Biopharmaceutical Sector

Weekly Update – October 30, 2023

STIFEL | Healthcare

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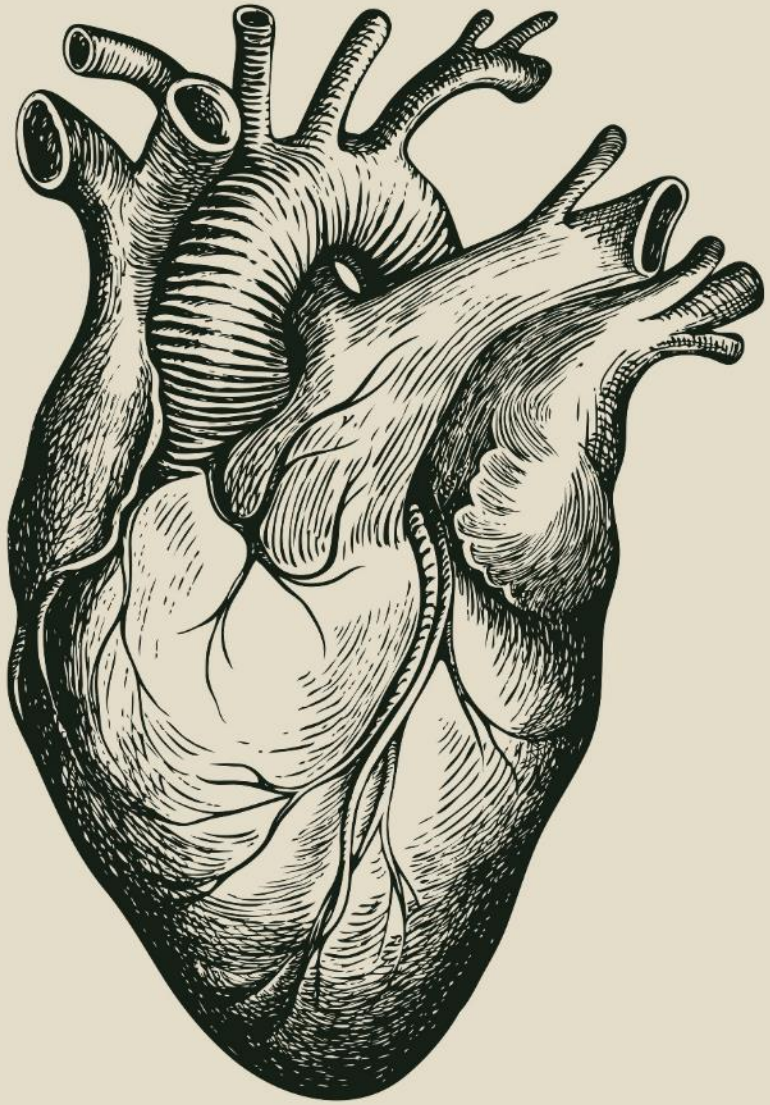

STIFEL | Healthcare

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Recent issues in case you missed and want to read:

October 23, 2023 (ESMO Review)
October 16, 2023 (Cancer Screening)
October 9, 2023 (Biosimilars, M&A)
October 2, 2023 (FcRn, Antibiotics)
September 25, 2023 (Target ID)
September 18, 2023 (Changing Pharma Strategy)
September 11, 2023 (US Health System)
September 5, 2023 (FTC, IRA, Depression)
August 21, 2023 (Covid, China)
August 7, 2023 (Employment, Summer reading)
July 24, 2023 (Alzheimer's Disease)
July 7, 2023 (Biotech market review – H1 '23)
July 1, 2023 (Obesity drugs)
June 19, 2023 (Generative AI)
June 12, 2023 (IRA, State of Industry)
May 29, 2023 (Oncology update)
May 22, 2023 (FTC case on Amgen/Horizon)

Bodelian Library, 1890s

Join Us at These Upcoming Events

Biotech Hangout held its latest event on October 27th.

The next event will be on November 3, 2023.

Please join us.

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

BIO-Europe convenes over 5,500 attendees, representing 60 countries and 2,220+ companies, making the event the industry's largest gathering of biopharma professionals in Europe.

To Learn More
https://informaconnect.com/bioeurope/

Macro Update

Frontispiece from Bernardino Genga's *Anatomia per uso et intelligenza del disengno*, 1691

The US Economy Grew at a Blistering Rate Despite High Interest Rates

Bryan Mena, CNN, October 26, 2023 (excerpt)

The US economy expanded at a remarkably strong pace in the third quarter, despite interest rates at their highest level in 22 years.

Gross domestic product, a measure of all goods and services produced in the economy, grew at an annualized 4.9% rate in the third quarter, the Commerce Department reported Thursday. GDP is adjusted for inflation and seasonal swings.

That's well above the second quarter's 2.1% pace and faster than economists' expectations of a 4.3% rate.

Robust consumer spending fueled growth in the third quarter, a sign of the economy's surprising resilience in the face of tougher borrowing costs and persistently high inflation. Spending grew from July through September by an annualized rate of 4%, its strongest pace since the fourth quarter of 2021. Americans splurged both on goods and services.

Indeed, packed Taylor Swift and Beyoncé concerts and record tickets sales for the "Barbie" film were a hallmark of this year's summer months. Americans also spent big on travel.

Americans chose to spend big in Q3 – among other things, on Taylor Swift concerts.

Source: https://www.cnn.com/2023/10/26/economy/us-economy-third-quarter-gdp/index.html

PCE Inflation Steady in September

Jeff Cox, CNBC, October 27, 2023 (excerpt)

Inflation accelerated in September, but consumer spending was even stronger than expected, according to a Commerce Department report Friday.

The core personal consumption expenditures price index, which the Federal Reserve uses as a key measure of inflation, increased 0.3% for the month, in line with the Dow Jones estimate and above the 0.1% level for August.

Even with the pickup in prices, personal spending kept up and then some, rising 0.7%, which was better than the 0.5% forecast. Personal income rose 0.3%, one-tenth of a percentage point below the estimate.

Including volatile food and energy prices, the PCE index increased 0.4%. On a year-over-year basis, core PCE increased 3.7%, one-tenth lower than August, while headline PCE was up 3.4%, the same as the prior month.

PCE (Personal Consumption Expenditures) inflation is the preferred inflation measure of the Fed. There was nothing in the news last week to give comfort to the Fed that inflation and spending are coming under control. The markets understood this.

Source: https://www.cnbc.com/2023/10/27/key-fed-inflation-gauge-rose-0point3percent-as-expected-in-september-spending-tops-estimate.html

Market Expecting Fed to Remain on Guard for Inflation

Gregg Robb, Marketwatch, October 27, 2023 (excerpt)

The Federal Reserve will hold interest rates steady at its meeting next week, extending the pause that began after the last rate hike in July.

The central bankers are giving off signals that they'd like to remain on the sidelines for some time, but will continue to keep alive the possibility of a hike in December, said Josh Shapiro, chief U.S. economist at MFR Inc.

"They're not going to do anything. I think that they're hoping they are done, but I don't think they are at all ready to commit to that," Shapiro said.

Stephen Stanley, chief U.S. economist at Santander, agreed the Fed would hold steady: "The FOMC has clearly decided to sit on its hand for another six weeks, hopefully giving time for some of the uncertainties hanging over the outlook to resolve."

Fed officials will meet on Oct. 31- Nov. 1. The Fed will issue a statement at 2 p.m. Eastern on Wednesday after their meeting ends. Fed Chairman Jerome Powell will hold a press conference at 2:30 p.m.

Source: https://www.marketwatch.com/story/fed-wont-raise-rates-next-week-and-hopes-that-theyre-done-4a9d22d0

Many Observers See Q3 GDP Numbers as the Peak

There is a broad sense that the U.S. economy in 2024 won't be great

Zachary Warmbrodt, *Politico*, October 26, 2023 (excerpt)

Economists are expecting growth to slow heading into next year.

Borrowing costs are rising, pandemic financial buffers are being drawn down and student loans are coming due – not to mention the hot wars playing out in the Middle East and Ukraine. The talk among CEOs is that they aren't thrilled about what's in store for the economy next year.

It underscores that the third-quarter GDP number may be stellar, but it's a dated snapshot.

The question then becomes: To what extent will Jerome Powell's data-driven Fed take action based on the new stat, which could suggest more work is needed to head off inflation? The Fed is expected to hold interest rates steady when it meets next week.

"That's where I constantly feel this tension between the Fed having been and continuing to be extremely data dependent — and backward-looking as a result — versus what would be optimal in the current environment, which is a forward-looking perspective," EY-Parthenon chief economist Gregory Daco said Wednesday.

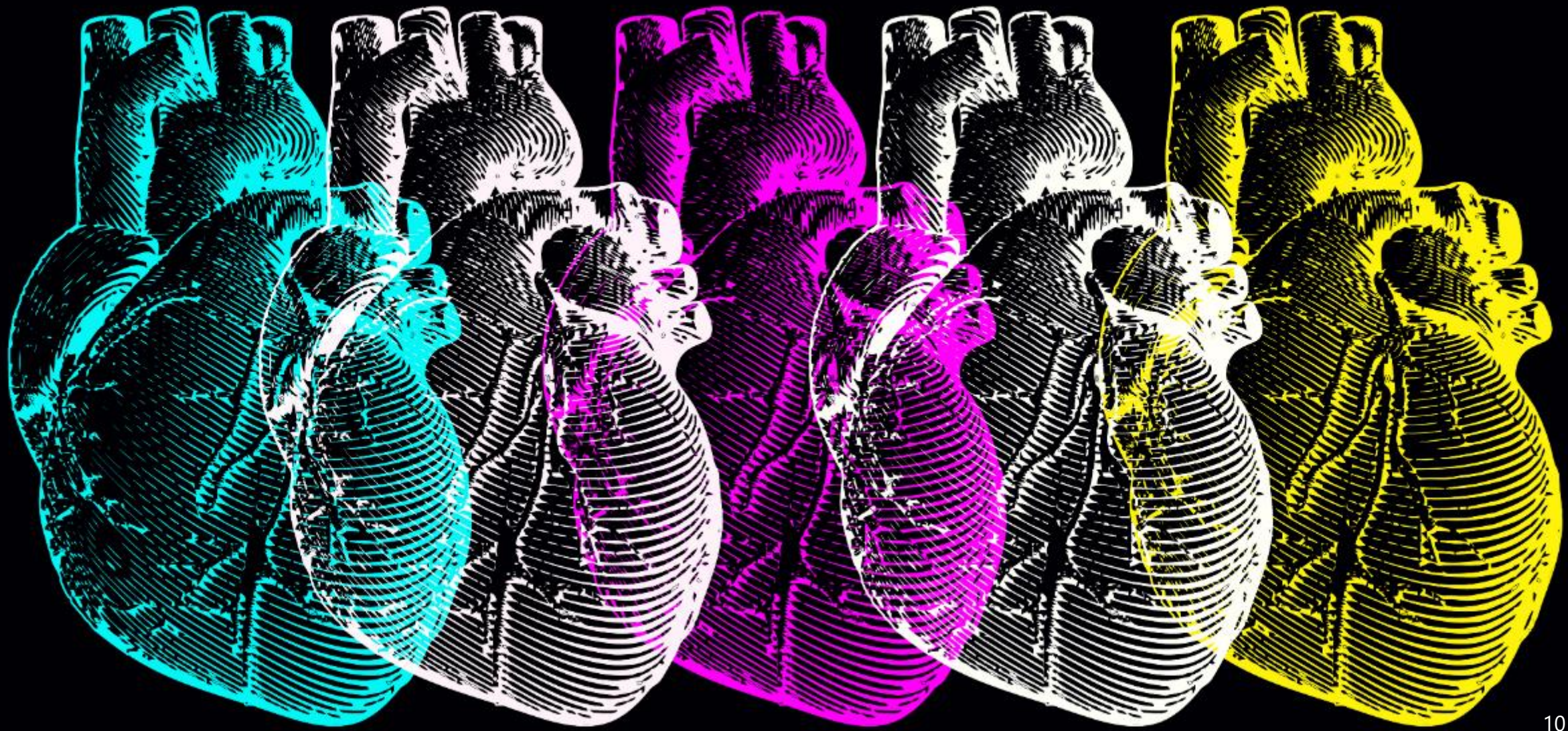
The key issue, according to Daco, is whether consumers and business leaders still have the buffers they need to keep spending into 2024 amid a persistently high-cost, high-interest rate environment.

"The answer to that question, in my opinion, is no," he said. "But depending on how you respond to that question, you're going to want to be more or less hawkish in terms of monetary policy."

Source: https://www.politico.com/news/2023/10/26/bidenomics-gdp-economy-00123706

Alexandria Center for Life Sciences, South San Francisco, CA. Source: Stifel

Biopharma Market Update



Rendering of hearts

XBI Closed at 64.1 Last Week (Down 4.2%)

The XBI was down against last week. The XBI is now down 22.7% for the year. The bear market in biotech has continued due to continued concerns regarding inflation and rates.

Biotech Stocks Down Last Week

Return: Oct 21 to Oct 27, 2023

Nasdaq Biotech Index: -4.1%
Arca XBI ETF: -4.2%
Stifel Global Biotech EV (adjusted): -2.7%*
S&P 500: -2.5%

Return: Jan 1 to Oct 27, 2023

Nasdaq Biotech Index: -13.7%
Arca XBI ETF: -19.4%
Stifel Global Biotech EV (adjusted): -17.9%*
S&P 500: +7.2%

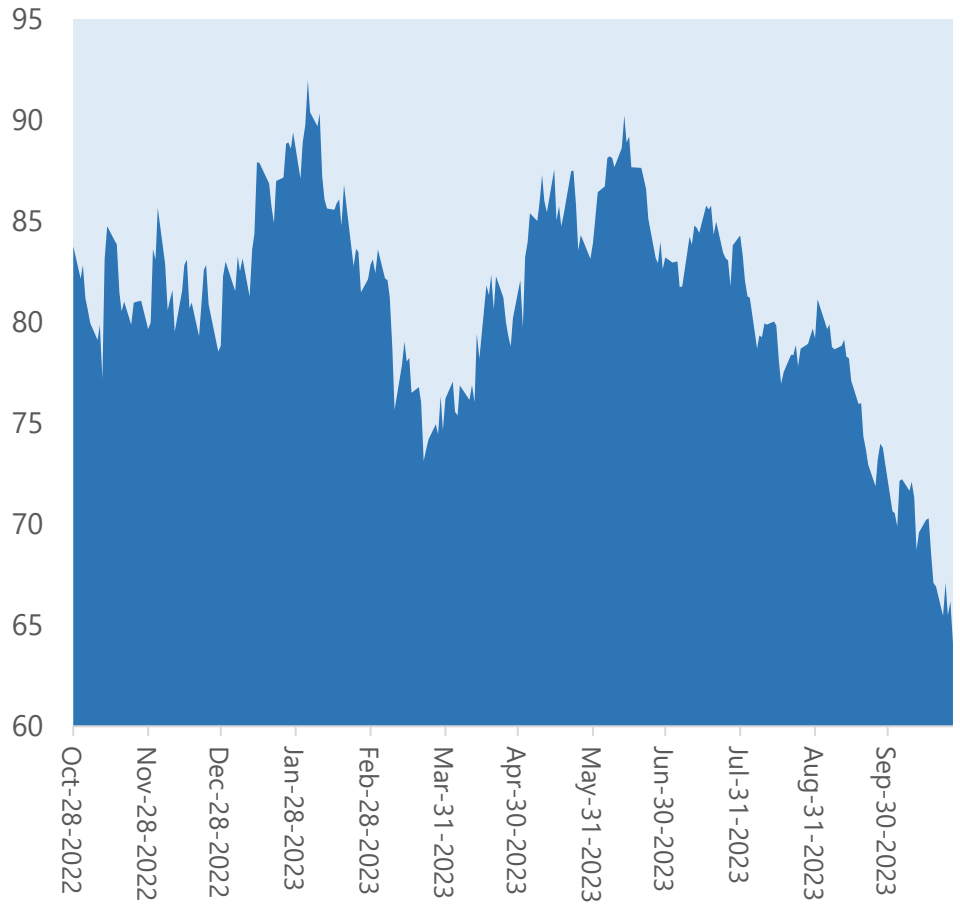
VIX Flat

Oct 21: 29.7%
Jan 20: 19.9%
May 26: 18.0%
July 21: 13.6%
Sep 29: 17.3%
Oct 13: 19.3%
Oct 20: 21.7%
Oct 27: 21.2%

10-Year Treasury Yield Down

Oct 21: 4.2%
Jan 20: 3.48%
May 26: 3.8%
July 21: 3.84%
Sep 29: 4.59%
Oct 13: 4.63%
Oct 20: 4.98%
Oct 27: 4.86%

XBI, Oct 28, 2022 to Oct 27, 2023

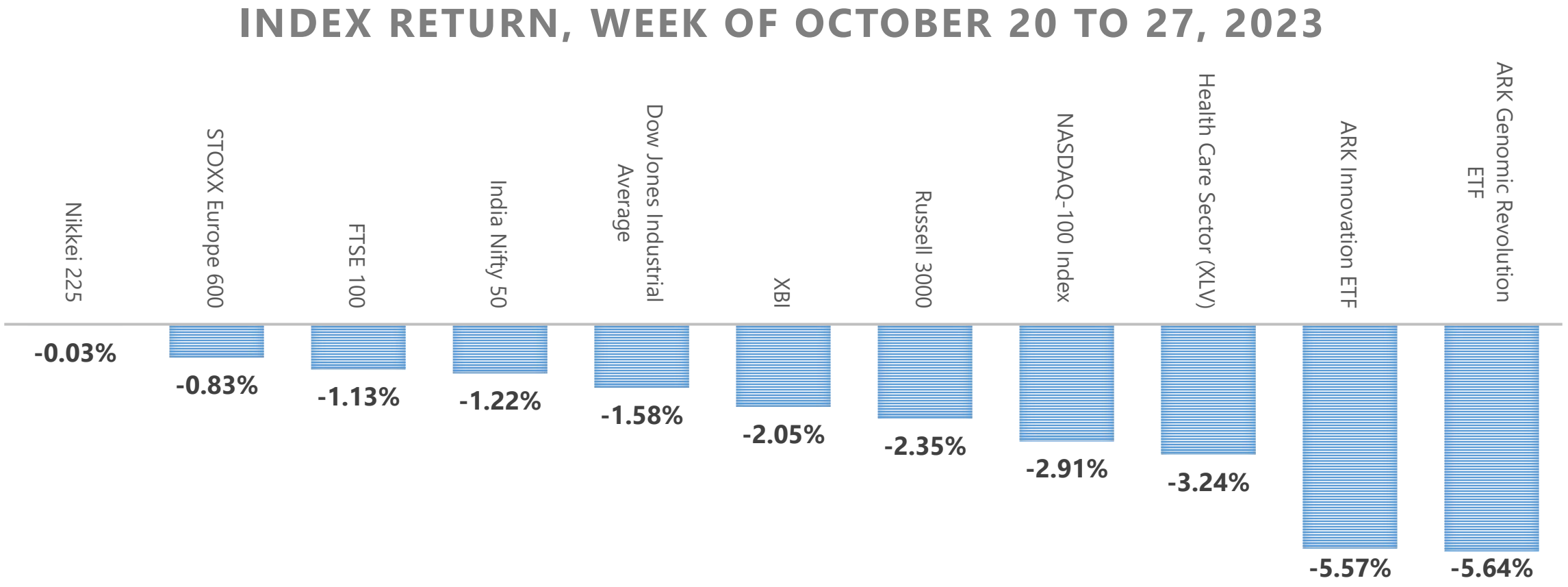


* Change by enterprise value. The adjusted number accounts for the effect of exits and additions via M&A, bankruptcies and IPOs.

Source: S&P Capital IQ and Stifel analysis

Last Week Was One of the Biggest "Risk Off" Periods of 2023

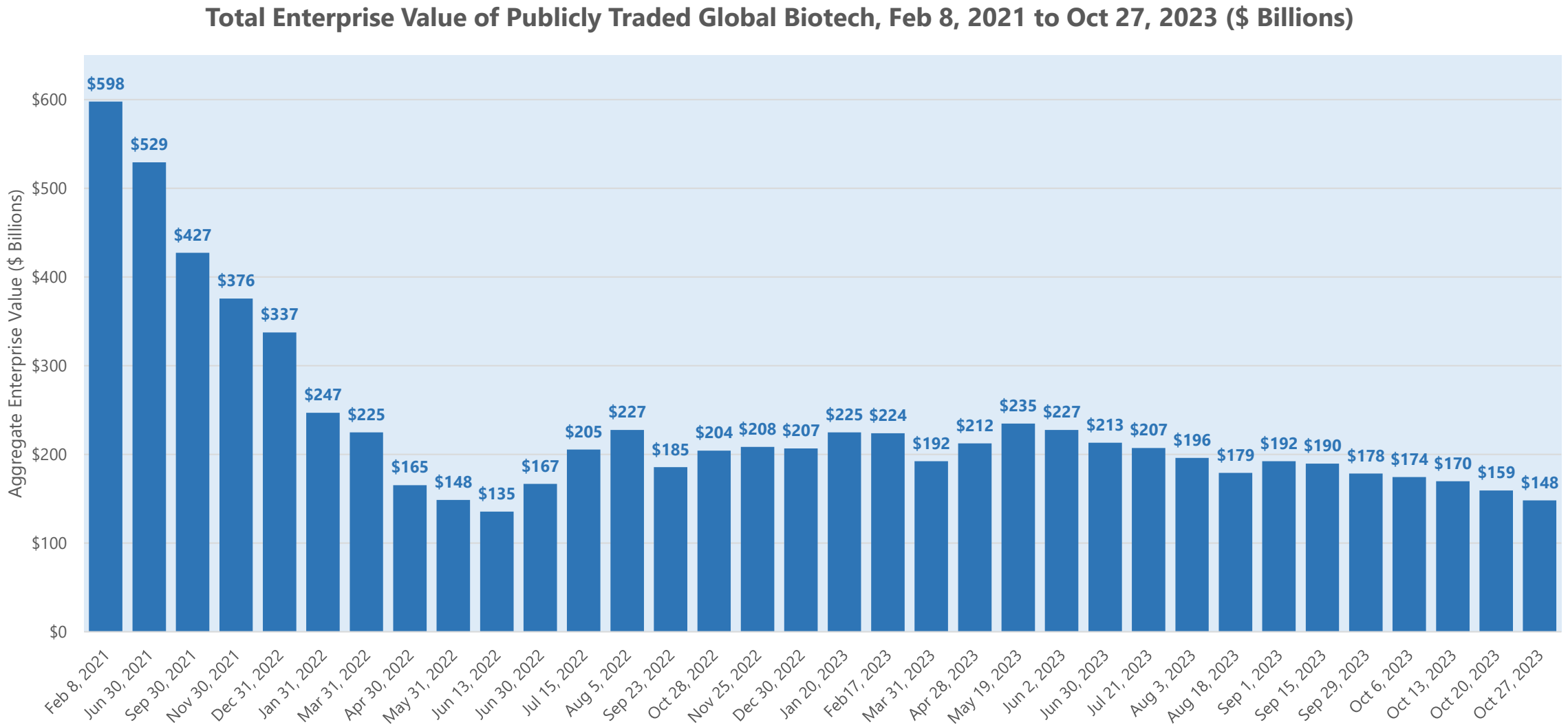
Investment dollars flowed away from higher risk asset classes (e.g., the ARK Genomic Revolution ETF). Asset prices were steady in lower risk asset classes such as the Nikkei 225. The market is not anticipating good things from the Fed's press conference next week on rates and inflation. Investors appear to be avoiding rate and risk sensitive assets classes a result. The swoon in biotech last week was clearly part of a larger and ongoing rotation out of riskier assets.



