Biopharma Market Update

November 3, 2025

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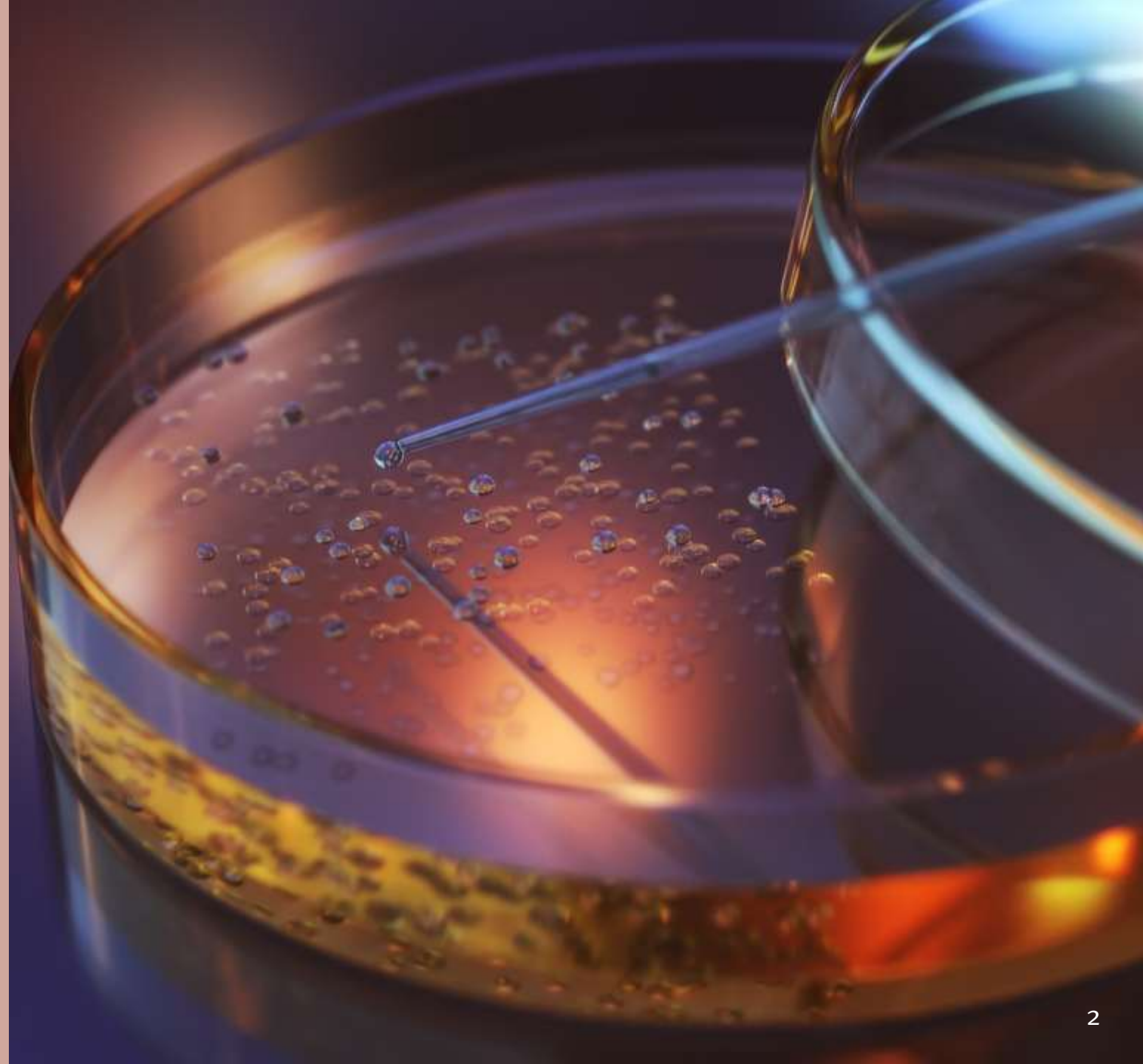

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[Oct 28, 2025]

Medicine, Progress & AI

[Sep 11, 2025]

Obesity Drug Update

[July 9, 2025]

Oncology Update

[Jun 5, 2025]

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[May 30, 2025]

Aging Biology, Part I

[Mar 26, 2025]

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[November 22, 2023]

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Biopharma Market Update

Money is Flowing into Biotech

Just six weeks ago (Sep 16th) we wrote “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 and (7) the much-needed “biotech cleanse” is behind us.”

Our expressed view was that we should end the year with the XBI somewhere around 120 – and that it will be heading well north from there in 2026. Yeah, we know… We are on a LOT of Prozac. Clearly.

Since then, the XBI has gone from 93 to 112.7 (up 21%). There is a saying that sometimes it is better to be lucky than good. We’ll take “lucky” this time.

It’s as if we are living in a different world. Money is flowing into biotech now. Fast. Capital markets activity has picked up materially. And the pace of M&A takeouts is accelerating.

What we are seeing today is exceptional and surprising to many.

Sources of Heightened Capital Flows

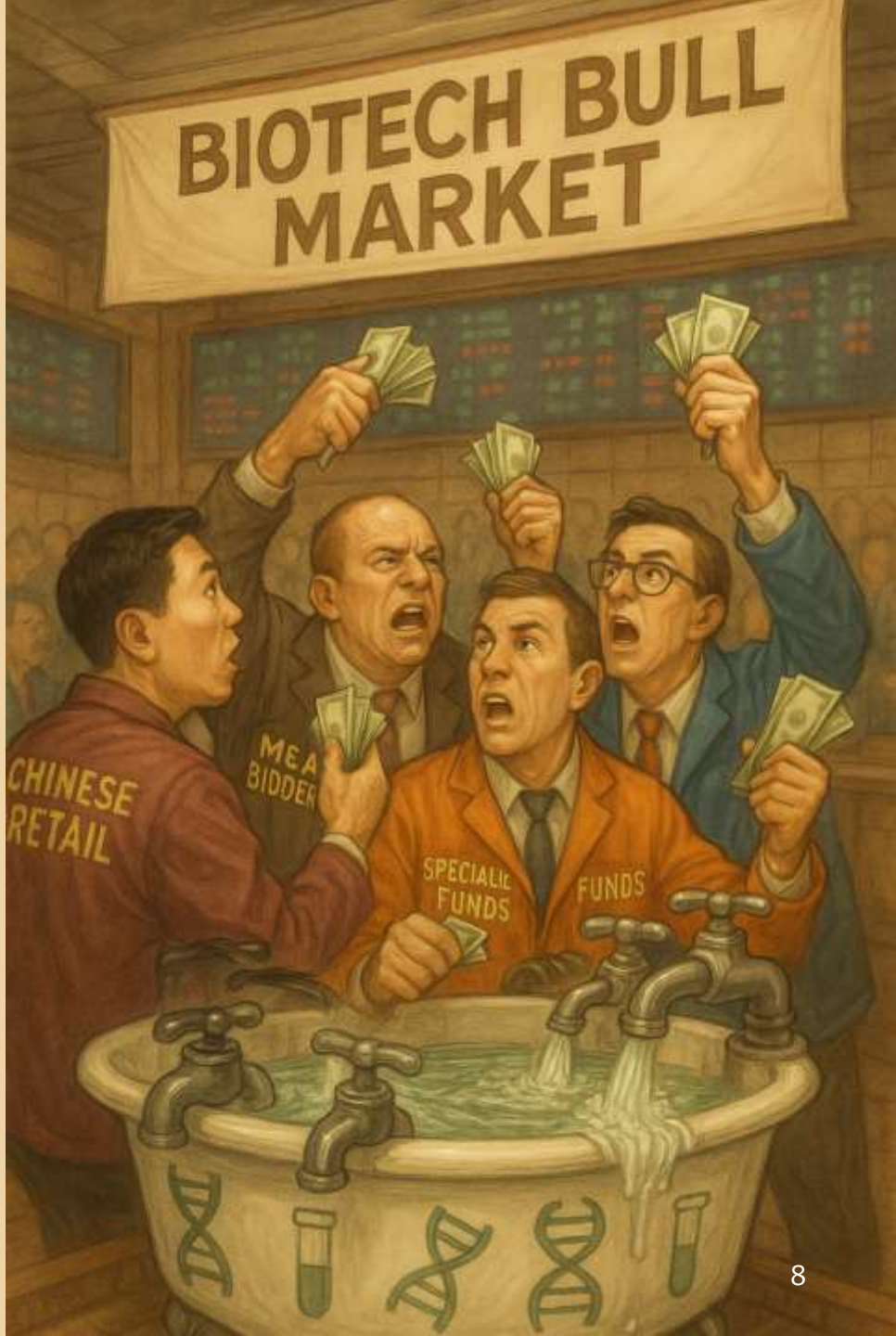
As little as four weeks ago words were being used in investor conversations about the market like “constructive” but “mixed”.

In other words, investor sentiment had turned somewhat positive and previous fears seemed to be melting away. The language today, in contrast, is “enthusiastic”, “positive” and the like.

The main complainers we are hearing now are from long-short funds or those who are net short saying that the market isn’t “making sense” anymore. “Alnylam is too high” etc. Sorry buddy. Tough day for you, I guess. Sort of.

So, the question is where is this money coming from all of a sudden? There is good reason to expect that a lot of the initial September inflow was sourced from global retail, particularly those in China and the MidEast. China has more than 100 million retail accounts. Many fund families have both specialist subfunds and generalist subfunds. We started to see those generalist subfunds put more into biotech. Now, we are seeing broader generalist buying and interest in biotech – for the first time in a long time.

We spoke to one aggregator of biotech capital on Friday who indicated that last week he was being offered investment money from “all sorts of places” around the world and worried that there was no place to put it. What has been so striking about this rally is its speed – those who were on strike on buying biotech have turned very quickly back into the sector.



“Risk On” Sentiment Rising

We at Stifel have acted as bookrunner on 14 financings since Labor Day for $3.2 bn in capital raised, including one IPO.

What we have noted in the last few weeks is high oversubscription on secondary deals. Completely different than six months ago.

It’s clearly a “risk on” market.

We should hasten to add that this risk on sentiment is now well established and reflective of broader changes in the market.

The Fed cut rates last week again and there is a sense that more cuts are on the way. We have seen the value of other riskier asset classes rise as FOMO spreads. At one point last week there was one $5 trillion market cap tech company (NVDA) and two $4 trillion companies (AAPL, MSFT). Gold and crypto have also been subject to substantial speculative buying. There is huge interest right now in tech secondaries.

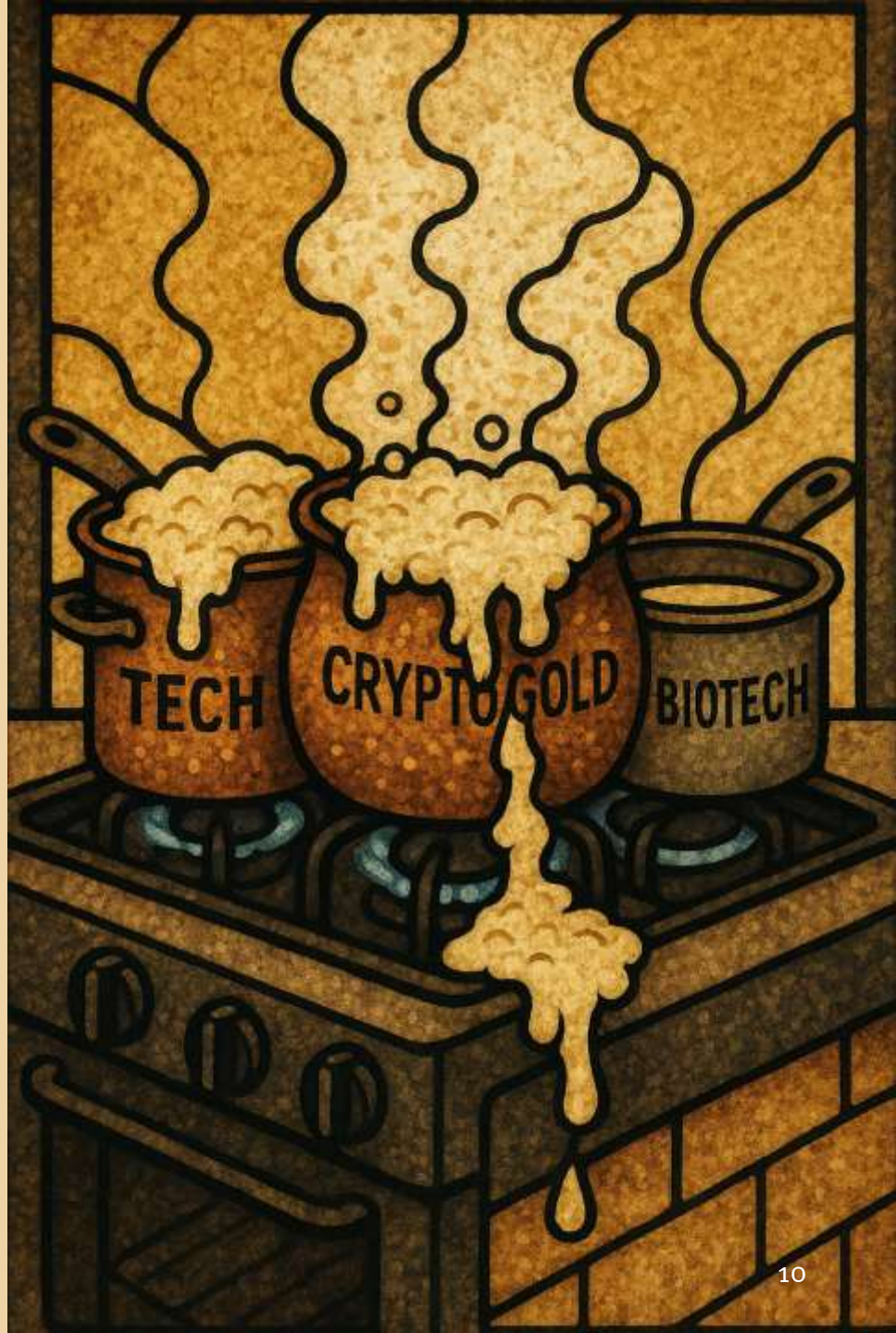
Most large investors in the world are waking up and realizing at the same moment that they are underweight biotech. Like way underweight.

Some worry that biotech is getting overheated in what is clearly becoming an increasingly “risk on” environment.

Is Biotech Overheated?

Our own view is that biotech is not overheated at all. We cannot speak for fair value of tech stocks, gold or crypto, nor can we vouch for whether any biotech stock is fairly valued, but we can say a few things:

1. Unlike the S&P500 as a whole, biotech is still well down from its all-time highs.
2. We frequently run NPV's on biotech and pharma stocks as part of our M&A work with various buyers. We are still finding that most interesting targets right now are trading *below* fair value – not above fair value.
3. The macro fundamentals are likely to get even better. We see rates continuing to moderate.
4. The M&A bid for biotech is not going away. If anything, as we get closer to the big upcoming patent expiries –M&A is going to rise. Last week's eruption over Metsera typifies what we think we will be seeing more of ahead.
5. The policy environment continues to be relatively permissive. Importantly, the Republicans will be facing the voters in the U.S. in a year and they know it. It's time for less culture war and more "economy" right now. Trump has been conspicuously steering away from anti-pharma crusades lately, knowing what he is going to be dealing with in 2026.

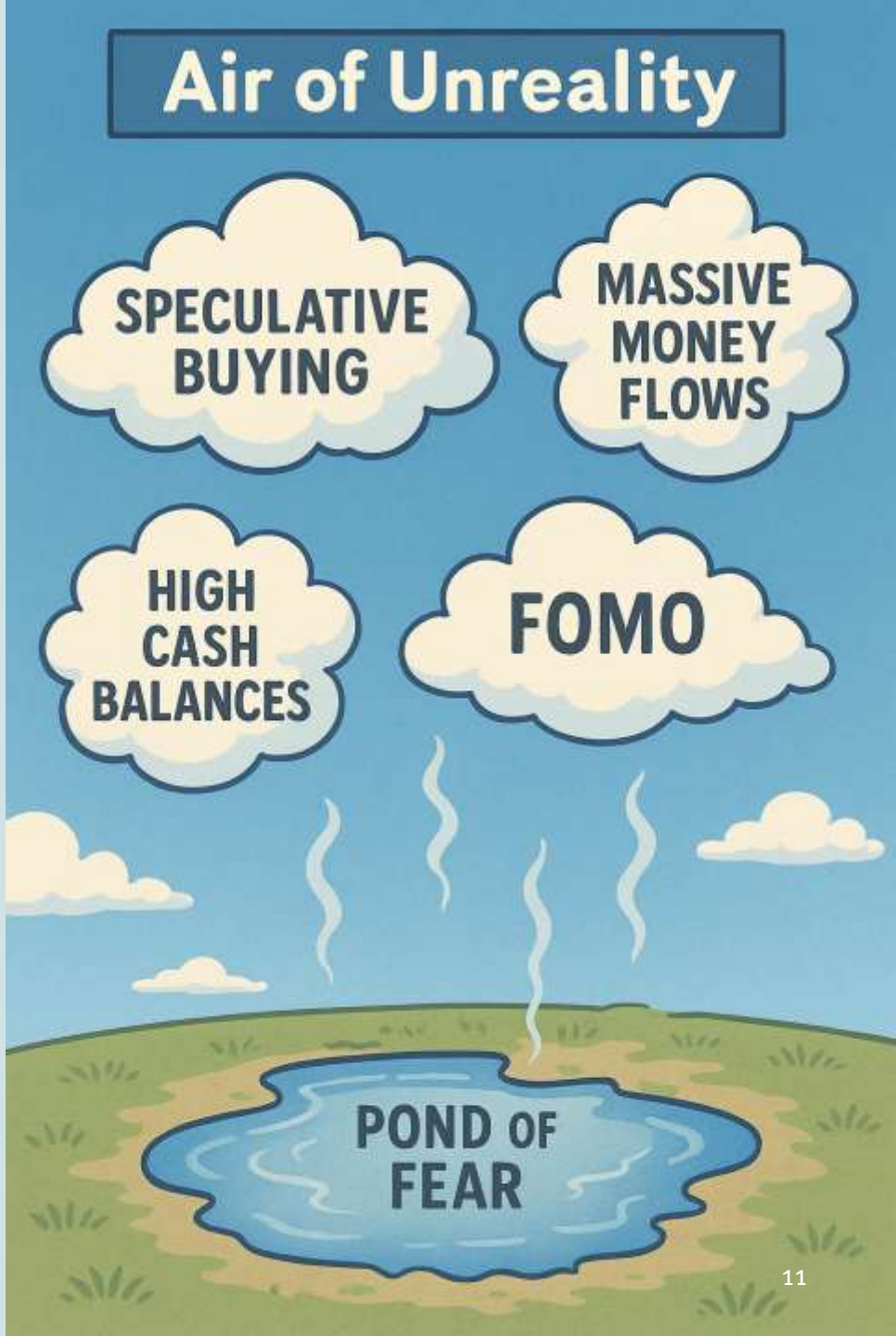


An Air of Unreality, Perhaps?

OK, you might say, so biotech is not overheated, but at least let us all agree that there is an air of unreality to this market. We appear to have come way too far – way too fast. How can it be that six months ago a common conversation was about investors leaving the biotech market, people quitting the profession of being a biotech CEO and talk of shifting biotech stocks to crypto and other such fluffiness?

Today, money is coming into our market with extraordinary vigor. The top seven tech stocks have gained $3 trillion dollars in value since August. And the US biotech sector has tacked on about $60 billion in value since then (not that much in the greater scheme of things).

Where is all this money coming from? It all seems a bit unreal. Of course, we cannot know with any certainty about the "where". But we can note a few things: (1) the level of money parked in cash in the Summer was at record levels, (2) the scale of investable "retail" wealth in China, India, the MidEast, tech entrepreneurs today is extraordinary and (3) the value of the biotech sector had gotten so low that even modest capital inflows would result in large percentage value gains. The sheer *scale* of capital pools today seems far larger than the investable tech and biotech markets than before. The "Cathie Wood" Days of Risk-taking Yore seem quaint versus today's forces in their ability to move equity markets far and fast. There is still a lot of capital on the sidelines – which could move markets more.



The XBI Closed at 112.7 On Friday (Oct 31), Up 4% Last Week

The Stifel Global Biotech Value Tracker rose by 4.9% last week, a bit more than the XBI. Treasury yields are in the low 4's. The XBI is up 25% for the year while the Stifel Global Biotech Value Tracker is up 67% for the year (reflective of the boom in China which is not included elsewhere).

