Biopharmaceutical Sector

Weekly Update – Jan 15, 2024

St. Francis Hotel. Site of #jpm24 Conference.. Photo: Tim Opler

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Herbert Hotel by #JPM24 Conference. Photo: Tim Opler

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If you are not on the mailing list for this publication and wish to be added, please notify Natasha Yeung (yeungn@stifel.com). Recent issues in case you missed and want to read:

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Dec 18, 2023 (Expectations for Future)
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Dec 4, 2023 (Big Pharma, CEA)
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May 29, 2023 (Oncology update)
May 22, 2023 (FTC case on Amgen/Horizon)

Macroeconomics Update

U.S. CPI Inflation of 0.3% in December

NPR, January 4, 2024

Inflation ticked up a little in December on the back of higher costs for housing and car insurance. The overall cost of living in December was up 3.4% from a year ago, a slightly larger increase than the 3.1% rate in November, according to data from the Labor Department on Thursday.

The cost of motor vehicle insurance rose 1.5% in December from the previous month, marking a 20.3% increase compared to the previous year.

The cost of housing accounted for more than half the monthly increase in consumer prices. Food and energy prices were also up in December. The so-called "core" inflation rate, which excludes food and energy prices, was 3.9% last month.

While the market viewed this inflation report somewhat negatively, the change in CPI in December was the same for November if energy was excluded.

We do not view this inflation report as alarming.

Source: https://www.npr.org/2024/01/11/1224044520/cpi-inflation-december-labor-department-interest-rate-fed

NY Fed President Speech Last Week

Julie Lasson, Jan 10, 2024, NY Fed (excerpt)

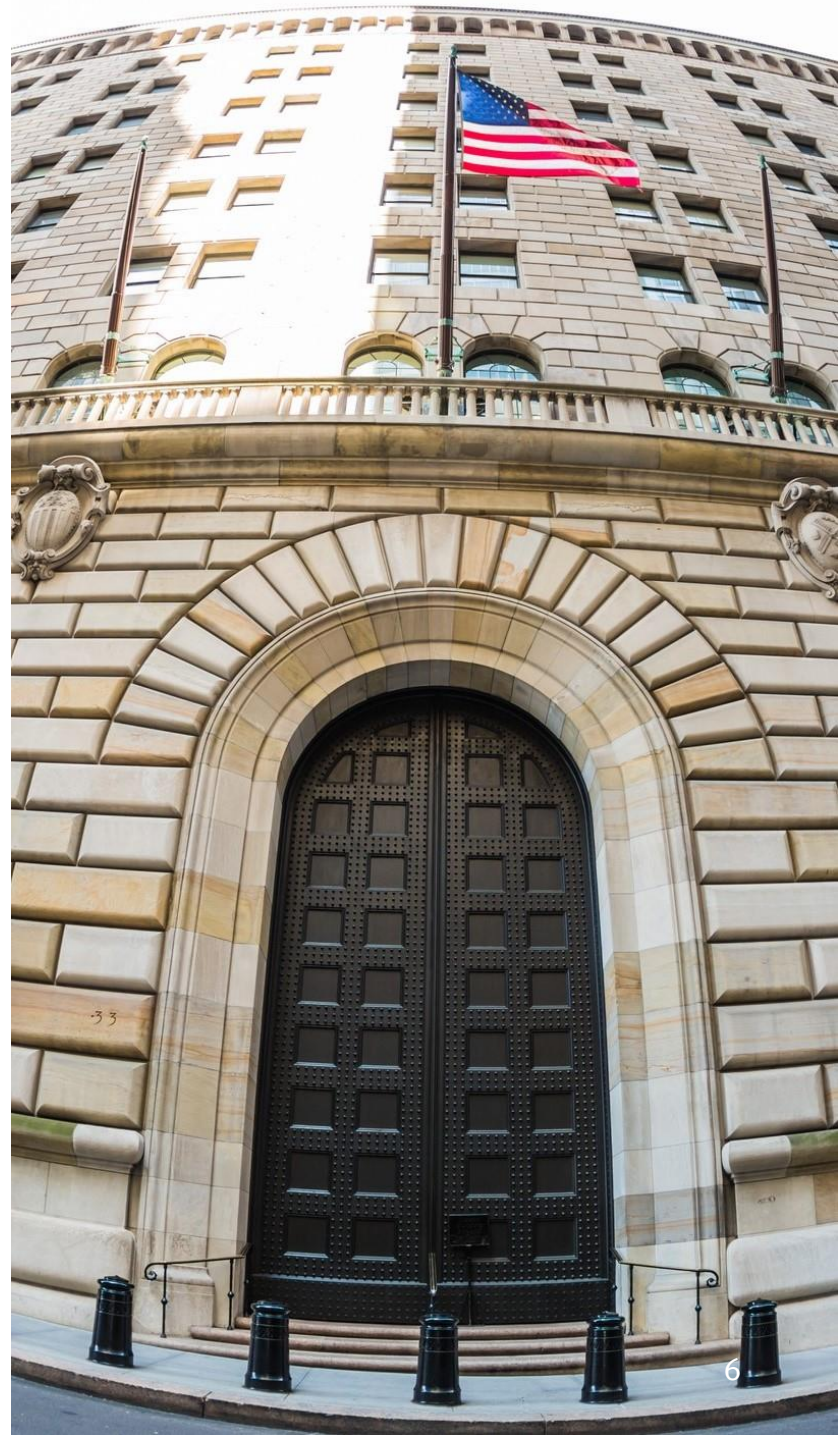
New York Fed President John C. Williams spoke about his economic outlook and monetary policy before a group of real estate and business leaders from across the greater New York metropolitan area on January 10, 2024.

He said: “I expect that we will need to maintain a restrictive stance of policy for some time to fully achieve our goals, and it will only be appropriate to dial back the degree of policy restraint when we are confident that inflation is moving toward 2 percent on a sustained basis.”

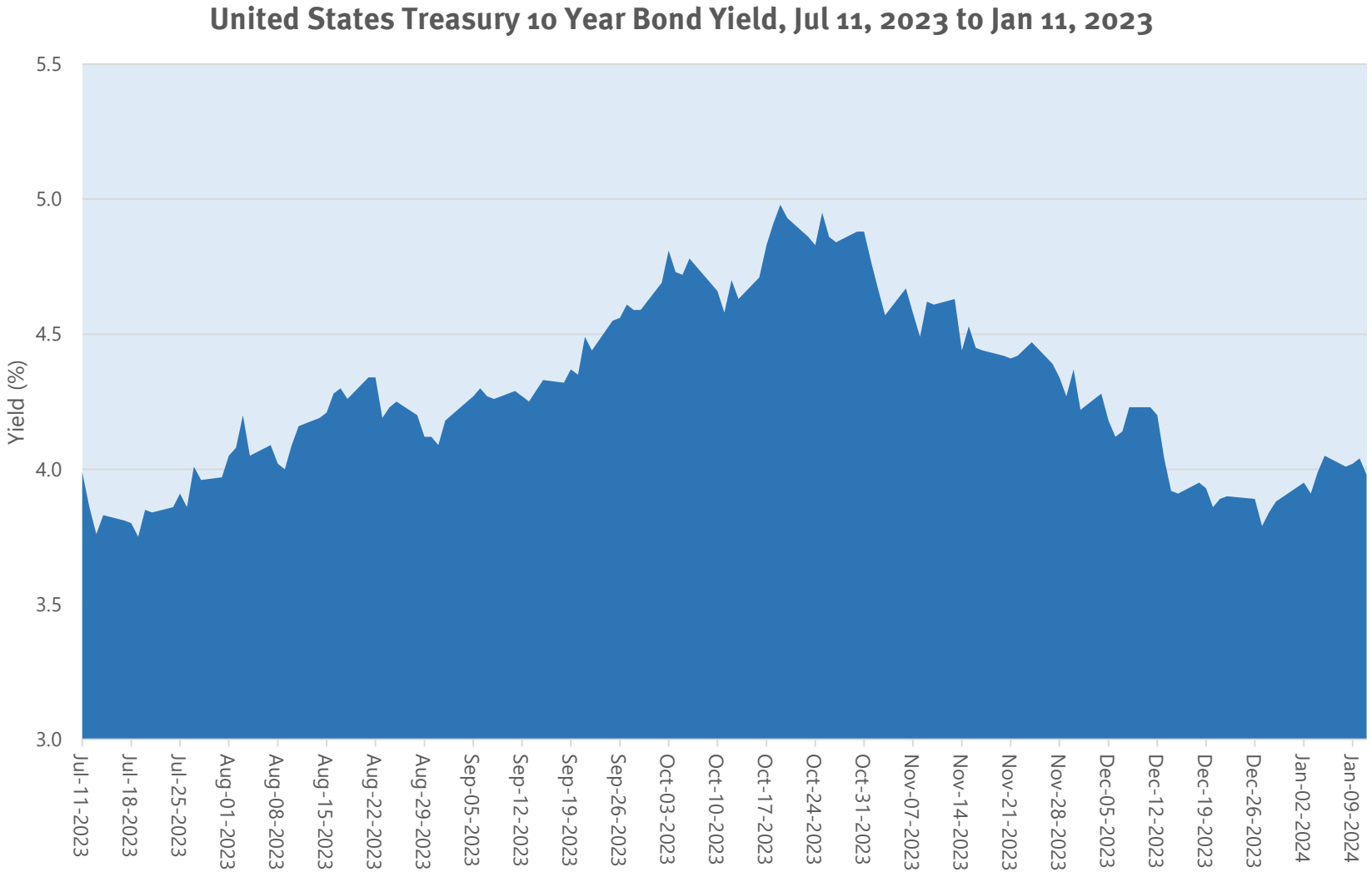
“The outlook remains highly uncertain, and I will continue to carefully watch and assess the data to judge whether the stance of policy is best positioned to achieve our goals.”

He pointed out that inflation, as measured by the personal consumption expenditures (PCE) price index, surged to a 40-year high of about 7 percent in June of 2022, but fell back to just over 2-1/2 percent over the past year and a half. “This decrease is a clearly positive development, but it is important to stress that we still have a ways to go to get inflation back to the FOMC’s longer-run goal of 2 percent,” he added.

Source: https://tellerwindow.newyorkfed.org/2024/01/10/key-takeaways-from-president-williamss-speech-on-the-economic-outlook-and-monetary-policy-8/



U.S. Ten-Year Treasury Dipped Back Below 4% Last Week



Ten-Year US Treasury Bond Yields have dropped by over 100 basis points since peaking in October.

The yield dipped below 4% last week despite some negative inflation news.

This is bullish for biotech.

Source: S&P CapitalIQ.

Don’t Be So Certain Trump Has the Nomination Locked

Charlie Mahtesian, *Politico*, Jan 11, 2024 (excerpt)

Sure, at the moment, it looks like Donald Trump will win the 2024 Republican nomination. But it smells a bit like 2016, when there was near unanimity in the press and the political class that he didn’t have a shot in hell against Hillary Clinton.

In an unstable, unconventional time, it’s not inconceivable to imagine a scenario in which the bottom suddenly falls out for the former president and a rival ambushes him on his way to the GOP convention in Milwaukee. Like Nikki Haley.

Let’s review the last quarter-century of presidential elections.

The GOP’s Electoral College lock has been picked. The Democratic Blue Wall has been breached. Ohio, a longtime bellwether, has gone red. Georgia and Arizona, longtime GOP stalwarts, have gone blue. Jeb Bush, a GOP juggernaut, lost to a reality TV star. Joe Biden, a dead letter after the first 2020 primaries, is now president.

If we’ve learned anything, it’s that the laws of political gravity or axioms about elected politics don’t always apply anymore. Traditional voting habits have been thrown out the window. Polling has proved unreliable. And yet here we are, again, operating with utter certainty that the GOP primary is already cooked.

After Iowa, it’s on to New Hampshire, where expectations will be higher. She’s already nipping at Trump’s heels in the latest polls, so anything less than a second-place finish could prove fatal to Haley’s campaign.

But New Hampshire is also uniquely suited for her. Polls suggest it is the early state where Trump is weakest. She has spent time and directed resources there and it shows — she has doubled her support over the past two months.

This year’s U.S. election is more than a little consequential for the pharma sector.

The most pharma friendly candidate is Nikki Haley.

She has been gaining rapidly on Donald Trump in polls for the upcoming New Hampshire primary.

Source: https://www.politico.com/news/magazine/2024/01/11/nikki-haley-donald-trump-gop-00134902

Biopharma Market Update

#JPM24 Conference crowd crush in Four Seasons Hotel. Photo: Tim Opler

Heard at #JPM24: Industry Buzz

We had numerous illuminating conversations with industry participants at #JPM24 last week. Here is what we picked up at the conference.

It was nice to largely have beautiful weather last week (versus rain hell the year before) at #JPM24.

The mood was generally positive – boosted by an improving economic picture, a heavy dose of M&A and an abundance of business opportunities. We don't think we heard the word "COVID" once in the whole week.

At least 30,000 people showed up and getting around the main streets and hotels was more than a little challenging.

We started with meetings on Saturday and wrapped up Thursday at the end of the day and can report that five straight days of meetings can start to scramble the brain. Stifel met with over 1,000 industry participants.

Pharma CEOs reported that it was a lot easier to buy biotechs in 2023 than before, as boards were more realistic about value and open to change of control deals. They expressed high interest in understanding and getting ahead on AI. There was also a sense that M&A activity is not going down in 2024. Certain companies that we visited with made it crystal clear that 2024 is going to be a *very busy* year for M&A – particularly in the cardiometabolic sphere.

#JPM24 photo of Takeda event. Photo: Gwen Melnyk.

The Takeda party was beautiful and businesslike.

Heard at #JPM24: Industry Buzz

Perhaps the biggest bit of industry news that popped up at the conference was the rumor reported in the *WSJ* that Novartis was buying Cytokinetics.

We had the pleasure of attending the Novartis cocktail event on Monday night (the same day of the rumor). Not only was senior management present (including top level M&A brass) but they were engaged and excited. Not stressed as one might guess if they were fighting to close a big M&A deal. By Wednesday, Novartis CEO, Vas Narasimhan made it clear that one should not expect them to buy CYTK anytime soon. All makes sense.

We met countless VCs and public markets investors and can report a general sense of enthusiasm and high interest in getting involved in PIPE deals and follow-ons – particularly in I&I and CV.

The big drugs for big diseases view seems to have now taken strong root in the industry and there is a broad sense that this is the way things are going to go.

Events for the tech VC's (e.g., Andreesen Horowitz) were completely mobbed and we came away with the feeling that the level of investment in AI/tech type stories is going up big in 2024. We also heard a lot of talk on CAR-T/B-cell and radiopharma.

#JPM24 photo of Novartis event. Photo: Gwen Melnyk.

Senior management of Novartis was present and happy at their cocktail party when the CYTK M&A rumor surfaced.

#JPM24 Buzz (Continued)

Another theme were heard more than a few times regarded the return of the crossover round.

While IPO's have yet to materialize in force there seemed to be a broad consensus that IPOs are coming back in 2024 and that this is a good time to get involved in better crossover rounds.

You won't be surprised to hear that the obesity area was widely discussed. We met with a number of key parties in this area and picked up: (1) much more nuanced views of oral players, (2) a report that the oral space is getting super crowded (more than 50 groups according to one pharma tracking the area), (3) an interest in Obesity Plus. That is, might one get better reimbursement for obesity drugs if you could address pathologies and diseases that accompany obesity.

Jay Bradner, newly installed as CSO for Amgen, was quoted in Reuters as being quite positive on AMG133. This is perhaps the most anticipated drug of 2024 and Dr. Bradner sounded very comfortable with the prospects of this product.

Another interesting set of meetings for us were with senior management at top payors. Think CVS, Humana etc.

We can report an unambiguously negative point of view on GLP-1 reimbursement. One executive put it succinctly to us "we don't pay for weight loss. Period."

We continue to think that the private pay obesity market is going to be important in 2024.

We heard high excitement about neuroscience from both buyers and the various biotechs in the space. Some of the big leaders in this space expect big things to happen in targeted brain therapies in 2024 and expect much higher business development / M&A activity to unfold.

We should also report that Chinese biotech and pharma was out in force at the confab. Pharma is waking up to the China opportunity. Pfizer, for example, held a special event to attract various potential China partners. One senior industry exec wondered out loud in our earshot whether Chinese biotech pipelines have been completely picked over at this point. We would say "no" based on what we are seeing. China will remain hot.

We would be remiss if we didn't report that a minority of people we met with remained pessimistic on the macro picture.

One prominent industry leader on the financial services side remains negative on the Fed's easing plan and thinks that the XBI might have gotten a bit ahead of things. We'd disagree but time will tell who's calling it correctly.

Newly Optimistic, Biotech Investors Weigh Lessons of Sector's Downturn

Ben Fidler, *Biopharma Dive*, Jan 11, 2023 (excerpt)

The J.P. Morgan Healthcare Conference, a yearly temperature taker for the biotechnology industry, had a different feel in 2024.

For the first time in awhile, young drugmakers and their backers were optimistic the sector's downturn might finally be over. An improving macroeconomic picture, combined with a recent run of dealmaking, has led many to hope investors may again see biotech as a worthy bet.

"This event is always the canary in the coal mine for the year," said Andreesen Horowitz general partner Jorge Conde. "This year, we have a happy canary."

Yet underneath the optimism remain concerns the rebound may be short lived. Private funding rounds and initial public offerings are still difficult for biotech companies to pull off.

Early technologies aren't getting the same support they were three years ago. Among nearly a dozen investors and executives interviewed by BioPharma Dive, all expect changes in how biotechs are built and that industry layoffs, which regularly made headlines last year, will continue.

An election and geopolitical conflict could also bring uncertainty for a sector already defending itself against drug pricing legislation and an aggressive Federal Trade Commission. The Federal Reserve, which has signaled interest rate cuts, may still surprise markets, too.

"There's a lot of stuff going on in the world that no one in this room really can control," said Kristina Burow, a managing director at Arch Venture Partners. "2024 is probably going to be a roller coaster."

