Biopharmaceutical Sector

Update – Nov 25, 2024

STIFEL | Healthcare

Table of Contents

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Past Issues

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

Nov 18, 2024 (New Administration)
Nov 4, 2024 (Election, Obesity)
Oct 21, 2024 (China, Pfizer)
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)
June 8, 2024 (Oncology Review)
May 27, 2024 (GLP-1's)
May 20, 2024 (Returning Capital)
May 13, 2024 (Brain, AlphaFold 3)
May 6, 2024 (Earnings, Obesity)
April 29, 2024 (M&A, Japan)
April 22, 2024 (Pharma Pricing)
April 15, 2024 (AI in Pharma)
April 8, 2024 (The Buyside)
April 1, 2024 (Biotech Balance Sheets)
March 25, 2024 (Women's Health)
March 18, 2024 (Inflammasome)
March 11, 2024 (IRA, Immunology)
March 4, 2024 (Biotech Employment)
Feb 26, 2024 (Biotech Strategy)
Feb 19, 2024 (Big Drugs, Autoantibodies)
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)
November 13, 2023 (AHA, Bear Market)
November 7, 2023 (Unmet Needs)
October 30, 2023 (ADCs)
October 23, 2023 (ESMO Review)
October 16, 2023 (Cancer Screening)
October 9, 2023 (Biosimilars, M&A)
October 2, 2023 (FcRn, Antibiotics)
September 25, 2023 (Target ID)
September 18, 2023 (Pharma Strategy)
September 11, 2023 (US Health System)
September 5, 2023 (FTC, IRA, Depression)
August 21, 2023 (Covid, China)
August 7, 2023 (Employment, Reading)
July 24, 2023 (Alzheimer's Disease)
July 7, 2023 (Biotech market review – H1 '23)
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 These Upcoming Events

Please join us this Friday at noon EST for the latest episode.

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

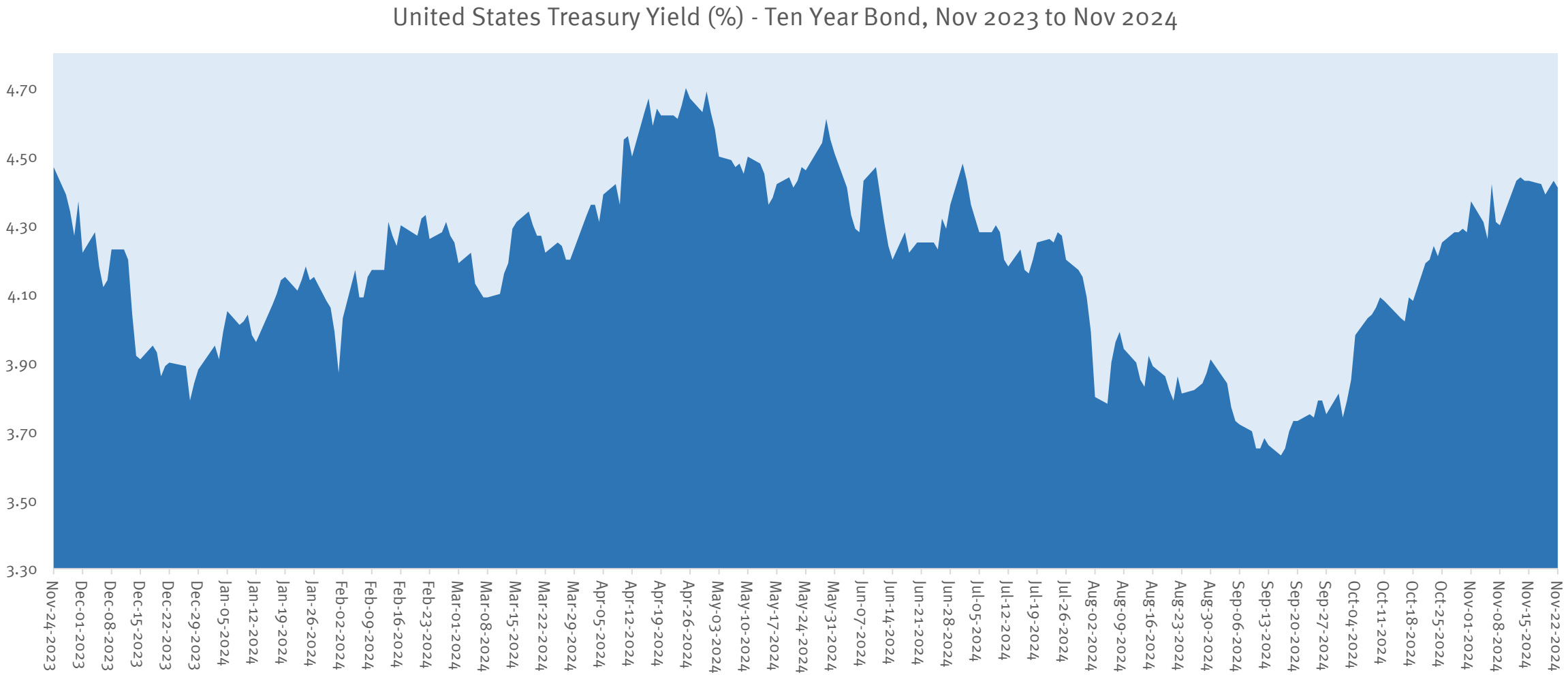
The week of Jan 13, 2025 will feature over 30,000 biopharma professionals in SF for JPM, Biotech Showcase and many other events. Stifel will be hosting an industry cocktail party on Jan 13th.

To meet with Stifel
yeungn@stifel.com

Macro Update

U.S. Treasury Bond Yields Remain Stubbornly High

Not good for biotech at all.



Source: S&P Capital IQ

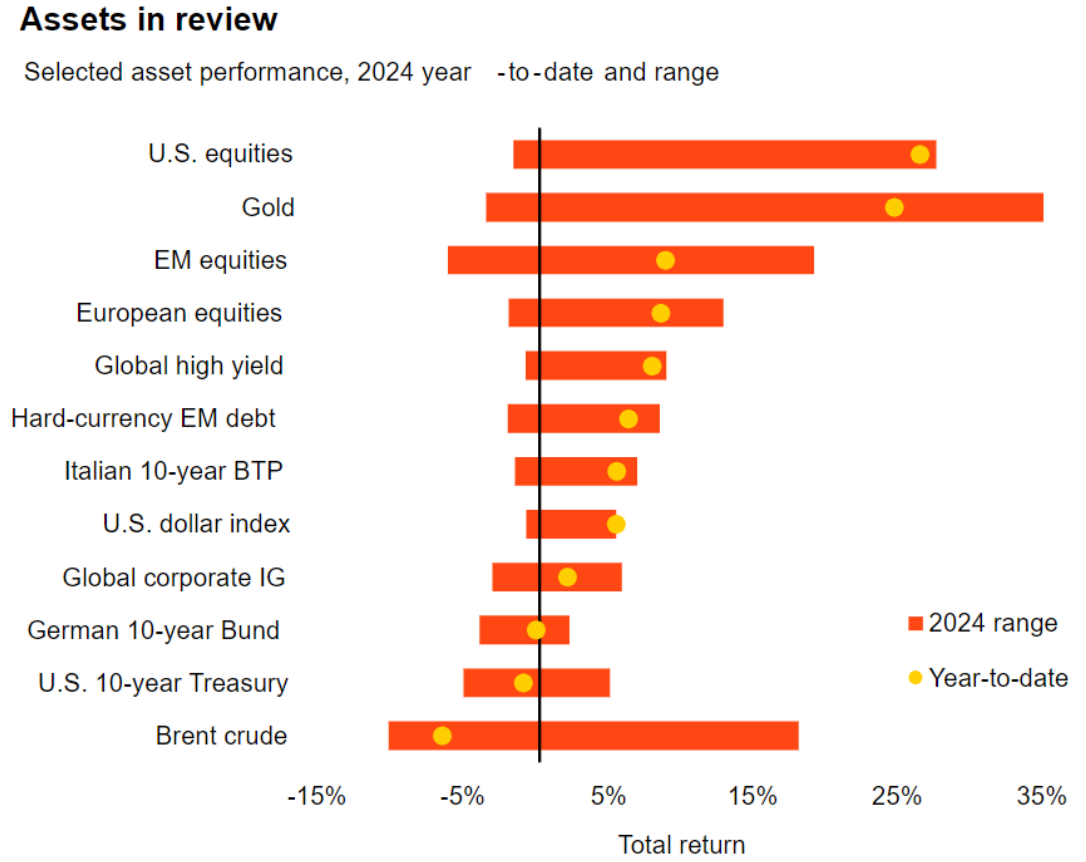
Blackrock Foresees Persistent Inflation Following Trump Election

Jean Boivin and Colleagues, Blackrock Investment Institute, Nov 18, 2024 (excerpt)

BlackRock.

Mega forces are playing a bigger role in shaping markets and economies – and driving returns now and in the future. Some of President-elect Donald Trump's proposed policies, such as large-scale tariffs, reinforce why we see persistent inflation in the medium term and interest rates staying above pre-pandemic levels.

If implemented, those policies could reinforce geopolitical fragmentation and economic competition. Plans to reduce legal immigration could impact the labor market. And we expect persistent budget deficits – one factor we see pushing up long-term U.S. Treasury yields.



Source: https://www.blackrock.com/us/individual/insights/blackrock-investment-institute/weekly-commentary

This Week's Inflation Report Will Heavily Influence the Fed's Direction on Rates

Jennifer Hughes, Mari Novik and Shotaro Tani, "How Bumpy is US Inflation?," *Financial Times*, November 24, 2024 (excerpt)

US inflation data on Wednesday will provide clues for investors on the likely timing and speed of interest rate cuts by the Federal Reserve next month.

Chair Jay Powell pushed the issue of rising prices back into the spotlight this month when he warned that progress on inflation had been more "bumpy" than expected.

Wednesday sees the latest reading for the Personal Consumption Expenditures index, the Fed's preferred inflation gauge. It is also a crucial piece of information ahead of the central bank's December meeting to set interest rates.

The core index, which strips out volatile food and energy costs, rose 0.3 per cent month on month in October, according to economists polled by Reuters. The headline rate is expected to have risen 0.2 per cent. In his speech, Powell said core PCE prices looked likely to have risen 2.8 per cent year on year in October.

Investors have sharply scaled back rate cut bets in the past month on a combination of already sticky inflation figures, Powell's comments and expectations that the incoming Trump administration's policies, such as plans to raise tariffs, will add to inflation and reduce the Fed's room to cut interest rates next year.

Deutsche Bank's US economists this week forecast PCE would stall "at or above" 2.5 per cent next year, up from previous expectations it would ease to 2 per cent. "The primary driver of this upward revision is a significant increase in tariffs," said Matthew Luzzetti, the bank's chief US economist.

Futures market bets that rates in June would be at least a full percentage point below current levels have fallen from a 50 per cent chance four weeks ago, to just a 10 per cent probability. Investors are still pricing in a 60 per cent change for a quarter-point cut in December. Jennifer Hughes

Source: https://www.ft.com/content/919027f1-9f7a-47ec-b77b-2c1f015d3908

Newly Chosen Treasury Secretary Focused on Tax Cuts

By Brian Cheung, Olympia Sonnier and Zoë Richards, *CNBC*, November 22, 2024 (excerpt)

President-elect Donald Trump on Friday announced he had asked Scott Bessent, a hedge fund executive and top fundraiser to his campaign, to serve as secretary of the Treasury Department.

In a statement regarding his pick, Trump said that Bessent "will help me usher in a new Golden Age for the United States."

"Unlike in past Administrations, we will ensure than no Americans will be left behind in the next and Greatest Economic Boom, and Scott will lead that effort for me," Trump said.

If confirmed by the Senate, Bessent will helm the fiscal policies for an economy that weathered high inflation in recent years, an issue that remained top of mind for many voters who helped send Trump back to the White House in the election earlier this month.

Trump's pick will be tasked with implementing any tax cuts that a Republican-controlled Congress may pursue. And with Trump proposing aggressive tariffs on imports from countries spanning the globe, the new Treasury Department chief will have to manage relationships with global finance ministers who may choose to retaliate with tariffs of their own.

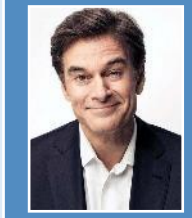
Source: https://www.nbcnews.com/politics/donald-trump/trump-picks-scott-bessent-serve-treasury-secretary-rcna180171

Trump Health Appointments

Current List of Healthcare Appointees in Trump Administration

President-Elect Donald Trump completed making his healthcare appointees late last week. Of the new appointees, those with the highest importance to the biopharmaceutical industry are Mehmet Oz (Head of CMS) and Martin Makary (Head of FDA). We will dig into these appointments in this section.

Robert F. Kennedy, Jr. (appointee), Department of Health and Human Services, Secretary



Mehmet Oz, MD (appointee), Head Centers for Medicaid and Medicare Services, CMS

Dave Weldon, MD (appointee), Head Centers for Disease Control and Prevention (CDC)

Martin Makary, MD (appointee), Head, Food and Drug Administration (FDA)

Janette Neshiewat MD (appointee) Surgeon General

Note: there has not been a new appointment made to head the NIH. In his last administration, Trump did not replace Francis Collins, the head of the NIH at the time.

Mehmet Oz Appointed to CMS Role

Tami Luhby, Kate Sullivan and Alayna Treene, *CNN*, November 19, 2024 (excerpt)

"President-elect Donald Trump has picked Dr. Mehmet Oz to serve as the administrator for the Centers for Medicare and Medicaid Services, a key federal agency that oversees health insurance coverage for more than 150 million Americans.

"I have known Dr. Oz for many years, and I am confident he will fight to ensure everyone in America receives the best possible Healthcare, so our Country can be Great and Healthy Again!" Trump said in a statement on Tuesday. "Dr. Oz will be a leader in incentivizing Disease Prevention, so we get the best results in the World for every dollar we spend on Healthcare in our Great Country."

Trump, who is also seeking to slash spending in the federal government and has long had Medicaid in mind for reductions, also promised Oz would take a scalpel to the massive agency. "He will also cut waste and fraud within our Country's most expensive Government Agency, which is a third of our Nation's Healthcare spend, and a quarter of our entire National Budget," the president-elect said in his statement.

His views on Covid-19, however, sparked controversy. Early on in the pandemic, for instance, Oz talked up the antimalarial drug hydroxychloroquine as a way to treat the coronavirus — despite the lack of firm scientific evidence that it was an effective treatment. Many of Oz's perspectives were praised by Republicans at the time.

Oz's selection continues Trump's string of unconventional picks for key roles in his administration, including Robert F. Kennedy Jr. for secretary of the Department of Health and Human Services. If they are both confirmed, Kennedy would be Oz's boss. For CMS administrator in his first term, Trump chose Seema Verma, who had a long history in health policy and consulting with a specialty in Medicaid. (continued)

Source: https://www.cnn.com/2024/11/19/politics/mehmet-oz-trump-medicare-medicaid/index.html

Oz has long voiced support for Medicare Advantage, a fast-growing program in which the federal government pays private insurers to provide coverage to senior citizens and disabled Americans. In his Senate campaign, he supported a health care plan called "Medicare Advantage Plus," an expansion of the popular program."

Not All Are Positive on Dr. Oz

Helaine Olen, reporter in residence at the Omidyar Network, Editorial, *MSNBC*, Nov 21, 2024 (excerpt)

There are many reasons to oppose Donald Trump's decision to appoint Dr. Mehmet Oz to lead the Centers for Medicare and Medicaid Services. Oz is a snake oil salesman who has promoted quack cures on television and hawked bogus weight loss products. He has zero experience leading a large bureaucracy, never mind a large health care one like CMS. But Oz's track record on Medicare, which covers about 66 million people, should concern us the most.

History suggests Oz will seek to boost the use of Medicare Advantage, further privatizing the program — and that he'll do it with the support of Trump. This, in turn, will drain government coffers while leaving many seniors in poorer health. Medicare Advantage is, in fact, a worthy target for the volunteer commission known as Department of Government Efficiency, led by Elon Musk and Vivek Ramaswamy, which ostensibly aims to make government less wasteful and costly.

At the same time, the increasingly consolidated health care conglomerates offering up Medicare Advantage plans are raking in the bucks. The gross margins on the plans covering Americans over the age of 65 are more than double those of other health insurance offerings, including the coverage Americans receive via their employers. Such profits are helping fuel an epic mergers and acquisitions spree by the health care giants, which puts further strain on the American health care system. That Oz likes Medicare Advantage and thinks everyone, regardless of age, should have it shouldn't come as a surprise. Like the once and future president appointing him to run CMS, he is a huckster at heart. (Research published in the British Medical Journal in 2014 found that less than half of the medical recommendations on Oz's TV show were supported by evidence. During the early days of the coronavirus pandemic, he also, contrary to evidence, suggested chloroquine and hydroxychloroquine were effective treatments for that virus.)

Last week's media stories about Dr. Oz's appointment to the CMS position were almost universally negative.

While we agree that Dr. Oz does not have substantial administrative experience, his views on Medicare Advantage are not necessarily a negative as this program has many positives. It's worth bearing in mind that more than half of Medicare beneficiaries have *voluntarily chosen* to join this program.

Perhaps more concerning, privatization of traditional Medicare is not necessarily good for pharma as it may concentrate more power in groups like UnitedHealthcare and CVS that negotiate against pharma on drugs prices and also have PBM subsidiaries. Our sense is that the Trump Administration is well aware of the risks of this dynamic.

Source: https://www.cnn.com/2024/11/19/politics/mehmet-oz-trump-medicare-medicaid/index.html

Trump Nominates Martin Makary to Lead FDA: A Bold Move for U.S. Healthcare

***DevDiscourse*, November 23, 2024 (excerpt)**

U.S. President-elect Donald Trump has nominated Dr. Martin Makary to head the FDA, aiming to streamline processes and improve public health standards. Makary, a Johns Hopkins surgeon and author, emphasizes reducing overtreatment in healthcare and questioned COVID vaccine mandates, signaling a shift in the agency's direction.

In a significant reshuffle, U.S. President-elect Donald Trump has appointed Dr. Martin Makary, a respected surgeon and author, to lead the U.S. Food and Drug Administration (FDA). This nomination aims to revamp the agency, responsible for regulating drugs, devices, and food safety within the nation's vast healthcare market.

Dr. Makary is widely known for his work at Johns Hopkins Hospital and his recent book, 'Blind Spots: When Medicine Gets It Wrong.' He has been vocal about the issue of overtreatment in American healthcare, calling it an epidemic. Makary's appointment suggests an upcoming shift in the FDA's focus towards addressing inefficiencies and unnecessary treatments.

Makary will report to the nominee for the Department of Health and Human Services, Robert F. Kennedy Jr., if confirmed by the Senate. **Under his leadership, the FDA may introduce reforms to expedite the approval of medical cures and treatments, aligning with Trump's vision of cutting bureaucratic red tape.**

We have spoken to a number of healthcare investors who are enthusiastic about Dr. Makary's FDA appointment for biotech.

He has written more than 100 articles that show a rational, thoughtful man who is deeply interested in getting medicine right.

At the same, Dr. Makary is an iconoclastic individual – quick to point out the foibles of modern medicine and instances where regulatory agencies may not have gotten all decisions right.

We would expect that Makary will be data driven and industry friendly. We think reasonable moves can be expected like (1) considering data from foreign countries without full replicative trials in the US, (2) taking a Bayesian approach, (3) considering the costs of trials and FDA rules relative to the societal risks and potential benefits. His views are likely to be aligned with those of Vivek Ramaswamy and also echo, in many ways, those of Mark McLellan, FDA Commissioner under George W. Bush.

Source: https://www.devdiscourse.com/article/health/3167710-trump-nominates-martin-makary-to-lead-fda-a-bold-move-for-us-healthcare

‘We Dodged a Bullet’: Biotech and Pharma React to Selection of Marty Makary for FDA commissioner

Stat+, November 23, 2024 (excerpt)

STAT reporters reached out to key figures in biotech, pharma, and medical devices to find out what they think about President-elect Trump’s pick of Johns Hopkins pancreatic surgeon Martin “Marty” Makary as commissioner of the Food and Drug Administration. Makary, like Trump’s intended Health and Human Services selection, Robert F. Kennedy Jr., is part of the “Make America Healthy Again” movement, focused on addressing chronic disease. He was also a critic of some Covid-19 pandemic measures, including vaccine mandates.

Anonymous biotech investor

“We dodged a bullet. I didn’t want someone who would just approve everything without efficacy standards, nor did I want someone who would say no to any pharma drug, or see pharma companies as corrupt entities, no matter what. Marty Makary is neither extreme.

“How do FDA staff react to this pick? That’s the more interesting question, and still my biggest concern as a long-time investor in the sector. Had the pick been one of the other insane clown-car folks, I would have absolutely sold my portfolio down. With Makary, I am more wait and see, but at least somewhat reassured by the pick.”

Anonymous biotech VC

There is a “great opportunity for him to bring the FDA forward” with “pragmatic, patient-focused reform.” His nomination is “going to be very well received by patients and the industry, because he understands science and data, but also that the system is broken. The key issue is retaining people. FDA needs leadership. There hasn’t been good leadership since Scott Gottlieb. … [Robert] Califf is a non-entity. [The FDA] needs a leader who will get more drugs on the market. Stirring it up a little is good.

“People have been worried about RFK Jr. [Makary’s nomination] means some change at the FDA, but data-driven change. I’ve asked around with some people I know, and Makary will be well-received. Not universally — there are some controversial views. But there’s some opportunity in all this.

“There will be uncertainty for a while. But in the long term, the biggest risk to industry is over-regulation, that there are promising therapies that never see the light of day.”

Anonymous biotech VC

“I think there’s a sigh of relief across the industry. … He’s not gonna blow up the agency. I think that’s right on balance. And everyone in the ecosystem has every incentive to work with whoever is out forward. And on the credentials, he’s at least above bar.”

Source: https://www.nytimes.com/2024/11/22/health/fda-commissioner-marty-makary-rfkjr.html

FDA Commissioner Designate Will Fight for Science

> **I believe Marty Makary is a man of science. I think he will look at the scientific evidence carefully and interpret it using the training and skills that he has.**

Jennifer Nuzzo
Director of the Pandemic Center and Professor of Epidemiology
Brown University
Nov 24, 2024

Source: https://www.nytimes.com/2024/11/22/health/fda-commissioner-marty-makary-rfkjr.html

Trump's Choices for Health Agencies Suggest a Shake-Up Is Coming

Emily Anthes and Emily Baumgaertner, *New York Times*, Nov 23, 2024 (excerpt)

A longtime leader of the anti-vaccine movement. A highly credentialed surgeon. A seven-term Florida congressman. A Fox News contributor with her own line of vitamins.

President-elect Donald J. Trump's eclectic roster of figures to lead federal health agencies is almost complete — and with it, his vision for a sweeping overhaul is coming into focus.

Mr. Trump's choices have varying backgrounds and public health views. But they have all pushed back against Covid policies or supported ideas that are outside the medical mainstream, including an opposition to vaccines. Together, they are a clear repudiation of business as usual.

"What they're saying when they make these appointments is that we don't trust the people who are there," said Dr. Paul Offit, director of the Vaccine Education Center at Children's Hospital of Philadelphia and an adviser to the Food and Drug Administration.

Some doctors and scientists are bracing themselves for the gutting of public health agencies, a loss of scientific expertise and the injection of politics into realms once reserved for academics. The result, they fear, could be worse health outcomes, more preventable deaths and a reduced ability to respond to looming health threats, like the next pandemic. "I'm very, very worried about the way that this all plays out," Dr. Offit said.

But other experts who expressed concerns about anti-vaccine views at the helms of the nation's health agencies said that some elements of the picks' unorthodox approaches were welcomed. After a pandemic that closed schools across the country and killed more than one million Americans, many people have lost faith in science and medicine, surveys show. "We are playing with fire with the shake-ups and choices, but at this point change is needed," said Dr. Michael Mina, an epidemiologist and former Harvard professor. He said the agencies were often too slow and bureaucratic, and their leaders too unwilling to engage with the public's concerns. "At least there's a better chance of positive change compared to complacency and more of the same," he said.

One thing seems certain: It will not be more of the same.

Source: https://www.nytimes.com/2024/11/23/health/trump-kennedy-health-agencies-vaccines-covid.html

Accelerating Innovation at HHS / FDA a Key Priority to Get Costs Down

> Healthcare is a critical frontier for DOGE. I met with Marty Makary, Mehmet Oz, and other incoming health appointees this week. It's clear they're serious about reducing cost & they understand innovation is a key part of the solution (not the problem). I left impressed with the team @RobertKennedyJr is building. I don't say that lightly.

