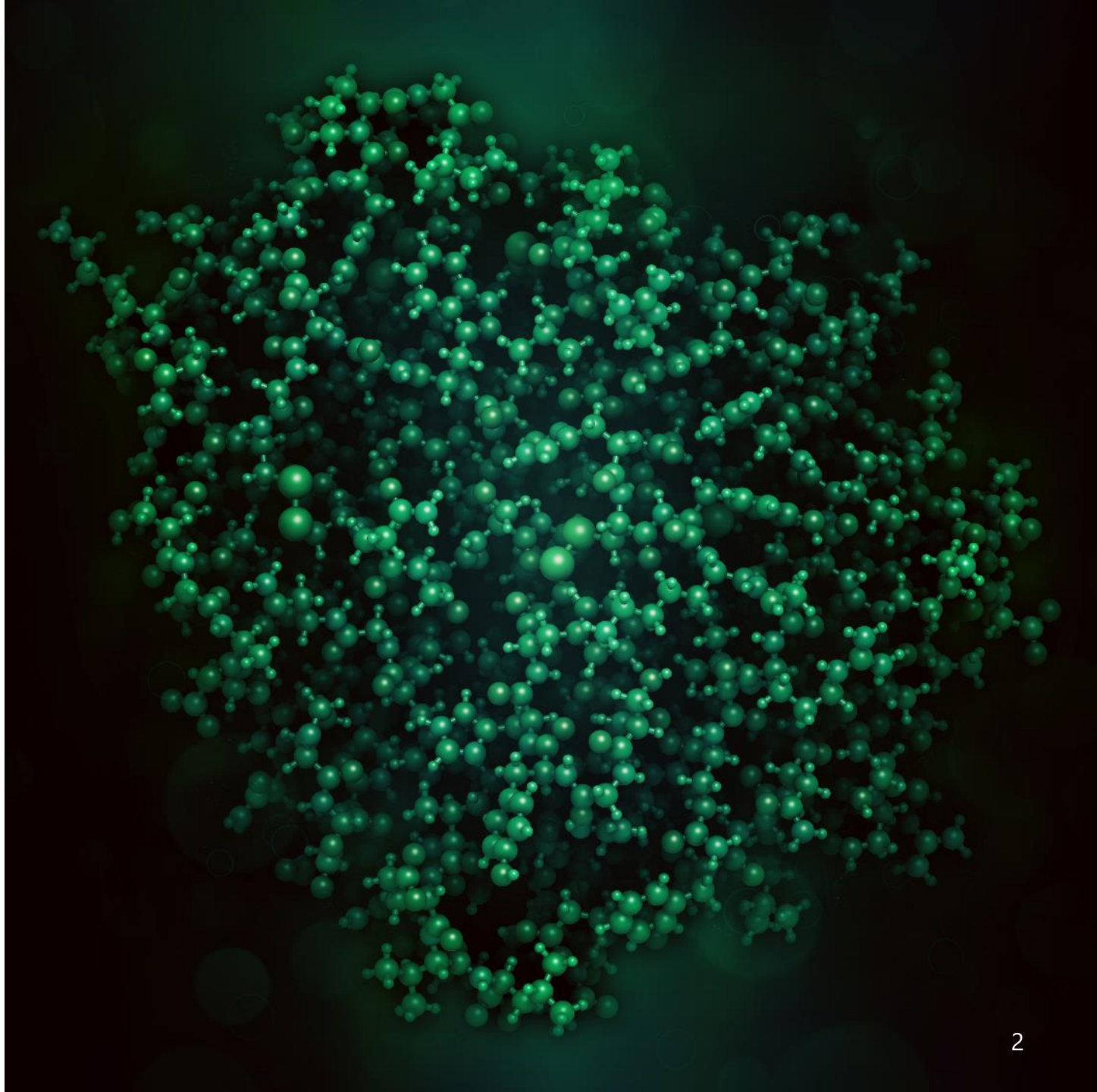
Biopharmaceutical Sector

Weekly Update – October 23, 2023

STIFEL | Healthcare

Table of Contents



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Recent issues in case you missed and want to read:

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

Join Us at These Upcoming Events

Biotech Hangout held its latest event on October 20th.

The next event will be on October 27, 2023.

Please join us.

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

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

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

Macro Update

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

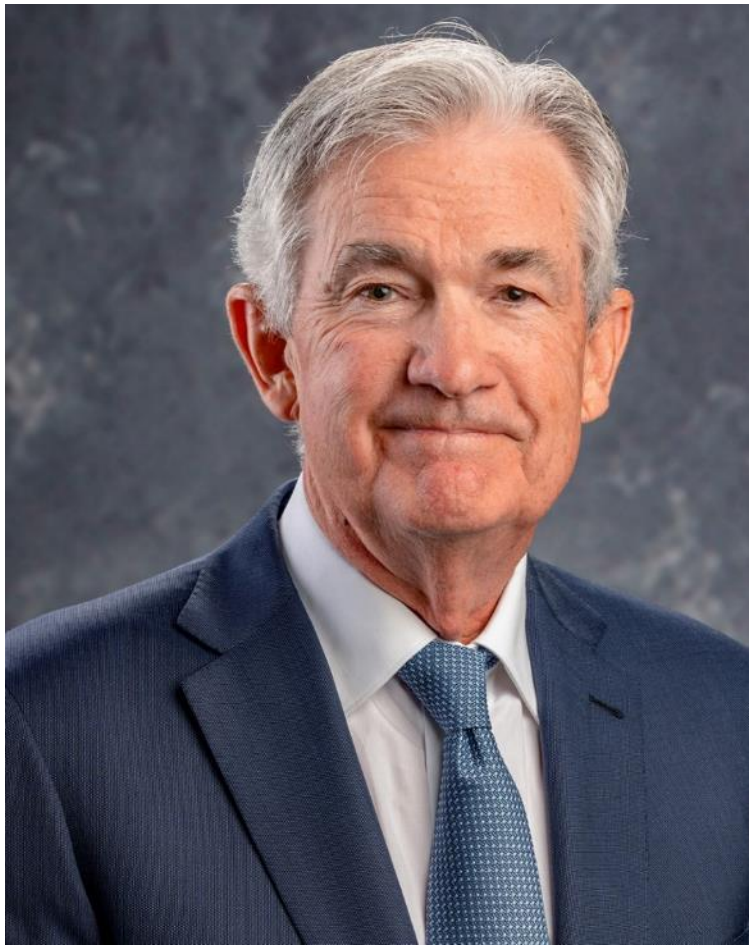
Fed Last Week Signalled that Rate Increases May Not Be Done

Jeanna Smialek, *New York Times*, October 19, 2023 (excerpt)

Jerome H. Powell, the chair of the Federal Reserve, reiterated the central bank's commitment to moving forward "carefully" with further rate moves in a speech on Thursday. But he also said that the central bank might need to raise interest rates more if economic data continued to come in hot.

"We are attentive to recent data showing the resilience of economic growth and demand for labor," Mr. Powell acknowledged on Thursday. "Additional evidence of persistently above trend growth, or that tightness in the labor market is no longer easing, could put further progress on inflation at risk and could warrant further tightening of monetary policy." Mr. Powell called recent growth data a "surprise," and said that it had come as consumer demand held up much more strongly than had been expected.

The S&P 500 ended almost 1 percent lower for the day. The move came alongside a further rise in crucial market interest rates, with the 10-year Treasury yield rising within a whisker of 5 percent, a threshold it hasn't broken through since 2007.

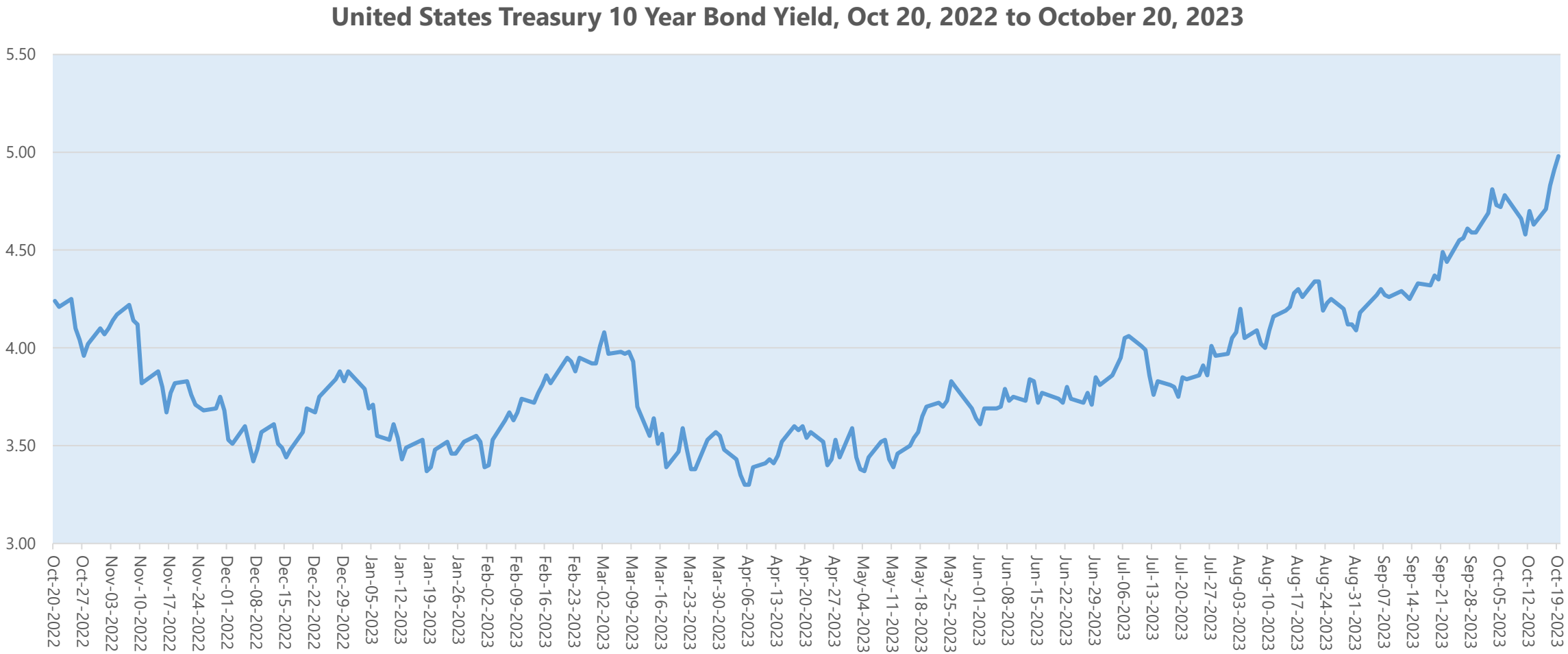


Fed Chair, Jay Powell

Source: https://www.nytimes.com/2023/10/19/business/economy/powell-fed-interest-rates.html

Long Bond Yields Rose After Powell's Remarks

After a two week respite in increasing long bond rates, we saw the ten-year Treasury yield resume its upward march last week. The 10-year yield hit 5% last Friday – a first since 2007. This is *not* good news for biotech.



Source: CapitalIQ

Negative Market Mood Caused by a Dollop of Fed Reality

Katherine Greifeld and Vildana Hajric, *Bloomberg*, Oct 20, 2020

Benchmark 10-year Treasury yields soared 30 basis points this week, taking the rate within a whisker of 5% for the first time in more than 16 years. By contrast, yields on two-year Treasuries — the tenor most sensitive to monetary policy expectations — rose just 2 basis points. That dynamic sent the 2- to 10-year yield curve to just negative 17 basis points, the least inverted level in over a year. Commodities only added to the drama, with oil and gold notching a second straight week of gains.

Powell spoke Thursday and was emphatic that relief in the form of rate cuts isn't in the cards. While inclined to hold policy steady at its next meeting, the Fed chief suggested that another hike may be warranted should policymakers see further signs of resilient economic growth, adding that inflation is still "too high."

"The reality that has begun to sink in over the past month since the FOMC meeting is that the Fed is not cutting rates back to pre-pandemic levels when inflation cools. Rates will settle back in at higher level," said Michael O'Rourke, chief market strategist at JonesTrading. "That means that the discount rate one uses for investment-valuation models needs to be higher, which means multiples contract and valuations come down."

Source: https://www.bloomberg.com/news/articles/2023-10-20/bond-market-s-bad-tidings-start-to-overwhelm-miracle-stock-rally

Biopharma Market Update

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

XBI Closed at 66.92 Last Week (Down 3.9%)

The XBI was down 3.9% on bad rate news last week. The XBI is now down 19.4% for the year. Total global biotech value dropped 6.1% for the year. After adjusting out the effect of exits and entries (M&A and IPO's), total biotech is down 15.8% for the year (not quite as bad as the XBI).

Biotech Stocks Down Last Week

Return: Oct 14 to Oct 20, 2023

Nasdaq Biotech Index: -3.7%
Arca XBI ETF: -3.9%
Stifel Global Biotech (EV): -6.1%*
S&P 500: -2.4%

Return: Jan 1 to Oct 13, 2023

Nasdaq Biotech Index: -10.0%
Arca XBI ETF: -19.4%
Stifel Global Biotech: -22.9%*
Stifel Global Biotech (adjusted): -15.8%*
S&P 500: +10.0%

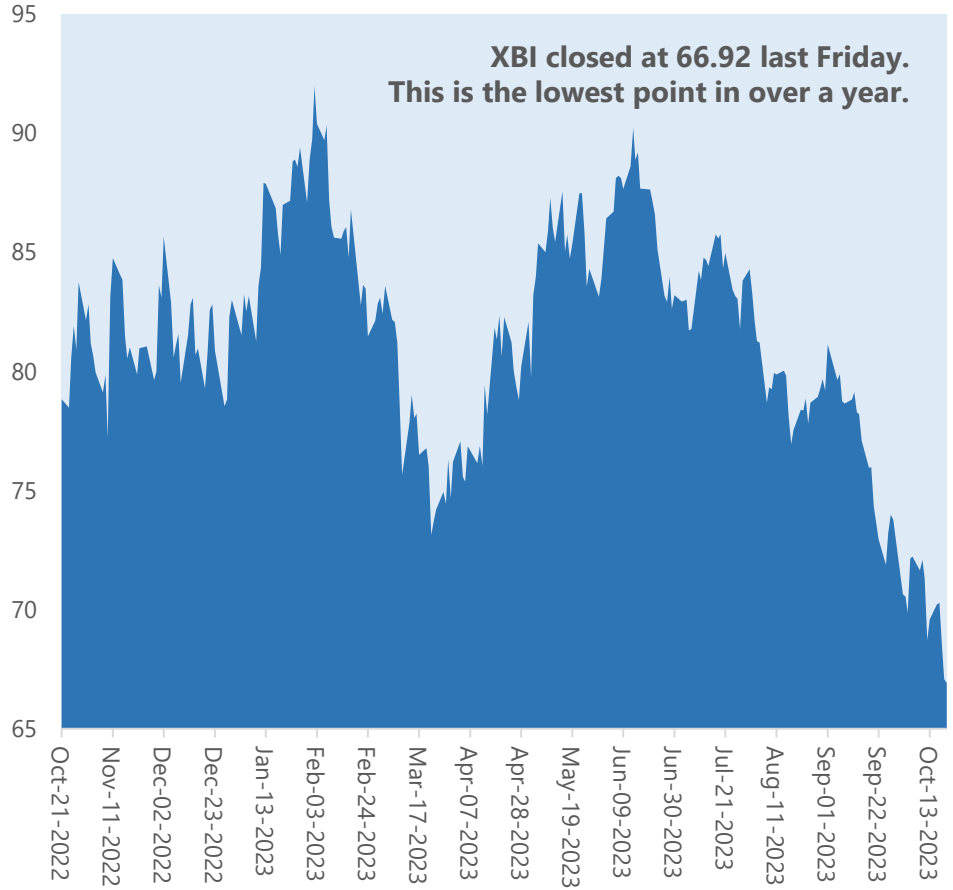
VIX Up

Oct 21: 29.7%
Jan 20: 19.9%
May 26: 18.0%
July 21: 13.6%
Sep 29: 17.3%
Oct 6: 17.4%
Oct 13: 19.3%
Oct 20: 21.7%

10-Year Treasury Yield Down

Oct 21: 4.2%
Jan 20: 3.48%
May 26: 3.8%
July 21: 3.84%
Sep 29: 4.59%
Oct 6: 4.78%
Oct 13: 4.63%
Oct 20: 4.98%

XBI, Oct 21, 2022 to Oct 20, 2023

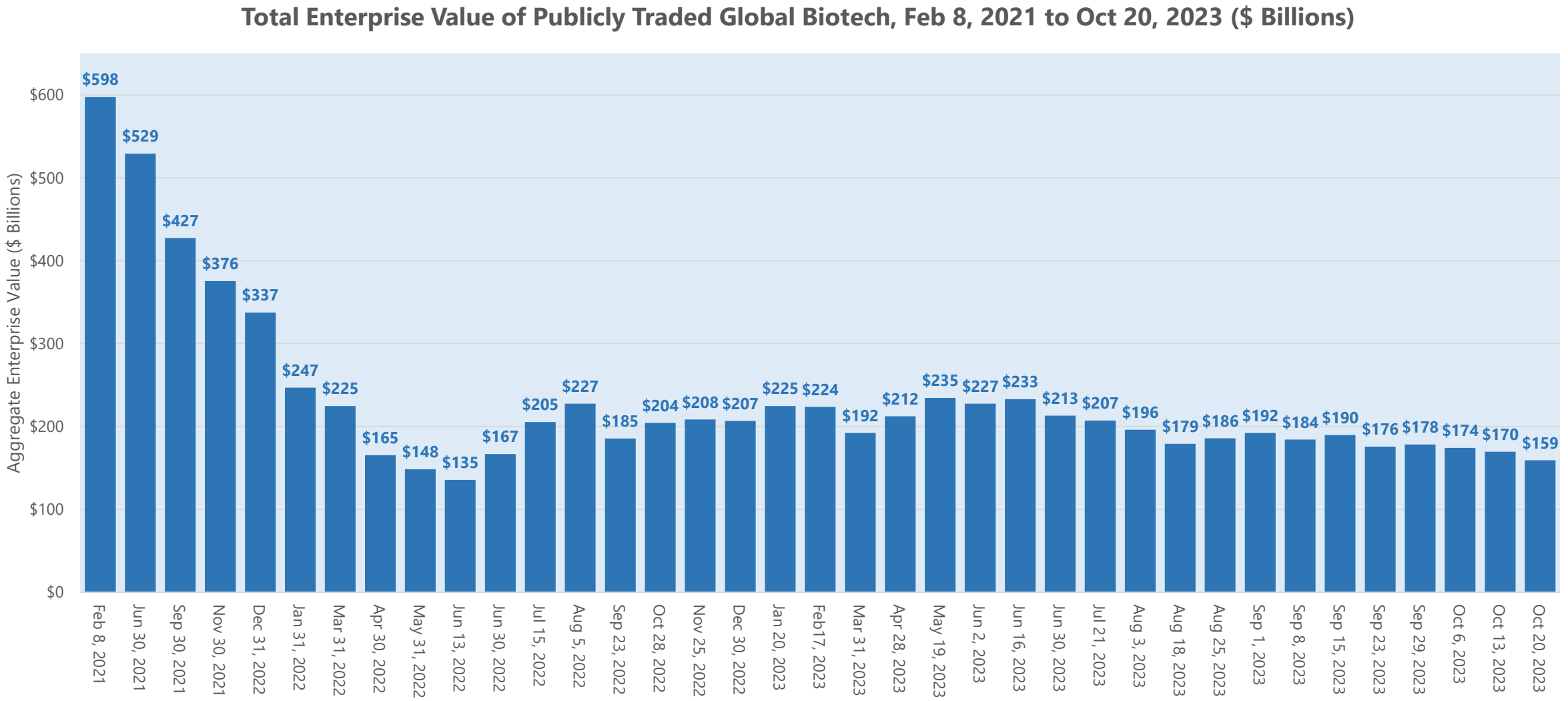


* Change by enterprise value. The adjusted number accounts for the effect of exits and additions via M&A, bankruptcies and IPOs.

Source: S&P Capital IQ and Stifel analysis

Total Global Biotech Sector Value Down Last Week

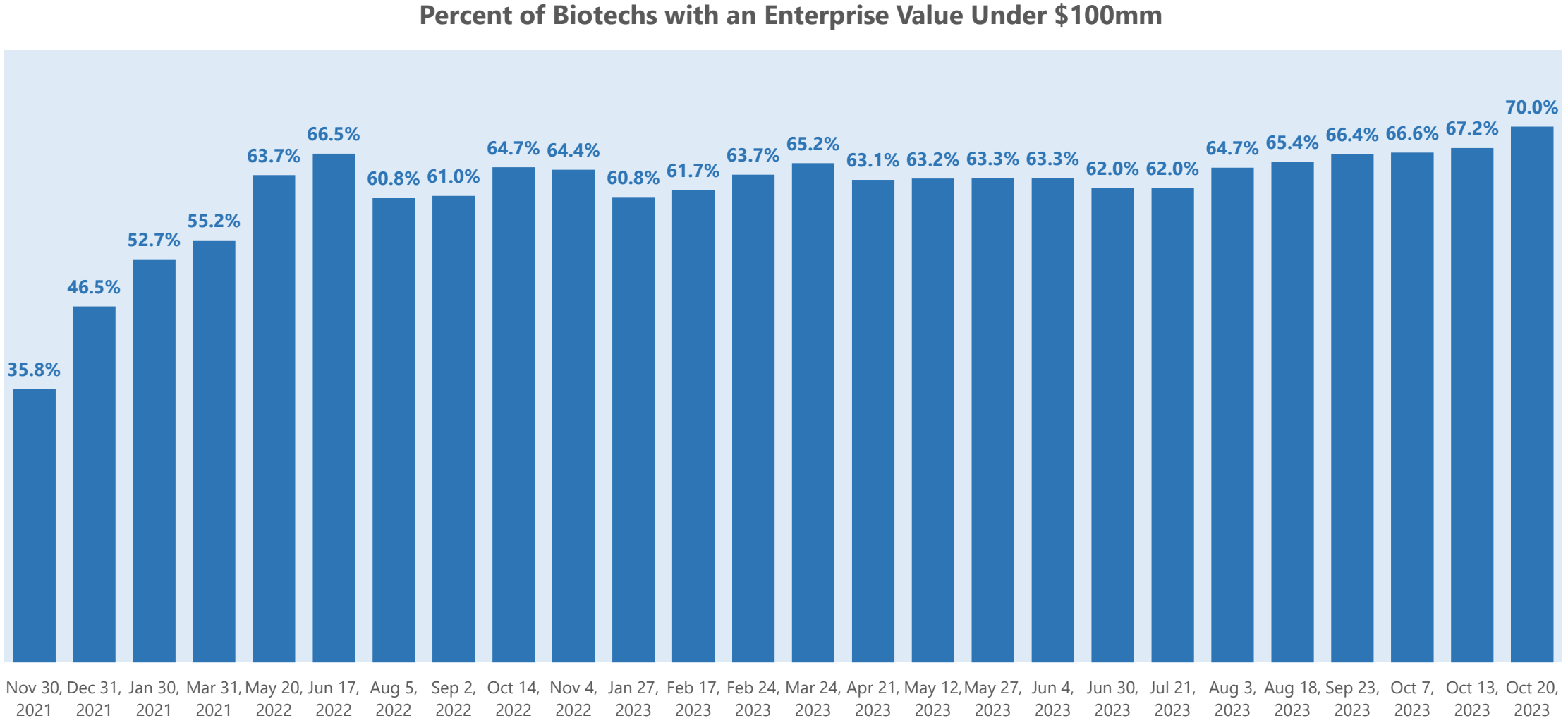
The total value of the global biotech sector fell by 6.1% last week and is now down over 15.8% for the year after adjusting out for exits and entries.