Source: https://www.biopharmadive.com/news/biotech-startups-venture-capital-funding-outlook-2024/704289/

‘Let The Good Times Roll Again’: VCs Confident in Biotech Activity for ’24

Tyler Patchen, *Biospace*, Jan 11, 2023 (excerpt)

Several experts on a panel Wednesday at JPM’s Biotech Showcase expressed positive attitudes for the coming year on the investment side, with Andrew Lam, the principal of special investments at Ally Bridge Group, commenting that the panel’s title should be “Biotech in 2024: Let the good times roll.”

“What’s exciting is despite the hard times in 2023 . . . the last two months of the year have been quite productive, November and December,” noted panelist Maha Katabi, general partner at Sofinnova Investments. “We closed the year with 23 M&A deals in the industry. . . . And the last time we exceeded that number was . . . in 2002.”

On the IPO front, Lam noted that more companies could go public as soon as next week and expressed cautious optimism about the prices. This will give investors even more confidence as more capital is being “infused” into the sector. While Lam did say valuations are being compressed and raises are shrinking in deal size compared to previous years, the market is getting better, and sizes are bound to increase.

As for topics such as the IRA, which has also been a significant subject of discussion all week in San Francisco, Katabi said that while the IRA will be debated and refined, it will be a “non-issue” and should be regarded more as a patent expiration date and not necessarily the “dominant factor” in the conversation.

As for advice to companies on navigating the coming year, Lam said to condition your board early, as funding could be a 12-month process due to investors being “inundated with opportunities,” and there is a wide range of opportunities for investors to put their money into. Thus, he said it’s important to budget responsibly.

“Have a clear plan for what your current investors are doing versus new investors,” Katabi said.

Source: https://www.biospace.com/article/-let-the-good-times-roll-again-vcs-confident-in-biotech-activity-for-24/

The XBI Closed at 90.4 Last Friday (Jan 12). Up 1.4% YTD

Biotech Stocks Up Slightly Last Week

Return: Jan 7 to Jan 12, 2024

Nasdaq Biotech Index: +1.8%
Arca XBI ETF: 1.31%
Stifel Global Biotech EV (adjusted): +2.0%*
S&P 500: 1.8%

Return: Jan 1 to Jan 12, 2024

Nasdaq Biotech Index: +0.2%
Arca XBI ETF: +1.3%
Stifel Global Biotech EV (adjusted): 2.2%*
S&P 500: +0.2%

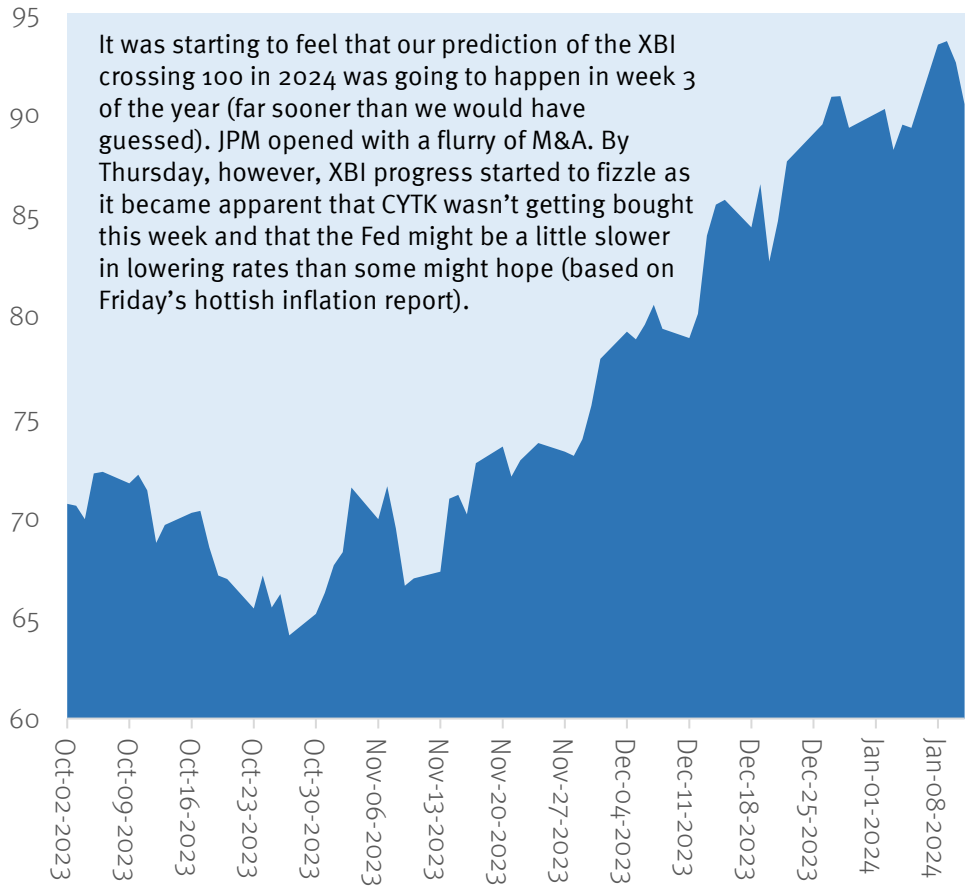
VIX Down

Jan 20: 19.9%
May 26: 18.0%
July 21: 13.6%
Sep 29: 17.3%
Oct 27: 21.2%
Dec 1: 12.6%
Dec 29: 12.45%
Jan 3, 2024: 13.2%
Jan 12, 2024: 12.7%

10-Year Treasury Yield Sub-4

Jan 20: 3.48%
May 26: 3.8%
July 21: 3.84%
Sep 29: 4.59%
Oct 27: 4.86%
Dec 1: 4.24%
Dec 29: 3.88%
Jan 3, 2024: 3.95%
Jan 12, 2024: 3.96%

XBI, Oct 1, 2023 to Jan 11, 2024

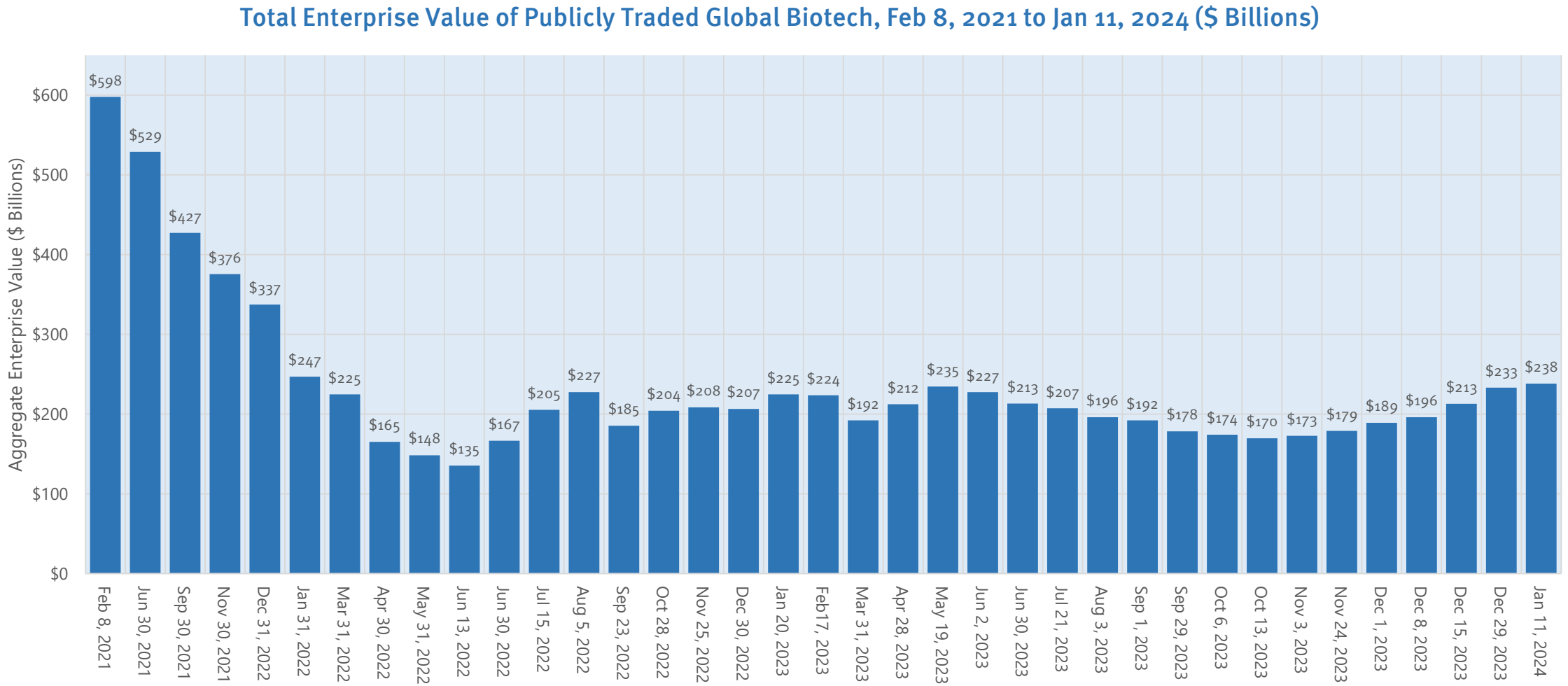


* Change by enterprise value. The adjusted number accounts for the effect of exits and additions via M&A, bankruptcies and IPOs.

Source: S&P Capital IQ and Stifel analysis

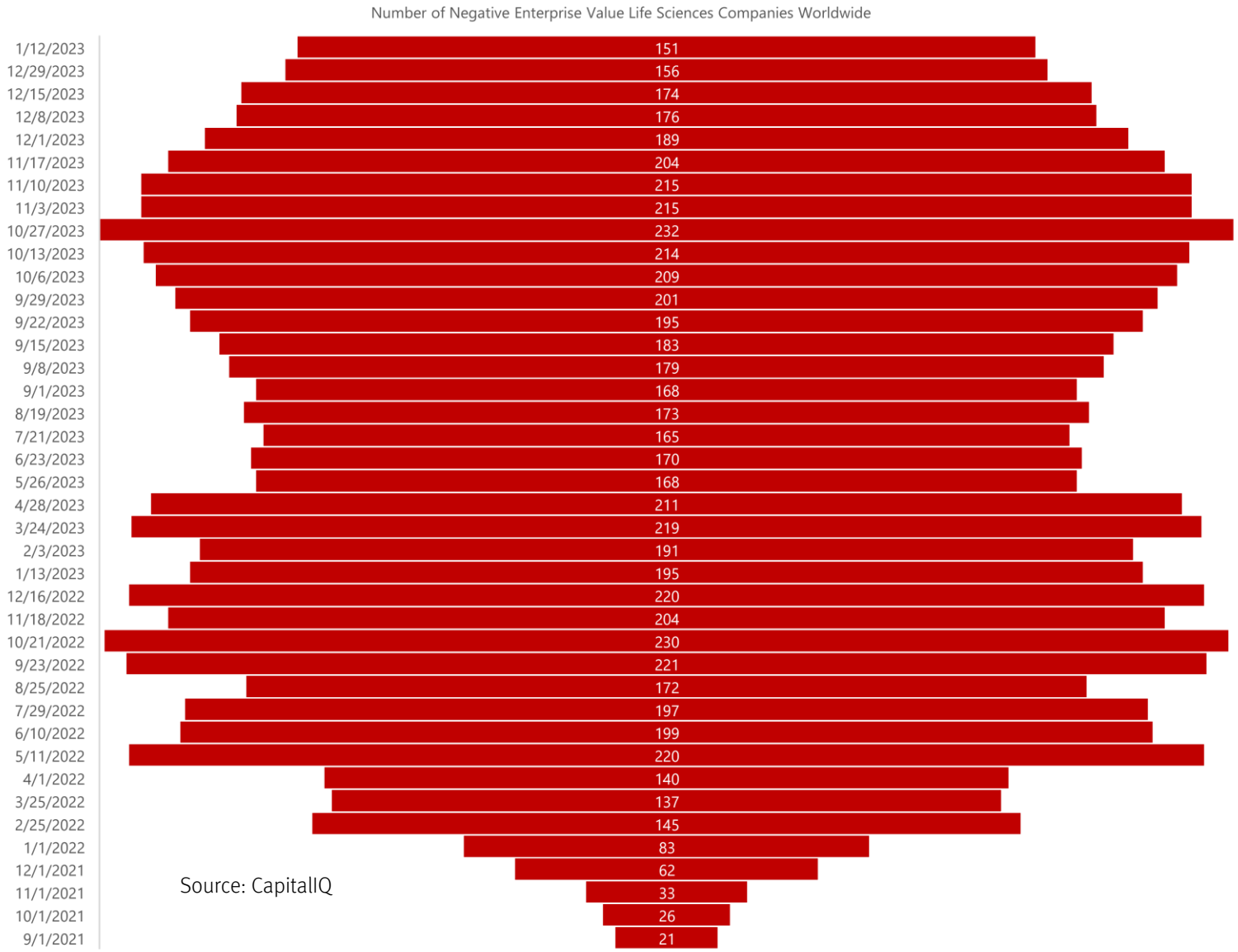
Total Global Biotech Sector is Now Up 47% in Recent Rally

The total enterprise value of the global biotech sector is up 2.2% for the year to date. The rally that started 12 weeks ago has started to slow down in the face of incrementally negative macro news in 2024.



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

Number of Negative Enterprise Value Life Sciences Companies Fell to 151 in Last Week



Source: CapitalIQ

The count of negative EV life sciences companies worldwide fell from 156 two weeks ago to 151 last Friday.

This is the lowest number in almost two years.

The negative EV life science company population has shrunk by 35% since peaking on Oct 27, 2023.

Life Sciences Sector Up 1.2% Last Week

Last week saw a 1.2% increase in life sciences stocks worldwide. Devices, Biotech and CDMOs were up the most.

Sector	Firm Count	Enterprise Value (Jan 12, 2024, $millions)	Change in Last Week (percent)	Change in Last Month (percent)	Change in Last Year (percent)
API	81	$84,797	-1.8%	-0.5%	-1.5%
Biotech	804	$285,872	3.4%	10.5%	-5.1%
CDMO	40	$145,084	3.1%	5.3%	-27.1%
Diagnostics	83	$275,462	-0.1%	0.3%	2.5%
OTC	31	$29,341	0.9%	2.8%	-5.4%
Pharma	717	$6,057,612	0.6%	4.6%	3.2%
Pharma Services	38	$194,543	-0.6%	-4.9%	-10.5%
Tools	52	$674,043	0.5%	0.2%	-13.9%
Devices	181	$1,666,590	3.7%	3.2%	2.9%
HCIT	10	$21,536	0.2%	-1.9%	-30.4%
Total	2037	$9,434,879	1.2%	3.8%	1.0%

Source: CapitalIQ

Capital Markets Update

#JPM24 view of Bay Bridge at dawn. Photo: Tim Opler

Stifel Comment on Capital Markets Status in 2024

Overall Market

Overall, we are positive as to capital markets direction in 2024 with a constructive tone coming out of the JPM conference last week.

We're seeing a nice rebound in the markets (XBI crossing 93 earlier in the week) following multiple M&A announcements and an extremely active first two weeks of the year from an equity deal activity standpoint.

Renewed interest in high quality private capital raises

1. Many issuers raising crossover rounds have received term sheets and are now looking to round out syndicates
2. Balance between valuation and quality of syndicate is a paramount consideration. Issuers appreciate the importance of getting the right syndicate of investors involved who will support the Company for the long term (through IPO and beyond)

Initial Public Offerings

Set-up for IPO market is constructive:

1. Currently 4 IPOs in the publicly filed backlog: CG Oncology, Arrivent and Metagenomi
2. Confidentially filed backlog continues to build – everyone is watching and rooting for the first wave of 2024 IPOs to price and trade well
3. Trends from 2023 still remain – IPOs launching covered from existing investor support and new demand uncovered from robust testing the waters processes

Source: Stifel ECM Desk, Jan 12, 2023

Stifel Comment on Capital Markets (continued)

Equity Follow-Ons

Follow-on market is performing well as deals are pricing and trading well:

1. In the first 2 weeks of the year, we've seen 11 Follow-ons / PIPEs / Registered Direct's price, of which 9 raised over $100mm in proceeds
2. Tight discounts: Average/median file-to-offer discounts of (4.6%)/(7.2%)
3. Strong aftermarket performance: 8 of 11 traded up on day 1, on average +8%
4. While a large portion of deals are completed on the back of positive data events/catalysts, there is a market again for opportunistic financings (4 of 11 were opportunistic)

M&A Market and Specialist Funds

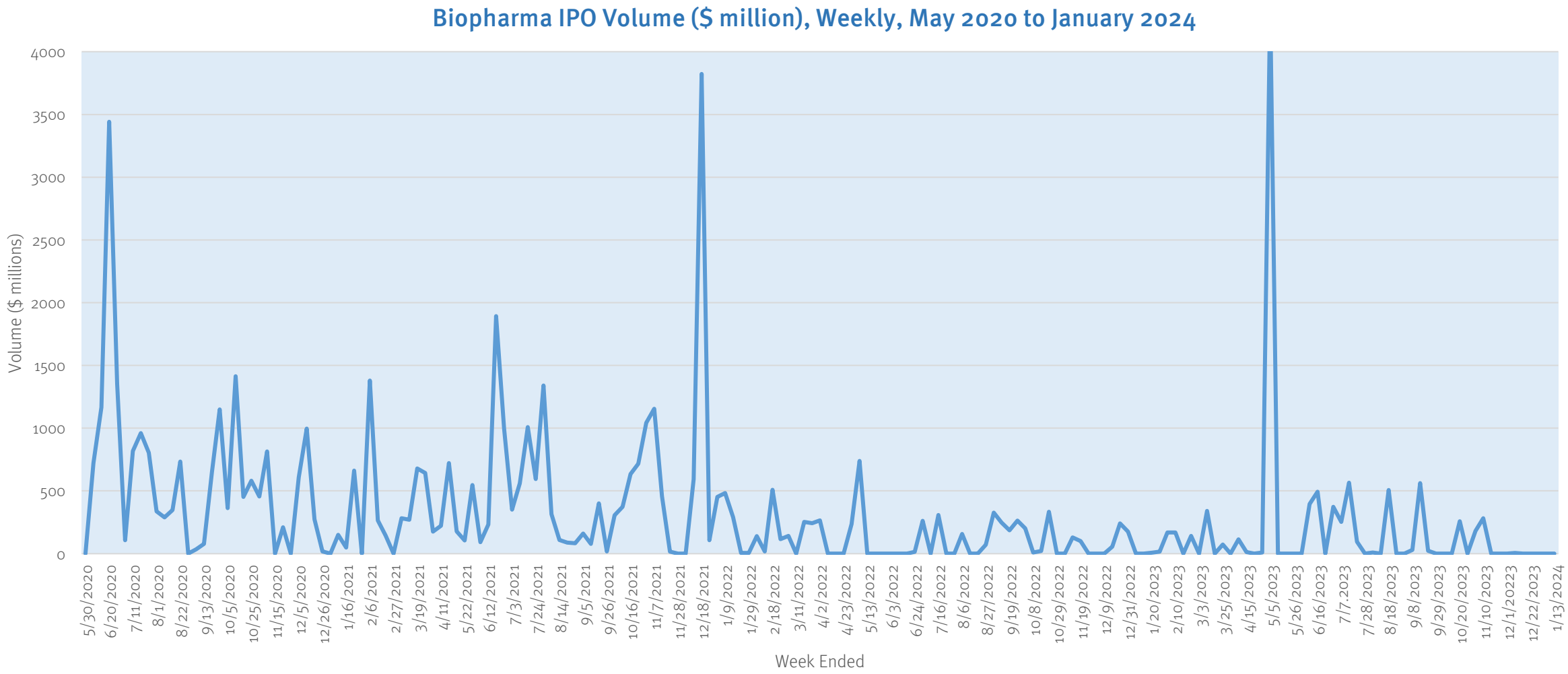
M&A activity in December/early January has brought life back into the market – positive returns leave investors with capital to re-deploy back into the sector:

1. Healthy mix of mutual funds and other long-only funds and healthcare dedicated hedge funds have been top investors in the 10+ biopharma companies acquired over the past 2 months.
2. These beneficiaries have included RA Capital, Fidelity, T Rowe Price, Wellington, Logos, Orbimed, Paradigm, Redmile, Rock Springs, Sofinnova, TCGx, Venrock, Viking, Vivo, Bain, Janus and others

Overall, investors are eager to deploy capital into good biotech stories in 2024.

