Biopharmaceutical Sector

Market Update – June 19, 2023

STIFEL | Healthcare

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STIFEL | Healthcare

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Human organ systems. Source: Getty Images.

Join Us at These Upcoming Events

1

Biotech Hangout held its last event on June 16th.

The next event will be on June 23rd.

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

Please join us.

June 16th Replay
https://twitter.com/i/spaces/1YqKDoEnNyaxV

June 23 Session:
https://twitter.com/i/spaces/1gqxvyaAZakJB

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

2

BIOTECH ceosummit

We'll be at the Biotech CEO Summit USA in La Jolla on July 17 to 19.

Would be great to see you there.

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

Macro Update

Stock market and economy. Source: Getty Images.

Substantially Improved May CPI Number in U.S.

U.S. BUREAU OF LABOR STATISTICS **June 13, 2023**

The Consumer Price Index for All Urban Consumers (CPI-U) rose 0.1 percent in May on a seasonally adjusted basis, after increasing 0.4 percent in April, the U.S. Bureau of Labor Statistics reported today. Over the last 12 months, the all items index increased 4.0 percent before seasonal adjustment.

The index for shelter was the largest contributor to the monthly all items increase, followed by an increase in the index for used cars and trucks. The food index increased 0.2 percent in May after being unchanged in the previous 2 months. The index for food at home rose 0.1 percent over the month while the index for food away from home rose 0.5 percent. The energy index, in contrast, declined 3.6 percent in May as the major energy component indexes fell.

The index for all items less food and energy rose 0.4 percent in May, as it did in April and March. Indexes which increased in May include shelter, used cars and trucks, motor vehicle insurance, apparel, and personal care. The index for household furnishings and operations and the index for airline fares were among those that decreased over the month.

The all items index increased 4.0 percent for the 12 months ending May**; this was the smallest 12-month increase since the period ending March 2021.** The all items less food and energy index rose 5.3 percent over the last 12 months. The energy index decreased 11.7 percent for the 12 months ending May, and the food index increased 6.7 percent over the last year.

Source: https://www.bls.gov/news.release/cpi.nr0.htm

Board of Governors of the Federal Reserve System

The Federal Reserve, the central bank of the United States, provides the nation with a safe, flexible, and stable monetary and financial system.

June 14, 2023

Federal Reserve issues FOMC statement

The Committee seeks to achieve maximum employment and inflation at the rate of 2 percent over the longer run. **In support of these goals, the Committee decided to maintain the target range for the federal funds rate at 5 to 5-1/4 percent.** Holding the target range steady at this meeting allows the Committee to assess additional information and its implications for monetary policy. In determining the extent of additional policy firming that may be appropriate to return inflation to 2 percent over time, the Committee will take into account the cumulative tightening of monetary policy, the lags with which monetary policy affects economic activity and inflation, and economic and financial developments.

Source: https://www.federalreserve.gov/newsevents/pressreleases/monetary20230614a.htm

This was the first FOMC meeting in 11 meetings where the Fed chose to not raise rates. In the post meeting press conference, Chairman Powell indicated that the Fed expects to raise rates a few more times in 2023. Overall, this is good news for the system and biotech.

Some Observers See No Further Fed Rate Increases

Ryan Herzog, Professor of Economics, Gonzaga University, *The Conversation,* June 14, 2023

The latest data, not to mention several other factors, however, suggests it's time for a full stop. As an economist who follows the central bank's actions closely, I believe there's good reason to think the Fed's brief hiatus is likely to turn into a permanent vacation.

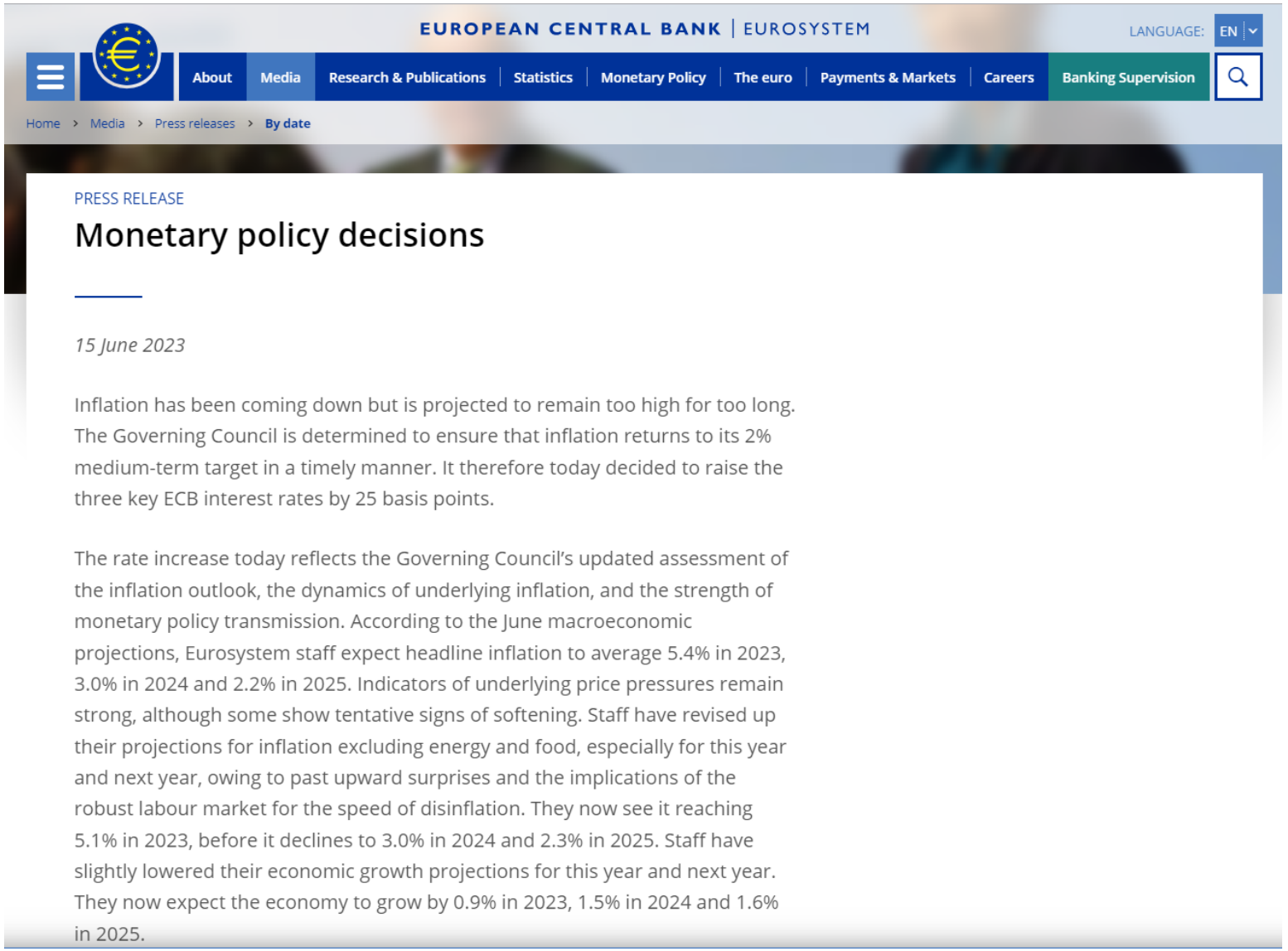
The Bureau of Labor Statistics relies on a survey that gauges rental prices from 50,000 leases, many of which were signed during the rental bubble in 2021 and 2022. A better measure of current market rents is the Zillow Observed Rent Index. That index suggests rates are declining – rents rose 4.8% year over year in May, aligning with pre-pandemic rates.

Comparing the two measures suggests the official consumer price index data lags behind the market by four to six months. Using current rents would put inflation much closer to where the Fed wants it to be. Jason Furman, former chair of the government's Council of Economic Advisors, created a modified version of core inflation – which uses a market-based measure of shelter prices – at 2.6%.

Ryan Herzog
Gonzaga University

Source: https://theconversation.com/why-the-federal-reserves-epic-fight-against-inflation-might-be-over-207693

ECB Hikes Interest Rates to Highest Level Since 2001



The European Central Bank raised interest rates by a quarter of a percentage point on June 15th and signaled another hike to come next month.

The ECB has now hiked rates at eight meetings since July in order to temper inflation. The benchmark rate in the euro area is now 3.5%, the highest since May 2001.

Source: https://www.ecb.europa.eu/press/pr/date/2023/html/ecb.mp230615~d34cddb4c6.en.html

Biopharma Market Update

Process biology. Source: Getty Images.

Biotech Stocks Update

The XBI was flat last week (0.0% movement) despite great inflation news. The XBI is up 5.6% for the year and our tracker of biotech aggregate value is up 12.8% for the year to date.

Biotech Stocks Flat Last Week

Return: June 10 to June 16, 2023

Nasdaq Biotech Index: +2.0%
Arca XBI ETF: 0.0%
Stifel Global Biotech (EV): +1.0%*
S&P 500: +2.6%

Return: Jan 1 to June 16, 2023

Nasdaq Biotech Index: 0.4%
Arca XBI ETF: +5.6%
Stifel Global Biotech: +12.8%*
S&P 500: +14.8%

VIX Down Again Last Week

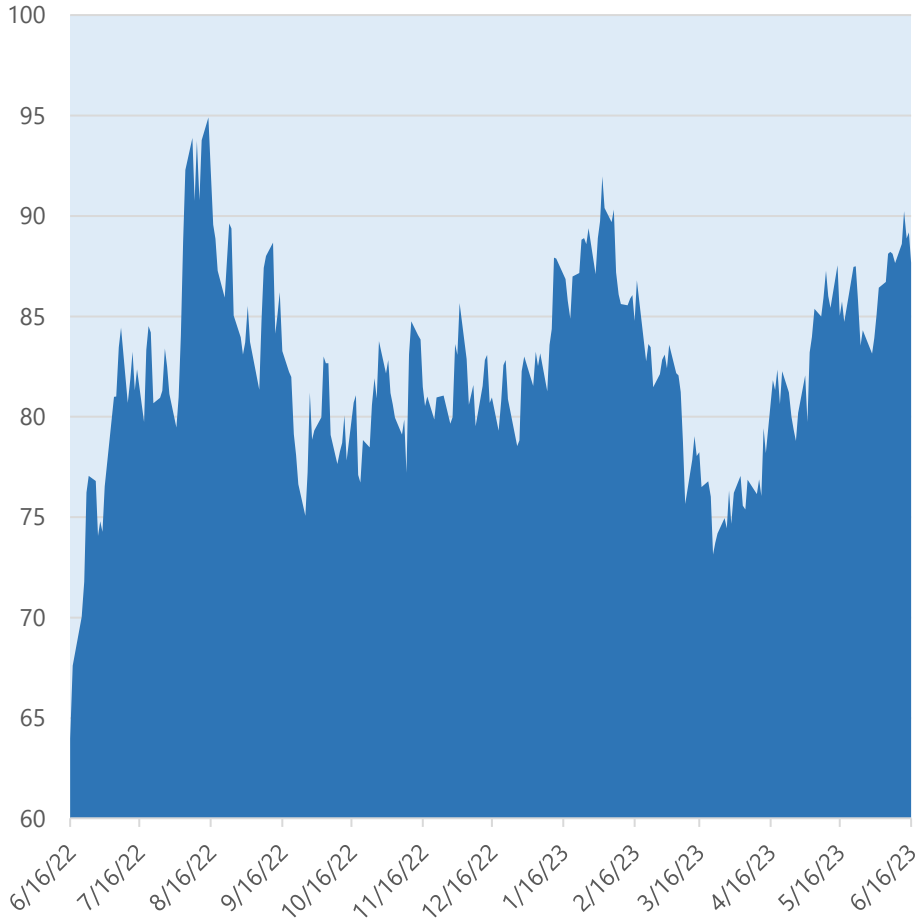
Oct 21: 29.7%
Jan 20: 19.9%
Mar 17: 24.6%
Apr 28: 15.8%
May 26: 18.0%
June 2: 14.6%
June 9: 13.7%
June 16: 13.5%

Lowest since early 2020

10-Year Treasury Yield Flat

Oct 21: 4.2%
Jan 20: 3.48%
Mar 17: 3.39%
Apr 28: 3.44%
May 26: 3.8%
Jun 2: 3.69%
June 9: 3.75%
June 16: 3.77%

XBI, Jun 16, 2022 to June 16, 2023

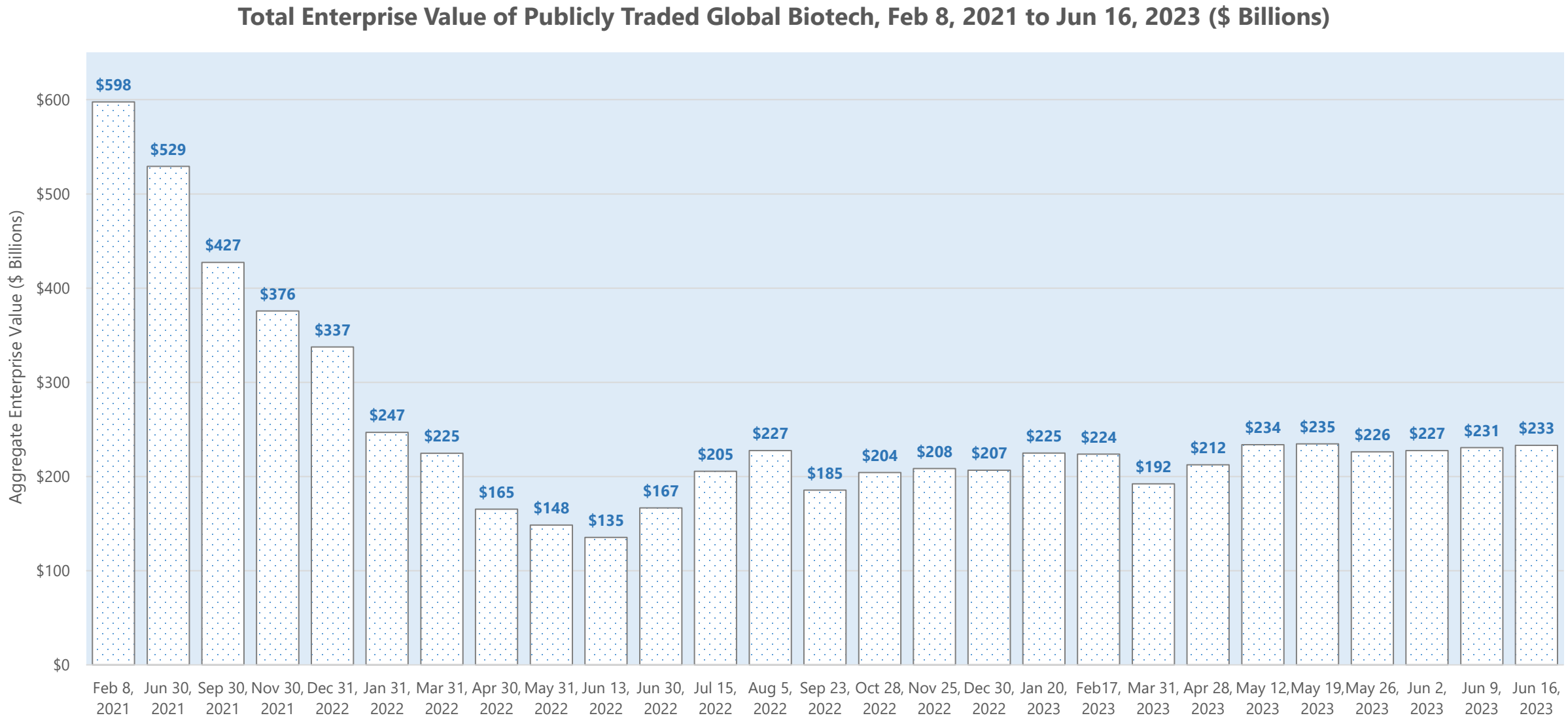


* Change by enterprise value.

Source: S&P Capital IQ and Stifel analysis

Total Global Biotech Sector Valuation Up 1% Last Week

The total value of the global biotech sector was up 1% last week. The overall biotech market is up 12.8% YTD.



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

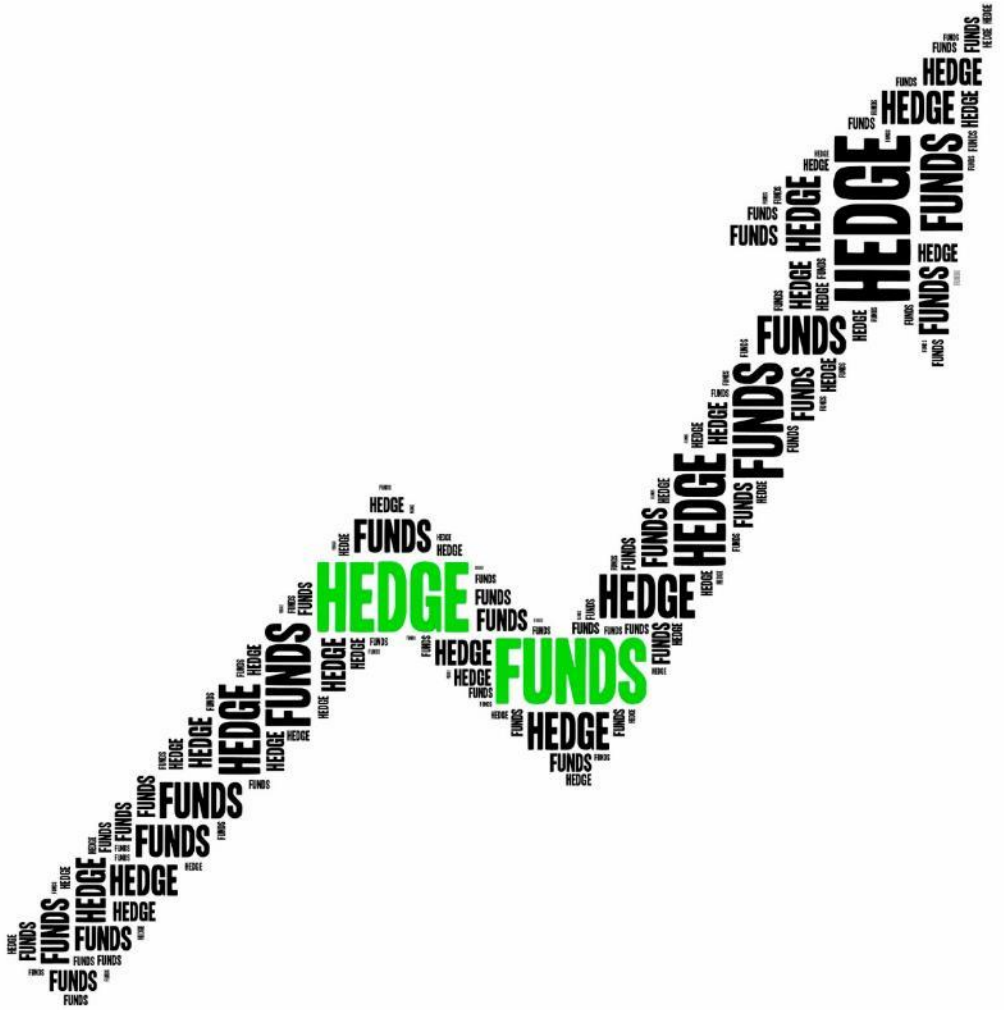
Biopharma Hedge Funds Rebounded in May 2023

Stephen Taub, *Institutional Investor*, June 14, 2023

Another month, another big round of performance for a number of biopharma-focused healthcare hedge funds.

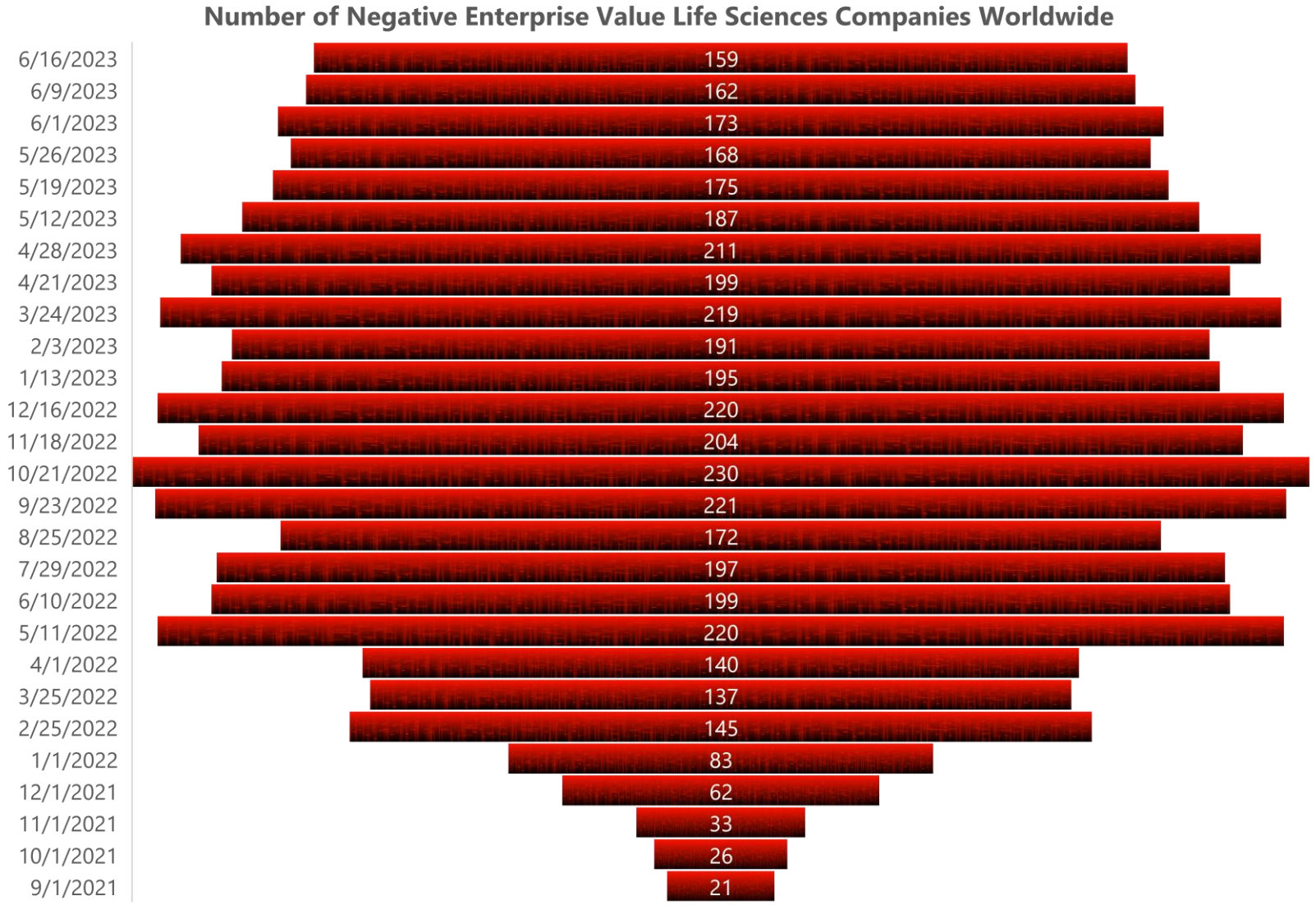
Many of the funds posted strong gains in May, and this helped several of them move back into the black for the year, if only temporarily.

The top performer in May was Casdin Capital, which has suffered perhaps the roughest ride in recent years. The firm headed by Eli Casdin posted a 4.72 percent gain last month in its biopharma hedge fund and is now up 10.7 percent for the year. RA Capital Management, meanwhile, surged 7.8 percent in May, putting the firm's hedge fund back into the black for the year by 1.2 percent. Elsewhere, Soleus Capital Management, one of the only biopharma funds to make money in 2022, moved back into the black for the year when it posted a 4.4 percent gain in May. The firm is up 3.4 percent over the first five months of 2023. Perceptive Advisors was up 2.4 percent for the month, extending its gain for the year to 8.4 percent. RTW Investments gained 1.8 percent in May and is up 6.4 percent for the year, while Averill Partners was up 1.5 percent last month and 2.6 percent for the year.



