enough to address inflation. The Michigan survey showed that Americans are now fearful of higher inflation on the horizon.

Investors grew fearful that weak consumer sentiment could lead to a pullback in Americans' shopping habits. Consumer spending makes up more than two-thirds of the US economy.

Also dragging down stocks was UnitedHealth, a key Dow component, which sank 7% on a Wall Street Journal report that the US Department of Justice is investigating the company for its Medicaid billing practices. The company strongly denied the Journal's report.

Source: https://www.cnn.com/2025/02/21/investing/stock-market-dow-jones/index.html

Fed's QT pause, Treasury's debt plans may offer fleeting relief to US bonds

Davide Barbuscia, *Reuters*, Feb 21, 2025 (excerpt)

NEW YORK, Feb 21 (Reuters) - A potential slowdown of the Federal Reserve's balance sheet drawdown and Treasury Secretary Scott Bessent's assurance against imminent long-term debt hikes could offer relief in the near term to bond market jitters as fiscal concerns linger.

Fed minutes from the January 28-29 rate-setting meeting released this week showed officials weighed a possible pause or slowdown of the Fed's balance sheet reduction, known as quantitative tightening (QT), as a binding government debt cap could complicate the central bank's ability to gauge market liquidity. Meanwhile, Bessent said in an interview with Bloomberg Television on Thursday that, for now, expanding long-dated government debt issuance is not on the table.

Treasury yields, which move inversely to prices, declined after the Fed minutes on Wednesday and Bessent's interview injected further optimism pushing yields lower on Thursday.

Still, his remarks did not disrupt market expectations of increased government debt, as investors and analysts anticipate the Treasury will eventually need to borrow more to offset a drop in government revenues from President Donald Trump's proposed tax cuts.

Brij Khurana, a fixed-income portfolio manager at Wellington Management, said it was encouraging to have a Treasury Secretary "who is mindful of the funding costs." Bessent said earlier this month the focus of the Trump administration was to contain the benchmark 10-year Treasury yields.

"The push and pull here is that on one side you have what looks to be a meaningful increase in deficit spending from the tax deal, and on the other side there's potentially ... some savings to be found from DOGE, maybe some budget cuts," said Brian Kennedy, a portfolio manager at Loomis, Sayles & Company.

Source: https://www.reuters.com/markets/rates-bonds/feds-qt-pause-treasurys-debt-plans-may-offer-fleeting-relief-us-bonds-2025-02-21/

Trump Wants to Bring Down Treasury Yields. Here's What to Know.

Sam Goldfarb, *Wall Street Journal*, Feb 16, 2025 (excerpt)

Forget the Federal Reserve. To lower borrowing costs for Americans, the Trump administration says it is going to cut spending and increase energy production.

Although President Trump continues urging the Fed to reduce short-term interest rates, Treasury Secretary Scott Bessent has suggested recently that both he and Trump are focusing less on the central bank and more on bringing down the key rate set by financial markets: the yield on the 10-year Treasury note.

The task isn't easy. A benchmark for rates on everything from mortgages to corporate bonds, the 10-year yield shifts with market and economic forces largely beyond the control of the White House. Yields on Treasurys fall when their prices rise, so any effort to lower them would either need to reduce government borrowing—thereby decreasing the supply of bonds—or make U.S. debt more appealing to investors.

Here is a look at how Trump might try to accomplish those things and what he's up against.

How could a president bring down yields?
The most obvious way that presidents can move Treasury yields is through fiscal policy. A smaller budget deficit means less government borrowing and a reduced supply of new Treasurys. That can push up the prices of existing bonds, driving their yields lower.

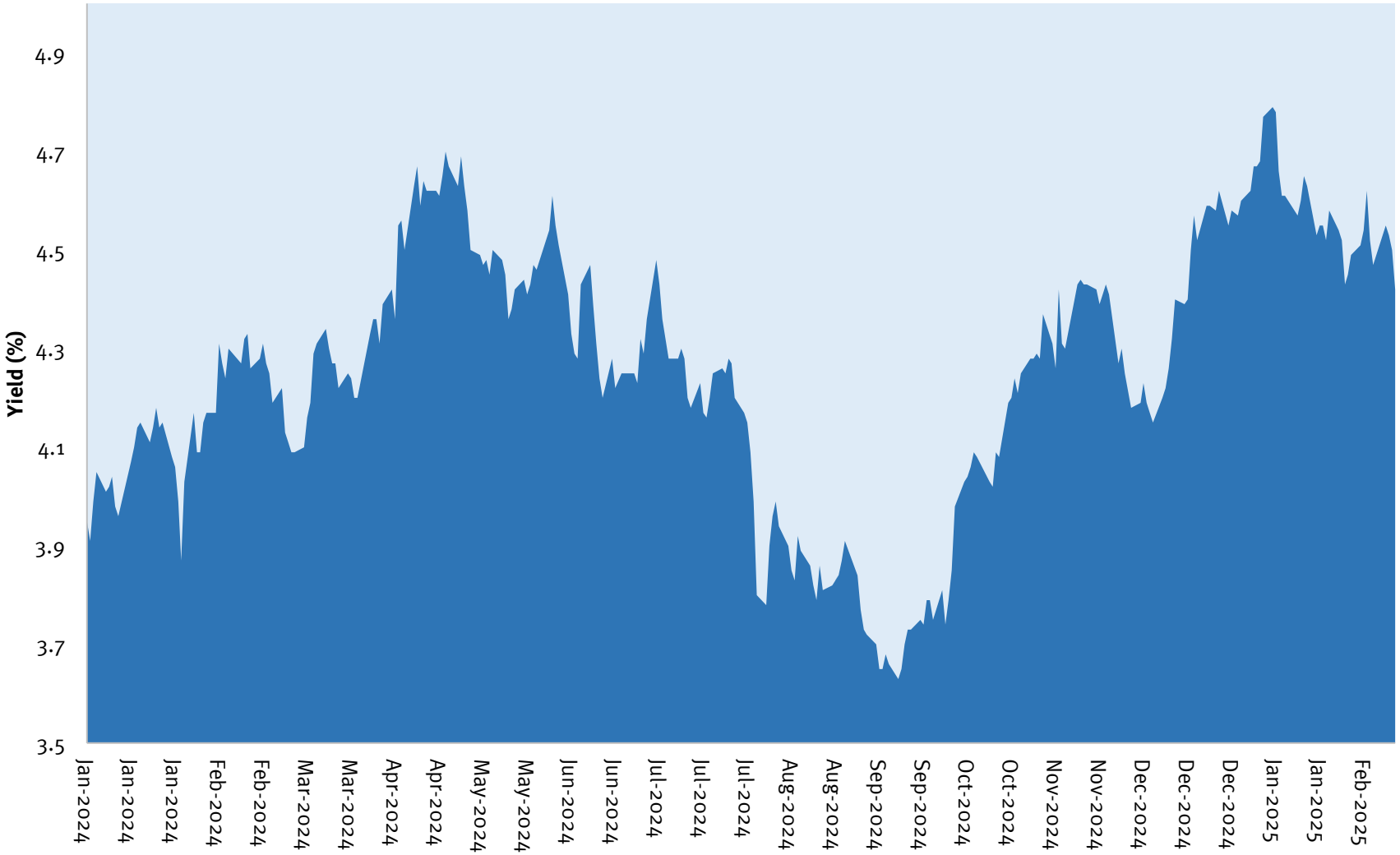
Bessent recently leaned into this idea in an interview with Bloomberg Television, arguing that the 10-year yield could decline if the Elon Musk-led Department of Government Efficiency is able to reduce government spending.

Republicans over decades have shown that "we like spending—we just wanted to raise it less, the Democrats want to raise it more," Bessent said. But, he added, "what if it actually goes down because of everything we're doing right now?"

Source: https://www.wsj.com/economy/10-year-treasury-yields-bonds-trump-explained-d988bd4e

U.S. Treasury Bond Yields Starting to Come Down

United States Treasury 10 Year Yield, Jan 1, 2024 to Feb 21, 2025



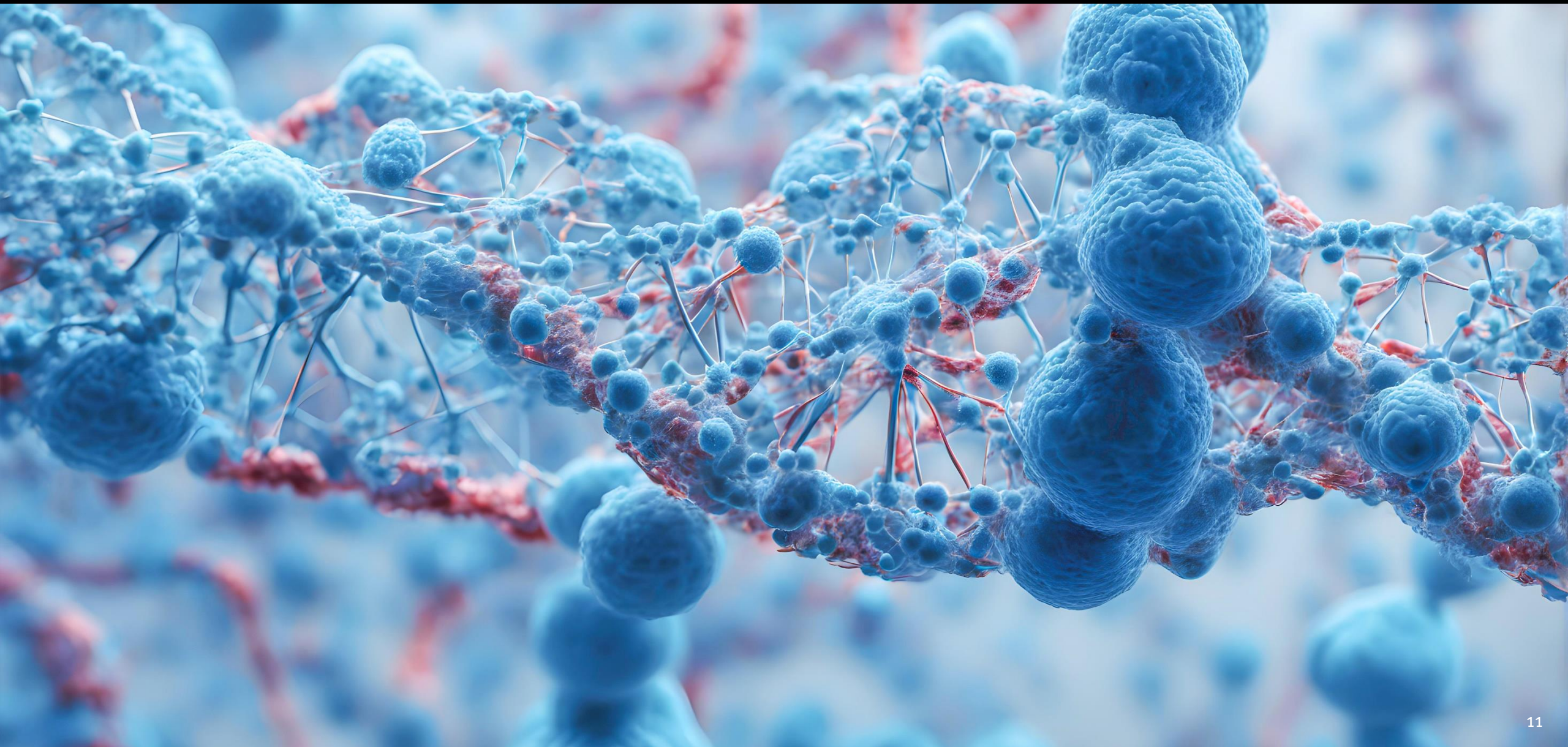
10-year US Treasury yields started to come down a month ago as it becomes clear that the Trump Administration is serious about control of fiscal deficits.

In total the yield has fallen by 35 basis points since Jan 12th. This is a positive for biotech.

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



Investors Focused on Fundamentals

We have spoken to a half dozen or so leading public investors in the last two weeks and can report that biotech sentiment on the public side isn't great.

While bargains abound, investors are concerned about Trump Administration signals on using the IRA and the industry's political position.

Last week's Black History Month event at the White House where Pfizer's CEO was booed by the crowd shows that the populace remains ambivalent towards pharma and the healthcare industry more broadly. With a bill in Congress to allow Americans to import drugs from Canada, investors are acutely aware of the industry's political fragility.

The recent M&A (aka "takeunder") of Bluebird hasn't exactly boosted investor confidence in the last week.

One investor spoke about the importance of being on top of breaking science and figuring out which companies will be successful. The specialist investor appears to be responding to the current environment by becoming even more specialized.

Another investor last week spoke of the importance of the excellent drug launches we are seeing these days from emerging biopharma.

One specialist investor attributed the lack of generalist interest in biotech to the availability of China molecules.f

Fund Redemptions Behind Us

Traditionally, hedge funds give their limited partners a specific time window in which they can withdraw their investments.

Hedge fund withdrawals are a normal part of business and can be accompanied by seeing other investors put money in.

However, because biotech has underperformed the S&P 500 for two years running, it has not been surprising to see multiple funds experience an imbalance of withdrawals.

This has been accentuated by a relatively poor performance of some well-known hedge funds in the industry.

According to recent media reports, at least one prominent fund has had to give their withdrawing LP's "IOU's" (promises to pay later) – essentially gating withdrawal.

The problem with this is that if there are forced sellers in the market due to heavy fund outflows, one can see fear spread in the market as fundamentals cease to matter.

Our previously discussed belief is that exactly this sort of phenomenon played out last December and into the first few weeks of 2025.

Our conversations with LP's in recent weeks indicate that outflows have halted and, if anything, money is going into funds.

Fund redemption time is behind us.

This perspective is supported by the numbers (reported shortly) which showed that last week was the second best for biotech so far this year. We saw both the XBI and the Stifel Total Global Biotech tracker turn positive for the year by the end of last week.

We Remain Early in the Recovery

We are hearing a somewhat different message from generalists.

Specifically, generalists are saying “show me the money.” Investors want to see commercial success. There appears to be a gradual shift from the imperative of “guess which companies will get bought” to “buy into companies that can generate revenue and cash flow.” This renewed interest in fundamentals strikes us as healthy.

Our own view is that we remain quite early in a classic sector recovery. The historical analogue of the Reagan Administration resonates with us. While Reagan entered office Jan 1981, the market did not start to really move up until late 1983. The nagging uncertainties associated with inflation, foreign policy issues and high gas prices continued to hold back the market. Reagan faced strong opposition, resistance and skepticism from the market. The U.S. was highly polarized at the time.

But eventually, Springtime hit with the Crocuses piercing snow and soon enough it was high Summer.

While history never quite repeats, we think the analogue is highly relevant today. If Trump can successfully lower taxes, reduce regulation and trim Federal spending, we should see quite a healthy capital market emerge – with all the positives for the 1biopharmaceutical sector.

But, as before, it is going to take time for a strong recovery to take hold.

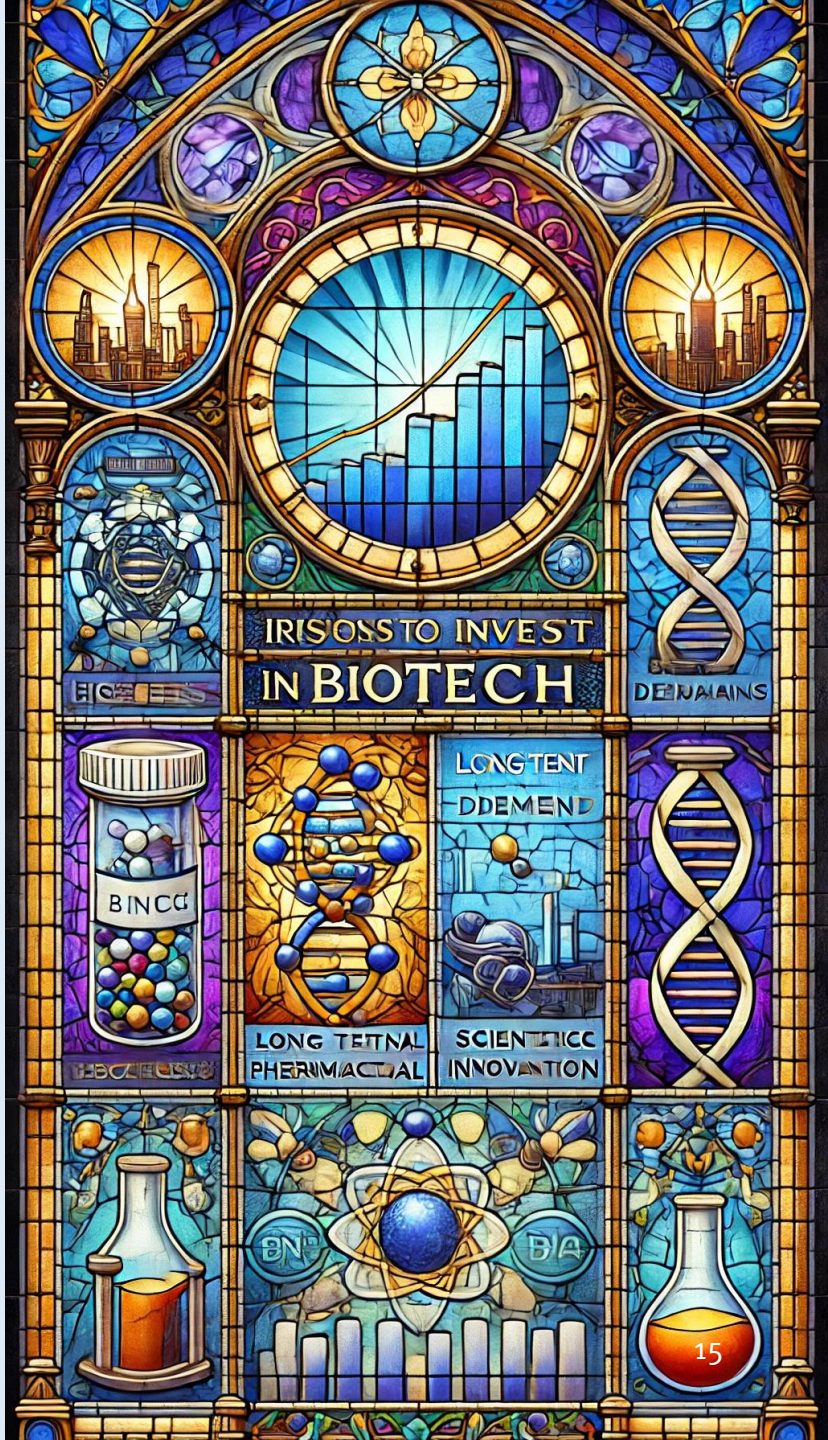
But do not doubt. A recovery will come. And its presence will be unmistakable. Our industry continues to enjoy very strong fundamentals and now is a very good time for bargain-minded investors to back high potential biotech companies.that

The Biotech Catechism

There are obviously more than a few biotech doubters in the market at present. It never hurts to review the excellent reasons to own biotech for the long run. These factors were detailed in a report we issued in 2023:

1. The biopharma sector has outperformed the S&P 500 for more than 50 years. Further, biotech, the phrase we use for emerging biopharma, is up more than twenty-fold in the last 30 years.
2. The factors that drove this surprisingly good performance are even more relevant for the future:
    a) Spend on pharma is going to rise rapidly over time in real terms. This is because pharma spend accelerates with rising incomes – and real global income keeps rising. Further, there is the "longevity dividend". That is, the more longevity is created by pharmaceuticals, the more demand is created for pharmaceuticals because illness persists. The fraction of the social budget spent on pharmaceuticals has increased fivefold in the last century and is likely to continue increasing.
    b) The pace of underlying scientific innovation and translatability of science to drugs is accelerating as the inevitable result of the Scientific Enlightenment that started in the early 1600's. The long-term buildup of knowledge upon knowledge is both irreversible and accelerating. That is, the more we learn, the more quickly we can learn – up to a point, of course. The revolution in genetics and molecular biology is making even easier to design appropriate therapeutics.
    c) The extent of opportunities for high value, civilization-changing innovation in areas such as obesity, neuroscience and aging is rising over time.
3. Macroeconomic trends are highly favorable:
    a) The current Administration is pursuing anti-inflationary policies. There is a determination to manage down the long bond yield and to reduce spend. This is hugely positive for long duration biotech.
    b) The Federal Reserve has raised rates considerably over a period of three years. There is a substantial policy lag for this to take effect and historical timing would suggest that both 2025 and 2026 will very likely see the fruits of higher rates in the form of lower inflation.

An important theme is that the political process will ultimately reflect underlying free market forces. We live in a capitalist society – where business interests ultimately drive politics. That is, if our society can produce an accelerating innovation curve and long-term income growth then the political process will follow. This is the ultimate reason not to worry too much about today's highly visible political theatrics.



