Biopharma Market Update

Mar 31, 2025

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Photo of statue of Pia de' Tolomei and Nello della Pietra in Palazzo de Pitti, Florence, taken on Bio-Europe Trip, March 2025. The unfortunate story of Pia de' Tolomei, whose husband Nello unfairly suspected her of adultery and locked her up in his castle in Maremma, where she died of malaria was summarized in a few verses in Dante's Purgatory.

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Macro Update

‘Modest Stagflation’ Risk Climbs for Trump

Sam Sutton, *Politico*, March 28, 2025 (excerpt)

Inflation climbed in February as consumers braced for the potential onslaught of higher prices from President Donald Trump’s sweeping tariffs on U.S. trading partners. The Commerce Department reported Friday that prices rose at a higher-than-expected annual rate of 2.8 percent last month, excluding food and energy items, a signal that prices could spike even further in the coming months. That doesn’t augur well for price-sensitive businesses and consumers — or for Trump’s big plans for the U.S. economy. While administration officials like Treasury Secretary Scott Bessent argue that tariff-related inflation will be transitory, most of Trump’s planned levies haven’t yet taken effect. Wall Street analysts are increasingly warning that the U.S. could fall into a period of at least some stagflation — a politically toxic combination of low growth and higher inflation that the country hasn’t seen in more than four decades.

“Today’s data has the general pattern of what many observers will be looking for in the months ahead as new tariffs and other policy changes begin to bite: weaker-than-expected spending and stronger-than-expected inflation,” David Alcaly, the lead macroeconomic strategist at Lazard Asset Management, said in a research note. “Much remains uncertain, and it’s premature to be drawing judgments about impacts, but seeing this pattern in hard data and not just surveys could feed apprehension.”

February’s personal consumption expenditures report did not reflect the 25 percent tariffs on steel and aluminum imports that kicked in on March 12. Nor did it incorporate the effects of most of the new levies attached to Chinese, Mexican or Canadian goods. It predates auto industry tariffs — snarled auto supply chains were a major driver of post-pandemic inflation — as well as so-called reciprocal tariffs that are scheduled to be imposed next week.

Barely two months after Inauguration Day, voters are sounding alarms over Trump’s lack of progress on cost-of-living issues. A Gallup poll released Thursday had him 18 points underwater on his handling of the economy. Future tariff-related sticker shocks are unlikely to improve those margins.

Source: https://www.politico.com/news/2025/03/28/stagflation-risk-inflation-trump-economy-tariffs-00256500

US Consumer Spending Barely Rises, Key Inflation Gauge Picks Up

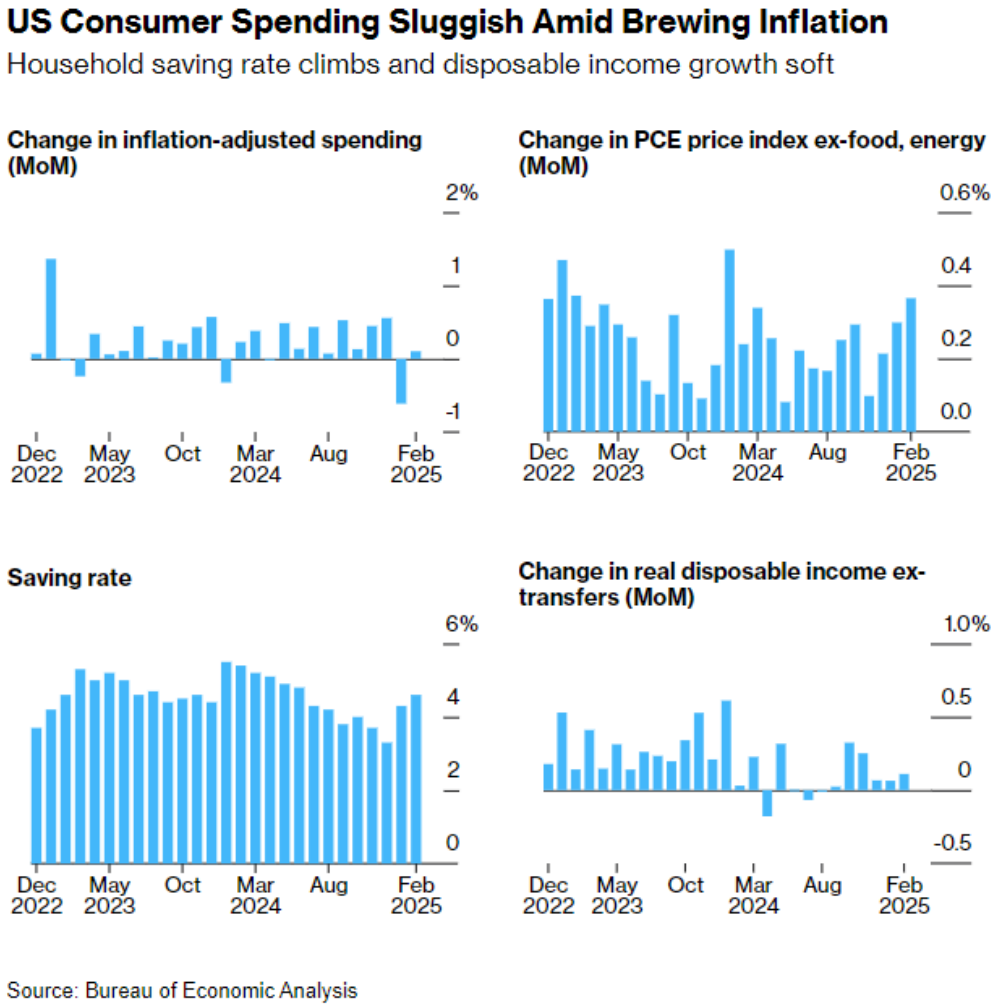
By Augusta Saraiva, *Bloomberg*, March 28, 2025 (excerpt)

Consumer spending was weaker than expected again in February while a key inflation metric picked up, in a double whammy for the economy before the brunt of tariffs.

Inflation-adjusted consumer spending edged up 0.1%, on the low end of economists' estimates, after a slump January that analysts mostly blamed on bad weather. Notably in February, Americans reduced spending on services for the first time in three years in the face of higher prices — including on dining out.

"Consumers are resistant to price increases," Neil Dutta, head of US economics at Renaissance Macro, said in a note. "Ultimately, inflation boils down to a household's budget constraint and conditions are deteriorating here."

The Federal Reserve's preferred inflation rose 0.4% from January, the most in a year, according to Bureau of Economic Analysis data out Friday. The so-called core personal consumption expenditures price index, which excludes food and energy items, was up 2.8% from last year, remaining stubbornly above the Fed's 2% target.



Source: https://www.bloomberg.com/news/articles/2025-03-28/us-pce-inflation-accelerates-spending-is-weaker-than-forecast

Dow Closes 700 Points Lower as Inflation and Tariff Fears Worsen

Pia Singh and Sarah Min, *CNBC*, March 28, 2025 (excerpt)

Stocks sold off sharply on Friday, pressured by growing uncertainty on U.S. trade policy as well as a more grim outlook on inflation.

The Dow Jones Industrial Average closed down 715.80 points, or 1.69%, at 41,583.90. The S&P 500 shed 1.97% to 5,580.94, ending the week down for the fifth time in the last six weeks. The Nasdaq Composite plunged 2.7% to settle at 17,322.99.

Shares of several technology giants dropped, putting pressure on the broader market. Google-parent Alphabet lost 4.9%, while Meta and Amazon each shed 4.3%.

This week, the S&P 500 lost 1.53%, while the 30-stock Dow shed 0.96%. The Nasdaq declined by 2.59%. With this latest losing week, Nasdaq is now on pace for a more than 8% monthly decline, which would be its worst monthly performance since December 2022.

Stocks took a leg lower on Friday after the University of Michigan's final read on consumer sentiment for March reflected the highest long-term inflation expectations since 1993.

Friday's core personal consumption expenditures price index also came out hotter-than-expected, rising 2.8% in February and reflecting a 0.4% increase for the month, stoking concerns about persistent inflation. Economists surveyed by Dow Jones had been looking for respective numbers of 2.7% and 0.3%. Consumer spending accelerated 0.4% for the month, below the 0.5% forecast, according to fresh data from the Bureau of Economic Analysis.

"The market is getting squeezed by both sides. There is uncertainty around next week's reciprocal tariffs hitting the major exporting sectors like tech alongside concerns about a weakening consumer facing higher prices hitting areas like discretionary spending," said Scott Helfstein, head of investment strategy at Global X.

Source: https://www.cnbc.com/2025/03/27/stock-market-today-live-updates.html

High-Conviction Wall Street Bets Unravel in ‘Trump Trade’ Rebuke

Denitsa Tsekova and Isabelle Lee, *Bloomberg*, March 28, 2025 (excerpt)

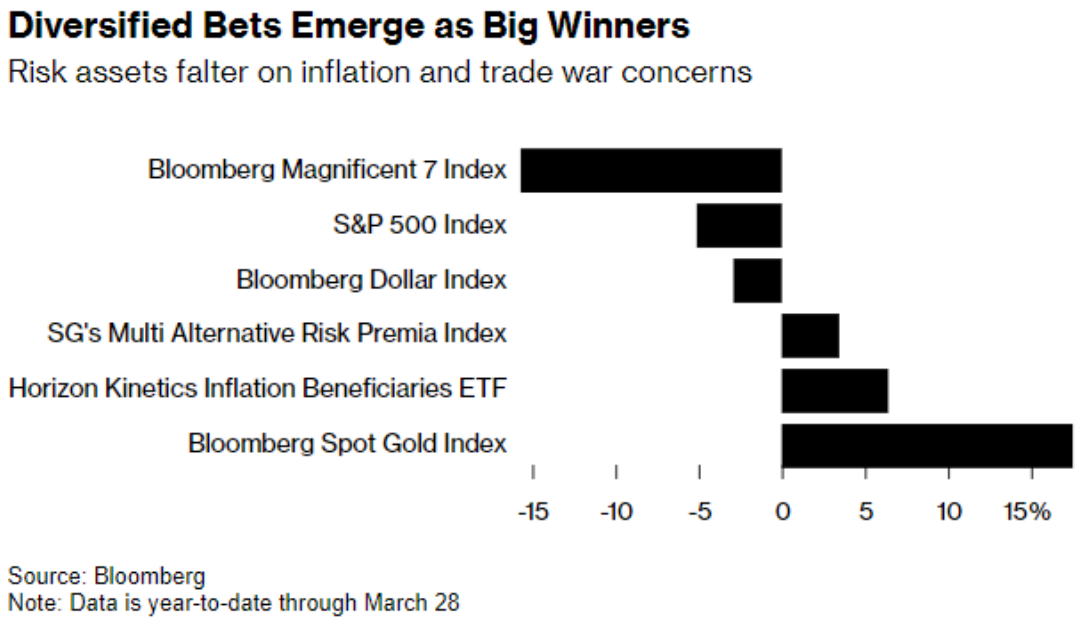
Coming into the new presidency the playbook for traders was obvious. Bet it all on a core of America First-linked champions, from Tesla Inc. and crypto to smaller companies.

Turns out, amid spiraling policy shifts and worsening economic data, whittling yourself down to just a few bold calls has been one of the worst things to do in the era of Donald Trump.

That’s bad news for followers of this approach — including would-be market timers and those with concentrated portfolios — after another crushing week on Wall Street.

As trade tensions flared, risk bulls were hit Friday by reports showing that consumer confidence plunged and inflation ticked up — just before tariff ‘Liberation Day.’ The Nasdaq 100 sank 2.6%, Treasuries jumped, a gauge of credit risk rose, and gold hit yet another record.

Altogether, it’s a fresh gut-punch for investors wedded to big macro bets on one-shot themes, like America First trading or the Big Tech era. Few escaped unscathed but, once again, institutional pros who’ve long touted the virtues of spreading out market bets fared the best.



Multi-faceted portfolios are outperforming anew, including those packing in systematic-like trades, inflation-hedged assets like commodities and other physical assets, and cheap — rather than expensive — securities. It’s a diverse group of market winners, but call this the real Trump trade: dynamic hedging for the era of policy uncertainty.

Source: https://www.bloomberg.com/news/articles/2025-03-28/high-conviction-wall-street-bets-unravel-in-trump-trade-rebuke

Americans Feel Bad About the Economy. Whether They Act on It Is What Really Matters.

Justin Lahart and Matt Grossman, *Wall Street Journal*, March 29, 2025 (excerpt)

Americans are in the dumps about the economy. The big question: What will that pessimism mean for the economy?

The University of Michigan on Friday reported that its index of consumer sentiment, which measures people's view of the economy, fell to 57 this month from 64.7 in February, hitting its lowest level since 2022. Respondents' feelings about the current economy were gloomy but relatively stable. Their views about the economy's future got much worse.

The Michigan report follows on a series of other surveys showing that the mood among both American consumers and businesses has markedly deteriorated over the course of the first quarter. The Conference Board, a business-research group, on Tuesday reported that its overall index of consumer confidence fell sharply this month. Its measure of future expectations dropped to the lowest level in 12 years.

The Michigan sentiment index, for example, fell sharply from the middle of 2021 to the middle of 2022 as inflation soared. Yet while Americans felt bad about the economy, they kept spending money.

In contrast, when sentiment fell sharply over the year leading up to the 2008-09 financial crisis, pinched consumers were reining in spending.

To Joshua King, angsty headlines about tariffs and DOGE layoffs feel far removed from his work at an aircraft-charter company in Tulsa, Okla. A recent bachelor party in New Orleans brought together 11 of his college friends, all with steady jobs. "No one was pinching pennies," King said.

Others said concern about the economy is leading them to cut back. "I'm definitely not planning any vacations this year," said Robin Suggs, a community-nonprofit worker who lives in Robbinsville, N.C. Suggs said federal spending cuts are taking a toll on the rural area where he works.

What is different now is that hiring has slowed, while pandemic savings have been spent down. "Those supports just are weakening or disappearing altogether," Hsu said.

History shows that sentiment counts for something. Americans' sentiment fell sharply, according to the Michigan index, after Saddam Hussein invaded Kuwait in August 1990. A recession started around the same time.

The incident helped prompt a 1994 paper from Christopher Carroll, Jeffrey Fuhrer and David Wilcox, who were then Federal Reserve economists. Their research found that the expectations component of the Michigan survey, in particular, had some predictive value when it came to consumer spending.

Source: https://www.wsj.com/economy/consumers/trump-economy-consumer-business-sentiment-fbfb1db5

Biopharma Market Update

The XBI Closed at 84.4 Last Friday (Mar 28), Down 3.1% for the Week

The Stifel Global Biotech Value Tracker fell by 2.2%, a little less than the XBI (-3.1). Treasury yields were flat. The XBI is down 6.6% for the year. Last week saw big pharma substantially outperform the S&P 500 amidst broad market uncertainty – visible in the rise in the VIX.

Biotech Stocks Down Last Week

Return: Mar 21 to Mar 28, 2025

Nasdaq Biotech Index: -1.4%
Arca XBI ETF: -3.1%
Stifel Global Biotech EV (adjusted): -2.2%*
S&P 500: -1.5%

Return: Dec 31, 2024 to Mar 28, 2025 (YTD)

Nasdaq Biotech Index: +1.8%
Arca XBI ETF: -6.3%
Stifel Global Biotech EV (adjusted): -6.6%*
S&P 500: -5.1%

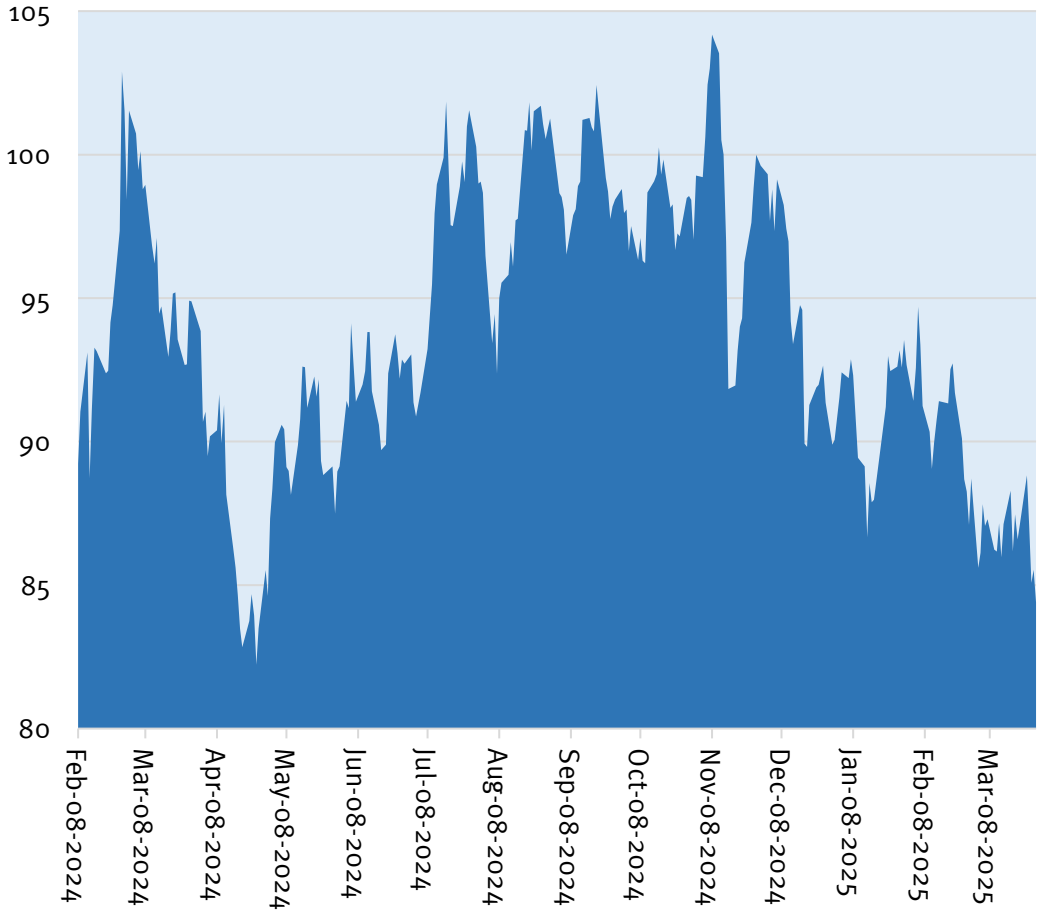
VIX Up

Dec 29, 2023: 12.45%
Mar 29, 2024: 13.0%
Aug 2, 2024: 23.4%
Dec 13, 2024: 13.8%
Jan 24, 2025: 14.2%
Feb 21, 2025: 18.2%
Mar 21, 2025: 19.2%
Mar 28, 2025: 21.7%

10-Year Treasury Yield Flat

Dec 29, 2023: 3.88%
Aug 2, 2024: 3.80%
Dec 13, 2024: 4.4%
Jan 24, 2025: 4.6%
Feb 21, 2025: 4.4%
Mar 21, 2025: 4.25%
Mar 28, 2025: 4.27%

XBI, Feb 8. 2024 to Mar 28, 2025

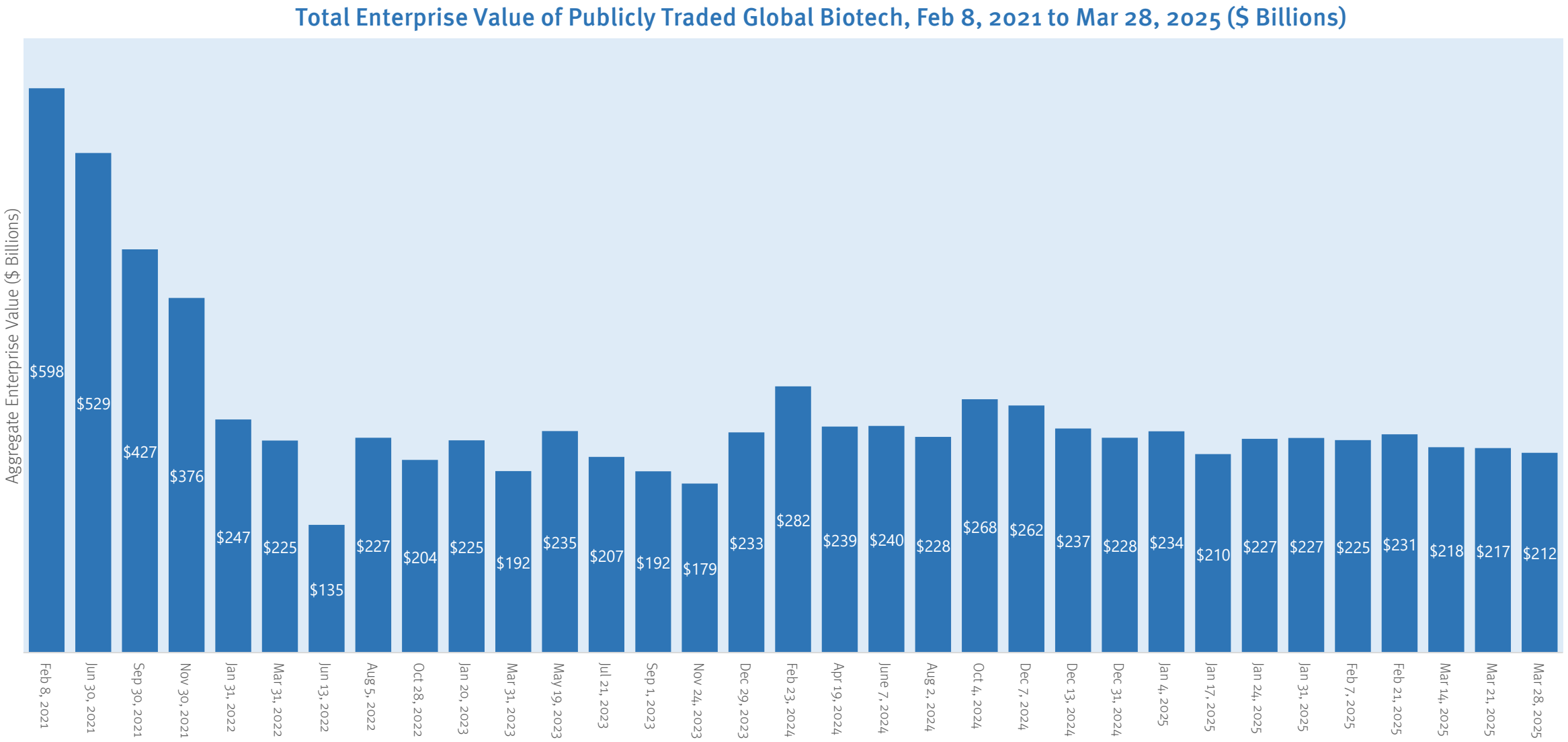


* Change by enterprise value. The adjusted number accounts for the effect of exits and additions via M&A, bankruptcies and IPOs. The annual change by market cap is even higher.

Source: S&P Capital IQ and Stifel analysis

Total Global Biotech Sector Fell 2.2% Last Week

Biotech stocks fell 2.2% in the last week –less than the XBI. By our math, the total global biotech sector is down 6.6% for the year.

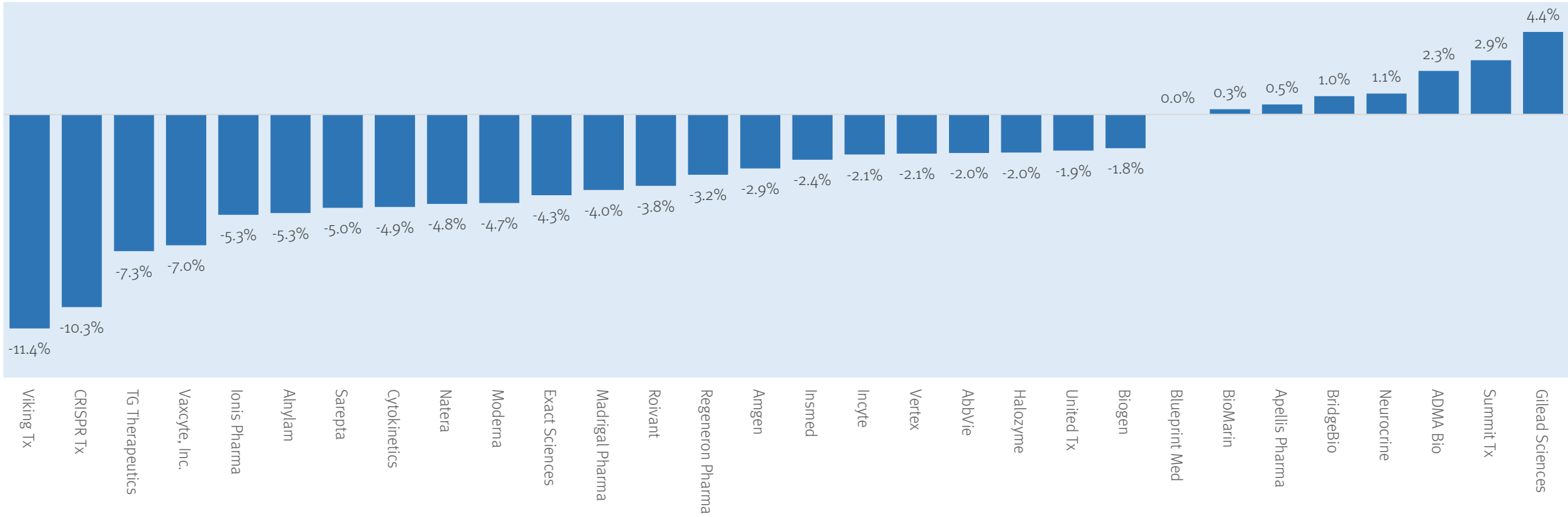


Source: CapitalIQ. Biotechs are defined as any therapeutics company without an approved product on any global stock exchange.

XBI 30 Performance Mixed Last Week

This chart shows the change in market cap this year for the 30 most influential stocks in the XBI. These 30 stocks comprise 60% of the weight of the XBI (out of 138 stocks total). The mean percentage change in value last week was -2.9%. The median change was -2.6%. Viking and CRISPR Therapeutics fell the most. TG fell following substantial upwards momentum. Sarepta continued to lose ground after the recent patient death. Gilead performed well as it became clear that federal budget cuts are not going to impact HIV spend. Summit rose in sympathy with positive momentum for VEGF/PD1 bispecifics (from BioNTech SCLC data). The XBI overall remains highly bifurcated. Large caps are up 13% for the year while all other size buckets are down 5% to 10% for the year.

Top 30 XBI Influencers, Pecent Change in Market Cap, Week of Mar 21 to Mar 28, 2025

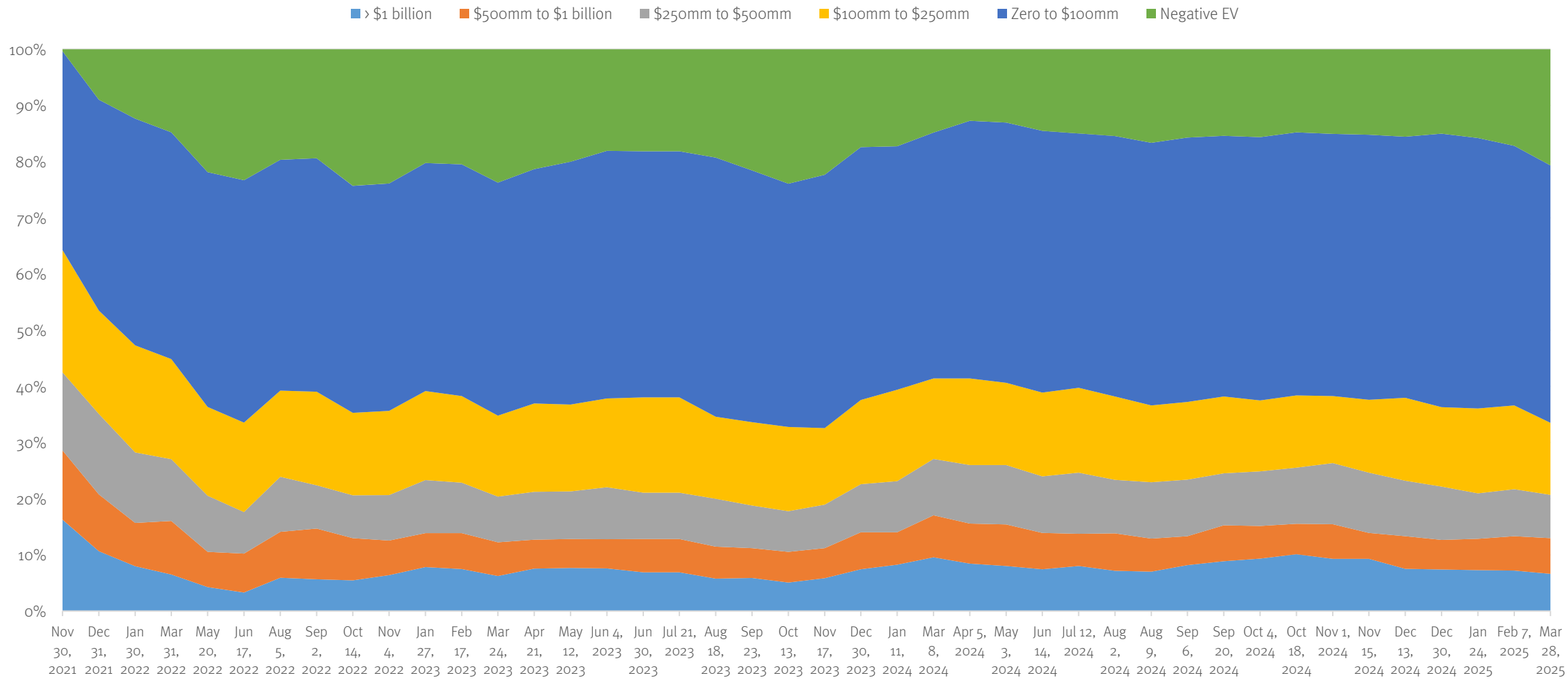


Source: CapitalIQ. Biotechs are defined as any therapeutics company without an approved product on any global stock exchange.

Global Biotech Neighborhood Analysis

The population of biotechs trading for less than cash continues to expand rapidly.

Global Biotech Universe by Enterprise Value Category, Nov 30, 2021 to Mar 28, 2025



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

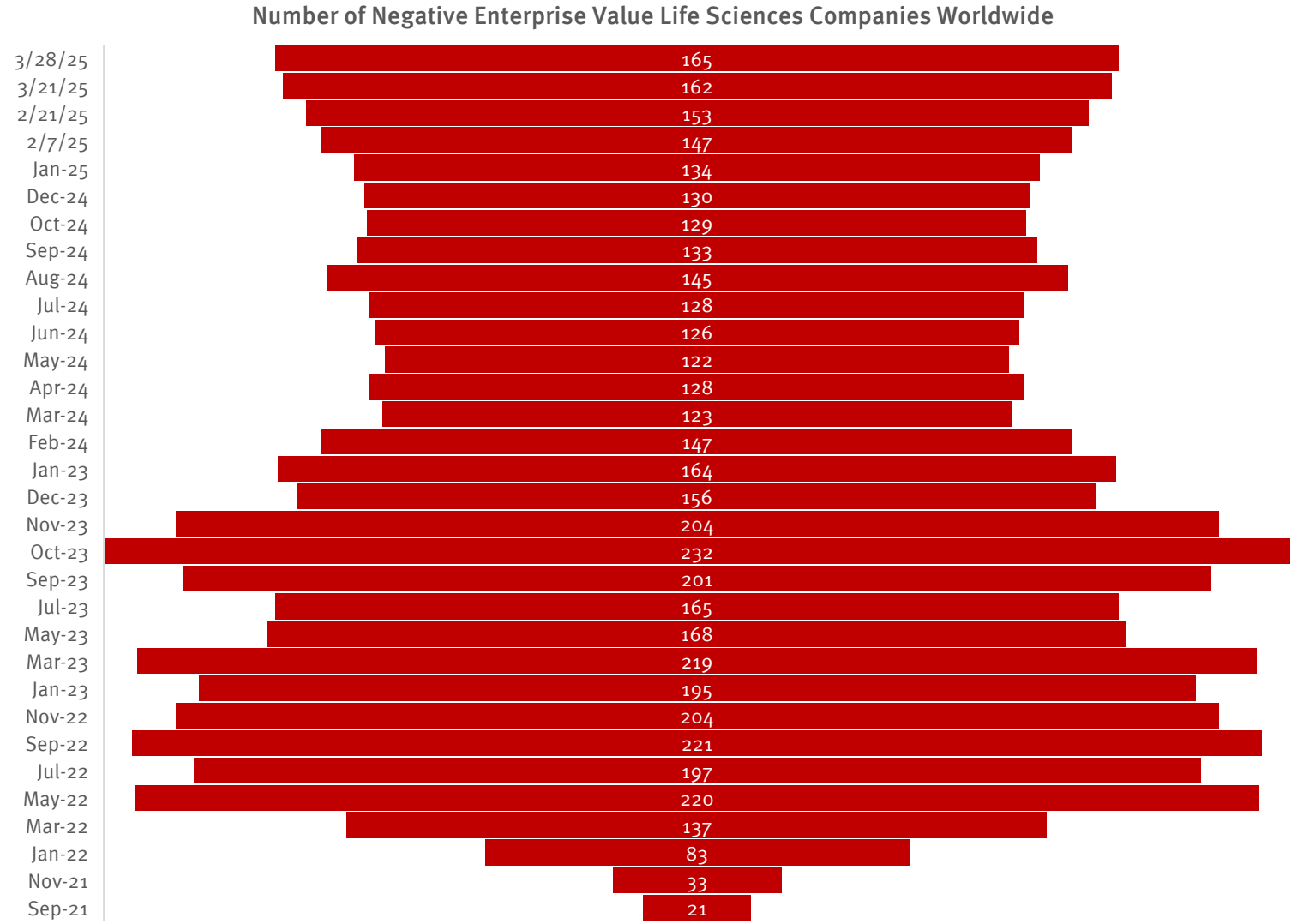
Life Sciences Sector Lost $155 Billion in Value Last Week (-1.6%)

Last week saw strength in API. All other subsectors lost value with HCIT, diagnostics, life science tools and biotech falling the most.

