Biopharmaceutical Sector

Update – Oct 21, 2024

STIFEL | Healthcare

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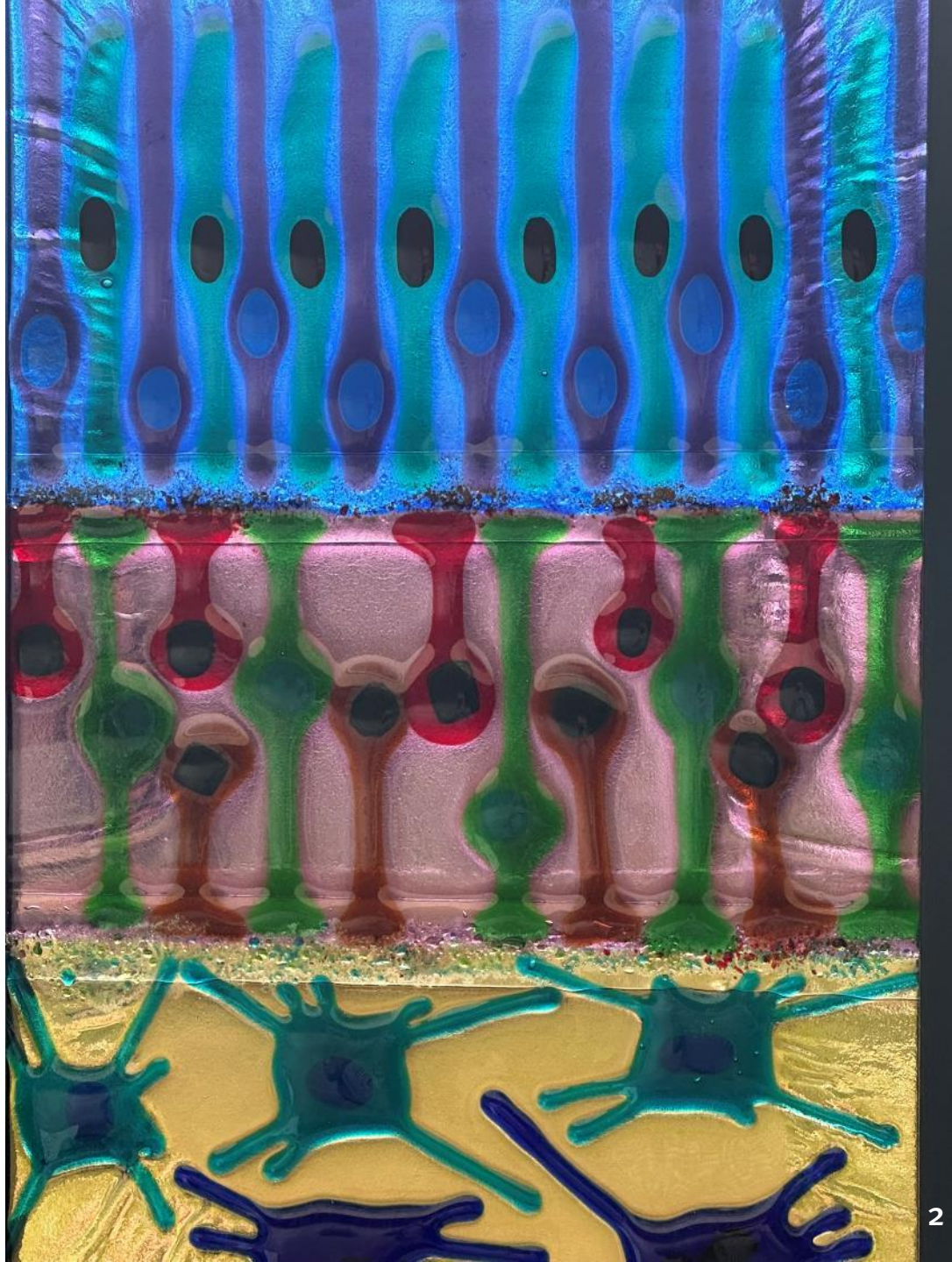

Stained glass rendering of the retina by Joel Kowit. On view at Harvard Medical School, Sep 2024.

Past Issues

If you wish to be added to the mailing list for this publication, please notify Natasha Yeung (yeungn@stifel.com). Past issues:

Oct 7, 2024 (VC update)
Sep 23, 2024 (The Fed Rate Cut)
Sep 9, 2024 (Sector Outlook)
Aug 12, 2024 (Biotech Market)
July 15, 2024 (Halftime Report)
July 8, 2024 (Obesity Market Update)
June 17, 2024 (Lab Market)
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March 11, 2024 (IRA, Immunology)
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Feb 12, 2024 (Fibrosis, Endometriosis)
Feb 5, 2024 (Severe Disease in Women)
Jan 29, 2024 (Pharma R&D Productivity)
Jan 22, 2024 (AI in medicine)
Jan 5, 2024 (Sector Outlook for 2024)
Dec 18, 2023 (Expectations for Future)
Dec 11, 2023 (ASH, R&D Days)
Dec 4, 2023 (Big Pharma, CEA)
November 22, 2023 (Bullish on Biotech)
November 20, 2023 (M&A)
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July 1, 2023 (Obesity drugs)
June 19, 2023 (Generative AI)
June 12, 2023 (IRA, State of Industry)
May 29, 2023 (Oncology update)
May 22, 2023 (FTC case on Amgen/Horizon)

Join Us at Biotech Hangout This Friday

And meet us at a number of upcoming conference events:

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

New York City
@Cure
October 28-30, 2024
https://biofuture.com/

To meet with Stifel at BioFuture:
yeungn@stifel.com

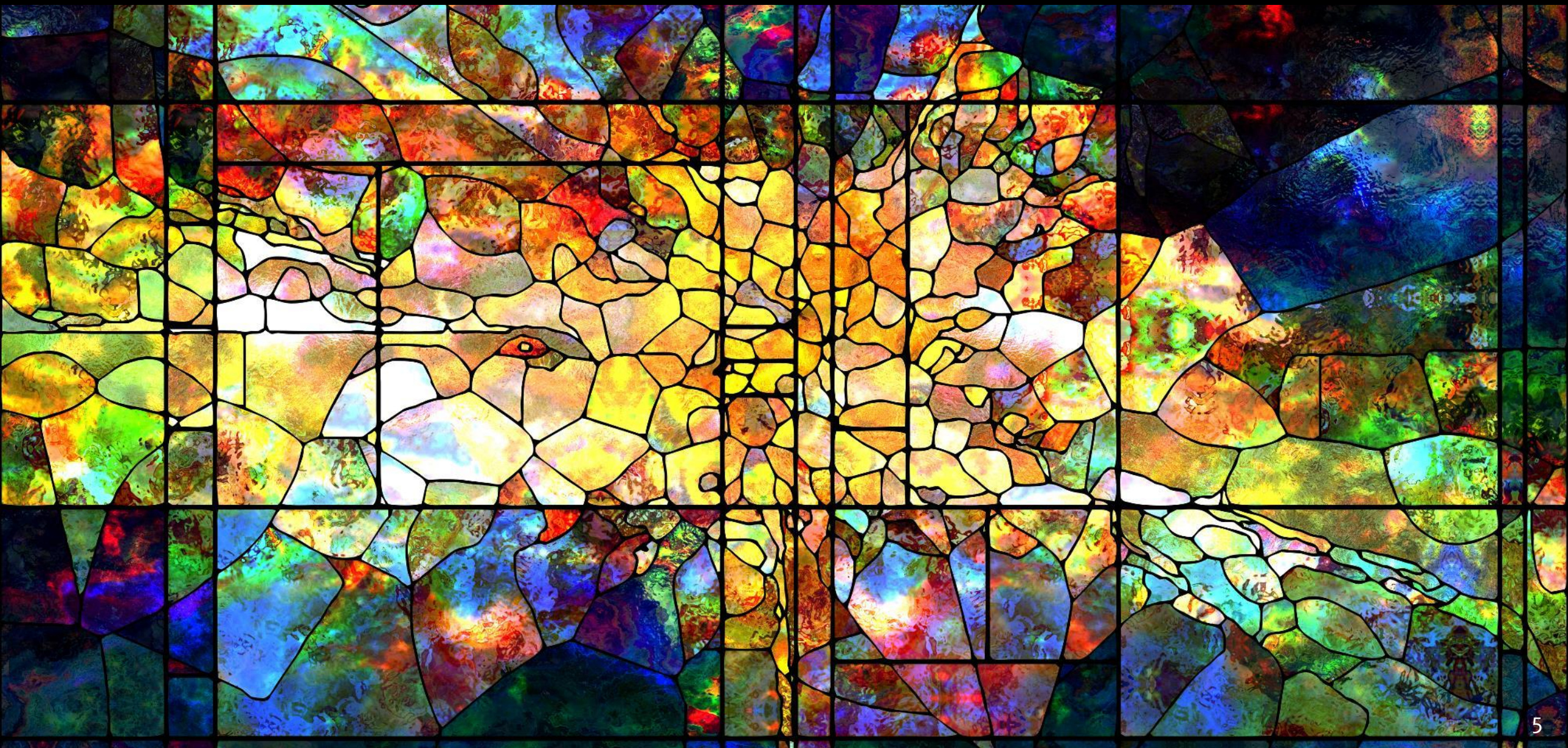
The week of Nov 4 will feature over 5,000 biopharma professionals in Stockholm for Bio-Europe. We'd love to meet you there.

https://informaconnect.com/bioeurope/

To meet with Stifel @ Bio-Europe
yeungn@stifel.com

The Macro Picture and the Election

Beautiful but murky stained-glass window



U.S. Inflation Well Under Control

***LEXINGTON, Ky, Lex18*, Oct. 15, 2024 (excerpt)**

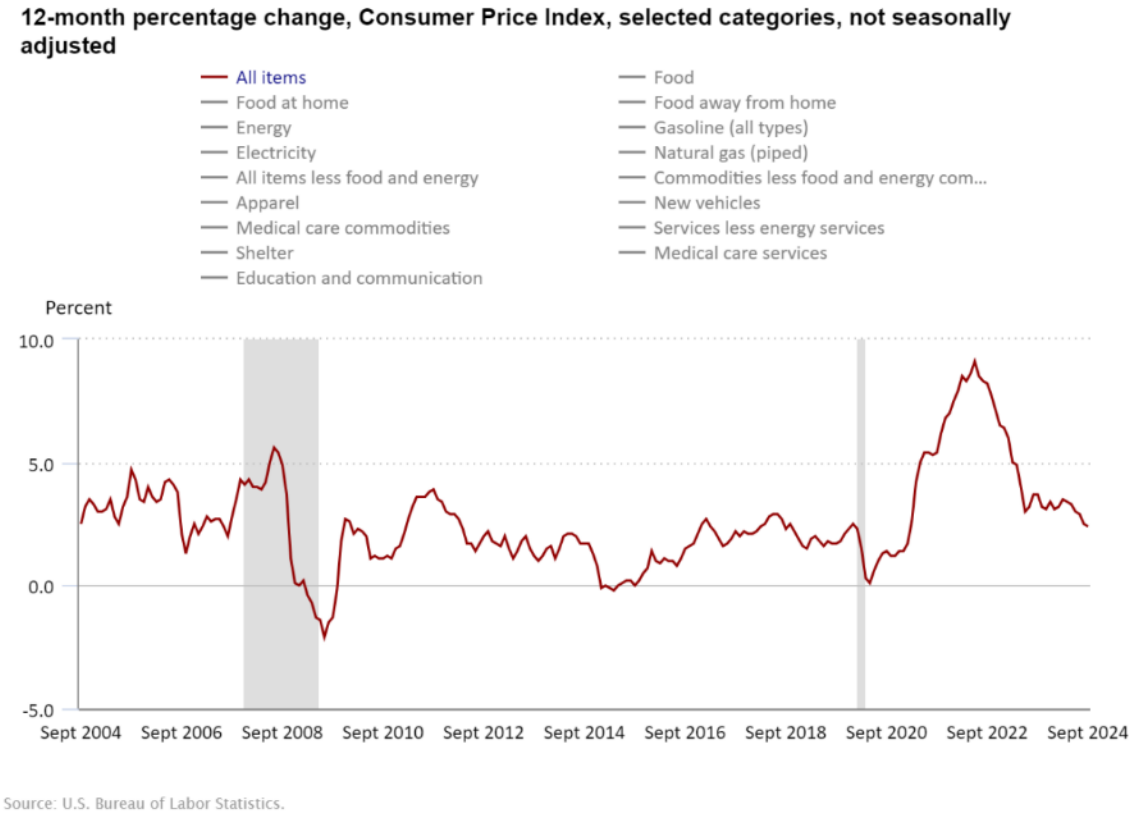
LEXINGTON, Ky. (LEX 18) — The U.S. Bureau of Labor Statistics released its monthly consumer price index report last week, revealing the inflation rate hit a low in September, a rate that has not been seen in three years.

That could mean a more stable economy heading into the holiday shopping season. The overall consumer price index increased 2.4% from last September, the smallest year-over-year increase since February 2021, when the increase was just 1.7%.

The report comes as average price increases begin to plateau for food and apparel, and prices begin to deflate for gasoline and vehicles.

He said the latest CPI report is good news for consumers. It could also serve as a signal to the Federal Reserve to adjust interest rates.

"As we continue to see inflationary pressures ease, that will allow them to reduce interest rates even further," Clark noted.



Source: U.S. Bureau of Labor Statistics.

Source: https://www.lex18.com/news/covering-kentucky/national-inflation-rate-hits-a-3-year-low-heres-what-that-means-for-consumers

Americans say the Economy is a Top Election Issue. Here's how Economists are Grading it.

***CBS News*, Oct. 18, 2024 (excerpt)**

With less than three weeks until the U.S. presidential election, millions of Americans say the economy is a top issue as they decide how to cast their vote — an understandable focus after the rollercoaster of the past four years, which included everything from a bear market to the hottest inflation since the 1980s.

But with the chaos of the pandemic behind us and inflation edging close to its pre-2020 levels, the U.S. economy is ripe for a fresh assessment of its strengths and weaknesses, along with whether the Biden administration's economic policies have paid off.

By many measures, the U.S. economy has regained its footing, emerging from the health crisis with the type of growth that it experienced prior to 2020. Gross domestic product is growing solidly, while unemployment and the labor market have also rebalanced, remaining close to their pre-pandemic levels. Critically, inflation has dropped to a three-year low and is approaching the Federal Reserve's annual target of 2%.

Source: https://www.cbsnews.com/news/trump-kamala-harris-policies-how-strong-is-the-economy-election/

"In the 35 years I've been an economist, I've rarely seen an economy performing as well as it is," Mark Zandi, chief economist of Moody's Analytics who has previously advised presidential candidates from both parties, told CBS MoneyWatch. "I'd give it an A+."

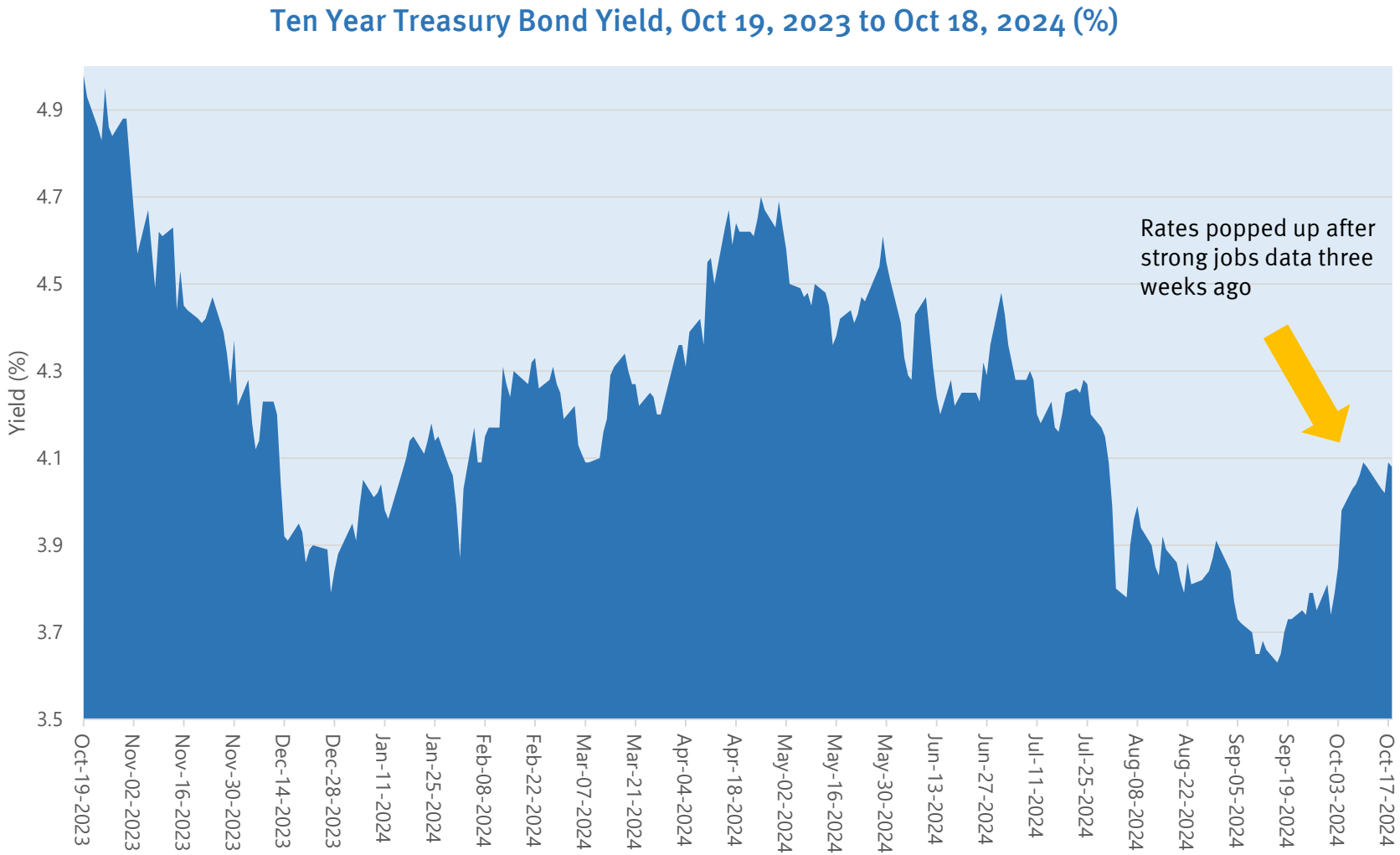
Like Zandi, many other experts are giving the economy strong marks. The U.S. economy is "hot, hot, hot," noted Yardeni Research in an October 17 report. Yet many Americans might scoff at such bullish assessments: 6 in 10 now describe the U.S. economy as either "fairly bad" or "very bad," according to CBS News polling.

That's not lost on Zandi and other economists. "The difference between the happy talk of economists and what people say has never been this wide," he noted.

Only 1 in 10 Americans rate the economy as "very good," according to a CBS News poll of registered voters taken between October 8-11. Meanwhile, about 52% of Americans say they and their family are worse off today than they were four years ago, Gallup found in a new poll.

The discordant economic views among experts and typical Americans reflects several factors. First, and perhaps most pressing in the short-term, prices around the U.S. remain elevated even as the searing inflation that followed the pandemic descends to normal levels.

Treasury Bond Yields Creeping Up



Source: S&P CapitalIQ

Treasury bond yields have risen over the past month because of concerns over persistent inflation, strong jobs data and the possibility of prolonged higher interest rates.

This is puzzling in some ways because the latest CPI data were really positive.

Further, other countries like the UK, have also made substantial progress on inflation.

Investors also remain concerned about high budget deficits and don't see either candidate as likely to help reduce the U.S. debt anytime soon.

Trump has Gained in 538's Forecast, but the Election is Still a Toss-up

***G. Elliot Morris*, 538, ABC News, Oct 18, 2024 (excerpt)**

The closest election of the century keeps getting closer. Two weeks ago, 538's forecast of the presidential election gave Vice President Kamala Harris just a 58-in-100 chance of defeating former President Donald Trump on Nov. 5. Now — just 18 days away from Election Day — our forecast gives Trump the bare advantage in the race with a 52-in-100 chance to win.

You might be tempted to make a big deal about our forecast "flipping" to Trump, but it's important to remember that a 52-in-100 chance for Trump is not all that different from a 48-in-100 chance for Harris — both are little better than a coin flip for the leading candidate. While Trump has undeniably gained some ground over the past couple weeks, a few good polls for Harris could easily put her back in the "lead" tomorrow. Our overall characterization of the race — that it's a toss-up — remains unchanged.

The reason our forecast is close is that the polls are close — well within the range that even a small polling error could be decisive. According to our polling averages, the margin between Trump and Harris is 2 percentage points or less in all seven major swing states (Arizona, Georgia, Michigan, Nevada, North Carolina, Pennsylvania and Wisconsin). And in our average of national polls, Harris leads Trump by only 2.0 points.

Source: https://abcnews.go.com/538/trump-gained-538s-forecast-election-toss/story?id=114907042

As Election Day Nears, Trump and Harris Veer in Different Directions on Pharma

Amy Baxter, *Biopharma Dive*, Oct 15, 2024 (excerpt)

With just a few weeks left until the election, Vice President Kamala Harris and former President Donald Trump are making their final appeals to the American public in their runs for the oval office. While Harris has sharpened her agenda, Trump has changed his stance on some of the pharma-targeting policies he previously supported. In particular, Trump's publicly stated views are now more aligned with industry lobbyists looking to gut provisions of the Inflation Reduction Act, among them Medicare's new authority to negotiate drug prices. The pharmaceutical industry has vehemently opposed those negotiations, referring to them as equivalent to price setting and a threat to drug research. Yet their legal challenges have been rebuffed by the courts so far, allowing the process to move forward and the results of the first round of talks to go into effect in 2026. Drugmakers, then, have a lot on the line in the coming election.

Harris' plan promises to expand several IRA policies, including the $35 monthly insulin cap and $2,000 annual out-of-pocket maximum for Medicare recipients to all Americans, even those with private insurance, while ramping up the speed of drug price talks. In general, her plan outlines that she aims "to cover more drugs and lower prices faster." She also doubled down on how she would use Medicare savings last week during an appearance on "The View," stating, without details, that expanded savings from price negotiations could go toward Medicare's coverage of in-home healthcare.

Harris is also zeroing in pharmacy benefit managers, aiming to "crack down on pharmaceutical companies that block competition and abusive practices by pharmaceutical middlemen who squeeze small pharmacies' profits and raise costs for consumers."

During his first run for president in 2016, Trump repeatedly vowed to lower prescription drug prices, including by giving Medicare the type of authority it now has under the IRA. Yet as Harris noted in their Sept. 10 debate, Trump never followed through, with many proposals either losing momentum or falling apart due to legal action. He's since further aligned himself with positions favored by the industry lobbying group PhRMA. For instance, Trump signed an executive order in 2020 for a "most-favored nations" policy designed to link Medicare reimbursement for certain drugs to prices paid abroad. Trump has since dropped support for the policy, his campaign confirmed to media outlets this month. The move falls in line with the position of PhRMA, the industry's largest lobbying group with a budget of $16.9 million, according to Open Secrets.

Source: https://abcnews.go.com/538/trump-gained-538s-forecast-election-toss/story?id=114907042

Trump White House Official: Medicare Part D is a ‘Time Bomb’

Katherine MacPhail, *Stat+*, October 18, 2024 (excerpt)

Should former President Donald Trump resume office, Republicans will need to repeal or revisit President Joe Biden’s signature drug pricing reform and expanded Affordable Care Act premium subsidies, according to Joe Grogan, a former Trump White House official.

Grogan argued that Biden’s Inflation Reduction Act destabilized Medicare Part D, the program’s prescription drug pricing benefit. He forecast that higher premiums would send the Part D program into an inevitable “death spiral,” and said lawmakers should consider repealing it.

To replace Medicare Part D, Grogan suggested transferring all beneficiaries into the privately-run Medicare Advantage program or offering a combination of MA and health savings accounts.

Grogan also maintained that the GOP should not extend the enhanced ACA subsidies for lower healthcare premiums. The subsidies, which the Biden administration passed in its Covid relief bill and extended through the IRA, are set to expire in 2025. He dismissed concerns that many of the people who benefit from the subsidies live in Republican-led states and said that there is an “intolerable” amount of fraud in the program.

Biopharma Market Update

Alexandria Center for Life Sciences, South San Francisco, CA. Source: Stifel

The XBI Closed at 99.8 Last Friday (Oct 18), Up 1.2% for the Week

The XBI was up slightly last week despite rising Treasury yields. The XBI has been in neutral as investors are (1) waiting until the U.S. election is passed and (2) looking to the Fed for further guidance on the speed of rate cuts. We are seeing the broader biotech market perform well.