Source: Stifel ECM Desk, Jan 12, 2023

No Biopharma IPO's in Last Eight Weeks



Source: Data from CapitalIQ and Stifel research.

Market Sees IPO Window Opening in 2024

Jules Adam, "Is the biotech industry poised for recovery in 2024?," *Labiotech*, Jan 8, 2024 (excerpt)

There is particular optimism surrounding the Initial Public Offerings (IPO) market in 2024. After a period of decline, analysts at Bernstein forecast a recovery of biotech companies and IPOs in 2024 as high-interest rates begin to ease.

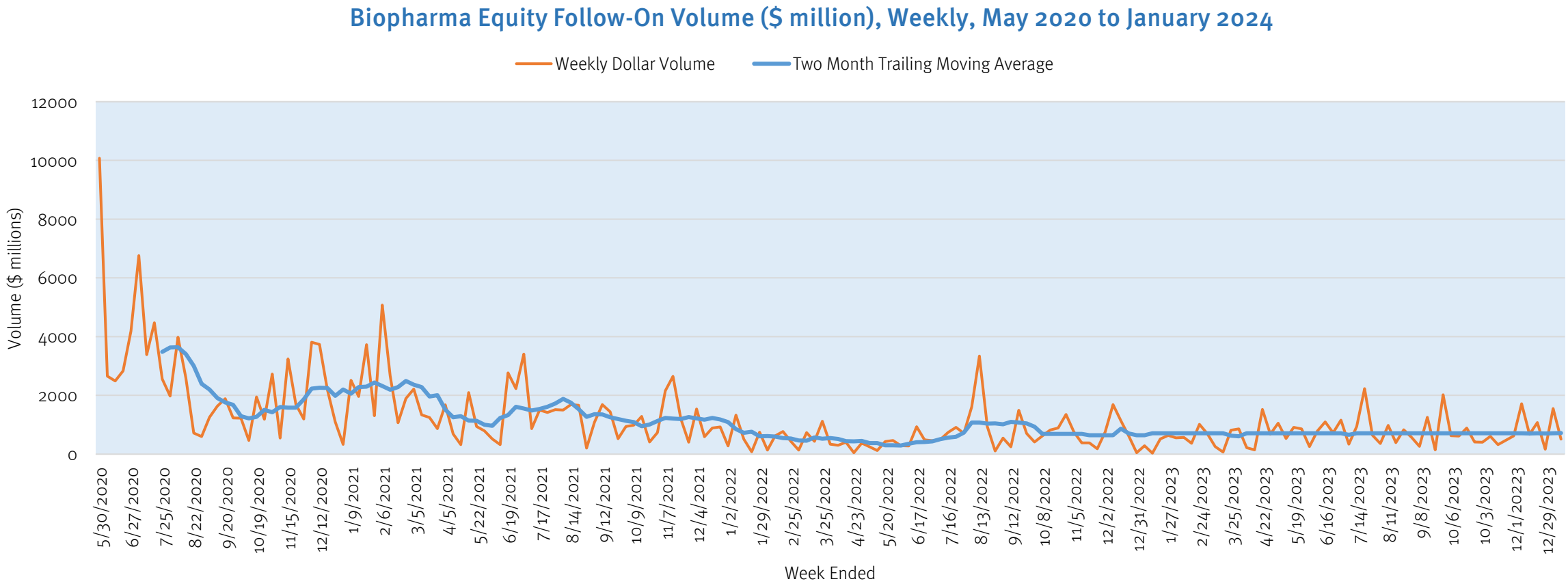
The S&P Biotech ETF (XBI), a key performance indicator, saw a rise of 7.6% in 2023, marking a shift in the market after a significant fall in the preceding year suggesting a biotech recovery in 2024. This positive trend offers a glimmer of hope for the IPO market, which had a subdued performance in 2023, raising only $2 billion across nine IPOs that exceeded $50 million versus more than a hundred IPOs in 2021 for a total exceeding $15 billion. Bernstein analysts express hope for 2024 as the year of resurgence for the IPO market, indicating potential for upward momentum.

Further supporting this outlook, PwC analysts predict that the biotech IPO window will "gradually reopen" in 2024. This reopening is likely to favor companies with strong clinical data, reflecting a selective but optimistic approach by investors toward biotech offerings.

Source: https://www.labiotech.eu/trends-news/biotech-recovery-2024/

Follow-On Market Robust Thus Far in 2024

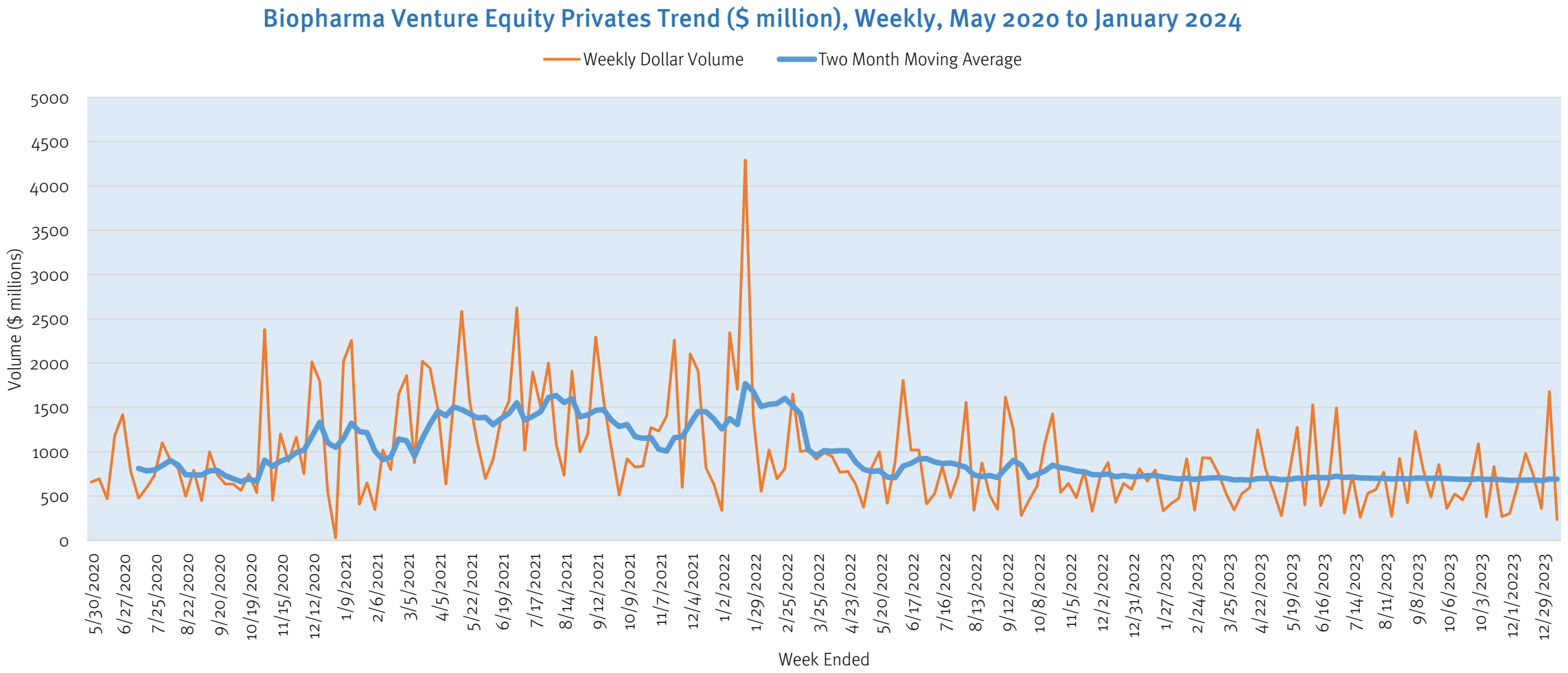
The first week of the year saw $1.6 billion in follow-on issuance volume. The second week saw $700mm in issuance for a total of $2.3 billion in the first two weeks. To compare, 2021 set the record for all-time issuance volume and saw $2.8 billion of issues in the first two weeks. Last year volume was $300 million in the same period and in 2022 volume was $1.6 billion. We see capital issuance as much more solid in 2024.



Source: Data from CapitalIQ and Stifel research.

First Two Weeks of 2024 Have Seen $1.9 Billion in Venture Privates

The $1.7 billion in privates issuance in the first week of the year was the busiest since mid-2022. The privates market is picking up.



Source: Data from CapitalIQ, Crunchbase.

Biotech Venture Ecosystem: Quick Health Check

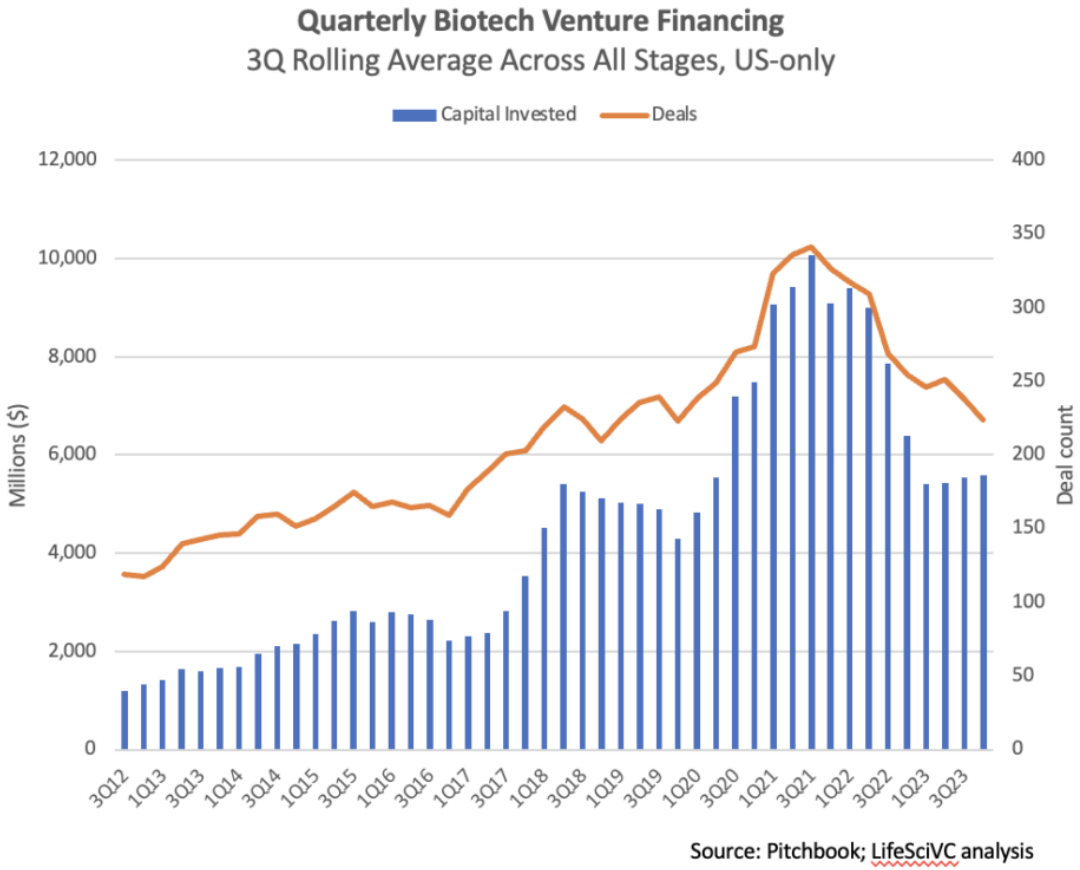
Bruce Booth, LifeSci VC, January 12, 2024

Biotech feels like it's got some wind in its sails here at the start of 2024, with positive sentiments from the JPM conference. Indeed, the public equity markets feeling somewhat buoyant for the first time in ages.

With the close out of 2023, it's time to take stock of the health of the private venture ecosystem. Analyzing Pitchbook data for venture funding into US-based biopharma companies, at least four themes are worth highlighting related to overall funding, startup creation, mega-rounds, and valuations.

1. VC funding overall has stabilized at around $5B per quarter, which is a historically very healthy amount of capital.

Overall venture funding for US-based biopharma companies was just shy of $5B in 4Q2023, softer than the prior quarter. To smooth out some of the quarterly variability, taking a three-period rolling average of the quarterly funding data reveals what appears to be real stabilization in terms of overall funding. While off the peak quarterly funding level by ~50%, by all historic measures this is a robust level of financing, and supports 800+ private biotech companies each year in the US alone.



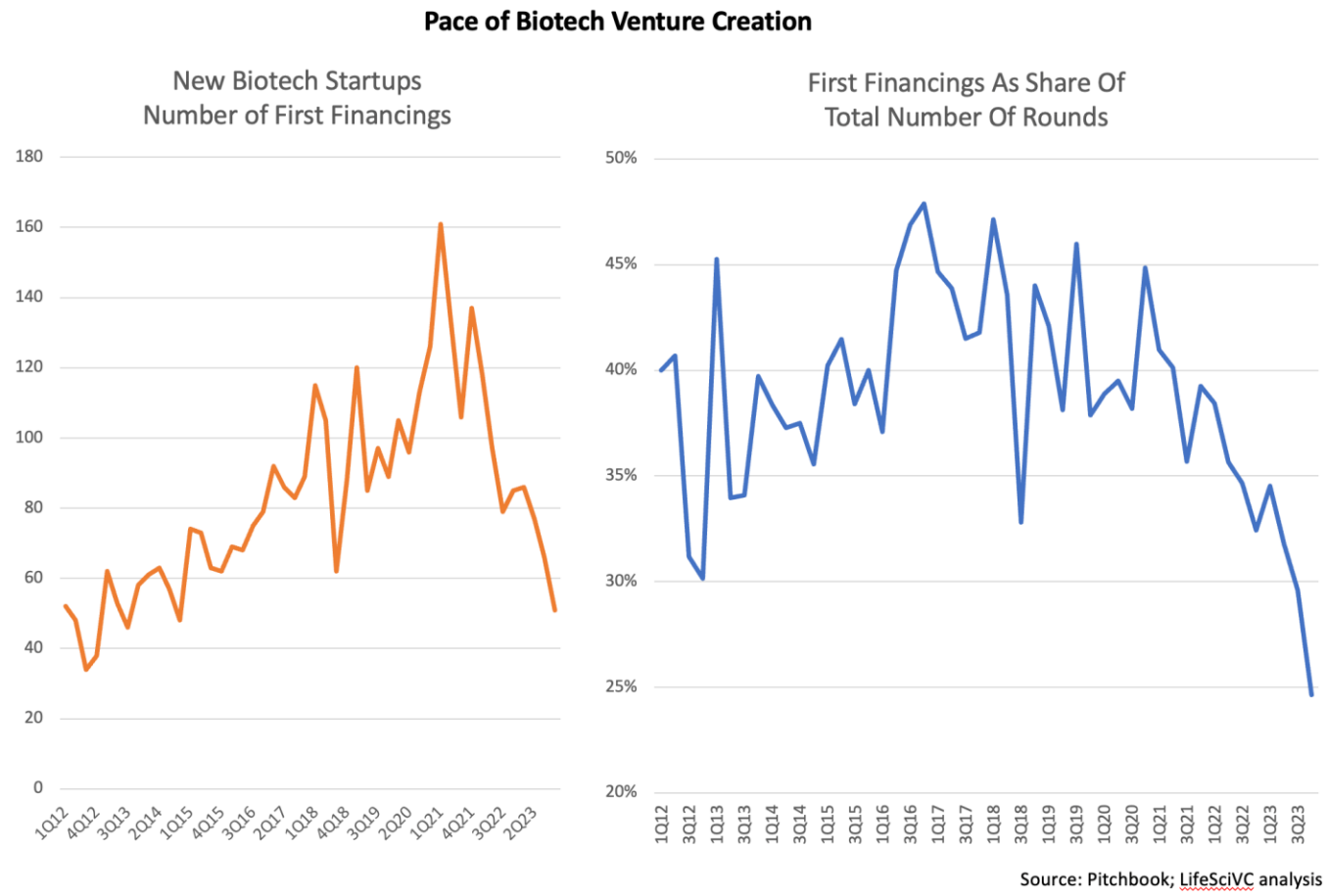
Source: https://lifescivc.com/2024/01/biotech-venture-ecosystem-quick-health-check/

Biotech Venture Ecosystem (continued)

2. Pace of new startup creation has slowed considerably, and the proportion of private rounds going into new startups is the lowest its ever been.