Source: CapitalIQ

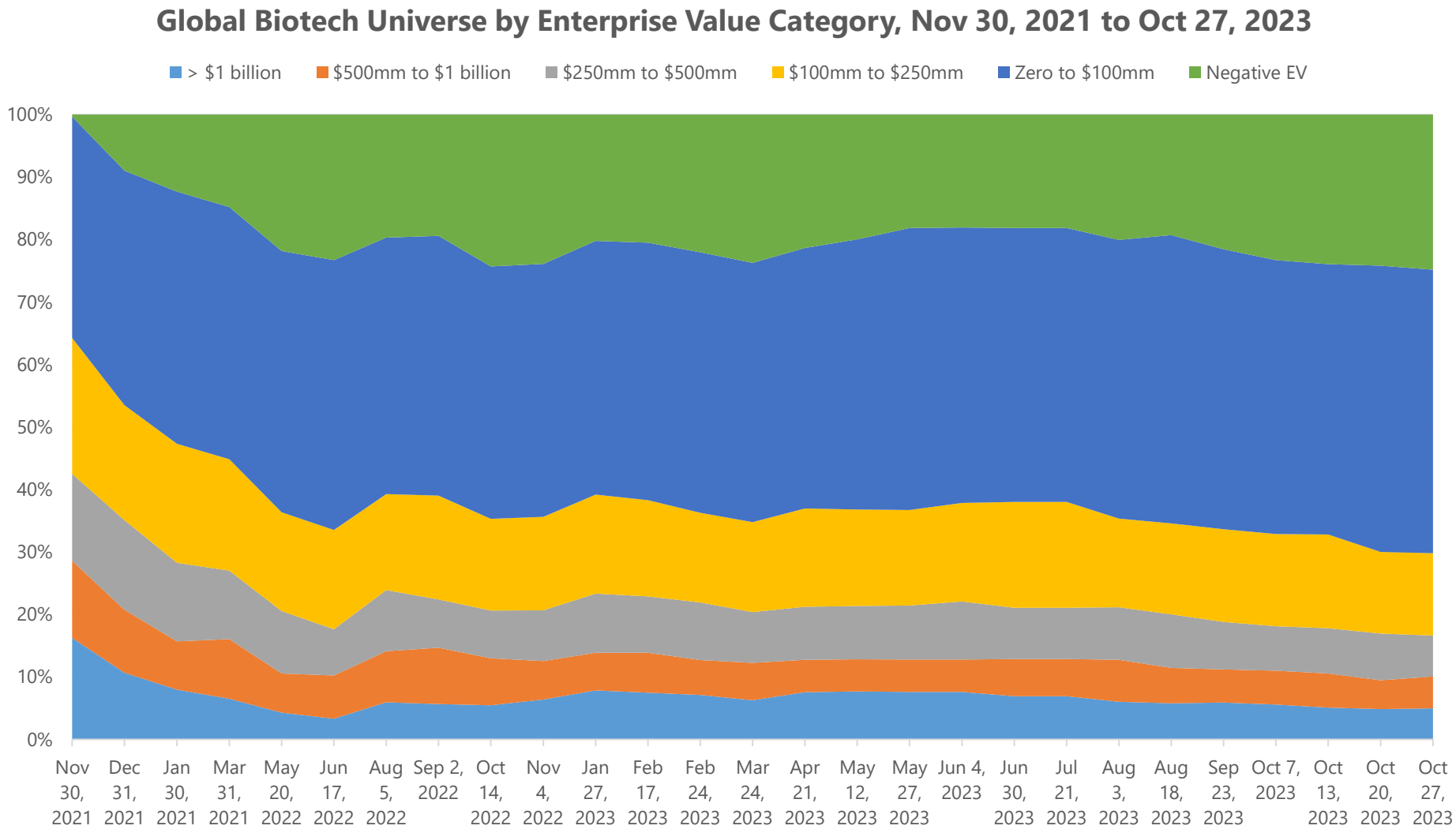
Total Global Biotech Sector Value Down Last Week

The total enterprise value of the global biotech sector fell by 2.7% last week (on an adjusted basis) and is now down over 17.9% for the year after adjusting out for exits and entries.



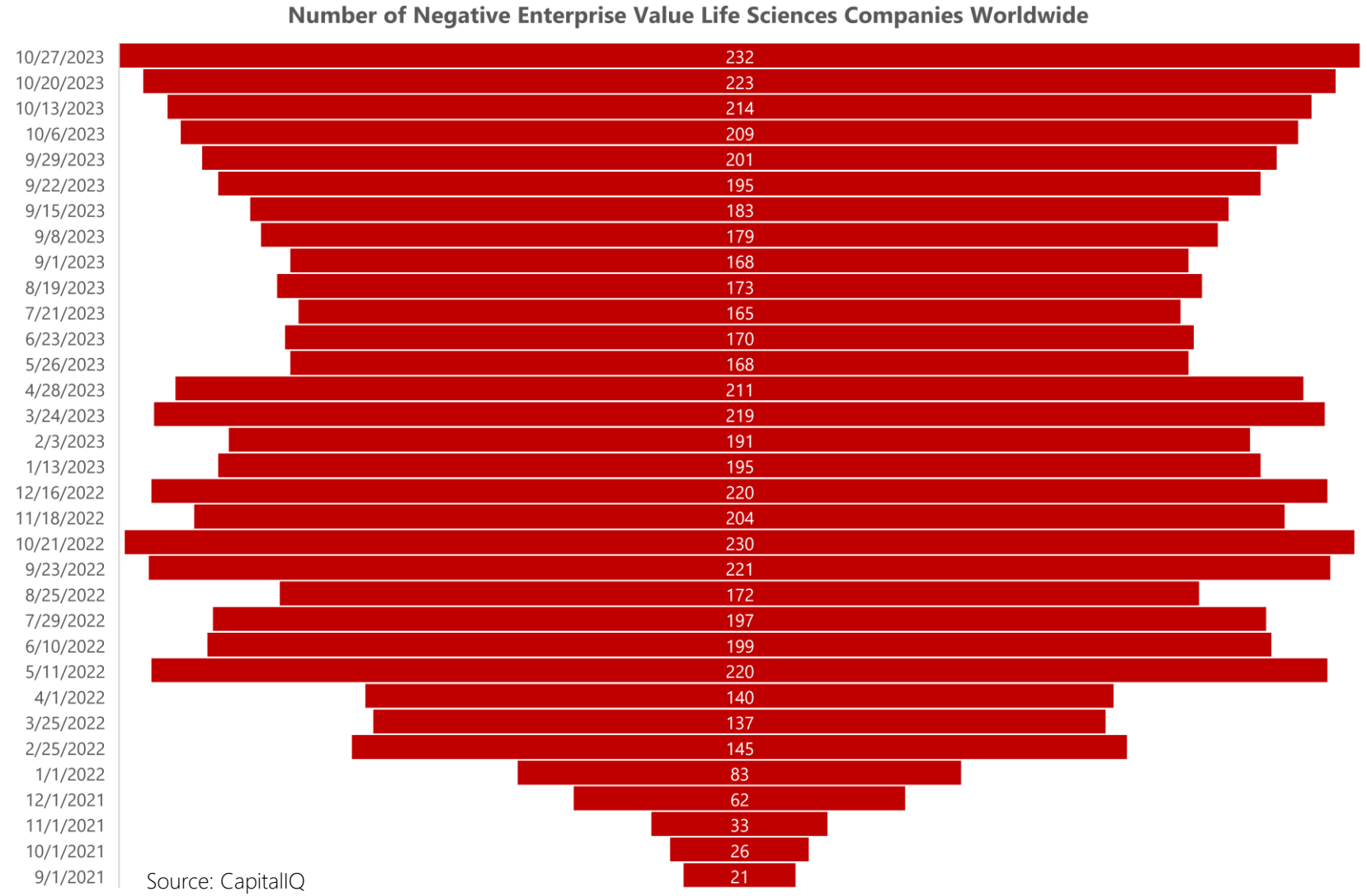
Source: CapitalIQ. Biotechs are defined as any therapeutics company without an approved product on any global stock exchange. Last week included a removal of a commercial company with a $7bn value.

Biotech Neighborhood Continues to See Growth in Sub-$100mm Companies



More than 70% of the global biotech sector now trades with an enterprise value of $100 million or less.

Number of Negative Enterprise Value Life Sciences Companies Rose to 232 in Last Week



Source: CapitalIQ

The count of negative EV life sciences companies worldwide rose from 223 a week ago to 232 last Friday.

This count surpasses the historical record of 230 companies that was set on October 21, 2022.

Public Life Sciences Sector Value Down Last Week

Last week was challenging, in general, for the life sciences sector. The sector lost $274 billion in value. The biggest value drops took place in life science tools (-7%), healthcare IT (-5%), commercial pharma (-3.1%) and medical devices (-3%). The total value of the global sciences sector stands at $8.3 trillion – well down from over $10 trillion at the peak of the Pandemic.

Sector	Firm Count	Enterprise Value (Oct 27, 2023, $millions)	Change in Last Week (percent)	Change in Last Month (percent)	Change in Last Year (percent)
API	81	$77,631	0.7%	-3.5%	-2.4%
Biotech	814	$148,287	-2.7%	-15.9%	-5.1%
CDMO	40	$145,845	-1.0%	-5.9%	-12.2%
Diagnostics	83	$217,213	-2.1%	-7.5%	-8.7%
OTC	31	$27,275	-1.5%	-7.5%	-6.1%
Commercial Pharma	725	$5,491,207	-3.1%	-4.9%	0.2%
Pharma Services	40	$188,430	-1.0%	-6.0%	1.4%
LS Tools	53	$564,238	-7.0%	-15.4%	-21.2%
Medical Devices	181	$1,402,808	-3.0%	-7.7%	-6.6%
HCIT	11	$21,071	-5.0%	-4.0%	-10.2%
Total	**2059**	**$8,279,005**	**-3.2%**	**-6.5%**	**-3.7%**

Source: CapitalIQ

Big Pharma Update

Alexandria Center for Life Sciences, South San Francisco, CA. Source: Stifel

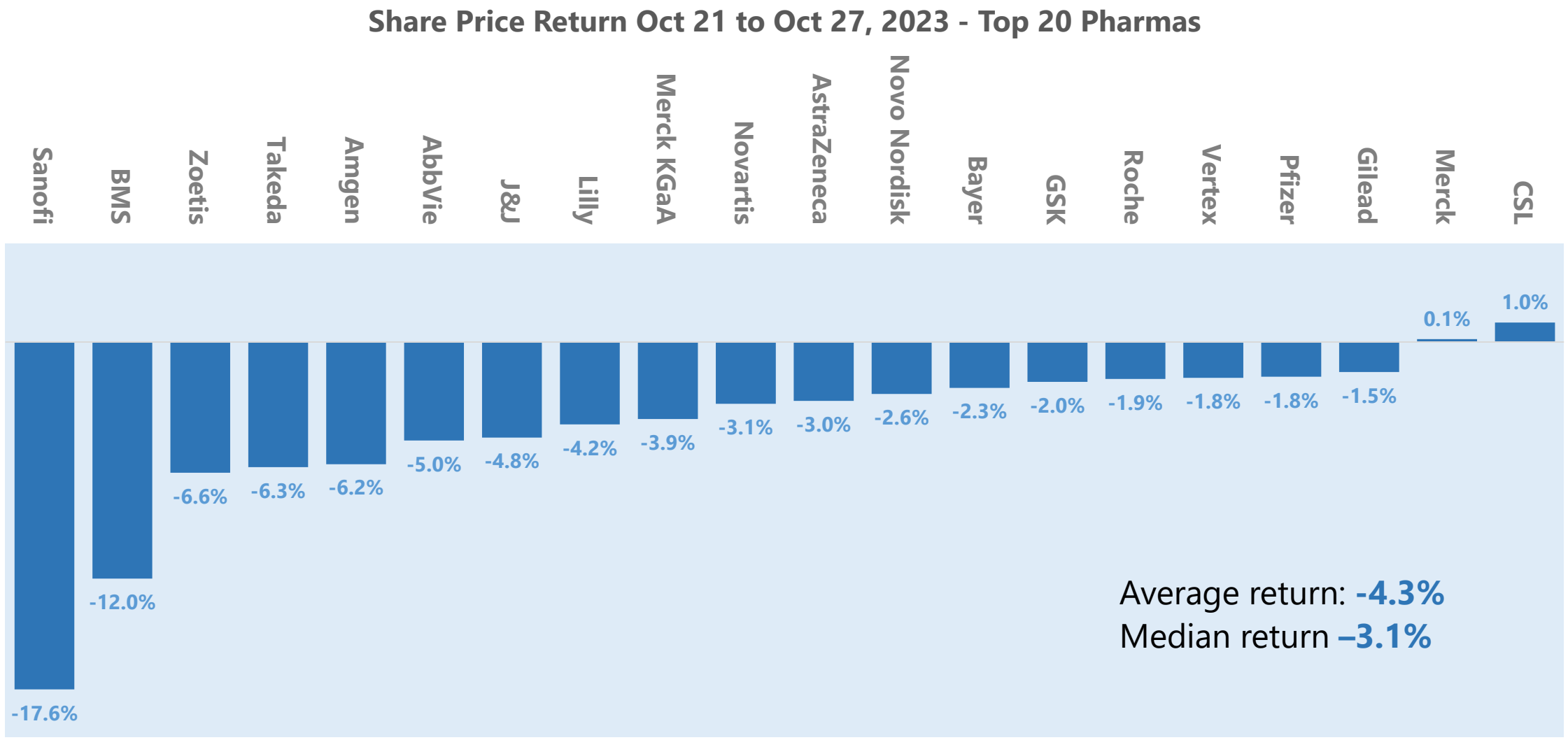
A Difficult Week for Large Pharma

Last week saw the top 20 pharmas lose $145 billion in value. Compare this to a total value loss in 2023 YTD of $190 billion. Only two companies went up in value last week. These were CSL and Merck. Merck reported strong earnings growth last week and was basking in the glow of spectacular data on multiple programs it picked up prior to ESMO.

Company Name	Headquarters	Enterprise Value ($mm)	Market Cap ($mm)	Weekly Value Change ($mm)	YTD Value Change ($mm)	Return Year to Date	Monthly Return	Weekly Return
Lilly	United States	$519,328	$503,808	-$21,952	$158,950	45%	3%	-4%
Novo Nordisk	Denmark	$417,357	$418,876	-$11,314	$114,583	38%	1%	-3%
Johnson & Johnson	United States	$368,957	$350,600	-$17,819	-$111,248	-24%	-7%	-5%
AbbVie	United States	$297,877	$245,218	-$12,885	-$45,981	-14%	-9%	-5%
Merck	United States	$291,490	$260,908	$381	-$9,048	-7%	-1%	0%
Roche	Switzerland	$237,283	$211,950	-$4,028	-$71,131	-24%	-3%	-2%
AstraZeneca	United Kingdom	$214,556	$190,648	-$5,853	-$23,836	-9%	-8%	-3%
Novartis	Switzerland	$203,617	$190,756	-$6,155	-$1,027	-2%	-10%	-3%
Pfizer	United States	$191,163	$170,000	-$3,049	-$97,589	-41%	-6%	-2%
Amgen	United States	$167,210	$139,914	-$9,222	-$155	0%	-3%	-6%
BMS	United States	$135,190	$103,813	-$14,137	-$55,721	-35%	-15%	-12%
Sanofi	France	$122,303	$108,161	-$23,096	-$13,804	-10%	-19%	-18%
Gilead	United States	$112,220	$95,470	-$1,470	-$13,136	-11%	2%	-2%
GSK	United Kingdom	$88,106	$70,564	-$1,451	$270	0%	-5%	-2%
CSL	Australia	$83,995	$71,852	$700	-$9,550	-24%	-8%	1%
Bayer	Germany	$83,530	$42,154	-$1,004	-$5,588	-17%	-10%	-2%
Vertex	United States	$79,870	$91,696	-$1,698	$14,689	24%	1%	-2%
Zoetis	United States	$76,879	$71,823	-$5,091	$4,403	5%	-10%	-7%
Merck KGaA	Germany	$75,736	$65,855	-$2,671	-$18,127	-22%	-8%	-4%
Takeda	Japan	$75,294	$42,295	-$2,862	-$7,197	-13%	-13%	-6%
Total ($mm)		**$3,841,960**	**$3,446,360**	**-$144,677**	**-$190,245**			

Source: CapitalIQ

Top 20 Pharma Share Price Returns Last Week



Tricks and Treats as Biopharma's Q3 Earnings Season Gets Underway

Greg Slabodkin, *Biospace*, Oct 27, 2023 (excerpt)

The third-quarter earnings season is upon us with major biopharma companies reporting mixed financial results, providing a litmus test for the state of the industry and the opportunity to revise expectations for the final quarter of 2023 and beyond. There have been some pleasant and unpleasant surprises for investors this week as clear Q3 winners and losers have emerged.

In the winner's column is Merck, which reported third-quarter revenue and adjusted earnings that topped Wall Street expectations led by strong sales of its blockbuster cancer drug Keytruda, HPV vaccine Gardasil and—surprisingly—COVID-19 antiviral drug Lagevrio. Looking ahead, Merck increased its full-year sales forecast to between $59.7 billion and $60.2 billion, slightly higher than its previous guidance in the range of $58.6 billion to $59.6 billion.

Another winner this week was Novartis, which continued to beat earnings expectations. The Swiss pharma reported a 12% sales increase and 21% core operating growth for the third quarter, while raising its full-year earnings forecast for the third time.

On the negative side of the ledger, Takeda shared financial results for the first half of fiscal year 2023 on Thursday, reporting a disappointing net loss from Phase III fails while dropping net profit projections for the fiscal year by 71%. The Japanese company attributed losses to the exchange rate, tax assumptions and developmental setbacks from two asset failures: Crohn's disease stem-cell therapy Alofisel and non-small cell lung cancer drug Exkivity.

However, at the top of the Q3 loser's column is Sanofi. Just days before Halloween, the French drugmaker spooked investors with a profit warning that sent Sanofi's shares down nearly 20% on Friday. The news: it has abandoned its previous goal of a 32% operating profit margin for 2025—instead focusing on "long-term" profitability by deepening its investment in R&D.

"If this move in Sanofi holds, it would be the largest negative single-day stock move across global pharma in more than 10 years," Jared Holz, Mizuho healthcare equity strategist, told The Wall Street Journal.

Questions are also being asked about Bristol Myers Squibb's mid-term future after it pushed back target sales projections for its new drugs. BMS now expects more than $10 billion in new product sales in 2026, despite previously forecasting $10 billion to $13 billion in sales in 2025. The company's third-quarter revenue also decreased by 2%, which was the fifth consecutive quarterly decline. The main culprit in Q3 was multiple myeloma drug Revlimid, with sales dropping a whopping 41%. Trick or treat!

Source: https://www.biospace.com/article/tricks-and-treats-as-biopharma-s-q3-earnings-season-gets-underway-

Sanofi Increasing R&D Investment and Spinning Off Consumer Business

Paul Hudson
Chief Executive Officer

"We have made tremendous progress on our Play to Win strategy by bringing new and transformative products to market and building an industry-leading immunology pipeline, evidenced by our recent, strong flow of positive R&D data readouts. In this new chapter of our strategy, we are deepening our investment in R&D, taking steps toward becoming a pure play biopharma company, and further optimizing our cost structure. This will help us accelerate innovation and strengthen our growth drivers, while ensuring long-term profitability and enhancing shareholder value. We are excited to build on the success of our strategy and confident in the long-term value our investments will generate for all Sanofi stakeholders."

Source: https://www.sanofi.com/en/media-room/press-releases/2023/2023-10-27-05-30-00-2768148

Sanofi Rebases Guidance in its Q3 Earnings Announcement

Press Release

Sanofi Enters Next Chapter of Play to Win Strategy

2023 Guidance and Preliminary 2024 and 2025 Outlook[1]

Sanofi reiterates its 2023 guidance of mid-single digit[2] Business EPS[3] growth at constant exchange rates.

As a result of changes to global tax regulations, Sanofi's effective tax rate is expected to increase from 19% in 2023 to 21% in 2024. Due to the increased R&D investment, Sanofi expects 2024 Business EPS to remain roughly stable to 2023 levels excluding the impact of the expected tax rate change, and therefore decline low-single digits including the higher expected tax rate.

In 2025, Sanofi expects a strong rebound in business EPS growth, driven by continued sales growth supported by its leading franchises, the full benefit from planned efficiency initiatives, and its expectation of relatively stable R&D expenses year on year.

