# Biopharmaceutical Sector

Update – Dec 17, 2024



STIFEL | Healthcare

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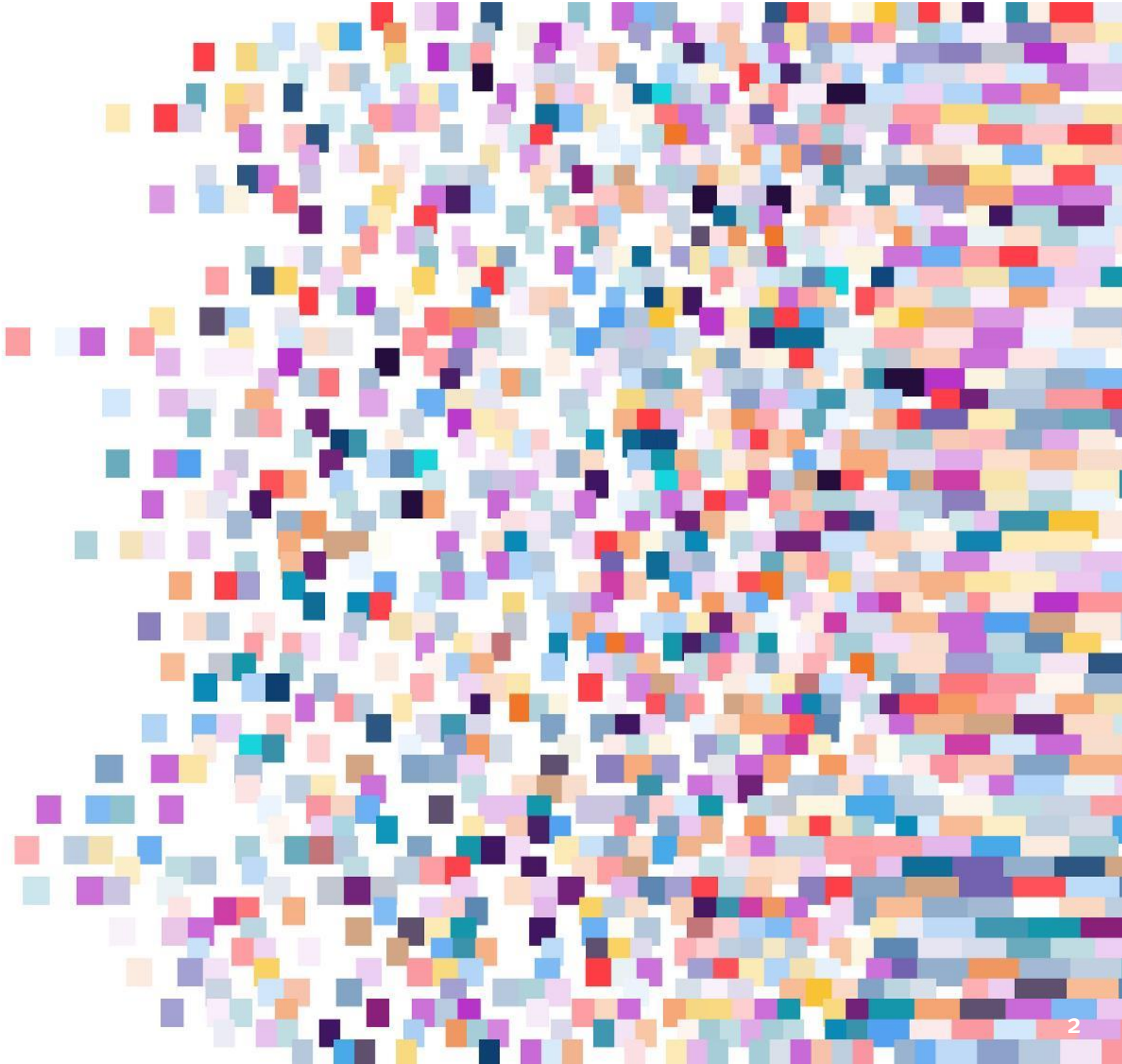


# Publishing Schedule Update

We will not be publishing on the week of Dec 25th. We will publish twice in the weeks leading up to the JPM conference.

If you are not on the mailing list for this publication and wish to be added, please notify Natasha Yeung (yeungn@stifel.com).

Wishing you a great holiday and a Happy New Year in advance!

# Past Issues

Past issues of this publication can be read online at:

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)
August 7, 2023 (Employment, Reading)
July 24, 2023 (Alzheimer's Disease)
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)
May 29, 2023 (Oncology update)
May 22, 2023 (FTC case on Amgen/Horizon)

# Feel Free to Join Us at These Upcoming Events


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

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


The week of Jan 13, 2025 will feature over 30,000 biopharma professionals in SF for JPM, Biotech Showcase and many other events. Stifel will be hosting an industry cocktail party on Jan 13th.

**To meet with Stifel**
yeungn@stifel.com

# Please Join at Two Panel Events at #JPM25

## Saturday, January 11

*1st Annual BioPharma Obesity Innovation Forum, Sachs Associates*
Marines' Memorial Club, 609 Sutter Street, San Francisco

8:50am

**Potential Magnitude of Obesity Market & Impact on the Healthcare System Panel**

*Moderators*: Jeff Berkowitz, CEO, Real Endpoints
Tim Opler, Managing Director, Healthcare Group, Stifel

Panel Members:

David Kendall, CMO, Zealand Pharma A/S
Enrique Conterno, Board Member, Zealand Pharma A/S
Kent Rogers, CEO, EveryONE Medicines

## Monday, January 13

*Biotech Showcase*
Hilton, Imperial Ballroom, 12:00-1:30 PM

**The "New" Policy Landscape: Now that the Election is Behind Us, Where Do We Go from Here?**
Join us for a discussion on the Trump Administration, the Inflation Reduction Act (IRA), the decision to overturn Chevron deference, and other issues that are impacting the healthcare landscape. This panel of experts will explore how these pivotal changes could reshape regulatory environments, funding opportunities and innovation.

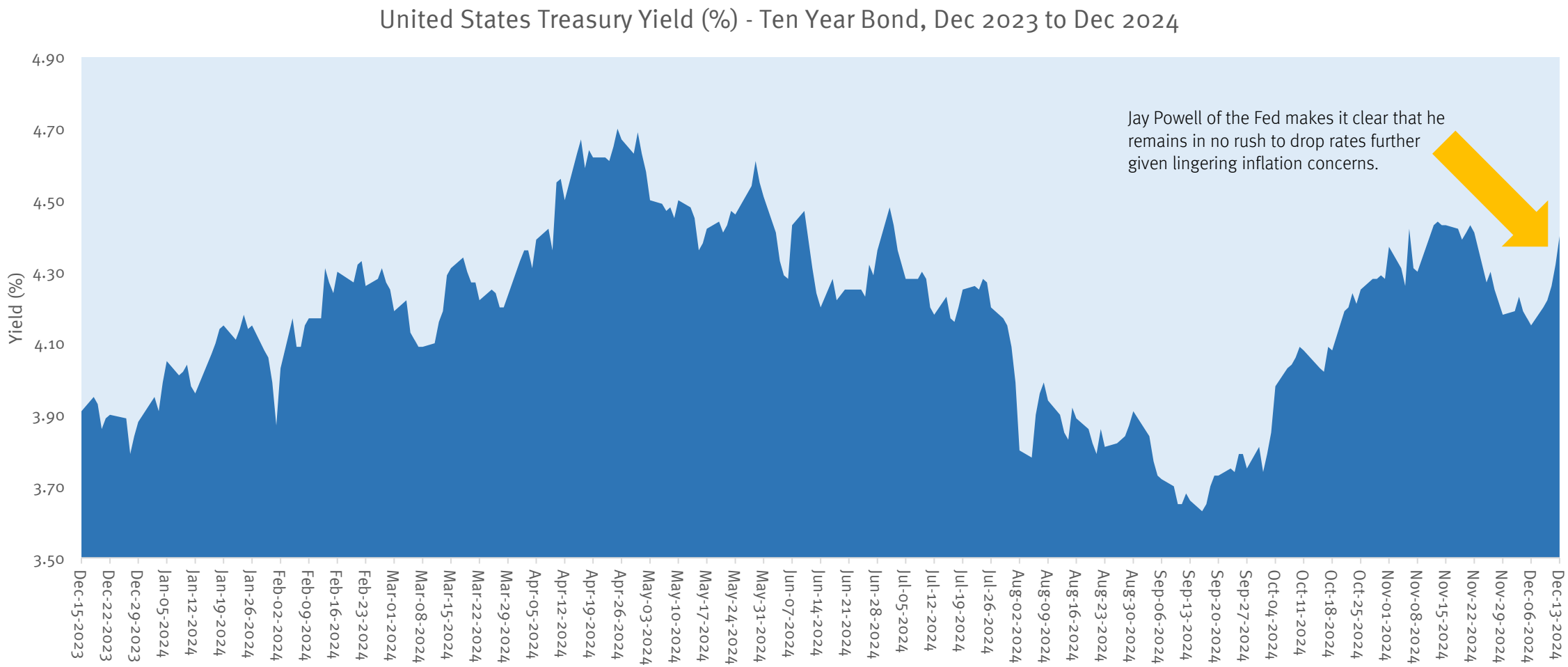
*Moderator*: Tim Opler, Managing Director, Healthcare Group, Stifel
Panel:

- Grace Colón, CEO & Co-Founder, Inaya Therapeutics, BIO Executive Committee Member
- Nouhad Husseini, SVP, Business Development & Corporate Strategy, Regeneron Pharmaceuticals
- Tony Lanzone, Global Head, Consulting, Syneos Health
- Ted Love, Chair, Board of Directors, Biotechnology Innovation Organization (BIO)
- Beth Neitzel, Partner, Foley Hoag

# Macro Update

# U.S. Treasury Bond Yields Remain Stubbornly High

**Not good for biotech at all.**




Source: S&P Capital IQ

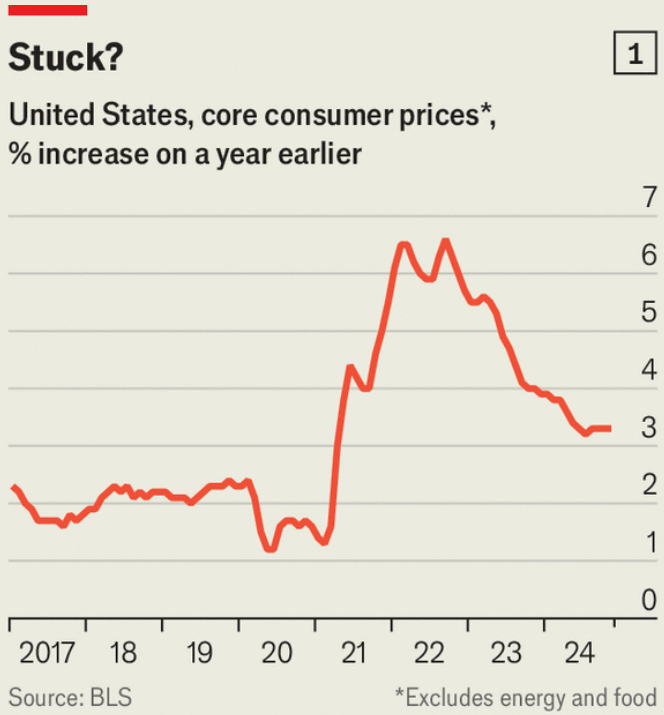
# The Federal Reserve takes on Trump—and Stubborn Inflation

*The Economist*, Dec 12, 2024 (excerpt)

A lot is riding on the numbers after the decimal point. In the argot of investors, inflation in America is back to having a “two-handle” (that is, running above 2% but below 3%). It is a far better position to be in than a couple of years ago, when price rises were threatening to hit double digits. But there is a big difference between inflation decelerating towards 2% in the coming year or getting stuck nearer 3%. Not only would the latter forestall aggressive interest-rate cuts by the Federal Reserve, it would also put the central bank on a collision course with Donald Trump—a double-whammy of monetary hawkishness and political turbulence that would cast a shadow over the global economy.

For most of the past year the baseline forecast of most economists has been quite rosy. When the Fed last published its quarterly outlook in September, for instance, a solid majority on its monetary-policy committee projected that their most important inflation gauge would retreat to 2.2% next year. That, they thought, would let them cut rates by a full percentage point in 2025, before taking them still lower in 2026. In such a scenario, Mr Trump would presumably be satisfied enough with the central bank that he would feel little compulsion to snipe at Jerome Powell, the Fed’s chairman, or, worse, to start a legal battle by trying to oust Mr Powell before his term expires in May 2026. With the possibility of turmoil off the table, markets could breathe a sigh of relief.

Yet in the past couple of months a more awkward situation has emerged. Some economists—Sarah House of Wells Fargo, a bank, among them—now worry that inflation, having come down sharply since mid-2022, is stalling at around 3%. It is “getting stuck”, she warns, pointing to a series of gauges. The consumer price index (cpi), which often dominates newspaper headlines, rose by 2.7% in November, compared with a year earlier, reversing some of the softening seen a few months previously. Core cpi, which strips out volatile food and energy costs, has proved to be even more stubborn, hovering around 3.3% year-on-year since late spring (see chart 1). **And the core reading of the personal consumption expenditure (pce) price index, which the Fed watches most closely, has shifted in the wrong direction: it rose at an annualised pace of 3.3% in October, its highest in half a year.**




Source: https://www.economist.com/finance-and-economics/2024/12/12/the-federal-reserve-takes-on-trump-and-stubborn-inflation

# Fed Determined to Take Down Inflation

"Overall, I feel like an MMA fighter who keeps getting inflation in a chokehold, waiting for it to tap out, yet it keeps slipping out of my grasp at the last minute. But let me assure you that submission is inevitable—inflation isn't getting out of the octagon."

**Christopher Waller, Member, Federal Reserve, Board of Governors, Dec 2024**

Source: https://www.economist.com/finance-and-economics/2024/12/12/the-federal-reserve-takes-on-trump-and-stubborn-inflation
(image licensed from Getty Images)

# Jay Powell Has to Worry About Inflation Due to Trump Tariff Threat

**Desmond Lachman, *American Enterprise Institute*, Dec 12, 2024 (excerpt)**

One has to pity Federal Reserve Chair Jerome Powell as he tries to secure his legacy by meeting the Fed's dual mandate of attaining price stability and maximum employment. Not only will Powell have President-elect Donald Trump now looking closely over his shoulder and putting inordinate pressure on him to keep interest rates low to goose up the economy and the stock market. He will also have to deal with more than the usual degree of policy uncertainty and of external economic and geopolitical instability.

A basic fact that makes monetary policy difficult even in the best of times is that it operates with what Milton Friedman characterized as long and variable lags. This means that it takes time for the full effect of any monetary policy change to work its way through the economy. To make the right interest rate decisions, the Fed has to take a view on the basic forces that will be influencing the economy in the quarters that lie ahead. Next year, those forces will be very much more difficult than usual to gauge.

Start with the economic policy agenda of the incoming Trump administration. On the campaign trail, Trump made a number of radical economic policy commitments. If fully implemented and if not counteracted by higher interest rates, those commitments would drive inflation well past the Fed's two percent inflation target.

A 60 percent tariff on imports from China together with a 10–20 percent import tariff on the rest of our trade partners would cause sharp increases in import prices. The deportation of up to 10 million undocumented immigrants would drive up food prices and building costs given how dependent the agricultural and construction sectors have become on illegal immigrants. Meanwhile, aggregate demand would be boosted substantially by the promised extension of the 2017 Jobs and Tax Cut Act and the elimination of taxes on social security benefits and tips.

A key problem that Powell now has in responding to the incoming Trump administration's economic policy agenda is that he cannot be sure to what extent it will be implemented. Maybe, once Trump takes office, his Treasury Secretary and other responsible adults in the room will persuade him how damaging fully fulfilling his campaign's promises will be to the American and world economies. On the other hand, maybe Trump will persist in carrying out his radical agenda of punitive import tariffs, mass deportations, and budget-busting tax cuts. Only sometime after January 20, once Trump assumes office, will Powell know the answer to that question.

A more basic problem for Powell is that no one can be sure what the impact of Trump's disruptive economic policies will be on the long-run inflation outlook and on the economy's overall performance.

Source: https://www.aei.org/economics/jerome-powells-2025-inflation-challenge/

# Economists Trim Fed Rate Cut Estimates on Fear of Trump Inflation Surge

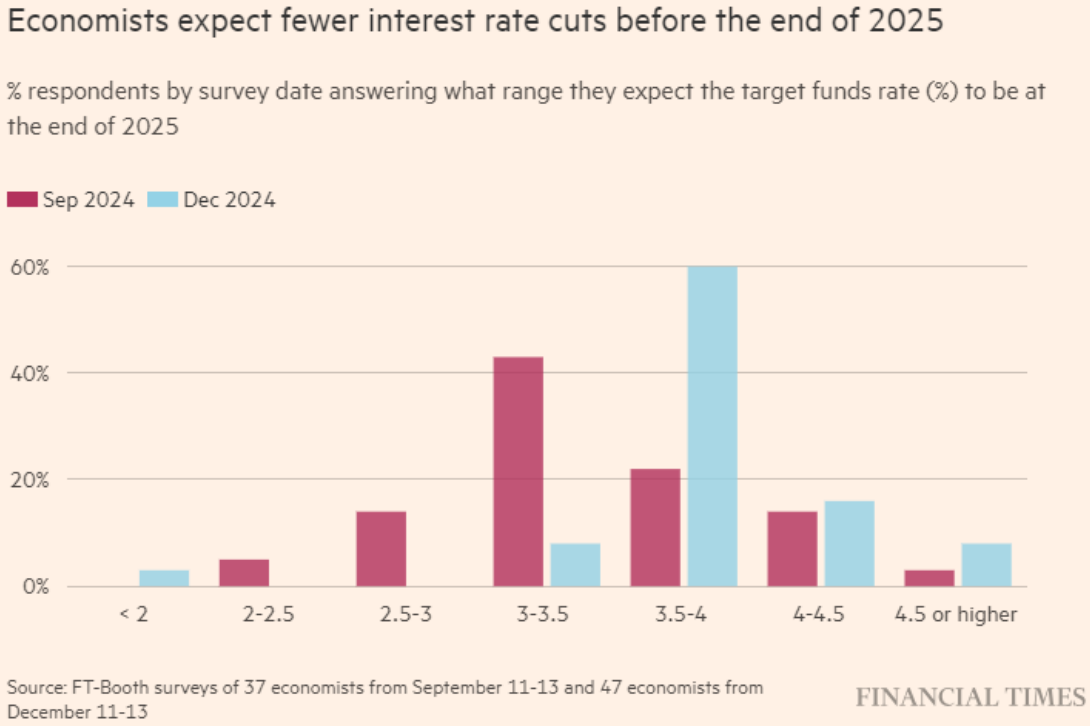
**Colby Smith and Eva Xiao, *Financial Times*, Dec 15, 2024 (excerpt)**

The Federal Reserve is set to take a more cautious approach to interest rate cuts on fears that the Trump administration's policies will stoke higher inflation, according to academic economists polled by the Financial Times.

The economists, who were surveyed between December 11 and 13, moved up their forecasts for the federal funds rate next year compared to the previous FT-Chicago Booth poll in September.

