



# Biopharmaceutical Sector

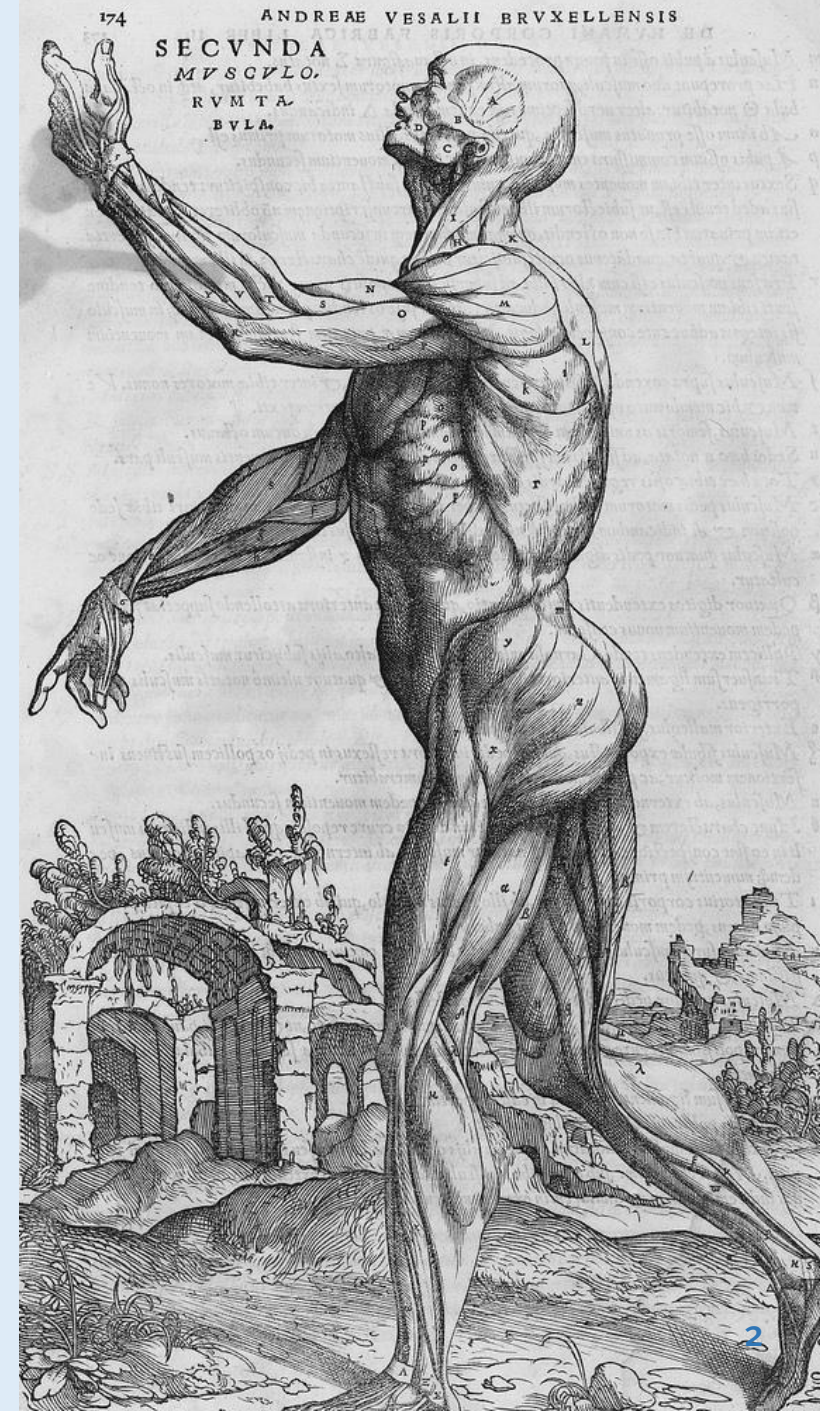
Weekly Update – April 8, 2024

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## From the Crypt

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When you think of Asbestos you think of Johns-Manville

## San Diego's 1st biotech product wins approval

By Craig D. Rose  
 STAFF WRITER

Agouron Pharmaceuticals Inc. broke a long shutout for San Diego's biotechnology industry yesterday by winning approval for the first locally developed

drug, an AIDS treatment expected to gain widespread acceptance.

The U.S. Food and Drug Administration gave Agouron clearance to begin marketing Viracept, a member of a new class of drugs credited with stabilizing HIV-infected patients.

The drugs, called protease inhibitors, block the replication of the AIDS-causing virus by chemically binding a



**Viracept:**  
 Should be available next week.

See **AGOURON** on Page A-18

# Join Us at Biotech Hangout This Friday



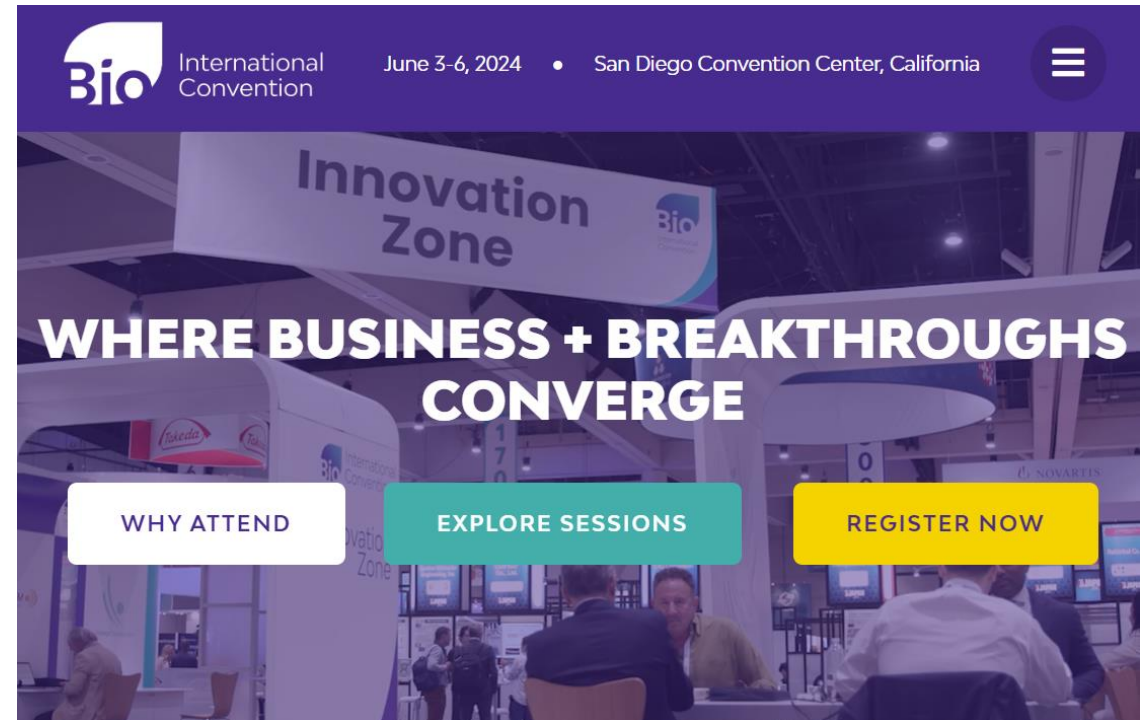
Biotech Hangout held its latest event on April 2, 2024.

The next event will be on April 9, 2024.

Please join us.

**To Learn More**

<https://www.biotechhangout.com/>



Please join us at BIO on June 3 to 6, 2024.

For details on attending please go to:

<https://convention.bio.org/>

We will also be at [ASCO](#) from May 31 to June 2<sup>nd</sup>. Happy to meet up there as well.

# Macroeconomics Update



# U.S. March Jobs Report Very Strong

Rob Wile, *NBC News*, April 5, 2024 (excerpt)

The U.S. economy added 303,000 jobs in March, blowing past expectations and indicating that economic growth remains on a firm footing.

The reading matches the largest one-month boost in payrolls since May 2023 and is a significant increase from the 270,000 added in February and the 256,000 in January. Economists had forecast that about 200,000 jobs would be added for March. The unemployment rate declined slightly to 3.8%, and wage growth came in at 4.1% over the last 12 months, the Bureau of Labor Statistics said.

The strong data point **may prompt the Federal Reserve to continue to push back the interest rate cuts** it had been signaling for this year.



# Powell Sticks With Fed's Cautious Rate-Cut Strategy

Howard Schneider and Abhirup Roy, *Reuters*, April 3, 2024 (excerpt)

Federal Reserve officials including U.S. central bank chief Jerome Powell on Wednesday continued focusing on the need for more debate and data before interest rates are cut, a move financial markets expect to occur in June.

"Recent readings on both job gains and inflation have come in higher than expected," Powell said in a speech to the Stanford Graduate School of Business. While policymakers generally agree that rates can fall later this year, he said this will happen only when they "have greater confidence that inflation is moving sustainably down" to the Fed's 2% target.

His remarks repeated language the Fed has adopted as it tries to balance the risks of cutting interest rates before inflation is truly controlled with the risks of suppressing economic activity more than is needed.

As new data arrives, however, as many questions have been raised as answered. In separate comments to CNBC on Wednesday, Atlanta Fed President Raphael Bostic said rates should likely not be reduced until the fourth quarter of this year. Bostic anticipates only one quarter-percentage-point cut will be appropriate in 2024, well below the three or more cuts most of his colleagues anticipate.

Fed Governor Adriana Kugler, for one, agreed with the assessment from Bostic, Powell and other officials that recent progress on inflation has been "bumpy." Still, Kugler said in comments at Washington University in St. Louis, "I expect the disinflationary trend to continue" and help pave the way for rate cuts over the course of the year.



# 10-Year Treasury Yield Going Up

U.S. Constant Maturity 10-Year Treasury Bond Yield - Oct 6, 2023 to Apr 5, 2024



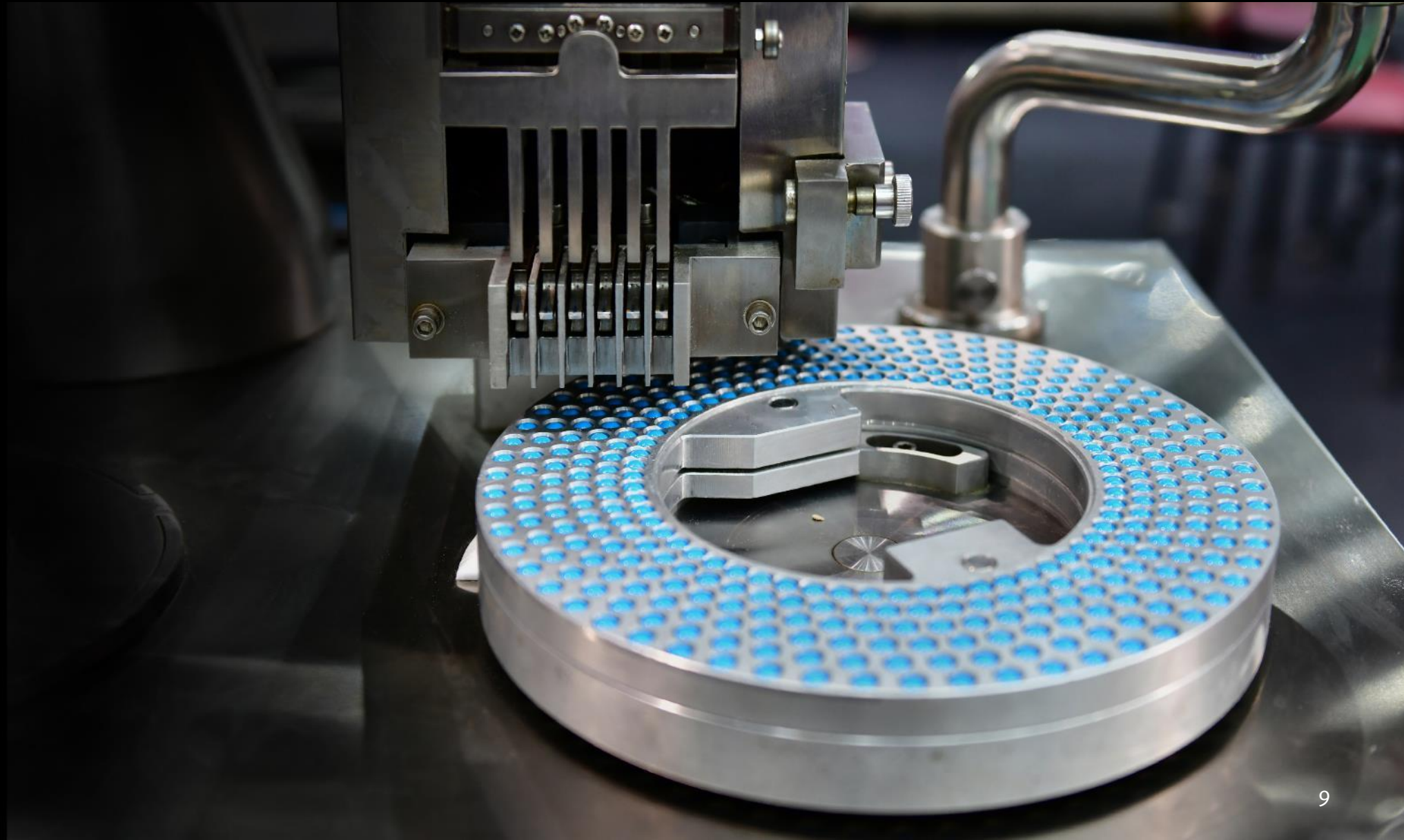
Last week's 19 basis point jump in the 10-year yield was not welcome news for biotech stocks at all.

Last year's late biotech rally can be linked to the big drop in the long bond yield visible in this chart.

Once the yield bottomed and reversed at the start of the year, the biotech market has been flattish.



# Biopharma Market Update



# Red Light, Green Light: The Weird Vibes of Biotech's Start-Stop Recovery

Drew Armstrong, *Post Hoc*, Weekly Newsletter, *Endpoints News*, April 5, 2024 (excerpt)

It's a weird time to be watching the biotech stock market. Over the last few months, it feels inevitable that whenever somebody writes a piece of analysis declaring that biotech markets are back (we're guilty, too!), biopharma stocks drop the very next day.

Markets like narratives, and it's been hard to find a truly linear one this winter and spring. Generalists were going to get pulled back to the sector when interest rates get cut — but the Fed keeps stalling based on strong inflation and jobs data. Big private rounds are booming — but only for the privileged few. IPOs are happening — but not quite catching on fire. And every time the S&P's biotech index flirts with \$100, it gets slapped back down.

Welcome to biotech's start-stop recovery. I've been thinking about why this market feels strange and caught up with Stifel's Tim Opler a few days ago. Opler publishes a weekly note that digs into a load of market data and tries to answer some of the "what's actually happening here?" questions about who's buying what and why they're buying it.

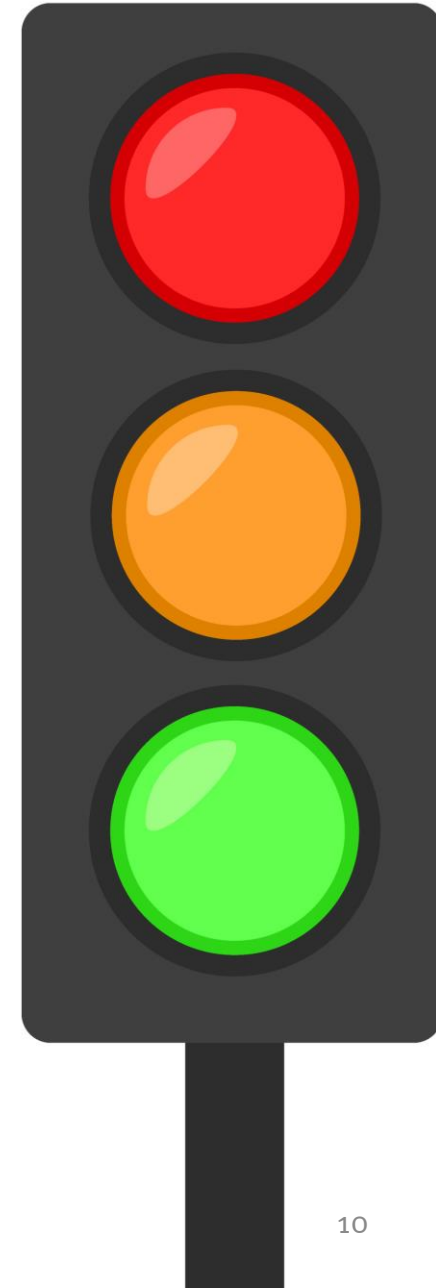
One thing Opler flagged is that while the {\$XBI} is up a few middling percentage points this year to date, the broader universe of biotech stocks (many of which aren't on the index) were up almost 30% for the quarter.

"This is a very different biotech market than we've seen before," Opler said. "Generalist funds and index funds have not come into the market." But hedge funds have, Opler notes, and they're taking positions in smaller companies where they can make more concentrated bets (the XBI biases toward larger market caps).

If you could forget (cue sad laugh) about the pandemic years, biotech is actually trading right about where it was in late 2019 — which back then was an all-time high. A lot of industry positives have happened since — the obesity drug revolution, an explosion of new genetic treatments and an increasingly flexible FDA.

But none of it has been enough to create that dominant, linear narrative (AI owns that, for now) and haul back in the generalists. And whether generalist money is the "lifeflood" of the industry, or "cocaine" (as one biotech CEO anonymously described it to me) probably depends where you sit.

But it's hard not to look at the way the signals are lining up and conclude that the factors that are in the industry's control — R&D, data, financings — are moving in the right direction



# The XBI Closed at 90.18 Last Friday (April 5), Down 5% for the Week

The XBI is up 1% since the year began. The biotech market sank last week in light of hawkish comments from Fed Chairman Powell. A hot jobs report did not help matters. Next week brings CPI inflation data that will help to set direction of the biotech market.

