Biopharma Market Update

April 28, 2025

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2024 Biotech Mid-Year Outlook

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Why Invest in Biotech?

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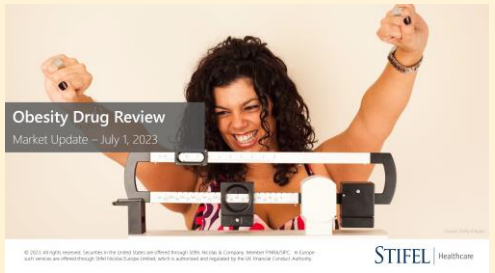
Obesity Drug Review



[July 1, 2023]

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All Eyes on Washington DC

“Liberation Day” Was Just Four Weeks Ago

It seems like an eternity has gone by since President Donald J. Trump announced unprecedentedly high tariffs on “Liberation Day”. But, in fact, it’s been only four weeks since the fateful announcement on the Rose Garden Lawn (April 2, 2025).

What transpired was a violent negative market reaction, leading many observers to worry that an economic depression was imminent.

Importantly, China countered Trump’s tariffs with reciprocal actions.

The “Liberation Day” actions coincided with a launch of threatened federal funding cuts against Harvard University. On April 11th, Harvard received a letter (see next page) that went well beyond prior insistence that it take steps to address anti-semitism with a threat to cut off all funding unless highly intrusive steps be taken to improve viewpoint diversity and the like.

Because Harvard receives very large amounts of NIH funding for medical research this action had potentially significant implications for the biotech industry.

This has all coincided with significant concern in the American populace about the story of an apparently wrongly deported man.

Letter Sent to Harvard University on April 11th

April 11, 2025

Dr. Alan M. Garber
President
Harvard University
Office of the President
Massachusetts Hall
Cambridge, MA 02138

Penny Pritzker
Lead Member, Harvard Corporation
Harvard Corporation
Massachusetts Hall
Cambridge, MA 02138

Dear Dr. Garber:

The United States has invested in Harvard University's operations because of the value to the country of scholarly discovery and academic excellence. But an investment is not an entitlement. It depends on Harvard upholding federal civil rights laws, and it only makes sense if Harvard fosters the kind of environment that produces intellectual creativity and scholarly rigor, both of which are antithetical to ideological capture.

Harvard has in recent years failed to live up to both the intellectual and civil rights conditions that justify federal investment. But we appreciate your expression of commitment to repairing those failures and welcome your collaboration in restoring the University to its promise. We therefore present the below provisions as the basis for an agreement in principle that will maintain Harvard's financial relationship with the federal government.

If acceptable to Harvard, this document will constitute an agreement in principle, which the parties will work in good faith to translate into a more thorough, binding settlement agreement. As you will see, this letter incorporates and supersedes the terms of the federal government's prior letter of April 3, 2025.

- **Governance and leadership reforms.** By August 2025, Harvard must make meaningful governance reform and restructuring to make possible major change consistent with this letter, including: fostering clear lines of authority and accountability; empowering tenured professors and senior leadership, and, from among the tenured professoriate and senior leadership, exclusively those most devoted to the scholarly mission of the University and committed to the changes indicated in this letter; reducing the power held by students and untenured faculty; reducing the power held by faculty (whether tenured or untenured) and administrators more committed to activism than scholarship; and reducing forms of governance bloat, duplication, or decentralization that interfere with the possibility of the reforms indicated in this letter.

- **Merit-Based Hiring Reform**. By August 2025, the University must adopt and implement merit-based hiring policies, and cease all preferences based on race, color, religion, sex, or national origin throughout its hiring, promotion, compensation, and related practices among faculty, staff, and leadership. Such adoption and implementation must be durable and demonstrated through structural and personnel changes. All existing and prospective faculty shall be reviewed for plagiarism and Harvard's plagiarism policy consistently enforced. All hiring and related data shall be shared with the federal government and subjected to a comprehensive audit by the federal government during the period in which reforms are being implemented, which shall be at least until the end of 2028.

- **Merit-Based Admissions Reform**. By August 2025, the University must adopt and implement merit-based admissions policies and cease all preferences based on race, color, national origin, or proxies thereof, throughout its undergraduate program, each graduate program individually, each of its professional schools, and other programs. Such adoption and implementation must be durable and demonstrated through structural and personnel changes. All admissions data shall be shared with the federal government and subjected to a comprehensive audit by the federal government—and non-individualized, statistical information regarding admissions shall be made available to the public, including information about rejected and admitted students broken down by race, color, national origin, grade point average, and performance on standardized tests—during the period in which reforms are being implemented, which shall be at least until the end of 2028. During this same period, the dean of admissions for each program or school must sign a public statement after each admissions cycle certifying that these rules have been upheld.

- **International Admissions Reform**. By August 2025, the University must reform its recruitment, screening, and admissions of international students to prevent admitting students hostile to the American values and institutions inscribed in the U.S. Constitution and Declaration of Independence, including students supportive of terrorism or anti-Semitism. Harvard will immediately report to federal authorities, including the Department of Homeland Security and State Department, any foreign student, including those on visas and with green cards, who commits a conduct violation. As above, these reforms must be durable and demonstrated through structural and personnel changes; comprehensive throughout all of Harvard's programs; and, during the reform period, shared with the federal government for audit, shared on a non-individualized basis with the public, and certified by deans of admissions.

- **Viewpoint Diversity in Admissions and Hiring**. By August 2025, the University shall commission an external party, which shall satisfy the federal government as to its competence and good faith, to audit the student body, faculty, staff, and leadership for viewpoint diversity, such that each department, field, or teaching unit must be individually viewpoint diverse. This audit shall begin no later than the summer of 2025 and shall proceed on a department-by-department, field-by-field, or teaching-unit-by-teaching-unit basis as appropriate. The report of the external party shall be submitted to University leadership and the federal government no later than the end of 2025. Harvard must abolish all criteria, preferences, and practices, whether mandatory or optional, throughout its admissions and hiring practices, that function as ideological litmus tests. Every department or field found to lack viewpoint diversity must be reformed by hiring a critical mass of new faculty within that department or field who will provide viewpoint diversity; every teaching unit found to lack viewpoint diversity must be reformed by admitting a critical mass of students who will provide viewpoint diversity. If the review finds that the existing faculty in the relevant department or field are not capable of hiring for viewpoint diversity, or that the relevant teaching unit is not capable of admitting a critical mass of students with diverse viewpoints, hiring or admissions within that department, field, or teaching unit shall be transferred to the closest cognate department, field, or teaching unit that is capable of achieving viewpoint diversity. This audit shall be performed and the same steps taken to establish viewpoint diversity every year during the period in which reforms are being implemented, which shall be at least until the end of 2028.

- **Reforming Programs with Egregious Records of Antisemitism or Other Bias.** By August 2025, the University shall commission an external party, which shall satisfy the federal government as to its competence and good faith, to audit those programs and departments that most fuel antisemitic harassment or reflect ideological capture.
  - The programs, schools, and centers of concern include but are not limited to the Divinity School, Graduate School of Education, School of Public Health, Medical School, Religion and Public Life Program, FXB Center for Health & Human Rights, Center for Middle Eastern Studies, Carr Center for Human Rights at the Harvard Kennedy School, Department of Near Eastern Languages and Cultures, and the Harvard Law School International Human Rights Clinic.
  - The report of the external party shall include information as to individual faculty members who discriminated against Jewish or Israeli students or incited students to violate Harvard's rules following October 7, and the University and federal government will cooperate to determine appropriate sanctions for those faculty members within the bounds of academic freedom and the First Amendment.
  - The report of the external party shall be submitted to University leadership and the federal government no later than the end of 2025 and reforms undertaken to repair the problems. This audit shall be performed and the same steps taken to make repairs every year during the period in which reforms are being implemented, which shall be at least until the end of 2028.

- **Discontinuation of DEI**. The University must immediately shutter all diversity, equity, and inclusion (DEI) programs, offices, committees, positions, and initiatives, under whatever name, and stop all DEI-based policies, including DEI-based disciplinary or speech control policies, under whatever name; demonstrate that it has done so to the satisfaction of the federal government; and demonstrate to the satisfaction of the federal government that these reforms are durable and effective through structural and personnel changes. By August

- **Transparency and Monitoring**. The University shall make organizational changes to ensure full transparency and cooperation with all federal regulators. No later than June 30, 2025, and every quarter thereafter during the period in which reforms are being implemented, which shall be at least until the end of 2028, the University shall submit to the federal government a report—certified for accuracy—that documents its progress on the implementation of the reforms detailed in this letter. The University must also, to the satisfaction of the federal government, disclose the source and purpose of all foreign funds; cooperate with the federal government in a forensic audit of foreign funding sources and uses, including how that money was used by Harvard, its agents, and, to the extent available, third parties acting on Harvard's campus; report all requested immigration and related information to the United States Department of Homeland Security; and comply with all requirements relating to the SEVIS system.

We expect your immediate cooperation in implementing these critical reforms that will enable Harvard to return to its original mission of innovative research and academic excellence.

Sincerely,

Josh Gruenbaum
Comm'r of the Fed. Acquisition Serv.
General Services Administration

Sean R. Keveney
Acting General Counsel
U.S. Dep't Health & Human Servs.

Thomas E. Wheeler
Acting General Counsel
U.S. Dept. of Education

...

Highly Intrusive

Two Fateful Weeks in April

The imposition of tariffs and attack on Harvard University coincided with a behind the scenes conversation with the pharmaceutical industry about taking steps to bring more jobs home to the United States and to narrow international price differentials from those in the United States.

And, to make matters even more interesting, we learned on April 1st (called the "April Fool's Firings") that the FDA would let go many thousands of staffers.

This followed visits to the FDA from members of the Department of Government Efficiency (DOGE) and requests from DOGE to thousands of MD's at the FDA that they submit the five things that they did that week to DOGE. Oh, and by the way, show up at the office five days a weeks as well.

The day after these firings it emerged that Elon Musk would be leaving DOGE. Tesla stock had been cut in half since the election.

Senior FDA staffers began to resign *en masse* (fired or not) and the well-respected Peter Marks stepped down from his role leading CBER on March 28th. In his resignation letter, Marks wrote: "As you are aware, I was willing to work to address the Secretary's concerns regarding vaccine safety and transparency by hearing from the public and implementing a variety of different public meetings and engagements with the National Academy of Sciences, Engineering, and Medicine. However, it has become clear that truth and transparency are not desired by the Secretary, but rather he wishes subservient confirmation of his misinformation and lies."

To say the least, the two weeks following March 28th were not good one for the biotech market. The XBI went from 84.1 on Friday, March 28th to 66.5 in intraday trading on April 8th.

The S&P 500 plummeted at the same time as U.S. equity values dropped four trillion dollars in just ten days. And then the value of U.S. Treasury bonds started to drop rather precipitously.

“Shock and Awe” Tactics Fizzle

In the afternoon of April 9th, President Trump announced that tariffs would be delayed for 90 days for all nations except China.

Then, in the next weeks, after it emerged that Harvard was going to fight hard against the Trump Administration, indicating that it would be happy to end up in the Supreme Court (where, interestingly, a majority of justices either graduated from Harvard University or formerly taught there). Unnamed sources in the Administration distanced themselves from the Harvard letter, indicating that Harvard should have known that the letter was sent *by mistake*.

And now we are hearing that FDA staffers are no longer required to show up five days a week in the office and that the FDA plans to substantially increase the pace of drug approvals, particularly for rare disease.

The conversation about China tariffs has been particularly interesting. Chinese financial markets have done really well since the tariffs were announced and, puzzlingly, Trump has unilaterally *lowered* tariffs on China.

What is odd about this is that the Chinese apparently refuse to meet with the Administration despite claims from Washington that there is dialogue underway. It’s not at all obvious that the U.S. has a winning hand with China.

Importantly, we have not seen *new* broadsides launched against allies, industry or academia in the last two weeks. We are reminded of how quickly past revolutionaries (think Robespierre, Trotsky or Cromwell) faded from the scene.

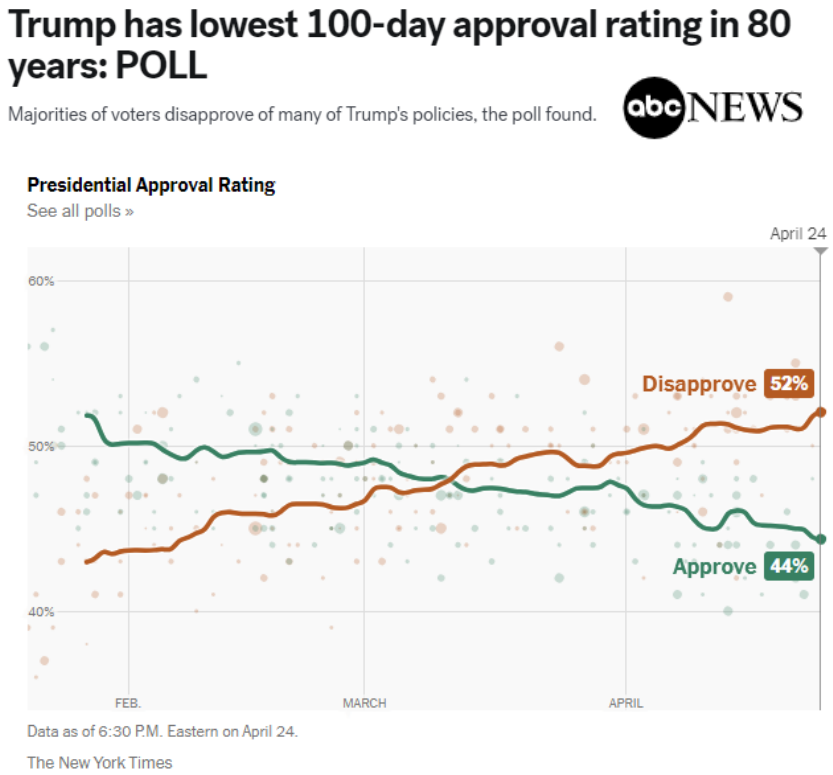
Something very fundamental appears to have changed in the White House in recent weeks. It appears that the Trump 2.0 “Shock and Awe” campaign seems to have fizzled.

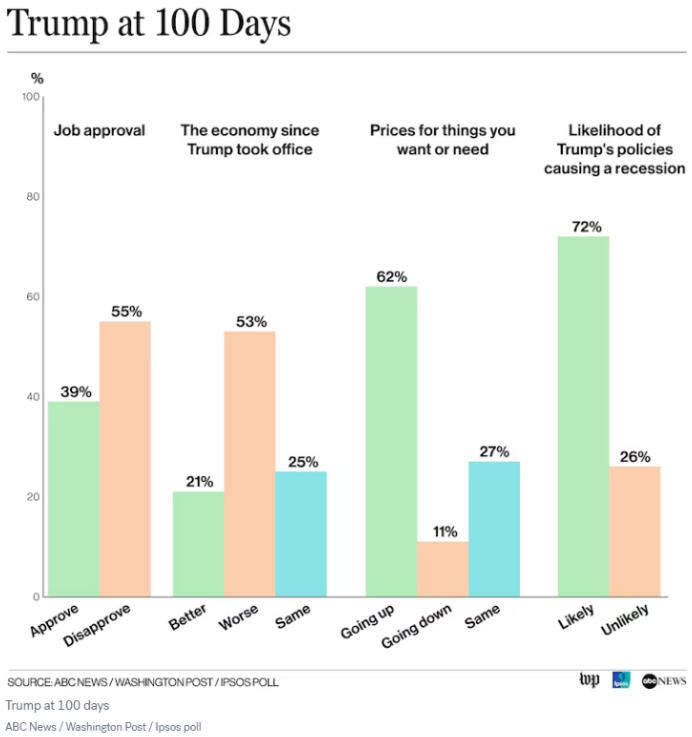
The question is why.

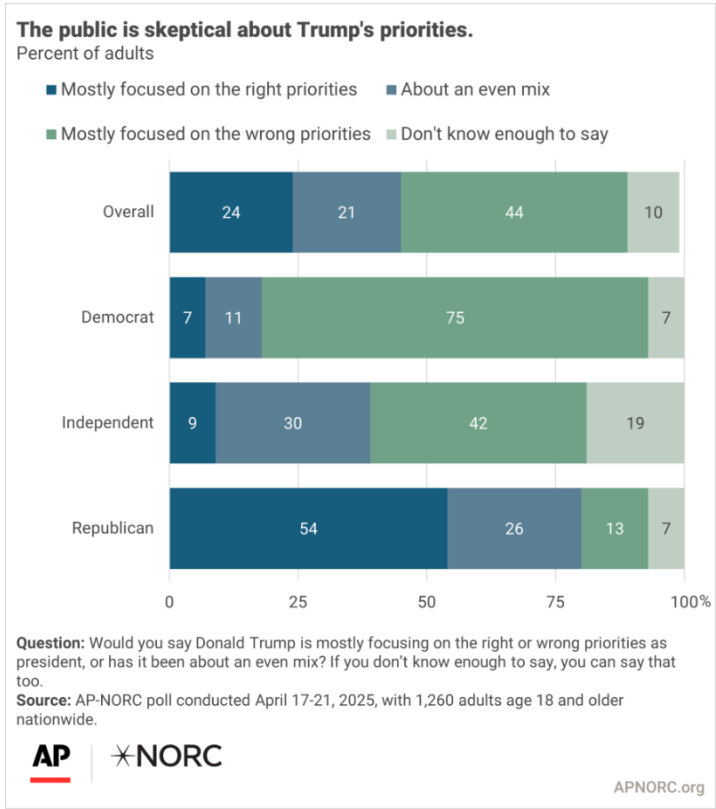
Trump’s Shock and Awe Campaign Shook Up Financial Markets Badly in the First Half of April

Trump Support from Republicans & Independents Weakens

The story behinds the Administration's shift in emphasis appears related to dropping popularity with voters. Roughly three fourths of U.S. voters disapproved of Trump's policies, and his overall approval rating has dropped substantially since his inauguration. Almost half of Republicans did not indicate that Trump is "mostly focused on the right priorities" in a recent AP-NORC poll. Importantly, a large majority of Americans believe that Trump's tariff policies will be inflationary and talk of a resounding defeat in upcoming congressional elections started to spread in second week of April. Independents who make up a large amount of the U.S. electorate supported Trump in last year's election but largely disapprove of his actions overall. Trump has quite low approval ratings for this point in his presidency compared to other presidents in the past and appears to be dialing back some of his less liked policies.