Biotech Stocks Up Big Last Week

Return: Oct 24 to Oct 31, 2025

Nasdaq Biotech Index: +3.4%
Arca XBI ETF: +4%
Virtus LifeSci Biotech ETF (BBC): +5.5%
Stifel Global Biotech EV (adjusted): +4.9%*
S&P 500: +0.7%

Return: Dec 31, 2024 to Oct 31, 2025 (YTD)

Nasdaq Biotech Index: +24.5%
Arca XBI ETF: +25.1%
Virtus LifeSci Biotech ETF (BBC): +34.7%
Stifel Global Biotech EV (adjusted): +67%*
S&P 500: +16.3%

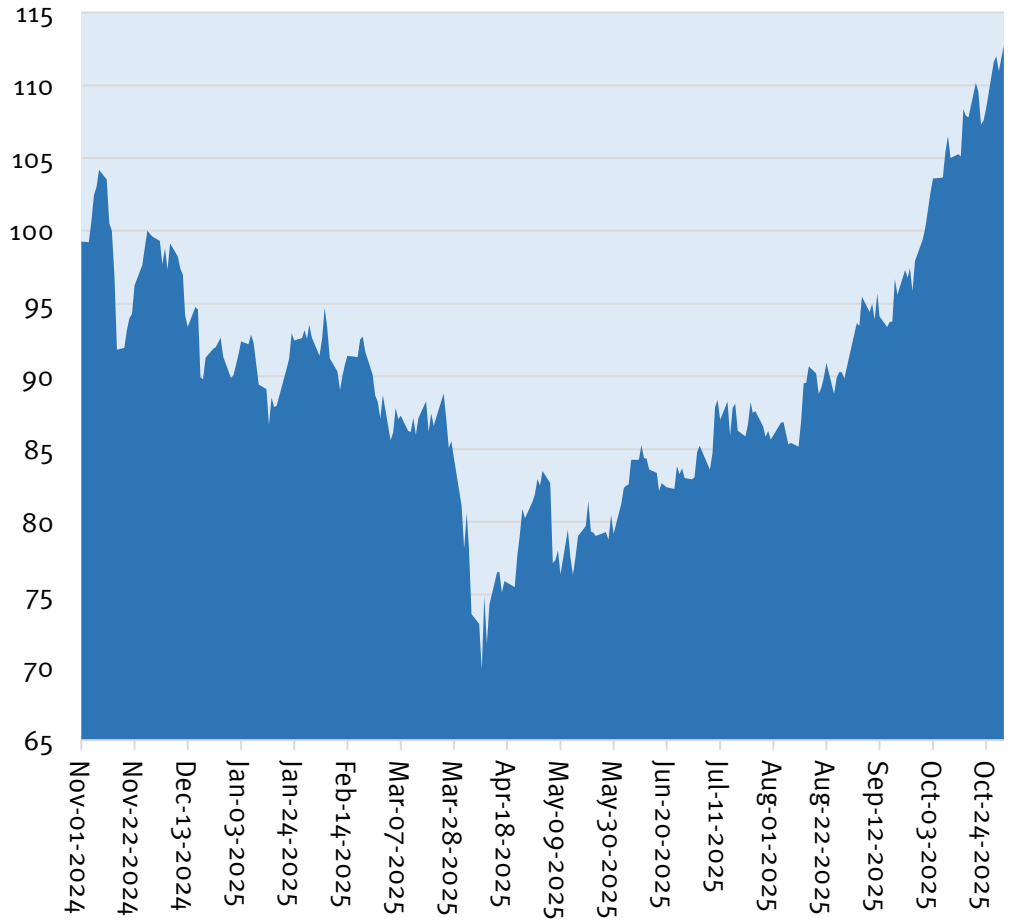
VIX Up a Bit

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%
Oct 3, 2025: 16.6%
Oct 31, 2025: 17.7%

10-Year Treasury Yield Flat

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%
Oct 3, 2025: 4.1%
Oct 31, 2025: 4.11%

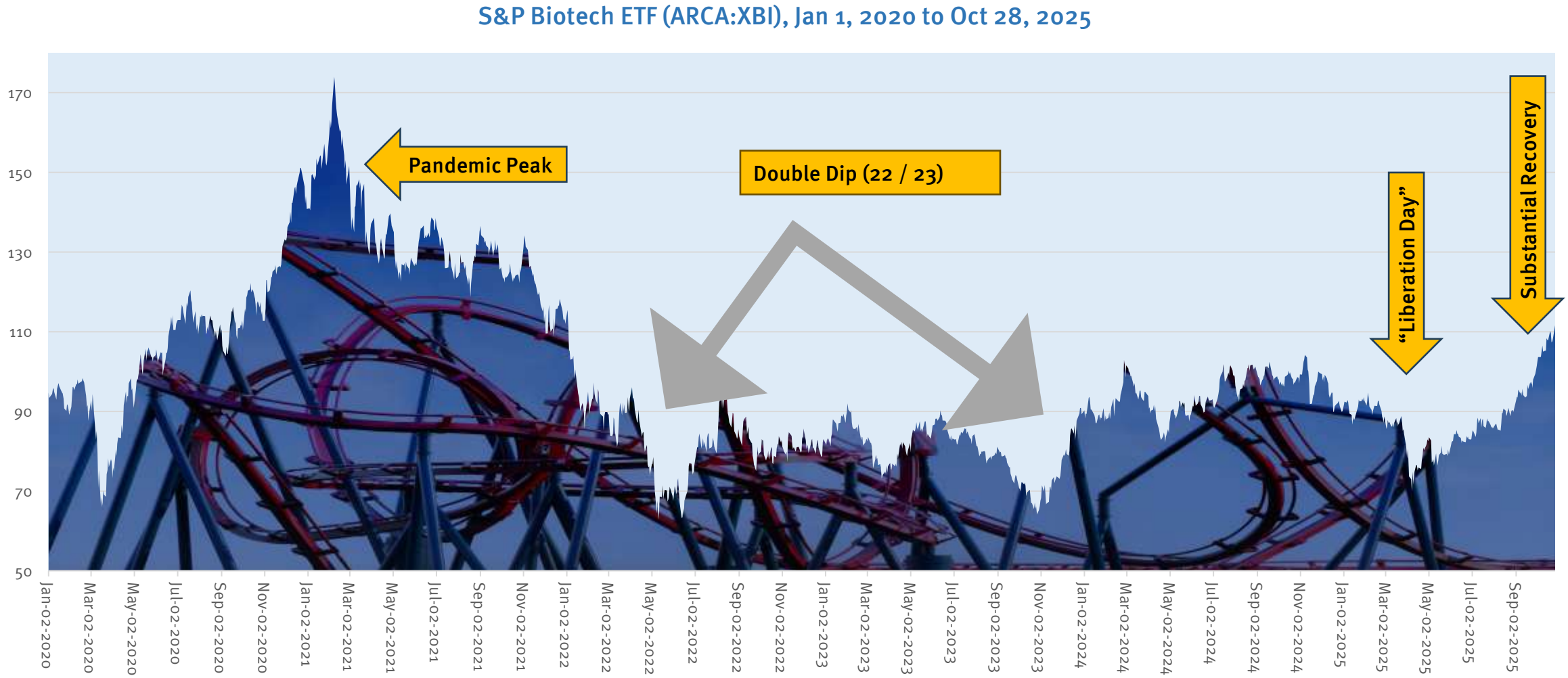
XBI, Nov 1, 2024 to Oct 31, 2025



* Change by enterprise value. The adjusted number accounts for the effect of exits and additions via M&A, bankruptcies and IPOs.

Source: S&P Capital IQ and Stifel analysis

The Last Five Years Have Been Quite Volatile

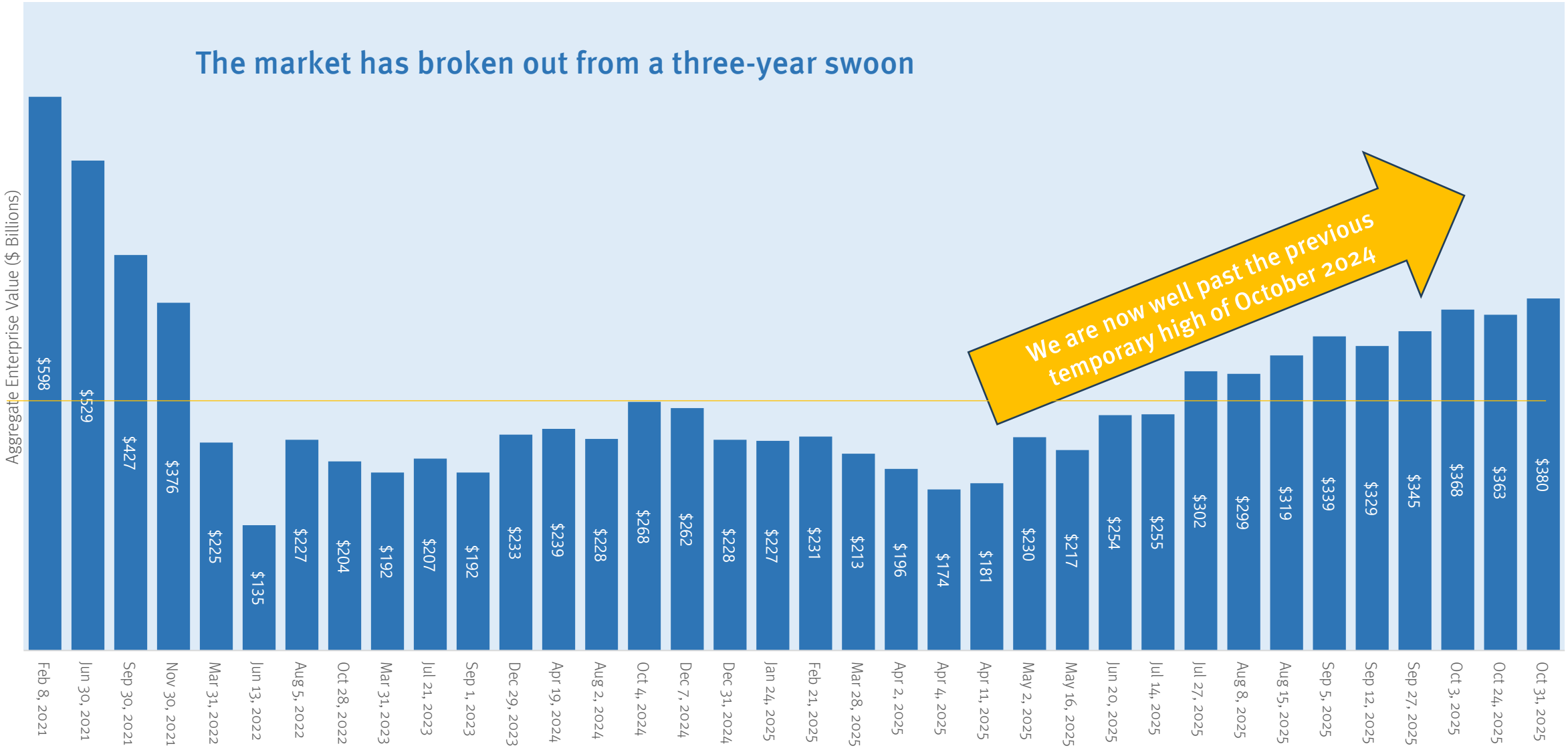


Source: CapitalIQ.

Biotech Stocks are up 113% Since Liberation Day and 67% for the Year

Total Enterprise Value of Publicly Traded Global Biotech, Feb 8, 2021 to Oct 31, 2025

($ Billions, Addition / Exit Adjusted)

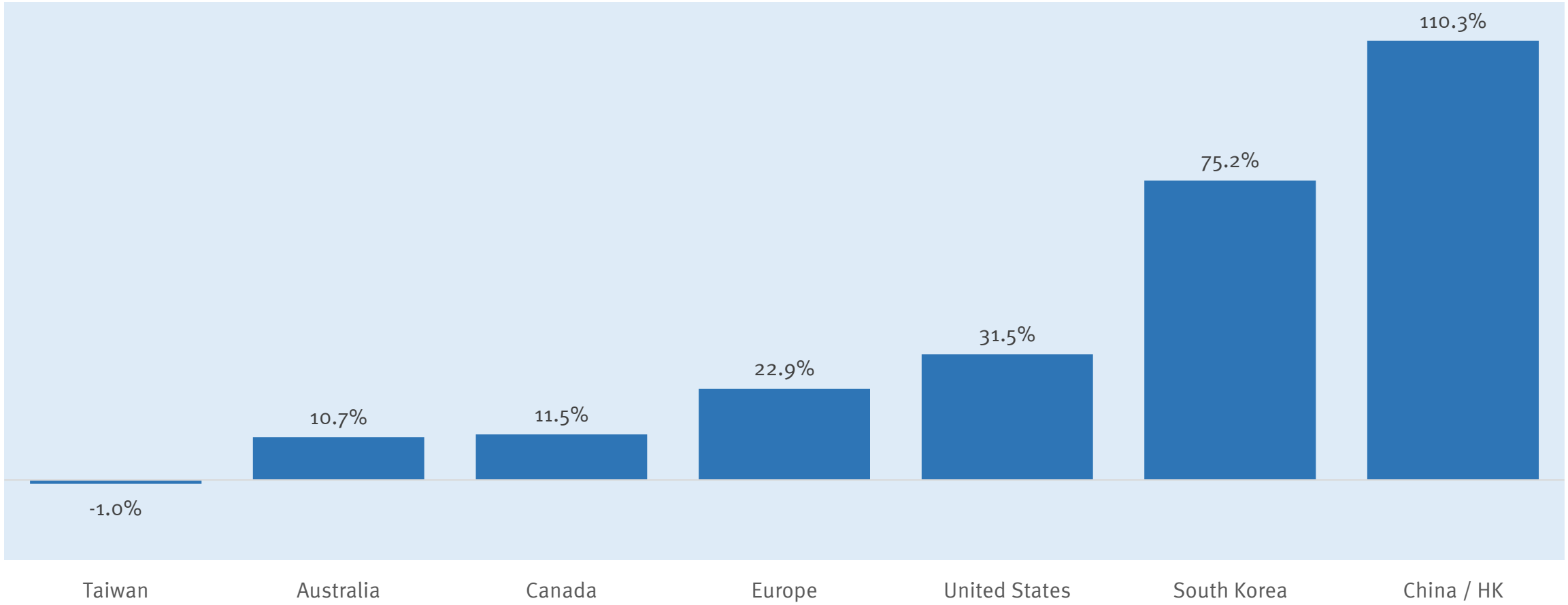


Source: CapitalIQ. Biotechs are defined as any therapeutics company without an approved product on any global stock exchange.

China, Korea and US Biotechs Have Done Well This Year

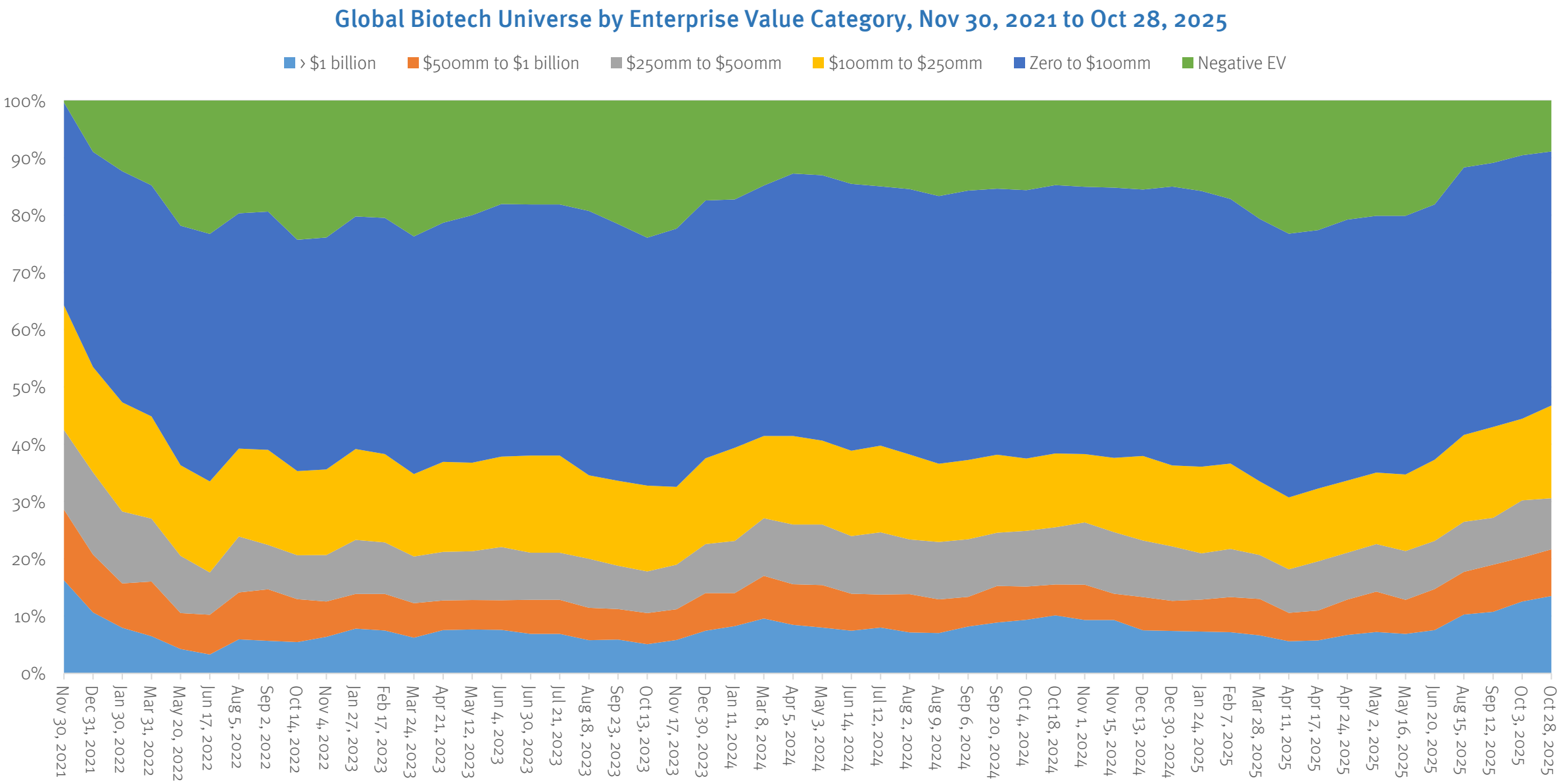
China biotech is up 110% this year. South Korea is up 75% while the U.S. is now up 31.5%. Amazingly, the U.S. biotech sector was down more than 30% just six months ago.

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



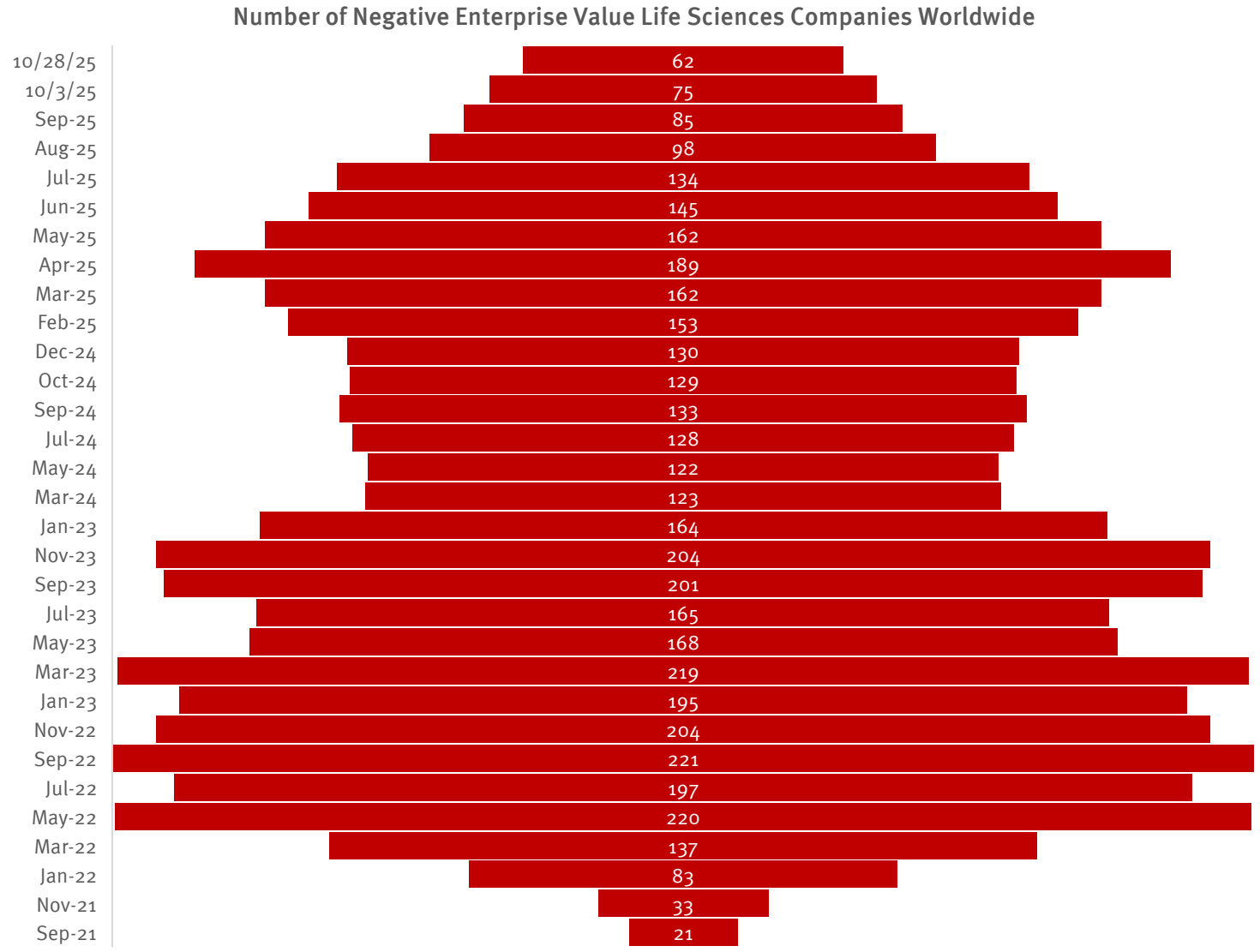
Source: CapitalIQ and Stifel analysis. Biotechs are defined as any therapeutics company without an approved product on any global stock exchange. Europe biotech includes companies from all major EU countries.

Global Biotech Neighborhood is Getting a Lot Richer



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.

Number of Negative Enterprise Value Life Sciences Companies is Down Massively

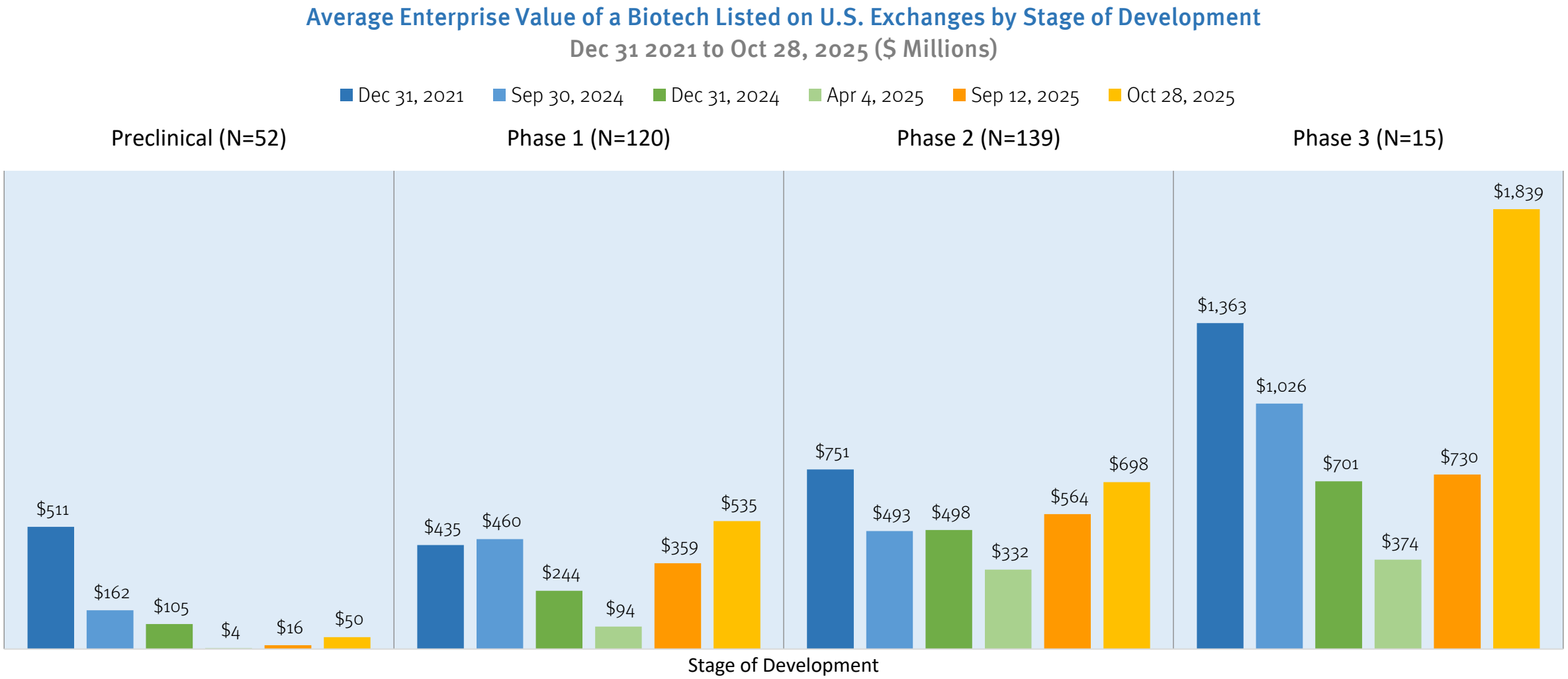


This measure of sector distress continues to go in the right direction.

