

First Half Market Review – July 2023

STIFEL | Healthcare

Table of Contents

Section	Page
Biotech Sector Update	5
RA Capital View of Biotech Sector	24
Large Cap Pharma is Evolving Fast	32
The IPO Market	47
The Follow-On Equity Market	57
Venture Equity Market	62
Private Debt & Royalty Market	71
Venture Fund Capital Raising	76
Partnership Deal Environment	79
Mergers and Acquisitions Environment	97



Life Sciences Market: H1 2023

Innovation is the Ultimate Market Fundamental

The last 18 months have been an exceptionally difficult time for the life sciences industry. With the end of the Pandemic, we have seen many life science companies struggle in the capital markets while simultaneously dealing with layoffs, macroeconomic headwinds and a less than helpful political environment.

We remain optimistic about the environment going forward. To begin, we are seeing robust recoveries this year in the follow-on equity market and the M&A market (charts at right). This is great news as both strategic players and major investors are clearly committed to the market.

The underlying fundamentals of the sector could not be more positive. We have seen numerous medical breakthroughs this year, pathbreaking scientific discoveries and patients everywhere benefitting from novel modalities, medicines, diagnostics and devices.

We at Stifel see the market recovery continuing, if at times in fits and starts, through the rest of 2023. We encourage you to be steadfast in understanding that this market recovery will not be deterred, as it is driven by the ultimate fundamental: delivering highly innovative life sciences products to patients.

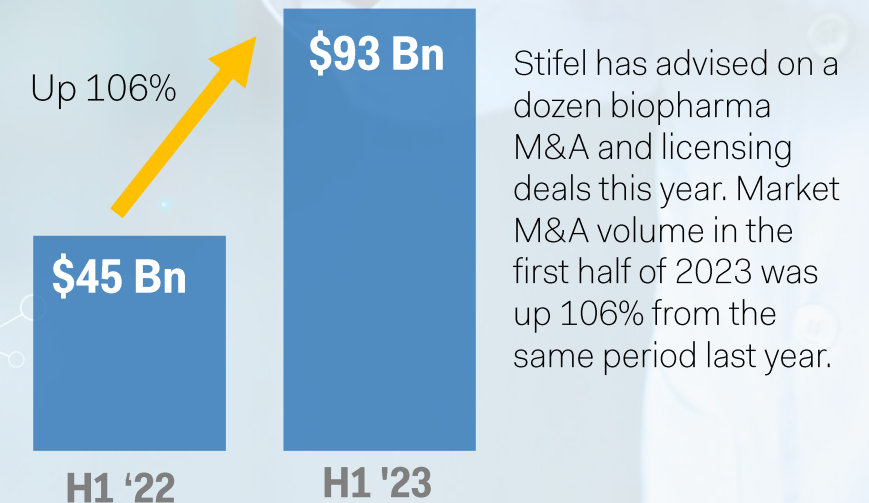
Note: Details and sourcing on the M&A and follow-on data are provided inside this presentation.

Stifel Market Observations

U.S. Biotech Follow-On Recovery in H1 2023



Robust Biopharma M&A Volume Recovery in 2023



<p>£16,700,000</p> <p>Yourgene Health</p> <p>Potential Sale</p> <p>Advisor to Seller Ongoing</p>	<p>\$64,474,282</p> <p>immunome</p> <p>Has Agreed to Merge with</p> <p>morphimmune</p> <p>Advisor to Buyer Pending</p>	<p>WraSer PHARMACEUTICALS</p> <p>Has Agreed to Sell Certain Assets to</p> <p>blue water biotech</p> <p>Advisor to Seller Pending</p>	<p>€154,430,010</p> <p>BIOCORP</p> <p>Has Agreed to be Acquired by</p> <p>novo nordisk</p> <p>Advisor to Seller Pending</p>	<p>\$60,000,000</p> <p>KAMADA</p> <p>PIPE</p> <p>Financial Advisor to the Special Committee of the Board of Directors Pending</p>	<p>cyclerion</p> <p>Has Agreed to Sell Certain Assets to</p> <p>NewCo</p> <p>Advisor to Seller Pending</p>	<p>MEI Pharma</p> <p>Has Agreed to Merge with</p> <p>Infinity PHARMACEUTICALS</p> <p>Financial Advisor Pending</p>	<p>erytech</p> <p>Has Merged with</p> <p>PHERECYDES PHARMA</p> <p>Financial Advisor June 2023</p>	<p>Ongoing</p> <p>UPSHER-SMITH</p> <p>Divestiture of Assets</p> <p>TONIX PHARMACEUTICALS</p> <p>Advisor to Seller June 2023</p>	<p>\$120,000,000</p> <p>Igm Biosciences, Inc.</p> <p>Confidentially Marketed Follow-on Offering Joint Bookrunning Manager June 2023</p>	<p>\$210,000,000</p> <p>aeglea</p> <p>PIPE</p> <p>Joint Placement Agent June 2023</p>
<p>\$157,780,000</p> <p>disc)medicine</p> <p>Follow-on Offering Joint Bookrunning Manager June 2023</p>	<p>\$200,000,000</p> <p>TRICIDA</p> <p>Chapter 11 Restructuring</p> <p>Investment Banker for Tricida Inc. June 2023</p>	<p>\$575,000,000</p> <p>IONIS</p> <p>Convertible Senior Notes</p> <p>Co-Manager June 2023</p>	<p>\$65,023,725</p> <p>X4 PHARMACEUTICALS</p> <p>PIPE</p> <p>Co-Lead Placement Agent May 2023</p>	<p>Up to \$600,000,000</p> <p>LaNova 礼新医药</p> <p>Out-Licensing of LM-305 to</p> <p>AstraZeneca</p> <p>Advisor to Licensor May 2023</p>	<p>\$100,000,000</p> <p>HILLEVAX</p> <p>At-the-Market Offering</p> <p>Sole Agent Commenced May 2023</p>	<p>\$350,000,000</p> <p>ARCELLX</p> <p>At-the-Market Offering</p> <p>Sole Agent Commenced May 2023</p>	<p>£176,000,000</p> <p>30 TECHNOLOGY Antimicrobial Nitric Oxide Platform</p> <p>Has Been Acquired by</p> <p>convatec</p> <p>Financial Advisor April 2023</p>	<p>\$50,000,000</p> <p>daré bioscience</p> <p>At-the-Market Offering</p> <p>Joint Agent Commenced March 2023</p>	<p>STERICON</p> <p>Has Been Acquired by</p> <p>NIRMA</p> <p>Advisor to Seller March 2023</p>	<p>\$460,000,000</p> <p>KARUNA THERAPEUTICS</p> <p>Follow-on Offering Joint Bookrunning Manager March 2023</p>
<p>\$150,000,000</p> <p>DICC</p> <p>At-the-Market Offering</p> <p>Joint Placement Agent Commenced March 2023</p>	<p>Dr.Reddy's</p> <p>Has Sold Certain Assets to</p> <p>Eris ERIS LIFESCIENCES LIMITED</p> <p>Advisor to Seller March 2023</p>	<p>\$220,800,000</p> <p>MINERALYS</p> <p>Initial Public Offering Joint Bookrunning Manager February 2023</p>	<p>RICBT OneCBT</p> <p>Has Been Acquired by</p> <p>REFRESH Mental Health</p> <p>Advisor to Seller February 2023</p>	<p>\$115,000,000</p> <p>TREACE Medical Concepts, Inc.</p> <p>Confidentially Marketed Follow-on Offering Joint Bookrunning Manager February 2023</p>	<p>\$20,300,000</p> <p>renalytix</p> <p>PIPE</p> <p>Sole Placement Agent and Nomad February 2023</p>	<p>FREELINE</p> <p>CMC-focused Subsidiary in Germany and Certain IP Has Been Acquired by</p> <p>ascend gene & cell therapies</p> <p>Advisor to Seller February 2023</p>	<p>ApicBio</p> <p>Out-license of APB-102</p> <p>uniQure</p> <p>Advisor to Licensor February 2023</p>	<p>\$227,843,965</p> <p>geron</p> <p>Follow-on Offering Joint Bookrunning Manager January 2023</p>	<p>Up to \$30,000,000</p> <p>MINA Therapeutics</p> <p>Debt Private Placement</p> <p>Sole Financial Advisor January 2023</p>	<p>ayaia pharmaceuticals</p> <p>Has Been Acquired by</p> <p>ADVAXIS IMMUNOTHERAPIES™</p> <p>Advisor to Seller January 2023</p>

All transaction announcements appear as a matter of record only. Stifel collectively refers to Stifel, Nicolaus & Company, Incorporated and other affiliated broker-dealer subsidiaries of Stifel Financial Corp. Unless otherwise indicated, information presented herein with respect to the experience of Stifel also includes transactions effected and matters conducted by companies acquired by Stifel, including, but not limited to the acquisition of Torreya Capital LLC and its affiliated entities.

Biotech Sector Update



Biotech Stocks Flat in the First Half of 2023

The XBI closed last Friday June 30th at 83.2. At the start of the year, it was 83.0. Basically, the XBI has not changed despite a set of extraordinarily positive clinical developments. In contrast, the S&P 500 Index rose 15.9% in the first half on the back of a strong rally in AI-driven tech stocks. As of July 6th close (Thursday), the XBI had dropped to 81.7.

Biotech Stocks Down Last Week

Return: June 26 to June 30, 2023

Nasdaq Biotech Index: -1.6%

Arca XBI Index: -2.26%

Stifel Global Biotech (EV): +0.4%

S&P 500: +2.3%

Return: Jan 1 to June 30, 2023

Nasdaq Biotech Index: -3.2%

Arca XBI Index: 0.2%

Stifel Global Biotech: +3.4%*

S&P 500: +15.9%

* Change by enterprise value of R&D stage public therapeutics players worldwide. Not an index. Impacted by entry of Acelyrin and exits of Bellus and Prometheus. If adjusted out, would be up 7% for year.

VIX Flat Last Week

Oct 21: 29.7%

Jan 20: 19.9%

Mar 17: 24.6%

May 26: 18.0%

June 9: 13.7%

June 16: 13.5%

June 23: 13.4%

June 30: 13.6%

10-Year Treasury Yield Up

Oct 21: 4.2%

Jan 20: 3.48%

Mar 17: 3.39%

May 26: 3.8%

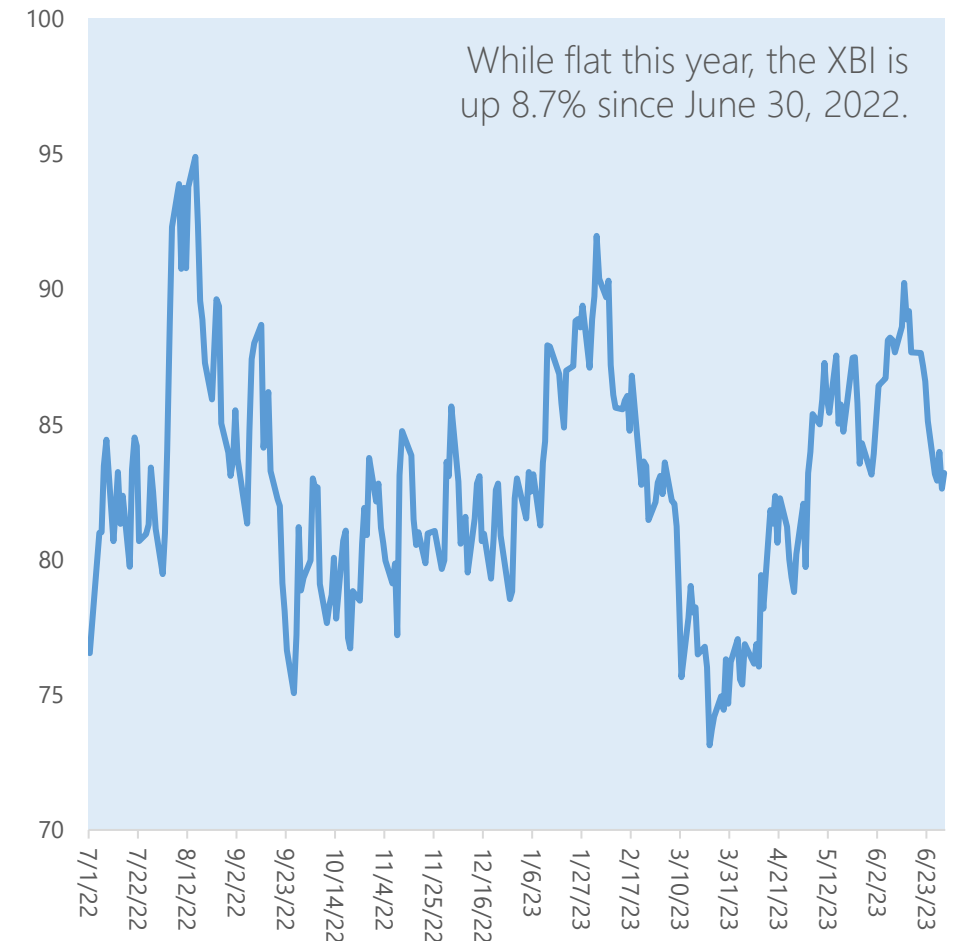
June 9: 3.75%

June 16: 3.77%

June 23: 3.74%

June 30: 3.81%

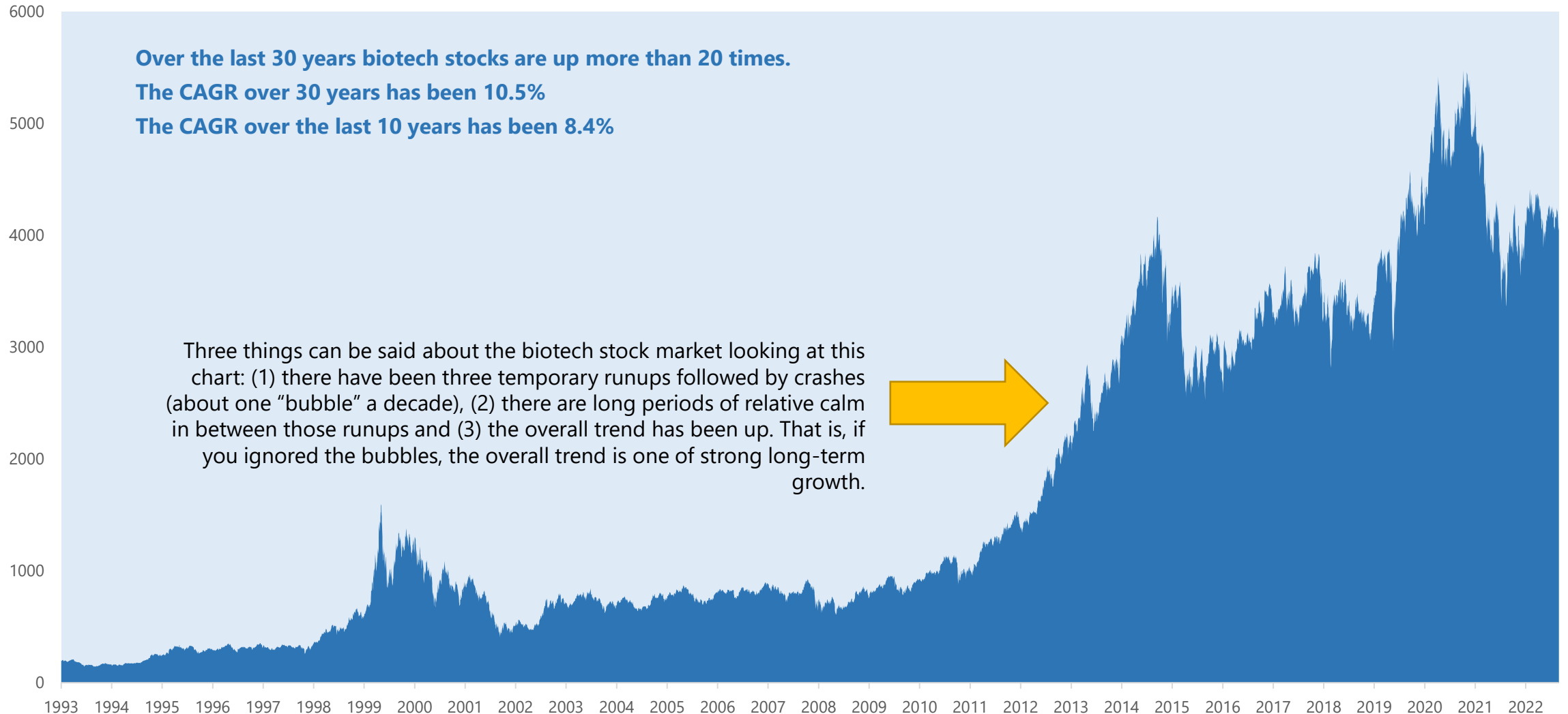
XBI Index, July 1, 2022 to June 30, 2023



Source: S&P Capital IQ and Stifel analysis

The Long View: Biotech Up Big

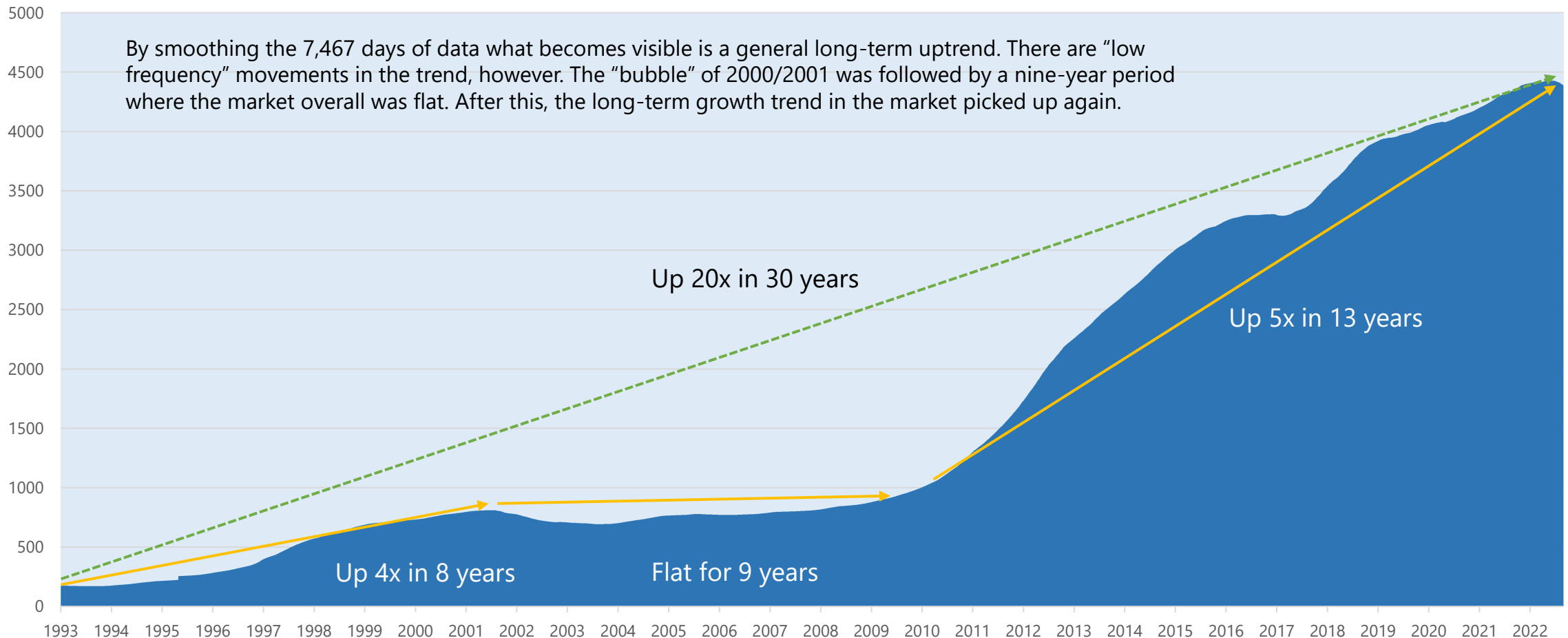
Nasdaq Biotech Index (NBI), Nov 1993 to June 2023



Smoothed Look at 30 Years of NBI Data

When one looks at the underlying market trend, it's very clear that biotech investing involves a long-term uptrend. But one must be prepared for occasional long periods of flat performance.

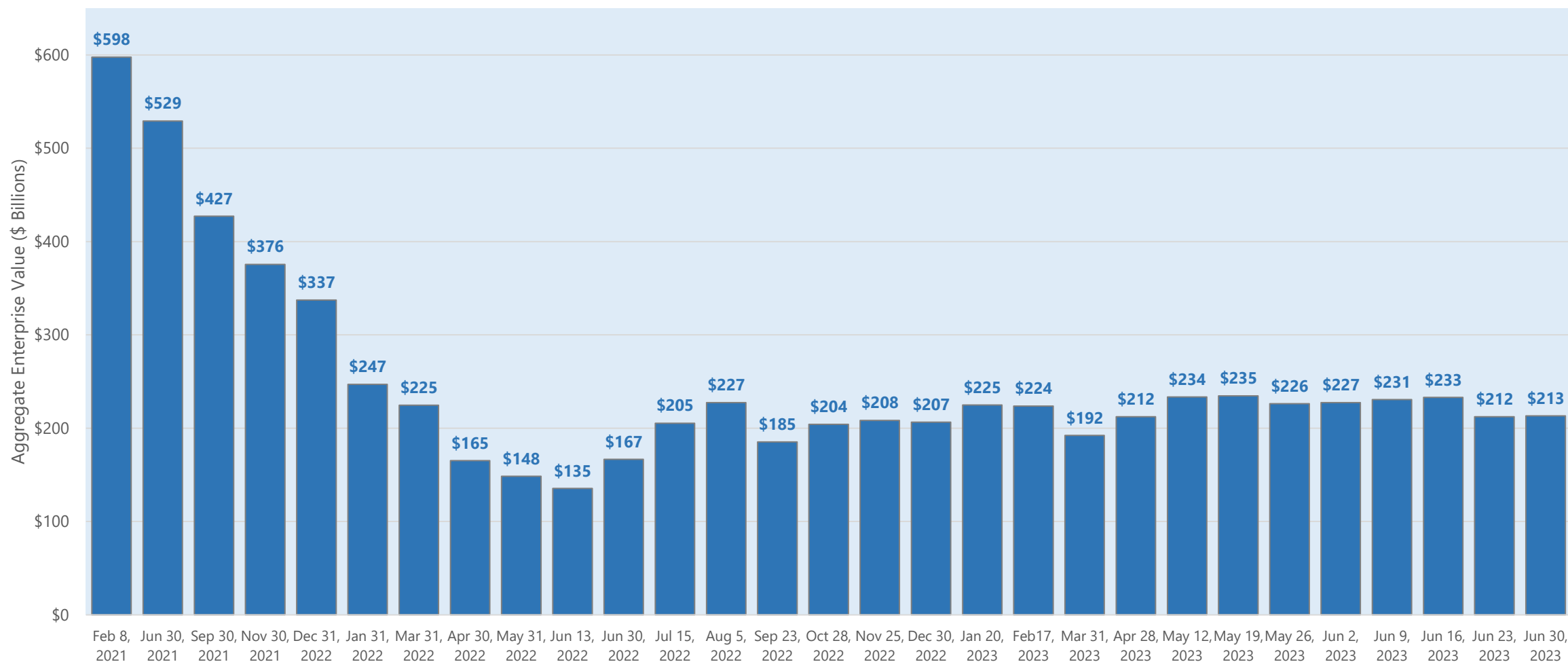
Nasdaq Biotech Index, Centered Moving Average of 1200 Days, Nov 1993 to June 2023



Total Global Biotech Sector Valuation Up Last Week

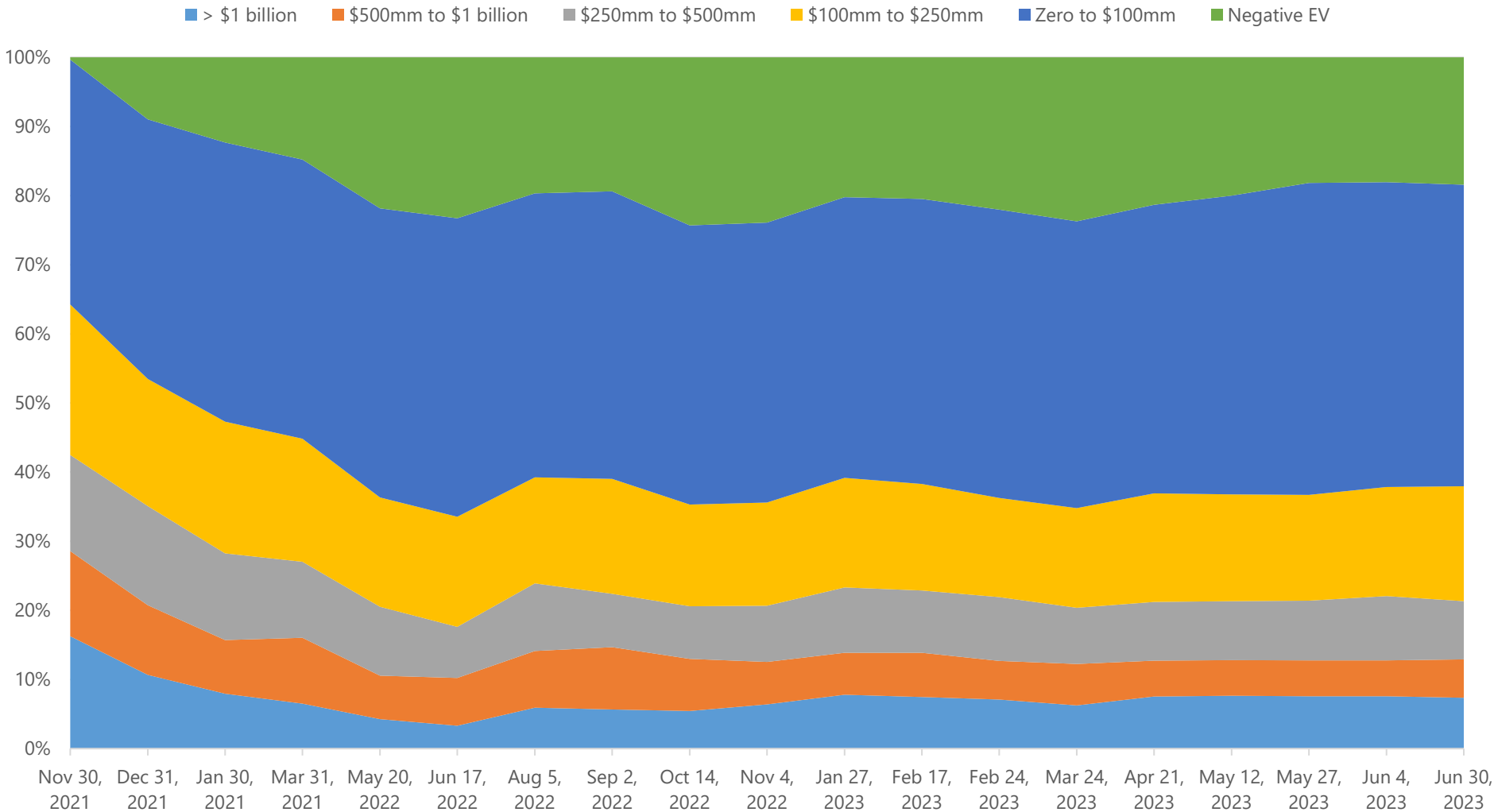
The total value of the global biotech sector was up 3.4% in the first half despite a significant number of disappearances including Bellus and Prometheus. Overall, the sector is performing flat to well.

Total Enterprise Value of Publicly Traded Global Biotech, Feb 8, 2021 to Jun 30, 2023 (\$ Billions)



Biotech Neighborhood Analysis

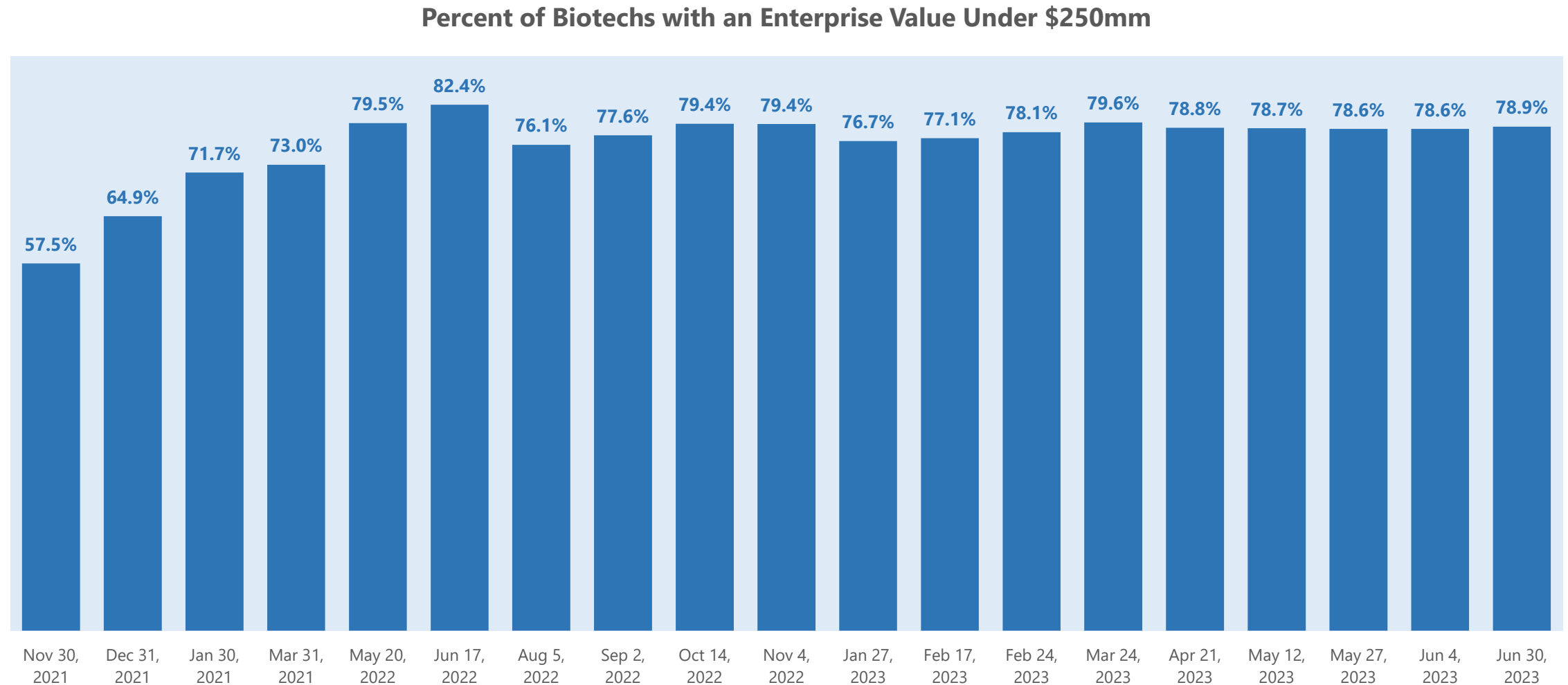
Global Biotech Universe by Enterprise Value Category, Nov 30, 2021 to Jun 30, 2023



The global biotech populations at both extremes are shrinking. There are fewer negative EV biotechs today and fewer valued over \$1 billion.

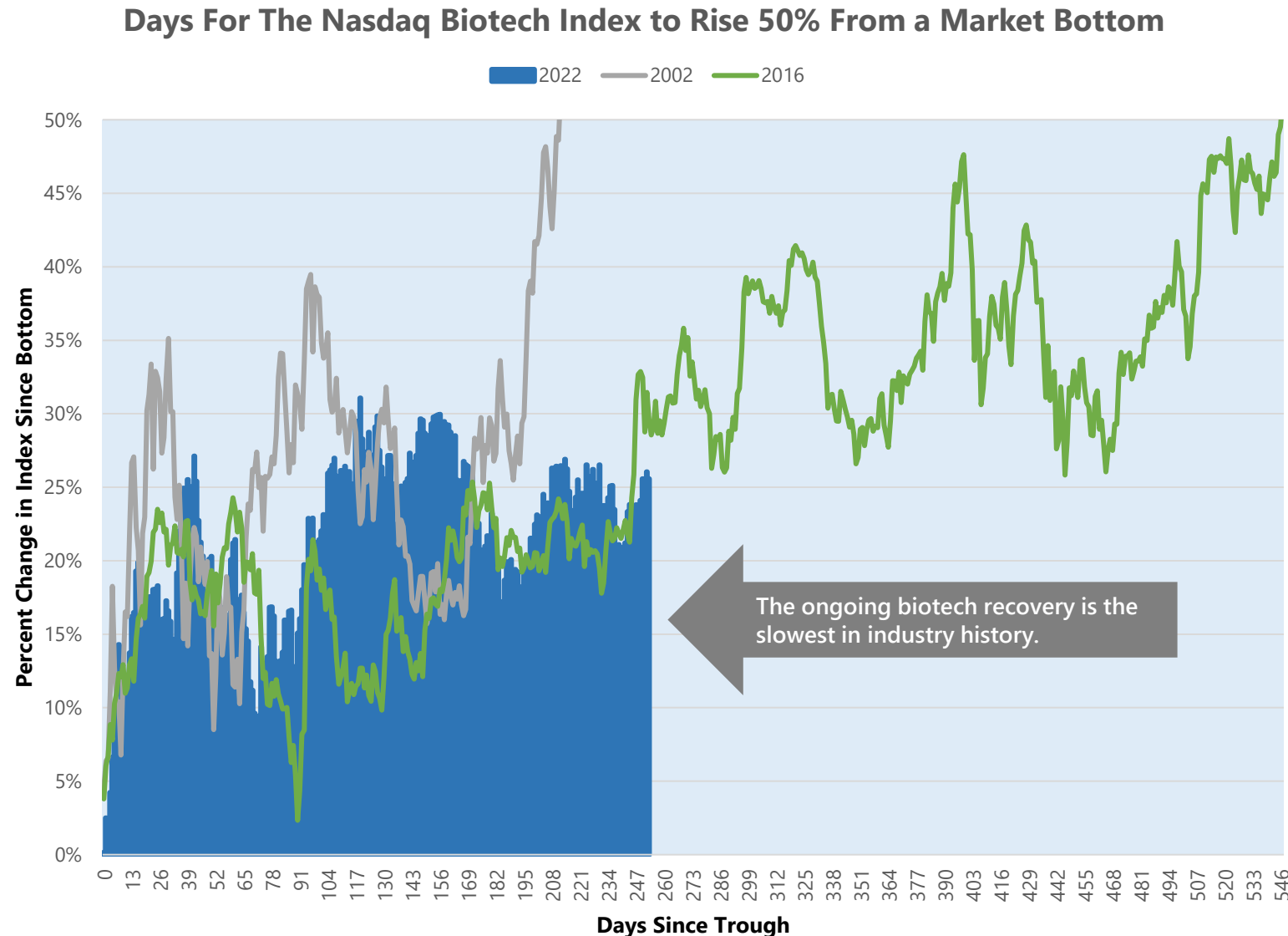
The biggest growth has been in companies with an EV between \$100mm and \$250mm. This group's census is up 10% in size since May 27th.

Percentage of Global Biotechs Trading Under \$250mm Steady



Source: CapitalIQ

Biotech Recovery To Date Weak by Historic Standards



Source: CapitalIQ, Stifel Analysis.

It's been 253 trading days since we saw the trough of this downturn (June 2022).

Compared to the market recoveries seen after other deep downturns in biotech in both 2002 and 2016 we are well behind in seeing the market come back. At this point following the 2016 downturn, the market was up 33% (versus 25% for the current market). Following the 2002 downturn the market had long since been up 50% or more (around day 200).

For whatever reason, we are seeing a substantially slower reaction to the market correction following the biotech bubble of 2021.

There are a lot of reasons that one could give to explain this. One is that AI in tech has taken off at the very moment that biotech should be reattracting generalist investors. Another is that there are just too many companies in the market, and it will take time to fund them all. Others might argue that it has become very difficult to play in the market as a generalist as the science has far more difficult for a non-expert investor to parse through effectively.

Biotech Condition by Country

Country	Firm Count	Total Enterprise Value (\$mm)			Balance Sheet Cash (\$mm)	Average Years of Burn	Percent Negative EV
		6/30/2023	12/30/2022	Change Over Last Six Months			
United States	433	\$123,655	\$108,034	14%	\$70,598	1.61	26%
South Korea	42	\$6,143	\$6,766	-9%	\$1,257	3.20	0%
United Kingdom	36	\$6,703	\$6,844	-2%	\$3,017	1.86	14%
China	35	\$24,260	\$31,304	-23%	\$10,859	6.25	26%
Sweden	35	\$3,522	\$3,919	-10%	\$653	1.99	9%
Canada	33	\$3,487	\$3,238	8%	\$1,999	1.42	15%
France	31	\$2,848	\$2,211	29%	\$990	1.16	6%
Taiwan	29	\$5,366	\$4,625	16%	\$720	3.62	10%
Australia	29	\$10,423	\$10,253	2%	\$1,280	4.90	0%
Japan	23	\$2,767	\$3,359	-18%	\$682	1.51	0%
Israel	16	\$564	\$203	178%	\$413	0.89	13%
Switzerland	14	\$7,320	\$2,944	149%	\$2,616	1.15	7%
Germany	13	\$2,538	\$2,607	-3%	\$985	1.37	8%
Denmark	10	\$3,897	\$3,403	15%	\$813	0.96	20%
Norway	8	\$303	\$438	-31%	\$101	1.50	0%

Source: CapitalIQ and Stifel analysis. Top 15 countries by public company count included. Country is chosen based on location of headquarters rather than listing location.

U.S. biotech valuations have improved nicely since the year began but many have negative enterprise value and average burn is under two years. U.S. biotech today accounts for 58% of the total sector's value (up from 52% six months ago).

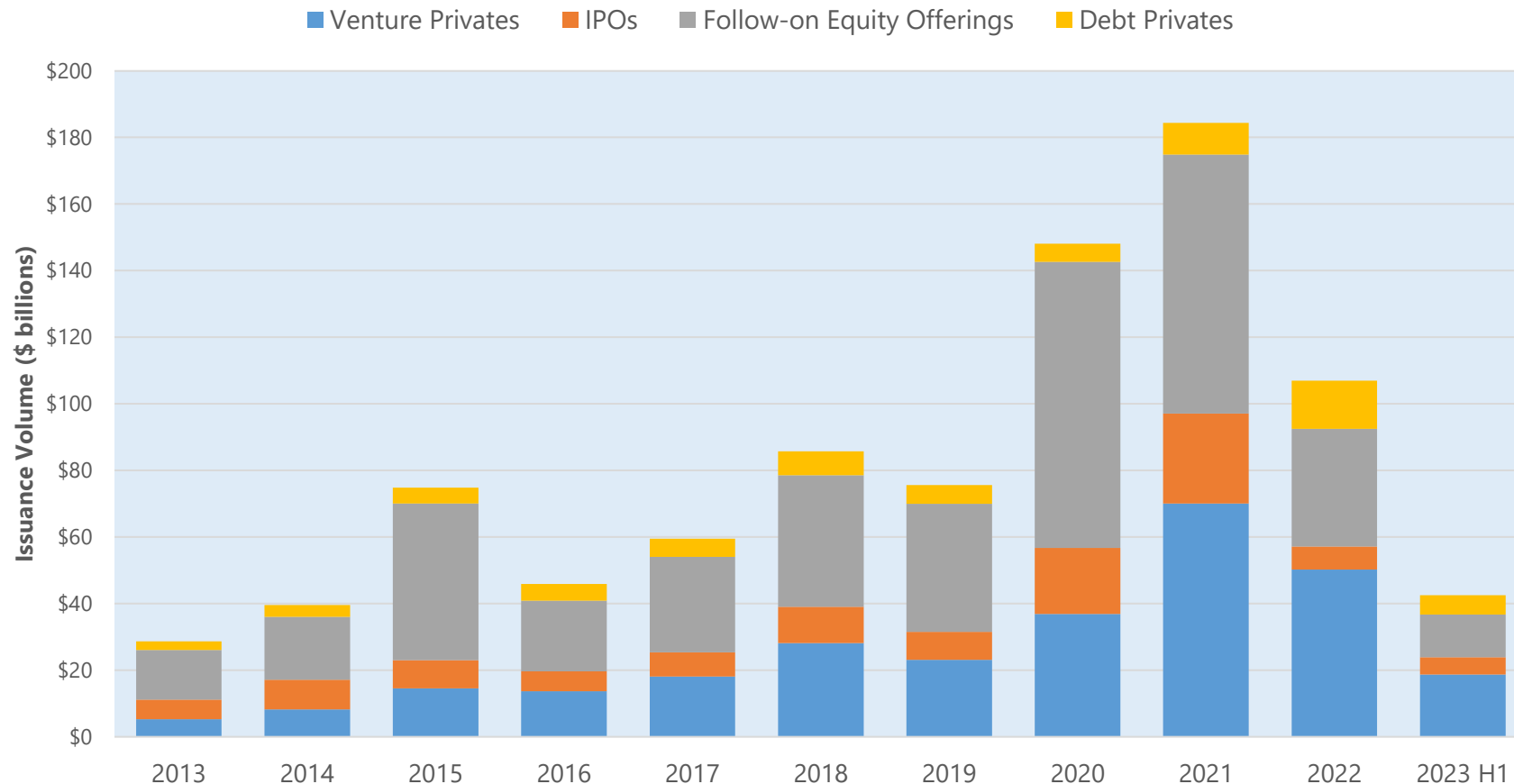
In contrast, the South Korea sector and the China sector are much better capitalized relative to burn. Biotechs in these countries run with *much less burn* than do U.S. companies.

The Chinese sector has numerous distressed companies today – which is indicated by fact that 26% have negative EV.

Both Israel and Switzerland have seen strong rebounds in their biotech sectors. Average remaining years of burn, however, in Switzerland is quite low – as it is in Denmark, France, Germany and Canada.

Overall Biopharma Capital Raised Thus Far in 2023 on an Annualized Basis Is Down 20.6% Versus 2022

Equity Raised, Private Debt Raised in the Biopharma Sector, 2013 - H1 2023 (\$ Billions, Worldwide)

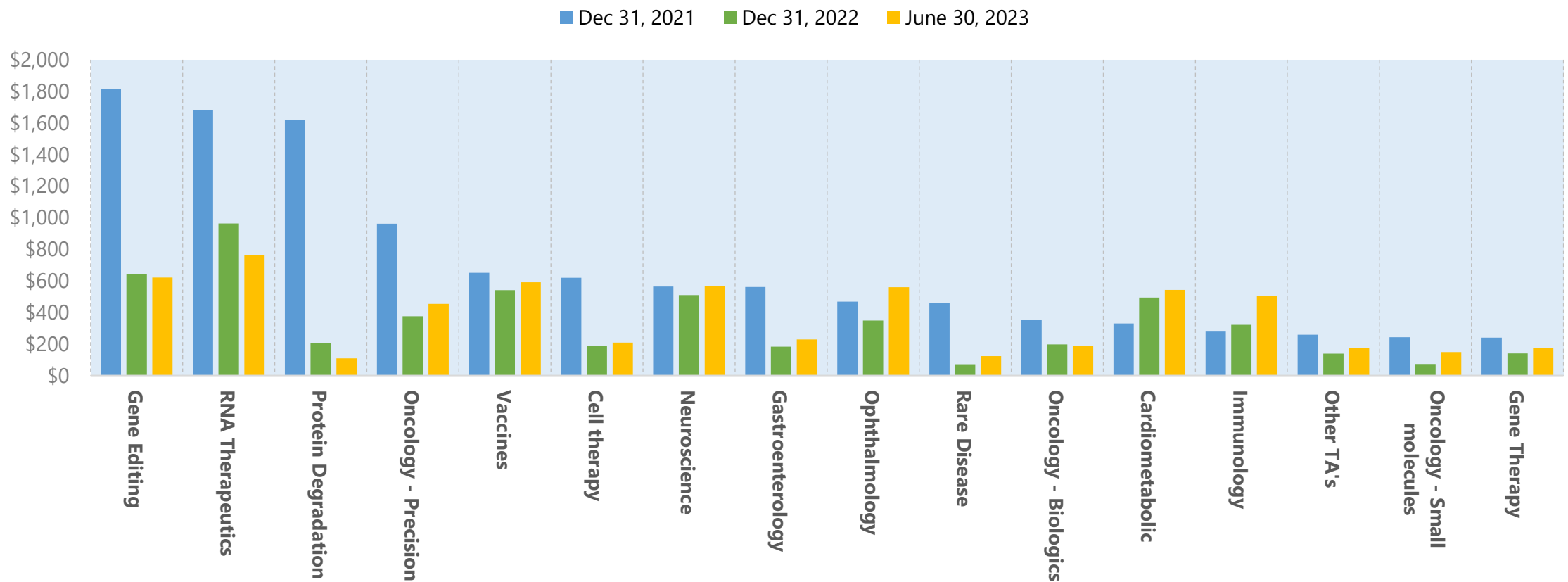


Venture privates' volume and follow-on equity volume this year has been down quite substantially compared to 2021 and 2022.