On the venture creation side of things, using the proxy of "first financings" as a good metric for new startup formation, things have clearly tightened up significantly over the past year or so. With a little over 50 new startups raising capital in 4Q24, we're back to levels not seen for nearly a decade, at the start of the biotech secular bull market in 2013-2014.

Further, the share of rounds going towards startups raising their first financings, versus follow-on rounds, is the lowest ever recorded, according to Pitchbook data, coming in just below 25% in 4Q24. This is clear evidence for the "digestion" process – the venture ecosystem experienced rampant startup formation in 2020-2021, and now has to work through that backlog of existing startups.

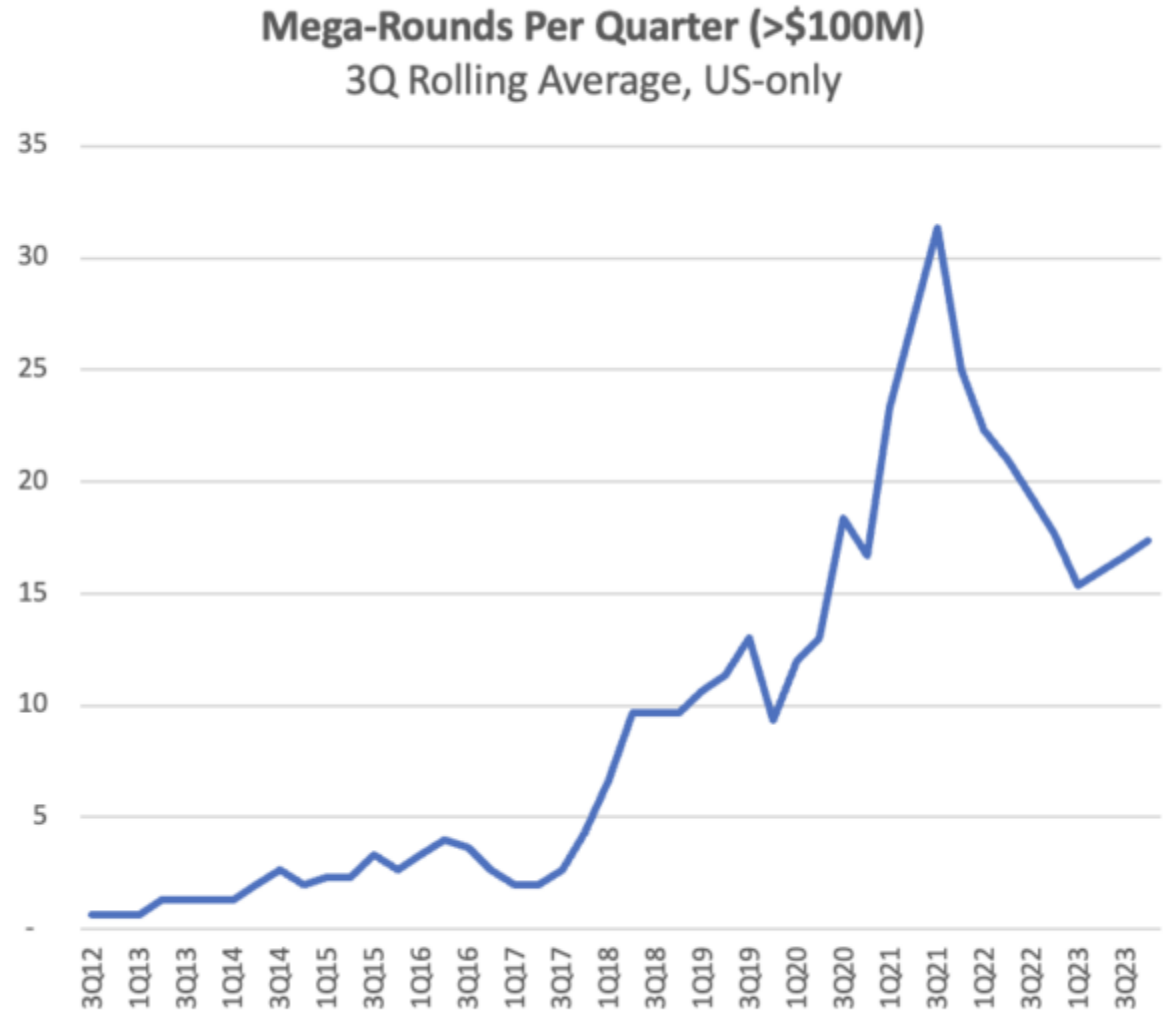


Biotech Venture Ecosystem (continued)

3. Mega-rounds greater than $100M continue to be fairly common.

Starting in 2018, large rounds became more frequent in biotech venture funding. These peaked in the pandemic bubble, but have not returned to their 2018-2019 levels. We've seen at least one mega-round per week, on average, throughout 2023.

Multiple reasons for this: larger rounds help hedge future financing risk in choppy markets; bigger VC funds have been raised in recent years which require bigger check sizes, driving rounds larger; and, among other things, costs and burn rates continue to climb, especially for funding complex modalities and later stage assets privately (given lack of an IPO market).

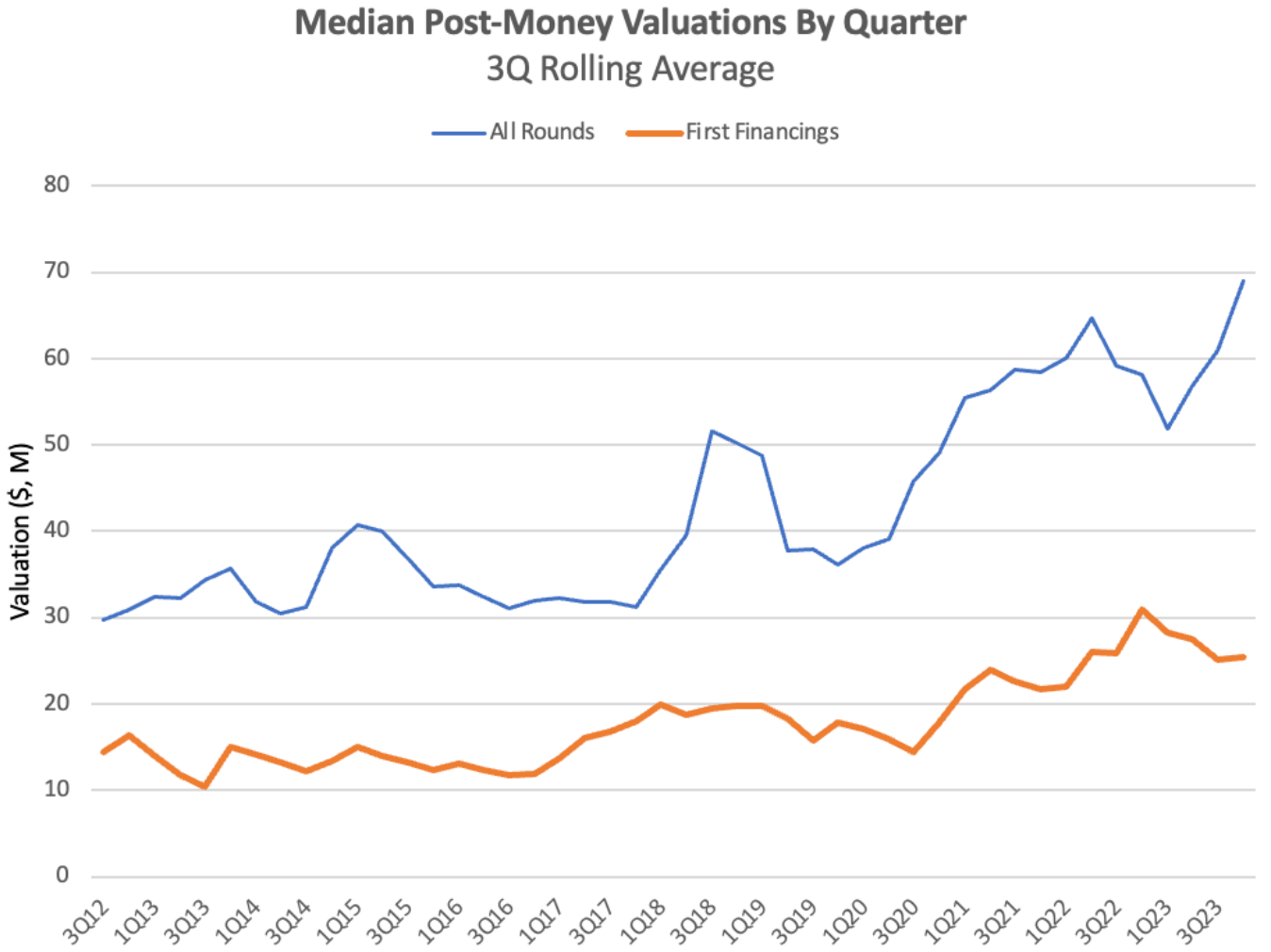


Source: Pitchbook; LifeSciVC analysis

Biotech Venture Ecosystem (continued)

4. Private round valuations have remained surprisingly robust despite 2022-2023's choppy market turbulence and resetting of public equity valuations.

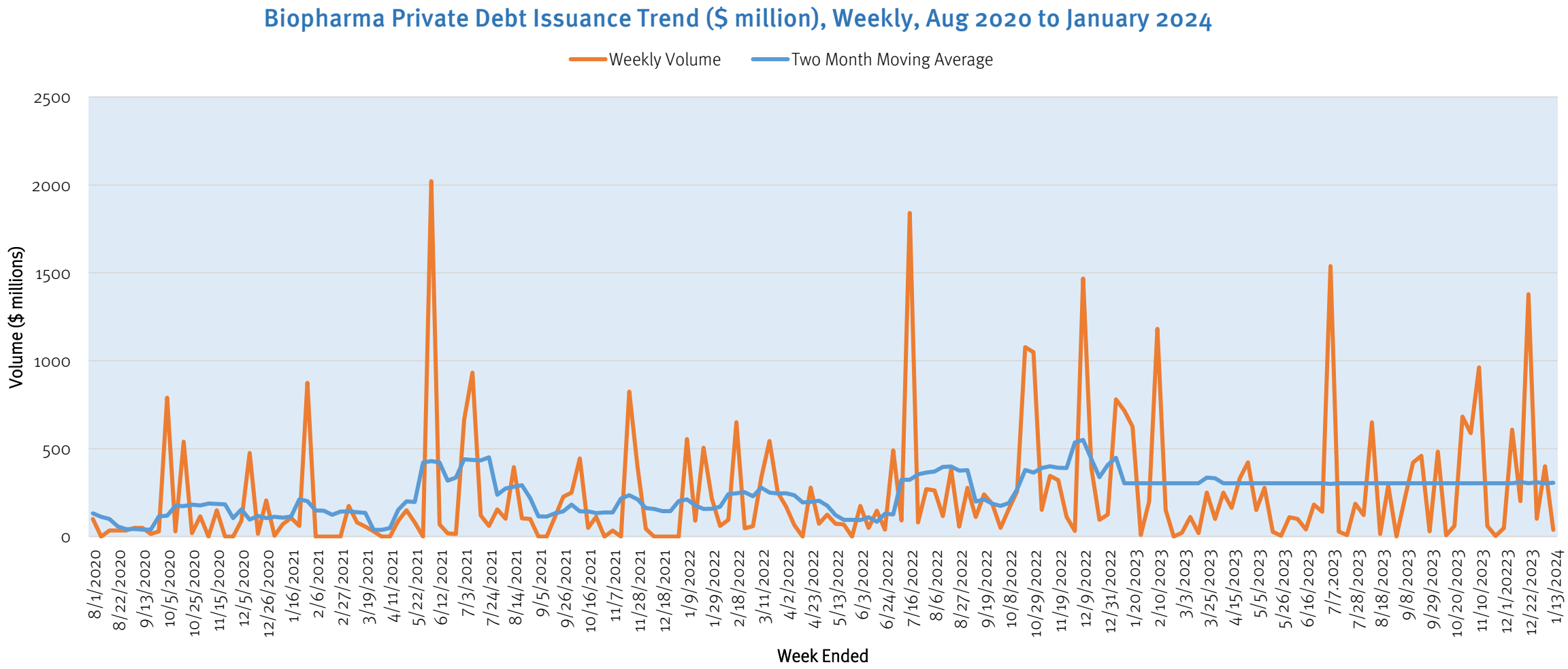
Post-money valuations in private deals have held up remarkably well in 2023: the median post-money in the 2H of 2023 was ~$70M+, higher than it's ever been, and more than 100% greater than a decade ago. A significant driver of this relates to the prior observations: as more venture funding activity was focused on later stage rounds in 2023 relative to prior periods, as well as the persistence of these mega-rounds, it has pulled up the median post-money valuations. That said, even first round valuations remain robust, holding up at roughly twice the valuation of 5-10 years ago.



Source: Pitchbook; LifeSciVC analysis

Weekly Global Biopharma Private Debt Placement Market Open in December

We have seen $438 million in private debt deals get done in the first two weeks of 2024. The market is open and active.

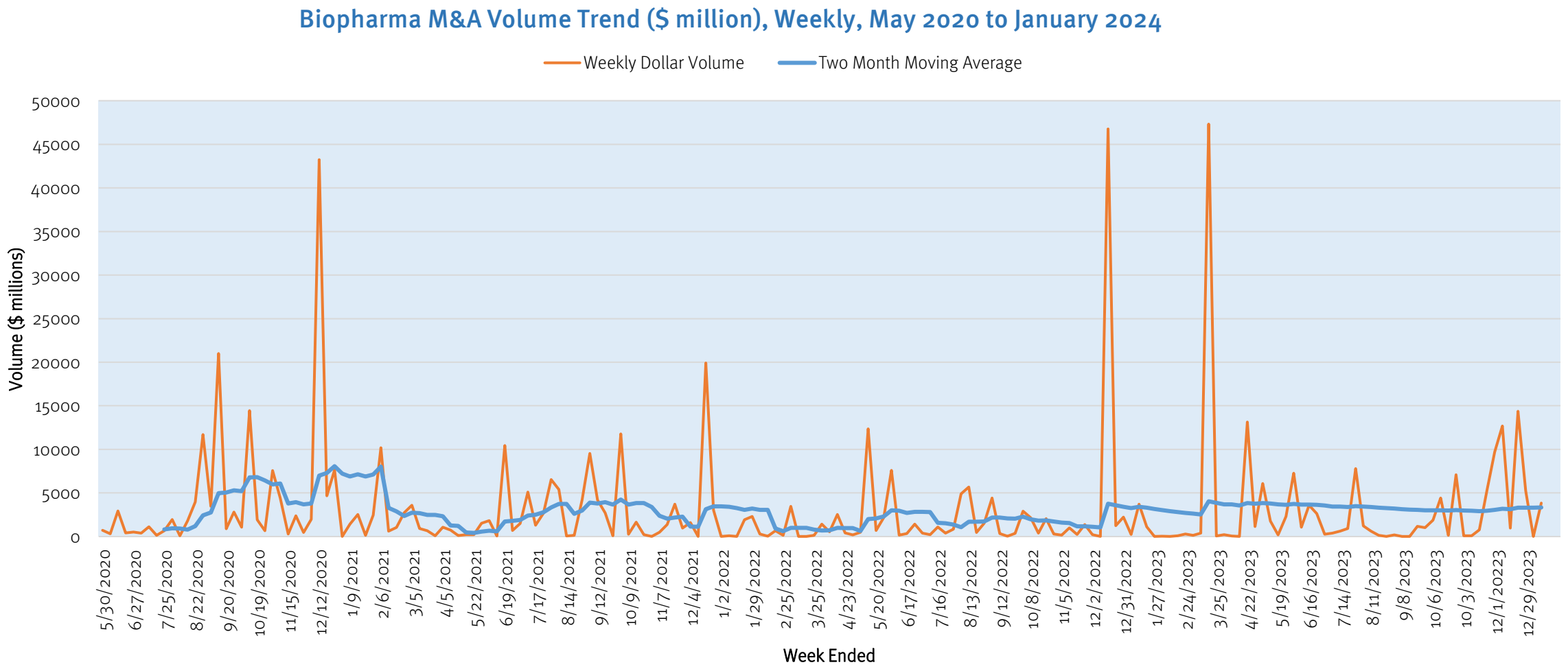


Source: Data from CapitalIQ, Crunchbase.

