

# Biopharmaceutical Outlook for 2025

Jan 8, 2025

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# Past Issues

Past issues of this publication can be read online at:

[Dec 17, 2024](#) (Biotech Blues)  
[Nov 25, 2024](#) (Biotech Balance Sheets)  
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[Dec 18, 2023](#) (Expectations for Future)  
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[July 24, 2023](#) (Alzheimer's Disease)  
[July 7, 2023](#) (Biotech market review – H1 '23)  
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# Feel Free to Join Us at These Upcoming Events



**BIOTECH HANGOUT**  
Join Us on X (formerly Twitter) Spaces  
Fridays, 12-1pm EDT  
REPLAYS AVAILABLE ON  
BIOTECHHANGOUT.COM, SPOTIFY & APPLE PODCASTS

The graphic features a grid of 18 circular headshots of participants, including Paul Woffles, Michael Yee, Grace Colon, Dawn Bell, Sam Fazzell, Nicholas Garabedian, Daphne Zohar, John Madiganone, Yaron Hershkov, Brad Longair, Lisa Kitzmann, Josh Schimmer, Julian Sobole, Jim O'Neil, Bruce Bogert, and Brian Persson.

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 13<sup>th</sup>.

**To meet with Stifel**  
[yeungn@stifel.com](mailto: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:

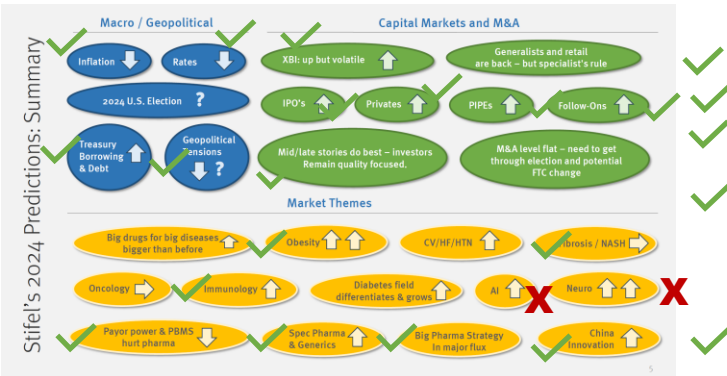
- Grace Colón, CEO & Co-Founder, Inaya Therapeutics, BIO Executive Committee Member
- Nouhad Husseini, SVP, Business Development & Corporate Strategy, Regeneron Pharmaceuticals
- Tony Lanzone, Global Head, Consulting, Syneos Health
- Ted Love, Chair, Board of Directors, Biotechnology Innovation Organization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



# 1. What Happened in 2024?







### Our Views on the Macro and Political Outlook in 2024

- Inflation continues to drop in 2024 and other macro negatives also continue to disappear.
- Declining rates put some pressure on commercial banks but they manage through it.
- Treasury gets back to what it loves to do - borrow lots of money. The U.S. Treasury Quarterly Refunding Announcement in Q4 was very friendly to market - most likely by design. That can't last as the deficit is just too big for light borrowing. U.S. borrowing will keep some upward pressure on long rates - we don't get back to sub-2% yields of 2019 for a long time. This will work to prevent an absolute explosion in the XBI.
- US election gets a lot of attention, will be close and is likely to be quite nasty.
- It feels like Trump's momentum won't get stopped by the many legal challenges as the Supreme Court won't let it happen.
- The question will be how much the improving economy helps Biden. It should but voters don't seem to love the man.
- Nikki Haley emerging as key challenger to Trump. She has no record of using anti-pharma rhetoric in chasing votes and is a non-populist, fiscal conservative. If she does well in the primaries it could be a major positive for pharma.
- The election doesn't change the biotech market's positive direction - historically, it hasn't.
- IRA legal challenges continue to make progress in 2024 - which creates pressure to rewrite the law.
- However, the IRA doesn't get fixed until after the election - and it's not a slam dunk that it happens.

### More Capital Markets Predictions in 2024 (continued)

- Substantial increase in IPO activity
  - Mid to late stage therapeutics are favored. We don't see a return to preclin IPOs as we had in 2021
  - A few big AI stories get out like Valo. Interest in AI and biopharma remains off the charts
  - More obesity/CV companies get out like Kallyope and Rivus
- Significant increase in equity privates:
  - We could easily set an all-time volume record in the equity privates area in 2024
  - Activity slowed down a lot in 2023 but as the market picks up, the many well financed funds will stop throttling back investment volume and shift to an offensive stance on deploying capital - can't raise a new fund until you deploy the old one
  - PIPE interest remains off the charts and PIPE deals remain quite important throughout the year
  - Healthtech efforts of groups like Andreessen Horowitz/GC etc continue to be really interesting
  - Incursion of tech VC's into healthcare accelerates - particularly at the margins (e.g., AI in drug discovery)
- The "old days" stay the "old days" - generalists don't take over and healthcare specialists continue to rule:
  - Twenty years ago, specialty funds less important and retail/generalists drove the market - creating enormous swings etc.
  - We are going to see well-performing healthcare specialist funds like Cormorant, Deep Track and RA get a lot bigger in 2024
  - The ability of these funds to move/influence/drive small/midcaps is going to grow
  - While generalists come back and retail comes back the world will be much more specialist influenced than ever before
  - PE/biotech hybrid funds like General Atlantic and Patient Square that are able to gather funds well (especially from MidEast), get ever greater market influence

### Our Views on the Biopharma Capital Markets in 2024

- Big funds flow into biopharma and biotech
  - Generalists come in and retail gets new interest - FOMO factor is real
  - Many healthcare savvy investment groups continue to come out of cash and net short positions
- The XBI goes over 100 again but doesn't get anywhere near 150 this year.
- Investors stay focused on stock picking and funding the best stories. Preference for great science, mid/late stage biopharma and commercial growth opportunities. No general euphoria sweeps the market
- Turbulence and volatility remain in market:
  - Some hedge funds continue with drawdowns
  - Electoral jawboning on pharma pricing
  - Volatility / gamma managing quant funds continue to accentuate the wild swings we have been seeing
- Lots, lots more M&A in 2024:
  - But M&A volume not up from 2023 which was a record for biotech M&A.
  - Prices go up - a lot
  - Biotech consolidation / cleanup continues as smallco's that can't finance well continue to merge or disappear
- Continued interest in hot areas like I&I (e.g., Gracell M&A in Dec) and radiopharma (e.g., Rayze takeout in Dec)
- Substantial growth in the follow-on market as returning investors seek large blocks of quality biopharma companies.

### How The Market Could Play Out in 2024

As the saying goes history never quite repeats itself but it does rhyme.

We have been through a reasonably similar time - the dotcom collapse of 2000/2001.

Biotech plummeted by more than 75% as genomics names like Human Genome and Incyte couldn't find interested investors in the post-apocalyptic period. The market got steadily worse and hit bottom some time in mid 2002. The market got better in 2003 with Novartis buying Idenix and the merger of Biogen and Idex. The fundamentals were quite positive with numerous approvals that year.

A key development at that time was investors deepening appetite for taking risk. Those with long memories will remember that a lot of great companies raised money in 2003.

For example, IPOs got done in 2003 for companies like Myogen (bought by Gilead for \$2.5bn in 2006).

We see 2024 as a year that will be similar to the 2003/2004 period.

Good companies will be able to go public. There will be more than a few IPOs and the follow-on market will be robust.

We see 2024 as a year when biotech and growth players in life sciences will raise substantial capital as investors have money that needs to be put to work and will fear losing out on the ongoing M&A wave.

2024 will be a big year for raising capital.

### How The Market Could Play Out in 2024 (continued)

But there is an even larger trend emerging here.

No one really wants to openly speak the truth - which is that today's user of GLP-1 agonists is more likely to be a slightly overweight woman in Beverly Hills than a morbidly obese poor person in Mississippi or Alabama.

Overwhelmingly, GLP-1 users are private pay patients based in coastal areas where incomes are higher.

If anti-vaxxers tended to be Trump Republicans found in Missouri or Wyoming, then GLP-1 users tend to be more Democratic, more wealthy, much more health conscious and much more likely to live in a wealthy coastal city.

What's interesting is just how big this market is. We have previously estimated that based on recent surveys the *private pay* market alone for obesity drugs in the U.S. could go over \$100 billion in size.

That's stunning.

The entire business model of pharma can be shifted by providing consumers what they really want.

To be thin. To live longer. To be able to quit smoking. To get rid of their diabetes. And so on.

It strikes us that the modern obesity drug is profoundly disruptive to the existing ecosystem that delivers and pays for medicines in the US.

Because of poor reimbursement, today's obesity drug user is more likely to be found on Rodeo drive than Southern Alabama.

Shown at left are slides from our Jan 4, 2024 [sector outlook](#) report.

We got a **lot right** including the improved macro situation, the election outcome, the geopolitical picture and the XBI. We correctly foresaw the chaos in big pharma ranks, the growth of immunology, the relatively moderate performance of oncology stocks, the growing consumerization of the obesity drug market, the importance of China innovation and the resurgence of specialty pharma and generics. There were also a number of areas where we were **clearly wrong**:

- We said M&A would be flat but, in fact, it was *down*.
- We said it would be a big year for neuro. It was a tough year for neuro.
- We said AI would be big but it wasn't. If anything, AI stories fizzled in 2024.
- We said the private venture market would take off. It rose but didn't exactly "take off".

One area that we **nailed** was the strength of the public follow-on market. As we forecast, the PIPE market was huge and follow-ons were up really big in 2024.

# We Weren't the Only Prescient Ones

Our Dec 18, 2023 issue highlighted predictions for 2024 from Deloitte, Janus Henderson and Venrock.

Looking back, a number of predictions that seemed non-obvious to us turned out to be right.

**Deloitte.**

Deloitte correctly highlighted the high focus on health equity measures.

**Janus Henderson**  
INVESTORS

Janus Henderson predicted numerous additional health benefits of GLP-1 agonists would become apparent in 2024.

Like ourselves, they were too optimistic about the market in 2024.

**venrock**

Venrock's predictions from Bob Kocher and Brian Roberts were **spookily good**. They correctly foresaw nothing happening to PBMs, turnover in management of managed care, CMS hitting its drug negotiation deadline, crumbling of VC-backed brick and mortar startups, Supreme Court protecting access to mifepristone and rapid growth in usage of GLP-1s.





# Investor Mood Glum

We have spoken to quite a few investors in recent weeks and can report that biotech market sentiment definitely worsened from earlier in 2024.

Somehow, the New Years' champagne was quite as bubbly as was a year ago.

Apparently, flat champagne is the same thing as mediocre chardonnay.

And the market was definitely mediocre.

What we have seen transpire in late December was the arrival of quite a few specialist hedge fund annual letters recounting the year's performance. On the whole, the letters weren't good. Most funds were flat for the year. Some like Casdin, Janus Henderson and RA, were up substantially. But far too many were down.

The problem is that the S&P 500 index registered a 23% gain in 2024. And that was on the heels of a 24% rise in 2023.

You can imagine that biotech hedge fund LP's aren't exactly dancing in the streets right now. Quite a few funds are out saying *now* is the time to load up on biotech. Mr. LP, "please put money in our fund now – you won't regret it." They are very likely correct.

The issue is that funds were saying all of this last year.

And they turned out to be wrong.

The chart on the next page summarizes the recent divergence between broad market indices and biotech.

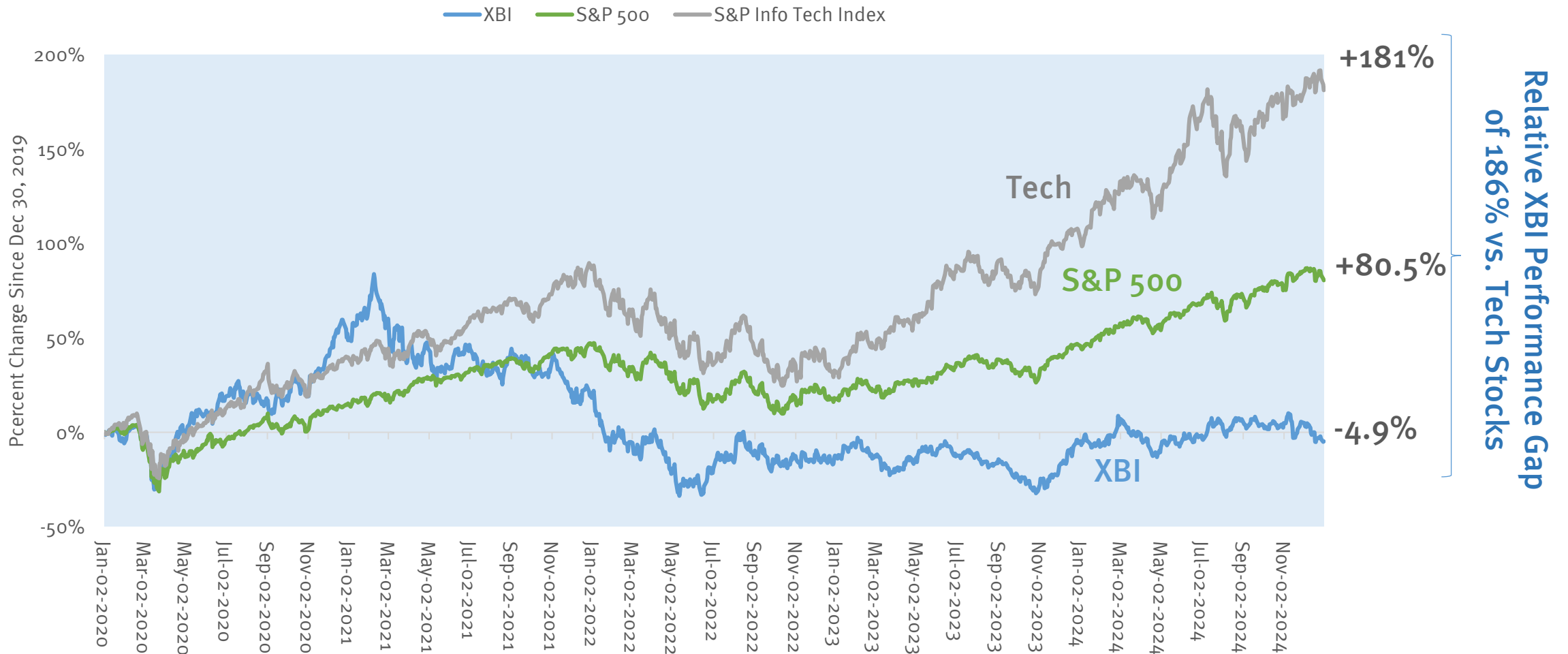
Apparently, day old flat champagne is the same thing as mediocre chardonnay.



# Biotech Has Dramatically Underperformed in Last 5 Years

We began 2023 with a 106% differential between the S&P IT Index and the XBI since the start of 2020. By year end the gap had hit a mind-boggling 186%.

Cumulative Percent Return of the XBI vs. S&P 500 and S&P Info Tech Index, Jan 1, 2020 to Dec 30, 2024





# Preposterous Underperformance

It wasn't just that biotech had a tepid 2024. It's that while the XBI was up for the year, the gap between the performance of the S&P IT index and the XBI widened by 80% percentage points.

This is crazy.

Biotech is an awesome sector. And, while tech is great too, this performance differential seems hard to explain based on any obvious fundamental factors.

We spoke to one highly discouraged hedge fund limited partner on December 30<sup>th</sup> who was recounting negative fund letter after negative fund letter.

He said “maybe biotech just isn't that great of a place to be.” “Maybe we should own up to the fact that most of good performance in biotech was driven by just a few lucky years.” Perhaps, he mused “we need to recognize that the clinical risk in this sector combined with systemic management overspending makes biotech a poor place to invest.”

These are all perfectly human responses to watching one's wallet shrink without explanation.

Before shifting to some more optimistic themes, please indulge us for a moment while we wallow a bit in this mire of negativism.

What actually took place in 2024? What's actually going on in the market?

We don't pretend to have all of the answers, but we would like to share a bit of a story – a narrative if you will – for how the biotech market has underperformed so much in recent years.



# Four Factors Underly the Biotech Market's Relative Underperformance in 2024

1

## REDEMPTIONS

We can confirm that several large hedge fund groups received unwelcome redemptions in 4Q24. These hit in the week following Trump's election and, in that period, when it felt that the market should be headed up based on Fed talk, a great FTC decision (for biotech) and a relatively benign FDA appointment, the market headed down and stayed down. This reflected forced selling of biotech stocks and caused December to be a weak month for the XBI.

2

## M&A MARKET

More than almost any other industry, the biotech sector depends on a steady diet of M&A deals to bolster public stocks. The many stocks that investors thought might get bought in 2024 didn't. There were no public biotech takeouts for more than \$5 billion all year. This was a definite negative because investors didn't get the pops and they also didn't get fresh capital to redeploy in the many new stories that hit the market in 2024.

3

## SCALE & AI

Biotech performance was only half the story behind divergence over the last five years. The other part was the stellar performance of tech. Tech companies have become really large and new ways of organizing companies have helped to overcome traditional diseconomies of scale. Built-in economies associated with AI, lock-in, operating system control and the cloud propelled stellar earnings growth in the tech sector.

4

## CONFIDENCE

In many of our missives in 2024 we argued that the market *should* go up. We don't think our arguments, in retrospect, lacked merit. The issue, rather, involved a confluence of relatively low investor confidence in the market coupled with the notable absence of entry into the market by generalist investors. Economists like to refer to "multiple equilibria" in markets. We got stuck in the bad equilibrium in 2024.



# On the Scale Point

We spent the weekend before Christmas visiting a friend who works for Amazon in Seattle. She took us around many of Amazon's facilities in the downtown and we started to learn a little bit about how large their cloud business is and how it works. Amazon is doing more than \$100 billion in revenue in its cloud business and enjoys outstanding profit margins by allowing anyone to access computing and data storage over the net virtually. This business has been growing in the 10 to 20% range and, based on what we heard, could see its growth *accelerate* in the years ahead. The underlying story is that this business is massively scalable and much harder to imitate than you might think. For example, we learned that competitors have a very hard time competing on cost because Amazon uses chips from a fab that it owns (called Annapurna Labs) that are optimized for cloud computing infrastructure. Amazon is massively more efficient in the cloud.

More broadly, we are seeing very high growth rates from the large tech players fueled by business models that involve customer lock-in, powerful network effects and direct relationships with consumers. We have argued elsewhere that pharma needs to wise up to the possibilities available in healthcare but there is no sign anywhere (that we can see at least) that this is happening.

Traditional ideas about economies of scale were outlined by Alfred Marshall in the 1890s who noted that at some point the inefficiencies of business scale tend to swamp the higher productivity gains associated with larger plants. Oliver Williamson later argued that larger organizations are less efficient because managers have inherently limited span of control and can't manage too many people. Others like Alfred Chandler argued that hierarchical management structures instituted in the 1920s at organizations like GM were instrumental in redefining the limits to scale despite the Williamson point.

What we learned on our trip to Amazon is that the leverage per employee can be massive and that software and AI can fundamentally redefine the span of control in a modern enterprise. That is, in tech, you don't need some insane, GM-like organizational spider web to manage a large business. It's not clear to us that the limits to scale in a technology-enabled enterprise have been remotely reached. We left our trip thinking (1) the boom in tech stocks is far from done and (2) the healthcare industry needs to figure this out before the tech industry figures out healthcare. AI is very much something to keep an eye on.

## Further Reading and Sources

Marshall, Alfred (1890). *Principles of Economics*; Chandler, Alfred D. Jr. (1993). *The Visible Hand: The Management Revolution in American Business*; Oliver Williamson (1992), *The Theory of the Firm as Governance Structure: From Choice to Contract*. Alfred Sloan Jr., (1964). *My Years at General Motors* (<https://www.macsmotorcitygarage.com/bookshelf-my-years-with-general-motors-by-alfred-p-sloan-jr/>). Tim Laseter (2003). The Big, the Bad, and the Beautiful (<https://www.strategy-business.com/article/03402>), Geoffrey West (2017). *Scale: The Universal Laws of Life, Growth and Death in Organisms, Cities and Companies*.



# On Investor Confidence

An equally academic discussion can be had about investor confidence and financial markets. Grizzled Wall Street veterans will be the first to tell you that markets can be vastly inefficient. Mike Milken was featured in an article in *Forbes* in the 1990s alongside Merton Miller, eventual Nobel-Prize winner and University of Chicago Professor (aka the “High Priest of Market Efficiency”). Milken argued that it can be perfectly rational for participants in the market to reach the wrong conclusion about what security prices should be.\* Of course, Miller disagreed on this point.

Our own experience tends to back up Milken’s observations. In the long run, for example, the cash flows from a biotech or its M&A price will determine its value. But in the short and medium run, investor fashion and sentiment can cause its share price to stray far from the type of rational probabilized NPV that Miller might want to see.

These ideas have been further legitimized in the last forty years by economists such as Cass Sunstein, Mike Woodford and Roger Farmer who note that it is perfectly possible to have multiple equilibria in an economic model of perfect competition. This applies both to markets for goods and markets for securities.\*\* What is interesting is that the market can end up in the “wrong place” for an extended period as a function of investor sentiment. One remarkable fact about the biotech market is that it involves both high information processing costs (don’t try to figure out degraders if you don’t have a Ph.D.) and high amounts of information asymmetry. This plays very much into the hands of so-called specialist investors. Such markets are particularly subject to pricing inefficiency.\*\*\*

Our own gut instinct is that we saw ever stronger specialist investors in 2024, who played a strong hand in the market – participating, for example, in an advantaged way in the PIPE market.

\* See <https://www.mikemilken.com/fincareer.taf?page=securities>.

\*\* See, for example: [https://en.wikipedia.org/wiki/Sunspots\\_\(economics\)](https://en.wikipedia.org/wiki/Sunspots_(economics)), <https://www.aeaweb.org/articles?id=10.1257/aer.20210972>.

\*\*\* See Jess Benhabib’s paper on this topic: <https://www.sciencedirect.com/science/article/abs/pii/S002205311400180X>.

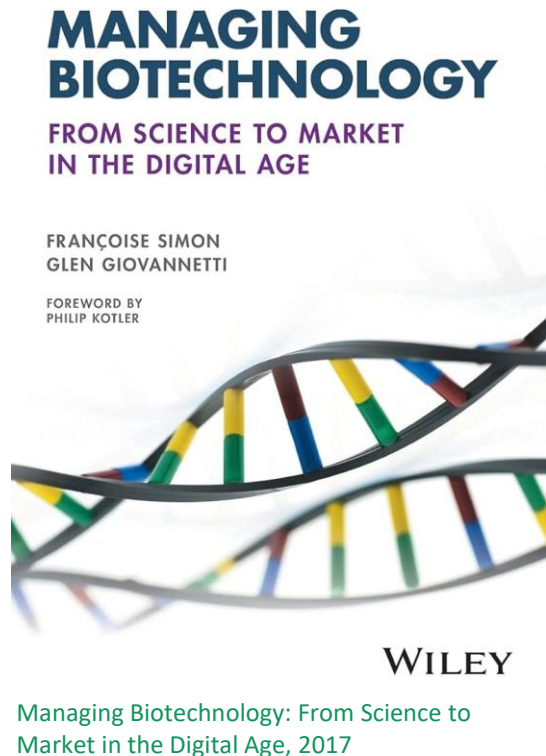


**Mike Milken engaging with Merton Miller in 1989.**

While individually rational for each fund, our fear is that generalists and retail investors have increasingly realized that biotech is a tough game for them to participate in given the rise of specialists. Getting left out of sweet PIPE deals doesn’t help. In contrast, investing in tech stories like Amazon is easier for the generalist to understand. There’s nothing subtle going on. While we don’t think this confidence narrative fully explains the vast gulf in biotech versus tech performance, we do believe that part of the issue in biotech is the increasing relative influence of specialists (and index funds) has made it a tougher place for the uninitiated to invest.



# Restating the Obvious: Biotech is not an Easy Place to Invest



**Many risks: scientific risk, regulatory risk, financing risk, payor risk and risk of irrelevance**

The primary way that biotechnology companies create long-term value for society and their investors is through the development of innovative products that address significant unmet medical needs. This is an inherently high-risk, high-reward activity. The simple fact is that most drug development efforts do not result in a product approval [1]. Founders and funders must contend with a number of different types of uncertainty, including scientific risk, regulatory risk, financial risk, and, increasingly, payer risk. As a result, a core competency entrepreneurs must develop is the ability to market the company's story to investors, including addressing how inherent risks will be mitigated. Among these risks is how the product or technology under development will result in improved outcomes (and therefore differentiated value) for patients and increasingly value-conscious payers, even if that result is a decade or more away. As Ed Mathers, a partner at NEA Ventures, notes

“We still ask ‘will it work?’, but now we also ask ‘will it matter?’. If a new product or platform doesn't matter to payers and pharma companies, then we are unlikely to invest in it. Nowadays, the product must not only work clinically and provide some measurable benefit relative to the standard of care, it must also offer economic advantages in terms of impacting the overall cost of therapy” [2].

## The Long Game

**Decade long cycle times plus extreme high costs**

Despite significant advances in scientific understanding and advanced clinical development strategies that leverage the latest digital and other enabling technologies, drug development, on average, still requires a decade or more and significant amounts of capital—all before the first dollar of profit is realized [3]. Indeed, including the expenditures associated with failed drugs and the cost of capital, in November 2014, the Tufts Center for the Study of Drug Development estimated that it costs \$2.6 billion to successfully develop a drug [4]. Even if one counts only the costs of successfully bringing a specific drug to market, as companies tackle increasingly complex diseases and development times lengthen, it is not uncommon for companies to require more than \$500 million (and at times, substantially more) prior to launching a first product.

**Rapid change in environment and underlying technology**

Katrine Bosley, CEO of gene editing pioneer Editas Medicine, notes, “Even if the CEO thinks two or three steps ahead, the reality he or she responds to will be different from the plan. By thinking through multiple scenarios over several years, the CEO has a better grasp of how much capital will be required to reach the next value-creating milestone” [6].

# Biotech Stock Prices Can Stray Far From Fundamentals

## 1 Extreme Variations in Volatility

Thakor et.al. (2017) Looked at all U.S. traded biotech and pharma from 1930 to 2015. They found that biotech share returns volatility (standard deviation of returns) is around 25% but in two periods it jumped to over 40% and went over 60% during the crash of 2001.

Thakor RT, Anaya N, Zhang Y, Vilanilam C, Siah KW, Wong CH, Lo AW. Just how good an investment is the biopharmaceutical sector? *Nat Biotechnol.* 2017 Dec;35(12):1149-1157.

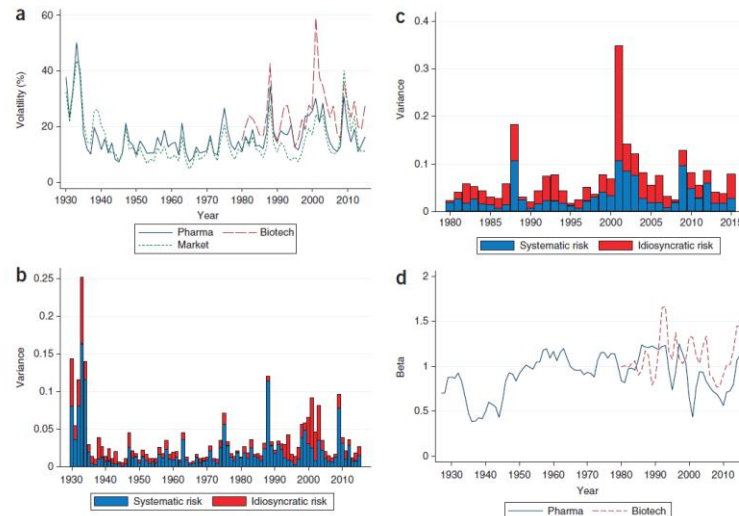


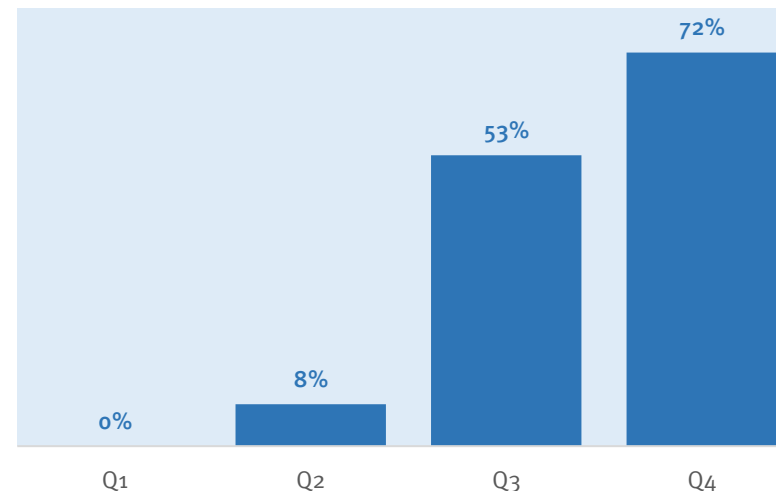
Figure 3 Risk in the biopharmaceutical sector. (a) Annualized total stock return volatility over time of the pharmaceutical (blue), biotech (red), and market (green) portfolios. Volatilities are calculated by taking the s.d. of the daily returns of each portfolio for each year, and are annualized. (b) The total variance of the pharma value-weighted portfolios, decomposed into systematic and idiosyncratic risk. (c) The total variance of the biotech value-weighted portfolio decomposed into systematic and idiosyncratic risk. Variances are calculated using daily returns within each year, as well as beta estimates for each portfolio. (d) Capital Asset Pricing Model (CAPM) market beta estimates of the pharma (blue) and biotech (red) portfolios. Betas are calculated by estimating the CAPM each month, using the past two years of daily returns.

## 2 Biotech Market Overreacts to Bad News

Exler and Pradel looked at bad news events in biotech (113 negative trial readouts) and found a highly statistically significant positive return after the initial negative news gets reported. Specifically, in the four quarters following the bad news, the share price of the unlucky biotech companies, on average, rose by 72%.

“Do investors overreact to negative clinical trial results in the biotechnology industry?,” Sara Exler and Claudia Pradel, Stockholm School of Economics, Thesis Report, 2013.

### Average Stock Price Return in the 12 Months Following Publication of Negative Clinical Results (Cumulative Percentage Return)



## 3 High Uncertainty Feeds Capricious Market Pricing

**Bixia Xu, Information Uncertainty, Capricious Behavior, and Share Price Volatility: Evidence from the Biotech Industry (June 14, 2006), Social Science Research Network**

“Capricious market behavior is theoretically documented in the literature as a competing description of investors' behavior in terms of response to new information. Empirical evidence on the existence of this behavioral bias is rather limited. Moreover, causes of this behavior and its effect on market variables are largely unexplored. In the setting of the biotech industry which is characterized by high share price volatility, I find information uncertainty causes capricious market expectation revisions, which results in high share price volatility.

...the cross-section research on information uncertainty documents a time series consistent market (under)reaction to uncertain information (Liang 2003, Zhang 2006, Francis et al. 2005). This study provides evidence that information uncertainty in the biotech setting actually causes capricious market behaviour (i.e., a time-series inconsistent reaction).”



# Unwillingness to Bargain Shop

One of the most remarkable aspects of investor conversations in the first week of 2025 has been the lack of interest in bargain conversations.

It's not unusual after a few bad weeks in the market for investors to indicate the beaten down stock that they favor the most for acquisition.

As highlighted in a "Heard on the Street" column by David Wainer in the *Wall Street Journal* on Jan 6, 2025 there is no [shortage of bargains](#) in healthcare at the moment.

Uncertainty about the direction of the overall market is high after two great years in the S&P 500 and with the Trump Administration coming in, there is a desire to see what this all means for healthcare.

The first week of 2025 has turned out to be quite a tough one and, as a result, a number of planned IPOs were moved back to February or postponed indefinitely.

Similarly, we didn't see substantial buying in beaten down shares. We think the basic confidence issue associated with potential fund redemptions and forced selling needs to be worked through.

This will happen. But only in time. And then we do expect to see serious buying resume.





# Brighter Days Lay Ahead

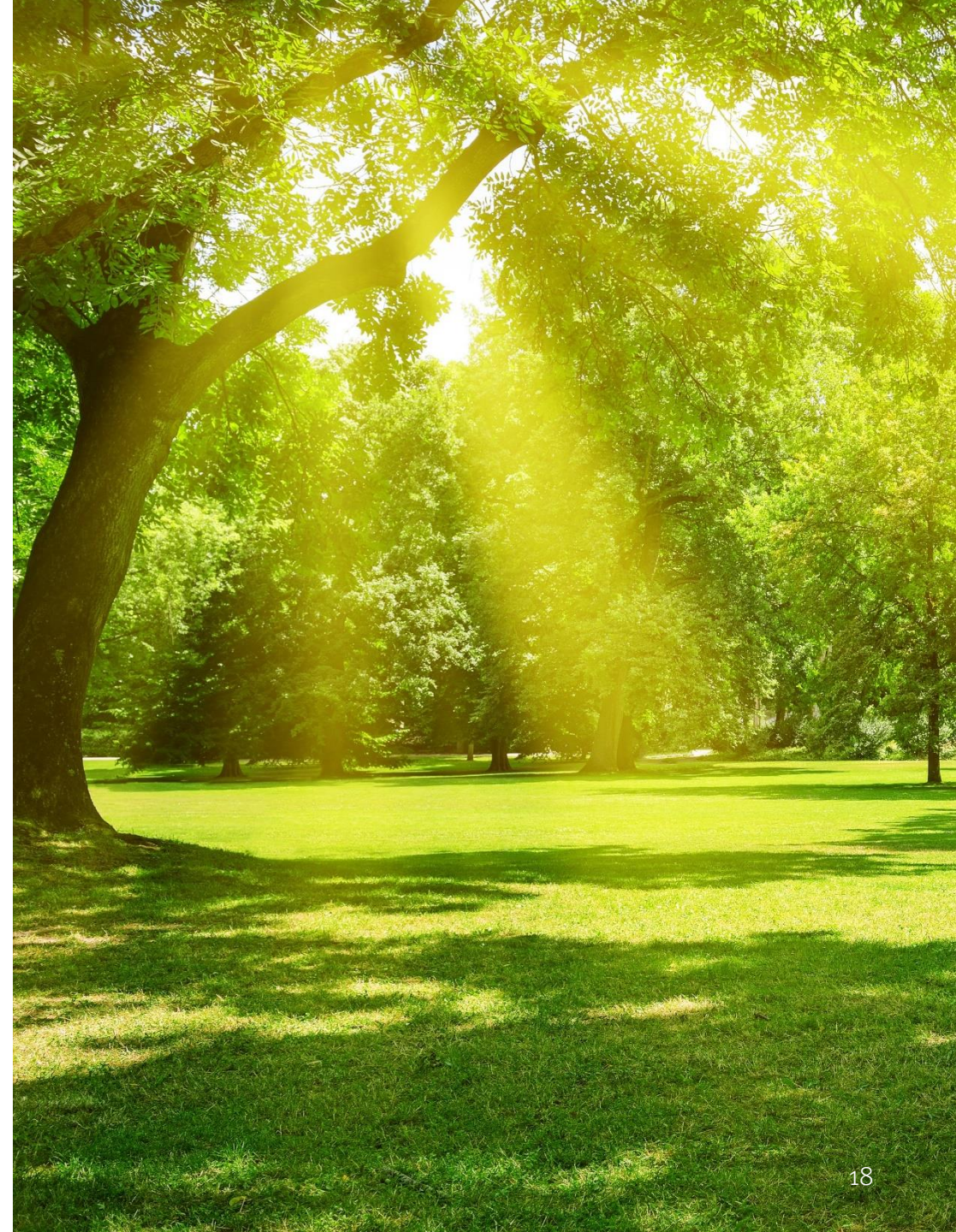
We probably “protest too much” here, taking up so much of your valuable time to explain that we haven’t really lost our mind - one can explain last year’s biotech market by looking at the redemptions hitting hedge funds and evidence on how stock markets can behave in the face of high uncertainty and informational asymmetry.

Basically, we think that the biotech market is a good place to invest but that one has to be able to ride out periods when market participants miss how positive the fundamentals really are.

It is hard to justify the poor performance of the XBI in 2024 using any story regarding fundamentals. Yes, it’s true that M&A was light. And, inflation has been a problem. Oh, and the tech sector is doing really well. But there has been so much positive in biotech to talk about:

1. Inflation has come down massively
2. Numerous positive market developments (see next page)
3. Strong underlying scientific progress (see page two hence)
4. We have an administration in the U.S. that, while unpredictable., is likely to be far more friendly to biopharma on pricing and antitrust than the last
5. Underlying R&D productivity is improving
6. Tax cuts are on the way, and they will fundamentally positive for biotech
7. Long-term trends support the growth of the sector

History tells us that brighter days lay ahead for biotech. To reiterate a point we have made in the past: the value of biotech stocks is up *twenty times* over the last thirty years. That’s no anomaly. That’s an indicator of a great place to put capital.

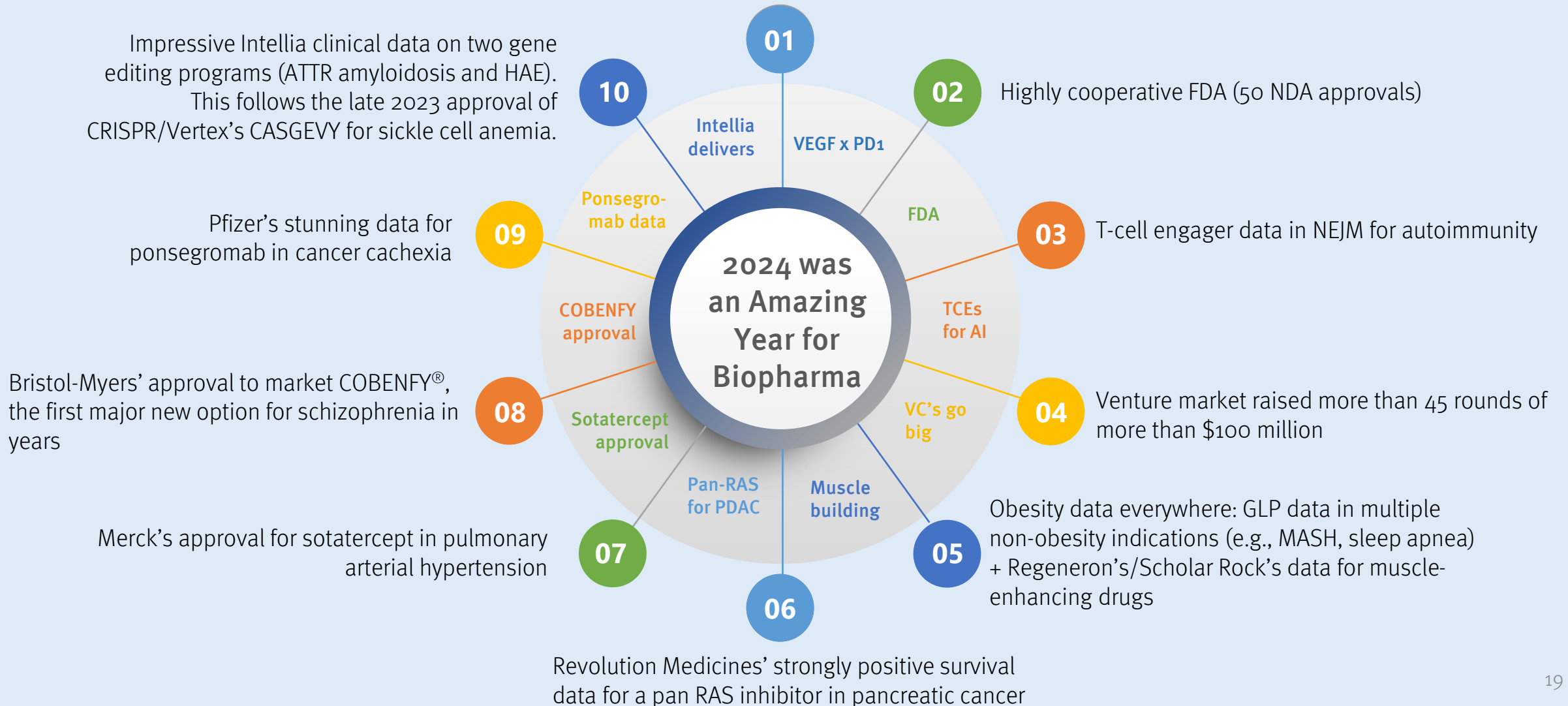




# Ten Major Positive Biopharma Market Developments in 2024

This chart highlights the “wheel of good fortune” that has hit biotech in the last year. We can’t think of a recent year that developed more impressive scientific breakthroughs for patients.