Sources: https://www.nytimes.com/2025/04/23/us/politics/trump-approval-rating.html, https://apnorc.org/projects/100-days-in-and-the-public-feels-trumps-presidency-is-proceeding-mostly-as-expected/, https://abcnews.go.com/Politics/trump-lowest-100-day-approval-rating-80-years/story?id=121165473

Unpopular Presidential Policies Tend to Disappear Quickly

George W. Bush — Privatization of Social Security (2005)

After winning reelection, Bush pushed for partly privatizing Social Security, letting workers invest some of their payroll taxes in private accounts. It was deeply unpopular (especially with older voters), met bipartisan resistance, and died quietly by 2006.

Woodrow Wilson — League of Nations Membership (1919–1920)

After World War I, Wilson's top goal was to join the League of Nations. It faced huge opposition in the U.S. Senate (especially from isolationists and Republicans).The U.S. never joined, despite Wilson basically staking his presidency on it.

Barack Obama — “Cadillac Tax” on Health Insurance (Affordable Care Act, 2010)

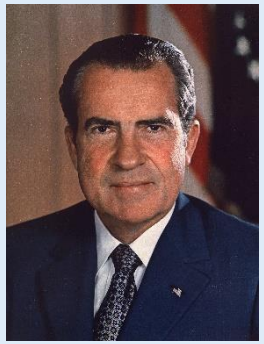
As part of Obamacare, there was a tax planned on high-cost employer health plans (nicknamed the "Cadillac Tax"). It was hated by labor unions and businesses. Although technically law for years, it was repeatedly delayed and finally repealed in 2019, before it ever went into effect.

Donald J. Trump — Family Separation Policy (2018)

Trump's administration implemented a "zero tolerance" immigration policy that led to family separations at the border. It provoked a massive public outcry, even from conservatives. Trump signed an executive order ending it after just a few months.

Herbert Hoover — Smoot-Hawley Tariff (1930)

Hoover signed a huge tariff increase on thousands of imports, intending to protect American industries. It was hugely unpopular internationally, worsened the Great Depression, and was reversed by later trade agreements (like FDR’s Reciprocal Trade Agreements Act of 1934).



Richard Nixon — Wage and Price Controls (1971–1973)

Nixon froze wages and prices to fight inflation, something usually considered un-Republican. It was initially popular but quickly unraveled, causing distortions and shortages. The policy collapsed by 1974, with most controls phased out or repealed.

On Major Economic Decisions, Trump Blinks, and Then Blinks Again

David Sanger, *New York Times*, April 23, 2025 (excerpt)

After weeks of bluster and escalation, President Trump blinked. Then he blinked again. And again.

He backed off his threat to fire the Federal Reserve chairman. His Treasury secretary, acutely aware that the S&P 500 was down 10 percent since Mr. Trump was inaugurated, signaled he was looking for an offramp to avoid an intensifying trade war with China.

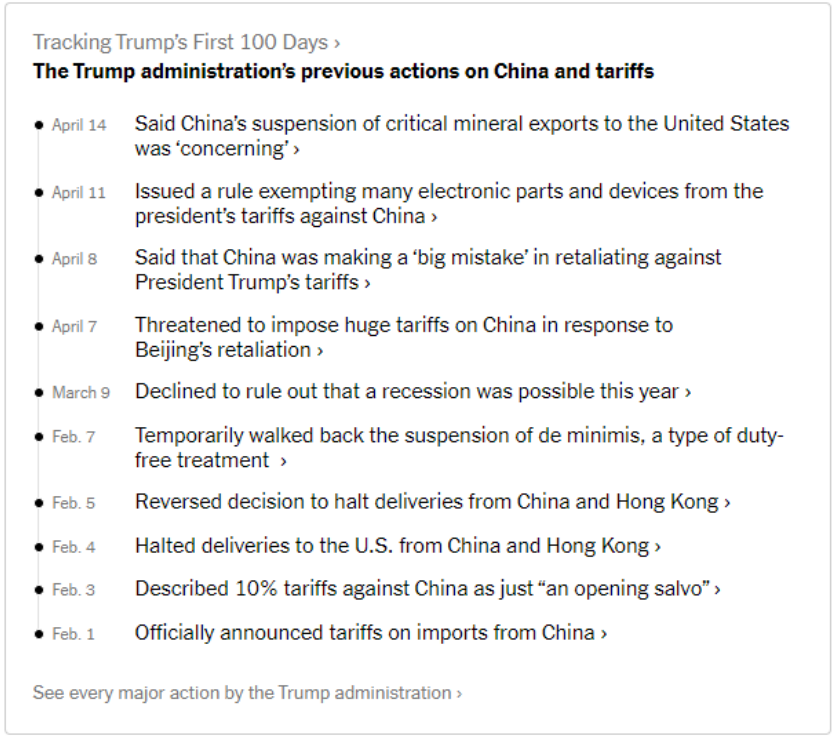
And now Mr. Trump has acknowledged that the 145 percent tariffs on Chinese goods that he announced just two weeks ago are not sustainable. He was prompted in part by the warnings of senior executives from Target and Walmart and other large American retailers that consumers would see price surges and empty shelves for some imported goods within a few weeks.

Mr. Trump's encounter with reality amounted to a vivid case study in the political and economic costs of striking the hardest of hard lines. He entered this trade war imagining a simpler era in which imposing punishing tariffs would force companies around the world to build factories in the United States.

He ends the month discovering that the world of modern supply chains is far more complex than he bargained for, and that it is far from clear his "beautiful" tariffs will have the effects he predicted.

Mr. Trump himself insisted to reporters at the White House that everything was going according to plan.

"We have a lot of action going on," he said, repeating his now-familiar line that "we're not going to be a laughingstock that got taken advantage of by virtually every country in the world." He suggested again that the United States needed to return to the halcyon era from 1870 to 1913 — the year the country began to impose income taxes — when tariffs funded the government and "we had more money than anybody."


Tracking Trump's First 100 Days ›

The Trump administration's previous actions on China and tariffs

- April 14 — Said China's suspension of critical mineral exports to the United States was 'concerning' ›
- April 11 — Issued a rule exempting many electronic parts and devices from the president's tariffs against China ›
- April 8 — Said that China was making a 'big mistake' in retaliating against President Trump's tariffs ›
- April 7 — Threatened to impose huge tariffs on China in response to Beijing's retaliation ›
- March 9 — Declined to rule out that a recession was possible this year ›
- Feb. 7 — Temporarily walked back the suspension of de minimis, a type of duty-free treatment ›
- Feb. 5 — Reversed decision to halt deliveries from China and Hong Kong ›
- Feb. 4 — Halted deliveries to the U.S. from China and Hong Kong ›
- Feb. 3 — Described 10% tariffs against China as just "an opening salvo" ›
- Feb. 1 — Officially announced tariffs on imports from China ›

See every major action by the Trump administration ›

Source: https://www.nytimes.com/2025/04/23/us/politics/trump-tariffs-economy.html

What Happens Next?

We are hesitant to make prognostications given how unpredictable the policy environment has been.

Interestingly, our calls on what's transpiring in the market have been fairly on point in recent weeks and so we'll give this all a go but take our views for what they are worth: an attempt to reason through an occasionally unreasoning world.

Our belief is that President Trump is an intelligent and largely rational man. Impulsive perhaps, but he clearly cares about his cause and his long-term legacy.

Given this, it is of paramount importance for the Administration to focus on its most important priorities and regain its mandate well ahead of next year's congressional elections. Culture wars, attacks on science, immigration stunts and the like are not likely the right place to focus now – although these will not disappear.

Now is the time to focus on the pocketbook of the average American. This means removing the tariff / inflation threat and boosting economic growth to avoid a recession.

By far the most important Administration priority then will be to be seen as guiding the U.S. economy into a good direction through implementation of tax cuts. Those tax cuts are the central promise of the Trump Administration and should stimulate the economy rapidly – and in time for the next election cycle.

A tax cut package has already made it through the Senate and the current battlefield is in the U.S. House of Representatives where the Administration is pushing for "one big, beautiful bill" that combines tax cuts with large spending cuts.

Congress returns to session this week and according to a recent article in *The Guardian* "there will be little beautiful about the negotiations to come…" There are major differences within the Republican party about spending cuts, and it feels to us that the House will take many weeks to squeeze out a spending and tax bill.

The Republican majority in the House is quite narrow and the Senate's recently passed bill largely dodged the question of spending cuts, leaving this up to the House.

It appears difficult to predict the next steps of the Trump Administration.

The Upcoming Budget Battle in Washington

Our best guesses are as follows:

1. The upcoming battle on the Republican side of the House is going to be protracted and painful – going on for six weeks or more.
2. It is likely that most of the proposed tax cuts will pass.
3. But we would expect that the tax cuts will need to be trimmed back given the number of budget hawks on the Republican side of the House and the implied size of deficits.
4. This means that some cuts to Medicaid and other entitlement programs are likely to go through as well.
5. Importantly, while Medicare recipients vote often and are frequently Republican, *Medicaid* recipients tend to be Democrat and vote much less.
6. Things like federal coverage for obesity drugs are unlikely to get anywhere given the severity of budget deficits.
7. The 44% cut for the 2026 NIH budget proposed by the Trump Administration is not likely to get through due to strong Republican support for the agency, but the NIH is going to take some pain.
8. While this budget battle goes on, the Administration will want to marshal political leverage and thus is highly incentivized to deescalate the tariff situation with China, reach tariff agreements with other countries and the like.
9. Further, given that many Senators and Representatives attended Ivy League schools, the cultural war against Harvard will likely de-escalate quickly. This is not a winner in the midst of a budget battle.

What Does This Mean for Biotech?

Our basic view of the biotech market is that the rebound from the first months of Trump 2.0 is *just getting started*.

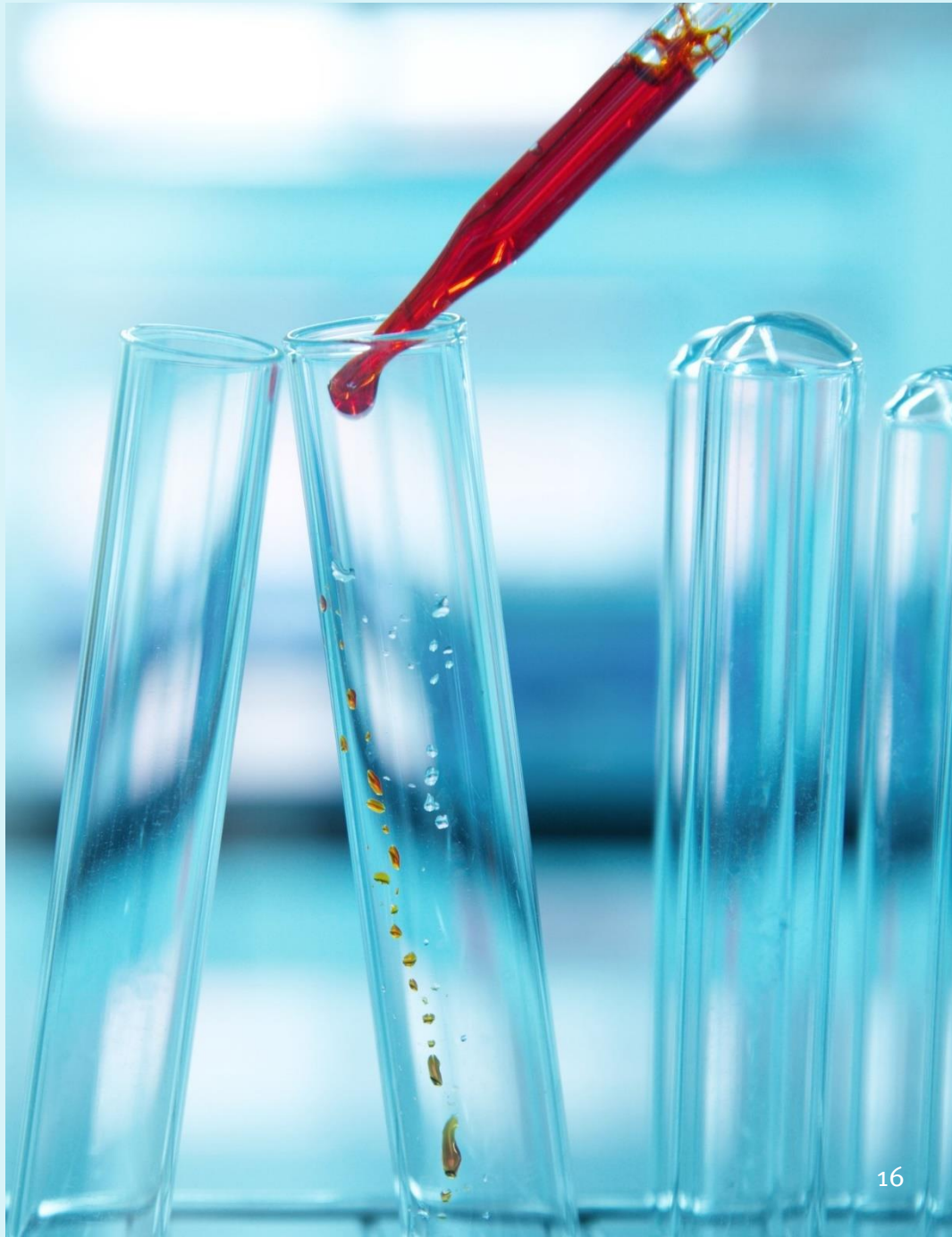
There is substantial upside from here in biotech stocks. Here is our reasoning:

Tariff and Trade Wars to De-Escalate

1. The Trump Administration needs to repair damage to the stock market quickly and the best way to do this is to get some tariff concessions – most likely from our allies.
2. The Trump Administration needs to deescalate its trade war with China quickly because it is likely to be inflationary at home – and that will not go well in the upcoming congressional election.

FDA to Deliver

1. FDA's capacity to perform is not that impaired from last year and the motivation of the agency to deliver approvals for industry and patients is quite high.
2. We expect to see positive developments in this area as early as *this week*. We expect to see surprisingly rapid approval paths emerge for a number of biotechs that have, heretofore, had appallingly low market caps.
3. The recent rally in biotech looks more driven to us by short covering and quants/specialists coming in from the sidelines rather than deep buying in anticipation of what the FDA is going to do.
4. When it becomes apparent what the FDA will be doing over the next eight weeks, we expect biotech to *perform* and tickle investors.
5. If you will, we haven't seen anything yet. In our view, the last two weeks were not another roller coaster bump but rather the beginnings of a sustained rally.



Biotech Rally Ahead

6. FDA concerns will turn out to be overblown: (a) the employees who have recused themselves from reviewing files will get back to work because the external job market is not good and because the “five day a week in the office” mandate is being reversed and (b) it will emerge that removing layers of policy professionals from the agency was probably a pretty good idea.

Improving Macroeconomic Picture

1. Last month’s great inflation numbers will likely persist. While the apparent impact of tariffs on inflation looks scary, the reality is that tariffs on goods coming into the U.S. are unlikely to persist while post-Pandemic supply-side driven inflation will continue to cool.
2. The impact of foreign selling of dollars and bonds on Treasury yields is unlikely to persist as tariff battles get settled out in the weeks and months ahead.
3. Lowered trade barriers outside the U.S. are very likely to be help boost growth at home. This should all be good for the stock market as a whole.
4. Tax cuts and deregulation have historically delivered good economic growth. This takes years but as it becomes clear that the U.S. economy has good prospects we expect (hope) to see the type of long-term rally that accompanied the Reagan Administration.
5. A hidden benefit of a strong market, lowered rates and economic growth is the rise of “risk-on” market conditions as investors begin to look for other sources of return in a market where yields decline.

Biopharma M&A to Jump in the Rest of 2025

Investors Remember the Fundamentals

1. Amnesia about all the great reasons to own biotech will fade away in the months ahead.
2. In our view the top three reasons to own biotech are: (1) accelerating innovation and quality of disease cures, (2) economic growth stimulates pharma spend in the long run as it has before and (3) big pharma M&A is a real thing.
3. M&A comes back as pharma works through its negotiations with the Administration. The issue of price differentials between U.S. and foreign drugs will need to get sorted out but it's not likely to involve big U.S. price cuts. Specifically, M&A has been artificially suppressed as pharma figures out what impact tariffs and various pricing policies, if any, will have on their future.
4. As it becomes apparent that Trump 2.0 doesn't fundamentally change the economic value proposition of being a pharma company, we will see quite a few biotech takeouts transpire this year.
5. A very interesting question is will biotech stocks jump so far that pharma gets priced out of a number of the more obvious M&A opportunities.
6. We continue to see underlying innovation as the #1 value driver ahead. We see the next five years as likely to bring a number of exciting and fundamentally disruptive changes from the biotechnology industry including (1) huge growth in the obesity drug market, (2) breakthroughs in neuroscience drugs, (3) breakthroughs in drugs for aging and (4) realization of potential of industrial biotechnology.