Biotech Stocks Up Last Week

Return: Oct 11 to Oct 18, 2024

Nasdaq Biotech Index: +1.2%
Arca XBI ETF: +1.1%
Stifel Global Biotech EV (adjusted): +6.1%*
S&P 500: +0.1%

Return: Dec 29, 2023 to Oct 18, 2024 (YTD)

Nasdaq Biotech Index: +10.5%
Arca XBI ETF: 11.8%
Stifel Global Biotech EV (adjusted): +43.8%*
S&P 500: +22.3%

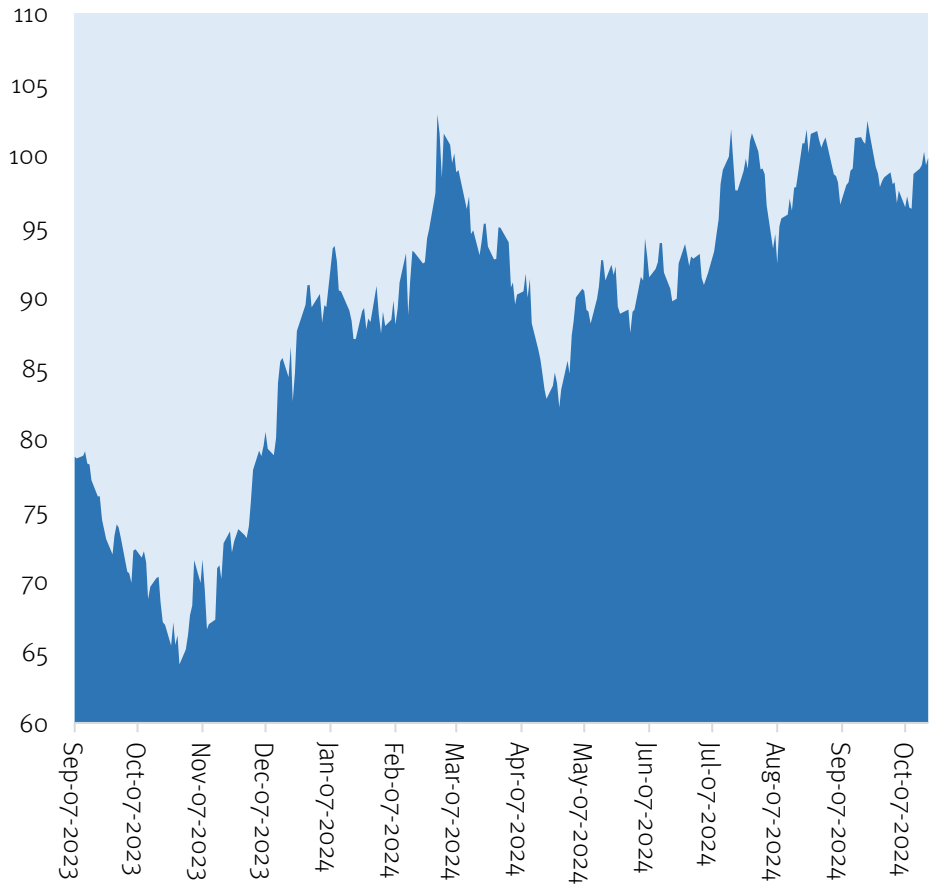
VIX Down

Sep 29, 2023: 17.3%
Dec 29, 2023: 12.45%
Mar 29, 2024: 13.0%
May 17, 2024: 12.0%
Aug 2, 2024: 23.4%
Sep 20, 2024: 16.1%
Oct 4, 2024: 19.2%
Oct 19 2024: 18.0%

10-Year Treasury Yield Up

Sep 29, 2023: 4.59%
Dec 29, 2023: 3.88%
Mar 29, 2024: 4.20%
May 17, 2024: 4.42%
Aug 2, 2024: 3.80%
Sep 20, 2024: 3.73%
Oct 4, 2024: 3.98%
Oct 19, 2024: 4.08%

XBI, Sep 7, 2023 to Oct 18, 2024



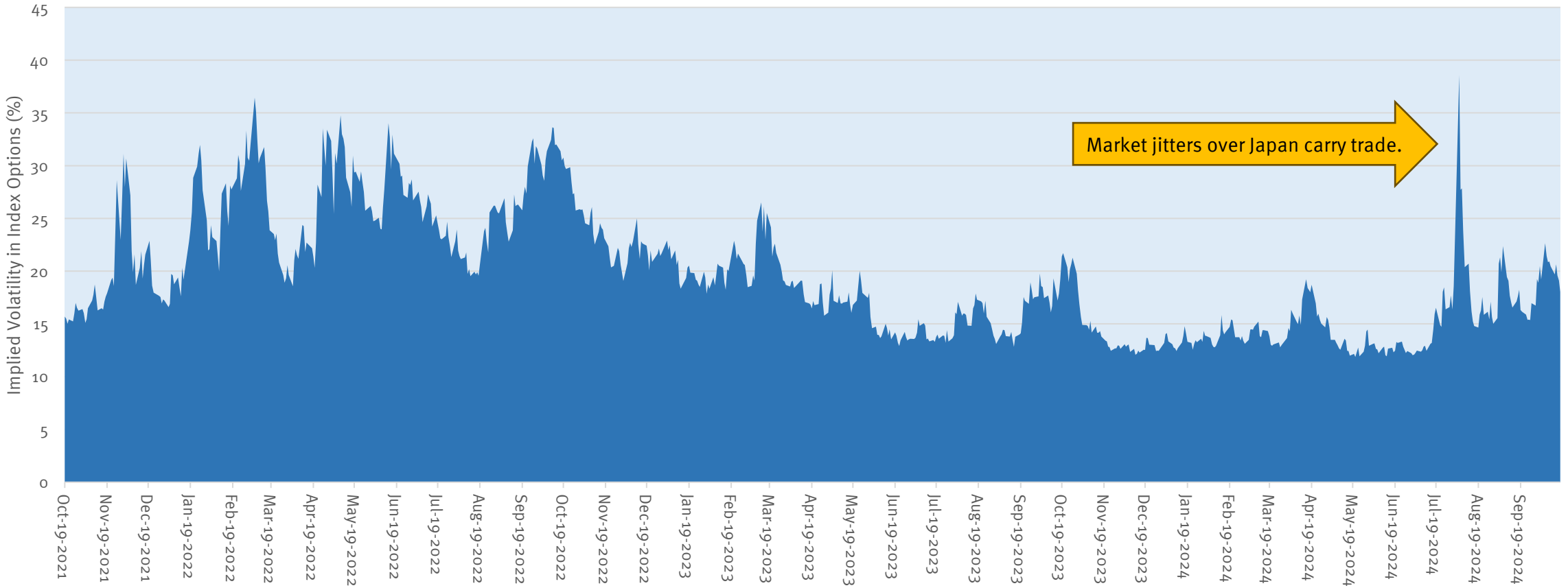
* Change by enterprise value. The adjusted number accounts for the effect of exits and additions via M&A, bankruptcies and IPOs. The annual change by market cap is even higher.

Source: S&P Capital IQ and Stifel analysis

VIX is Gradually Normalizing

In early August we saw the VIX go well over 35% as the market was worried about stability of major players due to planned increase in rates in Japan – causing losses on the so-called carry trade. Market volatility has come down since then and is now around 18%. Historically, a VIX under 20% has been a good time for equity underwriting activity to pick up.

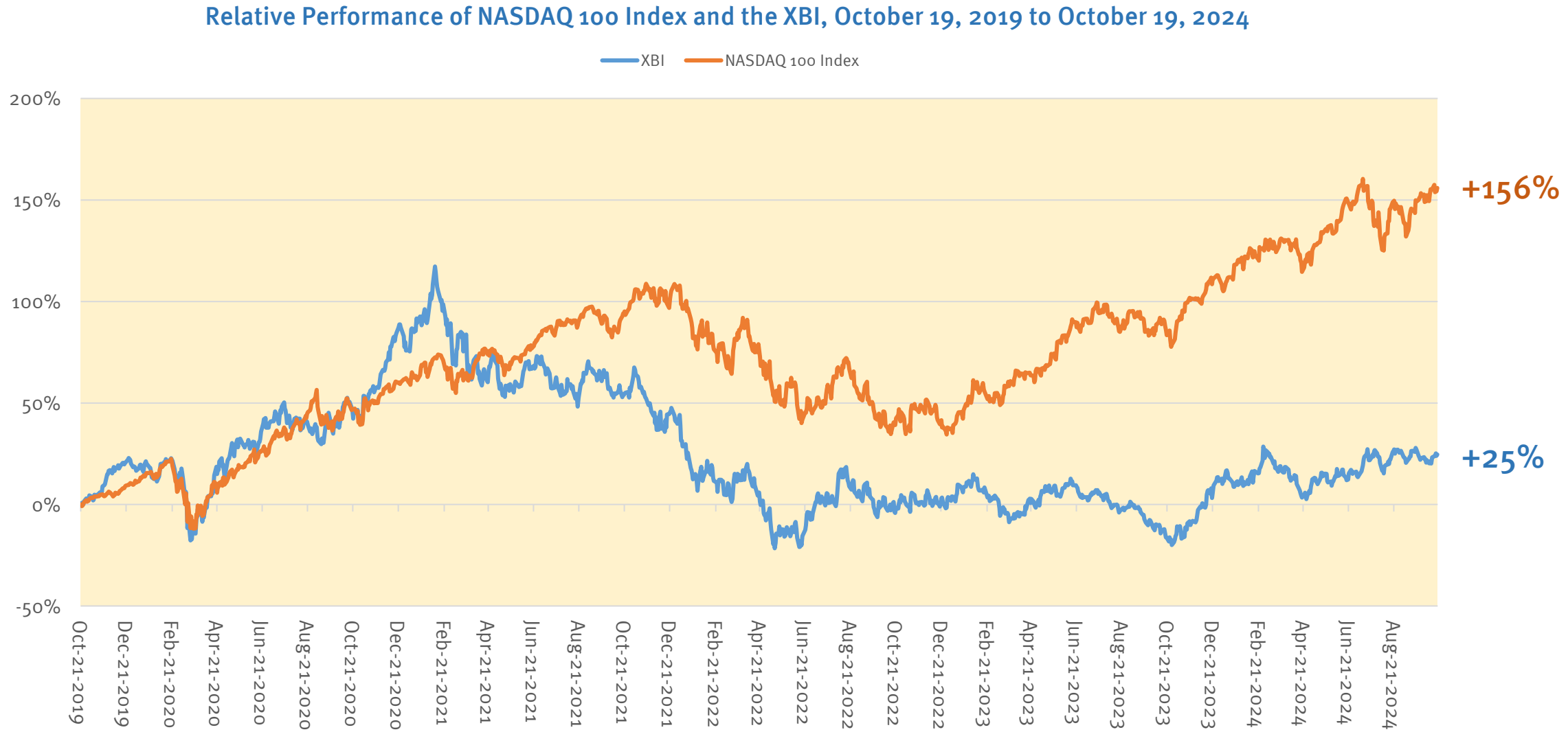
CBOE Volatility S&P 500 Index (VIX) – Level from October 19, 2021 to October 19, 2024



Source: S&P Capital IQ and Stifel analysis

Tech / Biotech Divergence Continues to Grow

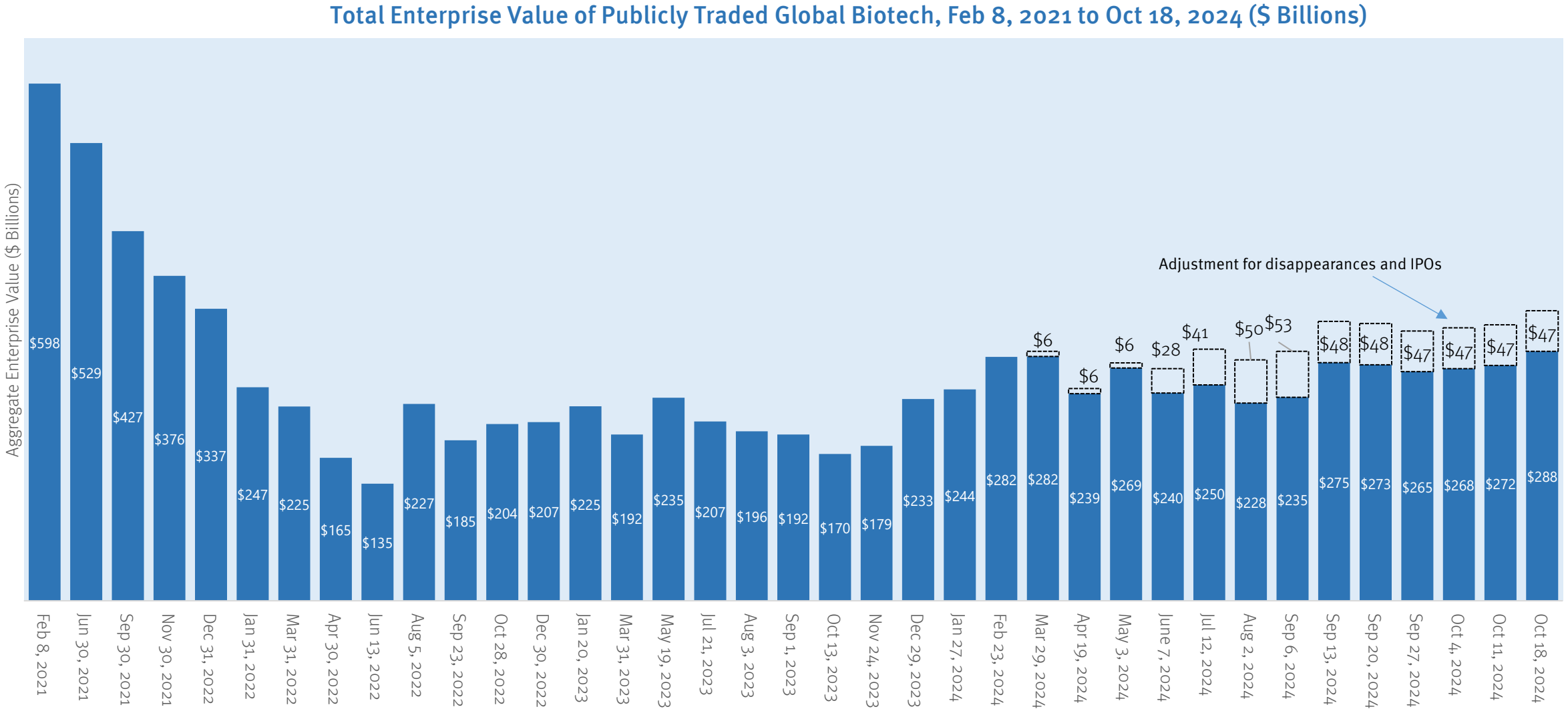
The massive gap between relative performance of the tech-heavy NASDAQ 100 and the XBI has widened throughout 2024.



Source: S&P Capital IQ and Stifel analysis

Total Global Biotech Sector Up 6.1% Last Week

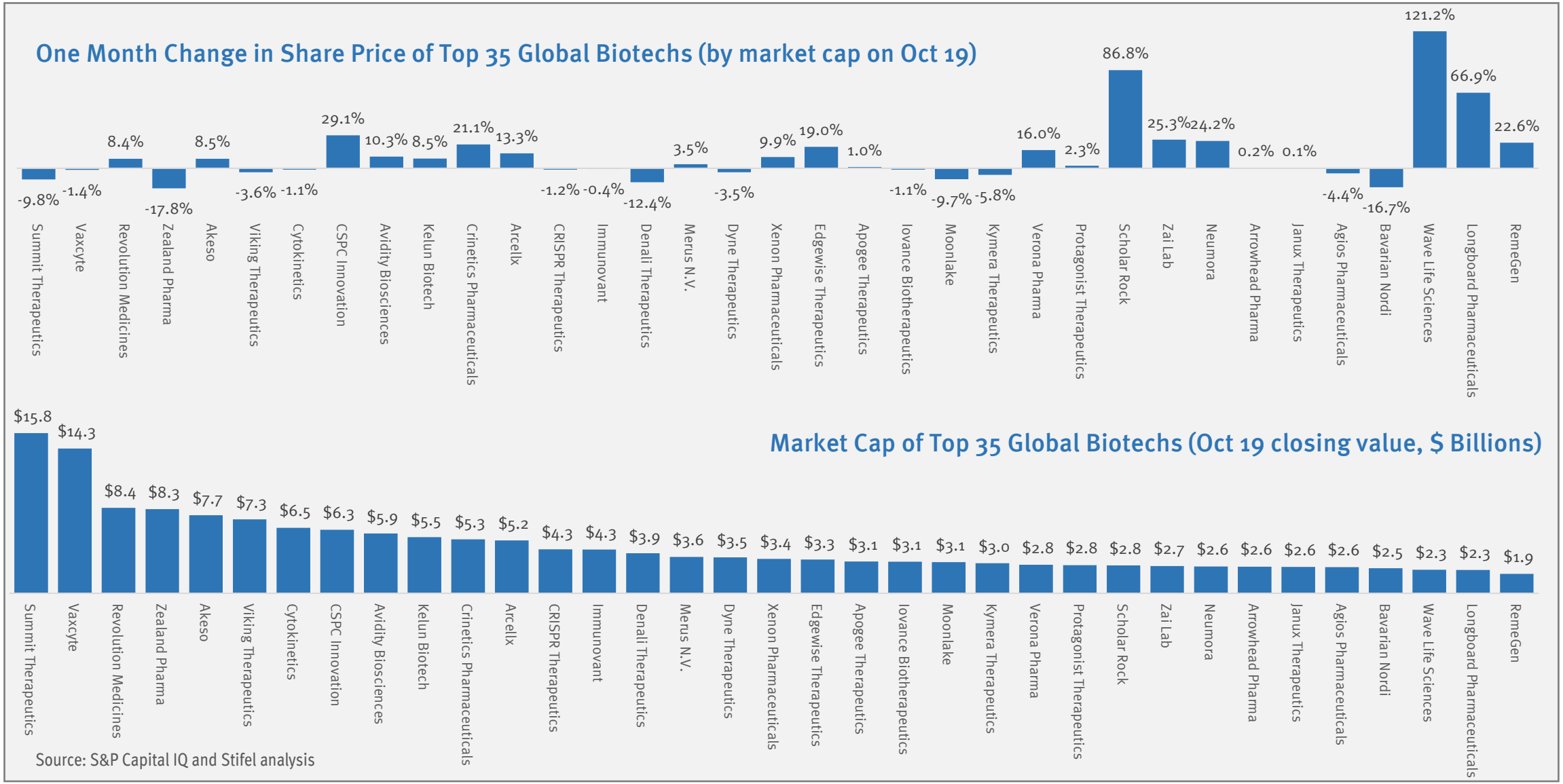
Biotech stocks were up 6.1% in the last week. On a disappearance adjusted basis, biotech is up 43.8% for the year to date (enterprise value). Last week was the first good week in a month.



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

Performance of the Top 35 Biotechs Over the Last Month

There has been some profit taking at a few of the market's biggest success stories including Summit, Zealand Pharma and Moonlake. Positive data and an acquisition have powered up Scholar Rock, Wave Life Sciences and Longboard.



Source: S&P Capital IQ and Stifel analysis

Why Was the Total Biotech Market Up So Much More than the XBI Last Week?

A recurring theme in our reports is that the XBI doesn't necessarily capture the value of the R&D-stage therapeutics sector.

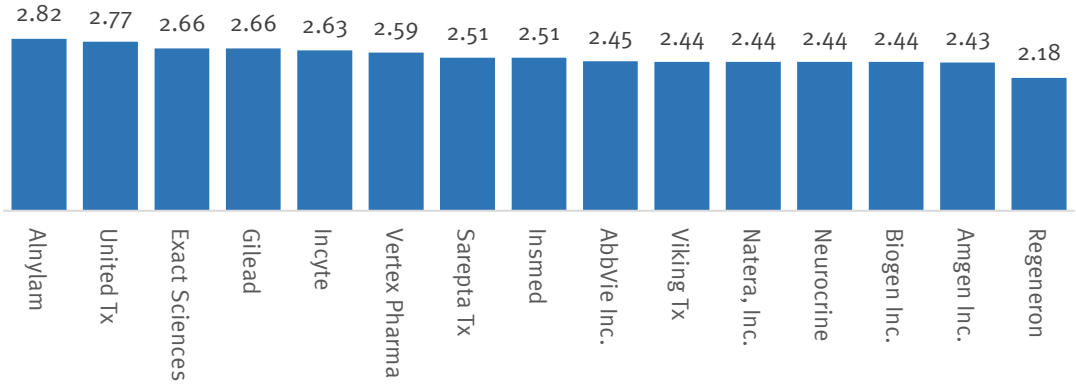
We are having a very good year for biotech, but you wouldn't necessarily know it by looking at the XBI. The Stifel biotech tracker looks at the *entire R&D therapeutics sector globally* and its movements give one a value-weighted view. This is because we simply add up the enterprise value of every public biotech each week and report that as the total sector value.

We are seeing ever greater divergence between changes in our tracker value and that of the XBI. The XBI is up 11% this year while our tracker is up 44% in 2024 YTD. Last week our tracker was up 6% while the XBI barely moved.

We wish to highlight a few things:

1. Looking at enterprise value via the Stifel EV tracker rather than market cap does not explain the divergence with the XBI. The total market cap of the biotech sector jumped by 4.6% over the last week. The exit adjusted market cap of the biotech sector is up 53.5% so far this year, more than the adjusted enterprise value.
2. The XBI selects and weights mature commercial biopharma rather than emerging stage. The commercial companies in the XBI have, on average, risen by 75% less in 2024 than the R&D stage companies.
3. To illustrate this point, consider the fact that the top 60 stocks in the XBI (by weight) make up 81% of the value of the ETF. Only 20 of these stocks are R&D stage and those account for only 18% of the value of the ETF. As noted in the chart below, only one of the top 15 stocks in the XBI (Viking) is R&D-stage. These 15 stocks were flat on a weighted basis last week while R&D companies were up big. Yet R&D stage companies comprise only 5% of the value of the XBI.
4. For reasons that are not entirely clear, the XBI generally tends not to include so many companies that have lots of inflection points. For example, last week saw great performance from Wave, Scholar Rock and Longboard. Wave and Longboard are not in the XBI at all, and Scholar Rock has a very small weight (it's roughly one three hundredths of the value of the XBI).

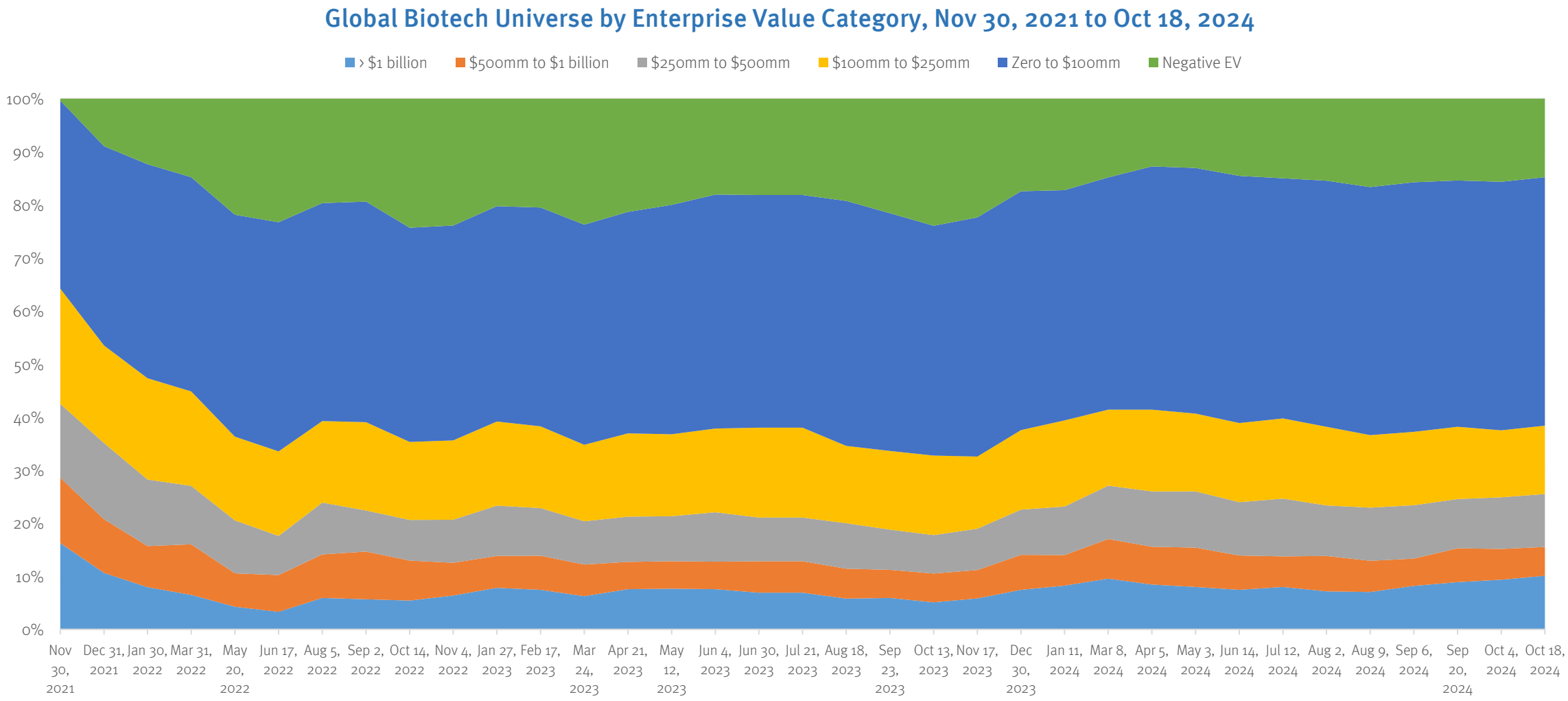
Percentage Weights of the Top 15 Stocks in the XBI, Oct 19, 2024



Source: S&P Capital IQ and Stifel analysis

Global Biotech Neighborhood Analysis

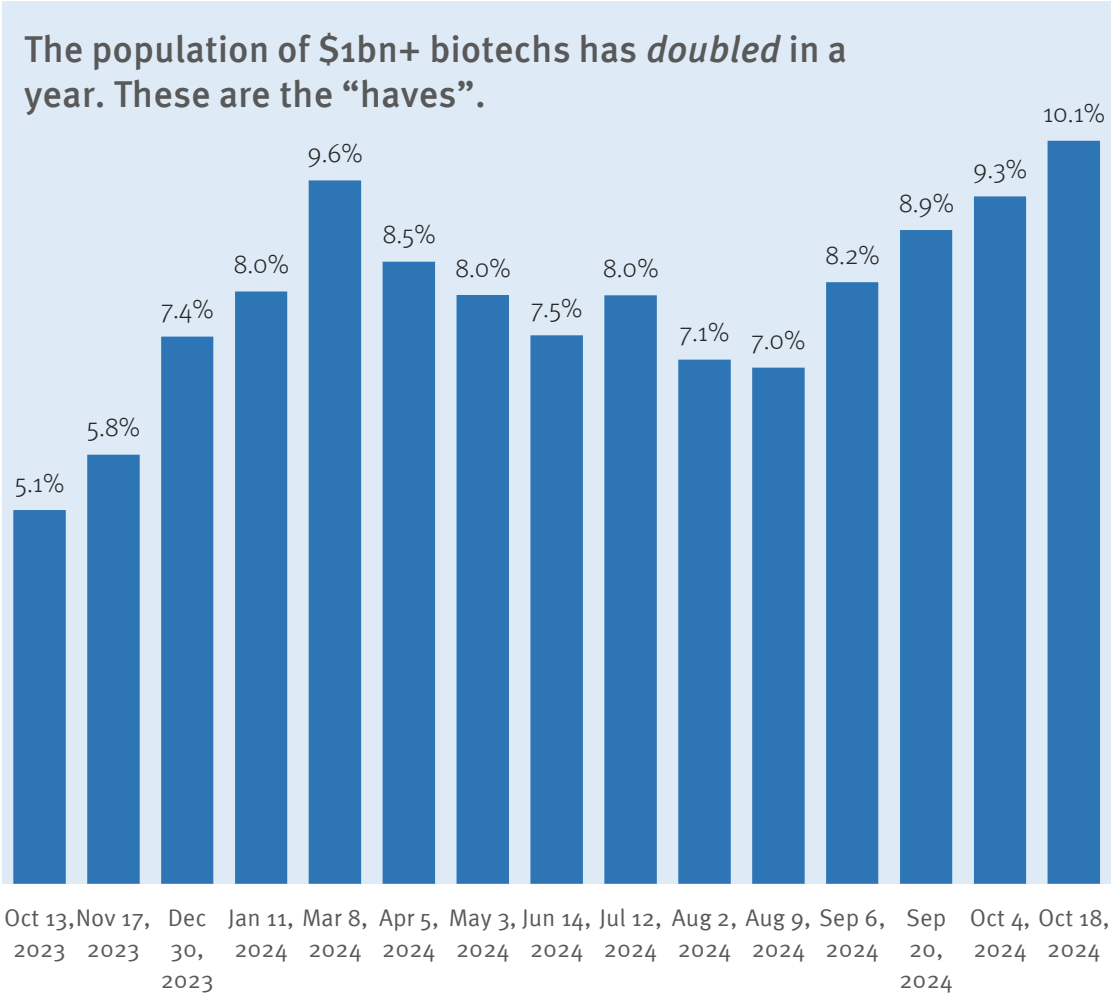
The population of high valued biotechs continues to grow. The population of companies with negative EV has shrunk meaningfully in recent weeks.