Sector	Firm Count	Enterprise Value (Mar 28, 2025, $millions)	Change in Last Week (percent)	Change in Last Month (percent)	Change in Last Year (percent)
API	79	$88,333	1.0%	3.0%	14.9%
Biotech	730	$216,081	-2.2%	-5.7%	-5.1%
CDMO	37	$150,446	-2.1%	-4.5%	8.4%
Diagnostics	76	$244,247	-3.1%	-7.5%	-14.6%
OTC	29	$24,051	-0.5%	-0.5%	-12.2%
Pharma	697	$6,172,009	-1.8%	-3.3%	-1.7%
Services	38	$159,922	-2.3%	-3.6%	-19.7%
Tools	50	$588,839	-2.9%	-5.9%	-18.6%
Devices	174	$1,771,574	-0.1%	-5.0%	3.6%
HCIT	7	$24,467	-5.8%	-16.2%	25.9%
Total	**1917**	**$9,439,968**	**-1.6%**	**-4.0%**	**-2.9%**

Source: CapitalIQ and Stifel analysis

Number of Negative Enterprise Value Life Sciences Companies Jumped in Last Week



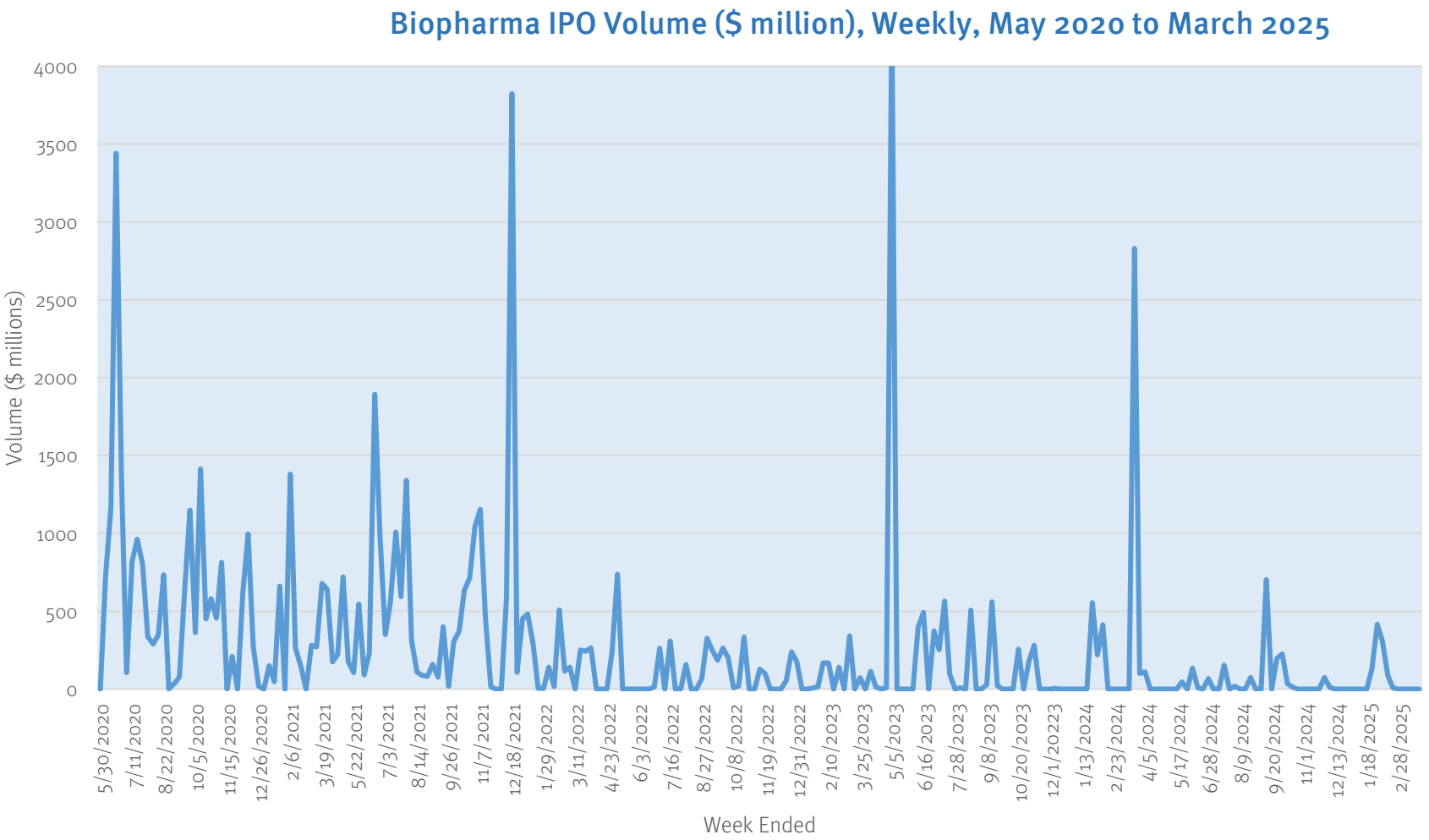
The count of negative EV life sciences companies worldwide rose from 162 a week ago to 165 last Friday.

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

Source: CapitalIQ

Capital Markets Update

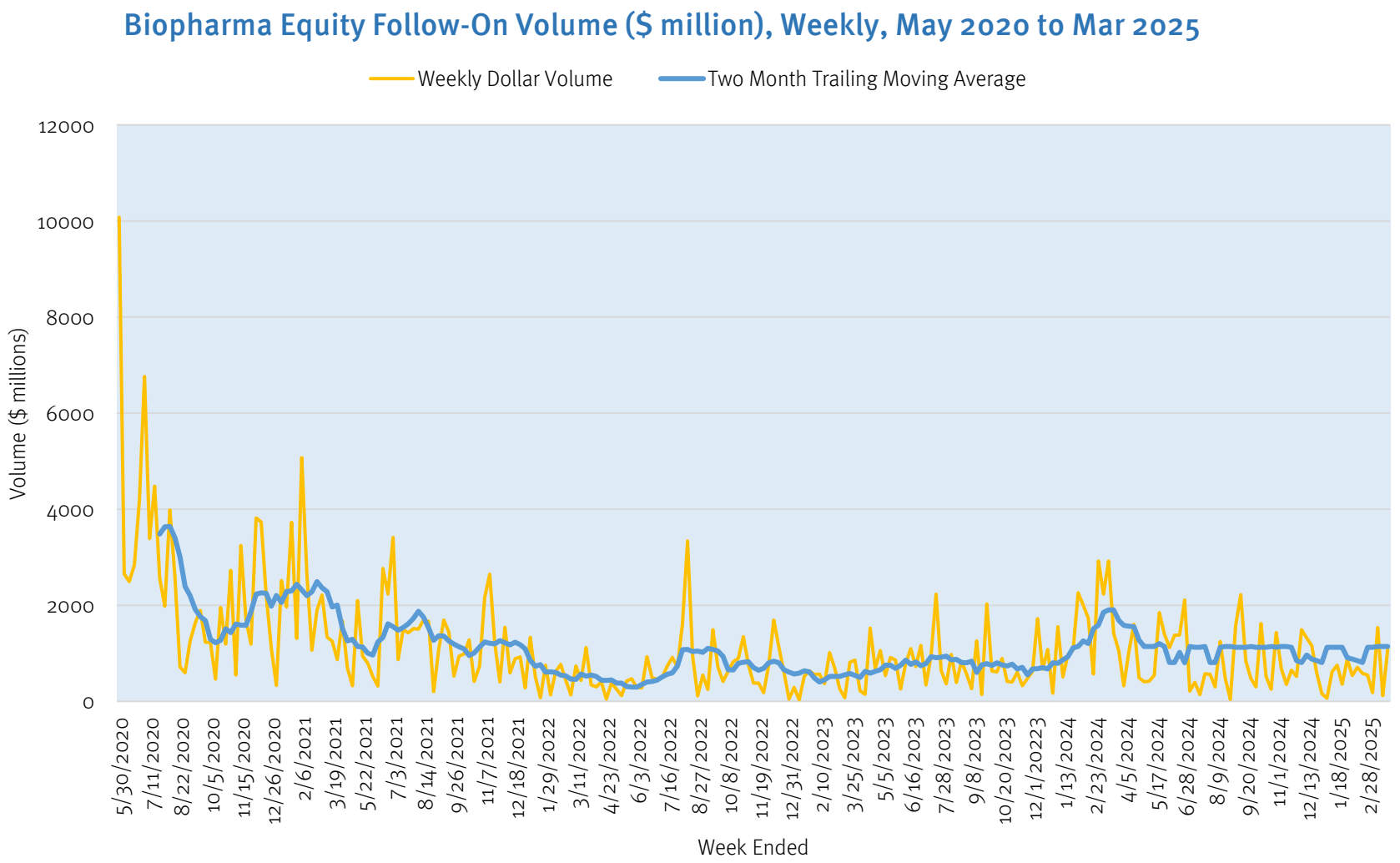
IPO Market Has Quieted Down



Last week saw no IPO's price in the market. With the VIX over 20% and a down market, conditions were not conducive to efforts by companies to go public in the market.

Source: Data from CapitalIQ and Stifel research.

$1.1 Billion in Follow-On Equity Financings Last Week



Last week was one of the stronger weeks for follow-ons (globally) in two months.

The largest deal in the market was a $175 million PIPE deal done by Surrozen to fund a novel back of the eye drug candidate.

The second and third largest deals were by Chinese biotechs, raising money on the hot HK market. These companies were Livzon ($138mm raise) and HBM Holdings ($105mm raise).

Source: Data from CapitalIQ and Stifel research.

Burst PIPEs? So-so Returns for Biotech's Once-buzzy Financing Vehicle

***Adam Feuerstein, STAT*, Mar 27, 2025 (excerpt)**

This newsletter launched in the middle of the biotech PIPE frenzy. You may recall, between January and April 2024, biotechs raised nearly $7 billion via these privately negotiated transactions.

As I wrote at the time, for developmental-stage biotechs, PIPEs were an increasingly common method to raise new capital, eclipsing traditional follow-on stock offerings. For investors on the other side of the table, PIPEs were viewed as a new source of alpha — the investment edge needed to beat the market. Lubricating the deals with privileged access to material, non-public information helped, too.

How'd that work out?

Big picture: The average return for the 50 PIPE transactions that I tracked in the early part of last year is currently 4% — not stellar, but better than the XBI's -2% performance in the same timeframe.

The median return on these PIPE deals, however, was -20%. Nearly twice as many PIPEs have lost money than gained.

Comparing these PIPEs to the XBI may not be completely fair because riskier, cash-burning, development-stage companies are particularly out of favor with investors during this biotech bear market. Consider: A larger basket of development-stage biotechs tracked by this ETF is down 20%.

Avidity Biosciences pulled off one of the better-performing PIPEs at that time, raising $400 million in late February 2024 at $16.50 per share. Investors who bought into that deal and still own the stock are up 96%.

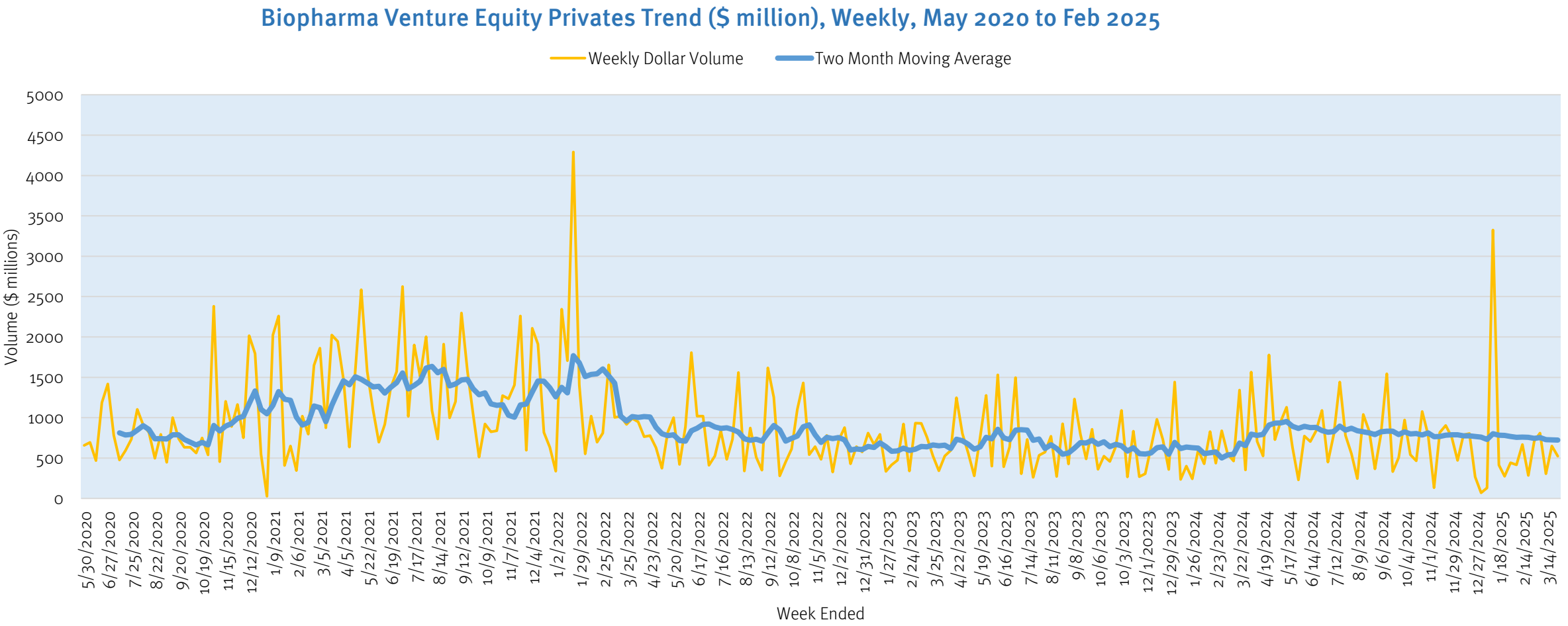
This was a "wall-crossed" PIPE — investors in the Avidity syndicate, including Adage Capital, RA Capital, Boxer Capital, and Janus Henderson, were given confidential access to new clinical data that were reported publicly days later.

Had you been among the hoi polloi forced to wait for the public data announcement before buying Avidity shares, you'd be up 68%.

Source: https://www.statnews.com/2025/03/27/pipes-biotec-financing-performance-actinium-regenexbio/

Venture Privates Market Continues to Slow Down

The first six weeks of 2024 saw private raises of $900mm a week, on average. Last week saw $523 get raised in the privates market. Activity is definitely slowing down in recent weeks. The largest deal was a $93mm investment into Character Biosciences.



Source: Data from CapitalIQ, Crunchbase.

Character Biosciences Raises $93 Million

Jersey City, Mar 25, 2025 (BUSINESS WIRE) Character Biosciences, a precision medicine company transforming drug development for polygenic diseases, announced today an oversubscribed $93 million Series B financing round to accelerate the advancement of its pipeline of precision therapies to treat degenerative eye diseases, starting with age-related macular degeneration (AMD). The funding was co-led by new investors aMoon and Luma Group, with additional participation from Bausch + Lomb and Jefferson Life Sciences, alongside existing investors Innovation Endeavors, Catalio Capital Management, S32, and KdT Ventures.

AMD affects one in eight people over 50 and is the leading cause of blindness for older adults worldwide. Despite its complexity, AMD has long been treated as a uniform disease, contributing to high failure rates in drug development. To apply a precision medicine approach to this disease, Character Bio has partnered with over 150 ophthalmology treatment centers across the US to conduct an AMD-focused observational trial, integrating genetics with longitudinal clinical and imaging data for over 6,500 consented patients. This proprietary resource enables the company to reclassify AMD into genetically-defined subtypes, discover and prioritize therapeutic targets, and optimize patient selection for clinical trials.

This data-driven approach has led to the discovery and advancement of its lead candidates, CTX203 and CTX114, which target key drivers of retinal cell death and vision loss. CTX114, a best-in-class complement inhibitor, is designed to slow the progression of geographic atrophy in advanced dry AMD, while CTX203, a first-in-class lipid regulator, aims to prevent progression to advanced AMD. Both programs are expected to enter clinical trials in the next year. The company is also leveraging its AI-driven, genomics-based platform to expand its pipeline into additional ophthalmic diseases.

"Millions of patients suffering from degenerative eye diseases lack effective treatments that delay disease progression. By identifying the genetic modifiers of their disease progression, we can develop therapeutics to more precisely target the root causes of disease and improve clinical translation. This funding allows us to advance our lead programs into first-in-human trials, with the goal of bringing new therapies to patients who urgently need them."

Cheng Zhang
Chief Executive Officer
Character Biosciences

Source: https://www.businesswire.com/news/home/20250325445846/en/Character-Biosciences-Raises-%2493-Million-Series-B-to-Advance-Precision-Medicine-for-Progressive-Eye-Diseases

Augustine Therapeutics Raises $85 Million

LEUVEN, Belgium – 24 March 2025 Augustine Therapeutics NV ("Augustine" or "the Company"), a biotechnology company focused on developing new therapies for neuromuscular, neurodegenerative and cardio-metabolic diseases through the inhibition of the cytosolic Histone DeACetylase 6 (HDAC6) enzyme, today announced it has successfully completed its Series A financing round raising a total of EUR 77.7 million (USD 84.8 million). The oversubscribed financing was co-led by Novo Holdings and Jeito Capital, supported by existing investors Asabys Partners, who led an initial EUR 17.5 million closing in 2024, Eli Lilly and Company, AdBio partners, V-Bio Ventures, PMV, VIB, Gemma Frisius Fund, the US-based Charcot-Marie-Tooth (CMT) Research Foundation and Newton Biocapital.

HDAC6 is involved in neurodegeneration and tissue aging-related cellular processes, and pharmacologic inhibition of HDAC6 is a promising approach in a number of diseases. Augustine Therapeutics have designed a unique next-generation approach to selectively inhibit HDAC6 while preserving its beneficial non-catalytic functions. This novel non-hydroxamate, non-hydrazine producing approach seeks to avoid the limitations of previous HDAC6i and has significant potential in CMT, the most common hereditary disorder of the peripheral nervous system, affecting approximately three million people worldwide.

The Company's scientific foundation originates from the ground-breaking research of Prof. Ludo Van Den Bosch from the VIB-KU Leuven Center for Brain and Disease Research, who identified HDAC6 inhibition as a promising approach for the treatment of CMT and other neuropathies. Augustine was initially formed and seed-funded by V-Bio Ventures, AdBio Partners, VIB, PMV, and Gemma Frisius Fund. The Company recently appointed experienced biopharma leader Gerhard Koenig, PhD, who had served as Executive Chairman since June 2024, to lead the Company as CEO in January 2025.

The proceeds will be used to advance Augustine's lead candidate, AGT-100216, through a Phase I/II proof-of-concept clinical trial in CMT. Beyond AGT-100216, Augustine has two other programs in discovery targeting peripherally-restricted and blood-brain barrier-penetrant HDAC6i for undisclosed neurodegenerative and cardio-metabolic indications.

Source: https://www.globenewswire.com/news-release/2025/03/24/3047524/0/en/Augustine-Therapeutics-raises-oversubscribed-EUR-78-million-USD-85-million-Series-A-financing-round.html

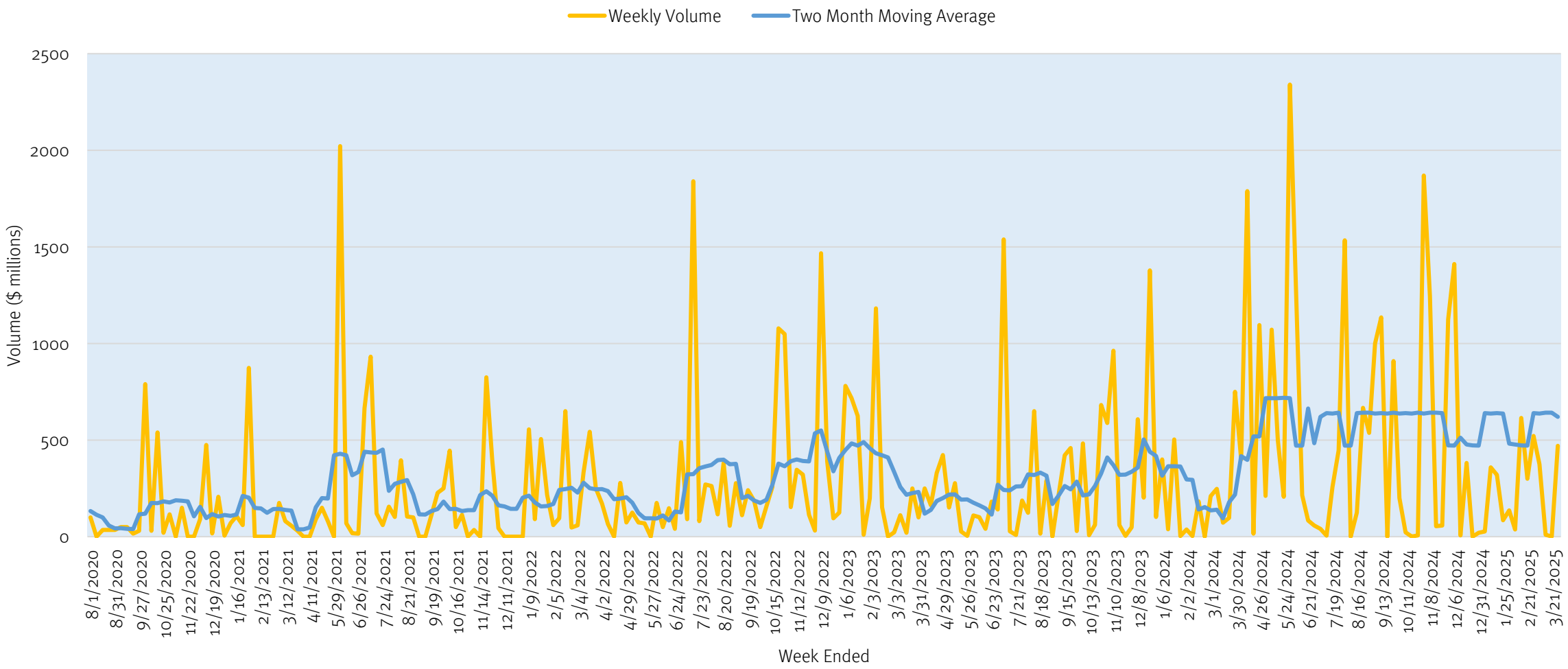
"This significant financing is a testament to the innovative medicinal chemistry that Augustine was founded on, which acts via a unique mechanism of action. The therapeutic potential of HDAC6 is widely recognized in our industry, but previous drug approaches have been sub-optimal, particularly for chronic diseases. At Augustine, we believe we have solved these challenges with a novel non-hydroxamate, non-hydrazide producing chemotype…

Gerhard Koenig, Ph.D.
Chief Executive Officer
Augustine Therapeutics

Global Biopharma Private Debt Placement Solid Last Week

Last week saw four companies take down private debt. These deals were led by Eurofins which did a $431mm private placement of debt.

Biopharma Private Debt Issuance Trend ($ million), Weekly, Aug 2020 to March 2025



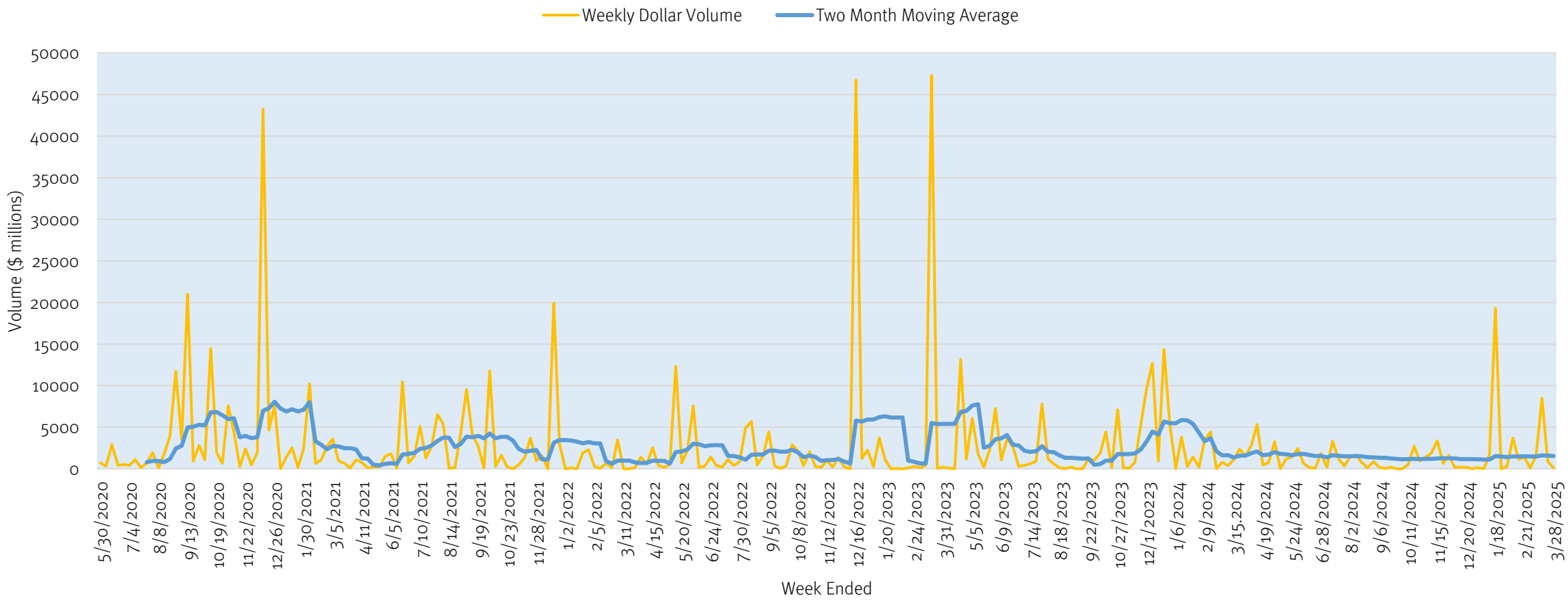
Source: Data from CapitalIQ, Crunchbase.

M&A Update

M&A Market Quiet Last Week

The M&A market was not active last week. The largest deal in the market was a $58mm purchase of Summit Veterinary Pharmaceuticals by Swedencare. Bluebird received a rival offer from Ayrmid, the owner of Gamida Cell.

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



Source: S&P, CapitalIQ

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

Bluebird bio Receives Rival M&A Bid Worth 50% Higher Than Carlyle-SK Offer

Angus Liu, *FiercePharma*, Mar 28, 2025 (excerpt)

A rival bidder has emerged to acquire struggling gene therapy specialist bluebird bio. Ayrmid has offered to buy bluebird for $4.5-apiece upfront, plus a one-time contingent value right (CVR) of $6.84 per share tied to a sales milestone, bluebird said Friday.

The upfront tag is 50% higher than the $3-per-share selling price that bluebird has previously penned with Carlyle and SK Capital Partners. That private equity duo's buyout offer also includes a $6.84-per-share CVR.

For now, bluebird's board has not changed its mind and the company remains bound by the original merger agreement. But it's willing to look at the new unsolicited non-binding written proposal.

"Consistent with its fiduciary duties, the bluebird Board of Directors is carefully reviewing the Ayrmid proposal in consultation with its legal and financial advisors," the Massachusetts biopharma said Friday.

A higher price would be good news for bluebird, as the Carlyle-SK offer valued the biotech at a discount, which highlights the challenge the company has faced in commercializing its gene therapies. Bluebird's cheap sale cast a dark shadow over the entire gene therapy field, which is undergoing an industry-wide reckoning.

Per bluebird's merger agreement with the private equity group, the company's board, on the condition of not breaching its non-solicitation obligations, may withdraw its recommendation for the deal if a more attractive offer emerges. In that case, bluebird's board must first provide the Carlyle-SK group a right to make counterproposals, according to a securities filing.

If bluebird eventually endorses a rival bid, it must pay a termination fee of $1.5 million, which the Ayrmid offer would more than cover. While the original deal values bluebird at about $29 million, the new offer is worth about $45 million upfront.

U.K. entity Ayrmid is known as the parent company of Gamida Cell, which is a cell therapy company using a nicotinamide technology to create allogeneic cell products for blood caners. Gamida sells Omisirge, an FDA-approved allogeneic hematopoietic progenitor cell therapy for use in patients 12 years and older with hematologic malignancies who are set to receive an umbilical cord blood transplantation.

Source: https://www.fiercepharma.com/pharma/bluebird-bio-receives-rival-ma-bid-worth-50-higher-carlyle-sk-offer

Alcon Gains Upper Hand in Aurion Power Struggle via Majority Stake, Removing CEO

James Waldron, *FierceBiotech*, Mar 27, 2025 (excerpt)

Eye care giant Alcon appears to have gained the upper hand in the ongoing power struggle with Aurion Biotech by securing a majority stake in the clinical-stage company and replacing its CEO.

The move will see Aurion "operate as a separate company with full support from Alcon to advance its clinical-stage allogeneic cell therapy asset, AURN001, into phase 3 for corneal edema secondary to corneal endothelial disease during the second half of 2025," an Alcon spokesperson told Fierce Biotech.

As part of the transaction, Alcon said in a March 26 release that it has promoted Aurion Chief Scientific Officer Arnaud Lacoste, Ph.D., to replace Greg Kunst as CEO "effective immediately."

The two companies have been locked in a struggle for months over Aurion's desire to list on the New York Stock Exchange. Alcon's subsidiary Alcon Research, which is an investor in Aurion, tried to block the IPO plans in court, arguing that its rights were being violated by Aurion's plans to go public. Aurion countersued, claiming that the investor was trying to trap the biotech so it could buy Aurion at a low price.

On one point raised by the lawsuit, regarding Alcon's ability to vote its full share of the 40% ownership stake it has had in Aurion since October 2024, the judge backed Alcon, saying the company "has the right to vote its full block of stock."

Deerfield Management, another one of Aurion's investors, came to the biotech's defense last month. The firm sued Alcon to stop what it described as "an unrelenting campaign to take over Aurion" at a cheaper price.

Deerfield's intervention was triggered by what the firm called a "Valentine's Day massacre," where Alcon had entered into an agreement to buy Aurion stock from fellow investor Petrichor Opportunities Fund on Feb. 14, a move that would give Alcon a majority of voting shares. Later that day, Aurion's executive chair of the board Thomas Frinzi resigned, and Petrichor and Alcon swapped out a Petrichor board appointee for an Alcon designee, which resulted in Alcon holding three of six total board seats, according to the suit.

Source: https://www.fiercebiotech.com/biotech/alcon-gains-upper-hand-aurion-power-struggle-majority-stake-removing-ceo

The Trump Antitrust Stance? M&A Pros are Still Guessing

Michael Bodley, *Pitchbook*, Mar 28, 2025 (excerpt)

The widespread uncertainty around the Trump administration's emerging stance on antitrust has sent M&A professionals searching for a regulatory roadmap.

Though some sizable deals have been finalized since President Donald Trump took office, investors say many others have been put on hold. How Trump's Federal Trade Commission and Department of Justice define a monopoly or unfair competitive advantage is still largely an open question. The common Wall Street view as recently as the fourth quarter of 2024 boiled down to expectations that Trump's appointees would approach antitrust enforcement far more lightly than their predecessors under former President Joe Biden and that deals would surge accordingly.

But that hypothesis has yet to be borne out, according to Zheng (Jonathan) Zhou, an M&A-focused partner at law firm Freshfields. From venture-backed acquisitions to private equity purchases to public company transactions, dealmakers say they're proceeding with caution until they have more clarity on antitrust enforcement. Still, prominent VCs including SoftBank have introduced new funds in the mold of Andreesen Horowitz's "American Dynamism" model, targeting manufacturing, education, supply chain and military sectors.

But there are already some signs that the Trump administration will apply ample scrutiny to sizable deals. **The FTC, for example, sued to stop the $627 million purchase of healthcare startup Surmodics by GTCR, a private equity firm**. Regulators are also looking at deals among public companies, like Hewlett Packard Enterprise's $14 billion proposed acquisition of Juniper Networks, which the DOJ sued to block in January.

At the same time, there have been substantial staffing changes within the US regulatory agencies. Last week, Trump fired two Democratic FTC commissioners with no clear replacement. (Those individuals are suing Trump, accusing him of executive overreach.) And the Securities and Exchange Commission is reportedly moving to slash at least 10% of its workforce.

Not everyone, however, is preoccupied with the new administration's antitrust agenda. "Anyone who was acting surprised wasn't paying much attention to the current administration's viewpoints," said Justin Abelow, a managing director at Houlihan Lokey who works on PE deals.

There have been more than 1,500 US M&A deals struck this year to date as the first quarter comes to a close, according to PitchBook data. That's not on pace with the 8,387 transactions recorded in Q1 2024. Indeed, other factors may be bigger culprits when it comes to the sluggish M&A in 2025. Interest rates remain relatively high, and tariffs are roiling public and private markets. Geopolitical conflict isn't stopping either. "If you're drawing a decision tree for the market, do you have a close nexus to the global supply chain?" Abelow said. "If the answer is yes, take a nice vacation."

Source: https://pitchbook.com/news/articles/the-trump-antitrust-stance-m-a-pros-are-still-guessing

Trump Turbulence Stalls Large Pharma and Biotech Deals, Bankers Say

Sabrina Valle, *Reuters*, Mar 26, 2025 (excerpt)

NEW YORK, March 26 (Reuters) - Large deals involving pharmaceutical and biotech companies are stalling as executives grapple with mercurial White House economic policies that have roiled markets and set off a global trade war, according to four top healthcare investment bankers.

The excitement late last year over U.S. President Donald Trump's election victory and prospects for a subsequent flurry of mergers and acquisition deals have quickly faded, they say.

The political uncertainty is pushing some deals out by a few months or even quarters, said the four bankers, who lead healthcare deals at some of the most active U.S. M&A banks.

C-suite meetings scheduled to talk about company valuations and price negotiations are now spent guiding bewildered executives through Trump's shifting policy moods, whether they directly impact their companies or not.

"They say 'Gosh, I didn't see that coming.' Or, 'We're having tariffs, we're not having tariffs. We're having tariffs, we're not having tariffs,'" said one of the top healthcare dealmakers.

"It's a massive distraction factor for CEOs," he said. "I try to get off the topic, because what do I have to add to it? It doesn't get us anywhere."

He and the other bankers interviewed by Reuters asked not to be identified so they can freely criticize the government without fear of retribution. The White House did not respond to a request for comment.

It's not tariffs and stock market volatility that have bankers most worried, they said. Trump's decision to install a vaccine skeptic as health secretary, dismiss thousands of employees of the U.S. Food and Drug Administration and other agencies, push for cuts to drug prices and slash federal research grants all have the potential to erode revenue and reduce the future pipeline for new drugs.

Smaller healthcare deals should still drive M&A growth this year, bankers say. But fewer or smaller deals can indicate economic uncertainty, lack of capital to finance businesses, or less confidence in future growth prospects, the bankers and analysts said.

Source: https://www.reuters.com/business/healthcare-pharmaceuticals/trump-turbulence-stalls-large-pharma-biotech-deals-bankers-say-2025-03-26/

Industry Update

HHS Announces Transformation to Make America Healthy Again

HHS Press Release, Mar 27, 2025 (excerpt)

Today, the U.S. Department of Health and Human Services (HHS) announced a dramatic restructuring in accordance with President Trump's Executive Order, “Implementing the President’s ‘Department of Government Efficiency’ Workforce Optimization Initiative.”