## Biotech Stocks Down Last Week

### Return: Mar 29 to Apr 5, 2024

Nasdaq Biotech Index: -3.5%

Arca XBI ETF: -5.0%

Stifel Global Biotech EV (adjusted): -5.4%\*

S&P 500: -1%

### Return: Dec 29, 2023 to Apr 5, 2024 (YTD)

Nasdaq Biotech Index: -2.1%

Arca XBI ETF: +1%

Stifel Global Biotech EV (adjusted): +23%\*

S&P 500: +9.1%

## VIX Up

Jan 20, 2023: 19.9%

July 21, 2023: 13.6%

Sep 29, 2023: 17.3%

Dec 29, 2023: 12.45%

Jan 26, 2024: 13.26%

Feb 23, 2024: 13.5%

Mar 29, 2024: 13.0%

Apr 5, 2024: 16.0%

## 10-Year Treasury Yield Up

Jan 20, 2023: 3.48%

July 21, 2023: 3.84%

Sep 29, 2023: 4.59%

Dec 29, 2023: 3.88%

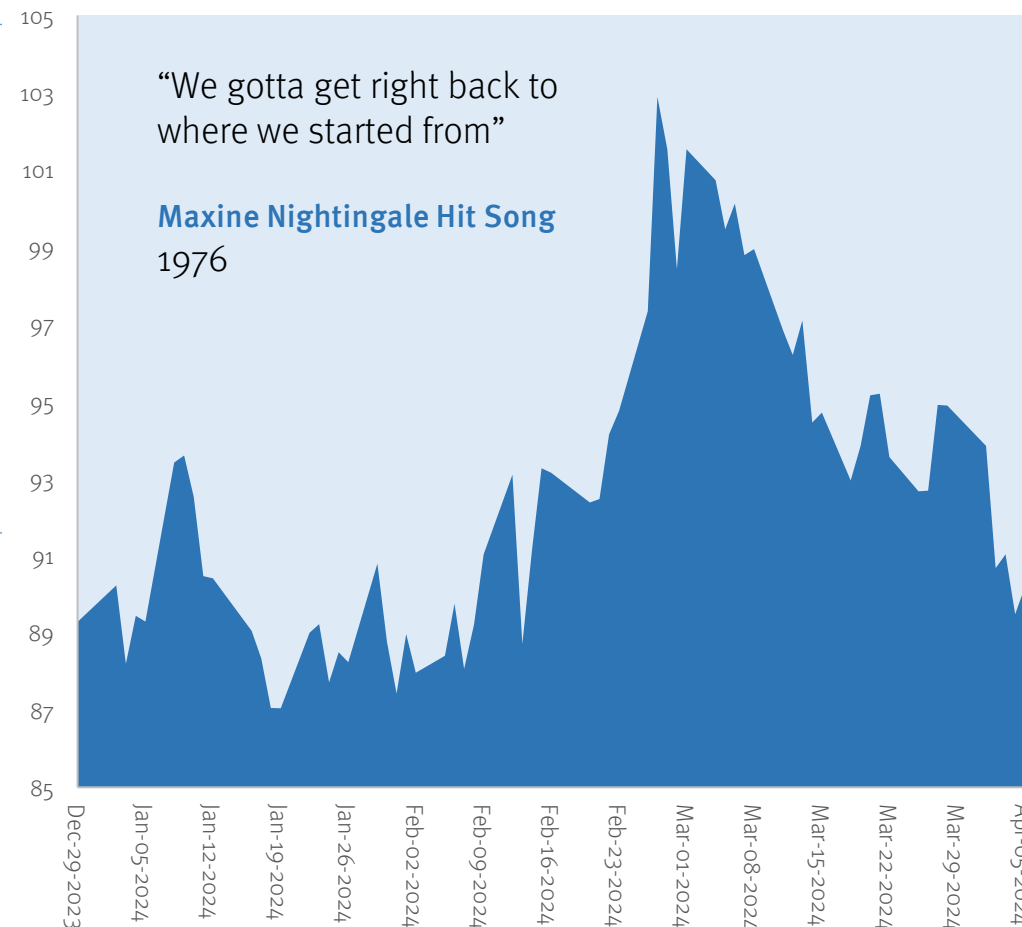
Jan 26, 2024: 4.15%

Feb 23, 2024: 4.26%

Mar 29, 2024: 4.20%

Apr 5, 2024: 4.39%

## XBI, Dec 29, 2023 to Apr 5, 2024

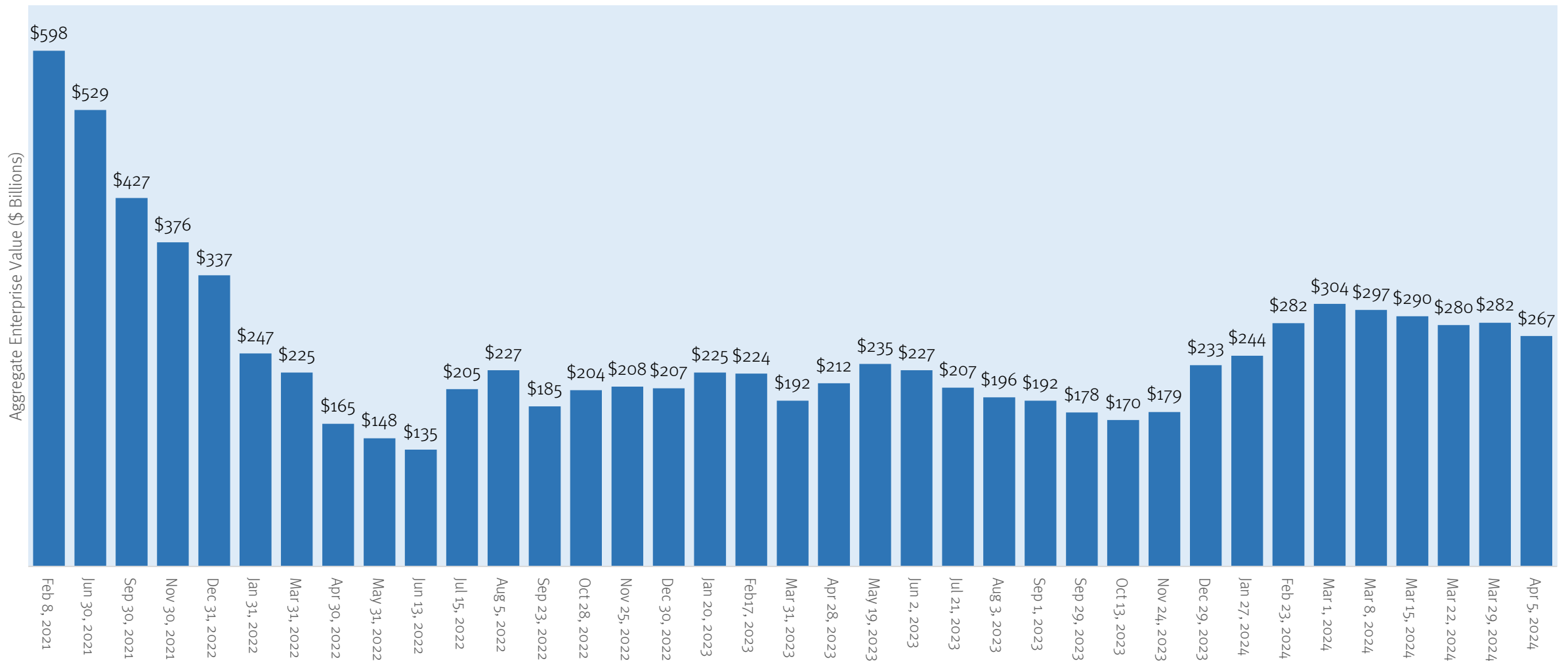


\* Change by enterprise value. The adjusted number accounts for the effect of exits and additions via M&A, bankruptcies and IPOs.

# Total Global Biotech Sector Value Down 5.4% Last Week

The total enterprise value of the global biotech sector is up 23.3% year-to-date on an addition/exit corrected basis. Before correcting for exits the market is up only 14.5%.

Total Enterprise Value of Publicly Traded Global Biotech, Feb 8, 2021 to Apr 5, 2024 (\$ Billions)

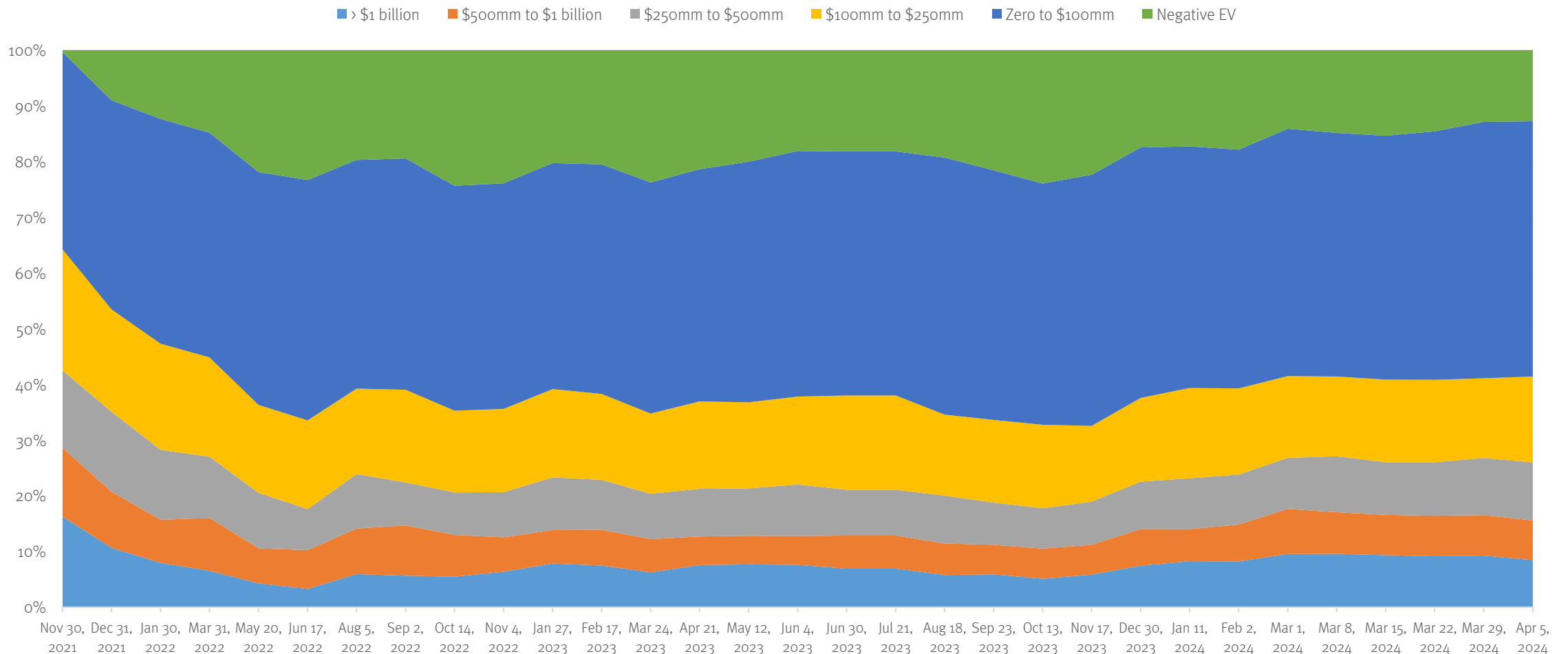


Source: CapitalIQ. Biotechs are defined as any therapeutics company without an approved product on any global stock exchange.

# Global Biotech Neighborhood Analysis

The “very rich” (\$1bn+ caps) and “very poor” (negative EV) segments of biotech both shrunk last week. This means the zero to a billion value group grew, especially the zero to \$250mm segment. Time to celebrate the middle class!

Global Biotech Universe by Enterprise Value Category, Nov 30, 2021 to Apr 5, 2024



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

# Life Sciences Sector Total Value Dropped 2.1% Last Week

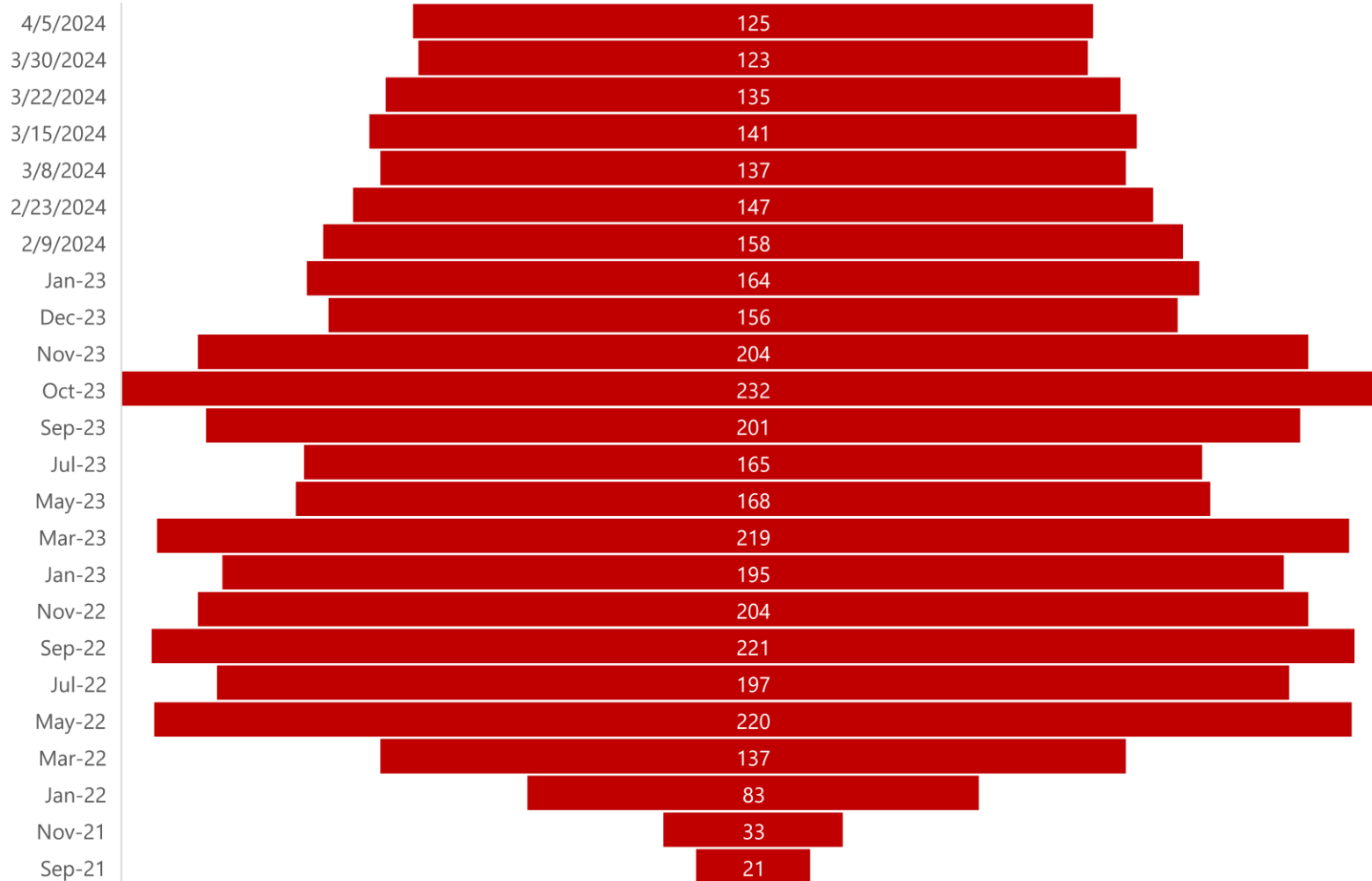
It was not a pleasant week for the life sciences. As a whole, the sector dropped in value by over 2% (\$207 billion). HCIT and biotech were hardest hit subsectors.

Sector	Firm Count	Enterprise Value (Apr 5, 2024, \$millions)	Change in Last Week (percent)	Change in Last Month (percent)	Change in Last Year (percent)
API	81	\$79,497	3.1%	-1.5%	-1.9%
Biotech	798	\$267,055	-5.4%	-5.4%	-5.1%
CDMO	40	\$151,266	-2.1%	1.2%	-20.1%
Diagnostics	81	\$274,649	-1.9%	-2.2%	1.7%
OTC	30	\$27,213	-2.7%	-2.3%	-7.7%
Pharma	719	\$6,160,201	-2.1%	-2.2%	5.7%
Services	38	\$194,793	-2.0%	-2.8%	-5.5%
Tools	51	\$713,144	-1.8%	-3.8%	-3.9%
Devices	181	\$1,696,340	-2.0%	-2.8%	2.9%
HCIT	10	\$18,119	-8.1%	-12.1%	-29.7%
<b>Total</b>	<b>2029</b>	<b>\$9,572,277</b>	<b>-2.1%</b>	<b>-2.5%</b>	<b>4.2%</b>

Source: CapitalIQ

# Number of Negative Enterprise Value Life Sciences Companies Was Flat Last Week

Number of Negative Enterprise Value Life Sciences Companies Worldwide



Source: CapitalIQ

The count of negative EV life sciences companies worldwide rose from 123 from 125 last week.

In past weeks with a big down move in the market, we have seen the number of negative EV companies shoot up.

This did not happen last week as it appears that some investors have learned to generate returns by taking advantage of inefficiency in this market segment.

# Biotech Ripe for ‘Cascade of Dealmaking’

Thomas Monteiro, *Investing.com*, April 5, 2024 (excerpt)

Few corners of the market have been as prone to dealmaking over the last couple of years as the life sciences industry.

Fueled by strong demand for innovation, the cyclical nature of patent cliffs, and substantial cash reserves among major players, the sector has consistently presented attractive opportunities for investors who can identify and capitalize on the right trends.

Not by coincidence, healthcare merger activity remained resilient throughout 2022 and 2023, when tight financial conditions led to an overall drop of 37% and 25% in global M&A volumes, respectively. Now, as US and global dealmaking stage a substantial rebound, and as the Fed prepares to cut rates, the industry may be on the verge of a ‘cascade of takeovers,’ says an industry source consulted by Investing.com.

Consulted exclusively by Investing.com, Pharma giant AstraZeneca hinted it is, indeed, scanning the market for opportunities. “We are always scanning the horizon to look for new technologies that complement our portfolio, and we’re making strategic investments in new technologies and platforms that we believe have the potential to transform the future of medicine through the end of the decade and beyond” said a spokesperson for the company.

## Healthcare Consolidation on the Rise - Oncology Leads the Way

The positive outlook has already resulted in several mergers this year. According to Needham Research, the biotech sector experienced a total of 13 M&A deals in Q1, of which seven were among public traded companies and six private transactions. These figures are substantially higher than the quarterly average of 8.2 observed since 2018.

Among the most prominent is AstraZeneca’s recent acquisition of Fusion Pharmaceuticals (NASDAQ:FUSN) for \$2.4 billion, a 97% premium to Fusion’s closing price before the deal. “[The acquisition] marks a major step forward in us delivering on our ambition to transform cancer treatment and outcomes for patients by replacing traditional regimens like chemotherapy and radiotherapy with more targeted treatments,” AstraZeneca told Investing.com.

This follows Johnson & Johnson's (NYSE:JNJ) takeover of cancer drug developer Ambrx Biopharma for \$2 billion in January and Merck's (NYSE:MRK) \$680 million buyout of Harpoon Therapeutics (NASDAQ:HARP), strengthening the group’s pipeline of cancer treatments.



# Cascade Article (continued)

The recent flurry of mergers shows that companies are strategically targeting the oncology market, which is anticipated to soar to \$323 billion by 2028, boosted by a new generation of drug discovery and development.

“Oncology is AstraZeneca’s largest therapy area, representing 40% of our total revenue in 2023, a 21% increase year-over-year,” explained AZN.

“Radiopharmaceuticals hold the potential to gain traction following the recent AstraZeneca M&A of \$2B for Fusion Pharmaceuticals. Given its oncology sales of \$17.15 billion in 2023, this move aligns with AZN’s strategy to innovate beyond traditional therapies,” explains Aaron Rafferty, co-founder and CEO of technology incubation hub Standard.

Another key factor for increasing activity is the number of impending patent cliffs within the industry.

“As patent expiries draw closer, M&A is becoming a vital tool for pharma companies looking to bulk up near-term revenue and strengthen drug pipelines,” explains Bryan Luchs, Partner at White & Case.

## Success in Obesity Drugs Another Tailwind

The recent boom in obesity drugs, such as Eli Lilly's (NYSE:LLY) Zepbound and Novo Nordisk's (NYSE:NVO) Ozempic, is another tailwind for acquisitions within the industry as companies hoard more cash into their already hefty balance sheets.

The increasing competition for innovation within the sector may also lead to the payment of high premiums for smaller target companies, which could result in hefty gains for investors positioned in such stocks.

## M&A Framework: Who’s Ripe For the Next Takeover?

Despite the focus on oncology-related deals since the start of the year, other areas of the life sciences industry also appear prone to increased merger activity.

“Big pharma is looking for transformative assets – advanced-stage therapeutics with proven efficacy, like Inspirna’s Ompenaclid, or innovative modalities such as Umoja’s in-situ CAR-T candidates,” adds Aaron Rafferty.

# What's Going on with the Biotech Buyside?



# Update of the Stifel Buyside Study

We previously published reports on the biotech buyside in our November 21, 2022 and April 17, 2023 issues.

Today, we are updating this using data on fund holdings as of December 31, 2023.

We have accessed Form ADV's which are filed with the SEC by Registered Investment Advisors in the U.S. Any fund holding more than \$110mm and managing money for at least two persons needs to file a Form ADV. This captures most groups but would miss institutions that manage their own money or small funds.

These include Novo Holdings and family office type investors such as Tang Capital or Ridgeback Capital.

We also collected fund level data as of the start of April on biotech holdings from S&P CapIQ. These would draw off of Form 13G, 13F and 13D reports filed by investors earlier. These data will largely reflect holdings of the buyside as of Dec 31, 2023.

A particularly thorny issue that we wish to be upfront about is that our definition of biotech (R&D stage) therapeutics and that of CapitalIQ is not the same. CapitalIQ's definition of biotech is hard to fathom and encompasses about 75% of R&D stage therapeutics companies but also includes AbbVie, Gilead, Moderna and many other commercial stage companies.

Nonetheless, we have found that there is a lot to be learned from the available data and are happy to share our latest findings with you.