The XBI Closed at 91.7 Last Friday (Feb 21), Flat for the Week

The Stifel Global Biotech Value Tracker rose by 1.7% - much more than the XBI (up 0.3%). Treasury yields fell. The XBI is up 2% 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: Feb 14 to Feb 21, 2025

Nasdaq Biotech Index: +1.5%
Arca XBI ETF: +0.3%
Stifel Global Biotech EV (adjusted): +1.7%*
S&P 500: -1.7%

Return: Dec 31, 2024 to Feb 21, 2025 (YTD)

Nasdaq Biotech Index: +6.5%
Arca XBI ETF: +1.8%
Stifel Global Biotech EV (adjusted): +1.3%*
S&P 500: +2.2%

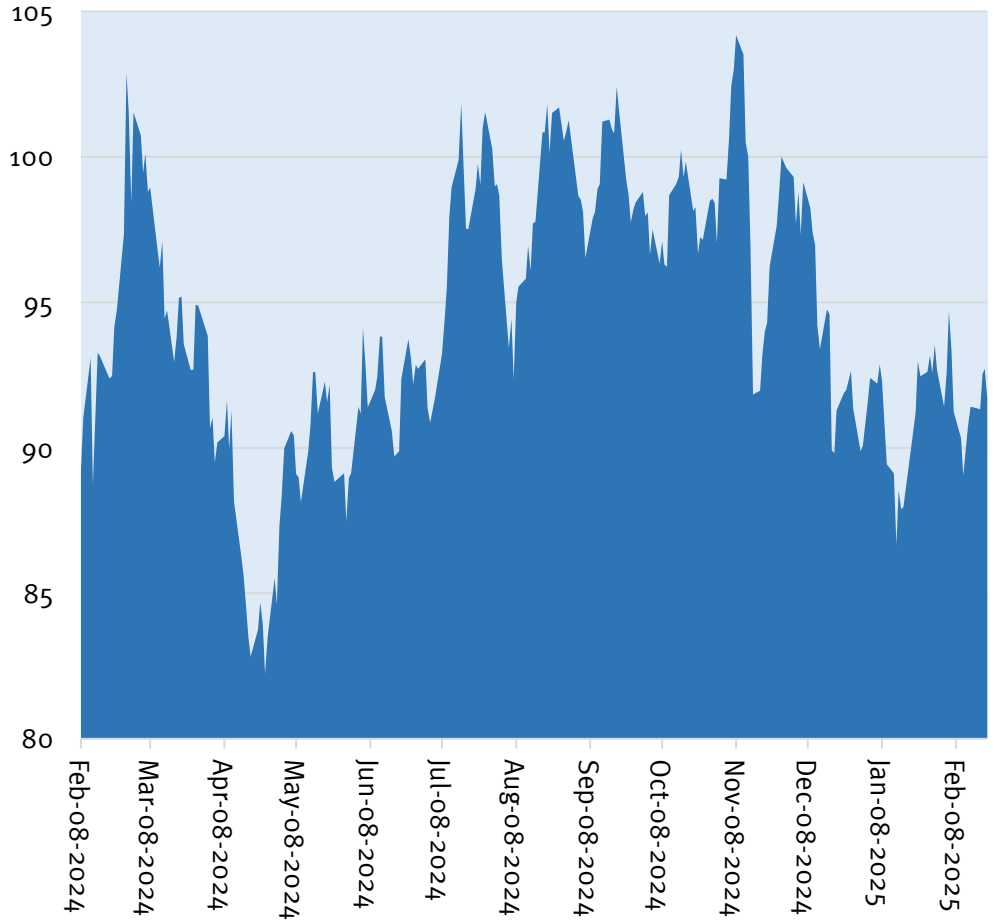
VIX Up

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%
Feb 21, 2025: 18.2%

10-Year Treasury Yield Flat

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%
Feb 21, 2025: 4.4%

XBI, Feb 8. 2024 to Feb 21, 2025

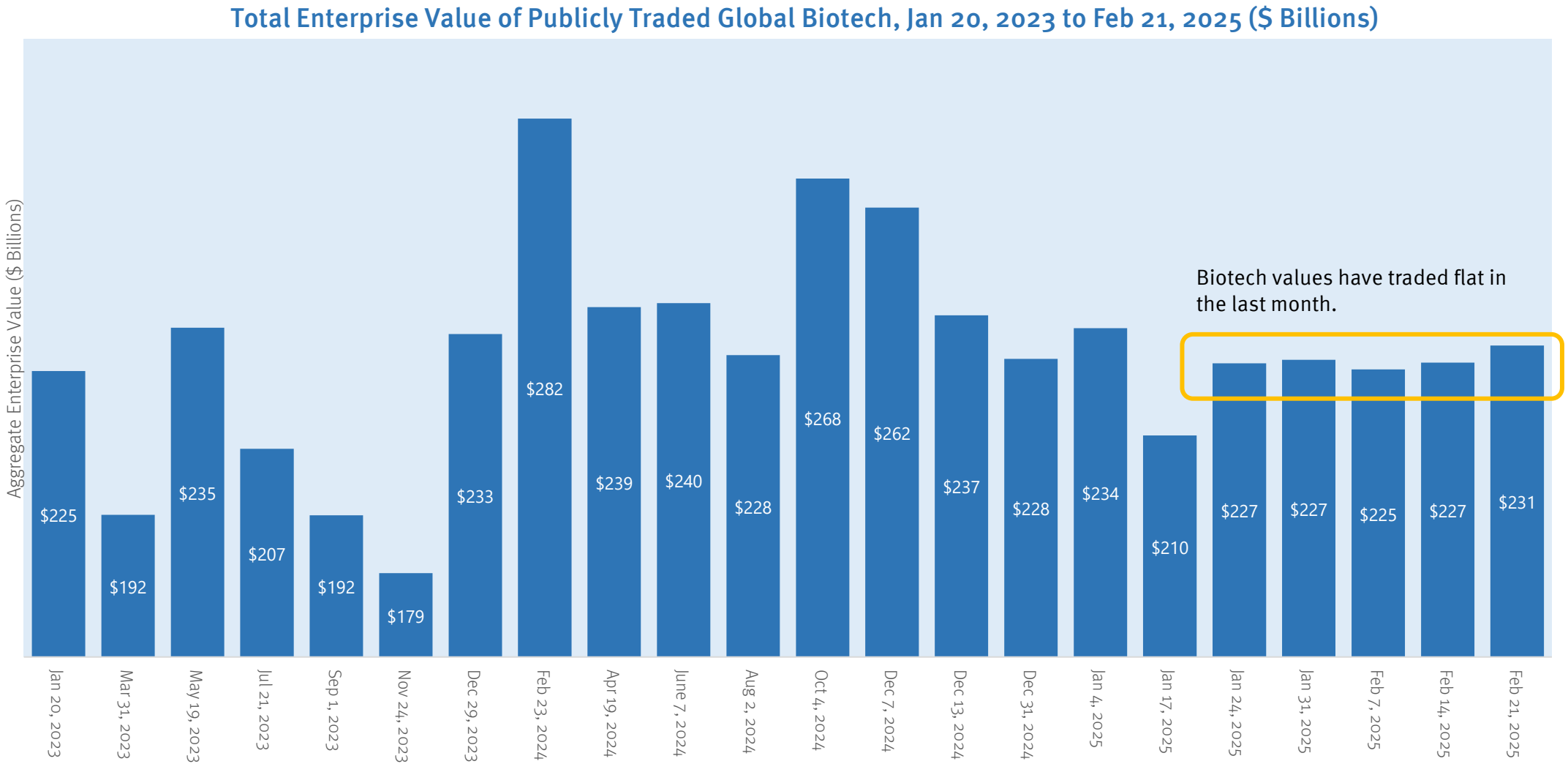


* Change by enterprise value. The adjusted number accounts for the effect of exits and additions via M&A, bankruptcies and IPOs. The annual change by market cap is even higher.

Source: S&P Capital IQ and Stifel analysis

Total Global Biotech Sector Rose 1.7% Last Week

Biotech stocks rose 1.7% in the last week – more than the XBI. By our math, the total global biotech sector is up 1.3% for the year. While not what one would call a rally, the sector was down for the year just a week ago.

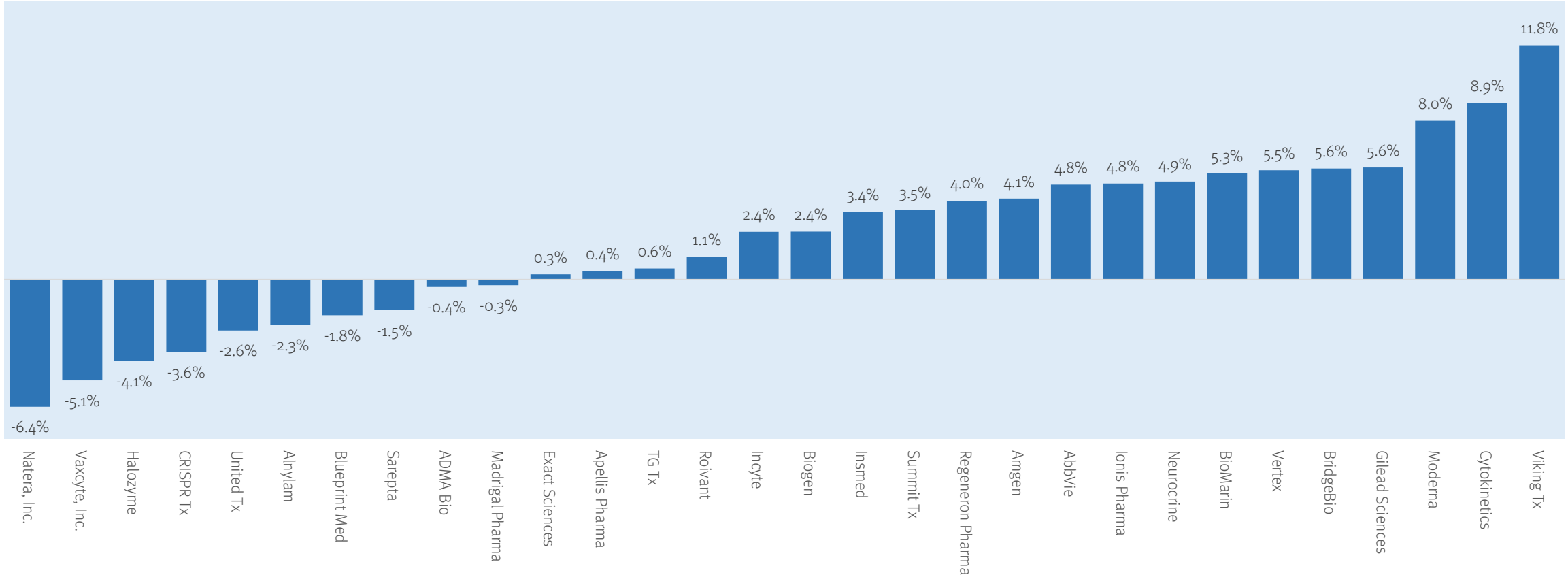


Source: CapitalIQ. Biotechs are defined as any therapeutics company without an approved product on any global stock exchange.

XBI 30 Performance Solid 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 +2%. The median change was 2.4%. Viking and Cytokinetics did well on M&A speculation. Moderna also did well. Natera, Vaxcyte and Halozyme were the biggest decliners.

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

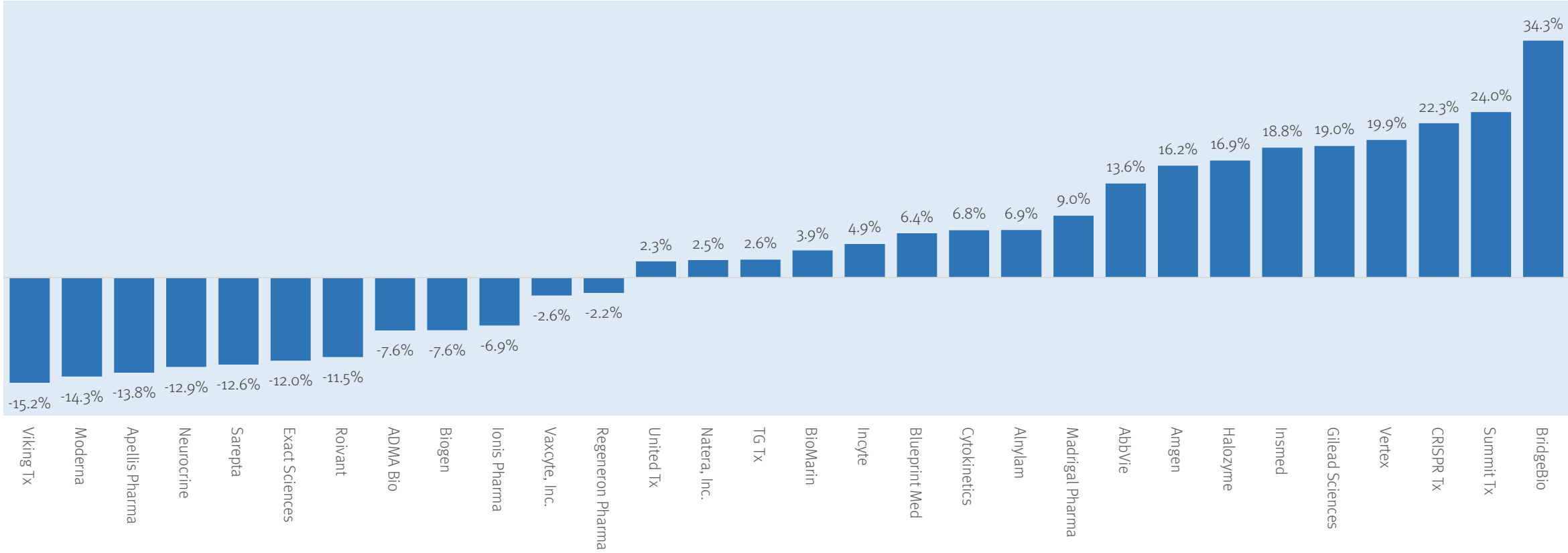


Source: CapitalIQ. Biotechs are defined as any therapeutics company without an approved product on any global stock exchange.

XBI 30 Performance Solid Year to Date

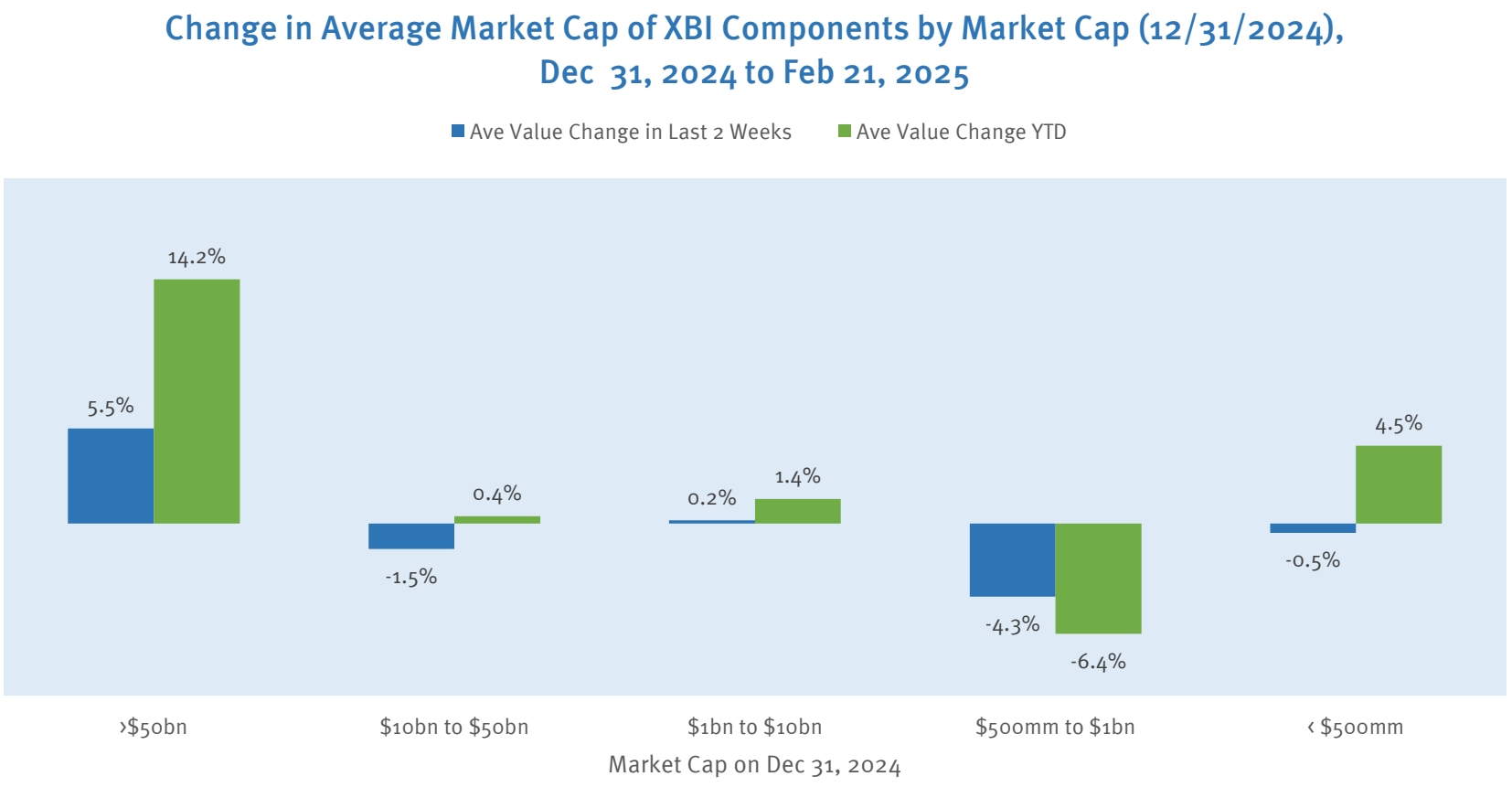
This chart shows the change in market cap this year for the 30 most influential stocks in the XBI. These 30 stocks comprise 60% of the weight of the XBI (out of 138 stocks total). The mean percentage change in value this year is up 3.7%. BridgeBio, Summit and CRISPR have been the best performers for the year. Viking, Moderna and Apellis have all been down.

Top 30 XBI Influencers, Pecent Change in Market Cap, Week of Dec 31, 2024 to Feb 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.

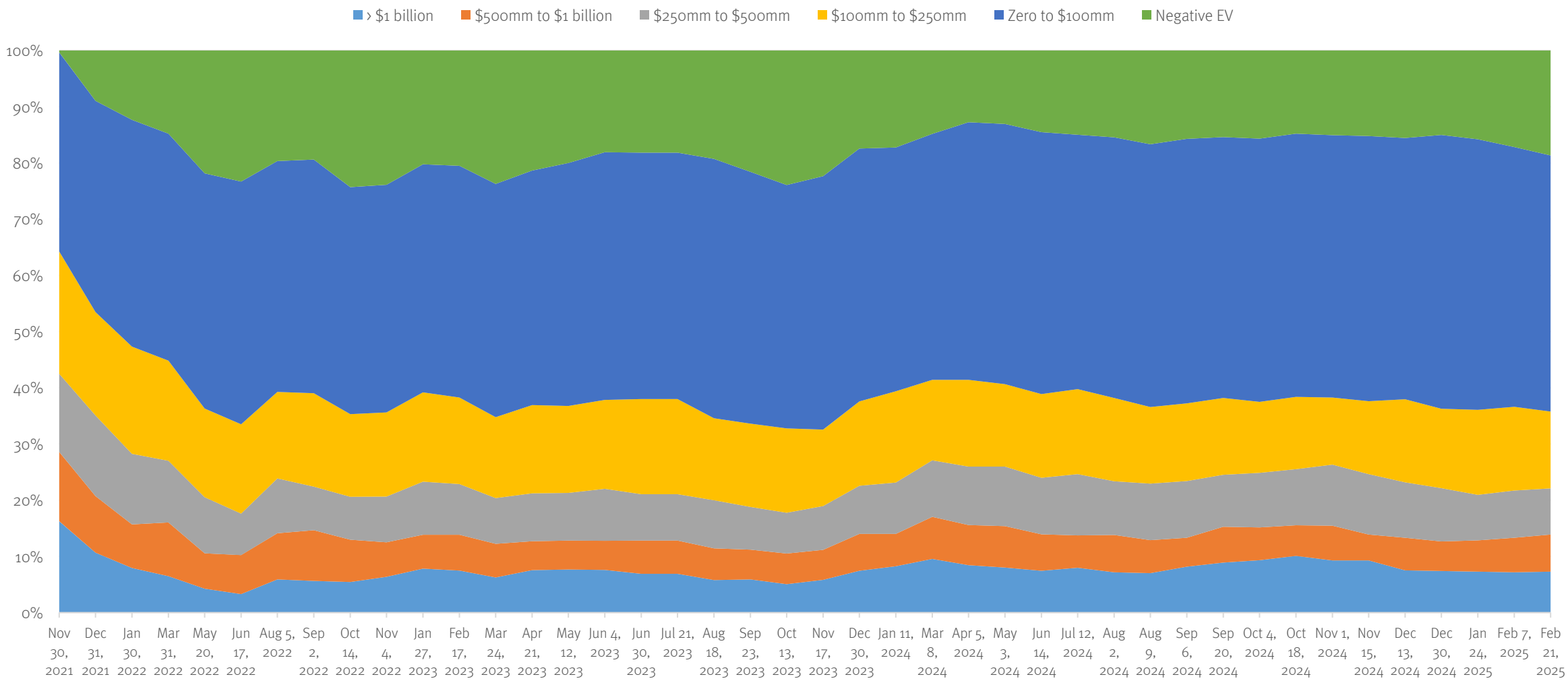
Big cap are up 14% YTD and rose 5.5% last two weeks.

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

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.

