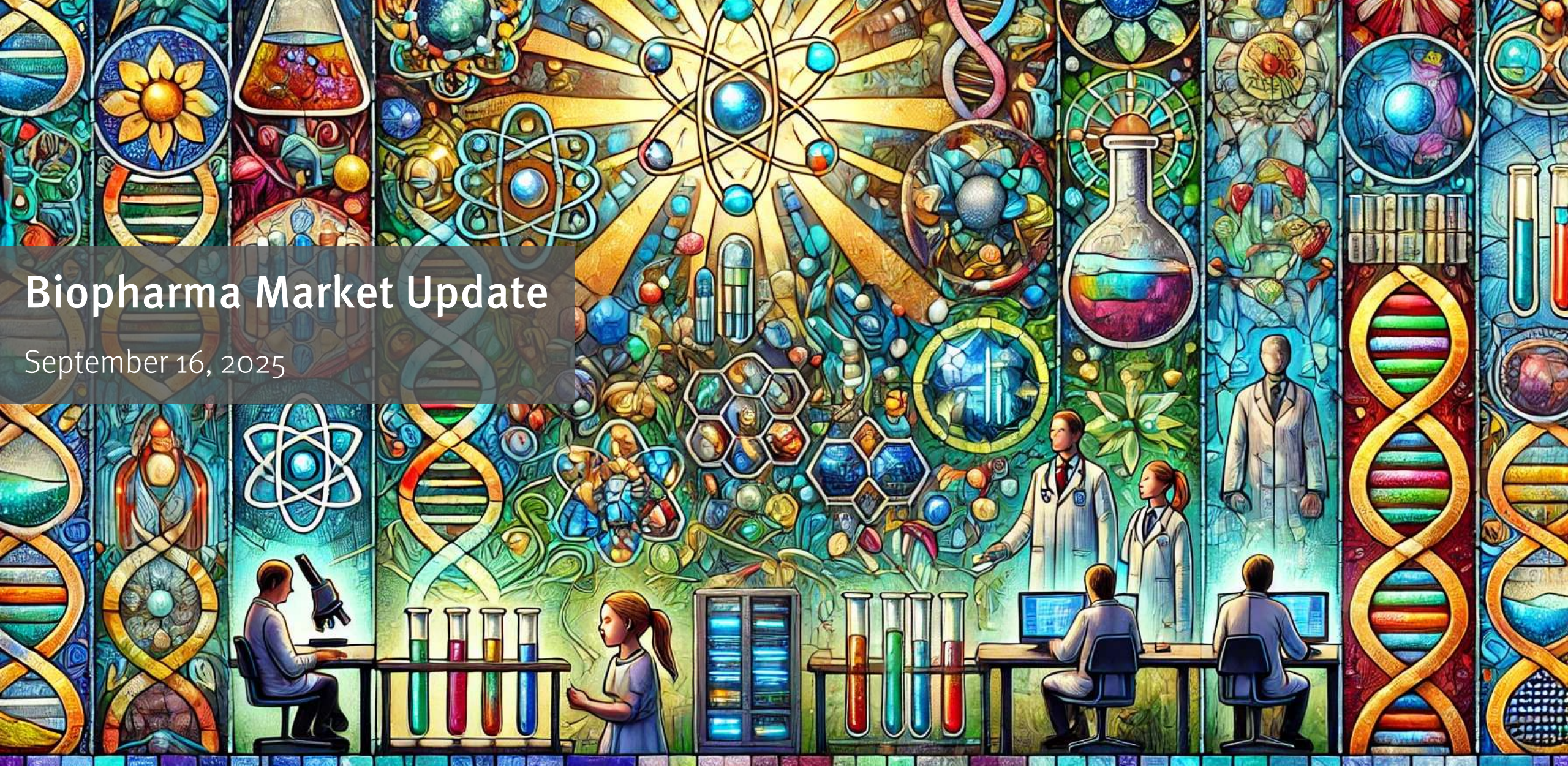

Biopharma Market Update

September 16, 2025

STIFEL | Healthcare

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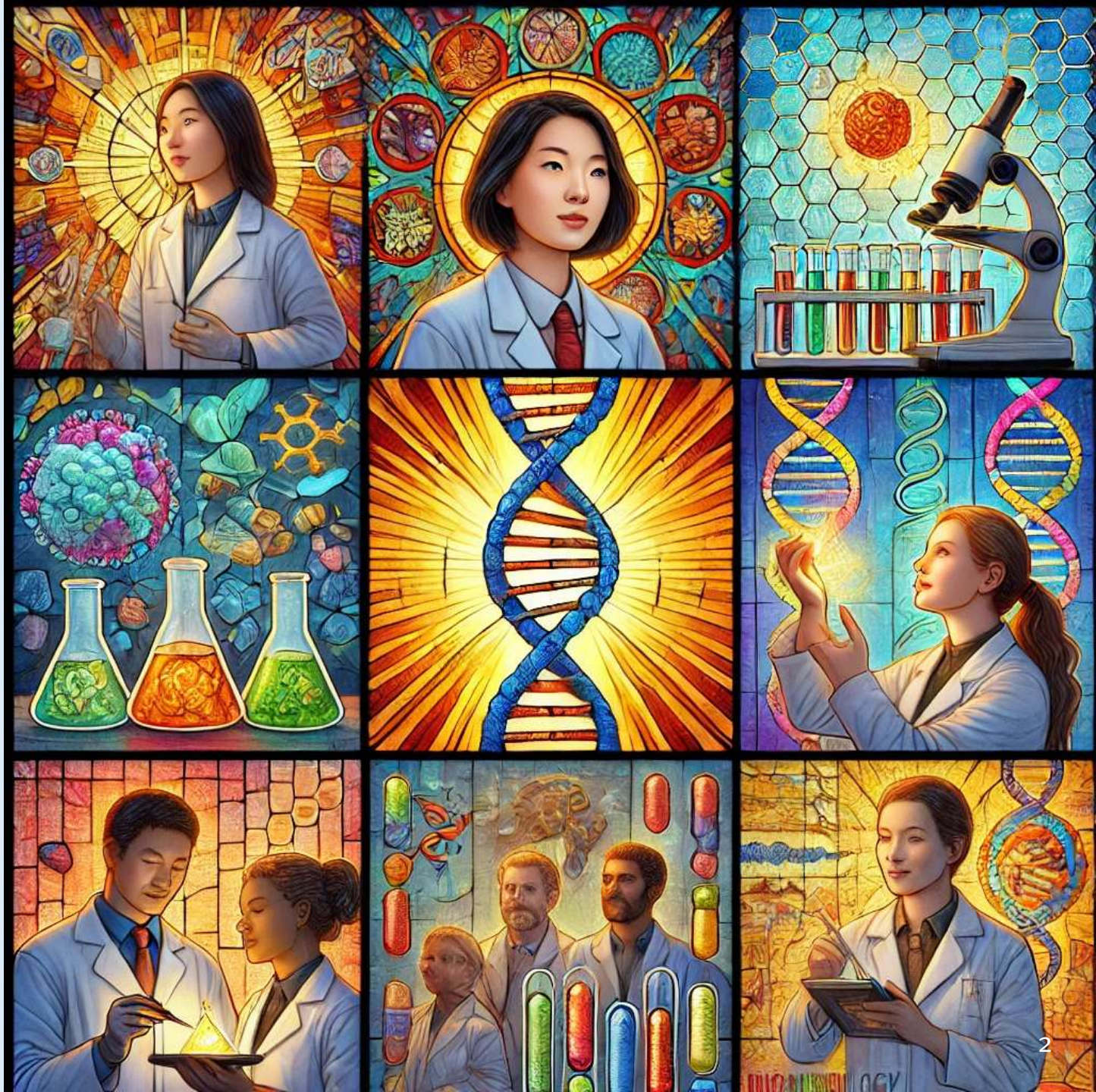

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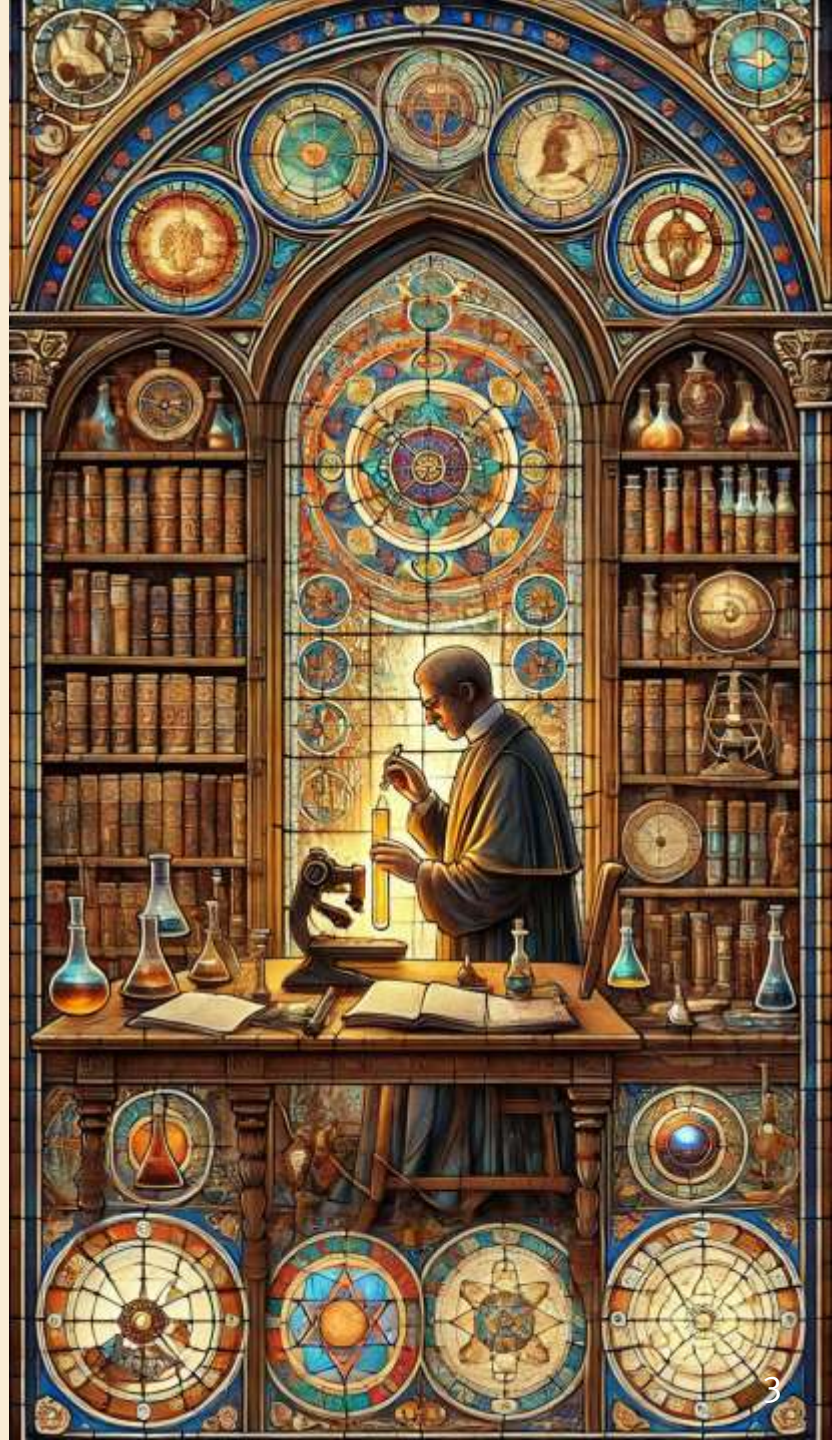

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[Jun 5, 2025]

Aging Biology, Part I

[Mar 26, 2025]

2025 Biotech Outlook

[Jan 8, 2025]

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Macro and Political Update

Rise in U.S. Inflation Is Likely to Keep Fed Cautious on Pace of Rate Cuts

Colby Smith, *New York Times*, September 11, 2025 (excerpt)

U.S. inflation accelerated in August at a speed that is likely to keep the Federal Reserve cautious about lowering borrowing costs too quickly once it restarts cuts as soon as next week.

The Consumer Price Index, released on Thursday by the Bureau of Labor Statistics, rose 2.9 percent from the same time last year, the fastest annual pace since the start of 2025.

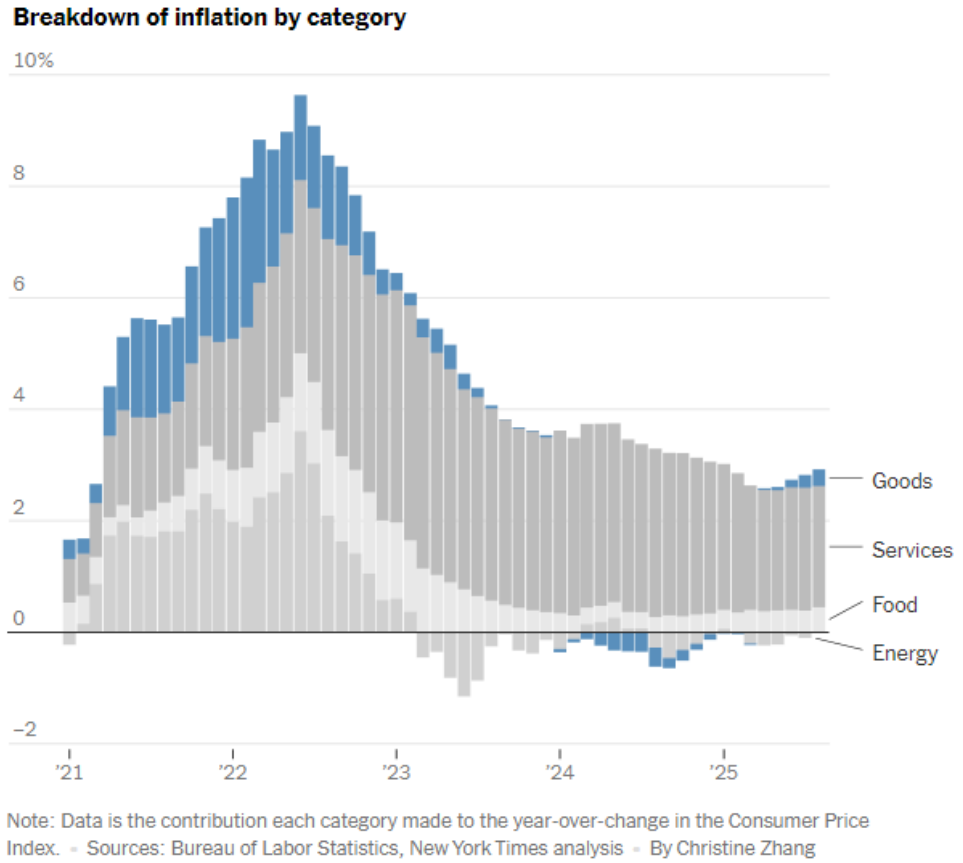
“Core” inflation, which the central bank tracks as a gauge of underlying inflation since it strips out volatile items like energy and food prices, steadied at 3.1 percent.

The overall measure of inflation rose 0.4 percent for the month, slightly higher than economists had expected. The core measure rose 0.3 percent.

The inflation data has been pivotal to the Fed’s debate about not only when it should lower interest rates again after a long pause but also the speed at which the central bank moves as that process kicks off.

The issue for the Fed is that Mr. Trump’s levies have pushed up costs across a wide range of goods, upending earlier progress on bringing inflation down. Declines in other categories have limited the overall increase, helping to placate earlier fears that the resulting inflation surge would be much more intense.

Source: https://www.nytimes.com/2025/09/11/business/cpi-inflation-fed-rate-cuts.html



Trump Tariffs are Fueling Inflation, Budget Chief Says

Erin Doherty, CNBC, September 15, 2025

Congressional Budget Office director Phillip Swagel said Monday that President Donald Trump's tariffs appear to have pushed inflation up higher than CBO analysts had initially expected.

His views differ from those of Wall Street analysts, many of whom have been bracing for tariff-driven price hikes, but have yet to see them in materialize.

Speaking on CNBC's "Squawk Box," Swagel said the CBO analysis shows the economy has weakened since January, which he would expect to exert downward pressure on inflation.

Swagel also shared his office's long-term view of the impact of Trump's tariffs: The CBO expects the levies to reduce the U.S. budget deficit by $4 trillion over the next decade by pouring money into the federal coffers.

"So $3.3 trillion of revenue and then $700 billion of averted debt costs," he said. "That would be a big reversal in terms of the deficit."

Source: https://www.cnbc.com/2025/09/15/trump-trade-inflation-tariffs-cbo.html

Phil Swagel

Director, Congressional Budget Office

Investors Seek Fed's View of Shaky Labor Market as Rate Cut Looms

Lewis Krauskopf, *Reuters*, Sep 14, 2025 (excerpt)

Investors will look for the Federal Reserve to communicate how worried it is about the flagging U.S. labor market at its meeting next week and they expect the central bank to cut interest rates for the first time in nine months to shore up employment.

On Thursday, inflation data came in slightly hotter than expected. Still, market players did not expect this would dissuade the Fed from easing rates on Wednesday, following several downbeat reports about U.S. job growth.

With some recent stability in trade and fiscal policy, "the Fed has moved back onto the front burner for investors going forward," said Chris Fasciano, chief market strategist at Commonwealth Financial Network. "Now that the labor market is weakening, the Fed becomes the dominant story for investors as to how they address that," Fasciano said.

Expectations that the Fed will reduce interest rates have helped lift the major U.S. stock indexes to record highs, along with excitement over the potential of artificial intelligence, strong corporate earnings and calming fears about the economic fallout from President Donald Trump's tariffs. The benchmark S&P 500 (.SPX), opens new tab is up 12% so far in 2025.

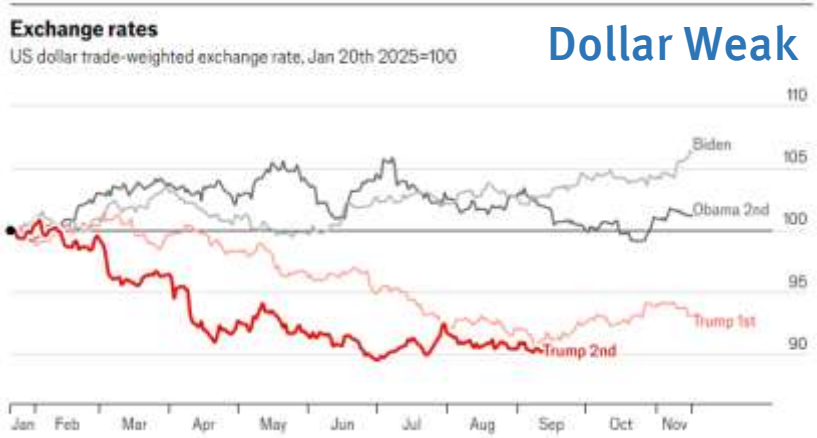
As of Thursday, Fed fund futures indicated that markets were expecting a 90% chance that the Fed lowers rates by 25 basis points in next Wednesday's policy decision, according to LSEG data. The balance of expectations left about a 10% chance for a larger-than-standard 50 bp cut.

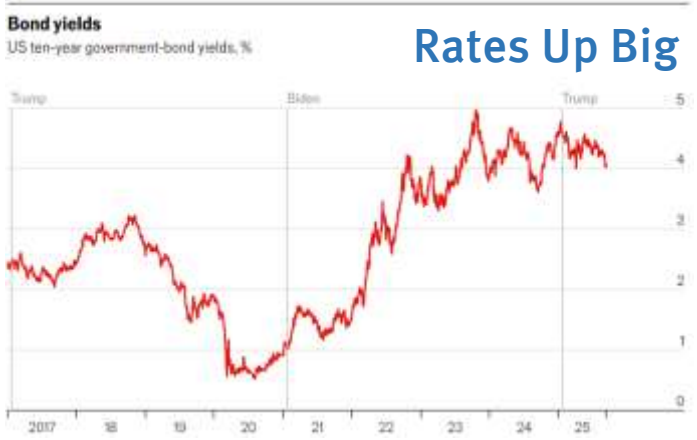
Source: https://www.reuters.com/business/wall-st-week-ahead-investors-seek-feds-view-shaky-labor-market-rate-cut-looms-2025-09-12/

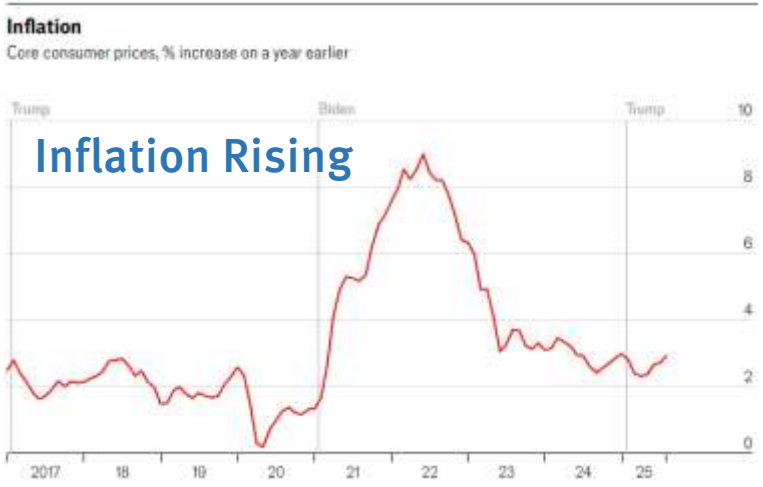
Nine Months Into Trump's Term: The Economy

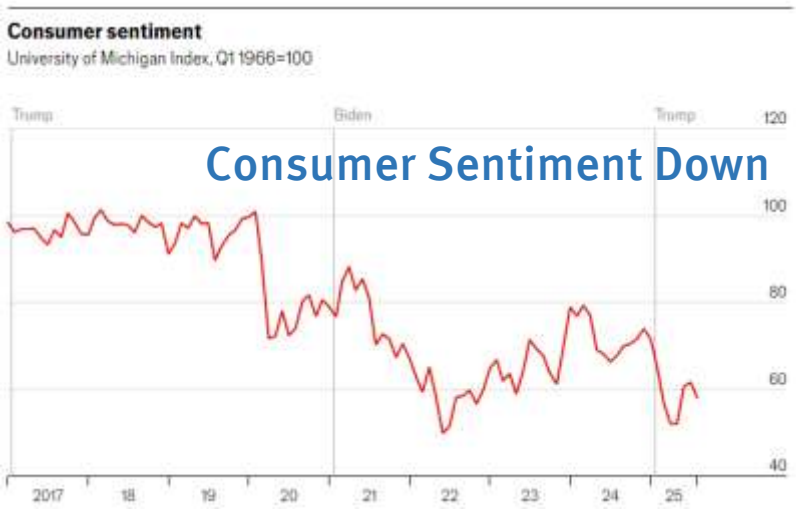
***Economist*, Sep 14, 2025 (excerpt)**

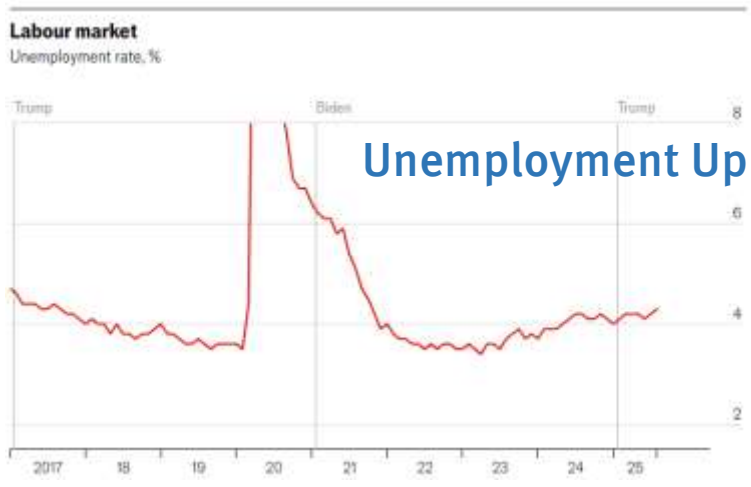
GDP grew in the second quarter, but the healthy headline figure was flattered by a sharp drop in imports (in the first quarter the reverse was the case). But strains are starting to show: retail sales are weakening, housing starts have dropped to their lowest since mid-2020 and an immigration crackdown is tightening labour supply. And the labour market may be softening: America added just 73,000 jobs in July, far below economists' expectations.











Source: https://www.economist.com/interactive/trump-approval-tracker/economy

Trump is Selling a Strong Economy. Voters Aren't Buying It

Megan Messerly, *Politico*, Sep 13, 2025 (excerpt)

President Donald Trump this week insisted Americans are experiencing the "best economy we've ever had." Privately, White House officials acknowledge people just aren't feeling it.

The economy grew faster in the second quarter than initially anticipated, productivity was revised upwards, inflation hasn't surged despite new tariffs and gas prices have fallen to levels not seen in decades. Republicans also avoided what would have amounted to a major tax increase with Trump's One Big Beautiful Bill earlier this year. But polls show Americans remain anxious about high prices, and there are signs the economy's resilience is starting to fray, making it harder for the administration to close the delta between how the economy looks on paper and how people feel. The Congressional Budget Office also said Friday that the megalaw will have little effect on economic growth before the 2028 election, its gains blunted by the president's tariffs and immigration crackdown.

"That's a thing that I know the White House political team is nervous about because there's a reality and there's a perception. And the reality is the economy is doing fine and the perception is people are still worried about things like grocery prices, which are still high, and still growing," said Stephen Moore, an outside economic adviser to Trump who the president featured in an impromptu Oval Office press conference last month.