Given Sanofi's decision to support the full realization of its pipeline's long-term potential, its continued investment around the new launches, as well as pricing headwinds in General Medicines, the Company will no longer target a 32% BOI[4] margin for 2025 while maintaining a focus on long-term profitability.

The company reiterates its goal to generate over €22 billion in sales in immunology, and over €10 billion in sales in vaccines by 2030[1].

Sanofi guided down 2024 and 2025 earnings from analyst expectations.

Source: https://www.sanofi.com/en/media-room/press-releases/2023/2023-10-27-05-30-00-2768148

Sanofi's Shares Drop 18% on Friday's Earnings Guidance Drop

Sanofi Analyst Consensus Earnings / Share Going Into Q3

	2022	2023	2024	2025	2026	2027
Consensus	8.75 A	8.75 E	9.30 E	10.48 E	11.30 E	11.98 E
Reguided	8.75 A	9.11 E 4%	8.83 E -3%	9.71 E 10%		
Difference	None	4.0%	-5.1%	-7.3%		

Source: CapIQ

Sanofi effectively guided down 2024 earnings by 5%, and 2025 by more relative to analyst consensus.

The timing could not be worse. Investors are extremely skittish at the moment and know that when large corporates guide down it's not a good thing. Investors believe that management teams tend to underguide them to keep "sand in the pocket" so reducing guidance from what was already viewed as a conservative level is considered a bad sign.

The average historical share price decline followed lowering of earnings guidance has been -9.6%.* Sanofi's coupling of reduced guidance with a major spinout, bad news on taxes, the general medicine business, exchange rates and R&D spend appear to have set off alarm bells with investors.

* Lynn Rees & Brady Twedt (2011) The stock price effects from downward earnings guidance versus beating analysts' forecasts: which effect dominates?, *Accounting and Business Research*, 41:2, 95-118

Sanofi CEO Shocks Investors With Investment Plan, Few Details

Tim Loh, *Bloomberg*, October 27, 2023

When the day began, Paul Hudson, Sanofi's perennially upbeat chief executive officer, was sitting pretty with a double-digit share gain this year, a world-beating drug in Dupixent and few of the patent cliff worries weighing on his big pharma rivals.

That changed when he stunned investors with a profit warning and plans for higher research-and-development spending that raised doubts about future earnings — and then said he'd fill in details at an investor event in about six weeks.

The move to cut some of Sanofi's financial targets for the next two years in service of speeding up the pipeline of medicines had one big effect on Friday: blunting the impact of Sanofi's decision, long anticipated, to separate its consumer health division.

Instead of benefiting from that announcement, Sanofi's shares plunged the most ever, wiping about €25 billion ($26.5 billion) from its market value and erasing all of this year's gains and more besides. By Friday afternoon, at the end of a 75-minute call with Wall Street analysts and with the stock sliding anew, Hudson was left insisting that his gamble will pay off.

"We have reached the point where we believe we can create more value by taking this approach and we understand there's some short-term disappointment," Hudson said. "We'll show you why it was the right decision."

Source: https://www.bloomberg.com/news/articles/2023-10-27/sanofi-ceo-shocks-investors-with-investment-plan-few-details

Why Drug Companies Don't Want to Sell OTC Allergy Medicines and Bandages Anymore

Sanofi plans to spin off division with brands such as Allegra, IcyHot and Aspercreme.

By Jared S. Hopkins and Adrià Calatayud, Wall Street Journal, October 27, 2023 (excerpt)

Big Pharma is almost finished with the cough and cold medicine business.

French drug giant Sanofi said Friday it plans to spin off its consumer-health business, which includes well-known brands like allergy medicine Allegra and the pain treatments IcyHot and Aspercreme.

The drugmaker is the latest—after rivals Johnson & Johnson, Pfizer and GSK—to hive off a division selling over-the-counter medicines and other retail products to focus on more commercially lucrative but scientifically riskier prescription drugs.

Once the split is completed as early as the fourth quarter next year, there will be just one consumer-health business left under the umbrella of a big drugmaker parent. Germany's Bayer will be the largest drugmaker with such a business.

Yet the companies lose the crutch of a reliable source of cash flow, and now face more pressure to hit on breakthrough medicines with large sales potential.

Sanofi shares fell as much as 16% in trading in Europe after the company announced the consumer-health split because the firm said its earnings next year would decline due to higher taxes and plans to boost research-and-development investment.

The consumer-health separations signal just how much the pharmaceutical industry has moved past its cough-and-cold remedy roots to complex therapies, often delivered by intravenous infusion and based on advanced molecular biology, for debilitating diseases.

The consumer products were key sources of revenue. They also sometimes offset the ups-and-downs of the more volatile prescription drug sales.

As many pharmaceutical investors seeking higher returns have also noticed, prescription products can command higher prices and generate bigger profits.

Cancer, cystic fibrosis and other therapies can list for more than $100,000 and in some cases more than $1 million, while big retailers like Amazon.com and Walmart can squeeze the margins on consumer-health products because of their online presence.

Sanofi, which generated roughly 43 billion euros, the equivalent of about $45 billion, in total company sales last year, saw its consumer business bring in more than $5 billion last year, an 8.6% increase from the prior year.

Source: https://www.wsj.com/health/healthcare/sanofi-plans-to-spin-off-consumer-healthcare-business-ab808c6f

Takeda Operating Profit Down 9.5%

Takeda Announces FY2023 H1 Results; Updates Full-Year Forecasts While Remaining on Track Towards Management Guidance

Revenue Growth of +6.4% at Actual Exchange Rate (AER); +1.4% Growth at Constant Exchange Rate (CER), Driven by Growth & Launch Products (+13% at CER)
Core Operating Profit Year-on-Year Change of -9.5% at CER Reflecting Generic Impact, Lower Demand for Coronavirus Vaccines and Increased Investment in R&D and Data & Technology
Reported Operating Profit and Net Profit Impacted by Non-Cash Impairment of Intangible Assets Booked in Q2
Raising Full Year Revenue and Core EPS Forecasts to Reflect Updated FX and Tax Rate Assumptions; Lowering Full-Year Profit Forecasts on a Reported Basis Due to Non-Core Items Booked in Q2
No Change to Free Cash Flow Outlook or Management Guidance

FINANCIAL HIGHLIGHTS
Results for FY2023 H1 Ended September 30, 2023

(Billion yen, except percentages and per share amounts)	REPORTED		CORE[c] (Non-IFRS)[a]		
	FY2023 H1	vs. PRIOR YEAR (Actual % change)	FY2023 H1	vs. PRIOR YEAR (Actual % change)	vs. PRIOR YEAR (CER % change[d])
Revenue	2,101.7	+6.4%	2,101.7	+6.4%	+1.4%
Operating Profit	119.2	-53.2%	588.8	-5.8%	-9.5%
Margin	*5.7%*	*-7.2pp*	*28.0%*	*-3.6pp*	
Net Profit	41.4	-75.2%	407.7	-8.7%	-13.8%
EPS (yen)	27	-75.4%	261	-9.4%	-14.4%
Operating Cash Flow	291.3	-4.6%			
Free Cash Flow (Non-IFRS)[a][b]	-71.1	N/A			

(a) Further information regarding certain of Takeda's Non-IFRS measures is posted on Takeda's investor relations website at https://www.takeda.com/investors/financial-results/quarterly-results/.

Source: https://www.takeda.com/newsroom/newsreleases/2023/Takeda-Announces-FY2023-H1-Results/

Takeda CEO Comments on Outlook

“We continue to pursue our vision to discover and deliver life-transforming treatments, making further progress in the first half of our fiscal year to address unmet medical needs and provide new treatment options to improve patient outcomes and quality of life. Our pipeline is robust and we anticipate a number of important milestone in the second half of the fiscal year, including potentially up to three new product approvals in the U.S., for TAK-755, fruquitinib, and TAK-721.

Development setbacks with EXKIVITY® and ALOFISEL®, which impacted our reported profit in FY2023 Q2, highlight the inherent risk in research and development in the pharmaceutical business, but do not hinder our strategy for a return to growth in the near-term and our confidence in the long-term strength of the business remains firm.”

Christophe Weber
President and CEO
Takeda

Source: https://www.takeda.com/newsroom/newsreleases/2023/Takeda-Announces-FY2023-H1-Results/

Q3 2023 Performance

Bristol Myers Squibb™

Commercial & Financial Execution

Q3 Global Net Sales

- **11.0B;** (2%) YoY; (3%) Ex-FX*

In-Line Brands & New Product Portfolio

- **~$9.3B;** +8% YoY; +7% Ex-FX*

Earnings per Share (EPS)

- GAAP **$0.93,** +24% YoY
- Non-GAAP* **$2.00,** +1% YoY

Financial Outlook

Medium-Term Financial Targets*

Reaffirms[1]:

- Low-to-mid single digit revenue CAGR[2]
- Low double-digit revenue CAGR[2] ex-Rev/Pom
- $8-10B revenue growth from in-line brands[3]

Adjusts:

- >$10B growth from new product portfolio in 2026
- Operating margin to >37%[4]

Business Development

MIRATI THERAPEUTICS

- Entered into acquisition agreement with planned close by 1H 2024
- Strengthens & diversifies Oncology portfolio

Pipeline Execution

- **Reblozyl:** U.S. approval in 1L MDS associated anemia (COMMANDS)
- **Opdivo:** U.S. & EU approval in Stage II adj. melanoma (CM-67K); positive Ph3 in SC nivolumab (CM-67T) & peri-adj. lung (CM-77T)
- **LPA_1 antagonist:** Established PoC in PPF

*See "Forward-Looking Statements and Non-GAAP Financial Information" and "Bristol Myers Squibb Company Reconciliation of Certain GAAP Line Items to Certain Non-GAAP Line Items"

1. 2020-2025 Financial Targets 2. At constant exchange rates on a risk-adjusted basis 3. Primarily I-O & Eliquis 4. Target through 2025

Source: https://www.bms.com/investors.html

Bristol Myers Squibb™

Solid Momentum in Q3 & Accelerating Future Growth

Key In-Line Products

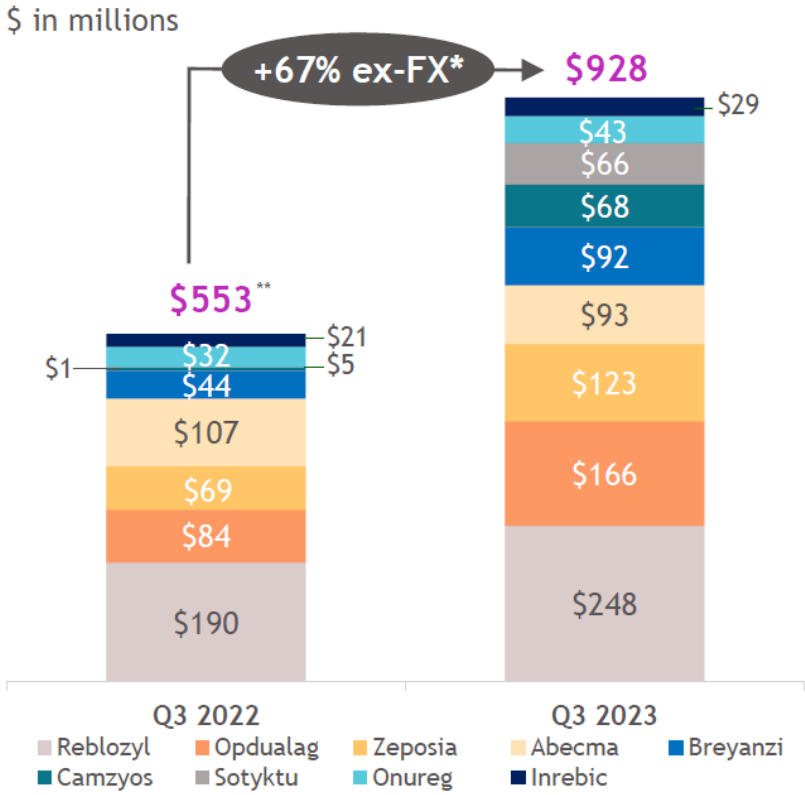
Eliquis apixaban

- Strong U.S. demand growth offset by gross-to-net adjustments

OPDIVO (nivolumab) INJECTION FOR INTRAVENOUS USE 10 mg/mL

- Continued demand growth
- Delivered key clinical milestones to enable future growth

New Product Portfolio



Outlook*

- Expect **>$10B revenue** from new product portfolio in 2026
- Focused on product **acceleration** to enable future growth
- Planned expansion of **new product portfolio** with repotrectinib[1] & Krazati[2]

*See "Forward-Looking Statements and Non-GAAP Financial Information"
**Q3 2022 sales: Camzyos - $5M & Sotyktu - $1M

1. U.S. PDUFA: November 27, 2023
2. Subject to satisfaction of customary closing conditions; anticipated closing by 1H 2024

Source: https://www.bms.com/investors.html

Bristol Myers Shares Dropped on Pushing Back Topline Expectations for New Products

Bristol Myers Squibb™

Medium-Term Financial Targets

The company is updating its previously communicated medium-term targets:

July (Prior)	October (Revised)
Low-to-mid single digit revenue CAGR[1] from 2020-2025	Reaffirms low-to-mid single digit revenue CAGR[1] from 2020-2025
Low double-digit revenue CAGR[1] Ex-*Revlimid/Pomalyst* from 2020-2025	Reaffirms low double-digit revenue CAGR[1] Ex-*Revlimid/Pomalyst* from 2020-2025
$8-$10 billion growth from in-line brands[2] from 2020-2025	Reaffirms $8-$10 billion growth from in-line brands[2] from 2020-2025
$10-$13 billion from new product portfolio in 2025	Adjusts to >$10 billion revenue from new product portfolio in 2026
40%+ Non-GAAP operating margin through 2025	Adjusts Non-GAAP operating margin target to >37% through 2025

[1] At constant exchange rates on a risk-adjusted basis.
[2] Primarily I-O and *Eliquis*.

Source: https://www.bms.com/investors.html

AbbVie Raises Guidance

Full-Year 2023 Outlook

AbbVie is raising its adjusted diluted EPS guidance for the full year 2023 from $10.86 - $11.06 to $11.19 - $11.23, which includes an unfavorable impact of $0.27 per share related to acquired IPR&D and milestones expense incurred year-to-date through the third quarter 2023. The company's 2023 adjusted diluted EPS guidance excludes any impact from acquired IPR&D and milestones that may be incurred beyond the third quarter of 2023, as both cannot be reliably forecasted.

AbbVie Raises 2024 EPS Guidance Floor

AbbVie is raising its adjusted diluted EPS guidance floor for the full year 2024 from $10.70 to $11.00, which excludes any impact from acquired IPR&D and milestones, as both cannot be reliably forecasted. This is an update to guidance that was initially issued in February 2023 as part of AbbVie's fourth quarter 2022 earnings call. As a result of this update, AbbVie does not expect adjusted diluted EPS for full year 2024 to be below $11.00 per share. The company will issue its formal 2024 adjusted diluted EPS guidance range in conjunction with fourth quarter 2023 results.

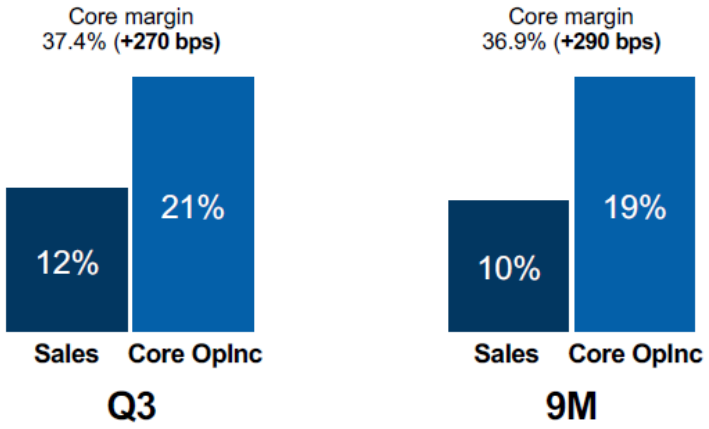
Source: https://investors.abbvie.com/static-files/296839c1-fd45-44b5-875e-c11e77924358

Novartis Raises Guidance

Novartis delivers strong sales growth, robust margin expansion and raises guidance. Successfully spun Sandoz

Growth and productivity[1]

% cc



FY 2023 guidance raised[1]

Sales expected to grow high single digit; Core OpInc expected to grow mid to high teens (from low double digit to mid teens)

Successful spin-off of Sandoz

Completed October 4, 2023

Several major innovation milestones in Q3

- **Cosentyx®** IV formulation approved in US (PsA, AS, nr-axSpA)
- **Leqvio®** approved in China and Japan
- **Kisqali®** submitted in EU; US submission planned in Q4 2023

Clinically meaningful and statistically significant Ph3 data for multiple assets with blockbuster potential

- **Pluvicto®** mCRPC pre-taxane
- **Iptacopan** IgAN
- **Remibrutinib** CSU
- **Lutathera®** GEP-NETs

1. Continuing operations. Constant currencies (cc), core results are non-IFRS measures; explanation can be found on page 48 of Condensed Interim Financial Report. Unless otherwise noted, all growth rates refer to same period in PY. OpInc – operating income.

Source: https://www.novartis.com/investors

Merck Delivers Great Numbers

Strong Q3 sales performance and earnings growth[1]

Q3 Worldwide Sales

$16.0B

+7%

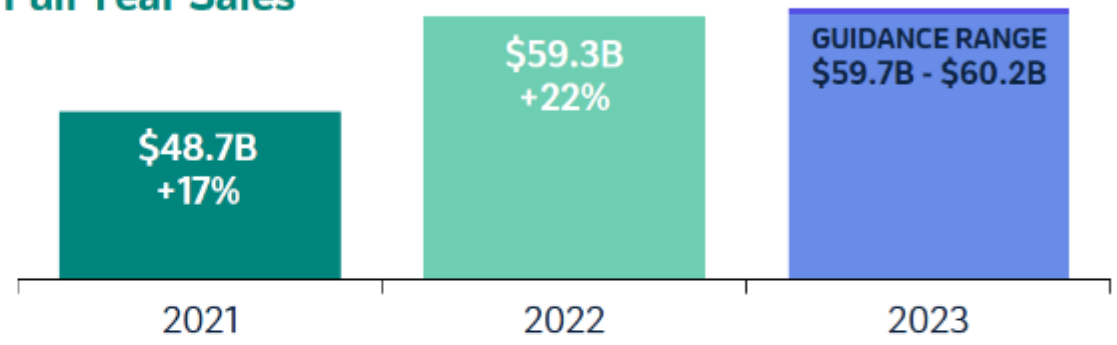
+8% ex-Exchange, ex-LAGEVRIO[2]

Q3 Non-GAAP EPS[3,4]

$2.13

+15%

Full Year Sales



Full Year Non-GAAP EPS[3]

1. Results from continuing operations attributable to Merck & Co., Inc. 2. Excludes Lagevrio sales of $640 million in 3Q23 and $436 million in 3Q22. 3. Merck does not exclude expenses for upfront and milestone payments related to collaborations and licensing agreements, or charges related to pre-approval assets obtained in transactions accounted for as asset acquisitions from its non-GAAP results. YTD 2023 non-GAAP results include an aggregate $11.6 billion or $4.52 per share of R&D expenses related to the Prometheus and Imago acquisitions and upfront payment for the license and collaboration agreement with Kelun-Biotech. Full year 2022 non-GAAP results include $690 million or $0.22 of such charges. Full year 2021 non-GAAP results include $1.7 billion or $0.65 of such charges. For 2023, guidance includes an additional $5.5 billion or $1.70 per share related to the collaboration with Daiichi Sankyo, and guidance does not assume any additional significant potential business development transactions. 4. GAAP EPS of $1.86.

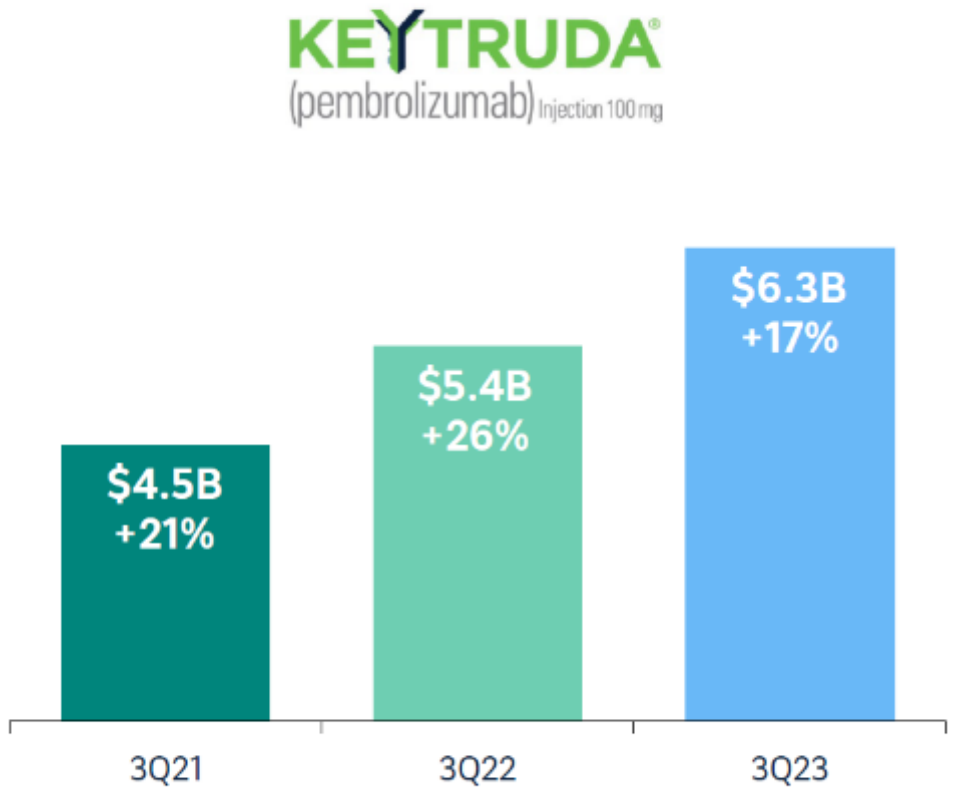
MERCK 6

Source: https://www.merck.com/investor-relations/events-and-presentations/

KEYTRUDA® Revenues Continue to Impress

Oncology: KEYTRUDA continues to drive exceptional growth

- KEYTRUDA sales of $6.3B increased 17% year-over-year, driven by global uptake in earlier stage cancers and continued strong global demand from metastatic indications
  - In the U.S., growth of 14% reflects strong utilization across metastatic indications and earlier stage cancers, such as TNBC
  - Ex-U.S., 22% increase driven by uptake in earlier stage cancers, including high-risk early-stage TNBC and adjuvant RCC, as well as increased demand in advanced RCC and certain types of H&N cancer



Growth rates exclude the impact of foreign exchange.