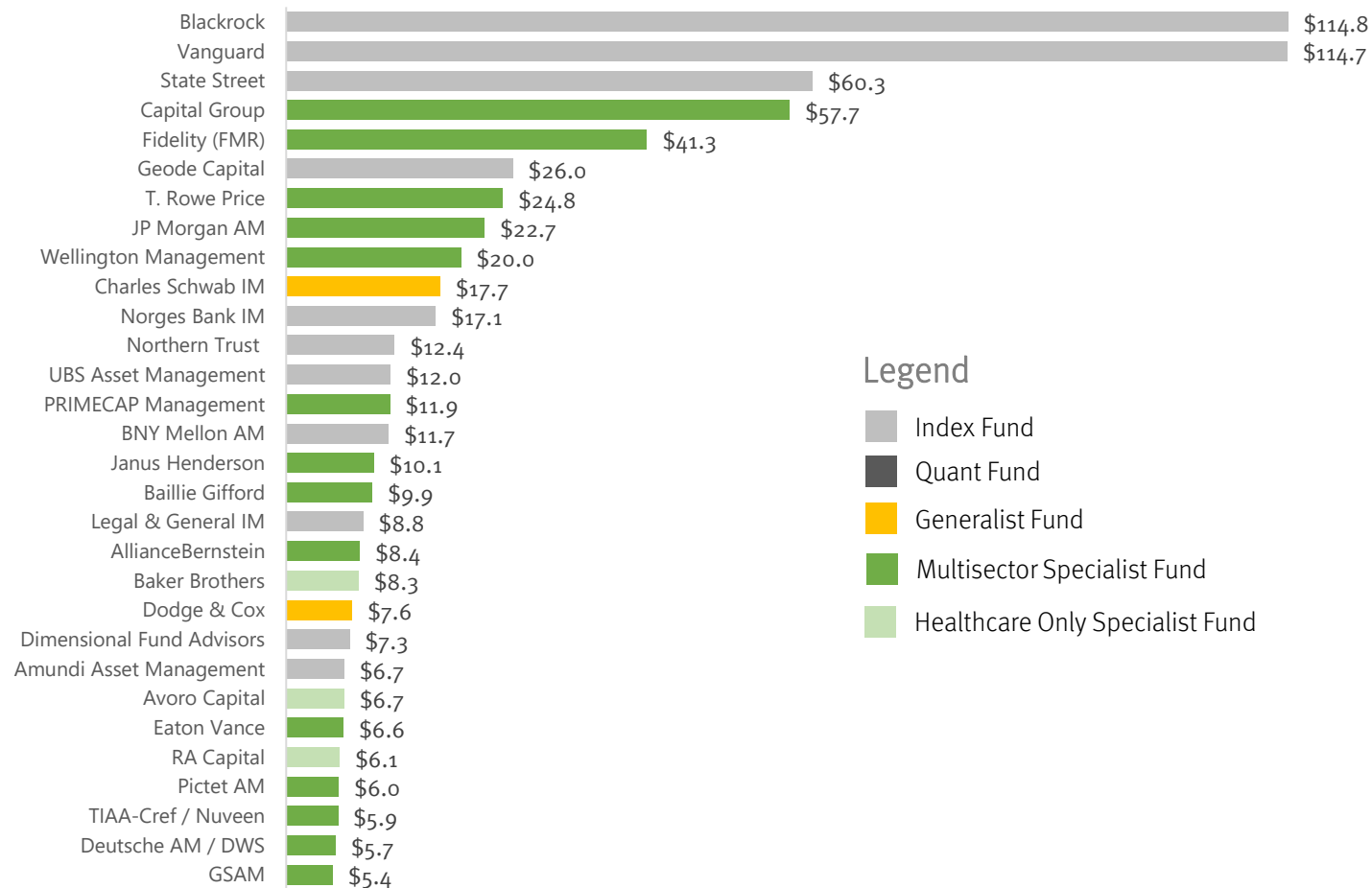
The timing of today's analysis is propitious as Form ADV's which provide total AUM data for RIA's as of Dec 31, 2023 were due on March 31, 2024.



# Who Are the Largest Owners of Biotech Stocks?

## Largest Disclosed Holders of Biotechnology Stocks on April 5, 2024

(\$ Billions, CapitalIQ Definition of Biotechnology, Shows holdings as of Dec 30, 2023)



### Legend

- Index Fund
- Quant Fund
- Generalist Fund
- Multisector Specialist Fund
- Healthcare Only Specialist Fund

These data are from S&P CapitalIQ and show the level of biotech holdings as of Dec 30, 2023 and are ranked by amount owned. Recall that these data reflect some holdings of large pharmas such as AbbVie given that the data on biotechnology holdings are sourced from CapitalIQ. The valuation of the holdings is as of April 3, 2023.

There was a total of \$845 billion of biotech stocks held by funds that we track in our database. This is based on holdings as of Dec 30, 2023. This is up from \$800bn a year earlier.

The data reveal that index and quant funds account for \$423 billion of the holdings of top biotech funds (almost exactly half).\*

These funds are not proactive and simply follow indices like the Russell 3000 and buy whatever companies are included in an effort to mimic the market return at a low cost.

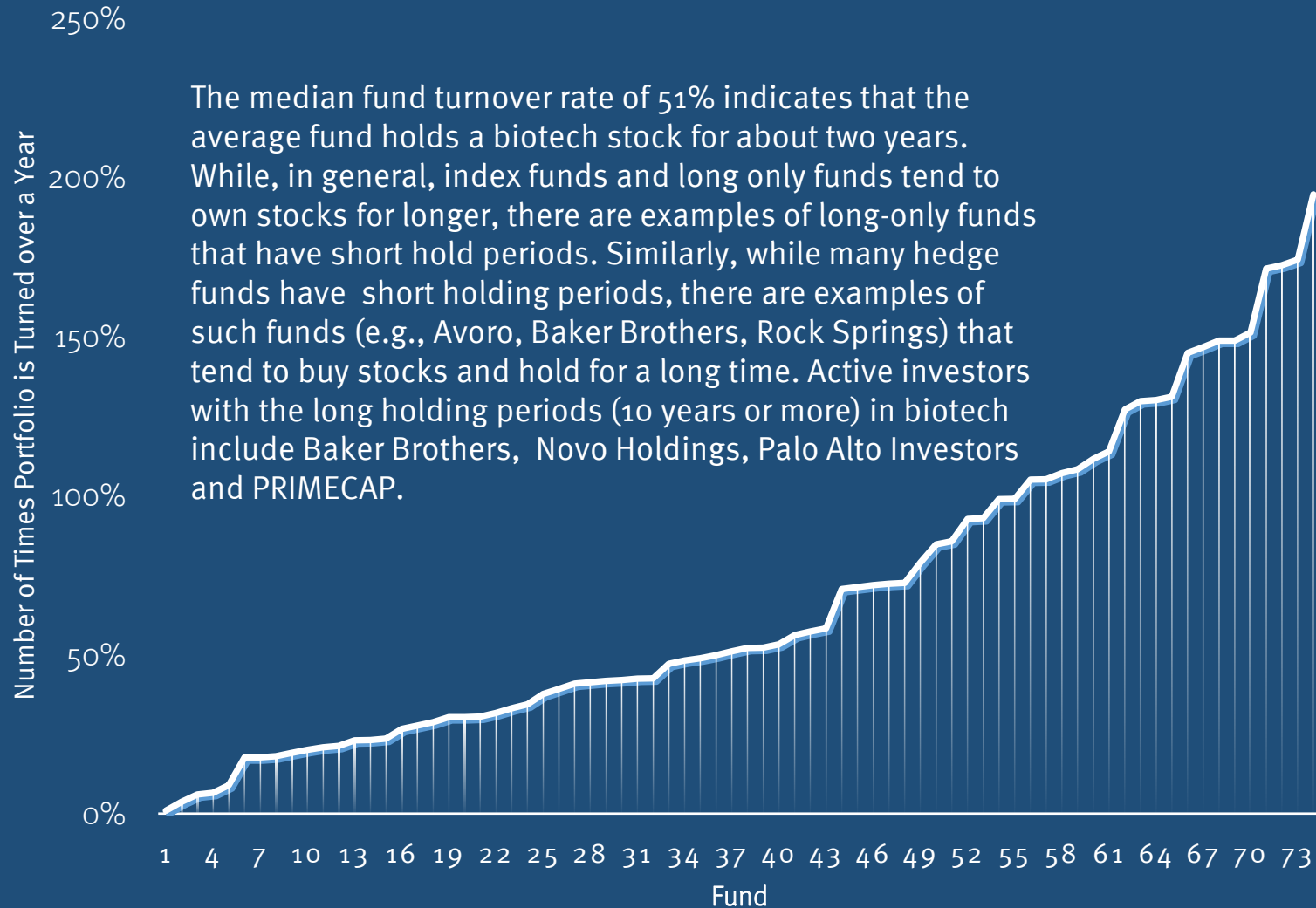
Specialist multisector funds investors such as Janus Henderson account for another \$260bn+ or so of holdings. Generalist funds (think Charles Schwab Investment Management) are not as important in the market (holding only \$32bn of biotech assets).

This analysis does not include retail investors at all and so may overstate the relative importance of indexers and specialists but certainly gives a sense of the ownership structure of the biotech market.

An important observation here is that index funds, overall, have substantially more ownership of biotech stocks than do specialist funds.

# On Average, Biotech Stocks are Held for About Two Years

## Annualized Portfolio Turnover Rate of Leading Holders of Biotech Stocks



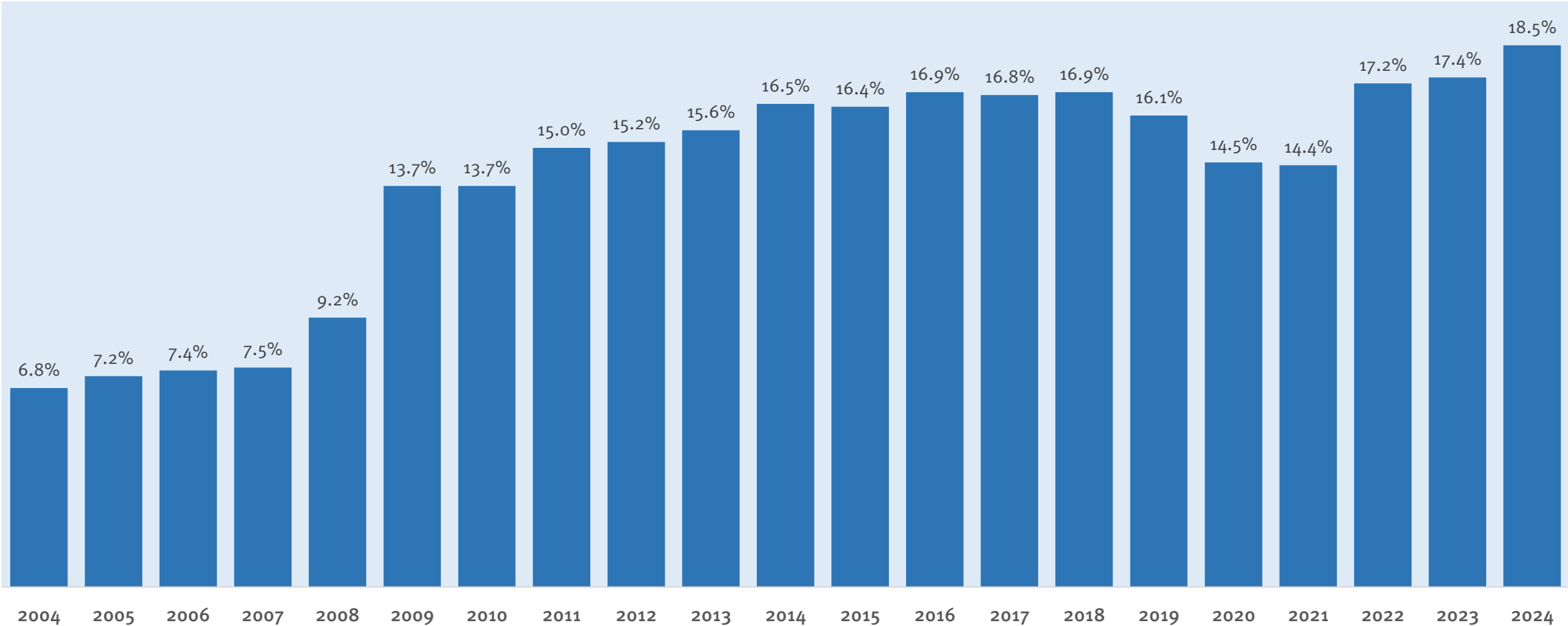
Only about a quarter of the investor population holds stocks for a half year or less. These are all hedge funds, and they tend to be event driven. The mindset of an event investor is to benefit from market inefficiency in the stock move around an event and profit by anticipating either the data or by how other investors will react going into the data.

A long-term buy-and-hold investor, in contrast seeks to benefit from other investor's inability to see the capital appreciation potential embedded in a company's business plan. These investors often buy stocks in companies that will have big drugs but need time to get there. Other investors play a medium-term game, anticipating that a company is near a value inflection with multiple positive data or commercial readouts. It's very common for CEO's to complain that their holders are too short-term and abandon them at their hour of need. We are sympathetic to such complaints but would encourage management and IR team to think of strategies that will work to the benefit of short and medium horizon investors.

# Index Fund Ownership of Biotech at an All-Time Peak

The ownership of the biotech market by indexers has nearly tripled over the last twenty years. Biotech ownership by top index funds is at an all time high. More than half of the biotech market today is owned by passive asset managers (index funds or quant funds).

Percent of CapIQ Biotech Stocks Owned by a Top 5 Index Fund, December 2004 to April 2024



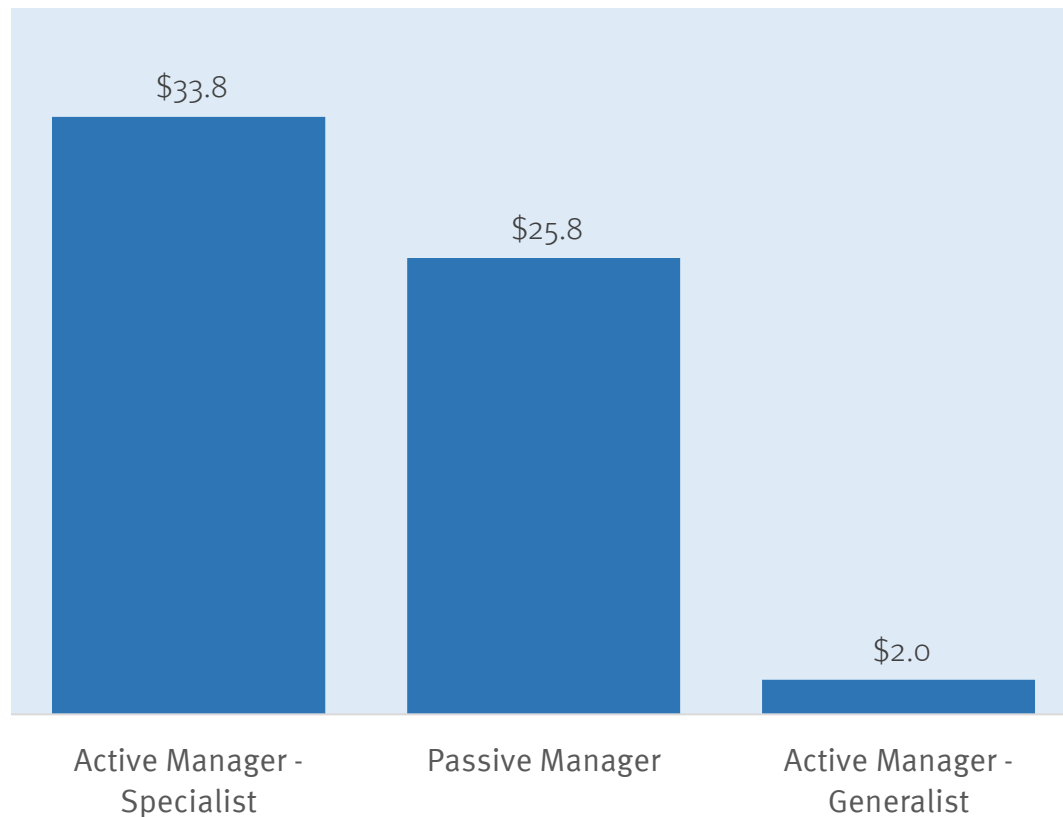
Source: CapitalIQ Holdings data and Stifel analysis of data. This chart shows the market value of shares owned by Blackrock, Geode Capital, Norges Bank, State Street and Vanguard divided by the total value of biotech stocks. For each year, the shares are valued on Dec 30<sup>th</sup>. For 2023 and 2024 shares are valued as of the start of April. 22

# What Types of Funds Added Assets in 2023?

Last year saw the highest growth in assets under management (AUM) by active specialist managers and more modest aggregate AUM growth among both passive managers and active managers with a generalist style.

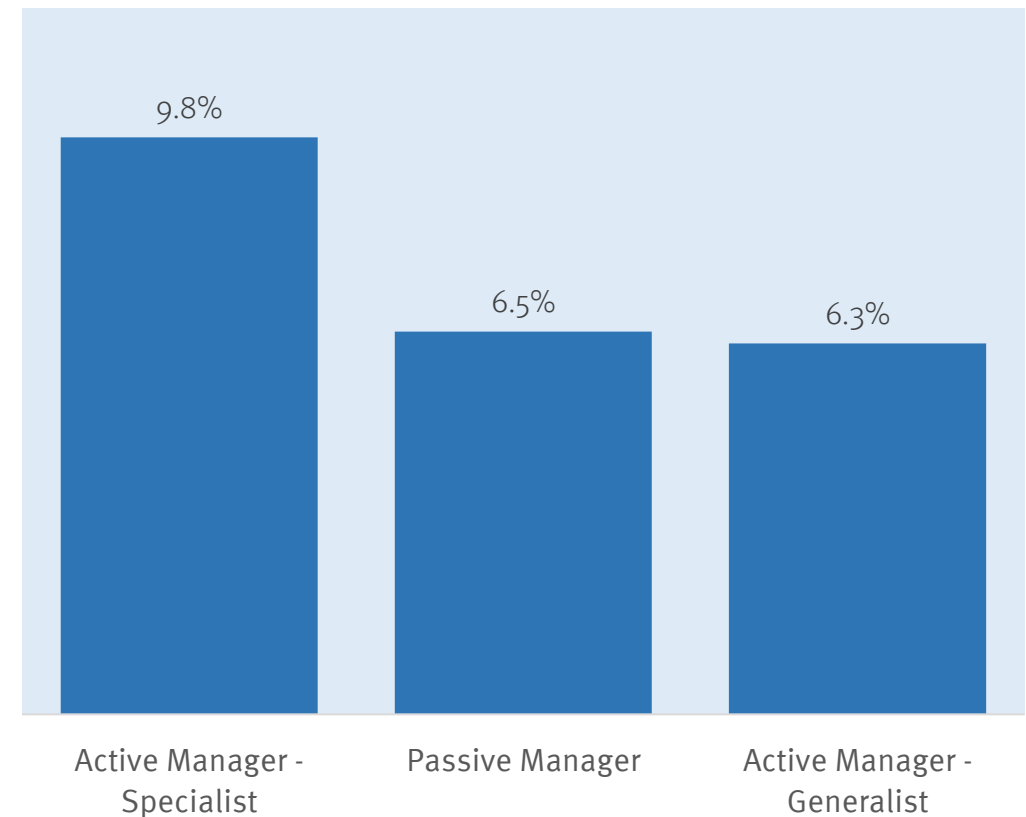
**Change in AUM (\$bn) by Fund Manager Type**

Dec 30, 2022 to Dec 30, 2023



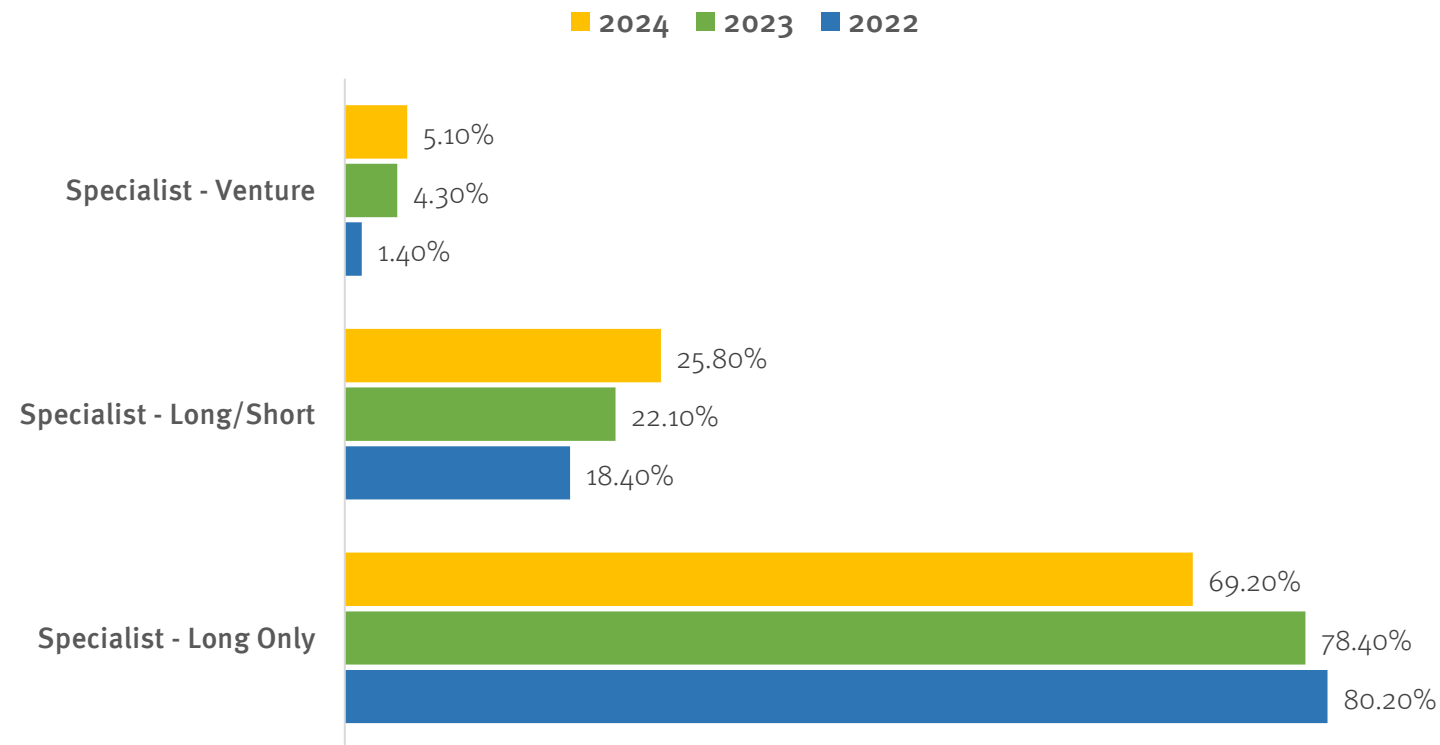
**Percent Change in AUM (\$bn) by Manager Type,**

Dec 30, 2022 to Dec 30, 2023



# Within the Specialist Group, Long-Short Hedge Funds Continue to Gain Value Share from Traditional Long Funds

Percentage Sector Ownership of Tracked Specialist Funds in CapIQ  
Biotech Group, June 2022 to April 2024



The chart at left looks at ownership share within the healthcare specialist group.