The market is rapidly normalizing.

Source: CapitalIQ

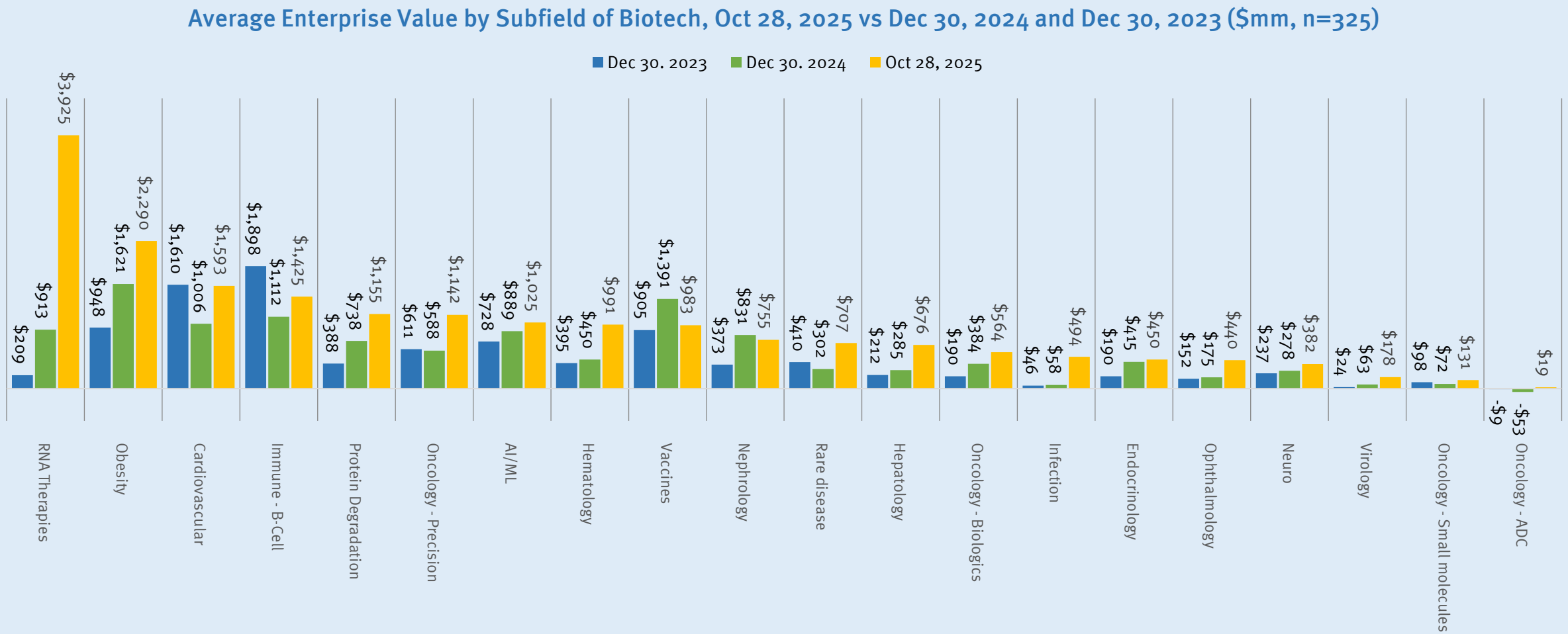
U.S. Phase 1 and 2 Biotechs Back at Peak Values. Phase 3's are Beyond Peak Values and Early-Stage Way Below the Last Peak



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.

U.S. Biotech Values Today Highest in RNA, Obesity, CV and B-Cell

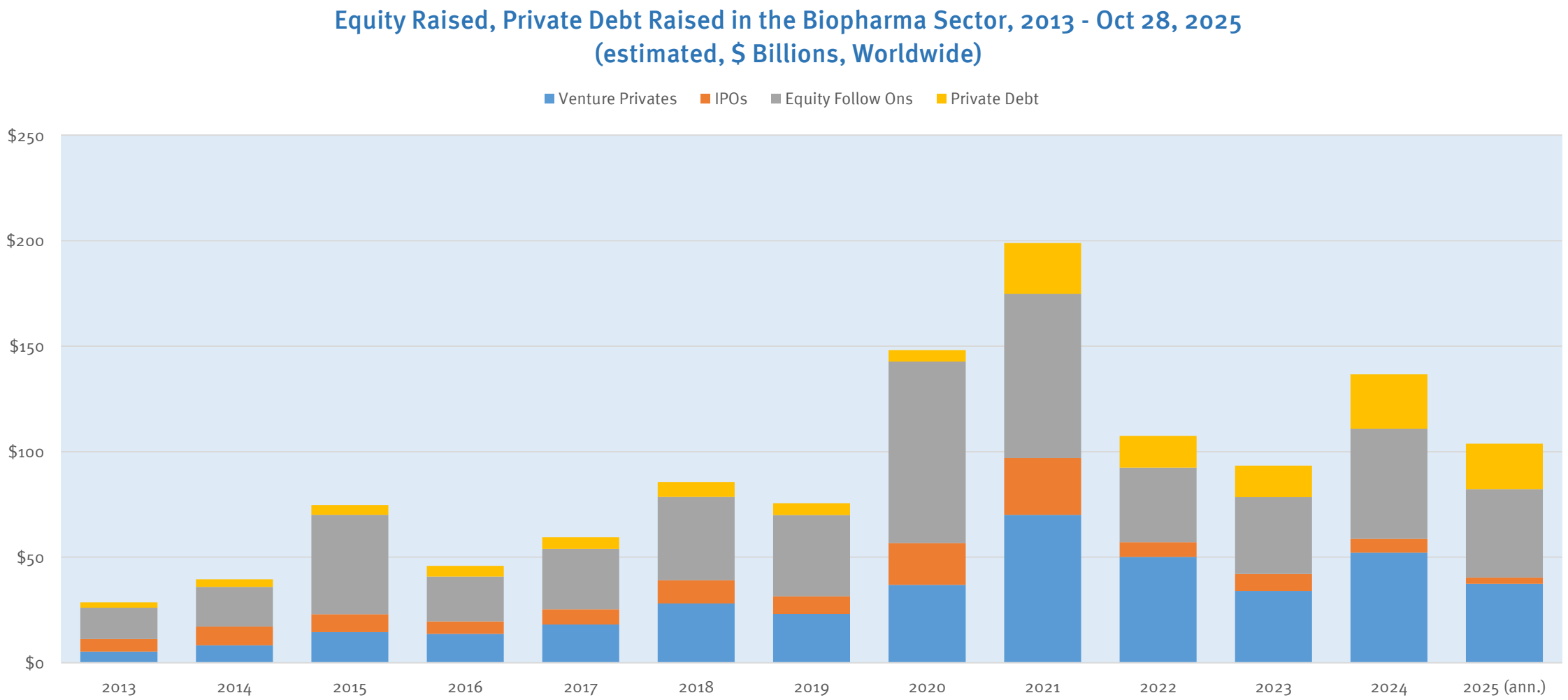
The most valued sectors in biotech today are in RNA, obesity and B-cell immunology. The scale of value changes in the last 21 months are quite notable. It's important to remark that the RNA and obesity pick ups are influenced by takeouts for Avidity and Metsera.



Source: S&P CapitalIQ and Stifel analysis.

Capital Markets Update

Financing Market on Track to Match 2022 Levels

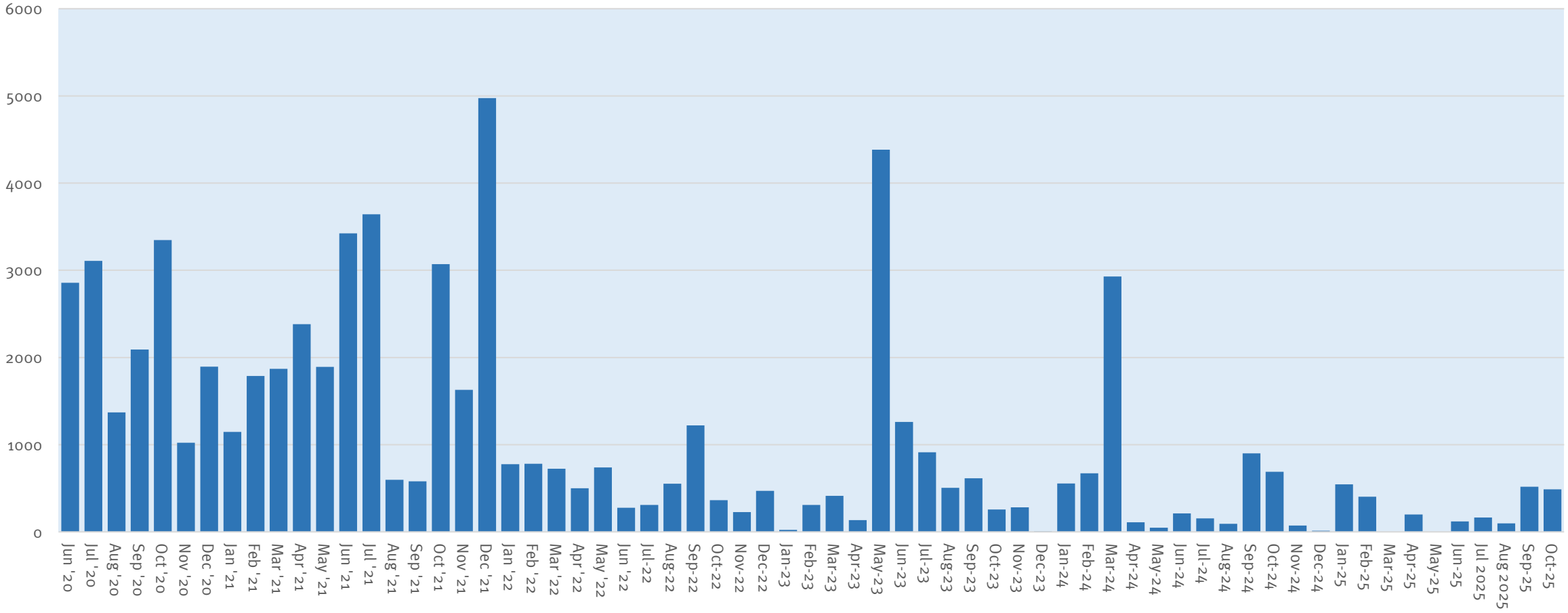


Source: CapitalIQ and Stifel Investment Banking Calculations

IPO Market Remains Fairly Quiet

Last week saw Maplight price its IPO. We expect IPO volume to pick up substantially from here.

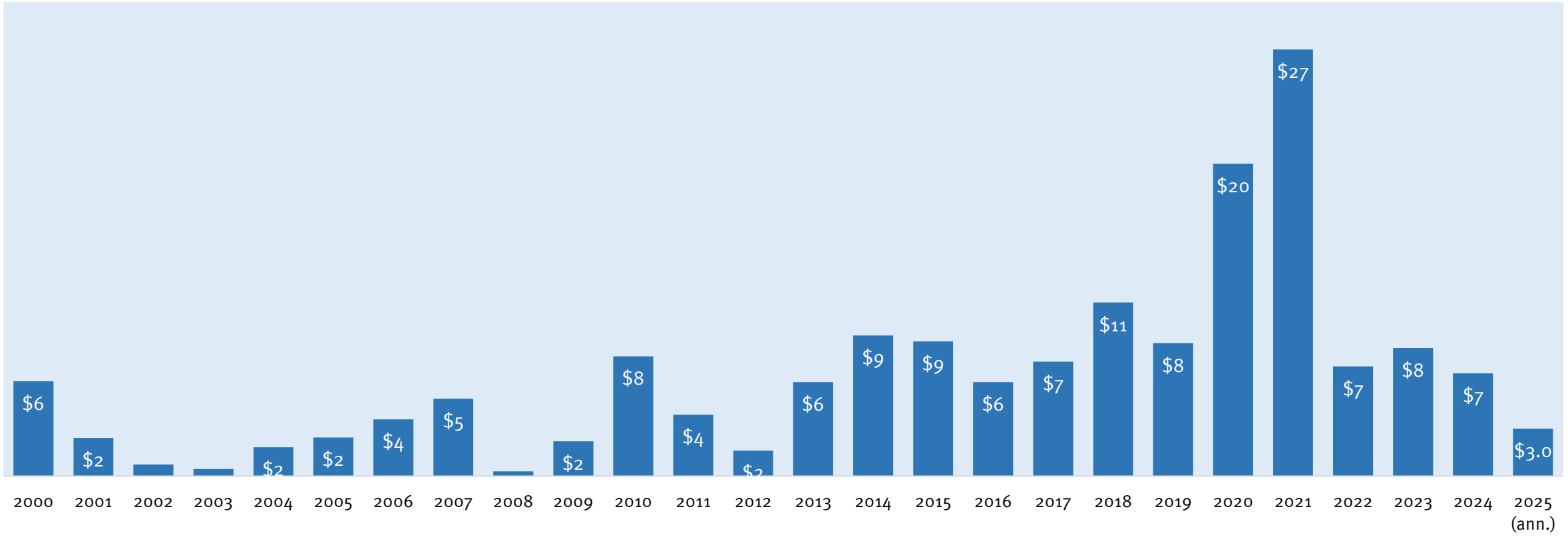
IPO ($volume, $mm), June 2020 to October 2025



Source: Data from CapitalIQ and Stifel investment banking department.

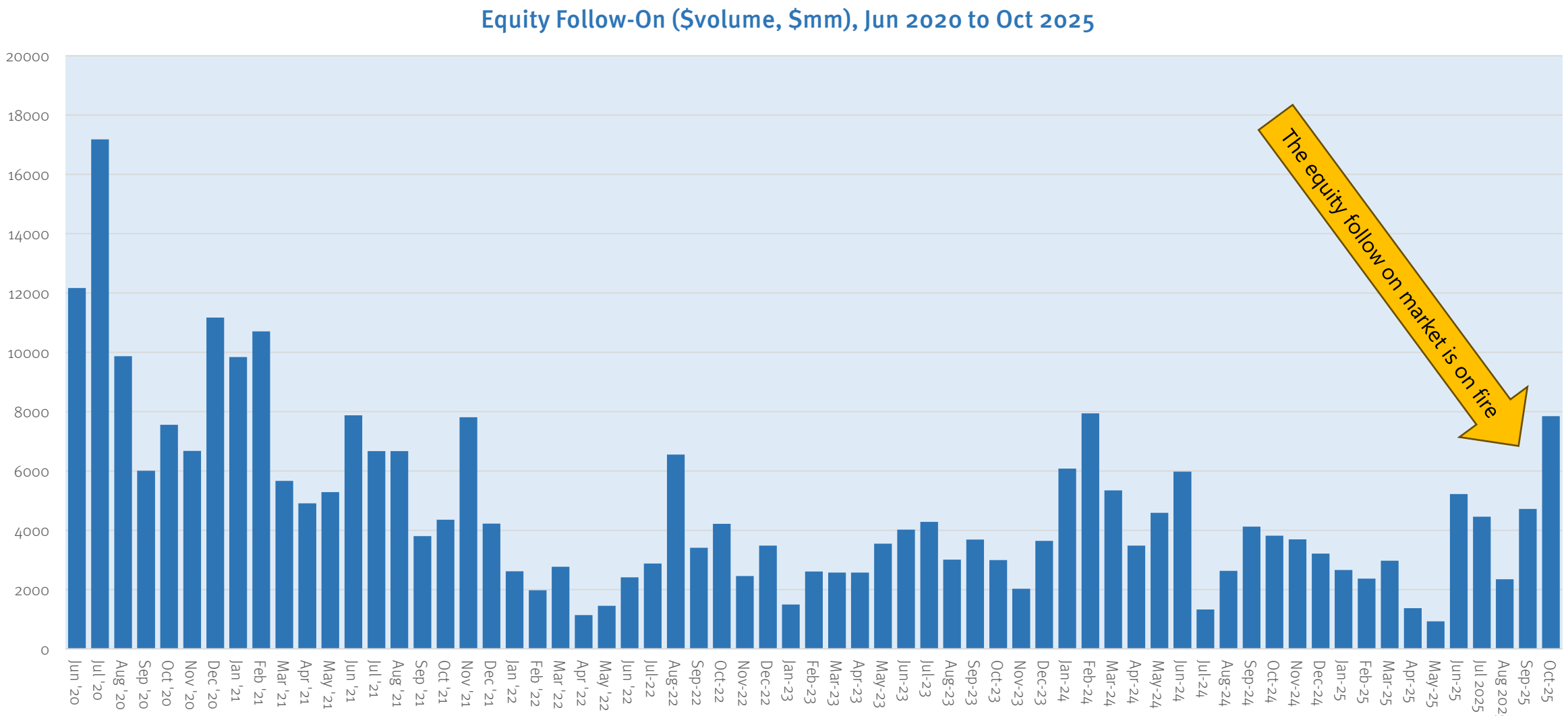
This is Not the Year to Set IPO Volume Records

Global IPO Volume in the Biopharma Sector, Jan 2000 – Oct 2025
($ Billions, Worldwide)



Source: Data from CapitalIQ and Stifel investment banking department.

$8 Billion in Follow-On Volume in October 2025

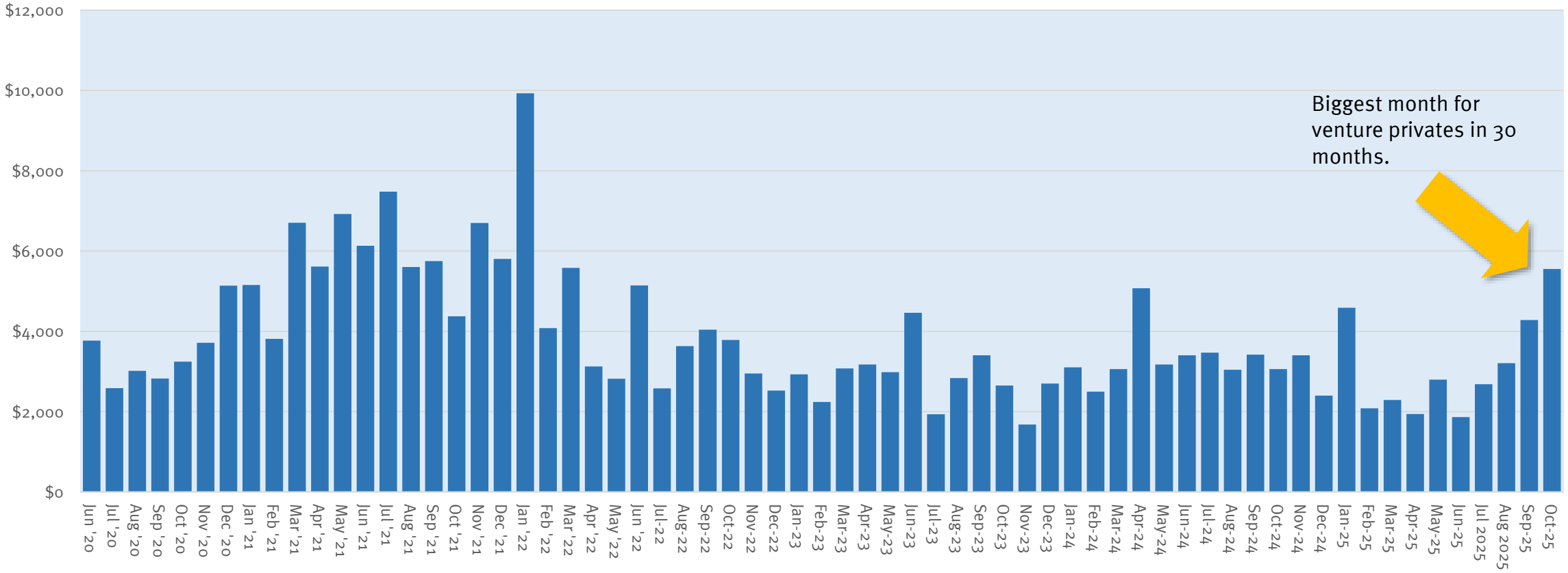


Source: Data from CapitalIQ and Stifel investment banking department..

Venture Privates Market is Picking Up with the Market

Venture equity financings have picked up rather substantially since "Liberation Day". We are not back at Pandemic levels, but the market is quite strong now. The last time we had a month this busy was March 2022 (over three and a half years ago).

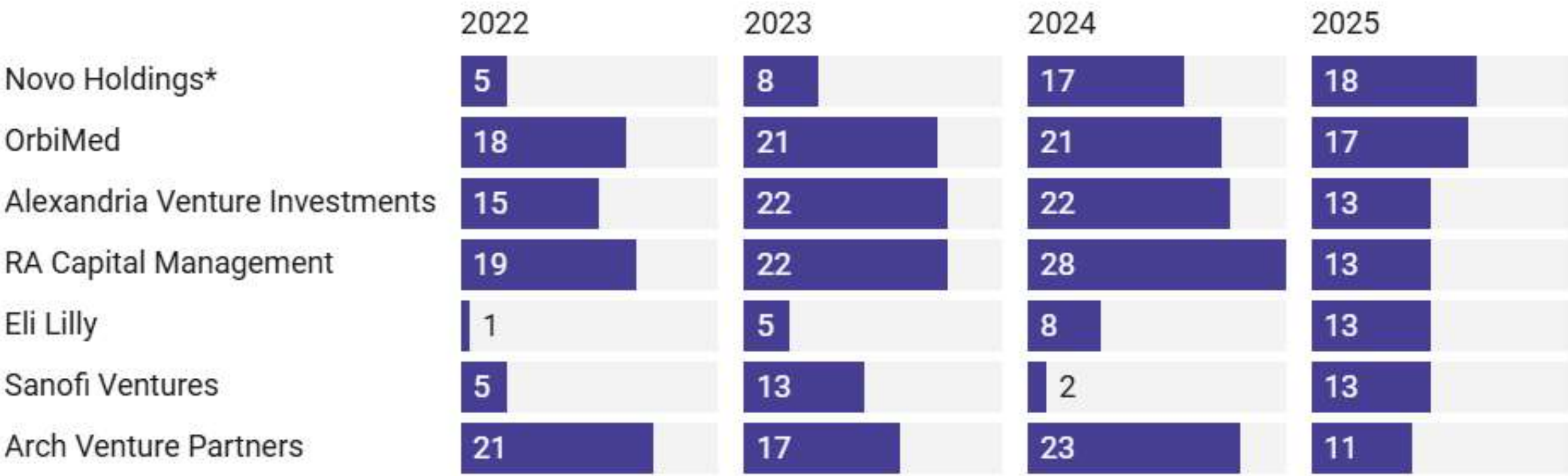
Monthly Private Equity Placement ($volume, $mm), Jun 2020 to Oct 2025



Source: Data from CapitalIQ, Crunchbase.