While signs of market improvement have appeared in recent months the markets have been softer in 2023 than in 2021 and 2022.

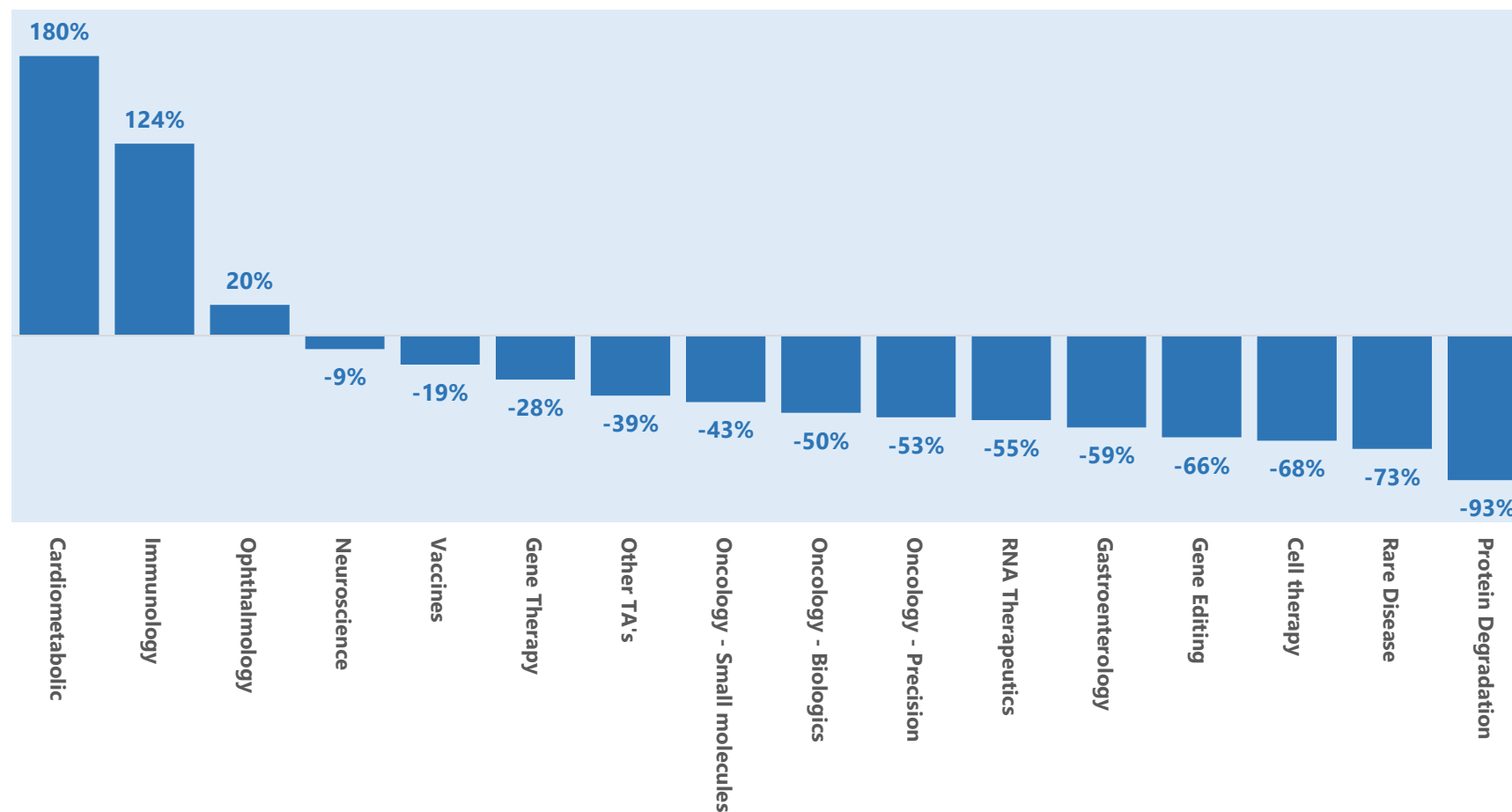
Biotech Valuations Down in Once “Hot” Areas Like Gene Editing, RNA Therapeutics, Protein Degradation and Precision Oncology. In Contrast, Immunology and Cardio Doing Well

Average Enterprise Value of U.S. Biotechs by Field, Dec 31, 2021 to June 30, 2023 (\$ millions)



Change in U.S. Biotech Average Valuations by Field Over the Last 18 Months

Percent Change in Average Enterprise Value of U.S. Domiciled Biotechs by Lead Asset Therapeutic Area / Modality, Dec 31, 2021 to June 30, 2023



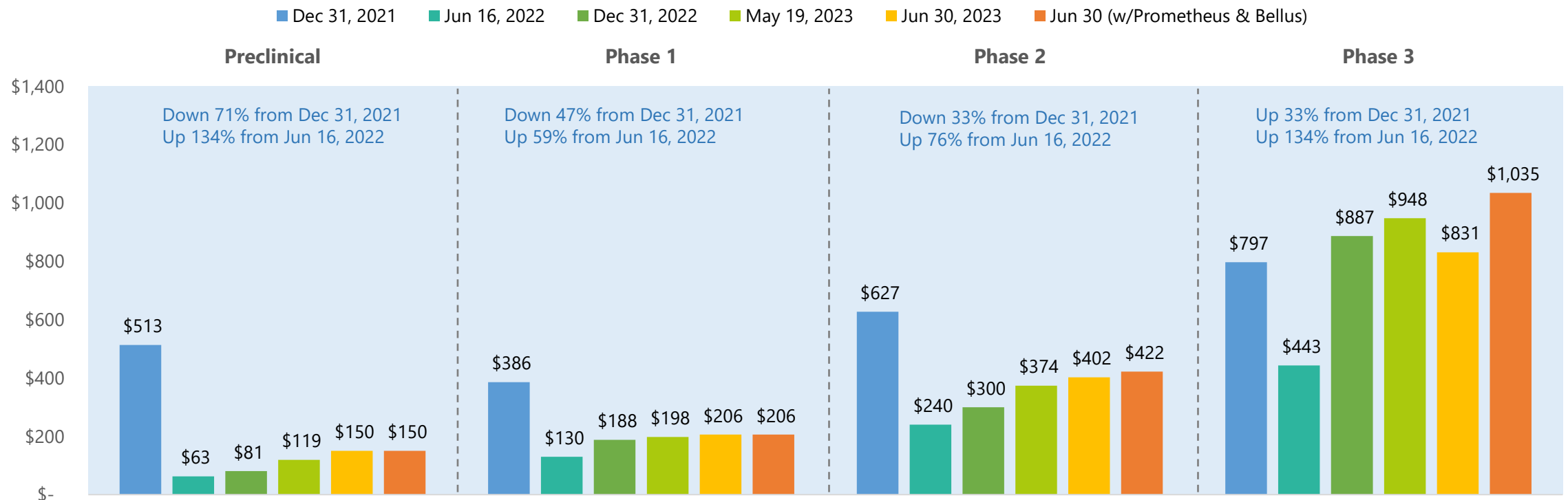
Investor's therapeutic tastes have changed quite a lot in the last 18 months.

In sympathy with pharma valuations and M&A interest, companies focused on cardiomatabolic disease and immunology have seen big jumps in value. In contrast, companies working in the fields of protein degradation, rare disease, cell therapy, gene editing, GI and RNA therapeutics have fared less well. There have also been major value declines in the field of oncology.

U.S. Biotech Average Valuations by Stage of Development of Lead Compound, Last 18 Months

Declines in value have been far greater for preclinical companies than those which are late stage. Early companies remain far below their Pandemic valuations. Phase 2 companies, on average, are also down from their Pandemic peak. In contrast, Phase 3 companies today are trading at higher levels. The recent exit of Prometheus at \$11bn substantially reduced the average value of the Phase 3 companies (there are only 35 in our dataset). Thus, we show the average Phase 3 value with and without Prometheus for comparison's sake.

Average Enterprise Value of a U.S. Domiciled Public Biotech by Last Completed Stage of Development, Dec 31, 2021 to June 30, 2023 (\$ Millions)

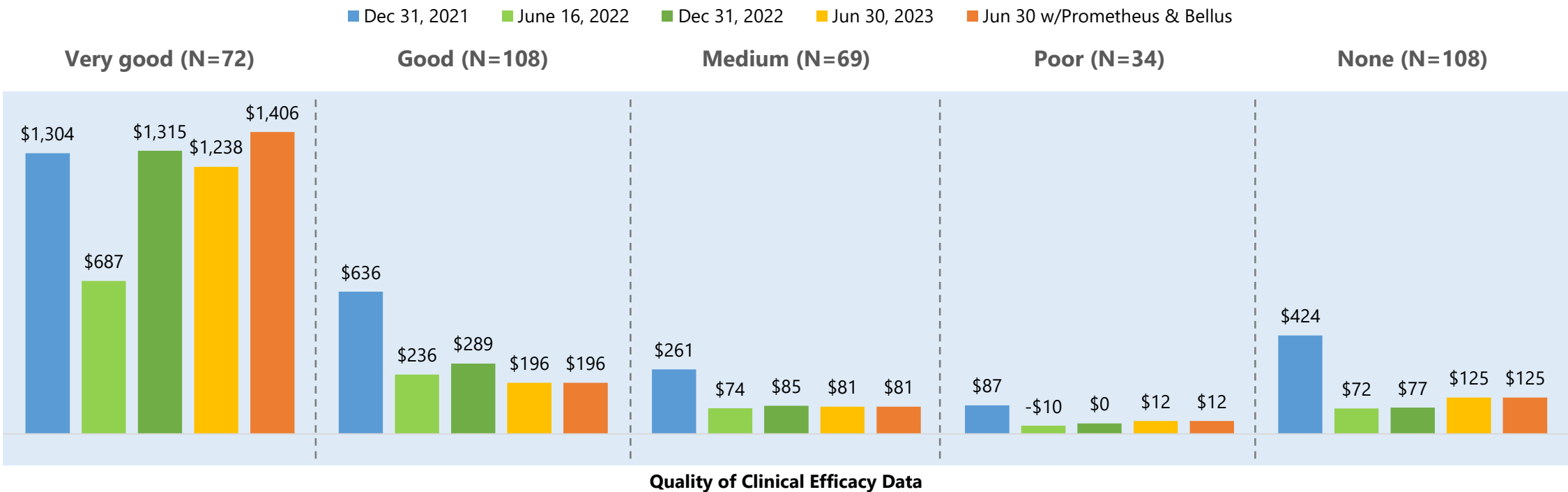


Notes: These data are sourced from CapitalIQ and based on Stifel research on the company's development stage. We required that the company have data in that stage. So, for example, if a company was dosing a Phase 1 study but had not yet reported data, we classified the company as preclinical.

U.S. Biotech Average Valuations by Quality of Data for Lead Compound, Last 18 Months

Companies with very good datasets have held their value since the Pandemic period. If anything, these companies are trading at historically high levels. Companies with good datasets are down almost 70% since the Pandemic peak. Similarly, those with medium quality, poor datasets or no data are down quite substantially. The companies recovering the most in 2023 those with no data. We are seeing quality platform companies that are early-stage bounce back quite a bit (think Beam, Sana, Verve etc.)

Average Enterprise Value of a U.S. Domiciled Public Biotech by Quality of Efficacy Data, Dec 31, 2021 to Jun 30, 2023 (\$ Millions)



Notes: These data are sourced from CapitalIQ and based on Stifel research on the dataset quality for a company's lead asset. We classified datasets that indicated a high probability that the drug would meaningfully improve on the standard of care for a disease as "very good". We classified "good" data as data that might beat the standard of care. Medium data was data that was unlikely to beat the standard of care, was very early or came from a study with a mixed signal. Poor data reflects situations where a drug did not perform well at all in a clinical trial.

The Market is Rewarding Late-Stage Companies with Great Datasets Even More than During the Pandemic. Those with Weaker Data or No Data Are Trading for Less Than Before

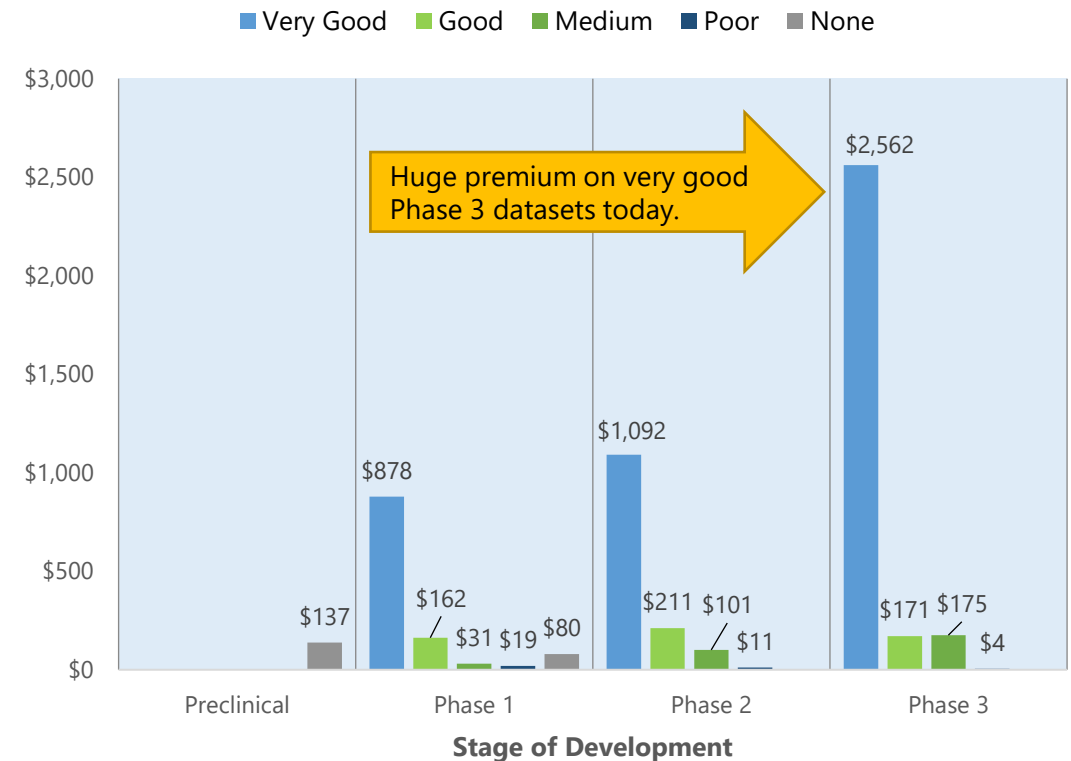
Peak of the Pandemic

Average Enterprise Value of a U.S. Domiciled Biotech by Stage of Development and Quality of Data, December 31, 2021 (\$ millions)



Today

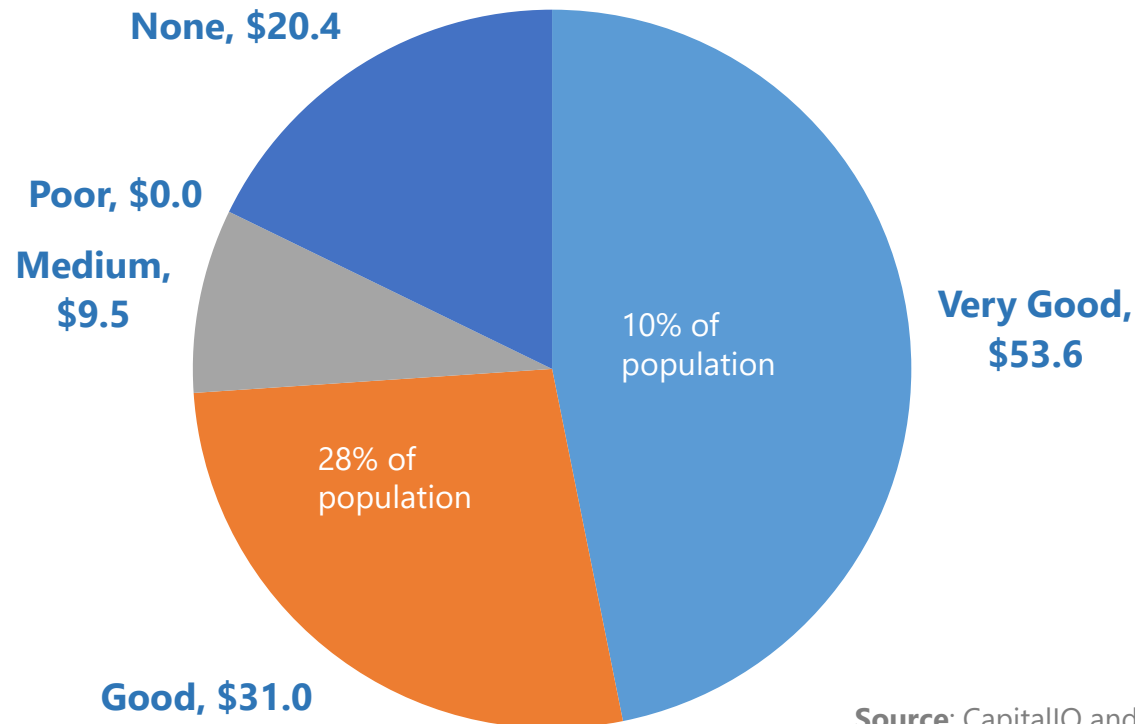
Average Enterprise Value of a U.S. Domiciled Biotech by Stage of Development and Quality of Data, June 30, 2023 (\$ millions)



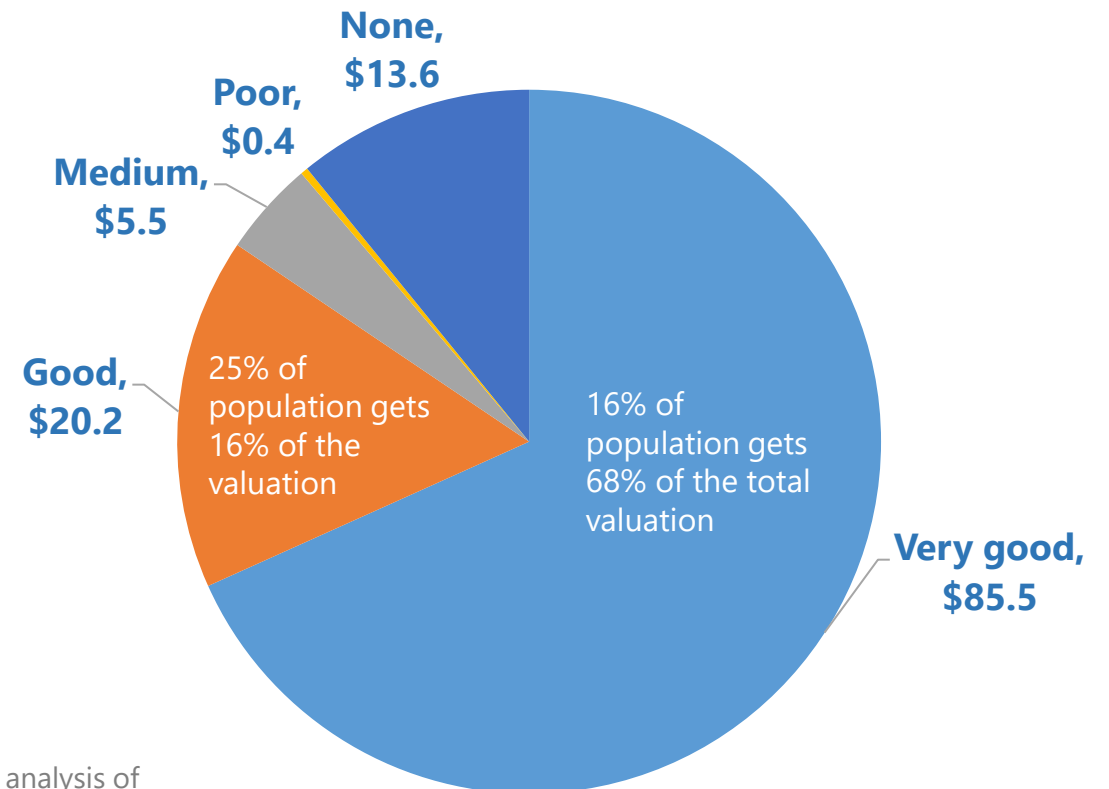
Data Quality is Very Important in Today's Biotech Market

Roughly 60 percent of the public U.S. biotech population has no clinical data yet, poor or medium quality clinical data. These companies get little of the value pie. In contrast, just 16% of the U.S. biotech population has a very good dataset (defined as clear clinical evidence of potential superiority over the standard of care for a disease) and enjoys 68% of the market's total valuation. What matters today can be summarized simply: "data, data, data".

Total Enterprise Value (\$ billions) of the U.S. Biotech Sector by
Quality of Dataset on Last Completed Stage of Development,
Nov 30, 2022



Total Enterprise Value (\$ billions) of the U.S. Biotech Sector
by Quality of Dataset on Last Completed Stage of
Development, June 30, 2023



Source: CapitalIQ and Stifel analysis of
company press releases.

Strong Class of \$2bn+ Valued U.S. Listed R&D-Stage Biotechs

This table shows U.S. listed biotechs with \$2bn or more in enterprise value. These value leaders largely have late-stage drug candidates for large markets with exceptional efficacy profiles. We doubt that we have ever had such a good group of leading U.S. biotechs.

 (EV = \$6.7bn)	 (EV = \$5.0bn)	 (EV = \$3.9bn)	 (EV = \$3.8bn)	 (EV = \$3.4bn)	 (EV = \$3.3bn)
 (EV = \$3.0bn)	 (EV = \$2.9bn)	 (EV = \$2.8bn)	 (EV = \$2.6bn)	 (EV = \$2.6bn)	 (EV = \$2.3bn)
 (EV = \$2.2bn)	 (EV = \$2.1bn)	 (EV = \$2.1bn)	 (EV = \$2.1bn)	 (EV = \$2.0bn)	

We count seventeen U.S. listed biotechs with an enterprise value today of \$2 billion or more. The total value of the group is \$53 billion – less than a sixth of the value of, say, Merck. The same portfolio was worth \$44 billion on Dec 31, 2022, and \$27 billion on June 30, 2022. This group has fifteen drugs in development that we rate today as having “very good” efficacy (incontrovertible data showing a clinical profile better than the current standard of care).^{*} Further, overwhelmingly the companies have peak sales estimates for the lead drug in excess of \$2 billion. Overall, the bar in today’s biotech market to fetch a high valuation is incredibly high. The market is discerning, and the quality of companies in the market is extraordinary. Incidentally, we published a similar list (a dozen companies) four months ago (Feb 27th). Two companies on that list (Prometheus and Iveric) were since targeted for acquisition.

^{*} Prothena and Revolution have yet to show PoC data for their lead programs.

Public Life Sciences Sector Value Up 3% Over Last Year

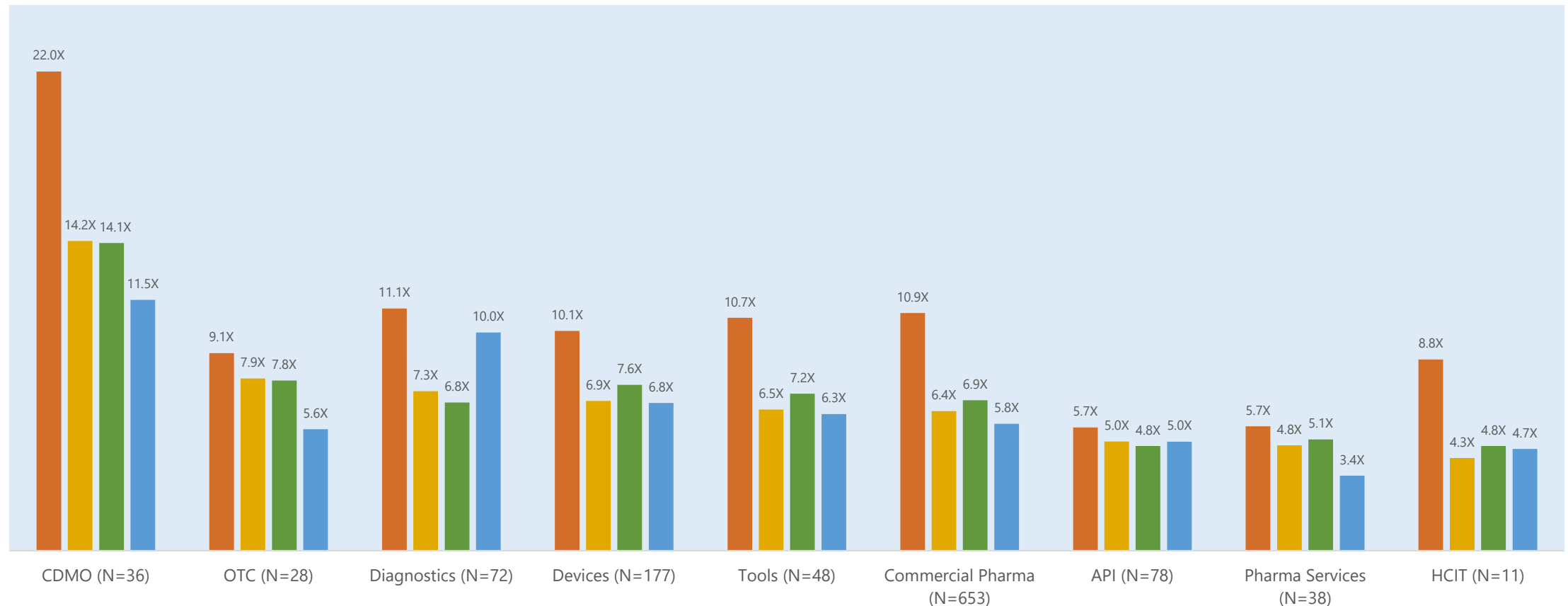
The aggregate enterprise value of the publicly traded life sciences sector is up 3.2% over the last year. The market recovery has been uneven with biotech value up 29% in a year while both pharma services and healthcare IT have traded down roughly 15%. We are also seeing robust recovery in valuations in the diagnostics and device field.

Sector	Firm Count	Enterprise Value (June 30, 2023, \$millions)	Change in Last Week (percent)	Change in Last Month (percent)	Change in Last Year (percent)
API	81	\$77,168	0.9%	-1.3%	-14.7%
Biotech	831	\$232,650	-1.6%	-4.9%	29.4%
CDMO / Manufacturing	40	\$166,066	-0.3%	-6.9%	-19.1%
Diagnostics	83	\$277,168	1.3%	1.3%	17.2%
OTC	32	\$30,807	1.1%	3.0%	16.0%
Pharma	726	\$5,833,055	-0.3%	-0.2%	3.3%
Pharma Services	41	\$206,878	2.5%	1.6%	-15.4%
Life Science Tools	54	\$694,834	0.2%	0.0%	-7.1%
Devices	183	\$1,734,109	1.7%	3.3%	9.7%
HCIT	11	\$26,049	5.8%	-0.1%	-14.6%
Total	2082	\$9,261,429	0.2%	0.3%	3.2%

Revenue Multiples for Pharma Services and CDMO's Continue to Drop While Valuations for Commercial Diagnostics Bouncing Back

Average Revenue Multiples by Subsector of the Global Life Sciences Sector, Feb 2021 to Jun 2023

Feb 11, 2021 (peak) May 20, 2022 Jul 29, 2022 Jun 30, 2023



Source: CapitalIQ. Revenue multiple was defined as the ratio of enterprise value to trailing 12 months revenue. Companies with revenue multiples over 100x and below 0.5x were excluded from this analysis.

RA Capital View of Biopharma Sector

RACAPITAL **SEMPER MAIOR**

RA Capital's 1H23
Core Biotech Report

July 1, 2023

We are sharing an excerpt of this July 1 report. You can read the full report (and subscribe to RA Capital's future reports) by going to rapport.bio.

RA Capital Analysis Shows that Specialist Fund Sponsored Biotech is Well Capitalized and Benefitting from M&A

By Peter Kolchinsky, July 1, 2023

This is the second of RA Capital's *Semper Maior* biotech series and the first update of the kinds of analyses we introduced in the first article. In that first piece, we broke down all the cash-burning companies in the development-stage public biotech universe by what we called Core (owned by at least one biotech specialist fund) and Peripheral (not owned by any specialists) and then further broke them down by whether or not they were in a financing Danger Zone.

Importantly, we looked at the weightings of Danger Zone companies as well as other categories (e.g., those trading below cash) relative to the overall Core set to make the case that while there were hundreds of struggling companies, their overall weighting in the sector was small, which is to say that they had already been substantially written down and their further decline would not weigh much on the sector's performance or specialists' performance.

Our January [2023] piece was not intended for those small, struggling companies, to whom it would offer no comfort. We wrote it for the broader audience of potential biotech investors, including generalists and specialist fund LPs, who might be intimidated by reading other biotech sector analyses that emphasized its number of struggling companies and ignored their low weighting in the portfolios of the specialist investors that companies count on for funding.

The bottom line then was that development-stage biotech as a whole was well positioned to achieve continued positive performance thanks to cash-rich strategics acquiring promising companies to replenish their own pipelines, injecting cash into the ecosystem.

Six months on, we have updated our data and make the case here that our thesis has been playing out and will continue to play out.

RA Analysis of Balance Sheet Position of Biotech Universe

	UNIVERSE			CORE			PERIPHERAL		
	2022 YE	2023 Q2	% Change	2020 YE	2023 Q2	% Change	2022 YE	2023 Q2	% Change
Total Number	656	620	-5%	388	348	-10%	268	272	1%
Number Trading Below Cash (Market Cap Weighted %)	214 (5.2%)	153 (4.2%)	-29%	119 (5%)	79 (4.1%)	-34%	95 (6.4%)	74 (5.3%)	-22%
Number Trading with <2 Years of Cash (Market Cap Weighted %)	430 (34.9%)	450 (50.3%)	5%	210 (31.7%)	214 (46.9%)	2%	220 (56.2%)	236 (76.6%)	7%
Number Trading with <2 Years of Cash and 25%+ Burn /Market Cap Ratio (Market Cap Weighted %)	361 (12.3%)	344 (11.7%)	-5%	169 (10.4%)	152 (10.2%)	-10%	192 (25.7%)	192 (23.4%)	0%
Cumulative Market Capitalization	\$324.6B	\$320.6B	-1%	\$282.9B	\$284.0B	0%	\$41.7B	\$36.5B	-12%
Cumulative Annual Burn (% of Total Market Cap)	\$61.6B (19%)	\$57.3B (17.9%)	-7%	\$49.2B (17.4%)	\$46.7B (16.4%)	-5%	\$12.4B (29.6%)	\$10.6B (29%)	-14%
Cumulative Annual Burn, <2 Years of Cash (% of Total Market Cap)	\$32.4B (10%)	\$37.4B (11.7%)	15%	\$23.2B (8.2%)	\$28.8B (10.1%)	24%	\$9.2B (22.1%)	\$8.6B (23.5%)	-7%
Cumulative Annual Burn, <2 Years of Cash, and 25%+ Burn/Market Cap Ratio (% of Total Market Cap)	\$24.7B (7.6%)	\$23.1B (7.2%)	-7%	\$17.0B (6%)	\$16.5B (5.8%)	-3%	\$7.7B (18.4%)	\$6.5B (17.8%)	-15%

This chart identifies 348 biotech companies where at least one specialist fund is an investor at the end of Q2 2023. Of these, 152 have less than 2 years of cash and has a burn to market cap ratio over 25%. But the market cap of these companies is only 5.8% of the universe market cap.

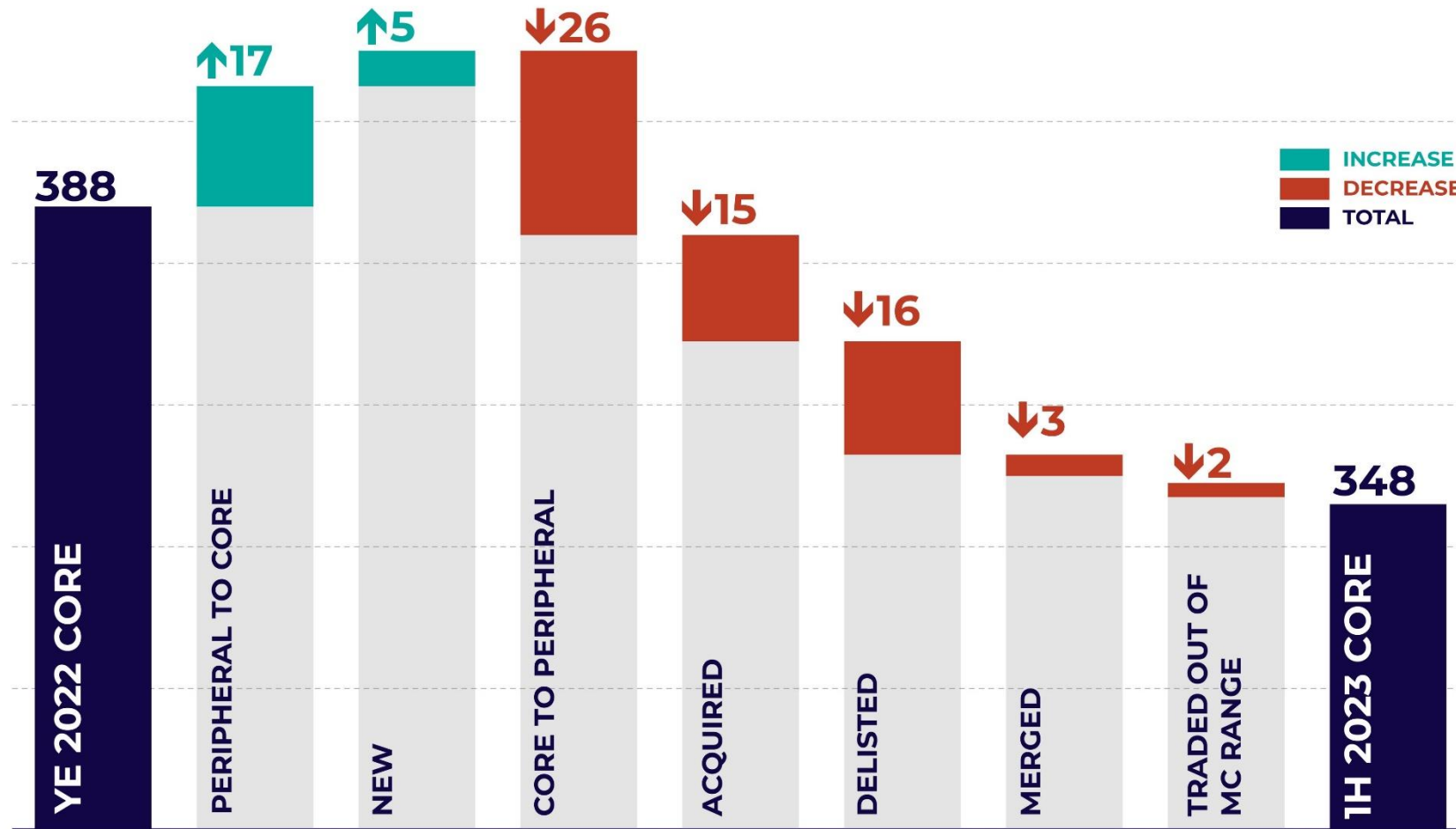
RA's main point is that, broadly speaking, specialist sponsored companies are well capitalized.

Non-specialist sponsored companies ("peripheral") have a much lower market cap overall.

DANGER ZONE

Composition and characteristics of our biotech Universe and its Core and Peripheral sub-sets at the start and end of 1H23. We also include data on how well capitalized companies in these sets are. Where you see percentages in parentheses, they are telling you what the market cap weighting is for a particular set of companies as a proportion of the total market cap of that group. For example, there are 79 Core companies trading below cash, whose market cap represents 4.1% of the total market cap of the Core set.

What Happened to the “Core” Set of Biotechs in the Last Six Months?



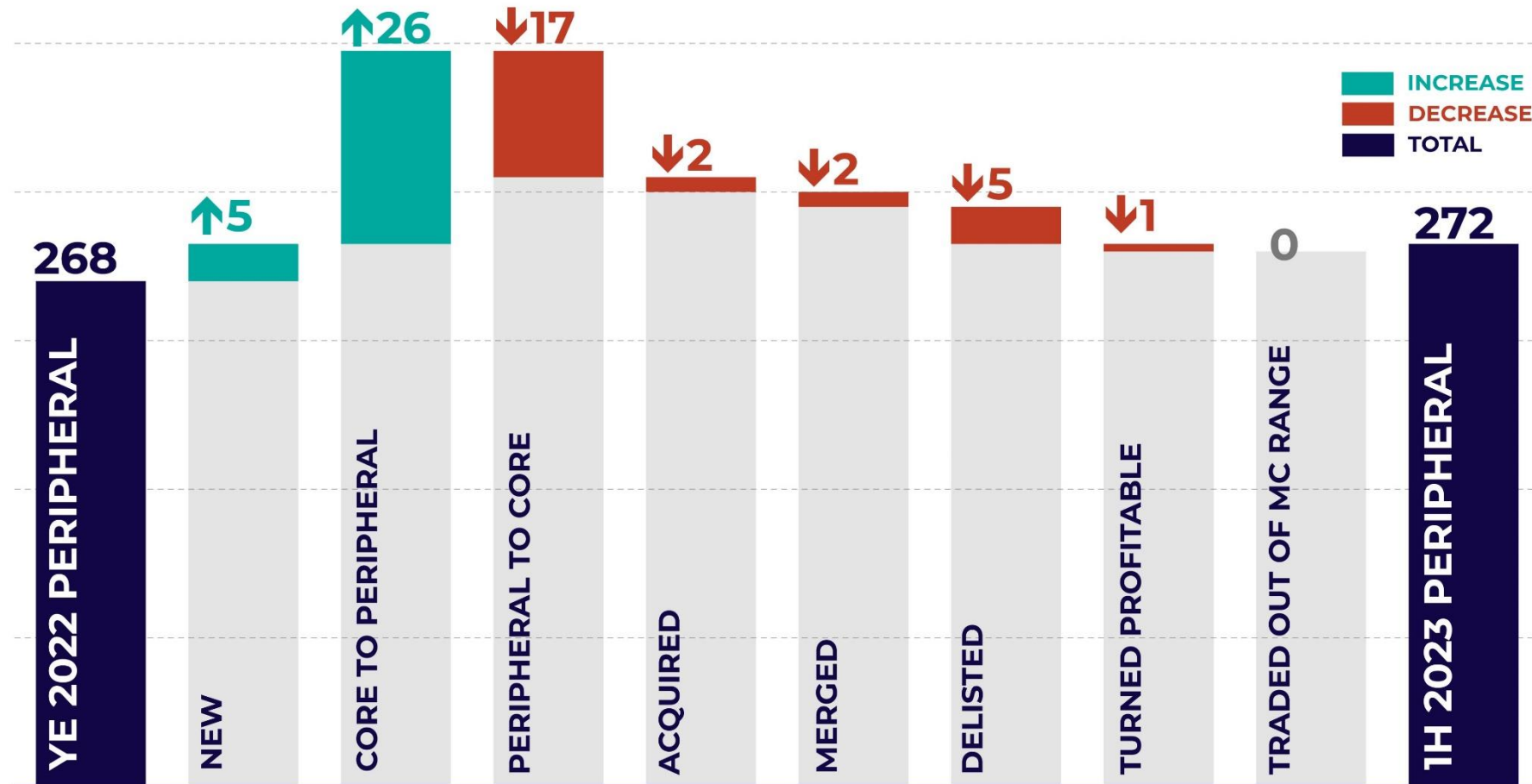
The additions of companies by IPOs and entry into the core set (presumably due to positive data outcomes or other positive developments) was more than offset by exit from this group, delistings, acquisitions and mergers.

It's interesting to compare our global biotech list to this one. We see less attrition in biotech over the last six months. We think there are two reasons: (1) we include a global list and there has been less attrition outside the U.S. and (2) we include *all* companies and those that are not sponsored did not see the same attrition (next page).*

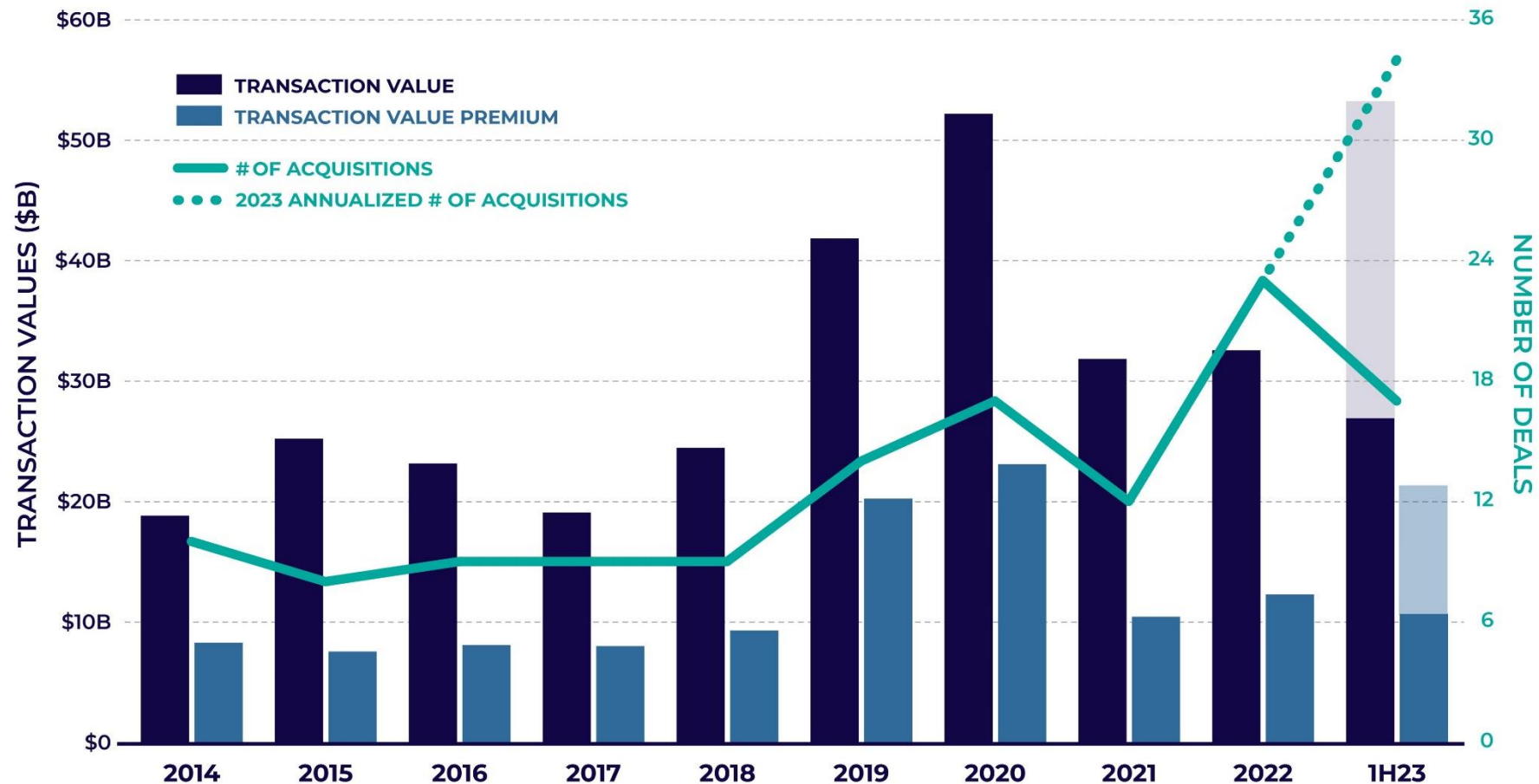
Source: <https://rapport.bio/all-stories/semper-maior-1h23-core-biotech-report>

* It's also noteworthy that our definition of "biotech" is not the same. RA's listing includes commercial stage companies whereas we only define R&D-stage innovative therapeutics companies as being "biotechs".