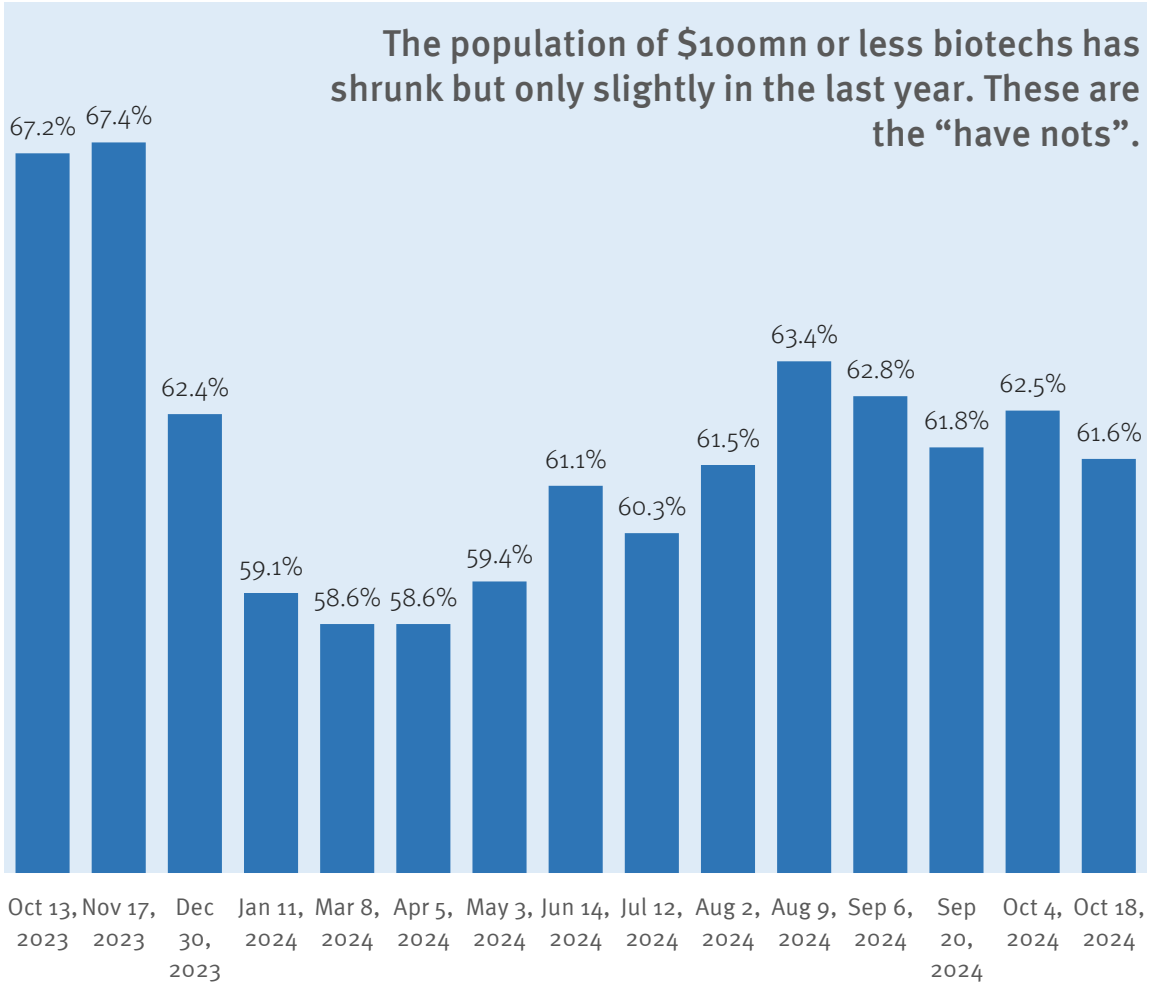
Source: CapitalIQ and Stifel analysis. Biotechs are defined as any therapeutics company without an approved product on any global stock exchange.

A Tale of Two Biotech Cities

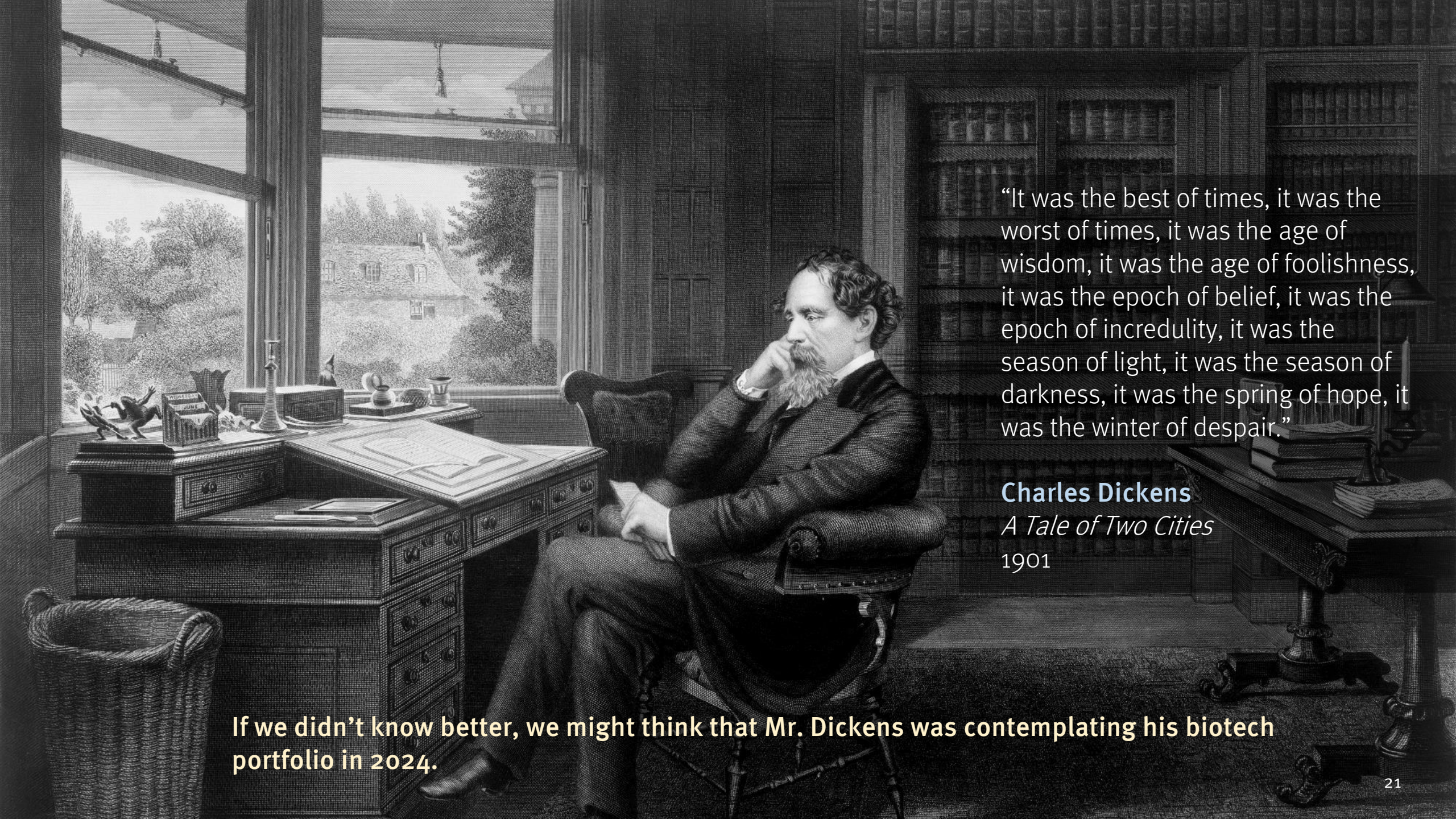
Percent of Biotechs with an Enterprise Value of $1bn or More (Oct 13, 2023 to Oct 18, 2024)



Percent of Biotechs with an Enterprise Value Under $100mm (Oct 13, 2023 to Oct 18, 2024)



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



"It was the best of times, it was the worst of times, it was the age of wisdom, it was the age of foolishness, it was the epoch of belief, it was the epoch of incredulity, it was the season of light, it was the season of darkness, it was the spring of hope, it was the winter of despair."

Charles Dickens
A Tale of Two Cities
1901

If we didn't know better, we might think that Mr. Dickens was contemplating his biotech portfolio in 2024.

Life Sciences Sector Total Value Up 0.3% Last Week

The top performing life sciences sectors last week included biotech, medical devices and CDMO's. HCIT and diagnostics underperformed.

Sector	Firm Count	Enterprise Value (Oct 18, 2024, $millions)	Change in Last Week (percent)	Change in Last Month (percent)	Change in Last Year (percent)
API	79	$97,250	-1.1%	8.9%	27.1%
Biotech	774	$282,447	6.1%	4.5%	-5.1%
CDMO	39	$172,309	1.6%	3.8%	17.0%
Diagnostics	81	$251,014	-1.3%	-0.7%	13.5%
OTC	29	$26,521	-0.1%	-3.2%	-2.6%
Commercial Pharma	712	$6,778,140	-0.3%	-0.5%	20.5%
Pharma Services	38	$185,974	0.6%	2.5%	-1.7%
Life Science Tools	50	$728,136	0.4%	-0.1%	21.7%
Medical Devices	180	$1,838,149	1.9%	2.7%	28.2%
HCIT	10	$23,131	-3.7%	8.5%	18.0%
Total	**1992**	**$10,383,072**	**0.3%**	**0.4%**	**22.6%**

Source: CapitalIQ and Stifel analysis

Count of Negative Enterprise Value Life Sciences Companies Has Dropped in Recent Weeks

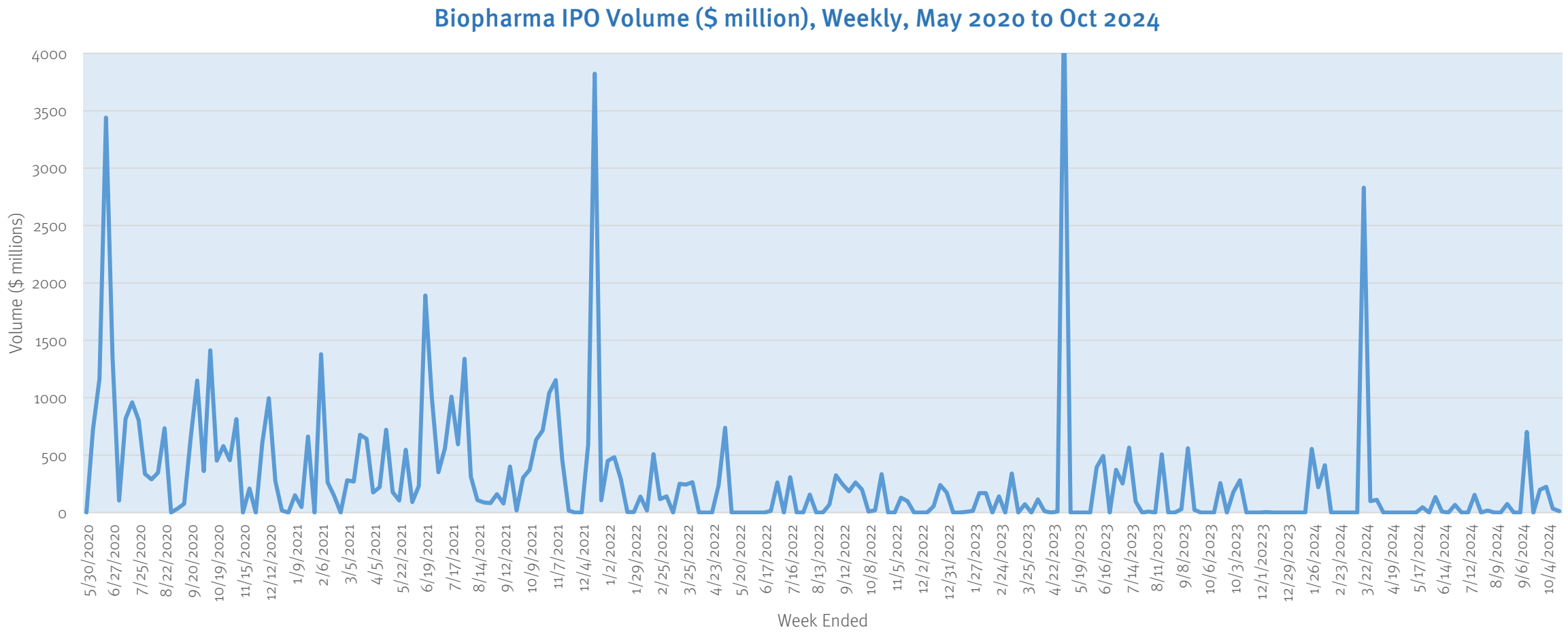
The number of negative EV life sciences companies fell from 136 two weeks ago to 129 last Friday.

Source: CapitalIQ and Stifel analysis

Capital Markets Update

IPO Market Has Been Quiet

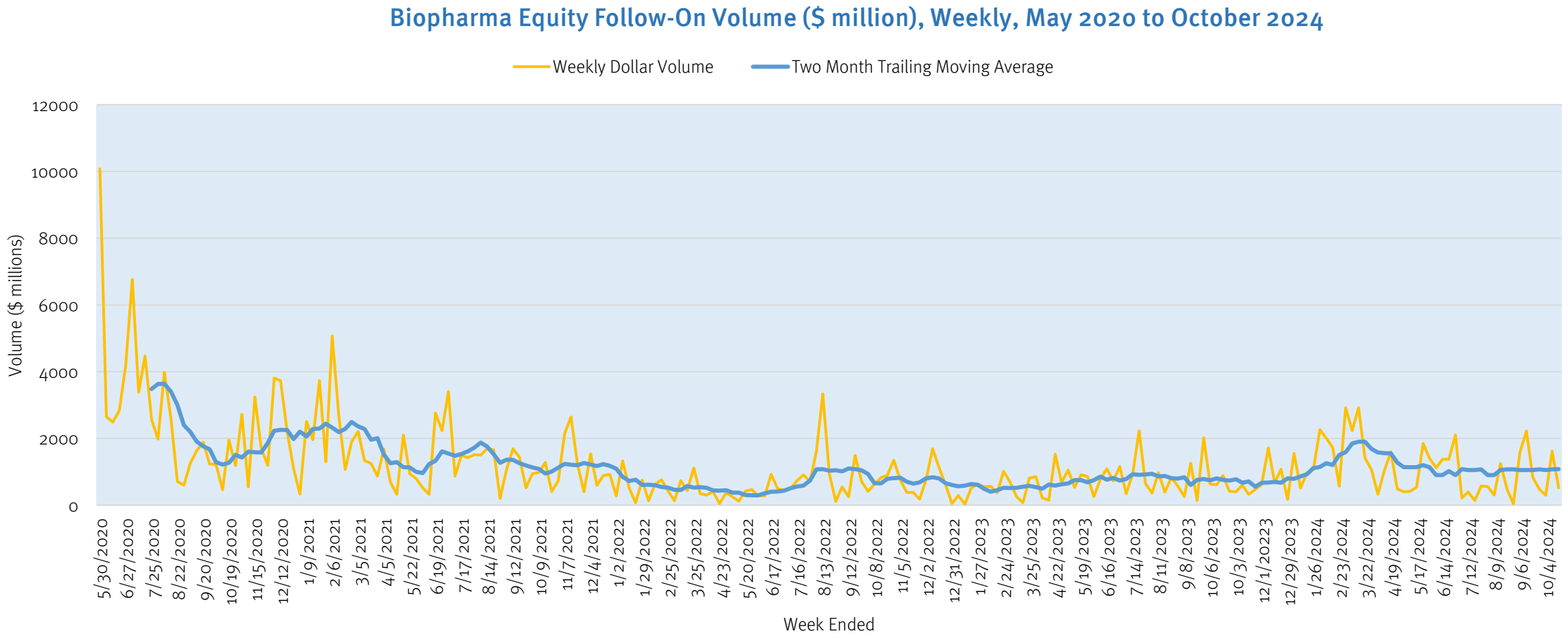
The IPO market perked up nicely after Labor Day and the issues that went out then have traded well. Despite this, we have not seen a new crop of IPO's price in the market for at least a month's time.



Source: Data from CapitalIQ.

Equity Follow-On Market Steady

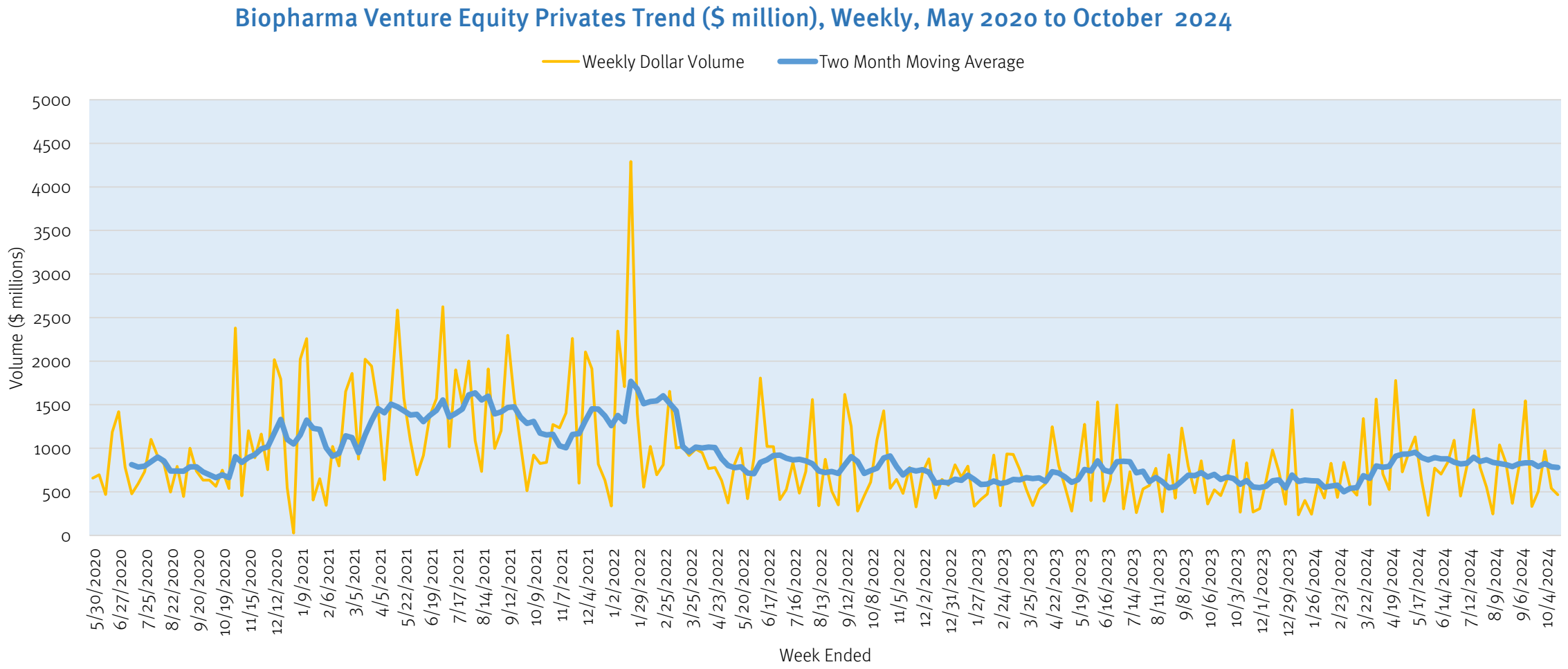
While not matching the torrid pace of early September, we have seen $2.1 billion in follow-on's in the last two weeks. This puts the market well above its pace from Q2 and Q3 of this year.



Source: Data from CapitalIQ.

Private Venture Equity Market Normal in Recent Weeks

Weekly volume of venture privates this year has averaged $750mm. The volume in recent weeks has been below this, averaging $500mm a week.



Source: Data from CapitalIQ, Crunchbase.

Terray Therapeutics Closes $120M Series B to Advance Its AI Pipeline of Small Molecule Therapeutics to the Clinic

Press Release, Los Angeles, October 17, 2024

Terray Therapeutics, a biotechnology company improving human health by transforming the speed, cost, and success rate of small molecule drug development using computation integrated with novel data at scale, today announced Series B funding of $120 million. The funding will progress internal programs into clinical trials and further enhance Terray's integrated AI platform, tNova, which it uses to power both internal and partnered programs.

The round was led by new investor Bedford Ridge Capital and existing investor NVentures (NVIDIA's venture capital arm), with participation from new and existing investors including Maverick Capital, Goldcrest Capital, Madrona Ventures, Two Sigma Ventures, XTX Ventures, Digitalis Ventures, and Alexandria Ventures. Sid Shenai, who partnered with Bedford Ridge Capital on this financing, will join Terray's Board of Directors.

With its proprietary experimental platform, Terray has built the world's largest chemistry dataset, having quantitatively measured 5 billion+ target-ligand interactions in the past 3 years–roughly 50X the entirety of all publicly available chemistry data. This dataset is doubling annually.

Terray's unique data advantage enables best-in-class AI capabilities to identify and optimize novel small molecule solutions to the most complex problems. Terray applies this expertise to its own internal pipeline focused on immunological diseases and to additional challenging targets in partnership with Bristol Myers Squibb and Calico.

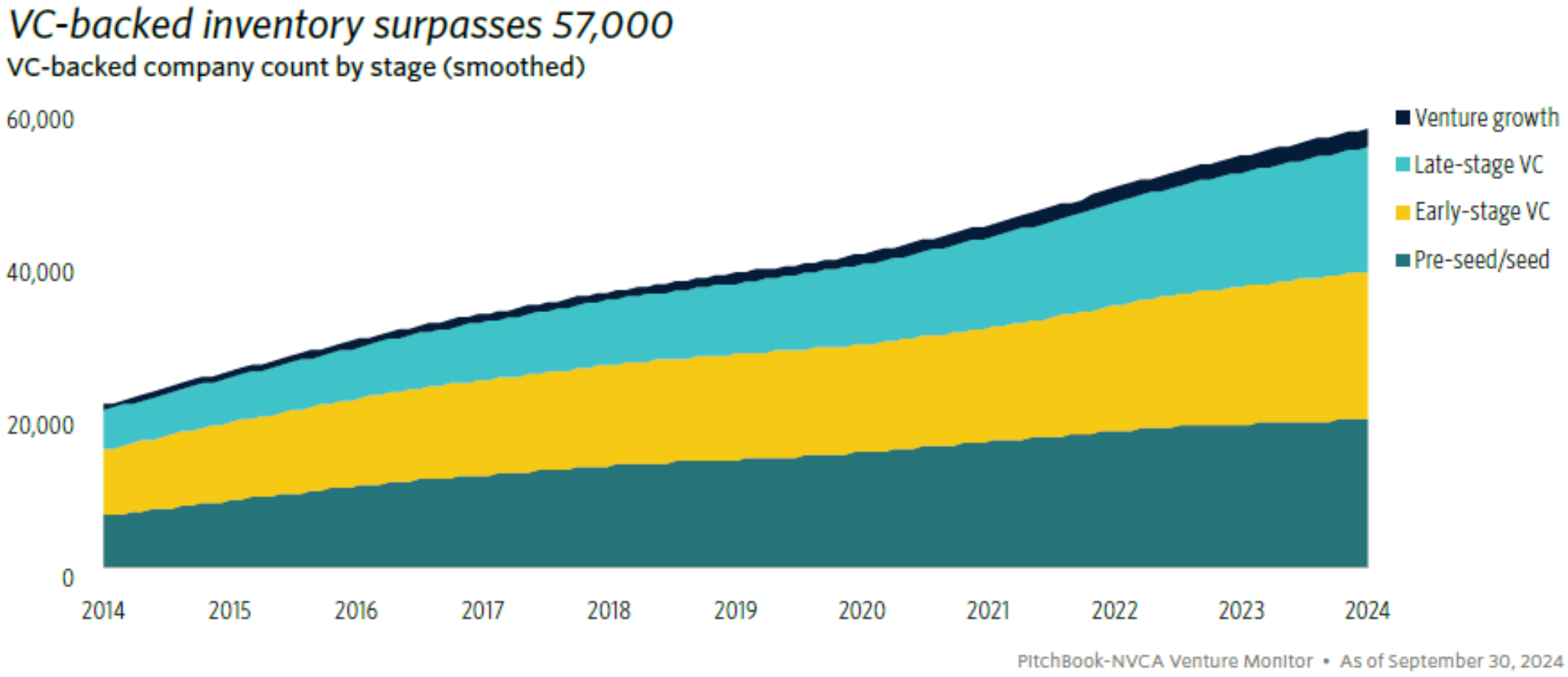
"Terray's unique, high-quality data generation enables continuous advanced generative AI development, like their COATI models," said Kimberly Powell, vice president of healthcare at NVIDIA. "Rapid experiments combined with advanced AI creates a molecule discovery and design flywheel able to take on the most difficult and yet to be discovered targets."

"We're delighted that this funding will help us bring new medicines forward for patients in need. That's why we all work at Terray. Knowledge of what causes human disease has exploded in the 'omics' era, but the ability to discover and develop new molecules to treat those diseases hasn't kept pace. Trained on rapidly iterating, precise data generated at unprecedented scale in our labs, Terray's AI will dramatically improve the success rate of small molecule development and bring relief to patients."

Jacob Berlin, Ph.D,
CEO of Terray Therapeutics

Source: https://www.terraytx.com/press/terray-therapeutics-closes-oversubscribed-120m-series-b-to-advance-its-generative-ai-pipeline-of-small-molecule-therapeutics-to-the-clinic

Very Large Inventory of Unrealized VC Deals



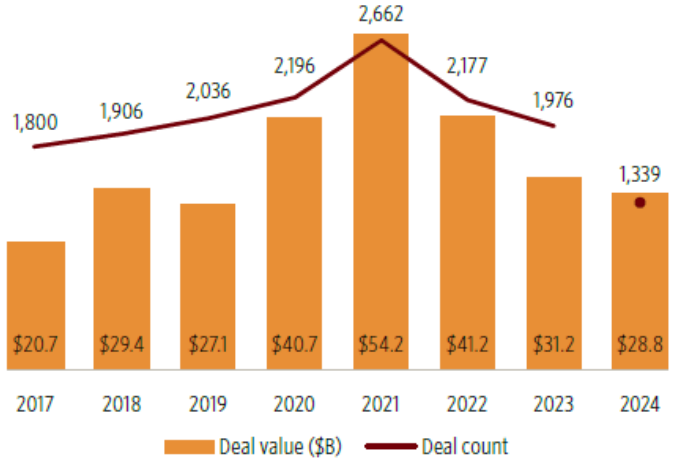
Source: https://pitchbook.com/news/reports/q3-2024-pitchbook-nvca-venture-monitor'

Pitchbook Data: Life Sciences Deal Activity Down But Not Out in 2024

Life sciences

Deal counts continue to decrease

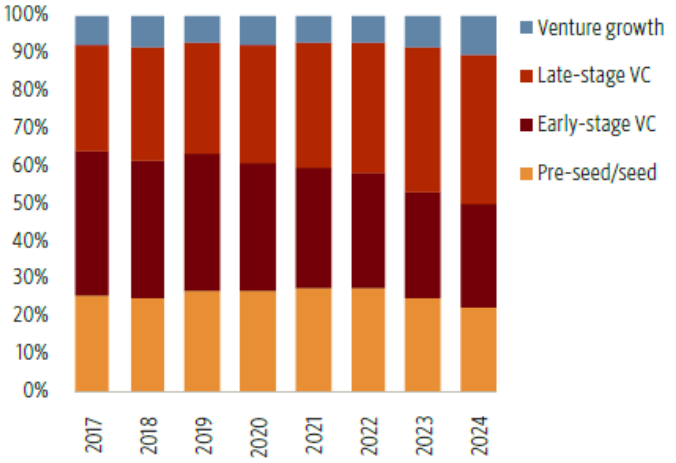
Life sciences VC deal activity



PitchBook-NVCA Venture Monitor • As of September 30, 2024

Greater proportion of later-stage life sciences deals

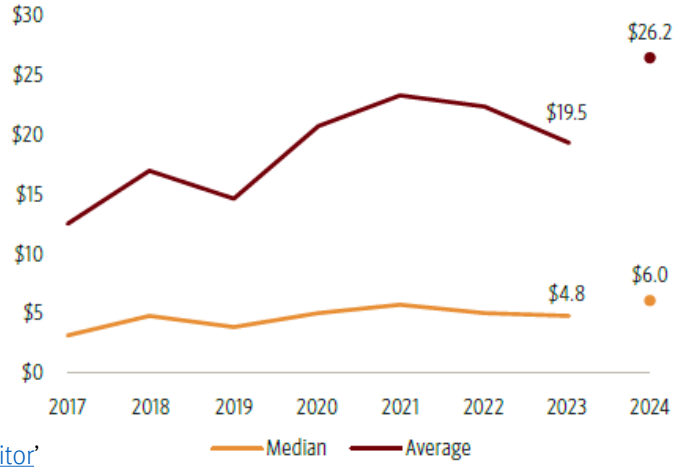
Share of life sciences VC deal count by stage



PitchBook-NVCA Venture Monitor • As of September 30, 2024

Completed life sciences deals are getting larger

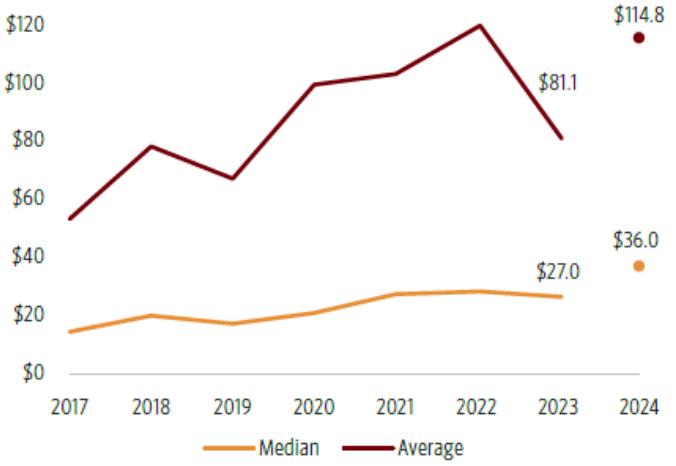
Median and average life sciences VC deal values ($M)