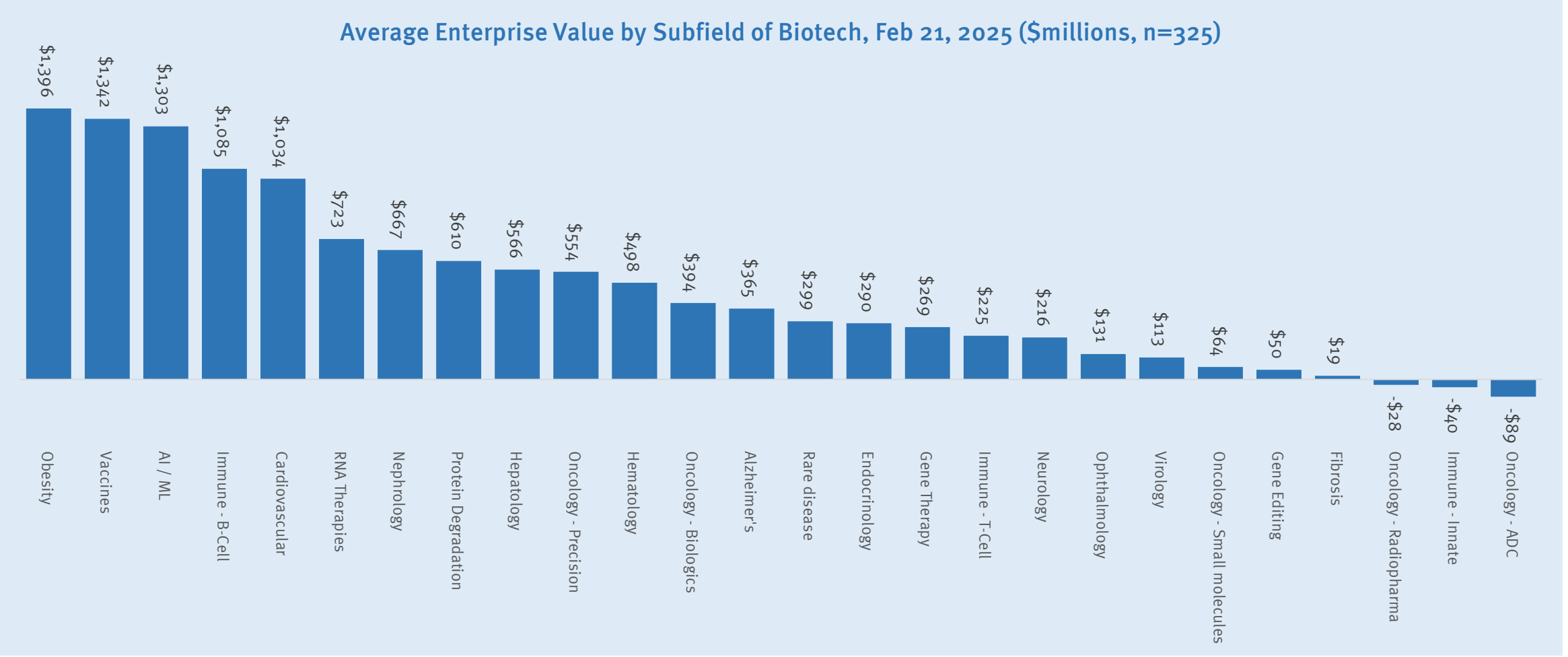
Global Biotech Universe by Enterprise Value Category, Nov 30, 2021 to Feb 21, 2025



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

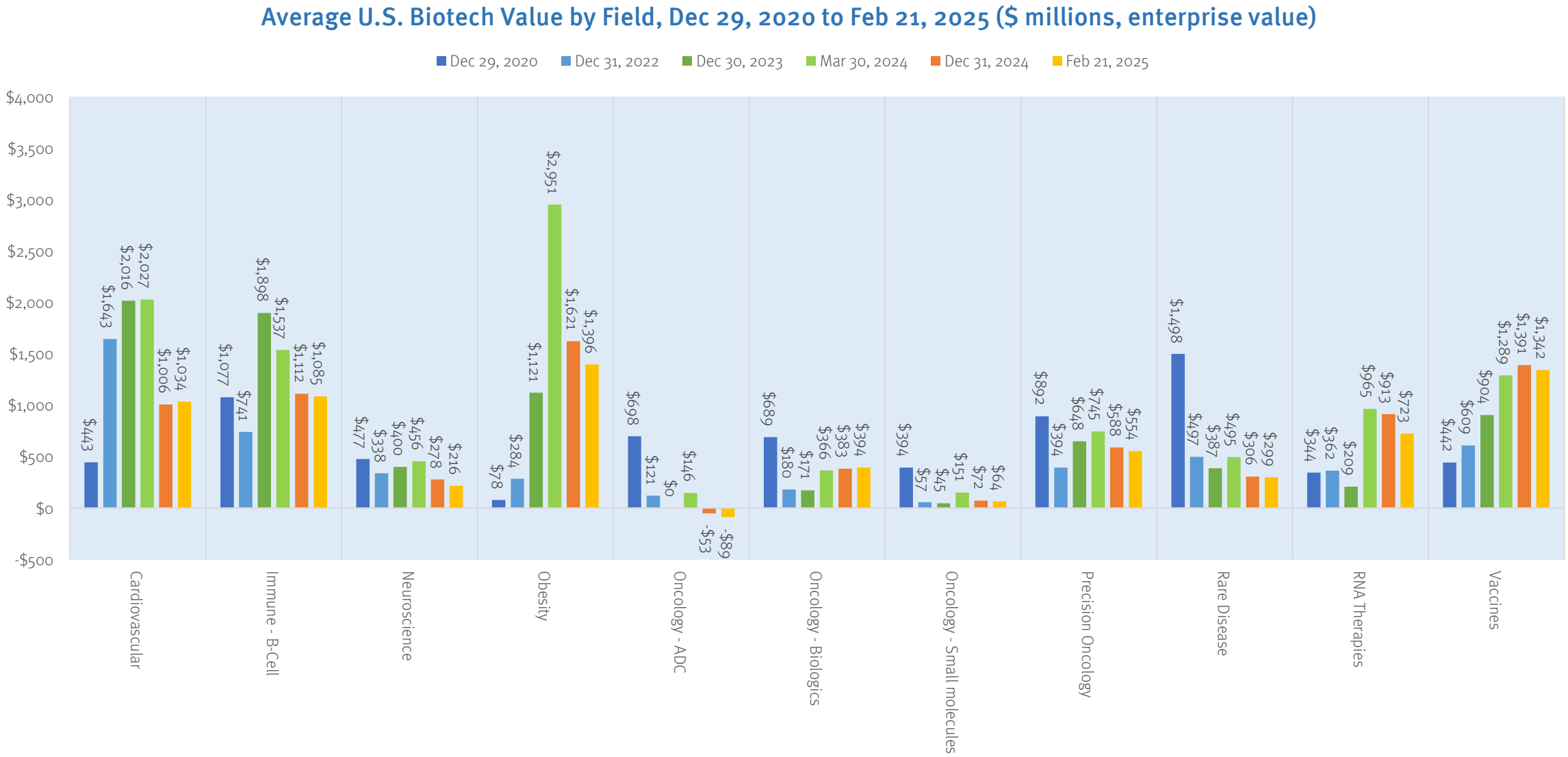
U.S. Biotech Values Today Highest in Obesity, Vaccines and AI

The most valued sectors in biotech today are obesity, vaccines 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, innate immunology, radiopharma and gene editing.



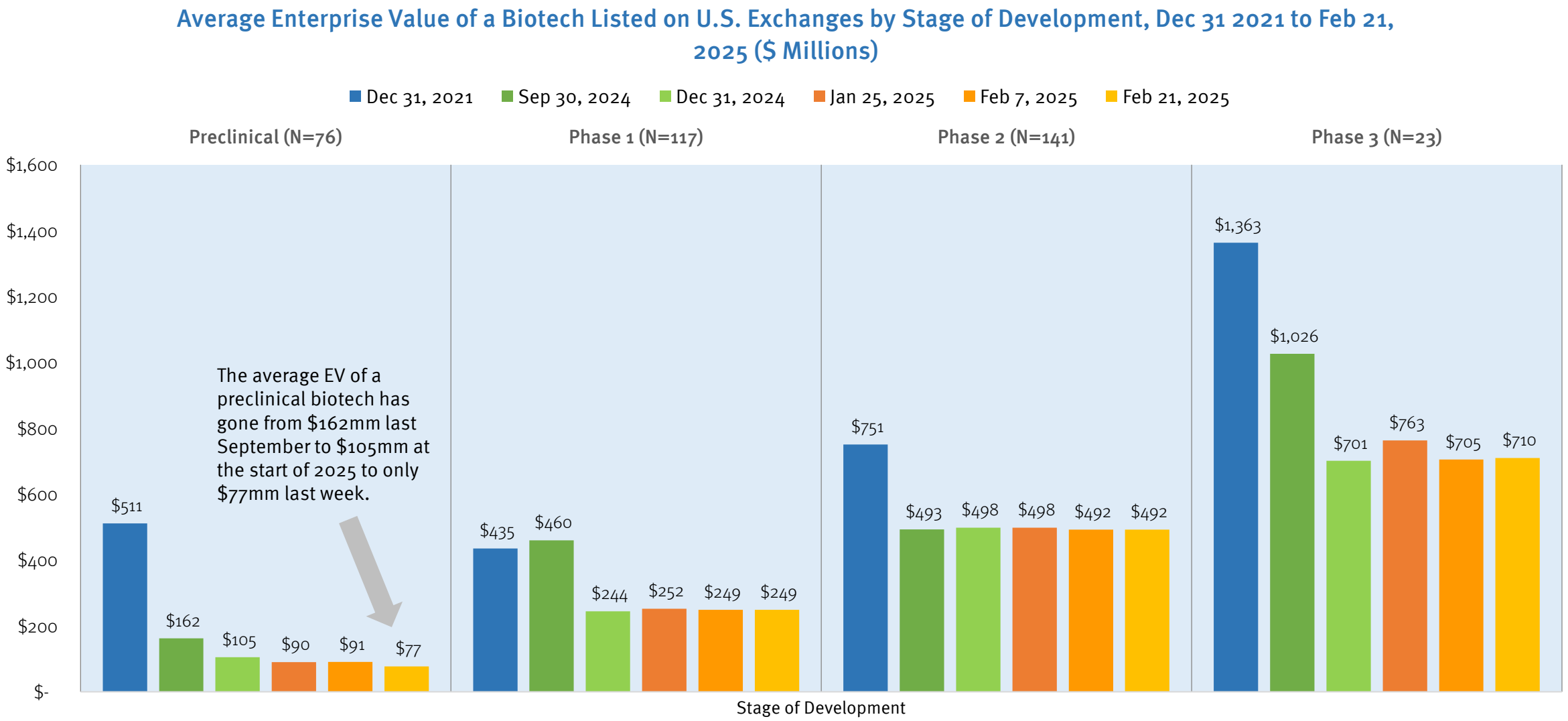
Source: S&P CapitalIQ and Stifel analysis.

In 2025 We Are Seeing Softening of Obesity and RNA Therapeutics Valuations



Source: S&P CapitalIQ and Stifel analysis.

Preclinical Stocks Dropping in Value in Recent Months



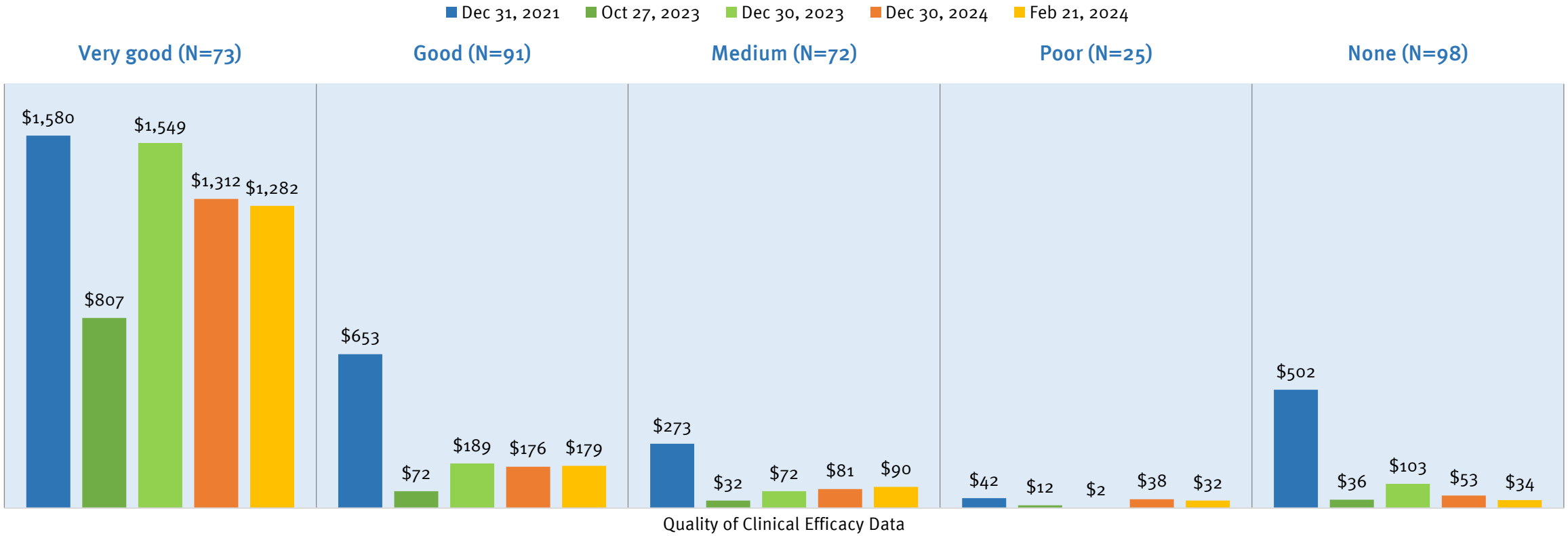
Source: CapitalIQ and Stifel analysis. Phase of development is defined by release of at least some efficacy data from a given stage of clinical development.

Biotech Quality Premium Holding Steady in 2025

One of the distinctive characteristics of the biotech downturn of 2022 to 2024 has been an extreme quality premium. Companies with “very good” data have traded at a value of five to ten times companies with a “good” dataset. We are seeing the value of the average company today with “very good” data little changed since the year began. In contrast companies with a poor dataset or no dataset have steadily lost value as 2025 has rolled on.

Average Enterprise Value of a Biotech Listed by Quality of Efficacy Data

Dec 31, 2021 to May 10, 2024, ($ Millions, US Exchanges Only, N=377)

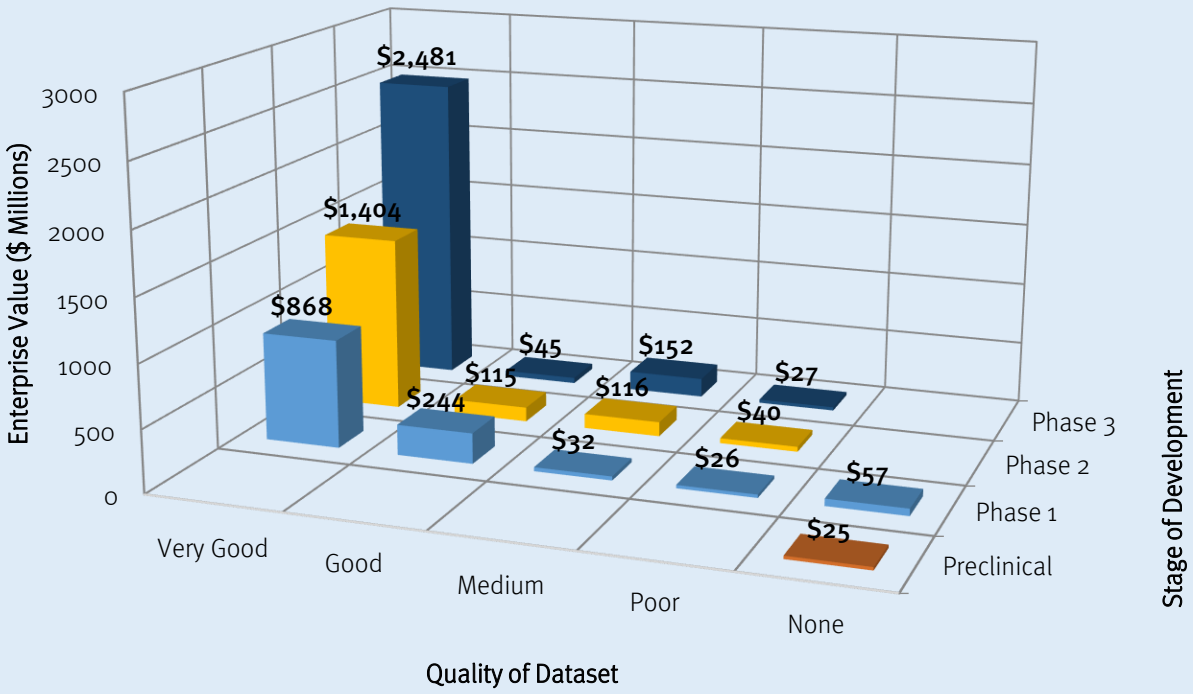


Note: These data are sourced from CapitalIQ and based on Stifel research on the dataset quality for a company’s lead asset. We classified datasets that indicated a high probability that the drug would meaningfully improve on the standard of care for a disease as “very good”. We classified “good” data as data that might beat the standard of care. Medium data was data that was unlikely to beat the standard of care, was very early or came from a study with a mixed signal. Poor data reflects situations where a drug did not perform well at all in a clinical trial.

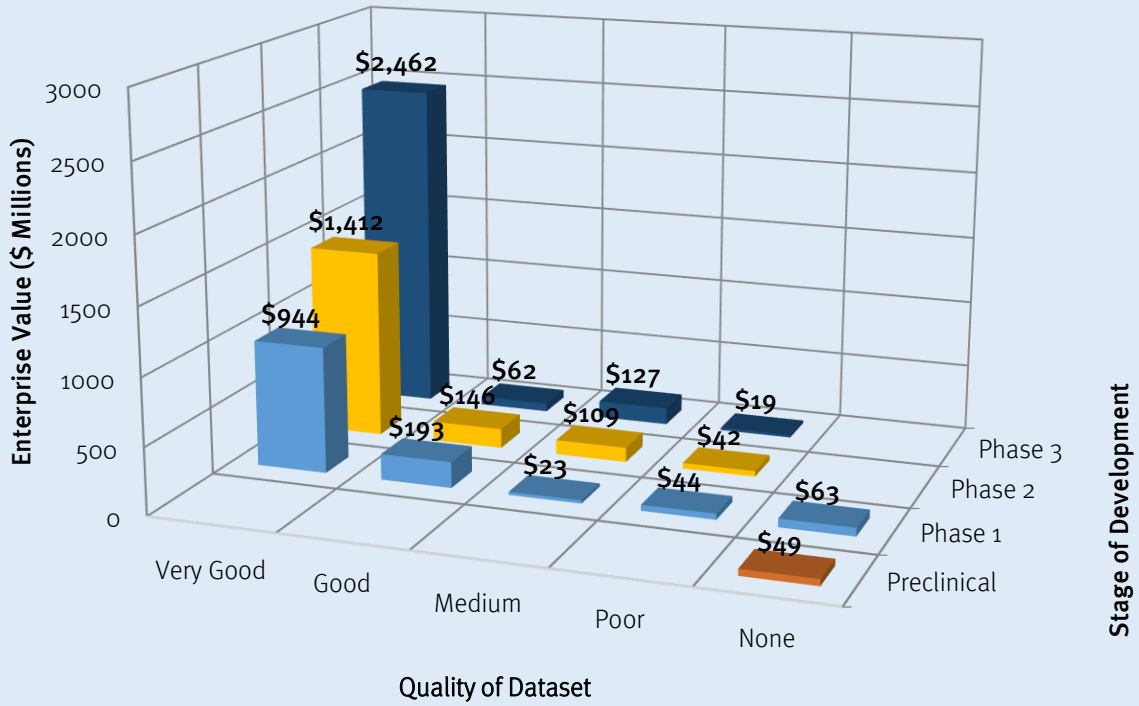
The Most Valued Biotechs are Those With “Very Good” Phase 3 Data

The valuation tiering of the biotech market by stage of development and dataset quality hasn’t changed much since 2025 began.

Average Enterprise Value of a Biotech Listed on U.S. Exchanges by Stage of Development and Quality of Data, Feb 21, 2025



Average Enterprise Value of a Biotech Listed on U.S. Exchanges by Stage of Development and Quality of Data, Dec 31, 2024



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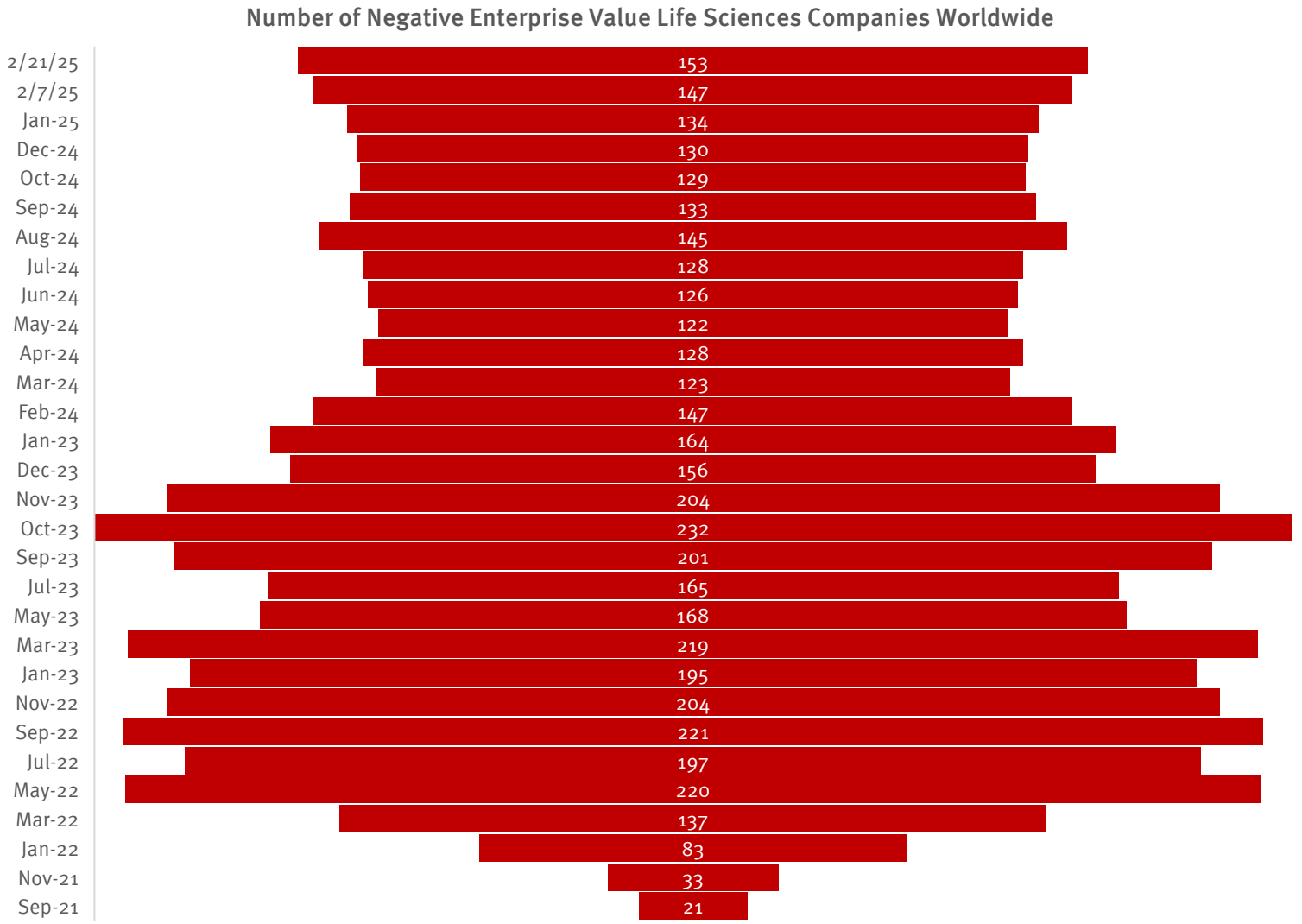
Life Sciences Sector Gained $162 Billion in Value Last Week (1.7%)

Last week was quite good for the life sciences sector with big gains in commercial pharma and pharma services. The HCIT and CDMO sectors have recovered nicely in the last month while life science tools stocks have not fared well as of late.

Sector	Firm Count	Enterprise Value (Feb 21, 2025, $millions)	Change in Last Week (percent)	Change in Last Month (percent)	Change in Last Year (percent)
API	79	$86,219	-1.0%	-3.9%	6.3%
Biotech	732	$237,955	1.7%	0.2%	-5.1%
CDMO	37	$159,056	0.2%	8.8%	18.5%
Diagnostics	77	$260,459	-1.6%	-0.2%	-2.8%
OTC	29	$24,219	-0.1%	1.3%	-12.3%
Commercial Pharma	699	$6,310,992	2.9%	5.3%	0.8%
Pharma Services	38	$167,965	3.0%	-1.6%	-15.3%
Life Sciences Tools	50	$625,880	0.5%	-10.5%	-11.6%
Devices	174	$1,867,613	-1.0%	-0.3%	8.9%
HCIT	7	$30,613	-3.3%	42.2%	51.2%
Total	1922	$9,770,971	1.7%	2.7%	1.2%

Source: CapitalIQ and Stifel analysis

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



The count of negative EV life sciences companies worldwide rose from 147 two weeks ago to 153 last Friday.

This measure of sector distress is starting 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

Why Biotech's Future is Threatened by Zombies

Adam Feuerstein, *Stat+*, Feb 20, 2025 (excerpt)

I was a bit worried last week's angst-y rant on the bleak state of biotech investing would turn folks off. In fact, it was my most popular newsletter ever, with the version posted to STAT's website delivering a ton of new subscribers. Thank you!