The “Peripheral” Biotech Population Grew Slightly in the Last Six Months



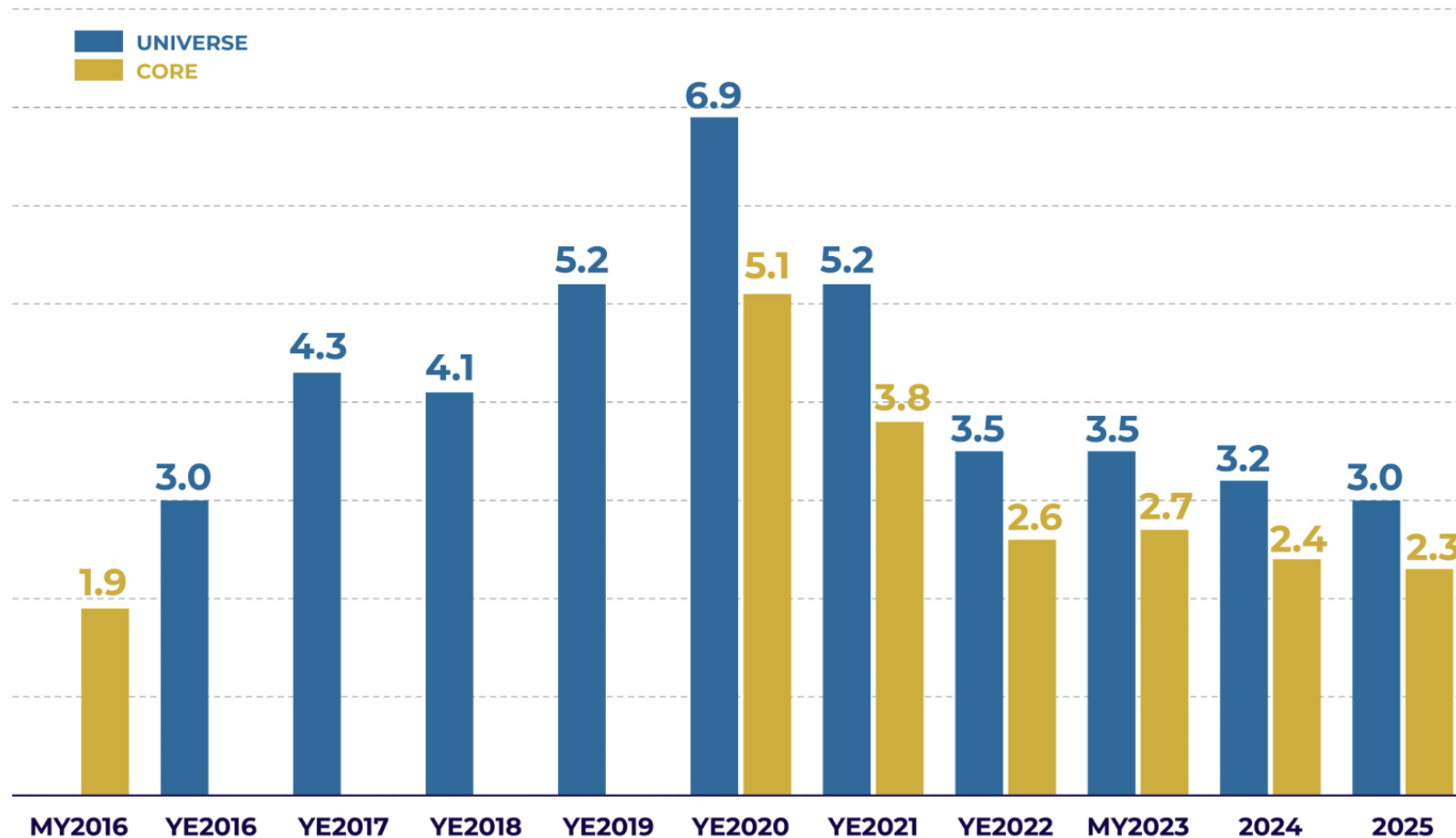
M&A is Very Strong in 2023



2023 M&A transactions are outpacing 2022 in both value and deal count, likely fueled by how relatively inexpensive the sector remains. The faded extensions of the 1H23 bars reflect a simple doubling to convey what the values would be if the M&A we have seen in 1H23 were to continue through the rest of 2023.

Sector Inexpensive Relative to Acquiror Pocketbooks

FIGURE 3: The Sector's Acquisition Ratio - Years of Strategics' Free Cash Flow to Acquire Smid Cap Biotechs for a 100% Premium



M&A conditions are favorable based on how few years worth of strategics' Free Cash Flow it would take to acquire the whole Universe or just the Core set for a 100% premium, which is what we call the sector's Acquisition Ratio. We did not calculate the Core values for YE2016 or 2017-2019 because it's tedious to do so and it's enough to eyeball the trend evident in the Universe data. MY2023 values correspond to the current data as of the end of 1H23. 2024-2025 rely on sell-side projections of biopharma free cash flow to project what the acquisition ratios would be in future years if current valuations remained the same.

Almost All M&A Premium Accruing to Companies with One or More Specialist Investors Present

Number of specialist investors




	UNIVERSE	PERIPHERAL	1+ CORE	2+ CORE	3+ CORE	1-2 CORE
# of Companies	620	272 (44%)	348 (56%)	270 (44%)	207 (33%)	141 (23%)
Value (Total Market Cap)	\$321B	\$37B (11%)	\$284B (89%)	\$259B (81%)	\$228B (71%)	\$56B (18%)
Historical Share of M&A Premium	100%	0.5%	99.5%	94.8%	87.7%	11.8%
Return on Value from Share of \$11B of M&A Premium	3.4%	0.1%	3.9%	4.0%	4.2%	2.3%

Large Cap Pharma is Evolving Fast



Reordering of Largest Players by Value in Life Sciences

Enterprise Value (\$mm) of Top Life Sciences Companies, Feb 8, 2021 to June 30, 2023

	Value Rank (Jun 30 , 2023)	Company	Jun 30, 2023	Value Rank (June 17, 2022)	Jun 17, 2022	Value Rank (Dec 31, 2021)	Dec 31, 2021	Value Rank (Feb 8, 2021)	Feb 8, 2021
	1		\$491,331	1	\$446,793	1	\$450,711	1	\$441,136
↑	2		\$459,931	4	\$275,160	6	\$262,418	8	\$199,050
↑	3		\$360,891	6	\$239,281	8	\$252,890	10	\$163,171
↑	4		\$313,226	7	\$236,919	11	\$210,056	6	\$211,317
	5		\$270,071	2	\$310,463	4	\$307,886	3	\$267,777
	6		\$270,006	3	\$278,801	2	\$349,544	2	\$301,332
↑	7		\$248,828	9	\$212,736	11	\$209,520	11	\$150,063
	8		\$233,280	8	\$226,761	5	\$272,609	7	\$207,897
	9		\$228,384	11	\$188,764	10	\$224,014	5	\$231,398
	10		\$223,530	5	\$273,875	3	\$341,892	4	\$246,412
	11		\$192,325	10	\$193,248	7	\$260,455	9	\$185,995

Lilly is now the world's second largest life sciences company (up from a ranking of #8 at market peak on Feb 8, 2021) and is positioned to challenge J&J for the top spot. Roche was #2 at the start of the Pandemic and is now #6 as it has failed to overcome drug LOE's with new products fast enough.

In Feb 2021 Novartis was the fifth largest player and dropped to #11 before coming back to #9 over the last year on the strength of new drugs. One can't help but be impressed by AZ's move from #11 to #7 – now larger than Pfizer which once tried to buy it through a hostile takeover.

Impressively, Novo Nordisk has climbed from #10 to #3.

We have shifted from a world where performance in cardiometabolic disease is shaking up the industry and where COVID-19 drugs are largely a memory of the past.

The pharma rankings have been massively reshuffled in just 30 months.

Significant Historical Change in Big Pharma Rankings

The list of the top 15 big pharma from 1974 is barely recognizable today, containing only 6 companies that are still around. The ranks of the top players in the industry are highly dynamic as the advent of new products and modalities and patent expiries on the old, drive dramatic change. Also notable is the decline in the EU pharma sector – once the source of most industry sales. This is likely not a failure on the part of companies in this part of the world but rather a reflection of the declining importance of Europe as a source of sales related to pricing changes there. Also noteworthy is the industry's massive long-term growth (6% revenue growth after inflation, on average since 1974 – far above GDP growth). Our suspicion is that when we get to 2027 the face of the industry will be far different than it is forecast to be today because of ongoing disruptive forces.

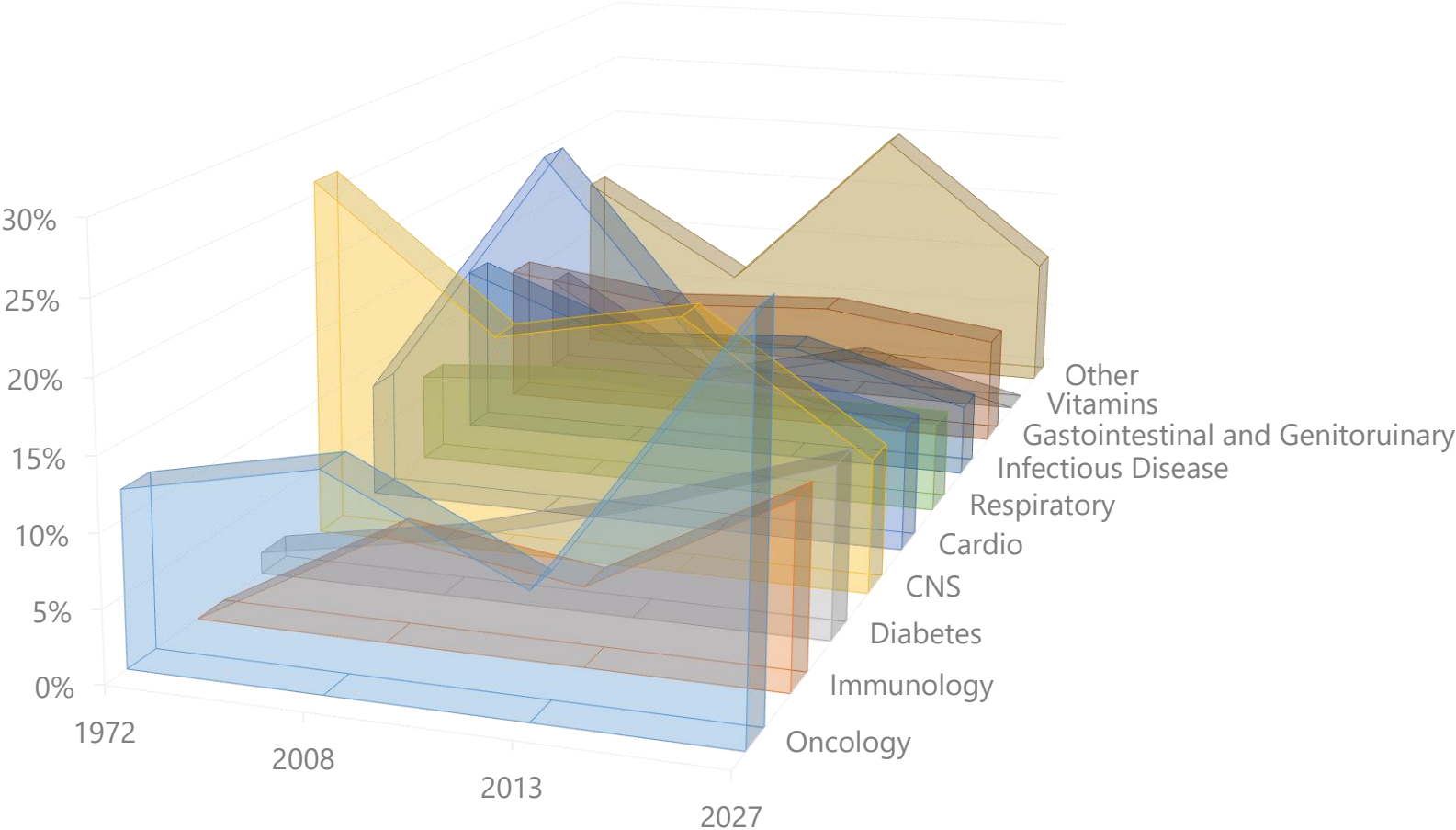
Top 15 Pharma Players Ranked by Revenue \$mm, 1974-2027

1974		1988		2005		2014		2022		2027 (est.)	
Company	Revenue (\$mm)	Company	Revenue (\$mm)	Company	Revenue (\$mm)	Company	Revenue (\$mm)	Company	Revenue (\$mm)	Company	Revenue (\$mm)
Roche	\$1,386	Merck	\$4,984	Pfizer	\$44,280	Novartis	\$53,717	Pfizer	\$92,951	Merck	\$72,550
Merck	\$1,197	Glaxo	\$4,213	GlaxoSmithKline	\$33,960	Pfizer	\$49,605	Merck	\$57,869	Pfizer	\$68,900
Hoechst	\$1,174	Hoechst	\$3,868	Sanofi-Aventis	\$32,340	Sanofi	\$41,287	AbbVie	\$53,729	AbbVie	\$60,770
Ciba-Geigy	\$1,063	Bayer	\$3,628	Novartis	\$24,960	Roche	\$40,129	Novartis	\$52,222	Sanofi	\$60,100
Bayer	\$862	Ciba-Geigy	\$3,466	AstraZeneca	\$23,950	Merck	\$36,042	Sanofi	\$50,194	AstraZeneca	\$59,600
Sandoz	\$847	American Home Products	\$3,218	Johnson & Johnson	\$22,320	Johnson & Johnson	\$32,213	Roche	\$50,013	Novartis	\$59,390
Eli Lilly	\$789	Sandoz	\$3,089	Merck	\$3,089	GlaxoSmithKline	\$28,939	Bristol-Myers Squibb	\$45,848	Eli Lilly	\$55,940
American Home Products	\$758	Takeda	\$3,076	Wyeth	\$3,076	AstraZeneca	\$26,095	Johnson & Johnson	\$45,572	Novo Nordisk	\$53,880
Pfizer	\$740	Eli Lilly	\$2,680	Bristol-Myers Squibb	\$2,680	Gilead Sciences	\$24,890	AstraZeneca	\$43,840	Johnson & Johnson	\$51,000
Upjohn	\$683	Abbott	\$2,599	Eli Lilly	\$2,599	Amgen	\$20,063	GlaxoSmithKline	\$32,818	Roche	\$50,000
Warner-Lambert	\$611	Pfizer	\$2,539	Abbott	\$2,539	AbbVie	\$19,960	Takeda	\$30,297	Bristol-Myers Squibb	\$47,900
Rhone-Poulenc	\$595	Warner Lambert	\$2,509	Roche	\$2,509	Eli Lilly	\$19,616	Eli Lilly	\$27,691	GlaxoSmithKline	\$44,280
Sterling	\$566	Bristol-Myers	\$2,509	Amgen	\$2,509	Bristol-Myers Squibb	\$15,879	Gilead	\$27,483	Amgen	\$32,680
Abbott	\$551	Eastman Kodak	\$2,500	Boehringer-Ingelheim	\$2,500	Novo Nordisk	\$14,434	Novo Nordisk	\$27,459	Gilead	\$29,770
Boehringer-Ingelheim	\$506	Roche	\$2,365	Takeda	\$2,365	Boehringer Ingelheim	\$13,424	Amgen	\$26,190	Takeda	\$27,650
Sales of Top 15	\$12,328	Sales of Top 15	\$47,243	Sales of Top 15	\$205,676	Sales of Top 15	\$436,292	Sales of Top 15	\$664,177	Sales of Top 15	\$774,410
Sales in 2023 dollars	\$77,419	Sales in 2023 dollars	\$123,638	Sales in 2023 dollars	\$326,048	Sales in 2023 dollars	\$570,663	Sales in 2023 dollars	\$702,525	Sales in 2023 dollars	\$819,123
Percent European	52%	Percent European	44%	Percent European	42%	Percent European	41%	Percent European	39%	Percent European	42%

Sources: CapitalIQ and 2022 Torrey Pharma 1000 report data for 2014 to 2022 period. Harvard Business School for 1974 to 2005 data (see <https://www.hbs.edu/ris/Publication%20Files/09-118.pdf>). CapitalIQ analyst consensus average revenue estimates taken for 2027 revenue except for J&J and Roche where analyst reports were analyzed to take the pharma division revenue estimate average for 2027. U.S. CPI index used to inflation adjust numbers to 2023 (<https://www.minneapolisfed.org/about-us/monetary-policy/inflation-calculator/consumer-price-index-1913->).

Substantial Shift in Therapeutic Area Mix Over Time

Therapeutic Area Share of Total Pharma Revenue, 1972 to 2027



The instability in the rankings of who's who in big pharma is accentuated by frequent shifts in the relative importance of therapeutic areas served by the pharmaceutical industry. This is related, of course, to product cycles and increasing prices over time. The table below shows sales by TA, for example, in the 1972-82 period. This distribution of sales by TA is completely different than today's.

TABLE 3
Domestic Sales of Ethical Drugs for Human Use, by Product Class
1972, 1978, and 1982

Class	Relative Share of Sales		
	1972	1978	1982
Central Nervous System	26.0%	23.6%	25.2%
Anti-Infectives	12.8	15.0	17.0
Gastrointestinal and Genitourinary	10.7	11.8	8.9
Neoplasms and Endocrine	12.0	9.7	13.5
Vitamins and Nutrients	7.6	9.6	8.3
Cardiovasculars	8.4	9.4	17.0
Respiratory System	6.6	7.8	5.2
Dermatologicals	3.3	2.9	2.8
Other	12.6	10.2	2.1
Totals	100.0%	100.0%	100.0%

Source: PMA Fact Book 1984 and U.S. Department of Commerce, Bureau of Census, Current Industrial Report 1982

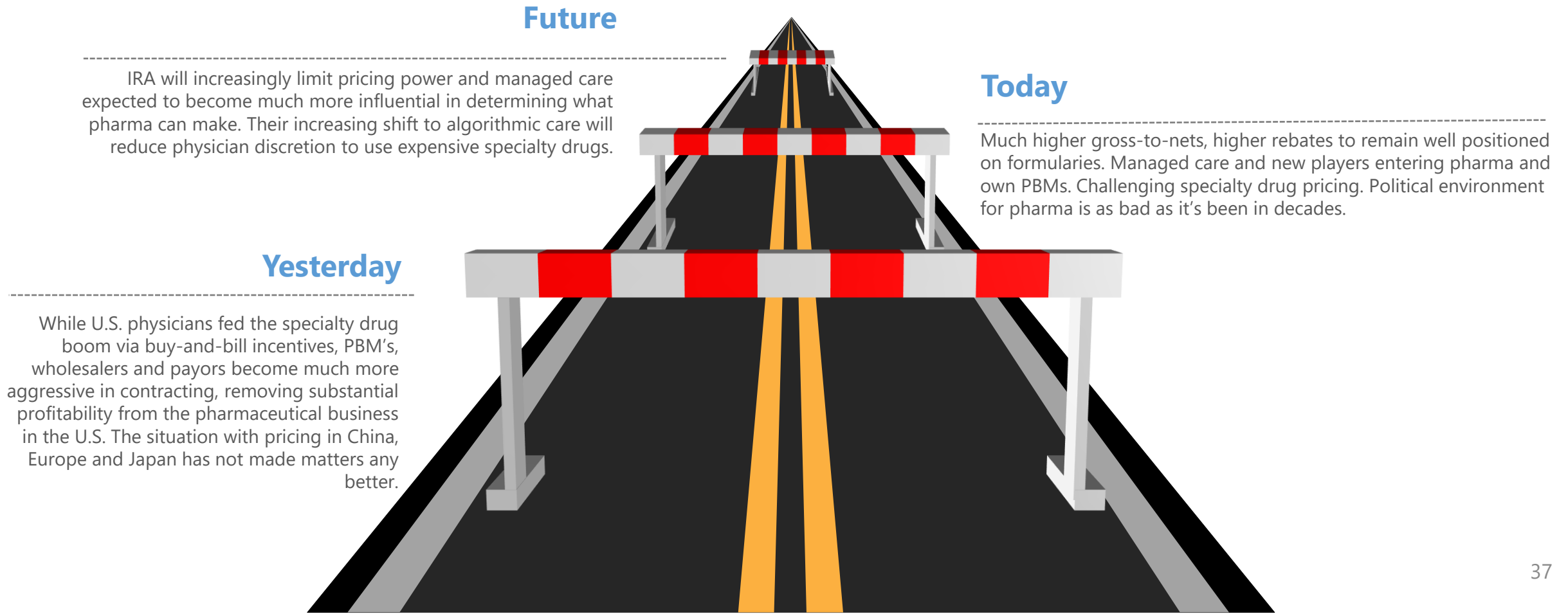
Three Key Factors Disrupting Big Pharma Today

The previous slide highlights the constant change and historical disruptions in the pharma sector. There are three major forces at work today in the sector.



#1. Value-Based Care and a Challenging Payor Ecosystem

As pharma sales have grown, pricing pressures on big pharma have grown. The obvious squeeze has been from the largest payor, the U.S. government (e.g., most-favored nation pricing, the IRA etc.). The growing power of managed care companies and co-owned PBM's has further eroded the specialty drug model that has emphasized profitability from oncology drugs and niche disease drugs, especially biologics. We expect that these pressures will grow over time.



#2. The Shift to the “Big Drugs for Big Diseases” Theme

Key Thought Process: “Go Big” But Charge “Real Prices” for Drugs That Impact Many Patients

- Since the end of Pandemic, we have seen exceptional value growth in companies that are developing drugs with more than \$30 billion in end market potential.
- In the same sense that Humira® got quite big by addressing multiple inflammatory diseases well there is a growing realization that the best route to success in pharma is to develop “big drugs” for “big diseases”.
- The idea is to invent drugs that truly impact the health of many patients and to charge a “medium price” rather than a “rare disease price”. The key is to avoid categories where effective generics exist – but rather show outcomes benefits over best available care and then charge for it.*
- While payors fight the exigency of having to pay for these drugs, the pressure to deliver medically necessary care to patients in need has ultimately allow pricing to be realized that is very different than what used to be charged for blood pressure meds, statins and the like. Even with larger sales force requirements, this approach to the market can pay off very big.
- One popular approach to achieving giant market potential for a drug is to develop it for many different indications. Abbott pioneered this idea with development of Humira® – running massive label expanding studies over time. Abbott started calling this the “pipeline in a product” (or PiP approach). Merck wasn’t far behind, massively outspending rival BMS to build the label for Keytruda up to \$30bn market size.
- This sea change in market thinking has been difficult for many companies that have been charging headlong into specialty care, especially oncology. It takes years to rebuild R&D capacity in the newly popular areas after it has been disassembled. Think of how many well-known companies exited CVM.
- Everything else is not so fashionable today. It’s just very hard to take a cancer drug for 5,000 patients and turn it in to anything that looks like a billion-dollar drug. Payor behavior has made it very difficult to do this as payors generally force patients to go on less expensive drugs first.



Up until the Pandemic most big pharmas couldn't exit genericized “primary care” therapeutic areas fast enough. A few stayed in, including Lilly and Novo Nordisk who have been committed to serving diabetes patients for a century. These two companies are now reaping disproportionate rewards as their R&D know-how in incretin biology has borne fruit. Today, investors understand the shift that has taken place very well. Areas where drugs can impact major cardiometabolic, respiratory diseases or immunologic conditions can become very big and overcome barriers imposed by payors. It's now a “Go Big or Go Home” market.

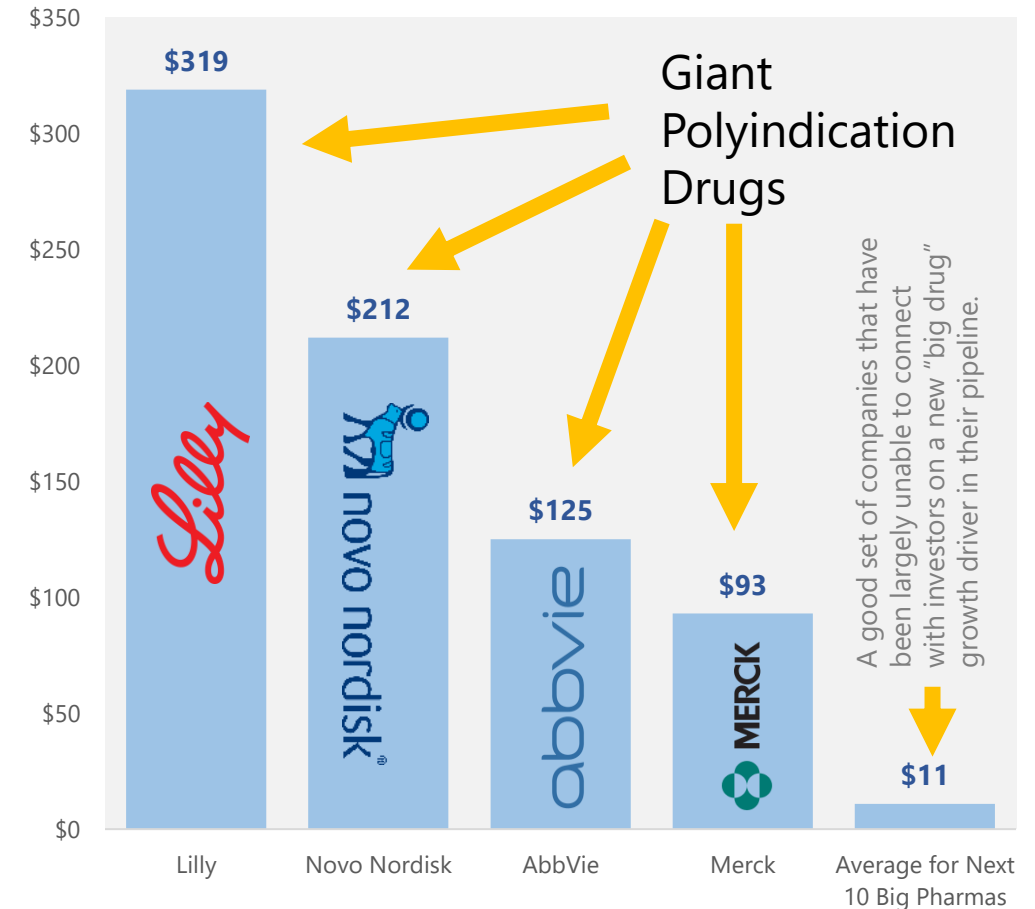
* This is not as easy as it looks. Earlier efforts to introduce biologics for cholesterol management via injectable PCSK9 inhibitors failed to gain traction with payors by pricing in the \$1k to \$2k / month area.

Value Growth Has Accrued to the “Go Big” Thinkers

Giant Polyindication Drugs are in Vogue Today

- The chart at right shows the change in enterprise value of the top 14 pharma since the start of the Pandemic (Feb 19, 2020) until June 30, 2023.
- Since Feb 2020 AbbVie has made visible two massive pipeline in a product drugs (Rinvoq® and Syrizi®). They are progressing clinical studies that build out the label for these drugs at a breakneck pace.
- Since Feb 2020 Lilly has made a “real drug for real disease” visible in tirzepatide that is also a pipeline in a drug. Since then, Lilly has progressed with donanemab for Alzheimer’s and orforglipron and retatrutide for obesity. While competitors are running giant oncology trials, they are running huge outcomes study to build a polyindication label for Tirzepatide.
- Since Feb 2020 Novo has made big progress in “real drugs for real disease” with Rybelsus® and Wegovy® approvals and is now preparing to fight Lilly for the obesity market with its new drug CagriSema.
- Since Feb 2020 Merck has continued to make huge progress with trials for Keytruda® developing a “pipeline in a drug” with this PD-1 inhibitor. The spend on clinical trials is not stopping despite an upcoming LOE event – in part because of a switch to SubQ. Merck has recently picked up a highly promising immunology drug from Prometheus (PRA023, a TL1A antagonist) and can be expected to invest heavily in building the label for this drug. Merck’s peak sales from Keytruda and PRA023 could easily exceed \$40 billion.

Change in Enterprise Value of Big Pharmas (\$billions), Feb 19, 2020 to June 30, 2023



Stifel's Analysis Identifies At Least \$100-Billion Market Potential in Obesity Drugs

Whether or not payors go along with the price for obesity drugs set by Lilly and Novo, consumers are going to pay for the drugs themselves. The private pay market alone would make this the largest drug class in history . . . by far.

Recent Harris/Stat+ Poll Implies a Giant Private Pay Market for Obesity Drugs

Prevalence of Obesity in the United States: **41.9%** (CDC).

Number of adults in the U.S.: **258 million** (US Census)

Number of obese adults in the U.S.: **108 million**

Total Market Sizing:

Monthly Price Point of \$1000: 5% of 108mm people @\$12,000 annually = **\$154.8 billion**

Monthly Price Point of \$500: 11% of 108mm people @\$9000 annually = **\$170.3 billion**

Monthly Price Point of \$375: 17% of 108mm people @\$4500 annually = **\$197.4 billion**

Monthly Price Point of \$175: 23% of 108mm people @\$2100 annually = **\$124.6 billion**

Monthly Price Point of \$50: 44% of 108mm people @\$600 annually = **\$68.1 billion**

If 30% of the Obese in the U.S. Were Reimbursed for GLP-1's at a Discount to Today's Price, it would be \$208 Billion Market

Prevalence of Obesity in the United States: **41.9%** (CDC).

Number of persons in the U.S.: **332 million** (US Census)

Number of obese persons in the U.S.: **139 million**

Market Sizing:

10% of U.S. obese persons (4% of population) on GLP-1s @\$5000 a year: **\$69.5 billion**

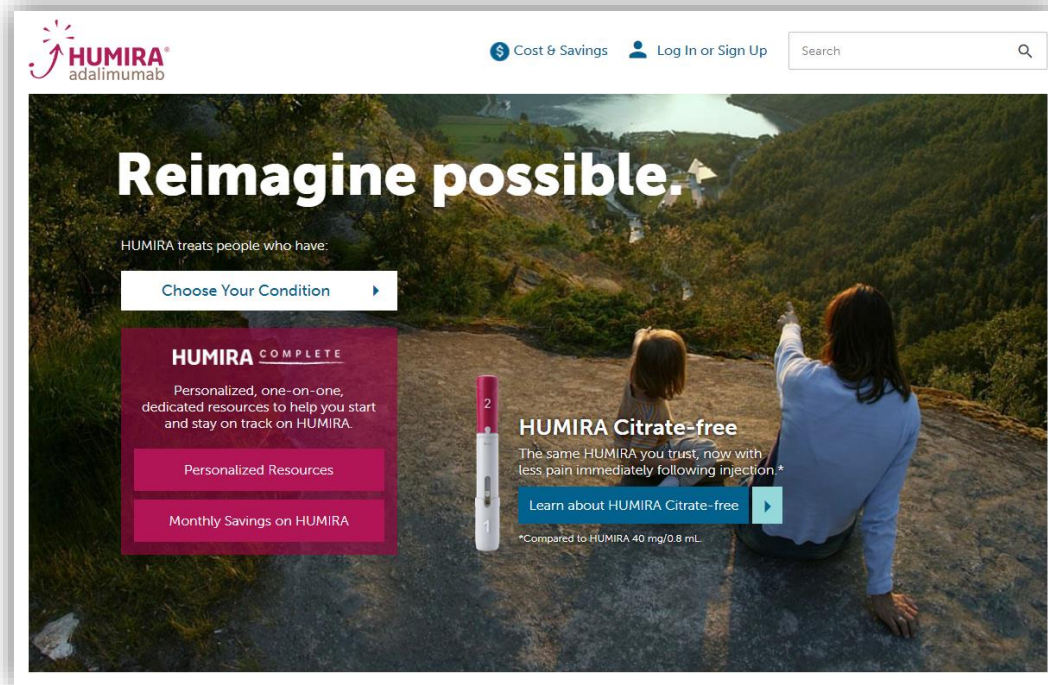
20% of U.S. obese persons (8% of population) on GLP-1s @\$5000 a year: **\$139 billion**

30% of U.S. obese persons (12% of population) on GLP-1s @\$5000 a year: **\$208.5 billion**

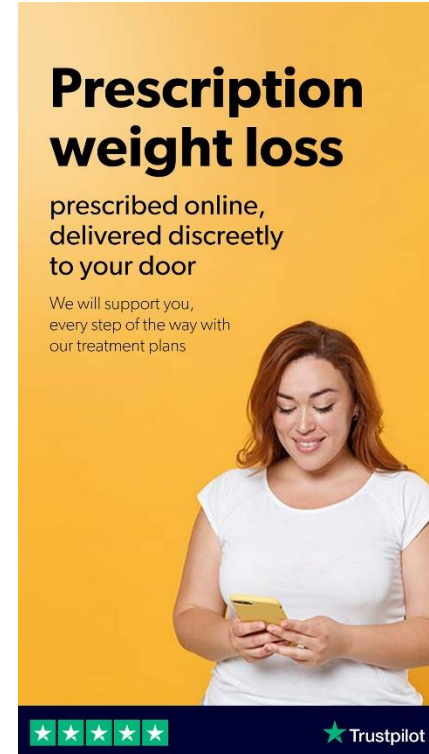
A Not-So-Subtle Change is Underway: Consumerization

The traditional relationship between governments and their populations is being challenged in many countries because of the power of social media. Similarly, the consumer is increasingly taking charge of their medical care and obviously prefers drugs for symptomatic diseases that are important to them personally.

The Old Days: Massive Direct-to-Consumer Advertising Campaigns



Today: The Consumer Learns Online (e.g., social media) and Buys Online (or gets a drug via a Doc)



Consumers have become increasingly sophisticated about pharmaceutical products and are buying the drugs online via e-Prescribing websites or are shopping for a physician to prescribe.

The widespread use of telehealth during the Pandemic and growing digital sophistication of the consumer is accelerating this change.

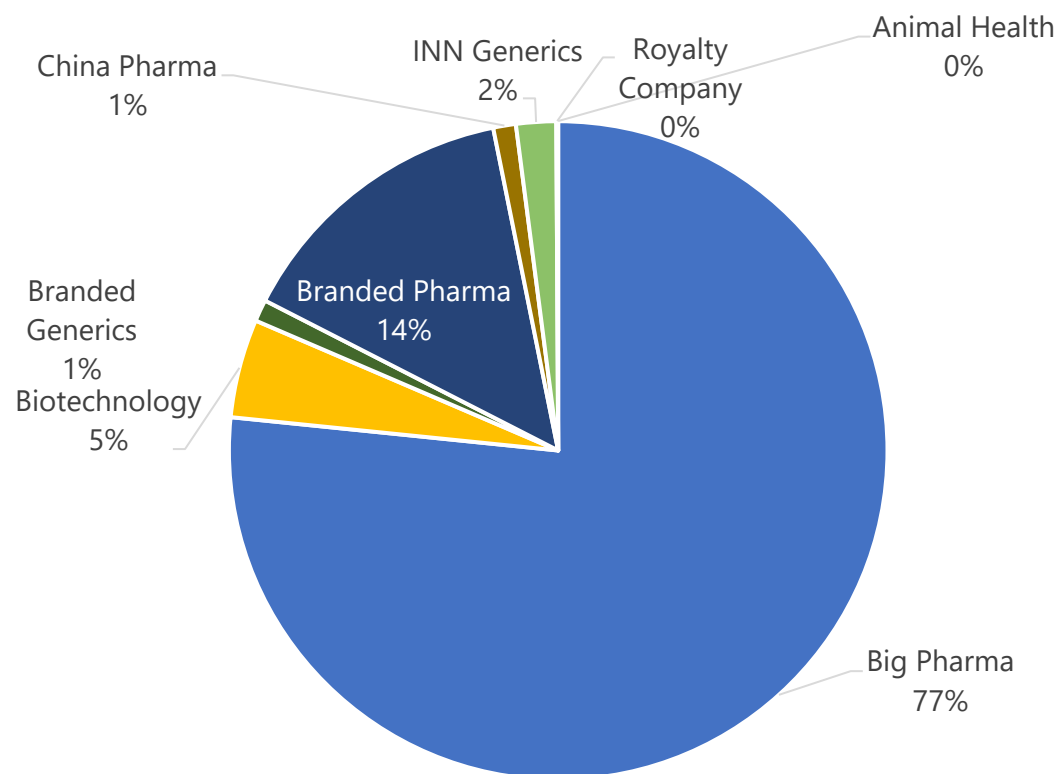
Fascinatingly, today Novo Nordisk is trying to slow down websites that sell prescription Semaglutide and is in shortage due to unexpectedly high consumer demand for its GLP-1 agonist for weight loss.

We believe that the impact of the consumerization of pharma is only just beginning its impact on the sector.

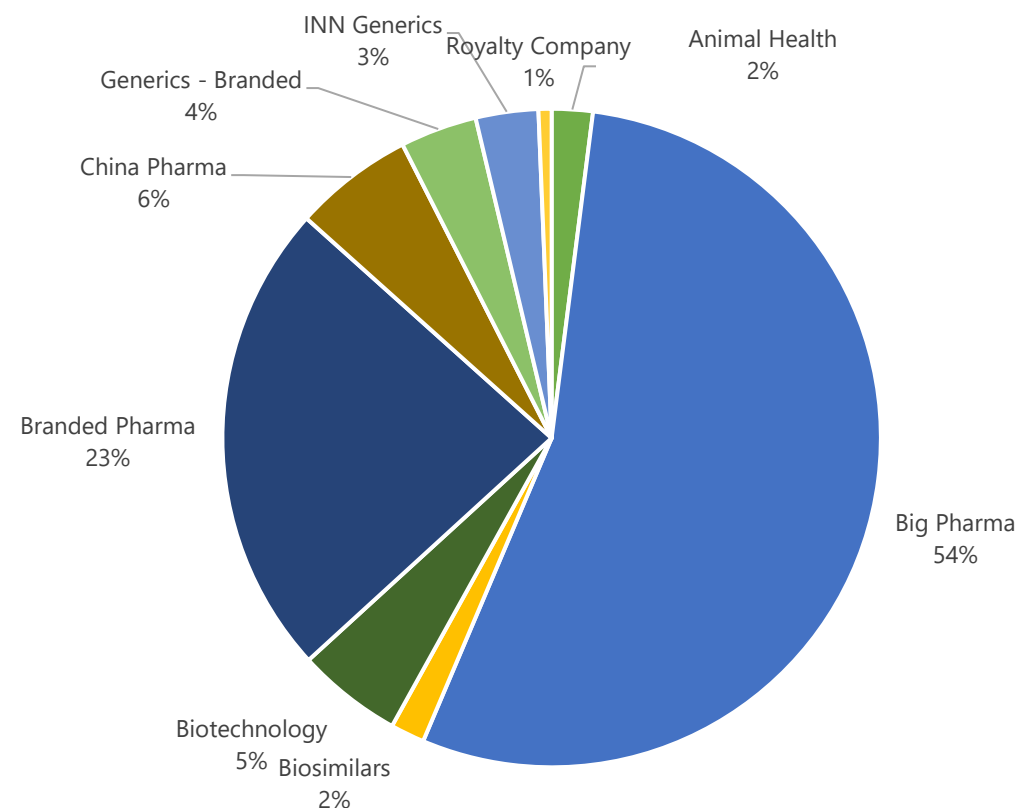
#3. Long-Term Theme: Democratization of Pharma Sector

The pharmaceutical sector has democratized since 2003. While big pharma has grown, other parts of the industry have grown faster. Key changes over the last two decades include growth of branded pharma and the growth of the Chinese pharma sector. Far from consolidating, big pharma is fighting a losing battle for industry share. In the old days, Amgen and Gilead emerged from “biotech” to become “Big Pharma”. Now, there are many more biotechs that have a credible case to drive “big pharma” type revenue (\$25bn+) on their own (think BioNTech/Moderna/Argenx/Alnylam). These companies are mastering new modalities and technologies before big pharma can get there. The key to this has been democratization of technology access and execution of drug discovery and clinical trials.

VALUE SHARE OF PHARMACEUTICAL
SUBSECTORS, SEPTEMBER, 2003 (Ent Value)



VALUE SHARE OF PHARMACEUTICAL
SUBSECTORS, MAY 2023 (Ent Value)

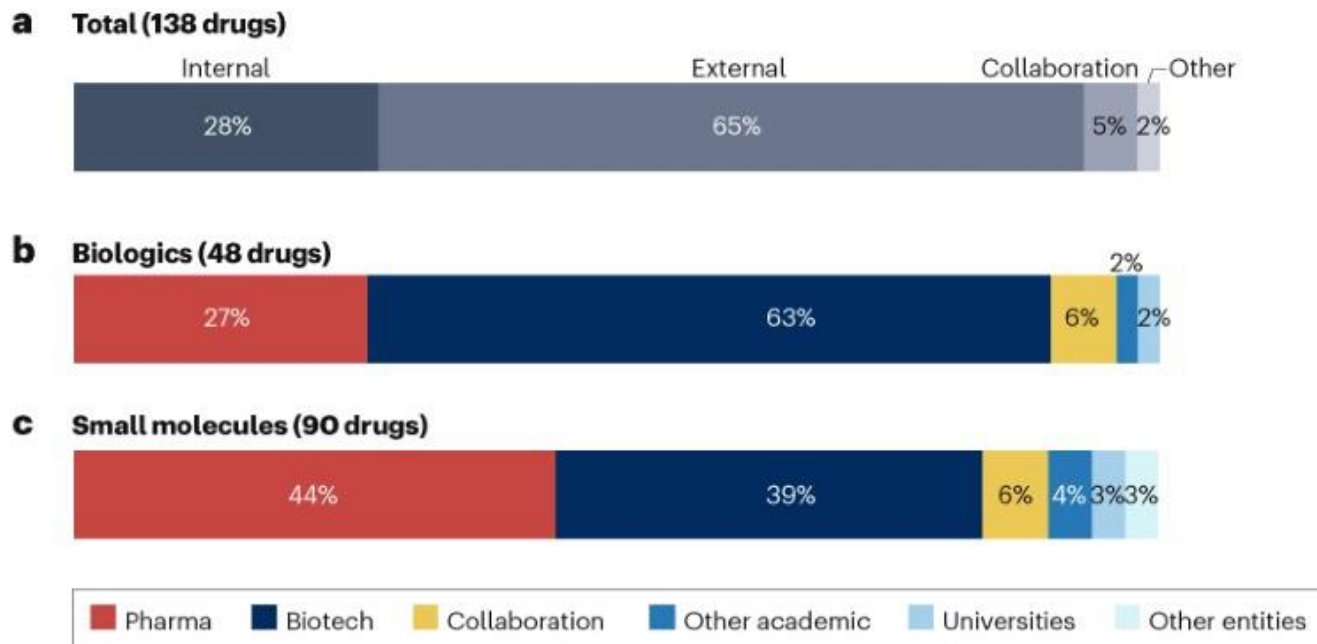


Source: Stifel analysis, May 2023. “Big pharma” is classified as the 18 largest companies in the sector by value. The biotech sector seems smaller than some might have expected. This is because we classify a company with no approved product as a “biotechnology company” and a company with a marketed product that is not a big pharma, not a Japan pharma nor a China branded generic pharma as a branded pharma company.