The restructuring will address this and serve multiple goals without impacting critical services. First, it will save taxpayers $1.8 billion per year through a reduction in workforce of about 10,000 full-time employees who are part of this most recent transformation. When combined with HHS’ other efforts, including early retirement and Fork in the Road, the restructuring results in a **total downsizing from 82,000 to 62,000 full-time employees**.

Secondly, it will streamline the functions of the Department. Currently, the 28 divisions of the HHS contain many redundant units. The restructuring plan will consolidate them into 15 new divisions, including a new Administration for a Healthy America, or AHA, and will centralize core functions such as Human Resources, Information Technology, Procurement, External Affairs, and Policy. Regional offices will be reduced from 10 to 5.

Third, the overhaul will implement the new HHS priority of ending America’s epidemic of chronic illness by focusing on safe, wholesome food, clean water, and the elimination of environmental toxins. These priorities will be reflected in the reorganization of HHS.

Finally, the restructuring will improve Americans’ experience with HHS by making the agency more responsive and efficient, while ensuring that Medicare, Medicaid, and other essential health services remain intact.

“We aren't just reducing bureaucratic sprawl. We are realigning the organization with its core mission and our new priorities in reversing the chronic disease epidemic,” HHS Secretary Robert F. Kennedy, Jr. said. “This Department will do more – a lot more – at a lower cost to the taxpayer.”

Source: https://www.hhs.gov/about/news/hhs-restructuring-doge.html

Kennedy's 'MAHA' Quest Begins: 10,000 Jobs Expected to Be Cut at Health Agencies

Berkeley Lovelace Jr., Brandy Zadrozny and Corky Siemaszko, *NBC News*, Mar 28, 2025 (excerpt)

Thousands of federal workers were bracing for pink slips Friday as Health and Human Services Secretary Robert F. Kennedy Jr. begins dismantling the sprawling federal agency responsible for protecting America's health.

Some 10,000 full-time jobs were on the chopping block as part of the White House's "reduction in force" plan to effectively shutter or downsize a number of divisions under the HHS umbrella, including virtually eliminating some offices tasked with tackling HIV and improving minority health.

HHS oversees 13 agencies, including the Centers for Disease Control and Prevention, the Food and Drug Administration and the National Institutes of Health. Overall, the cuts will shrink the health department's workforce from 82,000 to 62,000 when combined with its earlier layoffs, Andrew Nixon, a senior spokesperson for HHS, said Thursday.

Federal health workers, who spoke to NBC News on the condition of anonymity because they weren't authorized to speak to the media, said it's likely to get ugly. "No matter what happens, this is going to be a bad day," one CDC official said. "It feels like we're participating in the 'Hunger Games' reaping."

An endangered FDA worker said they were told that if they're not laid off on Friday to take their laptops home in the event they get a termination notice over the weekend. "Our director said our center would be heavily impacted and the RIF (reduction in force) notices are going out this afternoon into the weekend," a CDC worker in the Division of HIV Prevention said.

And a worker at the Centers for Medicare and Medicaid Services said employees were told to expect "layoffs of large number" at the agency's Office of Minority Health, a division focused on eliminating health disparities.

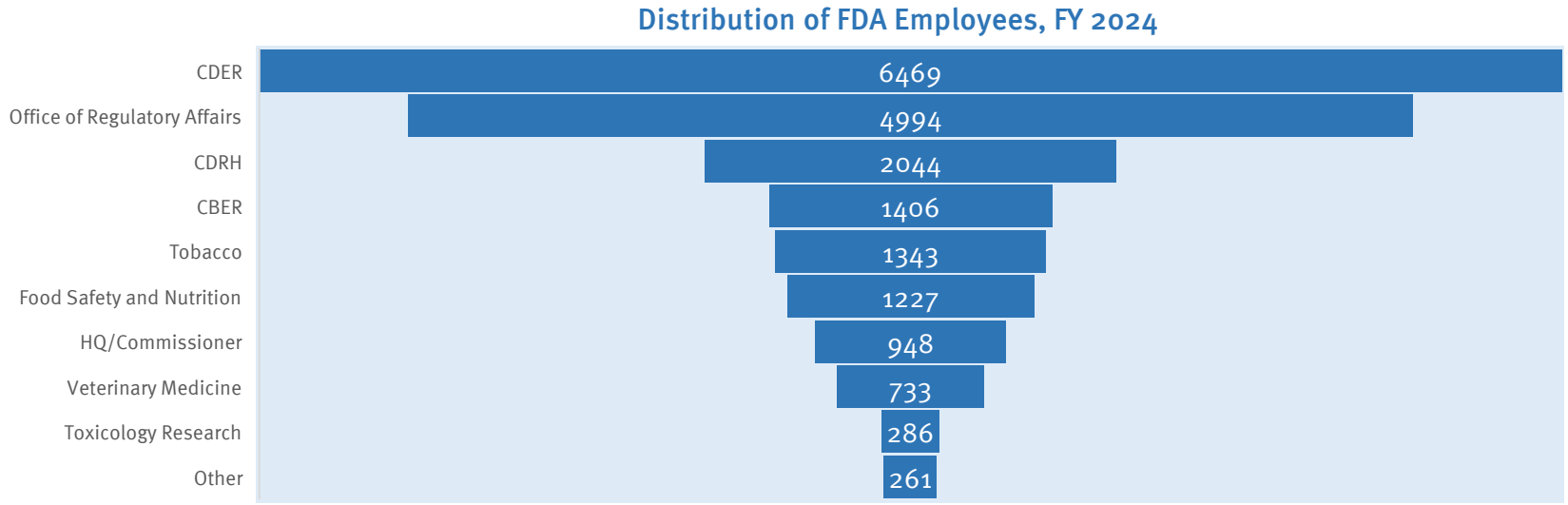
The layoffs add to growing evidence that Kennedy, who tried to strike a moderate tone during his Senate confirmation, is set to pursue an agenda that could radically reshape public health across the U.S.

Source: https://www.nbcnews.com/health/health-news/hhs-kennedy-health-agencies-mass-layoffs-rcna198549

How Meaningful Are the Cuts at FDA?

As is evident from the employee distribution chart below, most of the FDA's personnel goes for the regulation and approvals of drugs. Another big chunk of the employees and budget are for the regulation of human foods. There is also substantial budget allocated to the regulation of tobacco products and animal drugs. With 3,500 personnel cut in the latest HHS announcement and another 1,000 departures (estimated) from the recent voluntary resignation program, we would look at taking the agency from 19,700 people to 15,200. That's a 23% cut.

HHS has emphasized that the cuts are not likely to impact the FDA's ability to regulate and approve drugs; in fact, most of the CDER and CBER employees are paid for by user fees so it would be tough to cut there. Looking at the chart below if one were to spare CBER, CDRH and CDER, you would be looking at a 44% cut to all other functions. That doesn't sound too bad until you look at what the largest remaining function (Office of Regulatory Affairs) actually does. ORA is responsible for inspecting manufacturing sites, screening imported goods for safety and responding to food emergencies with recalls. This function has been chronically understaffed before, leading to delayed inspections and slower drug approvals, shortages of generic drugs and the like. Let's say, hypothetically, you wanted to keep ORA and not touch it, nor touch CDER, CBER and CDRH. You would then need to cut more than 90% of all other FDA jobs which would wipe out the agency's ability to regulate animal medicines, tobacco and foods.



Source: https://web.archive.org/web/20241130125725/https://www.fda.gov/media/176925/download?attachment

Peter Marks Resigns from FDA

In his resignation letter, Dr. Peter Marks cited 'misinformation and lies' from Health and Human Services Secretary RFK Jr.

Liz Essley Whyte, *Wall Street Journal*, March 28, 2025 (excerpt)

The Food and Drug Administration's top vaccine official has been pushed out, according to people familiar with the matter.

Dr. Peter Marks, who played a key role in the first Trump administration's Operation Warp Speed to develop Covid-19 vaccines, stepped down Friday. He submitted his resignation after a Health and Human Services official earlier in the day gave him the choice to resign or be fired, people familiar with the matter said.

The letter was addressed to acting FDA Commissioner Sara Brenner. His resignation takes effect April 5, the letter said.

"If Peter Marks does not want to get behind restoring science to its golden standard and promoting radical transparency, then he has no place at FDA under the strong leadership of Secretary Kennedy," an HHS official said.

Marks, who has been with the FDA since 2012, has led its division responsible for overseeing vaccines, biotech drugs and blood products since 2016. Part of the division's role is making sure vaccines work and are safe.

"It has become clear that truth and transparency are not desired by the Secretary, but rather he wishes subservient confirmation of his misinformation and lies. My hope is that during the coming years, the unprecedented assault on scientific truth that has adversely impacted public health in our nation comes to an end."

Peter Marks, M.D., Ph.D.
Former Director
Center for Biologics Evaluation and Research
U.S. Food and Drug Administration

Source: https://www.wsj.com/politics/top-vaccine-official-out-at-fda-f39a5a16

Peter Marks Commentary on His Efforts with HHS Secretary on Vaccines

Over the past 13 years I have done my best to ensure that we efficiently and effectively applied the best available science to benefit public health. As you are aware, I was willing to work to address the Secretary's concerns regarding vaccine safety and transparency by hearing from the public and implementing a variety of different public meetings and engagements with the National Academy of Sciences, Engineering, and Medicine. However, it has become clear that truth and transparency are not desired by the Secretary, but rather he wishes subservient confirmation of his misinformation and lies.

My hope is that during the coming years, the unprecedented assault on scientific truth that has adversely impacted public health in our nation comes to an end so that the citizens of our country can fully benefit from the breadth of advances in medical science. Though I will regret not being able to be part of future work at the FDA, I am truly grateful to have had the opportunity to work with such a remarkable group of individuals as the staff at FDA and will do my best to continue to advance public health in the future.

Sincerely,

Peter Marks

Peter Marks, MD, PhD

Marks does not pull his punches. Unusual to see such stark language even in a resignation letter.

Will Pharma Tariffs Achieve their Goals?

Marta Wosińska, *Brookings*, Mar 27, 2025 (excerpt)

Tariffs, which are taxes on imported goods, are a key part of President Trump's policy agenda. Pharmaceuticals are among the sectors targeted for tariffs. The administration has highlighted at least two objectives for tariffs on pharmaceuticals: securing U.S. drug supply chains by onshoring drug production and creating U.S. manufacturing jobs.

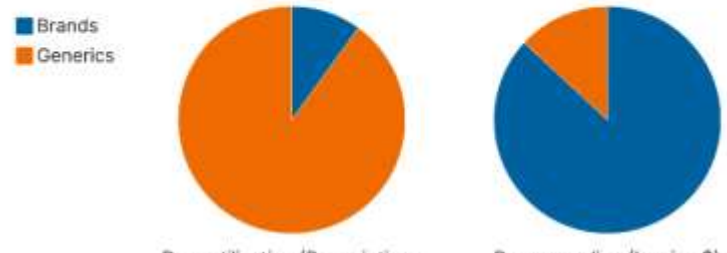
Understanding the impact of tariffs on pharmaceuticals is important because of the role prescription drugs play in the lives of Americans—61% of American adults (157M) and 20% of children (15M) fill at least one prescription each year through retail or mail pharmacies. Many of the same patients also get drugs administered in virtually all inpatient hospital stays. And millions of patients receive physician-administered drugs in the outpatient setting, for conditions like cancer or autoimmune diseases.

At the time of writing this article, there are two potential versions for sector-wide pharmaceutical tariffs. One is a 25% across-the-board tariff on pharmaceuticals. The other comes in the form of not yet defined reciprocal tariffs that would reflect any subsidies, including tax treatments, that foreign governments use to support specific domestic industries. These proposed tariffs would supplement tariffs already in place on all Chinese products, set at 20% for pharmaceuticals, and 25% tariffs on Canadian and Mexican products.

When new drugs come to market, they benefit from market exclusivity that prevents others from making copies primarily because of patents. A branded drug may need to compete with other brands, but the level of competition is lower than when they face exact copycats. Once market exclusivity ends, generic and biosimilar versions can come on the market: generic for small molecule drugs, and biosimilar for biologic drugs. Of the about 257 large-molecule biologic drugs, about 6% have biosimilar competition. Of the about 2,900 approved small drug molecules, about half have generic competition. Within a year or two of generic entry, prices drop precipitously leading the off-patent branded version molecule to exit the market. Because older drugs are effective for many conditions and because of their price, Americans primarily take small molecule generic drugs. Generics represent 92% of U.S. retail and mail pharmacy prescriptions (Figure 1). They also represent about three-quarters of volume (doses) in the smaller hospital setting… **What is relevant for segment-specific tariffs is that only FDF and API products are specific to pharmaceuticals, with the rest of the supply chain (marked in orange in Figure 2) shared with other industries.** Excipients, such as starch, lactose, or titanium dioxide, are used in foods and cosmetics. Key starting materials and enabling chemicals are all fine chemicals with many industrial uses.

Source: https://www.brookings.edu/articles/pharmaceutical-tariffs-how-they-play-out/

Figure 1: Role of generics in pharmacy drug spending and utilization



Center on Health Policy at Brookings

Source: IQVIA (2024), The U.S. Generic and Biosimilar Medicines Savings Report
Note: Retail and mail pharmacy spending and utilization; does not include physician-administered drugs

Figure 2: Typical drug supply chain for small molecule drugs

Note: Items marked in orange are not used exclusively in drug supply chains. For biologics, steps marked with * would be replaced with cell culture and purification, all done in one facility.

More on Pharma Tariffs (continued)

Many observers will raise higher prices as an argument against tariffs. I take a more nuanced approach—we may have to accept higher prices for generic drugs if we want to have resilient supply chains.

However, I am worried that without further policy interventions, tariffs will not make supply chains more resilient. In fact, I am worried that the resilience of many supply chains, already weak for drugs like sterile injectable generics, will be significantly challenged.

Of course, the scope and level of tariffs will matter for how they affect specific markets in the short and long run. It will also depend on the structure of specific markets, with generic sterile injectable drugs at the most risk of disruption that might lead to shortages. Most importantly, the impact will depend on what other policy actions the administration and Congress might take to buffer the supply chain.

This paper is not intended to provide a comprehensive policy proposal for how to supplement the tariffs, but four main themes arise if the administration intends to move forward with across-the-board pharmaceutical tariffs affecting branded and generic drugs alike.

First, the administration should add pressure valves to prevent shortages. This is important because generic margins will be threatened, leading manufacturers to pull unprofitable products from the market. A big factor here is the limited ability of manufacturers to pass on tariffs onto buyers. Some of it has to do with private contracts, but it also relates to the congressionally mandated Medicaid inflation rebates on multisource drugs and the spillover they have on sales to 340B entities. Another policy to consider is substantially delaying tariffs on API used by domestic manufacturers, with it improving their profitability.

Second, the administration should increase, not decrease, FDA's capacity to oversee drug manufacturing. One reason is that generic drug margin squeeze may lead manufacturers to cut costs by cutting corners, which, especially if coupled with weakened FDA oversight, could lead to a higher rate of substandard drugs being shipped to American patients. Another reason is that any onshoring of facilities will increase the existing demand for FDA services—services that are critical for assuring that facilities are set up to consistently manufacture products to specification, with that assuring the safety of drugs that American patients take.

Third, the administration should directly finance generic drug onshoring, in recognition that tariffs alone will not create a sufficiently strong business case to attract private investment in pharmaceutical infrastructure. Identifying sources of funding for such initiatives can be challenging. However, here, branded drug tariffs will likely generate significant revenue, which could then be used to stimulate onshoring of generics.

The fourth point is perhaps the most challenging—de-risking drug supply chains from China will be significantly more challenging, if not counterproductive, without collaboration with India and Europe.

Source: https://www.brookings.edu/articles/pharmaceutical-tariffs-how-they-play-out/

Mineralys Therapeutics Announces Late-Breaking Data from Advance-HTN Pivotal Trial of Lorundrostat in Uncontrolled and Resistant Hypertension Presented at ACC

Press Release, March 29, 2025

Mineralys Therapeutics, Inc. (Nasdaq: MLYS), a clinical-stage biopharmaceutical company focused on developing medicines to target hypertension, chronic kidney disease (CKD), obstructive sleep apnea (OSA) and other diseases driven by dysregulated aldosterone, today announced detailed results from the Phase 2 Advance-HTN trial, one of two pivotal trials evaluating lorundrostat in patients with confirmed uncontrolled hypertension (uHTN) or resistant hypertension (rHTN). In the trial, lorundrostat 50 mg demonstrated a 15.4 mmHg absolute reduction and a 7.9 mmHg placebo-adjusted reduction at week 12. Additionally, lorundrostat demonstrated a favorable safety and tolerability profile, with modest changes in potassium, sodium and eGFR, and a low discontinuation rate.

“With the recent announcement of data from our two pivotal trials, we now have a comprehensive dataset demonstrating the robust and consistent blood pressure reductions of lorundrostat in two distinct but complementary patient populations—real-world setting in Launch-HTN, and those with optimally treated yet uncontrolled hypertension in the specialist setting in Advance-HTN,” stated Jon Congleton, Chief Executive Officer of Mineralys Therapeutics. “These findings underscore lorundrostat’s clinical utility across diverse care settings and also provide critical insights for both primary care providers, who manage the vast majority of hypertension patients, and specialists, who treat the most complex cases. We are excited about the potential impact lorundrostat could have as a novel treatment to address a significant unmet need in hypertension care.”

“Twenty-four-hour ambulatory blood pressure monitoring is the gold standard for assessing the true impact of an antihypertensive therapy, as it provides a more comprehensive picture of blood pressure control beyond the office setting, including overnight readings,” stated Luke Laffin, M.D., co-director of the Center for Blood Pressure Disorders in the Heart, Vascular & Thoracic Institute at Cleveland Clinic and the study’s lead author. “Along with rigorous evaluations in the Advance-HTN trial, the double-digit drop in blood pressure readings observed with lorundrostat in this trial are particularly notable given the complex characteristics of the patient population, which included a high proportion of individuals who have been historically underrepresented in hypertension clinical trials and who face a disproportionate burden of treatment-resistant hypertension.”

Following the recently announced positive topline data from both Advance-HTN and Launch-HTN pivotal trials, detailed results from Advance-HTN were presented in a late-breaking session at the American College of Cardiology’s Annual Scientific Session & Expo (ACC.25) on Saturday, March 29, 2025, at 1:30 p.m. CT.

Source: https://www.globenewswire.com/news-release/2025/3/29/3051760/0/en/Mineralys-Therapeutics-Announces-Late-Breaking-Data-from-Advance-HTN-Pivotal-Trial-of-Lorundrostat-in-Uncontrolled-and-Resistant-Hypertension-Presented-at-the-American-College-of-C.html

Enzyme Engineering Opens Door to Novel Therapies for Parkinson's, Cancers and Other Hard-to-Target Protein Diseases

Scripps Press Release, March 26, 2025

Scientists have long struggled to target proteins that lack defined structure and are involved in cancer, neurodegenerative disorders like Parkinson's disease, and other serious illnesses. Now, a new study from Scripps Research demonstrates a proof of concept for a new strategy: engineering proteases—enzymes that cut proteins at specific sites—to selectively degrade these elusive targets with high precision in the proteome of human cells.

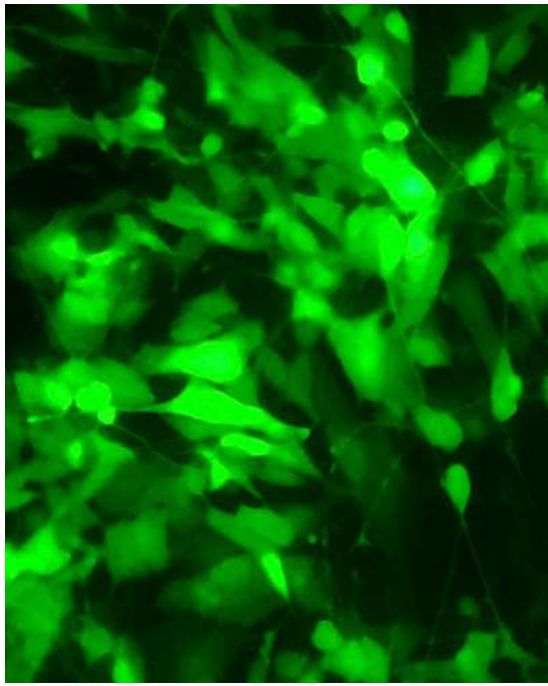
Published on March 24, 2025, in the *Proceedings of the National Academy of Sciences*, the study shows how to **reprogram a protease from botulinum toxin to target α-Synuclein**—a protein with unstructured regions used here as a model. The study marks one proof point in a broader approach that could be applied to a wide range of targets across the proteome.

"This work highlights how we can use the power of laboratory evolution to engineer proteases that offer a new way to treat diseases caused by hard-to-target proteins," says senior author Pete Schultz, the President and CEO of Scripps Research, where he also holds the L.S. "Sam" Skaggs Presidential Chair. "It's an exciting step toward developing new therapeutic strategies for diseases that lack effective treatments."

The research builds on botulinum toxin, a bacterial protein best known for its use in Botox, a medication utilized for cosmetic purposes and certain medical conditions. This toxin naturally contains a protease. In its original form, the protease only targets SNAP-25—a protein essential for transmitting signals between nerve cells. By degrading SNAP-25, botulinum toxin disrupts nerve signaling, leading to the temporary paralysis effect seen after Botox treatments.

To reprogram this precision for α-Synuclein, the research team modified the enzyme using directed evolution, a laboratory process that involves introducing mutations and selecting variants with improved function over multiple cycles. The result: Protease 5. The challenge, however, wasn't just reprogramming the protease to target α-Synuclein—it was ensuring that it attacked only α-Synuclein and nothing else. Past attempts to evolve proteases for therapeutic use have resulted in enzymes that targeted too broad a range of proteins, cleaving multiple unintended molecules and causing toxicity in cells.

"α-Synuclein is an incredibly hard protein to target because it doesn't have a stable structure," says first author Philipp Sondermann, a postdoctoral fellow at Scripps Research. "Most drugs work by latching onto structured proteins, but α-Synuclein is more like a shifting tangle."



α-Synuclein modulates neurite outgrowth as seen here in human cells, potentially suggesting involvement of the protein in learning processes of the brain. However, dysregulated α-Synuclein leads to neurotoxic aggregates associated with incurable Parkinson's disease. Credit: Scripps Research

Source: https://www.scripps.edu/news-and-events/press-room/2025/20250326-schultz-enzyme-engineering.html

Gene-Modified Pig-to-Human Liver Xenotransplantation

KF Dou and colleagues, *Nature*, March 26, 2025

The shortage of donors is a major challenge for transplantation; however, organs from genetically modified pigs can serve as ideal supplements. Until now, porcine hearts and kidneys have been successively transplanted into humans.

In this study, heterotopic auxiliary transplantation was used to donate a six-gene-edited pig liver to a brain-dead recipient. The graft function, haemodynamics, and immune and inflammatory responses of the recipient were monitored over the subsequent 10 days.

Two hours after portal vein reperfusion of the xenograft, goldish bile was produced, increasing to 66.5 ml by postoperative day 10. Porcine liver-derived albumin also increased after surgery. Alanine aminotransferase levels remained in the normal range, while aspartate aminotransferase levels increased on postoperative day 1 and then rapidly declined.

Blood flow velocity in the porcine hepatic artery and portal and hepatic veins remained at an acceptable level. Although platelet numbers decreased early after surgery, they ultimately returned to normal levels. Histological analyses showed that the porcine liver regenerated capably with no signs of rejection.

T cell activity was inhibited by anti-thymocyte globulin administration, and B cell activation increased 3 days after surgery and was then inhibited by rituximab. There were no significant peri-operative changes in immunoglobulin G or immunoglobulin M levels. C-reactive protein and procalcitonin levels were initially elevated and then quickly declined. The xenograft remained functional until study completion.

Source: https://www.nature.com/articles/s41586-025-08799-1

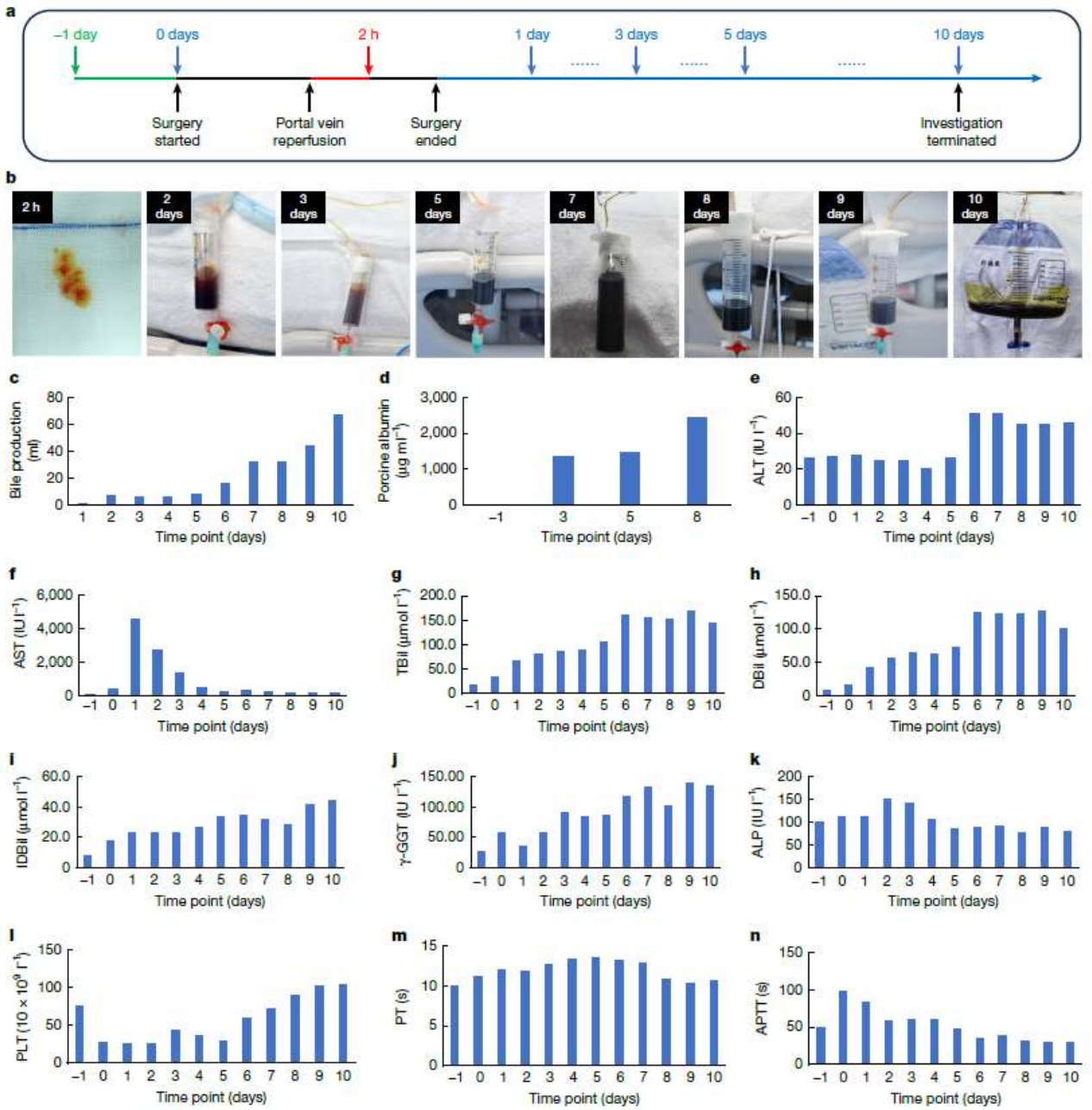


Fig. 2 | Xenograft function. **a**, Schematic depiction of the study, showing various time points of the investigation. **b**, Photographs of the bile secreted from the xenograft at different time points throughout the study. **c**,**d**, Amounts of bile (**c**) and porcine albumin (**d**) produced by the xenograft at different time points throughout the study. **e**–**k**, Amounts of ALT (**e**), AST (**f**), total bilirubin (**g**), direct bilirubin (**h**), indirect bilirubin (**i**), γ-GGT (**j**) and alkaline phosphatase (**k**) in the recipient's serum at different time points throughout the study. **l**–**n**, Amounts of PLT (**l**), PT (**m**) and APTT (**n**) of the recipient at different time points throughout the study. **c**–**n** contain one biological and technical repetition. DBil, direct bilirubin; IDBil, indirect bilirubin; IU, international unit; TBil, total bilirubin.

Scientists Transplant a Gene-Edited Pig Liver Into a Person

Alice Park, *Time*, March 26, 2025

Alice Park, Time

In the past year, doctors have performed history-making transplants, placing genetically modified pig kidneys and pig hearts into patients. Now, a group of doctors and scientists in China report they have done the same with a pig liver.

In a study published in *Nature*, the group describes transplanting a gene-edited pig liver into a brain-dead patient. At the request of the patient's family, the study was terminated after 10 days and the pig liver was removed. The patient's original liver was not removed, so the experiment served as a way to test whether a pig liver could supplement the function of failing livers for patients waiting for a transplant.

"The transplanted pig liver successfully secreted bile and produced liver-derived albumin, and we think that is a great achievement," said Dr. Lin Wang, a surgeon at Xijing Hospital, Fourth Military Medical University and one of the senior authors of the paper, during a briefing. "It means the pig liver could survive together with the original liver in a human being—and would give additional support to an injured liver, maybe, in the future."

Pigs are promising sources of organs, but the human immune system rejects transplanted pig tissue. Scientists have been getting around this by genetically modifying the pigs that provide the organs. The donor liver in this case came from a pig that had received six modifications to certain genes in order to remove major pig proteins that would have led to rejection; the editing technique also added genes that made the liver appear more human to immune cells.

Earlier this year, a surgical team at the University of Pennsylvania reported connecting a brain-dead patient to a gene-edited pig liver that remained outside of the patient's body, but the results were not published in a peer-reviewed journal. In the Chinese case, Wang and his team transplanted the liver into the patient, connecting major blood vessels to monitor how well it could produce key compounds like bile and albumin.

Wang said the blood flow to and from the liver, as well as measures of things like bile and albumin production, were encouraging, even if not all functions were sufficient enough to completely mimic a human liver. There were changes in platelets and clotting functions soon after the transplant, but those seemed to resolve after a few days. The pig liver began producing bile two hours after the transplant, and levels of albumin began increasing as well following the operation. When the team analyzed the liver after removing it 10 days later, there were "no signs of immune rejection," they wrote in the paper.

Source: https://time.com/7271780/scientists-pig-liver-transplant/

Optimal Dietary Patterns for Healthy Aging

Gausch-Ferré and colleagues, *Nature Medicine*, March 24, 2025

As the global population ages, it is critical to identify diets that, beyond preventing noncommunicable diseases, optimally promote healthy aging. Here, using longitudinal questionnaire data from the Nurses' Health Study (1986–2016) and the Health Professionals Follow-Up Study (1986–2016), we examined the association of long-term adherence to eight dietary patterns and ultraprocessed food consumption with healthy aging, as assessed according to measures of cognitive, physical and mental health, as well as living to 70 years of age free of chronic diseases. After up to 30 years of follow-up, 9,771 (9.3%) of 105,015 participants (66% women, mean age = 53 years (s.d. = 8)) achieved healthy aging. For each dietary pattern, higher adherence was associated with greater odds of healthy aging and its domains. The odds ratios for the highest quintile versus the lowest ranged from 1.45 (95% confidence interval (CI) = 1.35–1.57; healthful plant-based diet) to 1.86 (95% CI = 1.71–2.01; Alternative Healthy Eating Index).

When the age threshold for healthy aging was shifted to 75 years, the Alternative Healthy Eating Index diet showed the strongest association with healthy aging, with an odds ratio of 2.24 (95% CI = 2.01–2.50). Higher intakes of fruits, vegetables, whole grains, unsaturated fats, nuts, legumes and low-fat dairy products were linked to greater odds of healthy aging, whereas higher intakes of trans fats, sodium, sugary beverages and red or processed meats (or both) were inversely associated. Our findings suggest that dietary patterns rich in plant-based foods, with moderate inclusion of healthy animal-based foods, may enhance overall healthy aging, guiding future dietary guidelines.

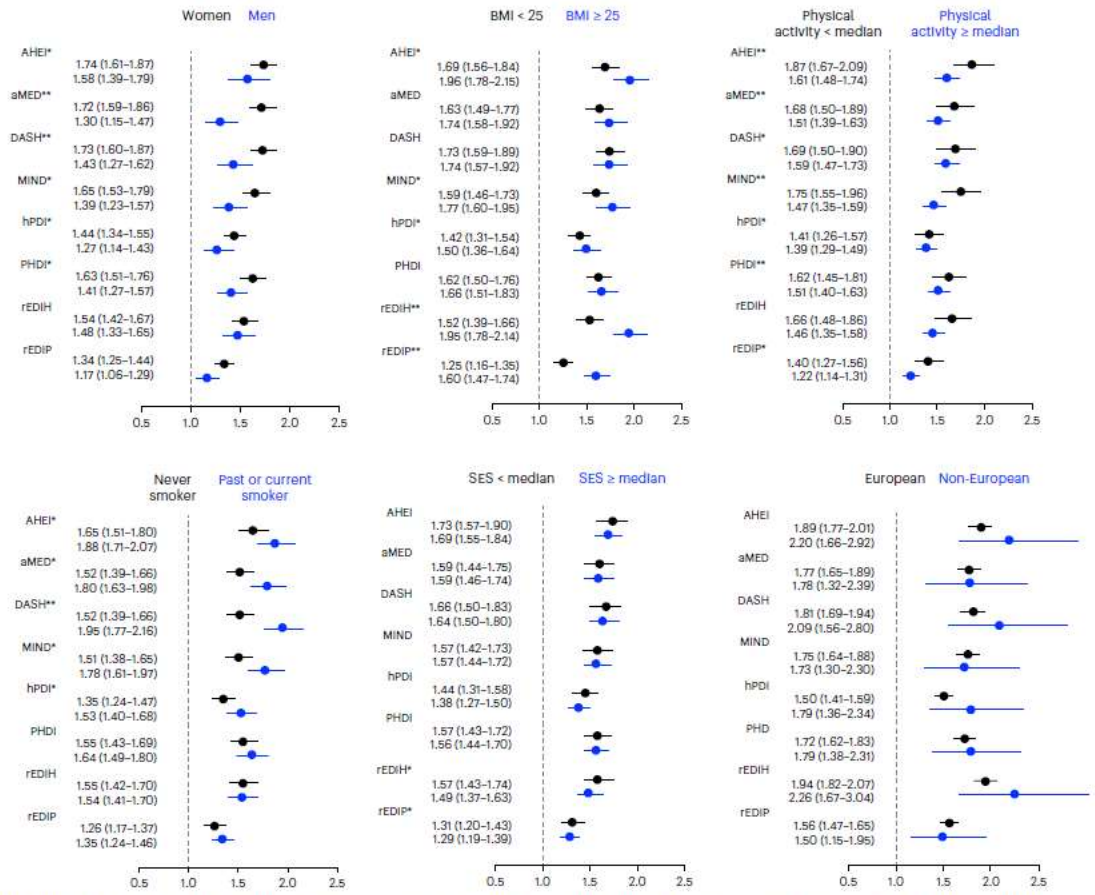


Fig. 5 | Subgroup analysis of the associations between average dietary pattern scores and healthy aging in the main pooled dataset (n = 105,015). The forest plots show the ORs comparing the 90th to the 10th percentile for each of the dietary patterns (visually represented by the centers of the error bars) and 95% CIs (visually represented by error bars). Logistic regressions were used to estimate the ORs and were adjusted for age at baseline (1986), cohort (sex), BMI (kg m^{-2}), ancestry (European, Asian, African-American, Other), smoking status (never, former, current smoker: 1–14 cigarettes per day, 15–24 cigarettes per day and ≥25 cigarettes per day), alcohol intake (g per day), physical activity (MET-h week^{-1}), multivitamin use ever (yes/no), family history of myocardial infarction (yes/no), family history of type 2 diabetes, family history of cancer, family history of dementia (yes/no), postmenopausal status (yes/no) and menopausal hormone use (no, past, or current hormone use; women only), SES at baseline, marital status (yes/no), living alone ever (yes/no) and history of depression (yes/no), excluding the stratified variable where applicable, in the pooled cohorts. ** two-sided P interaction <0.0001 (not adjusted for multiple comparisons). *Two-sided P interaction < 0.05 (not adjusted for multiple comparisons); sex, AHEI P = 0.022; MIND P = 0.001; hPDI P = 0.002; PHDI P = 0.0008; BMI, AHEI P = 0.001; MIND P = 0.024; and hPDI P = 0.015. For physical activity, DASH P = 0.0003; hPDI P = 0.0005; rEDIP P =0.023. For smoking, AHEI P = 0.005; aMED P = 0.010; MIND P = 0.0007; hPDI P = 0.002. For SES, rEDIH P = 0.019; rEDIP P = 0.023.