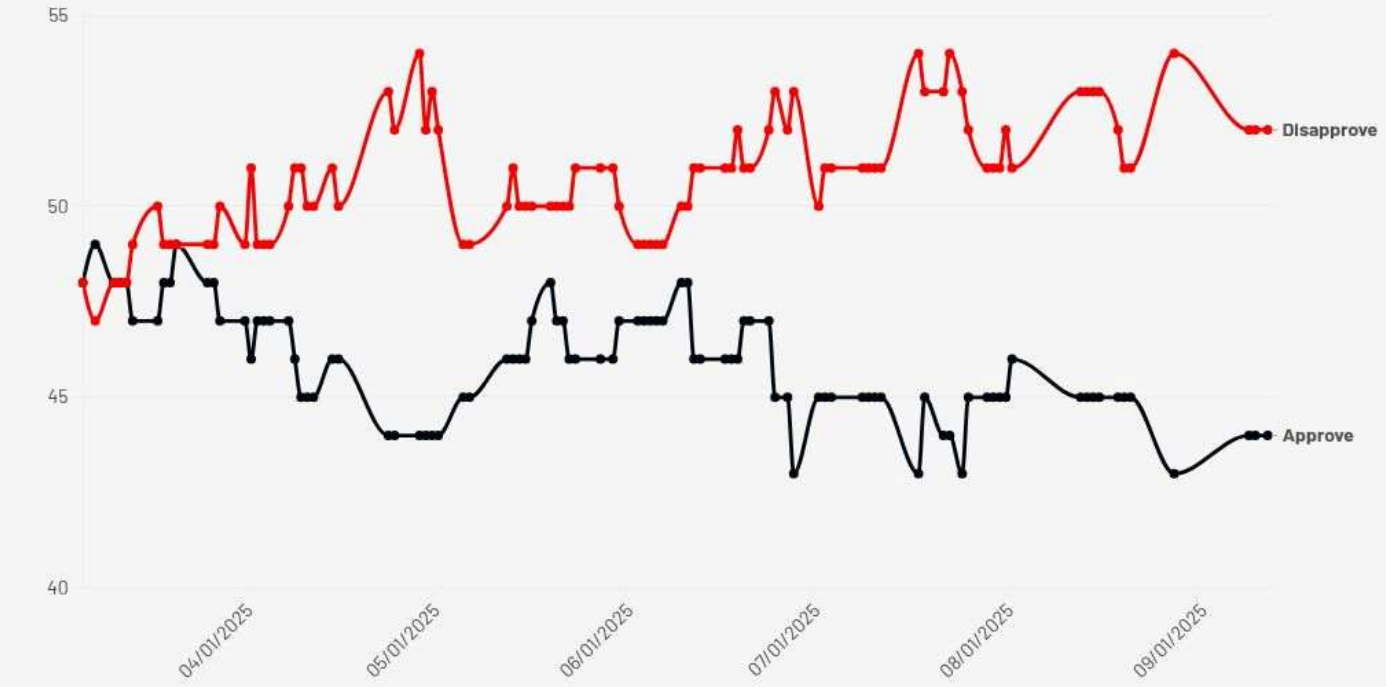
Trump, in an interview on "Fox & Friends" Friday, pointed to the trillions of dollars of investments in the U.S. that companies have promised since he took office and the record high stocks hit on Thursday, insisting that Americans are experiencing the "best economy we've ever had." Trumpeting positive economic statistics in the face of sagging sentiment is a political trap that has ensnared many administrations, including, most recently, the Biden White House. During former President Joe Biden's term, the president and his aides insisted that economic statistics vindicated their policies even as that data failed to move frustrated voters.

Republicans could face a similar problem as they head into what is expected to be a difficult fight for control of the House. A recent CBS News poll found that just 36 percent of Americans say the economy is "good," while the New York Federal Reserve said Monday that people believe there is a 45 percent chance they can find a new job if unemployed — the weakest reading since the survey began in 2013. Together, the numbers sketch a picture of an American electorate more jittery than jubilant.

The August jobs report also came in weaker than expected, inflation remains above the Fed's target and jobless claims just hit their highest level since late 2021.

Source: https://www.politico.com/news/2025/09/13/trump-is-selling-a-strong-economy-voters-arent-buying-it-00561986

Trump Approval Ratings Struggling



Sources: https://www.newsweek.com/donald-trump-approval-rating-polls-economy-2128978

Attack on Lisa Cook: ‘Trump’s Going to Take the Fed Over’

Vittoria Guida, *Politico*, Sep 11, 2025 (excerpt)

Wall Street has shrugged off President Donald Trump’s attempt to fire Federal Reserve official Lisa Cook, even as the matter is destined to reach the Supreme Court.

But the central bank’s insulation from the president could eventually hinge on whether investors start to panic.

If the court ultimately gives Trump broad authority to decide the grounds on which Fed board members can be ousted, it could create a pathway to removing other central bank officials — even, theoretically, Chair Jerome Powell, an event that would send shockwaves through the global economy.

But for now, the range of possible outcomes is so broad that it’s hard for investors to bet on any result with precision.

So, short of Trump moving against Powell, what would cause markets to react?

The answer I heard from several people on Wall Street: The freakout might not come until the Fed actually starts behaving less independently. BNY chief economist of investments Vincent Reinhart told me that pervasive fears about the loss of central bank independence could be an “amplifier” of market stress if there’s a worrying increase in inflation.

Source: https://www.politico.com/news/magazine/2025/09/11/trump-powell-fed-cook-markets-00557651

Appeals Court Says Lisa Cook Can Remain on Fed Board

Tony Romm, Colby Smith and Ben Casselman, *New York Times*, September 15, 2025 (excerpt)

A federal appeals court on Monday denied a last-minute attempt by President Trump to block Lisa Cook, a governor on the Federal Reserve, from participating in a meeting of the central bank, in a move that will allow her to cast a vote this week on interest rates.

The ruling marked the second legal defeat for Mr. Trump, who has sought to install a roster of political loyalists at the Fed. With Ms. Cook, the president has labored to oust her over allegations of mortgage fraud, even though she hasn't been charged with a crime.

The decision from the U.S. Court of Appeals for the District of Columbia Circuit upheld the work of a lower judge, who temporarily blocked Mr. Trump earlier this month from firing Ms. Cook while the two sides war over the legality of her dismissal. The court rejected the president's emergency request to halt that order, which would have allowed him to proceed with the firing.

Mr. Trump and his top deputies had claimed that Ms. Cook falsified records to obtain favorable mortgage terms before her arrival at the Fed. But Ms. Cook, who has been neither charged with nor convicted of a crime, sued on grounds that her dismissal was unlawful under the Fed's chartering statute.

Source: https://www.nytimes.com/2025/09/15/us/politics/lisa-cook-fed-appeals-court-decision.html

Lisa Cook

Governor, Federal Reserve Board

China is Ditching the Dollar, Fast

The Economist, Sep 10, 2025 (excerpt)

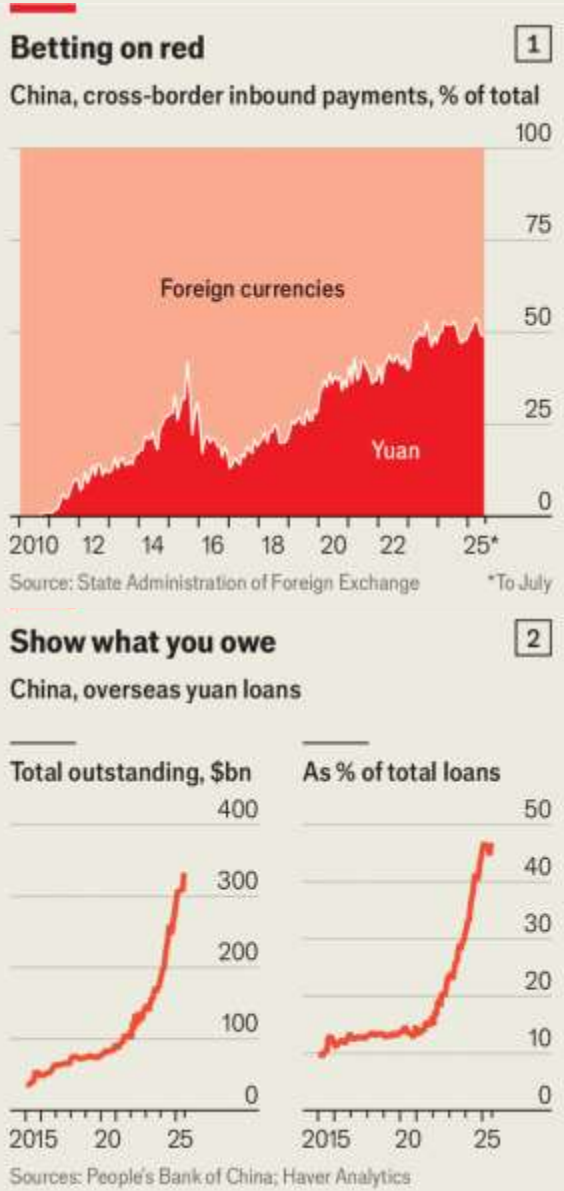
China's leaders sense an epic opportunity. President Donald Trump's erratic trade policy, gaping fiscal deficits and threats to the independence of America's Federal Reserve risk badly hurting the dollar. It has slumped 7% on a trade-weighted basis since January, and had its worst start to a year since 1973. By contrast, China's tightly controlled currency, the yuan, has reached its highest level since Mr Trump was re-elected in November. Foreign investors are piling in. So are many governments looking for dollar alternatives.

Such keen interest is not new. Neither is China's desire to internationalise the yuan. The country's first such push began in 2009 and saw it loosen some capital controls. That ended painfully back in 2015, when a stockmarket rout and currency devaluation saw money rush for the exits. A capital clampdown followed and ended the yuan's nascent rise. This time around, officials are eager to ensure that progress is lasting and that they retain a tighter grip over capital flows.

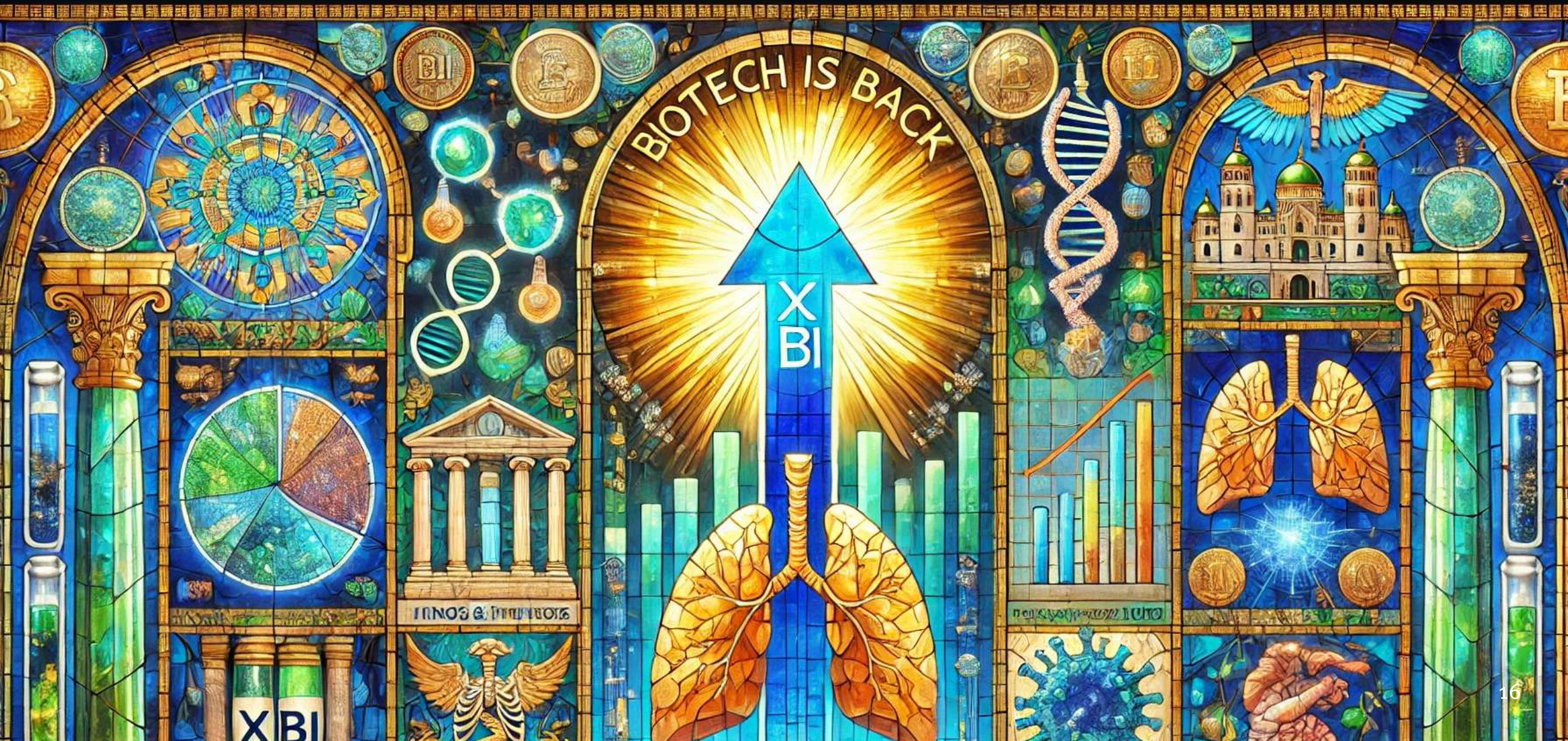
China's leaders think a globally accepted yuan can insulate their exporters from movements in the dollar's value and blunt the threat of America's financial sanctions. Some officials hope that foreign firms and investors will overlook the state's rigid control and, perhaps, even come to see it as an asset. In recent years they have made surprising gains.

So what has China achieved so far? By any measure, the yuan lacks cachet. Though China is responsible for nearly a fifth of global economic activity, its tender is used in only 4% of international payments by value (compared with 50% for the dollar). Yuan assets make up just 2% of global central-bank currency reserves (compared with 58% for dollar assets). A lot of this mismatch can be blamed on China's controls on money flowing in and out of the country. Many economists think that internationalising the yuan is impossible while they remain in place.

Source: https://www.economist.com/china/2025/09/10/china-is-ditching-the-dollar-fast



Biopharma Market Update



Biotech Sector Shows No Signs of Slowing

Doug Busch, *Barron's*, Sep 9, 2025 (excerpt)

Biotech stocks are on a winning streak that might just continue through the rest of the year.

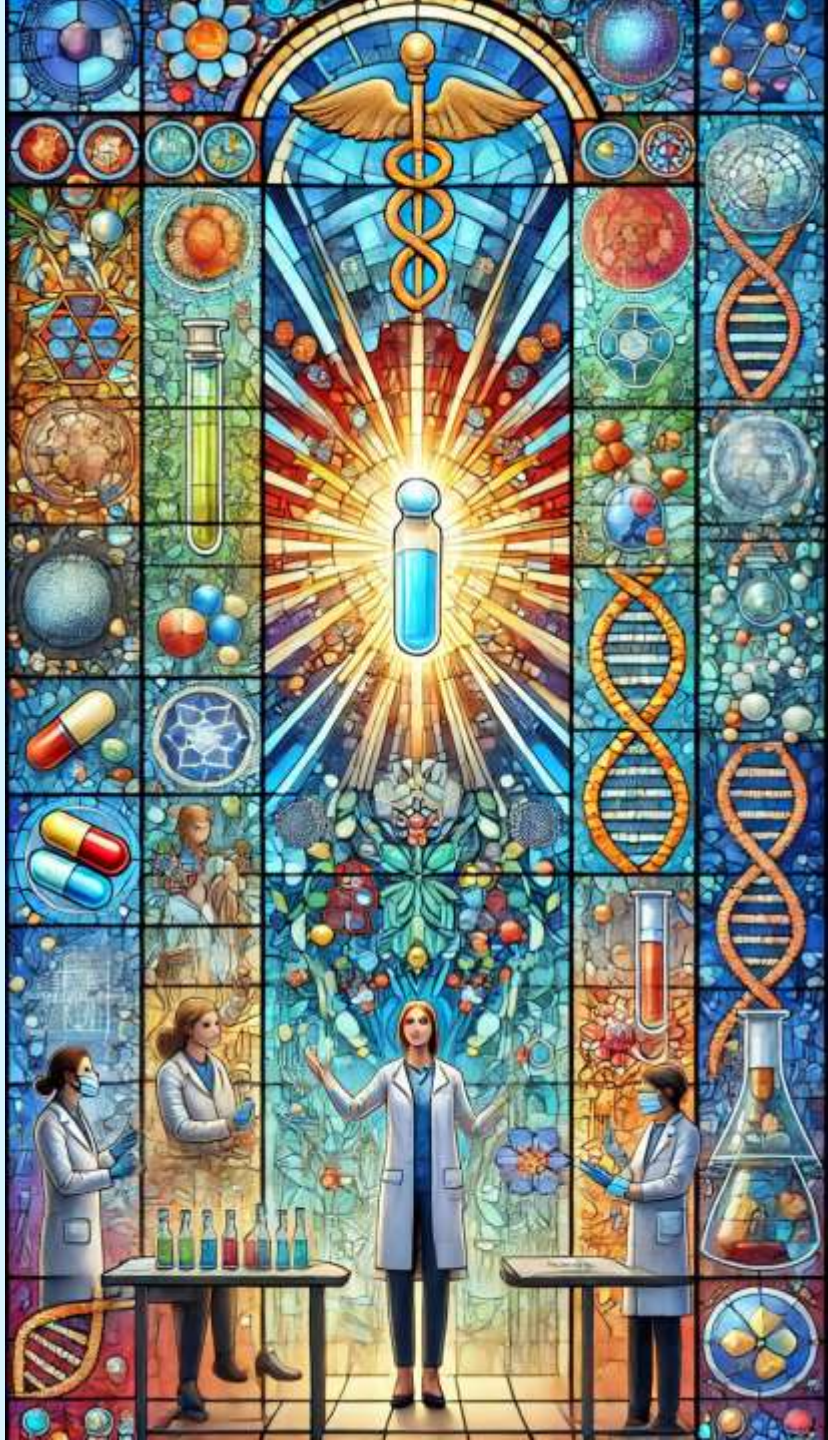
Last week, the SPDR S&P Biotech exchange-traded fund (ticker: XBI) surged 6%, contrasting with a 0.8% decline in the broader healthcare space, as measured by the Health Care Select Sector SPDR fund (XLV).

When the biotech sector shows signs of renewed strength, it often signals a broader risk-on sentiment among investors.

The biotech ETF, up 5% in 2025, is poised for its third consecutive annual percent gain in the single digits.

Could the sector be gearing up for a meaningful rally into year-end? We last discussed this possibility in July, and technical analysis of recent price action says yes. The monthly chart reveals a bullish breakout above a long-term bearish head and shoulders pattern. That breakout projects a push toward the very round $100 level near term, and a potential advance to $115 by the first quarter of 2026.

Source: https://www.barrons.com/articles/biotech-stocks-incyte-merus-crispr-d56d1cf9



Biopharma Hedge Funds Rebounded Sharply Last Month

Stephen Taub, *Institutional Investor*, Sep 11, 2025 (excerpt)

A number of biopharma and life sciences hedge funds posted extraordinary gains in August, catapulting them into the black for the year. The big question moving forward is whether this signals a bottom for the embattled sector or just a one-month blip.

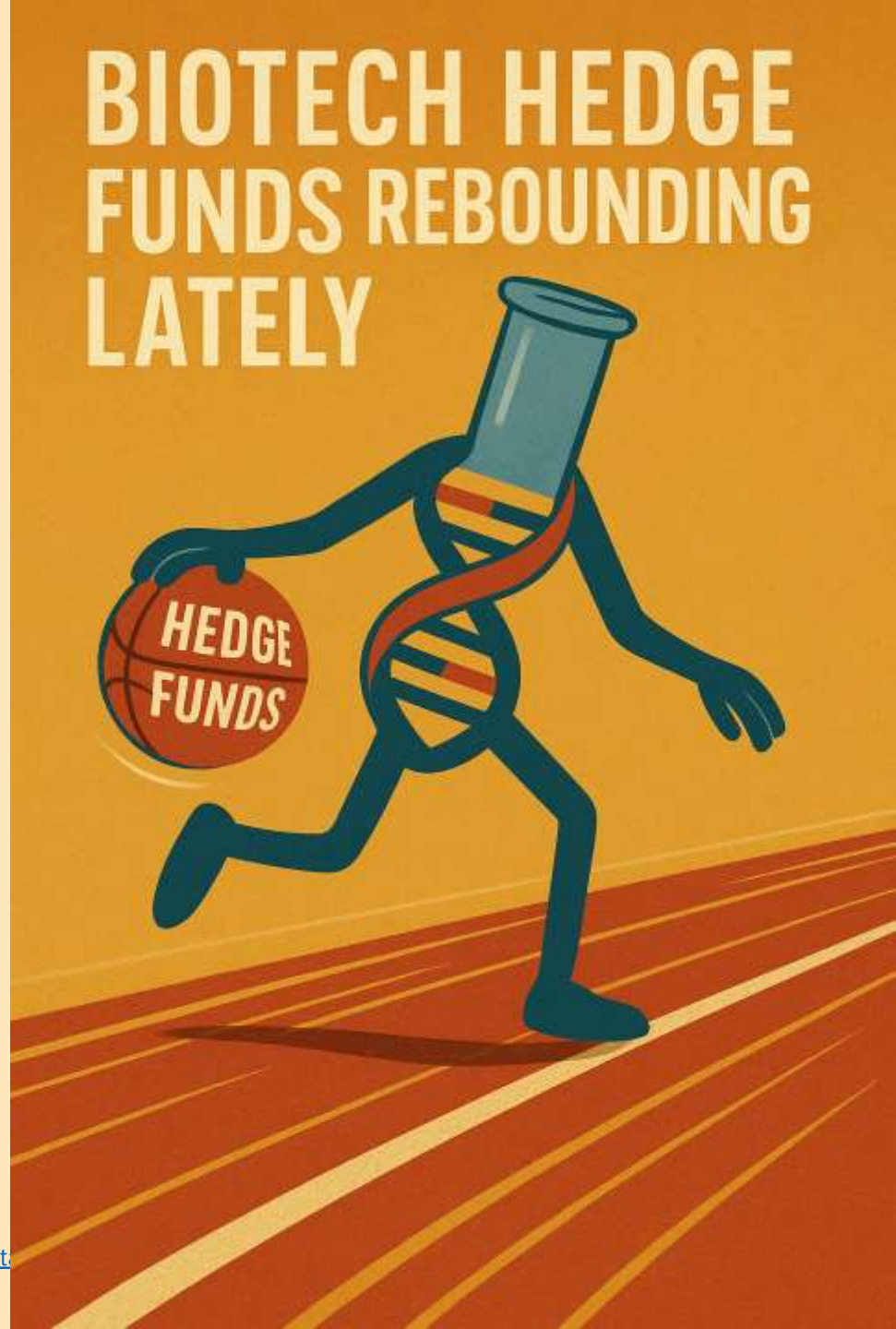
The group has been hurt in part by the Trump administration's antivaccine policy and purging of many key people in the various health care–related agencies. However, a recent spate of acquisitions and joint ventures involving biopharma companies has acted like a needed shot in the arm for many of these stocks.

For example, last month Royalty Pharma announced it had acquired a royalty interest in Amgen's drug Imdelltra from BeOne Medicines for $885 million, according to a press release. The drug is described as a first-in-class bispecific T-cell engager. The agreement includes an option for BeOne to sell additional Imdelltra royalties to Royalty Pharma for up to $65 million within the next 12 months.

Perhaps the top-performing biopharma-focused hedge fund in August was Avoro Capital Advisors, which climbed by high teens and is now up about 6 percent, says an investor. Ascendis Pharma, its largest long, accounting for more than 15 percent of assets, rose nearly 12 percent last month.

RTW Investments saw a 10.5 percent increase in August and is up more than 20 percent in 2025, according to someone who has seen the results. It too was boosted by Madrigal, its largest long. Soleus Capital Management swelled by 9.5 percent last month and is now up 6 percent for the year, says an investor. The hedge fund has never lost money in a single year.

Source: https://www.institutionalinvestor.com/article/premium/biopharma-hedge-funds-rebounded-sharply-last-month-it-sust



Biotech Investor Sentiment Improving

It's always nice to welcome many biotech management teams to New York in the first few weeks of September. This is a moment of magic weather and sincere serious business discourse.

In addition, we have had ample opportunity to speak to many venture fund managers and public investors in recent weeks.

We are long past the desperate and dark days of April. Our sense is that every week that goes by, investors are learning to take Trump's many pronouncements and policy initiatives in stride for what they are – attempts to shape debate, behavior and, not necessarily anything remotely resembling actual policy.

With the XBI getting ever closer to 100, we are looking at a market that is up 40% or more since early April.

Investor sentiment is much improved, although some parties still report bearish sentiment and "mixed" views on the future. We have noted exceptional personnel reshuffling among many hedge funds in recent weeks, triggered in part by unfortunate bets against the market made some of the leading "pod" shops.