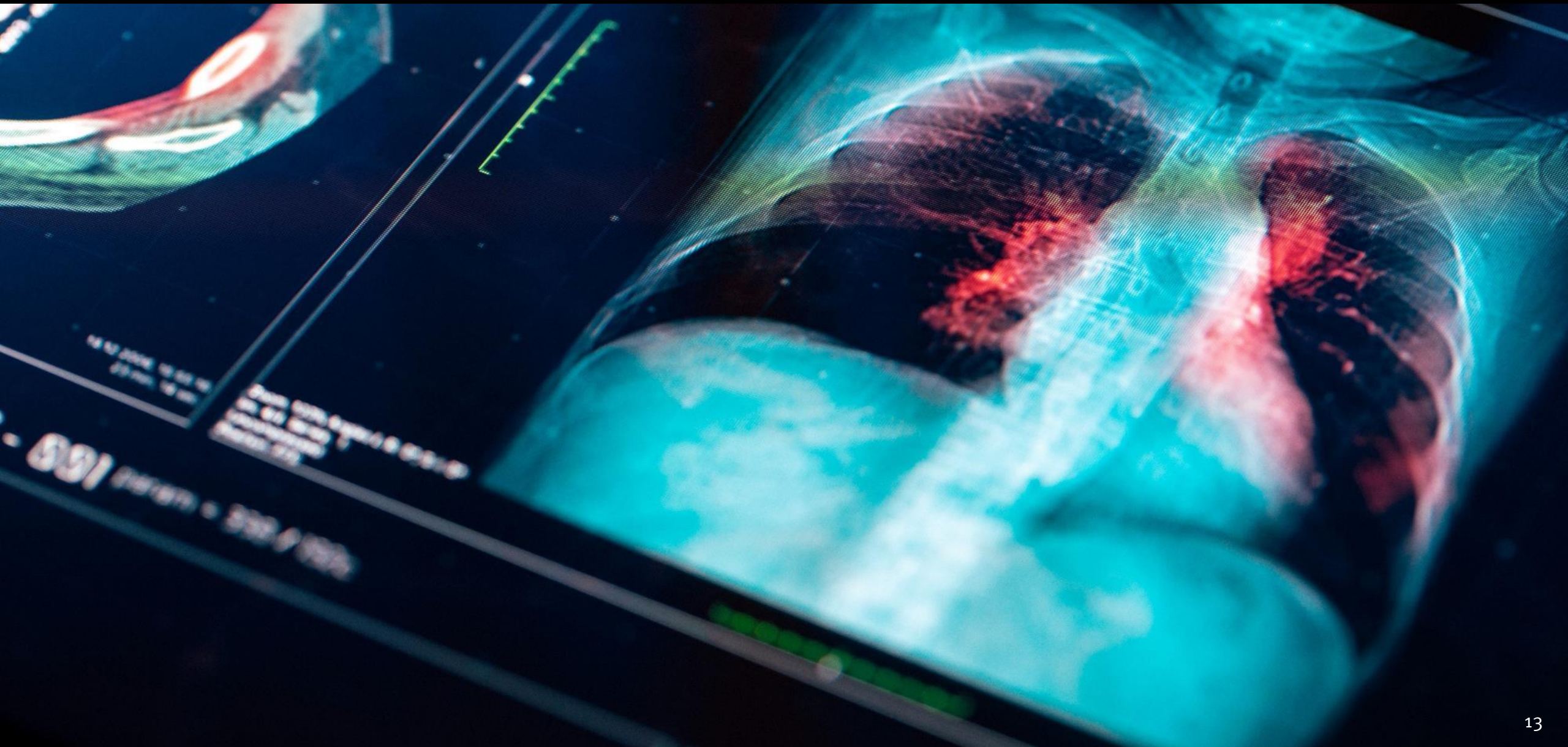
The vast majority thought it would hover at 3.5 per cent or higher by the end of 2025, whereas most respondents in September said it would probably fall below 3.5 per cent by that point.

If the Fed follows through with a quarter-point cut at its meeting next week as expected the policy rate will stand at 4.25-4.5 per cent.




Source: https://www.ft.com/content/50ec8049-58ca-4a8f-abe5-9036a0cb0317

# Biopharma Market Update



# The XBI Closed at 93.4 Last Friday (Dec 13), Down 5.8% for the Week

The XBI lost substantial ground last week on a steady stream of negative clinical news. Despite positive hopes from many quarters, the biotech sector has not been attracting generalists in December. The XBI is up only 4.6% for the year.

## Biotech Stocks Down Last Week

**Return: Dec 8 to Dec 13, 2024**

Nasdaq Biotech Index: -4.0%
Arca XBI ETF: -5.8%
Stifel Global Biotech EV (adjusted): -9%*
S&P 500: -0.6%%

**Return: Dec 29, 2023 to Dec 13, 2024 (YTD)**

Nasdaq Biotech Index: +1.8%
Arca XBI ETF: 7.8%
Stifel Global Biotech EV (adjusted): +22%*
S&P 500: +26.9%

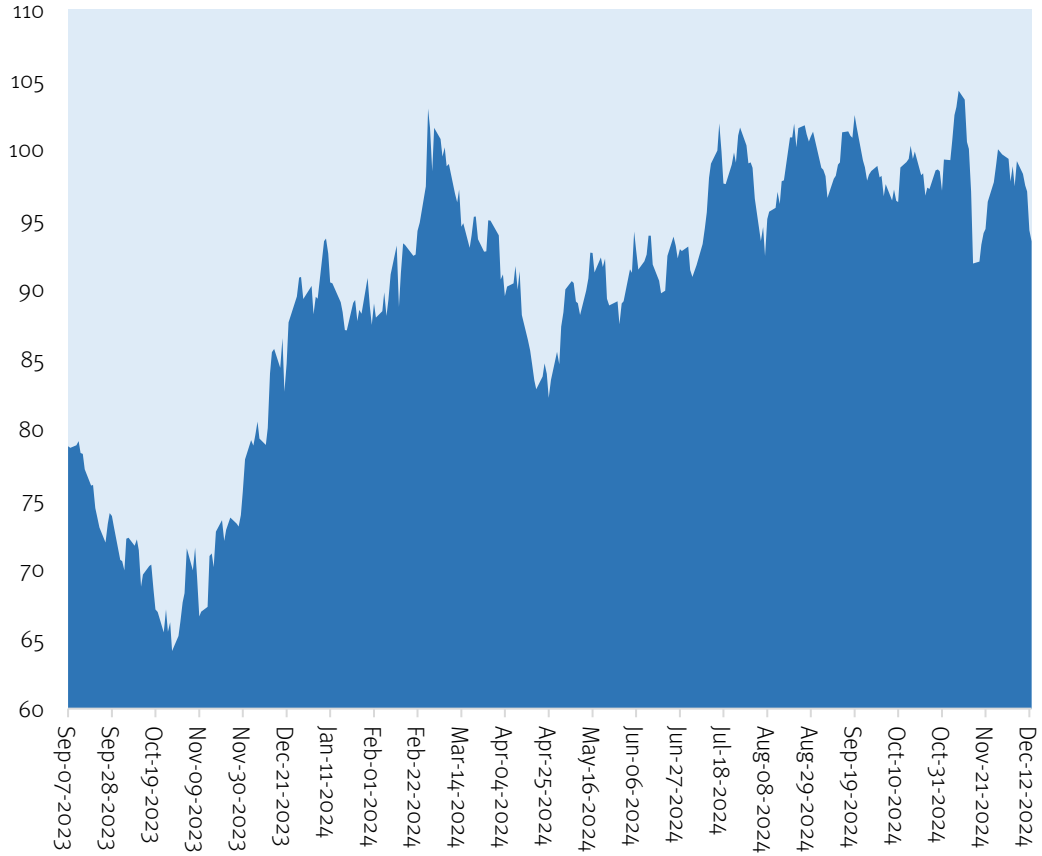
## VIX Down

Dec 29, 2023: 12.45%
Mar 29, 2024: 13.0%
May 17, 2024: 12.0%
Aug 2, 2024: 23.4%
Sep 20, 2024: 16.1%
Oct 19, 2024: 18.0%
Dec 13, 2024: 13.8%

## 10-Year Treasury Yield Flat

Dec 29, 2023: 3.88%
Mar 29, 2024: 4.20%
May 17, 2024: 4.42%
Aug 2, 2024: 3.80%
Sep 20, 2024: 3.73%
Oct 19, 2024: 4.08%
Nov 23, 2024: 4.41%
Dec 13, 2024: 4.4%

## XBI, Sep 7, 2023 to Dec 13, 2024




* 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

# Market Rose 1.5% on Monday, Dec 16th

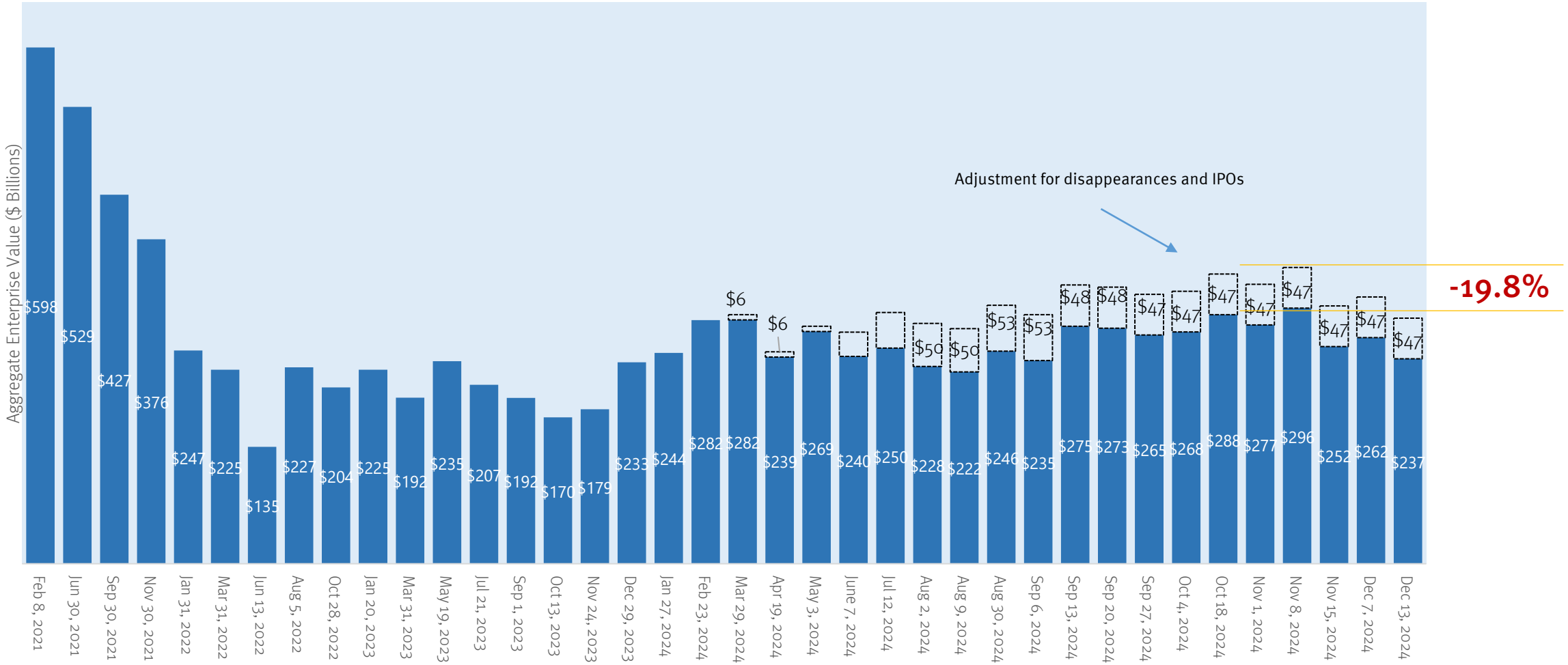

**This Monday, Dec 16, was a little cheerier than last week with positive news from Edgewise and Puretech.**

**Nonetheless, the XBI is down a full ten points since Nov 8th – the day the post-election market "Sugar Rush" ended.**

# Total Global Biotech Sector Down 9% Last Week

Biotech stocks fell 9% in the last week far more than the XBI. On a disappearance adjusted basis, biotech is up 22% for the year to date (enterprise value). Larger cap biotechs (see next page) were not sheltered. From the week after the election (Nov 8) to last Friday (Dec 13), biotech is down 20%.

## Total Enterprise Value of Publicly Traded Global Biotech, Feb 8, 2021 to Dec 13, 2024 ($ Billions)

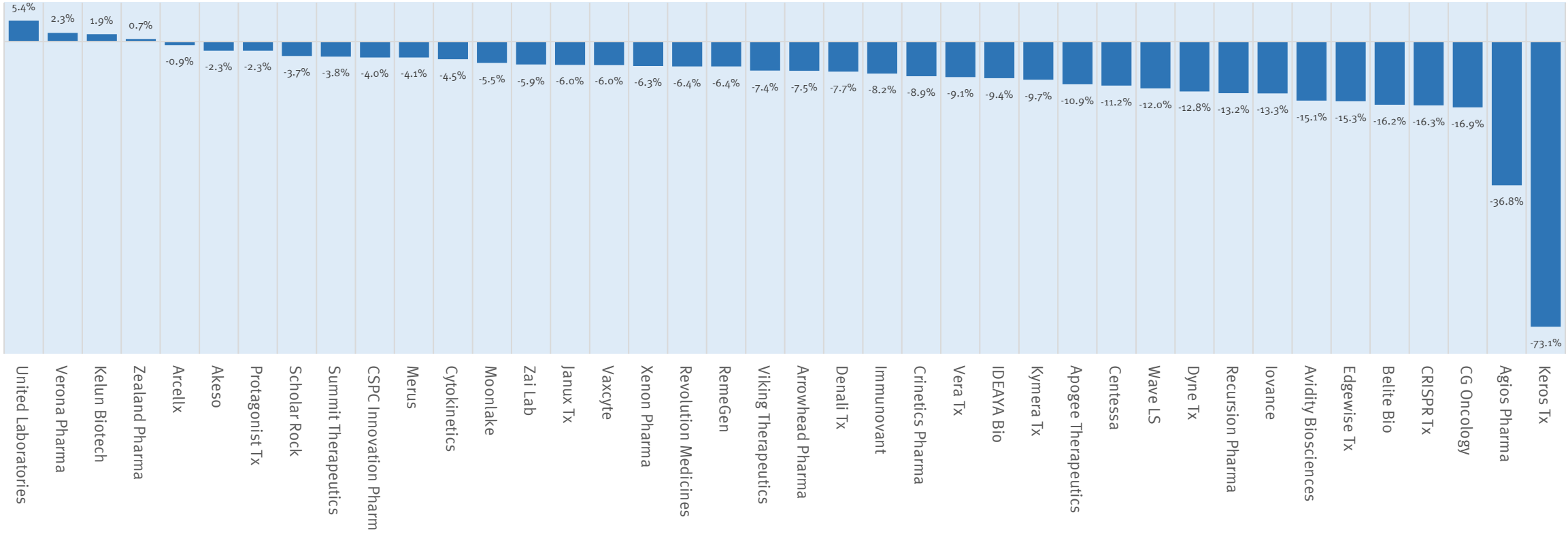



Source: CapitalIQ. Biotechs are defined as any therapeutics company without an approved product on any global stock exchange.

# A Tough Week for Biotech

This chart shows the change in market cap last week for the top 40 biotechs worldwide by their market cap at start of week. The mean percentage change in value was -9.8%. Keros and Agios were all hit hard based on data events. Keros failed a key trial. Shares of Agios Pharmaceuticals lost 21% last Monday after management revealed that two thalassemia patients who received its sole-marketed drug mitapivat across two late-stage studies reported hepatocellular (liver) injury in the first six months of treatment.

**Average Percent Change in Market Cap for Week Ended Dec 13, 2024, Top 40 Global Public Biotechs,**

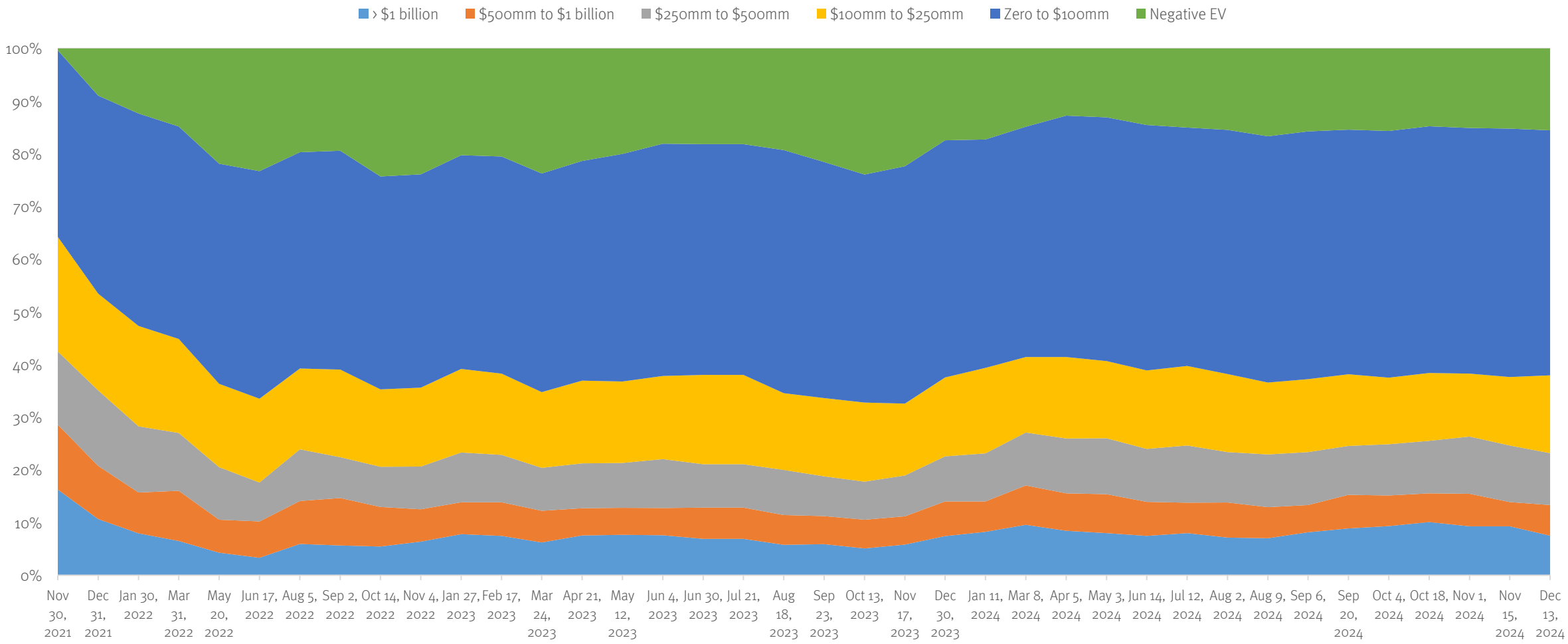



Source: CapitalIQ. Biotechs are defined as any therapeutics company without an approved product on any global stock exchange.