Democratization of R&D: Only 28% of Big Pharma's Drugs Approvals in the 2015-2021 Period Came From Internal R&D

Investigating the origins of recent pharmaceutical innovation

Alexander Schuhmacher, Markus Hinder, Alexander Dodel, Oliver Gassmann & Dominik Hartl, *Nature Reviews Drug Discovery*, July 5, 2023

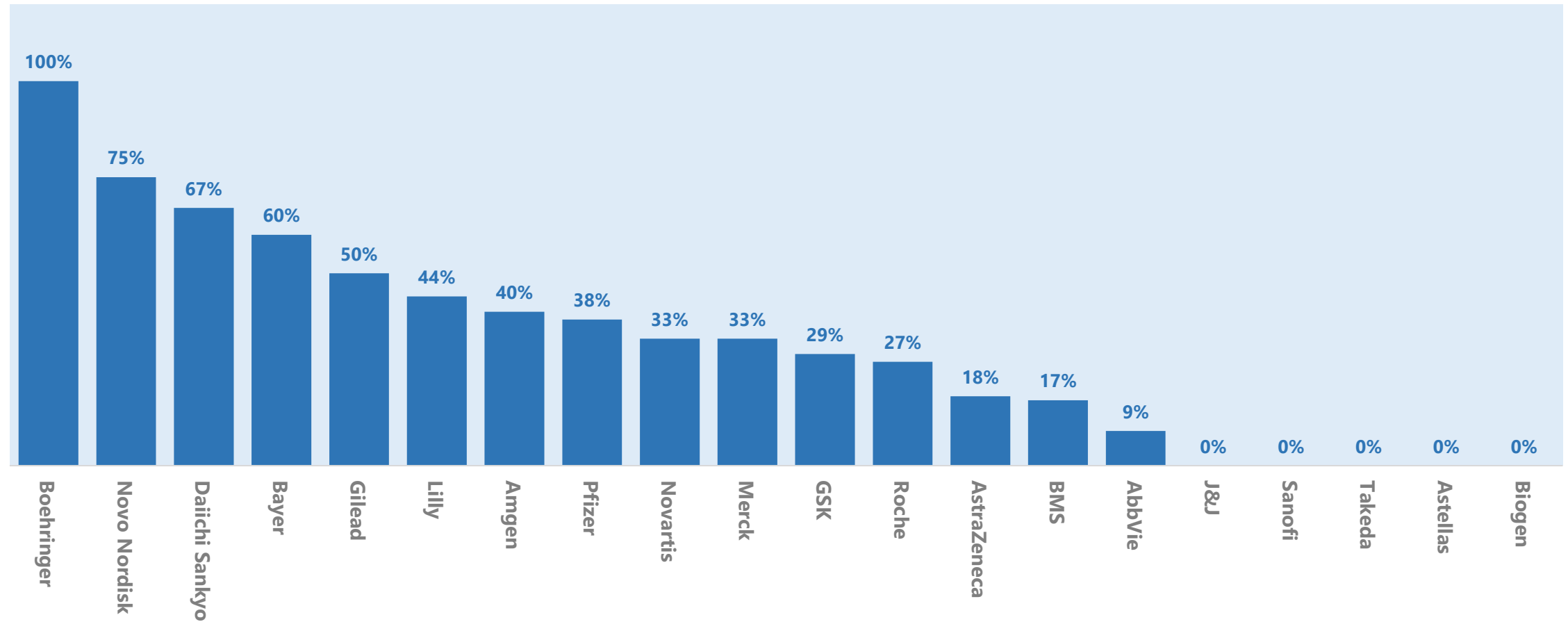


"The FDA approved 323 new drugs between 2015–2021, of which 138 were filed for approval by the top 20 biopharma companies. The majority (65%) of these new drugs originated from external sources, whilst 28% were invented internally."

41% of approvals were from M&A and 25% were from licensing.

Fraction of New Drug Approvals in 2015 to 2021 That Were Internally Invented

Percent of New Drug Approvals From 2015 to 2021 Were Internally Invented



Further Innovation That May Have Long Run Industry Impact

We believe that the pharma sector will change much more in the next twenty years than it did in the last twenty due to acceleration of innovation. Some of the interconnected innovation themes to keep an eye on include:

#1

GENERATIVE AI



Without optimization, generative AI is already better with patients than doctors and massively smarter to boot. We are likely to see the care system reorganized with massively improved “theranostic” approaches in time. In the old days pharma worked on “companion diagnostics” and “digital health” tools. In the future, pharma will integrate with AI-driven care.

#2

ALGORITHMIC CARE



Breakthroughs in ‘Omics now make it possible to screen much better for disease. It’s also possible to design much better forms of precision medicine than are used today. We predict that proprietary care algorithms start to become more important than drugs themselves at some point. This can trigger an earthquake in pharma.

#3

CONSUMERIZED CARE



We have highlighted the consumer’s increasing interest in care. We are going to see this coming the other way as well from groups like Amazon and CVS – very good offerings for the consumer. This will make much easier to sell consumer-friendly drugs. Think obesity, stomach upsets, pediatrics etc. Today’s focus on oncology/rare may change.

#4

BIOELECTRONICS



Read / write access to the human electrical system (known as the central nervous system) is a huge opportunity. It’s just a lot easier to impact diseases with small electric signals than via complex chemical drugs. Watch out for a splash from Neuralink, Elon Musk’s company in this area. Also keep an eye on pharma’s that have invested here.

A Vision of the Evolution of the Pharma Sector

The 1980s to 2010

Big Pharma Era

1. Blockbusters are born starting with Tagamet® which crossed \$1bn in sales in 1986.
2. Generics are born.
3. Employer health insurance takes off.
4. Big Pharma gets big.
5. Big drugs like Humira®, Lipitor®, Viagra® and Zyprexa® define how important pharmaceuticals can be to humanity.
6. Roche oncology franchise becomes very large.
7. In 1980 Bayer was the biggest pharma. By 2010 the largest player had become Pfizer.
8. Shareholder returns are awesome.

2011 to 2021

Specialization Era

1. Blockbuster movement continues but drugs get bigger.
2. Despite cost pressures industry continues to explode.
3. Focus shifts to oncology and drugs for less common diseases.
4. Merck Keytruda® franchise become very big.
5. Biotech gets larger.
6. Generics get a lot larger but don't move the value needle.
7. Providers get a lot larger.
8. Pharma industry hits the Pandemic and shines.
9. Technology (especially mRNA) matters. A lot.
10. Big pharma shareholder returns aren't great.

2022 to 2035

Polyindication Era

1. Due to advancing science, pharma gets a lot smarter about designing polyindication drugs.
2. The GLP1, GIP, FcRn, TYK2's, integrins and NLRP3s become gigantic.
3. Collectively could do a quarter trillion in revenue, dwarfing past peaks.
4. But now in chronic diseases rather than rare diseases.
5. New technologies like degraders, RNA therapies, cell therapies really matter.
6. Some aging research pays off.
7. We get at least one trillion-dollar healthcare company.
8. Gravity still wins. Drugs go off patent and shareholder returns, while better, aren't great.

2036 to 2050

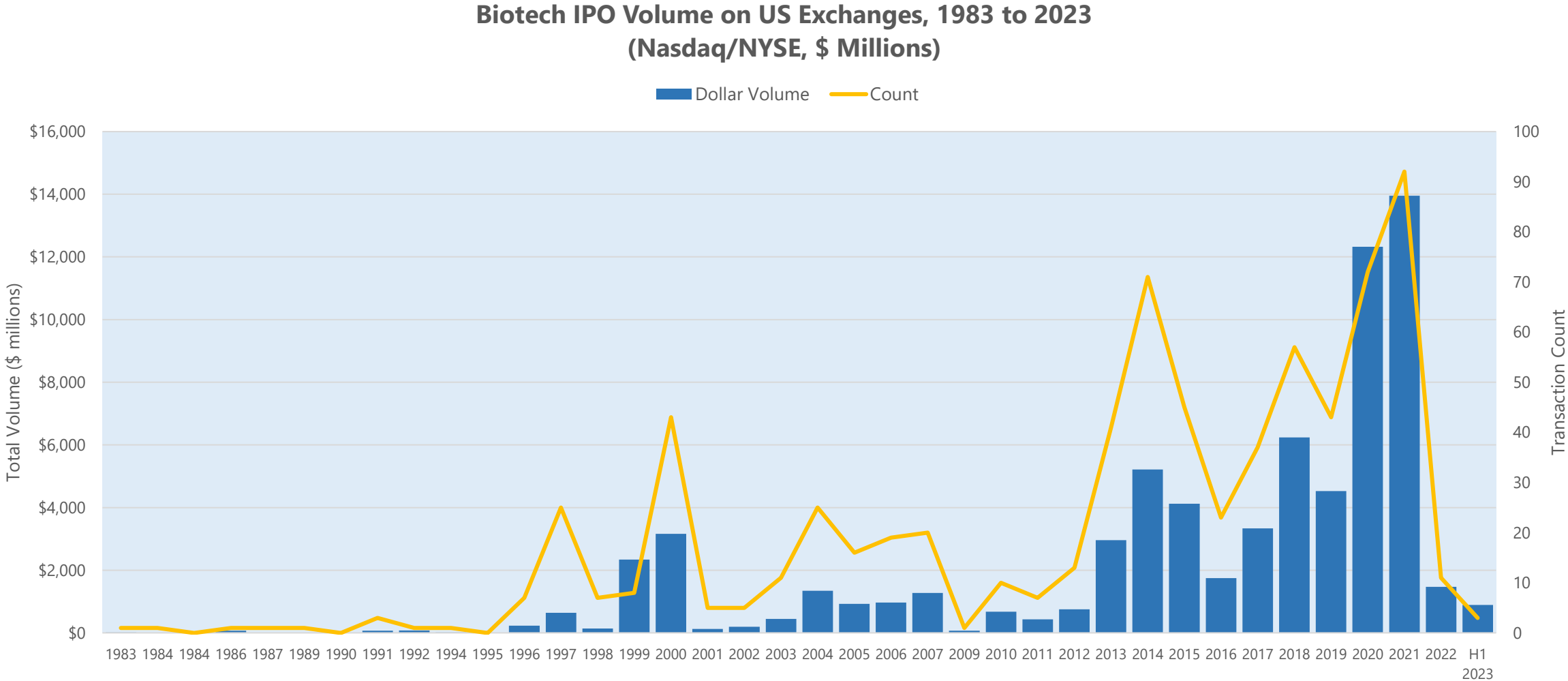
The Algorithm Era

1. Algorithms for treatment become integrated with pharma, devices and the provision of care.
2. Bioelectronics matures and starts to dominate, back integrating into AI algorithms.
3. Much greater consumerization of healthcare experience. A consumer-focused healthcare company could take over. Could become world's largest firm.
4. Drugs still matter but algorithms matter a lot more. The industry formerly known as "pharma" seems almost quaint.
5. Aging research really pays off.
6. Life expectancy at birth crosses 100 in an Asian country.
7. Multiple trillion-dollar players.
8. Not clear that a traditional big pharma wins here. May be a company from Silicon Valley that takes the industry. Or, it could be an insurance company.

The Biopharma IPO Market



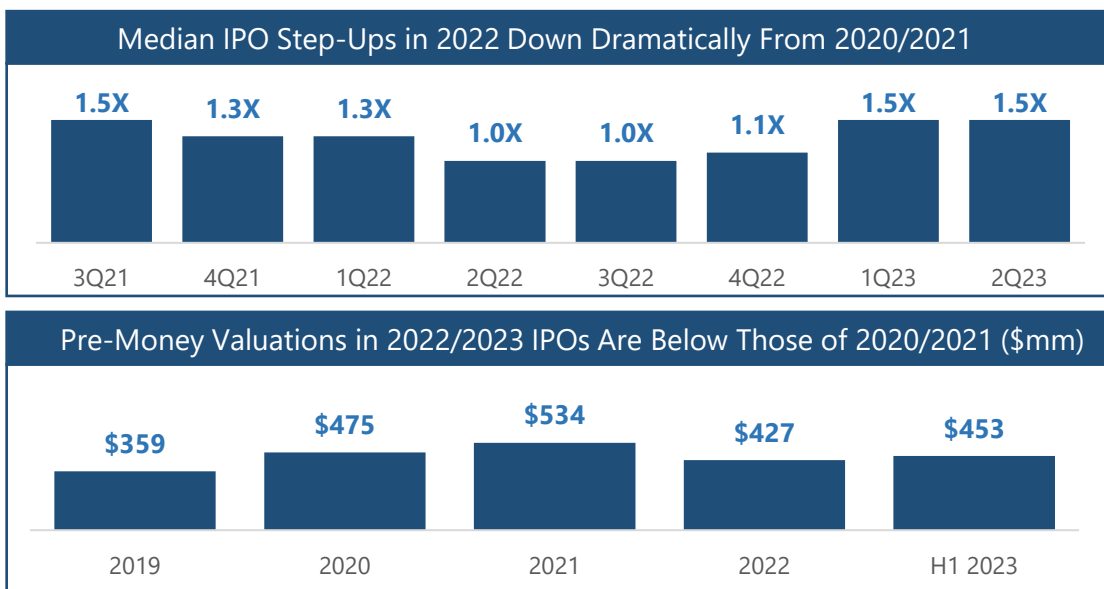
Annualized 2023 U.S. Biotech IPO Volume Down 87% From 2021 And 61% From 2019



Source: CapitalIQ. Biotech companies are defined as R&D-stage therapeutic development companies.

U.S. Biotech IPO Market Conditions

- All three U.S. biotech IPO's this year have been either in immunology (I&I) or cardiometabolic. The market is open to high quality issuers in those sectors.
- These IPOs came at a median step-up to last round valuation of 1.5x. 2023 step-ups have been substantially higher than for companies that issued in 2022. Those step-ups were down dramatically from the Pandemic period.
- After-market performance for the 2023 IPO class has been solid. Median after-market performance for the 2022 IPO class has been -16.1%.
- The market remains selectively open with two U.S. biotech issuers currently publicly on file: Turnstone Biologics and Apogee Therapeutics.
- The tone of the market is benefitting from a lower VIX and we expect that it will improve significantly when after-market performance of IPO's picks up.



Source: Stifel Capital Markets. Pre-money values are fully diluted, accounting for options and warrants using the Treasury Stock Method.

30 Most Recent Biotech IPOs

(\$ in millions)

Issuer	Offer Date	Issuance Amount	Pre-Money Valuation	Pricing vs. Range	Step-Up	Price Change Offer to	
						Day 1	Current
ACELYRIN, Inc.	05/04/23	\$540.0	\$1,221.5	High End	1.5x	30.6%	(1.9%)
Mineralys Therapeutics, Inc.	02/09/23	192.0	452.8	High End	1.7x	15.3%	(0.3%)
Structure Therapeutics, Inc.	02/02/23	161.1	414.3	High End	1.2x	73.3%	95.5%
Acrivon Therapeutics, Inc. ⁽³⁾	11/14/22	99.4	183.0	Below	0.9x	33.1%	9.2%
Prime Medicine, Inc.	10/20/22	175.0	1,501.9	Midpoint	1.2x	(9.6%)	(11.8%)
Third Harmonic Bio, Inc.	09/14/22	185.3	496.0	Midpoint	1.0x	15.8%	(70.6%)
PepGen, Inc.	05/05/22	108.0	169.1	Below	0.8x	7.4%	(16.1%)
HilleVax, Inc.	04/28/22	200.0	449.8	Midpoint	1.3x	12.3%	(2.7%)
AN2 Therapeutics, Inc.	03/25/22	69.0	230.7	Midpoint	1.0x	2.7%	(50.3%)
Arcellx, Inc.	02/04/22	123.8	436.7	Low End	1.3x	12.0%	121.9%
Vigil Neuroscience, Inc.	01/07/22	98.0	329.0	Below	1.4x	(9.6%)	(31.4%)
Amylyx Pharmaceuticals, Inc.	01/07/22	190.0	955.8	Midpoint	1.9x	(4.9%)	21.4%
CinCor Pharma, Inc.	01/07/22	193.6	417.9	Midpoint	1.2x	0.0%	NA
Vaxxinity Inc	11/11/21	78.0	1,720.2	Below	1.0x	27.3%	(80.7%)
IO Biotech, Inc. ⁽⁴⁾	11/04/21	100.1	300.6	Low End	1.0x	11.8%	(86.7%)
Evotec SE	11/03/21	435.0	3,411.2	Below	NA	1.1%	(46.4%)
LianBio	11/01/21	325.0	1,490.0	Midpoint	1.7x	(14.4%)	(84.9%)
Entrada Therapeutics, Inc	10/28/21	181.5	455.3	Midpoint	1.3x	19.8%	(26.3%)
Aura Biosciences Inc	10/28/21	75.6	349.3	Low End	1.3x	5.7%	(10.0%)
Xilio Therapeutics Inc	10/21/21	117.6	339.4	Low End	1.2x	0.0%	(82.9%)
Ventyx Biosciences, Inc.	10/20/21	151.6	690.2	Midpoint	1.3x	31.4%	104.9%
Pyxis Oncology, Inc.	10/07/21	168.0	394.5	High End	1.5x	(17.5%)	(83.4%)
Theseus Pharmaceuticals, Inc.	10/06/21	160.0	500.2	High End	1.1x	16.1%	(40.5%)
Exscientia Plc ⁽⁵⁾	09/30/21	464.7	2,146.2	High End	1.9x	23.2%	(71.0%)
DICE Therapeutics, Inc.	09/14/21	204.0	415.2	High End	1.3x	117.0%	174.7%
Tyra Biosciences, Inc.	09/14/21	172.8	515.8	High End	1.5x	62.5%	9.4%
Eliem Therapeutics, Inc.	08/09/21	80.0	263.9	Below	0.8x	27.2%	(81.3%)
Adagio Therapeutics, Inc.	08/05/21	309.4	1,683.5	Midpoint	1.1x	22.8%	(93.7%)
Rani Therapeutics Holdings, Inc.	07/30/21	73.3	454.9	Below	1.5x	0.0%	(60.8%)
Tenaya Therapeutics, Inc.	07/29/21	180.0	434.7	Midpoint	1.2x	2.3%	(61.7%)

Last 30 IPO Summary Statistics:

Mean	\$187.1	\$760.8	1.3x	17.2%	(19.3%)
Median	\$170.4	\$451.3	1.3x	12.1%	(31.4%)

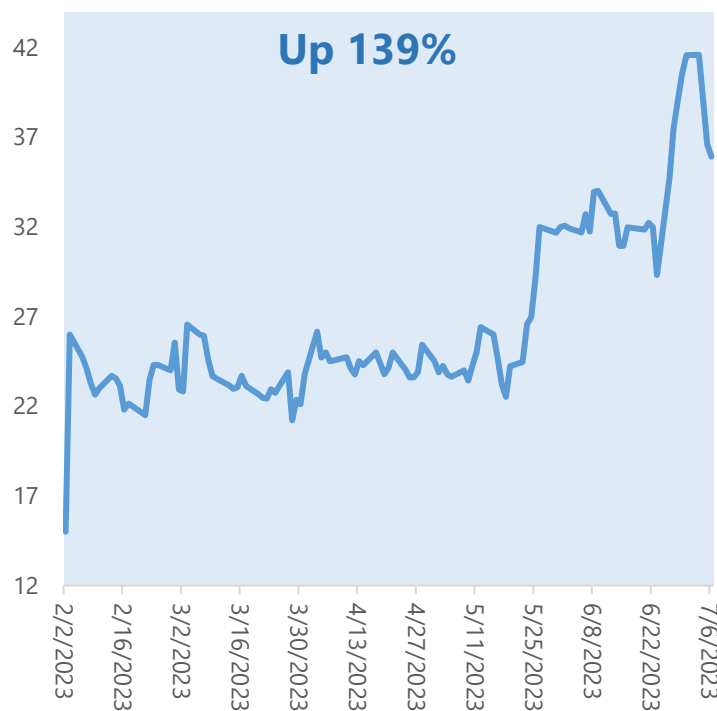
Shows U.S. market listings and excludes companies that raised less than \$50 million or more than \$1bn. Price change to current is computed to June 23, 2023. IPO's highlighted in yellow are those where Stifel acted as an underwriter. Source: Stifel Capital Markets.

Offer to Current of IPO Class of 2023

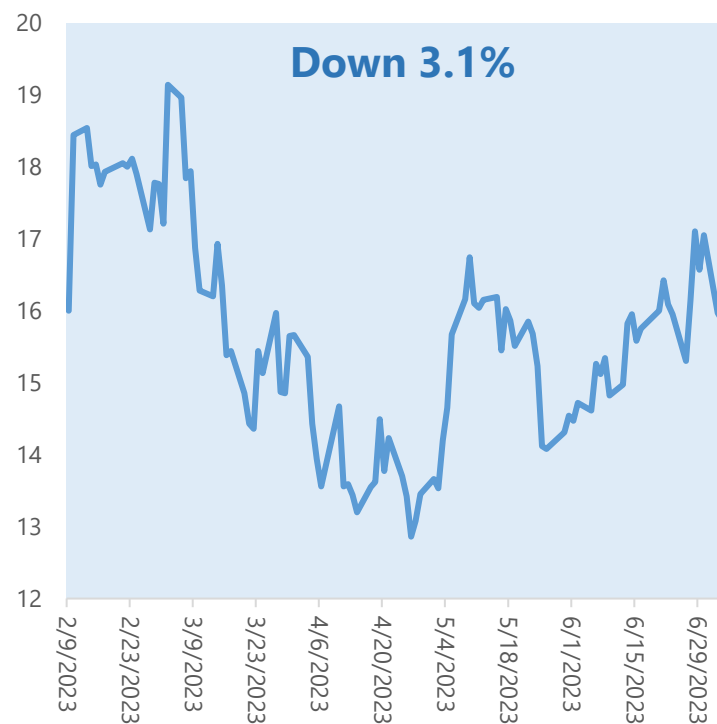
On average, the current to offer of the three IPO's to price this year is 49%.



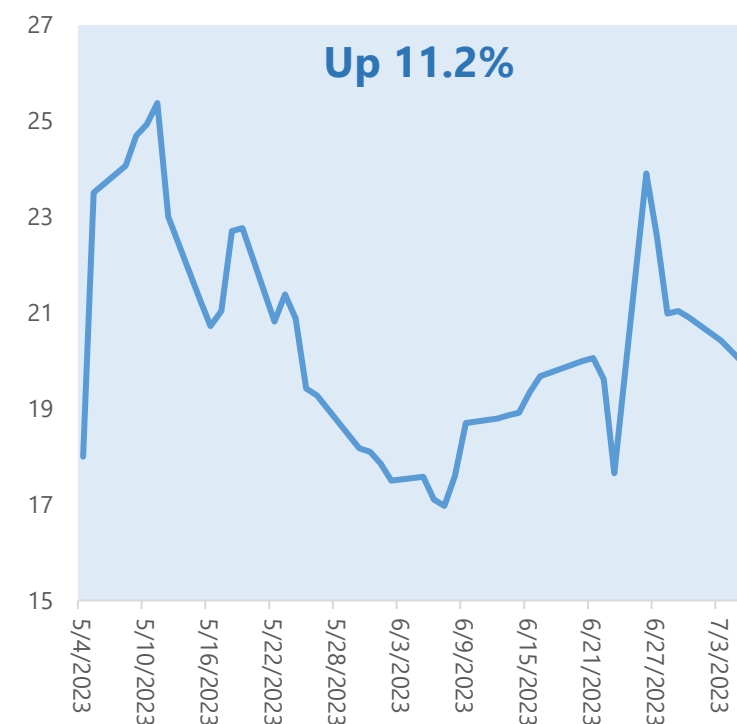
Share Price Since IPO
(Feb 2 to Jul 6, 2023)



Share Price Since IPO
(Feb 9 to Jul 6, 2023)



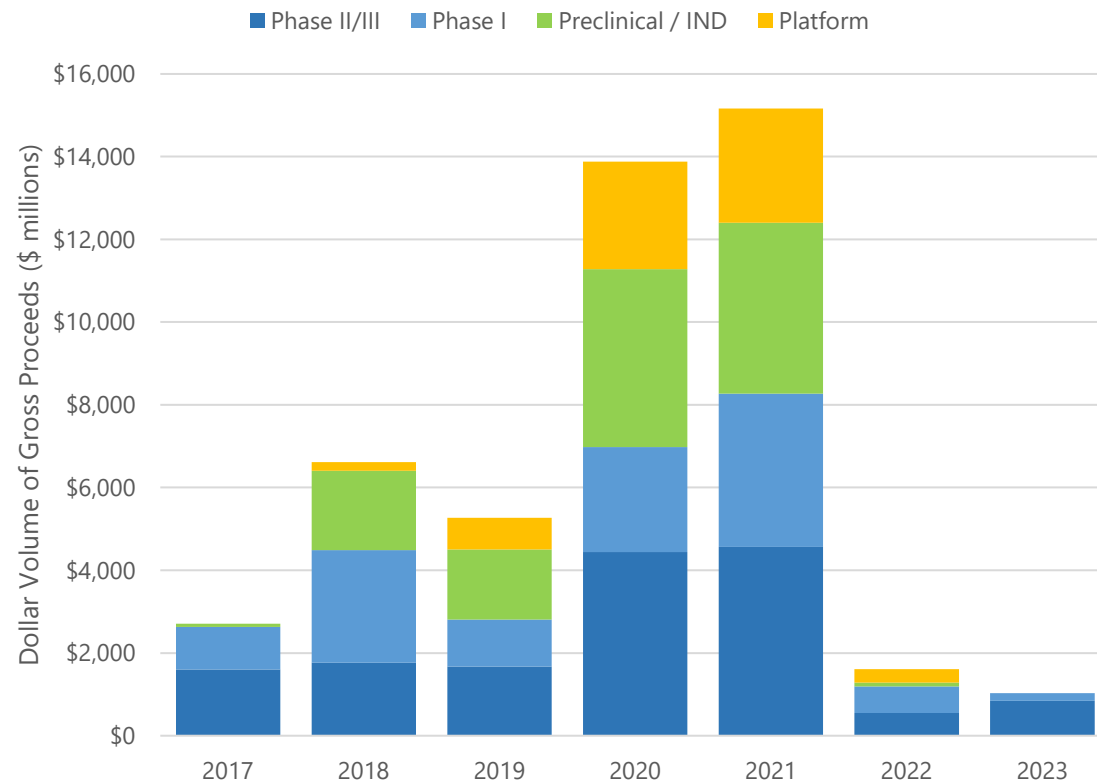
Share Price Since IPO
(May 4 to Jul 6, 2023)



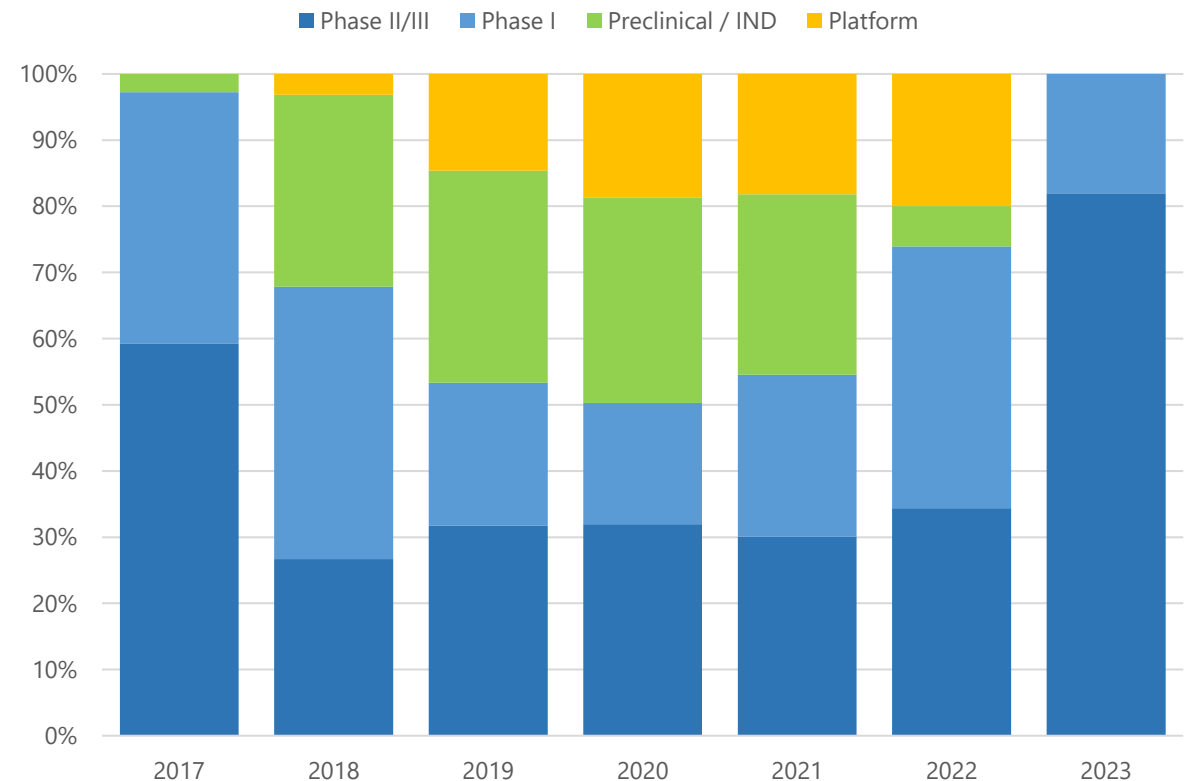
U.S. IPO's this Year Are More Frequent For Clinical Stage Companies

We have not seen any pre-clinical or a platform companies go public in 2023. In contrast, in 2020 half of IPOs were for pre-clinical or platform companies.

U.S. IPOs by Stage of Development of Lead Product at Time of Listing, 2017 to 2023



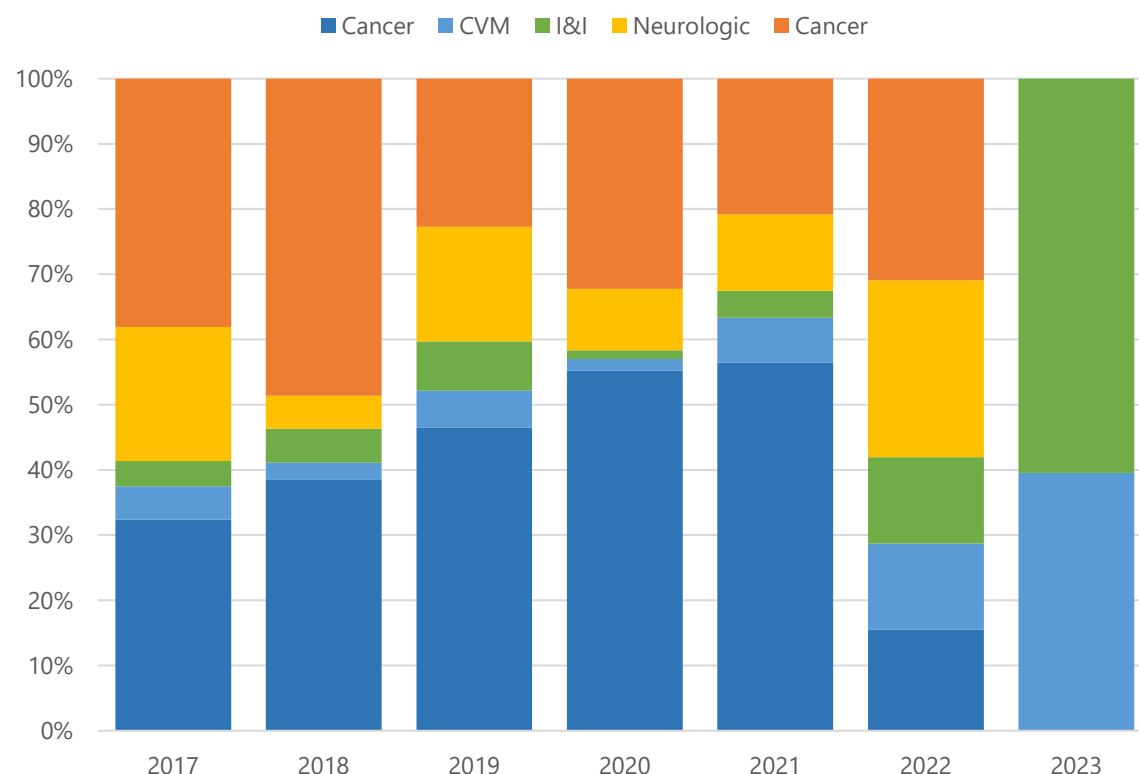
Fraction of U.S. IPOs by Stage of Development of Lead Product at Time of Listing, 2017 to 2023



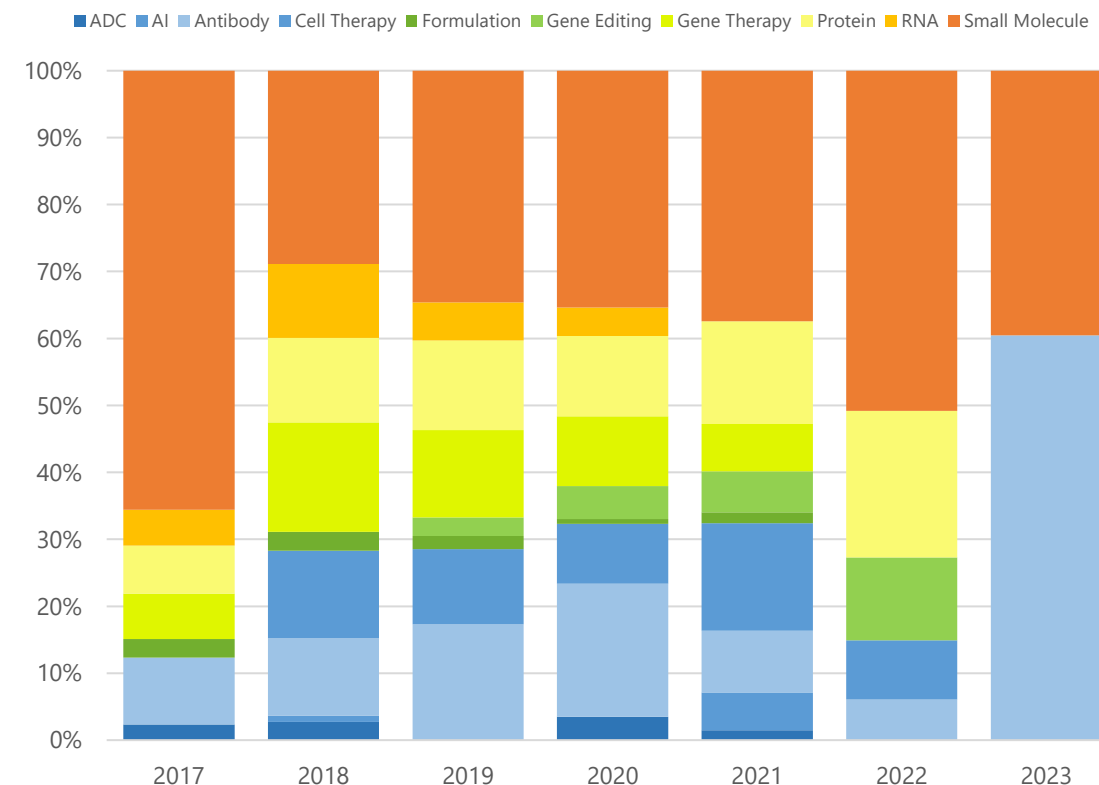
The U.S. IPO Market Has Been Selectively Open to Quality Companies in Cardiometabolic (CVM) and Immunology (I&I). No Novel Modalities.

The IPO market has been accommodating this year to companies pursuing cardiometabolic disease stories and immunology stories. All U.S. IPO's so far have either been built on therapeutic antibodies or small molecule chemistries. We have not seen companies go public based on the promise of novel modalities in some time.

Fraction of U.S. IPOs by Therapeutic Area of Lead Product at Time of Listing, 2017 to 2023



Fraction of U.S. IPOs by Modality of Lead Product at Time of Listing, 2017 to 2023

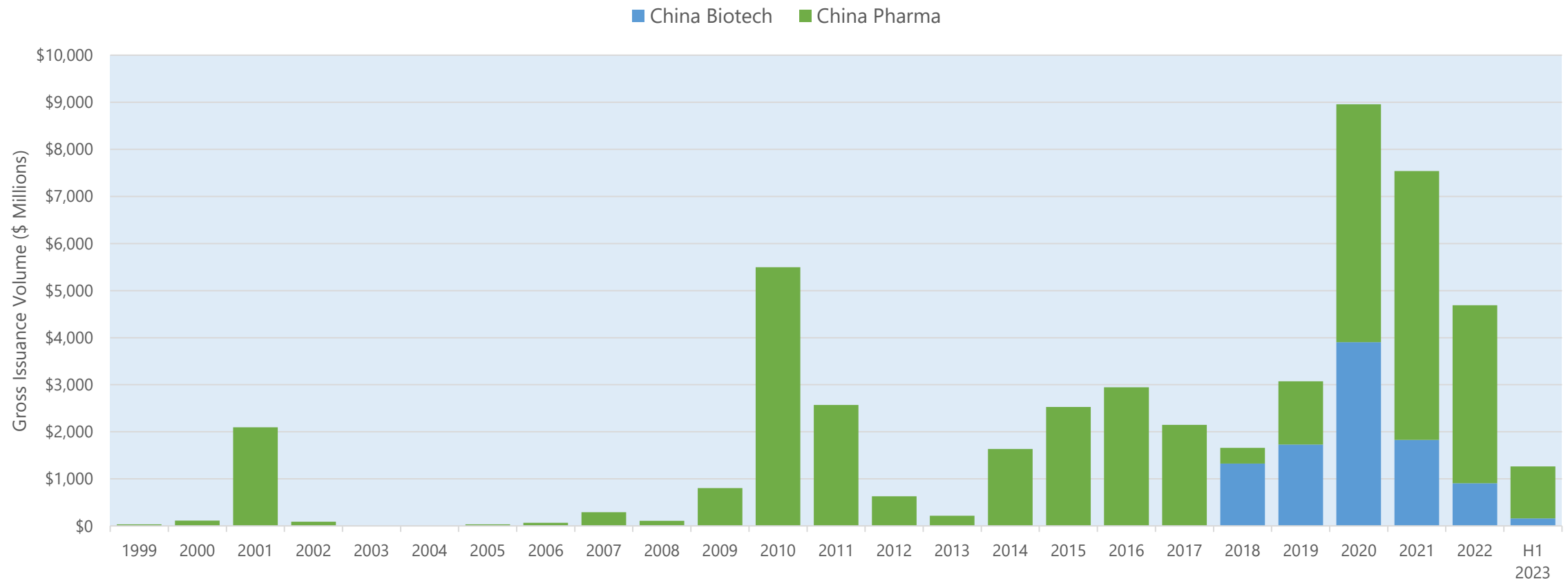


Source: DealForma. IPOs are shown for Nasdaq and NYSE listed R&D-Stage companies that raised at least \$50 million. I&I encompasses investments in autoimmune and inflammation. CVM encompasses, cardiometabolic, diabetes and chronic kidney disease.

China IPO Volume by Exchange and Company Type

The China IPO market has remained open in 2023 to commercial stage pharma companies but biotech offerings are slim. This is changing as Laekna went public last week on the Hong Kong exchange and this week Kelun Biotech is going public. China biotech offering levels in 2023 on an annualized basis are down 82% from 2021.

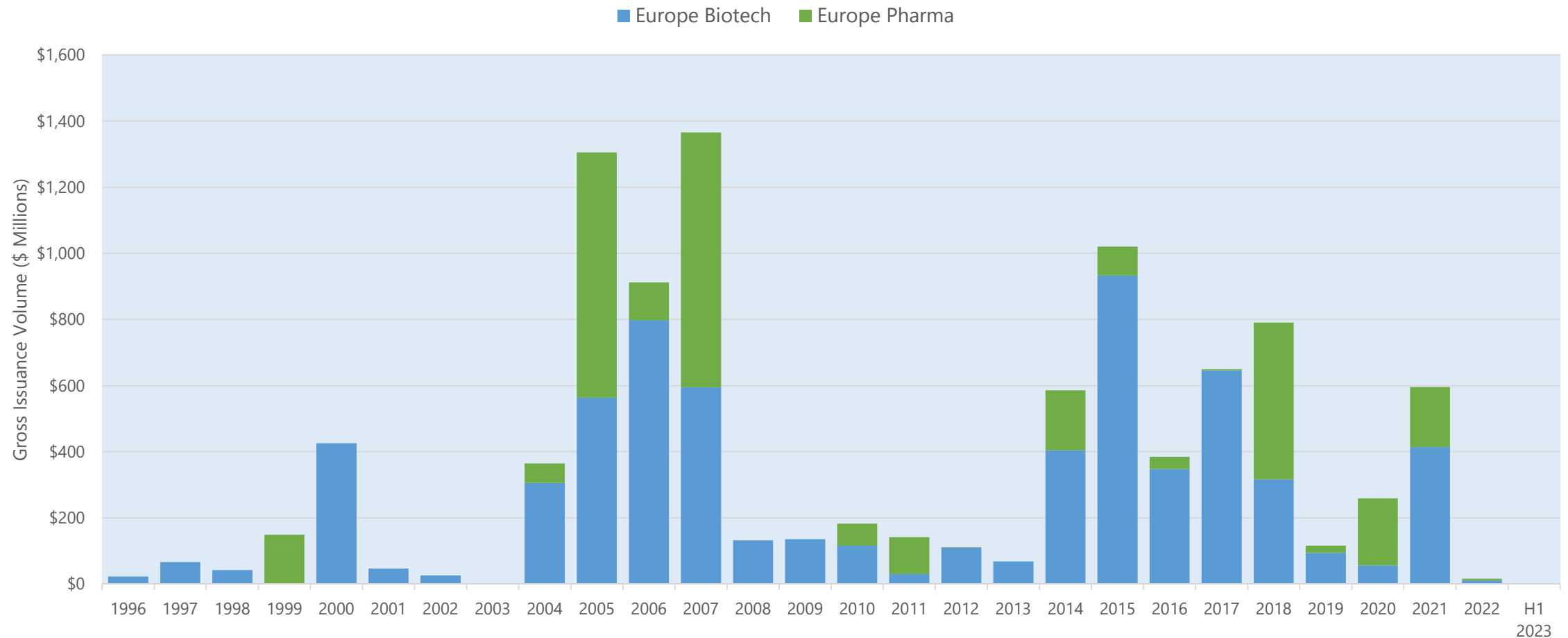
China Biopharma IPO Volume, 1999 to 2023



European Exchange Biopharma IPO Volume by Company Type

The European biotech and commercial pharma IPO market has been quiet since 2021. Volumes in Europe are quite low as many issuers there have shifted to U.S. exchanges where the market is more liquid and has more specialty investors.