Vivek Ramaswamy

Nov 24, 2024

Views Expressed by Martin Makary in his Recent Book “Blind Spots”

Positive on GLP-1’s But Would Like to See Long-Term Studies on Survival Effect. Interested in Measures to Preserve Muscle Mass During Weight Loss

Highly celebrated GLP-1 medications like Ozempic and Rybelsus appear to be effective not only for losing weight, but also in reducing the health problems associated with obesity such as heart disease, liver disease, and renal failure. But studies showing these benefits have looked at outcomes in the first few years of use. In the long run, are these medications good for your health? While we can have our opinions, the truth is we don’t yet know.

This class of medications appears to both reduce excess fat *and* muscle mass. Muscle mass is the leading predictor of longevity. Loss of muscle mass is a component of the frailty syndrome.[62] And loss of muscle mass is one reason why doctors who prescribe GLP-1 drugs are keen to make sure that people taking them exercise and get enough protein in their diet.

While it appears that we are seeing exciting health benefits from these medications, we have to be open to the fact that future research could tell us that people on them long-term ultimately live longer, or shorter lives.

p. 216

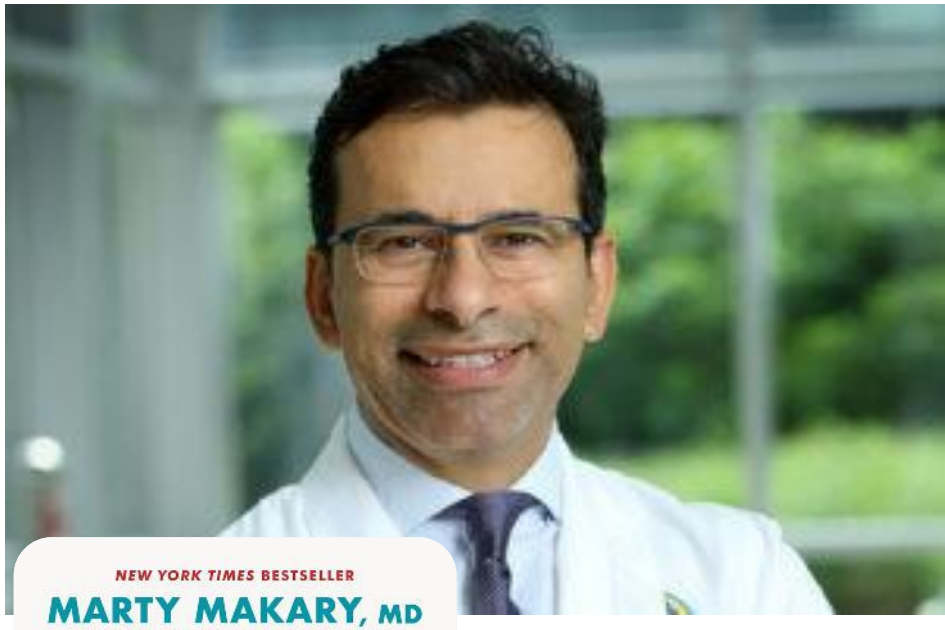
Sees a Medical Establishment that Doesn’t Ask The Right Questions. Sees HRT in menopause as a positive.

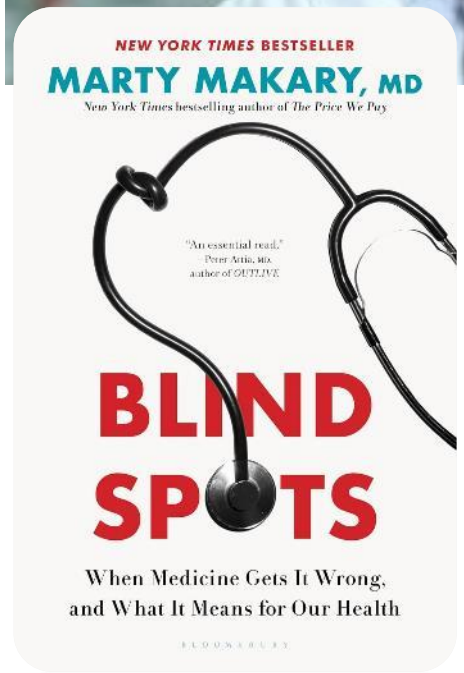
p. 220

In science, you have to be able to ask questions. So let me pose a big one: Could it be that many of our modern-day health crises were caused by (or hastened by) the hubris of the medical establishment?

Experts told people *for decades* that opioids were not addictive—igniting the opioid crisis. They insisted infants avoid peanut butter—fueling the peanut allergy epidemic. They demonized natural fat in foods—driving people to processed carbohydrates as obesity rates soared. They prescribed antibiotics haphazardly—altering the gut microbiomes of a generation and causing a drug-resistant bacteria epidemic. They unfairly used fear to scare women away from HRT, resulting in a generation of women being denied the life-extending and quality of life benefits. And some might say that “experts” experimented on a bat coronavirus in the lab for no good reason, causing a global pandemic.

Medical dogma continues to looms large. Sometimes because people are railroaded for asking questions, and sometimes because loud medical establishment leaders who got things perfectly backward have never apologized for their decades-long hubris.





Source: https://www.amazon.com/dp/1682193519/

More Views Expressed by Martin Makary in his Recent Book

Bitingly Critical of Opponents of HRT in Menopause – not Positive on Expensive Alternatives to HRT

The first study looked at 56,000 women over two decades. Researchers from the University of Minnesota and the NIH found that the women who took HRT had a 25 to 45% decreased risk of colon cancer, depending on the type and duration of HRT used.[35] Another study, by the American Cancer Society, analyzing 67,000 women, found that HRT use was associated with a 24% decreased risk of colorectal cancer.[36] Finally, the *Journal of Clinical Oncology* reported in a study of more than 2,600 Israeli women that HRT was associated with a 63% reduction in the risk of colorectal cancer in postmenopausal women.[37] The microbiome, the bacterial layer that lines the gut, may also play a role, a topic we'll explore in the next chapter.

Other Surprising Benefits

One reason couples stop having sex when a woman goes through menopause is because of vaginal dryness, making sex painful for some women. Estrogen reduces vaginal dryness. Incidentally, women also report that HRT alleviates the dryness they notice in their nose, mouth, eyes, and scalp. Doctors tell me they have saved marriages by prescribing HRT to women. "The mental health improvement is palpable," one of them told me.

HRT may also help prevent diabetes. WHI researchers, with all their skepticism about HRT, reported in 2004 that women on HRT had a 21% lower risk of diabetes.[38] One possible mechanism for the reduction in diabetes is that women on HRT feel better, may be more active, and thus have less of the weight gain typically seen with menopause. That could be why a systematic review published in 2017 found that HRT delays the onset of Type 2 diabetes.[39,40] While the data are considered less definitive than for the other benefits of HRT, the potential implications are significant. One in seven U.S. women has diabetes.[41,42]

Finally, because HRT helps with bone density, there is also a dental benefit. A 2017 study found that severe gum disease was 44% lower in women who were taking HRT.[43] Another study by South Korean researchers found that postmenopausal women had a higher risk of gum disease, and that HRT could reduce its incidence.[44] Yet another little-known health benefit of HRT.

Overall, HRT may do more to improve the health of women over age 50 on a population level than any other medication in history.

A Few Notable Exceptions

While HRT has a long list of dramatic short-term and long-term health benefits, it is not for everyone. Some oral forms of estrogen have been suggested to slightly increase the risk of a blood clot. But this is not the case for transdermal estrogen. The very low risk of a blood clot is akin to that of oral contraceptive pills. Women with risk factors for developing a blood clot may be advised against the oral form.

For some women with endometriosis, estrogen can make it worse. Furthermore, some women who take HRT may not tolerate it because it can cause a resumption of bleeding or irritability and moodiness. Not everyone does well with it. Also, as above, no one recommends starting HRT more than ten years after menopause. Women should also be aware that the type and quality of estrogen and progesterone matter. There are "pill mills" carrying HRT made with poor quality control. Some clinics say they only offer surgically implanted pellets for HRT when women should really be offered all options, including topical, oral, and implantable.

Lowering Drug Costs

As I write this book, the FDA just approved the first medication to treat hot flashes, Veozah.[45] Already I'm noticing a barrage of Veozah ads on TV. While the ads do not have the standard people dancing and singing, Veozah does market itself as hormone-free. The obvious question that comes to my mind: Why would a healthy woman take this new medication to treat one menopausal symptom when she could take HRT to treat the same symptom and get the full spectrum of short- and long-term health benefits?

For a woman who can't take HRT, such as someone with a predisposition to blood clots or someone with active breast cancer, Veozah seems like a great medication. But otherwise, it makes no sense to me. Plus, it's much more expensive than HRT. A one-year supply of Veozah costs $7,386 at my local Costco.

As politicians scratch their heads trying to figure out how to lower drug costs in the U.S., here's a simple idea: The best way to lower drug costs in the U.S. is to stop encouraging patients to take expensive drugs when there are less expensive alternatives.

The Aftermath and Legacy

Drs. Avrum Bluming, Carol Tavris, Phil Sarrel, and others have dedicated their lives to educating doctors about the truth about HRT. Dr. Sarrel is among a group of experts from around the country who now run a foundation to educate women and physicians about the best data on the topic.[46] Visana is another group helping women navigate the healthcare system to find good care.

The leaders of the WHI have done tremendous damage to public health. Dr. Sarrel and a team of researchers published a study that estimated that up to 91,000 women have died prematurely from HRT avoidance in the first decade after the infamous WHI press conference. Dr. Sarrel told me that in the last ten years, there have been at least another 50,000 premature deaths due to the misinformation put forth by WHI leaders.[47] Looking back, telling women to avoid HRT because it causes breast cancer may have been the biggest error in modern medicine.

Women deserve an apology.

Yet, inexplicably, the dogma is still alive and well. This year, the U.S. Preventive Services Task Force, an influential board of doctors in America, renewed its guidance to avoid HRT to prevent chronic conditions because of the risk of breast cancer. The Task Force's statement read, "The USPSTF recommends against the use of combined estrogen and progestin for the primary prevention of chronic conditions in postmenopausal persons." In response, strong articles by Dr. Langer and others pointed out the fallacy of the recommendation and urged them to take a hard look at the evidence.[48,49]

More Views Expressed by Martin Makary in his Recent Book

Positive on Testosterone Replacement for Men p. 209-210

When we doctors are asked about a new treatment, our first reaction is to find out if it's backed up by a robust study. If we don't have a study, we get uncomfortable with uncertainty. We are trained to dismiss the issue. Until recently, testosterone replacement for men has been in that gray zone. (The role of food and vitamins in overall health has also been relegated to the same medical purgatory.)

It's also easy to be turned off by all the shady pill shops pushing testosterone. But if we're being objective, we shouldn't dismiss something because we don't like those who are supporting it.

Many midlife men struggle with low energy, weight gain, sleep apnea, depressed mood, and sexual dysfunction. Sometimes they discover their free testosterone level is low upon testing and told about the option of testosterone replacement therapy (TRT).

New research is emerging about the benefits of TRT in men with low T. Doctors who frequently prescribe TRT for men tell me that they are seeing their patients feel better, increase their libido, and lose weight, which can subsequently alleviate their sleep apnea. Dr. Mark McCormick in South Florida tells me he's seen people come off their CPAP machines with TRT. Wow. Imagine the potential implications for better health through better sleep, not to mention the savings of being off the CPAP. Poor sleep is bad for the heart and contributes to high blood pressure, weight gain, and possibly Alzheimer's.[43] Dr. McCormick is also seeing his patients on TRT exercise more and improve their self-confidence.

There are both similarities and important differences between TRT in men and hormone replacement therapy (HRT) in women. HRT and TRT work differently, and thus TRT should not be regarded as the male equivalent of HRT. Estrogen offers more profound benefits by keeping blood vessels soft and healthy in postmenopausal women. To varying degrees, both HRT and TRT result in higher bone density[44] and lower fat mass,[45] and help with blood-sugar levels in people with Type 2 diabetes.[46]

In the same way that HRT has been accused of causing breast cancer, TRT has been alleged to cause prostate cancer, an allegation that has not been well supported in studies. There are also cardiovascular concerns. TRT may increase the risk of cardiovascular problems by a small effect size in everyone who takes it, and that risk may increase when men start TRT after the onset of heart disease.

Negative on Grail's Early Cancer Detection Test p. 203

I don't mean to rain on the parade, but before we throw $60 billion in taxpayer dollars at this test, let's see how many lives it truly saves. We should also weigh the cost against other ways we could spend that large amount of money: on prenatal vitamins, buying food for hungry children in America, and ending the dumping of raw sewage into my local river.

Would I trust handing over my genetic information to this company? Not at this point. It's not hard to imagine the mishandling of this collected genetic data. In 2023, the company mistakenly sent letters to 400 of its customers informing them they might have cancer. Half of the people had not even had the Galleri test done yet. *Yikes!* Even more concerning is that the company knew about this error but failed to disclose it until *after* its shareholder proxy vote.

I believe in early cancer detection and hope liquid biopsies can save lives in the future, but this test is not quite ready. If it is broadly rolled out now, I worry about the hundreds of thousands of people who will undergo invasive tests because of false negative results. Certainly, the medical-industrial complex is poised to generate a lot of business, but will it improve health? Before we as a medical profession and country get sold on testing all Medicare beneficiaries with a novel test, let's make sure it saves more lives than it destroys.

Worries About Legalization of Marijuana p. 200

The belief that marijuana is safe and definitely not a gateway drug looms large in society today, even among some doctors. Two dozen states have legalized recreational use of marijuana, as of 2023,[4] and its use has become mainstream. But could it be that we are convincing ourselves what we want to be true?

The marijuana of today is not the marijuana of hippies from decades ago. In the last several years, manufacturers got smart and now, compared to the 1970s, it includes ten times as much *tetrahydrocannabinol*, the psychoactive component better known as THC.[5] It also may be more harmful to adolescents than to adults,[6] which is why an adult's anecdotal experience should not become the basis of a firm scientific position on the issue in children. The developing adolescent brain may be more susceptible to long-term damage.

A study by Swedish researchers found that young people who used marijuana had up to a sixfold increased risk of developing schizophrenia compared to those who did not. Other studies have found that as many as 1 in 10 young people who use marijuana will develop psychotic symptoms later in life. In a review by Ann Abouseif at Harvard University, she found "an apparent correlation between early cannabis use and several neurological and psychological adverse consequences in adolescence and continuing into adulthood."[7]

Marijuana also seems to be worsening our teenagers' mental health crisis. A McGill–Oxford meta-analysis found a 37% increased risk of depression and more than a 300% increase risk in suicidal ideation among adolescents who used cannabis.[8]

Marijuana may also affect intelligence. One study suggested that an earlier onset and frequent use during adolescence was directly associated with declines in verbal IQ and executive function tasks, such as trial and error learning and conditional association learning.[9]

Finally, it's well known in the field of cardiology that marijuana use increases the risk of heart attack and stroke—a 25% and 42% increase respectively, according to a 2024 study published in *JAMA*.[10]

Between the risk of psychosis, increased rates of anxiety and depression, and cardiovascular disease, "harmless" is not the word I would use to describe the drug. Sure, it may be less lethal than cocaine, but it's not exactly an organic kale salad.

People should be aware of these risks. Afterall, marijuana is the most common drug used by adolescents.[11]

I'll acknowledge that there are *underappreciated* health benefits to THC, the active ingredient in marijuana. I've seen patients with Crohn's disease and terminal cancer benefit from "medical marijuana." But that doesn't mean it's safe for young developing minds.

Wants Us to Try Alternatives to Pharmaceuticals First p. 192

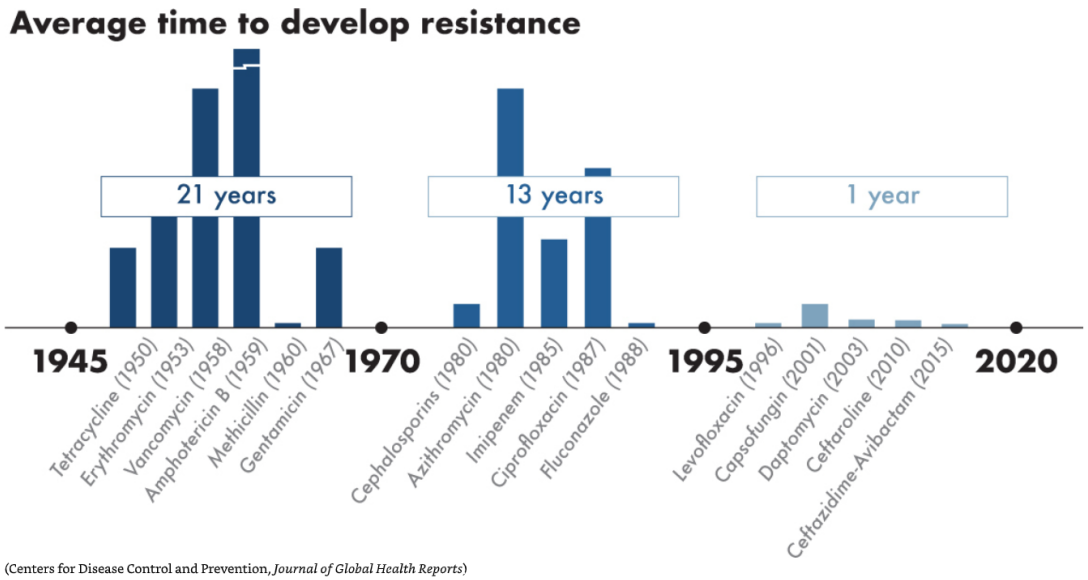
I'm encouraged by a new generation of health professionals who are willing to get off the hamster wheel of medicine. They aspire to be renaissance thinkers, not cogs on a corporate wheel. They have no allegiance to tradition when it conflicts with an opportunity to make a difference. Social justice is a generational value, and to do something bigger they are willing to explore hybrid medical careers.

Many are starting companies or joining start-ups that are disrupting the way medicine is delivered. Together, we're asking new questions. For example:

- Can diabetes be more effectively treated with a cooking class than by prescribing insulin?
- Can we lower high blood pressure by improving sleep quality and reducing stress instead of throwing anti-hypertensive medications at people?
- Can we discuss school lunch programs, not just bariatric surgery and Ozempic?
- Can we treat the epidemic of loneliness by fostering communities instead of simply prescribing antidepressants?
- Can we study the impact of body inflammation on health?
- Can we study environmental exposures that cause cancer, not just the chemotherapy to treat it?

Source: https://www.amazon.com/dp/1682193519/

Martin Makary Highly Concerned About Antibiotic Resistance



(Centers for Disease Control and Prevention, *Journal of Global Health Reports*)

It used to take 21 years on average for bacteria to become resistant to a new antibiotic. Now it takes an average of one year. Today, the CDC lists different types of antibiotic-resistant bacteria that are circulating in the U.S. It classifies five of them as "urgent threats" to human health.[46] This is an emerging crisis. The patient I operated on was but one casualty.

The carnage of the Covid pandemic is now clear to everyone. As people try to predict the odds of a future pandemic, the reality is that the next pandemic has already begun. It's not one that rips through countries in a matter of months. It's a slower-growing pandemic, yet it is projected to kill 10 million people a year by 2050.[47]

Antibiotics should be prescribed precisely to save a life or prevent disability. We've discussed overuse, but under-use can also be a problem. Some children are tragically *not* given antibiotics they need for severe ear infections, and as a result they can experience hearing loss and perhaps even fall behind in school because it goes unrecognized. Antibiotics can rescue a patient dying of pneumonia and they can restore sight to a person with an eye infection. But people should stop demanding antibiotics from their doctor for conditions in which they don't even work. In addition, doctors should not prescribe them just to get a five-star rating online. The modern-day consumerist culture is contributing to the epidemic. The purpose of this chapter is not to demonize antibiotics, it's to stop the overkill of prescribing them when they are not medically indicated.

The alarming current trajectory of bacterial resistance means antibiotics will become increasingly less efficient. They may even stop working, threatening to undo a century of progress in medicine. Surgery could once again become a dangerous procedure as it was in the 1800s and maternal mortality from childbirth could soar. Antibiotic stewardship is everyone's responsibility.

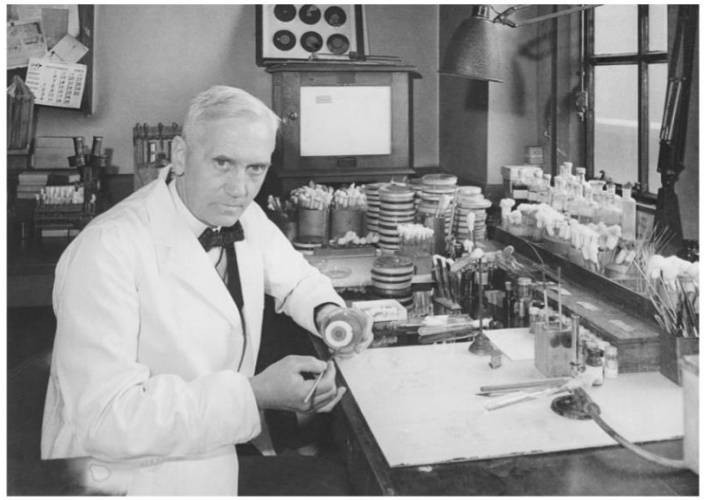
We Can't Say We Weren't Warned

One day, walking into his laboratory after returning from vacation, Dr. Alexander Fleming discovered that the window in his lab had been inadvertently left open. A fungus had blown in and landed on his petri dishes where he was growing bacteria. He soon noticed that the bacteria were dead in the spots where the fungus had landed. The year was 1928, and that fungus would soon become known to the world as penicillin. It would revolutionize every field of medicine. Within a few decades, women would no longer routinely die from childbirth, children would not lose their hearing from ear infections, and surgery would be safe for the first time.

Many people know that penicillin ushered in the modern era of medicine, but what they may not know is that in 1945, as the antibiotic was beginning to be commonly used, Dr. Fleming issued an ominous warning. The "public will demand" the new miracle drug, he said, and that demand would begin "an era . . . of abuses." In an interview later that same year, he issued a stern warning: "The thoughtless person playing with penicillin treatment is morally responsible for the death of the man who succumbs to infection with the penicillin-resistant organism. I hope this evil can be averted."[48] His discovery was an accident, but his warning was deliberate.

Fleming's warning was also prophetic. The overuse of antibiotics is driving resistance and creating superbugs that are killing people. At the root of the overprescribing problem is a cavalier attitude reflected in sayings such as "Antibiotics probably won't help, but they won't hurt." It may be one of the most damaging myths of modern medicine.

It's amazing how much time we spend in medical school on memorizing and regurgitating information that we never need to know on the fly. What's lost in that rote style of education is the wisdom to know what's appropriate in medical care.



Alexander Fleming, the discoverer of penicillin
(Photo by Bettmann/Getty Images)

The problem of overprescribing antibiotics is getting so bad that, at many U.S. hospitals, doctors are not allowed to prescribe certain antibiotics without an infectious diseases doctor approving the request.

Source: https://www.amazon.com/dp/1682193519/

Makary Likes Medical History and Mavericks that Were Right

Servetus – Heretic Who Was Right Gets Burned at the Stake

p. 164

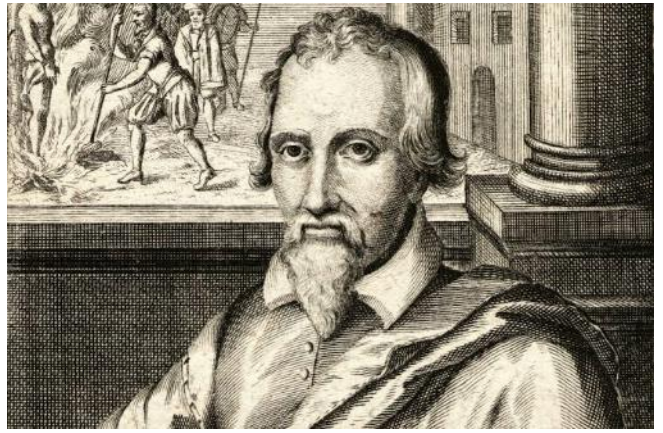
In the Middle Ages, doctors believed the body turned food into blood, and blood just sat in the body stagnant. (I still think that's true of some of my early morning students sleeping in the front row.) Blood doesn't circulate, they believed. It would only be replaced by eating more food that then converted to blood. The heart—the pounding thing everyone could feel in their chests—was thought to be a source of heat.

But then in the 16th century, Spanish theologian Michael Servetus dared to postulate otherwise. Servetus wasn't shy of controversy. In a book called *The Restoration of Christianity*, he criticized the church. But what changed our understanding of the body was the bizarre addendum to his theological treatise in which he provided an accurate description of the body's circulatory system. I guess he tried to publish his theory anywhere he could.

It was a "good-news-bad-news" situation for Servetus.

The good news? His circulation theory turned out to be correct.

The bad news: His theological beliefs got him in trouble. John Calvin had him arrested for heresy and he was burned at the stake. Publish or perish, they say. Sadly for Servetus, it turned out to be both.