# Global Biotech Neighborhood Analysis

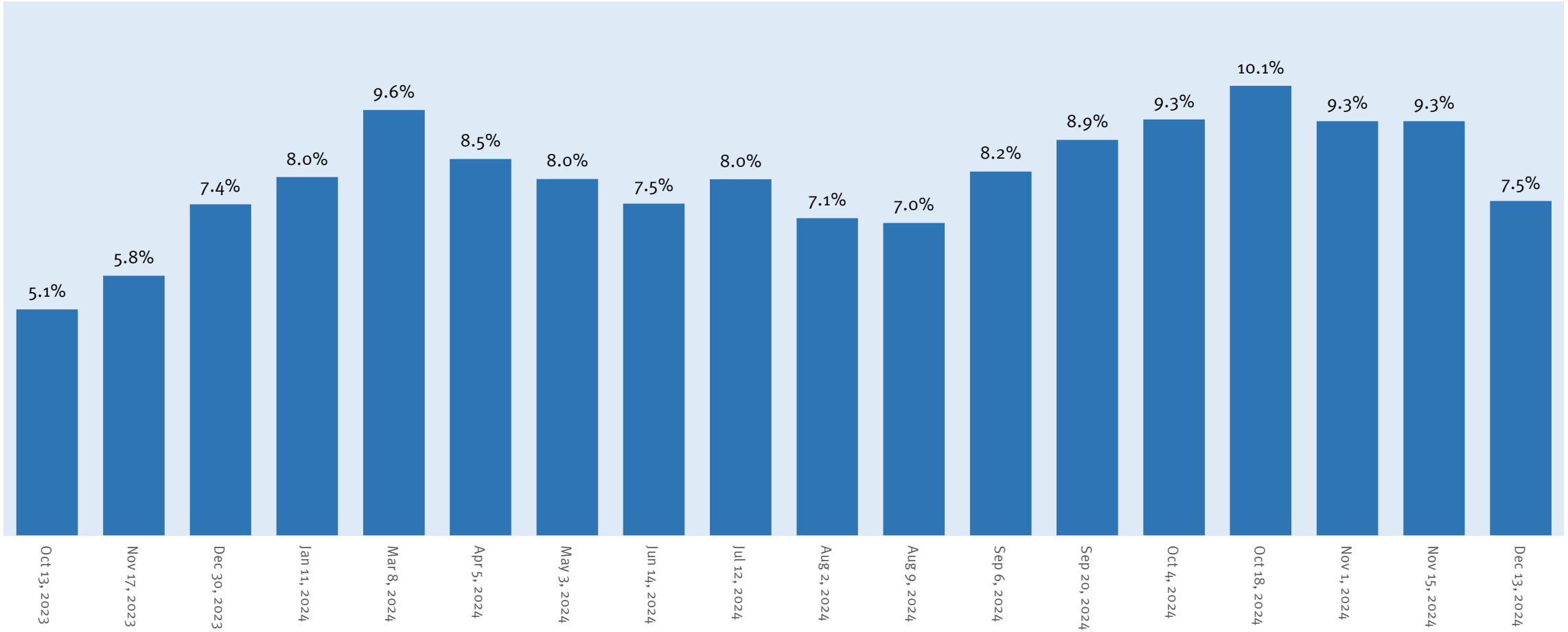
Last week saw growth in the group of companies that are worth $1bn or more get squeezed down hard. The population of companies worth $100mm to $250, is the “growth area” in biotech real estate lately.

## Global Biotech Universe by Enterprise Value Category, Nov 30, 2021 to Dec 13, 2024




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

# Percent of Public Biotechs Worth $1 Billion or More



# Understanding the Biotech Blues

If you ask us, it is not at all obvious why biotech investors are suffering from the blues.

Perhaps we are on Prozac or something, but we see plenty of cause for optimism.

So how could biotech be down 20% over the last five weeks?

That's not exactly a small move.

We have spoken to roughly a half dozen funds in recent weeks to gain insight into what is going in the market.

And, specifically, we have focused on what happened last week. Why a 9% drop?

If you will forgive us for a moment, we would think that last week could have been a really *good* week.

# There is a Strong Case for Optimism

For all of you “glass is half empty” people (whoever you are), there is plenty of argument to say that the biotech glass right now is half full.

Or even a lot more than half full.

In a sense, one could not imagine a **better week** for our sector. Specifically, Trump has announced that FTC head Lina Khan will be replaced by Andrew Ferguson, a known light hand on merger enforcement of antitrust laws.

Under Ms. Khan we have not had much in the way of M&A.

To make it more interesting, Trump has also designated Gail Slater, a known conservative pro-business lawyer to lead the DoJ’s antitrust division.

# So Why Not Biotech Rock and Roll?

So, shouldn't it be rock and roll time for biotech?

To be clear, a key driver of biotech market performance historically has been the M&A market (see upcoming chart). And we have not had much of one lately.

Remember, pharma *has* to buy biotech. And, they have been remarkably shy at doing so in the last 18 months. And they will tell you that antitrust has had a *lot* to do with it.

To make it even more interesting, Trump and Ferguson have made it clear that they want the FTC to pursue pro-innovation policies.  We would have a hard time inventing a fake news story this good.

Basically, the **brakes will be off** of biotech M&A next year.

Hello!

# FTC's Ferguson is Supposed to be Pro-Innovation and Pro-Merger

**We would have had a hard time inventing a piece of news this positive for biotech last week.**

**Donald J. Trump**
@realDonaldTrump

I am pleased to appoint Andrew N. Ferguson to be the next Chair of the Federal Trade Commission. Andrew has a proven record of standing up to Big Tech censorship, and protecting Freedom of Speech in our Great Country. Sworn in as a Commissioner on April 2, 2024, he will be able to fight on behalf of the American People on Day One of my Administration.

Andrew most recently served as Solicitor General of the Commonwealth of Virginia. Prior to Government service, he was an antitrust litigator at several Washington, D.C. law firms. He earned his undergraduate degree and law degree from the University of Virginia. Andrew also clerked for Judge Karen L. Henderson on the U.S. Court of Appeals for the D.C. Circuit, and U.S. Supreme Court Justice Clarence Thomas.

Andrew will be the most America First, and pro-innovation FTC Chair in our Country's History.
CONGRATULATIONS ANDREW!

**784** ReTruths **3.19k** Likes Dec 10, 2024 at 5:58 PM

## FTC Commissioner Andrew N. Ferguson for FTC Chairman

Commissioner Ferguson is the America First, pro-innovation choice for Chairman of the Federal Trade Commission. Ferguson has impeccable legal credentials, proven loyalty to President Donald Trump, and a track record of standing up to Big Tech Censorship, DEI-wokeism, and the anti-business, anti-innovation agenda of the radical left. President Trump can designate Ferguson as Chairman of the FTC on Day 1 of the Trump Administration – no Senate confirmation is needed for sitting FTC Commissioners to become Chairman, and his term does not expire until 2030.

### Major Accomplishments

- Sued the Biden Administration to halt its lawless environmental, immigration, and gun policies.
- Directed Virginia Attorney General's efforts to bring down the Department of Homeland Security's "Disinformation Board."
- Represented Virginia and numerous other States in a landmark antitrust suit against Google's ad-tech monopoly.
- Successfully fought to end the Biden FTC's anti-business policy of refusing to end merger investigations early and allow firms to close their deals as soon as the FTC finds no competitive harm ("early termination").
- Oversaw the effort to confirm President Trump's judicial nominations in the Senate, transforming the Supreme Court as well as the lower courts. Lead staffer for both the Kavanaugh and Barrett nominations.
- Senate staff architect of President Trump's two impeachment acquittals.

### Agenda for the FTC

#### Reverse Lina Khan's Anti-Business Agenda

- Repeal burdensome regulations and provide businesses with the certainty they need. Businesses deserve to know what they can and can't do.
- Support strong American companies that can beat foreign competitors. Foster innovation that improves our quality of life and makes our country greater than ever before.
- Stop Lina Khan's war on mergers. Most mergers benefit Americans and promote the movement of the capital that fuels innovation. Focus FTC resources on the mergers that harm competition and hinder innovation, while permitting mergers that keep capital flowing to innovators.
- End the FTC's attempt to become an AI regulator.
- No more novel and legally dubious consumer protection cases. Demand honesty and fairness to consumers, but businesses should not fear that the FTC will punish them for honest conduct that offends the sensibilities of beltway bureaucrats.
- Stop abusing FTC enforcement authorities as a substitute for comprehensive federal privacy legislation.

#### Hold Big Tech Accountable and Stop Censorship

- Focus antitrust enforcement against Big Tech monopolies, especially those companies engaged in unlawful censorship.
- Pursue structural and behavioral legal remedies under the antitrust laws and the FTC Act to make sure large platforms treat all Americans fairly and to prevent them from using their market power to box out new entrants and stymie innovation.

#### Protect Freedom of Speech and Fight Wokeness

- Investigate and prosecute collusion on DEI, ESG, advertiser boycotts, etc.
- End Lina Khan's politically motivated investigations.
- Terminate all initiatives investigating so-called "disinformation," "hate speech" or AI "bias."
- End the FTC's attacks on online anonymity.
- Fight back against the trans agenda. Investigate the doctors, therapists, hospitals, and others who deceptively pushed gender confusion, puberty blockers, hormone replacement, and sex-change surgeries on children and adults while failing to disclose strong evidence that such interventions are not helpful and carry enormous risks.
- Stop pursuing cases under lawless disparate impact discrimination theories. Such cases are designed to force companies to adopt de facto quotas and affirmative action policies.

#### Fight the Bureaucracy to Implement President Trump's Agenda

- The Constitution requires that all federal employees, even the heads of so-called independent agencies, answer to the President.
- Terminate uncooperative bureaucrats.
- Advance the President's agenda by taking on entrenched left-wing idealogues at the FTC who take their agenda from liberal journalists and activists. Only a strong, Trump-aligned Chairman can resist their influence.

### Biographical Highlights

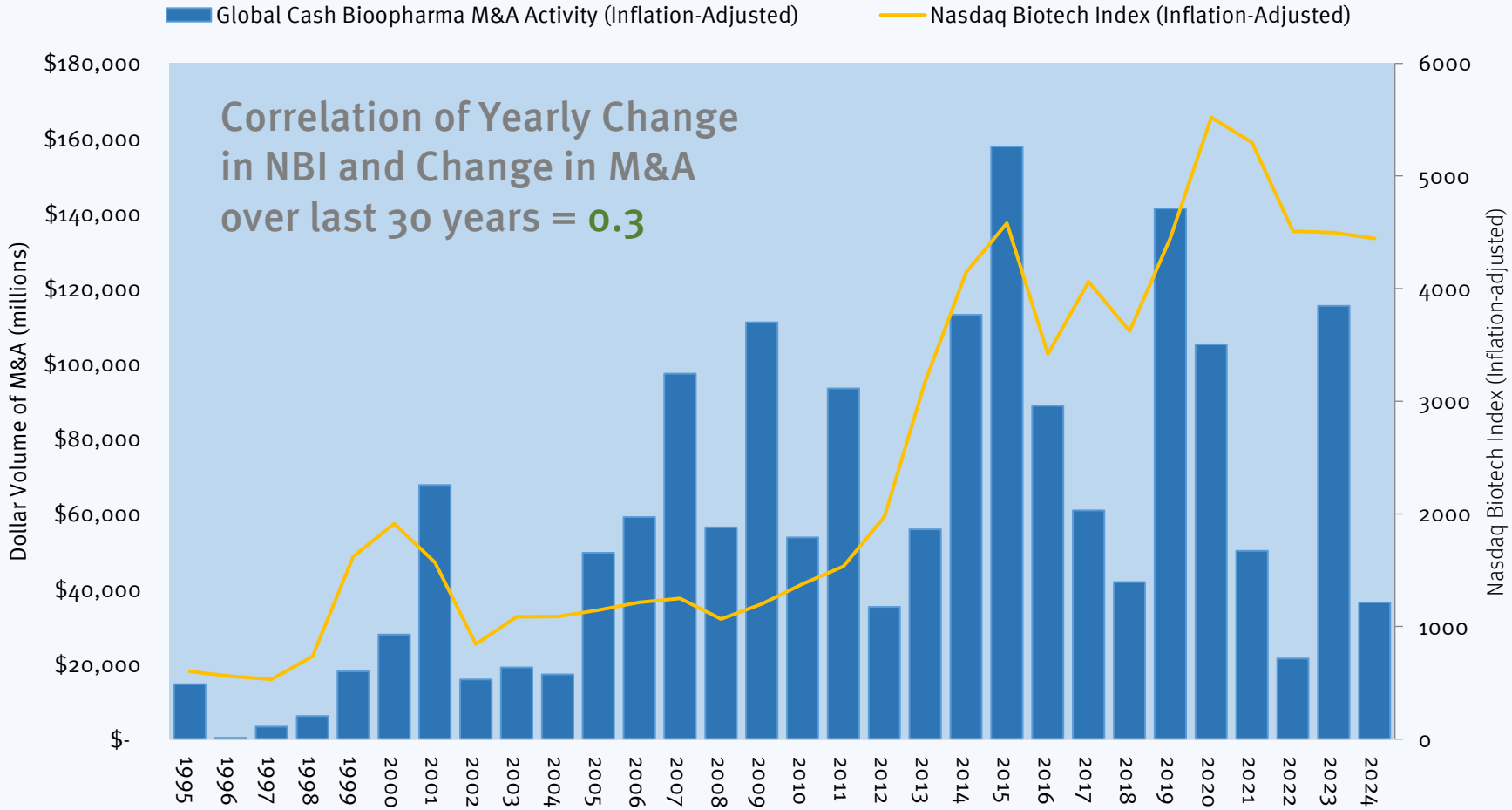
- Solicitor General of Virginia
- Law Clerk to Supreme Court Justice Clarence Thomas. Also clerked on D.C. Circuit. B.A. & J.D. from the University of Virginia.
- Chief counsel for nominations to the Senate Judiciary Committee.
- Chief Counsel to Senate Majority Leader Mitch McConnell. Ferguson served as a strong voice that supported President Trump's agenda within McConnell's office.

# The Biopharma Market Rises in Strong M&A Years

**This chart confirms what most of us think intuitively: a strong M&A market is generally going to be a strong year for biopharma stocks.**

**The correlation between changes in M&A volume and changes in the NBI is high and statistically significant but far from perfect. Of course, the ultimate driver of the market is the underlying performance of the individual companies involved but the volume of M&A takeout activity is highly relevant.**

**Cash Acquisitions of Biopharma Companies, 1995 to 2024 vs. the Nasdaq Biotech Index**
(inflation adjusted)



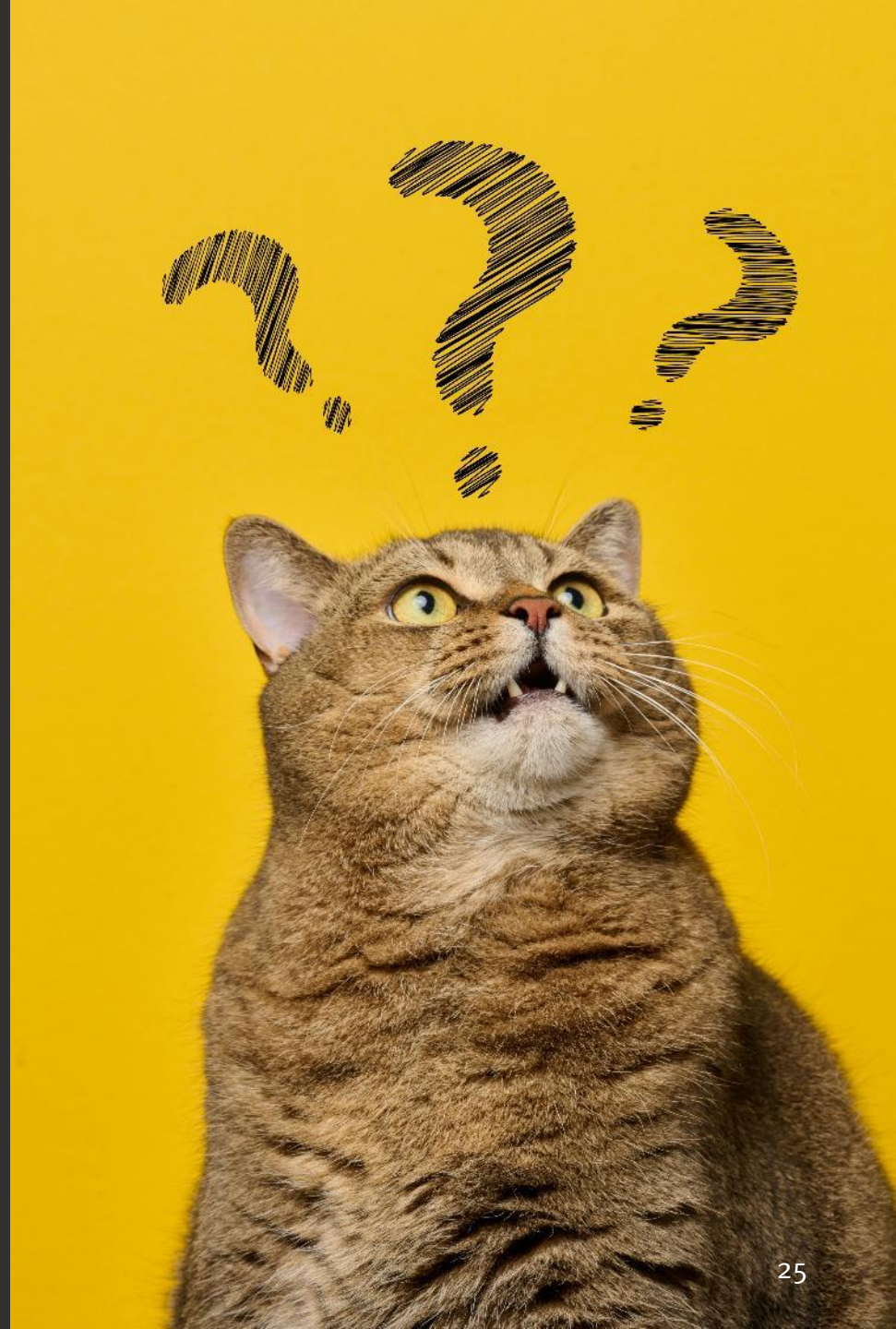

Source: S&P CapitalIQ

# So, What's the Story?

Obviously, what we think doesn't drive the market. What matters is what's going through fund managers minds.

So back to those conversations we have been having.  There are three things that we are hearing. First and foremost, we have heard that investors **hate uncertainty**. And there is a lot of it. One commentator quipped to us that they would never have imagined a two-week period in which: (1) the head of United Healthcare would be assassinated, and that the assassin would be *receive strong support* from the general population, (2) that Syria would fall and (3) that mysterious drones would show up over New Jersey.

Indeed, it has been a bizarre couple of weeks. But really? If anything, the UNH news, tragic as it was, could spark a national conversation about the power of managed care (something we have discussed before) and what to do about it. That would likely be *good* for pharma. Further, the apparent weakening of the Iran/Russia/China axis (apparent in Syria) is not likely a *bad* thing for the U.S. And we don't know what to say about that drone thing. Perhaps they are lost generalist investors looking for the biotech market? And, by the way, the S&P 500 was unchanged last week. Shouldn't that have dropped too on all of this uncertainty. The S&P is up nicely since the Trump election. It's really biotech that is not. The divergence in the last three years between biotech and the S&P is increasingly surprising. For some reason, the market is **out of love** with biotech.



# Bad Luck Has Played a Part

The second point that we are hearing is that the market has had a run of bad luck.

It was **Friday the 13th** last week after all.

One prominent market player emailed us the following:

*"9 clinical trials failures last week, OUCH, $1 B in biotech specialist outflows, a big biotech fund had layoffs, Specialist YTD performance being pac-manned - little Christmas cheer in Dec so far this year..."*

OK, we get it, we had some ugly clinical failures last week. The Keros news was unexpected and ugly. The adverse events at Agios were not good.

But last week also saw some **great news** as well. Chimerix announced that it was unexpectedly filing for early approval of dordivaprone (stock up 256%). Companies with good news included Puretech, X4, Candel, Cardiff, RegeneX, Uniqure, NewAmsterdam and others.

We don't see, on balance, that it was **that bad** of a week. Certainly, not cause for a 10% market drop.