It's Not all Bubbles

Of course, there are real risks to U.S. and European biotech that will remain despite the improving outlook including (a) strengthened Chinese competition, (b) the potential for more aggressive drug price negotiations from HHS, (c) ongoing therapeutic crowding and (d) disruptions caused by emerging technologies including AI. Furthermore, underlying geopolitical risks do not seem to be ebbing as an emerging multipolar world accelerated by recent policy moves may have unknown consequences that could prove dangerous for financial markets.

Biopharma Market Update

The XBI Closed at 80.25 Last Friday (Apr 25), Up 5.7% for the Week

The Stifel Global Biotech Value Tracker rose by 10% last week, substantially more than the XBI (+5.7%) and about the same as the BBC which tracks R&D-stage small / mid cap biotech. Treasury yields came down but remain high. The XBI is down 10.9% for the year while the Stifel Global Biotech Value Tracker is down 7.5% for the year.

Biotech Stocks Up Last Week

Return: Apr 19 to Apr 24, 2025

Nasdaq Biotech Index: +4.1%
Arca XBI ETF: +5.7%
Virtus LifeSci Biotech ETF (BBC): +10.1%
Stifel Global Biotech EV (adjusted): +10.0%*
S&P 500: +4.6%

Return: Dec 31, 2024 to Apr 24, 2025 (YTD)

Nasdaq Biotech Index: -4.0%
Arca XBI ETF: -10.9%
Virtus LifeSci Biotech ETF (BBC): -23.4%
Stifel Global Biotech EV (adjusted): -7.5%*
S&P 500: -6.1%

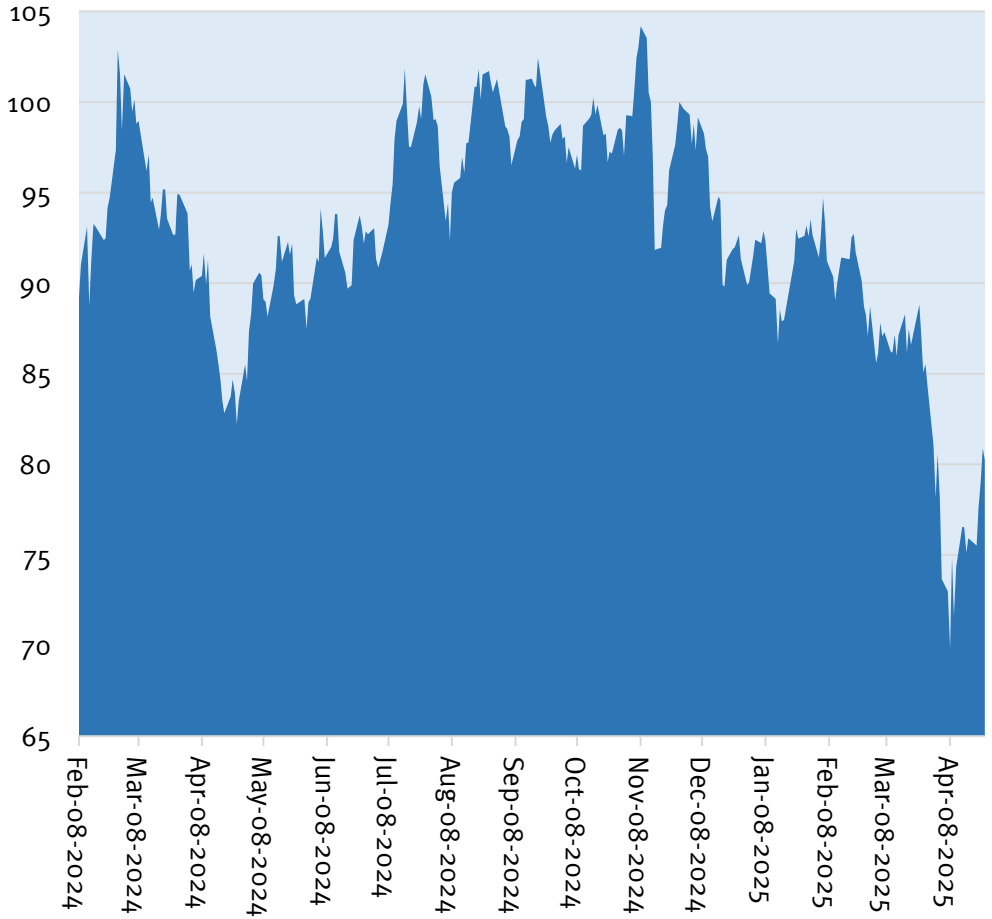
VIX Down

Aug 2, 2024: 23.4%
Dec 13, 2024: 13.8%
Jan 24, 2025: 14.2%
Feb 21, 2025: 18.2%
Mar 28, 2025: 21.7%
Apr 11, 2025: 37.6%
Apr 18, 2025: 29.7%
Apr 24, 2025: 24.8%

10-Year Treasury Yield Down

Aug 2, 2024: 3.80%
Dec 13, 2024: 4.4%
Jan 24, 2025: 4.6%
Feb 21, 2025: 4.4%
Mar 28, 2025: 4.27%
Apr 11, 2025: 4.48%
Apr 18, 2025: 4.34%
Apr 24, 2025: 4.29%

XBI, Feb 8. 2024 to Apr 24, 2025

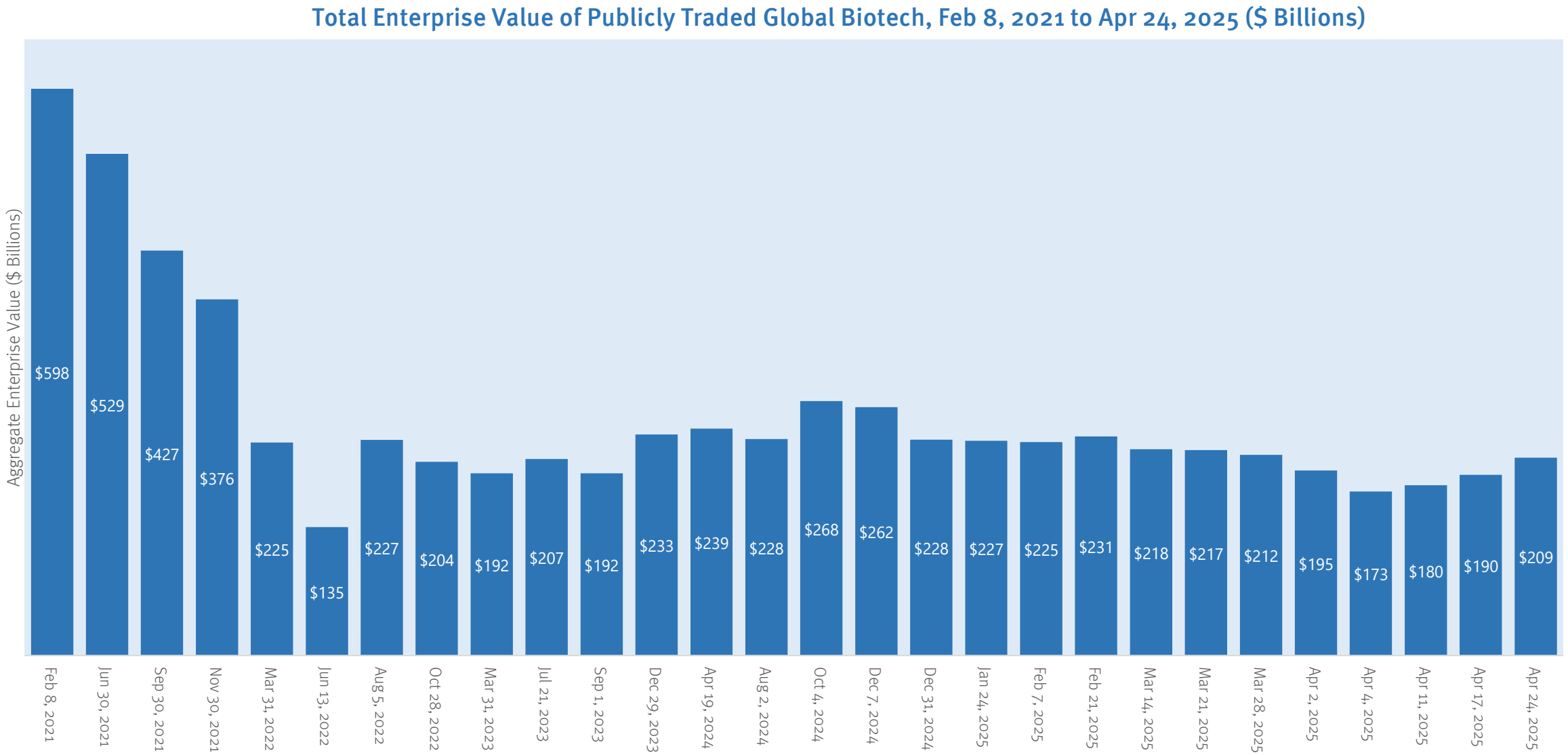


* Change by enterprise value. The adjusted number accounts for the effect of exits and additions via M&A, bankruptcies and IPOs. The annual change by market cap is even higher.

Source: S&P Capital IQ and Stifel analysis

Total Global Biotech Sector Rose 10% Last Week

Biotech stocks rose 10% in the last week, much more than the XBI. Biotech stocks are up 21% since hitting a low point three weeks ago.

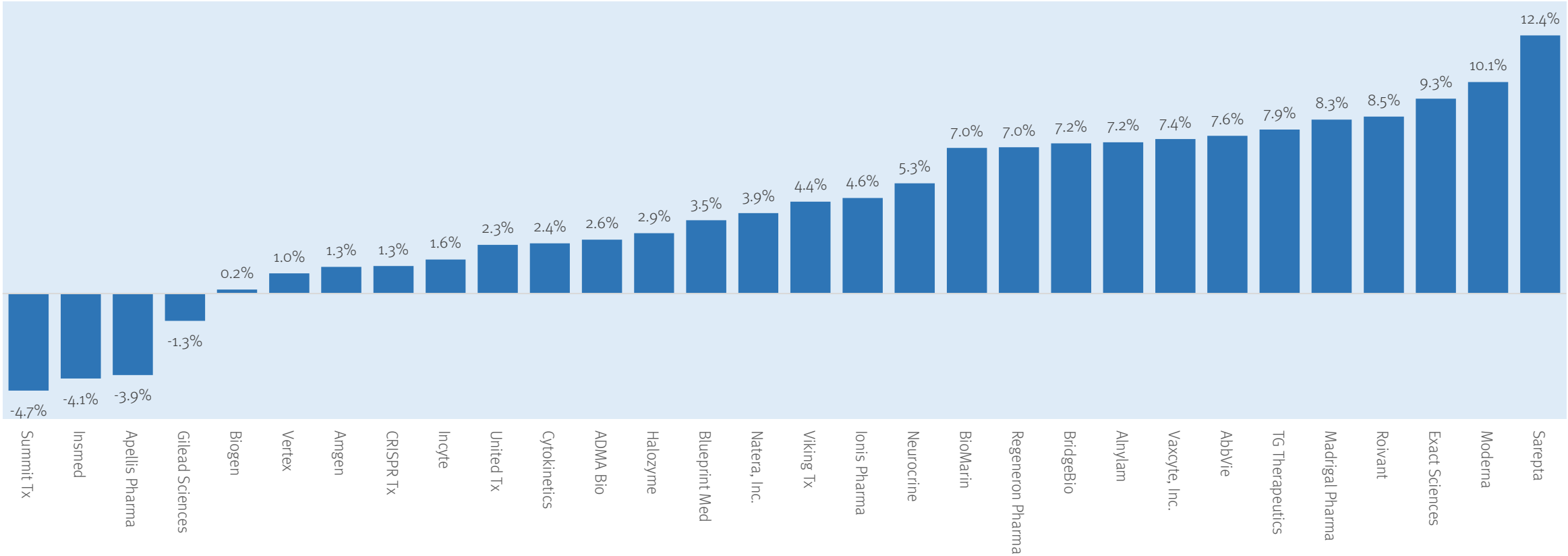


Source: CapitalIQ. Biotechs are defined as any therapeutics company without an approved product on any global stock exchange.

XBI 30 Performance Up Last Week

This chart shows the change in market cap this year for the 30 most influential stocks in the XBI. These 30 stocks comprise 60% of the weight of the XBI (out of 138 stocks total). The mean percentage change in value last week was +4.1%. The median change was +4.1%. Sarepta did well based on a perception that the FDA will be more receptive to rare disease stocks. Moderna and Exact Sciences performed well despite the lack of news.

Top 30 XBI Influencers, Pecent Change in Market Cap, Week of Apr 19 to Apr 25, 2025

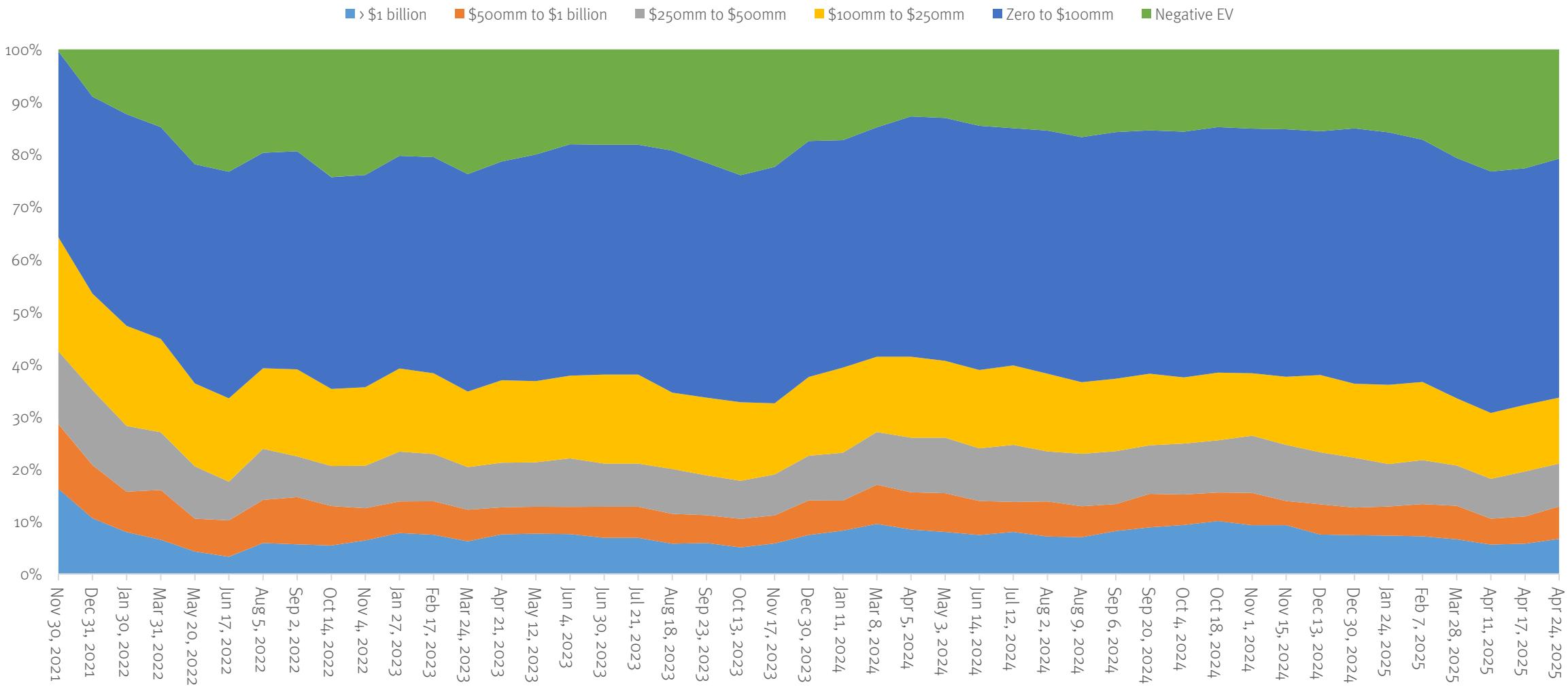


Source: CapitalIQ. Biotechs are defined as any therapeutics company without an approved product on any global stock exchange.

Global Biotech Neighborhood Analysis

We saw a significant positive turn in the number of negative EV companies last week. Valuations of micro caps turned around dramatically.