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

Total Global Biotech Sector Neighborhood Shifting

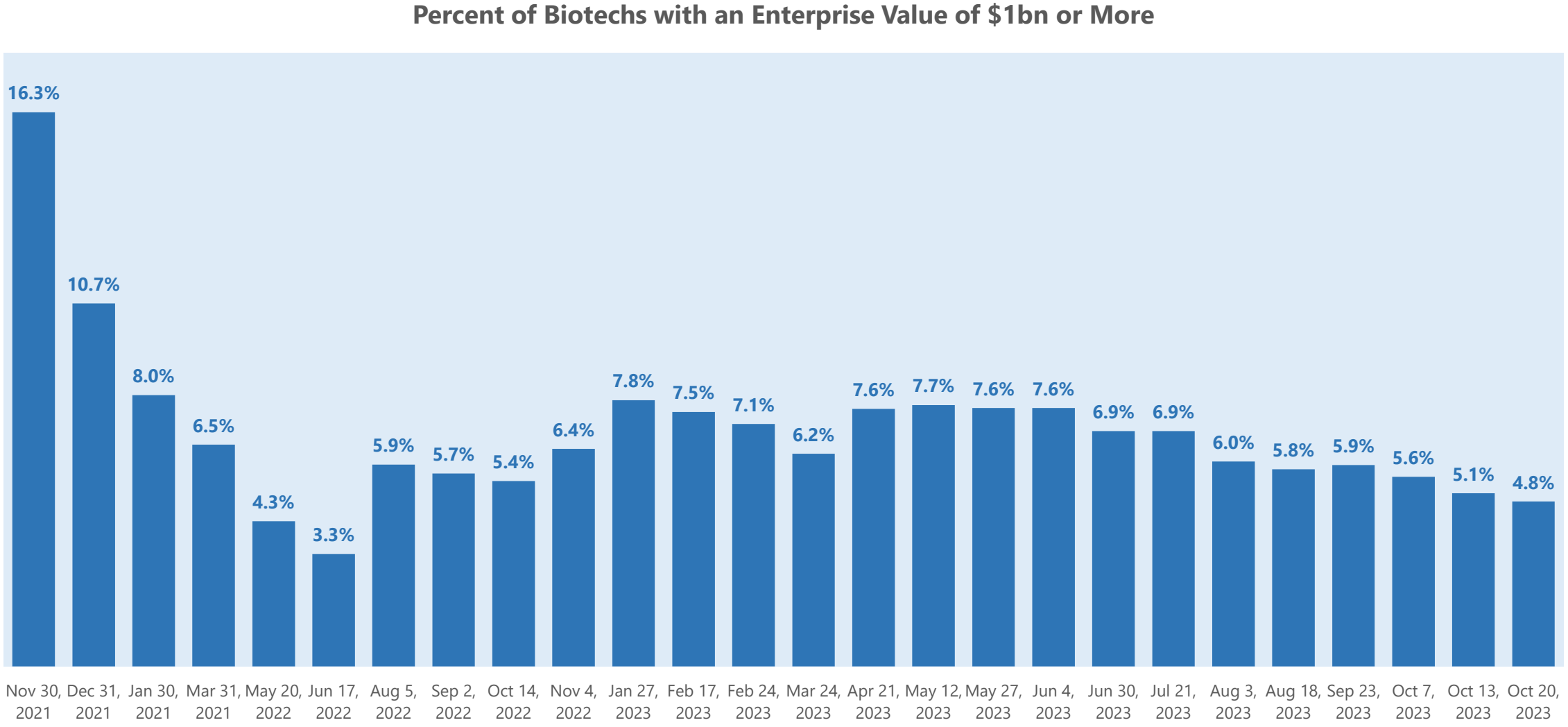
The number of global biotechs worth $100mm or less rose quite a lot last week. At no point in this cycle have there been more companies worth $100mm or less.



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

Less Than 5% of Biotechs Worth Over $1 Billion

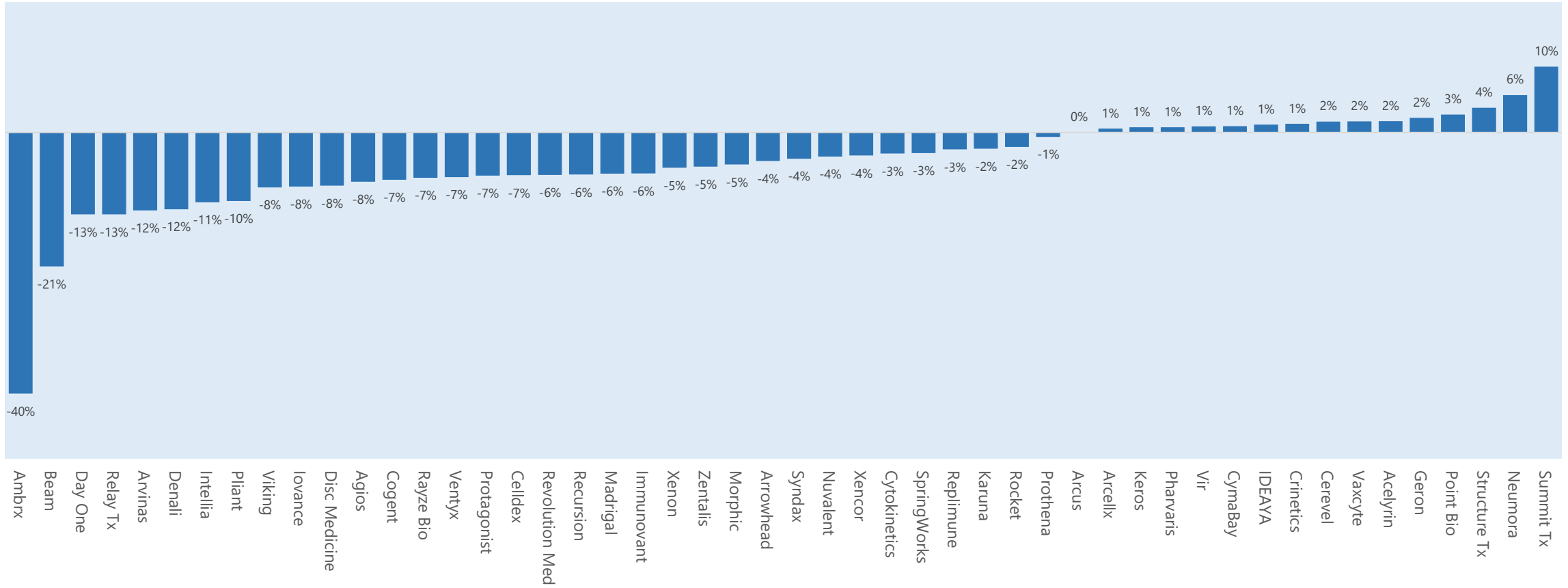
The number of global biotechs worth $1bn or more dipped below 5% last week.



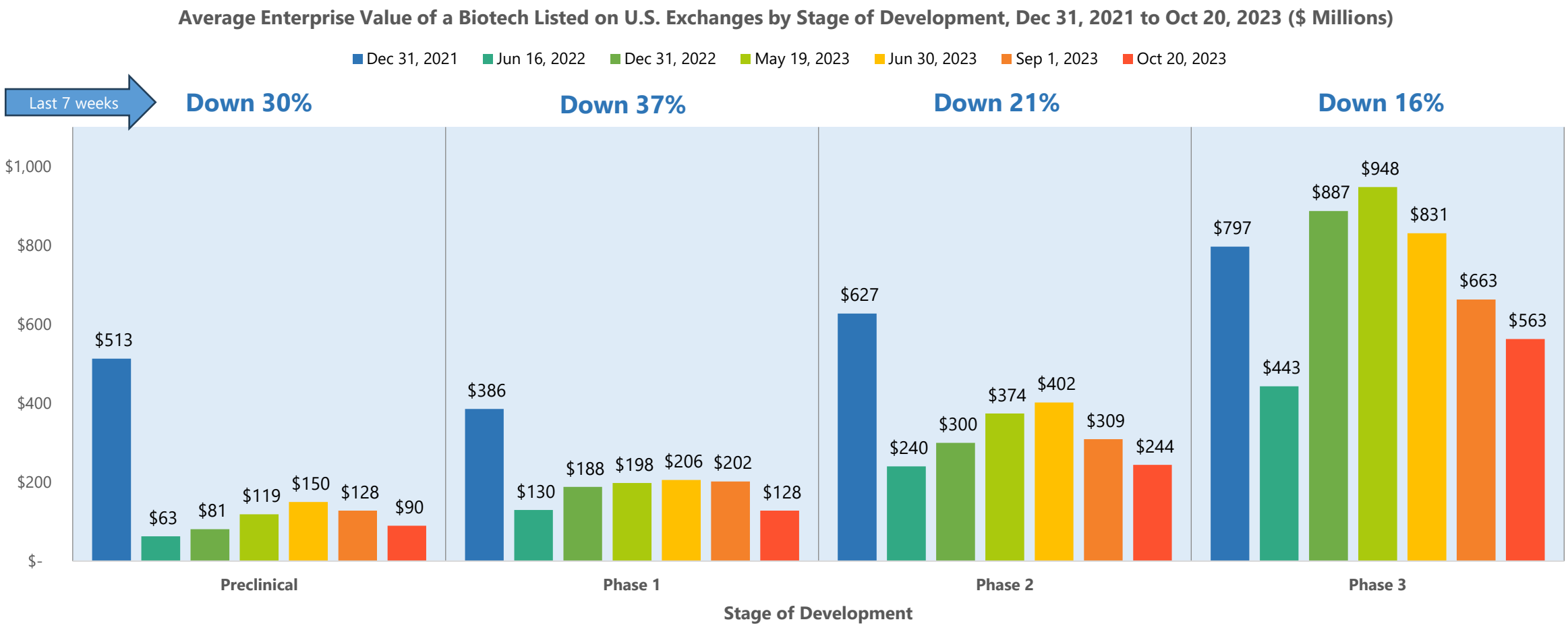
Source: CapitalIQ. Biotechs are defined as any therapeutics company without an approved product on any global stock exchange.

Returns of Top 50 U.S. Biotechs by Market Cap a Week Ago

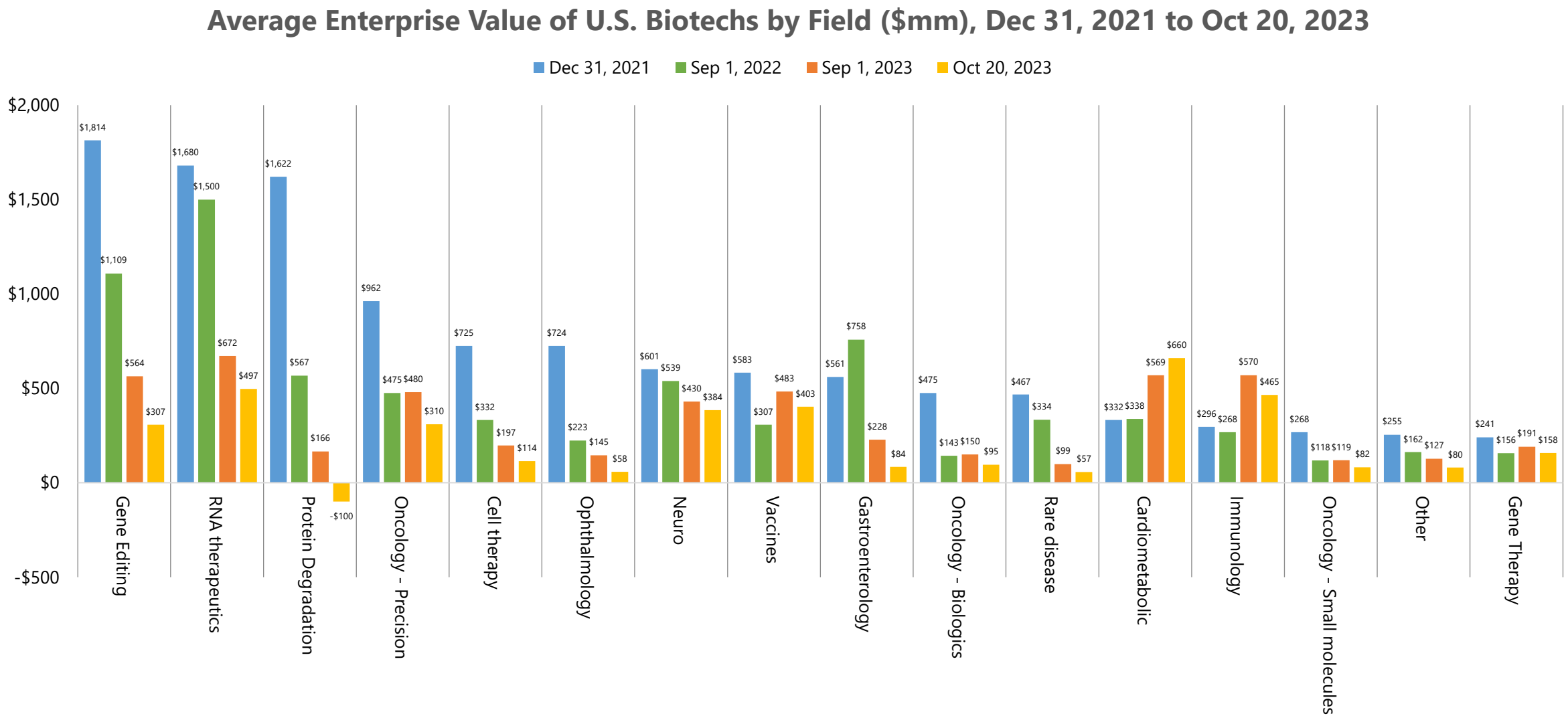
Last week was very tough for the biotech sector as many of the higher quality names saw big drops in value. Gene editing, base editing and precision oncology stocks were particularly hard hit. The average top 50 biotech return was -4.6% last week. The median was -4.2%.



Phase 1 and Preclinical Biotechs Down Around 30% Over Last Seven Weeks While Phase 3's Down 16%



Evolution of Value Structure by Field, Last Seven Weeks, U.S. Public Biotechs

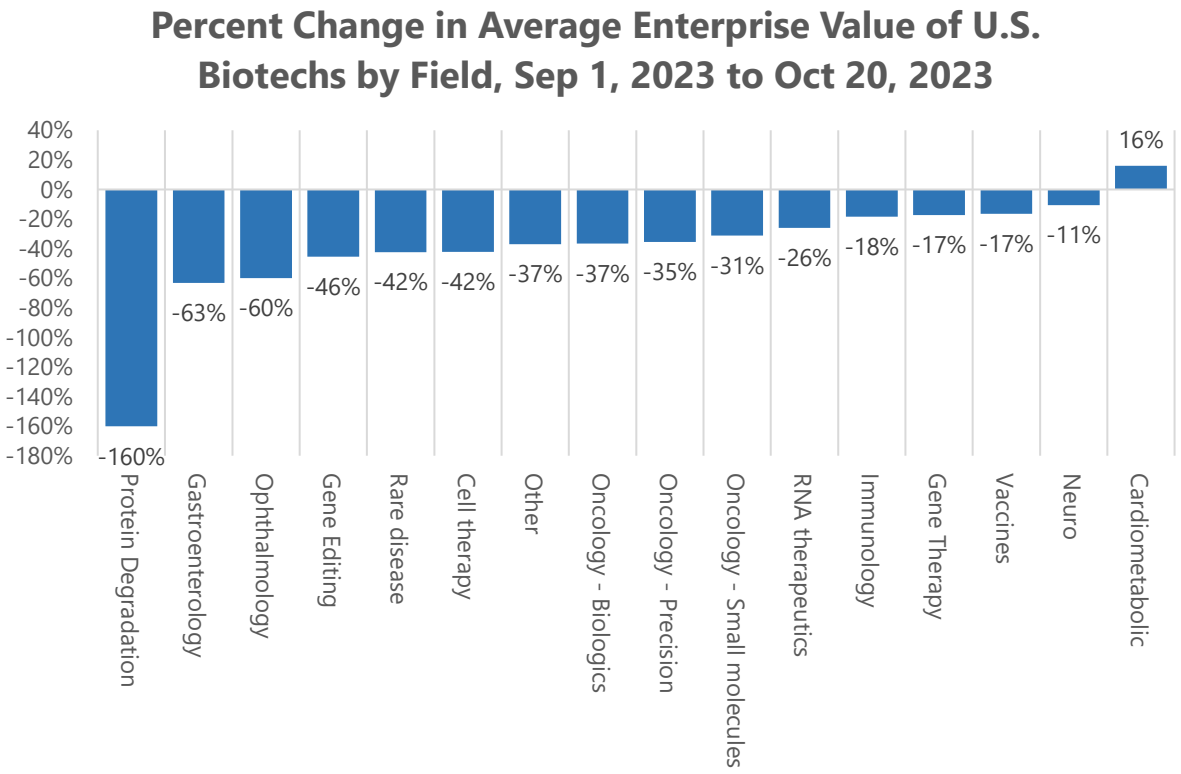


Source: CapitalIQ and Stifel analysis.

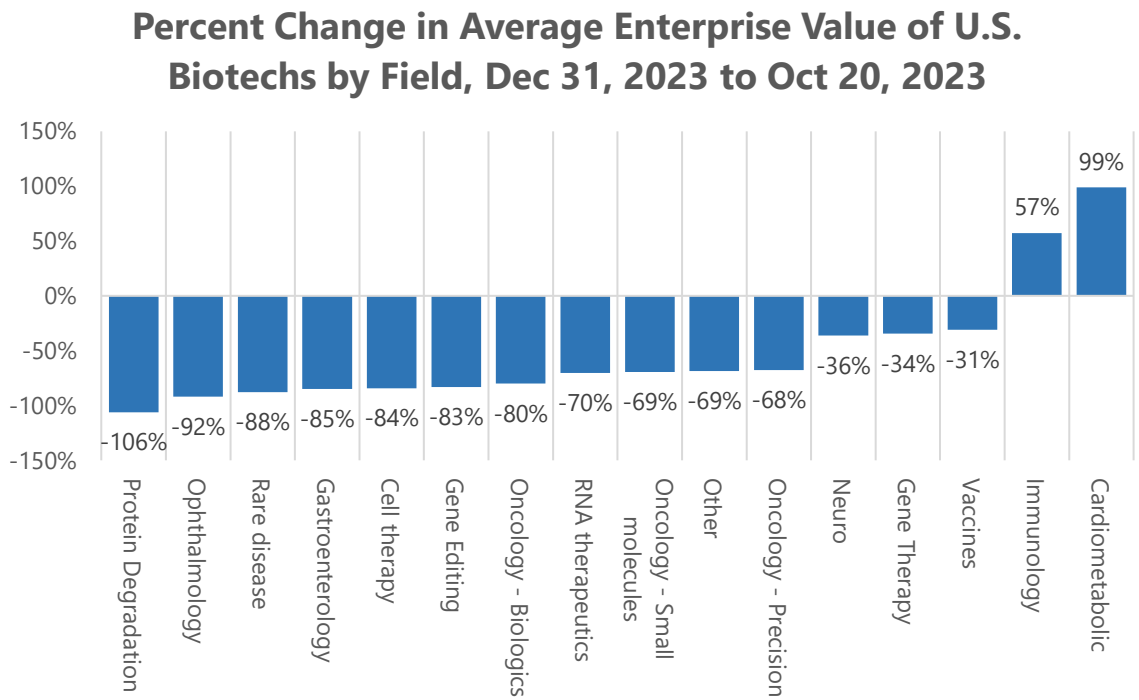
Average Percent Change in Enterprise Value by Field

The last seven weeks have seen significant weakness in protein degrader stocks, gastroenterology stocks and ophthalmology stocks while cardiometabolic biotechs have fared best. If one goes back to Dec 31st, 2021 it is evident that CVM and immunology biotechs have fared best while vaccine, gene therapy and neuro stories have also fared well in a relative sense.

Last Seven Weeks

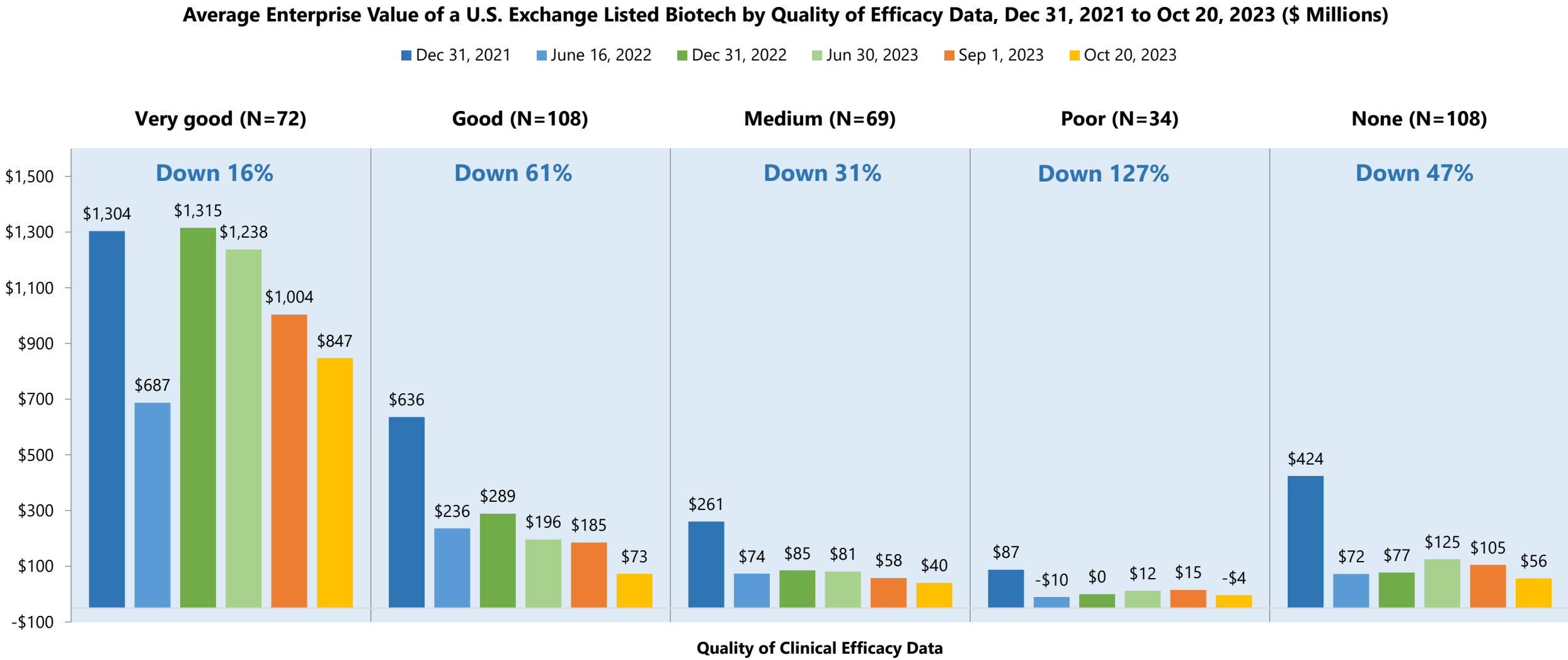


Since Dec 31, 2021



Source: CapitalIQ and Stifel analysis.