# Year-End Fund Positioning

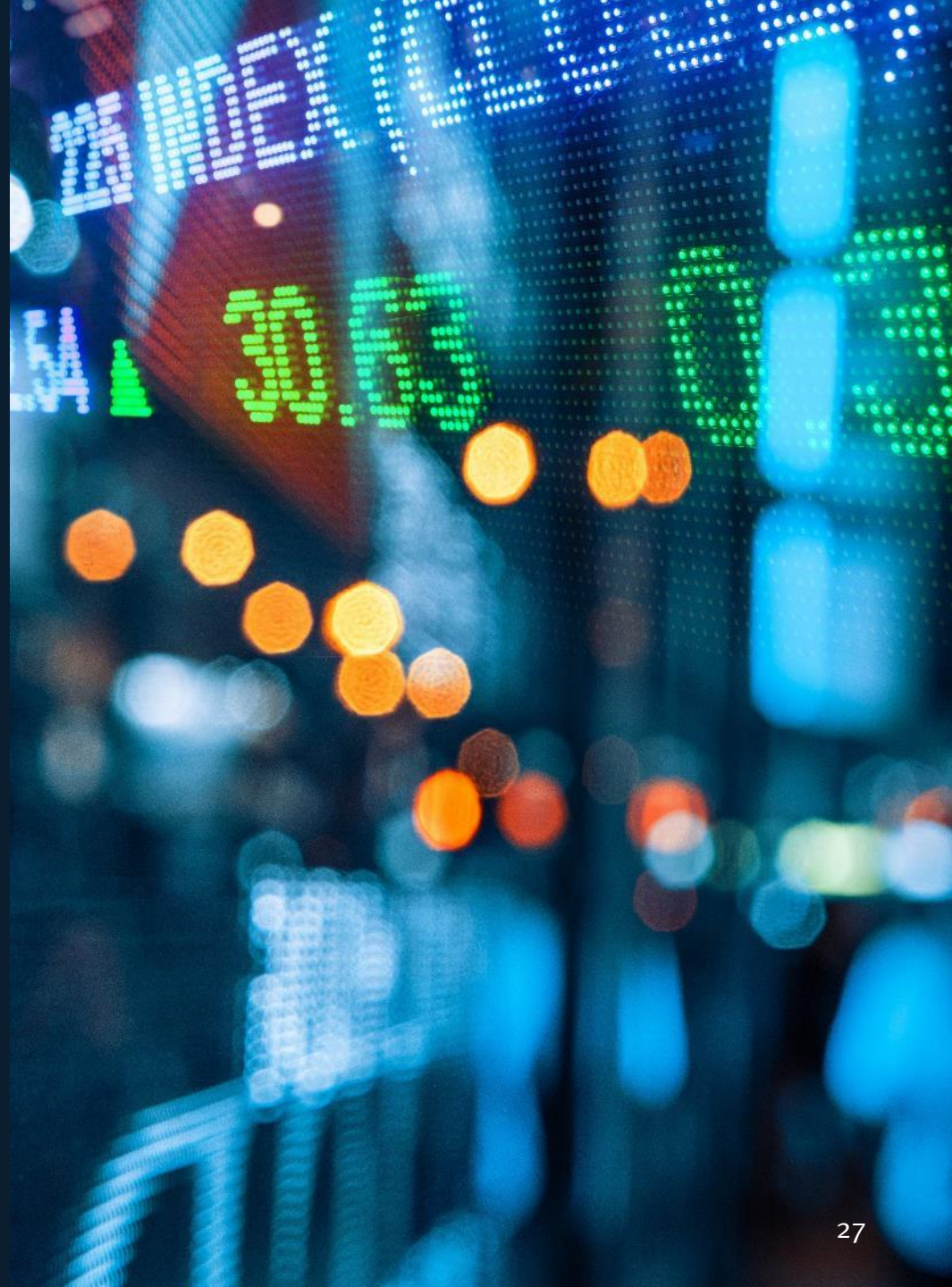
What does matter is the year end and what is going on with specialist funds. And these days, unfortunately, that largely means hedge funds.

Money is **flowing out of the market** at the same moment that biotechs are hitting the secondary window and it's true, hedge funder resumes are floating all over the place.

Some hedge funds have not had a great year, and a few may be getting redemption notices from LP's. Further, some appear to be reducing exposure in order to lock in the year's gains and associated performance fees.

We think that is the general explanation for what is going on. Funds are moving to cash and are **locking in the gains** that they have. We are hearing that many funds have had a really good year and want to keep it that way. Hence, the reduction in market exposure.

For those that are staying in stocks, we are hearing frequent conversations about who is going to get bought rather than underlying fundamentals. Many funds are focused on the near term and don't seem to positioning for what we think will be a great five years ahead of us for biotech.



# Many Life Sciences Hedge Funds Failed to Beat the Broader Market

**Stephen Taub, *Institutional Investor*, Dec 10, 2024 (extract)**

In November, most biopharma and life sciences hedge funds were in the black, though not all have returned to their high-water marks. The funds were helped by the biopharma rebound that was mainly sustained in 2024 — after several years of sharp losses. Still, many funds are on pace to significantly lag the broader market for the year.

Biopharma stocks in general started rallying in the final nine weeks of 2023 along with the rest of the stock market — especially small-caps — when the Federal Reserve signaled a potential interest rate cut in 2024. The rally led to a surge of investors covering their shorts, putting upward pressure on the stocks.

Casdin Capital is by far the leader heading into the final month of 2024, with its public portfolio up about 40 percent through November. The hedge fund, however, is still below its high-water mark after losing about 63 percent in 2022 and 30 percent in 2021.

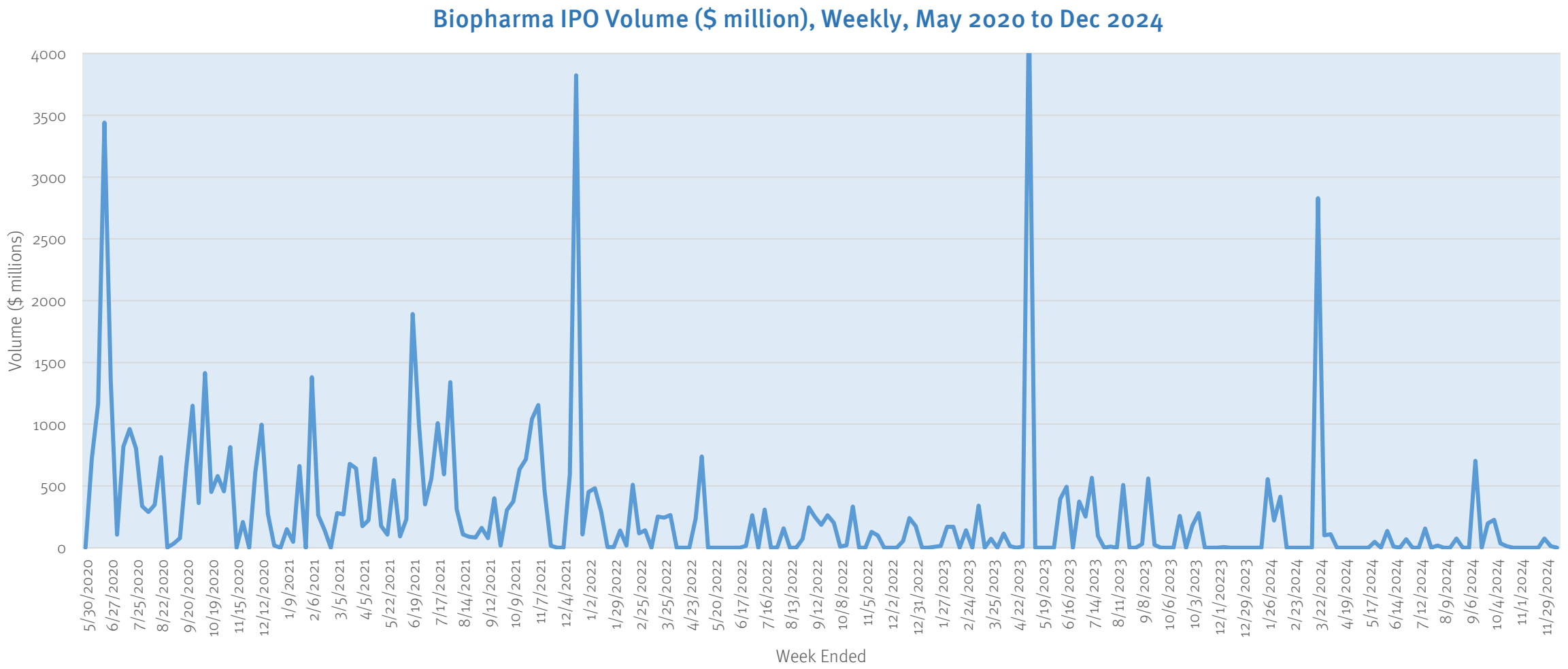
Elsewhere, Affinity Healthcare gained more than 4 percent last month and is now up 33.5 percent for the year, according to a hedge fund database. The fund, which specializes in therapeutics, manages about $450 million, per the database.

Most other biopharma and life sciences funds are lagging the broader market despite strong showings in November.

**Source**: https://www.institutionalinvestor.com/article/2e4vf75fmihj287joh9ts/premium/casdin-leads-life-sciences-funds-in-a-recovery-year

# Capital Markets Update

# No IPOs Last Week




Source: Data from CapitalIQ and Stifel research.

# IPO Activity Picked Up in 2024

## Jules Adam, *Labiotech*, Dec 10, 2024 (excerpt)

**As 2024 comes to a close, and while we will soon be thinking about 2025 and the trends that will shape the biotech industry, now is a good time to look back at what happened this year.**


In 2024, the biotech sector experienced a resurgence in public market activities, notably in initial public offerings (IPOs). After a subdued period, the year began with a promising uptick in biotech IPOs, with momentum building significantly by late summer. A remarkable instance was in September, when three companies – Bicara Therapeutics, Zenas BioPharma, and MBX Biosciences – collectively raised over $700 million on Nasdaq in a single day, signaling renewed investor confidence in the sector.

This revival was further exemplified by Upstream Bio's October debut, where shares opened 26.5% above the initial public offering (IPO) price, valuing the company at $1.1 billion. Overall, the healthcare sector, with biotech as a significant contributor, led U.S. IPO activities in 2024, accounting for 23% of total IPO proceeds and raising $6.6 billion. This resurgence indicates a robust recovery in biotech public market activities, with expectations of continued momentum into 2025. Europe's biotech IPO landscape was more subdued.

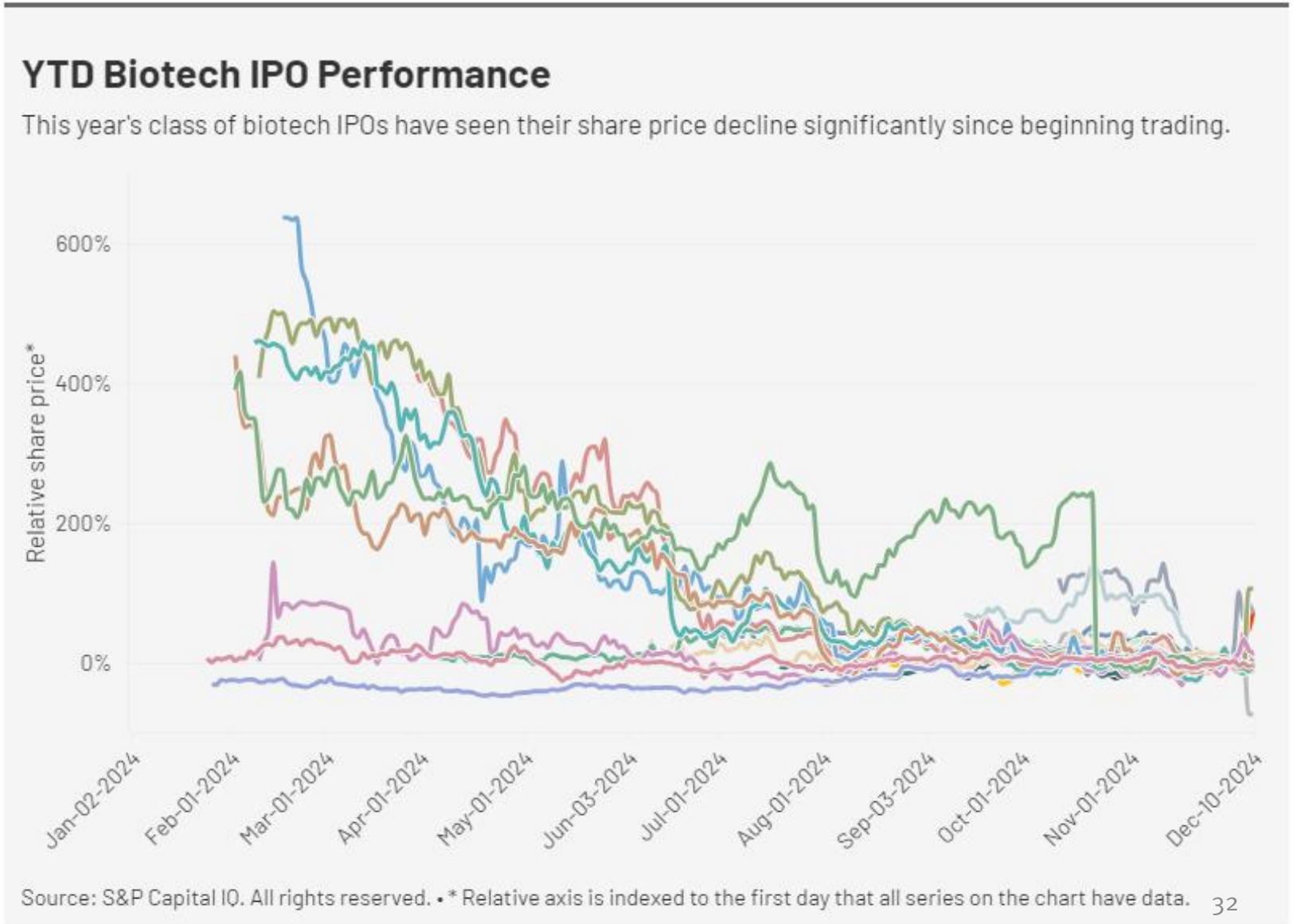
Source: https://www.labiotech.eu/more-news/biotech-2024-retrospective/

# After Making the IPO Jump, Biotechs Landed On a Slippery Slope

**Annalee Armstrong, *Biospace*, Dec 11, 2024 (excerpt)**

The IPO window cracked open in 2024, just long enough for a couple dozen biotechs to sneak out. What they found on the other side, however, was a slippery slope.

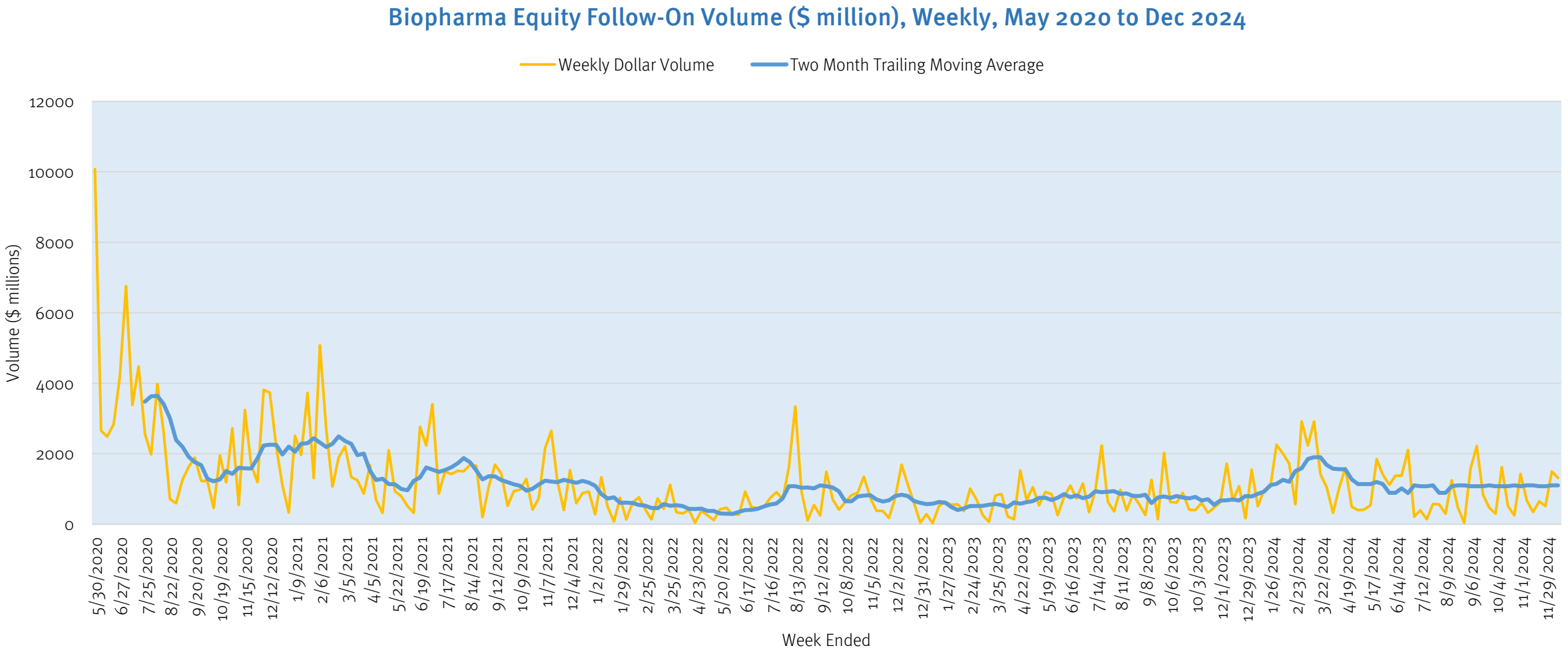
About 25 companies have gone public this year, the majority of them in the early months. And most have tumbled from their original offer price, now hovering around the S&P XBI, which tracks U.S. biotechnology stocks and is commonly used as an overall measure of the sector's performance.