Summit’s pathbreaking HARMONi-2 data on VEGF/PD1 bi-specifics in Lung Cancer



# Bioscience Delivers in 2024

Progress in basic science and understanding of biology was stunning last year and reflects the inexorable accumulation of knowledge associated with improved life sciences tools like single cell sequencing and deeper analysis of the genome, proteome and transcriptome. Here's our list of the top ten most impressive advancements in bioscience in 2024:

## 1 Gilead's Lencepavir Trial in HIV Prevention

Gilead reported [data](#) on June 20, 2024 that its HIV-1 capsid inhibitor, lenacapavir, demonstrated 100% efficacy for the investigational use of HIV prevention in women. What's so impressive is that this is a twice a year treatment for treating HIV.

## 2 Lichtman Lab Maps a cubic mm of the Brain

Working with Google, Jeff Lichtman and colleagues at Harvard [mapped](#) a cubic millimeter of the brain in spectacular detail. The mapping found that the brain has far more connections than realized. Further, a number of new brain features were found.

## 3 Princeton Team Maps the Fruit Fly Brain

Neuroscientists have created the most complete brain [map](#) of a single fruit fly marking a major milestone in neuroscience. The map, developed over four years by the FlyWire consortium includes nearly 140,000 neurons and 54.5 million synapses.

## 4 Better ALK Inhibitors

The team at Nuvalent last year showed strong [results](#) from NVL-655, a novel brain-penetrant ALK inhibitor. This molecule is a tour-de-force of chemistry. Also impressive was the approval of Xcovery's ensartinib for ALK-Positive NSCLC.

## 5 Alnylam's Helios-B Data

The [HELIOS-B](#) study evaluated vutrisiran in patients with TTR amyloidosis with cardiomyopathy. The drug led to a 28% reduction in the composite endpoint of all-cause mortality and recurrent CV events compared to placebo. Wow!

## 6 Brain-Computer Interface Work Progresses

Elon Musk's [Neuralink](#) reported excellent progress in 2024 for its brain-computer interface (BCI). Neuralink went well beyond previous BCI demos to show that its technology could be broadly useful for a person with limited mobility. This space is growing rapidly.

## 7 Obesity Memory

A [paper](#) from ETH Zurich showed that adipocytes retain epigenetic "memory" of obesity after weight loss. Mice carrying obesogenic memory show accelerated rebound weight gain. Transcriptional deregulation occurs in response to high-fat diet feeding.

## 8 Explanation of Female Autoimmunity Found

Four in five persons with autoimmunity are female. Howard Chang of Stanford (now Amgen) showed that this was not due to hormone differences but rather [ribonucleoproteins](#) in place to prevent transcription from a second X chromosome. Wow!

## 9 Lp(a) Matters

An impressive [study](#) by Paul Ridker of the Brigham (and collaborators) looked at 30-years of cardiovascular outcomes in women and found that baseline Lp(a) was just as important as LDL cholesterol and CRP in predicting incident cardiovascular events.

## 10 Massively Parallel Gene Editing in Agriculture

Last year was a really big year for companies like [Cibus](#) and [Inari](#) which are using gene editing to alter multiple traits in crops. Unlike us mere humans, it's possible to dramatically improve crop yields, drop nitrogen use and reduce water use with clever edits.

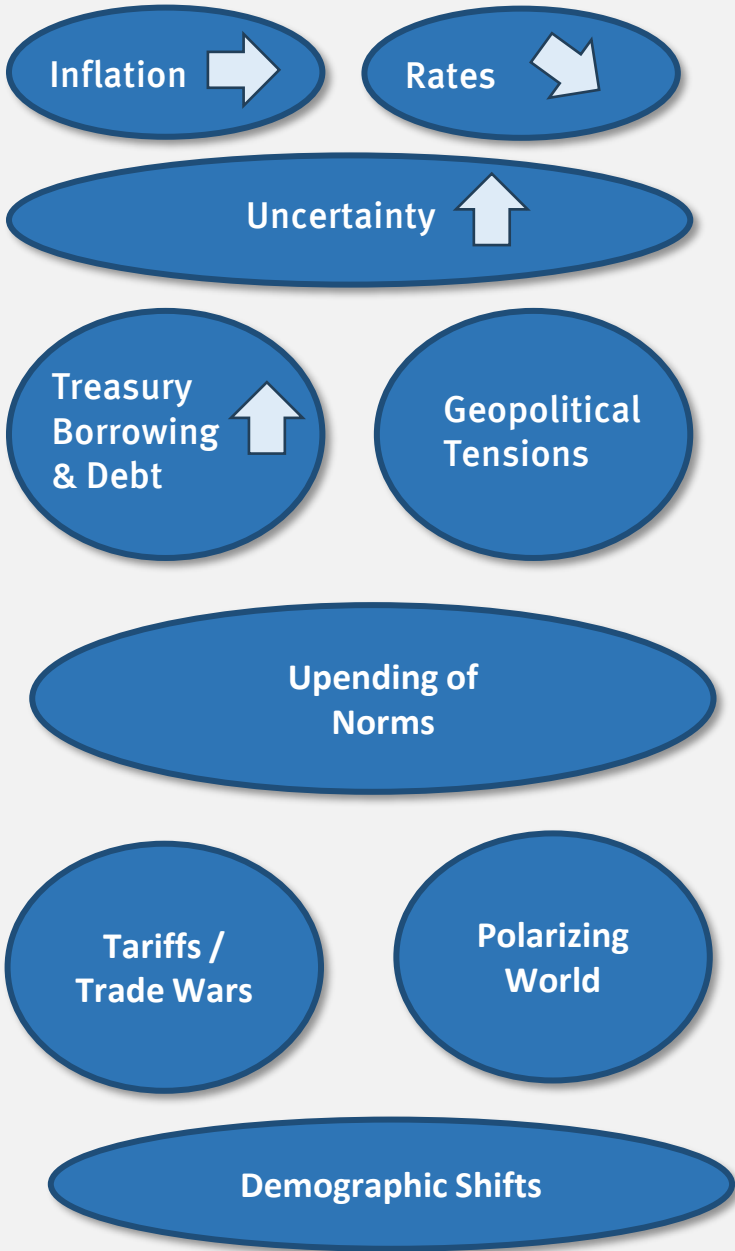


# 2. Predictions for 2025



Stifel's 2025 Predictions: Summary

Macro / Geopolitical

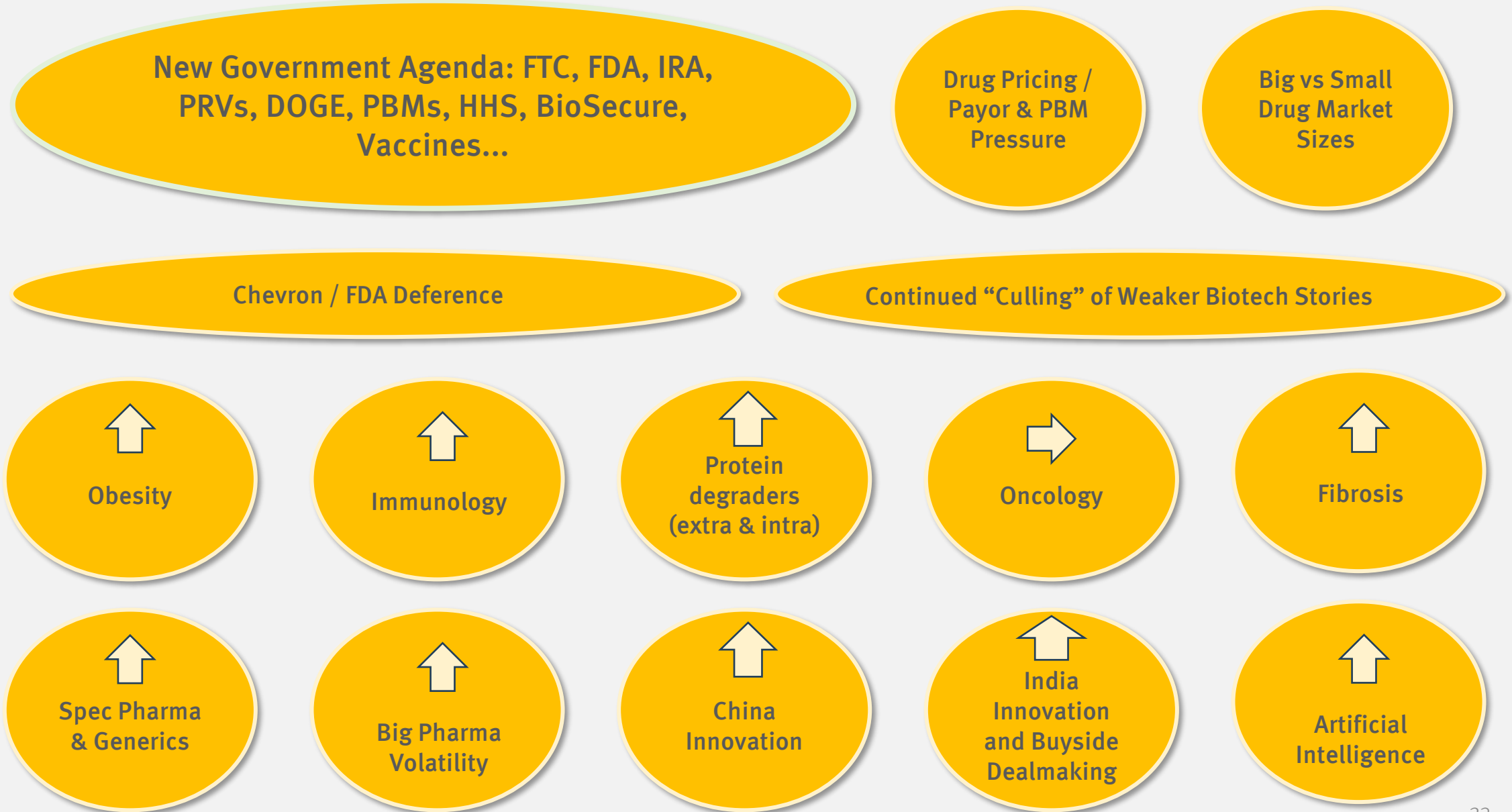


Capital Markets and M&A





## Market Themes



# Our Views on the Macro and Political Outlook in 2025

1. The #1 and #2 concerns in biotech going into 2024 were macro and geopolitical risk.
2. Coming into 2025 the risk of inflation appears to be less and key geopolitical hot spots appear much more manageable.
3. There is a school of thought that Trump Administration policies (e.g., tariffs and deportations) will be inflationary. We're not so worried here because Trump and his advisors understand that re-igniting inflation would be political suicide. If there's one thing they want to do, it is to create economic growth and bring interest rates down.
4. We see Trump Administration policies as fundamentally good for biotech. Lower taxes and pro-innovation policies should prove to be a big positive for the sector. We'll see bombast here and there, but we think the Trump bark is likely to be far worse than its bite (as it pertains to the biotech and pharma sectors). This said, there is high uncertainty associated with new faces in unexpected places (e.g. RFK in HHS, Oz in CMS etc.).
5. Numerous buysiders cite "high uncertainty" in the current environment as a big negative. Looking back at the weak market in December, we blamed RFK/Oz for risk and uncertainty but now know that a toxic combination of fund performance-triggered redemptions and negative catalysts were the real cause of poor biotech market performance.
6. We do think that the IRA gets redesigned in the Trump Administration as it's fundamentally a Democratic construct. We see Trump preferring jawboning as a mechanism to control pharma prices rather than direct negotiations against drugmakers.
7. The focus of groups like "No Patient Left Behind" on fighting against cost-effectiveness analysis (CEA) requirements built into the IRA will remain well-founded as both governmental and private groups like ICER are going to continue to try to use CEA as a blunt weapon against the pharmaceutical industry.
8. The real question is how quickly and how well will biotech investors and external generalists regain confidence in the market. We think success will beget success in this market but it's going to take time for this to all play out.



# Our Views on the Public Biopharma Capital Markets in 2025

1. We saw substantial volume of follow-ons and some IPOs in 2024.
2. We saw the XBI rise for 2024 but not as much as one would have liked.
3. A consistent feature of the market was a high quality premium (investors stuck to later stage and derisked stories that were seen as better M&A bets). If anything, this premium *went up* throughout the year.
4. For 2025 we foresee:
  - a) Another positive year for biotech with the XBI up *materially* this year versus last.
  - b) A gradual decline in the quality premium and greater willingness of investors to take risk on emerging stories.
  - c) This will all be fueled by tax cuts in Washington – which get signed by President Trump by mid-year. These energize the market very much as they did in the Reagan Administration in 1980.
5. Biotech investors stay focused on stock picking and funding the best stories. Preference for great science, mid/late stage biopharma and commercial growth opportunities. No general euphoria sweeps the market.
6. A continued *very strong* follow-on market for quality names:
  - a) As the quality premium comes down there will be more access for companies that don't have positive data catalysts.
  - b) But the market remains highly bifurcated with much less access to fresh capital afforded to companies with market caps under \$250 million. This doesn't change for some time to come.
7. Turbulence and volatility remain in market:
  - a) Some hedge funds continue with drawdowns while others attract fresh capital.
  - b) Quant funds continue to create market volatility and bizarre situations where good news events are followed by share price declines.

# More Capital Markets Predictions in 2025 (continued)

8. Continued strong performance of cash flowing, revenue positive companies in areas like generics, biosimilars and specialty pharma. In an early recovering market, we expect that commercial stage companies will perform the best in 2025.
9. An improvement in M&A volume:
  - a) A relaxed FTC will help
  - b) Some big LOE gaps remain ahead that will motivate external pick ups of pipeline.
10. There are some brakes on the M&A market that will very likely keep volume to an “average” level rather than a blowout level.
  - a) Pharma isn’t going to be hitting the big red “M&A deal” button so quickly as it will still risk antagonizing government authorities which have substantial discretion in pricing conversation.
  - b) The availability of good mid-stage drug candidates from China at prices far below those in the U.S. biotech market pushes pharma to license certain technologies rather than to buy them in the biotech market (more on this later).
  - c) The very best biotech names are expensive due to the aforementioned quality premium – pharma may choose to wait it out
  - d) Big pharma balance sheets that are not as strong as they were in previous years.
11. Companies with strong balance sheets that are less vulnerable to adverse pricing discussions (think players like Genmab or Incyte) will continue to be more likely to resort to the M&A market.
12. Substantial increase in IPO activity:
  - a) Mid to late-stage therapeutics are favored. We don’t see a return to preclin IPOs as we had in 2021.
  - b) We continue to expect to see strong obesity stories like Kailera and Metsera will do well in IPOs in 2025.
  - c) We think that there will be some big “story type IPO’s” in emerging fields like brain-computer interface (think Neuralink) and AI/medicine (think a Verily or Ada Health).

# More Capital Markets Predictions in 2025 (continued)

13. PIPE market picks up in 2025:
  - a) While strong in Q1 2024 the market cooled down as 2024 rolled on.
  - b) We see the PIPE market picking up substantially in H1 2025.
  - c) The ability to give specialist funds real time to analyze a deal before committing is an enduring positive of the PIPE market
  - d) Incursion of tech VC's into healthcare accelerates – particularly at the margins (e.g., AI in drug discovery).
14. Healthcare specialists continue to rule the public markets:
  - a) Ever fewer generalist public investors participate in biotech (think of groups like Royce Funds).
  - b) More and more funds with access to Ph.D.'s and MD's (ideally on staff) experience high growth in the market.
  - c) We will also see relative growth from groups like Deerfield, Orbimed, Perceptive and RA that invest across multiple asset classes in the life sciences (e.g., venture, public and credit).
  - d) We will see more groups like Bain, Fairmount and RA sponsors public newcos into the markets as was commonplace in 2024.
  - e) We will see relative growth of specialist groups despite some poor performance in Q4 of '24.
  - f) The ability of specialist groups to move/influence/drive small/midcaps is going to grow.
  - g) Generalists will eventually return to the market – along with retail – but this will be more of a 2026/2027 phenomenon than a 2025 thing.
  - h) Funds with good access to top family offices and MidEast money will grow disproportionately in 2025 (e.g., Patient Square).



# More Capital Markets Predictions in 2024 (continued)

15. Venture capital funds thrive in '25:
  - a) We see volume as being up in 2025 but it will not surpass the record seen in 2021
  - b) The trend towards larger round size will remain in 2025 as firms find that more scaled up companies and stories do better overall
  - c) Funds that tend to sponsor their own companies as opposed to invest in those of others do particularly well (think groups like Atlas, Column Group and Versant)
  - d) These groups use cap table control to engineer better returns and use better returns to be able to afford great teams that keep the circle of virtue turning
  - e) Healthtech efforts of groups like Andreessen Horowitz/GC etc continue to grow
  - f) Incursion of tech VC's into healthcare accelerates – particularly in areas like AI in healthcare delivery and brain-computer interface
16. Private equity comes roaring back and is a lot more sophisticated than before
  - a) More and more PE platforms understand the life sciences sector well
  - b) Despite a paucity of exits the disorder in public markets early in an upcycle plays well to PE firms
  - c) Credit markets quite healthy right now – which feeds the upcoming PE wave
  - d) Today's market very similar to that in the early '80s (Reagan era) when PE took off

# Key Biopharma Market Predictions for 2025

1. Continued shift towards big drugs for big diseases - this trend is just getting started:
  - a) This theme evolves a bit – more to what we call “cures over treatments” for “diseases that matter” – the emphasis is on transformational treatment for reasonably large groups of patients in real need.
  - b) Examples of drugs that should be “really good” for “big diseases” include TCE’s for autoimmunity and VEGFxPD1 bispecifics for lung cancer.
  - c) Oncology has been waning in recent years and comes back in 2025 but not in the same way as before. Less focus on mutations and more focus on larger indications.
  - d) Cancer ultimately becomes one of the very biggest areas in pharma but only when we get good pan-cancer drugs. This is in the cards for the next five years but not necessarily in 2025.
2. Cardio gets even hotter with particular interest in highest unmet needs such as heart failure, hypertension, rhythm disorders, atherosclerosis and PAD.
3. Asthma/COPD/IPF get a lot bigger.
4. Fibrosis does well in 2025 thanks to big progress at companies like Agomab, Alentis and Boehringer.
5. I&I focus starts to differentiate more. The relevance of B-cell and innate pathways gets ever higher:
  - a) Immune cell engagers (e.g., doubles and triples) do really well.
  - b) We see some comeback for CAR-t in autoimmune.
  - c) We see really strong results from some extracellular IgG degraders in autoimmune (think Biohaven / Lycia etc).

# Biopharma Market Predictions for 2025 (continued)

6. Neuroscience continues to deliver breakthroughs with its usual share of heartbreaks, particularly in areas like psych (e.g., orexins), PD (e.g., Bluerock), degeneration (e.g., Monument) and epilepsy (e.g., Neurona)
7. Degraders have a really big year in 2025
  - a) This is the year where we see results from the likes of Arvinas, C4, Kymera, Monte Rose, Nurix
  - b) Technical evolution in this area with novel types of molecular glues continues to shine
8. Other areas of high innovation remain important
  - a) RNA therapies dazzle
9. More consolidation on payor/provider side which continues to put pressure on pharma:
  - a) Pressure on pharma from United/CVS/Humana (step edits/rebates/pricing drops) gets worse than before
  - b) PBM reform does not happen but pressure from new entrants continues to catalyze sector change
  - c) Reforms that cap total drug spend prove to be rocket fuel for pharma sector
  - d) Generics and biosimilars industry continues its comeback.
10. RFK Jr. focus on foods and basic health fails to resonate
  - a) The masses keep eating Wendy's and fried chicken despite exhortations about food supply
  - b) No real support for change in nutrition exists
  - c) National debate on improving access to GLP-1's ultimately accelerates



# Biopharma Market Predictions for 2025 (continued)

11. Pharma strategy continues to evolve in the face of disruption from upstarts like Regeneron and Vertex
  - a) More interest in involvement with health systems / population health
  - b) More waking up to the China innovation opportunity
  - c) More interest in top-down strategy formation
12. Money flows heavily into spec pharma in 2025 due to abundance of bargains
13. Tech enabled healthcare services sector continues to grow rapidly
14. AI effect on health systems starts to become real
  - a) Agents start to really move the needle
  - b) Unexpected applications shine (e.g., using the computer to negotiate endless insurance company paperwork)
  - c) Use of AI for the underserved becomes a thing
15. ADC's continue to excel:
  - a) Not quite as much attention as those immune cell engagers
  - b) Hybrid platforms become ever interesting. For example, we are watching Sutro's immune + ADC engager platform with interest
  - c) We are watching pan-tumor targets like CTLA4 and Epcam with interest for data in 2025 (e.g., CytomX/BioAtla)

# Biopharma Market Predictions for 2025 (continued)

16. China importance to our ecosystem gets bigger as the wave of biopharma innovation continues there
  - a) We start to see China IPOs of quality biotechs (e.g., BeiGene) hit U.S. shores
  - b) At the same time the tensions between the U.S. and China gradually improve with greater collaboration in the biotech sectors
  - c) Recent moves by groups in Congress and our own BIO organization to distance the U.S. from the Chinese life sciences ecosystem (e.g., BioSecure Act) lose momentum as its recognized that such measures are unlikely to have much positive effect on national security
17. “America first” theme matters ever more in CDMO space
  - a) Recent sale of Wuxi CGT business highlights trend
  - b) More interest from PE’s in domestically located biologics facilities
  - c) Strategic acquisitions of domestic capacity grow throughout 2025
18. Obesity drugs become even more embedded in American society in 2025:
  - a) If there is one change we’ve noted in our personal lives it is how many friends and family members benefitted from GLP-1s
  - b) We see the obesity getting even bigger in 2025 than we think it can as more and more data comes out
  - c) While there have been some notable setbacks in recent months with drugs like MariTide and Cagrisema, we are going to see fresh data out in 2025 on numerous novel MOA’s in obesity and the odds are that the market evolves positively
  - d) Muscle becomes an ever bigger theme in the obesity landscape (e.g., Scholar Rock, iBio)
  - e) The consumer becomes an ever bigger theme in the obesity landscape (highlighted by names like Gan&Lee / Metsera)

# Big Hopes for M&A at the JPM Conference

Annalee Armstrong, *Biospace*, “Biopharma Heads to JP Morgan Seeking an M&A Spark to Improve Sentiment,” Jan 6, 2024

**M&A didn't return as hoped for in 2024. The biopharma industry is heading into the J.P. Morgan Healthcare Conference next week in a grim mood.**

Despite the cautious optimism a year ago, 2024 did not exactly bust the biopharma industry out of the prolonged downturn that followed the pandemic boom. Going into the 2025 J.P. Morgan Healthcare Conference, leaders in the space are a bit more pessimistic.

“Sentiment is really bad in general in biotech,” Seaport Therapeutics CEO Daphne Zohar told BioSpace.

That said, Zohar and others are looking forward to potentially big news that could spark that optimistic attitude once again. The annual gathering in San Francisco is a who's who of biopharma with thousands of executives descending on the Bay Area looking to strike deals. The meeting, which officially begins next Monday, Jan. 13, sets the tone for the year, and for many executives who spoke to BioSpace, a few high-profile transactions could really change the tune. But, Zohar commented, it needs to happen early.

“If we don't see a lot of M&A between now and, like, the Tuesday of J.P. Morgan, I think we'll have kind of negative sentiment,” Zohar said in a late December interview. “I always feel like, by Monday, if you're not seeing a lot, then people begin to assume that there's not much that's going to happen.”

Linda Marbán, CEO of cell and exosome-based therapy biotech Capricor Therapeutics, agreed that the industry will be watching closely. And despite the swirling gloom, some of last year's “cautious optimism” still exists, she wrote in an email to BioSpace.

“While challenges like clinical failures remind us of the complexity of developing transformative therapies, they also reinforce the importance of innovation and persistence,” she said. “I think everyone is eager to see what opportunities JPM will bring.”

Another big headwind over the industry is the presidential transition. Donald Trump will re-take the presidency on January 20, just after the JPM meeting concludes. Zohar and Gebauer both said that the wait for the new administration has suppressed deal activity.

Immunic Therapeutics Chief Operating Officer Jason Tardio said the macroeconomic stars are aligning for a year full of deal activity: the cost of capital has come down and interest rates are declining. On the policy front, the incoming Trump administration and Republican-led Congress are expected to ease corporate taxes, regulatory hurdles and drug pricing provisions like the Inflation Reduction Act.

“2025 could see significant megadeals as companies look to fill their growth gaps ahead of the looming loss of exclusivity in 2028,” Tardio said.

Whether the deals come now or later, Zohar is similarly confident that deal activity will return, fueled by Big Pharma. “They really need to fill their pipeline, so at some point they're going to get pretty aggressive.”



# Recent Bain Survey Shows How Much GLP-1s are Impacting Americans

## How GLP-1 drugs change consumers

### During treatment

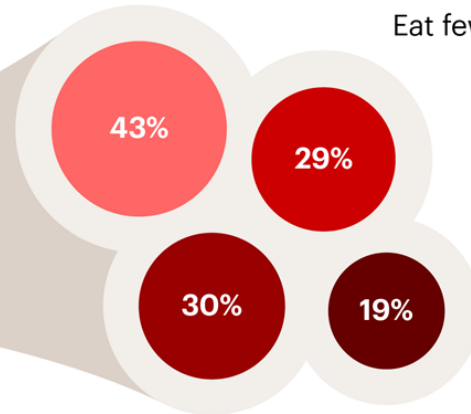
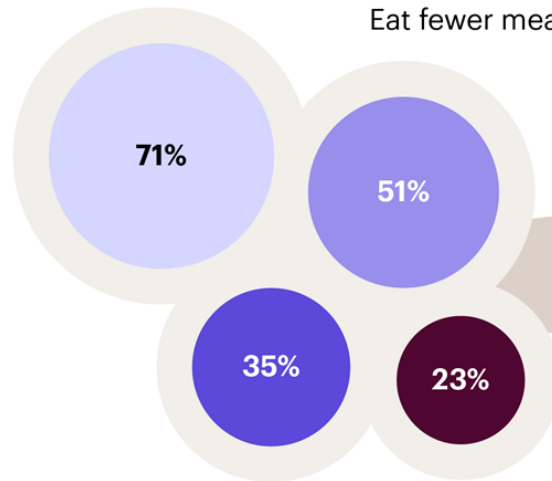
### Once lapsed

Eat less at each meal

Eat fewer meals

Eat less at each meal

Eat fewer meals



Exercise more

Drink less alcohol

Exercise more

Drink less alcohol

Source: Bain & Company GLP-1 Survey, Q4 2024 (n=4,378 including 1,147 current and 218 former GLP-1 users)

Source: <https://www.bain.com/insights/weight-loss-drugs-arent-just-changing-waistlines-snap-chart/>

From Stifel's Mark Dempster and Tim Opler: It's very clear that widespread use of GLP-1's and their clear overall health benefits are affecting people's overall view of wellness.

We know a number of people who are on GLP-1's and the prospect/success of them losing weight and feeling better is leading them to live healthier lives generally (work out more/eat better/etc).

Couple this with the literature on the negative effects of alcohol, the explosion of Non-Alcoholic beer and wine and the Surgeon General's recent proclamation that alcohol is the number 1 cause of avoidable cancer, and it feels like a broader shift is underway in our society which GLP1s are playing a big part of.

We also think the consumer sentiment against the healthcare system generally is a theme that will continue and is something that some politicians can't miss. The recent tragic killing of the United HC CEO started a discussion that highlights societal concerns about the cost of healthcare in America. Interestingly, this shifts the conversation more onto healthcare overall than just pharma pricing *per se*. We see this dialogue continuing in 2025 with less demonization of pharma and a broad examination of healthcare costs.

One of the most striking ironies in this evolving consumer picture is that most insurers like United Health are very reluctant to cover weight loss drugs and the U.S. government doesn't pay for them at all. We see important change taking place in this area in the next several years.

# Summary: What We Think is Going to Work in Public Biotech Markets in 2025

## What Has Worked

We believe that the public market has largely understood and valued the implications of promising therapeutic areas such as:

1. Cardiometabolic disease, especially obesity and heart
2. Immunology
3. Targeted protein degradation
4. Genetically-targeted oncology
5. Effective, rare disease therapeutics
6. Pneumococcal vaccines
7. T-cell engagers and ADCs in oncology
8. RNA therapeutics

## What Is Likely to Work

We believe that the public market has yet to fully value the implications of emerging therapeutics in areas that include:

1. Orally delivered drugs that modulate GPR75, GIP and other novel targets for obesity
2. Novel developments in neuroscience, particularly mutation-targeted therapies, selected cell therapeutics and orexins
3. T-cell engagers in immunology, particularly triples
4. Degraders in immunology and cardiology
5. Muscle targeting drugs, particularly myostatin inhibitors
6. Further developments in Fc gamma receptors and IgG Tx

# What We Think is Going to Work in Biopharma in 2025

In we remain in a declining rate environment, we expect to see particularly good returns associated with **lower risk, medium duration assets** that include:

Private equity plays (have been bottled up for awhile)

Credit plays

Commercial growth equity plays

Specialty pharma / Gx plays (have performed well lately)

The scenario discussed herein where biotech can double or triple will come more in the medium-term as risk-premia shrink



# Private Venture Market Themes for 2025 and Beyond

## Approaching Translational Readiness

Just as obesity shifted into a translationally ready field around five years ago, we expect to see translational readiness hit a number of gigantic areas with strong implications for returns in the decade ahead:

1. Drugs to increase lifespan
2. Bioelectronics
3. Fibrosis
4. Hair regrowth therapies
5. Female-predominant diseases
6. Pan-tumor approaches (e.g., Myc/Elane)
7. Gene editing for agriculture

## Giant IPOs of the Future (ex Pharma)

Other commercial areas where explosive growth (and large IPOs) lay ahead include:

1. Innovative value-based care delivery models that leverage biosciences know-how
2. Applications of 'Omics technologies to areas like healthcare and life insurance
3. AI-enabled consumer-driven comprehensive care, particularly for patients that do not have good access to care
4. AI-enabled hospitals and urgent care ambulatory clinics (e.g., emergency department decision-making)

# Evaluate Pharma Analysts Predict M&A, IPO Uptick in 2025 But Don't Expect 'Floodgates to Suddenly Open'

Nick Paul Taylor, *FierceBiotech*, Jan 3, 2024 (excerpt)

Will 2025 be better? After another tough year, the answer to that question will shape the prospects of innumerable drug candidates and the lives of people who work in biotech. Evaluate analysts made predictions in their 2025 preview—and anyone expecting a dramatic turnaround should look away now.

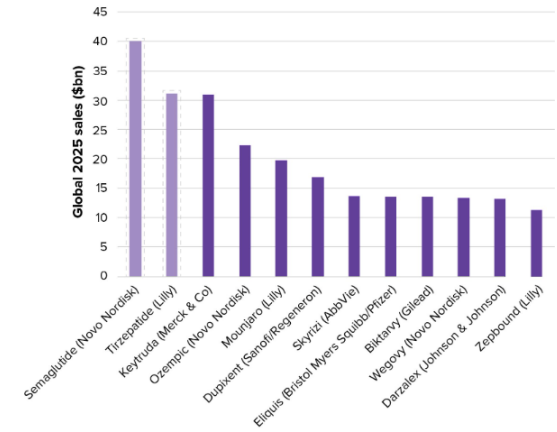
Green shoots were evident in 2024. Evaluate tracked an increase in the number of IPOs and the amount they raised, as well as an uptick in the number of venture capital rounds. Companies that navigated the challenges of the past few years are closing in on approvals, with Cytokinetics' aficamten and Insmed's brensocatib scoring places on the analysts' list of the potential biggest launches of 2025.

Yet, 2024 only looked good compared to the disastrous 2022 and 2023. The number and value of IPOs were well down on the highs of 2020 and 2021, the amount raised in venture rounds continued a slide that began in 2022, and the analysts characterized dealmaking as “subdued.”

Evaluate analysts said the pace of IPO activity is expected to pick up again after pausing around the U.S. election late last year. There is huge pent-up demand “in the private world,” the analysts said, but only the safest bets and companies heavily supported by existing investors are expected to go public in the early months of the year.

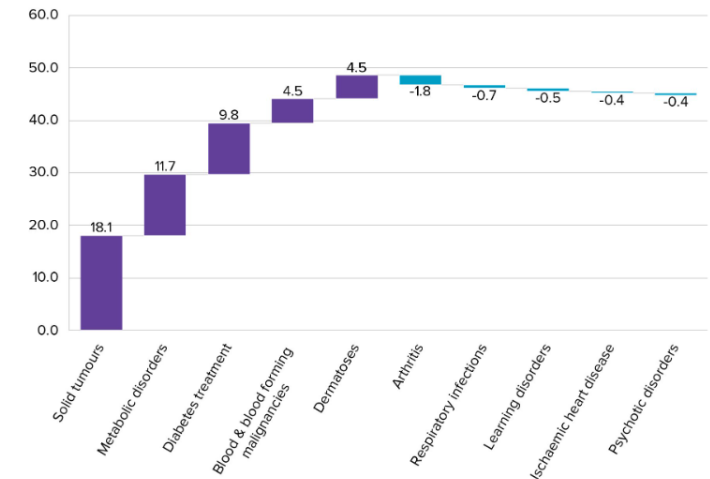
Sources: (1) FierceBiotech writeup <https://www.fiercebiotech.com/biotech/analysts-great-new-year-muted-optimism-after-tough-2024>  
(2) EvaluatePharma Report: <https://www.evaluate.com/thought-leadership/2025-preview/>

Top selling drugs in 2025



Note: Forecasts include sales booked by all global marketing partners, where relevant. Source: Evaluate Pharma consensus forecasts.

Therapy areas: growth drivers and brakes



# Evaluate Report on Drug Launches in 2025

## Biggest potential drug launches of 2025

Product	Companies involved	Description	Status	2030e sales (\$bn)
Vanza Triple	Vertex	Triple combination CFTR modulator for cystic fibrosis	PDUFA January 2, 2025; EU approval Q2'25	8.3
Datopotamab Deruxtecán	Daiichi Sankyo/AstraZeneca	Anti-Trop2 ADC for lung and breast cancers	US and EU decisions due Q1'25	5.9
Suzetrigine	Vertex	Nav1.8 channel blocker for acute and neuropathic pain	PDUFA January 2025	2.9
Aficamten	Cytokinetics	Cardiac myosin inhibitor for hypertrophic cardiomyopathy	US and EU decisions due Q4'25	2.8
Tolebrutinib	Sanofi	BTK inhibitor for multiple sclerosis	Filing planned before YE'24	1.4
Mazdutide	Innovent/Lilly	GLP-1 & glucagon receptor agonist for T2D and obesity	China obesity approval due H1'25; T2D due H2'25	1.3
Depemokimab	GSK	Long-acting anti-IL-5 Mab for severe allergic asthma	Filing planned before YE'24	1.2
MenABCWY	GSK	Meningococcal A, B, C, W-135 & Y vaccine	PDUFA February 14, 2025	1.2
Brensocatib	Insméd	DPP1 inhibitor for neutrophil-mediated diseases	Filing planned by YE'24 (priority review expected)	1.2
Nipocalimab	J&J	FcRn antagonist in broad autoimmune development programme	US and EU decisions due H1'25	1.2

Note: T2D = type 2 diabetes. Source: Evaluate Pharma.

Source: <https://www.evaluate.com/thought-leadership/2025-preview/>

# The Regulatory Environment

Source: <https://www.evaluate.com/thought-leadership/2025-preview/>

Next year holds the potential to see a historically high number of novel approvals, with Evaluate Omnium yielding 71 projects with a good chance of reaching the US market.

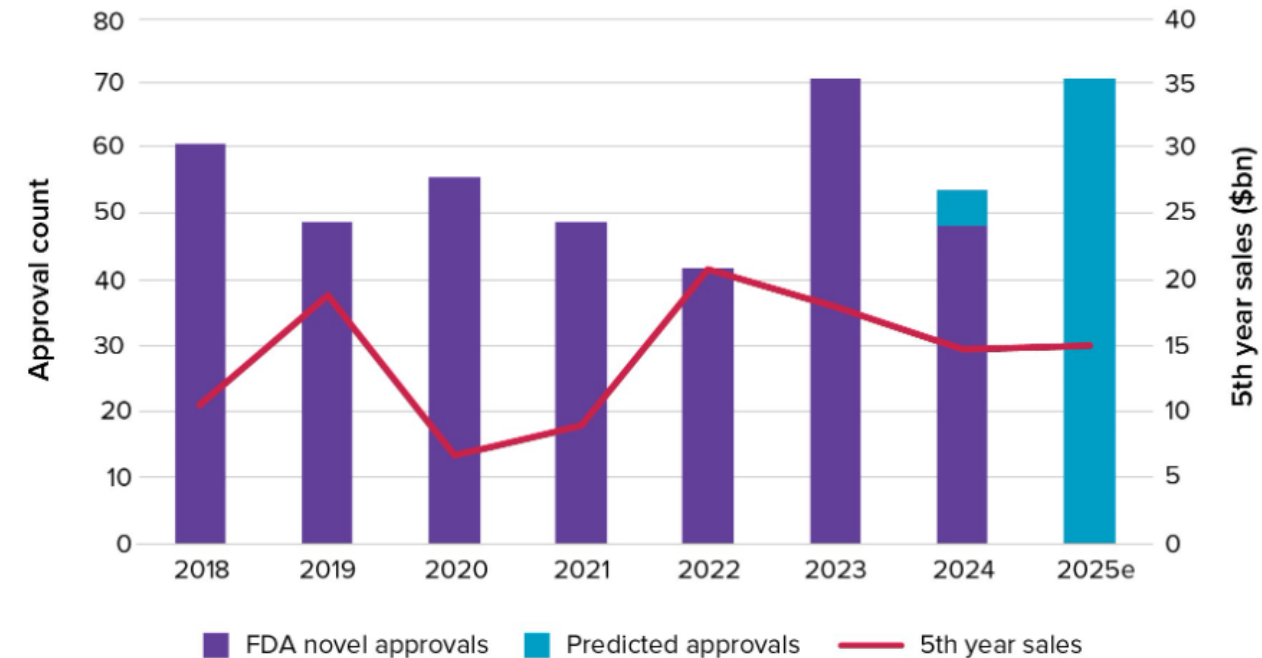
This includes the 10 detailed earlier which are seen as the most commercially promising. This estimate is far from set in stone, of course, with both small and large companies liable to encounter regulatory hick ups. Matching 2023's record 71 novel approvals would be notable, however.

The chart here shows how biopharma and the FDA have filled in the hole that Covid-19 put in sector productivity. The pandemic impact can really be seen in fifth-year sales, with the classes of 2020 and 2021 showing substantially lower market potential than surrounding years, presumably as the sector focused its efforts on combating the virus.

The big unknown for the FDA regulator next year is the identity of its new commissioner, and what agenda they might pursue. Martin Makary, Trump's pick for the job is, like the incoming President's other nominees, a controversial name who has criticised the agency on several issues. Vaccine sceptic Robert F. Kennedy Jr. has been proposed to run the U.S. Department of Health and Human Services, which is technically in control of the FDA.

What the following years might hold for drug regulation – and the biopharma sector more widely – depends a lot on the people that end up with the top jobs in Trump's new administration. It is also

## Tracking US approvals



Note: Count includes novel therapeutics approved by both CDER and CBER. Source: FDA and Evaluate Pharma.



# Big Hopes for M&A at the JPM Conference

Annalee Armstrong, *Biospace*, “Biopharma Heads to JP Morgan Seeking an M&A Spark to Improve Sentiment,” Jan 6, 2024 (excerpt)

**M&A didn’t return as hoped for in 2024. The biopharma industry is heading into the J.P. Morgan Healthcare Conference next week in a grim mood.**

Despite the cautious optimism a year ago, 2024 did not exactly bust the biopharma industry out of the prolonged downturn that followed the pandemic boom. Going into the 2025 J.P. Morgan Healthcare Conference, leaders in the space are a bit more pessimistic.

“Sentiment is really bad in general in biotech,” Seaport Therapeutics CEO Daphne Zohar told BioSpace.

That said, Zohar and others are looking forward to potentially big news that could spark that optimistic attitude once again. The annual gathering in San Francisco is a who’s who of biopharma with thousands of executives descending on the Bay Area looking to strike deals. The meeting, which officially begins next Monday, Jan. 13, sets the tone for the year, and for many executives who spoke to BioSpace, a few high-profile transactions could really change the tune. But, Zohar commented, it needs to happen early.

“If we don’t see a lot of M&A between now and, like, the Tuesday of J.P. Morgan, I think we’ll have kind of negative sentiment,” Zohar said in a late December interview. “I always feel like, by Monday, if you’re not seeing a lot, then people begin to assume that there’s not much that’s going to happen.”

Linda Marbán, CEO of cell and exosome-based therapy biotech Capricor Therapeutics, agreed that the industry will be watching closely. And despite the swirling gloom, some of last year’s “cautious optimism” still exists, she wrote in an email to BioSpace.

“While challenges like clinical failures remind us of the complexity of developing transformative therapies, they also reinforce the importance of innovation and persistence,” she said. “I think everyone is eager to see what opportunities JPM will bring.”

Another big headwind over the industry is the presidential transition. Donald Trump will re-take the presidency on January 20, just after the JPM meeting concludes. Zohar and Gebauer both said that the wait for the new administration has suppressed deal activity.