Source: https://www.institutionalinvestor.com/article/b8z4th2qcgf8q0/Biopharma-Funds-Rebound-in-May

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



Source: CapitalIQ

Last week saw another decline in the count of negative EV companies. The last time we had this few negative EV companies was April 2022.

Investors are increasingly aware of the arbitrage possibilities presented by negative enterprise value companies.

As of their latest filing dates, the 159 companies mentioned here held $23.3 billion in cash. Just 20 companies hold half of that cash. These companies are listed on the following page.

Top 20 Life Sciences Companies With The Most Negative Enterprise Values (June 16, 2023)

Company Name	SubSector	HQ Country	Exchange:Ticker	Enterprise Value ($mm, June 16, 2023)	Market Capitalization ($mm)	LTM EBITDA ($mm)	Cash (Last Reporting Period $mm)	Enterprise Value on June 16, 2022	Enterprise Value on Feb 8, 2021
Galapagos NV	Europe Biotech	Belgium	ENXTAM:GLPG	-$1,541.0	$2,800	-$198	$4,335	-$1,403	$668
Atea Pharma	US Biotech	United States	NasdaqGS:AVIR	-$273.9	$344	-$130	$620	-$175	$7,377
Nuvation Bio	US Biotech	United States	NYSE:NUVB	-$257.5	$385	-$110	$647	$11	$233
I-Mab	China Biotech	China	NasdaqGM:IMAB	-$235.3	$254	-$270	$500	$191	$3,743
Nektar	US Biotech	United States	NasdaqGS:NKTR	-$220	$108	-$151	$457	$41	$2,770
Vanda Pharma	Spec Pharma	United States	NasdaqGM:VNDA	-$127	$364	$19	$501	$106	$519
Genor Pharma	China Biotech	China	SEHK:6998	-$118.5	$107	-$109	$230	-$94	$1,293
Achilles Therapeutics	Europe Biotech	United Kingdom	NasdaqGS:ACHL	-$110.7	$40	-$67	$158	-$131	$0
Abbisko	China Biotech	China	SEHK:2256	-$109.6	$228	-$71	$345	-$103	$0
Kronos Bio	US Biotech	United States	NasdaqGS:KRON	-$100.9	$95	-$127	$226	-$92	$1,791
Fulcrum Therapeutics	US Biotech	United States	NasdaqGM:FULC	-$100	$185	-$112	$298	-$2	$276
Graphite Bio	US Biotech	United States	NasdaqGM:GRPH	-$98.6	$161	-$101	$264	-$218	$0
Antengene	China Biotech	China	SEHK:6996	-$92.9	$158	-$126	$260	$220	$1,829
NextCure	US Biotech	United States	NasdaqGS:NXTC	-$92.8	$46	-$68	$145	-$82	$63
Ilsung Pharma	Asia Pharma	South Korea	KOSE:A003120	-$92.2	$149	$1	$236	$43	$64
Vaccitech	Europe Biotech	United Kingdom	NasdaqGM:VACC	-$92.2	$88	-$23	$191	-$41	$0
Ascletis Pharma	China Biotech	China	SEHK:1672	-$91.7	$267	-$47	$360	$113	-$14
iTeos Therapeutics	US Biotech	United States	NasdaqGM:ITOS	-$91.1	$506	-$17	$602	-$161	$1,099
Malin Corporation	Biotech / Investor	Ireland	ISE:MLC	-$88	$102	-$3	$186	$112	$394
Passage Bio	US Biotech	United States	NasdaqGS:PASG	-$88.3	$53	-$109	$168	-$131	$760

Source: CapitalIQ. Note: LTM EBITDA means earnings before interest, taxes, depreciation and amortization over the previous 12 months of financial reporting.

Public Life Sciences Sector Worth $9.4 Trillion on June 16, 2023

The total enterprise value of the publicly traded life sciences sector rose by 2.1% last week ($193 billion). For the last twelve months, the sector is up 11.3%. Big gaining sectors last week were pharma services, devices, diagnostics and life science tools. This was one of the strongest weeks of the year for life sciences stocks.

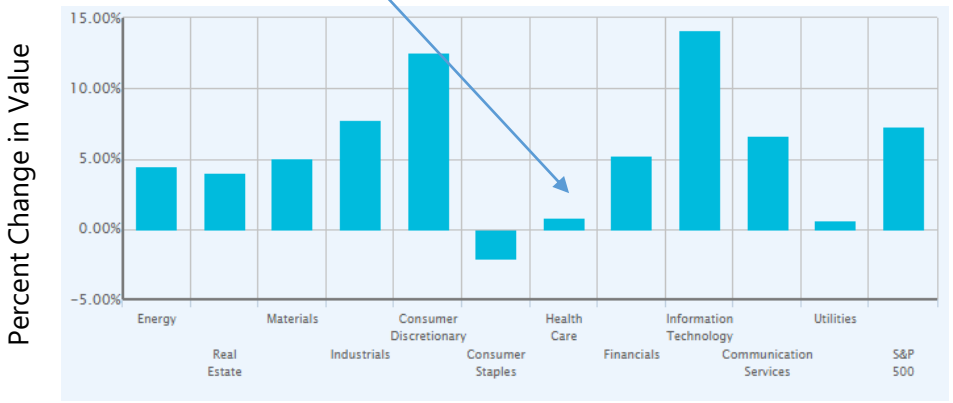
Sector	Firm Count	Enterprise Value (June 16, 2023, $millions)	Change in Last Week (percent)	Change in Last Month (percent)	Change in Last Year (percent)
API	81	$78,532	2.4%	2.2%	-12.6%
Biotech	828	$232,650	1.0%	4.6%	65.3%
CDMO	40	$181,008	2.4%	3.7%	-9.9%
Diagnostics	83	$279,637	3.8%	2.8%	26.5%
OTC	32	$31,048	1.4%	5.2%	20.3%
Commercial Pharma	728	$5,917,241	1.3%	0.6%	11.4%
Pharma Services	41	$209,615	3.9%	4.1%	-8.4%
Tools	54	$712,033	3.2%	2.8%	2.0%
Devices	183	$1,725,406	3.9%	1.3%	15.7%
HCIT	11	$26,394	2.9%	1.7%	-7.3%
Total	**2081**	**$9,395,724**	**2.1%**	**1.2%**	**11.3%**

Source: CapitalIQ

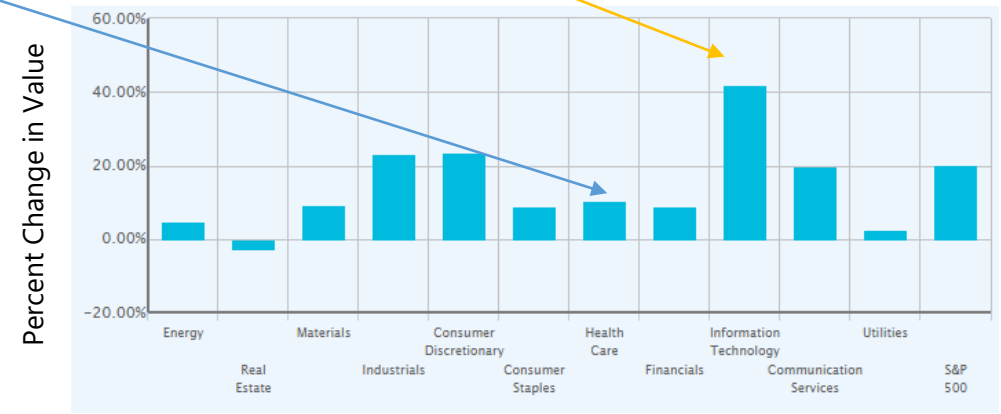
Change in S&P Component Indices in Recent Months

We are seeing the Fed start showing signs of dovishness in recent months as inflation eases up. Healthcare has not performed well as the sector has been dealing with the end of the Pandemic, a hostile FTC and the IRA. In contrast, the tech sector has been *flying* with strong AI tailwinds.

Last 30 Days



Last 12 Months



Source: CapitalIQ

Oracle Founder Larry Ellison Confirms New Gen AI Service With Cohere During Earnings Call Last Week

Venture Beat, June 12, 2023

"Oracle Corp., the software giant known for its database technology, is joining the chorus of enterprise cloud vendors betting big on generative AI services.

On Monday, the company revealed that it was developing a new cloud service with Cohere, a Toronto-based startup that specializes in building and training large language models (LLMs).

Oracle's founder and chief technology officer, Larry Ellison, confirmed the partnership during the company's fourth-quarter earnings call, where he also reported strong growth in Oracle's cloud business. Ellison said that Oracle and Cohere were working together to make it easy for enterprise customers to train their own customized LLMs using their private data, while protecting their data privacy and security."

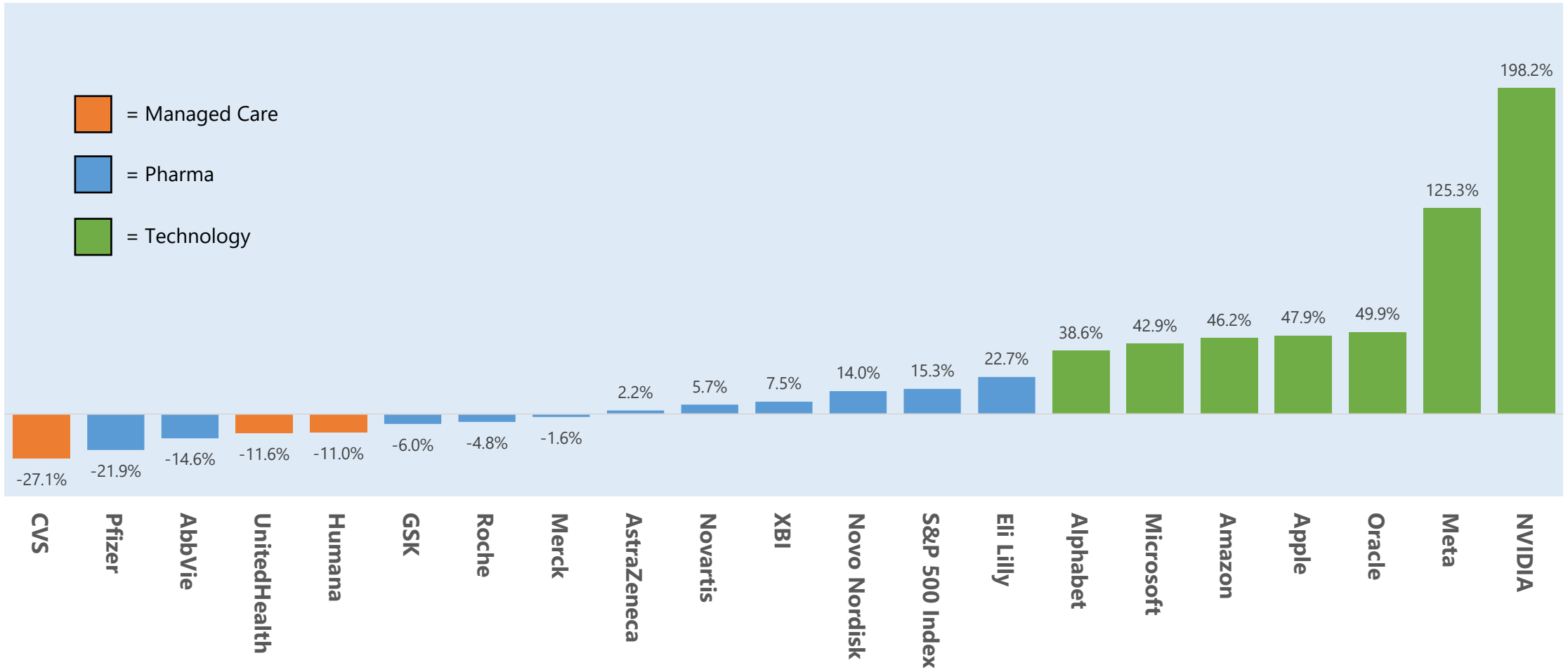
Oracle's Market Cap Up $80bn in Last Month on AI News and Cloud Growth

Sources: https://venturebeat.com/data-infrastructure/oracle-founder-larry-ellison-confirms-new-gen-ai-service-with-cohere-during-earnings-call/ and Google Finance.

Tech Stock Outperformance Driving the Market in 2023

YTD Returns of Top Pharma, Managed Care and Tech Stocks

Jan 1, 2023 to Jun 16, 2023 (% change in share price)



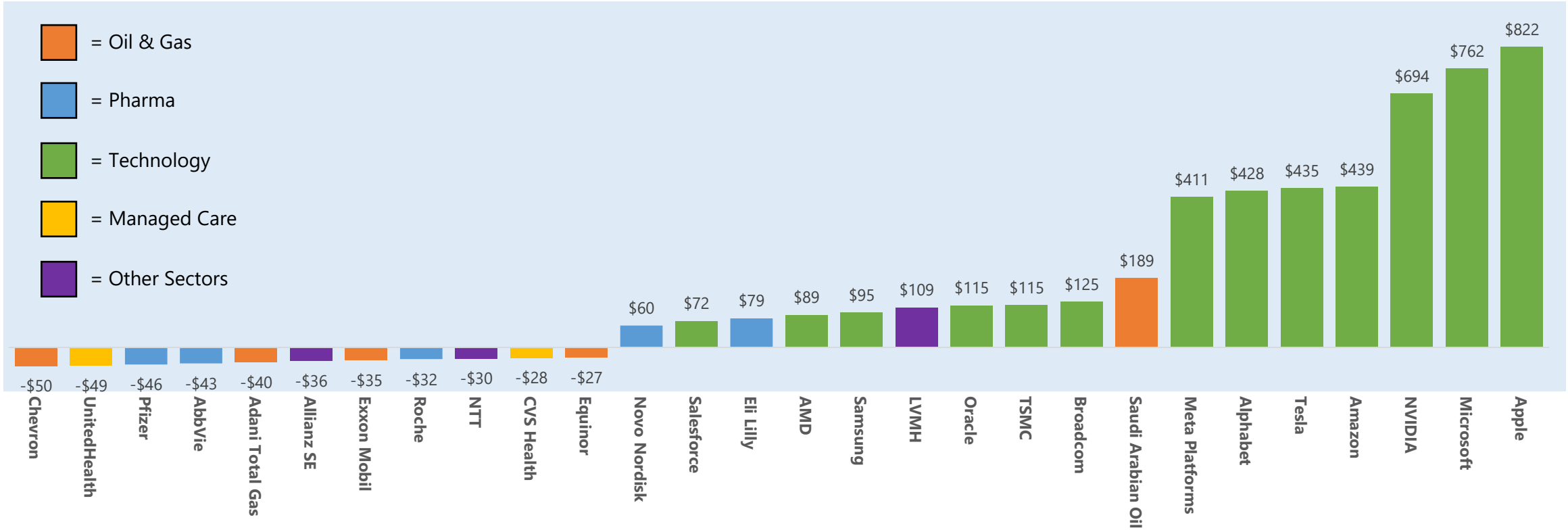
Source: CapitalIQ

Tech Stock Outperformance Driving the Market in 2023

This chart shows total change in EV year-to-date and includes sectors beyond tech and healthcare. Thirteen tech stocks have added more EV this year than the healthcare value champ (Lilly). The top fourteen techs have added $4.5 trillion in value. In contrast, the two pharma champs (Lilly and Novo) have added $0.14 trillion in value (3% as much). Further, five of the top ten value decliners this year have been in healthcare and three have been in pharma.

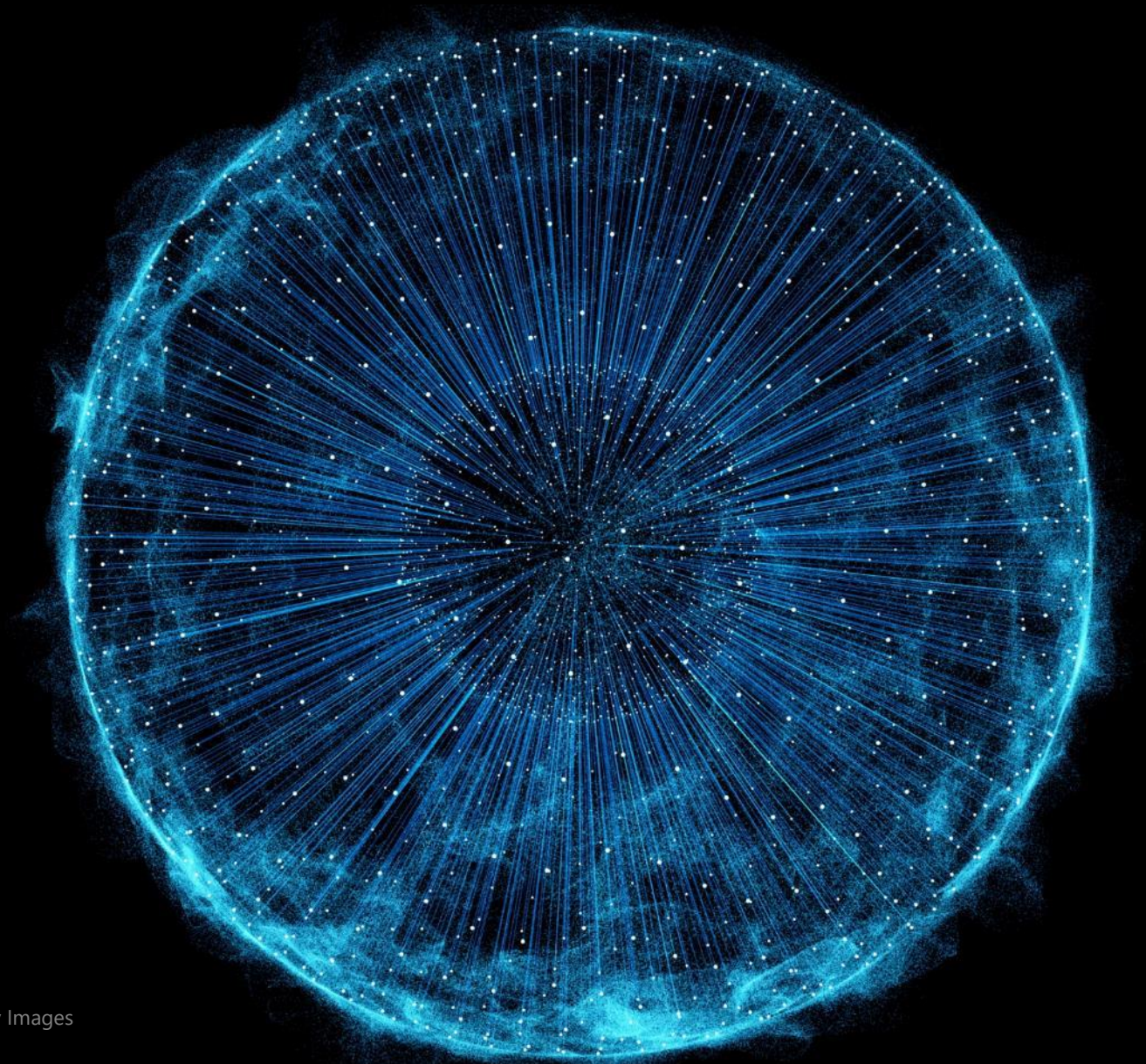
Top Global Change in Enterprise Value, Jan 1, 2023 to Jun 16, 2023 ($ billions)

(included total market gainers of $60bn or more or decliners of $25bn or more)



Source: CapitalIQ

Industry News



Representation of biological control. Source: Getty Images

U.S. Health Expenditures to Hit $7.2 Trillion by 2031

HEALTH AFFAIRS > AHEAD OF PRINT

National Health Expenditure Projections, 2022–31: Growth To Stabilize Once The COVID-19 Public Health Emergency Ends

Sean P. Keehan, Jacqueline A. Fiore, John A. Poisal, Gigi A. Cuckler, Andrea M. Sisko, Sheila D. Smith, Andrew J. Madison, and Kathryn E. Rennie

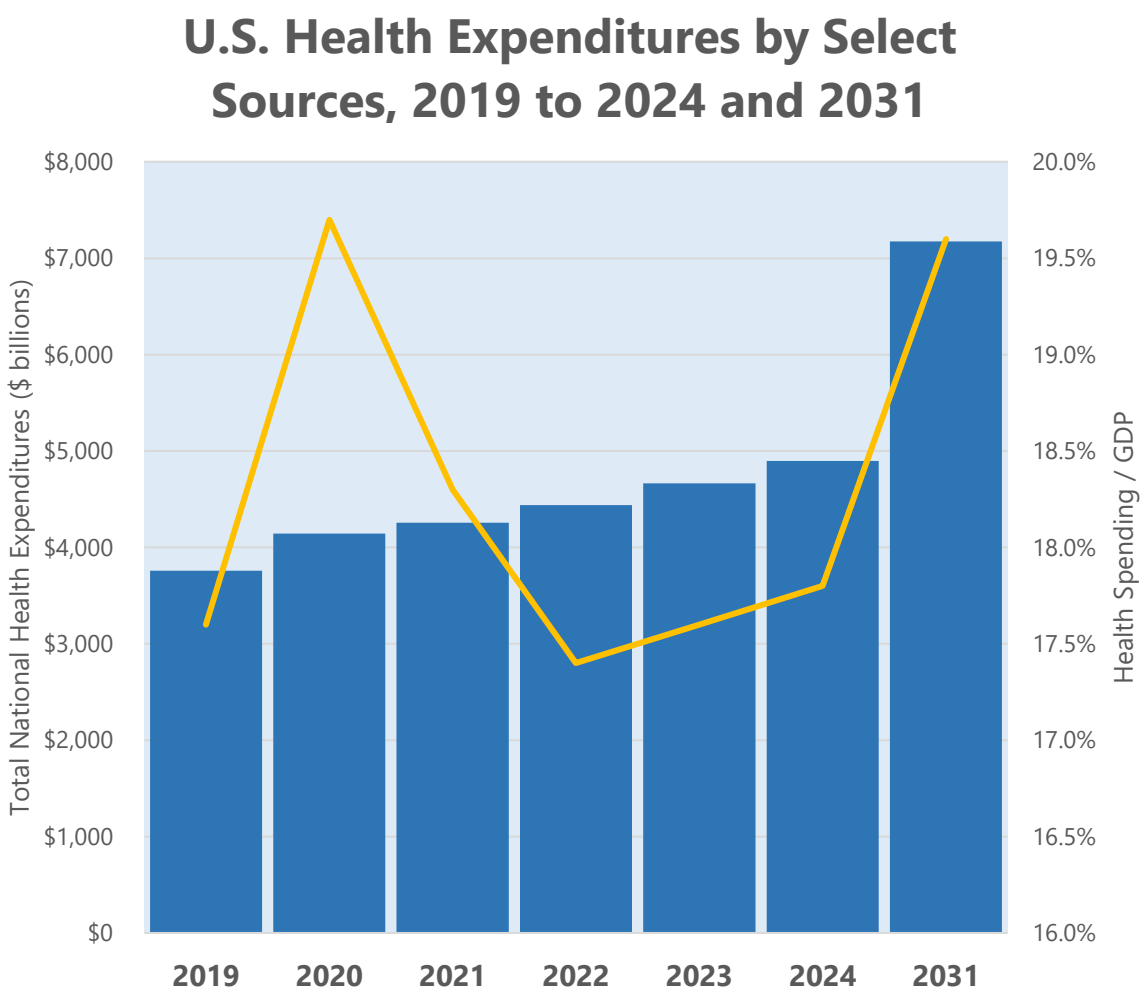
AFFILIATIONS

PUBLISHED: JUNE 14, 2023 Open Access https://doi.org/10.1377/hlthaff.2023.00403

SECTIONS VIEW PDF PERMISSIONS SHARE TOOLS

Abstract

National health expenditures are projected to grow 5.4 percent, on average, over the course of 2022–31 and to account for roughly 20 percent of the economy by the end of that period. The insured share of the population is anticipated to exceed 92 percent through 2023, in part as a result of record-high Medicaid enrollment, and then decline toward 90 percent as coverage requirements related to the COVID-19 public health emergency expire. The prescription drug provisions of the Inflation Reduction Act of 2022 are anticipated to lower out-of-pocket spending for Medicare Part D enrollees beginning in 2024 and to result in savings to Medicare beginning in 2031.