Source: https://www.merck.com/investor-relations/events-and-presentations/

MERCK

Industry News

St. Thomas Hospital London, 1840

After Reaching FDA First, CRISPR-Vertex's Gene Editing Therapy Will get 'Benign' Review by Committee

Annalee Armstrong, *Fierce Biotech*, October 27, 2023 (excerpt)

A historic moment in pharmaceuticals will happen next week: an FDA advisory committee is set to review the first-ever CRISPR gene editing-based therapy, Vertex Pharmaceuticals and CRISPR Therapeutics' exa-cel for sickle cell disease (SCD).

But what would be even more industry changing would be securing the first such approval. Before they can do that, Vertex and CRISPR Tx will need to convince the FDA that the therapy, also known as exagamglogene autotemcel, does not cause off-target effects.

The FDA has asked the Cellular, Tissue, and Gene Therapies Advisory Committee to discuss just one question: the applicants' off-target analysis and any recommendations for additional studies, if needed, to assess the off-target risk for exa-cel.

To support their case, the companies submitted data from in silico and cellular assays. The first uses gRNA sequence information to scan the human reference genome to find potential off-target editing. But since this method only uses the reference genome, the FDA is concerned that edits specific to an SCD patient may be missed.

"The small target sample size in this database may not be sufficient for the safety assessment as it may not adequately capture variants in this population across the United States," the FDA wrote in its briefing documents.

The FDA recommended a potentially more diverse data tool called CRISPRme that allows for the study of potential off-target effects with gene editing. A recent study on the tool used the same gene that exa-cel edits, finding a few off-target effects present in African ancestry samples.

Source: https://www.fiercebiotech.com/biotech/crispr-vertexs-gene-editing-1st-get-narrow-review-fda-committee-and-thats-good-thing

NIH Nominee Monica Bertagnolli Clears Senate Panel with Bipartisan Support Despite Sanders' Drug Pricing Qualms

Lia DeGroot, Endpoints News, October 25, 2023 (excerpt)

National Cancer Institute director Monica Bertagnolli received the Senate health committee's stamp of approval to helm the NIH — but as promised, Bernie Sanders strayed from Democratic colleagues and voted against her nomination.

The independent senator from Vermont joined five Republicans in voting no, voicing concerns that Bertagnolli isn't prepared to take on the pharma industry's "greed." At her nomination hearing last week, Bertagnolli largely skirted Sanders' direct questions about how she would lower prescription drug costs.

Sanders was alone among Democratic committee members in opposing her nomination.

"I like her," Sanders said in remarks. "But I think this is a moment where we need leadership at the NIH, which is really prepared to take on the greed of the pharmaceutical industry, lower prescription drug prices in America, and move the NIH in a very, very different direction."

Source: https://endpts.com/nih-nominee-monica-bertagnolli-clears-senate-panel-with-bipartisan-support-despite-sanders-drug-pricing-qualms/

Who Earns More Money From Generic Drug Sales: PBMs or Drug Manufacturers?

Jason Shafrin, *Healthcare Economist*, October 26, 2023

If you guessed manufacturers, you would be incorrect. At least that is according to a new study by Mattingly et al. (2023) in *JAMA Health Forum*. Using a sample of the 45 generic drugs with >$100m in Part D and used by >1m beneficiaries, the authors found that:

"…Medicare Part D spent $11.8 billion for 690 million claims (mean, $22.50 per claim; 95% CI, $18.28-$26.72 per claim), representing 5.5% of all Part D spending ($216 billion) in 2021. The $22.50 was distributed as follows: $9.18 (40.8%) represents PBM gross profit; $3.87 (17.2%), pharmacy gross profit; $2.71 (12.0%), wholesaler gross profit; and $6.73 (29.9%), manufacturer revenue. Total intermediary gross profit (PBM, wholesaler, and pharmacy) ranged from −12.3% to 88.6% of Medicare Part D spending."

See https://www.healthcare-economist.com/2023/10/26/who-earns-more-money-from-generic-drug-sales-pbms-or-drug-manufacturers/ and https://jamanetwork.com/journals/jama-health-forum/fullarticle/2810783

KaufmanHall Survey Last Week Finds Serious Staffing Shortages in U.S. Hospital System

KaufmanHall

Volume and Revenue (continued)

FIGURE 10: Staffing Shortages Have Required Organization to Run at Less Than Full Capacity

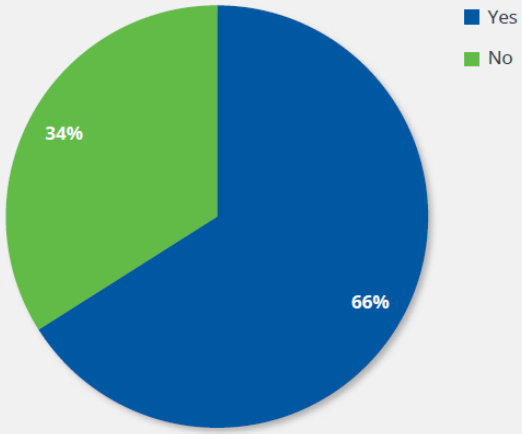
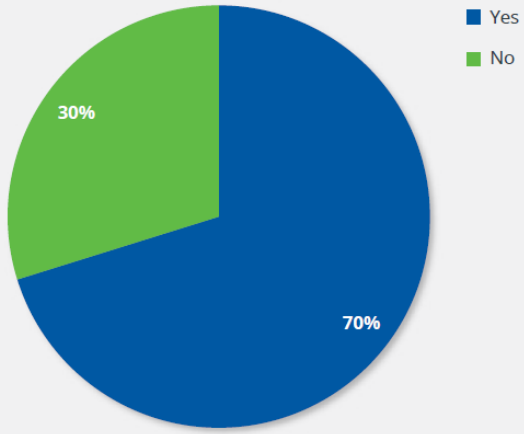


FIGURE 11: Lack of Staffing or Bed Capacity Requires Boarding Patients in ED or PACU



Staffing issues still pose challenges for hospital and health system volumes and patient throughput. The percentage of respondents reporting that staffing shortages required their organization to run at less than full capacity some time over the past year remained at 66%, the same percentage as in last year's report (Figure 10). And an even higher percentage of respondents reported that their organizations are boarding patients in the emergency department or post-anesthesia care unit (PACU) because of a lack of staffing or bed capacity (Figure 11).

> *"We could solve our financial problems by solving two issues: labor costs and throughput."*
>
> — Survey Respondent, Regional Health System

Workforce-related challenges persist, however, keeping costs high and contributing to issues with patient access to care. The percentage of respondents who report that they have run at less than full capacity at some time over the past year because of staffing shortages, for example, remains at 66%, unchanged from last year's *State of Healthcare Performance Improvement* report. A solid majority of respondents (63%) are struggling to meet demand within their physician enterprise, with patient concerns or complaints about access to physician clinics increasing at approximately one-third (32%) of respondent organizations.

Source:
https://www.kaufmanhall.com/sites/default/files/2023-10/KH-Report_2023-State-Healthcare-Performance-Improvement.pdf?utm_source=agcy&utm_campaign=performance-improvement-report&utm_medium=pr&utm_term=231024

Thermo Fisher Erases $12 Billion Value on China, Biotech Growth Slumps

By Angel Adegbesan and Madison Muller, *Bloomberg*, October 25, 2023 (excerpt)

Thermo Fisher Scientific Inc. has erased more than $12 billion from its market value so far this week as a growth slump in China and slowing demand from drug makers hit the laboratory tools maker.

Shares of the company dropped 5.5%, the biggest one-day decline since November 2020, after the firm — which earns roughly a tenth of its revenue from China — cut its profit outlook for the second time this year. Rival testing and equipment companies also fell.

Thermo and life science companies in the S&P 500 have been left out of the broader market gains this year, with the sector falling more than 20%. Tool-makers, which get most of their revenue selling lab equipment and supplies that drug developers use to research, discover and produce new treatments, have been hit hard by a slump in the health-care sector.

Source: https://www.bloomberg.com/news/articles/2023-10-25/thermo-fisher-erases-15-billion-value-on-china-biotech-growth-slumps

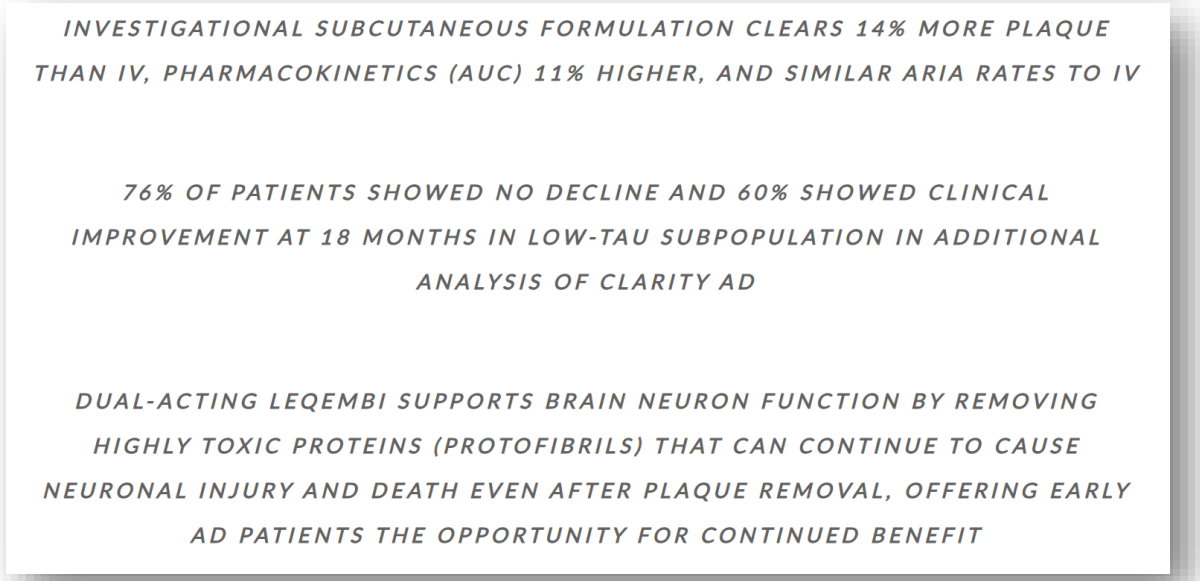
More Convenient Form of Breakthrough Alzheimer's Drug Leqembi Shows Promising Results in Study

Annika Kim Constantino, CNBC, Oct 24, 2023

Eisai on Wednesday said an injectable version of the Alzheimer's drug Leqembi showed promising initial results in a clinical trial, potentially paving the way for a new and more convenient option for administering the antibody treatment.

However, the injection did not cause lower rates of brain swelling and bleeding, which are Leqembi's most concerning side effects.

Leqembi, made by Eisai and its partner Biogen, is the first medicine proven to slow the progression of Alzheimer's in people at the early stages of the memory-robbing disease. U.S. regulators in July approved a version of Leqembi that is administered twice monthly through the veins, which is a method known as intravenous infusion.



Sources: https://www.cnbc.com/2023/10/25/alzheimers-drug-leqembi-shows-promise-as-injection.html, https://media-us.eisai.com/2023-10-25-EISAI-PRESENTS-NEW-LEQEMBI-R-LECANEMAB-IRMB-INVESTIGATIONAL-SUBCUTANEOUS-FORMULATION-INTERIM-STUDY-RESULTS-AND-CLINICAL-IMPROVEMENT-DATA-IN-EARLIER-STAGES-OF-EARLY-ALZHEIMERS-DISEASE-FROM-ADDITIONAL-ANALYSES-OF-CLARITY-AD-AT-THE-CLINICAL-TRIALS

The NEW ENGLAND JOURNAL of MEDICINE Oct 24, 2023

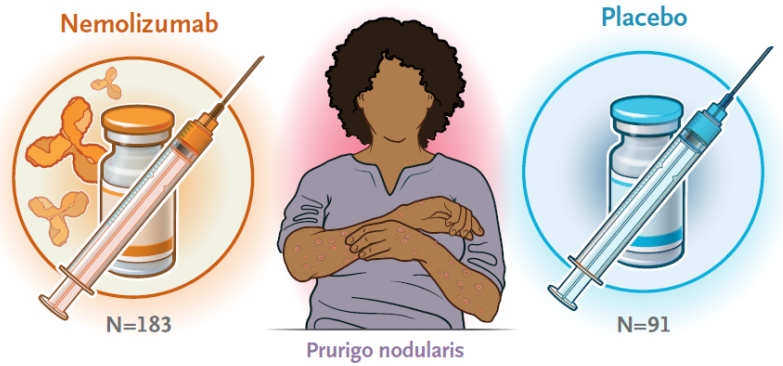
RESEARCH SUMMARY

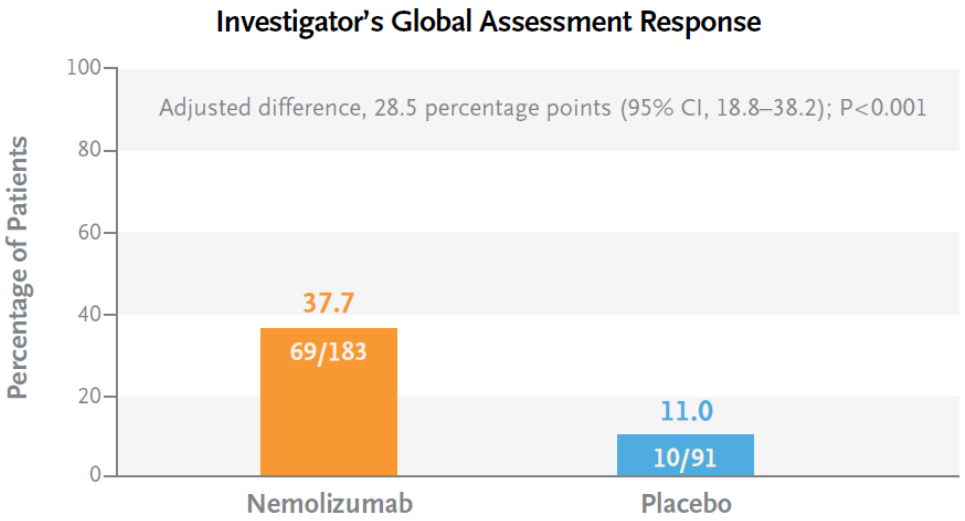
Phase 3 Trial of Nemolizumab in Patients with Prurigo Nodularis

Kwatra SG et al. DOI: 10.1056/NEJMoa2301333

CLINICAL PROBLEM

Prurigo nodularis is a chronic and debilitating neuroimmunologic skin disease characterized by severe pruritus and widespread nodular lesions. Interleukin-31 is increased in patients with prurigo nodularis, and dermal interleukin-31 levels are positively associated with itch intensity. In a phase 2 trial, nemolizumab — an interleukin-31 receptor alpha antagonist — showed promise for reducing pruritus and skin-lesion severity in patients with prurigo nodularis, but additional data are needed.





CONCLUSIONS

In patients with moderate-to-severe prurigo nodularis, treatment with nemolizumab resulted in a greater reduction in itch intensity and skin lesion severity over 16 weeks than placebo.

Source: https://www.nejm.org/doi/full/10.1056/NEJMoa2301333

The Total Mass, Number, and Distribution of Immune Cells in the Human Body

The total mass, number, and distribution of immune cells in the human body

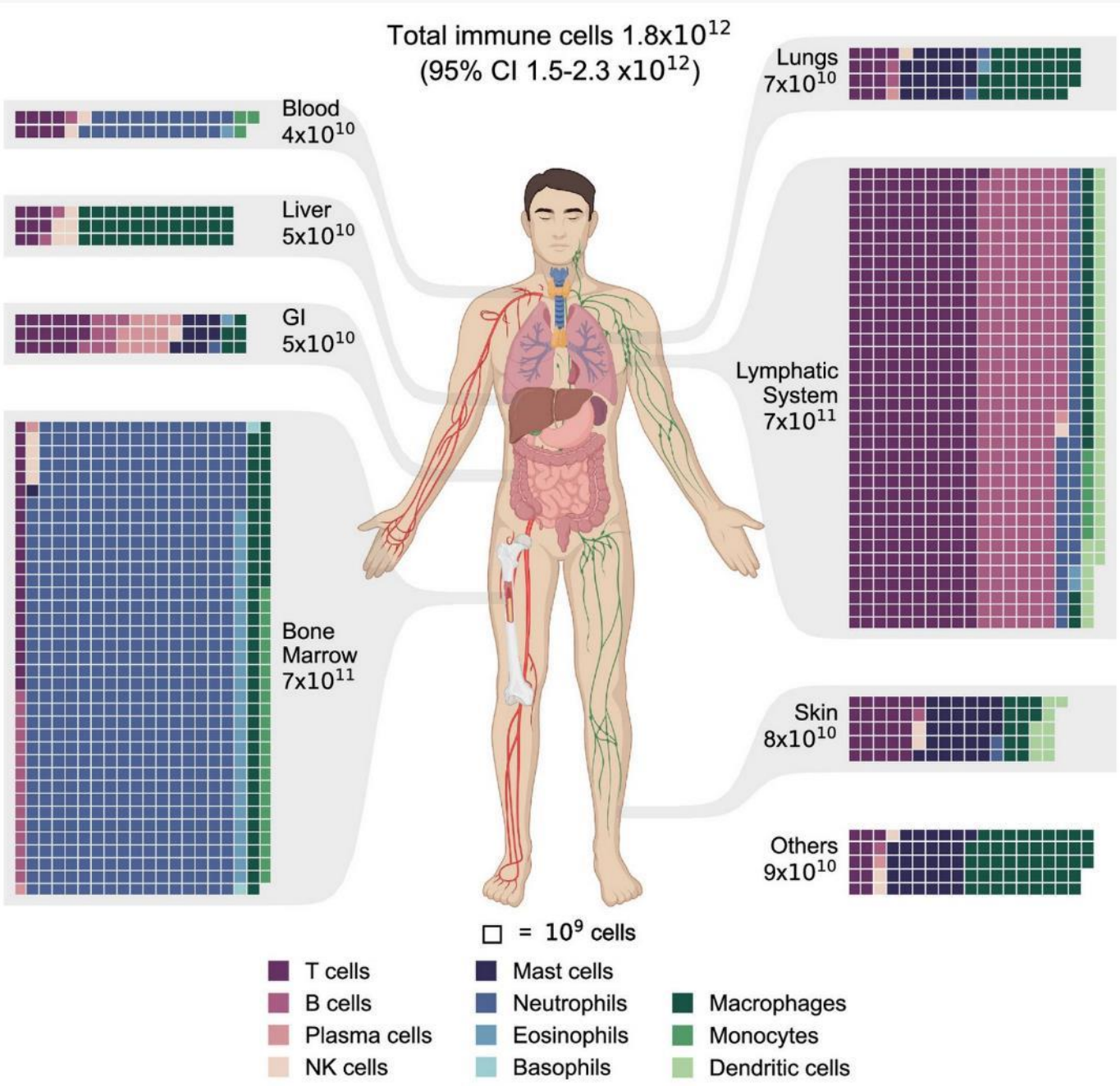
Ron Sender, Yarden Weiss, Yoav Navon, +6, and Ron Milo Authors Info & Affiliations

Edited by David Baker, University of Washington, Seattle, WA; received May 21, 2023; accepted September 11, 2023

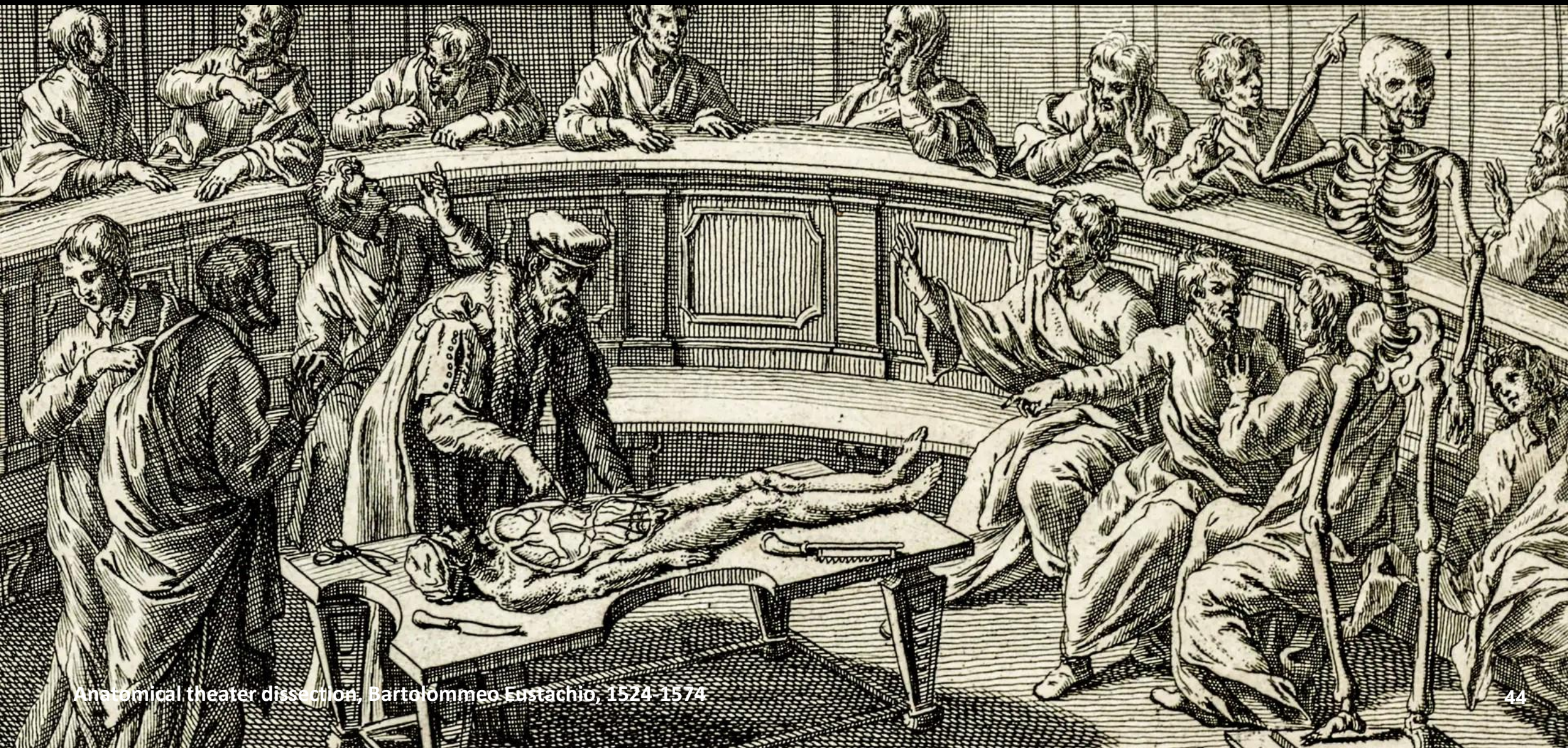
October 23, 2023 | 120 (44) e2308511120 | https://doi.org/10.1073/pnas.2308511120

PNAS

The immune system is a complex network of cells with critical functions in health and disease. However, a comprehensive census of the cells comprising the immune system is lacking. Here, we estimated the abundance of the primary immune cell types throughout all tissues in the human body. We conducted a literature survey and integrated data from multiplexed imaging and methylome-based deconvolution. We also considered cellular mass to determine the distribution of immune cells in terms of both number and total mass. Our results indicate that the immune system of a reference 73 kg man consists of 1.8 × 1012 cells (95% CI 1.5–2.3 × 1012), weighing 1.2 kg (95% CI 0.8–1.9). Lymphocytes constitute 40% of the total number of immune cells and 15% of the mass and are mainly located in the lymph nodes and spleen. Neutrophils account for similar proportions of both the number and total mass of immune cells, with most neutrophils residing in the bone marrow. Macrophages, present in most tissues, account for 10% of immune cells but contribute nearly 50% of the total cellular mass due to their large size. The quantification of immune cells within the human body presented here can serve to understand the immune function better and facilitate quantitative modeling of this vital system.