Despite underlying policy uncertainty there is much to like in the current set up for biotech:

1. **Rates are likely to come down, starting this week.**
2. **Risk appetite across the market is expanding.**
3. **M&A is at very high levels given that we are not seeing mega merger deals take place.**
4. **More big M&A is likely given high patent cliffs and record levels of pharma financial firepower.**
5. **Underlying innovation trends are exceptionally strong.**
6. **Today's FDA willing to fast track drugs for rare disease that have exceptional datasets**
7. **Much-needed "biotech cleanse" is behind us. Far fewer companies in the market today without data or a plan to get there in a reasonable period.**

History Guides Us to a Bull View for Biotech

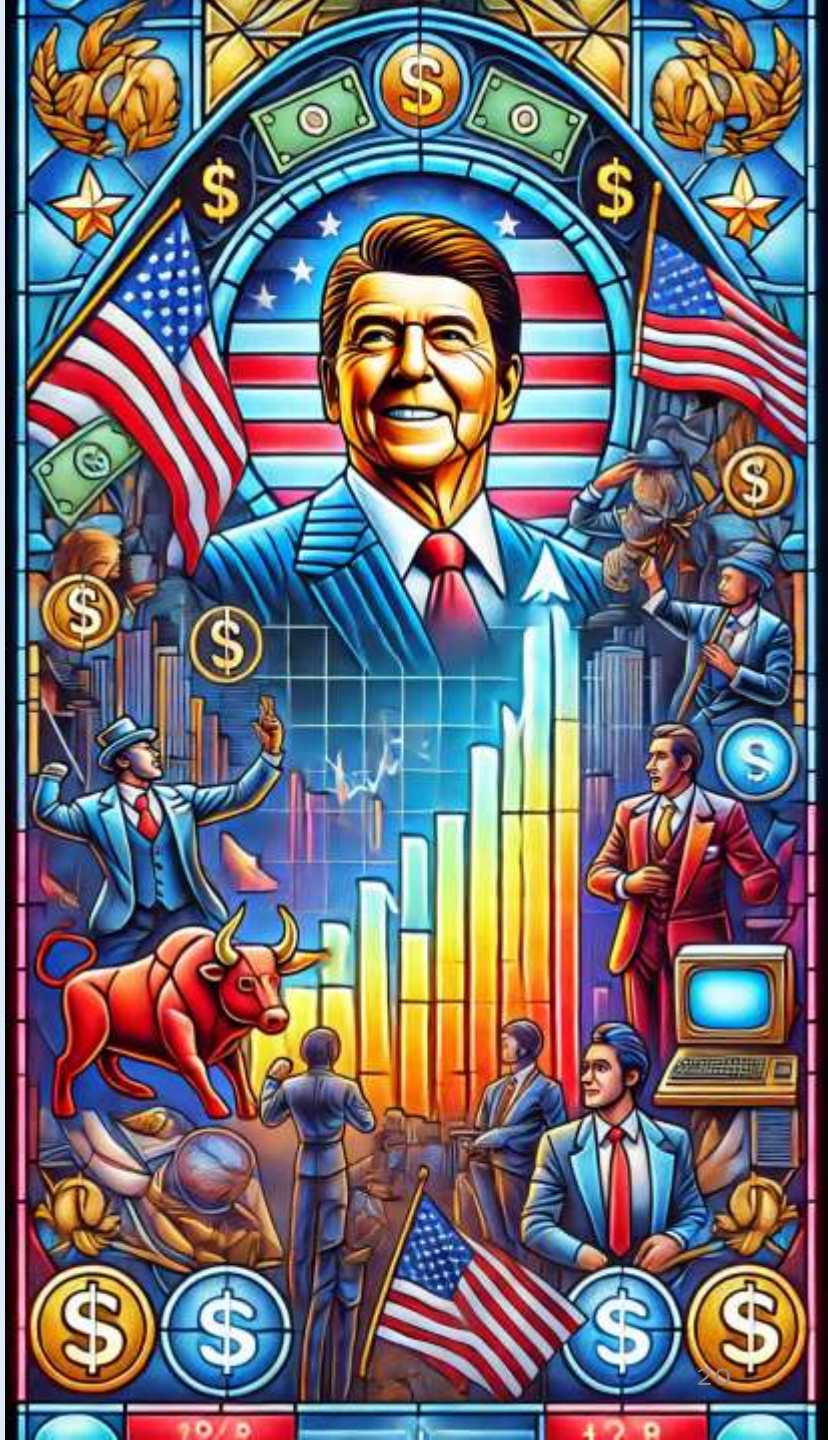
History has so much to say about the current moment. To be clear, we have an unpopular president who has fought for tax reductions and is trying to get federal spending down.

The biotech market has not been easy this year with the tariff announcements and relatively persistent high rates.

But we have seen this all before. Reagan's first term in office was accompanied by similar divisions, Oval Office unpopularity, tax reductions and spending cuts.

The market took its time as the Fed worked through a series of interest rate reductions as Carter-era inflation cooled. But the market started to move seriously in 1982 (a very similar moment to today) and went vertical in the 1984 to 1990 period (M&A took off in this time period). In all, the Dow Jones Industrial Average rose two and a half fold in the decade after Reagan came in and eleven times by 2000. Confidence in the markets took quite the turn as investors fell in love with the market again. We see similar dynamics playing out today.

We see improving confidence in biotech as contagious. We think we will see improvements in market conditions, including IPOs and follow-ons for many years to come. Initially, these improvements will be gradual and later frenzied.



The XBI Closed at 93.4 On Monday (Sep 15), Down 2% Since Sep 6

The Stifel Global Biotech Value Tracker fell by 3.2% last week, more than the XBI. Treasury yields are starting to improve. The XBI is up 4% for the year while the Stifel Global Biotech Value Tracker is up 45% for the year (largely reflective of movements in China).

Biotech Stocks Down a Bit Last Week

Return: Sep 6 to Sep 15, 2025

Nasdaq Biotech Index: -1.6%
Arca XBI ETF: -2.2%
Virtus LifeSci Biotech ETF (BBC): -1.1%
Stifel Global Biotech EV (adjusted): -3.2%*
S&P 500: +1.6%

Return: Dec 31, 2024 to Sep 15, 2025 (YTD)

Nasdaq Biotech Index: +10.6%
Arca XBI ETF: +3.7%
Virtus LifeSci Biotech ETF (BBC): +0.7%
Stifel Global Biotech EV (adjusted): +45%*
S&P 500: +10.6%

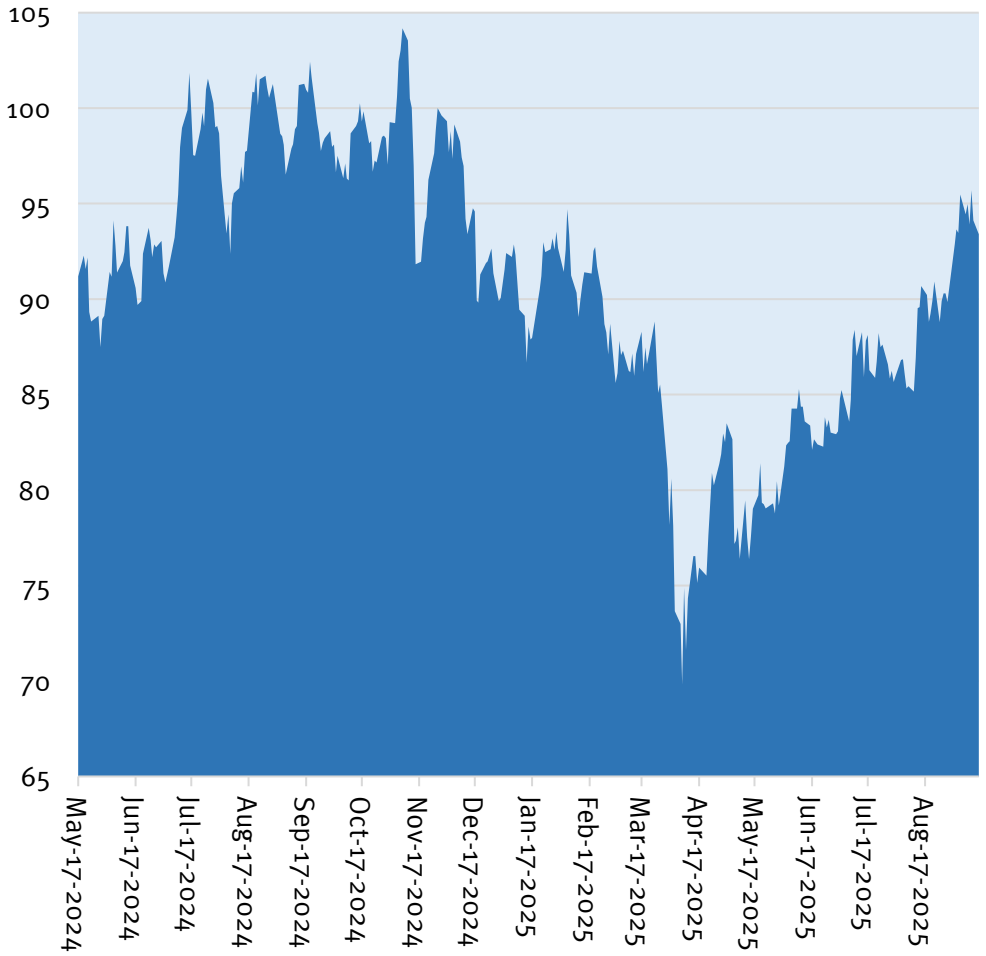
VIX Up

Dec 13, 2024: 13.8%
Mar 28, 2025: 21.7%
Apr 11, 2025: 37.6%
May 16, 2025: 18.4%
Jun 20, 2025: 20.4%
Jul 12, 2025: 16.4%
Aug 15, 2025: 15.1%
Sep 15, 2025: 15.7%

10-Year Treasury Yield Down

Dec 13, 2024: 4.4%
Mar 28, 2025: 4.27%
Apr 11, 2025: 4.48%
May 16, 2025: 4.43%
Jun 20, 2025: 4.3%
Jul 12, 2025: 4.43%
Aug 15, 2025: 4.3%
Sep 15, 2025: 4.05%

XBI, May 16, 2024 to Sep 15, 2025

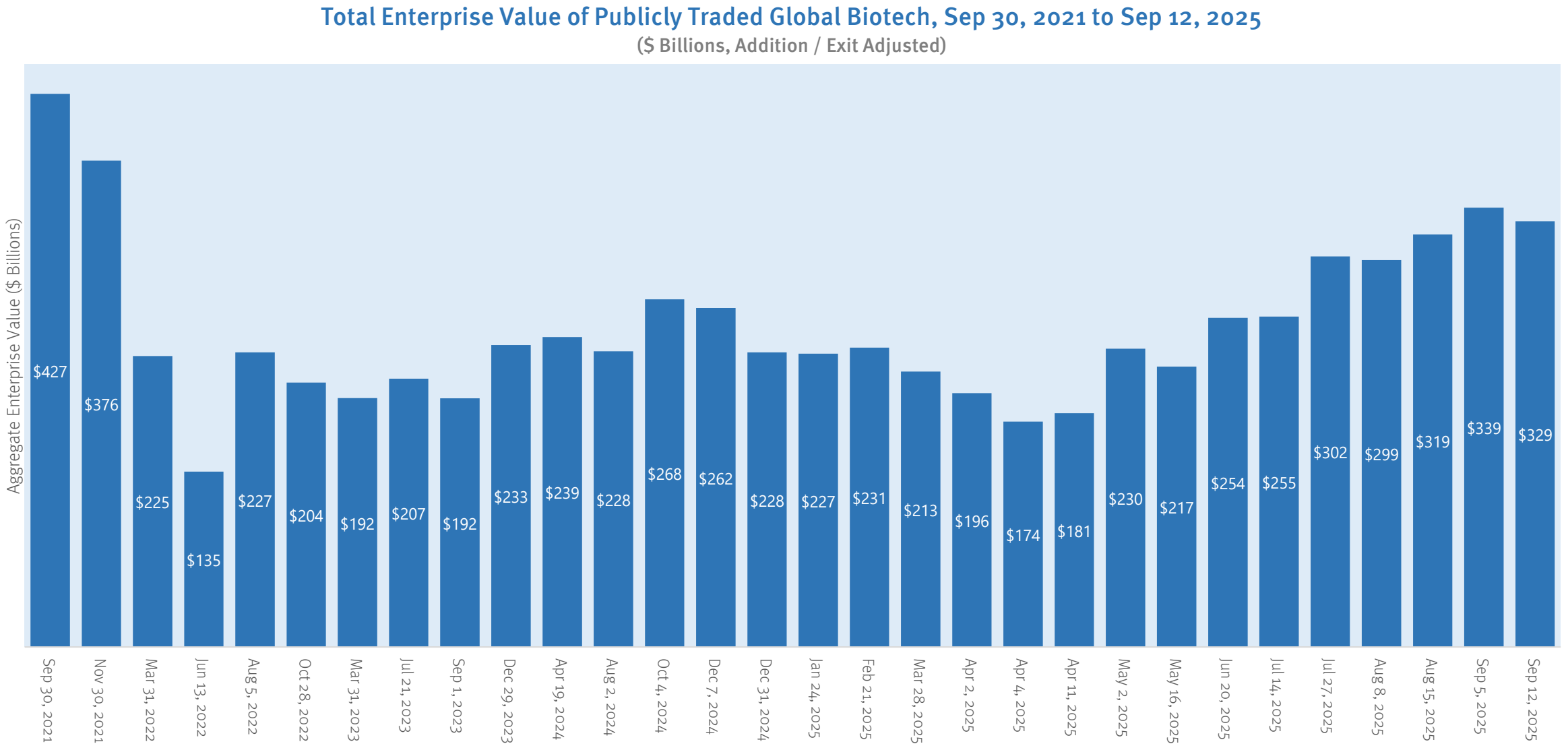


* Change by enterprise value. The adjusted number accounts for the effect of exits and additions via M&A, bankruptcies and IPOs. The annual change by market cap is even higher.

Source: S&P Capital IQ and Stifel analysis

Total Global Biotech Sector Fell 3.2% Last Week

Biotech stocks are up 89% since hitting a low point on Apr 4, 2025. Biotech stocks ended last week up 45% for the year.

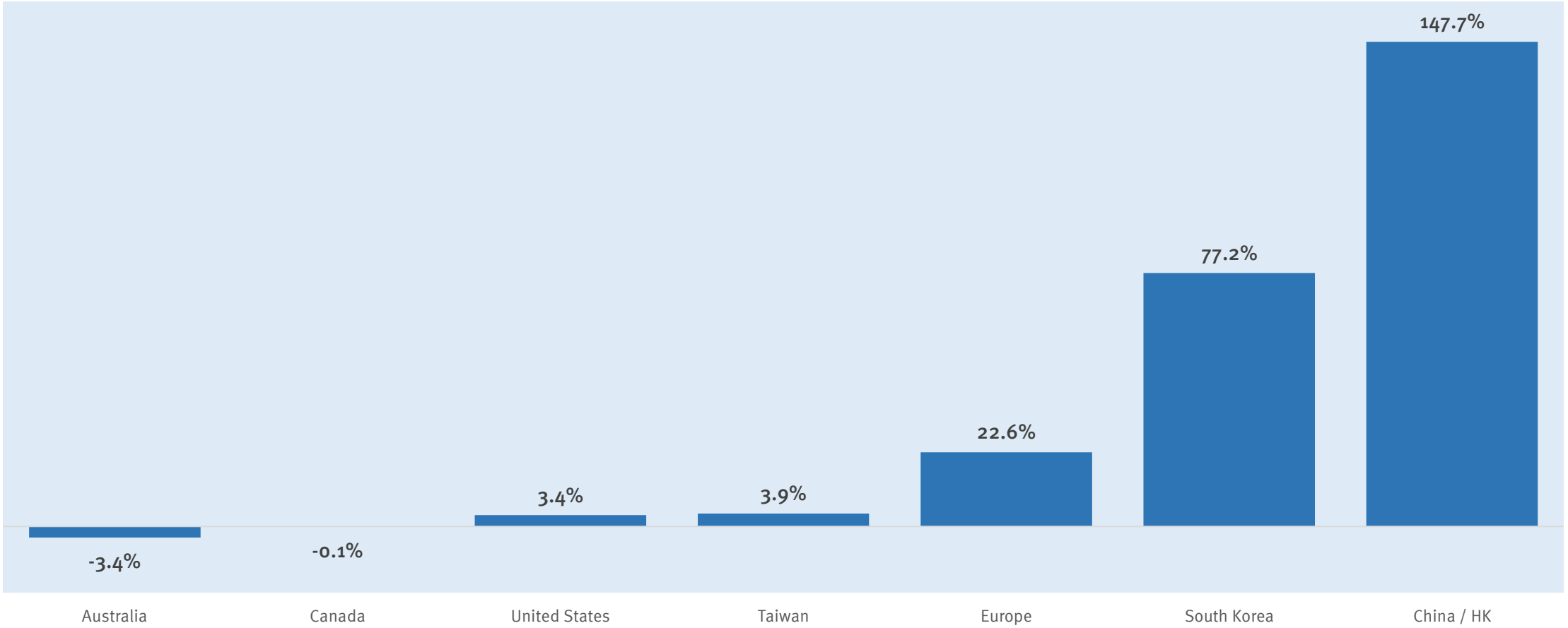


Source: CapitalIQ. Biotechs are defined as any therapeutics company without an approved product on any global stock exchange.

China Biotech Has Done Extremely Well This Year

China biotech is up 148% this year. South Korea and Europe are up while the U.S. remains is up 3%. However, it's important to recall that the U.S. biotech sector was down more than 30% just five months ago.

Percent Change in Total Market Cap of Public Biotech by Country/Region, Dec 31, 2024 to Sep 12, 2025

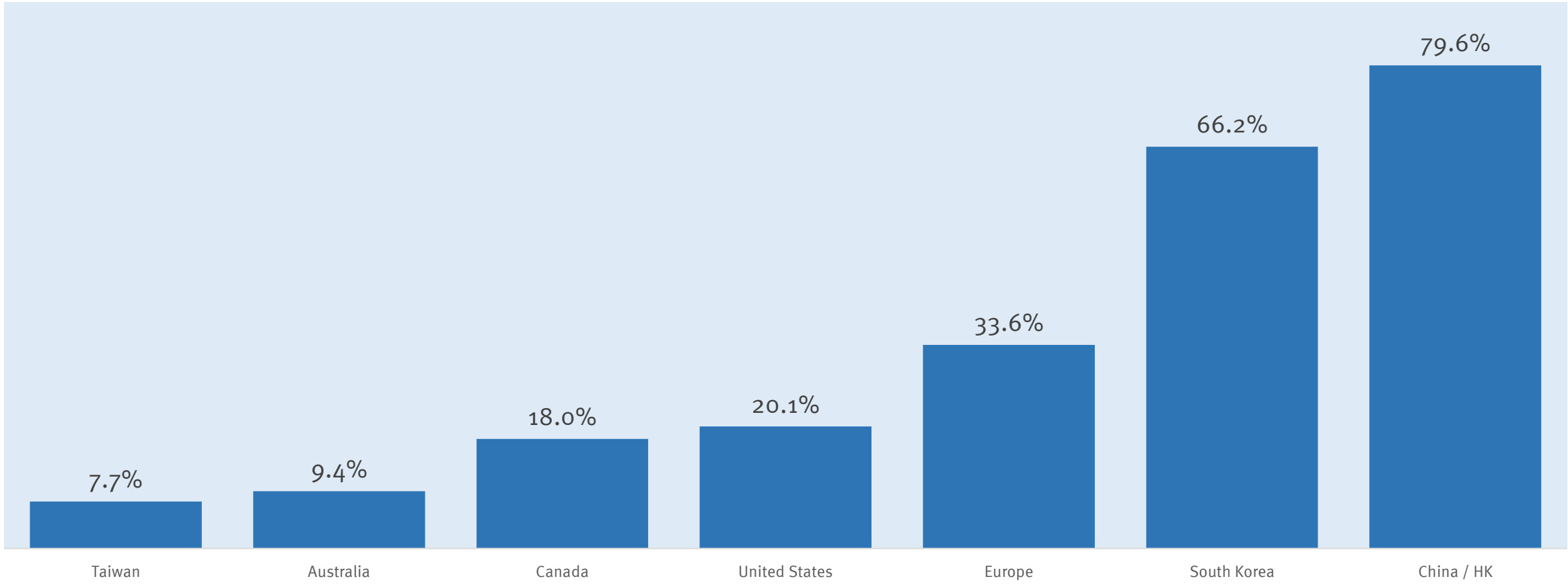


Source: CapitalIQ and Stifel analysis. Biotechs are defined as any therapeutics company without an approved product on any global stock exchange. Europe biotech includes companies from all major EU countries.

China Biotech Has Done Best Since “Liberation Day”

The China biotech sector has had stellar performance since early April. U.S. biotech has recovered from sharp losses and is now up 18% since that time. Europe is up 28% and South Korea is up 39%.

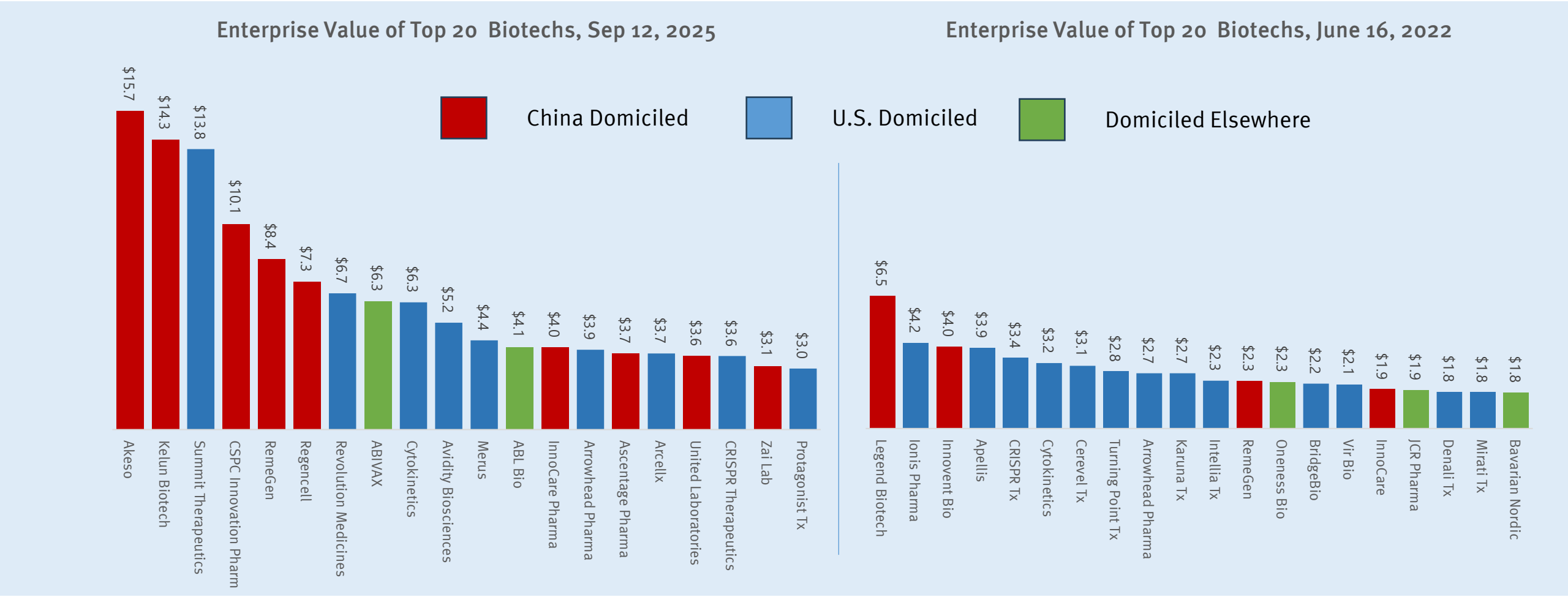
Percent Change in Total Market Cap of Public Biotech by Country/Region, Apr 3, 2024 to Sep 12, 2025



Source: CapitalIQ and Stifel analysis. Biotechs are defined as any therapeutics company without an approved product on any global stock exchange. Europe biotech includes companies from all major EU countries.

Seeing Red: Half of Top 20 Biotech Value Today is Chinese – Compare This to a Quarter in 2022

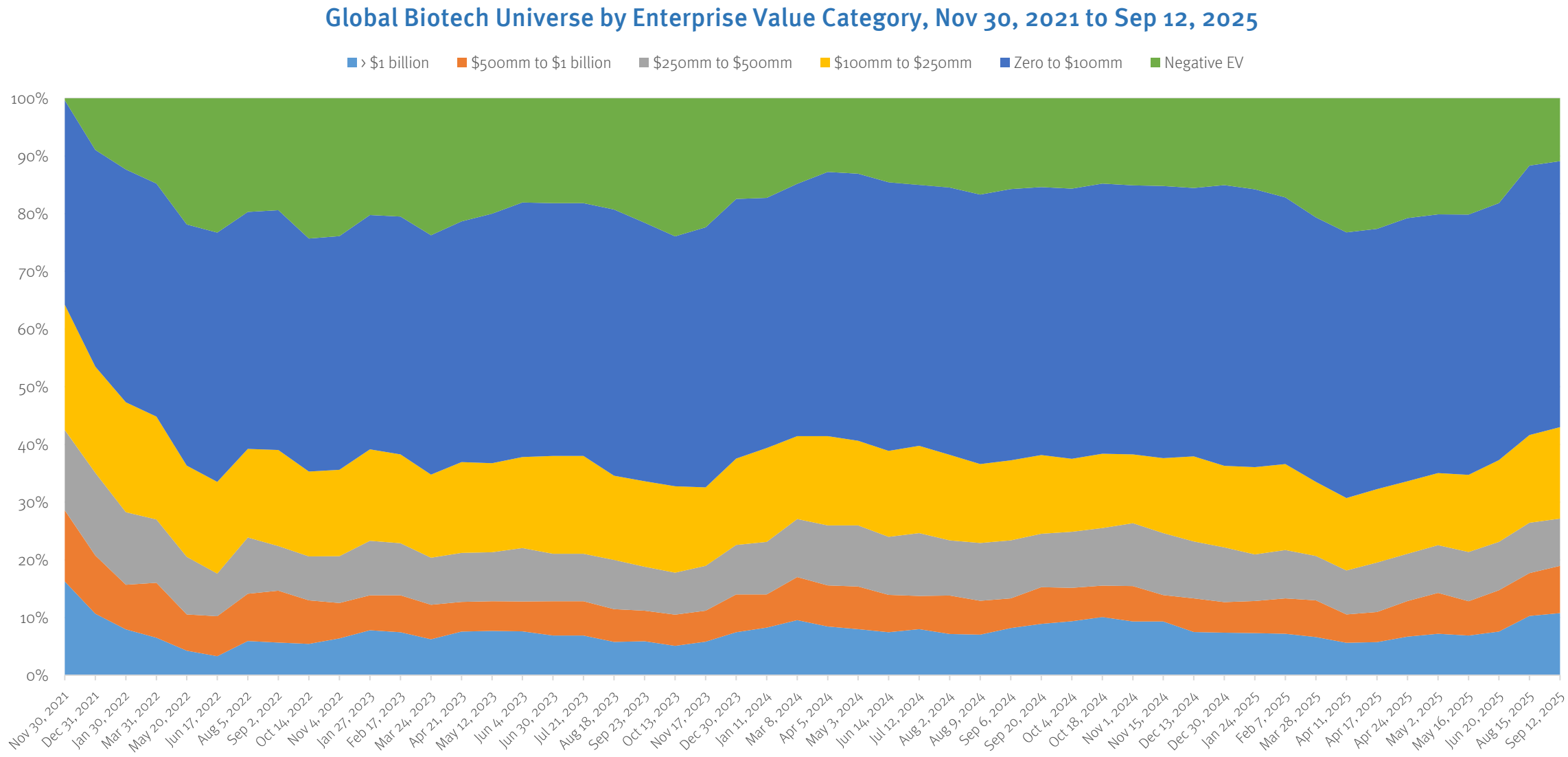
The world is changing fast. Only ten of the top twenty biotech's by EV today are U.S. domiciled. This was thirteen of twenty 39 months ago.