Deals Update

M&A Market Active

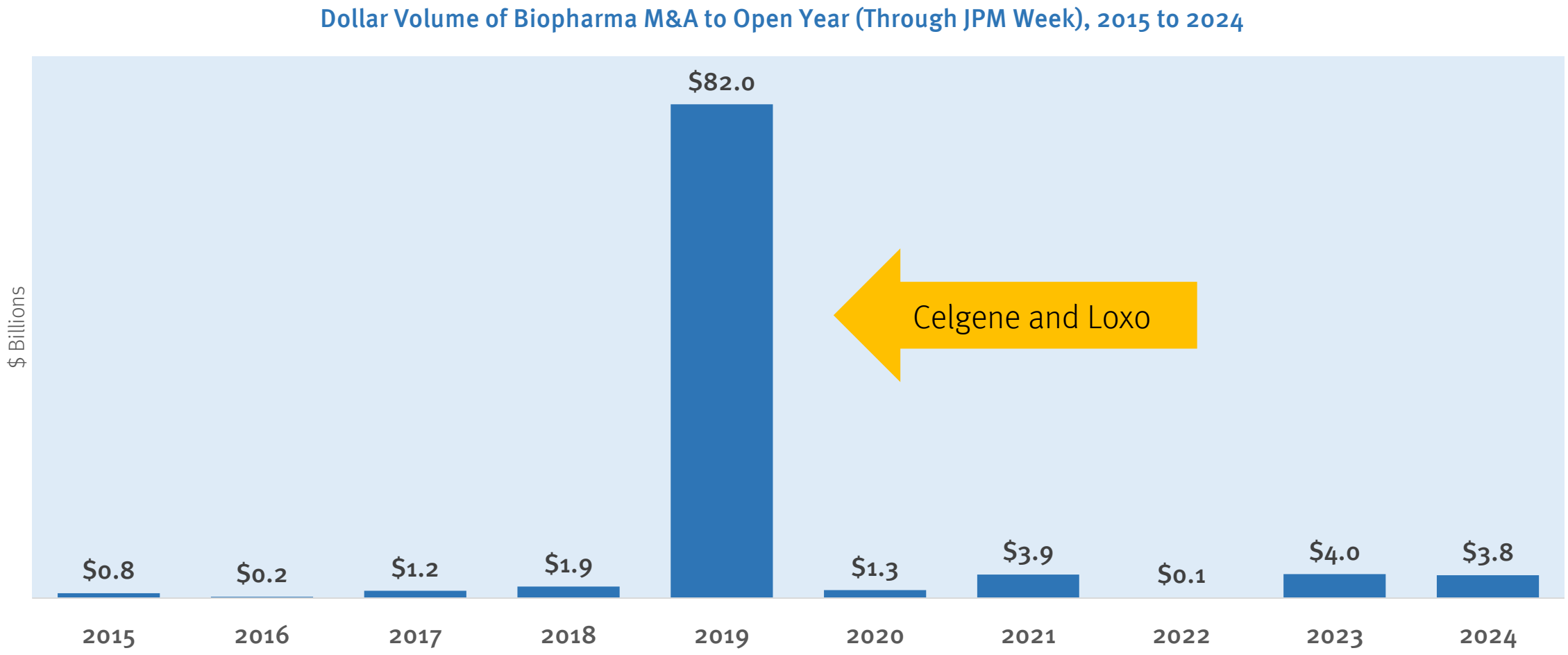
Last week saw four big pharma M&A deals led by J&J's $2bn acquisition of Ambrx. There were widespread rumors that Cytokinetics could be bought.



Source: S&P, CapitalIQ

Activity Through JPM Week Fourth Busiest of Last Decade

While there is no typical opening to M&A for the year, we would say that the year so far has been relatively normal in terms of M&A activity since 2019. The level of M&A announcements YTD in 2024 was quite similar to that of 2021 and 2023.



Source: S&P, CapitalIQ

Johnson & Johnson to Acquire Cancer-Treatment Developer Ambrx for $2 Billion

Ben Glickman, *Wall Street Journal*, Jan 8, 2024 (excerpt)

Johnson & Johnson will acquire cancer-treatment developer Ambrx Biopharma in a $2 billion cash deal.

The pharmaceutical giant said Monday that the deal to acquire all shares of Ambrx for $28 each was expected have a value of $1.9 billion net of estimated cash required.

Ambrx said the deal represented a premium of 105% on the Jan. 5 closing price.

Ambrx is currently developing candidates for treatments for multiple types of cancer, including for metastatic castration-resistant prostate cancer, metastatic breast cancer and renal cell carcinoma.

Johnson & Johnson said the deal presented an opportunity to "design, develop and commercialize targeted oncology therapeutics."

The acquisition is expected to close in the first half of the year, subject to approval by Ambrx shareholders.

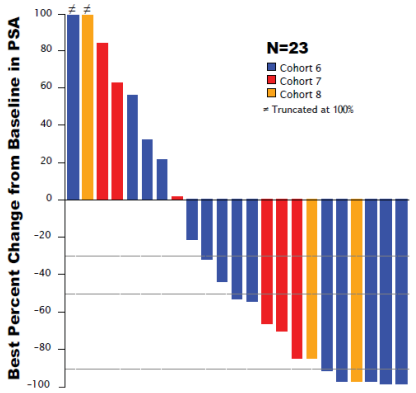
Source: https://www.wsj.com/health/pharma/johnson-johnson-to-acquire-cancer-treatment-developer-amrbx-for-2b-f7fbafea?mod=pharma_news_article_pos5

Why Would J&J Spend $2Bn on a Phase 2 Prostate Cancer Drug? Answer: An ADC That Can Compete Against Radiopharma Drug

Radiopharmaceutical products have the benefit, in general, of higher efficacy, albeit with the downside of requiring generation of an isotope with a limited half life. The Ambrx PSMA ADC was not good news for radiopharma at all – as its emerging efficacy profile was competitive against Pluvicto® - the star drug to date from the radiopharma armamentarium. It will be interesting to see if ADC's can continue to shine relative to RLT's for other targets in the future.

AMBRX

52% (12/23) of Patients Experienced ≥50% PSA Reduction at 2.0 – 2.88 mg/kg in Patients Who Have Exhausted Available and Appropriate Treatment Options

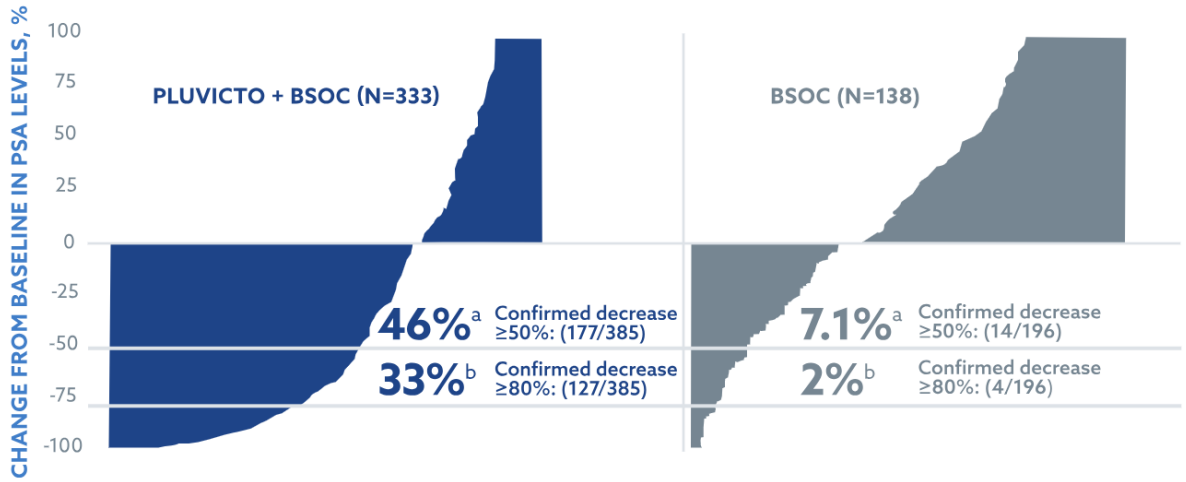


	Cohort 6 (n = 14)	Cohort 7 (n = 6)	Cohort 8 (n = 3)	Cohorts 6-8 (n=23)
≥30% PSA	64%	50%	67%	61%
≥50% PSA	50%	50%	67%	52%
≥90% PSA	36%	0	33%	26%

PSA waterfall includes patients with at least two on-treatment PSA assessments or discontinued before the second assessment.
Presented at ESMO 2023.

PLUVICTO®
lutetium Lu 177 vipivotide tetraxetan
INJECTION FOR INTRAVENOUS USE

PSA response from baseline (additional secondary end point)



Merck to Acquire Harpoon Therapeutics

Merck Press Release, January 8, 2024

RAHWAY, N.J. & SOUTH SAN FRANCISCO, Calif.--(BUSINESS WIRE)-- Merck (NYSE: MRK), known as MSD outside of the United States and Canada, and Harpoon Therapeutics, Inc. (Nasdaq: HARP) today announced that the companies have entered into a definitive agreement under which Merck, through a subsidiary, will acquire Harpoon for $23.00 per share in cash for an approximate total equity value of $680 million.

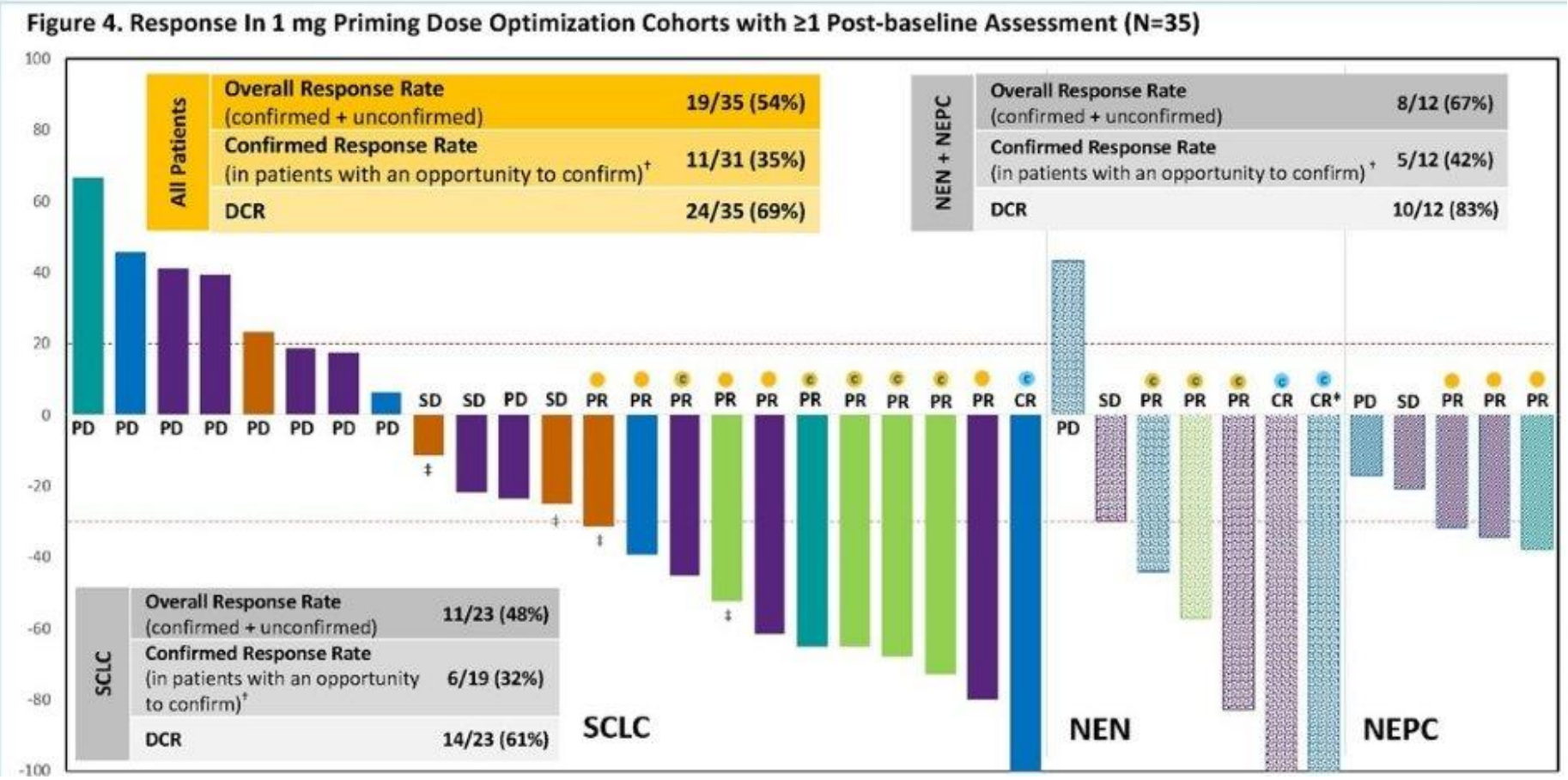
“At Merck, we continue to enhance our oncology pipeline through strategic acquisitions that complement our current portfolio and advance breakthrough science to help address the needs of people with cancer worldwide,” said Dr. Dean Y. Li, president, Merck Research Laboratories. “This agreement reflects the creativity and commitment of scientists and clinical development teams at Harpoon. We look forward to further evaluating HPN328 in innovative combinations with other pipeline candidates.”

Harpoon has developed a portfolio of novel T-cell engagers that employ the company’s proprietary Tri-specific T cell Activating Construct (TriTAC®) platform, an engineered protein technology designed to direct a patient’s own immune cells to kill tumor cells, and ProTriTAC™ platform, applying a prodrug concept to its TriTAC® platform to create a therapeutic T-cell engager that is designed to remain inactive until it reaches the tumor.

Harpoon’s lead candidate, HPN328, is a T-cell engager targeting delta-like ligand 3 (DLL3), an inhibitory canonical Notch ligand that is expressed at high levels in small cell lung cancer (SCLC) and neuroendocrine tumors. HPN328 is currently being evaluated in a Phase 1/2 clinical trial (NCT04471727) evaluating the safety, tolerability and pharmacokinetics of HPN328 monotherapy in patients with advanced cancers associated with expression of DLL3. The study is also evaluating HPN328 in combination with atezolizumab in patients with SCLC. In October 2023, Harpoon announced the presentation of positive interim tolerability and response data for HPN328 in certain patients with SCLC and neuroendocrine tumors.

Source: https://www.merck.com/news/merck-to-acquire-harpoon-therapeutics-further-diversifying-oncology-pipeline/

Harpoon DLL3 T-Cell Engager Data at ESMO (Oct 2023)



Confirmed ORR of 32% in SCLC with Harpoon's HPN328 was competitive with the 40% we saw with the 10mg dose of Amgen's T-cell engager tarlatamab.

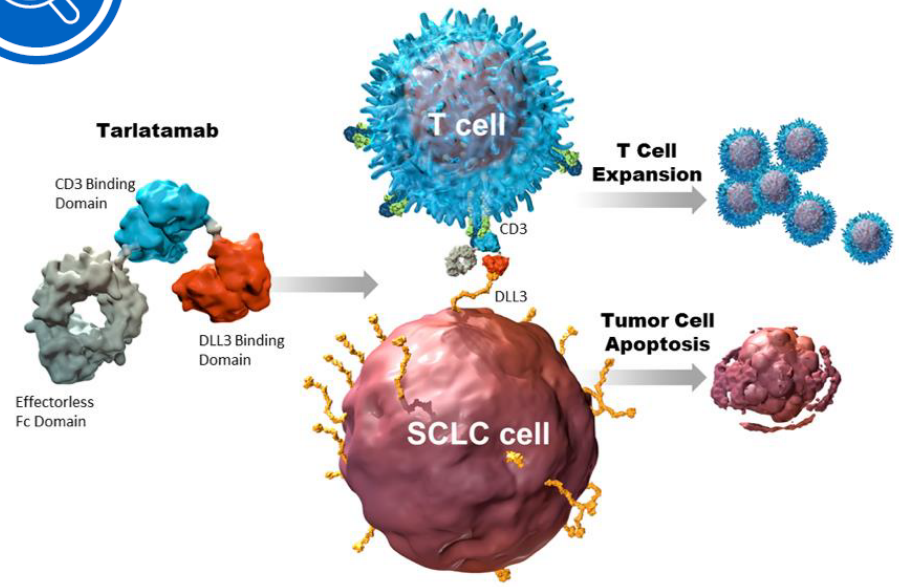
Importantly, this creates new options for patients with SCLC, a long-standing area of unmet need.

Merck can combine HPN328 with Keytruda to improve ORR.

Amgen Updates on its DLL3 Engager at #JPM24

TARLATAMAB: A POTENTIAL BREAKTHROUGH IN ADVANCED SMALL CELL LUNG CANCER

ONCOLOGY: SELECTED PIPELINE PROGRAMS



- PDUFA date of June 12, 2024
- Response rate of 40%, with 6-month survival of 73% in advanced small cell lung cancer
- Initiating Phase 3 trials in earlier lines
- First T-cell engager to demonstrate activity in a common solid tumor

Merck will obviously need to move quickly given Amgen's speed to market with Tarlatanab.

Merck's opportunity is to create combo's that should allow a competitive profile against the Amgen molecule.

U.S. DRUG-TREATED POPULATION OF ~35K ACROSS ALL LINES OF DISEASE

DLL3 - delta-like ligand 3; CD3 = cluster of differentiation 3; Fc = fragment crystallizable; SCLC = small cell lung cancer; PDUFA = Prescription Drug User Fee Act.

11 Provided January 8, 2024, as part of an oral presentation and is qualified by such, contains forward-looking statements, actual results may vary materially; Amgen disclaims any duty to update.

AMGEN

IQVIA: Strong Deal Catalysts for 2024

Markus Gores and William Harries, *IQVIA Blog*, January 12, 2023 (excerpt)

As 2024 gets underway, the fundamentals in support of dealmaking continue to be strong:

Deal capacity: Already by 2023, big pharma amassed a formidable war chest, equating to $0.8Tn deal capacity among the top 15 companies, which we expect to grow to $1.2Tn through 2025. The stellar success of Novo's and Lilly's GLP-1 franchises in both diabetes and obesity, possibly to be followed to some extent by other market entrants, will further add to the available M&A firepower. Much of this dry powder has yet to be deployed.

Growth gap: Between 2023 and 2030, $210-$250Bn of biopharma industry revenue is facing LoE exposure in the critical US market alone, thus creating an urgency to replenish pipelines and portfolios to drive future growth.

Supply side: Innovation continues to be dominated by Emerging Biopharma Companies (EBPs), accounting for over 280 unpartnered assets currently in phase 3 which are owned by pre-commercial biotech companies without any revenues.

In addition to these strong fundamentals, there are incremental positive catalysts to provide further support for deal momentum in 2024:

New threats to growth: Challenges from new policies and cost-containment measures are a common theme across major pharmaceutical markets and increase the need to replenish revenue via deals. For example, the IRA in the U.S., including the prospect of direct price negotiations by Medicare; the GKV-FinStG, Germany's Statutory Health Insurance System Financial Stabilization Act, freezing drug prices until 2026, while increasing mandatory rebates from 7% to 12% and reducing the free-pricing period from 12 to 6 months, alongside other measures; or the new EU Pharmaceutical Legislation, e.g., proposing to shorten Regulatory Data Protection and orphan drug exclusivity, adding potential medium-term risk for which companies may want to start preparing in 2024.

