Biopharmaceutical Sector

Market Update – May 29, 2023

Abstract imagery of life. Source: Getty Images.

STIFEL | Healthcare

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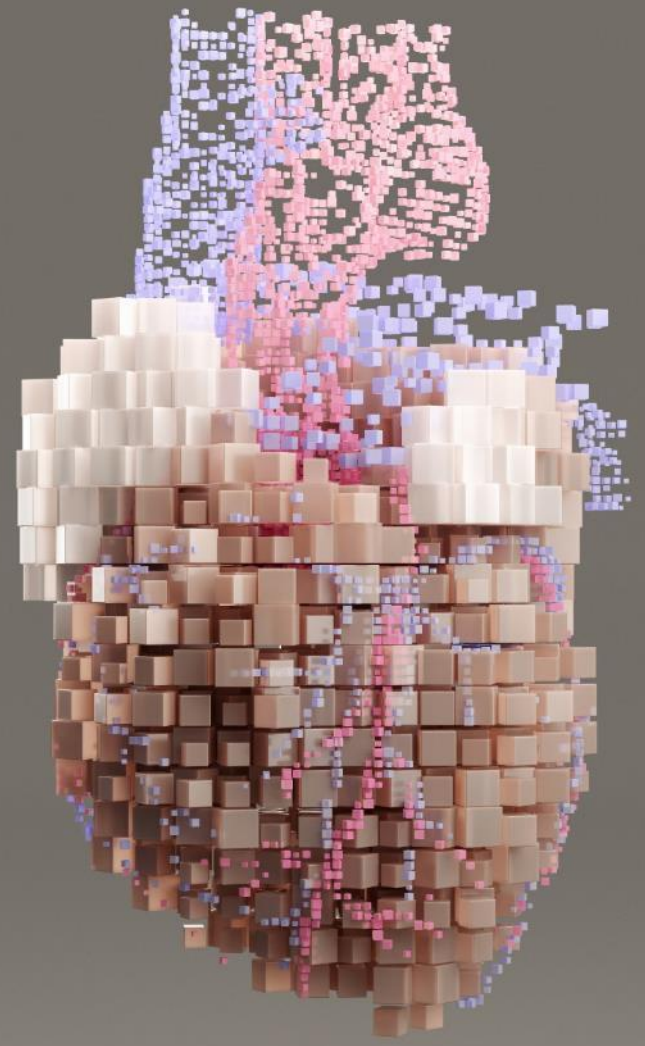
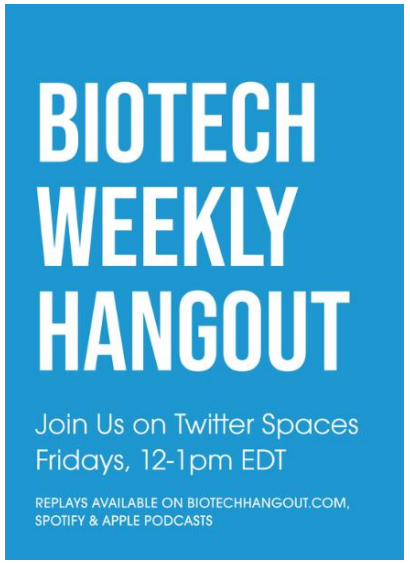
555 Madison Ave, Suite 1201, New York NY 10022, +1-(212) 257-5801
Web: www.stifel.com



Rendering of heart. Source: Getty Images.

Join Us at These Upcoming Events

1



Biotech Hangout held its last event on May 19th.

The next event will be on June 2nd.

Note that the time for the event has changed to noon EDT.

Please join us.

May19th Replay: https://twitter.com/i/spaces/1mnGeRvjevNJX

June 2nd Session: https://twitter.com/i/spaces/1lDGLnrBlAbxm

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

2

We'll be at **BIO** from June 5 to 8 and hope to see you there. To set up a meeting with Stifel at BIO please contact:

Allison Bobzin (bobzina@stifel.com).

Details on the meeting: https://www.bio.org/events/bio-international-convention

3

BIOTECH ceosummit

We'll be at the Biotech CEO Summit USA in La Jolla on July 17 to 19 and the Biotech CEO Summit EU in Barcelona on June 12 to 14.

Would be great to see you there.

Details on the meeting: https://www.biotechceosummit.com/

Macro Update

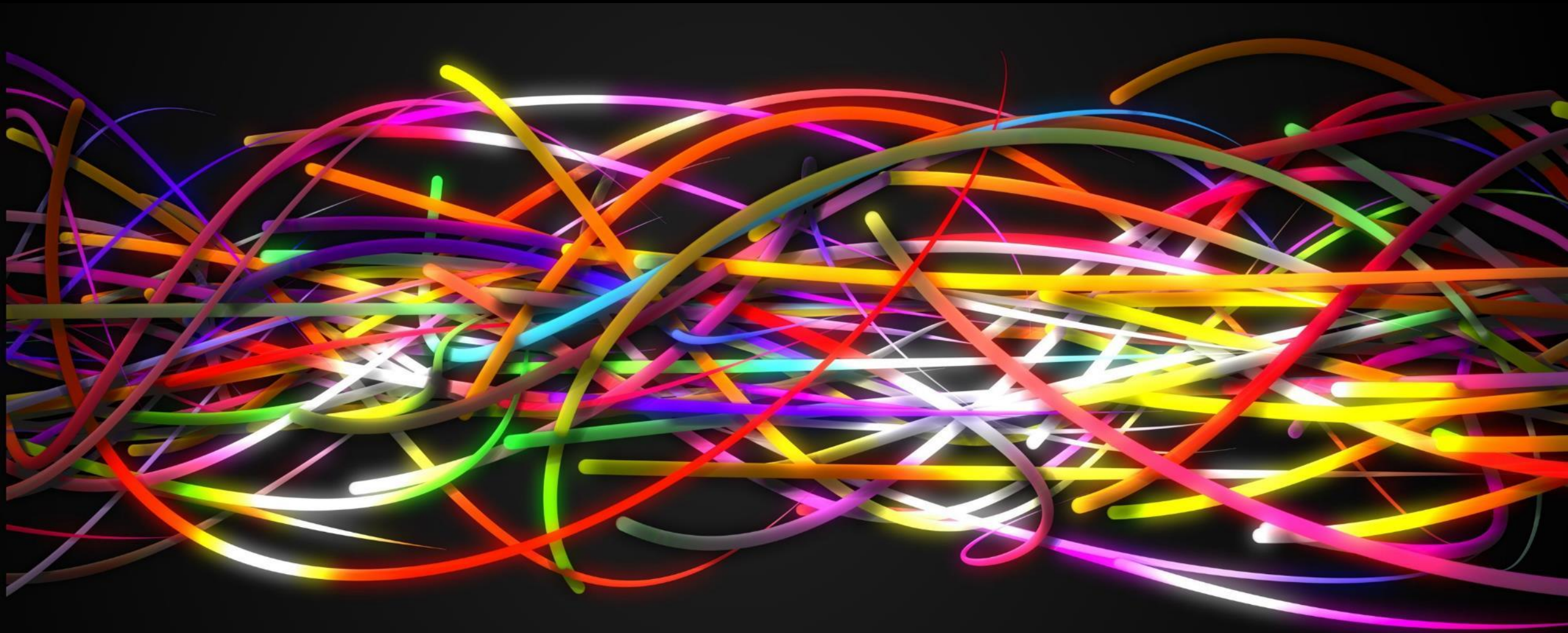


Illustration: Representation of economic activity. Source: Getty Images.

Debt Ceiling Deal is Reached

Reuters, May 28, 2023

WASHINGTON, May 28 (Reuters) - After tough negotiations to reach a tentative deal with the White House on the U.S. borrowing limit, the next challenge for House Speaker Kevin McCarthy is pushing it through the House, where it may be opposed by both hardline Republicans and progressive Democrats.

As Democratic and Republican negotiators iron out the final details of an agreement to suspend the federal government's $31.4 trillion debt ceiling in coming days, McCarthy may be forced to do some behind-the-scenes wrangling.

The deal does just that, sources briefed on it say: it suspends the debt ceiling until January 2025, after the November 2024 presidential election, in exchange for caps on spending and cuts in government programs.


House Speaker Kevin McCarthy

Source: https://www.reuters.com/world/us/mccarthys-next-challenge-sell-debt-ceiling-deal-congress-2023-05-28/

PCE Inflation of 0.4% in April Implies 3.6% Inflation Run Rate

Personal Income and Outlays, April 2023

Personal income increased $80.1 billion (0.4 percent at a monthly rate) in April, according to estimates released today by the Bureau of Economic Analysis (table 3 and table 5). **Disposable personal income** (DPI) increased $79.4 billion (0.4 percent) and **personal consumption expenditures** (PCE) increased $151.7 billion (0.8 percent).

The **PCE price index** increased 0.4 percent. Excluding food and energy, the PCE price index increased 0.4 percent (table 9). **Real DPI** increased less than 0.1 percent in April and **Real PCE** increased 0.5 percent; goods increased 0.8 percent and services increased 0.3 percent (table 5 and table 7).

	2022	2023			
	Dec.	Jan.	Feb.	Mar.	Apr.
	Percent change from preceding month				
Personal income:					
Current dollars	0.2	0.6	0.3	0.3	0.4
Disposable personal income:					
Current dollars	0.3	2.2	0.5	0.3	0.4
Chained (2012) dollars	0.1	1.6	0.2	0.2	0.0
Personal consumption expenditures (PCE):					
Current dollars	0.0	1.9	0.1	0.1	0.8
Chained (2012) dollars	-0.2	1.3	-0.2	0.0	0.5
Price indexes:					
PCE	0.2	0.6	0.3	0.1	0.4
PCE, excluding food and energy	0.4	0.6	0.4	0.3	0.4
Price indexes:	Percent change from month one year ago				
PCE	5.3	5.4	5.1	4.2	4.4
PCE, excluding food and energy	4.6	4.7	4.7	4.6	4.7

The April PCE inflation run rate was 3.6%.

On the one hand this is below the Y-o-Y 4.4% inflation rate.

On the other hand, this is well above the Fed's target inflation rate of 2% and portends more Fed tightening ahead.

Source: https://www.bea.gov/news/2023/personal-income-and-outlays-april-2023

Investors Expect Higher Interest Rates as Inflation Pressures Mount

Financial Times, May 26, 2023

Stronger than expected US inflation and a bump in consumer spending have fuelled worldwide expectations that interest rates will go higher, as predictions about future monetary policy rapidly shift.

The Federal Reserve's preferred measure of inflation overshot expectations in April, data published on Friday showed, while US consumer spending rose last month and new orders for long-lasting goods unexpectedly increased.

Kristalina Georgieva, the IMF's head, on Friday warned US interest rates would need to stay higher for longer to tame inflation that had been more persistent than anticipated. She added that a loss of confidence in US Treasury markets would mean turmoil for the global economy. Yields on short-term government debt in the US, UK and eurozone have begun to rise again as investors switch from betting on an economic slowdown to anticipating more prolonged rate increases to contend with price rises.

Source: https://www.ft.com/content/236c2aeb-5dfe-4564-814f-e88044efedad
Photo from Getty Images

Biopharma Market Update

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

Laboratory photography. Source: Getty Images.

Biotech Stocks Update

The XBI was down slightly last week despite positive economic news on a U.S. debt ceiling deal. The XBI remains up for the year but only slightly. Stifel's biotech total sector value tracker is up 11.4% for the year. We have gone from a nice rally to three weeks of biotech doldrums. Treasury yields and the VIX up as a debt ceiling deal still not fully worked out.

Biotech Stocks Down a Bit Last Week

Return: May 20 to May 26, 2023

Nasdaq Biotech Index: -2.5%
Arca XBI ETF: -1.2%
Stifel Global Biotech (EV): -1.9%*
S&P 500: +0.3%

Return: Jan 1 to May 26, 2023

Nasdaq Biotech Index: -3.2%
Arca XBI ETF: +1.6%
Stifel Global Biotech: +11.4%*
S&P 500: +9.5%

VIX Up Last Week

Jan 3: 16.6%
Oct 21: 29.7%
Jan 20: 19.9%
Mar 17: 24.6%
Apr 28: 15.8%
May 12: 17.8%
May 19: 16.8%
May 26: 18.0%

10-Year Treasury Yld Up

Jan 3: 1.63%
Oct 21: 4.2%
Jan 20: 3.48%
Mar 17: 3.39%
Apr 28: 3.44%
May 12: 3.39%
May 19: 3.7%
May 26: 3.8%

XBI Index, April 1, 2021 to May 26, 2023

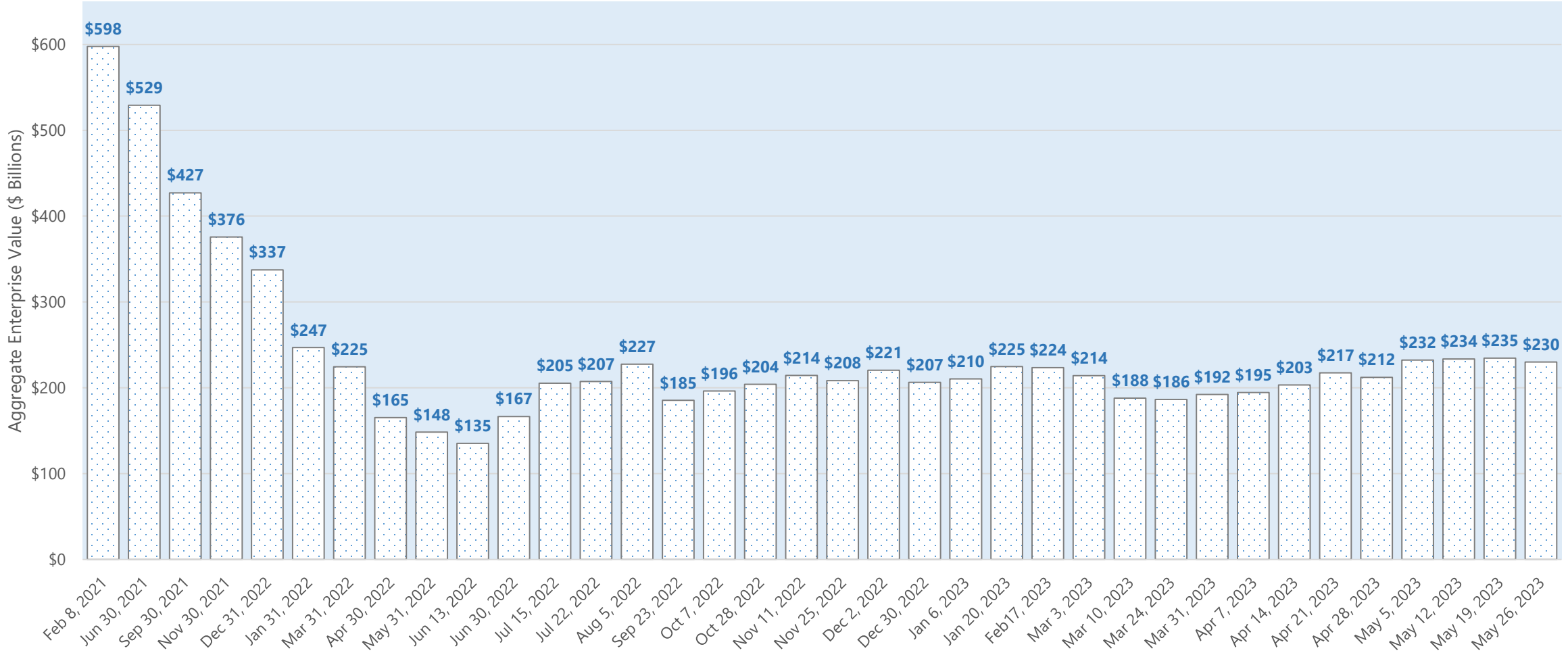
* Change by enterprise value.

Source: S&P Capital IQ and Stifel analysis

Total Global Biotech Sector Valuation Down Last Week

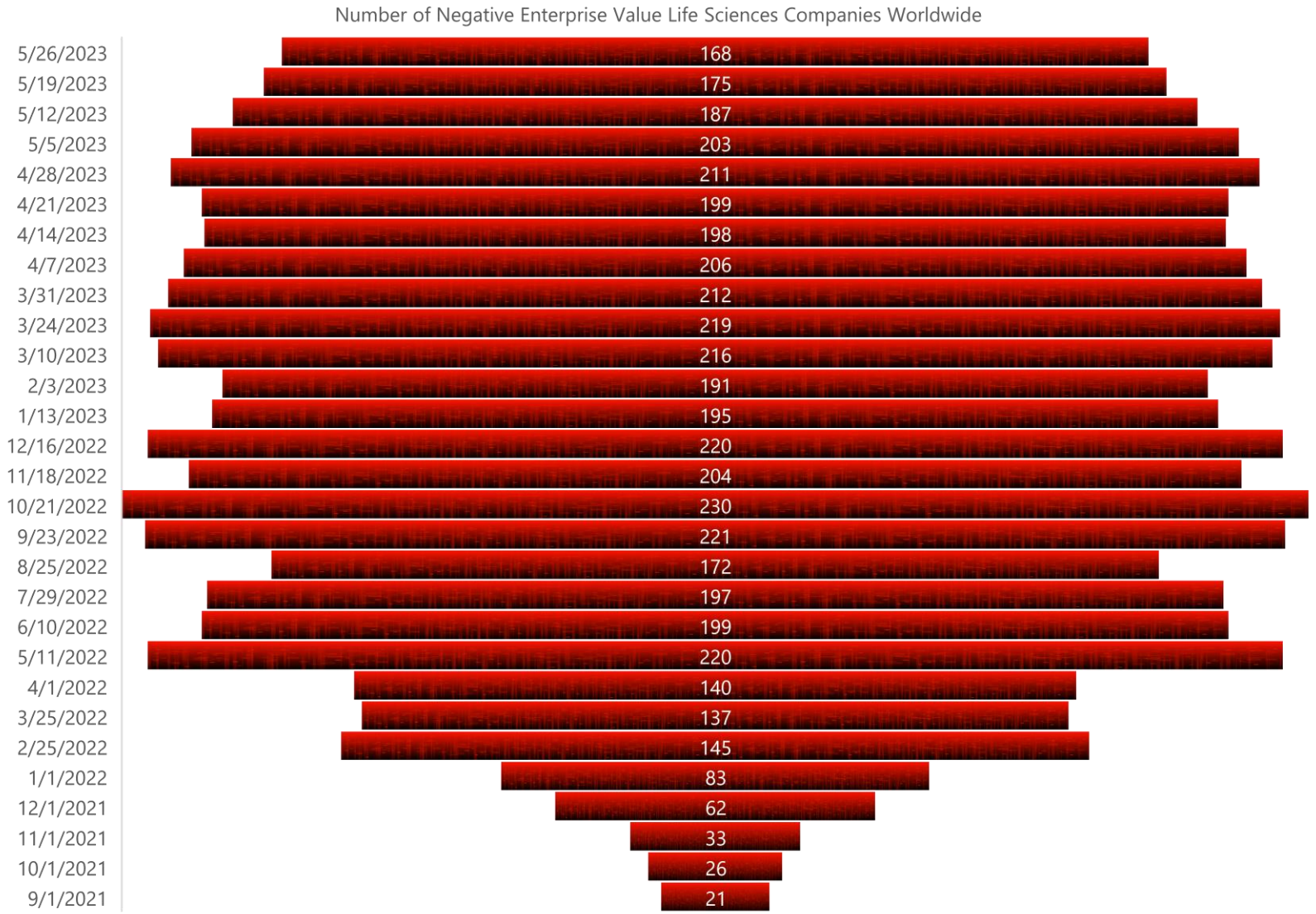
The total value of the global biotech sector was down 1.9% last week. This took place after news of persistent U.S. inflation. The total biotech sector is up 11.4% for the year.

Total Enterprise Value of Publicly Traded Global Biotech, Feb 8, 2021 to May 26, 2023 ($ Billions)



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

Number of Negative Enterprise Value Life Sciences Companies Fell Again Last Week



Source: CapitalIQ

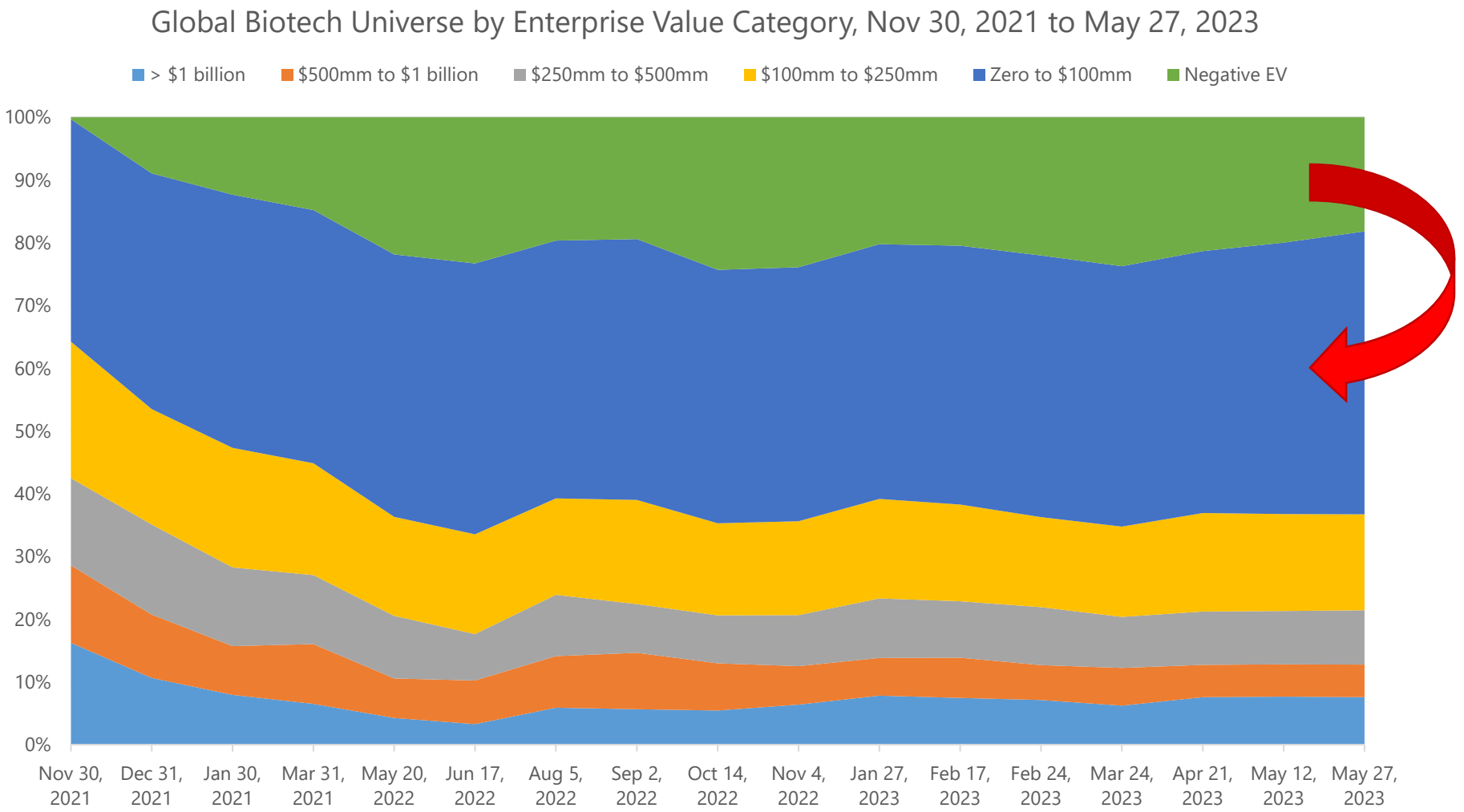
Despite the flat market, last week saw a drop in the number of negative EV companies again in life sciences. The count went from 175 to 168 such companies.

Of these 168 companies, 151 were in biotech.

Bargain hunters and activists are pushing these companies into positive EV territory. We haven't seen so few negative EV companies for 13 months.

So Where Are All Those Negative EV Biotechs Going?

Negative EV biotech companies are moving into the poor neighborhood across the street. The number of companies with EV's over $100mm has been shrinking as the negative population has been declining.



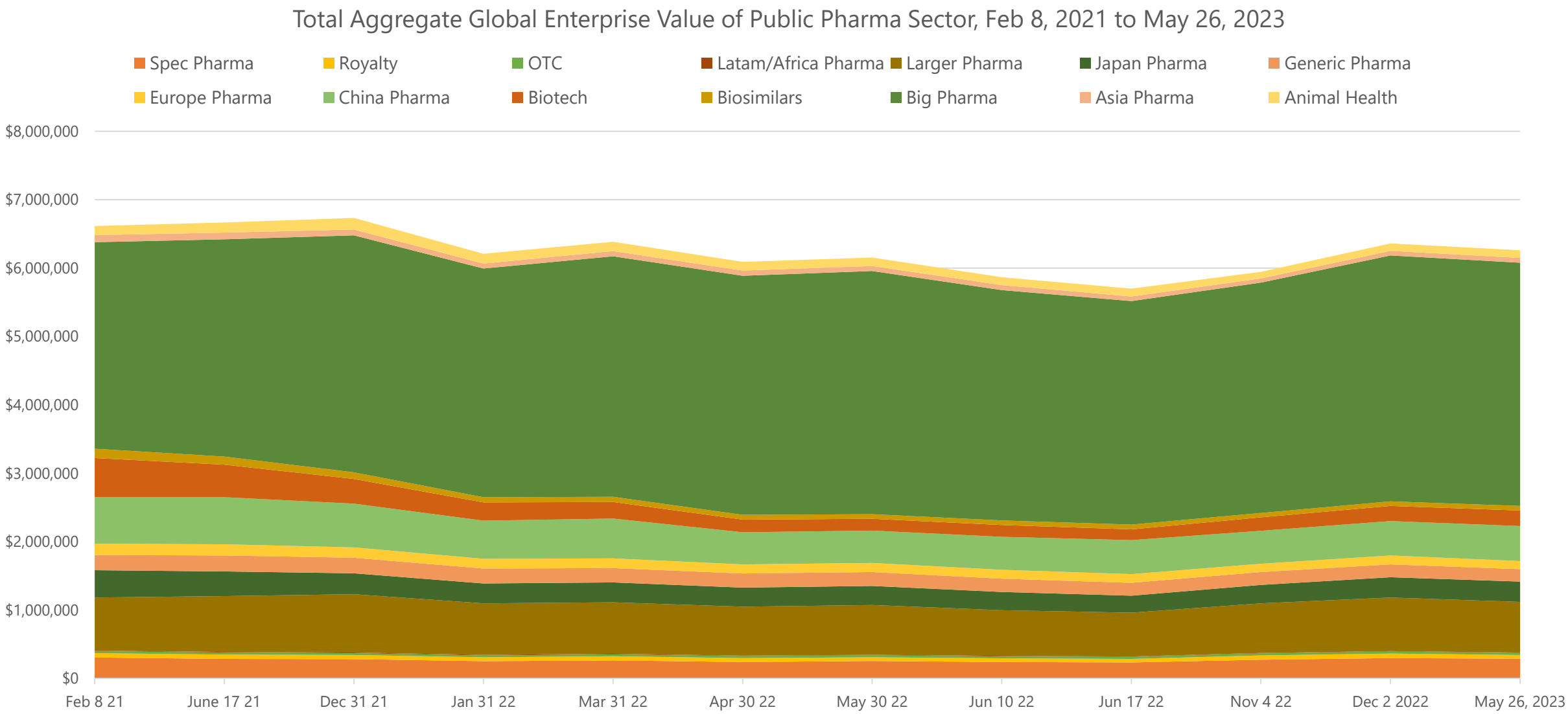
Five weeks ago (Apr 21), we had 178 biotechs with negative EV. Now we have only 151 of them.

The zero to $100mm EV population in biotech has gone from 348 to 375 companies.

The population of companies with EV's over $100mm shrunk from 308 to 305 in the same time period.