William Harvey and Discovery of Blood Circulation – Didn't Get Burned at Stake

p. 165

Dr. William Harvey was born 25 years after Servetus's execution. Since Servetus had been regarded as a heretical nut job, few took his circulation theory seriously. But Dr. Harvey didn't write him off. He objectively considered the circulation theory. Seeing what had become of poor Servetus, Dr. Harvey used a more data-driven approach.

Dr. Harvey was a British prodigy. At 16, he was awarded a scholarship to study medicine at Cambridge University, where he focused on Aristotle.[2] He also learned under a famous anatomist in Italy and became a rising figure among doctors in Europe.[3] Before the age of 30, Harvey was accepted into the Royal College of Physicians. Years later, he became a physician for King James I and then King Charles I. It sounds cool but trust me, VIP patients can be a pain in the butt.

Dr. Harvey conducted autopsies on animals and humans to learn more about the heart and circulatory system. In 1628, at age 50, Harvey published the culmination of his life's work.[4] He argued that the heart pumped a significant volume of blood with each contraction—too much blood for the body's tissue to absorb. The blood had to go somewhere! He theorized that it moved through the body and returned to the heart in a circle-like pattern, with the heart serving as the engine. He published mathematical calculations to show how it worked.

Naturally, Dr. Harvey got criticized for getting it exactly right. Many found his findings to be ludicrous. He said at the time that his practice took a big hit (in his words it "fell mightily") and that physicians were against his opinion.[5] Even worse, he was called "crack-brained," a term I gather, despite my ignorance of medieval vernacular, is not exactly a compliment.

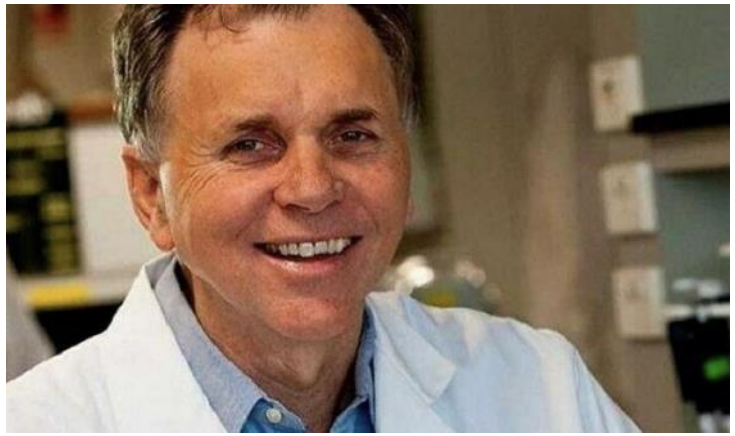
Some historians have called Dr. Harvey's description of the circulatory system the greatest medical discovery of all time.[6]

And even better, he didn't get burned at the stake.

Source: https://www.amazon.com/dp/1682193519/

Likes Mavericks that Were Right (continued)

Barry Marshall – Found Cause of Ulcers But Was Repeatedly Told He Was Wrong p. 162



In the early 1980s, Dr. Barry Marshall, a researcher in Australia, was studying the cause of ulcer disease. He was intrigued by a nonconventional idea—one that had been suggested in studies published over the previous hundred years. The studies speculated that ulcers were caused not by stress, but by a spiral bacteria. He read about a Greek physician named Dr. John Lykoudis who had success treating 10,000 ulcer patients with antibiotics in the 1960s only to have his medical license revoked because the treatment departed from accepted medical practice.[1]

The more Dr. Marshall learned, the more emboldened he became to challenge establishment thinking. He wanted to test the hypothesis that ulcers were caused by the bacteria and that they could be treated with a short course of antibiotics. But he faced powerful opposition. He tried several times to voice his perspective and got laughed out of the room.

So Dr. Marshall pursued his hypothesis on his own. He did a formal study on a series of ulcer patients. He even performed an experiment on himself! He drank the bacteria to give himself the disease and then had his stomach biopsied to prove the cause and effect. Then he cured himself with a short course of antibiotics. He did many other experiments that worked. He demonstrated that stomach ulcers were caused by one specific bacteria that he isolated: *Helicobacter pylori*. It was one of the greatest breakthroughs in medicine. Instead of requiring major surgery, stomach ulcers could be cured with an antibiotic.

Katalin Kariko – and the mRNA Vaccine p. 171

When the Covid pandemic hit, researchers used mRNA technology to rapidly develop a vaccine, and now it's being tested to fight other diseases. But few people know that the technology was developed several years before the pandemic by Dr. Katalin Karikó at the University of Pennsylvania. Using her discovery, the genetic code for making a Covid spike protein was built into the mRNA, just as any code could be set to make any desired protein in the body.

But Dr. Karikó was initially disparaged for the work. In fact, she faced so much opposition that mRNA almost didn't happen.

The University of Pennsylvania moved her office to the outskirts of the campus and cut her pay, and many faculty disdained her, reported the *Wall Street Journal*.[27] She later said doing the work had cost her professionally. "I was demoted four times," she told CNBC.[28]

But Dr. Karikó insisted on continuing.

In her 2023 memoir, she calls the highly acclaimed director of the Gene Therapy Program at Penn one of her early detractors. She said that he demanded she stop speaking Hungarian with her colleagues and refused to use grant money to fund her mRNA projects. She was described as a "difficult" employee by a supervisor for insisting on researching mRNA vaccines.[29] Dr. Karikó said that she was denied basic lab supplies to conduct her experiments, got passed up for a promotion, and was in a dire situation.

Source: https://www.amazon.com/dp/1682193519/

Views Expressed by Martin Makary in his Book "The Price We Pay"

Does Not Like PBM Rebates, Spread Pricing and Other Shenanigans

p. 197

If "the spread" is the leading shenanigan of PBMs, rebates are a close second. Rebates are the smoke bomb of the PBM world. Pharmaceutical companies offer rebates for medications, but the employer paying for medication doesn't know the amount of the rebate, or that it even exists. The PBM keeps all or part of the pharma rebate for itself, for "administrative work." This could also be called a "kickback."

In his presentation, Danny Toth enumerated so many schemes that I couldn't keep up. There are so many that they add up to a lot of money. A 2018 study in the *Journal of the American Medical Association* showed that customers overpaid for one quarter of their prescriptions, with an average overpayment of $7.69 per prescription. Overpayments totaled $135 million during a six-month period.[3]

Justin Simon is a respected health care analyst and investor. I met Justin for lunch in Washington, D.C., and he confirmed everything Toth had said. It's a burden to health plans all over America, he said. Simon said one of the biggest problems he's seeing with PBMs is that they now often own the pharmacies filling the prescriptions.

"PBMs claim they are saving you money by managing your medication costs," Simon said. "But the more the pharmacies sell, the more they make. It's a conflict of interest."

The fundamental conflict is that the PBM claims to reduce what you spend on drugs while owning a pharmacy that profits when you spend more. This leads to yet another PBM shenanigan: signing up patients for mail order drug delivery.

It goes like this: A PBM figures out in their data that you, the patient, had a medication refilled. The PBM then calls you incessantly trying to get you to sign up for their mail order program, enticing you with a lower copay. But once you get on the mail order train, it's hard to get off. All of a sudden, you're getting stockpiles of medications you don't want or need because the PBM is getting your doctor to sign a refill request even though you never asked for one. When the doctor's office receives a refill request they often just sign it. I've done it myself.

The PBM has a different spin. They report that they are increasing patient compliance. But then I have to ask: Does sending a medication to a patient's house mean the patient actually took it?

"THE SPREAD"

Difference between what a PBM charged one employer and what they paid out to a pharmacy

DRUG NAME (brand name example)	STRENGTH	QUANTITY	AMOUNT PBM CHARGED THE EMPLOYER	AMOUNT PBM PAID TO PHARMACY*	"THE SPREAD"
Omeprazole (Prilosec)	40 mg	30	$70.85	$0.00	$70.85
Bupropion XL (Zyban)	300 mg	30	$188.88	$0.00	$188.88
Escitalopram (Lexapro)	10 mg	30	$103.47	$0.00	$103.47
Losartan (Cozaar)	50 mg	90	$204.00	$25.22	$178.78
Azithromycin (Zithromax Z-pack)	250 mg	6	$46.70	$0.00	$46.70
Fluoxetine (Prozac)	20 mg	30	$126.03	$59.50	$66.53
Ketorolac (Acular)	10 mg	20	$43.14	$14.00	$29.14
Pantoprazole (Protonix)	40 mg	30	$159.85	$0.00	$159.85
Meloxicam (Mobic)	15 mg	30	$145.33	$0.00	$145.33
Lisinopril (Zestril)	30 mg	30	$45.21	$2.75	$42.46
Paroxetine (Paxil)	30 mg	90	$253.35	$35.63	$217.72
Simvastatin (Zocor)	40 mg	90	$442.85	$34.94	$407.91
Baclofen (Gablofen)	10 mg	270	$667.17	$126.49	$549.68
Quetiapine (Seroquel)	200 mg	10	$129.37	$5.07	$124.30
Fluocinonide Cream (Vanos)	0.1 %	240gm	$3,174.47	$997.00	$2,177.74
Atorvastatin (Lipitor)	20 mg	30	$173.02	$0.00	$173.02

*$0.00 indicates the patient's copay covered the entire cost of the medication, thus the PBM charged the employer for the medication but paid the pharmacy nothing.

Source: https://www.amazon.com/Price-We-Pay-American-Care

Views Expressed by Martin Makary in his Book "The Price We Pay"

Not a Fan of How Medicare Advantage Plans Get Sold Through Brokers

p. 180

"Marty, the dirty little secret in health care that no one is talking about is the way we brokers get paid," Phil said. He was about to retire so he wasn't worried about breaking the code of silence. He said he simply couldn't stand it anymore. "I went into this business because I thought it was noble to advise employers on the right health insurance coverage for their employees. But this business is not what I thought it was."

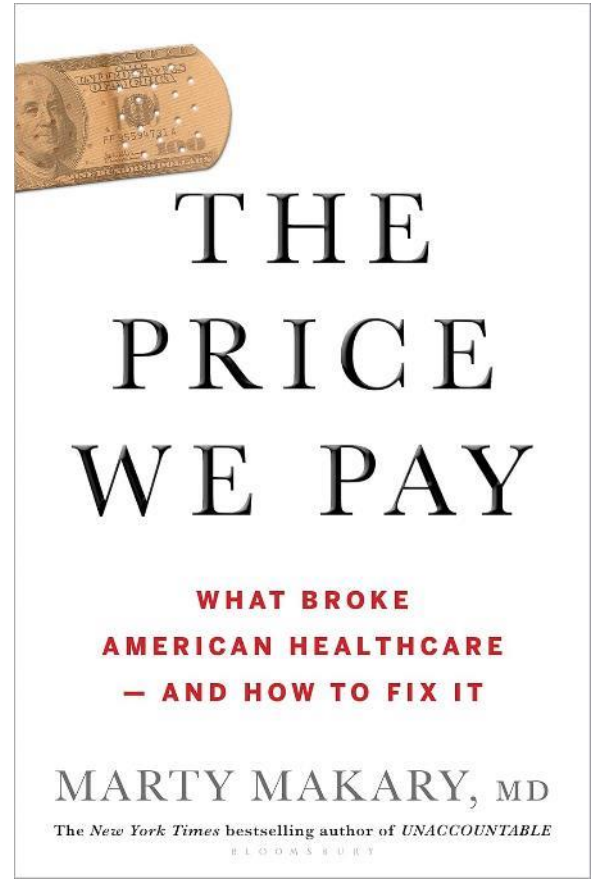
That night, I learned things they don't teach in health policy textbooks or graduate schools. I learned, in vivid detail, exactly how insurance brokers get kickbacks for selling health insurance and pharmacy benefit manager plans to employers, just as Contorno had explained to me. I realized that brokers are often the shepherds leading the sheep. They can convince an employer to buy an overpriced plan or a great value plan. They can convince an employer to switch insurance carriers, stick with their current carrier, go to the mat for a better price, or bypass health insurance and simply self-insure. Brokers have a lot of power. Employers grow to trust them. But what employers don't know is how insurance companies use cash to control the brokers. At the Orlando conference, I heard story after story of companies calling brokers to dangle a big bonus in front of them if they kept an employer on the hook.

I barely knew what a health insurance broker did before I attended that conference. Phil and his colleagues got me up to speed fast as we sipped piña coladas in the Florida heat. Slouching back in cozy chairs at the terrace bar, they spoke candidly about the business. I was leaning forward, taking notes, my eyes popping out of my head.

"The way brokers are paid is one reason people are paying too much for health insurance, and I can't believe no one is talking about it." Phil said. Throughout his career, he had regularly been offered hundreds of kickbacks from insurance companies, ranging from $30,000 to $100,000 (often referred to in the industry as "bonuses," "overrides," "persistency bonuses," or "contingent income").

"Sometimes that money pushed me to put employers into plans that were way too expensive for them," Phil admitted.

But as I learned from Contorno's experience of getting blackballed by Blue Cross Blue Shield of North Carolina, health insurance companies don't just use carrots, they also use sticks. Brokers told me if they lost a key employer, an insurance company might "fire" them from their entire book of business. That means the broker would be cut off from the gravy train—the 1 to 5% commission on every premium dollar the broker had brought to that company. That's a few hundred dollars *per employee* going to the commission payout every year! And as the employers' costs rise, so, too, does the broker's revenue. One broker, who switched an employer to a different health insurance plan, told me how he got blackballed, then trash-talked by the carrier who was telling other employers to avoid him simply because he was fired from working with them. The bad-mouthing was not merely to get revenge on that one broker. It sent a signal, loud and clear, to other brokers who might want to encourage employers to switch to a different plan.



Source: https://www.amazon.com/Price-We-Pay-American-Care

Views Expressed by Martin Makary in his Book "The Price We Pay"

Negative on GPOs and Positive on Domestic Manufacturing

p. 208

I sat at my desk a few months ago and caught up on my backlog of 58,465 unread emails. I replied to an FYI email from about two years ago with a "thanks," then noticed a new email warning me about a critical shortage of saline bags. Saline bags were in reportedly short supply because Hurricane Maria had damaged a factory that made them in Puerto Rico.[5] I wondered how our country became so dependent on this one factory. Salt and water are the two most common elements on planet Earth. And now we had a shortage?

This was not the first critical supply shortage I've had come across my email. It happens dozens of times a year. Epinephrine, propofol, heparin, and other drugs that have been around for more than 50 years are suddenly rare-earth materials. In the case of heparin, a blood thinner given to almost every patient who has surgery, the drug had been adulterated from a source in China and led to the death of more than 100 Americans.

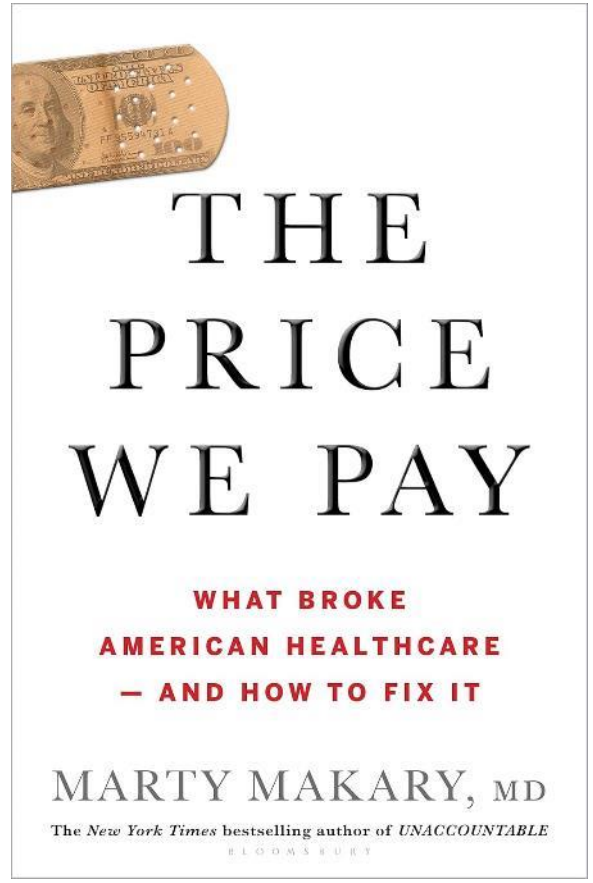
There are indications that the market power of GPOs could be associated with the shortages. Often, only one or two manufacturers are responsible for an entire regional or national supply chain. If a factory has production problems, this reliance on a narrow supply chain can have an adverse effect on hospital inventories.

A 2016 GAO study concluded that there was a strong association between critical drug shortages and a decline in the number of drug suppliers.[6] Furthermore, GPOs were a significant focus in a U.S. House of Representatives report on drug shortages that stated, "The GPO structure reduces the number of manufacturers producing each generic drug."[7]

As I spoke with more and more people in the field, it became clear to me that GPOs can make it difficult for manufacturers to enter the market. They may reward fewer, larger manufacturers, which increases health care's dependence on a smaller number of drug producers. Conversely, I also found that there are "better" GPOs that do not demand kickbacks and choose to list as many options as possible in their catalogs. By doing so, they are eliminating barriers to entry for new products and promoting a healthy competitive marketplace.

Whenever we have a critical shortage, we blame a factory or a storm. But the real question is how we became so dependent on so few factories.

Dependence on foreign factories threatens our national security, especially during a health emergency. Having domestic manufacturing of medications, ventilators, and personal protective equipment (PPE) is an underappreciated yet critical part of our nation's health security.

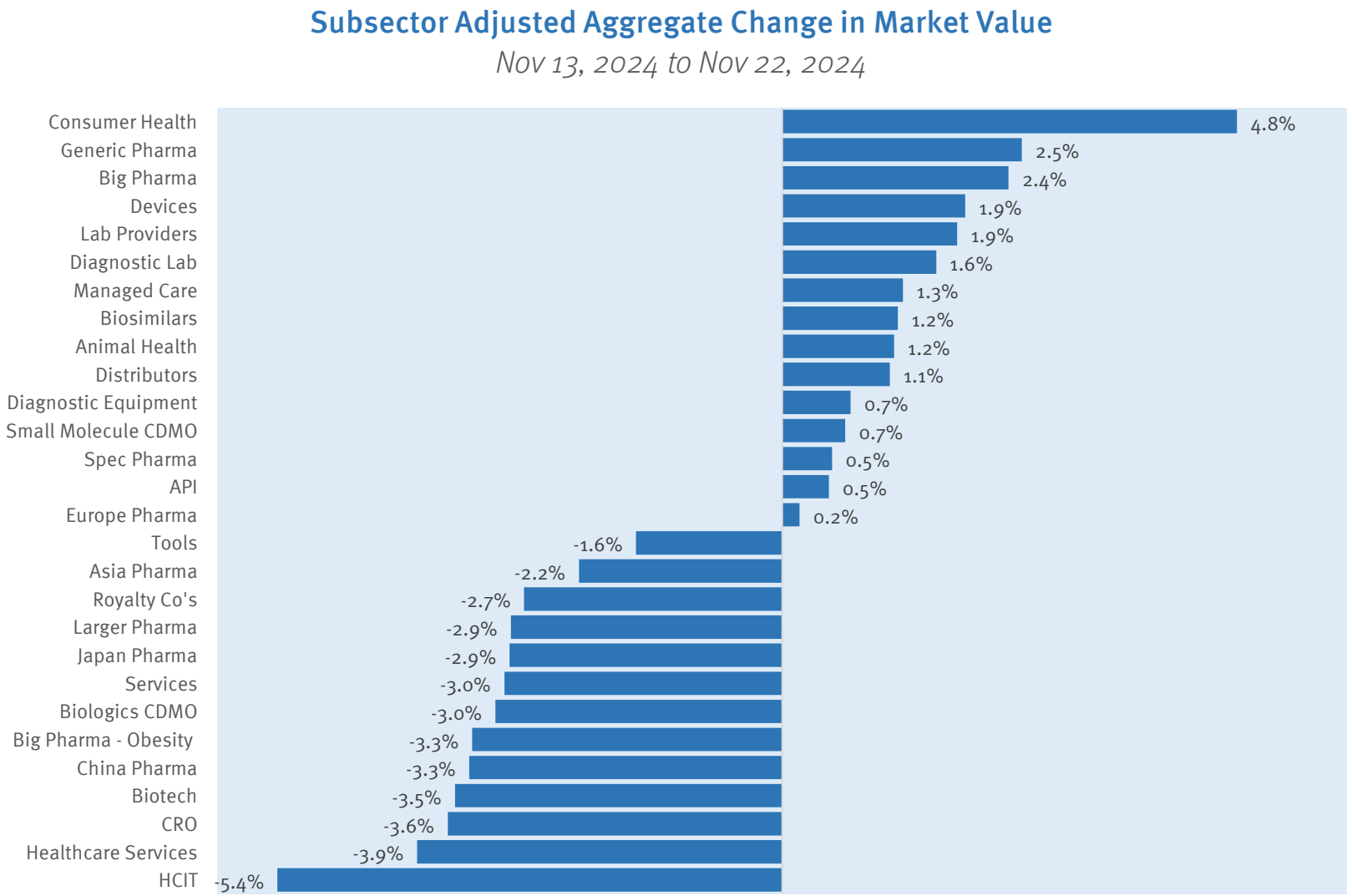


Source: https://www.amazon.com/Price-We-Pay-American-Care

Potential Areas of Change at FDA in Drug Evaluations and Approvals

In Person Presence	•Trump Administration expressing interest in having employees show up on site •In person sponsor discussions and AdComms likely to accelerate development with more direct, clear communication
Biosimilars	•Potential for approvals based on comparability studies •Potential for approval of studies with ex-US data on comparability alone
NCE's with ex-U.S. data	•Potential to gain approval with small bridging studies •Different than current standard of a full extra Phase 3 study
Antimicrobial Resistance	•Potential to push through the Pasteur Act •Potential to promote and incentivize alternatives to antibiotics including antibodies (e.g., Vir, Yumab) and phage therapies (e.g., Armata, BiomX, Phaxiam)
Oncology Drugs	•Last administration under Rick Pazdur made it harder to get approvals due to Project Optimus and vigorous vigilance on post-approval commitments of sponsors •Pazdur initiatives have favored patient safety over industry – potentially resulting in fewer NDA/BLAs due to longer, more expensive drug development pathways •Possible to put in place a Bayesian approach that provides for limited approvals that expand as additional dosing / efficacy experience obtained
Chronic Diseases	•The reality is that requirements for outcomes data and two large Phase 3 studies has discouraged sponsor investment in this area •One could envision an "exchange" where sponsors provide RWE on safety/efficacy in exchange for earlier approvals or doing a single Phase 3 study •Patrizia Cavazzoni (Head of CDER) has consistently advocated precision approaches to chronic disease – her ideas could be accelerated under Makary •Opportunity to create incentives like those with the pediatric and rare disease voucher program for sponsors who push through expensive but socially beneficial drug programs in areas of the highest need like T2DM, COPD, asthma, atherosclerosis, major depression and the like.
Vaccines	•Potential to require long-term safety monitoring •Potential to push universal approaches •Potential to push approaches that can adapt to changing antigens
Gene and Cell Therapy	•Peter Marks interest in allowing approvals for GCT drugs that are customized to the patient could get energized •Possible to accelerate idea of "mass customization" of drugs. FDA leadership seems aligned here.
Plant Inspections	•FDA has been woefully understaffed in the facility inspection area and will often refuse to travel to some countries such as China •There is a clear opportunity to improve the supply chain and speed of approvals with a a better staffed system here
Women's Health	•Incoming FDA commissioner has a strong interest in improving the label of HRT •Possible that FDA will take action in this area

The “RFK Effect”



Source: S&P CapitalIQ and Stifel analysis

This chart shows how the aggregate value of life sciences subsectors worldwide has changed since RFK Jr. was announced to the HHS role. We take the percent change in total market cap of each subsector from last Friday to the close before RFK Jr’s announcement and then subtract the average change in the sector (2.4%).

Relatively speaking then, consumer health, generic pharma and big pharma have all done well since RFK’s announcement.

HCIT, biotech, service providers and CRO’s have been down.

The two big pharmas that are biggest in obesity (Lilly and Novo) are down 3.3% vs the average. That’s a fairly big move.

Distributors, biosimilars and managed care have all gone up since the announcement.

We might have expected to see an even bigger move in biosimilars. We looked at the data and saw the sole U.S. public biosimilar company (Coherus) rose over 30%.

Biopharma Market Update

The XBI Closed at 96.2 Last Friday (Nov 22), Up 4.8% for the Week

The XBI regained about half of the ground it lost the week before. Investors were calmed as word spread that Marty Makary might take the FDA post. The XBI is up 7.8% for the year.