Long-short specialist funds have substantially increased their share of ownership in the last year.

Long-short funds were obviously able to shield themselves from losses in this time interval by shorting the market.

Further, they are much better staffed with experts given higher fees. This has likely led to good performance which has helped to grow AUM.



# The Specialist Biopharma Fund Universe

We often speak of specialist fund managers in biotech in a broad sense. But specifically, how many are there? How much do they manage? And, how many, like Perceptive, are “healthcare only”?

The data at right show rapid growth in AUM and the number of funds that are healthcare only.

Most dedicated healthcare funds are small. For example, a year ago we counted 45 HC-only specialist funds with \$1 billion or more in assets. Today, we count 53 such funds. This implies, the other 145 HC-only funds are managing less than a billion in assets.

\* There are some specialist funds that do not need to file as an investment advisor. SEC Rule 203A-1 permits an investor to avoid registering if they do not provide investment advice to others (in other words, if they are solo, this is not required) or if they manage less than \$110 million. Many groups that manage less than \$110 million still file Form ADV due to state securities rules. Examples of well-known funds that do not file an ADV include Pivotal, Quogue, Ridgeback and Tang. These are effectively family office investors.

Here is our accounting of the specialist biopharma fund universe:

**\$388 billion**

of biotech assets as of Apr 7, 2023 are held by specialist funds.\* This is up from \$365bn a year ago and \$315bn on June 30, 2022.

**43 stocks**

The average healthcare only specialist fund has 43 biotech positions.\*

\* Using S&P's definition of biotech.

**198 funds**

We count 198 funds that invest in Biopharma with at least one MD or Ph.D. on staff. Compare to 149 funds in June 2022.





















**94 funds**

We count 94 healthcare only specialist funds (up from 79 a year ago). These funds have \$240bn in AUM.

# Top 20 Healthcare Only Investment Managers by AUM

Baker Brothers returned capital to LPs due to the Seagen sale in Q1 of this year. This caused Orbimed to move into the #1 position of HC only asset managers by AUM. Deerfield has held onto its #2 position while RA Capital is picking up assets rapidly. A new entrant on this list is Patient Square which has been highly successful in raising capital for diversified life sciences investment model. Patient Square debuts at the #7 position.

Assets Under Management (Q1 2024 / End of 2023, \$ Billions, From Form-ADV Filings made in late Q1 2024)

 <p><b>OrbiMed</b> Healthcare Fund Management</p> <p>\$17.5 Billion</p>	 <p><b>Baker Brothers Investments</b></p> <p>\$15.6 Billion</p>	 <p><b>PERCEPTIVE ADVISORS</b></p> <p>\$9.7 Billion</p>	 <p><b>Blackstone</b></p> <p>\$7.2 Billion</p>	 <p><b>BainCapital</b> LIFE SCIENCES</p> <p>\$6 Billion</p>	 <p><b>ARMISTICE</b></p> <p>\$5.9 Billion</p>	 <p><b>VIVO</b> CAPITAL</p> <p>\$5.8 Billion</p>	
 <p><b>DEERFIELD</b> Advancing Healthcare™</p> <p>\$16.1 Billion</p>	 <p><b>RACAPITAL</b></p> <p>\$11.3 Billion</p>	 <p><b>RTW</b> Investments</p> <p>\$8.8 Billion</p>	 <p><b>Redmile</b></p> <p>\$6.5 Billion</p>	 <p><b>AVORO</b> CAPITAL</p> <p>\$5.6 Billion</p>	 <p><b>DEEP TRACK</b> CAPITAL</p> <p>\$5.1 Bn</p>	 <p><b>BRAIDWELL</b></p> <p>\$4.9 Bn</p>	
		 <p><b>PATIENT SQUARE</b> CAPITAL</p> <p>\$7.9 Billion</p>	 <p><b>BVF</b> PARTNERS L.P.</p> <p>\$6.1 Billion</p>	 <p><b>AVIDITY</b> PARTNERS</p> <p>\$5.3 Billion</p>	 <p><b>ROCKWELL</b> CAPITAL</p> <p>\$4.0 Bn</p>	 <p><b>ECOR1</b> CAPITAL</p> <p>\$3.9 Bn</p>	 <p><b>ROCK SPRINGS</b> CAPITAL</p> <p>\$3.7 Bn</p>

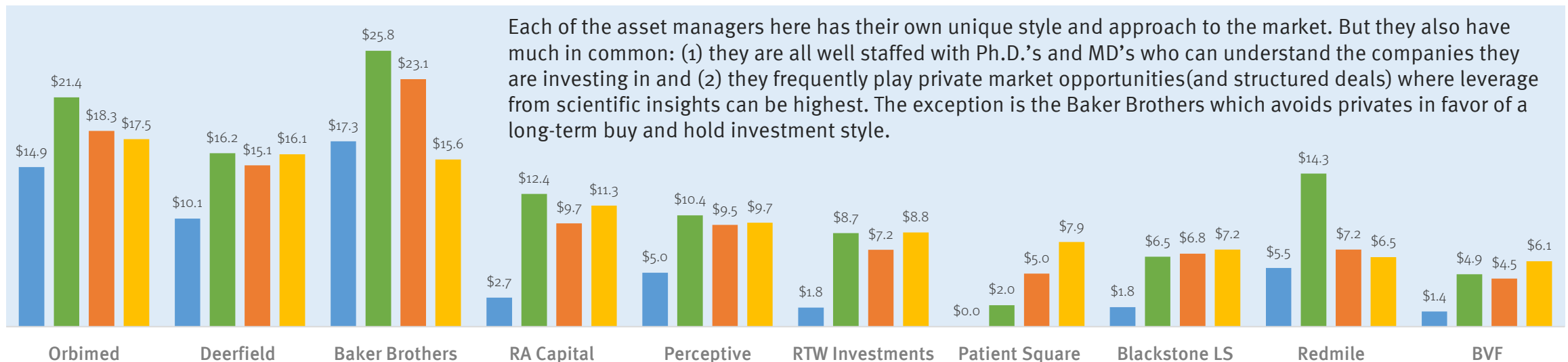
Source: U.S. Securities and Exchange Commission Filings. \*Note: Armistice is largely healthcare but also does some small investments in other sectors.

# Top 10 Healthcare Only Specialist Funds Evolution Over the Last Six years

Last year was an *annus horribilus* for many asset managers that were whipsawed by the interplay between rates, inflation and the Fed. Even the most astute clinical minds had a hard time getting biotech stock picks right last year. If there was a year that would lead to market capitulation and wipe out buy-side managers last year would have been it. Nonetheless, except for the Baker Brothers who returned substantial capital to their LPs, there is not a single fund listed here that has December 2023 AUM below where it was at the end of 2018. Healthcare specialist style investment grew massively after the Pandemic and has held up well despite difficult market conditions. Funds who were able to use specialist knowledge, short strategies and private investment strategies to hold onto assets in a challenging market. There are some funds lost assets last year that have fallen down the rankings. Surprisingly few. We presume last year saw redemptions from LP's that had been gated in 2022.

**Assets Under Management at Top 10 Healthcare Only Fund Managers, Year End 2018 to Year End 2023 (\$ Billions)**

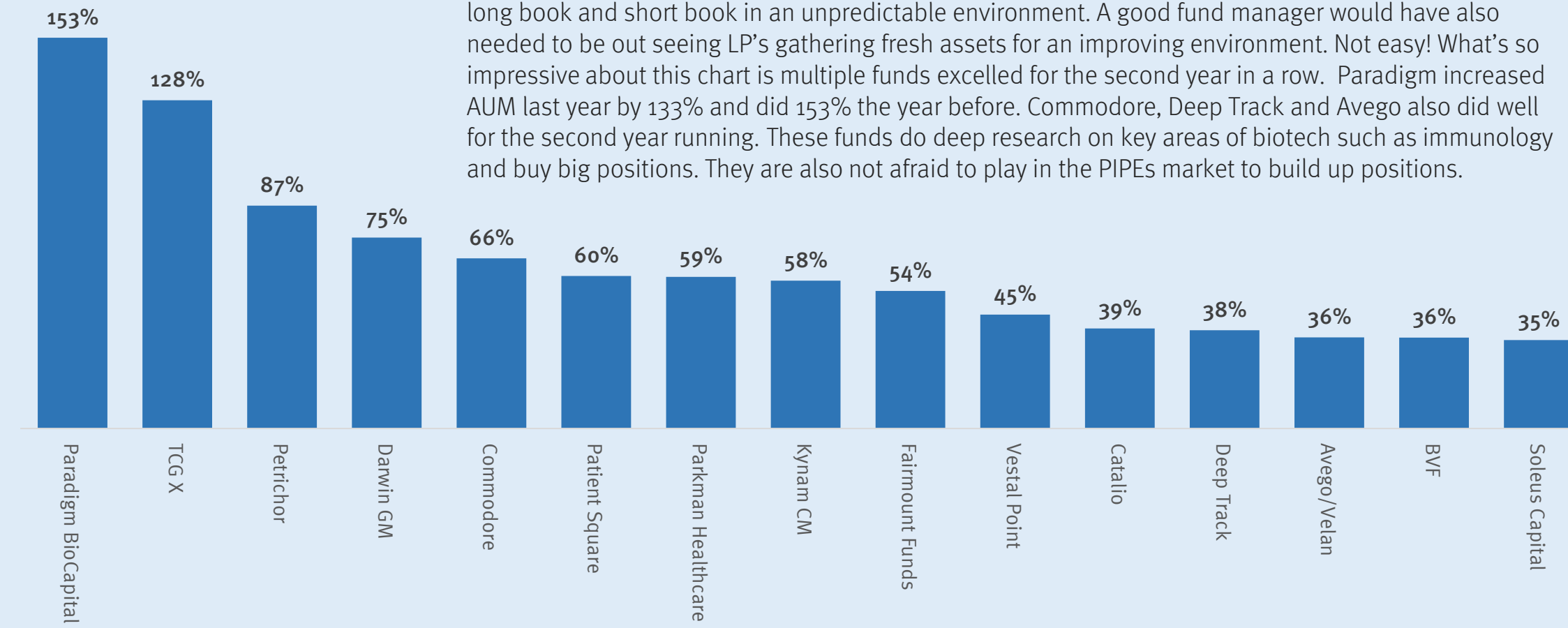
■ 2018 ■ 2021 ■ 2022 ■ 2023



# Top 15 Healthcare Only Specialist Funds by Gain in Percent Change in AUM During 2023

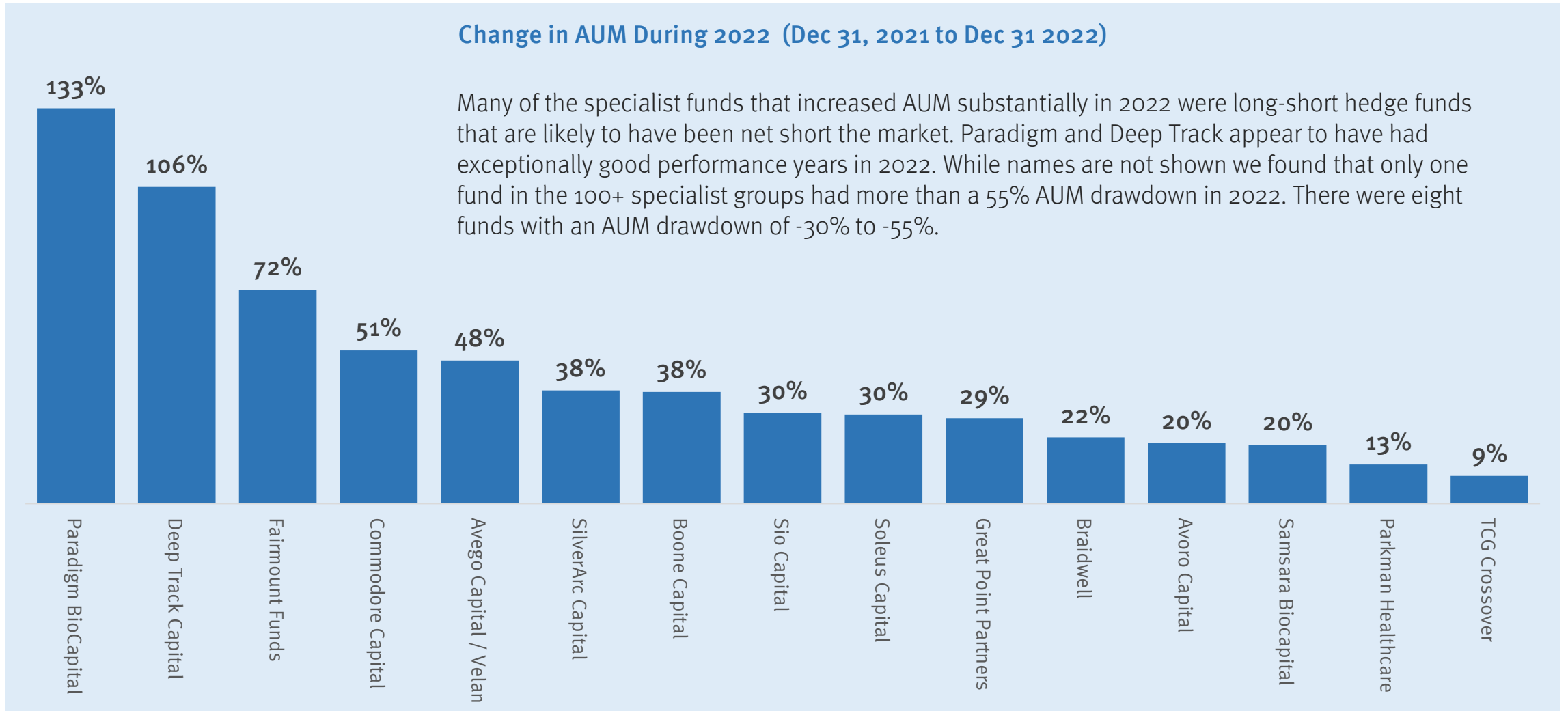
## Change in AUM During 2022 (Dec 31, 2022 to Dec 31 2023)\*

Last year was a volatile year that was ultimately up. A successful fund would have needed to time its long book and short book in an unpredictable environment. A good fund manager would have also needed to be out seeing LP's gathering fresh assets for an improving environment. Not easy! What's so impressive about this chart is multiple funds excelled for the second year in a row. Paradigm increased AUM last year by 133% and did 153% the year before. Commodore, Deep Track and Avego also did well for the second year running. These funds do deep research on key areas of biotech such as immunology and buy big positions. They are also not afraid to play in the PIPEs market to build up positions.



\* only included funds with \$500mm+ in AUM at end of 2022. Source: U.S. Securities and Exchange Commission Form ADV Filings.

# Comparison: Top 15 Healthcare Only Specialist Funds by Gain in Percent Change in AUM During 2022



# Top 60 Investors in the Biopharma PIPE Market YTD

This table shows the top investors in privates into public companies (PIPEs). PIPEs are quite the fashion this year with 34 deals done that were over \$50mm in size by specialist investors through April 5th. The 60 investors shown here account for 95% of disclosed involvement in the biotech PIPEs that have come to market. We are impressed by the number of companies doing PIPEs and the number of investors participating. Some specialist investors are obviously much more active than others. Commodore Capital has led the market in the number of deals done so far (11 of the 34) while the Baker Brothers have deployed the most capital (over a half billion in just three months).