PitchBook-NVCA Venture Monitor • As of September 30, 2024

Median valuation shows swift uptick

Median and average life sciences VC pre-money valuations ($M)

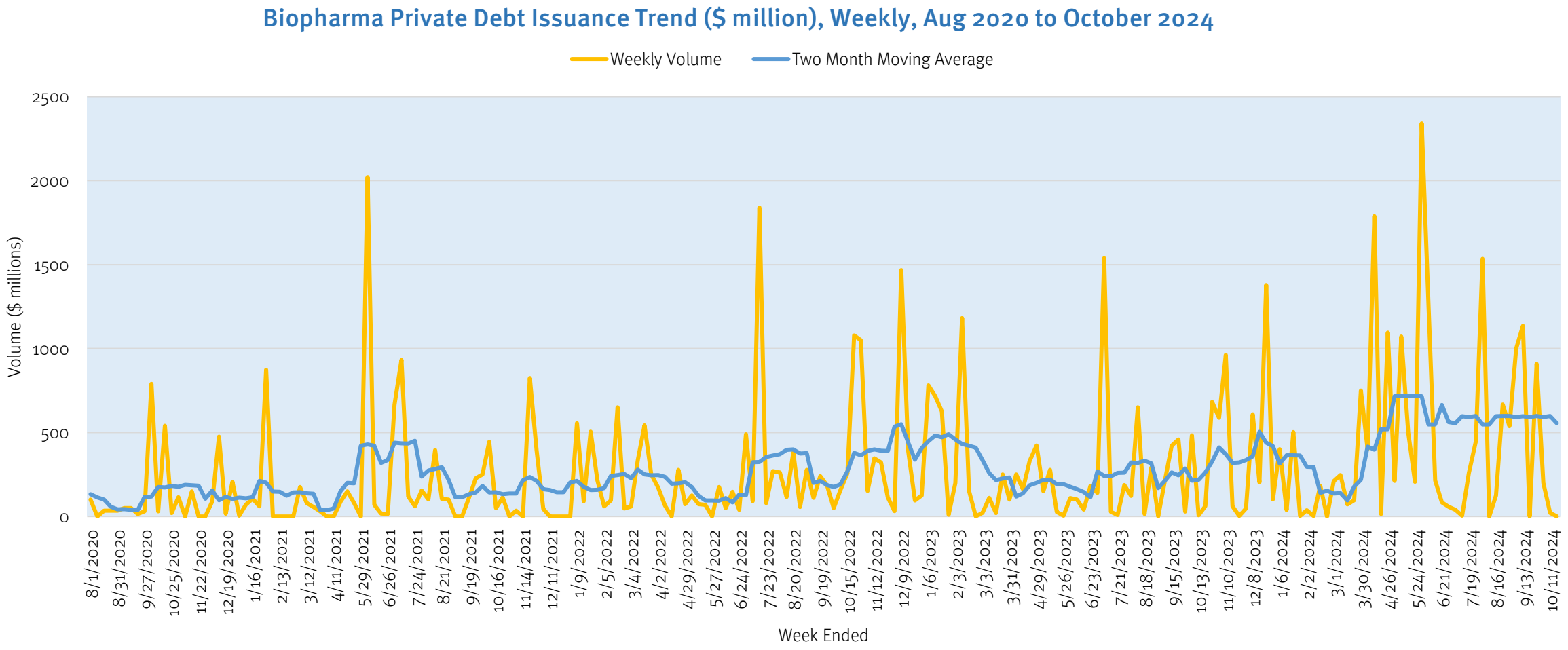


PitchBook-NVCA Venture Monitor • As of September 30, 2024

Source: https://pitchbook.com/news/reports/q3-2024-pitchbook-nvca-venture-monitor'

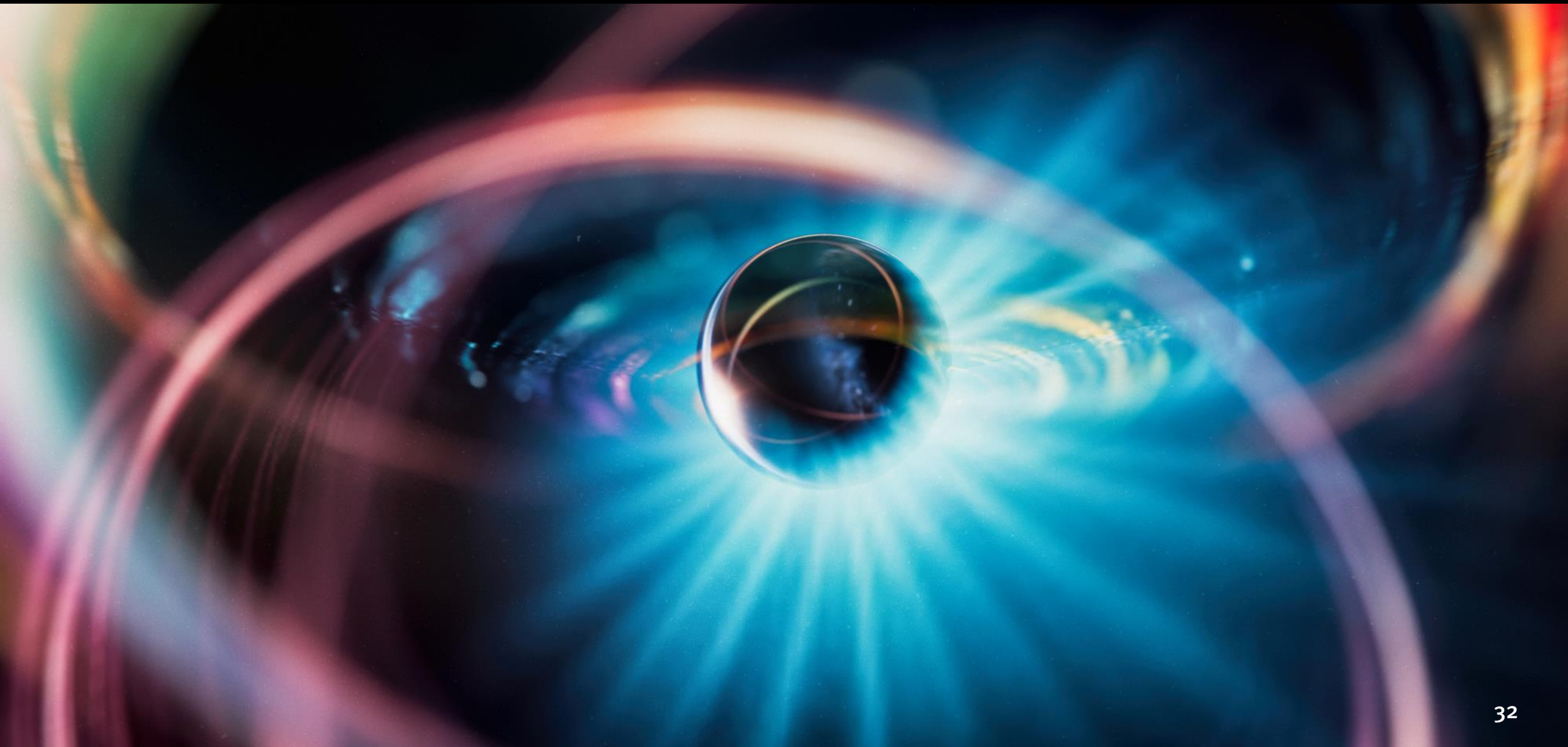
Biopharma Private Debt Market Slowing Down

The volumes in the private debt market have been light in recent weeks. Not included here was a $1.46 credit deal done by Gevo for renewable jet fuels based on bioproduction principles.



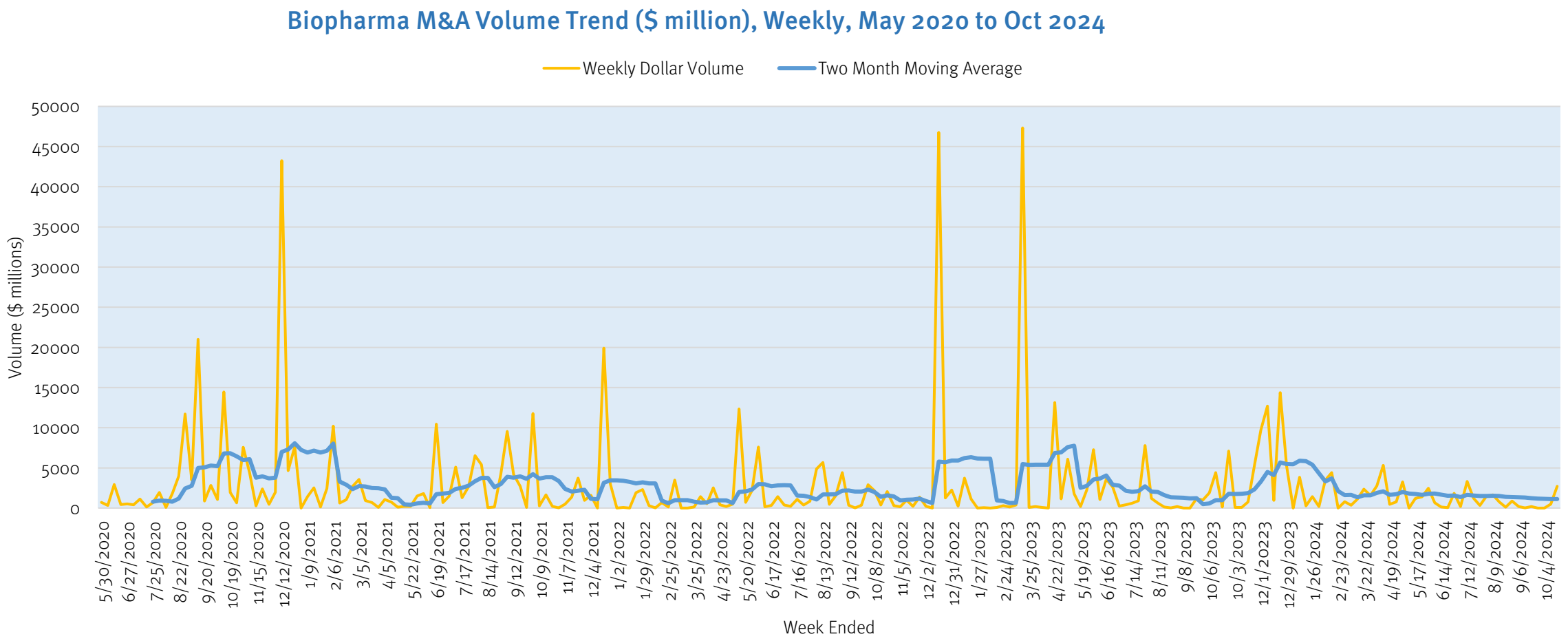
Source: Data from CapitalIQ, Crunchbase, Stifel research.

Deal News



Last Week Saw the First Billion Dollar M&A Offer in Months

Last week saw the largest deal announcement since July with H. Lundbeck offering to acquire Longboard Pharmaceuticals for $2.5 billion (net of cash). Nonetheless, the overall pace of M&A activity remains muted compared to any reasonable interval over the last decade.



Source: S&P CapitalIQ

Lundbeck to acquire Longboard Pharmaceuticals in a strategic deal, significantly enhancing its neuroscience pipeline

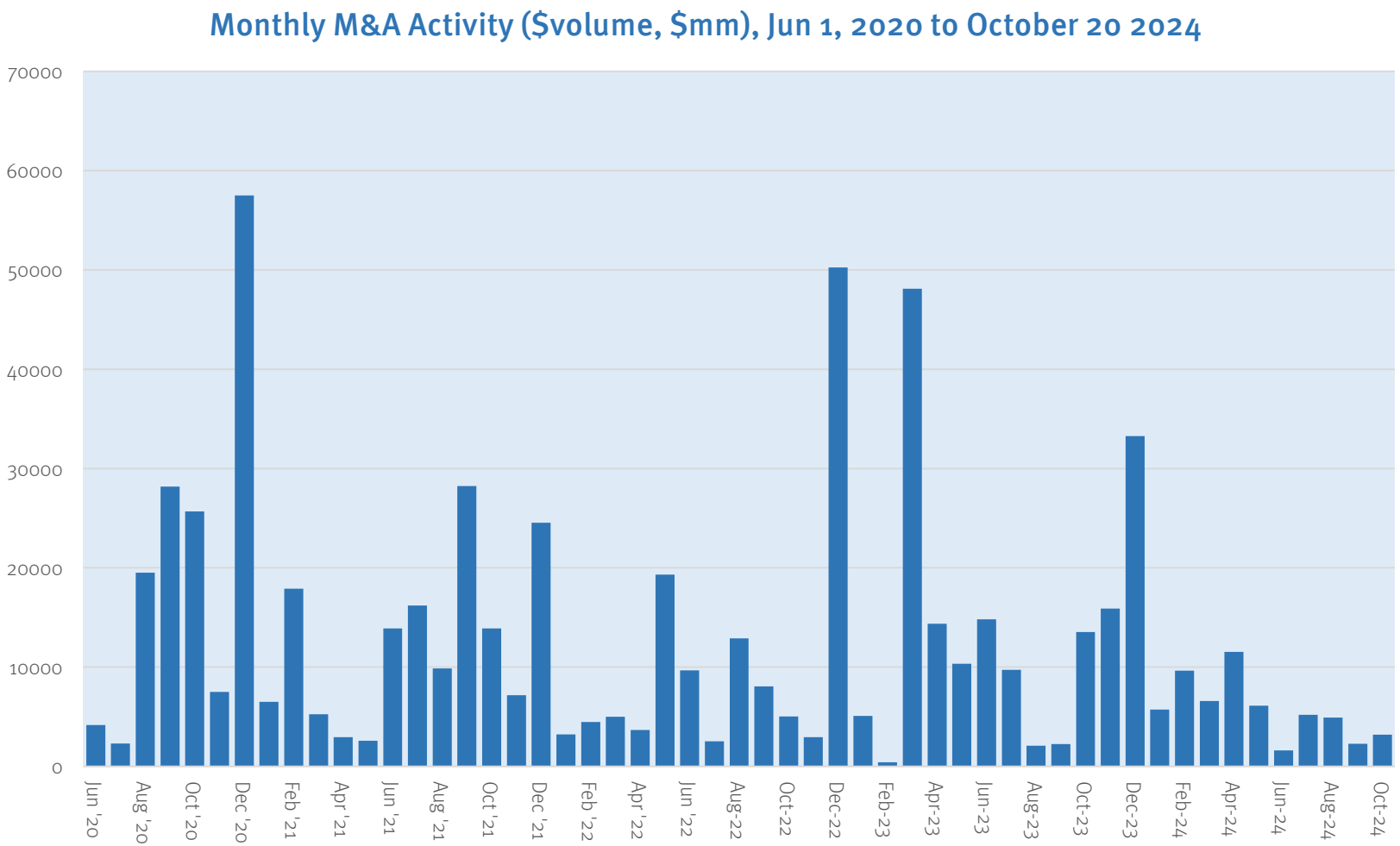
October 14, 2024

- The proposed acquisition represents a significant step forward in Lundbeck's Focused Innovator strategy, adding a highly innovative and complementary product in late-stage development for Developmental and Epileptic Encephalopathies (DEEs) - an area of high unmet medical need
- The acquisition will enhance and complement Lundbeck's capabilities and presence within neuro-rare conditions
- The lead asset, bexicaserin, holds blockbuster potential and is in development for the treatment of DEEs in a program enrolling patients diagnosed with Dravet syndrome, Lennox-Gastaut syndrome, and other DEE syndromes
- Bexicaserin has shown encouraging anti-seizure effects to date in preclinical and clinical studies, with its next-generation superagonist mechanism specifically targeting 5-HT_{2C} receptors, supporting bexicaserin's potential to offer a highly differentiated and best-in-class profile
- A global phase III trial (*DEEp SEA*) evaluating bexicaserin for the treatment of seizures associated with Dravet syndrome was initiated in September 2024
- Total transaction value of approximately USD 2.6 billion equity value and USD 2.5 billion net of cash (approximately DKK 17 billion). Funding will be through existing cash resources and bank financing

Source: https://www.lundbeck.com/global/press/news-archive/2024/lundbeck-to-acquire-longboard-pharmaceuticals-in-a-strategic-dea

Longboard Deal Doesn't Get Us Out of the M&A Doldrums

Through two thirds of October, we are still looking at a very slow month for M&A. The overall pace of M&A in 2024 remains quite weak relative to past years.



Source: Data from CapitalIQ, Stifel research.

Longboard Deal the Fifth Largest Biopharma Industry M&A Transaction Announcement of 2024

Announcement Date	Target	Buyer	Field	Stage of Lead Asset	Upfront Deal Value ($ millions)	Contingent Payments ($millions)
4/10/2024	Alpine Immune Sciences	Vertex Pharmaceuticals Inc.	Immunology	Phase II	4,900	0
2/12/2024	CymaBay Therapeutics	Gilead Sciences Inc.	Hepatology	Phase III	4,300	0
7/08/2024	Morphic Therapeutic	Eli Lilly and Co.	Immunology	Phase II	3,200	0
2/05/2024	MorphoSys AG	Novartis AG	Oncology	Approved	2,900	0
10/14/2024	Longboard Pharmaceuticals	H. Lundbeck A/S	Neurology	Phase III	2,600	0
4/29/2024	Deciphera Pharmaceuticals	Ono Pharmaceutical Co. Ltd.	Oncology	Approved	2,400	0
3/18/2024	Fusion Pharmaceuticals	AstraZeneca plc	Oncology	Phase II	2,000	400
1/08/2024	Ambrx Biopharma	Johnson & Johnson	Oncology	Phase II	2,000	0
4/03/2024	ProfoundBio Co.	Genmab A/S	Oncology	Phase II	1,800	0
1/23/2024	Inhibrx Inc.	Sanofi S.A.	Rare Disease	Phase II	1,700	500

Source: DealForma

Other Deals Last Week

"Zentiva AG entered into a share sale and purchase agreement to acquire 37.50% stake in Apontis Pharma AG from Paragon Partners GmbH for €28.1 million on October 16, 2024. In related transaction Based on the Investment Agreement, Zentiva AG will launch a voluntary public purchase offer. Zentiva will offer APONTIS PHARMA shareholders a price of €10.00 for each outstanding share of APONTIS PHARMA in cash. The consideration represents a premium of 52.9% over the closing share price on 15 October 2024, and a premium of 38.3% based on the weighted average price of the APONTIS PHARMA share over the three months ending 15 October 2024.

"Werfen, S.A. acquired Omixon Biocomputing Ltd. for $25 million on October 16, 2024. The acquisition is funded with cash on hand. The transaction is subject to regulatory and antitrust approvals and completed the acquisition after obtaining all necessary regulatory and antitrust approvals."

CD&R Nears Sanofi OTC Deal After Signing With Government

Pamela Barbaglia, Dinesh Nair, and Aaron Kirchfeld, *Bloomberg*, October 20, 2024 (excerpt)

Clayton Dubilier & Rice is nearing a deal to acquire control of Sanofi's consumer health unit after the American buyout firm signed social commitments with the French government, according to people familiar with the matter.

CD&R agreed to pledges around local jobs, investments and production linked to the consumer health unit Opella with the French government late Sunday, the people said, asking not to be identified because the information is private. Sanofi and the US buyout firm are set to announce exclusivity as early as Monday, they said.

The consumer health unit is valued at around €15 billion ($16.3 billion), Bloomberg News has reported. Sanofi confirmed earlier this month it's in talks to sell a 50% controlling stake in the business to CD&R, which beat out PAI Partners in the year-long bidding process. PAI representatives declined to comment.

Source: https://www.bloomberg.com/news/articles/2024-10-20/cd-r-said-to-near-sanofi-otc-deal-after-signing-with-government

FTC Guidelines are Impacting the Pharma Industry

Rajiv Khanna, *Norton Rose Fulbright Blog*, October 2024 (excerpt)

The Federal Trade Commission's (FTC) revised merger guidelines issued in 2023 signify a substantial alteration in antitrust enforcement, notably impacting industries like pharmaceuticals where consolidation is prevalent.

The updated guidelines provide reduced Herfindahl-Hirschman Index (HHI) and market share requirements, signifying a more stringent method for assessing the anticompetitive nature of mergers. A significant modification is that mergers resulting in a corporation possessing over 30 percent of market share may now be deemed to contravene Section 7 of the Clayton Act, even with minimal competitive overlap. Moreover, the rules abandon the reliance on a 30 percent market share as a conclusive indicator of market dominance, instead prioritizing the assessment of dominance by direct proof or sustained market power.

The revised guidelines notably remove the 30 percent market share barrier as a conclusive indicator of market dominance. The recommendations emphasize evaluating dominance by actual evidence or indicators of sustained market power. They aim to obstruct mergers that may enable a firm dominating in one market to reinforce or expand its influence into other markets, regardless of whether the merger has any current activities in those sectors. These transactions may be considered as infringing upon both Section 2 of the Sherman Act and Section 7 of the Clayton Act. Moreover, the recommendations tackle issues of companies employing a strategy of numerous minor acquisitions to attain anticompetitive results, even if no single transaction would separately violate antitrust regulations.

The revised guidelines expand the range of evidence assessed in evaluating anticompetitive risks, incorporating the acquiring firm's previous M&A strategies—regardless of completion—in various markets or industries, alongside its prospective acquisition intentions and those of other industry participants. The initial draft's general "catchall" guideline was supplanted with more specific instances, offering clearer and more actionable direction for firms. The modification entailed the elimination of draft Guideline 13, which asserted that "Mergers Should Not Otherwise Substantially Lessen Competition or Tend to Create a Monopoly." The FTC has expanded its competitive analysis to evaluate mergers based on their effects on direct competition as well as their influence on access to vital resources and customers. A significant alteration is the integration of the "ecosystem theory," enabling regulators to contest acquisitions if a company's wider ecosystem may inhibit competition. This notion was formerly employed in the United Kingdom. In the US, the concept of "ecosystem competition," which originated in the EU, is currently implemented to handle situations where a dominant corporation providing a range of products and services may be limited by the combinations of offerings from competing providers. The guidelines also present the notion of a nascent threat, characterized as a firm with the potential to evolve into a significant competitor, bolster the expansion of other rivals, or otherwise undermine the influence of an incumbent. **The guidelines emphasize the importance of maintaining incentives for innovation in pharmaceutical research and development, cautioning against mergers that may diminish these incentives or establish significant obstacles to entry for new competitors**. Nonetheless, although these guidelines indicate heightened regulatory oversight, they lack legal authority—agencies must still convince federal courts to implement them.

Source: https://www.nortonrosefulbright.com/en-ke/knowledge/publications/33212c9e/ftcs-watchdog-role-in-pharma-mergers-road-bumps-and-the-way-forward

Industry News

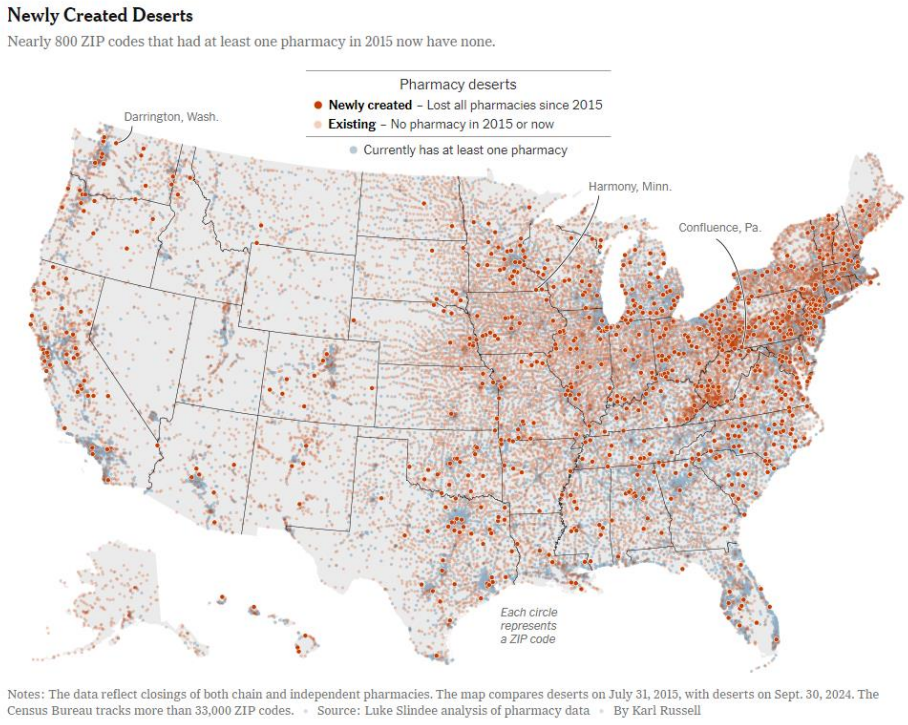
PBM Discriminatory Pricing Putting Independent U.S. Pharmacies Out of Business

Reed Abelson and Rebecca Robins, *New York Times*, October 19, 2024 (excerpt)

[A] New York Times investigation found that P.B.M.s, which employers and government programs hire to oversee prescription drug benefits, have been systematically underpaying small pharmacies, helping to drive hundreds out of business. The pattern is benefiting the largest P.B.M.s, whose parent companies run their own competing pharmacies. When local drugstores fold, the benefit managers often scoop up their customers, according to dozens of patients and pharmacists.

The benefit managers' power comes from two main sources. First, the three biggest players — CVS Caremark, Express Scripts and Optum Rx — collectively process roughly 80 percent of prescriptions in the United States. Second, they determine how much drugstores are reimbursed for medications that they provide to patients. Pharmacies buy those drugs from wholesalers, in the hope that P.B.M.s will reimburse them at a profit when the medications are provided to patients. But the largest benefit managers have strong incentives to set those rates as low as possible. A key reason: They make money in part by charging employers more for certain drugs than what the P.B.M.s pay pharmacies for them.