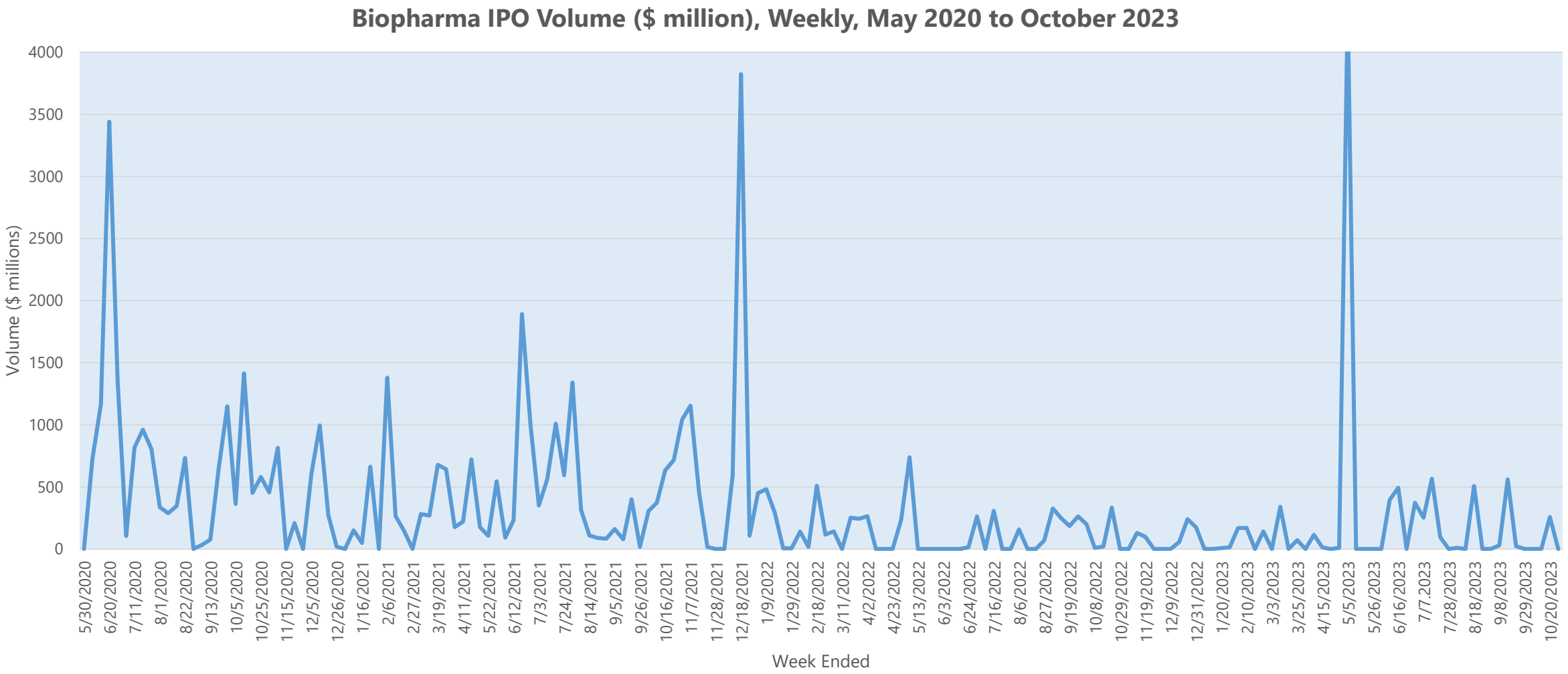


Capital Markets Environment



Anatomical theater dissection, Bartolommeo Eustachio, 1524-1574

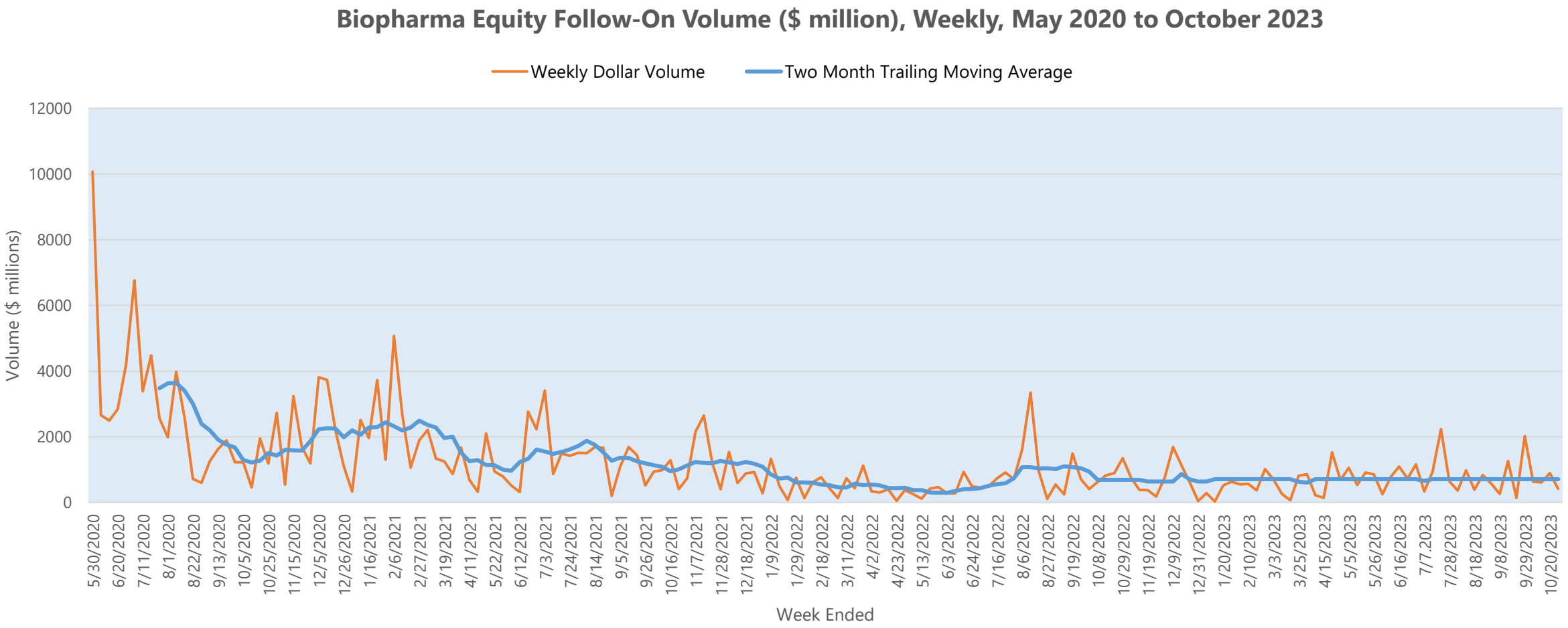
IPO Market Saw No Transactions Last Week



Source: Data from CapitalIQ and Stifel research.

Last Week Was Quiet for Follow-On Offerings

Last week saw $414 million in follow-on equity volume across 19 deals. The largest transaction was a $143 million financing by IDEAYA Biosciences.



Source: Data from CapitalIQ and Stifel research.

IDEAYA Biosciences Announces Pricing of $143 Million Offering of Common Stock

SOUTH SAN FRANCISCO, Calif., Oct. 27, 2023 /PRNewswire/ -- IDEAYA Biosciences, Inc. (Nasdaq:IDYA) today announced the closing of its underwritten public offering of 5,797,872 shares of its common stock at a public offering price of $23.50 per share, before underwriting discounts and commissions, and pre-funded warrants to purchase 319,150 shares of common stock at a public offering price of $23.4999 per pre-funded warrant, before underwriting discounts and commissions. This includes the exercise in full by the underwriters of their option to purchase up to an additional 797,872 shares of common stock in the offering. The gross proceeds from the offering, before deducting underwriting discounts and commissions and other offering expenses payable by IDEAYA, were approximately $143.8 million.

IDEAYA is pursuing precision medicine therapeutics, with a broad pipeline based on synthetic lethality for oncology, such as Darovasertib (IDE196), a PKC inhibitor.

Source: https://ir.ideayabio.com/2023-10-27-IDEAYA-Announces-Closing-of-Public-Offering-Including-Full-Exercise-of-Underwriters-Option-to-Purchase-Additional-Shares

Harpoon Raises $100 Million in PIPE Deal

SOUTH SAN FRANCISCO, Calif., Oct. 23, 2023 (GLOBE NEWSWIRE) -- Harpoon Therapeutics, Inc. (NASDAQ: HARP) (the "Company"), a clinical-stage immunotherapy company developing novel T cell engagers, today announced that it has entered into a securities purchase agreement for a private placement in public equity ("PIPE") financing that is expected to result in upfront gross proceeds of approximately $100 million, with up to an additional approximately $50 million of gross proceeds upon cash exercise of warrants, before deducting placement agent fees and offering expenses. The PIPE financing was led by a leading biotechnology investor associated with one of the largest alternative asset managers, with participation from new and existing investors including Soleus Capital, Commodore Capital, New Leaf Venture Partners, Cormorant Asset Management, RA Capital Management, Invus, Surveyor Capital (a Citadel company), K2 HealthVentures, Ally Bridge Group, Lion Point Capital, and a large mutual fund.

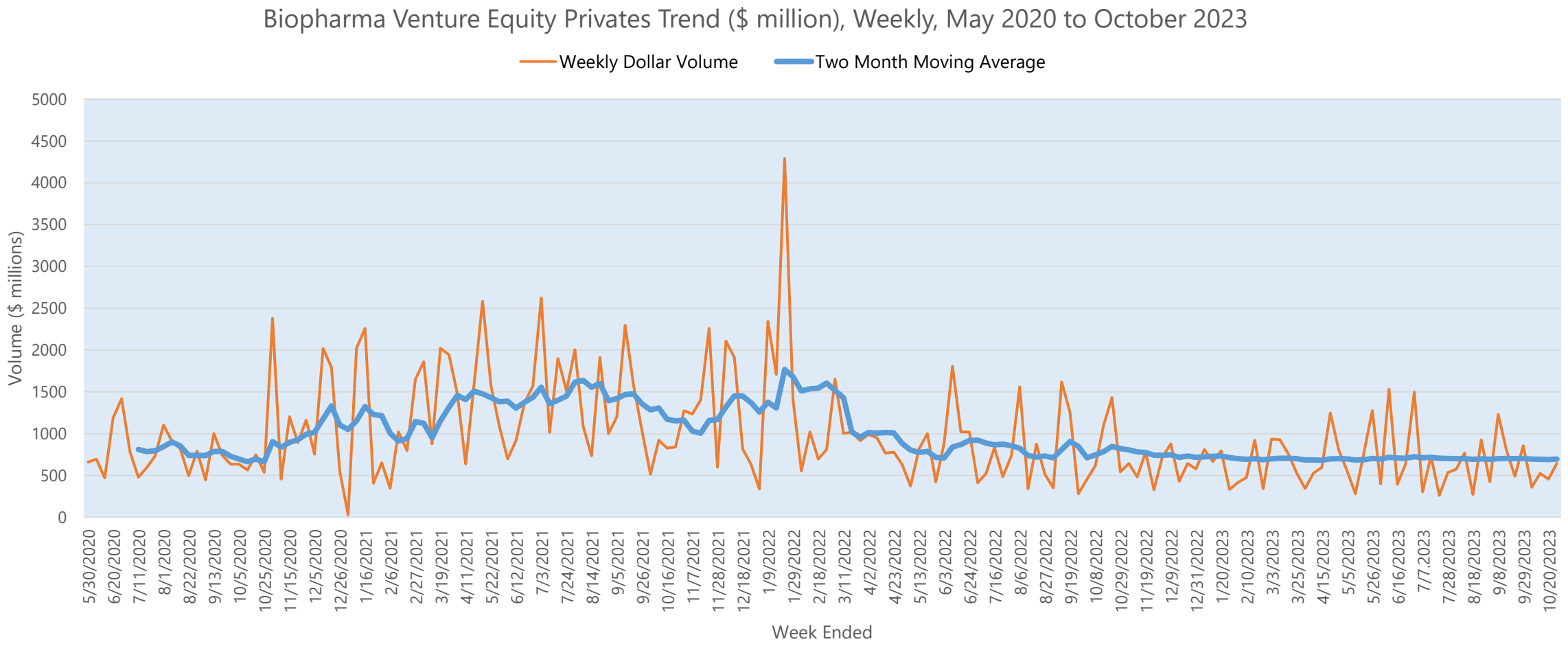
HARPOON Therapeutics

Harpoon Therapeutics is a clinical-stage immunotherapy company developing a novel class of T cell engagers, using its proprietary Tri- specific T cell Activating Construct (TriTAC®) platform.

Source: https://ir.harpoontx.com/news-releases/news-release-details/harpoon-therapeutics-announces-150-million-private-placement

Venture Equity Market Active Last Week

Last week saw 25 companies raise $643 million in the venture equity market. The largest deal in the market was a $245 million raise by Aiolos Bio.



Source: Data from CapitalIQ, Crunchbase.

Aiolos Bio Launches with $245 Million Series A

October 24, 2023: SAN FRANCISCO & LONDON--(BUSINESS WIRE)--Aiolos Bio, Inc. ("Aiolos" or "the Company") today announced its launch as a clinical-stage biopharmaceutical company focused on addressing the unmet treatment needs of patients with respiratory and inflammatory conditions. Aiolos launches with an oversubscribed $245 million Series A investment co-led by Atlas Venture, Bain Capital Life Sciences, Forbion, and Sofinnova Investments with additional investment from RA Capital Management (collectively the "Investor Group"). The Company will advance its lead drug candidate, AIO-001, into a Phase 2 clinical trial in moderate-to-severe asthma patients and is actively evaluating additional development opportunities.

AIO-001 is an anti-thymic stromal lymphopoietin (TSLP) monoclonal antibody that has the potential to be administered only twice per year due to its differentiated potency and long half-life. TSLP inhibition has a proven role in addressing symptoms of severe asthma and is currently under investigation for additional immune conditions like Chronic Obstructive Pulmonary Disorder (COPD) and Chronic Spontaneous Urticaria (CSU).

Aiolos Bio acquired exclusive rights for global development and commercialization of the drug outside of greater China from Jiangsu Hengrui Pharmaceuticals Co., Ltd ("Hengrui") in August 2023. In multiple clinical studies, AIO-001 has demonstrated encouraging safety, tolerability, pharmacokinetics, and biological activity in healthy volunteers and asthma patients, with low immunogenicity.

Khurem Farooq, Co-founder and Chief Executive Officer, is a seasoned biopharmaceutical executive with more than 25 years of drug development and operational leadership experience. Mr. Farooq has been appointed a member of the Board of Directors. Prior to joining Aiolos, he was Chief Executive Officer of Gyroscope Therapeutics and previously served as Senior Vice President and Head of the Immunology and Ophthalmology business unit at Genentech, a member of the Roche Group.

"Aiolos has a unique opportunity to positively impact patients' asthma outcomes. I'm excited for the opportunity to lead this innovative Company and the wealth of experience our talented team brings to bear, from operating large-scale clinical trials in asthma, to overseeing more than 30 FDA approvals, to leading successful product launches in immune conditions like asthma, rheumatoid arthritis, and IPF."

Khurem Farooq
Chief Executive Officer

Source: https://www.businesswire.com/news/home/20231024577944/en/Aiolos-Bio-Launches-with-245-Million-Series-A-Investment-to-Advance-Development-of-Novel-Phase-2-Ready-TSLP-Antibody

OrbiMed Raises $4.3 Billion Across Private Investment Funds

NEW YORK, Oct. 24, 2023 /PRNewswire/ -- OrbiMed, a global healthcare investment firm, is pleased to announce it has raised more than $4.3 billion in commitments for its latest private investment funds, including OrbiMed Private Investments IX, OrbiMed Asia Partners V and OrbiMed Royalty & Credit Opportunities IV.

Consistent with their predecessors, these new funds enable OrbiMed to invest globally, from seed stage for start-ups incubated by OrbiMed through growth capital opportunities. OrbiMed works closely with its portfolio companies to provide tailored financing solutions, which can include equity, credit and royalty-based financing. OrbiMed focuses on innovative and growth-oriented opportunities across healthcare sub-sectors, including biopharmaceuticals, medical devices, diagnostics and technology-enabled healthcare services.

OrbiMed is led by its 21 partners, with a growing team exceeding 130 professionals that contribute diverse, complementary skills across company incubation, strategy, operations and finance. The firm's professionals are based in a dozen global locations across key healthcare markets in North America, Europe and Asia.

"OrbiMed is deeply appreciative of the continued support we've received from many long-standing partners who've invested in these funds," said Carter Neild, a Managing Partner of OrbiMed. "We will endeavor to meet our partners' high expectations in the coming years."

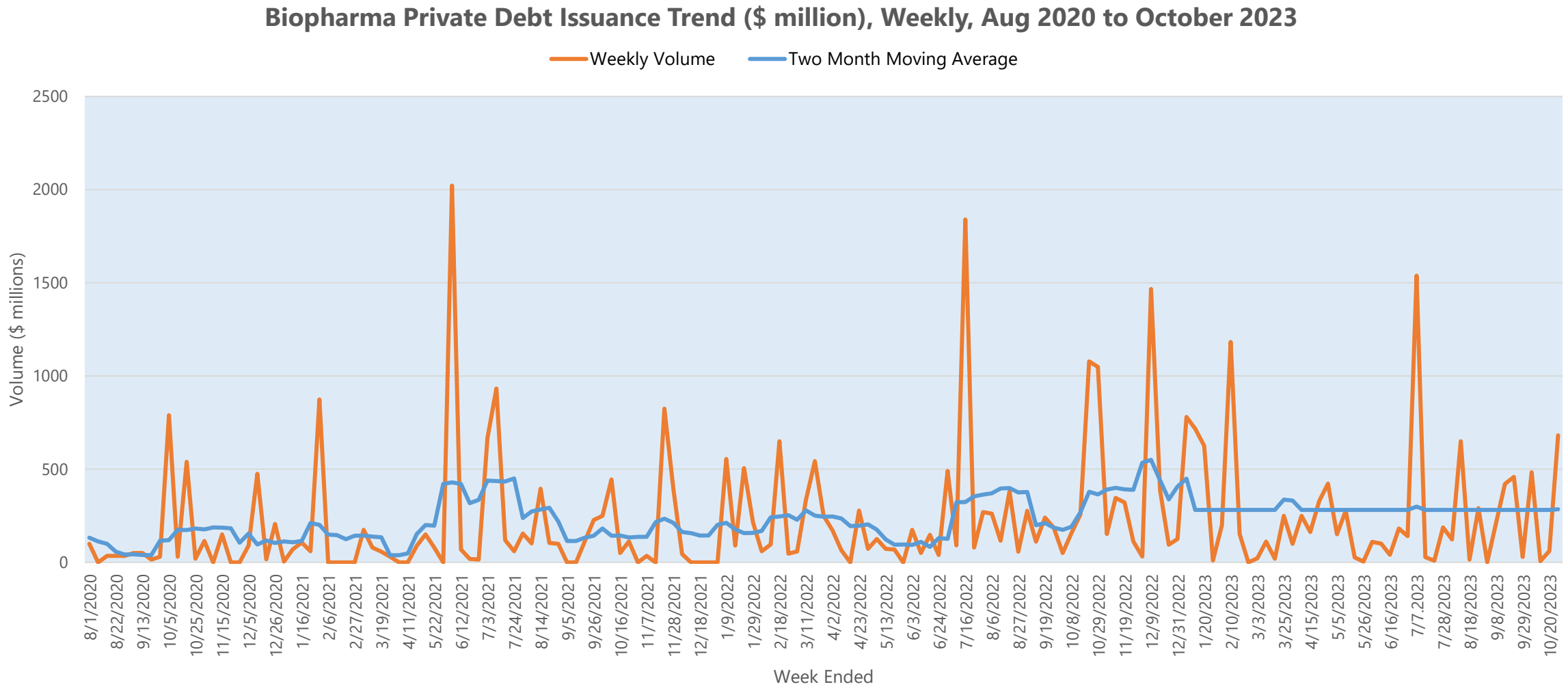
This would be an impressive fund raise in the best of times. To round up $4.3 billion at the bottom of the biopharma cycle is particularly impressive and speaks volumes about Orbimed's performance and outstanding team.