Immunic Therapeutics Chief Operating Officer Jason Tardio said the macroeconomic stars are aligning for a year full of deal activity: the cost of capital has come down and interest rates are declining. On the policy front, the incoming Trump administration and Republican-led Congress are expected to ease corporate taxes, regulatory hurdles and drug pricing provisions like the Inflation Reduction Act.

“2025 could see significant megadeals as companies look to fill their growth gaps ahead of the looming loss of exclusivity in 2028,” Tardio said.

Whether the deals come now or later, Zohar is similarly confident that deal activity will return, fueled by Big Pharma. “They really need to fill their pipeline, so at some point they’re going to get pretty aggressive.”

# Venrock Predictions for 2025



## Dr. Oz turbocharges Medicare Advantage and everyone monitors their glucose: 10 health care predictions for 2025 from top investors

By Bryan Roberts and Bob Kocher, Dec 2024 (excerpted)

Welcome back to health care predictions season! We invite you to join us and gaze into our crystal ball as we look ahead to 2025. But first, let's look back and grade last year's performance.

In 2024, we did better than usual. We got eight and a half out of 10 predictions right. We feel smug about our prediction that Medicare Advantage's (MA) underperformance would lead to turnover at big payors with CEO Karen Lynch departing CVS Health (we are rooting for Steve Nelson and Sree Chaguturu at CVS). We were sadly right that nothing happened to pharmacy benefit managers (PBMs) other than public shaming (but the PBM-branded biosimilars are a cool thing to watch). And we correctly predicted that the Supreme Court would protect access to Mifepristone (though the Trump Administration may now set their sights on the Comstock Act to restrict mail order access). Finally, as anticipated, once mighty unicorns revealed themselves as bad businesses and the Federal Trade Commission set its sights on health care monopolies by unveiling its case against United Healthcare. We are saddened and send our condolences to Brian Thompson's family and his United Healthcare colleagues.

We were surprised by how emphatically our prediction that artificial intelligence (AI)/large language models (LLMs) would be adopted has proved out. Businesses like Abridge, Nuance, and Suki all experienced astonishing growth and continue to accelerate. We correctly predicted that the Centers for Medicare and Medicaid Services (CMS) would complete drug price negotiations which, at the time of our prediction, was tied up in the courts. However, we were disappointed that the negotiated prices were essentially cost-neutral since the reductions were really just the value of the rebates. Finally, the cracks we predicted in the brick-and-mortar services businesses were larger than we expected. Oak Street Health and VillageMD struggled to cut costs, while Cano Health and Caremax went bankrupt and Forward shut down.

We were less proficient soothsayers about payors playing hardball with hospitals. The opposite actually came true as several hospitals turned the tables on payors, dropping MA insurance plans. We were also overly optimistic about the cost-effectiveness and ease of access to GLP-1s. On this one, we think it is only a matter of time and give ourselves partial credit since adoption was extraordinary, even as many payors tried to restrict access. We believe increasing GLP-1 rebates and more data should make cost-effectiveness clearer over the near term, though incoming Health and Human Services leadership may slow things a tad.

Source: <https://www.venrock.com/insights/dr-oz-turbocharges-medicare-advantage-and-everyone-monitors-their-glucose-10-health-care-predictions-for-2025-from-top-investors-2/>

# Venrock Predictions for 2025 (continued)

## 1. All the health care policy action will be in the courts, not Congress

Although Trump is entering the White House with an electoral mandate, we do not believe he will spend any political capital on health care legislation. Congress will not try, for the 101st time, to repeal the Affordable Care Act and no major health care legislation will be passed in 2025. Instead, all the action will be in the courts. In 2024, in *Loper Bright*, the Supreme Court ended decades of deference to administrative agencies and opened the door to a world of challenges to existing regulations. This, in turn, led to a flurry of cases questioning CMS and Food and Drug Administration (FDA) rulemaking on matters like risk adjustment, MA Stars, broker commissions, and FDA authority.

## 2. Illumina gets sold as the dream ends

Illumina has gone from being the darling of the human genome project to losing its way for the last five years, punctuated by the disaster of buying and divesting Grail, destroying \$10 billion of value.

Today, Illumina faces stiff competition and slowing growth. Its market cap is in the \$20 billion range, down 50% over the past years which, along with new management, makes it a ripe takeover target for one of the life sciences tools aggregators (our bet is on Danaher).

## 3. Multiple down exits in health tech M&A and IPOs

After several years of no liquidity, WE ARE SO BACK! Combine a laissez-faire Trump administration attitude toward antitrust with pent-up demand from growth businesses, large payors, pharma, and tech will all be active acquirers. We also think M&A premiums and tax cuts will fuel public markets and open the IPO window—the hitch being that pricing will be well below what these companies were prepared to pay at the peak. Nonetheless, management teams and investors will accept “okay” prices four years post-market bust.

## 4. Litigation and Dr. Oz-led CMS make Stars easier, and Medicare Advantage grows faster

More 4 Star plans would help an Oz-led CMS achieve its goal of Medicare Advantage growth and private sector involvement and innovation in Medicare.

Cessation of the data analytics sleight of hand and tricky foreign language secret shoppers would make Stars cutoffs more predictable and bonuses easier to achieve or at least less foot-fault binary. Additionally, the new administration will have no appetite for more lawsuits like SCAN’s and Elevance’s successful challenges in 2024.

# Venrock Predictions for 2025 (continued)

## 5. At-risk primary care rebounds in 2025 after a disastrous 2024

2024 was a disaster for risk-bearing primary care providers (PCPs). Changes to the CMS V28 risk adjustment model, overly generous health plan benefits eating into their revenues, and lower-than-inflation-rate increases conspired to cause losses, divestitures, and cost cuts. With better cost structures, it's time to figure out how to win in V28, and with plans cutting benefits in 2025, profits and growth will return to these groups (and continue to improve into 2026).

## 6. Healthcare Service Corporation (HCSC) walks from Cigna's MA business due to Cigna's rich AEP offerings

While several MA plans cut benefits in a big way in 2024, Cigna's cuts were much more limited. We believe this was in order to show strong membership growth for the sale (and maybe they didn't get the Inflation Reduction Act memo and recognize the landmine that is Part D risk).

These benefit designs, especially around drug costs, are attracting a bunch of adverse risk. Realizing they overshot the growth versus profitability balance, in early November Cigna (along with several others, such as Elevance) informed brokers that they would not pay commissions on these plans. But that will have been too late. We expect that HCSC, realizing this, will decide that this mess is too big to clean up, walk, and find another way to grow their MA business.

## 7. More leadership turnover at big payors

## 8. Apple does glucose monitoring well

If you have ever tried Dexcom or Freestyle Libre glucose monitors, you have dealt with so-so software and needles. Enter Apple who will bring world-class software and design to non-invasive glucose monitoring. Needleless glucose monitoring is a much more appealing product and will lead glucose monitoring to be as omnipresent as sleep tracking across the population.

## 9. Health tech AI startups prove to be features, not businesses

While AI has been the investor darling of 2024, with 39 AI companies raising rounds of \$100 million or more, most of the health tech-focused AI startups are going to be disappointing. Most health tech AI companies are commercializing a novel feature that is better as part of a broader product or can be easily emulated once the use case is realized.

## 10. Cell therapy gets out of the doghouse

After several years of being avoided like Bob and Bryan at their 1980s high school dances, cell therapy bounces back. Clinical data in solid tumors and manufacturing improvements across the board rekindle the promise to bring the extraordinary efficacy that a few blood cancer patients have benefited from to a much broader population. Not in autoimmunity, however, where things actually cool off because T-cell engagers show efficacy, rendering cell therapy products less needed.



# Sachin Jain's Predictions for 2025

**Sachin H. Jain, CEO SCAN Health, *Forbes*, Dec 2024 (excerpt)**

What I undeniably see is a year ahead in American healthcare that will be like no other in recent memory:

## **1) Wellness Will Be Front and Center**

The RFK Jr. Effect will be real. People will begin wondering why we normalized overeating processed foods and consuming high volumes of neurotoxic alcohol and marijuana. Heretofore fringe ideas about wellness and disease causation and medications will continue to go mainstream. Traditional allopathic medicine and public health will be on non-stop defense. Doctors, nurse practitioners, and pharmacists will have to do more than ever before to continue to encourage adherence to medicines about which the public will be more skeptical than ever (with the exception, of course, of Ozempic and other GLP1s!).

## **2) Misinformation Will Get (Much) Worse**

Coming off the pandemic, a whole swath of American society has de-credentialed the medical profession. And there is no easy pathway back to a place where physicians and other healthcare professionals are fully trusted for their knowledge and, more importantly, their judgment. Logging on to X, the social media site formerly known as Twitter, you get the feeling that everyone is an MD and a PhD these days with the confidence to make claims that once required clinical experience and data and analysis.

## **3) Medicare Advantage Will Make A Roaring Comeback**

The last few years have been dark days for Medicare Advantage. Enter the incoming Trump administration and Dr. Mehmet Oz, the likely new administrator of the Centers for Medicare and Medicaid Services (CMS) who has been unabashedly supportive of Medicare Advantage leading up to his appointment. With a Republican House and Senate and Presidency, will they go so far as to push (as Oz has before—and, I have, too, for that matter) for Medicare Advantage for All? Will “repeal and replace” take the form of a broadened Medicare Advantage program? I doubt it. Nonetheless, I expect that they will ease up the regulatory environment surrounding Medicare Advantage and make it an even more attractive alternative to traditional Medicare....

## **4) Obscure Government Deputies Will Matter More Than Ever**

## **5) The Health Equity Field (As We Know It) Will End**

## **6) There Will Be More Turnover at The Top**

## **7) Big Transactions Will Return**

## **8) The AI Revolution Will Accelerate**

## **9) Regulators Will Scrutinize Private Equity's Role in Healthcare (Even More)**

## **10) Digital Health Will Continue to Spin**

# Deloitte Predictions for 2025

**Alex Phillipidis, Deloitte, *GenEng News*, Jan 3, 2024 (excerpt)**

Of 150 C-suite executives from pharmaceutical, biotechnology, and other life sciences companies surveyed by the Deloitte Center for Health Solutions across the U.S., Europe, and Asia, 75% said they believe 2025 will indeed be a happy new year for their companies and the broader industry. They based that optimism on a combination of factors that include expectations for strong growth (68% anticipated revenue increases) and the pace of science and technology innovation.

Some of these predictions are among the seven biopharma-related trends that GEN has uncovered in its interviews with experts and other industry stakeholders, and in its reviews of reports and public statements. These trends are detailed below:

## **AI: Growth beyond discovery algorithms**

Having ensconced itself in drug discovery and development, artificial intelligence (AI) is poised for even further growth. Nearly 60% of biopharma executives surveyed by Deloitte said they plan to increase generative AI investments across their value chains.

“We are moving from the experimentation and hype stage to the ‘How am I using it to improve my business?’ stage. That shift happened over the course of this year, and I think we’ll see it even more next year,” Pete Lyons, a vice chair with Deloitte and the firm’s U.S. Life Sciences Sector Leader, told GEN Edge.

Executives plan to expand AI use beyond drug discovery algorithms, to greater use of gen AI at scale across business operations, Lyons said: “I think it will change jobs, not necessarily cost jobs. And this isn’t the first technology that we’ve seen over the last many decades that has come through to make folks more efficient.

More AI in biopharma is expected to spur more growth for leading AI-based drug developers. Recursion combined with Exscientia for a reported \$688 million in November... Insilico Medicine published peer-reviewed details of its inflammatory bowel disease program and has grown its pipeline to 31 programs, 10 of them progressing to clinical phases—led by ISM001-055, an idiopathic pulmonary fibrosis candidate the company plans to advance into a potentially pivotal trial.

While some drug developers will continue building out their own AI platforms, others will simply partner with other companies: “people have largely migrated to in-licensing to get those AI technologies, as promising as they may be, deployed in their own internal development programs,” Roel Van den Akker, a partner with PwC US and the firm’s Pharmaceutical and & Life Science Deals Leader, told GEN Edge.

A growing presence in biopharma AI helped propel Silicon Valley-based microprocessing giant Nvidia to a market capitalization—the product of the share price and the number of outstanding shares—surpassing \$3 trillion in 2024, and a 10-for-1 stock split that took effect in June. Heading into 2025, those new Nvidia shares have all but plateaued, finishing December down 0.55%.

# Deloitte Predictions (cont.)

## **CANCER VACCINES: Gathering late-stage data**

The quest to develop a cancer vaccine will see continued late-stage data gathering in 2025. Among leading developers, Moderna and Merck in October launched their third Phase III trial (NCT06623422) for their individualized neoantigen therapy (INT) that Moderna calls mRNA-4157 and Merck, V940. INTerpath-009 is evaluating the combination of adjuvant INT plus Merck's Keytruda® (pembrolizumab) for some types of non-small cell lung cancer (NSCLC) following Keytruda and chemotherapy.

“We do continue to discuss with our partner, Merck additional Phase III programs. We will start new ones in the coming year that we haven't yet announced,” Moderna's President Stephen Hoge told analysts November 7 on the company's quarterly earnings call.

## **VC deals, IPOs bouncing back**

Biopharma startups are likelier to see larger venture capital (VC) financings and more of them in 2025 if encouraging figures seen in the third quarter of 2024 continue their positive direction.

The VC market has fallen from post-COVID highs of \$44 billion in 756 deals in 2021, skidding to \$27.9 billion in 543 deals the following year, then further tumbling to \$23.5 billion in 464 deals in 2023.

## **GENE EDITING: Revenue, reform, and history**

2024 saw Vertex Pharmaceuticals generate its first commercial revenue from the first patient dosed with the first FDA-approved CRISPR therapy, Casgevy® (“exa-cel” or exagamglogene autotemcel).

Far more in revenue could be potentially generated from CRISPR therapies—and far more such treatments could reach the patients who need them, Fyodor Urnov, PhD, director, technology & translation at the Innovative Genomics Institute and professor of molecular and cell biology at University of California, Berkeley, asserted in a 6,000-word guest editorial in the October 2024 issue of The CRISPR Journal (a sister journal of GEN, published by Mary Ann Liebert, Inc.)

Gene editing technologies beyond CRISPR also advanced during 2024 and stand poised to progress further. During 2025, Prime Medicine expects to report initial clinical data from the first human trial of a prime editing therapy, a Phase I/II study (NCT06559176) of PM359, an ex vivo autologous hematopoietic stem cell (HSC) product designed to treat chronic granulomatous disease (CGD) patients with a mutation in p47phox. Prime gained FDA clearance for the first human trials of a prime editing therapy last April.

Also in the new year, Wave Life Sciences anticipates sharing multi-dose data from its Phase Ib/IIa RestorAATion-2 trial (NCT06405633) assessing its alpha-1 antitrypsin deficiency (AATD) candidate WVE-006. Wave made clinical history in October when it announced that WVE-006 succeeded in the first-ever clinical demonstration of RNA editing in humans by achieving positive proof-of-mechanism in RestorAATion-2.

# Deloitte Predictions (cont.)

## **M&A: Patent cliff to drive mid-range deals**

The improving VC and IPO markets are giving market watchers hope for a rebound in the merger and acquisition (M&A) activity long cherished by investors as the most lucrative avenues for cashing in on their investments.

Deloitte's Lyons said larger biopharmas are eager to replenish pipelines that will shrivel in coming years through "patent cliff" loss of exclusivity on numerous blockbuster drugs—such as Johnson & Johnson/Bayer's blood thinner Xarelto® (rivaroxaban), Boehringer Ingelheim/Eli Lilly's Jardiance® (empagliflozin), and AstraZeneca's top-selling drug Farxiga® (dapagliflozin). Jardiance and Farxiga are both sodium-glucose cotransporter 2 (SGLT2) inhibitors indicated for type 2 diabetes, chronic kidney disease, and heart failure.

As a result, M&A is expected to bounce back from a year-over-year decrease in the dollar volume and number of transactions during the first three quarters of 2024.

In 2025, PwC's Van den Akker said, his firm expects sustained M&A activity for mid-range transactions ranging in value from \$5 billion and \$15 billion—deals priced below the values of blockbuster combos like Pfizer-Seagen, but above "bolt-on" acquisitions of under \$5 billion.

Source: <https://www.genengnews.com/insights/trends-for-2025/seven-biopharma-trends-to-watch-in-2025/>

## **OMICS: Expansion and consolidation**

Next-generation sequencing (NGS) tools developers will further grow their footprints into multiomics tools and tech following expansion efforts during 2024. NGS leader Illumina catapulted into multiomics in July when it acquired Fluent BioSciences, a single-cell technology developer, for an undisclosed price. Spatial biology will see fewer but larger tools developers among leading companies following consolidations during 2024.

## **TRUMP 2.0: Going "wild" on biopharma, health**

Trump signaled his intent to disrupt both days after his election win by announcing he wanted Robert F. Kennedy Jr. to "go wild on health" by nominating him for HHS. Kennedy will head a subgroup of Trump appointees committed to his "Make America Healthy Again" agenda, along with Marty Makary, MD, as FDA commissioner, and Jay Bhattacharya, MD, PhD, as NIH director. All three have severely criticized measures promulgated to limit the spread of COVID-19, with Kennedy also taking aim at the safety of the messenger RNA (mRNA) vaccines...

One area of medicine that Kennedy has pledged to encourage at HHS is psychedelic drugs. Several public companies in the space saw their stocks rise soon after Kennedy emerged as Trump's choice for HHS, on the expectation that he would catalyze psych drug development. "He is a free thinker and slightly unpredictable, I would say, but to me it feels as if he is interested in radically reforming the way medications are being approved. So, he may be a catalyst. But I think it all boils down to the data," said Hans Eriksson, MD, PhD, CMO of HMNC Brain Health



# Comments and Thoughts on the Market From Our Friends

We shared a draft of this report with various friends inside Stifel and industry and received quite a few comments, including:

## John Maraganore, Former Alnylam CEO:

1. I agree with your comments on the current investor mood, and I've heard this from many of my hedge fund friends. Everyone thought 2024 would be THE turnaround year, and it's hard to be optimistic in 2025 right now given the uncertainty.
2. it's interesting to reflect on how the XBI would look if Lilly and Novo were included in the index. After all, these 2 pharmas are leading the most important innovation in the biopharma sector right now. The lines between "biotech" and "pharma" are therefore blurred. I wonder if there's an interesting analysis to do on this.
3. One theme that I think you're missing is the implications of Casgevy and Elvidys commercial performance on investor interest in "one and done" gene editing and gene therapy technologies. It almost seems like investors are looking for signs of commercial reward for those type of multi-million therapies before putting money behind gene editing and gene therapy names. Sadly, will scientific and medical *cures* get stymied by lack of commercial execution?

## Jeff Jay, Head, Great Point Partners

1. I am not real optimistic about IPOs in early 2025. The 2024 class came out at valuations that were too high. The median IPO was down 29% and as of year end 75% were below their issue price. New IPOs in 2025 need to come out as a down round to the most recent crossover or the IPO market will close pretty quickly in my humble opinion.
2. I am pretty optimistic about M&A. The dollar value (not number of deals) was at a 10 year low last year. Lina Kahn drove that, so I feel with a Republican FTC Head the pendulum will swing back here.
3. The biotech ecosystem does not work without active M&A – plain and simple. One product companies will not generate enough free cash flow with their own sales force to make the ROI work for the sector. A salesperson needs multiple products in the bag. And investors need some stocks that pop 50 to 100% because of synergies that can be achieved. The cash then of course gets recycled back into the sector.
4. Your report is too optimistic. I hope that I am wrong

# More Comments and Thoughts on 2024 and 2025:

## **Brad Loncar, CEO, Biotech TV:**

1. I'm sorry to say that I mostly agree with the hedge fund manager you quoted.
2. I think we can have a good year every now and then, but I do think biotech is going through structural change that most people don't want to admit, and it is unlikely to have big streaks of outperformance like we saw from 2010 to 2015.
3. Those years were peak years of commercial companies getting away with anything they wanted to charge for drugs, and also development stage companies getting away with IPOing based on hopes and dreams.

## **Ed Saltzman, Senior Advisor, Lumanity (and frequent strategy advisor to biotech CEOs and boards):**

1. The excesses of the "Covid era" are hanging over the market a lot longer than many would have expected or hoped. There are still hundreds of public companies going nowhere but yet still hanging around. Their performance counts in the indexes though which is a problem.
2. The over hyping of early stage biotechs has scared away retail investors from the sector- possibly for good. Biotech and their many stakeholders have to own their version of "The Big Short" It may have been legal but it was probably immoral and definitely not pretty. A lot of people felt snookered and this tends to make people angry while turbocharging their memory.

3. At some point the sector will have to face up to the fact that the majority of money made in the business is not associated with the development of important new therapies but rather raising money and then more money. This needs to be fixed. Some of today's mega round VC deals could easily be reported in The Onion.
4. M&A is in a lull for more reason than FTC excess. It turned out to be a bad idea in retrospect but for a decade or more the majority of all venture investment went into immune-oncology programs that Pharma now has little to no interest in. Ditto for rare disease. Ditto for cell therapies. I suspect half or more of the deals we do see will be for obesity and metabolics companies. I fear the same bubble may now be approaching for all the I&I companies funded over past 5 years.
5. The practice of drug commercialization in the US has become almost comically hard (except it's not funny). Most VCs and biotech CEOs (as well as their Boards) claim to be aware of these hurdles but are really clueless as to just how high these hurdles are.
6. Finally, I suspect that in order for the sector to sustainably rebound we will need not only a lot of positive data (this alone has not worked for a lot of programs) but quality companies pursuing thoughtfully chosen corporate development strategies which best align risk and reward with cost of capital. I know this sounds pretty basic which makes it all the more depressing that it is actually very rare. I have maintained for years that strategic failure is a bigger killer of biotechs than scientific or clinical failure.

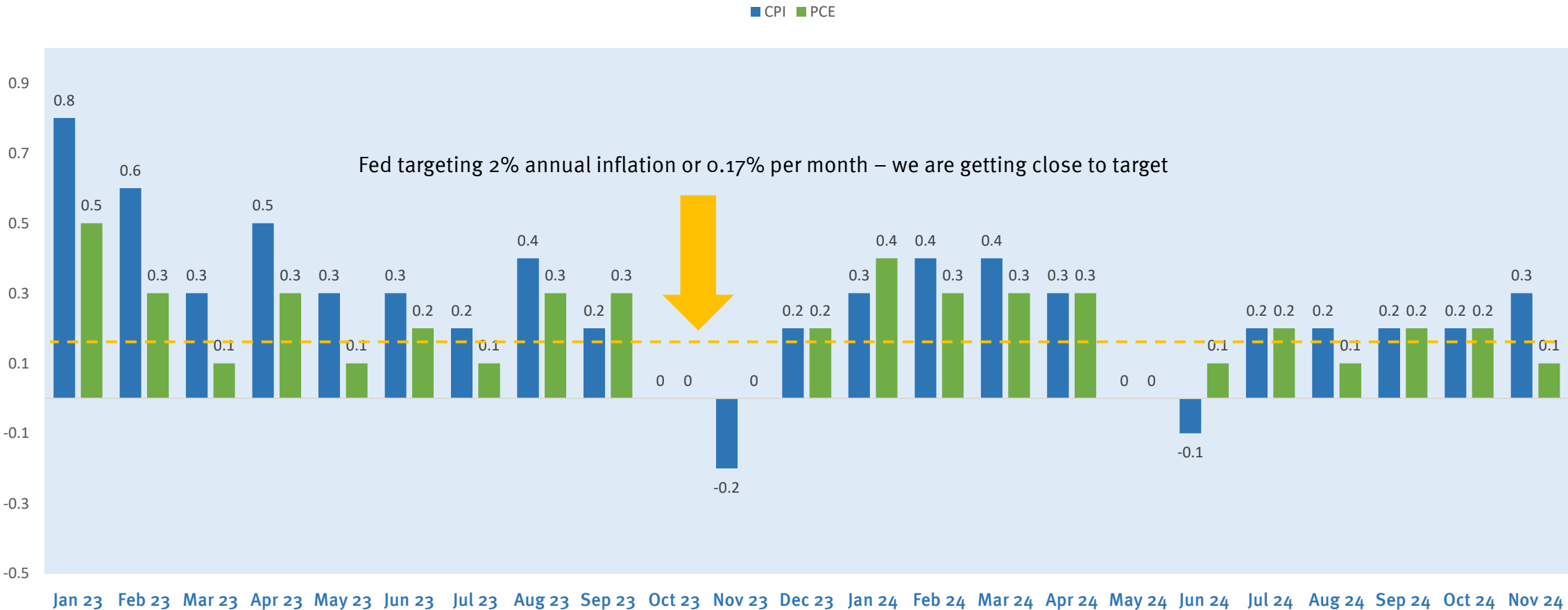
# 3. Macro and the Markets



# U.S. Inflation Picture Shows Control

The U.S. inflation picture in late 2024 looks far brighter than it did 18 months ago. Inflation is very close to the Fed’s target rate of 2%. Nonetheless, we have not seen CPI inflation in the U.S. go below 0.2% per month since July, hence the Fed’s recent slowdown in rate cuts and the associated collateral damage on the XBI. The Fed is also nervous about how Trump policies might affect inflation.

Monthly U.S. Inflation Jan 2023 to Nov 2024 (% change in price index)



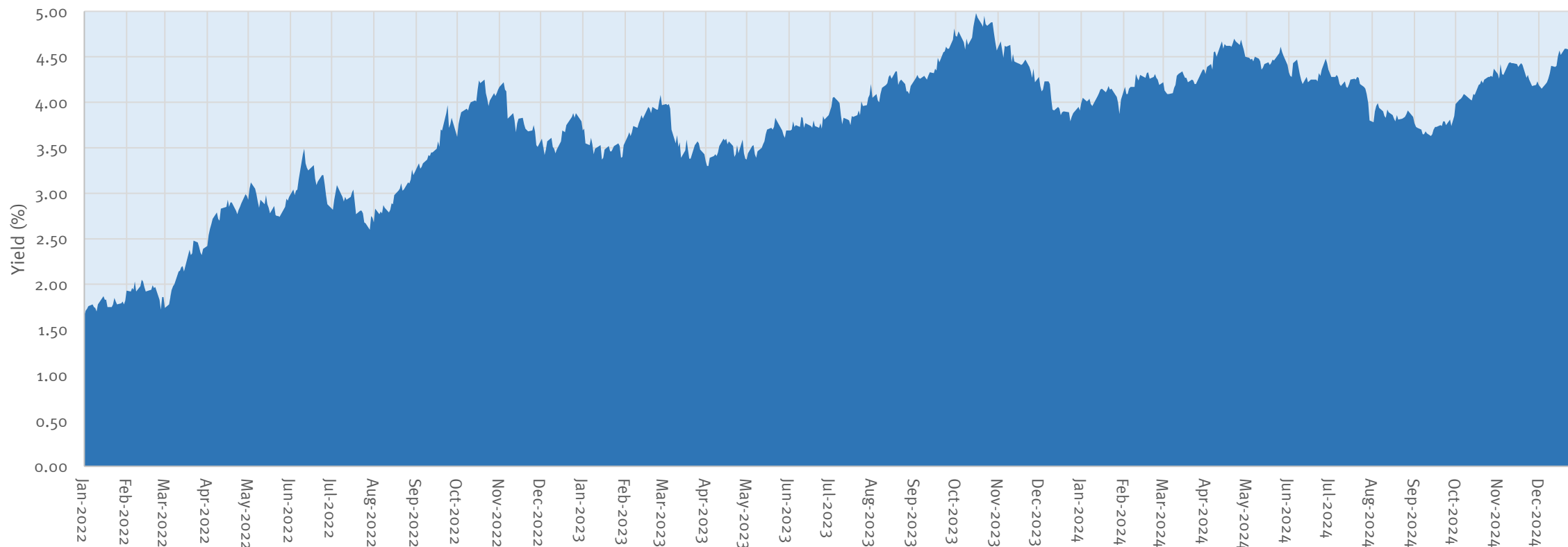
Source: U.S. Bureau of Labor Statistics



# Long Bond Rates Remain Stubbornly High

The biotech story of 2024 has been very much linked to interest rates. We saw rates down on positive inflation news in January and February. The XBI took off and the PIPE / follow-on market became volcanic. In April we saw our second unpleasant inflation read in a row and the XBI headed south, the follow-on market headed south, and biotech bears started to come out of hibernation. As inflation has come back since September 2024, Fed messaging has understandably toughened, rates have come back up and the XBI has gone in the wrong direction. Today, rates are as high as they were in May of 2024.

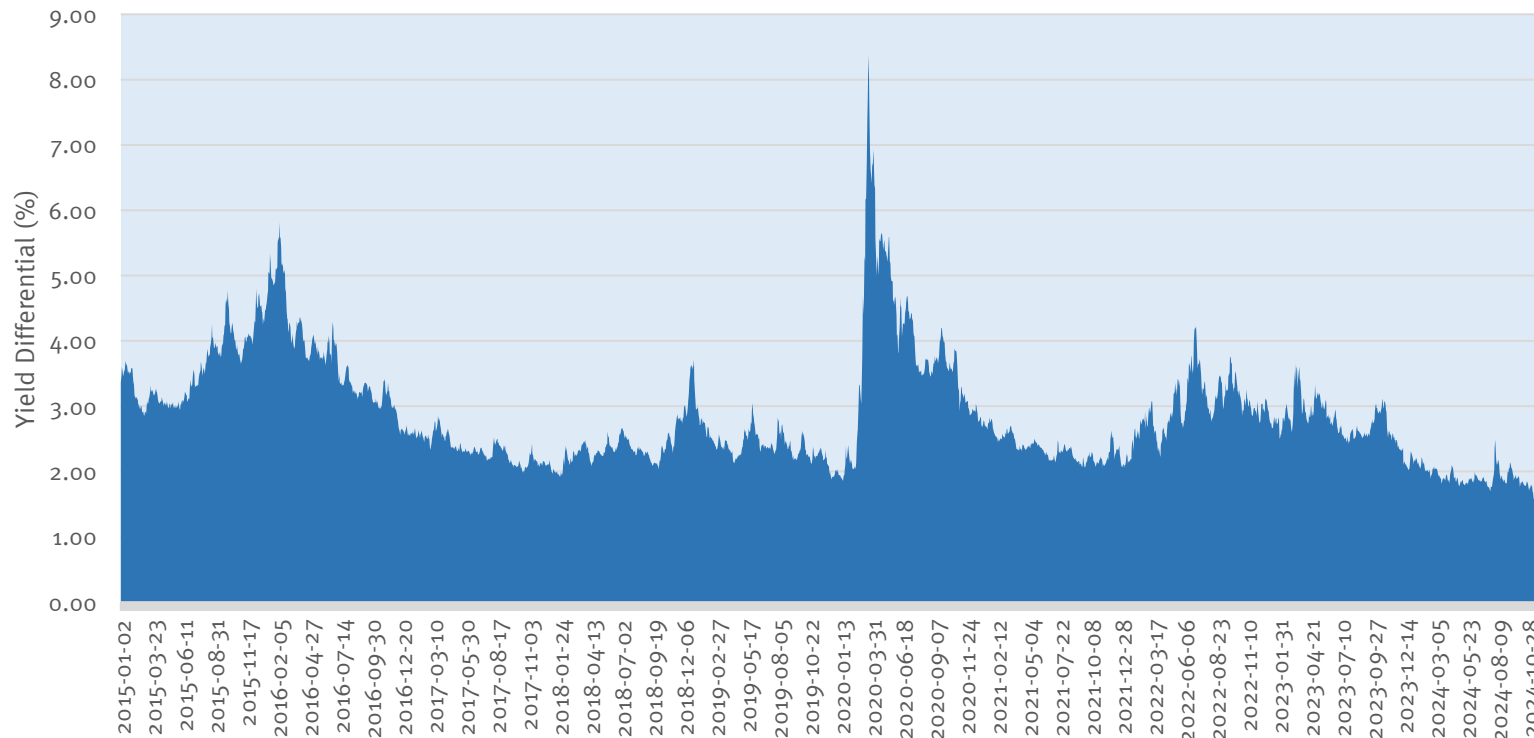
United States Treasury 10 Year Yield, Jan 2, 2022 to Jan 3, 2025



# Credit Spreads Highly Favorable and Can Fuel PE Deals

Credit market conditions today are quite favorable. We are in a period of relative economic strength and investors are chasing yields. As a result, we have seen the differential between junk bond yields and equivalent duration Treasuries fall below 2% in 2024. Low credit borrowing costs are a big positive for private equity deals which tend to substitute debt in the capital structure for equity. Interestingly, with upcoming Trump tax cuts, receding inflation and cheap credit, we may be poised for the type of private equity boom that took place in the early 1980s under President Reagan.

Spread Between Yield on BB U.S. Bonds and Equivalent Duration Treasuries, 2015 to 2025



**Wikipedia on Buyouts in the Early 1980s:** “The beginning of the first boom period in private equity would be marked by the well-publicized success of the Gibson Greetings acquisition in 1982 and would roar ahead through 1983 and 1984 with the soaring stock market driving profitable exits for private equity investors. In January 1982, former US Secretary of the Treasury William E. Simon, Ray Chambers and a group of investors, which would later come to be known as Wesray Capital Corporation, acquired Gibson Greetings, a producer of greeting cards. The purchase price for Gibson was \$80 million, of which only \$1 million was rumored to have been contributed by the investors. By mid-1983, just sixteen months after the original deal, Gibson completed a \$290 million IPO and Simon made approximately \$66 million. Between 1979 and 1989, it was estimated that there were over 2,000 leveraged buyouts valued in excess of \$250 billion. Because of the high leverage on many of the transactions of the 1980s, failed deals occurred regularly, however the promise of attractive returns on successful investments attracted more capital. With the increased leveraged buyout activity and investor interest, the mid-1980s saw a major proliferation of private equity firms.”

# Credit Spreads Haven't Looked This Good Since the 2000s. Can They Get Better?

**Kristin Broughton, *Wall Street Journal*, Dec 30, 2024 (excerpt)**

Companies took advantage of favorable financing conditions this year to issue debt at levels not seen since the pandemic, adding cash to the balance sheet to pay for future refinancing needs and other projects.

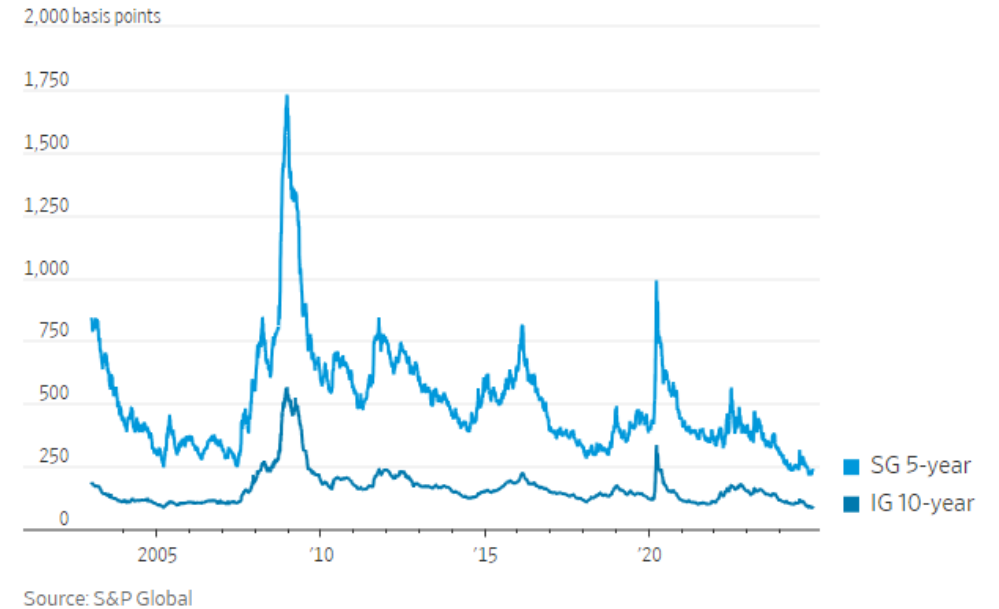
Underpinning the surge in debt issuance: credit spreads, a metric that finance chiefs watch when deciding when to pull the trigger on a bond sale. That metric—the additional amount that companies pay above a Treasury of a similar maturity—tightened throughout 2024, ending the year at levels not seen since at least the mid-2000s.

Whether debt issuance remains as strong in 2025 will depend in part on whether spreads remain attractive, advisers said. If companies issue more debt to fund acquisitions or capital investments, that could bolster issuance, as well.

As the Federal Reserve trims interest rates, total borrowing costs in the corporate bond market are expected to decline, though that could change if the central bank moves slower or faster than investors expect, causing spreads to widen. Borrowing costs in the bond market don't always move in sync with the Fed. The central bank said this month that it will be cautious about further rate cuts.

The improvement in spreads in 2024, alongside strong debt issuance throughout the year, surprised some bankers, advisers and analysts, given earlier uncertainty about the potential for a U.S. recession, as well as a contentious presidential election. But the year also featured strong economic data, solid corporate earnings and a surge in demand from investors.

**Credit spreads on investment- and speculative-grade bonds**



Source: <https://www.wsj.com/articles/credit-spreads-havent-looked-this-good-since-the-2000s-can-they-get-better-bfcf6094>

# Geopolitical Hotspots Cool Down

We saw 2023 bring into the open a loose axis of interests between China, Russia, Iran, North Korea and their proxies. While this axis is ultimately threatening to global stability and the markets, it is remarkable how little progress was made by Russia and Iran in 2024. Russia gave up 400,000 lives in 2024 to gain 6% of Ukraine territory while Iran's interests were beaten badly by Israel. We see the impact of geopolitics on the biotech market as inherently limited in 2025. We are optimistic that 2025 will be a year of geopolitical calm. A key question will involve the Trump Administration's engagement with China and potential tariffs on that country. We are hopeful that we will see more normal relations emerge with China in the months ahead.



## China – U.S. Friction Over Taiwan

We are not experts on China politics but easing of tensions between the U.S. and China in 2024 was notable. The Chinese government faces significant internal economic issues and President Xi has been continuing to focus on domestic matters while continuing to increase dialogue with the U.S. counterparts. President Trump has appointed a China hawk to Secretary of State and it is not obvious that the relationship between the U.S. and China gets better in the next four years.



## Russia – Ukraine War

While Ukraine has not been successful in removing Russia from its soil the toll of the war on Russia is unmistakable. Russia faces high inflation and, tragically, a shrinking population due to massive and shocking war losses. A recent missile attack on Ukraine energy supplies caused little damage. Ultimately, a stalemate works against the attacker and appears likely that the Ukraine situation will not to boil over into something bigger in 2025. Trump will be incentivized to see emergence of peace in Ukraine.



## Israel – Hamas Conflict

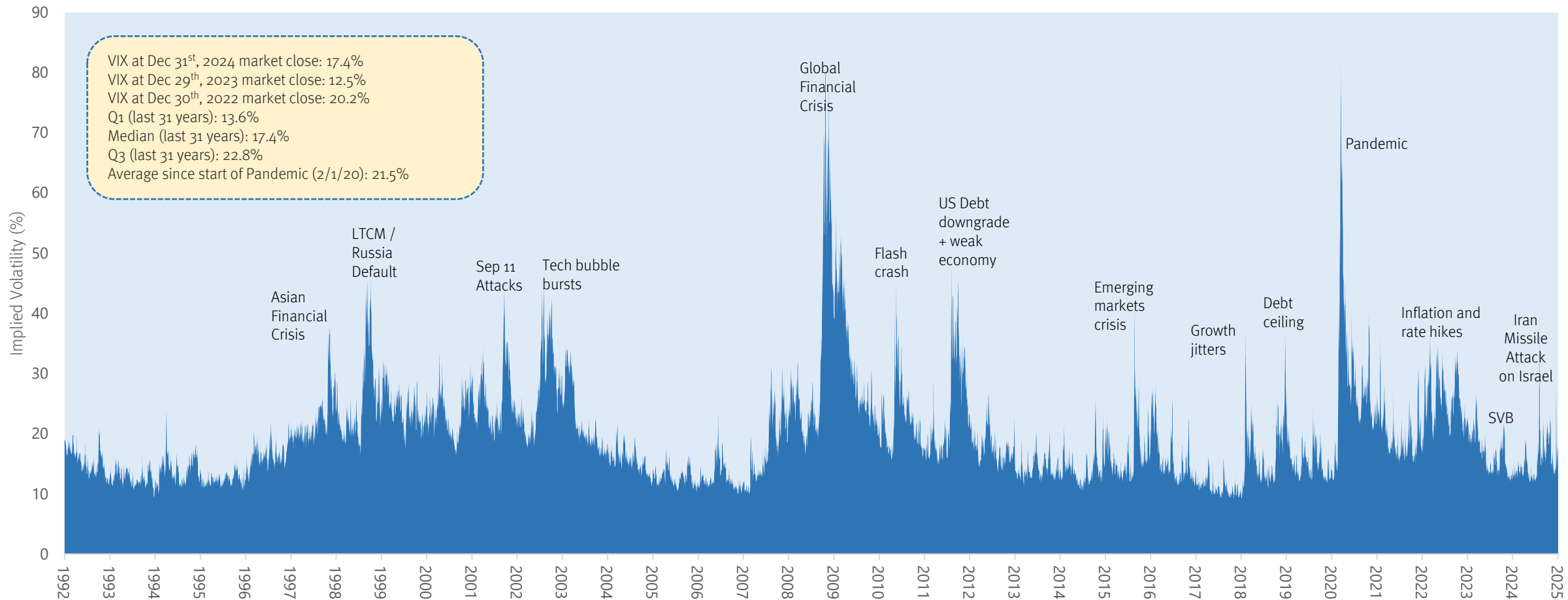
Unlike Ukraine, the Israeli war with Hamas is not a stalemate. Israel has not only removed Hamas from Gaza but has also humiliated Hezbollah and is now going to work on Houthi rebels in Yemen. An Iran missile attack on Israel was spectacularly unsuccessful. The change of regime in Syria was surprising and a major setback for Russia and Iran. While wider regional conflict remains possible, most reports indicate that Iran has little stomach to ramp up offensive efforts given recent developments.