Fear of missing out: The emergence of new growth platforms meets growth-seeking big pharma companies eager to secure a stake in those opportunities, for example, novel modalities such as ADCs or radiopharmaceuticals; or the revival of stalled TAs as a result of breakthrough innovation, e.g., GLP-1s in obesity or novel MoAs for treating a range of CNS indications, e.g., Alzheimer's, schizophrenia or depression. M&A provides an attractive route for quickly establishing a presence and closing any portfolio gaps.

Renaissance of high prevalence conditions: Commercialisation of the new wave of transformative therapies for conditions with sizeable patient populations, such as obesity, NASH or Alzheimer's, compounded by the absence of an effective standard of care, requires extensive market shaping and the engagement of a large customer universe. The commercial infrastructure and investment levels needed put self-commercialisation beyond the reach of most EBPs, even if well-funded, and thus force such companies to seek commercialisation partners for their assets, including via the M&A route.

Source: https://www.iqvia.com/blogs/2024/01/biopharma-m-and-a-outlook-for-2024

JPM24: Roche's Pharma BD Chief Explains Renewed ADC Interest

Angus Liu, *FierceBiotech*, Jan 12, 2024 (excerpt)

As one of the first Big Pharmas to embrace antibody-drug conjugates (ADCs), Roche plans to make further bets on the popular cancer modality, according to the company's global head of pharma partnering, James Sabry, Ph.D. But biotechs looking for an alliance must first meet an invisible bar.

"We plan to do more deals, and we plan to do internal work in ADCs," Sabry said in an interview with Fierce Biotech on the sidelines of the 2024 annual J.P. Morgan Healthcare Conference.

Sabry's comments—and a recent licensing deal—marked a change of public tone at Roche toward ADCs. Back in mid-2022, chairman and then-CEO Severin Schwan told reporters that Roche had "rather limited interest" in ADCs despite other companies' growing investments in the field.

Still, getting on Roche's good side won't be an easy task for prospective ADC partners—Sabry's team reviews around 6,000 opportunities across all disease areas each year.

"For Roche, what the biotech companies are competing with is our internal work," he said. But that internal work isn't necessarily visible to outsiders. When asked what internal capabilities Roche has built around ADCs, Sabry said, "You'll see when the products come."

Source: https://www.fiercebiotech.com/biotech/jpm24-roches-pharma-bd-chief-explains-renewed-adc-interest-and-invisible-bar-all-dealmaking


James Sabry, Roche

Roche Also Looking to Beef Up in the Obesity Area

Naomi Kresge, *Bloomberg*, Jan 10, 2024 (excerpt)

Roche Holding AG isn't done making moves in the obesity market after last month's agreement to buy Carmot Therapeutics Inc. for as much as $3.1 billion.

The Swiss drugmaker said Tuesday that it's on the hunt for additional biotech partners to help it challenge weight-loss leaders Novo Nordisk A/S and Eli Lilly & Co. Roche is looking for new ways of adjusting metabolism that could ultimately be combined with treatments it's gaining in the Carmot deal.

"This is opening up a whole new vista for us," James Sabry, Roche's head of partnering, said in an interview on the sidelines of the JPMorgan Healthcare Conference in San Francisco.

Carmot was one in a flurry of recent deals Roche has made to bolster its pipeline. The company is also interested in oncology, neurology and ophthalmology as well as cardiovascular medicine, Sabry said.

While many companies are trying to break into the hot weight-loss market, Sabry said Roche is one of only a handful of suitors with the size and global reach to run the large, costly trials necessary to bring new drugs to market. Marketing obesity medicines is also more complicated than other areas like cancer because drugmakers need to deal with primary-care doctors instead of a few specialized treatment centers, he said.

"When we're trying to get a deal done, we find more competitors in oncology," he said. "You'd think everyone must be competing with you for metabolism drugs, but it's not that way."

Source: https://www.bloomberg.com/news/articles/2024-01-10/roche-hunts-for-more-deals-to-challenge-lilly-novo-on-obesity

Other Big Pharma M&A Comments at #JPM24

1. **Eli Lilly** most likely to do smaller deals. Won't rule out larger deals but they are unlikely to meet the company's investment criteria.
2. **Gilead** could do a deal in the $5bn to $25bn range this year. Oncology of highest interest to them.
3. **Merck** will look at all deal sizes and is most interested in oncology. Also interested in drugs that will lower weight while treating specific aspects of metabolic syndrome such as liver disease or diabetes.
4. **Novo Nordisk** will be very active in 2024 and will focus on areas that they know including diabetes, obesity and cardiovascular.
5. **Pfizer** will not be doing larger deals but will be opportunistic in areas of interest.

Ozempic Mania Fuels Deal Optimism Across Drug Industry

Naomi Kresge, Michelle Davis and Robert Langreth, *Bloomberg*, January 10, 2023 (excerpt)

The world's biggest drugmakers are racing to buy up biotech companies to fill looming holes in their pipelines and pounce on new discoveries, bringing a hopeful buzz back to JPMorgan Chase & Co.'s big health-care conference in San Francisco.

"Opening new markets like obesity is adding optimism," said Victor Bulto, president of the US unit for Novartis AG on the sidelines of the JPMorgan Healthcare Conference, which draws the heads of the world's biggest drug companies who use the annual confab to broker multibillion-dollar deals.

The renewed energy in biotech, which has been pummeled in recent years, applies even for companies that aren't working in obesity, Bulto said. "The realization that there's still a substantial unmet need" is boosting the excitement, he said.

"There was definitely the sentiment of, you know, 'We've got more than enough money. We don't need you,'" Teresa Graham, chief of the pharmaceutical unit at Roche Holding AG, said at the conference. Enthusiasm for the sector cooled as Covid faded and it got costlier to borrow money, sending biotech share prices tanking. Now interest rates are stabilizing, making more deals possible.

Prices for biotech companies have reached "a better, more realistic place," Graham said. "There is a lot of energy around what is out there."

Now, big drugmakers are in a hurry. As many as 170 drugs could lose exclusivity by the beginning of the next decade, representing close to $400 billion in annual sales for big pharmaceutical companies, according to data compiled by Bloomberg Intelligence. At Bristol Myers Squibb Co., for example, three drugs that have been among their biggest sellers are at risk.

That's why the deals are coming in. On the first day of the conference alone, about $6.4 billion worth of health deals were announced. Merck & Co. spent $680 million for cancer drugmaker Harpoon Therapeutics Inc., Boston Scientific Corp. spent $3.7 billion on a device-maker and Johnson & Johnson spent $2 billion for a cancer drugmaker. It follows an even busier December when Bristol and AbbVie Inc. each announced an acquisition within days of doing another deal.

Source: https://www.bloomberg.com/news/articles/2024-01-10/obesity-drugs-biotech-deals-feature-at-jpmorgan-healthcare-conference

Rumors Fly on Cytokinetics

Tristan Manalac, *Biospace*, Jan 12, 2024 (excerpt)

Novartis is reportedly backing off of its rumored potential acquisition of California–based cardiovascular disease specialist Cytokinetics, according to a Thursday report from The Wall Street Journal, citing a source familiar with the matter.

On Monday, the WSJ reported that the Swiss drugmaker was in “advanced talks” to buy Cytokinetics. According to the Journal’s sources, the agreement could have been inked “as soon as this week” amid the 42nd annual J.P. Morgan Healthcare Conference, which is widely recognized in the biopharma industry as a hub of dealmaking activity.

At the time, however, there was no potential purchase price.

A Reuters article earlier this week also identified AstraZeneca and Johnson & Johnson as potential suitors of Cytokinetics, however noting that they were likely to be outdone by Novartis.

On Thursday, Amgen emerged as another potential suitor, according to Seeking Alpha. Cytokinetics is reportedly holding out for $130 to $145 a share, per Betaville, which cited sources familiar with the matter. Amgen has history with Cytokinetics. The larger biopharma terminated a development and collaboration agreement for small molecule cardiac myosin activator omecamtiv mecarbil in 2020.

In response to reports Novartis backing away from the potential deal, Cytokinetics’ shares crashed by as much as 28% on Thursday, as per Seeking Alpha.

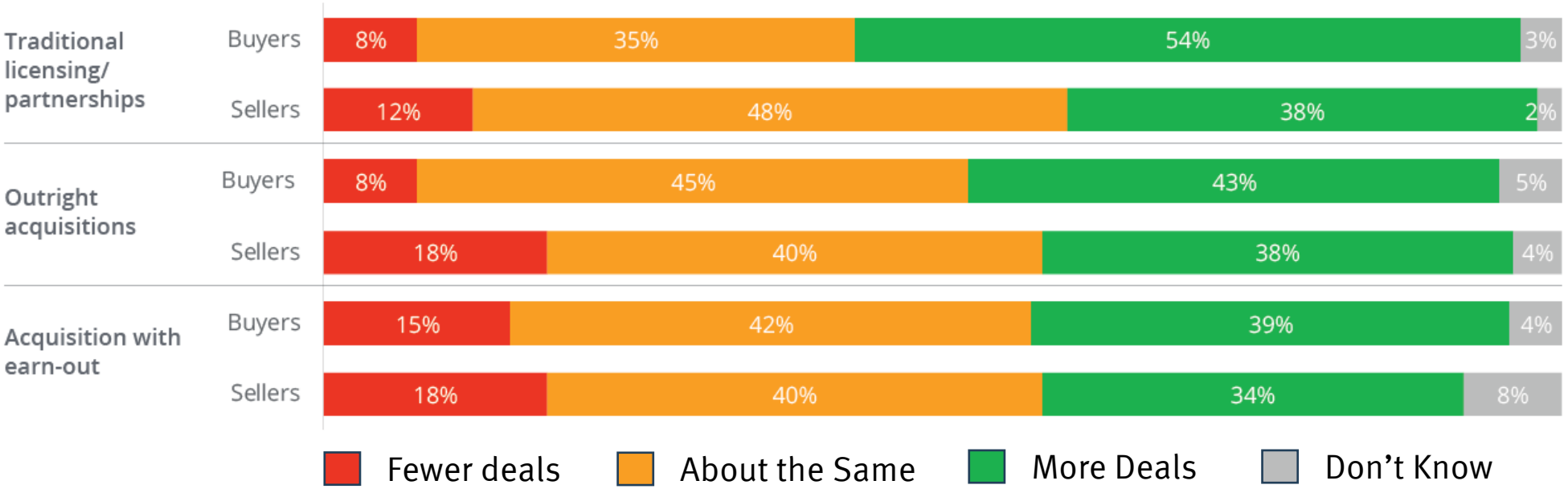
Source: https://www.biospace.com/article/novartis-pulls-away-from-rumored-cytokinetics-deal-while-amgen-emerges-as-a-contender-reports/

Syneos Survey of Dealmakers Intentions for 2024

Syneos Health Report, Jan 8, 2024

Figure 3. Expectations by deal and financing types

Expectation by Deal Type (Compared to the trailing 12 months in 2022-2023*)
"buyers" vs. "sellers"



Source: https://www.syneoshealth.com/insights-hub/dealmakers-intentions-survey-2024

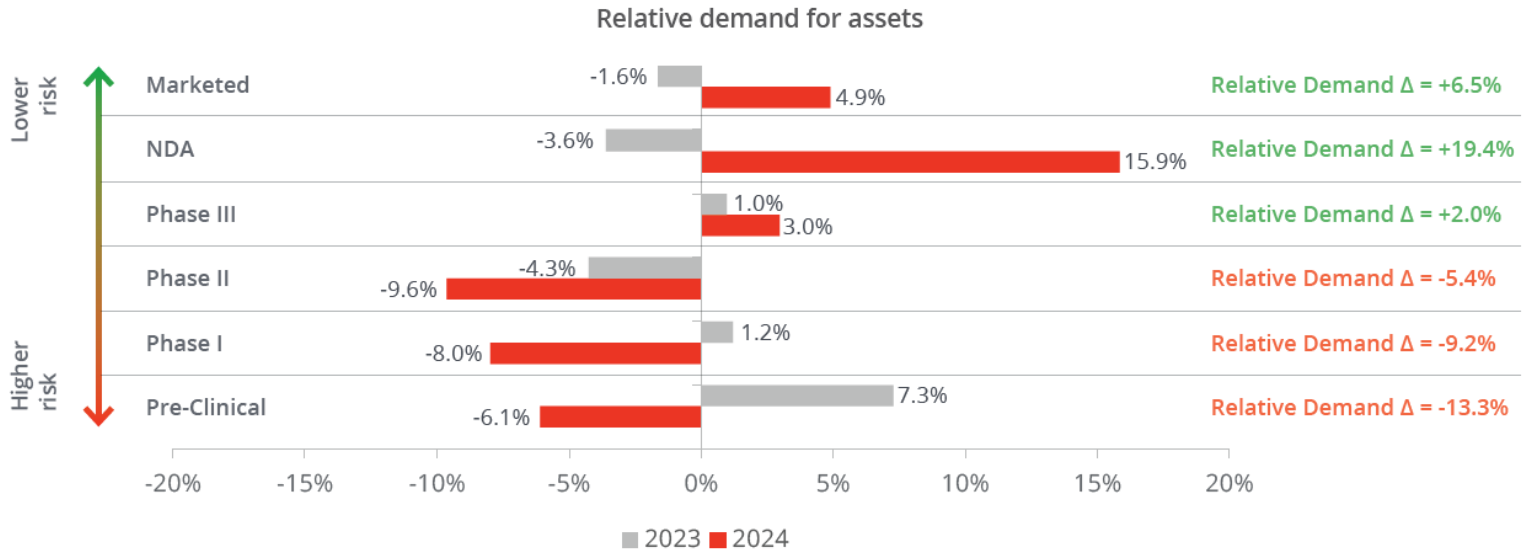
Dealmakers Focused on Approved Products

Syneos Health Report, Jan 8, 2024

Healthy appetite for approved products

The relative demand for assets across stages of development continues to favor lower-risk opportunities including marketed, NDA-level and Phase III assets. In addition to weaker appetite for risk associated with early-stage assets, pharma and biotech companies are seeking out products to fill their near-term revenue gaps amidst patent expirations and pipeline disappointments. Despite this trend favoring later stage assets, we observed strong demand for Phase I oncology treatments (see Figure 8).

Figure 4: Assets across different stages of development



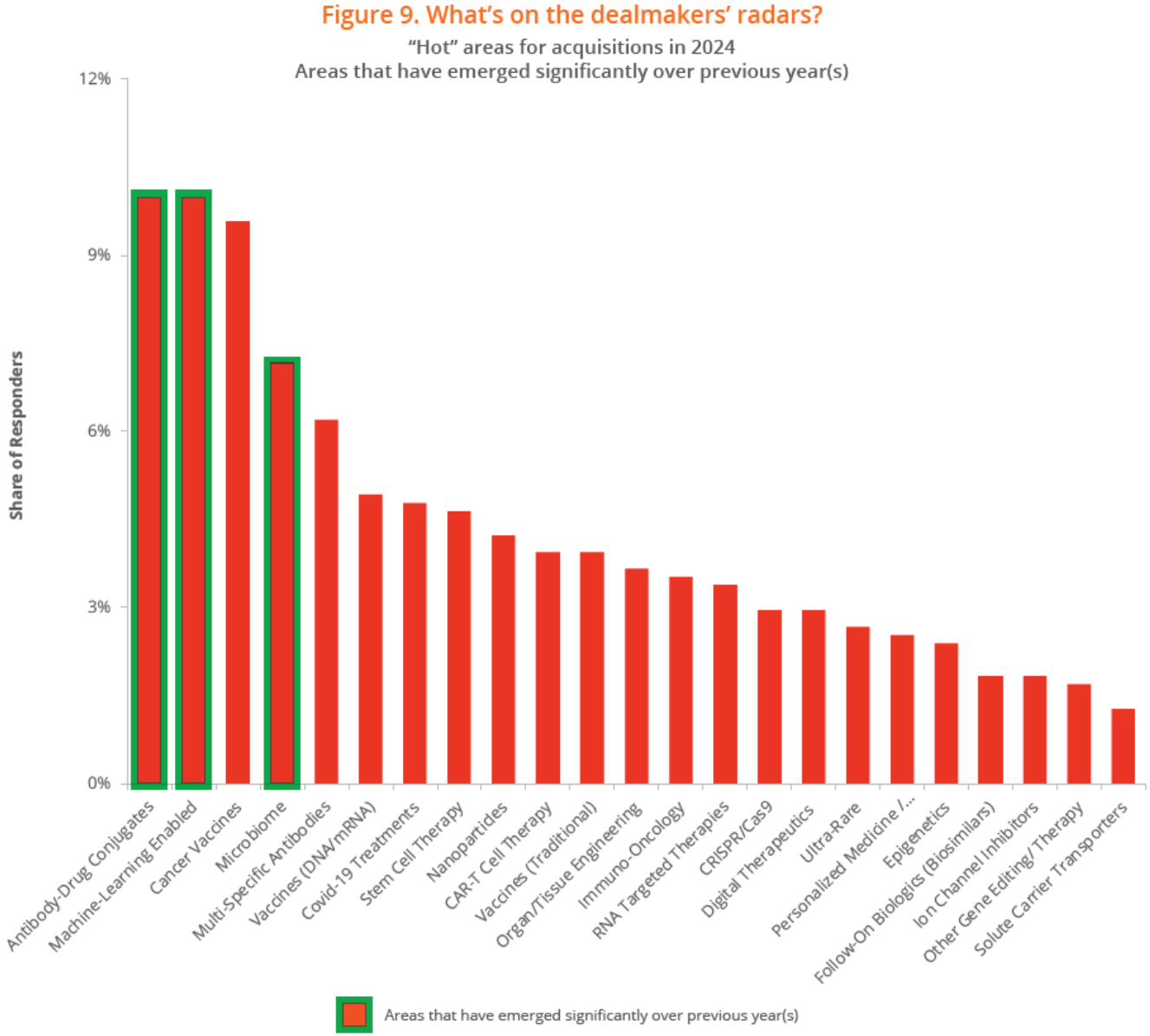
Source: Syneos Health Consulting, Inc. Dealmakers Intentions 2024. N=119 for buyers and N=50 for sellers.