Biotech Stocks Up Last Week

Return: Nov 16 to Nov 22, 2024

Nasdaq Biotech Index: +3.0%
Arca XBI ETF: +4.8%
Stifel Global Biotech EV (adjusted): +1.5%*
S&P 500: +1.7%

Return: Dec 29, 2023 to Nov 15, 2024 (YTD)

Nasdaq Biotech Index: +3.7%
Arca XBI ETF: 7.8%
Stifel Global Biotech EV (adjusted): +29.6%*
S&P 500: +25.0%

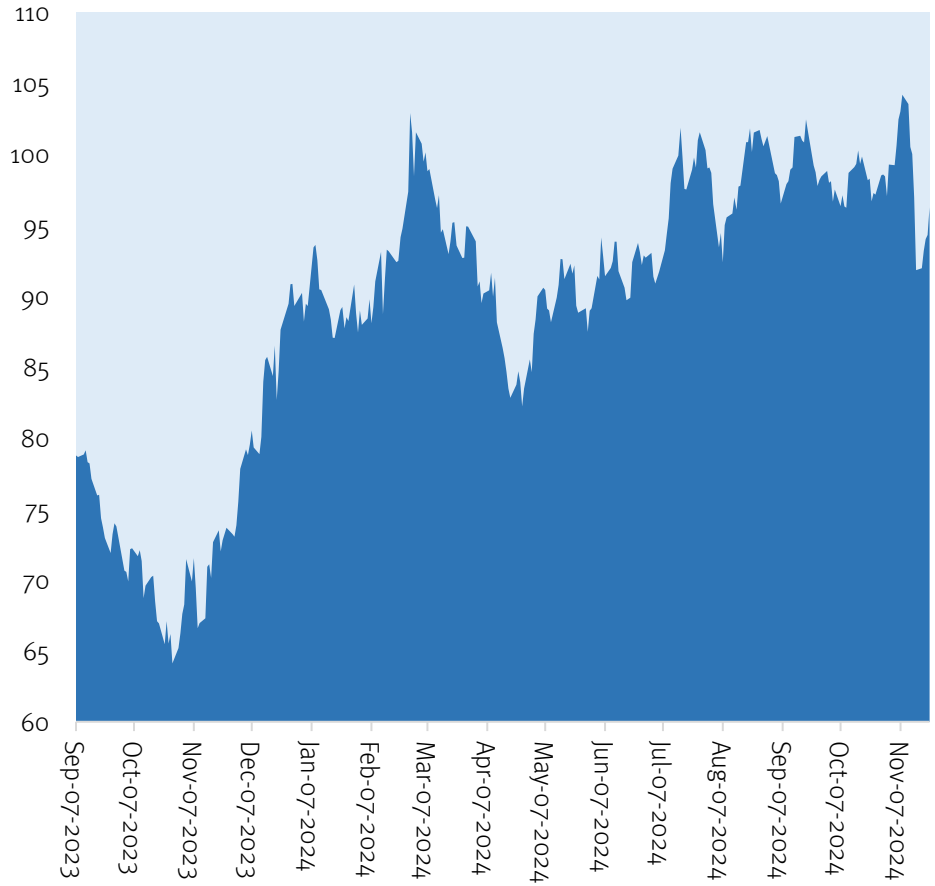
VIX Down

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 19, 2024: 18.0%
Nov 15, 2024: 16.1%
Nov 23, 2024: 15.2%

10-Year Treasury Yield Down

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 19, 2024: 4.08%
Nov 15, 2024: 4.43%
Nov 23, 2024: 4.41%

XBI, Sep 7, 2023 to Nov 23, 2024



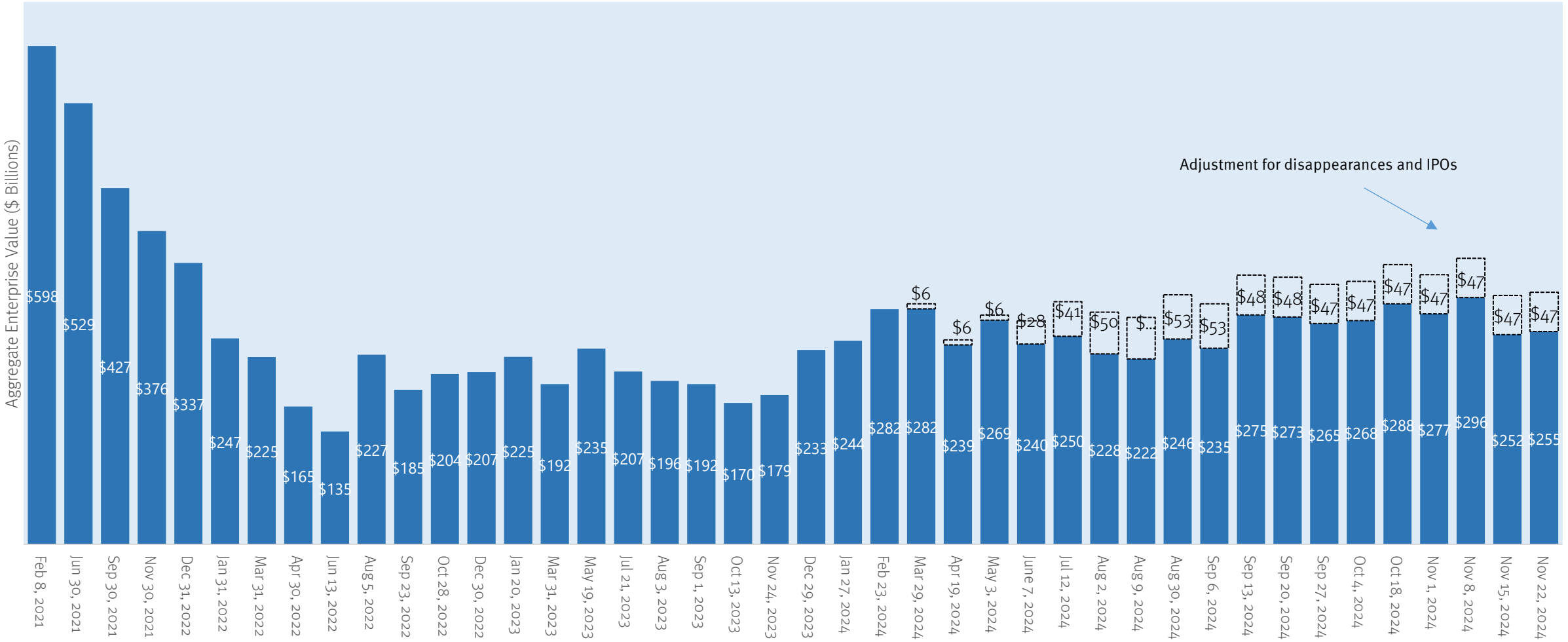
* Change by enterprise value. The adjusted number accounts for the effect of exits and additions via M&A, bankruptcies and IPOs. The annual change by market cap is even higher.

Source: S&P Capital IQ and Stifel analysis

Total Global Biotech Sector Up 1.5% Last Week

Biotech stocks rose 1.5% in the last week gaining less in total than the XBI. On a disappearance adjusted basis, biotech is up 30% for the year to date (enterprise value). An interesting factoid is that biotechs worth under $2 billion a week ago lost value for the week while all of the gain that took place was in the 30 or so companies worth more than $2bn.

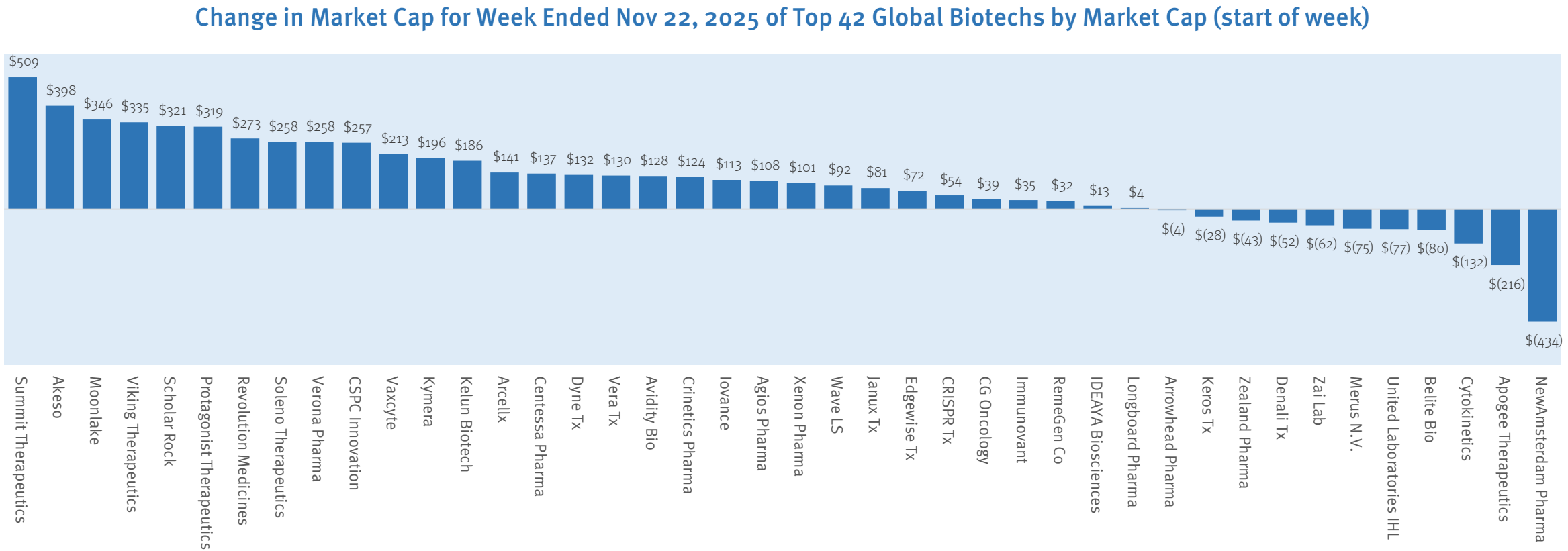
Total Enterprise Value of Publicly Traded Global Biotech, Feb 8, 2021 to Nov 22, 2024 ($ Billions)



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

A Solid Week for Top Biotech

This chart shows the change in market cap last week for the top 42 biotechs worldwide by their market cap at start of week (only companies worth $2bn or more at start of week were included). The median percentage change in value was 2.7% and the median gain in value was $115 million. The VEGF x PD1 story keep gaining stem with Summit and Akeso showing strength last week. Moonlake, Viking, Scholar Rock and Protagonist also performed quite well last week.

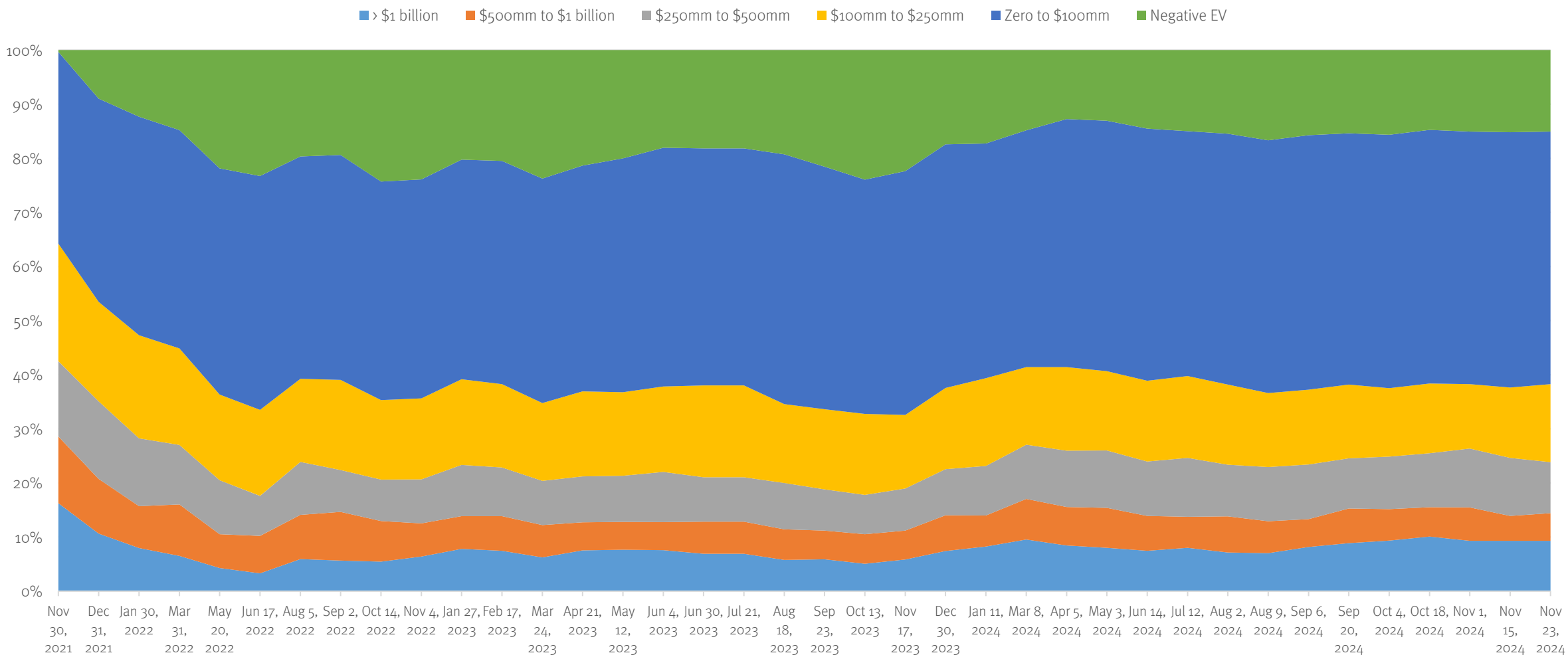


Source: CapitalIQ. Biotechs are defined as any therapeutics company without an approved product on any global stock exchange.

Global Biotech Neighborhood Analysis

Last week saw growth in the group of companies that are worth $1bn or more than those that are worth $250mm or less. The “middle class”, in contrast, got squeezed hard.

Global Biotech Universe by Enterprise Value Category, Nov 30, 2021 to Nov 22, 2024



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

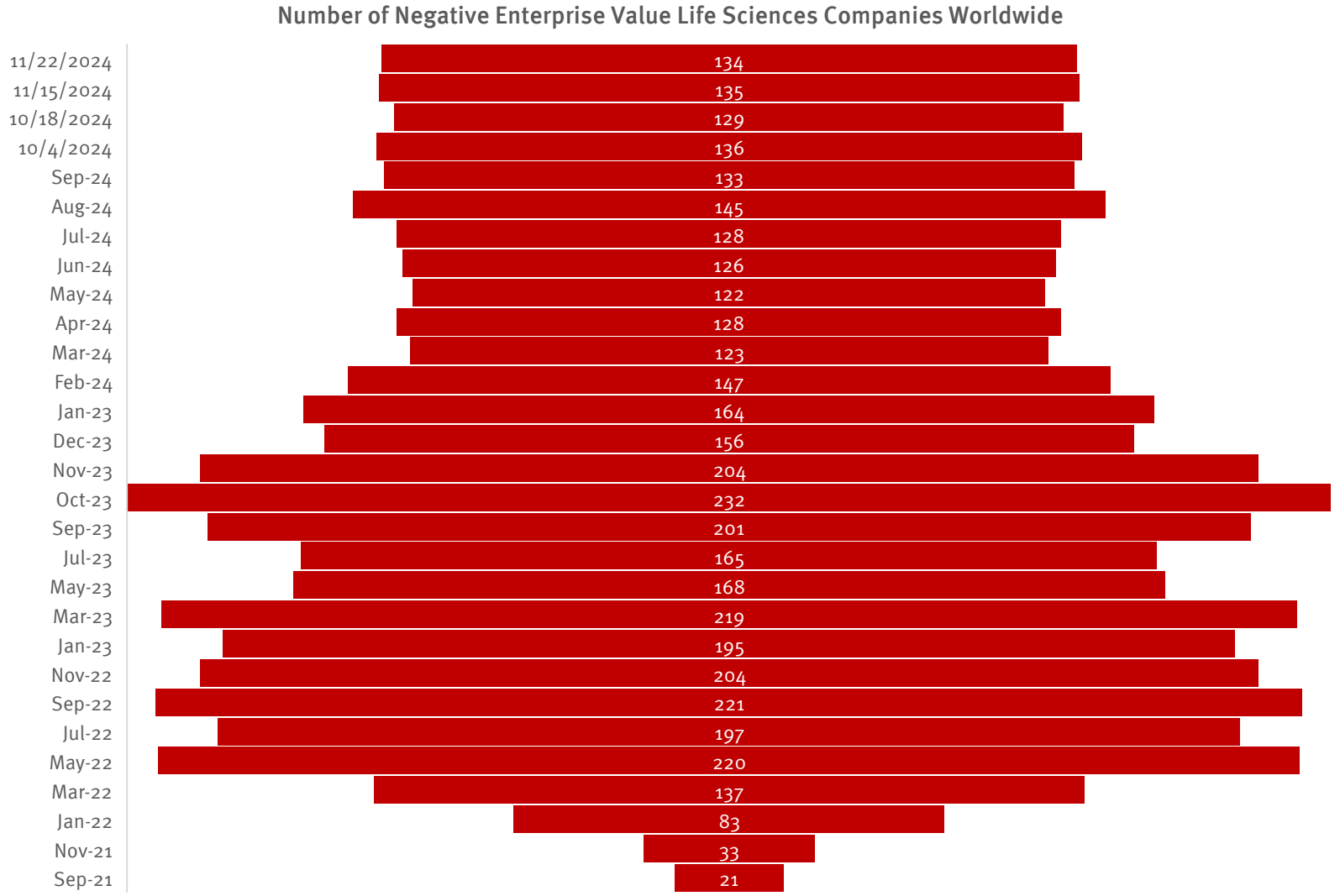
Life Sciences Sector Gained $95 Billion in Value Last Week (5.7%)

The life sciences sector gained back a sixth of the value it had lost in the previous week's rout.

Sector	Firm Count	Enterprise Value (Nov 24, 2024, $millions)	Change in Last Week (percent)	Change in Last Month (percent)	Change in Last Year (percent)
API	79	$93,041	-0.9%	-3.2%	9.8%
Biotech	774	$255,152	1.5%	-8.8%	-5.1%
CDMO	39	$157,591	-0.4%	-8.4%	4.6%
Diagnostics	81	$243,491	1.2%	-1.6%	-4.8%
OTC	29	$25,156	1.1%	-3.7%	-8.3%
Commercial Pharma	712	$6,146,551	1.0%	-8.2%	7.7%
Pharma Services	38	$168,722	1.0%	-4.1%	-17.2%
LS Tools	50	$651,310	1.7%	-3.7%	4.0%
Medical Devices	178	$1,805,214	1.0%	0.6%	18.1%
HCIT	10	$20,720	-1.7%	-5.8%	0.9%
Total	**1990**	**$9,564,948**	**1.0%**	**-6.1%**	**9.1%**

Source: CapitalIQ and Stifel analysis

Count of Negative Enterprise Value Life Sciences Companies Was Flat Last Week



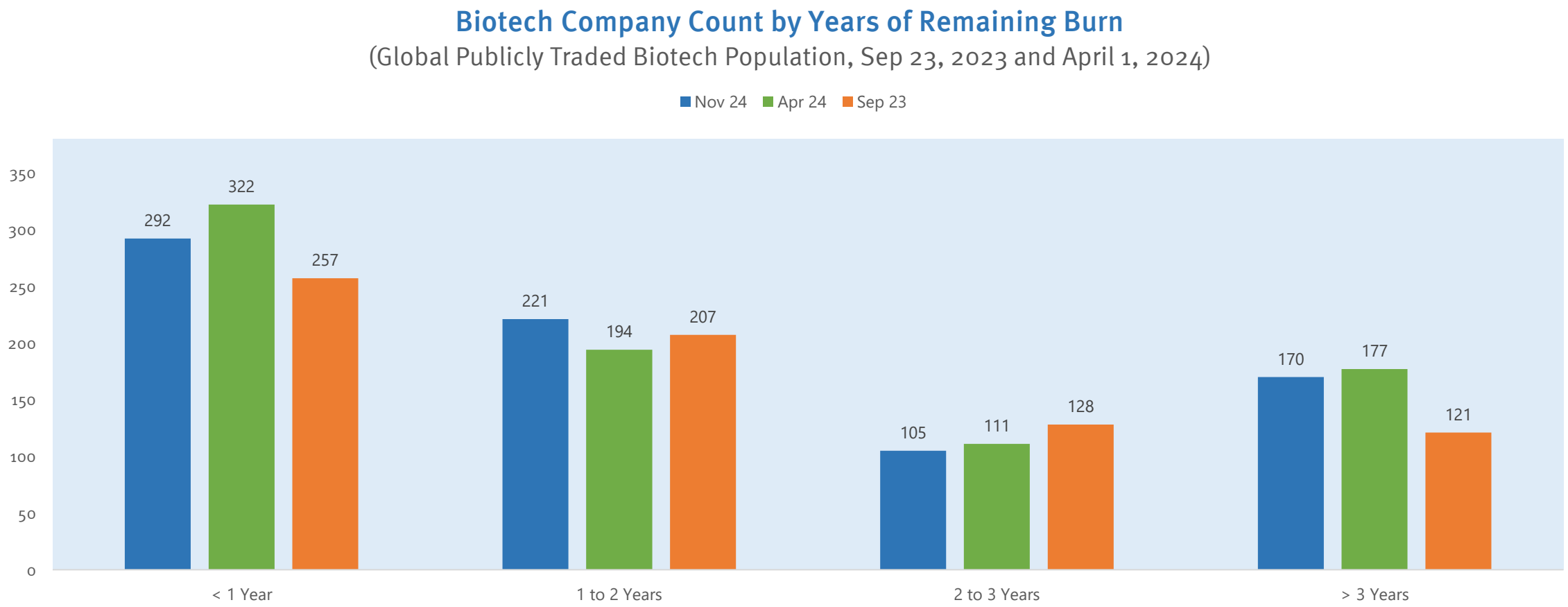
The number of negative EV life sciences companies fell from 135 a week ago to 135 last Friday (Nov 22nd).

Source: CapitalIQ and Stifel analysis

Biotech Balance Sheet Condition

Biotech Sector Seeing Fewer Companies Tight on Cash

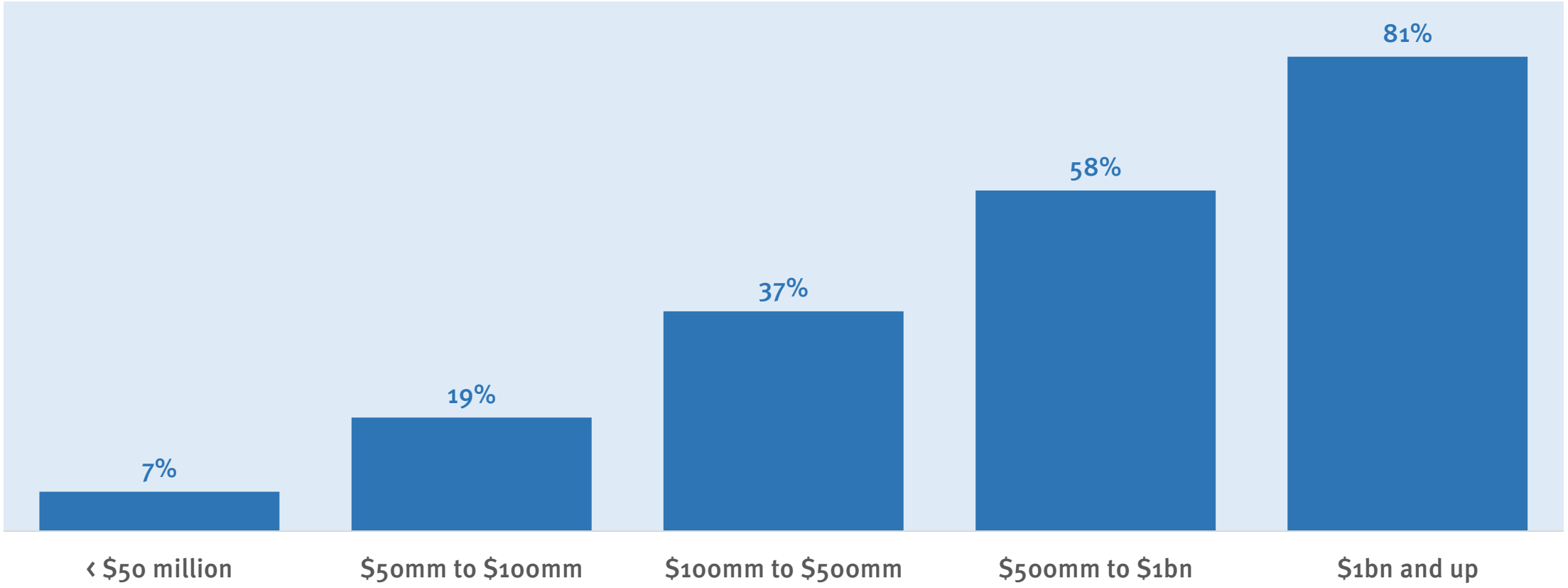
If one looks at all 788 public biotech companies in our database worldwide, there is a substantial fraction that have less than a year of cash. On the other hand, the fraction of companies in this predicament has fallen (in part, due to an improved fund-raising environment and, in part, due to Darwinian forces).