Corporate venture activity surged in 2025

Number of rounds involving the most active venture firms tracked by BioPharma Dive



** Note: Novo Holdings is the parent company of Novo Nordisk. 2025 numbers as of Oct. 28.*

Chart: Gwendolyn Wu • Source: BioPharma Dive • Get the data • Download image • Created with Datawrapper

Source: https://www.biopharmadive.com/news/corporate-venture-capital-biotech-startup-funding/804015/

European VC Biotech Dealmaking Rebounds to Record Highs

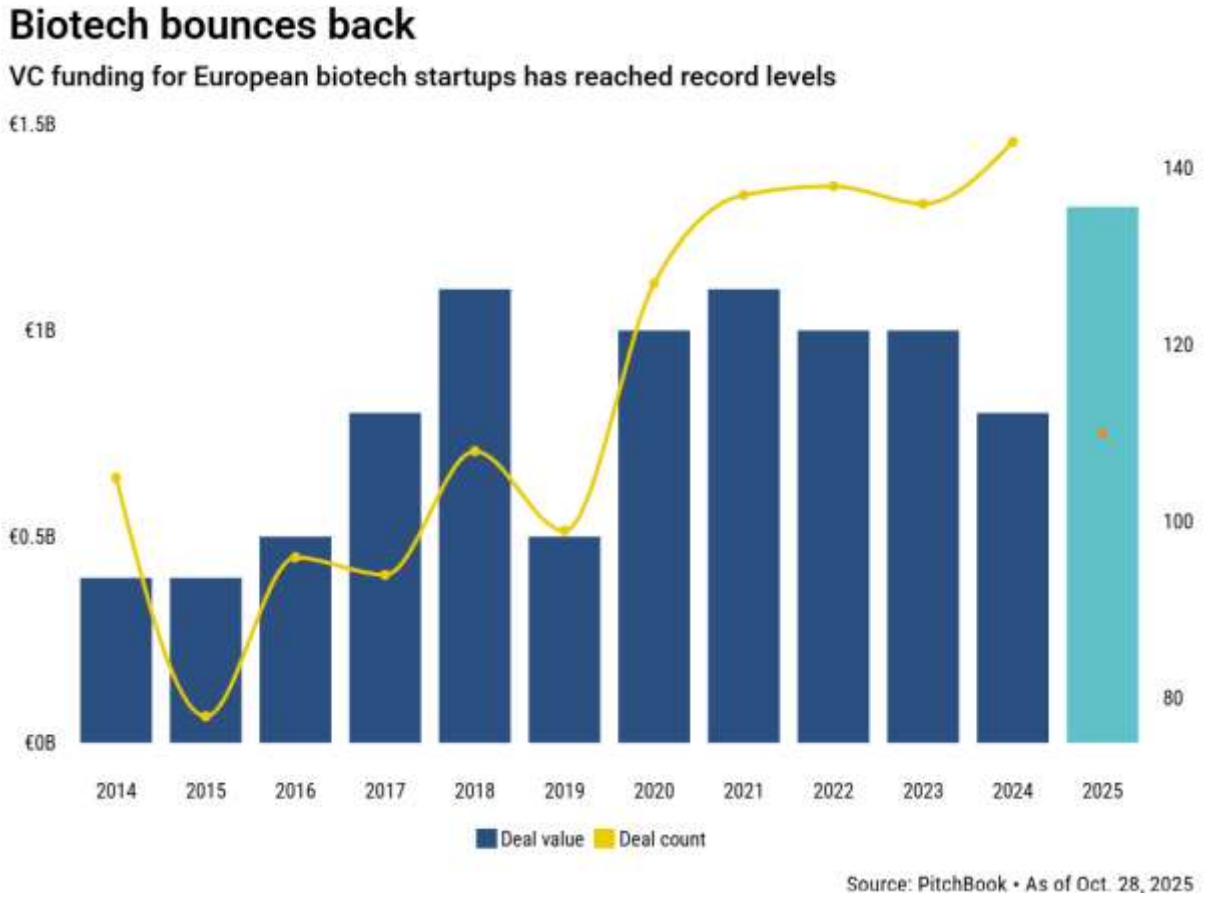
Leah Hodgson, *Pitchbook*, October 31, 2025 (excerpt)

Biotech VC investing in Europe has rallied this year, with deal value already reaching record levels. According to PitchBook data, €1.3 billion (about $1.5 billion) has been invested in the sector, an increase of 62.5% over last year's total and exceeding the previous peak in 2021.

The deal count has slowed somewhat this year, but is still expected to remain within a similar range as 2024's figure, which was at its highest in a decade. VC investment in European biotech surged during the pandemic years, but contracted with the broader market correction in 2022. The downturn reset valuations and deal sizes, setting the stage for a rebound this year. Several outsized deals have closed in 2025. Drug discovery startup Isomorphic Labs' $600 million raise in March is currently the year's largest round, underscoring investor appetite for biotech companies that intersect with AI.

The rapid pace of AI development is encouraging more VCs to explore opportunities in biotech. Fields such as drug discovery are especially attractive because AI can speed up years-long processes, cut costs and shorten the timeframe for bringing products to market. Other notable deals include protein engineering startup GlycoEra's $130 million Series B and cancer-focused CellCentric's $120 million Series C.

Early-stage rounds now account for the largest share of both deal value and count, reflecting investor confidence in the growing pipeline of European life science startups and university spinouts. Positive signals in Europe's biotech exit market may also be boosting investor interest in the sector. Although still below 2021's peak, 2025 has seen an uptick in acquisitions, with eight closing this year compared to six in 2024.



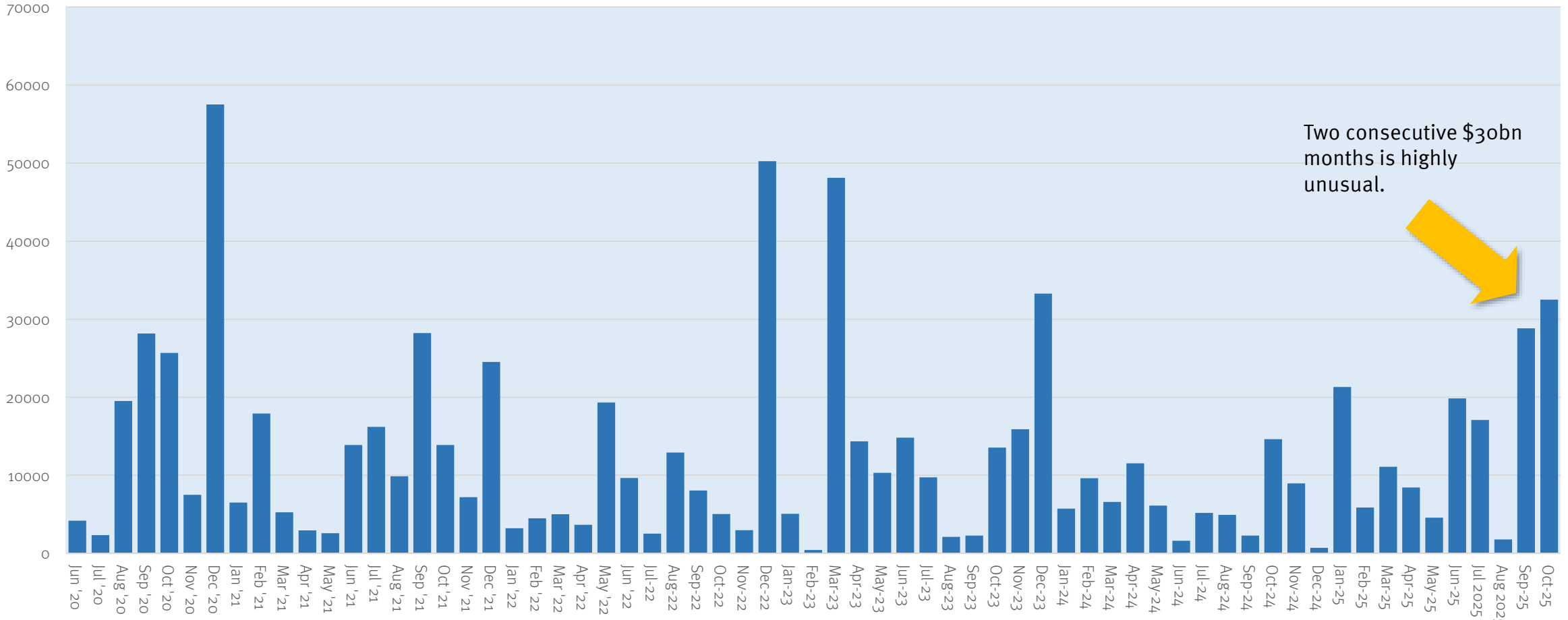
Source: https://pitchbook.com/news/articles/european-vc-biotech-dealmaking-rebounds-to-record-highs

M&A Update

M&A Market Very Strong in the Last Two Months

We are seeing high volume of biotech and spec pharma M&A so far in the second half of 2025. We expect this to continue.

Monthly M&A Activity ($volume, $mm), Jun 1, 2020 to October 2025



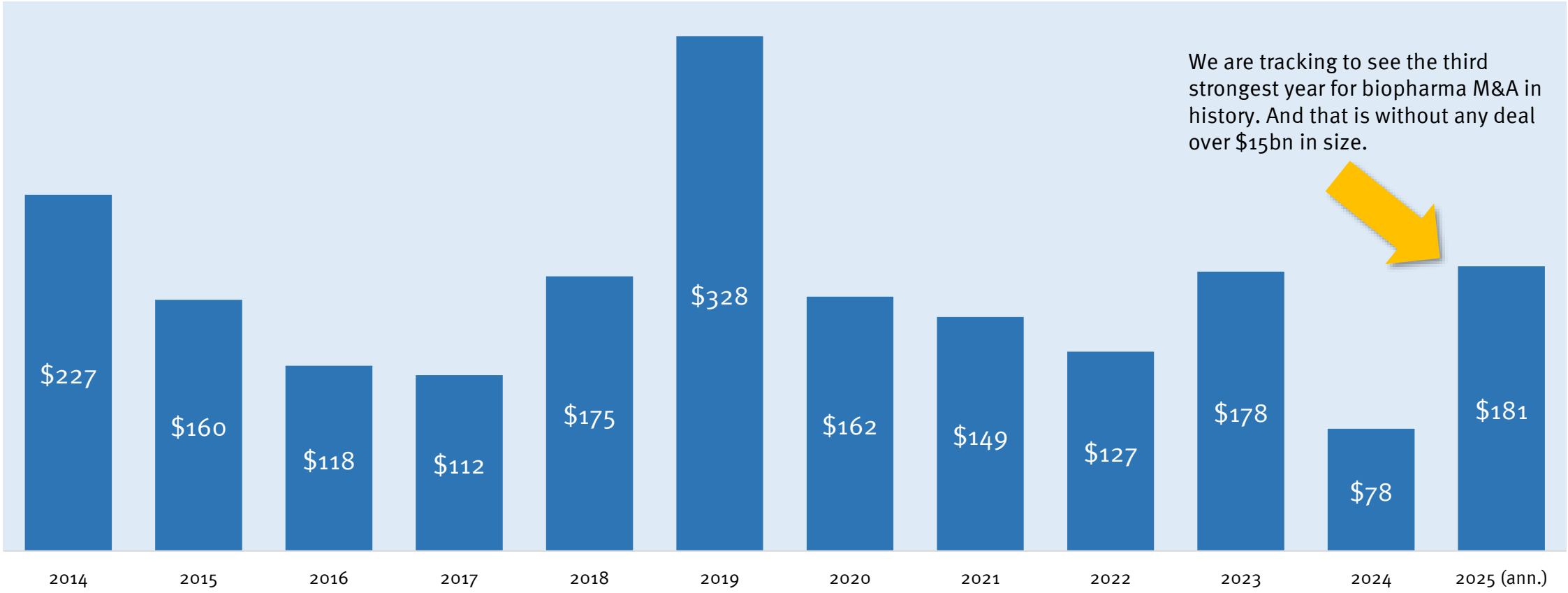
Source: S&P, CapitalIQ. Note: there are two offers on the table for Metsera presently. We counted the largest offer only.

We are Tracking for the Strongest Year in M&A Since 2019

The recent pace of biopharma M&A is very high. If the pace of the last two months continued for a year, it would surpass the all-time record of 2019. What is so remarkable this year is that there have been no deals over $15bn in size. And we are still running at record levels.

M&A Volume in the Biopharma Sector, 2014 - 2025

($ Billions, Worldwide)



Source: S&P, CapitalIQ. Note: there are two offers on the table for Metsera presently. We counted the largest offer only. 2025 data annualized as of Oct 31, 2025.

Novartis' $12B Avidity Deal Shows a Willingness to Take Big Swings in Neuroscience

Michael Gibney, *PharmaVoice*, October 28, 2025 (excerpt)

With the weekend announcement that Novartis would acquire neuroscience RNA biotech Avidity Biosciences for $12 billion, the pharma giant's long-term business development strategy is coming into clearer focus.

Just a few months ago, PharmaVoice sat down with Novartis chief strategy and growth officer Ronny Gal, a former Wall Street analyst, to talk about the direction he and fellow company execs planned to take the Swiss drugmaker.

Ultimately, Novartis wants to become a streamlined innovation machine by leaning into the areas where it can have the biggest impact — and is willing to drop a significant amount of cash to bring in the right candidates, Gal indicated.

And the Avidity deal illustrates Novartis' willingness to spend on assets the company can nurture with its own expertise. So while Novartis paid a more than 45% premium for Avidity based on the biotech's market share, the purchase coincides with the big-picture roadmap Gal drew up at the time.

The large cash infusion from Novartis also shows the value biopharma circles still place on RNA technology, which Avidity uses to treat rare neuromuscular conditions. While mRNA served as the basis of successful COVID-19 vaccines during the pandemic, the genetic breakthrough has recently faced a backlash from regulators and health leaders.

For Novartis, the Avidity deal is still a risk. But that's part of what Gal called Novartis' "secret sauce" — taking a big swing with scientific backing and applying the company's own talent to bring it to fruition... Even as RNA was hitting its stride with several new approvals a few years ago, Avidity was applying its delivery approach in ways no other company was attempting. The company has also explored earlier-stage cardiovascular delivery, resulting in programs that will be spun off into a new company prior to the Novartis acquisition.

Source: https://www.pharmavoice.com/news/novartis-avidity-biosciences-acquisition-rna-12b-pharma-drug/803907/

Novo Makes Bombshell $6.5B Counteroffer to Pfizer's Acquisition of Obesity Biotech Metsera

James Waldron, *FierceBiotech*, October 30, 2025 (excerpt)

Novo Nordisk has thrown a curveball at Pfizer by attempting to outbid the U.S. pharma for obesity biotech Metsera. Until this morning, Pfizer's acquisition of Metsera had appeared done and dusted, with the Big Pharma announcing more than a month ago that the biotech's board had "unanimously approved" the sale of the company for $4.9 billion, with a further $2.4 billion also on the table in relation to certain milestones.

Metsera is advancing a pipeline led by MET-097i, a phase 2b injectable GLP-1 receptor agonist that could support monthly dosing. The biotech's clinical-phase pipeline also features a monthly injectable amylin analog, which could be combined with MET-097i, and an oral GLP-1 that is designed to drive more weight loss than small molecules and avoid the scalability challenges of other oral peptides.

Now, Novo has decided to shake things up by offering Metsera shareholders an equity value of $6.5 billion for the biotech, with another $2.5 billion tied to milestones.

Pfizer came out fighting this morning, branding Novo's offer a "reckless and unprecedented proposal."

"It is an attempt by a company with a dominant market position to suppress competition in violation of law by taking over an emerging American challenger," Pfizer claimed in its own Oct. 30 release.

"The proposal is illusory and cannot qualify as a superior proposal under Pfizer's agreement with Metsera, and Pfizer is prepared to pursue all legal avenues to enforce its rights under its agreement," the U.S. Big Pharma added.

Pfizer claimed that Metsera had previously turned down an offer by Novo and instead opted for Pfizer as its purchaser due to the greater degree of certainty that the U.S. pharma could buy 100% of the biotech's equity.

Source: https://www.fiercebiotech.com/biotech/novo-makes-surprise-65b-counter-offer-pfizers-acquisition-obesity-biotech-metsera

Bruce Booth of Atlas Venture Reflects on Dealmaking

The cliché is true: BD deals are never done until the ink is dry. I've seen too many deals fall apart at literally the 11th hour. 11:59 in fact. Press releases agreed, champagne on ice… only to have a wonderful pharma "partner of choice" change their mind. Getting that phone call is a gut punch. It's so painful, and often hurts the morale of executive teams and damages the cohesion of a Board… the blame game ensues out of the deal wreckage and there are usually casualties. You really can't count your chickens until they're hatched. **The other axiom in BD is that "time kills deals" which is also certainly true. Don't let minor non-critical, non-business issues drag on too long.** Lawyers get paid to redline and "add value" by fighting to win every point during contracting, but it can come at the cost of time. BD fatigue is real and partners can and do walk because of it. If there's an impasse in the deal dialogue (either at term sheet or in contracting), don't let it fester – escalate it quickly to the right senior business principal (often the Head of R&D or BD, or in some cases the CEO) to get it resolved. Don't be shy about doing that. Where needed, leverage your investors' relationships to help – I've made that call to senior Pharma executives countless times to facilitate getting a deal done.

Companies are bought not sold – but with caveats. The gravity of Big Pharma's balance sheets is too big for most emerging biotechs to escape over the long run, which is why M&A is a fairly common exit, at some point, for those firms developing or commercializing high impact new medicines. **But putting a "for sale" sign up in front of an emerging biotech is generally not a great way fetch an attractive acquisition offer.** Instead, planning for the long-term and executing on the business plan is frequently what attracts M&A interest. But, obviously, you can put yourself into the position of being an acquisition target by proactively engaging Pharma around BD discussions. Bankers will frequently acknowledge that 80% of M&A deals start as partnering/licensing discussions, and then flip into M&A through the deal dialogue. If you didn't engage in any BD discussions at all, M&A likely wouldn't happen (especially not for earlier stage companies) – so there is a subtle balance in most deals. Sure, you aren't selling yourself, but you are helping potential buyers appreciate the great things you have going on in your pipeline. Add into the mix a good set of strategic deal advisors and the boundary between getting bought vs getting sold blurs even more.

Source: https://lifescivc.com/

China Update

Notes from Our October “Road Trip” Trip to China

We travelled to China to visit biotechs in the week of October 20th.

Activity off the charts. Four biotech conferences in the same week held at the St Regis Shanghai. Felt like JPM in January in SF but with lots of Chinese food instead. Hello Char Shiu. Goodbye Fisherman’s Wharf. Met tons of familiar faces from large pharma who were in the country.

U.S. venture presence increasingly visible. One prominent US group had sent two scouts to meet as many Chinese good biotechs as possible. Very smart move. A little weakening in the Hong Kong Stock Exchange in the last six weeks. This is accompanied by a huge IPO queue. Over 200 companies trying to go public there all at once. Obviously, not all of them are going to get listed. Chinese government approval required for these IPOs and it’s increasingly hard to get.

We have heard from multiple sources that there is a lot of Chinese retail going into biotech. We think the weakening of HK biotech and simultaneous strengthening of the Nasdaq biotech since Labor Day is, in part, the result of retail capital migration to the U.S. market which has obviously been much less heated up than the Hong Kong market. Feels almost coordinated in some way as if there is a bit of an “invisible hand” directing capital flows.

St. Regis Shanghai

Trip Notes (continued)

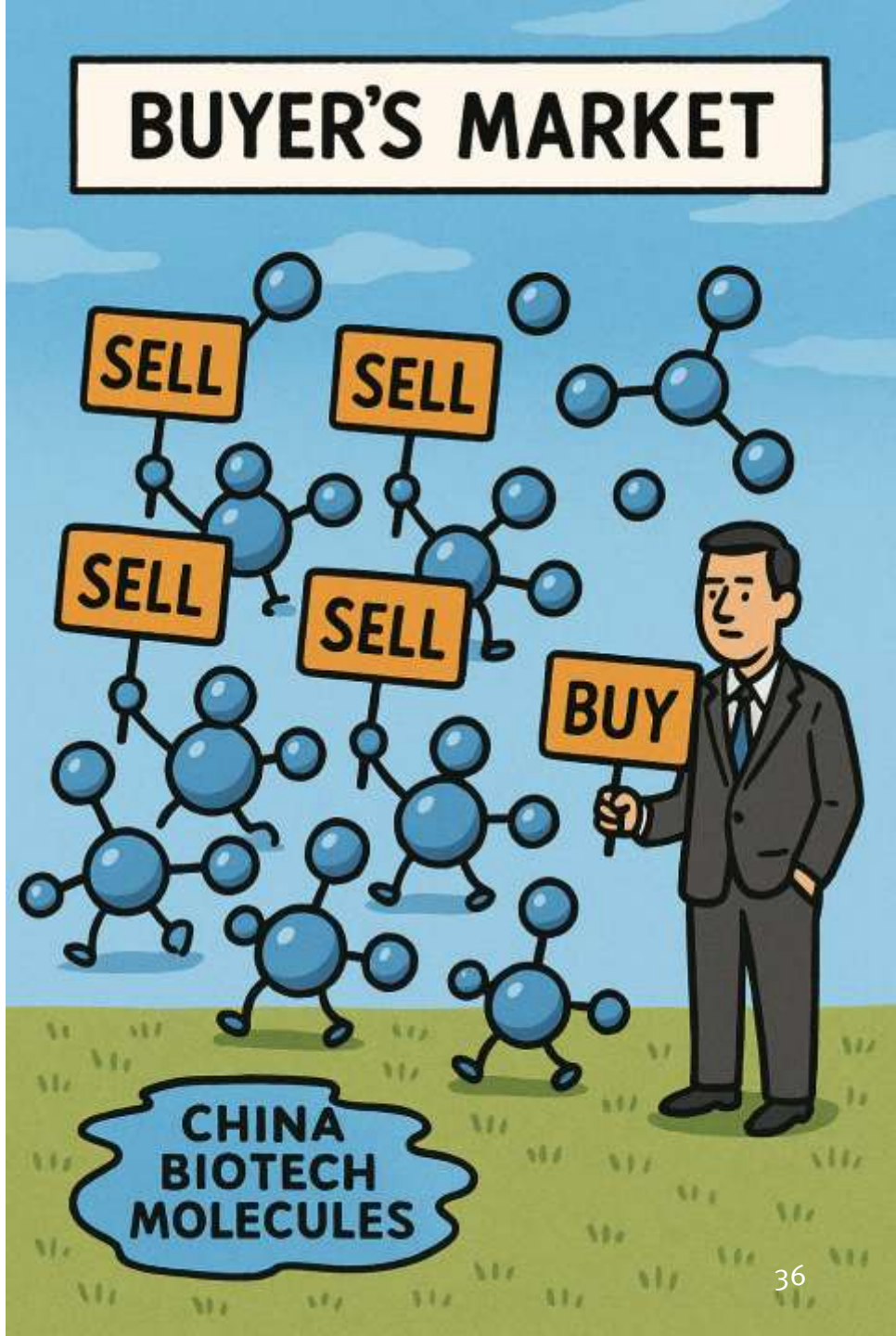
Overall, Chinese biotech pipelines continued to strengthen. Pharma interest remains high although we met quite a few companies that were super keen to license out their molecules. It remains a buyers market given the abundance of product. We continue to see quite a few companies that have first-in-class or highly innovative molecules.