Source: https://www.biospace.com/business/after-making-the-ipo-jump-biotechs-landed-on-a-slippery-slope

# Last Week Average for Follow-On Offerings

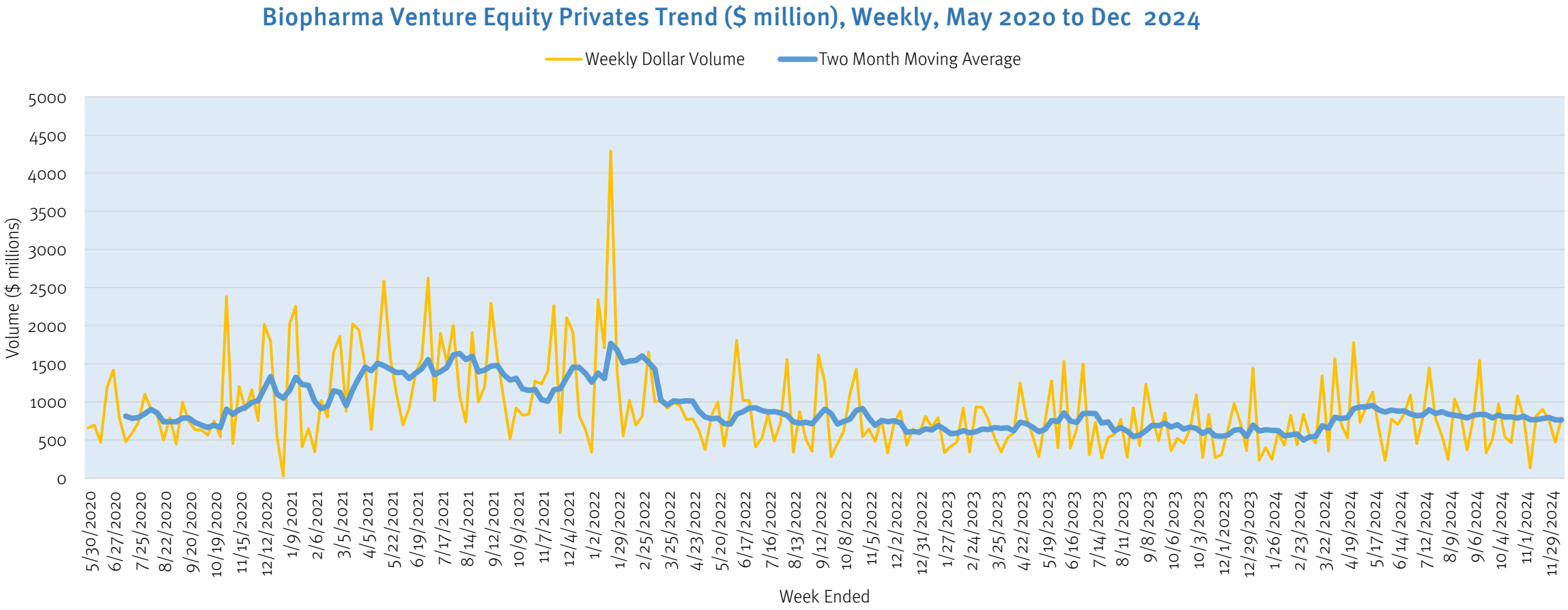
**Last week saw $1.3 billion in follow-on biopharma volume. The last two weeks have been quite active as issuers rush to complete their raises before the holidays set in.**




Source: Data from CapitalIQ and Stifel research.

# Last Week Saw $787 Million in Venture Privates

**The market for privates last week was right at its median point. The largest deals in the market were Noema (raised $147 million), Angitia Biopharmaceuticals Guangzhou Limited (raised $120 million) and Citryll (raised $90 million). Notably, the three largest deals all took place outside the U.S.**




Source: Data from CapitalIQ, Crunchbase.

# Noema Pharma Raises CHF 130 Million

**BASEL Dec. 11, 2024 (BUSINESS WIRE)** Noema Pharma, a clinical-stage biotech company targeting debilitating central nervous system (CNS) disorders, announced the successful close of a Series B extension financing round with an investment from EQT Life Sciences, bringing the total capital raised in the round to CHF 130 million (approx. USD 147 million). With its investment in Noema Pharma, EQT Life Sciences joins the syndicate of previous Series B investors including Forbion, Jeito Capital, Sofinnova Partners, Gilde Healthcare, Polaris Partners, Invus and UPMC Enterprises.

The new financing will support Noema Pharma's four active Phase 2 trials, with key data readouts anticipated in 2025. This includes additional development activities for basimglurant (NOE-101), an mGluR5 negative allosteric modulator currently in Phase 2 trials for severe pain in trigeminal neuralgia (TN) and seizures in tuberous sclerosis complex (TSC); gemlapodect (NOE-105), a PDE10a inhibitor in a Phase 2b trial for Tourette syndrome and under development for childhood-onset fluency disorder (COFD or stuttering); and NOE-115, a broad-spectrum monoamine modulator in a Phase 2 trial for vasomotor symptoms and other symptoms of menopause.

Felice Verduyn-van Weegen, Partner at EQT and member of the Board at Noema, commented: "Noema Pharma's innovative approach to CNS disorders aligns very well with our investment strategy and we are excited to support their late-stage clinical pipeline and transformative therapies. Having worked with Ilise Lombardo on a previous successful investment, her exceptional leadership as a repeat entrepreneur reinforces our confidence in Noema's potential to deliver meaningful impact to patients in need."

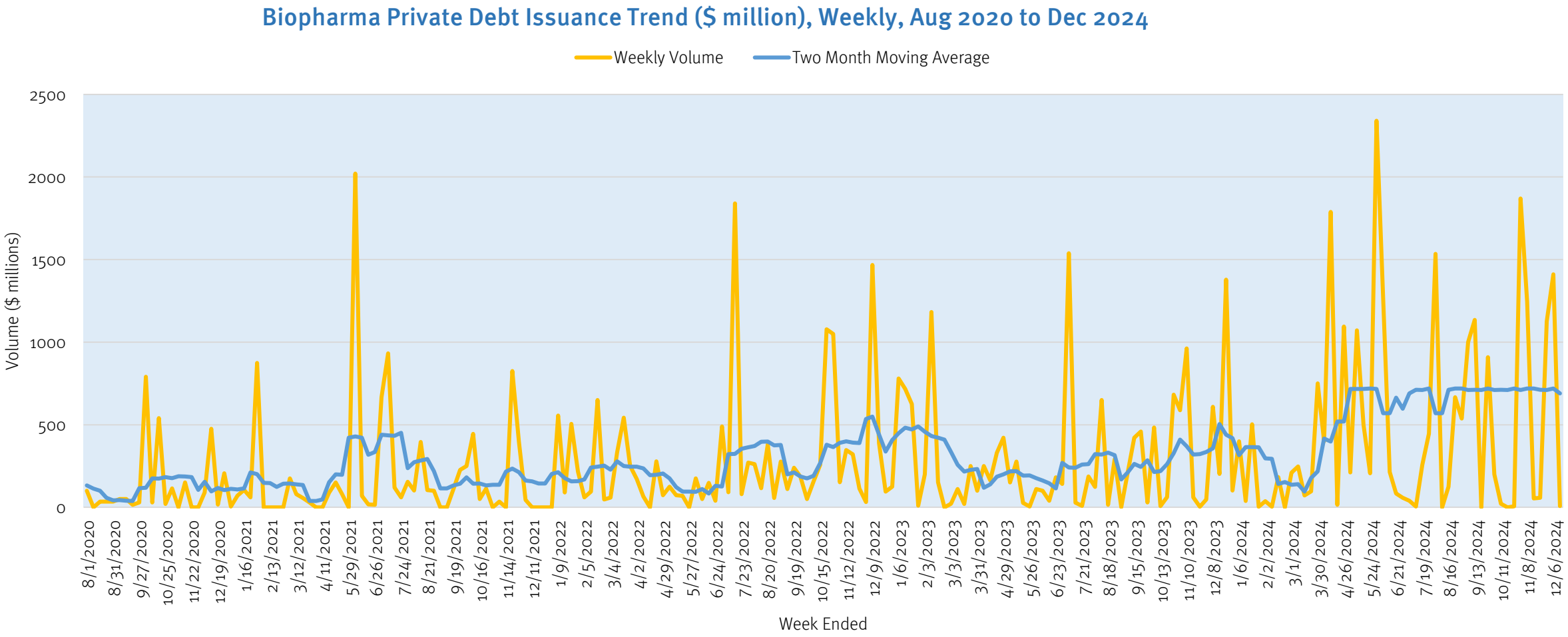
"This latest financing underscores the strong support and confidence from investors in Noema's vision to treat neuroscience-based conditions. We are thrilled to welcome EQT Life Sciences into this strong syndicate of investors and have Felice join our Board. EQT's support and expertise alongside our syndicate of investors will be invaluable as we progress our clinical programs and strive to make a meaningful impact on patients' lives."

**Ilise Lombardo, MD**
*Chief Executive Officer*
Noema Pharma

Source: https://www.businesswire.com/news/home/20241211787741/en/Noema-Pharma-extends-Series-B-financing-round-closing-at-CHF-130-Million-147-Million

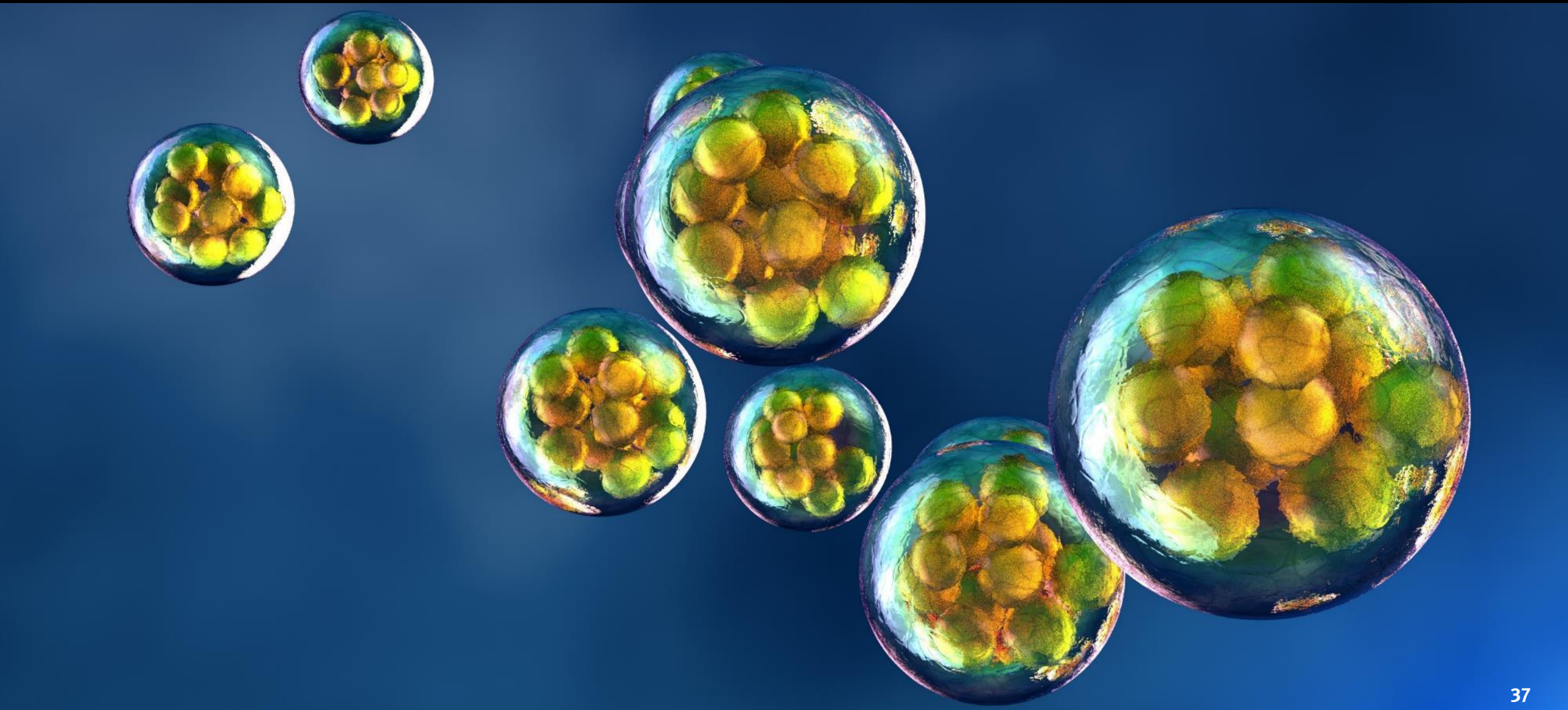
# Weekly Global Biopharma Private Debt Placement Market Open in December

**We saw $7 million in private debt deals get done last week. While the week was quiet the overall pace of activity in November and December has been robust.**




Source: Data from CapitalIQ, Crunchbase.

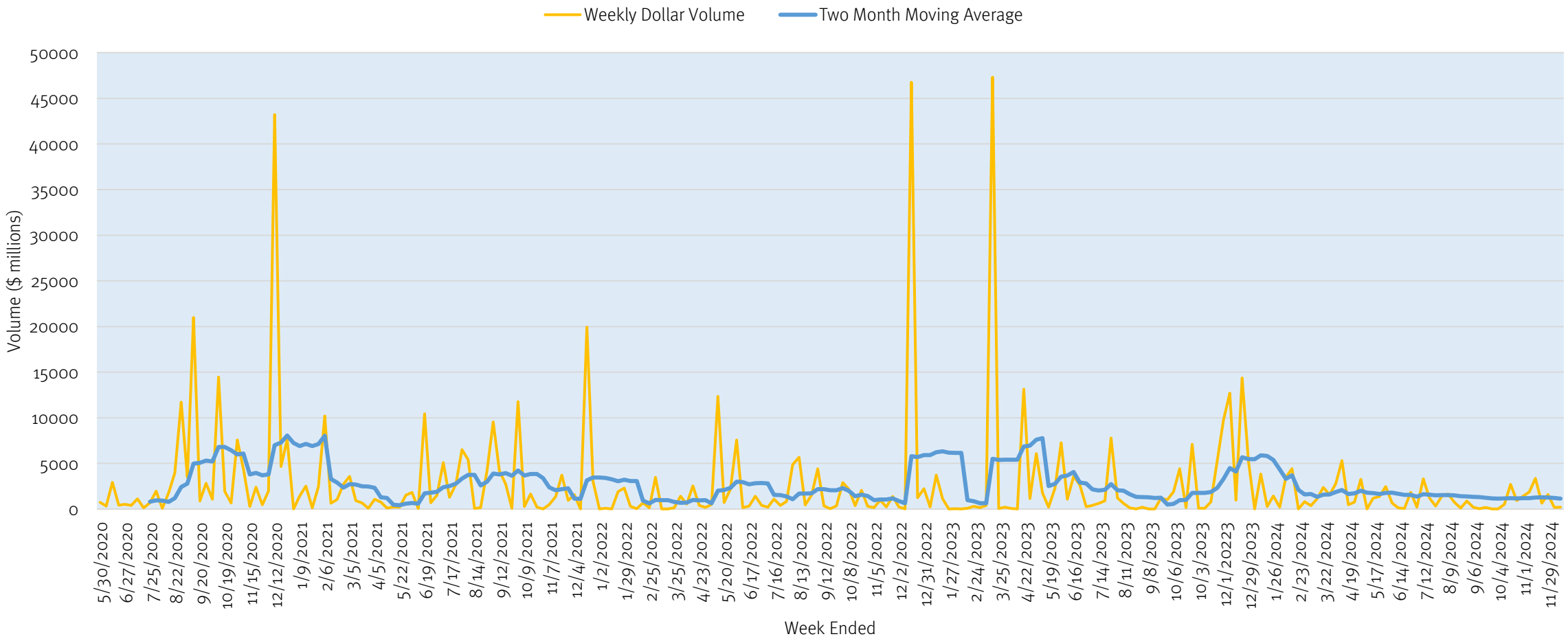
# Deals Update



# M&A Market Quiet in Recent Months

**Last week saw AbbVie acquire Nimble Therapeutics for $200 million upfront.**

## Biopharma M&A Volume Trend ($ million), Weekly, May 2020 to Nov 2024




Source: S&P, CapitalIQ

# AbbVie to Acquire Nimble Therapeutics, Further Strengthening Immunology Pipeline

**NORTH CHICAGO, Ill. and MADISON, Wis., Dec. 13, 2024**

AbbVie (NYSE: ABBV) and Nimble Therapeutics today announced a definitive agreement under which AbbVie will acquire Nimble, including its lead asset, an investigational oral peptide IL23R inhibitor in preclinical development for the treatment of psoriasis and a pipeline of other novel oral peptide candidates with potential across several autoimmune diseases. Additionally, AbbVie will acquire Nimble's peptide synthesis, screening, and optimization platform, which uses proprietary technology to help drive rapid discovery and optimization of peptide candidates for a range of targets.

"The addition of Nimble's pipeline to AbbVie's existing pipeline, combined with our deep clinical and translational expertise in immunology, represents an important growth opportunity," said Jonathon Sedgwick, Ph.D., senior vice president and global head of discovery research, AbbVie. "Together, AbbVie and Nimble have the potential to help address the significant unmet medical need for people living with autoimmune diseases."

"Nimble Therapeutics is committed to transforming the discovery of oral peptide-based medicines. With AbbVie's world-class expertise in developing and commercializing medicines on a global scale, Nimble's novel oral therapies will be well-positioned to reach more people living with autoimmune diseases," said Jigar Patel, Ph.D., founder and chief executive officer, Nimble Therapeutics. "The talented, passionate and dedicated team at Nimble has made great progress over the past few years and we are pleased that AbbVie has recognized the tremendous potential of our proprietary platform and emerging immunology pipeline."

Nimble's preclinical-stage IL23R inhibitor is an investigational oral therapy for the treatment of psoriasis and inflammatory bowel disease (IBD). IL23R is a clinically validated therapeutic target in certain autoimmune diseases and a major contributing factor to psoriasis and IBD pathogenesis and progression through increased inflammation and amplified immune responses.

Under the terms of the agreement, AbbVie will make a cash payment of $200 million at closing to acquire Nimble, subject to certain customary adjustments, in addition to certain interim funding payments. Nimble's shareholders remain eligible for a potential payment, subject to the achievement of a development milestone. The transaction is subject to the satisfaction of customary closing conditions, including the applicable waiting period under the Hart-Scott-Rodino Antitrust Improvements Act.

Source: https://news.abbvie.com/2024-12-13-AbbVie-to-Acquire-Nimble-Therapeutics,-Further-Strengthening-Immunology-Pipeline

# Novo to Close the Catalent Acquisition

**SOMERSET, NJ and COPENHAGEN, Denmark, Dec 14, 2024**

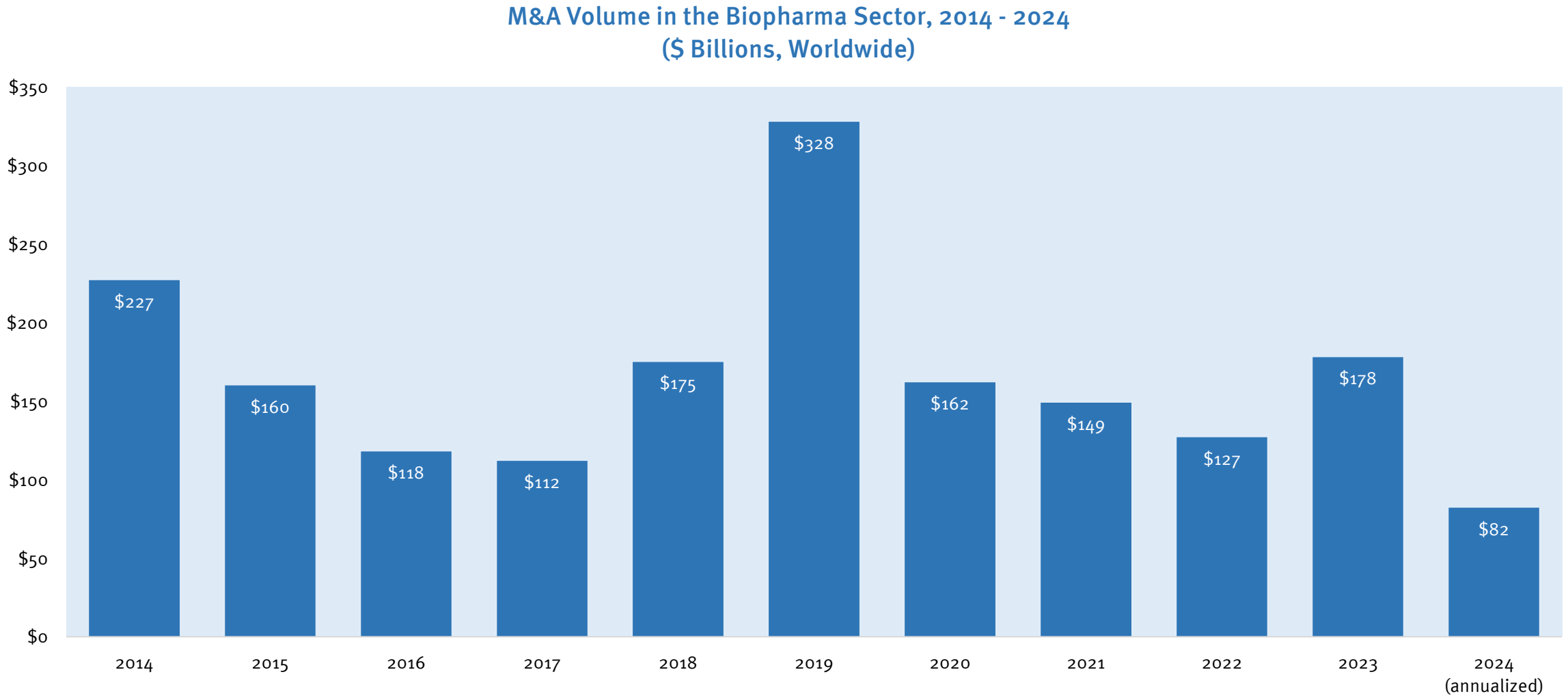
Catalent, Inc. (“Catalent,” NYSE: CTLT), a leader in enabling the development and supply of better treatments for patients worldwide, and Novo Holdings A/S (“Novo Holdings”), a global life sciences investment firm, today announced that the companies have fulfilled all regulatory closing conditions for their pending transaction. The companies now expect to close the transaction in the coming days.