Source: https://www.healthaffairs.org/doi/full/10.1377/hlthaff.2023.00403

JUNE 16, 2023

President Biden Announces Intent to Appoint Dr. Mandy Cohen as Director of the Centers for Disease Control and Prevention

Today, President Biden announced his intent to appoint Dr. Mandy Cohen as Director of the Centers for Disease Control and Prevention.

FTC Stance on Amgen/Horizon Merger Risks Chilling Innovation

Jamie Smyth, "Big Pharma dealmaking recovers with $85bn M&A splurge," *Financial Times*, June 12, 2023

"Amgen said it would fight the decision in court but this did not temper industry-wide concerns that the action would chill M&A activity when many smaller biotechs face funding constraints. "Blocking that deal is absolutely uninformed. The more volatility there is the harder it is for investors to invest," said Paul Hastings, chief executive of Nkarta, an early-stage biotech company specialising in cell therapies that target cancers.

Paul Hastings, an industry veteran who is outgoing chair of Bio, the biotech industries' main lobbying group, warned that US antitrust authorities' tougher stance on pharma/biotech deals risks upending a decades-long business model that underpins innovation.

This model attracts investors to biotechs that are pursuing high-risk research in the knowledge that large companies may later buy them and supply the funds needed to complete expensive clinical trials and commercialise new drugs, he said. The importance of small to midsize biotechs to drug development has grown rapidly over the past two decades.

Last year emerging biopharma companies were responsible for a record 65 per cent of the molecules in the R&D pipeline without a larger company involved, up from less than 50 per cent in 2016 and 34 per cent in 2001, according to the Iqvia Institute.

Bio's concerns were echoed by Seagen, whose shareholders recently backed a proposed $43bn takeover by Pfizer — the largest deal in the sector since AbbVie agreed to buy Allergan in 2019. Seagen chief executive

David Epstein told the *Financial Times* that if the FTC took away the possibility of Big Pharma acquiring biotechs then "funding" and "innovation" would soon dry up in the sector. 'I hope that the FTC can come to understand how the ecosystem works,' he said in an interview."

Source: https://www.ft.com/content/e03d746c-e74c-4e95-8d12-d1edef2880d7

BMS and U.S. Chamber of Commerce Sue CMS over Constitutionality of IRA (Joining Merck's Suit of Last Week)

IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF NEW JERSEY
TRENTON VICINAGE

BRISTOL MYERS SQUIBB COMPANY,

Plaintiff,

v.

XAVIER BECERRA, U.S. Secretary of Health & Human Services; CHIQUITA BROOKS-LASURE, Administrator of Centers for Medicare & Medicaid Services; U.S. DEPARTMENT OF HEALTH & HUMAN SERVICES; CENTERS FOR MEDICARE & MEDICAID SERVICES,

Defendants.

Civil Action No. _____

COMPLAINT

INTRODUCTION

1. When Congress enacted the Medicare "Drug Price Negotiation Program" (the Program) in the Inflation Reduction Act (IRA) last summer, it did so under the guise of merely empowering Medicare to "negotiate" directly with pharmaceutical companies to enter voluntary price "agreements" for certain medications. In truth, however, Congress did something entirely different. Contrary to its name, the Program does not involve "negotiations" in any ordinary sense of the word. Nor does it result in real "agreements" between Medicare and pharmaceutical companies.

2. Rather, the Program creates an unprecedented regime whereby the Secretary of the U.S. Department of Health and Human Services (HHS) dictates a price at which pharmaceutical companies are compelled to sell their most innovative and

IN THE UNITED STATES DISTRICT COURT
FOR THE SOUTHERN DISTRICT OF OHIO
WESTERN DIVISION

DAYTON AREA CHAMBER OF COMMERCE
8 N. Main Street, Suite 100
Dayton, OH 45402;

OHIO CHAMBER OF COMMERCE
34 S. Third Street, Suite 100
Dayton, OH 45402;

MICHIGAN CHAMBER OF COMMERCE
600 S. Walnut Street
Lansing, MI 48933;

CHAMBER OF COMMERCE OF THE UNITED STATES OF AMERICA
1615 H Street NW
Washington, DC 20062,

Plaintiffs,

v.

XAVIER BECERRA, in his official capacity as Secretary of the U.S. Department of Health and Human Services
200 Independence Avenue SW
Washington, DC 20201;

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
200 Independence Avenue SW
Washington, DC 20201;

CHIQUITA BROOKS-LASURE, in her official capacity as Administrator of the Centers for Medicare and Medicaid Services
7500 Security Boulevard
Baltimore, MD 21244;

CENTERS FOR MEDICARE AND MEDICAID SERVICES
7500 Security Boulevard
Baltimore, MD 21244,

Defendants.

No. _____

COMPLAINT

Plaintiffs Dayton Area Chamber of Commerce ("Dayton Area Chamber"), Ohio Chamber of Commerce ("Ohio Chamber"), Michigan Chamber of Commerce ("Michigan Chamber"), and Chamber of Commerce of the United States of America ("U.S. Chamber") bring this action for declaratory and injunctive relief against the Department of Health and Human Services ("HHS") and the Centers for Medicare & Medicaid Services ("CMS") and the heads of those agencies in their official capacities (collectively, "Defendants"), alleging as follows:

INTRODUCTION

1. This lawsuit is a constitutional challenge to the prescription drug price control program established by the "Inflation Reduction Act of 2022" ("IRA"), 42 U.S.C. § 1320f *et seq*. The IRA uses the term "negotiation" to mislead the public into believing that a voluntary and fair bargaining process will take place between the government and pharmaceutical companies. The reality, however, is that Congress has not set up a negotiation at all. Congress created an unprecedented, one-sided regime that forces manufacturers to sell drugs at government-set prices. The appropriate term for this is "mandated price control," not "negotiation."

2. The IRA's price control program is not only a disastrous error of public policy; it is illegal. The program is a violation of America's fundamental constitutional requirements of limited government, property rights, the rule of law, and the separation of powers.

3. When Congress delegates authority to an administrative agency to impose price controls, the momentous nature of the delegation and the potential consequences for both private rights and the public as a whole raise fundamental separation-of-powers and other serious constitutional concerns.

4. It is therefore incumbent upon Congress to abide by traditional and constitutionally required guardrails for protecting private rights and avoiding abuses of power by government officials. Congress must provide legal standards to constrain the agency to ensure that the prices

Also see: https://www.vox.com/2023/6/16/23760650/medicare-big-pharma-prescription-drug-prices-lawsuit

Source: https://www.scribd.com/document/653447129/U-S-Chamber-of-Commerce-IRA-Medicare-Lawsuit

AstraZeneca Considering a Spin Off of China Business

AstraZeneca drafts plan to spin off China business amid tensions

Anglo-Swedish drugmaker views listing a separate unit in Hong Kong as potential shelter from global strife

Financial Times, June 18, 2023

AstraZeneca has drawn up plans to break out its China business and list it separately in Hong Kong as a way to shelter the company against mounting geopolitical tensions.

The Anglo-Swedish drugmaker began discussing the idea with bankers several months ago and is among a growing number of multinational companies now considering that option, according to three people familiar with the talks.

A separation might not ultimately take place, the same people cautioned. One of the people said listing the entity in Shanghai was also possible. The discussion shows the significant restructuring multinational corporations could be forced to undertake as they adapt to growing friction between China and the US and its allies.

Source: https://www.ft.com/content/d195f3d0-0101-414e-b190-9691e6c5661d

New Bayer Chief Plans a Radically Different Style to Cut Bureaucracy

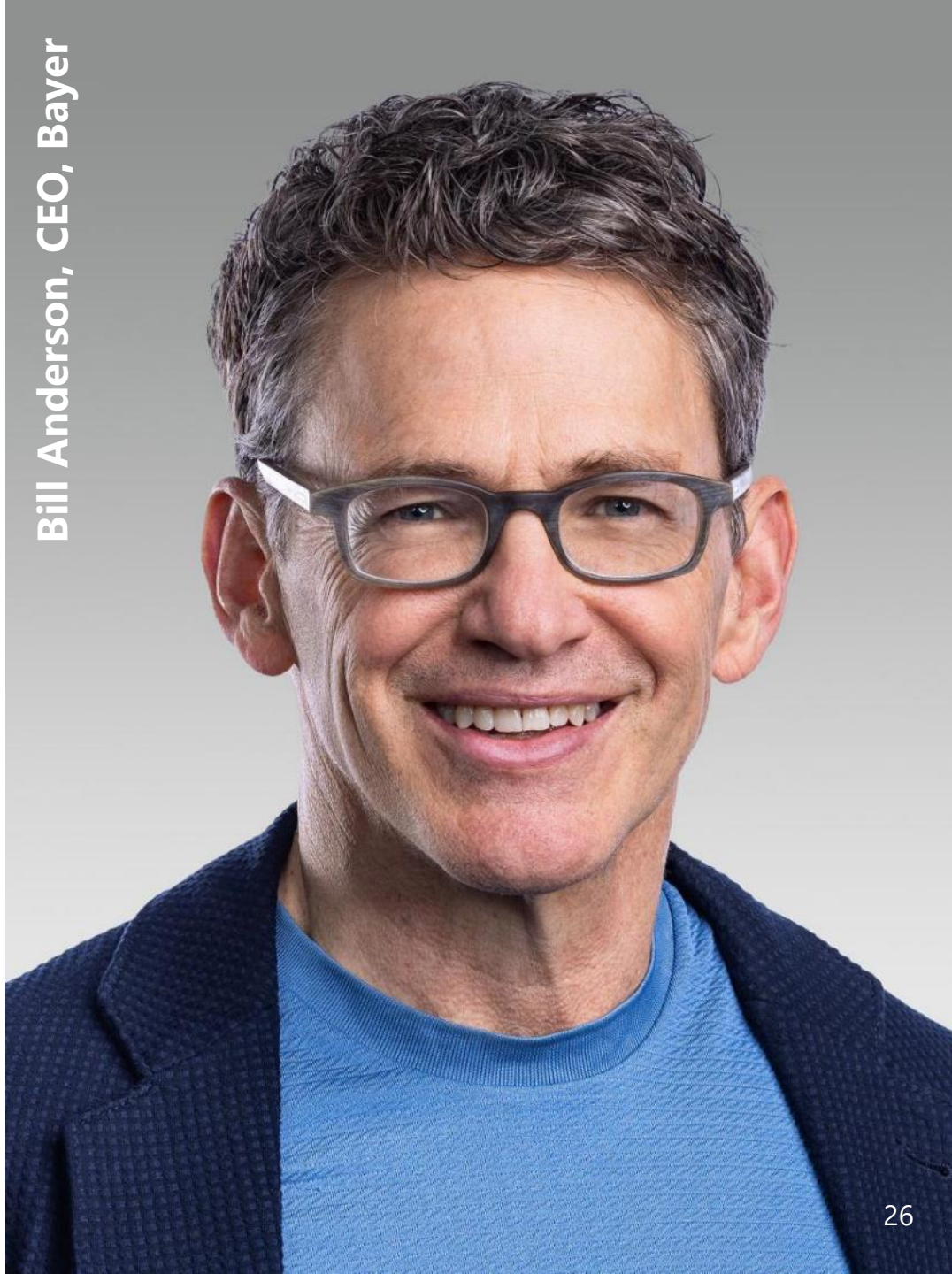
Olaf Storbeck, *Financial Times*, June 18, 2023

Article Summary: Bayer's new CEO, Bill Anderson, is planning to address internal bureaucracy in an effort to make the company more innovative and efficient. Facing pressure from shareholders and the aftermath of its acquisition of Monsanto, Anderson aims to give scientists and operational managers more influence in decision-making processes. His focus is on empowering staff, eliminating red tape, and making individuals more accountable without resorting to job cuts. Anderson wants to create a radically different approach to work organization, resource allocation, and budget determination, granting every employee the same level of impact and accomplishment.

With over 100,000 employees and a diverse range of products, Bayer is a major European corporation that has been grappling with the debt and legal costs resulting from the Monsanto acquisition. Anderson intends to shift away from the traditional top-down approach and foster a team dynamic where managers relinquish control, allowing teams to develop their own strategies. Drawing inspiration from the film "2001: A Space Odyssey," he emphasizes the need for a change in the flawed system that inhibits employee potential. Anderson also plans to eliminate traditional budgets, enabling scientists and team leaders to drive innovation by responsibly using company resources.

Anderson's approach to leadership emphasizes decentralized decision-making and empowering employees. He believes that decisions should be made by those best suited to make them, rather than relying solely on top-level management. By eliminating bureaucracy and budgets, he aims to foster a culture of accountability and resource optimization. Anderson recognizes that implementing such changes will require experimentation and collaboration from various employees, avoiding a top-down approach that revolves around his own ideas. His vision is to transform Bayer into a more efficient and innovative organization by empowering individuals and fostering a collaborative environment.

Source: https://www.ft.com/content/1d0112ad-b523-4b78-aaa3-586b1f05ccb6. Article summarized by ChatGPT. Photograph from Bayer website.



Paul Janssen R&D Philosophy

Dr. Paul Janssen, the founder of Janssen pharmaceutica (now J&J), was one of the most prolific drug discovery scientists ever. Between 1953-1991 Janssen and his team discovered >70 new medicines.

Alex Telford, a consultant on pharma R&D, enjoyed this paper about his R&D philosophy over last weekend:

R&D MANAGEMENT

Successful pharmaceutical discovery: Paul Janssen's concept of drug research

Paul J. Lewi, Adam Smith

First published: 03 September 2007 | https://doi.org/10.1111/j.1467-9310.2007.00481.x | Citations: 10

See text at right.

We are struck that Bill Anderson's emerging approach at Bayer has parallels with that described at right.

Source: https://twitter.com/Atelfo

Janssen relied on two basic criteria for effective research, both of which are frequently at odds with current practice. Firstly, he believed that research should be centered around competent people rather than around predefined processes. Secondly, the specific goals of research were not to be imposed, but should instead result from continuous critical questioning. Janssen believed that the criteria used for research were necessarily different from those applied to development, production, marketing and sales. Janssen understood that the nature of research is such that discoveries and inventions are often unplanned and unpredicted. They are made by self-motivated and inquisitive people who are encouraged to persevere in the face of adversity. Ideally researchers must be given the freedom to pursue their own research interests.

Thus the organization needs to adapt to the competences of the people who are present, or who may join the organization, rather than the other way round. In this respect, the research organization behaved more like a living organism than a preprogrammed machine.

Health insurance stocks slide after UnitedHealth warns more surgeries will drive up medical costs

CNBC, June 14, 2023

"Health insurer stocks dropped Wednesday after UnitedHealth Group warned of higher medical costs as older Americans start to catch up on surgeries they delayed during the Covid-19 pandemic.

Shares of UnitedHealth, the largest U.S. health-care provider by market value, closed around 6% lower. Medicare-focused insurer Humana declined 11%.

Insurance companies have benefited in recent years from a delay in nonurgent procedures due to hospital staffing shortages and the pandemic, which saw hospitals inundated with Covid patients. Hospitals at that time were widely seen as too risky to enter for elective procedures."

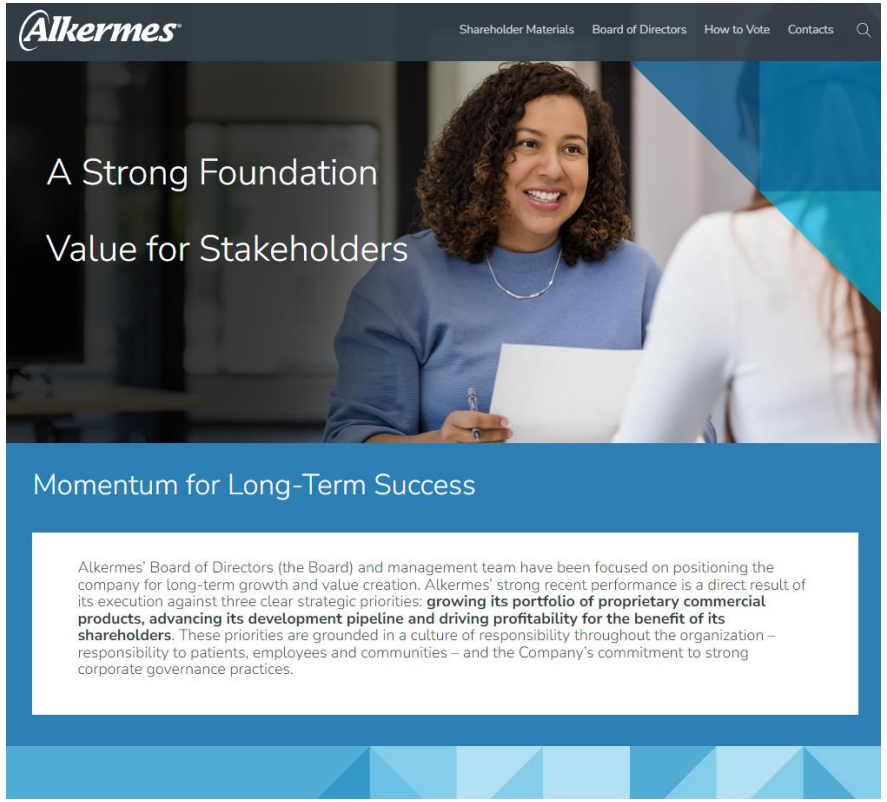
With the Pandemic over, more seniors are going in for elective knee and hip replacements.

Source: https://www.cnbc.com/2023/06/14/health-stocks-slide-after-unitedhealth-warns-of-higher-medical-costs.html. Photo from Getty Images.

Pitched Proxy Fight Underway for Alkermes Board Seats

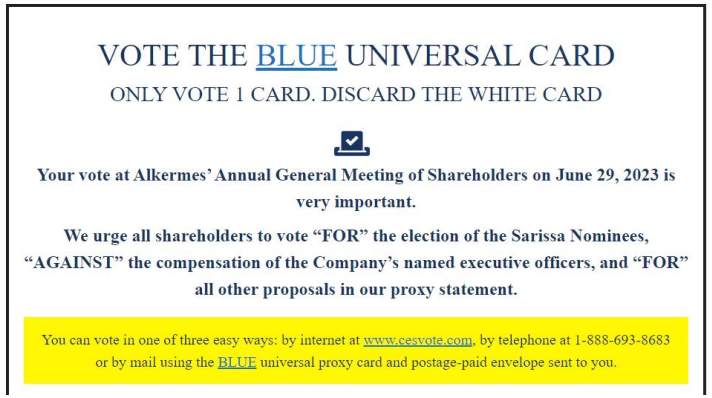
Pro Status Quo at Alkermes

www.alkermesvalue.com



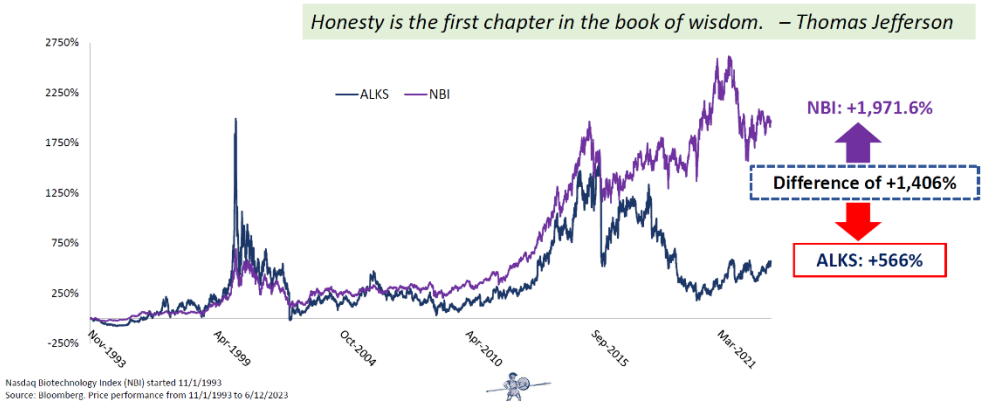
Pro Change at Alkermes

www.upgradealkermes.com



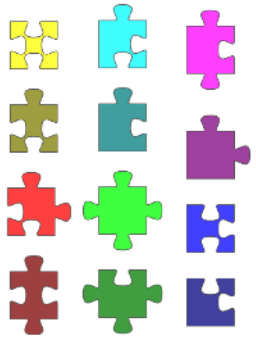
Sarissa Argues Alkermes Has Underperformed and Run Losses

Alkermes has underperformed the market for >30 years with Pops at the helm

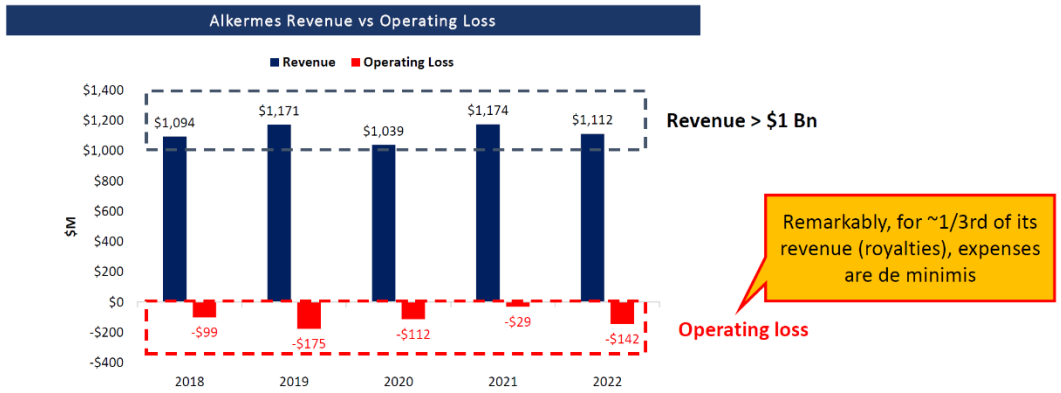


Pops has made Alkermes into a fundamentally inefficient and hodgepodge of subscale businesses

Royalties from drugs with licensed Alkermes technology	Billions of cheap free cash flows from royalties burned
Commercial products for addiction and mental illnesses	Bloated infrastructure, subscale and competing against pharma giants
Manufacturing	Manufacturing not a core strength and likely unprofitable venture
Research and Development Oncology (to be spun)	Hundreds of millions of annual R&D spend with little regard for ROI



Alkermes touts recent revenue growth but with years of revenues exceeding $1 Bn, Alkermes continues to operate at a loss



Only after 30 years and shareholder pressure did Alkermes consider shareholders

SARISSA CAPITAL MANAGEMENT LP

ELLIOTT

+ Other shareholders

Shareholder pressure

It's obvious that Alkermes only agreed to profitability targets as a result of shareholder pressure. Without shareholders pressure, Alkermes would likely continue their multi-decade status quo of underperformance