Source: https://www.syneoshealth.com/insights-hub/dealmakers-intentions-survey-2024

Hot Areas for Acquisitions

Syneos Health Report, Jan 8, 2024

Buyers and sellers share strong interest in oncology and antivirals, two of the 'hotter' therapeutic areas emerging In the survey, ADCs, machine-learning enabled products—perhaps including generative AI—and microbiome-related technologies were identified as "hot" acquisition targets in 2024. Survey responses also indicated sustained demand for cancer vaccines following the clinical success of personalized vaccine combination regimens from Moderna and Merck. Gene therapy categories were separated out in the survey so the percentages individually seem smaller. However, combining the individual categories suggests a continued high level of interest.



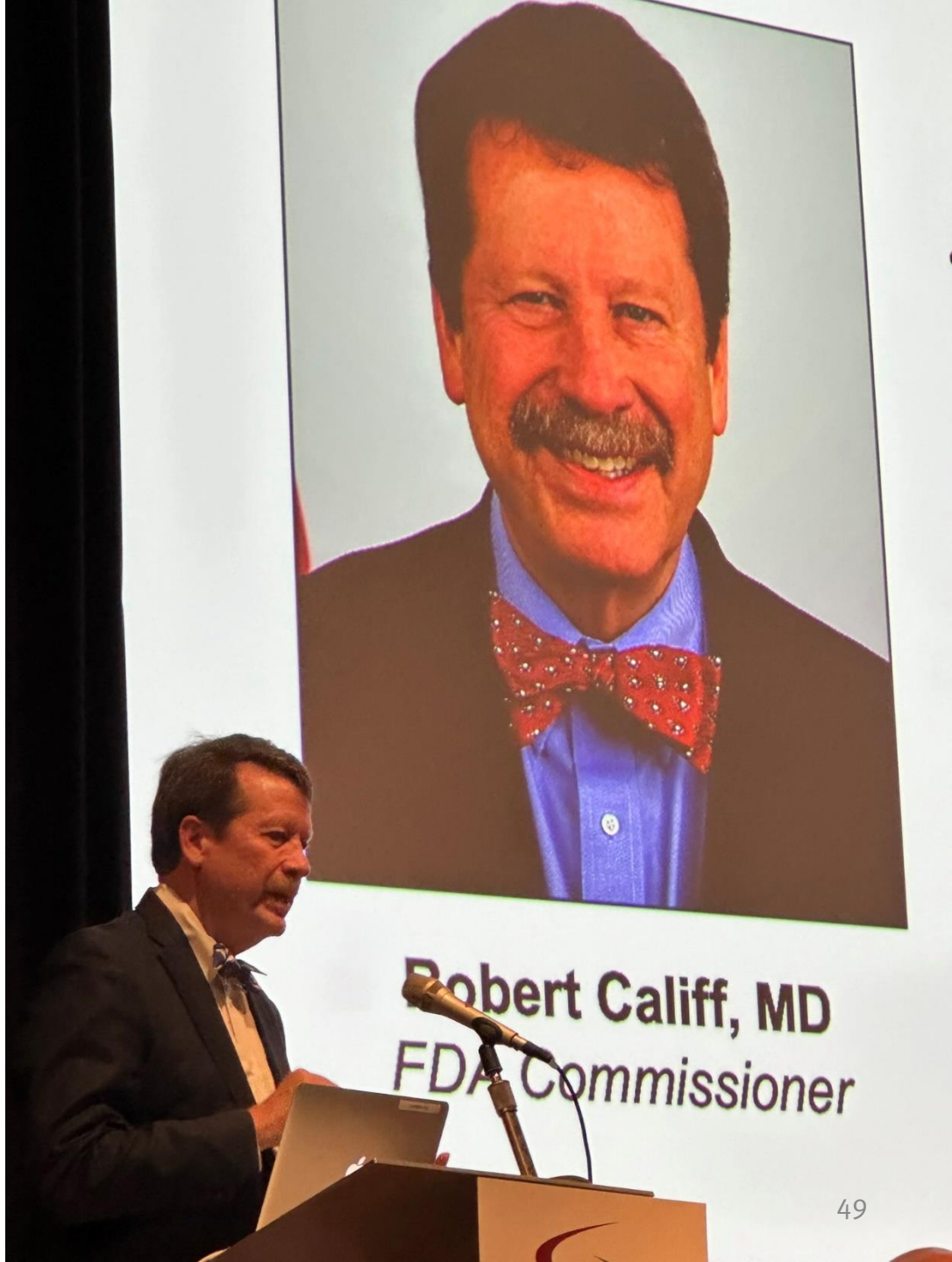
Source: Syneos Health Consulting, Inc. Dealmakers Intentions 2024. N=119 for buyers and N=50 for sellers. Respondents could select multiple areas.

Source: https://www.syneoshealth.com/insights-hub/dealmakers-intentions-survey-2024

Industry News

FDA Commission Musings at CERSI Conference on Jan 7, 2024

- How can it be that we can be at the top of innovation pack and yet our nation's life expectancy is on the bottom of the pile in terms of high-income countries?
- Hundreds of generic drugs are in shortage. We need to fix this.
- Low cost devices (e.g., hospital gowns and masks have moved back to China) and are also frequently in shortage. We need to figure out what to do here.



Rob Califf on Key Policies and Priorities for the FDA in 2024

1. **Tobacco**. As you well know we have proposed rules for menthol and flavored cigars. Flavored cigars now exceed cigarettes in terms of use by teenagers. We are working on a rule that would reduce the level of nicotine to a sub-addictive level. Won't be enacted until the next administration.
2. **Food labelling**. If you ask me the label for a food product should be on the front of the package. Where a consumer could actually read it. You would be amazed by the level of opposition to this simple idea.
3. **Food labelling**. We are working to redefine the word "healthy". That's hotly contested.
4. **Food**. Enormous need for research on ultraprocessed food. We are growing by a pound a year in our population – we need to know if it caused by ultra processed foods. Some are saying yes.
5. In devices we are focused diagnostic **LDT's**. It's me vs. academic medical centers. We made it clear that Congress should pass a law. We are now putting a rule that if you say a test does something you have to prove it. You'd be surprised by the level of opposition.
6. **AI** is a huge thing. Everyone is talking about it. We are in a good spot relative to a field where nowhere knows what will happen. Implications for healthcare and food are significant.
7. AI and device **platforms** are a focus for us in 2024. There are many areas need a relook here. Integrated device structures. If you are in the OR you would like to have the best surgeon available who can scrub in virtually. That's going to involve a bunch of interconnected devices. Same is true with homes. We need to figure out how to better regulate here.
8. **Substances**. We need a center for bad decisions. We need a way to protect people from harm. CBD gummy bears are a good example. We are having a lot of issues with these. They are barely regulated and are becoming an ever bigger problem.
9. **Gene modification** is increasingly an issue for us. An enormous issue for animals where multiple gene edits can happen.
10. Data and **enterprise transformation** at the FDA is also a priority for us.

Six Takeaways from JP Morgan 2024

Jonah Comstock, *Pharmaphorum*, January 12, 2024 (excerpt)

With another JP Morgan in the rearview mirror, it's time to take stock of the announcements, the presentations, and, above all, the vibes. While the event and its attendant satellite events comprise more content than anyone could ever consume, it also serves an important function to align goals and expectations for the year to come. So. for those of you who couldn't make it, or those of you who were there, but your head's still spinning, here are my six big takeaways from the show:

1. **Dealmaking is back on the menu (at least for late-stage assets)**. I've been working on my own 2024 predictions piece (still to come) and I started doing calls for that in mid-December. At that point, I was hearing doom and gloom about M&A reminiscent of 2023's JP Morgan. But then the industry got an early Christmas present in the form of news that BMS was acquiring Karuna Therapeutics for $14 billion, followed by RayzeBio for $1.4 billion. Then AstraZeneca put up $1.2 billion for Gracell. Then, at the show itself, J&J, Novartis, and MSD all kicked in the door with acquisition announcements, as did GSK. At this point, predicting a big year for acquisitions seems reminiscent of Mean Girls' Karen Smith telling us there's a 60% chance it's already raining. Nonetheless, there are lots of reasons to believe more acquisitions are coming, and there seemed to be a consensus on that at JPM. The headwinds make sense: big pharma has a lot of dry powder and is facing a patent cliff over the next few years, along with the still-uncertain effects of the Inflation Reduction Act (IRA). Diversifying portfolios with more assets is the best hedge they have and, with the economy on an upturn, prices might be as good right now as they're going to get for a while.
2. **Big tech is more than dipping its toe into life sciences, but they're not going alone**. Chipmaker NVIDIA announced a major push into Generative AI (GenAI) for drug discovery, working with high-profile partners like Recursion and Amgen. The demos were impressive and it was clear from CEO Jensen Huang's fireside chat that the company is deeply invested in the vertical. Alphabet spinout Isomorphic Labs signed big-dollar deals with Eli Lilly and Novartis for AI drug hunting. And Amazon marched on with its gradual push into healthcare, announcing a programme with digital health stalwart Omada Health that takes the company into the chronic condition management space. At one memorable panel at Fierce JPM Week, Vivodyne CEO Abraham Heifets described how tech and pharma are almost opposites in how they do business: tech companies secure a first-mover advantage early, then dominate the space for as long as they can, reinvesting to stay ahead of the competition (think Google in search, Amazon in commerce, Apple in mobile devices); pharma companies, on the other hand, have to extract value quickly from their leadership positions and then be ready with the next thing when they lose exclusivity.

Source: https://pharmaphorum.com/market-access/six-takeaways-jp-morgan-2024

Six Takeaways (Continued)

3. **Everyone's talking about AI. But only some people have anything to say.** Look, of course AI was going to be the topic du jour this year at JP Morgan. But for good reason: 2023 was the year that AI became table stakes for life sciences companies. But applications go way beyond that, especially with the advent of large language models (LLMs). There are AI applications starting to transform the whole R&D value chain, from clinical trial recruitment to protocol writing and study design, and to data collection and analysis. Not to mention applications on the commercial side and in medical affairs, particularly for GenAI. It's no longer enough to say, "We use AI." What are you using AI for? Are your models high-quality? Are they trained on high-quality data? How are you solving for bias and hallucination? AI winners and losers will emerge based on companies' ability to answer those questions. The strength of ChatGPT is that anyone can use it, but that makes it inherently commodified. The question pharma companies have to answer is, "What can my AI application do that Chat GPT can't?"
4. **Answers are starting to emerge to cell and gene therapies' big questions**. If the most discussed topic at JP Morgan was AI, cell and gene therapy may have been the second-most-discussed. With the meeting coming just a month after the FDA's landmark approval of two gene therapies for sickle cell disease, perhaps it's no surprise that it was top of mind. There is optimism and positive energy around cell and gene therapy, but the hurdles are far from cleared. And some of the start-ups working in that space may not make it if the various pieces don't move fast enough. Andrew Obershain, CEO of bluebird bio, said as much on stage. A year before the FDA approved his company's gene therapy for sickle cell, he was telling reporters that the company was running out of runway and might shut down.
5. **ADCs are poised for a third act.** One of the best single talks of the show for me was Daiichi Sankyo CEO Ken Keller, who told the story of how his company restructured around oncology when it became apparent how much opportunity was in ADCs. "The success of Enhertu has put a new kind of feeling into this space," he said. "In 2013, there were 32 trials in this space. Last year there were over 300 [...] So, something that was thought of as old has truly become the hot new thing. And now that we've cracked the code on these ADCs, the sky's the limit."
6. **A real world evidence paradigm shift is coming... Eventually.** AI has made it possible to use synthetic data to replace the placebo arm in drug trials, something that is increasingly necessary, as the drugs with accelerated approvals struggle to recruit for post-market studies and maintain the integrity of their placebo groups. As Tracy Hayne from Slipstream IT put it, we shouldn't be expecting people to voluntarily put their lives on the line for science, but that's what we're asking 50% of people to do when we enrol an RCT of a drug that's already in the market.

Source: https://pharmaphorum.com/market-access/six-takeaways-jp-morgan-2024

Pfizer Focusing on Cost and Commercial Structure in 2024

2023: Moving Beyond a Challenging Year

A challenging 2023 with missed expectations, yet significant achievements seeding success for 2024 onward

2023 Achievements

- Treated >600M patients with our medicines and vaccines[1]
- Reported highest revenue YTD Q3 2023 among peers[2]
- Received record number of FDA approvals[3]
- Closed Seagen transaction

A Strong Foundation for 2024+

- Removed many COVID product uncertainties
- Enhanced commercial structure
- Launched cost realignment program designed to right-size cost base
- Reduced COVID product inventory to reflect anticipated future demand

* See Slide 5 for footnotes..

Source: https://investors.pfizer.com/Investors/Overview/default.aspx

Merck Highlights Broad, Diverse Pipeline

Progressing broad pipeline across key therapeutic areas

Vaccines & Infectious Disease

Pneumococcal Disease: Adults
V116 (PCV, Filed)

RSV
Clesrovimab (mAb, Phase 3)

HIV: Treatment
Islatravir (NRTTI, Phase 3)

Dengue
V181 (LATV, Phase 2)

HIV: PrEP
MK-8527 (NRTTI, Phase 2a)

Pneumococcal Disease: Pediatrics
V117 (PCV, Phase 1)

Cardiometabolic

PAH
Sotatercept (activin signaling inhibitor, Filed)

Lipid Lowering
MK-0616 (Oral PCSK9 inhibitor, Phase 3)

Chronic Heart Failure (without worsening event)
VERQUVO (sGC stimulator, Phase 3)

PAH
MK-5475 (Inhaled sGC stimulator, Phase 2/3)

Thrombosis
MK-2060 (Factor XI inhibitor, Phase 2)

NASH
MK-6024 (GLP-1/glucagon receptor dual agonist, Phase 2b)

Immunology

Inflammatory Bowel Disease
Tulisokibart (MK-7240) (TL1A inhibitor, Phase 3)

Vitiligo, Lupus
MK-6194 (IL-2 mutein, Phase 2a)

Immune Mediated Disease
MK-8690 (CD30L antagonist, Phase 1)

Neuroscience

Schizophrenia
MK-8189 (PDE10 inhibitor, Phase 2)

Alzheimer's Disease
MK-2214 (Anti-Tau mAb, Phase 1)

Alzheimer's Clinical Syndrome
MK-4334 (Alpha 7 Nicotinic Acetylcholine Receptor PAM, Phase 1)

Narcolepsy
MK-6552 (Undisclosed, Phase 1)

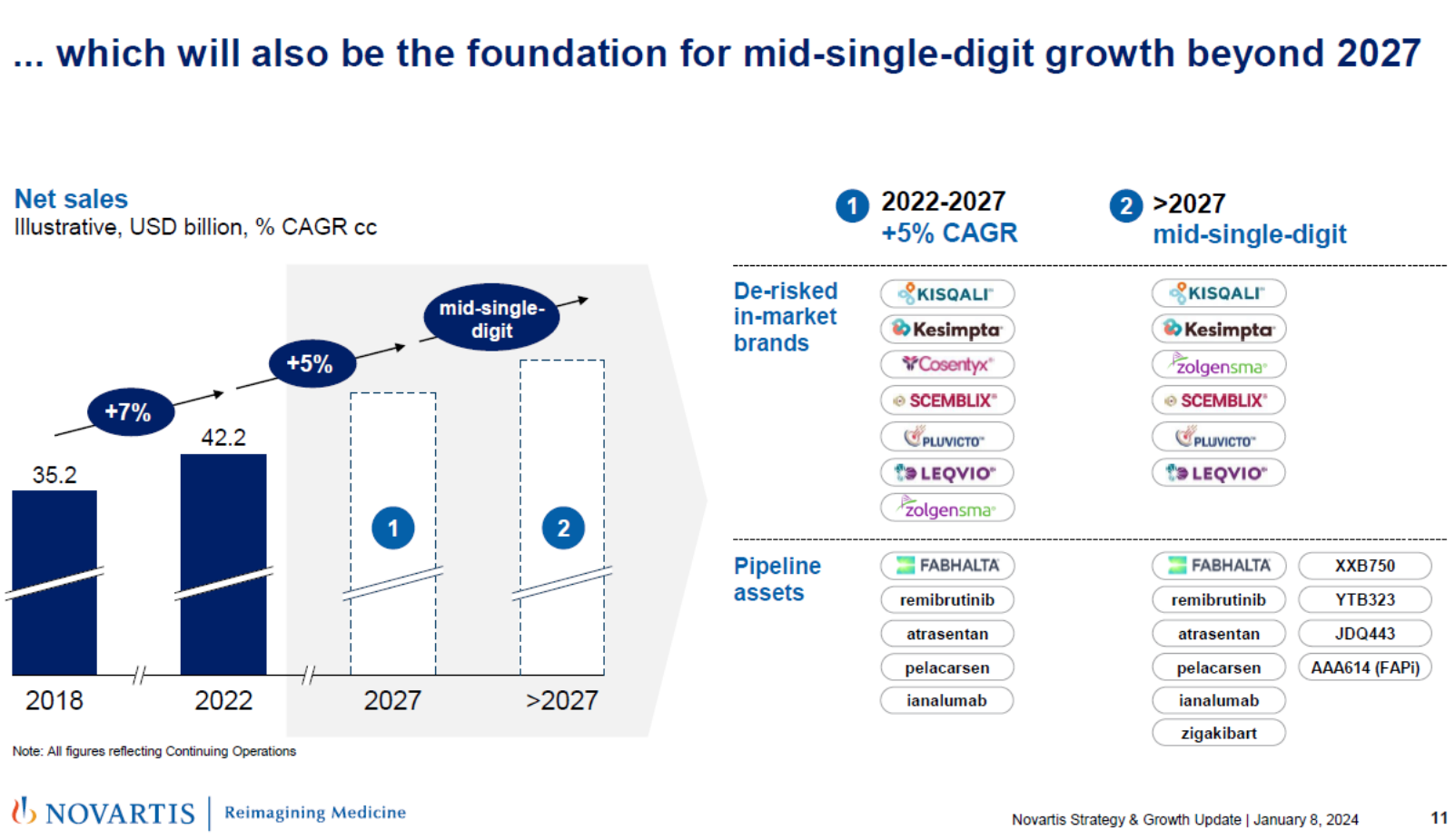
Primary completion date in 2024 per clinicaltrials.gov

MERCK 12

Merck showed off a deep ADC pipeline for 2024 and notes numerous readouts this year in vaccines, cardio, immunology and neuroscience.