P.B.M.s frequently pay the pharmacies at rates that do not cover the costs of the drugs, according to more than 100 pharmacists around the country and dozens of examples of insurance paperwork and legal documents. **In every state, The Times identified at least one example since 2022 in which an independent drugstore closed and the pharmacist blamed P.B.M.s. In some states, like Pennsylvania, such closings have become routine. They have disproportionately affected rural and low-income communities, creating so-called pharmacy deserts that make it harder for residents to get prescriptions and medical advice.**

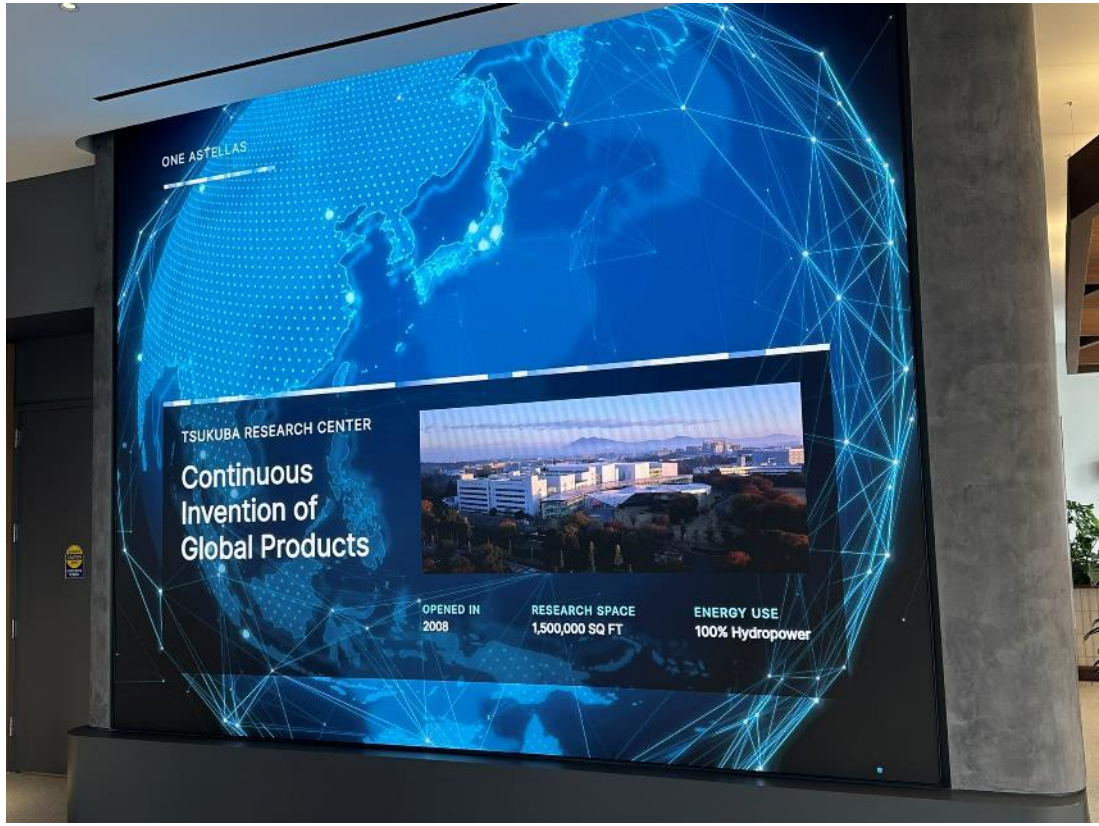


Source: https://www.nytimes.com/2024/10/19/business/drugstores-closing-pbm-pharmacy.html

FDA Approves Astellas Claudin18.2 Antibody

Katherine Lewin, *Endpoints News*, October 18, 2024 (excerpt)

The FDA on Friday approved Astellas' treatment for a type of gastric cancer, marketed as Vyloy (zolbetuximab). The approval came three weeks ahead of its scheduled PDUFA date of Nov. 9. Vyloy targets a protein called Claudin18.2 that is expressed on the surface of some gastric cancer cells. The drug is now approved in combination with chemotherapy for the first-line treatment of locally advanced unresectable or metastatic HER2-negative gastric or gastroesophageal junction adenocarcinoma. According to the company, Claudin18.2 is expressed by 38% of patients with advanced gastric cancer. The treatment previously won approval in Japan in March based on data from two Phase 3 clinical trials, with Astellas saying at the time that it's the first of its class to receive approval worldwide. The drug was also authorized in Europe in September and approved by the UK in August. Data from the Phase 3 SPOTLIGHT and GLOW trials showed statistically significant improvements in progression-free survival and overall survival compared to standard of care chemotherapy.



Source: https://endpts.com/fda-approves-astellas-gastric-cancer-drug-vyloy-ahead-of-schedule/

FDA Not Taking Compounded Tirzepatide off the Market

Taylor O'Bier, Scripps News, October 15, 2024

Pharmacists can continue making compounded versions of generic tirzepatide, the active ingredient in popular medications Mounjaro and Zepbound, the Food and Drug Administration said in a recent court filing.

The agency will revisit its decision to remove the drug from its nationwide shortage list earlier this month in response to the lawsuit filed by a trade group of compounding pharmacies claiming the drug was still in short supply.

When a drug is on the FDA's shortage list, it allows compounding pharmacies to legally make generic, copied versions of the medications by ordering ingredients in bulk and producing the medications themselves. But when the FDA announced on Oct. 2 that the shortage of tirzepatide had ended, that meant compounding pharmacies had to stop making it.

One of the key criteria of whether a drug is on shortage according to the FDA is whether a drug is available in the supply chain.

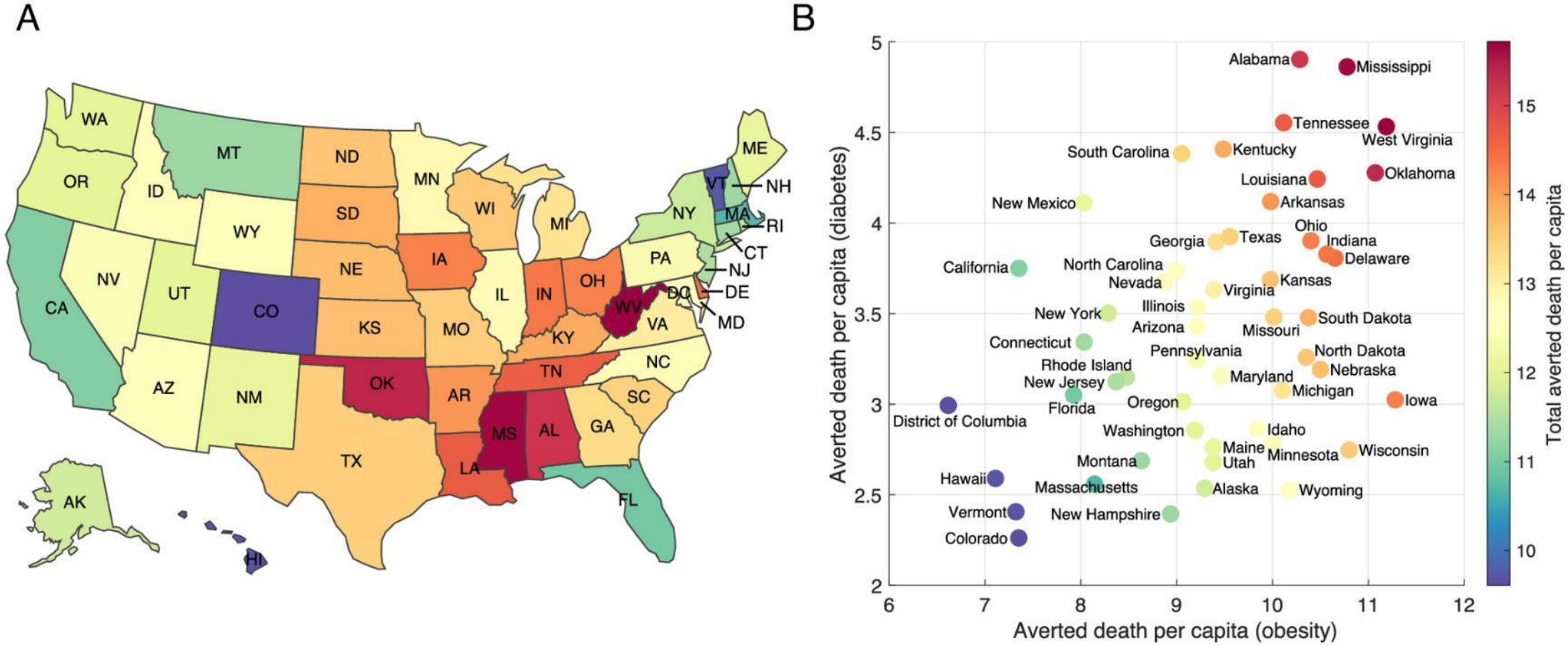
An informal discussion with people that we know who use tirzepatide (or would like to) in October 2024 in the U.S. would indicate that it remains tough to the find the drug. Patients report having to contact multiple pharmacies to find drug if they can get it at all.

Source: https://www.scrippsnews.com/health/medicine/fda-is-reconsidering-its-decision-to-take-tirzepatide-off-its-drug-shortage-list

Expanding Access to GLP-1's Would Save Thousands

Expanding access to new, highly effective weight-loss medications could prevent more than 40,000 deaths a year in the United States, according to a new study led by researchers at Yale School of Public Health and the University of Florida.

Pandey et.al., "Estimating the lives that could be saved by expanded access to weight-loss drugs," PNAS, Oct 15, 2024



(*A*) State-level annual deaths averted per 100,000 population. (*B*) Distribution of averted deaths per capita among overweight and obese individuals with type 2 diabetes and obese individuals without type 2 diabetes.

Source: https://www.pnas.org/doi/10.1073/pnas.2412872121

Wave Sees RNA Editing Validation in Early Trial Results

Ben Fidler and Ned Pagliarulo, *Pharmavoice*, Oct 17, 2024 (excerpt)

Clinical trial results released by Wave Life Sciences Wednesday appear to provide early validation for the company's newest drugmaking technology as well as a burgeoning field of genetic medicine, RNA editing.

The data are from just two patients, the first treated in a Wave study of the biotechnology firm's medicine for an inherited lung and liver disease called alpha-1 antitrypsin deficiency, or AATD. Still, Wave claims the data show convincing evidence its medicine successfully edited the messenger molecules cells use to turn DNA blueprints into proteins.

According to the company, this kind of effect hasn't before been demonstrated in clinical testing.

"Achieving the first-ever therapeutic RNA editing in humans is a significant milestone for our organization, for our GSK collaboration, and for the entire oligonucleotide field," said Wave CEO Paul Bolno in a statement.

Source: https://www.pharmavoice.com/news/wave-rna-editing-aatd-first-trial-data/730139/

Book Review: Confessions of a Grizzled Biotech Survivor

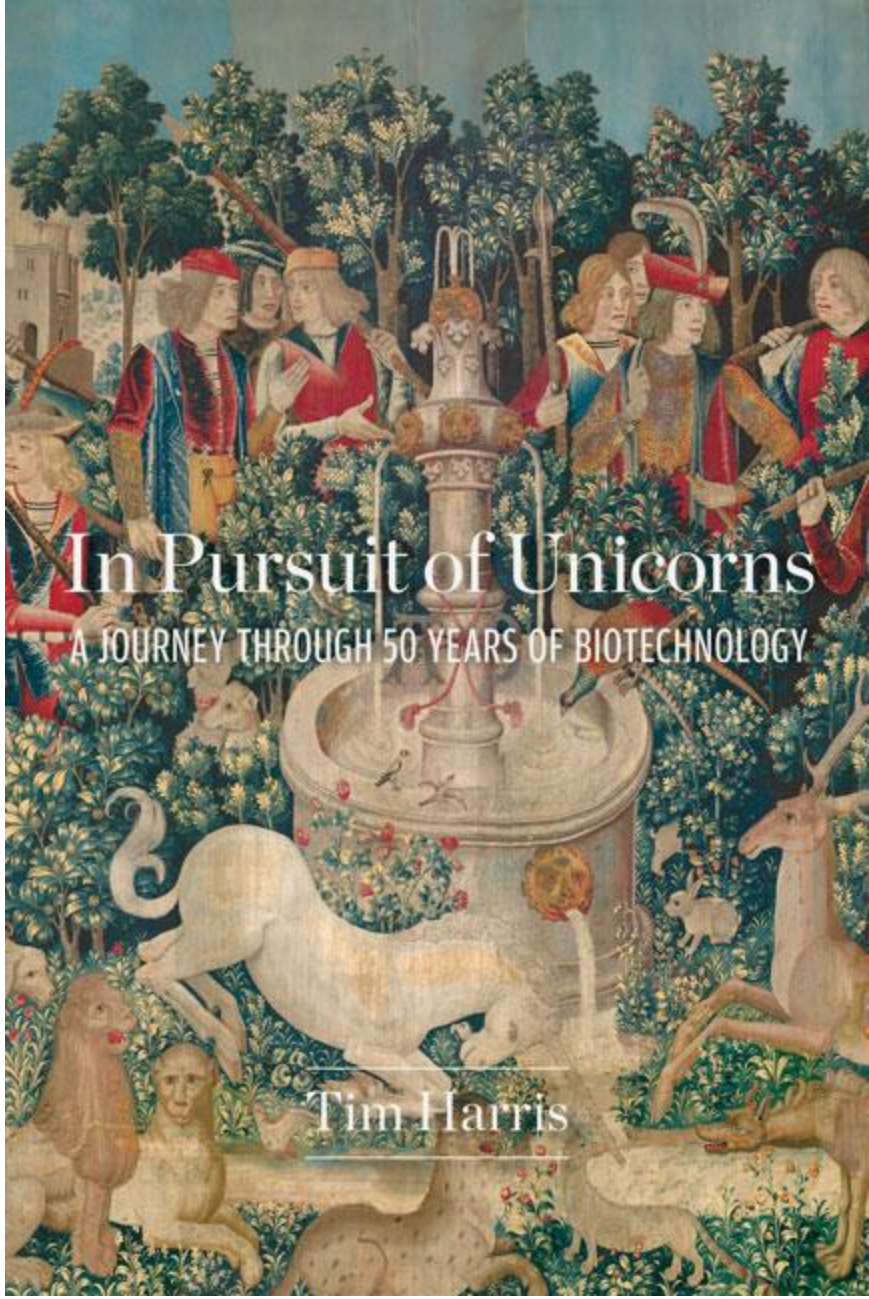
John Sterling, *GEN*, Oct 17, 2024 (excerpt)

“We wish to suggest a structure for the salt of deoxyribose nucleic acid (D.N.A.). This structure has novel features which are of considerable biological interest.”

Those famously understated words introduced a research paper written by James Watson and Francis Crick that appeared in Nature in April 1953. The second sentence set wheels in motion that ultimately revolutionized life science research and provided the foundation for the eventual emergence of the international biotechnology industry.

But as Tim Harris, PhD, points out in his remarkable new book, In Pursuit of Unicorns: A Journey through 50 Years of Biotechnology, modern biotechnology really began with the creation of recombinant DNA plasmids, which could be transferred into bacteria that would manufacture human proteins from the microbes’ coded genes.

With publication of the in-depth scientific description of recombinant DNA technology by Stanley Cohen and Herbert Boyer in an article in PNAS in November 1973, the blueprint for genetic engineering in the biotech business was laid out. Harris should know. An English molecular biologist, he began his career in 1974 and later joined one of the first British biotech companies, Celltech, in 1981 in the U.K. Harris continued to work as both a scientist, executive and entrepreneur, who went on to create several companies. He currently serves as a venture partner at SV Health Investors.



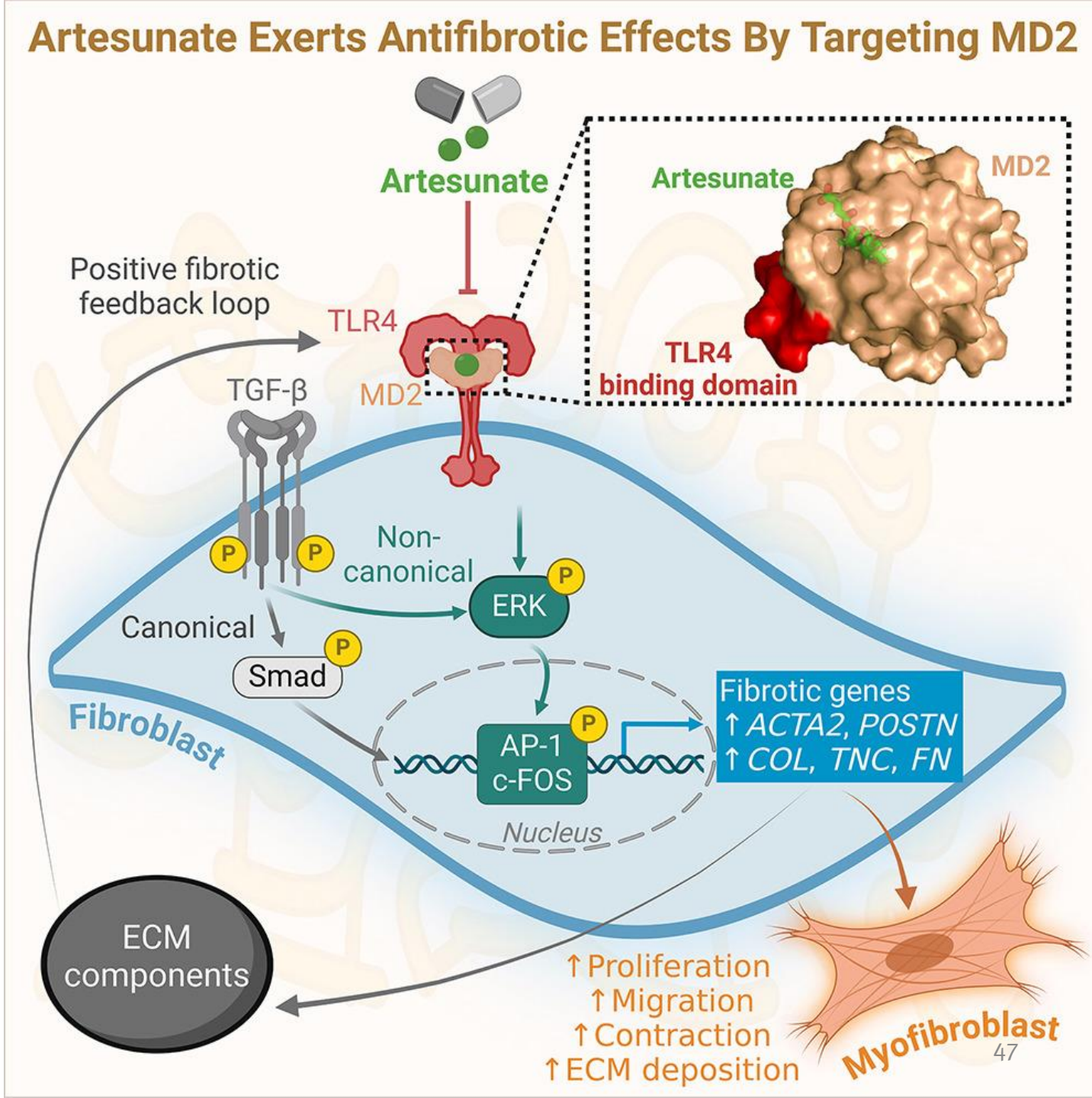
Sources: https://www.genengnews.com/topics/genome-editing/confessions-of-a-grizzled-biotech-survivor/, https://www.cshlpress.com/default.tpl?cart=17294548581111273454

MD2 As a Target for Heart Failure and Fibrosis

Zhang H et.al. Multiscale drug screening for cardiac fibrosis identifies MD2 as a therapeutic target. *Cell*. Oct 12, 2024.

Cardiac fibrosis impairs cardiac function, but no effective clinical therapies exist. To address this unmet need, we employed a high-throughput screening for antifibrotic compounds using human induced pluripotent stem cell (iPSC)-derived cardiac fibroblasts (CFs). Counter-screening of the initial candidates using iPSC-derived cardiomyocytes and iPSC-derived endothelial cells excluded hits with cardiotoxicity. This screening process identified artesunate as the lead compound. Following profibrotic stimuli, artesunate inhibited proliferation, migration, and contraction in human primary CFs, reduced collagen deposition, and improved contractile function in 3D-engineered heart tissues. Artesunate also attenuated cardiac fibrosis and improved cardiac function in heart failure mouse models. Mechanistically, artesunate targeted myeloid differentiation factor 2 (MD2) and inhibited MD2/Toll-like receptor 4 (TLR4) signaling pathway, alleviating fibrotic gene expression in CFs. Our study leverages multiscale drug screening that integrates a human iPSC platform, tissue engineering, animal models, in silico simulations, and multiomics to identify MD2 as a therapeutic target for cardiac fibrosis.

Source: https://www.cell.com/cell/abstract/S0092-8674(24)01092-4



The Pfizer Activist Attack

He Made Pfizer a Household Name. Wall Street Wants More

With Pfizer's stock down sharply, an activist investor is pushing for CEO Albert Bourla to improve performance

Jared Hopkins, *Wall Street Journal*, October 18, 2024 (excerpt)

When a novel coronavirus struck in early 2020, Pfizer's chief executive, Dr. Albert Bourla, saw an opportunity to help save the world. He pushed the drugmaker to deliver a Covid-19 vaccine at lightning speed. The Greek-born CEO's bold bet paid off. The shot turned Pfizer into a household name, while ringing up tens of billions of dollars in sales. Bourla's cellphone hummed with calls from leaders around the world. The experience, he said in a commencement speech afterward, showed the virtue of "setting ambitious goals that are seemingly impossible."

But now Bourla is under attack because Pfizer's stock price is way down, in part because it miscalculated demand for its Covid-19 vaccine, and some of the ambitious goals Bourla has set in the years since the pandemic have yet to pan out.

An activist investor is leading the charge. Starboard Value, a hedge fund that has waged fights in recent months against Autodesk, Salesforce and Tinder parent Match Group recently took a roughly $1 billion stake in Pfizer. The sides held their first meeting on Wednesday, after Starboard accused the company of pressuring two former executives who had been working with Starboard to express support for Bourla.

But Pfizer so far has been unable to escape its postpandemic slump. After the Covid-19 emergency receded, sales of the company's vaccine and antiviral tanked, much more than executives forecast. New drug launches under-delivered. Pfizer's first stab at the booming anti-obesity market flamed out.

Wall Street noticed, sending Pfizer stock down. Today Wall Street values Pfizer at roughly $166 billion, roughly half its peak during the pandemic.

Some analysts and investors have said Bourla overspent on those acquisitions, some of which have yet to bear fruit. Pfizer recently pulled a sickle-cell disease drug, Oxbryta, from the market. The launch of the migraine drug, Nurtec, started slowly.

A closely watched pill in development for treatment of obesity disappointed during testing, setting back Pfizer's efforts to join one of the pharmaceutical industry's hottest markets. Pfizer is now advancing another version of the anti-obesity drug.

Some of Pfizer's R&D programs "haven't worked out. It's the nature of the business. A lot have," Gottlieb said. "In this business you have to be willing to lean forward."

Source: https://endpts.com/wuxi-companies-may-sell-units-impacted-by-biosecure-report/

Four Reasons to be Optimistic on Pfizer

It's true that Pfizer miscalculated its post-Pandemic earnings and has had blow ups on a few acquisitions like GBT, but there is a lot to like. On balance, our view is that Pfizer management has been executing well – despite various bumps in the road.

1 Seagen's Pipeline

- The Seagen pipeline is quite strong and was not particularly "visible" to the Street at the time of the Pfizer merger.
- Since the acquisition, Pfizer has been quiet about the large number of first-in-class ADC's in development and their potential.
- There is no reason to educate rivals about how well the pipeline is going.
- Key pipeline opportunities include ADCs for LIV-1, ALPL2, CD228A and B7H4.
- The POS of ADC's has historically been quite high.

2 Ponsegromab

- The drug has as very large potential.
- We have seen supportive care biologics drugs cross $10 billion in sales before.
- The data for this drug are exceptionally good.
- Cancer cachexia is a killer – accounting for 25% of cancer deaths.
- Ponsegromab can make a major difference in this cause of death from the disease.
- The math is highly favorable – 6mm cases of cancer in G7 countries and a third are candidates for Pon.
- Assuming $50k pricing / patient that is a $100 billion TAM.

3 The "fix" in commercial and cost reductions

- Pfizer is targeting $4 billion in savings by the end of 2024.
- Despite a strong growth pipeline Pfizer is trading at just 11x current earnings – this well below peers
- There is substantial leverage in the stock from cutting expenses.
- Further, Pfizer is substantially restructuring and upgrading its commercial organization – an area of substantial opportunity
- There is substantial operating leverage if Pfizer can raise revenues from the drugs it already has through better commercial execution.

4 Vaccine Powerhouse

- Next-generation pneumococcal vaccine candidate now in Phase 2
- COVID/flu combo vaccine has a Phase 3 readout this year
- A combo vaccine is likely to work and will be appealing to a very large audience
- While the use of antivirals is not as strong as Pfizer might want, there is no decrease in desire for vaccines
- With Covid persisting it is highly likely that a combo vaccine would have high uptake
- This market is quite large and creates substantial upside for Pfizer.

What Critics of Pfizer Are Getting Wrong

The activist investment firm Starboard Value has launched a proxy fight again Pfizer, questioning the company's management under CEO Albert Bourla. Yale SOM's Jeffrey Sonnenfeld and co-author Steven Tian write that the critics are demonstrating the same impatience that has led investors to underestimate Pfizer in the past.

Jeffery Sonnenfeld and Steven Tian, *Yale Insights*, October 14, 2024 (excerpt)

The brewing proxy fight between activist Starboard Value and pharmaceutical giant Pfizer has already taken a hostile turn. Anonymous sources have been disparagingly suggesting that Pfizer CEO Dr. Albert Bourla should be removed. After news reports suggested they initially sided with the activists, former Pfizer CEO Ian Read and former CFO Frank D'Amelio switched sides, abandoning their erstwhile Starboard allies and expressing their support for Bourla. Then, Starboard Value founder Jeff Smith reportedly issued a fiery letter to Pfizer's board, alleging intimidation and coercion.

We don't know for sure what Starboard's turnaround plan contains. It has allegedly created an "extensive 50-page slide deck on its turnaround plans" which it is yet to reveal publicly. But one can easily guess what the primary complaints about Bourla might be since these criticisms have now been repeated so many times in anonymous leaks to the media: that Pfizer stock has gone sideways under Bourla's watch; that he supposedly overpaid in several major acquisitions and squandered tens of billions of Pfizer's COVID-19 vaccine windfalls; that Pfizer's business is in deep trouble after the demand for COVID vaccines fell off faster than anyone thought possible. There's just one problem: These criticisms are simply not factual, no matter how many times they may be repeated, as we reveal in our original detailed analysis and 36-page slide deck.

Source: https://insights.som.yale.edu/insights/what-critics-of-pfizer-are-getting-wrong

Of course, what is undeniably true is that Pfizer's stock price has gone sideways during Bourla's tenure, to the understandable frustration of some shareholders. However, the underperformance of Pfizer stock isn't all that it appears to be. In fact, Pfizer stock has performed in line with, if not a bit stronger than, pharmaceutical peers such as Merck, Johnson & Johnson, and Bristol-Myers Squibb this year.

Pharma stocks have been reduced to a "haves vs. have nots": a stark divide between GLP-1-driven stocks, namely Novo Nordisk and Eli Lilly who have soared to record heights, and all other pharma companies, many of whom languish trading near record-low multiples as investor sentiment plummets. This is a reversal from the COVID-19 pandemic when those now-soaring stocks (Novo Nordisk and Eli Lilly) looked weak for having missed the COVID vaccine and therapeutics boom and were attacked by critics, while COVID-powered stocks benefitted. To pin the blame for see-saw swings in the stock market on Bourla, considering Pfizer stock is performing exactly in line with non-Novo Nordisk, non-Eli Lilly pharma peers, one would have to fault Bourla for not developing a GLP-1 drug sooner, despite the fact virtually the entire pharmaceutical industry—like virtually every investor—was caught off guard by the speed with which these new obesity drugs were commercialized.

Sonnenfeld and Tian Article (continued)

Similarly, the persistent critique that Dr. Bourla overpaid and made bad deals during his post-COVID M&A spree—a criticism that seems to have become a rallying cry for investors upset with Bourla's leadership—isn't all that it appears to be.

For sure, one of Pfizer's four biggest deals, the smallest deal of the four, Pfizer's acquisition of Global Blood Therapeutics, has been a disaster so far by most objective measures (though not unsalvageable).

However, the return on investment for the three larger deals—the $6.7 billion acquisition of Arena, the $11.6 billion acquisition of Nurtec from Biohaven, and most importantly, the transformative, bet-the-farm $43 billion acquisition of Seagen—seem to be surpassing even the more optimistic internal and external projections so far, as we describe in more depth in our original analysis.

And regardless of the ROI numbers, a simple fact that many seem to have forgotten is that it is just plain too early to judge these deals as defeats. So much of the value of these deals is locked up in the research and development (R&D) pipeline of prospective drug candidates that Pfizer acquired—and it'll take many years for these pipeline projects to reach maturation. As the old pharma saying goes, the trouble with research is you don't know whether you've done the right thing for 10 years. Until that pipeline reaches maturity, writing off these deals as failures is equivalent to throwing in the towel after the first inning with eight innings left to go.

That is the trap that critics have consistently fallen into. Dating back decades, growth through M&As has been the Pfizer way, and each time, financial markets have mistakenly underestimated Pfizer's acquisitions only for those deals to pay off handsomely with time, as we show in our analysis.