Source: CapitalIQ

Pharma Sector Overall Down Slightly in Last 25 Weeks

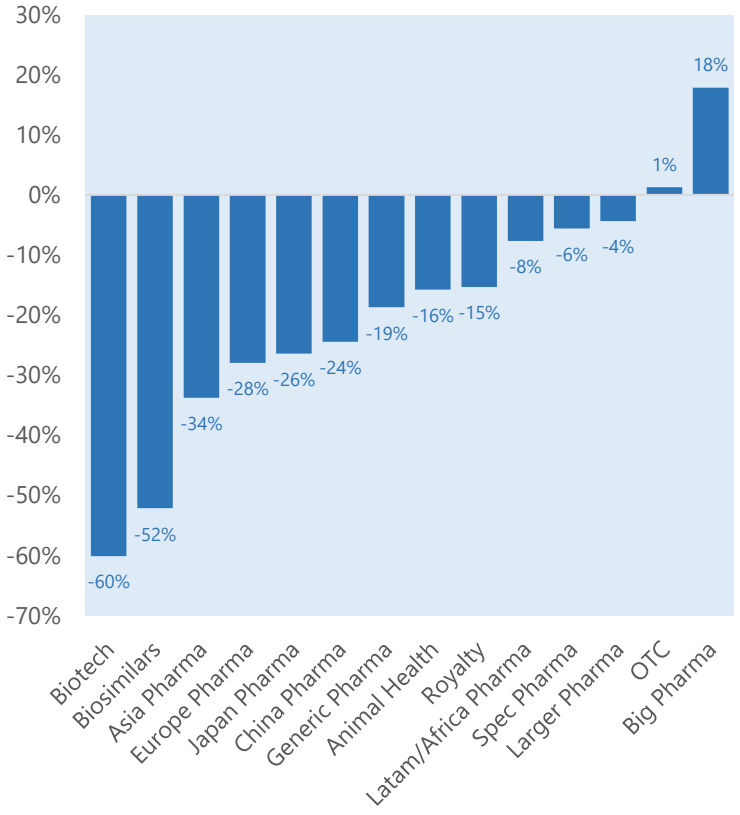


Source: CapitalIQ

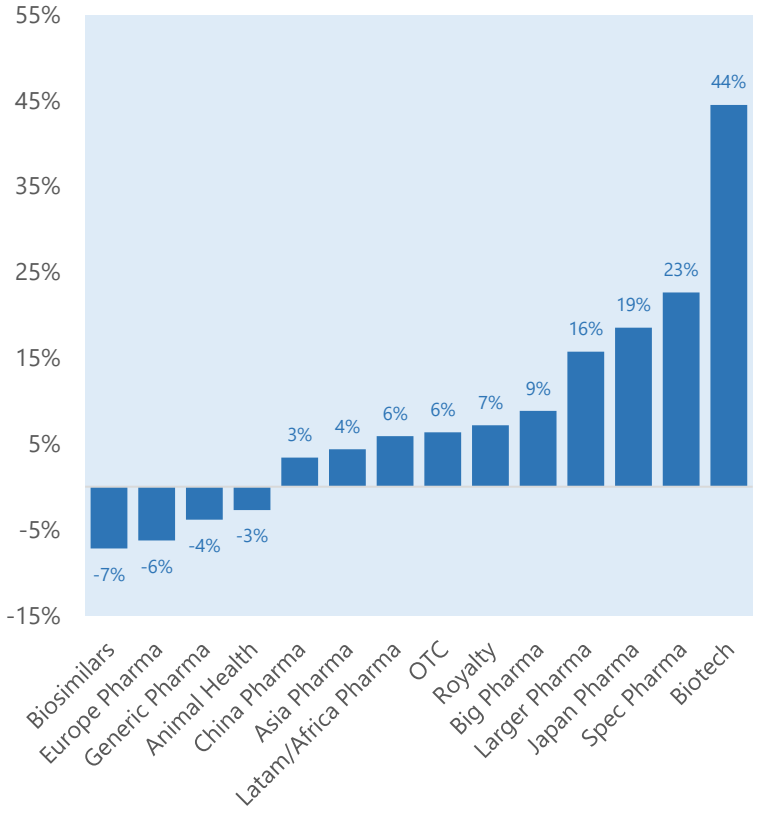
Recent Pharma Subsector Performance

All parts of the pharma sector except big pharma and OTC are down since the Pandemic peak. Since market bottom, biotech, spec pharma and Japan pharma have come back big. In the last 25 weeks we have seen the royalty sector take a big hit. This sector is quite rate sensitive and the news that rates aren't coming down soon has impacted royalty players.

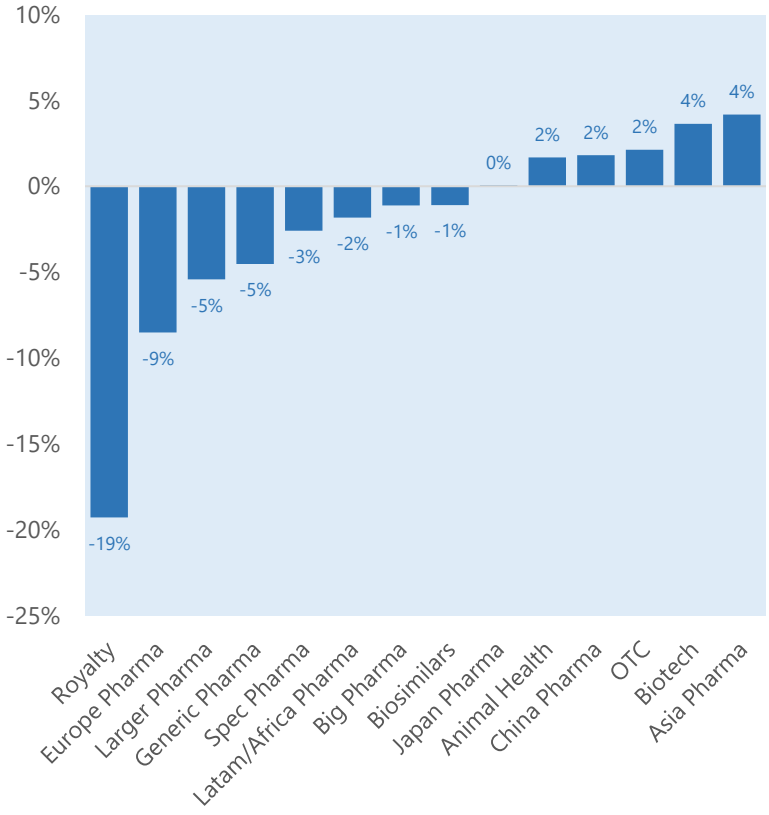
Change in Aggregate EV Since Feb 8, 2021 Market Peak



Change in Aggregate EV Since Jun 17, 2022 Market Bottom



Change in Aggregate EV Since Dec 2, 2022 (Last 25 Weeks)



Source: CapitalIQ

Value of Public Life Sciences Companies by Subsector

The total value of the public life sciences market dropped by 2.4% last week (-$223 billion). This was driven principally by substantial drops in pharma and device company valuations.

Sector	Firm Count	Enterprise Value (May 26, 2023, $millions)	Change in Last Week (percent)	Change in Last Month (percent)	Change in Last Year (percent)
API	81	$78,915	1.9%	-1.3%	-11.2%
Biotech	832	$227,243	-0.1%	10.3%	54.5%
CDMO	40	$174,821	-1.3%	-3.0%	-12.9%
Diagnostics	83	$263,412	-1.8%	-4.2%	3.4%
OTC	32	$29,301	-1.1%	-0.5%	7.4%
Pharma	727	$5,806,082	-2.2%	-1.0%	2.1%
Services	41	$199,835	-1.7%	-0.2%	-15.9%
Tools	54	$691,192	-0.9%	-2.9%	-12.4%
Devices	184	$1,640,765	-4.2%	-4.4%	-1.9%
HCIT	11	$24,831	-2.4%	-13.8%	-11.4%
Total	**2085**	**$9,136,399**	**-2.4%**	**-1.7%**	**0.1%**

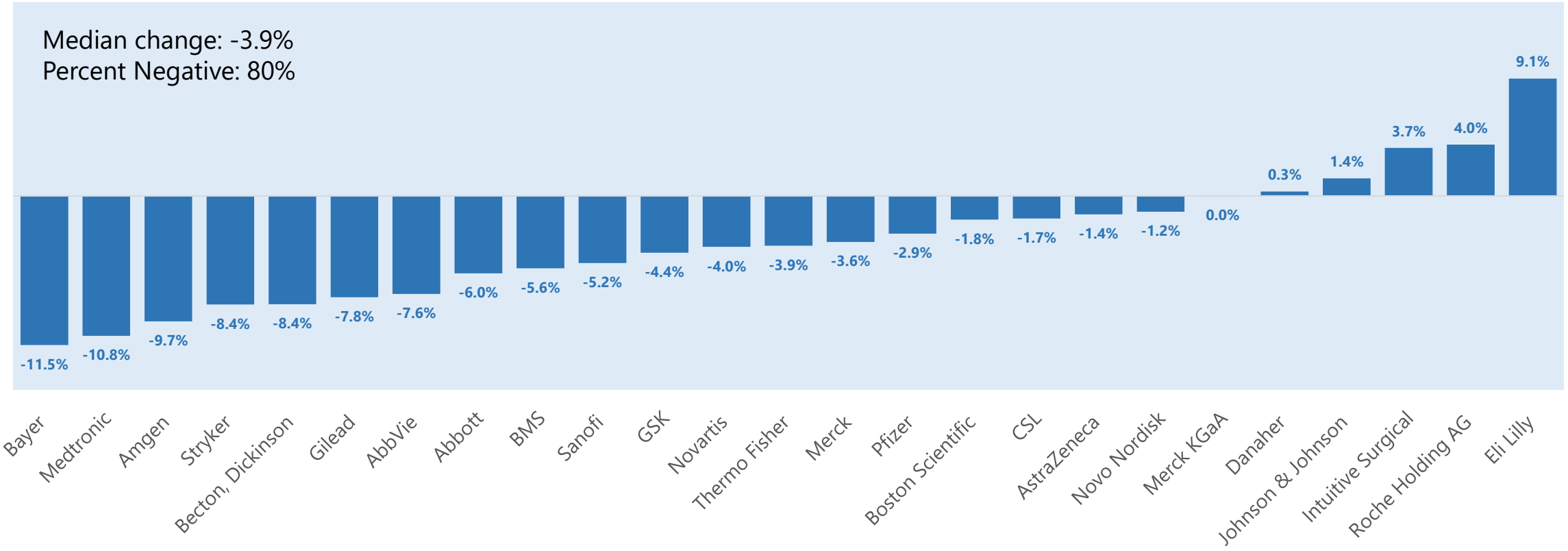
Source: CapitalIQ

Large Cap Life Sciences Performance in Last Month Poor

Top device and pharma players have been a safe haven in an economic storm. We are seeing investors rotate out of life sciences and into IT in the last month. Only one in five life sciences large caps have been up in the last month.

Top 25 Life Sciences Companies Share Price Return Over Last Month

(Percent Change in Enterprise Value, April 26 to May 26, 2023)



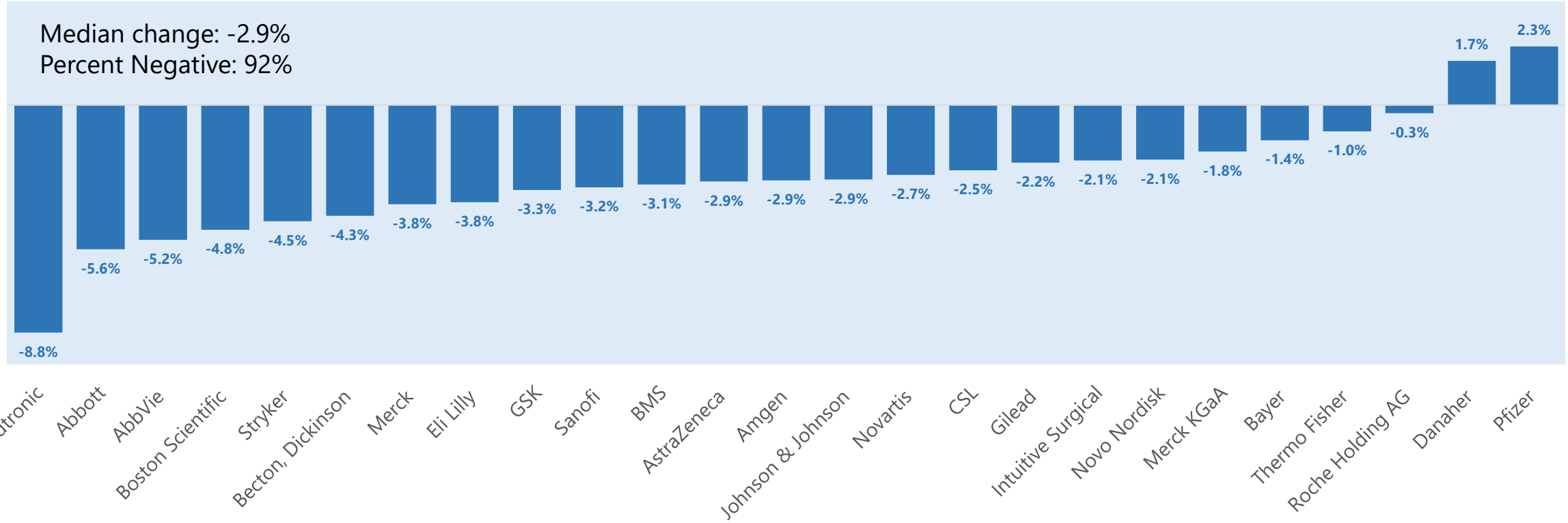
Source: CapitalIQ

Large Cap Life Sciences Performance Last Week Not Great

Last week was particularly bad for large cap players in life sciences. The 25 companies below lost $125 billion in total market cap in a week. Only two of twenty-five companies traded up. Device companies performed particularly poorly on the heels of an OK outlook from Medtronic in its earnings last week. Pfizer rose on the back of favorable data for its oral GLP-1 agonist.

Top 25 Life Sciences Companies Share Price Return Over Last Week

(Percent Change in Enterprise Value, May 19 to May 26, 2023)

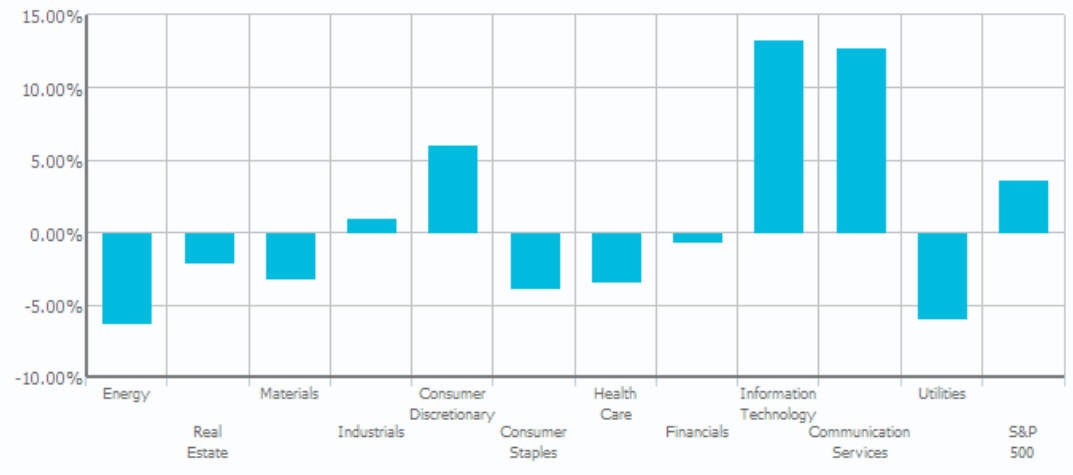


Source: CapitalIQ

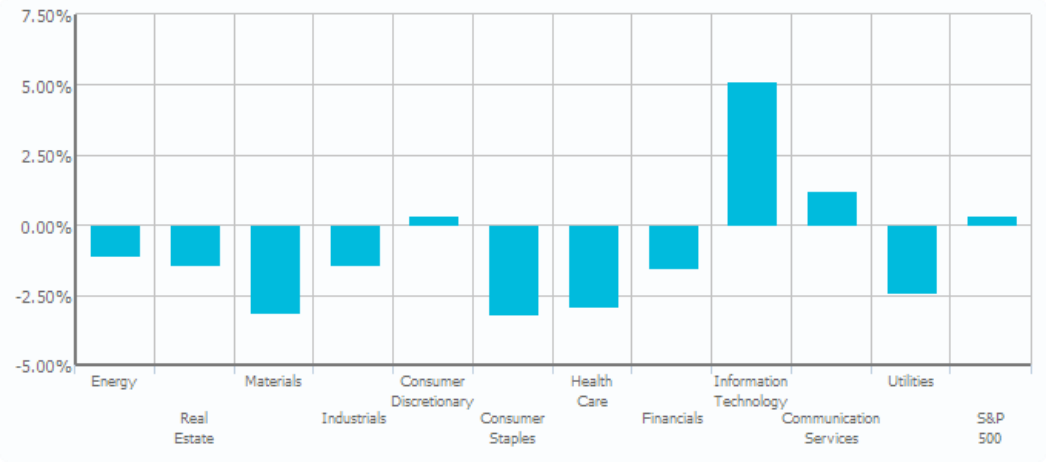
Top Performing Segments in S&P Indices

The healthcare sector is not the only one seeing investor rotation. In the last week there were significant declines in materials, consumer staples, healthcare and utilities as investors pulled money out to invest in semiconductors, AI and tech.

Last Month



Last Week



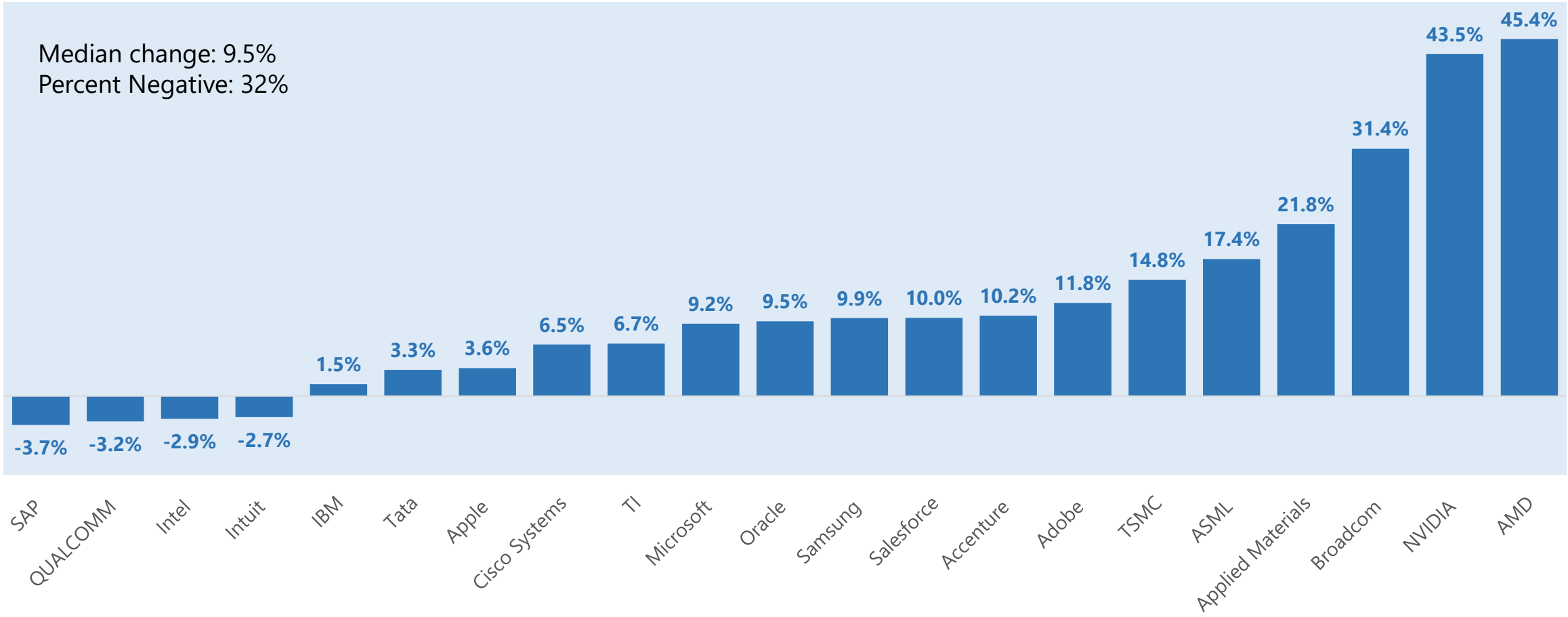
Source: CapitalIQ

Large Cap Performance in Info Tech Last Month

Key players in semiconductors and AI were on fire last week. The IT sector has added a trillion dollars in market cap in four weeks.

Top 20 Global IT Companies Share Price Return Last Month

(Percent Change in Market Cap, Apr 26 to May 26, 2023)



Source: CapitalIQ

A Revenue Beat for the Ages

NVIDIA Announces Financial Results for First Quarter Fiscal 2024

May 24, 2023

- Quarterly revenue of $7.19 billion, up 19% from previous quarter
- Record Data Center revenue of $4.28 billion
- Second quarter fiscal 2024 revenue outlook of $11.00 billion

NVIDIA (NASDAQ: NVDA) today reported revenue for the first quarter ended April 30, 2023, of $7.19 billion, down 13% from a year ago and up 19% from the previous quarter.

GAAP earnings per diluted share for the quarter were $0.82, up 28% from a year ago and up 44% from the previous quarter. Non-GAAP earnings per diluted share were $1.09, down 20% from a year ago and up 24% from the previous quarter.

"The computer industry is going through two simultaneous transitions — accelerated computing and generative AI," said Jensen Huang, founder and CEO of NVIDIA.

"A trillion dollars of installed global data center infrastructure will transition from general purpose to accelerated computing as companies race to apply generative AI into every product, service and business process.

"Our entire data center family of products — H100, Grace CPU, Grace Hopper Superchip, NVLink, Quantum 400 InfiniBand and BlueField-3 DPU — is in production. We are significantly increasing our supply to meet surging demand for them," he said.

NVIDIA's high speed, high throughput chips are essential for datacenters that run generative AI LLM's.

NVIDIA announced 19% quarterly revenue growth and is forecasting 53% revenue growth for Q2 2023.

This was 40% over analyst consensus. Yowza. This does not happen often.

With no new net capital in the market, investors have understandably been taking money out of less exciting sectors like medical devices and consumer staples and putting it in AI-linked tech stocks.

Source: https://nvidianews.nvidia.com/news/nvidia-announces-financial-results-for-first-quarter-fiscal-2024

Industry News

Astellas Pharma Lobby, Source: Astellas

No ‘Magic Wand’ for Financial Pressures, Hunt Tells Pharma Groups

Hannah Kuchler, *Financial Times*, May 25, 2023

The government will on Friday unveil reforms worth £650mn to boost the life sciences sector as part of a wider package of measures. Drugmakers have condemned the government for this year increasing a tax on sales of drugs to the NHS to 26.5 per cent, from 5.1 per cent over the past two years.

“I’m very honest with drug companies that we don’t have a magic wand to deal with these financial pressures. Responsible public finances are absolutely essential if we’re going to have economic stability.”

Hunt said the government wanted to work with companies to find a “win-win” outcome as they negotiate an agreement on the NHS drugs bill for the coming years.

Jeremy Hunt, Chancellor of the Exchequer, United Kingdom

Source: https://www.ft.com/content/8bdea0bd-6cea-47fb-9c5f-8becf456d32b

Record Number of People in U.S. Have Health Insurance

Caroline Hanson, Claire Hou, Allison Percy, Emily Vreeland, Alexandra Minicozzi, Congressional Budget Office, Health Insurance For People Younger Than Age 65: Expiration Of Temporary Policies Projected To Reshuffle Coverage, 2023–33, Health Affairs, May 24, 2023.

The Congressional Budget Office estimates that in 2023, 248 million people in the US who are younger than age sixty-five have health insurance coverage (mostly through employment-based plans), and twenty-three million people, or 8.3 percent of that age group, are uninsured—with significant variations in coverage by income and, to a lesser extent, by race and ethnicity. The unprecedented low uninsurance rate is largely attributable to temporary policies that kept beneficiaries enrolled in Medicaid and enhanced the subsidies available through the health insurance Marketplaces during the COVID-19 pandemic. As the continuous eligibility provisions unwind in 2023 and 2024, an estimated 9.3 million people in that age group will transition to other forms of coverage, and 6.2 million will become uninsured. If the enhanced subsidies expire after 2025, 4.9 million fewer people are estimated to enroll in Marketplace coverage, instead enrolling in unsubsidized nongroup or employment-based coverage or becoming uninsured. By 2033 the uninsurance rate is projected to be 10.1 percent, which is still below the 2019 rate of about 12 percent.

Source: https://www.healthaffairs.org/doi/full/10.1377/hlthaff.2023.00325

Illumina shareholders oust board chair, CEO survives Carl Icahn proxy battle

PUBLISHED THU, MAY 25 2023•1:21 PM EDT | UPDATED THU, MAY 25 2023•2:52 PM EDT

CNBC: "Activist investor Carl Icahn on Thursday won enough support from Illumina shareholders to oust the biotech company's board chair.

Shareholders booted Chairman John Thompson. An Illumina spokesperson said a new chair will be chosen in the next few weeks.

Icahn had urged shareholders to vote off the company's CEO, Francis deSouza, and Thompson from the nine-member board. DeSouza survived the proxy fight.

Shareholders also voted to install one of Icahn's three board nominees, Andrew Teno, a portfolio manager at Icahn Capital LP, an entity where Icahn manages investment funds."

Source: https://www.cnbc.com/2023/05/25/illumina-installs-carl-icahn-board-nominee-ousts-chair-.html

Robert Coury Exits Viatris Board

PITTSBURGH, May 22, 2023 /PRNewswire/ -- Viatris Inc. (NASDAQ: VTRS), a global healthcare company, announced today that as a result of the strength and stability that Viatris has achieved since its formation in 2020, including its ninth consecutive quarter of solid execution and performance, as well as the successful completion of the integration of its two legacy companies, Robert J. Coury, the key architect behind Viatris' unique and powerful global platform, will once again transition his role, this time from his current position of Executive Chairman to Chairman Emeritus and Senior Strategic Advisor to the board and management following the company's 2023 annual meeting of shareholders. The annual meeting for 2023 is anticipated to occur in mid-December of this year, at which time Mr. Coury will not be standing for re-election.

Given his longstanding and critical connection to, as well as direct oversight of, many of Viatris' significant ongoing business matters and strategic development opportunities, Coury will continue to serve the company in this new non-employee, strategic advisor capacity until the end of 2025 when the term of his contract would have otherwise expired. This will not only ensure a smooth transition but also help limit potential business or strategic disruptions. The Viatris board will select a new independent chair of the board who will be announced in the coming months and whose tenure is intended to begin following the 2023 annual meeting.

Robert J. Coury said, "Given the success and stability of Viatris to date and the sustainable future I see ahead for the company as we near the completion of our Phase 1 long-term strategic plan, I am very pleased to be in a position to plan a clear and orderly transition for the company. This will provide an opportunity for its leaders to further progress and grow, while I also remain available to continue to advise the board and management on ongoing matters and help ensure the success of the company's long-term goals. With Viatris' powerful foundation now securely in place, with Scott A. Smith at the helm as our new CEO, and with the clear and defined path that we established for growth going forward, I have never been more confident in the future of our company, our employees and all of our stakeholders than I am today."

Source: https://www.prnewswire.com/news-releases/robert-j-coury-to-transition-from-executive-chairman-of-viatris-to-chairman-emeritus-and-senior-strategic-advisor-to-the-board-and-management-at-the-end-of-the-year-301830676.html

FDA Approves Lexicon's SGLT1/SGLT2 Inhibitor for Heart Failure

The Woodlands, Texas, May 26, 2023 – Lexicon Pharmaceuticals, Inc. (Nasdaq: LXRX) today announced that the U.S. Food and Drug Administration (FDA) has approved INPEFA™ (sotagliflozin), a once-daily oral tablet to reduce the risk of cardiovascular death, hospitalization for heart failure, and urgent heart failure visit in adults with: heart failure or type 2 diabetes mellitus, chronic kidney disease, and other cardiovascular risk factors.