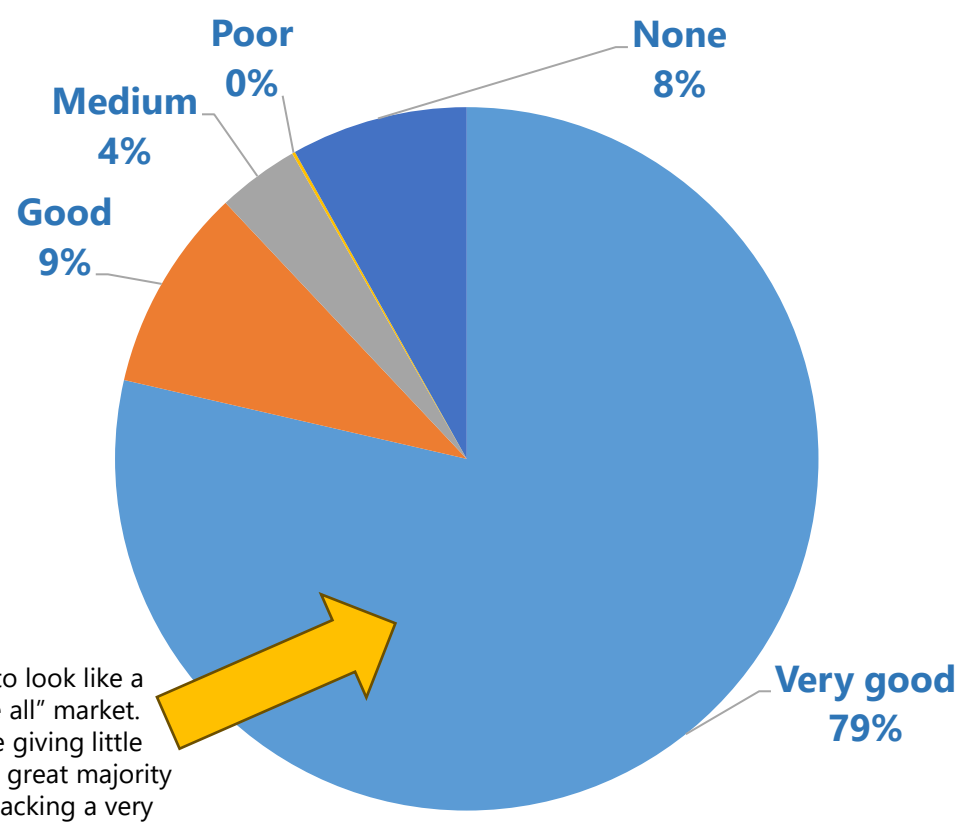
Companies with Excellent Data Down 16% in Last Seven Weeks While Those with Poor or No Data Down Much More



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

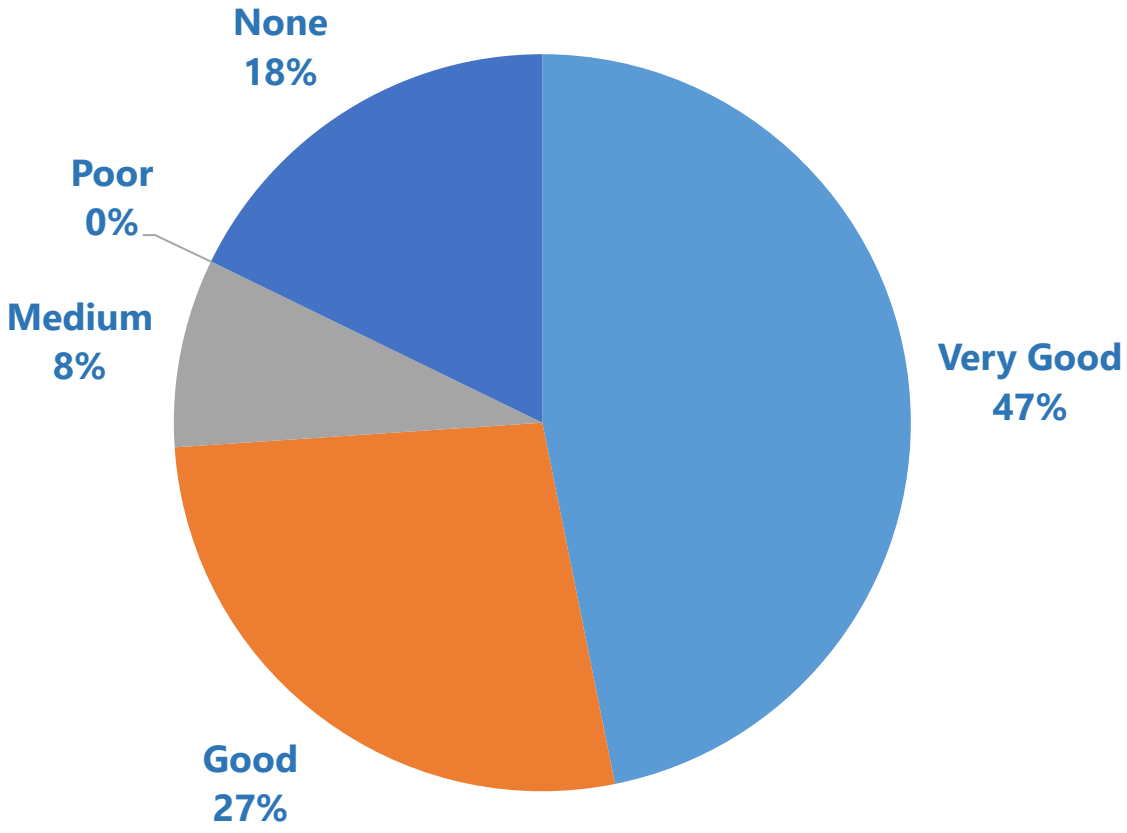
Today, 79% of Value of U.S. Biotech Companies is in 17% of Companies with Very Good Datasets. Big Change from Last November When Only 47% of Market Was in Such Companies

Total Enterprise Value of the U.S. Biotech Sector by Quality of Dataset on Completed Stage of Development, Oct 20, 2023



It's starting to look like a "winner take all" market. Investors are giving little credit to the great majority of biotechs lacking a very good dataset.

Total Enterprise Value of the U.S. Biotech Sector by Quality of Dataset on Completed Stage of Development, Nov 30, 2022



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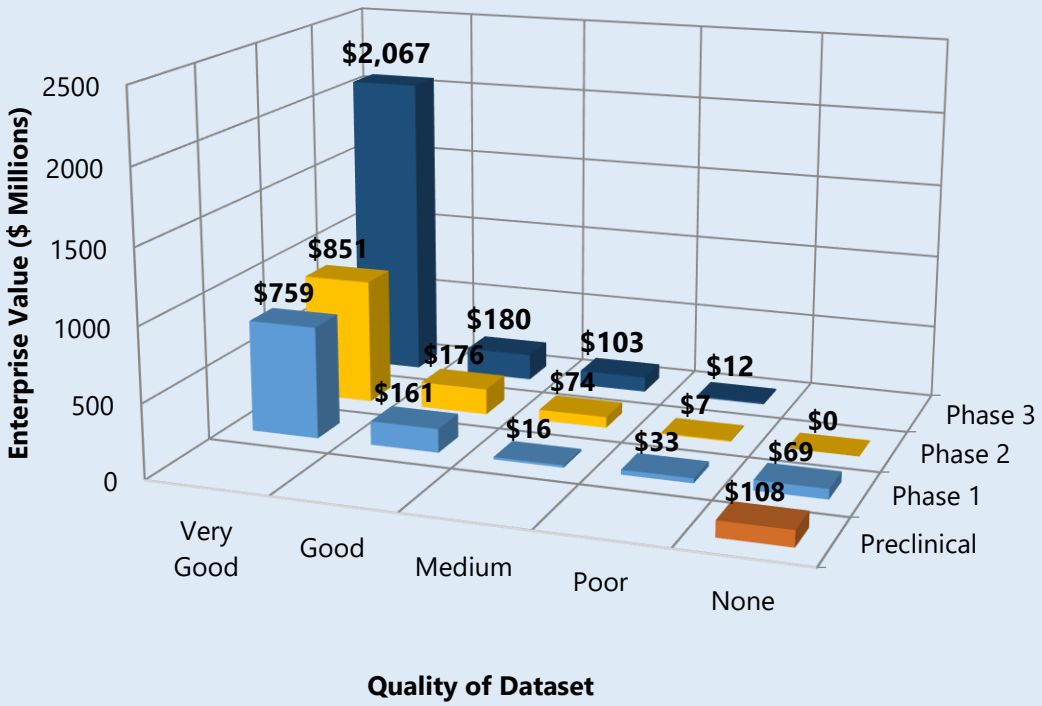
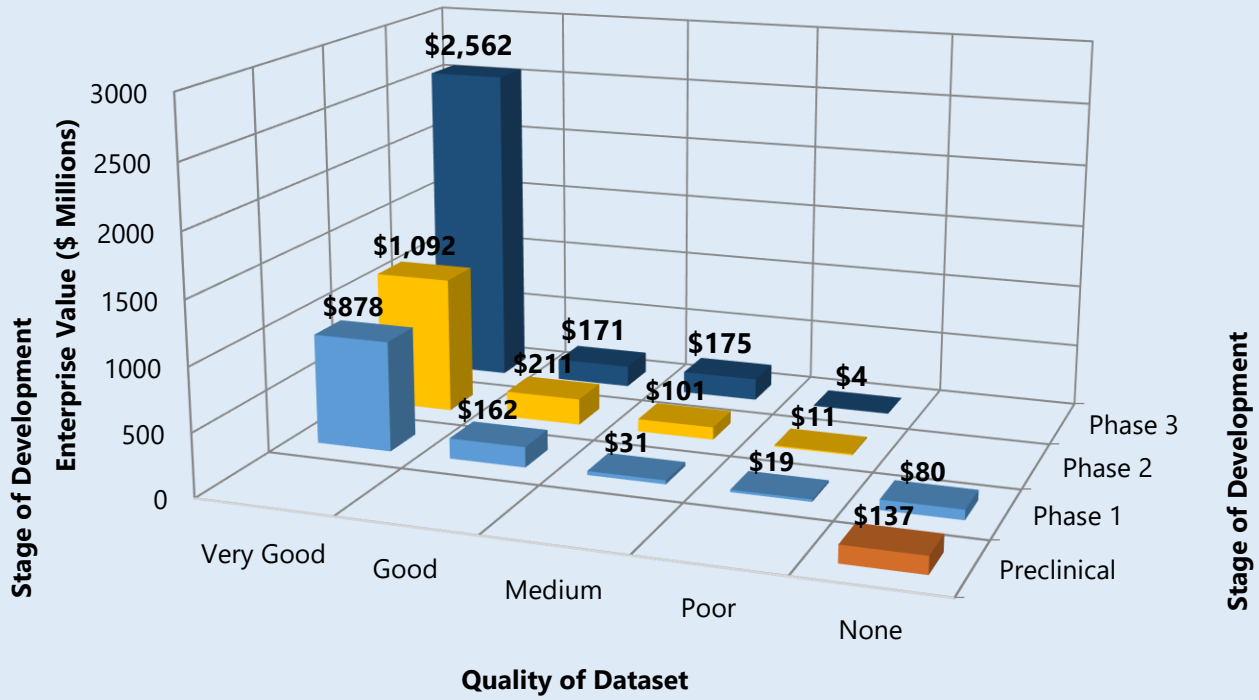
The Only Remaining Refuge Where One Can Expect a Billion Dollar Value is to Have "Very Good" Phase 3 Data

The quality premium is down across the board today versus mid-year.

Average Enterprise Value of a Biotech Listed on U.S. Exchanges by Stage of Development and Quality of Data, Oct 20, 2023



Average Enterprise Value of a Biotech Listed on U.S. Exchanges by Stage of Development and Quality of Data, Jun 30, 2023



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Biotech Stocks are in a Post-Pandemic Slump and Recovery in 2024 is Questionable

Jurica Dujmovic, *MarketWatch*, Oct 20, 2023 (excerpt)

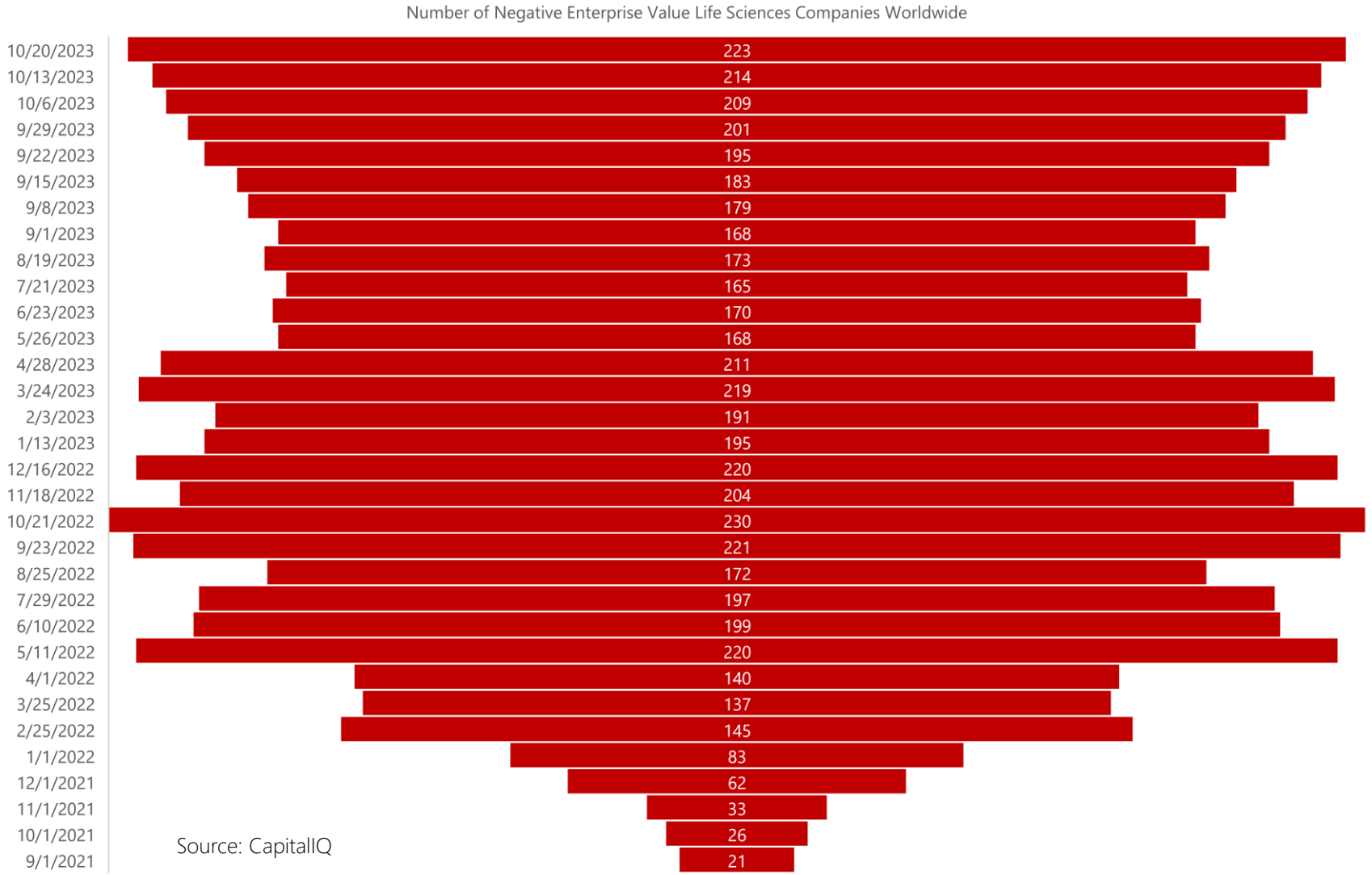
These [vaccine biotech] challenges are symptomatic of a larger trend within the biotech sector, where companies are grappling with a sugar crash — a post-pandemic reality marked by normalized revenues and increased scrutiny. The industry, once buoyed by the demand for COVID-19 vaccines and treatments, is now experiencing a sobering leveling out.

Regulatory pressures are also intensifying, with recent Federal Trade Commission (FTC) activity and the introduction of the U.S. Inflation Reduction Act (IRA) raising concerns about the potential stifling of innovation and implications for pricing and reimbursement. The industry is navigating a tougher regulatory landscape, as FDA approvals dropped in 2022, though returned to pre-pandemic levels in the first quarter of 2023.

Financing also has hit a rough patch, with all types of biotech financing experiencing a significant decrease since 2022. According to Ernst & Young, the biotech IPO market is down 93% compared to 2021, and around 29% of publicly traded biotech companies in the U.S and Europe have less than one year of cash on hand. This constrained financing environment is a stark reminder for companies like Novavax, which, despite having cash on its balance sheet, continues to face financial challenges.

Source: https://www.marketwatch.com/story/biotech-stocks-are-in-a-post-pandemic-slump-and-recovery-in-2024-is-questionable-344e8e9f

Number of Negative Enterprise Value Life Sciences Companies Rose to 223 in Last Week



Source: CapitalIQ

The count of negative EV life sciences companies worldwide rose from 214 a week ago to 223 last Friday. There has been only one week with as many companies with negative EV on this chart (Oct 21, 2022).

Public Life Sciences Sector Value Flat Last Week

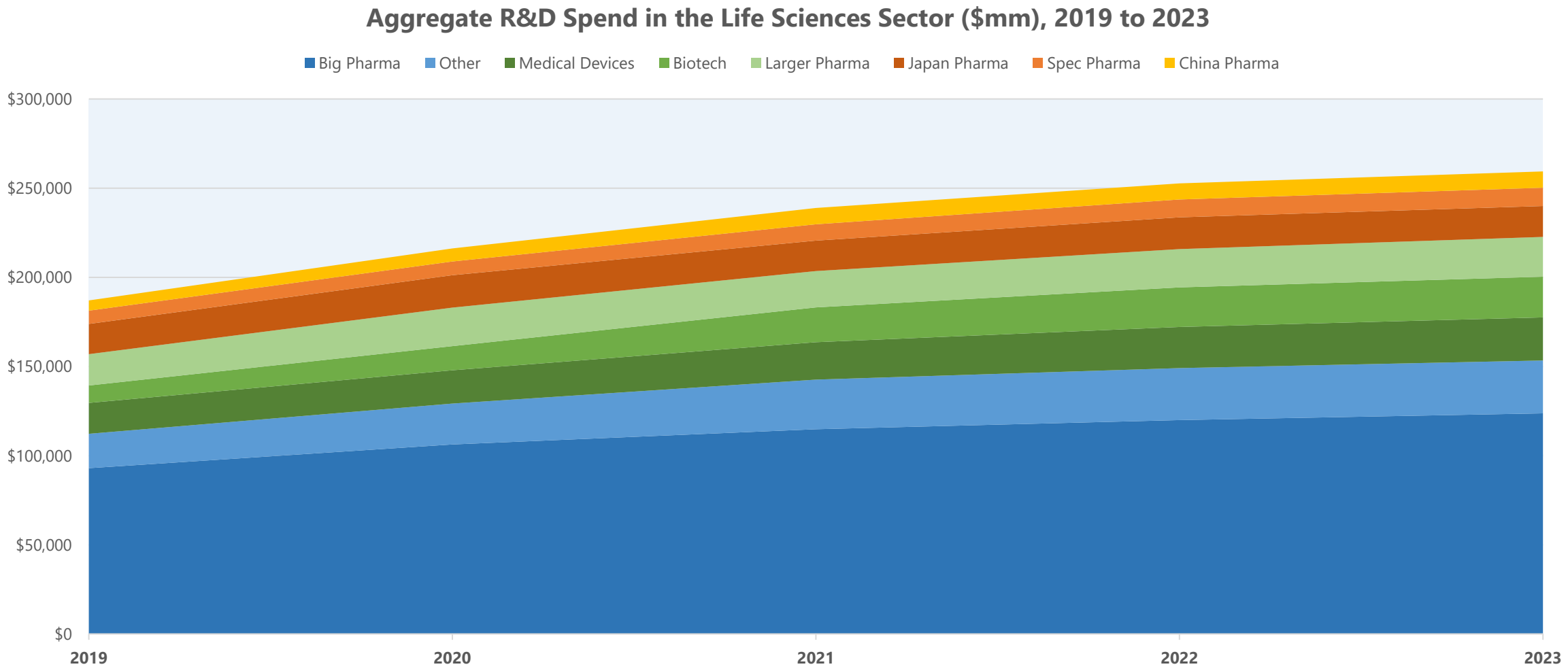
The total enterprise value of the publicly traded life sciences sector was down last week by 2.8% (-$247 billion). The sectors that were hardest hit include CDMO's, biotech, pharma services and API.