# Market Volatility Measured by VIX is Down From Pandemic

The Pandemic period was remarkable for high market volatility. The VIX, a measure of investor fear, has averaged 23% since the Pandemic. Today's VIX value of 16% is down substantially from Pandemic levels although up a smidge from this time a year ago. It's well understood that a low VIX is a positive for market performance and for biotech issuance activity, especially IPOs.\*

VIX - Implied Volatility on CBOE S&P 500 Option Contracts, 1992 to 2025



# Tax Cuts are on the Menu in 2025

Brian Faler, *Politico*, Jan 4, 2024 (excerpt)

Washington is geared up for a big debate over trillions of dollars in tax cuts. It's going to be long, slow and messy. As the utter chaos that erupted as lawmakers struggled to write a year-end bill to fund the government demonstrated, the GOP has a tenuous grip on the House. President-elect Donald Trump has a penchant for chaos. And Republicans are at odds over a long list of issues, beginning with whether they should take up tax first this year or immigration.

Deficit concerns are running hot in the House, where many Republicans say a tax bill ought to be completely paid for. That's anathema to party heavyweights like House Ways and Means Chair Jason Smith (R-Mo.) and Senate Finance Chair Mike Crapo (R-Idaho), not least because it would be extremely difficult to find enough offsets to cover the projected \$4 trillion cost.

Lawmakers could split the difference, and just pay for part of it. It's possible they would decide that only certain types of provisions have to be offset. Crapo says extending current policy, like the tax cuts from Trump's first term that are set to expire at the end of this year, shouldn't cost anything. Nor should what he calls "pro-growth" provisions — leaving only new ideas that don't do much for the economy needing offsets.

Lawmakers haven't really begun wrestling with this question in earnest, though, and it could take a long time to sort out. But they can at least start hashing out a plan with only a rough idea of how much they'll ultimately spend.

Back in 2017, when they passed Trump's plan, it took Republicans months to settle on the original \$1.5 trillion price tag for their tax cuts. Republicans would like to extend their tax cuts for as long as possible, and 10 years has become the norm. But lawmakers could drastically reduce costs, and the need for payfors, by adopting a shorter extension.

Rolling over the full slate of the 40 or so provisions due to expire would cost roughly \$400 billion per year, according to budget analysts. While a shorter extension might reduce sticker shock, it would also seriously disappoint many Republicans.

Source: <https://www.politico.com/news/2025/01/04/trump-tax-cuts-congress-chaos-00195363>





## 4. The Biopharma Market



# Subsection 4.A

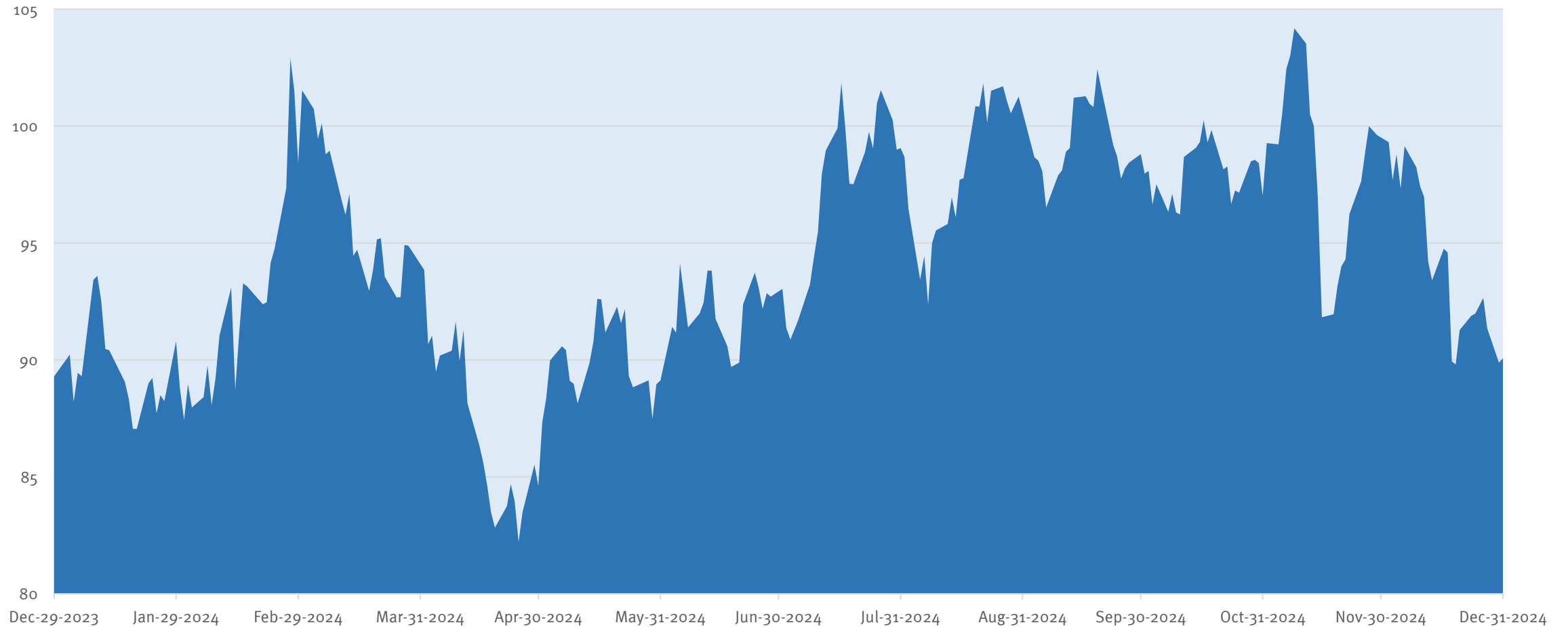
How Did Global Biotech Perform in  
2024?



# XBI Unchanged in 2024

After a year of furious rallies and tough downdrafts the XBI ended within 1% of where it began. In total, the XBI was up 0.9% for 2024.

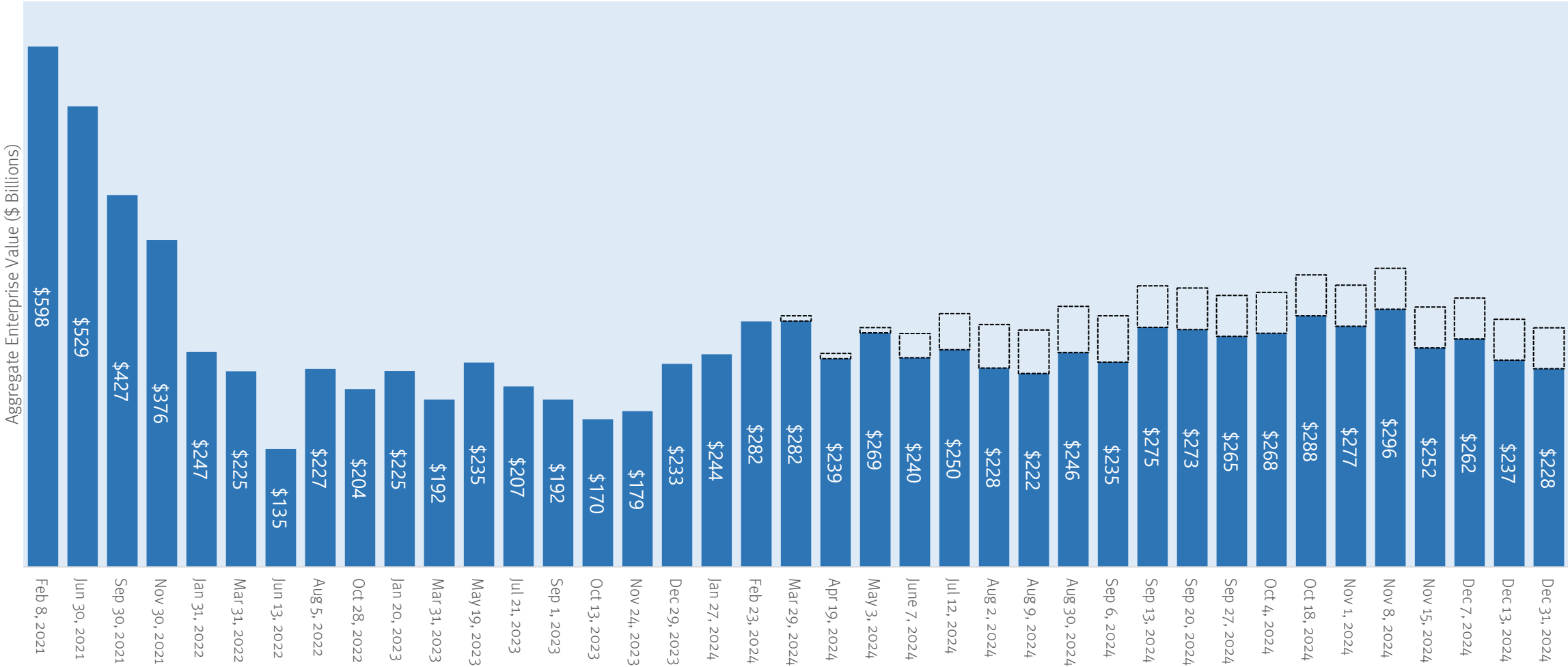
XBI, Dec 29, 2023 to Dec 30, 2024



# Stifel Measure of Biotech Sector Value Rose by 22% in 2024

The total enterprise value of the global biotech sector rose by 22% in 2024 after adjusting for exits and entries. While impressive, the last two months of the year were brutal. The total sector EV was up 47% on Nov 8, 2024 and gave back more than half of the year’s gain in just two months.

Total Enterprise Value of Publicly Traded Global Biotech, Feb 8, 2021 to Dec 31, 2024 (\$ Billions)

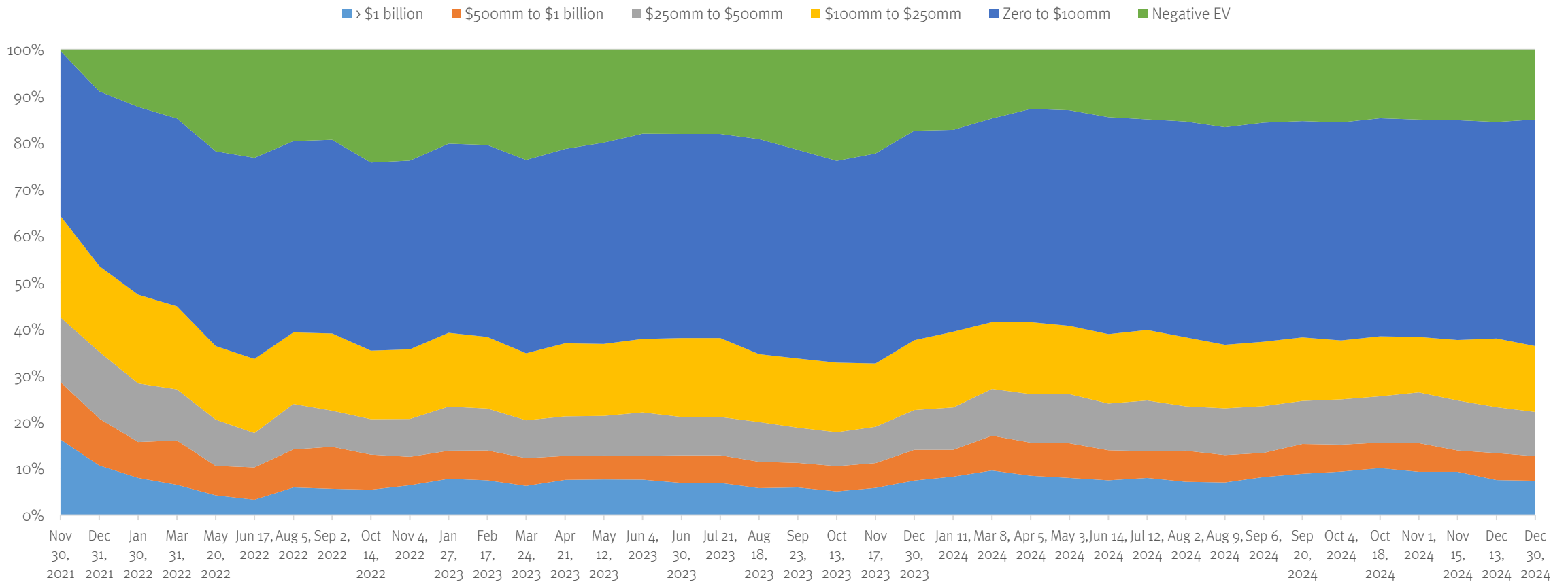


Source: CapitalIQ. Biotechs are defined as any therapeutics company without an approved product on any global stock exchange.

# Biotech Neighborhood Analysis

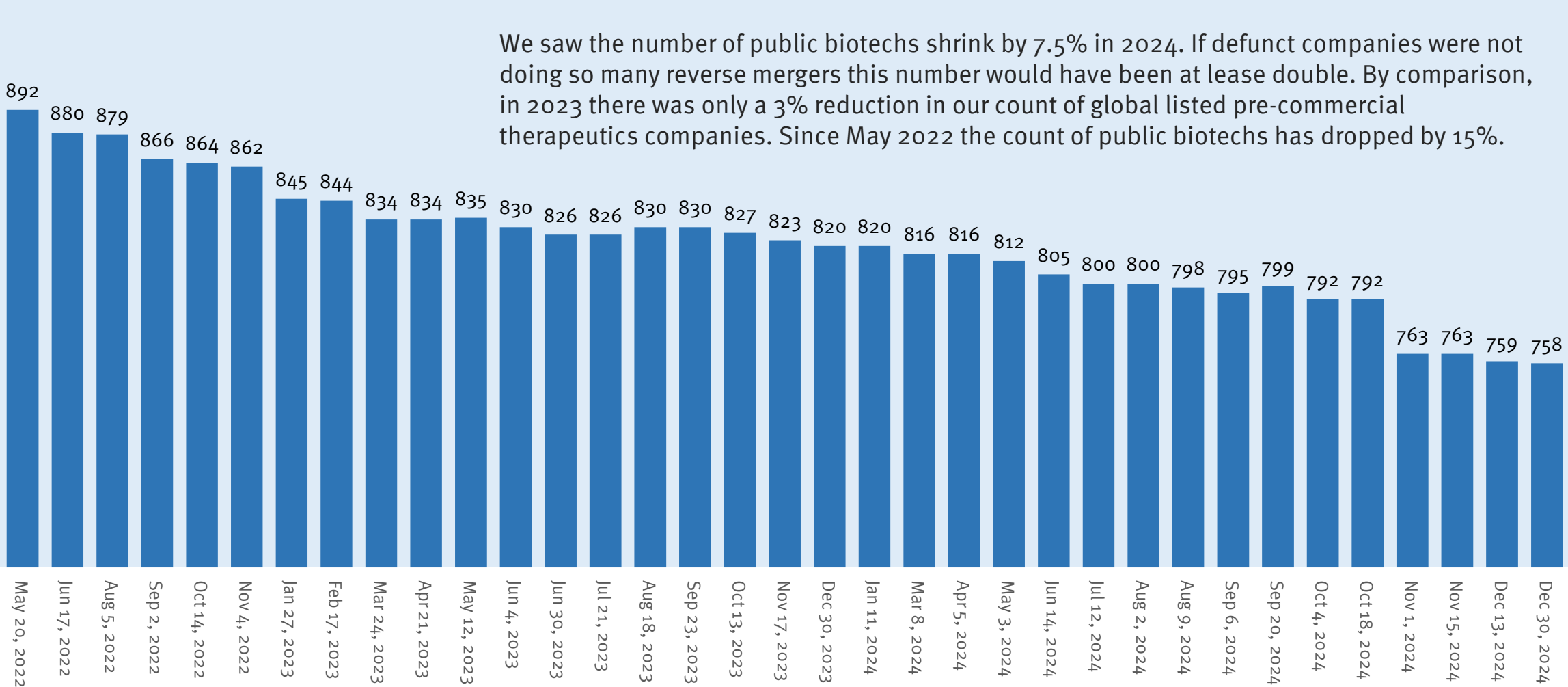
Far fewer companies today are at negative EV than were a year ago. On Dec 30, 2023 we found that 17.4% of all biotechs worldwide had negative EV. On Dec 31, 2024, that percent had fallen to 15%.

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



# Public Biotech Company Count Shrunk by 7.5% in 2024

Number of Publicly Traded Biotech Companies Worldwide, May 2022 to Dec 2024



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



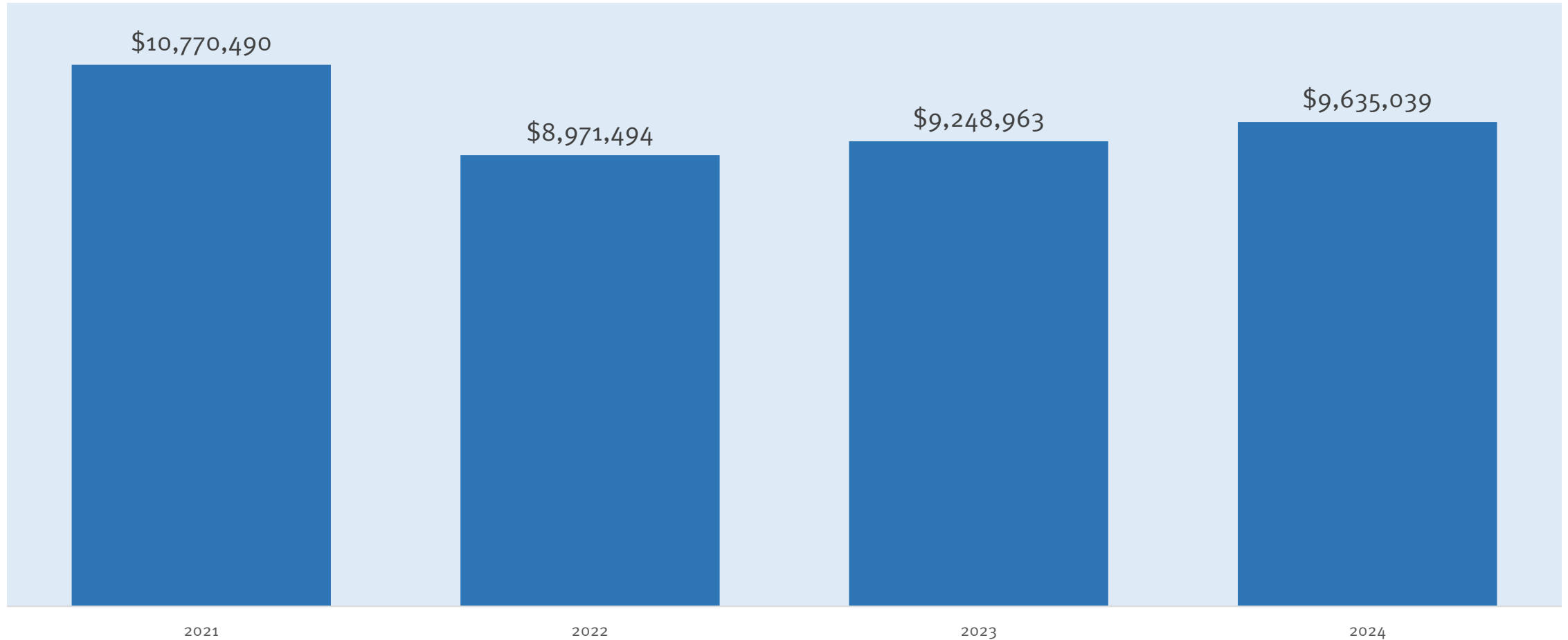
## Subsection 4.B

How Did the Life Sciences Sector  
Perform in 2024?

# Life Sciences Sector Up 4.2% in 2024

Last year saw a 4.2% rise in life sciences stocks worldwide. The sector's value rose by \$386 billion to end the year at \$9.6 trillion. Most of this reflected growth in obesity-oriented pharmas.

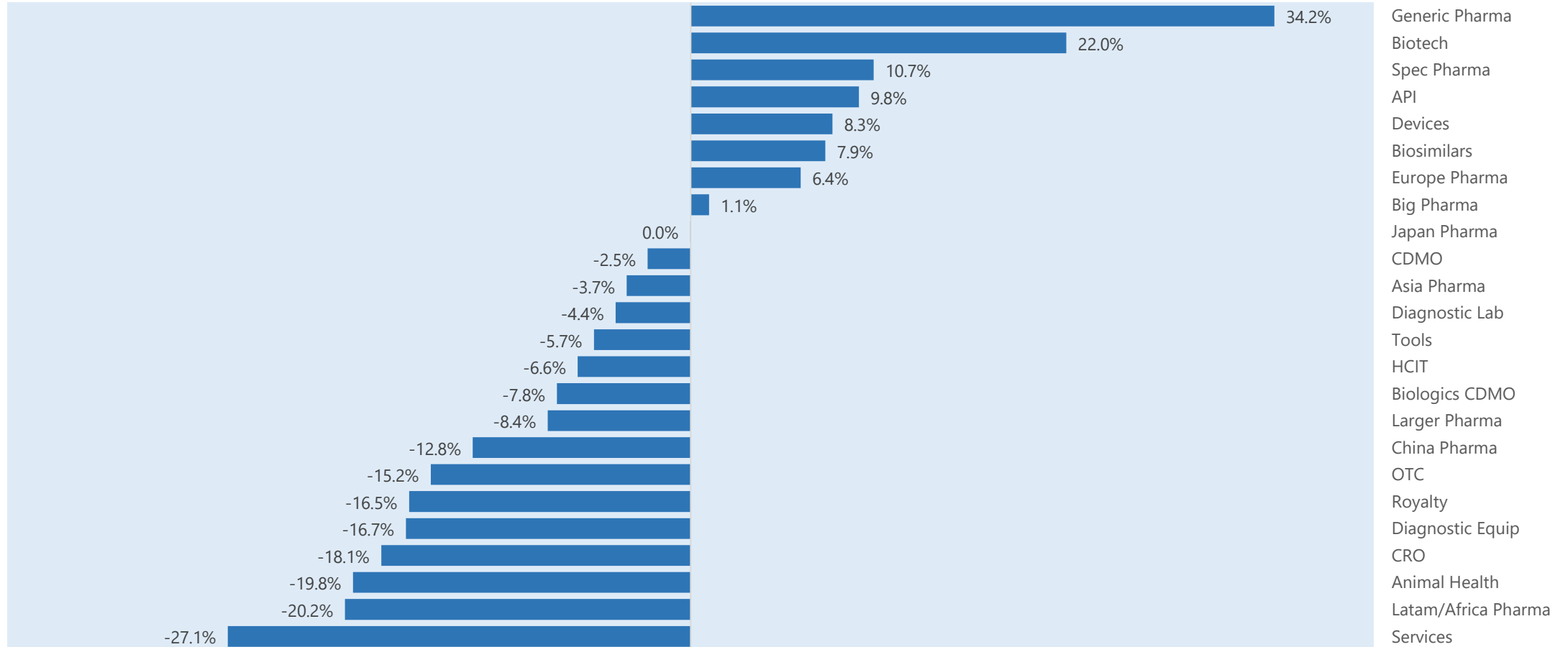
Total Value of the Publicly Traded Life Sciences Sector Worldwide at Year End, 2021 to 2024



# Life Sciences Subsector Performance During 2024

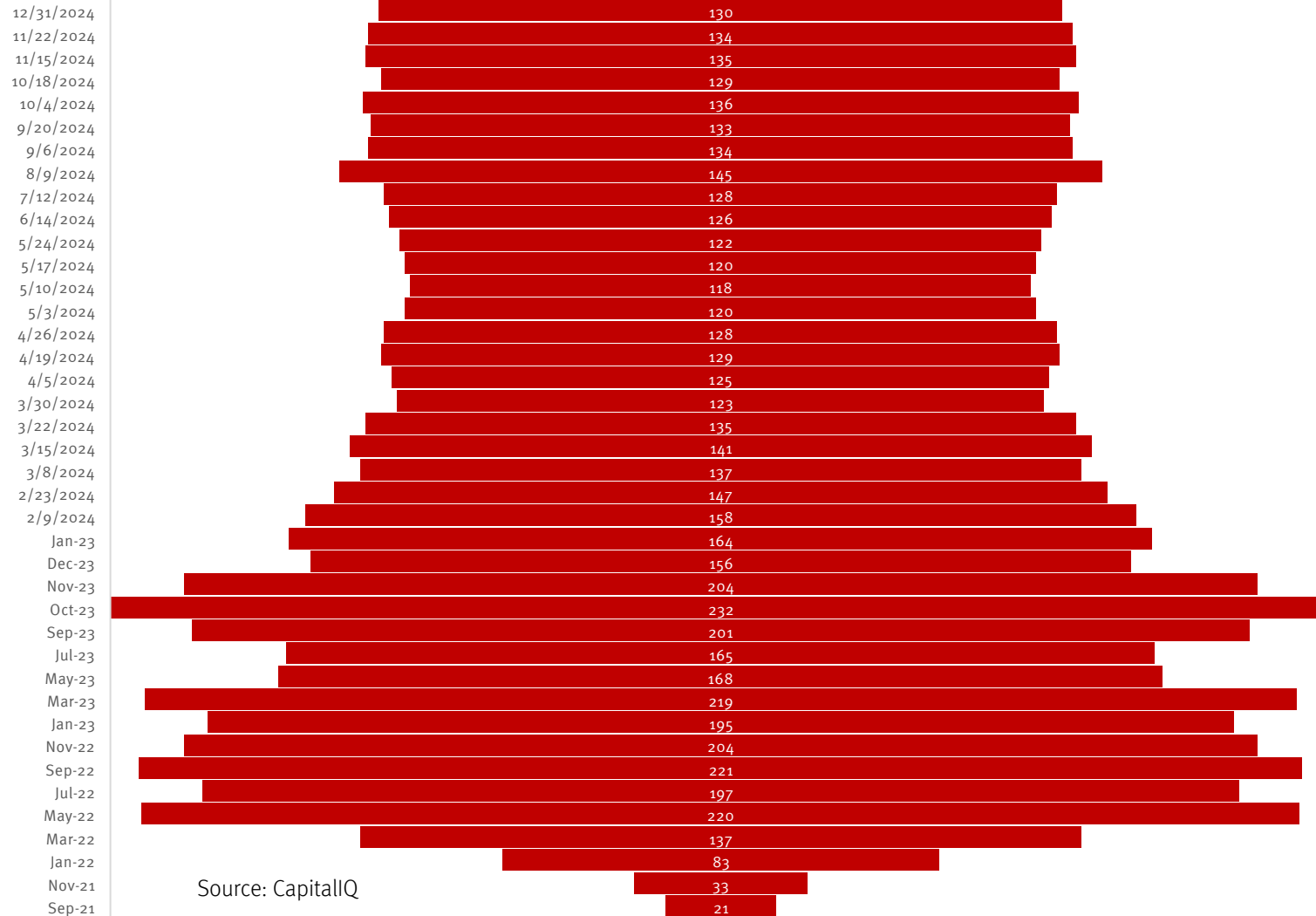
Generic pharma, spec pharma and biotech all did well last year. API, medical devices and biosimilars showed solid performance. In contrast, pharma services, animal health, CRO's and diagnostic equipment companies underperformed in 2024

Aggregate Value Change (Dec 30, 2023 to Dec 31, 2024, \$ millions)



# Number of Negative Enterprise Value Life Sciences Companies Fell to 130 at Year End

Number of Negative Enterprise Value Life Sciences Companies Worldwide



Source: CapitalIQ

The count of negative EV life sciences companies worldwide fell from 156 at the start of the year to 130 by year end.

A year prior the count was 220 so there has been substantial normalization of the measure of sector distress.

Even if the total number of biotechs didn't shrink that much, the number of companies where market participants seem to suggest a company is better off "dead than alive" dropped dramatically throughout 2024.

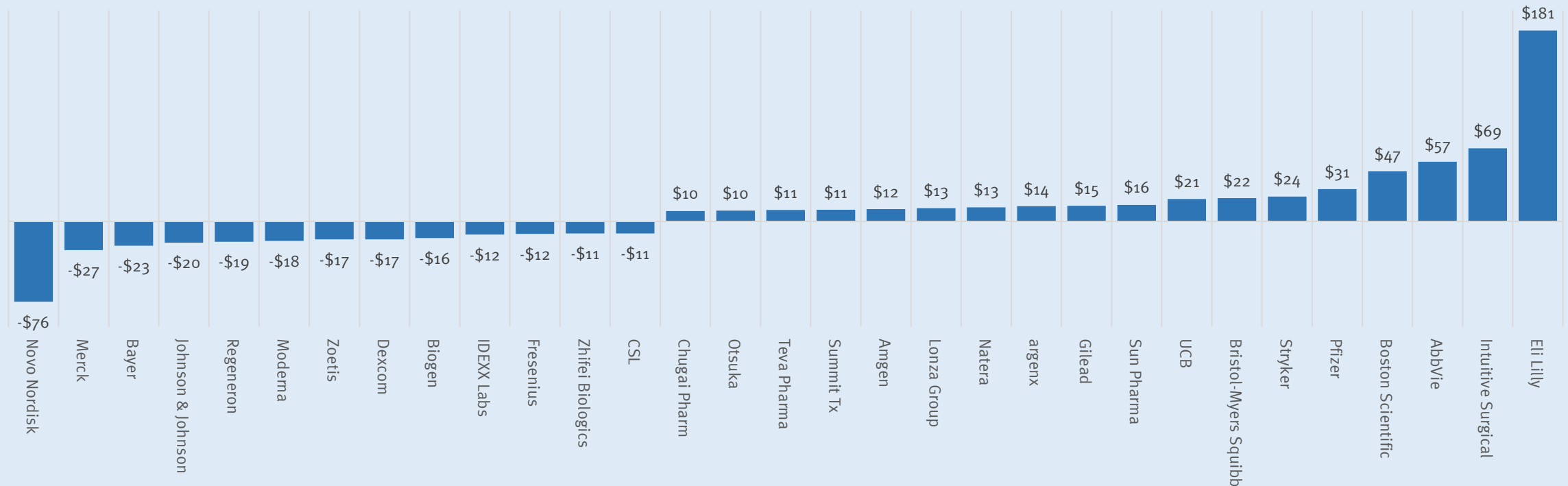


# Greatest Value Swings Among Life Sciences Companies in 2024

Lilly managed to add \$181 billion in value in 2024. Intuitive Surgical, AbbVie and Boston Scientific also delivered very impressive value gains. The third best value add in pharma was from Pfizer which is well down the road of a turnaround. Strong value addition is also quite notable at BMS and Gilead. UCB, argenx and Sun Pharma are mid-sized companies that added tremendous value in 2024. Novo Nordisk lost substantial value after its CagriSema clinical readout was disappointing.

**Life Sciences Sector, Greatest Swings in Enterprise Value, Dec 30, 2023 to Dec 31, 2024**

(companies gaining or losing \$10bn or more included in this chart)

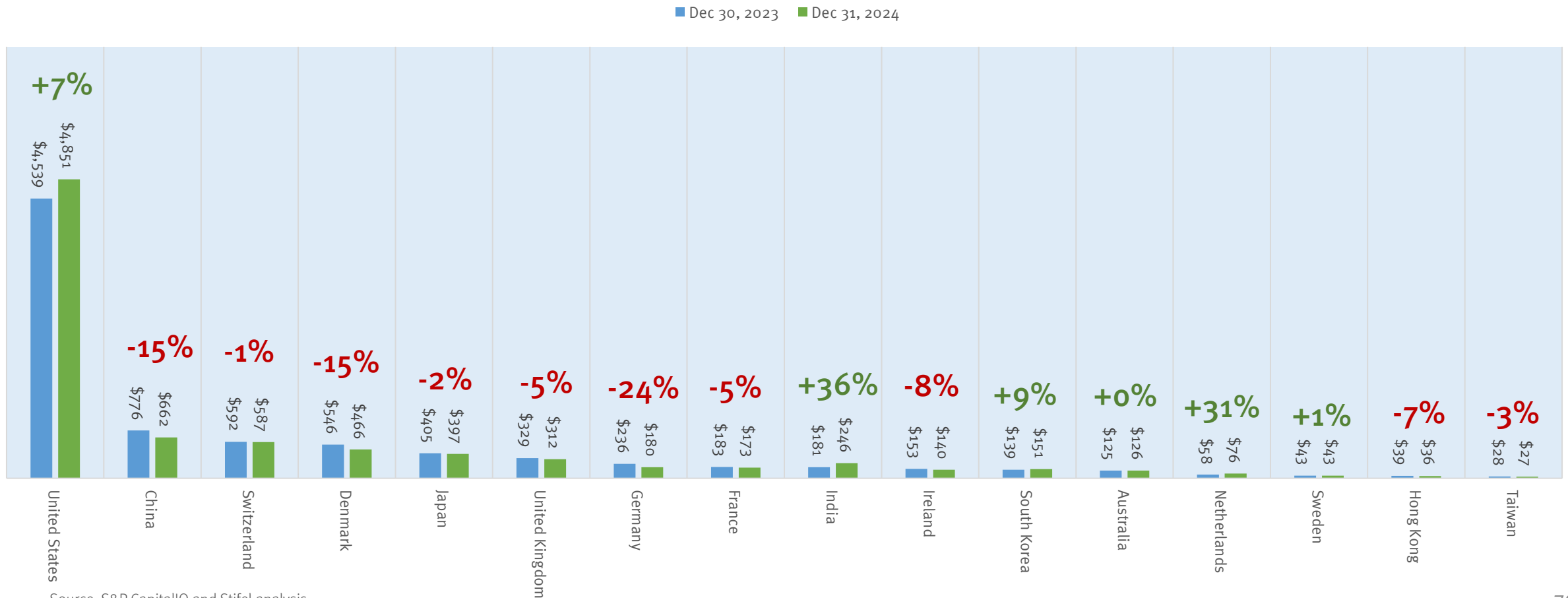


# Life Sciences Sector Performance in 2024 by Country

The U.S. did well – mainly because of the performance of Lilly and Intuitive Surgical. China took a hit as pricing in that country worsened and its pharma services groups (e.g., Wuxi Apptec) were hit by geopolitical issues. Denmark dropped on Novo’s decline. India did the best of any country in 2024 on a resurgent generics market and a strong domestic market. Netherlands did well due to argenx. In general, many countries were down a bit. This largely reflects our accounting for performance in US dollars in a year where the dollar rose.

## Total Market Cap of Life Sciences Companies by HQ Country, Dec 30, 2023 vs. Dec 31, 2024

(\$ Billions, Percent Change Shown Above Each Country, Sorted by Aggregate Cap on Dec 30, 2023)

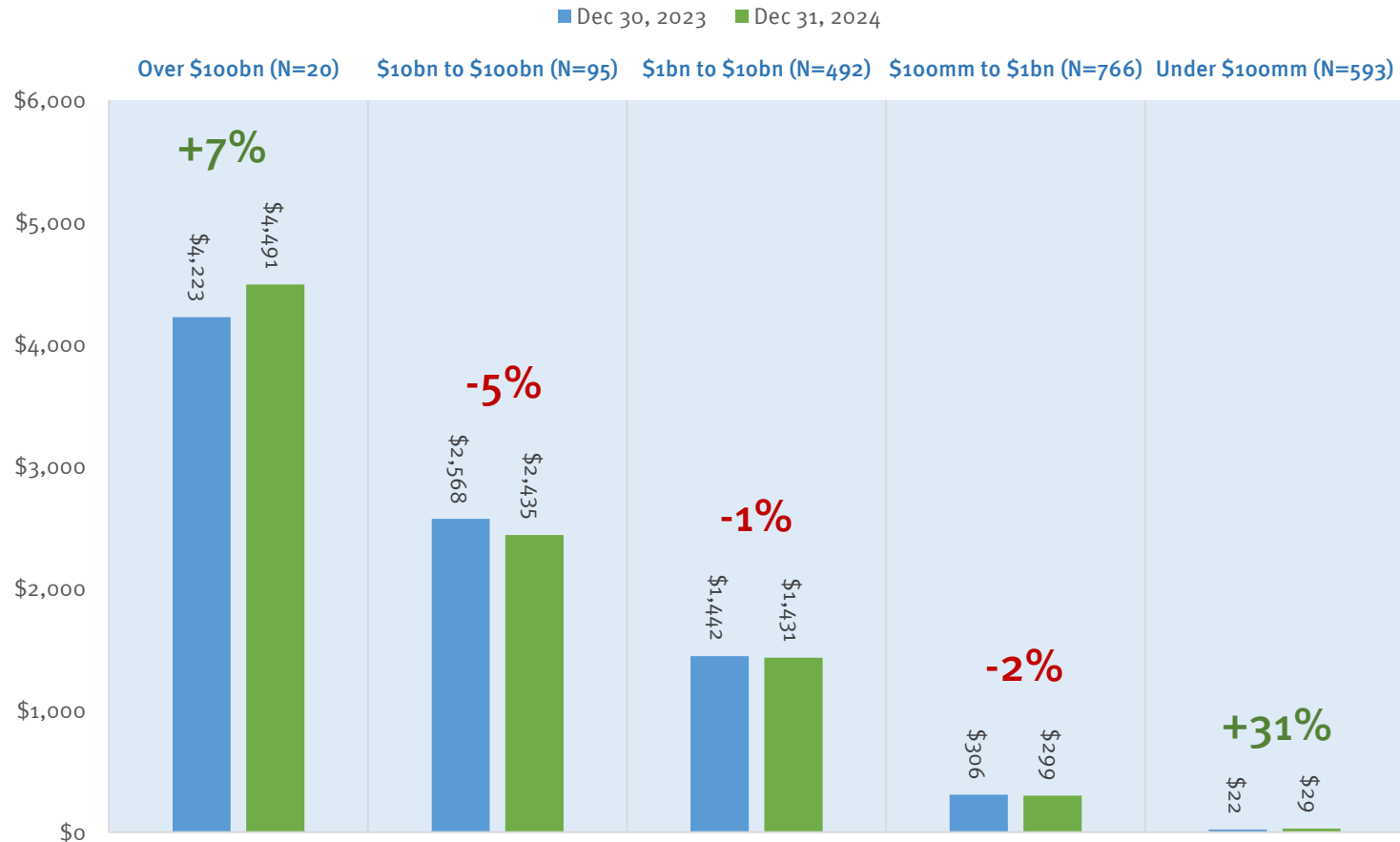


Source: S&P CapitalIQ and Stifel analysis.

# Large Caps and MicroCaps Life Sciences Players Outperformed in 2024

## Total Market Cap of Life Sciences Companies by Size Class Dec 30, 2023 vs. Dec 31, 2024

(\$ Billions, Percent Change Shown Above Each Size Class, Size based on market cap on Dec 30, 2023)



Large caps did well thanks largely due to Eli Lilly which gained substantial value on the back of the obesity boom.

Microcaps did well but, in aggregate, picked up only \$7 billion in total value. These stocks had been beaten down badly during the post-Pandemic period.