The broad label encompasses heart failure patients across the full range of left ventricular ejection fraction (LVEF), including preserved ejection fraction and reduced ejection fraction, and for patients with or without diabetes.

"The approval of INPEFA along with the breadth of the label, is a major milestone in Lexicon's path to fulfilling its mission of pioneering medicines that transform patients' lives," said Lonnel Coats, Lexicon's chief executive officer. "We expect this important innovation to be commercially available in the U.S. market by the end of June 2023."

The approval is based on two randomized, double-blind, placebo-controlled Phase 3 cardiovascular outcomes studies of INPEFA in patients with heart failure or at risk of heart failure. Together, SOLOIST-WHF (Worsening Heart Failure) and SCORED enrolled almost 12,000 patients. Results from SOLOIST-WHF showed that INPEFA significantly reduced risk of the composite of hospitalizations for heart failure, urgent visits for heart failure, and cardiovascular death by 33% compared to placebo in patients who had been recently hospitalized for worsening heart failure.

INPEFA is an inhibitor of both sodium-glucose co-transporter type 2 (SGLT2) and type 1 (SGLT1).

Source: https://www.lexpharma.com/media-center/news/2023-05-26-lexicon-announces-fda-approval-of-inpefa-sotagliflozin-for-treatment-of-heart-failure

Dupixent® (Dupilumab) Late-Breaking Phase 3 COPD Results Presented at ATS and Simultaneously Published in the New England Journal of Medicine

Sanofi, May 21, 2023

Dupixent® (dupilumab) late-breaking Phase 3 COPD results presented at ATS and simultaneously published in the New England Journal of Medicine

- Dupixent is the first and only investigational biologic for COPD that has demonstrated a significant reduction in moderate or severe acute exacerbations by 30% compared to placebo
- Dupixent is the first and only investigational biologic for COPD that has significantly improved lung function at 12 and 52 weeks, with numerical improvements seen as early as 2 weeks
- Dupixent significantly improved quality of life, with numerical improvements as early as 4 weeks after initiating treatment, and respiratory symptoms
- COPD is the third leading cause of death worldwide, with no new treatment approaches approved in more than a decade; trial enrolled patients with moderate-to-severe disease and evidence of type 2 inflammation (i.e., blood eosinophils ≥300 cells/µL)

Paris and Tarrytown, N.Y. May 21, 2023. Positive Phase 3 results evaluating the investigational use of Dupixent® (dupilumab) compared to placebo in adults currently on maximal standard-of-care inhaled therapy (triple therapy) with uncontrolled chronic obstructive pulmonary disease (COPD) and evidence of type 2 inflammation were shared today in the 2023 American Thoracic Society (ATS) International Conference session "New England Journal of Medicine and JAMA. Discussion on the Edge: Reports of Recently Published Pulmonary Research" and simultaneously published in the *New England Journal of Medicine* (*NEJM*). These results will also be presented in the "Breaking News: Clinical Trial Results in Pulmonary Medicine" session on May 22.

Source: https://www.sanofi.com/en/media-room/press-releases/2023/2023-05-21-18-17-12-2672904

Vanda Pharmaceuticals Reports Results from a Phase III study of Tradipitant in Motion Sickness

May 25, 2023

WASHINGTON, May 25, 2023 /PRNewswire/ -- Vanda Pharmaceuticals Inc. (Vanda) (Nasdaq: VNDA) today announced the results from its Phase III study of tradipitant in motion sickness, confirming the previously reported results demonstrating that tradipitant is effective in the prevention of vomiting associated with motion sickness. The Phase III study was conducted in real-world conditions on boats in the coastal waters of the United States (U.S.).

The Motion Syros study was a multicenter, randomized, double-blind, placebo-controlled study where 365 participants embarked on boat trips under varied sea conditions and received tradipitant 170 mg, tradipitant 85 mg, or placebo. Study participants had a prior history of motion sickness and were distributed across thirty-four boat trips that took place between November 2021 and April 2023. Sea conditions and participant evaluation of the symptoms of motion sickness were recorded for each trip. The primary endpoint of the study was the effect of tradipitant on vomiting induced by motion sickness.

Both 170 mg and 85 mg tradipitant doses were shown to be superior to placebo in preventing vomiting with only 18.3% and 19.5% of participants experiencing vomiting on tradipitant 170 mg and 85 mg respectively, as compared to 44.3% of participants on placebo ($p < 0.0001$ for both).

Motion sickness remains an unmet need as various pharmacological and non-pharmacological interventions suffer from low efficacy, substantial side effects, or both. The U.S. Food and Drug Administration (FDA) has not approved a new medication for motion sickness in over forty years, since the approval of scopolamine, a transdermal patch placed behind the ear, in 1979.

Vanda plans to continue the motion sickness clinical program and pursue FDA approval upon completion of additional efficacy and safety studies.

Table 1: Results of Motion Syros study for the Overall population across all sea conditions

		% Vomiting	Difference v. Placebo	P-value
Tradipitant 170 mg	n=120	18.3 %	26.0 %	< 0.0001
Tradipitant 85 mg	n=123	19.5 %	24.8 %	< 0.0001
Placebo	n=122	44.3 %		

Source: https://vandapharmaceuticalsinc.gcs-web.com/node/15401/pdf

Link Between Mental Stress and Inflammatory Diseases Clarified

Cell, May 25, 2023

Mental health profoundly impacts inflammatory responses in the body. This is particularly apparent in inflammatory bowel disease (IBD), in which psychological stress is associated with exacerbated disease flares. Here, we discover a critical role for the enteric nervous system (ENS) in mediating the aggravating effect of chronic stress on intestinal inflammation. We find that chronically elevated levels of glucocorticoids drive the generation of an inflammatory subset of enteric glia that promotes monocyte- and TNF-mediated inflammation via CSF1. Additionally, glucocorticoids cause transcriptional immaturity in enteric neurons, acetylcholine deficiency, and dysmotility via TGF-β2. We verify the connection between the psychological state, intestinal inflammation, and dysmotility in three cohorts of IBD patients. Together, these findings offer a mechanistic explanation for the impact of the brain on peripheral inflammation, define the ENS as a relay between psychological stress and gut inflammation, and suggest that stress management could serve as a valuable component of IBD care.

Source: https://www.cell.com/cell/fulltext/S0092-8674(23)00475-0?

nature computational science

Article

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The high-dimensional space of human diseases built from diagnosis records and mapped to genetic loci

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Gengjie Jia[1,20,21], Yu Li[2,3,4,20], Xue Zhong[5], Kanix Wang[6,7], Milton Pividori[6,8], Rabab Alomairy[9,10], Aniello Esposito[11], Hatem Ltaief[9], Chikashi Terao[12,13,14], Masato Akiyama[12,15], Koichi Matsuda[16], David E. Keyes[9], Hae Kyung Im[6], Takashi Gojobori[2,17], Yoichiro Kamatani[12,16], Michiaki Kubo[12], Nancy J. Cox[5], James Evans[18], Xin Gao[2,3,21] & Andrey Rzhetsky[6,19,21]

Human diseases are traditionally studied as singular, independent entities, limiting researchers' capacity to view human illnesses as dependent states in a complex, homeostatic system. Here, using time-stamped clinical records of over 151 million unique Americans, we construct a disease representation as points in a continuous, high-dimensional space, where diseases with similar etiology and manifestations lie near one another.

We use the UK Biobank cohort, with half a million participants, to perform a genome-wide association study of newly defined human quantitative traits reflecting individuals' health states, corresponding to patient positions in our disease space. We discover 116 genetic associations involving 108 genetic loci and then use ten disease constellations resulting from clustering analysis of diseases in the embedding space, as well as 30 common diseases, to demonstrate that these genetic associations can be used to robustly predict various morbidities.

Source: https://www.nature.com/articles/s43588-023-00453-y

ASCO Abstracts and Oncology News

McCormick Place Chicago. Source: Getty Images.

Evaxion Personalized Vaccine + PD-1 Inhibitor Shows Strong Phase 1 Responses

EVAXION

COPENHAGEN, Denmark, May 25, 2023 (GLOBE NEWSWIRE) -- Evaxion Biotech A/S (NASDAQ: EVAX) ("Evaxion" or the "Company"), a clinical-stage biotechnology company specializing in the development of AI-powered immunotherapies, to present promising clinical data from its EVX-01 Phase 1 clinical trial in metastatic melanoma on June 3, at the 2023 ASCO annual meeting, in Chicago, Illinois.

"We are excited to report that the EVX-01 Phase 1 trial achieved its primary objectives. EVX-01 was well tolerated and induced a higher objective response rate than previously reported for standard of care treatment. Importantly, EVX-01 induced a broad immune response that correlated with clinical outcome, which is very encouraging for the further development of Evaxion's personalized cancer vaccine programs," said Per Norlén, CEO at Evaxion.

The Phase 1 trial aimed to evaluate the safety, feasibility, and immunogenicity of the personalized cancer vaccine EVX-01 in patients with metastatic melanoma, in combination with a check-point inhibitor. EVX-01 builds on Evaxion´s proprietary AI platform, PIONEER™, which plays a central role in identifying unique and immunogenic neoantigens for each patient.

In brief, the study showed the following:

- Eight out of the twelve patients (67%) had an objective response, including two complete responders and six partial responders
- Broad neoantigen T-cell responses were induced in all 12 patients
- 58% of vaccine neoantigens induced an immune response, of which 85% were *de novo* responses
- EVX-01 treatment was well tolerated with only mild grade 1-2 adverse events (AEs) being related to the vaccine
- The personalized vaccine was successfully manufactured within 8 -weeks for all patients

Per Norlén concluded: "The promising clinical and immunological results of the study validate the precision of the AI platform PIONEER™ in selecting immunogenic neoantigens for personalized cancer vaccine candidates. The successful completion of the Phase 1 trials is a significant milestone for Evaxion, reaffirming the company's commitment to deliver innovative therapies for cancer patients. Looking ahead, we expect to report interim results from our ongoing Phase 2 study of EVX-01 in Q4 2023."

Source; https://www.evaxion-biotech.com/press-releases/255-23-evaxion-announces-promising-clinical-phase-1-data-for-its-personalized-cancer-vaccine-evx-01

Geron ASCO Data for Imetelstat Hint at Superiority for the Treatment of Lower-Risk MDS Patients

***Title:* "Results from a Phase 3, Randomized, Double-Blind, Placebo-Controlled Study of Imetelstat in Patients (pts) With Heavily Transfusion Dependent (TD) Non-Del(5q) Lower-Risk Myelodysplastic Syndromes (LR-MDS) Relapsed/Refractory (R/R) to Erythropoiesis Stimulating Agents (ESA)."**

Presenter: Amer Methqal Zeidan, Yale School of Medicine

The abstract recaps top-line results from IMerge Phase 3 with a data cut-off of October 2022. As reported in January 2023, the primary endpoint of 8-week transfusion independence (TI) was met with high statistical significance (P<0.001) for imetelstat-treated patients (39.8%) vs. placebo (15.0%). Key secondary endpoint of 24-week TI and hematologic improvement erythroid (HI-E) under 2018 IWG criteria were also met with high statistical significance (P<0.001 for each) for imetelstat-treated patients vs. placebo.

In addition, the rate of 8-week TI was significantly higher with imetelstat vs. placebo across subgroups, including ring sideroblast (RS) negative patients. Median TI duration was significantly longer for imetelstat-treated patients vs. those on placebo (51.6 vs 13.3 weeks, P< 0.001). Patients receiving imetelstat had significantly higher mean hemoglobin (P < 0.001) and fewer transfusions (P = 0.042) over time than those on placebo.

In three of four genes frequently mutated in MDS, variant allele frequency (VAF) reduction was significantly greater in patients treated with imetelstat than placebo: *SF3B1* (P< 0.001), *TET2* (P= 0.032), *DNMT3A* (P= 0.019) and *ASXL1* (P= NS). *SF3B1* VAF reduction correlated with longer TI duration (P< 0.001).

Source: https://ir.geron.com/investors/press-releases/default.aspx

ASCO Abstract for Regeneron Lag-3 mAb Highly Impressive in Advanced Melanoma

Evaluate Vantage, May 25, 2023

With interest in the Lag3 mechanism recently piqued by lung cancer data on Immutep's eftilagimod alpha, Regeneron is working hard to stay ahead of the pursuing pack. And data just unveiled in an Asco abstract confirm the leading activity of its contender, fianlimab.

That molecule's Libtayo combo had already impressed at last year's Esmo meeting, with 64% ORR in front-line melanoma beating Bristol Myers Squibb's Opdualag across trials. But the Asco data are intriguing for another reason: fianlimab plus Libtayo appears active in melanoma patients who have already progressed on PD-(L)1 blockade in the perioperative setting.

In earlier iterations of this dataset "we couldn't believe how good the results were", Israel Lowy, Regeneron's senior vice-president of oncology translational and clinical sciences, tells Evaluate Vantage. And now his optimism is holding up: "I don't know why our efficacy is better than Bristol's, but we'll take it."

Source: https://www.evaluate.com/vantage/articles/news/trial-results-conferences/asco-2023-regeneron-nips-bristols-heels-lag3

Immutep's Lag-3 Effective in Head and Neck Cancer Treatment

- New data published from Part C of TACTI-002 Phase II Trial evaluating eftilagimod alpha plus pembrolizumab in metastatic 2nd line head and neck squamous cell carcinoma
- Deep, durable responses seen across all PD-L1 subgroups with a 13.5% Complete Response rate and median Duration of Response not yet reached (minimum follow-up of 17 months)
- In the overall patient population, regardless of PD-L1 expression, a strong response rate of 29.7% and 12-month overall survival rate of 46.0% were achieved
- In patients with a PD-L1 Combined Positive Score of ≥20, a very promising response rate of 60% and 12-month overall survival rate of 66.7% were achieved
- Treatment was safe and well tolerated with no new safety signals

Conclusions:

Efti + pembrolizumab is safe, showing encouraging antitumor activity in platinum and partially cetuximab pre-treated, 2nd line HNSCC patients. TACTI-003 (NCT04811027) a randomized study in 1st line HNSCC is currently recruiting. Response by iRECIST: Clinical trial information: NCT03625323.

	Overall (ITT) N=37	PD-L1 CPS ≥20 N=15	PD-L1 CPS <20 N=17
CR, n (%)	5 (14)	4 (27)	1 (5.9)
PR, n (%)	6 (16)	5 (33)	1 (5.9)
ORR, n (%)	11 (30)	9 (60)	2 (11.8)
DCR, n (%)	14 (38)	9 (60)	4 (23.5)
mPFS, mo	2.1	13.6	2.0
6-mo PFS rate, (%)	32.4	53.3	17.7
mOS, mo	8.7	15.5	7.5
12-mo OS rate, (%)	46.0	66.7	35.3
mDoR, mo	NR	NR	12.0
12-mo DoR rate, (%)	80.0	87.5	50.0

NR: not reached.

Source: https://meetings.asco.org/abstracts-presentations/218549, https://www.immutep.com/detail/immutep-announces-publication-of-abstracts-for-asco-2023-annual-meeting.html

Merck-Kelun Trop2 ADC Shines in Advanced Lung Cancer Study

ASCO Abstract, May 25, 2023, "SKB264 (TROP2-ADC) for the treatment of patients with advanced NSCLC: Efficacy and safety data from a phase 2 study"

This is a Phase 1/2, multicenter dose-escalation/expansion study in pts with relapsed or refractory locally advanced/metastatic NSCLC and other tumor types (NCT04152499). All NSCLC pts received SKB264 at 5 mg/kg IV Q2W. Tumor assessments based on RECIST 1.1 were performed every 8 weeks by investigators.

As of February 9th, 2023, 43 pts (63% male, 88% ECOG PS 1, median age 58 yrs [44-74]) were enrolled. Median follow-up was 11.5 months (mo; 95% CI, 10.4-12.2). Median treatment duration was 5.7 mo (range, 0.5-14.1). **Among 39 response-evaluable pts, the ORR was 44% (17/39, 15 confirmed and 2 pending confirmation),** median DoR was 9.3 mo (range, 1.3+ to 11.2+), 6-month DoR rate was 77%. For EGFR wild type subgroup (previously received median 2 lines of therapy including anti-PD-1/L1), the ORR was 26% (5/19), DCR was 89% (17/19), median PFS was 5.3 mo, and 9-month OS rate was 80.4%. For subgroup with TKI resistant EGFR mutant NSCLC (50% also failed at least one line of chemotherapy), the ORR was 60% (12/20), DCR was 100% (20/20), median PFS was 11.1 mo, and 9-month PFS rate was 66.7%. 67.4% (29/43) of pts had Grade ≥ 3 treatment-related adverse events (TRAEs). The most common Grade ≥3 TRAEs (occurred in ≥5% of pts) were neutrophil count decreased (32.6%), anemia (30.2%), white blood cell count (WBC) decreased (23.3%), stomatitis (9.3%), rash (7.0%), and lymphocyte count decreased (7.0%). Grade 4 TRAEs occurred only for neutropenia and WBC decreased. Most of the hematology toxicity occurred within the first two months of treatment and resolved after treatment with granulocyte colony stimulating factor or erythropoietin without blood transfusions. 23.3% (10/43) of the pts experienced dose reduction due to TRAEs. No neuropathy or drug-related ILD/pneumonitis was reported. No TRAEs led to treatment discontinuation or death.

Source: https://meetings.asco.org/abstracts-presentations/218898

Roche TIGIT mAb Clobbers Standard of Care in Liver Cancer

ASCO Abstract, May 25, 2023, "Results from the MORPHEUS-liver study: Phase Ib/II randomized evaluation of tiragolumab (tira) in combination with atezolizumab (atezo) and bevacizumab (bev) in patients with unresectable, locally advanced or metastatic hepatocellular carcinoma (uHCC)."

Atezo + bev is the current first-line standard of care for uHCC based on the IMbrave150 study, which demonstrated superior overall survival, progression-free survival (PFS), and objective response rate (ORR) vs sorafenib (Finn, et al. New Engl J Med 2020; Cheng, et al. J Hepatol 2022). TIGIT is a novel inhibitory immune checkpoint present on activated T cells and NK cells. Tira (anti-TIGIT) may synergize with other immunotherapies, such as PD-L1/PD-1 inhibitors. The MORPHEUS platform comprises multiple phase Ib/II trials to identify early efficacy signals and safety of treatment combinations across cancers. Here we report data from a cohort of the MORPHEUS-liver study (NCT04524871) evaluating the combination of tira + atezo + bev vs a control arm (atezo + bev) in patients with uHCC.

A total of 58 patients were randomized (tira + atezo + bev, n=40; atezo + bev, n=18). As of 28 November 2022, median follow up was 14.0 months in the tira + atezo + bev arm and 11.8 months in the control arm. **Confirmed ORR was higher in the tira + atezo + bev arm (42.5%) vs the control arm (11.1%).** Median PFS was longer with tira + atezo + bev (11.1 months; 95% CI: 8.2–NE) vs control (4.2 months; 95% CI: 1.6–7.4), corresponding to a PFS hazard ratio (HR) of 0.42 (95% CI: 0.22–0.82). A similar pattern of increased ORR and PFS was observed for the treatment arms in both PD-L1+ (n=23) and PD-L1– (n=27) subgroups. For tira + atezo + bev vs control arm, grade 3/4 treatment-related AEs were 27.5% vs 33.3% and AEs leading to any treatment discontinuation were 22.5% vs 22.2%, respectively.

Source: https://meetings.asco.org/abstracts-presentations/219773

Use of Precision Oncology Drugs Suboptimal

ASCO Abstract, May 25, 2023, "Real-world rates of FDA-approved targeted therapy and immunotherapy prescriptions for metastatic colorectal cancer patients in the VA's National Precision Oncology Program (NPOP)."

Colorectal cancer is the fourth most common cancer among Veterans and the third leading cause of cancer-related death in the USA. Use of comprehensive genomic profiling (CGP) to guide administration of FDA-approved biomarker directed therapies can improve outcomes among metastatic CRC (mCRC) patients. We sought to compute the rates of actionable biomarkers and prescriptions of associated FDA-approved therapies among Veterans in NPOP.

Rates of actionable biomarkers associated with FDA-approved therapies were as follows: NRAS/KRAS/BRAF wildtype (34.4%), TMB-H (9.6%), BRAF V600E (7.7%), MSI-H (5.6%), TMB-H and MSI-H (5.6%), and NTRK Fusion or rearrangement (0.3%). Among the 424 eligible patients, the frequencies of FDA-approved CGP-directed therapy prescriptions were as follows: MSI-H (70.7%), TMB-H (47.4%), NRAS/KRAS/BRAF wildtype (38.5%), and BRAF V600E (17.1%). Across all included biomarkers, African Americans (53.4%) were more likely to receive these therapies than whites (36.8%); and patients with prescriptions were more likely to be younger that those without (all $p < 0.01$).

Nearly 30% of patients with MSI-H mCRC did not receive efficacious ICIs, and though disease laterality data was not readily available, a substantial number of eligible patients also did not receive EGFR inhibitors. This underuse of EGFR inhibitors has been reported previously.There were racial and age differences in prescription rates. Further studies should evaluate the barriers to prescribing CGP-directed therapies in the care of mCRC patients. Keywords: molecular testing, metastatic colorectal cancer, comprehensive genomic profiling, actionable biomarkers, FDA approved therapies, veterans.

Source: https://meetings.asco.org/abstracts-presentations/219773

IQVIA Institute Report on Global Oncology Trends

Young girl with cancer. Source: Getty Images.

IQVIA Institute Publishes Report on Global Oncology Trends Last Week

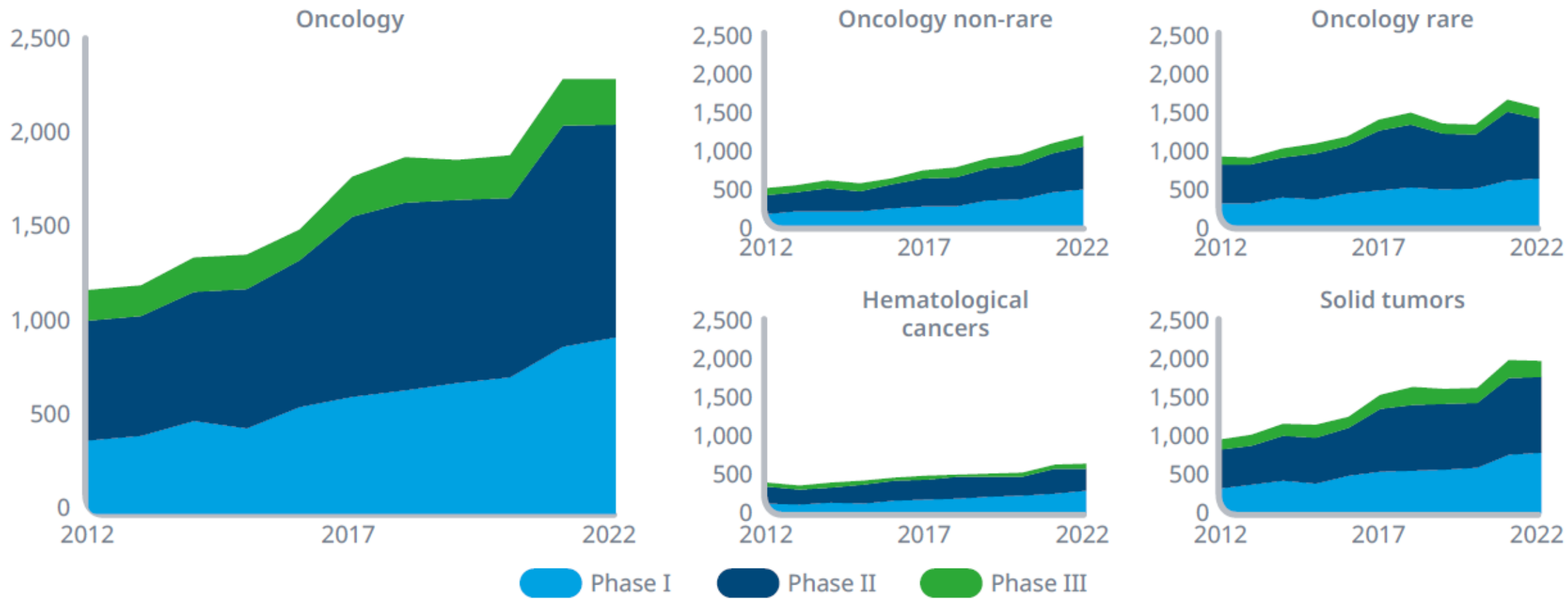
Key findings:

1. Oncology trial starts remained at historically high levels in 2022, up 22% from 2018
2. The global number of treated patients has increased annually by an average of 5% over the past five years
3. Spending on cancer medicines is expected to reach $375Bn globally by 2027, up from $196Bn in 2022
4. Oncology clinical trial representation for Black/African American and Hispanic patients was 80% and 61% below the 2019 U.S. cancer incidence respectively
5. Emerging biopharma companies led innovation in oncology in 2022 and account for 71% of the pipeline

Source: https://www.iqvia.com/insights/the-iqvia-institute/reports/global-oncology-trends-2023

Oncology trial starts remained at historically high levels in 2022, up 22% from 2018 and primarily focused on rare cancers

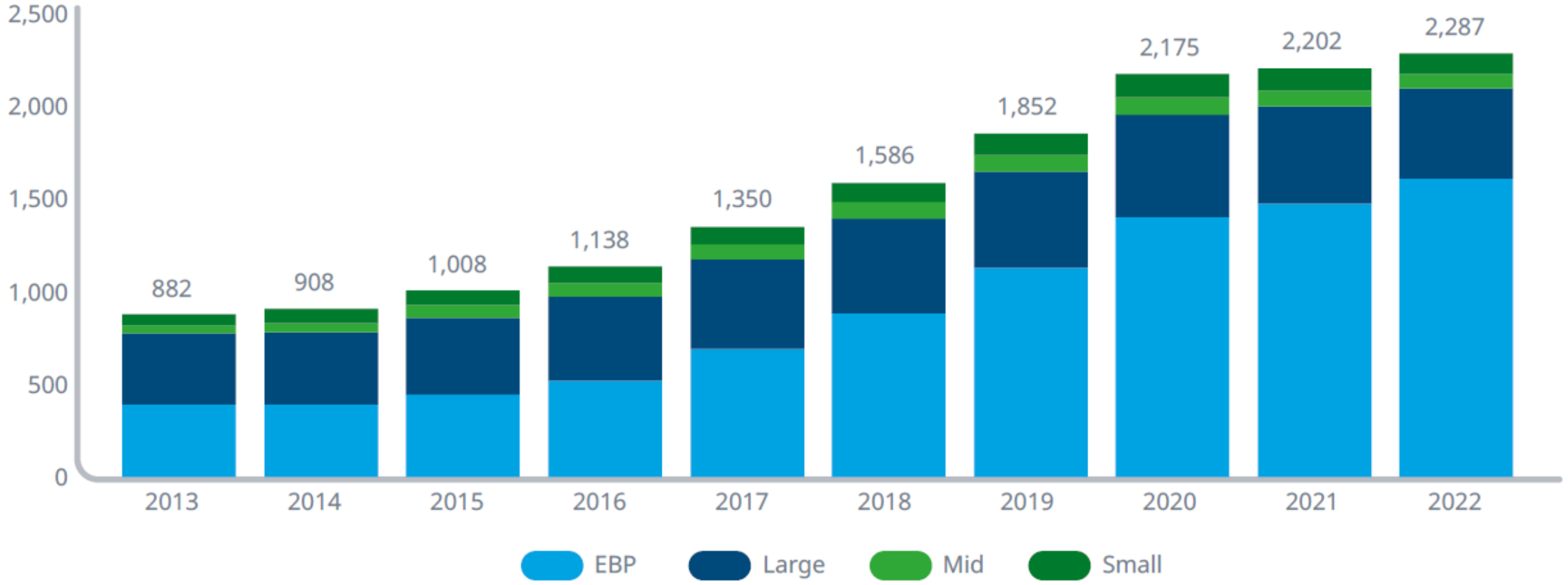
Exhibit 1: Clinical trial starts by year, 2012–2022



Source: Citeline Trialtrove, IQVIA Institute, Jan 2023.