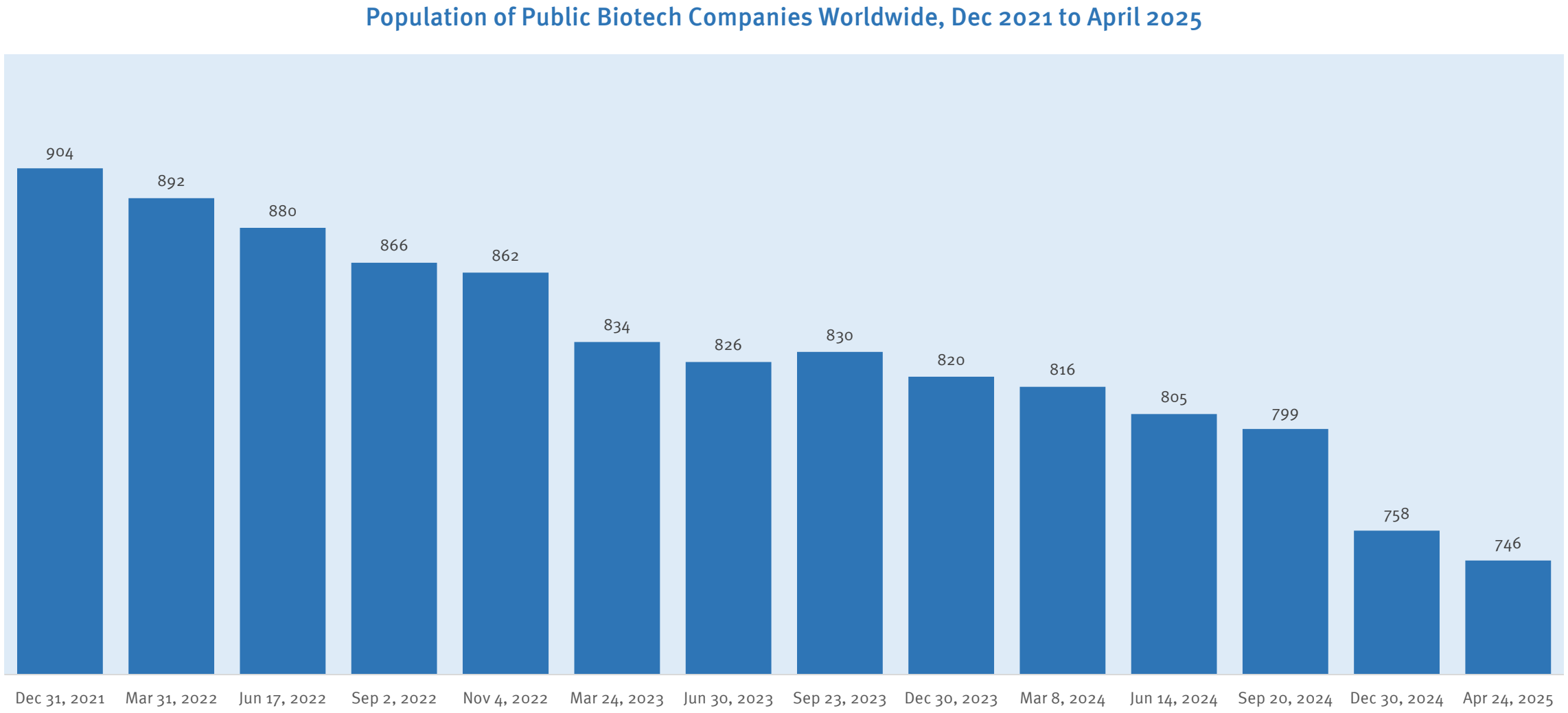
Global Biotech Universe by Enterprise Value Category, Nov 30, 2021 to Apr 24, 2025



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

Continued Drop in Public Biotech Population

We have seen an 18% drop in the number of public biotechs over the last forty months.

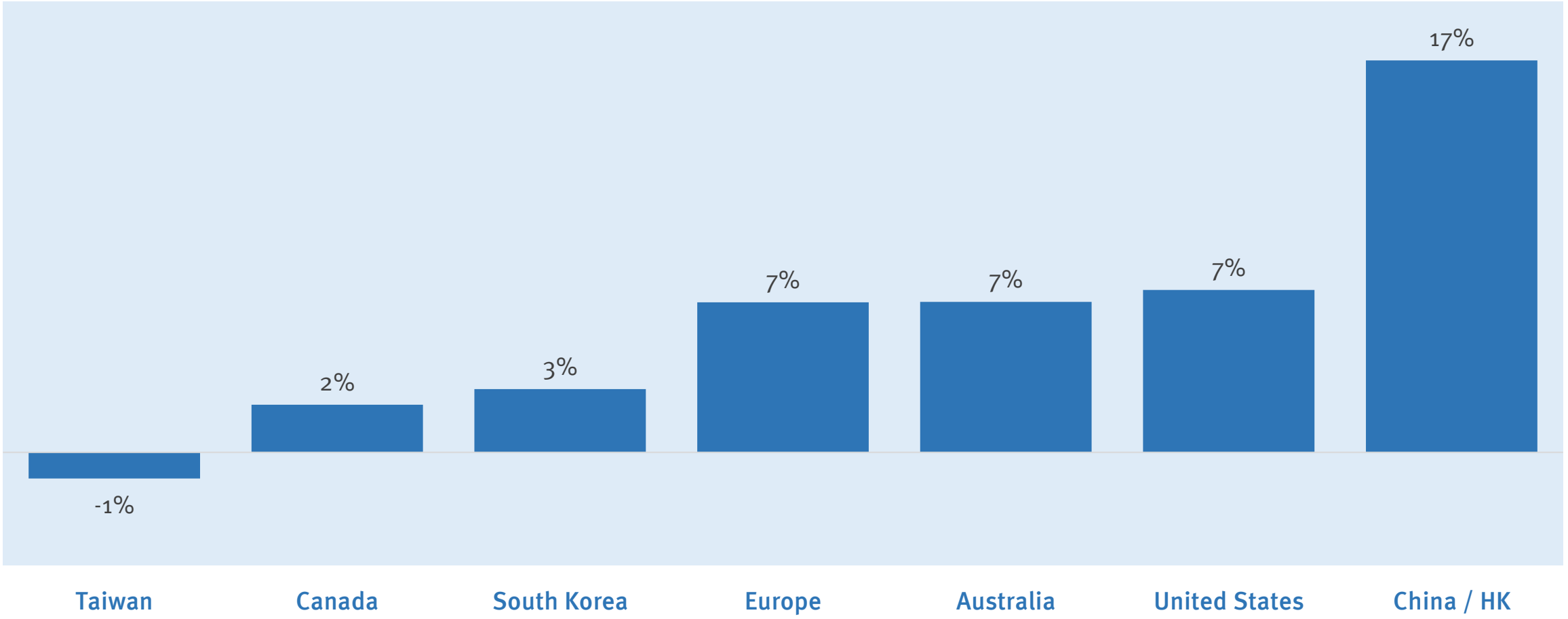


Source: CapitalIQ and Stifel analysis. Biotechs are defined as any therapeutics company without an approved product on any global stock exchange. There was a big drop after Sep 2024. This is when we removed approximately 30 companies that had a zero market cap.

Biotech Performance by Region

Last week saw a strong recovery take place in U.S. biotech (up 7%, change in total market cap) but this was a faint shadow of the 17% jump that took place in China and HK stocks. The China market was energized by the approval of Akeso's VEGF/PD-1 bispecific antibody.

Percent Change in Total Market Cap of Public Biotech by Country/Region, Apr 18, 2024 to Apr 24, 2025



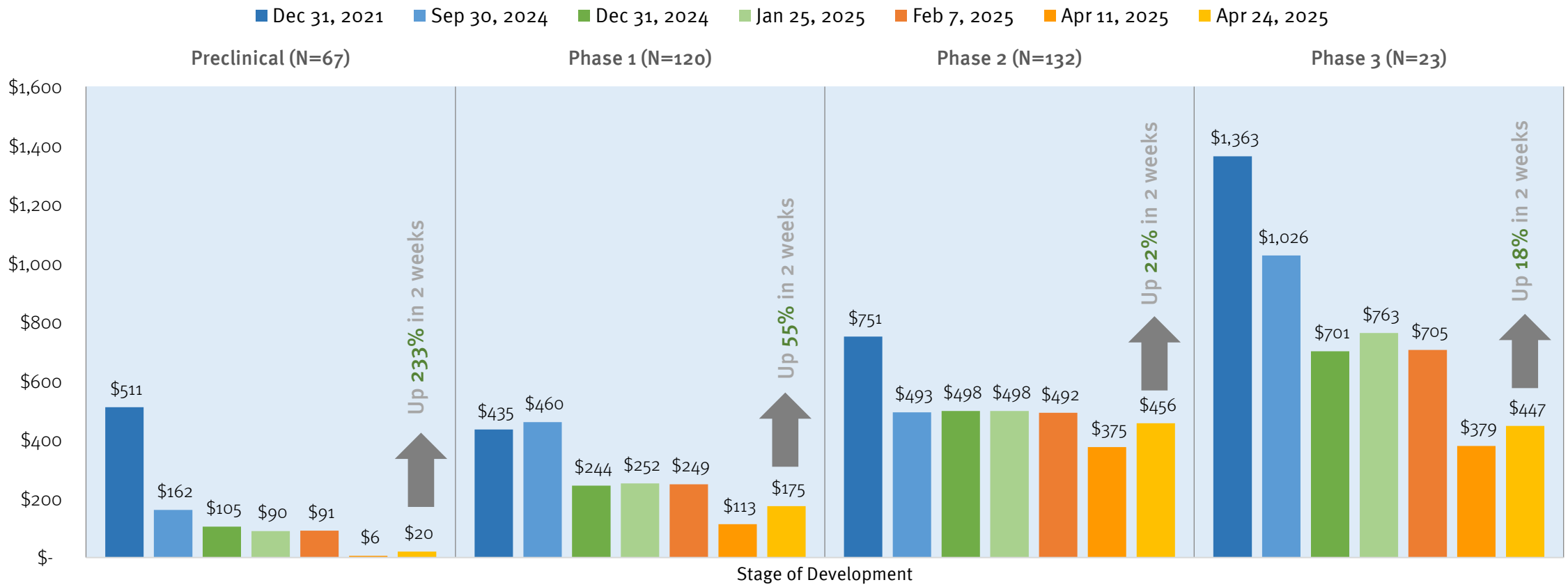
Source: CapitalIQ and Stifel analysis. Biotechs are defined as any therapeutics company without an approved product on any global stock exchange.

Rally Strongest for Early-Stage Stories in Last Two Weeks

The biotech market is very much reacting to Makary's statements that drug approval pathways will be shorter. Pre-clinical stories are up over 200%. Phase 1 stories are up 55% while Phase 2 and Phase 3 stories are up around 20%, on average. One strange artifact in the recent data is the inversion of average Phase 2 and Phase 3 values. A Phase 2 biotech today, technically, has a higher value, on average, than a Phase 3 biotech. This, in part, reflects the drop in value of Summit Therapeutics last week.

Average Enterprise Value of a Biotech Listed on U.S. Exchanges by Stage of Development

Dec 31 2021 to Apr 24, 2025 ($ Millions)

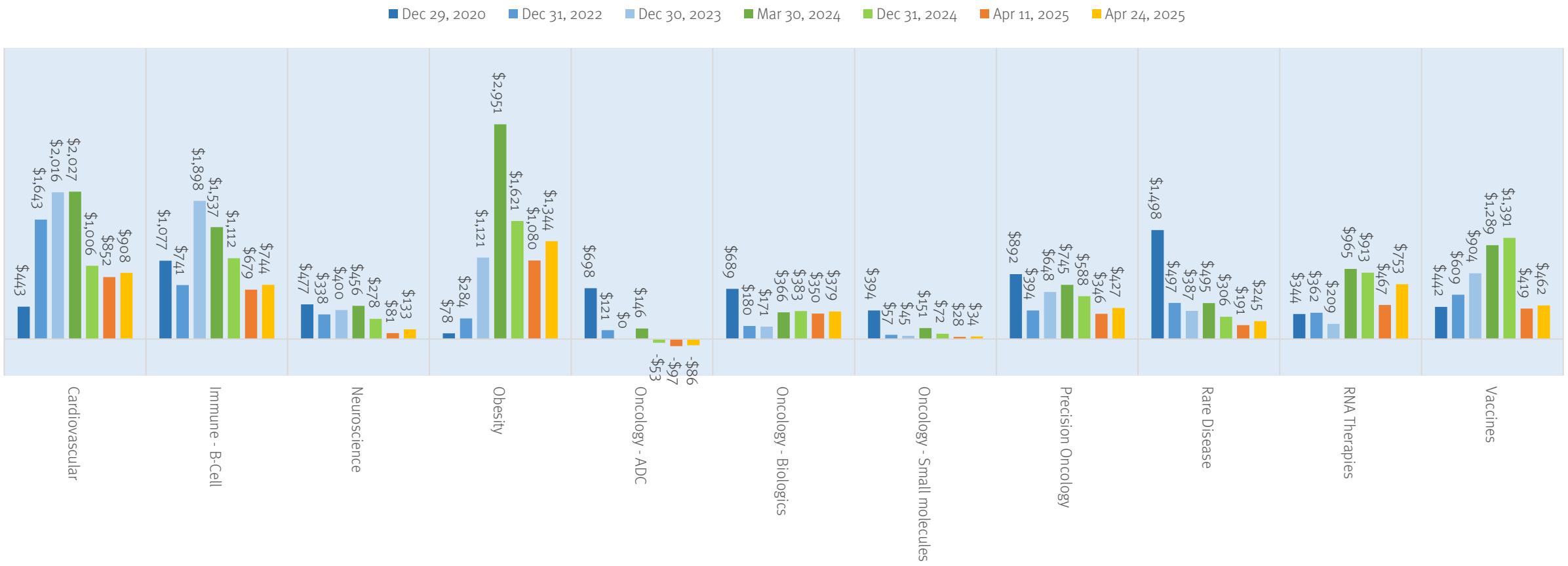


Source: CapitalIQ and Stifel analysis. Biotechs are defined as any therapeutics company without an approved product on any global stock exchange.

Biggest Two-Week Bounce in RNA Therapeutics and Neuro

The market is very much reacting to Makary's statements that new pathways to approval are opening up in fields where sponsors may have impactful but sparse datasets. In recent weeks, for example, biotech companies like Beam have done well. Our own view is that the market may be missing the bigger implications of Makary's message for fields like B-cell therapies and rare disease (which has bounced back but not that much). This is one of the reasons why we think the nascent rally has much longer to run.

Average U.S. Biotech Value by Field, Dec 29, 2020 to Apr 24, 2025 ($ millions, enterprise value)



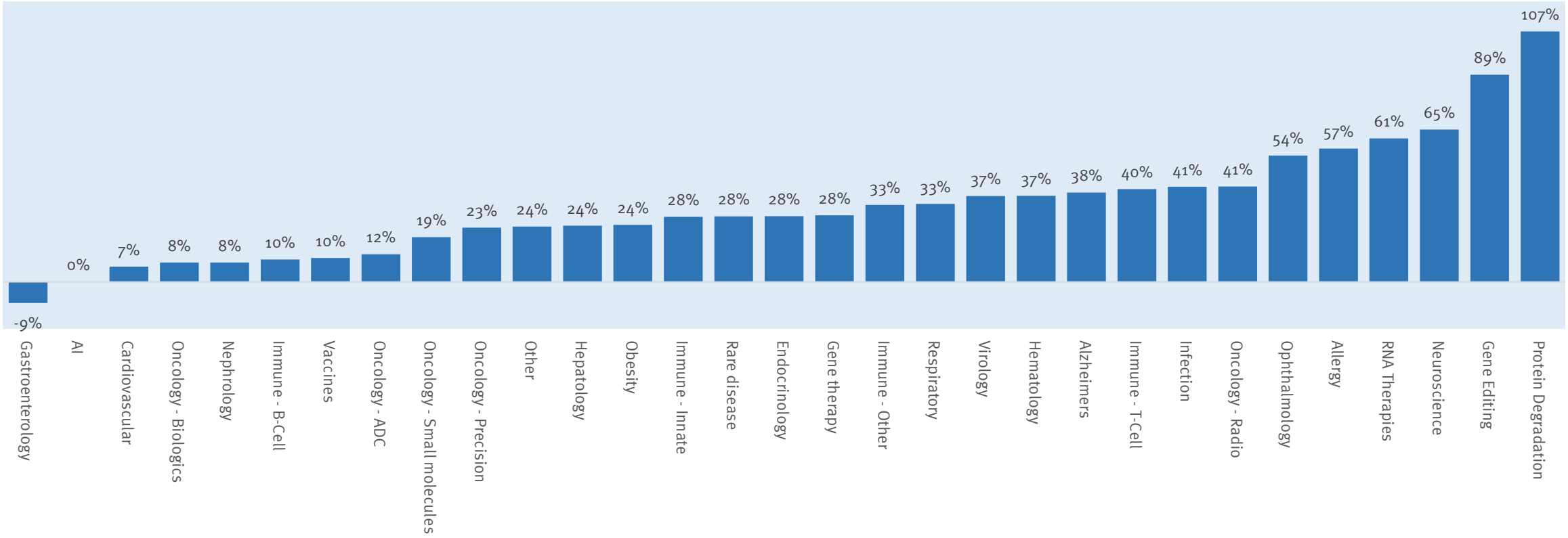
Source: CapitalIQ and Stifel analysis. Biotechs are defined as any therapeutics company without an approved product on any global stock exchange.

Rally Also Strong in Protein Degradation, Gene Editing and RNA

It's interesting to see higher risk and "high tech" modalities bounce back the most in the last few weeks. While these have, indeed, been areas that have been beaten down, our own view is that the market may be missing the broader opportunity to identify companies that are eligible for early approvals under the new FDA regime in fields like rare disease, B-cell and endocrinology.