# Subsection 4.C

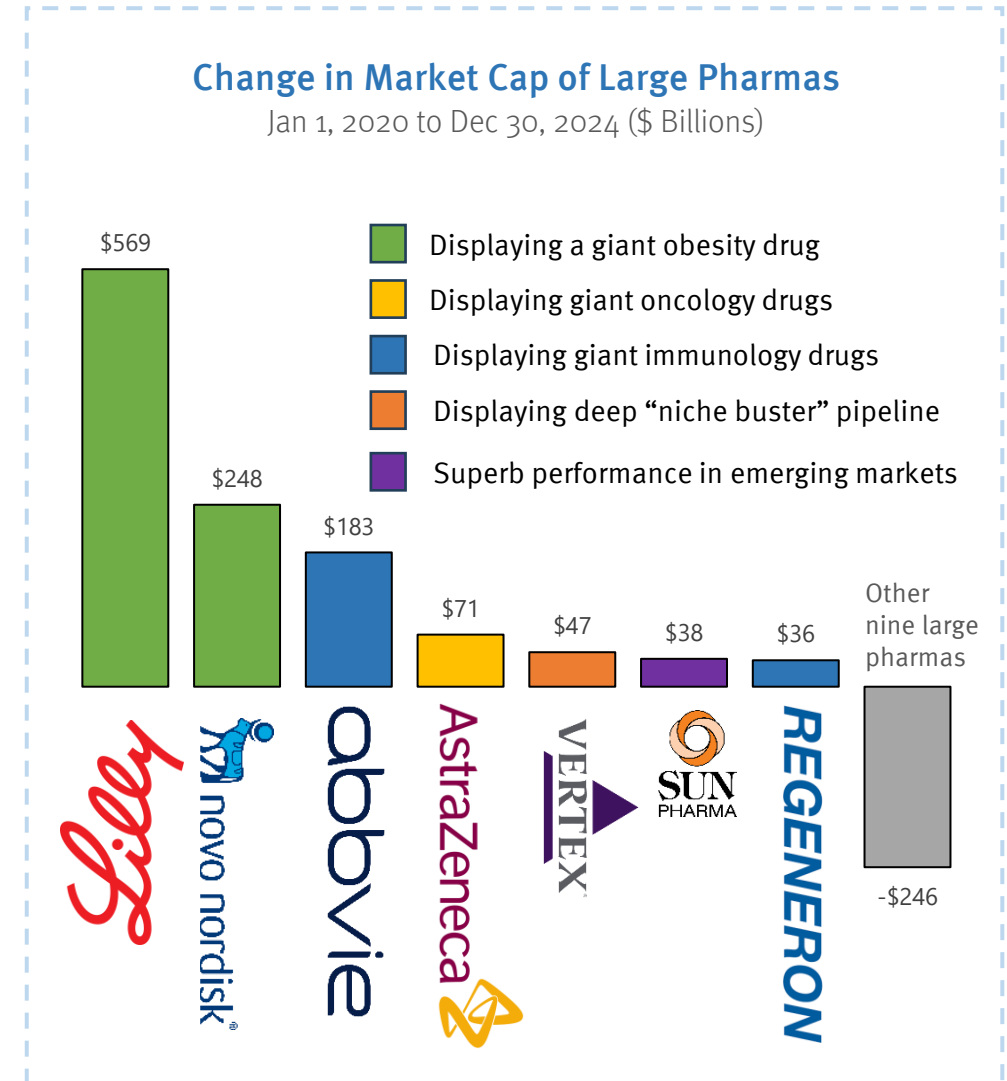
How Did Big Pharma Perform in 2024? And How Can Pharma Compete Against Tech?



# What's Happened to Big Pharma in the Last 48 Months?

The rules of the pharma game changed coming out of the Pandemic. There is a new thought process: “Go Big or Go Home”

- Real drugs for real diseases with real data are now in vogue.
- Massive “pipeline in a product” (“PiP”) drugs are in vogue.
- The big moves have been in **obesity drugs** where there is massive scale possible due to many indications and widespread application.
- Go for “efficacy on big markets” is the new mantra. Precision on narrow markets was the old mantra.
- Everything else is not so fashionable. This is visible in change in enterprise value of top pharmas since the start of the pandemic. See chart at right.
- The nine pharmas that are not successful engaging the market on a “go big” strategy are down \$246bn in aggregate market cap since Jan 1, 2020.
- There are several interesting counterexamples. Vertex Pharma has followed a “niche buster” strategy – a succession of \$3bn+ drugs for indications like cystic fibrosis and Type 1 diabetes.
- Sun Pharma has had two phenomenal years, adding more value since 2020 than even Regeneron (up \$38 billion in value). Sun’s strategy is to be a generic player in rapidly growing emerging markets and a highly efficient branded player in developed markets like the U.S. Sun is rapidly scaling up.



Source: CapitalIQ

# What We See Happening in 2025 Among the Largest Pharma

- **Novo Nordisk comeback:** With heavy ownership by a foundation Novo has amazing investor disclosure but very little hype about its pipeline.
  - We are the first to admit that Novo underwhelmed in 2024 on both monlunabant and CagriSema.
  - Further, Novo's key composition of matter patent on semaglutide (US patent 8536122) expires in 2026.
  - While Novo has many other Orange Book patents going out to 2033 most of its real patent protection will be gone after 2026. The remaining key 10,335,462 patent relates to specific dosing regimens of semaglutide.
  - However, rather than risk having this patent invalidated, Novo settled litigation last year with a group of generic companies led by Viatris. While the date of entry into the semaglutide market by Viatris is unknown, we would guess that this would be sometime around 2030, meaning that Novo has six years or so of semaglutide cash flows ahead.
  - Given the size of the market, this should work out to something in the range of \$100 billion to \$200 billion in free cash flow to come.
  - Our optimism on Novo stock stems from its CV portfolio which includes three phase 3 trials underway for ziltivekimab for atherosclerosis and Phase 1 studies of an NLRP3 in CV and an ANPTL3. Zilti could be an absolutely massive drug if the trial hits.
  - Further, Novo has multiple unannounced obesity programs involving novel MOA's. We think there is a good chance that some of these could work well.
- **Continued Strength from Lilly:** Lilly has an extraordinarily good pipeline with strength in both oral GLP-1's and next generation obesity drugs. The free cash flow from this pipeline alone could exceed \$500 billion. Further, free cash flow from tirzepatide could hit a similarly large value. Lilly seems to have fallen back a bit in Q4 2024. We don't particularly see the rationale particularly given the rest of the pipeline, particularly their Lp(a) drug.
- **Merck Likely to Deliver:** We really like Merck's position right now and can't quite understand why their shares didn't do better in 2024. Merck has a great CV pipeline, a monster product in WINREVAIR® for PAH, a strong vaccine portfolio, a very promising TLA1, an extraordinary set of ADCs from a partnership with Daiichi, a promising prostate drug and three newly in-licensed products from China (Curon's TCE for autoimmunity, Lanova's VEGF<sub>x</sub>PD1 bispecific and Hansoh's GLP-1 oral). Merck has the clinical prowess to turn this pipeline into large sales.
- **AZ Likely to Shine:** AstraZeneca has publically said that they intend to hit \$80 billion in revenue by 2030. We think they have the pipeline to get there between their extraordinary strength in oncology, rare disease and cardiovascular. We like AZ's oral GLP-1 from Eccogene a lot and note that they have a surprisingly respectable portfolio in the respiratory and immunology field.
- **Sun Pharma Momentum Continues:** Sun Pharma has a surprisingly strong position in emerging markets (#1 in India) and should be able to ride the growth in that region for years to come. Further, we really like Sun's portfolio in North America and Europe and expect to see further growth ahead.

# Gap Between Top Healthcare and Tech Stocks Widened in 2024

The world's top five tech companies are worth **\$14.8 trillion** at the end of 2024. Compare this to \$10.3 trillion at the end of 2023.

The world's top five healthcare companies were worth **\$2.4 trillion** at the end of 2024. Compare this to \$2.2 trillion at the end of 2023.

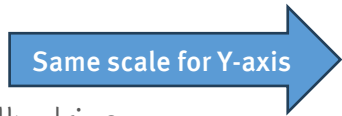
Each of the top four techs are individually larger than the top five healthcare companies **combined**.

The gap widened in 2025 from approximately 4.6:1 to 6.3:1.

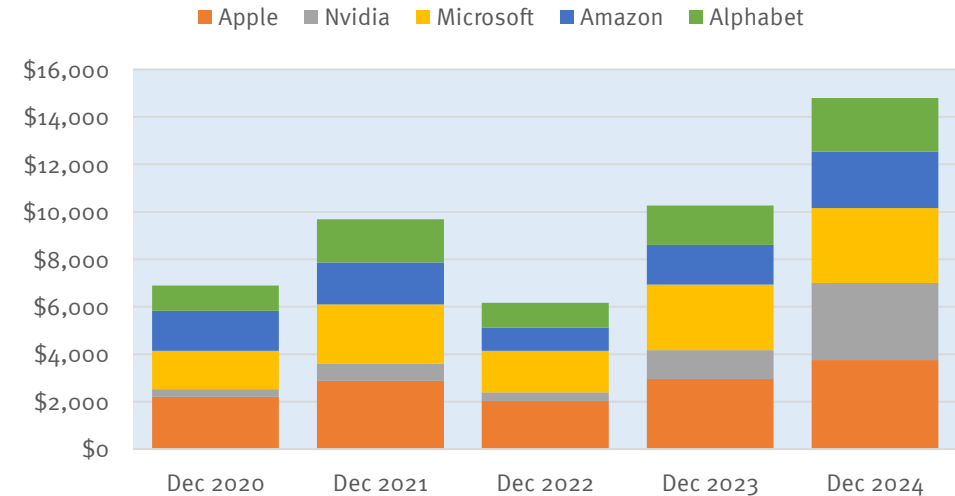
But the GDP contribution of healthcare is far larger than the GDP contribution of technology.

Fundamentally, the patent rules on drugs have led the healthcare sector to have lousy monopolies compared to those of the tech sector.

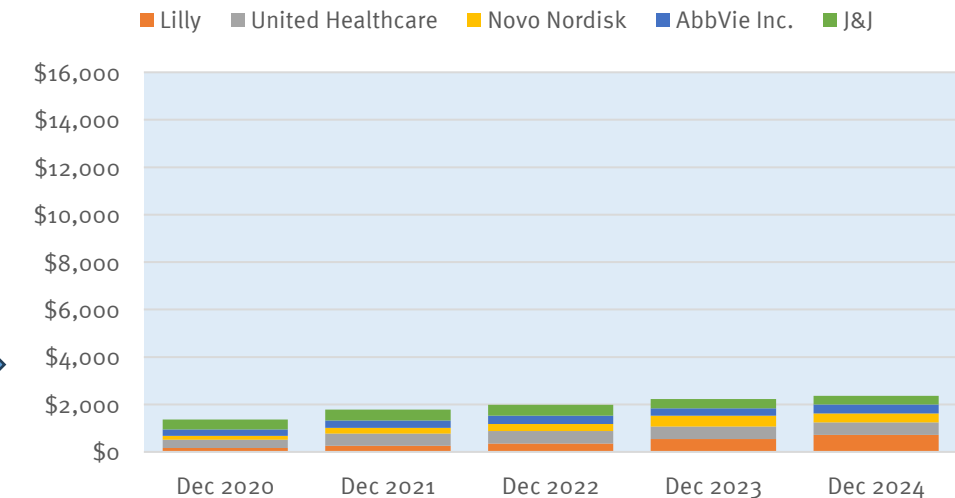
On the next two pages we reprint some pages from past presentations arguing that pharma companies need to and can start to act more like tech companies to get beyond the lousy monopolies created by the current patent system. The core idea is to integrate drugs with treatment that is algorithmically driven.



**Top Five Tech Companies Enterprise Value (\$ billions) Dec 2020 to Dec 2024**



**Top Five Healthcare Companies Enterprise Value (\$ billions) Dec 2020 to Dec 2024**



Source: CapitalIQ

# Pharma Needs to Bust Out of the LOE Trap: Algorithmic Competition is One Way to Do It

## Is there an opportunity to redefine healthcare product scale and profitability?

### Specifically...

Can one build a highly profitable healthcare company that has \$170 billion or more in sustainable revenue?

Pharmas trade today at 6X revenue. This is what it would take to get to a \$1 trillion pharma / healthcare co.

## Comment on UnitedHealth Business Model Versus That of a Pharma

1. UnitedHealth has a very powerful business model: become the leading Medicare insurer and, simultaneously, build out the largest health insurance footprint in the United States in Medicaid, employer and individual segments.
2. Compete wherever possible for value-based care contracts where a broad platform would be useful.
3. Focus on maximizing value of each beneficiary using analytics on incoming data feeds and send out nurse practitioners to the homes of high-risk Medicare beneficiaries who miss their Annual Wellness Visits.
4. **An important element is the integration of physician care and associated services in Optum.** The reasons are many. First, one can direct insureds to Optum sites where physician incentives are aligned with the insurer. Second, care in itself is a good business and synergies gained from the data platform in treating so many millions of patients can prove to be quite helpful.
5. A further value element is the **adoption of standardized care algorithms from mining claims data.** It is not unusual to find that one way to delivering care is less expensive while good for patients. Once this is done it can be adopted by all 70,000 physicians who work for United.
6. The integration of a PBM has obvious value to both government and employer customers. United can focus on delivering the best pharmaceuticals to maximize customer healthcare outcomes while control overall payroll spend with an integrated PBM.
7. This business model has high long-term growth and allows the vertically-integrated payor to build a strong consumer brand, build a data moat and, potentially, lock in consumers.
8. **Pharma models are radically different** – involving high R&D spend, relatively low returns on R&D and finite monopolies, impacted by generic competition and 20-year patent lives.

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## Article: The Biggest Company in The World

andressen  
horowitz Its time to build

By Daisy Wolf and Vijay Pande, Nov 12, 2022

We think the biggest company in the world will be a consumer health tech company.

This may sound crazy to some, but why shouldn't this be true? Four of the top five biggest companies in the world are consumer companies, and healthcare is one of the nation's biggest industries.

In fact, those massive consumer companies—Google, Apple, Facebook, Amazon (GAFA, for short)—are all working to move into healthcare because they realize the size of the opportunity: a \$4 trillion American industry that makes up 20% of US GDP (and growing).

Source: <https://a16z.com/2022/11/11/the-biggest-company-in-the-world/>

On the other hand, the world's biggest healthcare company (the 8th biggest company in the world), UnitedHealth Group (UHG), is not a tech company and is also seriously lacking in the consumer engagement department. While they're technically a consumer company, selling half of their products direct to consumer (DTC), their poor consumer engagement—reflected in their NPS of 4—will always cap their potential and keep them trapped as the 8th biggest company in the world.

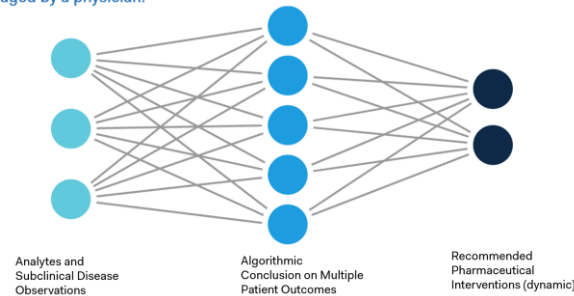
**Our bet is the future's biggest company, the consumer health giant, won't be one of today's big tech or incumbent healthcare companies. It will be a consumer-obsessed, healthcare-native tech company that reimagines what care can look like.**

When many people think "consumer health company," they think Hims or Ro, but a consumer health company doesn't need to be DTC for distribution nor does the consumer have to be the one paying. Instead, what matters is that consumers know they're interacting with the company and have the opportunity to feel loyalty toward it.

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## A Future Potential Model: Similar to Neural Net in Structure

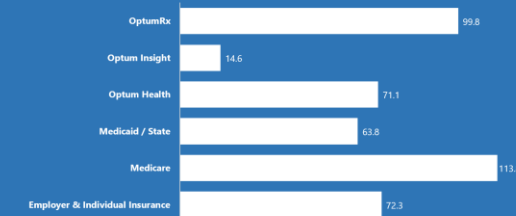
Multiple pills for multiple diseases (and subclinical states) recommended by computer but managed by a physician.



The core idea

## UnitedHealth Has Built an Impressive, Vertically Integrated Healthcare Payor and Provider Platform

Revenue by Segment, UnitedHealth, 2022 (\$ Billions)



United's PBM (OptumRx) is a huge business with \$99.8 billion in revenue although this business only has a 5% operating profit before tax margin. The OptumHealth segment provides access to networks of care provider specialists, health management services, and care delivery. This business generated \$71 billion in 2022 revenue and \$6 billion in operating profits. The OptumInsight segment offers software and information products. United's Medicare business is particularly large at \$113.8bn and we estimate generates more than 40% of UnitedHealth's operating cash flow.

Source: <https://www.unitedhealthgroup.com/newsroom/2023-01-13-fourth-quarter-full-year-results.html>

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## Big Potential for Pharma in These Ideas

Today we have one example of a major integrated provider of diagnostics and therapies which is Roche.

1. Roche is principally developing precision assays for cancer therapies via genomic and histological assays.
2. However, there is very little *real integration* between the drug development teams at Roche and the diagnostics side.
3. Roche does not appear to be thinking about how to leverage diagnostics to drive pharma sales in a transformative way.
4. We believe that a future therapeutics company could generate as much value through disease state algorithms as via therapies themselves.
5. Therapies can be state-specific and adjusted in real-time. The algorithm and the pharmaceutical intervention(s) are *one and the same*.
6. All of the benefits of the tech competition model would accrue to a pharma who followed this approach.
7. Just as importantly it becomes much more difficult for a branded or generic competitor to overcome a company that combines pharmaceutical products with diagnostic algorithms in cooperation with a medical provider.

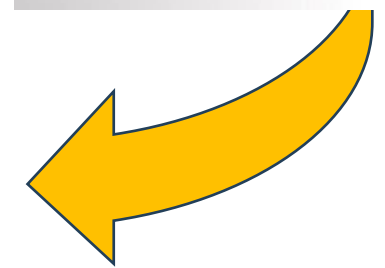
# Previously Proposed Model of Pharma's to Feel More Like TechCo's: Algorithmic Competition

## A Vision of the Evolution of the Pharma Sector



"I think the biggest company in the world will be one that can invent technology to prevent or reverse disease (or both) and vertically integrates (like tech has done, and like you mention) to own the entire care system. Disintermediating hospitals and Pharma. Better for people."

**Bob Nelsen**  
Partner  
ARCH Venture Partners  
*(reacting to A16z article on twitter)*



Also see: <https://www.youtube.com/watch?v=d0ljiuwkJC4>



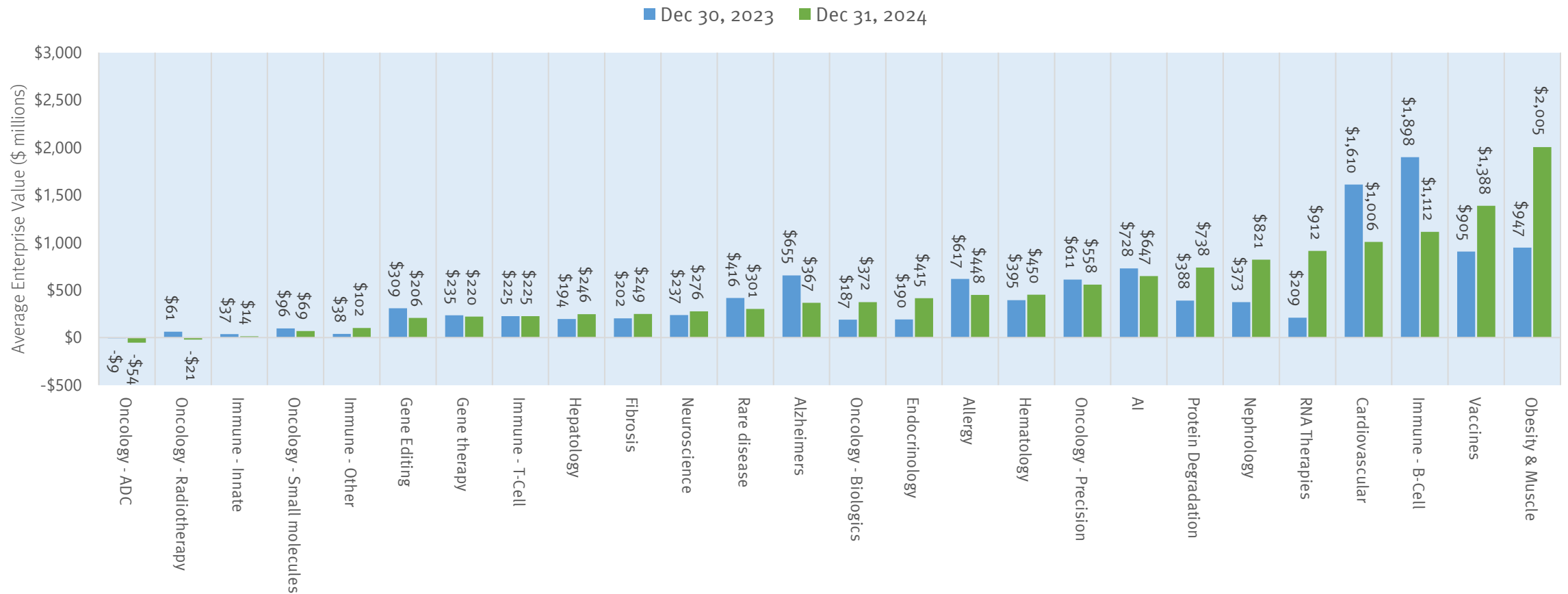
# Subsection 4.D

What Drove U.S. Biotech  
Performance in 2024?

# U.S. Biotech Values Today Highest in Obesity, Vaccines and B-Cell

The most valued sectors in biotech today are in obesity, vaccines and B-cell immunology. We have seen substantial values drop in cardiovascular, gene editing and Alzheimer's and strong value pick-ups in RNA therapeutics, protein degraders and oncology biologics (principally engagers).

Average Enterprise Value by Subfield of Biotech, Dec 31, 2024 vs. Dec 30, 2023 (\$mm, n=330, U.S. biotech only)

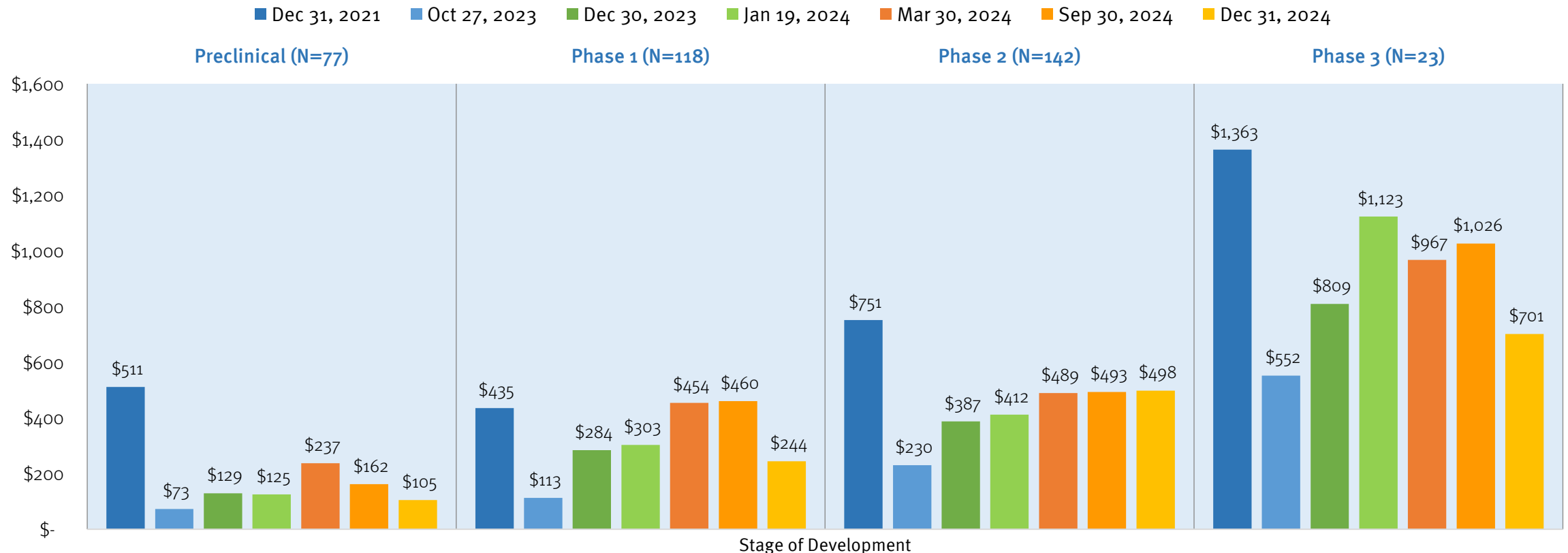


# Last Quarter Saw a Big Drop in Values of Early-Stage Biotech

The average preclinical biotech was worth \$511 million three years ago. One year ago, that value had dropped to \$125 million. As of last week, the value dropped further to \$105 million. We saw a big drop in the value of Phase 1 biotechs in Q4 last year. Phase 2 biotechs held up well (this is where some of the stronger stories in the market lay). In contrast, Phase 3 biotech values fell quite a lot in Q4.

## Average Enterprise Value of a U.S. Biotech Listed by Stage of Development, Dec 31 2021 to Dec 31, 2024

(\$ Millions, U.S. Exchanges, N=360)

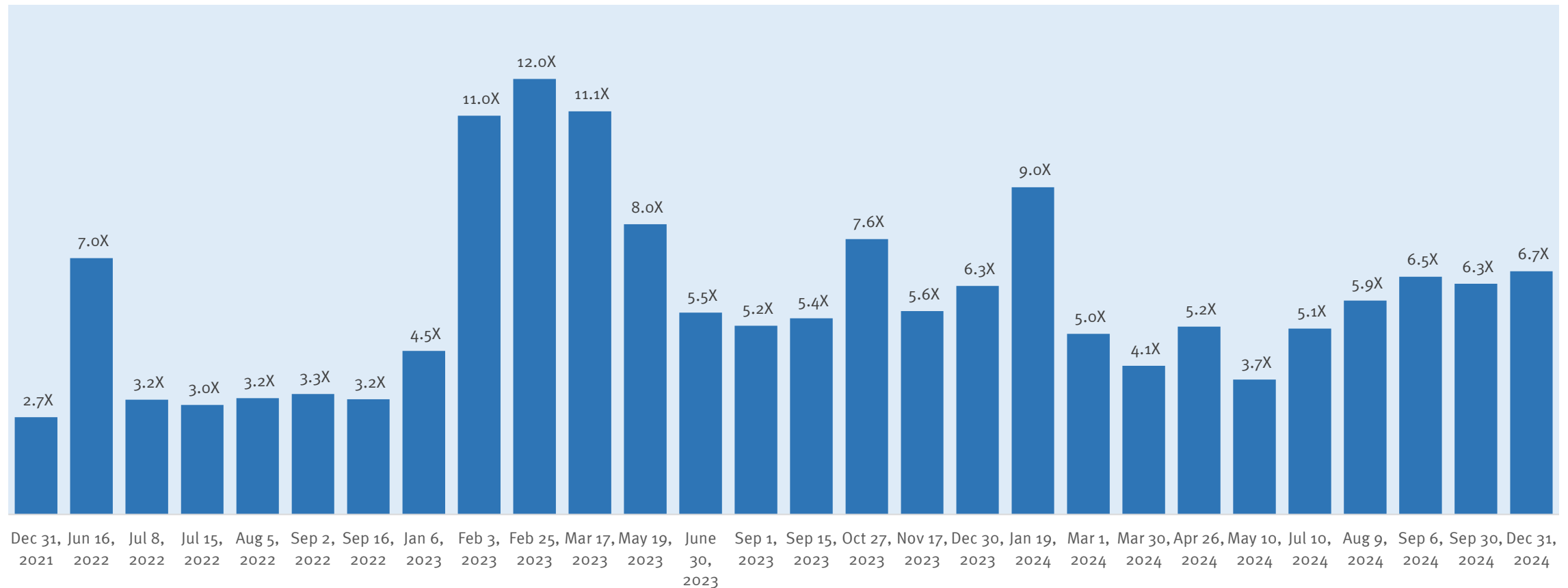


Source: CapitalIQ and Stifel analysis. Phase of development is defined by release of at least some efficacy data from a given stage of clinical development.

# The Effect of High Interest Rates on Biotech Remains Clear

Investors tend to flock into later stage biotech stories when interest rates rise. This is perfectly rational. When the 10-year Treasury came down in mid-2024 you could see the relative value of preclinical biotechs come up. As long rates ground up during the year, you can see the hit that these stocks took relative to later stage stories.

Ratio of Average Value of a U.S. Phase 3 to a Preclinical Stage Biotech, 2021 to 2024



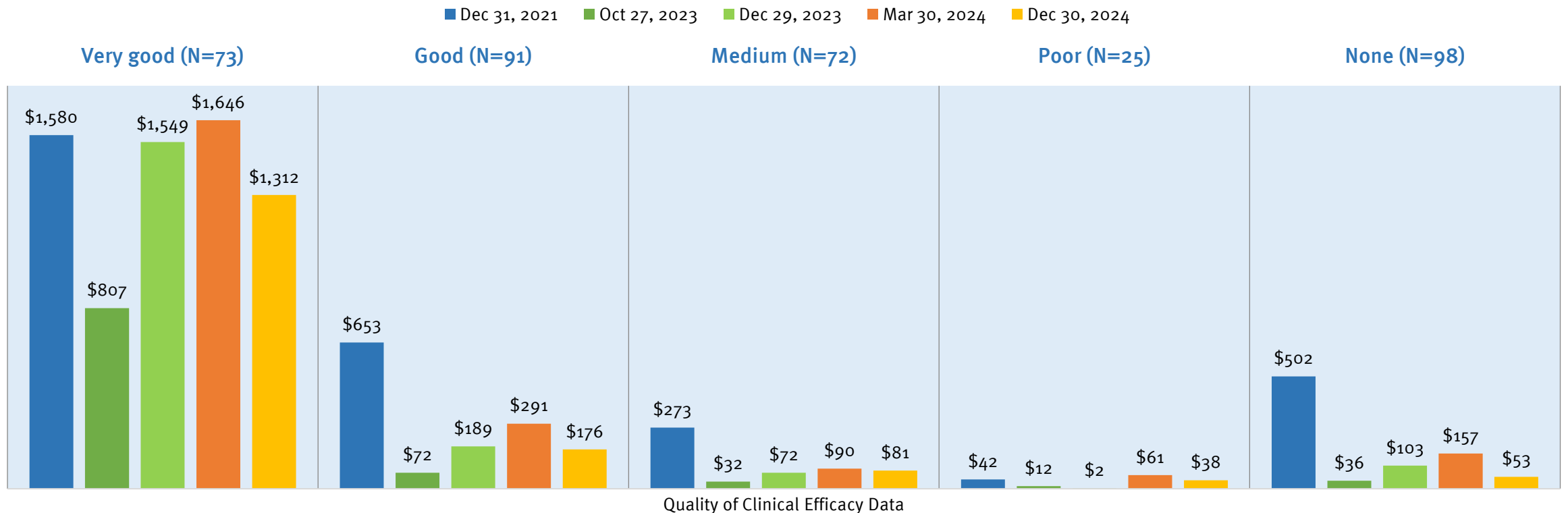
Source: CapitalIQ and Stifel analysis. Phase of development is defined by release of at least some efficacy data from a given stage of clinical development.

# Biotech Quality Premium Has Risen in 2024

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. Investors flee to quality in tough times. In Q4 of 2024 the value of companies with “very good” data fell but held up relatively well given the strength of the downdraft in the market. Unfortunately, we saw a huge drop in 2024 among companies with no dataset. At present, the public markets are a very tough place for a “biotech story stock” to live before it has produced clinical data. This is a complete turnabout from the Pandemic period.

## Average Enterprise Value of a U.S. Biotech Listed by Quality of Efficacy Data

Dec 31, 2021 to May 10, 2024, (\$ Millions, US Exchanges Only, N=359)



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.

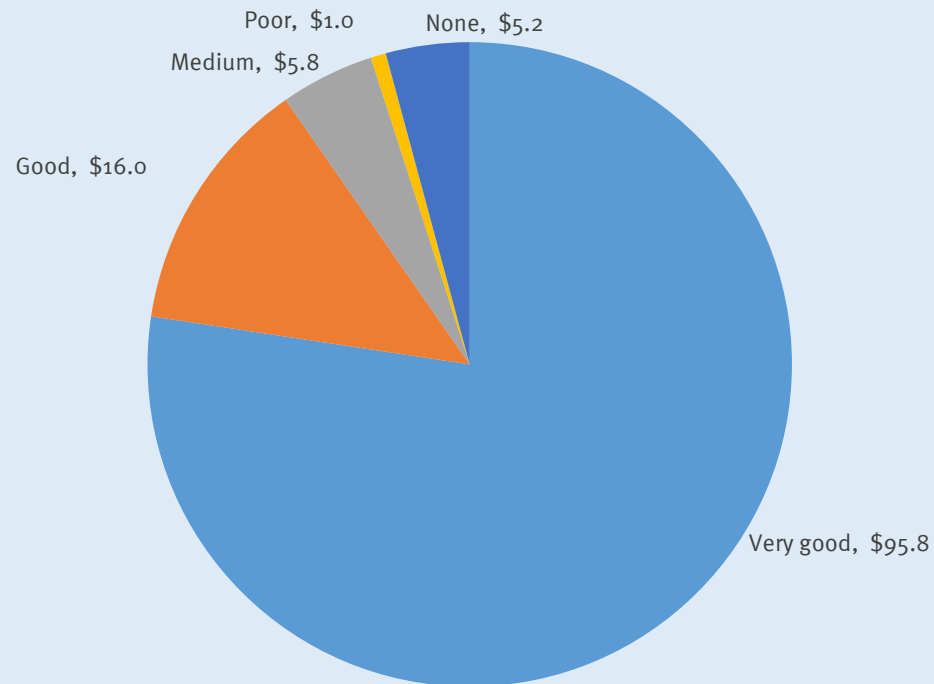


# The Public Biotech Market Has Become a “Winner Take All” World

Today, only 22.6% of U.S. public biotech value flows to companies with less than a “very good” dataset. Just 23 months ago, more than a majority of biotech value flowed to such companies.

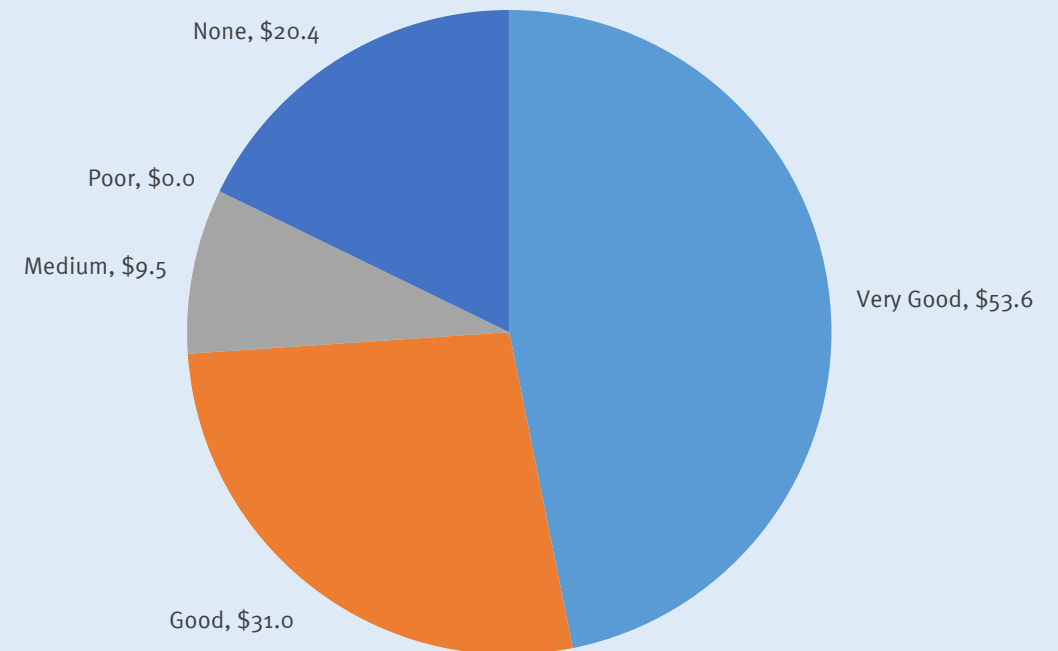
**2024**

Total Enterprise Value (\$ billions) of the U.S. Biotech Sector by Quality of Dataset on Last Completed Stage of Development, Dec 31, 2024



**2022**

Total Enterprise Value (\$ billions) of the U.S. Biotech Sector by Quality of Dataset on Last Completed Stage of Development, Nov 30, 2022

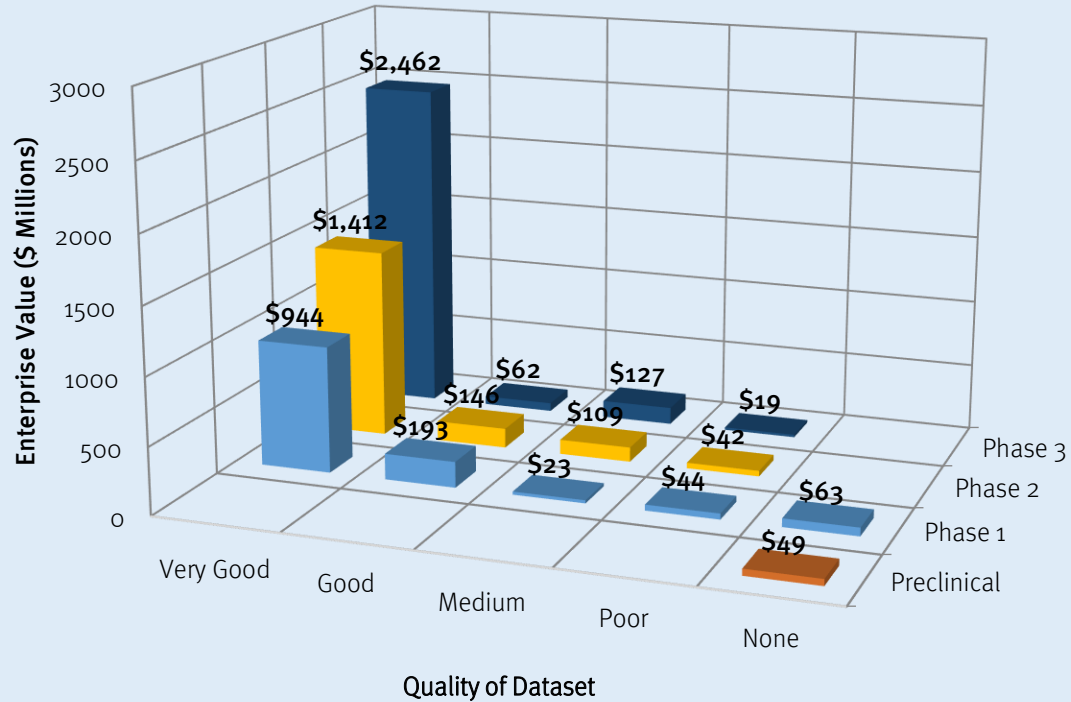


Note: These data are sourced from CapitalIQ and based on Stifel research on the dataset quality for a company’s lead asset. We classified datasets that indicated a high probability that the drug would meaningfully improve on the standard of care for a disease as “very good”. We classified “good” data 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.

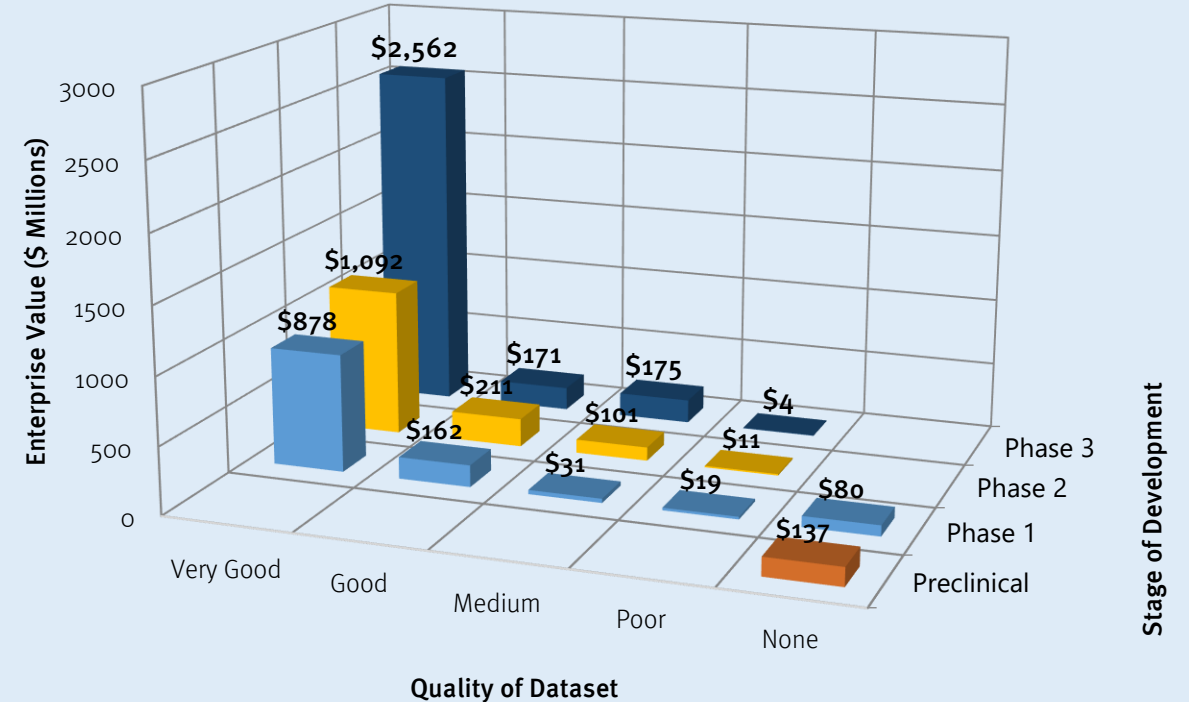
# The Most Valued Biotechs are Those With “Very Good” Phase 3 Data

The biotech market is looking for really strong clinical data.