Emerging biopharma companies were responsible for 71% of the oncology pipeline in 2022, up from 45% a decade ago

Exhibit 2: Number of Phase I to regulatory submission oncology pipeline products by company segment, 2013–2022

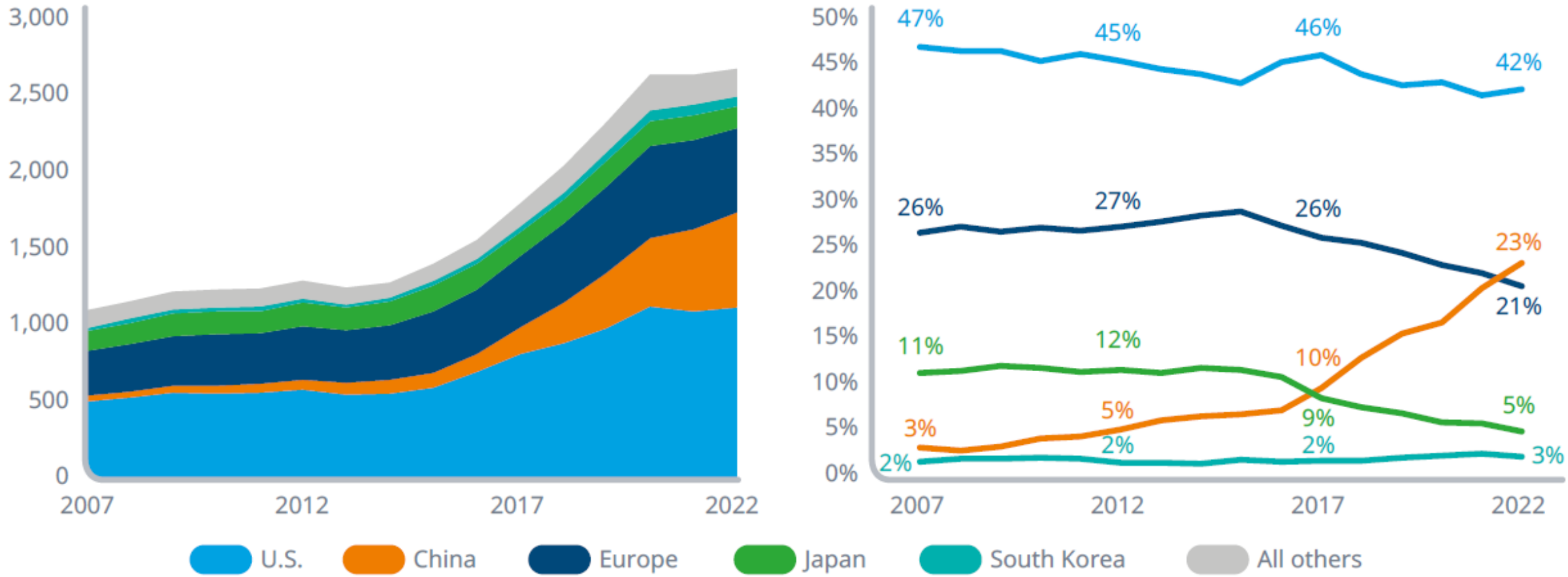


Source: IQVIA Pipeline Intelligence, Dec 2022; IQVIA Institute, Apr 2023.

Note: EBP = emerging biopharma

Drugs from China-headquartered companies have risen to 23% of the oncology pipeline from only 5% a decade ago

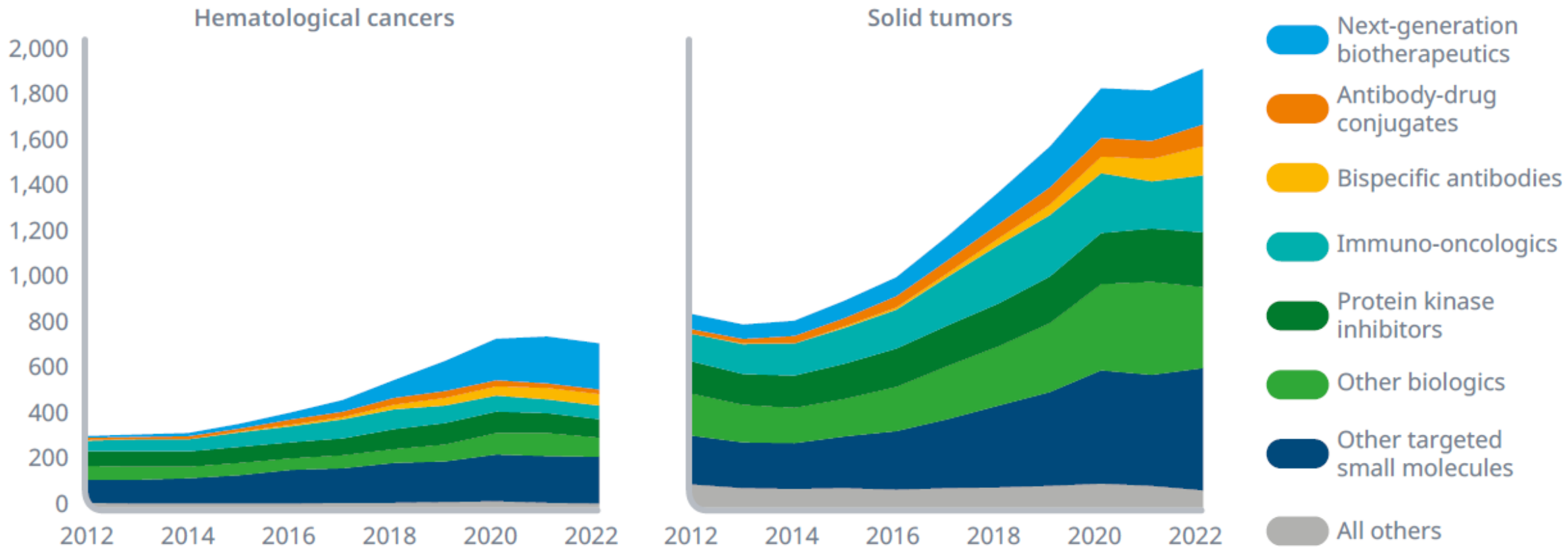
Exhibit 3: Number of oncology drugs over time and country share of pipeline Phase I to regulatory submission based on company headquarters location, 2007–2022



Source: IQVIA Pipeline Intelligence, Dec 2022; IQVIA Institute, Apr 2023.

Oncology development is focused on solid tumors with next-generation biotherapeutics growing across all cancers

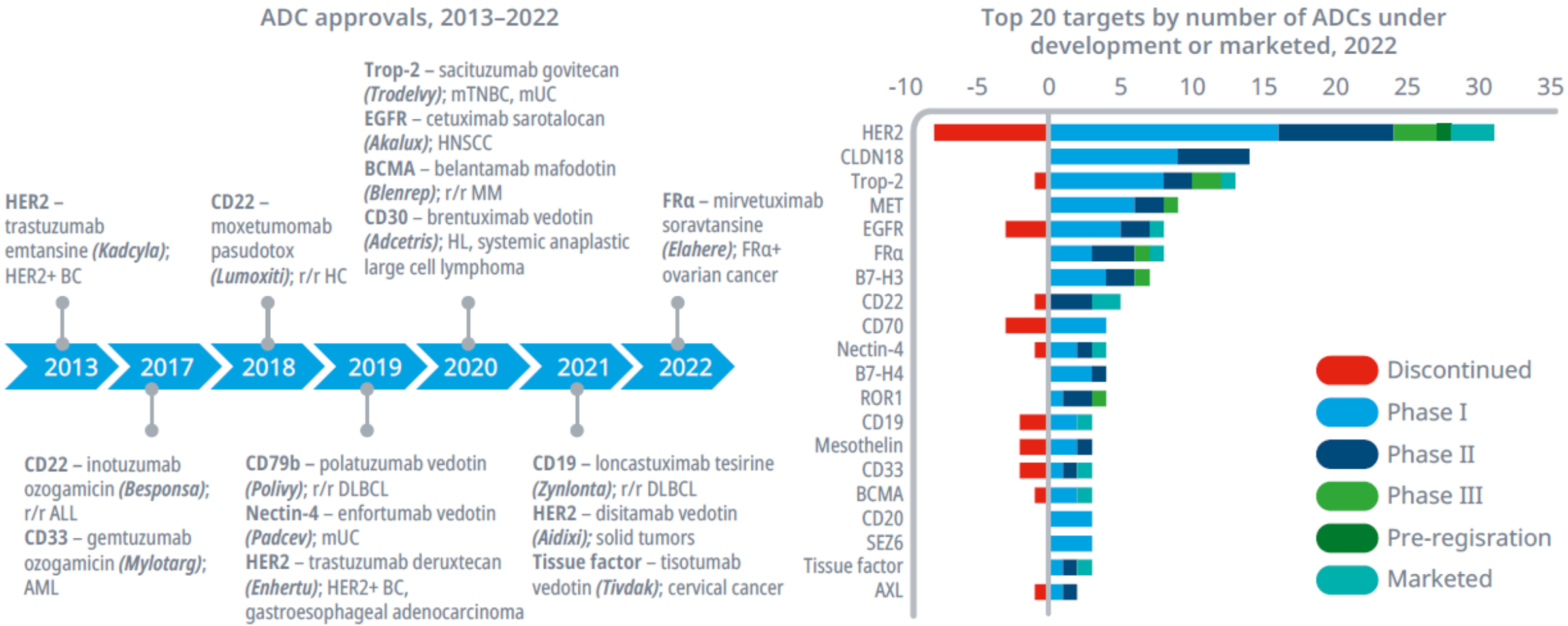
Exhibit 4: Oncology R&D pipeline Phase I to regulatory submission by type, 2012–2022



Source: IQVIA Pipeline Intelligence, Dec 2022; IQVIA Institute, Jan 2023.

Antibody-drug conjugates are emerging with significant efficacy across a broad range of targets with varying success

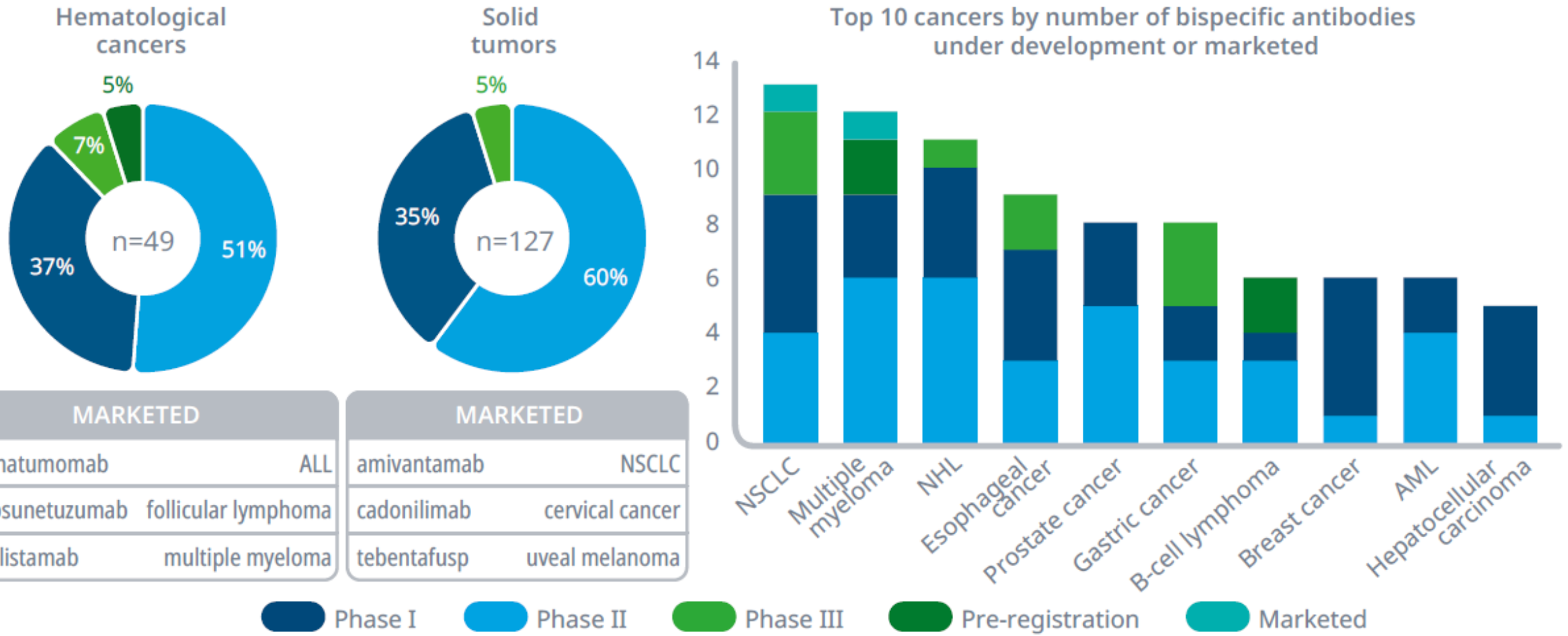
Exhibit 6: Antibody-drug conjugates approved and under development by target



Source: Citeline Trialtrove, IQVIA Pipeline Intelligence, IQVIA Institute, May 2023.

6 bispecific antibodies are marketed globally for oncology with many in development for rare hematological cancers

Exhibit 7: Bispecific antibody pipeline by tumor and phase, 2022



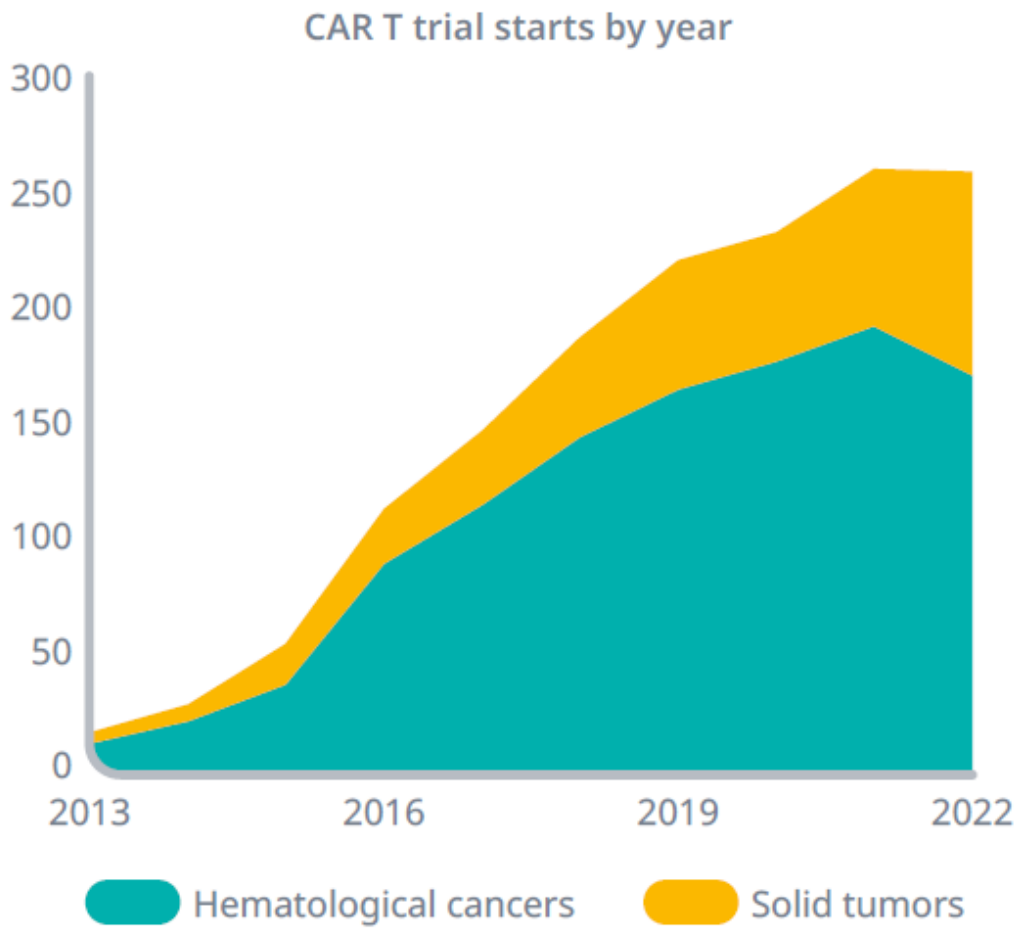
MARKETED	
blinatumomab	ALL
mosunetuzumab	follicular lymphoma
teclistamab	multiple myeloma

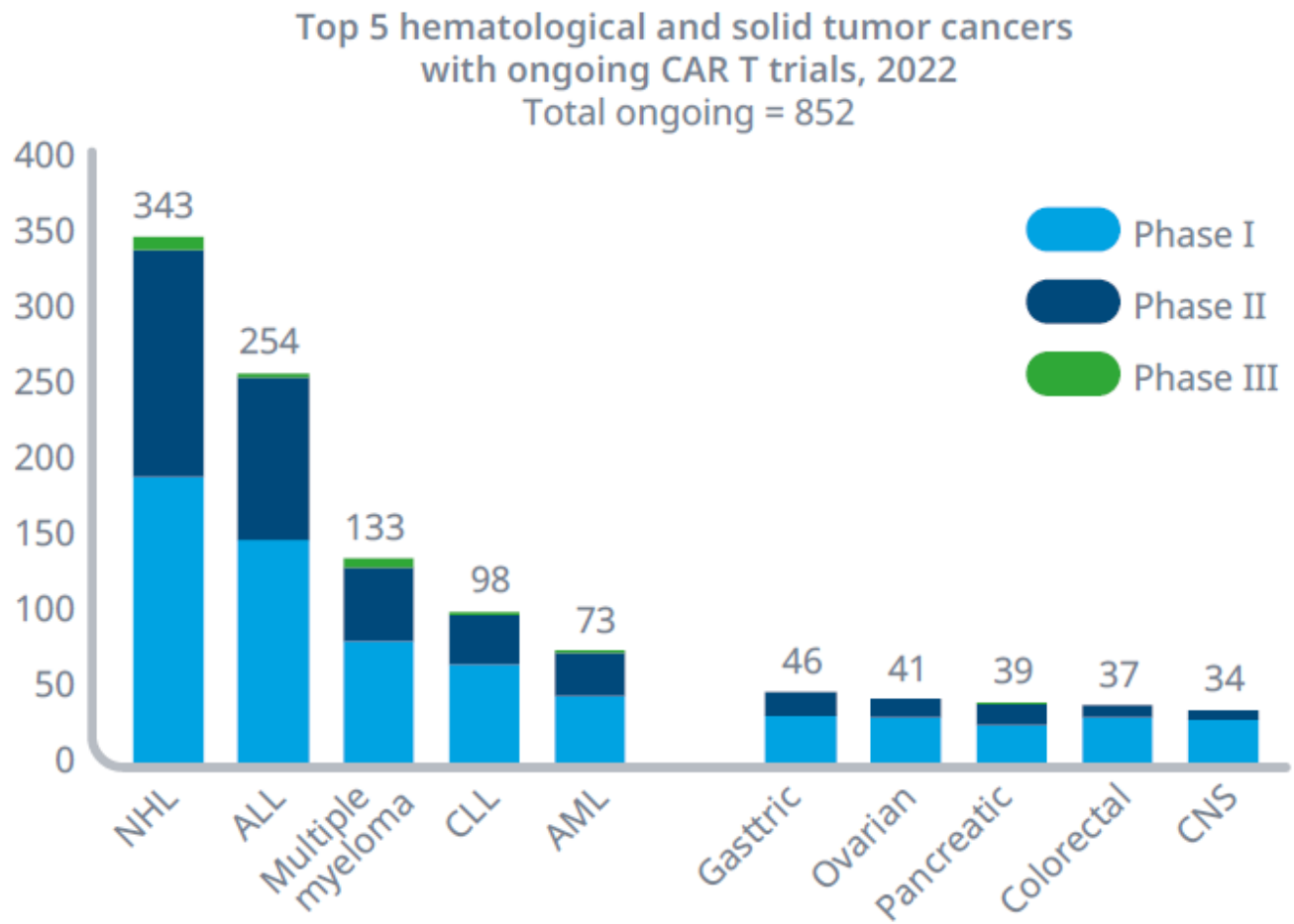
MARKETED	
amivantamab	NSCLC
cadonilimab	cervical cancer
tebentafusp	uveal melanoma

Source: IQVIA Pipeline Intelligence, Dec 2022; IQVIA Institute, Apr 2023.

Nearly 250 trials testing CAR T-cell therapies in oncology started in 2022 with a growing number across a range of solid tumors

Exhibit 9: Oncology CAR T-cell therapy clinical trial starts and ongoing trials by top tumors

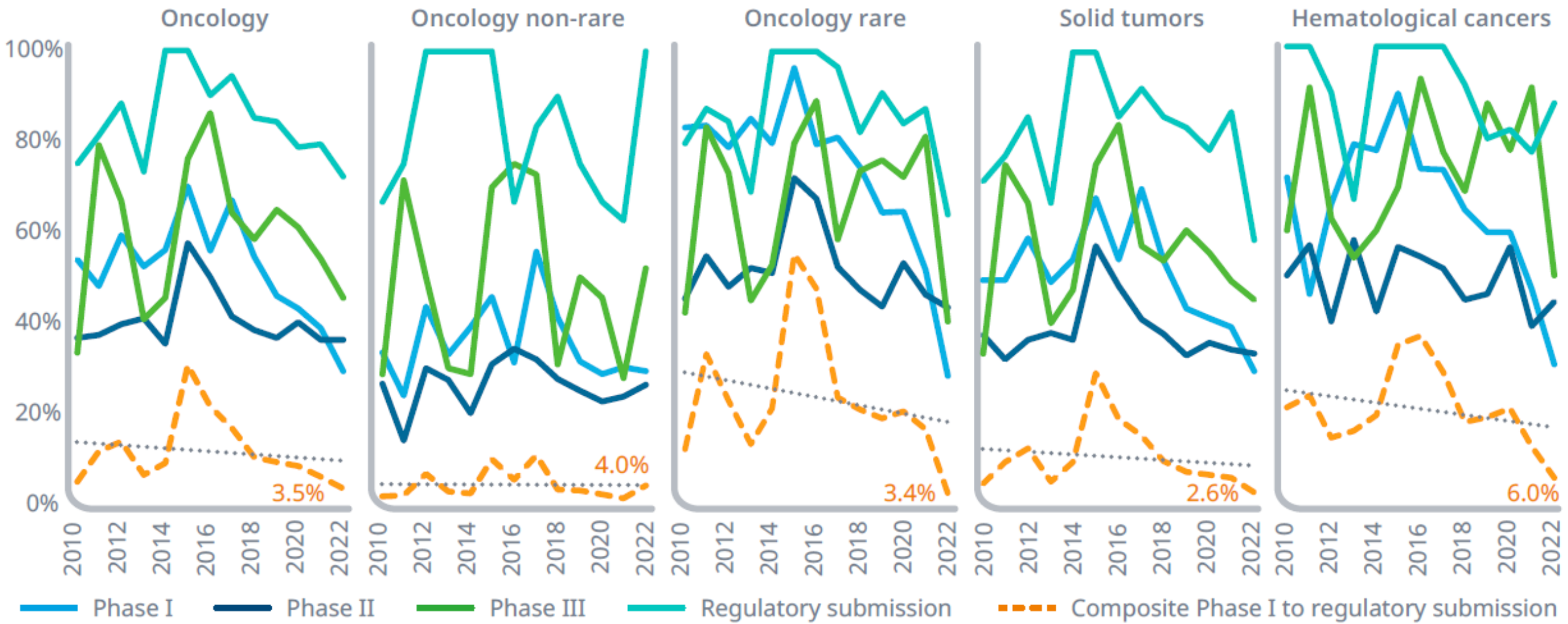




Source: Citeline Trialtrove, IQVIA Institute, Apr 2023.

Composite success rates in oncology have been trending down since 2015 while hematological cancers remain the highest

Exhibit 12: R&D phase and composite success rates by therapy area, 2010–2022



Source: IQVIA Pipeline Intelligence, Dec 2022; IQVIA Institute, Apr 2023.

There were 10 new cancer medicines launched in the U.S. in 2022, with 9 that were orphan designated

Exhibit 27: Oncology novel active substances launched in the U.S. in 2022

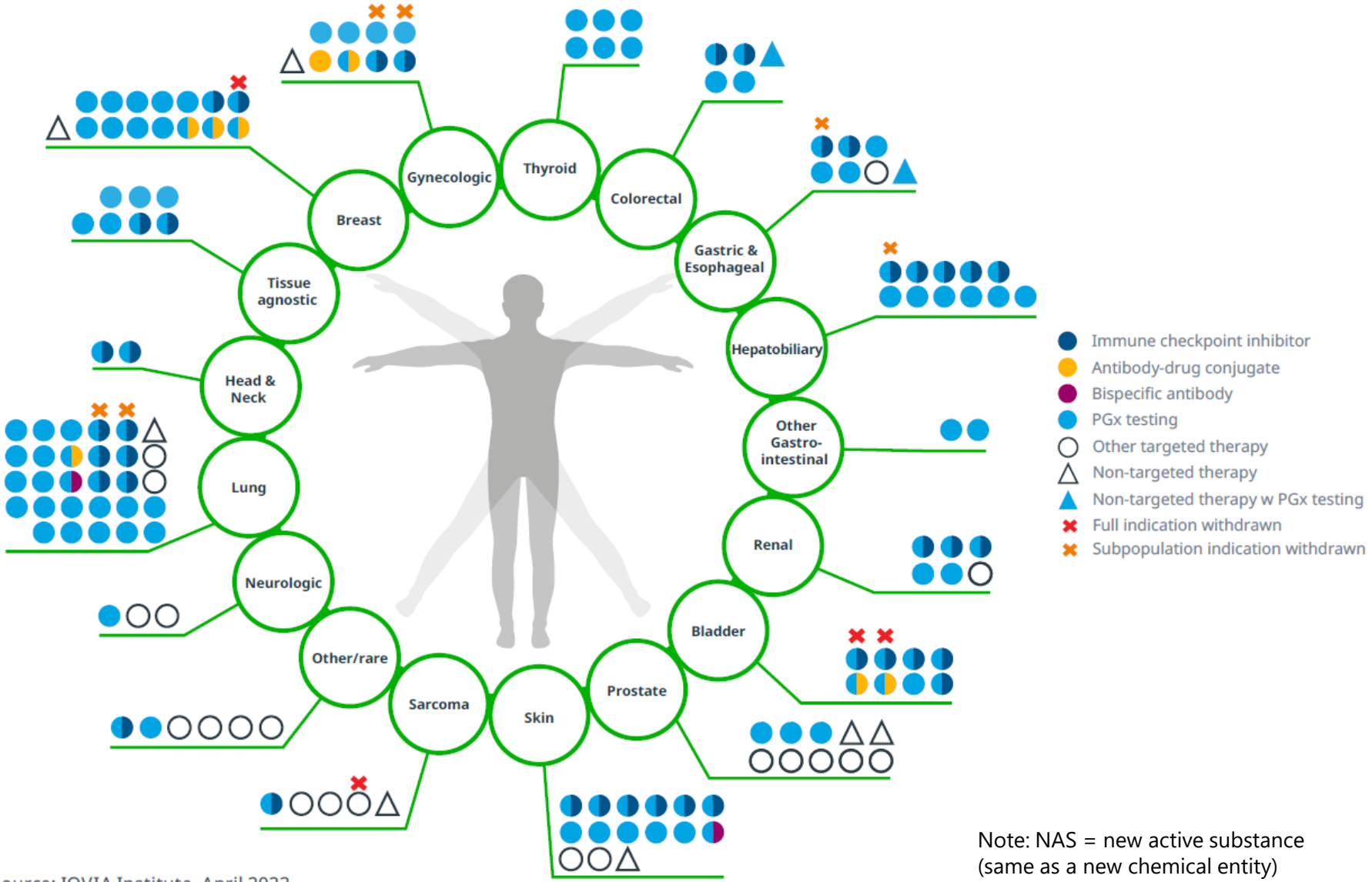
*ATTRIBUTES KEY: 1 = Oral 2 = Biologic 3 = Specialty 4 = Next-gen biotherapeutic 5 = Orphan 6 = First-in-class 7 = Expedited review 8 = U.S. patent to launch ≤5 years 9 = EBP originated 10 = EBP launched

THERAPY AREA	INDICATION	MOLECULE	BRAND	ATTRIBUTES									
				1	2	3	4	5	6	7	8	9	10
Oncology	Acute myeloid leukemia	olutasidenib	Rezlidhia	●		●		●			●	●	●
	FRα positive, platinum-resistant epithelial ovarian, fallopian tube, or primary peritoneal cancer	mirvetuximab soravtansine	Elahere		●	●		●	●	●		●	●
	Hepatocellular carcinoma	tremelimumab	Imjudo		●	●		●		●			
	Myelofibrosis	pacritinib	Vonjo	●		●		●		●		●	●
	Non-small cell lung cancer (NSCLC)	adagrasib	Krazati	●		●		●		●	●	●	●
	Prostate-specific membrane antigen (PSMA)-positive metastatic castration-resistant prostate cancer (mCRPC)	lutetium (177Lu) vipivotide tetraxetan	Pluvicto			●			●	●		●	
	Relapsed or refractory multiple myeloma	ciltacabtagene autoleucel	Carvykti		●	●	●	●		●		●	
		teclistamab	Tecvayli		●	●		●	●	●			
	Unresectable or metastatic melanoma	nivolumab + relatlimab	Opdualag		●	●		●	●	●			
	Unresectable or metastatic uveal melanoma	tebentafusp	Kimmtrak		●	●		●	●	●		●	●
Totals				3	6	10	1	9	5	9	2	7	5

Source: IQVIA Institute, Apr 2023.