Source: https://www.nature.com/articles/s41591-025-03570-5

China Biotech Update

Hangzhou China, Skyline

Observations from a Trip to China

We visited a number of biotechs and VC's in China on a weeklong trip in the week of March 10th. This was a follow up trip from our visit in November 2024.

The last trip involved visits to Shanghai and Beijing. On this trip we spent time in Hangzhou, Suzhou and Shanghai. We spent a lot more time on this trip visiting VC's.

What was striking to us was how quickly things are changing in China. Sort of like watching a five-year-old grow, you could tell the difference in the country's biotech sector in just four months time.

Some of our key observations from the trip are:

1. Higher energy level and better mood overall in the Chinese biotech community – triggered by the recovery of the biotechs on the Hong Kong Stock Exchange.
2. Ironically, perhaps, this has been triggered by migration of money back to China from the NASDAQ following Trump's election. The U.S. has been increasingly seen as an unstable place to put money.
3. At the same time the Chinese government has made it clear that it will do what it can to support its biotech sector, although no dramatic pronouncements have been made.
4. The biotech areas of Suzhou felt little different than driving to see biotech companies in the Bay Area. Same type of facilities and smart people.
5. The energy level was particularly high in Hangzhou. This secondary Chinese city is the home of Deepseek and there was a lot of talk about other similarly very good startups in the city (see next page for some projects coming out of there). The city government has taken a "hands off" policy but has been putting up beautiful new buildings to house the many startups popping up across the city. We saw at least five really good biotechs in Hangzhou.


Hangzhou at Night

HANGZHOU CHINA 杭州

City of Innovation

Robot dogs join Hangzhou city's forest firefighting team

The forest fire brigade in Xihu district of Hangzhou, capital of East China's Zhejiang province, recently caused a real stir when it welcomed five new high-tech recruits in the form of robot dogs.

March 10, 2025

Chinese robots show skills

China will work to effectively combine digital technologies with its manufacturing and market strengths under the AI Plus initiative.

March 10, 2025

Hangzhou news program adds AI-generated hosts

A television channel in Hangzhou has launched an innovative newscast featuring AI-generated anchors, drawing significant attention and sparking discussions about the role of artificial intelligence in the media industry.

March 4, 2025

Hangzhou's BrainCo starts producing smart bionic prosthetics

BrainCo, one of the rising tech innovators in Hangzhou – capital of East China's Zhejiang province – has launched full production of its advanced bionic prosthetics.

February 26, 2025

Robot made by Hangzhou-based Unitree wows with kung fu moves

Leading robot developer Unitree Robotics recently revealed it had taken its humanoid robots to the next level of skills.

February 26, 2025

Hangzhou: The city behind DeepSeek's rise and why it's just the beginning

Why there could be 100x more DeepSeeks on the way

Baiguan: Hangzhou isn't just the home of DeepSeek; it's a city that thrives on innovation. While many know it as the birthplace of Alibaba (NYSE: BABA) and NetEase (NASDAQ: NTES), Hangzhou's tech ecosystem extends far beyond e-commerce and the internet. The city is a breeding ground for cutting-edge companies in AI, robotics, gaming, and hard tech

Hangzhou-based Star Vision to send robots to moon

Star Vision, an aerospace startup founded in Hangzhou, Zhejiang province, just three years ago, is set to contribute micro-exploration robots to China's Chang'e-8 mission, planned for 2028.

January 28, 2025

World's 1st emergency rescue robot, transport robot unveiled in China, operate from -20 C to 55 C

March 28, 2025

FIFA World Cup Asian qualifier to boost Hangzhou economy with record-high attendance

March 20, 2025

China's first zero-carbon metro line debuts in Hangzhou

January 9, 2025

Cyborg-like walking assistance device targets China's expanding elderly market

March 20, 2025

AI innovators head to Hangzhou for Win with AI+ Future Camp

February 27, 2025

Zero-magnetic therapy devices embrace new progress in Hangzhou

February 7, 2025

Source: https://www.ehangzhou.gov.cn/hz_technology.html, https://www.baiguan.news/p/deepseek-chinese-ai-startup-hangzhou-innovation-hub-alibaba-black-myth-unitree-brainco-population-inflow-talent-attraction-hukou-entrepreneurial-culture-government-policies

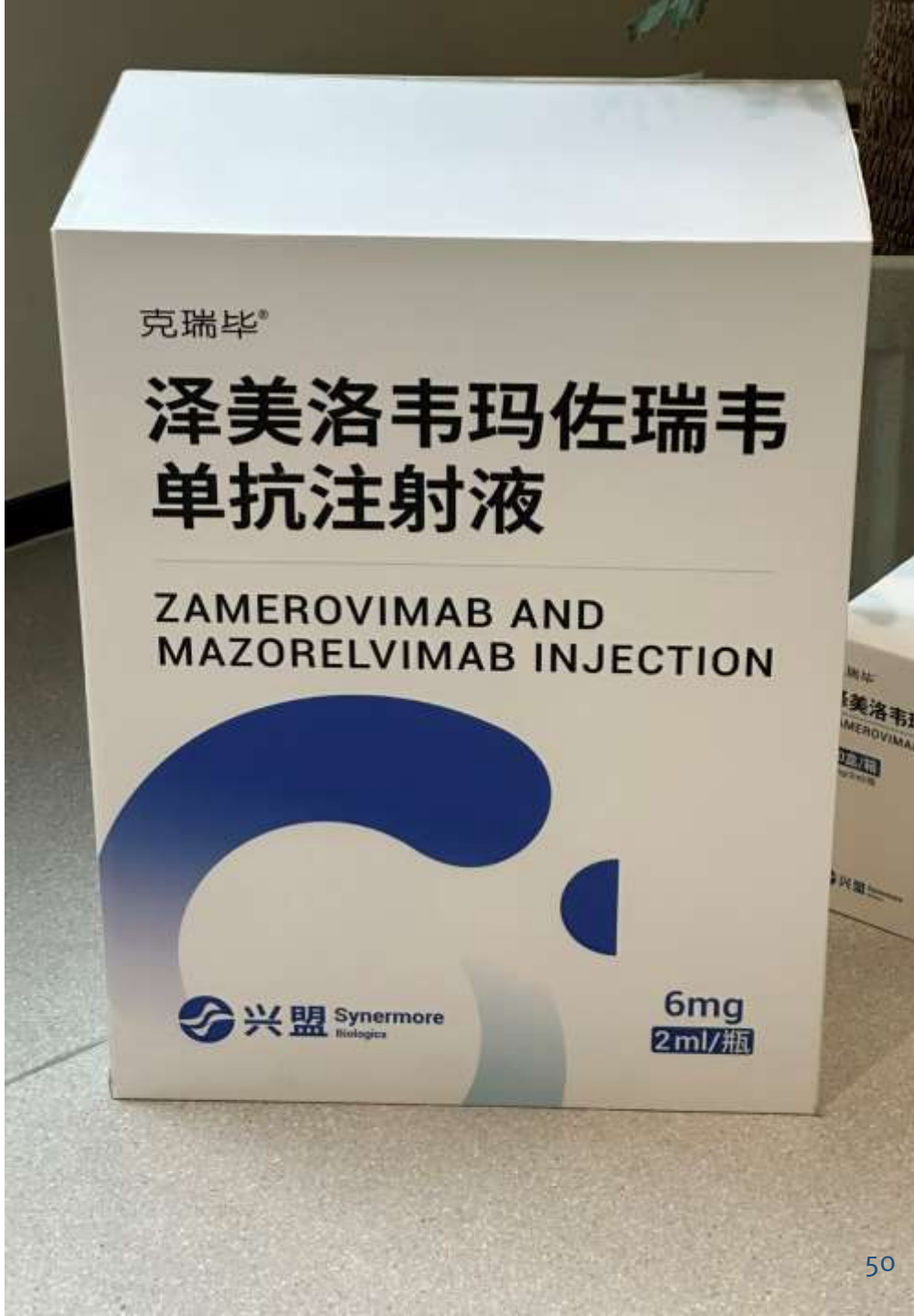
Observations from Our China Trip

6. A tangible improvement in the quality of the innovation stories in the last year. There has been a move away from relatively commoditized areas like antibodies to more biologically informed innovation across a wider range of modalities.
    - Just like the U.S. biotech ecosystem, Chinese biotechs are highly heterogenous. Some are a lot better than others.
    - The best biotechs tended to be funded by mainstream, name brand Chinese VC's such as Decheng Capital, OrbiMed China, Lilly Asia Ventures, Qiming and Tailong.
    - There just seemed to be more "really good" biotech stories – companies that could go public even on NASDAQ in a tough year or that had assets that a large pharma might want to acquire.
    - The average biotech we saw on the trip was closer to the leading edge of science relative to what we had seen in November.
7. At the very moment where fundraising the U.S. and Europe is at its most challenging, the spigots for Chinese biotech capital appear to be reopening:
    - Many biotechs reported fresh rounds of capital (none of which seem to get reported)
    - IPOs and follow-ons in the Hong Kong market are picking up, in part due to relaxation of listing rules under section 18A (see https://www.charltonslaw.com/hong-kong-law/listing-pre-revenue-biotech-companies/, https://www.kroll.com/en/insights/publications/valuation/valuation-insights-h2-2024/hong-kong-ipos-china-unicorns-new-listing-rules-chapter-18c).
    - The Shanghai STAR market remains largely closed to biotech.
8. The pace of interest from global pharma continues to rise. Many of the top VC's reported big pharma senior management "stop ins" in recent months.
9. Ever greater sophistication about U.S. "newco" type dealmaking. How to cut the deals and the like.
10. The China licensing market remains a "buyers market". There remain many more sellers than buyers in the market. The scale of the available pipeline is enormous.

Brand new building opened in March 2025 for tech / biotech startups: Sign on left reads Hangzhou High-tech Industrial Development Zone, Zhejiang Future Technology Smart Land Committee

Further Observations from China

1. We saw so much happening that was away from autoimmunity and oncology. Many companies were innovating in harder therapeutic areas which included women's health, ophthalmology, vaccines, and cardiovascular. First-in-class, high risk innovation stories were not hard to find.
2. Some of the companies we saw included:
    - A Chinese biotech that was well positioned to compete as the world's best evaporative dry eye company. While early, they had a 5 for 5 "cure" of dry eye. Disease gone with a novel approach.
    - A very strong SubQ drug for thyroid eye disease well into Phase 3 (Minghui).
    - A Chinese-backed gene therapy company with a credible shot a curing Stargardt Disease.
    - Hope Medicines with highly promising Phase 2 data for a new treatment for endometriosis.
    - A drug with Phase 2 data showing nice plaque reduction in atherosclerosis – holy grail stuff.
    - A Chinese biotech with a very strong, differentiated story for an anticoagulant backed by a five-person senior team out of Gilead.
    - A Chinese company with a very strong late-stage dataset in macrophage activation syndrome (MAS)
    - An oral GLP-1 in Phase 2b from Regor that avoids receptor internalization (similar to the Roche CT-966)
    - A Chinese biotech (Yoltech) with very good in vivo gene edited drugs targeting PCSK9, TTR, HAO1 etc. Good data in beta thal from an IIT study.
    - A Chinese company that is filing the first recombinant immunoglobulin for rabies.
    - A Chinese biotech with a credible shot on goal for a functional cure for HIV (in vivo CAR-t approach).



On the Oncology Front

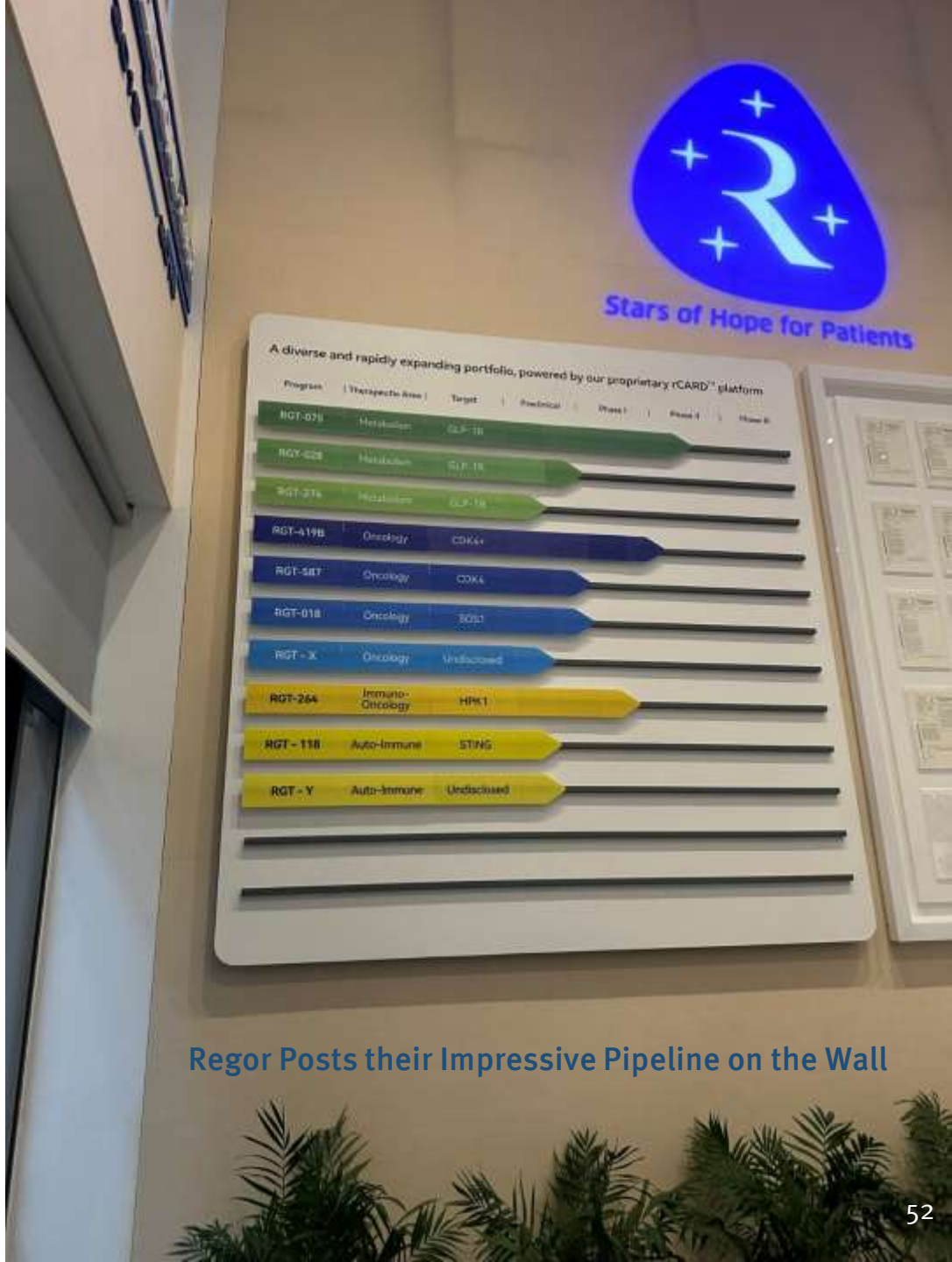
Some of the items we picked up in oncology included:

1. Whispers of very positive data coming up from upcoming readouts involve a PD1 x CTLA4 trial were fairly audible from multiple sources. In U.S. both Macrogenics and Xencor developing PD1 x CTLA4's. Word from China is that this could work well.
2. Whispers of stunning data coming up from PD-L1 ADC's also heard from two sources in China. Pfizer starting up a PDL1 ADC trial for PF-08046054 in China now; there are a number of others in Chinese pipelines.
3. Impressive data in late-stage CRC from Innovative Cellular Therapeutics (ICT).
4. The current PD1 x VEGF bispecific landscape feels like it is fragile in light of upcoming data releases.
5. We saw a lot more of the "same" – fast followers in fields like ADC's and PD1xVEGFs where companies were chasing known targets with technological or incremental targeting improvements. To this point, we visited a shopping mall in Shanghai which had seven coffee shops in one foodcourt. We asked our Chinese biotech friend who met us there for coffee if this was normal and had anything to do with biotech in the country. She laughed and said "yes, we let the competitors show up and fight it out – that's partly how we get to great drugs."
6. Phrontline is showing very good data with an EGFR x B7H3 TCE. In general, we saw lots of trispecific TCE's in cancer and immunology and lot of the same in ADC's (both Duality and VelaVigo had amazing pipelines in this area).
7. Impressive oncology pipelines at AlphaMab, Duality, LaNova, Regor and VelaVigo.
8. IMPACT Therapeutics incredibly excited by its PARP1 inhibitor being developed with Eikon Therapeutics.

On the Immunology Front

Some of the items we picked up in immunology included:

1. Discussion of results from IIT studies in China using CD19 CAR-t. The word is that no one is quite repeating Schett's data in China. Groups are seeing good initial responses but the idea of full "wipe out" of autoimmune diseases is not being replicated with CD19's was widely discussed. Parties are finding out that reducing the lymphodepletion dosing causes the CAR-t results to be substantially worse.
2. Perhaps the best data we've seen in China is from IASO with its BCMA CAR-t. They have seen multiple durable full remissions in myasthenia gravis.
3. There is a lot of interest in tuning CAR-t and many efforts underway. A promising company was Bioheng Therapeutics which is going after autoimmune with *in vivo* allogenetic CAR-t. They are apparently seeing solid results in IIT studies.
4. Widespread discussion of CD19 TCE's in IIT studies. The results seen in *NEJM* studies last year are being replicated in China although no one is claiming long-term durability of response.
5. A very strong oral peptide platform with multiple clinical shots on goal on important I&I targets like TNFa, TSLP, activins etc.
6. A Chinese company that is looking to leapfrog groups like Lycia and Biohaven in extracellular ASPGR degraders for autoimmune disease (coming at the problem in a new way).
7. A late-stage brain-penetrant TYK2 molecule that seemed well positioned to compete in the MS market (LYNK). LYNK also has what appears to be a late-stage credible competitor to RINVOQ®.
8. An impressive clinical stage SubQ FcRn with a completely novel scaffold (Staidson).



Regor Posts their Impressive Pipeline on the Wall

China Biotech is Not Monolithic

For all of the excitement of what we saw in China it's important to note that there is an increasing recognition among Western pharmas and newco entrepreneurs that not all Chinese science is great. Not all Chinese biotechs are doing great work. Not every China biotech is amazing. Despite monolithic vending machines, China is not a monolithic threat in biotech.

Some of the back channel talk we are hearing indicates:

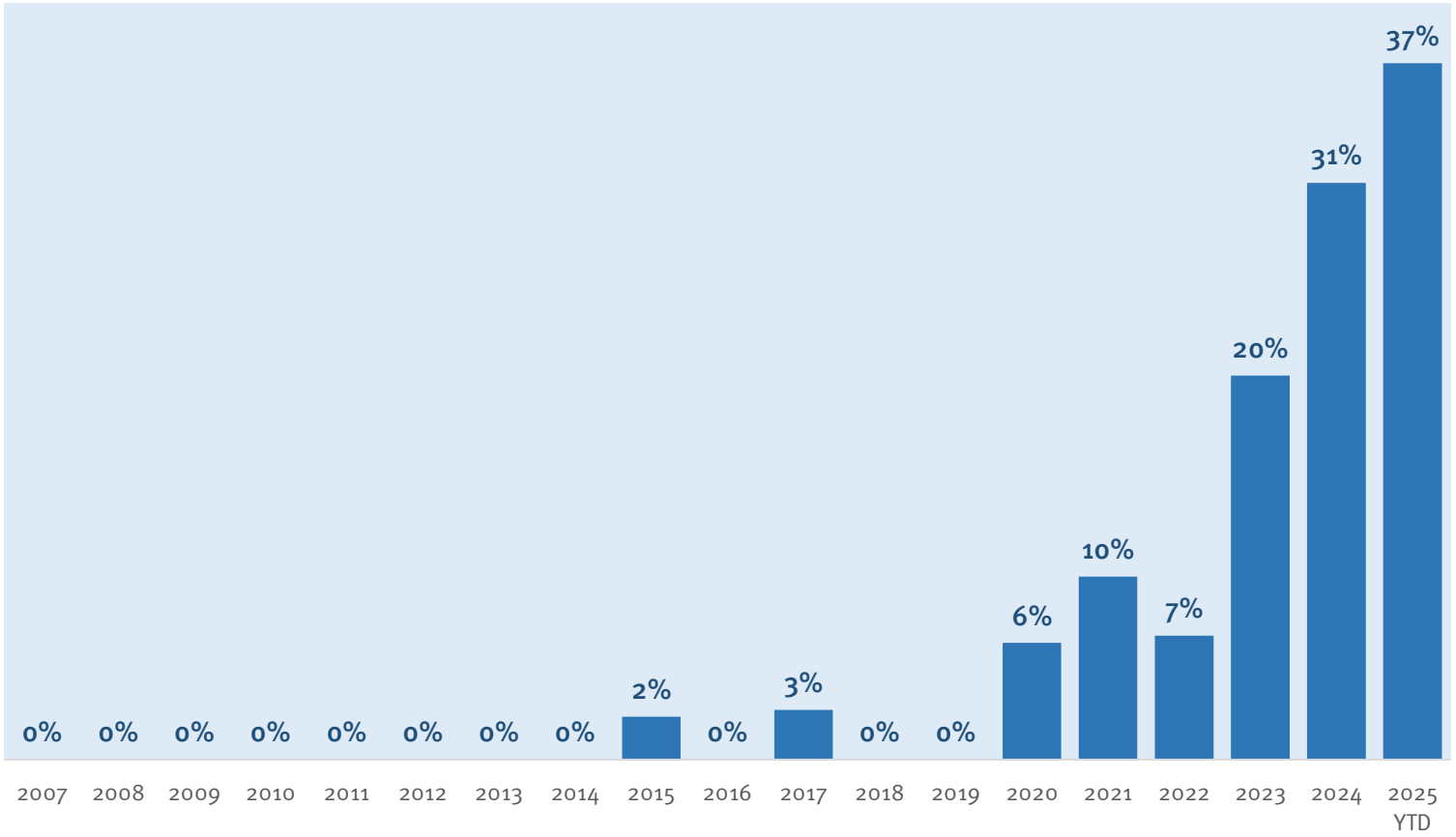
1. The CMC work on Chinese biologics is often not as good as one would hope. Wuxi Biologics makes a great antibody, but the problem is that many Chinese biotechs aren't using Wuxi these days. A few Western pharma are feeling a little burnt by some of the assets that they have paid big upfronts for – not because of the molecules but because of the extra CMC work that is required.
2. The transparency on clinical and pre-clinical data packages is often not great. It's very much a "buyer beware" market where Western assumptions about the quality of preclinical studies and the like doesn't always hold. Several parties note that the larger more reputable pharmas and biotechs (think Innovent or Hengrui) do a much better job than some of the less well-known companies.
3. It is also not uncommon for less well-known Chinese companies to put together items in a pipeline that barely exist, hoping to find a licensing partner (pipeline "spoofing"). One has to be careful when visiting a company to confirm the status of a molecule and where it actually is in development.

When the Japanese bought Rockefeller Center in the 1980s, as Americans recognized that owning a Toyota over a Chevy might be a good idea, there were many who thought Japan would surpass the U.S. in industrial might. This did not happen. U.S. automotive makers responded with better cars and Japan experienced a "lost decade" of slow growth following a burst property bubble in Tokyo. Japan did not come close to putting the U.S. out of business. Similarly, Chinese biotechs aren't going to put Western biotechs out of business anytime soon. But some Chinese biotechs are strong players and are going to be in global biopharmaceutical industry as worthy contributors for decades hence.

10-foot tall Coca-Cola vending machine in Shanghai

Ever More Licensed Molecules Going Into Big Pharma Are Coming from China in 2025

Percent of Big Pharma License Deals with $50mm+ Upfronts Sourced From China, 2007 to March 29, 2025

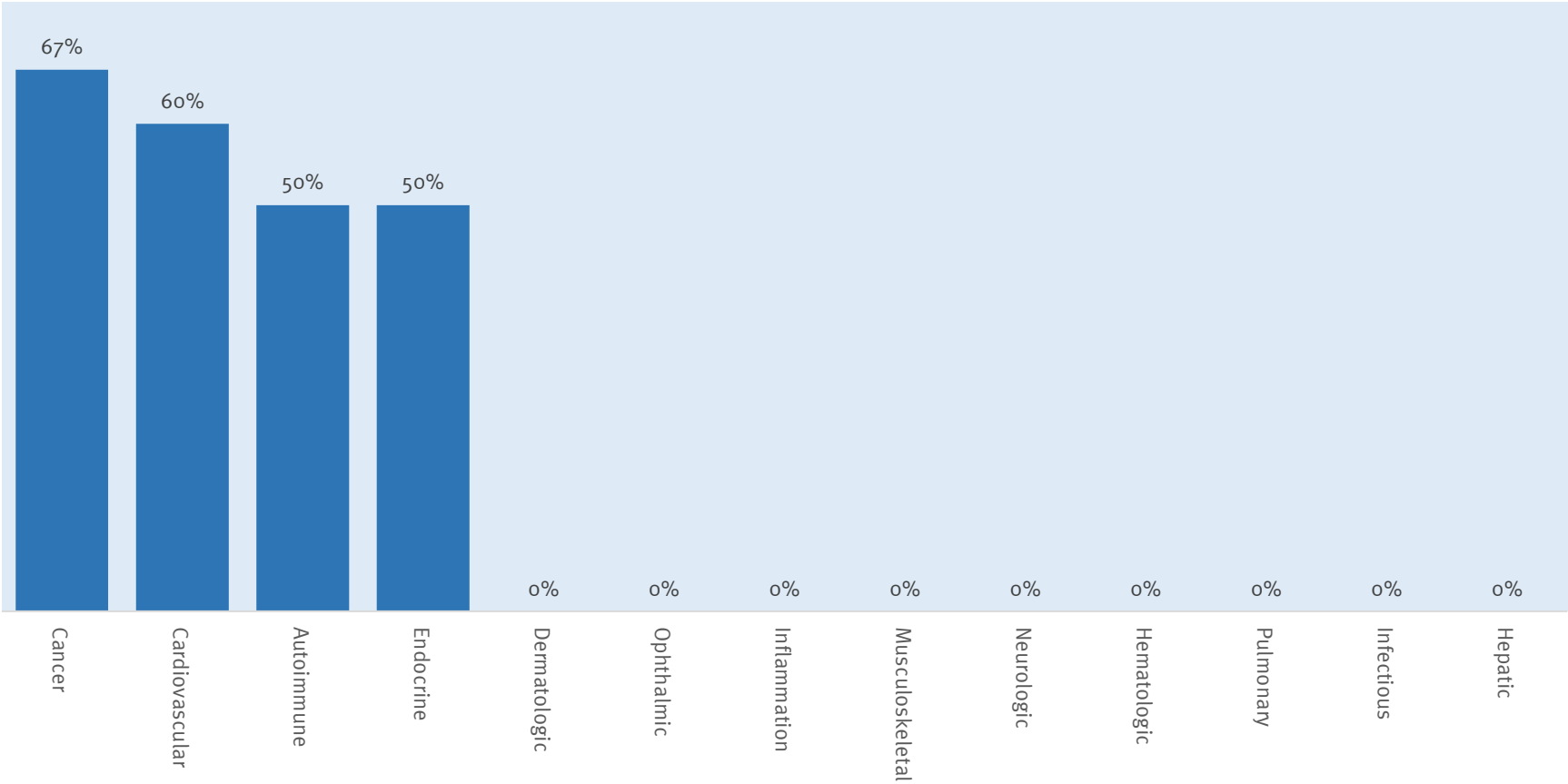


China has become even more important as a source of innovation molecules to big pharma in 2025.

Source: DealForma

Big Pharma Licensing Activity from China Highly Concentrated by Therapeutic Area

Percent of Large Pharma License Deals for $50mm or More Sourced from China, 2024 and 2025 (through Mar 23rd)



Big pharma has sourced 60% of its larger licensing deals in cancer and CV from China in the last 15 months. 50% of deals in autoimmune and endocrine have come from China. But for most therapeutic areas, there have been no transactions sourced from China with upfronts of $50mm or more.

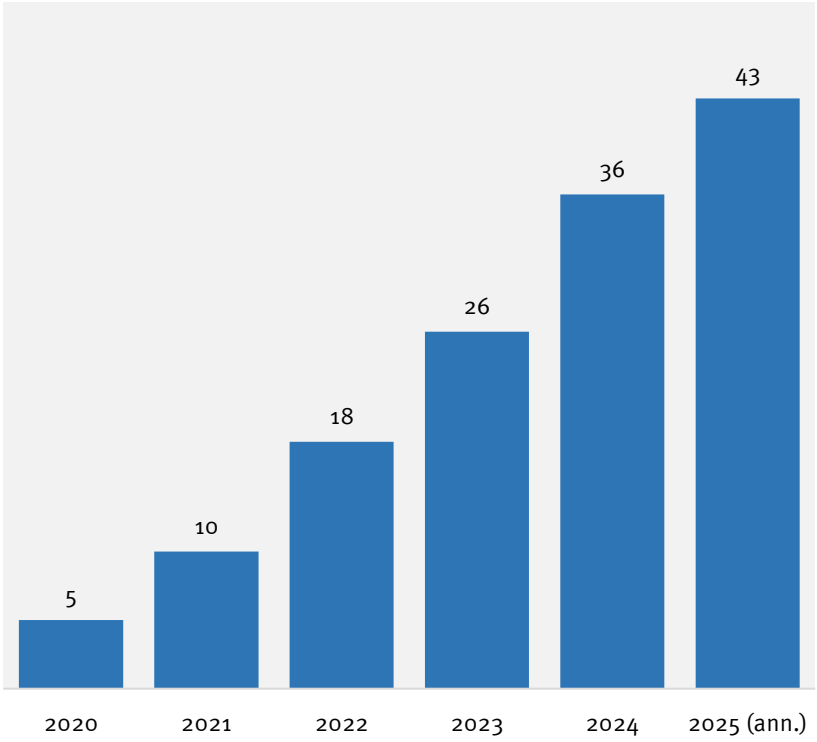
Source: DealForma

Our Perception of the China Market: Huge Imbalance of Sellers Versus Buyers

Despite concerns that all the good assets are gone, China is very much a buyer's market today.