Sector	Firm Count	Enterprise Value (Oct 20, 2023, $millions)	Change in Last Week (percent)	Change in Last Month (percent)	Change in Last Year (percent)
API	81	$76,892	-5.5%	-3.1%	-6.3%
Biotech	814	$154,799	-6.1%	-13.3%	-5.1%
CDMO	40	$147,340	-8.0%	-5.3%	-11.0%
Diagnostics	83	$221,847	-0.1%	-3.5%	1.1%
OTC	31	$27,678	-1.2%	-7.2%	-4.2%
Pharma	723	$5,627,299	-3.2%	-2.5%	6.3%
Services	40	$190,326	-6.0%	-3.2%	8.7%
Tools	53	$606,760	-2.2%	-9.3%	-12.6%
Devices	181	$1,444,497	-0.2%	-5.7%	-1.3%
HCIT	11	$22,187	-3.2%	1.5%	0.8%
Total	**2057**	**$8,522,905**	**-2.8%**	**-3.9%**	**2.4%**

Source: CapitalIQ

R&D Spending Trends in Life Sciences, 2019 to 2023

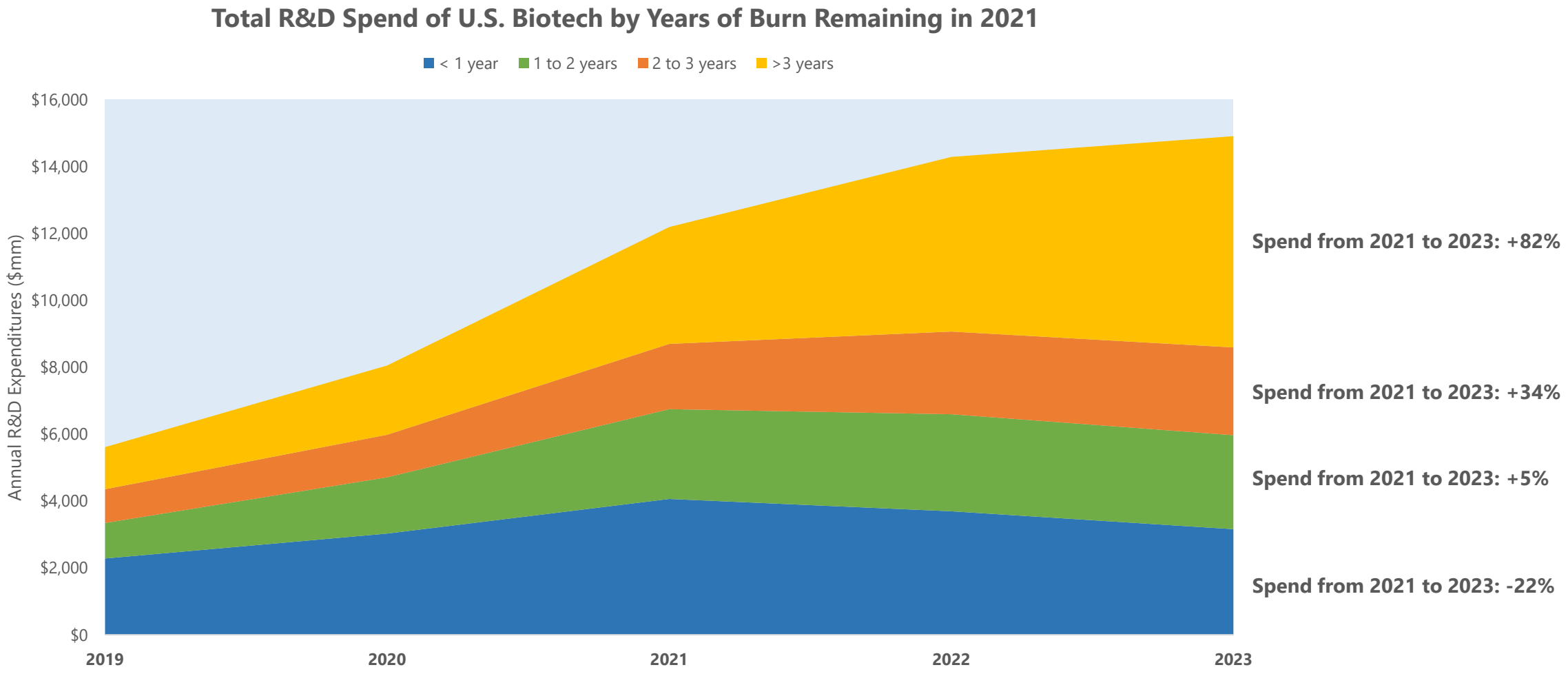
Growth in total R&D spend of the public life sciences sector has slowed from 15.6% per annum between 2020 and 2019 to 2.7% over the last 12 months. Big pharma accounts for roughly half of all R&D spending in the sector.



Source: CapitalIQ

How Has Biotech R&D Changed Since 2019?

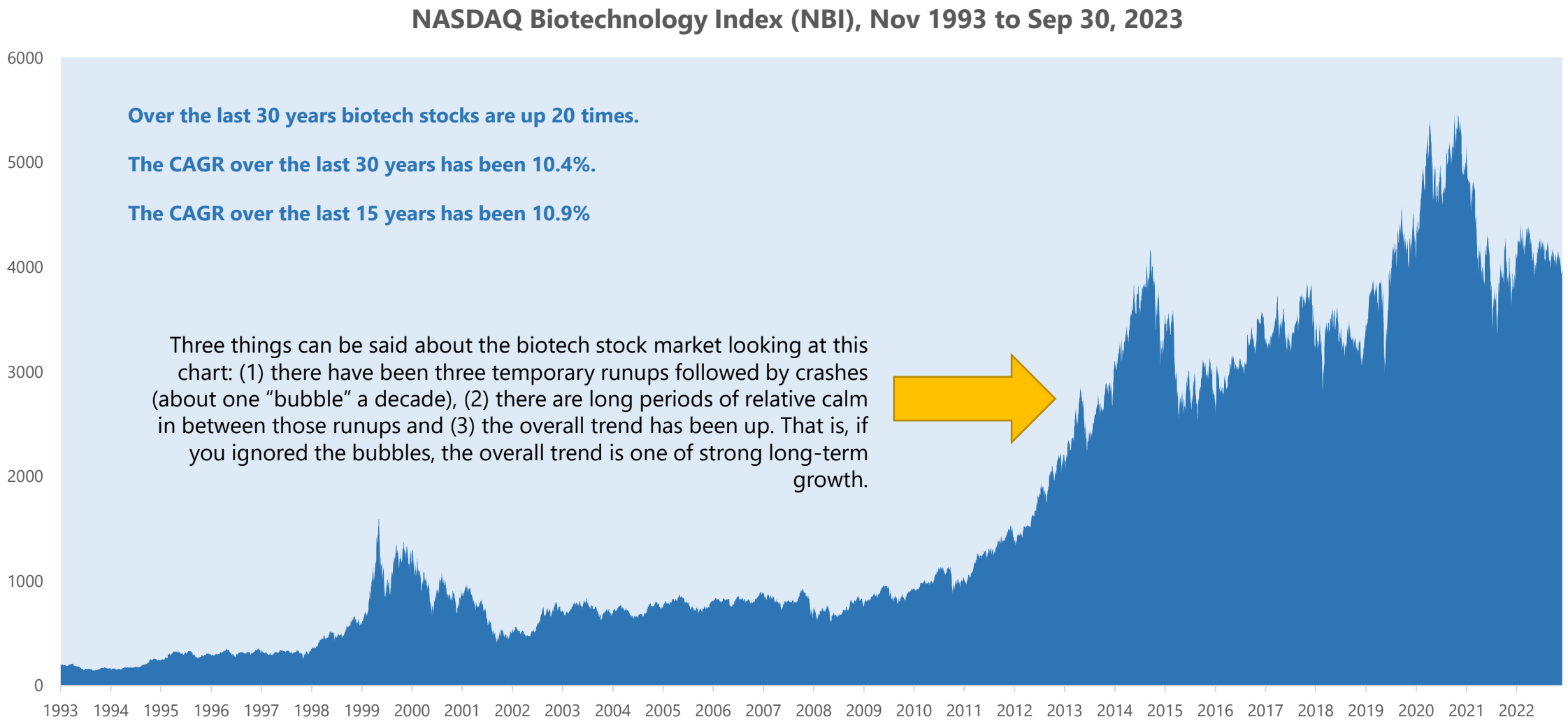
Growth in total R&D spend of U.S. listed biotech companies is slowing down in 2023 substantially versus prior years. Most of the slowdown is confined to companies that had low years of burn remaining in cash in 2021.



Source: CapitalIQ

Fundamental Reason for Optimism:

Biotech Up Big in Long Run



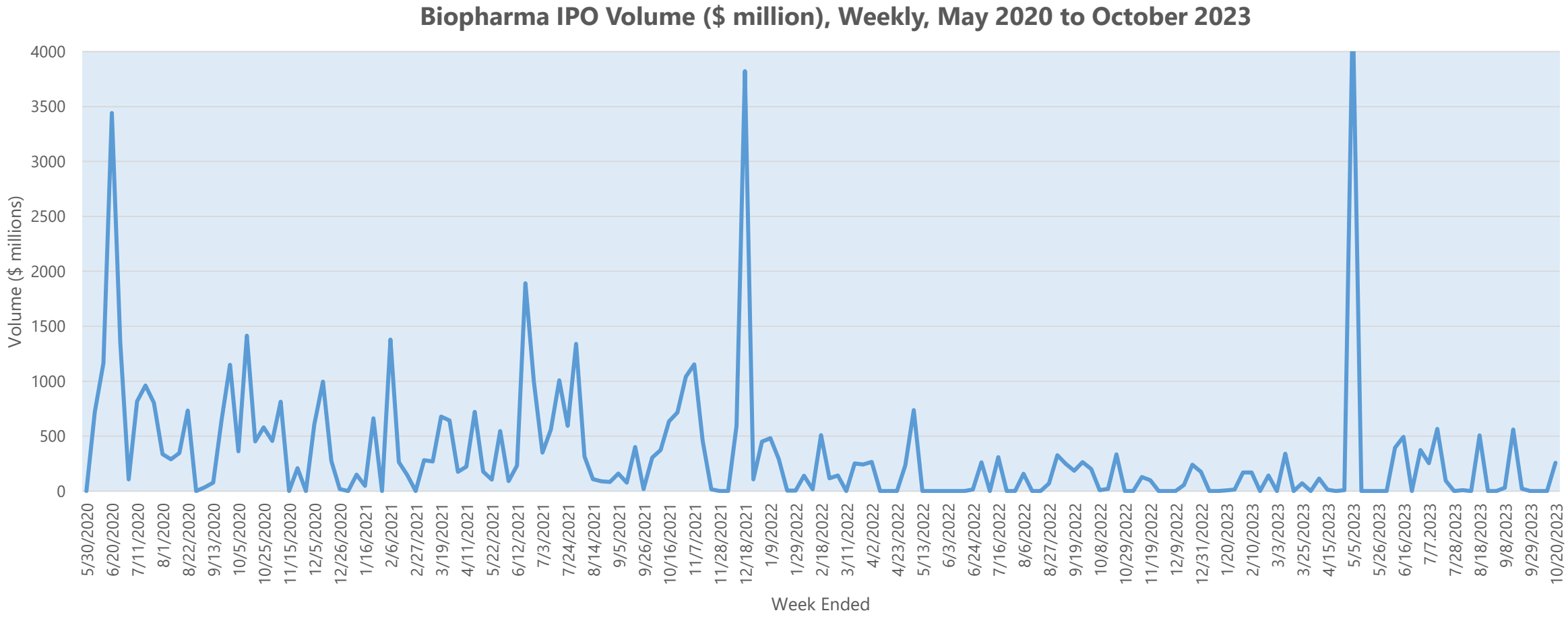
Source: CapitalIQ

Capital Markets Environment

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

IPO Market Saw One Transaction Last Week

There was a $10.6mm IPO on the Japan exchanges last week by K Pharma and a $236mm U.S. Listing by Abivax on the Nasdaq. Abivax was already listed in Europe.



Source: Data from CapitalIQ and Stifel research.

Abivax Prices €223mm Offering on Friday with U.S. Listing

PARIS, France, October 20, 2023 – 3:00 p.m. (CEST) – Abivax SA (Euronext Paris: FR0012333284 – ABVX) ("**Abivax**" or the "**Company**"), a clinical-stage biotechnology company focused on developing therapeutics that harness the body's natural regulatory mechanisms to modulate the immune response in patients with chronic inflammatory diseases, announced today the pricing of its initial public offering on the Nasdaq Global Market by way of a capital increase of 20,325,500 new ordinary shares (the "**New Shares**"), consisting of a public offering of 18,699,460 ordinary shares in the form of American Depositary Shares ("**ADSs**"), each representing the right to receive one ordinary share, in the United States (the "**U.S. Offering**") and a concurrent offering of 1,626,040 ordinary shares in certain jurisdictions outside of the United States to certain investors (the "**European Private Placement**" and together with the U.S. Offering, the "**Global Offering**"). The offering price was set at $11.60 per ADS in the U.S. Offering and a corresponding offering price of €10.9864 per ordinary share based on an exchange rate of €1.00 = $1.0559 as published by the European Central Bank on October 19, 2023. The aggregate gross proceeds are expected to be approximately $235.8 million, equivalent to approximately €223.3 million, before deduction of underwriting commissions and estimated expenses payable by the Company. The Global Offering is expected to close on October 24, 2023, subject to the satisfaction of customary closing conditions.

All securities to be sold in the Global Offering will be offered by the Company. The ADSs have been approved for listing on the Nasdaq Global Market and are expected to begin trading on October 20, 2023 under the ticker symbol "ABVX". The Company's ordinary shares are listed on the regulated market of Euronext Paris ("**Euronext Paris**") under the symbol "ABVX".

Source: https://ir.abivax.com/news-releases/news-release-details/abivax-announces-pricing-its-initial-public-offering-nasdaq

ABIVAX

Obefazimod—Abivax's lead drug candidate—is an oral, first-and-only small molecule with a novel mechanism of action that demonstrates enhanced expression of miR-124, which plays a critical role in the regulation of the inflammatory response.
Currently, obefazimod is being tested in phase 3 trials for the treatment of adults with moderately to severely active ulcerative colitis (UC). The initiation of these late-stage trials is building upon the success of the obefazimod phase 2 trials, which demonstrated an onset of symptom relief by day 8 of dosing, with meaningful reductions in rectal bleeding and stool frequency scores.
Abivax is also initiating a phase 2a clinical trial for obefazimod in Crohn's disease (CD) in Q1 2024.

Weak Debut for Abivax

Colin Kellaher, MarketWatch, Oct 20, 2023

American depositary shares of Abivax tumbled in their trading debut Friday after the Paris-based clinical-stage biotechnology company's U.S. initial public offering was priced at the bottom of expectations.

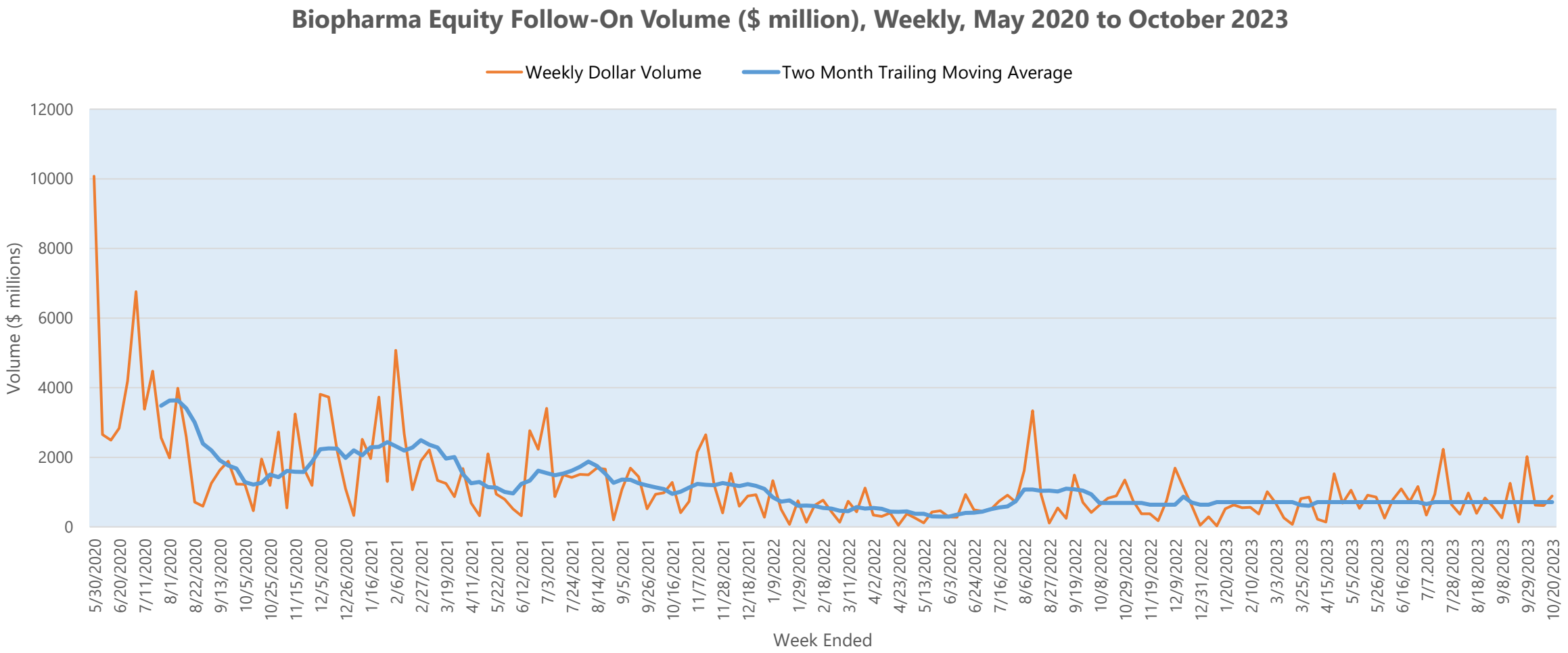
Abivax sold nearly 18.7 million ADSs at $11.60 apiece in the IPO, compared with an expected price range of $11.60 to $13.

Abivax ADSs were recently changing hands at $9.99, down nearly 14%, after opening at $11.60. They closed Friday at $8.30 (down 28.4%).

Source: https://www.marketwatch.com/story/abivax-adss-slide-in-trading-debut-after-u-s-ipo-priced-at-low-end-8b10355d

Last Week Was Solid for Follow-On Offerings

Last week saw $891 million in follow-on equity volume. The largest transactions were $300mm raises by Nuvalent and Ultragenyx.



Source: Data from CapitalIQ and Stifel research.

Nuvalent Announces Pricing of $300 Million Offering of Common Stock

CAMBRIDGE, Mass., Oct. 16, 2023 /PRNewswire/ -- Nuvalent, Inc. (Nasdaq: NUVL), a clinical-stage biopharmaceutical company focused on creating precisely targeted therapies for clinically proven kinase targets in cancer, today announced the pricing of its previously announced underwritten public offering of 5,357,143 shares of Class A common stock at a price to the public of $56.00 per share. All shares are being offered by Nuvalent. The gross proceeds to Nuvalent from the offering, before deducting underwriting discounts, commissions and other offering expenses, are expected to be approximately $300.0 million. The offering is expected to close on October 19, 2023, subject to the satisfaction of customary closing conditions. In addition, the underwriters have a 30-day option to purchase up to an additional 803,571 shares of Class A common stock at the public offering price less underwriting discounts and commissions.

Source: https://www.prnewswire.com/news-releases/nuvalent-announces-pricing-of-public-offering-of-common-stock-301958188.html

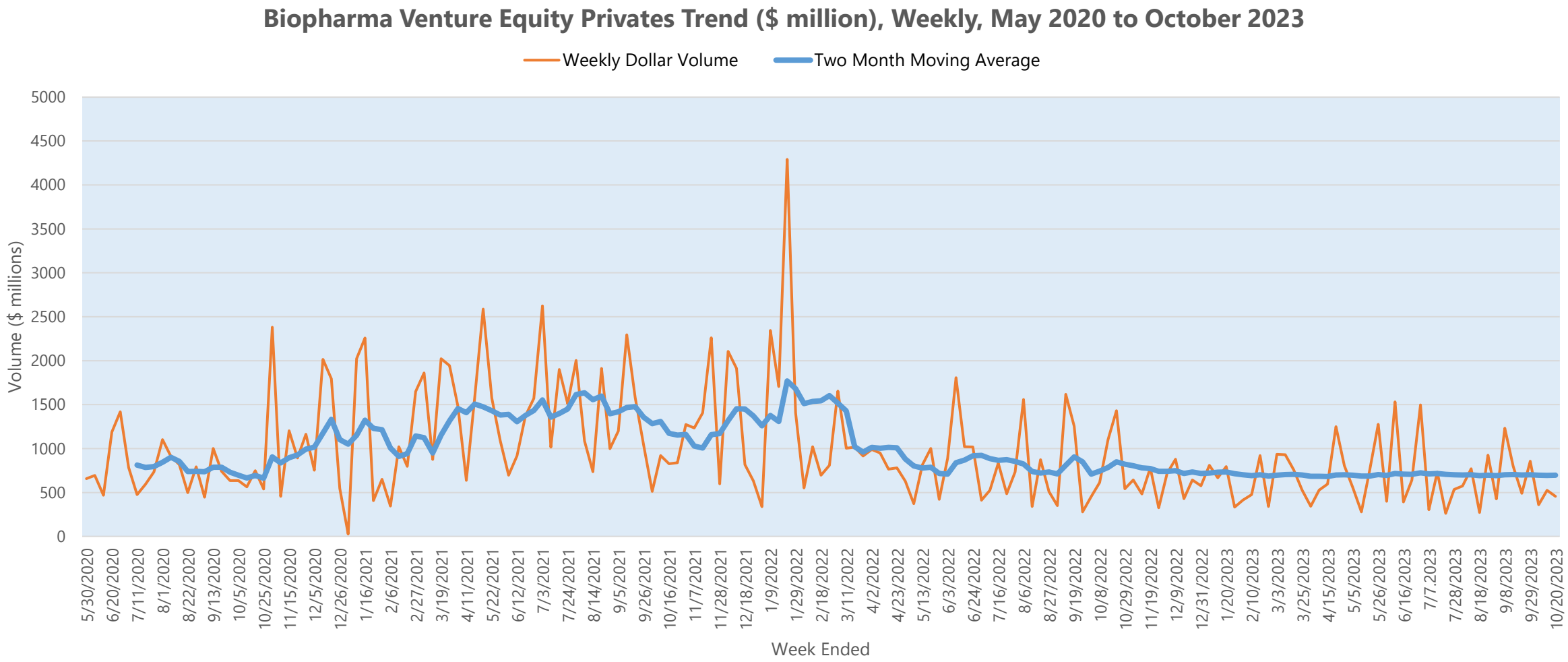
Ultragenyx Announces Pricing of $300 Million Offering of Common Stock

NOVATO, Calif., Oct. 18, 2023 (GLOBE NEWSWIRE) -- Ultragenyx Pharmaceutical Inc. (NASDAQ: RARE), a biopharmaceutical company focused on the development and commercialization of novel therapies for rare and ultrarare diseases, today announced the pricing of its underwritten public offering of 8,333,334 shares of its common stock at a price to the public of $30.00 per share. In addition, in lieu of issuing common stock to certain investors, the company is offering pre-funded warrants to purchase 1,666,722 shares of its common stock at a purchase price of $29.999 per pre-funded warrant, which equals the public offering price per share of the common stock less the $0.001 exercise price per share of each pre-funded warrant. The aggregate gross proceeds to the company from this offering is expected to be $300 million, before deducting underwriting discounts and commissions and other offering expenses, and excluding the exercise of any pre-funded warrants. In addition, the company has granted the underwriters of the offering an option for a period of 30 days to purchase up to an additional 1,500,000 shares of the company's common stock at the public offering price, less the underwriting discount.