We won't have the final statistics until next Spring but we suspect that this raise will vault Orbimed into the #1 or #2 rank in the largest private asset managers in the life science sector.

Source: https://www.prnewswire.com/news-releases/orbimed-raises-4-3-billion-across-private-investment-funds-301964935.html

Weekly Global Biopharma Private Debt Placements

We saw three deals in the private debt market last week with $681 raised.



Source: Data from CapitalIQ, Crunchbase.

HealthCare Royalty Announces Closing of Credit Facility and New Debt Focused Fund

October 26, 2023 - STAMFORD, Conn.–HealthCare Royalty, a leading middle market royalty acquisition firm that has raised $7.6 billion in capital since inception, today announced several important firm developments:

Closing of Credit Facility for New Operating Business

HCRx is pleased to announce that the new permanent capital company, HCRx Holdings, L.P. (“HCRx Holdings”), it formed in 2022 held a final closing on a $680 million credit facility. The credit facility includes a $380 million term loan and a $300 million revolving credit facility; the revolving credit facility remains undrawn.

With the closing of this financing, the Company has over $1 billion of liquidity. HCRx Holdings will use its capital to expand its leading presence in the biopharmaceutical royalty acquisition space during a time of unprecedented market opportunity.

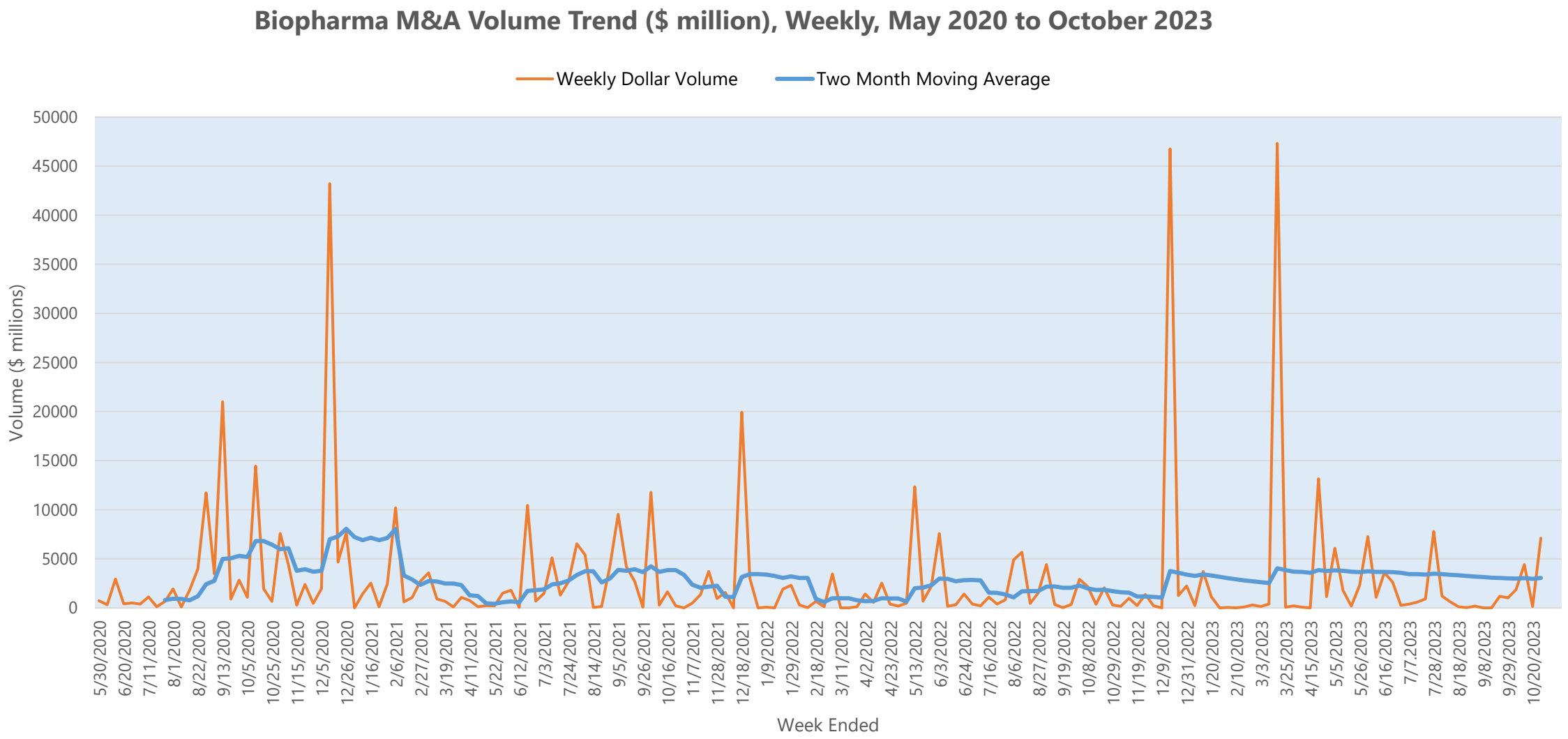
“We appreciate the confidence shown by our bank group and investors in HCRx’s differentiated business model, strategic vision, and operational excellence,” said Clarke B. Futch, Founder, Chief Executive Officer and Chairman at HCRx. “It is an attractive time to be in the royalty financing market and HCRx is on track for a very productive year having already purchased royalties in a diverse set of products including Hemgenix, Relistor, Lumify, Rezurock, and Bexacat. We are also excited to have a source of capital focused on debt opportunities as that market looks much more attractive to us today than it has in years.”

Source: https://www.hcrx.com/healthcare-royalty-announces-closing-of-creditfacility-new-debt-focused-fund-andappointment-of-josh-house-as-west-coast-lead/

Deals Environment Update

M&A Market Active Last Week

Last week saw Roche acquire the Televant subsidiary of Roivant Sciences for $7.1 billion.



Roche to Acquire Televant and TLA1 Antibody for $7.1 Billion

Basel, 23 October 2023 - Roche (SIX: RO, ROG; OTCQX: RHHBY) announced today the entry into a definitive agreement to acquire Telavant Holdings, Inc. (Telavant), a Roivant company, owned by Roivant Sciences Ltd. and Pfizer Inc. The agreement includes the development, manufacturing and commercialisation rights in the US and Japan for Telavant's RVT-3101, a novel TL1A directed antibody. RVT-3101 is a promising new therapy in development for people suffering from inflammatory bowel disease, including ulcerative colitis and Crohn's disease. Inflammatory bowel disease is a group of chronic gastrointestinal disorders with almost 8 million people diagnosed worldwide and 80% of all individuals not experiencing lasting remission. Given the antibody's novel mode of action targeting both inflammation and fibrosis, it has potential to be applied in multiple other diseases.

RVT-3101 has been investigated in the TUSCANY-2 phase 2b study in patients with moderate to severe ulcerative colitis. The global, randomised, double-blinded, placebo controlled trial delivered the first long-term, dose finding data in a large number of patients (n=245). The maintenance treatment phase following induction resulted in improved clinical remission (36% at week 56) and endoscopic improvement (50% at week 56) at the proposed Phase 3 dose administered subcutaneously every month. Beyond the efficacy results, the maintenance dosing period of RVT-3101 also showed a favourable safety profile across all patients.

Under the terms of the agreement, Roche will pay a purchase price of US$ 7.1 billion upfront and a near-term milestone payment of US$ 150 million. Upon closing of the transaction, Roche will have full rights to further develop and manufacture RVT-3101 and commercialise it in the US and in Japan pending clinical and regulatory success. Roche is committed to starting a global Phase 3 trial for RVT-3101 as soon as possible to bring this promising therapy to the patients suffering from inflammatory bowel disease. Outside of the US and Japan, Pfizer holds commercialisation rights.

Source: https://www.roche.com/media/releases/med-cor-2023-10-23

This $5 Billion Biotech Home Run Took Less Than a Year

David Wainer, *Wall Street Journal*, October 24, 2023 (excerpt)

You can't completely blame Pfizer's executives, yet Roche's $7 billion acquisition of a bowel-disease treatment that it owned until last year isn't a great look.

In a deal that now feels like a biotech version of "Moneyball," Roivant announced it was selling an asset that only 11 months ago it got for free from Pfizer. (The Wall Street Journal had reported the talks back in July). Big pharma companies focused on the drug industry equivalent of free agent signings will often overlook one of their own hot prospects. In fact, Republican presidential candidate Vivek Ramaswamy founded Roivant on the idea that pharma's trash can be another company's treasure. But this one became an almost instant All-Star.

Pfizer out-licensed the monoclonal antibody to Roivant back in December with the idea that the biotech would shoulder the heavy costs of developing the drug, which targets a protein linked to inflammation called TL1A, while Pfizer would hold on to a 25% equity stake. The speed at which the drug went from Pfizer to Roivant and then to Roche stunned even Wall Street veterans long accustomed to seeing pharma pass on promising compounds. Pfizer certainly didn't anticipate one of its big pharma rivals swooping so quickly.

Source: https://www.wsj.com/health/pharma/this-5-billion-biotech-home-run-took-less-than-a-year-94e1c0df

BMS Repurchases China Rights to Mavacamten From LianBio

SHANGHAI and PRINCETON, N.J., Oct. 24, 2023 (GLOBE NEWSWIRE) -- LianBio (Nasdaq: LIAN), a biotechnology company dedicated to bringing innovative medicines to patients in China and other major Asian markets, today announced that the company has entered into an agreement with Bristol Myers Squibb (BMS), whereby BMS has obtained LianBio's exclusive rights to develop and commercialize mavacamten in Mainland China, Hong Kong, Macau, Taiwan, Singapore and Thailand, in conjunction with termination of the exclusive license agreement LianBio previously entered into with MyoKardia, Inc., now a wholly owned subsidiary of BMS, in August 2020 to acquire such rights.

Under the terms of the agreement, LianBio will receive a one-time payment of $350 million. In addition, LianBio will be released from payment obligations of up to $127.5 million in remaining milestone payments under the MyoKardia license agreement.

In April 2023, the China National Medical Products Administration (NMPA) accepted with Priority Review a New Drug Application (NDA) for mavacamten for the treatment of adults with symptomatic obstructive hypertrophic cardiomyopathy (oHCM). LianBio received approval in Macau and Singapore for mavacamten for the treatment of adults with symptomatic oHCM in 2023.

Source: https://investors.lianbio.com/news-releases/news-release-details/lianbio-enters-agreement-bristol-myers-squibb-mavacamten-china

Arbitrage Opportunity in a Distressed Market?

LianBio Share Price Reaction to Recent Asset Sale

LianBio shares went from $1.39 each to $3.90 at Friday close but are they still too cheap?

LianBio had $267mm in cash at its June quarter end. Let's suppose it's now $210mm. They just picked up another $350mm. Lets suppose that transaction expenses and taxes will be $75mm (the company had minimal NOL carryforwards). This would leave the company with $485 million. As of Friday, it's market cap was $419 million. Plus, it has a full pipeline with cash value as shown at right.

The company has indicated that it will undertake a strategic review, indicating the willingness on the part of its board to liquidate assets and return cash to shareholders. Some of the assets are very good (e.g., infigratinib – already FDA approved).

This appears to be a sign of the times. It's not quite a "cash and carry arbitrage" situation but it looks highly likely that the shares of the company are trading well below liquidation value.

Pipeline of Innovative Medicines – 5 Clinically Validated Therapeutic Candidates

Clinically Validated | Global Development Status[1]

Therapeutic Area	Program	Indication	Phase 1	Phase 2	Phase 3 / Pivotal	Approved	Catalyst / Next step in China	Partner
Cardiovascular	Mavacamten[2]	Obstructive Hypertrophic Cardiomyopathy (oHCM)					NDA on file in China, approval anticipated mid-2024	Bristol Myers Squibb
		Non-obstructive Hypertrophic Cardiomyopathy (nHCM)					Join ongoing global Phase 3 trial	
		Heart Failure with Preserved Ejection Fraction (HFpEF)					Conduct registration-enabling trial	
Oncology	NBTXR3[3]	Head and Neck Squamous Cell Carcinoma (HNSCC)					Global NANORAY-312 Phase 3 trial ongoing in China	NANOBIOTIX
		Solid Tumor IO Combinations					Join future global Phase 3 trial	janssen
	BBP-398	Advanced Solid Tumors					China Phase 1 monotherapy trial ongoing	navire
		Non-Small Cell Lung Cancer (NSCLC)					China Phase 1 osimertinib combo trial ongoing	Bristol Myers Squibb / bridgebio
	Infigratinib[4]	Gastric Cancer w/ FGFR2 Amplification[5]					Initiate registration-enabling trial 1H24	QED therapeutics
Ophthalmology	TP-03	Demodex Blepharitis					Topline P3 data 4Q23; U.S. FDA approval granted July 2023	tarsus
		Meibomian Gland Disease					Join future global Phase 3 trial	
Inflammatory Disease	NX-13	Ulcerative Colitis					Join potential future global Phase 3 trial	LANDOS
	Omilancor	Ulcerative Colitis					Potential to join future global Phase 3 trial	NIMMUNE BIOPHARMA
	LYR-210	Chronic Rhinosinusitis (CRS)					Conduct China standalone Phase 3 trial	LYRA THERAPEUTICS

1. The commercialization of each of our product candidates will require regulatory approval in the respective jurisdiction in which we intend to market such product candidate; however, obtaining and maintaining regulatory approval in one jurisdiction does not guarantee we will be successful in obtaining or maintaining regulatory approval of the product candidate in other jurisdictions that are material to the success of LianBio. 2. Mavacamten has received FDA approval in the US, which is not a part of our licensed territory, for the treatment of NYHA class II-III obstructive HCM. 3. NBTXR3 has received European market approval (CE mark) in the EU, which is not a part of our licensed territory, for the treatment of locally advanced soft tissue sarcoma. At present, we are not pursuing NBTXR3 in relation to this STS indication. 4. Infigratinib has received FDA approval in the US, which is not a part of our licensed territory, for the treatment of previously treated, unresectable locally advanced or metastatic cholangiocarcinoma with FGFR2 fusion or other rearrangement. 5. Phase 2a gastric cancer and other FGFR-driven tumor standalone clinical trial in China. Separate investigator sponsored Phase 2 clinical trial of infigratinib in FGFR-driven tumors is ongoing in the United States.

6

Arbitrage Opportunity in a Distressed Market?

Roivant Share Price Reaction to Recent Asset Sale

The Roivant story is also puzzling. Roivant shares were at $9.70 at Monday open and the company closed at $8.38 / share on Friday. This implies a $6.5bn market cap.

Let's walk through the logic here. The sale of Televant generates a $7.1 bn windfall. Roivant gets 75% of it. The total payments to Roivant will equal $5.3 billion. Roivant has not said what its tax bill will be but the company is a Bermuda corporation, so we expect that to be minimal. The company also has billions of NOLs to use for any U.S. taxes that it would be assessed.

Roivant had $942mm in net cash as of its last 10-Q filing. It's stake in Immunovant is worth $2.7 billion. Its stake in Arbutus is worth $67 million. The company burns $250mm a quarter.

It's commercial Dermavant business and brepocitinib franchises are easily worth $500mm, if not substantially more. It has numerous other subs with obvious value.

Assuming the subs are worthless, the total value of the company's assets, by our math, is $9.25 billion (at least). There appears to be a substantial valuation disconnect.

ROIVANT SCIENCES

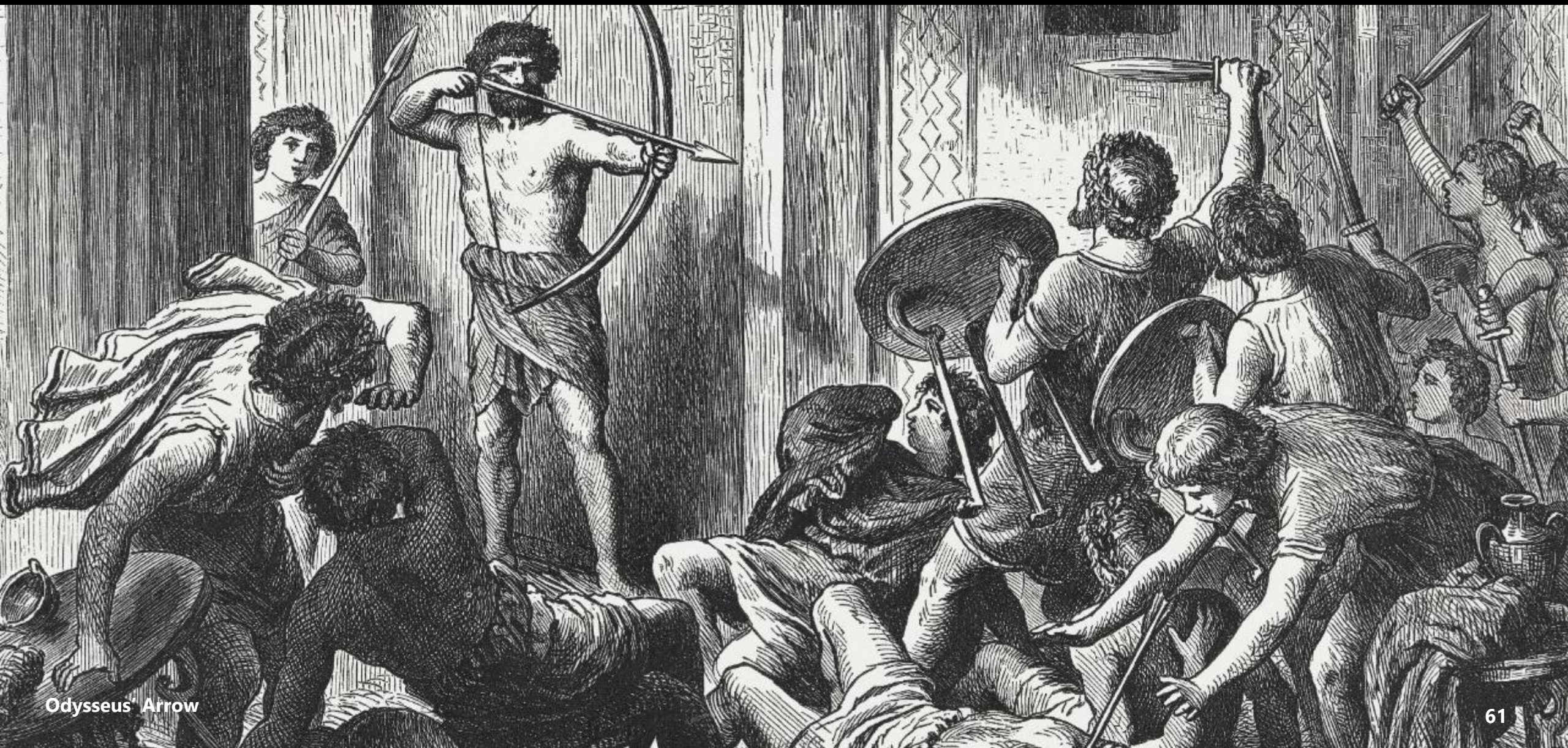
Robust Late-Stage Pipeline Post-Transaction

Seven ongoing registrational trials in multi-billion dollar markets

	Modality	Preclinical	Phase 1	Phase 2	Phase 3	Approved
VTAMA (tapinarof) cream 1% Psoriasis | *Dermavant*	*Topical*					▶
VTAMA (tapinarof) cream 1% Atopic Dermatitis | *Dermavant*	*Topical*				Completed	
BREPOCITINIB Dermatomyositis | *Priovant*	*Small Molecule*				▶	
BREPOCITINIB Systemic Lupus Erythematosus | *Priovant*	*Small Molecule*			▶		
BREPOCITINIB Other Indications | *Priovant*	*Small Molecule*			▶		
BATOCLIMAB Myasthenia Gravis | *Immunovant*	*Biologic*				▶	
BATOCLIMAB Thyroid Eye Disease | *Immunovant*	*Biologic*				▶	
BATOCLIMAB Chronic Inflammatory Demyelinating Polyneuropathy | *Immunovant*	*Biologic*			▶		
BATOCLIMAB Graves' Disease | *Immunovant*	*Biologic*			▶		
IMVT-1402 Numerous Indications | *Immunovant*	*Biologic*		▶			
NAMILUMAB Sarcoidosis | *Kinevant*	*Biologic*			▶		
RVT-2001 Transfusion-Dependent Anemia in Patients with Lower-Risk MDS | *Hemavant*	*Small Molecule*		▶			

Source: https://investor.roivant.com/

Antibody Drug Conjugate (ADC) Market Update



Odysseus' Arrow

ADCs and Immune Cell Engagers Shined at ESMO

Just as we thought ADCs couldn't get any more prominent, they did at ESMO. We saw multiple practice changing developments in breast cancer, blader cancer, prostate cancer and ovarian cancer.