Since 2013, 89 NASs were launched in the U.S. to treat solid tumors with some approved for multiple indications

Exhibit 29: U.S. NASs in solid tumors launched 2013–2022 with indications, including those granted after initial launch

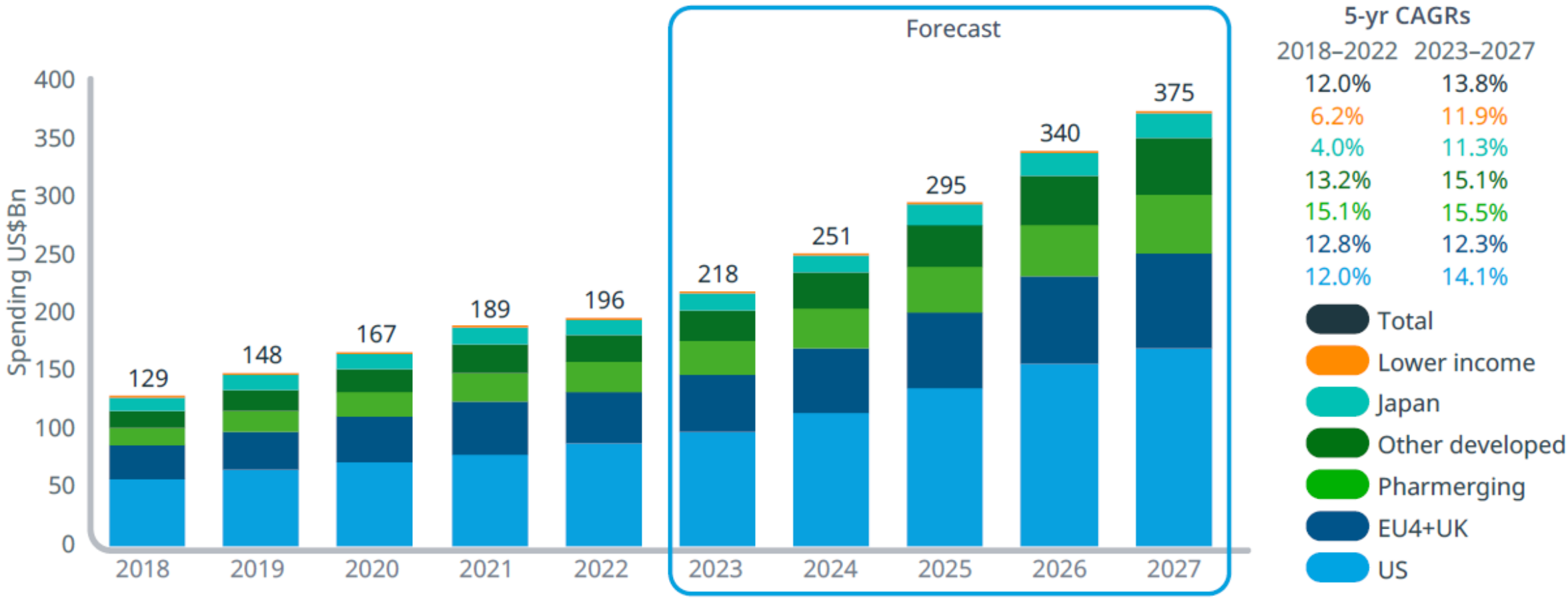


Source: IQVIA Institute, April 2023.

Note: NAS = new active substance (same as a new chemical entity)

Cancer medicine spending rose to $196Bn globally in 2022 and is expected to reach $375Bn by 2027

Exhibit 48: Oncology spending by region, US$Bn



Source: IQVIA Oncology Link, Apr 2023.

Chiesi Report on Burden of Rare Disease

Rare disease Day Imagery. Source: Getty Images.

May 25, 2023

The Burden of Rare Diseases: An Economic Evaluation

Pedro Andreu, PhD; Jenny Karam, PharmD; Caroline Child, BSc; Giacomo Chiesi, MBA; Gina Cioffi, JD

Key findings from the study

Rare diseases impose a substantial economic burden that is reduced by treatment availability.

- The burden of rare diseases is approximately 10x higher than mass market diseases on a per patient per year (PPPY) basis.
- A lack of treatment for a rare disease is associated with a 21.2% increase in total costs PPPY.
- The cost for 8.4 million patients in the U.S. impacted by 373 rare diseases considered in this analysis is estimated to be $2.2 trillion per year.
- Based on this estimate, the societal responsibility for all known rare diseases may be in the range of $7.2 trillion to $8.6 trillion per year. Investment in diagnostic tools, newborn screening, and development of new therapies is justified.
- Empirical studies need to consider many aspects of healthcare costs to gain a full picture of the overall burden of rare diseases.
- Access to therapies for people living with rare diseases generates significant value for society.

Source: https://chiesirarediseases.com/assets/pdf/chiesiglobalrarediseases.whitepaper-feb.-2022_production-proof.pdf
Also see: https://fortune.com/2023/05/25/why-the-underestimated-economic-burden-of-rare-diseases-could-be-costing-the-u-s-trillions-of-dollars/

Selected rare diseases across therapeutic areas

Metabolic disorders

- Fabry disease
- Gaucher disease type I
- Mucopolysaccharidosis (Hunter, Hurler)
- Ornithine transcarbamylase deficiency
- Phenylketonuria

Hematologic disorders

- Acquired aplastic anemia
- Acute intermittent porphyria
- Atypical hemolytic uremic syndrome
- Beta thalassemia major
- Sickle cell disease

Immunological disorders

- Autoimmune encephalitis
- Common variable immune deficiency
- Juvenile idiopathic arthritis
- Myasthenia gravis
- Pemphigus vulgaris

Congenital disorders

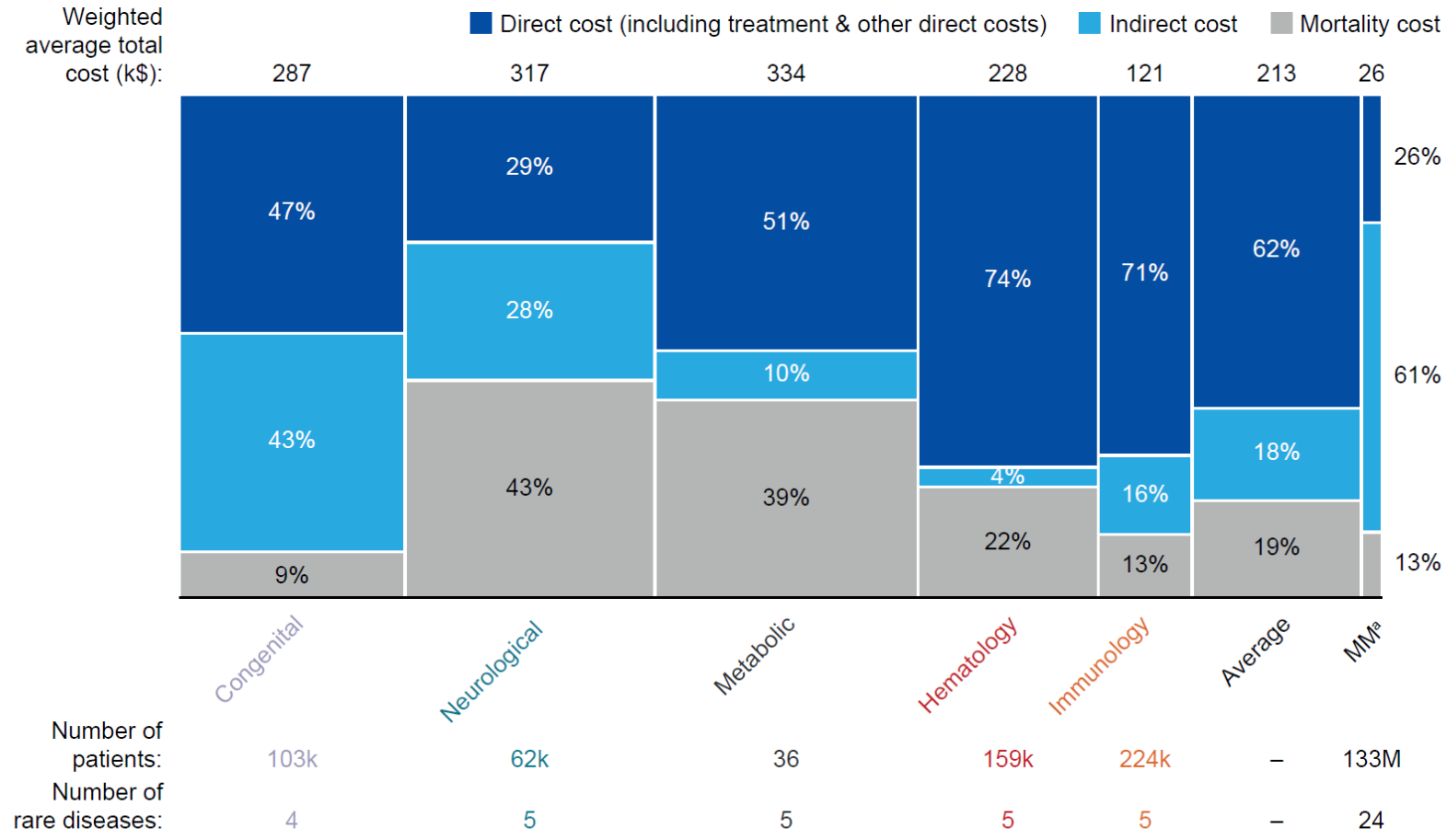
- Angelman syndrome
- Christianson syndrome
- Deletion 5p
- Fragile X syndrome

Neurological disorders

- Amyotrophic lateral sclerosis
- Ataxia telangiectasia
- Duchenne muscular dystrophy
- Early onset familial Alzheimer's disease
- Spinal muscular atrophy type I (proximal)

Source: https://chiesirarediseases.com/assets/pdf/chiesiglobalrarediseases.whitepaper-feb.-2022_production-proof.pdf
Also see: https://fortune.com/2023/05/25/why-the-underestimated-economic-burden-of-rare-diseases-could-be-costing-the-u-s-trillions-of-dollars/

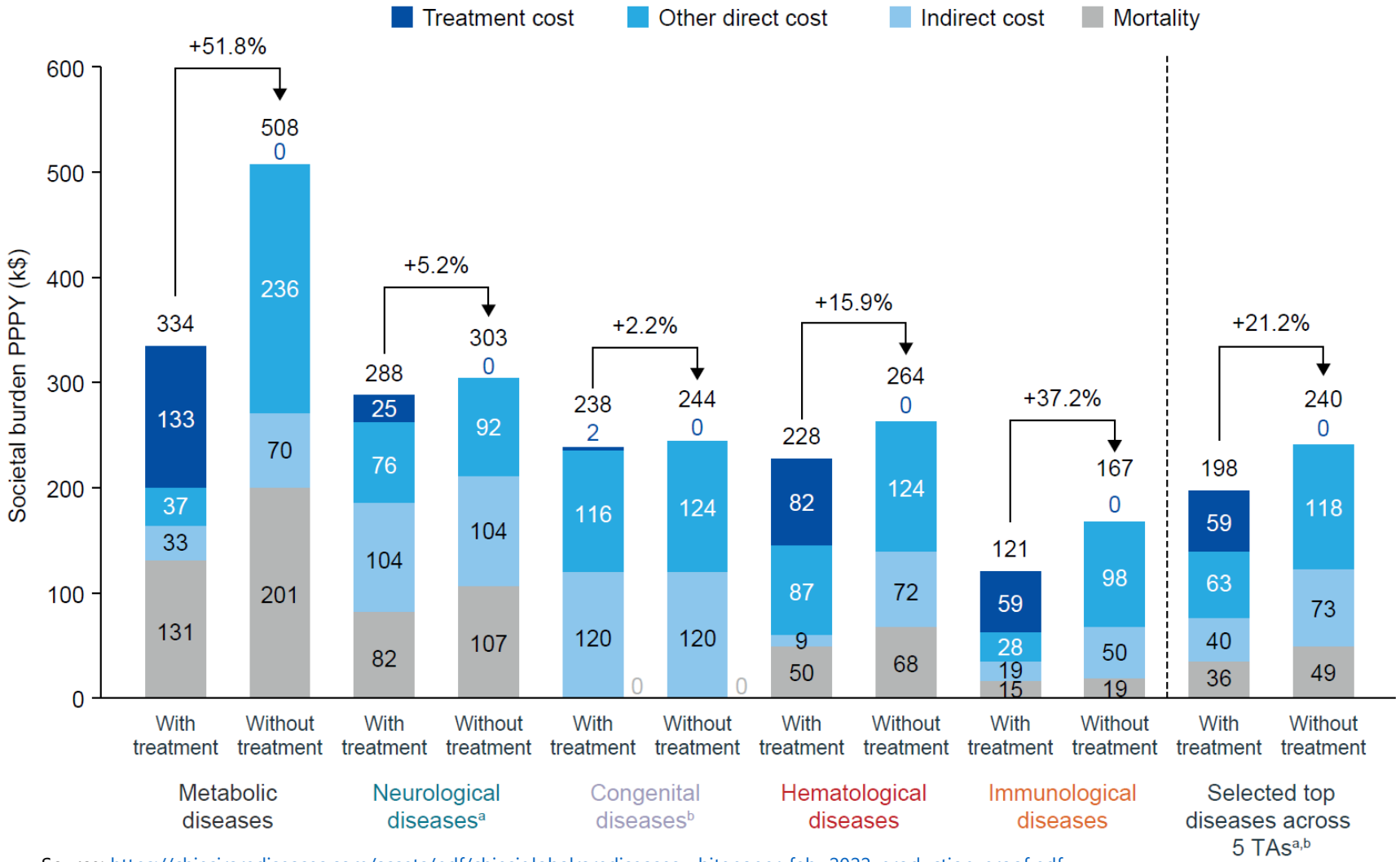
Average burden of rare disease therapeutic areas PPPY across 24 rare diseases



This study revealed that for 24 rare diseases selected for a deep-dive analysis the total cost to society is approximately $125 billion with an overall economic burden PPPY ranging from $121,000 to $334,000 (average overall cost of $266,000 PPPY), which is approximately 10x the cost associated with mass market diseases ($26,000 PPPY). Overall, burden was generally driven by direct and mortality costs. Indirect costs, while substantial, represent the smallest proportion of cost burden for rare diseases. The overall burden was highest for metabolic ($334,000 PPPY) and neurological disorders ($317,000 PPPY).

Source: https://chiesirarediseases.com/assets/pdf/chiesiglobalrarediseases.whitepaper-feb.-2022_production-proof.pdf
Also see: https://fortune.com/2023/05/25/why-the-underestimated-economic-burden-of-rare-diseases-could-be-costing-the-u-s-trillions-of-dollars/

Burden of Disease PPPY Across Rare Diseases With and Without Treatment and Value Assessment



Source: https://chiesirarediseases.com/assets/pdf/chiesiglobalrarediseases.whitepaper-feb.-2022_production-proof.pdf

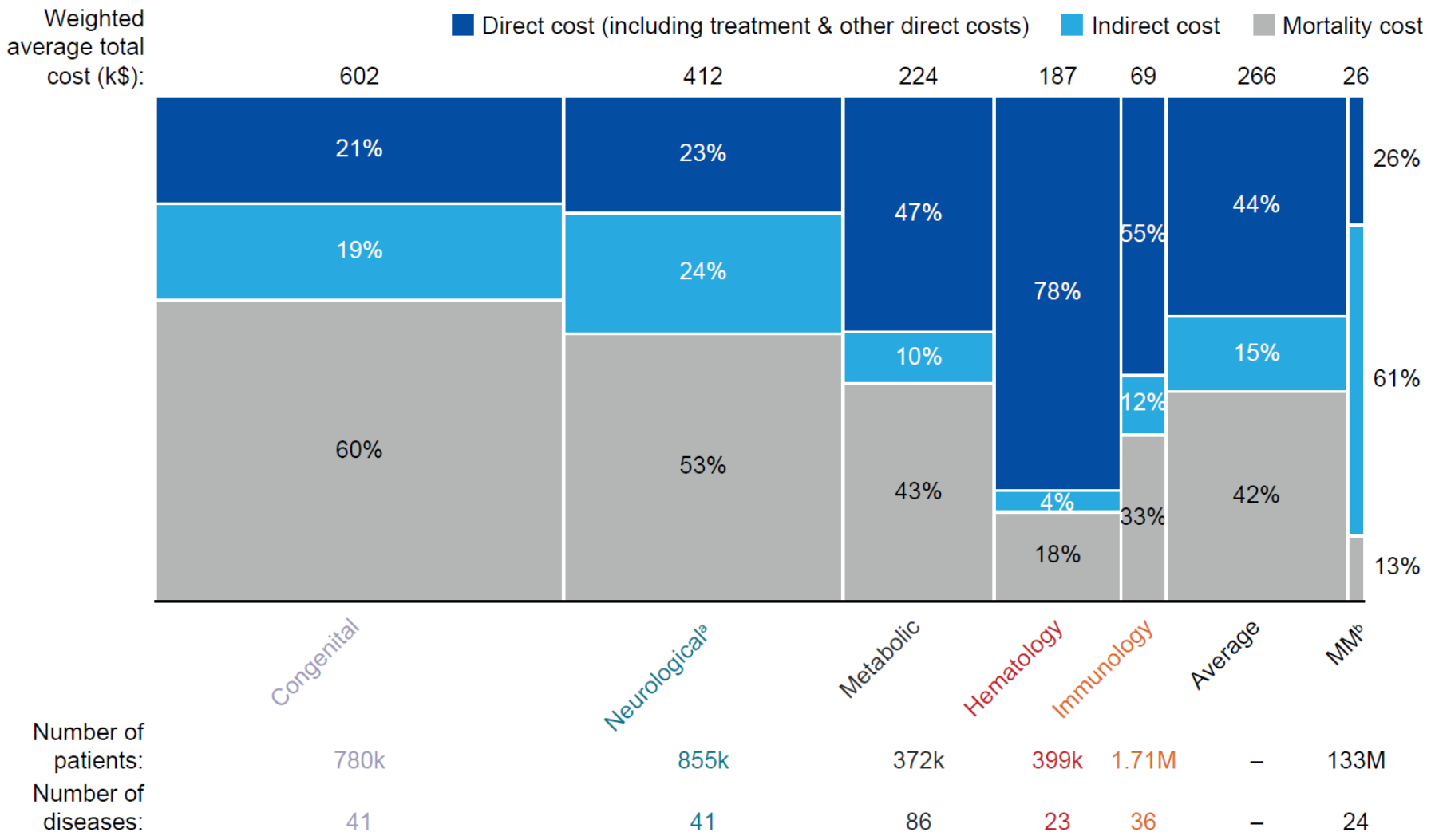
A scenario analysis was conducted to assess the average cost if treatments were not available and found that a lack of treatment was associated with a 21.2% increase in total costs PPPY. The percentage increases ranged from a 2.2% increase for congenital diseases to 51.8% for metabolic diseases.

- Direct costs: $63,000 PPPY with treatment vs. $118,000 PPPY without treatment
- Indirect costs: $40,000 PPPY with treatment vs. $73,000 PPPY without treatment
- Mortality costs: $36,000 PPPY with treatment vs. $49,000 PPPY without treatment

Importantly, across all the therapeutic areas assessed, access to treatment effectively shifts burden relating to indirect and mortality costs into direct costs (treatment and other direct costs). These costs are more likely to be financed by private and public payers.

Value of treatment is further demonstrated by decreases in PPPY indirect costs. When no treatments were available the range for productivity loss was approximately $33,000 to $61,000 for patients and $25,000 to $61,000 for caregivers, compared with approximately $3,000 to $22,000 for patients and $4,000 to $5,000 for caregivers when treatments were available. These findings highlight that providing access to rare disease treatments generally generates substantial value for society because it lowers the associated economic burden on patients and caregivers.

Extrapolated Average Burden of Rare Disease Therapeutic Areas PPPY Across 227 Rare Diseases



When these results were extrapolated to 227 rare diseases belonging to the five priority therapeutic areas, similar results were obtained. The average cost of rare diseases was again approximately 10x higher than for mass market diseases. If extrapolated again to the total of 8.4 million people in the U.S. impacted by the 373 rare diseases in this analysis, the overall cost of rare diseases in the U.S. is estimated to be **$2.2 trillion per year** compared with $3.4 trillion per year for 133 million patients with mass market diseases.

These overall findings may represent an underestimate because social costs (including impact on health-related quality of life) were not part of this analysis. A previous systematic literature review of qualitative research suggested that living with a rare disease is associated with a substantial psychological and social impact. These observations highlight the need to consider as many aspects of healthcare costs as possible to gain a full picture of the overall burden of rare diseases.

Source: https://chiesirarediseases.com/assets/pdf/chiesiglobalrarediseases.whitepaper-feb.-2022_production-proof.pdf

Lumanity Report on First Time Biotech Commercializers

Pharma sales rep pitching a drug to a physician. Source: Getty Images

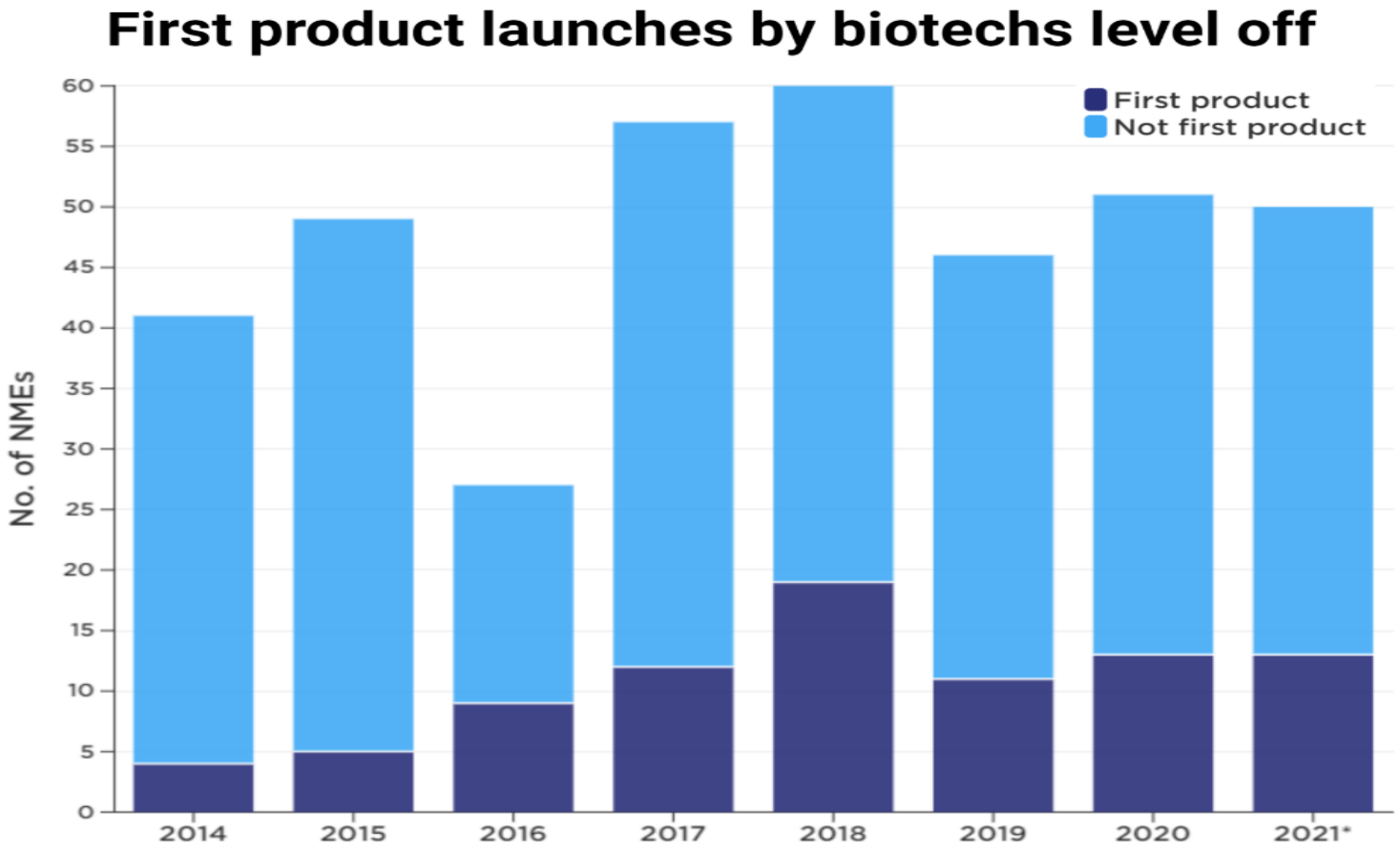
The Growing Pipeline of First-time Commercializers and the Challenges of New Enterprise Commercialization

Ed Saltzman and Dennis Chang, May 2023

Also see the talk online at https://vimeo.com/827612097/

Lumanity Clarion | A LUMANITY BUSINESS

Number of Biotech *First-Time Commercializers* Has Typically Not Exceeded 10 in a Year: Majority Have Been "Intentional Commercializers" in Rare Diseases



Source: BIoCentury, Biotechs are bringing their drugs to market, alone, December 9, 2021

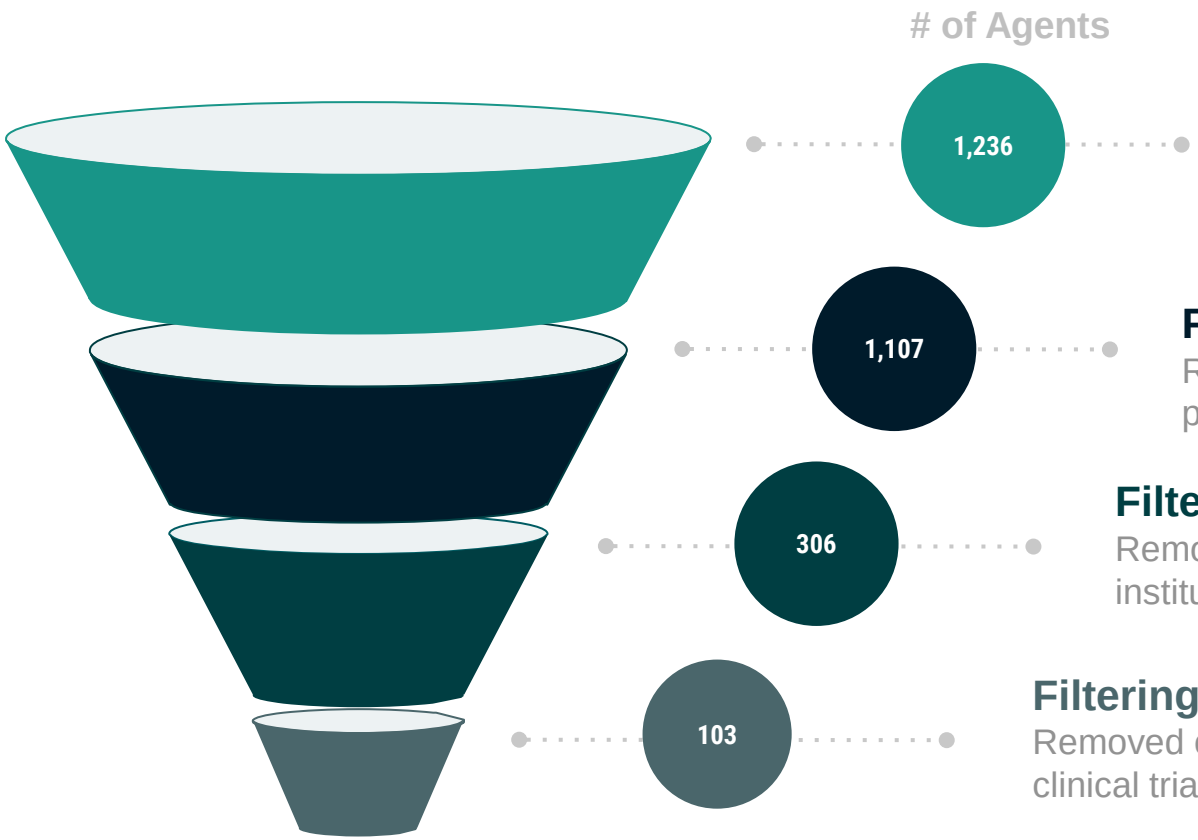
But Imbalance of "Available" Post-PoC Programs and Lack of Buyside Interest Points to Unprecedented Numbers of "*Non-Rare*" Biotechs Facing Need to Commercialize for First Time

Applying rough attrition estimates (clin dev failure, regulatory failure) to P3 unpartnered inventory suggests potential for at least a *doubling* of first time commercializers over next several years.