Source: https://upgradealkermes.com/wp-content/uploads/2023/06/PR-06152023.pdf

Alkermes Argues It Is On The Right Track

Executing on our Strategy to Drive Shareholder Value

June 7, 2023

Executive Summary: Transformation Has Delivered Significant Value

The Board Recognized the Need for Change and Has Led a Program of Transformation

- **Transformation plan is working, as reflected in the Company's strong stock price performance**
  - Alkermes stock price has increased ~49% since the Company announced its Value Enhancement Plan on December 10, 2020, and the Company's total shareholder return (TSR) has outperformed its peers[1] by 61%, the XBI biotech index by 83% and the NBI biotech index by 56% through the unaffected date[2]
  - The Company's TSR has also outperformed its peers and the aforementioned indices since the unaffected date through yesterday's close of business
- **Driven by the Company's share performance, operational considerations, and shareholder feedback, the Board and management recognized the need in 2019 to realign the Company's priorities, refine its strategic and operational focus, and effect certain governance changes**
  - Implemented a Board-led transformation across multiple facets of the Company, including governance and operations
  - In December 2020, we announced the Company's "Value Enhancement Plan" (Board Refreshment, Profitability Targets, Strategic Options Evaluation) following dialogue with investors, including Elliott Management ("Elliott")
- **The Board oversaw the establishment of three core strategic priorities to drive further shareholder value**
  - *Commercial*: Grow the Company's portfolio of proprietary commercial products
    - Revenues from proprietary products up ~75% from 2019 – 2023E, reaching $918M in 2023E[3]
  - *Pipeline*: Leverage the Company's medicinal chemistry and protein engineering capabilities to advance a pipeline with high ROI[4] potential
    - 2 new internally developed product approvals yielding $212M in 2022 sales, advanced nemvaleukin alfa into potential registrational studies, and orexin 2 receptor agonist into phase 1
  - *Profitability*: Drive profitability through cost optimization and operating leverage
    - Established profitability targets for 2024 and 2025, realized in excess of $40M in annual savings from headcount reductions, and announced planned separation of the oncology business to accelerate neuroscience profitability, simplify capital allocation and refine strategic focus

[1] Peers include: Acadia Pharmaceuticals Inc., Alnylam Pharmaceuticals, Inc., Blueprint Medicines Corporation, Emergent BioSolutions Inc., Exelixis, Inc., Incyte Corporation, Ionis Pharmaceuticals, Inc., Ironwood Pharmaceuticals, Inc., Jazz Pharmaceuticals plc, Neurocrine Biosciences, Inc., PTC Therapeutics, Inc., Sage Therapeutics, Inc., Sarepta Therapeutics, Inc., Ultragenyx Pharmaceutical Inc., United Therapeutics Corporation
[2] Share prices from 12/9/2020, the last trading day before Alkermes announced its Value Enhancement Plan, through 2/3/2023, the last trading day prior to Sarissa's Schedule 13D/A disclosing its notice of director nominations
[3] Reflects midpoint of financial expectations provided on June 6, 2023, which are effective only as of such date. The Company expressly disclaims any obligations to update or reaffirm these financial expectations
[4] Abbrev: ROI - Return on Investment

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Established Three Strategic Priorities to Drive Shareholder Value

Grow Commercial Portfolio

Grew proprietary revenues by 75% since 2019[1]

Overall revenues increased by 39% over the last 4 years[1,2]

LYBALVI® launch has exceeded expectations

Advance Development Pipeline

Progressed ALKS 2680, our orexin 2 receptor agonist for the treatment of narcolepsy, into phase 1 trials

Advanced nemvaleukin alfa into potential registrational trials and received FDA Fast Track designation in multiple indications

Drive Long-Term Profitability

Established profitability targets overseen by the Financial Operating Committee, including NGNI margins of 25% and 30% for 2024 and 2025, respectively

Achieved $40M annual cost savings and margin improvement over last three years[3]

Oncology separation to accelerate profitability

Alkermes stock has increased 49% since announcement of the VEP[4] - significantly beating our peers and the XBI[5]

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Qualified Board Driving Growth, Profitability, and Value Creation

Richard F. Pops – Chairman / CEO (2011)
- Chairman / CEO of Alkermes
- **Current Outside Public Boards**: Neurocrine Biosciences
- **Other Relevant Boards**: Biotechnology Industry Organization (BIO) and Pharmaceutical Research and Manufacturers of America (PhRMA)

Industry Leader w/ Practical Operational Experience

Emily Peterson Alva – Independent Director (2021)
- Former M&A Partner at Lazard (focus on transactions and strategic evaluations, with specific expertise in Healthcare)
- Strategic Advisor to CEO and Board of Constellis
- **Current Outside Public Boards**: Amneal Pharma

Global M&A Banker w/ Expertise in Complex Healthcare Transactions

Brian P. McKeon – Independent Director (2020)
- EVP / CFO / Treasurer of IDEXX Laboratories
- Former EVP / CFO of Iron Mountain
- Former EVP / CFO of Timberland Co.

Public Company Finance and Capital Allocation Leadership

Shane M. Cooke – Independent Director (2018)
- Former President of Alkermes (retired 2018)
- Former EVP / Head of Drug Technologies / CFO of Elan Corp.
- **Current Outside Public Boards**: Prothena Corp., Endo International

Global Biopharma Executive Leadership & Irish Resident Director

David A. Daglio, Jr. – Independent Director (2020)
- Former EVP / Chief Investment Officer / Executive Director of Mellon Investments Corp.; also served as Mellon's head of Opportunistic Value Strategies
- Former management consultant at Deloitte

Distinguished Equity Portfolio Manager

Nancy J. Wysenski – Lead Independent Director (2013)
- Former EVP / Chief Commercial Officer at Vertex
- Former COO at Endo Pharma, Endo International, and Endo Pharma Solutions
- **Current Outside Public Boards**: Cytokinetics

Proven Commercial Pharma Leader

Richard B. Gaynor, M.D. – Independent Director (2019)
- President, Chief of Research and Development at BioNTech US
- Former SVP, Clinical Development and Medical Affairs at Eli Lilly
- **Current Outside Public Boards**: Infinity Pharma, Zai Lab

R&D Expertise Across Various Disciplines (Academic/Operational)

Cato T. Laurencin, M.D., Ph.D. – Independent Director (2021)
- CEO, Cato T. Laurencin Institute for Regenerative Engineering
- University Professor at University of Connecticut
- Member of the National Science Foundation and NIH Advisory Council
- **Current Outside Public Boards**: MiMedx Group

Medical and Public Health Expertise in Various Therapeutic Areas

Christopher I. Wright, M.D., Ph.D. – Independent Director (2022)
- Chief Medical Officer at Ring Therapeutics
- Former SVP, Chief Medical Officer at Axovantibio
- Former SVP, Chief Medical Officer at Cyclerion Therapeutics
- Former Associate Professor of Neurology at Harvard Medical School and board-certified practicing neurologist at Brigham and Women's Hospital

Extensive Clinical Development Experience w/ Neuroscience Expertise

Nancy L. Snyderman, M.D. – Independent Director (2016)
- Consulting Professor in the School of Global Health at the Stanford University Center for Innovation in Global Health
- Former Otolaryngologist at California Pacific Medical Center
- **Current Outside Public Boards**: Axonics, Lyra Therapeutics, Future Health ESG Corp.

Experienced Physician w/ Communications Background

Frank Anders ("Andy") Wilson – Independent Director (2019)
- Former SVP / CFO / Chief Accounting Officer at PerkinElmer
- Former VP, Investor Relations and Finance at Danaher Corp.
- Former VP, Finance / Division CFO at AlliedSignal (now Honeywell International)
- **Current Outside Public Boards**: Cabot Corp., Novanta

Finance / Accounting Expertise in Life Sciences

Legend:
- Committee Chair
- Joined since 2019
- Up for Election in 2023
- A Audit and Risk Committee
- C Compensation Committee
- F Financial Operating Committee
- N Nominating and Corporate Governance Committee

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Source: https://www.alkermesvalue.com/getmedia/6d0bc892-81ec-4a98-9d6d-2c353713261d/alkermes-investor-presentation-6-7-23.pdf

Catalent Finally Reports Earnings: Revenue Down 19%

“June 12, 2023 (Reuters) - Catalent's shares shot up 12% on Monday as the contract drug manufacturer posted third-quarter revenue ahead of estimates after a long delay caused by persistent production issues at its major facilities.

The company reported a larger-than-expected quarterly loss and cut its annual revenue forecast for the second time, but strength in its biologics unit drove quarterly sales past tempered Wall Street estimates.

Catalent's "results cleared an admittedly low bar", Stephens analyst Jacob Johnson said.”

Catalent®

Source: https://www.reuters.com/business/healthcare-pharmaceuticals/catalent-reports-bigger-than-expected-loss-production-challenges-2023-06-12/

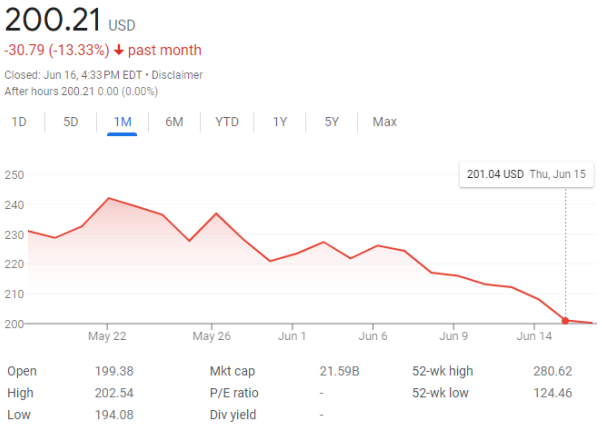
AbbVie Sues BeiGene Over Zanubrutinib Patent

Biospace, June 15, 2023

"AbbVie has filed a lawsuit accusing China-based BeiGene's new blood cancer drug Brukinsa (zanubrutinib) of infringing on its patent for Imbruvica (ibrutinib). Imbruvica was co-developed by J&J's Janssen and AbbVie's Pharmacyclics and approved in 2014 by the FDA as a treatment for chronic lymphocytic leukemia.

Brukinsa, which gained its FDA approval in January 2023, had its patent issued on Tuesday. Through its complaint, filed that same day in federal court in Delaware, AbbVie is seeking a declaratory judgment of infringement plus damages, Bloomberg Law reported.

BeiGene's shares in Hong Kong and mainland China have fallen more than 10% since the announcement."



We don't have particular insight into the legal matters here but would note that a previous suit between Acerta (AZ) and AbbVie over ibrutinib patents was settled confidentially.

Source: https://www.biospace.com/article/abbvie-files-patent-infringement-lawsuit-against-beigene-s-brukinsa/

BeiGene to Vigorously Defend Patent Infringement Allegations by Pharmacyclics

BASEL, Switzerland & BEIJING & CAMBRIDGE, Mass.—June 15, 2023--(BUSINESS WIRE)--BeiGene (NASDAQ: BGNE; HKEX: 06160; SSE: 688235), a global biotechnology company, is aware that Pharmacyclics LLC has filed a complaint against BeiGene, Ltd. and BeiGene USA, Inc., alleging that BeiGene's BRUKINSA® infringes a Pharmacyclics patent issued on June 13, 2023. BeiGene's work is original, and we will vigorously defend against all allegations of patent infringement.

It is an unfortunate but rather regular occurrence that companies make allegations that a competitive product potentially infringes their intellectual property rights, even more so in response to a clearly differentiated medicine for cancer patients as BRUKINSA.

BeiGene has developed original and novel intellectual properties around BRUKINSA to demonstrate its differentiated profile. BRUKINSA's broad global development and registration program includes more than 4,900 patients in 35 trials across 29 markets. BRUKINSA is now approved in more than 65 markets around the world and is approved in chronic lymphocytic leukemia (CLL) or small lymphocytic lymphoma (SLL), Waldenström's macroglobulinemia (WM), mantle cell lymphoma (MCL), and relapsed or refractory (R/R) marginal zone lymphoma (MZL) in the United States.

Most recently, the ALPINE study, a head-to-head comparison between BRUKINSA and IMBRUVICA® in R/R CLL/SLL, demonstrated BRUKINSA's superior efficacy (PFS and ORR) and safety (atrial fibrillation) over IMBRUVICA. The study also reported zero sudden cardiac death events for BRUKINSA versus a 1.9% rate for IMBRUVICA.

As a science-based, global biotech company with over 9,400 people and operations on five continents, BeiGene highly values and respects valid and enforceable intellectual property rights. BeiGene remains confident in BRUKINSA's intellectual property and will continue its mission to discover and develop innovative oncology treatments that are more efficacious and safer. BeiGene also remains committed to making medicines that are more affordable and accessible to cancer patients worldwide.

Source: https://www.businesswire.com/news/home/20230615020330/en/BeiGene-to-Vigorously-Defend-Patent-Infringement-Allegations-by-Pharmacyclics

Drugmaker Warns US Data Rules Threaten Access to Alzheimer's Treatment

Jamie Smyth, *Financial Times*, June 17, 2023

"Eisai has warned that mandatory data collection by US health authorities could restrict patient access to the Japanese drugmaker's new Alzheimer's treatment. The company said a decision by Centers for Medicare and Medicaid Services to restrict financial support for Leqembi to Alzheimer's patients whose doctors participate in a health agency database could have "unintended consequences".

CMS said the database, also known as a registry, would collect evidence about how the drug works in practice and make it available to researchers to conduct studies about Leqembi and similar drugs. It marks the first time that Medicare — the US government health scheme for people aged over 65 — has made such a data-gathering requirement mandatory for a drug deemed safe and effective by regulators."

Source: https://www.ft.com/content/8596a170-bad1-4e32-b11b-37e1b1daa4ab. Photo from Getty Images.

Ipsen Achieves Approval Last Week for Odevixibat in Alagille Syndrome

PARIS, FRANCE, 13 June 2023 – Ipsen (Euronext: IPN: ADR: IPSEY) today announced that the U.S. Food and Drug Administration (FDA) has approved Bylvay® (odevixibat) for the treatment of cholestatic pruritus in patients from 12 months of age with Alagille syndrome (ALGS). Bylvay is a once-daily, non-systemic ileal bile acid transport inhibitor (IBATi) that acts locally in the small intestine and has minimal systemic exposure. Bylvay was approved as the first drug treatment option for patients living with cholestatic pruritus due to progressive familial intrahepatic cholestasis (PFIC) in the U.S., and for the treatment of PFIC in Europe, in 2021. Bylvay is immediately available via prescription for eligible ALGS patients.

"Today's approval of Bylvay in a second indication allows patients and physicians to access an additional treatment option that has the potential to improve the management of pruritus, or intense itch, in this distressing condition that tends to affect young children," said Howard Mayer, Executive Vice President and Head of Research and Development for Ipsen. "We are proud to have achieved FDA approval for Bylvay as a treatment for ALGS in the U.S. and we are committed to making it available to many more eligible patients across the world."

Positive data from the Phase III ASSERT study, presented at the 2022 American Association for Study of Liver Diseases congress, demonstrated that Bylvay provided highly statistically significant and clinically meaningful sustained improvements in pruritus, starting early after initiation of treatment. More than 90% of patients were pruritus responders (≥ 1 point change at any time during 24 weeks). The overall incidence of treatment-emergent adverse events was similar to placebo. No patients discontinued the study and 96% of patients rolled over into the open-label extension study.

First approved by FDA for cholestatic pruritus caused by PFIC, Ipsen's odevixibat (Bylvay®) has now won an FDA approval for cholestatic pruritus due to Alagille syndrome in patients 12 months of age and older.

With analysts attributing $750mm to $1bn in peak sales to this label, Ipsen's recent acquisition of Albireo for $952 million plus a modest CVR looks positively brilliant.

This is quite the turnaround for Ipsen in rare disease which had previously paid $1.3 billion for Clementia – only to later take a $750mm write down after the deal disappointed.

Source: https://www.ipsen.com/press-releases/u-s-fda-approves-bylvay-for-patients-living-with-cholestatic-pruritus-due-to-alagille-syndrome/

Mersana Down 60% on Partial Clinical Hold

Mersana Therapeutics Announces Partial Clinical Hold on UP-NEXT and UPGRADE-A Clinical Trials

CAMBRIDGE, Mass., June 15, 2023 (GLOBE NEWSWIRE) -- Mersana Therapeutics, Inc. (NASDAQ: MRSN), a clinical-stage biopharmaceutical company focused on discovering and developing a pipeline of antibody-drug conjugates (ADCs) targeting cancers in areas of high unmet medical need, today announced that the U.S. Food and Drug Administration (FDA) has issued a partial clinical hold pausing new patient enrollment in UP-NEXT and UPGRADE-A, the company's ongoing clinical trials of UpRi in platinum-sensitive ovarian cancer. UPLIFT, Mersana's ongoing clinical trial of UpRi in platinum-resistant ovarian cancer, completed enrollment in October 2022. Patients who are already enrolled in these trials may continue receiving UpRi. Mersana expects to lock its UPLIFT clinical trial database and disclose UPLIFT top-line data by early August.

The partial clinical hold follows a submission by Mersana of a recent aggregate safety report of all patients dosed with UpRi (approximately 560 patients) evaluating bleeding events.

Although data on the background rate of bleeding in platinum-resistant ovarian cancer are limited, Mersana's recent assessment determined that serious bleeding events appear to occur at a higher rate than background. While most bleeding cases in this aggregate safety analysis were low-grade, five (<1%) Grade 5 (fatal) bleeding events were observed among the approximately 560 patients dosed to date. The causes of bleeding events remain under investigation.

"Patient safety is always at the forefront for us, and work is now underway to compile further analyses that may inform FDA," said Anna Protopapas, President and Chief Executive Officer of Mersana Therapeutics. "Additionally, with UPLIFT top-line data on the near-term horizon, we will soon have a much more complete assessment of both the efficacy and safety profile for UpRi in platinum-resistant ovarian cancer."

Sources: https://ir.mersana.com/news-releases/news-release-details/mersana-therapeutics-announces-partial-clinical-hold-next-and and Google Finance.

Kura Shows Impressive Menin Inhibitor Data at EHA

SAN DIEGO, June 11, 2023 (GLOBE NEWSWIRE) -- Kura Oncology, Inc. (Nasdaq: KURA), a clinical-stage biopharmaceutical company committed to realizing the promise of precision medicines for the treatment of cancer, today announced updated clinical data from KOMET-001, a Phase 1/2 clinical trial of the Company's potent and selective menin inhibitor, ziftomenib, including significant clinical activity in patients with heavily pretreated and co-mutated relapsed/refractory NPM1-mutant acute myeloid leukemia (AML).

The updated clinical data are being featured during a late-breaking oral session today at the 2023 European Hematology Association (EHA) Annual Congress in Frankfurt, Germany. A copy of the presentation is available in the Posters and Presentations section on Kura's website.

"Our goal with our ziftomenib program is to transform the standard of care for patients with acute leukemias," said Stephen Dale, M.D., Chief Medical Officer of Kura Oncology, "and we are delighted to share new clinical and preclinical data that we believe further demonstrate its potential best-in-class product profile. The emerging data for ziftomenib include: high clinical activity in relapsed/refractory NPM1-mutant AML patients, including 35% achieving durable complete remissions (CR) with maintained full count recovery on ziftomenib monotherapy; a lower frequency of MEN1 resistance mutations; a favorable safety and tolerability profile; strong evidence of mechanistic synergy with standards of care such as venetoclax and FLT3 inhibitors; and convenient once-daily, oral dosing and optimal pharmaceutical properties for combination. We believe ziftomenib has the ideal properties to become a cornerstone of therapy across the continuum of treatment, and we intend to build on the growing momentum as we continue to execute on our registration-enabling study in NPM1-mutant AML and move rapidly into combinations."

As of the data cutoff on April 12, 2023, seven of the 20 patients (35%) with NPM1-mutant AML treated at the recommended Phase 2 dose (RP2D) of 600 mg achieved a CR with full count recovery. Notably, 33% (2/6) of patients with FLT3 co-mutations and 50% (4/8) of patients with IDH co-mutations achieved a CR on ziftomenib. Two patients underwent a stem cell transplant (SCT) and remain in remission as of the data cutoff, including one on post-SCT ziftomenib maintenance therapy. An eighth patient who had a CR with incomplete recovery (CRi) at the time of transplant subsequently evolved to a CR and remains on study.

Source: https://ir.kuraoncology.com/news-releases/news-release-details/kura-oncology-presents-late-breaking-clinical-data-menin

Bristol Myers Squibb's Breyanzi Delivers Deep and Durable Responses in Relapsed or Refractory Follicular Lymphoma as Presented at ICML 2023

June 17, 2023 - PRINCETON, N.J.--(BUSINESS WIRE)-- Bristol Myers Squibb (NYSE: BMY) announced the first disclosure of primary analysis results from two pivotal studies, TRANSCEND FL, an open-label, global, multicenter, Phase 2, single-arm study evaluating Breyanzi (lisocabtagene maraleucel; liso-cel) in patients with relapsed or refractory follicular lymphoma (FL) and the relapsed or refractory mantle cell lymphoma (MCL) cohort of TRANSCEND NHL 001, an open-label, multicenter, Phase 1, single-arm, seamless-design study evaluating Breyanzi. These data were presented in late-breaking oral presentations at the 2023 International Conference on Malignant Lymphoma (ICML) on Saturday, June 17.

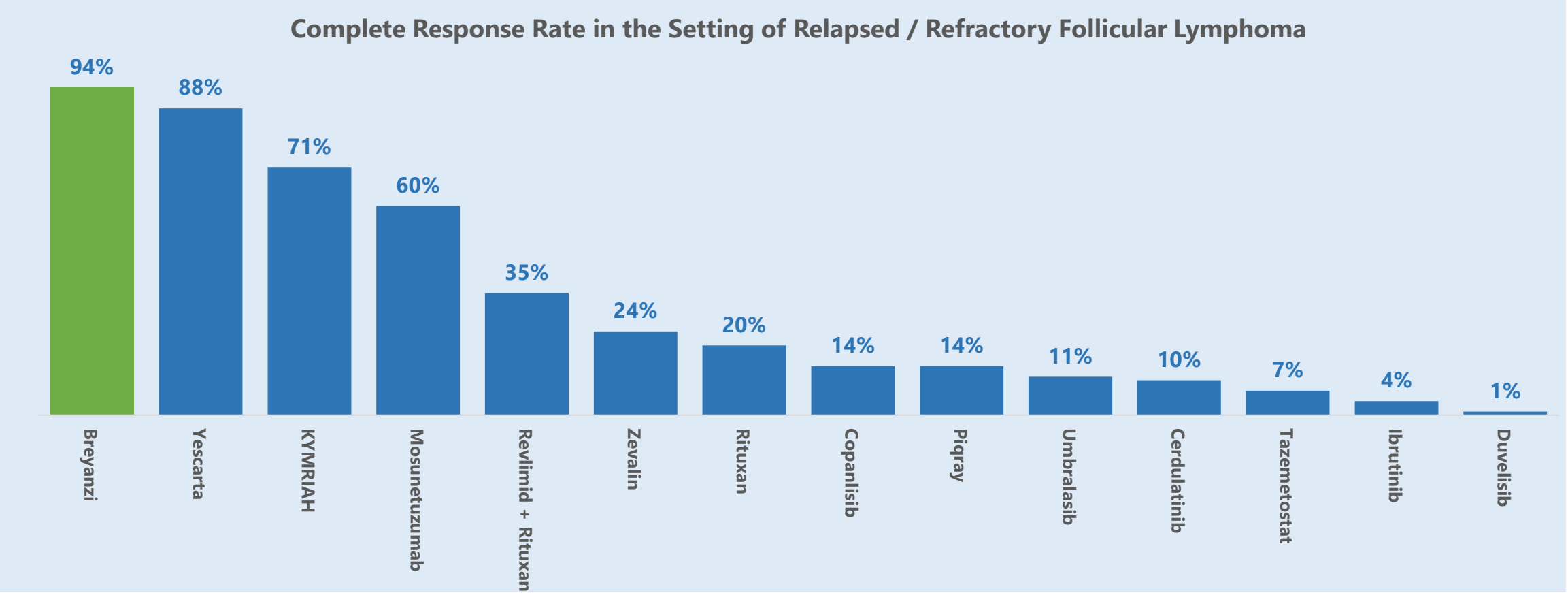
"With Breyanzi, we're dedicated to delivering a CAR T cell therapy with a differentiated profile to transform outcomes for some of the most difficult-to-treat lymphomas," said Anne Kerber, senior vice president, head of Cell Therapy Development, Bristol Myers Squibb. "Based on results from TRANSCEND FL and TRANSCEND NHL 001, Breyanzi continues to demonstrate the ability to elicit significant deep and durable responses alongside a manageable safety profile, potentially addressing areas of high unmet need and reinforcing our commitment to advancing innovative solutions for the broadest array of hematologic malignancies of any CD19-directed CAR T cell therapy."