Source: https://ir.ultragenyx.com/news-releases/news-release-details/ultragenyx-announces-pricing-public-offering-common-stock-and

Venture Equity Market Quiet Last Week

Last week saw 33 companies raise $457 million in the venture equity market. The largest deal in the market was an $83mm raise by Atom Bioscience.



Source: Data from CapitalIQ, Crunchbase.

Atom Bioscience Raises $83M in a D-Round Financing to Support Global Pivotal Clinical Trials of ABP-671 For Gout

JIANGSU, China–October 16, 2023-- Atom Bioscience (Jiangsu Atom Bioscience and Pharmaceutical Co., Ltd.), a clinical stage biotechnology company developing best-in-class treatments for inflammatory and metabolic diseases, announced today completion of a D-round financing of approximately $83 million (CNY 600 million) for completion of global pivotal clinical trials of ABP-671, its unique orally administered URAT1 inhibitor for chronic gout. The funds also will be used to advance to clinical stage the company's innovative pipeline of drugs for inflammatory and metabolic diseases. This round of financing includes new and existing investors and was led by Kaitai Capital. Other investors include Fortune Capital, Huajin Investment, Unifortune and NNFE Investment. After this round of financing, Atom has raised a total of nearly $165 million.

"We appreciate the support of every investment institution involved in the D-round financing and previous investors," said Dr. William Dongfang Shi, CEO, Chairman and Founder of Atom Bioscience. "We are honored to have their trust as we strive to promote innovative best-in-class drugs benefiting gout patients worldwide."

Source: https://atombp.us/2023/10/16/atom-bioscience-raises-83m-in-a-d-round-financing-to-support-global-pivotal-clinical-trials-of-abp-671-a-new-treatment-for-chronic-gout/

KKR Buys Minority Stake in Life Sciences Investor Catalio Capital

Brian Gormley, *Wall Street Journal*, October 17, 2023 (excerpt)

KKR has acquired a minority stake in Catalio Capital Management, a firm that manages venture-capital and other medical-investment funds, adding to a trend of private-equity firms moving upstream in life sciences through deals with earlier-stage investors.

Private-equity firms are increasingly recognizing opportunities emerging in life sciences fields such as biotechnology that the Covid-19 pandemic has highlighted. By backing firms experienced in earlier-stage investments, they aim to capture a greater proportion of the market opportunity.

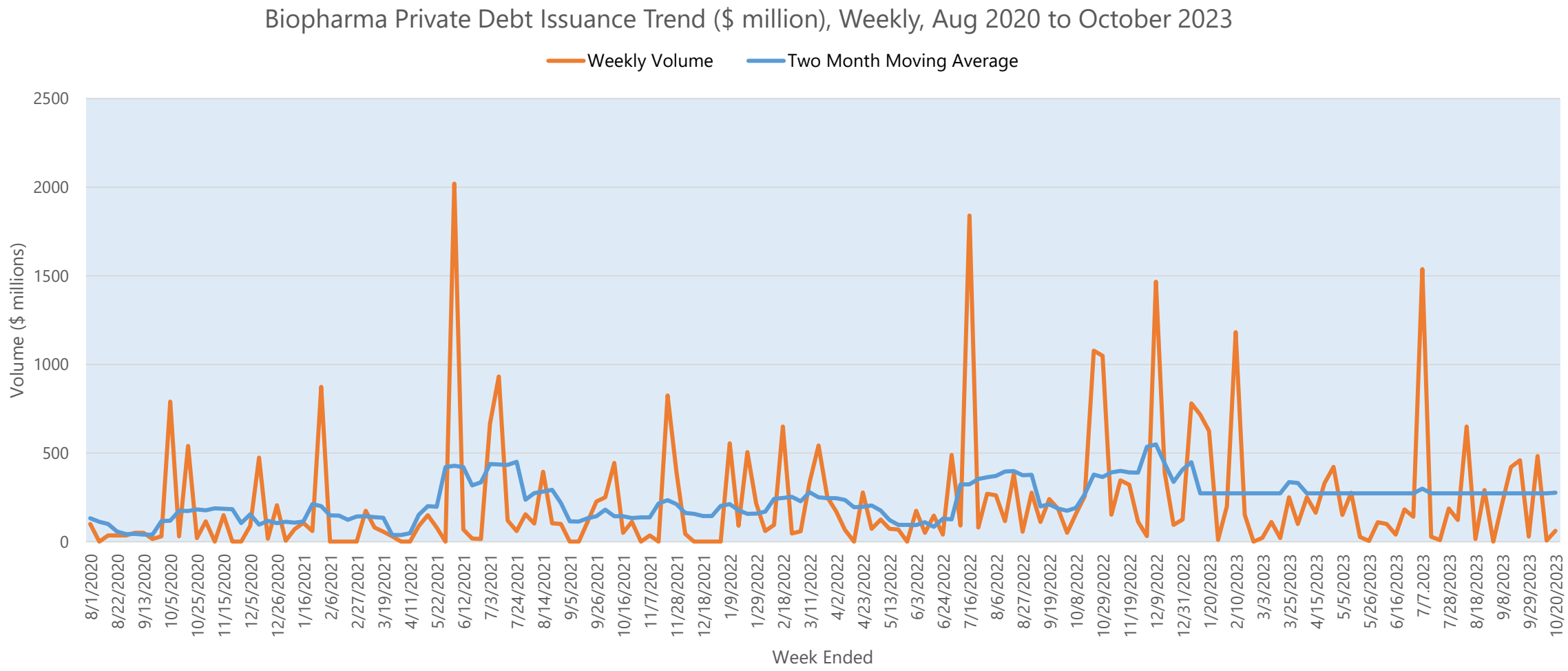
Venture investors, for their part, seek access to deeper-pocketed investors who can help portfolio companies scale.

"There's a realization that the life sciences opportunity is real, it's tangible," said Ali Satvat, a partner and head of healthcare strategic growth for New York-based KKR.

Source: https://www.wsj.com/articles/kkr-buys-minority-stake-in-life-sciences-investor-catalio-capital-e4ee84e

Weekly Global Biopharma Private Debt Placements

We saw two deals in the private debt market last week with $61 million raised. It was a quiet week on the debt front.



Source: Data from CapitalIQ, Crunchbase.

AVITA Secures up to $90 Million of Debt with OrbiMed to Support Growth Initiatives

VALENCIA, Calif., Oct. 18, 2023 (GLOBE NEWSWIRE) - AVITA Medical, Inc. (NASDAQ: RCEL, ASX: AVH) (the "Company"), a regenerative medicine company leading the development and commercialization of first-in-class devices and autologous cellular therapies for skin restoration, today announced third quarter 2023 financial highlights and the closing of a debt financing facility for up to $90 million with OrbiMed, a healthcare investment firm. The non-dilutive capital provides financial flexibility to support portfolio expansion, global initiatives, and the further development and commercialization of approved indications.

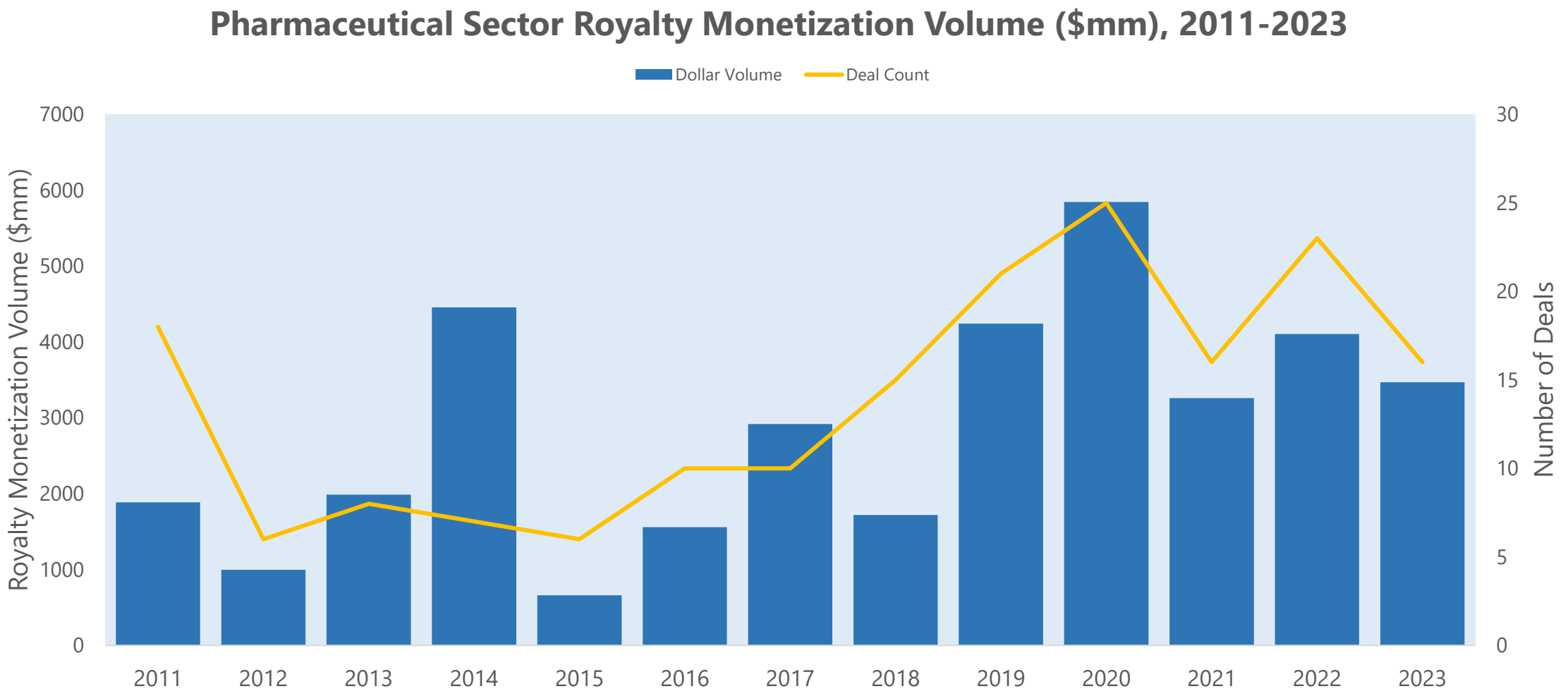
Under the terms of the Credit Agreement (the "Credit Agreement") with OrbiMed, the Company borrowed $40 million at closing. In addition, an aggregate of an additional $50 million is available in two tranches at the Company's option, based on the achievement of certain revenue thresholds. The Credit Agreement has a five-year term that matures in October 2028. AVITA Medical also issued OrbiMed a warrant to purchase 409,661 shares of the Company's common stock, with an exercise price of $10.9847.

"After another strong quarter, we are excited to be partnering with OrbiMed," said Jim Corbett, Chief Executive Officer of AVITA Medical. "This transaction provides us with the capital to execute strategic growth initiatives as we continue to transform our business. We believe this financing provides us with sufficient capital to meet our goals without the near-term need of equity financing and positions us to reach profitability during 2025."

Matthew Rizzo, General Partner of OrbiMed, added, "We are excited to support AVITA Medical as they pursue their strategic objectives, providing them with the necessary capital for financial flexibility, enabling future portfolio expansion, global initiatives, and the continued advancement and commercialization of their approved indications, solidifying their position as a leader in regenerative medicine."

Source: https://ir.avitamedical.com/news-releases/news-release-details/avita-medical-announces-preliminary-third-quarter-2023-financial

Royalty Monetization Volume This Year To Date is In Line with the Last Five Years



PTC Therapeutics Announces Evrysdi® Royalty Agreement with Royalty Pharma for Up To $1.5 Billion

SOUTH PLAINFIELD, N.J., Oct. 19, 2023 /PRNewswire/ - PTC Therapeutics, Inc. (NASDAQ: PTCT) today announced an agreement with Royalty Pharma plc. to monetize up to $1.5 billion of the Evrysdi royalty stream. Under the agreement, Royalty Pharma acquires additional royalties on Evrysdi for $1.0 billion upfront. The agreement includes options for PTC to sell up to all of its retained royalties on Evrysdi for up to $500 million or for Royalty Pharma to acquire half of such retained royalties for up to $250 million at a later date. PTC maintains all economics associated with up to $250 million in remaining commercial sales milestones associated with Evrysdi global net sales.

This agreement builds on the previous strategic partnership established with Royalty Pharma in 2020. The initial agreement was for the monetization of approximately 43% of the Evrysdi royalty stream for $650 million. As a result of the current agreement, PTC will maintain ownership of approximately 19% of the Evrysdi royalty stream pending any exercise of future options by PTC or Royalty Pharma.

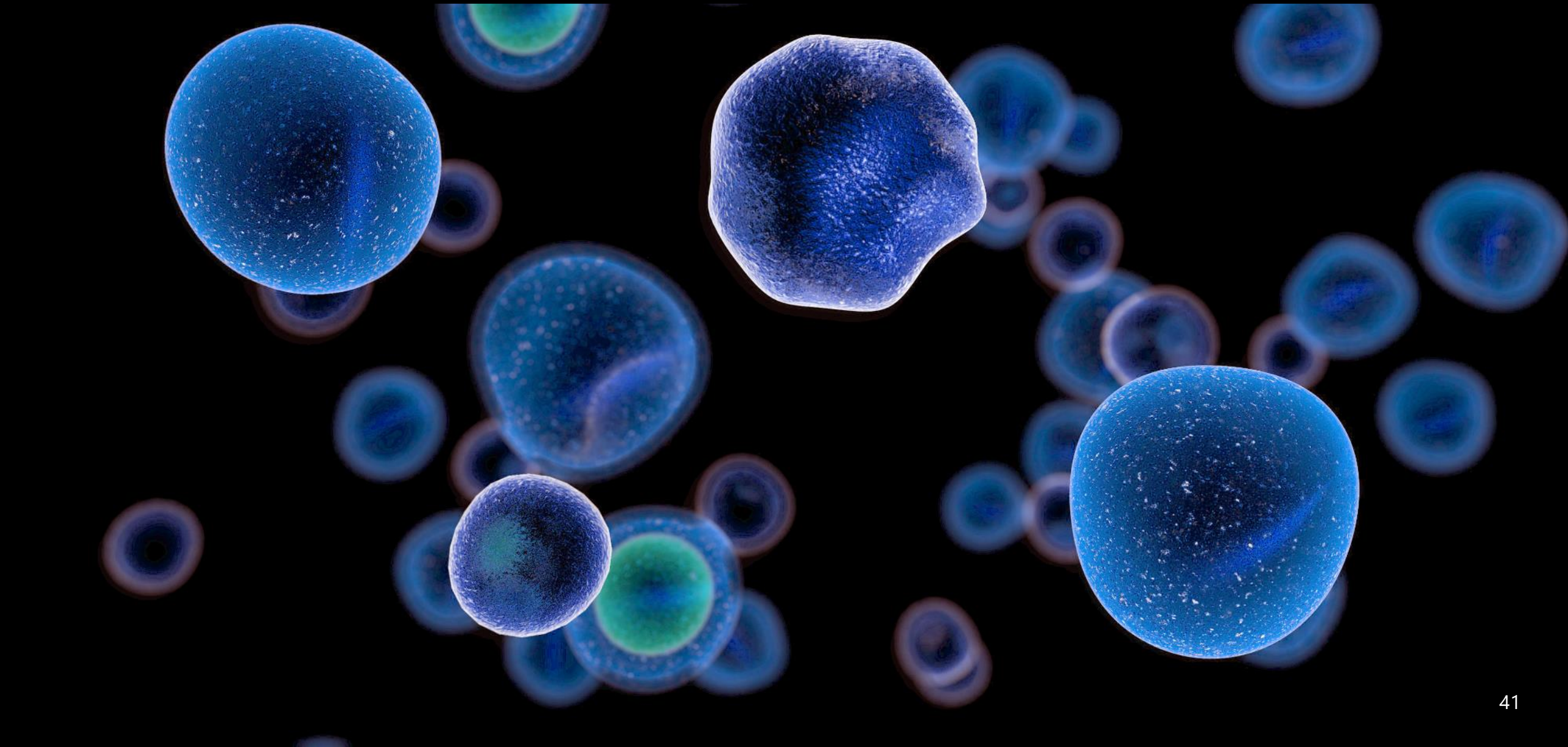
The proceeds from the financing will be used to retire all outstanding debt obligations with Blackstone Life Sciences and to fund planned operations.

"We are pleased to expand our existing strategic partnership with Royalty Pharma," said Matthew B. Klein, M.D., Chief Executive Officer, PTC Therapeutics. "This non-dilutive financing provides PTC with the capital to support operations and allows for increased operational and financial flexibility by removing the Blackstone debt obligation from our balance sheet. In addition, the deal structure provides important flexibility for additional non-dilutive capital over the next two years."

Evrysdi is a survival motor neuron 2 (SMN2) splicing modifier designed to treat SMA

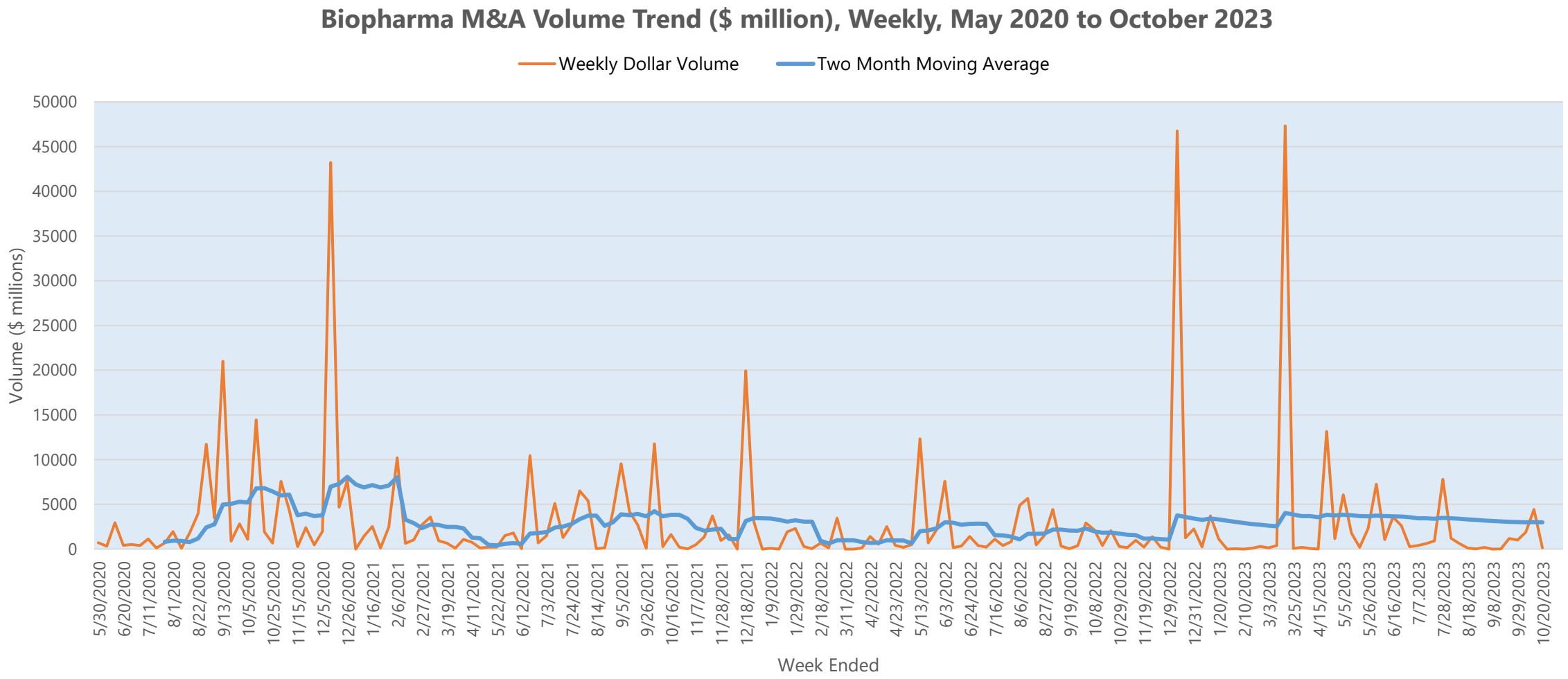
Source: https://ir.ptcbio.com/news-releases/news-release-details/ptc-therapeutics-announces-evrysdir-royalty-agreement-royalty

Biopharma Strategic Deals Environment



M&A Market Quiet Last Week

Last week saw $143 million in M&A deals announce across six deals. The largest was an acquisition of Yingu Pharma in China and an unsolicited offer by Concentra to acquire Rain Oncology.



Source: S&P, CapitalIQ

Rain Oncology Confirms Receipt of Unsolicited Proposal from Concentra Biosciences

NEWARK, Calif., October 16, 2023 – Rain Oncology, Inc. (NasdaqGS: RAIN) ("Rain") confirmed that it has received an unsolicited proposal from Tang Capital, LP on behalf of Concentra Biosciences LLC to acquire all outstanding shares of common stock of Rain for $1.25 per share in cash, plus a contingent value right ("CVR") representing the right to receive 80% of the net proceeds payable from any license or disposition of Rain's programs.

Rain's Board of Directors and management team regularly review opportunities to generate stockholder value and are committed to acting in the best interests of all stockholders.

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

Rain's stockholders are advised to take no action at this time.

Source: https://www.rainoncology.com/news-press-releases/rain-oncology-confirms-receipt-of-unsolicited-proposal-from-concentra-biosciences

Lilly makes another ADC play, buying Mablink

Pharmaphorum, Phil Taylor, October 19, 2023 – Eli Lilly has agreed a deal to acquire French antibody-drug conjugate (ADC) specialist Mablink, continuing a series of transactions that build its position in what has become one of the fastest-growing therapeutic classes in oncology.