Source: Stifel analysis of S&P CapitalIQ Data. Note: Biotech's are defined as drug companies that began 2025 without a commercial product.

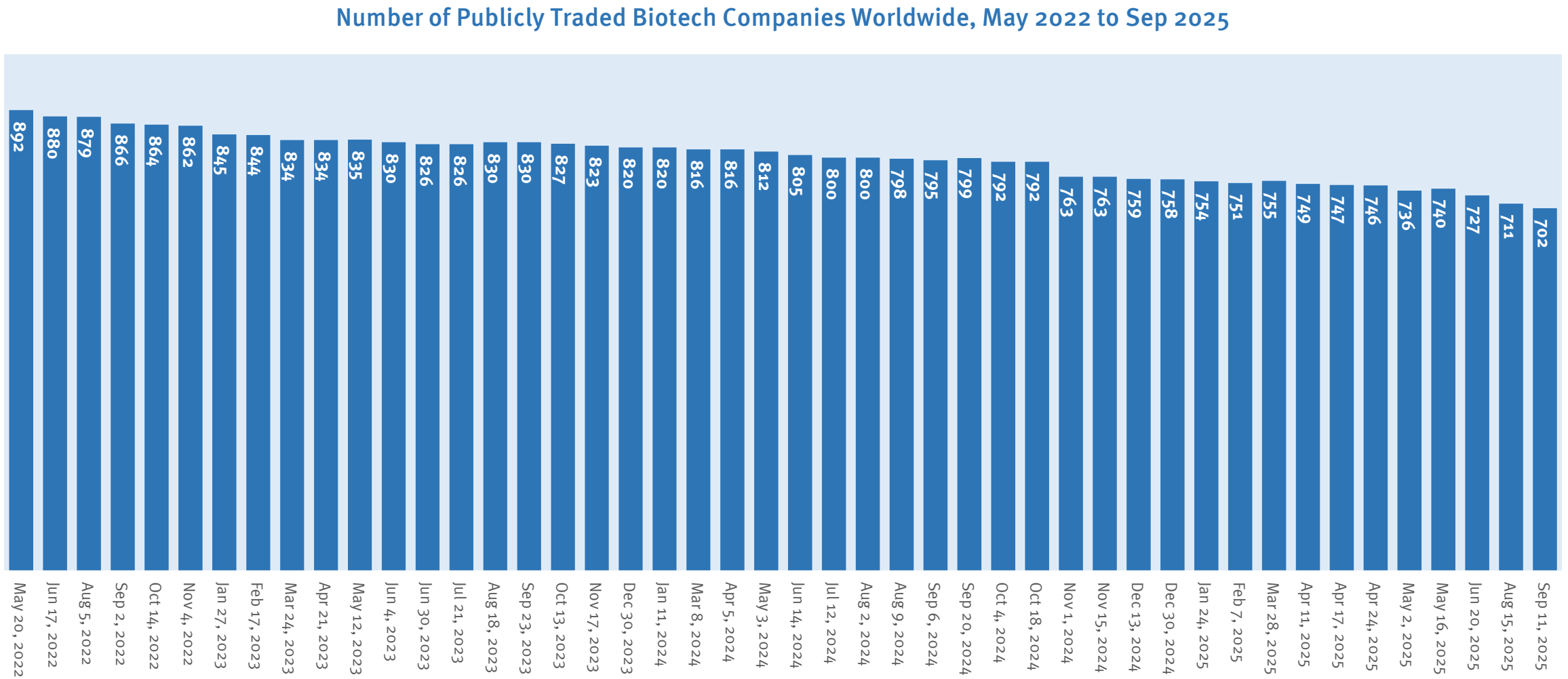
The “Good Neighborhood” in Biotech is Growing Fast

We have seen huge shrinkage in the negative EV population in the last five months.



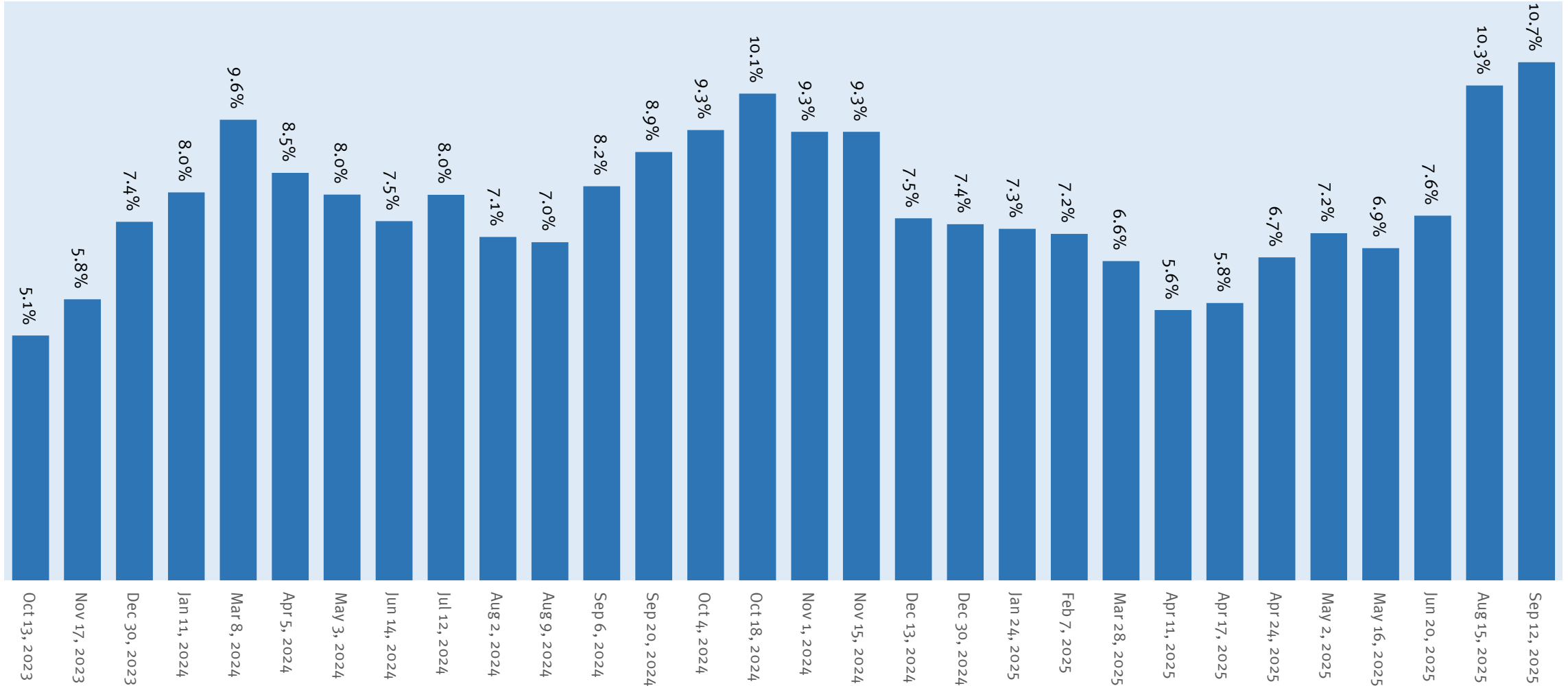
Source: CapitalIQ and Stifel analysis. Biotechs are defined as any therapeutics company without an approved product on any global stock exchange.

Public Biotech Population Has Dropped Over 20% In Last 40 Months



Billion Dollar Biotech Population Has Jumped in Recent Months

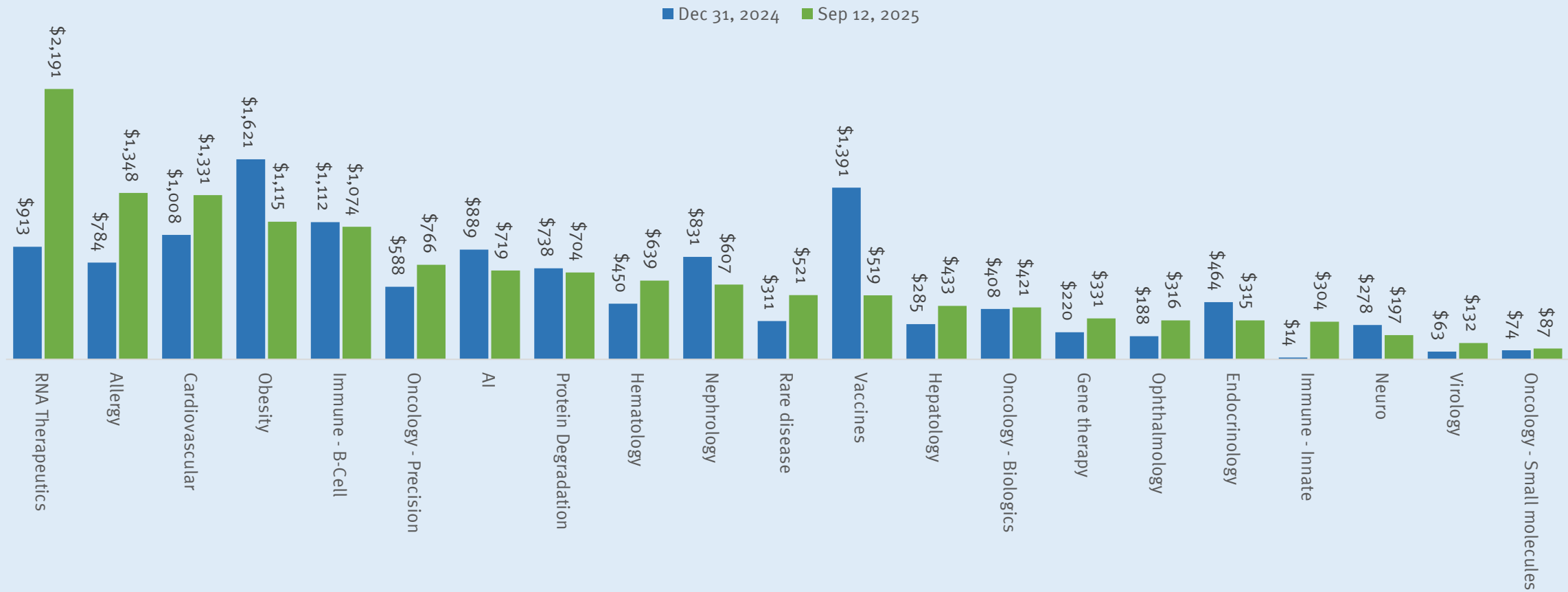
Percent of Biotechs with an Enterprise Value of $1bn or More, Oct 2023 to Sep 2025



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

U.S. Biotech Value Today Highest in RNA, Allergy, CV and Obesity

The most valued sectors in biotech today are in RNA therapies, allergy, cardiovascular, obesity and B-cell. We have seen substantial values drop in vaccines, obesity, nephrology and neuro. Precision oncology, hematology, rare disease, hepatology, gene therapy, innate immune and ophthalmology have all done quite well in 2025.

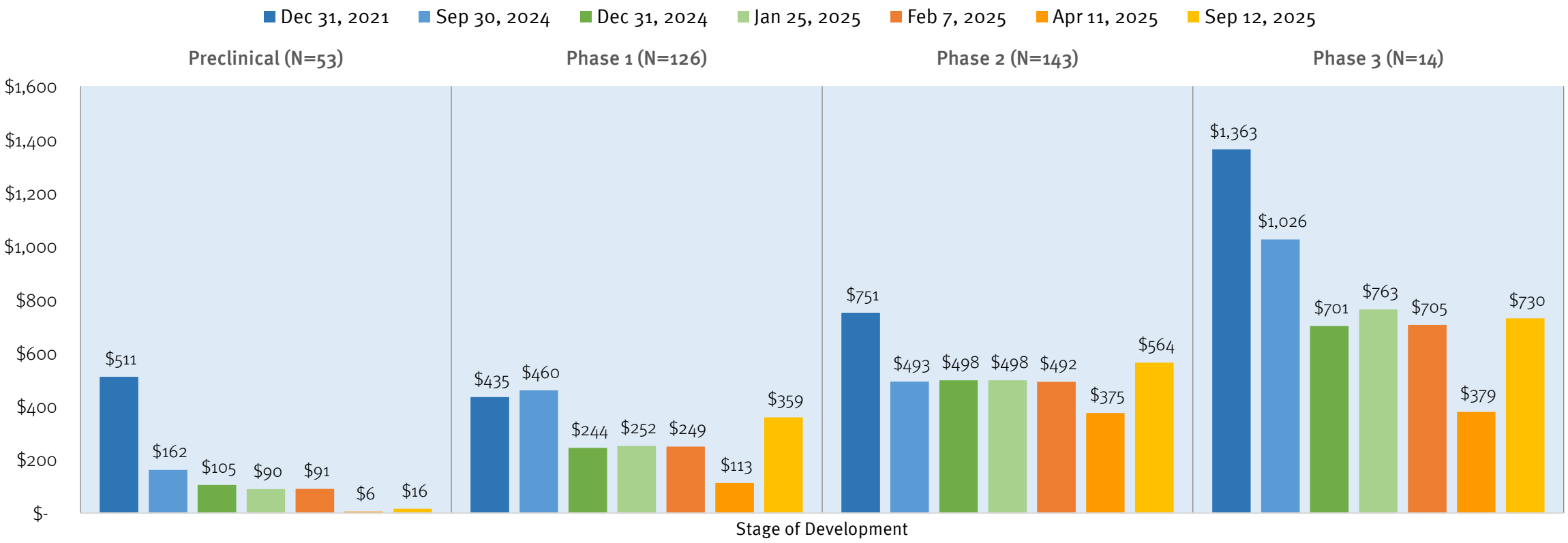


Source: S&P CapitalIQ and Stifel analysis.

Mid and Late-Stage U.S. Biotech Values Recovered While Preclinical Stories Remain in the Basement

The average preclinical biotech was worth $511 million four years ago. One year ago, that value had dropped to $125 million. As of last week, the value stood at $16 million. This value has not recovered since April. In contrast, we have seen Phase 1 stories and their Phase 2/3 brethren come back strong since “Liberation Day”.

Average Enterprise Value of a Biotech Listed on U.S. Exchanges by Stage of Development, Dec 31 2021 to Sep 12, 2025 ($ Millions)



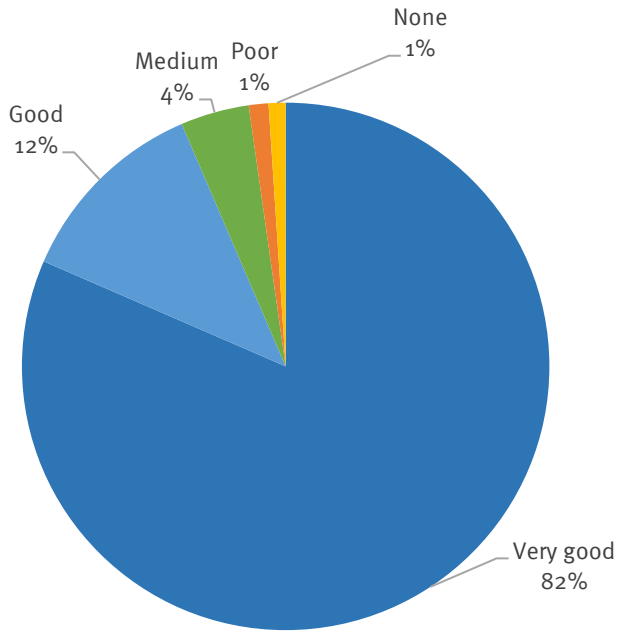
Source: CapitalIQ and Stifel analysis. Phase of development is defined by release of at least some efficacy data from a given stage of clinical development.

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

In today’s market, 82% of public U.S. biotech value is held by companies that have a “very good” dataset. Compare this to 77% in 2024 and 47% in 2022. Interestingly, the relative value of companies with these differentiated positive datasets versus those without is not rising. Rather, there are simply more companies in the market today with really good datasets. The market has systematically weeded out companies with weak data.

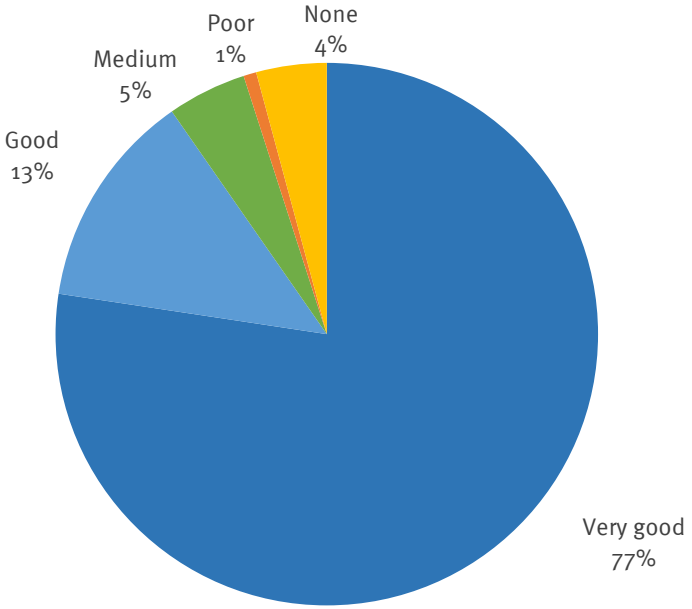
2025

Total Enterprise Value ($ billions) of the U.S. Biotech Sector by Quality of Dataset on Last Completed Stage of Development, Sep 12, 2025



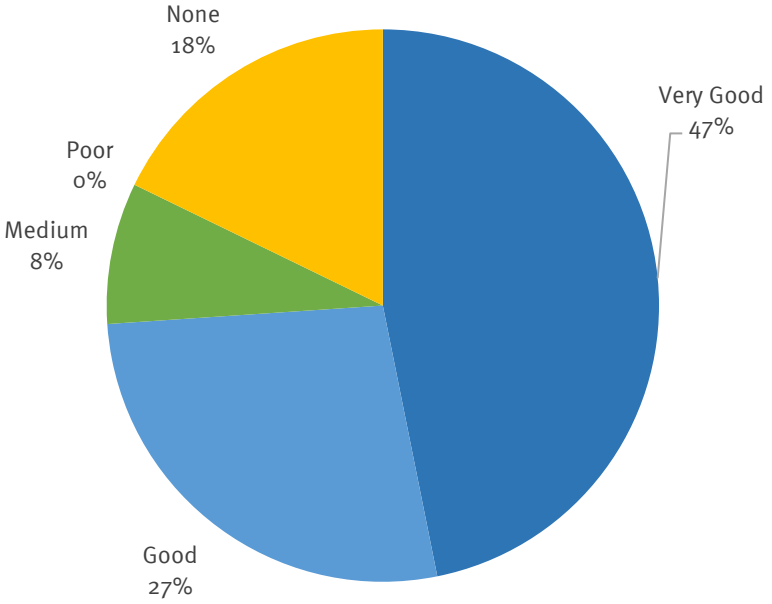
2024

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.

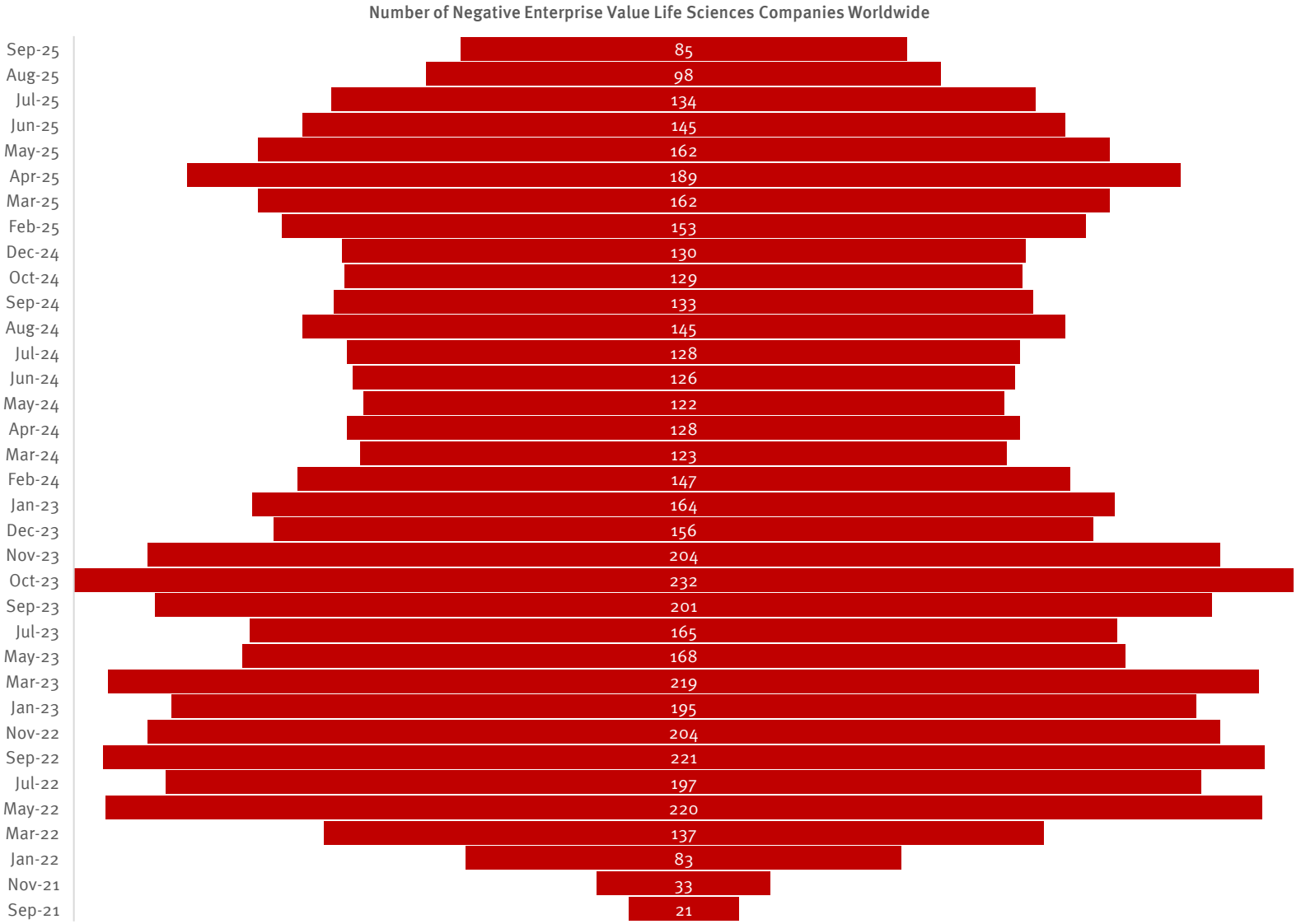
Life Sciences Sector Down 0.9% Last Week

The life sciences sector is worth $9.9 trillion and fell in value by 0.9% last week. The biotech sector and life science tools sector lost the most value while healthcare IT was up last week. Commercial pharma and Pharma Services were flat.

Sector	Firm Count	Enterprise Value (Sep 12, 2025, $millions)	Change in Last Week (percent)	Change in Last Month (percent)	Change in Last Year (percent)
API	79	$101,542	1.2%	2.0%	12.2%
Biotech	686	$318,732	-3.5%	1.9%	-5.1%
CDMO	36	$168,336	-1.1%	2.3%	14.9%
Diagnostics	74	$280,265	-0.7%	0.0%	8.5%
OTC	28	$23,266	-1.3%	0.5%	-15.7%
Commercial Pharma	685	$6,403,577	-0.5%	1.5%	-6.4%
Pharma Services	38	$195,937	0.0%	1.8%	9.6%
Life Science Tools	48	$567,598	-3.2%	-4.0%	-21.7%
Devices	170	$1,804,510	-1.3%	-0.7%	0.8%
HCIT	7	$31,555	4.9%	18.3%	57.0%

Source: CapitalIQ and Stifel analysis

Number of Negative Enterprise Value Life Sciences Companies Continues to Decline



The count of negative EV life sciences companies worldwide fell from 98 a month ago to 85 on Sep 12, 2025.

This is similar to the level in January 2022.

While negative EV companies are not yet an endangered species, they are becoming far less common in the life sciences sector. The combination of better results, dissolutions, continued takeouts of these companies by the likes of Concentra and Xoma, and crypto conversions has helped to cut the population of negative EV companies by 45% in just four months.

It's been quite a long time but the evidence that the biotech sector is normalizing is growing ever stronger.