- There is little internal capital for development – buyers are forced to sell assets if a licensee shows up
- There is a huge imbalance between sellers and buyers.
- Consensus biotech count in China is over 5,000 companies (we surveyed over 20 people on our last trip on how many biotechs are in the country)
- Assume four pipeline drugs for each company (conservative)
- That would be mean that there are 20,000 pipeline items
- Last year, there were 36 deals for $10mm or more upfront
- If you are the Chinese biotech, your odds that an asset of yours would be one of the lucky few was basically 1 in 500
- While Chinese biotechs are aggressive at present in negotiating for better upfronts the opportunity to pick up good assets at affordable prices in China is quite good

Count of China Out License Deals with Upfronts of $10mm or More, 2020 to 2025



Source: DealForma

Top China Outbound License Deals, Jan 1, 2025 to Mar 29, 2025

Date	Chinese Partner	Global In-Licensor	Asset	Deal Structure	Upfront Cash ($mm)	Total Deal Value ($mm)	Stage Signed
03/25/2025	Hengrui Pharmaceuticals	Merck & Co. Inc.	Oral LP(a)	License	$200	$1970	Phase 2
03/24/2025	United Laboratories	Novo Nordisk	Triple incretin agonist	License	$200	$2000	Phase 2
03/21/2025	Syneron Technology	AstraZeneca plc	Macrocyclic peptides	License	$75	$3475	Platform
03/21/2025	Harbour BioMed	AstraZeneca plc	Unspecified	Collaboration/Option	$280	$4680	Platform
01/10/2025	Sciwind Biosciences	Verdiva Bio Inc.	GLP-1 agonist	License	$70	$2470	Phase 1
01/07/2025	Duality Biologics	Avenzo Therapeutics	EGFR x HER3 ADC	License	$50	$1200	Preclinical
01/01/2025	Innovent Biologics Inc.	Roche	DLL3 ADC	License	$80	$1080	Phase 1

Source: DealForma

Top China Outbound License Deals, Jan 1, 2022 to Dec 30, 2024

Date	Chinese Partner	Global In-Licensor	Asset	Deal Structure	Upfront Cash ($mm)	Total Deal Value ($mm)	Stage Signed
12/18/2024	Hansoh	Merck	Oral GLP1	License	$112	$2,012	IND Ready
12/12/2024	CSPC	BeOne	MAT2A inhibitor	License	$150	$150	Phase 1
11/14/2024	LaNova	Merck	PD-1/VEGF bispecific	License	$588	$3,288	Phase 1
10/28/2024	Chimagen	GSK	T-cell engager	Asset Purchase	$300	$850	Phase 1
10/7/2024	CSPC Pharma	AstraZeneca	Oral LP(a) inhibitor	License	$100	$2,020	IND Ready
9/30/2024	Regor Therapeutics	Roche	CDKx Platform	Asset Purchase	$850	NA	Phase 1
8/9/2024	Curon Biopharmaceutical	Merck	T-cell engager	Asset Purchase	$700	$1,300	Phase 1
6/14/2024	Ascentage Pharma	Takeda	BCR-Abl Modulator	License Option	$100	$1,300	Phase 2
6/13/2024	Mingji Biopharm	AbbVie	TLA1 mAb	License	$150	$1,710	IND Ready
1/7/2024	Argo Bio	Novartis	RNA tx for CV	License	$185	$4,165	Phase 1
12/26/2023	Gracell Biotechnologies	AstraZeneca	CAR-t platform	Acquisition	$1,000	$1,200	Phase 1
12/20/2023	Hansoh Pharma	GSK	B7-H3 ADC	License	$185	$1,710	Phase 2
12/11/2023	Systimmune	BMS	EGFRxHER3 ADC	License	$800	$8,400	Phase 3
11/9/2023	Eccogene	AstraZeneca	Oral GLP1 agonist	License	$185	$2,010	Phase 1
10/30/2023	Hengrui Pharma	Merck KGaA	PARP1 inhibitor	License	$170	$1,487	Phase 1
4/3/2023	Duality Biologics	BioNTech	ADC portfolio	License	$170	$1,670	Phase 2
1/23/2023	Hutchmed	Takeda	VEGF inhibitor	License	$400	$1,130	Phase 3
12/22/2022	Kelun-Biotech	Merck	ADC portfolio	License	$175	$9,513	IND Ready
12/5/2022	Akeso Bio	Summit Tx	PD-1/VEGF bispecific	License	$500	$5,000	Phase 2
1/4/2022	3SBio	Syncromune	PD1 mAb	License	$100	$100	Phase 2

Source: DealForma

China NewCo Deals with US Investors in 2024

Date	Financial Partner	Seller	Previous Partners	NewCo	Product	MoA	Indication	Stage @ Deal	Equity	Upfront	Total	Royalty
Nov-24	Monograph capital	康诺亚	Roche	Platina Medicines	CM336	BCMAxCD3 bsAb TCE	r/r MM, autoimmune diseases	Phase 1/2	Und.	$16	$626	Tiered
Nov-24	ArtiumBio	Leads Biolabs	BeOne	Oblenio	LBL-051	CD19xBCMAxCD3 Tri- TCE	Autoimmune disorders	PC	Und.	$35	$614	Tiered
Sep-24	FORESITE LABS	EpimAb	almirall	Vignette Bio	EMB-06	BCMAxCD3 bsAb TCE	Multiple myeloma	PC	Und.	$60	$635	Tiered
Aug-24	TWO RIVER THIRD ROCK	GENOR	GO THERAPEUTICS	TRC 2004	GB261	CD20XCD3 bsAb TCE	B-NHL	Phase 1/2	Und.	>$10	>$443	Single to double digits
Jul-24	OrbiMed (50.26%)	康诺亚	Roche	Belenos	CM512 CM536	bsAbs	Atopic Dermatitis Und.	Phase 1/2 PC	30%	$15	$185	Tiered
May-24	BainCapital rtw (39% /19%)	HENGRUI	Multiple	Hercules	HRS-7535 HRS9531 HRS-4729	GLP-1	T2D, obesity	PC to Phase 3	20%	$110	$6,035	Low single digits to low double digits

- A best-in-class potential asset in a high potential growth area of biotech is a key requirement to pull off a strong “NewCo” type deal
- On average, the upfront payments on NewCo deals tend to run lower than upfronts on large pharma transactions.

1st Quartile	$15	$486
Mean:	$41	$1,423
Median:	**$26**	**$620**
3rd Quartile	$54	$633

Sources: Evaluate Pharma and public websites

Select China Asset Purchase and M&A Deals in 2024

(in $mm)

Date	Type	Target	Existing Partners	Buyer	Lead Program	MOA	Indication	Status @ Deal	Tech Platform?	Upfront	CVR	Total Value
Nov-24	Cash/ WholeCo	BIOTHEUS	BIONTECH	BIONTECH	BNT327	PD-L1 x VEGF bsAb	NSCLC, BC	Phase 2	Yes	$800	$150	$950
Oct-24	Cash/ Asset	CHIMAGEN BIOSCIENCES	N/A	GSK	CMG1A46	CD3xCD19xCD20 Tri-TCE	SLE, LN	Phase 1	/	$300	$250	$550
Sep-24	Cash/ Asset	Regor Therapeutics	Lilly	Genentech	RGT-419B	CDK2/4/6 inhibitor	ER+, HER2- Breast Cancer	Phase 1	/	$850	Und.	>$850
Aug-24	Cash/ Asset	启润 CURON	N/A	MERCK	CN201	CD3 x CD19 bsAb	NHL, ALL	Phase 1	/	$750	$600	$1,350
Apr-24	Cash/ WholeCo	ProfoundBio	Synaffix	Genmab	Rina-S	FRα-targeted Topo 1 ADC	PROC, Solid Tumors	Phase 2	Yes	$1,800	$0	$1,800
Mar-24	Stock / WholeCo	AnHeart		Nuvation Bio	Taletrectinib	ROS1/NTRK inhibitor	NSCLC	Pivotal	No	$252	$0	$252
Jan-24	Cash/ WholeCo	SanReno	CHINOOK	NOVARTIS	Atrasentan (China rights)	ERA antagonist	IgAN	Phase 3	No	Und.	Und.	Und.

- This table shows asset purchase and M&A deals done in 2024
- The most popular areas remain oncology and autoimmune
- Most of the deals are for biologics
- Deals are getting done at the clinical stage
- Transactions for entire assets rather than licenses are increasingly common

1st Quartile	$838	$250	$1,250
Mean	$792	$200	$959
Median	**$775**	**$150**	**$900**
3rd Quartile	$413	$0	$625

Sources: Evaluate Pharma and public websites

Rationale and Details on these Asset/M&A Deals

	BIOTHEUS 普米斯生物技术	CHIMAGEN BIOSCIENCES	Regor Therapeutics	同润 CURON	ProfoundBio	AnHeart Therapeutics	SanReno 信诺泰
Therapeutic Area	✓BsAb ✓Targeting blockbuster indication	✓Tri-specific TCE ✓TCE's potential in autoimmune diseases	✓Monotherapy potential to treat ER+, HER2- breast cancer	✓BsAb ✓TCE's potential in autoimmune diseases	✓ADC ✓Linker-drug technology	✓NSCLC, blockbuster indication	✓IgAN
Strategic Fit	✓BioNTech has been very active in buying ADC, BsAb assets from China	✓GSK has been a pioneer in the treatment of lupus	✓Genentech has a big breast cancer franchise	✓Merck has been very active in acquiring TCE (Harpoon TX)	✓Technology platform is synergistic to Genmab's antibody platform	✓Nuvation was actively looking for strategic alternative with good story for capital market	✓Novartis acquired Chinook
Good Target	✓PD-L1x VEGF ✓PD-1/TGF-β	✓CD3xCD19x CD20	✓CDK4/6	✓CD3/CD19	✓FRα ✓PTK7 ✓EGFR ✓cMET	✓TKI inhibitor	✓ERA antagonist
Brand Partners/ Investors	✓Collaborated with BioNTech before the acquisition	✓Invested by Foresite Capital	✓Licensed metabolic pipeline to Eli Lilly	✓Invested by Wuxi Biologic	✓Technology platform collaborated with Synaffix	✓Lead program is licensed from Daiichi Sankyo	✓Chinook's JV
Differentiation	✓Phase 2 data at ESMO is pretty good	✓The first CD3xCD19x CD20 entering into clinical development	✓Targeting CDK2 to mitigate drug resistance and toxicity of CDK4/6	✓The only clinical stage CD3x CD19 TCE in China with very good data	✓ProfoundBio's ADC technology deliver very good PK profiles ✓Rina-S data (N=10) is promising	✓Taletrectinib was very close to get approved in China and filed NDA in US	✓Atrasentan showed pretty good Phase 3 data in US before Novartis acquired SanReno

Sources: Evaluate Pharma and public websites

Bloomberg Discussion of China Biotech Sector

You've heard about Chinese EVs. You've heard about Chinese batteries and solar panels. And recently you learned that China is near the cutting edge of AI research. Here's another category: biotech. In 2019, the Chinese share of molecules licensed to Big Pharma companies was 0%. In 2024, it's now 31%. On this episode we speak with Tim Opler, a biotech industry investment banker at Stifel. He explains how this industry has taken off in such a short period of time. Among the factors he cites: a generation of Chinese research scientists working in the US who hit a ceiling in terms of promotion and thus went back home to start companies. It's also far cheaper to run clinical trials in China, due to the structure of the healthcare system. We also talk about the broad history of the pharmaceutical industry, how it's evolved, and what impact, if any, AI will have on drug discovery.

Click to listen to the podcast.

AstraZeneca Details $2.5B Investment in China's Political Center, Funding R&D Center, Biotech Pacts

Nick Paul Taylor, *FierceBiotech*, March 21, 2025 (excerpt)

AstraZeneca has shown its commitment to China amid investigations into its executives and activities, outlining plans to establish a global strategic R&D center in Beijing as part of a $2.5 billion investment in the city.

Chinese authorities detained AstraZeneca's former China head Leon Wang last year and revealed a probe into potential illegal drug importation early this year. Against that backdrop, AstraZeneca has reiterated its commitment to China and voiced confidence in the leadership team that is in place in the country. AstraZeneca put a dollar value on that commitment Friday.

Tallying up a wide range of investments, AstraZeneca said it is pumping $2.5 billion into Beijing. The figure includes outlays on partnerships with Harbour BioMed, Syneron Bio and BioKangtai and cash for establishing a new R&D center in Beijing. The company plans to grow its head count in Beijing, the political center of China, to 1,700.

AstraZeneca has partnered with Syneron to develop macrocyclic peptides and formed a joint venture with BioKangtai to develop, manufacture and sell vaccines for respiratory and other infectious diseases in China. The BioKangtai collaboration will see AstraZeneca set up its first vaccine manufacturing facility in China.

The partners will build the manufacturing plant in Beijing International Pharmaceutical Innovation Park, a campus that hosts biotechs, research hospitals and China's National Medical Products Administration. AstraZeneca has also picked the park as the location of its new R&D center.

Beijing will become AstraZeneca's sixth R&D center globally and second in China, where the company already operates a site in Shanghai. Once operational, the Beijing site will support early-stage research and clinical development.

Source: https://www.fiercebiotech.com/biotech/astrazeneca-details-25b-investment-chinas-political-center-funding-rd-center-biotech-pacts

U.S. Cuts in Research Funding Ill-Timed Given Chinese Competition

Sujai Shivakumar, Charles Wessner, and Julie Heng, *CSIS*, March 18, 2025 (excerpt)

For years, China has played a leading role in manufacturing active pharmaceutical ingredients and generic drugs. While securing the supply chain for active pharmaceutical ingredients is increasingly recognized as a national security priority by policymakers, China's growing role in biotechnological innovation has generally received less attention.

The need for more attention was revealed last year when a drug from a little-known Chinese biotech outperformed one of the world's top-selling medications. As the Wall Street Journal reported, Akeso's Ivonescimab outperformed Merck's Keytruda, a drug that generates over $30 billion annually, in what some are calling a "DeepSeek moment" for biopharmaceuticals.

It is important to note that this is not a one-off event. There are increasing numbers of new drugs in development, accompanied by a surge in clinical trials, licensing agreements, and acquisitions in China. According to The Economist, Western pharmaceutical companies struck nearly a third of large licensing deals—those valued at $50 million or more—with Chinese firms in the past year, a threefold increase since 2020. In 2024, the value of drugs licensed from China to the West reached $48 billion, 15 times higher than in 2020. Reflecting this growth, China is emerging as a major force in the global biopharmaceutical industry. Since 2006, China has prioritized biotechnology, implementing a long-term national strategy to develop its biopharmaceutical industry. Chinese authorities have overhauled the regulatory ecosystem to achieve this goal, enabling drug testing to be done more quickly and affordably than in the United States.

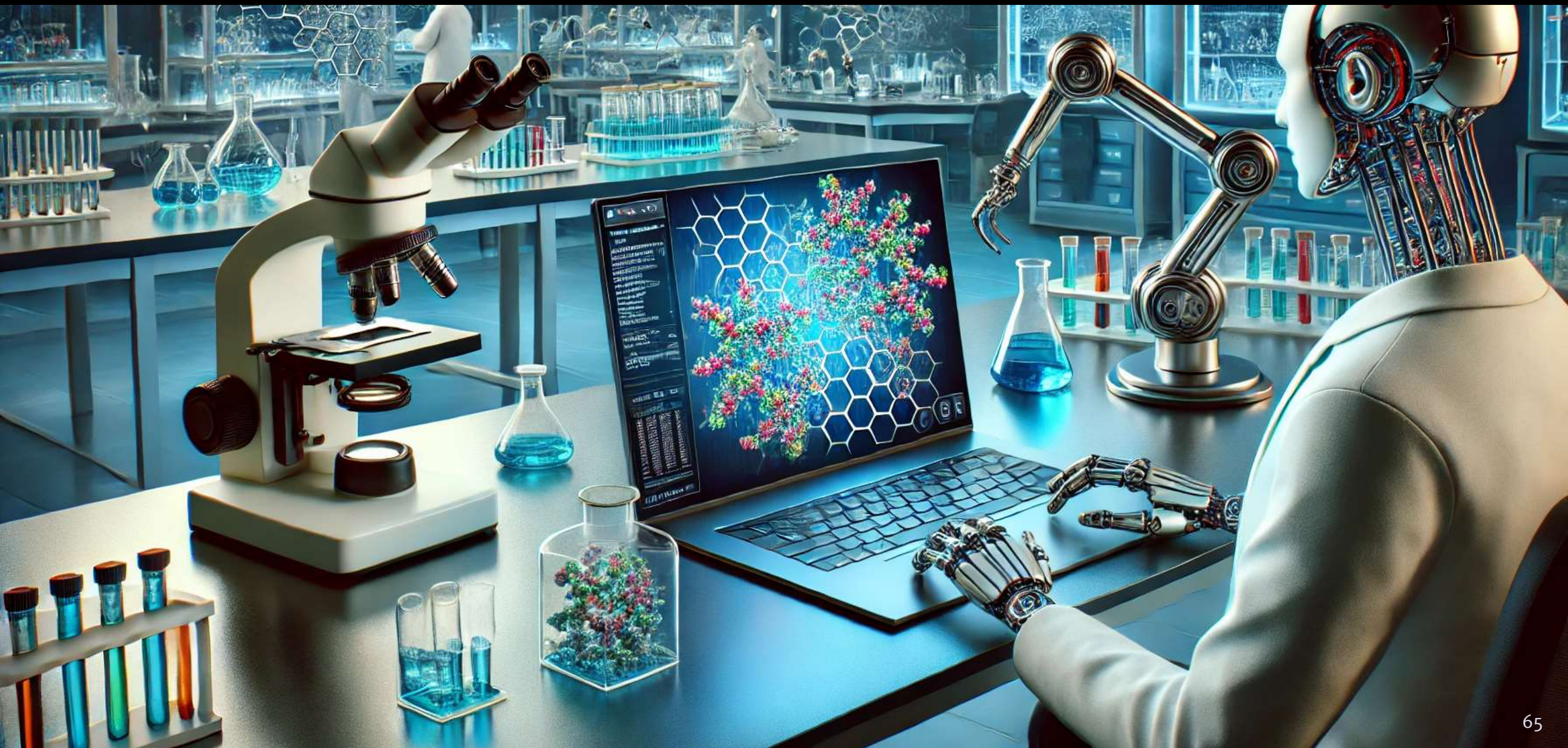
Additionally—and somewhat ironically—China is strengthening its intellectual property framework and investing heavily in both basic and applied research among other supportive measures. These policies, and the substantial resources devoted to the sector, have enabled China to make significant strides in biopharmaceutical innovation. Crucially, some estimate that clinical development in China has become 50–100 percent faster than in the United States or Europe.

This sustained support has enabled a U.S. biopharmaceutical innovation system that is the envy of the world, one that supports 300,000 researchers in every U.S. state. Yet it now appears under threat from within. Government investments in research, through the NIH, have been stagnant for years. Last year, the Biden administration cut federal research funding even as Chinese funding for research surged, and now the additional cuts projected by the Trump administration risk undermining our leadership. Compounding these concerns, in February, the NIH announced that it would limit funding for universities' indirect research costs to 15 percent, down from a historical average of 40 percent. If fully implemented, this could represent a massive reduction in funding for the university research enterprise, perhaps as much as $4 billion a year.

At a time when China is intensifying investment in biopharmaceutical innovation, the United States cannot afford major cuts in funding for this leading research enterprise. Innovation leadership depends on a country's ability to continue to make new health-enhancing discoveries and bring them to market at affordable cost. Yet, since the NIH announced cuts to indirect research funding, at least 20 U.S. universities have announced hiring freezes, and 33 have reduced PhD admissions for this year, most notably in biomedical programs.

Source: https://www.csis.org/analysis/united-states-cannot-afford-disarray-china-strengthens-its-biopharmaceutical-industry

Is Biotech Dead? Business Model Designs for Coping with Commoditization



Elliot Hershberg: Essay on Commoditization and China

Ten years ago, the scientologist (no, not scientist) Bob Duggan sold his American biotech startup to AbbVie for $21 billion (no, not million). His company, Pharmacyclics, had developed a highly promising cancer drug and was handsomely rewarded for it. In fact, Duggan's payout of over $3.5 billion was reported to be one of the largest returns from a public buyout in history.

Aside from the eccentricities of Duggan as a founder—and the other large characters involved that made all of this book worthy—this was a relatively normal deal. A Big Pharma company was under serious pressure to find a new source of revenue as one of its blockbuster products reached the end of its patent exclusivity. An American startup's breakthrough drug became that new source.

Much of the biotech industry is predicated on this dynamic. Small startups have become the primary source of innovation, running the majority of early-stage clinical trials each year. Big Pharma companies buy these startups at a rich premium to continually replenish their pipelines.

But things are changing. A decade later, Duggan is back. This time, he's got a new drug that beat Keytruda—Merck's cancer immunotherapy drug that grosses $30 billion a year—in a clinical trial. Crucially, Duggan didn't find this drug in an American lab. He licensed it from a Chinese company.

Unlike Pharmacyclics, this story didn't end with a massive multi-billion dollar acquisition. Instead, Merck went to the same source, buying their own version of the same drug type for $500M from another Chinese company. This is a really big deal. Much like we recently saw in AI, China has become a serious competitive threat in biotech, demonstrating the capacity to rapidly develop new drugs that can rival—or surpass—those being produced in American labs. In other words, "the drug industry is having its own DeepSeek Moment."

Consider another example. As GLP-1 drugs became an explosive success, pharma companies raced to get their hands on their own next-generation versions of this product class to compete with Novo Nordisk and Eli Lilly for market share. Again, Merck looked to China, acquiring an oral GLP-1 drug for $112M upfront. The deal was backloaded with milestones up to $1.9B based on commercial success.

For context, Viking Therapeutics, an American biopharma company with an oral GLP-1/GIP agonist in its pipeline, currently has a $3.8B market cap. Rather than pursuing a wholesale buyout of Viking, why not just grab a molecule from China for a bargain and see if it works?

In a moment where the biotech market is depressed, the heightened external competition makes things even harder. While the M&A market has already been slow, now founders and investors alike are losing sleep over deals falling apart at the last minute because of stealthy Chinese competitors they had never even heard about.

This whole situation has spurred a lot of analysis. Some of my favorites so far are David Li's reflection as a Chinese American biotech startup founder, his subsequent analysis in the *Timmerman Report*, Bloomberg's coverage, and Alex Telford's characteristically thoughtful take on the question: Will all our drugs come from China?

Source: https://centuryofbio.com/p/commoditization

Hershberg Essay (cont)

Source: https://centuryofbio.com/p/commoditization

Here, I want to zoom out and consider how we got here.

In 1987, Merck was featured on the cover of Fortune Magazine as “America’s Most Admired Corporation” for “betting on magic molecules.”

In the decades prior, Merck scientists were responsible for producing breakthrough molecules for hypertension, some of the most successful vaccines in history (Maurice Hilleman, one of the most prolific vaccinologists of all time, was a scientist at Merck), the first statins, and entire new classes of antibiotics.

Now, for two of the hottest products in the market, Merck has looked outside of the American biotech startup ecosystem—which was still struggling to come into existence in 1987—and acquired molecules from the Chinese ecosystem—which wasn’t a major source of innovation until very recently.

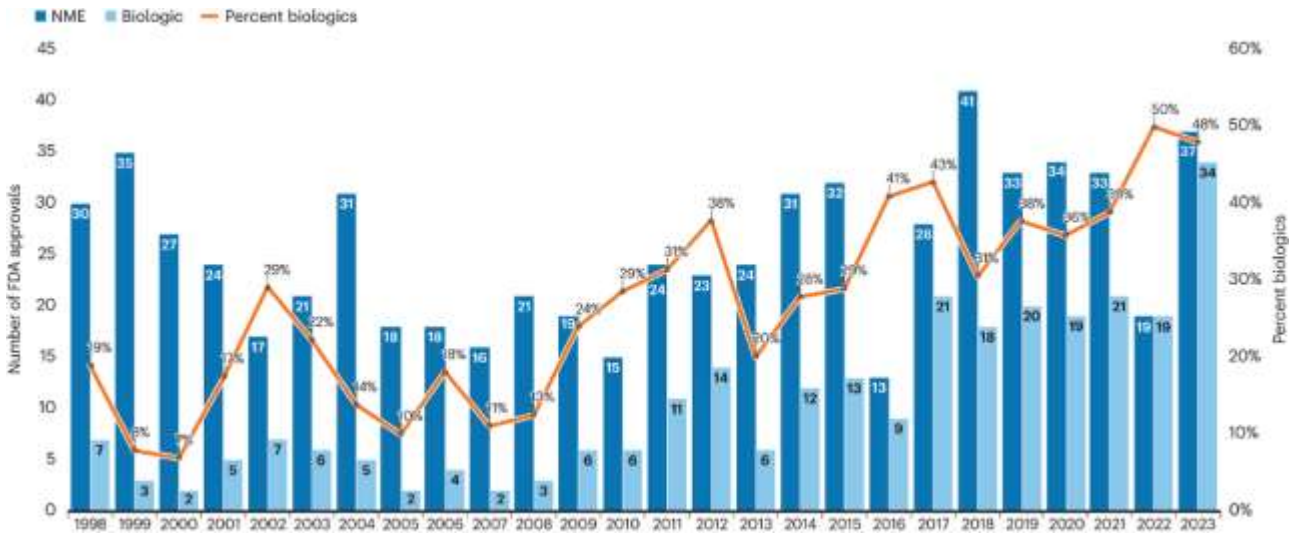
Clearly, the global drug discovery industry has undergone considerable evolution. At this juncture, I think it’s worth considering the long arc of commoditization for drug discovery technologies, as well the implications of this historical pattern for the future of the industry.

The Long Arc of Modality Commoditization

Let’s think about biologics.

For most of history, nearly all drugs were plant-based chemicals with a useful impact on human physiology that humans had serendipitously discovered. Over time, tools were developed to more systematically search through chemical space for useful small molecules. Another small category was the set of proteins, such as insulin, that could be isolated from animals and used to treat disease.

The recombinant DNA revolution that gave rise to Genentech’s founding in 1976 planted a seed of radical change. Using the tools of genetic engineering, it became possible to produce biologically derived molecules to mitigate disease in entirely new ways. Fifty years later, there are nearly as many biologics approved each year as there are small molecules.



Hershberg Essay (continued)

But there was an important kernel of truth at the center of this bubble: recombinant DNA really was a transformative tool for making new medicines. Even in a more sober environment, the companies with the resources, technology, talent, and grit to survive kept churning out products.

After synthetic insulin, Genentech produced seven more biologics throughout the 80s and 90s. Amgen, another early biologics pioneer founded in 1980, had their own string of breakthrough medicines that set them apart from the rest of the struggling competition. Regeneron, which was founded in 1988 after the initial boom, differentiated themselves over time with a keen focus on human genetics and a powerful technology platform for producing monoclonal antibodies—which proved to be one of the most important types of biologic.

While there were still many skeptics, the scope of biologics continued to expand across medicine, reaching the point in 2022 where their volume of approvals was first on par with small molecules. (The graph we looked at earlier.)

The commercial success for these first movers is also undeniable. Genentech was acquired by Roche in 2009 for $46.8B, where it still operates as a highly impactful independent subsidiary. Amgen currently has a market cap of $168B. Regeneron is now worth $78B, with a share price nearly 4000% higher than at their IPO.

This evolution is almost a textbook example of the phenomenon known as the Gartner hype cycle. An initial “innovation trigger” causes a big spike in hype and excitement. When the hype isn’t immediately justified, the market cools. If the initial trigger has substance, there is a more gradual rebound over time.

And we do seem to have entered a “plateau of productivity.” The ability to produce biologics is no longer a secret guarded by a small set of companies. Scientists around the world have now spent decades refining the tools for developing these drugs. An entire wave of companies has cropped up to offer antibody development as a service.

What’s interesting to note is that across each generation, the magnitude of the businesses decreases by roughly one order of magnitude. The first movers grew into ~$100B+ companies. The leading service providers that followed became ~$10B+ companies. Now, the new entrants in the discovery market are ~$1B+ companies.

To me, this looks like the textbook definition of commoditization, which is the gradual process of making a good or service into a commodity and competing on price. A commodity is a good or service that is interchangeable with other commodities of the same type.

Think about electronics. At the start, very few companies could produce the best TVs. These companies charged a large premium. Over time, this premium was competed away. Now, a large number of companies sell massive flat screens packed with smart features for hundreds of dollars at Costco. This is commoditization.

Similarly, it’s getting increasingly hard to distinguish between antibody discovery providers, with many companies using similar technologies to produce antibodies against the same drug targets.

So far, we’ve exclusively focused on the history of antibodies. But I want you take a leap with me that will potentially annoy some drug developers: **no discovery technology is immune from the inescapable pull towards commoditization—like virtually every other technology.**

Source: https://centuryofbio.com/p/commoditization

Hershberg Essay (continued)

For big and small molecules alike, once discovery technologies—whether it's high-throughput screening, in silico screening, in vitro or in vivo models, or an analytical assay—become standardized, companies around the world will compete to offer them as a service.

This is The Long Arc of Modality Commoditization.

Over time, revolutionary ideas become universal building blocks for the next wave of innovation.

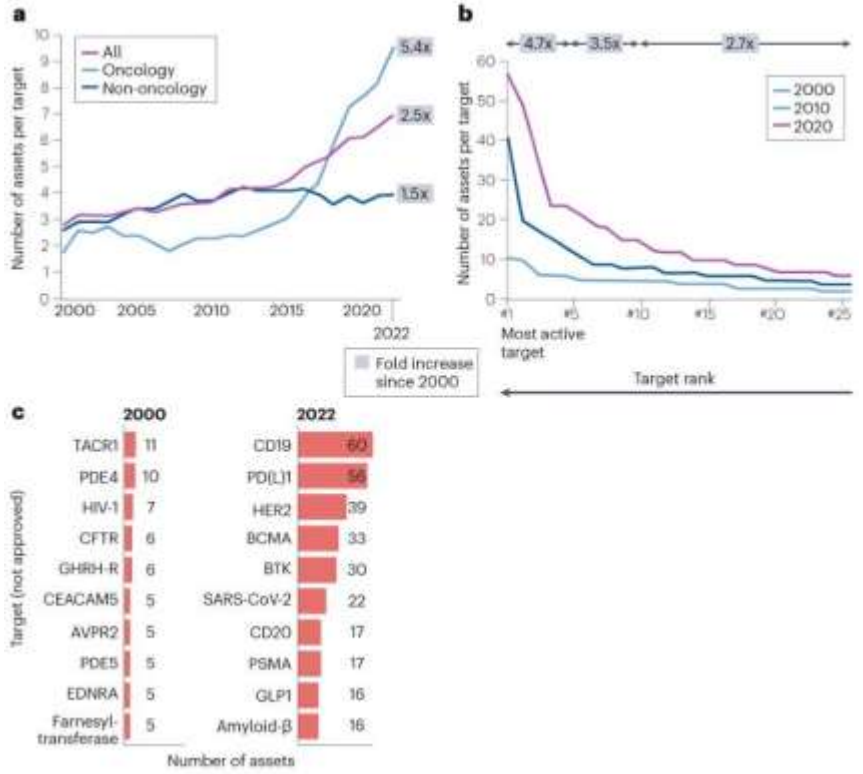
Biotech's Strategic Evolution

In parallel to the standardization and commoditization of discovery technologies, biotech investing became professionalized. With many decades of refinement, the industry moved towards standardized models for valuing companies. New strategies emerged.

One strategy that has gained considerable popularity is the "fast follower" approach where a new drug is developed to be "best-in-class" for a target with other drugs on the market, rather than to be "first-in-class" for a wholly new drug target. An analysis published in 2003 pointed out two key benefits to the "quest for the best." First, these drugs clearly have a lower risk profile because the target has already been validated by a drug approval based on human evidence. Investors typically talk about the amount of "biology risk" they are underwriting for a new target hypothesis.

A clear example of this strategy is Merck's acquisition of the oral GLP-1 agonist we looked at earlier. Novo Nordisk and Eli Lilly took on a lot of risk proving out the efficacy of the first GLP-1 drugs. Now, other companies are competing for fast-followers with improved properties, like formulation in a pill rather than dosing via injection.

Many biotech investors have taken this type of analysis to its logical extreme. As the size of early-stage rounds—and the funds financing them—have swelled, it's gotten harder to justify risking big pools of capital on totally unproven target hypotheses. In practice, this has led to substantial crowding around validated targets.



Source: https://centuryofbio.com/p/commoditization

Hershberg Essay (continued)

To make things even more efficient, “virtual biotechs” became prominent around the 2010s, where all research and development was outsourced to discovery partners like Adimab. The goal was often to rapidly produce a best-in-class molecule against a known target that could be sold to a Big Pharma for late-stage development and commercialization.

This industry history is essential for understanding the recent explosion of Chinese licensing deals, because many of the top outsourcing partners were Chinese Contract Research Organizations (CROs).

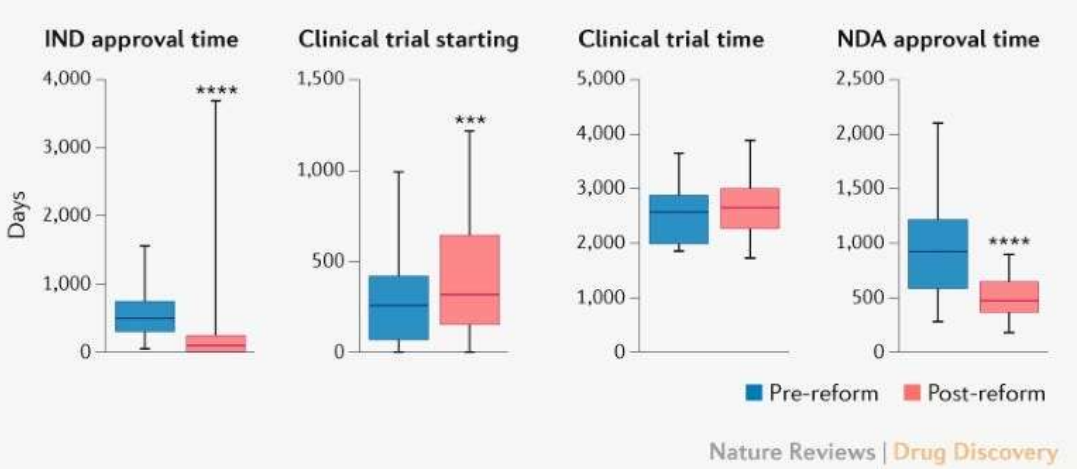
WuXi Biologics, a sprawling Chinese company offering a large suite of biologics discovery and manufacturing services, has become the second largest outsourcing partner in the world, capturing over 10% of the global market.

Now, the extremely logical strategic evolution from China, encoded in a new set of policies in 2015, is to develop their own drugs rather than just remaining a service provider. In a world where most people are using commoditized discovery technologies against the same drug targets, China has two key advantages:

1. Speed. The new set of reforms made it possible to launch clinical trials much more quickly.

2. **Cost.** Salaries for Chinese scientists are a fraction of those for American scientists. An army of highly-skilled—often American-trained—researchers can be thrown at far more problems.

Source: https://centuryofbio.com/p/commoditization



Source: *Trends in innovative drug development in China* (Thanks again to Alex Telford’s excellent blog post for putting this figure on my radar!)

With these advantages, Chinese startups and biopharma companies have seemingly saturated the space of known drug targets. Companies place cheap “call options” on a wide range of targets in the form of pre-clinical or early-stage assets. When a specific target or product idea gains traction with Big Pharma, these “options” can be exercised by pouring gas on the existing program to race it forward.

This puts intense pressure on the fast-follower strategy. When American scientists go to bed at night, the machines in the labs of their competitors on the other side of the world keep humming.

So far, we’ve traced the history of commoditization for drug discovery technologies and the subsequent professionalization of biotech investing. These changes help to contextualize the “DeepSeek moment” for the industry.

Hershberg: AI Could be the Last Wave of Commoditization

Over the last few years, a lot of money has been poured into companies with moonshot visions to transform drug discovery with AI. Some companies, like Xaira Therapeutics, which started with $1B in "Seed" funding, aim to develop their own medicines. But many others, such as EvolutionaryScale, Profluent, Chai Discovery, and Latent Labs, are considering strategies more akin to Adimab, where this new technology is offered as a broadly enabling piece of infrastructure.

When Latent Labs was launched, Tony Kulesa at Pillar wrote:

What emerged was a clear vision for democratizing access to advanced AI tools in drug discovery. While every biotech and pharma company searching for therapeutic molecules understands the role AI can play, most aren't in a position to develop their own models and tooling at the cutting edge. Simon's insight was that by giving partners instant access to the best tools, Latent Labs could accelerate drug design across the entire industry.

The combination of large funding rounds and new business models has drawn a mix of intrigue and skepticism. Andy Dunn at *Endpoints* wrote, "Latent's launch shows how AI-focused startups can buck tradition in biotech. Most biotechs are formed around a molecule, research paper or key intellectual property. Instead, Latent's investors are betting on AI talent in Kohl and Alex Bridgland, another ex-DeepMind developer of AlphaFold, to figure it out." Let's consider the bear case and the bull case for this investment thesis. In the bear case, none of these technical directions—whether the focus is on novel data generation, scaling models, architecture improvements, or some combination of all three—meaningfully move the needle when compared to commoditized technologies.