Notes: Data from CapitalIQ and Stifel Analysis. Data on burn and cash not available for all companies in dataset. Biotechs were defined as companies in the biopharma sector that do not yet have a commercial product.

Balance Sheet Condition Much Better in High Market Cap Biotechs

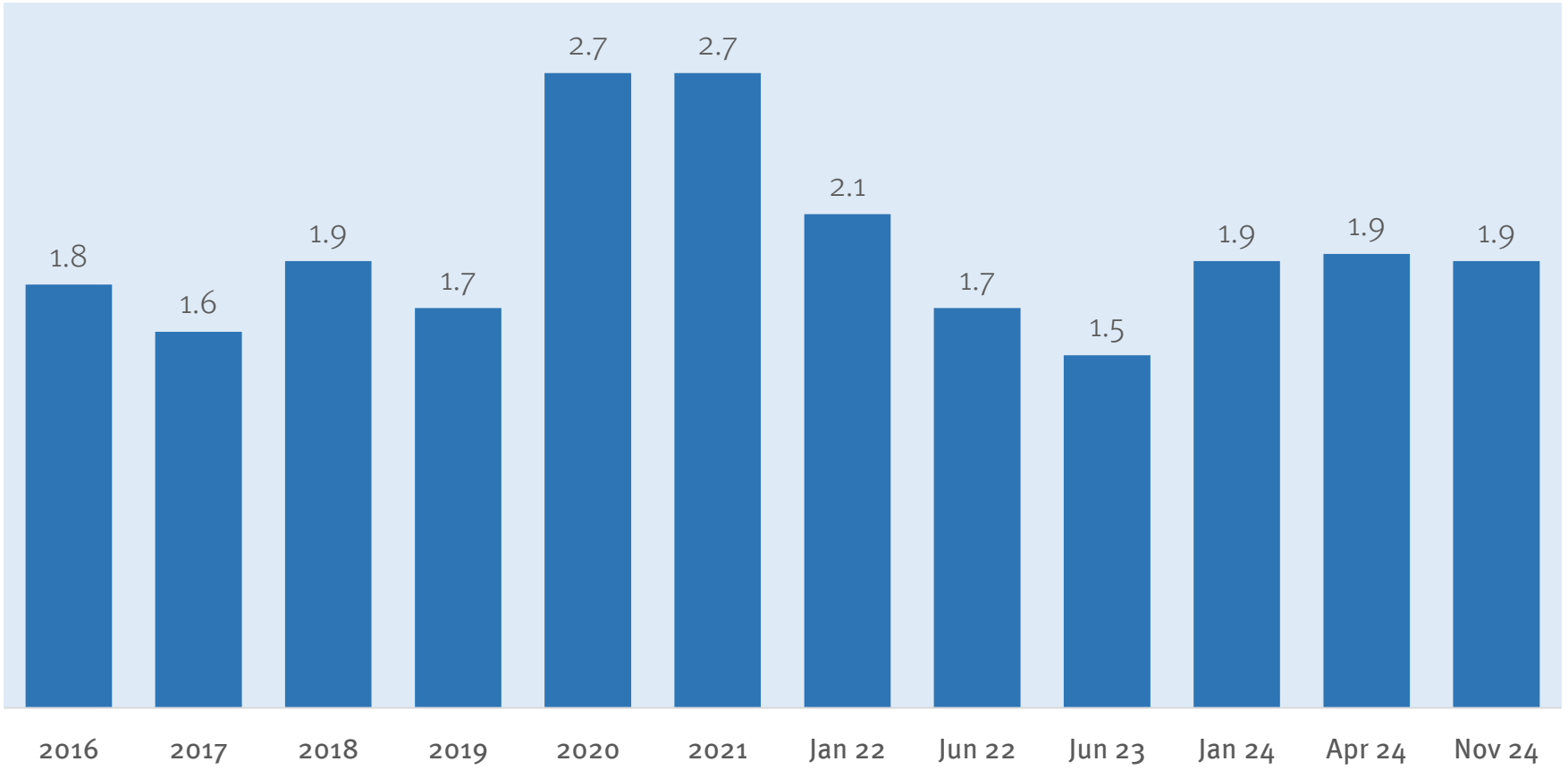
Percent of Companies with Two Years or More of Burn by Market Cap as of Nov 2024 (U.S. Public Biotech, N=388)



Source: CapitalIQ

Median Years of Burn of Top 500 Public Biotechs Reverses its Sharp Decline that Ran Into Mid-2023

Median Years of Burn Among Top 500 Global Biotechs
(only including companies that burn cash)



This page looks at the top 500 biotechs by market cap.*

Cash positions for quarter ended Dec 30, 2023 have now been fully reported.

The median Top 500 biotech company at 2023 year-end had 1.9 years of burn on its balance sheet.

By the end of the third quarter of 2024 the median years of burn was steady at 1.9 years.

* Data from CapitalIQ. We took all public biotech companies in Sep 2021 and chose the largest 500 by enterprise value at the time for this analysis. This chart tracks the balance sheets of this cohort to June 2023 (and back to 2016 for historic reference). Years of burn is defined as net cash at last quarter end dividend by trailing 12-month EBITDA. After that we looked at the top 500 companies by market cap at quarter end 2024. For April 2024 estimated burn we added funds raised via disclosed ATM use, follow-ons, royalty deals and debt deals. We then deducted 25% of trailing annual EBITDA.

Atlas Venture Update on Industry Environment (Excerpts)

YEAR IN REVIEW 2024

ATLAS VENTURE

PRESENTED ON

November 7, 2024

PRESENTED BY

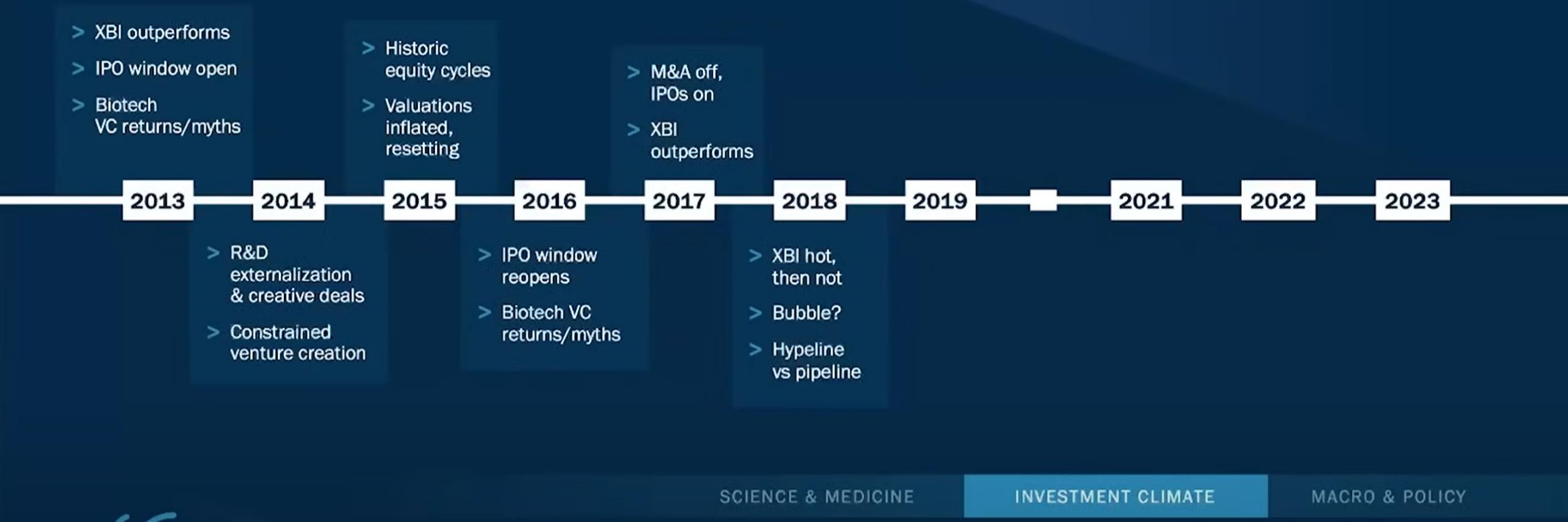
Bruce Booth
Partner
Atlas Venture

DESIGN BY

Edward Goin
www.medeina.io
egoin@medeina.io

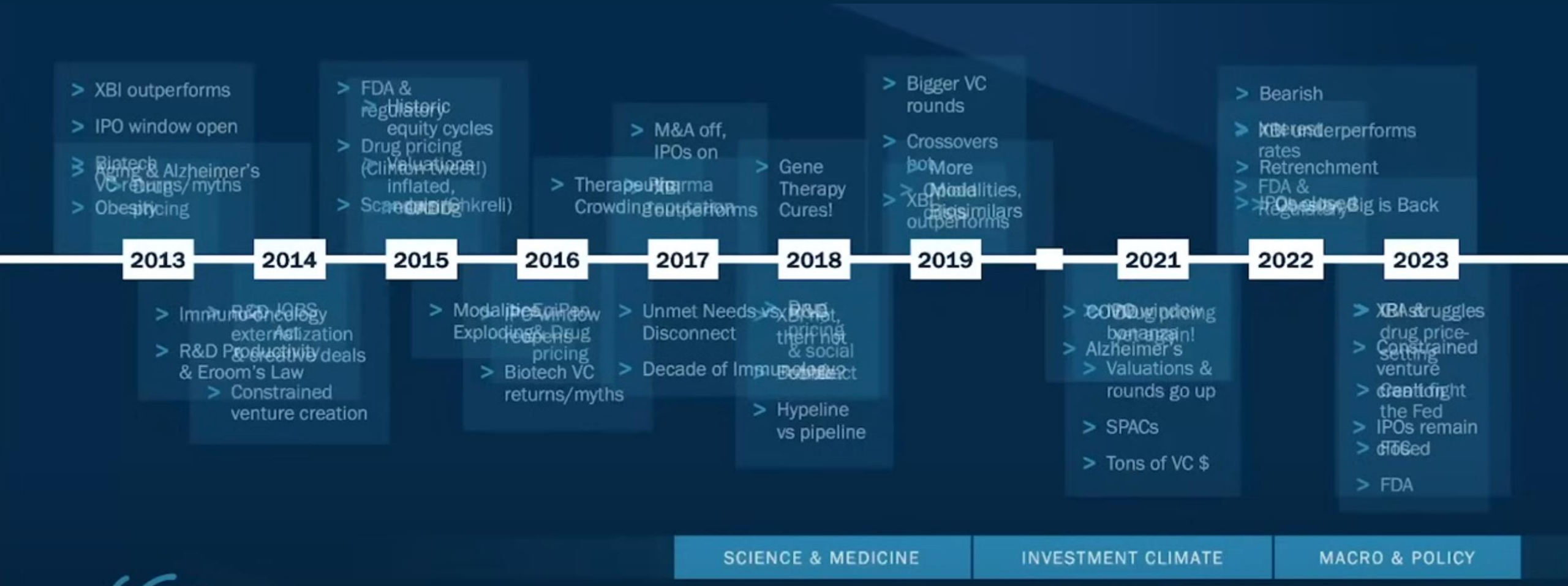
Bruce Booth of Atlas Reviewed a Lot of History in Preparing This Year's Report

Link to Review the Report Directly Yourself:
https://www.youtube.com/watch?v=szwRUERnoOM



YEAR IN REVIEW 2024

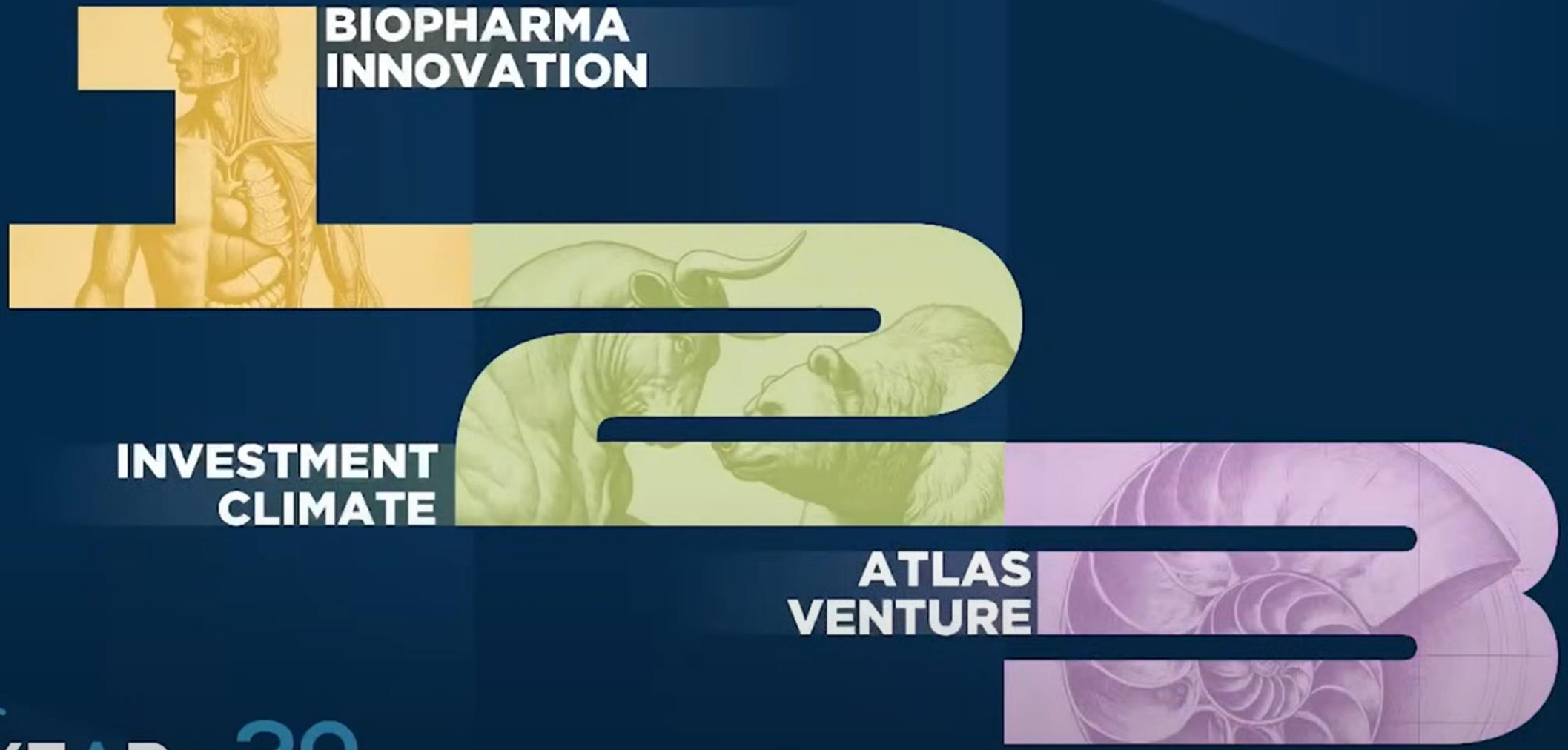
History Does Not Perfectly Repeat But the Key Themes Recur