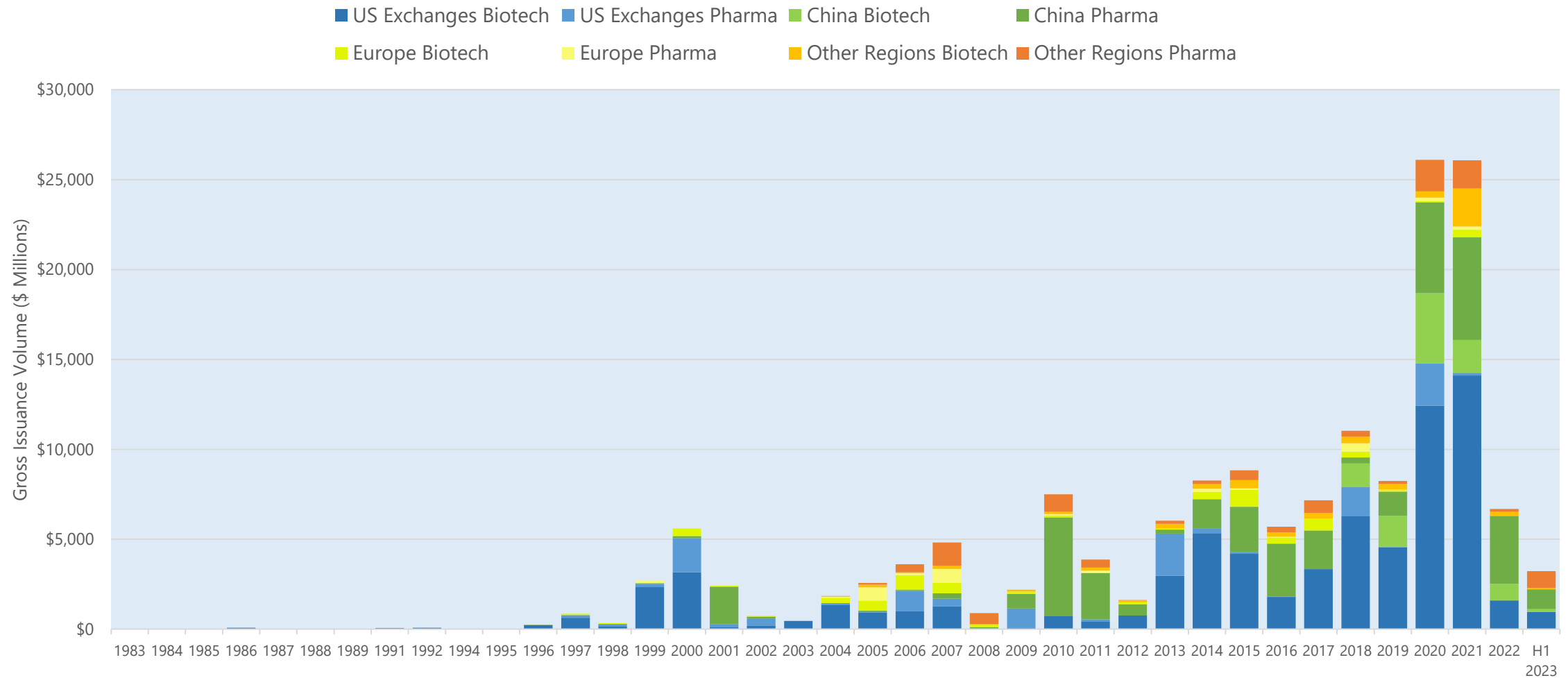
Europe Biopharma IPO Volume, 1996 to 2023



Source: CapitalIQ. Biotech companies are defined as R&D-stage therapeutic development companies. Pharma companies are defined as those that are commercial stage.

Aggregate Global IPO Volume in 2023 is Down 75% From 2021 Levels

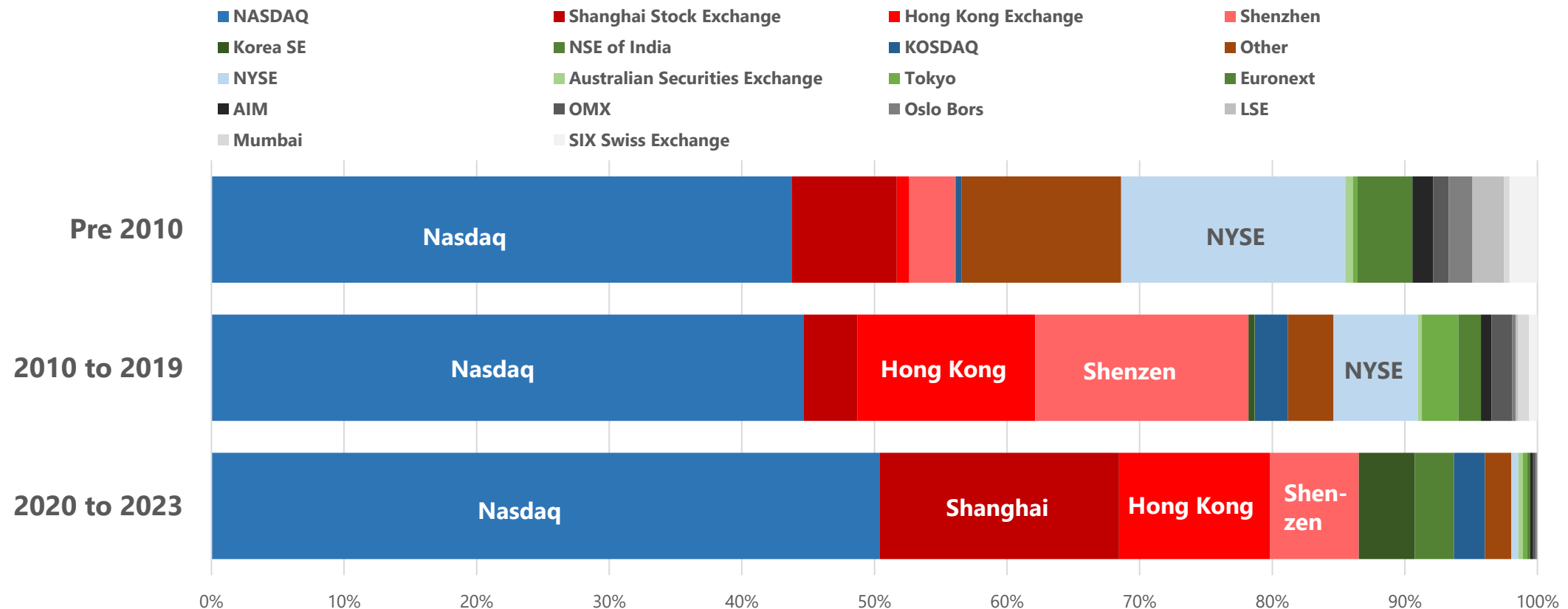
Global Biopharma IPO Volume, 1983 to 2023



Nasdaq and Chinese Exchanges Dominate Biopharma IPO Market

Slightly over half of all IPO dollars in the 2020 to 2023 period were raised on the Nasdaq. Another 36.2% were raised on the Chinese Exchanges (Shanghai, Shenzhen and HK). There is no doubt that the Chinese markets have been starting to challenge the Nasdaq for market share. The NYSE had 16.9% share of new listings in the pre-2010 period. Today, it's share is 0.5%.

Market Share by Dollar Volume of IPO Listing Exchange for Biopharma Stocks, 1983 to 2023



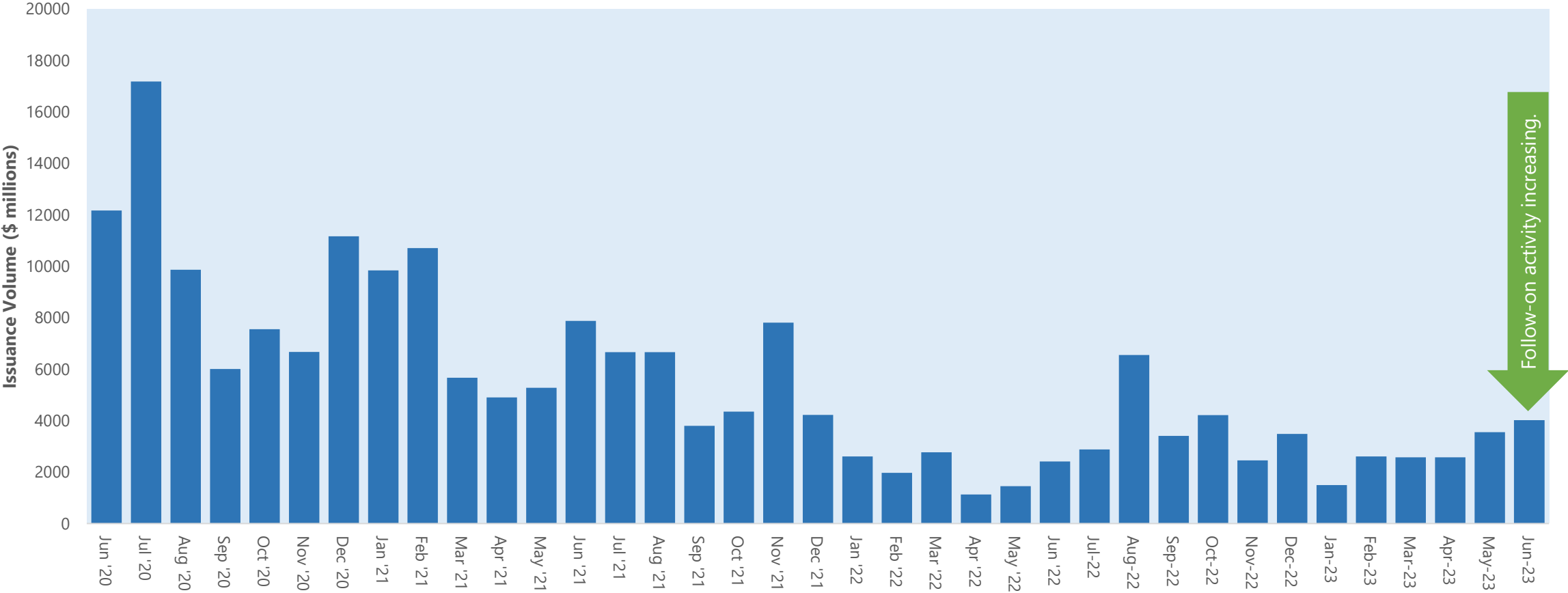
The Biopharma Follow-on Equity / Secondary Market



Monthly Global Biopharma Follow-on Equity Volume

Last month saw over \$4 billion in follow-on volume in the equity capital markets for the first time in eight months. The biotech equity capital markets are clearly improving. Nonetheless, market activity is nowhere near where it was in 2020.

Equity Follow-On (\$volume, \$mm), June 2020 to June 2023

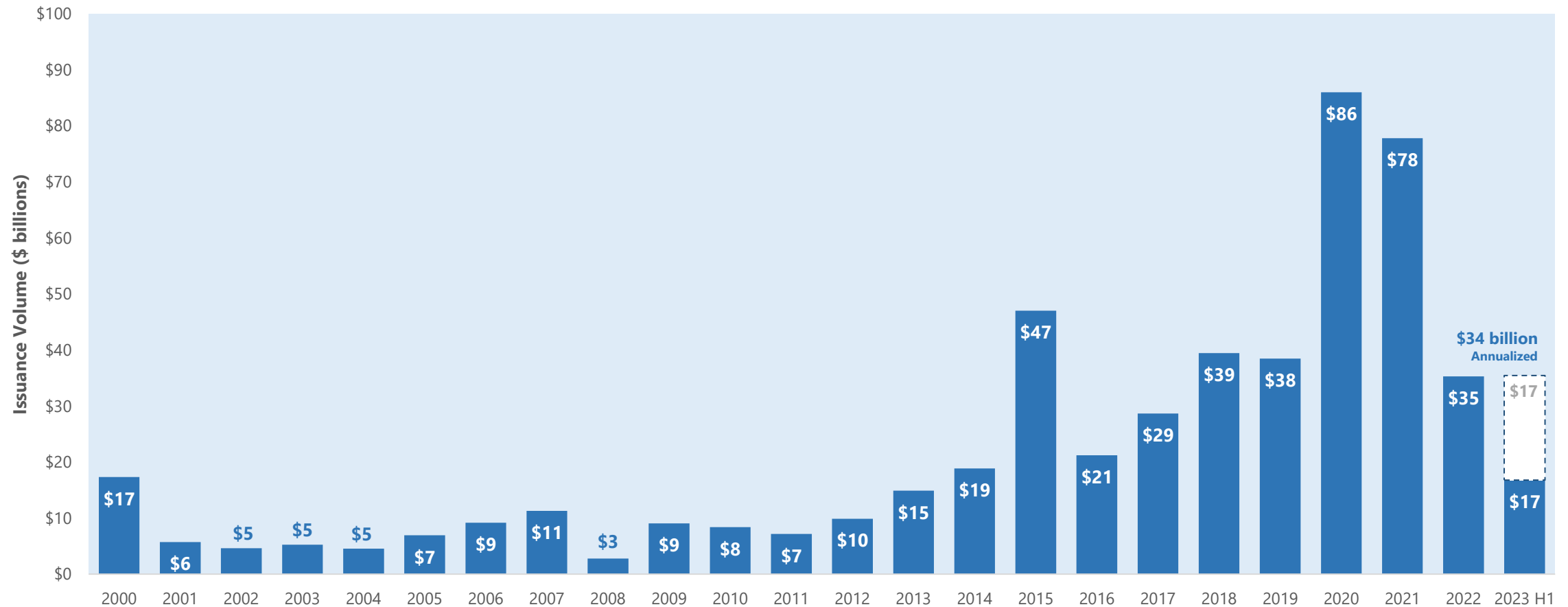


Source: Data from CapitalIQ. Follow-ons from all countries and valuations are included in this analysis.

This Year's Follow-On Volume In Line with Levels Seen in the 2017 to 2019 Period

Follow-on Equity Volume in the Biopharma Sector, 2000 - First Half 2023

(\$ Billions, Worldwide)



Source: Data from CapitalIQ and Stifel Database

Biopharma Follow-On Offerings, H1 2023, Market Cap < \$500mm

Investors have been making money on follow-ons in 2023. The average current to offer is over 10% and stocks are up from offer price over 70% of the time. This is a big positive for the market going forward.

Follow-ons for NASDAQ Listed Biopharma (Market Cap > \$500mm), H1 2023

Ann. Date	Issuer	Type	Raise Amount \$mm	Issue Price / Share	Cap at Issue Date	Discount	Current / Offer	One Day Share Price Reaction
06/28/2023	Axsome Therapeutics	Registered Offering	\$225	\$75.00	\$3,268	0.0%	-3.9%	-2.5%
06/26/2023	MoonLake Immuno	Registered Offering	\$350	\$50.00	\$2,183	-8.8%	0.2%	12.7%
06/15/2023	Zentalis Pharmaceuticals	Registered Offering	\$500	\$22.66	\$1,598	18.3%	25.2%	-0.5%
06/14/2023	Editas Medicine	Registered Offering	\$250	\$10.00	\$779	9.8%	-18.6%	-16.3%
06/13/2023	Kura Oncology	Registered Offering	\$150	\$11.50	\$787	9.6%	-7.8%	-9.8%
06/12/2023	Disc Medicine	Registered Offering	\$62	\$49.00	\$970	-0.3%	-10.8%	4.1%
06/06/2023	Day One Biopharmaceuticals	Registered Offering	\$200	\$13.00	\$956	9.5%	-9.6%	0.3%
06/06/2023	NewAmsterdam Pharma	Registered Offering	\$200	\$11.50	\$940	16.5%	3.4%	-16.5%
06/06/2023	Cogent Biosciences	Registered Offering	\$100	\$12.00	\$851	7.9%	2.0%	-10.2%
06/01/2023	Lexicon Pharmaceuticals	PIPE	\$150	\$2.60	\$618	4.1%	-13.8%	1.3%
05/23/2023	Phathom Pharmaceuticals	Registered Offering	\$150	\$11.75	\$643	10.1%	16.2%	-10.4%
05/21/2023	Krystal Biotech	PIPE	\$325	\$92.50	\$2,386	3.7%	28.1%	22.4%
05/16/2023	Akero Therapeutics	Registered Offering	\$131	\$42.00	\$2,324	9.5%	7.3%	-0.2%
05/11/2023	ANI Pharmaceuticals	Registered Offering	\$100	\$39.50	\$654	10.1%	37.1%	-5.2%
05/04/2023	4D Molecular Therapeutics	Registered Offering	\$70	\$16.00	\$532	0.5%	16.5%	5.3%
05/03/2023	ImmunoGen	Registered Offering	\$125	\$12.50	\$2,826	-2.0%	51.9%	8.3%
05/02/2023	Morphic Holding	Registered Offering	\$125	\$45.00	\$1,786	7.2%	28.2%	5.6%
04/24/2023	IDEAYA Biosciences	Registered Offering	\$55	\$18.50	\$895	8.7%	23.3%	-8.0%
04/17/2023	Vaxcyte	Registered Offering	\$85	\$41.00	\$3,281	3.2%	21.2%	4.2%
04/04/2023	Protagonist Therapeutics	Registered Offering	\$125	\$20.00	\$1,026	7.2%	14.7%	-16.4%
03/29/2023	Viking Therapeutics	Registered Offering	\$60	\$14.50	\$1,137	9.0%	8.8%	8.8%
03/29/2023	Biomea Fusion	Registered Offering	\$60	\$30.00	\$888	7.3%	-25.8%	-1.2%
03/29/2023	Avadel Pharmaceuticals	Registered Offering	\$50	\$8.50	\$548	4.4%	76.0%	-4.2%
03/22/2023	89bio	Registered Offering	\$50	\$16.25	\$849	-18.8%	16.9%	23.8%
03/06/2023	BridgeBio Pharma	Registered Offering	\$75	\$17.00	\$2,573	-2.9%	-0.2%	12.3%
02/22/2023	Apellis Pharmaceuticals	Registered Offering	\$62	\$63.00	\$7,011	4.3%	42.0%	1.7%
02/13/2023	Morphic Holding	PIPE	\$50	\$35.35	\$1,363	9.4%	63.3%	5.5%
02/06/2023	CureVac	Registered Offering	\$75	\$9.25	\$1,803	12.6%	15.5%	-11.3%
02/01/2023	Roivant Sciences	Registered Offering	\$65	\$7.50	\$5,441	12.2%	35.9%	-11.1%
01/17/2023	Fulcrum Therapeutics	Registered Offering	\$210	\$13.00	\$677	7.1%	-74.2%	-11.2%

Average	\$141	\$27.01	\$1,720	5.6%	12.3%	-0.6%
Percent Positive					70.0%	46.7%
Q1	\$63	\$11.81	\$802	3.3%	-3.0%	-10.1%
Median	\$112	\$16.63	\$998	7.2%	15.1%	-0.4%
Q3	\$188	\$40.63	\$2,288	9.6%	27.4%	5.5%

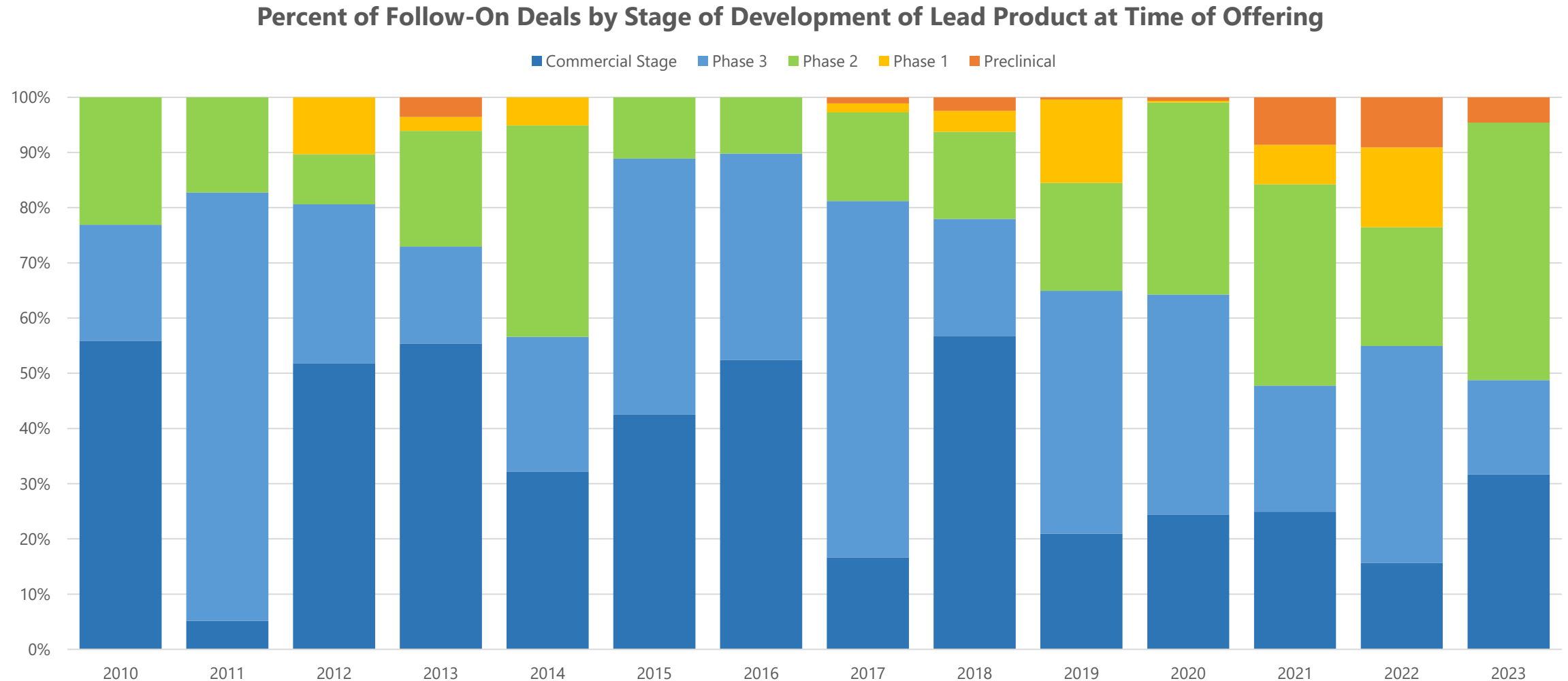
Follow-ons for NASDAQ Listed Biopharma (Market Cap < \$500mm), H1 2023

Ann. Date	Issuer	Type	Raise Amount \$mm	Issue Price / Share	Cap at Issue Date	Discount	Current / Offer	One Day Share Price Reaction
06/30/2023	Black Diamond Therapeutics	Registered Offering	\$400	\$5.00	\$183	-4.2%	1.0%	0.0%
06/29/2023	Immunome	PIPE	\$160	\$5.91	\$72	40.3%	23.2%	2.7%
06/24/2023	ORIC Pharmaceuticals	PIPE	\$350	\$7.00	\$316	13.0%	-7.9%	0.0%
06/22/2023	Aeglea BioTherapeutics	PIPE	\$400	\$0.29	\$19	57.3%	36.4%	-12.3%
06/21/2023	IGM Biosciences	Registered Offering	\$137	\$8.00	\$346	17.9%	9.7%	7.6%
06/21/2023	AlloVir	Registered Offering	\$240	\$3.75	\$337	-16.0%	23.9%	-35.7%
06/20/2023	Pharvaris	PIPE	\$220	\$10.07	\$341	45.5%	13.6%	-1.9%
06/15/2023	Verastem	Registered Offering	\$75	\$9.75	\$163	-18.5%	9.9%	-5.0%
06/15/2023	Praxis Precision Medicines	Registered Offering	\$100	\$0.95	\$61	27.4%	-5.0%	18.2%
06/08/2023	Elevation Oncology	Registered Offering	\$250	\$2.25	\$55	-32.7%	20.2%	-32.3%
06/06/2023	Vaxart	Registered Offering	\$125	\$0.94	\$127	-21.3%	24.4%	-27.4%
05/31/2023	Lexicon Pharmaceuticals	Registered Offering	\$275	\$2.60	\$493	-13.8%	21.2%	-17.9%
05/26/2023	Lyra Therapeutics	PIPE	\$120	\$1.78	\$57	130.3%	31.3%	0.0%
05/25/2023	TScan Therapeutics	Registered Offering	\$100	\$2.00	\$48	17.0%	17.7%	31.3%
05/24/2023	Kamada Ltd.	PIPE	\$250	\$4.75	\$225	6.5%	12.0%	-0.2%
05/22/2023	Icosavax	Registered Offering	\$125	\$8.10	\$336	6.2%	-2.9%	24.8%
05/17/2023	Caballetta Bio	Registered Offering	\$150	\$12.00	\$376	-0.3%	1.1%	1.4%
05/17/2023	Prelude Therapeutics	Registered Offering	\$87	\$5.75	\$275	-20.7%	8.7%	-11.4%
05/15/2023	Coherus BioSciences, Inc.	Registered Offering	\$159	\$4.25	\$342	5.9%	13.1%	5.9%
05/15/2023	X4 Pharmaceuticals, Inc.	PIPE	\$125	\$1.52	\$186	26.3%	0.0%	15.8%
05/03/2023	MeiraGTx Holdings	PIPE	\$250	\$5.75	\$280	18.3%	1.5%	7.9%
05/03/2023	Reneo Pharmaceuticals, Inc.	Registered Offering	\$85	\$8.00	\$201	-16.3%	18.9%	-1.4%
04/28/2023	Eledon Pharmaceuticals, Inc.	PIPE	\$68	\$2.31	\$32	-40.3%	-10.0%	0.0%
04/27/2023	Zura Bio Limited	PIPE	\$107	\$4.25	\$117	88.0%	46.9%	-14.9%
04/23/2023	Applied Therapeutics, Inc.	PIPE	\$200	\$0.95	\$45	40.7%	0.1%	16.3%
04/18/2023	Immuneering Corporation	Registered Offering	\$85	\$11.00	\$291	-12.5%	17.7%	-3.2%
03/30/2023	Checkpoint Therapeutics, Inc.	Registered Offering	\$62	\$3.60	\$42	-32.2%	-7.5%	-32.8%
03/30/2023	Akari Therapeutics, Plc	Registered Offering	\$75	\$0.15	\$11	8.1%	0.0%	21.1%
03/30/2023	RedHill Biopharma Ltd.	PIPE	\$100	\$4.00	\$9	-69.5%	9.9%	-7.9%
03/23/2023	Generation Bio Co.	PIPE	\$80	\$6.10	\$400	-17.2%	-22.0%	1.6%
02/28/2023	Zseventy bio, Inc.	Registered Offering	\$51	\$11.50	\$449	-11.9%	14.8%	-18.4%
02/23/2023	Omega Therapeutics, Inc.	Registered Offering	\$63	\$5.78	\$318	-14.2%	1.4%	-2.0%
02/21/2023	Verrica Pharmaceuticals Inc.	Registered Offering	\$198	\$6.75	\$282	-9.8%	19.3%	-3.2%
02/15/2023	Galera Therapeutics, Inc.	Registered Offering	\$50	\$2.10	\$60	41.8%	-26.2%	-4.2%
02/10/2023	Fusion Pharmaceuticals Inc.	PIPE	\$140	\$3.40	\$152	38.2%	1.2%	0.0%
02/02/2023	ADC Therapeutics SA	Registered Offering	\$57	\$5.00	\$403	-57.6%	-2.0%	-5.5%
01/24/2023	Precigen	Registered Offering	\$90	\$1.75	\$364	-33.7%	20.1%	-24.7%
01/24/2023	Verastem	PIPE	\$59	\$0.75	\$13	960.0%	89.8%	4.1%
01/18/2023	bluebird bio	Registered Offering	\$60	\$6.00	\$498	-44.3%	0.4%	-1.7%

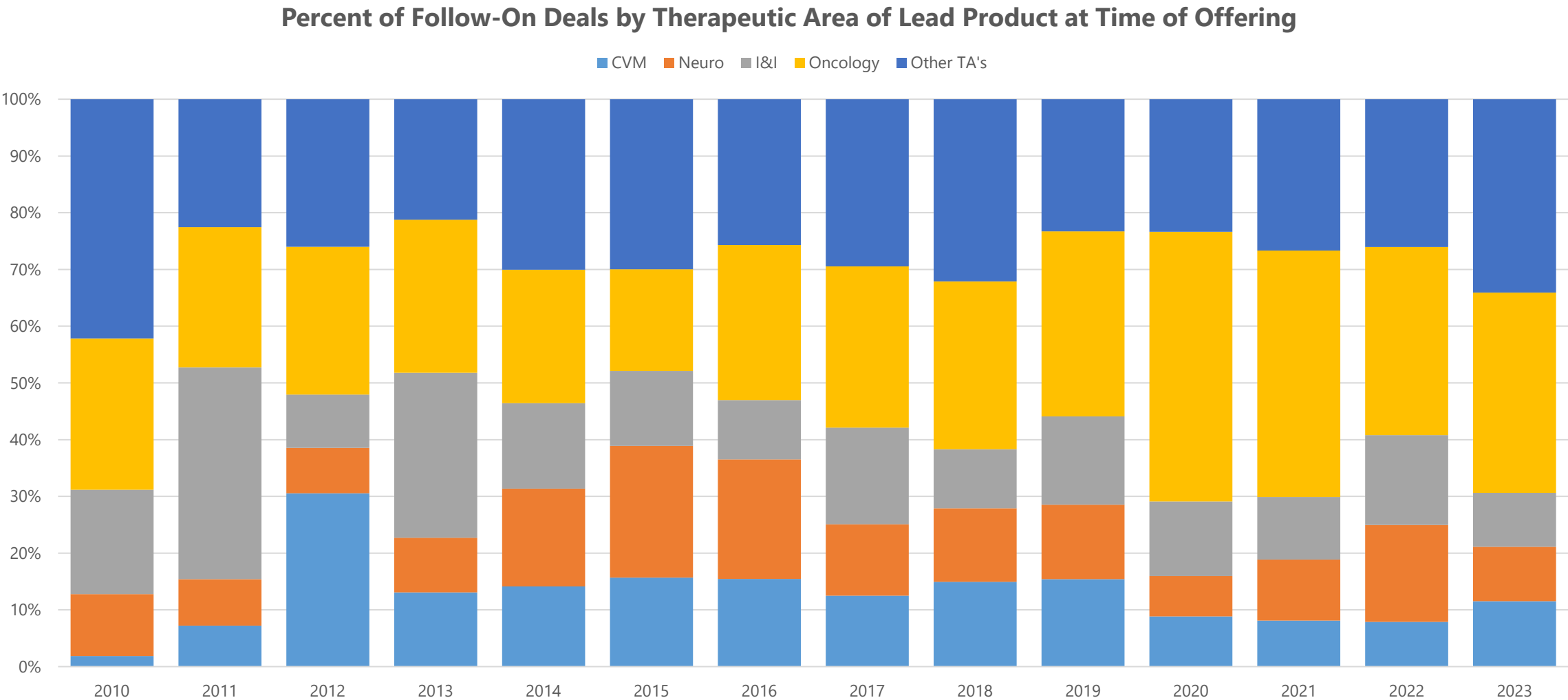
Average	\$147	\$4.74	\$213	28.2%	10.9%	-2.7%
Percent Positive					74.4%	33.3%
Q1	\$77	\$2.02	\$58	-17.8%	0.1%	-9.7%
Median	\$120	\$4.25	\$201	-0.3%	9.9%	-1.4%
Q3	\$199	\$6.59	\$339	26.9%	19.7%	3.4%

Preclinical and Phase 1 Follow-On Deals Nearly Extinct in 2023

- Deals Overwhelmingly for Companies with Clinical Data



Thus Far in 2023, the Follow-on Market has Seen Increased Volume in Cardiometabolic (CVM) While Oncology Has Held Steady



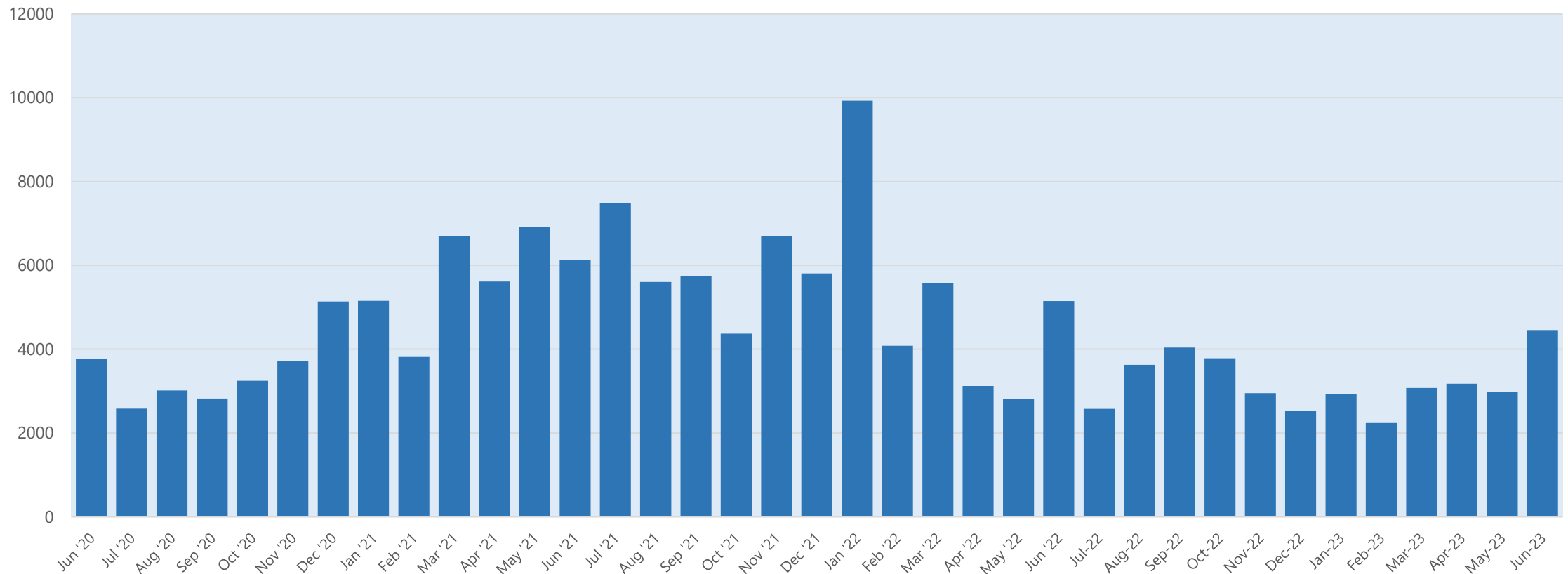
Venture Equity Environment



Monthly BioPharma Private Equity / Venture Placement Volume Picked up Significantly in June 2023

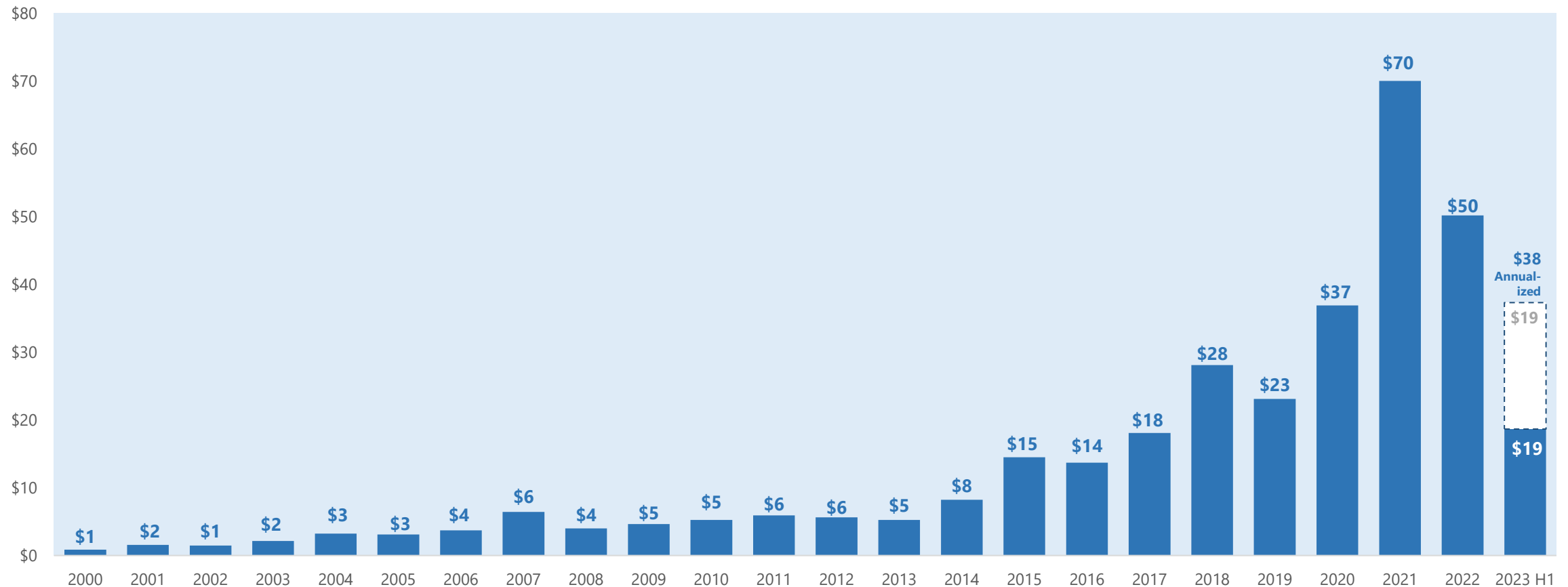
June equity privates' volume was the highest in a year's time reflecting an increase in larger rounds getting done. This was distorted, however, by a \$1bn raise last week by Galderma. But even if that deal were omitted, June 2023 would have been the most active month in eight months.

Monthly Private Equity Placement (\$volume, \$mm), Jan 2020 to June 2023



We Are On Track To Do \$38 Billion in Venture Equity Deals in 2023; Volume Down Substantially From 2021/2022 Period











Venture Privates in the Biopharma Sector, 2000 - First Half 2023
(\$ Billions, Worldwide)



Top Venture Equity Rounds For U.S. Companies

This year has seen a blend of very strong platform stories via large Series A financings, particularly in the RNA field. Other companies such as Alkeus, Upstream or Carmot have instead been able to finance around high potential clinical stage assets.

Largest Venture Raises for U.S. Domiciled R&D Stage Biotech Companies, Jan 1 to June 30, 2023

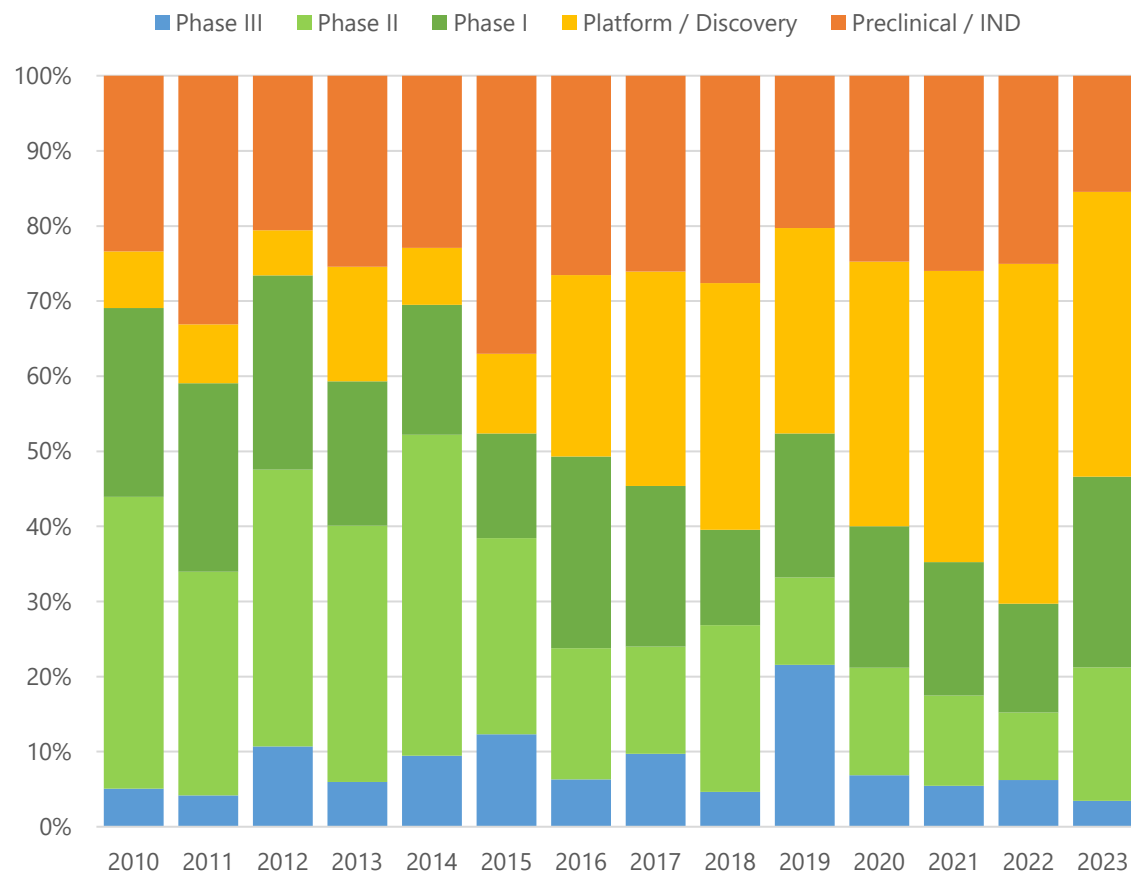
Announcement Date	Company	Subsector	Technology	Stage of Development	Lead Investor	Round	Amount (\$mm)
5/23/2023	 ReNAgade THERAPEUTICS	Multiple	RNA Editing	Platform / Discovery	MPM Capital	Series A	\$300
4/26/2023	 ORBITAL THERAPEUTICS	Multiple	RNA Delivery	Platform / Discovery	ARCH	Series A	\$270
3/1/2023	 CARGO THERAPEUTICS	Heme Malignancies	CAR-t	Phase 1	Third Rock	Series A	\$200
6/8/2023	 UpstreamBIO™	I&I	TSLP Antibody	Phase 2	Enevate / Venrock	Series B	\$200
2/16/2023	 ERA THERAPEUTICS	Gene Therapy	Large payloads	Platform / Discovery	ARCH	Series B	\$193
5/01/2023	 Retro	Aging	Cell Reprogramming	Platform / Discovery	Undisclosed	Series A	\$180
4/13/2023	 T* R L BIOTHERAPEUTICS	Oncology	Claudin Antibodies	Phase 1	Goldman Sachs Asset Management	Series B	\$158
3/27/2023	 ARRIVENT	Oncology	Precision Oncology / Small Molecule	Phase 1	Sofinnova Investments	Series B	\$155
6/05/2023	 Alkeus PHARMACEUTICALS	Ophthalmology	Small Molecule	Phase 2	Bain Life Sciences	Series B	\$150
5/25/2023	 CARMOT THERAPEUTICS	Cardiometabolic	Protein Therapeutics	Phase 1	Deep Track Capital	Series E	\$150

Source: CapIQ, Crunchbase, Torrey Research

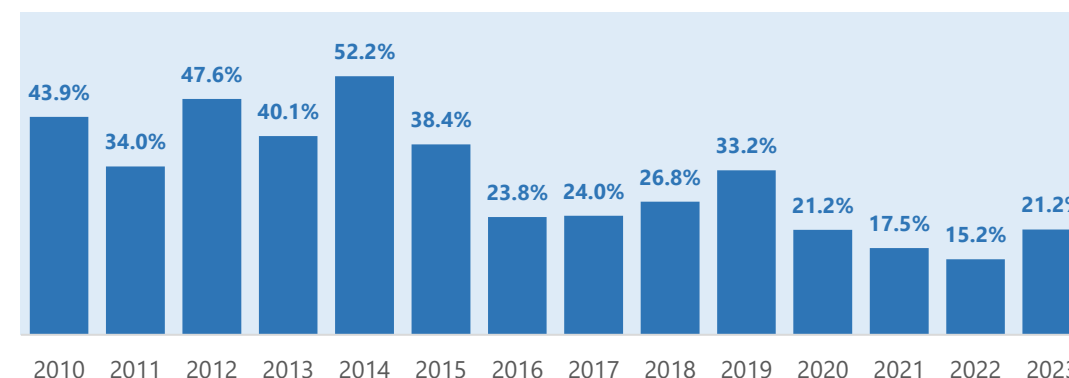
This Year Saw More Late-Stage Venture Investments

The share of venture dollars invested in later stage molecules went up in 2023. However, over a longer period, we saw distinctly less late-stage investments after 2019 (presumably because these companies could go public). Platform investment levels fell slightly in 2023. However, over the long-term, the popularity of investing in platform companies is a relatively new thing, taking off in a meaningful way only in 2016 – and peaking last year when over 45% of all venture dollars went into discovery stage deals and platforms.