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



Average Enterprise Value of a Biotech Listed on U.S. Exchanges by Stage of Development and Quality of Data, Jun 30, 2023



**Notes:** 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. Stage of development refers to the stage of the last completed trial rather than the stage of ongoing clinical trials.

# Subsection 4.E

## **The China Syndrome:**

Is Chinese Sourced Innovation an  
Existential Threat to Western Biotech?

# China Innovation is Here to Stay

It's not exactly a secret that the Chinese have gotten really good at biotech.

As illustrated on the next page Chinese molecules became increasingly important in 2023 and 2024. At this point nearly a third of molecules sourced by big pharma through licensing deals are coming from China. [Thanks to Chris Dokomajilar from DealForma for pulling together this data for us on the fly].

Obviously, in a slow biotech M&A environment, one has to ask the question: Is the availability of good molecules from China a problem for U.S. biotech?

The answer is obvious.

The availability of Chinese molecules is not a good thing. At least, if you are Western biotech company.

Chinese molecules are generally well designed and available to pharma at prices that are less than what it would cost to buy them on the biotech market.

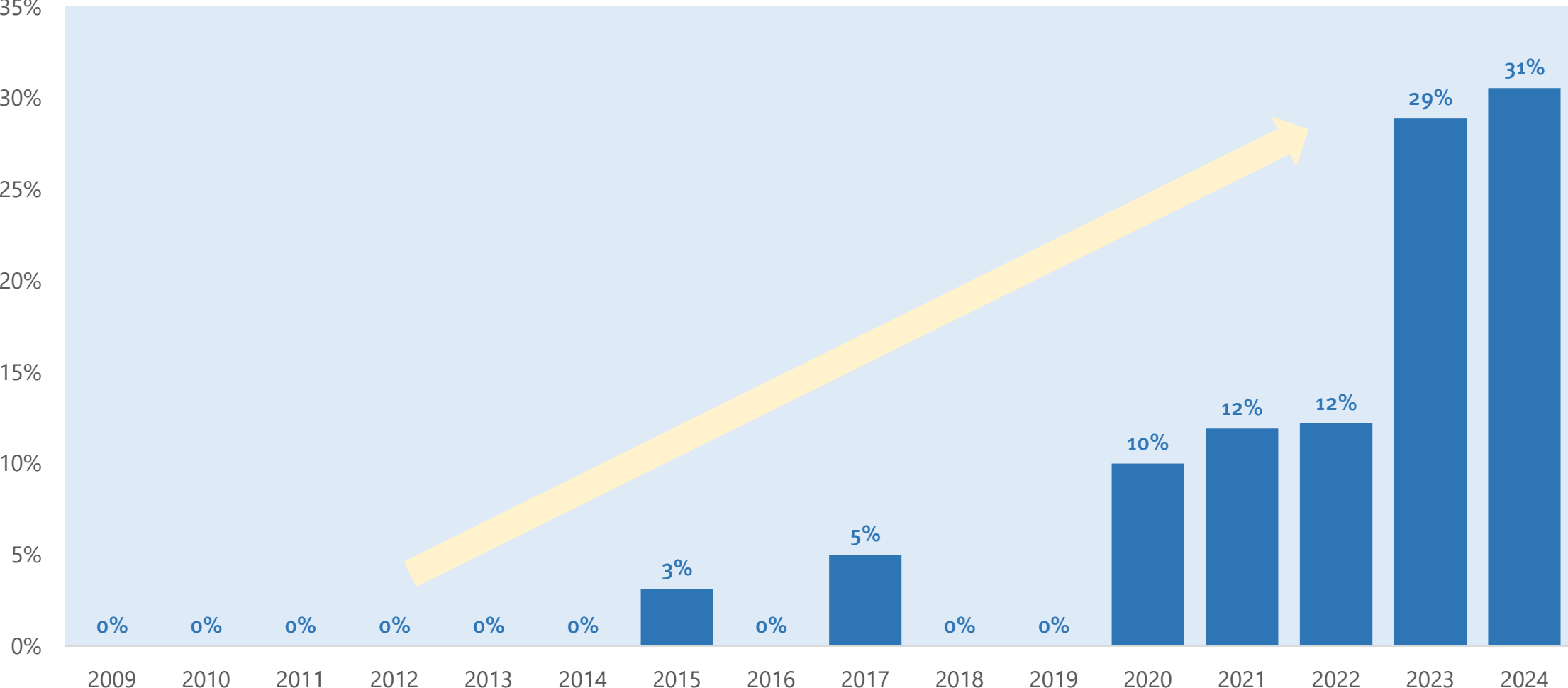
To illustrate, Structure Therapeutics has roughly a \$1.6 billion market cap. With a normal premium it would cost something like \$2.4 billion to buy them. If they would even sell when you made that phone call. Merck went out last year and bought a perfectly good clinic ready oral GLP-1 from Hansoh for \$112 mm upfront. The molecule is not as advanced as Structure's lead but Merck also gets a molecule at roughly a twentieth of the cost of what it would have cost to access Structure's. Merck made a choice. Don't buy Structure. Do buy the Hansoh molecule.



# Pharma is Sourcing Nearly a Third of External Molecules from China

## Percent of Large Pharma In-Licensed Molecules Sourced from Chinese Biotechs

(Upfronts of \$50mm or more), 2009 to 2024



Source: Dealforma



# China Innovation is an Issue for Biotech

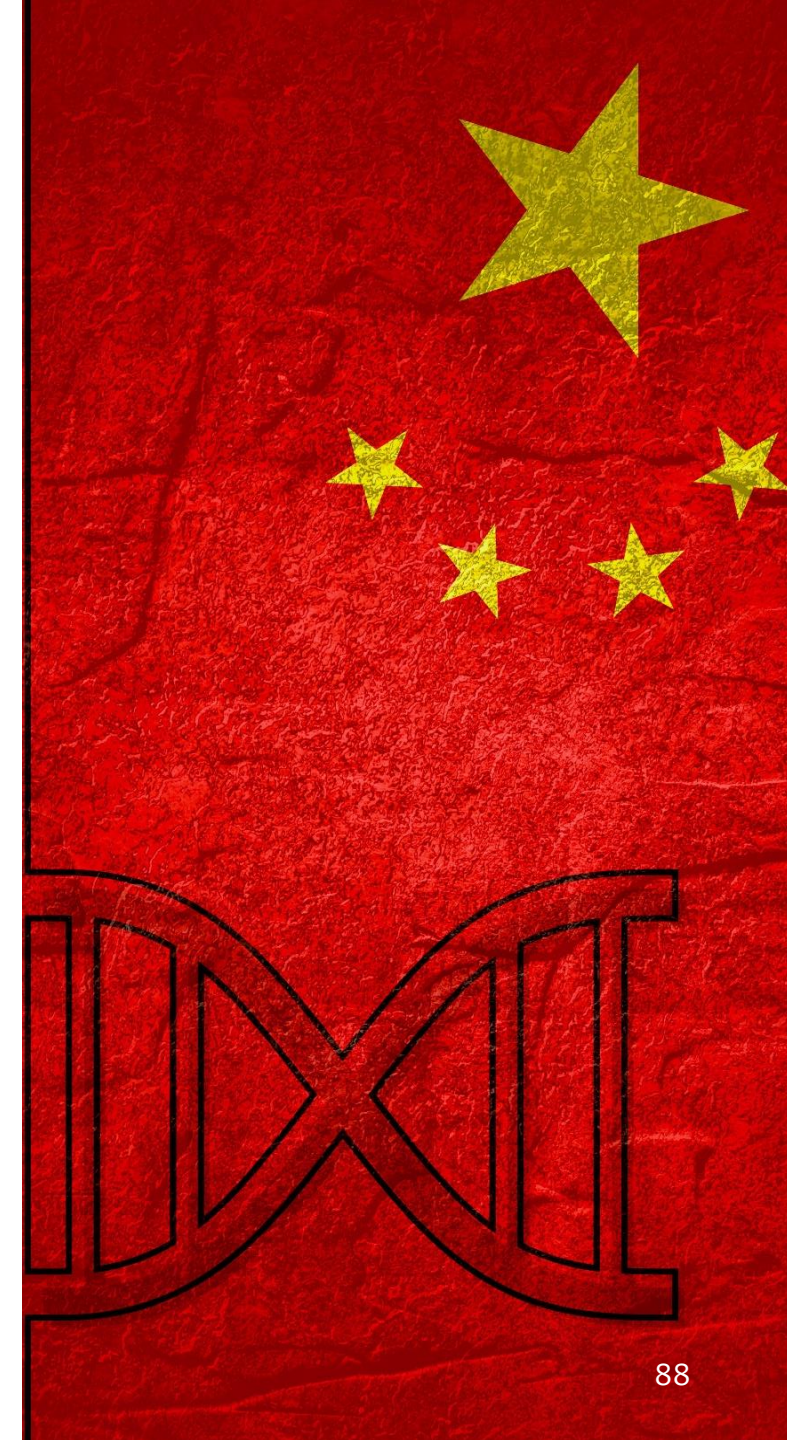
We have spoken directly to multiple large pharmas and they have made it clear that they are comfortable buying molecules from China and appreciate the ability to save their shareholders dollars versus equivalent molecules sourced from U.S. or European biotech M&A.

Our own view is that this trend is just getting started. We spoke to Jeff Jay of Great Point Partners and he had this to say:

“I feel all the Phase I and preclinical compound deals being done with Chinese companies are very, very bad for the US VC biotech ecosystem. It is even tougher to track the clinical progress of these compounds and they bite US private and public investors when data is released like being shot by a covert sniper. By our count, these Chinese licensing deals are almost half of the private pharma & large biotech licensing deals in number, up from close to *zero* ten years ago. These are deals that would otherwise be done with a US VC backed company focused on the same target. But they are done at about a third of the up front money, generally are fast followers with better efficacy and milestones appear to be about a third of US VC deals. The Chinese are delivering a better product at a lower price point. I don't think the VC community has figured out just how bad this is for them if this trend continues.”

Credit to Jeff for coming out and saying what should be on the mind of every VC. Of course, there have been some amazing deals happening such as the situation when RTW, Bain and Atlas picked up a TSLP from Hengrui to create Aiolos and turned around and sold it for a large multiple to GSK less than a year later. These guys are giving Roivant a run for their money!

The issue with this type of VC molecule “flipping” is that the VC's can (and are) get disintermediated by the pharmas who can go direct themselves. On a recent trip to China, one observer said that the majority of Western large pharma Heads of R&D had been in the country in the same month last year.



# Innovation Competition is Going to Get Worse

We received further input on this topic from Brad Loncar CEO of Biotech TV:

“This China competition issue is real. Over the last year, \$6B of licensing upfronts went to China companies for licensing deals...this competition did not exist before, and in prior years the money would have gone to XBI companies. Last year was just the start of that and if some kind of protectionism is not put in place, it's going to have a big effect on the future number of smaller type companies that exist in the U.S. and their chance of success.”

Our own view is that competition in biotech is going to accelerate in the years ahead and not go back the other way. It's been with us from day one. Remember the jostling way back when between Genentech / Lilly and Novo Nordisk on recombinant insulin in 1976 or the battle between Genetics Institute (now part of Pfizer), J&J and Amgen over EPO in the early 1980s?

Chinese innovation is just part of a broader trend – the availability of great molecules from a wide variety of sources. Specifically, bear the following in mind:

1. It's not just China. Competition for biomolecule development is broadly globalizing. For example, India is now getting into the game in a serious way. Glenmark's Ichnos sub reported first-in-class [data](#) for a triple TC engager at ASH in December. We were *wowed* by the data. Zydus of India is now out [ahead](#) of Novartis and Roche in the NLRP3 space. They are planning to run a pivotal study in 2025 for their NLRP3 and they also have a PPAR that looks just as [good](#) as Cymabay's molecule.
2. The Chinese are moving quickly to build first in class innovation capabilities and are advancing fast in basic biologic science. The VEGF x PD1 idea, for example, started in China and China remains far ahead in this area.
3. The billions of pharma upfront money going into Chinese biotech are fueling more pipeline investment which will only heighten the competition.

Not that anyone is asking but if you sat down and spoke to Chinese biotech CEOs about their point of view you might hear something like this:

1. You hired us as your scientists in your American pharma labs. You took our work but didn't let us advance, perhaps because our English wasn't great or, maybe, because we were foreign. We learned everything there was to learn about how to make great antibodies, ADC's, you name it. When you failed to promote us to the VP positions we earned, we left and moved back to China and started up our own shops. Don't complain now that you see how good we are.



# Some Perspectives on China Biotech

2. Our biotechs are so much more efficient than yours. You don't need all those FTE's, fancy executive suites, salary surveys and the like that we see in U.S. biotechs. You spend way too much time in the U.S. in project meetings and not enough time on innovation. You spend way too money for what you are getting.
3. You accuse of stealing your secrets. Really? It's not that hard to find novel epitopes on a protein. It's not that hard to figure out phage display. We can innovate the same way you do and we probably work harder.
4. You decided that Wuxi is a threat somehow to you. We're happy to have them back working on our molecules. Wuxi Biologics can go from a protein sequence to an IND ready biologic in six months and do so at a fraction of the cost of a Lonza. Please don't complain when we license great molecules done at Wuxi to large pharmas.

There is much to be learned from the recent success of China in biotech and we would share our own views here:

1. The fact that the Chinese can develop biologics quickly and inexpensively is great news for patients and should motivate U.S. biotechs to do the same. The recent progress by Akeso and Summit emblemizes this.
2. Why don't more U.S. biotechs and pharmas set up their own shops in China where innovation can be done very efficiently?



“East Asian Americans have been a meaningful part of the biotech sector, particularly at the entry and research levels for decades. Unfortunately, that success has not translated to ascending to positions of leadership. While our community has made progress, the numbers remain painfully small, particularly in Big Pharma/Biotech. There are no East Asian-American CEO's in Big Pharma/Biotech and one can count on one hand those that have made it to the C-suite.”

**Chen Yu**

*Managing Partner*

TCG X, Jan 2025



# The Real Answer to Competition is Innovative Excellence

The value of a Western biotech has to come from doing something truly innovative really well. Not in being third or fourth to market.

Peter Kolchinsky of RA Capital expresses the following view on the topic:

“We don't see China meeting most of pharma's significant demand for assets. Certain kinds of modalities and targets are unique to companies. And being early in a race to market still counts. Those same Chinese companies are also a source of assets for us VCs to start US companies.”

If a U.S. VC has a business plan which is to make a “fast follower” to a drug on an already validated target, it is perhaps best to source the molecule from China, India or some other efficient source.

As for those who are U.S. public investors, there is another obvious idea, which is to entertain IPOs from Chinese companies on the U.S. market.

Who says that there can't be more BeiGene's. If a company is located in Asia but has truly excellent science and products, why not invite them to participate in domestic capital markets?





# 5. Biopharma Capital Markets Review

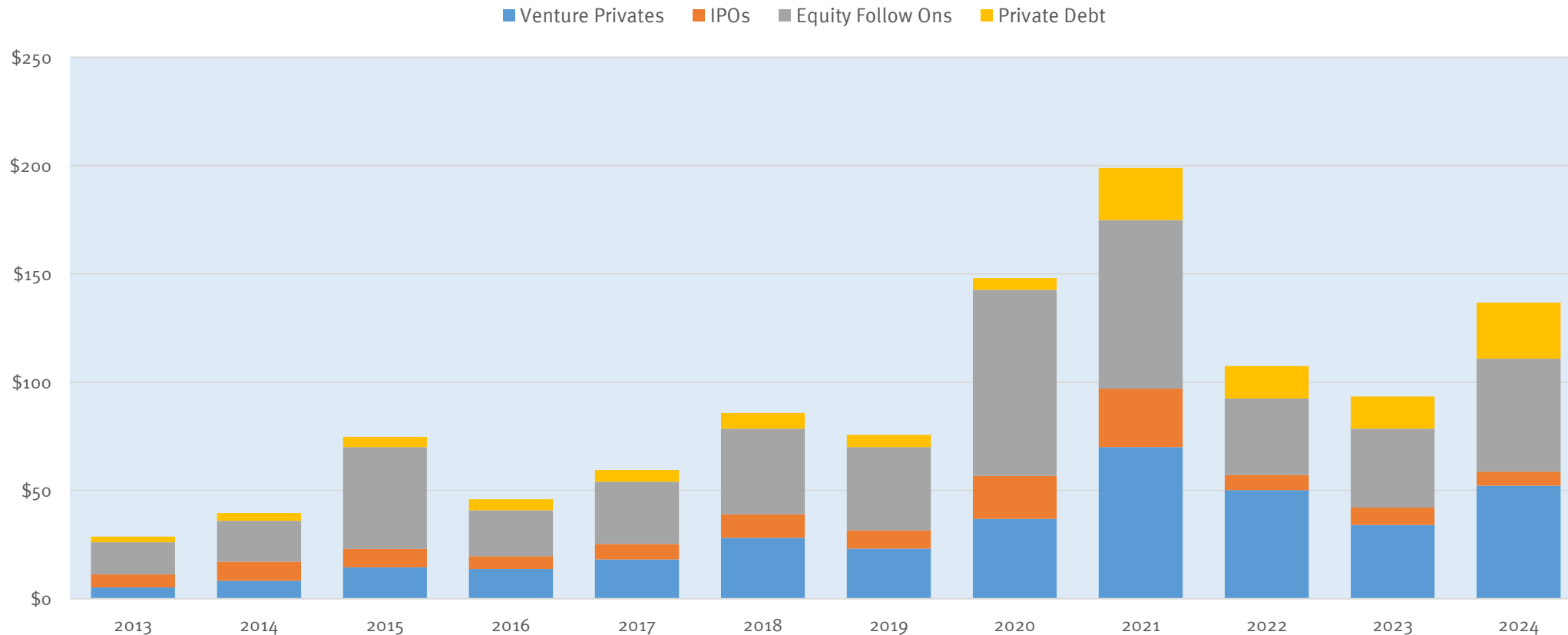




# Overall Biopharma Capital Raised in 2024 To Date is Up 47% Versus 2023

While it's not 2021, 2024 ended up as the third most active year for biotech fundraising in history.

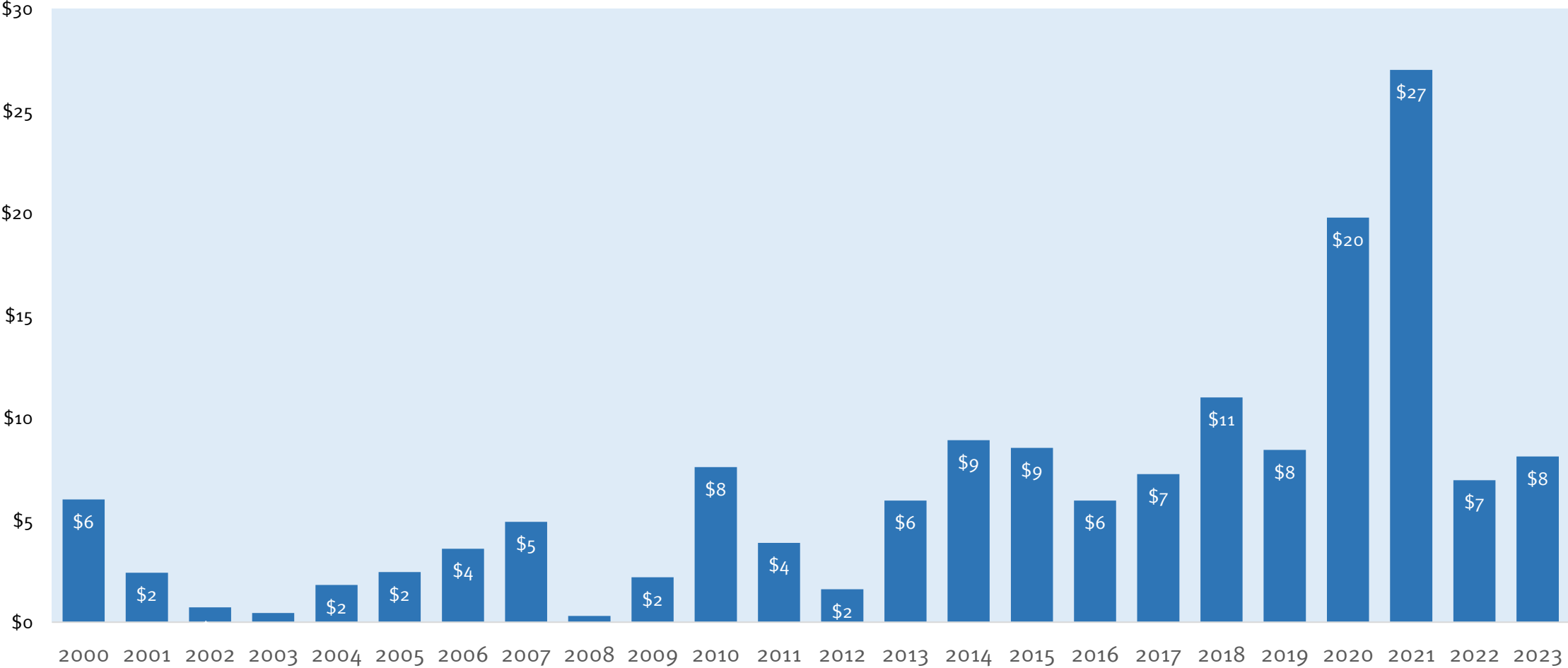
Equity Raised, Private Debt Raised in the Biopharma Sector, 2013 - Dec 31, 2024  
(\$ Billions, Worldwide)



Source: CapitalIQ and Stifel research

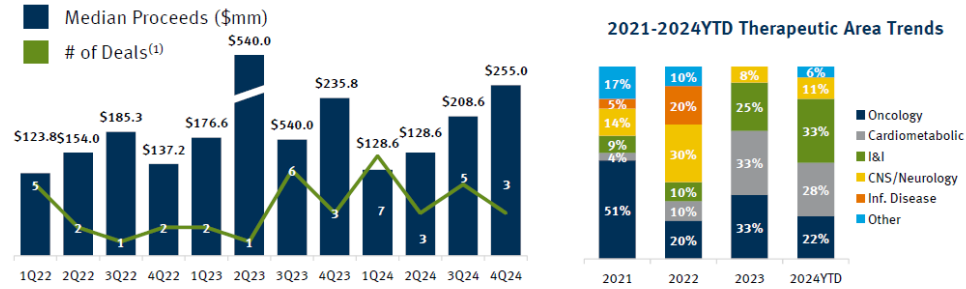
# Biopharma IPO Volume in 2024 Was Up Slightly from 2023

Global IPO Volume in the Biopharma Sector, 2000 - 2024  
(\$ Billions, Worldwide)

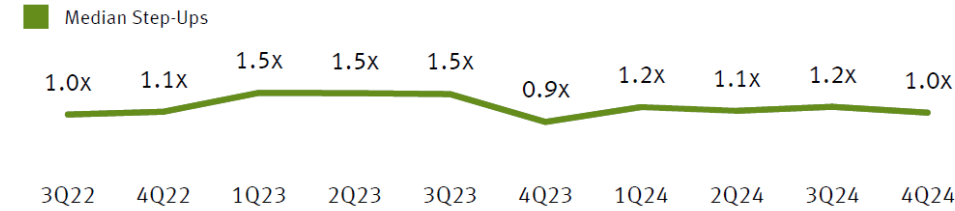


Source: Data from CapitalIQ and Stifel Database

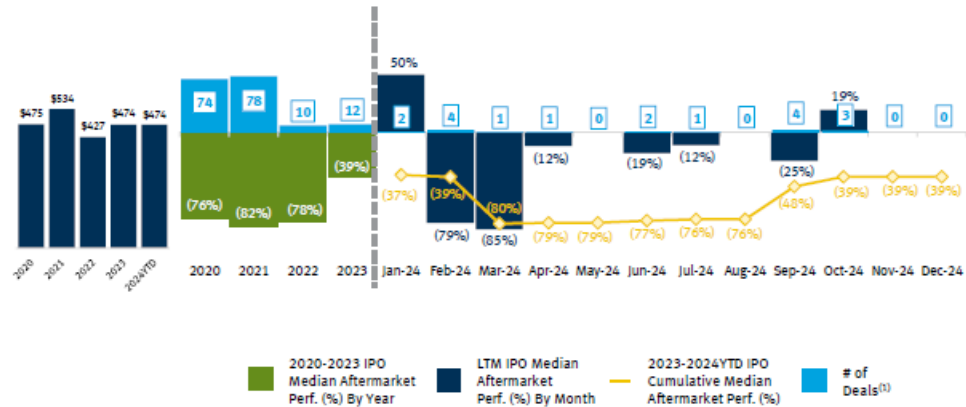
## Biopharma IPO Market Remains Highly Selective



## IPO Step-Ups Remain Deal Dependent



## Pre-Money Valuations Have Rebounded And Performance Has Been Lackluster<sup>(2)</sup>



## 30 Most Recent Biotech IPOs

(\$ in millions)

Issuer	Offer Date	Issuance Amount	Pre-Money Valuation	Pricing vs. Range	Step-Up	Price Change Offer to	
						Day 1	Current
Septerna, Inc.	10/24/24	\$288.0	\$509.3	\$1.00 Above	1.7x	18.9%	24.4%
Upstream Bio, Inc.	10/10/24	255.0	693.0	High End	1.0x	29.4%	19.1%
CAMP4 Therapeutics Corp.	10/10/24	75.0	146.2	Below	0.7x	(2.5%)	(30.6%)
BioAge Labs, Inc. <sup>(5)</sup>	09/25/24	208.6	451.9	Midpoint	1.2x	1.7%	(76.2%)
Bicara Therapeutics Inc.	09/12/24	315.0	689.7	High End	1.4x	30.1%	(2.8%)
Zenas BioPharma, Inc.	09/12/24	225.0	484.7	Midpoint	1.1x	6.8%	(47.5%)
MBX Biosciences, Inc.	09/12/24	163.2	375.1	High End	1.3x	47.8%	18.4%
Artiva Biotherapeutics, Inc	07/18/24	167.0	122.8	Below	0.2x	0.0%	(11.5%)
Alumis, Inc. <sup>(4)</sup>	06/27/24	250.0	676.1	Low End	1.1x	(16.9%)	(47.6%)
Rapport Therapeutics, Inc. <sup>(3)</sup>	06/06/24	154.0	479.4	Midpoint	1.2x	22.4%	10.4%
Contineum Therapeutics, Inc.	04/04/24	110.0	319.2	Low End	1.1x	(3.8%)	(12.3%)
Boundless Bio, Inc.	03/27/24	100.0	295.8	Midpoint	1.2x	(10.9%)	(84.6%)
Metagenomi Technologies, LLC	02/08/24	93.8	469.2	Low End	0.6x	(31.3%)	(78.4%)
Kyverna Therapeutics, Inc.	02/07/24	319.0	652.3	\$3.00 Above	2.6x	36.4%	(79.9%)
Alto Neuroscience, Inc.	02/01/24	128.6	321.8	High End	1.5x	29.4%	(76.1%)
Fractyl Health, Inc.	02/01/24	110.0	606.6	Midpoint	0.8x	(14.3%)	(86.4%)
ArriVent BioPharma, Inc.	01/25/24	175.0	435.1	Midpoint	1.1x	11.1%	48.4%
CG Oncology, Inc.	01/24/24	380.0	911.7	\$1.00 Above	1.5x	95.6%	51.4%
CARGO Therapeutics, Inc.	11/09/23	281.3	329.4	Low End	1.1x	(3.1%)	(8.4%)
Lexeo Therapeutics, Inc.	11/02/23	100.0	187.0	Below	0.6x	(8.6%)	(37.5%)
Abivax SA <sup>(6)</sup>	10/20/23	235.8	495.0	Low End	NA	(28.4%)	(38.7%)
Adlai Nortye Ltd. <sup>(7)</sup>	09/29/23	97.5	769.3	In Range	1.2x	(34.8%)	(90.0%)
RayzeBio, Inc.	09/14/23	311.0	800.6	High End	1.4x	33.3%	NA
Neumora Therapeutics Inc.	09/14/23	250.1	2,509.6	Midpoint	1.5x	(4.4%)	(39.3%)
Turnstone Biologics Corp.	07/20/23	80.0	194.1	Low End	0.5x	(8.3%)	(96.0%)
Sagimet Biosciences Inc.	07/13/23	85.0	301.4	Midpoint	1.5x	(0.3%)	(72.6%)
Apogee Therapeutics, Inc.	07/13/23	300.1	505.8	High End	2.0x	24.9%	161.8%
ACELYRIN, Inc.	05/04/23	540.0	1,221.5	High End	1.5x	30.6%	(82.1%)
Mineralys Therapeutics, Inc.	02/09/23	192.0	452.8	High End	1.7x	15.3%	(25.6%)
Structure Therapeutics, Inc.	02/02/23	161.1	414.3	High End	1.2x	73.3%	108.3%

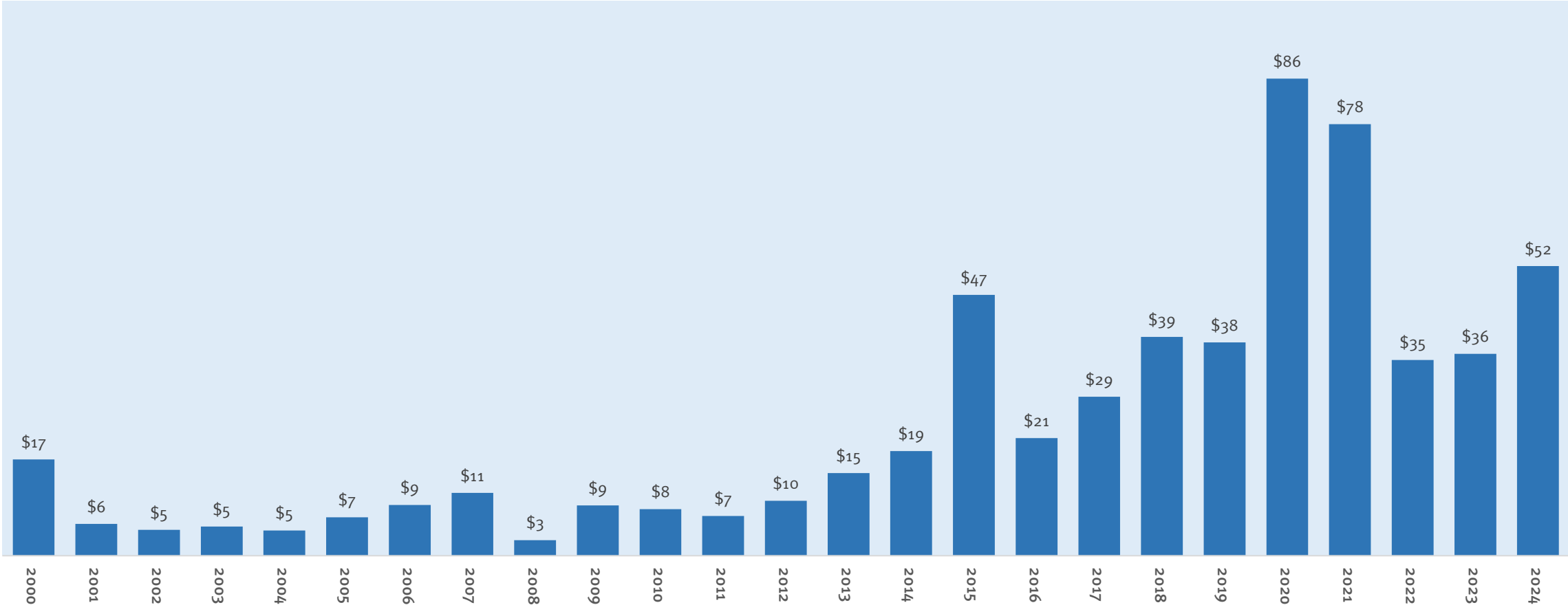
### Last 30 IPO Summary Statistics:

	Mean	Median	Step-Up	Day 1	Current
Mean	\$205.0	\$560.7	1.2x	11.3%	(23.5%)
Median	\$183.5	\$474.3	1.2x	4.2%	(37.5%)

Source: Stifel Capital Markets as of December 31, 2024. Note: Amounts raised in concurrent private placements are included as part of the IPO issuance amount. Pre-money equity values at pricing are fully diluted, accounting for options and warrants using the Treasury Stock Method. Excludes IPOs with total proceeds of less than \$50.0mm or greater than \$1.0bn. Note: Highlighted IPOs represent Stifel bookrun offerings. "NA" means not applicable. (1) Number of deals includes re-IPOs (companies with a previous foreign listing that list on a U.S. exchange). (2) Median aftermarket performance represents current performance. (3) Includes concurrent private placement of 588,888 of common stock. (4) Includes concurrent private placement of 2,500,000 of common stock. (5) Includes concurrent private placement of 1,058,824 of common stock. (6) Includes concurrent European private placement of 1,626,040 shares of common stock. (7) Includes concurrent private placement of 5,217,371 shares of common stock.

# 2024 Biopharma Follow-On Volume Was the Third Busiest in History

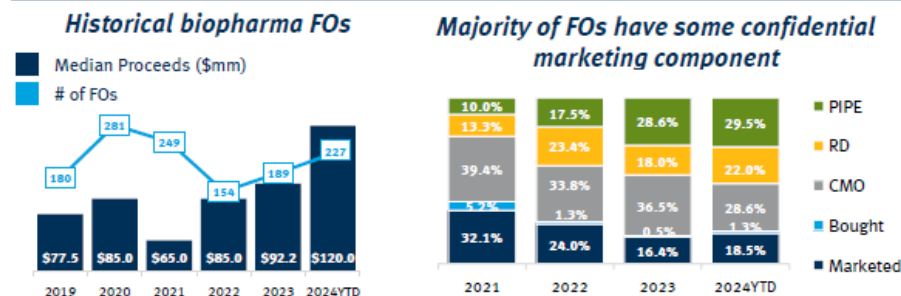
Follow-On Equity Issuance in the Biopharma Sector, 2000 - 2024 (annualized)  
(\$ Billions, Worldwide)



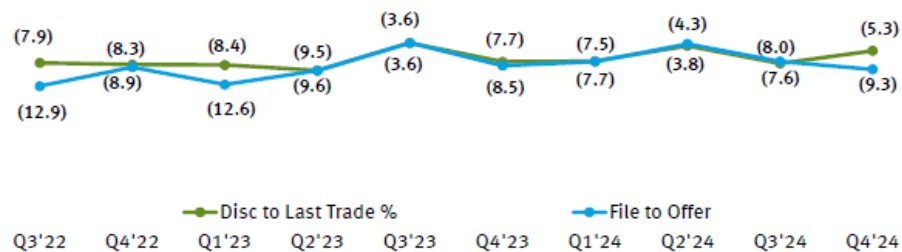
Source: Data from CapitalIQ and Stifel Database

# Biotech Follow-On Market Active

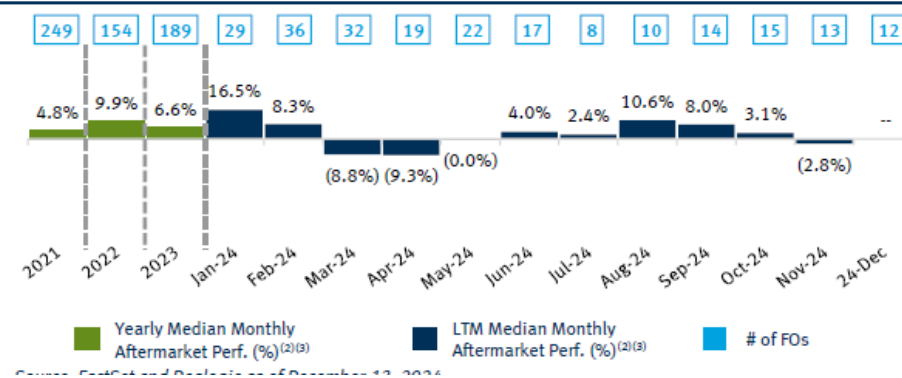
## Follow-On Market Has Been Active 2024YTD<sup>(1)</sup>



## Discounts Have Historically Been in line<sup>(2)</sup>



## Aftermarket Performance Has Been Mixed<sup>(1)</sup>



Source: FactSet and Dealogic as of December 13, 2024

## Recent Biotech FOs By Market Cap<sup>(2)</sup>

Pricing Date	Issuer	Execution Format	Market Cap (\$mm)	Total Proceeds (\$mm)	File to Offer (%)	% Change		Deal Catalyst	Warrants?
						Offer to 1 Day (%)	Offer to Current (%)		
<b>Recent FOs with Market Cap &gt;\$2.5bn</b>									
12/11/24	ImmunityBio, Inc.	CMO	\$3,233.3	\$100.0	(35.3%)	5.0%	(4.3%)	✓	
12/04/24	Janux Therapeutics Inc	Marketed	3,287.6	350.0	5.2%	5.2%	(3.0%)	✓	
12/03/24	Revolution Medicines Inc	Marketed	8,713.8	750.0	(11.2%)	4.9%	(2.2%)	✓	
11/14/24	Zai Lab Ltd	Marketed	2,983.3	200.0	(14.9%)	6.1%	3.3%	✓	
10/29/24	Vera Therapeutics Inc	Marketed	2,595.5	300.0	(11.3%)	(3.2%)	4.9%	✓	
10/08/24	Crinetics Pharmaceuticals, Inc.	CMO	4,137.8	500.0	(3.3%)	1.4%	7.3%	✓	
10/08/24	Scholar Rock Holding Corp	Marketed	3,326.6	300.0	(17.6%)	(1.7%)	48.6%	✓	
10/01/24	Biohaven Ltd.	CMO	4,724.3	250.0	(4.9%)	2.3%	(19.0%)	✓	
09/19/24	Ascendis Pharma A/S	Marketed	8,669.5	300.0	0.8%	0.8%	(13.4%)	✓	
09/16/24	Nuvalent Inc	Marketed	5,666.6	500.0	14.4%	4.8%	(13.1%)	✓	

Average (n=10)	\$4,733.8	\$355.0	(7.8%)	2.6%	0.9%
Median (n=10)	\$3,732.2	\$300.0	(8.1%)	3.5%	(2.6%)

<b>Recent FOs with Market Cap \$500mm - \$2.5bn</b>									
12/12/24	CG Oncology Inc	Marketed	\$2,279.1	\$224.0	(16.9%)	2.7%	2.7%	✓	
12/11/24	NewAmsterdam Pharma Co NV	Marketed	2,488.5	416.5	(6.5%)	2.4%	0.8%	✓	
12/11/24	Rocket Pharmaceuticals, Inc.	CMO	1,273.8	165.0	(7.5%)	7.0%	(3.8%)	✓	
11/25/24	Replimune Group Inc	Marketed	1,173.9	140.0	(12.9%)	10.6%	(3.5%)	✓	
11/18/24	Spyre Therapeutics, Inc.	CMO	1,484.9	200.1	(4.1%)	(2.2%)	(12.3%)	✓	
11/12/24	89bio, Inc.	CMO	970.2	125.0	(6.1%)	4.9%	(9.5%)	✓	
11/07/24	Traverse Therapeutics, Inc.	CMO	1,378.4	125.0	(9.4%)	24.1%	8.3%	✓	
10/29/24	EyePoint Pharmaceuticals Inc	Marketed	661.9	140.0	(9.2%)	4.2%	(32.2%)	✓	
10/17/24	Capricor Therapeutics, Inc.	CMO	827.2	75.0	(17.1%)	8.8%	(22.0%)	✓	
10/10/24	Immatics NV	Marketed	1,141.4	150.3	(16.4%)	1.0%	(22.1%)	✓	

Average (n=10)	\$1,367.9	\$176.1	(10.6%)	6.3%	(9.4%)
Median (n=10)	\$1,223.9	\$145.2	(9.3%)	4.5%	(6.7%)

<b>Recent FOs with Market Cap &lt;\$500mm</b>									
12/13/24	Inovio Pharmaceuticals, Inc.	CMO	\$106.2	\$30.0	(43.9%)	(22.7%)	(22.7%)	✓	✓
12/12/24	Candel Therapeutics, Inc.	CMO	318.3	80.0	(38.8%)	12.5%	12.5%	✓	
12/10/24	Cardiff Oncology, Inc.	RD	124.8	40.0	6.6%	45.4%	50.8%	✓	
12/09/24	Protara Therapeutics, Inc.	CMO	202.3	100.1	(6.3%)	0.0%	(4.3%)	✓	
11/21/24	Verrica Pharmaceuticals Inc.	CMO	41.8	42.0	(17.2%)	11.2%	(14.5%)		✓
11/20/24	Lineage Cell Therapeutics, Inc.	RD	170.0	30.0	(15.9%)	(15.6%)	(33.4%)		
11/12/24	Alpha Cognition Inc	Marketed	63.5	50.0	(42.5%)	(0.9%)	(5.7%)		
11/04/24	KalVista Pharmaceuticals, Inc.	RD	495.5	60.0	(5.7%)	16.3%	(13.1%)	✓	
10/29/24	Eledon Pharmaceuticals, Inc.	RD	197.5	85.0	8.3%	(1.6%)	20.0%	✓	
10/25/24	Molecular Partners AG	RD	220.8	20.0	(8.8%)	18.2%	(1.1%)	✓	

Average (n=10)	\$194.0	\$53.7	(16.4%)	6.3%	(1.2%)
Median (n=10)	\$183.7	\$46.0	(12.3%)	5.6%	(5.0%)

Average (n=30)	\$2,098.6	\$194.9	(11.6%)	5.1%	(3.2%)
Median (n=30)	\$1,223.9	\$140.0	(9.3%)	4.5%	(4.1%)

Source: FactSet and Dealogic as of December 13, 2024. Note: File to offer represents “all-in” discount for offerings with warrants. (1) Includes marketed, bought, confidentially marketed, registered direct and PIPE offerings with proceeds of \$20.0 million and greater. (2) Only includes marketed, confidentially marketed and registered direct offerings with proceeds of \$20.0 million and greater, excludes bought and PIPE offerings. (3) Median monthly aftermarket performance represents +30 day performance.