“Today represents an important step in our transition to private ownership under Novo Holdings, a leading life sciences investment firm,” said Alessandro Maselli, President and Chief Executive Officer of Catalent. “As we approach transaction close, I want to thank the Catalent team for all their hard work and share my excitement for our company’s bright future. With the support of Novo Holdings and access to additional resources, Catalent will be well-positioned to drive innovation and enhance offerings for the benefit of customers and the patients they serve, ultimately accelerating our strategy to create value for stakeholders.”

“We are pleased to have achieved this latest milestone, which we believe reflects the significant benefits the proposed transaction is expected to deliver,” said Jonathan Levy, Senior Partner, Novo Holdings. “As we near close, we are enthusiastic about partnering with and supporting the Catalent team in its mission to drive innovation in the healthcare system and improve patient outcomes.”

Source: https://www.catalent.com/catalent-news/catalent-and-novo-holdings-fulfill-all-regulatory-closing-conditions-for-pending-transaction/

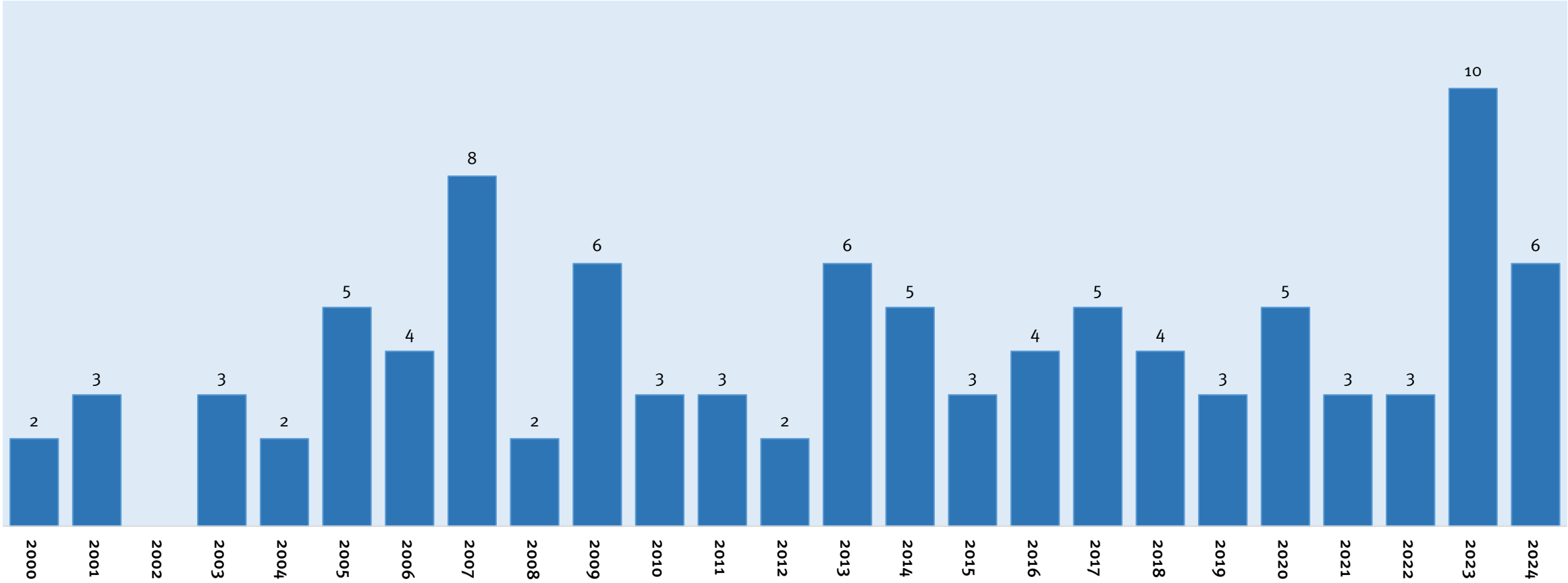
# We are Wrapping up a Weak Year for M&A Volume




Source: CapitalIQ and Stifel Analysis

# Public Biopharma Takeouts ($1bn+) Solid in 2024 – But Nowhere Near the Record Level Seen in 2023

**Number of Acquisitions of Public Biopharma Companies for $1bn or More, 2000 to 2024**
(Inflation-adjusted deal count)



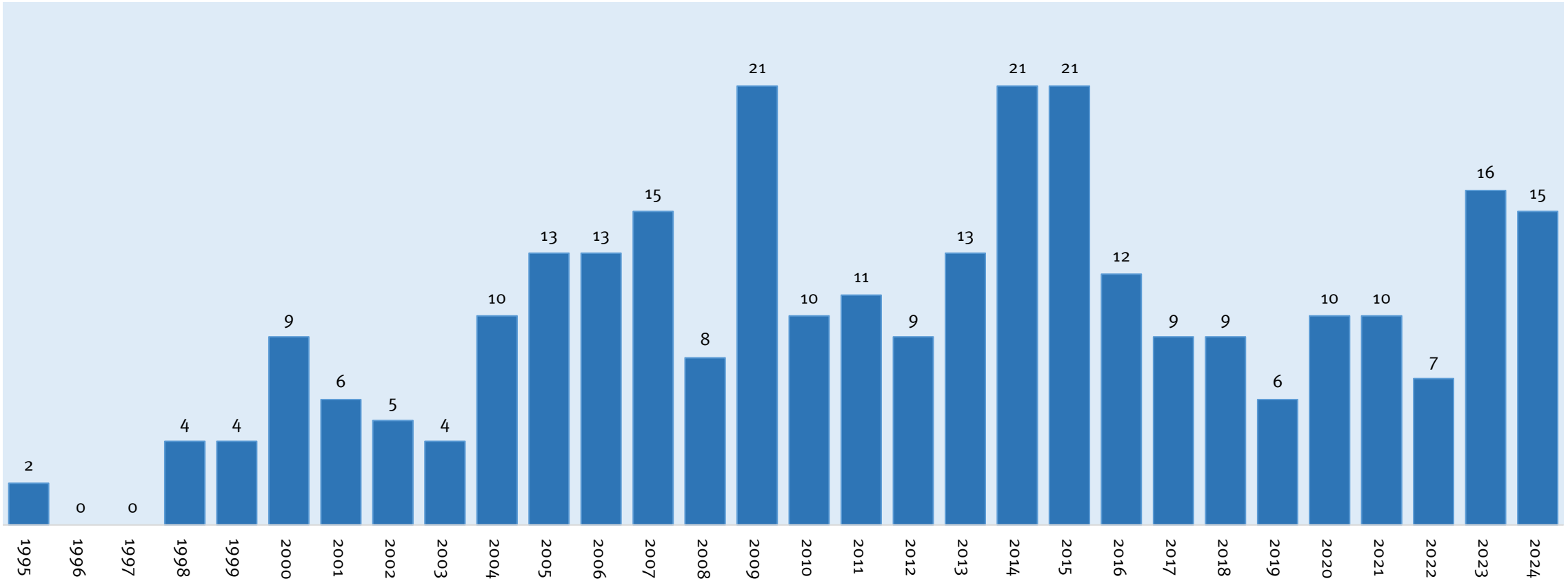

Source: S&P CapitalIQ

# Total $1bn Biopharma M&A Deals Relatively High in 2024

This chart includes all biopharma deals that are $1bn or more since 1995. This includes horizontal big pharma deals and private target deals. This year's total of $1bn+ is quite respectable by historical standards (15 such transactions). This would be the sixth highest total since 1995 (a 30-year period).

**Number of Acquisitions of Biopharma Companies for $1bn or More, 1995 to 2024**

(Inflation-adjusted deal count)




Source: S&P CapitalIQ

# PWC Report Notes a Drop in Life Sciences M&A in 2024

## Deal volumes and value down in the last 12 months

**Value by the numbers**

$205B

8%

Decrease in deal value vs. prior period

**Volume by the numbers**

252

2%

Decrease in deal volumes vs. prior period

Source: PwC analysis
*Data through November 15, 2024

## Top 2024 PLS deals YTD*

| | Target name | Industry | Acquirer | Value of transaction ($billions) |
|---|---|---|---|---|
| 1 | Catalent | Pharma | Novo Holdings | 16.7 |
| 2 | Shockwave Medical | Medical devices | Johnson & Johnson | 13.9 |
| 3 | Alpine Immune Sciences | Biotech | Vertex Pharmaceuticals | 5.0 |
| 4 | MorphoSys | Biotech | Novartis | 4.8 |
| 5 | CymaBay Therapeutics | Pharma | Gilead Sciences | 4.4 |
| 6 | Critical Care Group of Edwards Lifesciences | Medical devices | Becton, Dickinson and Company | 4.2 |
| 7 | Vantive Health | Medical devices | The Carlye Group | 3.8 |
| 8 | Axonics | Medical devices | Boston Scientific | 3.7 |
| 9 | Morphic | Biotech | Eli Lilly | 3.2 |
| 10 | China Traditional Chinese Medicine Holdings | Pharma | Sinopharm Common Wealth | 3.1 |

Source: PwC analysis
*Data as of November 15, 2024. Reflects transactions announced during 2024 (some of which may not have closed yet)

Source: https://www.pwc.com/us/en/industries/health-industries/library/pharma-life-sciences-deals-outlook.html

# PWC Sees M&A Pick Up in 2025

**PWC Study, Dec 14, 2024 (excerpt)**

Beginning with the first of several anticipated rate cuts by the Federal Reserve and following through to the implications of the recent election, the market has begun to see resolution to some of these challenges and we expect it will drive deal values and volumes higher in 2025.

We expect transactions between $5 billion and $15 billion to see sustained activity while recognizing geopolitical factors that could bring headwinds.

Pharma continues to see significant loss of exclusivity gaps in their product pipelines that will need to be filled soon. The potential for a change in the perspectives of anti-trust regulators could give them more confidence in their ability to close the larger deals needed to fill these gaps. Further, the sheer size of the cardio-metabolic market following the success of GLP-1s in 2024 will make it a therapeutic area that players will want to be in. Companies that weren't first movers will be looking for entry points through M&A to supplement potential in-house clinical development pathways.

Despite the challenging funding environment in recent years, many early to mid-stage biotech companies continue to innovate and have become attractive buyout targets for larger players in the sector. Signs of a reopening of the IPO market also bode well for the subsector as the continued funding of R&D activities is critical to getting their products to market. We expect areas such as radiopharmaceuticals and immunology to see healthy activity and expect that the nascent trend of China-to-the-West licensing deals will continue given the quality of clinical innovation in China and the impacts of the Biosecure Act.

Source: https://www.pwc.com/us/en/industries/health-industries/library/pharma-life-sciences-deals-outlook.html

# Biopharma M&A Deals get Smaller and Earlier

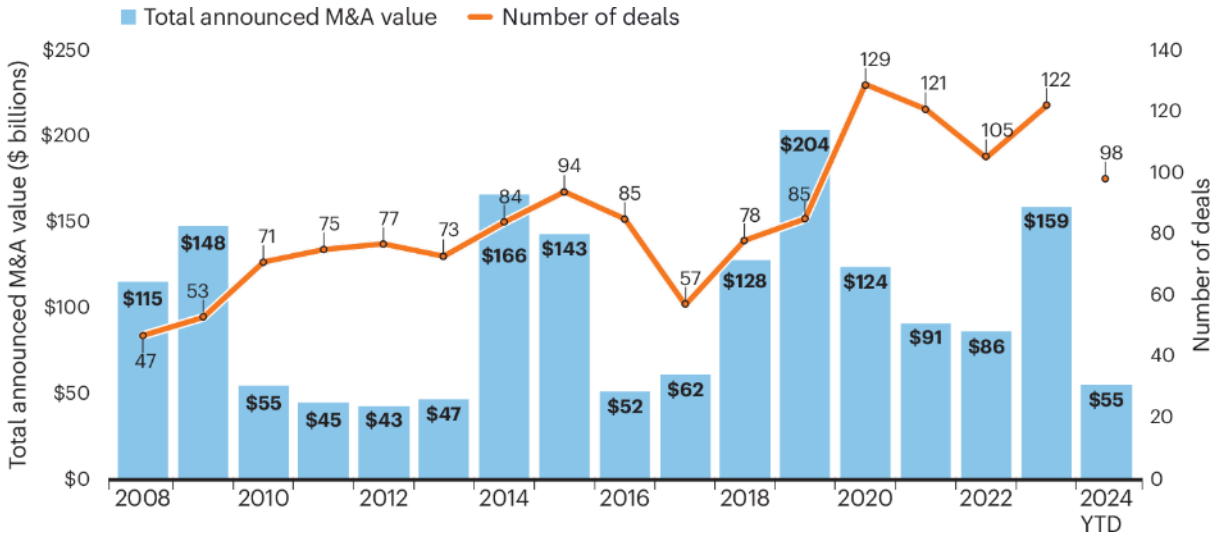
**Merger and acquisition activity is at a seven-year low in 2024 as buyers digest prior deals and US election jitters delayed further spending. Expect a pick-up in 2025.**

## Melanie Senior, *Nature Biotechnology*, Dec 13, 2024 (excerpt)

So far in 2024, biopharma merger and acquisition (M&A) activity has been lackluster. Granted, the previous year was always going to be a hard act to follow, with Pfizer's $43 billion acquisition of Seagen and a flurry of other multi-billion-dollar transactions around late-stage or marketed drugs.

But with just $55 billion of biopharma M&A by the end of September 2024, full-year value is tracking at less than half of 2023's total. Barring a huge deal in the last weeks of 2024, that would mark the cheapest shopping year since 2017, according to DealForma data tracking biopharma-related transactions (Fig. 1).

The number of M&A deals in 2024 is on track to surpass 2023's and is significantly greater than those in pre-pandemic 2019. But this year's deals are smaller and involve earlier-stage assets. No single transaction has exceeded $5 billion in cash (Vertex's April 2024 acquisition of Alpine Immune Sciences came close, at $4.9 billion), although 17 deals reached the $1 billion mark, according to BioCentury (Table 1). The share of Big Pharma acquisitions involving phase 3 or approved assets has halved to 20% so far this year, from more than 40% in 2023.

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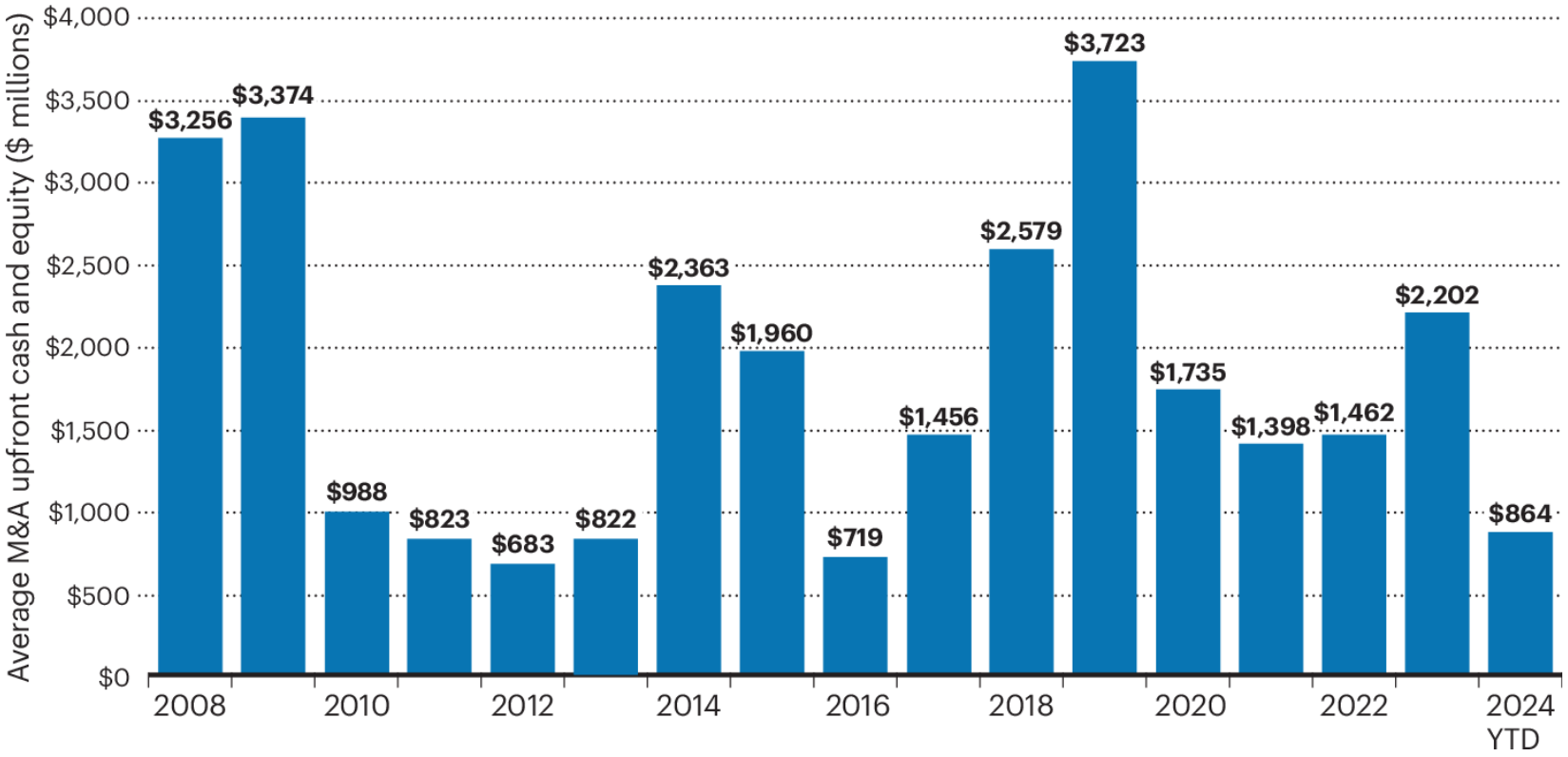
Source: https://www.nature.com/articles/s41587-024-02506-7

# Smaller and Earlier M&A Story (continued)

Earlier-stage assets are higher risk and attract smaller sums, though. Average upfront cash payments are at an eight-year low, tracking at under half 2023's values (Fig. 2).