Source of all the money for Chinese biotech becoming more clear. One VC told us that they had received over $300mm from the Hangzhou government. McKinsey presentation (more in a sec) also indicated that more than half of venture dollars sourced from the government.

Interestingly, several of the larger venture groups we met on the trip went to lengths to tell us that they are turning down Chinese government money. It comes with strings attached and these funds want the ability to maximize returns for their LP's.

Quite a few leaders of the Chinese biopharma ecosystem attending the BioCentury-BayHelix conference at the St. Regis last week.

Conversations in the halls were highly informative of developments in the country.



Trip Notes (continued)

There is a broad recognition that China's moment has arrived but that its capital formation system has not kept up with its molecules.

It's well understood that Chinese public market investors tend to chase the speculative buck too much and are not aware enough of the underlying quality of the molecules that they are investing in.

This is one of the main vulnerabilities of China vis-à-vis the U.S.

The U.S. has such an amazingly good specialist investor system that China lacks.

If China catches up here, that would not be good for the U.S.

Chinese investment in RNAi picking up and we saw some very good molecules and efforts.

All of a sudden there are over 100 China in vivo CAR-t players.

So many and so quickly.

We picked up continued awareness of the absolute importance of TCE's in immunology. TCE's continue to be a major theme in China.

Trip Notes (continued)

There is high awareness of crowding in this space but the October 15, 2025 *NEJM* publication on TCE's by Ricardo Grieshaber-Bouyer (and Georg Schett) has stunned many.

In his ten-patient series, individuals with refractory diseases including systemic sclerosis, Sjögren's syndrome, rheumatoid arthritis, and IgG4-related disease received a single course of teclistamab. B-cell depletion lasted a median of five months, and autoantibody levels dropped sharply, with normalization of disease biomarkers such as IgG4 and C-reactive protein. Six patients achieved drug-free remission lasting up to fifteen months, while others showed marked improvement in pulmonary and systemic manifestations. Cytokine-release syndrome occurred frequently but was mild, and no neurotoxicity was observed.

The publication bodes well for Candid in the U.S. which has licensed Epimab's Chinese BCMA TCE.

TCE's were very much on the agenda at the Prostate Cancer Foundation scientific meetings last week with one prominent speaker emphasizing the dual role of TCE's: attracting T-cells to the site of interest and *activating* the cells. The speaker argued that the stoichiometry of TCEs is very important for the latter function.

BCMA T-Cell Engager Therapy in Patients with Refractory Autoimmune Disease

TO THE EDITOR: T-cell engagers redirect T-cell cytotoxicity for precision cell depletion and are emerging as a promising therapeutic method in autoimmune diseases.[1-4] Teclistamab, a bispecific antibody approved for multiple myeloma,[5] binds to CD3 on T cells and to B-cell maturation antigen (BCMA) on B cells and plasma cells. Here, we report on the safety and efficacy of teclistamab in 10 patients with six different refractory autoimmune diseases, with up to 15 months of follow-up.

The patients — all of whom had active, multidrug-resistant autoimmune diseases with characteristic serologic profiles — received teclistamab therapy under compassionate use (Table 1). The median age of the patients was 55 years (range, 24 to 66); 60% of the patients were women. Five-month follow-up has been reported previously[3] for Patients 1 through 4; these patients are included in this report with 10 to 15 months of follow-up.[3] All the patients had a history of treatment failure with more than three immunomodulatory drugs (Table S1 in the Supplementary Appendix, available with the full text of this letter at NEJM.org). Notably, nine patients had received previous B-cell depletion with rituximab.

Teclistamab was administered as standard step-up dosing during a 5-day period in an inpatient setting (at a dose of 0.06 mg per kilogram of body weight on day 1, 0.3 mg per kilogram on day 3, and 1.5 mg per kilogram on day 5). The initial administration of teclistamab was followed by a one-time maintenance dose of 1.5 mg per kilogram after 4 weeks, as described previously[3] (see the Supplementary Appendix). Two weeks before the initiation of teclistamab, glucocorticoids were tapered to less than 5 mg per day, and all other immunosuppressive medication was stopped.

Teclistamab induced rapid B-cell depletion, with a median B-cell aplasia of 157 days (Fig. S1A in the Supplementary Appendix). Free kappa and lambda light chains dropped below detection limits in all the patients (Fig. S1E and S1C), which indicated successful depletion of the plasma-cell compartment, and serum immunoglobulin levels substantially decreased (Fig. S1D, S1E, and S1F).

Cytokine release syndrome occurred in 8 patients (grade 1 in 4 patients and grade 2 in 4 patients) within 2 days after induction therapy and resolved with a single dose of tocilizumab. No grade 3 or 4 cytokine release syndrome and no neurotoxicity occurred. Mild upper respiratory tract infections were common (in 8 of 10 patients) (Table 1). Patient 1 received inpatient hydration to treat viral gastroenteritis. Two bacterial infections warranted antibiotic therapy (*Clostridium difficile* infection in Patient 7 and urinary tract infection in Patient 3). Hypogammaglobulinemia developed in all 10 patients, with a median onset of 4 weeks after induction therapy; all cases were treated with a median of two immune globulin infusions.

Levels of disease-specific autoantibodies decreased, and seroconversion was observed for multiple antibodies, including Scl-75, Scl-100, RF, SS-A, PM75, Mi2a, and Mi2 (Fig. S2). In Patients 9 and 10 who had IgG4-related disease, levels of IgG4 and C-reactive protein (markers of humoral inflammation) normalized (Fig. S2), a change that was accompanied by a substantial improvement in constitutional symptoms.

Clinical responses were observed in all but 1 patient (Patient 8) (Fig. S3A). Among the 5 patients with interstitial lung disease for whom longitudinal data on pulmonary diffusion capacity were available, symptoms abated and diffusion capacity improved in 4 patients, whereas both measures worsened in 1 patient, with an overall average change from a median carbon monoxide transfer coefficient of 45% to 53% (Fig. S3A). In the patient with Graves disease, magnetic resonance imaging showed reduced exophthalmos and muscle thickness (Fig. S3B). In Patient 9, who had IgG4-related disease, FAPI-PET-CT (fibroblast activation protein inhibitor–positron-emission tomography–computed tomography) showed reduced stromal-cell activation in the tissue (Fig. S3C). At the latest follow-up, 6 of 7 patients who were evaluated were not taking glucocorticoids, and 8 of 10 patients were not taking immunosuppressants (Table S1).

After a single treatment course, 6 patients were in drug-free remission, with a median recorded response of 11 months (range, 8 to 15); 3 patients had progression after a median of 5 months (Fig. S3D). In 2 patients, teclistamab was administered again, which was followed by a second response. The median duration of response across all patients was 10 months (range, 4 to 15), without concomitant glucocorticoid and immunomodulatory therapy.

Teclistamab appeared to show durable efficacy as rescue therapy across six different refractory autoimmune diseases. The incidence of cytokine release syndrome was common but mild and manageable with tocilizumab. Hypogamma-

Trip Notes (continued)

Several impressive groups working to put together hub-and-spoke models for China. A recognition that there are so many good molecules that one could prosecute more of them using this model than by doing newco after newco.

A growing sense in hallway that developments in China may be more worrying for large pharma than U.S. biotech.

Chinese ability to develop molecules at low cost and lightning speed profoundly threatening to large pharma business models which tend to optimize development rather than satisfice. Multiple large pharmas spending over $10bn a year on R&D with relatively low molecule output. Seems at variance with what's possible. Very nice McKinsey presentation highlights this threat by spelling out just how much more efficient China ecosystem is (reproducing a few of their slides in a bit).

Also, a very nice presentation by Simone Fishburn of *BioCentury* who showed how agile Chinese biotechs are in responding to changing tastes of large pharma.

She also showed that the majority of outbound Chinese licensing deals done to biotech rather than pharma.

Quite interesting.

Chinese Biotech Industry Shows no Signs of Slowing as Threat of U.S. Restrictions Loom

Brian Yang, *Stat+*, October 27, 2025 (excerpt)

As the U.S. government moves to guard against an increasingly competitive Chinese biotech industry, Chinese drugmakers are striking major deals with their global counterparts — including some in the U.S.

Last week, Innovent Biologics announced a deal with the Japanese pharmaceutical giant Takeda that will provide it $1.2 billion up front — including a $100 million equity investment — and more than $10 billion in potential "milestone" payments for rights to a pair of cancer medications. Under the agreement, the biggest deal yet for Chinese-developed antibodies, the two will jointly develop and commercialize one of the drugs in the U.S.

Earlier this month, Zenas Biopharma, a U.S. biotech company developing therapies for autoimmune diseases, announced it would license three drugs from China's InnoCare, which will receive up-front and "near-term" milestone payments of up to $100 million, along with far larger long-term potential revenue if the programs advance.

The agreements follow a string of others between Chinese drugmakers and their international counterparts. They have been dominated by licensing deals for bispecific antibodies and antibody-drug conjugates, next-generation cancer treatments aimed at targeting tumors more precisely while reducing side effects. But they also come as a rivalry heats up between Chinese and U.S. companies, and their respective governments. The Trump administration has made a priority of trying to onshore American drug manufacturing and cast the country's pharmaceutical supply chain as a national security issue.

It has also engaged in some saber-rattling toward China. The New York Times reported last month that the administration was considering a draft executive order that could restrict the flow of Chinese experimental treatments in various ways. But doing so, including by imposing heavier scrutiny on U.S. licensing deals with Chinese companies, would potentially block innovative treatments from reaching American patients.

Some experts think that is a step the administration won't take. "It is hard to see a scenario where the U.S. government would deny its citizens access to a best-in-class drug, for lung cancer for example, made in China," Franck Le Deu, a former senior partner at global consultancy McKinsey & Company, said in an interview. He has spent over two decades advising pharma and biotech clients in Shanghai and Hong Kong.

Source: https://www.statnews.com/2025/10/27/china-biotech-drugmakers-partnerships/

China's Biotech Deal-Making Matures Beyond Licensing to Navigate 'Crazy' Valuations and Global Headwinds

Zhang Yushuo, *Yicai*, October 30, 2025 (excerpt)

China's biotech industry is fast evolving from a "product export" market to a "value export" powerhouse, reshaping cross-border deal-making, valuation models, and long-term global strategies, according to industry leaders gathering for the International Biopharma Industry Week and 12th BioCentury-BayHelix China Healthcare Summit in Shanghai.

For years, licensing products out was the standard for Chinese biotech companies seeking global validation and cash. It was an essential, efficient, direct one-time deal that could quickly improve cash flow, Gao Lu, vice president for business development at Shanghai Medicilon, told Yicai in an interview on Oct. 26.

Licensing remains a dominant model. The value of the licensing-out deals signed by Chinese biotech firms in the first half of the year reached USD66 billion, surpassing last year's total of USD51.9 billion, according to industry data.

However, the so-called NewCo model, where Chinese biotech firms establish new entities to manage and develop their assets overseas, often backed by foreign venture capital, is becoming increasingly popular.

The NewCo model is an evolution from product export to value export that allows companies to share their assets' long-term value through equity stakes while retaining greater research and development control, Gao explained. For example, Medicilon's partner Hengrui Pharma has secured over USD14 billion in deals with global giants over its novel drugs as of August.

Multinational corporations are paying close attention to the development of NewCos.

These new investor-led entities can be seen as both competition and complementation, Deepa Talapade, SVP and head of business development and licensing for oncology and radiology at German pharmaceutical giant Bayer, told Yicai during the BioCentury BayHelix China Healthcare Summit that ended on Oct. 24.

The first NewCos that were established mostly focused on mature, late-stage products with abundant clinical proof of concept and relatively low risks, James Li, venture partner at Frazier Life Sciences and former chief executive officer of JW Therapeutics, said in a recent podcast.

Source: https://www.yicaiglobal.com/news/chinese-biotech-firms-expand-beyond-licensing-toward-newco-model-experts-say

Yicai Story (continued)

But as these mature products were quickly secured by either direct licensing deals or VC-backed NewCos, more and more NewCos began evolving toward early-stage products in Phase I clinical trials or even in the pre-investigational new drug stage, Li noted.

The emergence of the NewCo model has increased market competition, thus making it more complex and more expensive for overseas companies to acquire Chinese assets. However, this also has some positives, as direct overseas funding can provide NewCos with more cash for clinical trials, which can help multinationals obtain clinically positive data, Talapade explained.

The industry has become very crowded, as every multinational now boasts large teams tasked with hunting for Chinese assets, Li said, adding that they are not only competing with each other but also with foreign VC-backed NewCos.

New High-Valuation Standard

Biotech deals over Chinese assets have become more and more expensive, and a debate about whether prices are excessive has inevitably arisen. "The deal prices in the last six months have gone crazy," Talapade said.

The problem is that investors are going to benchmark to these high-priced deals, and some of the smaller biotech firms might get hurt because they will ask for too much, she explained. If the deals fall apart because multinationals do not agree to the high prices, startups may not have enough funds to continue developing the assets on their own.

On the other hand, if the multinationals agree to the high prices, they would be facing high risks. In fact, while the startups would secure hefty upfront payments, multinationals would be the only ones bearing the risks of clinical trials if they miss the high expectations.

Gao was asked if she believes these valuations are too high, as some think they are actually fair or even 'bargains.' She said that these opposite views are actually an inevitable phenomenon that the market experiences when seeking a balance.

The exorbitant prices are nothing more than a fundamental shift in the market, as early-stage innovative assets with global first-in-class or best-in-class potential are now valued the same as mature products before, Gao noted.

"Valuations, high or low, are determined by the global clinical value and commercialization potential of the innovative asset," she explained.

Source: https://www.yicaiglobal.com/news/chinese-biotech-firms-expand-beyond-licensing-toward-newco-model-experts-say

The Relentless Rise of China's Biotechs

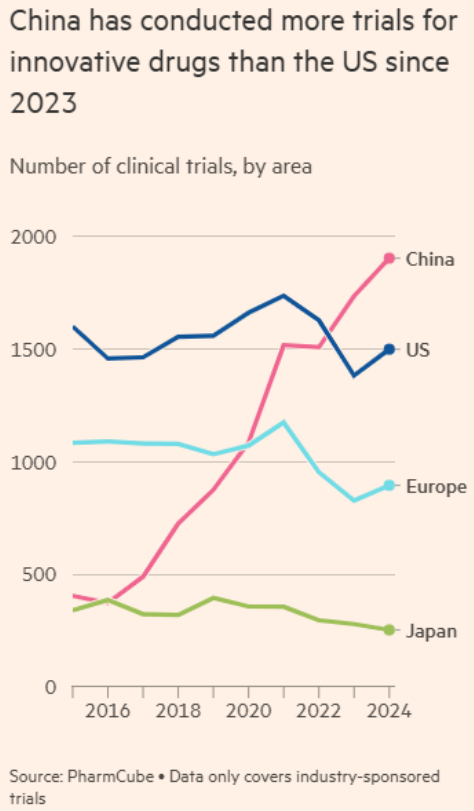
Eleanor Olcott, Haohsiang Ko and William Sandlund, *Financial Times*, October 27, 2025 (excerpt)

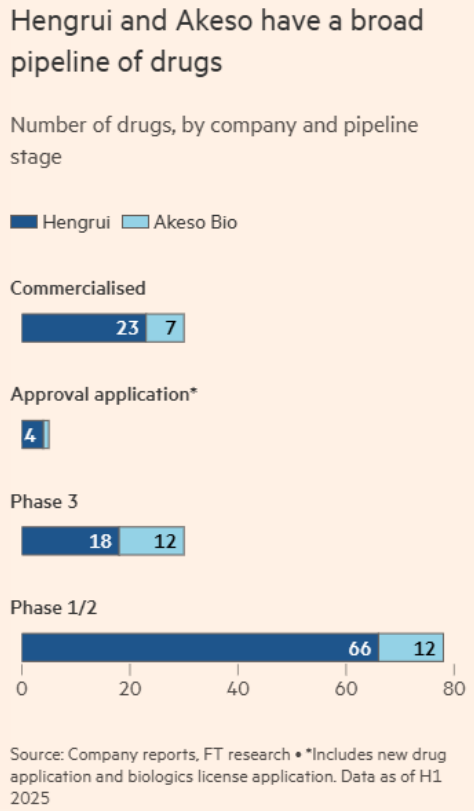
Chinese drugmakers have struck a record number of deals this year to sell their assets overseas, sending biotech stocks surging as investors bet the country will become a driving force in global drug discovery.

There have been 93 overseas licensing deals in the first eight months of 2025, worth a combined $85bn, according to Chinese data provider PharmCube — with domestic companies selling the international rights to homegrown drugs. The total value of deals is on track to hit its sixth consecutive annual record, underscoring the speed at which the country's pharmaceutical sector is internationalising.

Meanwhile, the rapid growth of clinical trials and drugs in early-stage development from companies, including Jiangsu Hengrui and Akeso, indicates that the trend of Chinese biotechs selling their drugs to global pharmaceutical companies is set to continue — a stark reversal from a decade ago. "Ten years ago, China didn't have a biotech sector to speak of. For the most part, the companies were developing generic drugs. Fast forward to today, and every big pharma is doing most of their shopping in China for novel therapies," said Brad Loncar, an expert on Chinese biotech.

Beijing introduced reforms in the mid-2010s that made it easier for biotech companies to raise capital and pursue innovation. These changes, coupled with the relative speed and low cost of doing drug development and clinical trials, have turbocharged the industry's growth. Hong Kong's Hang Seng biotech index has surged more than 80 per cent this year on growing investor excitement.





Source: https://www.ft.com/content/c0a1b15b-84ee-4549-85eb-ed3341112ce5

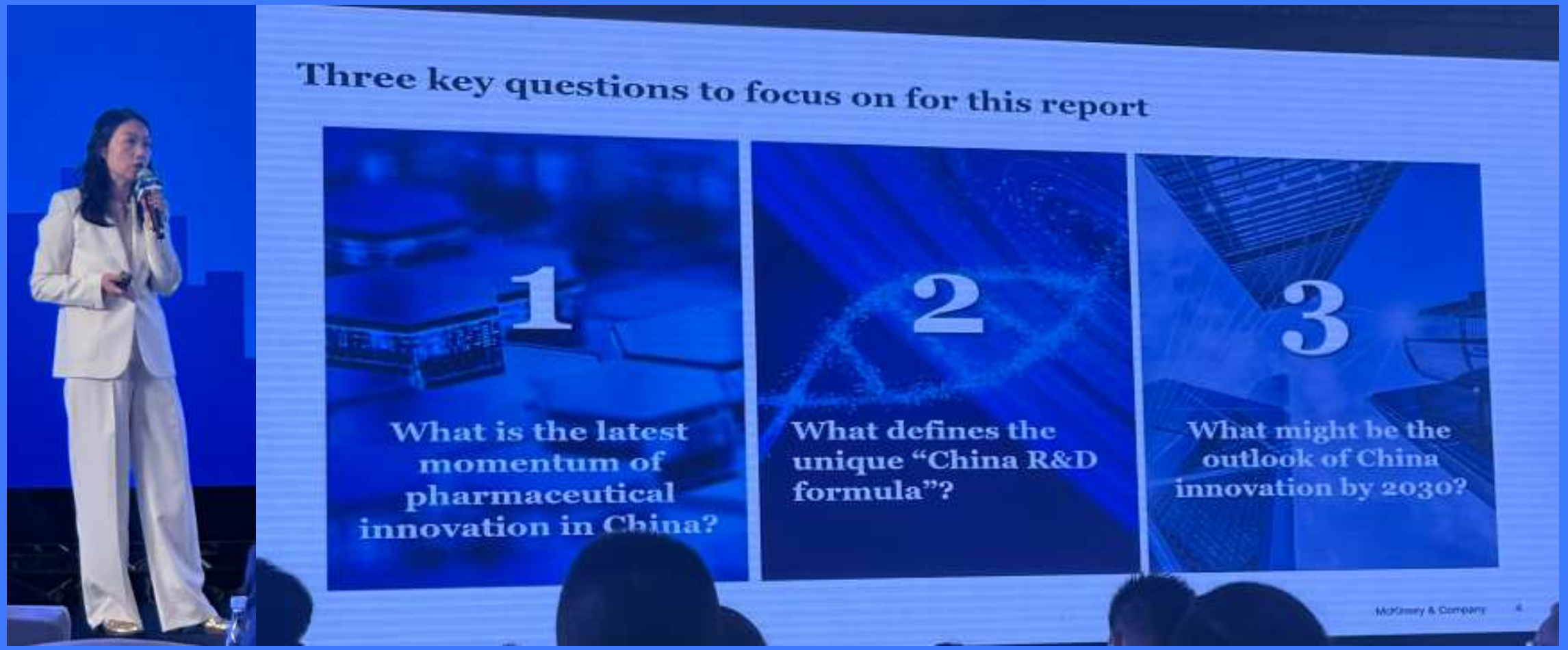
Asia Society Paper on "Healthy China" Initiative

Lizzi Lee, Chang Liu and Jing Qian, *Asia Society*, October 29, 2025 (excerpt)

- "Health" has moved to the center of China's governance agenda and, increasingly, to the core of Asia-Pacific regional cooperation. This paper argues that Healthy China 2030 is more than a public health initiative. It is a flagship political project designed to address the twin pressures of demographic aging and chronic disease while positioning China as an emerging, resilient global leader in innovative development. In alignment with China's other long-term blueprints, including the Five-Year Plans and the Made in China 2025 industrial strategy, Healthy China 2030 promotes the state's capacity for resilience and sustainable economic development.
- Domestically, China's health reforms remain hampered by weak primary care, bureaucratic fragmentation, and misaligned incentives, placing its demographic transition under ever-increasing pressure. This is a global challenge faced by other Asia-Pacific Economic Cooperation (APEC) economies and most countries across the world. In China, the urgency is even greater.
- To address these significant challenges, Beijing is simultaneously pushing at the frontiers of biotech innovation, regulatory reform, the return of scientific talent, and advances in artificial intelligence (AI). These initiatives have transformed China into a credible and leading force in novel therapies, generating cost-effective products with huge potential benefits for the international community, society, and global health markets. However, this progress is still somewhat limited by the risks of fragile financing, rigid institutions, and geopolitical uncertainty.
- The wider region stands to benefit from a framework that both strengthens collective health security and accelerates regulatory and technological convergence. By pooling data, expertise, and financing through APEC mechanisms, member economies can scale best practices in preventive care, aging policy, and biotechnology, reducing duplication and closing capacity gaps between developed and developing economies. In turn, this can foster a more resilient and inclusive regional health ecosystem — one that aligns economic integration with human well-being.
- For the world, it opens a rare domain of intersection, where U.S.-China collaboration and U.S.-China–led multilateral cooperation can advance with fewer political frictions and yield substantial shared gains in economics, science, and public health.
- A cooperative APEC agenda on health innovation and governance provides a model for tackling transnational challenges as a whole: even amid strategic competition, joint stewardship of human welfare remains not only possible but also mutually beneficial.