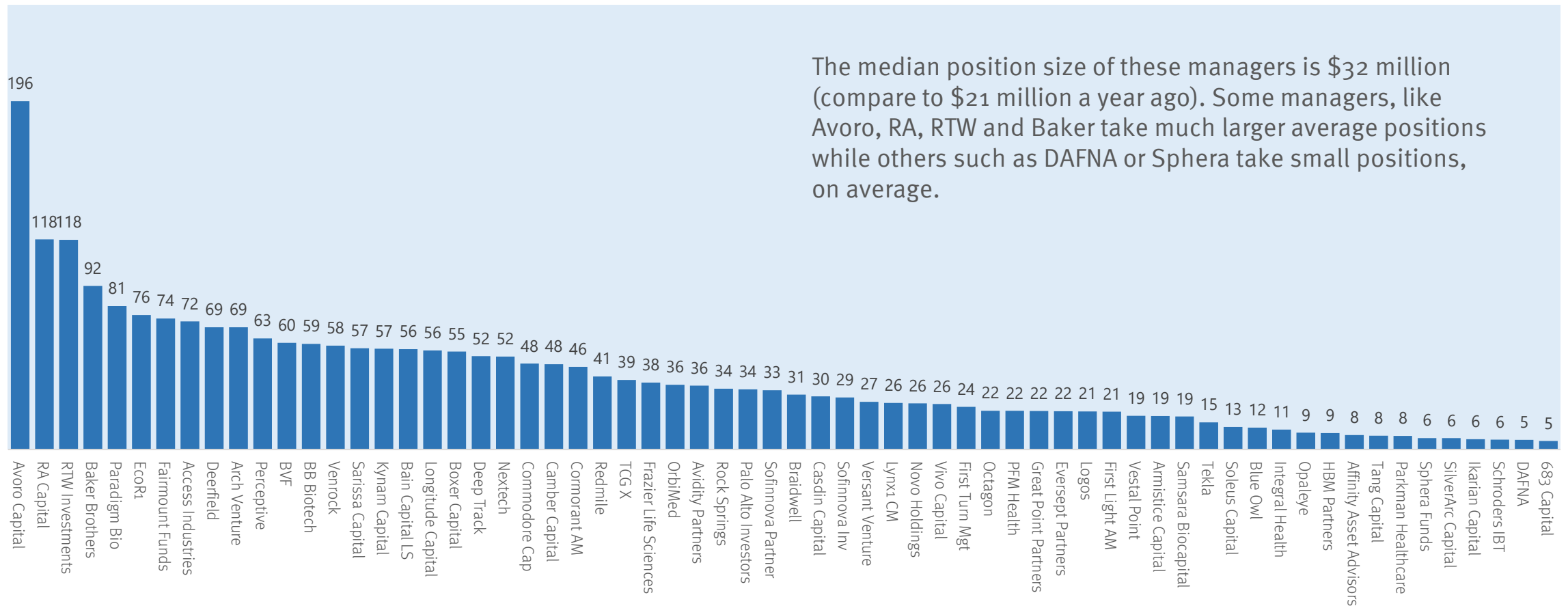
Fund	Deals	Ave Bite Size (\$mm)	Total Invested	Fund	Deals	Ave Bite Size (\$mm)	Total Invested	Fund	Deals	Ave Bite Size (\$mm)	Total Invested
Baker Brothers	5	\$94	\$565,961,463	Nnextech	4	\$12	\$60,000,400	Foresite Capital	1	\$13	\$25,000,000
Avoro	4	\$41	\$205,007,879	Fairmount Funds	4	\$20	\$58,812,500	Vestal Point	4	\$5	\$23,000,005
EcoR1	3	\$51	\$202,500,636	Capital Research	1	\$27	\$53,604,392	Suvretta	2	\$7	\$22,000,057
Invus	4	\$38	\$191,500,045	Great Point Partners	6	\$11	\$52,622,899	Braidwell	4	\$7	\$21,996,042
RA Capital	10	\$24	\$191,389,710	Bain Capital LS	2	\$15	\$45,000,005	Samsara Biocapital	3	\$5	\$21,159,769
Venrock	10	\$21	\$185,849,872	Frazier Life Sciences	3	\$11	\$42,509,999	First Light	1	\$10	\$20,816,040
RTW Investments	4	\$38	\$150,005,974	Franklin Advisors	5	\$7	\$42,495,029	Woodline	8	\$3	\$20,072,019
TCG X	6	\$24	\$145,500,034	GMS	1	\$20	\$40,349,995	Driehaus	4	\$5	\$20,000,014
Fidelity	6	\$19	\$134,112,000	Viking Global	1	\$20	\$40,000,000	Paradigm BioCapital	2	\$10	\$20,000,000
Commodore Capital	11	\$15	\$120,373,497	BVF	2	\$13	\$39,500,094	Kynam	1	\$10	\$19,999,995
Deep Track Capital	10	\$16	\$112,003,353	Vivo Capital	3	\$10	\$38,500,250	Darwin	2	\$9	\$17,500,000
Perceptive Advisors	8	\$14	\$109,378,664	Blue Owl Healthcare	3	\$8	\$33,847,597	Balyasny	2	\$6	\$17,496,200
Janus Henderson	8	\$12	\$99,520,015	OrbiMed	5	\$7	\$32,999,897	Altium	4	\$4	\$16,000,015
T. Rowe Price	4	\$19	\$95,528,947	5AM Ventures	4	\$6	\$30,500,189	Sphera	6	\$3	\$15,932,098
Adage Capital	10	\$10	\$85,747,448	Redmile	4	\$10	\$30,000,398	Rock Springs	4	\$4	\$15,214,801
Farallon Capital	5	\$17	\$83,344,917	Tang Capital	2	\$9	\$27,510,000	Casdin	2	\$8	\$15,000,002
Logos Global	10	\$9	\$80,949,880	Boxer Capital	4	\$6	\$27,503,199	Octagon Capital	6	\$3	\$11,074,999
Deerfield	7	\$11	\$76,500,057	Surveyor / Citadel	5	\$7	\$27,500,031	Soleus Capital	3	\$4	\$10,500,000
Point72	3	\$18	\$72,500,034	Armistice Capital	2	\$9	\$26,999,984	GordonMD	1	\$5	\$10,000,032
Avidity	5	\$15	\$61,124,300	NEA	3	\$7	\$26,600,001	Cormorant	2	\$5	\$10,000,000

**Data source/Notes:** We obtained the data here from SEC filings on 34 PIPE transactions that were \$50mm or more in size that took place between Jan 1 and April 3, 2024. Our analysis excludes PIPEs done by strategics such as Gilead's investment into Arcus. Investment dollar values are obtained from SEC registration statements, proxy statements and holdings disclosures. These were available for 27 of the 34 transactions that took place. Transaction count data were used for all 34 deals analyzed but average bite size is computed only using transactions where dollar amounts of investments were disclosed.

# Some Funds Take Highly Concentrated Larger Positions While Others Are Much More Diversified

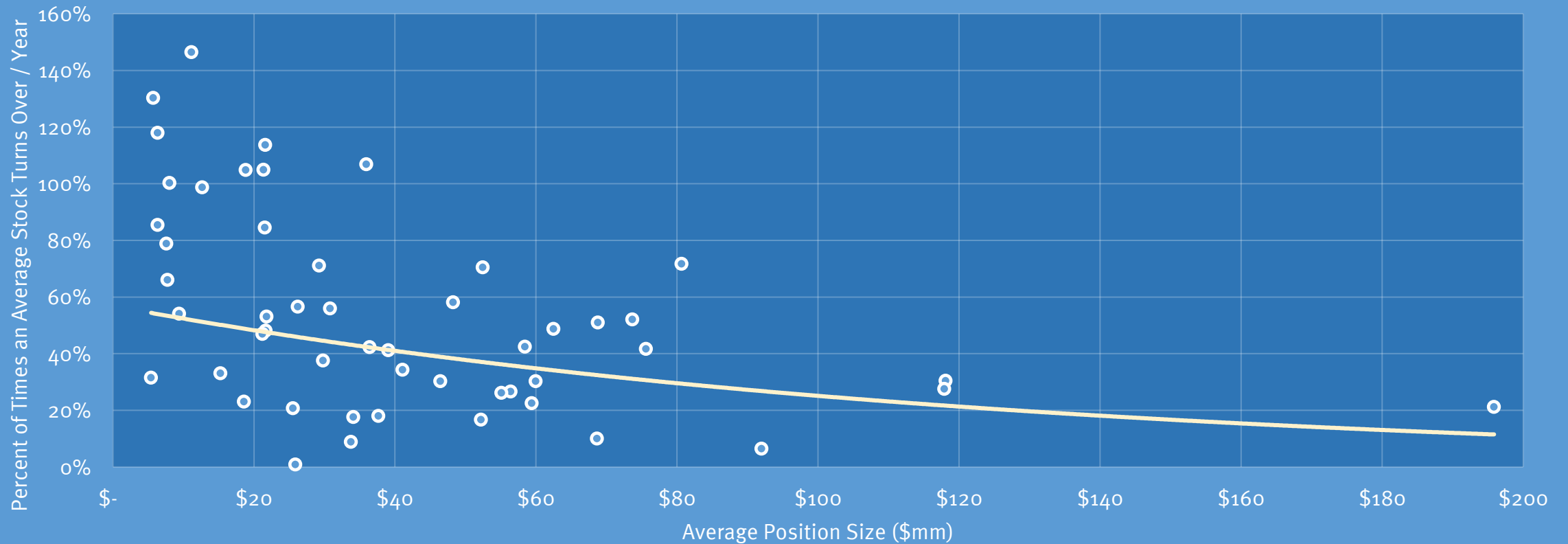
## Average Long Position Size of Healthcare Only Specialist Managers

(\$ Millions, Based on Dec 31, 2023 Holdings and April 5, 2024 Valuations)



# Funds with Large Position Sizes Tend to Turn Over Their Portfolio Less


## HEALTHCARE ONLY FUNDS: PORTFOLIO TURNOVER PER ANNUM VS. AVERAGE POSITION SIZE





# Summary: The Evolving Healthcare Investor

- The specialist life science buy-side is **quite large**.
  - Nearly \$400 billion of assets are held by biotech specialist funds.
  - The AUM of these funds has more than **doubled** in the last four years.
  - We count 198 specialist life sciences funds and 94 healthcare only specialist funds today. This is up substantially year-on-year despite a challenging market in 2023.
  - Or, as we suggest below, perhaps **because** of it.
- Overall, the specialist healthcare investor is in great shape as of April 2024. In fact, the specialist is steadily gaining assets in a market where generalists have feared to tread.
- Other facts of note include the ongoing growth of index funds. Their share of the total market is rising. **Passive investors own more than 50% of biotech in 2024.**
- The stock market is a highly Darwinistic place where asset managers that generate above-average returns thrive and gather more assets. Others don't survive (and some investors didn't make it through the last two year's market swoon). The biotech market is slowly squeezing out retail and generalist active managers which tend to have higher fees than index funds but may not be well equipped to parse through scientific stories and pick winners in a down market.



Biotech investing offers great opportunity but also peril to those that can't analyze the companies in the system. In this Darwinian environment we are seeing two investment styles (specialist and passive) dominate and squeeze out other investors. This has been playing out since 2021. We don't see any particular factors that will reverse this anytime soon.

- Index funds ignore the battle between styles and assume that, overall, the market will perform. If the market is led by specialist investors who know how to pick winners, then great. We should have even better companies in the ecosystem to passively buy up. This investment style free rides on work done by other managers and hopes the market is right on average.
- The weakness of the index style is that it is always slow to the party as indexes are balanced in arrears. In a world where a specialist wouldn't own all companies all the time the indexer is always playing catch up but benefits from lower overhead costs.
- As we look forward into the rest of 2024 and 2025, it strikes us that the sector is poised for growth and that we have an exceptionally bright and battle-tested investor group that should be able to provide ample capital where needed to emerging therapeutics companies. The depth the specialist investor community is one of the great strengths of the U.S. biotech ecosystem.

# 1Q Healthcare Investing: Still Cleaning up after the Party

Jim Flynn, Managing Partner, Deerfield, *Pulse*, April 2, 2024

The stock market and its many participants are fascinating creatures, reminiscent of a school of fish. At one moment, they are all lackadaisically drifting along, seemingly oblivious to the dangers swimming alarmingly nearby, and then, all at once, shoot off to gorge or escape threats that are suddenly universally realized. But in these disconnected, opposite, and discordant behaviors, and despite some losses along the way, a sustaining evolutionary sensibility somehow persists.

The advancement of new therapies and healthcare technologies rely on this curious aquarium, as the markets provide a vital step along the path of innovation. Innovation often starts with an idea developed through academic research, then progresses when funded by venture capital. The public markets provide the significant risk capital that is subsequently required to prove out business models or fund expensive clinical programs. Unfortunately, for most of the last two years, despite the ever-improving likelihood of developing important new therapeutics and technologies, the markets have been largely closed to new healthcare IPOs.

In the fourth quarter of last year and the first quarter of this year, things did pep up a bit, but with many cross currents. M&A activity, a true test of value in the market and which brings with it the promise of realized profits to investors, has been strong, particularly among therapeutics companies.



In the fourth quarter of 2023 and the first quarter of 2024 combined, there was in excess of \$90 billion in acquisition activity by large pharmaceutical companies alone. This is higher than the full year for 2021 and 2022 and very similar to the full year of 2018 and 2020. Eli Lilly and Novo Nordisk, which are both benefiting from their highly successful GLP-1 launches, were the most noteworthy. From June 2023 to present, those two companies made 11 acquisitions out of the 37 total. Novartis made four acquisitions over that period, and Bristol-Myers and AstraZeneca each made three.

# 1Q Healthcare Investing (Continued)

As is the norm, the majority of these acquisitions were for companies where the market had done its job by funding proof-of-concept human clinical trials.

IPO activity has also perked up. Public offerings in the first quarter of 2024 were the highest they have been in over two years. These were not all clean deals in the sense that there was normal demand. In many cases, companies needed to take investors over the wall to present new data to convince them that there was value to be gained. Nonetheless, the money flowed. Convertible offerings are still well depressed compared to the booming late teens and 2020. Still, towards the end of the quarter, several notable convertible offerings came at seemingly attractive prices for the companies that offered them. It is somewhat surprising that convertibles have not been more utilized, as convertible arbitrage players are hungry with demand for new issues and convert strike price premiums offer dilution advantages to the issuer over common equity.

An active public market is a prerequisite for venture firms to make significant investments in new technologies, and these are collectively more positive signals than we have seen for a couple of years. For markets to be fully open, however, the clean-up of the rest of the excesses of prior years is likely necessary. In the first quarter, Invitae joined medical technology companies Nanostring and Sientra in filing for bankruptcy.

While there will always be additional healthcare companies and technologies that fail to make it, companies such as Invitae represent some of the last of the highfliers to come back down to earth.

At the end of the day, returns are what drive market participation. In this regard, healthcare stock performance, outside of takeouts, remains unremarkable at best. In the first quarter of 2024, the Russell 2000 Healthcare index was up under 5% compared to the S&P 500 Total Return of over 10%. This adds to the significant underperformance from last year when the Russell 2000 Healthcare was also up less than half of the surging S&P 500.

In part, this was caused by strong outflows from mutual fund investors, which occurred almost continuously through October of last year and, after a brief reversal around year-end, resumed in the first quarter of this year. With interest rate volatility and populist rhetoric mounting as the election cycle progresses, these fund flows are not surprising. What will be surprising is if we look back a few years hence and the evolutionary sensibility of the market has not fully recognized and rewarded the continuous, high-value innovations that are emerging across healthcare.

# Biotech Buyside Getting More Active in Venture Deals

Stephen Taub, *Institutional Investor*, April 2, 2024.

The venture capital market appears to be coming back to life — at least when it comes to the life sciences and biopharma sectors. This is evident from the activity among hedge fund firms that either have separate VC arms or include privates in their long-short and long-only portfolios. In the first quarter, at least four firms that specialize in the life sciences areas saw a burst of activity that puts them on pace to make more new investments in 2024 than they did last year.

In fact, several firms are set to exceed the total in 2021, the last hot year for VC investing. They were led by RA Capital Advisors, which made 25 new investments in the first quarter — nearly double the 13 it made in the fourth quarter and more than half the 46 it made in 2023.

The sharp increase in investment activity in the life sciences sector is in stark contrast to the technology, internet, and consumer areas, where investment activity has all but dried up, with little sign of any meaningful rebound or resurgence. The most glaring examples: Tiger Global Management and Coatue Management. Only a couple of years ago, they were two of the most active firms in the venture capital market in general, but each completed only a handful of deals in the first quarter.

RA Capital's surge in activity is not surprising. Institutional Investor reported last September that the firm was raising money for a new venture capital fund and an offshore equivalent, according to regulatory filings. The firm, headed by founder Peter Kolchinsky and managing partner Rajeev Shah, previously launched three VC funds under the name of Nexus. Of RA Capital's 25 first-quarter investments, 16 were either post-IPO equity or debt private placement deals, says Crunchbase. Most recently, RA Capital led the investment in more than 2.5 million units for CervoMed, a clinical-stage company focused on developing treatments for age-related neurologic disorders, per a press release. Each unit comprises one share of common stock or one prefunded warrant to purchase shares of common stock and has a purchase price of either \$19.745 or \$19.744. Armistice Capital and Soleus Capital also participated in the deal.

Perceptive Advisors was the second-most-active VC investor among firms best known for their hedge funds, completing at least 15 deals in the first quarter. This compares with three in the fourth quarter and 19 all of last year, according to Crunchbase. In July 2022, it reported that Perceptive was raising money for Perceptive Credit Opportunities Fund IV and an offshore equivalent, its fourth dedicated credit fund. The firm was targeting \$1.25 billion, said an investor at the time. The new fund was designed to provide loans to public and private health care companies.

The third-most-active firm in the VC market in the first quarter was Cormorant Asset Management. It made eight investments during the period after making the same number in the fourth quarter, with a total of 23 deals in all of 2023.

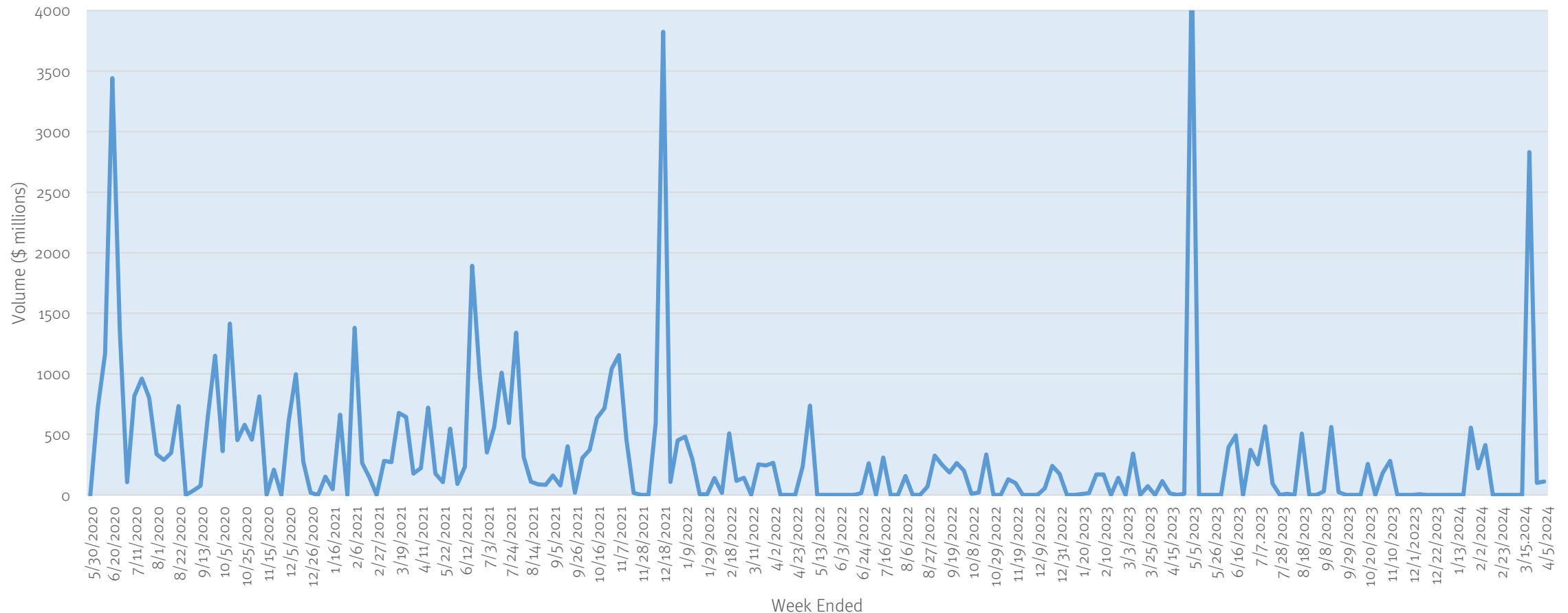
# Capital Markets Update



# Weekly IPO Activity in the Biopharma Sector Modest

Last week saw Contineum price their debut market offering. Otherwise, the IPO market was quiet.

Biopharma IPO Volume (\$ million), Weekly, May 2020 to April 2024

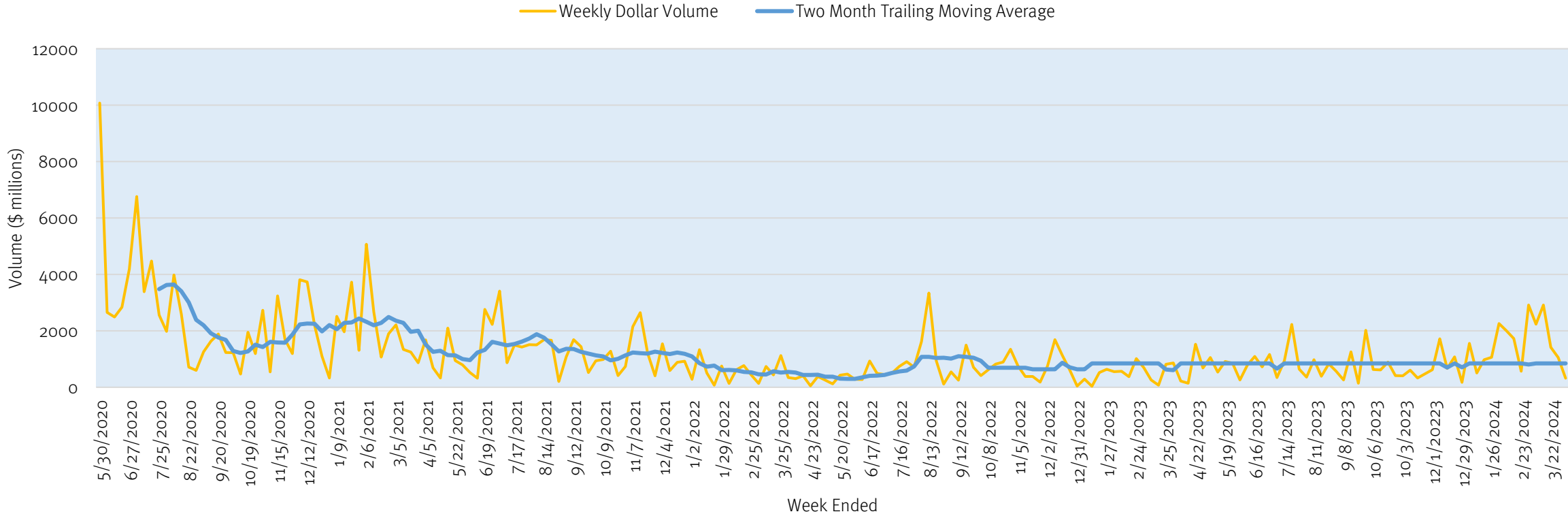


Source: Data from CapitalIQ and Stifel research.