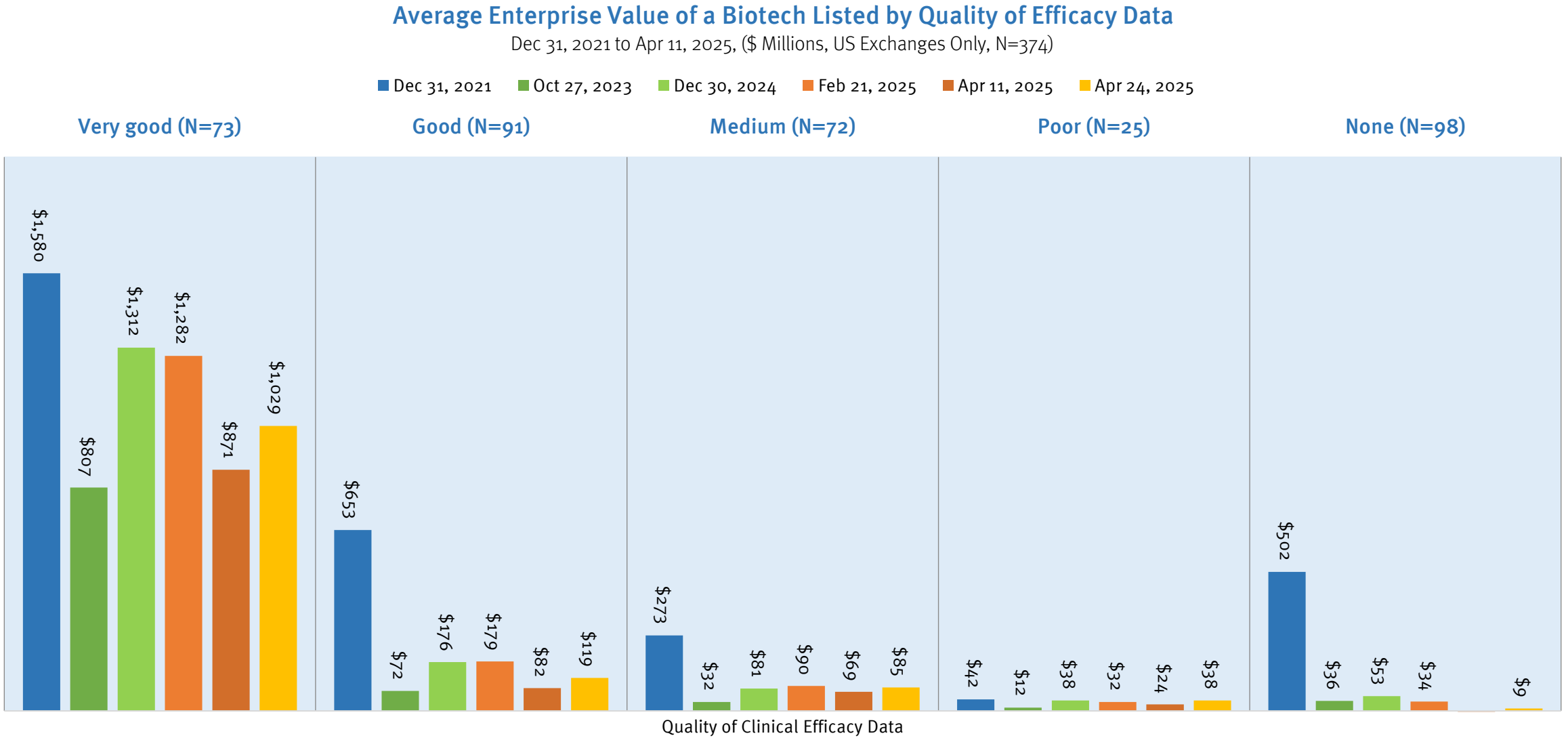
Two Week in Change Average Enterprise Value of U.S. Public Biotechs in Key Therapeutic Areas

Apr 24 vs Apr 11, 2025 ($ millions)



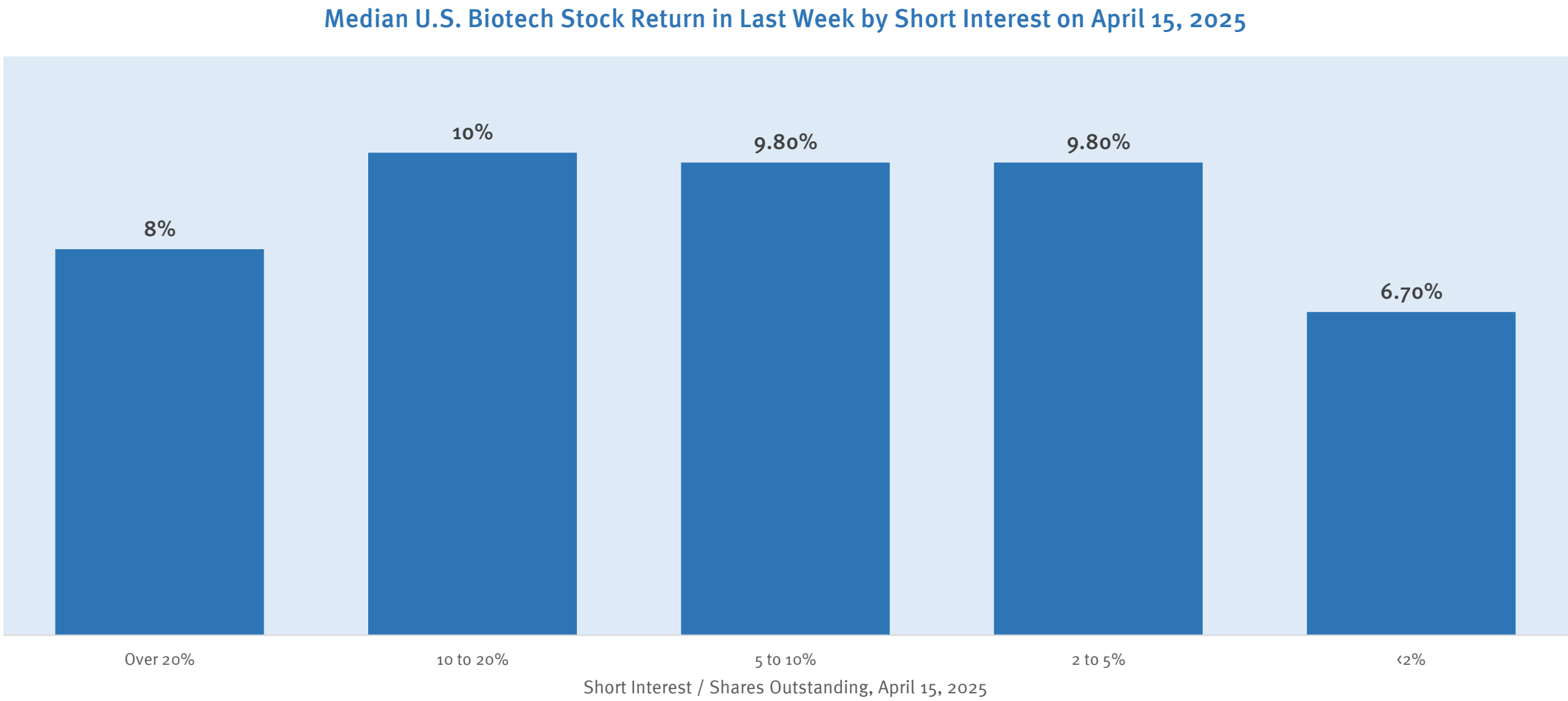
Source: CapitalIQ and Stifel analysis. Biotechs are defined as any therapeutics company without an approved product on any global stock exchange.

Substantial Bounce in Recent Weeks for Firms with Very Good Datasets



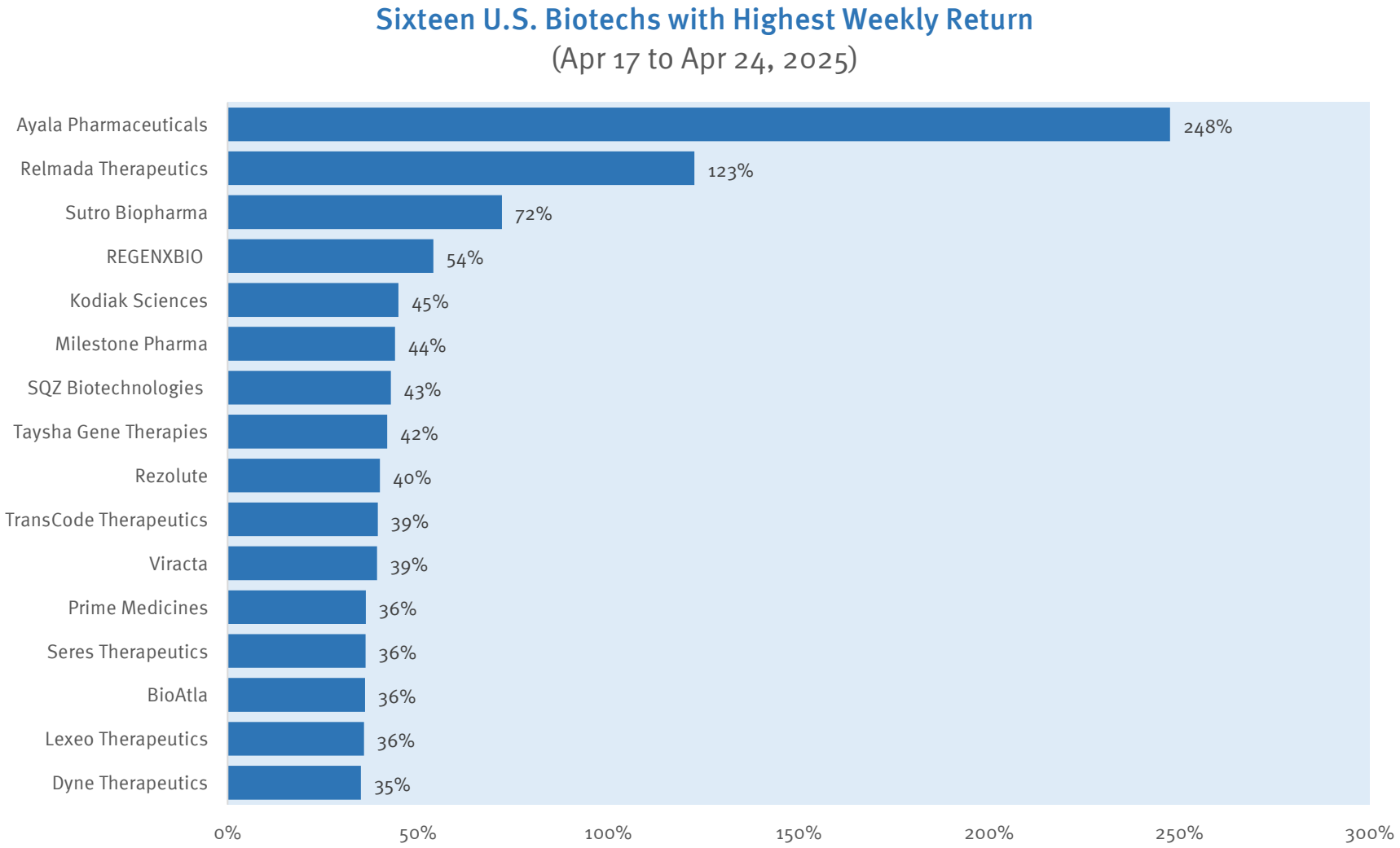
Source: CapitalIQ and Stifel analysis. Biotechs are defined as any therapeutics company without an approved product on any global stock exchange.

Rally Does Not Appear Linked to Short Covering



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

Rally Strongest Where Probability of FDA Approval Seems to Have Moved Most



We do not wish to overinterpret any signal in this data.

Nonetheless, a number of companies here fall into one of three buckets: (1) companies with a reasonable but not great signal in a rare disease where approval now seems more likely, (2) companies with a strong data signal but in a limited number of patients (e.g, certain gene therapy / gene editing stories like Lexeo) and (3) companies that would have ordinarily needed to do another trial for approval that might be eligible for a post-approval study (e.g., Milestone Pharma).

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

Life Sciences Sector Gained $230 Billion in Value Last Week (+2.6%)

Last week saw strength across the board in the life sciences sector. In just two weeks we have seen a 5% jump in values of life science companies worldwide.

Sector	Firm Count	Enterprise Value (Apr 25, 2025, $millions)	Change in Last Week (percent)	Change in Last Month (percent)	Change in Last Year (percent)
API	79	$87,966	3.2%	-0.8%	8.8%
Biotech	727	$209,310	10.0%	-3.2%	-5.1%
CDMO	37	$151,173	1.4%	-0.3%	17.6%
Diagnostics	75	$249,280	4.1%	0.9%	-6.3%
OTC	29	$24,198	2.9%	0.1%	-8.4%
Pharma	695	$5,998,658	2.1%	-2.4%	-0.8%
Pharma Services	38	$146,303	4.2%	-9.4%	-21.5%
Tools	50	$543,192	2.9%	-9.2%	-21.1%
Devices	173	$1,764,079	3.2%	-1.3%	8.1%
HCIT	7	$23,675	4.3%	-6.2%	36.7%
Total	**1910**	**$9,201,834**	**2.6%**	**-2.6%**	**-1.1%**

Source: CapitalIQ and Stifel analysis

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

The count of negative EV life sciences companies worldwide fell from 185 a week ago to 172 last Friday.

A big drop. This was the second week in over a month where this metric of sector health improved.

Source: CapitalIQ

Biotech is Back, Baby! It's All Upside From Here

Adam Feuerstein, *Stat+*, April 24, 2025 (excerpt)

I leave for a week and when I get back, biotech is wonderful, again!

I'm putting all the "Biotech Doom Loop" panic-mongering of my last newsletter aside. For this week's edition, I am luminescent moonbeams and downy-soft puppies, vibrant rainbows, and warm embraces. Everything is awesome! Since bottoming on April 7, the XBI is up 14%.

The BBC, the index of development-stage biotechs that has become the must-watch proxy for small and mid-cap stocks, is up 30% in the same time period. You might ask, but what about the performance year to date? The hole remains deep. To which I say, "Sunshine day!"

The 'new' FDA wants to approve a lot of drugs

Investors loved FDA Commissioner Marty Makary's interview with Megyn Kelly. I'm not here to argue whether that sentiment is right or wrong. This was the first time investors heard Makary speak on his vision for the FDA since his confirmation hearing. I'm simply telling you the market reacted — and is reacting — with a big sigh of relief.

There were some cringey moments during the Kelly interview, but the takeaway message investors heard from Makary was that the FDA is open for business even with the turmoil caused by DOGE cuts, and that finding ways to cut administrative red tape and accelerate drug approvals, particularly for rare diseases, is an agency priority.

I spoke to Tim Opler, Stifel's health care market strategist, earlier this week. He's convinced the FDA is going to be a strong tailwind for biotech in 2025 and beyond. Sentiment has been horrible and market losses extremely painful, Opler conceded, but that's caused investors to experience cognitive dissonance as it relates to the drug-friendly message Makary is actually sending.

How does Makary deal with a MAHA movement that distrusts, even hates, pharma? By couching reforms and drug approvals through the lens of helping patients. "Nothing Makary is proposing is being done for the benefit of pharma, it's to benefit patients," Opler believes. This might be a distinction without a difference, because patients and pharma (biotech, too) both benefit from faster drug approvals, but… shhhh… don't tell anyone.

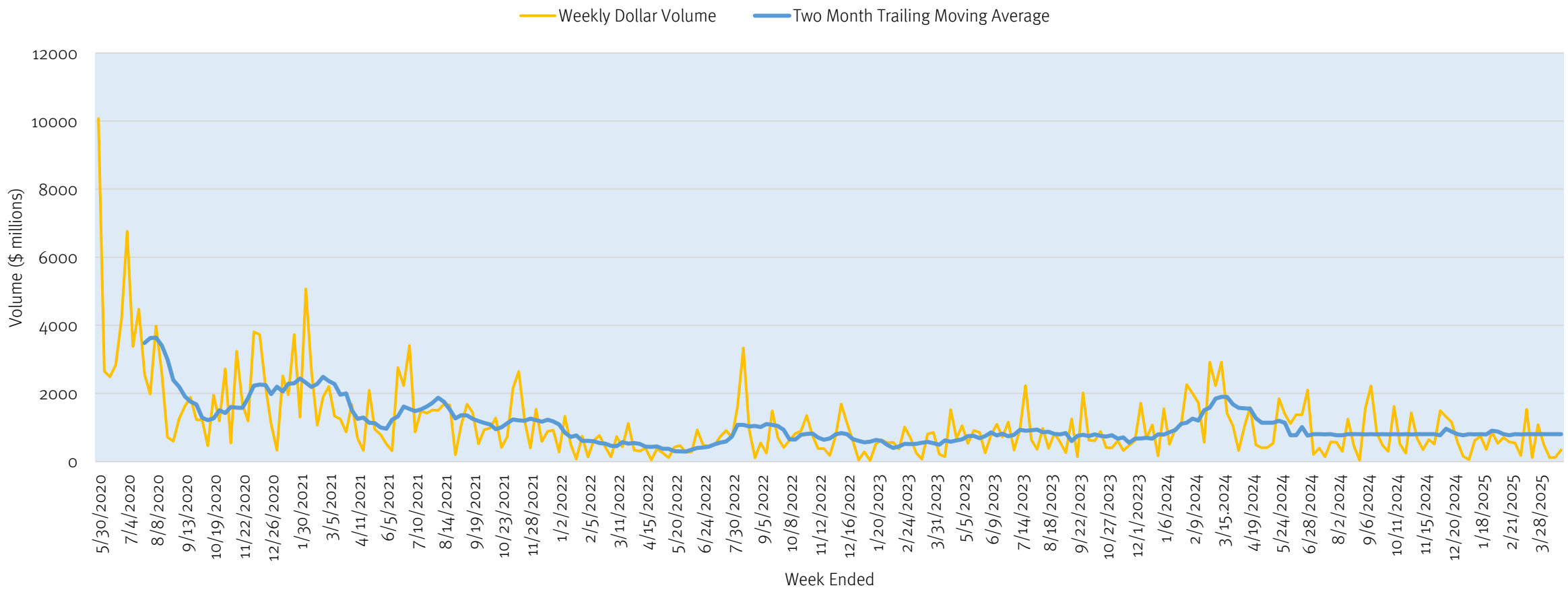
Source: https://www.statnews.com/2025/04/24/biotech-is-back-baby-upside-following-doom-loop/

Capital Markets Update

Public Market Equity Financings Very Slow this Month

While the biotech market has rallied strongly in the last two weeks the financing and deal markets have been more or less frozen – not due to any fundamental uncertainty, but in a pause while larger macropolitical uncertainties are worked out and as the surprising rally took place. We did see some life in the follow-on market with $344 million in offerings led by a $90mm follow-on for Rezolute.