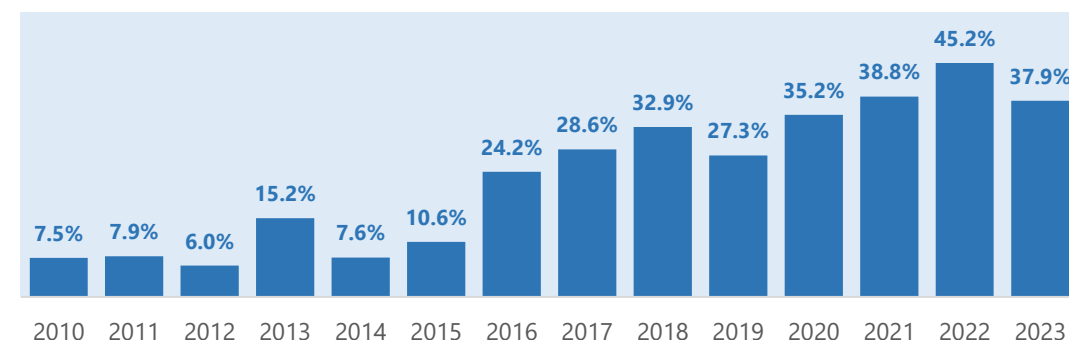
Fraction of Biopharma Venture Dollars by Stage of Development by Year



Fraction of Biopharma Venture Dollars Invested in Phase 2/3 Molecules (Versus All Stages), 2010 to H1 2023

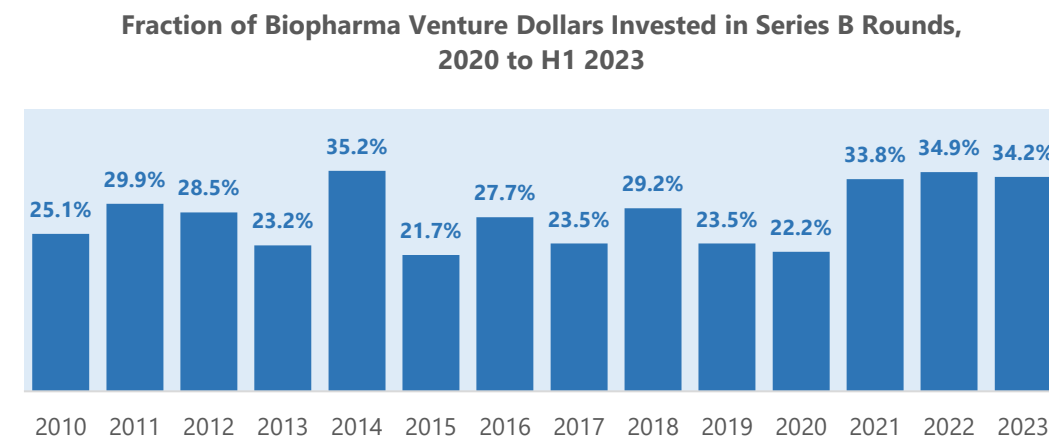
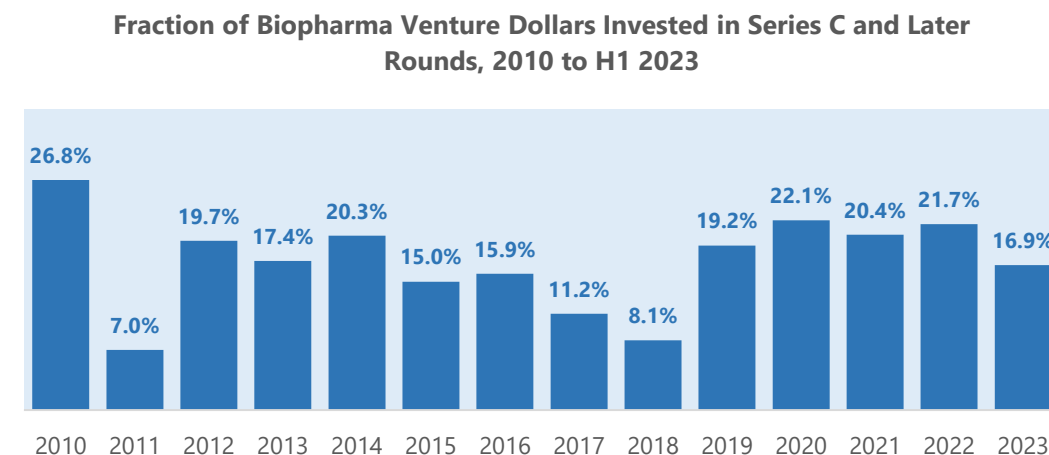
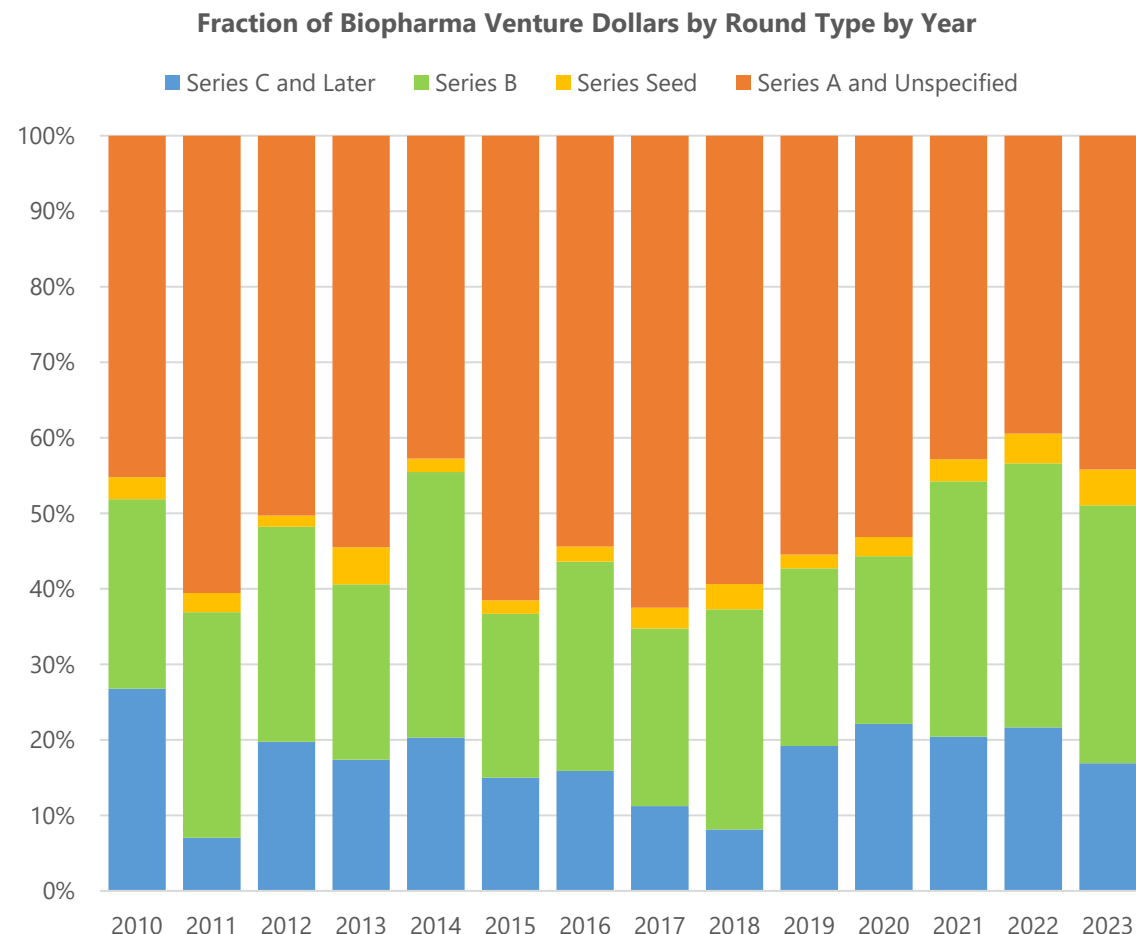


Fraction of Biopharma Venture Dollars Invested in Platform / Discovery Stage Technologies (Versus All Stages)



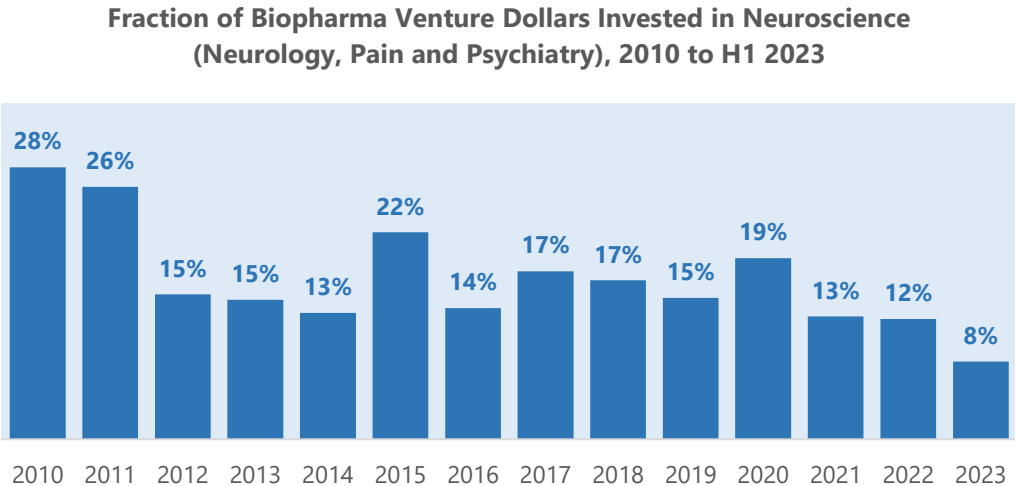
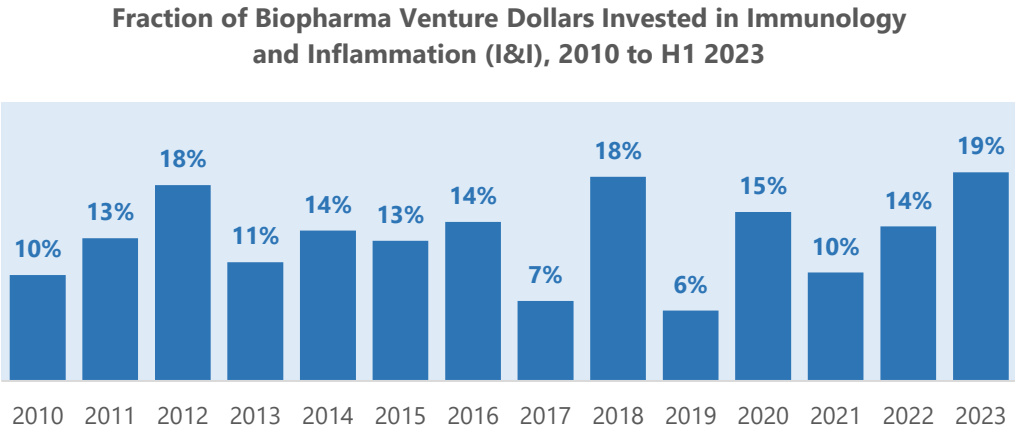
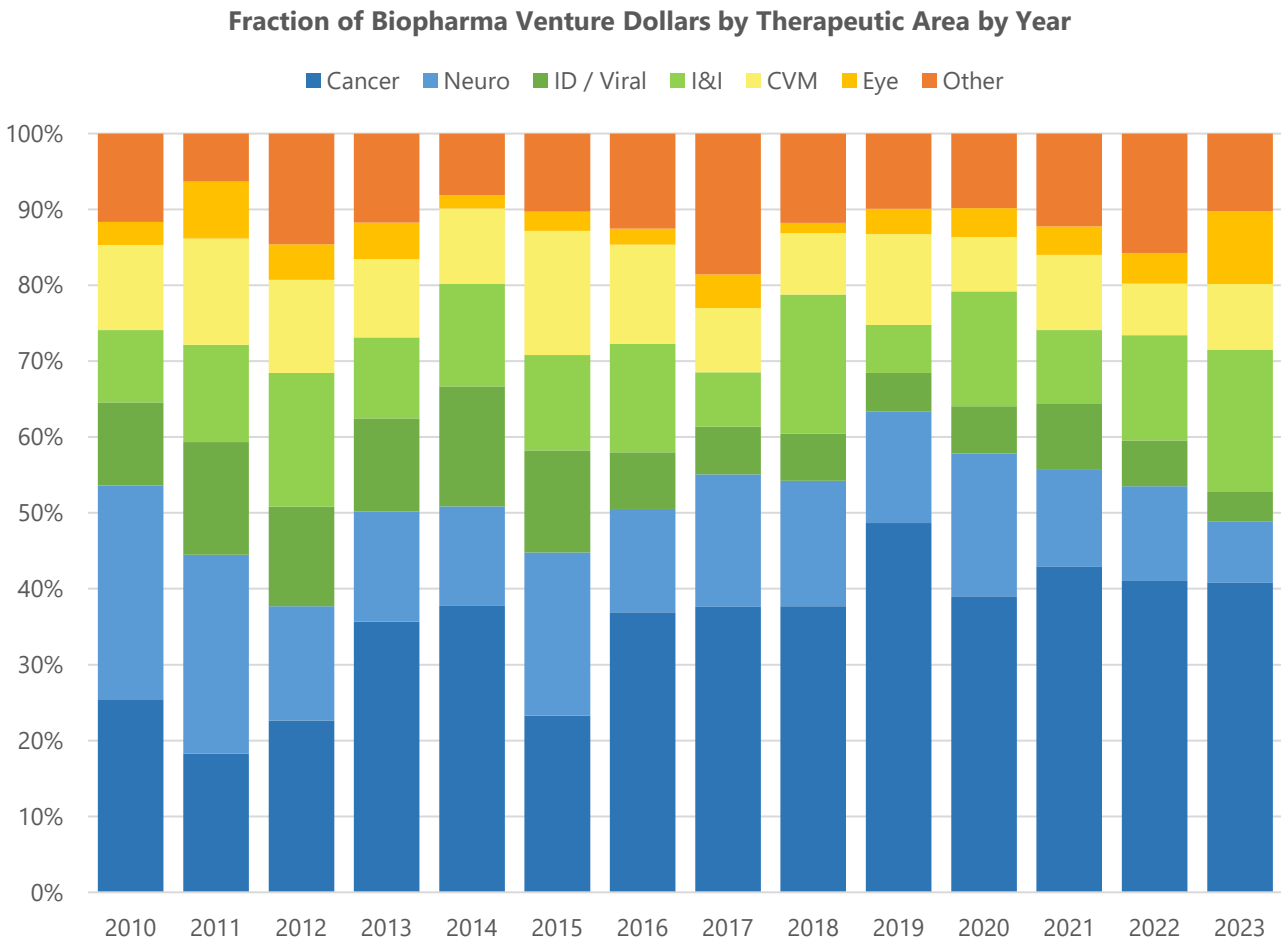
This Year Saw More Series A Stage Rounds Getting Done

The share of money going into Series Seed and Series A deals went up in 2023 while the share of money going into Series B rounds held steady. In contrast, Series C and later rounds saw less activity in 2023 versus earlier years.



Immunology Investment Area Strongest in 2023

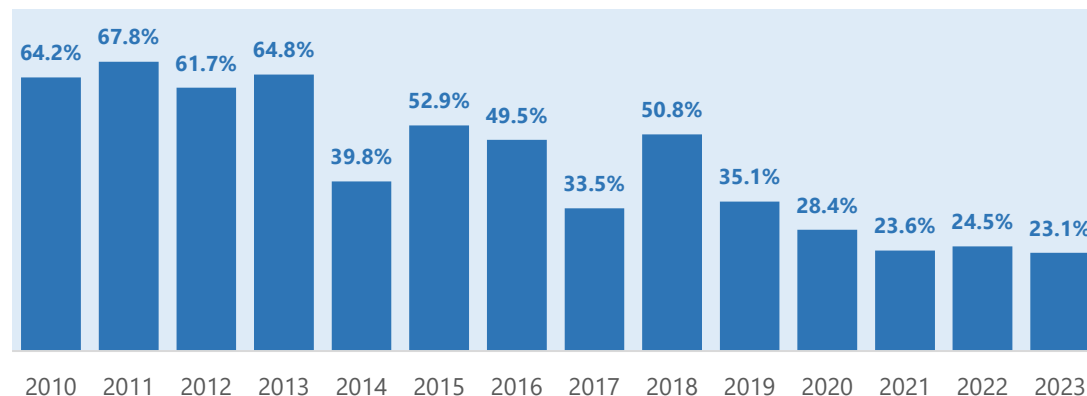
We have seen venture investments into oncology companies hold steady in 2023, investments into I&I companies rise in 2023, investments into neurology companies continue a long-term decline (on a relative basis) and investments into eye-related disease jump.



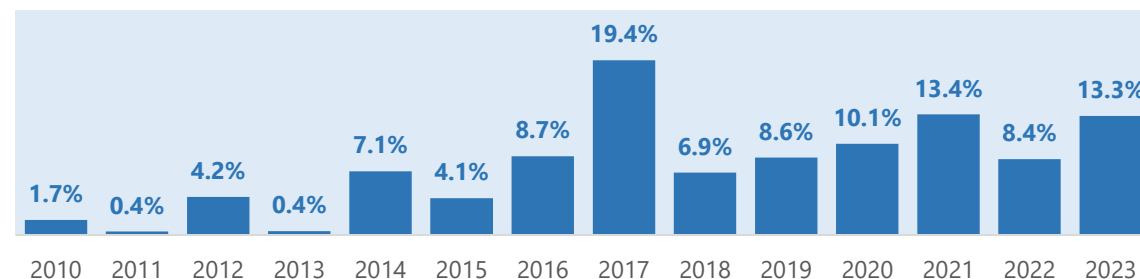
This Year Saw More Focus on Biologics and RNA Therapies

Small molecule type investments are down while biologics, particularly RNA therapeutics, investments is up. Cell therapy investments are holding steady while investments in genetic medicine, particularly gene editing, were down in the first half of 2023.

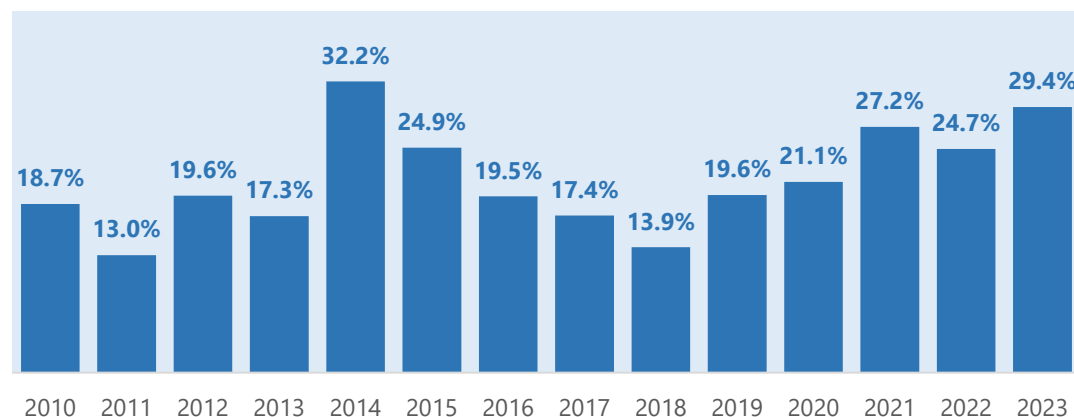
Fraction of Biopharma Venture Dollars Invested in Small Molecules



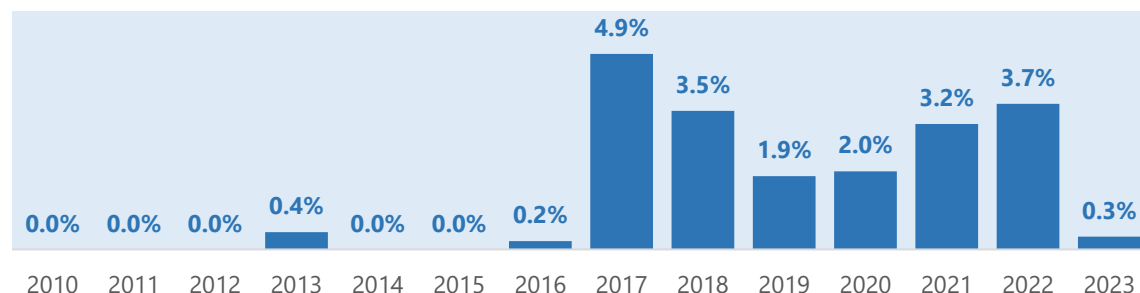
Fraction of Biopharma Venture Dollars Invested in Cell Therapy Companies



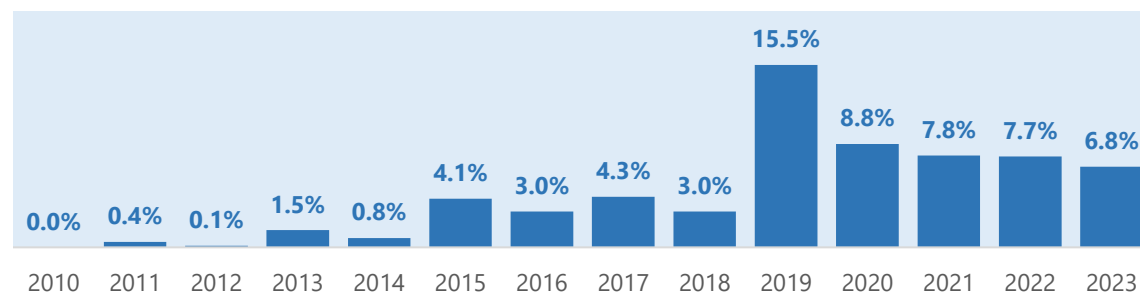
Fraction of Biopharma Venture Dollars Invested in Biologics
(Antibodies, Proteins, DNA and RNA Therapies)



Fraction of Biopharma Venture Dollars Invested in Gene Editing / CRISPR



Fraction of Biopharma Venture Dollars Invested in Gene Therapy Companies



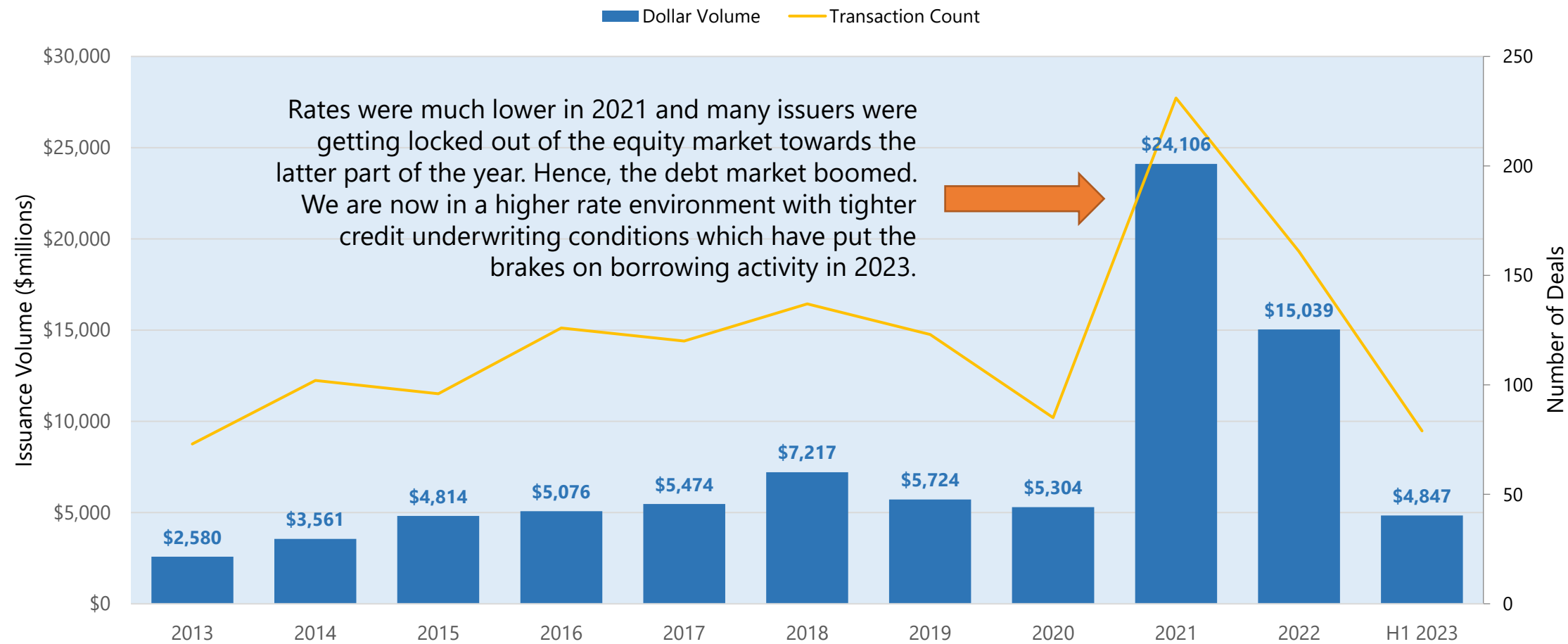
Source: DealForma. Venture investments into the biopharma sector. Data for 2023 through June 30th.

Private Debt Environment



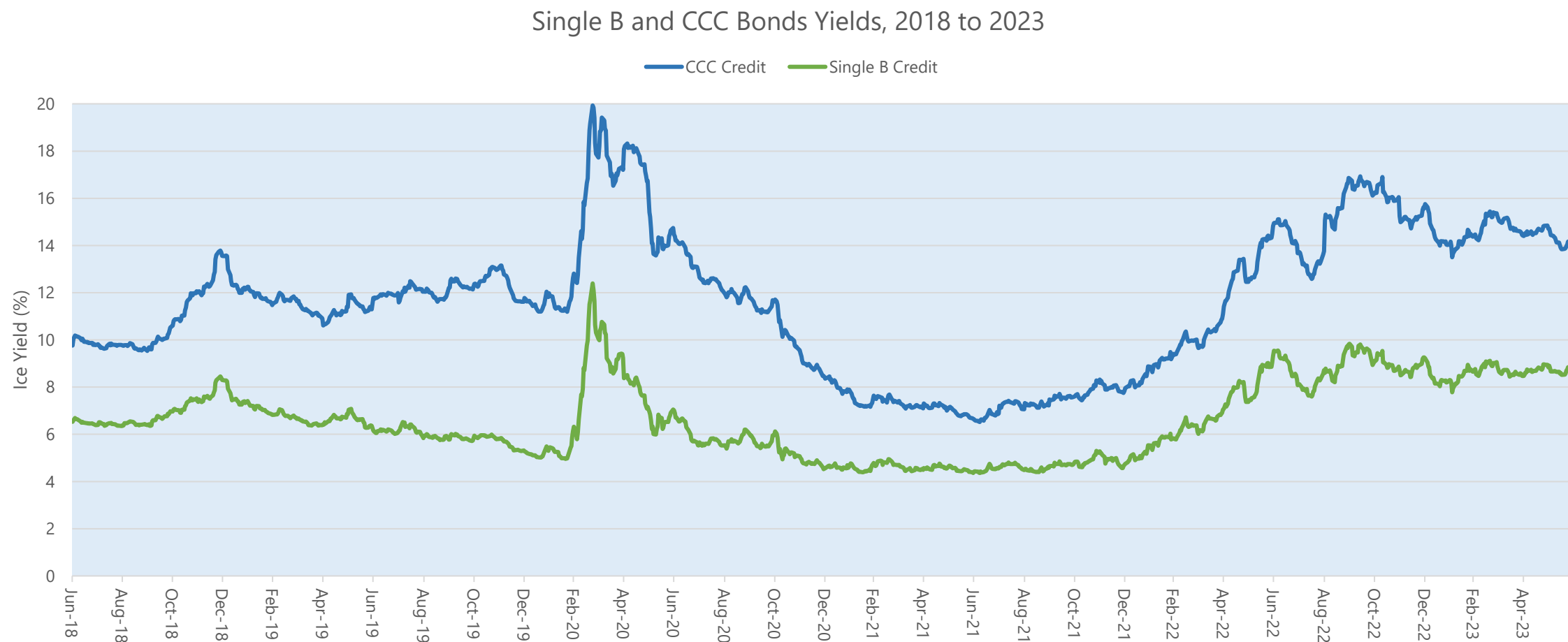
On An Annualized Basis, Debt Market Transaction Dollar Volume is Down 35% from 2022

Private Debt Market Volume in Life Sciences, 2013-2021 (\$ millions)

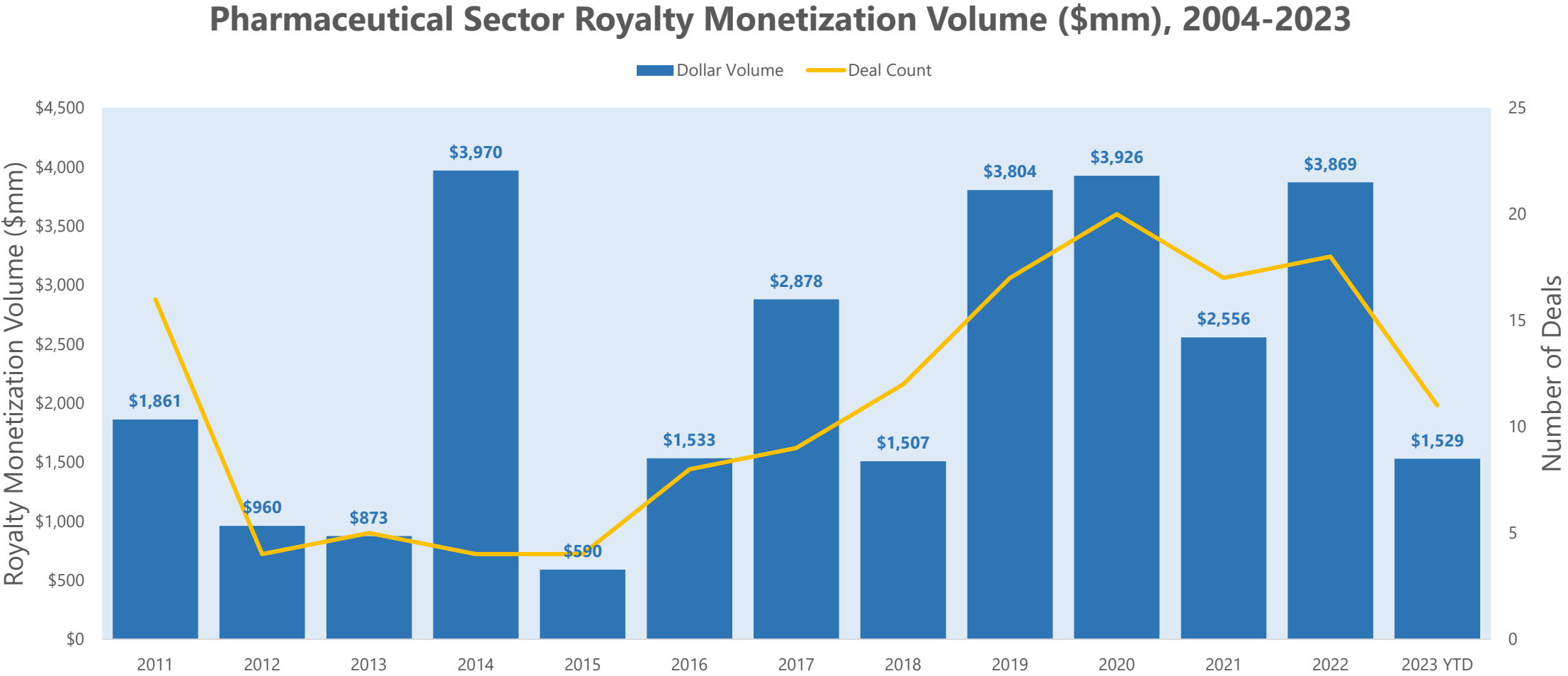


Source: Stifel Debt Transaction Database

Credit Market Yields for CCC Bonds Today are around 14% - Down from a Peak Last Year of 17%.



On an Annualized Basis, the Pharma Royalty Monetization Market Has Been in Good Shape in 2023



Source: Stifel Pharma Royalty Transaction Database

Oaktree Is Betting on Life Sciences With \$2.3-Billion Fundraise

- This is the firm's first dedicated life sciences fund
- Non-dilutive financing said to be attractive for growing firms

Bloomberg, June 23, 2023

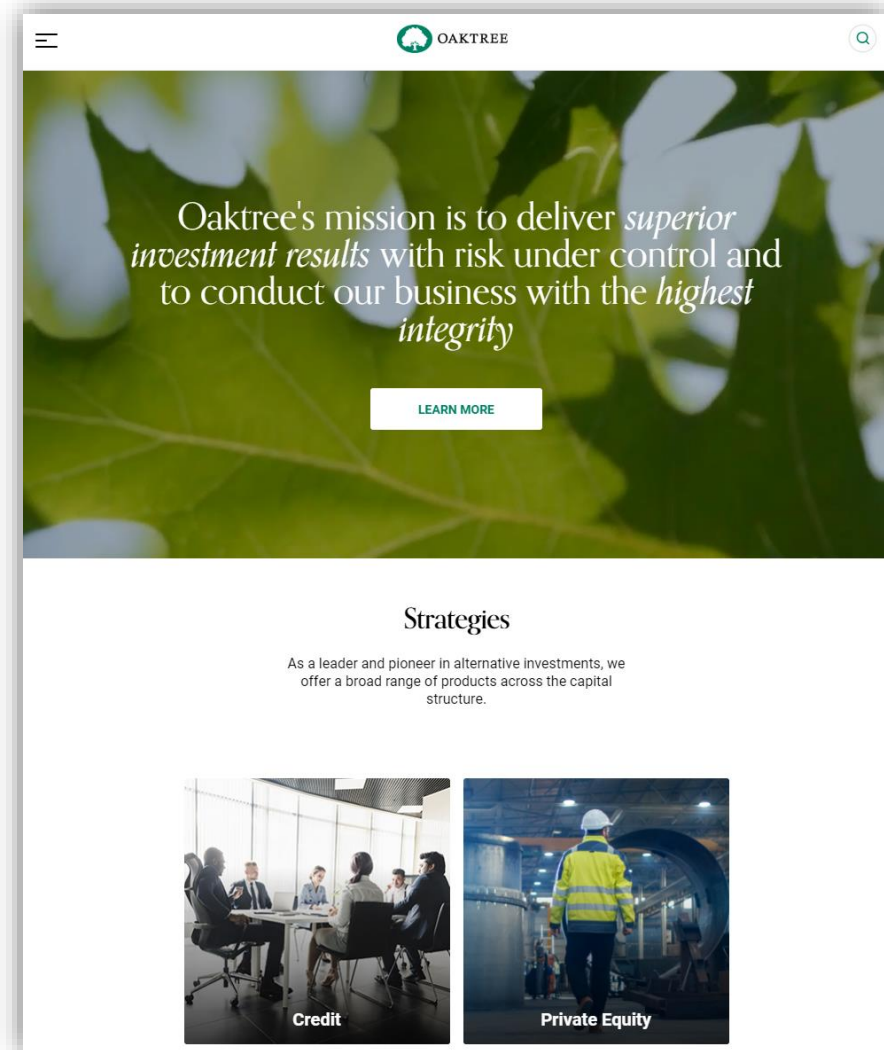
Oaktree Capital Management has raised more than \$2.3 billion for its first private credit fund dedicated to life sciences companies, according to a statement seen by Bloomberg.

The Oaktree Life Sciences Lending Fund will lend directly to biopharmaceutical and medical device companies across the globe, focusing on firms that have strong intellectual property or late-stage assets targeting difficult-to-treat medical conditions.

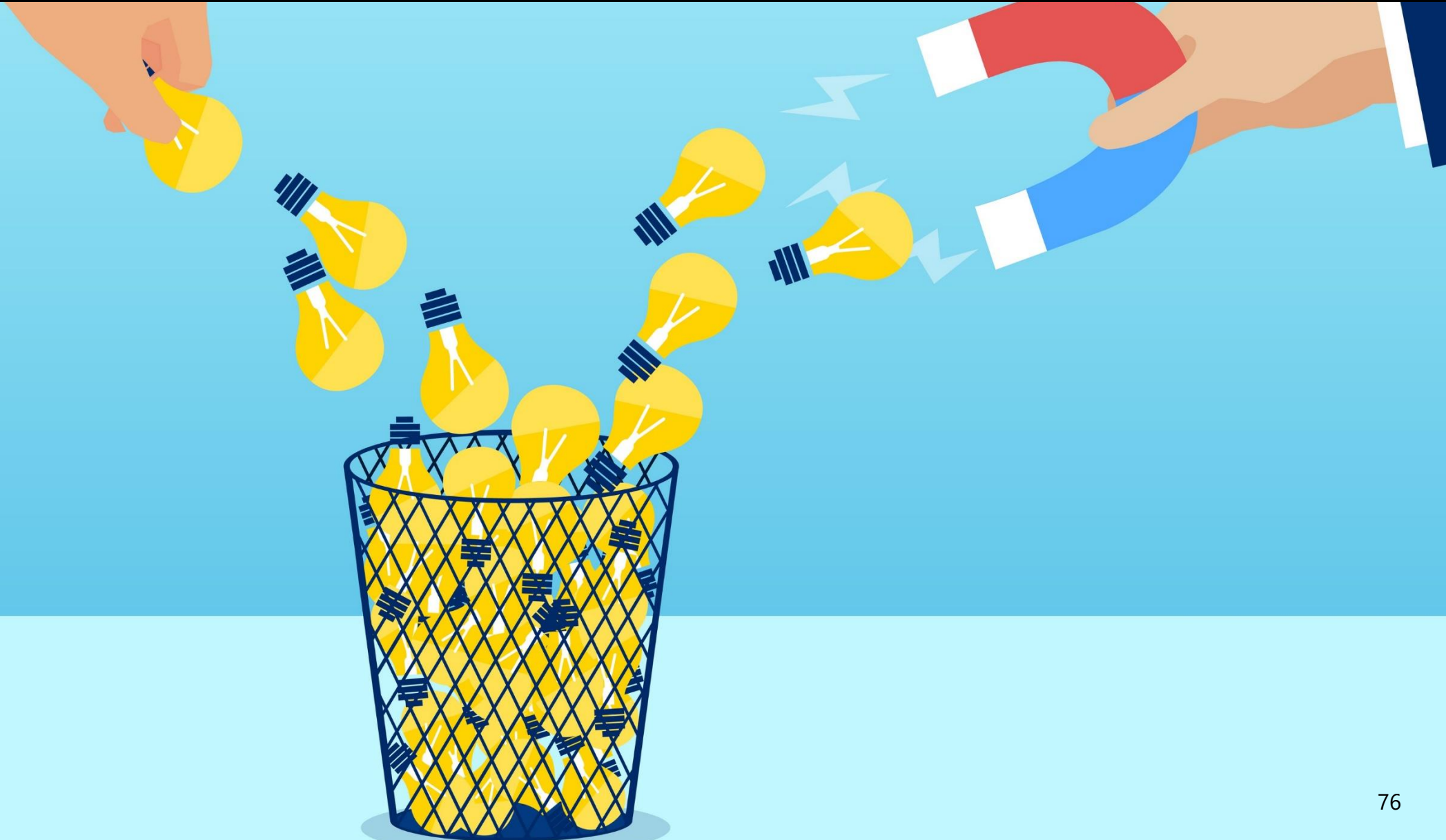
Oaktree seeks to provide non-dilutive financing to companies in the sector that typically raise capital through the equity markets to support their capital-intensive needs, said Aman Kumar, co-portfolio manager of life sciences lending at Oaktree.

"There are a couple of key changes starting to shift the demand to non-dilutive financing," Kumar said. "A decade ago, 70% of innovations in the life sciences space was done in large-cap companies. Now 70% is coming from small to mid-cap companies that can't access the broadly syndicated market and previously primarily relied on raising equity."