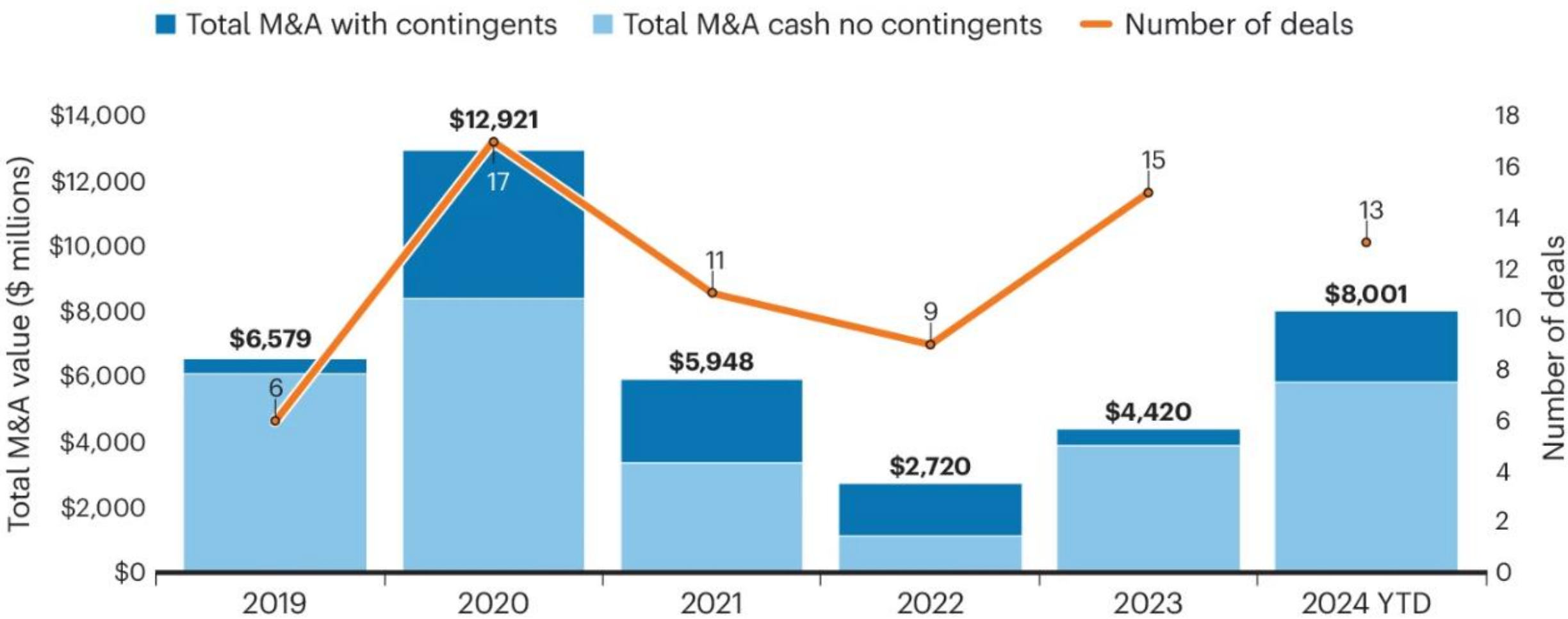



There has also been an uptick in contingent payments—cash that materializes only if certain milestones are reached. The total value of M&A deals around phase 1 assets (a sweet spot for buyers seeking access before proof-of-concept data ratchets up competition and price) is already higher than in 2023, but contingents account for much of the increase (Fig. 3). These deals are still tightly linked to data read-outs, but those read-outs may lie in the future. Other drivers of contingent payments include a rise in transactions involving private firms, for which due diligence can be more of a challenge than for listed companies, and a buyers' market.

Source: https://www.nature.com/articles/s41587-024-02506-7

# Fig. 3: Biopharma M&A by target stage—phase 1.

From: Biopharma deals get smaller and earlier




Phase 1 M&A deals made a comeback in 2024, but contingent payments comprise much of the value increase. YTD, year to date (through 30 September).

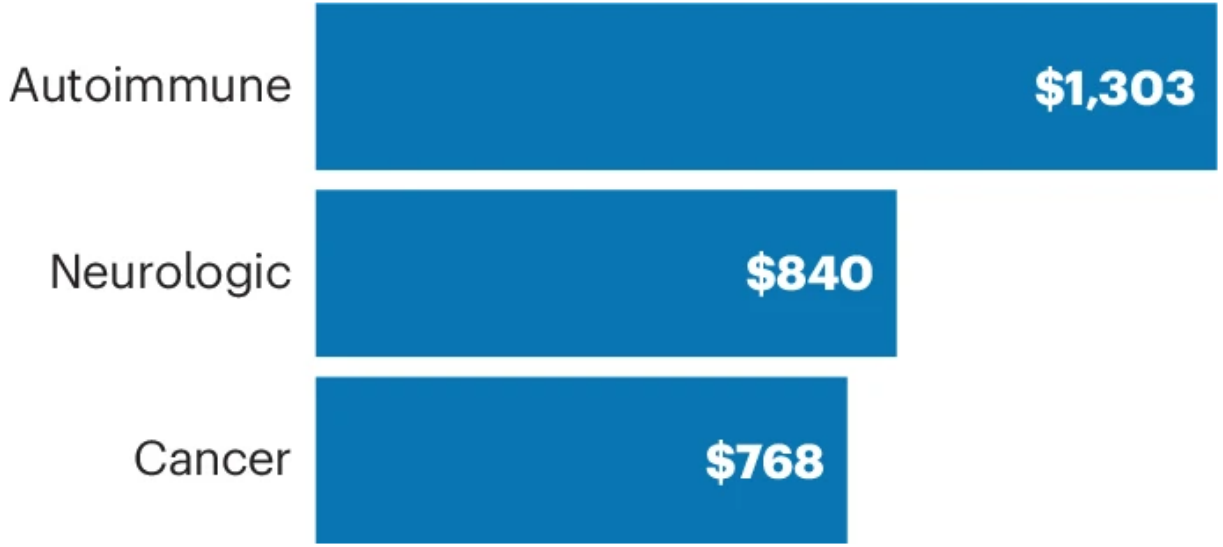
Source: DealForma Database.

Source: https://www.nature.com/articles/s41587-024-02506-7

# Smaller and Earlier M&A Story (continued)

**Fig. 5: Upfront cash and equity across various fields.**

From: Biopharma deals get smaller and earlier

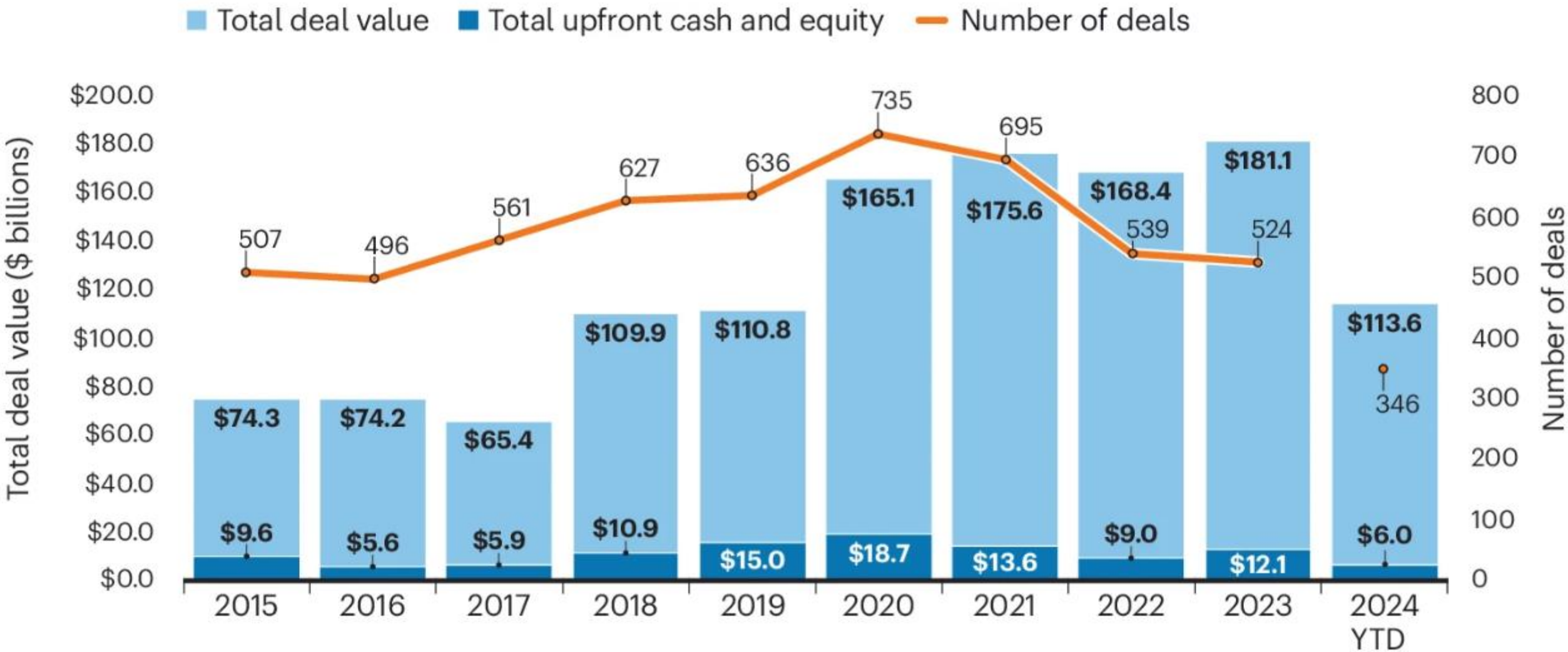



Autoimmune- and neurology-focused M&A command higher average upfront payments (in $ millions) than cancer. Source: DealForma Database.

Source: https://www.nature.com/articles/s41587-024-02506-7

# Fig. 7: R&D partnerships.

From: Biopharma deals get smaller and earlier




Total R&D partnership value for 2024 is at a five-year low. YTD, year to date (through 30 September). Source: DealForma Database.

# Industry News

# Trump Administration Downplaying Anti-Vax Talk

**KFF News, Dec 16, 2024**

## RFK Jr. Hopes To Win Over The Senate With Less Talk About Vaccines

Robert F. Kennedy Jr.'s plan is to play down his vaccine skepticism, and play up healthy food and chronic disease prevention in his attempt at confirmation to lead HHS. Meanwhile, Sen. Mitch McConnell, who battled polio as a child, said in a statement: "Efforts to undermine public confidence in proven cures are not just uninformed — they're dangerous."

**The Wall Street Journal: RFK Jr. Has A Battle Plan To Get Senate Confirmation**

Robert F. Kennedy Jr.'s attempt to win over Capitol Hill starts this week with a strategy to play down the topic of vaccines, adhere tightly to President-elect Donald Trump's messaging on abortion and talk up healthy food and preventing chronic disease, according to people familiar with his thinking. ... Kennedy is slated to be on the Hill several days this week, sitting down with over two dozen senators and a team of Republican staffers, people familiar with his plans said. His team is hoping to assuage senators' concerns about his broad criticism of vaccines, according to people familiar with his strategy. He is likely to tell senators that, if confirmed to lead HHS, he isn't planning to take anyone's vaccines away and instead wants to promote transparent, safe, effective vaccines, the people said. (Whyte, Peterson and Andrews, 12/16)

**The Hill: RFK Jr. Seeks To Win Over Senate GOP Skeptics As He Begins HHS Meetings**

"He's in a good spot. You haven't really heard much consternation about his nomination at all in recent weeks," one Senate GOP aide told The Hill, adding they expect Kennedy's focus to be on his "Make America Healthy Again" (MAHA) priorities and assuaging Republicans that he does not still support abortion. "If that turns out to be true, I think he'll be on a glide path to being confirmed," the aide added. (Weixel and Weaver, 12/15)

## Trump says he's a big believer in the polio vaccine

**CNN, Dec 16, 2024**

President-elect Donald Trump said he's a "big believer in polio vaccines" amid questions about Robert F. Kennedy Jr.'s view on the crucial inoculation. CNN previously reported that a lawyer associated with Kennedy has petitioned the US Food and Drug Administration to revoke approval of the vaccine used in the United States.

Sources: https://kffhealthnews.org/morning-breakout/rfk-jr-hopes-to-win-over-the-senate-with-less-talk-about-vaccines/, https://www.cnn.com/2024/12/16/politics/video/donald-trump-polio-vaccine-remarks-digvid

# Trump Administration Has Met with Pharma Execs

**Michael Scherer and Rachel Roubein, *Washington Post*, Dec 16, 2024 (excerpt)**

President-elect Donald Trump set two tables for a dinner party this month with his choice for health and human services secretary, Robert F. Kennedy Jr., and drug company executives like the ones Kennedy once accused of belonging to a “criminal enterprise” that knowingly killed patients for profit.

They gathered first in a side dining room at his Mar-a-Lago estate, until Trump made clear that he wanted the meal to proceed as something less formal. He proposed that the diners — who included the chief executives of Pfizer, Eli Lilly and the trade group PhRMA — relocate to a second round table on the patio, where music was playing, to better enjoy the winter Palm Beach evening, according to three people familiar with the dinner’s discussion, who spoke on the condition of anonymity to describe the private event.

Trump directed the conversation to the role pharmacy benefit managers play in the costs of prescription drugs — a major sore point for drug manufacturers who have launched a lobbying crusade accusing the middlemen of driving up prices.

The incoming president made clear that he wanted to do something to help drugmakers, and they discussed recent efforts to increase U.S.-based manufacturing of pharmaceutical drugs, according to two of the people familiar with the meeting. Another person said the comments were focused on helping patients save money.

When the topic turned to vaccines, the discussion was not about banning the products, the three people said. Kennedy spoke about the need for better study of the vaccine dosing schedule for newborns and the rise in chronic disease, while also rattling off statistics about the increase in autism rates despite multiple studies that have shown no link between vaccines and the disorder and World Health Organization estimates that immunizations have saved 154 million lives, according to two of the people.

Sources: https://www.washingtonpost.com/politics/2024/12/14/rfk-jr-trump-pharma-ceos-vaccines/

# DOGE has a Plan for Medicare, Medicaid. Will it Work?

**Ben Leonard and Chelsea Cirruzo, *Politico*, December 13, 2024**

Biotech entrepreneur Vivek Ramaswamy, co-leader of President-elect Donald Trump's Department of Government Efficiency, is eyeing Medicare and Medicaid as potential sources to cut federal spending by trillions, Ben reports.

The goal of DOGE — an outside group that will recommend spending and regulation cuts — is a tall task that would likely involve cutting entitlement programs to extract significant savings. Ramaswamy said last week on CNBC that "hundreds of billions of dollars in savings" could come from just "basic program integrity measures" in Medicare, Medicaid and Social Security.

He's generally in the right ballpark for the numbers. HHS estimated that, in fiscal year 2024, Medicare and Medicaid accounted for about $86 billion in improper payments, and other estimates peg fraud and waste higher annually.

But the devil's in the details.

Jessica Farb, managing director of the Government Accountability Office's health care team, noted that most of the improper payments in HHS' estimates are due to insufficient documentation. "If these documentation errors were corrected, it is very possible that these payments would no longer be considered improper and therefore there would not be any 'savings' to the programs," Farb said, adding that she doesn't know what estimates Ramaswamy was using. "Improper payment rate is not an estimate of fraud or waste."

Controlling fraud might be more difficult than Ramaswamy suggests because many before him have pointed to curbing fraud, waste and abuse as a way to control government spending. Experts on health care fraud say there are ways to reduce it.

"Internal controls are extremely important in trying to deter fraudulent activity from occurring, and to be honest, the government has the worst system of any organization," Patrick Malloy, program coordinator at the University of New Haven's health care fraud, waste and abuse program, told Pulse.

Source: https://www.politico.com/newsletters/politico-pulse/2024/12/13/doge-has-a-plan-for-medicare-medicaid-will-it-work-00194118

# UnitedHealth Group CEO Addresses Brian Thompson Death, says Health-care System is 'Flawed'

**Annika Kim Constantino, *CNBC*, Dec 13, 2024 (excerpt)**

UnitedHealth Group  CEO Andrew Witty on Friday mourned the death of Brian Thompson, who led the company's insurance arm, and acknowledged that the U.S. health-care system is "flawed" and in need of reform.

"We know the health system does not work as well as it should, and we understand people's frustrations with it," Witty wrote in a New York Times opinion piece. "No one would design a system like the one we have. And no one did. It's a patchwork built over decades."

UnitedHealth Group's "mission is to help make it work better," he said.

"We are willing to partner with anyone, as we always have—health care providers, employers, patients, pharmaceutical companies, governments and others—to find ways to deliver high-quality care and lower costs," Witty added.

The New York Times piece marks Witty's first public comments since last week's fatal shooting of Thompson, CEO of UnitedHealthcare, the largest private insurer in the U.S. UnitedHealth Group is the nation's biggest health-care conglomerate based on revenue. Its nearly $475 billion market cap has shrunk since Thompson's death on Dec. 4.

Luigi Mangione, 26, is accused of fatally shooting Thompson outside the Hilton hotel in midtown Manhattan as the CEO headed to UnitedHealth Group's investor day. Investigators have said Mangione was a critic of the health-care industry, a widely held view among Americans.  The killing has unleashed a wave of pent-up resentment and anger toward the insurance industry, which has become a popular villain blamed for spiraling health-care costs and difficulties accessing care. From denied claims, rising premiums and unexpected bills, to an overall lack of transparency, patients have flooded social media with stories about their own negative experiences with insurance.

Still, the killing comes after a challenging year for the insurers, which are under pressure to shore up profits. This year in particular, companies grappled with higher medical costs due to seniors opting for surgeries they had delayed during the Covid-19 pandemic.

Source: https://www.cnbc.com/2024/12/13/unitedhealth-group-ceo-andrew-witty-addresses-brian-thompson-death.html

# What Doctors Like Me Know About Americans' Health Care Anger

**Helen Ouyang, Associate Professor, Columbia University, *New York Times*, Dec 8, 2024 (excerpt)**

The killing of Brian Thompson, the chief executive of UnitedHealthcare, the country's largest health insurer, has reignited people's contempt for their health plans. It's unknown if Mr. Thompson's tragic death was related to health care, and the gleeful responses have been horrifying. But that reaction, even in its objectionable vitriol, matters for how it lays bare Americans' deep-seated anger toward health care. Around the country, anecdotes were unleashed with furor.

Among these grievances is the great unknown of whether a treatment recommended by a doctor will be covered. It's critical for me as a physician to build trust with my patients by giving them clear answers. But the conversations we're seeing now about health care remind me that insurance unknowns don't just compromise the care I can deliver to my patients — they also undermine the fragile doctor-patient trust. It's an unsustainable dynamic.

I've been on the other side of the American health insurance quagmire, too, as a patient. Recently, my primary care physician recommended I undergo additional testing to assess my risk for certain diseases. The patient in me instinctively asked if my insurance covered it, even though I knew she wouldn't know the answer. "They should," she said. "It seems most insurers are paying for it." I recognized her response — it's the same optimistic but vague one I often give.

When doctors can't give a straight or accurate answer, patients may lose faith in them. What's more, when insurers reject claims, they usually blame the provider — the medical code used was wrong, the diagnosis wasn't specific enough — which can further erode the relationship between patients and their doctors.