# Follow-On Volume Slowed Way Down Last Week

We saw only two offerings over \$50mm in the follow-on market last week. Sutro raised \$75 million on the back of an impressive partnership deal and Aquestive Therapeutics raised \$100mm. With only \$322 million in volume, it was the quietest week for follow-ons since the year began. The story of what’s going on is clear. The macro picture and the 5% drop in the XBI created inhospitable conditions for follow-on issuers last week.

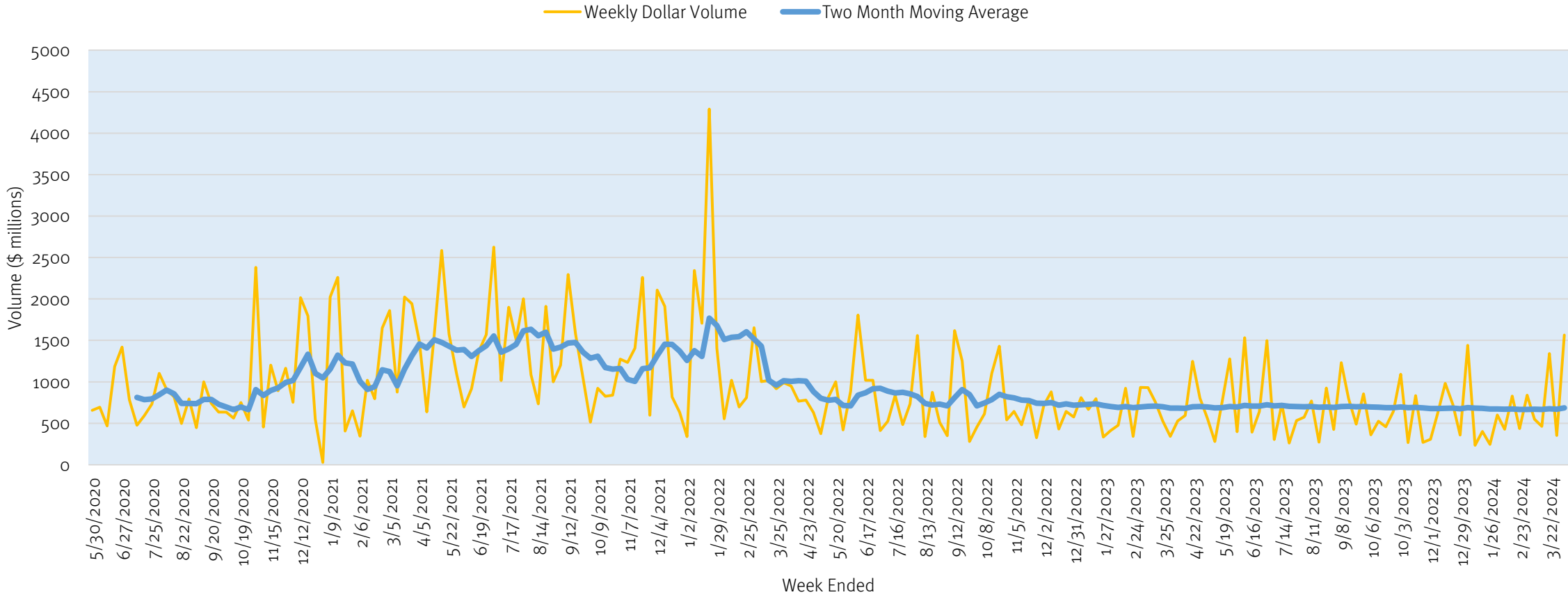
**Biopharma Equity Follow-On Volume (\$ million), Weekly, May 2020 to April 2024**



# Biggest Week for Private Venture Equity Investments in 18 Months

The venture private market went into overdrive last week with nearly \$1.6 billion in deals getting announced. There were four raises over \$100mm. It feels like the privates market is coming back to life.

Biopharma Venture Equity Privates Trend (\$ million), Weekly, May 2020 to April 2024



Source: Data from CapitalIQ, Crunchbase.



# Obsidian Therapeutics Announces Oversubscribed \$160.5 Million Series C Financing to Drive OBX-115 Clinical Development

**CAMBRIDGE, Mass., April 03, 2024** - Obsidian Therapeutics, Inc., a clinical-stage biotechnology company pioneering engineered cell and gene therapies, today announced it has closed a significantly oversubscribed \$160.5 million Series C financing with a top-tier syndicate of life science investors led by new investor, Wellington Management. Additional new investors participating in the financing include Foresite Capital, Janus Henderson Investors, Novo Holdings A/S, Paradigm BioCapital, RTW Investments, funds and accounts advised by T. Rowe Price Associates, Inc., and Woodline Partners LP. Existing investors Atlas Venture, Blue Owl Healthcare Opportunities, Bristol Myers Squibb, Deep Track Capital, Logos Capital, RA Capital Management, TCGX, Samsara BioCapital and Surveyor Capital (a Citadel company) also participated in the financing.

Proceeds from the financing will advance Obsidian's lead engineered tumor-infiltrating lymphocyte (TIL) program, OBX-115, in its ongoing trials for patients with melanoma and non-small cell lung cancer (NSCLC). The Company is focused on enrolling patients and reaching key clinical and regulatory milestones, as well as manufacturing scale-up ahead of pivotal trial readiness.

The Company also announced the appointment of Ray Camahort, Ph.D., Partner in the Venture Investments group at Novo Holdings US, to its Board of Directors. "Obsidian's engineered TIL cell therapy is highly differentiated and has the potential to bring transformational efficacy to patients with solid tumors," said Dr. Camahort. "We look forward to supporting Obsidian's team on their journey to bring OBX-115 to additional patients."

"Wellington is excited to be supporting Obsidian through its next phase of growth, as the Company continues demonstrating the potential of OBX-115 to address the unmet need of patients with immune checkpoint inhibitor-resistant advanced or metastatic melanoma. The Company has been generating momentum with its novel cytoDRiVE technology and advancing OBX-115 into late-stage clinical trials," commented Irina Margine, Ph.D., Biotech Sector Lead at Wellington Management.

**Source:** <https://obsidiantx.com/news-releases/obsidian-therapeutics-announces-oversubscribed-160-5-million-series-c-financing-to-drive-obx-115-clinical-development/>



"The strong demand and support from this syndicate of premier investors is a testament to the promise of OBX-115 for patients with treatment-resistant advanced melanoma. This financing provides funding through key clinical readouts in melanoma and is the catalyst to continue expanding OBX-115 into NSCLC, where there is significant potential and high unmet need."

**Madan Jagasia, M.D., M.S**

*Chief Executive Officer*  
Obsidian Therapeutics

# Diagonal Therapeutics Launches with \$128 Million to Develop Antibodies for Debilitating Diseases



**CAMBRIDGE, Mass., April 03, 2024** - Diagonal Therapeutics, a biotechnology company pioneering a new approach to discovering and developing agonist antibodies, launched today with \$128 million in financing. The Series A was co-led by BVF Partners and Atlas Venture, with participation from Lightspeed Venture Partners, RA Capital Management, Frazier Life Sciences, Viking Global Investors, Velocity Capital, and Checkpoint Capital. Diagonal was co-founded by Chief Executive Officer, Alex Lugovskoy, Ph.D., and Atlas and previously seeded by Atlas, Lightspeed Venture Partners, and Velocity Capital. The financing will support further advancement of the company's proprietary DIAGONAL platform and pipeline of novel therapeutics to value-creating milestones, including its lead program for the treatment of hereditary hemorrhagic telangiectasia (HHT), a severely debilitating bleeding disorder with limited therapeutic options, through clinical proof-of-concept. Diagonal's agonist antibody activates a receptor complex in the TGF- $\beta$  superfamily genetically impaired in HHT patients. In preclinical models of HHT, Diagonal's agonist antibodies prevent and reverse the formation of pathological vascular malformations.

“The biopharmaceutical industry has a robust, growing toolkit of approaches to inhibit disease-associated pathways. However, we still lack systematic pharmacologic approaches to activate biological pathways to treat diseases caused by deficient signaling,” said Michael Gladstone, Partner at Atlas Venture and Board Chair of Diagonal. “Diagonal’s platform addresses this unmet need by rapidly identifying antibodies that activate key pathways. I am excited to support them as they advance their therapeutic candidates for patients in need.”

Unlike most approved antibodies, which inhibit a cellular function, agonist antibodies activate a signaling cascade by binding two receptors and bringing them together in a highly specific conformation that enables their activation. Given the many potential binding sites between each receptor and an antibody, nearly infinite binding configurations exist, of which only a small subset will result in the desired agonistic activity. Historically, this has made identifying or rationally designing agonist antibodies difficult. The DIAGONAL platform solves this challenge, combining proprietary computational and experimental techniques that enable Diagonal scientists to sift through billions of combinations at unprecedented speeds and with high fidelity.



“We are fundamentally changing how agonist antibody therapies are developed. The DIAGONAL platform allows us to overcome technical limitations that hindered agonist antibody discovery in the past, and we have demonstrated that we can efficiently advance novel drug candidates for diseases where patients have limited or no treatment options. Our approach enables us to treat a wide range of disorders where signaling pathways have been disrupted with agonist antibodies that have superior potency and selectivity, tunable and sustained pharmacology, excellent developability, and low immunogenicity.”

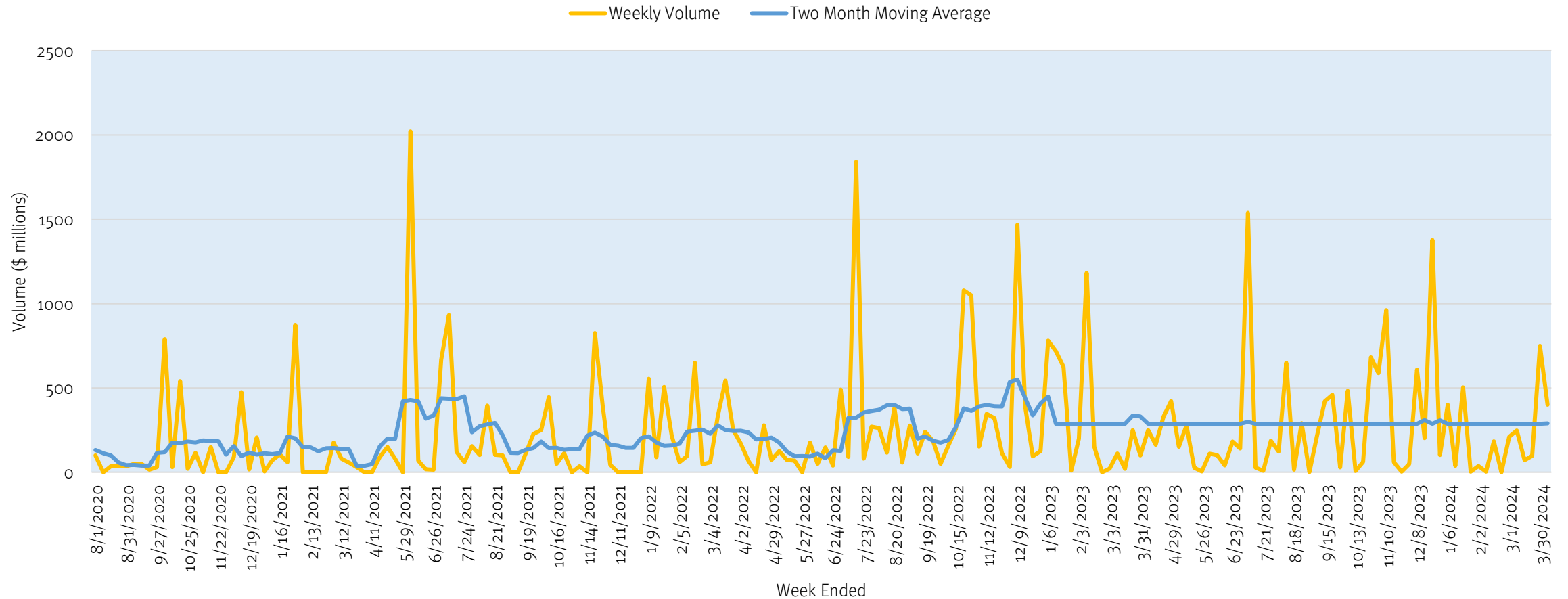
**Alex Lugovskoy**  
*Chief Executive Officer*  
Diagonal Therapeutics

**Source:** <https://www.globenewswire.com/news-release/2024/04/03/2856722/0/en/Diagonal-Therapeutics-Launches-with-128-Million-in-Financing-to-Pioneer-a-New-Approach-to-Discovering-and-Developing-Agonist-Antibodies-to-Tackle-the-Underlying-Causes-of-Severely-.html>

# Biopharma Private Debt Market Solid Last Week

Last week saw Endo raise \$1.60 billion in a debt deal and Catalent's debt offering come to market as part of its buyout deal.

### Biopharma Private Debt Issuance Trend (\$ million), Weekly, Aug 2020 to April 2024



Source: Data from CapitalIQ, Crunchbase, Stifel research.

# Endo, Inc. Announces Proposed New Senior Secured Credit Facilities



**MALVERN, PA, April 1, 2024** -- Endo, Inc. ("Endo"), a newly formed entity, today announced that its wholly-owned subsidiary Endo Finance Holdings, Inc. (the "Borrower") intends to enter into new senior secured credit facilities consisting of: (i) a \$400.0 million five-year super-priority revolving credit facility (the "New Revolving Facility"); and (ii) a \$1,250.0 million seven-year term loan facility (the "New Term Loan Facility", and together with the New Revolving Facility, the "New Credit Facilities").

The New Credit Facilities will be guaranteed by Endo and certain of the Borrower's subsidiaries (collectively, the "Guarantors") and will be secured by first priority liens on substantially all assets of the Borrower and the Guarantors, subject to certain exceptions. Endo intends to use the net proceeds of the New Term Loan Facility, together with the proceeds of the rights offerings under the Plan (as defined below), certain other debt and cash on hand to, among other things: (i) make settlement payments under the Fourth Amended Joint Chapter 11 Plan of Reorganization of Endo International plc and its affiliated debtors (the "Plan") to various trust beneficiaries and the U.S. federal government; (ii) make cash distributions to first lien claimholders under the Plan; (iii) pay restructuring expenses and other fees and expenses; and (iv) fund Endo's prospective operations.

Endo currently expects the Plan to be effective on or around April 23, 2024.

The New Credit Facilities are subject to market and other conditions and are anticipated to close substantially concurrently with the effectiveness of the Plan. However, there can be no assurance that the New Credit Facilities will be consummated on the terms described herein or at all.

# Catalent Financing Taken by Blue Owl and Ares

Bloomberg, April 6, 2024

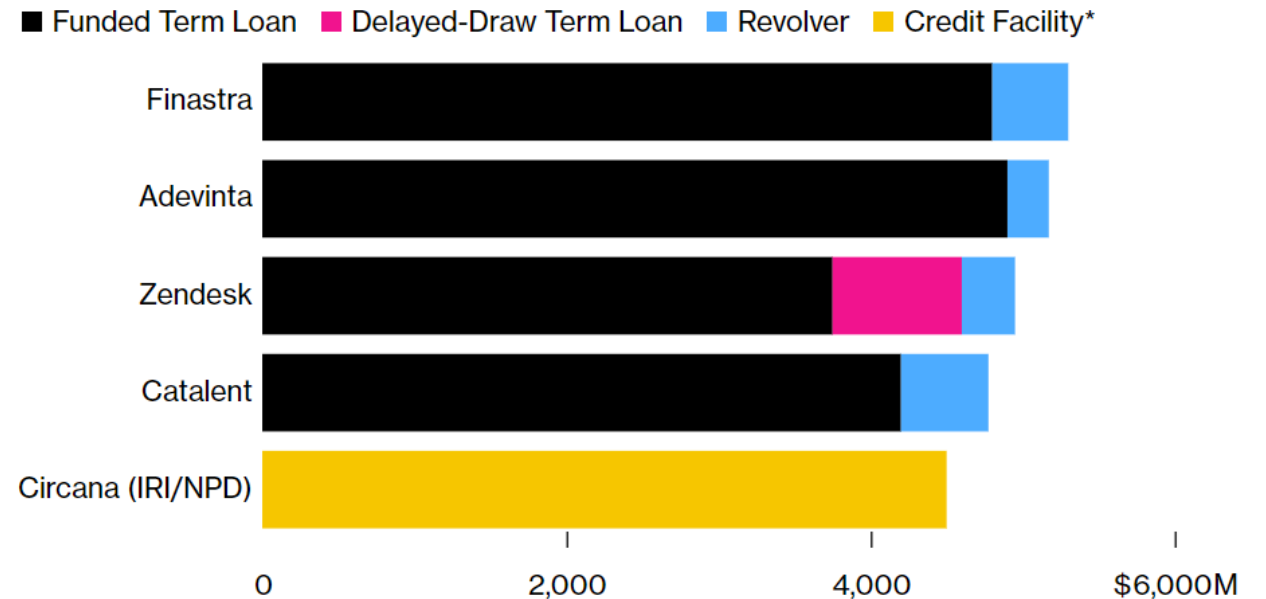
Ares Management Corp. and Blue Owl Capital Inc. are leading a group of private credit lenders providing \$4.8 billion of debt financing for the acquisition of pharmaceuticals manufacturer Catalent Inc., according to people with knowledge of the matter.

The financing — one of the largest private credit transactions on record — will help fund the \$16.5 billion acquisition of Catalent by Novo Holdings, the controlling shareholder of weight loss drugmaker Novo Nordisk A/S. The package is made up of a \$4.2 billion term loan and \$575 million revolving line.

The financing is one of the biggest ever arranged by private credit lenders and the biggest so far this year, according to data compiled by Bloomberg News. It's a win for direct lenders such as Ares and Blue Owl, which have faced renewed competition from banks in providing debt for large acquisitions and buyouts in recent months.

## Jumbo Deals

Largest direct loans arranged by private credit lenders



Source: Bloomberg News

Note: \*Total credit facility size is displayed when a breakdown is not available. Excludes deals that have grown through add-on transactions. Adevinta is shown in US dollar-equivalent as of Nov. 22, 2023.

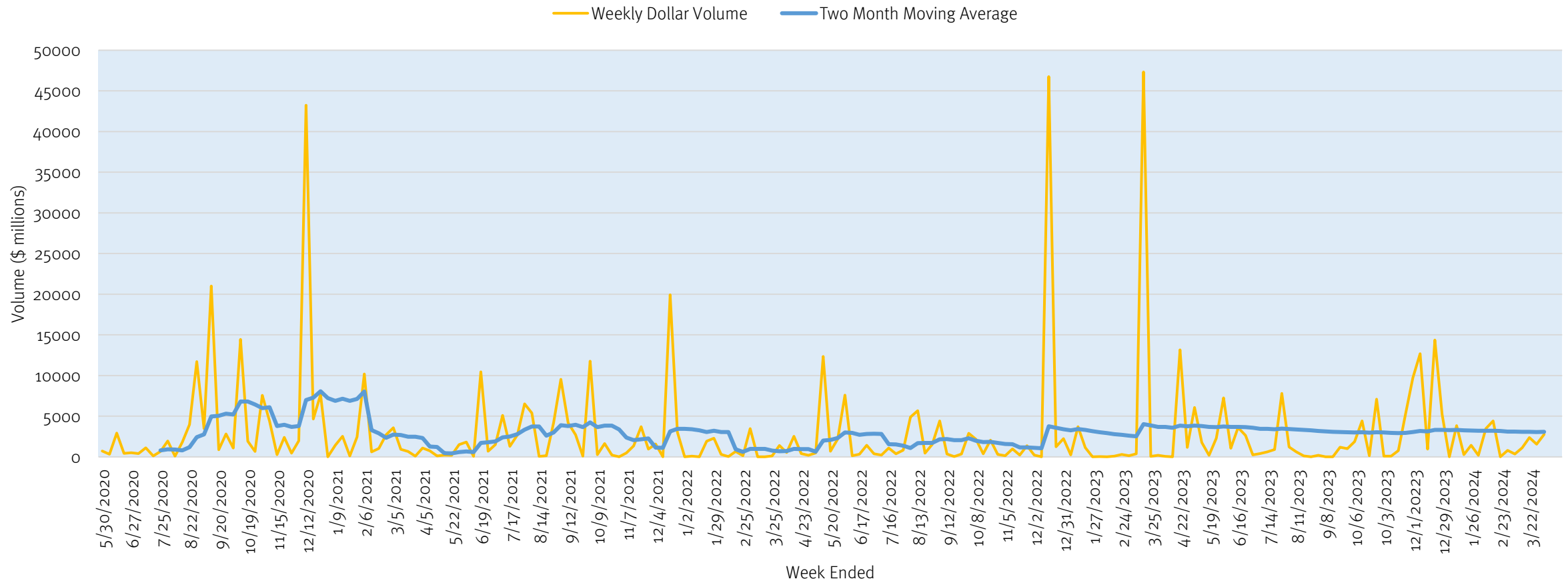
# Deals Update



# Last Week Saw \$3.1 Billion in M&A Volume.

The largest deals last week was Genmab's acquisition of ProfoundBio for \$1.8bn and Apotex's acquisition of Searchlight Pharma. It was the fourth busiest M&A week of the year.