Source: https://asiasociety.org/policy-institute/healthy-china-2030-apec-opportunities-health-first-domestic-reform-biotech-innovation-and

McKinsey Presentation at BioCentury Oct 2025



Source: McKinsey Analysis, BioCentury-BayHelix China Conference, Oct 24, 2025

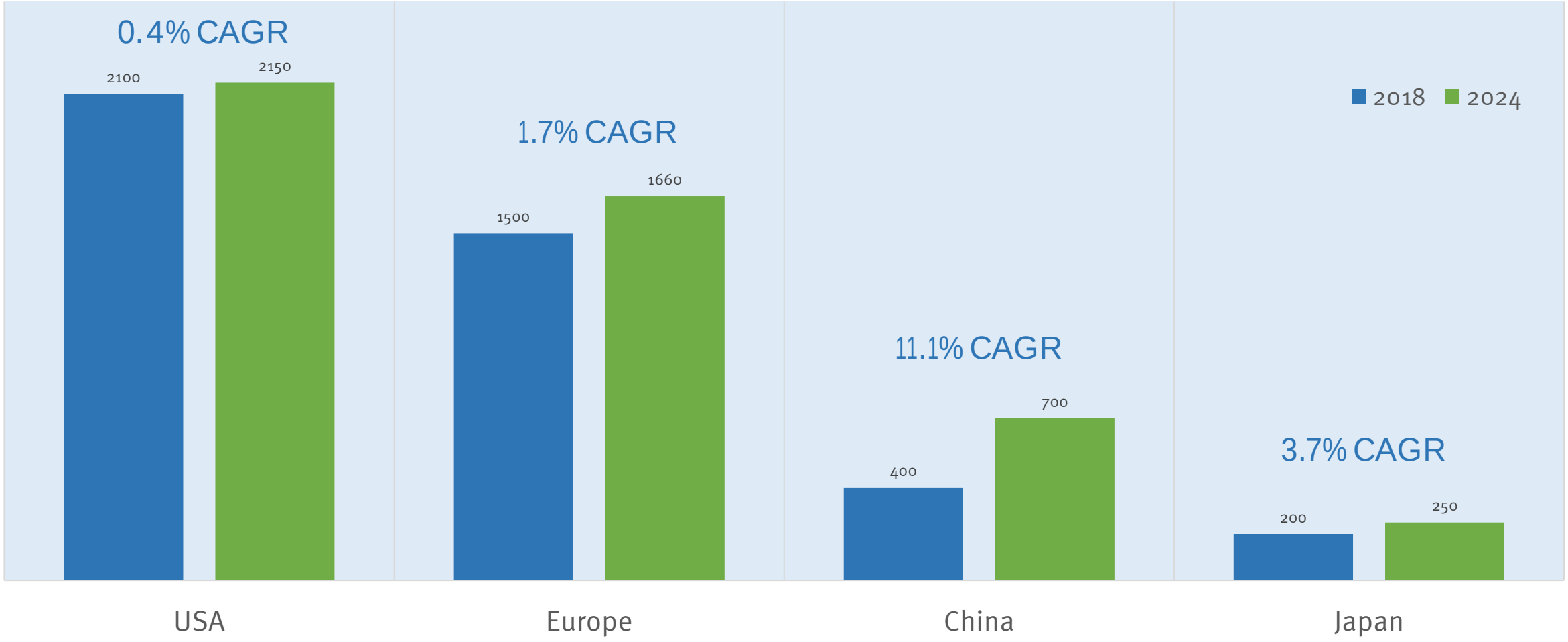
Capital: Funding Sources for China Biotech Diversifying

		Out-licensing	NewCo	M&A	IPO	VC Investment
2025 YTD	# of deals	47	13	5	9	43
	Total amount USD Bn	81	13.9	1.3	1.1	0.9
	Upfront amount USD Bn / Total	3	0.4			
2024	# of deals	42	8	6	4	82
	Total amount USD Bn	40	9	4.4	0.3	1.7
	Upfront amount USD Bn / Total	4	0.3			

Source: McKinsey Analysis, Biocentury China Conference, Oct 24, 2025

China BioScience Activity Up Tremendously

Count of Biomedical Research Papers in Cell, Nature and Science Journals by Author's Country Affiliations, 2018 to 2024



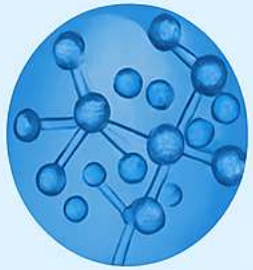
Source: McKinsey Analysis, Biocentury China Conference, Oct 24, 2025

China Innovators' Speed and Efficiencies Driven by Three Factors

China speed & efficiency	Discovery	Clinical development
Speed	**2–3x faster** from target nomination to IND submission	**2–5x** faster in patient enrolment
Efficiency	**⅓ to ½ of costs** vs. global best practices*	**<50%** per patient cost of USA/EU

Underlying drivers

Strong macro environment



Scaled end-to-end local ecosystem & infrastructure

Delivery focused ways of working

Source: McKinsey Analysis, Biocentury China Conference, Oct 24, 2025

Discovery: Delivery Focused Ways of Working

Focused fast-to-signal approach

- Leaner data package: focus on critical path
- Parallel processing for early signal
- Iterative exploration and experimentation rather than optimize and develop

Delivery-focused decision making and culture

- Involution: fierce competition among locals, speed of delivery key to survival esp. for fast-following assets
- Agile decision-making
- Execution intensity: flexible scheduling and extended working hours, hands-on senior leaders

What we hear from industry leaders

We first focus on most critical experiments to test core hypotheses; at each step we ask ourselves which experiments are on the critical path.
— *Leading Biotech CEO*

We've built in-house animal testing capabilities and frontload multi-model testing of several compounds for rapid signal, which gives us a competitive advantage.
— *Leading Chinese investor*

CEO needs to role model hands-on execution such as frequent trouble shooting with CROs including on weekends sometimes, to secure high-quality output, in our case, 2–3× faster at half of the cost.
— *Leading Biotech CEO*

Source: McKinsey Analysis, Biocentury China Conference, Oct 24, 2025

McKinsey Views of China Biopharma

McKinsey & Company

MNC / Big Pharma Engagement

- Top-20 multinational pharmas now source ~40% of new deals from Chinese firms.
- Share of Chinese-origin assets in large (› $50 M upfront) deals rising sharply.
- Half of these assets involve next-generation modalities, especially bispecifics and cell/gene therapy.

Clinical Development at Scale

- Enrollment 2–5× faster across therapeutic areas, esp. oncology and immunology.
- Supported by ›1,500 clinical sites, many Phase-I capable, with integrated biomarker testing.
- Large treatment-naïve patient pools concentrated in major hospitals.

Government initiatives promote 'Full-Value Chain for Innovation'

- Fast-track 30-day clinical review pathway.
- Frameworks for tech transfer and translational research.
- 10 B+ RMB funds (e.g., Shanghai) supporting early-stage development. Beijing offering 20 B+ RMB to foster a range of technologies (including biotech)

China Biopharma to Play on the Global Stage

- There are four archetypes of Chinese biopharmas: Fast follower, new combinations, optimized validated targets, novel biology.
- We expect that China biopharma will drive 10–15% of global launches across modalities by 2030.
- Momentum tempered by geopolitical and financing dynamics but structurally robust.

Source: McKinsey Analysis, Biocentury China Conference, Oct 24, 2025

IQVIA Institute: Eight $2bn+ China Deals Through July

Exhibit 8: M&A and Alliance/Collaboration/Licensing Deals Valued >$2Bn involving China headquartered companies YTD July 2025

COMPANIES	VALUE $BN	THERAPY AREAS	DESCRIPTION
GSK + Jiangsu Hengrui	12.5	Multiple	GSK and Hengrui Pharma to develop up to 12 medicines, including HRS-9821, across respiratory, immunology, inflammation and oncology worldwide excluding mainland China, Hong Kong, Macau and Taiwan
Pfizer + *3SBio*	6.2	Oncology	Pfizer to develop and commercialize 3SBio's SSGJ-707 against cancers worldwide, excluding China with an option
Astrazeneca + CSPC Pharmaceutical Group	5.3	Immunology	Astrazeneca and CSPC Pharmaceuticals Group to discover and develop preclinical candidates for immunological diseases worldwide
Astrazeneca + *Harbour Biomed*	4.7	Oncology	Harbour and Astrazeneca to develop antibodies for immunology and oncology worldwide, with an option for two preclinical immunology programs
Vor Biopharma + *Remegen*	4.2	Immunology	Vor Bio to develop and commercialize Remegen's telitacicept against generalized myasthenia gravis, systemic lupus erythematosus and rheumatoid arthritis worldwide excluding Greater China
Verdiva Bio + *Hangzhou Sciwind Biosciences*	2.5	Metabolic/Obesity	Verdiva Bio agreed license and collaboration agreement with Hangzhou Sciwind Biosciences for global development and commercialization of a portfolio of metabolic diseases therapies in territories outside of Greater China and South Korea
Regeneron + Hansoh	2	Metabolic/Obesity	Regeneron to develop and commercialize Hansoh's HS-20094 against obesity worldwide excluding China, Hong Kong, and Macao
Novo Nordisk + *The United Bio-Technology (Hengqin) Co*	2	Metabolic/Obesity	Novo Nordisk to develop and commercialize United Bio-Technology's UBT-251 against obesity, type 2 diabetes and other diseases worldwide excluding Chinese mainland, Hong Kong, Macau, and Taiwan

Source: BioWorld, Jul 2025, IQVIA Pharma Deals, Jul 2025.

EBP companies in *italics*.

Source: https://www.iqvia.com/insights/the-iqvia-institute/reports-and-publications/reports/expanding-options-for-emerging-biopharma-in-the-us-a-decade-of-change

Industry Update

Trump's Pharma Agreements Signal a Shift Toward Direct-To-Consumer Pricing

Rita Numerof, *Forbes*, Nov 1, 2025 (excerpt)

President Trump's recent agreements with Pfizer and AstraZeneca have drawn attention for lowering drug costs and incentivizing domestic manufacturing. Equally important, they make direct-to-consumer purchasing a national priority, an evolution that could reset industry incentives.

Direct-to-consumer pricing isn't new, but its integration into federal policy is. If implemented thoughtfully, it could lower costs by advancing transparency, streamlining distribution and strengthening accountability across the pharmaceutical supply chain.

As I wrote in a recent column, the administration's negotiations with Pfizer and AstraZeneca signal that the president and his team are pushing for a structural reset in pharma, and willing to apply pressure to get it. Both agreements exchange tariff relief for lower prices and greater U.S. investment, and the launch of TrumpRx.gov signals that direct-to-consumer purchasing is now central to the drug affordability agenda.

This development builds on earlier private-sector efforts, like Eli Lilly's decision to sell its obesity drug Zepbound directly to patients at a steep discount, the topic of a recent column of mine. While the concept isn't new, the scale and legitimacy will be. When the federal government creates an infrastructure for DTC purchasing, it gives the model permanence, and potentially, broad consumer adoption.

The DTC approach also aligns with the administration's broader strategy: using negotiation and leverage to correct imbalances without imposing formal price controls. By linking affordability to domestic production and transparency, it reframes how pharmaceutical value is defined—through measurable benefit rather than intermediated pricing.

For decades, the drug-pricing ecosystem has rewarded opacity. Pharmacy benefit managers and other intermediaries operate between manufacturer and patient, profiting from rebates negotiated off inflated list prices. These rebates often obscure real costs, leaving employers, taxpayers and patients in the dark about who benefits from discounts that were meant to lower prices.

Source: https://www.forbes.com/sites/ritanumerof/2025/11/01/trumps-pharma-agreements-signal-a-shift-toward-direct-to-consumer-pricing/

FDA Reconsidering Comparative Efficacy Study Requirement for Biosimilars

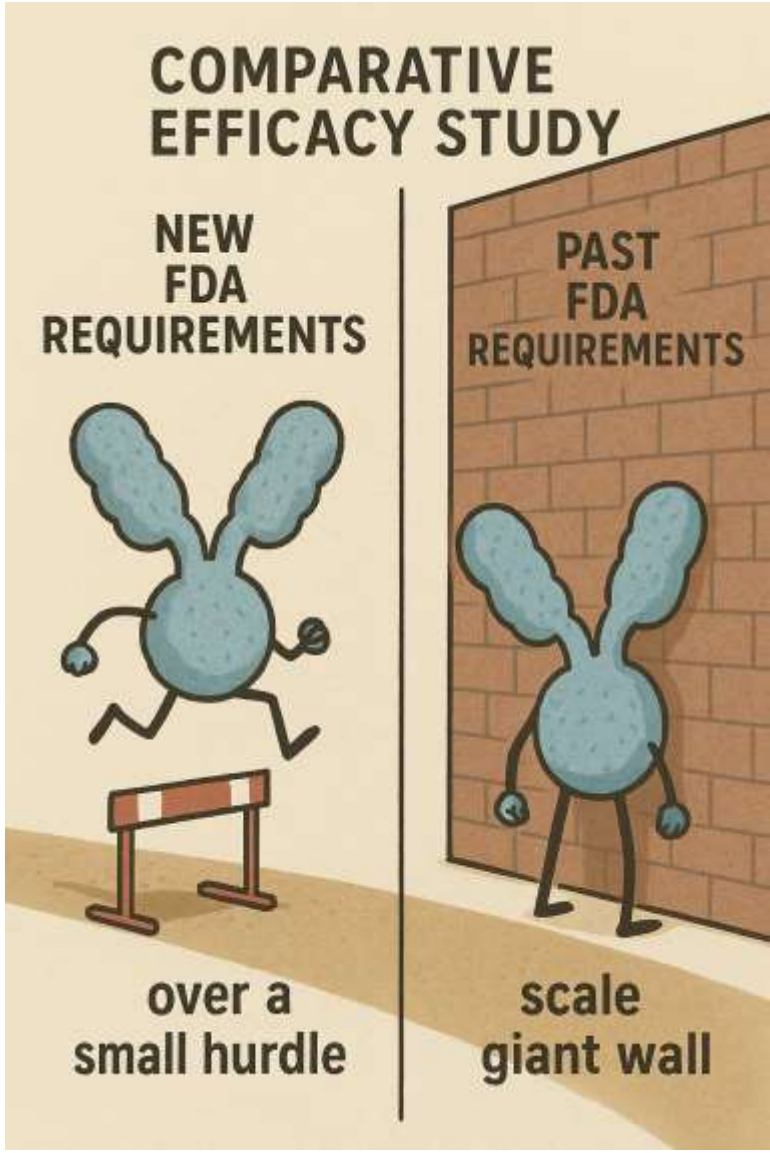
Zachary Brennan, *Endpoints News*, Oct 29, 2025 (excerpt)

The FDA on Wednesday published new draft guidance outlining how biosimilar developers can cut out Phase 3 comparative efficacy studies, potentially reducing development timelines and cutting costs.

The move, first disclosed by FDA Commissioner Marty Makary at an Association for Accessible Medicines conference in Maryland on Wednesday morning, follows years of work by regulators across multiple countries to bring down the barriers to market entry for biosimilars.

The four-page draft guidance says that the agency's thinking around comparative efficacy studies for biosimilars "has evolved, and FDA has gained significant experience in evaluating data from comparative analytical and clinical studies used to support a demonstration of biosimilarity."A streamlined approach can be used when the biologic and proposed biosimilar are made from clonal cell lines, when the quality attributes are understood for the reference biologic, and when pharmacokinetic studies are feasible and clinically relevant, the draft says.

An ICH meeting next month will also discuss formalizing this policy across more countries, which has been in the works since at least 2023.The guidance and Makary's remarks follow similar comments Tuesday from the agency's biosimilar lead Sarah Yim, who noted the FDA is pushing toward making the biosimilar development process more similar to generic drugs.



Source: https://endpoints.news/fda-to-reduce-regulatory-red-tape-for-biosimilars/

New CBO Report Confirms 340B's Ballooning Costs. Congress Must Act

Dan Crippen (former CBO director), *Healthcare Dive*, Nov 1, 2025

In its first report on the 340B drug discount program's effect on the budget, the Congressional Budget Office revealed that a previously obscure federal program originally meant to help a few dozen safety-net hospitals has exploded into a multibillion-dollar subsidy for thousands of nonprofit hospitals, driving up healthcare costs for patients — burdening taxpayers and contributing to the federal deficit — while delivering little measurable benefit to patients in need.

The [340b] program allows qualifying hospitals and clinics to buy prescription drugs at steep discounts that manufacturers are required, by law, to provide. The idea was simple: Hospitals would use the savings to expand care to indigent patients. But in practice, the program has evolved into something very different — and far more costly. Today, 340B discounted drugs can be sold to any out-patient (including commercially insured) for any price.

Recent CBO analysis shows that **340B spending rose from $6.6 billion in 2010 to nearly $70 billion in 2023.** During that same time, brand-name drug spending across the rest of the market grew at just 4% per year. So what's driving the surge? CBO identifies several culprits.

First, the report points to hospital consolidation. Between 2013 and 2021, the number of off-site outpatient clinics enrolled in 340B grew from about 6,100 to nearly 28,000. These "child sites" let hospital systems pull in more prescriptions under the program — even when those sites serve commercially insured patients in higher-income neighborhoods.

Second, contract pharmacies — retail drugstores that dispense 340B medicines — are fueling the furious pace of growth. CBO found that 340B purchases made at contract pharmacies grew at an average of 34% per year from 2010 to 2021 to over 30,000 pharmacies — nearly 60% of all eligible pharmacies. The problem is the savings from these drugs don't reach many patients, who still pay their full copay at the counter, while hospitals capture the discount as profit.

Third, and most importantly, the program's incentives are upside down. Because hospitals can pocket the difference between the discounted 340B price and the insurer's reimbursement, they're financially rewarded for prescribing higher-priced drugs. CBO puts it bluntly: These incentives "lead to higher prices or an increased use of drugs and other health care services" — and that translates to higher federal spending across Medicare, Medicaid, and private plans while costing taxpayers billions.

Source: https://www.healthcaredive.com/news/new-cbo-report-340b-ballooning-costs-congress-must-act-dan-crippen-cbo/804109/

AbbVie Lifts Profit Outlook as Sales Rise

AbbVie Press Release, Oct 31, 2025

NORTH CHICAGO, Ill., Oct. 31, 2025 /PRNewswire/ -- AbbVie (NYSE:ABBV) announced financial results for the third quarter ended September 30, 2025.

"AbbVie continues to deliver outstanding results, with significant momentum across key areas of our portfolio. We are also making great progress advancing our pipeline and investing in innovation to support AbbVie's long-term growth," said Robert A. Michael, chairman and chief executive officer, AbbVie. "Based upon the strength of our business and its promising outlook, we are once again raising our quarterly cash dividend.“

Worldwide net revenues were $15.776 billion, an increase of 9.1 percent on a reported basis, or 8.4 percent on an operational basis.

- Global net revenues from the immunology portfolio were $7.885 billion, an increase of 11.9 percent on a reported basis, or 11.2 percent on an operational basis.
- Global Skyrizi net revenues were $4.708 billion, an increase of 46.8 percent on a reported basis, or 46.0 percent on an operational basis.
- Global Rinvoq net revenues were $2.184 billion, an increase of 35.3 percent on a reported basis, or 34.1 percent on an operational basis.
- Global Humira net revenues were $993 million, a decrease of 55.4 percent on a reported basis, or 55.7 percent on an operational basis.

- Global net revenues from the neuroscience portfolio were $2.841 billion, an increase of 20.2 percent on a reported basis, or 19.6 percent on an operational basis.
- Global Vraylar net revenues were $934 million, an increase of 6.7 percent.
- Global Botox Therapeutic net revenues were $985 million, an increase of 16.1 percent on a reported basis, or 15.8 percent on an operational basis.

Source: https://www.prnewswire.com/news-releases/abbvie-reports-third-quarter-2025-financial-results-302600511.html

Eli Lilly Blows Past Estimates, Hikes Guidance as Zepbound and Mounjaro Sales Soar

Annika Kim Constantio, CNBC, Oct 30, 2025 (excerpt)

Eli Lilly on Thursday reported third-quarter earnings and revenue that topped estimates and hiked its full-year outlook, as the company continued to see strong demand for its blockbuster weight loss drug Zepbound and diabetes treatment Mounjaro.

Shares of the company closed more than 3% higher Thursday.

The pharmaceutical giant now expects its fiscal 2025 revenue to come in between $63 billion and $63.5 billion, up from previous guidance of $60 to $62 billion. Eli Lilly also expects full-year adjusted profit to come in between $23 and $23.70 per share, rising from its previous outlook of $21.75 to $23 a share.