Biopharma Equity Follow-On Volume ($ million), Weekly, May 2020 to Apr 2025

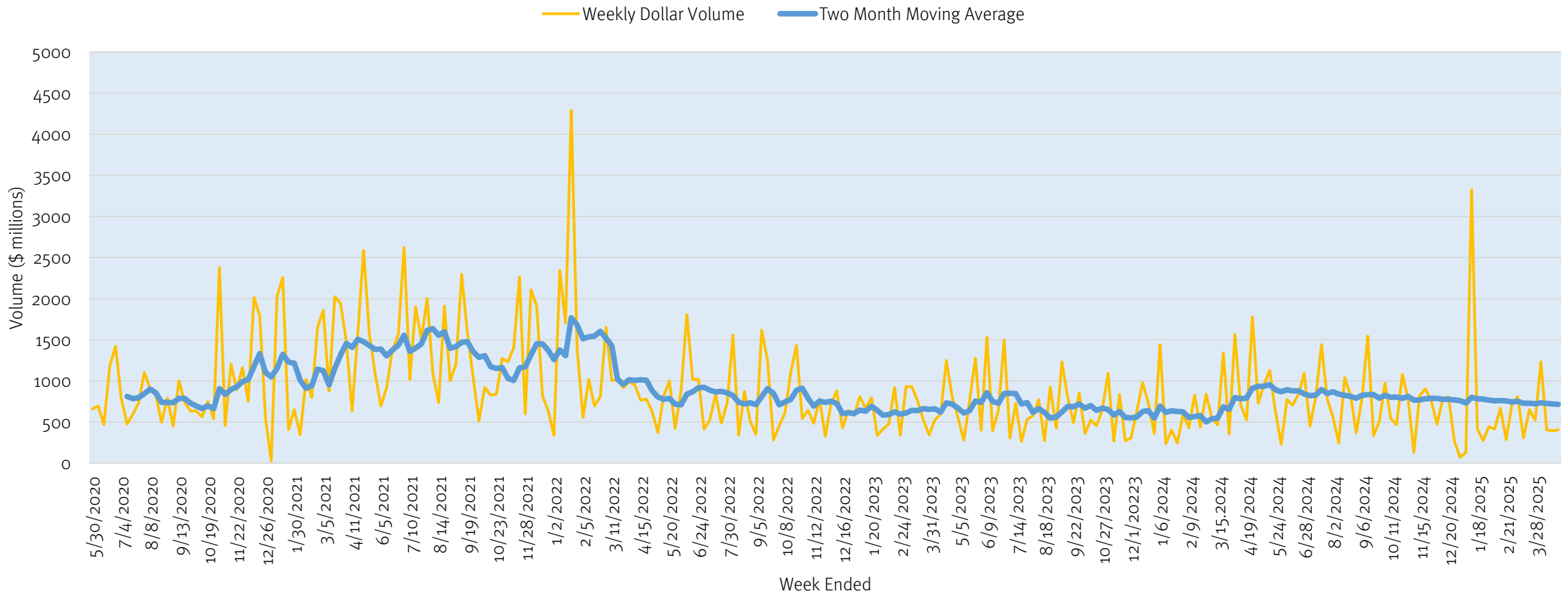


Source: Data from CapitalIQ and Stifel research.

Venture Privates Remained Subdued

Recent weeks have seen modest activity in the venture privates market. Last week saw $404 million in deals. Compare this to an average volume of $900mm in the first two months of 2025. The largest deal was a $100mm raise by Bioliq.

Biopharma Venture Equity Privates Trend ($ million), Weekly, May 2020 to Apr 2025

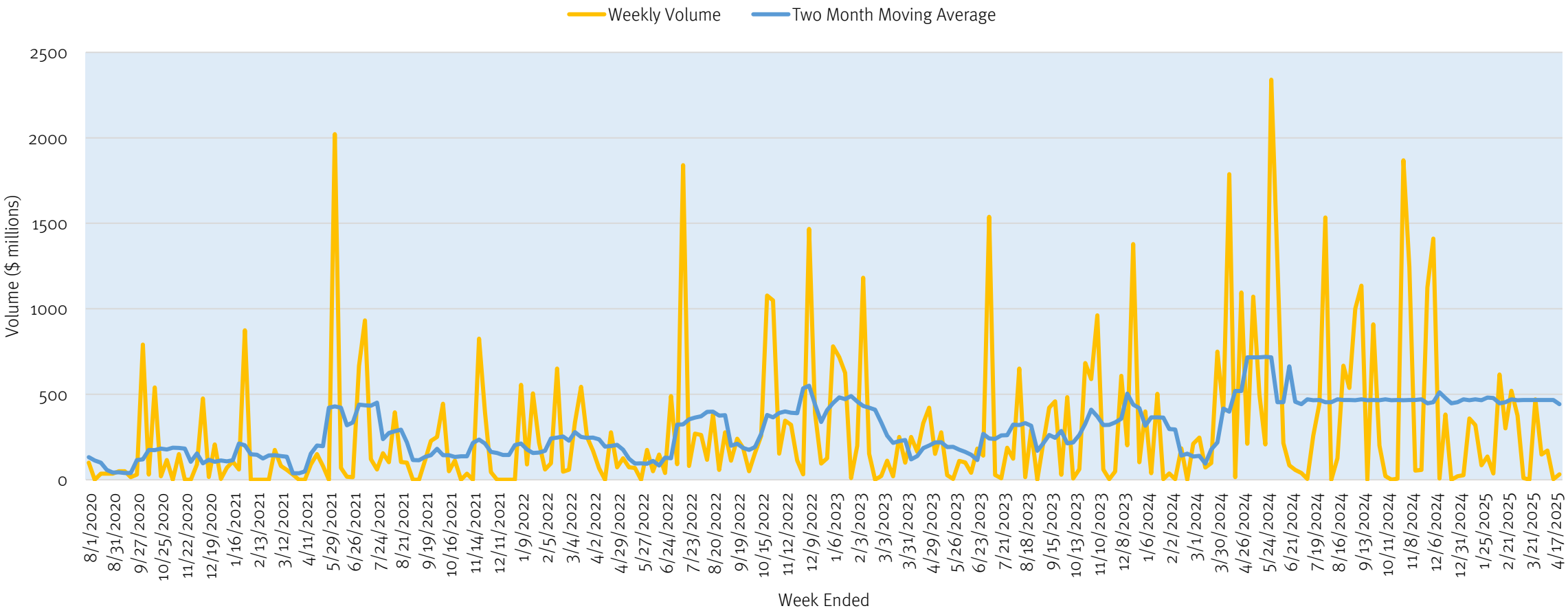


Source: Data from CapitalIQ, Crunchbase.

Global Biopharma Private Debt Placement Volume Low

Private debt issuance last week was slow with $33 million raised across three deal prints. The volumes in this market appear to have been dropping in recent weeks due to high uncertainty in credit markets linked to Trump's tariff actions.

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

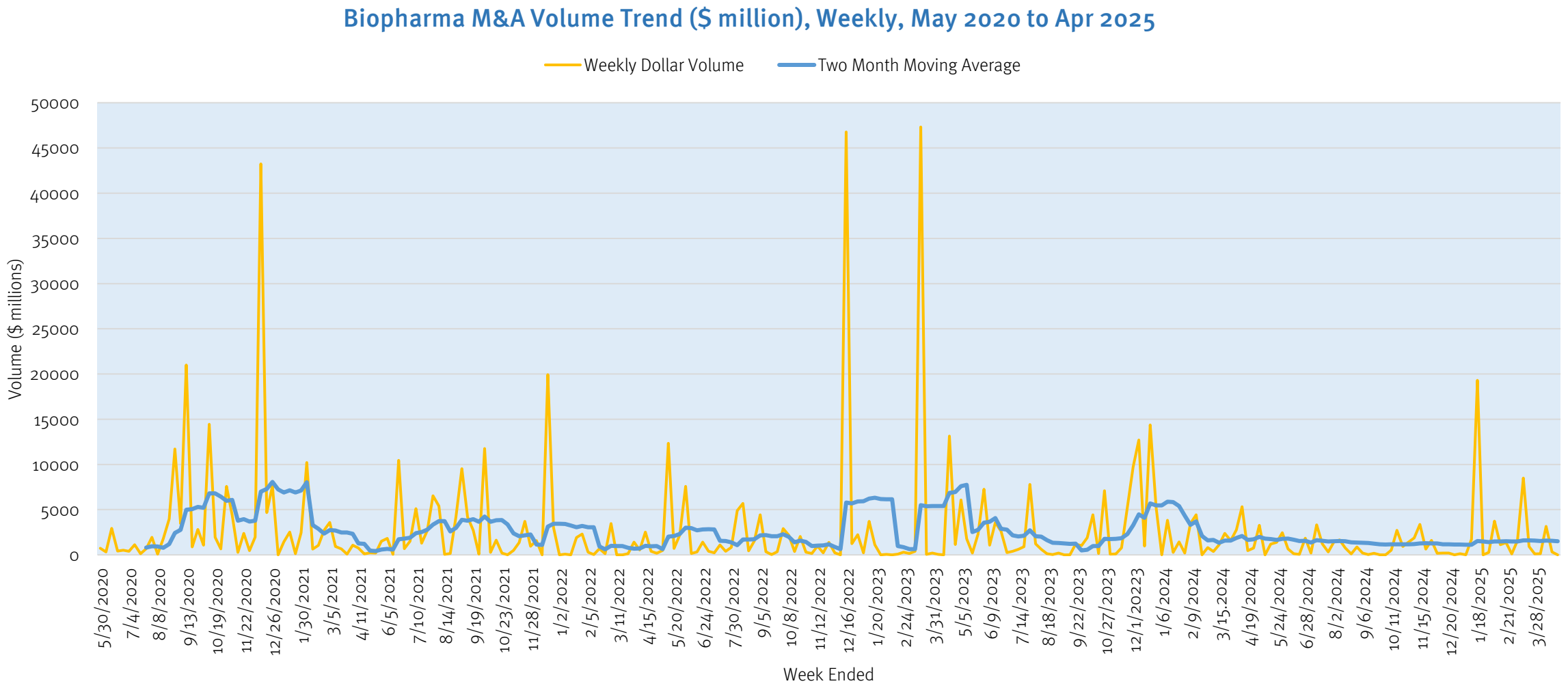


Source: Data from CapitalIQ, Crunchbase.

Deals Update

M&A Market Lightening Up in April

There were no M&A deals last week. This was only the second zero volume M&A deal week of the year.



Source: S&P, CapitalIQ

Germany's Merck Nears Roughly $3.5 Billion Deal for SpringWorks

Ben Dummett and Lauren Thomas, *Wall Street Journal*, April 24, 2025 (excerpt)

Germany's Merck KGaA is finally nearing a roughly $3.5 billion deal for SpringWorks Therapeutics, a U.S. biopharmaceutical company that specializes in rare diseases and cancer.

The two parties are discussing a deal around $47 per share, Merck said in a statement Thursday, confirming an earlier report in The Wall Street Journal. Merck said no final agreement had been made.

A deal could be completed as soon as Monday, assuming the talks don't hit any more last-minute snags, people familiar with the matter had said.

The German life-sciences and chemicals company had said in February it was in advanced talks to buy SpringWorks, after signaling it was on the lookout for deals.

After the deal didn't quickly materialize, SpringWorks's shares slumped. On Thursday, the stock closed up 9% to $44.93 following the Journal report. In February, shares were changing hands closer to $60.

Recent market volatility with President Trump's global trade war has added complexity to the deal discussions.

Merck, which is based in Darmstadt, Germany, has a market value of almost $60 billion which should make SpringWorks easily digestible despite the overall market uncertainty.

Source: https://www.wsj.com/business/deals/germanys-merck-nears-roughly-3-5-billion-deal-for-springworks-2c7258b9

Roche in ‘Very, Very Good Position’ To Weather Trump Tariffs but M&A May Suffer

Tristan Manalac, *Biospace*, April 24, 2025 (excerpt)

Roche’s exposure to the tariffs is mostly limited to four medicines, three of which it already produces in the U.S., according to CEO Thomas Schinecker, who declined to reveal what these assets are.
Roche is confident that it will be able to absorb financial impacts from President Donald Trump’s tariffs, but dealmaking may go by the wayside as the industry awaits the true impact of the import taxes.

In a media call after releasing first-quarter earnings on Tuesday, CEO Thomas Schinecker said that the pharma has been working to ensure that it is “well-positioned as a company [for] whatever may come our way.”

According to Schinecker, just four of Roche’s assets account for some 90% of the company’s exposure to possible tariffs. Three of these are produced in the U.S., the CEO continued, adding that Roche has already “increased the volume of manufacturing” of these medicines domestically. Meanwhile, the company began tech transfer for the final drug “weeks ago,” with an eye toward producing it in the U.S. as well.

Schinecker declined to identify what these four assets were.

Still, Schinecker expects that tariffs will have some appreciable impact on its business, particularly in terms of dealmaking. While Roche will “continue to look at the science” for its deals, it will also consider whether or not they “make financial sense.”

“If there are questions around tariffs, it will be more difficult to make financial sense of any M&A deals,” Schinecker said during the call, adding that in such a climate, parties across the industry and worldwide might slow down dealmaking to “see how things develop.”

Source: https://www.biospace.com/business/roche-in-very-very-good-position-to-weather-trump-tariffs-but-m-a-may-suffer

M&A Remains 'Top Priority' for Big Pharmas in the Face of Tariff Threat

James Waldron, *FierceBiotech*, April 25, 2025 (excerpt)

Big Pharmas aren't letting the looming threat of potential tariffs divert them from their M&A strategies for the year—at least for the time being.

As the dust settles on the first significant week of quarterly earnings calls since the Trump administration made clear that tariffs on pharmaceutical imports are a live option, executives at some of the biggest drugmakers insisted they are staying focused on their existing plans.

In a call with analysts yesterday, Bristol Myers Squibb CEO Chris Boerner, Ph.D., declared that business development "remains a top priority" for the company. The pharma is planning to slash $2 billion in costs by the end of 2027, on top of a $1.5 billion initiative unveiled last year that targeted more than 2,000 layoffs. These efforts to make BMS "more efficient and agile" have given the company the "financial flexibility to be … much more engaged on business development," Boerner said.

This is "way more important than any of the exogenous factors" that could affect the industry more widely, such as the threat of tariffs or the restructuring at the FDA, the CEO added. When it comes to potential acquisitions that BMS has in its sights, Boerner would only say that the company is "focused on strengthening our position in the core TAs that we operate in."

"That's bringing in promising areas of science, assets where we can improve the growth profile of the company," he added. "And what's important is that we like the science and we feel we're the rightful owners; the financials make sense; and again, that's strengthening the growth profile in key areas."

Meanwhile, Merk & Co. is already counting the costs of the Trump administration's current tariff policy. Even before any pharmaceutical tariffs become a reality, the Big Pharma expects the existing tariffs implemented between the U.S. and China, plus Canada and Mexico, will lead to incremental costs of $200 million.

Despite this, Merck's CEO Rob Davis echoed BMS' sentiment by stating that business development remains a "top priority."

"Our desire and belief that we need to continue to identify new science-based opportunities to continue to build on the pipeline is unchanged," Davis told analysts in response to a specific question about the impact of tariffs. "And so our strategy continues."

Source: https://www.fiercebiotech.com/biotech/ma-remains-top-priority-big-pharmas-face-tariff-threat

Industry Update

Europe’s Pharma Industry Braces for Pain as Trump Tariff Threat Looms

Jeanna Smialek, Liz Alderman and Melissa Eddy, *New York Times*, April 27, 2025 (excerpt)

Insulin, heart treatments and antibiotics have flowed freely across many borders for decades, exempt from tariffs in a bid to make medicine affordable. But that could soon change.

For months, President Trump has been promising to impose higher tariffs on pharmaceuticals as part of his plan to reorder the global trading system and bring key manufacturing industries back to the United States. This month, he said pharmaceutical tariffs could come in the “not too distant future.”

If they do, the move would have serious — and wildly uncertain — consequences for drugs made in the European Union. Pharmaceutical products and chemicals are the bloc’s No. 1 export to America. Among them are the weight-loss blockbuster Ozempic, cancer treatments, cardiovascular drugs and flu vaccines. Most are name-brand drugs that yield a large profit in the American market, with its high prices and vast numbers of consumers.

“These are critical things that keep people alive,” said Léa Auffret, who heads international affairs for BEUC, the European Consumer Organization. “Putting them in the middle of a trade war is highly concerning.”

European companies could react to Mr. Trump’s tariffs in a range of ways. Some pharmaceutical companies trying to dodge the tariffs have already announced plans to increase production in the United States, which Mr. Trump wants. Others could decide to move production there later.

Other companies appear to be staying put, but could raise their prices to cover the tariffs, pushing up costs for patients. And higher prices could affect not only American consumers, but also patients in Europe. Some companies have begun to argue that Europe should create more favorable conditions for their businesses by dismantling some of the rules that keep drug prices down.

Source: https://www.nytimes.com/2025/04/27/world/europe/tariffs-pharmaceuticals-drugs-medicine-trump.html

Pharma Tariffs Would Raise U.S. Drug Costs by $51 Billion Annually, Report Finds

Maggie Fick, *Reuters*, April 25, 2025 (excerpt)

A 25% U.S. tariff on pharmaceutical imports would increase U.S. drug costs by nearly $51 billion annually, boosting U.S. prices by as much as 12.9% if passed on, a report commissioned by the industry's U.S. trade group and reviewed by Reuters shows.