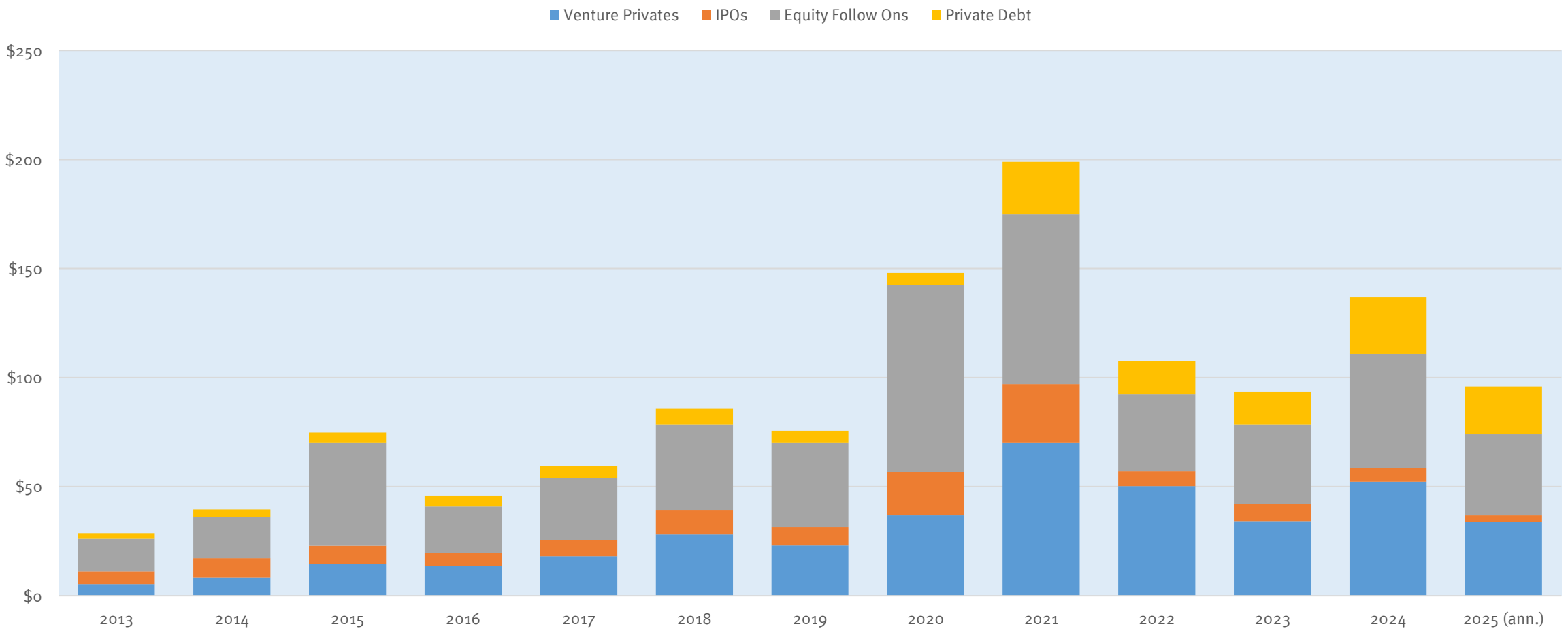
Source: CapitalIQ

Capital Markets Update

Capital Raising Pace in 2025 Now Ahead of 2023

The rapid pace of financings of the last ten weeks has pushed up our estimates of total financing volume for 2025 to be above the levels of 2023. There is a reasonable chance that this ends up being the fourth most active financing year on record despite a very slow first half.

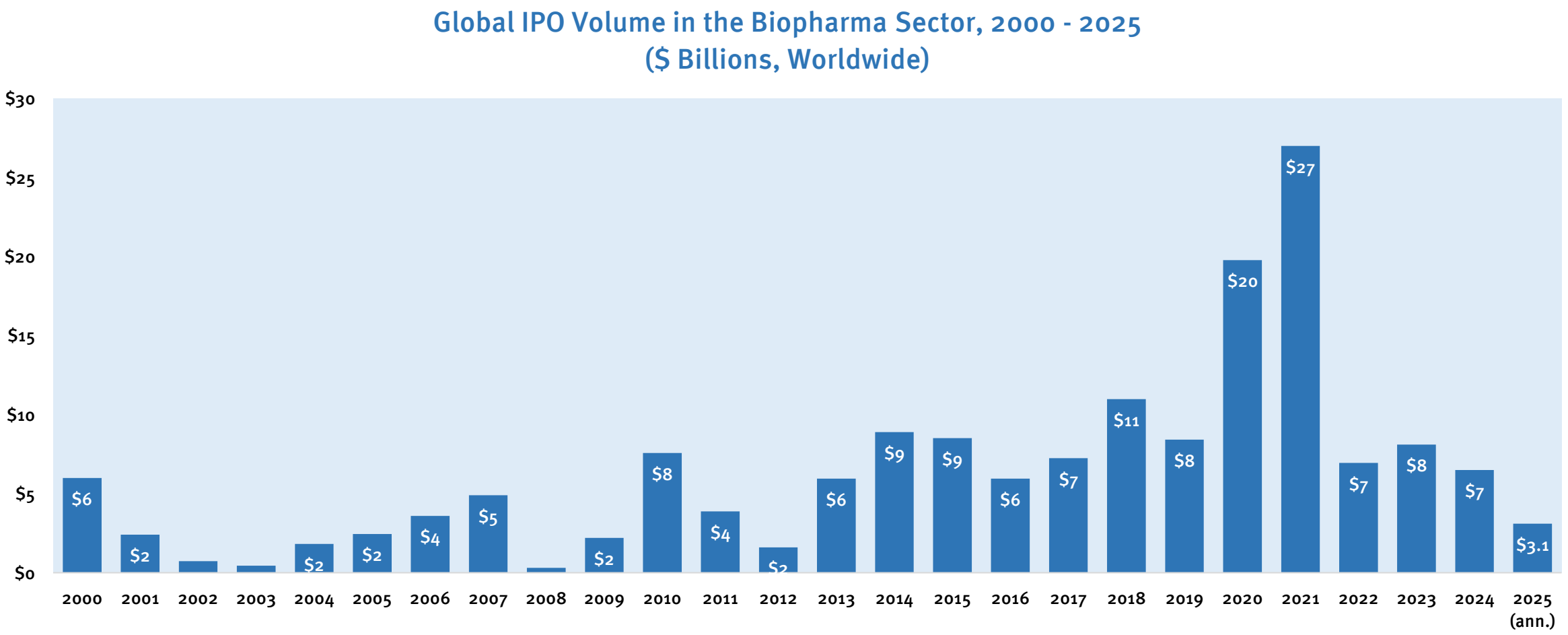
Equity Raised, Private Debt Raised in the Biopharma Sector, 2013 - Sep 30, 2025 (estimated, $ Billions, Worldwide)



Source: Data from CapitalIQ. Note: Data for 2025 is annualized based on results as of Sep 12, 2025.

IPO Market Picked Up Nicely Last Week

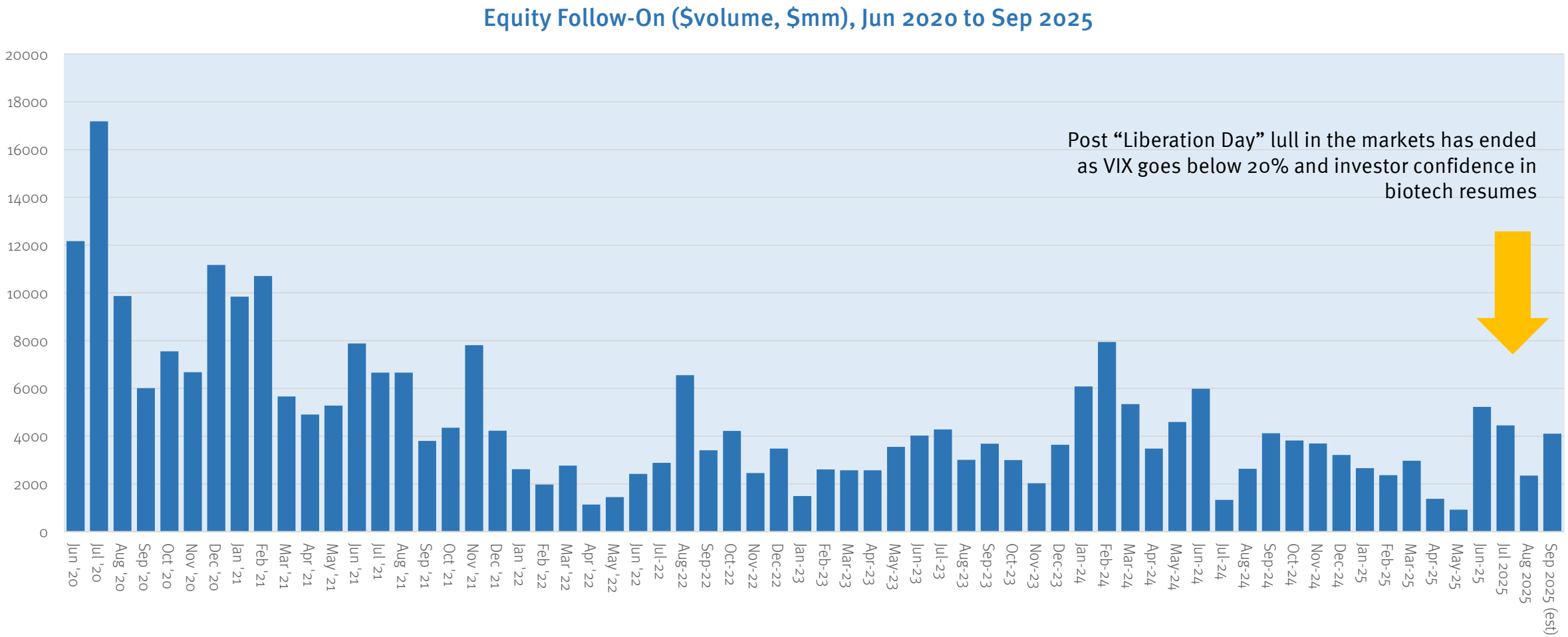
Last week saw the first company to go public since February. We do think that the remainder of 2025 looks like a more normal IPO market as the calendar continues to fill in with quality offerings.



Source: Data from CapitalIQ. Note: Data for 2025 is annualized based on results as of Sep 12, 2025.

Global Follow-On Market Strong in Last 14 Weeks

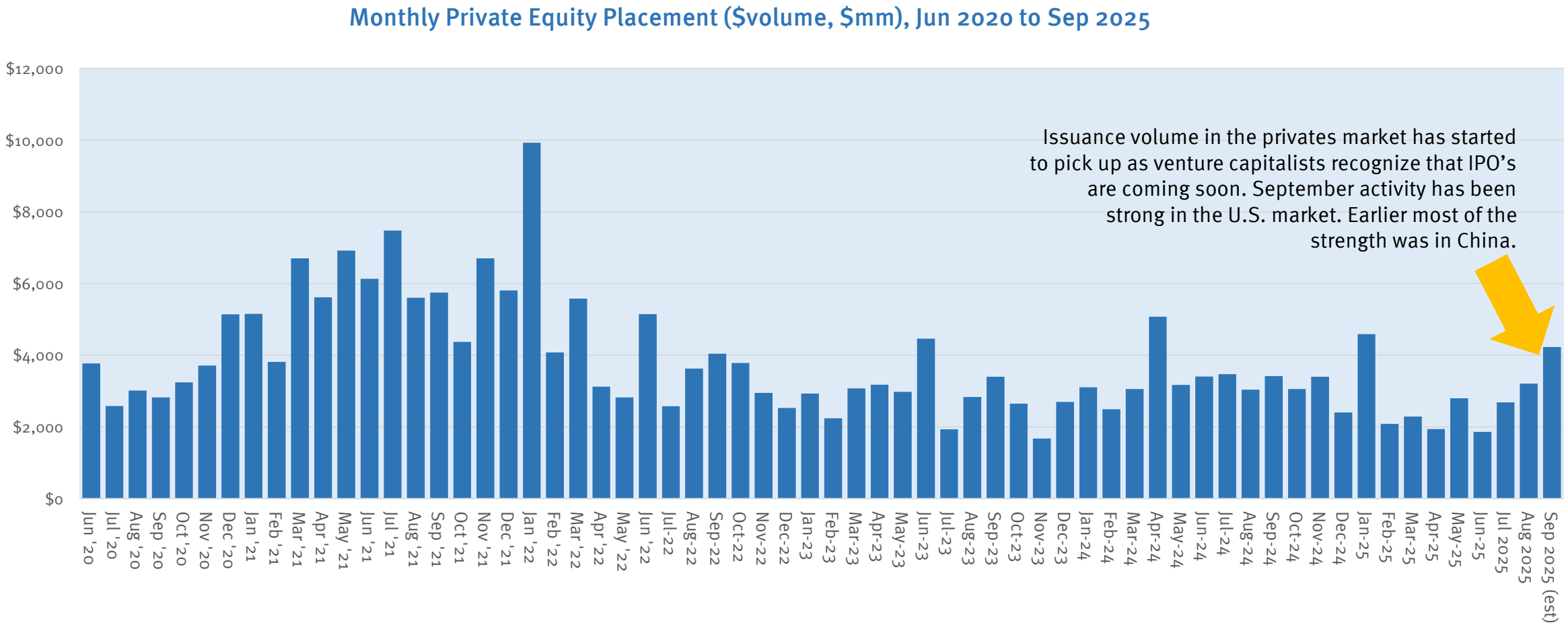
The follow-on market has shown a substantial pickup in activity as the XBI has begun to rise and normalization has spread throughout the markets. Last week was particularly strong with $2.4 billion in paper getting priced in the market. Stifel was active as a bookrunner on last week's $288 million financing by Dianthus and $250 million financing by Rapport Therapeutics.



Source: Data from CapitalIQ, Crunchbase. Data for Sep 2025 is extrapolated based on results through July 11th.

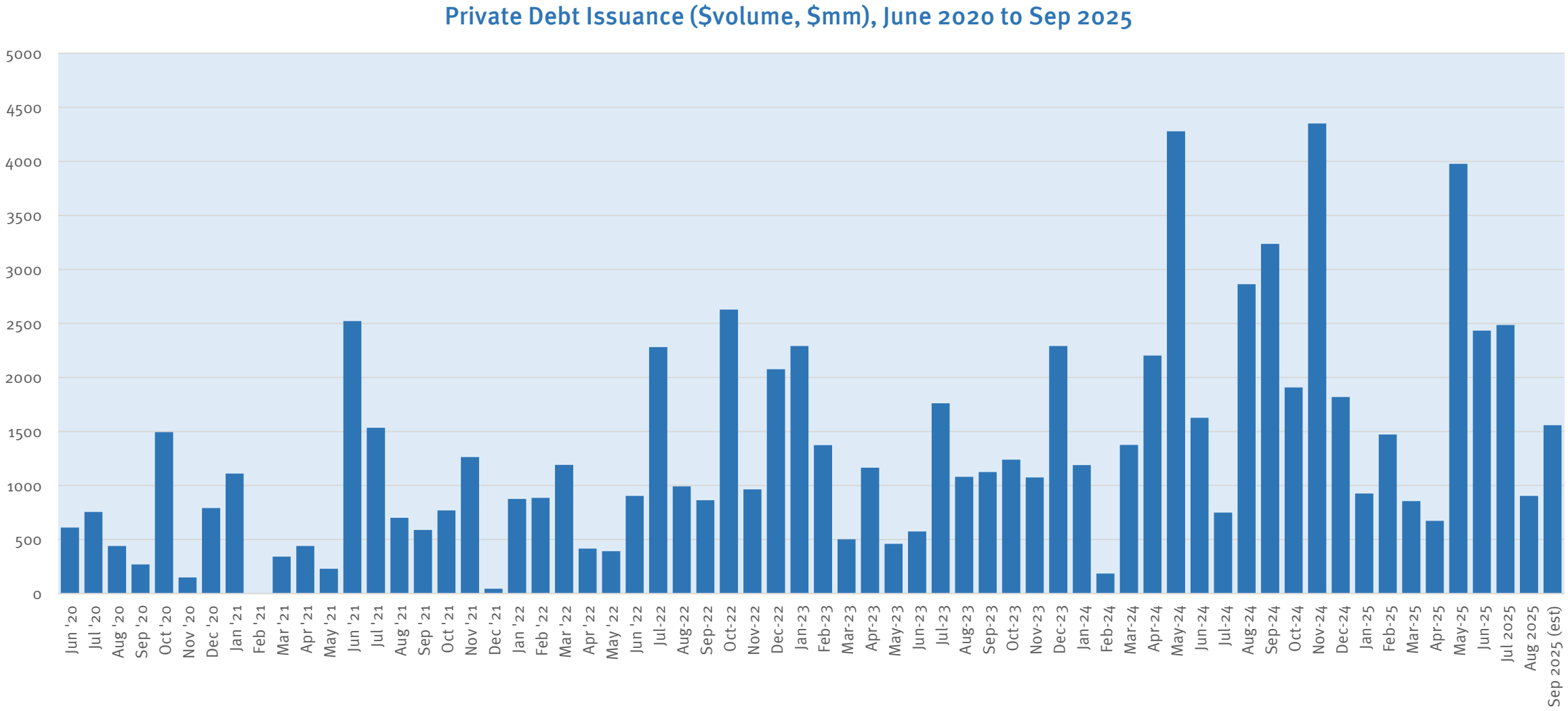
Venture Equity Private Deal Pace Showing Strength

The market for venture privates has picked up quite a bit this month following the Summer holidays. Last week saw three companies (NRG, Amsilk and Epigenic) raise between $60mm and $70mm. This followed an exceptional week that kicked off September.



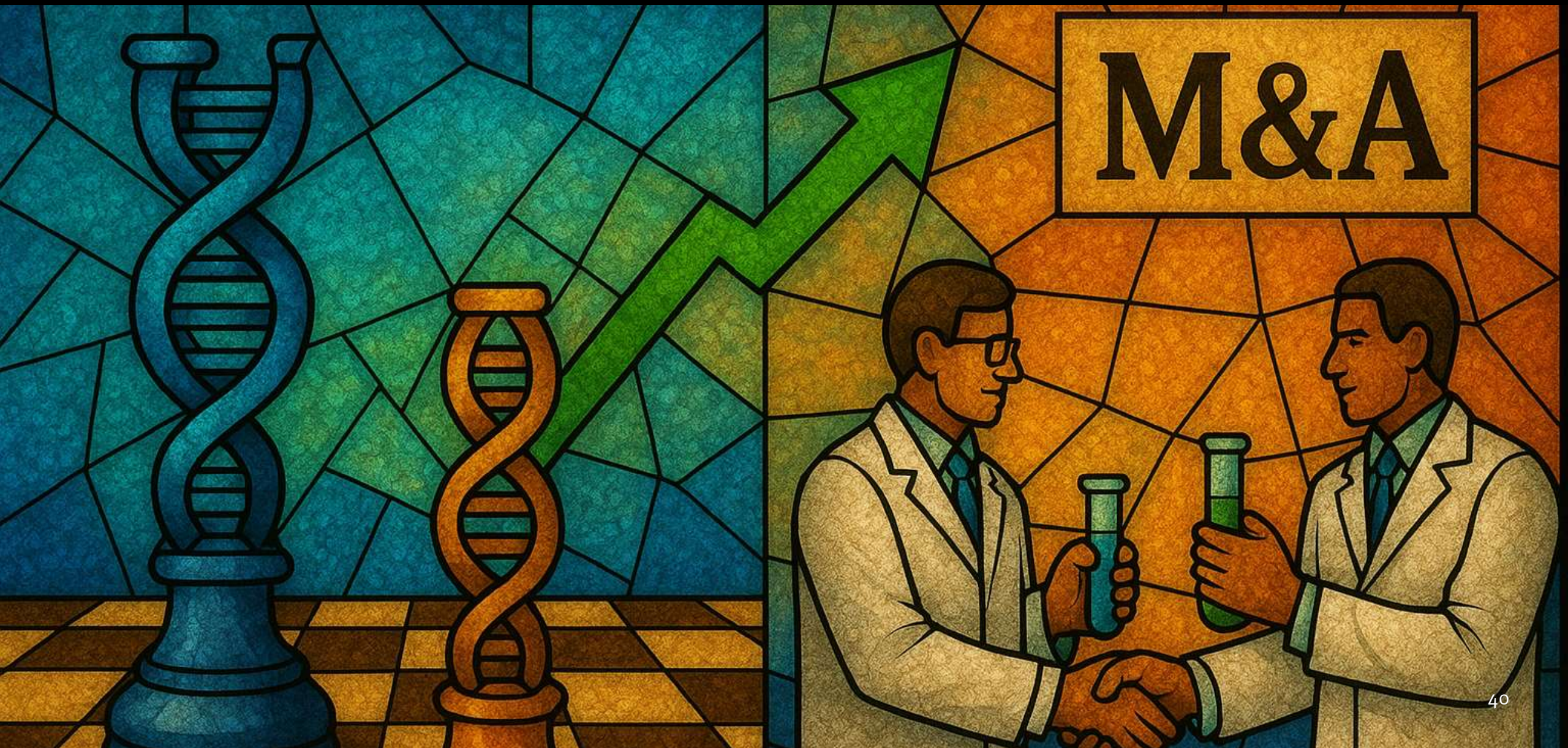
Source: Data from CapitalIQ, Crunchbase. Data for Sep 2025 is extrapolated based on results through August 15th.

Biopharma Private Debt Placement Volume Solid This Month



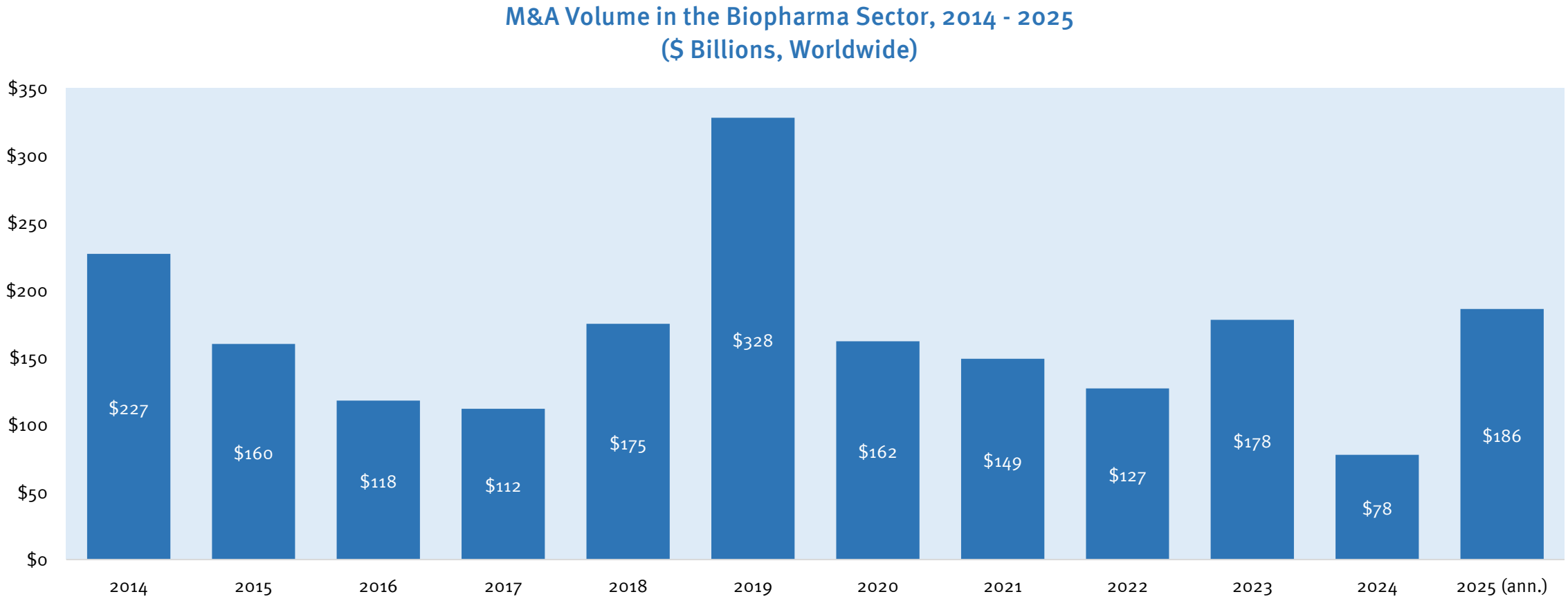
Source: Data from CapitalIQ, Crunchbase. Data for Sep 2025 is extrapolated based on results through Aug 15th.

Deals Update



M&A Market Is Picking Up Steam

September has been solid with takeouts of Tourmaline by Novartis ($1.4 billion), Zentiva acquired by GTCR for €4.1 billion. And CapVest acquired a 70% stake in Stada at a valuation of approximately €10 billion. If one extrapolates M&A volume YTD we are looking for 2025 to be the strongest M&A year since 2019 and the third strongest year in history. What is remarkable is that there are no large ($20bn+) deals that have transpired so far in 2025.



Source: S&P, CapitalIQ

Zentiva, a Leading European Generics Pharma, Announces Sale from Advent to GTCR

Prague, Czech Republic; London, UK; Chicago, US — September 11, 2025

Zentiva, a leading European generics pharmaceutical company, Advent and GTCR – two leading global private equity investors – today announce the sale of Zentiva by Advent to GTCR.

Since acquiring Zentiva from Sanofi in 2018, Advent has worked closely with the management team to successfully transform the business, whilst investing to expand Zentiva's portfolio of medicines and manufacturing footprint, both organically and through targeted M&A. This transformation programme has built Zentiva into a highly successful standalone business, with a strong focus on operational excellence and R&D capabilities, serving millions of patients across Europe.

GTCR is a leading private equity firm with a long history of investments in the healthcare sector and deep domain expertise in the pharmaceutical industry specifically, having invested behind several leading platforms and completed dozens of acquisitions in the space in the last 20 years. With GTCR's track record in the pharmaceutical space and its focus on partnering with management teams to build market-leading companies through organic growth, product innovation and strategic acquisitions, it is well-positioned to support Zentiva in this next phase of growth.