In his field notes from the Molecular Machine Learning conference at MIT, Simon Barnett from Dimension wrote, "my interpretation of [the co-founder of Adimab] Dr. Wittrup's talk was that he views monoclonal antibody (mAb) discovery as **a mostly solved problem** and that the impact of machine learning (ML) to this domain is exaggerated."

If AI techniques prove to only make a small numerical difference on problems like antibody discovery, the companies offering these solutions could join the long line of companies competing to offer these services.

We could expect to see <$1B companies rather than ~$50-100B+ generational behemoths.

What about the bull case?

Squint with me for a second, and imagine a trajectory of AI progress that leads to a *qualitative* difference, genuinely moving us into a world of *design* rather than *discovery*. Imagine a model that spits out zero-shot predictions of the platonic antibody—perfect affinity and specificity, exquisitely optimized along every dimension—for any target. Put in a target product profile (TPP), get out a drug.

That would probably be a pretty big deal.

Source: https://centuryofbio.com/p/commoditization

Hershberg Essay (continued)

One commonly invoked comparison is Cadence Design Systems, which is a $66B company that generates most of their revenue from licensing their software and IP for electronic design automation (EDA) for the semiconductor industry.

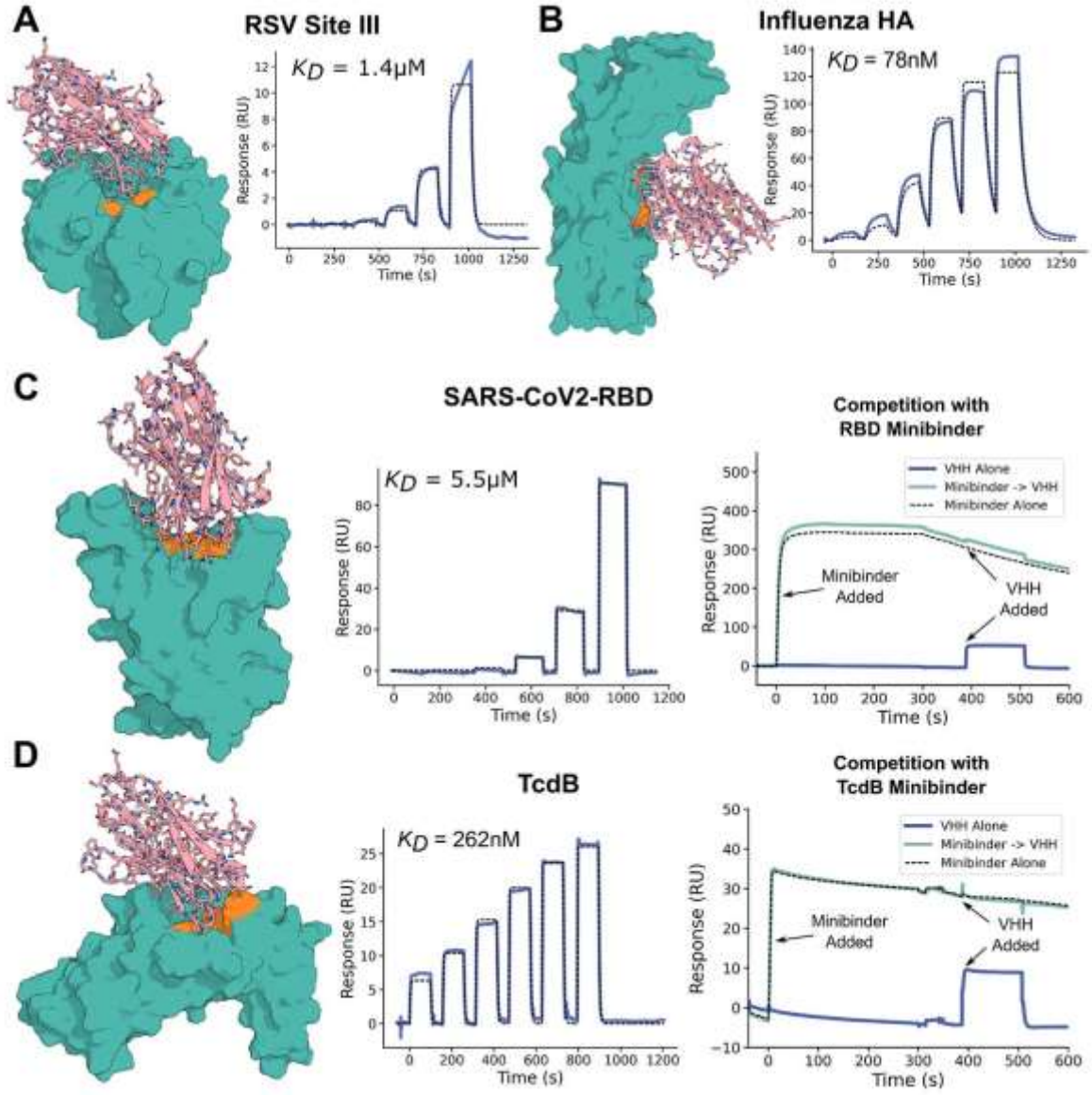
Is there any evidence for this technological trajectory?

Last year in March, the Baker Lab at the University of Washington published a preprint entitled Atomically accurate de novo design of single-domain antibodies. Building on decades of leading work on computational protein design, they introduced an AI model that could effectively generate miniature antibodies (called VHHs or nanobodies) for a given target.

These results stirred up an enormous amount of excitement and interest—including the $1B bet to launch Xaira. But the work was a proof of concept, not a magical black box capable of spitting out perfect antibodies.

Slightly less than a year later, the Baker Lab "significantly updated" their original preprint, renaming it to Atomically accurate de novo design of antibodies with RFdiffusion. As you might guess, the title was changed because the work was extended beyond just VHH design. The updated preprint also demonstrated the design of single-chain variable fragments (scFvs) which are another antibody format that have two variable domains rather than the single variable domain of a VHH.

Source: https://centuryofbio.com/p/commoditization



Part of Figure 2 from Atomically accurate de novo design of single-domain antibodies. The binders are shown in pink, with the target protein in turquoise. The specified epitope—which is the region that the antibody binds to—is shown in orange.

Hershberg Essay (continued)

Another important update was a response to the concerns about affinity. The authors wrote, “While initial computational designs exhibit modest affinity, affinity maturation using OrthoRep enables production of single-digit nanomolar binders that maintain the intended epitope selectivity.” In other words, AI doesn’t produce perfect binders yet, but they can be quickly tuned with existing experimental techniques.

So that’s about a year. At the risk of drawing a line between two data points, progress seems pretty rapid. Moving forward, what if somebody creates a giant set of training data for affinity using OrthoRep and that step moves out of the realm of atoms and becomes encoded in the world of bits…

In the next five years, what will prevent the continued march from VHHs to scFvs to full-fledged monoclonal antibodies?

Again, just squinting, it appears that we could be on the cusp of digitizing the development of biologics. If the advantages in speed and cost—and potentially quality—are substantial, this could lead to consolidation in the discovery market…

Now let’s consider what the world looks like if we take the concept of “foundation model” seriously. What if important underlying patterns of biological structure and function are learned across many tasks? As Simon Kohl from Latent Labs told Endpoints, “The vision is grander. I think we can expand from there, and we will find over time many other areas beyond the molecular interactions level will be steerable with generative models.”

Source: https://centuryofbio.com/p/commoditization

So if this—or any part of what I just outlined—is true, some of these companies could become really big.

But one of the biggest threats is likely to be… commoditization! After all, the entire “DeepSeek Moment” framing comes from the abrupt leap in AI capabilities from Chinese research groups with less resources than their American counterparts.

And there are already signs of this.

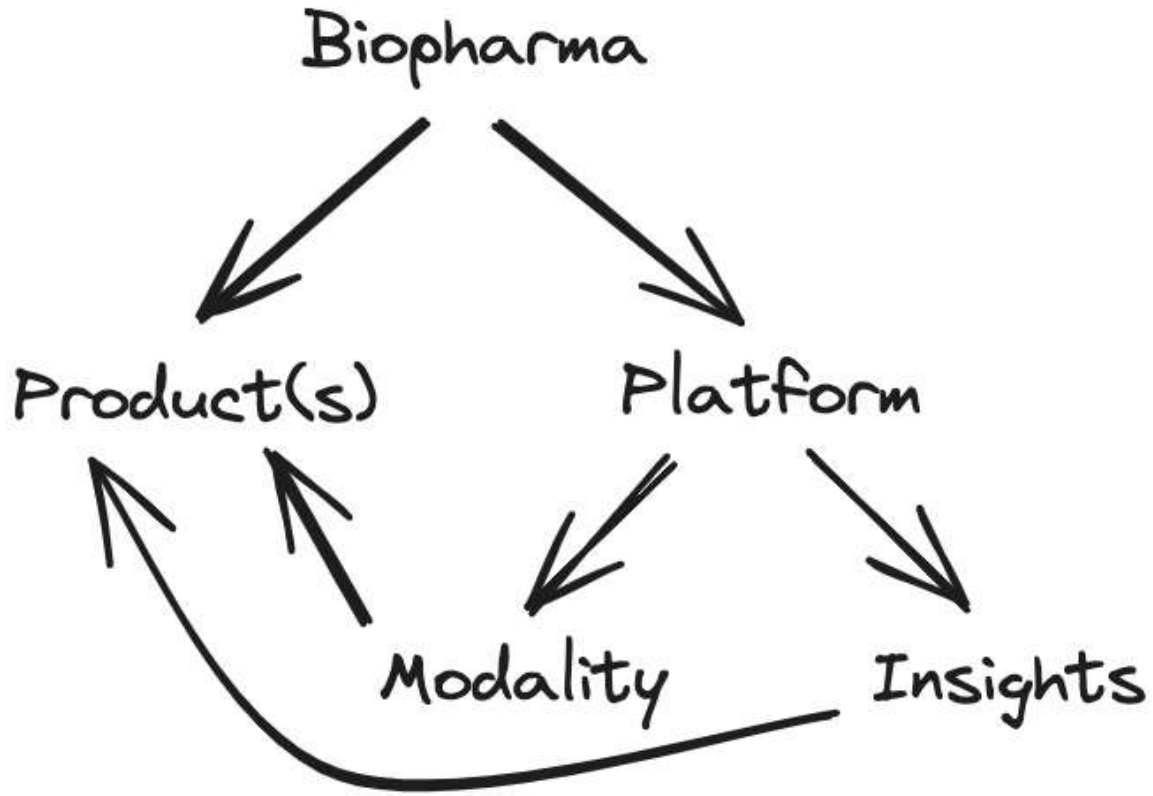
So far, Demis Hassabis, the co-recipient of the Nobel Prize for protein structure prediction and CEO of both DeepMind and Isomorphic Labs, has been betting on algorithm innovation rather than the development of a proprietary data moat for model defensibility. In a recent interview, he said, “make your algorithms better, your models better. You do have enough data — if you were innovative enough on your algorithm side.” It’s been amazing how quickly serious algorithmic competitors have emerged.

In May of 2024, Isomorphic and DeepMind published a paper describing AlphaFold3, their latest and greatest structure prediction model. In September of 2024, Chai Discovery published and open-sourced a state-of-the-art model. Roughly two months later, a research group at MIT produced another open-source version with comparable performance.

It will be interesting to see where value accrues in this new AI race. No matter what, all of these advances will open up new opportunities for innovation in other parts of the drug discovery stack.

Hershberg Essay (continued)

Not all biotech platforms focus on therapeutic modalities. Some companies focus on the other side of the coin: the identification of new biological targets to drug. In Steve Holtzman's "typology of platform companies" these are "insight platforms."



Source: https://centuryofbio.com/p/commoditization

Focusing on disease insights comes with its own basket of strategic challenges. In his original post, Holtzman wrote,

HOWEVER, Genus 2, Species A Platform Companies face a set of challenges not faced by Genus 1 Platform Companies. These arise intrinsically from the fact that the output of the Genus 2, Species A Platform Companies is data/information/insights, NOT, as with the Genus 1 Platform Companies, New Chemical Entities (NCEs) and biologic therapeutics.

1. The history of data in the biopharmaceutical industry is the history of its **commoditization**.
2. Companies whose "life's blood" is drugs/products have a vested interest in rendering data "pre-competitive" (or, at least doing so after they have had proprietary access for a time). They win based on their products; they don't want to be held captive by the owner of the information.
3. A more restrictive intellectual property (IP) environment: gone are the days when a transcriptional profile showing over-expression of a gene in a diseased tissue (or a genetic mutation in the diseased state) could get you an issued patent of the logical form, **"a method of treating disease X comprising modulating target A by any means"** (with dependent claims stating that the "means" could be an antibody, an antisense, an RNAi, a gene therapy, a small molecule, etc.).

Let's break this down. First, it's important to understand that data generation technologies have their own long arc of commoditization. (That's technology, folks!) Next, the main issue in the past has been the asymmetric negotiation with larger partners—who used to have proprietary access to discovery technologies that gave them an unfair advantage in actually creating chemical matter against new targets.

Hershberg Essay (continued)

This dynamic has already started to shift. The growth and maturation of the CRO industry has already made it possible for insight companies to show up to partner discussions with their own NCEs rather than just patents around target insights. What if AI accelerates this dynamic? Over time, as modalities become increasingly commoditized, the time and cost from target insight to developable chemical matter could be compressed even further.
In this world order, the pendulum could swing. New disease insights could become more valuable than any incremental starting point in chemical space against a known target.

The $100B+ GLP-1 success story, after all, was built on a biological insight, not a modality advance.

There are a few economic and technical realities that could slow down progress on this front.

In terms of economics, as David Yang nicely laid out, part of the reason GLP-1 was a *pharma* success rather than a *biotech* success is because of the centrality of M&A in the industry. Most early-stage biotech investors are banking on large acquisitions for liquidity, which means they keep a very close eye on the shopping list of pharma buyers. And pharma buyers really don't like spending billions of dollars to test new biological hypotheses—especially when the size of the market opportunity is uncertain. How can we change this and unleash a new wave of more innovative medicines? We'll need to continue to decrease the time and cost for every part of the stack—from discovery, to development, to commercialization.

Source: https://centuryofbio.com/p/commoditization

Doing this would make early-stage drug discovery a lot more valuable.

Improving discovery and commercialization both seem like technology problems. Accelerating development may require new technology *and* regulatory reforms. Taking a page out of China's book (for a change!) and studying their recent reforms could be a good starting point for the latter.

On a technical level, it's important to recognize that modeling human biology is a much more difficult AI problem than modeling a specific modality. Consider two questions. Does my antibody bind this target with higher affinity? What impact will activating the GLP-1 receptor have on the totality of human physiology? The tools to definitively answer the first question in the lab are readily available. The answer to the second question can't fully be known until first-in-human trials, because our pre-clinical models are only rough approximations of human biology.

More effectively simulating human biology will likely require substantial data generation and continued progress in new AI paradigms.
Over time, tackling these economic and technical challenges could dramatically reshape the biopharma landscape, leading to a new wave of commercial biotechs advancing bold new therapies.

But all of these rapidly compounding technologies could also lead to an even more radical departure from traditional biotech business models in the long run.

Hershberg Essay: Moats Could Look Very Different

In most industries, there are multiple viable strategies to create enduring competitive advantages over competitors. The canonical 7 Powers framework developed by Hamilton Helmer is an attempt to enumerate the most prevalent approaches.

The 7 Powers are:

1. **Scale Economies** — A business where per unit costs decline as volume increases.
2. **Network Economies** — A business where the value realized by a customer increases as the userbase increases.
3. **Counter Positioning** — A business adopts a new, superior business model that incumbents cannot mimic due to the anticipated cannibalization of their existing business.
4. **Switching Costs** — A business where customers expect a greater loss than the value they gain from switching to an alternate.
5. **Branding** — A business that enjoys a higher perceived value to an objectively identical offering due to historical information about them.
6. **Cornered Resource** — A business that has preferential access to a coveted resource that independently enhances value.
7. **Process Power** — A business whose organization and activity set enables lower costs and/or superior products that can only be matched by an extended commitment.

At the risk of oversimplifying, only two of these Powers matter in biopharma. Big Pharma companies benefit from Scale Economies because they can amortize the costs of development and commercialization with revenue from their existing portfolio.

For biotechs, basically the only real source of Power is control over a Cornered Resource in the form of new intellectual property (IP).

As Peter Drucker once wrote, "The pharmaceutical industry is an information industry." The value of a small molecule drug has nothing to do with its physical instantiation, which is worth very little. The ability to charge the highest margins for any physical product in existence is purely a function of the IP. Once the IP expires, generic drug makers can swoop in and offer substantially lower prices.

This is "The Biotech Social Contract," as Peter Kolchinsky at RA Capital would frame it.

Scientists and entrepreneurs are rewarded patent exclusivity for innovation. But the exclusivity is finite. When it expires, the innovative drugs become cheap commodities for all future generations.

Source: https://centuryofbio.com/p/commoditization

Elliot Hershberg Essay (continued)

Source: https://centuryofbio.com/p/commoditization

Personalized cancer vaccines are another form of therapy with this type of form factor. There is no single composition of chemical matter at the core of this type of medicine. Instead, each dose is produced by a complex combination of patient measurements, algorithms, and manufacturing steps.

This has really interesting consequences. For the first time, this could be a medicine with Network Economies. Because each dose is designed with an algorithm, the quality could be improved as more data is collected. Patients could benefit from taking the medicine produced by the company with the largest data moat. This approach also clearly benefits from Process Power. Over time, the winner for this new modality could even accrue a clear Branding advantage as the market leader.

If more forms of medicine start to look like this, we could see a wave of biotechs directly competing to establish themselves as an entirely new generation of pharmaceutical company.

In considering this, I can't help but think of my good friend Packy McCormick's writing around Vertical Integrators. In his words, there are several defining characteristics of these companies:

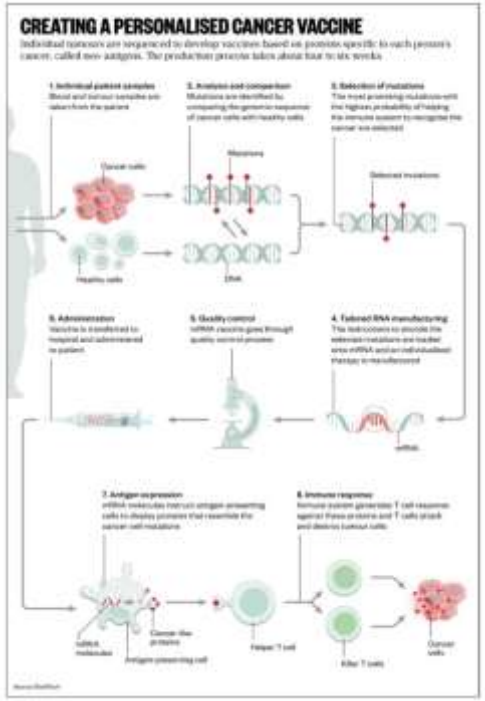
Vertical Integrators are companies that:

1. Integrate multiple cutting-edge-but-proven technologies.
2. Develop significant in-house capabilities across their stack.
3. Modularize commoditized components while controlling overall system integration.
4. Compete directly with incumbents.
5. Offer products that are better, faster, or cheaper (often all three).

For Vertical Integrators, the integration is the innovation. Just as before, there are clear challenges with this strategy. There is no free lunch!

A massive hurdle will likely be financing and capital formation. This approach to company creation is totally distinct from how most biotech investors think about generating returns. It's completely unclear if a Big Pharma company would be willing to buy a company with such a complex product without definitive proof of commercial viability.

Winners in this space may need to look elsewhere for capital. One possible option is to tap the growing pool of "Deep Tech" venture capital that is focused on underwriting breakthrough advances in hardware and innovation in the world of atoms. Later stage investment could come from generalist growth equity firms rather than traditional biotech crossover funds.



Hershberg Essay: Building a Vertical Integrator in Biotech

Attempting to build a Vertical Integrator in biotech is not for the faint of heart.

Combining multiple technologies in new ways is hard. Financing will be hard. Scaling commercial efforts will be hard. It could take a lot longer to achieve success.

Because of all of these factors, biotech investing could start to mirror the rest of the private market's evolution. Companies could stay private longer. Consider SpaceX, which has raised nearly $10B over its 23 years as a private company and is now valued at $350B. Liquidity for early investors and employees has come from secondary markets rather than M&A transactions or IPOs.

Despite the hurdles, the prize is potentially massive.

Measurement tools that were once unimaginable are now commonplace in biology. The foundational insights that gave birth to the last wave of generational biotechs have been refined and commoditized. AI is accelerating biology's transition into a predictive and quantitative discipline.

Tackling big problems that have evaded prior approaches—like cancer, infectious disease, and brain health—will likely require creative solutions that integrate multiple digital and physical building blocks.

If the companies solving these global problems establish moats in new ways, we could see the first $1T+ biotech firms come into existence.

The public biotech market is pretty gloomy right now. And for American biotechs, the steady uptick in Chinese acquisitions has further threatened their prospects of success. As Adam Feuerstein wrote, "Sentiment is lousy and the bad mood is relentless, to the point where people are seriously wondering if a sector turnaround is ever possible."

At the same time, the early-stage market is brimming with potential. The pace of technological innovation is equivalently relentless. Entrepreneurs equipped with hard-earned lessons and powerful tools are pursuing wholly new ideas.

Perhaps the right question isn't whether the market will rebound. Because it will. Markets are cyclical. Instead, the question is if biotech is on the cusp of a phase shift into something new altogether. If it is, it's never been a better time to build.

In other words…

Biotech is Dead. Long Live Biotech!

Source: https://centuryofbio.com/p/commoditization

Obesity Update

Soleno Wins FDA Approval for Prader-Willi Hyperphagia Treatment

The drug, named Vykat XR, will be available to patients in the US with Prader-Willi syndrome from April 2025.

Jenna Philpott, *Pharmaceutical Technology*, March 27, 2025 (excerpt)

Soleno Therapeutics has won US Food and Drug Administration (FDA) approval for diazoxide choline – which will be branded as Vykat XR – to treat extreme hunger in patients with Prader-Willi syndrome.

This approval follows a three-month delay from the FDA. In November 2024, the agency classified responses from Soleno as a "major amendment" to its new drug application (NDA), requiring additional time to review. However, the agency did not raise concerns about the drug's safety, efficacy, or manufacturing.

Prader-Willi syndrome is a rare genetic disorder caused by abnormalities in chromosome 15. Symptoms include low muscle tone, developmental delays, and behavioural challenges. Extreme hunger – known as hyperphagia, is one of the most serious and defining characteristics of the disorder and can lead to severe obesity and associated health complications if unmanaged. Vykat XR is now the only FDA-approved treatment specifically addressing hyperphagia in Prader-Willi syndrome.

The FDA approval of Vykat XR was based on data from the Phase III Study C602-RWP clinical trial (NCT03714373). Efficacy was demonstrated during a 16-week randomised withdrawal study period. Patients who switched to a placebo demonstrated a statistically significant worsening of hyperphagia compared to those who remained on Vykat XR.

The drug was also studied in the Phase III DESTINY-PWS trial (NCT03440814), which enrolled 127 individuals with genetically confirmed Prader-Willi syndrome. The trial did not demonstrate a statistically significant difference in hyperphagia reduction overall, but Soleno reported "nominally significant" reductions in fat mass, and general improvements in condition as assessed by investigators.

Vykat XR is set to launch in the US in April 2025, according to Soleno's 26 March announcement. Vykat XR – an extended-release tablet containing a crystalline salt formulation of diazoxide – works by activating the adenosine triphosphate (ATP)-sensitive potassium (KATP) channel, which plays a role in hunger regulation.

The approval was welcomed by the Prader-Willi Syndrome Association: "Today marks a historic day for the PWS community. The FDA's approval of Vykat XR represents a monumental step forward in addressing the longstanding unmet needs of individuals living with PWS and their families," said Stacy Ward, CEO of the Association.

Source: https://www.pharmaceutical-technology.com/news/soleno-wins-fda-approval-for-prader-willi-hyperphagia-treatment/

Novo Nordisk's Diabetes Pill Slashes Risk of Cardiovascular Complications by 14% After Four Years

Annika Kim Constantino, CNBC, Mar 29, 2025

Novo Nordisk on Saturday said its diabetes pill Rybelsus showed cardiovascular benefits in a late-stage trial, paving the way for it to become a new treatment option for people living with diabetes and heart disease.

The pill lowered the risk of cardiovascular-related death, heart attack and stroke by 14% compared to a placebo after four years on average in patients with diabetes and established heart disease, with or without chronic kidney disease. The Danish drugmaker presented the results on Rybelsus, which is already approved for Type 2 diabetes, at the American College of Cardiology's Annual Scientific Session in Chicago.

Novo Nordisk has already applied in the U.S. and EU to expand the pill's approval to include lowering the risk of serious cardiovascular complications, Stephen Gough, the company's global chief medical officer, said in an interview.

Rybelsus is the once-daily oral formulation of Novo Nordisk's blockbuster diabetes injection Ozempic, which is taken once a week. Both treatments, as well as the company's weekly weight loss injection Wegovy, contain the active ingredient semaglutide.

Wegovy in March 2024 won U.S. approval for slashing the risk of major cardiovascular events in adults with cardiovascular disease and who are obese or overweight. But the pill data presented on Saturday suggests that patients who are hesitant to take injections, such as those who are afraid of needles, could soon access treatment in a more convenient way.

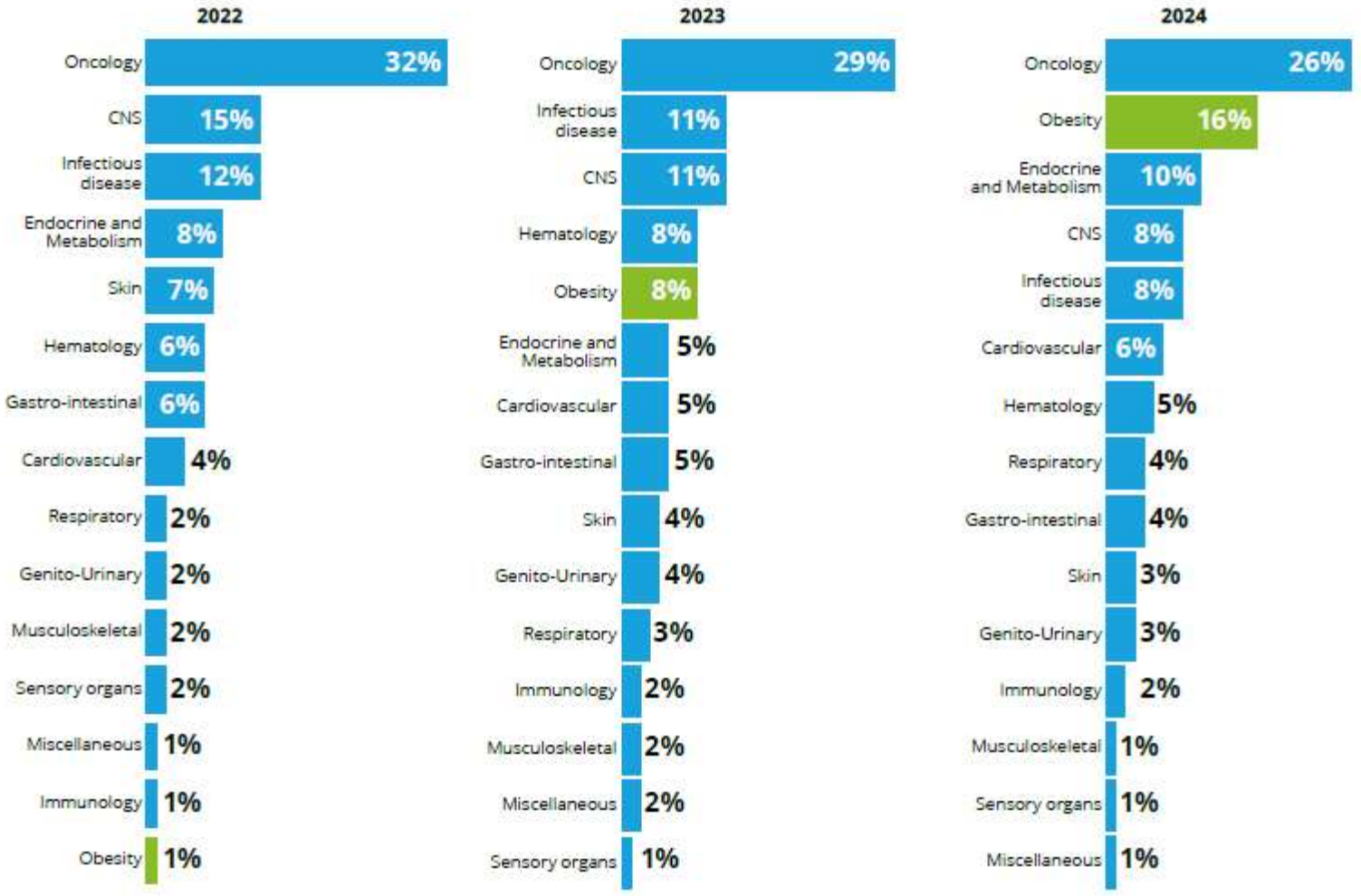
"We know not everybody wants an injection, whether it is painful or not, they want the option of an oral medication," Gough told CNBC. "We provide that option, that you can have one or the other, depending on what the patients and the healthcare professional think is right in that joint discussion."

The data comes as a slate of other drugmakers, including Eli Lilly,
work to develop oral GLP-1s for diabetes, weight loss and other conditions, such as sleep apnea.

Source: https://www.cnbc.com/2025/03/29/novo-nordisks-diabetes-pill-rybelsus-slashes-cardiovascular-risk.html

Deloitte: Obesity Importance is Rising Fast. Oncology Down.

Figure 7. Forecast revenue for the top 20 cohort by therapy area, 2022-2024



Source: Deloitte analysis of Evaluate Pharma data, 2025

The remarkable growth trajectory of GLP-1s, particularly in the obesity market, underscores the substantial return potential of addressing unmet needs at a population health level. Forecast revenue from obesity indications has increased from one per cent of total revenue in 2022, to eight per cent in 2023 and 16 per cent in 2024. (see Figure 7).

Source: https://www2.deloitte.com/us/en/pages/life-sciences-and-health-care/articles/measuring-return-from-pharmaceutical-innovation.html

Novo's Obesity Pipeline Keeps Evolving With up to $1B Lexicon Deal

Tristan Manalac, *Biospace*, March 28, 2025 (excerpt)

Lexicon's LX9851 targets ACSL5, a liver enzyme involved in fat metabolism that helps moderate fat accumulation and slow down gastric emptying.

In its search for its next-generation obesity drug, Novo Nordisk on Friday put $1 billion on the line for Lexicon Pharmaceuticals' non-incretin obesity drug.

Under the terms of the agreement, Novo will hand over up to $75 million in upfront and near-term milestone payments. Lexicon, meanwhile, will be eligible to receive additional development, regulatory and sales-based milestone payments, with the total deal value reaching $1 billion. The Texas-based biotech will also be able to claim tiered royalties on net sales, in the event of approval.

The star of Wednesday's deal is Lexicon's molecule called LX9851. Unlike Novo's blockbuster product semaglutide—marketed as Ozempic for type 2 diabetes and Wegovy for chronic weight management—LX9851 is not an incretin drug.

In November 2024, Lexicon presented in vivo preclinical data for LX9851, showing that the drug candidate could lead to "significant" drops in food intake, fat mass and overall weight in mice. LX9851 also mitigated weight regain even after patients stopped semaglutide treatment and had positive effects on liver steatosis.

Source: https://www.biospace.com/business/novos-obesity-pipeline-keeps-evolving-with-up-to-1b-lexicon-deal

Rajkumar et al. BMC Medical Genetics (2016) 17:56
DOI 10.1186/s12881-016-0320-4

BMC Medical Genetics

RESEARCH ARTICLE Open Access

Acyl-CoA synthetase long-chain 5 genotype is associated with body composition changes in response to lifestyle interventions in postmenopausal women with overweight and obesity: a genetic association study on cohorts Montréal-Ottawa New Emerging Team, and Complications Associated with Obesity

Abishankari Rajkumar[1,3], Gilles Lamothe[2], Pierrette Bolongo[3], Mary-Ellen Harper[1], Kristi Adamo[4,5,6], Éric Doucet[6], Remi Rabasa-Lhoret[7,8], Denis Prud'homme[6,9] and Frédérique Tesson[3,10*]

Abstract

Background: Genetic studies on Acyl-CoA Synthetase Long-Chain 5 (ACSL5) demonstrate an association between rs2419621 genotype and rate of weight loss in women with obesity in response to caloric restriction. Our objectives were to (1) confirm results in two different populations of women with overweight and obesity (2) study rs2419621's influence on body composition parameters of women with overweight and obesity following lifestyle interventions.

Methods: rs2419621 genotype was determined in women with overweight and obesity who participated in the Montréal-Ottawa New Emerging Team (MONET $n = 137$) and Complications Associated with Obesity (CAO $n = 37$) studies. Genotyping was done using TaqMan MGB probe-based assay. Multiple linear regression analyses were used to test for associations.

Results: When studying women with overweight and obesity, rs2419621 [T] allele carriers had a significantly greater decrease in visceral fat, absolute and percent fat mass and a greater increase in percent lean mass in response to lifestyle intervention in comparison to non-carriers. Studying only individuals with obesity showed similar results with rs2419621 [T] allele carriers also displaying a significantly greater decrease in body mass index following the lifestyle intervention in comparison to non-carriers.

Conclusion: Women with overweight and obesity carrying the ACSL5 rs2419621 [T] allele are more responsive to lifestyle interventions in comparison to non-carriers. Conducting such genetic association studies can aid in individualized treatments/interventions catered towards an individual's genotype.

Table 8 Regression analysis studying lifestyle intervention effect in CT/TT vs CC women with obesity

Multiple regression model	Dependent variable	Number of subjects (*n*)	Parameter estimate	Standard error	Variable *p*-value	r^2 model	r^2 adjusted model	Model *p*-value
1	Δ BMI	87	−2.14	1.05	0.045	0.129	0.087	0.022
2	Δ Lean Mass	85	0.49	1.07	0.645	0.151	0.086	0.041
3	Δ Fat Mass	85	−5.13	1.97	0.011	0.212	0.151	0.004
4	Δ % Lean Mass	85	3.12	1.19	0.010	0.257	0.189	0.001
5	Δ % Fat Mass	85	−3.30	1.30	0.013	0.252	0.194	0.001
6	Δ Visceral fat	85	−9.53	3.47	0.007	0.214	0.164	0.002
7	Δ Muscle attenuation	87	1.20	0.72	0.098	0.177	0.126	0.007

* Multiple linear regression analysis was conducted. Parameter estimate of independent variable = Xt was studied. Physiological factors (dependent variables) were studied while adjusting for confounding factors independent for each model (Table 2). Analysis was conducted on MONET and CAO studies combined

The Lexicon drug candidate would cause a patient to be more likely to lose weight with a GLP-1 or lifestyle intervention.