The analysis, conducted by Ernst & Young, found the United States imported $203 billion in pharmaceutical products in 2023, with 73% coming from Europe -- primarily Ireland, Germany and Switzerland. Total U.S. sales of finished pharmaceuticals that year were $393 billion.

The report, dated April 22 and not made public, was commissioned by the main U.S. pharmaceutical lobby, the Pharmaceutical Research and Manufacturers of America.

Last week, the Trump administration announced probes into pharmaceutical imports, citing national security concerns over reliance on foreign drug production.

The move triggered a 21-day public comment period as part of the investigation led by the Commerce Department. Drugmakers see the probe as a chance to show the administration that high tariffs would hinder their efforts to swiftly ramp up U.S. production, and to propose alternatives, said Ted Murphy, a trade lawyer at law firm Sidley Austin, which is advising companies on their submissions to the Commerce Department.

Drugmakers have also lobbied Trump to phase in tariffs on imported pharmaceutical products in hopes of reducing the sting from the charges.

Source: https://www.reuters.com/business/healthcare-pharmaceuticals/us-pharma-tariffs-would-raise-us-drug-costs-by-51-bln-annually-report-finds-2025-04-25/

Merck Takes $200M Tariff Hit Trimming its Gross Profits

Jonathan Gardner, *Biopharma Dive*, April 24, 2025 (excerpt)

Merck's first-quarter earnings are among the first signs of the financial impact President Donald Trump's tariff threats will have on pharmaceutical companies. Johnson & Johnson already reported a $400 million impact from tariff costs, primarily in its medical device business, but didn't alter its forecast for the year. Other companies, such as Sanofi and Bristol Myers Squibb, have also reiterated or increased their financial outlooks, citing the lack of clarity about what their dues might look like.

Merck's adjustment was minimal, too, with only a half-percent change — from 82.5% at the beginning of the year to 82% — in the guidance for its gross margin. The company also added $200 million to its operating expenses estimate and trimmed 6 cents from its earnings per share outlook, which is now expected to fall between $8.82 and $8.97. Both of those numbers will be affected by payments to development partners.

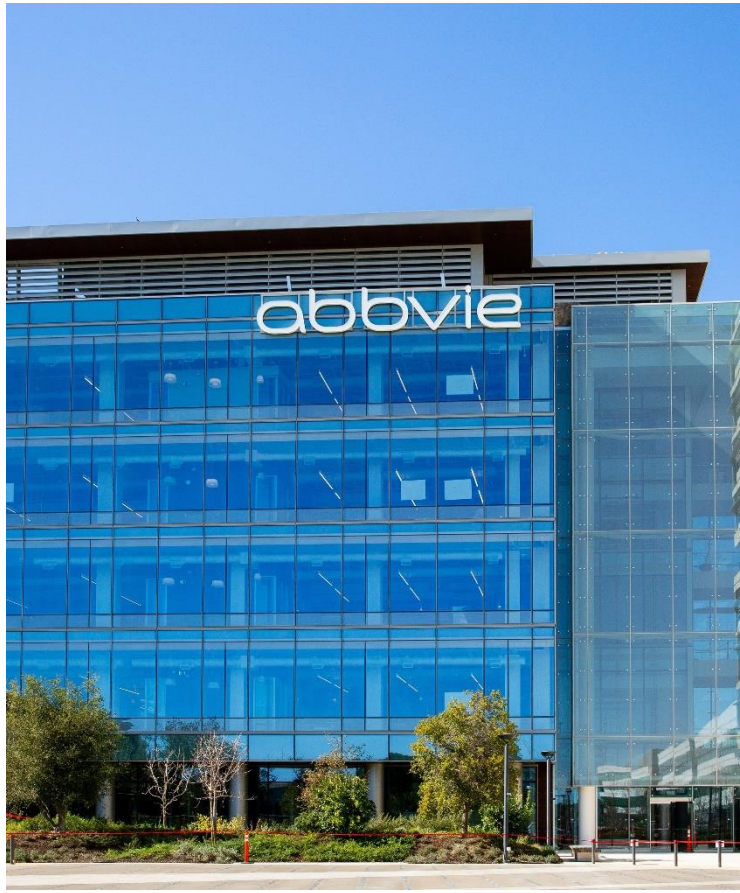
Davis expects that Merck's longstanding plan to onshore drug manufacturing — which has been underway since 2017 — should help protect it from substantial tariff costs. Those moves, he said, have stimulated $12 billion in U.S. capital spending so far, along with another $9 billion in planned investments.

"As you look at 2025, we're well-positioned with inventory to be able to mitigate anything we could see in the short term," Davis said. "In the medium to long term, we've already started to identify where we can either reposition our own manufacturing, change the the priorities of existing plants, bring on external manufacturing, in some cases, to bridge gaps, and then finally, to build internal manufacturing."

Source: https://www.biopharmadive.com/news/merck-tariffs-first-quarter-earnings-guidance/746227/

AbbVie Lifts Profit Guidance as Newer Drugs Drive Sales Beat

Madison Muller, *Bloomberg*, April 25, 2025 (excerpt)



AbbVie Inc. raised its profit outlook for the year on better-than-expected sales from newer autoimmune treatments, but warned its forecast doesn't take into account any potential changes in trade policy.

The drugmaker raised its 2025 adjusted earnings by 10 cents to a range of $12.09 to $12.29 a share. That "does not reflect any trade policy shifts, including pharmaceutical sector tariffs, that could impact AbbVie's business," according to a statement.

The company said it expects a $30 million charge from tariffs that are already in place, mostly related to its aesthetics business.

Investors have been focused on how companies are navigating existing tariffs and the potential for new levies to be imposed on pharmaceutical imports to the US. Larger competitors like Johnson & Johnson and Merck & Co. already warned tariffs will cost them hundreds of millions of dollars.

Potential tariff impacts would be "in line" with AbbVie's peers, Chief Executive Officer Rob Michael said on a call with investors. The company plans to invest $10 billion in the US over the next decade, he said.

AbbVie has looked to Skyrizi and Rinvoq — a pair of newer autoimmune medicines — to make up for fading revenue from its aging blockbuster Humira. That strategy is showing signs of working: Both drugs beat estimates in the first quarter, with combined sales of $5.14 billion.

That helped the company surpass quarterly revenue expectations. AbbVie recorded $13.34 billion in overall sales, beating analyst estimates. Adjusted earnings for the quarter were $2.46 a share, above Wall Street's expectations.

Source: https://www.bloomberg.com/news/articles/2025-04-25/abbvie-lifts-profit-guidance-as-newer-drugs-drive-sales-beat

Bristol Myers Squibb Tops Quarterly Estimates, Hikes Outlook as Drugmaker Braces for Tariffs

Annika Kim Constantino, *CNBC*, April 24, 2025 (excerpt)

Bristol Myers Squibb on Thursday beat first-quarter estimates and hiked its revenue and profit guidance for the year, as the drugmaker cuts costs.

The company now expects 2025 revenue to come in between $45.8 billion and $46.8 billion, up from a previous outlook of around $45.5 billion. Bristol Myers also projects full-year adjusted earnings of $6.70 to $7 per share, which compares with its prior forecast of $6.55 to $6.85 per share.

Notably, the company said its guidance revisions include the estimated impact of current tariffs on U.S. products shipped to China. China is a critical market for Bristol Myers. The company has previously outlined its "China 2030 Strategy," which is a plan to bring more of its medicines to the nation to address unmet medical needs in areas like gastric cancer and include more Chinese patients in clinical trials.

But the new outlooks do not account for any of President Donald Trump's planned tariffs on pharmaceuticals imported into the U.S., Bristol Myers said.

In an earnings call Thursday, Bristol Myers Squibb CEO Christopher Boerner said the company appreciated the Trump administration's efforts to increase U.S. manufacturing, but noted that it "needs to be done in a very thoughtful and deliberate way" in the pharmaceutical sector.

"We have a tremendous amount of flexibility to be able to move our manufacturing around should any potential tariffs come up," said the company's CFO David Elkins on the call. He added that Bristol Myers has a broad global manufacturing network, which includes a significant presence in the U.S.

Source: https://www.cnbc.com/2025/04/24/bristol-myers-squibb-bmy-earnings-q1-2025.html

Johnson & Johnson's TAR-200 Demonstrates High CR Rate in Bladder Cancer

Press Release, J&J, April 26, 2025 (excerpt)

Johnson & Johnson (NYSE: JNJ) today announced new data from Cohort 2 of the pivotal Phase 2b SunRISe-1 study evaluating TAR-200—an intravesical gemcitabine releasing system—for patients with certain types of bladder cancer. The findings demonstrate the highest complete response rate without reinduction with more than half of responders remaining cancer-free for at least 12 months. These results highlight the potential of TAR-200 as a breakthrough for people with Bacillus Calmette-Guérin (BCG)-unresponsive, high-risk non-muscle-invasive bladder cancer (HR-NMIBC) with carcinoma in situ (CIS), with or without papillary tumors who are ineligible or refuse radical cystectomy (RC). These results were featured in the Paradigm-Shifting, Practice-Changing Clinical Trials in Urology plenary session at the 2025 American Urological Association (AUA) Annual Meeting.

As of March 2025, 82.4 percent of the 85 enrolled patients in the study achieved a complete response (CR) (95 percent confidence interval [CI], 72.6-89.8), meaning their cancer was undetectable following treatment. This high response rate translated into sustained disease control, with 52.9 percent of responders maintaining complete response at one year. The median duration of response (DOR) was 25.8 months (95 percent CI, 8.3-not estimable), indicating that many patients remained cancer-free for over two years without the need for reinduction therapy. At 12 months, 86.6 percent (95 percent CI, 76.6-92.6) of responders remained cystectomy-free. Importantly, the treatment was well-tolerated, with most adverse events being mild urinary symptoms. These findings show that TAR-200 offers a highly effective and durable treatment option for patients with certain types of BCG-unresponsive HR-NMIBC.

TAR-200 is inserted directly into the bladder by a healthcare professional in a brief outpatient procedure, without the need for anesthesia. Designed to remain in the bladder, it does not interfere with daily activities and provides sustained release of treatment throughout the day. To date, TAR-200 has been placed more than 10,000 times as part of the SunRISe clinical program.

Phase 2b SunRISe-1 study shows more than 82 percent of patients achieved complete response (CR) with more than half of responders remaining cancer-free at one year after CR

Results reinforce potential of TAR-200 to transform outcomes for certain types of BCG-unresponsive, high-risk non-muscle invasive bladder cancer

Source: https://www.jnj.com/media-center/press-releases/johnson-johnsons-tar-200-monotherapy-demonstrates-highest-complete-response-rate-with-sustained-clinical-benefits-in-patients-with-certain-types-of-bladder-cancer

Akeso wins Chinese Approval for Cancer Drug Positioned to Rival Merck's Keytruda

Jonathan Wosen, *Stat+*, April 25, 2025 (excerpt)

Akeso, a Chinese biotech that made headlines for beating Merck's Keytruda in a head-to-head trial, won approval in China this week for the therapy, a company spokesperson confirmed to STAT. New data show early hints of the medicine improving patient survival — the gold standard outcome of any cancer study.

The drug, ivonescimab, was approved for previously untreated patients with non-small cell lung cancer who had detectable levels of PD-L1, a protein that tamps down immune responses. China's National Medical Products Administration greenlit the therapy based on results from a late-stage trial, HARMONi-2, which found Akeso's therapy reduced patients' risk of tumor progression by 49% compared with Keytruda.

In an email to STAT, an Akeso spokesperson noted that the interim analysis was not powered for statistical significance and that the company plans to conduct formal analyses of survival once 232 and 280 deaths have occurred in the trial.

Ivonescimab's approval as a monotherapy comes just a few days after the biotech announced that another late-stage study, HARMONi-6, showed that the drug in combination with chemotherapy "decisively beat" chemo and Tevimbra, a BeiGene drug that shares the same target as Keytruda, in improving progression-free survival.

Summit's stock price dropped sharply Friday after the ivonescimab survival analysis from the HARMONi-2 study was reported. While several analysts said the 22% reduced risk of death matched expectations at the interim analysis, some investors described the result as borderline meaningful, raising concerns that it could worsen, and not improve, when a final analysis is conducted. In a statement issued Friday, Summit noted the interim survival analysis was conducted with only 39% of the data mature, leaving ample room for improvement.

It's fascinating to see how high expectations were for ivonescimab OS data. The drug resulted in a 22% percent improvement in survival versus Keytruda®, the leading drug in the oncology market.

Source: https://www.statnews.com/2025/04/25/akeso-wins-chinese-approval-for-cancer-drug-ivonescimab-keytruda-rival/

Real World Data and Diagnostics Improving Clinical Trials in Oncology

Ashita Batavia, J&J, *McKinsey Interview*, April 2025 (excerpt)

Early on, we used real-world data to help us understand the populations we used for a trial, so they can help us understand the current standard of care and unmet needs. That supplementary research can help us down the road when we're looking to submit applications for regulatory approval. In larger trials, the real-world data can help you understand what centers to prioritize and where you can have the most efficiency for enrollment.

Also, real-world data that is collected retrospectively can help us find patients with a subset of the criteria, so we can flag them for closer evaluation before they are offered a trial or screening. This step can help accelerate enrollment and can streamline collection of care through technology interfaces.

We've also been able to use diagnostic-testing-based imaging algorithms to find patients. With the retrospective data, this effort can provide a lot of value for drug development. For example, if there is a promising new therapy in oncology or a rare disease, you don't want the standard of care to be random. An external control arm can populate the trial with prospective, real-world data and provide important context to improve the efficacy of a trial.

Real-world data can also be used to shape post-marketing commitments, safety signals, and clinical-trial tokenization. There's a wealth of applications of real-world data across that drug development continuum.

Ashita Batavia, Head of hematology and oncology data sciences, R&D, at Johnson & Johnson Innovative Medicine

Source: https://www.mckinsey.com/industries/life-sciences/our-insights/j-and-js-ashita-batavia-on-advancing-oncology-clinical-trials-with-data

Giant Drop in DNA Sequencing Cost

Jules Adam, *Labiotech*, April 25, 2025 (excerpt)

The journey of genome sequencing began in 1977 with Frederick Sanger's introduction of the chain-termination method, revolutionizing DNA sequencing by enabling the reading of longer DNA fragments with higher accuracy. This technique laid the groundwork for future genomic research and earned Sanger his second Nobel Prize, this time, shared with Walter Gilbert.

Building on this foundation, the Human Genome Project (HGP) was launched in 1990, aiming to map the entire human genome. After 13 years and an investment exceeding $2 billion, the HGP successfully completed the first human genome sequence in 2003.

The early 2000s have seen the emergence of next-generation sequencing (NGS) technologies, which transformed genomic research by significantly reducing sequencing costs and increasing throughput. In 2005, 454 Life Sciences introduced the GS20 platform, pioneering massively parallel sequencing. Not too long after, Illumina's acquisition of Solexa led to the development of sequencing-by-synthesis technology.

This all contributed to the significant decrease in sequencing costs, from approximately $95 million per genome in 2001 to around $600 by 2023. This cost reduction made genome sequencing more accessible for research and clinical applications.

While NGS technologies excelled in speed and cost-effectiveness, they often produced short reads, posing challenges in assembling complex genomic regions. This is why long-read sequencing technologies emerged, offering longer read lengths and improved assembly of repetitive regions. Companies like Pacific Biosciences and Oxford Nanopore Technologies have been at the forefront of this innovation.

Additionally, the pursuit of affordable whole-genome sequencing has been a driving force in genomics. In 2014, Illumina announced the HiSeq X Ten system, aiming for the $1,000 genome. By 2023, MGI Tech introduced the DNBSEQ-T20x2 sequencer, claiming to achieve a sub-$100 genome at scale. In 2024, Illumina's NovaSeq X series further reduced sequencing costs to approximately $200 per genome, bringing the $100 genome within reach.

Source: https://www.labiotech.eu/in-depth/genome-sequencing/

- **1977 – Sanger sequencing is born**

  British biochemist Frederick Sanger develops a technique for reading DNA, laying the groundwork for modern genomics.

- **1990 – The Human Genome Project begins**

  A massive international effort launches with the goal of decoding the entire human genome.

- **2003 – The first human genome is completed**

  After 13 years and over $2 billion, researchers finish sequencing the human genome, revealing more than 20,000 genes.

- **2005 – Next-generation sequencing kicks off**

  454 Life Sciences (later acquired by Roche) and other early platforms launch a new era of high-throughput sequencing, cutting costs and time.

- **2014 – Illumina introduces the $1,000 genome**

  With its HiSeq X Ten system, Illumina approaches a major affordability milestone, fueling clinical adoption.

- **2015 – Oxford Nanopore launches MinION**

  The first desktop, USB-connected sequencer, another step toward accessibility.

- **2021 – The first complete human genome is published**

  The Telomere-to-Telomere (T2T) consortium fills in all remaining gaps, delivering the first truly complete human sequence.