SIMILAR THEMES, DIFFERENT YEARS

YEAR IN REVIEW 2024

Three Parts to the Review

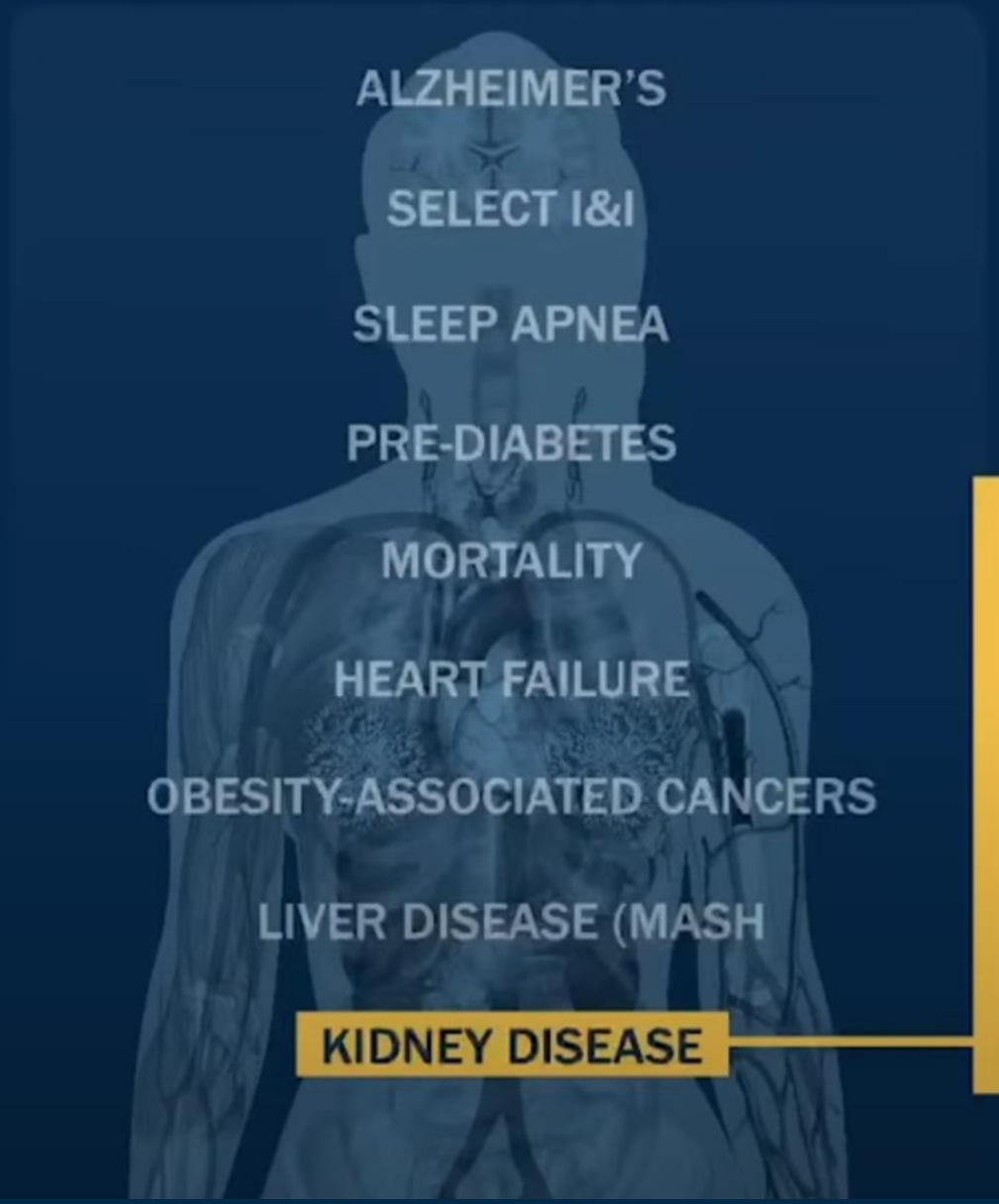


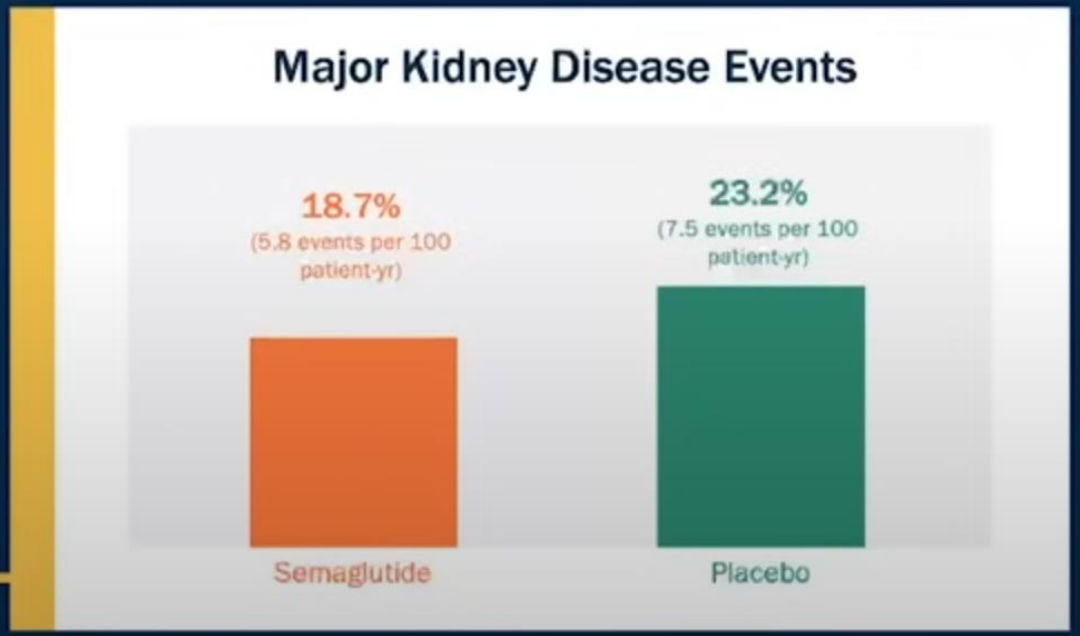
YEAR IN REVIEW 2024

Six Topics Are Most Important in 2024…

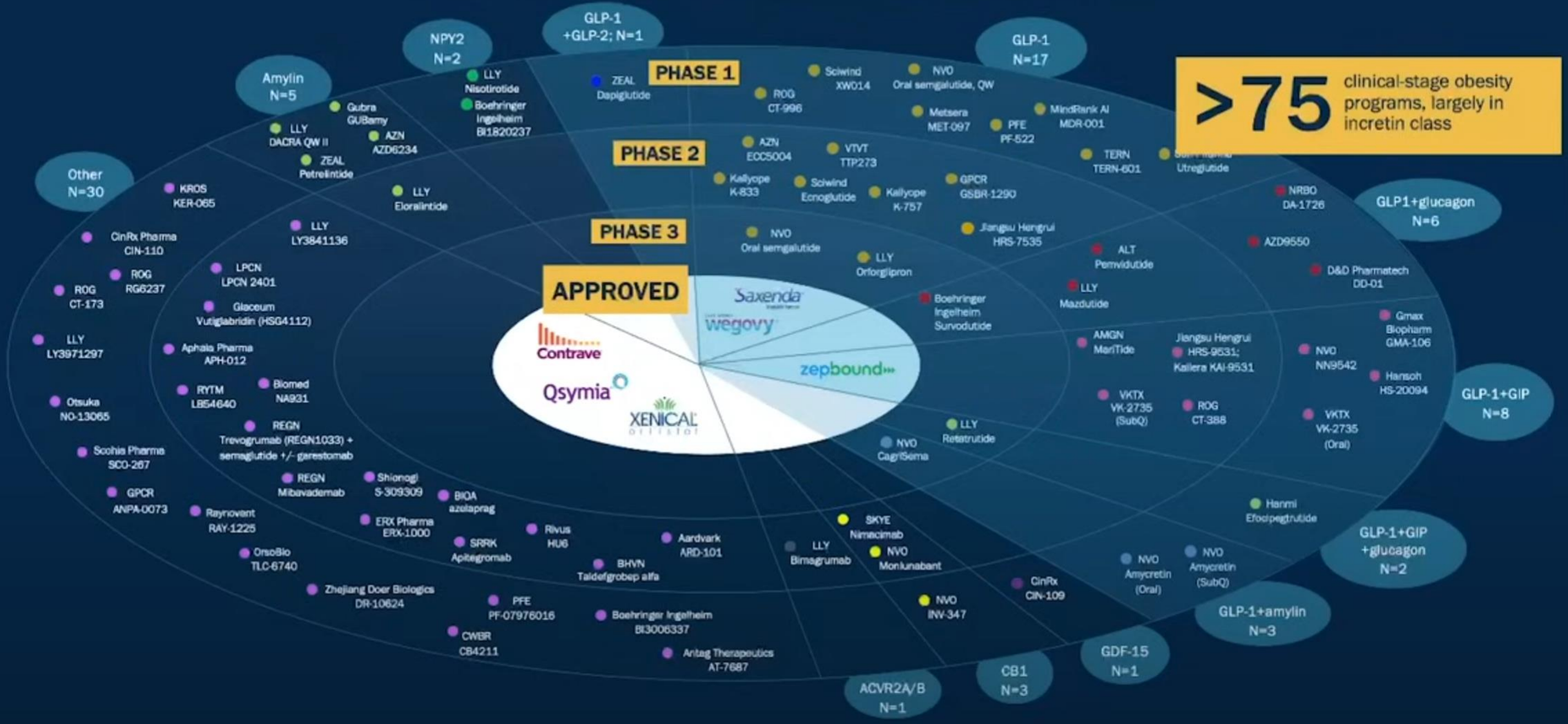
Obesity is the “Biggest” Theme in 2024

HEALTH BENEFITS OF INCRETINS CONTINUE TO BROADEN

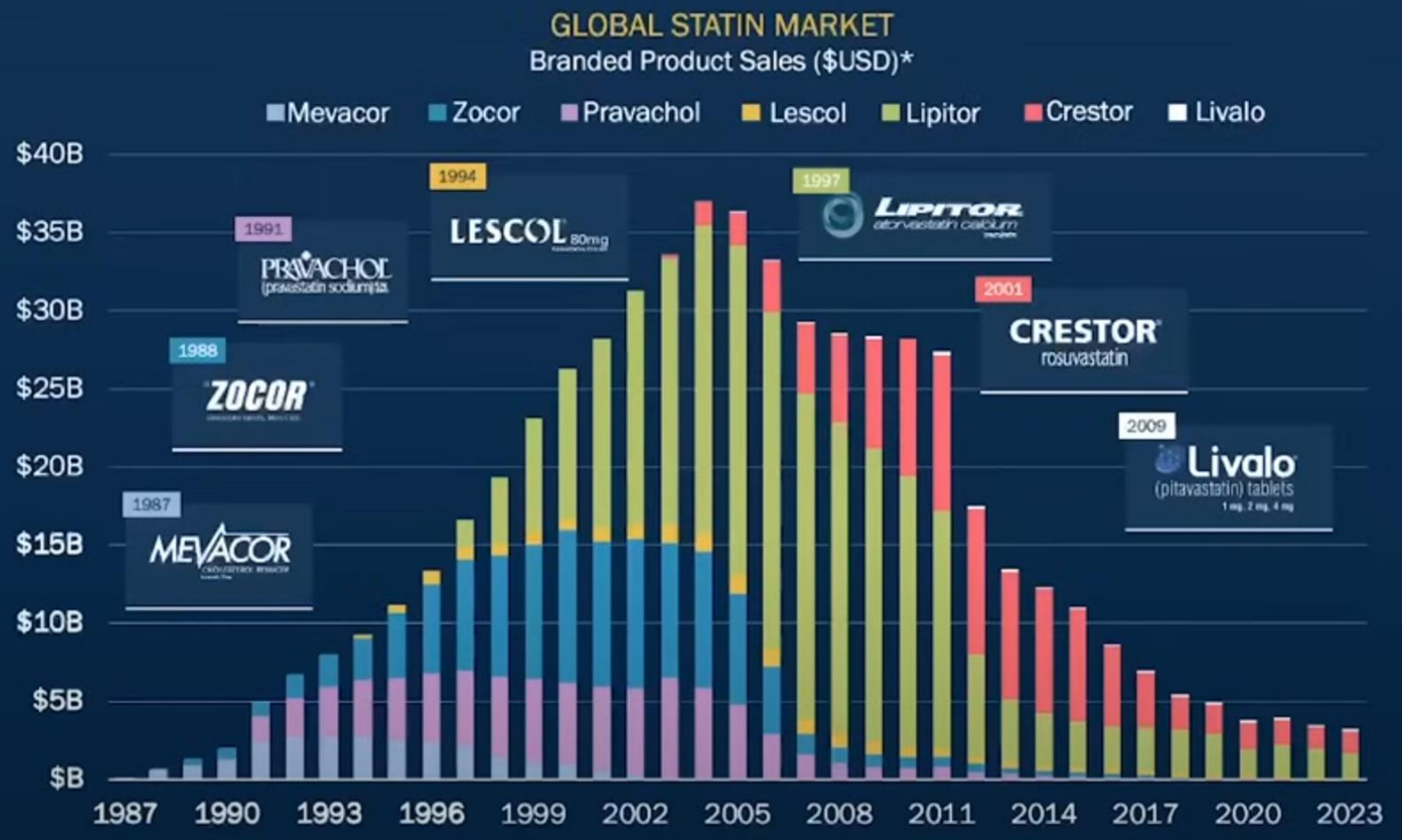




Sources: Lincoff et al., NEJM (2023); Perkovic et al., NEJM (2024); Kosiborod et al., NEJM (2023); Eli Lilly Q2 2024 presentation; company PR; Wang et al., Alzheimer's Dement (2024)


BURGEONING PIPELINE IN OBESITY
>75 clinical-stage obesity programs, largely in incretin class
PHASE 1
PHASE 2
PHASE 3
APPROVED
Saxenda
wegovy
Contrave
zepbound
Qsymia
XENICAL
GLP-1 +GLP-2; N=1
NPY2 N=2
GLP-1 N=17
Amylin N=5
Other N=30
GLP1+glucagon N=6
GLP-1+GIP N=8
GLP-1+GIP +glucagon N=2
GLP-1+amylin N=3
GDF-15 N=1
CB1 N=3
ACVR2A/B N=1
LLY Nisotirotide
Boehringer Ingelheim BI1820237
Gubra GUBamy
LLY DACRA QW II
AZN AZD6234
ZEAL Petrelintide
LLY Eloralintide
ZEAL Dapiglutide
ROG CT-996
Sciwind XW014
NVO Oral semaglutide, QW
Metsera MET-097
PFE PF-522
MindRank AI MDR-001
AZN ECC5004
VTVT TTP273
Kallyope K-833
Sciwind Ecnoglutide
Kallyope K-757
GPCR GSBR-1290
TERN TERN-601
Utreglutide
NRBO DA-1726
KROS KER-065
CinRx Pharma CIN-110
ROG RG6237
ROG CT-173
LLY LY3971297
LLY LY3841136
LPCN LPCN 2401
Glaceum Vutiglabridin (HSG4112)
Aphaia Pharma APH-012
RYTM LB54640
Biomed NA931
Otsuka NO-13065
REGN Trevogrumab (REGN1033) + semaglutide +/- garetosmab
Scohia Pharma SCO-267
GPCR ANPA-0073
Raynovant RAY-1225
REGN Mibavademab
Shionogi S-309309
ERX Pharma ERX-1000
OrsoBio TLC-6740
BIOA azulaprag
SRRK Apitegromab
Rivus HU6
BHVN Taldefgrobep alfa
Aardvark ARD-101
Zhejiang Doer Biologics DR-10624
PFE PF-07976016
CWBR CB4211
Boehringer Ingelheim BI3006337
Antag Therapeutics AT-7687
NVO Oral semaglutide
LLY Orforglipron
Jiangsu Hengrui HRS-7535
Boehringer Ingelheim Survodutide
LLY Mazdutide
ALT Pemvidutide
AZD9550
D&D Pharmatech DD-01
AMGN MariTide
Jiangsu Hengrui HRS-9531; Kailera KAI-9531
NVO NN9542
Gmax Biopharm GMA-106
Hansoh HS-20094
VKTX VK-2735 (SubQ)
ROG CT-388
VKTX VK-2735 (Oral)
LLY Retatrutide
NVO CagriSema
Hanmi Efocipegtrutide
SKYE Nimacimab
LLY Bimagrumab
NVO Monkunabant
CinRx CIN-109
NVO INV-347
NVO Amycretin (Oral)
NVO Amycretin (SubQ)

STATINS: CLOSEST PARALLEL?



- From Discovery (1970s) to Blockbuster status (1990s) took two decades
- Best-in-class differentiation enabled late-to-market entrants who secured most value over time
- Exuberance about broader health benefits (e.g. Alzheimer's)
- Evolution to combinations and new MoAs (e.g., PCSK9) to further improve LDL-C lowering and cardio benefit

INEGY VYTORIN Caduet Roszet

- Hard for pharma to NOT be in the class

Note: * Inflation-adjusted data using CPI; does not include drugs removed from market for safety reasons (e.g., Baycol)

Source: BCG and EvaluatePharma; Atlas analysis of GlobalData, Citeline, Jie Jack Li In: Triumph of the Heart: the Story of Statins (Oxford University Press, 2009), Chen et al., AHDB (2023), Lin et al., JAMA Netw Open (2021), CNN, NYTimes, Pharma quarterly earnings reports

China is the Second Biggest Theme in 2024

Many Cross-Border China to West Deals Have Happened

CHINA: AN INNOVATION TRANSFORMATION

EXEMPLARY CHINA-TO-WEST **ONCOLOGY** DEALS
In the Past 10 Years (2013 To 2024)

CHINESE COMPANY	GLOBAL PARTNER	UPFRONT VALUE	TOTAL DEAL SIZE
GRACELL	AstraZeneca	$1,000M	$1.2B
Akesobio	Summit Therapeutics	$515M	>$5B
			>$1.7B
			~$1.7B
			>$9B
HENGRUI	MERCK	$169M	~$1.7B
康诺亚 Kelun-Biotech	AstraZeneca	$63M	~$1.2B
MABCARE	Day One Biopharmaceuticals	$55M	~$1.2B

Akeso & Summit Therapeutics
Recent World Lung data supports combo beat vs. Keytruda

>5 months mPFS benefit vs. Keytruda alone

By 2024

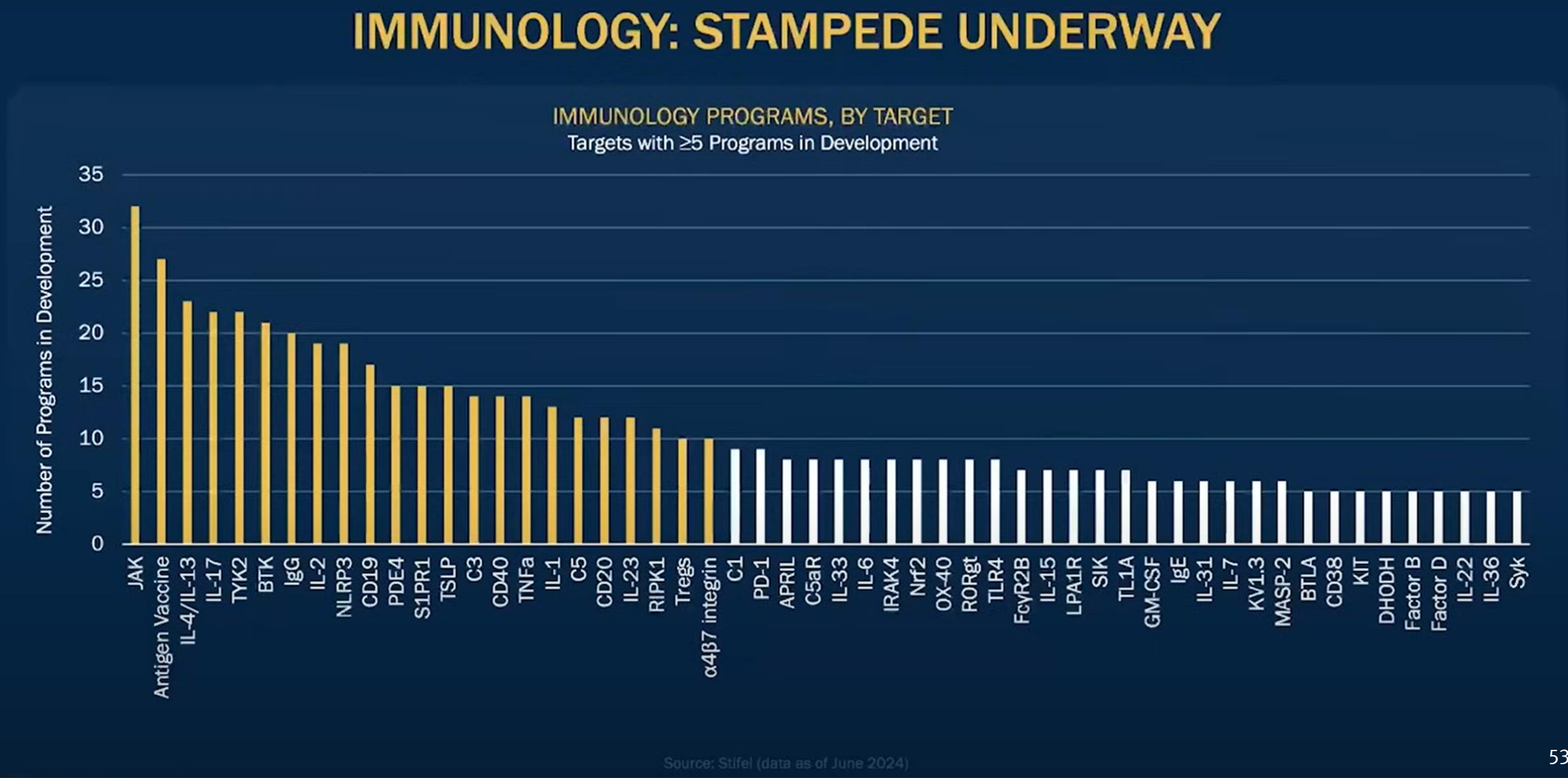
- Source of innovative new patented drugs
- Home of successful global players (e.g. Beigene)
- Huge market (#2 in the world)

EXEMPLARY CHINA-TO-WEST **NON-ONCOLOGY** DEALS
In the Past 10 Years (2013 To 2024)

CHINESE COMPANY	GLOBAL PARTNER	UPFRONT VALUE	TOTAL DEAL SIZE
CURON	MERCK	$700M	$1.3B
Argo Biopharma	NOVARTIS	$185M	>$4B
ECCOGENE 诚益生物	AstraZeneca	$185M	>$2B
FutureGen 明济生物	abbvie	$150M	~$1.7B
HENGRUI	kailera	$100M	>$6B
HENGRUI	AILOS BIO	$21.5M	>$1B

Source: Atlas analysis of company press releases & Citeline

Growth in Immunology Programs is a Third Big Theme



SIGNIFICANT ASSET-CENTRIC M&A ACTIVITY IN AUTOIMMUNITY

KEY IMMUNOLOGY M&A (2023 to 2024)

ACQUIRER	TARGET	TOTAL DEAL VALUE
MERCK	Prometheus Biosciences	$10.8B
Roche	Telavant	$7.25B
Takeda	nimbus THERAPEUTICS	$6B
VERTEX	ALPINE	$4.9B
Lilly	MORPHIC	$3.2B
Lilly	DICE	$2.4B
Biogen	HI·Bio	$1.8B
GSK	AIOLOS BIO	$1.4B
Johnson&Johnson	NUMAB	$1.25B
sanofi	teva	$1B
Johnson&Johnson	PROTEOLOGIX	>$825M

Source: Atlas analysis of company PR and Citeline

>$40B

in M&A

for Autoimmune Diseases

HOT SPACES FOR INVESTORS IN THE AUTOIMMUNE FIELD

CAR-T in LUPUS

T & B CELL DEPLETERS

HALF-LIFE EXTENSION FOR KNOWN MECHANISMS

STAT6 ORALS

BISPECIFICS

Theme #4 is AI – This Will be Gradual

AI/ML WILL IMPACT R&D PROCESS

DRUG DISCOVERY

- Target/pathway ID
- Predict structure (e.g., AlphaFold)
- Literature reviews
- Repurposing old drugs, new uses
- Antibody & protein design

PRECLINICAL DEVELOPMENT

- Tox predictions
- ADME in silico
- Regulatory documentation
- Synthetic route optimization
- Human dose modeling

CLINICAL TRIALS

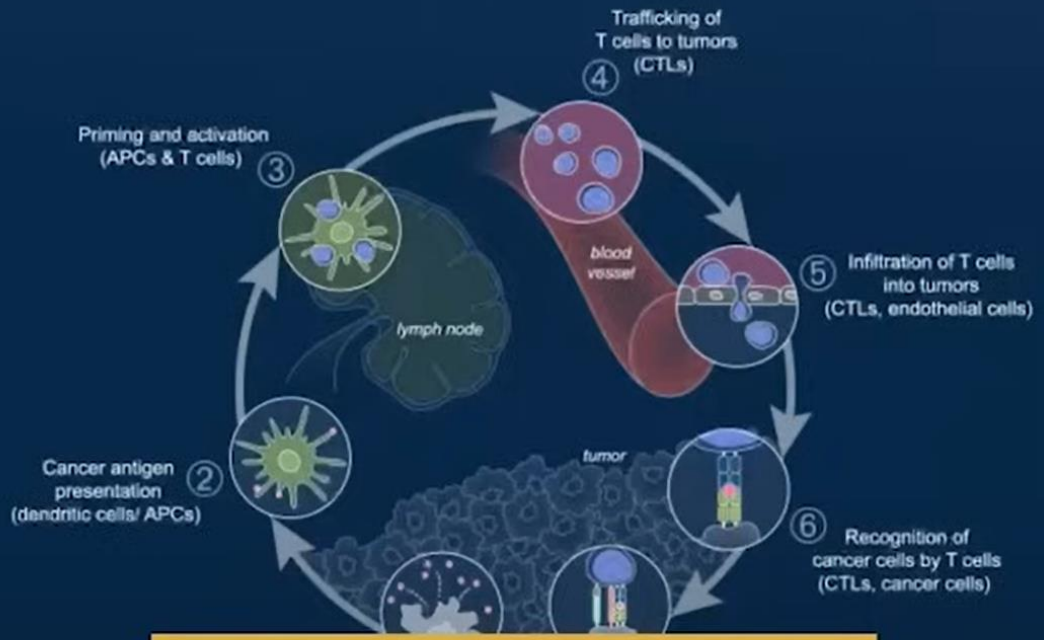
- Patient selection / subgroups
- Data analysis
- Trial designs
- Synthesis and reports
- Trial enrollment

Given complexity of human biology,
the impact of AI/ML on R&D likely more evolution ***than revolution***

Theme #5: R&D Dynamism

R&D DYNAMISM: ONCOLOGY

2013 - 2014 Immuno-oncology



Keynote-001 Goldrush 2014+

- **Thousands** of trials
- **Billions** of dollars
- *...yet few new I/O breakthroughs*

What's Hot in 2024

- ADCs
- Radiopharma
- Precision Oncology Redux
- Degraders
- Bispecific T-Cell Engagers

R&D DYNANISM: MODALITIES

EXPLOSION OF "MODALITIES"

- Winners and losers: only some modalities will be broadly useful
- Manufacturing and distribution complexity
- Concern around permanent changes/terminal therapies
- Oral pills remain preferred modality

HEADWINDS

- Autologous cell therapy
- Viral gene Rx
- Digital therapies
- Gene editing

TAILWINDS

- PROTACs
- T-Cell Engagers
- Non-viral delivery
- Targeted therapies (ADC, Radio, Oligo)

PATIENT IMPACT: NEW DRUGS

AMTAGVI (lifileucel) Suspension for IV infusion
IOVANCE BIOTHERAPEUTICS

casgevy (exagamglogene autotemcel) suspension for IV infusion
CRISPR THERAPEUTICS | VERTEX

kisunla (donanemab-azbt) injection for IV infusion
Lilly

lenmeldy (atidarsagene autotemcel)
Orchard therapeutics

Livdelzi seladelpar
GILEAD

COBENFY (xanomeline and trospium chloride) capsules
Bristol Myers Squibb

nemluvio (nemolizumab-ilto) for injection 30 mg
GALDERMA

ojemda (tovorafenib) 100 mg tablets 25 mg/mL for oral suspension
Day One BIOPHARMACEUTICALS

Rezdiffra: resmetirom tablets
Madrigal Pharmaceuticals

Note: Approvals through 10/04/24
Source: AV analysis of CDER and CBER approvals

EXCITING NEW DRUGS TO WATCH...

WVE-006
RNA editor

— FOR —
Alpha-1 Antitrypsin Deficiency

WAVE LIFE SCIENCES

KRRO-110
KORRO BIO

CD19 THERAPIES
B cell / plasmablast depletion

— FOR —
Autoimmune (notably SLE)

CAR-T
- kyverna
- Cabaletta Bio
- NOVARTIS

T-Cell Engagers
- cullinan THERAPEUTICS
- MERCK
- CURON

TEZEPELUMAB
anti-TSLP

— FOR —
COPD

AMGEN AstraZeneca

AIO-001
AIOLOS BIO GSK

REVUMENIB; ZIFTOMENIB
Menin inhibitor

— FOR —
AML

Syndax KURA ONCOLOGY

RMC-6236
KRAS inhibitor (incl. G12X, G13X, Q61X)

— FOR —
PDAC, NSCLC, other solid tumors

Revolution Medicines

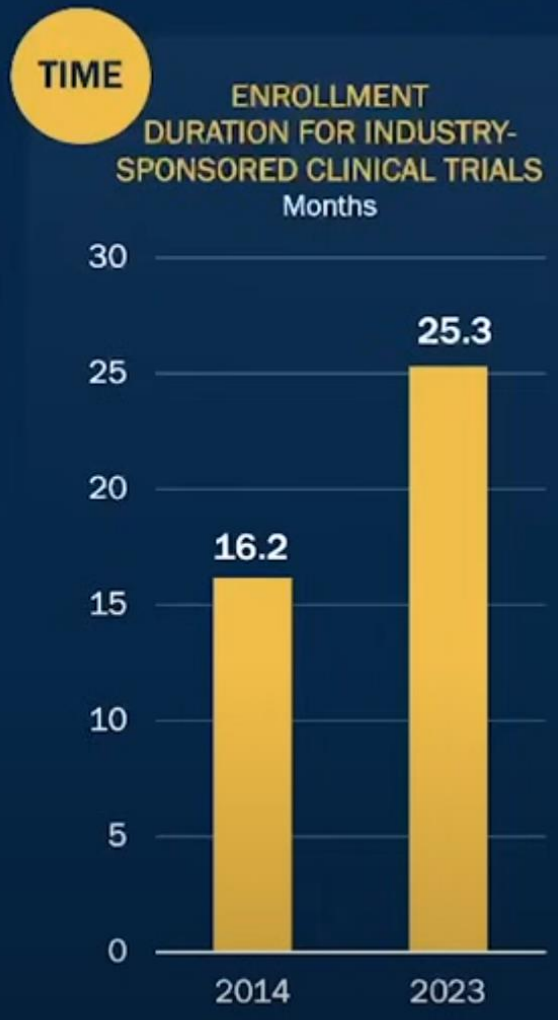
APITEGROMAB
Myostatin inhibitor

— FOR —
Spinal Muscular Atrophy

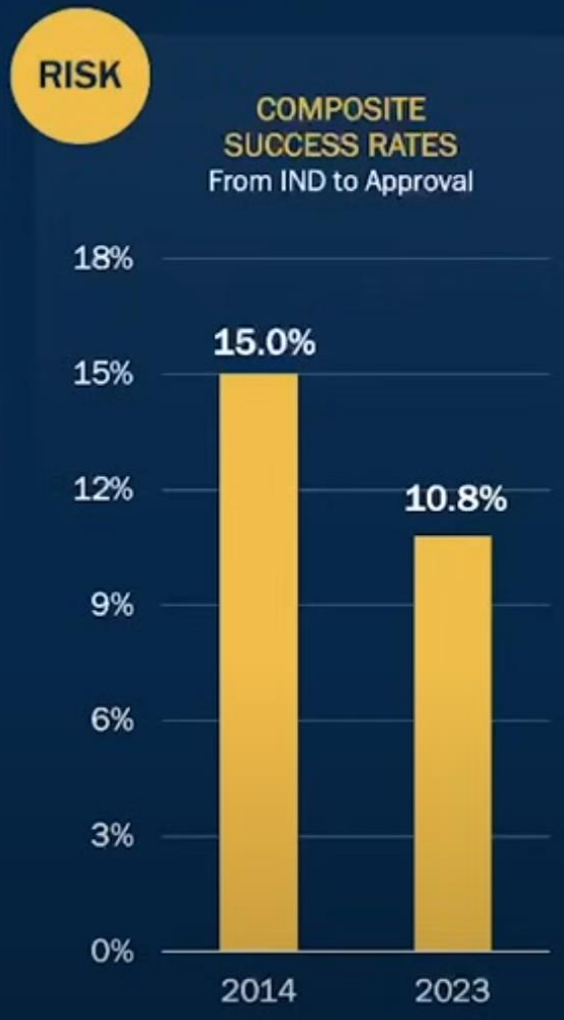
Scholar Rock

TOUGH BUSINESS

Source: Deloitte Annual Report on the Returns from Pharmaceutical Innovation (April 2024)



Source: IQVIA report "Rethinking Clinical Trial Country Prioritization" (2024)

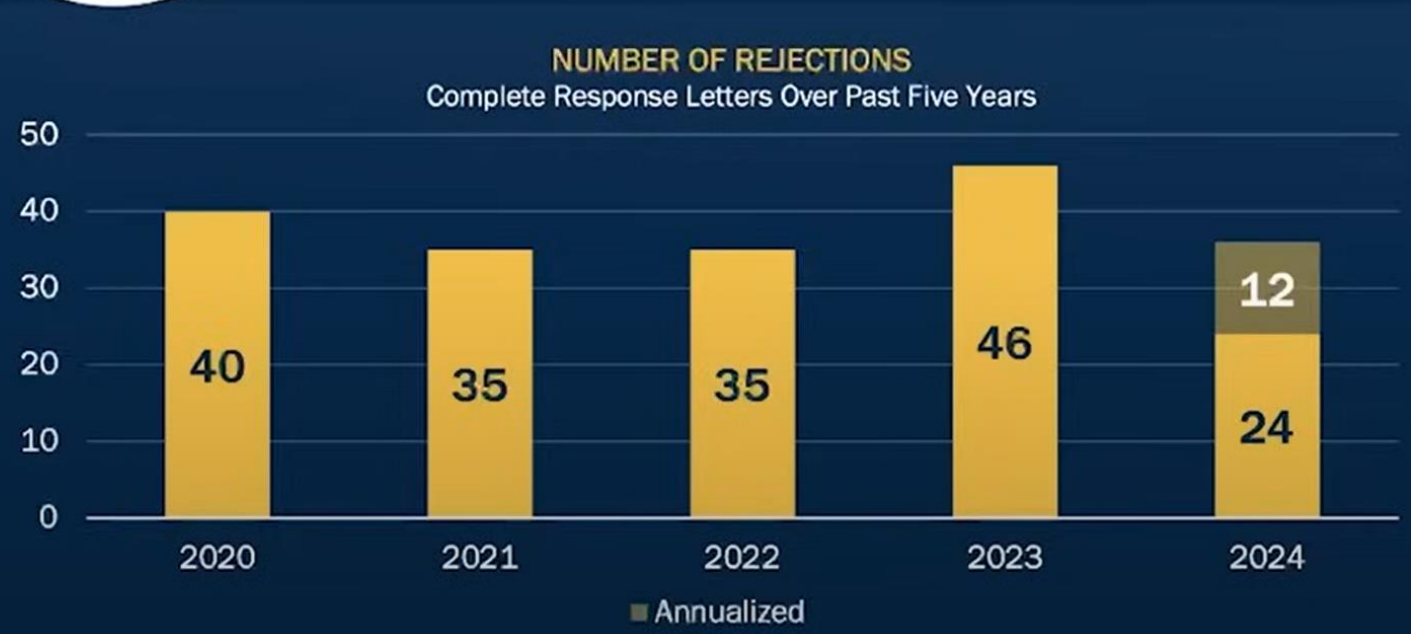


Source: IQVIA "Global Trends in R&D 2024"

Source: Deloitte Analysis (April 2024)

FDA: TOO TIGHT, TOO LOOSE?