Why did "Biotech is in a dark place" resonate with so many of you? Because it's true! Collectively, we're all frustrated after running in place for five-plus years, and by recognizing the problem, hopefully, some cages are rattled and positive change happens.

Cargo exemplifies the industry's zombie problem. The company is dead, but also alive. It has no future, no reason to exist as a standalone company, but its corpse walks the biotech world, nourished by residual bank funds.

One zombie might not be so bothersome, but there's no such thing as a single zombie. (We know this from the movies.)

As I mentioned last week, 200 of the 700 public companies that I track trade at a negative enterprise value — the finance term for zombie — and they have more than $30 billion in excess cash to waste.

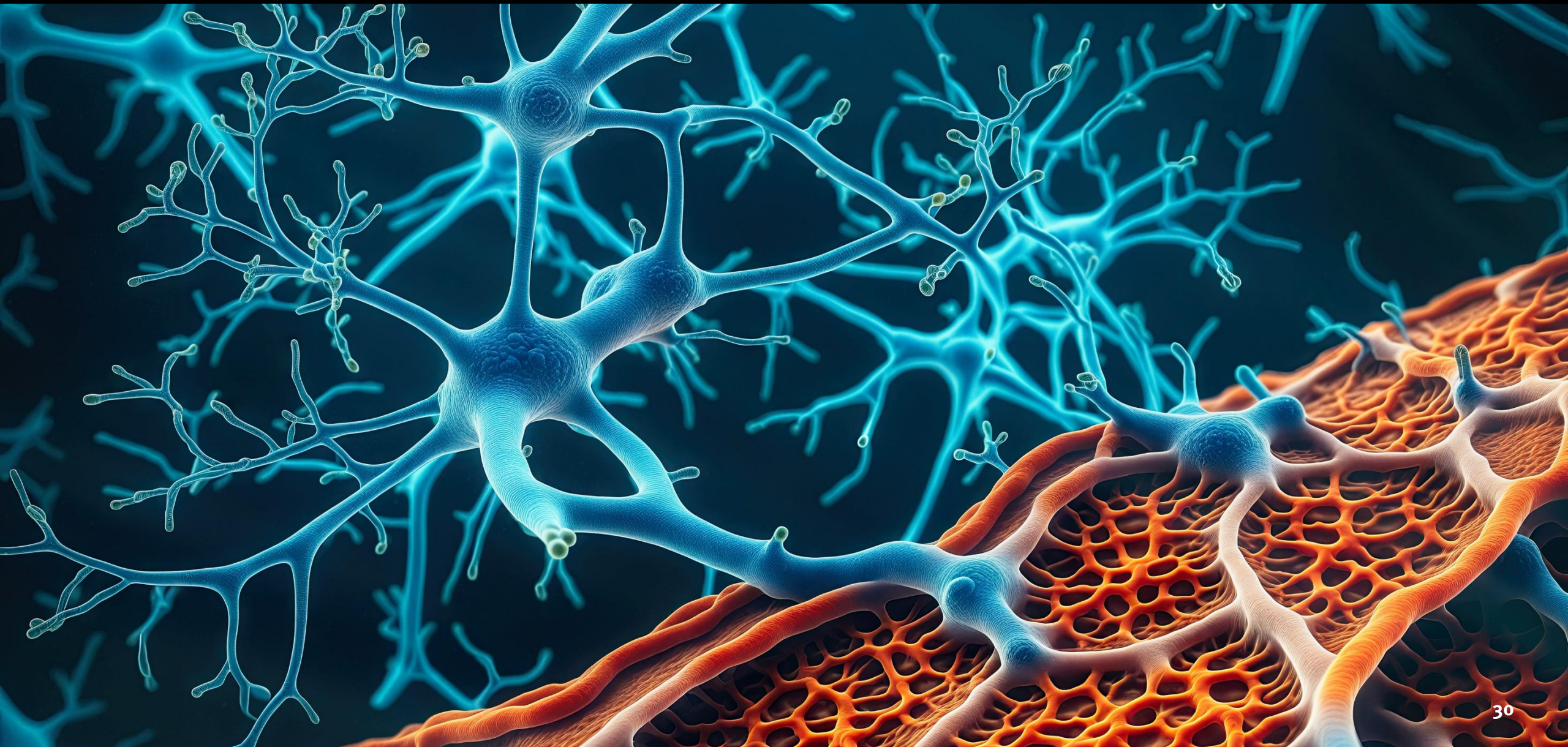
$30 billion!

You think, maybe, all that money might be invested more productively somewhere else?

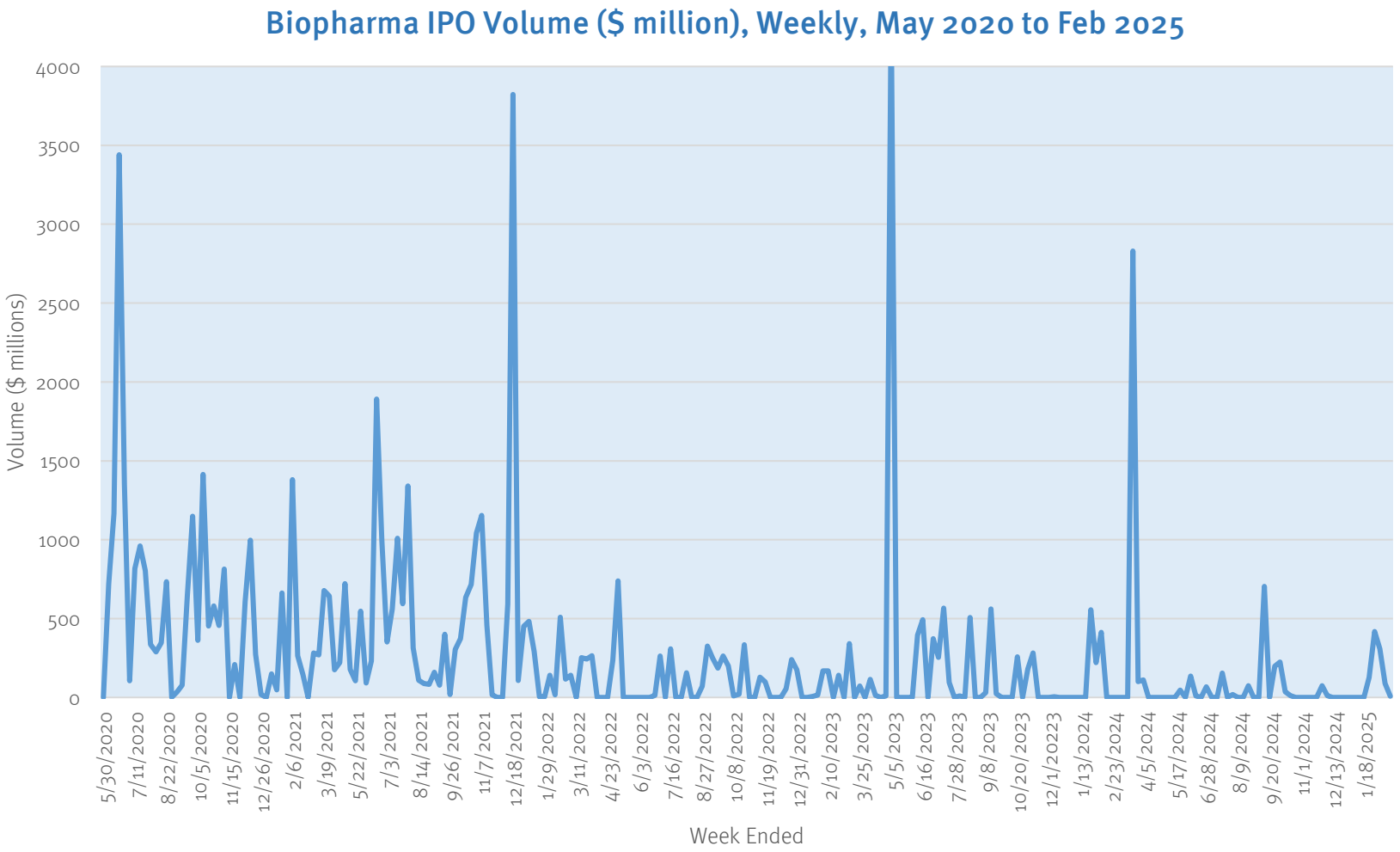
No single solution will lift biotech from its dark place, but killing the zombies is a start.

Source: https://www.statnews.com/2025/02/20/why-biotechs-future-is-threatened-by-zombies/

Capital Markets Update



IPO Market Has Quieted Down



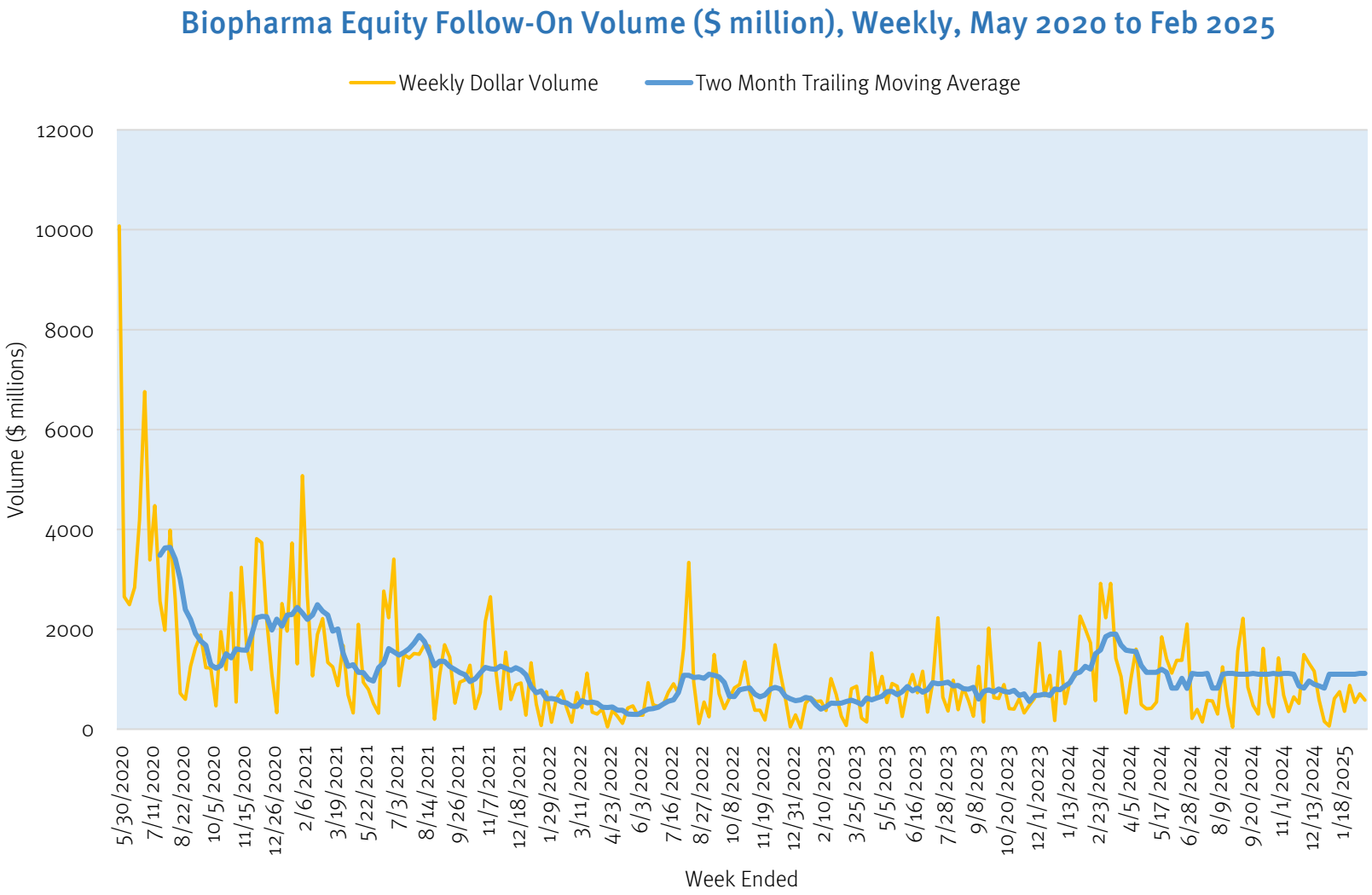
Last week saw no IPOs for $50mm or more. The week before saw Aardark Therapeutics go public. The pace of IPO activity has come down substantially since the start of February where we saw four issuers go out and price deals.

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

Not a bad start to the year.

Source: Data from CapitalIQ and Stifel research.

Follow-On Equity Financing Market Continues to be Soft



The first seven and a half weeks of 2025 have seen $4.5 billion in follow-on ("FO") biopharma offerings.

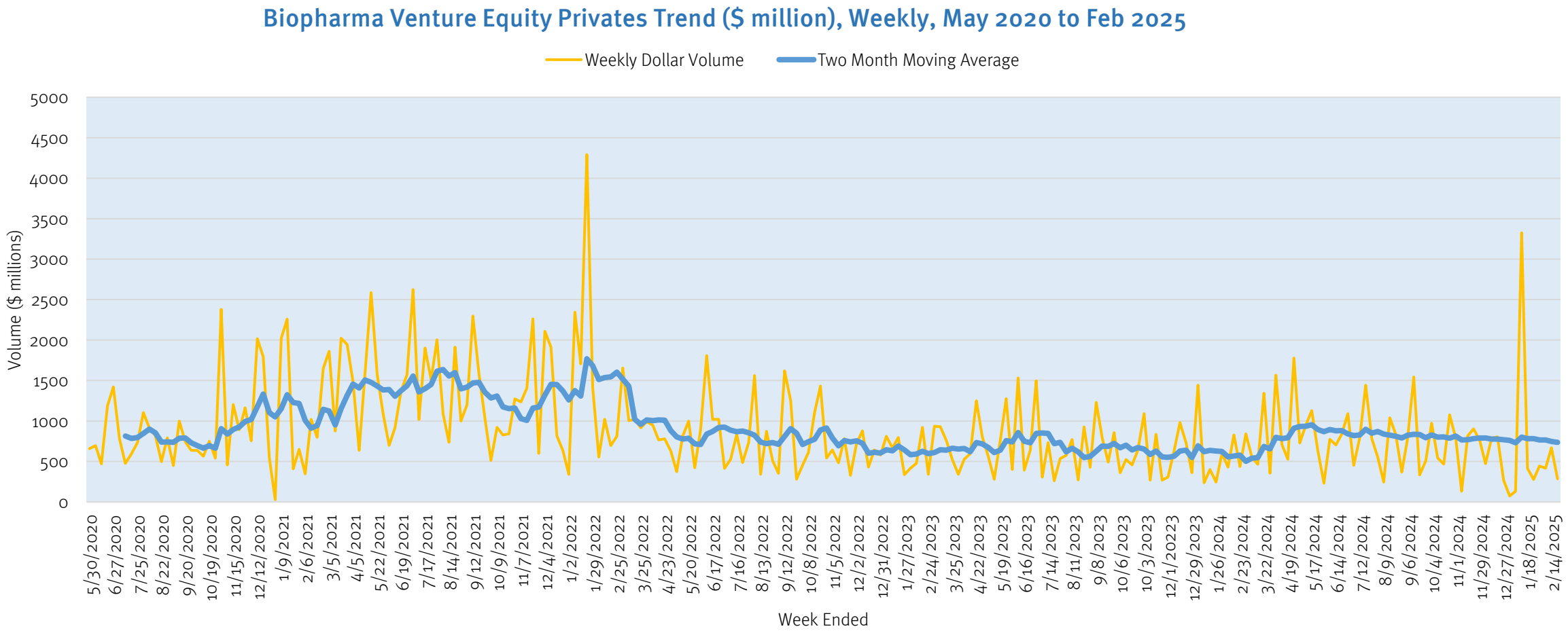
Thus far, we have seen $1.8 billion in offerings price in February (through Feb 21) – a pace of $600mm a week.

This is well below the $1bn a week pace that was seen in Q4 2024. While deals are getting done, investor sentiment has been a headwind on activity.

Source: Data from CapitalIQ and Stifel research.

Venture Privates Market is Slowing Down

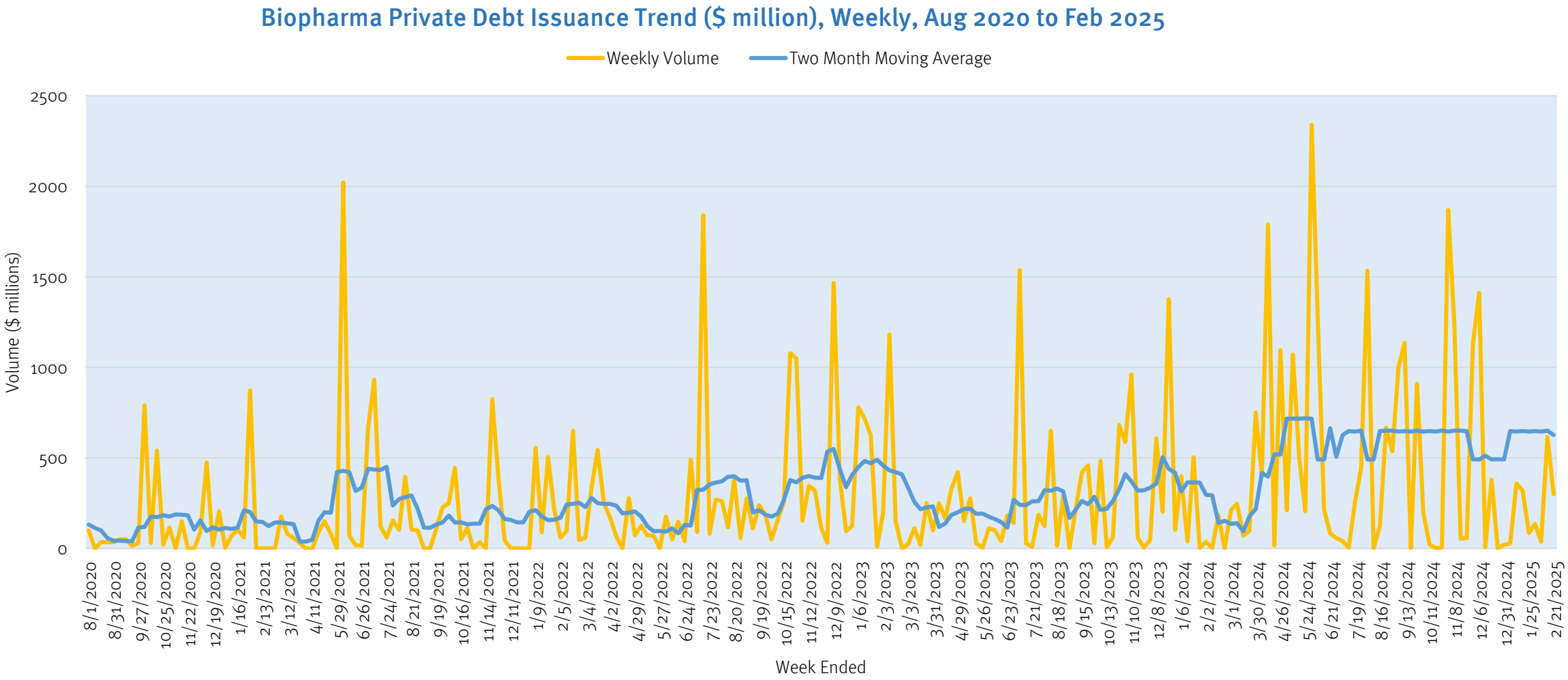
The first six weeks of 2024 saw private raises of $900mm a week, on average. The pace of the last three weeks has been roughly half of that level ($450mm a week). Last week was particularly slow with $285mm raised, although it was a holiday shortened week.



Source: Data from CapitalIQ, Crunchbase.

Global Biopharma Private Debt Placement Market Cooling in 2025

After a January hiatus, the private debt market has been stronger in February with $950mm raised in the first three weeks of the month. Last week saw Tempus raise $300 million in debt from Ares.



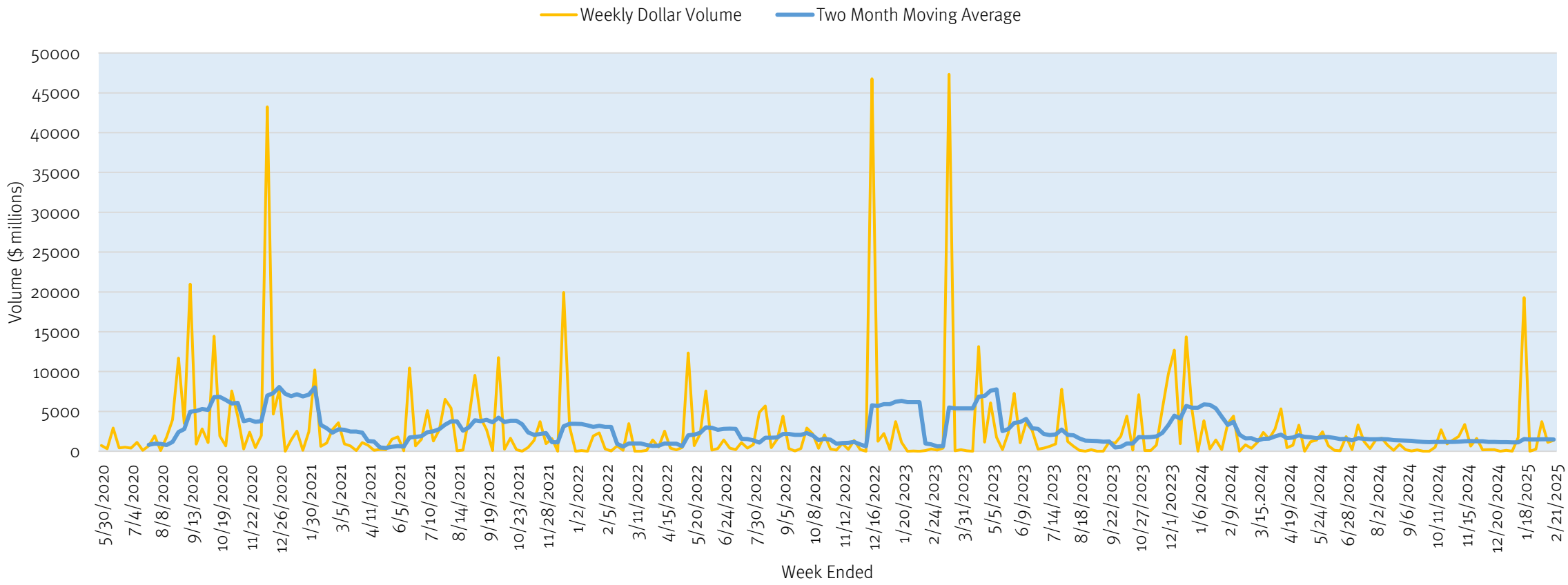
Source: Data from CapitalIQ, Crunchbase.