Steffen Saltofte, CEO, Zentiva, said, "Advent has been an exceptional partner in Zentiva's transformation journey. Their commitment to investing in our capabilities, pipeline, and manufacturing base has been instrumental in our growth and in ensuring we can better serve millions of patients across Europe. As we move forward with GTCR, we are excited to build on this momentum to ensure continued growth and expand access to high-quality, affordable medicines."

Tom Allen, Managing Director at Advent, said, "When we acquired Zentiva from Sanofi in 2018, we saw the opportunity to build an independent European leader in affordable medicines. By actively working with the management team and investing in the company's capabilities, Zentiva has more than doubled its revenue and EBITDA, establishing a strong foundation for the future. Zentiva exemplifies Advent's ability to carve out and transform non-core divisions into thriving, market-leading businesses. We are proud of what has been achieved and confident Zentiva will continue to excel under GTCR's ownership." The transaction is subject to customary regulatory approvals and its closing is expected to take place in early 2026.

Source: https://www.gtcr.com/zentiva-a-leading-european-generics-pharmaceutical-company-announces-sale-from-advent-to-gtcr/

Novartis Acquires Tourmaline for $1.4 Billion

Tourmaline Press Release, Sep 9, 2025

NEW YORK, Sept. 09, 2025 (GLOBE NEWSWIRE) -- Tourmaline Bio, Inc. (“Tourmaline”) (NASDAQ: TRML), a late-stage clinical biotechnology company developing transformative medicines that establish new standards of care for patients with life-altering inflammatory and immune diseases, today announced that it has entered into a merger agreement with Novartis AG (“Novartis”), pursuant to which Novartis will acquire Tourmaline for $48.00 per share in cash at closing, or a total equity value of approximately $1.4 billion. This represents a premium of 59% to Tourmaline’s closing stock price on September 8, 2025, the last trading day before the announcement of the transaction, and 127% to Tourmaline's 60-day volume-weighted average stock price as of that same date. The transaction has been unanimously approved by the Boards of Directors of both companies.

“Our mission at Tourmaline has been to establish new standards of care in areas of high unmet medical need, and today’s transaction announcement both underscores our commitment to that focus and also delivers compelling shareholder value,” said Sandeep Kulkarni, MD, Co-Founder and Chief Executive Officer of Tourmaline. “We are thrilled that Novartis, a company with deep roots and a commitment to innovation in the cardiovascular, renal, and metabolic disease space, will continue to advance this mission. Novartis shares our conviction in the critical, but largely unaddressed, role of inflammation in driving cardiovascular diseases and will be an ideal partner to accelerate the development of pacibekitug. I want to extend my heartfelt thanks to our Tourmaline colleagues and advisors for their dedication and hard work, as well as to our investigators and clinical trial participants who have helped expand our understanding of cardiovascular inflammation.”

Transaction Details:
Under the terms of the merger agreement, a subsidiary of Novartis will commence a tender offer to acquire all of Tourmaline's outstanding shares for a price of $48.00 per share in cash at closing. The closing of the tender offer will be subject to certain conditions, including the tender of shares representing at least a majority of the total number of Tourmaline's outstanding shares and receipt of regulatory approvals, and other customary closing conditions.

Completion of the transaction is expected in the fourth quarter of 2025, subject to the satisfaction or waiver of customary closing conditions. Until that time, Tourmaline will continue to operate as a separate and independent company.

Source: https://ir.tourmalinebio.com/news-releases/news-release-details/tourmaline-bio-enters-agreement-be-acquired-novartis-ag

CapVest to Acquire Majority Stake in STADA

Stada Press Release, Bad Vilbel, Germany and London – 1 September 2025

CapVest Partners LLP (“CapVest”), a leading global investment firm, has today signed a definitive agreement with Bain Capital and Cinven to acquire the majority stake in STADA Arzneimittel AG “(STADA” or “the Company”), a leading healthcare and pharmaceuticals company specializing in Consumer Healthcare, Generics and Specialty pharmaceuticals.

Headquartered in Bad Vilbel, Germany, STADA is a leading European pharmaceutical company focused on three strategic pillars: Consumer Healthcare, Generics and Specialty Pharmaceuticals. The company was acquired by Bain Capital and Cinven in 2017. Working with management, the two international investment firms helped transform the company from a traditional German generics business into a leading, diversified global healthcare platform with a strategic focus on Consumer Healthcare, Generics and Specialty Pharmaceuticals. During this period, STADA grew into a multifaceted, resilient company, generating revenues in excess of €4 billion, delivering a compound annual net sales growth rate of 9%, and more than doubling EBITDA since 2017. The firm currently employs approximately 11,600 people worldwide.

A leading international private equity investor that partners with ambitious companies supplying essential goods and services, CapVest brings deep sector expertise and a strong track record of over 20 years of investing in the healthcare industry, making the firm ideally positioned to support STADA in its next phase of growth. Following completion of the transaction, Bain Capital and Cinven will each retain a minority stake in STADA, underscoring their confidence in the company’s future growth trajectory and commitment to supporting the management team.

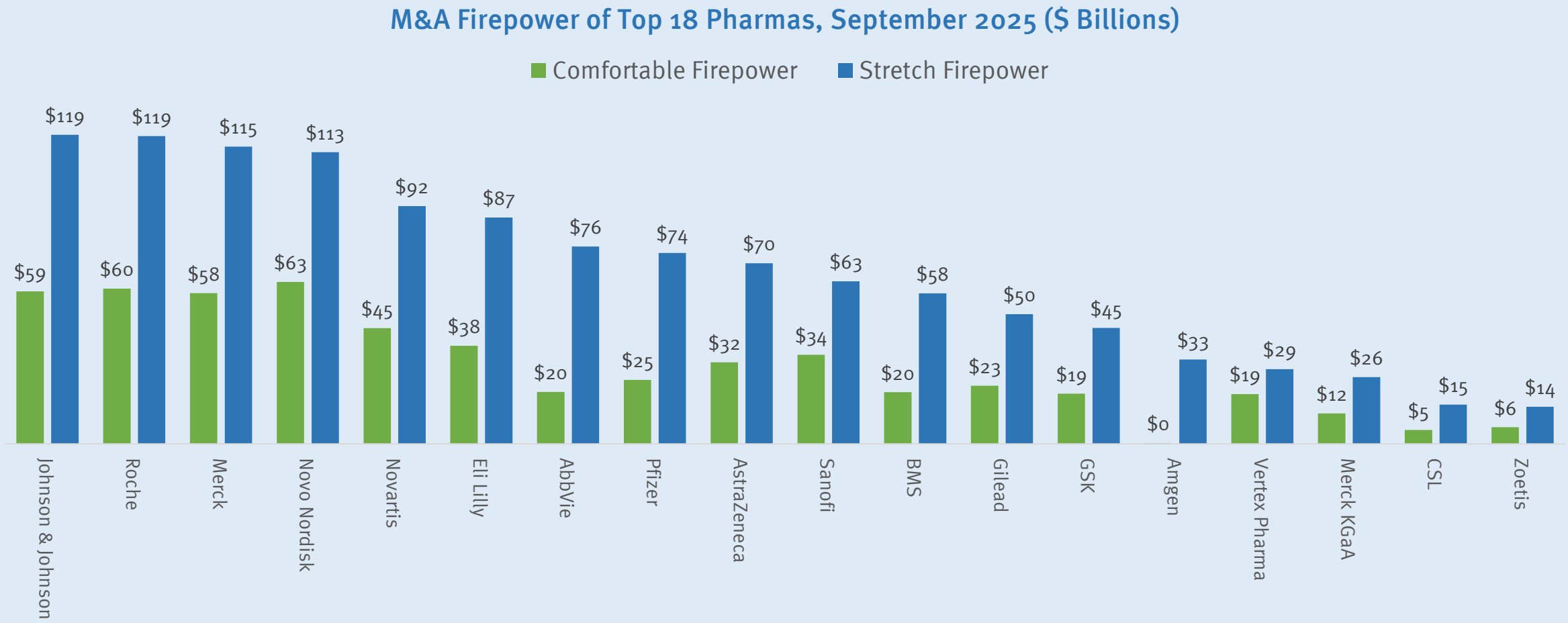
The terms of the transaction have not been disclosed and are subject to regulatory approvals and other customary closing conditions. Closing of the transaction is expected in early in 2026.

Matthew Fargie of CapVest said: “We have admired STADA for several years, including its deep heritage, leading product portfolio and a culture underpinned by caring for people's health. Peter and the entire STADA team have a best-in-class track record of performance. STADA is a unique strategic platform through which we will leverage our significant healthcare and consumer expertise to accelerate the development of the company in Germany and internationally. We intend to deploy significant new capital towards this objective. We look forward to working with Peter Goldschmidt and his team as custodians of this great company in its next phase of development.”

Source: https://www.stada.com/blog/posts/2025/september/capvest-to-acquire-majority-stake-in-stada-from-bain-capital-and-cinven

Top Pharma Have $1.2 Trillion of M&A Firepower Today

This chart shows firepower of top pharmas. We define comfortable firepower as the amount of debt a company can take on given current EBITDA levels to arrive at a ratio of net debt to EBITDA of 3X. Stretched firepower would take a company to a ratio of net debt / EBITDA of five times. Historically, some companies like AZ and Takeda have been willing to go well beyond the 3X net debt / EBITDA comfort levels. In contrast, J&J and Roche have been reluctant to use obvious balance sheet capacity in order to be fully prepared for industry rainy days. Today, there is $1.2 trillion of stretch firepower and $500+ billion of comfortable firepower among the top 18 companies listed here. This has gone up from 2023 and 2020, other occasions upon which we carried out firepower analysis.



Source: S&P CapitalIQ

Massive Pharma Patent Cliffs Ahead

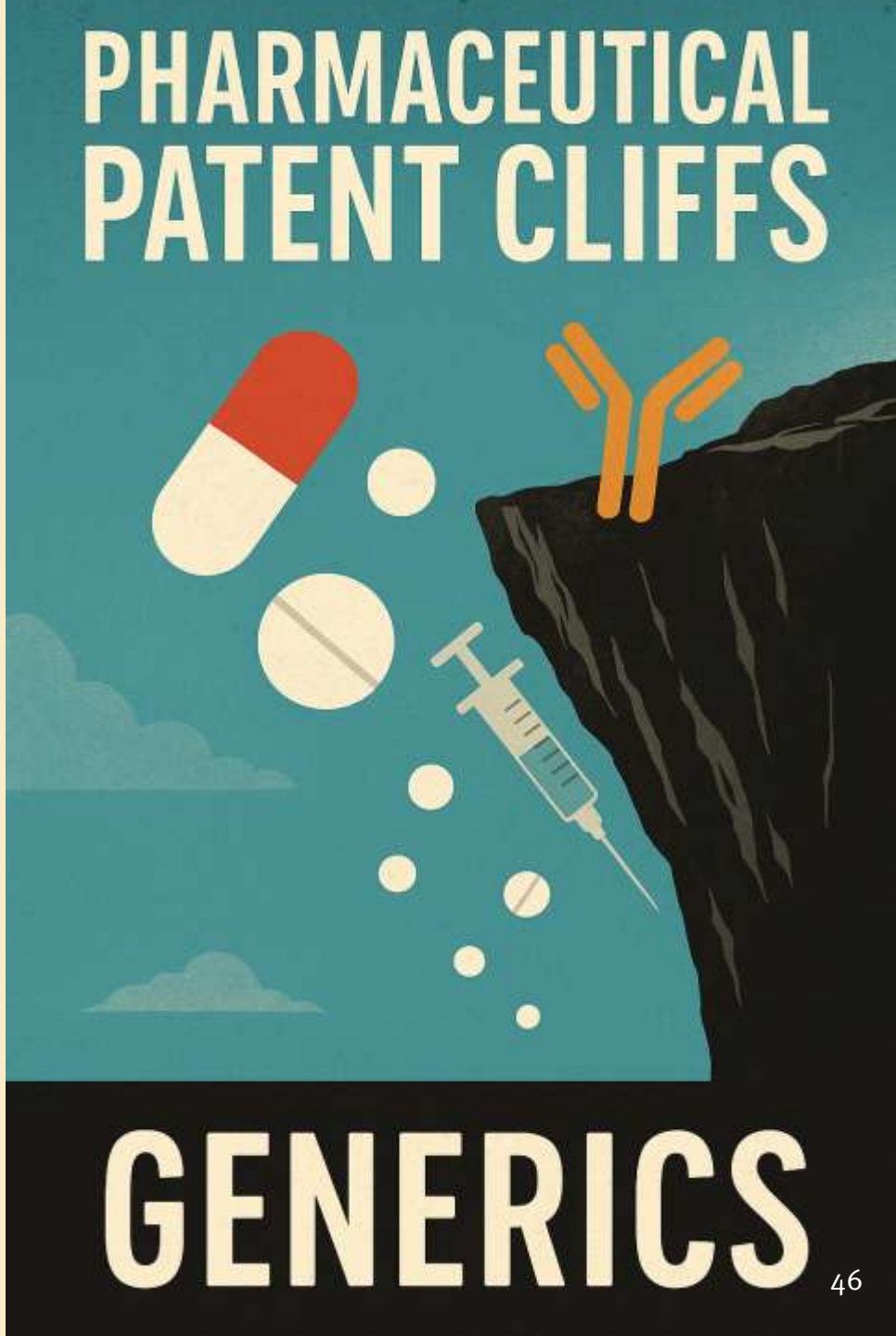
Rosie Bradbury, *Pitchbook*, Sep 12, 2025 (excerpt)

Across the board, from J&J to Pfizer and Eli Lilly, the country's pharmaceutical giants are facing a patent cliff that could spur M&A as they move to fill out their pipelines and close revenue gaps. Analysts estimate some $180 billion in big pharma revenue is at risk by 2030. Pfizer alone has predicted a revenue loss of $17-18 billion by 2030 as a direct result of patent expirations of key drugs. "It's a big, big problem for the big boys of our industry," said Ross Morton, managing partner at Nodenza Capital Partners, a venture firm focused on biotech.

Historically, patent cliffs have been a respite for slow M&A cycles. Pharmaceutical companies' own R&D is usually far from enough to generate the needed additional revenue, so they turn to acquisitions of smaller companies with newly approved or nearly approved drugs to satisfy their shareholders. For VCs hungry for liquidity in a stalled IPO market and early-stage companies struggling to land financing, this patent cliff could be a game-changer. But they still face the huge roadblocks, including high interest rates, supply chain uncertainty and softening biotech valuations, that have been holding back Big Pharma from making the usual blockbuster deals.

There were 23 acquisitions in biopharma in the first two quarters of 2025. Only one, J&J's $14.6 billion acquisition of Intracellular Therapies, crossed the 11-figure mark. "It is just so difficult to be sure of valuations when there's that volatility," said Nicole Daley, a partner at A&O Shearman's M&A practice. Buyers are still hesitant to pull the trigger on large deals, although therapies are experiencing much more buyer interest, she added.

Source: https://pitchbook.com/news/articles/as-big-pharmas-next-patent-cliff-looms-biotech-investors-see-dollar-signs



Interview with Devang Bhuva, Head of M&A at Gilead

Chase Feiger, Kinara, September 12, 2025

Gilead Sciences SVP, corporate development Devang Bhuva arrived at the company five years ago from the financial world, where he'd spent the first decade-plus of his career working across a range of clients and industries. Now established as one of Gilead's primary development execs, he has moved aggressively to add assets that bolster the organization's presence in virology, oncology and inflammation.

Q: What distinguishes Gilead's approach to business development and M&A?

A: When you look at Gilead's history, so much of it has been built upon external innovation—our early antivirals from the acquisition of Triangle Pharma really created the foundations for what became our HIV franchise. Then when you look at what we've done to cure hepatitis C, a huge portion of it was due to acquiring a company called Pharmasset that started the backbone of our first therapy for hepatitis C and allowed us to continue innovating on top of it. What differentiates us today, I think, is that Gilead has this mindset that there's one Gilead portfolio. It doesn't matter if something came from internal research or from external innovation; we'll have the same mindset toward developing it to its fullest potential.

Q: There are a lot of biotech companies that would love to get corporate development or acquisition interest from an organization like Gilead and they're excited to learn a little bit about how the typical deal cycle works. What does the arc usually look like when you're evaluating these opportunities?

A: There's no one way that it happens, or a typical timeline or process it follows. We pride ourselves on being agile and nimble and flexible in how we approach getting deals done. What's fundamental for us is: Has this company solved a key problem? Have they come up with something that we think can be first-in-class or best-in-class, and ideally both? We're looking for that level of innovation and what we bring to the table is a phenomenal research and development organization that has been working on these products for years and years.

Q: Does competitive tension ever influence your timeline or decision making?

A: We get calls all the time from venture capitalists or investors or bankers saying, "Hey, this company that you guys have been meeting with for six months now has a proposal from somebody else." In those situations where we were otherwise taking a more pragmatic approach to a deal, we'll rally the troops and come to the table and say, "Okay, we thought we were going to solve this issue within a couple months.

Source: https://kinara.co/article/the-mechanics-of-pharma-m-a-a-q-a-with-gilead-sciences-devang-bhuva/

Gilead Looking for Strong Scientific Assets that Help Solve a Key Problem in Medicine

The Pharma Industry Public Relations Problem

Pharma Industry Has the Worst Image of any Major American Industry

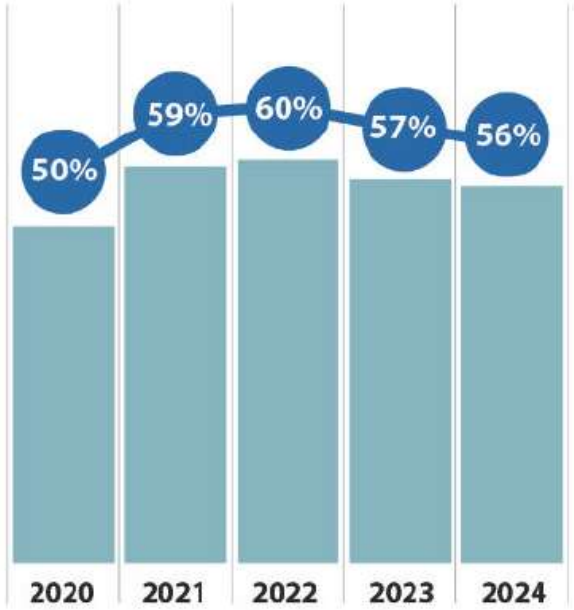
What does it take for a company — or an industry — to get back in the good graces of the American public once it has a poor reputation? Apparently, it takes more than 380 million doses of a vaccine distributed free-of-charge to the public. We know this because **the pharmaceutical industry remains the least-trusted industry in the U.S., according to our 2021 poll**. In 2013 we first observed the close correlation between the public's view that an industry is untrustworthy and its opinion that the industry is also under-regulated. The pharmaceutical industry has been ranked both the least trustworthy and the most under-regulated sector for more than five years running. During that time, we've also seen a gradual decline in trust in the technology industry and a concomitant rise in public appetite for more oversight of tech firms.

Source: https://pac.org/public-affairs-pulse-survey-2021

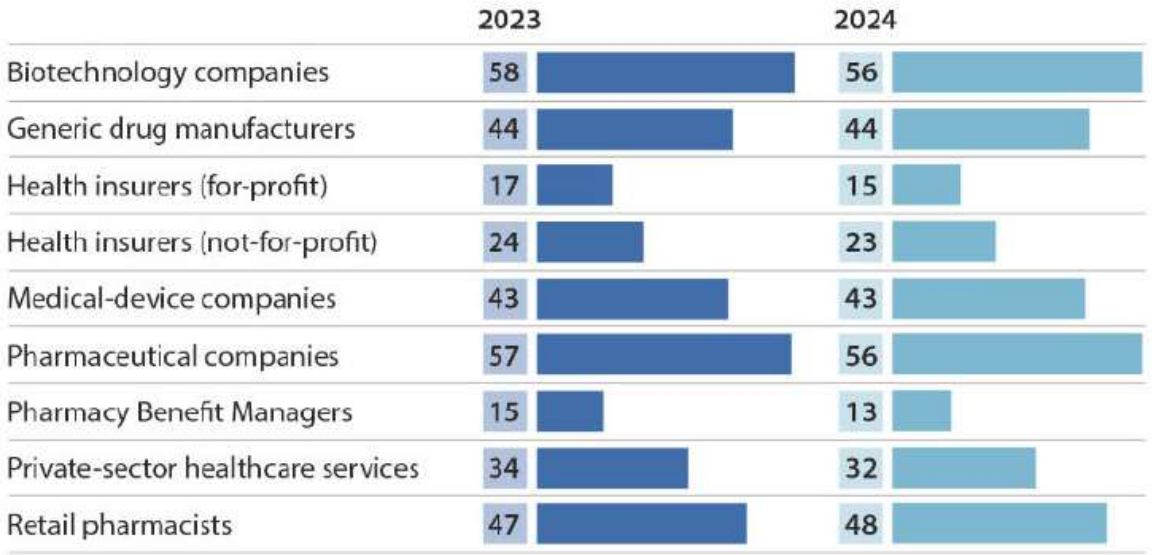
Patient Groups Have a Much More Positive View of Pharmaa

PatientView Survey, 2024

The corporate reputation of the pharma industry, according to respondent patient groups, 2020-2024
% of respondent patient groups, per year, stating "Excellent" or "Good"



The corporate reputation of the pharma industry, compared with that of other healthcare sectors, 2024 v. 2023—according to respondent patient groups
% of respondent patient groups, per year, stating "Excellent" or "Good"



Source: https://www.patient-view.com/wp-content/uploads/2025/04/CORP-REP-PHARMA-2024-PATIENTVIEW-PRESS-RELEASE.pdf

Resolving the Massachusetts Paradox

The biopharmaceutical industry's crisis communication plan begins at home

Peter Kolchinsky, RA Capital, Sep 15, 2025

In Washington, senators and representatives usually fight for their states' economic interests. Why then, when it comes to the biopharmaceutical industry that is so important to Massachusetts, are we such an outlier? Our Senators led the charge that resulted in the pill penalty. They urge for price controls to be expanded to all medicines and be applied earlier. And they did it because that's what Massachusetts voters wanted them to do. We can't expect our elected representatives to act differently until voters change their minds about our industry.

In this article, I'll examine the origins of this Massachusetts Paradox, what kinds of biopharma-related policies Massachusetts voters (and thus who we send to Washington) should logically support, and propose a new approach to rallying our neighbors to support those policies. Our campaign should be rooted in a kind of engaging storytelling that all of us in the biopharma ecosystem, from startup to pharma and from investor to banker, can and should contribute to. I'm talking about marketing, communication, education, and brand building, not lobbying.

As an industry, even in Massachusetts where we have home field advantage, we're terrible at connecting with the public. The majority of our creativity and communications effort goes into marketing our wins (e.g., DTC ads). Would the NFL have any fans if it played its games in private and then promoted the winner of every game? Hardly. Fans are forged by bringing them along on the quest to victory, with all its pitfalls, and letting them bond emotionally with the players.

Source: https://rapport.racap.com/all-stories/resolving-the-massachusetts-paradox

Massachusetts Paradox (continued)

We must bring the audience into the R&D ecosystem itself and let them see who we are if we're going to succeed. Only when the audience has connected with us as people, witnessing first-hand our effort, passion, struggles, and failures, will it tolerate and maybe even celebrate our high-priced wins they're already familiar with through traditional DTC-marketing. Only then will they care to learn to hold insurance companies accountable for making covered medicines affordable when patients – which is to say all of us eventually – need them. **Politicians will do what voters want them to, so we have to inspire them to want the biopharma industry to thrive and show them what kind of policy makes that possible.** And I mean show, through character-driven storytelling, not tell via fact-heavy op-eds.

Rather than delegate this effort to a few industry lobbying groups, I propose a **MA-rketing Coalition** inclusive of any companies, non-profits, universities, and state agencies that are inspired to contribute ideas, money, people, and follow-through, collaborating and competing to engage the public. I'll explore key points and terminology that all members should align on, examples of what we could produce together, the early efforts of No Patient Left Behind and others that have kickstarted this campaign, and which metrics would indicate that we're on the right track. If you're already compelled to join, then sign up here and get engaged.

Massachusetts is merely a laboratory for this communications R&D effort. Once we have developed the messages and materials that align Massachusetts voters with their own interests, our campaign can extend to other states. **Ultimately, our goal is to inspire America to solve affordability through insurance reform to lower out-of-pocket costs and to stop threatening price controls on novel medicines, preserving our innovation ecosystem.**

I'm proud to base my firm in Massachusetts, and I'm proud that we create many companies and many jobs here. But in what I've come to refer to as the **Massachusetts Paradox**, those same companies are constantly vilified by our own legislators. In the **horror movie that is public opinion** of the biopharma industry, the call for price controls on novel medicines – which make investors run away as effectively as any vengeful slasher in a hockey mask – is coming from inside the house!

If Massachusetts can't rally as a team in support of its economic crown jewel, then what hope is there of the rest of America embracing the value of our industry? And the Massachusetts Paradox only happens to focus on biotech at the moment; what will happen to other segments of our economy that have big price tags, such as climate tech and education, if/when Massachusetts helps enact counter-productive policies due to a failure to understand their value to our state and to the world?

We **have to pay for what we value** and, especially when it's a core export of our economy, it makes sense to let everyone else know that it's worth paying for, too. If that seems logical to you, then it's hard to unsee how illogically and self-destructively Massachusetts is behaving.

Inventing medicines boosts our local economy, improves the lives of Massachusetts residents, and ultimately saves us money since medicines can go generic and become inexpensive whereas hospitals never go generic. With proper insurance that doesn't charge high out-of-pocket costs, medicines can be both profitable for our companies and affordable to patients. Massachusetts leads on this front with the country's lowest uninsured rate (3%), thanks to the Obamacare precursor Romneycare.