AZ/DS Trop2 ADC

Antibody–drug conjugates improve outcomes for patients with inoperable or metastatic breast cancer

Seagen / Astellas Nectin-4 ADC (PADcEV)

Landmark Trial Produces New First-Line Standard for Advanced Bladder Cancer

— Enfortumab vedotin-pembrolizumab doubles OS, PFS versus chemotherapy

by Charles Bankhead, Senior Editor, MedPage Today October 22, 2023

B7H4 and TROP2 ADCs

ESMO 23: Kelun/Merck, Hansoh ADCs Impress With Early Data In Breast Cancer

20 Oct 2023 | ANALYSIS

Ambrx PSMA ADC

ESMO: Ambrx's 'reset' arrives at the last line of prostate cancer, offering the kind of safety rarely seen

By **Annalee Armstrong** · Oct 22, 2023 9:39am

Daiichi-Sankyo / Merck CDH6 ADC

Raludotatug Deruxtecan Continues to Demonstrate Promising Clinical Activity in Patients with Advanced Ovarian Cancer in Early Trial

- Encouraging overall response rate of 46% and disease control rate of 98% with a median duration of response of 11.2 months seen with raludotatug deruxtecan in heavily pretreated patients
- Plans underway to initiate late-stage trial of raludotatug deruxtecan in advanced ovarian cancer

‘Guided Missile Drugs’ Could Be Big Pharma’s Secret Weapon

David Wainer, *Wall Street Journal*, October 26, 2023 (excerpt)

A true home run in the drug industry is when a company develops a mega-blockbuster that transforms its finances for years.

But with Medicare trying to bring costs down by targeting the industry’s most expensive drugs, a portfolio of medium-size moneymakers that can keep your name off the U.S. government’s naughty list can be a wise strategy.

That is at least one reason why big pharma is investing heavily in biotech companies developing antibody-drug conjugates. Known as ADCs, these treatments work like a guided missile by pairing antibodies with toxic agents to fight cancer. In short, they enable a more targeted form of chemotherapy that goes straight into the cancer cells while minimizing harm to healthy cells.

While the three Daiichi ADCs in the Merck deal are promising, they aren’t going to be massive blockbusters.

A silver lining of having a portfolio of medium-size moneymakers is that it keeps your drugs from earning a spot on an ever-growing list of top-selling drugs selected later in their life by Medicare for negotiation. Under the Inflation Reduction Act passed last year, Medicare will now be able to negotiate the prices of drugs it spends the most on and that don’t face competition from less-expensive copies.

There are other provisions in the IRA that encourage ADC investments as well. For one, because they are complex biologics, they will be protected for longer than regular medicines. Price negotiation for small molecule medicines is allowed nine years after Food and Drug Administration approval compared with 13 years for large molecule biologics. In addition, because they are so complex to make, they also might avoid competition from copycat biosimilars well after their patents have expired, explains Andy Hsieh, an analyst at William Blair.

Source: https://www.wsj.com/health/pharma/guided-missile-drugs-could-be-big-pharmas-secret-weapon-437aa87f

ADC's Are Antibodies with a Toxic Payload That Internalized Into a Cancer Cell

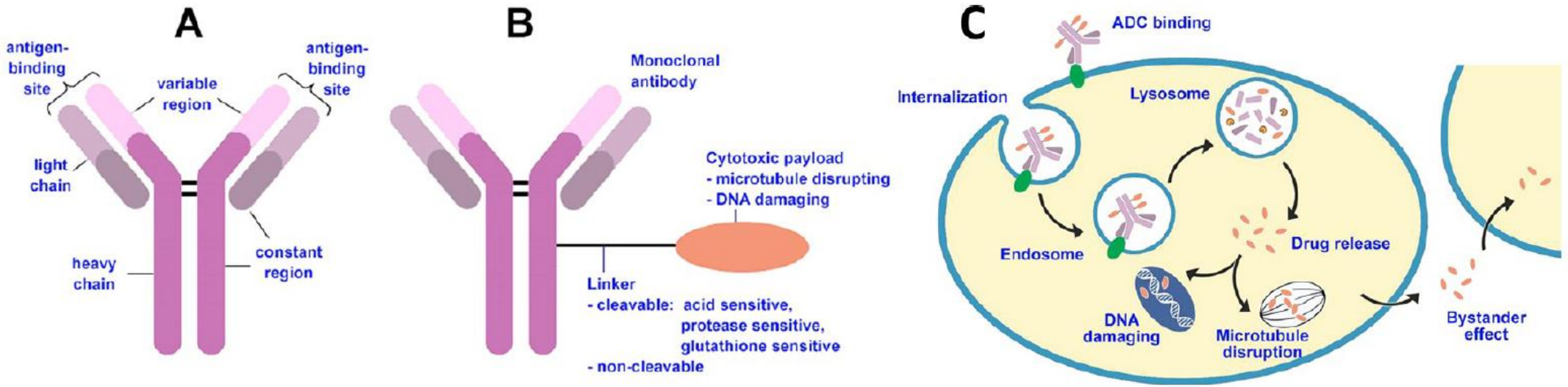


Figure 1. Structure and mechanism of action of ADCs. (A) Scheme of antibody structure including heavy chains, light chains, constant region, variable region, and antigen binding site. (B) Antitumor ADCs combine three key elements: a monoclonal antibody moiety that binds to an antigen preferentially expressed on the tumor cell surface, thereby ensuring specific binding to tumor cells; a covalent linker that warrants that the payload drug is not released in blood ahead of time, but is released within the tumor cell; and a cytotoxic payload that causes tumor cell apoptosis through targeting of key components such as DNA, microtubules. (C) ADC mechanism of action includes key sequential steps: binding to cell surface antigen; internalization of the ADC–antigen complex through endocytosis; lysosomal degradation; release of the cytotoxic payload within the cytoplasm; and interaction with target cell components. A fraction of the payload may be released in the extracellular environment and taken up by neighboring cells, known as the bystander effect.

Source: https://pubs.acs.org/doi/10.1021/acs.bioconjchem.3c00374

ADC Boom Has Been Result of Decades of Work

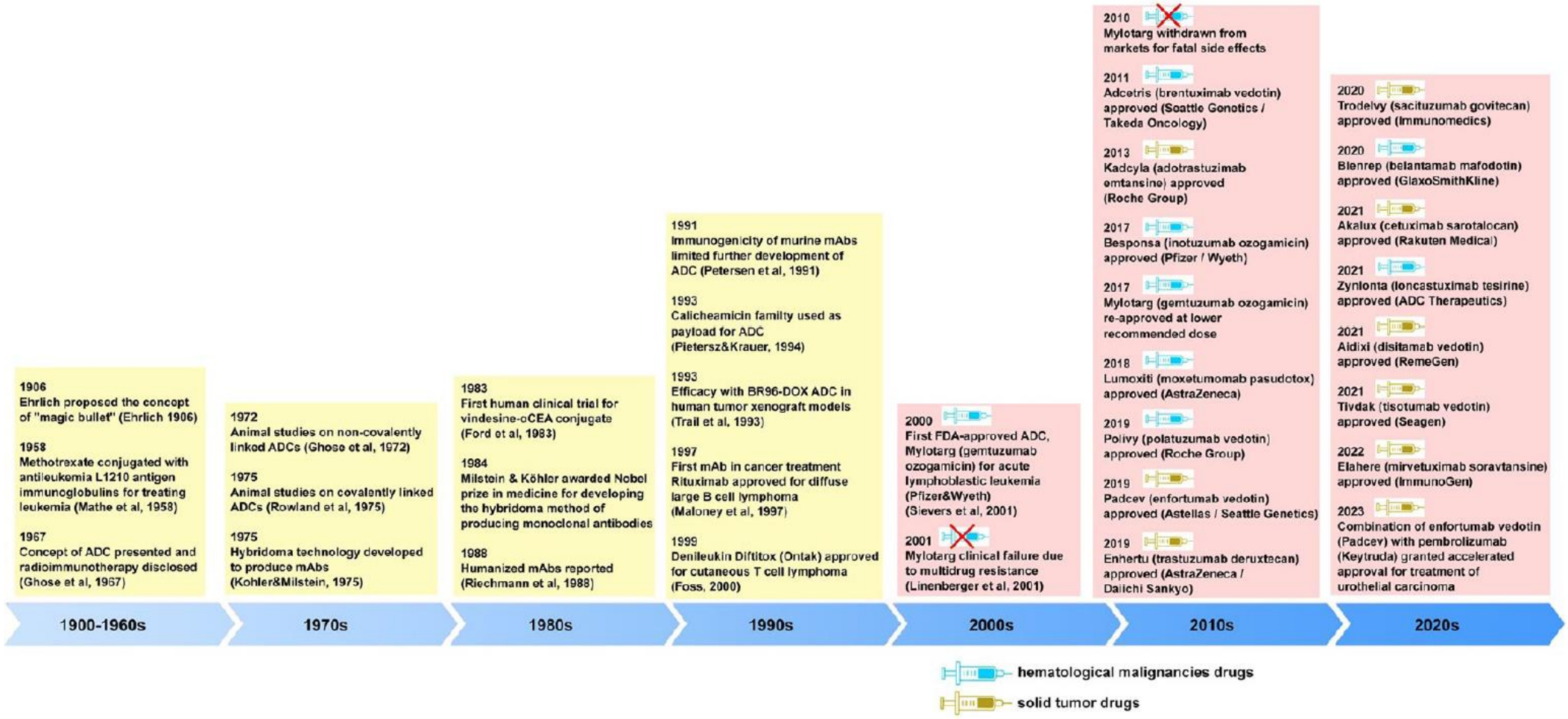
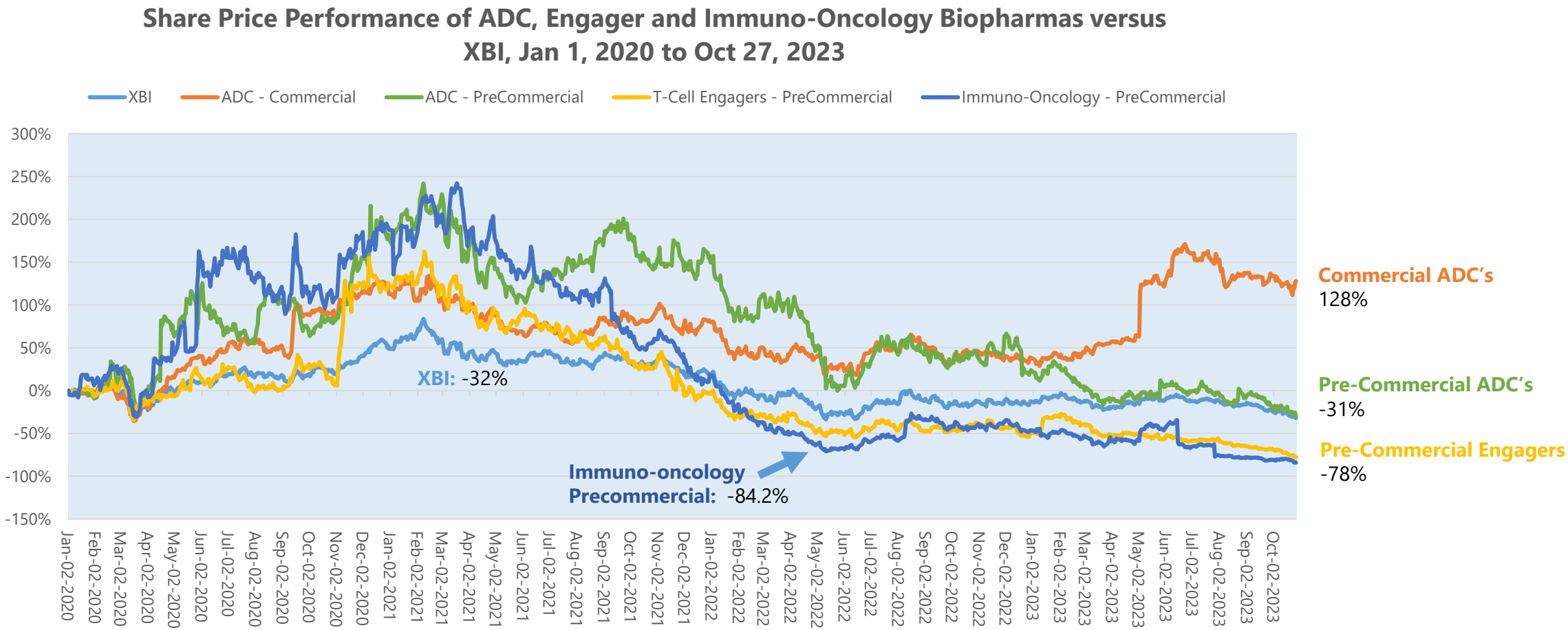


Figure 2. Timeline of key events and discoveries in the antibody–drug conjugate research and development.[21,24–27,29–34,36–80]

Source: https://pubs.acs.org/doi/10.1021/acs.bioconjchem.3c00374

Commercial ADC Players Have Performed Well While Precommercial ADC and Engager Biotechs Have Lost Substantial Value in Downturn



Notes: data sourced from CapitalIQ. All indices are equal-weighted. The commercial ADC index includes ADC Therapeutics, Daiichi-Sankyo, Immunogen, Immunomedics and Seagen. The pre-commercial ADC index includes BioAtla, CytomX, Mersana and Pyxis Oncology. The T-cell engager index includes Aptevo, Harpoon, IGM, Janux and Xencor. The immuno-oncology antibodies index includes Agenus, ALX Oncology Arcus and Iteos.

Improving the Therapeutic Index With ADC Technology Advances: HER2 Example

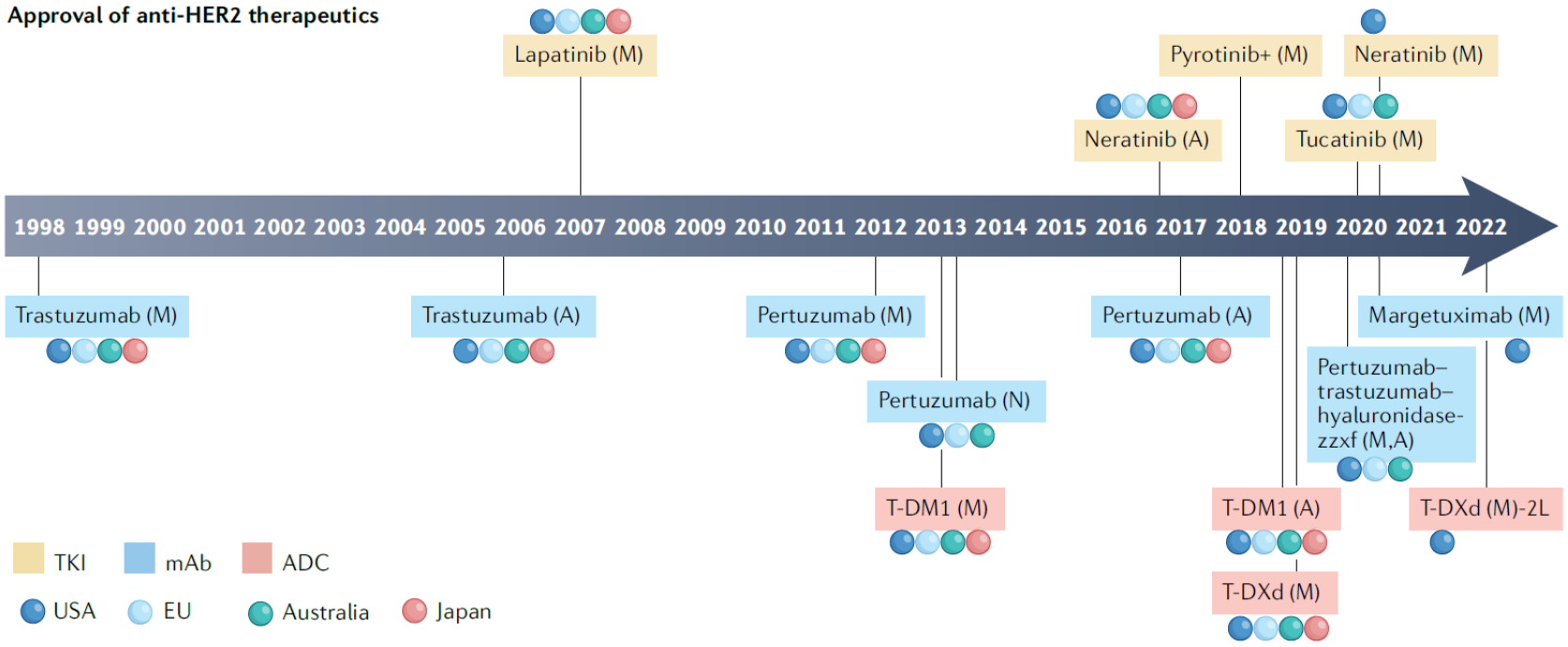


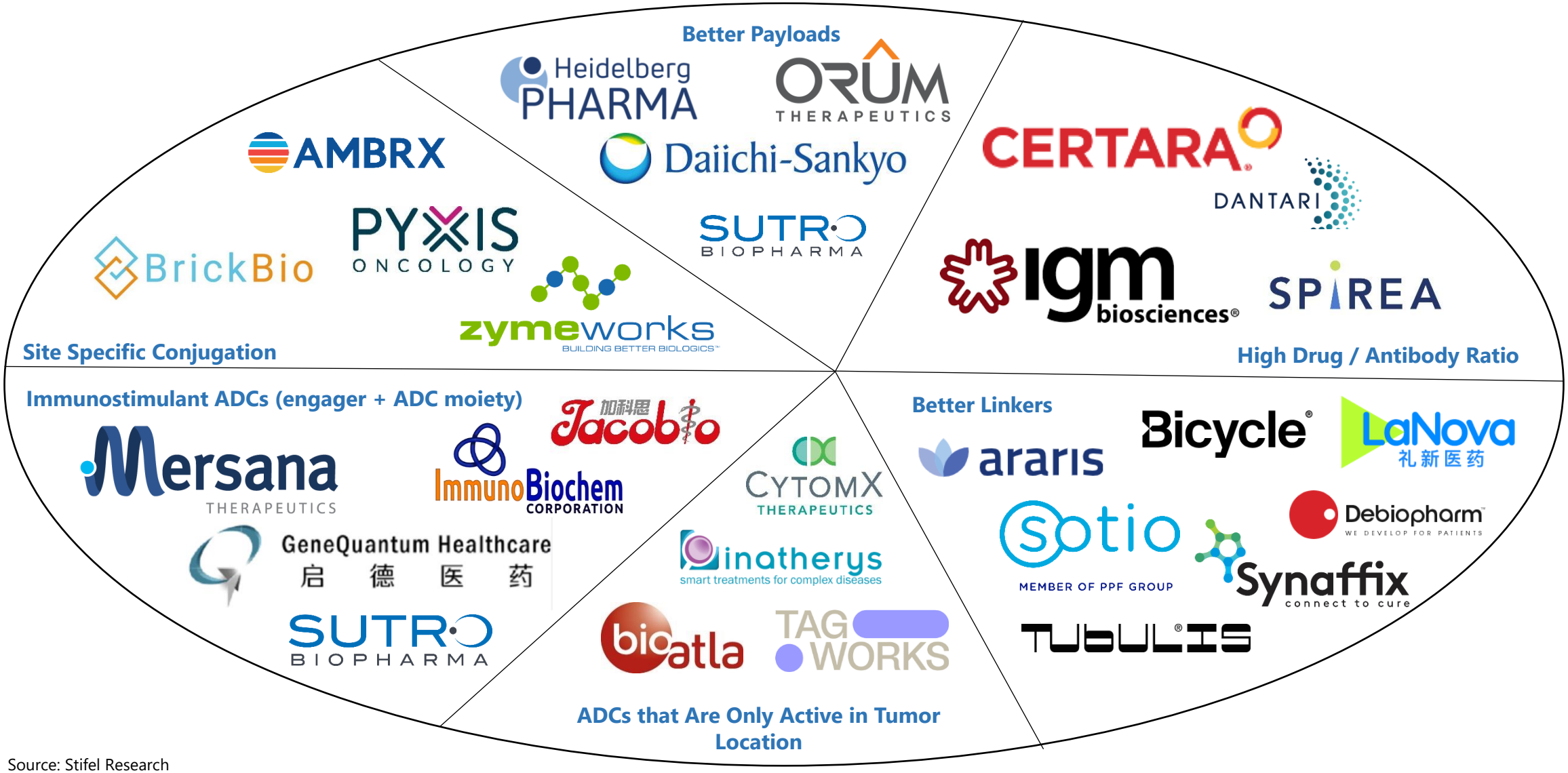
Fig. 1 | Evolution of HER2 as a biomarker and target for treatment for breast cancer. Timeline of preclinical discovery milestones for HER2 biology and regulatory approval for anti-HER2 therapies. A, adjuvant setting; M, metastatic setting; N, neoadjuvant setting; +, approved in China only; *, M. Bishop and H. Varmus awarded Nobel Prize in 1989 for this discovery; **, S. Cohen and R. Levi-Montalcini awarded Nobel Prize in 1986 for discovery of growth factors and their receptors.

Nature Reviews Drug Discovery | Volume 22 | February 2023 | 101–126

Trastuzumab was approved for HER2+ breast cancers in 1998. The drug's ORR was 18% and had a 15% incidence of Grade 3 AE's. By 2013, Kadcycla showed a 44% ORR and worse AE's. Enhertu (T-Dx) was approved in 2019 with a 61% ORR. Most recently, Ambrx's ARX-788 has achieved a 74% ORR rate with a much lower rate of Grade 3 AE – using site specific conjugation and a cleavable linker to improve its Therapeutic Index.