Beyond the persistent myths surrounding Pfizer's M&A track record, there is also a persistent narrative that Pfizer's business is in trouble after demand for COVID-19 vaccines fell off faster than anyone thought possible. Bourla's pandemic heroics, for which he has been widely saluted, need no retelling. There is no dispute that the brilliant partnership between Pfizer and BioNTech, his leadership through later-stage vaccine development and successful clinical trials, with seamless production execution and unrivaled distribution as well as such follow-up therapeutics as Paxlovid, profoundly changed the course of public health history and global economic resilience in hugely positive ways.

Pfizer management has taken accountability for being too optimistic in their recent aggressive forecasts for COVID-19 vaccine demand and are wisely right-sizing their cost structure accordingly. However, by analyzing Pfizer's sales product line by product line, it's clear that virtually the entirety of Pfizer's revenue decline was caused only by the drop-off in COVID-19 vaccine demand, and nothing else. All of Pfizer's other major product lines have seen significant year-over-year growth, including record growth in the crucial oncology division, with cancer therapies poised for continued rapid revenue growth in the years ahead.

It's easy to miss the green shoots of progress as Pfizer's post-COVID reset gains steam: Pfizer now has no less than 112 promising drug candidates in its vaunted pipeline, including several recent launches with blockbuster potential. Since Bourla became CEO, Pfizer has had a higher clinical trial success rate than many industry peers—a stark turnaround from the worst R&D returns of any pharma company under prior leadership.

Source: https://insights.som.yale.edu/insights/what-critics-of-pfizer-are-getting-wrong

Pharmaceuticals Investor Sentiment Near Record Lows Across The Board, GLP-1 Aside

Current and Historical Multiples Of Pharmaceutical Companies
(current multiples calculated with projected 2024 earnings and using stock price as of October 8, 2024)

Company	Current P/E Multiple	5-Year Historical Average P/E
Pfizer	10.3x	11.3x
Bristol-Myers Squibb	9.5x	10.3x
Merck & Co.	11.6x	15.2x
Johnson & Johnson	15.1x	18.6x
Novo Nordisk A/S	28.9x	26.7x
Eli Lilly	43.6x	37.4x

The stocks of Pfizer, Bristol-Myers Squibb, Merck, and Johnson & Johnson are all trading at near record-low multiples, with price-to-earnings ratios well below their historical average. Meanwhile, propelled by their hot GLP-1/obesity products, the stocks of Novo Nordisk and Eli Lilly are trading at technology-lite multiples rarely seen in the pharma industry.

Pfizer Has Long Relied On Mega-Deals To Replenish Product Pipeline – With Strong Track Record Of Success

List of Largest M&A Deals Within Pharmaceutical Industry In History

Rank	Year	Acquirer	Target	Deal Size
1	2000	Pfizer	Warner-Lambert	$90B
2	2000	Glaxo Wellcome	SmithKline Beecham	$76B
3	2019	Bristol-Myers Squibb	Celgene	$74B
4	2004	Sanofi	Aventis	$73.5B
5	2015	Actavis	Allergan	$70.5B
6	2009	Pfizer	Wyeth	$68B
7	2002	Pfizer	Pharmacia	$64.3B
8	2018	Takeda Pharmaceutical	Shire	$62B
10	2009	Merck	Schering-Plough	$47.1B
11	2009	Roche	Genentech	$44B
12	2023	Pfizer	Seagen	$43B

Of the twelve largest deals in the history of the pharma industry, four belong to Pfizer – no other company has more than one

Financial markets often misattribute and underestimate the value of pipeline drugs. Each of Pfizer's deals were met with initial skepticism by financial markets, and each time, the deals ended up working out better than expected

We've Seen This Before: Financial Markets Chronically, Mistakenly Underestimated Pfizer's Acquisitions Every Time

REUTERS

DEALS JANUARY 29, 2009 / 8:23 AM / UPDATED 14 YEARS AGO

Pfizer-Wyeth deal fails to create spark

By Ransdell Pierson 6 MIN READ

NEW YORK (Reuters) - Days after Pfizer said it would buy Wyeth for $68 billion, Pfizer shares fell to nearly a 12-year low and some shareholders are questioning the wisdom of the planned union.

Los Angeles Times

BUSINESS

Pfizer Deal Roils Its Stock

BY RONALD D. WHITE
JULY 16, 2002 12 AM PT

TIMES STAFF WRITER

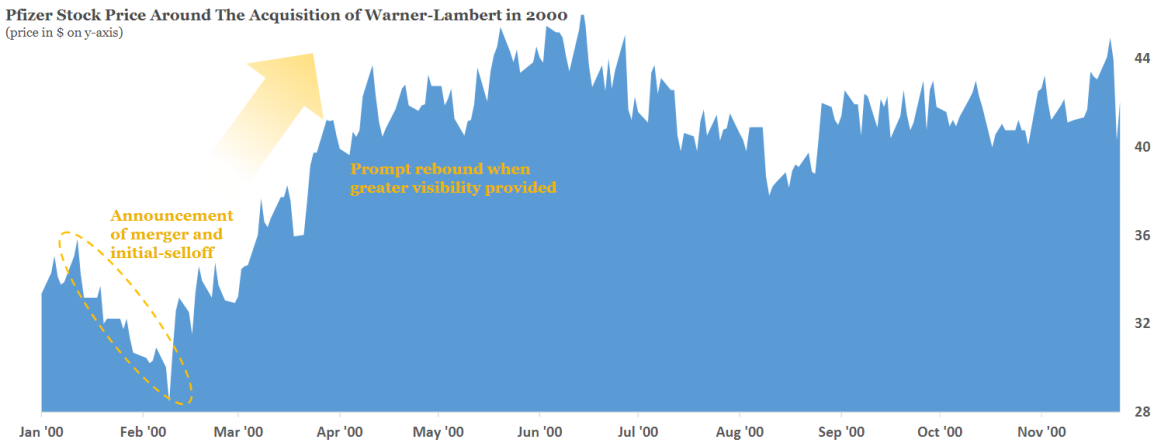
Investors hammered the stock of Pfizer Inc. on Monday, driving it down nearly 11% amid concerns over the price and timing of its proposed acquisition of Pharmacia Inc.

REUTERS

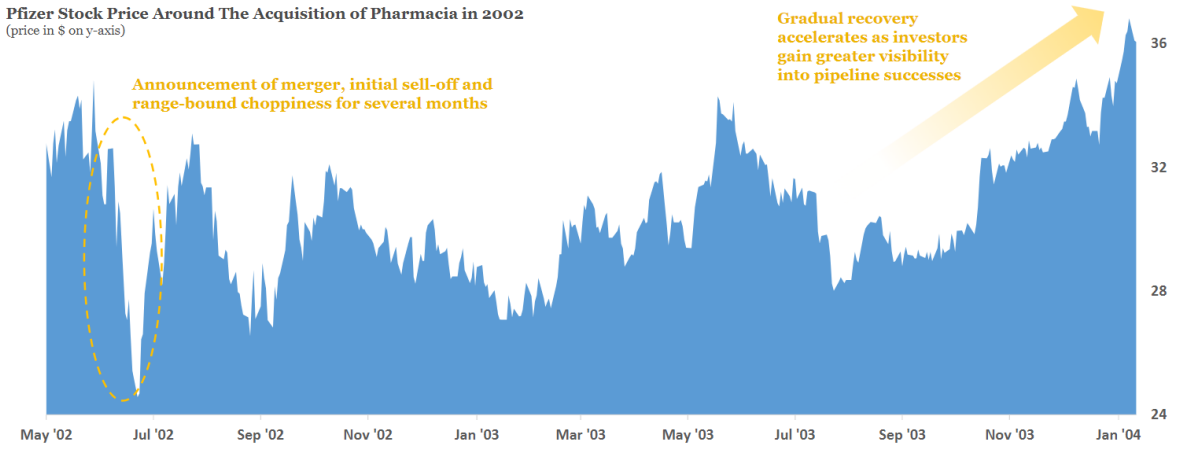
Faith slipping in meaningful Pfizer deal

By Ransdell Pierson, Jessica Hall 5 MIN READ

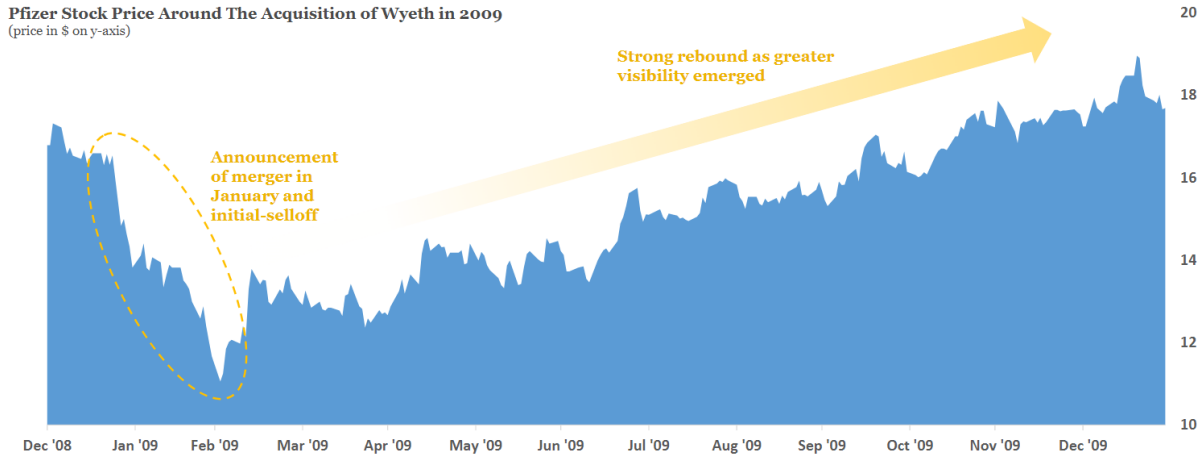
Financial Markets Mistakenly Underestimated Pfizer's $90 Billion Acquisition Of Warner-Lambert in 2000



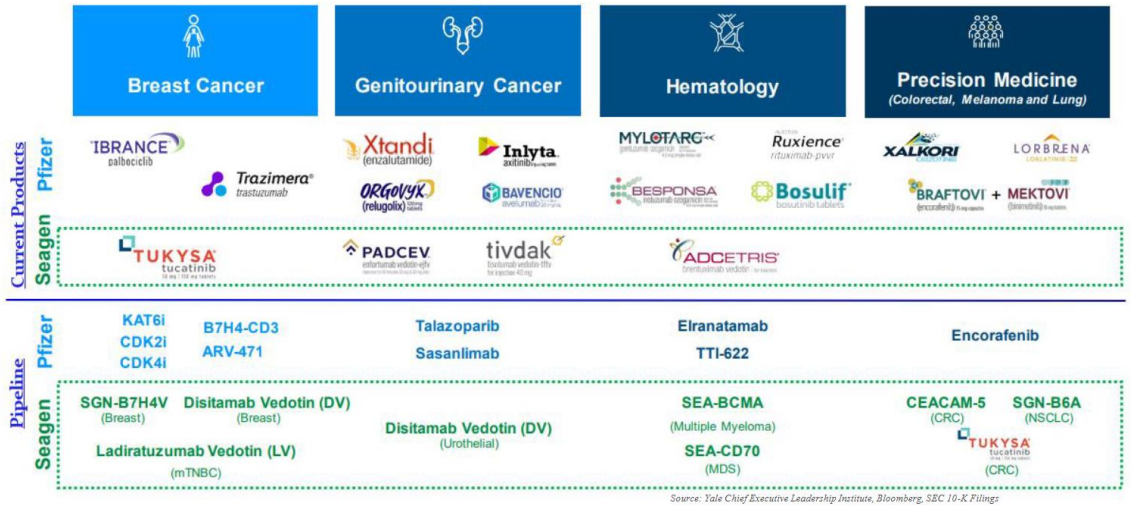
Financial Markets Mistakenly Underestimated Pfizer's $64.3 Billion Acquisition Of Pharmacia in 2002



Financial Markets Mistakenly Underestimated Pfizer's $68 Billion Acquisition Of Wyeth in 2009



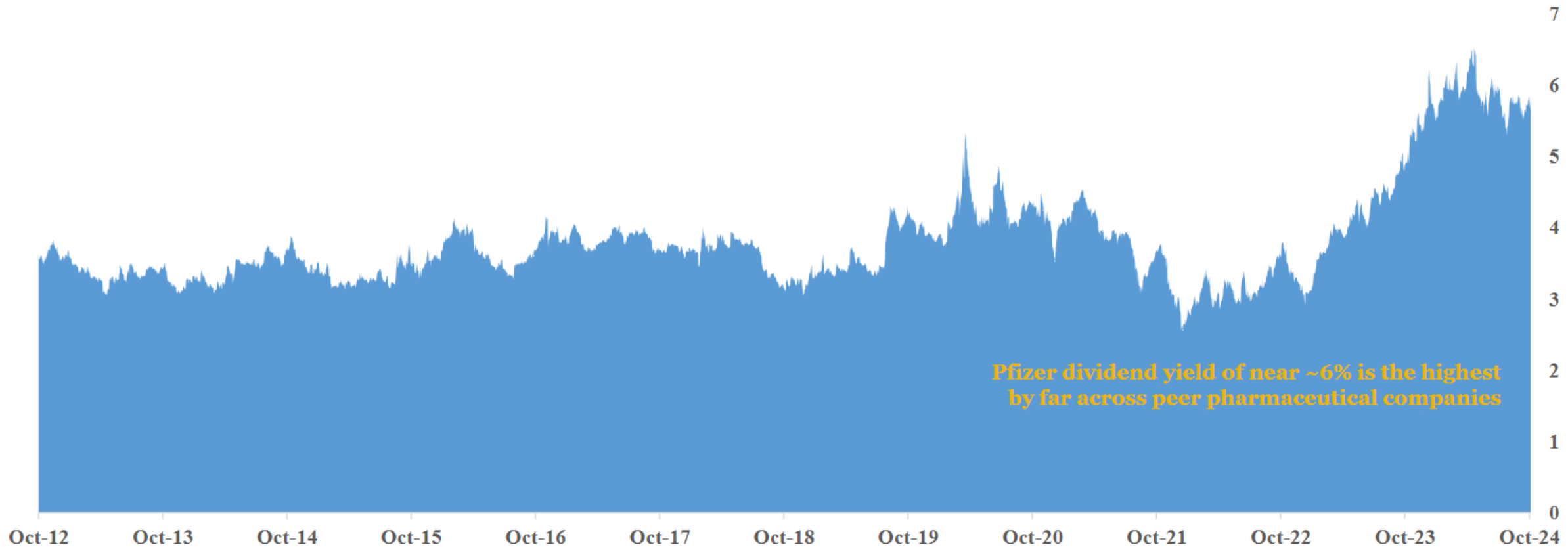
Seagen Portfolio And Pipeline Extremely Complimentary With Pfizer Portfolio



Source: Yale Chief Executive Leadership Institute, Bloomberg, SEC 10-K Filings

Pfizer Dividend Yield Near Record High; Management Reiterated Its Commitment To Maintaining And Increasing The Dividend, With 345 Consecutive Payouts

Pfizer Dividend Yield
(measured in %)



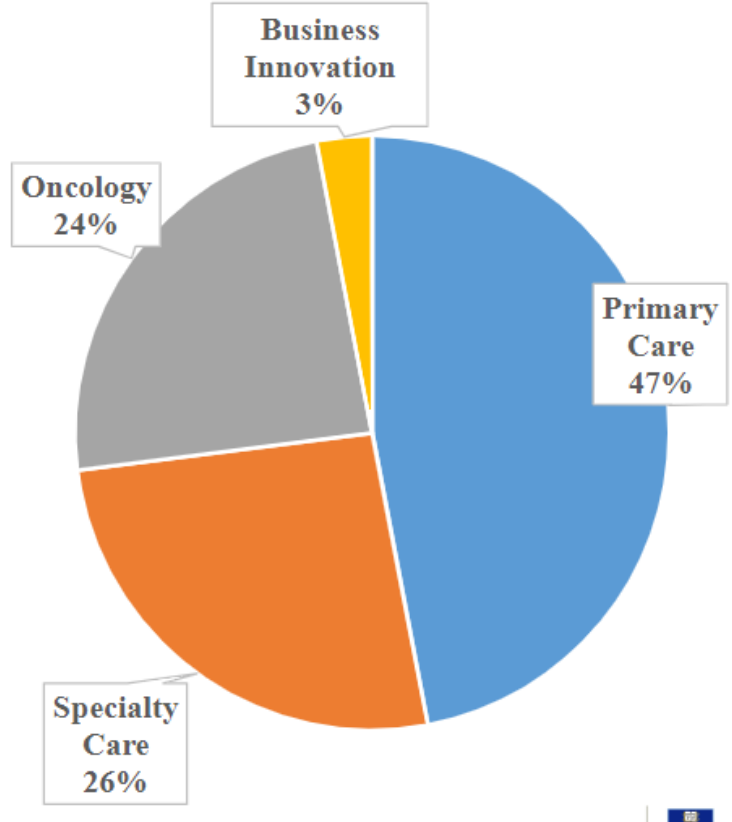
Source: Yale Chief Executive Leadership Institute, Bloomberg, SEC 10-K Filings

Much More Than Just COVID – Pfizer Has One Of The Most Expansive, Diversified Portfolios Of Any Pharma Company – Specialty Care and Oncology Products

Specialty Care Products	Description	2023 Revenues ($ Millions)
Vyndaqel	ATTR-CM and polyneuropathy	$3,321
Xeljanz/ Enbrel	RA, PsA, UC	$1,703
Enbrel	RA, juvenile arthritis	$830
Sulperazon	Bacterial infections	$757
Ig Portfolio	Various	$585
Genotropin	Replacement of human growth hormone	$539
Zavicefta	Bacterial infections	$511
Inflectra	Crohn's disease	$490
BeneFIX	Hemophilia B	$424
Zithromax	Bacterial infections	$406
Medrol	Anti-inflammatory glucocorticoid	$339
Oxbryta	Sickle cell disease	$328

Oncology Products	Description	2023 Revenues ($ Millions)
Ibrance	Metastatic breast cancer	$4,753
Xtandi	mCRPC	$1,191
Inlyta	Advanced RCC	$1,036
Bosulif	Myelogenous leukemia	$645
Lorbrena	ALK-positive metastatic NSCLC	$539
Zirabev	Metastatic cervical cancer	$424
Ruxience	Non-Hodgkin's lymphoma	$390
Xalkori	Advanced NSCLC	$374
Retacrit	Anemia	$340
Aromasin	Advanced breast cancer	$301
Besponsa	Lymphoblastic keukemia	$236
Braftovi	Metastatic melanova	$213

Segment Contribution As % Of Total Sales
(based on FY 24 estimated sales)



Source: Yale Chief Executive Leadership Institute, Bloomberg, SEC 10-K Filing; all calculations as of October 8, 2024

A Deep, Deep Dive Into Pfizer's R&D Pipeline – Which Could Add ~$20 Billion In Revenues By 2030

Product	Category	Indication	Launch	TAM ($MM)	Peak Sales Expectations ($MM)
mRNA Vaccines	High-Value Pipeline	Influenza + COVID/Flu + Shingles	2025+	> $16B in 2030 (Flu: $10B, Shingles: $6B, COVID: NM)	$10-15B
Oral GLP-1 Agonists	High-Value Pipeline	Type 2 Diabetes and Obesity	TBD	> $90B in 2030 (T2DM: $35-40B, Obesity: $50-55B)	~$10B
Migraine Portfolio (Nurtec/Vydura + Zavegepant)	New BD	Migraine Treatment/Prevention	2022/2023	NM	> $6B
Elrexfio	Near-Term Launch	Multiple Myeloma	2023	NM	> $4B (All lines of MM)
Inclacumab & GBT-601	New BD	Sickle Cell Disease	2026/2027	NM	> $3B
TTI-622	High-Value Pipeline	Hematological Malignancies	TBD	$46B in 2030 (MM: $33B, DLBCL: $10B, AML: $3B)	> $3B (All indications)
Abrysvo (Maternal & Older Adult)	Near-Term Launch	RSV Prophylaxis	2023	NM	> $2B
Anti-IFN-β	High-Value Pipeline	Dermatomyositis (DM) & Polymyositis (PM)	TBD	$6-12B (Advanced DM/PM therapies)	~ $1-3B
Etrasimod (Ulcerative Colitis)	New BD	Ulcerative Colitis	2023	NM	$1-2B (UC only)
Talzenna (Prostate Cancer)	Near-Term Launch	1L mCRPC	2023	$4.9B (PARPi for prostate, 2028)	> $1B
Litfulo	Near-Term Launch	Alopecia Areata	2023	NM	$1B
Total					**> $42- 50B**

	PRODUCT/CANDIDATE	PROPOSED DISEASE AREA
LATE-STAGE CLINICAL PROGRAMS FOR ADDITIONAL USES AND DOSAGE FORMS FOR IN-LINE AND IN-REGISTRATION PRODUCTS	Ibrance (palbociclib)[a]	ER+/HER2+ metastatic breast cancer
	Talzenna (talazoparib)	Combination with Xtandi (enzalutamide) for DNA Damage Repair-deficient mCSPC
	Ngenla (somatrogon)[b]	Adult growth hormone deficiency
	Braftovi (encorafenib) and Erbitux® (cetuximab)[c]	First-line $BRAF^{V600E}$-mutant mCRC
	Paxlovid (nirmatrelvir; ritonavir)	COVID-19 in high-risk children (6-11 years of age; >88lbs)
	Litfulo (ritlecitinib)	Vitiligo
	Elrexfio (elranatamab)	Multiple myeloma double-class exposed
		Newly diagnosed multiple myeloma post-transplant maintenance
		Newly diagnosed multiple myeloma transplant-ineligible
	Oxbryta (voxelotor)	Sickle cell disease (pediatric)
	Eliquis (apixaban)[d]	Venous thromboembolism (pediatric)
	Abrysvo (vaccine)	Active immunization to prevent RSV infection in adults (18-59)
	Padcev (enfortumab vedotin)[e]	Cisplatin-ineligible/decline muscle-invasive bladder cancer
		Cisplatin-eligible muscle-invasive bladder cancer
	Tukysa (tucatinib)	HER2+ adjuvant breast cancer
		2nd line/3rd line HER2+ metastatic breast cancer
		1st line HER2+ metastatic colorectal cancer
NEW DRUG CANDIDATES IN LATE-STAGE DEVELOPMENT	giroctocogene fitelparvovec (PF-07055480)[f]	Hemophilia A
	PF-06425090 (Vaccine)	Immunization to prevent primary clostridioides difficile infection
	sasanlimab (PF-06801591)	Combination with Bacillus Calmette-Guerin for non-muscle-invasive bladder cancer
	fordadistrogene movaparvovec (PF-06939926)	Duchenne muscular dystrophy (ambulatory)
	VLA15 (PF-07307405) vaccine[g]	Immunization to prevent Lyme disease
	PF-07252220 (quadrivalent mRNA-based vaccine)	Immunization to prevent influenza
	Vepdegestrant (PF-07850327)[h]	Breast cancer metastatic - 2nd line ER+/HER2-
	inclacumab (PF-07940370)	Sickle cell disease
	Ibrance + vepdegestrant[h]	ER+/HER2- metastatic breast cancer
	Dazukibart (PF-06823859)	Dermatomyositis, polymyositis
	Disitamab vedotin[i]	1st line HER2 (≥IHC1+) metastatic urothelial cancer
	PF-07926307 (COVID/flu combo vaccine)[j]	Immunization to prevent COVID infection and influenza
	sisunatovir (PF-07923568)	Respiratory syncytial virus infection (adults)

Source: Yale Chief Executive Leadership Institute, Bloomberg, SEC 10-K Filing, TD Cowen, Jefferies

On China and Biotech

Shanghai headquarters of Jemincare, a rapidly growing and innovative Chinese pharma company. Oct 2024

Challenges Remain in China Biotech Sector

We had the pleasure of visiting China last week and held conversations with dozens of pharma CEO's, biotech entrepreneurs and venture capital investors.

We opened every conversation with a question: what do you see happening to the Chinese biotech sector?

The answers we got back were diverse but, generally, pessimistic.

The pessimists note that the Chinese state has become substantially more interventionist since the Pandemic, has limited the ability of biotechs to go public (via the 18A process in Hong Kong) and is not providing the same level of financial support as before.

The pessimists note that very few Chinese companies are getting deals done with Western companies and that capital is dwindling fast – with the result that a large fraction of the Chinese biotech sector might be out of business in a few years.


Flowers from the Province of Yunnan

China Moving into the Biotech Big Time

Capital constrained or not, the quality of biotech portfolios in China is rising fast. China is particularly strong in platform innovations in areas like ADCs, bispecifics, GLP-1's and immunology drugs.

One Chinese VC told us that every major pharma's head of R&D has been to China at least once in the last year and that dozens of foreign R&D professionals are in the country at any given moment, visiting local biotech companies, seeking opportunities for cooperation and partnering deals. **The bottom line is that China is moving into the big time.** We count over 20 deals from Western companies in recent years where an upfront payment of $100mm or more was made for a biotech type asset. The quantity and quality of Chinese drug pipeline is exploding.

And the belief that China will never be a place where first in class innovation happens is quickly dissolving. Numerous Chinese companies are building true innovation capabilities. The next generation of younger entrepreneurs are particularly focused on first-in-class tech-heavy approaches to bioinnivation in up-and-coming places like Shenzen. As noted on the next page, there are numerous positives for the China biotech sector.

Shanghai lights up at night

Five Major Positives Underpin Growth of the China Biotech Sector

The emphasis in China is shifting from generic drugs to innovative treatments, which is driving consolidation in the generic drug market and is spurring the rise of biotech companies with strong economic prospects. We count five major long-term positives underpinning Chinese biotech.

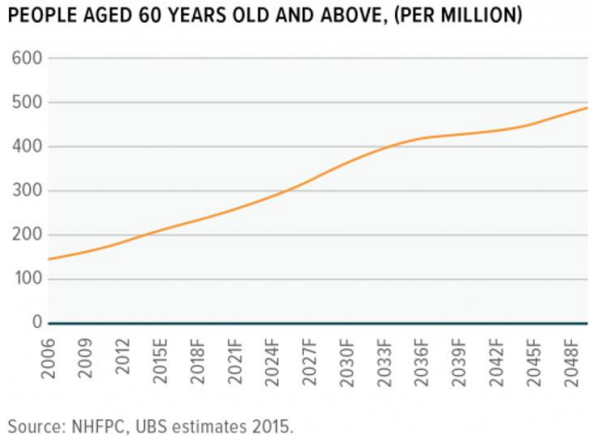
1. Many Chinese companies are mitigating these risks by developing "me-too" or "me-better" drugs, which improve upon existing therapies. Over time, the R&D focus is expected to evolve toward more innovative, first-in-class drugs.

2. The Chinese National Medical Products Administration (NMPA) is streamlining drug approval processes, making it more transparent and aligned with global standards. This encourages faster and more efficient development and approval of innovative biotech treatments.

3. China's aging population and urbanization are key factors driving the demand for advanced healthcare. By 2030, over 400 million people in China will be over 60, and increasing urbanization, coupled with rising disposable incomes, is fueling the demand for better healthcare. Intellectual property and regulatory challenges remain, but the sector is poised for growth.

4. The ability of the population to afford better healthcare is growing, with disposable incomes increasing significantly. This expanding purchasing power fuels demand for more sophisticated and innovative biotech products.

5. China's biotech sector benefits from lower operational costs for research, development, and manufacturing, attracting both domestic and international companies to develop and produce new drugs within the country.



Source: NHFPC, UBS estimates 2015.

Charts sourced from: https://www.am.miraeasset.com.hk/insight/innovation-revolution-chinese-biotech/

Just How Many Biotechs are in China Anyway?

One of the challenging things about China biotechs is that there isn't really a good database that tracks them all. Sources like EvaluatePharma aspire to it but we haven't found a good comprehensive source.

So, one of our questions to the various players we met was how many biotechs are in China? Everyone we talked agreed that there were more than 1,000 biotech companies. The consensus was that there were between 3,000 and 4,000 R&D-stage therapeutics companies.