Source: https://rapport.racap.com/all-stories/resolving-the-massachusetts-paradox

Summary of Key Points in Remainder of Paradox Article

Kolchinsky stresses that the industry has failed at connecting emotionally with voters. Most communication has focused on marketing approved drugs through ads, not sharing the human side of the R&D journey. Kolchinsky calls for a new approach modeled after sports fandom—inviting the public to witness scientists, investors, and patients navigating the ups and downs of drug discovery. This type of storytelling would build empathy, making people more tolerant of high drug prices and supportive of reforms that target insurance design rather than innovation itself.

The MA-rketing Coalition

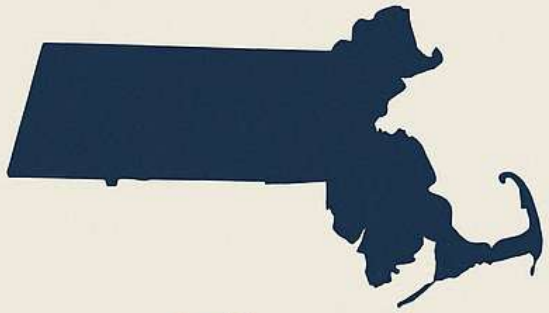
To shift sentiment, Kolchinsky proposes the creation of a "MA-rketing Coalition," a broad partnership of companies, universities, non-profits, and state agencies committed to funding and producing compelling public narratives. He points to early efforts like No Patient Left Behind's campaigns and suggests drawing inspiration from documentaries, podcasts, and even fictional dramas that humanize biopharma. By pooling stories across the ecosystem, Massachusetts can pilot messaging strategies that could later expand nationwide.

Constructive Policy Reforms

Kolchinsky underscores that voters need to be redirected toward reforms that lower out-of-pocket costs and curb abuses by pharmacy benefit managers, rather than blunt price controls on new medicines. He advocates for insurance reforms that make patients' costs predictable and affordable, combined with rules ensuring old drugs eventually go generic. These changes, he argues, would be good for patients, for innovation, and for Massachusetts' economic interests—unlike punitive measures that scare off investors and stall progress.

A Long-Term Commitment

Ultimately, Kolchinsky frames the MA-rketing campaign as an insurance policy against destructive policy shifts. Winning voter trust requires constant, authentic engagement—just as the immune system must remain vigilant even when we're healthy. Success would be measured not only in favorable legislation but also in shifting media narratives and public attitudes. By rallying Massachusetts voters to embrace the industry as hometown heroes, the state can preserve its role as the global hub of medical innovation and safeguard the incentives that fuel future cures.



The Massachusetts Paradox

Inspired Storytelling

Biogen

MA-RKETING COALITION

Constructive Reforms

Curb Insurer Abuses

Curb insurer abuses

Measure Progress

Ensure Commitment

Our Reactions to Kolchinsky's Article

The pharma industry ranks in the basement of least favorite industry groups in the United States. Right down there with lobbyists, the cable industry, politicians and the cigarette industry.

Here in NYC, we *don't* root for the Patriots. We don't root for the Red Sox. But we do want to see Boston-based biotechs be incredibly successful. Kolchinsky is right. If we can get Bostonians to like biotech, this could be a model for the nation.

One of the few things that both Democrats and Republicans agree on is that voters don't like the pharmaceutical industry. With passage of the IRA things have gotten seriously bad. We see a steady stream of negative news stories on the industry.

We agree with Kolchinsky that the solution to this perception problem starts with an industry effort to create greater awareness of the good that the industry does. His idea of humanizing innovation seems like a great approach. We also agree that the way that insurance works is not good for pharma. In other words, at the very moment that one is most vulnerable –when you are sick – you get a bill for an expensive therapeutic from a pharma company.

That is a recipe for becoming a very unpopular industry.

We absolutely must find a way to do a better job of reducing the out-of-pocket shock of specialty drug costs.

Peter Kolchinsky's article is right on the money. We should all read the article and think of our own views on how to improve pharma's abysmal PR problem. We are watching the Trump Administration skillfully take advantage of our industry's poor reputation. Collectively, we in the industry need to *own* this problem – rather than kick it over to industry associations. No one else is going to do it for us.

Our Views: Five Things That Would Help Pharma Perception

1 **Defeasance of out-of-pocket costs as is happening in Medicare needs to happen across all consumers.**

There is no way for the pharma industry to gain a favorable view from voters if patients get stuck with giant bills when they are sick. It's horrible PR.

2 **Investment in improving portrayals of pharma in the media.**

Groups like Gay & Lesbian Alliance Against Defamation (GLAAD) or the Media Empathy Foundation have been highly successful in reversing biases in the media against gays, overweight people and those with mental disorders. Likewise, a concerted effort to point out that there are very few positive portrayals of the pharma sector on television but constant shows that give a negative perception.

3 **Measures that allow pharma to more easily risk share on the outcomes of their products through risk-sharing in capitated care plans.**

While risk-sharing around things like expensive gene therapies is being explored pharma companies do not routinely get to participate in capitated care programs as do Medicare Advantage insurers. But MA insurers get to go the other way around by owning PBMs.

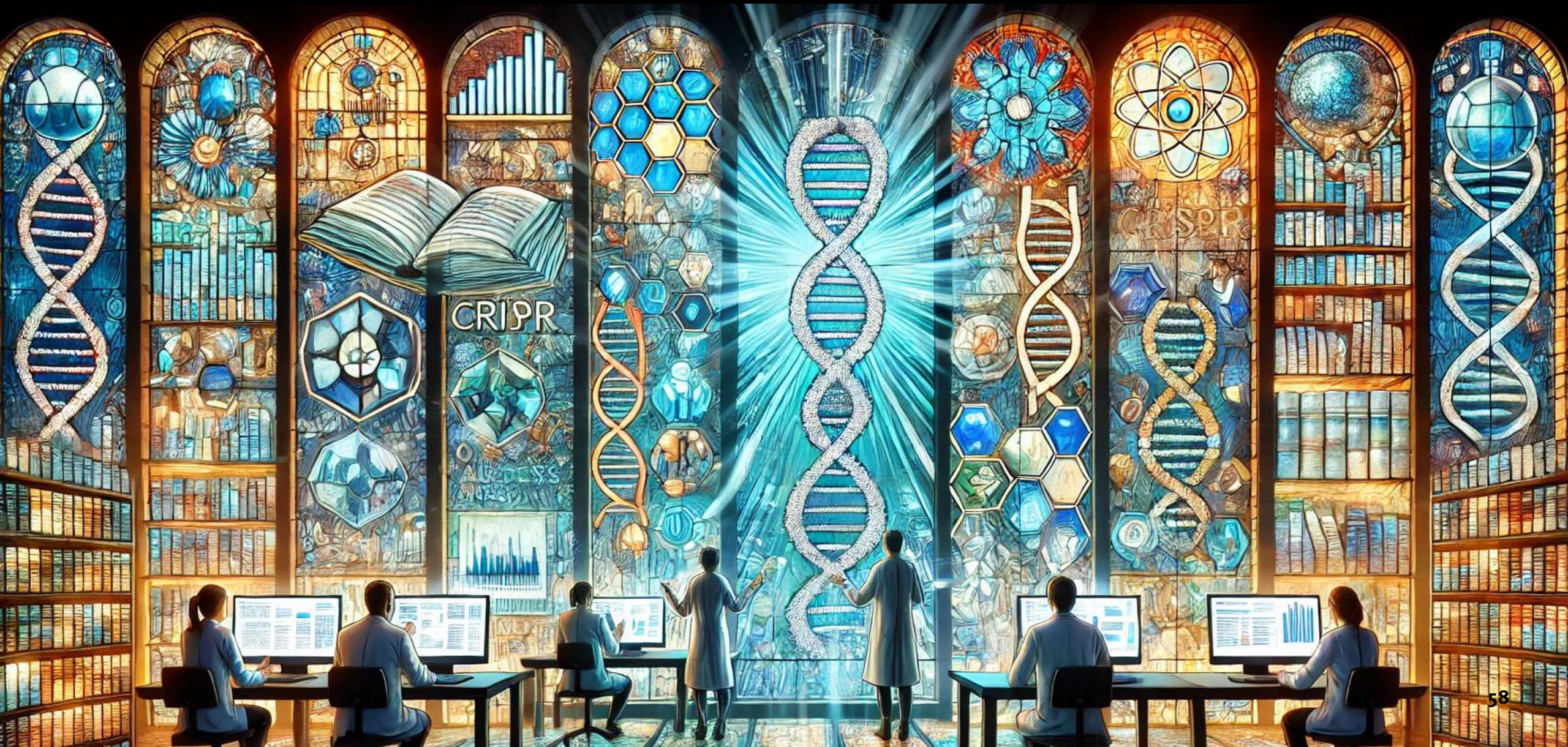
4 **More balance between the specialty drug model and more affordable large market drugs.**

The pharma industry has adopted pricing practices for most new drugs that require insurance companies to cover costs. Most new drugs to the market today are high priced and for niche populations. Henry Termeer's orphan drug pricing model has taken over the entire industry. Few drugs are in reach out of pocket any more for the average Joe. We believe that more focus on population health (e.g., efforts of Clive Meanwell's group Population Health Partners) would go a long way to helping pharma's PR problem.

5 **More connection with the consumer**

Pharma companies have been ditching their OTC brands in favor of specialty business models quickly. We think ideas of building more intimacy between the customer and the brand would help immensely on the PR front. There is no reason that a company like AbbVie can't be loved as much as Apple. This would start with growing DTC businesses and integrating those efforts with measures that help customers become more healthy. Today, pharma has left this idea to companies like HIMS that do not necessarily optimize brand.

Industry Update



I Run the F.D.A. Pharma Ads Are Hurting Americans.

Martin Makary, Editorial, *New York Times*, Sep 10, 2025

American drug advertisements are filled with dancing patients, glowing smiles and catchy jingles that drown out the fine print. It's not education — it's distraction by design. This is not how the practice of medicine is supposed to be.

Earlier this week, President Trump and the Food and Drug Administration took action to rein in misleading pharmaceutical ads targeted at consumers. An existing F.D.A. regulation states that ads must not create a "misleading impression," and that ads must offer a "fair balance" between a drug's benefits and risks.

For far too long, these ads have distorted the physician-patient relationship and have created increased demand for medications regardless of whether they are appropriate for the patient. It used to be that the F.D.A. properly enforced the regulations governing pharmaceutical ads and, as a result, pharmaceutical ads were rare. But over time, the F.D.A. has become too lax. In the past, the F.D.A. office charged with overseeing drug advertising sent more than 100 warning letters to pharmaceutical companies each year. But those numbers have dwindled. In 2023, the F.D.A. sent just one warning letter. And last year, it sent zero.

It's not just ads on television that are creating a misleading impression. Increasingly, social media influencers are paid to promote pharmaceutical products, often with no mention of side effects. A 2024 review in the Journal of Pharmaceutical Health Services Research found that many pharmaceutical ads on social media concealed risk information. The F.D.A. is taking action. Earlier this week, the agency sent approximately 100 cease-and-desist letters to pharmaceutical companies whose ads were found to violate the law. This includes several online pharmacies. The F.D.A. also sent thousands of letters to companies warning them to remove ads that violate the law and alerting them to our new diligent enforcement posture going forward.

Whether driven by patient protection concerns or fiscal responsibility principles, lawmakers across the political spectrum recognize that America's unique position as one of only two countries allowing widespread prescription drug advertising demands serious reform. There have been many efforts to rein in pharmaceutical ads, but none have worked — ads are more prevalent today than ever.

Source: https://www.nytimes.com/2025/09/13/opinion/i-run-the-fda-pharma-ads-are-hurting-americans.html

Trump Effort to Target Television Drug Ads Could Have Massive Implications

Dominic Mastrangelo, *The Hill*, Sep 14, 2025

An effort by President Trump's administration to curb advertising for pharmaceutical drugs on television is posing a potential marketing hurdle for some of the country's largest drugmakers while threatening a key revenue stream for media companies.

Advertising and pharmaceutical industry experts say an executive order Trump signed this week could pose an existential threat to the business model of both drugmakers and the media companies which raked in an estimated $5 billion in advertising revenue from pharmaceutical companies in 2024.

The order instructs the Department of Health and Human Services to ensure "transparency and accuracy" in direct-to-consumer advertising, including requiring greater disclosures of side effects in television and other ads. The order stops short of directing an outright ban on drug advertisements, though HHS Secretary Robert F. Kennedy Jr. has called for a wholesale end to direct-to-consumer advertising for prescription drugs.

"This is a shot across the bow from the administration telling these companies we're watching you, get your act together or we're going to come after you," said Robin Feldman, an expert in health law and a professor at the University of California. "The tone of the message matters as much as the language here." The administration has sent firm cease and desist letters to some of the country's largest drug manufacturers in recent says, warning scrutiny of the content in its advertisements is part of a broader push to combat "egregious violations demonstrating harm" in the marketing of high-cost prescription drugs.

The action is seen as an about-face from previous administrations, which thanks to a powerful healthcare lobby loosened restrictions on how drug makers market and sell their products, leading to a boom in Big Pharma ads on television in recent decades. White House officials have insisted they are not interested in pursuing an outright ban on direct-to-consumer drug ads but are instead interested in greater transparency and a more informed public on medicine and its side effects.

"Our goal is not to see a certain numeric reduction in ads," a senior administration official told reporters during a background call this week. "Our goal is to ensure that patients have proper information about drugs that have potential harms, and it's to rebuild public trust."

There could be major downstream impacts for media companies of drug manufacturers either spending less on advertising or placing greater scrutiny on how a drug commercial gets made.

Source: https://thehill.com/policy/healthcare/5500949-trump-administration-pharma-advertising-curbs/

Pharma's UK Frustrations Come to a Head as Lilly, Sanofi, AZ Pause Investments in the UK

Elizabeth Eaton, *FirstWord Pharma,* September 12, 2025 (excerpt)

Merck & Co.'s decision this week to walk away from a £1-billion ($1.4 billion) R&D facility in London — and pull its research activities out of the UK altogether — may have triggered a domino effect across big pharma, as Eli Lilly, Sanofi and AstraZeneca now seem to be rethinking their own investments in the country.

Following Merck's announcement, John Bell, an immunologist who was a member of the UK government's vaccine task force during the COVID-19 pandemic, appeared on the BBC Radio 4's Today podcast to warn that big pharmas are "not going to do any more investing in the UK" given how much the country spends on pharmaceuticals has fallen in recent years.

Merck's reasoning for moving its discovery efforts to mainly US-based sites was the UK's "overall undervaluation of innovative medicines and vaccines by successive UK Governments" — a sentiment that was echoed by a trio of pharmas on Friday.

An AstraZeneca spokesperson confirmed to FirstWord that it's pausing a planned £200-million ($271 million) investment in its Cambridge research site. It's the second UK project the pharma has backed out of, after it scrapped plans in January for a £450-million vaccine manufacturing facility in Liverpool — altogether, effectively cancelling a £650 million commitment to the UK's life sciences sector made in 2024.

Source: https://www.nature.com/articles/d41586-025-02578-8

U.S. Drugmakers Warn White House of Chaos as Trump Weighs Curbs on China

Rob Copeland and Rebecca Robbins, *New York Times*, Sep 12, 2025 (excerpt)

The Trump administration has been discussing severe restrictions on medicines from China that, if enacted, could upend the American pharmaceutical industry and availability of everything from generic drugs to cutting-edge treatments.

At the heart of the possible clampdown is a drafted executive order that threatens to cut off the pipeline of Chinese-invented experimental treatments. Major pharmaceutical companies have been buying the rights to drugs created in China for cancer, obesity, heart disease and Crohn's disease.

The prospect of the order, a draft of which was obtained by The New York Times, has set off furious behind-the-scenes lobbying efforts by two diametrically opposed groups — each with billions of dollars at stake.

Prominent investors and corporate executives with close ties to the White House, including the tech billionaire Peter Thiel, the Google co-founder Sergey Brin, the Koch family and staff at the investment firm run by President Trump's son-in-law Jared Kushner, have argued for a decisive crackdown against what they view as an existential threat by China to U.S. biotechnology, according to four people briefed on their lobbying who asked for anonymity to discuss private conversations.

On the other side are the world's largest drugmakers, including Pfizer and AstraZeneca. In the last few years, they have been on a shopping spree in China for low-priced experimental drugs, spurning smaller American biotech companies that are developing similar medicines.

A White House spokesman, Kush Desai, said in a statement on Monday that the administration was not "actively considering" the draft executive order. "Safeguarding our national and economic security is a top priority for the administration," Mr. Desai said.

Source: https://www.nytimes.com/2025/09/10/business/trump-medicines-china-biotech.html

MEMBER EXCLUSIVE

The Rise of US-China Biotech Partnerships: Opportunities and Emerging Challenges

China Market Intelligence
Banny Wang, June Xu ◇ September 11, 2025

KEY TAKEAWAYS

- Chinese biotech companies are becoming critical partners to American firms in early-stage drug development.
- MNCs maintain competitive advantages throughout innovative drug lifecycles, particularly in navigating global regulatory frameworks and leveraging resources during commercialization phases.
- US restrictions on bilateral biotech collaborations could limit these growth opportunities and weaken US pharmaceutical MNCs' competitiveness.

Turning Against Vaccines, America Is a Global Outlier

Damien Cave, *New York Times*, Sep 15, 2025 (excerpt)

That makes the United States an obvious outlier, though not because of public opinion, which still favors vaccination. Rather, experts say, it is because of the government. Health Secretary Robert F. Kennedy Jr. and other vaccine critics are now in charge of public health and — under a banner of MAHA or "make America healthy again" — they are stripping away support for vaccine development, promotion and distribution.

Florida recently became the first U.S. state to announce an end to mandates for vaccines. Experts say that weakens a policy devised to ensure that — in a decentralized and unequal health care system — nearly every child could be protected from horrific infections.

Mr. Kennedy has defunded vaccine research. He has replaced vaccine experts with critics on a key advisory panel, limited access to Covid shots and muddied official guidance on many others, worrying experts who see confusion eroding vaccine confidence worldwide.

As Heidi J. Larson, who leads the Vaccine Confidence Project at the London School of Hygiene and Tropical Medicine, recently put it in an essay for The Lancet: "The U.S.A., long a cornerstone of global health leadership, has become an unexpected source of global instability in vaccination confidence."

The Department of Health and Human Services, responding to such critiques from experts, said in an email that Mr. Kennedy was simply "being honest and straightforward about what we know — and what we don't know — about medical products, including vaccines."

But scientists see facts being cast aside, with effects that could last for years.

"The threat is this: that the U.S. style anti-vax movement linked to MAHA wellness-influencer grifting and authoritarianism is now globalizing," said Peter J. Hotez, a vaccine expert at Baylor College of Medicine and co-author of a new book, "Science Under Siege."

Source: https://www.nytimes.com/2025/09/15/world/asia/anti-vaccine-america-world-covid.html

Lasker Prizes Awarded Last Week

Carl Zimmer and Gina Kolata, *New York Times*, Sep 11, 2025 (excerpt)

The Lasker Awards, which honor fundamental discoveries and clinical advances that improve human health, were given on Thursday to scientists for discovering hidden complexity in cells, new states of biological matter, and a potent treatment for cystic fibrosis.

Lucy Shapiro of Stanford University received the Lasker-Koshland Special Achievement Award in Medical Science. Over the course of her 55-year career, she made profound discoveries about how proteins bring cells to life. At the time, biologists dismissed bacteria as mere bags of loose proteins. But Caulobacter's ability to make a tail at one end of a cell or a stalk at the other left Dr. Shapiro skeptical of the conventional wisdom.

She soon discovered that the interior of a bacterial cell is more like a carefully organized factory than a random molecular stew. Caulobacter moved certain proteins to specific spots in its cell. Only at those spots could they do their jobs. When the microbe made a new copy of its DNA, it carefully folded the stringlike molecule into intricate loops.

The Albert Lasker Basic Medical Research Award was presented to **Dirk Görlich and Steven McKnight** for discovering jellylike blobs in cells, which are essential to the survival of living things.

"It's a new kind of biological matter," said Dr. Görlich, a biochemist at the Max Planck Institute for Multidisciplinary Sciences in Göttingen, Germany.

A few years later, Steven McKnight of the University of Texas Southwestern Medical Center in Dallas independently came across similar gelatinous blobs. He had been studying a protein called FUS. When he and his colleagues purified the protein, it took on a jellylike consistency. "In all my years, that had never happened" with other proteins, Dr. McKnight recalled.

The Lasker-DeBakey Clinical Medical Research Award honors Dr. **Michael Welsh**, of the University of Iowa, and **Jesús González** and **Paul Negulescu**, who have both worked at Vertex Pharmaceuticals. The three men's research was instrumental in the discovery of drugs that transformed life for people with cystic fibrosis.

Source: https://www.nytimes.com/2025/09/11/health/lasker-awards-medicine.html

Lucy Shapiro

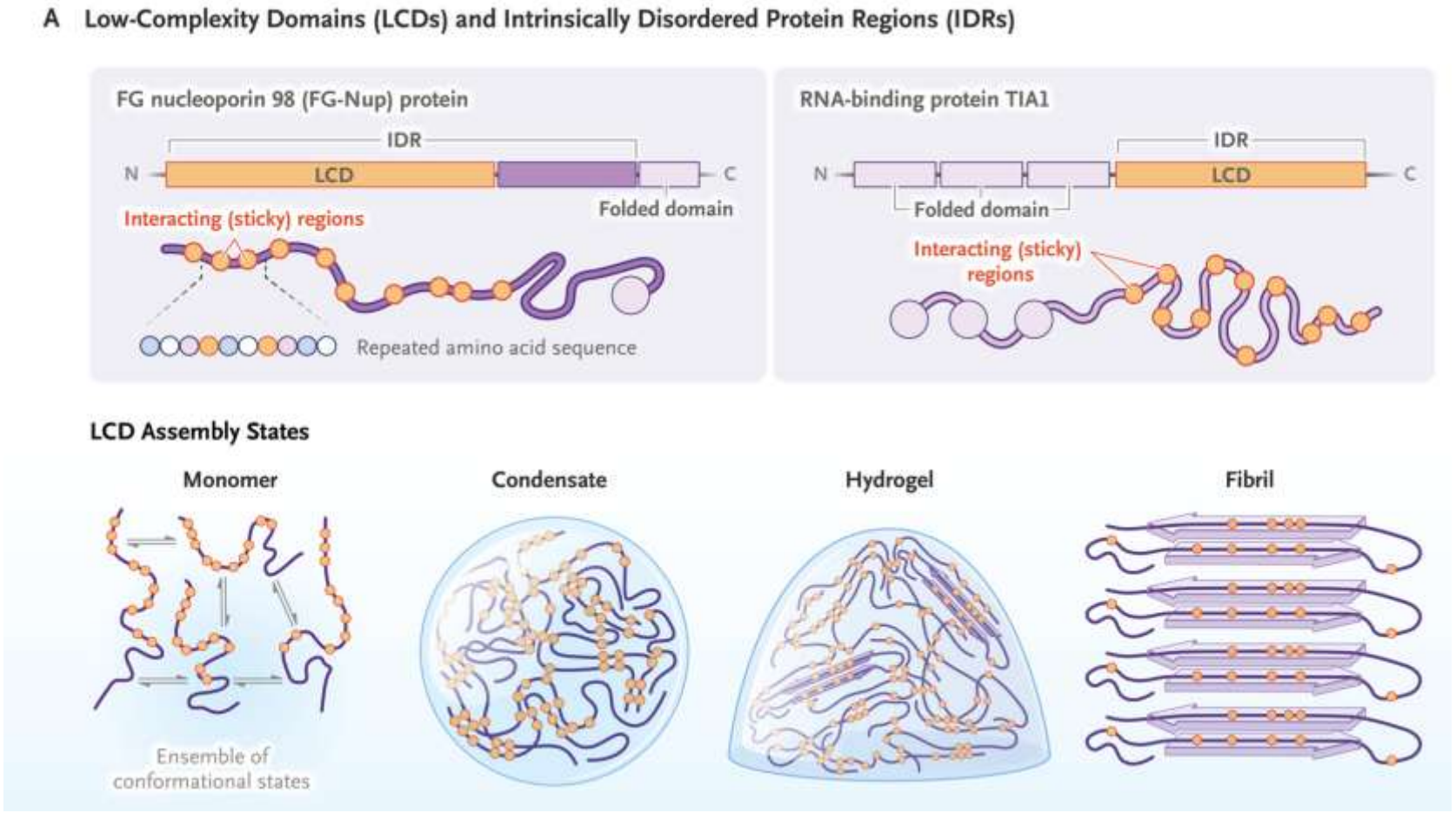
Dirk Görlich, who shared the Albert Lasker Basic Medical Research Award with Steven McKnight. Ines Bittcher-Gajewski/Max Planck Institute for Multidisciplinary Sciences, via Lasker Foundation

Steven McKnight of the University of Texas Southwestern Medical Center in Dallas. UT Southwestern Medical Center

Michael Welsh, Jesús González and Paul Negulescu. Michael Welsh and Jesús González, via Lasker Foundation; Dina Rudick/Anthem Multimedia, via Lasker Foundation

Dirk Görlich and Steven McKnight Work on Disordered Low-Complexity Domains (Lasker Award)

Intrinsically disordered protein regions (IDRs), which include low-complexity domains, do not adopt unique folded structures and therefore cannot be characterized by approaches such as x-ray crystallography that reveal the three-dimensional structures of folded proteins. Instead, IDRs adopt many different, typically unfolded, conformations that interconvert rapidly (Figure 1A).