Eli Lilly said the guidance reflects President Donald Trump's existing tariffs as of Thursday, but does not include his threatened levies on pharmaceuticals imported into the U.S.

Mounjaro raked in $6.52 billion in revenue for the quarter, up 109% from the same period a year ago. That blew past the $5.51 billion that analysts were expecting, according to StreetAccount.

Zepbound, which entered the market roughly two years ago, posted $3.59 billion in revenue for the third quarter. That's up 184% from the year-earlier period and slightly ahead of the $3.5 billion that Wall Street was expecting, according to StreetAccount estimates.

Source: https://www.cnbc.com/2025/10/30/eli-lilly-lly-earnings-q3-2025.html

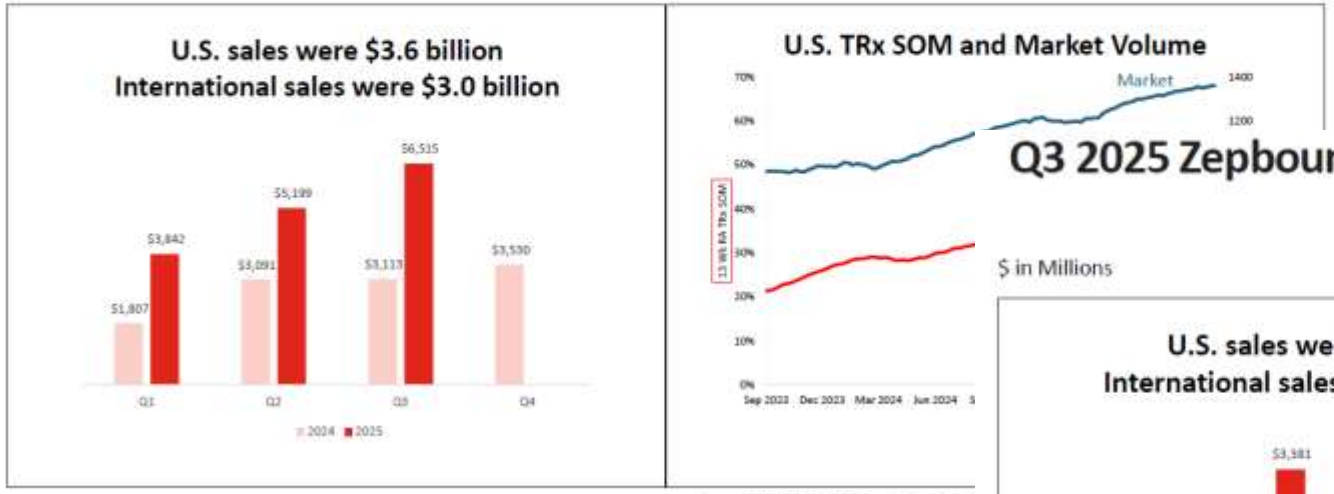
Lilly Sold $10.2 Billion of Tirzepatide in a Quarter

About 30% of this was sold outside the U.S.

This is on track to be the biggest sustained selling drug in history with a $40bn+ run rate.

Q3 2025 Mounjaro Sales Increased $3.4B

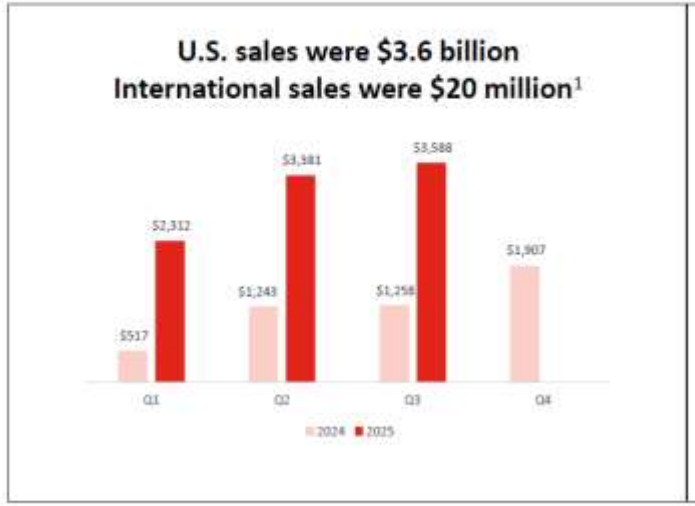
$ in Millions



Source: IQVIA NPA TRx 3MMA, weekly data Septer
TRx data is representative of the injectable incretin

Q3 2025 Zepbound Sales Increased $2.3B

$ in Millions



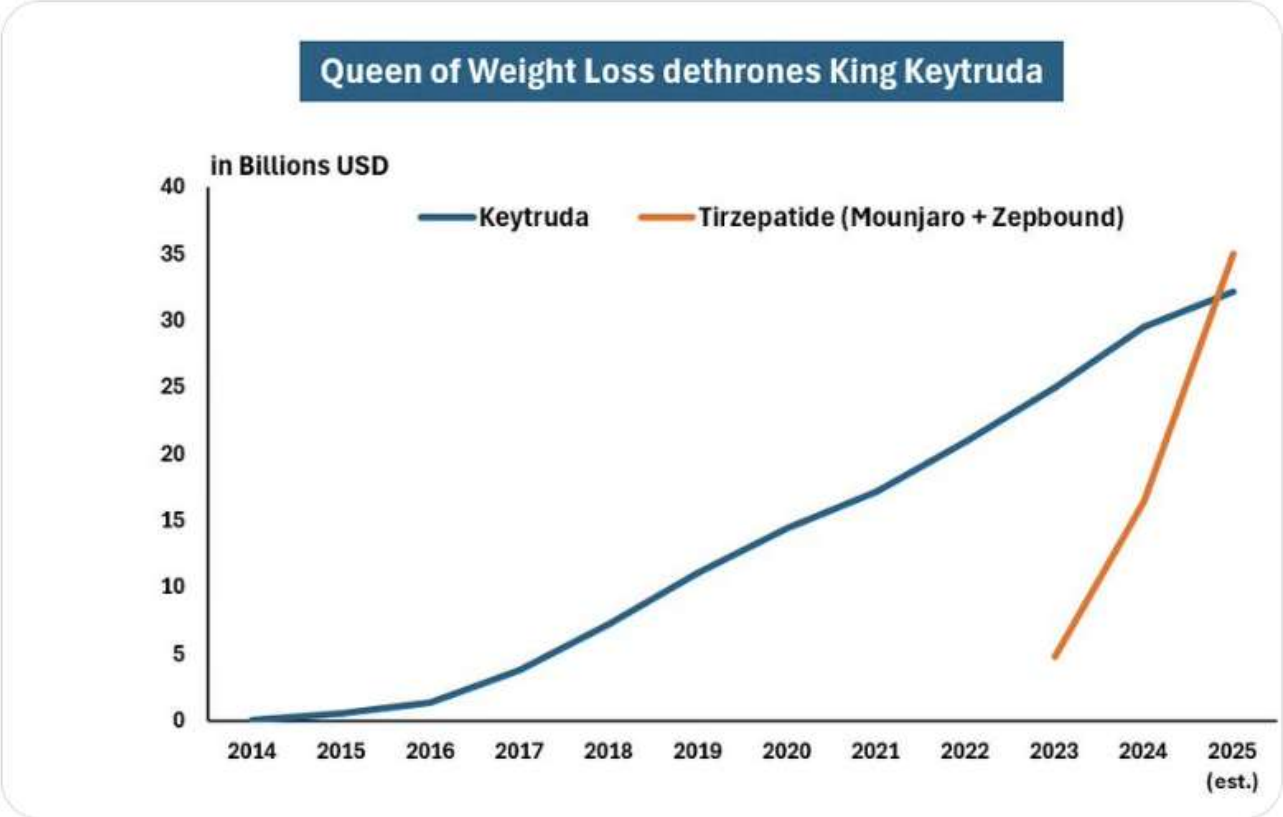
[1] Japan and Canada marketing authorization approved for obesity under the brand name Zepbound

Source: IQVIA NPA TRx 3MMA, weekly data September 26, 2025, RA = rolling average
TRx data is representative of the branded anti-obesity market

Source: https://investor.lilly.com/financial-information/quarterly-results

Paras Sharma @paras_biotech · 18h

In just 3 yrs, Eli Lilly's tirzepatide overtakes Merck's Keytruda — $35 B vs $31.8 B est in 2025. The fastest-growing drug ever. From oncology to obesity, the pharma crown shifts to GLP-1s.



Yowza!

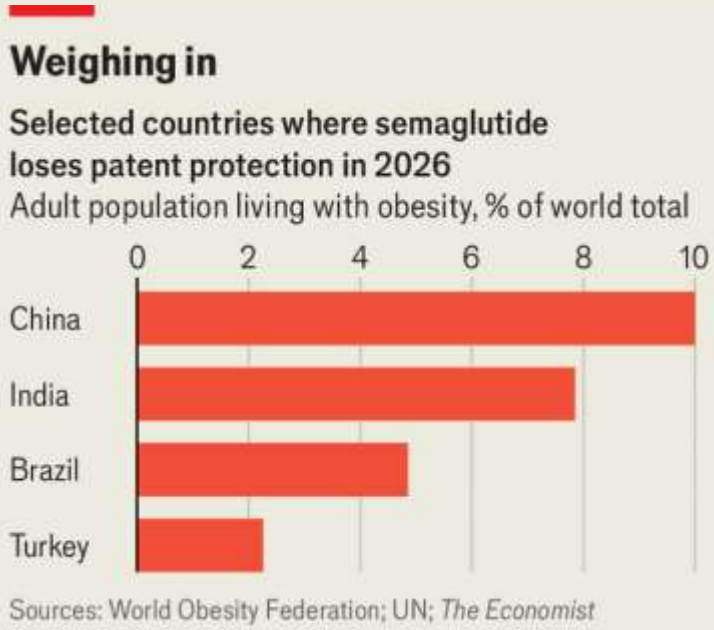
Weight-loss Drugs are Spreading Across the World

The Economist, Oct 28, 2025 (excerpt)

A new kind of instant gratification is catching on in India. Urban consumers, who have grown accustomed to groceries and gadgets arriving within minutes, can now order slimmer waistlines almost as quickly. Online pharmacies promise same-day delivery of weight-loss injections, and demand is booming. In March Eli Lilly, an American drugmaker, began selling Mounjaro, its obesity treatment, in India. A month's supply costs about $180—a quarter of the price in America, though still steep for most Indians. Even so, by September it was the country's second-bestselling branded medicine.

Until recently, GLP-1s, a powerful new class of weight-loss drugs, were confined mostly to rich countries. Yet the World Obesity Federation, a charity, reckons that two-thirds of the world's 1bn obese adults live in poorer countries. Excess weight is not merely cosmetic: it raises the risk of diabetes, heart disease and cancer. And GLP-1s may also treat sleep apnoea, kidney disease and Alzheimer's. For poorer countries, wider access to these medicines could transform the treatment of chronic illnesses. That may happen as early as next year, with the launch of cheaper generics alongside pill-based versions.

Demand for GLP-1s has been ravenous. Citeline, a research firm, reckons global sales of the drugs will exceed $26bn this year—double the figure in 2024. The market belongs to two firms: Eli Lilly and Novo Nordisk, the Danish maker of Wegovy. Mounjaro and Wegovy were approved by Chinese regulators in 2024, but with supplies tight, the two firms focused first on rich markets, particularly America, which accounts for four-fifths of sales of GLP-1s. Only now are the pair turning to large but poorer markets such as China and India.

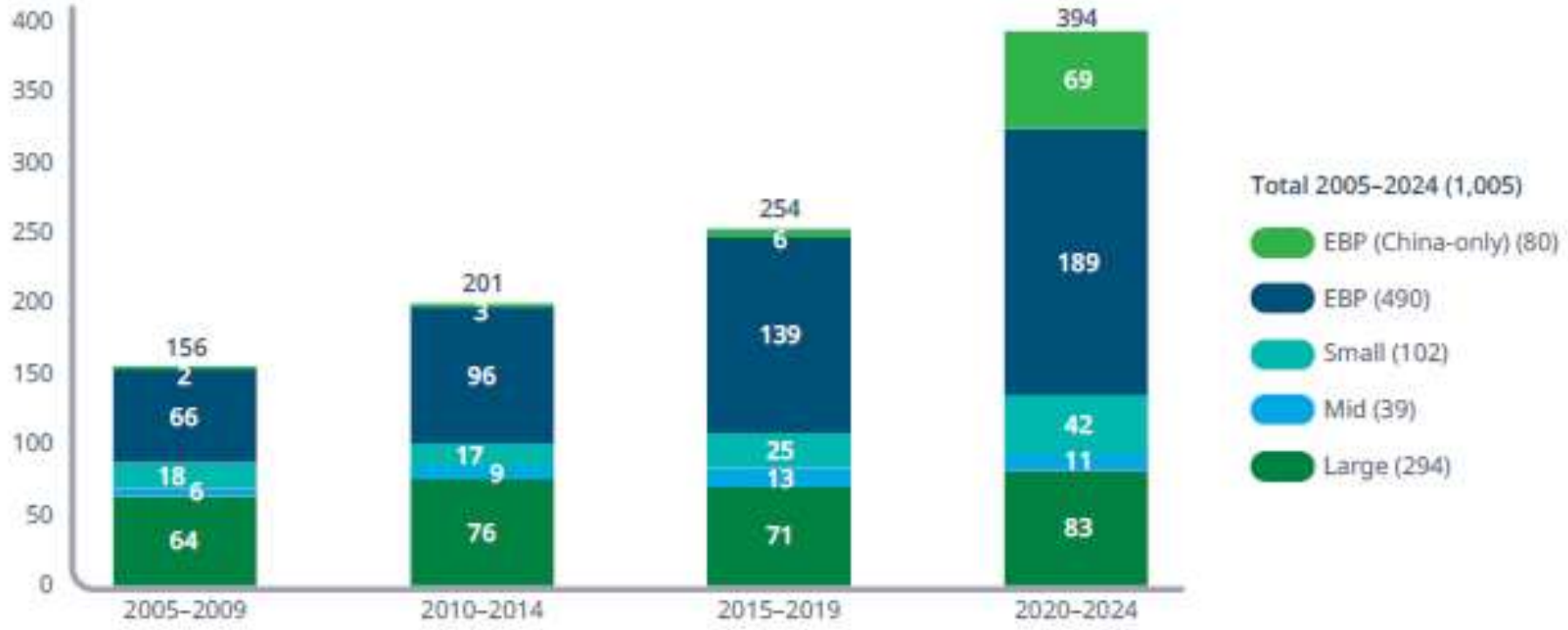


Source: https://www.economist.com/business/2025/10/28/weight-loss-drugs-are-spreading-across-the-world

Recent IQVIA Institute Report: More than Half of New Drug Launches in Last 20 Years Not from Large Pharma

Emerging biopharma companies originated the medicines for 570 of the 1,005 launches globally in the past 20 years

Exhibit 23: Global Novel Active Substance launches by originator company size, 2005–2024



Source: IQVIA Institute, Jul 2025.

Link to Report: https://www.iqvia.com/insights/the-iqvia-institute/reports-and-publications/reports/expanding-options-for-emerging-biopharma-in-the-us-a-decade-of-change

Drugmakers Continue ‘Thought-Provoking’ Price Talks with White House after Pfizer, AstraZeneca Deals

Alexis Kramer, *Endpoints News*, Oct 31, 2025

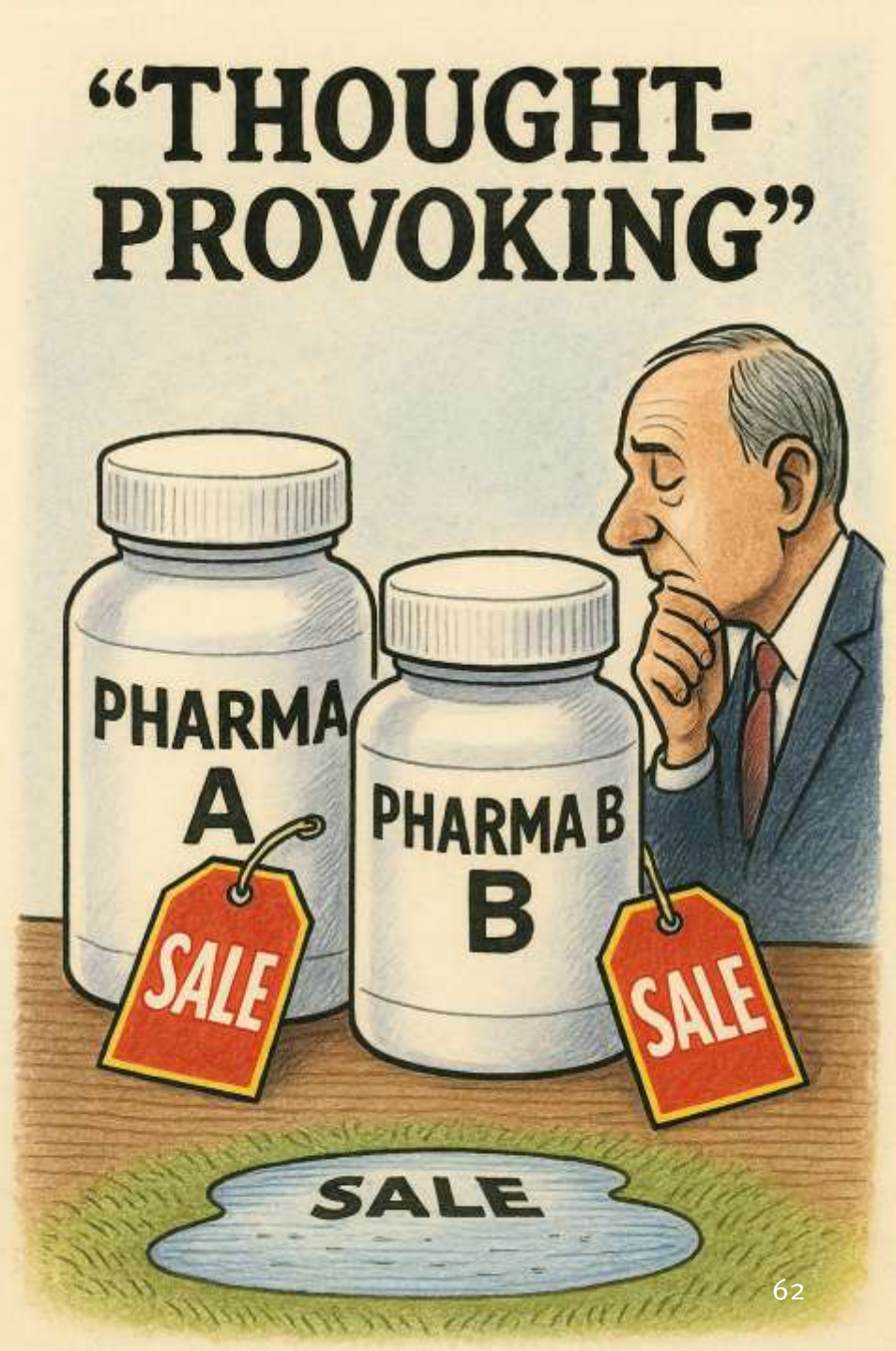
The Trump administration’s negotiations with large pharma companies are making gradual progress, according to top drugmaker CEOs, though none suggested that a new deal was imminent.

On quarterly earnings calls in recent days, executives from Bristol Myers Squibb, Novartis, and others said they’re having productive and frequent dialogue with the administration, after Pfizer and AstraZeneca reached “most favored nation” deals in the past month.

Some drugmakers declined to offer specific details on the talks, but the comments overall suggest a hopeful outlook from the industry as the White House works to bring more companies to the finish line.“I would characterize those discussions as frequent, and while not always fully aligned, they’re always constructive and thought-provoking on both sides,” Bristol Myers CEO Chris Boerner said Thursday. “Clearly, MFN and tariffs are front and center, but we continue to monitor a host of other issues, including the shutdown and what potential impact that could have downstream.”

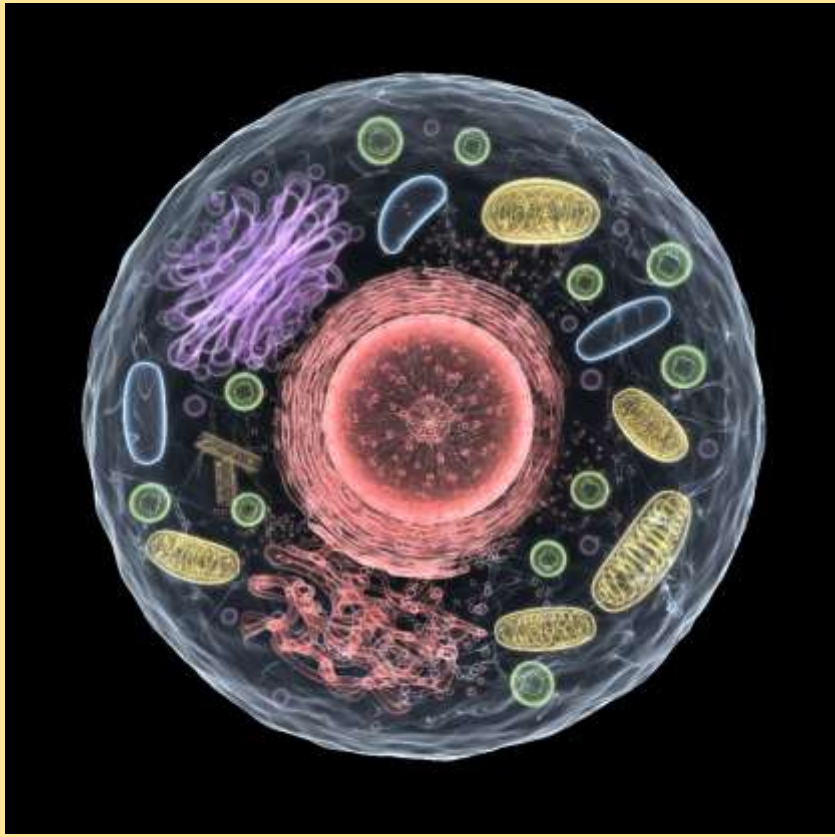
Novartis CEO Vas Narasimhan said Tuesday his company is “meeting with the administration weekly to look at what are the best solutions we can come up with.”

Source: https://endpoints.news/drugmakers-are-having-frequent-most-favored-nation-talks-with-white-house/



The Silicon Cell: AI Cell Models Could Transform Biomedicine—If They Work As Promised

Mitch Leslie, *Science*, Oct 30, 2025 (excerpt)



The human cell swarms with trillions of molecules, including some 42 million proteins and a plethora of carbohydrates, lipids, and nucleic acids. Crowded with organelles and other structures, the cell boasts an intricate organization that makes baroque architecture seem plain. Its cytoplasm is a frenzied chemical lab, with molecules continuously reacting, rearranging, and reshaping. In the nucleus, thousands of genes are constantly switching on and off to turn the seeming chaos into concerted actions that help the cell survive and reproduce.