- **2023 – MGI achieves sub-$100 genome at scale**

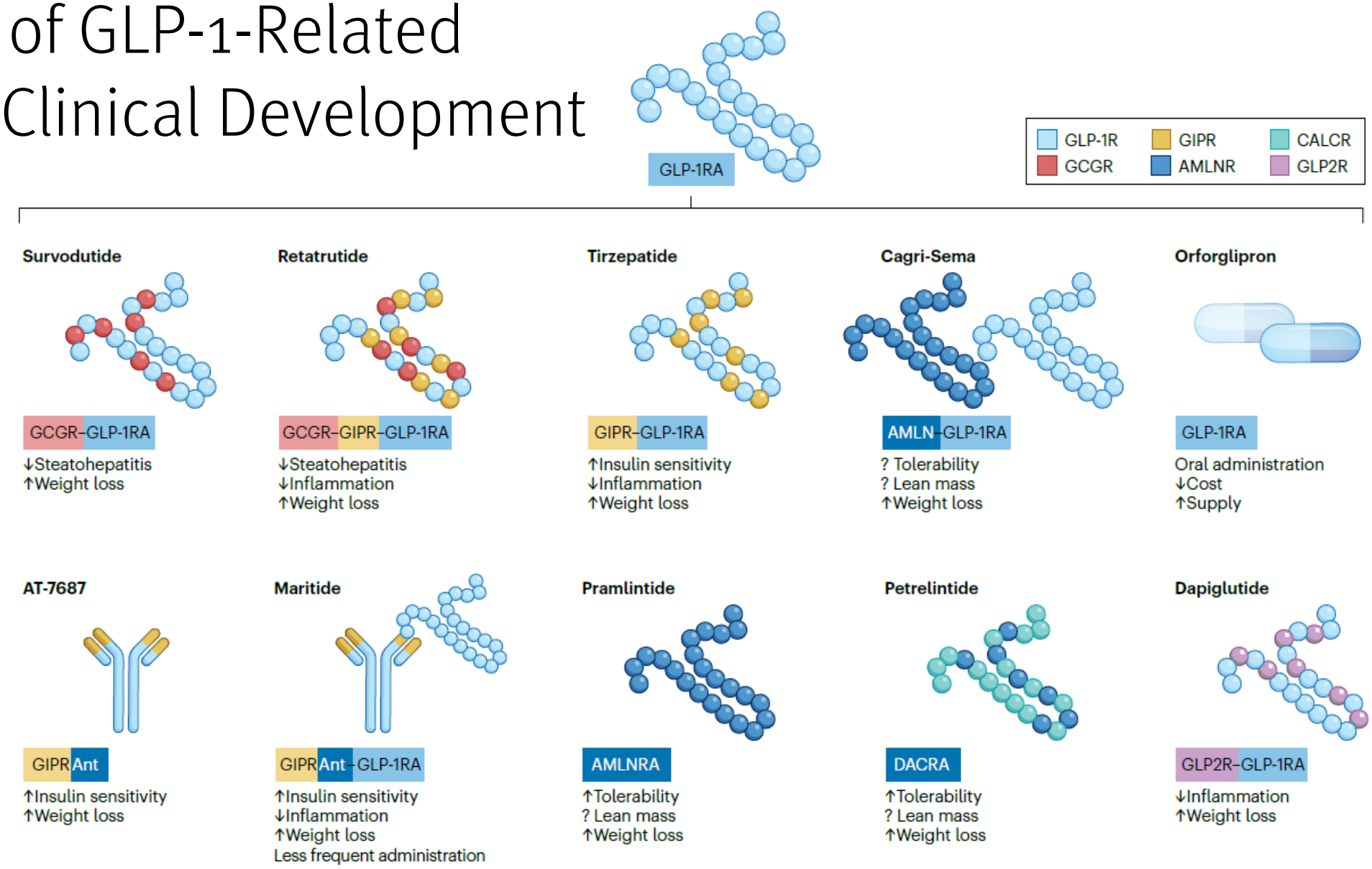
  Chinese company MGI unveils the DNBSEQ-T20×2 sequencer, breaking new cost barriers with industrial-scale throughput.

- **2024 – Illumina's NovaSeq X transforms the market**

  The new flagship platform boosts speed, reduces costs to ~$200 per genome, and brings clinical-grade sequencing closer to reality.

New Classes of GLP-1-Related Therapies in Clinical Development

Daniel Drucker, *Nature Reviews Drug Discovery*, April 25, 2025



Source: https://www.nature.com/articles/s41573-025-01183-8

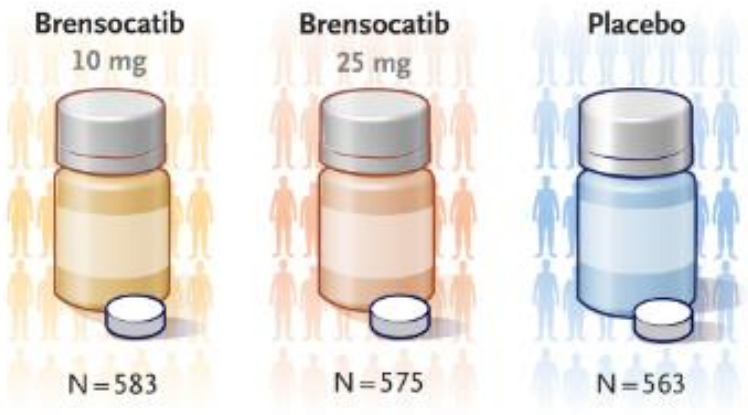
The NEW ENGLAND JOURNAL of MEDICINE

Phase 3 Trial of the DPP-1 Inhibitor Brensocatib in Bronchiectasis

A Research Summary based on Chalmers JD et al. | 10.1056/NEJMoa2411664 | Published on April 24, 2025

Patients

- 1680 adults; 41 adolescents
- Mean age, 60 years
- Female: 64%; Male: 36%

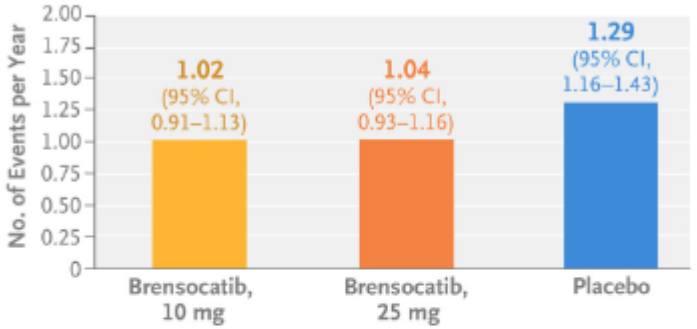


Annualized Rate of Pulmonary Exacerbations

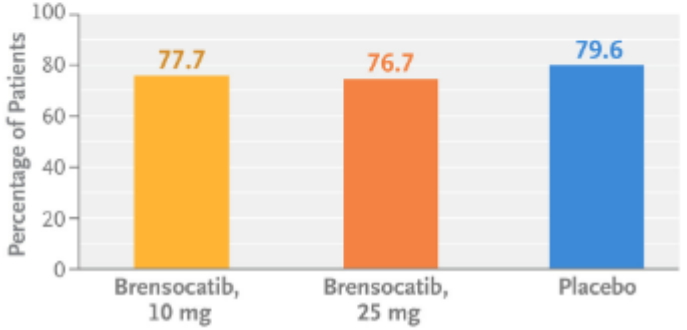
Rate ratio vs. placebo

Brensocatib 10 mg: 0.79 (95% CI, 0.68–0.92); adjusted P=0.004

Brensocatib 25 mg: 0.81 (0.69–0.94); adjusted P=0.005



Any Adverse Event



HOW WAS THE TRIAL CONDUCTED?

Adults and adolescents with non–cystic fibrosis bronchiectasis and exacerbations that led to antibiotic treatment in the previous year were assigned to receive brensocatib (10 mg or 25 mg) or placebo once daily for 52 weeks. The primary efficacy end point was the annualized rate of pulmonary exacerbations during treatment.

TRIAL DESIGN

- Phase 3
- Double-blind
- Randomized
- Placebo-controlled
- Location: 390 sites in 35 countries

RESULTS

The annualized rate of pulmonary exacerbations was significantly lower with both doses of brensocatib than with placebo. The incidence of adverse events overall and of adverse events leading to discontinuation of a regimen or withdrawal from the trial was similar across the groups.

Source: https://www.nejm.org/doi/full/10.1056/NEJMoa2411664

Fibromyalgia Eases After Doses of Gut Microbes

Humberto Basilio, *Nature*, April 24, 2025 (excerpt)

What Rina Green calls her “living hell” began with an innocuous backache. By late 2022, two years later, pain flooded her entire body daily and could be so intense that she couldn’t get out of bed. Painkillers and physical therapy offered little relief. She began using a wheelchair.

Green has fibromyalgia, a mysterious condition with symptoms of widespread and chronic muscle pain and fatigue. No one knows why people get fibromyalgia, and it is difficult to treat. But eight months ago, Green received an experimental therapy: pills containing living microorganisms of the kind that populate the healthy human gut. Her pain decreased substantially, and Green, who lives in Haifa, Israel, and is now 38, can go on walks — something she hadn’t done since her fibromyalgia diagnosis.

Green was one of 14 participants in a trial of microbial supplements for the condition. All but two reported an improvement in their symptoms. The trial is so small that “we should take the results with a grain of salt”, says co-organizer Amir Minerbi, a pain scientist at the Technion — Israel Institute of Technology in Haifa. “But it is encouraging [enough] to move forward.” The trial results and data from other experiments linking fibromyalgia to gut microbes are published today in Neuron.

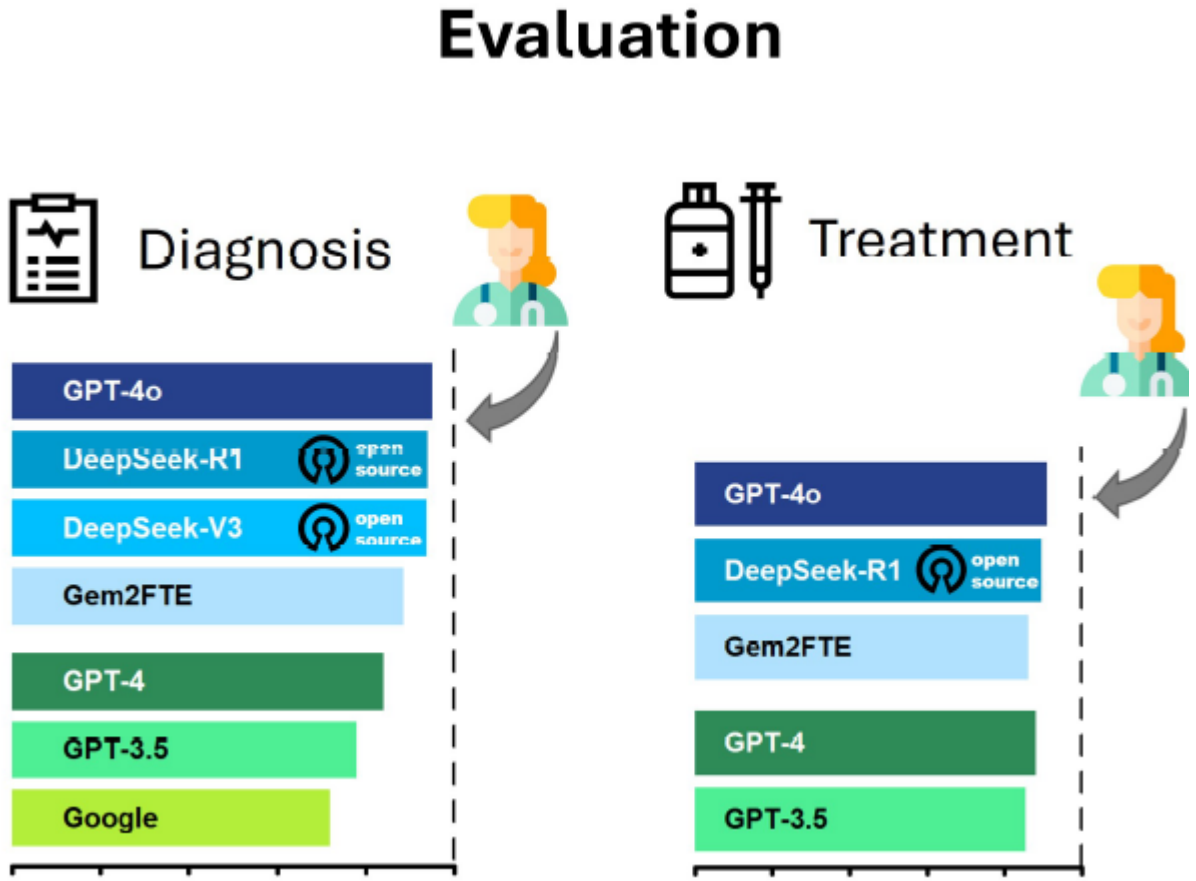
The trial had no control group, and all the participants knew that they were receiving the treatment — limitations that could skew the results. Even so, “these findings are really impressive”, says Andreas Goebel, a pain scientist at the University of Liverpool, UK, who was not involved in the research. He also notes the study’s limited sample size, but sees the improvements in some participants as a promising sign, given that people with treatment-resistant fibromyalgia “usually don’t respond to anything”, he says. “This is going in the right direction.”

Source: https://www.nature.com/articles/d41586-025-01290-x

DeepSeek Compares Quite Well to Proprietary LLM in Clinic

Sandmann, S., Hegselmann, S., Fujarski, M. et al. Benchmark evaluation of DeepSeek large language models in clinical decision-making. *Nature Medicine*, April 23, 2025

Large Language Models (LLMs) are increasingly transforming medical applications. However, proprietary models such as GPT-4o face significant barriers to clinical adoption because they cannot be deployed on site within healthcare institutions, making them non-compliant with stringent privacy regulations. Recent advancements in open-source LLMs such as DeepSeek models offer a promising alternative since they allow efficient fine-tuning on local data in hospitals with advanced IT infrastructure. To demonstrate the clinical utility of DeepSeek-V3 and DeepSeek-R1, we benchmarked their performance on clinical decision support tasks against proprietary LLMs, including GPT-4o and Gemini-2.0 Flash Thinking Experimental. Using 125 patient cases with sufficient statistical power, covering a broad range of frequent and rare diseases, we found that DeepSeek models perform equally well and in some cases better than proprietary LLMs. Our study demonstrates that open-source LLMs can provide a scalable pathway for secure model training enabling real-world medical applications in accordance with data privacy and healthcare regulations.

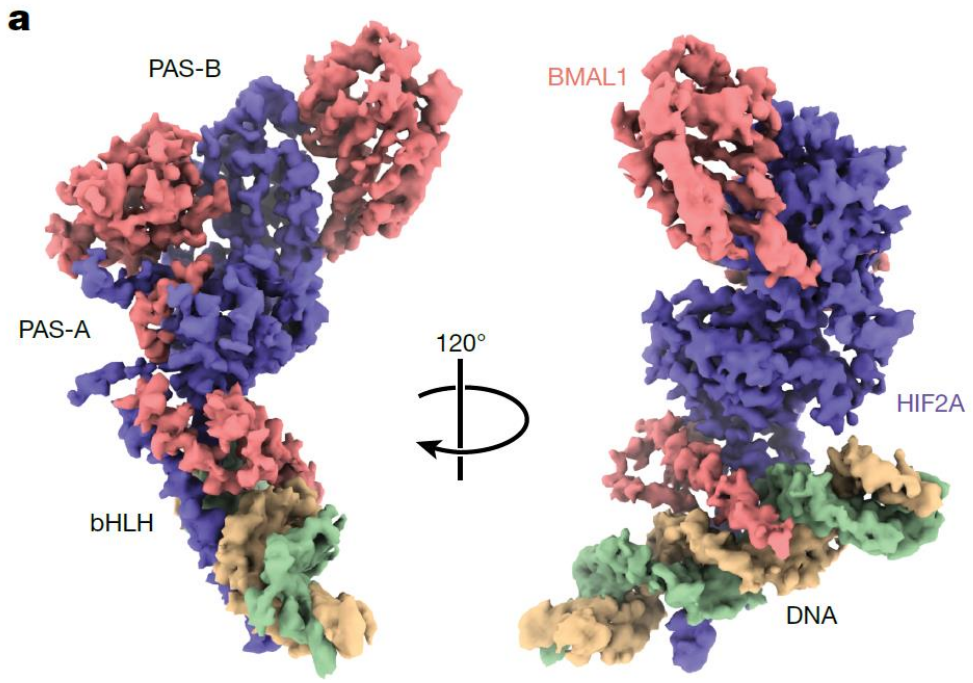


Source: https://www.nature.com/articles/s41591-025-03727-2

Why are Heart Attacks Worse in the Morning?

Ruan, W., Li, T., Bang, I.H. et al. BMAL1–HIF2A heterodimer modulates circadian variations of myocardial injury, *Nature*, April 23, 2025.

Acute myocardial infarction is a leading cause of morbidity and mortality worldwide. Clinical studies have shown that the severity of cardiac injury after myocardial infarction exhibits a circadian pattern, with larger infarcts and poorer outcomes in patients experiencing morning-onset events. However, the molecular mechanisms underlying these diurnal variations remain unclear. Here we show that the core circadian transcription factor BMAL regulates circadian-dependent myocardial injury by forming a transcriptionally active heterodimer with a non-canonical partner—hypoxia-inducible factor 2 alpha (HIF2A)—in a diurnal manner. To substantiate this finding, we determined the cryo-EM structure of the BMAL1–HIF2A–DNA complex, revealing structural rearrangements within BMAL1 that enable cross-talk between circadian rhythms and hypoxia signalling. BMAL1 modulates the circadian hypoxic response by enhancing the transcriptional activity of HIF2A and stabilizing the HIF2A protein. We further identified amphiregulin (AREG) as a rhythmic target of the BMAL1–HIF2A complex, critical for regulating daytime variations of myocardial injury. Pharmacologically targeting the BMAL1–HIF2A–AREG pathway provides cardioprotection, with maximum efficacy when aligned with the pathway's circadian phase.



Cryo-EM map of the BMAL1–HIF2A–DNA complex. The map was sharpened using DeepEMhancer. HIF2A and BMAL1 are coloured in purple and red, respectively, with two HRE DNA strands in green and yellow.

Source: https://www.nature.com/articles/s41586-025-08898-z

Disclosure

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