TRANSCEND FL, the largest clinical trial to date to evaluate a CAR T cell therapy in patients with relapsed or refractory indolent non-Hodgkin lymphoma, including FL, enrolled adults with relapsed or refractory disease treated with Breyanzi in the second-line and third-line plus setting. Patients received treatment with Breyanzi at a target dose of 100 x 106 CAR-positive viable T cells. In efficacy evaluable patients with relapsed or refractory FL treated with Breyanzi in the third-line plus setting (n=101), the overall response rate (ORR) was 97% (95% CI: 91.6-99.4; one-sided $p<0.0001$), with 94% of patients achieving a complete response (CR; 95% CI: 87.5-97.8; one-sided $p<0.0001$). Responses were durable with a median duration of response not reached at a median follow-up of 16.6 months. At 12 months, 81.9% of responders had an ongoing response. Median progression-free survival (PFS) was also not reached at a median follow-up of 17.5 months, with 12-month PFS achieved in 80.7% of patients.

With a median on-study follow-up of 18.9 months in the safety set (n=130), which included patients treated in the second-line plus setting, Breyanzi exhibited a manageable safety profile, with no new safety signals observed and low rates of severe cytokine release syndrome (CRS) and neurologic events (NE). Any grade CRS occurred in 58% of patients, with Grade 3 CRS occurring in 1% of patients and no Grade 4/5 CRS reported. Any grade NEs were reported in 15% of patients, with Grade 3 NEs occurring in 2% of patients and no Grade 4/5 NEs reported.

Source: https://investors.bms.com/iframes/press-releases/press-release-details/2023/Bristol-Myers-Squibbs-Breyanzi-lisocabtagene-maraleucel-Delivers-Deep-and-Durable-Responses-in-Relapsed-or-Refractory-Follicular-Lymphoma-and-Mantle-Cell-Lymphoma-in-TRANSCEND-Clinical-Trials-Presented-at-ICML-2023/default.aspx

Breyanzi® Efficacy Data in R/R Follicular Lymphoma Stunning



Note: BREYANZI is a CD19-directed genetically modified autologous T cell immunotherapy indicated for the treatment of adult patients with large B-cell lymphoma (LBCL).

Sources: https://ashpublications.org/blood/article/134/7/636/260715/High-rate-of-durable-complete-remission-in; https://pubmed.ncbi.nlm.nih.gov/29226764/; https://ascopubs.org/doi/full/10.1200/JCO.19.00010; https://www.cancerresearchuk.org/about-cancer/find-a-clinical-trial/a-trial-looking-at-zevalin-and-chemotherapy-for-relapsed-follicular-lymphoma; https://onlinelibrary.wiley.com/doi/10.1002/ajh.25659; https://www.hcp.aliqopa-us.com/efficacy/overall-response-rate; https://www.thelancet.com/journals/lanonc/article/PIIS1470-2045%2822%2900335-7/fulltext; https://twitter.com/lymphomahub/status/1304449307936993280; https://memoinoncology.com/ash-2021-english/promising-novel-approaches-in-various-b-cell-malignancies/.

Merck Abstract on Efinopegdutide Published Ahead of European Liver Meeting (EASL)

Merck reported data on its dual GLP-1/glucagon receptor co-agonist efinopegdutide in NAFLD last week and compared results to 1mg Semaglutide. Reductions in liver fat content were impressive and 8.4% weight loss was seen at 24 weeks.

OS-060

A Phase 2a, randomized, active-comparator-controlled, open-label study to evaluate the efficacy and safety of efinopegdutide in individuals with non-alcoholic fatty liver disease

Manuel Romero Gomez[1], Eric Lawitz[2], R. Ravi Shankar[3], Eirum Chaudhri[3], Jie Liu[3], Raymond Lam[3], Keith Kaufman[3], Samuel Engel[3]. *[1]University of Seville/Virgen del Rocio University Hospital, Institute of Biomedicine of Seville (HUVR/CSIC/US)/Digestive Diseases Unit and CIBERehd, Sevilla, Spain; [2]University of Texas Health Science Center at San Antonio-UT Health San Antonio, Texas Liver Institute, San Antonio, United States; [3]Merck and Co Inc, MRL, Rahway, United States*

Email: mromerogomez@us.es

Background and aims: Currently, there are no approved therapies for non-alcoholic steatohepatitis (NASH). This study was conducted to assess the effects of the GLP-1/glucagon receptor co-agonist efinopegdutide (EFI), relative to the selective GLP-1 receptor agonist semaglutide (SEMA), on liver fat content (LFC) in patients with non-alcoholic fatty liver disease (NAFLD), and to inform on the role of EFI as a therapy for NASH.

Method: This was a Phase 2a, randomized, active-comparator-controlled, parallel-group, open-label study in subjects with NAFLD (18–70 years, BMI 25–50 kg/m^2, stable body weight, without type 2 diabetes mellitus (T2DM), or with T2DM with an A1C ≤8.5% controlled by diet ± stable dose of metformin). During a 4-week screening period, an MRI-PDFF was performed to determine LFC. Participants with an LFC of ≥10% were randomized in a 1:1 ratio to open-label SC EFI 10 mg Q1W or SC SEMA 1.0 mg Q1W for 24 weeks, stratified according to concurrent diagnosis of T2DM. Both drugs were titrated to the target dose over an 8-week time period. The primary efficacy end point was the least squares (LS) mean relative reduction from baseline in LFC (%) after 24 weeks of treatment.

Results: Among 145 randomized subjects (EFI n = 72, SEMA n = 73), 55.2% were male, 35.2% were Hispanic and 33.1% had T2DM. At baseline, the mean BMI was 34.3 kg/m^2 and the mean LFC was 20.3%. The LS mean relative reduction from baseline in LFC at Week 24 was significantly ($p < 0.001$) greater with EFI (72.7% [95% CI: 66.8, 78.7]) than with SEMA (42.3% [95% CI: 36.5, 48.1]) (figure). Median relative reductions from baseline in LFC at Week 24 were 83.8% with EFI and 44.4% with SEMA. Greater proportions of participants had relative reductions from baseline at Week 24 in LFC of ≥30%, ≥50% and ≥70% with EFI (81.9%, 77.8%, and 70.8%, respectively) compared with SEMA (67.1%, 43.8%, and 12.3%, respectively) (figure). A greater proportion of participants achieved normal LFC (<5%) at Week 24 with EFI (66.7%) compared with SEMA (17.8%). Both treatment groups had an LS mean relative reduction from baseline in body weight at Week 24 ($p = 0.085$ for EFI 8.5% vs SEMA 7.1%). The relative reductions from baseline in LFC at Week 24 by weight loss category (≤5%, >5% to ≤10%, and >10% reduction in body weight from baseline) were greater in the EFI group (52.4%, 76.6%, and 86.2%, respectively) than in the SEMA group (13.4%, 39.6%, and 64.2%, respectively). There were no meaningful differences between the two treatment groups in the incidence of overall, serious, or drug-related adverse events, including adverse events that led to discontinuation.

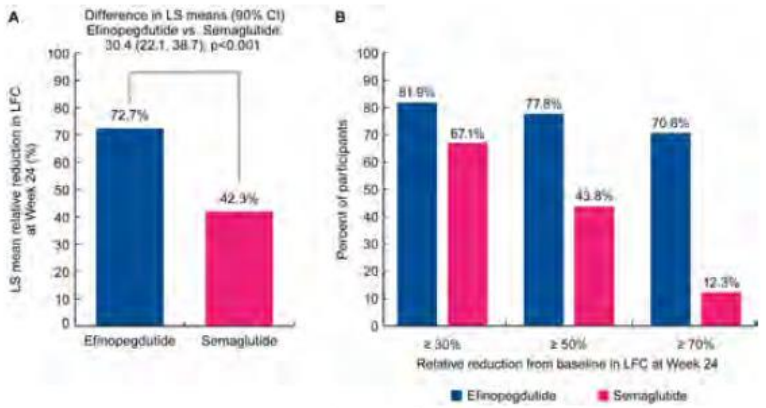
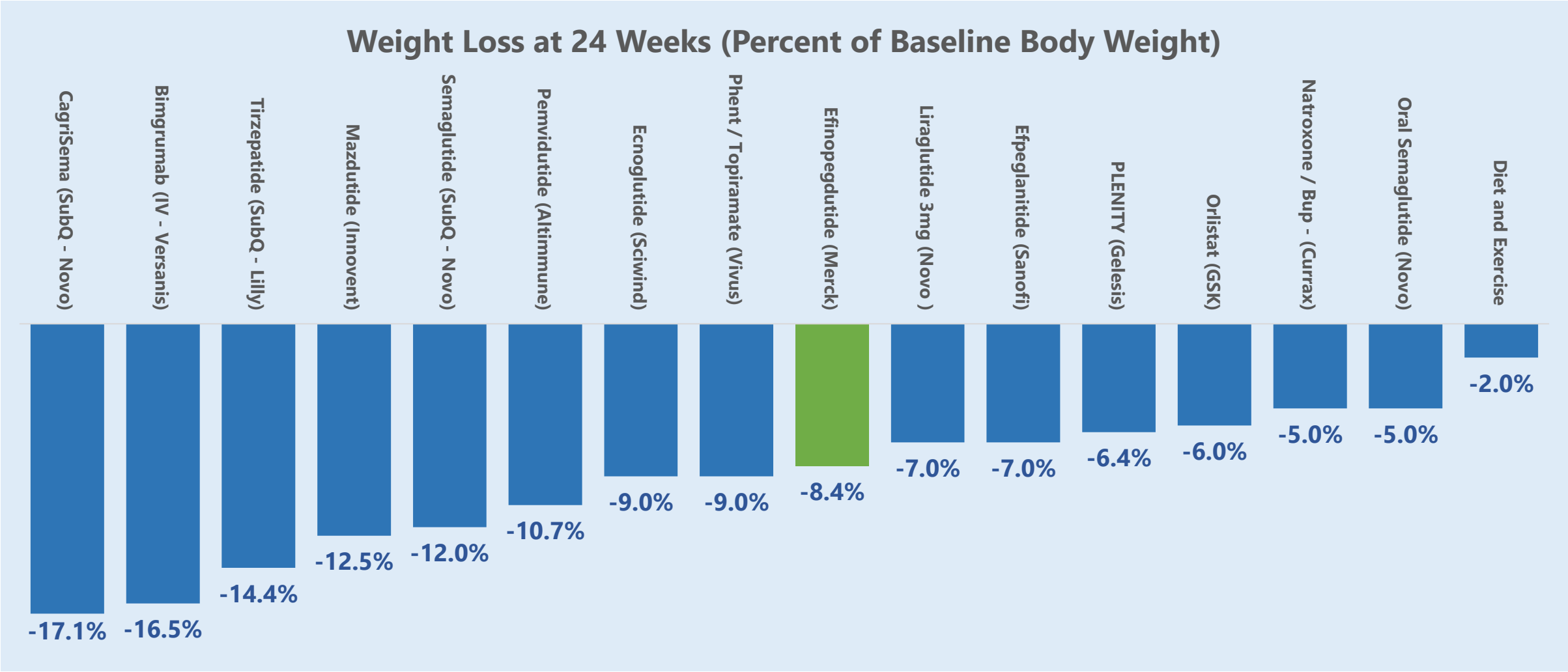


Figure: (A) LS mean relative reduction from baseline in LFC at Week 24 and (B) proportions of participants with relative reductions from baseline in LFC at Week 24 of ≥30%, ≥50% and ≥70%

Conclusion: In this study in patients with NAFLD, treatment with EFI 10 mg weekly led to a significantly greater reduction in LFC than SEMA 1 mg weekly. EFI may offer an effective treatment option for patients with NASH.

Source: https://www.easlcongress.eu/wp-content/uploads/2023/06/EASL_2023_Congress_Abstracts_version1_6June.pdf

Merck Efinopegdutide Molecule Not Particularly Competitive in 24 Week Weight Loss



Source: https://www.easlcongress.eu/wp-content/uploads/2023/06/EASL_2023_Congress_Abstracts_version1_6June.pdf

Intellia Therapeutics Announces Clinical Data from Phase 1 Study of NTLA-2002, a Treatment for Hereditary Angioedema

CAMBRIDGE, Mass., June 11, 2023 (GLOBE NEWSWIRE) -- Intellia Therapeutics, Inc. (NASDAQ:NTLA), a leading clinical-stage genome editing company focused on developing potentially curative therapeutics leveraging CRISPR-based technologies, today announced updated interim results from the Phase 1 portion of the ongoing Phase 1/2 study of NTLA-2002. NTLA-2002 is an *in vivo*, systemically administered CRISPR candidate being developed as a single-dose treatment for hereditary angioedema (HAE).

"After a single dose of our investigational CRISPR-based therapy, patients living with hereditary angioedema experienced durable elimination of their attacks. We are thrilled to see that the earliest-dosed patients are attack free for approximately a year or longer, with NTLA-2002 demonstrating a very favorable safety profile. These remarkable attack rate reductions have been consistent, even in patients with the most severe symptoms," said Intellia President and Chief Executive Officer John Leonard, M.D. "While early, these unprecedented interim data from the Phase 1 study continue to reinforce our belief that NTLA-2002 could be a potential functional cure for people with hereditary angioedema. In addition, these data strengthen our view that NTLA-2002 could address the significant treatment burden that exists, despite currently available, chronically administered therapies."

Across all patients, a 95% mean reduction in monthly attack rate was observed after a single dose of NTLA-2002 through the latest follow-up. The median duration of follow-up was 9.0 months (range of 5.6 - 14.1 months). At each dose level tested, a robust level of HAE attack rate reduction was achieved. Importantly, the elimination of HAE attacks has been sustained and long lasting. The first three patients dosed in the study with the longest follow-up to date have experienced attack-free durations of approximately one year or longer. Additionally, the reduction in HAE attacks has been persistent in patients with the most severe HAE symptoms. The three patients with the highest historic monthly HAE attack rates at the start of the study (16.8, 14.0 and 4.4 attacks per month, respectively) all became attack free by the end of the 16-week primary observation period and remained free of attacks through the latest follow-up. The longest attack-free duration in this patient group is 11.5 months and ongoing.

Source: https://ir.intelliatx.com/news-releases/news-release-details/intellia-therapeutics-announces-new-positive-clinical-data-phase

Verve Establishes Global Collaboration with Lilly to Advance Verve's In Vivo Gene Editing Program Targeting Lp(a)

BOSTON, June 15, 2023 (GLOBE NEWSWIRE) -- Verve Therapeutics, Inc. (Nasdaq: VERV) today announced an exclusive research collaboration with Eli Lilly and Company focused on advancing Verve's preclinical stage *in vivo* gene editing program targeting lipoprotein(a) (Lp(a)). Elevated Lp(a) is an established and genetically validated, independent risk factor for atherosclerotic cardiovascular disease (ASCVD), ischemic stroke, thrombosis, and aortic stenosis.

Under the terms of the collaboration, Verve will advance the research and development of the Lp(a) program through the completion of Phase 1 clinical development. Lilly will be responsible for subsequent development, manufacturing, and commercialization of the Lp(a) program.

"Verve was created with a singular focus to protect the world from ASCVD by developing single-course gene editing medicines that address the underlying causal drivers of the disease. Lp(a) is validated as one of these key drivers, and as such, this program represents another important step in our efforts to transform the care of ASCVD," said Sekar Kathiresan, M.D., co-founder and chief executive officer of Verve. "Blood concentrations of Lp(a) are determined almost entirely by inheritance, and unfortunately, lifestyle and currently approved lipid-lowering therapies have minimal to no impact. In patients with established ASCVD and elevated blood Lp(a), we believe there is a substantial opportunity for a single-course gene editing medicine to permanently lower Lp(a) levels, and we are thrilled to have joined forces with Lilly, an industry leader in cardiometabolic disease, to accelerate this program toward patients. Additionally, with the $60 million in capital expected from Lilly, we anticipate having a cash runway that extends into 2026."

Under the terms of the agreement, Verve will receive $60 million consisting of an upfront payment and equity investment. Research program costs through Phase 1 clinical trials will be funded by Lilly. Verve is also eligible to receive up to $465 million in research, development, and commercial milestones, as well as tiered royalties on global net sales. In addition, following the completion of Phase 1 clinical trials, Verve has the right to opt-in to co-fund and share margins globally on the Lp(a) program (in lieu of receipt of milestones and royalties).

Source: https://www.globenewswire.com/news-release/2023/06/15/2688718/0/en/Verve-Establishes-Global-Collaboration-with-Lilly-to-Advance-Verve-s-In-Vivo-Gene-Editing-Program-Targeting-Lp-a-for-the-Treatment-of-Atherosclerotic-Cardiovascular-Disease.html

Article

CD4+ T cell-induced inflammatory cell death controls immune-evasive tumours

Nature, June 14, 2023

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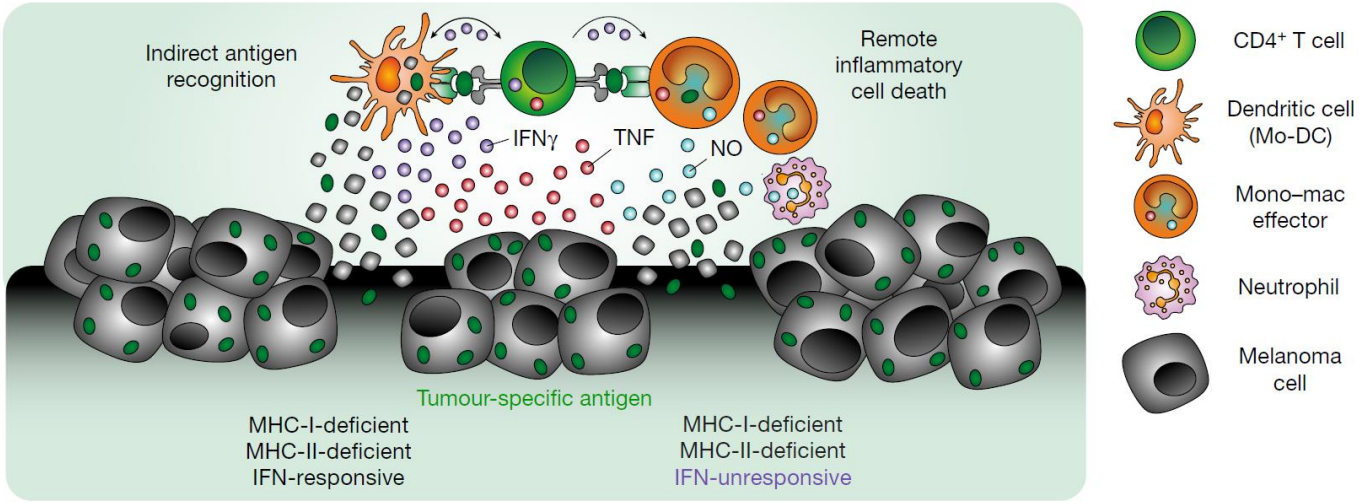


Source: https://www.nature.com/articles/s41586-023-06199-x

Most clinically applied cancer immunotherapies rely on the ability of CD8+ cytolytic T cells to directly recognize and kill tumour cells. These strategies are limited by the emergence of major histocompatibility complex (MHC)-deficient tumour cells and the formation of an immunosuppressive tumour microenvironment. The ability of CD4+ effector cells to contribute to antitumour immunity independently of CD8+ T cells is increasingly recognized, but strategies to unleash their full potential remain to be identified. Here, we describe a mechanism whereby a small number of CD4+ T cells is sufficient to eradicate MHC-deficient tumours that escape direct CD8+ T cell targeting. The CD4+ effector T cells preferentially cluster at tumour invasive margins where they interact with MHC-II+CD11c+ antigen-presenting cells. We show that T helper type 1 cell-directed CD4+ T cells and innate immune stimulation reprogramme the tumour-associated myeloid cell network towards interferon-activated antigen-presenting and iNOS-expressing tumouricidal effector phenotypes. Together, CD4+ T cells and tumouricidal myeloid cells orchestrate the induction of remote inflammatory cell death that indirectly eradicates interferon-unresponsive and MHC-deficient tumours. These results warrant the clinical exploitation of this ability of CD4+ T cells and innate immune stimulators in a strategy to complement the direct cytolytic activity of CD8+ T cells and natural killer cells and advance cancer immunotherapies.

Fusobacterium infection facilitates the development of endometriosis through the phenotypic transition of endometrial fibroblasts

AYAKO MURAOKA, MIHO SUZUKI, TOMONARI HAMAGUCHI, SHINYA WATANABE, KENTA IIJIMA, YOSHITERU MUROFUSHI, KEIKO SHINJO, SATOKO OSUKA, YUMI HARIYAMA, [...], AND YUTAKA KONDO +7 authors Authors Info & Affiliations

Science Translational Medicine, June 14, 2023

Retrograde menstruation is a widely accepted cause of endometriosis. However, not all women who experience retrograde menstruation develop endometriosis, and the mechanisms underlying these observations are not yet understood. Here, we demonstrated a pathogenic role of *Fusobacterium* in the formation of ovarian endometriosis. In a cohort of women, 64% of patients with endometriosis but <10% of controls were found to have *Fusobacterium* infiltration in the endometrium. Immunohistochemical and biochemical analyses revealed that activated transforming growth factor–β (TGF-β) signaling resulting from *Fusobacterium* infection of endometrial cells led to the transition from quiescent fibroblasts to transgelin (TAGLN)–positive myofibroblasts, which gained the ability to proliferate, adhere, and migrate in vitro. *Fusobacterium* inoculation in a syngeneic mouse model of endometriosis resulted in a marked increase in TAGLN-positive myofibroblasts and increased number and weight of endometriotic lesions. Furthermore, antibiotic treatment largely prevented establishment of endometriosis and reduced the number and weight of established endometriotic lesions in the mouse model. Our data support a mechanism for the pathogenesis of endometriosis via *Fusobacterium* infection and suggest that eradication of this bacterium could be an approach to treat endometriosis.

Source: https://www.science.org/doi/10.1126/scitranslmed.add1531

Endometriosis is a disease of adolescents and reproductive-aged women characterized by the presence of endometrial tissue outside the uterine cavity and commonly associated with chronic pelvic pain and infertility.

This disease impacts approximately 10% of women of reproductive age.

The idea that this disease might be caused by a bacterium is completely unexpected and one of the more interesting scientific findings we have seen so far in 2023.

The finding obviously points to a therapeutic strategy which would be to eradicate the bacterium.

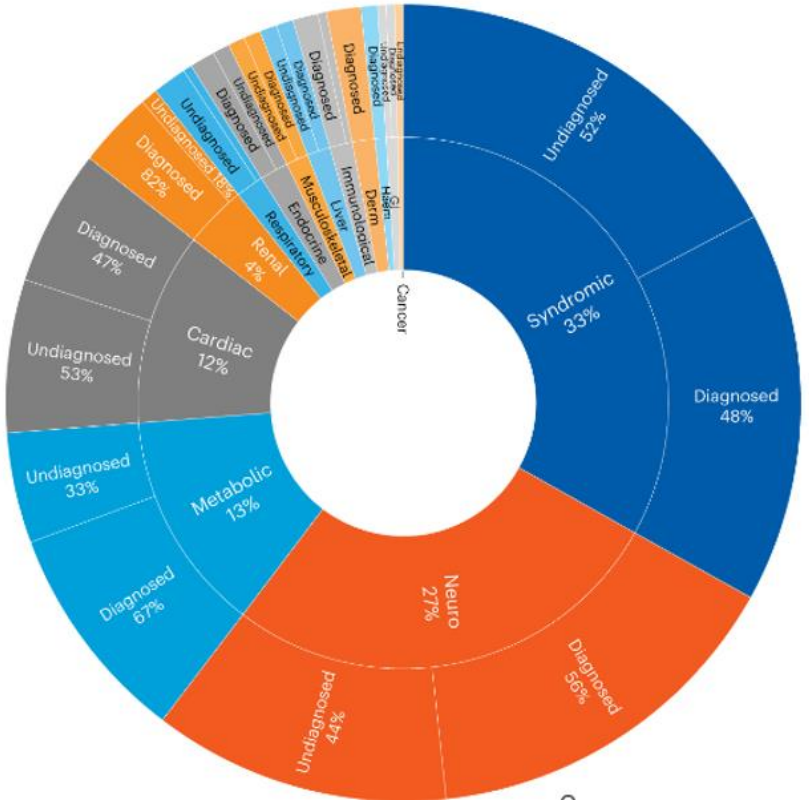
Hats off to extraordinary research out of the University of Nagoya, Japan!