That's a whole lot!

We had the pleasure of visiting a single biotech building in Beijing called the Zhongguancun Biotech Garden that had over 50 companies in it. If one wanders around a biotech building in San Diego, you might find five – even ten groups. But, these are high capacity units in China.

Life in the Zhongguancun Biomedical Garden

Life isn't bad at all for biotechs in the Zhongguancun Biomedical Garden. As shown at right, you get to play badminton with your mates at lunchtime. Not shown were an impressive set of ping pong tables. OK, from an appearance perspective, perhaps the place could use a little brush up from Alexandria.

But, there are central labs with all the toys you could ask for – including all the latest single cell analysis tools and pilot biologic facilities. On the other hand, those blue signs at a distance are put up by the Communist Party and exhort biotech entrepreneurs to stay true to the principles of the revolution. This comes with the territory in China.

We heard of several companies that had started there and had gone on to big things and large deals with Western companies.

Everyone we met was working hard, excited to be making a difference for patients and looking forward to the future.

Perhaps the most interesting thing about our trip was how many companies we saw had excellent pipeline. Just 18 months ago, we had the impression of way too many "me too" drugs. Another PD1? Another HER2? Really, a better TROP2 ADC? Those days are rapidly receding. We were consistently impressed by the quality of assets we saw. Some examples are shown on the next page.

Illustrative Innovation Seen from Recent China Biotech Conversations

ADCs

- Multiple trials of ADC's with better platforms and constructs
- Further very good data to be released at upcoming conferences

BCMA

- One company is pursuing BCMA CAR-t and has seen 20+ complete autoimmune disease remissions, including in myasthenia gravis

FcRn

- One Chinese biotech is not that far behind Immunovant in FcRn
- Has a fully SubQ drug that does not interfere with albumin binding on the FcRn protein – now in the clinic

VEGF x PD1

- Multiple Chinese companies chasing the Akeso/Summit ivonescimab molecule
- Most are far behind, but we met one company that has excellent data in lung cancer with over 180 subjects enrolled
- Concerns about tumor shrinkage/PFS not correlating with survival addressed well by this Chinese biotech

Incretins

- The Chinese incretins for obesity that have recently gone into Kailera from Hengrui look really good
- We visited another China player last week and got a long talk about manufacturing. This company uses *e. coli* for its GLP-1 and can drive high volumes at a low cost and thinks they can take on biosimilar semaglutide head-on with a better molecule.

Example of Innovation: LaNova Medicines Announces Initiation of Phase 1 Clinical Trial of Anti-PD-1/VEGF Bispecific Antibody LM-299 and Completion of $42 Million Series C1 Financing

SHANGHAI, Oct. 18, 2024 /PRNewswire/ -- LaNova Medicines Limited ("LaNova" or "The Company"), a privately-held clinical-stage innovation-driven biotech specializing in ADCs and immuno-oncology, announced the initiation of its Phase 1 clinical trial of LM-299, an anti-PD-1/VEGF BsAb, in China for advanced solid tumors and the successful completion of its $42 million Series C1 financing.

Founded in September 2019, LaNova's R&D engine is based on three proprietary platforms adept at tackling challenging targets and versatile modality development, which has so far enabled the in-house development of more than ten innovative programs, including monoclonal antibodies, ADCs and bispecific antibodies.

Following promising preclinical results demonstrating LM-299's strong inhibition of tumor growth in hPBMCs-humanized mice and well tolerated safety profile in NHP GLP tox study, LaNova has initiated its first-in-human clinical trial in China for advanced solid tumors. LaNova is planning to initiate an additional Phase 1 clinical trial in the US and expects to submit an IND in the second half of 2024.

The completed Series C1 financing was led by Sino Biopharmaceuticals and included participation from new investors Pudong Innovation Investment and Zhangjiang Haoheng, and existing investors, Qiming Venture Partners and Shanghai Healthcare Capital. Zhong Lun Law Firm acted as the legal advisor for this round of financing.

LaNova is a great example of a biotech company that many had never heard of two years ago. The company has a full pipeline today that has been developed with less than $40 million raised. The company is in Phase 3 with a best-in-class Claudin18.2 ADC, has a promising VEGFxPD1 bispecific and a full pipeline of first-in-class preclinical candidates. The company is developing novel approaches for conditionally activated ADC's and bispecifics as well.

Source: https://www.prnewswire.com/news-releases/lanova-medicines-announces-initiation-of-phase-1-clinical-trial-of-anti-pd-1vegf-bispecific-antibody-lm-299-and-completion-of-42-million-series-c1-financing-302280157.html

Newco Versus License

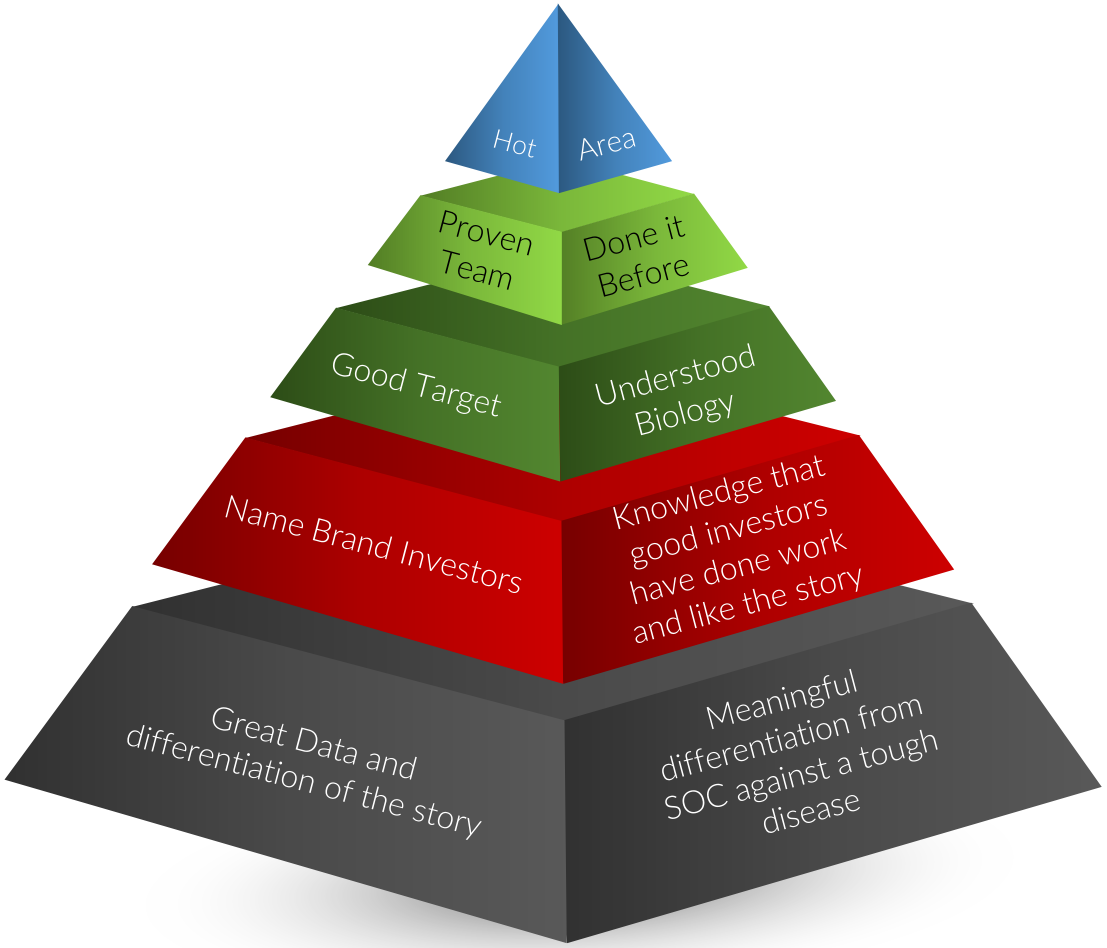
A consistent conversation with Chinese VC's and biotech CEO's surrounded the rapid growth of newcos in the U.S. ecosystem based on China assets like Kailera Therapeutics (Hengrui incretin portfolio), Summit (Akeso VEGF/PD1) or Candid Therapeutics (EpiMab TCE – and other assets).

A key question that came up was when to do a newco and when to do a license. We pointed to Hengrui's 20% stake in Kailera as likely to be worth far more than just the financial consideration offered. Newco's are prepared to pay real upfronts but usually a good global license deal will win out.

Most of the better companies we saw indicated that they were mobbed with large pharmas and U.S. VC players looking to create newcos and were realizing that they needed to be more proactive in controlling their destiny. We noted that Western companies like Pfizer and Merck Kgaa have historically played a proactive role in divestitures and have done really well with spinouts like Cerevel.

We pointed to the chart at right showing that a newco that can go public in the U.S. has to check multiple boxes that are not necessarily needed to do a license deal.

Typical Template for a U.S. Biotech IPO in 2024



Wellington's Take on What Makes for a Strong Newco IPO

Nilesh Kumar, Head of Biotech Private Investments and William Craig, Investment Director, *Institutional Investor*, October 17, 2024 (excerpt)

Key factors for a strong public listing

Every biotech IPO charts its own distinct path toward success or failure. But we believe there are certain characteristics that increase the probability of a positive public list. A few examples include:

Differentiated product pipeline – A strong product pipeline with a focus on a lead-asset that "matters." Main features of such assets can include:
• Clear evidence of a product's efficacy, safety, and market potential.
• Distinct mechanism of action and competitive edge over existing or other emerging therapies.
• Well-defined clinical development plan with realistic timelines and milestones.

Impact – Drugs that can change the existing "standard of care" or address unmet medical needs.
Experienced management team – A solid management team, with relevant expertise and track record.
Strong messaging – Communication of a clear and compelling story, with a coherent vision and strategy.
Strong and supportive investor base – A supportive, reputable, and reliable network of partners and stakeholders. This should include:
Capital, feedback, and endorsement from committed and credible investors to support companies through clinical progress and the associated inevitable delays.

Source: https://www.institutionalinvestor.com/article/2dvn6zxlxd16y3eb9x8u8/innovation/biotech-ipos-in-2025-quantity-quality-and-best-practices

Eli Lilly Expands Innovation Reach Via a Gateway Lab in China

Zoey Becker, *FierceBiotech*, October 15, 2024 (excerpt)

Eli Lilly is expanding its innovation digs to Beijing, opening two research centers called the Eli Lilly China Medical Innovation Center and Lilly Gateway Labs.

The newest Gateway Lab is the second to set up shop outside of the U.S. following a recently announced European branch planned in the U.K. The innovation incubators employ a flexible partnership model that allows researchers to lease space and take advantage of Lilly's resources and expertise during the drug development process.

So far, more than 20 biotechs have used the facilities, and more than 50 therapies are being developed at the labs, according to Lilly. The new setups in Beijing will "further deepen Eli Lilly's century-old business layout in China," Chief Scientific Officer and President of Lilly Research Laboratories Daniel Skovronsky, M.D., Ph.D., said in an Oct. 15 release.

"The new center will enable us to explore new clinical research designs to accelerate patient access to breakthrough therapies," Skovronsky added, while the Gateway Lab will "provide office space and research strategy guidance for domestic start-up biotechnology companies to help them develop a new generation of drugs for patients."

Lilly plans to register its Beijing Medical Innovation Center as an independent legal entity, according to the company. The drugmaker's work in China stretches back to 1918, when it established a Shanghai office. These days, Lilly employs more than 3,200 staffers in China.

Source: https://www.fiercebiotech.com/biotech/eli-lilly-expands-innovation-reach-another-global-gateway-lab-time-china

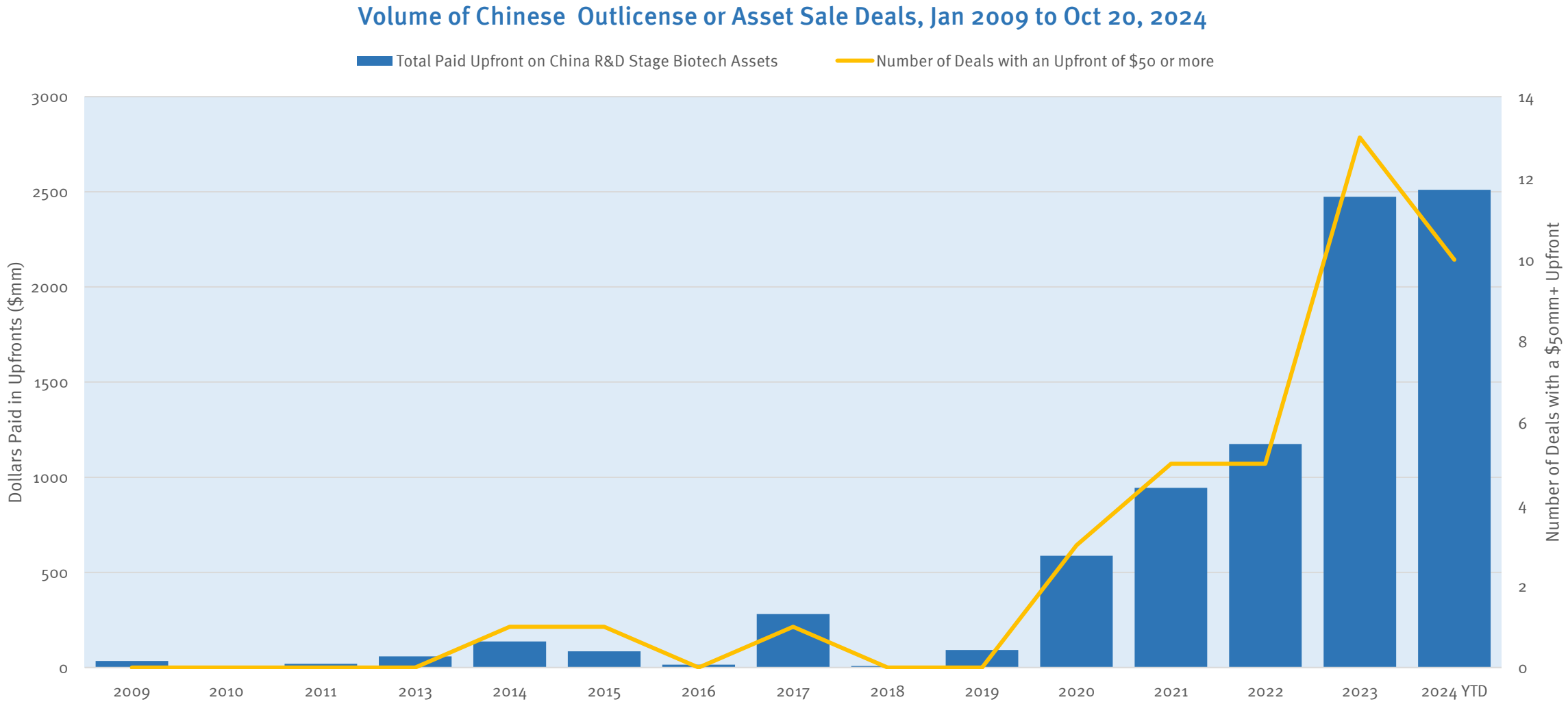
Shanghai skyline. Oct 2024

Twenty-Three Chinese Biotech Externalization Deals with an Upfront Payment of $100 Million or More

Date	Chinese Partner	Global In-Licensor	Asset	Deal Structure	Upfront Cash ($mm)	Total Deal Value ($mm)	Stage Signed
12/26/2023	Gracell Biotechnologies	AstraZeneca	CAR-t platform	Acquisition	$1,000	$1,200	Phase 1
9/30/2024	Regor Therapeutics	Roche	CDKx Platform	Asset Purchase	$850	NA	Phase 1
12/11/2023	Systimmune	BMS	EGFRxHER3 ADC	License	$800	$8,400	Phase 3
8/9/2024	Curon Biopharmaceutical	Merck	T-cell engager	Asset Purchase	$700	$1,300	Phase 1
12/5/2022	Akeso Biopharma	Summit Therapeutics	PD-1/VEGF bispecific	License	$500	$5,000	Phase 2
1/23/2023	Hutchmed	Takeda	VEGF inhibitor	License	$400	$1,130	Phase 3
12/20/2021	BeiGene	Novartis	TIGIT mAb	License	$300	$2,895	Phase 2
7/5/2017	BeiGene	BMS	PD1 mAb	License	$263	$1,393	Phase 1
8/9/2021	RemeGen	Seagen	HER2 ADC	License	$200	$2,600	Phase 2
1/7/2024	Argo Bio	Novartis	RNA tx for CV	License	$185	$4,165	Phase 1
12/20/2023	Hansoh Pharma	GSK	B7-H3 ADC	License	$185	$1,710	Phase 2
11/9/2023	Eccogene	AstraZeneca	Oral GLP1 agonist	License	$185	$2,010	Phase 1
9/4/2020	I-Mab Biopharma	AbbVie	CD47 mAb	License	$180	$1,940	Phase 1
12/22/2022	Kelun-Biotech	Merck	ADC portfolio	License	$175	$9,513	IND Ready
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
6/13/2024	Mingji Biopharm	AbbVie	TLA1 mAb	License	$150	$1,710	IND Ready
2/1/2021	Junshi Bio	Coherus	PD-1 mAb	License	$150	$845	Phase 2
10/26/2020	CStone Pharma	EQRx Inc.	EGFR inhibitor	License	$150	$1,300	Phase 2
7/12/2021	InnoCare Pharma	Biogen Inc.	BTK inhibitor	License	$125	$938	Phase 2
10/7/2024	CSPC Pharma	AstraZeneca	Oral LP(a) inhibitor	License	$100	$2,020	IND Ready
6/14/2024	Ascentage Pharma	Takeda	BCR-Abl Modulator	License Option	$100	$1,300	Phase 2
1/4/2022	3SBio	Syncromune Inc.	PD1 mAb	License	$100	$100	Phase 2

Source: DealForma and Stifel Research.

Substantial Growth in China Biotech Externalization Deals in 2023 and 2024



Source: DealForma

The Deeper Conversation: Nation-State Competition

Most Chinese CEO's and VC's that we met seemed very worried about the competition shaping up between the U.S. and China.

There was a sense that the U.S. is not welcoming China innovation that should be good for all.

The argument was that drugs invented in China should benefit patients anywhere in the world. The feeling was that the U.S., Japan and Europe have been doing most of the inventing and it's a point of pride that China should step up and do some.

But, somehow, Chinese innovation is being perceived by the West as some type of trade war that threatens livelihoods in places like the U.S.

A frequently expressed view is that China is far from threatening innovation in the U.S. An interventionist state and price controls are seen as problematic. Just as many in our industry in the U.S. are concerned about the impact of the IRA on prices with negative implications for innovation, Chinese entrepreneurs voiced similar concerns. The government is prioritizing price controls and not paying up for innovation. Multiple VC's indicated that just a little government support for innovation would go a long way and that the prices paid for results of biotech investment are key. It all sounded so familiar.

Nation-State Competition (continued)

The arguments, of course, are complex.

Some see a Chinese invasion of Taiwan as a real possibility and that reliance on Chinese CDMO's like Wuxi as a dangerous step.

This has been the motivation for the BIOSECURE Act – our biotechs should be self-reliant and not threatened by any type of "hot war" with China.

The pages that follow are meant to stimulate thought on this topic. We note (1) an article in *The Economist* last week on the importance of economic freedoms and capitalism in creating U.S. economic dominance (and the importance of the upcoming election), (2) Henry Kissinger's book *On China* which portrays China as unlikely to initiate military conflict but rather engaged in a long-term battle for economic supremacy and (3) Angus Maddison's study of long-term economic performance and its implications for life expectancy and the quality of life. Maddison notes that innovation helps to explain long-term economic performance and is associated with better life outcomes. All three of these publications seem particularly relevant at the current moment.

China is Challenging U.S. Dominance in Biotechnology

Sandra Barbosu, "How Innovative Is China in Biotechnology?," *ITIF Briefing*, July 30, 2024 (excerpt)

The United States remains the world's biotechnology leader with the highest level of new drug development. A sophisticated U.S. ecosystem, composed of national research funding sources, venture capital and private equity (VC/PE) start-up funding, large pharmaceutical firms that support life-sciences research and development (R&D), robust intellectual property (IP) protections, and strong commercialization ability have produced a globally unique environment that powerfully supports domestic biotechnology innovation. But this leadership position is at risk without a continually supportive domestic policy environment amidst robust foreign competition, particularly from China.

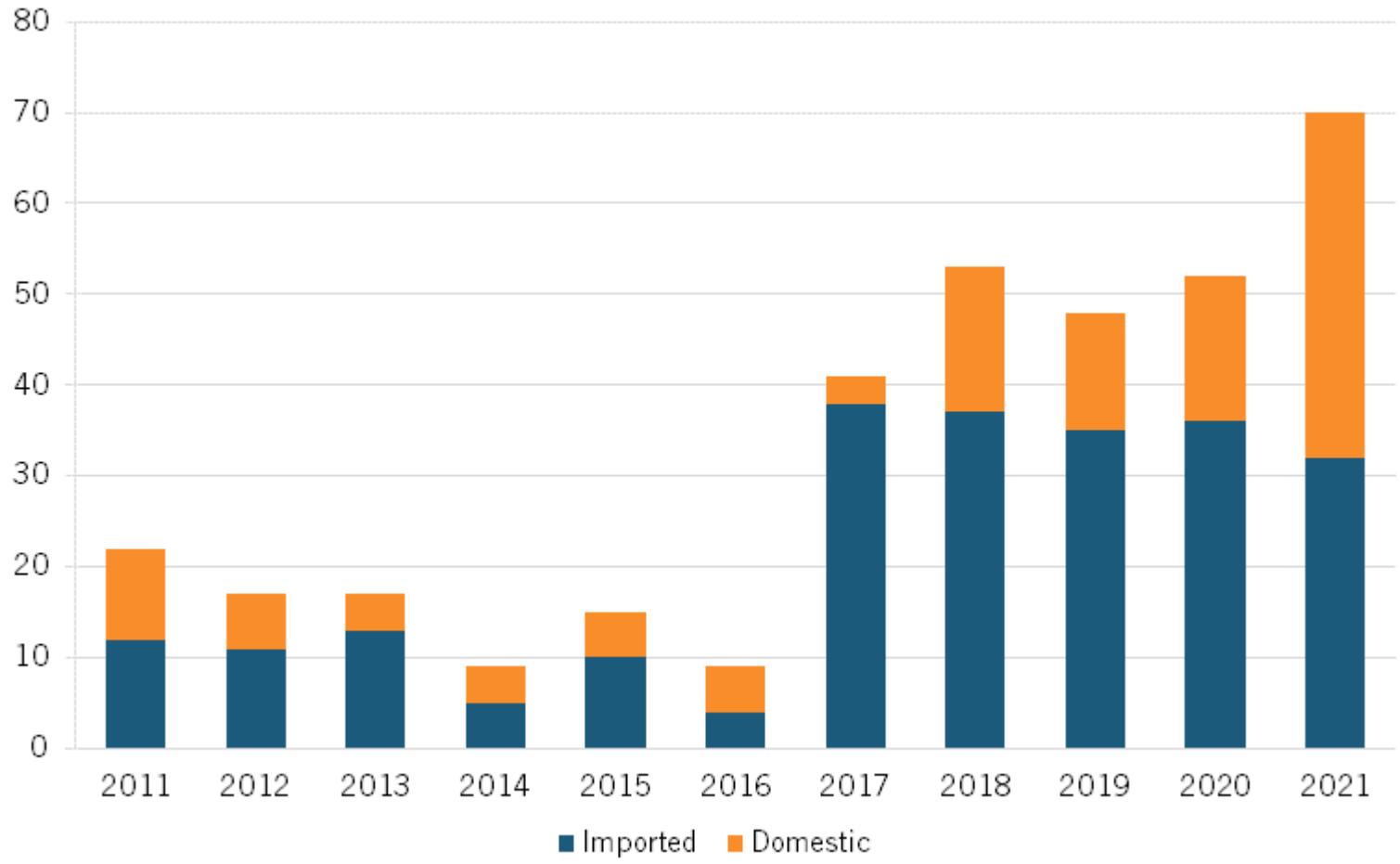
Until recently, China's playbook was to imitate the advances of industrialized countries, but since the 12th Five-Year Plan (2011–2015), the Chinese government has shifted its strategy toward incentivizing innovation, naming biotech as a strategic emerging industry and providing substantial support. In 2016, China committed itself to improving health outcomes for the Chinese population through its "Healthy China 2030" strategy, which focuses on medical innovation and improving access to drugs. More specifically, China has developed a comprehensive national strategy to enhance the innovation capabilities of its domestic biotech industry. The strategy includes subsidies; financial incentives; the initiation of national reimbursement for innovative therapies; the establishment of high-tech science parks, start-up incubators, and public-private partnerships; talent recruitment initiatives; reforms to expedite drug review, especially for domestic products; and efforts to enhance IP protection to foster innovation. China has set several milestones and goals for the industry, such as enhancing the originality of biotech through new technologies and products, creating a biotech innovation platform, and strengthening the industrialization of biotech.

Several recent indicators suggest that China's domestic biotech industry is indeed becoming more innovative. These include an uptick in the volume and quality of biotech-related scientific publications, a growing number of novel Chinese drugs approved by the U.S. Food and Drug Administration (FDA) and China's National Medical Products Administration (NMPA), an increase in out-licensing deals from small Chinese biotech companies, particularly in oncology, and a rise in clinical trials occurring in China.

Source: https://itif.org/publications/2024/07/30/how-innovative-is-china-in-biotechnology/

China Inventing More of its Own Drugs

Number of NMPA domestic and imported drug approvals in China, 2011 to 2021



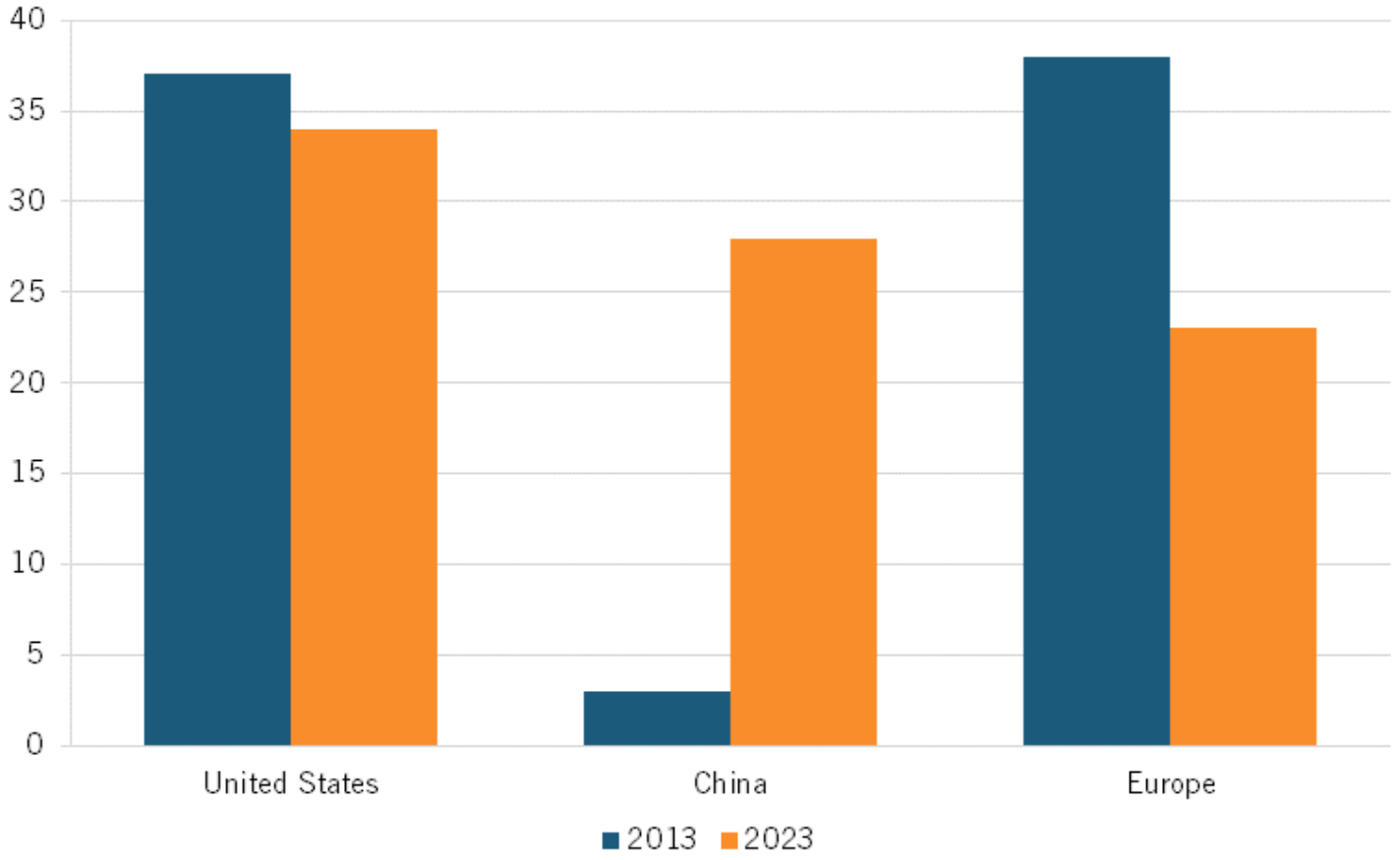
Source: https://itif.org/publications/2024/07/30/how-innovative-is-china-in-biotechnology/

In 2023, China had five first-in-class domestic drug approvals, a sign that domestic innovation is increasing. The five drugs approved were Glumetinib (Haihe Biopharma), Leritrelvir (Raynovent), Anaprazole (Xuanzhu Biopharma), Pegol-Sihematide (Hansoh Pharma), and Zuberitamab (BioRay Biopharmaceutical).