ADCs consist of an antibody targeting an antigen on cancer cells joined to a cytotoxic drug molecule, and are designed to boost the efficacy against tumours, whilst reducing off-target side effects.

Lyon-based Mablink is developing ADCs based on a proprietary linker technology, called PSARLink, which is designed to mask the cytotoxic payload carried by the drug molecules, reducing the chances that it will be released early.

The PSARLink molecule cordons off hydrophobic areas of cytotoxic drugs that can affect the properties of the antibody carrier, thereby preventing the drug molecule from breaking apart prematurely and causing toxicity, something that plagued the development of early ADC candidates.

Mablink's ADCs have shown a higher therapeutic index in animal models, according to the company. Preclinical results with its lead candidate MBK-103, targeting the folate alpha receptor (FOLR1), were reported at the American Association of Cancer Research (AACR) meeting in March.

The financial terms of the deal are not being disclosed, and it still needs to be approved by France's Ministry of the Economy before it can go ahead.

Source: https://pharmaphorum.com/news/lilly-makes-another-adc-play-buying-mablink

European Commission Approves Acquisition of Seagen by Pfizer

October 19, 2023: The European Commission has unconditionally approved the proposed acquisition of Seagen by Pfizer, under the EU Merger Regulation. The Commission concluded that the transaction would not raise competition concerns in the European Economic Area ('EEA'). Seagen and Pfizer are pharmaceutical companies. Seagen specialises in oncology therapies, primarily in antibody drug conjugates ('ADCs'). Pfizer's oncology portfolio largely consists of hormone therapies, immunotherapies, and targeted therapies.

In the EEA, the companies' marketed and pipeline products overlap in the treatment of several cancer types such as breast, bladder, colorectal, cervical and lung cancer, as well as in lymphoma and leukaemia. By acquiring Seagen's ADCs technology, Pfizer wishes to diversify its portfolio and accelerate the development and commercialisation of Seagen's ADCs drugs.

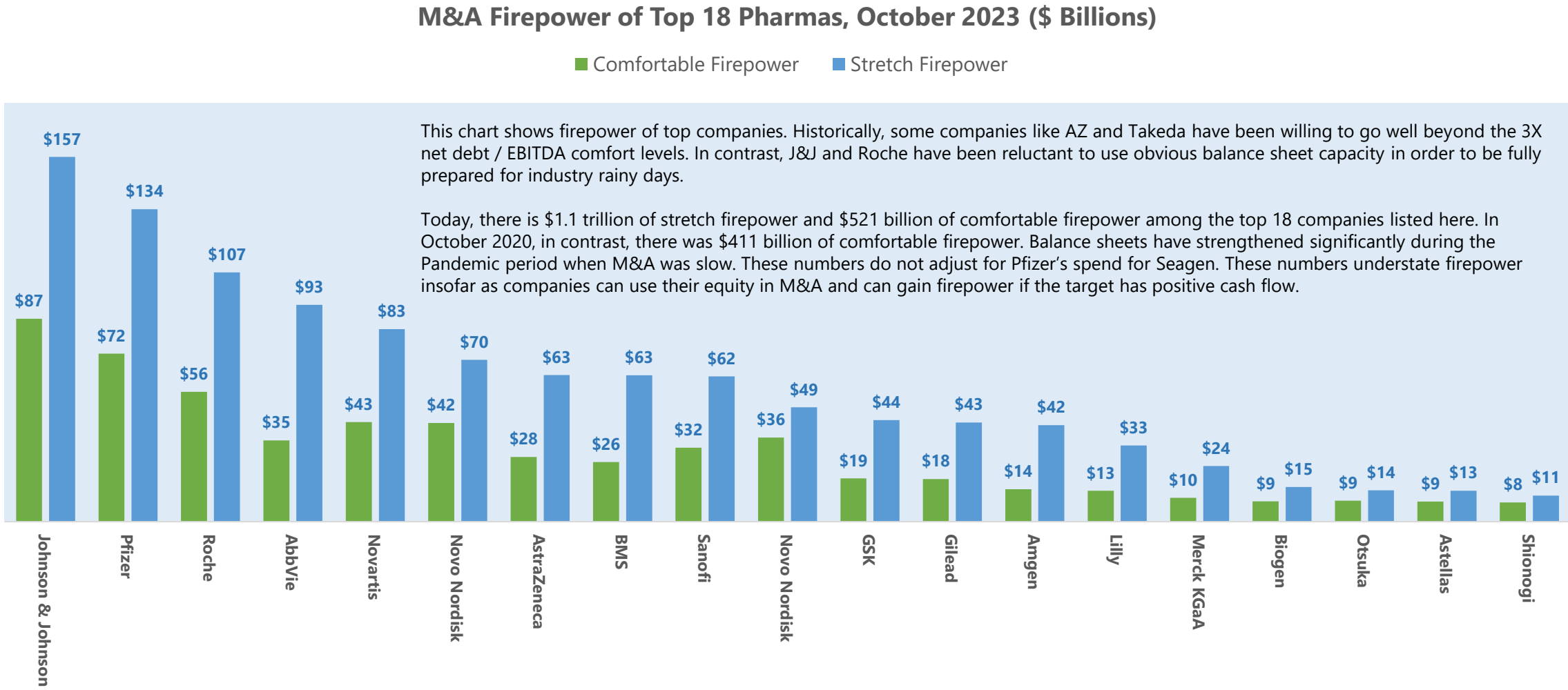
Based on its market investigation, the Commission found that the merger would not significantly reduce competition in the markets where their activities overlap within the EEA. In particular, the Commission focused its investigation on potential competition between the parties' marketed and pipeline products, and it found that the transaction would not lead to either the:

1. discontinuation, delay or re-orientation of the parties' ongoing and overlapping lines of research or pipeline projects. The parties' activities target different segments of patients, and they are not substitutable since they do not have the same mode of action and concern different lines of treatment; or
2. loss of innovation resulting from a structural reduction of the overall level of innovation, given that there is a significant number of players engaged in research & development activities in the broader oncology space and, more specifically, in ADCs, an area in which Pfizer wishes to grow.
3. Moreover, the Commission found that the transaction was unlikely to have negative impact on prices, given that the parties' offerings are differentiated and complementary and that the markets for the treatment of the various cancer types examined are sufficiently competitive.

Source: https://ec.europa.eu/commission/presscorner/detail/en/ip_23_5123

Over $500 Billion of M&A Firepower at Top 18 Pharmas

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



Source: S&P, CapitalIQ

Andrew Pannu: Pharma Using M&A and R&D to Replace Upcoming Patent Expiries

How is Pharma replacing LOEs?

Company	Core Focus Today	Key LOEs (TA)	$M Size of LOEs	R&D Focus by TA	Recent >$1B M&A
Lilly	CVMB, Oncology	Cyramza (Oncology), Trulicity (CVMB), Jardiance (CVMB)	$12,000	CVMB, Oncology	Dice Therapeutics (Immunology - $2.4B)
novo nordisk	CVMB	Victoza (CVMB)	$3,000	CVMB	N/A
Johnson&Johnson	I&I, Oncology	Stelara (I&I), Xarelto (Hematology), Imbruvica (Oncology), Opsumit (CV), Prezista (ID)	$22,250	Oncology, I&I	N/A
abbvie	I&I, Oncology, Aesthetics	Humira (I&I), Imbruvica (Oncology)	$27,000	Oncology	N/A
MERCK	Oncology	Keytruda (Oncology), Gardasil / Gardasil 9 (Vaccines), Januvia / Janumet (CVMB)	$40,000	Oncology	Prometheus Biosciences (Immunology - $10.8B), Imago Biosciences (Hematology - $1.0B)
Roche	Oncology, Neuro, I&I	Perjeta (Oncology), Tecentriq (Oncology)	$10,500	Oncology, Neuroscience	N/A
NOVARTIS	I&I, CVMB, Hematology	Glineya (Neuro), Entresto (CVMB), Promacta (Hematology)	$10,000	Oncology, I&I	Chinook Therapeutics (Rare Disease - $3.2B)
AstraZeneca	Oncology, CVRM	Brilinta (CVMB), Soliris (Rare Disease)	$4,100	Oncology, I&I, CVMB	CinCor Pharma (CVMB - $1.8B), TeneoTwo (Oncology - $1.3B)
AMGEN	I&I	Prolia / Xjeva (Bone), Otezla (I&I), Krypolis (Oncology), Aranesp (CVRM)	$12,000	Oncology, I&I	Horizon Therapeutics (Immunology - $26.9B), ChemoCentryx (Immunology - $3.5B)
Pfizer	COVID, Hematology, Oncology, I&I	Prevnar / Prevenar 13 (Vaccines), Xeljanz (I&I), Eliquis (Hematology), Inlyta (Oncology), Xtandi (Oncology), Ibrance (Oncology)	$27,700	Oncology, Vaccines	SeaGen (Oncology - $43.0B), Biohaven (CNS - $11.0B), Global Blood Therapeutics (Hematology / Rare Disease - $4.7B)
SANOFI	I&I, Vaccines, Rare Disease	N/A	N/A	Oncology, I&I	Provention Bio (CVMB - $2.9B)
Bristol Myers Squibb	Hematology, Oncology	Yervoy (Oncology), Pomalyst (Oncology), Eliquis (Hematology), Opdivo (Oncology)	$26,000	Oncology	Turning Point Therapeutics (Oncology - $2.9B)

Andrew Pannu @andrewpannu

Source: https://andrewpannu.com/

Daiichi Sankyo and Merck Collaboration for Three ADCs

BASKING RIDGE, N.J. & RAHWAY, N.J., October 19, 2023: Daiichi Sankyo (TSE: 4568) and Merck (known as MSD outside of the United States and Canada) (NYSE: MRK) have entered into a global development and commercialization agreement for three of Daiichi Sankyo's DXd antibody-drug conjugate (ADC) candidates: patritumab deruxtecan (HER3-DXd), ifinatamab deruxtecan (I-DXd) and raludotatug deruxtecan (R-DXd). The companies will jointly develop and potentially commercialize these ADC candidates worldwide, except in Japan where Daiichi Sankyo will maintain exclusive rights. Daiichi Sankyo will be solely responsible for manufacturing and supply.

All three potentially first-in-class DXd ADCs are in various stages of clinical development for the treatment of multiple solid tumors both as monotherapy and/or in combination with other treatments. Patritumab deruxtecan was granted Breakthrough Therapy Designation by the U.S. Food and Drug Administration in December 2021 for the treatment of patients with EGFR-mutated locally advanced or metastatic non-small cell lung cancer (NSCLC) with disease progression on or after treatment with a third-generation tyrosine kinase inhibitor (TKI) and platinum-based therapies. The submission of a biologics license application (BLA) in the U.S. is planned by the end of March 2024 for patritumab deruxtecan, which is based on data from the HERTHENA-Lung01 Phase 2 trial recently presented at the IASLC 2023 World Conference on Lung Cancer and simultaneously published in the Journal of Clinical Oncology.

Under the terms of the agreement, Merck will pay Daiichi Sankyo upfront payments of $1.5 billion for ifinatamab deruxtecan due upon execution; $1.5 billion for patritumab deruxtecan, where $750 million is due upon execution and $750 million is due after 12 months; and $1.5 billion for raludotatug deruxtecan, where $750 million is due upon execution and $750 million is due after 24 months. Merck also will pay Daiichi Sankyo up to an additional $5.5 billion for each DXd ADC contingent upon the achievement of certain sales milestones. When combined with the additional refundable upfront payment of $1 billion described below, total potential consideration across the three programs is up to $22 billion. Merck may opt out of the collaboration for patritumab deruxtecan and raludotatug deruxtecan and elect not to pay the two continuation payments of $750 million each that are due after 12 months and 24 months, respectively. If Merck opts out of patritumab deruxtecan and/or raludotatug deruxtecan, the upfront payments already paid will be retained by Daiichi Sankyo and rights related to such DXd ADCs will be returned to Daiichi Sankyo. As referenced above, Merck will pay an additional upfront payment of $1 billion ($500 million each for patritumab deruxtecan and ifinatamab deruxtecan), a pro-rated portion of which may be refundable in the event of early termination of development with respect to each program. For raludotatug deruxtecan, Merck will be responsible for 75% of the first $2 billion of R&D expenses.

Source: https://www.merck.com/news/daiichi-sankyo-and-merck-announce-global-development-and-commercialization-collaboration-for-three-daiichi-sankyo-dxd-adcs/

The Largest Licensing Deal Upfronts in History

Last week's Merck Daiichi-Sankyo deal involved the largest upfront seen in a pharma industry licensing deal in history.

Biggest upfront in history

Ann. Date	Licensor	Licensee	Deal Products	Upfront Cash ($mm)	Total Deal Value ($mm)	Primary TA	Stage Signed
10/19/2023	Daiichi Sankyo	Merck & Co. Inc.	Patritumab Dx (HER3); DS-7300; DS-6000	$4,000	$22,000	Cancer	Phase II
07/14/2019	Galapagos N.V.	Gilead Sciences Inc.	Ziritaxestat; GLPG-1972	$3,950	$6,525	Pulmonary	Phase III
06/30/2012	Bristol Myers Squibb Co.	AstraZeneca plc	BYETTA	$3,400	$3,535	Endocrine / Metabolic	Approved
07/27/2017	AstraZeneca plc	Merck & Co. Inc.	LYNPARZA; KOSELUGO	$1,600	$8,500	Cancer	Approved
03/28/2019	Daiichi Sankyo	AstraZeneca plc	CYAD-101+KEYTRUDA	$1,350	$6,900	Cancer	Phase III
07/27/2020	Daiichi Sankyo	AstraZeneca plc	Datopotamab deruxtecan	$1,000	$6,000	Cancer	Phase I
02/13/2018	Nektar Therapeutics	Bristol Myers Squibb	Bempegaldesleukin	$1,000	$3,630	Cancer	Phase I
05/06/2014	Bayer AG	Merck & Co. Inc.	ADEMPAS	$1,000	$2,100	Cardiovascular	Approved
06/02/2022	Sanofi S.A.	Regeneron Pharmaceuticals	LIBTAYO	$900	$1,100	Cancer	Approved
04/20/2021	CRISPR Therapeutics AG	Vertex Pharmaceuticals	Exagamglogene autotemcel	$900	$1,100	Hematologic	Phase II
11/27/2020	Sage Therapeutics Inc.	Biogen Inc.	Zuranalone	$875	$3,125	Neurologic	Phase III
11/17/2014	Merck KGaA	Pfizer Inc.	BAVENCIO	$850	$2,850	Cancer	Phase II
11/15/2018	Arena Pharmaceuticals	United Therapeutics	Ralinepag	$800	$1,200	Cardiovascular	Phase III
06/10/2020	Genmab A/S	AbbVie Inc.	Epcoritamab; GEN-3009; GEN-1044	$750	$3,900	Cancer	Phase I
01/13/2020	MorphoSys AG	Incyte Corp.	MONJUVI, MINJUVI	$750	$2,000	Cancer	Phase III
12/23/2019	Sarepta Therapeutics Inc.	Roche	Delandistrogene moxeparvovec	$750	$2,850	Musculoskeletal	Phase II
04/23/2014	Nogra Pharma Ltd.	Celgene Corp.	Mongersen	$710	$2,575	Autoimmune	Phase II
07/02/2021	Alector Inc.	GSK	GSK-4527223; AL-101	$700	$2,200	Neurologic	Phase II
07/14/2020	Blueprint Medicines	Roche	GAVRETO	$675	$1,702	Cancer	Phase I
07/22/2021	Arvinas LLC	Pfizer Inc.	Vepdegestrant	$650	$2,400	Cancer	Phase II

Source: DealForma

Merck Going All In on ADC's

Jacob Plieth, *Oncology Pipeline*, October 20, 2023 (excerpt)

It seems Merck & Co liked what it saw with Kelun's antibody-drug conjugates, but for its big bet on this modality it's turned to Daiichi Sankyo. Merck picking up three Daiichi ADCs for $5.5bn up front last night represents one of the biggest ever licensing deals in biopharma.

For Daiichi, therefore, ADCs continue to deliver. The Japanese group's first two shots, Enhertu and datopotamab deruxtecan, drew respective $1.4bn and $1bn up-fronts from AstraZeneca, and the three follow-on ADCs Merck has licensed use the same technology. It's worth remembering that Merck wanted to buy Seagen for around $40bn but was outbid by Pfizer, so clearly it's serious about ADCs.

Merck's deal spells out separate terms relating to the three Daiichi ADCs to which it's picking up global ex-Japan rights: patritumab deruxtecan, targeting HER3, raludotatug deruxtecan (CDH6) and ifinatamab deruxtecan (B7-H3).

The immediate up-fronts are $750m, $750m and $1.5bn respectively, followed by a further $750m in 12 months for patritumab and $750m in 24 months for raludotatug. Merck can opt not to pay out this additional $1.5bn, but since the amount appears not to be tied into any specific future milestone it's probably acceptable to include it in the total up-front deal valuation.

The most relevant downstream value, meanwhile, is captured largely as a commitment by Merck to fund R&D. This amounts to the company contributing $500m each to the development of patritumab and ifinatamab, and these amounts are also payable immediately, so technically can also be considered up front. There is also a separate Merck commitment to finance $1.5bn of the first $2bn of raludotatug's development.

Source: https://www.oncologypipeline.com/apexonco/after-failing-get-seagen-merck-turns-daiichi

Daiichi-Sankyo ADC Portfolio

Project	Target	Drug / Antibody Ratio	Key studies/tumours	Deal terms
Enhertu	HER2	8	Approved for HER2+ve breast, NSCLC & gastric cancers, & HER2-low breast cancer	Astra paid $1.35bn up front, $3.8bn due in regulatory and other milestones
Datopotamab deruxtecan (DS-1062)	TROP2	4	Tropion-Lung01 & Tropion-Breast01 data at ESMO 2023	Astra paid $1bn up front, $1bn due in regulatory approval milestones
Patritumab deruxtecan (U3-1402)	HER3	8	Herthena-Lung01 in post-Tagrisso+chemo EGFRm NSCLC	Merck paid $1.5bn up front ($750m of which is subject to decision in 12mths), plus $500m immediate R&D cost
Raludotatug deruxtecan (DS-6000)	CDH6	8	Ph1 in renal & ovarian cancers	Merck paid $1.5bn up front ($750m of which is subject to decision in 24mths)
Ifinatamab deruxtecan (DS-7300)	B7-H3	4	Ideate-01 trial in SCLC	Merck paid $1.5bn up front, plus $500m immediate R&D cost
DS-3939	TA-MUC1	?	Just started ph1/2 in solid tumours	Wholly owned by Daiichi, uses gatipotuzumab MAb licensed from Glycotope
DS-9606	Claudin 6	?	Ph1 in solid tumours	Wholly owned by Daiichi, described as a 2nd-gen ADC

GSK to Pay $85mm Upfront in License Agreement with Hansoh for HS-20089 (B7-H4 ADC)

October 20, 2023: GSK plc (LSE/NYSE: GSK) and Hansoh Pharma (HKEX: 03692), a Chinese biopharmaceutical company committed to discovering and developing life-changing medicines to help patients conquer serious diseases and disorders, today announced that they have entered into an exclusive license agreement for HS-20089, a B7-H4 targeted antibody-drug conjugate (ADC) currently in phase I (NCT05263479) clinical trials in China. Under the agreement, GSK will obtain exclusive worldwide rights (excluding China's mainland, Hong Kong, Macau, and Taiwan) to progress development and commercialisation of HS-20089.

Hesham Abdullah, SVP, Global Head Oncology, R&D, GSK, said: "Given early clinical data, we believe that HS-20089 has best-in-class potential in ovarian and endometrial cancer with opportunities in other solid tumours. This agreement is in line with our approach to advancing novel treatment options for patients with gynaecologic cancers."

In addition to targeting the B7-H4 surface antigen, which is overexpressed in ovarian and endometrial cancers and is often associated with poor prognosis, HS-20089 utilises clinically validated ADC technologies such as a topoisomerase inhibitor (TOPOi) payload.1 TOPOi is a validated mechanism of action in approved anti-cancer medicines and a proven standard of care in the treatment of breast and ovarian cancers.

Eliza Sun, Executive Director of Board, Hansoh Pharma, said: "In line with our commitment to deliver first- or best-in-class medicines to address unmet medical needs, Hansoh is excited to explore further development of HS-20089 to bring breakthrough medicines to cancer patients. GSK's R&D expertise and commercial footprint in developing therapies for gynaecologic cancers make them the ideal licensee to bring HS-20089 to patients outside of China."

Under the terms of this agreement, GSK will pay an $85 million upfront payment. In addition, Hansoh will be eligible to receive up to $1.485 billion in success-based milestones for HS-20089. Upon commercialisation of HS-20089, GSK will also pay tiered royalties on global net sales outside of China's mainland, Hong Kong, Macau, and Taiwan.

Source: https://www.gsk.com/en-gb/media/press-releases/gsk-enters-exclusive-license-agreement-with-hansoh-for-hs-20089/

ESMO 2023 – GSK sets up Pfizer battle in B7-H4

Madeleine Armstrong, *Oncology Pipeline*, October 21, 2023

The first day of ESMO saw one huge ADC-focused deal – plus another one not so huge. GSK's licensing of Hansoh Pharma's B7-H4-targeted asset HS-20089 yesterday might have been overshadowed by Merck & Co's tie-up with Daiichi Sankyo, but the UK group's new project had a chance to shine today.

Early data with HS-20089 in late-line triple-negative breast cancer look promising, but the project has a long way to go, and it isn't alone in this niche. Notably Seagen, soon to become part of Pfizer, also has a B7-H4-targeted ADC, which will feature at ESMO on Monday.

TNBC focus

Still, the latest results were clearly enough to tempt GSK, which on Friday licensed HS-20089 outside China for $85m up front, and up to $1.5bn in milestones.

The Chinese phase 1 dose-escalation trial of HS-20089 primarily enrolled breast cancer patients, with a focus on TNBC, but it also included a handful of ovarian and endometrial cancers. Across the study, subjects were heavily pretreated, with a mean five prior lines of therapy. Patients were not preselected for B7-H4 expression.

At a cutoff date of 17 August, there was a 29% ORR among 28 evaluable TNBC patients receiving various doses of HS-20089. Focusing on the 4.8mg/kg and 5.8mg/kg doses that are being taken forward, the ORR was 33% in 12 patients and 27% in 11 respectively.