Source: <https://www.bloomberg.com/news/articles/2023-06-23/oaktree-is-betting-on-life-sciences-with-2-3-billion-fundraise>

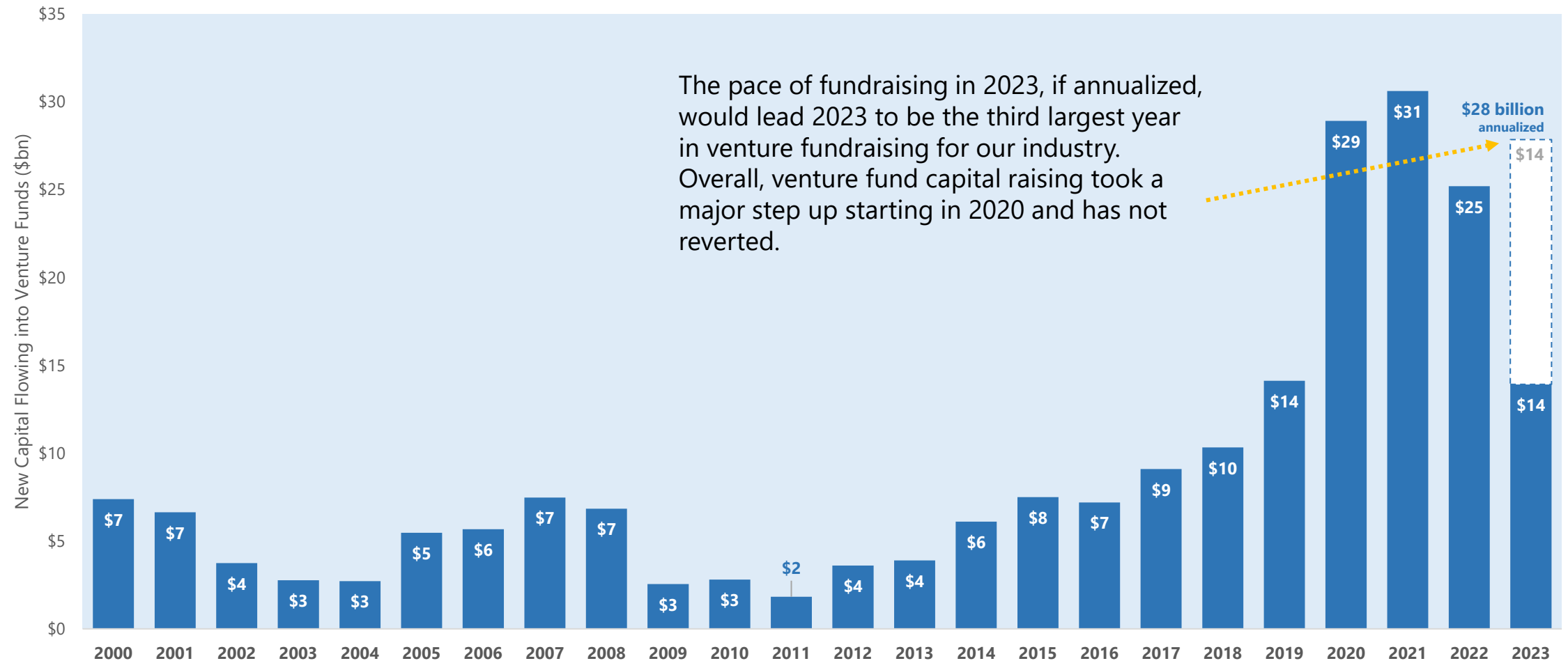


Venture Funds Capital Raising













New Capital Flows into Life Sciences Venture Funds Remain Brisk

Life Sciences Venture Capital Funds - Amount Raised \$Billions, 2000 to 2023



Top Ten Biopharma Fund Raises, First Half 2023

Month	Fund	Approach / Sweet Spot	Amount Raised (\$ millions)	Home Country
Feb-23	 PATIENT SQUARE CAPITAL	Life sciences platforms and strong management teams, mid-to-late stage with a patient, patient-centric approach	\$3,900	United States
Apr-23	 LUX	Lux Capital invests in life science companies with big ideas and the leaders to back them. Not afraid of early-stage investment.	\$1,115	United States
Apr-23	 Canaan	Canaan is an early-stage life science and tech venture capital firm that invests in visionaries with transformative ideas.	\$850	United States
Apr-23	 Forbion. Ventures	Forbion Ventures Fund VI invests in Series A and B therapeutics companies with a focus on European companies.	\$823	Netherlands
Apr-23	 Forbion. Growth	Forbion Growth Opportunities Fund II invests in innovative European later-stage biopharma companies focused on major market needs.	\$658	Netherlands
Apr-23	 Gilde HEALTHCARE	Gilde Healthcare Venture & Growth VI invests in growth companies with cost conscious good care solutions. Focus areas include digital, medtech and therapeutics.	\$657	Netherlands
Mar-23	 SR One	SR One Fund II collaborates with entrepreneurs to build high quality biotechs in the US and Europe. Does privates and public deals.	\$600	United States
May-23	 COWEN HEALTHCARE INVESTMENTS	Cowen Healthcare Investments IV invests in innovation in the healthcare sectors, with a particular focus on biopharma, diagnostics, and digital health. Will do privates and public deals.	\$550	United States
Feb-23	 Curie.Bio	Curie.Bio is a seed stage investor focused on a founder friendly model of launching new therapeutics companies.	\$520	United States
Mar-23	 B Capital Group	B Capital Group is focused on healthcare opportunities in digital and biotech. This company is partnered with BCG.	\$500	United States

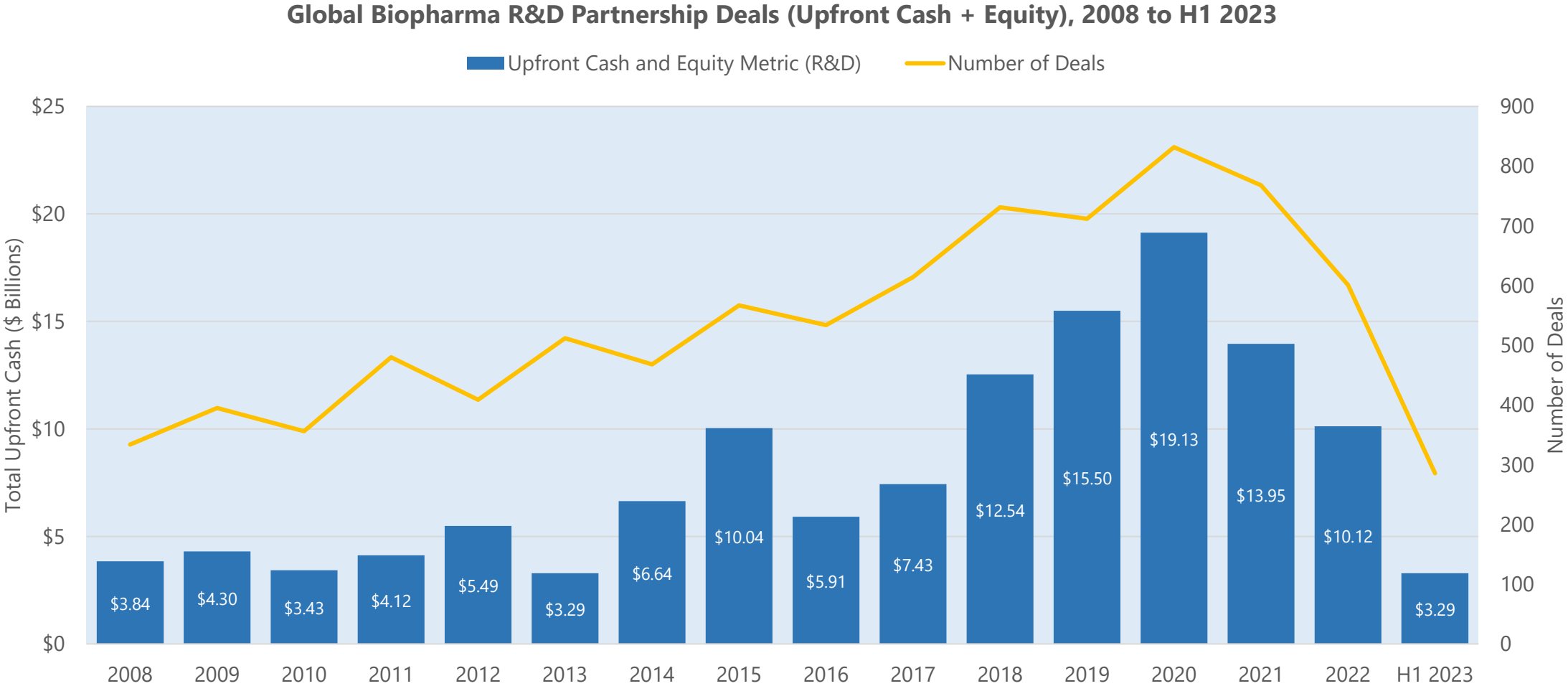
Source: Company press releases, Stifel research.

Licensing / Partnership Environment



Licensing Activity Down From Peak of Pandemic

We are seeing fewer biopharma licensing deals and less money upfront in the first half of 2023 (annualized) than in 2022. The annualized count of deals is only down 4.8% from 2022 although the average upfront per deal has dropped since the Pandemic's peak.























Source: DealForma. Biopharma licensors only. Data for 2023 through June 30th

Top Ten Licensing / Collaboration Deals in First Half of 2023

Four of these deals involved a China-based licensor. Five involved cancer drugs.

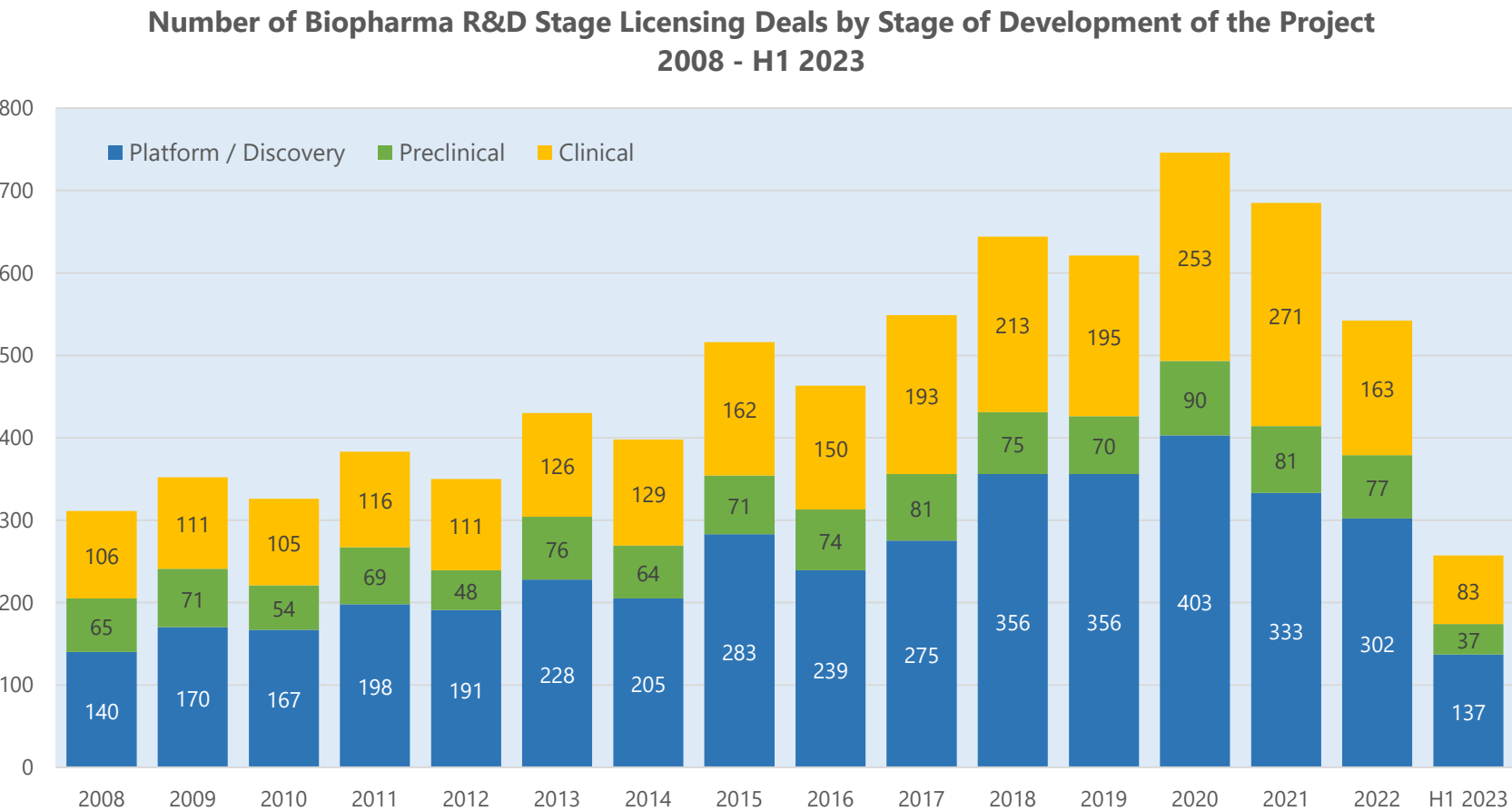
Ranked by Upfront (\$mm)

Date	Licensor	Licensee	Product Stage	Territories	Therapeutic Area	Modality	Upfront Cash (\$mm)	Total Deal Value (\$mm)
01/23/2023			Approved Drug	Global	Cancer	Small Molecule	400	1,130
05/02/2023			Phase 1	Global	Cancer	Cell Therapy	245	245
03/20/2023			Phase 2	Global	Cancer	Antibody	200	200
04/03/2023			Phase 2	Global	Cancer	Antibody Conjugate	170	1,670
01/08/2023			Preclinical	Global	Neurologic	Gene Therapy	136	4,410
03/23/2023			Phase 1	Global	Endocrine / Metabolic	Gene Editing/CRISPR	100	330
03/30/2023			Phase 3	Global	Infectious	Small Molecule	90	593
05/18/2023			Approved Drug	Global	Ophthalmic	Small Molecule	75	82.5
05/09/2023			Phase 1	Global	Cancer	Small Molecule	70	680
02/22/2023			Phase 3	Europe	Neurologic	Small Molecule	66	167

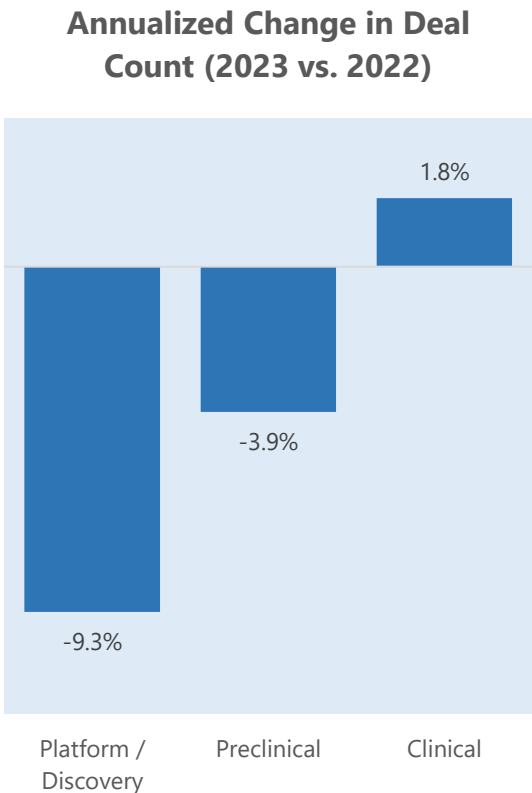
Source: DealForma. Biopharma licensors only. Data for 2023 through June 30th

Number of License Deals by Stage of Development of Project, 2008 to H1 2023

As we exit the Pandemic, licensees are much less focused on platform/discovery type access deals. We don't have specific insights as to why but would speculate that large pharmas have fuller pipelines and are more tooled up on new modalities.



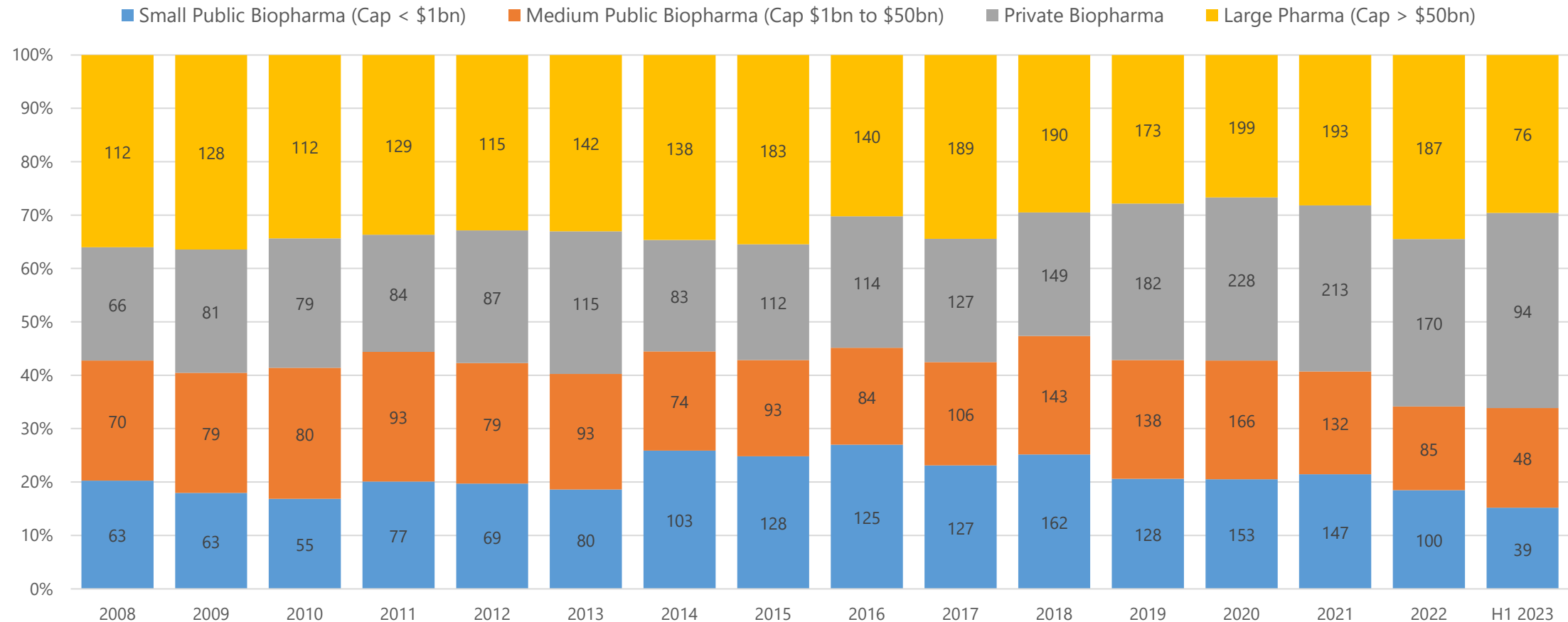
Clinical stage deal count is up in 2023.
Discovery stage deals are down over 9%.



Source: DealForma. Biopharma licensors only. Data for 2023 through June 30th

Decline in Licensing Activity Driven Most by Less Activity From Small Players

**Distribution of Biopharma R&D Partnership / Licensing Deal Count by Type of Licensee
2008 to H1 2023**

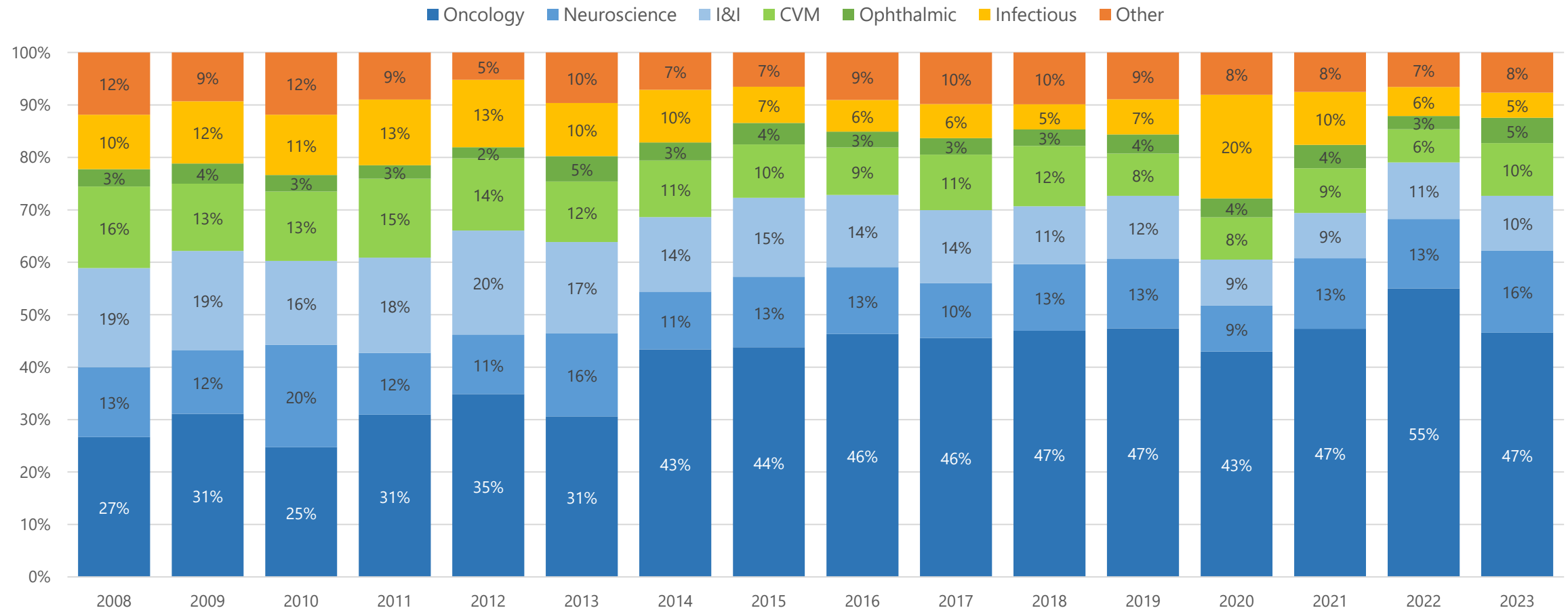


Source: DealForma. Biopharma licensors only. Data for 2023 through June 30th

Compared To Last Year, We Are Seeing More Licensing Activity in 2023 in Cardiometabolic, Neuro and Ophthalmology

The fraction of deals done in oncology has been on a long-term uptrend since 2008 and appears to have peaked in 2022.

R&D-Stage License Deals by Therapeutic Area, 2008 to H1 2023

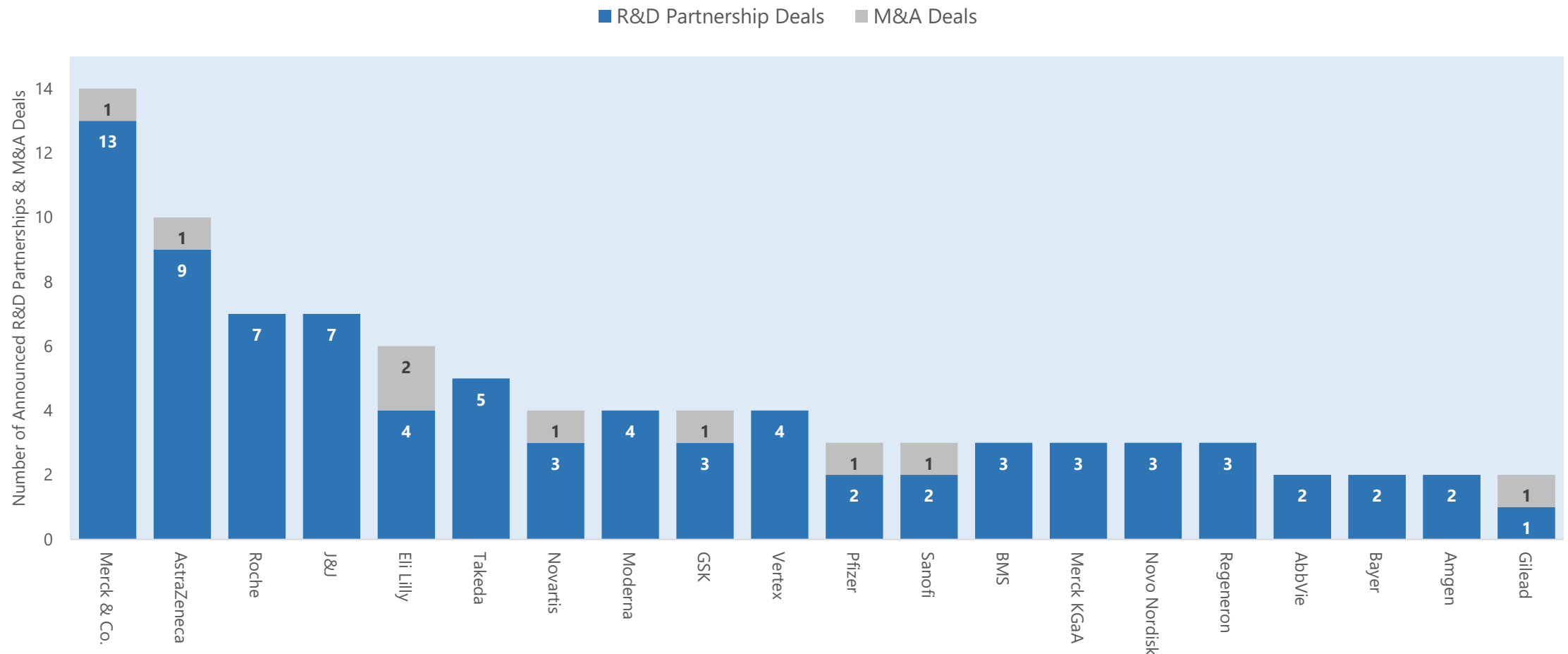


Source: DealForma. Biopharma licensors only. Data for 2023 through June 30th. I&I encompasses investments in autoimmune, GI, dermatology and inflammation. CVM encompasses, cardiometabolic, diabetes, endocrinology and renal.

Big Pharma Dealmaking Activity in 2023 (Deal Count)

Six of the twenty-two large pharma players have announced five or more transactions this year. Merck has been the most active player by far. Several traditionally active players such as AbbVie, Amgen and BMS have been relatively quiet.

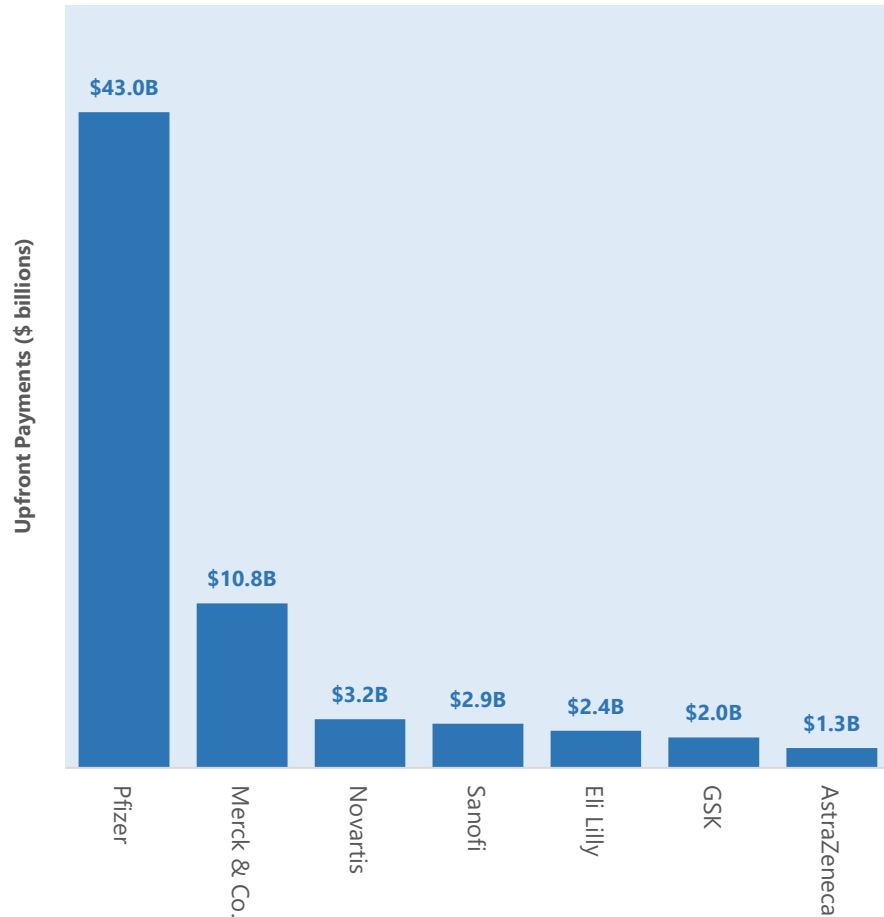
Big Pharma Dealmaking Activity in H1 2023



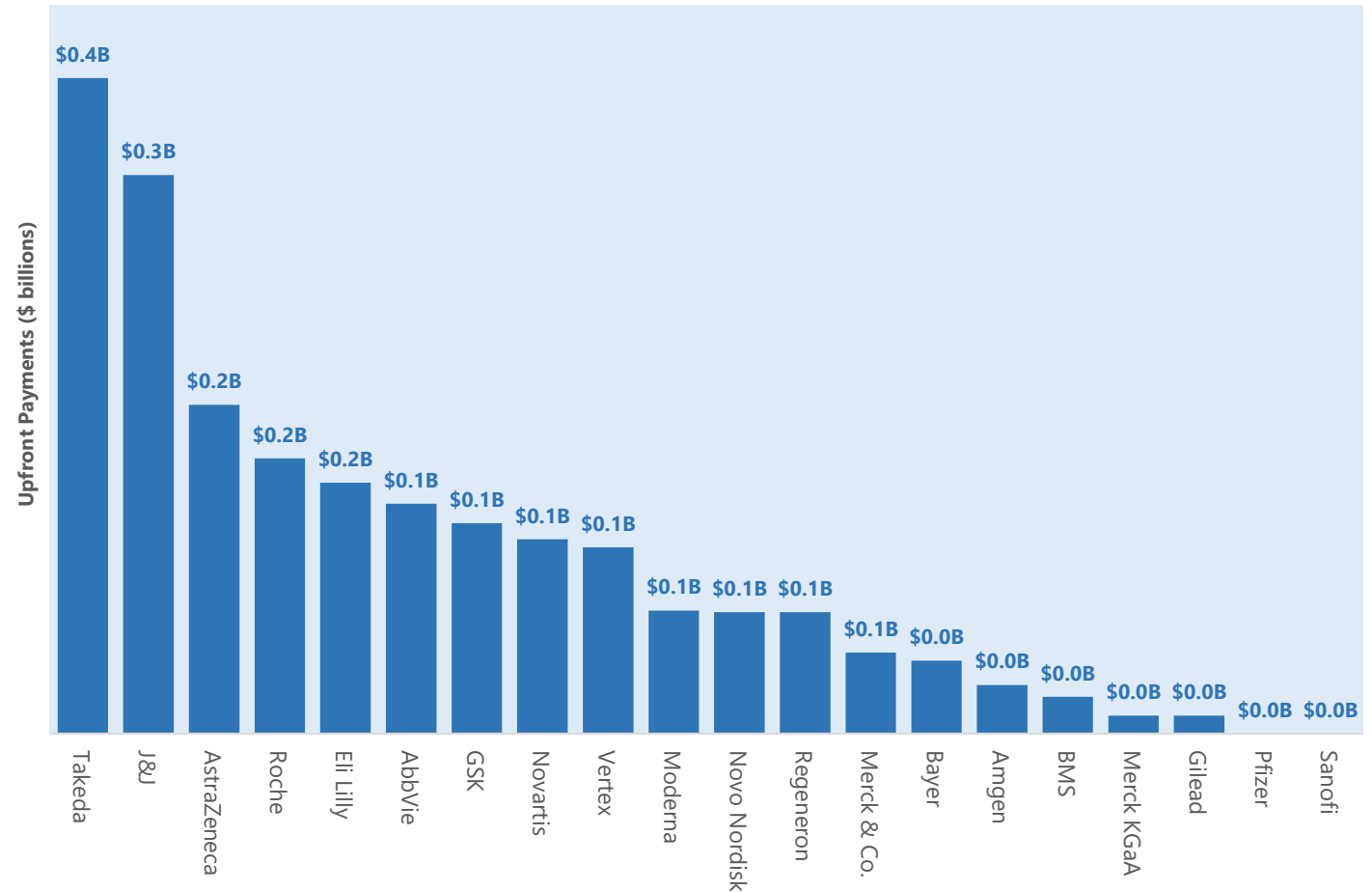
Big Pharma Dealmaking Activity in 2023 (Dollar Volume)

It's been a relatively asymmetric year from a dollar volume perspective. Pfizer's \$43 billion of spend for Seagen is larger than the total sum of M&A dollars and upfront dollars spent on all other M&A and partnership deals announced by the 22 players listed here. Some players such as Gilead and Merck KGAA have been uncharacteristically quiet in 2023.

Big Pharma M&A Activity in H1 2023 (Dollar Volume)



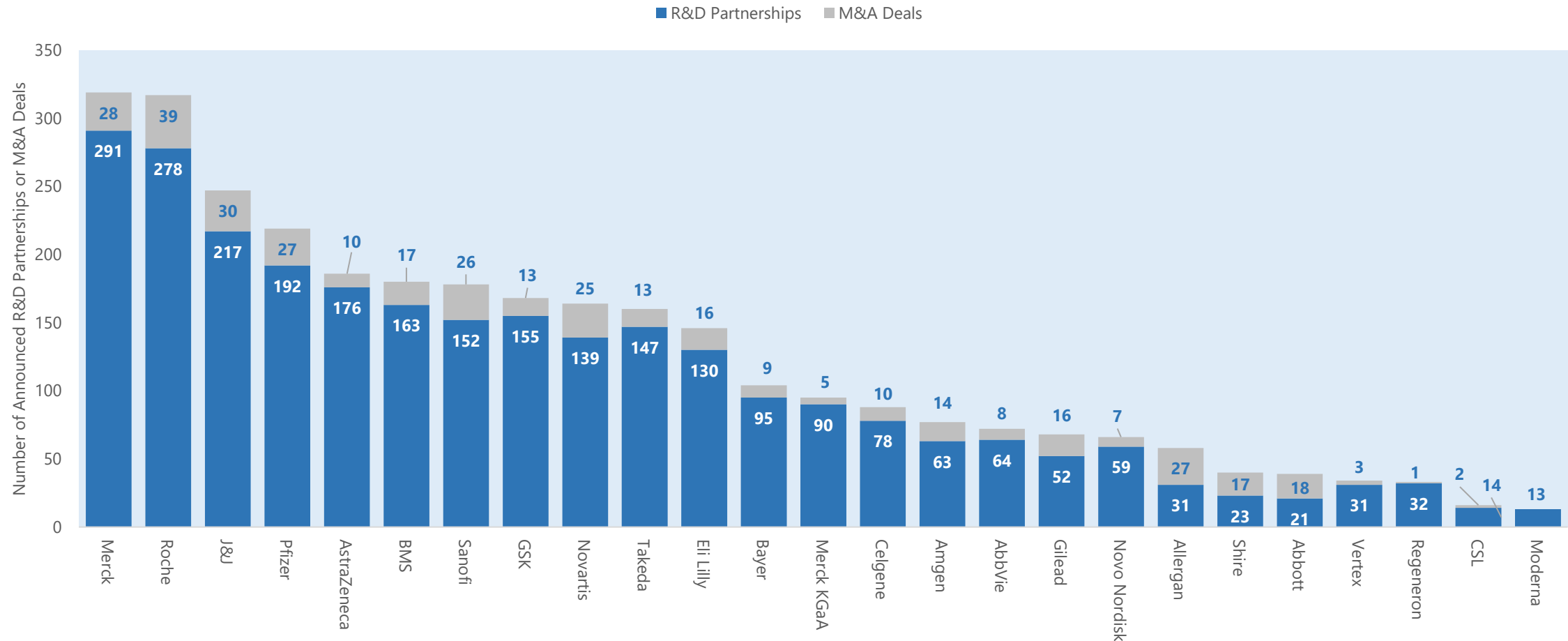
Big Pharma R&D Partnership Activity in H1 2023 (Total Upfronts Paid)



Big Pharma Dealmaking Activity from 2008-2023 (Deal Count)

Looking over the last 16 years, the most active pharma dealmakers have been Merck (28 M&A deals, 291 partnership deals) and Roche (39 M&A deals, 278 partnership deals). The next most active players have been J&J, Pfizer, AZ, BMS and Sanofi.

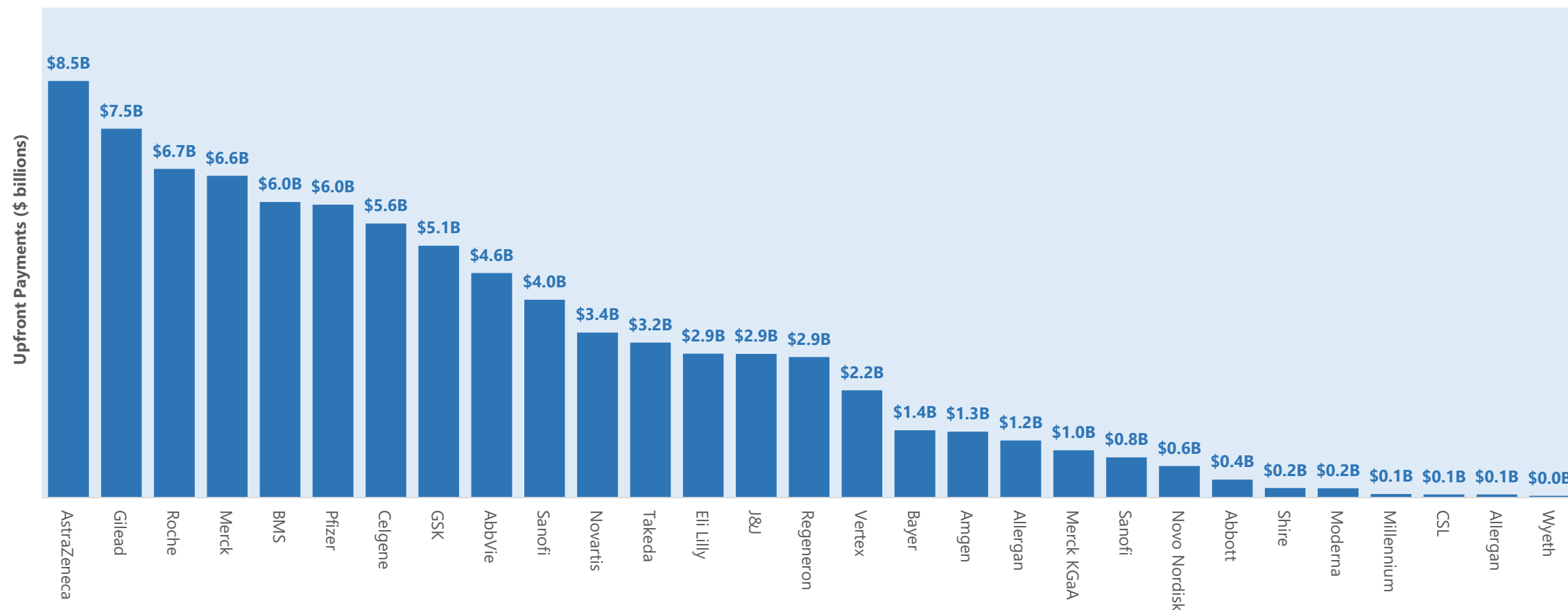
Big Pharma Dealmaking Activity, 2008-H1 2023



Big Pharma R&D Partnering Activity from 2008-2023 (Dollar Volume)

Over an extended period, AstraZeneca, Gilead, Roche, Merck, BMS and Pfizer have been the most likely to write meaningful upfront checks to access technology and drug candidates from biotech. These companies have each spent \$6 billion or more to access promising pipeline via R&D partnership deals.

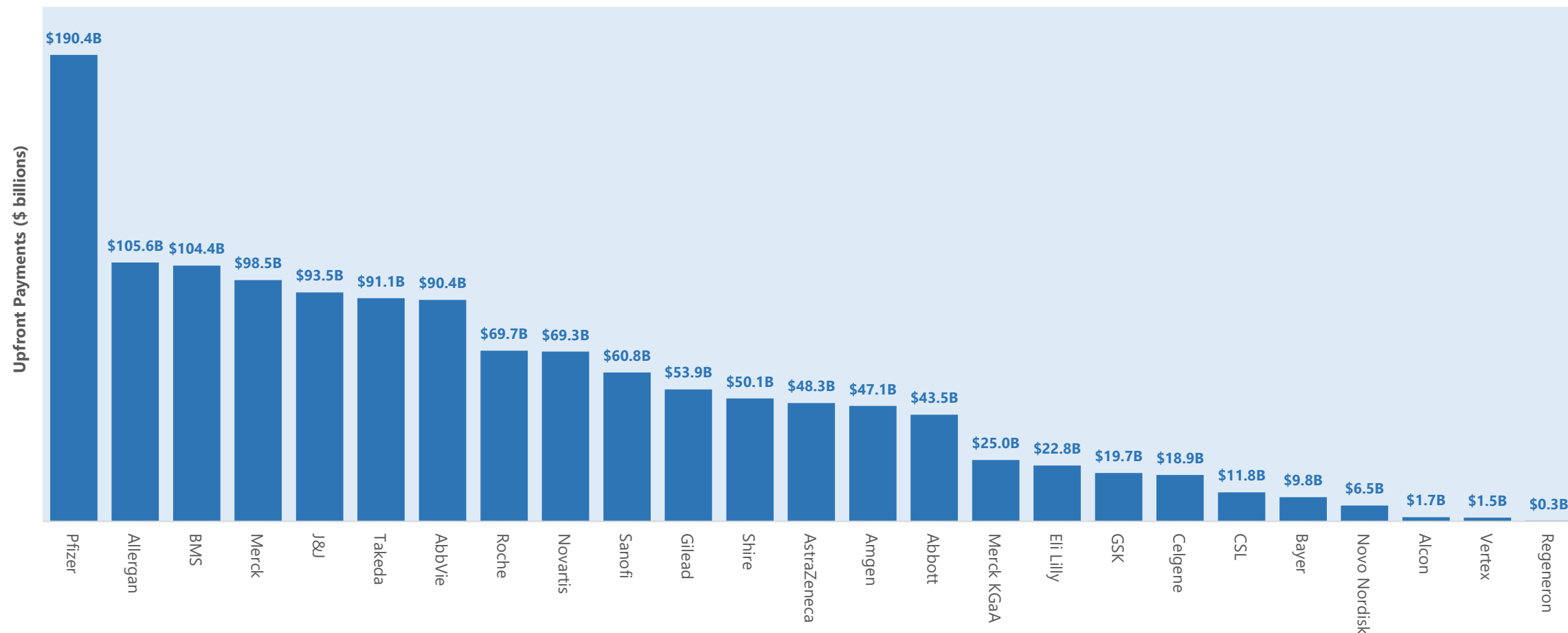
Big Pharma R&D Partnership Activity in the 2008 to 2023 Period (Total Upfronts Paid)



Big Pharma M&A Activity from 2008-2023 (Dollar Volume)

Pfizer has spent far more than any other player on M&A deal upfronts over the last 15 years. The other major spenders on M&A have been Allergan, BMS, Merck, J&J/Janssen, Takeda and AbbVie.

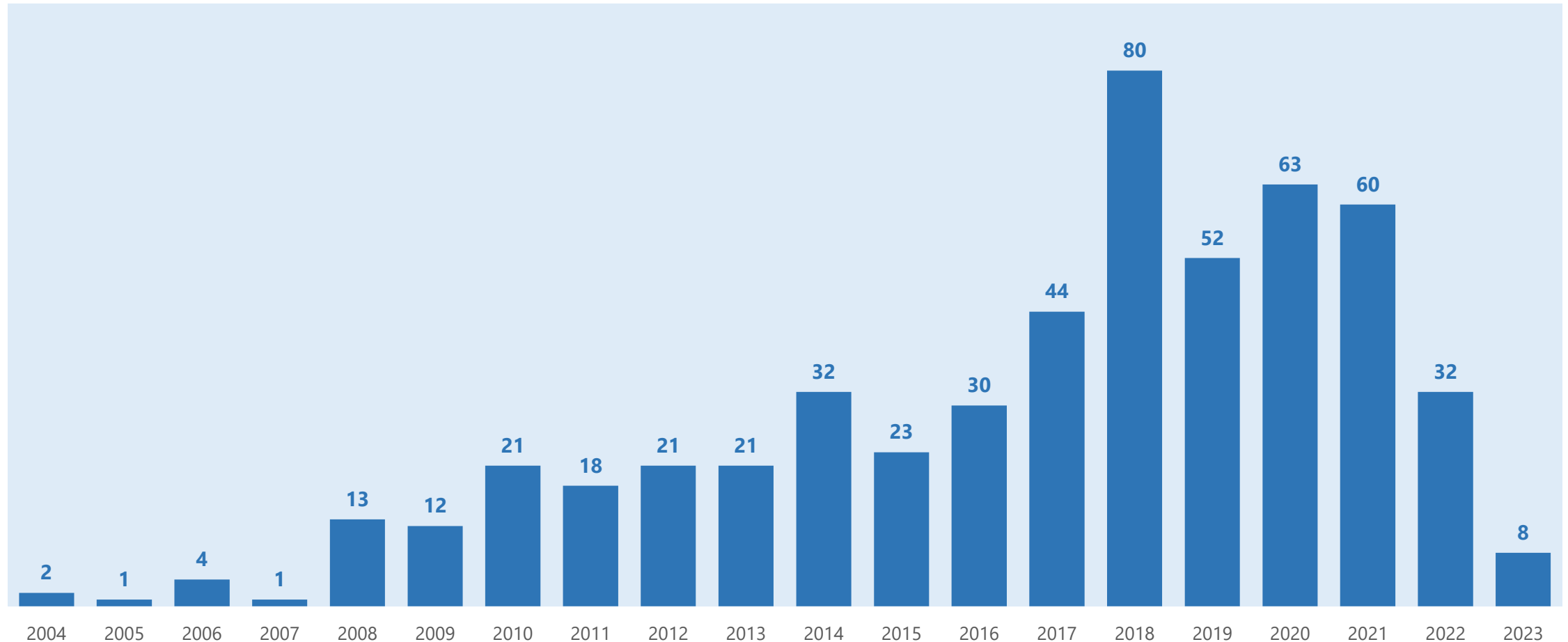
Big Pharma M&A Activity in the 2008 to 2023 Period (Total Upfronts Paid, \$Billions)



China Inbound License Deal Activity Down Substantially

Transactions for China territorial rights have fallen off quite a lot as the Chinese geopolitical situation has worsened. In addition, the shares of listed biotech companies in China have fallen giving these companies fewer resources with which to in-license assets.