Integrated Multi-omics for Rapid Rare Disease Diagnosis on a National Scale

Lunke et.al., *Nature Medicine*, June 2023

Critically ill infants and children with rare diseases need equitable access to rapid and accurate diagnosis to direct clinical management. Over 2 years, the Acute Care Genomics program provided whole-genome sequencing to 290 families whose critically ill infants and children were admitted to hospitals throughout Australia with suspected genetic conditions. The average time to result was 2.9 days and diagnostic yield was 47%. We performed additional bioinformatic analyses and transcriptome sequencing in all patients who remained undiagnosed. Long-read sequencing and functional assays, ranging from clinically accredited enzyme analysis to bespoke quantitative proteomics, were deployed in selected cases. This resulted in an additional 19 diagnoses and an overall diagnostic yield of 54%. Diagnostic variants ranged from structural chromosomal abnormalities through to an intronic retrotransposon, disrupting splicing. Critical care management changed in 120 diagnosed patients (77%). This included major impacts, such as informing precision treatments, surgical and transplant decisions and palliation, in 94 patients (60%). Our results provide preliminary evidence of the clinical utility of integrating multi-omic approaches into mainstream diagnostic practice to fully realize the potential of rare disease genomic testing in a timely manner.

Fig. 3: Summary of diagnostic outcomes.



Gene	Number of individuals
KMT2D	5
CHD7	3
PTPN11	2
PIK3CA	2
KCNQ2	6
PCDH19	2
HSD17B4	2
DNM1L	2
KCNT1	2
DMD	2
GLB1	2
ACAD9	2
LIPA	2
PDHA1	2
TNNT2	2
SCN5A	2
WT1	2
COL7A1	2
RYR2	4

Source: https://www.nature.com/articles/s41591-023-02401-9

Generative AI, Medicine and Pharma

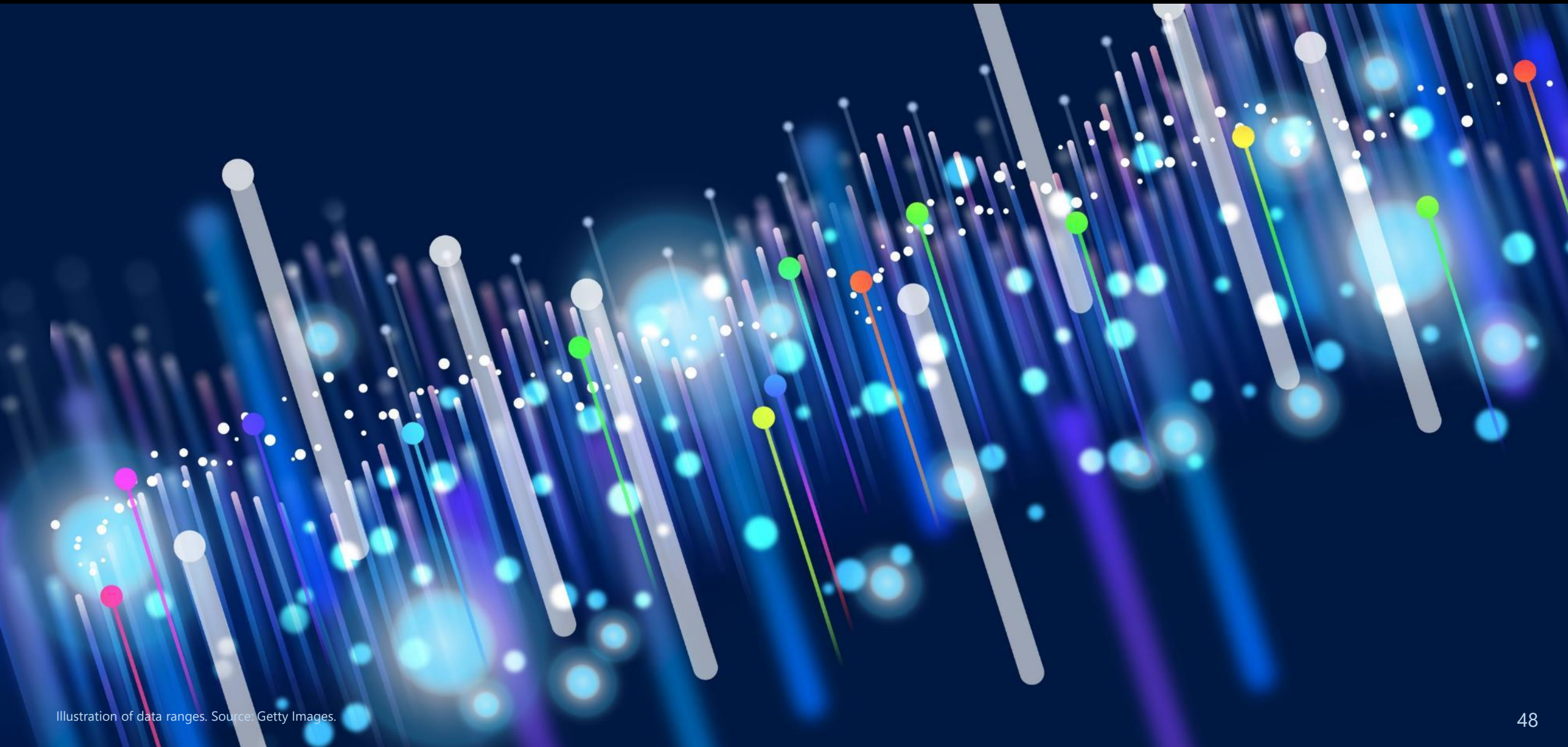


Illustration of data ranges. Source: Getty Images.

Size of Market for AI Products in Healthcare to Grow to $273 Billion by 2030

Press Release, June 15, 2023

"Bridge Market Research analyses that the artificial intelligence in healthcare market, which is $9.6 billion in 2022, is expected to reach $272.9 billion by 2030, at a CAGR of 51.9% during the forecast period 2023 to 2030."

Source: https://www.digitaljournal.com/pr/news/cdn-newswire/artificial-intelligence-in-healthcare-market-estimated-to-witness-exponential-growth-of-usd-272-91-billion-by-2030. Photo from Getty Images.

Research Letter

ONLINE FIRST

June 15, 2023

Accuracy of a Generative Artificial Intelligence Model in a Complex Diagnostic Challenge

Zahir Kanjee, MD, MPH[1]; Byron Crowe, MD[1]; Adam Rodman, MD, MPH[1]

» Author Affiliations

JAMA. Published online June 15, 2023. doi:10.1001/jama.2023.8288

"We used *New England Journal of Medicine* clinicopathologic conferences. These conferences are challenging medical cases with a final pathological diagnosis that are used for educational purposes; they have been used to evaluate differential diagnosis generators since the 1950s.

We used the first 7 case conferences from 2023 to iteratively develop a standard chat prompt that explained the general conference structure and instructed the model to provide a differential diagnosis ranked by probability. We copied each case published from January 2021 to December 2022, up to but not including the discussant's initial response and differential diagnosis discussion, and pasted it along with our prompt into the model. We chose recent cases because most of the model's training data ends in September 2021. Each case, including the cases used to develop the prompt, was run in independent chats to prevent the model applying any "learning" to subsequent cases.

Our prespecified primary outcome was whether the model's top diagnosis matched the final case diagnosis. Prespecified secondary outcomes were the presence of the final diagnosis in the model's differential, differential length, and differential quality score using a previously published ordinal 5-point rating system based on accuracy and usefulness (in which a score of 5 is given for a differential including the exact diagnosis and a score of 0 is given when no diagnoses are close). All cases were independently scored by Z.K. and B.C., with disagreements adjudicated by A.R.

Of 80 cases, 10 were excluded (4 were not diagnostic dilemmas; 6 were deleted for length). The 2 primary scorers agreed on 66% of scores (46/70; $\kappa = 0.57$ [moderate agreement]). The AI model's top diagnosis agreed with the final diagnosis in 39% (27/70) of cases. In 64% of cases (45/70), the model included the final diagnosis in its differential (Table). Mean differential length was 9.0 (SD, 1.4) diagnoses. When the AI model provided the correct diagnosis in its differential, the mean rank of the diagnosis was 2.5 (SD, 2.5). The median differential quality score was 5 (IQR, 3-5); the mean was 4.2 (SD, 1.3) (Figure).

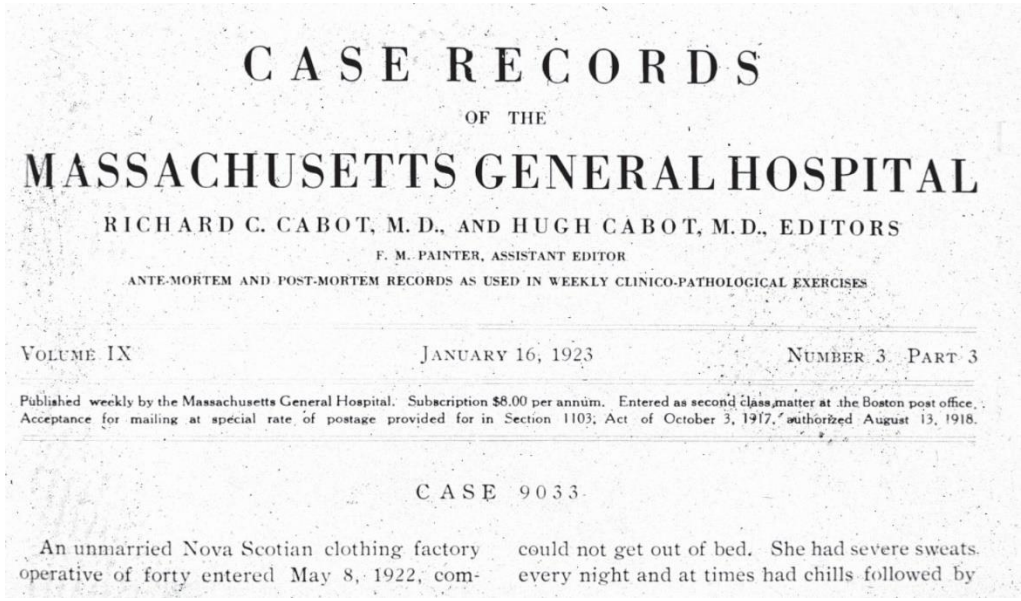
A generative AI model provided the correct diagnosis in its differential in 64% of challenging cases and as its top diagnosis in 39%. The finding compares favorably with existing differential diagnosis generators. A 2022 study evaluating the performance of 2 such models also using *New England Journal of Medicine* clinicopathological case conferences found that they identified the correct diagnosis in 58% to 68% of cases; the measure of quality was a simple dichotomy of useful vs not useful. GPT-4 provided a numerically superior mean differential quality score compared with an earlier version of one of these differential diagnosis generators (4.2 vs 3.8)."

Source: https://jamanetwork.com/journals/jama/fullarticle/2806457

Stump the Medical Expert

A.I., the CPC, and making the diagnosis

By Eric Topol, *Substack*, June 17, 2023



CASE RECORDS

OF THE

MASSACHUSETTS GENERAL HOSPITAL

RICHARD C. CABOT, M. D., AND HUGH CABOT, M.D., EDITORS

F. M. PAINTER, ASSISTANT EDITOR

ANTE-MORTEM AND POST-MORTEM RECORDS AS USED IN WEEKLY CLINICO-PATHOLOGICAL EXERCISES

VOLUME IX JANUARY 16, 1923 NUMBER 3 PART 3

Published weekly by the Massachusetts General Hospital. Subscription $8.00 per annum. Entered as second class matter at the Boston post office. Acceptance for mailing at special rate of postage provided for in Section 1103, Act of October 3, 1917, authorized August 13, 1918.

CASE 9033

An unmarried Nova Scotian clothing factory operative of forty entered May 8, 1922, com- could not get out of bed. She had severe sweats every night and at times had chills followed by

100 years ago, the first Case Records of the Massachusetts General Hospital was published in the Boston Medical and Surgical Journal, the precursor to the *New England Journal of Medicine*, which has been publishing what are known as clinicopathologic conferences (CPCs) since 1924 on a biweekly basis.

The CPC is a longstanding tradition that continues in many medical centers throughout the world, first introduced in the United States in 1898, undoubtedly influenced by Giovanni Battista Morgagni who published a book of 700 cases with anatomy-clinical correlations in 1761. As they evolved over the years, CPCs were extremely challenging patient cases to stump the medical expert. After presentation of the relevant data, the clinician expert would be asked to provide a differential diagnosis and presumptive final diagnosis, and the actual, definitive diagnosis was established via lab tests, scans, pathology, or autopsy. The CPC educational value is clearcut, but so was there entertainment to see if the noted expert might miss the diagnosis. Of course, there was the expectation that the master clinician—the doctor's doctor— would always get it right. I vividly remember trying to stump UCSF Professor Larry Tierney during my internal medicine residency training, but it was rare that he didn't have the right diagnosis in his differential.

That rarity of expert wrong diagnosis differs substantially from real world medicine. After a classic *Science* 1974 paper about uncertainty, one of its authors, Danny Kahneman, wrote about a study that compared the doctor's diagnosis before death to the autopsy findings. **"Clinicians who were completely certain of the diagnosis antemortem were wrong 40 percent of the time."**

Source: https://erictopol.substack.com/p/stump-the-medical-expert

Stump the Medical Expert: GPT-4 Beats Docs on CPC Diagnoses (Topol Article Continued)

"The New England Journal CPCs have been the benchmark for evaluating medical diagnostic reasoning, as used in the 1959 paper in Science Magazine, emphasizing the role of mathematical techniques and associated use of computers noting: "This method in no way implies that a computer can take over the physician's duties."

To date, the best DDx generator results that have been published are derived from Isabel Health's tool. In the most recent report with Isabel DDx data, two doctors (not medical experts) got 14 of 50 (28%) of the NEJM CPC final diagnoses. As the current report asserted, "GPT-4 provided a numerically superior mean differential quality score compared with an earlier version of one of these differential diagnosis generators (4.2 vs 3.8)."

We need to prospectively assess GPT-4 for its role in facilitating diagnoses. This is a major issue in medicine today: at least 12 million Americans, as out-patients, are misdiagnosed each year. There is real promise for GPT-4 and other large language models (LLMs) to help the accuracy of diagnoses for real world patients, not the esoteric, rare, ultra-challenging NEJM CPC cases. But that has to be proven, and certainly the concern about LLM confabulations is key, potentially leading a physician and patient down a rabbit-hole, towards a major wrong diagnosis and an extensive workup without basis, no less the possibility of an erroneous treatment.

Thee's been much buzz about ChatGPT, GPT 3.5, Med-PaLM, and GPT-4 surpassing the 60% pass threshold for the United States Medical Licensing exam (USMLE) (to reach ~86%). These are fairly contrived comparisons using a subset of representative questions and only those with text, not with visual media. It makes for nice bragging right for LLMs, but we aren't going to be licensing any of them to practice medicine! That's far less relevant than use of these AI tools for promoting accurate diagnoses.

I'm excited about this particular use case of LLMs in the future, especially as they undergo supervised fine tuning for medical knowledge. It clearly needs dedicated, prospective validation work, but ultimately may become a significant support tool for clinicians and patients. **If GPT-4 can perform well with arcane NEJM cases, imagine what might be in store for the common, real world diagnostic dilemmas.**"

Scripps Research

Eric Topol, MD
EVP, Scripps Research

Source: https://erictopol.substack.com/p/stump-the-medical-expert

When AI Overrules the Nurses Caring for You

Artificial intelligence raises difficult questions about who makes the call in a health crisis: the human or the machine?

Lisa Bannon, *Wall Street Journal*, June 15, 2023

Artificial intelligence and other high-tech tools, though nascent in most hospitals, are raising difficult questions about who makes decisions in a crisis: the human or the machine?

The technologies, which can analyze massive amounts of data with a speed beyond human capacity, are making extraordinary advances in medicine, from improving the diagnosis of heart conditions to predicting protein structures that could speed drug discovery. When it is used alongside humans to help assess, diagnose and treat patients, AI has shown powerful results, academics and tech experts say.

At the same time, the tools can be flawed and are sometimes implemented without adequate training or flexibility, say nurses and healthcare workers who work with them regularly, putting patient care at risk. Some clinicians say they feel pressure from hospital administration to defer to the algorithm.

"AI should be used as clinical decision support and not to replace the expert," said Kenrick Cato, a professor of nursing at the University of Pennsylvania and nurse scientist at the Children's Hospital of Philadelphia. "Hospital administrators need to understand there are lots of things an algorithm can't see in a clinical setting."

Source: https://www.wsj.com/articles/ai-medical-diagnosis-nurses-f881b0fe

McKinsey Study Published Last Week on Pharma and Data Management

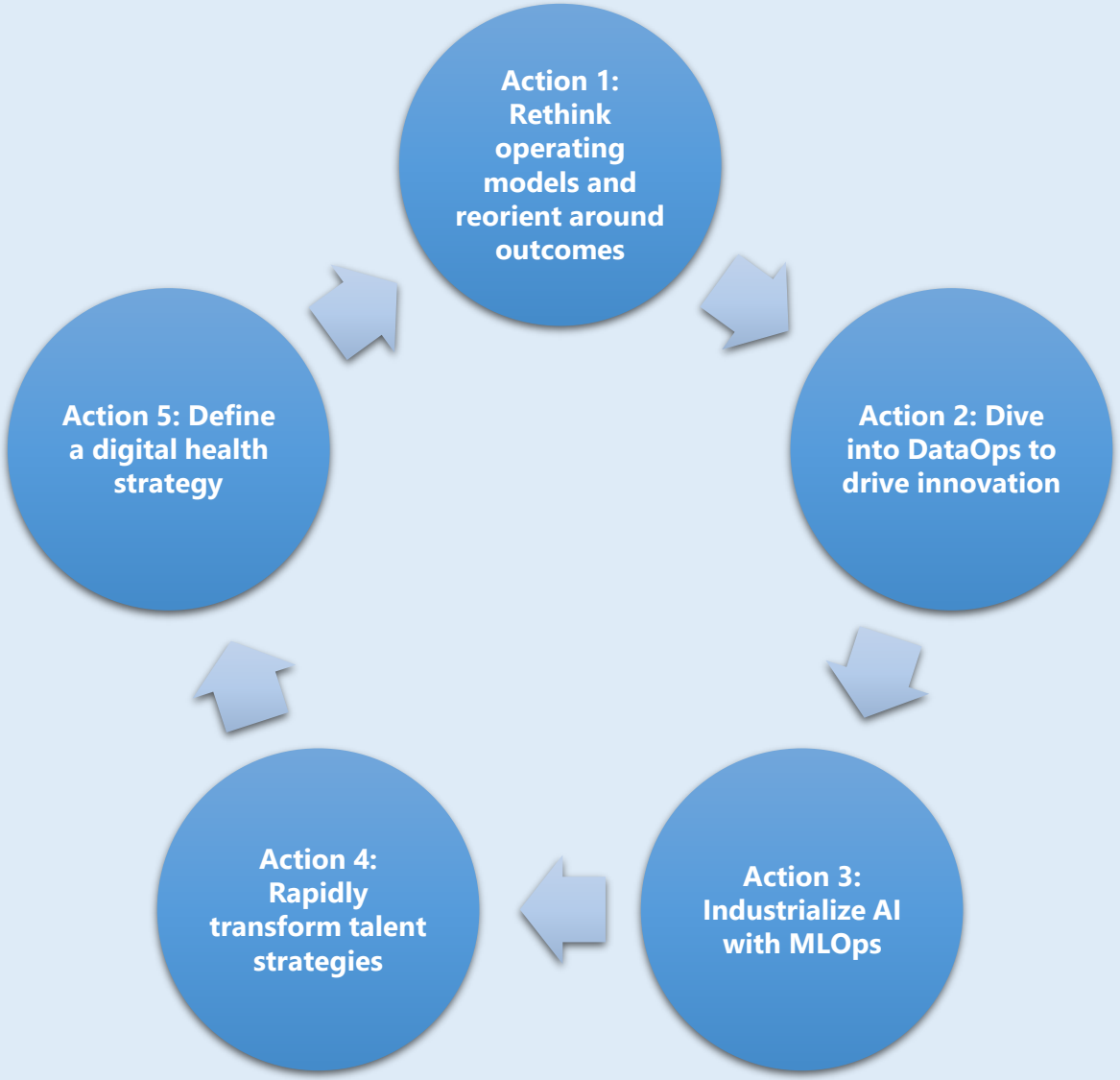
Virtually every pharmaceutical company recognizes the importance of digital technology to its business and has digital and analytics initiatives underway. Many firms now appoint dedicated chief digital and technology officers (CDTOs), experienced in leading such transformations, to head up their efforts. Leading players are incorporating digital and analytics into early-stage drug discovery and clinical development to shrink timelines and improve the probability of success. Many have also begun to reinvent their interactions with healthcare providers and patients, using technology to enhance and tailor experiences that achieve better treatment outcomes.

Still, as observed in McKinsey's 2022 review of the industry, pharmaceutical companies have only scratched the surface. Siloed use cases and impact stories abound, but investments have rarely led to profound organizational changes. Few have yet succeeded in deeply embedding digital and analytics throughout their organizations. Executives are growing frustrated by the lack of broader, transformational impact.

There is a way forward. McKinsey has examined companies that have successfully scaled their digital and analytics pilots into large-scale delivery and transformation with substantial bottom-line impact. That analysis suggests five proven actions pharmaceutical CEOs and CDTOs can take to advance from small-scale experimentation to industrialization of digital and analytics in the next 12 to 18 months.

Source: https://www.mckinsey.com/industries/life-sciences/our-insights/rewired-pharma-companies-will-win-in-the-digital-age

Five Key Actions Suggested by McKinsey on Data Front



Source: https://www.mckinsey.com/industries/life-sciences/our-insights/rewired-pharma-companies-will-win-in-the-digital-age

Embracing Generative AI: Why Its Disruption is Positive for Pharma

Sharlene Jenner, *Pharmaceutical Executive*, June 2023

"While we've focused on the marketing and sales aspects of generative AI, we cannot ignore the amazing impact this technology will have on the treatment side of the pharma industry. In the future, it may be possible to have generative AI create personalized treatment plans that are tailored to the specific needs of individual patients, leading to more effective treatments and improved patient outcomes.

We are already seeing generative AI make an impact on drug discovery. Due to its power in analyzing large sets of data and simulating drug interactions, it can identify potential drug candidates that may have been overlooked by traditional drug discovery methods. This could lead to the development of new treatments for diseases that previously had no effective therapies.

These are positive disruptors in our industry—forcing change and speeding up the processes in all aspects of the chain. As pharma marketers, we are always running in parallel with development teams, keeping up with the changes and making fast adjustments to engagement plans. Once again, we're talking about how generative AI gives us time. This includes time to think of strategy and build campaigns that bring awareness to diseases as well as time for HCPs to spend with their patients after learning about late-breaking treatment options from a sales representative. Generative AI is disrupting marketing in ways we never imagined, and that's a good thing."