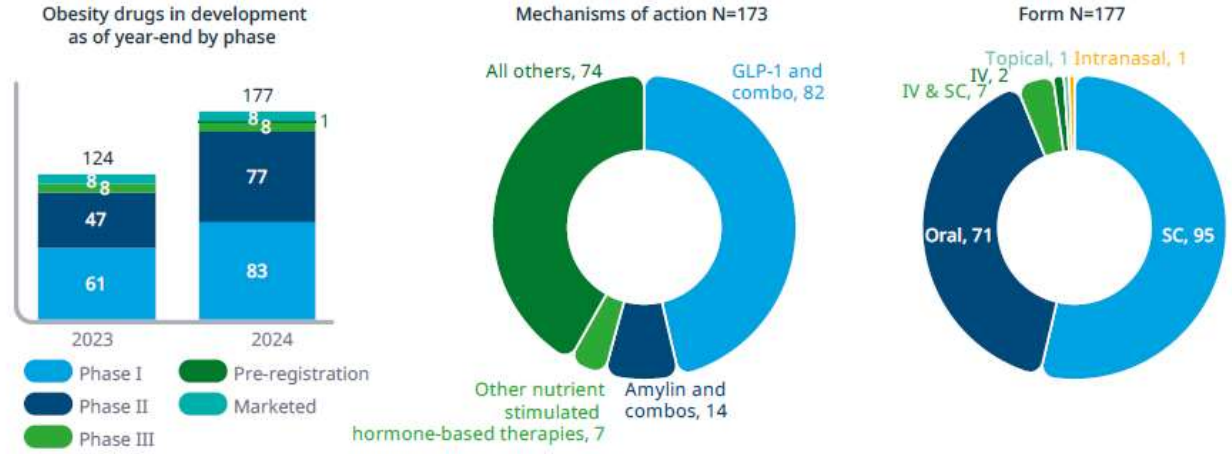
This is a potentially very clever approach to accelerate weight loss with GLP-1s.

Source: https://bmcmedgenet.biomedcentral.com/articles/10.1186/s12881-016-0320-4

IQVIA Institute: Clinical Stage Obesity Pipeline Exploding

There are 173 obesity medicines in development or marketed with multiple mechanisms beyond the leading GLP-1 therapies

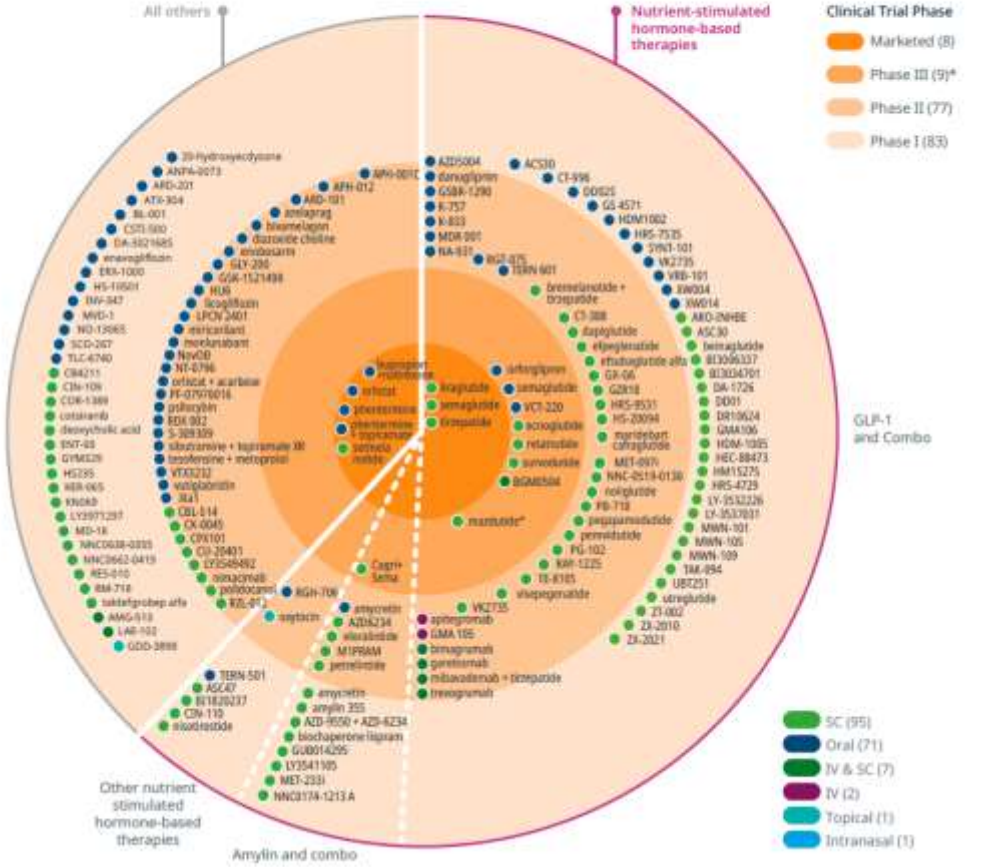
Exhibit 24: Obesity pipeline by phase, target and route of administration



Source: Citeline Trialtrove, Jan 2025; IQVIA Institute, Jan 2025.

GLP-1 and combination approaches account for the majority of obesity R&D programs

Exhibit 25: Obesity pipeline by phase, target and route of administration



Source: https://www.iqvia.com/insights/the-iqvia-institute/reports-and-publications/reports/global-trends-in-r-and-d-2025

Makary's FDA Has Options In Industry Fight Over Weight Loss Drugs

Arthur Kellermann, *Forbes*, Mar 27, 2025 (excerpt)

Americans pay more for prescription drugs than citizens in any other country — so much more that the U.S. accounts for half of world sales revenue from pharmaceuticals, but only consumes 13% of the total volume of prescription drugs. Compared to other wealthy nations in the Organization for Economic Co-operation and Development, the U.S. accounts for 60% of pharmaceutical revenues but only 24% of volume, according to a recent issue brief from the U.S. Department of Health and Human Services. If Dr. Marty Makary, the newly confirmed commissioner of the U.S. Food and Drug Administration, wants to change this lopsided deal, the fight over weight loss drugs is a good place to start.

For example, in 2023, the list price for a month's supply of Ozempic (semaglutide) in the U.S. was $936, more than five times higher than the list price in Japan ($169), and about 10 times the list price in Sweden, the United Kingdom, Australia and France, according to the Peterson-KFF Health System Tracker.

When the public learned that these drugs help people lose weight, demand quickly exceeded supply. This opened the door for FDA-licensed and state-licensed compounding pharmacies to produce lower-cost copies using the same active pharmaceutical ingredients (semaglutide or tirzepatide) as brand-name GLP-1 drugs at far lower cost. About 2 million Americans are currently using compounded GLP-1 medications, according to Kaiser Health News.

Big Pharma Strikes Back

This did not sit well with Novo Nordisk and Eli Lilly, the two multinational manufacturers of FDA-approved brand-name GLP-1 drugs. To reclaim market exclusivity as quickly as possible, they raced to boost production. Last month, the FDA announced that their brand-name GLP-1 drugs are no longer in shortage. On March 10, the agency notified compounding pharmacies that they should wind down production of medications containing semaglutide or tirzepatide or risk enforcement action.

Patients Are Worried

While the FDA focus is on availability, Americans are far more worried about the cost of brand-name GLP-1 drugs. This is particularly true for patients with health insurance that don't cover them.

Anticipating pushback, Novo announced earlier this week that it will directly sell Wegovy to cash-paying patients at a discounted price of $499 per month. Lilly already sells direct-to-consumer versions of its weight loss products at prices ranging from $349 to $699 monthly, depending on the dose.

Since these "discounted" monthly prices are significantly more expensive than those charged by compounders, its unclear how many cash-paying customers will be able to afford them.

What Are Makary's Options?

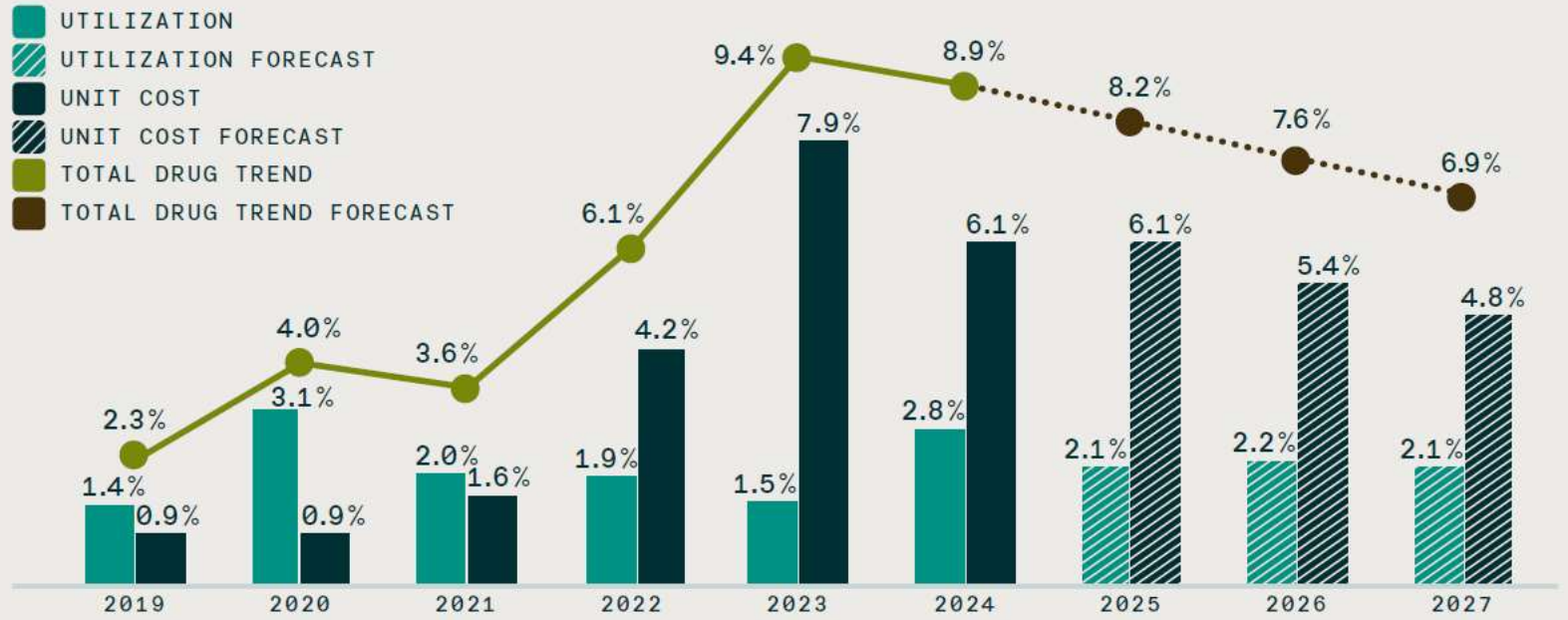
1: Allow FDA Enforcement To Proceed
2: Pause Enforcement And Pressure Manufacturers To Cut Prices
3: Limit FDA Enforcement To Compounders Making "Essential Copies" Of Brand-Name GLP-1 Drugs
4: On Behalf Of The States, Pursue Licensing Agreements With The Manufacturers
5: "The Nuclear Option"

Source: https://www.forbes.com/sites/arthurkellermann/2025/03/27/makarys-fda-has-options-in-industry-fight-over-weight-loss-drugs/

Evernorth Study: U.S. Total Drug Spend is Rising Rapidly

Evernorth Research Institute, March 25, 2025

Figure 1: Annual growth rate changes in total drug spend



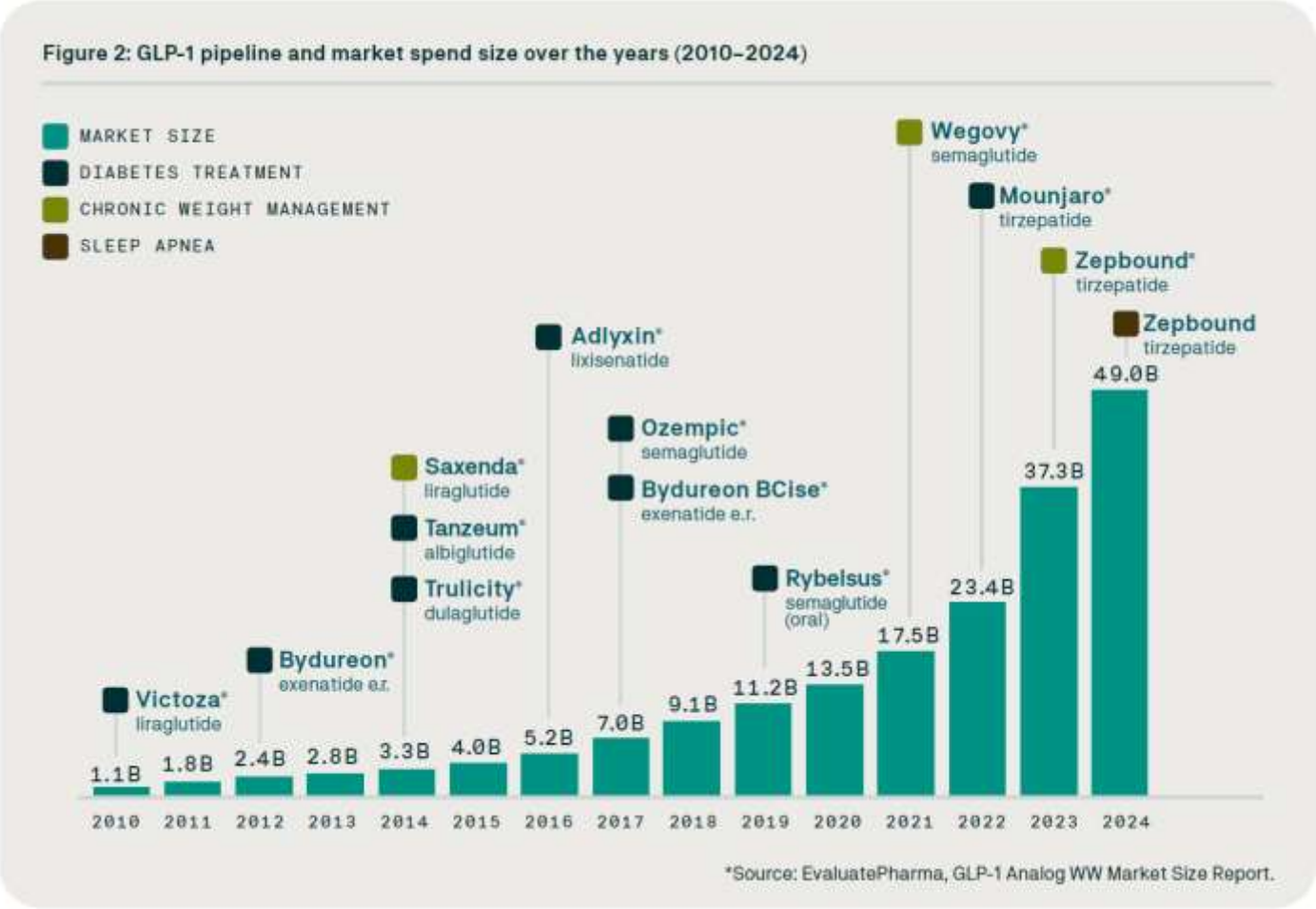
Evernorth Health Services is a health services subsidiary of The Cigna Group, established to deliver innovative and flexible health solutions aimed at improving health outcomes and increasing vitality. Launched in September 2020, Evernorth integrates and coordinates Cigna's health services capabilities, including pharmacy solutions, benefits management, and care solutions. The company encompasses several well-known brands and services:

1. **Express Scripts**: A pharmacy benefit management (PBM) company serving over 112 million Americans.
2. **Accredo**: Provides specialty pharmacy and related services for patients with complex and chronic health conditions.
3. **eviCore**: A medical benefits management company committed to ensuring the right delivery of care at the right time.
4. **MDLIVE**: Offers convenient and affordable virtual healthcare services to over 60 million members nationwide.

Source: https://www.evernorth.com/pharmacy-in-focus-2025

GLP-1 Spend Rising Very Rapidly

Evernorth Research Institute, March 25, 2025



Although GLP-1 therapy liraglutide was first approved for obesity in 2014, its adoption was limited, likely due to its daily injection requirement and perceived modest weight loss outcomes compared to other therapies. The landscape shifted dramatically in 2021 with the introduction of a once-weekly version—semaglutide—which triggered a surge in demand.

Looking ahead, GLP-1 therapies will continue expanding beyond obesity and diabetes treatment to other chronic conditions, accelerating their widespread adoption. While these advancements offer transformative potential in addressing the chronic disease epidemic, they also bring significant challenges raising critical questions about affordability, accessibility and long-term sustainability.

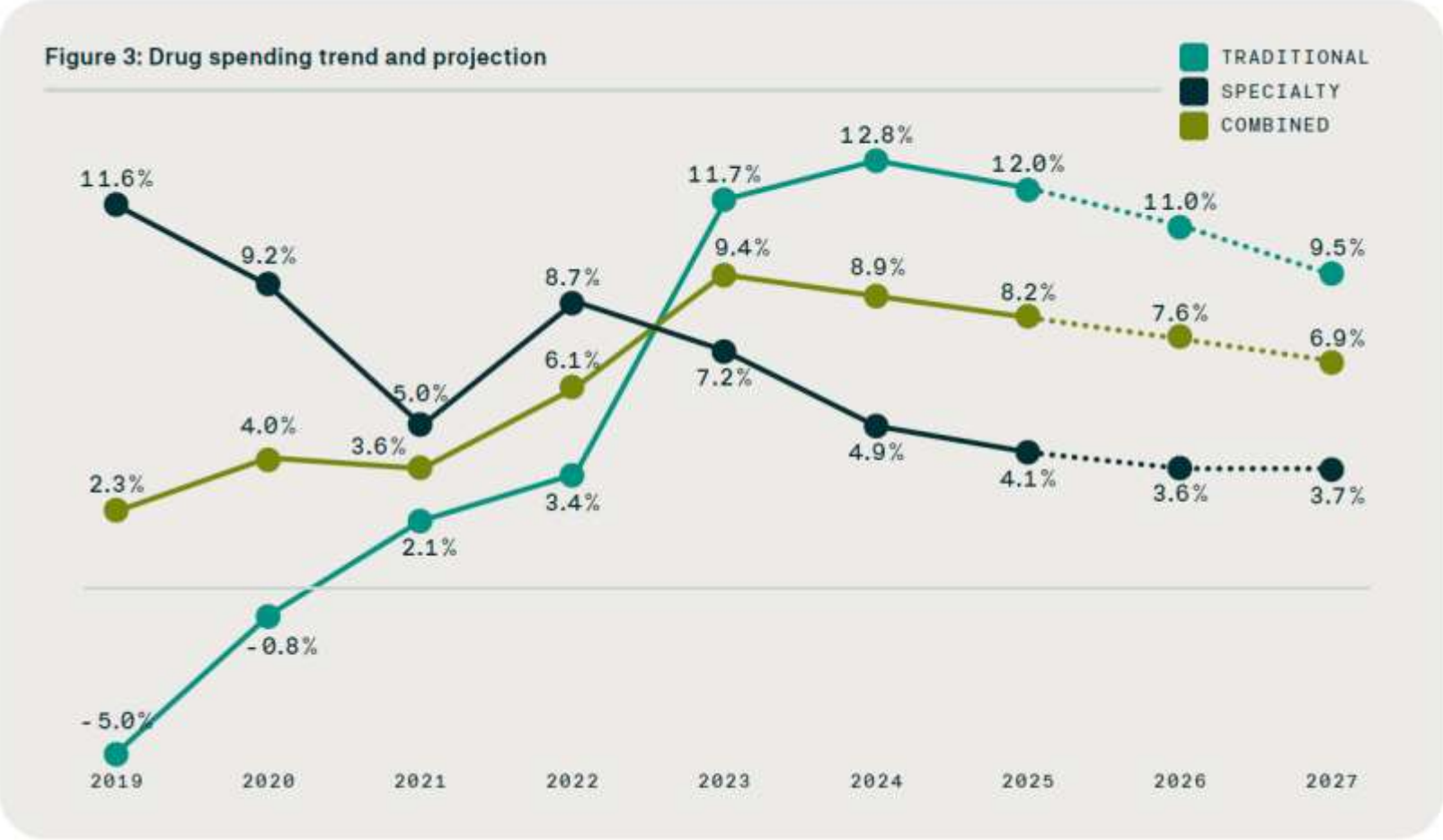
As we embrace their promise, we must also confront one of the greatest healthcare conundrums of our time: how to ensure these treatments remain accessible to those who need them most while preventing financial strain on healthcare systems, employers and individuals.

To better understand these dynamics, we conducted a comprehensive nationwide study of consumers with employer-sponsored health benefits, employers, providers, pharmacists and health plan leaders. Additionally, the study incorporated an extensive analysis of **28 million commercially insured individuals** and an evaluation of industry and scientific literature.

Source: https://www.evernorth.com/pharmacy-in-focus-2025

GLP-1 Spending Growth Causing Traditional Drug Spend to Outpace Specialty for the First Time in Years

Evernorth Research Institute, March 25, 2025

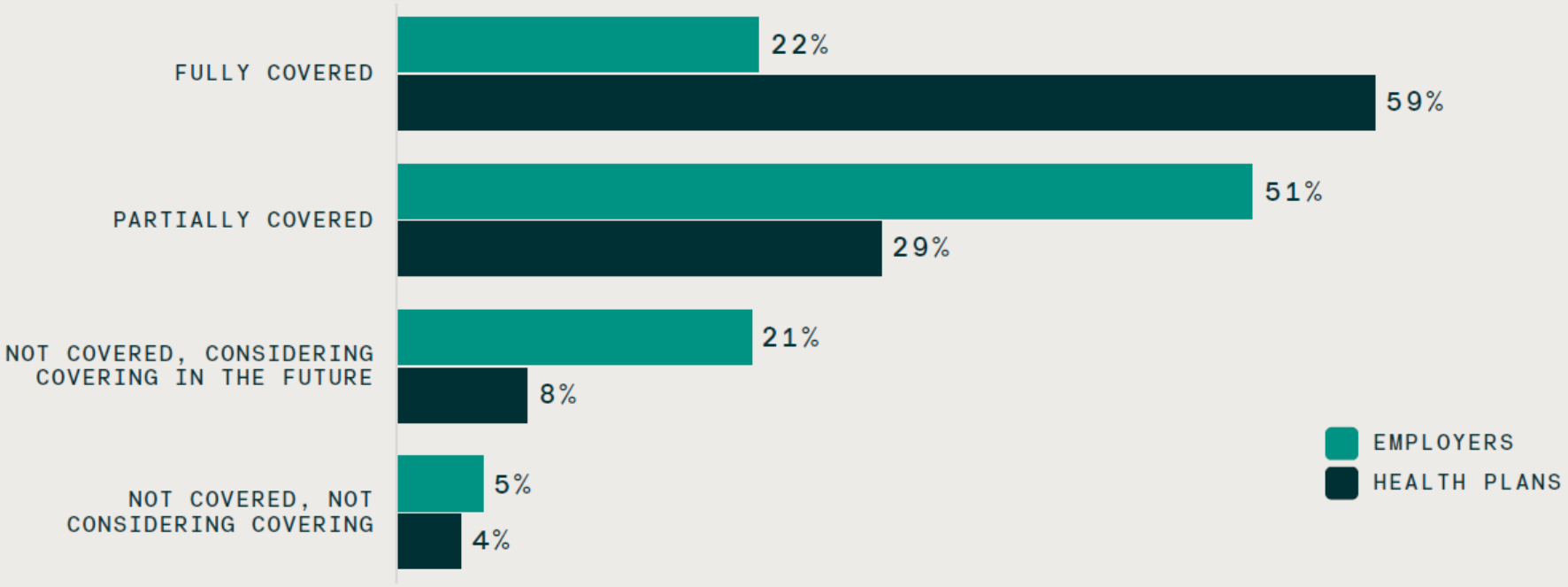


Traditional drugs are medications used to treat common health problems like infections, high blood pressure, high cholesterol and diabetes. They are widely accessible, available in both generic and brand-name versions, and are simpler to manufacture and administer than complex specialty medications. Their costs have also remained stable for years. However, **since the approval of semaglutide for chronic weight management in 2021, traditional drug spending has increased dramatically. The annual growth rate of spending changed from 2.1% in 2021 to 12.8% in 2024,** making a historic shift in pharmaceutical spending. For the first time, traditional drug-spending increases outpaced both specialty and overall drug-spending growth.

Source: https://www.evernorth.com/pharmacy-in-focus-2025

Substantial Insurer Coverage of GLP-1's for Weight Loss

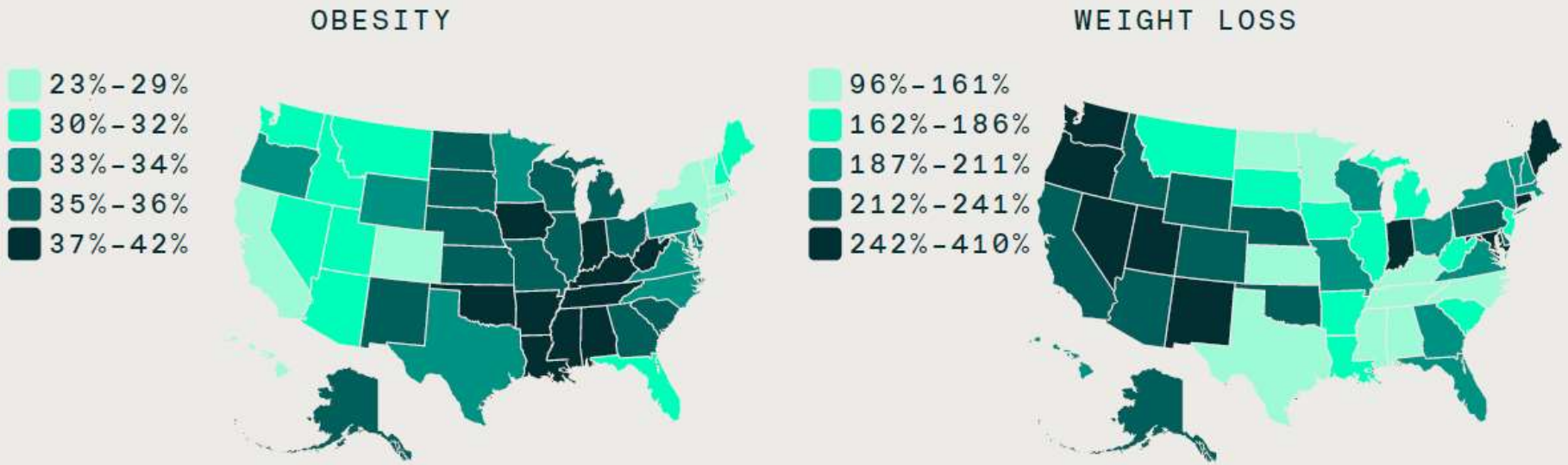
Figure 7: Coverage of GLP-1s for weight loss



Source: https://www.evernorth.com/pharmacy-in-focus-2025

Growth in GLP-1 Utilization Lowest in Midwest and South Where Obesity is Highest

Figure 8: Geographical differences between obesity rates and weight loss GLP-1 utilization growth



EVERNORTH HEALTH SERVICES

NAVIGATING THE GLP-1 CONUNDRUM | 10

Source: https://www.evernorth.com/pharmacy-in-focus-2025

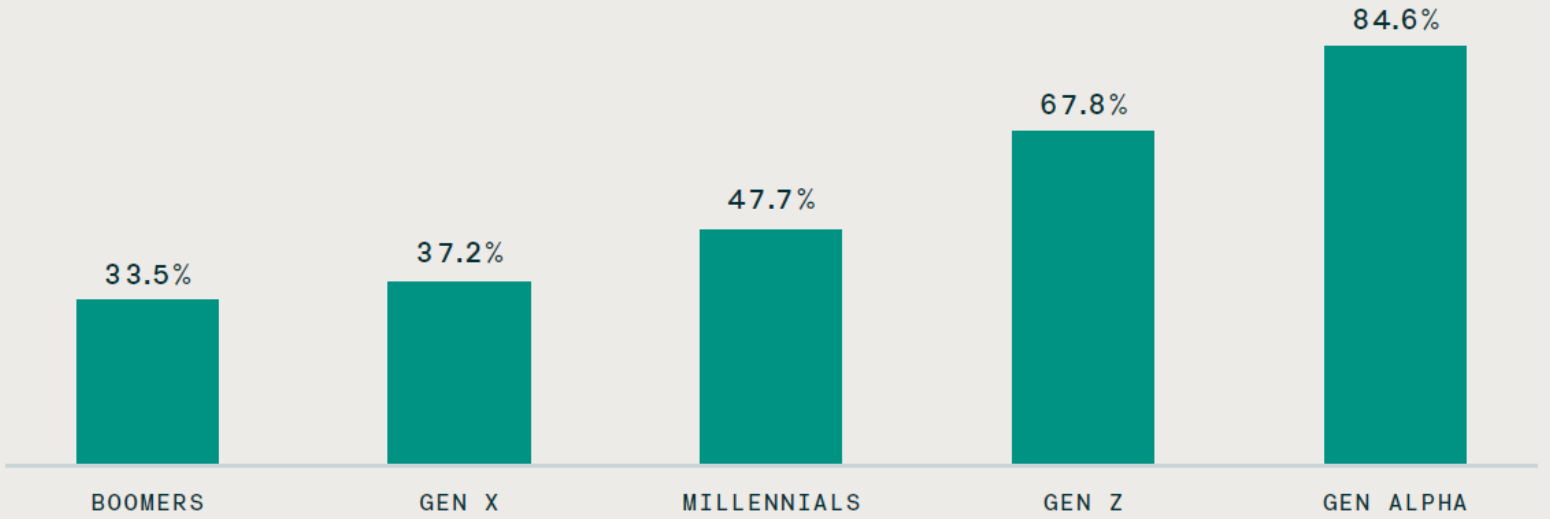
Younger Generation is Taking up GLP-1's Most Rapidly

INSIGHT 03

Surging GLP-1 use among youths amplifies sustainability and supply concerns.

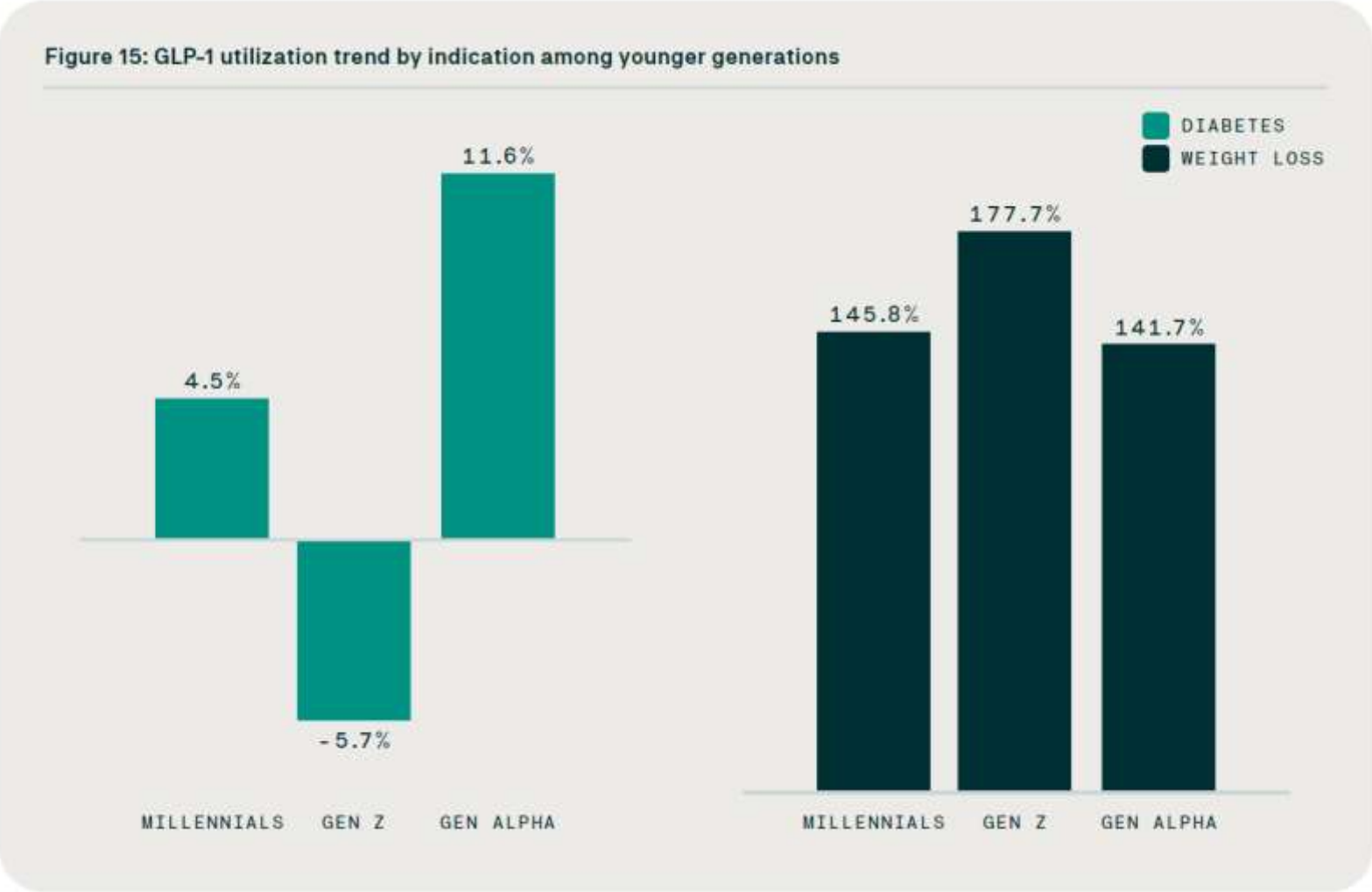
2024 data reveal a concerning increase in the use of GLP-1 drugs among younger generations. Early adoption of costly treatment can create an unsustainable burden on health plans, employers and communities because of potential lifelong reliance and the related comorbidities of these costly treatments.