U.S. FOOD
AND DRUG
ADMINISTRATION



Approved Drugs

– WITH –

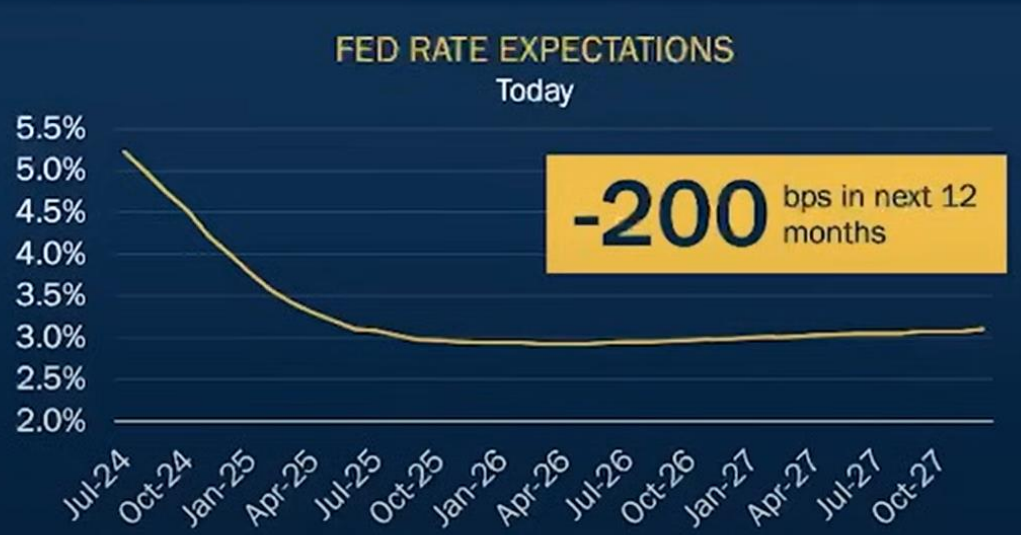
UNPROVEN AND/OR
UNCONFIRMED DATA

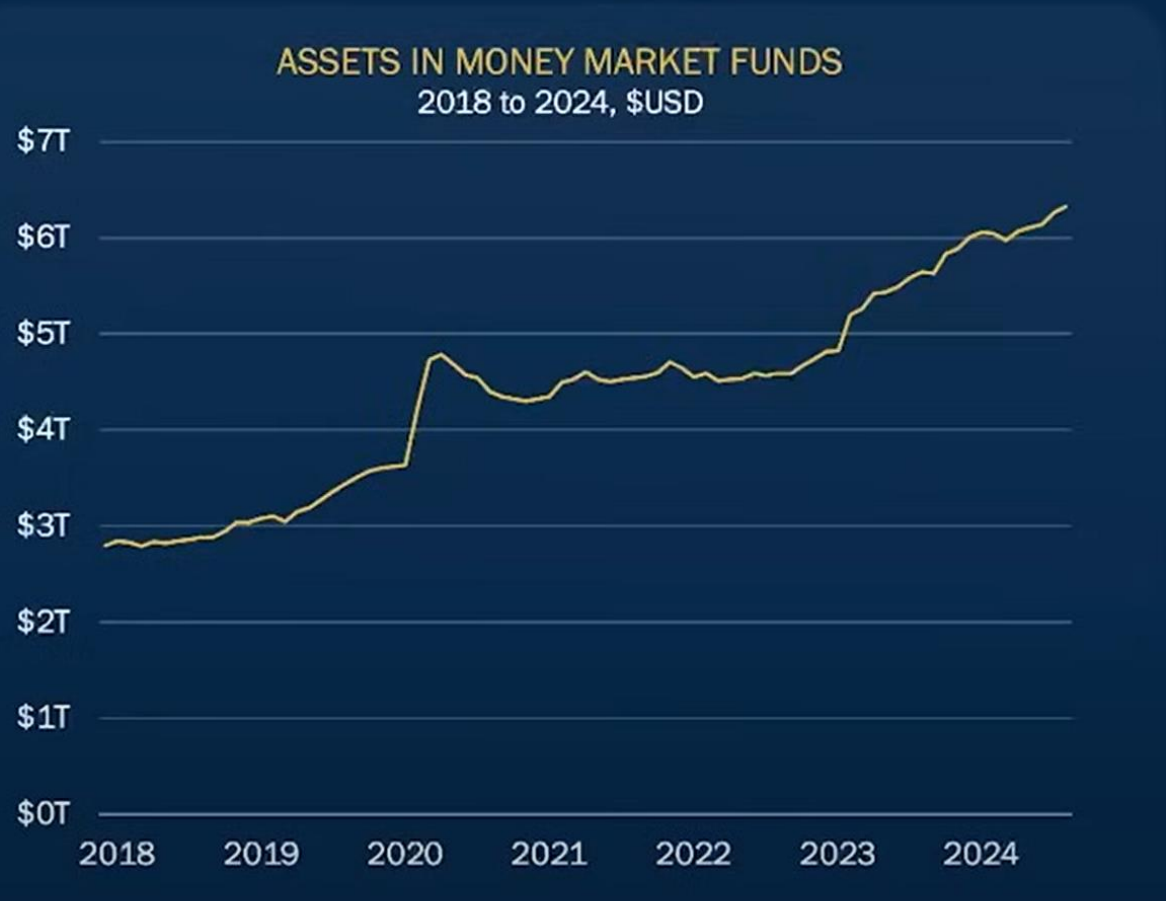
Aduhelm® (aducanumab-avwa) | 100 mg/mL injection, for intravenous use

Elevidys
delandistrogene
moxeparvovec-rokl
suspension for intravenous infusion

FED RATE CUT

INTEREST RATES



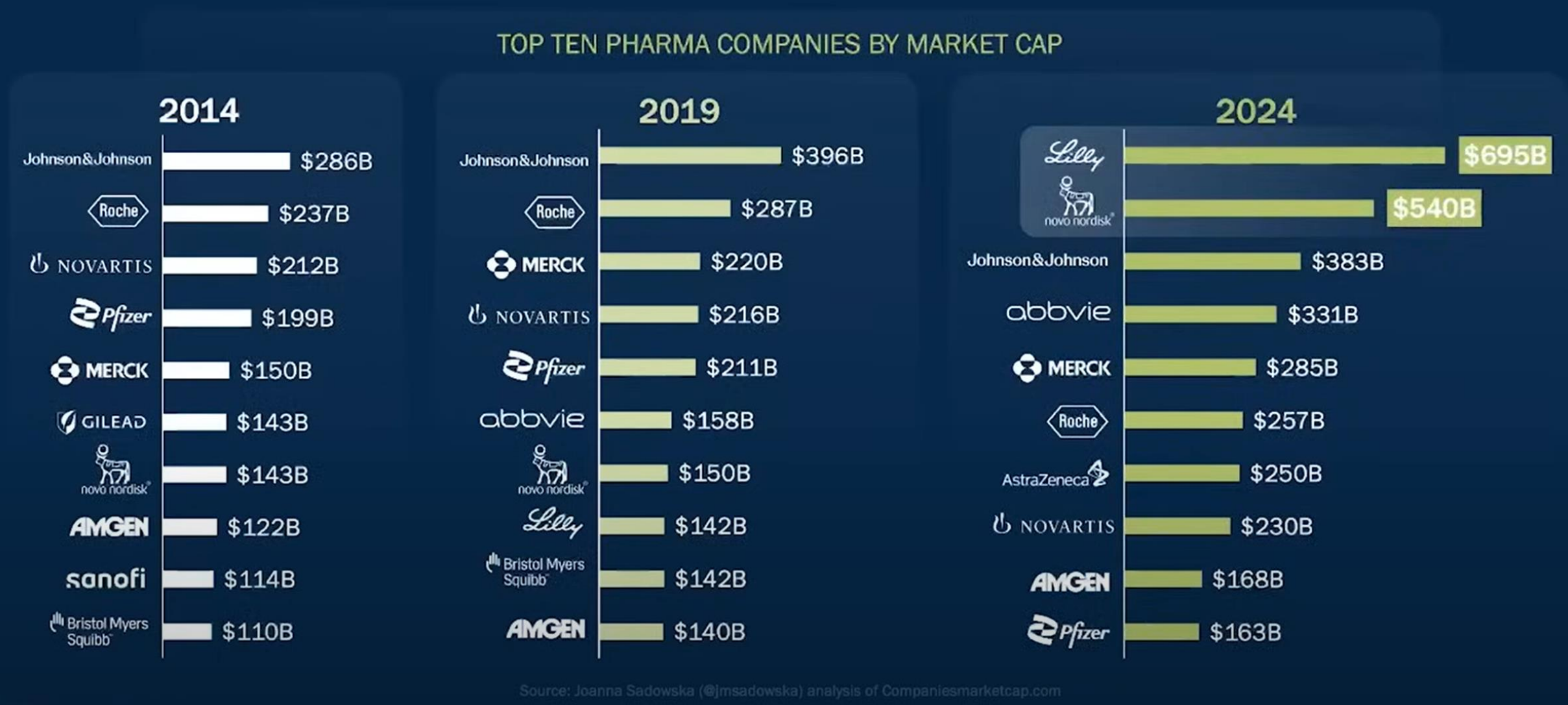


OBESITY PLAYERS HAVE OUTSIZED IMPACT

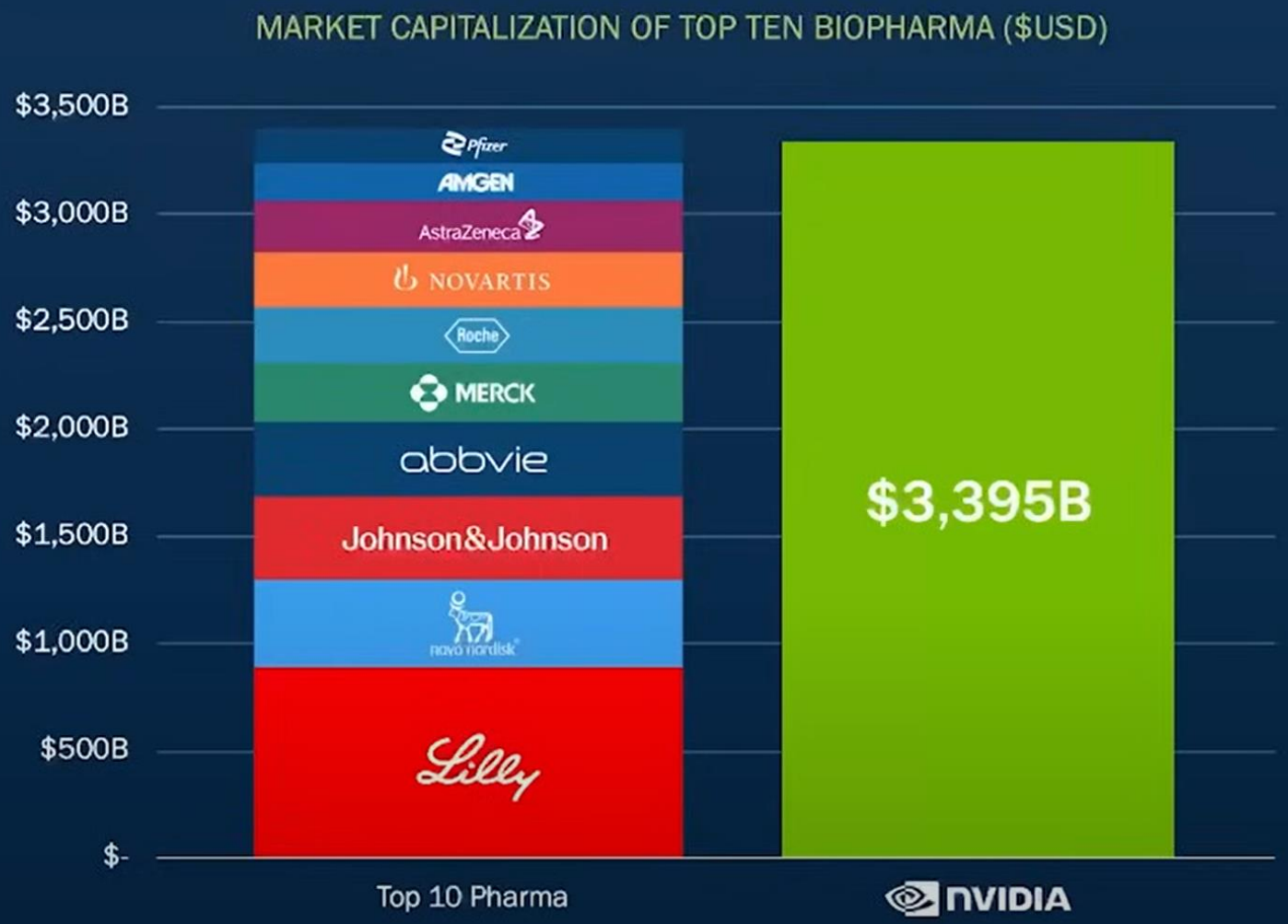
Source: AV analysis; Data as of 10/15/24

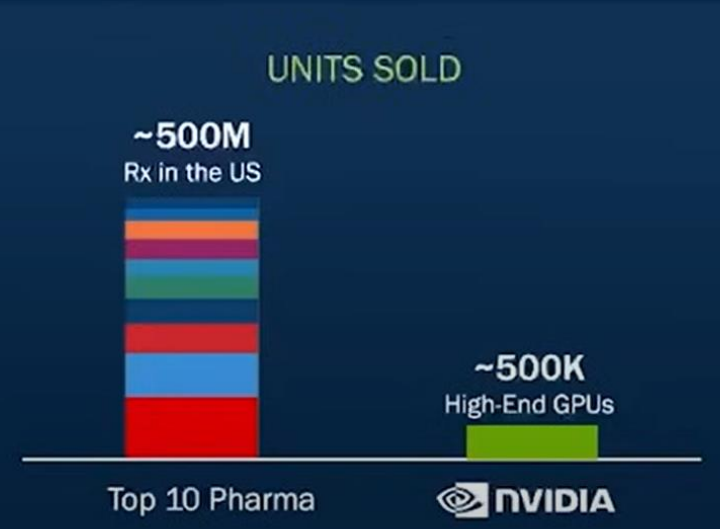
Note: * LLY, NOVO, AMGN, ZEAL, VKTX; obesity 5 and Big Pharma are equal-weighted to compare to XBI and S&P 500 indices

HUGE SHIFT IN THE LEAGUE TABLES



OBESITY HAS BEEN BIG, BUT AI/ML BIGGER!



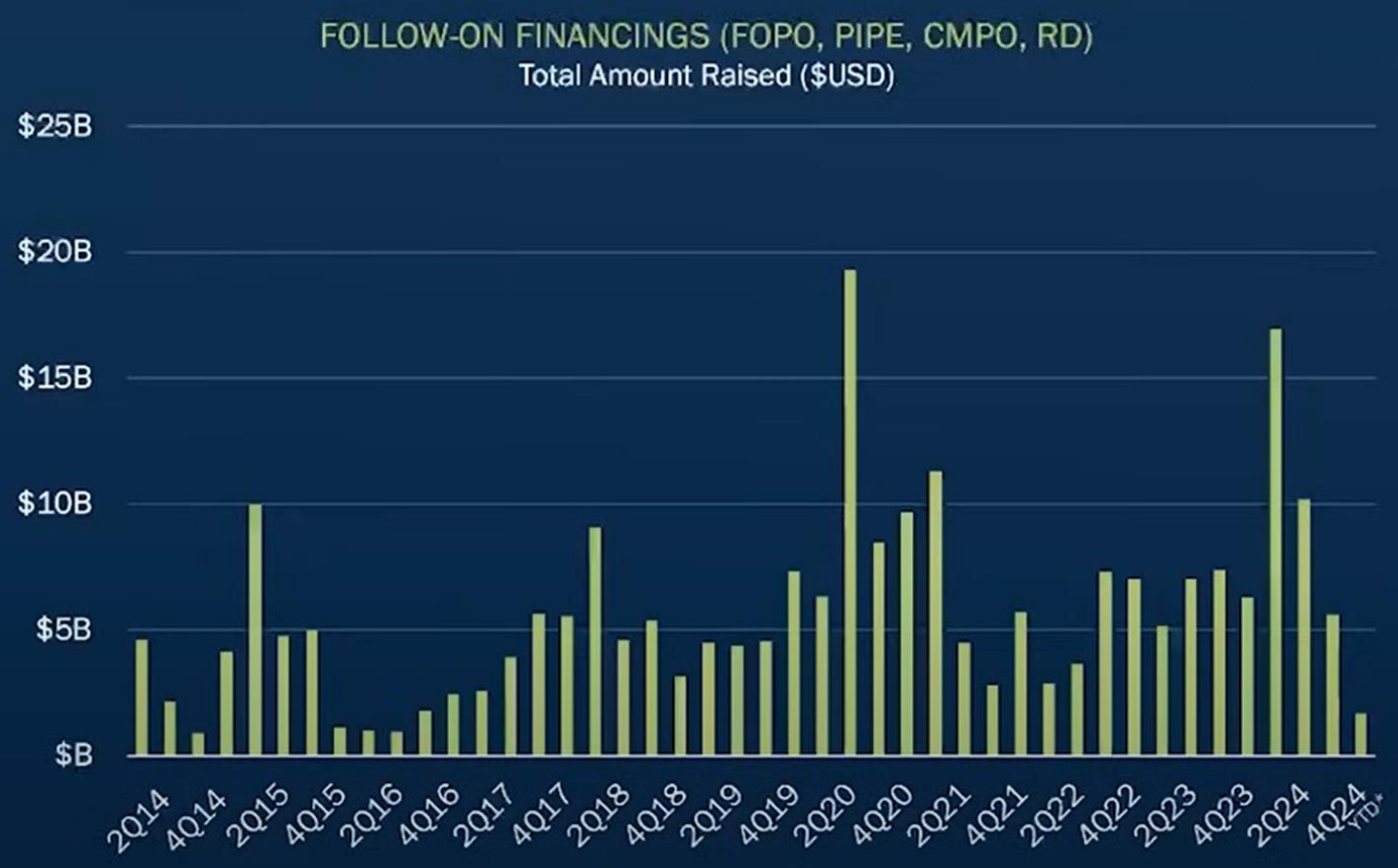


Source: AV analysis

Lilly and Novo Gains Dwarf All of Biotech

Source: LLY and NOVO data pulled from Yahoo Finance and Companiesmarketcap.com (data compared 9/13/21 vs. 9/13/24); Public biotech data courtesy of Tim Opler of Stifel, based on CapIQ analysis and includes Therapeutics IPOs of U.S.-domiciled biopharma companies. Atlas analysis of data from Stifel, Leerink, Cantor, and Morgan Stanley

FOLLOW-ON PUBLIC OFFERINGS: RECORD-BREAKING 1H



SELECTED FOPO RAISES OF 2024

COMPANY	AMOUNT RAISED ($USD)
VAXCYTE	$2.36B*^
Dyne	$719M*
Madrigal Pharmaceuticals	$690M
VIKING THERAPEUTICS	$633M
KYMERA	$575M*^
Cytokinetics	$570M
STRUCTURE THERAPEUTICS	$547M
Celldex therapeutics	$461M