SHARLENE JENNER
Vice President of Engagement Strategy, AbelsonTaylor

Source: https://www.pharmexec.com/view/embracing-generative-ai-why-its-disruption-is-positive-for-pharma

Press Release: Sanofi "all in" on Artificial Intelligence and Data Science to Speed Breakthroughs for Patients

Paris, June 13, 2023. Sanofi takes the next step in its company-wide digital transformation and rolls-out *plai* at scale. *plai*, Sanofi's industry-leading app developed with artificial intelligence (AI) platform company **Aily Labs**, delivers real-time, reactive data interactions and gives an unprecedented 360° view across all Sanofi activities. The app aggregates available company internal data across functions and harnesses the power of AI to provide timely insights and personalized "*what if*" scenarios to support thousands of Sanofi team's decision makers to take informed decisions in a simple and modern digital user experience.

Paul Hudson, CEO, Sanofi

"Our ambition is to become the first pharma company powered by artificial intelligence at scale, giving our people tools and technologies that focus on insights and allow them to make better everyday decisions. The use of artificial intelligence and data science already support our teams' efforts in areas such as accelerating drug discovery, enhanced clinical trial design, and improving manufacturing and supply of medicines and vaccines. We have just scratched the surface as to how we embrace these disruptive technologies to achieve our ambition of transforming the practice of medicine."

plai is an essential enabler in the company-wide digital transformation and data democratisation journey. AI-powered tools help Sanofi teams make better and faster data-driven decisions, hence boosting productivity

Source: https://www.sanofi.com/en/media-room/press-releases/2023/2023-06-13-12-00-00-2687072

The CEO of Pharma Giant Eli Lilly Shares 3 Ways AI Could Transform His Industry

Business Insider, June 15, 2023

A handful of biotech companies are testing AI-developed drugs in people. Meanwhile, digital-health companies, providers, and insurers are grappling with how to use technologies including ChatGPT to speed up tasks such as assessing patients and completing medical notes, while still maintaining the safety and privacy of their patients.

According to David Ricks, the CEO of the pharma giant Eli Lilly, the technology has the potential to upend the industry. Eli Lilly is developing dozens of drugs through clinical trials and expects to bring in more than $30 billion in revenue this year.

Ricks told *Insider* that AI is "one of the most exciting technological moves" he's seen in a long time.

A spokesperson for the company said that Lilly is investing in artificial intelligence and machine learning in areas including drug discovery, natural-language generation, robotic-process automation, and chatbots.

The goal is to grow what Lilly calls its "digital worker-equivalent workforce," a concept that the company says helps quantify the hours saved by using technology instead of human labor.

Image from Lilly booth at BIO

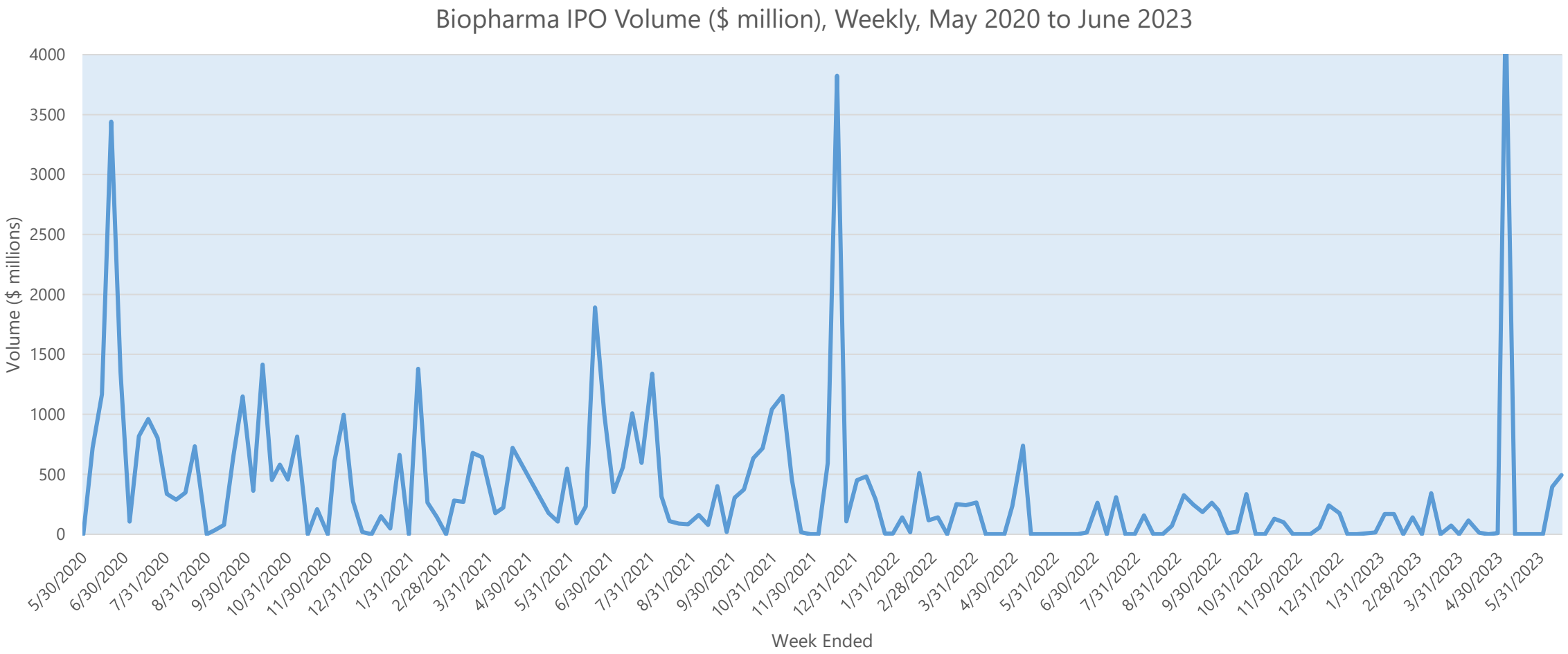
Source: https://ca.style.yahoo.com/ceo-pharma-giant-eli-lilly-193606225.html

Capital Markets Environment

Illustration of market activity. Source: Getty Images.

Two IPO's Priced Last Week

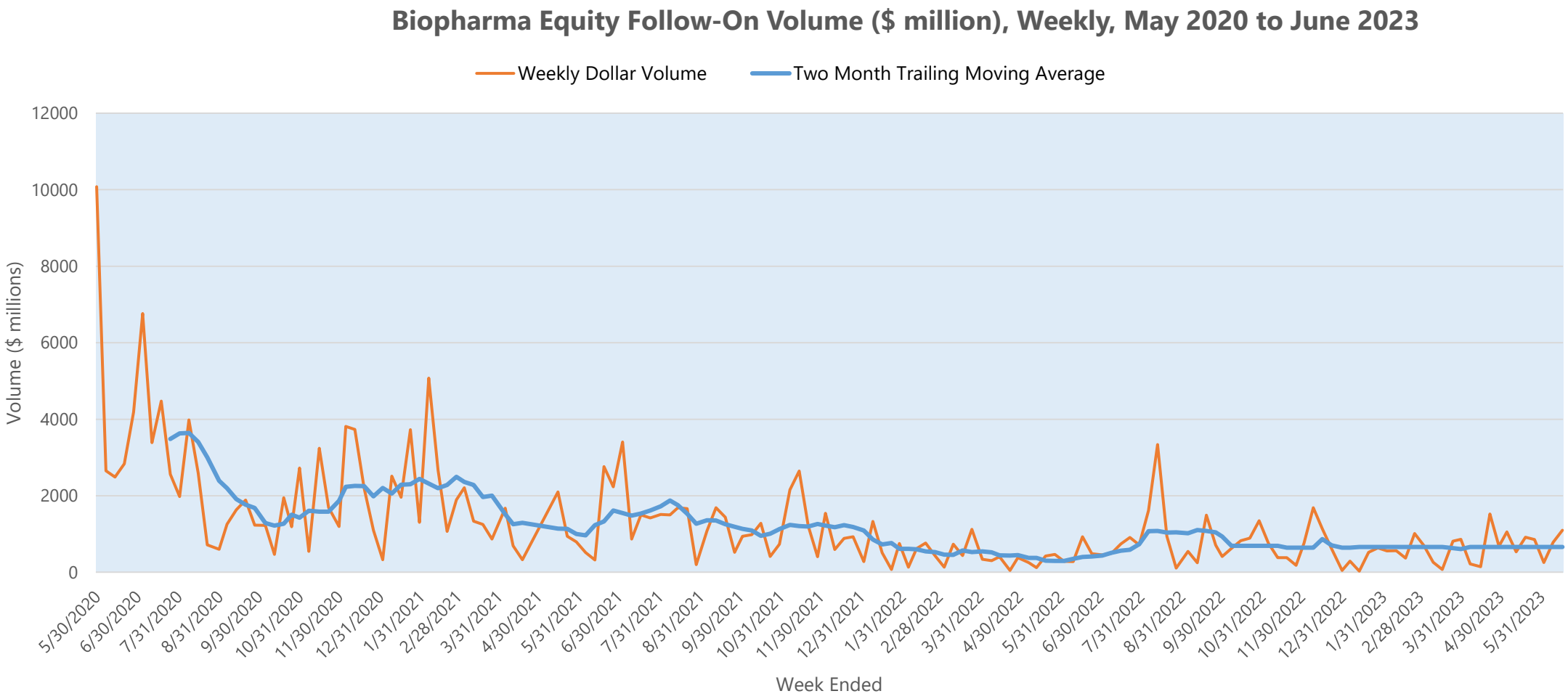
Last week saw Genrix Biopharma go public on the Shanghai Star Market, raising $485 million. Genrix is a biotech involved with antibodies and bispecifics. Further, Azitra went public on the NASDAQ, raising $7.5 million.



Source: Data from CapitalIQ and Stifel research.

Follow-on Equity Issuance Solid Last Week

The equity follow-on market remained active last week. Eighteen issuers raised a total of $1.1 billion. The largest issuers last week were Zentalis Pharma ($250 million), Almirall ($216 million), Disc Medicine ($137 million) and Editas ($125 million).



Source: Data from CapitalIQ and Stifel research.

Zentalis Pharma Raises $250 Million Follow-On

New York and San Diego, June 15, 2023 (GLOBE NEWSWIRE) -- Zentalis® Pharmaceuticals, Inc. (Nasdaq: ZNTL), a clinical-stage biopharmaceutical company discovering and developing clinically differentiated small molecule therapeutics targeting fundamental biological pathways of cancers, today announced the pricing of an underwritten offering of 11,032,656 shares of its common stock at an offering price of $22.66 per share, for total gross proceeds of approximately $250.0 million, before deducting underwriting discounts and commissions and offering expenses payable by the Company. All of the common stock is being offered by the Company. The offering is expected to close on June 20, 2023, subject to customary closing conditions.

The Company intends to use the net proceeds from the offering to fund ongoing and planned clinical trials, and for working capital and other general corporate purposes. Based on these planned uses of proceeds, the Company believes that the net proceeds from the offering and its existing cash, cash equivalents and marketable securities will be sufficient to fund its operating expenses and capital expenditure requirements into 2026.

Source: https://ir.zentalis.com/news-releases/news-release-details/zentalis-pharmaceuticals-announces-pricing-underwritten-0

Almirall Raises €200mm Follow-On

Barcelona Spain, 13 June 2023 -- Almirall S.A. (ALM) (the "Company"), a global biopharmaceutical company focused on skin health, has announced today the pricing and closing of its EUR 200,000,000 non pre-emptive share capital increase announced yesterday evening (the "Capital Increase") following completion of the accelerated book-building offering, which was carried out by J.P. Morgan and BNP PARIBAS as Joint Global Coordinators and Joint Bookrunners.

As a result of the Capital Increase, the Company has raised a total aggregate amount (including nominal amount and share issue premium) of EUR 199,999,992.60 through the issuance of 24,390,243 new ordinary shares of the Company belonging to the same class and series as the outstanding shares (the "New Shares"). The nominal amount of the Capital Increase has amounted to EUR 2,926,829.16 and the New Shares will be issued at a price of EUR 8.2 per New Share (of which EUR 0.12 corresponds to the nominal amount and EUR 8.08 to the share issue premium), representing a discount of 5.7% over the last available trading price of the shares of the Company (i.e., EUR 8.7 as of 12 June 2023).

The New Shares represent approximately 13.18% of the Company's share capital before the Share Capital Increase and approximately 11.65 % of its share capital thereafter.

As indicated in yesterday's press release, the Gallardo family, holding indirectly approximately 59.66% of the share capital of the Company has subscribed 15,559,000 New Shares in the Capital Increase via Grupo Plafín, S.A.U. ("Grupo Plafín") (a 100% subsidiary of its holding company Grupo Corporativo Landon, S.L.), therefore increasing its shareholding participation in the Company after the Capital Increase which will represent approximately 60.14% of the share capital after the Capital Increase.

The Company intends to use the net proceeds of the Capital Increase to retain financial flexibility and agility to actively pursue and swiftly execute inorganic growth opportunities (including bolt-on acquisitions and in-licensing opportunities) that are currently under analysis.

Source: https://www.almirall.com/media/newsroom/news-detail

Almirall Eyes Pipeline Expansion with €200m Funding

Phil Taylor, Pharmaphorum, June 13, 2023

Spanish pharma Almirall has closed a €200 million share capital raise that will be used in part to close pipeline-boosting activities – including bolt-on acquisitions and in-licensing deals – that it says are already being considered.

The Gallardo family – which holds a majority stake in the dermatology specialist – participated in the offering, raising its ownership fractionally to 60.14% of its share capital.

The financing comes after a somewhat turbulent period for Almirall, which said goodbye to its former chief executive Gianfranco Nazzi last November, with his role at the company taken on by board chairman Carlos Gallardo on an interim basis.

Earlier this year, it was confirmed that Gallardo would continue in the role for an extended period, and the search for a new CEO had been suspended.

Source: https://pharmaphorum.com/news/almirall-eyes-pipeline-expansion-eu200m-funding

Disc Medicine Raises $137mm Follow-On

WATERTOWN, Mass., June 13, 2023 (GLOBE NEWSWIRE) -- Disc Medicine, Inc. (NASDAQ: IRON) (Disc), a clinical-stage biopharmaceutical company focused on the discovery, development, and commercialization of novel treatments for patients suffering from serious hematologic diseases, today announced the pricing of its upsized underwritten public offering of shares of its common stock and, in lieu of common stock to certain investors that so choose, pre-funded warrants to purchase shares of its common stock. Disc is selling 2,595,919 shares of common stock and pre-funded warrants to purchase 204,081 shares of common stock in the offering. The shares of common stock are being sold at a public offering price of $49.00 per share, and the pre-funded warrants are being sold at a public offering price of $48.9999 per pre-funded warrant, which represents the per share public offering price for the common stock less the $0.0001 per share exercise price for each such pre-funded warrant. The aggregate gross proceeds to Disc from this offering are expected to be $137.2 million, before deducting underwriting discounts and commissions and other estimated offering expenses, excluding the exercise of any pre-funded warrants. In addition, Disc has granted the underwriters a 30-day option to purchase up to an additional 420,000 shares of its common stock at the public offering price less underwriting discounts and commissions. All of the securities being sold in the offering are being offered by Disc. The offering is expected to close on June 16, 2023, subject to the satisfaction of customary closing conditions.

Disc intends to use the net proceeds from the offering to fund research and clinical development of its current or additional product candidates, as well as for working capital and other general corporate purposes.

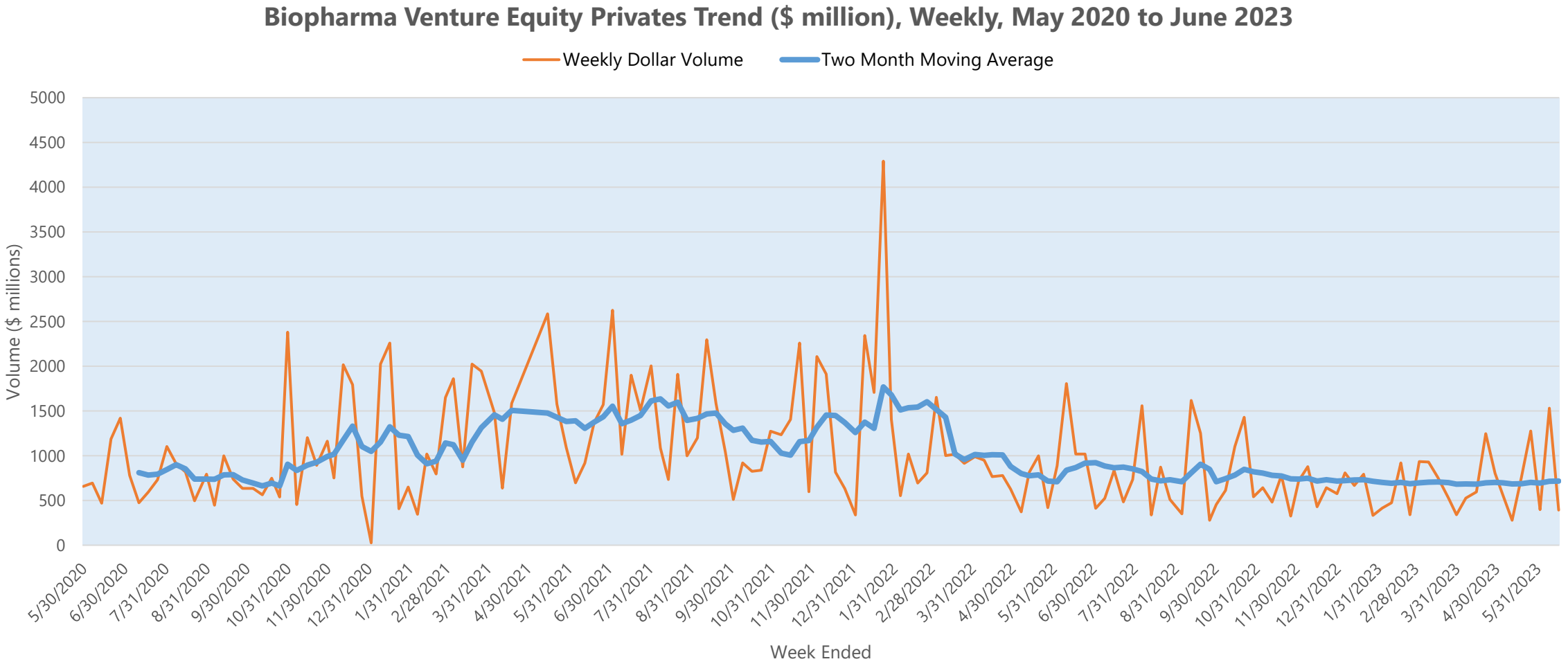
Disc Medicine raised $137 million on the back of positive Phase 2 data for Bitopertin in Patients with Erythropoietic Protoporphyria (EPP).

Stifel was pleased to act as a joint bookrunner on the offering.

Source: https://ir.discmedicine.com/news-releases/news-release-details/disc-medicine-announces-pricing-upsized-public-offering-common

Weekly Global Biopharma Venture Equity Placements

Last week saw 33 companies raise $400 million in the venture equity market. This week was much quieter than last. The largest deal was a $120mm raise by Beacon Therapeutics.



Source: Data from CapitalIQ, Crunchbase.

Beacon Therapeutics Launches With £96 Million ($120 mm)

London and Oxford, UK - 12 June 2023 – Beacon Therapeutics Holdings Limited, a leading ophthalmic gene therapy company with a purpose to restore and improve the vision of patients with retinal diseases, launches today and will develop a new generation of gene therapies to treat a range of rare and prevalent retinal diseases that result in blindness. Syncona Limited, with additional investors including OSE, has provided £96 million ($120 million) to fund the acquisition of AGTC and provide capital to take each of Beacon Therapeutics's development candidates through to value inflection points.

Beacon Therapeutics's lead clinical asset is AGTC-501, a gene therapy program currently in Phase II clinical trials for the treatment of XLRP that was acquired as part of Syncona's acquisition of AGTC in November 2022. XLRP is predominantly caused by mutations in the retinitis pigmentosa GTPase regulator (RPGR) gene. Unlike other approaches in the space, AGTC-501 correctly expresses the full length RPGR protein, thereby addressing the entirety of photoreceptor damage caused by XLRP, including both rod and cone loss.

Beacon Therapeutics's first pre-clinical asset is an intravitreally (IVT) delivered novel AAV based program for dry Age-related Macular Degeneration (dry AMD). Dry AMD is a leading cause of irreversible vision loss in people over 60, if left untreated. Around 20 million people in the United States suffer from AMD.

The second pre-clinical asset is targeting cone-rod dystrophy (CRD) which is caused by a null mutation in the Cadherin Related Family Member 1 (CDHR1) gene. To bolster its pipeline in the future, Beacon Therapeutics also has access to a target generation technology platform that will identify, screen, and search secreted proteins in the ophthalmology space.

beacon therapeutics

Beacon Therapeutics combines a broad development pipeline, a deep scientific foundation, a strong clinical network, and a highly experienced management team to drive forward a unique late-stage clinical and pre-clinical pipeline. With the 12-month data from our Phase II SKYLINE trial for AGTC-501 expected shortly and two highly innovative and differentiated pipeline assets for prevalent and rare blinding diseases, we are excited to be building a new leader in the ophthalmic gene therapy space

David Fellows
Chief Executive Officer
Beacon Therapeutics

Source: https://www.globenewswire.com/news-release/2023/06/12/2685957/0/en/Beacon-Therapeutics-launches-with-96-million-120-million-to-develop-a-new-generation-of-gene-therapies-for-retinal-diseases-resulting-in-blindness.html

America's largest public pension scheme, Calpers, which manages some $444 billion in capital on behalf of California's 1.5 million state, school, and public agency employees, is leaning into venture—even as **many LPs lean away**.

After years of bringing down its VC exposure to a 1% target, the institutional investor is now looking to increase its allocation by more than sixfold, from $800 million to $5 billion, the Financial Times reported. The strategy shift comes on the heels of steep losses in Calpers' venture strategy as well as losses related to Silicon Valley Bank's failure.

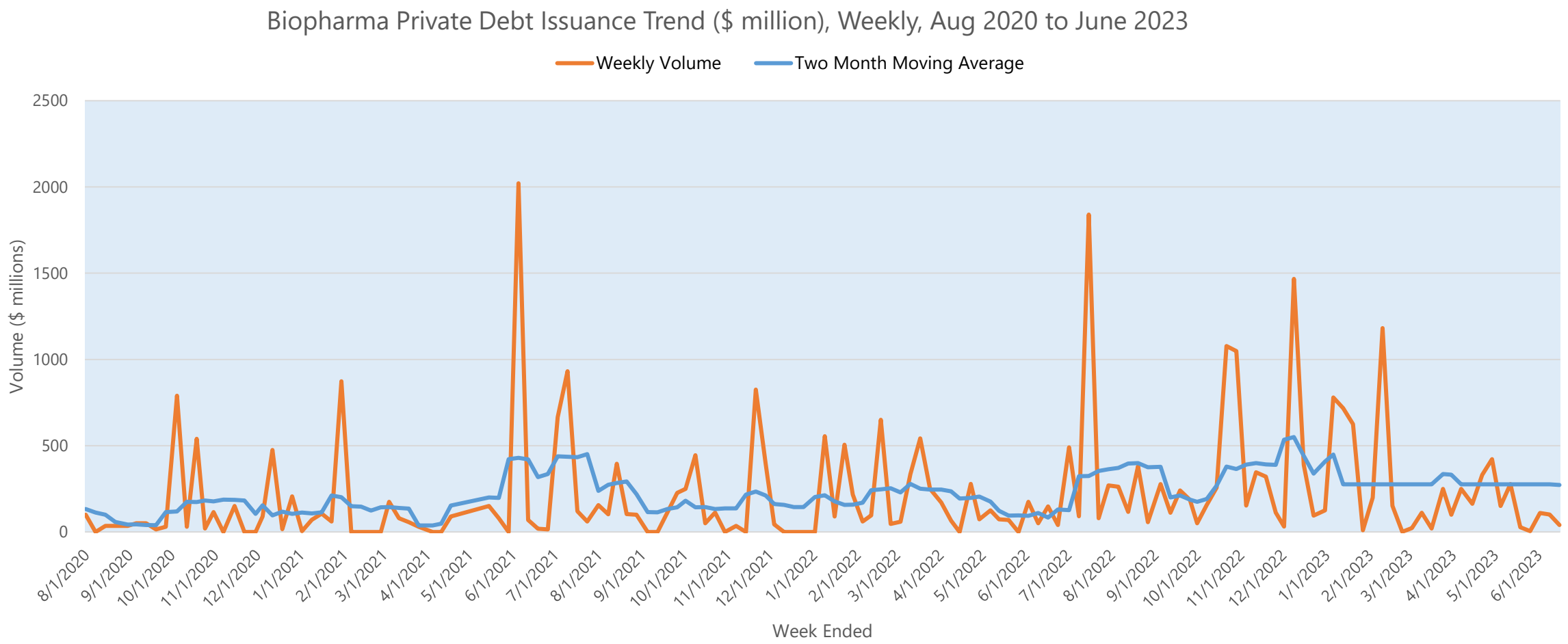
The pension manager suffered a "lost decade" coinciding with the venture boom, according to a new review of the program by managing investment director Anton Orlich.