Figure 14: Percentage increase in GLP-1 utilization by generation



Source: https://www.evernorth.com/pharmacy-in-focus-2025

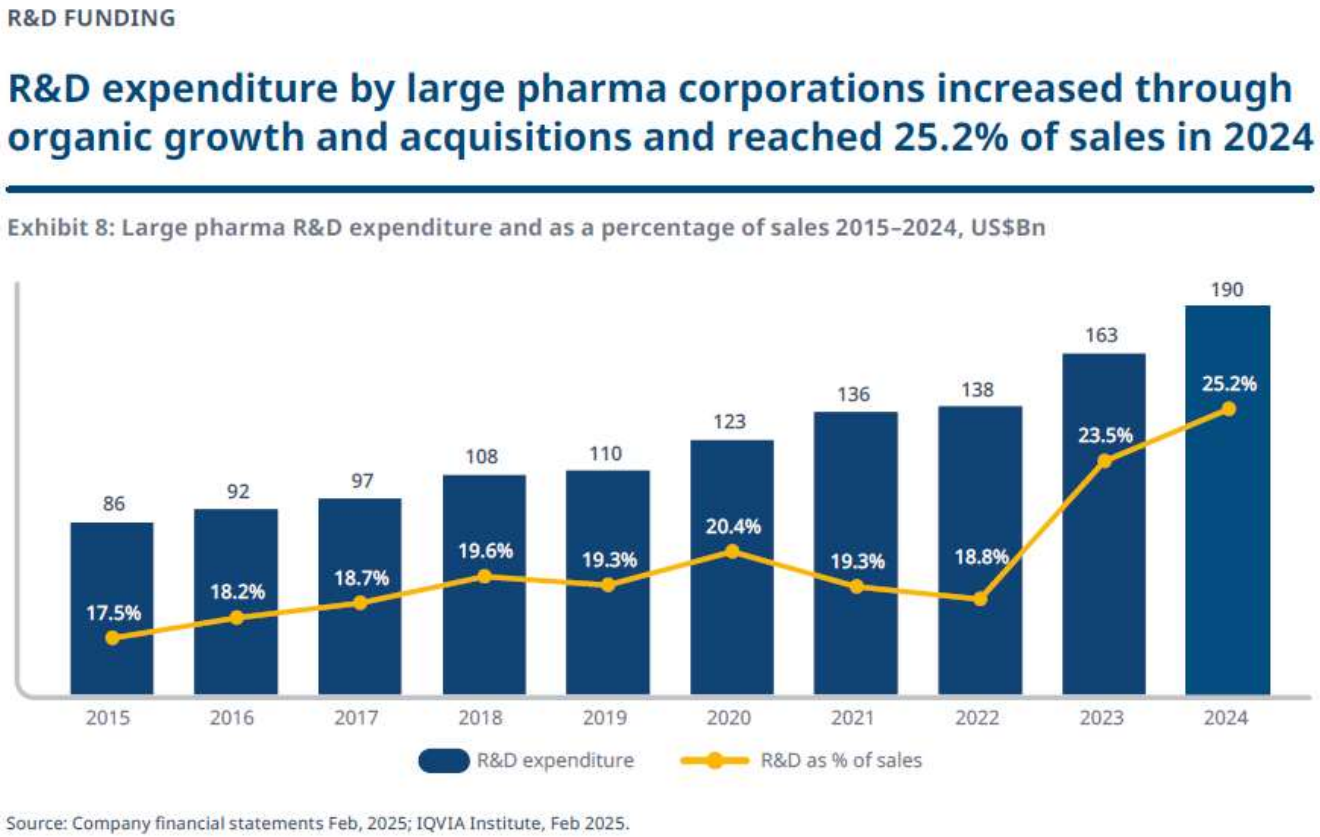
Younger Generation Utilization Growth of GLP-1's Driven by Interest in Weight Loss



Source: https://www.evernorth.com/pharmacy-in-focus-2025

IQVIA Institute 2025 R&D Trends Report

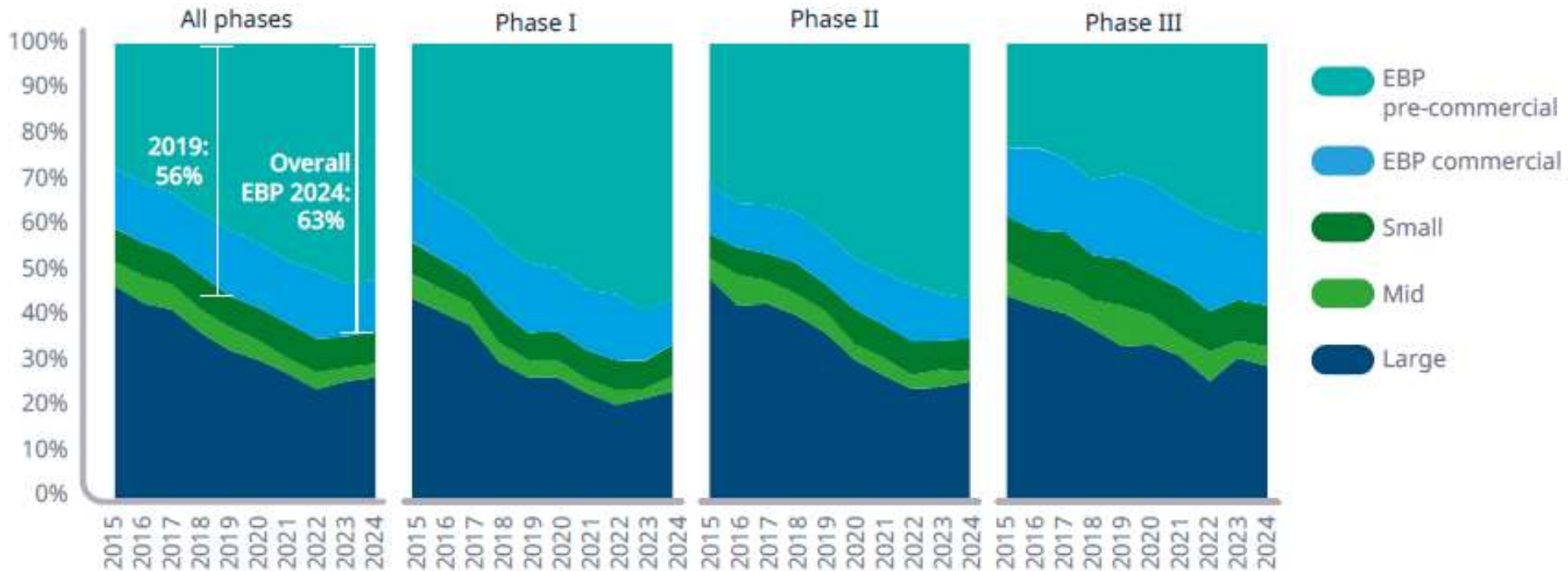
IQVIA Institute R&D Trends Report Out Last Week



Source: https://www.iqvia.com/insights/the-iqvia-institute/reports-and-publications/reports/global-trends-in-r-and-d-2025

Emerging biopharma companies — mostly pre-commercial — are responsible for 63% of trial starts, up from 56% in 2019

Exhibit 11: Share of clinical trial starts by phase and company segment, 2015–2024

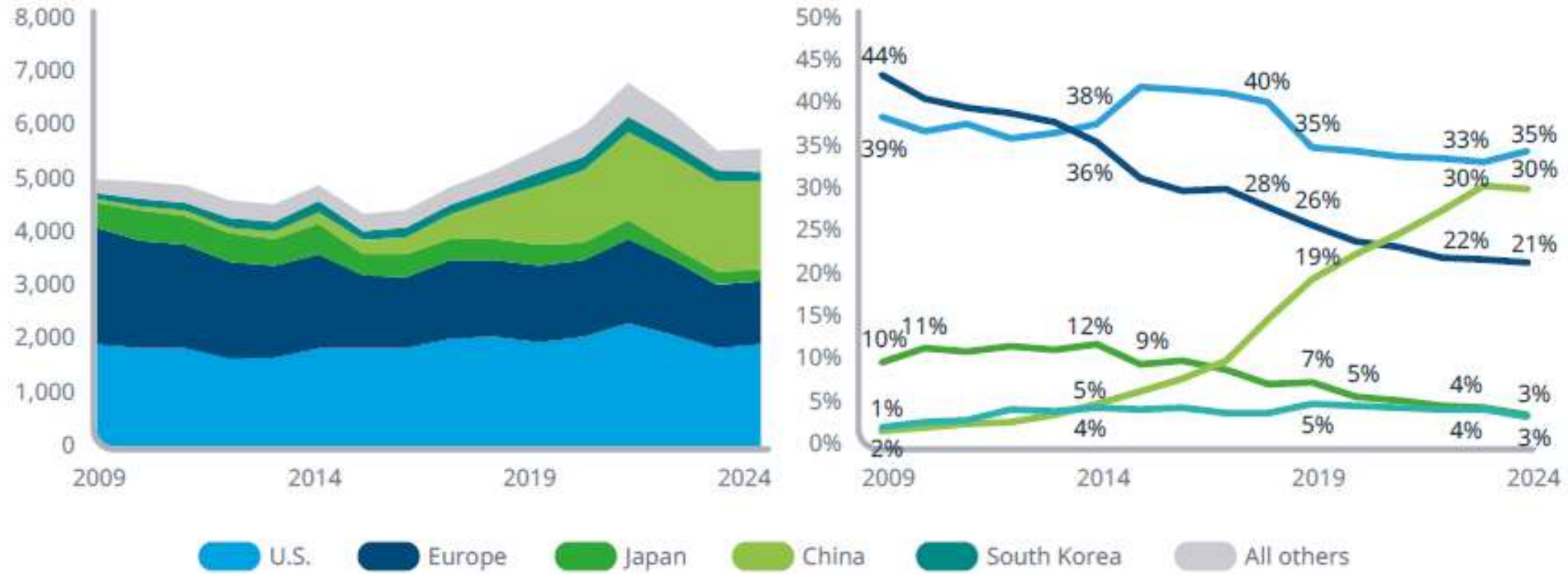


Source: Citeline Trialtrove, Jan 2025; IQVIA Institute, Jan 2025.

Source: https://www.iqvia.com/insights/the-iqvia-institute/reports-and-publications/reports/global-trends-in-r-and-d-2025

Trial starts from China-headquartered companies are now 30% of total trial starts, approaching the U.S. figure of 35%

Exhibit 13: Number of Phase I to III trial starts based on company headquarters location, 2009–2024

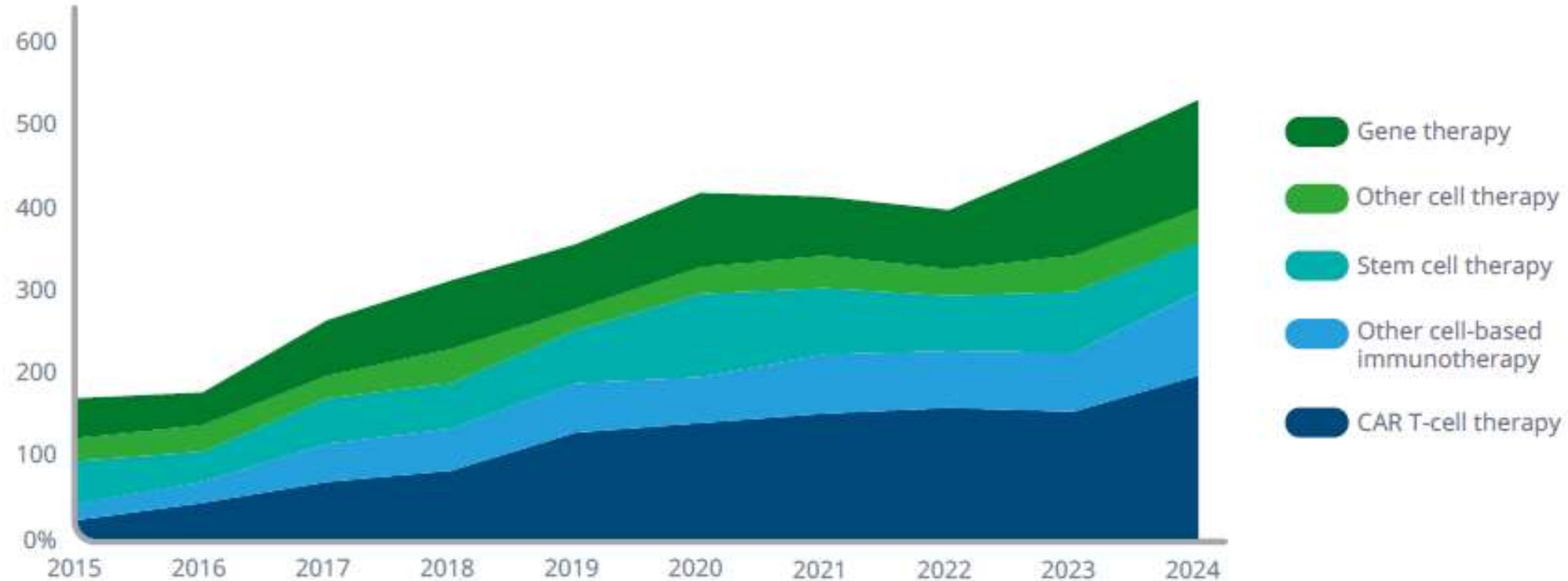


Source: Citeline Trialtrove, Jan 2025; IQVIA Institute, Jan 2025.

Source: https://www.iqvia.com/insights/the-iqvia-institute/reports-and-publications/reports/global-trends-in-r-and-d-2025

Cell and gene therapy trials have more than tripled over the last decade, driven by CAR T and other cell-based immunotherapies

Exhibit 22: Cell and gene therapy clinical trial starts by type, 2015–2024

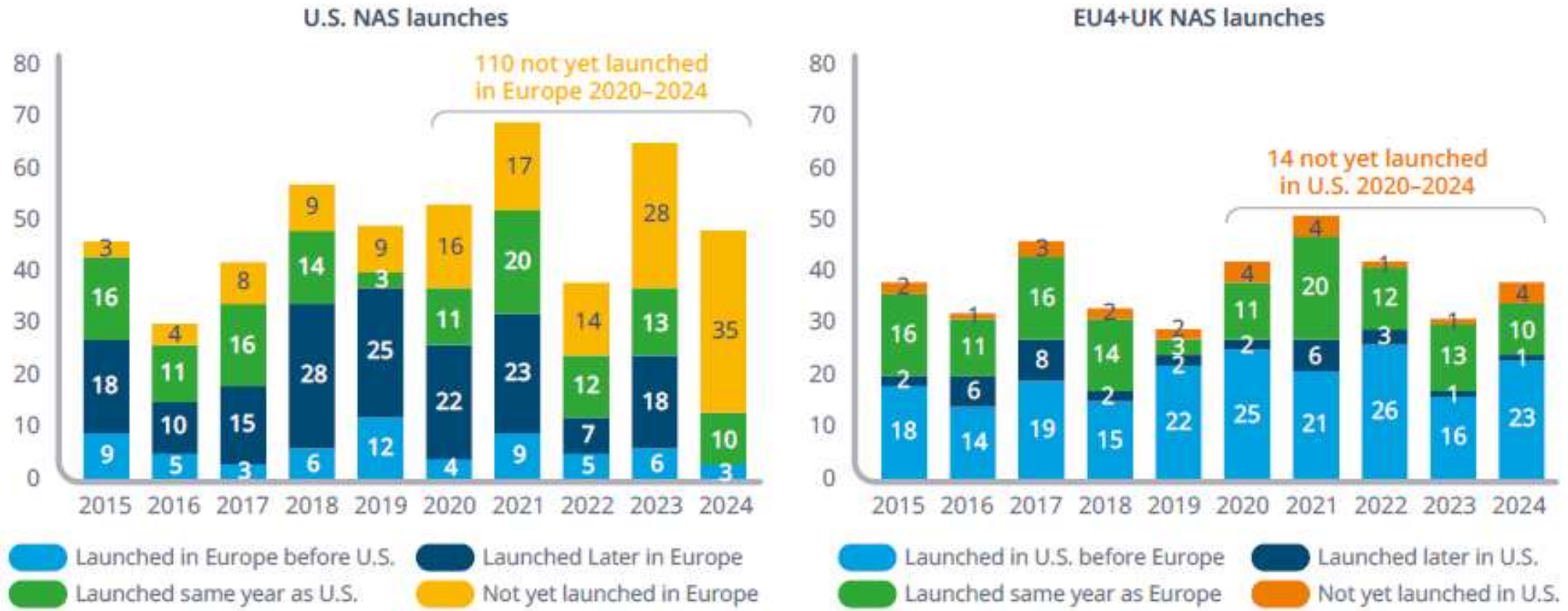


Source: Citeline Trialtrove, Jan 2025; IQVIA Institute, Feb 2025.

Source: https://www.iqvia.com/insights/the-iqvia-institute/reports-and-publications/reports/global-trends-in-r-and-d-2025

Since 2020, 110 NAS launched in the U.S. are not available in Europe while 14 European NAS are not available in the U.S.

Exhibit 32: NAS launches in the U.S. and EU4+UK, 2015–2024

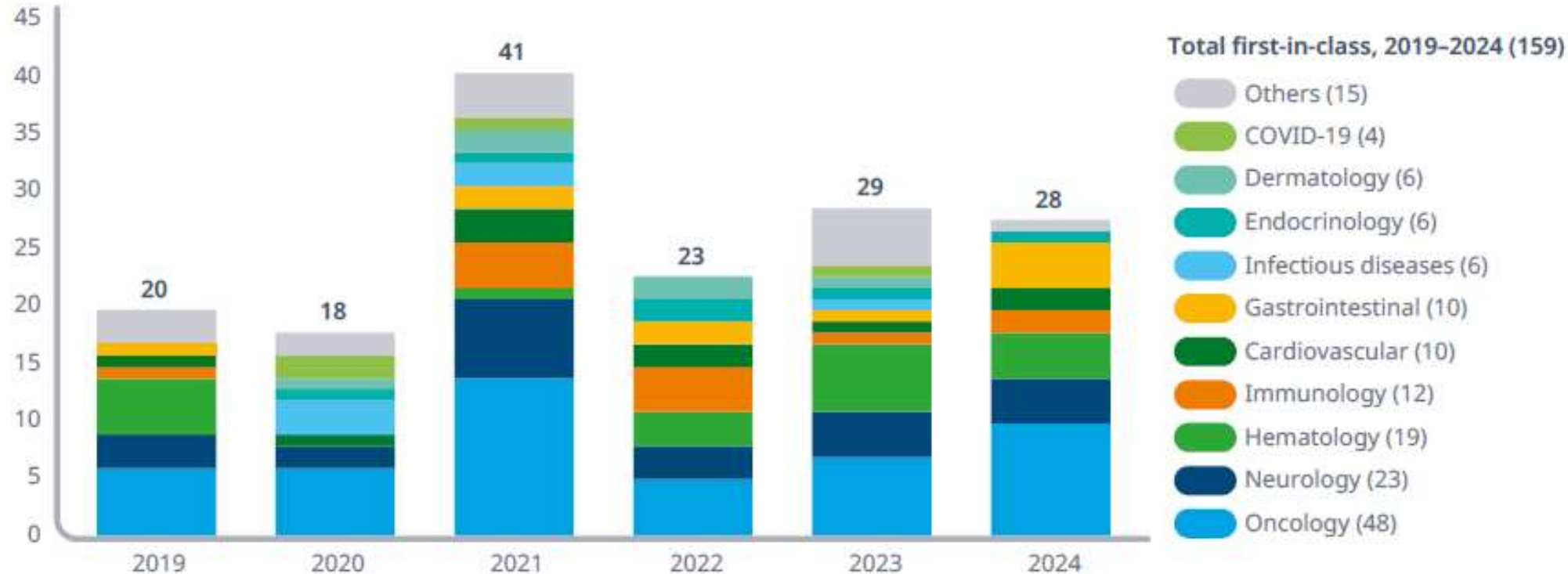


Source: IQVIA Institute, Jan 2025.

Source: https://www.iqvia.com/insights/the-iqvia-institute/reports-and-publications/reports/global-trends-in-r-and-d-2025

In the past 6 years, 159 first-in-class molecules emerged from research and reached the U.S. market

Exhibit 35: First-in-class U.S. novel active substance (NAS) by therapy area, 2019–2024

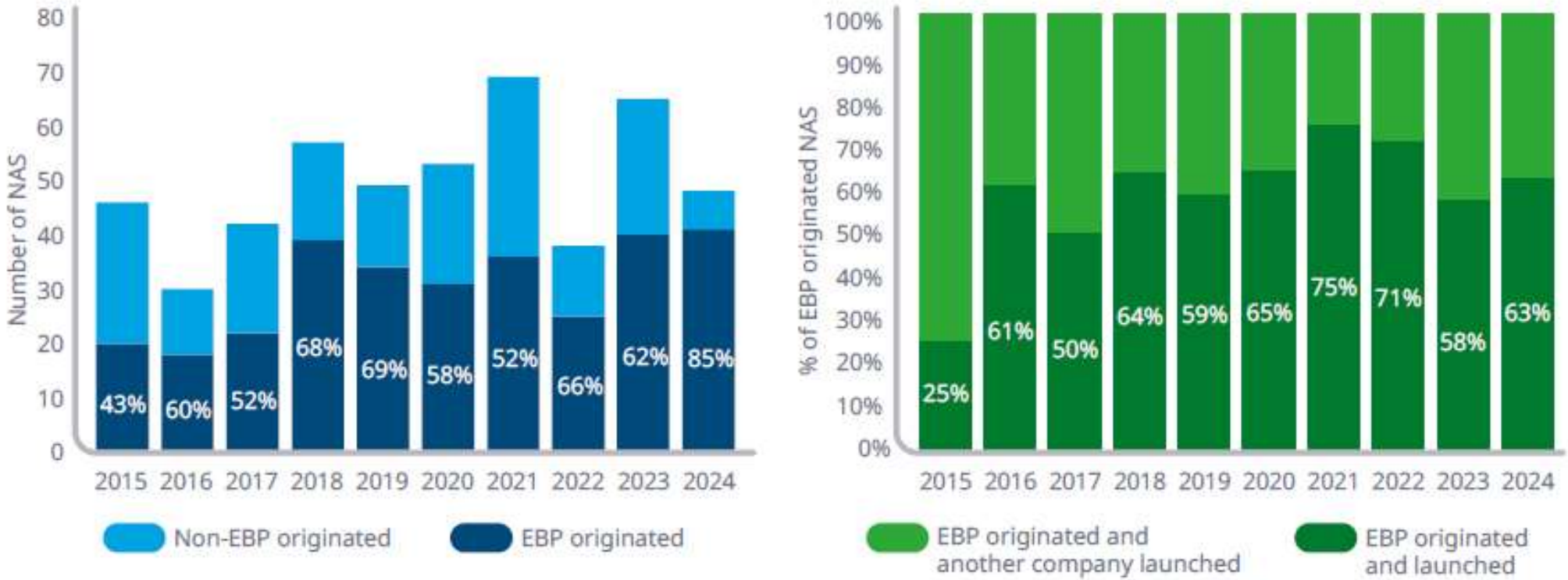


Source: IQVIA Institute, Jan 2025.

Source: https://www.iqvia.com/insights/the-iqvia-institute/reports-and-publications/reports/global-trends-in-r-and-d-2025

Emerging biopharma companies originated 85% of new drugs in 2024 and originated-and-launched 63% of them

Exhibit 37: Companies originating and filing FDA regulatory submissions for NAS and percent of launches by NAS launch year, 2015–2024



Source: IQVIA Institute, Jan 2025.

Source: https://www.iqvia.com/insights/the-iqvia-institute/reports-and-publications/reports/global-trends-in-r-and-d-2025

CLINICAL DEVELOPMENT PRODUCTIVITY

The composite Clinical Program Productivity Index rose in 2024, with a significant Phase III increase

Exhibit 45: Clinical program productivity by phase and overall, 2015-2024 indexed to 2010–14 average

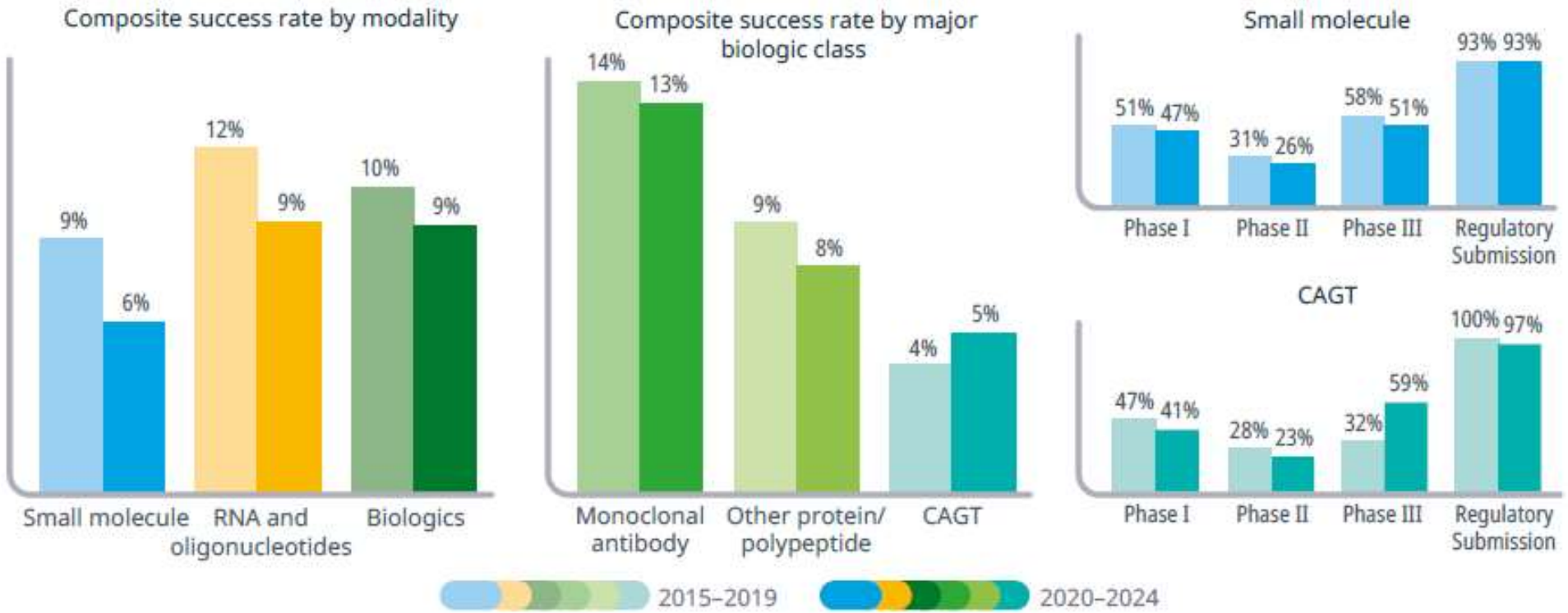
Source: Citeline Trialtrove, Pharmapremia, Jan 2025; IQVIA Institute, Jan 2025.

Source: https://www.iqvia.com/insights/the-iqvia-institute/reports-and-publications/reports/global-trends-in-r-and-d-2025

CLINICAL DEVELOPMENT PRODUCTIVITY

Small molecule success rates declined substantially in the last decade, while cell and gene therapy success rates increased

Exhibit 47: Program composite and between phase success rates, Phase I to approval, 2015–2024

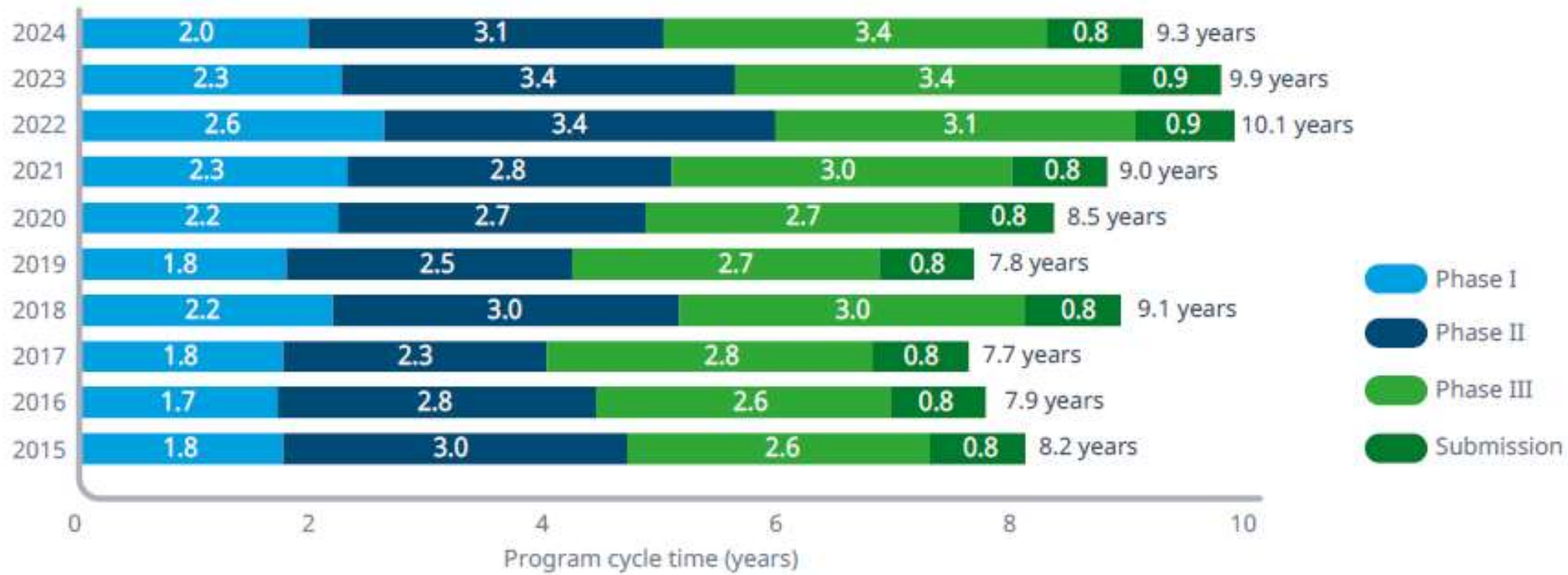


Sources: Citeline Pharmapremia, Jan 2025; IQVIA Institute, Jan 2025.

Source: https://www.iqvia.com/insights/the-iqvia-institute/reports-and-publications/reports/global-trends-in-r-and-d-2025

Total R&D program duration has increased since 2015 but has been stabilizing since 2022

Exhibit 62: Composite median R&D program phase progression duration (years), 2015–2024



Source: IQVIA Dataset, January 2022

Source: https://www.iqvia.com/insights/the-iqvia-institute/reports-and-publications/reports/global-trends-in-r-and-d-2025

Deloitte Analysis: Pharma R&D ROI Staying Positive

Deloitte Report, *Be Brave: Be Bold*, March 2025

Figure 1. Return on late-stage pipeline, 2013-2024

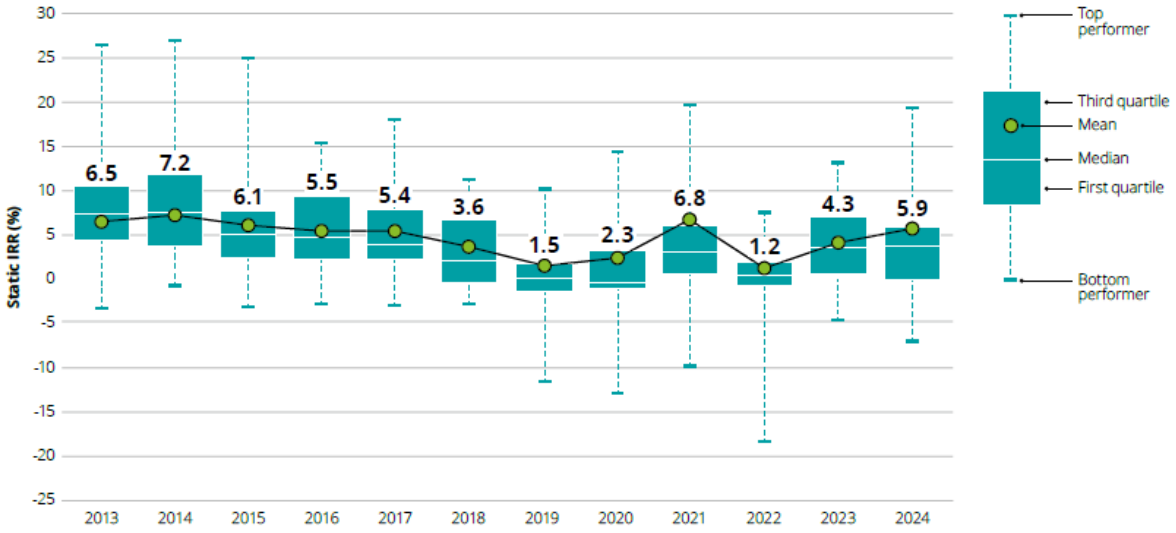
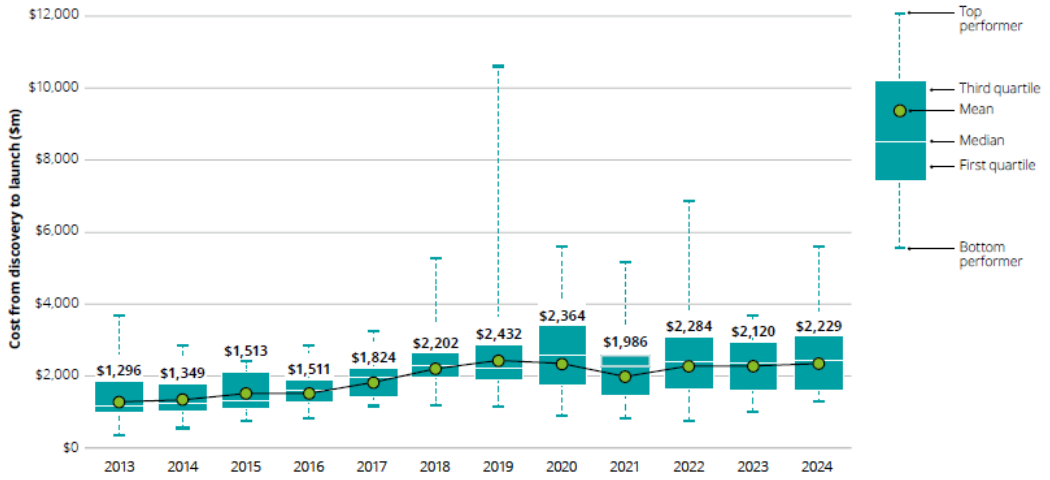


Figure 2. Average R&D cost to develop a drug from discovery to launch, 2013-2024



Our analysis shows that the 2024 IRR increased by 1.6 percentage points, to 5.9 per cent (see Figure 1), continuing the uptick seen in the previous year's analysis. Thirteen out of the 20 companies in our cohort, experienced growth in their IRR ranging between 0.4 and 6.9 per cent, with three companies exceeding a five per cent increase.

This year, the average cost per asset increased to $2.23 billion (see Figure 2), an upward trend observed in 12 out of the 20 companies analysed. While reported costs of pharma R&D, as declared in the cohort's annual returns, continue to increase year on year, since 2020 our cohort has reduced their increase in spend to a compound annual growth rate (CAGR) of 6.44 per cent, compared to 7.69 per cent in the years 2013 to 2020, reflecting the cohort's focus on improving the efficiency of R&D spending.

Source: https://www2.deloitte.com/us/en/pages/life-sciences-and-health-care/articles/measuring-return-from-pharmaceutical-innovation.html

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