Biopharma M&A Volume Trend (\$ million), Weekly, May 2020 to Apr 2024



Source: S&P, CapitalIQ

# Genmab to Broaden and Strengthen Oncology Portfolio with Acquisition of ProfoundBio



**COPENHAGEN, Denmark and SEATTLE, Washington, April 3, 2024**

Genmab A/S and ProfoundBio, Inc. announced today that the companies have entered into a definitive agreement for Genmab to acquire ProfoundBio in an all-cash transaction. ProfoundBio is a privately-owned clinical-stage biotechnology company developing next-generation ADCs and ADC technologies for the treatment of certain cancers, including ovarian cancer and other FR $\alpha$ -expressing solid tumors. Genmab will acquire ProfoundBio for USD 1.8 billion in cash, payable at closing (subject to adjustment for ProfoundBio's closing net debt and transaction expenses).

The transaction will further broaden Genmab's mid- to late-stage clinical pipeline and strengthen and complement Genmab's already validated suite of proprietary technology platforms. The acquisition will give Genmab worldwide rights to ProfoundBio's portfolio of next-generation ADCs, which consists of three clinical and multiple preclinical programs including Rina-S, a potential best-in-class, clinical-stage, FR $\alpha$ -targeted, Topo1 ADC, currently in Phase 2 of a Phase 1/2 clinical trial, for the treatment of ovarian cancer and other FR $\alpha$ -expressing solid tumors. In addition, the combination of ProfoundBio's novel ADC technology platforms with Genmab's proprietary antibody platforms will potentially create new opportunities to generate and develop new medicines with the potential to transform the treatment of cancer and improve the lives of patients.

The addition of Rina-S to Genmab's portfolio will enable Genmab to deepen its presence in the gynecologic oncology space and establish a firm foundation in solid tumors. As a potential best-in-class ADC, Rina-S aims to address a broader patient population than first-generation FR $\alpha$ -targeted ADCs. Based on the data from the ongoing Phase 1/2 clinical trial Genmab intends to broaden the development plans for Rina-S within ovarian cancer and other FR $\alpha$ -expressing solid tumors. In January 2024, the U.S. Food and Drug Administration (U.S. FDA) granted Fast Track designation to Rina-S for the treatment of patients with FR $\alpha$ -expressing high-grade serous or endometrioid platinum-resistant ovarian cancer.

"The proposed acquisition of ProfoundBio firmly aligns with our long-term strategy and our ambitious 2030 vision, to impact the lives of patients through innovative antibody medicines," said Jan van de Winkel, Ph.D., President and Chief Executive Officer of Genmab. "We believe that ProfoundBio's ADC candidates, proprietary technology platforms and talented team will be a great addition to Genmab and that, together, we will be able to accelerate the development of innovative, differentiated antibody therapies for cancer patients."

"Genmab shares our team's mission of developing novel therapies to improve outcomes for cancer patients. Genmab's deep expertise in antibody drug development and commercialization makes this a compelling union that will allow us to rapidly develop and realize the full potential of our ADC therapies to benefit patients," said Baiteng Zhao, Ph.D., ProfoundBio's co-founder, Chief Executive Officer and Chairman of the Board.



# Apotex to Acquire Searchlight Pharma, a Canadian Specialty Branded Pharmaceutical Leader

**TORONTO and MONTRÉAL, April 2, 2024**

Canada's largest pharmaceutical company, Apotex Inc. and Searchlight Pharma Inc., one of Canada's fastest growing companies, announced today that they have reached an agreement whereby Apotex will acquire Searchlight.

Searchlight is a private, top-growth Canadian specialty and innovative branded pharmaceutical company with global reach that executes best-in-class search, acquisition, commercialization, and focused development of innovative and unique specialty branded healthcare products.

For nearly five decades, Apotex has leveraged its strong Canadian footprint into adjacent verticals, and building on its recent transaction with Harrow, Inc. for the exclusive rights to certain branded ophthalmic products, with the addition of Searchlight, is positioned to become the partner of choice for pharmaceutical licensing and acquisition opportunities in the Americas. The acquisition further accelerates Apotex's growth within the specialty branded pharmaceutical market, adding a diverse portfolio of over 60 products and a full-service branded pharmaceutical platform, as well as established business development networks in Canada and internationally.

"Searchlight has an experienced and proven track record as one of Canada's fastest-growing companies with deep institutional knowledge across a range of domestic and international markets and a strong specialty and innovative branded product portfolio," said Allan Oberman, President and Chief Executive Officer at Apotex. "This acquisition is a strategic complement to Apotex's leading market position in generic and biosimilar pharmaceuticals, in alignment with our ongoing focus to expand into the high-value, innovative branded pharmaceuticals sector. We look forward to working with Searchlight's talented team as we plan the integration of our companies and a seamless transition for patients, customers and employees."

Mark Nawacki, Searchlight's President and Chief Executive Officer continued, "For the past decade, Searchlight has successfully pursued its branded pharmaceutical growth strategy by providing dependability and value to Canadian patients and healthcare professionals. Thinking forward to an ambitious future, we know that Apotex is the right partner for Searchlight given our shared purpose of providing access to innovative medicines that improve people's lives. We are confident and excited that joining forces to create a Canadian pharmaceutical champion and global health company will harness a combined passion, scale and talent that will accelerate our plans."



# Acorda Therapeutics Files for Bankruptcy

PEARL RIVER NY, April 1, 2024

PEARL RIVER, N.Y.--(BUSINESS WIRE)-- Acorda Therapeutics, Inc. (Nasdaq: ACOR) ("Acorda" or "the Company") today announced that it has entered into an asset purchase agreement with Merz Therapeutics to purchase substantially all of the assets of Acorda, including the rights to INBRIJA, AMPYRA, and FAMPYRA for \$185 million. Merz Therapeutics, a leader in the field of neurotoxins, is a business of the global family-owned company Merz, headquartered in Frankfurt am Main, Germany. To facilitate an orderly sale process, and in an effort to maximize the value for the Company's assets through a competitive auction process, with Merz serving as the "stalking horse" bidder, Acorda and certain of its affiliates filed voluntary petitions to commence Chapter 11 proceedings in the U.S. Bankruptcy Court for the Southern District of New York.

The decision to file for Chapter 11 protection follows a lengthy strategic review during which the Company explored a wide range of strategic options. The sale will be conducted through a court-supervised process under Section 363 of the U.S. Bankruptcy Code, which will provide potential buyers the opportunity to submit offers and is expected to conclude in June 2024.

Ron Cohen, M.D., Acorda's CEO and President, said, "Acorda's management team and board have evaluated all of our strategic options, and following an exhaustive process believe that this option is in the best interest of stakeholders. One of our top priorities is to ensure an uninterrupted supply of our medications to people with multiple sclerosis and Parkinson's disease. We are confident that Merz Therapeutics, if they are the ultimate acquirer, will be able to seamlessly continue serving these patients' needs, given Merz's longstanding dedication to improving the lives of people who suffer from movement disorders and other neurological conditions."

Acorda will continue operations while it works to complete the sale process. To enable this, the Company has filed motions with the court seeking to ensure the continuation of normal operations during this process. Upon court approval, Acorda expects to minimize the impact of the bankruptcy process on its employees, customers, patients, and other key stakeholders.

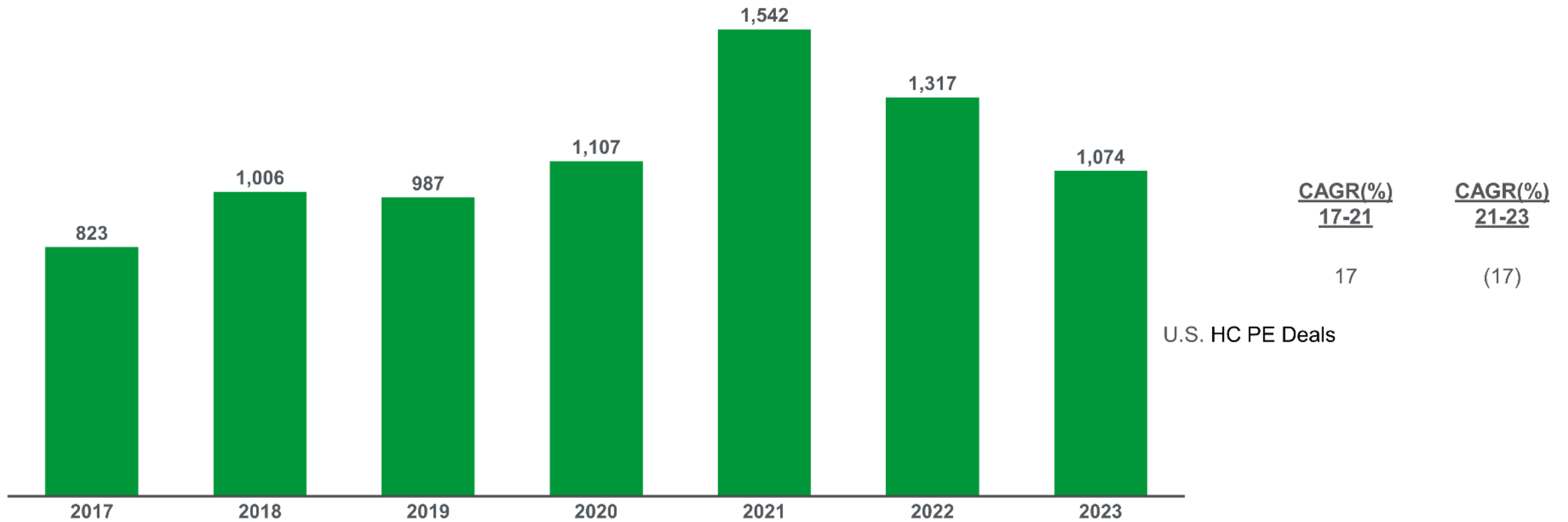
Acorda entered into a Restructuring Support Agreement with the holders of over 90% of its 6.00% Convertible Senior Secured Notes due 2024, which sets out certain milestones and conditions relating to the Section 363 sale process. In addition, in order to fund the continued operations of the Company during the bankruptcy process, Acorda and certain noteholders entered into a Debtor-in-Possession Financing Agreement to provide a term loan facility in the aggregate amount of \$20 million in new money, which is also subject to court approval.

The logo for Acorda Therapeutics, featuring the word "ACORDA" in a large, white, sans-serif font with a stylized lightning bolt or slash through the letter "O". Below "ACORDA" is the word "THERAPEUTICS" in a smaller, white, sans-serif font, separated by a thin horizontal line.

# Healthcare PE Deals Down in 2023

U.S. Healthcare PE Deal Count (2017-23)

Number of deals



Source: Pitchbook; L.E.K. research and analysis

Source: <https://www.lek.com/insights/pe/us/ar/healthcare-services-hot-topics-private-equity-2024>

# What Biotech Companies Should Know About M&A in Down Markets

Clary Estes, BIO Panel, Feb 29, 2024 (excerpt)

To kick off the discussion, moderator Arda Ural, Americas Leader for Life Sciences and Healthcare at EY (Ernst & Young), discussed the company's recent report, How life sciences can make the right deals in a time of change. The report places the era's current trends within a larger historical framework, contextualizing and alleviating some of the industry's anxiety today.

"I'm going to take us back to 2010," began Ural. "Try to compare how the top line of the industry was suspended or sustained by the bottom line or pipeline coming from the products launched in biotech in the prior five years. If you look at around 2010-12, it was mostly small molecules [that lead the market], and then the biologics kicked in to get us go into a sustainable growth we saw until 2020."

COVID, not surprisingly, was a singular event that shifted the market, the effects of which are playing out in different ways today. The top line for companies, Ural observes, exceeded the vaccine pipeline, but as the pandemic waned, those numbers have naturally slipped, and investors are looking for considerably more stable and mature deals.

To this point, the report's key takeaways include:

1. In 2023, Big Pharma began to embrace big dealmaking once again, as numerous key products face the loss of patent protection in the next five years.
2. Companies across the life sciences sector should do the right deals now to deliver value into the future.
3. Companies must nurture the partners, deal structures, therapeutic areas, and strategies to navigate a time of global business and regulatory upheaval.
4. Later during the panel, Mayukh Sukhatme, President & Chief Investment Officer at Roivant Sciences, observed, "There are two markets that are happening right now: the haves and the have-nots."

His observations are supported by the report, which found that "while the late stage assets (or biotech companies) enjoy a 73% premium one day post-announcement, 27% of biotechs in early stage development have less than one year of cash to sustain their operations."

# Industry News



# Roivant Announces \$1.5B Share Repurchase Program Including Purchase of Entire Sumitomo Stake for \$648M, Reducing Share Count by ~9%

Goal of repurchase program is to drive value creation for investors by taking advantage of price dislocation to reduce share count and shareholder concentration, while maintaining strong price discipline

Roivant is purchasing Sumitomo's full stake of 71.3M shares for \$9.10/share (\$648M), reducing share count by approximately 9%<sup>1</sup>

Board approved a share repurchase program of up to \$1.5B through a potential combination of open-market repurchases, tender offers and private transactions

We remain confident that our capital position is sufficient to fully fund our existing programs through profitability, expand our pipeline with business development opportunities and additional indications, and return capital to shareholders

# NIU Opportunity Parallels Other Blockbuster Orphan Indications, With Less Competition

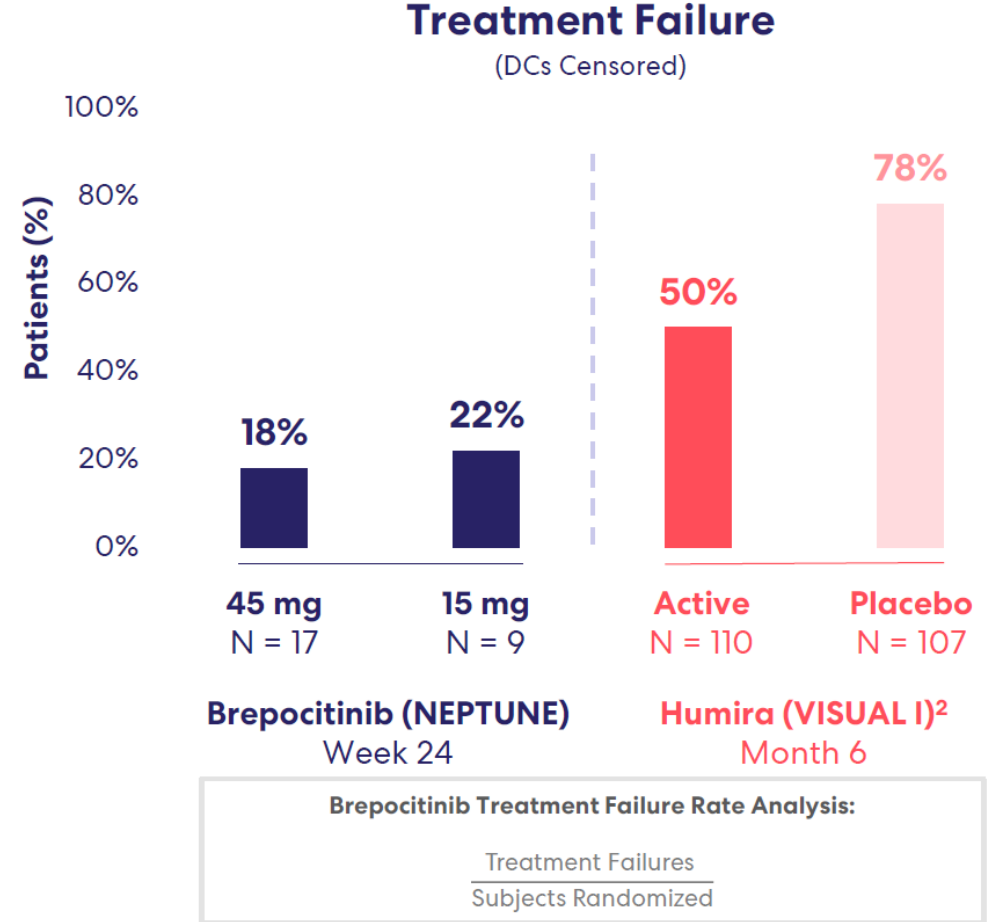
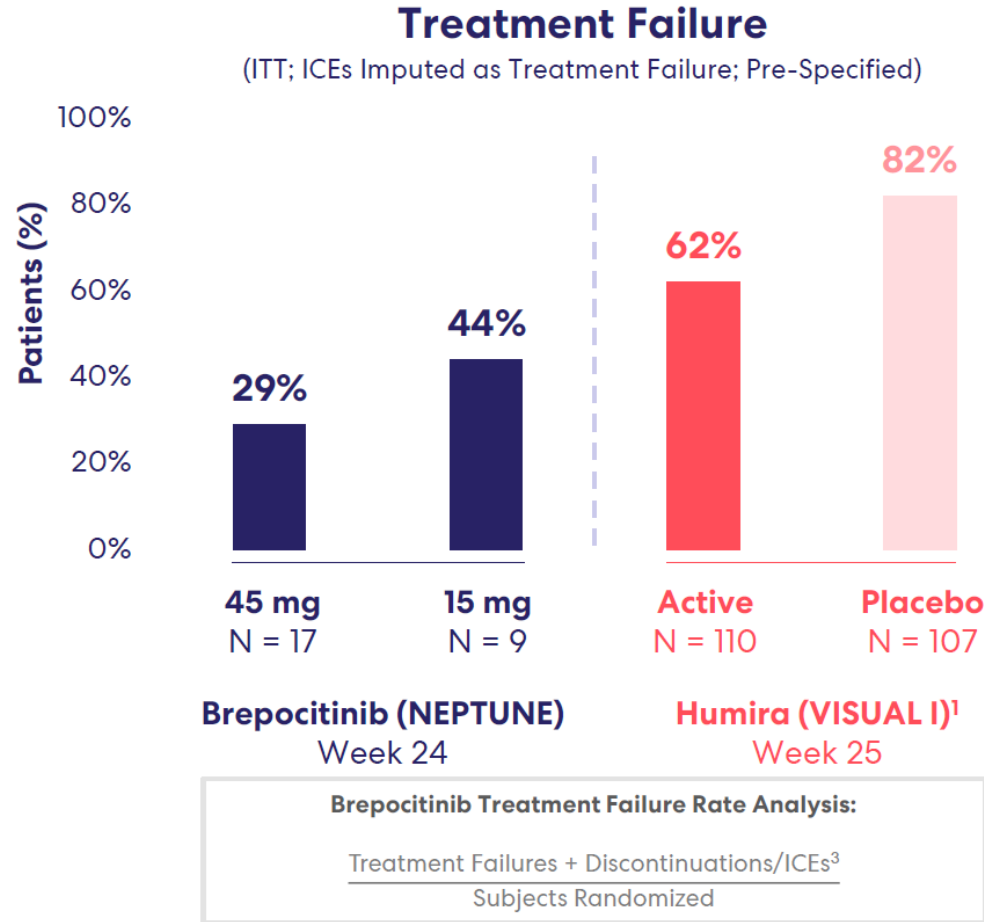
NIU = non-infectious uveitis

	Non-Infectious Uveitis	Hidradenitis Suppurativa	Thyroid Eye Disease	Myasthenia Gravis
Overall Prevalence	400,000 <sup>1,2</sup>	300,000	100,000	65,000
Prevalence in Relevant Sub-Population	70,000 - 100,000 <sup>2</sup> <i>(non-anterior)</i>	100,000 - 150,000 <i>(moderate / severe)</i>	15,000 - 20,000 <i>(active moderate / severe)</i>	55,000 <i>(AChR+)</i>
Humira Approved?	Yes	Yes	No	No
Morbidity	High <i>(blindness)</i>	High	High	High
Competitors in Phase 3	0 <sup>3</sup>	5	5	7

1. Joltikov KA, Lobo-Chan AM. Epidemiology and Risk Factors in Non-infectious Uveitis: A Systematic Review. Front Med (Lausanne). 2021 Sep 10;8:695904.  
 2. Thorne et al, JAMA Ophthalmol. (2016).  
 3. One therapy in Phase 3 for uveitic macular edema, which comprises a subset of non-anterior NIU patients.