Importantly, many of these opportunities likely were seen to require a large pharma partner because they fall primarily into 3 buckets where commercial headwinds are perceived as substantial:

Oncology	Large Chronic Diseases	Advanced Therapeutics
• Expensive and complex clinical development and clinical studies • Major post-launch investment	• Heavy trial expense • Requirement for commercial footprint • Existing generic SOC (especially in CNS and CVD)	• Programs gain early POC • Existing complex issues around manufacturing, supply chain, cost, and pricing

Lumanity Identified 103 Distinct Unpartnered Programs Now in P3 US Development in the Hands of Companies *Without* Commercial Revenues



Raw Pull
All active P3 agents pulled from ADIS Insights
Criteria: Phase 3, Unpartnered Biotech Companies, Clinical Trial Development in USA

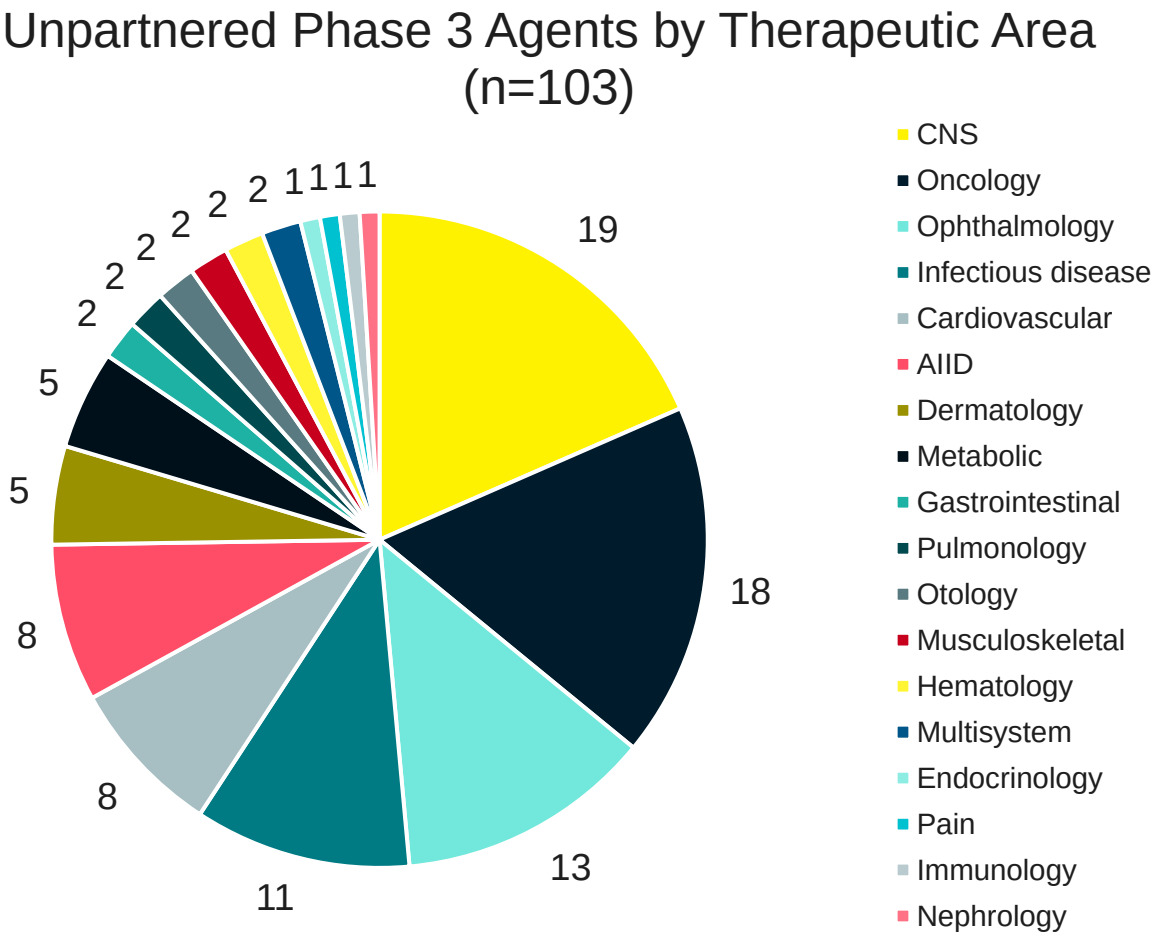
Filtering Step (1)
Removed biosimilars, reformulated assets, imaging/PET products, companion diagnostics, surgical theraputics

Filtering Step (2)
Removed large biotech/pharmaceutical companies, academic institutions, companies with a licensee or subsidiary

Filtering Step (3)
Removed companies with a marketed product, non-USA clinical trial developed assets

ADIS Insights, CT.gov

CNS, Oncology, and Ophthalmology Assets make up ~50% of the Unpartnered Phase 3 Agents: *Many Target Non-Rare and Large Population Indications*

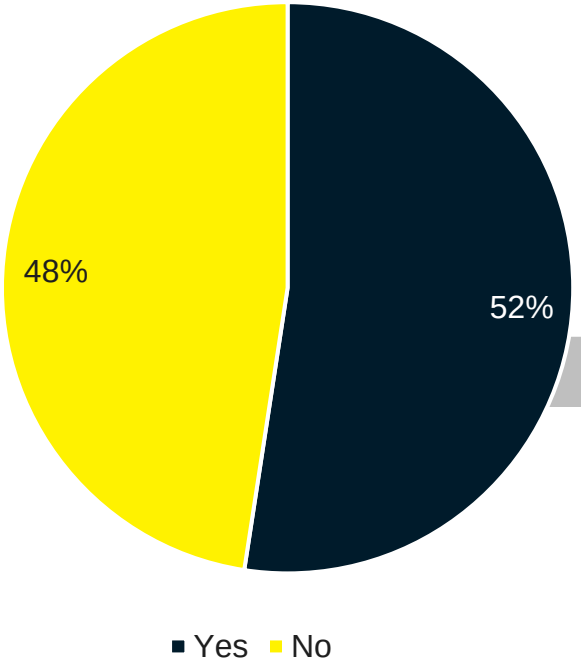


Example Indications	Therapeutic Area
Alzheimer's, Schizophrenia, ALS	CNS
Prostate cancer, AML	Oncology
Presbyopia, Glaucoma	Ophthalmology
COVID, Bacteremia	Infectious Disease
Hypertrophic cardiomyopathy	Cardiovascular
Ulcerative colitis, osteoarthritis	AIID
Burns, alopecia areata	Dermatology
Phenylketonuria, galactosemia	Metabolic
Postoperative ileus	Gastrointestinal
Cough, pulmonary sarcoidosis	Pulmonology
Meniere's disease, tinnitus	Otology
Cartilage disorders	Musculoskeletal
WHIM syndrome	Hematology
Prader-Willi syndrome	Multisystem
Hypocalcemia	Endocrinology
Sciatica	Pain
Leukocyte-adhesion deficiency syndrome	Immunology
Renal hypertension	Nephrology

1) ADIS Insights, 2) CT.gov

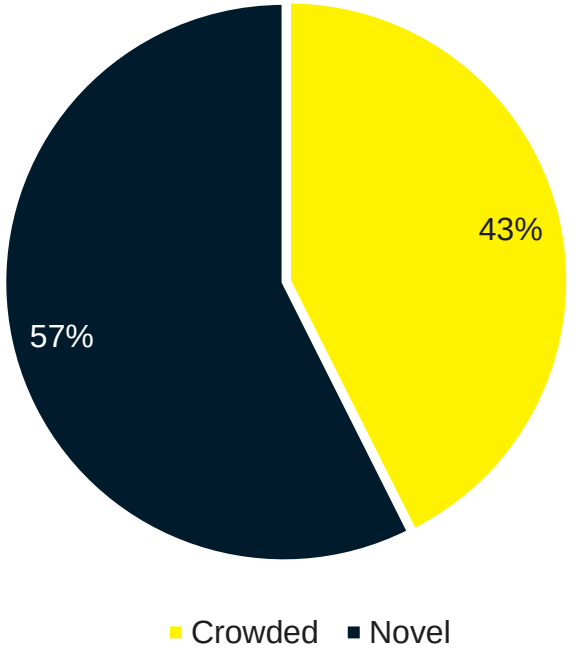
~Half of Unpartnered Phase 3 Drugs Are Entering Indications with Entrenched Standard of Care

Is the Drug Being Pursued in an Indication with an Entrenched SOC*? (n=103)



The unpartnered drugs pursuing indications with entrenched SOC (54/103) include a **mix of novel and crowded MOAs**

Is the Asset Within Crowded or Novel Therapeutic Class for Indication? (n=54)



An indication with an entrenched standard of care is defined as having an SOC that sets a high bar for adoption based on efficacy, cost-effectiveness, or physician satisfaction and is not easily supplanted by incoming agents.

1) ADIS Insights, 2) CT.gov

First-time Commercializer Categories and Examples

Unprecedented Indication

Parkinsons Psychosis
- Acadia's NUPLAZID
  - Launch Year: 2016
  - 2022/8 sales: $0.5/$1.3B

Tardive Dyskinesia
- Neurocrine's INGRESSA
  - Launch Year: 2017
  - 2022/8 sales: $1.3/$1.8B

T1D Onset Delay
- Provention's TZIELD
  - Launch Year: 2023
  - 2022/8 sales: N/A/$1.4B

Crowded or Generic SoC

Migraine
- Biohaven's NURTEC[1]
  - Launch Year: 2020
  - 2022/8 sales: $0.2/$3.7B

Schizophrenia, Bipolar
- Intra-Cellular's CAPLYTA
  - Launch Year: 2020
  - 2022/8 sales: $0.2/$2.2B

Plaque Psoriasis
- Arcutis's ZORVE
  - Launch Year: 2022
  - 2022/8 sales: $0.0/$0.9B

Gene or Cell Therapy

Retinal dystrophy
- Spark's LUXTURNA[2]
  - Launch Year: 2018
  - 2022/8 sales: $0.1/$0.1B

ß-thalassemia
- bluebird's ZYNTEGLO
  - Launch Year: 2020
  - 2022/8 sales: $0.0/$0.4B

EBV+ PTLD
- Atara's EBVALLO
  - Launch Year: 2023
  - 2022/8 sales: N/A/$0.5B

[1]Biohaven was acquired after product launch by Pfizer in 2022 for $11.6B; [1]Spark was acquired after product launch by Roche in 2019 for $4.8B; PTLD: post-transplant lymphoproliferative disease; 2022/8 sales are actual and projected (Source: EvaluatePharma)

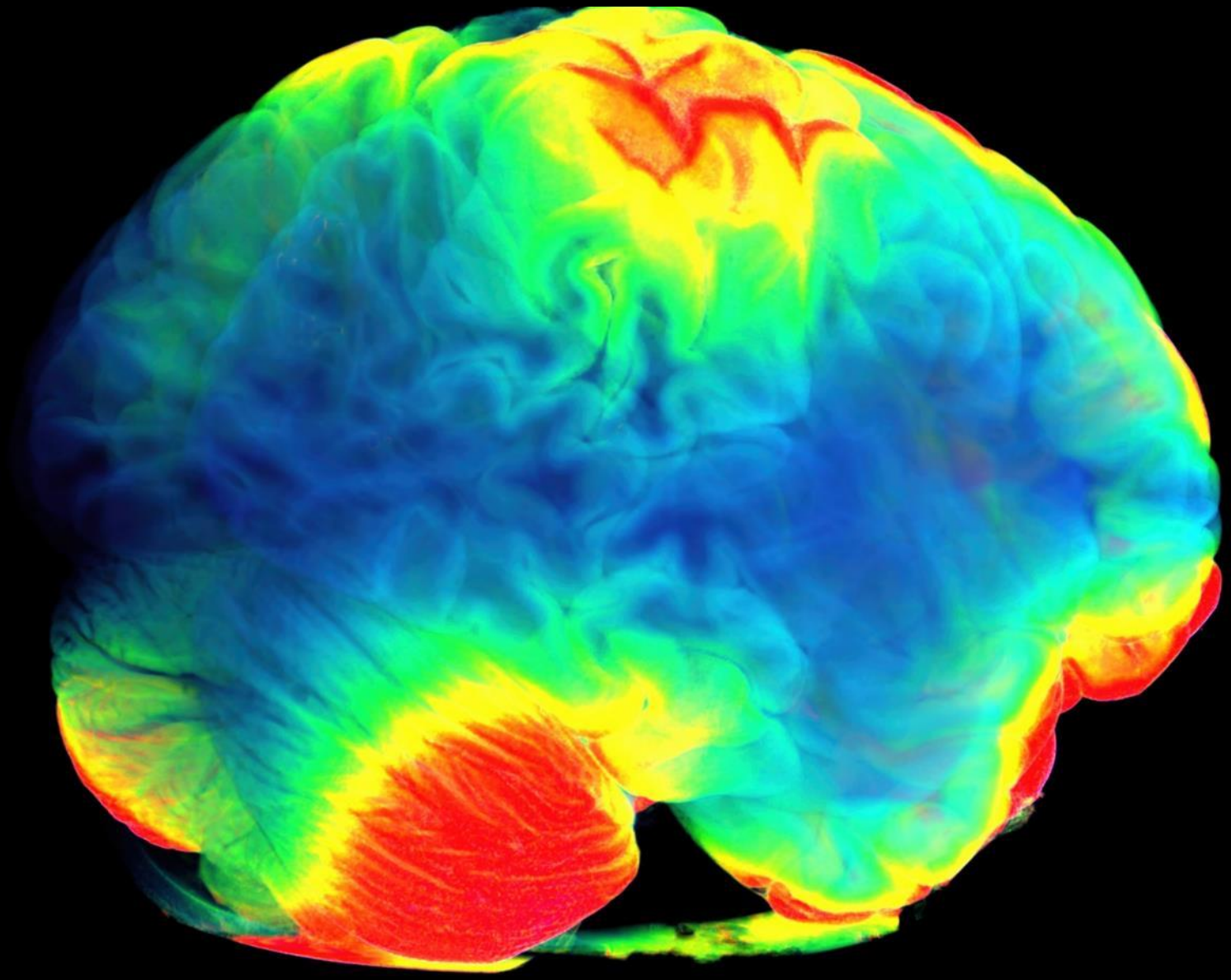
Requirements for new product commercialization (Phase 2 to launch)

Over 500+ activities

ILLUSTRATIVE

	25–30 mos	19–24 mos	13–18 mos	7–12 mos	0–6 mos	Launch
Brand Strategy	• Market understanding • Initial stakeholder insights • Product forecast • Initial go-to-market considerations	• Physician segmentation & prioritization • Patient profiling & segmentation • Market dev plan • Agency onboarding • PR strategy	• Positioning • Creative concept • Messaging • Pre-launch KPIs • Unbranded campaign	• Launch tactical plan & channel strategy • Branded asset dev & testing • Speak program development	• Branded materials • Launch PR plan • Post-launch KPIs • Consumer / patient education	
Regulatory	• Approval pathway identification • Label priorities	• Skeleton label development • NDA submission planning	• Pre-NDA meeting preparation • Full label development & negotiation strategy • NDA development	• Final NDA submission package • Inspection readiness • Ad Comm prep vendor engagement (if appl.)	• Label negotiation • Ad Comm prep (if appl.) • Post-approval filing preparation • OPDP submission (for pre-clearance)	
R&D / Clinical	• Phase 3 studies	• Phase 3 completion • Long term safety studies • Data gap identification	• Statistical analyses • Data packaging for NDA • LCM priorities defined • Ph 3b/4 study plan	• Areas of research interest defined • Grant submission process established (e.g., web portal)	• Ph3b/4 study setup • Investigator initiated studies grant evaluation	
Medical	• Pub & congress plan • Scientific lexicon & platform • KOL mapping & engagement strategy • Field medical strategy	• Congress presence ramp up (e.g., MA booth) • Pub author engagement • Medical PR • Advocacy strategy • Disease state pubs	• Core medical slide deck • Initial MSL training & deployment • CME grant support • Med Info services	• Phase 3 publication • Presence at key congresses • KOL ad boards • Ongoing KOL engagement	• Ongoing KOL engagement • Speaker training • Field training support • Payer engagement support	
Product Access	• Market access landscape • Initial payer & pricing insights	• Initial distribution & access support strategy • Gov't payer setup • Trade & distribution strategy	• Payer segmentation • Payer value proposition • Payer engagement & contracting strategy	• Pricing committee • Field reimbursement support strategy • Access support infrastructure	• Pricing finalized • NAM deployment • Payer prioritization & account strategies • Payer engagement materials	
Product Supply	• Clinical supply • Registration batch manufacturing • Stability testing initiated / continued	• Preliminary unit demand forecast • Commercial scale-up development • Packaging design • Supply chain plan	• Data packaging for NDA • Packaging artwork • Commercial scale mfg validation • Supplier infrastructure investment	• Launch supply & sample mfg plan • Commercial supply agreements in place • Packaging validation • Production scheduling	• Launch supply manufacturing • Post-approval product availability plan	

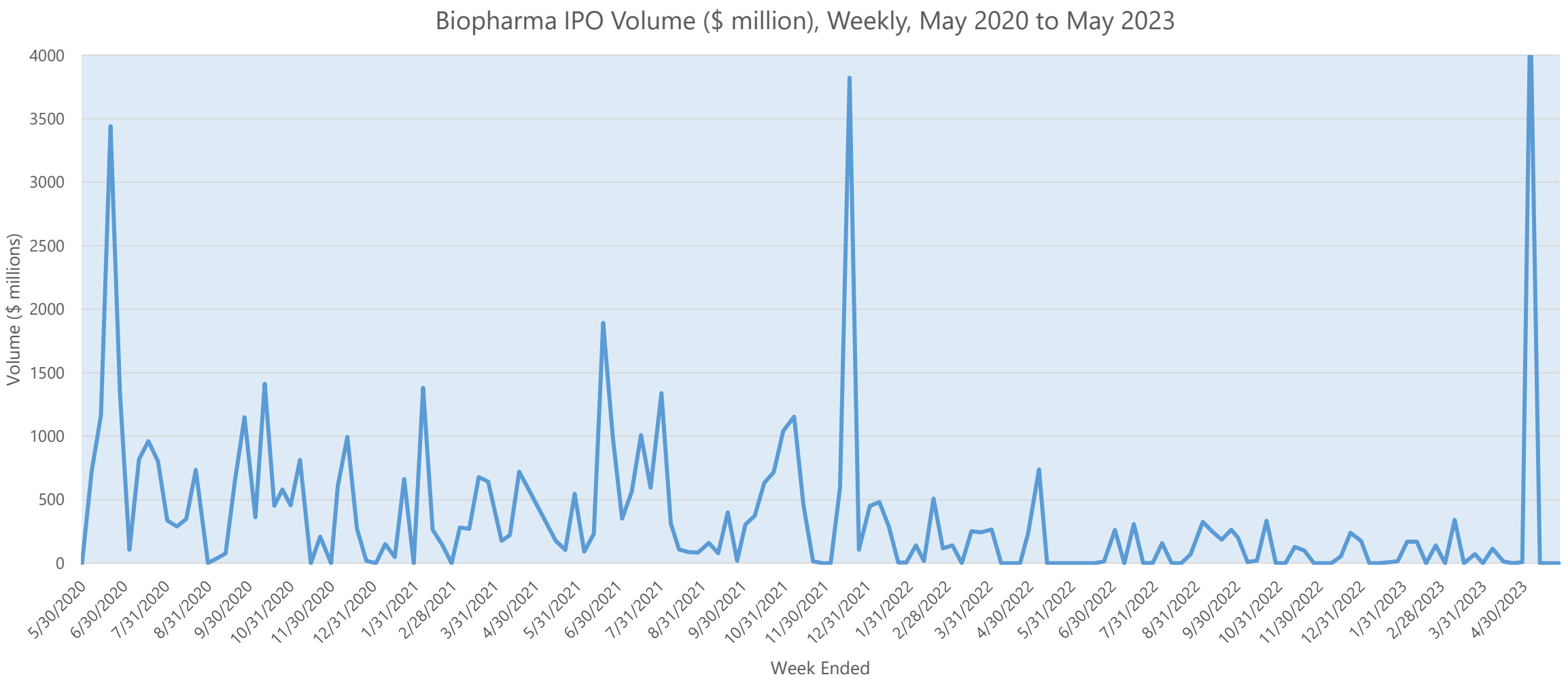
Capital Markets Environment



Brain PET image. Source: Getty Images.

IPO Update

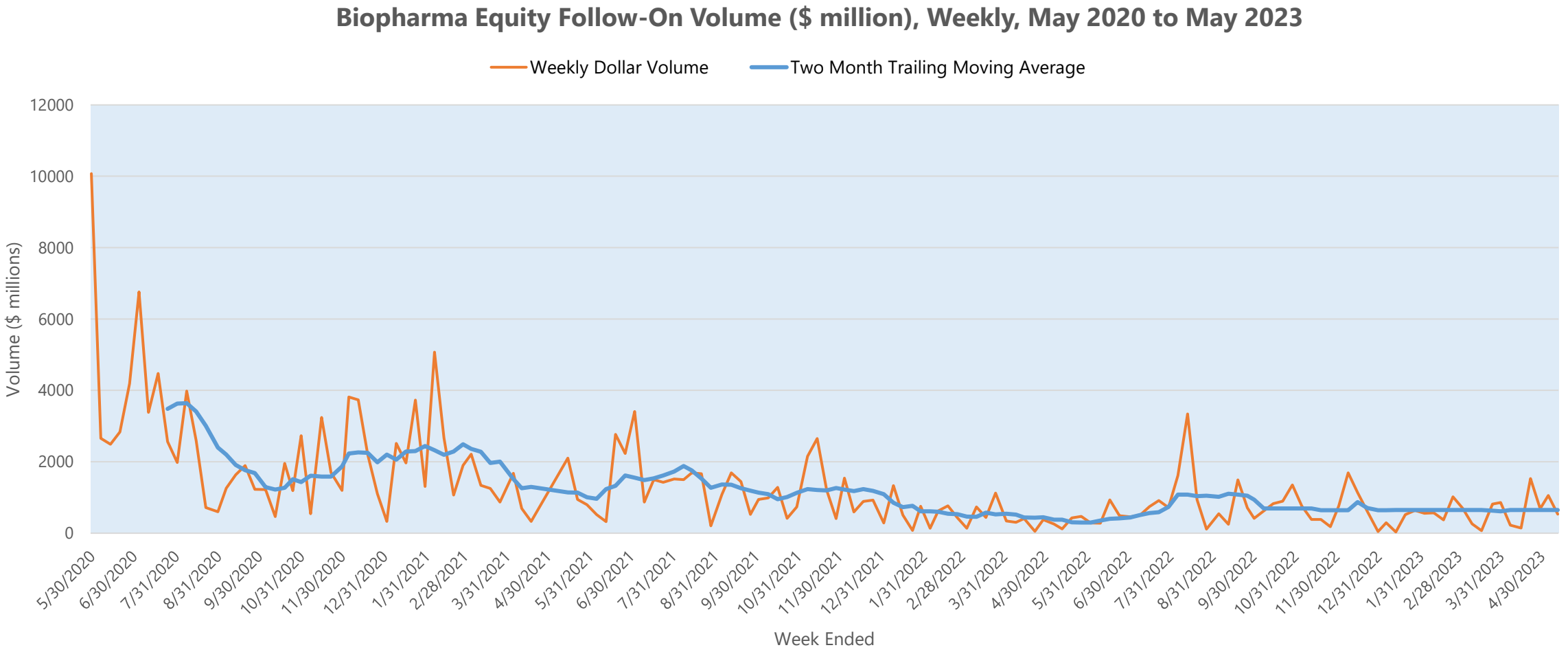
There were no IPO's in the market last week.



Source: Data from CapitalIQ and Stifel research.

Follow-on Equity Issuance Active Last Week

Last week was the fifth most active week of the year for follow-on offerings. We saw $857 million in deals price across 25 transactions. Nine deals used the PIPE format.



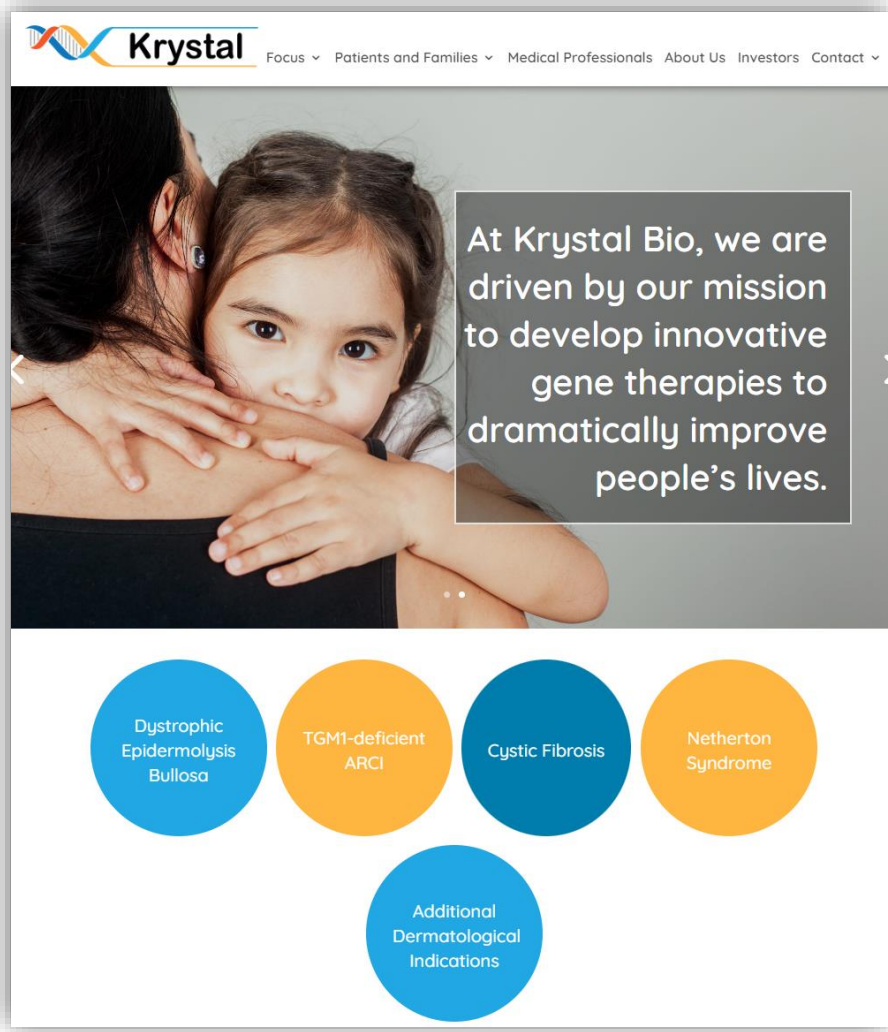
Source: Data from CapitalIQ and Stifel research.