The country is not heading toward a single-payer system, but that doesn't mean we have to continue leaving patients and their doctors in the dark. I loathe the fact that patients can't automatically get the care they need without thinking about costs. But they at least deserve clarity about what's covered before they acquiesce to expensive tests and treatments. Health insurance shouldn't be so opaque, up to the whims of different companies. Coverage shouldn't be so convoluted, mired in rigid codes and obfuscating wording. I should be able to tell my patient in the E.R. if his hospital stay will definitely be paid for. I know exactly how much of my dog's care will be covered; why can't I know the same for my patients?

Source: https://www.nytimes.com/2024/12/08/opinion/health-care-anger.html?unlocked_article_code=1.g04.NGgo._ki7WiuXsH-w&smid=url-share

# Biosimilar Competition Matters

**Benjamin Rome et.al., Use, Spending, and Prices of Adalimumab Following Biosimilar Competition, *JAMA Health Forum*, Dec 13, 2024 (excerpt)**

In this cross-sectional study, we found that in the first year of competition, adalimumab biosimilars constituted less than 2% of prescriptions in the US. However, there was a nearly 50% decrease in adalimumab net spending and prices, likely due to rebates by AbbVie to health plans and pharmacy benefit managers for maintaining Humira's position on formularies (list price increased while net price decreased). This study was limited by net sales excluding pharmacy and pharmacy benefit manager spending on intermediary fees and no measurement of how competition influenced patient out-of-pocket costs.

Lower health care spending is a goal of biosimilar introduction, but low uptake raises concerns that manufacturers may withdraw from the market or avoid developing future biosimilars. Compared with biosimilars, uptake of new generic drugs is often rapid, averaging 66% of the market share during the first year after brand-name market exclusivity ends. One reason is that all states allow or require pharmacists to automatically substitute generics in place of brand-name drugs; by contrast, biosimilars have additional requirements to be FDA certified as interchangeable, and state laws for biosimilar substitution are more stringent than for generics. To facilitate pharmacist substitution, Congress could eliminate the separate requirements for interchangeable biosimilars, as the FDA recommends.

By January 2024, nearly all Medicare Part D plans covered Humira, while only half covered biosimilars and less than 2% preferred biosimilars over Humira. To prevent manufacturers from leveraging confidential rebates to maintain exclusive preferred formulary status, policymakers could prohibit such rebates for biologics after initiation of biosimilar competition, facilitating direct price competition and possibly lowering patient out-of-pocket costs. In January 2024, CVS Health announced removal of Humira from its standard commercial formularies in favor of a colicensed biosimilar; the effects of this development on biosimilar uptake and spending should be assessed.

Source: https://jamanetwork.com/journals/jama-health-forum/fullarticle/2827711

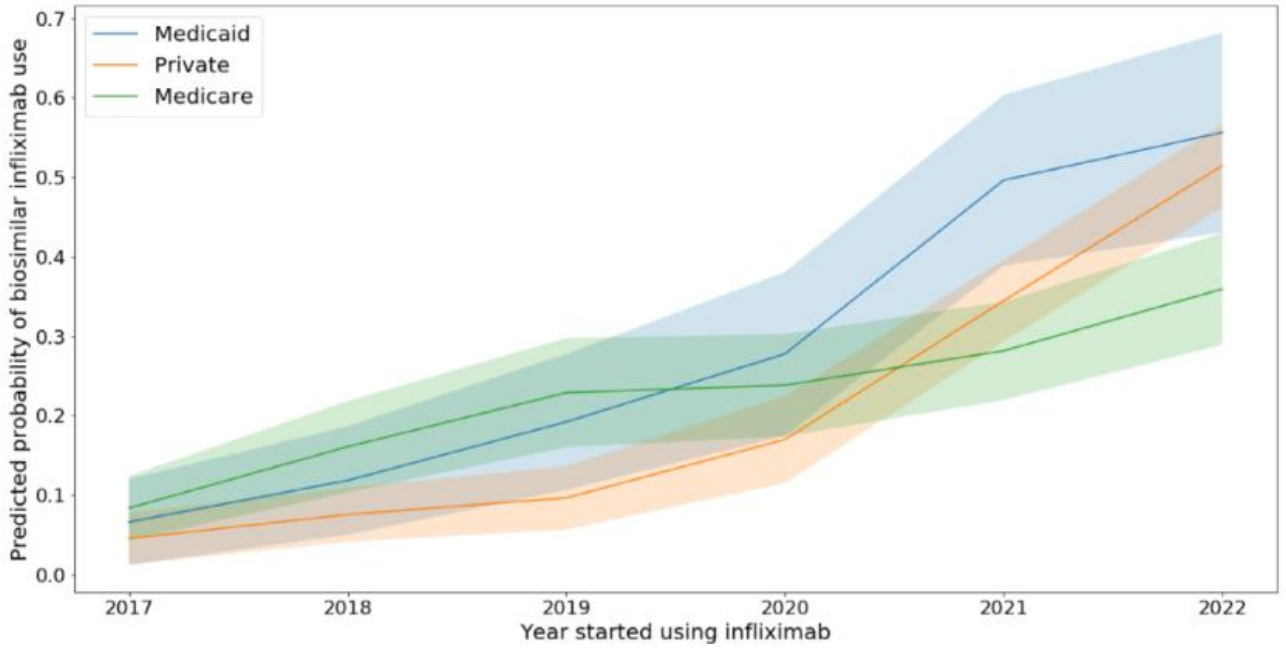
# How Many Patients are Switching to Biosimilars?

**Jason Shafrin, *Healthcare Economist*, Dec 11, 2024 (excerpt)**

Biosimilar initiation: The authors found that for patients initiating therapy, 21.6% received an infliximab biosimilar between 2017 and 2022. However, while <10% of patients initiated a biosimilar in 2017, by 2022 37% of Medicare patients, 51% of commercially insured and 55% of Medicaid patients initiated a biosimilar version of infliximab. Patients in the lowest socioeconomic status (as measured by Area Deprivation Index) were more likely to initiate a biosimilar (RR = 1.29, 95%CI 1.01–1.66).

Biosimilar switching. While there was an increasing trend to more biosimilar treatment initiation, switching from biologic to biosimilar was less common. "86.4% of users who received at least two doses of infliximab stayed with the formulation they were initially prescribed." Most of the switchers switched from biologic to biosimilar (11.5%) with 1% switching from biosimilar to biologic and <1% switching between biosimilar versions of infliximab.

Predicted probability of starting on biosimilar infliximab among new users of infliximab, by insurance and year of infliximab initiation




Source: https://www.healthcare-economist.com/2024/12/11/how-many-patients-are-switching-to-biosimilars/

*Figure 1* Deloitte Survey Indicates Optimism About Life Sciences Sector Outlook


Note: n = 150 (including 100 biopharma and 50 medtech respondents from several global markets).

Source: Deloitte's 2025 Life Sciences Outlook survey.

# GLP-1 Drug Compounding is in Limbo. Will the FDA Draw Out its Decision?

**Amy Baxter, *Biopharma Dive,* Dec 11, 2024**

When the Food and Drug Administration took Eli Lilly's Zepbound and Mounjaro off of its drug shortage list in October, companies making cheap "compounded" versions found themselves in a bind.

By ending compounders' ability to manufacture and sell their off-brand versions in bulk, the FDA's decision also left some patients wondering how they would be able to access the popular obesity and diabetes drugs at an affordable price. About 12% of American adults have taken a GLP-1 medication, according to a May poll from KFF Health. And compounded versions may account for as much as 20% of all GLP-1 prescriptions, CNN reported.

But when the FDA backed down, letting compound pharmacies resume their activities for the time being, the industry was left in something of a limbo.

"The FDA is probably feeling a lot of pressure to make sure they're not just siding with pharma to remove something because they think it's appropriate and making sure they have their due diligence," said Manny Jurado, principal at The Dedham Group.

Novo Nordisk and Eli Lilly, the dominant GLP-1 drugmakers, have ramped up their manufacturing and filed lawsuits against compound pharmacies to limit supply of the knock-off versions. Both companies have wrestled with shortages over the last year, though the FDA has now marked the medications as "available."

Compound manufacturers fought back after the FDA's October decision and sued the agency, leading to a reversal, which is rare, according to Jurado. He said the stakes are higher because of how lucrative GLP-1 drugs have become.

During the first nine months of the year, Eli Lilly's tirzepatide drugs Zepbound and Mounjaro raked in more than $11 billion in revenue, while Novo Nordisk reported combined revenue of more than $27 billion for its GLP-1 diabetes and obesity care business, including Wegovy and Ozempic, during the same time period.

As demand for the drugs have grown, a significant market around compounded versions has emerged in parallel, with digital healthcare companies such as Weight Watchers and Hims & Hers jumping on the trend and offering GLP-1 injectables.

Source: https://www.biopharmadive.com/news/glp-1-compounding-fda-decision-trump-administration/735231/

# Biohaven Reports Positive Phase 1 Degrader Data, Achieving Deep Targeted IgG Reductions in the Lowest Subcutaneous Dose Tested

**NEW HAVEN, Conn., Dec. 16, 2024** /PRNewswire/ -- Biohaven Ltd. (NYSE: BHVN) ("Biohaven"), a global clinical-stage biopharmaceutical company focused on the discovery, development, and commercialization of life-changing therapies to treat a broad range of rare and common diseases, today highlighted the achievement of several clinical and regulatory milestones across its proprietary Molecular Degrader of Extracellular Proteins (MoDE™) platform as well as its glutamate modulation and ion channel programs.

Subcutaneously administered BHV-1300 achieved deep lowering of targeted IgG, with reductions › 60% in the lowest subcutaneous dose tested in the ongoing multiple ascending dose (MAD) study. Subcutaneous BHV-1300 achieved progressive reduction in IgG within hours of each weekly dose administration in the MAD, and pharmacodynamic effects were sustained relative to baseline over the four-week study period. BHV-1300 has been safe and well-tolerated across the Phase 1 study. There were no clinically significant effects on albumin or liver function, and no increases in cholesterol were noted. Further enhancing the competitive safety profile and as intentionally designed, plasma IgG3 levels were preserved through the end of study week 4 to allow for healthy immune effector functioning. All AEs were mild, any drug-related AE resolved, and there were no discontinuations due to study drug related AEs. The optimized subcutaneous formulation in the MAD also showed substantially less inter-patient variability compared to previously reported intravenous BHV-1300. Escalating dose level cohorts of subcutaneous BHV-1300 are ongoing to explore the full range of IgG reductions possible with BHV-1300 for a wide range of future disease indications.

Tova Gardin MD, MPP, Biohaven's Chief Translational Officer, commented, "The results of subcutaneously delivered BHV-1300 from the first and lowest MAD dose cohort represent a monumental step forward for our MoDE platform with deep and rapid reduction in targeted IgG. Our results highlight the selectivity and precision of BHV-1300 in potentially treating IgG mediated immune diseases while the regulatory acceptance of three next generation degraders showcases the future of the MoDE technology in autoantibody disease. With speed, selectivity, and depth of lowering, BHV-1300 has the potential to transform the treatment of autoimmune disease and has paved the way for rapid innovation across the degrader platform. With the mechanistic validation of BHV-1300 and performance of the optimized subcutaneous formulation in Phase 1, we have begun the manufacturing of a convenient autoinjector that will further differentiate our approach in the clinic. The early autoinjector development to ensure a commercial ready, patient-administered device for BHV-1300 was important to derisking this aspect of our MoDE development program."

Source: https://ir.biohaven.com/news-releases/news-release-details/biohaven-reports-positive-phase-1-degrader-data-achieving-deep

Cell Metabolism

Article

Dec 13, 2024

# FcRn-dependent IgG accumulation in adipose tissue unmasks obesity pathophysiology

Lexiang Yu, Yong Xiao Yang, Zhen Gong, ..., Bao Ting Zhu, Liheng Wang, Li Qiang

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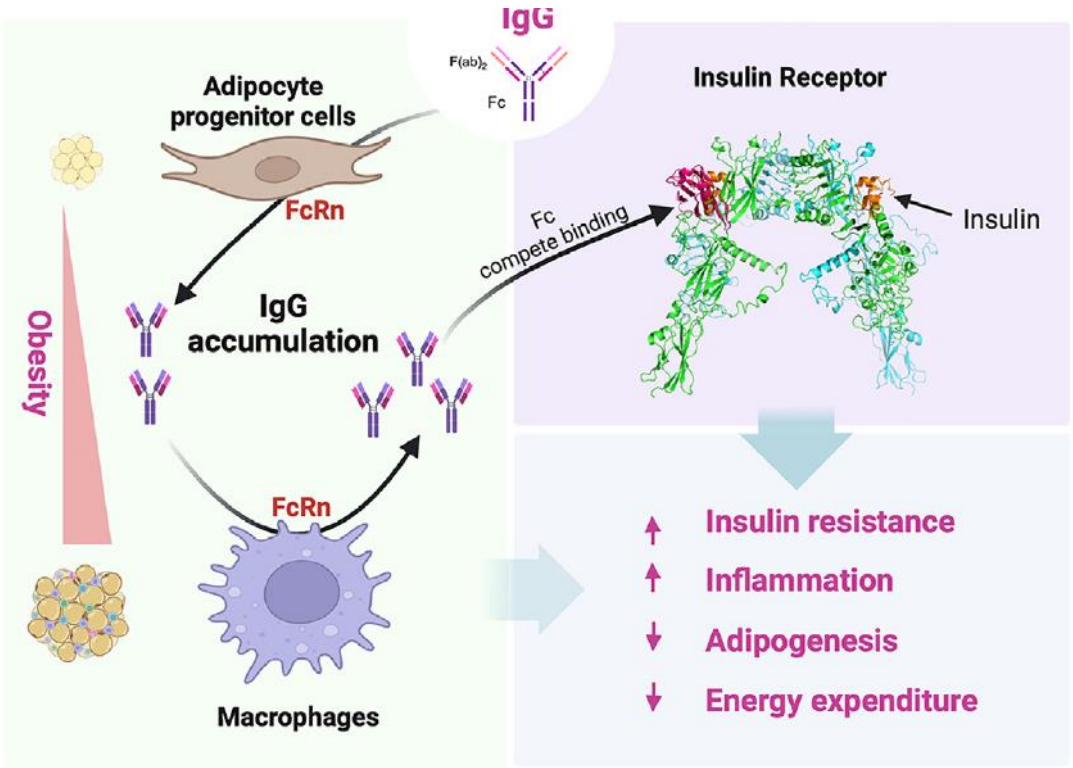
## In brief

Yu et al. found that in obesity, IgG accumulates preferentially in adipose tissue via FcRn-dependent recycling by adipose progenitor cells and macrophages. This buildup promotes macrophage infiltration and adipose inflammation and impairs insulin binding to its receptor, ultimately leading to insulin resistance and metabolic dysfunction.




Source: https://www.sciencedirect.com/science/article/pii/S1550413124004479

This is a surprising and highly relevant paper for the pharma sector, merging two of the hottest areas in biosciences: obesity management and IgG control.

Traditionally, immunoglobulin G is recognized as a plasma protein that neutralizes antigens for immune defense. However, this research from Yu et.al., demonstrates that IgG predominantly accumulates in adipose tissue during obesity development, triggering insulin resistance and macrophage infiltration. This accumulation is governed by neonatal Fc receptor (FcRn)-dependent recycling, orchestrated in adipose progenitor cells and macrophages during the early and late stages of diet-induced obesity (DIO), respectively.

Targeting FcRn abolished IgG accumulation and rectified insulin resistance and metabolic degeneration in DIO. The researchers further and unexpectedly uncovered an interaction between IgG's Fc-$CH_3$ domain and the insulin receptor's ectodomain. This interaction hinders insulin binding, consequently obstructing insulin signaling and adipocyte functions.

# ABHD56 Impacts Feeding Via Endocannabinoid System

***Genetic Engineering & Biotechnology News*, Dec 16, 2024 (excerpt)**

The nucleus accumbens (NAc) is a brain region that plays a key role in reward, motivation, and addiction. The NAc is rich in endocannabinoids, which are critical for many physiological functions that regulate human health. **An imbalance in the production of endocannabinoids, or in the body's responsiveness to them, can lead to clinical disorders, including obesity as well as neurodegenerative, cardiovascular, and inflammatory diseases.** Researchers from the University of Montreal Hospital Research Centre (CRCHUM) have now discovered in mice that targeting an enzyme in the brain that degrades a key endocannabinoid molecule could help fight obesity.

The findings are published in *Nature Communications* in an article titled, "ABHD6 loss-of-function in mesoaccumbens postsynaptic but not presynaptic neurons prevents diet-induced obesity in male mice," and led by Stephanie Fulton, PhD, a CRCHUM researcher.

For years, Fulton and her team have been unraveling the mechanisms in the human nervous system that control people's need to eat and engage in physical activity and how their metabolism affects their mood. In their new study, first co-authors David Lau, a University of Montreal doctoral student, and Stephanie Tobin, PhD, a former postdoctoral fellow, show that body-weight control in mice is strongly modulated by neurons in the NAc.

The team discovered the enzyme ABHD6 degrades a key endocannabinoid molecule known as 2-arachidonoylglycerol (2-AG).

With the discovery in 2016 that whole-body inhibition of ABHD6 reduced body weight and protected against diabetes—a finding made by the team of Marc Prentki, a researcher at the CRCHUM—the question arose as to what this enzyme does in the brain to affect appetite and body weight.

"We expected that increasing 2-AG levels would stimulate food intake by increasing cannabinoid signaling, but paradoxically found that when we deleted the gene encoding ABHD6 in the NAC in mice, there was less motivation for food and greater interest in physical activity," said Fulton.

Source: https://www.genengnews.com/topics/translational-medicine/targeting-a-brain-enzyme-may-be-the-key-to-unlocking-new-obesity-strategies/

# Dr. Thomas O'Brien, visionary who addressed dangers of antimicrobial resistance, dies at 95

**Bryan Marquard, *Boston Globe*, Dec 12, 2024 (excerpt)**

With insight few possessed decades ago, Dr. Thomas F. O'Brien sounded the alarm about the increasing danger of antimicrobial resistance in a world growing ever more connected. Drug-resistant strains of bacteria, viruses, and germs could emerge in far-flung places and hitch a ride on an unwitting tourist, who then headed home and spread the infection thousands of miles away.

If perils like that weren't daunting enough, the imprecise use of antibiotics in treatment could give rise to yet more deadly, drug-resistant superbugs. "An attempt to cure one patient may eventually prevent cure of another," Dr. O'Brien wrote in 2001.

To address these threats, he helped pioneer the use of databases that let doctors respond quickly to outbreaks of antibiotic resistance. Traveling the world, often to small hospitals in developing nations, he cultivated a network of physicians, researchers, and technicians whose observations and testing became part of a larger effort.

"A lot of what he did was create a family," said Dr. John Stelling, who codirected and cofounded, with Dr. O'Brien, the World Health Organization's Collaborating Centre for Surveillance of Antimicrobial Resistance. "Everybody contributes their little bit, and their little bit in aggregate tells a lot about emerging threats in close to real time."

Dr. O'Brien, who had served as the first director of the infectious diseases division at what is now Brigham and Women's Hospital, died Monday in his Brookline home. He was 95 and his health had been failing. His wife, Ruth Reardon O'Brien, who was the second woman partner at the Ropes & Gray law firm, was 92 when she died Thursday in their home.

"He was one of the very first people to call attention to the risks of antimicrobial resistance developing," said Dr. Daniel Kuritzkes, chief of the division of infectious diseases at Brigham and Women's and a professor at Harvard Medical School.

Source: https://www.bostonglobe.com/2024/12/12/metro/dr-thomas-obrien-obituary-conan-obrien/

# Disclosure

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