# Treatment Failure Rate at Week 24 *(lower rate = greater treatment benefit)*

Including Cross-Study Comparison to VISUAL I



*Disclaimer: Figures reflect cross-trial comparison and not results from a head-to-head study. Differences exist between trial designs and subject characteristics, and caution should be exercised when comparing data across studies.*



# Brepocitinib Proof-of-Concept in Potentially Resolving and Preventing Macular Edema

Data suggests potential to resolve macular edema and potential to prevent or reverse swelling before threshold for macular edema is reached and patient is formally diagnosed with UME

## In the 45 mg arm, at Baseline:

**10 patients**

did not have macular edema  
(CST < 300  $\mu\text{m}^1$ )

**7 patients**

had macular edema  
(CST  $\geq$  300  $\mu\text{m}$ )

## In the 45 mg arm, by Wk 24:

**0 patients**

developed macular edema  
**(0% occurrence rate)**

**3 of 7 patients**

had resolution of macular edema  
**(43% resolution rate)**

## By comparison:

In the VISUAL I study, among patients who did not have macular edema at baseline, **50% of placebo patients developed macular edema after 6.2 months<sup>1</sup>**

- 50% of Humira patients developed macular edema after 11.1 months<sup>2</sup>

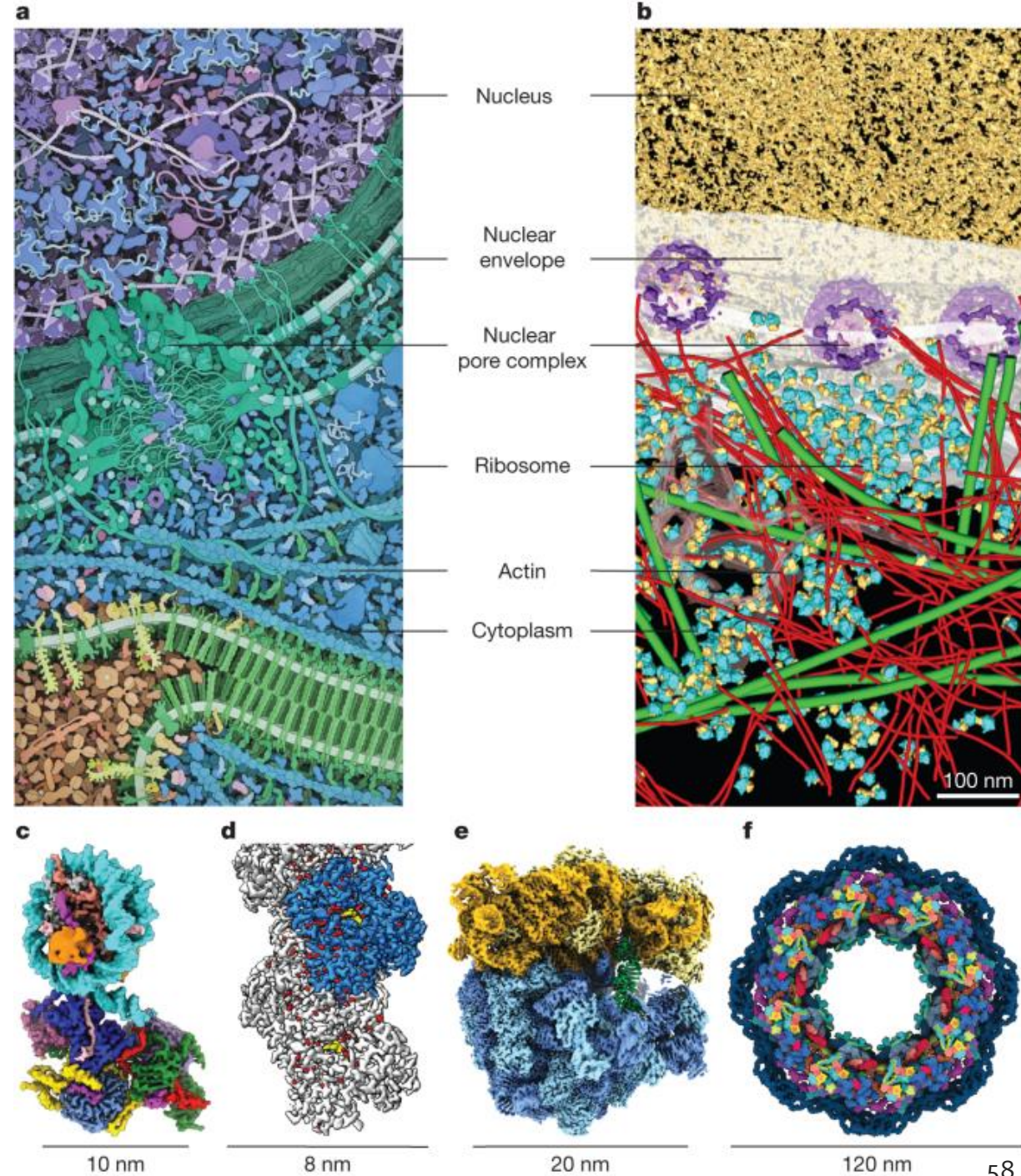
In a different study of patients with uveitic macular edema at baseline, **Humira resolution rates at Month 6 were 22%<sup>3</sup>**

*Disclaimer: Figures reflect cross-trial comparison and not results from a head-to-head study. Differences exist between trial designs and subject characteristics, and caution should be exercised when comparing data across studies.*

# A Structural Biologists Dream

Nogales, E., Mahamid, J. “Bridging structural and cell biology with cryo-electron microscopy,” April 3, 2024, *Nature* 628, 47–56

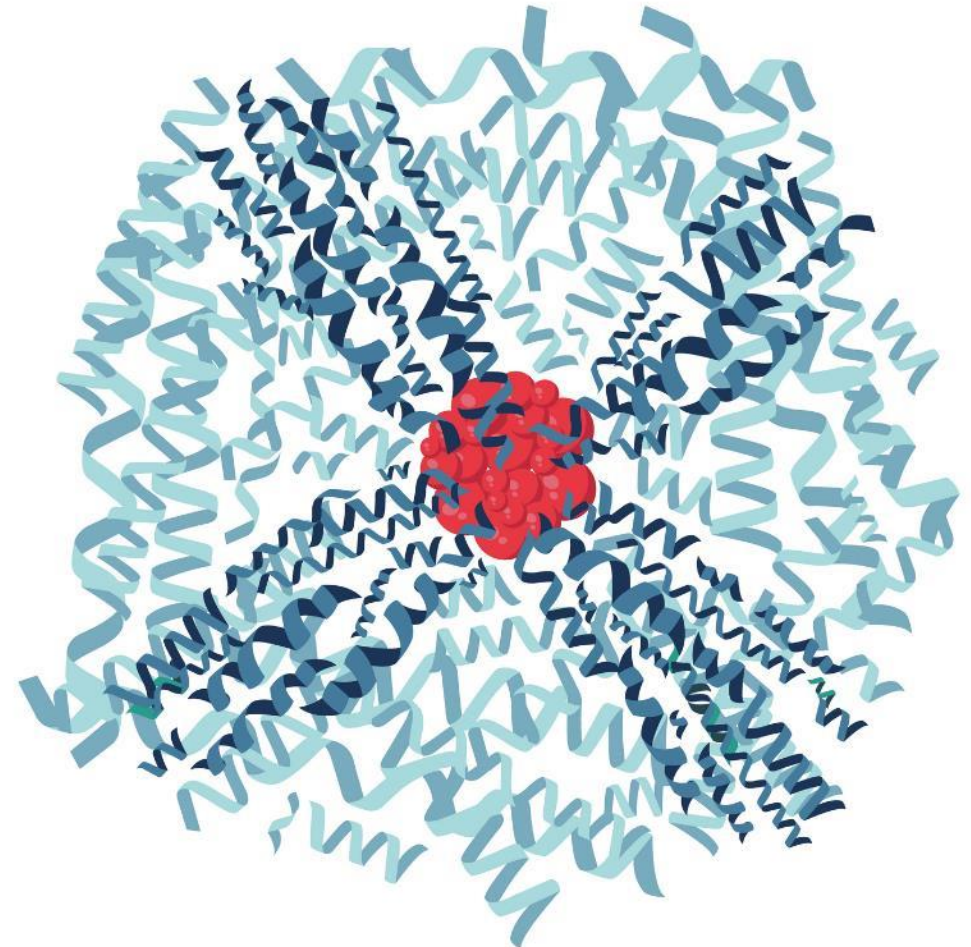
Most life scientists would agree that understanding how cellular processes work requires structural knowledge about the macromolecules involved. For example, deciphering the double-helical nature of DNA revealed essential aspects of how genetic information is stored, copied and repaired. Yet, being reductionist in nature, structural biology requires the purification of large amounts of macromolecules, often trimmed off larger functional units. The advent of cryogenic electron microscopy (cryo-EM) greatly facilitated the study of large, functional complexes and generally of samples that are hard to express, purify and/or crystallize. Nevertheless, cryo-EM still requires purification and thus visualization outside of the natural context in which macromolecules operate and coexist. Conversely, cell biologists have been imaging cells using a number of fast-evolving techniques that keep expanding their spatial and temporal reach, but always far from the resolution at which chemistry can be understood. Thus, structural and cell biology provide complementary, yet unconnected visions of the inner workings of cells. Here we discuss how the interplay between cryo-EM and cryo-electron tomography, as a connecting bridge to visualize macromolecules in situ, holds great promise to create comprehensive structural depictions of macromolecules as they interact in complex mixtures or, ultimately, inside the cell itself.



# The Heavy Subunit of Ferritin Stimulates NLRP<sub>3</sub> Inflammasomes in Hepatic Stellate Cells Through ICAM-1 to Drive Hepatic Inflammation

Fernandez-Rojo et.al., *Science Signaling*, April 2, 2024 (excerpt)

Serum ferritin concentrations increase during hepatic inflammation and correlate with the severity of chronic liver disease. Here, we report a molecular mechanism whereby the heavy subunit of ferritin (FTH) contributes to hepatic inflammation. We found that FTH induced activation of the NLRP<sub>3</sub> inflammasome and secretion of the proinflammatory cytokine interleukin-1 $\beta$  (IL-1 $\beta$ ) in primary rat hepatic stellate cells (HSCs) through intercellular adhesion molecule-1 (ICAM-1). FTH-ICAM-1 stimulated the expression of Il1b, NLRP<sub>3</sub> inflammasome activation, and the processing and secretion of IL-1 $\beta$  in a manner that depended on plasma membrane remodeling, clathrin-mediated endocytosis, and lysosomal destabilization. FTH-ICAM-1 signaling at early endosomes stimulated Il1b expression, implying that this endosomal signaling primed inflammasome activation in HSCs. In contrast, lysosomal destabilization was required for FTH-induced IL-1 $\beta$  secretion, suggesting that lysosomal damage activated inflammasomes. FTH induced IL-1 $\beta$  production in liver slices from wild-type mice but not in those from *Icam1*<sup>-/-</sup> or *Nlrp3*<sup>-/-</sup> mice. Thus, FTH signals through its receptor ICAM-1 on HSCs to activate the NLRP<sub>3</sub> inflammasome. We speculate that this pathway contributes to hepatic inflammation, a key process that stimulates hepatic fibrogenesis associated with chronic liver disease.



Ferritin Molecule

# Obesity Sector Update



# Metsera Funded With \$350 Million for Obesity

**Andrew Dunn, *Endpoints News*, April 3, 2024 (excerpt)**

Funded with \$350 million from top-tier VCs and led by a veteran pharma CEO, a new obesity startup called Metsera has been quietly building plans to get multiple drugs into the clinic over the next two years, *Endpoints News* has exclusively learned.

Metsera's CEO is Clive Meanwell, the former chief executive of The Medicines Company. The company was incorporated in 2022 by Population Health Partners, an investment firm started in 2020 by Meanwell and former Pfizer CEO Ian Read.

Operating in stealth mode, Metsera has in-licensed six obesity drug candidates from a Korean biotech, acquired a London-based biotech, and is targeting up to seven IND filings over the next 12 to 24 months. *Endpoints* pieced together Metsera's operations in the red-hot weight loss space through US and global legal filings, Korean press releases that outline the licensing deals, recent job postings, and an in-development-but-public-facing version of the startup's website. (After *Endpoints* reached out to Metsera, a password-protected login was added to access the site).

The young company has raised what could be one of biotech's biggest funding rounds of 2024 from some of biotech's highest-profile investors. The website describes Population Health and ARCH Venture Partners as its founders, with additional investors including GV, F-Prime Capital, Exor Ventures, Mubadala, Newpath Partners, SoftBank, the Abu Dhabi Investment Authority, and Americo. Metsera has raised \$250 million along with "an additional \$100 million committed from new and existing investors," according to a recent job opening description reviewed by *Endpoints*.

Source: <https://endpts.com/new-obesity-biotech-metsera-jumps-into-weight-loss-race-with-350m-in-vc-backing/>

**Clive Meanwell**

*Chief Executive Officer*

Metsera



# D&D Pharmatech, Metsera Expand Collaboration for New Obesity, MASH Treatments

**Lee-Han Soo, *Korea Biomedical Review*, March 18, 2024 (excerpt)**

D&D Pharmatech, a Korean biotech company, said it expanded its collaboration with the U.S.-based Metsera for new treatments.

This expansion includes amendments to a previously established agreement for an oral obesity treatment and the initiation of a new global technology transfer agreement for an injectable treatment targeting obesity and MASH (metabolic associated severe hepatopathy).

The original agreement covered the global technology transfer of D&D Pharmatech's peptide oral technology, ORALINK™, applied to obesity treatments DDo2S and DDo3, and METo6 for 550 billion won (\$412.1 million) in April of last year.

The updated agreement now includes the oral GLP-1/GIP dual agonist DD14 and oral amylin agonist DDo7, increasing the total possible license out fee by an additional 220 billion won to a total of 770 billion won.

DD14 is being developed as an oral formulation to enhance patient convenience over Eli Lilly's injectable obesity treatment, Zepbound, a GLP-1/GIP dual agonist. DDo7, an amylin receptor agonist previously approved for type 2 diabetes treatment, has shown potential for weight loss, especially when combined with GLP-1 agonists. In a separate move, D&D Pharmatech and Metsera have also entered into a new agreement for the global license of the injectable triple-G (GLP-1/GIP/GCG triple agonist) DD15, valued at approximately 280 billion won.

DD15, leveraging D&D Pharmatech's long-acting technology, aims to offer multifaceted benefits such as increased satiety, improved glycemic control, and enhanced fat breakdown, showcasing its potential not only as an obesity treatment but also for MASH.

D&D Pharmatech will continue preclinical development necessary for Investigational New Drug (IND) submissions, while Metsera will support all related costs, promising stable revenue generation for D&D Pharmatech beyond milestone payments.

"This expansion of the technology transfer items is believed to be the result of the mutual trust demonstrated through the joint research and development process between the two companies over time," D&D Pharmatech CEO Lee Seul-ki said. "Notably, based on D&D Pharmatech's early-stage material research and development know-how and Metsera's substantial financial support, we are committed to doing our best to grow into a leading company in the next-generation obesity treatment market by simultaneously advancing multiple product groups into clinical trials."

# They Thought Ozempic Would Help Them Lose Weight. It Didn't Work.

Sumathi Reddy, *Wall Street Journal*, April 1, 2024 (excerpt)

Behind the blockbuster success of drugs like Ozempic and Wegovy is a less-noticed phenomenon: Some people don't lose much weight on them.

There is wide variation in weight loss on these types of drugs, called GLP-1s. Doctors say roughly 10% to 15% of people who try them are “non-responders,” typically defined as those who lose less than 5% of their body weight. These patients, doctors say, don't experience enough appetite reduction to result in significant weight loss.

Researchers are studying why some people drop a lot of weight on them while others lose little. The answers might yield broader clues about weight loss and provide more insight into these medications, which have transformed the way Americans lose weight.

Doctors believe some people might be resistant to the drugs as a result of genetic differences. Other possible reasons could include certain medical conditions and medications, how much weight a person lost before taking the drugs, and differences in how people metabolize them.

## Wide range of weight loss

In a trial for the drug semaglutide—marketed as Wegovy and Ozempic—about 14% of patients lost less than 5% of their body weight. About a third lost less than 10%. In a trial for tirzepatide, sold as Mounjaro and Zepbound, 9% of people lost less than 5% of their body weight and 16% lost less than 10%.

Even among those who lost weight, amounts ranged from around 5% to upward of 20%.

“There's going to be extreme variability in how people respond,” says Dr. Eduardo Grunvald, an obesity-medicine physician at UC San Diego Health.

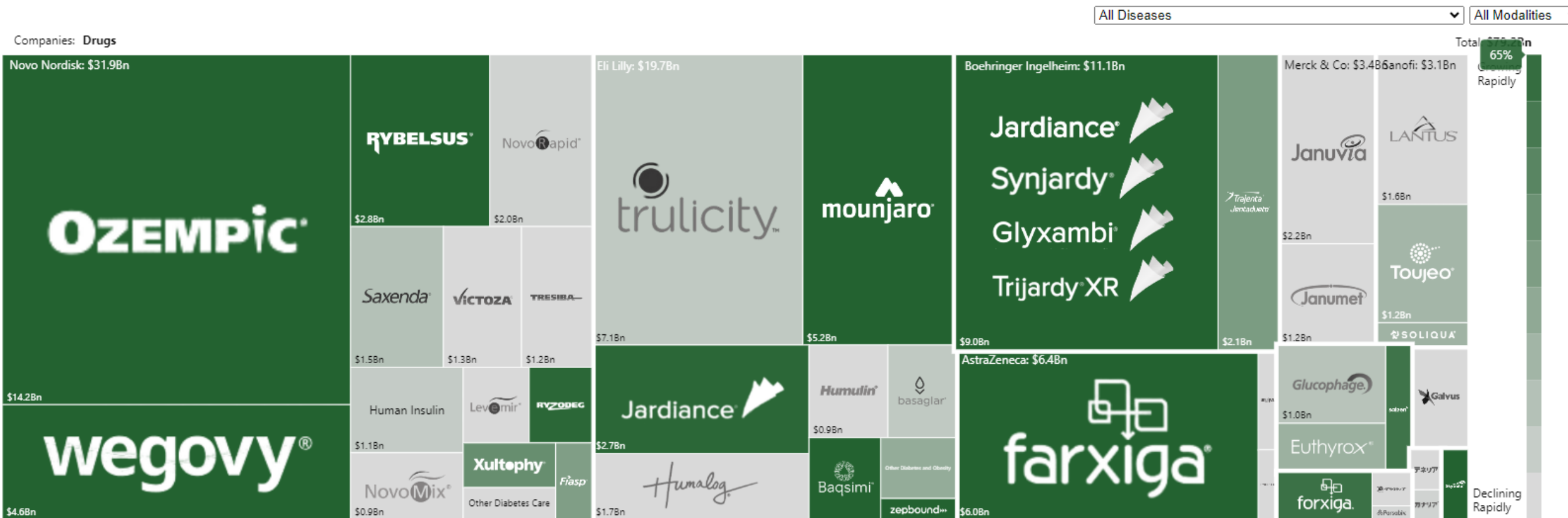
Source: <https://www.wsj.com/health/pharma/ozempic-weight-loss-drug-ineffective-why-6d7059bb>



# Pharma Obesity, Diabetes and Endocrinology Revenue > \$70Bn Last Year

## Obesity, Diabetes and Endocrinology, Market Map, 2023

Includes Branded Rx Drugs Only by Revenue



Source: PharmaSights (<https://www.pharmasights.com/>)



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