Krystal Biotech Raises $160 Million After FDA Approval

PITTSBURGH, May 22, 2023 (GLOBE NEWSWIRE) -- Krystal Biotech, Inc. (the Company) (NASDAQ: KRYS), a biotechnology company focused on developing and commercializing genetic medicines for patients with rare diseases, today announced that it has entered into a securities purchase agreement for the sale of 1,729,729 shares of its common stock at $92.50 per share in a private placement (the PIPE) to certain qualified institutional buyers. Gross proceeds from the PIPE are expected to be approximately $160 million, before deducting any offering-related expenses. The transaction is expected to close on May 22, 2023, subject to the satisfaction of customary closing conditions.

The PIPE financing was led by Avoro Capital Advisors and Redmile Group, LLC with participation from Braidwell LP and Frazier Life Sciences.

"We are extremely pleased to have the support of this strong investor group," said Krish S Krishnan, Chairman and CEO of Krystal Biotech, Inc. "These additional funds, together with our existing cash, cash equivalents and investments, should allow us to fund the VYJUVEK launch, future operations, and the advancement of our growing pipeline through the end of 2026. It also allows us to retain the optionality of monetizing the Priority Review Voucher we received in connection with the FDA approval of VYJUVEK at a future date with favorable terms and without any dilution."



Source: https://ir.krystalbio.com/news-releases/news-release-details/krystal-biotech-announces-160-million-private-placement-equity

Kamada Closes $60 Million PIPE

Stifel acted as financial advisor to Kamada on last week's financing.

REHOVOT, Israel, and Hoboken, NJ – May 24, 2023 — Kamada Ltd. (NASDAQ: KMDA; TASE: KMDA.TA) ("Kamada" or the "Company"), a commercial stage global biopharmaceutical company with a portfolio of marketed products indicated for rare and serious conditions and a leader in the specialty plasma-derived field, today announced that it has entered into a share purchase agreement (the "Purchase Agreement") with FIMI Opportunity Funds ("FIMI"), the leading private equity firm in Israel and a major shareholder of Kamada, to purchase $60 million of its ordinary shares in a private placement (the "Private Placement").

Under the terms of the Purchase Agreement, Kamada will issue an aggregate of approximately 12.6 million ordinary shares to FIMI at a price of $4.75 per share (which represents the average closing price of the Company's shares on NASDAQ during the 20 trading days prior to the date of the Purchase Agreement). Upon the closing of the transaction, FIMI is expected to beneficially own approximately 38% of Kamada's outstanding ordinary shares and will become a controlling shareholder of the Company, within the meaning of the Israeli Companies Law, 1999.
Proceeds from the Private Placement are expected to be used to support the Company's growth plans and execution of strategic business development opportunities.

The special committee of the Board of Directors retained Stifel, Nicolaus & Company, Incorporated as its financial advisor. The special committee of the Board of Directors also retained Prof. Aharon (Roni) Ofer as additional financial advisor and Erdinast, Ben Nathan, Toledano & Co. as its legal counsel. Naschitz, Brandes, Amir & Co. served as legal advisors to FIMI. Kamada retained Raymond James & Associates, Inc. as its financial advisor, and FISCHER (FBC & Co.) and Morrison & Foerster LLP served as its legal advisors.

Source: https://investors.x4pharma.com/news-releases/news-release-details/x4-pharmaceuticals-announces-65-million-private-placement-priced

TScan Closes $140 Million Follow-On Offering

May 26, 2023 Waltham-(GLOBE NEWSWIRE) -- -TScan Therapeutics, Inc. (Nasdaq: TCRX), a clinical-stage biopharmaceutical company focused on the development of T cell receptor (TCR)-engineered T cell therapies (TCR-T) for the treatment of patients with cancer, today announced the pricing of an underwritten public offering of 22,989,474 shares of its voting common stock at a public offering price of $2.00 per share, and pre-funded warrants to purchase up to an aggregate of 47,010,526 shares of its common stock at a price to the public of $1.9999 per pre-funded warrant, which represents the per share public offering price for the voting common stock less the $0.0001 per share exercise price for each such pre-funded warrant. In addition, TScan has granted the underwriters a 30-day option to purchase up to an additional 10,500,000 shares of its voting common stock at the public offering price, less underwriting discounts and commissions. The gross proceeds to TScan from this offering are expected to be approximately $140.0 million, before deducting underwriting discounts and commissions and other estimated offering expenses payable by TScan, assuming no exercise of the underwriter's option to purchase additional shares of voting common stock. The offering is expected to close on or about May 31, 2023 for the voting common stock, and June 1, 2023 for the pre-funded warrants, in each case, settlement is subject to customary closing conditions.

TSCAN THERAPEUTICS

TScan has had a lot of recent momentum with an Amgen partnership and encouraging data on TSC-100/101 in Post-Transplant AML/ALL/MDS at the ASGCT conference.

The company's recent offering was remarkable in that it is issuing 70 million shares and prepaid warrants off a previous base of 24 million common shares.

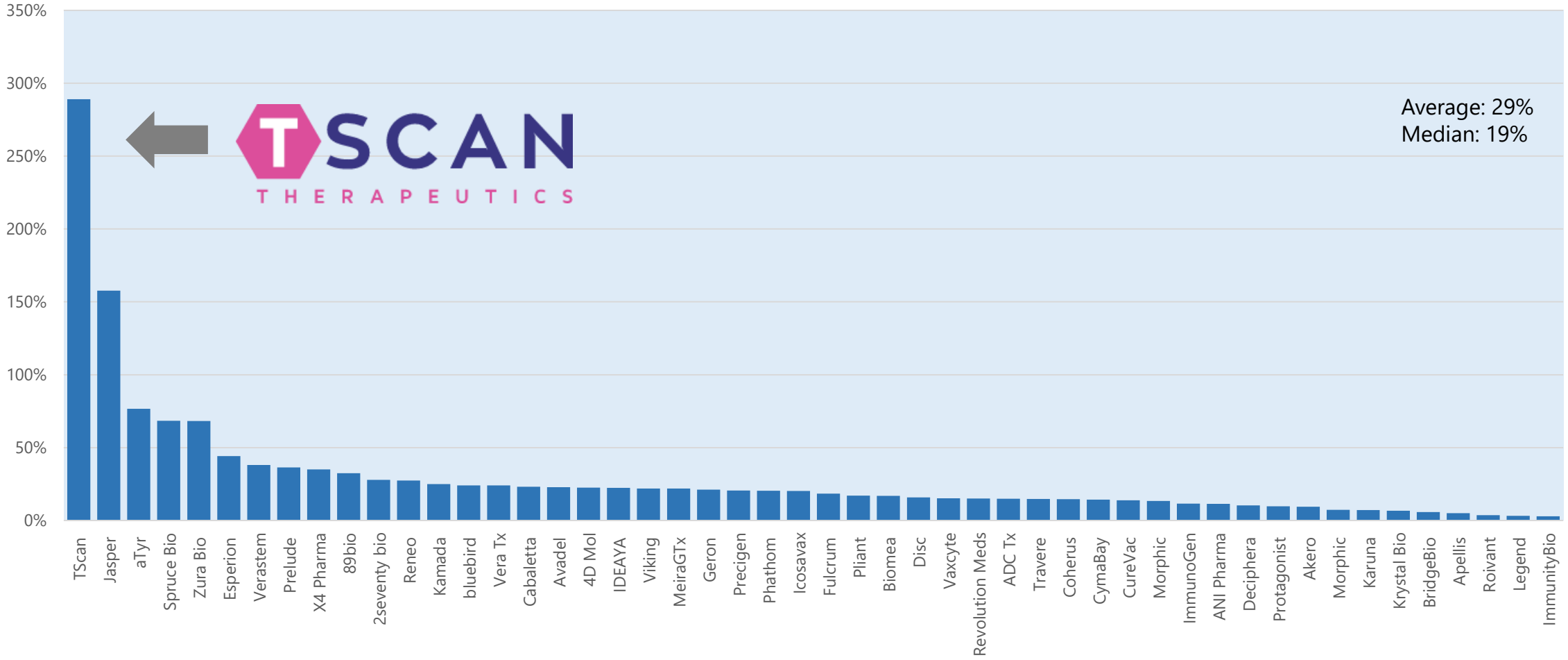
This is the largest offering to market cap ratio in 2023 for a deal over $50mm in size.

Source: https://ir.tscan.com/news-releases/news-release-details/tscan-therapeutics-announces-pricing-140-million-public-offering

TScan Offer Size to Market Cap Exceptional

Ratio of Offer Size to Market Cap of Follow-Ons on U.S. Exchanges, 2003 YTD

(Offerings of $50 million or more)



Source: CapitalIQ and Stifel analysis.

2003 Follow-on Market Statistics

(Offerings of $50mm or more on NASDAQ/NYSE for biopharma companies in 2023)

Key points:

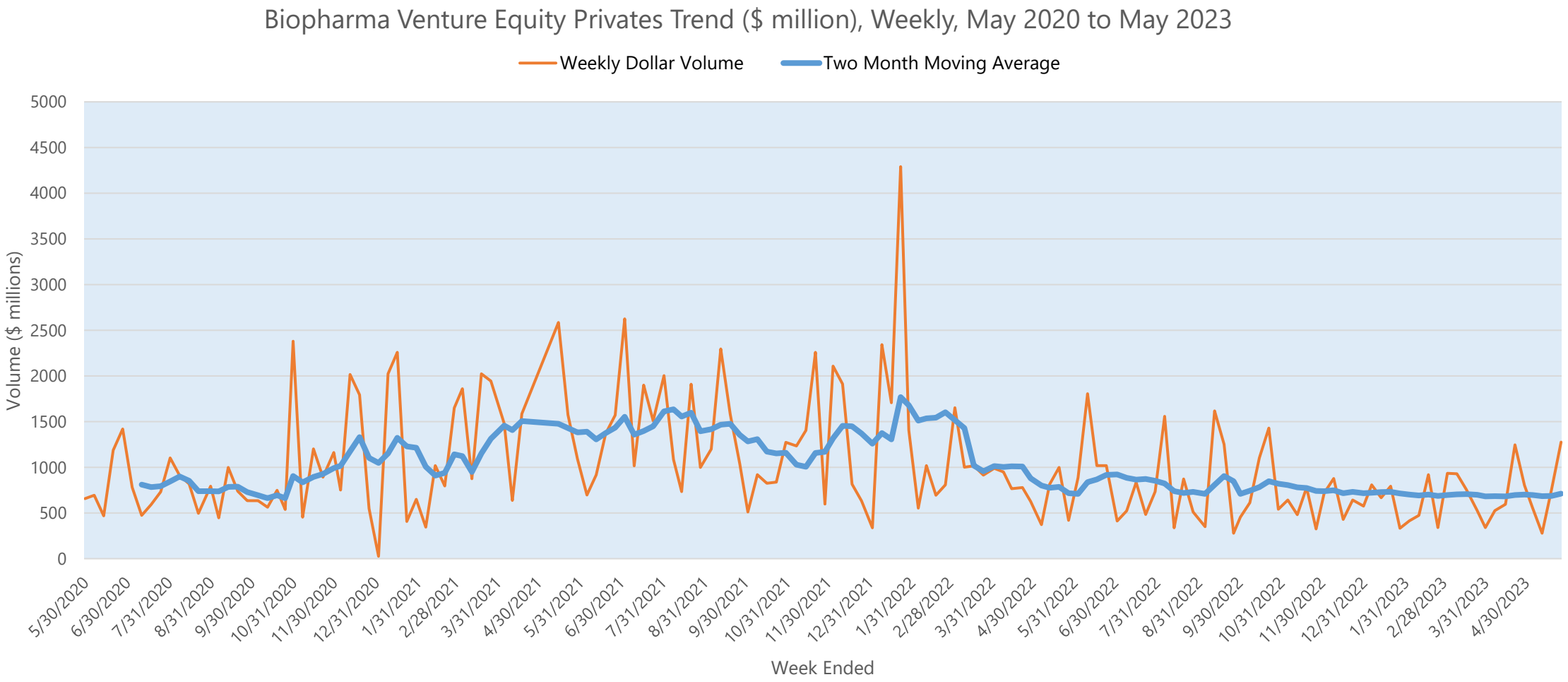
1. Current / offer is positive 68% of time and even higher for larger cap issuers.
2. Median discount is 7% (not accounting for warrants).
3. One day share price reaction is negative 54% of time but average effect small.

Announcement Date	Issuer	Warrant Coverage?	PIPE?	Amount Raised ($mm)	Issue/Cap	Current Price / Offer Price	Offer Discount to Last Trade	One Day Share Price Reaction
05/25/2023	TScan			$140.0	289%	60%	18%	31%
05/24/2023	Kamada		Yes	$60.0	25%	12%	12%	0%
05/23/2023	Phathom			$130.7	20%	0%	10%	-10%
05/22/2023	Icosavax			$67.8	20%	22%	-3%	25%
05/21/2023	Krystal Bio		Yes	$160.0	7%	30%	4%	22%
05/17/2023	Prelude			$100.0	36%	-4%	9%	-11%
05/17/2023	Cabaletta			$87.0	23%	-25%	1%	1%
05/16/2023	Akero			$220.0	9%	7%	9%	0%
05/15/2023	X4 Pharma		Yes	$65.0	35%	32%	0%	16%
05/15/2023	Coherus			$50.0	15%	2%	13%	6%
05/11/2023	ANI Pharma			$75.0	11%	17%	10%	-5%
05/08/2023	Legend			$350.0	3%	-1%	7%	-1%
05/04/2023	4D Molecular			$120.0	23%	10%	0%	5%
05/03/2023	Reneo			$55.0	27%	2%	19%	-1%
05/03/2023	MeiraGTx		Yes	$61.5	22%	14%	2%	8%
05/03/2023	ImmunoGen			$325.0	12%	12%	-2%	8%
05/02/2023	Morphic			$240.0	13%	27%	7%	6%
04/27/2023	Zura Bio	Yes	Yes	$79.9	68%	34%	47%	-15%
04/24/2023	IDEAYA			$200.0	22%	20%	9%	-8%
04/17/2023	Vaxcyte			$500.0	15%	19%	3%	4%
04/04/2023	Protagonist			$100.0	10%	31%	7%	-16%
03/29/2023	Avadel			$125.0	23%	63%	4%	-4%
03/29/2023	Viking			$250.0	22%	47%	9%	9%
03/29/2023	Biomea			$150.0	17%	5%	7%	-1%
03/22/2023	Esperion			$56.7	44%	-13%	-15%	7%
03/22/2023	89bio			$275.0	32%	9%	-19%	24%
03/20/2023	Karuna			$400.0	7%	36%	12%	-12%
03/06/2023	BridgeBio			$150.0	6%	-19%	-3%	12%
03/01/2023	Revolution Meds			$300.0	15%	16%	17%	-12%
02/28/2023	2seventy bio			$125.0	28%	4%	15%	-18%
02/27/2023	Travere			$200.0	15%	-22%	3%	2%
02/22/2023	Apellis			$350.0	5%	38%	4%	2%
02/15/2023	ImmunityBio	Yes		$50.0	3%	-40%	-22%	-8%
02/13/2023	Disc			$61.6	16%	41%	5%	0%
02/13/2023	Morphic		Yes	$100.0	7%	62%	9%	5%
02/08/2023	aTyr			$50.0	77%	4%	5%	-8%
02/08/2023	Spruce Bio	Yes	Yes	$51.1	68%	-23%	0%	-5%
02/06/2023	CureVac			$250.0	14%	-1%	13%	-11%
02/02/2023	ADC Tx			$60.0	15%	-54%	-2%	-6%
02/01/2023	Vera Tx			$100.0	24%	-49%	-77%	-16%
02/01/2023	Roivant			$200.0	4%	24%	12%	-11%
01/24/2023	Jasper			$90.0	158%	7%	11%	9%
01/24/2023	Verastem		Yes	$60.0	38%	35%	-23%	4%
01/24/2023	Precigen			$75.0	21%	-30%	20%	-25%
01/23/2023	Pliant			$250.0	17%	-28%	1%	9%
01/23/2023	CymaBay			$85.0	14%	25%	-6%	16%
01/18/2023	bluebird			$120.0	24%	-41%	0%	-2%
01/18/2023	Deciphera			$125.0	10%	-23%	13%	-9%
01/17/2023	Fulcrum			$125.0	18%	-78%	7%	-11%
01/04/2023	Geron			$198.1	21%	33%	23%	-22%
			Median	$122.5	19%	9.5%	7.0%	-0.7%
			Average	$152.4	29%	7.0%	4.2%	-0.4%
			Percent Positive			68%	76%	46%

Source: CapitalIQ and Stifel analysis.

Weekly Global Biopharma Venture Equity Placements

Last week saw 35 companies raise $1.28 billion in the venture equity market. This was the biggest week in more than six months for the venture market.



Source: Data from CapitalIQ, Crunchbase.

ElevateBio Announces $401 Million Series D Financing

Waltham, Mass., May 24, 2023 – ElevateBio, LLC (ElevateBio), a technology-driven company focused on powering the creation of life-transforming cell and gene therapies, today announced the closing of its $401 million Series D financing led by the AyurMaya Capital Management Fund, managed by Matrix Capital Management, and joined by a leading group of new and existing investors. ElevateBio's syndicate now includes new investors Woodline, Lee Family Office (Asia), and R&D partner Novo Nordisk, as well as existing investors: Matrix Capital Management, The Invus Group, Emerson Collective, SoftBank Vision Fund 2, Fidelity Management & Research Company, MPM Capital, F2 Ventures, Redmile Group, EcoR1 Capital, Samsara BioCapital, Surveyor Capital (a Citadel company), EDBI, Vertex Ventures, iTochu, and a large institutional investor. In connection with the financing, Khalil Barrage, Managing Director of The Invus Group, was appointed to ElevateBio's Board of Directors.

Proceeds from the financing will be used to further advance the company's technology platforms – Life Edit gene editing, induced pluripotent stem cells (iPSCs), and RNA, cell, protein, vector engineering – and BaseCamp®, its end-to-end genetic medicine current Good Manufacturing Practice (cGMP) manufacturing and process development business, to accelerate the design, manufacturing, and development of cell and gene therapies. The funding will also support ElevateBio's continued efforts to expand its geographic reach and increase its cGMP manufacturing capacity to provide its academic and industry partners with turnkey and scalable access to technologies and services across the full-product lifecycle.

"We have made significant strides in scaling our technologies and end-to-end capabilities in our pursuit to become the world's most indispensable cell and gene therapy technology company. We are thrilled to welcome Khalil to our Board as his expertise will be invaluable as the number of strategic partners harnessing the power of our integrated ecosystem continues to grow. We're emboldened by the pace of advancements to our technology platforms and continue to drive innovation from concept through commercialization and redefine how companies operate, how products are created, and how disease is treated."

David Hallal
Chairman and Chief Executive Officer
ElevateBio.

Source: https://elevate.bio/press-releases/elevatebio-announces-401-million-series-d-financing-to-further-accelerate-growth/

ReNAgade Therapeutics Launches with over $300 Million in Series A Financing

CAMBRIDGE, Mass., May 23, 2023 (Business Wire) -- ReNAgade Therapeutics, a company unlocking the limitless potential for RNA medicines to correct disease, today announced a $300 million Series A financing round led by MPM BioImpact and F2 Ventures.

ReNAgade has built a comprehensive and complementary platform that combines its proprietary delivery technologies, including novel lipid nanoparticles (LNPs), with a broad array of coding, editing, and gene insertion tools, in an all-RNA system. ReNAgade aims to address major limitations in RNA therapeutics by enabling the delivery of RNA medicines to previously inaccessible tissues and cells in the body, substantially expanding the potential addressable disease market. The Company has an established Joint Venture with Orna Therapeutics Inc., combining ReNAgade's delivery platform with Orna's circular RNA technology. Subsequently, Orna has entered into a collaboration with Merck, which includes technologies developed under the Orna/ReNAgade JV.

Founded by MPM BioImpact, ReNAgade is led by Chairman and Chief Executive Officer Amit D. Munshi, an industry veteran with more than 30 years of experience leading biotech companies and most recently the CEO of Arena Pharmaceuticals, with support from a world-class executive and scientific team with deep, translational expertise across multiple RNA modalities.

Amit Munshi
Chairman and Chief Executive Officer
ReNAgade Therapeutics

Source: https://www.businesswire.com/news/home/20230523005422/en/ReNAgade-Therapeutics-Launches-with-over-300-Million-in-Series-A-Financing-To-Unlock-the-Limitless-Potential-of-RNA-Medicine. Photo from company website.

Venture Fundraising in Healthcare Rises as Investment in Startups Slows

Looking past recent negative returns, VCs bet that biomedical innovation coupled with declining startup valuations will one day yield fat profits

Excerpt from Brian Gormley, *Wall Street Journal*, May 25, 2023

"Healthcare venture returns as well have slipped from pandemic-era highs. In the first quarter of 2021, for example, healthcare-focused venture funds posted a 22.5% return, according to market tracker PitchBook Data. Just a year later, that quarterly return had plummeted to a negative 9.5%, improving somewhat in the next three quarters.

But to abandon healthcare now would be to miss a digital revolution taking shape, some investors say, as startups apply machine-learning to ever-larger biological and medical data sets to create insights that will lead to new treatments and better patient care.

"Entrepreneurs have to do more with less," said Lynne Chou O'Keefe, founder and managing partner of digital-health investor Define Ventures, which has raised $460 million across two new funds. "They're much more focused, more tenacious and more clear in what they have to achieve.""

This is quite an interesting article.

VC's are raising more money than ever for healthcare despite negative returns in 2022.

While VC's and their LP's remain committed to the sector, the amount of money being put into startups is being dialed back forcing entpreneurs to "do more with less".

Source: https://www.wsj.com/articles/venture-fundraising-in-healthcare-rises-as-investment-in-startups-slows-67f3bd7c?tpl=vc

Funding for Early-Stage Companies Challenging

Biotech Financing Slowdown Hits Early-Stage Pharmaceutical Research — Talking Markets

Cecilia Butini, *Wall Street Journal*, May 24, 2023

Investment in biotechnology has been stalling due to a progressive increase in interest rates, recent developments such as the collapse of Silicon Valley Bank, and a postpandemic slowdown, and while analysts say there is no danger to industry-wide contagion, smaller companies focusing on early-stage drug development may be at risk.

Lower interest rates and an appetite for scientific ventures during the Covid-19 pandemic were a boon to the biotech industry, bringing liquidity to the market and prompting new and established companies to raise money, go public or improve their balance sheets. But after peaking in 2020, funding started to drop in 2021 and 2022 and is now at a comparable level to 2018 and 2019, according to analysts.

Source: https://www.wsj.com/articles/biotech-financing-slowdown-hits-early-stage-pharmaceutical-research-talking-markets-ef616a1f

Slowdown? Really? Where's the Drought?

A.I.-fueled biotech startups are having a moment

Lucy Brewster, *Fortune*, May 23, 2023

A $50 million seed round and a $300 million Series A deal: These don't sound like funding rounds taking place in a venture capital drought.

For some startups, especially in the biotech sector, this is turning out to be a surprisingly lucrative time to fundraise. "The challenge right now for the biotech investor scene is that the public markets have seized up for biotech, but at the same time, science is moving at a pace that's unprecedented," explained Amit D. Munshi, CEO of ReNAgade Therapeutics, which today announced a $300 million Series A round. "Positions are getting more concentrated, rounds are getting bigger, and they're picking the winners," he added.

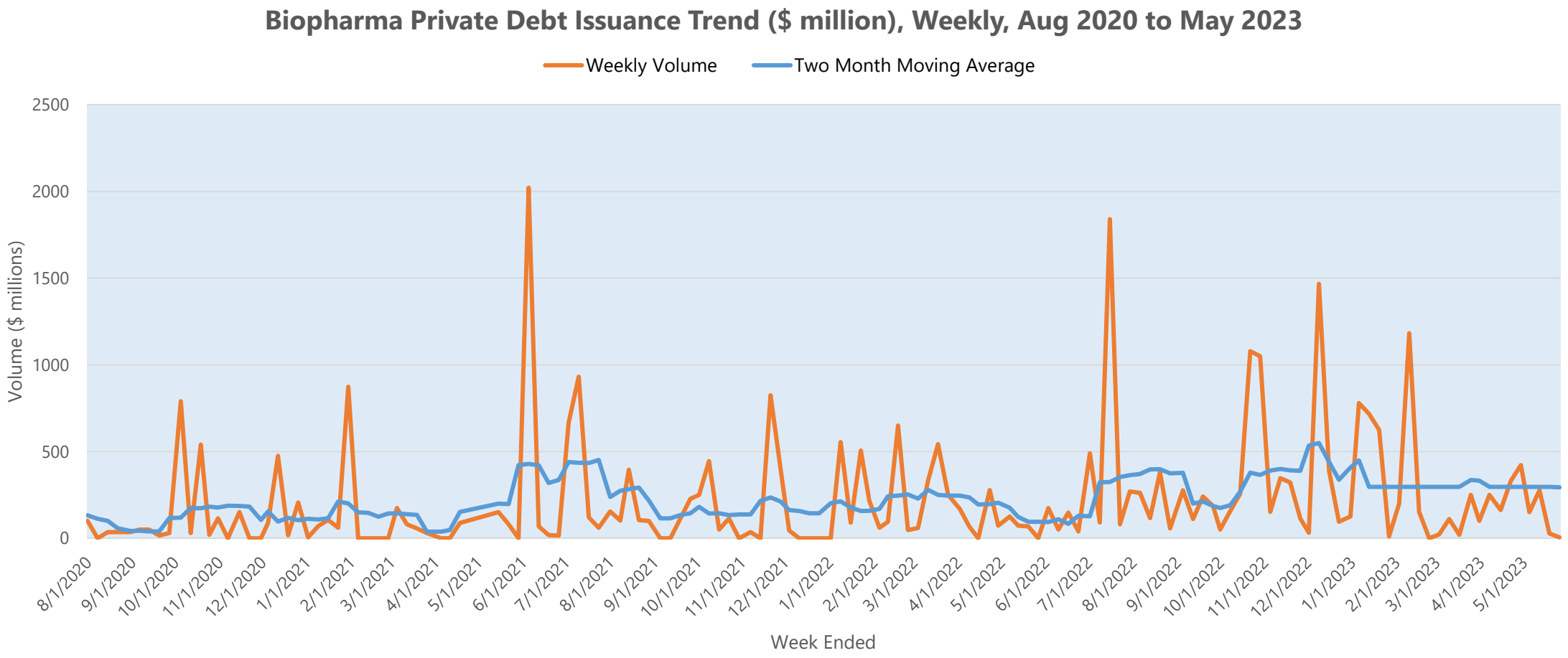
ReNAgade raised financing from investors like F2 Ventures and MPM BioImpact, an early-stage biotech investment fund that also helped found the company. The startup is developing its platform for breakthroughs in RNA medicine, which has applications across medicine for vaccines and a whole range of therapeutic treatments for genetic diseases.