Deals Update

M&A Market Well Ahead of 2024 Pace

We have seen $28 billion in M&A volume so far in 2025. This remains one of the strongest starts to the year seen in a long time. Last week saw a number of smaller and mid-size deals hit the tape including an offer by Concentra to acquire Acelyrin, Cosette's acquisition of Mayne Pharma and AZ's $160 million buy-in of FibroGen China.

Biopharma M&A Volume Trend ($ million), Weekly, May 2020 to Feb 2025



Source: S&P, CapitalIQ

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

Cosette Pharmaceuticals Acquires Mayne Pharma for $430 Million

February 20, 2025, *BRIDGEWATER, N.J.--(BUSINESS WIRE)*

Cosette Pharmaceuticals, Inc., a U.S.-based, fully integrated, pharmaceutical company, announced today that it has entered into a definitive agreement to acquire all the outstanding shares of Mayne Pharma Group Limited (ASX: Ticker MYX) (Mayne Pharma) at AUD$7.40/share for a total consideration of approximately USD $430 Million. The Boards of Directors of both companies have approved the transaction and Mayne Pharma's Board of Directors has unanimously recommended that its shareholders vote in favor of the transaction. The transaction is expected to close in the second quarter of 2025.

"This acquisition marks a transformational step for Cosette, adding patented, high-growth products to solidify our leadership in women's health in the U.S. and expanding our reach globally," said Apurva Saraf, President and CEO of Cosette Pharma. "By combining Cosette's strong portfolio with Mayne Pharma's proven commercial expertise, the combined company will be well positioned to further invest in innovation, portfolio expansion and better serve our patients. We look forward to a timely closing and welcoming Mayne Pharma to the Cosette family."

Cosette will utilize its market-leading commercial and operational capabilities, backed by its 350+ strong team and a leading portfolio of women's health and dermatology products alongside Mayne Pharma's complementary strength in these specialty areas. Mayne Pharma is backed by a 480+ strong team, including highly effective and successful sales and marketing teams in both specialties. The combined company will have two state-of-the-art FDA -approved manufacturing sites – one each in Lincolnton, North Carolina and Salisbury, South Australia – to service patients globally.

Source: https://www.businesswire.com/news/home/20250220569463/en/Cosette-Pharmaceuticals-Announces-Acquisition-of-Mayne-Pharma-Transforming-Company-into-a-Leader-in-Women%E2%80%99s-Health-and-Dermatology

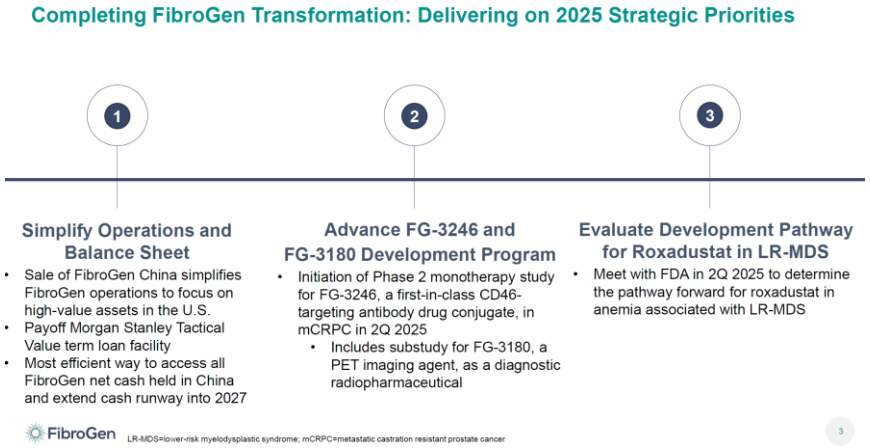
FibroGen Announces the Sale of FibroGen China to AstraZeneca for Approximately $160 Million

February 20, 2025, *SAN FRANCISCO (GLOBE NEWSWIRE)*

FibroGen, Inc. (NASDAQ: FGEN) today announced the sale of its China subsidiary to AstraZeneca for approximately $160 million.

“Today, we announced the sale of FibroGen China to AstraZeneca, our long-time strategic partner for roxadustat in China, bolstering our company on several fronts. It strengthens our financial position, meaningfully extending our cash runway into 2027, and enables us to continue progressing the clinical development program for FG-3246, our first-in-class, CD46 targeting antibody drug conjugate, and FG-3180, our companion PET imaging agent, in mCRPC,” said Thane Wettig, Chief Executive Officer of FibroGen. “After a thorough evaluation of alternatives, we believe selling our China operations and repaying our term loan is in the best interest of FibroGen’s stakeholders. We are grateful for our China colleagues, and in particular Christine Chung, our Head of China Operations, for their unwavering commitment to patients and successful commercialization of roxadustat in China. Now, we turn the page to the next exciting chapter for FibroGen.”

Under the terms of the agreement, FibroGen will receive an enterprise value of $85 million plus FibroGen net cash held in China at closing, currently estimated to be approximately $75 million, totaling approximately $160 million. The transaction is expected to close by mid-2025, pending customary closing conditions, including regulatory review in China. Following the close of the transaction, FibroGen will repay its term loan facility to investment funds managed by Morgan Stanley Tactical Value, further simplifying the Company’s capital structure. The combined transactions are expected to extend the Company’s cash runway into 2027. Upon closing, AstraZeneca will obtain all rights to roxadustat in China. Roxadustat is the category leader in brand value share for the treatment of anemia in chronic kidney disease with a pending regulatory decision for chemotherapy-induced anemia.



FibroGen China Sale: Summary of Key Commercial Terms

Purchase Price	▪ Enterprise value of **$85 million**
Value of FibroGen Cash Held in China	▪ Approximately **$75 million** of FibroGen net cash held in China at closing ○ Defined as net cash at closing held by FibroGen China, including FibroGen’s portion of Falikang net cash
Transaction Close Timing and Other Details	▪ Transaction expected to close by mid-2025, pending customary closing conditions, including regulatory review in China ▪ Transaction scope **does not** include the Eluminex license agreement, whose rights will be retained by FibroGen
Significant Balance Sheet Transformation	▪ Payoff of MSTV term loan facility at closing, simplifying the company’s capital structure ▪ Provides FibroGen full access to all cash in China ▪ Extends cash runway into 2027 ▪ Preliminary unaudited cash, cash equivalents, and accounts receivable of $121.1 million as of December 31, 2024

Source: https://investor.fibrogen.com/news-releases/news-release-details/fibrogen-announces-sale-fibrogen-china-astrazeneca-approximately

Concentra Offers to Buy Acelyrin, Endangering Proposed Merger With Alumis

Concentra has been able to win out in takeover contests by offering a price close to the target's cash level in recent years. Shareholder support for the Alumis deal will need to be strong to win against the proposed cash deal.

Tristan Manalac, *Biospace* Feb 21, 2025 (excerpt)

Acelyrin earlier this month agreed to an all-stock merger with fellow immune player Alumis, with their combined cash tiding the combined company over until 2027. Tang Capital's Concentra Biosciences is at it again, offering to acquire immunology specialist Acelyrin—potentially disrupting the biotech's plans to merge with Alumis.

Acelyrin announced Concentra's unsolicited offer early on Friday, disclosing that the Kevin Tang–controlled firm is willing to purchase all of its outstanding shares for $3 apiece. Concentra is adding on a contingent value right that would give Acelyrin 80% of the net proceeds from out-licensing deals or sale of its assets and intellectual properties.

Acelyrin stock was valued at $2.17 per share at Thursday close, rising to about $2.50 per share Friday morning. Acelyrin did not explicitly accept or decline the offer on Friday. Instead, the biotech said that its leadership "is committed to acting in the best interest of stockholders," adding that the company will provide additional information regarding its decision on the offer "in due course"—though no specific timeline was given.

Two weeks ago, Acelyrin announced it had entered into a definitive agreement to merge with fellow immune player Alumis. The all-stock arrangement would see Acelyrin fold into Alumis, creating a combined company with enough cash standing to last until 2027.

In its press release announcing the Concentra offer on Friday, Acelyrin said that it will stay "consistent … to its obligations under the merger agreement with Alumis."

Source: https://www.biospace.com/business/concentra-offers-to-buy-acelyrin-endangering-proposed-merger-with-alumis

bluebird bio Announces Definitive Agreement to be Acquired by Carlyle and SK Capital

February 21, 2025, *SOMERVILLE MA*

bluebird bio, Inc. (NASDAQ: BLUE) ("bluebird") today announced that it has entered into a definitive agreement to be acquired by funds managed by global investment firms Carlyle (NASDAQ: CG) and SK Capital Partners, LP ("SK Capital") in collaboration with a team of highly experienced biotech executives. David Meek, former CEO of Mirati Therapeutics and Ipsen, is expected to become CEO of bluebird upon closing. Carlyle and SK Capital will provide bluebird primary capital to scale bluebird's commercial delivery of gene therapies for patients with sickle cell disease, β-thalassemia, and cerebral adrenoleukodystrophy.

Under the terms of the agreement, bluebird stockholders will receive $3.00 per share in cash and a contingent value right per share, entitling the holder to a payment of $6.84 in cash per contingent value right if bluebird's current product portfolio achieves $600 million in net sales in any trailing 12-month period prior to or ending on December 31, 2027, for a potential total value of up to $9.84 per share in cash, subject to the tender of a majority of the outstanding shares of bluebird, receipt of applicable regulatory approvals, and other customary closing conditions. bluebird's Board of Directors (the "bluebird Board") unanimously approved the agreement and recommends that stockholders tender their shares. Following a comprehensive review of bluebird's strategic alternatives, including meeting with more than 70 potential investors and partners over a period of five months, and a third and final denial by the Federal Drug Administration of bluebird's appeal for a priority review voucher, the bluebird Board determined that, absent a significant infusion of capital, bluebird is at risk of defaulting on its loan covenants. The bluebird Board has decided that this transaction is the only viable solution to generate value for stockholders. Additional details on the process will be available in bluebird's Solicitation/Recommendation Statement on Schedule 14D-9, which will be filed with the U.S. Securities and Exchange Commission ("SEC").

"For more than a decade, bluebird has been at the forefront of gene therapy, delivering groundbreaking treatments to patients facing life-threatening genetic diseases. However, as our financial challenges mounted, it became clear that securing the right strategic partner was critical to maximizing value for our stockholders and ensuring the long-term future of our therapies. After an extensive review process, this acquisition represents the best path forward – maximizing value for stockholders and bringing significant capital, commercial expertise, and a commitment to provide more patients the opportunity to benefit from potentially transformative gene therapies."

Andrew Obershain, CEO, Bluebird

Source: https://www.carlyle.com/media-room/news-release-archive/bluebird-bio-announces-definitive-agreement-be-acquired-carlyle-and

A case study assessing the impact of M&A and licensing on FDA drug approvals of leading pharmaceutical companies

Alexander Schuhmacher [1,2,*], Kyrylo Grinchenko [2], Oliver Gassmann [2], Dominik Hartl [3,4], Markus Hinder [5,6]

[1] Technische Hochschule Ingolstadt Germany
[2] University of St Gallen Switzerland
[3] University of Tübingen Germany
[4] Granite-Bio Basel Switzerland
[5] Novartis Basel Switzerland
[6] University of Zürich Switzerland

Drug Discovery Today
Volume 30, Issue 3
March 2025

Despite a recent increase in FDA new drug approvals, leading pharmaceutical companies continue to face R&D productivity challenges. This highlights the need to better understand the context of their R&D concepts and related R&D outputs. Consequently, we conducted a systematic assessment of the impact of R&D expenditures, R&D intensities, mergers & acquisitions (M&A) deals and licensing agreements on new drug approvals of leading pharmaceutical companies between 2012 and 2021. Our analysis provides key insights into differentiating R&D factors: whereas R&D expenditures and the number of M&A deals correlate with the number of new drug approvals, our analysis shows no correlation with R&D intensity or the number of licensing agreements.

M&A a Net Positive for Pharma R&D Output

Conversely, and in contrast to previous findings of a negative impact of M&A on R&D results our insights provide strong indications of a positive effect of M&A on the R&D output of major pharmaceutical companies. This result, especially in the context that M&A can have positive impact on corporate performance, pro-vides a rationale why pharma executives should be more selective when recognizing, assimilating and integrating external assets to commercial ends and possibly focus more on M&A rather than on in-licensing.

A good example of a productive M&A is the acquisition of Celgene by BMS in 2019. The M&A deal did not only strengthen BMS's long-term capabilities in oncology and immunology but also included five new drugs (approved by the FDA between 2013 and 2020), including the two blockbusters Pomalyst® (pomalido-mide, total sales 2023 of US$3.44B) and Reblozyl® (luspaterzept,US$1.01B). Another very productive deal was the US $46.8B acquisition of Genentech by Roche in 2009, which generated 13 FDA new drug approvals (2012–2020) for Roche and pro-vided competitive advantage in the oncol-ogy and immunology field.

Source: https://www.sciencedirect.com/science/article/pii/S1359644625000194

TABLE 1

Key R&D figures of leading pharmaceutical companies (2012–2021)

Company	Total revenue (US$B)	Total (internal) R&D expenditures (US$B)	Average R&D intensity	Number of FDA-approved drugs	Number of M&A deals	Total M&A deal value (US$B)	Number of in-licensing agreements
Roche	638.97	119.91	19%	15	16	19.92	40
Pfizer	567.17	86.43	16%	12	11	41.09	34
Novartis	557.75	95.68	17%	18	13	36.59	28
Merck & Co.	469.08	86.39	19%	15	17	38.16	31
Sanofi	465.08	69.20	15%	11	8	30.12	19
GlaxoSmithKline	456.36	58.39	13%	13	4	9.21	18
AbbVie	327.42	50.13	16%	8	6	92.13	33
AstraZeneca	287.43	60.84	21%	14	16	61.38	26
Bristol-Myers Squibb	264.82	59.64	23%	7	11	110.56	29
Gilead Sciences	254.28	38.62	16%	9	10	43.31	23
Eli Lilly	245.73	59.97	24%	12	10	13.98	41
Amgen	244.03	44.20	18%	7	10	16.46	18
Takeda	226.45	39.69	18%	9	6	64.78	34
Boehringer Ingelheim	217.82	41.46	19%	5	6	1.43	28
Total	**5222.38**	**910.55**		**155**	**144**	**579.12**	**402**
Mean	**373.03**	**65.04**	**18.1%**	**11.07**	**10.29**	**41.37**	**28.71**
Standard deviation	**146.97**	**24.99**	**3.16%**	**3.73**	**4.10**	**31.54**	**7.46**

Source: https://www.sciencedirect.com/science/article/pii/S1359644625000194

Data source: annual reports (2012–2021), press releases (2012–2021), Refinitiv Eikon, GlobalData and FDA website (see methodology) – data normalized and cleaned. R&D intensity is calculated as the ratio of internal R&D expenditures to total revenue. Financial data originally reported in other currencies was converted to US$ by applying Refinitiv Eikon's embedded function.

R&D Output Highly Correlated with Both R&D Spend and M&A

But interestingly, the fraction of revenue spent on R&D (R&D intensity) is not tied to R&D output.

TABLE 3

Correlation of R&D strategy elements and R&D output of 14 leading pharmaceutical companies (2012–2021)

	R&D expenditure vs R&D output	Number of M&A vs R&D output	Number of in-licensing deals vs R&D output	Average R&D intensity vs R&D output
Observations	14	145	405	14
Pearson r				
r	0.7756	0.5970	0.1918	−0.08251
95% confidence interval	0.4163 to 0.9254	0.09724 to 0.8563	−0.3772 to 0.6557	−0.5874 to 0.4686
R^2	**0.6015**	**0.3564**	**0.0368**	**0.0068**
P value				
***P* (two-tailed)**	**0.0011**	**0.0242**	**0.5113**	**0.7792**
P value summary	**	*	ns	ns
Significant? (alpha = 0.05)	Yes	Yes	No	No
Number of XY pairs	14	14	14	14

Data source: annual reports (2012–2021), press releases (2012–2021), Refinitiv Eikon, GlobalData and FDA website (see methodology) – data normalized and cleaned. R&D expenditures (US$B) are inflation-adjusted to 2021. Financial data originally reported in other currencies was converted to US$ by applying Refinitiv Eikon's embedded function. Standard errors in parentheses: *, $P < 0.05$; ** $P < 0.025$; ***

Source: https://www.sciencedirect.com/science/article/pii/S1359644625000194

Industry Update

CBER's Deputy Director Departs as Staff Shakeup Continues

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

Celia Witten, deputy director of the FDA's Center for Biologics Evaluation and Research, has left the FDA, adding to a wave of departures at the agency and across the federal health infrastructure as Robert F. Kennedy Jr. takes control of HHS.

CBER's organizational chart, updated on Friday, notes at least a dozen departures, and that former FDA chief of staff Julie Tierney is the only deputy director of CBER. Tierney told Endpoints that she's been deputy director since Dec. 2023 but she did not comment on Witten's departure.

Witten's departure comes after a long career at FDA and amid an exodus of senior staff, including CDER Director Patrizia Cavazzoni and FDA's Principal Deputy Commissioner Namandjé Bumpus, leading to questions of who will lead the agency moving forward. Witten, who wrote in an out-of-office message, "I have left the FDA," also previously served as FDA's director of the Office of Cellular, Tissue and Gene Therapy.

Source: https://endpts.com/cbers-deputy-director-departs-as-staff-shakeup-continues/

More NIH Job Cuts Coming? Agency's Scientists Already Reeling after Week of Firings

Jocelyn Kaiser, *Science*, Feb 21, 2025 (excerpt)

Already bruised by the first round of firings of federal workers by President Donald Trump's administration, employees at the National Institutes of Health (NIH) faced more bad news. NIH's 27 institute directors were told this week the agency must cut staffing back to 2019 levels, or at least 10% below its 2024 tally, according to two sources.

All told, according to an authoritative NIH source, the biomedical agency has in recent days lost about 1200 employees, or just over 5% of its workforce of some 20,000 staff, as part of the firings of "probationary" employees with less than 1 or 2 years in their current position. They range from administrative staff who handle outside grants to NIH lab managers, staff scientists, and tenure-track investigators. The blows have left employees shaken and wondering about the future.

"The firings and uncertainty that have happened even just up to now have set back NIH science significantly," says one still-employed principal investigator on the NIH campus who declined to be identified for fear of retribution. "Ongoing projects have been disrupted, project plans are screwed up, people are looking for other jobs."

The cuts hit hard in NIH's in-house research program, which makes up about 11% of the agency's $47.4 billion. With 1200 principal investigators, the intramural program is the world's largest biomedical research institution, although that often goes unappreciated.

NIH this week sought permission to reinstate about 13 to 15 tenure-track principal investigators–young talent who had recently started up their labs. Several worked at a 4-year-old Center for Alzheimer's and Related Dementias that has had strong support from Republican lawmakers. Also on the list of 150 probationary worker firings being appealed was the scientist in line to serve as the center's acting head to replace its departing director, according to a memo obtained by Science.

Source: https://www.science.org/content/article/more-nih-job-cuts-coming-agency-scientists-already-reeling-after-week-firings

US Must Embrace a Winning Biotech Strategy

Drew Endy (Stanford Engineering Professor) and Mike Kuiken, *Boston Globe* (opinion), Feb 21, 2025 (excerpt)

When Cambridge-based *Cell* launched in 1974 as a "journal of exciting biology," all but one article was authored by American scientists. Last year, when Cell celebrated its 50th anniversary, it selected 50 inspiring scientists; of those involved in biology and related fields, 11 work in America and nine in China.

The United States has been the undisputed innovator and leader in biology and biotechnology. Molecular biology and genetic engineering were discovered, invented, and first commercialized here. It can be hard to imagine what no longer leading could look like.

How did we get here? Many scoffed when Beijing announced its Made in China 2025 strategy in 2015. But since then, China has realized massive strides in biotechnology and other key scientific areas. Last year, Niko McCarty, founding editor of Boston's science- and technology-focused Asimov Press, remarked on social media about China's impressive and enviable progress. In January, STAT cited Chinese "research parks that dwarfed biotech hubs like Kendall Square."

China's biotechnology strategy has evolved from following to leading. In 2012, the United States, China, and the United Kingdom developed a trilateral road map for synthetic biology. While Washington stood still, Beijing launched an all-out effort. Today, China equals or leads the world in biotechnology education, research, entrepreneurship, and manufacturing.

Beijing's motivations are crystal clear. China must feed four times as many people with three-quarters as much farmland compared to the United States; food security drives China's biotechnology acquisitions and innovations. China also understands that biology is emerging as a general-purpose technology. Anything bioengineers can learn to encode in DNA can be grown. Not just food, medicines, and materials but also things you would not expect biology could make, from explosives to computer components.

Why aren't Chinese researchers clamoring to run their experiments on platforms owned and operated by US companies? How did we default to a strategy of not losing? What would a winning strategy look like?

To start, we must urgently scale biomanufacturing. Each public dollar invested in pilot-scale biomanufacturing must be followed by $20 more for full-scale biomanufacturing. New manufacturing routes to essential medicines must be more than invented here. Medicines and everything else in the biological sciences must be brewed or grown in America.

Foundational wins are also key. The first nation to make routine the building of cells will own an "operating system" for life, coded in DNA rather than ones and zeros. The first nation to establish biomolecular standards — the "weights and measures" underlying the bioeconomy — will have a persistent competitive advantage. If we miss solving biotechnology's coordination problems, catching up later will become almost impossible. Without question, the United States can do these things, but a sustained whole-of-nation effort is required.

A new Congress and new administration must assess the trajectory of our investments, consider bold ideas, and act. China's bioeconomy is burgeoning. China's bio-infrastructure is becoming the envy of our best and brightest. America must turbocharge its own biotechnology century with the urgency that drove MIT's Vannevar Bush to declare an endless frontier and emboldened Brookline-born former president John F. Kennedy to launch the Apollo program.

Source: https://www.bostonglobe.com/2025/02/21/opinion/us-china-biotechnology-innovation-manufacturing

Eli Lilly Aims to Invest in “Big Problems Hiding in Plain Sight” Using Obesity Windfall

Angelica Peebles, *CNBC*, Feb 20, 2025 (excerpt)

Heart disease. Hearing loss. Addiction. Chronic pain. Alzheimer’s. ALS. These are some of the areas where Eli Lilly, flush with cash from its GLP-1 drugs, wants to make big bets.

These are the ideas that are “hiding in plain sight,” said Lilly Chief Scientific Officer Dan Skovronsky. They’re places where other pharmaceutical companies might not want to go because they’re hard problems to solve.

“As right now really the biggest health-care company in the world, probably the biggest health-care company in the world ever, we have an obligation,” Skovronsky said. “Investors have given us that vote of confidence. We see that as an obligation to invest in some of these big problems that are hiding in plain sight, to try and make a difference for the health of your community.”

Lilly’s tirzepatide, sold as Mounjaro for diabetes and Zepbound for obesity, has transformed the company. The company’s sales have grown almost 60% since Mounjaro was approved in 2022. Lilly’s stock price has rocketed 268% higher in the last three years, giving the company a market cap of $823 billion – the highest of any health-care company.