Share:

Source: https://pitchbook.com/news/articles/calpers-venture-asset-class-tiger-lightspeed

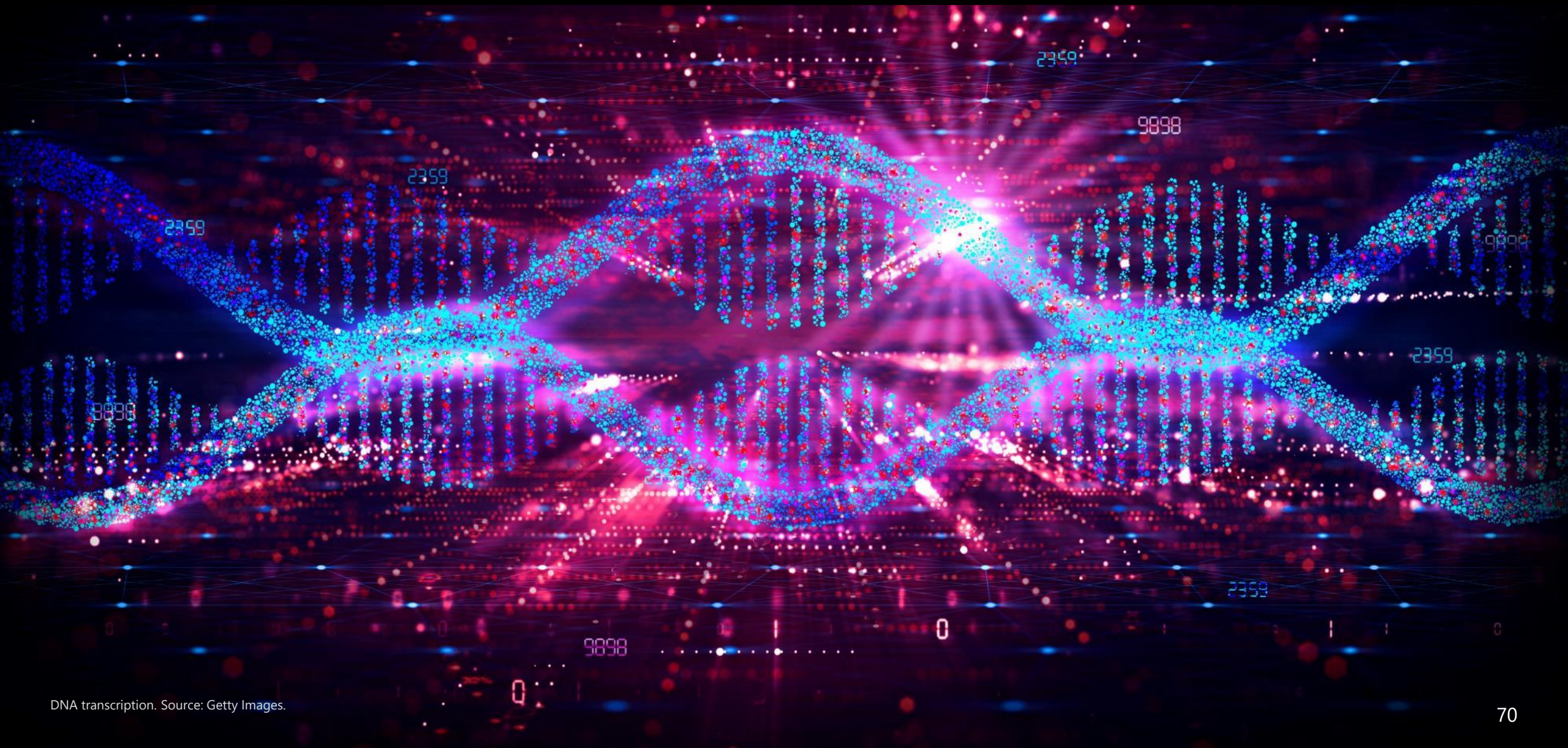
Biopharma Private Debt Volume Quiet Last Week

Last week saw two companies raise $40 million in the private debt market.



Source: Data from CapitalIQ, Crunchbase.

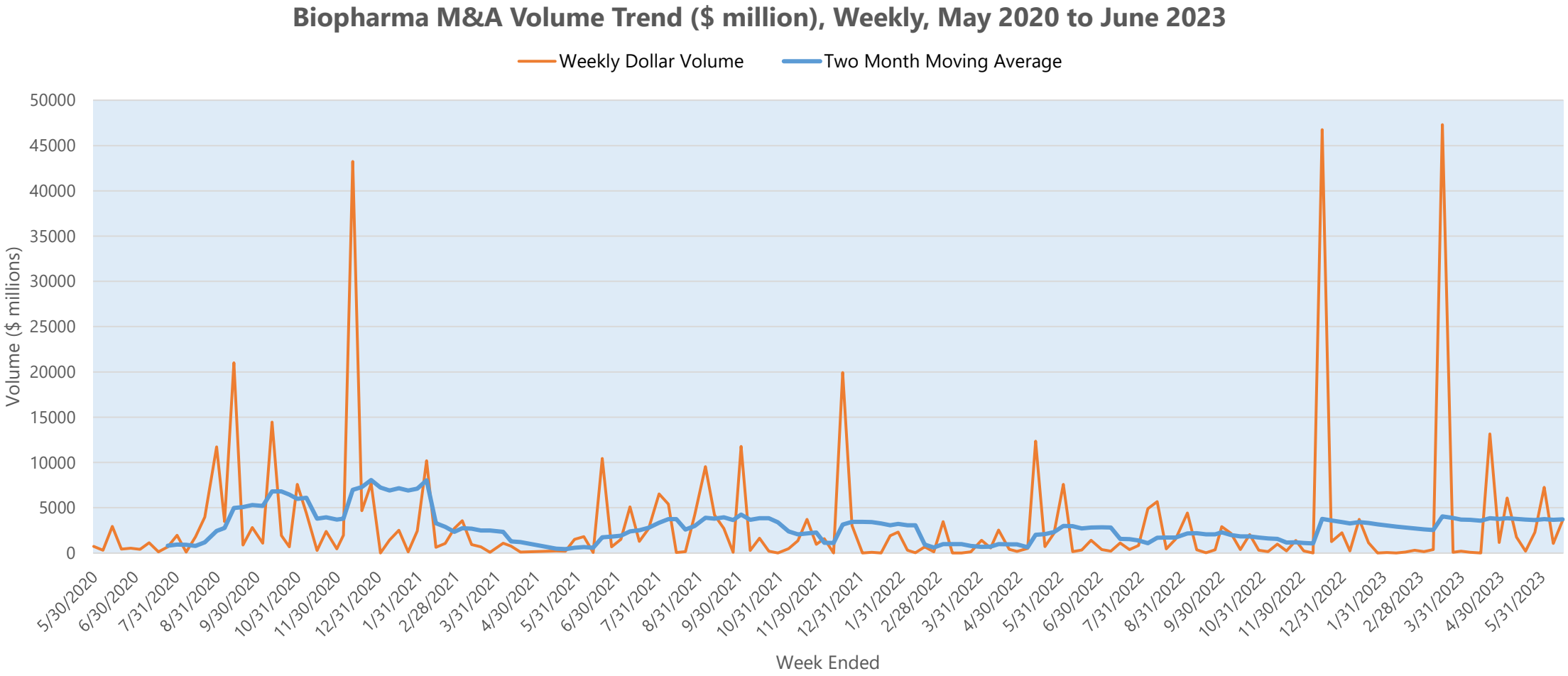
M&A Update



DNA transcription. Source: Getty Images.

Last Week Saw $3.6 Billion in M&A Volume

Last week saw $3.6 billion in announced biopharma M&A volume. The largest deal was Novartis' $3.5 billion bid for Chinook Therapeutics.



Source: S&P, CapitalIQ

Chinook to Be Acquired by Novartis for $3.5 Billion

SEATTLE, June 12, 2023 (GLOBE NEWSWIRE) -- Chinook Therapeutics, Inc. (Nasdaq: KDNY), a biopharmaceutical company focused on the discovery, development and commercialization of precision medicines for kidney diseases, today announced that it has entered into an agreement and plan of merger with Novartis AG pursuant to which Novartis will acquire Chinook for $40 per share in cash, or a total of $3.2 billion. This offer represents a premium of 83 percent to Chinook's 60-day volume-weighted average stock price and 67 percent to Chinook's closing price on June 9, 2023. In addition, Chinook shareholders will receive contingent value rights (CVRs) providing for payment of up to $4 per share upon the achievement of certain future regulatory milestones with respect to Chinook's lead product candidate, atrasentan. Total consideration including the contingent value right, if the milestones are achieved, would be approximately $3.5 billion. The transaction has been unanimously approved by the Boards of Directors of both companies.

"We are pleased that Novartis recognizes the significant value that the Chinook team has built with our pipeline of clinical and preclinical programs for patients with rare, severe chronic kidney diseases," said Eric Dobmeier, president and chief executive officer of Chinook Therapeutics. "We believe this transaction is great news for kidney disease patients and the programs we have built at Chinook. Through this merger, Novartis can apply its substantial resources to pursue broader development efforts and commercialization of atrasentan, zigakibart (BION-1301) and other programs in our pipeline to build its global renal therapeutic area."

Completion of the transaction is expected in the second half of 2023, pending approval by Chinook's stockholders and satisfaction of other customary closing conditions. Until that time, Chinook will continue to operate as a separate and independent company.

Source: https://investors.chinooktx.com/news-releases/news-release-details/chinook-therapeutics-enters-agreement-be-acquired-novartis-ag

Carson Block's Latest Short Bet Is Burned by Novartis M&A Deal

- Traders betting against Chinook down $58 million in 2023: S3
- Muddy Waters doubled down on position ahead of Novartis deal

Bloomberg, June 12, 2023

Carson Block's Muddy Waters wager against a hedge fund favorite, Chinook Therapeutics Inc., took a hit Monday after Novartis AG agreed to buy the drug developer in a deal for up to $3.5 billion.

With the stock surging 58%, its best day since 2015, short sellers betting against Chinook are looking at paper losses of $58 million, according to data from S3 Partners. Monday's rally erased bearish investors' gains for the year and put them on track for a mark-to-market loss of roughly $56 million for 2023

Muddy Waters' short report on Chinook completely ignored the company's promising APRIL antibody, BION-1301, which has the same promise as a similar drug in development by Remegen. We can only imagine that Novartis carefully considered the report and chose to take a different point of view on Atrasentan, the company's lead drug candidate.

Sources: https://www.bloomberg.com/news/articles/2023-06-12/carson-block-s-latest-short-bet-is-burned-by-novartis-m-a-deal, https://www.muddywatersresearch.com/research/kdny/muddy-waters-short-chinook/

SEC Charges Sabby Management with Naked Shorting

U.S. SECURITIES AND EXCHANGE COMMISSION

ABOUT | DIVISIONS & OFFICES | ENFORCEMENT | REGULATION | EDUCATION

ENFORCEMENT

- Accounting and Auditing Enforcement Releases
- Administrative Proceedings
- ALJ Initial Decisions
- ALJ Orders
- Amicus / Friend of the Court Briefs
- Delinquent Filings
- Fair Funds
- Information for Harmed Investors
- Litigation Releases
- Opinions and Adjudicatory Orders
- Receiverships
- Stop Orders
- Trading Suspensions

Securities and Exchange Commission v. v. Hal D. Mintz and Sabby Management LLC, No. 2:23-cv-03201 (D. N.J.) filed June 12, 2023

Litigation Release No. 25746 / June 14, 2023

SEC Charges Investment Adviser and Principal in Abusive Naked Short Selling Scheme

The Securities and Exchange Commission today charged investment adviser Sabby Management LLC and its managing partner, Hal D. Mintz, with fraud in connection with a long running scheme involving misrepresentations and violations of rules for short selling and order making, as well as other violative trading, that generated more than $2 million in illegal profits.

The SEC's complaint alleges that, from at least March 2017 through May 2019, Sabby and Mintz repeatedly circumvented trading rules to conduct unlawful trades in the stock of at least 10 public companies. Short selling is a legal practice where, generally, a trader borrows a security from a securityholder and sells the security at one price, speculating that the trader can buy the security at a lower price in the future before it must be returned to its owner. As alleged in the complaint, for example, Sabby and Mintz engaged in illegal "naked short selling" by intentionally and improperly placing short sales when they knew or were reckless in not knowing that they had not borrowed or located the shares, and then failed to make timely delivery of the shares. According to the SEC's complaint, the purpose of Sabby and Mintz's fraudulent scheme was to earn profits they could not have gained through legal trading.

It wasn't a great week for short-sellers.

In this complaint, the SEC alleges that Sabby Management has engaged in naked shorting – that is, short selling stocks, without borrowing the underlying stock.

Source: https://www.sec.gov/litigation/litreleases/2023/lr25746.htm

Coherus Acquiring Surface Oncology for Over $60 Million

REDWOOD CITY, Calif. and CAMBRIDGE, Mass., June 16, 2023 (GLOBE NEWSWIRE) -- Coherus BioSciences, Inc. (Coherus, Nasdaq: CHRS) and Surface Oncology, Inc. (Surface, Nasdaq: SURF) today announced that the companies have entered into a definitive merger agreement providing that, at the closing, Coherus will acquire Surface Oncology, a clinical-stage immuno-oncology (I-O) company developing next-generation immunotherapies that target the tumor microenvironment. The Surface acquisition adds two differentiated clinical stage assets to Coherus' novel I-O pipeline: SRF388, a novel IL-27-targeted antibody currently being evaluated in Phase 2 clinical trials in lung cancer and liver cancer, and SFR114, a CCR8-targeted antibody currently in a Phase 1/2 study as a monotherapy in patients with advanced solid tumors.

The transaction was unanimously approved by the boards of directors of both companies and is expected to close in the third quarter of 2023.

"This transaction is well-timed, as it coincides with the accelerating growth of our biosimilar revenues driven by the launch of CIMERLI® and near-term launch of YUSIMRY®. With the agreement to acquire Surface and the expected near-term approval of toripalimab, Coherus is positioned to become one of the very few I-O companies with demonstrated commercial expertise, significant product revenues, and unique, competitively positioned R&D programs addressing critical unmet medical needs," said Denny Lanfear, Chairman and Chief Executive Officer of Coherus. "Toripalimab has recently demonstrated potentially practice-changing overall survival data in nasopharyngeal carcinoma, and its differentiated mechanism of action defines it as a next-generation PD-1. Existing marketed PD-1's transformed the treatment of cancer over the past decade but are effective in only a minority of patients. Additional overall survival gains must come from novel combinations that more broadly target the cancer immunity cycle. The addition of Surface's IL-27 and CCR8 antibodies expands our next-generation I-O pipeline beyond checkpoint inhibition to agents targeting immune-suppressive mechanisms of the tumor microenvironment."

Source: https://investors.coherus.com/news-releases/news-release-details/coherus-acquire-surface-oncology

Grifols Announces a Potential Stake Sale

GRIFOLS

Grifols, S.A.

Avinguda de la Generalitat 152-158
08174 Sant Cugat del Vallès
Barcelona - ESPAÑA

Tel. [34] 935 710 500
Fax [34] 935 710 267

www.grifols.com

Pursuant to the provisions of article 226 of the Law 6/2023, of March 17, on Securities Markets and Investment Services Grifols, S.A. ("**Grifols**" or the "**Company**") hereby informs about the following

INSIDE INFORMATION

Grifols, as the largest shareholder of Shanghai RAAS ("**SR**"), has sent a notice to the latter informing them that they are planning major matters involving changes in the shareholding structure of SR. As of today, this matter is still in the planning stage and there's certain uncertainty.

Upon satisfactory closing of the deal, Grifols is expected to receive $1.5 bn and remain to be a significant shareholder of SR.

Grifols will continuously follow subsequent developments and perform the information disclosure obligation in accordance with the relevant provisions.

In Barcelona, on 14 June 2023

Grifols shares jumped by 7% on the news that it may sell a portion of its shares in Shanghai RAAS. Shanghai RAAS is one of the largest blood products companies in China.

Source: https://newsserviceweb.oslobors.no/message/42877

Bio & Pharma

Celltrion puts Takeda's assets on sale in three years

The S.Korean biosimilar giant plans new acquisitions after unloading Asia-Pacific sales rights for Takeda's products acquired in 2020

THE KOREA ECONOMIC DAILY
GLOBAL EDITION

June 18, 2023

"South Korea's Celltrion Inc. put Japanese Takeda Pharmaceutical Co.'s primary care assets acquired in 2020 on sale as the biosimilar giant is raising money to transform into a drug developer with consideration of investments of billions of dollars in acquisitions.

Celltrion selected JPMorgan Chase & Co. a manager to sell the sales rights for Takeda's pharmaceutical products and over-the-counter (OTC) products in Asia Pacific excluding South Korea, according to bio-industry sources in Seoul on Sunday. A number of major global pharmaceutical companies reportedly showed interest in the takeover.

Celltrion in June 2020 bought for $278 million the rights for patents, trademarks, permits and sales of 18 primary care assets for Takeda's pharmaceutical products sold in nine Asia Pacific countries such as South Korea, Thailand, Taiwan, Singapore, Malaysia and Australia. Those pharmaceutical products included diabetes treatment Nesina and hypertension medicine Edarbi, as well as OTC drugs such as cold medicine Whituben."

Source: https://www.kedglobal.com/bio-pharma/newsView/ked202306180003

Pfizer/Seagen Refile HSR Notification on June 14th

Our read of this filing is that Pfizer is giving FTC more time to consider its HSR filing and may be providing additional information to the FTC and DOJ.

UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

FORM 8-K

Current Report
Pursuant to Section 13 or 15(d)
of the Securities Exchange Act of 1934

Date of Report (Date of earliest event reported): June 14, 2023

Seagen Inc.
(Exact name of Registrant as specified in its charter)

Delaware	0-32405	91-1874389
(State or other jurisdiction of incorporation or organization)	(Commission File Number)	(I.R.S Employer Identification No.)

21823 30th Drive SE
Bothell, Washington 98021
(Address of principal executive offices, including zip code)

(425) 527-4000
(Registrant's telephone number, including area code)

Item 8.01 Other Events.

As previously disclosed, on March 12, 2023, Seagen Inc., a Delaware corporation (the "Company"), entered into an Agreement and Plan of Merger (the "Merger Agreement") by and among the Company, Pfizer Inc., a Delaware corporation ("Pfizer") and Aris Merger Sub, Inc., a Delaware corporation and a wholly-owned subsidiary of Pfizer ("Merger Sub"). Pursuant to the Merger Agreement, Merger Sub will be merged with and into the Company (the "Merger"), with the Company surviving the Merger as a wholly-owned subsidiary of Pfizer.

Also, as previously disclosed, on May 12, 2023, the Company and Pfizer each filed with the Federal Trade Commission ("FTC") and Department of Justice ("DOJ") a Notification and Report Form relating to the Merger Agreement and the Merger as required under the Hart-Scott-Rodino Antitrust Improvements Act of 1976, as amended (the "HSR Act").

As agreed with the Company, Pfizer withdrew its Notification and Report Form and will refile that form today, June 14, 2023. Accordingly, the statutory waiting period under the HSR Act will be scheduled to expire at 11:59pm ET on July 14, 2023. This statutory waiting period may be extended if the FTC issues a request for additional information and documentary material.

Additionally, on June 1, 2023, the Company and Pfizer referred the Merger to the European Commission (the "EC") for review under Article 4(5) of the EU Merger Regulation. If the EC obtains jurisdiction to review the Merger as a result of such referral, receipt of approval from the EC for the Merger would become a condition for the closing of the Merger.

As previously disclosed, the Company continues to expect that the Merger will be completed in late 2023 or early 2024, subject to fulfillment of customary closing conditions, including receipt of required regulatory approvals.

Source: https://d18rn0p25nwr6d.cloudfront.net/CIK-0001060736/4e87c484-76b7-43f1-97a4-f789baa3cc58.pdf

Life Sciences Firm Abcam Gets Takeover Approaches While It Battles Founder

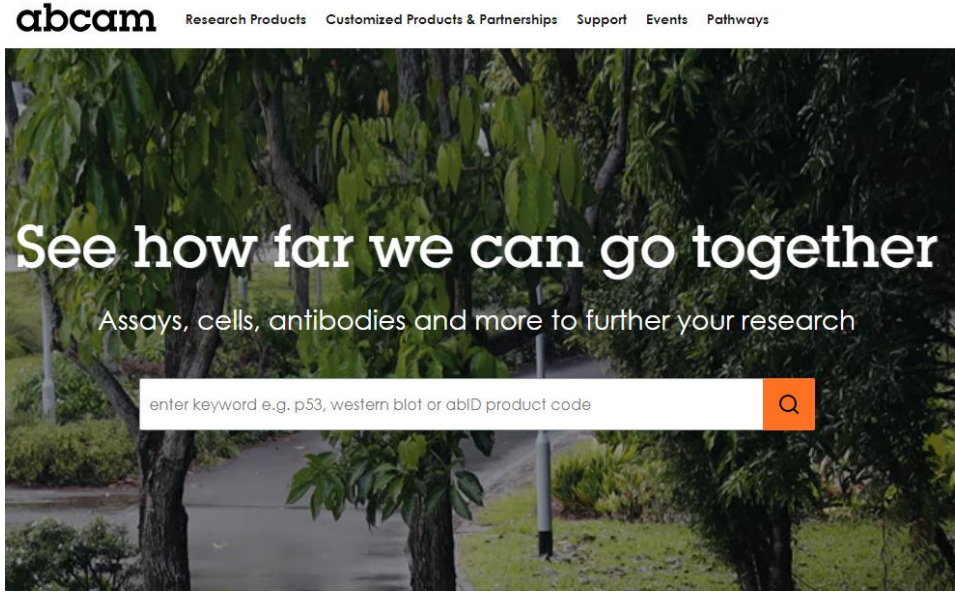
- Abcam draws interest from big US life-sciences tool makers
- $5 billion British company in talks on potential sale

Bloomberg, June 16, 2023

Abcam Plc, the biotechnology supplier whose founder is seeking to replace some of its board members, has received multiple takeover approaches.

The UK company has “received strategic inquiries from multiple parties over recent weeks,” likely due to the publicity around its upcoming shareholder meeting, Abcam said in a statement Friday. The board is aware of its fiduciary duties “and will work with its advisors to consider such inquiries as appropriate,” according to the statement.

Cambridge, England-based Abcam has attracted interest from suitors including some of the largest US suppliers of life-sciences tools and is in discussions on a potential sale, people with knowledge of the matter said. A representative for Abcam declined to comment beyond the statement.



Source: https://www.bloomberg.com/news/articles/2023-06-16/biotech-abcam-gets-takeover-approaches-while-battling-founder

Disclosure

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