Biotech is also drafting off some of the A.I. hype that has enraptured VCs and inspired them to invest heavily in machine learning technology. ReNAgade is utilizing A.I. as it builds out its computational biology group with an A.I. machine learning platform, according to Munshi. Hippocratic AI announced its eye-popping $50 million seed round on May 16, which was led by biotech veterans Andreessen Horowitz and General Catalyst. The company was founded by Munjal Shah and aims to build A.I. language models for the health care system.

Source: https://www.msn.com/en-us/money/savingandinvesting/ai-fueled-biotech-startups-are-having-a-moment/ar-AA1byVN1

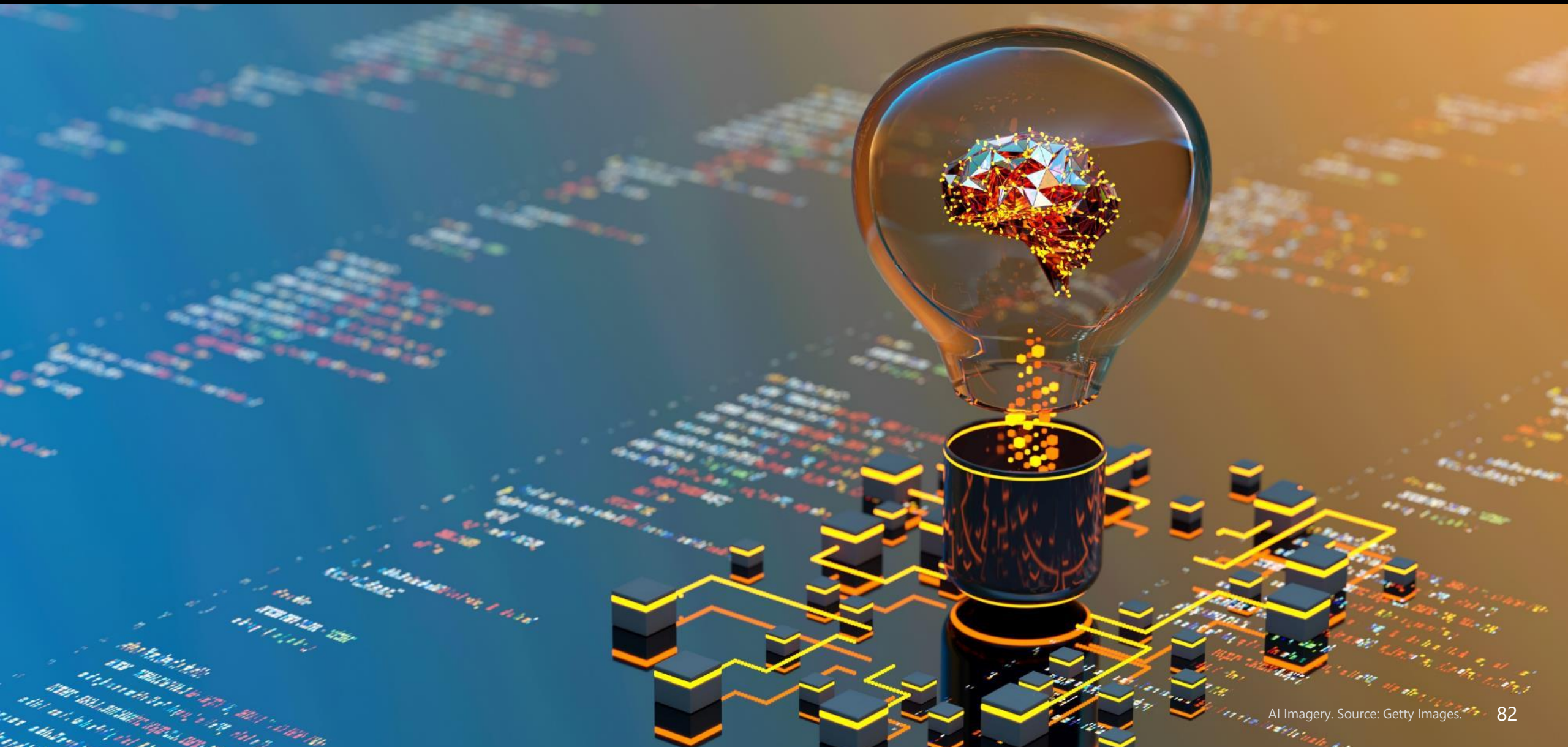
Global Biopharma Venture Debt Placements

Last week saw one private debt deal for $5mm. It was a light week.



Source: Data from CapitalIQ, Crunchbase.

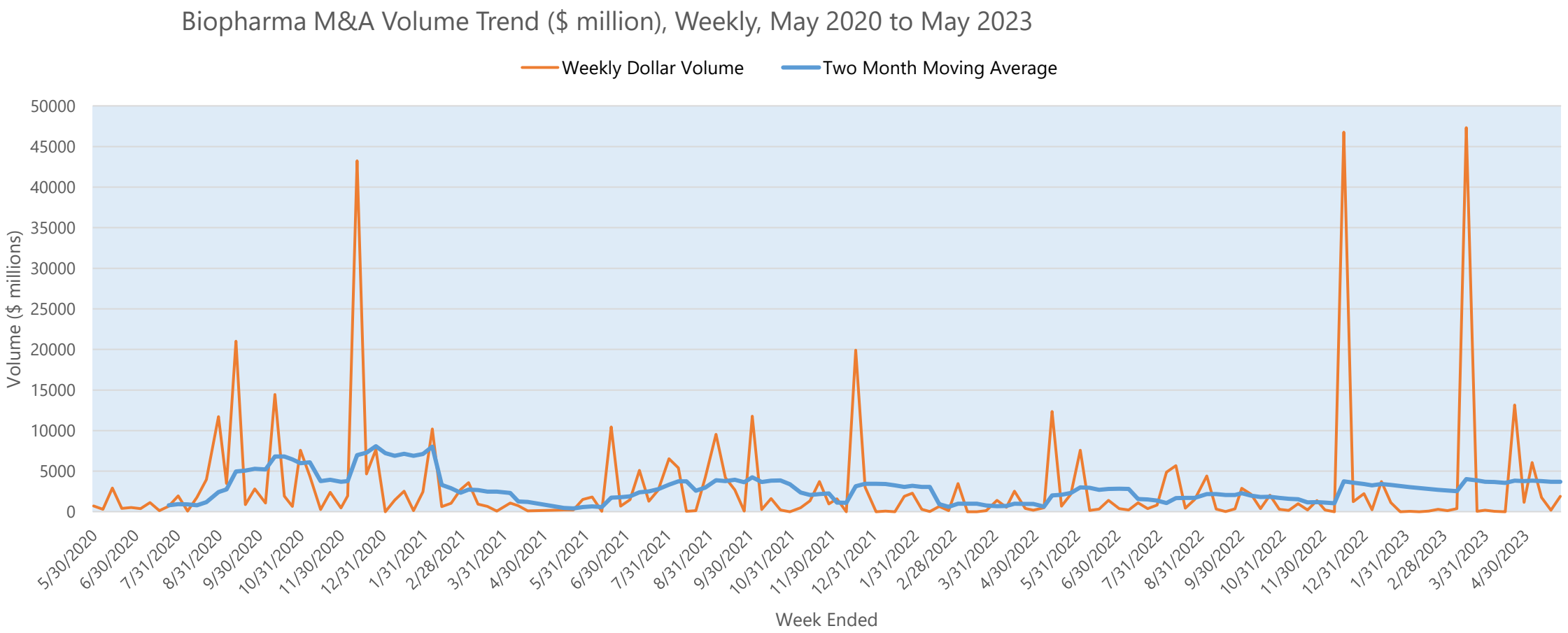
M&A Update



AI Imagery. Source: Getty Images.

Last Week Solid for M&A

Last week saw $2.23 billion in announced biopharma M&A volume. Key transactions including the proposed acquisition of VectivBio by Ironwood, the proposed acquisition of Atea by Kevin Tang, the acquisition of Purdue consumer and the acquisition of AVROBio's cystinosis program by Novartis.



Source: S&P, CapitalIQ

Ironwood to Acquire VectivBio

BOSTON & BASEL, Switzerland--(BUSINESS WIRE)--May 22, 2023--Ironwood Pharmaceuticals, Inc. ("Ironwood") (Nasdaq: IRWD), a GI-focused healthcare company, and VectivBio Holding AG ("VectivBio") (Nasdaq: VECT), a clinical-stage biopharmaceutical company pioneering novel, transformational treatments for severe rare gastrointestinal conditions, today announced that they have entered into a definitive agreement for Ironwood to acquire VectivBio for $17.00 per share in an all-cash transaction with an estimated aggregate consideration of approximately $1 billion, net of VectivBio cash and debt (the "Transaction"). The acquisition price represents a premium of 80% relative to the volume-weighted average share price over the previous 90 trading days. The Transaction was approved by both the Ironwood and VectivBio Boards of Directors and the Transaction Agreement was entered into on May 21, 2023. The Transaction is conditioned upon, among other things, the tender of shares representing more than 80% of VectivBio's issued and outstanding shares and other customary conditions. Orbimed, Forbion and Versant Ventures, and VectivBio's directors and officers, jointly representing 28.6% of VectivBio's shareholdings, entered into tender and support agreements pursuant to which such supporting shareholders agreed, among other things, to tender their shares in the tender offer.

Headquartered in Basel, Switzerland, VectivBio is a clinical-stage biotechnology company focused on the discovery and development of treatments for severe, rare conditions, including Short Bowel Syndrome with Intestinal Failure (SBS-IF) and acute Graft versus Host Disease (aGvHD). SBS-IF is a severe malabsorptive condition requiring ongoing I.V. administration of fluids and nutrients and is associated with significant morbidity and mortality, high economic burden, and an impaired quality of life. A substantial number of SBS-IF patients remain dependent on chronic parenteral support, and there is considerable unmet need in this patient population, which has an estimated addressable population of 18,000 adult patients across the U.S., Europe, and Japan1. aGVHD is an immunologically mediated disease occurring in individuals undergoing allogeneic hemopoetic stem cell transplantation (HSCT) where donor immune cells react against the host recipient. The gastrointestinal system is among the most common sites affected by acute GVHD, and severe manifestations of aGVHD of the gut portends a poor prognosis in patients after HSCT.

Ironwood®

is acquiring

VectivBio

$1.08 billion equity value

May 2023

Note: Ironwood is offering to acquire VectivBio for a premium of 43% to Vectiv's closing share price on the Friday close before deal announcement. Analysts project peak sales of $705 million. This implies a 1.4x price to peak sales multiple, which is below recent benchmarks.

Source: https://investor.ironwoodpharma.com/press-releases/press-release-details/2023/Ironwood-Enters-into-Definitive-Agreement-to-Acquire-VectivBio-a-Clinical-Stage-Biotech-Company-Pioneering-Novel-Treatments-for-Severe-Rare-Gastrointestinal-Diseases/default.aspx

Atea Receives Proposal from Concentra

BOSTON, May 23, 2023 (GLOBE NEWSWIRE) -- Atea Pharmaceuticals, Inc. (Nasdaq: AVIR) ("Atea") confirmed that it has received an unsolicited proposal from Tang Capital, LP on behalf of Concentra Biosciences LLC to acquire all outstanding common shares of Atea for $5.75 per share in cash, plus a contingent value right ("CVR") representing the right to receive 80% of the net proceeds payable from any license or disposition of Atea's programs.

Atea's Board of Directors and management team regularly review opportunities to generate shareholder value and are committed to acting in the best interests of all shareholders.

Consistent with its fiduciary duties, Atea's Board of Directors, in consultation with its independent financial and legal advisors, will carefully review and evaluate the proposal from Tang Capital Partners' affiliate, Concentra Biosciences.

Atea's shareholders are advised to take no action at this time.

Concentra Biosciences

has offered to acquire

ATEA Pharmaceuticals

$480 million equity value

May 2023

Note: Kevin Tang's Concentra is offering to buy Atea Pharma for $480mm. The company reported $620 million in cash in its last quarterly filing. This is the fourth attempted transaction of this type announced in recent months.

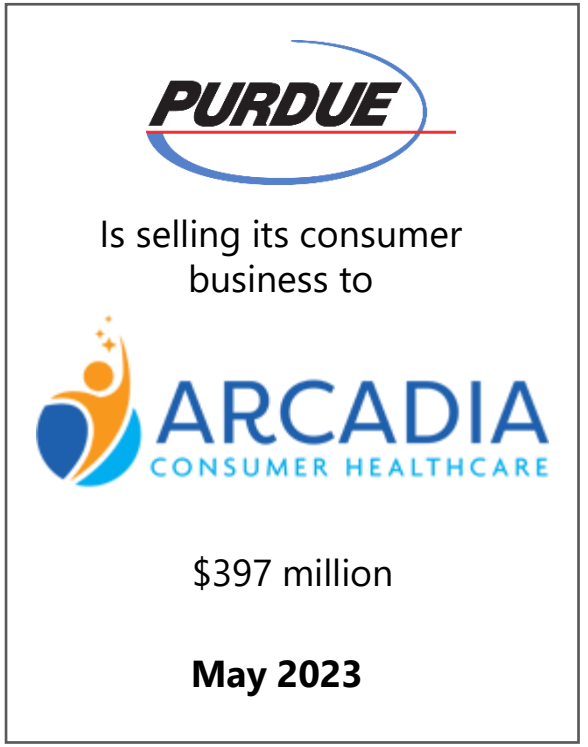
Source: https://ir.ateapharma.com/news-releases/news-release-details/atea-pharmaceuticals-confirms-receipt-unsolicited-proposal-tang

Purdue Pharma to sell Consumer Business for $397 Million

NEW YORK, May 23, 2023 (Reuters) - Bankrupt Purdue Pharma received a U.S. judge's permission on Tuesday to sell its consumer health business for $397 million to a subsidiary of Arcadia Consumer Healthcare.

U.S. Bankruptcy Judge Sean Lane approved Purdue's sale of Avrio Health at a hearing in White Plains, New York, allowing Purdue to begin liquidating its assets while it awaits a final ruling on a $10 billion settlement that would devote the company's remaining resources to combating the U.S. opioid epidemic.

Purdue's creditors' committee has pushed the company to use the proceeds from the sale to get started on that effort by compensating victims of the opioid crisis and funding addiction treatment programs.



Source: https://www.reuters.com/legal/purdue-pharma-sell-consumer-business-397-mln-2023-05-23/

CohBar Merging with Morphogenesis

BOSTON and SAN CARLOS, Calif., May 24, 2023 (GLOBE NEWSWIRE) -- Pyxis Oncology, Inc. ("Pyxis Oncology") MENLO PARK, Calif. and TAMPA, Fla. , May 23, 2023 (GLOBE NEWSWIRE) -- CohBar, Inc. (NASDAQ: CWBR) ("CohBar" or the "company") and Morphogenesis, Inc. ("Morphogenesis"), a privately-held Phase 2/3 clinical-stage biotechnology company developing novel personalized cancer vaccines and tumor microenvironment modulators to overcome resistance to current immunotherapies, today announced that they have entered into a definitive agreement for an all-stock transaction forming a company combining expertise and resources to advance a late-stage oncology pipeline. The combined company will focus on advancing Morphogenesis' two technologies that seek to overcome the major obstacles that limit the effectiveness of current immunotherapies in treating cancer.

"Following a thorough review and evaluation, we believe merging with Morphogenesis and leveraging their late-stage pipeline of novel immuno-oncology technologies represents the best path forward for our stockholders and has the potential to deliver near and long-term value," stated Dr. Joseph Sarret, CEO of CohBar. "Our board and management team believe that the combined company will be well-positioned to develop powerful new therapies with the potential to overcome resistance to current immunotherapies, an area of significant unmet need."

Under the terms of the merger agreement, subject to stockholder approval, each holder of CohBar common stock as of immediately prior to the closing of the transaction will be issued a dividend equal to approximately 3.30 shares of CohBar common stock on or about the effective date of the merger. On a pro forma basis taking into account the concurrent financing described below and the issuance of the stock dividend, pre-merger CohBar equityholders are expected to collectively own approximately 15% and pre-merger Morphogenesis equityholders are expected to collectively own approximately 77%, respectively, of the common stock of CohBar on a pro forma basis (assuming the exercise of all in-the-money warrants and options then outstanding).

Upon execution of the merger agreement, CohBar also entered into a stock purchase agreement with an affiliate of an existing investor in Morphogenesis for a $15 million private placement that is expected to close concurrently with the closing of the proposed merger. The proceeds from the private placement will be used to fund the advancement of the combined company's immunotherapy-focused development pipeline, with an anticipated cash runway through 2024. Immediately following the closing of the merger and the closing of the private placement, the shares issued in the private placement are anticipated to represent approximately 9% of the common stock of CohBar on a pro forma basis (assuming the exercise of all in-the-money warrants and options then outstanding).

CohBar INC

Has offered to merge with

Morphogenesis inc

$100 million equity value

May 2023

Note: This is a classic reverse merger. CohBar is offering to merge with Morphogenesis. The shares of CohBar jumped by more than 200% on the news of the transaction. As of its last quarterly filing CohBar had $14mm in net cash.

Source: https://www.cohbar.com/news-media/press-releases/detail/183/cohbar-inc-and-morphogenesis-inc-enter-into-definitive

Pyxis Oncology to Acquire Apexigen

BOSTON and SAN CARLOS, Calif., May 24, 2023 (GLOBE NEWSWIRE) -- Pyxis Oncology, Inc. ("Pyxis Oncology") (Nasdaq: PYXS), a clinical-stage company focused on developing next-generation therapeutics to target difficult-to-treat cancers, and Apexigen, Inc. (Nasdaq: APGN), a clinical-stage biopharmaceutical company focused on discovering and developing innovative antibody therapeutics for oncology, today announced a definitive agreement by which Pyxis Oncology will acquire Apexigen in an all-stock transaction for an implied value of $0.64 per Apexigen share. For each share of Apexigen, Pyxis Oncology will issue 0.1725 shares of its common stock, par value $0.001 per share, for a total enterprise value of approximately $16 million.

"This acquisition uniquely positions Pyxis Oncology at the forefront of antibody-drug conjugate (ADC) innovation by adding humanized antibody generation to our Flexible Antibody Conjugation Technology (FACT) ADC toolkit acquired from Pfizer, and expands our clinical pipeline into Phase 2 in select solid tumor types by leveraging our founding heritage of immuno-oncology expertise—all while maintaining our cash runway into 2025," said Lara S. Sullivan, M.D., President and Chief Executive Officer of Pyxis Oncology. "Sotigalimab is a CD40 agonist with best-in-class potential. It has demonstrated clear anti-cancer activity in patients who previously progressed on PD-(L)1 inhibitors, with impressive, durable remissions. This activity may not only be synergistic with immune checkpoint inhibitors, but also rescue their activity in patients who are refractory or have relapsed. We are excited about the potential to acquire the commercially and clinically validated APXiMAB platform to generate novel antibodies that can be optimized for targeted payload delivery. In combination with our proprietary FACT platform, we believe Pyxis Oncology is positioned with an unmatched, end-to-end system for designing and producing novel, next-generation ADC candidates with improved potency, stability and tolerability."

Under the terms of the definitive merger agreement, Pyxis Oncology expects to issue approximately 4.4 million shares of its common stock to Apexigen stockholders to acquire Apexigen. For each share of Apexigen common stock, Pyxis Oncology will issue 0.1725 shares of its common stock, par value $0.001 per share.

Upon closing of this business combination, Apexigen will become a wholly owned subsidiary of Pyxis Oncology. Pyxis Oncology's current stockholders will beneficially own approximately 90% of the combined company and Apexigen's stockholders will beneficially own approximately 10% of the combined company.

PYXIS ONCOLOGY

Has offered to acquire

Apexigen

$15.9 million equity value

May 2023

Note: Pyxis is entering to what appears to be a well thought through deal. Pyxis is not spending cash and picks up a suite of valuable royalties, a promising drug candidate and an antibody technology to complement its ADC platform.

Source: https://ir.pyxisoncology.com/news-releases/news-release-details/pyxis-oncology-acquire-apexigen

AVROBio Selling Cystinosis Program to Novartis

CAMBRIDGE, Mass.--(BUSINESS WIRE)--May 22, 2023-- AVROBIO, Inc. (Nasdaq: AVRO), a leading clinical-stage gene therapy company working to free people from a lifetime of genetic disease, today announced an agreement to sell its investigational hematopoietic stem cell (HSC) gene therapy program for the treatment of cystinosis to Novartis for $87.5 million in cash. AVROBIO retains full rights to its portfolio of first-in-class HSC gene therapies for Gaucher disease type 1 and type 3, Hunter syndrome and Pompe disease. Proceeds from this transaction are expected to extend the Company's cash runway into the fourth quarter of 2024. "This transaction strengthens AVROBIO's balance sheet, focuses our pipeline strategy and is a strong endorsement of our HSC gene therapy approach and plato® gene therapy platform," said Erik Ostrowski, AVROBIO's interim CEO and current CFO.

Transaction details

Pursuant to the terms of an asset purchase agreement, Novartis will pay AVROBIO $87.5 million in cash at closing, in consideration for the sale and transfer of certain assets related to the cystinosis program. In addition, AVROBIO has exclusively licensed to Novartis certain other assets, know-how and other intellectual property related to AVROBIO's gene therapy platform for use in cystinosis. To support the transition of the program, AVROBIO also has agreed to provide under a separate agreement certain transition, knowledge transfer and other related services.

AVROBIO

Has offered to sell its cystinosis gene therapy program to

NOVARTIS

$87.5 million

May 2023

Note: This asset sale buys AVROBio significant runway for its programs in Gaucher, Pompe and Hunter. The stock doubled on the news announcement, although the implied enterprise value upon close is now significantly negative.

Source: https://www.cohbar.com/news-media/press-releases/detail/183/cohbar-inc-and-morphogenesis-inc-enter-into-definitive

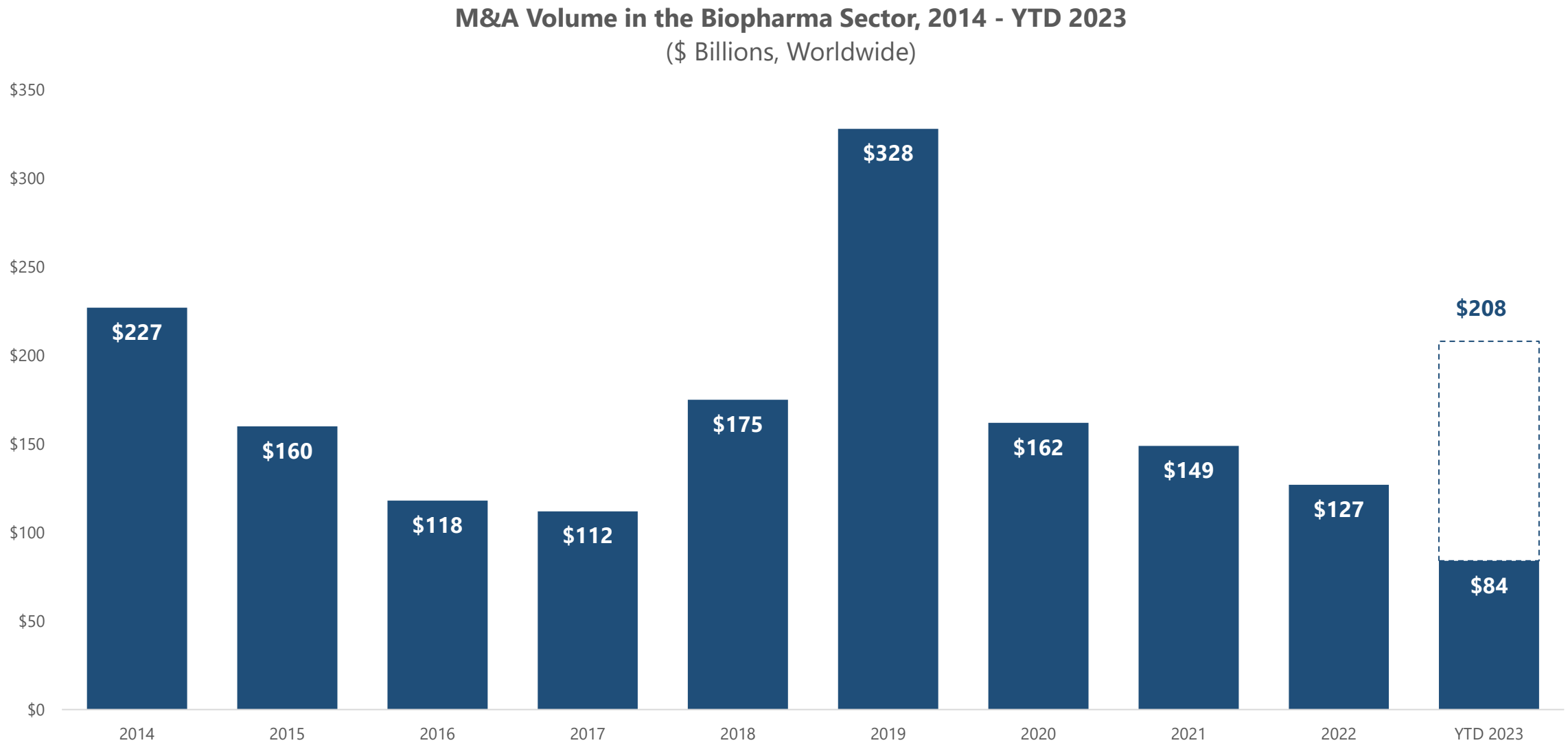
IVERIC Proxy Statement Out

See: https://www.sec.gov/Archives/edgar/data/1410939/000110465923063385/tm2316342-1_prem14a.htm

Key Points

- Iveric got its firm formal bid (from Astellas) on March 31. This coincided with a leak to the press of interest in Apellis a few days later.
- This press leak feels strategic – bankers appear to have been trying to get parties to look at Iveric – with the knowledge that Apellis might be for sale.
- Five parties of twelve contacted signed a CDA to look at Iveric. Only Astellas went forward with an acquisition but several companies appear to have done diligence.
- Iveric models peak sales at $3.7 billion – well above the Street consensus.

We are Tracking to a $208 Billion M&A Year



Source: CapitalIQ and Stifel analysis

Comment | May 26, 2023

After 2022 interest rate hikes spook investors, pharma M&A to resurge in late 2023

GlobalData Healthcare

M&A activity for pharma CMOs reached a peak in 2021, with 2022 seeing a slight decline in the number of deals.

M&A activity for pharma CMOs reached a peak in 2021, with 2022 seeing a slight decline in the number of deals. Top valuations were also higher in 2021, although there were high-value deals in 2022, such as Merck KGaA (Hessen, Germany) acquiring the injectables manufacturer Exelead Inc. (Indianapolis, IN, US) for $780m and private equity firm Advent International (Boston, MA, US) acquiring a 50.1% stake in CDMO Suven Pharmaceuticals (Hyderabad, India) for $761m. By contrast, in 2021, Thermo Fisher Scientific (Waltham, MA, US) acquired PPD (Wilmington, NC, US) and Danaher Corp (Washington, WA, US) acquired Aldevron LLC (Fargo, ND, US) for $20.9bn and $9.6bn, respectively. Russia's invasion of Ukraine in 2022 significantly added to inflationary pressures that were already at play when economies reopened after the pandemic. Rising inflation and interest rates in 2022 were the likely roots of reduced M&A activity, with CMOs reluctant to take on debt. CMO valuations contrast with the larger pharma industry, which recorded eight M&A deals above $1bn in Q1 2023, compared to five such deals in Q1 2022, according to GlobalData's publication *Global M&A Deals in Q1 2023*.

During 2018–2022, the CMO industry had 479 mergers and acquisitions of whole companies or individual facilities, a GlobalData analysis shows. The acquisition targets had a wide variety of manufacturing services, including API and dose manufacturing, packaging, and analytical services. The figure below is taken from an upcoming GlobalData publication entitled *M&A in the Contract Manufacturing Industry: Implications and Outlook – 2023 Edition* and indicates a general trend of CMO M&A activity increasing across 2018–2022. Although there is a slight dip in M&A activity in 2022 compared to 2021, it is still higher than levels in 2018–2020.

Source: https://www.pharmaceutical-technology.com/comment/pharma-ma-resurge-late-2023/

Disclosure

STIFEL | Healthcare

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