B7-H4 ADCs in clinical development

Project	Company	Paylod	Status	Note
HS-20089	GSK (via Hansoh Pharma)	Topoisomerase inhibitor	Ph1 China study in solid tumours	ESMO 2023: 29% ORR across TNBC pts; 27-33% ORR at target doses
SGN-B7H4V	Seagen (Pfizer)	Monomethyl auristatin E	Ph1 in solid tumours	ESMO 2023 abstract: responses in breast (7/25), ovarian (2/15), endometrial (1/16) & biliary tract (2/9) cancers; full data on Monday
XMT-1660	Mersana Therapeutics	Auristatin hydroxypropylamide	Ph1 in solid tumours	Dose escalation to complete 2023; dose expansion to begin 2024
Puxitatug samrotecan (AZD8205)	AstraZeneca	Topoisomerase inhibitor	Ph1/2 in solid tumours	Data expected >2024

Source: https://www.oncologypipeline.com/apexonco/esmo-2023-gsk-sets-pfizer-battle-b7-h4

Highlights of ADC Deals and Approvals

ADCs are HOT!

ADCs have become one of the most validated and sought-after therapeutic modalities

2019

Mar — AstraZeneca inks $6bn deal with Daiichi Sankyo for HER2 ADC

Jun — POLIVY (polatuzumab vedotin-piiq); CD79B; Genentech

Dec — PADCEV (enfortumab vedotin-ejfv); Nectin-4; Astellas Pharma

2020

Dec — ENHERTU (fam-trastuzumab deruxtecan-nxki); Her2; AZ/Daiichi Sankyo

Apr — TRODELVY (sacituzumab govitecan-hziy); TROP2; Immunomedics; *Accelerated approval*

Aug — BLENREP (belantamab mafodotin-blmf); BCMA; GSK0

Jul — AstraZeneca $6bn deal with Daiichi Sankyo for TROP2 ADC

Sep — Gilead acquires Immunomedics for $21bn

Sep — Merck inks $4.5bn deal with SeaGen

Nov — Merck acquires VelosBio for $2.8bn for ROR1 ADC

Dec — Boehringer acquires NBE-Therapeutics for $1.4bn

2021

Apr — Zynlonta (loncastuximab tesirine-lpyl); CD19; ADC Therapeutics

May — Zydus Cadila markets Ujvira®, the first ADC biosimilar of Roche's (Kadcyla®)

May — Daiichi Sankyo invests $13.8bn in 3 ADC programs

May — BMS acquires anti-FOLR1 ADC for $650m from Elsai

Aug — Seagen signs deal for up to $2.6 bn with RemeGen for HER2 ADC

Asset Purchase: Novo Nordisk to Acquire Ocedurenone for Uncontrolled Hypertension from KBP Biosciences

Bagsværd, Denmark and Singapore, 16 October 2023 – Novo Nordisk A/S and KBP Biosciences PTE., Ltd. today announced that Novo Nordisk has agreed to acquire ocedurenone for uncontrolled hypertension with potential application in cardiovascular and kidney disease from KBP Biosciences for up to 1.3 billion US dollars.

Ocedurenone is an orally administered, small molecule, non-steroidal mineralocorticoid receptor antagonist (nsMRA) that is currently being examined in the phase 3 trial CLARION-CKD in patients with uncontrolled hypertension and advanced chronic kidney disease (CKD). Uncontrolled hypertension is when a person's blood pressure remains high despite taking two or more blood pressure-lowering treatments.

"Hypertension is a leading risk factor for cardiovascular events, heart failure, chronic kidney disease and premature death," said Martin Holst Lange, executive vice president and head of Development at Novo Nordisk. "With its expected benefit-risk profile, ocedurenone has best-in-class potential in treating uncontrolled hypertension and could help address a major unmet medical need in people living with cardiovascular disease and chronic kidney disease."

"We are delighted to pass the ocedurenone torch to Novo Nordisk, a global leader in management of chronic diseases. We believe this transition could unlock the full potential of ocedurenone and benefit more patients with cardiovascular and kidney disease worldwide," said Dr. Zhenhua Huang, founder and chairman of KBP Biosciences. "The transition is an exciting inflection point in the discovery, research and development work on ocedurenone carried out by KBP, a young player still establishing itself in the global pharmaceutical industry," added Dr. Fred Yang, chief development officer of KBP Biosciences.

To date, ocedurenone has been investigated in nine clinical trials including the BLOCK-CKD Phase 2b trial. The BLOCK-CKD trial met its primary endpoint with ocedurenone demonstrating a clinically meaningful and statistically significant improvement in systolic blood pressure (SBP) from baseline to day 84 in patients with stage 3b/4 CKD and uncontrolled hypertension. There were no reports of severe hyperkalemia or acute kidney injury with ocedurenone in the trial1.

The CLARION-CKD phase 3 trial has been initiated in the US, Europe and Asia with the first patient dosed at the end of 2021 and will continue as planned with a total of more than 600 patients expected to be randomised by more than 150 sites. Novo Nordisk expects to initiate phase 3 trials in additional cardiovascular and kidney disease indications in the coming years, aiming to maximise the full potential of ocedurenone.

"We look forward to adding ocedurenone to our pipeline as it will complement our current development programmes in cardiovascular disease and chronic kidney disease," said Camilla Sylvest, executive vice president, Commercial Strategy & Corporate Affairs at Novo Nordisk. "This deal is closely aligned with our strategic focus on expanding from our core in diabetes into other serious chronic diseases, including through novel drug modalities, to help many more patients living with unmet medical needs."

Source: https://www.novonordisk.com/news-and-media/news-and-ir-materials/news-details.html?id=166329

Thermo Fisher Scientific to Acquire Olink, a Leader in Next-Generation Proteomics

WALTHAM, Mass. & UPPSALA, Sweden--(BUSINESS WIRE)—Oct 17, 2023: Thermo Fisher Scientific Inc. (NYSE: TMO) ("Thermo Fisher"), the world leader in serving science, and Olink Holding AB (publ) ("Olink") (Nasdaq: OLK), a leading provider of next-generation proteomics solutions, today announced that their respective boards of directors have approved Thermo Fisher's proposal to acquire Olink for $26.00 per common share in cash, representing $26.00 per American Depositary Share (ADS) in cash. This represents a premium of approximately 74% to the closing price of Olink's American Depositary Shares that trade on NASDAQ on October 16, 2023, the last trading day prior to the announcement of the transaction. Thermo Fisher will commence a tender offer to acquire all of the outstanding Olink common shares and all of the American Depositary Shares. The transaction values Olink at approximately $3.1 billion which includes net cash of approximately $143 million.

Olink offers leading solutions for advanced proteomics discovery and development, enabling biopharmaceutical companies and leading academic researchers to gain an understanding of disease at the protein level rapidly and efficiently. Olink's proprietary technology, Proximity Extension Assay (PEA), provides high throughput protein analysis for the very large installed base of qPCR and next-generation sequencing readout systems in the market. With a library of more than 5,300 validated protein biomarker targets, adoption of the technology has been very strong, leading to over 1,400 scientific publications. Headquartered in Sweden, Olink has operations in the Americas, Europe and Asia Pacific.

Olink is on track to deliver over $200M of revenue in 2024 and, as part of Thermo Fisher, is expected to grow mid-teens organically. In the first full year of ownership, the transaction is expected to be dilutive to adjusted EPS1 by $0.17. Excluding financing costs and non-cash deal related equity compensation costs, the transaction is expected to be accretive by $0.10 in that period. Thermo Fisher expects to realize approximately $125 million of adjusted operating income1 from revenue and cost synergies by year five following close. The expected strong long-term business growth and synergy realization profile make the financial returns on the transaction very compelling.

olink PROTEOMICS

Hats off to the founders and employees of Olink for a $3bn+ exit. The company's technology is transformational in the field of research proteomics.

We highlighted the value of Olink's technology in a recent write-up on emerging techniques used in pharma industry target identification.

Source: https://ir.thermofisher.com/investors/news-events/news/news-details/2023/Thermo-Fisher-Scientific-to-Acquire-Olink-a-Leader-in-Next-Generation-Proteomics/default.aspx

Gilead and Assembly Biosciences Partner to Develop Therapeutics for Serious Viral Diseases

October 17, 2023: Gilead Sciences, Inc. (Nasdaq: GILD) and Assembly Biosciences, Inc. (Nasdaq: ASMB), a biotechnology company developing innovative antiviral therapeutics targeting serious viral diseases, today announced that the companies have entered into a 12-year partnership to advance the research and development of novel antiviral therapies, with an initial focus in Assembly Bio's established areas of herpesviruses, hepatitis B virus (HBV) and hepatitis D virus (HDV).

Assembly Bio's current portfolio of small molecule antiviral therapeutics includes both clinical and preclinical programs, including next-generation core inhibitor ABI-4334 for the treatment of HBV, long-acting helicase-primase inhibitor ABI-5366 for herpes simplex virus (HSV), an orally bioavailable HDV entry inhibitor ABI-6250, and a pan-herpes polymerase inhibitor program.

"Advancing the next wave of innovation in virology remains a core focus for Gilead as we seek to address the unmet needs of people affected by serious viral infections around the world," said Tomas Cihlar, Senior Vice President of Virology Research, Gilead. "Collaborations and partnerships are key in the pursuit of the next wave of transformative innovations. We are excited to announce this partnership with Assembly Bio to synergize our efforts on advancing and accelerating the discovery and development of novel antiviral therapeutics."

Under the terms of the agreement, Assembly Bio will receive $100 million, consisting of an $84.8 million upfront payment and a $15.2 million equity investment from Gilead. Gilead's initial equity investment at a premium represents 19.9 percent of the outstanding voting stock of Assembly Bio as of the date of closing. In addition, subject to certain conditions, Gilead has agreed to purchase up to 29.9 percent of Assembly Bio's outstanding voting stock at a premium.

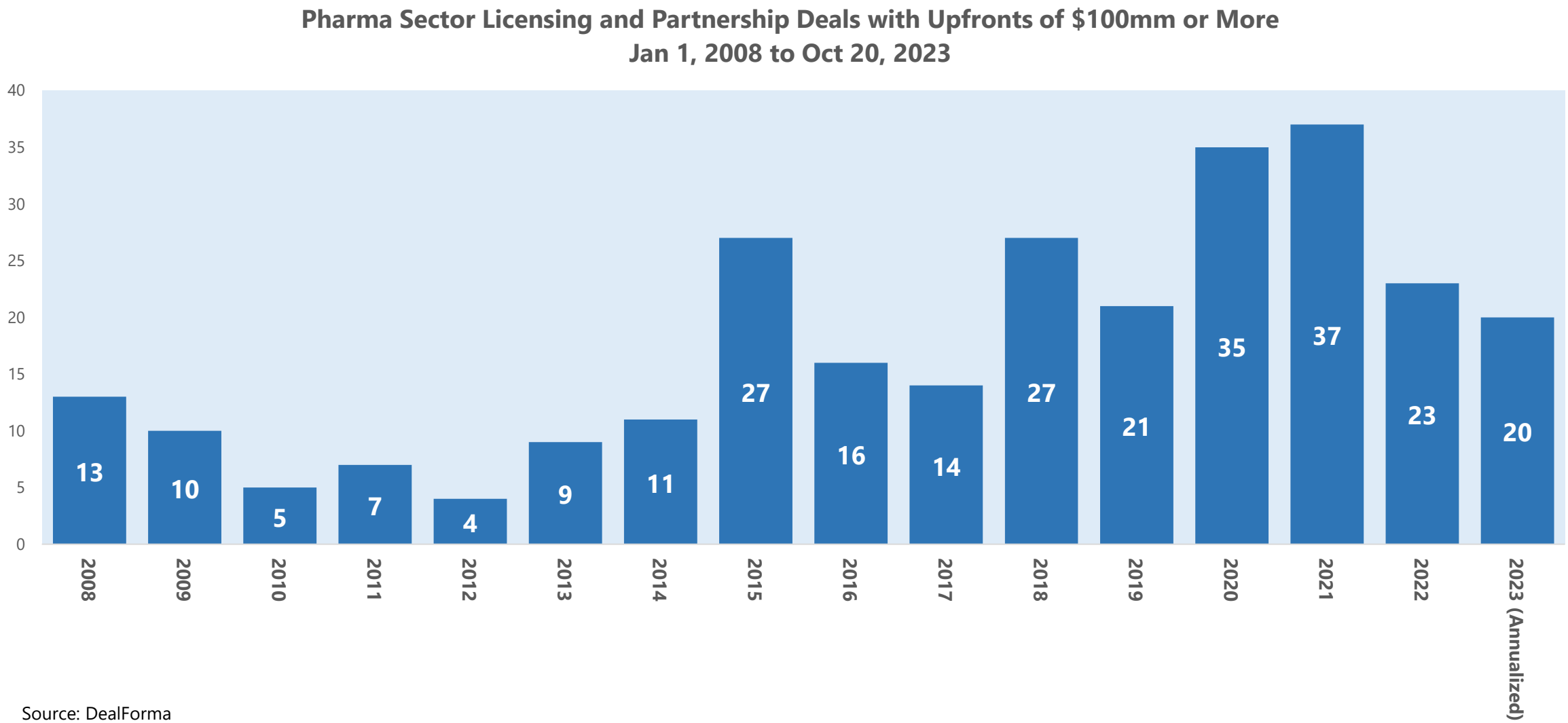
Gilead may opt-in to obtain exclusive rights for each of Assembly Bio's current and future programs, including two preclinical programs targeting HSV and transplant-associated herpesviruses that Gilead is licensing to Assembly Bio, upon payment of an opt-in fee of at least $45 million per program after clinical proof-of-concept is achieved. If Gilead opts-in to any current or future program under the collaboration, Assembly Bio is eligible to receive up to $330 million per program in potential regulatory and commercial milestones, in addition to royalties ranging from the high single digits to high teens.

assemblybio

Assembly has quietly built up an impressive next generation long-acting antiviral candidate for HSV and has a next generation core inhibitor for HBV in development. With a stock price in tatters, this deal with Gilead was eminently rational. Assembly gets needed capital and a great commercial partner who understands the value of their drug pipeline. Gilead gets a next generation antiviral portfolio. The deal was structured in a way similar to Gilead's partnerships with Arcus and Galapagos, coupling product rights with a significant equity investment giving both sides upside in ASMB stock. Surprisingly, ASMB shares were only up 33% for the week – highlighting challenging capital market conditions.

Source: https://www.gilead.com/news-and-press/press-room/press-releases/2023/10/gilead-and-assembly-biosciences-establish-partnership-to-develop-next-generation-therapeutics-for-serious-viral-diseases

The Recent Spate of Big Licensing Deals Not Enough to Overcome Drought Prior to September in Licensing Volume



Source: DealForma

EcoR1 Makes a Timely Bet

By Stephen Taub, *Institutional Investor*, Oct 16, 2020

Now this is what you call market timing.

Life sciences hedge fund EcoR1 Capital disclosed that as of September 22 it had initiated a stake of nearly 5.75 million shares of Mirati Therapeutics, making it the second-largest shareholder, with about 9.8 percent of the commercial-stage oncology company's shares. Mirati became EcoR1's fourth-largest U.S.-listed common stock long position.

Then, on October 8, Bristol Myers Squibb announced it had agreed to acquire Mirati — which is seeking to develop therapies for cancer — for $4.8 billion, or $58 per share. Under the deal, Mirati stockholders will receive one nontradable contingent value right for each Mirati share held, potentially worth $12 per share in cash and an additional $1 billion in value, according to a press release. Shares of Mirati surged 32 percent on the news, a big boost to hedge funds.

EcoR1 did not respond to requests for comment. The timely purchase, no doubt, is heavily boosting the hedge fund's October performance. But the deal's announcement did not come in time to prevent EcoR1 — and a slew of other life sciences funds that also hold large positions in Mirati — from reporting losses in September.

Although a surge in dealmaking between large pharmaceuticals companies and fledgling biopharma companies with promising drug pipelines is helping to boost the sector in general this year, the volume of deals has not been enough to lift the shares of other potential targets or the performance of the hedge funds that specialize in this sector.

Rather, in September EcoR1 lost 10 percent for the month alone, and it was down 12 percent for the year through the end of the third quarter, according to someone who has seen the results.

EcoR1 was badly hurt last month by its largest long, Prothena Corp., whose stock lost nearly 9 percent in September and is down about 35 percent since the end of July. At the end of the second quarter, shares of Prothena accounted for nearly 19 percent of U.S. common stock assets.

Source: https://www.institutionalinvestor.com/article/2cbstxl3mw8oxr8b4eb5s/premium/ecor1s-timely-bet

Biotech Firm Prothena Prepares for Potential Sale

By Michelle F Davis, Dinesh Nair, and Manuel Baigorri, *Bloomberg*, Oct 16, 2020

Prothena Corp., which is developing a closely-watched treatment for Alzheimer's disease, is preparing for a potential sale ahead of key data expected in the coming months, people with knowledge of the matter said.

The biotechnology company has been speaking to advisers as it gets ready to explore strategic options that may include a sale or partnership, according to the people.

Prothena rose 23% at 10:57 a.m. Monday in New York, putting the company on track for the biggest daily gain in over five months and giving it a market value of about $2.9 billion.

Source: https://www.bloomberg.com/news/articles/2023-10-16/biotech-firm-prothena-is-said-to-prepare-for-potential-sale

Jazz Pharmaceuticals Is Said to Explore Options Including Sale

By Michelle F Davis and Dinesh Nair, *Bloomberg*, Oct 19, 2020

(Bloomberg) -- Jazz Pharmaceuticals Plc is exploring strategic options including a potential sale, people with knowledge of the matter said.

The company is speaking with advisers to help field interest, said the people, who asked not to be identified because the information is private. Jazz Pharma is also studying possibilities that might include a breakup or divestment of parts of the business, the people said.

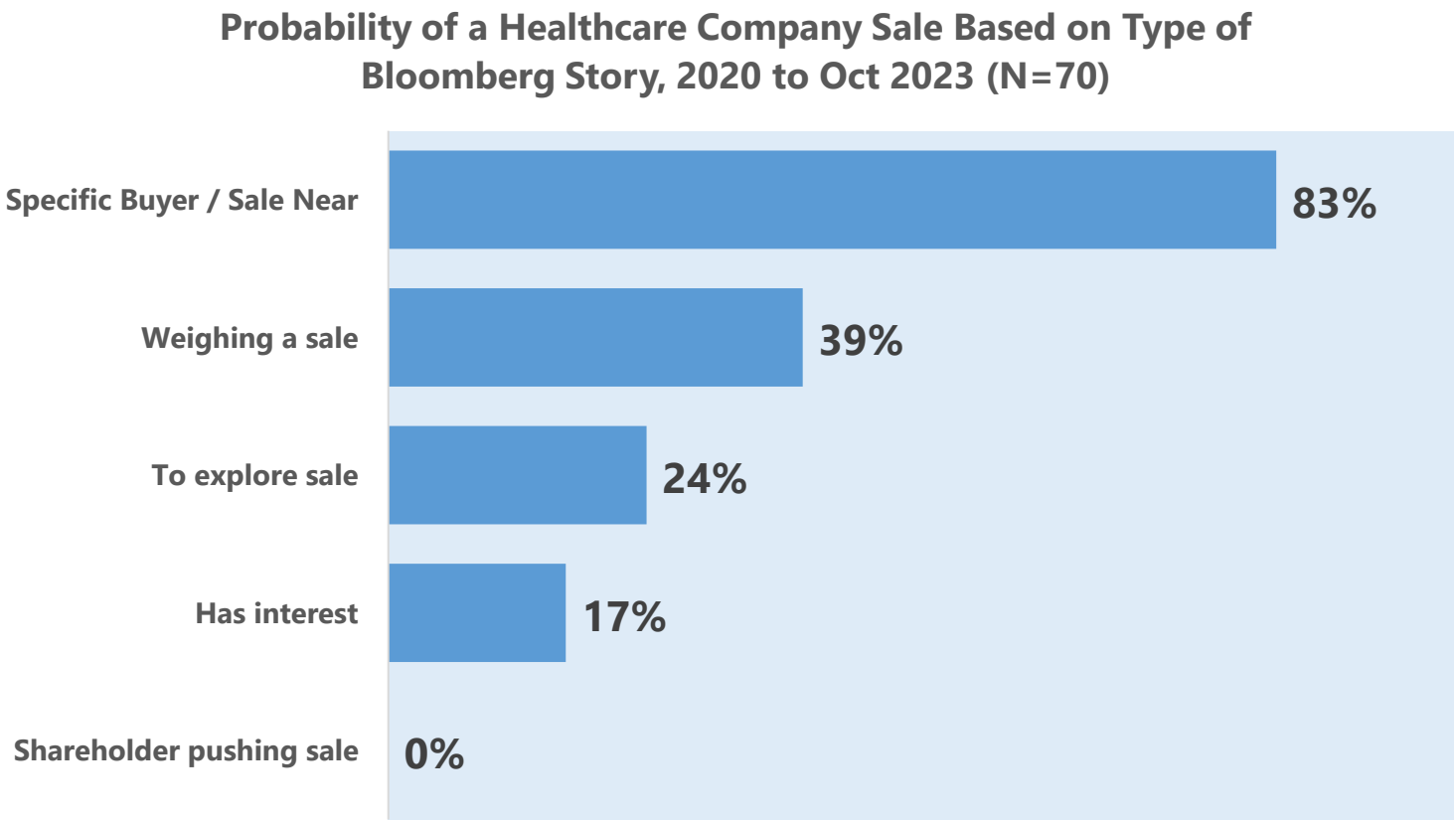
Separating its cannabinoid business from its oncology operations is one of the possibilities, the people said. Jazz Pharma agreed in 2021 to acquire GW Pharmaceuticals Plc, the maker of the first drug derived from the cannabis plant to win approval in the US, for $7.2 billion in cash and stock.

Jazz Pharma shares rose as much as 4% Friday in New York trading. They had lost 17% this year through Thursday's close.

Source: https://www.bnnbloomberg.ca/jazz-pharmaceuticals-is-said-to-explore-options-including-sale-1.1987117

Interpreting M&A Intelligence Stories from Bloomberg

It's hard to know what to make of Bloomberg stories indicating, for example, that Jazz or Prothena are exploring options. Do these stories reflect a reality that the company will be sold or, perhaps, an aspiration by the board or other shareholder that a company should be sold?



Source: Stifel research of Bloomberg stories and subsequent research of events using Google and CapIQ.

We went back and searched for stories in Bloomberg mentioning interest in a sale, interest from buyers, sale processes or impending sales in the period from June 2021 to July 2023. We then went to see what actually happened after the story ran. If a transaction occurred in the next 12 months on the mentioned asset, we indicates that the story successfully called the outcome.

The results of this analysis indicate that a story about a specific buyer who is near to the finish line forecasts the correct outcome 83% of the time. If a story says that the seller is weighing a sale (suggesting that there is real interest in an asset), a sale happened 39% of the time. The two recent cases of companies exploring a sale (Jazz and Prothena) are different. When a story indicates that a company will explore a sale, the event happens 24% of the time. When a story says that there is interest in an asset, a sale happens 17% of the time. And, when a story says a shareholder is pushing a sale, the sale happens 0% of the time.