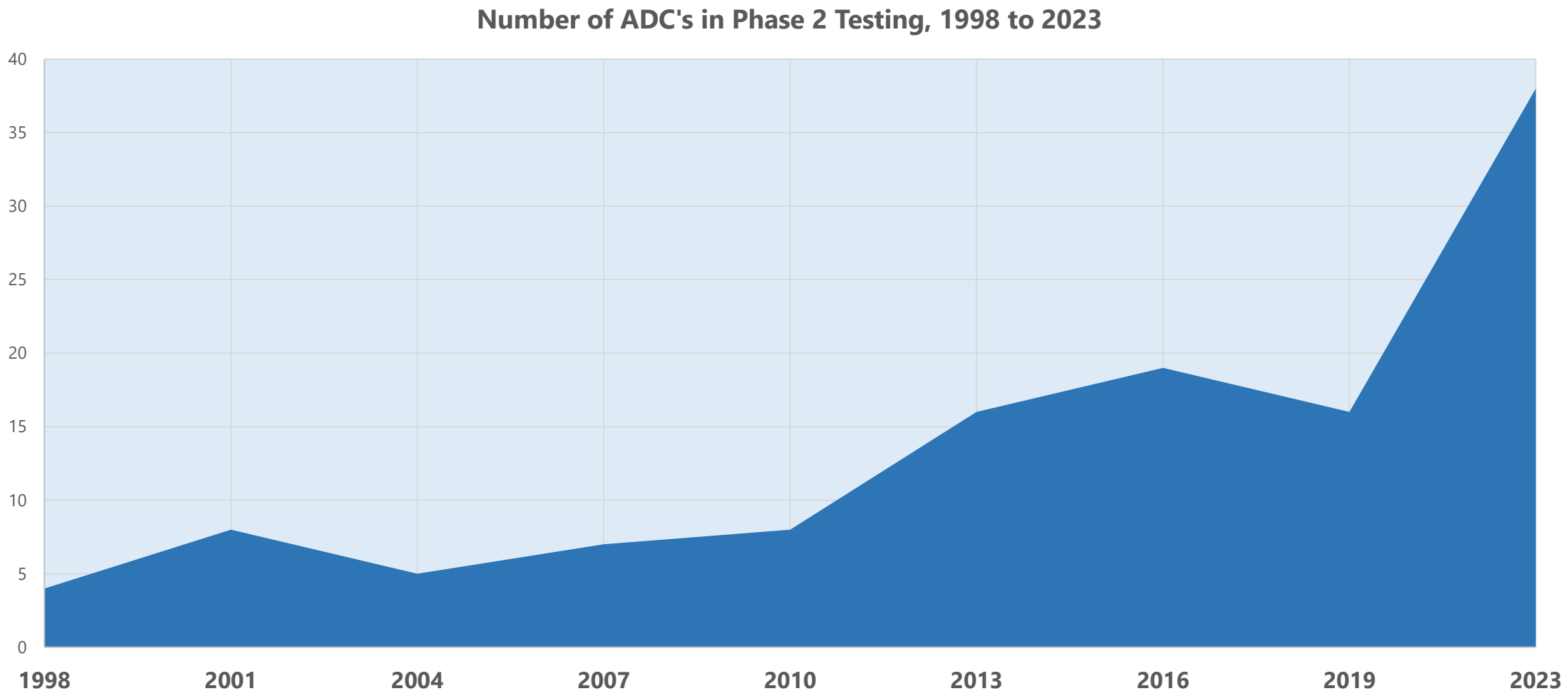
Source: https://www.nature.com/articles/s41573-022-00579-0

Key Technologies for Improving ADC Performance



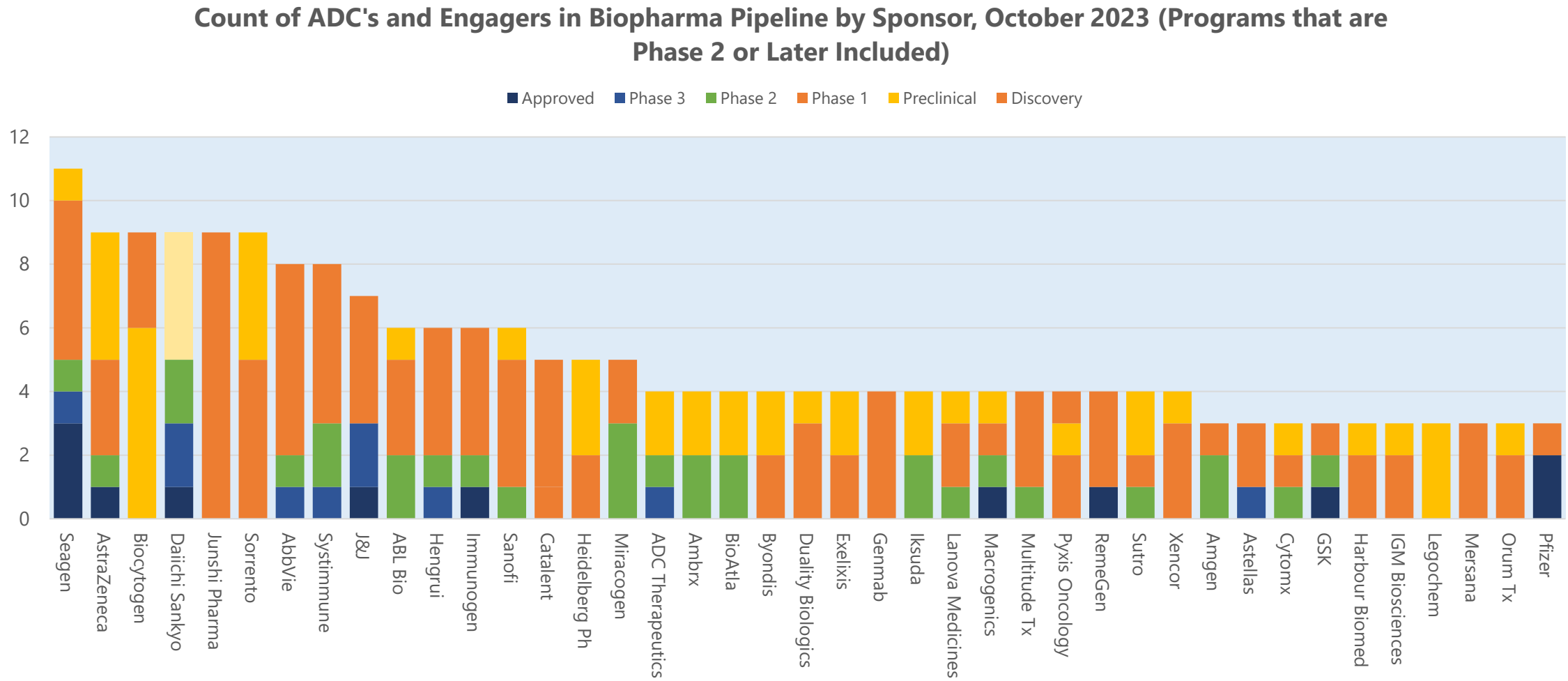
Source: Stifel Research

Size of ADC Pipeline is Exploding



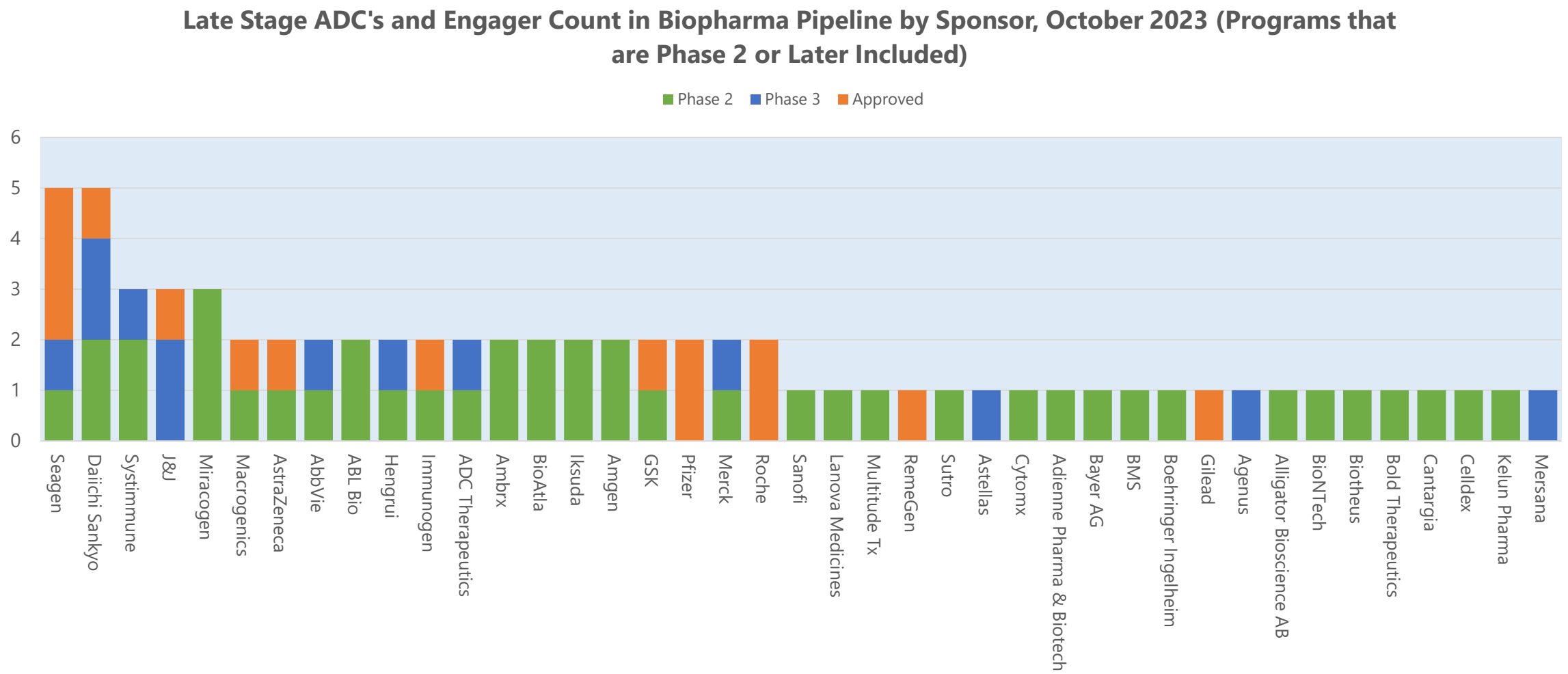
Source: Recon Strategies, Stifel

Seagen, Daiichi-Sankyo and AZ Lead the Pack in Terms of Pipeline Scale



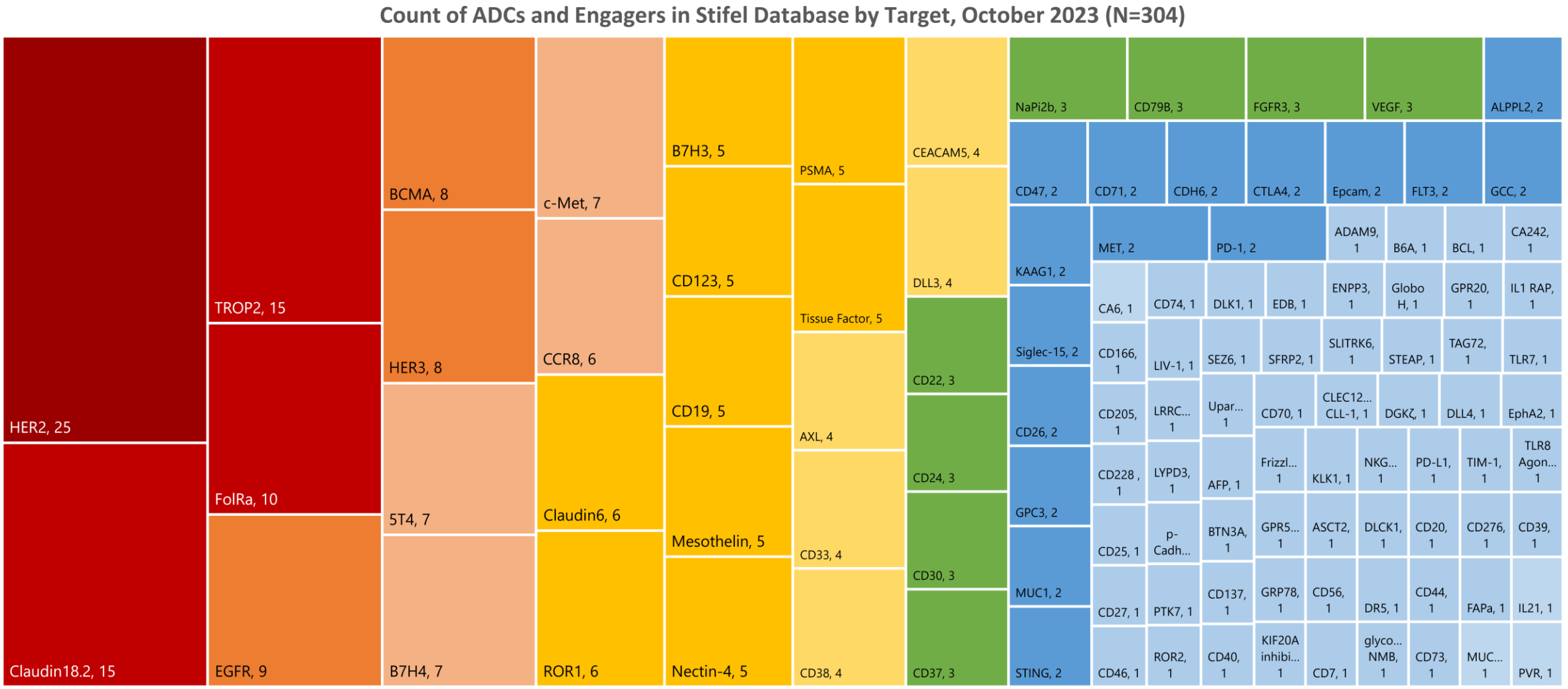
Source: Stifel Research

Late-Stage Pipeline: Seagen, Daiichi-Sankyo, Systimmune and J&J Have the Largest Pipelines (Phase 2 or Later)



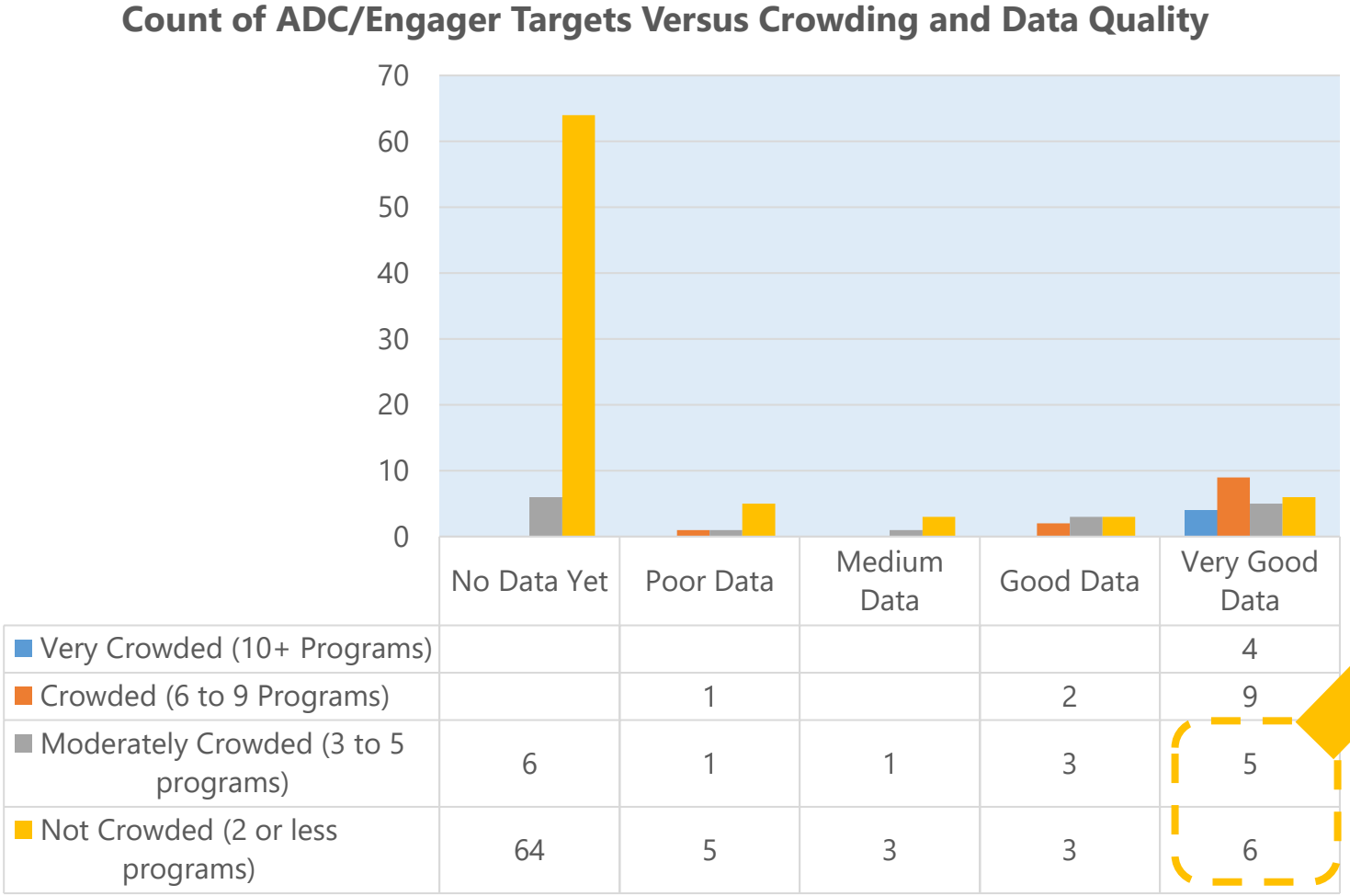
Source: Stifel Research

Roughly Half of ADCs and Engagers Concentrated in Top 17 (of 104) Targets



Source: Stifel Research

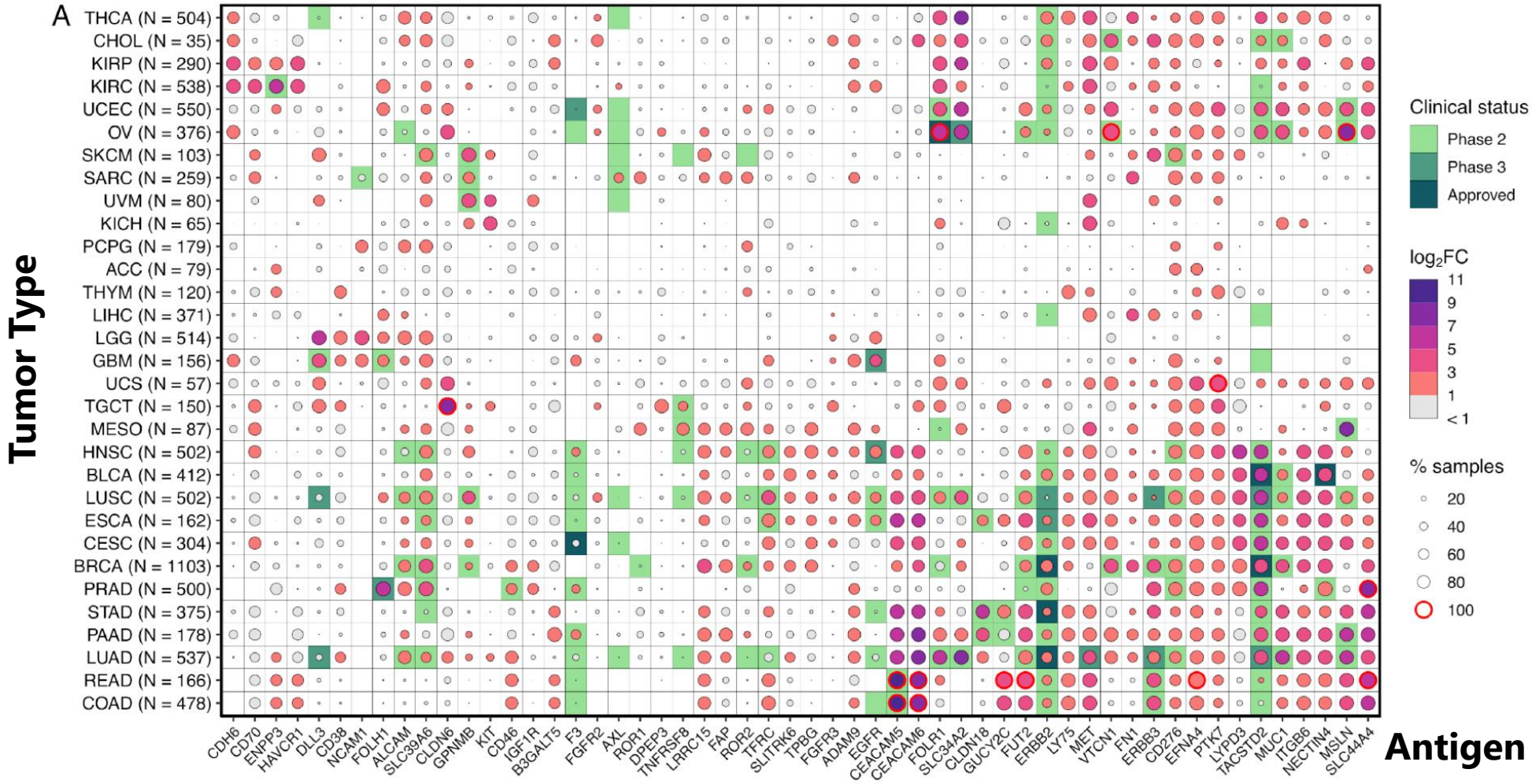
Locus of Opportunity: Less Crowded Targets Where Datasets are Good or Very Good



Antigen	Existing Data	Crowding
B7H3	Very Good	Moderate
CD30	Very Good	Moderate
CD71	Very Good	Low
CD79B	Good	Low
CDH6	Very Good	Low
CEACAM5	Good	Moderate
DLL3	Very Good	Moderate
FAPa	Good	Low
GPR5CD	Very Good	Low
NaPi2b	Good	Moderate
PSMA	Very Good	Moderate
STEAP1	Very Good	Low
Tissue Factor	Good	Moderate
VEGF	Very Good	Moderate

Source: Stifel Research

Bosi et.al., (Oct 2023): ADC Target Expression by Tumor Type



ADC target expression in primary tumours from The Cancer Genome Atlas (TCGA) and normal tissues from the Genotype-Tissue Expression (GTEx) repository. ADC targets are shown on the x-axis and cancer types on the y-axis. Fold-change (FC) of mean mRNA expression values (Log_2[TPM+1] mRNA counts) of ADC targets in cancer relative to all normal tissues in the GTEx. Darker dot colours indicate higher expression in cancer. Dot size is proportional to the percentage of tumour samples exceeding an expression threshold defined as the 80th centile of expression seen in pooled normal issues in the GTEx. The background colour of the squares indicates the clinical development stage in the given cancer type (white indicates phase 1 trials, light green phase 2 trials, darker shades of green phase 3 trials and approved indications, respectively).

Source: https://www.ejcancer.com/article/S0959-8049(23)00681-0

Disclosure

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