Source: https://www.merck.com/investor-relations/

Novartis Highlights Long-Term Growth Beyond 2027

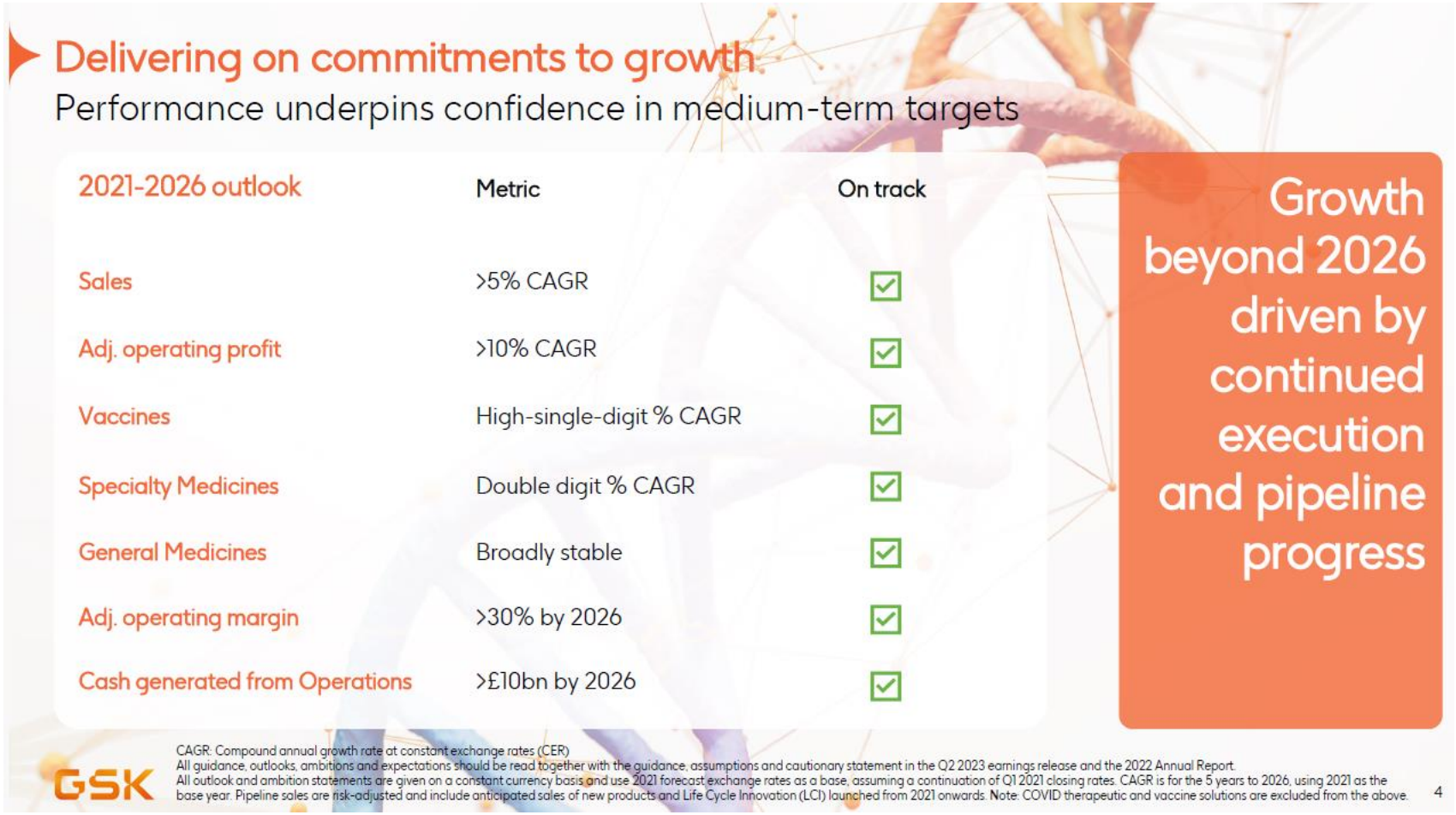


Novartis has steadily built up its case for long-term topline growth.

This page highlights potential for mid-single digit growth well into the next decade.

Source: https://www.merck.com/investor-relations/

GSK Highlights Long-Term Growth Trajectory



GSK is looking at topline growth of 5% or more beyond 2026.

GSK is acquiring Aiolos Bio to build up its already formidable respiratory pipeline.

Source: https://www.merck.com/investor-relations/

Lilly Highlights its Long-Term Commitment to Incretins

The long road to "overnight" success in incretins

Discovering and delivering breakthrough medicines requires persistence of R&D efforts

1996

Dr. John Eng licenses exendin-4 to Amylin

2002

Lilly-Amylin alliance for exenatide signed

2005

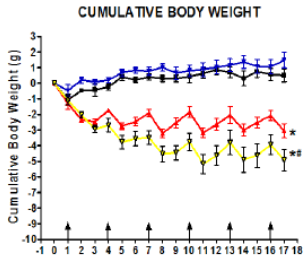
Approval of Byetta

2010

AWARD-1 Phase 3 study of dulaglutide in T2D begins

2010

Proof of concept in mice of weight loss from GIP+GLP-1

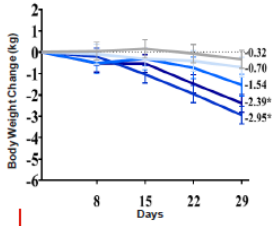


2014

FDA approval for Trulicity (dulaglutide once weekly injection)

2017

First in human data of tirzepatide showing weight loss



2017

Tirzepatide Phase 2 trial in T2D begins

2019

Trulicity REWIND CV outcomes study positive readout

2022

Mounjaro (tirzepatide) launches for T2D; SURMOUNT-MMO tirzepatide outcomes study in obesity begins

2023

Zepbound approved by FDA for chronic weight management

Source: https://investor.lilly.com/static-files/c700e00d-2474-42b0-9a92-6a539961e312

JPM24: Lilly CEO David Ricks to Biotechs: 'We're Open for Business

Annalee Armstrong, *FierceBiotech*, Jan 9, 2024 (excerpt)

Eli Lilly CEO David Ricks, speaking to the slow and steady progress that brought tirzepitide to the world, says the Indianapolis pharma is now ready to open up the chocolate factory.

"I know a number of biotechs are in the room at this conference so it's worth mentioning: we're open for business on external innovation," Ricks said at the J.P. Morgan Healthcare Conference Tuesday.

That doesn't just mean gobbling up companies. Ricks said the pharma's approach over the past few major acquisitions—see Loxo Oncology in 2019—has been to buy the companies and keep them operating more at an arm's length, retaining the talent and allowing them to continue bringing new, exciting ideas to the table.

"Most of the Big Pharma companies in our industry, and certainly Lilly for the longest time, thought about acquisition as grabbing an asset. Essentially, go into a company, take their work, thank them very much. The people move on to the next thing. And then as Big Pharma, we envelop that and prosecute it forward," Ricks said.

Lilly doesn't want to do that anymore. Starting with Loxo, the company began to prioritize the people more.

"We think about now, acquisition is not just assets, but people and methodologies and ways to make even more medicines," Ricks said. "Surely one of the ways that Big Pharma can grow R&D productively is by having more great minds around the table and more difference in how we think about creating drugs."

Source: https://www.fiercebiotech.com/biotech/jpm24-lilly-ceo-david-ricks-biotechs-were-open-business

Regeneron: AI is the Big Thing Right Now, But Real Tool is Genetics

Jim Cramer, *CNBC*, Jan 9, 2024 (excerpt)

Regeneron CEO Leonard Schleifer elaborated on the biotech company's latest ventures with CNBC's Jim Cramer on Tuesday and emphasized the importance of genetic research across the industry.

"The big thing for everybody these days is AI, that's the next big thing. But I don't believe that," Schleifer said. "It's a good tool. But for our business, the really, most important tool, I think, is genetics, it's genes."

Schleifer suggested that "associating genes with disease" is going to drive the pharmaceutical industry, explaining that innovative treatments can essentially repair certain genes and silence others.

In October of 2023, Regeneron shared preliminary results that gene therapy improved hearing in a child with a rare condition causing "profound genetic hearing loss." This specific gene therapy was developed in a collaboration between with Decibel Therapeutics, a company Regeneron recently acquired.

Len Schleifer
CEO, Regeneron

Source: https://www.cnbc.com/2024/01/09/regeneron-ceo-says-gene-therapy-is-the-next-big-thing-for-biotech.html

Regeneron to Test its Muscle Preserving Drugs with Semaglutide

Madison Muller, Bloomberg, January 10, 2024 (excerpt)

Regeneron Pharmaceuticals Inc. will soon start testing its antibody drugs in combination with Wegovy to see if they prevent muscle loss, a problem that drugmakers including Eli Lilly & Co. have been racing to solve.

GLP-1 drugs made by Lilly and rival Novo Nordisk A/S have exploded in popularity, but experts have started raising concerns that older patients may also be at risk of losing critical muscle mass that helps prevent injuries.

Up to 40% of the weight patients lose on GLP-1 drugs may actually be due to decreases in lean muscle mass, Regeneron's Chief Scientific Officer George Yancopoulos said in an interview at the annual JPMorgan Healthcare Conference in San Francisco. This could "potentially be a public health disaster," he said.

Later this year, Regeneron will start testing two of its antibody drugs in combination with Wegovy to see if they preserve or help to build muscle. The trial will also look at whether the combinations help prevent patients from rapidly regaining weight after they stop taking drugs such as Wegovy or Lilly's Zepbound.

Other companies are also trying to tackle the muscle-loss problem. Eli Lilly, for one, is studying Zepbound in combination with a drug it acquired from obesity startup Versanis Bio. It's also looking at combining the treatment with an experimental muscle-atrophy drug from BioAge Labs, a closely held California biotech company.

Source: https://www.bloomberg.com/news/articles/2024-01-10/regeneron-will-test-wegovy-drug-combos-to-protect-muscle-mass

Arena BioWorks Launches as a Privately Funded, Fully Independent Biomedical Institute

Press Release, Jan 12, 2024

Arena BioWorks announced today its launch as a biomedical research institute with a mission to uncover mechanisms of disease by engaging in basic biological research that will be translated into lifesaving biotech therapeutics. Inspired by the success of Bell Labs, Arena BioWorks is a dual-purpose entity aimed at achieving social good and creating long-term sustainable impact through the formation of for-profit biotechnology companies. It is located in a state-of-the-art facility in the Kendall Square biotech hub in Cambridge, MA and will collaborate globally to maximize societal benefit worldwide. As part of its novel model, discovery and company creation will occur seamlessly under one roof. By relying solely on private funding, Arena will be able to quickly translate insight into discovery, distinguishing it from traditional models. Arena will support development efforts with its drug discovery platforms through preclinical studies and beyond, when appropriate. Arena is led by a management committee that comprises preeminent chemical biology pioneer, Stuart Schreiber, Ph.D. as Chief Executive Officer to drive the scientific vision, former Co-Chair of Bain Capital and award-winning philanthropist, Steve Pagliuca, as Executive Chair, and Founder and Managing Partner of the life science venture capital firm Newpath Partners, Tom Cahill, M.D., Ph.D. as Institute Representative.

Source: https://www.prnewswire.com/news-releases/arena-bioworks-launches-as-a-privately-funded-fully-independent-biomedical-institute-to-shorten-the-path-from-insight-to-therapeutics-302033563.html

Genome Sequencing to Yield New Cancer Treatments, UK Study Finds

Clive Cookson, *Financial Times*, January 10, 2024 (excerpt)

Cancer patients stand to benefit from the expansion of genome sequencing of tumours that would enable the development of life-saving diagnostics and treatments, according to the word's largest study of the technology.

The results of the study, carried out in England and published in the journal Nature Medicine on Thursday, demonstrate that some common cancers have a genetic profile that could guide decisions about patient surgery and drug therapy.

The project, led by government-owned Genomics England in collaboration with the NHS, universities and hospital trusts involved 13,880 volunteers. Scientists analysed all the DNA present in cancerous and healthy tissue in each individual, relating genetic mutations to clinical data about their treatment and disease progression.

"This study is an important milestone in genomic medicine," said Nirupa Murugaesu of Guy's and St Thomas' NHS Trust, one of the project leaders. "We are showing how cancer genomics can be incorporated into mainstream cancer care across a national health system and the benefits that can bring patients.

"Discovering this DNA signature of tumours requires whole genome sequencing — reading all 3.2bn letters of genetic code in their DNA — rather than carrying out a more limited panel of genetic tests, which is currently the standard diagnostic technique.

Sir Mark Caulfield, professor of clinical pharmacology at Queen Mary University of London and former chief scientist at Genomics England, said the NHS had around £44mn to spend on expanding cancer genomics, though NHS England declined to comment on its planned expenditure.

Source: https://www.ft.com/content/e5981f66-784e-46b8-b75e-05117f9c956e

The Grand Challenge of Moving Cancer Whole-Genome Sequencing Into The Clinic

Akhoundova, D., Rubin, M.A. The grand challenge of moving cancer whole-genome sequencing into the clinic. Nat Med (2024).

The largest whole-genome sequencing study thus far has revealed myriad actionable alterations and potential biomarkers for 33 cancer types, but various logistical, technical and economic challenges must be overcome before this technique can become standard of care.

Whole-genome sequencing (WGS) is a powerful next-generation sequencing (NGS) tool that has enabled many advances and discoveries in the cancer research field. In this issue of *Nature Medicine*, Sosinsky et al. present an analysis of the largest real-world clinical WGS cohort thus far. They integrated data from the UK National Health Service Cancer Programme of the 100,000 Genomes Project — which analyzed 13,880 whole-cancer genomes from 33 cancer types — with matched clinical data from patients. The project demonstrates the potential clinical utility of this approach but also highlights many challenges on the road to implementing it.

WGS has, in theory, some clinical and technical advantages relative to targeted NGS. Seen as a molecular profiling 'one-stop shop', WGS could potentially serve as a universal molecular tumor-profiling test, allowing standardization across distinct assays and avoiding the need for multiple additional tests, such as fluorescence in situ hybridization, pharmacogenomics or even germline testing. Some technical advantages over targeted panels are a more-uniform sequencing depth, greater sequencing breadth (in the range of ~1,000-fold broader than the most extensive targeted panels), and the ability to detect less-common genomic rearrangements, intronic changes, splice-site alterations and genomic signatures, all with potential implications for treatment.

In summary, Sosinsky et al. present the most extensive real-world clinical WGS study thus far, underlining the feasibility and the considerable potential of linking paired genomic and clinical datasets. Moving this WGS precision oncology approach toward a standard of care will be difficult for logistical, technical and economic reasons. From a clinical perspective, focusing on alterations that can currently be treated is the main focus. Beyond predictive biomarkers, the added value and clinical implications of detecting larger numbers of prognostic alterations remain controversial. **A head-to-head comparison of WGS and targeted NGS will be needed to assess the prognostic and predictive value and clinical benefits of both approaches for patient outcomes.** However, looking to the future, it is possible that the greatest benefits will come from capturing as much data as possible — particularly if WGS is performed on diverse, real-world populations.

Source: https://www.nature.com/articles/s41591-023-02697-7

Disrupted Degradative Sorting of TLR7 is Associated with Human Lupus

Mishra H, Schlack-Leigers C, Lim EL, Thieck O, Magg T, Raedler J, Wolf C, Klein C, Ewers H, Lee-Kirsch MA, Meierhofer D, Hauck F, Majer O. Disrupted degradative sorting of TLR7 is associated with human lupus. Sci Immunol. 2024 Jan 11:eadi9575.

Hyperactive TLR7 signaling has long been appreciated as driver of autoimmune disease in mouse models. Recently, gain-of-function mutations in TLR7 were identified as a monogenic cause of human lupus. TLR7 is an intracellular transmembrane receptor, sensing RNA breakdown products within late endosomes. Here, we show that endosome dysfunction leads to unrestricted TLR7 signaling and is associated with human lupus. The late endosomal BORC complex together with the small GTPase Arl8b controls intracellular TLR7 levels by regulating receptor turnover. This requires a direct interaction between the TLR7-associated trafficking factor Unc93b1 and Arl8b. We identified an UNC93B1 mutation in a patient with childhood-onset lupus, which results in reduced BORC interaction and endosomal TLR7 accumulation. Therefore, a failure to control TLR7 turnover is sufficient to break immunological tolerance to nucleic acids. Our results highlight the importance of an intact endomembrane system in preventing pathological TLR7 signaling and autoimmune disease.

This article is highly topical as 2024 will feature three clinical readouts of TLR7 modulators for lupus.

The article shows how TLR7 signalling leads to lupus (via endosomal dysfunction).

Source: https://www.nature.com/articles/s41591-023-02697-7

Pipeline of TLR7 Inhibitors Aimed at Lupus

	EMD Serono	Bristol Myers Squibb	Eisai
Product	Enpatoran **(first in class)**	Afimetoran	E6742
Phase	Phase 2	Phase 2	Phase 1/2
Indication	SLE, CLE, Dermatomyositis & Polymyositis	SLE, CLE	SLE
MOA	Oral inhibitor of TLR7/8	Oral inhibitor of TLR7/8	Oral inhibitor of TLR7/8
Clinical Status	• In Ph2 trial among 440 SLE patients, expected to complete by Aug. 2024	• In Ph2 trial among 344 SLE patients, expected to complete by May 2025 • In Ph1 trial among 24 CLE patients, expected to complete by Jan. 2024	• In Ph1/2 trial among 24 SLE patients, expected to compete by Jan. 2024

Science Genome of girl with severe lupus pins down genetic target for treatments

"A new study fingers a gene called TLR7 that helps fight off viruses; when overactive, it unleashes the immune system on the body's organs and tissues. Although TLR7 is not the only gene implicated in lupus, targeting its activity or protein could help many patients. "TLR7 is likely to be a central hub, if not the central signaling pathway in lupus," says Carola Vinuesa, an immunogeneticist at the Francis Crick Institute who led the work, published today in Nature."

Source: https://www.science.org/content/article/genome-girl-severe-lupus-pins-down-genetic-target-treatments

Disclosure

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