Now the company wants that success to translate to other disease areas.

Lilly’s already testing whether its drug Kisunla can prevent Alzheimer’s disease. Kisunla is a monoclonal antibody that removes amyloid plaques from the brain, which are associated with the memory-robbing disease. It’s currently approved to treat people in the early stages of Alzheimer’s.

Dan Skovronsky
Chief Scientific Officer
Eli Lilly

Source: https://www.cnbc.com/2025/02/20/eli-lilly-to-take-big-swings-in-alzheimers-als-and-gene-therapy.html

GSK Struggles to Convince Market it Can Deliver on Pipeline Plans

Hannah Kuchler and Emma Dunkley, *Financial Times*, Feb 22, 2025 (excerpt)

UK drugmaker GSK is struggling to convince the market that it can deliver on its plans to refill its pipeline ahead of a key patent expiry, as US hedge fund Citadel took the largest short position against the company in more than a decade. Shareholders and analysts question GSK's plan to deliver £40bn in annual revenue by 2031, which is based on replacing income from its majority-owned blockbuster HIV drug dolutegravir towards the end of the decade. Ken Griffin's hedge fund has shorted the company at a time when its shares are trading below their price of a decade ago, having been knocked back by US lawsuits over the alleged cancer risks of discontinued heartburn drug Zantac. Even after GSK reached a $2.2bn settlement in October, resolving the majority of cases, its shares still did not bounce back.

GSK has historically been strong in vaccines and respiratory medicines. But Arexvy, its vaccine against respiratory syncytial virus, suffered a setback when a US immunisation advisory group delivered a more limited recommendation than its previous advice. Now, there is uncertainty over the whole market because of the appointment of vaccine sceptic Robert F Kennedy Jr as US health secretary. A top-30 shareholder said GSK had demonstrated some success in its pipeline and had made "rational decisions" but pointed to the "volatility in vaccines".

Tony Wood, GSK's chief scientific officer, acknowledged it might be easier to communicate the company's potential if he could point to "one big drug", but said: "It is in some ways an advantage that I'm not reliant on a single asset should something go wrong with that asset's performance."

Source: https://www.ft.com/content/67b15531-f7d3-4e60-b94d-80e9816a090b

Hims & Hers Shares Plunge as FDA Clears Weight-loss Drug Shortage

Axios, Feb 22, 2025

Ozempic and Wegovy, the popular GLP-1 drugs for diabetes and weight loss, are no longer in short supply, the FDA declared Friday.

Why it matters: That's good news for Novo Nordisk (whose stock rose 5% Friday) and potentially bad news for Hims & Hers (which fell 26%).
Between the lines: Novo makes Ozempic and Wegovy, while Hims has been making quite a bit of money offering copycat versions of the drugs in the U.S. for a fraction of the price.

The legal ability to sell these "compounded" versions of brand-name drugs relies, in large part, on the FDA's shortage designation.
State of play: That's setting up a potential standoff between Novo and Hims, who recently traded barbs after Hims' Super Bowl ad touting its alternative GLP-1s.

Friction point: Compounders now have 60 or 90 days, depending on their facility, to stop making drugs that are "essentially a copy" of Novo's products, the FDA said today.

Yes, but: Hims says it will continue to offer compounded semaglutide, the main ingredient in Ozempic and Wegovy.

It says despite the lift of the shortage designation, the FDA still allows compounding in the case of a "clinical need," such as when a patient has an allergy to a certain dye contained in a drug or cannot take it in its current form.

Source: https://www.axios.com/2025/02/22/ozempic-wegovy-weight-loss-drugs

Biggest-ever AI Biology Model Writes DNA on Demand

An artificial-intelligence network trained on a vast trove of sequence data is a step towards designing completely new genomes.

Ewen Callaway, *Nature*, Feb 19, 2025 (excerpt)

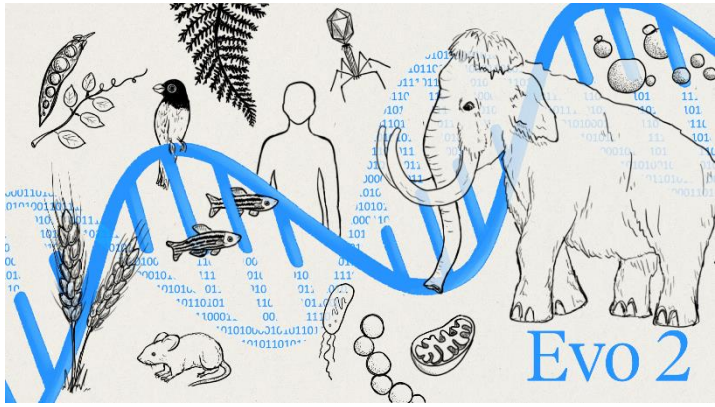
Scientists today released what they say is the biggest-ever artificial-intelligence (AI) model for biology.

The model — which was trained on 128,000 genomes spanning the tree of life, from humans to single-celled bacteria and archaea — can write whole chromosomes and small genomes from scratch. It can also make sense of existing DNA, including hard-to-interpret 'non-coding' gene variants that are linked to disease.

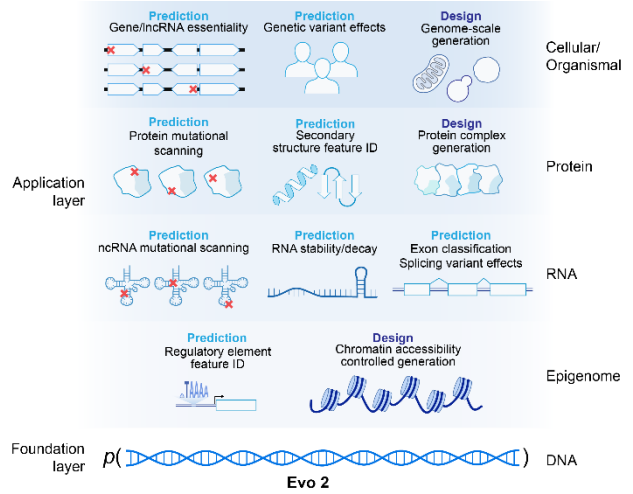
Evo-2, co-developed by researchers at the Arc Institute and Stanford University, both in Palo Alto, California, and chip maker NVIDIA, is available to scientists through web interfaces or they can download its freely available software code, data and other parameters needed to replicate the model.

The developers see Evo-2 as a platform that others can adapt to their own uses. "We're really looking forward to how scientists and engineers build this 'app store' for biology," Patrick Hsu, a bioengineer at the Arc Institute and the University of California, Berkeley, said at a press briefing announcing Evo-2's launch.

"We'll have to see how it holds up in independent benchmarks after the preprint is out," says Anshul Kundaje, a computational genomicist at Stanford University in Palo Alto. So far, he is impressed by the engineering that underpins the model.



You can now make your own organisms with EVO-2.



Source: https://www.nature.com/articles/d41586-025-00531-3

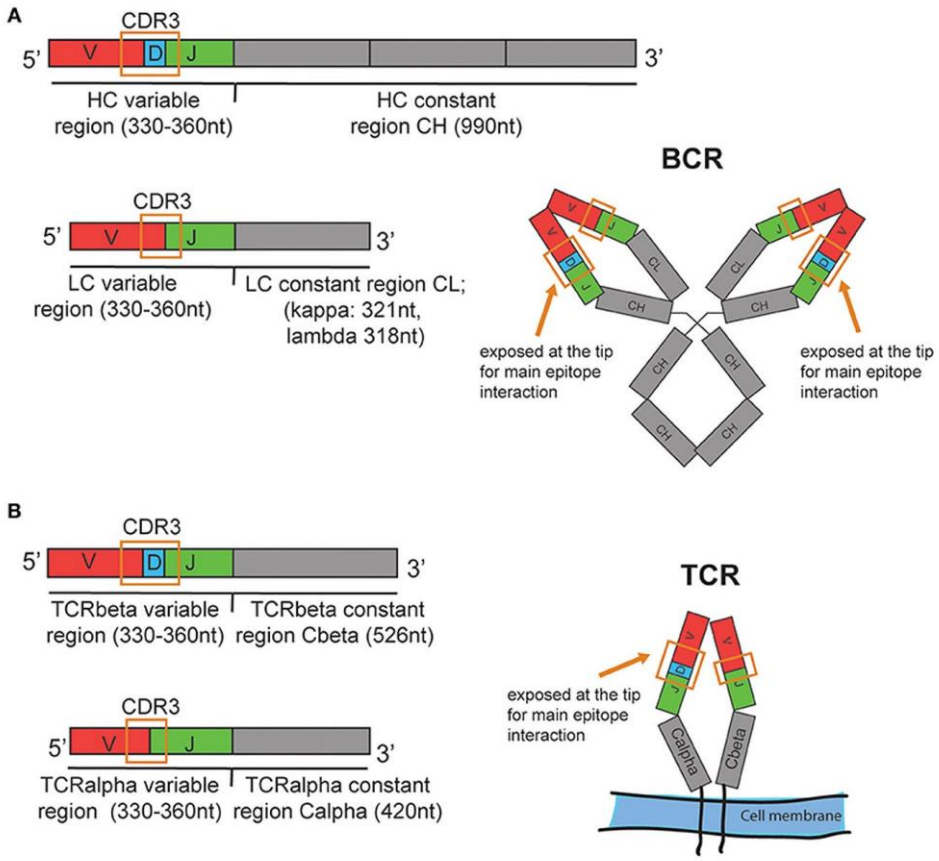
Eric Topol: Big Opportunity to Take a Precision Dx Approach to Autoimmunity

Eric Topol, Substack, Feb 22, 2025 (excerpt)

B and T lymphocytes contain a treasure chest of information about our immune response to pathogens, vaccination, environmental exposures, and untoward, self-directed attack (to our organs, tissues, and cells). The B and T cell receptors are like antennas, extending outside the cell (Figure below), that act as the sensors to mount a response to these different antigens. Their response is stored, but these receptors are exceedingly complex to decode because their diversity is extreme, with extensive gene rearrangements and somatic mutations. Until now, sequencing these receptors has not been used to diagnose an autoimmune condition or exposure to a pathogen. Their only clinical use case to date has been quite rare, in certain lymphomas for diagnosis and management.

Many autoimmune diseases are hard to accurately diagnose, require panels of expensive tests, and often lead to substantial delays. In fact, the average patient with an autoimmune disease requires visits with 4 doctors over 4.5 years to get an accurate diagnosis and treatment plan. The field has been waiting for a demonstration to unlock the potential of B and T cell repertoires—the complete collection of receptors express within an individual. In my prior post on Ground Truths, I outlined why it is so essential to have an immunome, since the only routine lab test we have today to assess a person's immune system is the ratio of neutrophils to lymphocytes, a crude marker, what can be considered as an icepick view of the body's most complex system. I'll come back to that later, since an immunome has promise well beyond diagnosing autoimmune conditions.

In Science this week, Maxim Zaslavsky and colleagues (and a who's who list of leading immunologists and rheumatologists in the US and Europe) published an extraordinary paper, the first sequencing of B (BCR) and T cell receptors (TCR) at scale across multiple diagnoses. This work included 63 people with acute Covid who were hospitalized, 86 with lupus (some were pediatric cases), 92 with autoimmune Type 1 diabetes, 95 with HIV, 37 who had a recent flu shot, and 220 different controls. A total of nearly 600 individuals (N=593). From blood samples, they sequenced the heavy chain of the B cell receptor and the beta chain of the T cell receptor (as seen in the Figure above) in tens of millions of lymphocytes.



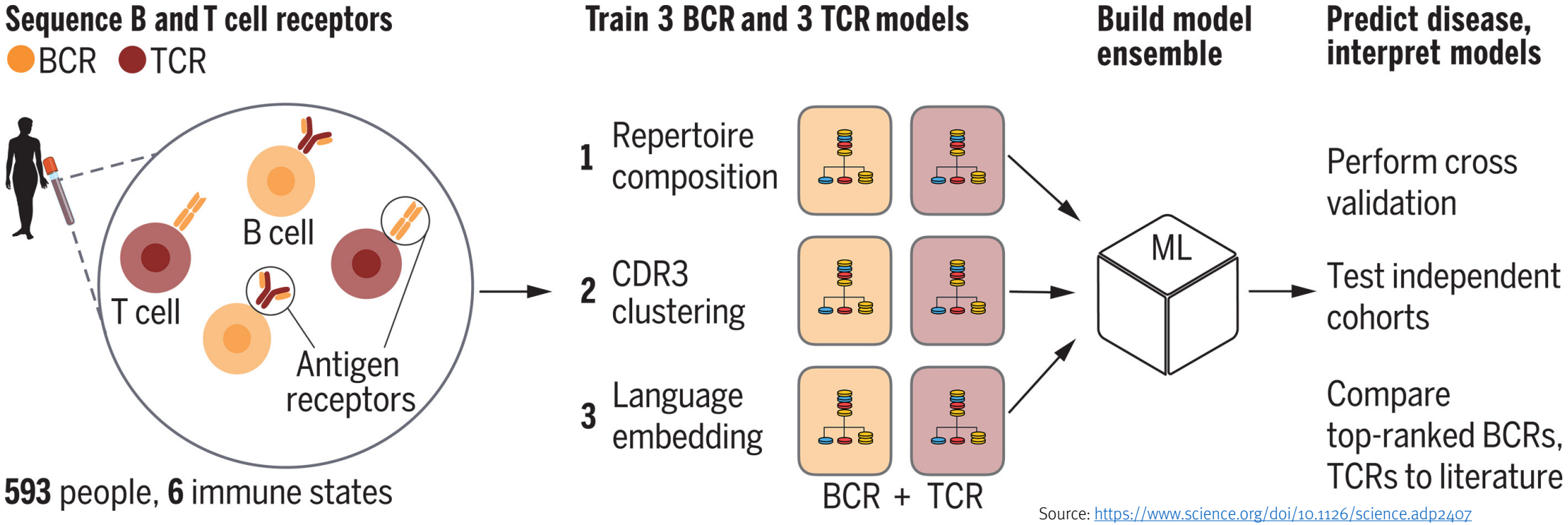
Source: https://erictopol.substack.com/p/the-first-diagnostic-immunome

The Science Paper Referenced by Topol: Disease Diagnostics Using Machine Learning of B Cell and T Cell Receptor Sequences

Maxim Zaslavsky et.al., *Science,* Feb 21 2025: 387(6736)

Clinical diagnosis typically incorporates physical examination, patient history, various laboratory tests, and imaging studies but makes limited use of the human immune system's own record of antigen exposures encoded by receptors on B cells and T cells. We analyzed immune receptor datasets from 593 individuals to develop MAchine Learning for Immunological Diagnosis, an interpretive framework to screen for multiple illnesses simultaneously or precisely test for one condition. This approach detects specific infections, autoimmune disorders, vaccine responses, and disease severity differences.

This pilot study demonstrates that **immune receptor sequencing data can distinguish a range of disease states and extract biological insights without prior knowledge of antigen-specific receptor patterns**. With further validation and extension, Mal-ID could lead to clinical tools that harness the vast information contained in immune receptor populations for medical diagnosis.



Source: https://www.science.org/doi/10.1126/science.adp2407

MYC in Cancer: From Undruggable Target to Clinical Trials

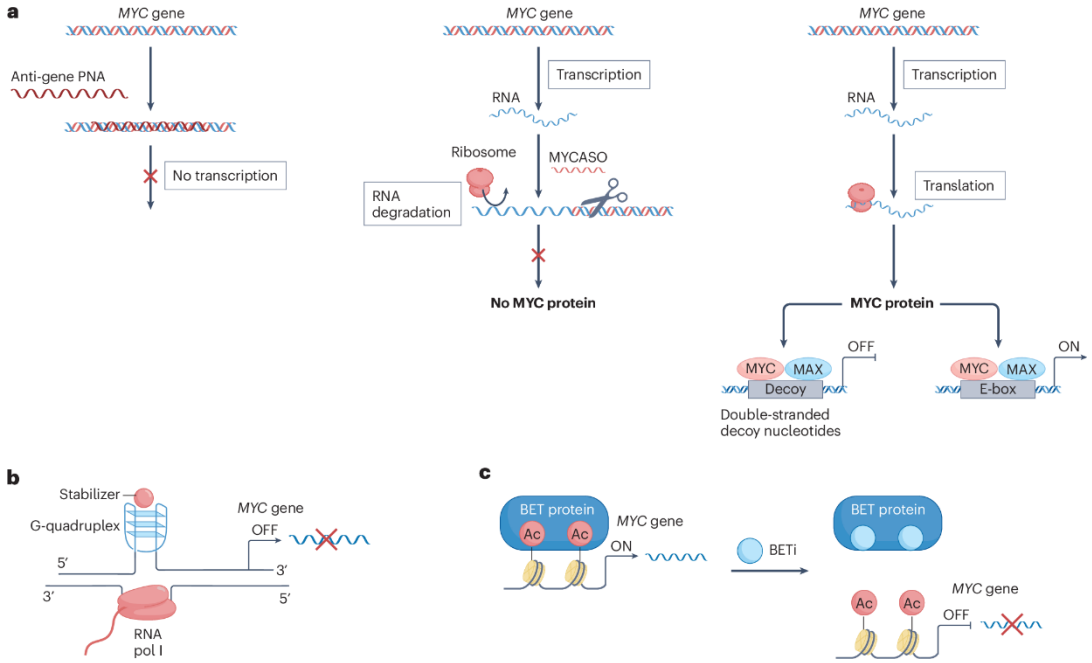
Whitfield, J.R., Soucek, L., *Nat Rev Drug Discovery*, Feb 19, 2025. (excerpt)

MYC is among the most infamous oncogenes in cancer. A notable feature that distinguishes it from other common oncogenes is that its deregulation is not usually due to direct mutation, but instead to its relentless activation by other oncogenic lesions. These signalling pathways funnel through MYC to execute the transcriptional programmes that eventually lead to the uncontrolled proliferation of cancer cells. Indeed, deregulated MYC activity may be linked to most — if not all — human cancers. Despite this unquestionable role of MYC in tumour development and maintenance, no MYC inhibitor has yet been approved for clinical use.

The main reason is that MYC has long fallen into the category of 'undruggable' or 'difficult-to-drug' targets, mainly because of its intrinsically disordered structure, which is not amenable to traditional drug development strategies. However, in recent years, attempts to develop MYC inhibitors have multiplied, and the first clinical trials have been testing their efficacy in patients. We are finally reaching the point at which its inhibition seems clinically viable. This Review provides an overview of the various strategies to inhibit MYC, focusing on the most recently described inhibitors and those that have reached clinical trials.

Source: https://www.nature.com/articles/s41573-025-01143-2

Fig. 2: Inhibitors of *MYC* transcription and translation.



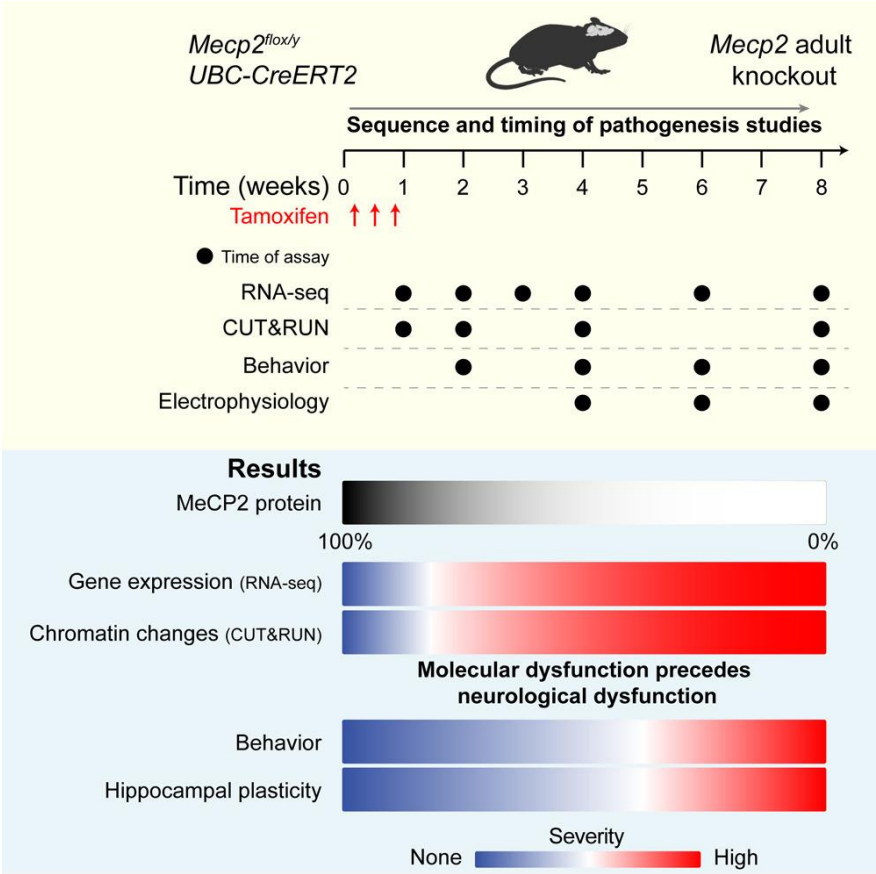
a, Oligonucleotide-based approaches to inhibit MYC can have various mechanisms of action. Anti-gene peptide nucleic acids (PNAs) hybridize with cDNA within the MYC gene promoter thereby blocking its transcription; MYC antisense oligonucleotides (MYCASOs) interfere with MYC mRNA, blocking its translation, and double-stranded decoy nucleotides compete with MYC targets for MYC–MAX binding, preventing their transcriptional activation. b, Binding of a stabilizer to the G-quadruplex prevents the advancement of RNA polymerase I (pol I) and transcription of the MYC gene. c, BET inhibitors (BETi) interact with BET proteins, preventing both their binding to the hyper-acetylated (Ac) region of the MYC gene and the recruitment of the transcription machinery. This results in reduced MYC transcription.

Rett Syndrome Linkage to MeCP2 Gene Shown to Work Through Transcriptomal Dysregulation

Bajikar SS et.al. Acute MeCP2 loss in adult mice reveals transcriptional and chromatin changes that precede neurological dysfunction and inform pathogenesis. *Neuron*. 2025 Feb 5;113(3):380-395.e8.

Mutations in the X-linked methyl-CpG-binding protein 2 (MECP2) gene cause Rett syndrome, a severe childhood neurological disorder. MeCP2 is a well-established transcriptional repressor, yet upon its loss, hundreds of genes are dysregulated in both directions. To understand what drives such dysregulation, we deleted Mecp2 in adult mice, circumventing developmental contributions and secondary pathogenesis. We performed time series transcriptional, chromatin, and phenotypic analyses of the hippocampus to determine the immediate consequences of MeCP2 loss and the cascade of pathogenesis.