These drugs treat a range of conditions: mild or moderate COVID-19 symptoms, acid reflux, anemia in chronic kidney disease, and cancer. Also in 2023, the FDA approved three new Chinese drugs: Loqtorzi (toripalimab), the first FDA-approved drug for nasopharyngeal cancer, Fruzaqla (fruquintinib) for metastatic colorectal cancer, and Ryzneuta (efbemalenograstim) for the treatment of chemotherapy-associated neutropenia.

Chinese Clinical Trial Activity Catching Up to U.S.

Share of clinical trial starts based on company headquarters location



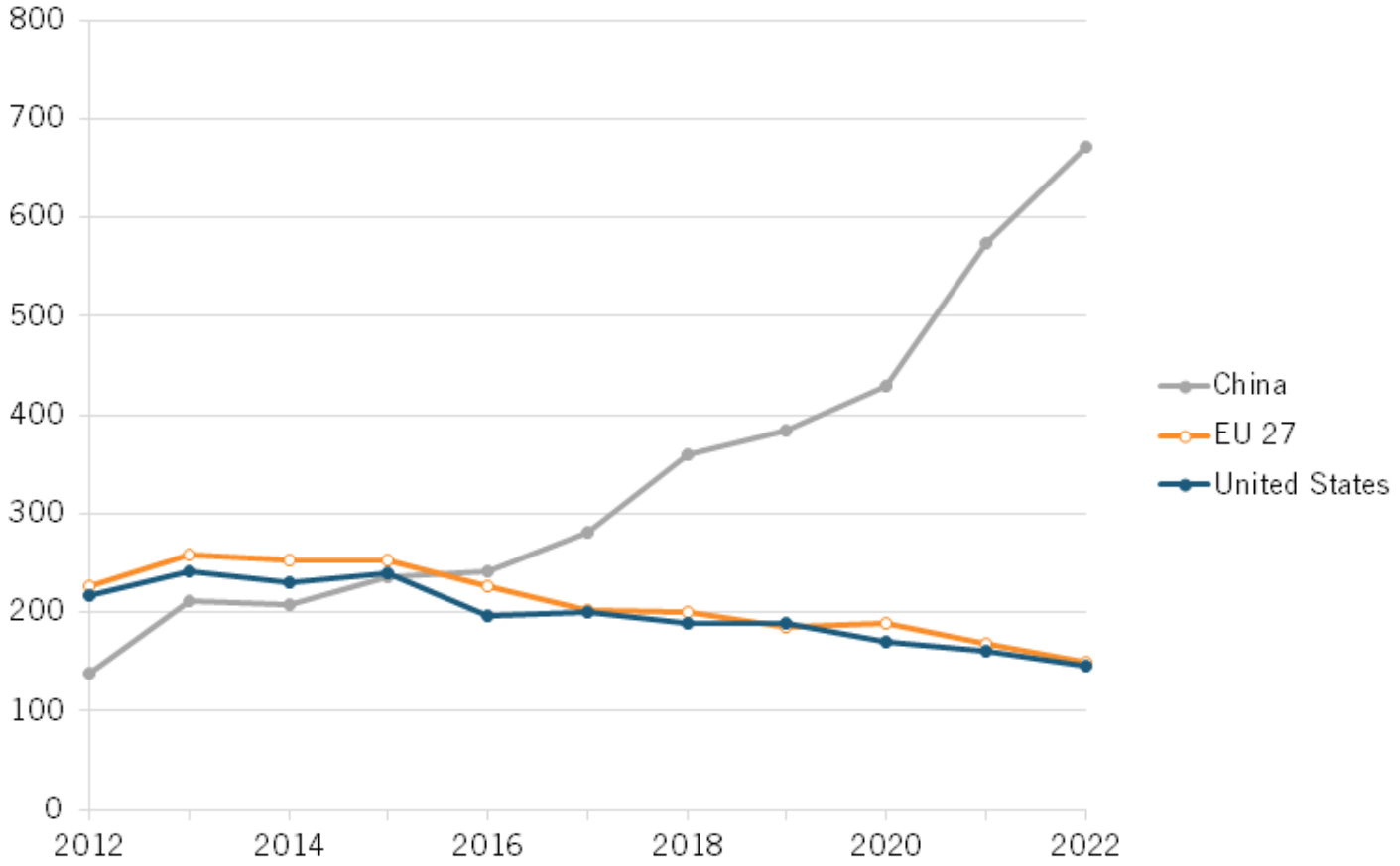
Further, a 2024 IQVIA report shows that the share of clinical trials launched by Chinese-headquartered biopharmaceutical companies rose from 3 percent in 2013 to 28 percent in 2023, suggesting a growing involvement of Chinese companies in early-phase drug development.

See chart at left.

Source: https://itif.org/publications/2024/07/30/how-innovative-is-china-in-biotechnology/

Chinese Clinical Trial Activity Catching Up to U.S.

Number of biotechnology publications in top 10 percent of most-cited publications



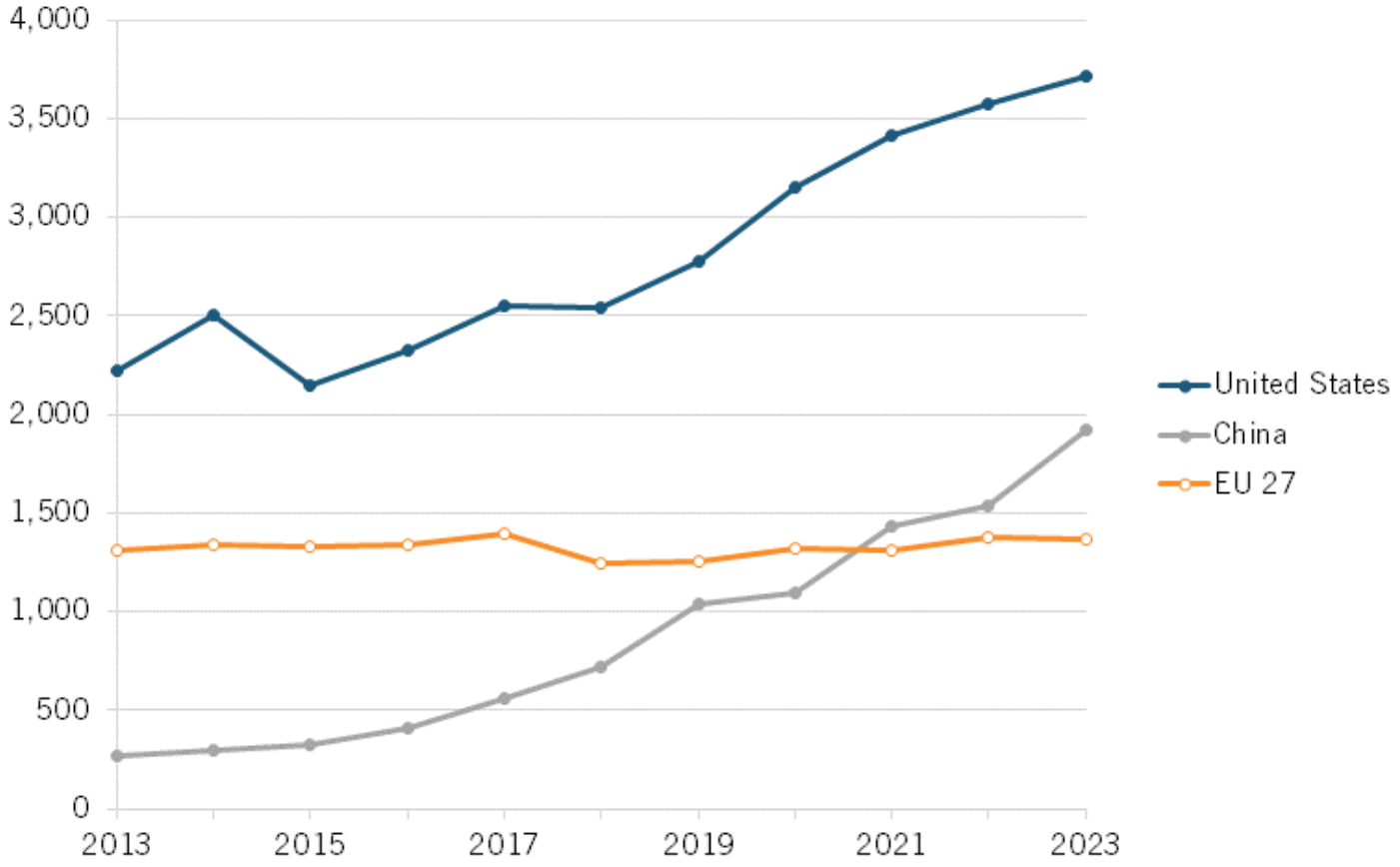
Chinese institutions are producing an increasing number of top-cited publications. In 2012, they published 139 biotech papers in the top 10 percent of most-cited publications. (See figure 10.) By 2022, that number had surged to 671 top-cited papers, an increase of more than 382 percent. Meanwhile, the number of publications from other countries has been relatively stable or slightly decreasing. In the United States, this number decreased from 218 in 2012 to 145 in 2022, a nearly 34 percent decrease.

See chart at left.

Source: https://itif.org/publications/2024/07/30/how-innovative-is-china-in-biotechnology/

Chinese Patenting Activity Catching Up to U.S.

Number of biotechnology publications in top 10 percent of most-cited publications

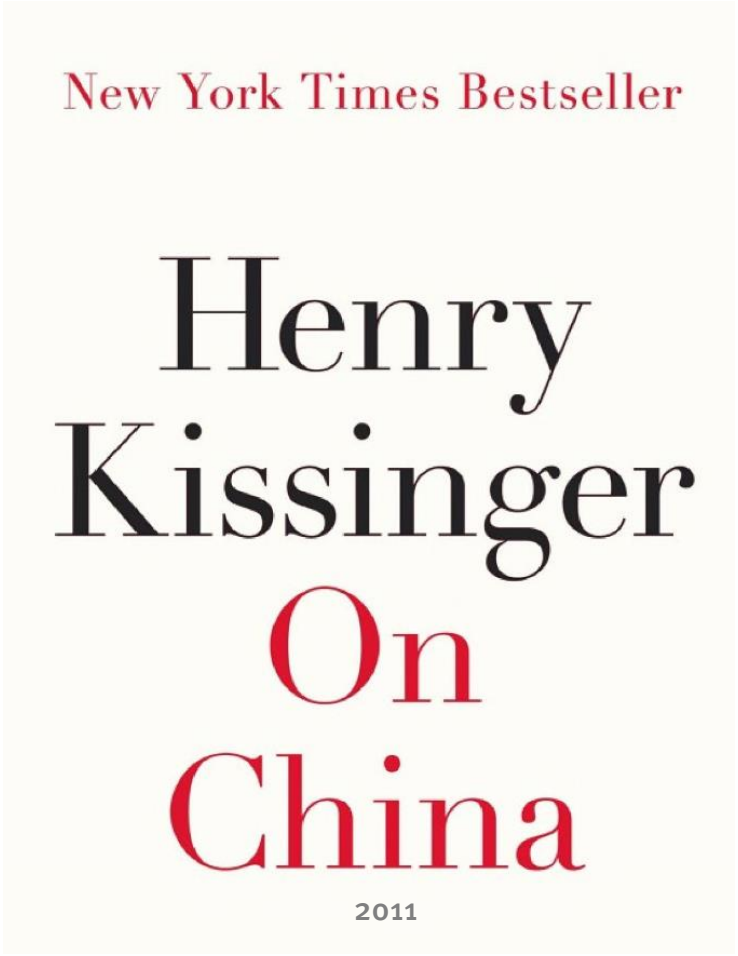


China has also made significant strides in turning its scientific publications into biotechnology patents. The Patent Cooperation Treaty (PCT), which entered force in 1978, allows innovators to seek protection for an invention simultaneously in each of a large number of countries through an “international” patent application.

From 2013 to 2023, the number of biotech PCT patents awarded to Chinese entities increased by more than 720 percent, from 266 to 1,920, exceeding the European Union’s annual number starting in 2021. While this represents a 622 percent increase (albeit from a low starting point), the number of patents awarded to U.S. filers over the same period increased by 67 percent. (See chart at left.)

Source: https://itif.org/publications/2024/07/30/how-innovative-is-china-in-biotechnology/

Henry Kissinger's Book “On China”



Source: https://en.wikipedia.org/wiki/On_China

FORTY YEARS AGO almost to the day, President Richard Nixon did me the honor of sending me to Beijing to reestablish contact with a country central to the history of Asia with which America had had no high-level contact for over twenty years. The American motive for the opening was to put before our people a vision of peace transcending the travail of the Vietnam War and the ominous vistas of the Cold War. China, though technically an ally of the Soviet Union, was in quest of maneuvering room to resist a threatened attack from Moscow.

In the interval I have been to China more than fifty times. Like many visitors over the centuries, I have come to admire the Chinese people, their endurance, their subtlety, their family sense, and the culture they represent. At the same time, all my life I have reflected on the building of peace, largely from an American perspective. I have had the good luck of being able to pursue these two strands of thinking simultaneously as a senior official, as a carrier of messages, and as a scholar.

This book is an effort, based in part on conversations with Chinese leaders, to explain the conceptual way the Chinese think about problems of peace and war and international order, and its relationship to the more pragmatic, case-by-case American approach. Different histories and cultures produce occasionally divergent conclusions. I do not always agree with the Chinese perspective, nor will every reader. But it is necessary to understand it, since China will play such a big role in the world that is emerging in the twenty-first century.

China avoids all-or-nothing war

Chinese *Realpolitik* and Sun Tzu's *Art of War*

The Chinese have been shrewd practitioners of *Realpolitik* and students of a strategic doctrine distinctly different from the strategy and diplomacy that found favor in the West. A turbulent history has taught Chinese leaders that not every problem has a solution and that too great an emphasis on total mastery over specific events could upset the harmony of the universe. There were too many potential enemies for the empire ever to live in total security. If China's fate was relative security, it also implied relative insecurity—the need to learn the grammar of over a dozen neighboring states with significantly different histories and aspirations. Rarely did Chinese statesmen risk the outcome of a conflict on a single all-or-nothing clash; elaborate multiyear maneuvers were closer to their style. Where the Western tradition prized the decisive clash of forces emphasizing feats of heroism, the Chinese ideal stressed subtlety, indirection, and the patient accumulation of relative advantage.

China sees itself as the central civilization

China's splendid isolation nurtured a particular Chinese self-perception. Chinese elites grew accustomed to the notion that China was unique—not just “a great civilization” among others, but civilization itself. A British translator wrote in 1850:

> An intelligent European, accustomed to reflect on the state of a number of countries enjoying a variety of different advantages, and laboring each under peculiar disadvantages, could, by a few well directed questions, and from very little data, form a tolerably correct notion of the state of a people hitherto unknown to him; but it would be a great error to suppose that this is the case with the Chinese. Their exclusion of foreigners and confinement to their own country has, by depriving them of all opportunities of making comparisons, sadly circumscribed their ideas; they are thus totally unable to free themselves from the dominion of association, and judge everything by rules of purely Chinese convention.[8]

Quotes from Kissinger's Book

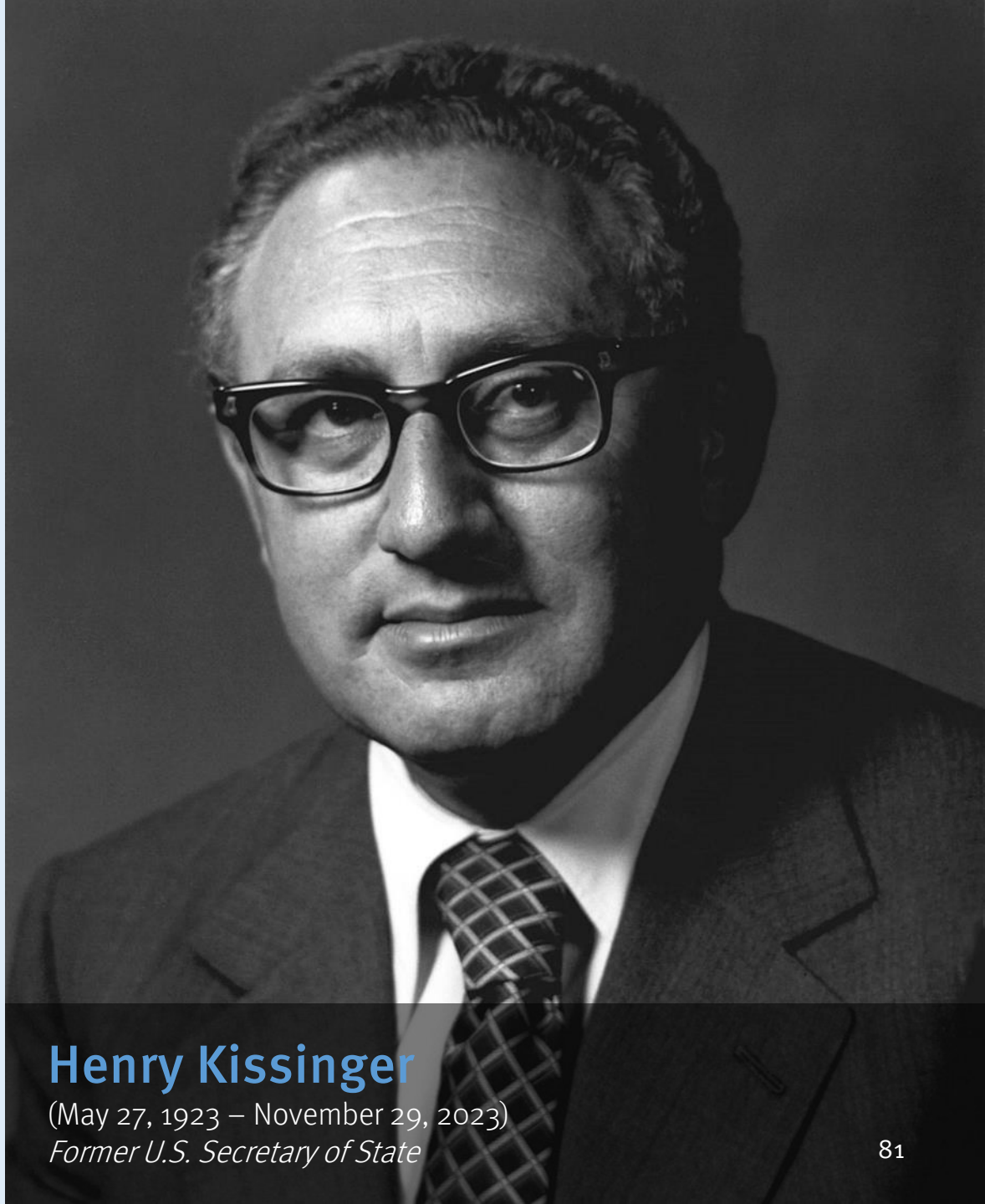
"China is a civilization pretending to be a nation."
China's perspective on international relations is deeply rooted in its ancient civilization, which spans millennia, not just its modern history as a nation-state.

"In the Chinese language, the term for crisis consists of two characters: one representing danger, the other, opportunity."
Kissinger highlights the Chinese perception of crisis, emphasizing the duality of danger and opportunity within difficult situations.

"For China, the game never ends."
China plays a long game, seeing strategy and foreign policy as continuous, without an end.

"The problem with China is not how to work with it or how to confront it; the problem is how to both confront and work with it at the same time."
Kissinger highlights the need for a dual strategy that involves cooperation in some areas while standing firm on disagreements in others.

"For centuries, China rarely expanded by conquest; instead, it influenced by osmosis."
Kissinger notes China's historical tendency to extend influence not by military force, but through culture, diplomacy, and economic ties.



Henry Kissinger
(May 27, 1923 – November 29, 2023)
Former U.S. Secretary of State

America's Economy is Bigger and Better than Ever

Will politics bring it back to Earth?

***The Economist*, Oct. 17, 2024 (excerpt)**

Few sights have better captured America's world-beating ingenuity. On October 13th a giant booster rocket built by SpaceX hurtled to the edge of the atmosphere before plunging back to Earth and being neatly caught by the gantry tower from which, only minutes earlier, it had taken off. Thanks to this marvel of engineering, big rockets could become reusable and space exploration cheaper and bolder. Yet, just as the launch was a testimony to American enterprise, so Elon Musk, SpaceX's founder, captures all that is going wrong with its politics. In his support for Donald Trump, Mr Musk has spread misinformation about voter fraud and hurricane relief and derided his opponents as ill-intentioned idiots.

America, too, continues to rack up a stellar economic performance even as its politics gets more poisonous. As they prepare to go to the polls in fewer than 20 days' time, Republicans and Democrats have never mistrusted or disagreed with each other more. Against that gloomy backdrop, can America's breathtaking economy possibly stay aloft?

Source: https://www.economist.com/leaders/2024/10/17/americas-economy-is-bigger-and-better-than-ever

Over the past three decades America has left the rest of the rich world in the dust. In 1990 it accounted for about two-fifths of the GDP of the G7. Today it makes up half. Output per person is now about 30% higher than in western Europe and Canada, and 60% higher than in Japan—gaps that have roughly doubled since 1990. Mississippi may be America's poorest state, but its hard-working residents earn, on average, more than Brits, Canadians or Germans. Lately, China too has gone backwards. Having closed in rapidly on America in the years before the pandemic, its nominal GDP has slipped from about three-quarters of America's in 2021 to two-thirds today.

This record is now in jeopardy. As America has become more partisan, both Kamala Harris and Mr Trump, the two presidential candidates, are focusing on policies that protect their own supporters, rather than expanding the overall economic pie. America is not about to lose its economic dominance. But, sooner or later, rotten politics will start to exact a heavy price, and by then it will be hard to reverse course.

Yet good policy has been important, too. America has long married light-touch regulation with speedy and generous spending when a crisis hits. Although supersized stimulus during the pandemic fuelled inflation, it has also ensured that America has grown by 10% since 2020, three times the pace of the rest of the G7. By contrast, stingier Germany is mired in recession for a second consecutive year.

The U.S. Economy is Vulnerable to Tariffs and High Budget Deficits

***The Economist*, Oct. 17, 2024 (continued)**

So far, America's worsening politics have had little visible effect on the economy. Over the past eight years Mr Trump and President Joe Biden have reached for protectionism and interventionism, in the name of helping factory workers, at the expense of the wider economy. Because America's economic strength has been so broad-based, it has not been overturned; and for many years stimulus has provided an offsetting sugar rush. Yet the economy is not immune from politics. And as the country grows more divided, Ms Harris and Mr Trump are promising ever more damaging policies—Mr Trump especially.

For a start, both candidates would tamper with the market forces that have served America so well, by protecting some companies at the expense of others. They could also limit the government's scope to swoop to the rescue next time a crisis hits. Both promise tax and spending giveaways—Ms Harris wants to spend more on families; Mr Trump to offer tax relief on everything from car loans to overtime work. Yet neither has a plan to rein in the budget deficit, which is running at around 6% of gdp, a level usually seen only during wartime or recession. Unchecked deficit spending could crowd out private investment and erode faith in American debt as a risk-free asset.

Mr Trump poses the bigger risk to America's extraordinary economy. He speaks of imposing ruinous tariffs on imports and embarking on huge programmes to deport millions of non-citizens, many of whom have been fully integrated into the labour market for years. He is cavalier about institutions, including the Federal Reserve and the rule of law. Should the independence of either be undermined, America would no longer attract the talent and money it needs to keep pushing relentlessly ahead. Nobody knows if Mr Trump means what he says, but the chance that he does hangs heavily over his candidacy, like Mr Musk's rocket over the launch pad.

Source: https://www.economist.com/leaders/2024/10/17/americas-economy-is-bigger-and-better-than-ever

Innovation is a Long-Term Driver of GDP Growth and Life Span

Angus Maddison's Essay on Long-Term Economic Performance

Angus Maddison, *Growth and Interaction in the Modern Economy*, 2005 (excerpt)

"There were … major intellectual and institutional changes in the West before 1820 that had a fundamental impact on economic performance and that had no counterpart in other parts of the world in this period. A fundamental change was the recognition of human capacity to transform the forces of nature through rational investigation and experiment. The first European university was created in Bologna in 1080. By 1500, there were seventy such centers of secular learning in Western Europe (see Goodman and Russell 1991, 25). Until the mid-fifteenth century, most of the teaching was verbal, and the learning process was similar to that in ancient Greece. Things changed after Gutenberg printed his first book in Mainz in 1455. Further changes in intellectual horizons occurred between the sixteenth and seventeenth centuries, when medieval notions of an earth-centered universe were abandoned. Thanks to the Renaissance, the seventeenth century scientific revolution, and the eighteenth-century enlightenment, Western elites gradually abandoned superstition, magic, and submission to religious authority. The scientific approach gradually impregnated the educational system. Circumscribed intellectual horizons were abandoned. A Promethean quest for progress was unleashed. The impact of science was reinforced by the creation of scientific academies and observatories which inaugurated empirical research and experiment."

Source: https://www.aei.org/wp-content/uploads/2017/02/Growth-and-Interaction-in-the-World-Economy.pdf

TABLE 1
LIFE EXPECTANCY, 1000–2002
(years at birth for both sexes combined)

	World	West	Rest
1000	24	24	24
1820	26	36	24
1900	31	46	26
1950	49	66	44
2002	66	79	64

SOURCE: Maddison (2001, 31), updated.

Maddison: "Over the past millennium, world population rose 23-fold, per capita income 14-fold, and GDP more than 300-fold. This contrasts sharply with the preceding millennium, when world population grew by only a sixth, with no advance in per-capita income. From 1000 to 1820, growth was predominantly extensive.

Most of the GDP increase went to accommodate a fourfold increase in population. The advance in per-capita income was a slow crawl—the world average increased only by half over a period of eight centuries.

In the year 1000, the average infant could expect to live about twenty-four years (see table 1). A third would die in the first year of life. Hunger and epidemic disease would ravage the survivors.

By 1820, life expectancy had risen to thirty-six years in the West, with no improvement elsewhere. After 1820, world development became much more dynamic. By 2001, income per head had risen ninefold, population nearly sixfold. Per-capita income rose by 1.2 percent a year, twenty-four times as fast as in 1000–1820. Population grew about 1 percent a year, six times as fast as in 1000–1820. Life expectancy increased to seventy-nine years in the West and sixty-four in the rest of the world."

Disclosure

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