This complexity is more than the human mind can yet fully understand or predict. But many researchers think artificial intelligence (AI), with its prodigious ability to assimilate and process information, might be up to the task. More than 2 decades ago researchers started to build systems of equations meant to simulate some of the cell's workings. Now, they have progressed to AI-driven replicas that, like the large language models taking business and popular culture by storm, ingest vast amounts of data to learn on their own. ChatGPT's attention-grabbing debut nearly 3 years ago inspired the virtual cell builders. "People want this kind of moment for biology," says Kasia Kedzierska, an AI research scientist at the Allen Institute.

How soon it is coming depends on whom you ask. Virtual cells that emulate their living counterparts would be a boon for many areas of research. In pharma labs, scientists could use them to quickly evaluate large numbers of potential drugs without the expense and difficulty of experiments. They might serve as test beds for engineering cells to perform novel functions. Virtual cells customized to match a patient's molecular profile could help doctors choose tailored medications. Researchers might even weave cell models into virtual tissues and organs to tackle questions such as how a tumor's environment affects its growth.

Source: https://www.science.org/content/article/can-ai-capture-mind-boggling-complexity-human-cell

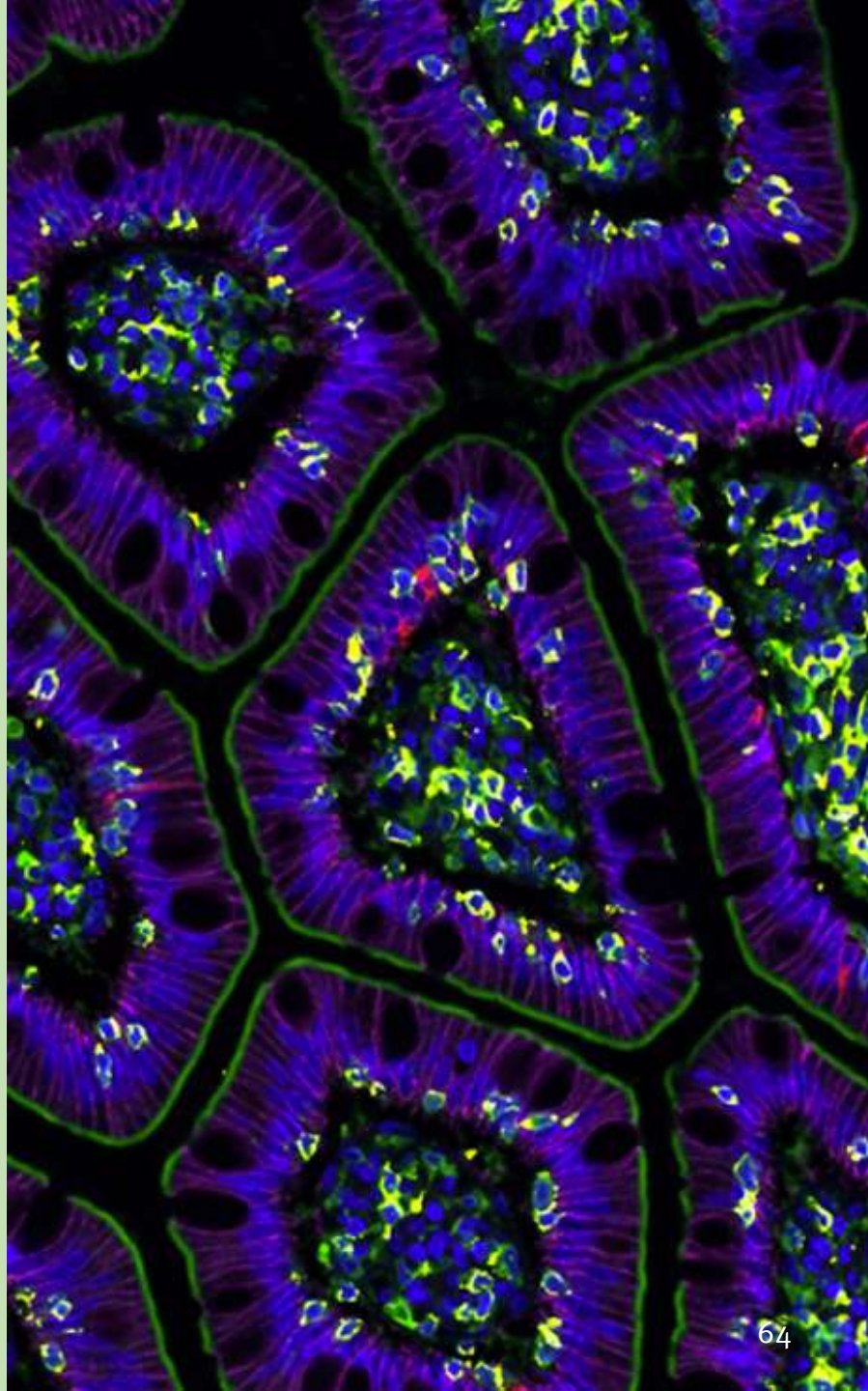
Silicon Cell Story (continued)

Such models could also help researchers make sense of the vast amount of diverse information pouring into molecular databases, says Theofanis Karaletsos, head of AI for science at the Chan Zuckerberg Initiative (CZI). An AI-powered cell mimic, Karaletsos says, “creates an integrated map of knowledge.”

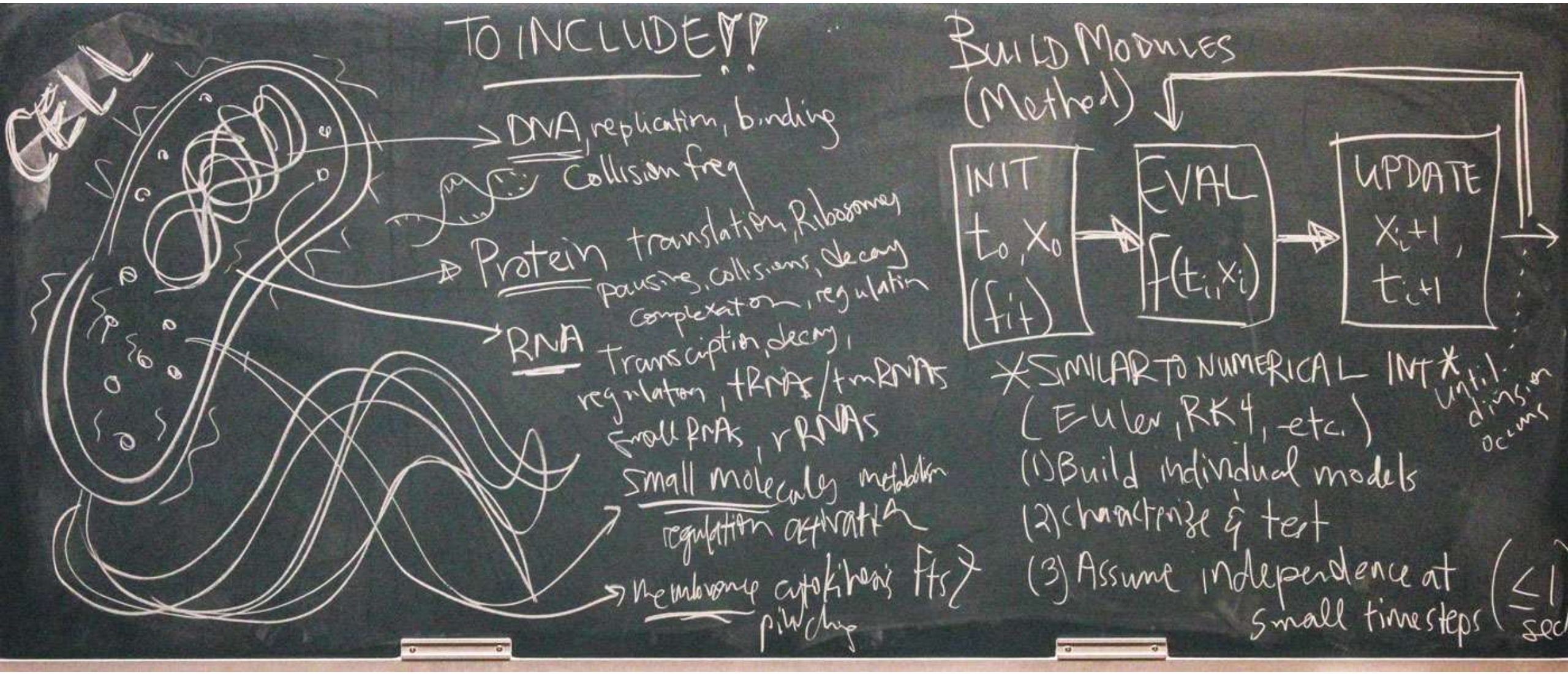
Like ChatGPT and its ilk, AI cell models have spawned big promises and hefty expectations. “Whenever a new model appears, it’s always the best,” says computational biologist Hani Goodarzi of the Arc Institute, who develops such models himself. In June he and more than 20 other researchers launched the Virtual Cell Challenge, a new contest that will put the models to the test annually. Much like a structural biology competition that started in 1994 and helped researchers largely solve the problem of how proteins fold, the Virtual Cell Challenge is meant to spur improvement in a very complex task. For its debut, it is asking AI aficionados to predict the effects of silencing certain genes in human embryonic stem cells.

So far, more than 1000 teams—with names like Cellamander, Zebulon Chow, SmartCell, and Mean Predictors—have entered and are vying for prizes donated by sponsors including Nvidia, the giant tech company that makes the graphics processing units (GPUs) at the heart of many AIs. On 6 December, contest organizers will reveal the final standings, with the top team taking home $100,000 in cash and GPU time. “We want to learn what works and what doesn’t work,” Goodarzi says.

The creators of the models say success is only a matter of time. “We haven’t solved the problem yet, but [the approach] is very promising,” says Bo Wang, head of biomedical AI for Xaira Therapeutics, a company that hopes to harness the technology for drug discovery.



Source: https://www.science.org/content/article/can-ai-capture-mind-boggling-complexity-human-cell



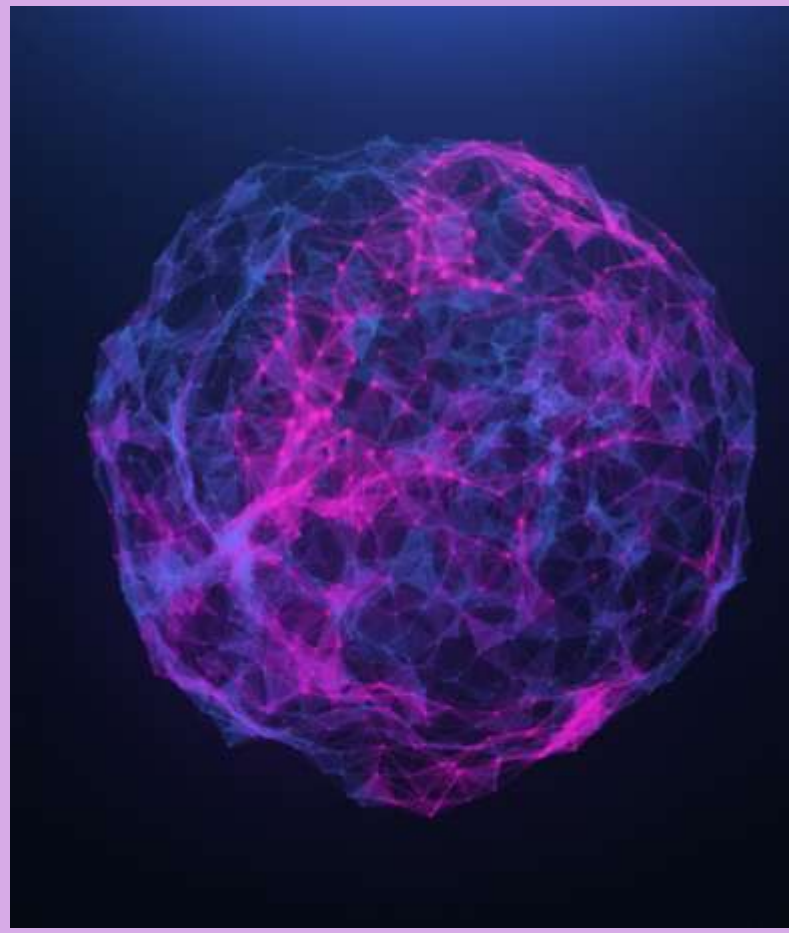
This chalkboard from 2012 depicts elements that went into the first published computational model of a whole cell, from Markus Covert's lab.ERIK JACOBSEN/THREESTORY

Silicon Cell Story (continued)

So, what's holding back virtual cells? For one thing, most current AI models rely on a single type of data: measurements of gene activity. Researchers are just beginning to include other types of information, such as cell images, that could lead to more powerful and useful models, Ma says. And even though the amount of cell data has exploded in recent years, there's still not enough to fuel the models. "The data limitation is a massive barrier to cell models," Karr says. "There's a limited set of questions we can pursue."

Karr notes that despite the debut of collections like CELLxGENE, many results don't end up in central storehouses where other scientists can easily access them. What the field needs, he says, is a repository like the Protein Data Bank (PDB), which was instrumental in the achievements of AlphaFold, the protein-folding predictor that is probably the most successful AI model in science. (Two of its developers shared a Nobel Prize in Chemistry in 2024.) The PDB houses almost every experimentally determined protein structure in a standard format, in part because most funders and journals required researchers to add any new structure they produced to the database. There's no such requirement for cell data, which are also far more diverse than protein structures, Karr says. "You can't characterize a cell with one technology."

To improve current models, researchers also need a good way to assess how well they work—but scientists are still trying to decide how to do that. After models complete their initial training, developers often educate them further to improve certain abilities before putting them to the test. That practice mirrors what happens with widely available foundation models, such as GPT-5, which undergo extensive fine-tuning before the public can use them. But some researchers argue that tests should measure a model's zero-shot performance. "If they are inferring a fundamental understanding of biology, it should be true before we fine-tune," Theis says.

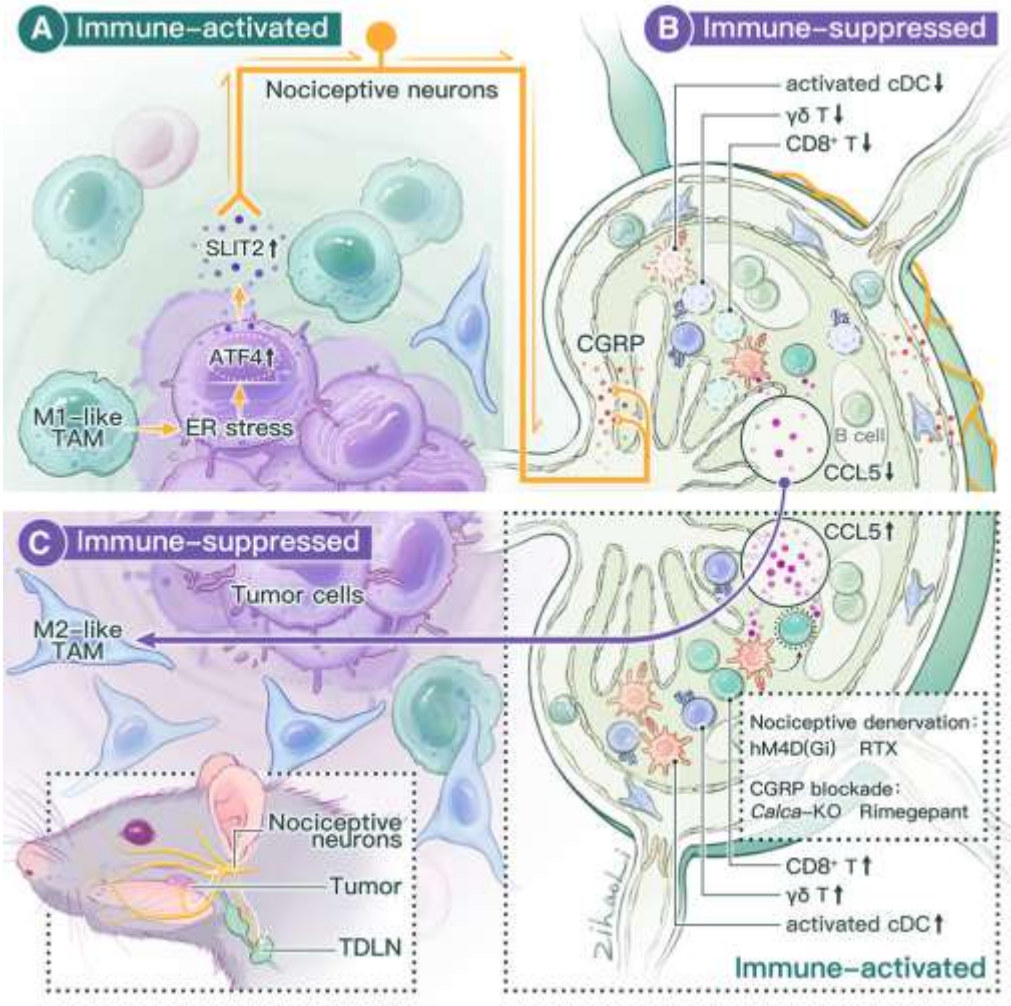


Source: https://www.science.org/content/article/can-ai-capture-mind-boggling-complexity-human-cell

Cancer Cells Co-opt an Inter-organ Neuroimmune Circuit to Escape Immune Surveillance

Zhang et.al., *Cell*, Oct 24, 2025 (excerpt)

Whether and how cancer exploits distant organs to escape immune surveillance remains largely unknown. Using clinical data from head and neck squamous cell carcinoma (HNSCC) patients and three murine oral cancer models, we find that cancer cells under immune pressure secrete slit guidance ligand 2 (SLIT2) through an activating transcription factor 4 (ATF4)-dependent pathway, which activates tumor-innervating nociceptive neurons and aggravates cancer-induced pain. This activation then stimulates tumor-draining lymph-node (TDLN)-innervating nociceptive neurons and increases calcitonin gene-related peptide (CGRP) secretion, remodeling TDLNs into an immune-suppressed state. Consequently, decreased CCL5 secretion from immune-suppressed TDLNs promotes M2-like polarization of tumor-associated macrophages, facilitating tumor growth and reducing immune checkpoint blockade (ICB) efficacy. Targeting nociceptive neurons or the ATF4-SLIT2-CGRP axis restores immune activity, alleviates cancer-induced pain, and improves ICB responses. Our findings reveal an inter-organ neuroimmune circuit co-opted by cancer to escape immune surveillance, suggesting potential therapeutic strategies to enhance immunotherapy.



Source: https://www.cell.com/cell/abstract/S0092-8674(25)01129-8

Molecular ‘Glues’ and ‘Bumpers’ on Receptors Can Bias Signalling Inside the Cell

***Nature*, Oct 29, 2025 (excerpt)**

The problemreceptors in humans and are targeted by more than 30% of approved therapeutics. They transmit signals into the cell by activating downstream ‘transducers’ — which include 16 Gα proteins and 2 β-arrestin proteins. More than 30 years ago, ‘biased’ compounds, which bind to GPCRs and preferentially activate a subset of downstream signalling pathways, were first discovered.

De novo design of biased compounds that act through the extracellular binding site is not yet feasible because the structural determinants of bias for such compounds are not well understood. We proposed that small molecules that target the GPCR–transducer interface inside the cell could change G-protein coupling through subtype-specific and predictable mechanisms. Such molecules would interact with both proteins directly and thereby act as either molecular ‘glues’ (encouraging complex formation with, and signalling through, some G proteins) or molecular ‘bumpers’ (preventing interaction with others). Modelling direct interactions is hard but feasible. Furthermore, there are inherent advantages to targeting areas on the receptor that are separate from its ligand-binding site1. These include improved receptor selectivity and cooperativity with the endogenous ligand, leading to reduced off-target effects and enhanced potency without displacing endogenous molecules. We tested our theory by using biosensors to monitor the signalling of the GPCR neurotensin receptor 1 (NTSR1) — a receptor for which we had an intracellular core-binding small molecule2 and a wealth of structural data3,4 — in real time in living cells (Fig. 1a).

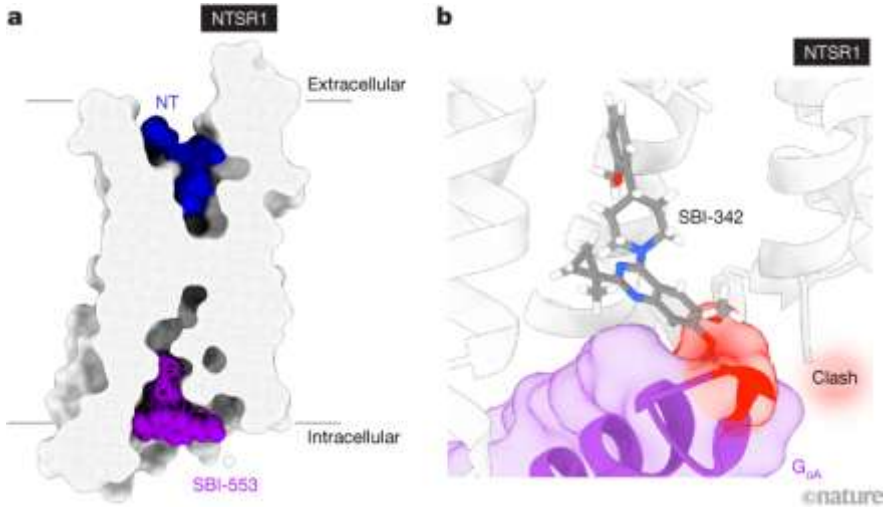


Figure 1 | At the intracellular interface between a G-protein-coupled receptor and a G-protein ‘transducer’, small molecules can act as molecular bumpers and glues. **a**, The active fragment of the neurotensin (NT) peptide binds to the G-protein-coupled receptor neurotensin receptor 1 (NTSR1) outside the cell, and the small molecule SBI-553 does so inside the cell, where G proteins usually bind[3]. SBI-553 acts as a bumper against a G_q protein and as a glue for a remodelled G_{oA} protein (not shown). **b**, Modelling indicated that changing the central ring of SBI-553 would cause the small molecule to clash with the G_{oA} protein, transforming it from a glue to a bumper. The small molecule SBI-342, an SBI-553 analogue, acts as a bumper for G_{oA}, for instance.Credit: Moore, M. N. *et al.*/*Nature* (CC BY-NC-ND 4.0)

Source: https://www.nature.com/articles/d41586-025-03461-2

Disclosure

STIFEL | Healthcare

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