We find that loss of MeCP2 causes immediate and bidirectional progressive dysregulation of the transcriptome. To understand what drives gene downregulation, we profiled genome-wide histone modifications and found that a decrease in histone H3 acetylation (ac) at downregulated genes is among the earliest molecular changes occurring well before any measurable deficiencies in electrophysiology and neurological function. These data reveal a molecular cascade that drives disease independent of any developmental contributions or secondary pathogenesis.



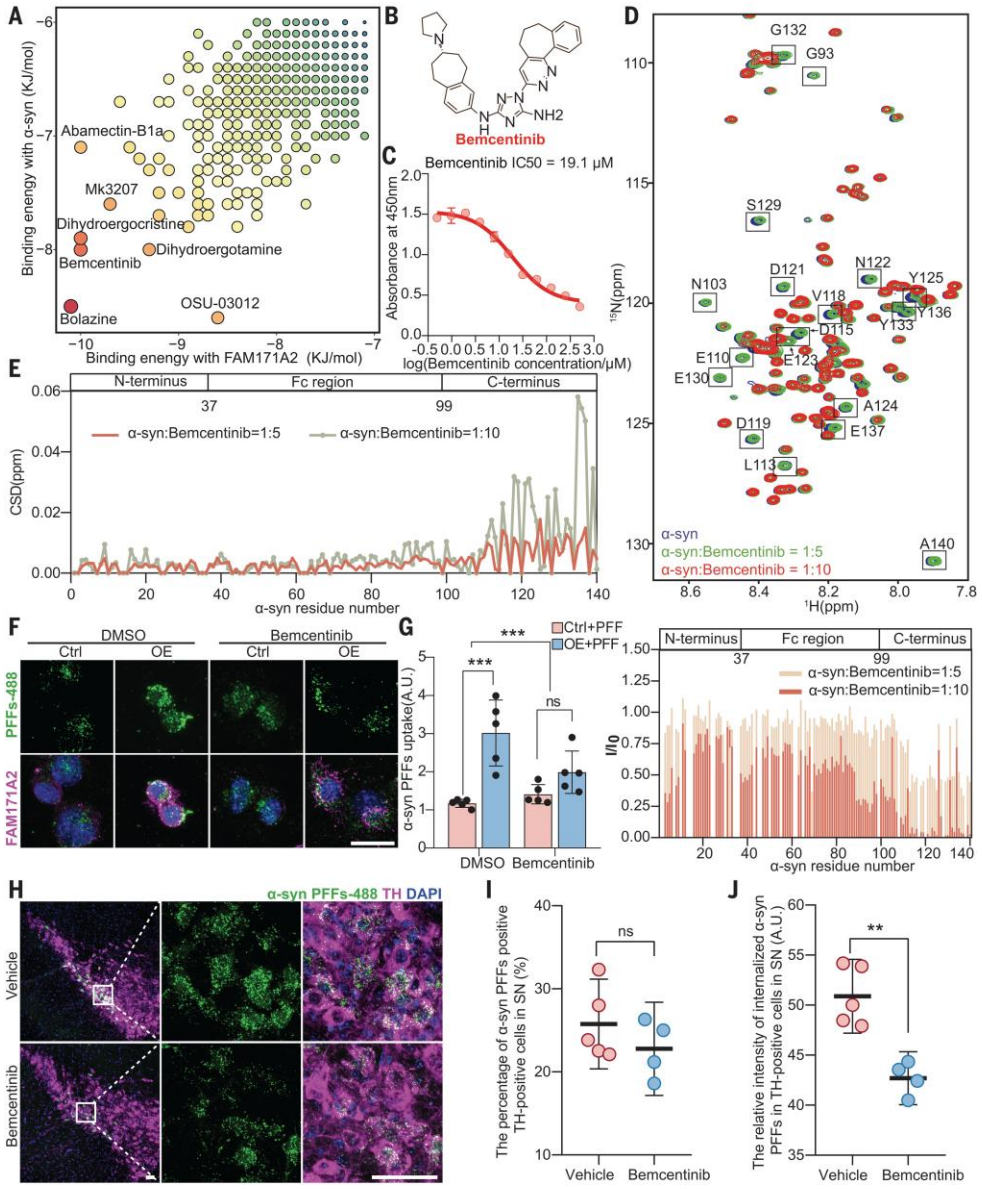
Source: https://www.cell.com/neuron/fulltext/S0896-6273(24)00806-7

Neuronal FAM171A2 Mediates α-synuclein Fibril Uptake and Drives Parkinson's Disease

KM Wu et.al. *Science*, Feb 21, 2025, pp. 892-900 (excerpt)

Neuronal accumulation and spread of pathological α-synuclein (α-syn) fibrils are key events in Parkinson's disease (PD) pathophysiology. However, the neuronal mechanisms underlying the uptake of α-syn fibrils remain unclear. In this work, we identified FAM171A2 as a PD risk gene that affects α-syn aggregation. Overexpressing FAM171A2 promotes α-syn fibril endocytosis and exacerbates the spread and neurotoxicity of α-syn pathology. Neuronal-specific knockdown of FAM171A2 expression shows protective effects.

Mechanistically, the FAM171A2 extracellular domain 1 interacts with the α-syn C terminus through electrostatic forces, with ›1000 times more selective for fibrils. Furthermore, we identified bemcentinib as an effective blocker of FAM171A2-α-syn fibril interaction with an in vitro binding assay, in cellular models, and in mice. Our findings identified FAM171A2 as a potential receptor for the neuronal uptake of α-syn fibrils and, thus, as a therapeutic target against PD.



Source: https://www.science.org/doi/10.1126/science.adp3645

IQVIA Update on U.S. Retail Prescription Marketplace at DSN

Feb 20, 2025
Selected Slides

DRUG STORE NEWS dsn

Speakers:

Doug Long
Vice President,
Industry Relations
IQVIA

Scott Biggs
Director of Supplier
Services
IQVIA

John Kenlon
Senior VP, Publisher
Drug Store News

EnsembleIQ

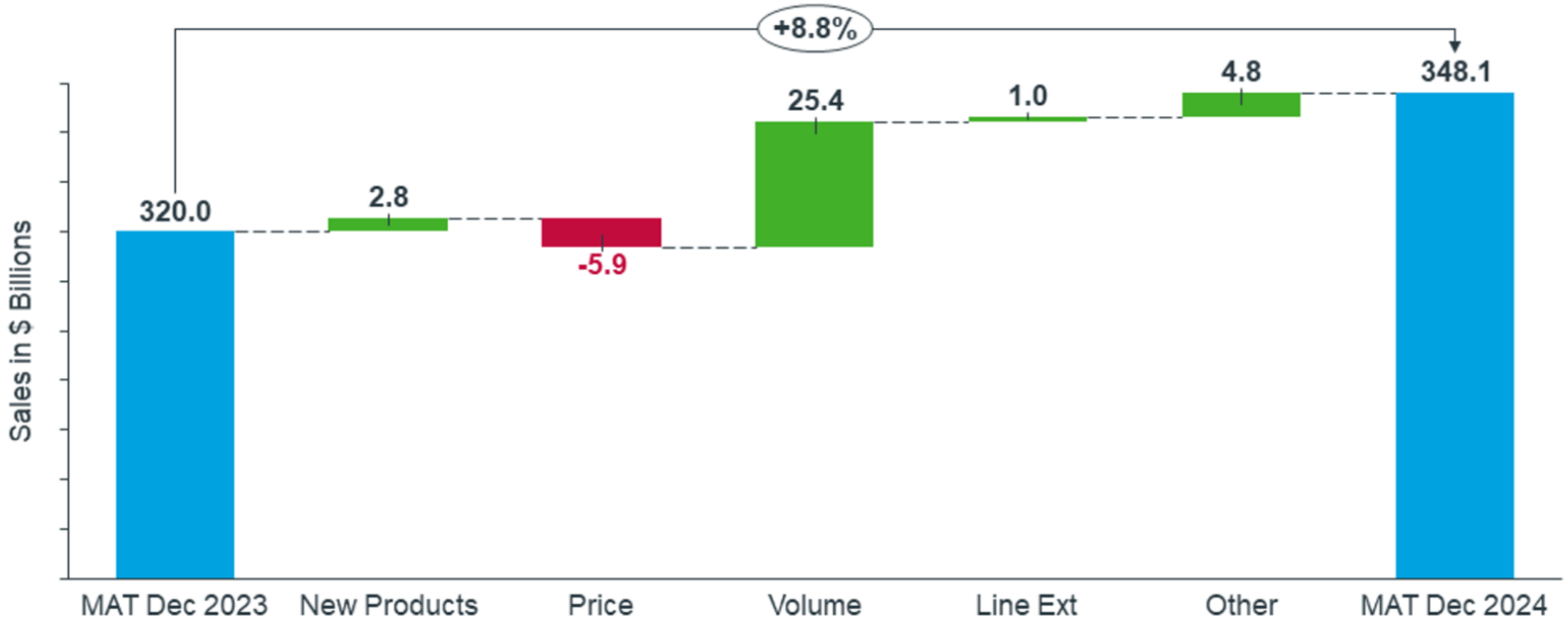
ASCEND Laboratories, LLC

IQVIA

Source: https://event.webcasts.com/viewer/event.jsp?ei=1705188

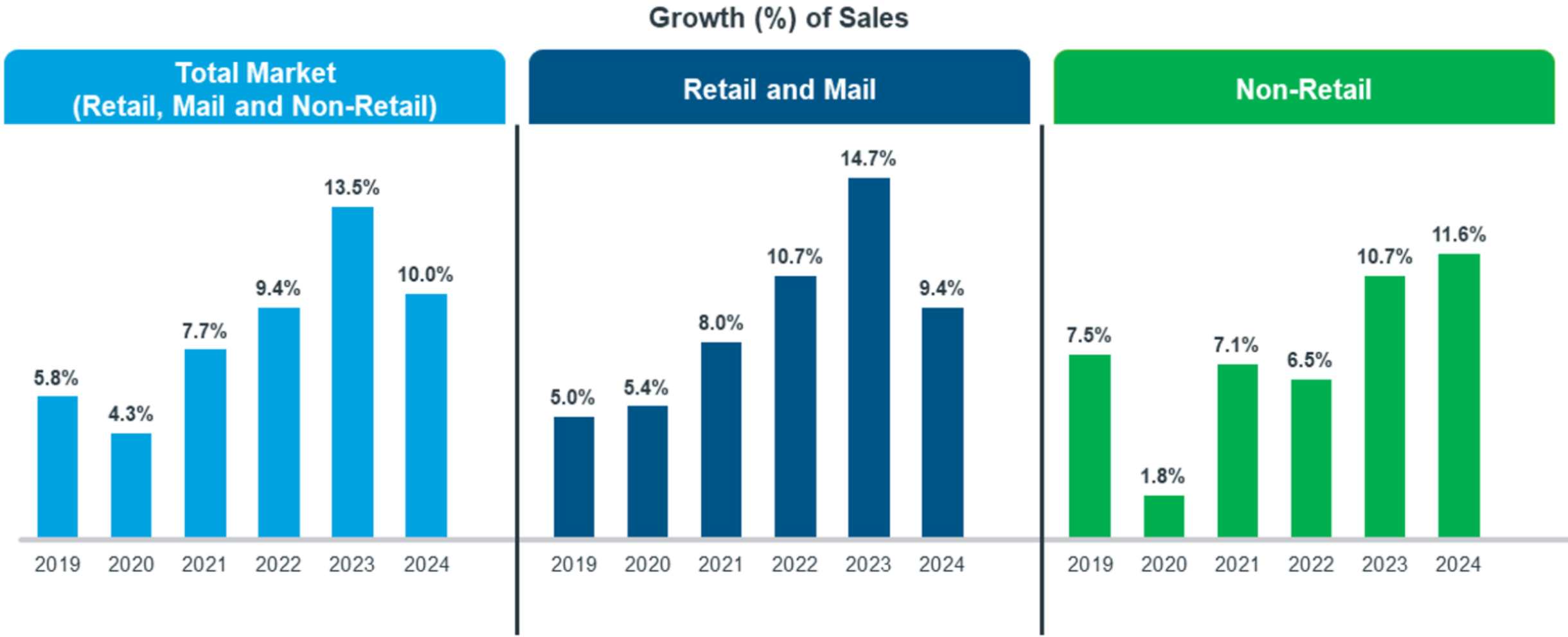
Rx Market Insights: Performance Trends and Outlook for 2025

The U.S. Retail pharmaceutical market grew 8.8% in 2024



Components contribution to Growth of 8.8%	0.9%	-1.9%	8.1%	0.3%	1.5%

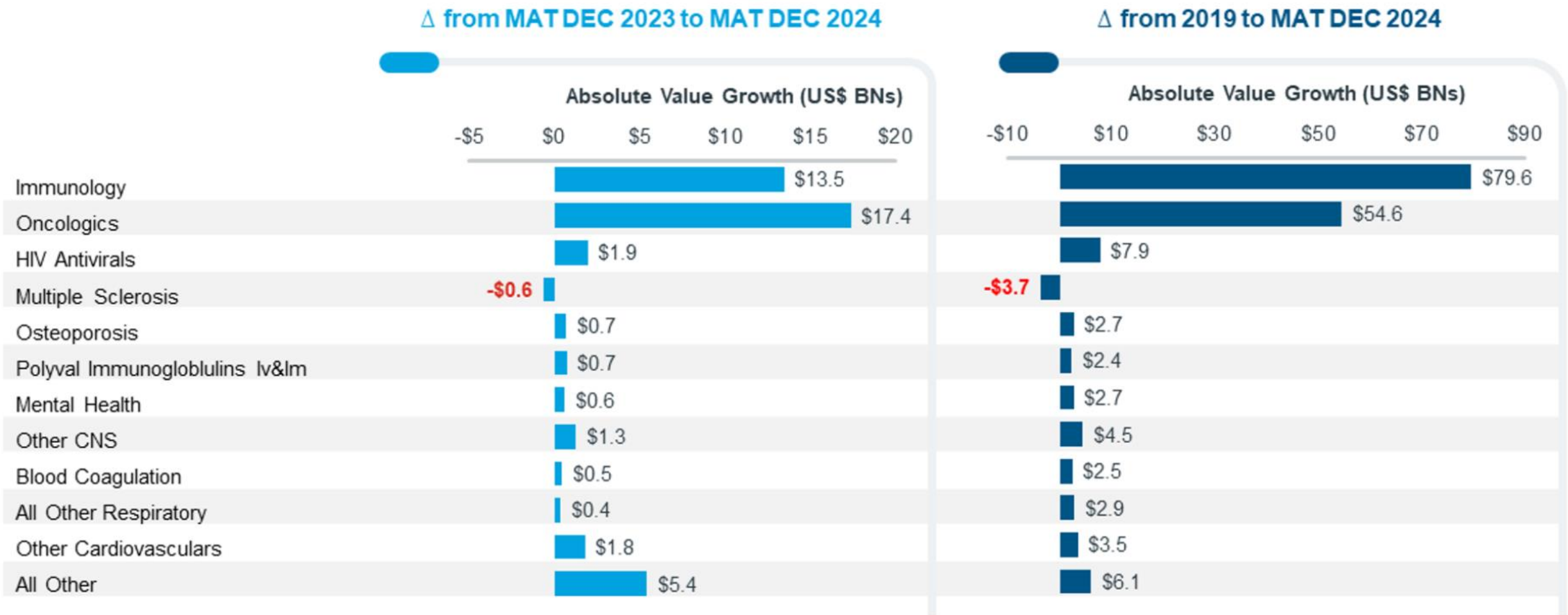
The Non-Retail channel showed higher growth in 2024 than Total Market and Retail and Mail



Source: IQVIA, National Sales Perspectives, December 2024
Note: Limited to Rx and OTC Insulins; Includes Retail, Non-Retail and Mail

Immunology and Oncologic contributed the most absolute value growth for specialty therapy areas

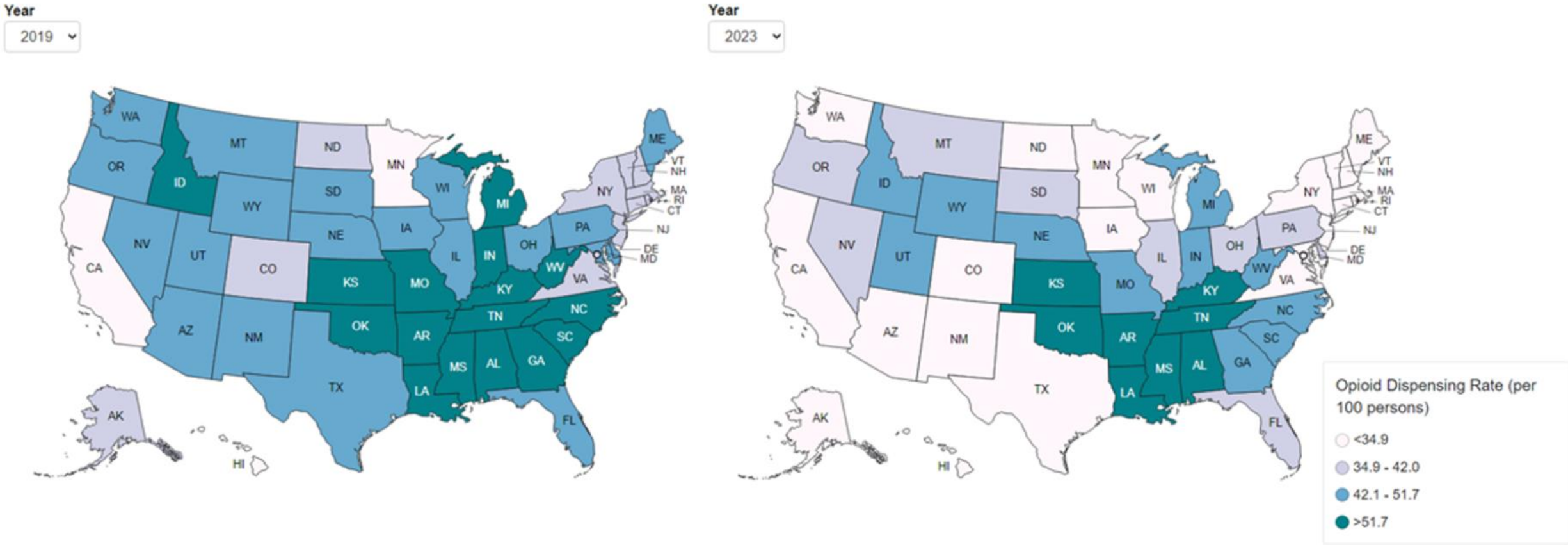
Absolute Value Growth for Top Specialty Therapy Areas



Source: IQVIA, National Sales Perspectives, December 2024
Note: top therapy areas ranked on MAT December 2024 non-discounted spend

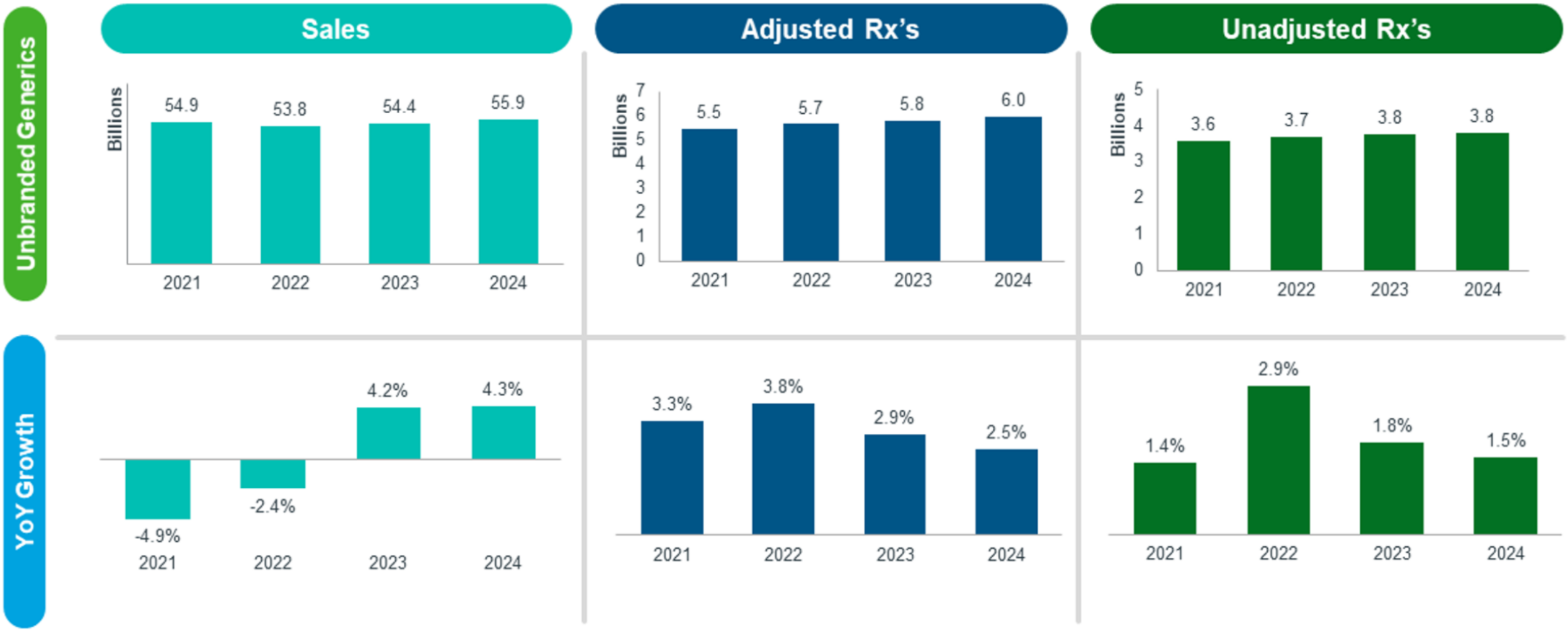
“The national opioid dispensing rate steadily declined from 46.8 Rxs per 100 persons in 2019 to 37.5 in 2023” per the CDC

State opioid dispensing rates



Source: Opioid Dispensing Rate Maps | Overdose Prevention | CDC, supported by the IQVIA Government Solutions team

Unbranded Generics sales and Rxs are positive



Source: IQVIA, National Sales Perspectives and RxInsights, 2024
Note: Limited to Rx and OTC Insulins; Includes Retail, Non-Retail and Mail

Launch Landscape as of December 2024

GLP-1s dominated previous years' launch sales and other products like Hyrimoz are growing in 2024
Neurology and oncology are the top therapy areas in 2024

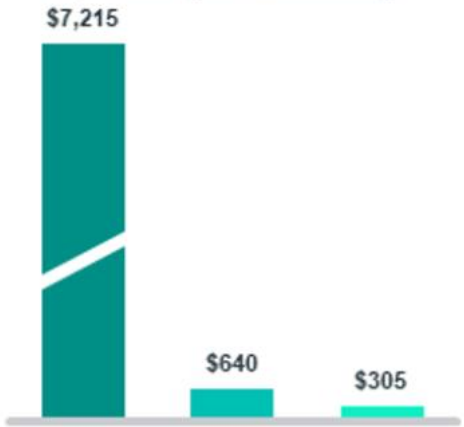
77 new launches through December 2024

Key Markets to Watch:
MASH
Respiratory vaccines
Humira biosimilars
GLP-1s (*Sleep Apnea*)