# Top PIPE and Registered Direct Investors

## Top 50 Disclosed Investors on ≥ \$50mm Biopharma PIPEs & Registered Directs Since 2023

#	Investor	# of PIPEs / RDs
1	RA Capital	31
2	Adage	29
4	Perceptive	27
3	Venrock	26
5	Janus	24
6	Deep Track	20
7	Logos	19
8	TCGx	19
10	BVF	19
9	Boxer	18
11	Surveyor	17
12	Frazier	17
13	Great Point	16
14	Vivo	15
15	Commodore	15
18	OrbiMed	15
16	Avidity	14
17	Woodline	14
19	EcoR1	13
20	Invus	13
22	RTW	13
21	Armistice	12
23	Samsara	12
24	Rock Springs	11
25	Bain	11

#	Investor	# of PIPEs / RDs
26	Octagon	10
27	Deerfield	10
28	Soleus	10
29	Cormorant	10
30	Nantahala	10
31	Fairmount	9
32	Paradigm	9
35	Redmile	9
33	Farallon	8
34	Braidwell	8
36	Nextech	7
37	Access Biotech	7
38	NEA	7
39	Blue Owl	7
40	Suvretta	6
41	Driehaus	6
42	Ally Bridge	6
43	Acorn	5
44	Novo	5
45	Baker Brothers	5
46	Vestal Point	5
47	Sphera	5
48	Wellington	5
49	5AM	4
50	Marshall Wace	4

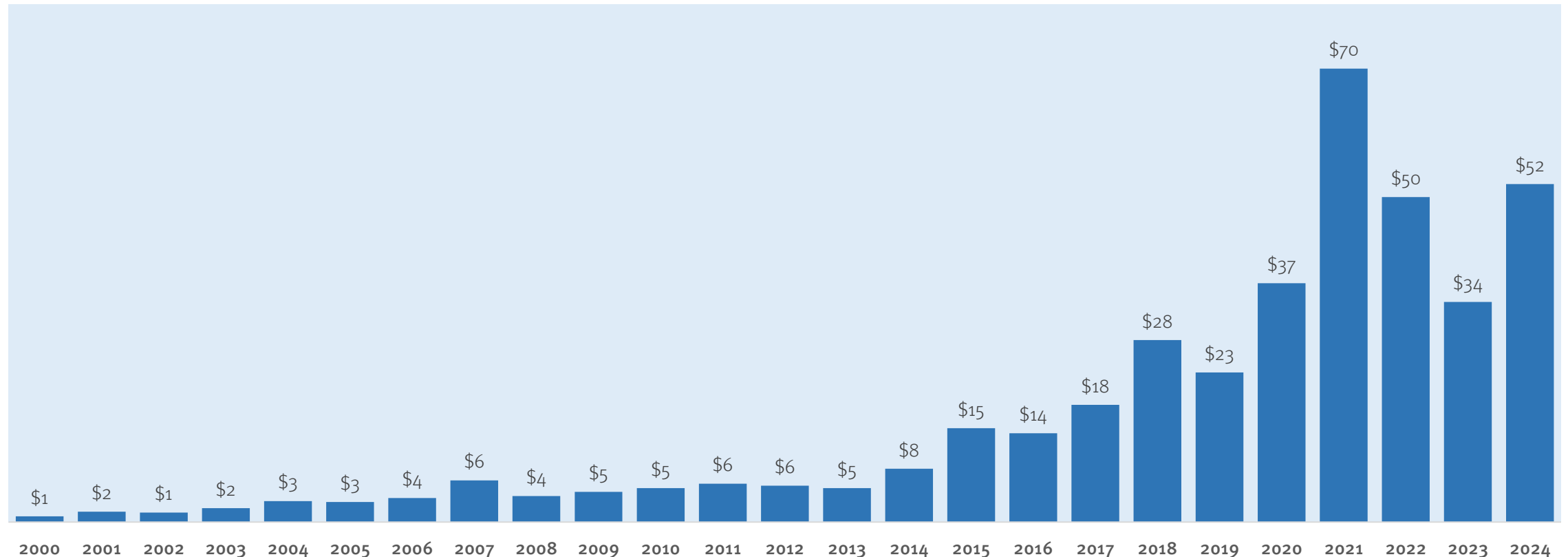
Source: FactSet, PrivateRaise and Dealogic as of January 3, 2025.

Note: Includes the top 50 investors publicly disclosed on ≥ \$50mm biopharma PIPE or registered direct since 2023.

# Biopharma Sector Venture Equity Deals Total Volume Up from 2023 But Down from Pandemic Period

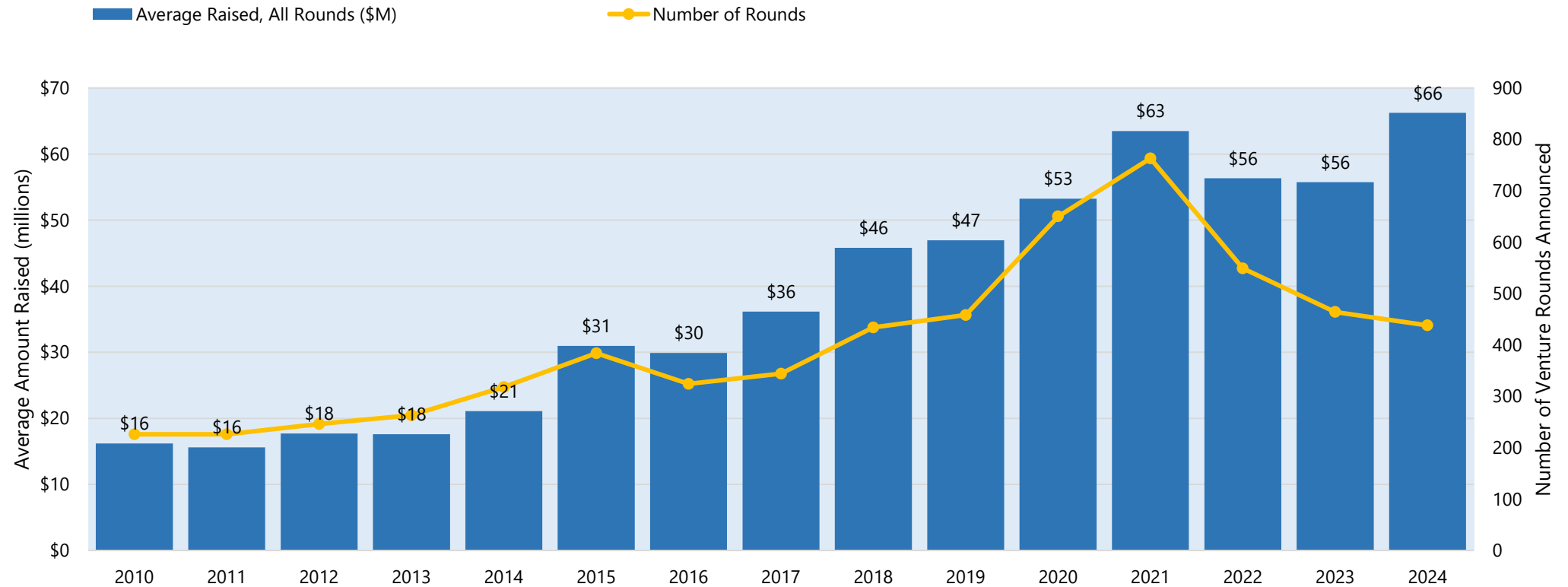
Looking back, 2024 turned out to be the second most active in history for venture investments in biopharma companies.

**Venture Privates in the Biopharma Sector, 2000 - 2024 (annualized)**  
(\$ Billions, Worldwide)



# While Venture Deals in Biopharma Fell by Number of Transactions, the Average Amount Raised Hit a Record in 2024

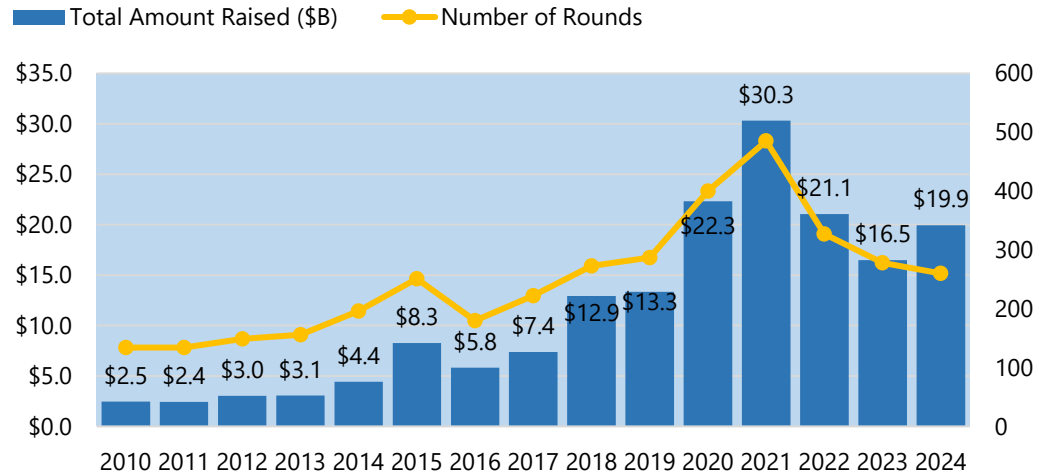
Venture **Averages** - Biopharma Tx and Platforms - **Global**



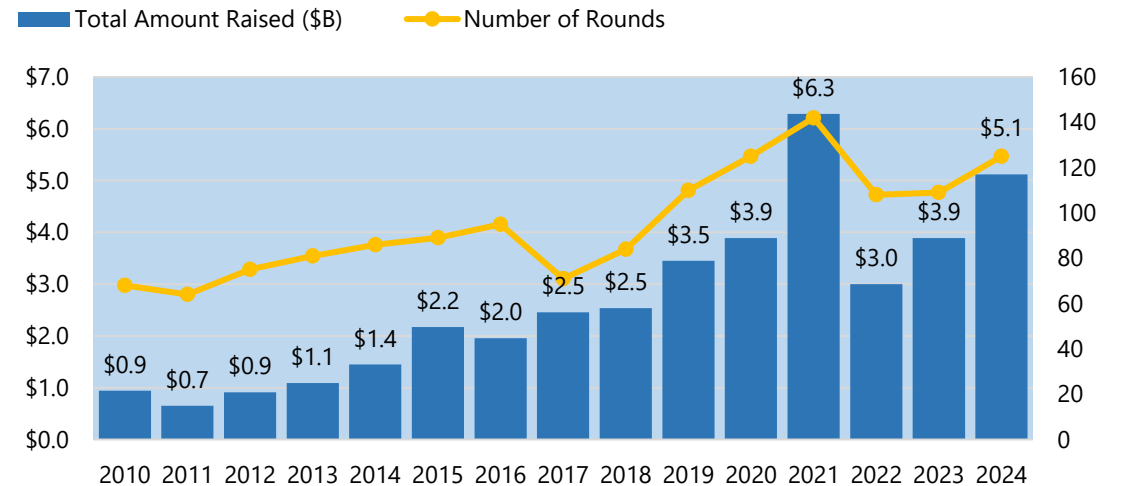
Source: DealForma Database

# China Venture Volume hit the Hardest Last Year. Europe and Japan Up Nicely

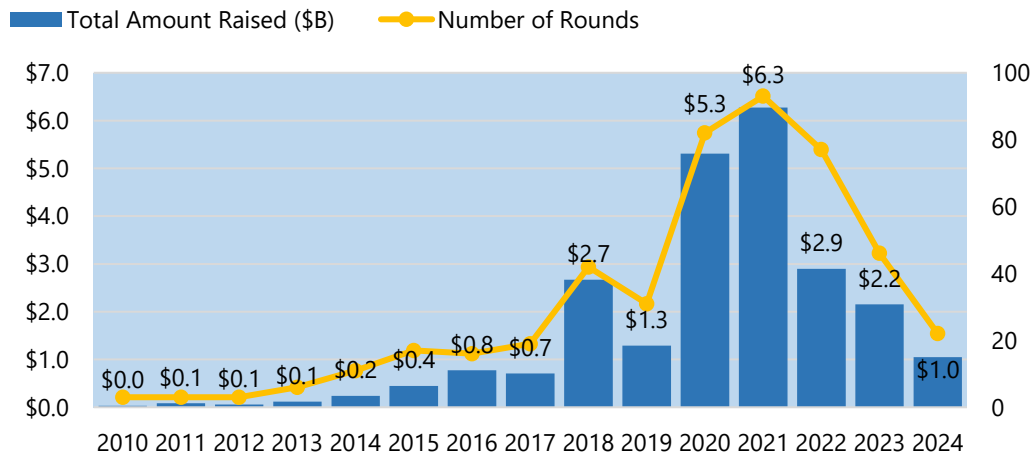
## Venture **Totals** - Biopharma Tx and Platforms - **U.S.**



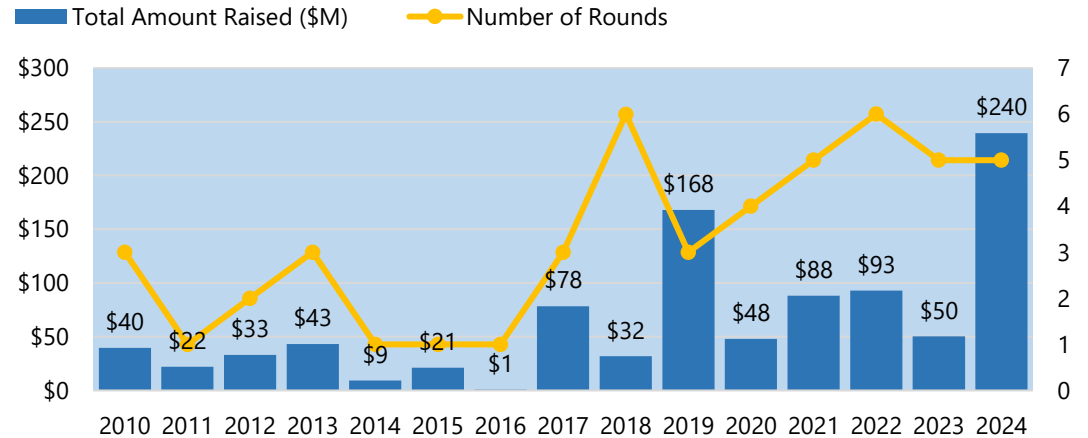
## Venture **Totals** - Biopharma Tx and Platforms - **Europe**



## Venture **Totals** - Biopharma Tx and Platforms - **China**

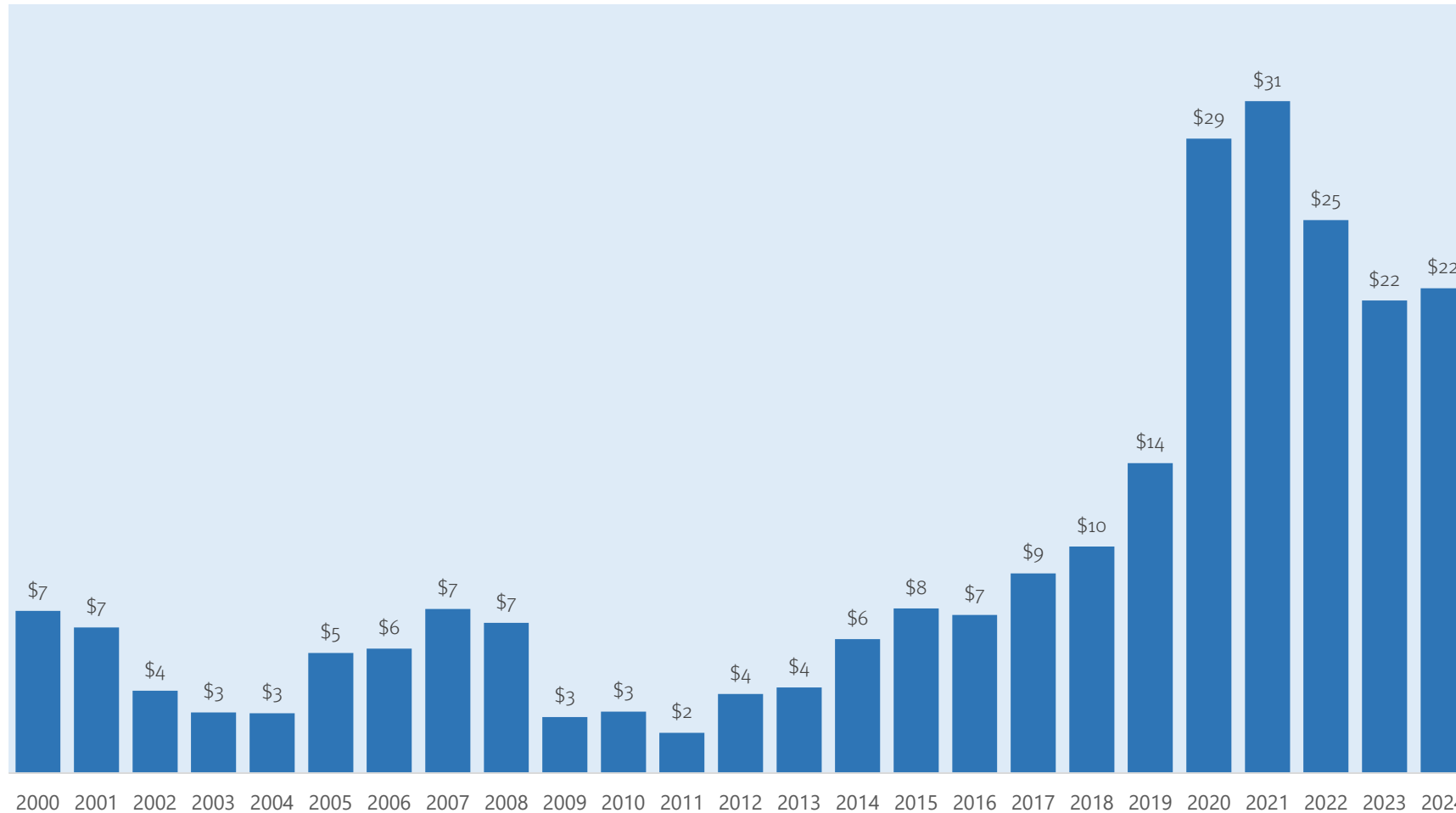


## Venture **Totals** - Biopharma Tx and Platforms - **Japan**



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

Biopharma Venture Capital Funds, Amounts Raise \$mm, 2000 to 2024



The total volume of new money flowing into life sciences venture funds in 2024 was \$22 billion, anchored by \$3bn+ funds from Arch, Bain and Flagship.

While volumes were nowhere near the Pandemic levels 2024 turned out to be the fourth best year in history.

Overall, venture fund capital raising took a major step up starting in 2020 and has not reverted.

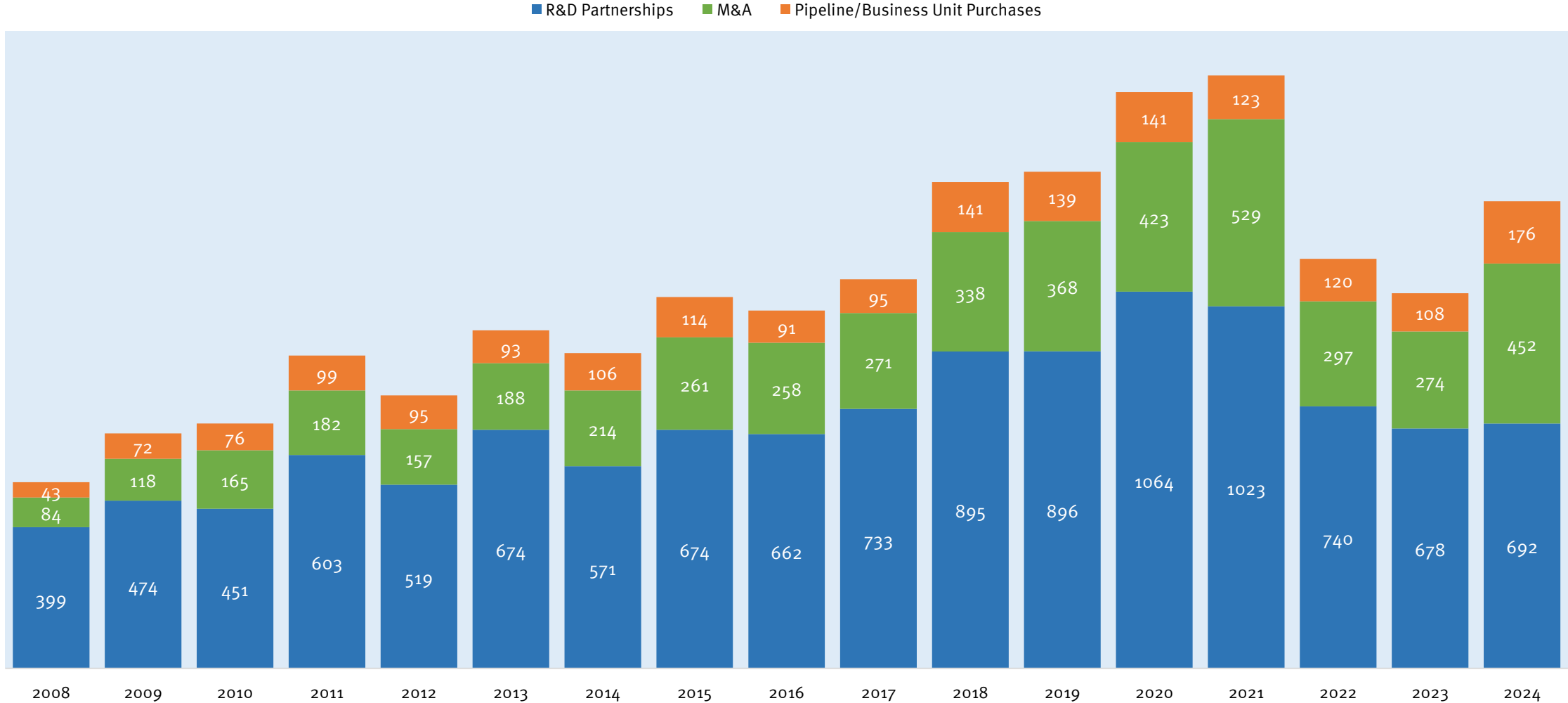


## 6. M&A and Partnership Deal Environment



# Healthcare and Life Science Deal Volumes Rose in 2024

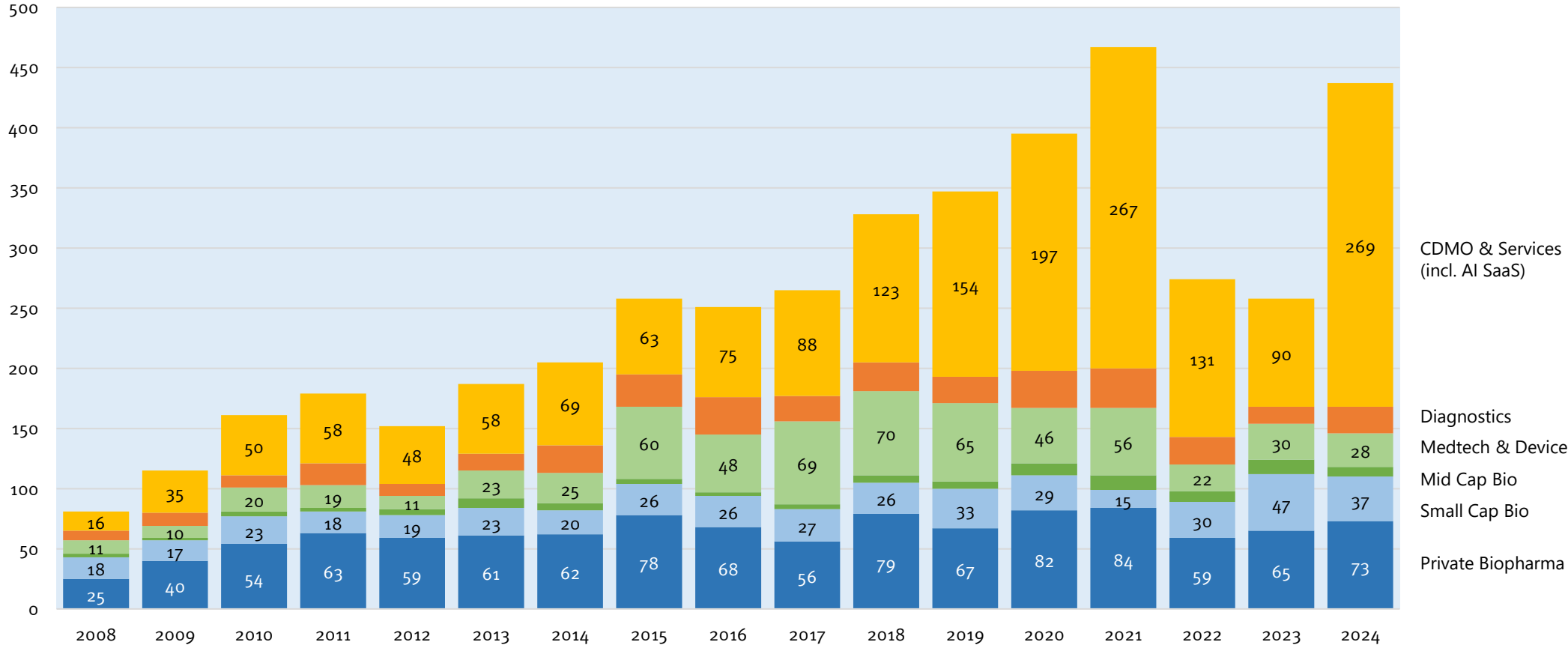
Number of Deals by General Structure - All Healthcare and Life Sciences, 2008 to 2024



Source: DealForma Database

# CDMO and Pharma Service M&A Deal Count Hit Record Level in 2024 After Two Slower Years

Life Sciences M&A Deal Count by Target Company Type, 2008 to 2024

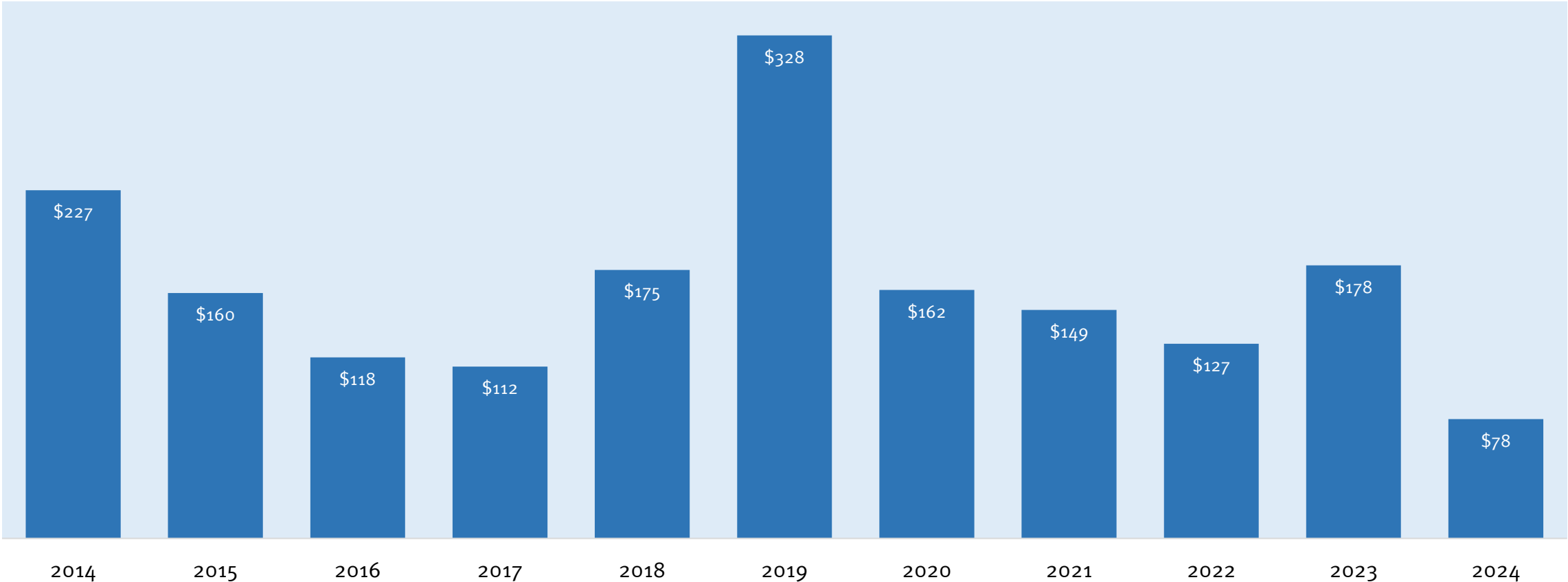


Source: DealForma Database

# Last Year Was Quite Slow for Biopharma M&A Volume

There were no transactions announced 2024 for a biopharma company for a deal value over \$5 billion. Interestingly, the *number* of deals announced this year was relatively normal, but the dollar volume was not - likely due to the Biden Administration's antitrust stance.

M&A Volume in the Biopharma Sector, 2014 - 2024  
(\$ Billions, Worldwide)

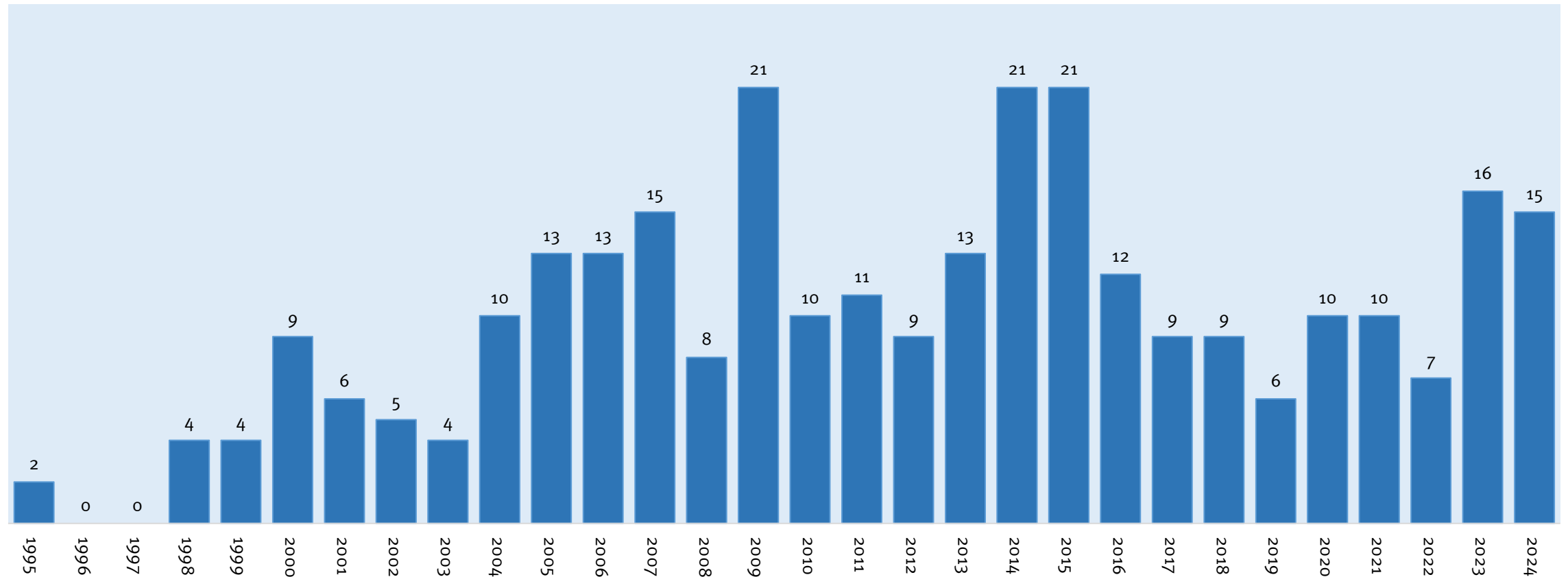


Source: S&P CapitalIQ and Stifel research. This includes all reported global therapeutics change of control transactions and included asset sales such as the Novartis Xiidra divestiture. Includes reverse mergers at equity value and transactions in human/animal health. Does not include SPAC mergers nor mergers in pharmaceutical services and non-therapeutic fields.

# Solid Pace of \$1bn+ Biopharma M&A Deals 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 was 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)

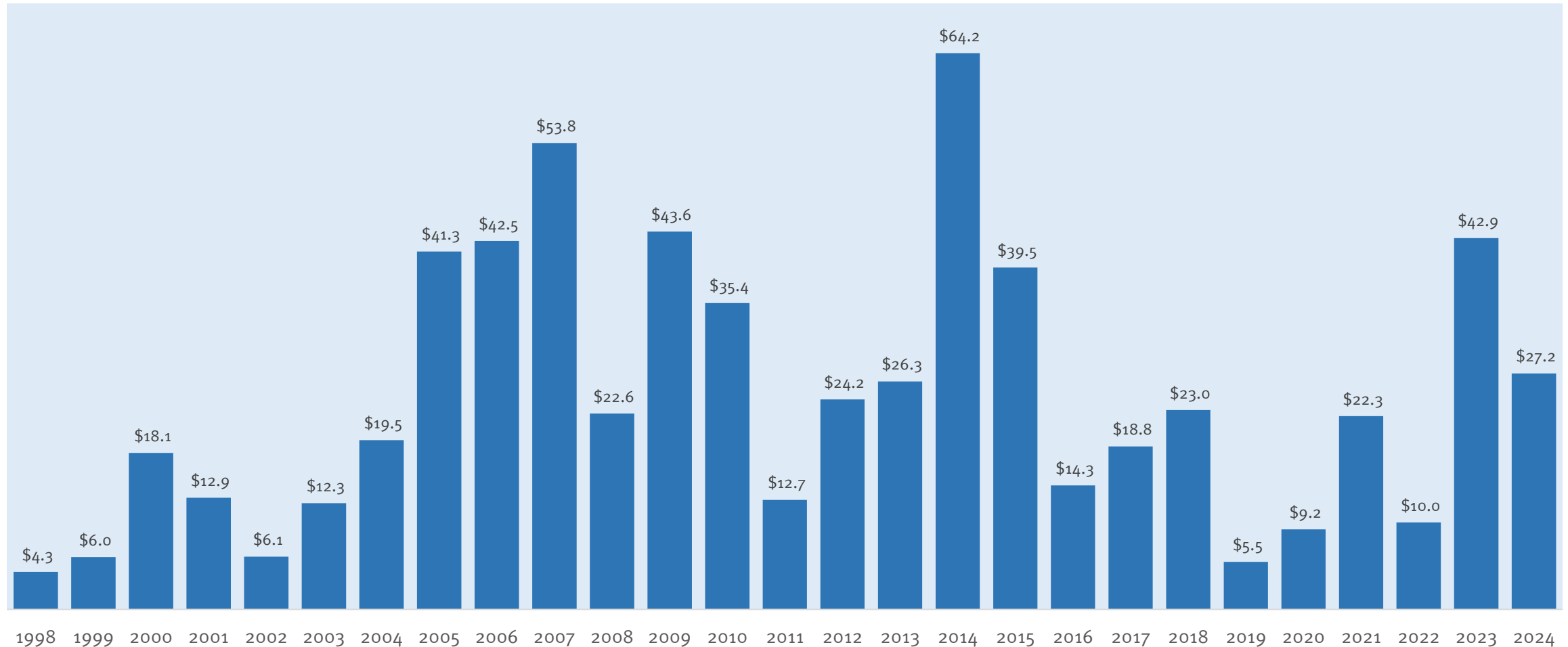




# While \$1bn M&A Deal Number Solid in 2024, Dollar Value Was Slow

This chart shows the aggregate dollar value of M&A deals in the \$1bn to \$10bn size bucket. It's notable that while the number of transactions was solid, the aggregate dollars returned to investors (\$27.2 billion) was well down from 2023.

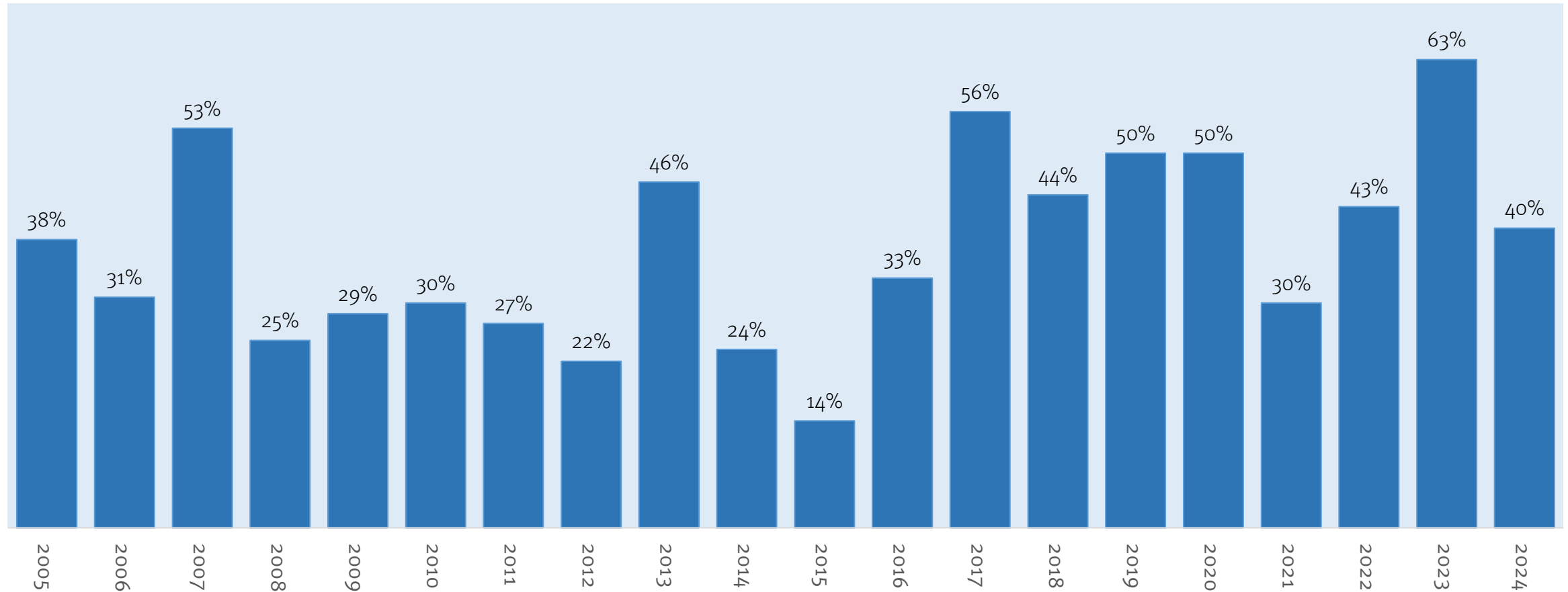
Dollar Value of \$1bn to \$10bn Biopharma M&A Deals, 1998 to 2024 (\$ billions)



# 40% of \$1bn+ M&A Takeouts in 2024 were Public

In some quarters we heard dismay in 2024 that so many of the larger takeouts were of private companies. In total 60% of the deals were for privates and 40% were for publics. It turns out that this is right at the median level over time. Historically, 38% of \$1bn biotech takeouts have been of public companies.