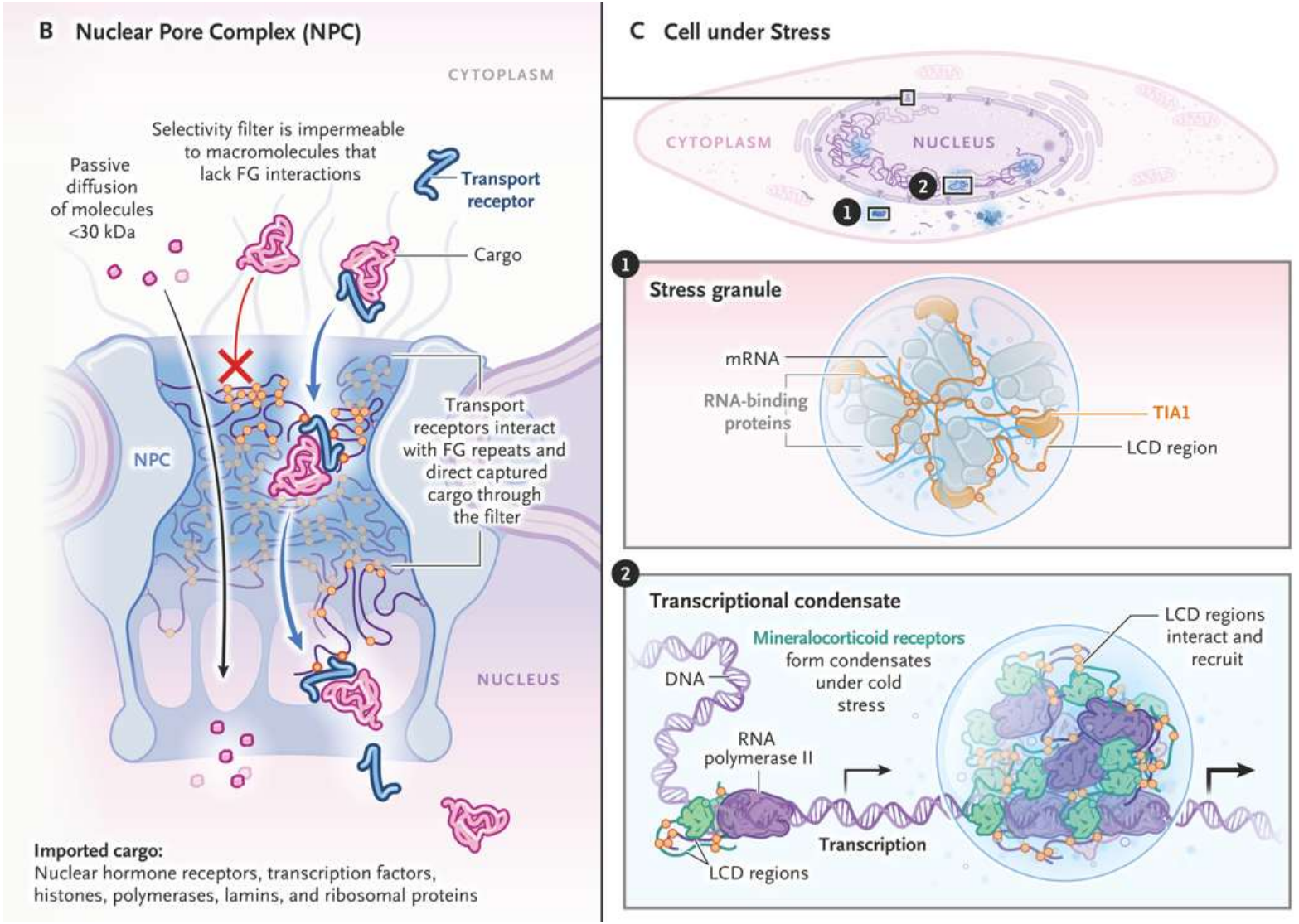


Association of Disordered Low-Complexity Domains (LCDs) into Different Assembly States.

LCDs comprise a subset of amino acids and function as monomers or assemble into condensates, hydrogels, or amyloid fibrils. The interiors of hydrogels can resemble those of condensates or be formed by amyloid fibrils (Panel A).

Source: https://www.nejm.org/doi/full/10.1056/NEJMcibr2509676

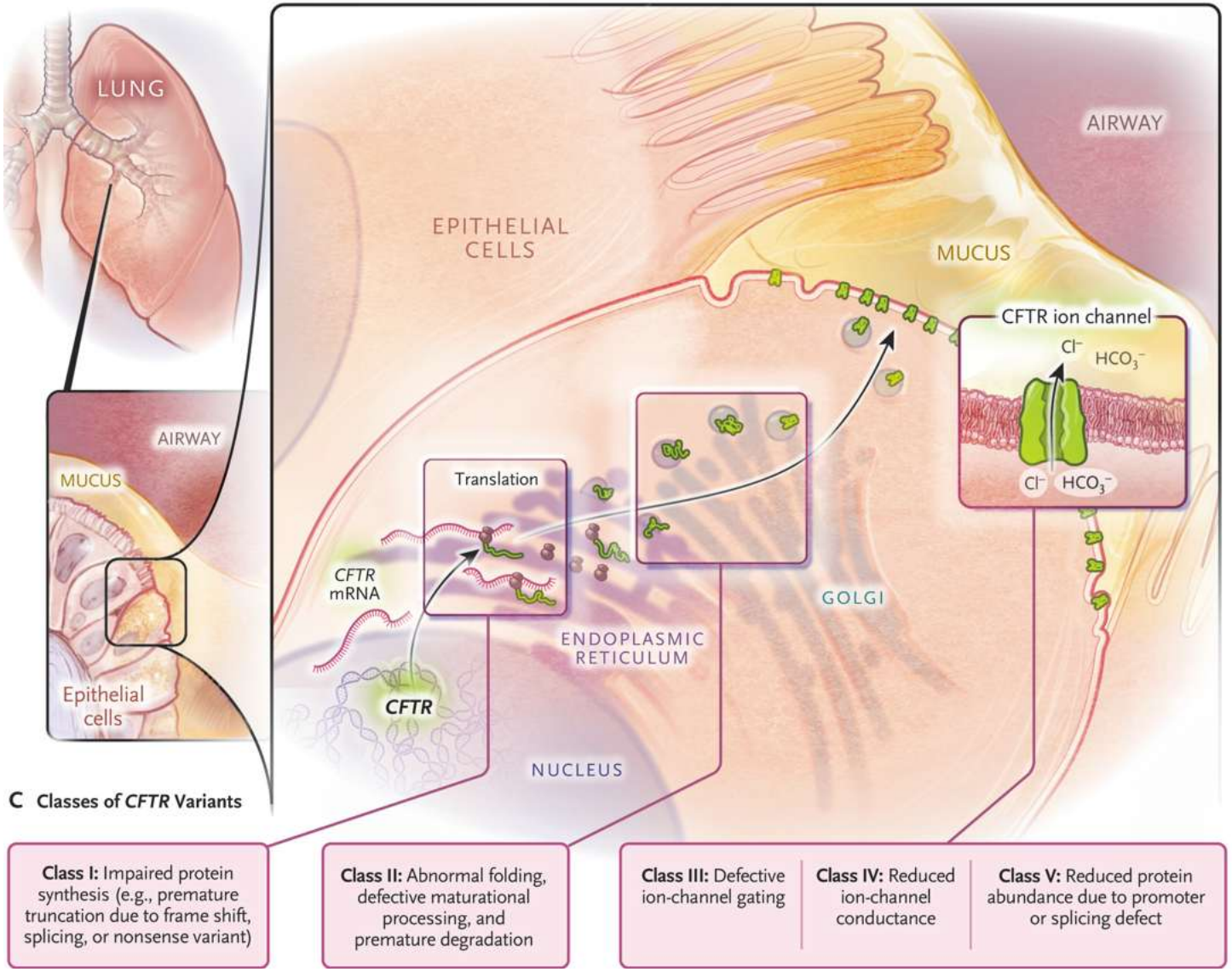
More on Dirk Görlich and Steven McKnight Work on Disordered Low-Complexity Domains (Lasker Award)



Phenylalanine–glycine (FG) nucleoporins form the semipermeable selectivity filter in nuclear pore complexes (NPCs) by forming a network of cohesive interactions (Panel B). Cargo larger than 30 kDa must be ushered through the filter by transport receptors that specifically recognize the cargo and interact with the FG nucleoporins. Under stress, cells form large assemblies mediated by LCD interactions (Panel C), including stress granules, which contain RNA-binding proteins such as T-cell–restricted intracellular antigen 1 (TIA1) and which function in RNA metabolism, and specific transcriptional condensates. The mineralocorticoid receptor forms condensates under cold stress and interferes with the quality of donor hearts. The term mRNA denotes messenger RNA.

Source: https://www.nejm.org/doi/full/10.1056/NEJMcibr2509676

Lasker Award in Cystic Fibrosis Work for Welsh, Gonzales and Negulescu



Over time, Michael Welsh, Jesús González, and Paul Negulescu would elucidate the pathogenesis, advance pharmaceutical science in remarkable new directions, and provide a transformational therapy for the disease. Their achievements are recognized by the 2025 Lasker–DeBakey Clinical Medical Research Award.

(figure) The cystic fibrosis transmembrane conductance regulator (CFTR) is an epithelial anion channel encoded by CFTR. CFTR regulates the composition and viscosity of airway epithelial and other exocrine secretions. In the lungs, the depth of the periciliary fluid layer, generation of submucosal glandular secretion, and mobilization of airway mucus depend on CFTR. Panel C shows the molecular mechanisms responsible for CFTR dysfunction. Hundreds of distinct CFTR variants are known to cause cystic fibrosis. The large majority can be grouped into classes, as shown. Class VI defects have also been described in which CFTR insertion, stability, or recycling at the plasma membrane are aberrant.

Source: https://www.nejm.org/doi/full/10.1056/NEJMcibr2510197

David Baltimore Dies at 87

David Baltimore (March 7, 1938 – September 6, 2025) was one of the towering figures in modern molecular biology — a scientist whose discoveries reshaped how we understand viruses, cancer, immunology and the interplay between genetics and disease. He won the Nobel Prize at just 37, cofounded major research institutions, led universities, and trained scores of young scientists. Here's a look at both his life and the significance of his death.

Baltimore was born in New York City and raised in Queens, later moving to Great Neck, Long Island. From an early age he displayed an aptitude for science, which was nurtured by academic summer programs and his undergraduate years at Swarthmore College. He earned his PhD at Rockefeller University in 1964, then held postdoctoral positions (at MIT among others) before beginning an independent research career. His best-known scientific breakthrough came in 1970, with the discovery of reverse transcriptase: the enzyme that allows certain RNA viruses to transcribe their RNA back into DNA.

This upended a fundamental assumption (the "central dogma") which held that information in biology flowed only from DNA to RNA to proteins. Baltimore's work, and parallel work by Howard Temin and Renato Dulbecco, showed that viruses like retroviruses could reverse that flow — a finding with deep implications for both basic biology and medicine.

Beyond that finding, Baltimore made major contributions in immunology (e.g. how antibodies are generated), the biology of tumor viruses, in shaping the field of biotechnology, and in establishing frameworks for responsible science (e.g. recombinant DNA, the regulation of biotechnology). He founded the Whitehead Institute, was President of Rockefeller University (briefly), and later President of Caltech, among many leadership and mentorship roles.

Dr. Baltimore was generous in giving time and energy to develop his Ph.D. students and leaves behind a legacy of excellent students.

Remembering David Baltimore, a Titan who Transformed Biology and Spoke Bluntly

Jon Cohen, *Science*, Sep 9, 2025 (excerpt)

David Baltimore, who died of cancer on 6 September at age 87, rewrote molecular biology, won a Nobel Prize before he was 40, and ran three major research institutions. He weathered a high-profile scientific fraud investigation directed at a collaborator with his reputation intact and helped shape safeguards for genetic engineering. He also had plenty of time for journalists, including me.

Like many others, I admired his outspokenness and ability to discuss the most complicated molecular biology and immunology in plain English. He served as one of my unofficial biology professors, who helped me explain cutting-edge research to others—a job he didn't sign up for—and our conversations often veered far from the intended subject to his childhood in New York City (his parents worked in the garment industry), jazz artists, and ideas for my future stories. We sometimes butted heads, yet he was unfailingly cordial and never condescending, even when he thought my ideas were misguided. He was allergic to bullshit.

When he was just 32 Baltimore reported in a rare solo author paper in Nature that the "central dogma" idea put forward by Francis Crick of DNA fame—that genetic information only flowed in one direction from DNA to RNA to proteins—needed an asterisk. In some viruses, he had found, the flow went the other way and RNA became DNA with the help of the reverse transcriptase (RT) enzyme. Tests for RT, which is used by retroviruses, would later play a key role in the discovery of HIV. That same year he and Alice Huang, a former postdoc whom he had married, described in a Nature article how disabled viruses could disrupt the replication of intact relatives, altering the course of a disease. These viral interfering particles continue to fascinate researchers, and some are testing them as a strategy to help cure HIV infections.

Five years later, in 1975, Baltimore shared the Nobel Prize in Physiology or Medicine for the RT discovery. He was becoming a public figure, and that year he helped organize the Asilomar Conference on Recombinant DNA, a landmark meeting of biologists attempting to self-regulate risky research.

Baltimore throughout his long working life was drawn to exploring uncertainty—and he knew how to dance with it, too. "Productive careers are unpredictable," he said to Ralf Pettersson, chair of the committee that awarded him the Nobel, in a 2001 interview. "I was never consciously directing myself so that I would end up somewhere. I was just following my nose and then not being afraid to take a step to the side or a step in a new direction when that opportunity seemed to be ripe."

Source: https://www.science.org/content/article/remembering-david-baltimore-titan-who-transformed-biology-and-spoke-bluntly

Pfizer PD1 x VEGF Strategy Focused on Creating Combo's for its ADC Portfolio

Max Gelman, *Endpoint News*, Sep 12, 2025 (excerpt)

But Pfizer isn't planning to conduct any trials pitting SSGJ-707 directly against standard of care or placebo at this time. Instead, it will run studies that combine the drug with the antibody-drug conjugates it acquired from Seagen, Pfizer's head of thoracic oncology Arati Rao told Endpoints News in a recent interview.

"For us to do a study like the Summit study, as a global study, would be tough," Rao said last month. "We have this great advantage at Pfizer of having this wealth of multiple ADCs that we can combine with, or work with, that we don't want to muddy those waters."

Rao said Pfizer could change course and still run a monotherapy trial for SSGJ-707, on which she has oversight. Rao and Jeff Legos, Pfizer's chief oncology officer, have said SSGJ-707 has the potential to be more efficacious than PD-1 checkpoint inhibitors alone on a call with investors in July. They describe it as "structurally distinct" from other PD-1xVEGF programs.

In lung cancer, however, Rao said the space is "pretty crowded right now," including Pfizer's other ADC trials. She pointed to a Phase 3 study in lung cancer for sigvotatug vedotin as a reason against launching a similar trial for SSGJ-707. Sigvotatug vedotin comes from Pfizer's roughly $43 billion acquisition of Seagen in 2023.

If Pfizer wanted to do a monotherapy trial in lung cancer, it would have to enroll only patients with at least 50% expression of PD-1 or PD-L1 on their tumor cells to beat the standard of care, Rao added.

"The bottom line is we don't need to have a monotherapy study," Rao said. "Our time is better spent treating patients who truly need this drug in combination with chemo or with something else."

Source: https://endpoints.news/pfizer-has-a-vegf-bispecific-strategy-and-its-very-different-than-summits/

Arati Rao, Head Thoracic Oncology, Pfizer

We like Pfizer's strategy. As discussed in our June oncology report, using VEGF x PD1 as a backbone therapy for ADC's and engagers appears to be a winning if risk-averse approach. BioNTech, BMS, Merck and Pfizer appear to be going down this road.

Lilly Weight Loss Drug Could be Approved by Year End

Deanna Beasley, *Reuters*, Sep 16, 2025 (excerpt)

Sept 16 (Reuters) - Eli Lilly's experimental weight-loss pill could be fast-tracked under a one- to two-month review process recently launched by the U.S. Food and Drug Administration, several Wall Street analysts said.

Analysts speculate that the drug, orforglipron, is a viable candidate given the growing cost burden of expensive injectable weight-loss drugs and the fact that Lilly is expanding its U.S. manufacturing - issues the Trump Administration has prioritized.

Lilly, based in Indianapolis, declined to comment.

The FDA is reviewing an oral version of Denmark-based rival Novo Nordisk's GLP-1 obesity drug, with a decision expected in the fourth quarter.

The FDA in July detailed terms of its new "Commissioner's National Priority Voucher" under which an experimental drug meeting certain criteria could be approved within a month or two. The agency's standard review takes 10 months.

"FDA policymakers have tried to come up with ideas to speed important products to market. ... It is in part directed to achieving some of the (Trump) Administration's goals," said Chad Landmon, chair of Polsenelli's patent and FDA practice.

Source: https://endpoints.news/pfizer-has-a-vegf-bispecific-strategy-and-its-very-different-than-summits/

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Novo Nordisk Amylin Phase 3 Data Worse Than Hoped

James Waldron, *Fierce Biotech*, Sep 16, 2025 (excerpt)

Novo Nordisk's injectable amylin alternative to Wegovy appears to have underperformed the approved obesity blockbuster in a phase 3 readout, but the pharma is still planning to push ahead with development.

The data unveiled this morning demonstrate the performance of a 2.4-mg weekly dose of cagrilintide, a long-acting amylin analogue, which was given to nondiabetic patients with obesity or who are overweight. Over 68 weeks, cagrilintide was tied to average weight loss of 11.8%, compared to 2.3% for the placebo cohort.

The data come from a sub-analysis of the Redefine 1 trial and were presented at the European Association for the Study of Diabetes congress in Vienna.

While trial-to-trial comparisons are difficult for several reasons, Novo's approved GLP-1 weight loss drug Wegovy achieved 14.9% average weight reduction in Step-1, a 68-week clinical trial of nondiabetic patients with obesity or who are overweight and have at least one weight-related comorbidity. Another study called Oasis 1 showed 15% weight loss after 68 weeks of treatment with the oral version of Wegovy, which is still under FDA review.

When it came to the safety of Novo's investigational asset, the Danish pharma giant said the drug was "well tolerated," with 1% of patients on cagrilintide discontinuing their treatment due to nausea compared to 0.1% in the placebo cohort.

Cagrilintide functions as a dual amylin receptor and calcitonin receptor agonist (DACRA), and analysts have suggested DACRAs have the potential for a more tolerable safety profile than GLP-1s.

Source: https://www.fiercebiotech.com/biotech/novo-sees-amylin-drug-underperform-wegovy-phase-3-pushes-ahead-development

Why is AI Struggling to Discover New Drugs?

Hannah Kuchler and Melissa Heikkilä, *Financial Times*, Sep 10, 2025 (excerpt)

In the mid-2010s, a spate of start-ups hoping to transform the laborious process of finding new drugs launched with big promises. Artificial intelligence would dramatically reduce the time it took to discover new medicines and cut the average of $2bn it takes to develop a drug. The emerging businesses attracted the attention of Big Pharma companies such as Bristol Myers Squibb and Sanofi, which signed deals worth billions of dollars pending the drugs' eventual approval. Press releases boasted of "breakthrough productivity gains" and "groundbreaking research collaborations".

But now, sceptics are asking: where are the drugs? It has been longer than the average 10 years that it takes to discover and develop a medicine, yet there are few AI-discovered candidates in late-stage clinical trials, and not one has been approved. Despite pledging to cut the industry's high failure rate, many of the companies' initial studies flopped. Some start-ups have struggled financially, launching in a period where investors have pulled money from the biotech sector in general. BenevolentAI, a British company that attracted lots of early excitement, saw its shares fall more than 99 per cent before it delisted in March, merging with a Japanese company. US-based Recursion snapped up rival Exscientia cheaply last year, paying $688mn — only $180mn more than the cash on its balance sheet and far less than the $2.9bn valuation it went public at three years before.

Alex Zhavoronkov, chief executive of AI for drug discovery company Insilico, says companies have been under pressure to prove their big claims about transforming drug discovery, by showing they had actual drugs. "In order to claim that you have a golden goose, you need to make sure that you have laid a few golden eggs. And if you don't have golden eggs, your golden goose is depreciating very, very quickly," he says.

Daphne Koller, chief executive of another, similarly named, AI for drug discovery start-up, Insitro, says fundamentally we are trying to fix something we do not understand because of the complexity of human biology. "I used to say we were the industry with the highest failure rates of anything but space exploration. And then space exploration started to work," she says. The idea of applying AI to drug discovery has been so attractive because investors see the pharmaceutical sector as a key area where slow and expensive processes are ripe for disruption. Venture capitalists poured money into companies trying to use AI to discover new drugs, seeing the industry as a promising field, especially as ageing populations increase medical costs around the world. Funding for AI drug discovery companies increased from $30mn in 2013 to a peak of $1.8bn in 2021, according to data from PitchBook.

Source: https://www.ft.com/content/9a8aee4e-9cf6-4bb3-b7ea-d95ddd0d5e79

Why is AI Struggling to Discover New Drugs? (cont)

> I used to say we were the industry with the highest failure rates of anything but space exploration. And then space exploration started to work

DAPHNE KOLLER — CHIEF EXECUTIVE OF INSITRO, AN AI FOR DRUG DISCOVERY START-UP

Source: https://www.ft.com/content/9a8aee4e-9cf6-4bb3-b7ea-d95ddd0d5e79

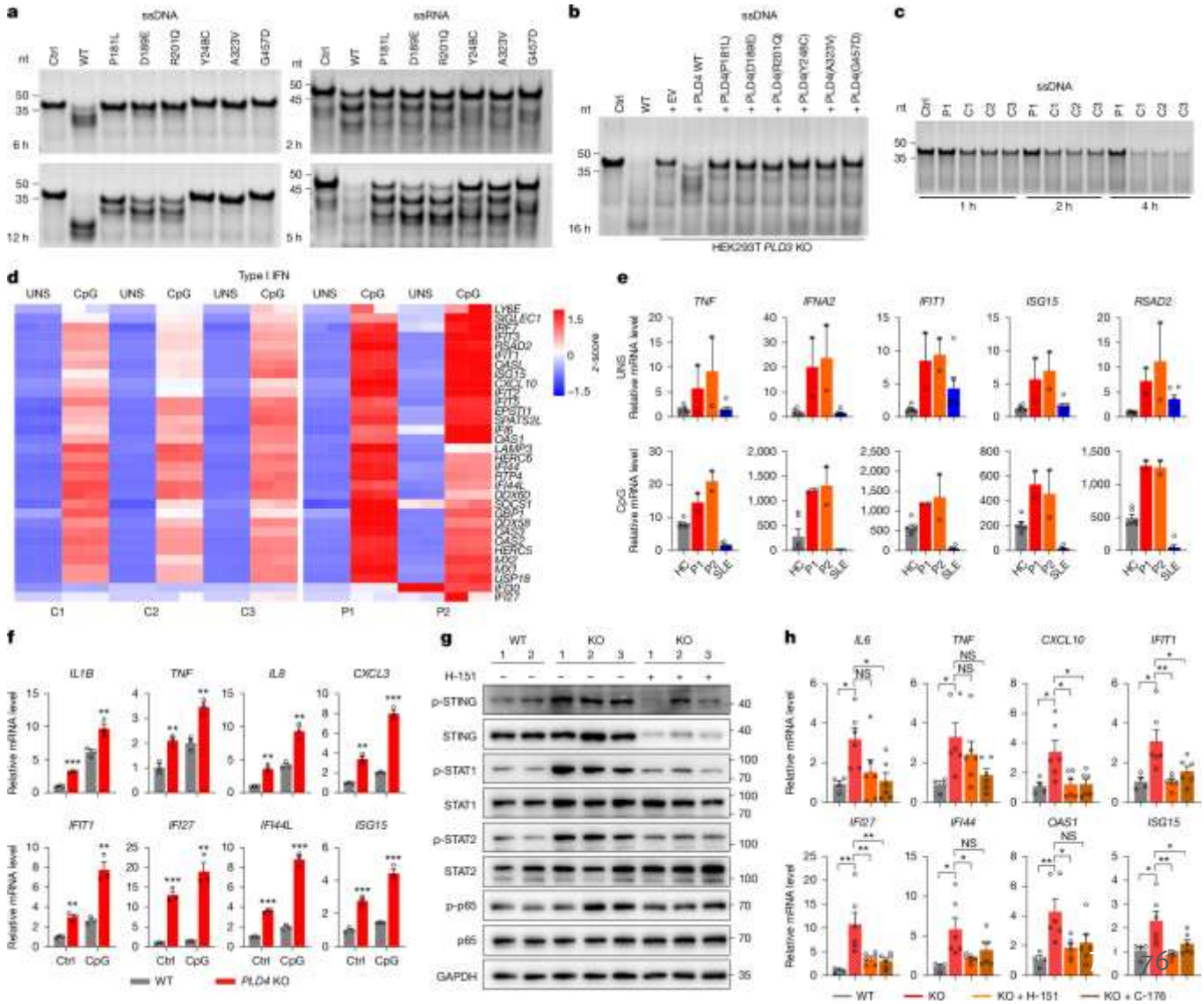
Loss-of-Function Mutations in PLD4 Lead to SLE

Qintao Wang et.al. *Nature*, Sep 10, 2025 (excerpt)

Monogenic lupus offers valuable insights into the underlying mechanisms and therapeutic approaches for systemic lupus erythematosus (SLE)1-3. Here we report on five patients with SLE carrying recessive mutations in phospholipase D family member 4 (PLD4). Deleterious variants in PLD4 resulted in impaired single-stranded nucleic acid exonuclease activity in in vitro and ex vivo assays. PLD4 loss-of-function mutations led to excessive activation of Toll-like receptor 7 (TLR7) and TLR9. Downstream inflammatory signalling pathways, especially type I interferon signalling, were hyperactivated in patient dendritic cells. Pld4-deficient mice presented with autoimmunity and cell-intrinsic expansion of plasmacytoid dendritic cells and plasma cells. Pld4-deficient mice responded to the JAK inhibitor baricitinib, suggesting that targeting type I interferon may be a potential therapy for patients with PLD4 deficiency.

Source: https://www.nature.com/articles/s41586-025-09513-x

Fig. 3: Mutations impair PLD4 exonuclease activity and result in aberrant type I IFN signalling activation.



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