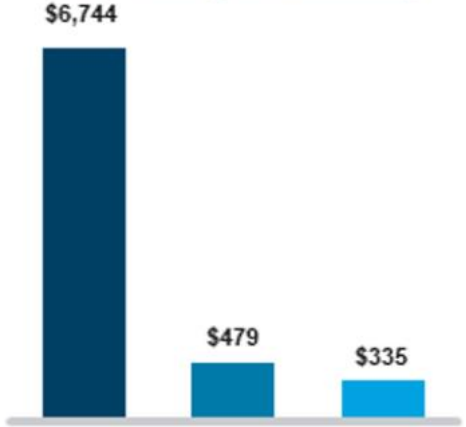
Top therapy areas *(share of launches)*

2024 n=77	Neurology 16%	Oncology 16%	Cardiovascular 13%
2023 n=96	Oncology 21%	Immunology 13%	Neurology 13%
2022 n=79	Oncology 17%	Neurology 12%	Cardiovascular 11%

Top 2022 launches by sales (USD millions)



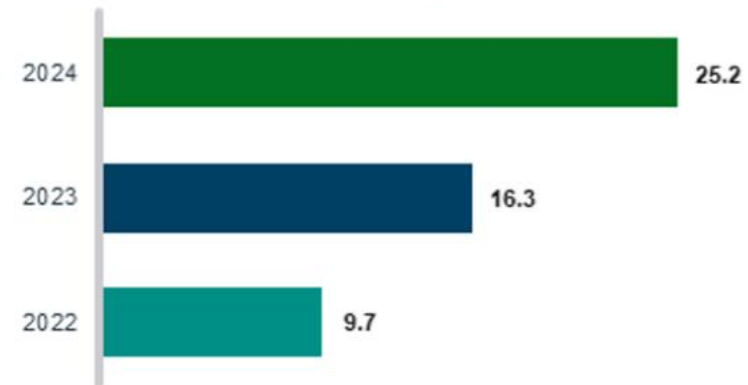
Top 2023* launches by sales (USD millions)



Top 2024* launches by sales (USD millions)

* Data through Dec 2024

Time-aligned average cumulative TRx at 9 months from launch, thousands

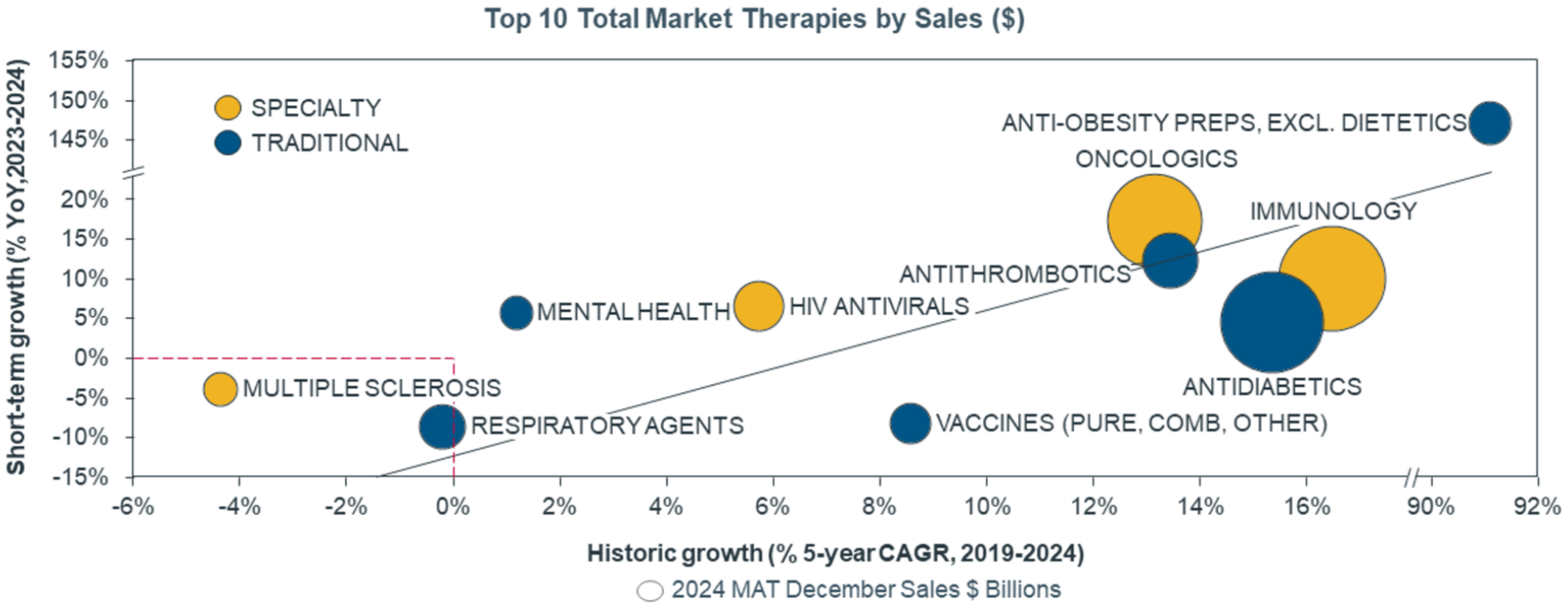


Excludes vaccines, Paxlovid, Mounjaro, Zepbound

IQVIA U.S. Launch Landscape Tracker, December 2024 Edition

Anti-obesity drugs led both long-term and short-term growth

COVID-19 Vaccines are not included in Sales



The GLP-1 category of drugs is affecting both sides of the pharmacy counter

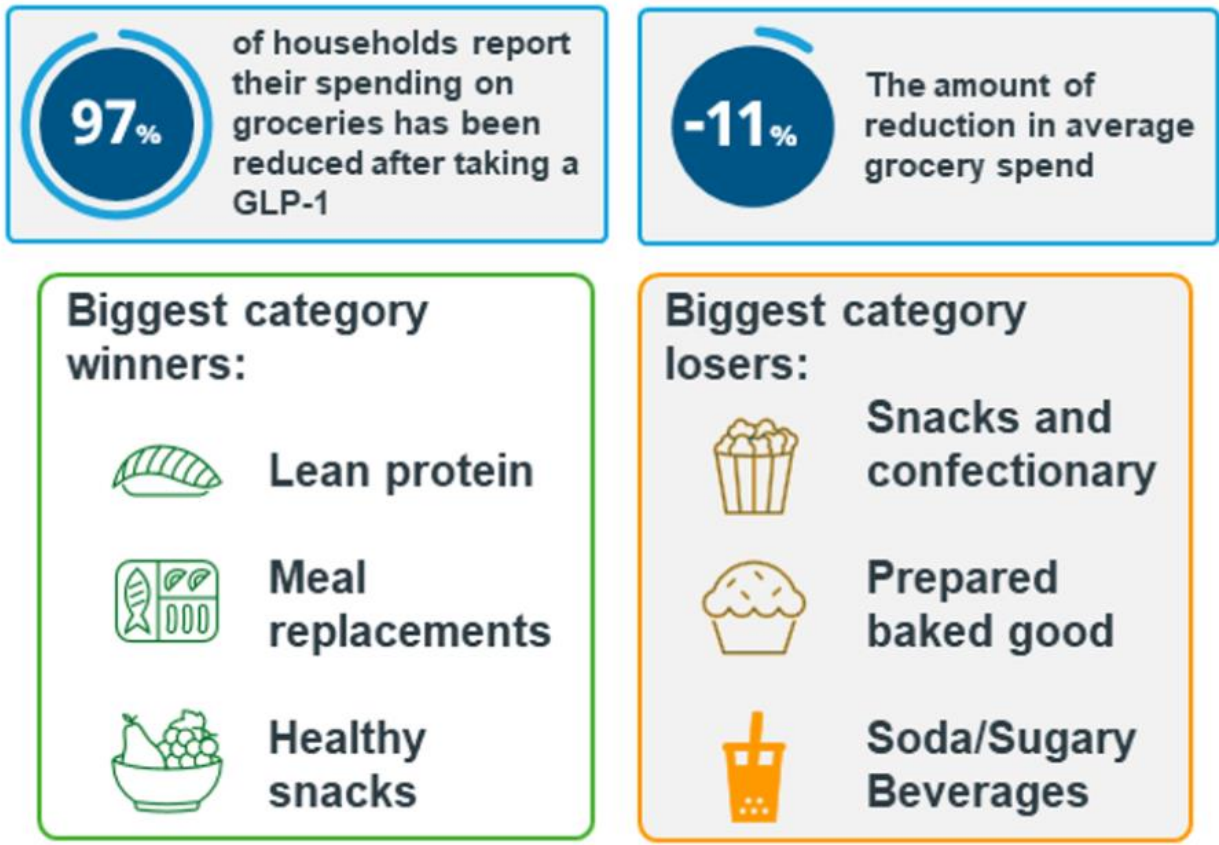
KFF Health Tracking Poll May 2024: The Public's Use and Views of GLP-1 Drugs

- **1** in **8** adults say they've taken a GLP-1 agonist
- **6%** say they are currently taking a GLP-1
- **32%** of adults say they have heard "a lot" about these drugs, up from **19%** in July 2023
- **62%** of adults who have taken GLP-1 drugs say they took them to treat a chronic condition including diabetes or heart disease
- **54%** of all adults who have taken GLP-1 drugs say it was difficult to afford the cost, including **22%** who say it was "very difficult"

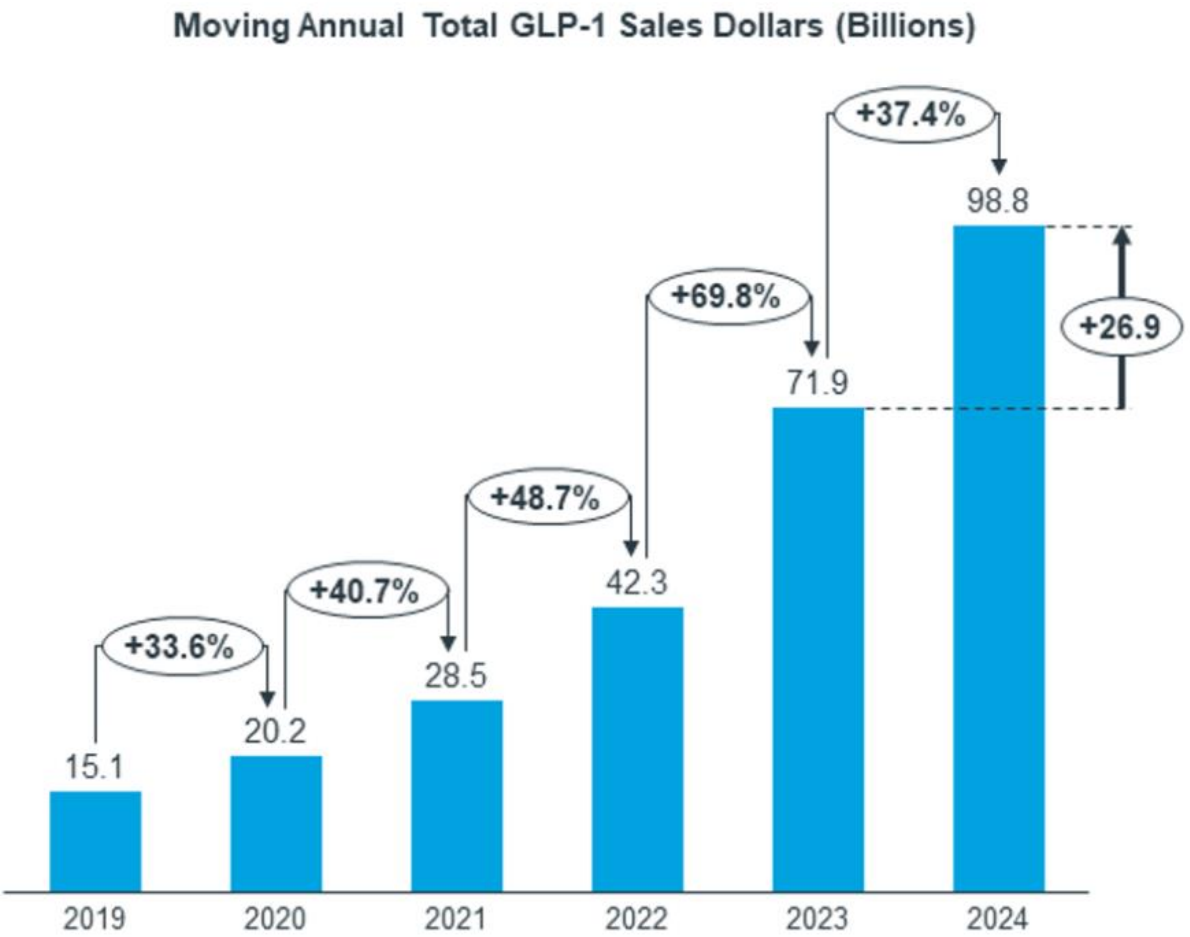
Source: https://www.kff.org/health-costs/poll-finding/kff-health-tracking-poll-may-2024-the-publics-use-and-views-of-glp-1-drugs/

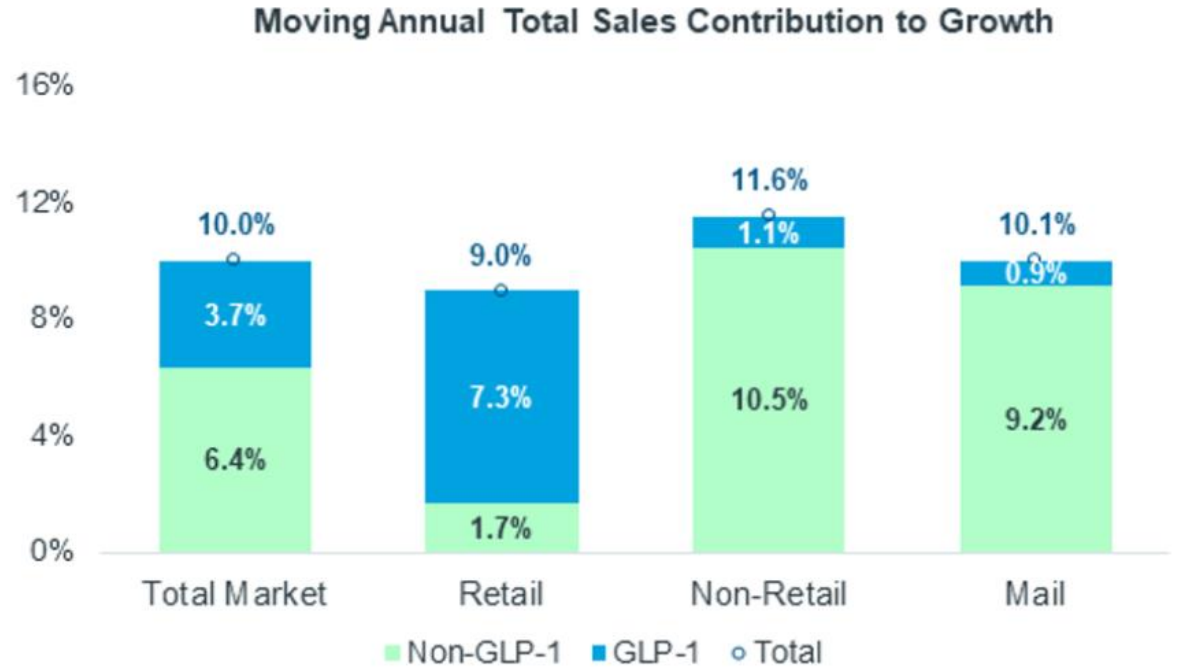
grocerydoppio's latest report continued to show how GLP-1s are impacting grocery shopping

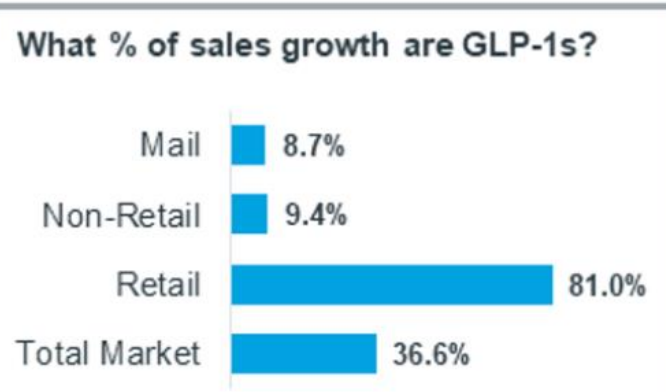
Source: grocerydoppio's 2024 Digital Grocery Takeaways, December 30, 2024



GLP-1s grew 37% over the last 12 months; 81% of Retail sales growth comes from GLP-1s



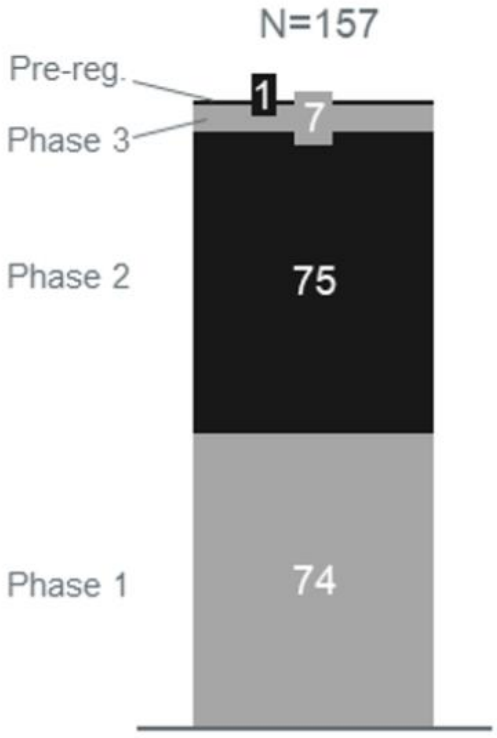




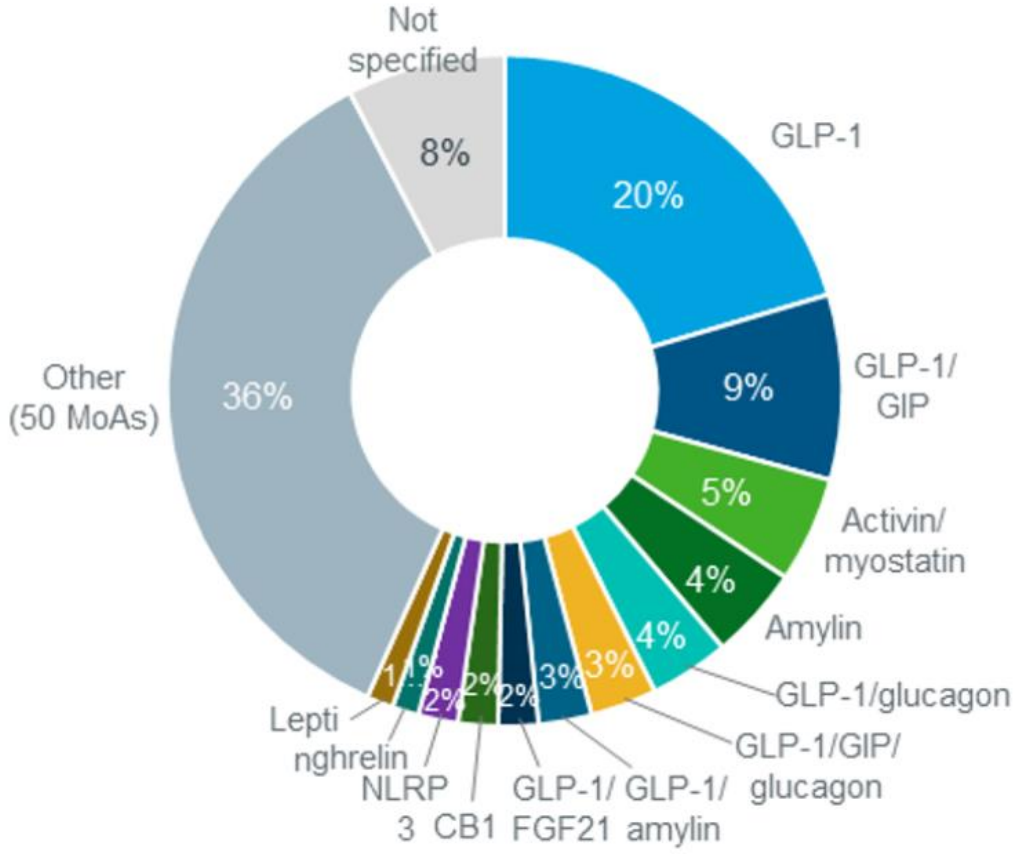
Updated with December 2024 Data

The Obesity pipeline is crowded: 157 new assets, 50+ MoAs and 70+ companies behind them

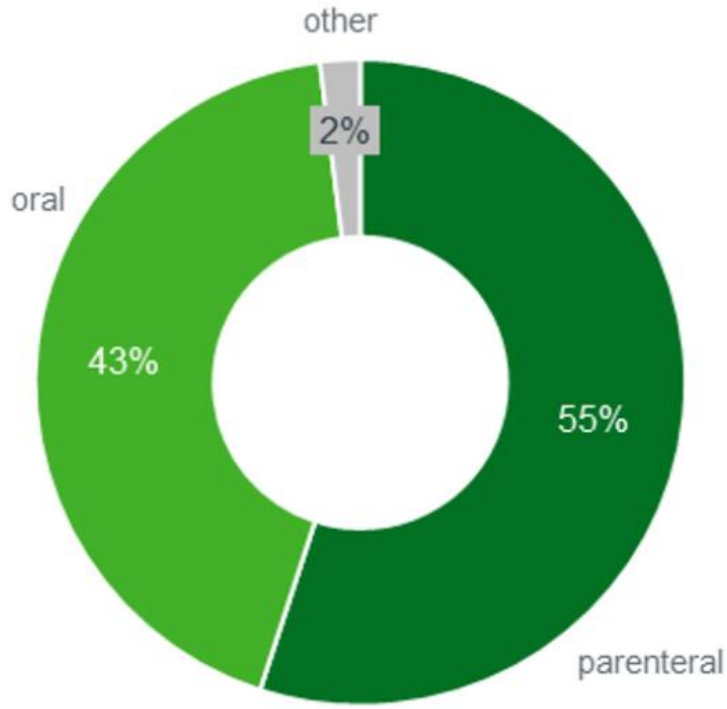
By phase
(Number of active assets)



By mechanism of action
(phase 1-pre−registration; N = 157)



By route of administration
(phase 1-pre−registration; N = 157)



Many companies in Obesity, from large to emergent

Disclosure

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