Percent of Acquisitions of Biopharma Companies of \$1bn or More that Were Public, 2005 to 2024



# Top Ten Biopharma M&A Deals of 2024 by Amount Paid Upfront

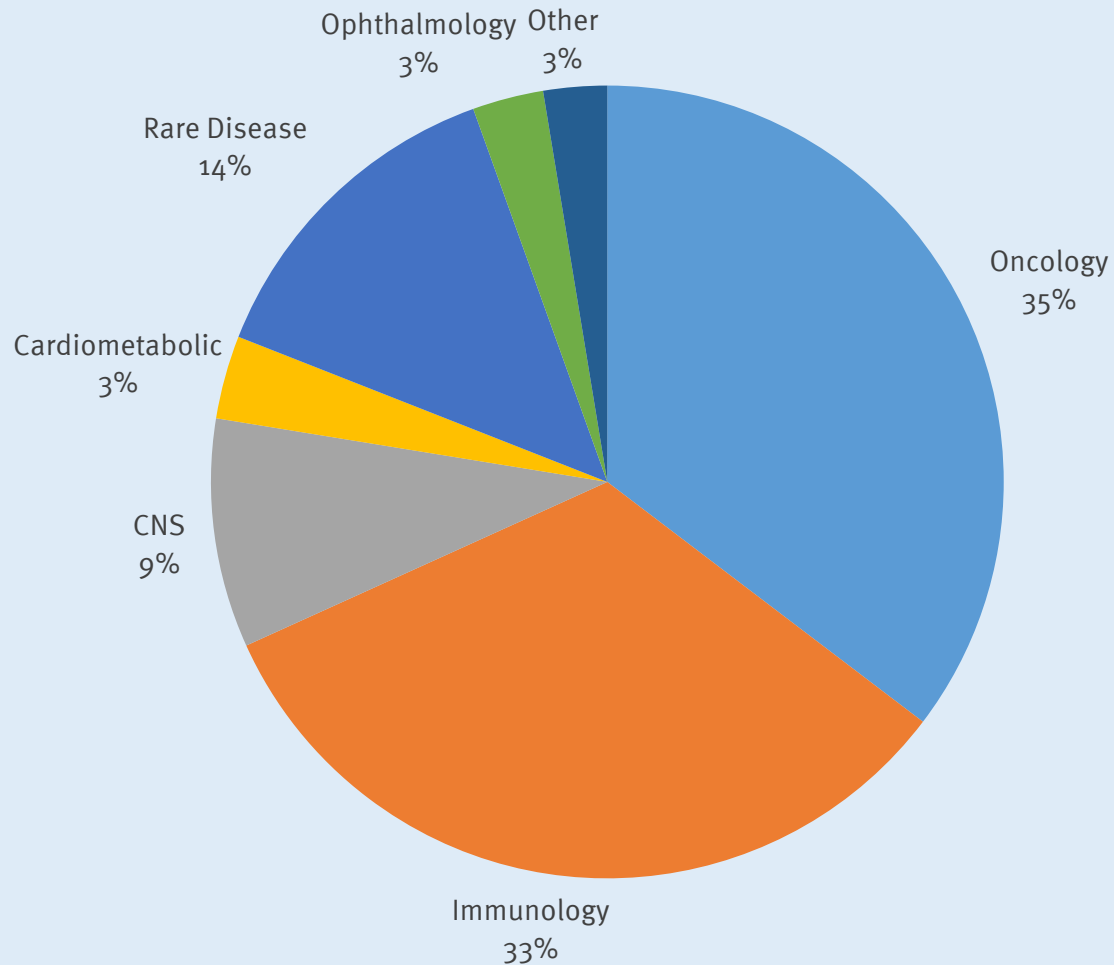
\$ millions

Date	Deal Type	Buyer	Seller	Asset	Therapeutic Area	Upfront	Total
04/10/24	Company Sale	Vertex Pharmaceuticals	Alpine Immune Sciences, Inc.	Povetacicept/ALPN-303	I&I	\$4,900.0	\$4,900.0
02/12/24	Company Sale	Gilead Sciences	CymaBay Therapeutics, Inc.	Seladelpar	Rare Disease	\$4,300.0	\$4,300.0
07/08/24	Company Sale	Eli Lilly and Company	Morphic Holding, Inc	MORF-057	I&I	\$3,200.0	\$3,200.0
02/05/24	Company Sale	Novartis AG	MorphoSys Ag	Pelabresib	Oncology	\$2,900.0	\$2,900.0
10/14/24	Company Sale	Lundbeck A/S	Longboard Pharmaceuticals, Inc	Bexicaserin	CNS	\$2,600.0	\$2,600.0
03/19/24	Company Sale	AstraZeneca PLC	Fusion Pharmaceuticals, Inc.	FPI-2265	Oncology	\$2,000.0	\$2,400.0
01/08/24	Company Sale	Johnson & Johnson	Ambrx Biopharma, Inc.	ARX517	Oncology	\$2,000.0	\$2,000.0
04/03/24	Company Sale	Genmab A/S	ProfoundBio	Rina-S	Oncology	\$1,800.0	\$1,800.0
01/23/24	Company Sale	Sanofi	Inhibrx	INBRX-101	Rare Disease	\$1,700.0	\$1,996.0
10/28/24	Company Sale	Abbvie	Aliada Therapeutics	ALIA-1758	CNS	\$1,400.0	\$1,400.0

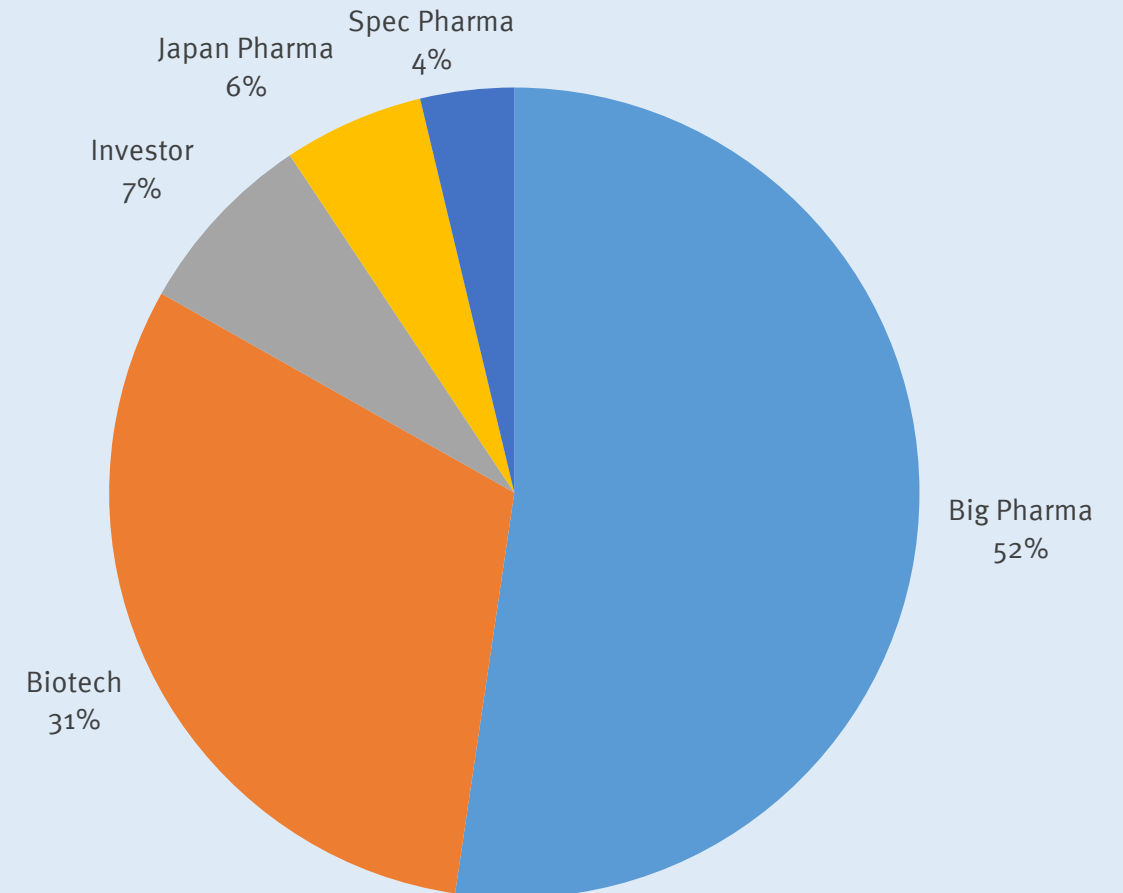
Source: CapitalIQ and Stifel analysis.

# Statistics on Biopharma M&A Deals in 2024

## Deal Value by Therapeutic Area

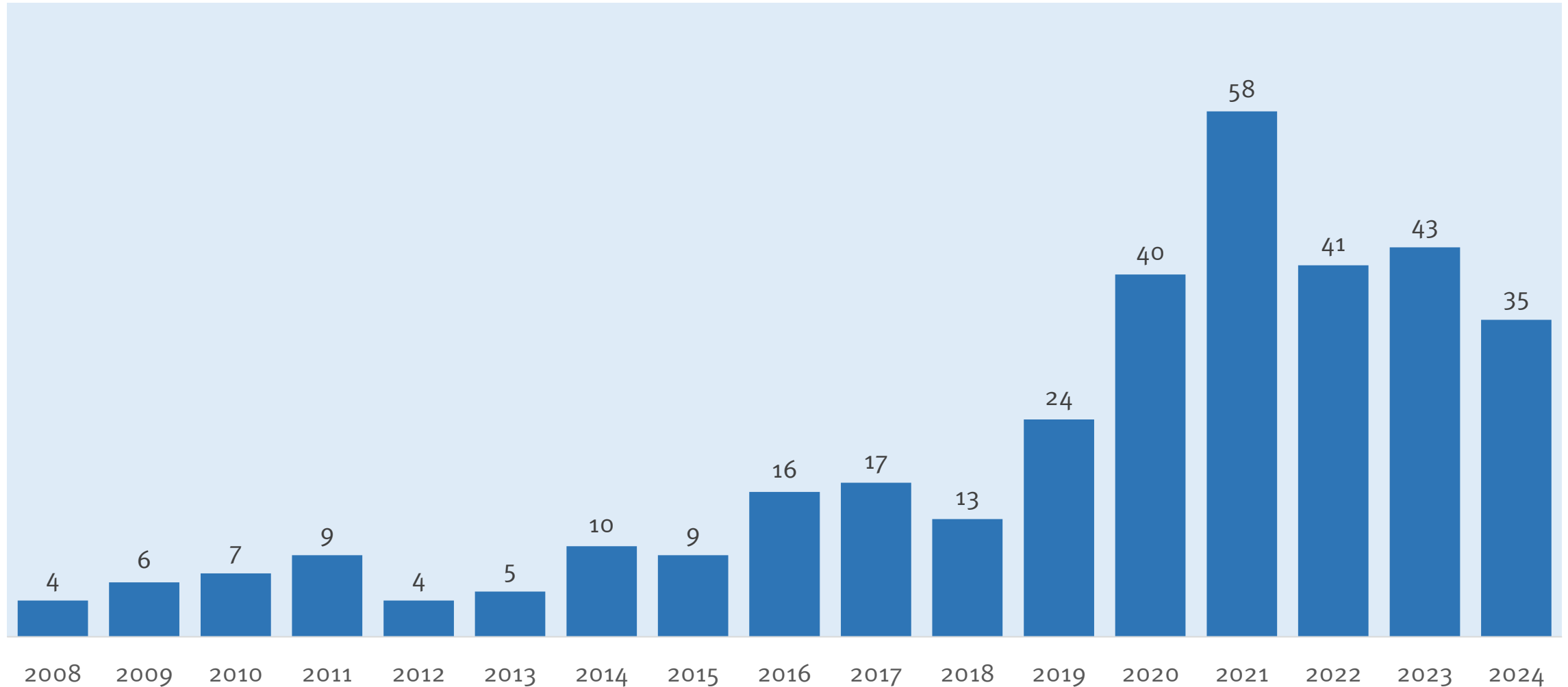


## Deal Value by Buyer Type



# Reverse Merger Activity Remained Elevated in 2024

Number of Life Sciences Sector Reverse Mergers, 2008 to 2024

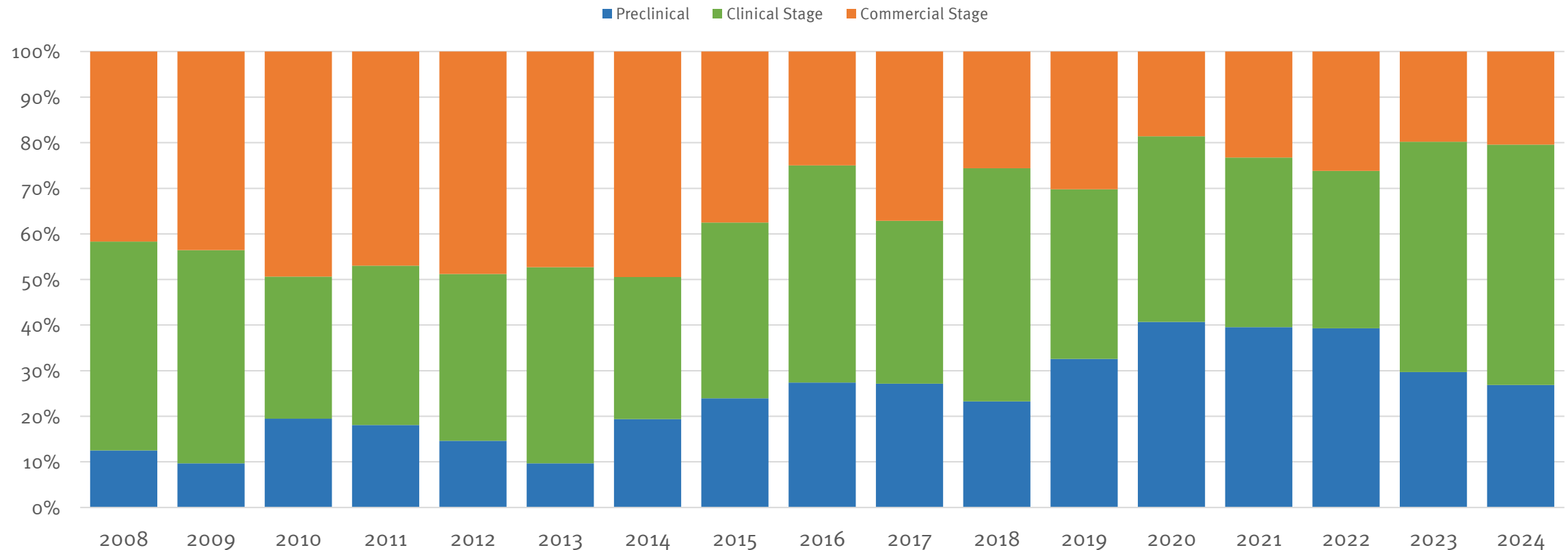




# We Have Seen a Significant Increase in Clinical Stage Versus Preclinical M&A Deals in 2024

In 2024 53% of M&A deals were for companies with clinical stage assets (Phase 1 to Phase 3). Compare this to an average of 45% in the 2019 to 2022 period. The fraction of M&A deals for approved assets is down as is the fraction of deals for platforms and preclinical assets.

**Distribution of Biopharma M&A Deals by Stage of Development of Target Company 2008 to 2024**

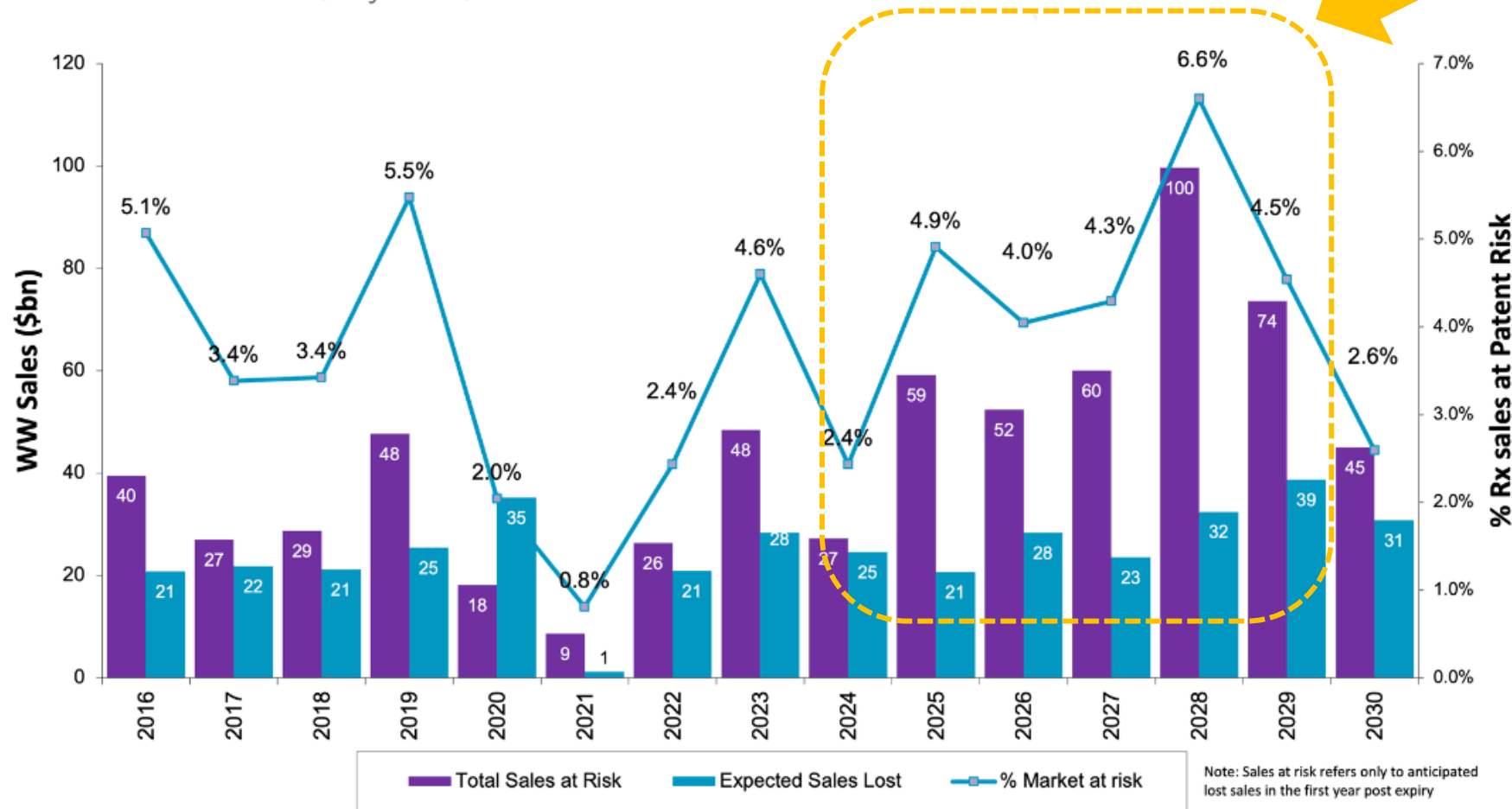


Source: DealForma. Only included therapeutics M&A deals with upfront payments (cash or equity) valued at \$100mm or more. Reverse merger / SPAC deals excluded.

# Evaluate Pharma: Huge Wave of LOEs is Coming

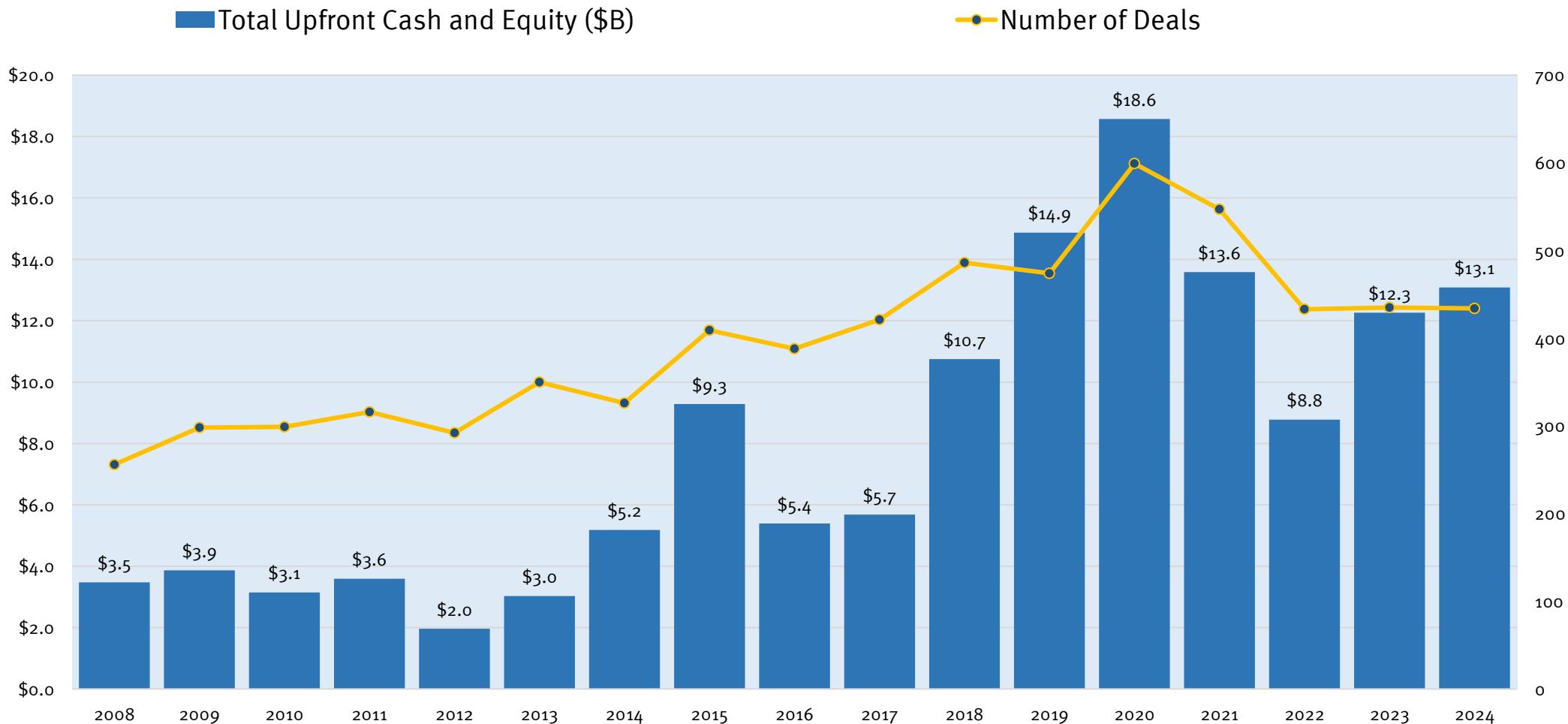
Figure 3: Worldwide Sales At Risk\* from Patent Expiration (2016-2030)

Source: Evaluate Pharma© (May 2024)

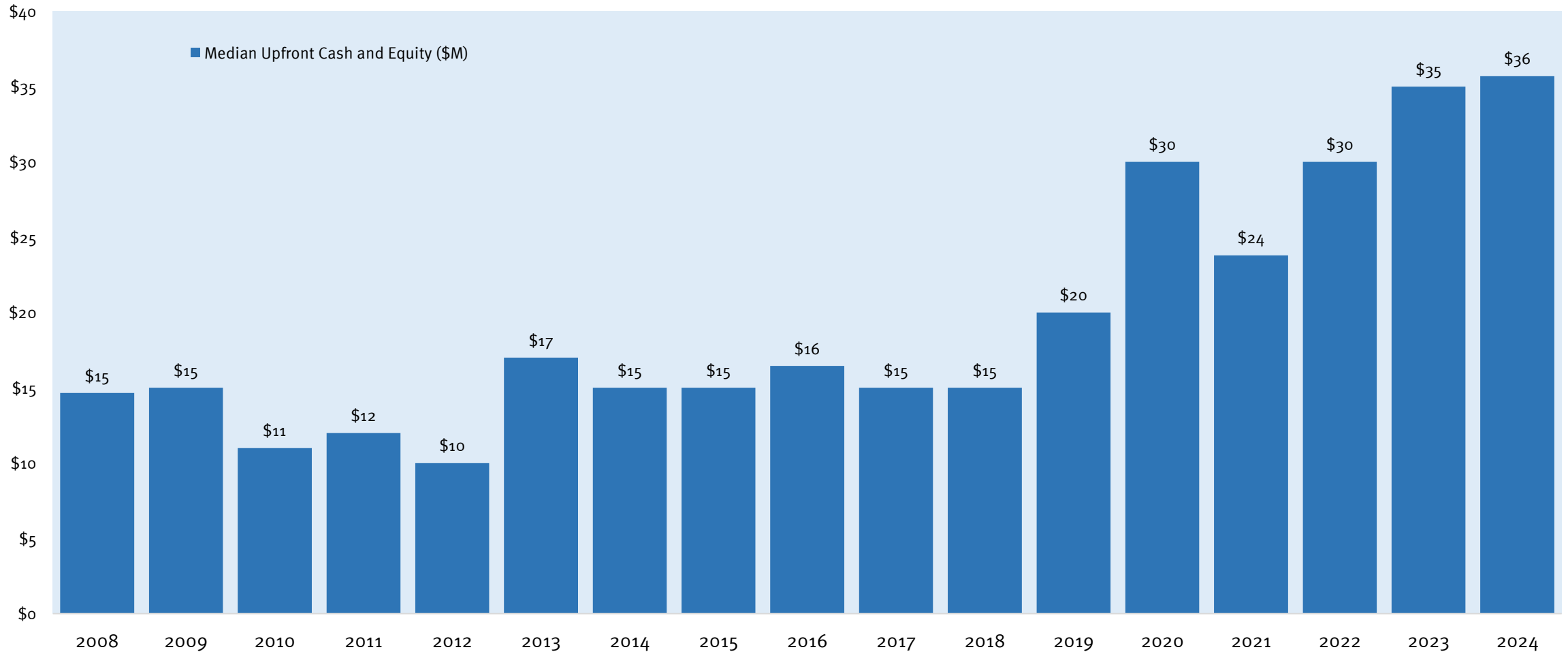


\$350 billion of LOE's scheduled in 2025 to 2029 period. Should be a major driver of M&A activity.

# Volume of Biopharma License Deals Was Flat Last Year



# Median Upfront on Biopharma License Deals Hit All Time Record Last Year



# Biopharma Licensing Deal Statistics by Therapeutic Area in 2024

Primary Therapy Area	Number of Deals	Total Deal Value (\$Bn)	Total Upfront Cash and Equity (\$Mil)	Average Upfront Cash and Equity (\$Mil)	Median Upfront Cash and Equity (\$Mil)
Cancer	163	\$68.6	\$6,105	\$103	\$45
Neurologic	59	\$36.5	\$2,607	\$97	\$27
Autoimmune	33	\$13.0	\$817	\$63	\$20
Cardiovascular	19	\$10.9	\$707	\$118	\$76
Endocrine / Metabolic	29	\$7.8	\$375	\$54	\$25
Inflammation	15	\$4.3	\$128	\$43	\$40
Hepatic	9	\$3.2	\$38	\$19	\$19
Infectious	12	\$3.0	\$943	\$314	\$432
Dermatologic	4	\$2.1	\$48	\$16	\$15
Musculoskeletal	6	\$1.9	\$215	\$72	\$80
Hematologic	3	\$1.3	\$200	\$200	\$200
Ophthalmic	10	\$0.7	\$119	\$30	\$13
Pulmonary	8	\$0.3	\$10	\$10	\$10
Renal	1	\$0.1	\$0	\$0	\$0
Gastrointestinal	2	\$0.0	\$0	\$0	\$0
Genitourinary	2	\$0.0	\$7	\$7	\$7
	<b>375</b>	<b>\$153.9</b>	<b>\$12,318</b>		



# Top Big Pharma M&A Dealmakers in 2024

2024 - By Number of Deals - Big Pharma Buy-Side			
Buyer	Number of Deals	Total Deal Value (\$B)	Total Upfront Cash and Equity (\$B)
J&J	6	\$18.9	\$17.8
Novartis	5	\$6.2	\$4.2
Merck	4	\$5.2	\$2.0
AbbVie	4	\$2.1	\$2.0
Novo Nordisk / Novo Holdings	3	\$17.6	\$16.5
AstraZeneca	3	\$3.5	\$2.8
GSK	2	\$1.5	\$1.1
Vertex	1	\$4.9	\$4.9
Gilead	1	\$4.3	\$4.3
Eli Lilly	1	\$3.2	\$3.2
Sanofi	1	\$2.2	\$1.7
Roche	1	\$1.5	\$1.0
<b>Total - These 10</b>	<b>32</b>	<b>\$71.0</b>	<b>\$61.4</b>

2024 YTD - By Total Deal Value - Big Pharma Buy-Side			
Buyer	Number of Deals	Total Deal Value (\$B)	Total Upfront Cash and Equity (\$B)
J&J	6	\$18.9	\$17.8
Novo Nordisk / Novo Holdings	3	\$17.6	\$16.5
Novartis	5	\$6.2	\$4.2
Merck & Co.	4	\$5.2	\$2.0
Vertex	1	\$4.9	\$4.9
Gilead	1	\$4.3	\$4.3
AstraZeneca	3	\$3.5	\$2.8
Eli Lilly	1	\$3.2	\$3.2
Sanofi	1	\$2.2	\$1.7
AbbVie	4	\$2.1	\$2.0
Roche	1	\$1.5	\$1.0
GSK	2	\$1.5	\$1.1
<b>Total - These 10</b>	<b>32</b>	<b>\$71.0</b>	<b>\$61.4</b>

2024 - By Upfront Cash & Equity - Big Pharma Buy-Side			
Buyer	Number of Deals	Total Deal Value (\$B)	Total Upfront Cash and Equity (\$B)
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Gilead	1	\$4.3	\$4.3
Novartis	5	\$6.2	\$4.2
Eli Lilly	1	\$3.2	\$3.2
AstraZeneca	3	\$3.5	\$2.8
Merck	4	\$5.2	\$2.0
AbbVie	4	\$2.1	\$2.0
Sanofi	1	\$2.2	\$1.7
GSK	2	\$1.5	\$1.1
Roche	1	\$1.5	\$1.0
<b>Total - These 10</b>	<b>32</b>	<b>\$71.0</b>	<b>\$61.4</b>

# Appendix: About Stifel's Life Science Franchise



# Stifel Healthcare: Bullish on the Life Sciences Sector

## STIFEL | Healthcare

Our Deep Sector Knowledge and Differentiated Capabilities Drives Strong Results For Our Clients

<p><b>100+</b> Investment bankers, globally</p>	<p><b>Deep Team Covering 4 Industry Verticals</b> Biopharma &amp; Spec Pharma   HCIT   Medtech &amp; Diagnostics   Healthcare Services</p>	<p><b>15</b> Research analysts covering <b>230</b> companies</p>
<p>Bookrun <b>251</b> financings raising over <b>\$48.3bn</b> 2020 - 2024</p>	<p><b>Prolific Underwriting Experience</b> IPOs   Follow-ons   CMOs   RDs   ATMs   144As   Private Placements   PIPEs   Converts   Debt</p>	<p>Raised <b>\$129.4bn</b> for <b>333</b> healthcare companies in <b>679</b> transactions<sup>(2)</sup></p>
<p><b>175</b> Advisory transactions 2020 - 2024 <b>\$29.1bn</b> of value<sup>(1)</sup></p>	<p><b>Dedicated M&amp;A Franchise</b> Mergers   Acquisitions   Divestitures   Collaborations   Partnerships   Activist / Defense   Other Financial Advisory Situations</p>	<p><b>388</b> transactions since 2010<sup>(2)</sup> <b>176+</b> cross-border deals since 2010<sup>(2)</sup></p>
<p><b>2022</b> Investment Bank of the Year – Americas<sup>(3)</sup> <b>#1</b> ranked bank for virtual roadshows in 2022<sup>(4)</sup></p>	<p><b>Backed by Full Service Investment Bank</b> Research   Trading &amp; Distribution   M&amp;A   Equity Capital Markets   Debt Capital Markets   Restructuring Advisory   Private Capital Markets</p>	<p><b>Research-led Healthcare Conferences</b></p> <ul style="list-style-type: none"> <li>- Stifel Healthcare Conference</li> <li>- Biotech Ski Summit Conference</li> <li>- Content driven equity research events</li> </ul>

Note: Accounts for Stifel's recent acquisition of Torrey Capital LLC and its affiliated entities, which closed on March 1, 2023.

(1) Only includes value where purchase price was disclosed.

(2) Since Q4 2010.

(3) Global M&A Network as of February 6, 2023.

(4) Investor Relations magazine as of February 7, 2023.



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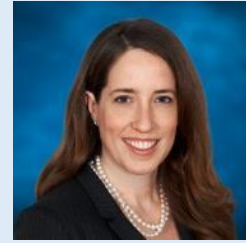
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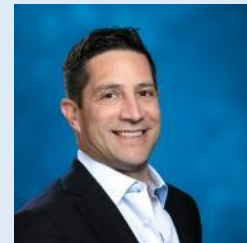
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# Stifel Active in Life Sciences Sector Advisory Transactions

Today, biopharma companies find themselves in a fast-moving environment characterized by great opportunity. This environment calls for getting the best possible advisor by your side. Stifel's Global Healthcare Group brings senior level attention and intense focus on execution to its clients. The group has been active in 2024's dynamic deal environment. Since the formation of the Global Healthcare Group in 2010, Stifel's team has advised on close to 400 strategic transactions.

## Mergers and Acquisitions

 Has Acquired  Advisor to Buyer December 2024	A\$120,000,000  Has Acquired  Advisor to Buyer December 2024	 Has Merged with  Advisor to Pieris December 2024	 Has Acquired  Advisor to Buyer October 2024
 Has Been Acquired by  Advisor to Seller August 2024	 Has Been Acquired by  Advisor to Seller April 2024	 Has Acquired  Financial Advisor March 2024	\$175,000,000  Has Been Acquired by  Advisor to Seller December 2023
 Has Agreed to be Acquired by  Advisor to Seller Pending	\$90,833,010  Has Merged with  Advisor to Buyer October 2023	\$235,000,000 Plus Pass-through Payments  Has Been Acquired by  Advisor to Seller August 2023	 Has Merged with  Financial Advisor June 2023

## Licensing Transactions

 Out-License of Sugemalimab in MENA and South Africa Region  Advisor to Licensor November 2024	 Has Sold its Rights to Contepo (Fosfomycin for Injection) to  Advisor to Seller July 2024	Up to \$51,300,000  Out-License of Sugemalimab in CEE Region  Advisor to Licensor May 2024	 Strategic Agreements  Advisor to Seller January 2024
\$245,000,000+  In-Licensing of the Japan Rights to Three Rare Endocrinology Drugs from  Advisor to Licensee November 2023	Up to \$132,500,000  Out-License of Zetomizomib in Greater China, South Korea and SE Asia to  Advisor to Licensor September 2023	Up to \$600,000,000  Out-Licensing of LM-305 to  Advisor to Licensor May 2023	 Out-license of APB-102  Advisor to Licensor February 2023
Up to \$113,000,000  Ebopirant License Agreement Has Been Acquired by  Advisor to Seller November 2022	 Has Out-Licensed Bexacat™ to  Advisor to Licensor June 2022	Up to \$1,200,000,000  Out-Licensing of LM-302 to  Advisor to Licensor May 2022	 Out-license of U.S. Rights to Posimir to  Advisor to Licensor December 2021

## Asset Sales

<b>Global Biopharma Company</b> Purchase of a Rare Pediatric Disease Priority Review Voucher from <b>Global Biopharma Company</b> Advisor to Buyer September 2024	 Sale of Controlling Stake in OSD Business to  Advisor to Seller August 2024	 Has Sold its Long-acting Insulin Products to  Advisor to Seller July 2024	<b>Top 50 Pharma Company</b> Sale of its Rare Pediatric Disease Priority Review Voucher to <b>Top 10 Large-Cap Pharma Company</b> Advisor to Seller March 2024
\$100,000,000  Has Acquired U.S. and Canadian Rights to  Advisor to Buyer December 2023	 Has Acquired API Unit from  Advisor to Buyer August 2023	<b>Top 50 Pharma Company</b> Sale of Rare Pediatric Disease Priority Review Voucher (PRV) to <b>Top 10 Large-Cap Pharma Company</b> Advisor to Seller July 2023	 Has Agreed to Sell Certain Assets to Tisento Therapeutics Advisor to Seller July 2023
 Has Agreed to Sell Certain Assets to  Advisor to Seller Pending	 Has Sold Certain Assets to  Advisor to Seller March 2023	 Has Acquired Bulk Formulation Manufacturing Facility from  Advisor to Buyer April 2023	 Divestiture of Assets  Advisor to Seller June 2023



# Stifel Continues To Lead in Biopharma Financings

## Select 2024 Stifel Financings

<p>\$55,550,000</p>  <p>PIPE Sole Placement Agent December 2024</p>	<p>\$50,000,000</p>  <p>Registered Direct Joint Bookrunning Manager December 2024</p>	<p>\$257,600,000</p>  <p>Follow-on Offering Joint Bookrunning Manager December 2024</p>	<p>\$402,500,000</p>  <p>Follow-on Offering Joint Bookrunning Manager December 2024</p>	<p>\$60,000,000</p>  <p>Registered Direct &amp; PIPE Joint Bookrunner &amp; Joint Placement Agent November 2024</p>	<p>\$200,000,000</p>  <p>PIPE Joint Placement Agent November 2024</p>	<p>\$300,000,000</p>  <p>PIPE Joint Placement Agent October 2024</p>	<p>\$200,000,000</p>  <p>PIPE Joint Placement Agent Pending</p>	<p>\$575,000,000</p>  <p>Follow-on Offering Joint Bookrunning Manager September 2024</p>	<p>\$187,680,000</p>  <p>Initial Public Offering Joint Bookrunning Manager September 2024</p>	<p>\$362,250,000</p>  <p>Initial Public Offering Joint Bookrunning Manager September 2024</p>
<p>\$258,750,000</p>  <p>Follow-on Offering Joint Bookrunning Manager September 2024</p>	<p>\$200,536,320</p>  <p>PIPE Joint Placement Agent September 2024</p>	<p>\$230,000,000</p>  <p>Follow-on Offering Joint Bookrunning Manager September 2024</p>	<p>\$258,800,000</p>  <p>Confidentially Marketed Follow-on Offering Joint Bookrunning Manager August 2024</p>	<p>\$130,000,000</p>  <p>Registered Direct Joint Bookrunning Manager August 2024</p>	<p>\$174,400,000</p>  <p>Initial Public Offering Joint Bookrunning Manager June 2024</p>	<p>\$60,000,000</p>  <p>Registered Direct Joint Bookrunning Manager May 2024</p>	<p>\$374,325,000</p>  <p>Follow-on Offering Joint Bookrunning Manager May 2024</p>	<p>\$75,000,000</p>  <p>Registered Direct Sole Bookrunning Manager May 2024</p>	<p>\$280,000,000</p>  <p>PIPE Joint Placement Agent April 2024</p>	<p>\$201,250,000</p>  <p>Confidentially Marketed Follow-on Offering Joint Bookrunning Manager April 2024</p>
<p>\$118,778,912</p>  <p>Initial Public Offering Joint Bookrunning Manager April 2024</p>	<p>€65,500,000</p>  <p>PIPE Joint Lead Placement Agent February &amp; April 2024</p>	<p>\$240,100,310</p>  <p>Registered Direct Joint Bookrunning Manager March 2024</p>	<p>\$150,000,000</p>  <p>Registered Direct Joint Bookrunning Manager March 2024</p>	<p>\$180,000,000</p>  <p>PIPE Joint Placement Agent March 2024</p>	<p>\$54,207,127</p>  <p>Registered Direct Joint Bookrunning Manager March 2024</p>	<p>\$95,000,000</p>  <p>PIPE Joint Placement Agent March 2024</p>	<p>\$482,999,902</p>  <p>Follow-on Offering Joint Bookrunning Manager March 2024</p>	<p>\$140,000,000</p>  <p>Follow-on Offering Joint Bookrunning Manager March 2024</p>	<p>\$632,540,250</p>  <p>Follow-on Offering Joint Bookrunning Manager February 2024</p>	<p>\$147,936,000</p>  <p>Initial Public Offering Joint Bookrunning Manager February 2024</p>

Stifel Has completed 679 Healthcare Financing Transactions since Q4 2010 raising over \$129.4bn for clients

Source: Dealogic and Stifel Capital Markets as of December 31, 2024.

Note: Deal values and dates represented are as of the announcement that the definitive agreement was signed. Stifel transactions include deals completed by Stifel, Nicolaus & Company, Incorporated and its affiliated entities and Torrey Capital LLC and its affiliated entities. Any pending IPO transaction tombstones on this page are neither an offer to sell nor a solicitation of an offer to buy any of these securities. An offer may only be made by the prospectus for the offering.

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