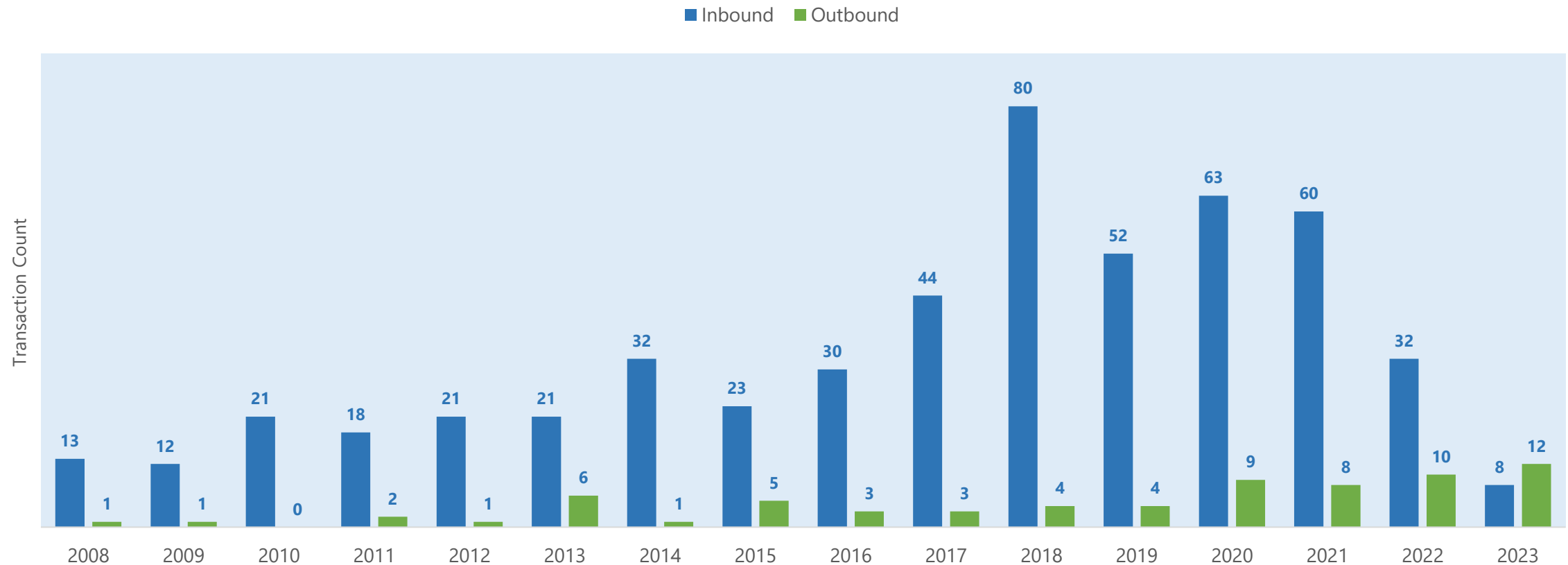
Count of China Territory Biopharma License / Partnership Deals, 2004 to 2023



This is The First Year That China Has Become a Net Exporter of Pharmaceutical Innovation

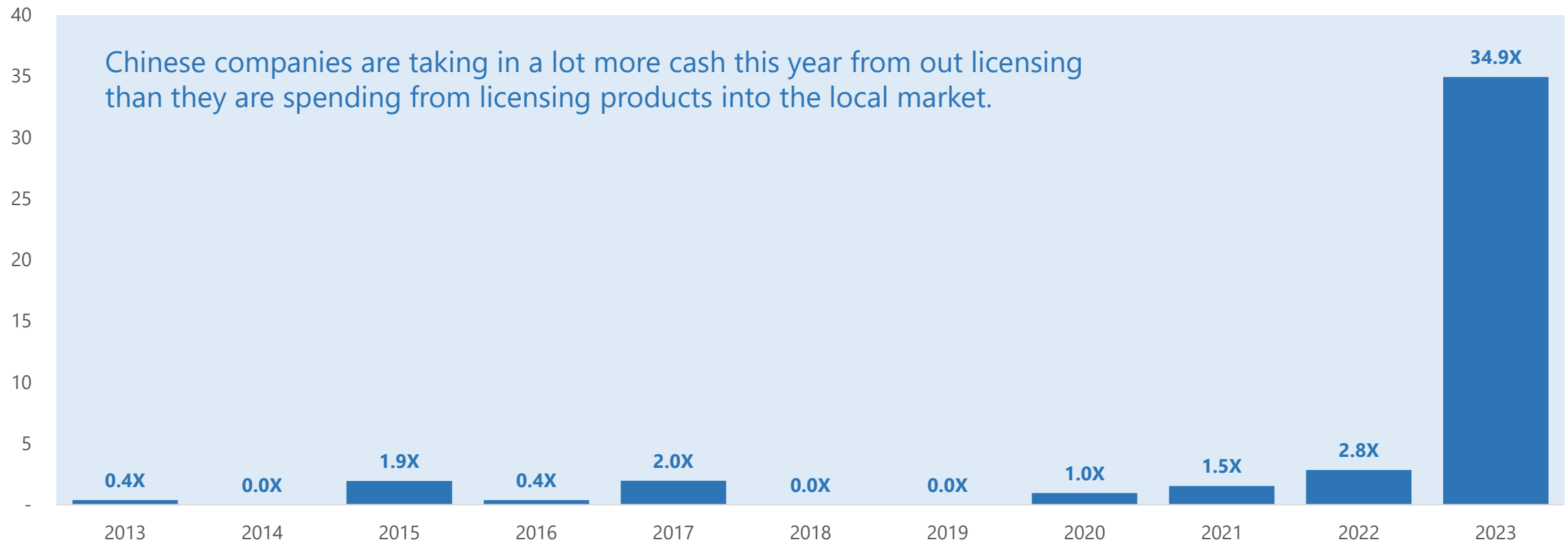
In a challenging geopolitical climate, China has invested massively in its own biotech infrastructure. The investment is paying off as Chinese biotechs have become significant exporters of rights to pharmaceutical products.

Number of Inbound Deals to China Territory Versus Outbound Deals From China to West, 2008 to H1 2023



Funds Flow Into China From Biopharma License Deals Versus Funds Flowing Out for Local In-licensing Has Become Imbalanced

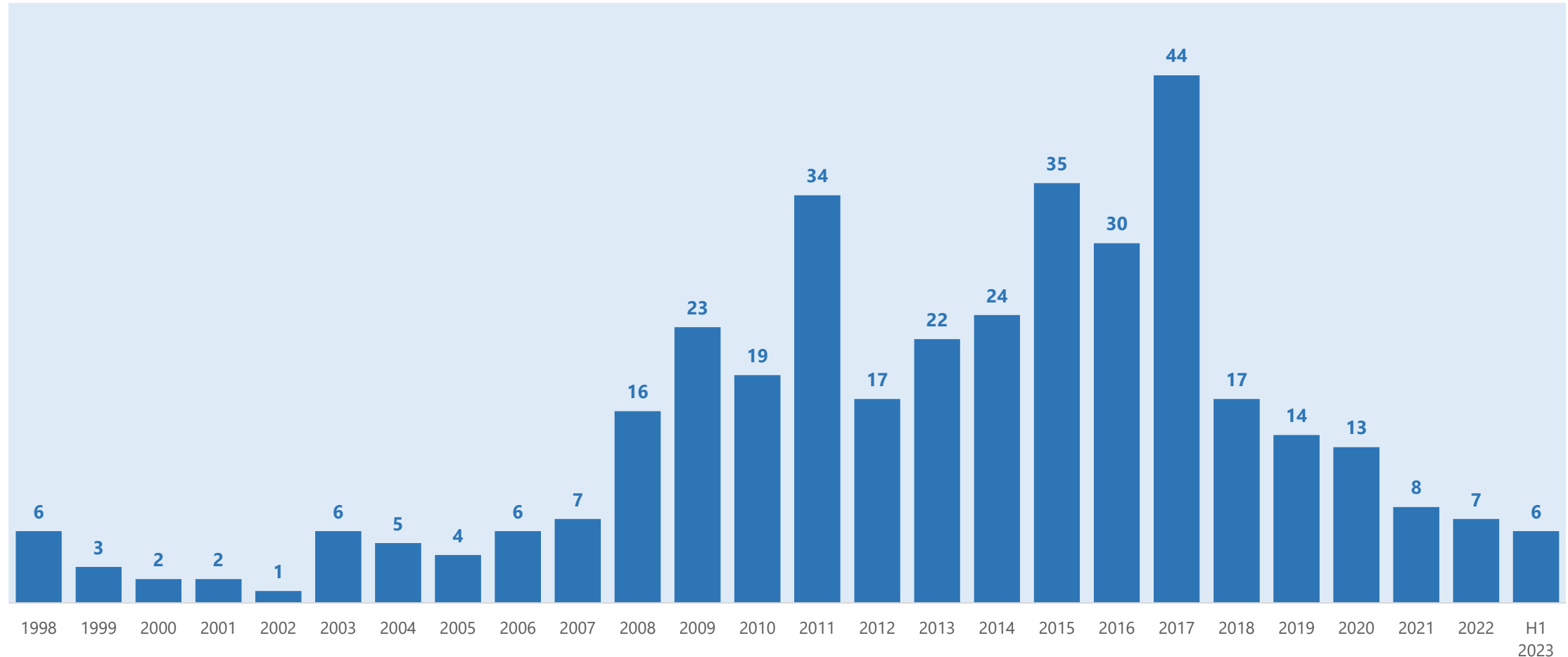
Multiple of Upfronts Paid on Deals to Chinese Companies for Global Product Rights Divided to Upfronts Paid by Chinese Companies for China Product Rights, 2013 to 2023



Japan Inbound License Deal Activity Down Substantially

Transactions for Japan territorial rights have fallen off quite a bit as Japanese companies increasingly globalized and the economics of operating in the domestic market worsened. This said, the six deals YTD 2023 put this to be the most active year since 2020.

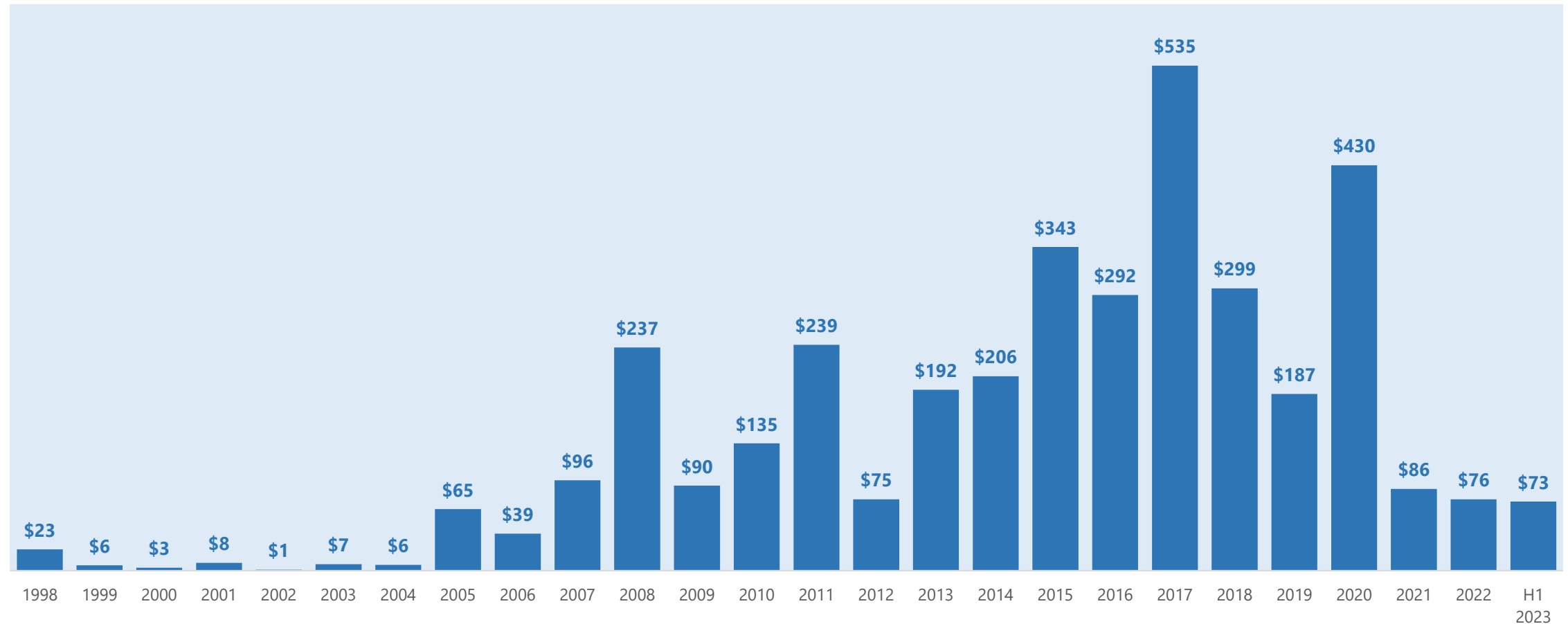
Count of Japan Territory Biopharma License / Partnership Deals, 1998 to 2023



Total Upfronts Paid on Japan License Deals Down Substantially

The total upfronts paid on Japan deals have dropped significantly since the market peaked in 2017. We saw high payments in 2020 as Japanese companies sought to tech transfer projects for dealing with the Pandemic.

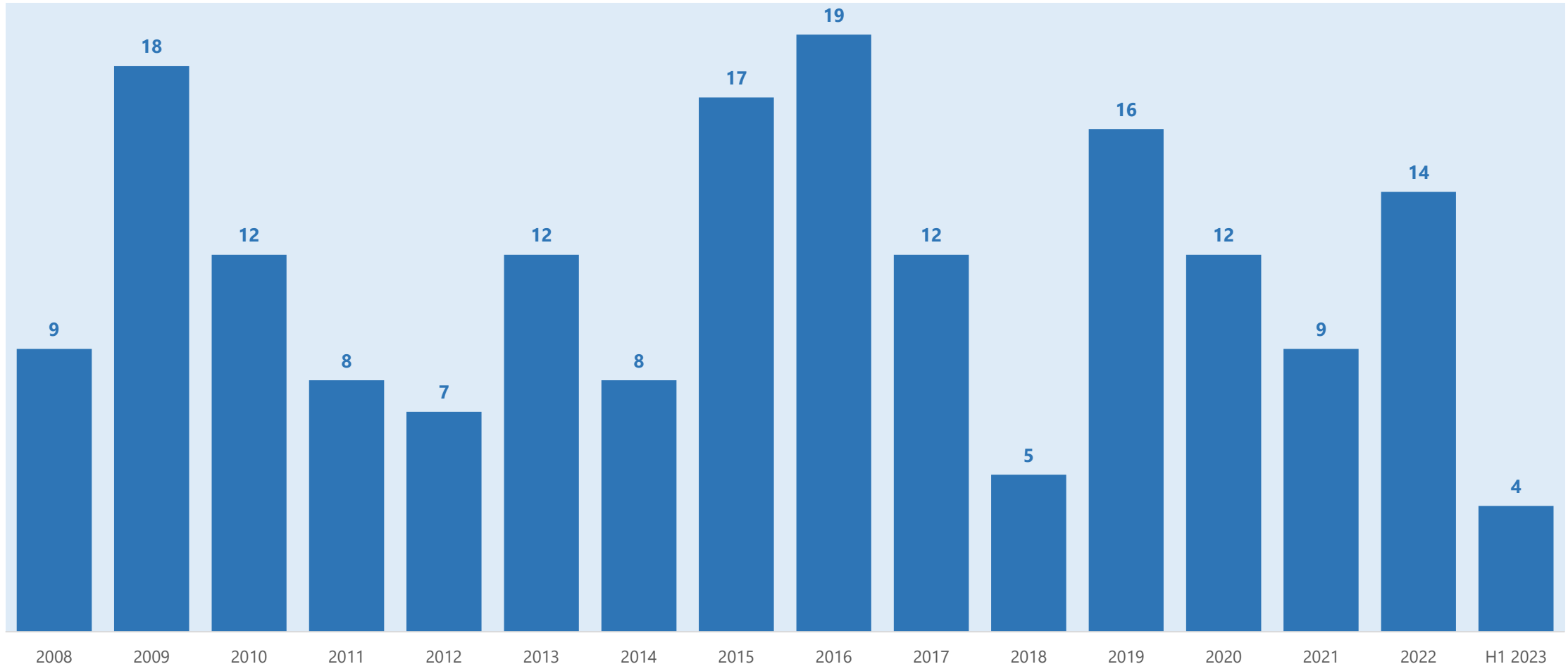
Aggregate of Upfronts Paid on Japan Territory Rights, 1998 to 2023 (\$ mm)



Europe Inbound License Deal Activity Down Substantially

Transactions for European territorial rights have held steady over time. With four deals done in the first half of 2023 we are on track for a somewhat normal year from a deal count perspective.

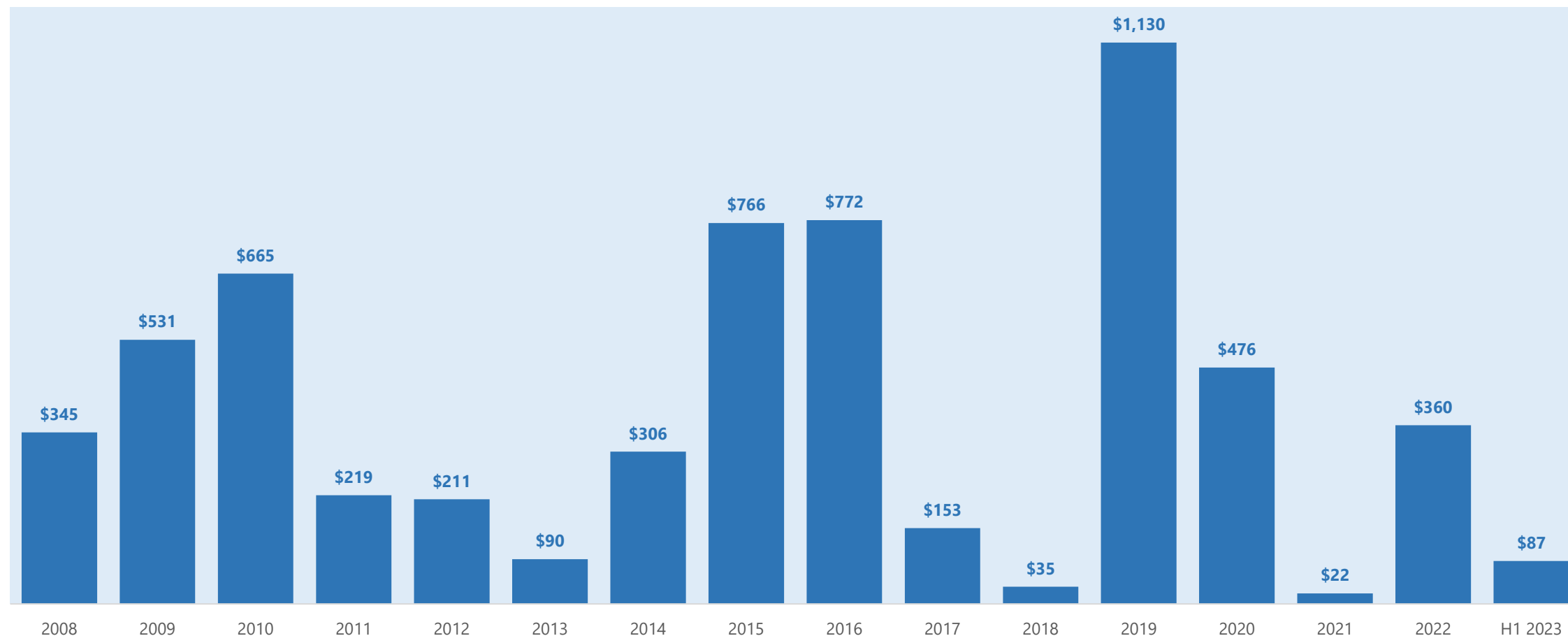
Europe Territory License Deals, 2008 - 2023



Total Upfronts Paid on Europe License Deals Not Big in 2023

The total upfronts paid on Europe deals have dropped significantly since 2019 which was a banner year. With \$87mm paid in the first half of 2023 this year is not on track to be one of the larger years for these type of deals.

Aggregate of Upfronts Paid on Europe Territory Rights, 2008 to 2023 (\$ mm)

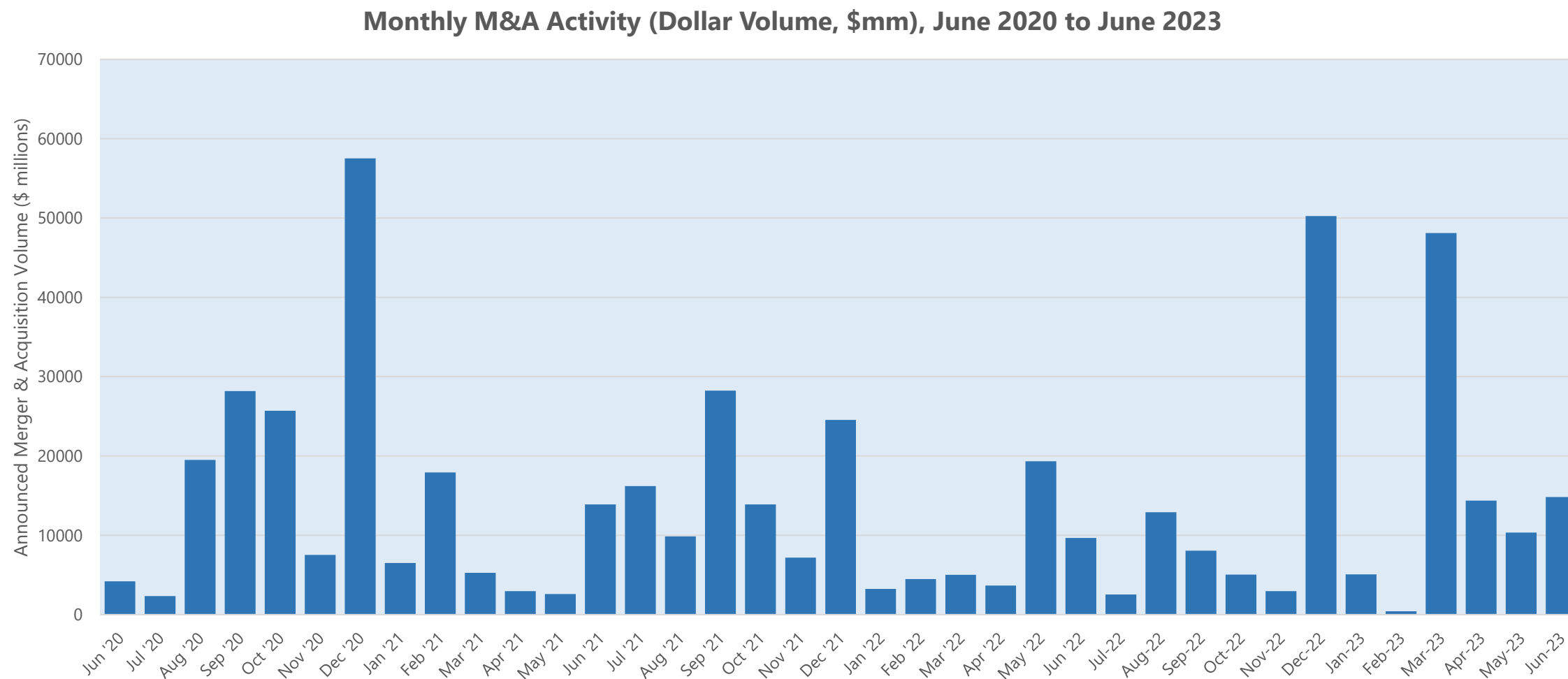


M&A Environment



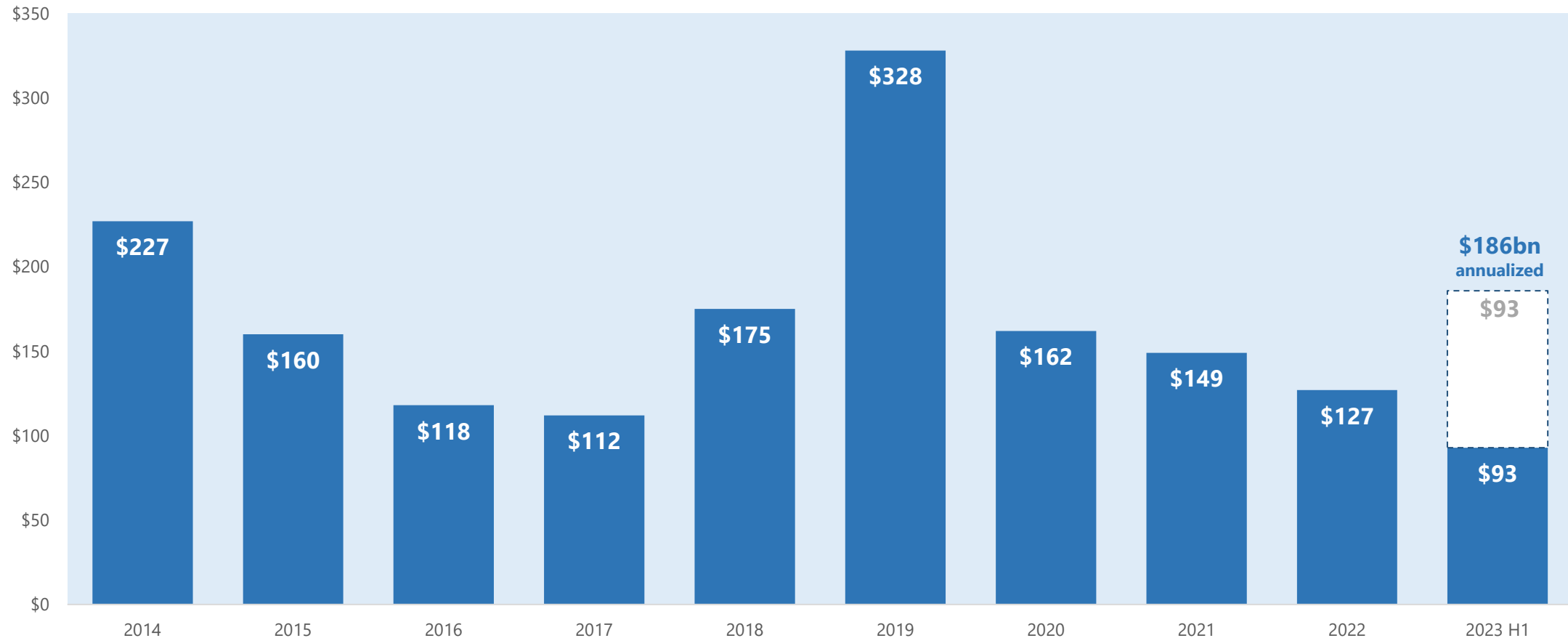
Monthly M&A Volume Solid in June

June 2023 was the second most active M&A month of the year. The M&A market has clearly picked up over the last four months.



We are on Track for a \$186 Billion M&A Year in Biopharma – The Busiest Since 2019










M&A Volume in the Biopharma Sector, 2014 - First Half 2023
(\$ Billions, Worldwide)



Source: S&P CapitalIQ and Stifel research. This includes all reported global therapeutics change of control transactions but excluded asset sales such as the recent Novartis Xiidra divestiture. Includes reverse mergers at equity value and transactions in human/animal health. Does not include SPAC mergers.

Top Ten Biopharma M&A Deals in First Half of 2023

Ranked by Upfront Cash Paid (\$mm) on Announced and Closed Transactions in the Pharmaceutical Sector, Jan to June 2023

Date	Target	Buyer	Status	Product Stage	Therapeutic Area	Modality	Upfront Cash (\$mm)	Contingent Payments (M)
03/13/2023	 Seagen®	 Pfizer	Pending	Commercial	Cancer	ADCs	\$43,000	\$0
04/16/2023	 Prometheus Biosciences	 MERCK	Closed	Phase 2	Immunology	Antibody	\$10,955	\$0
04/30/2023	 IVERIC	 astellas	Pending	Phase 3	Ophthalmology	Biologics	\$6,000	\$0
06/02/2023	 Dechra	 IEQTADIA	Pending	Commercial	Animal Health	Small Molecules	\$5,600	\$0
06/12/2023	 CHINOOK THERAPEUTICS	 NOVARTIS	Pending	Phase 2	Renal	Small Molecule / Antibody	\$3,150	\$350
03/13/2023	 proventionbio intercepting and preventing disease	 sanofi	Closed	Commercial	Endocrine / Immunology	Antibody	\$2,900	\$0
06/20/2023	 DICE	 Lilly	Pending	Phase 2	Immunology	Small Molecule	\$2,400	\$0
04/18/2023	 Bellus HEALTH	 GSK	Closed	Phase 2	Respiratory	Small Molecule	\$2,000	\$0
05/10/2023	 CTi	 sobi	Pending	Commercial	Cancer	Small Molecule	\$1,700	\$0
01/09/2023	 CINCOR	 AstraZeneca	Closed	Phase 2	Cardiovascular	Small Molecule	\$1,300	\$500

Three of ten M&A deals thus far in 2023 have been in immunology, two have been in oncology and the other five have been spread out across a range of areas. These deals involved traditional modalities, and all were Phase 2 or later.

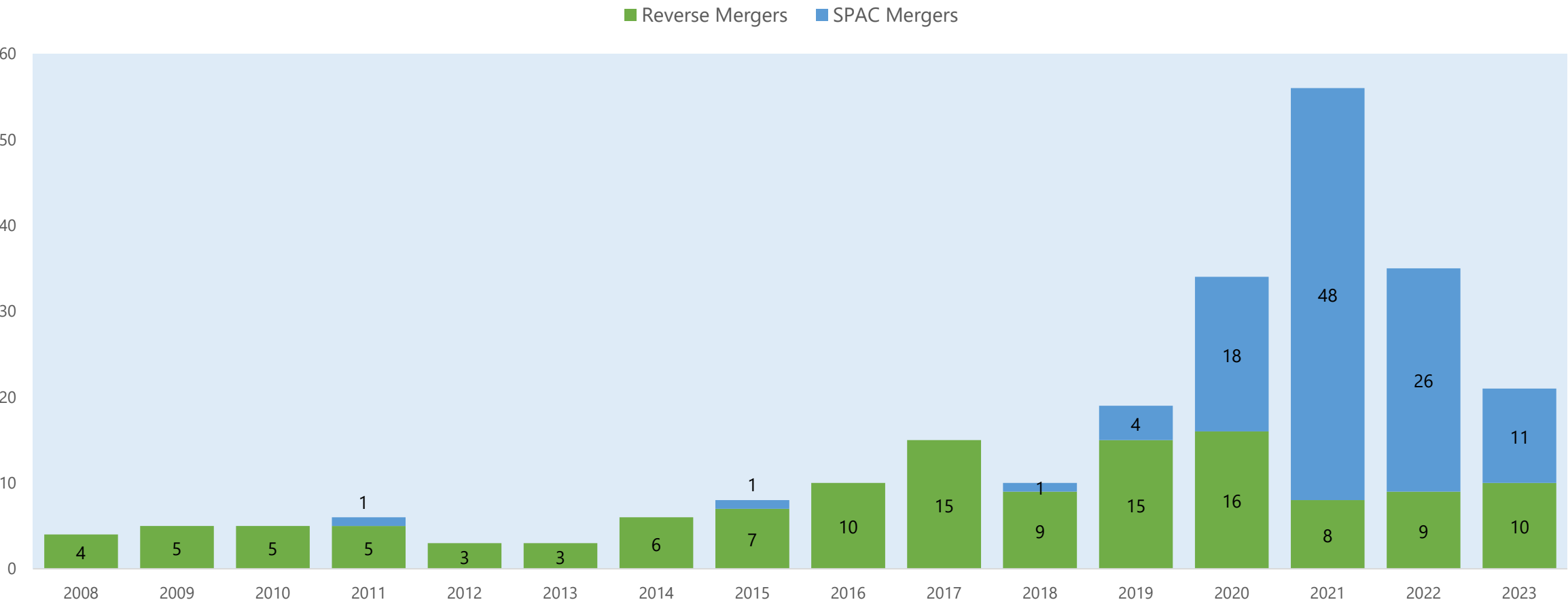
This year's M&A market is relatively "plain vanilla" with pharma scooping up attractive assets in a down market. Notably, eight of ten transactions did not have a contingent payment (a sign of agreement on price between parties).

Also, it's worth noting that all targets were public.

Reverse Mergers and SPAC Deals Remain Important

The availability of reverse mergers and SPAC deals as a way of going public has been responsible for 112 biopharma companies entering the public markets since 2021 without going through the traditionally underwritten IPO process.

Number of Biopharma Reverse Mergers and SPAC Mergers by Year, 2008 to H1 2023

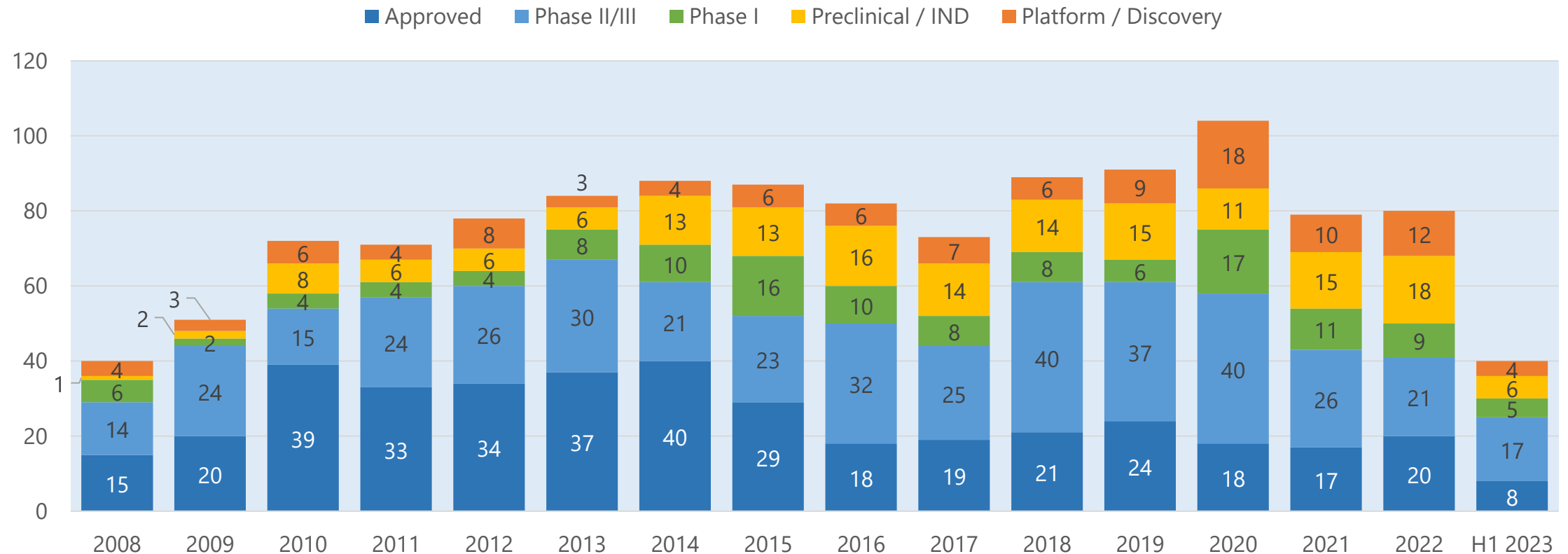


Source: DealForma. Data for 2023 are through June 30th.

We are Seeing A Significant Increase in Clinical Stage Versus Preclinical M&A Deals This Year

This year, 55% of M&A deals have been for companies with clinical stage assets (Phase 1 to Phase 3). Compare this to an average of 47% in the 2019 to 2022 period. The fraction of M&A deals for approved assets is down as is the fraction of deals for platforms and preclinical assets.

Number of Biopharma M&A Deals by Stage of Target Company, 2008 to 2023

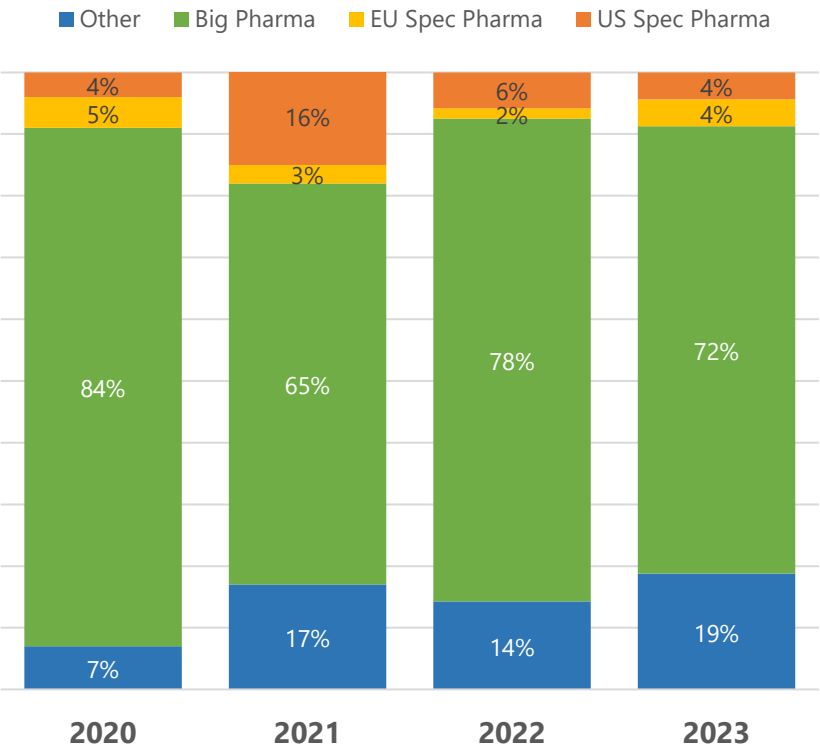


Source: DealForma. Data for 2023 are through June 30th.

Big Pharma and PE Most Active in Late-stage M&A

Big pharma has retaken share from U.S. spec pharma in 2022 and 2023. PE backed deals (most of “Other”) have also been very important in 2023.

Buyer Composition (By Value)



Horizon, Seagen, Kenvue spinoff

Prometheus, Chinook, IVERIC

We expect increased strategic activities from big pharma in 2023 driven by both internal and external factors

Internal Factors

- Huge LOE’s coming up
- Need to plug big holes in future revenue charts
- Need to refresh growth trajectory
- Ample cash balance available for M&A
- Internal R&D POS remains unsatisfactory

External Factors

- Fear of missing out on innovation / technology is more real than ever
- Stock price pressures and interest rates
- Need to catch up on immunology, CVM, renal and obesity market
- Uncertainty around pricing reform and potential disruption

Analysis of Buyer Activity (by Deal Count)

Most Active Buyers in 2020		Most Active Buyers in 2021	
	5		5
	3		3
Most Active Buyers in 2022		Most Active Buyers in 2023	
	2		2
	2		2

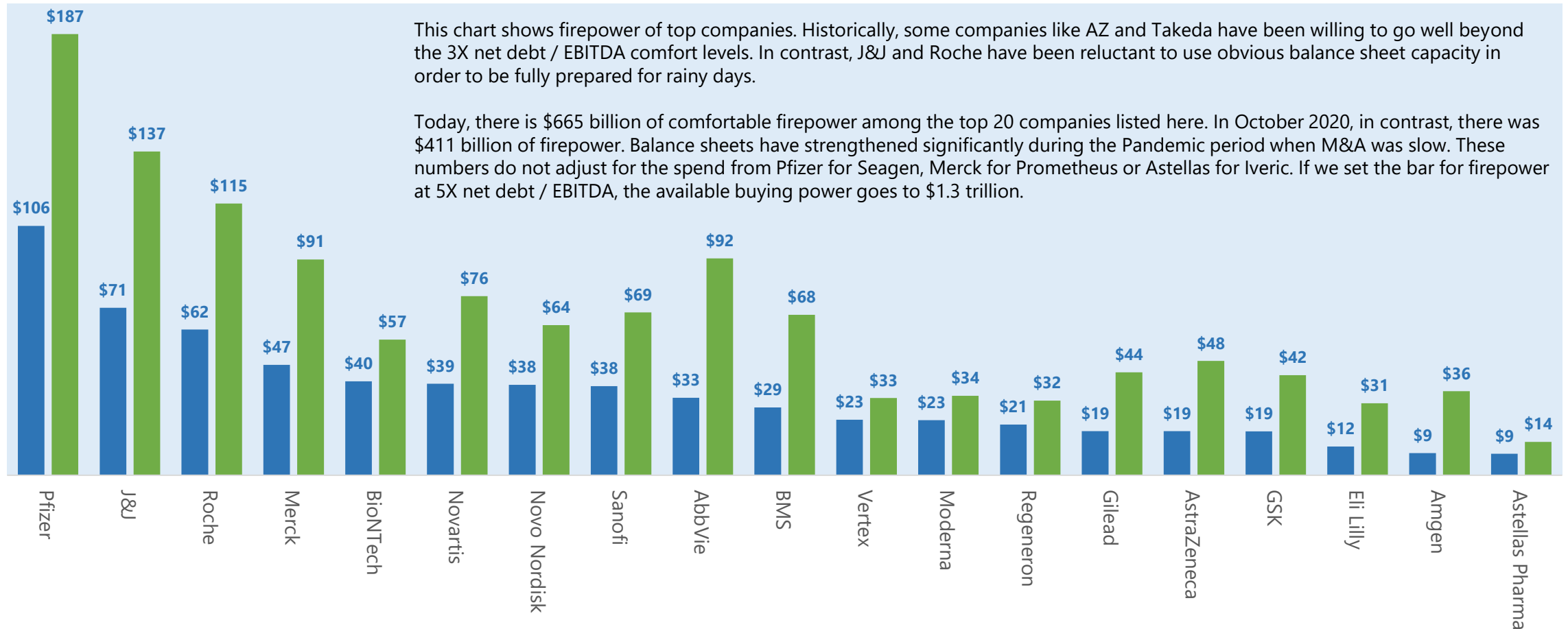
Source: Capital IQ and company press releases; analysis only includes deals with upfront > \$50mm and exclude generics, services, Dx, animal health, and reverse mergers.

\$665 Billion of M&A Firepower at Top 20 Pharma Companies

We define comfortable firepower as the amount of debt a company can take on given current EBITDA holds to arrive at a ratio of net debt to EBITDA of 3X. Stretched firepower would take a company to a ratio of net debt / EBITDA of five times.

M&A Firepower (\$ Billions, June 2023)

■ Comfortable Firepower ■ Stretched Firepower



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