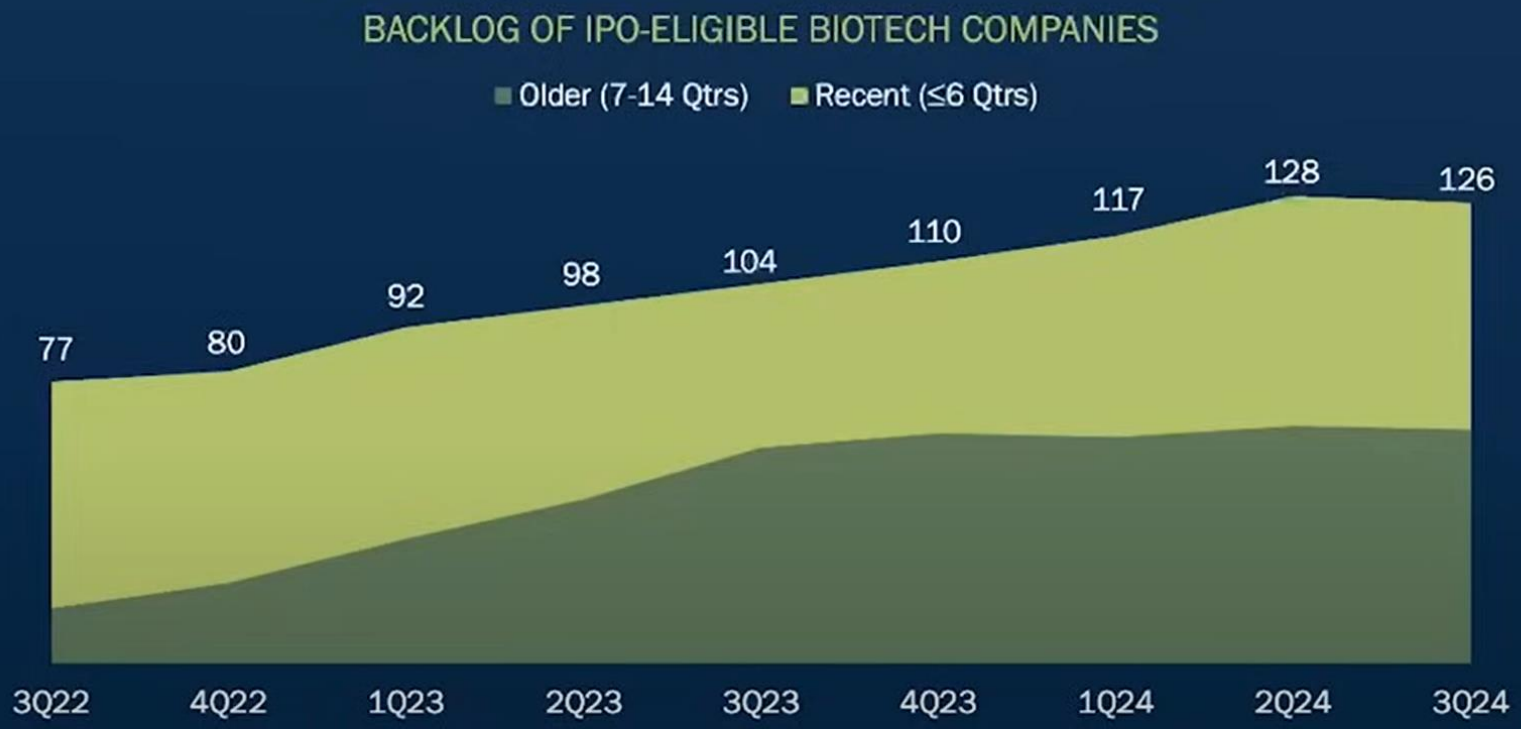
IPOs

Valuations have been robust by historic measures

Aftermarket performance has some early winners and losers

IPO LOGJAM: LATE STAGE PRIVATES

Backlog of private companies waiting to go public…



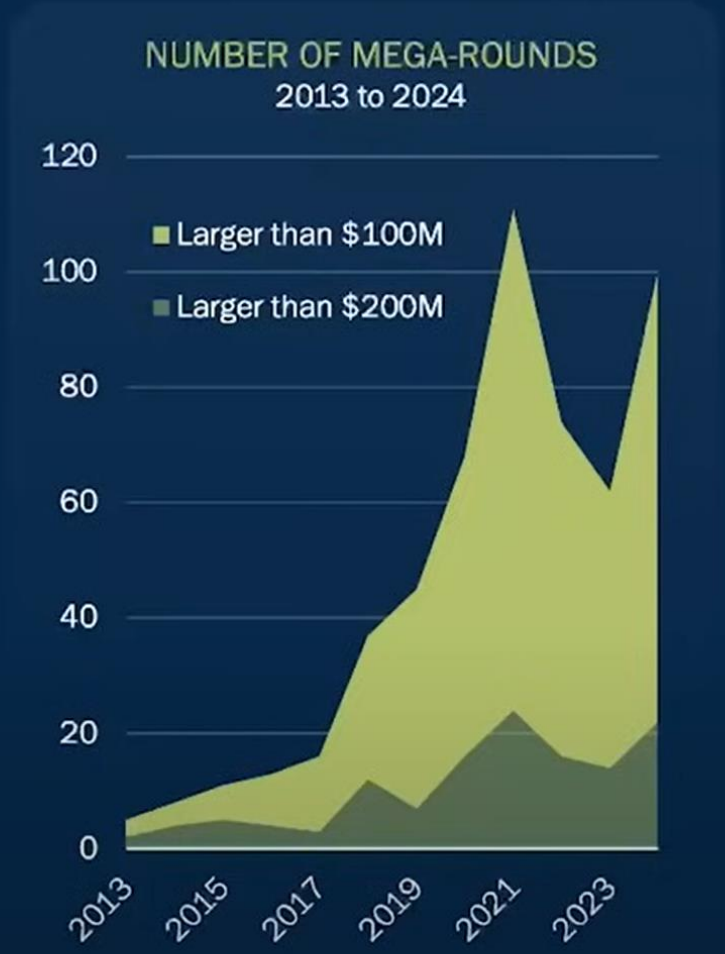
- Huge number of companies waiting with confidential S1's on file
- Many considering alternatives like Reverse Mergers or M&A
- Many will need to refinance over next 12-24 months at challenging valuations

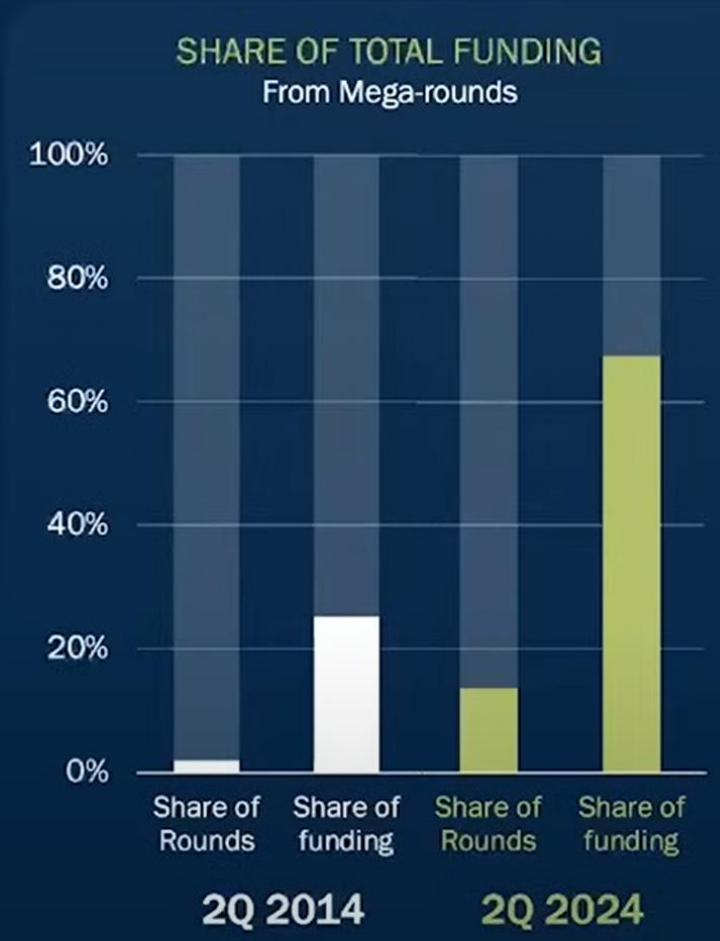
VENTURE CAPITAL FUNDING NORMALIZED

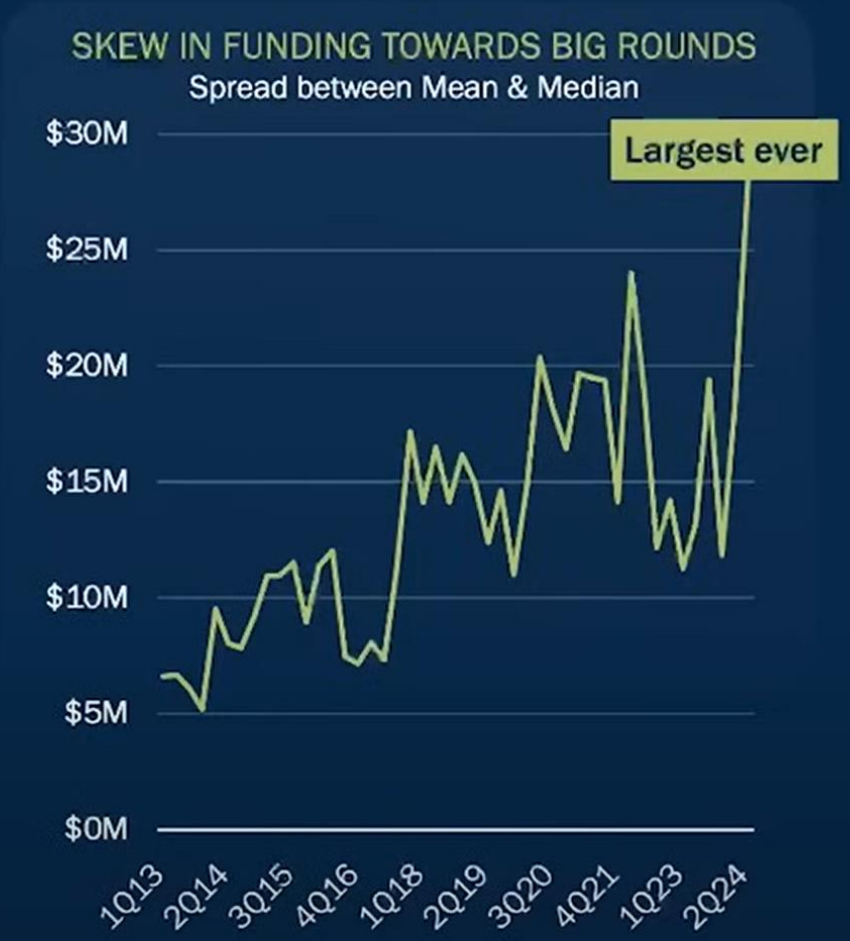
Source: Pitchbook, Data as of 10/11/24

- Robust $6-8B of funding per quarter
- Mostly from traditional VCs, but crossovers getting more active again
- Preferred stock terms shifting towards later stage investors

VC: HUGE SKEW REVEALS HAVE'S & HAVE NOT'S



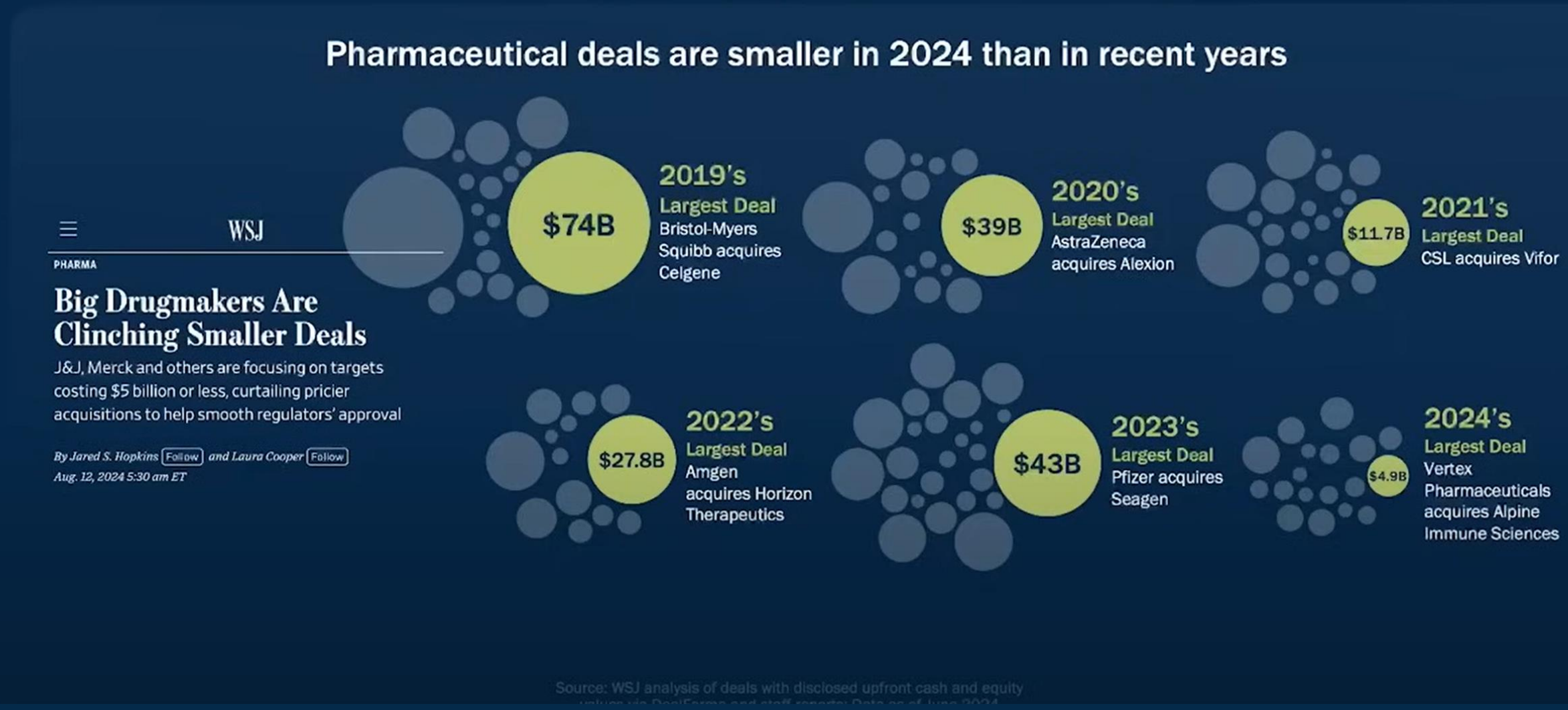




Note: U.S.-based private biopharma

LICENSING COLLABORATIONS: SLOWING DOWN

M&A: SMALLER DEALS IN 2024



M&A: SMALLER DEALS IN 2024

Pharmaceutical deals are smaller in 2024 than in recent years

Source: WSJ analysis of deals with disclosed upfront cash and equity values via DealForma and staff reports; Data as of June 2024

R&D-STAGE PUBLIC BIOTECH M&A

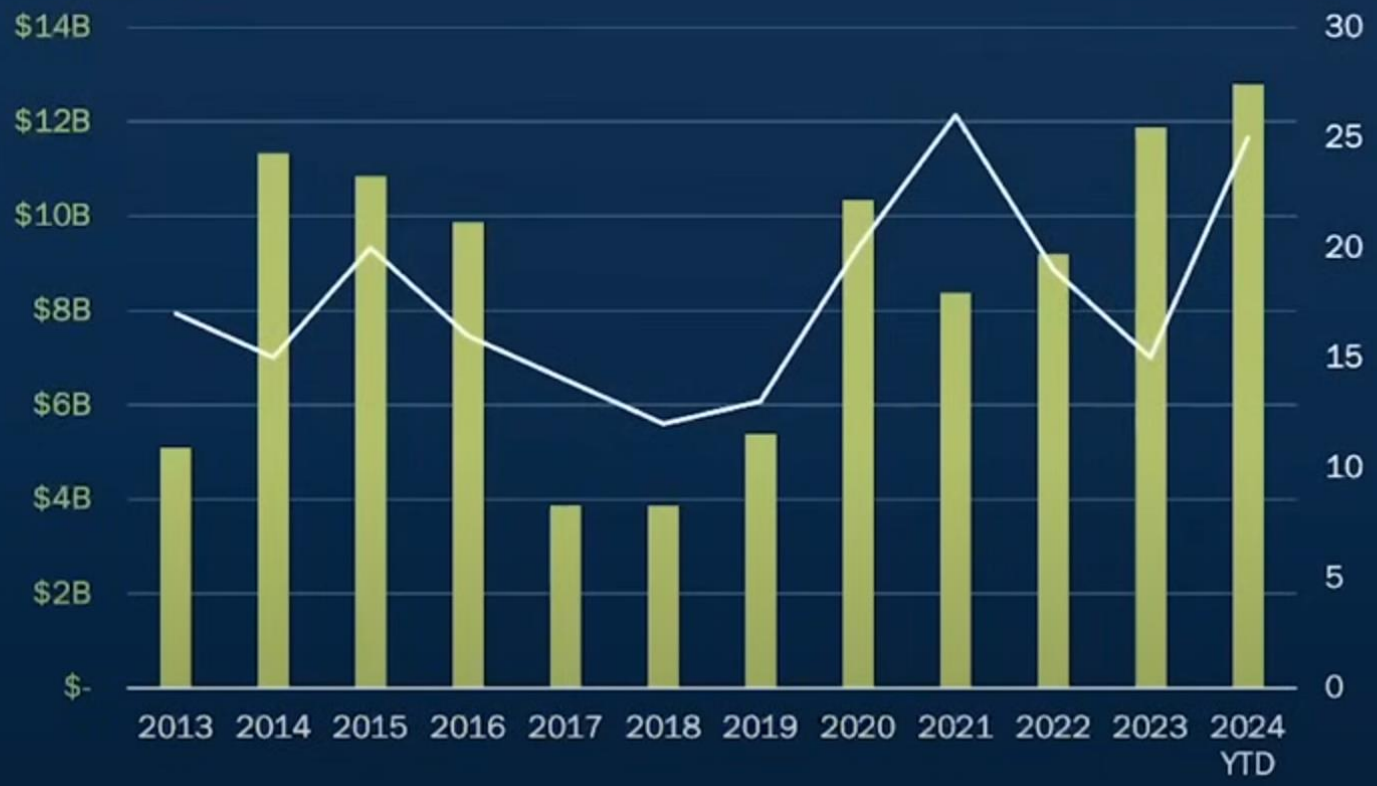
Source: BMO Capital; Cantor; Jefferies; Public pre-commercial M&A over $100M; Data through 9/20/24

NOTABLE PUBLIC M&A

TARGET	ACQUIRER	TOTAL DEAL VALUE
Alpine Immune Sciences	Vertex	$4.9B
CymaBay Therapeutics	Gilead	$4.3B
Morphic	Lilly	$3.2B
Morphosys	Novartis	$2.9B
Longboard Pharmaceuticals	Lundbeck	$2.6B
Fusion	AstraZeneca	$2.4B

PRIVATE M&A HEATING UP

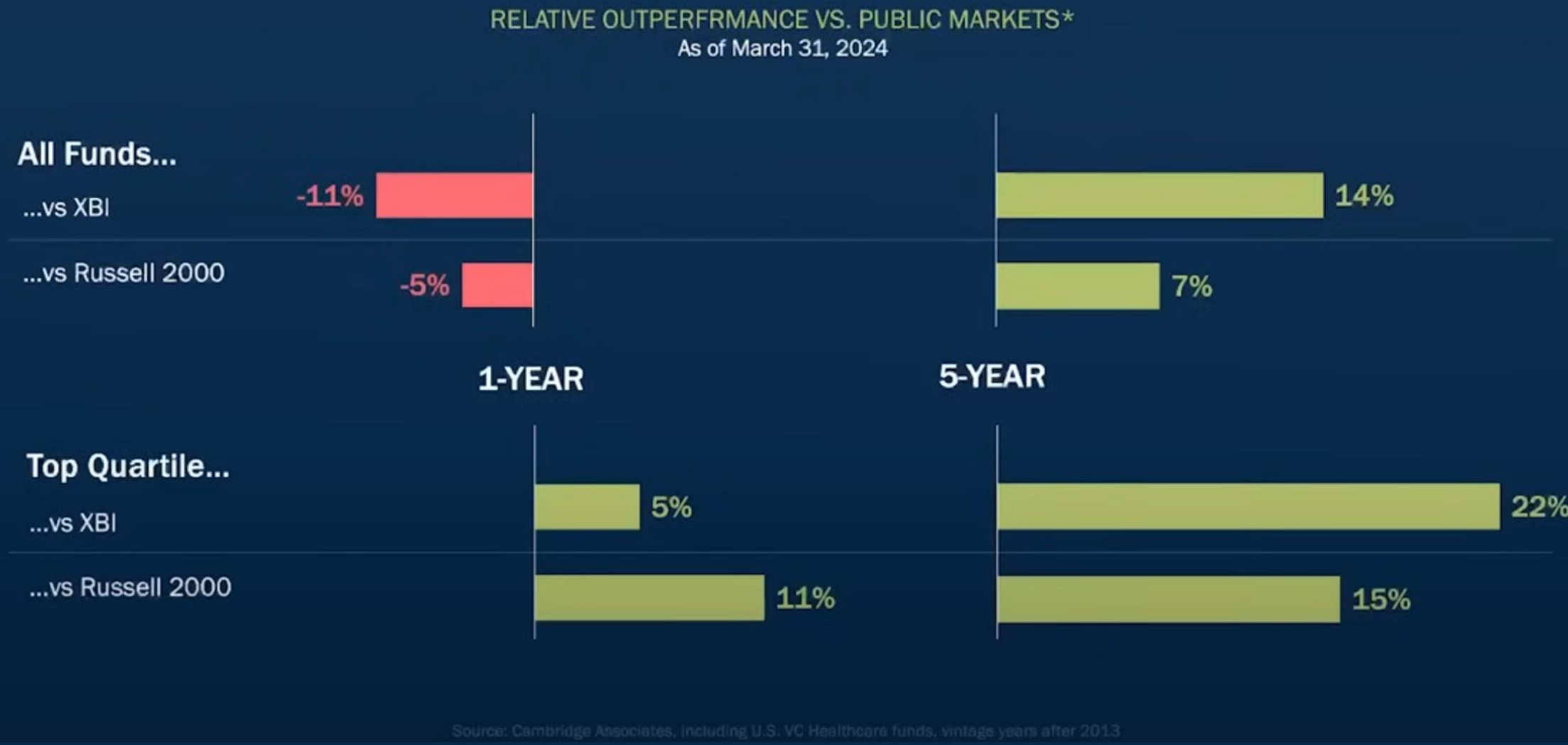
PRIVATE BIOTECH M&A



TOP 10 VC-BACKED PRIVATE M&A

TARGET	ACQUIRER	TOTAL DEAL VALUE
EyeBio	MERCK	$3.0B
ProfoundBio	Genmab	$1.8B
HI-Bio	Biogen	$1.8B
mariana ONCOLOGY	NOVARTIS	$1.8B
AIOLOS BIO	GSK	$1.4B
ALIADA	abbvie	$1.4B
CURON	MERCK	$1.3B
numab	Johnson&Johnson	$1.3B
jnana	Otsuka	$1.1B
AMOLYT PHARMA	AstraZeneca	$1.0B
PROTEOLOGIX	Johnson&Johnson	~$1B
escient	Incyte	$0.75B

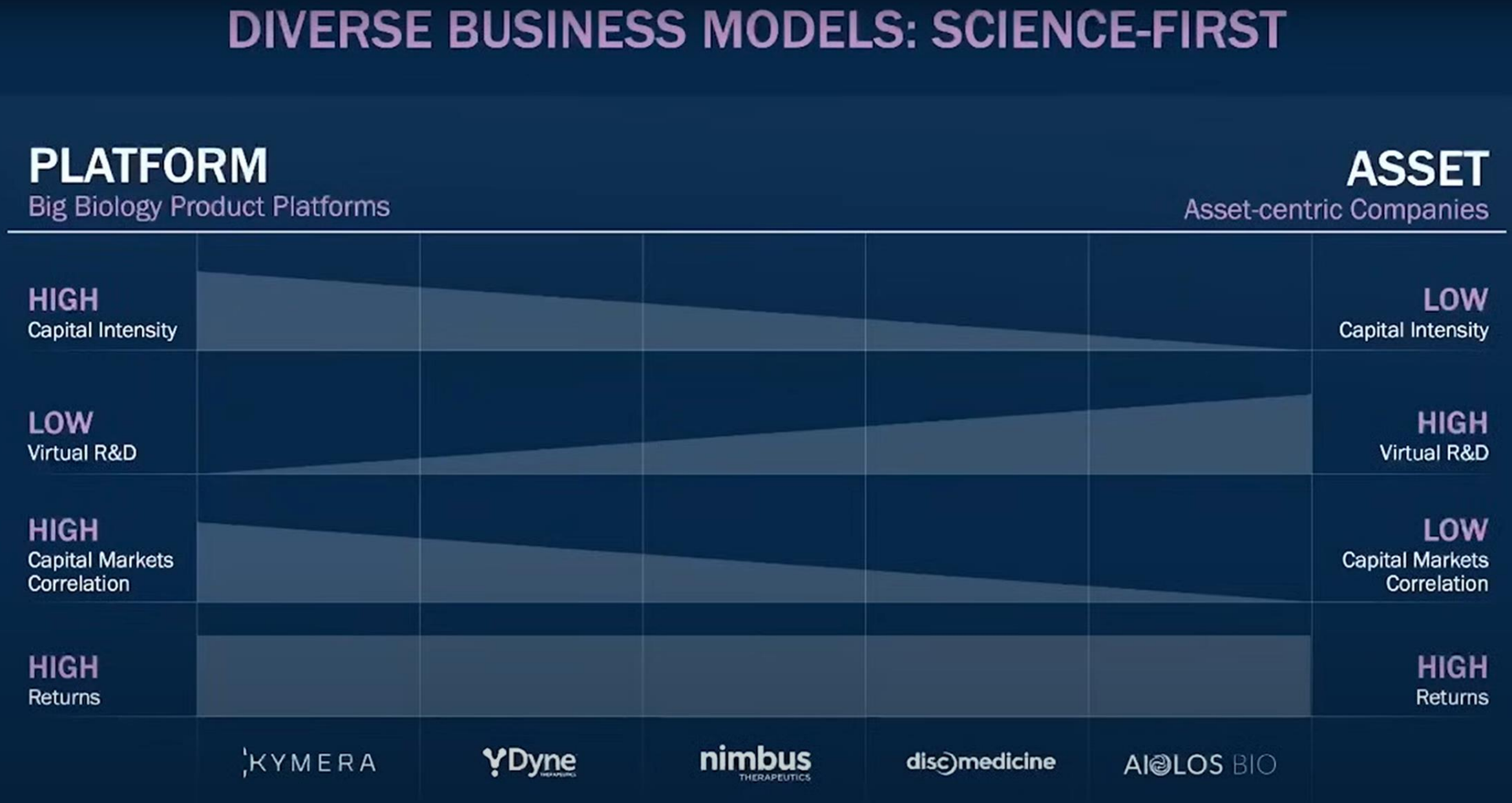
VC RETURNS: SOFTENED POST-2021, BUT STELLAR



Source: Cambridge Associates, including U.S. VC Healthcare funds, vintage years after 2013

Atlas Venture Delivering the Goods in a Tough Environment

Atlas Puts Science First and Adapts Business Models to the Circumstance



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