Biogen CEO Chris Viehbacher: Immunology is a Natural Fit at Biotech, Calls for 'Reinvention'

Jaimy Lee, *Endpoints News*, October 20, 2023

"Biogen has launched a significant revamp under Viehbacher, including the recent hire of Jane Grogan, an immunologist, as its new head of research. And on Thursday, the CEO pointed to the company's history in multiple sclerosis as an indicator that the company has long been focused on immunology."

I don't think we're going to get into" rheumatoid arthritis, Viehbacher said Thursday at the STAT Summit, "but moving into immunology is a natural adjacency for us, and so is rare disease."

It's been nearly a year since Viehbacher, who once ran Sanofi, took over as CEO of Biogen amid the company's recent struggles with a faltering pipeline and the controversial approval and launch of Aduhelm, its first Alzheimer's disease treatment."

Source: https://endpts.com/biogen-ceo-chris-viehbacher-immunology-is-a-natural-fit-at-biotech-calls-for-reinvention/

Dan Skovronsky Talks About Deals and Lilly's Future

***Endpoints News*, October 17, 2023**

Kyle LaHucik (Endpoints): Let's talk about M&A. There's Point. DICE. Versanis. Sigilon. Emergence. All of them are relatively small tuck-ins. Why not a mega deal?

Dan Skovronsky: Mega deals haven't been a particularly productive way of generating shareholder value. Sometimes companies go to mega deals in a position of relative weakness in terms of their pipeline. We're not looking to fill a particular revenue gap or looking to transform the company.

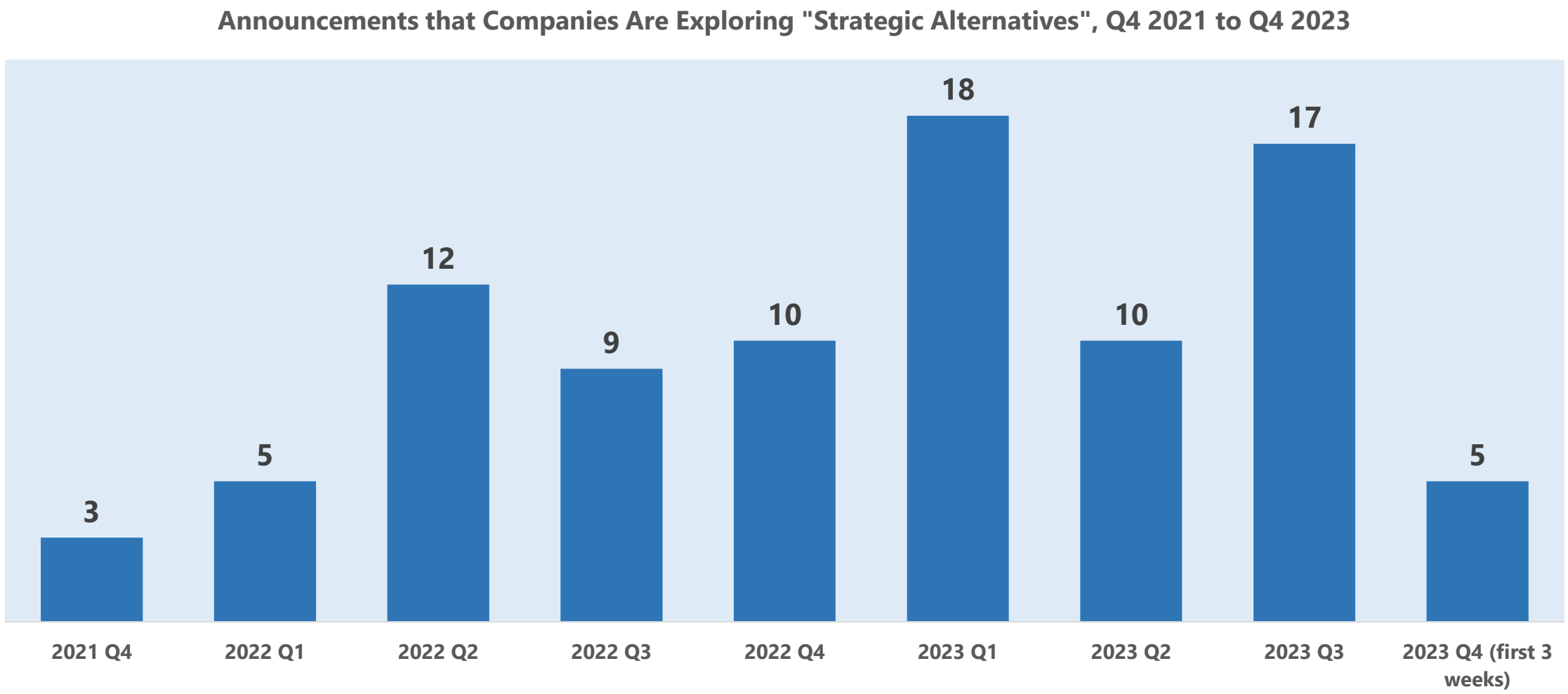
The deals you mentioned are actually just the tip of the iceberg. Lilly, for the last two years, has been the most prolific dealmaker in Big Pharma, but focused on early-stage deals, even research-stature or preclinical things. They're smaller, and they don't capture the headlines.

It needs to either be a target we haven't been able to pursue internally or aren't pursuing internally, is far more advanced than what's around internally, or a new modality to address a target we have conviction about. When we have conviction against a target, we won't be afraid to go after multiple directions. Some of those could come from business development.

Dan Skovronsky
Chief Scientific and Medical Officer
Eli Lilly

Source: https://endpts.com/qa-lilly-science-chief-dan-skovronsky-talks-dealmaking-ai-and-consistent-investing/

High Volume of Biopharma Companies Exploring "Strategic Alternatives"



Source: Stifel Research of news stories and company press releases.

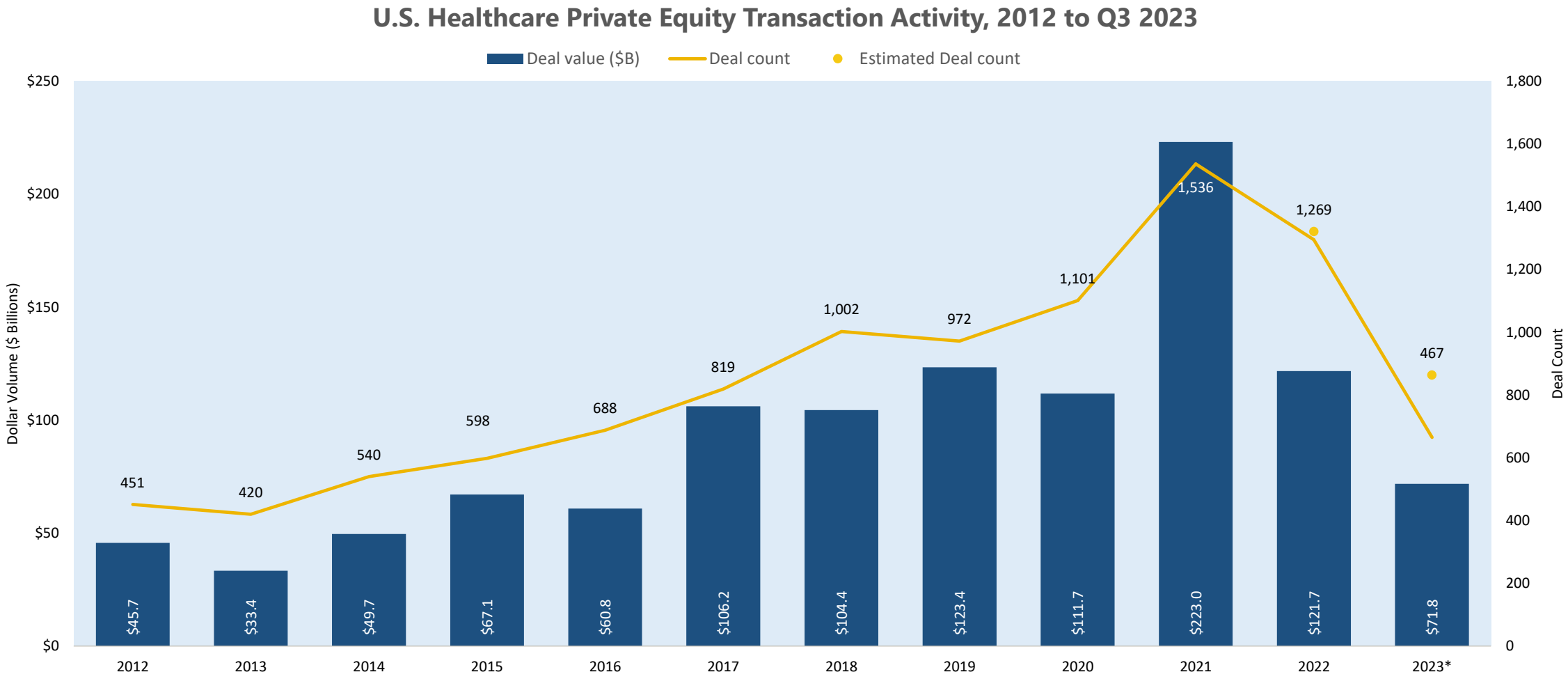
List of Companies Exploring Strategic Alternatives Today

We count 45 biopharma companies that are exploring strategic options today. This number is unprecedentedly high.

Ticker	Company	Announcement Date	Last Cash ($mm)	Enterprise Value ($mm, Oct 20, 2023)
EVLO	Evelo Biosciences	10/17/2023	$7.6	$57.9
JAZZ	Jazz Pharma (rumored in press to be looking at options)	10/20/2023	$1,362.3	$12,869.5
ATHX	Athersys	10/16/2023	$1.8	$22.8
RAIN	Rain Oncology (offer from Concentra)	10/16/2023	$86.3	-$49.0
IMPL	Impel Pharmaceuticals	10/5/2023	$15.2	$100.2
GLTO	Galecto	9/26/2023	$52.1	-$36.1
ARAV	Aravive	8/21/2023	$18.4	-$1.7
GRTX	Galera Therapeutics	8/14/2023	$38.8	$120.8
TCRT	Alaunos Therapeutics	8/14/2023	$18.3	$8.2
SLRX	Salarius Pharmaceuticals	8/8/2023	$11.5	-$8.9
NBSE	Neubase	8/3/2023	$13.8	-$6.6
AVTX	Avalo Therapeutics	8/3/2023	$6.3	$33.5
VXL	Vaxil Bio	8/2/2023	$0.8	$0.2
FIXX	Homology Medicines	7/27/2023	$127.1	-$38.8
SQZB	SQZ Biotechnologies	7/25/2023	$24.7	-$1.2
ELYM	Eliem Therapeutics	7/20/2023	$102.6	-$29.7
RKDA	Arcadia Biosciences	7/20/2023	$18.5	-$13.6
NMTR	9 Meters	7/19/2023	$0.0	$0.0
PIRS	Pieris Pharma	7/18/2023	$54.9	-$16.4
AVRO	AvroBio	7/12/2023	$124.7	-$52.8
HSTO	Histogen	7/5/2023	$7.3	-$2.3
RVLP	RVL Pharmaceuticals	7/5/2023	$19.2	$42.1
SPEX	Spexis	6/30/2023	$1.0	$20.3
AUPH	Aurinia Pharmaceuticals	6/29/2023	$350.4	$826.5
BLPH	Bellorophon Therapeutics	6/24/2023	$10.6	-$9.8
ONCR	Oncorus	6/1/2023	$45.0	$24.8
NOVN.Q	Novan	5/31/2023	$12.5	$24.5
GMDA	Gamida Cell	5/15/2023	$54.1	$142.3
IMVI.Q	IMV	5/1/2023	$21.2	$7.8
INFI	Infinity Pharma	3/28/2023	$0.4	$1.5
BLCM	Bellicum Therapeutics	3/14/2023	$7.4	$21.1
FRTX	Fresh Tracks Therapeutics	3/7/2023	$8.9	-$3.1
GRPH	Graphite Bio	2/23/2023	$284.0	-$152.0
EVFM	Evofem Biosciences	2/23/2023	$7.7	$81.0
ALRN	Aileron	2/21/2023	$12.1	-$6.3
GTTX	Genetether	2/8/2023	$2.0	$1.0
AXLA	Axcella Therapeutics	12/14/2022	$8.9	$15.7
MEIP	MEI Pharma	12/6/2022	$100.7	-$41.3
SNGX	Soligenix	11/10/2022	$17.0	$4.0
HGEN	Humanigen	10/31/2022	$3.1	-$3.0
XCUR	Exicure	9/26/2022	$15.6	-$3.0
TENX	Tenax Therapeutics	9/14/2022	$13.4	-$6.1
GLMD	Galmed	6/15/2022	$22.4	-$12.0
ABIO	Arca Bio	4/18/2022	$43.9	-$12.0
ADMA	ADMA Biologics	10/21/2021	$62.5	$799.7

Source: Stifel Research of news stories and company press releases.

Private Equity Deal Drought in Healthcare Continues



Source: Pitchbook. * Data for 2023 current through Sep 30, 2023.

Industry News

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

Britain's Life Sciences Sector Needs a Shot in The Arm

Editorial Board Opinion, *Financial Times*, October 18, 2023 (excerpt)

Shortly after this year's 70th anniversary of British researchers' discovery of the double helix, Prime Minister Rishi Sunak declared, as he unveiled a plan to turn the UK into a scientific "superpower", that science and innovation "have been in our DNA for decades". Yet for life sciences, a vaunted UK strength, the future is cloudy. Even as Merck of the US prepares to break ground on a £1bn London research centre, its research chief warned this week that Britain needs to become more welcoming to drugs companies. Warm words and historical credentials can only go so far: the government has to deliver a holistic remedy to the UK's waning pharma competitiveness.

Companies cite UK drug pricing as a disincentive to invest. A voluntary scheme agreed in 2019 caps growth in the NHS bill for branded medicines at 2 per cent a year; drugmakers have to pay back any excess. Blockbuster spending in recent years, due to the pandemic, means drugs companies will this year have to return £3.3bn, or 26.5 per cent of sales — double a similar clawback in Germany and triple that in France.

The voluntary scheme is due to expire at the year-end and be renegotiated, or companies will revert to a similar statutory system. This offers an opportunity to revise the arrangement — which a report for the Association of the British Pharmaceutical Industry estimated will otherwise cost the UK £5.7bn in lost investment in research and development between 2024 and 2028 — to bring the UK more into line with EU counterparts. But a balance must be struck to ensure this does not push up NHS costs.

Britain is also falling down global rankings in running clinical trials; Novartis recently scrapped a major trial of a cholesterol drug. The NHS can potentially offer access to a large population for testing treatments, but these are carried out at the level of regional NHS trusts, adding complexity and cost. A centralised approach would be possible, as the pandemic showed. The Recovery trial, a large-scale study into Covid treatments, suspended the usual practice and included more than 170 hospitals.

Source: https://www.ft.com/content/7c9bb23e-8106-4596-8b7a-4eb30117900b

Senators Grill Bertagnolli on NIH Priorities, Drug Costs

Ariel Cohen, *Roll Call*, Oct 18, 2023

President Joe Biden's nominee to lead the National Institutes of Health faced detailed policy questions about drug costs and biomedical research but few political fireworks during her Wednesday appearance in front of the Senate Health, Education, Labor and Pensions Committee. The relatively bipartisan nature of nominee Monica Bertagnolli's confirmation hearing came as somewhat of a surprise, considering the tumult that preceded her Senate appearance and how politicized the agency became during the COVID-19 pandemic.

Democrats on the committee quizzed the nominee on what she would do to lower drug costs, while Republicans focused on restoring public trust in the agency. Ranking member Bill Cassidy, R-La., told Bertagnolli, who currently heads the National Cancer Institute, that, if confirmed, much of her tenure would involve rebuilding the agency's trust with the American public.

"There are no questions regarding your scientific qualifications. But there are questions about your ability to lead NIH through this next phase," he said, noting the many lightning rods surrounding the NIH, including gain-of-function research and care for transgender youth.

Sanders, I-Vt., reiterated those concerns during the hearing, noting the high cost of drugs in the U.S. compared to other western nations. Over the past 20 years, the average cost of new treatments co-developed by NIH scientists was $111,000, Sanders said, pointing to a committee report released in June. "We pay for the research, drug companies develop the drug, and they make millions," Sanders said. "It doesn't make sense to me."

Bertagnolli told Sanders that she had sat in the clinic next to patients of her own who could not afford their cancer treatments, and told him she would work to lower drug costs.

Source: https://rollcall.com/2023/10/18/18bertagnolli/

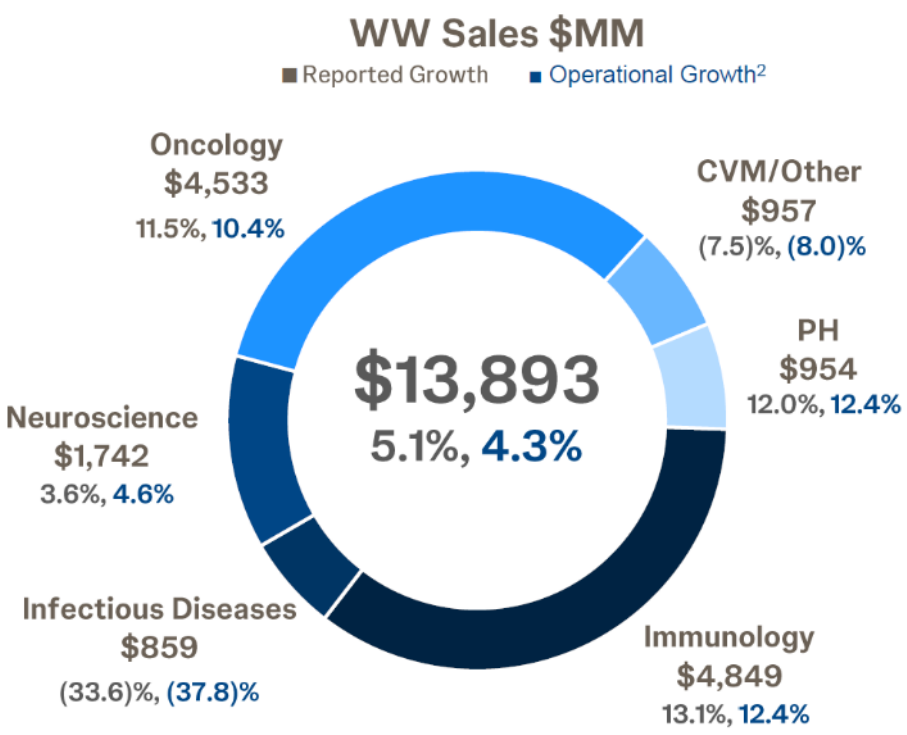
Solid Earnings Growth from J&J Last Week

Innovative Medicine[1] Highlights – 3rd Quarter 2023

Strong operational growth[2] of 8.2% excl. COVID-19 Vaccine driven by Oncology and Immunology

Reported: WW 5.1%, U.S. 10.9%, Int'l (2.3)%

Operational[2]: WW 4.3%, U.S. 10.9%, Int'l (4.3)%



Key Drivers of Operational Performance[2]

Immunology	• STELARA increase driven by patient mix, market growth, and continued strength in IBD • Growth in TREMFYA due to patient mix, market growth, and continued strength in PsO/PsA • SIMPONI/SIMPONI ARIA growth driven by market growth and favorable mix • REMICADE decline due to biosimilar competition
Infectious Diseases	• COVID-19 Vaccine revenue decline
Neuroscience	• SPRAVATO growth driven by ongoing launches as well as increased physician confidence and patient demand • Growth partially offset by declines in RISPERDAL/RIPSERDAL CONSTA and the paliperidone long-acting injectables due to the XEPLION loss of exclusivity in EU
Oncology	• DARZALEX increase driven by continued share gains in all regions and market growth • ERLEADA increase driven by continued share gains and market growth in mCSPC • CARVYKTI increase driven by ongoing launch, share gains, and capacity improvements • Growth in OTHER ONCOLOGY driven by launch of TECVAYLI • Growth partially offset by ZYTIGA loss of exclusivity and IMBRUVICA decline due to global competitive pressure
Cardiovascular / Metabolism / Other (CVM/Other)	• XARELTO decline due to unfavorable mix and access changes
Pulmonary Hypertension (PH)	• UPTRAVI and OPSUMIT growth driven by favorable patient mix, share gains and market growth • Continued declines in Other Pulmonary Hypertension

Adjusted Operational Sales[3]: WW 4.4%, U.S. 10.9%, Int'l (4.1)%

J&J

[1] Previously referred to as Pharmaceutical
[2] Non-GAAP measure; excludes the impact of translational currency; see reconciliation schedules in the Investor Relations section of the company's website
[3] Non-GAAP measure; excludes acquisitions and divestitures and translational currency; see reconciliation schedules in the Investors section of the company's website
Note: Values may not add due to rounding

J&J Innovative Medicine 8

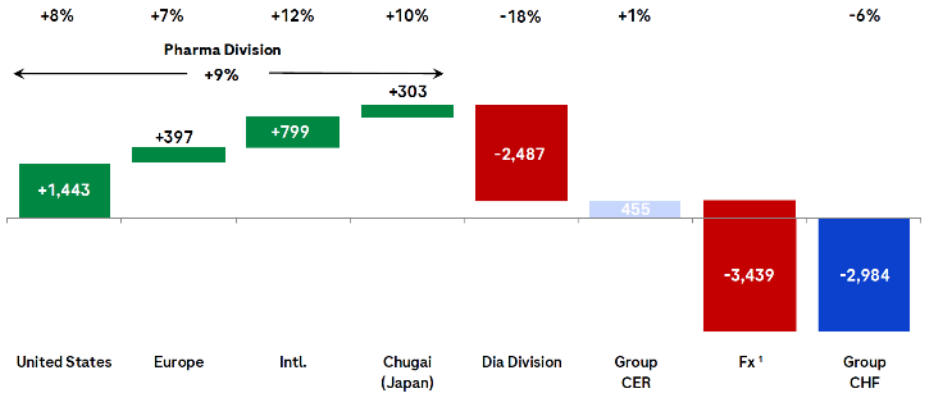
Source: https://www.investor.jnj.com/events-and-presentations/events/event-details/2023/Johnson--Johnson-Third-Quarter-2023-Earnings-Call-and-Webcast-2023-4SvirR-WpO

Flat Topline Growth at Roche in Q3 2023

Roche is facing negative growth in diagnostics related to the end of the Pandemic and, while positive, pharma growth is restrained due to the impact of biosimilars on its legacy portfolio.

YTD Sep 2023: Regional sales development

CER Group sales increase of +1% driven by Pharma Division



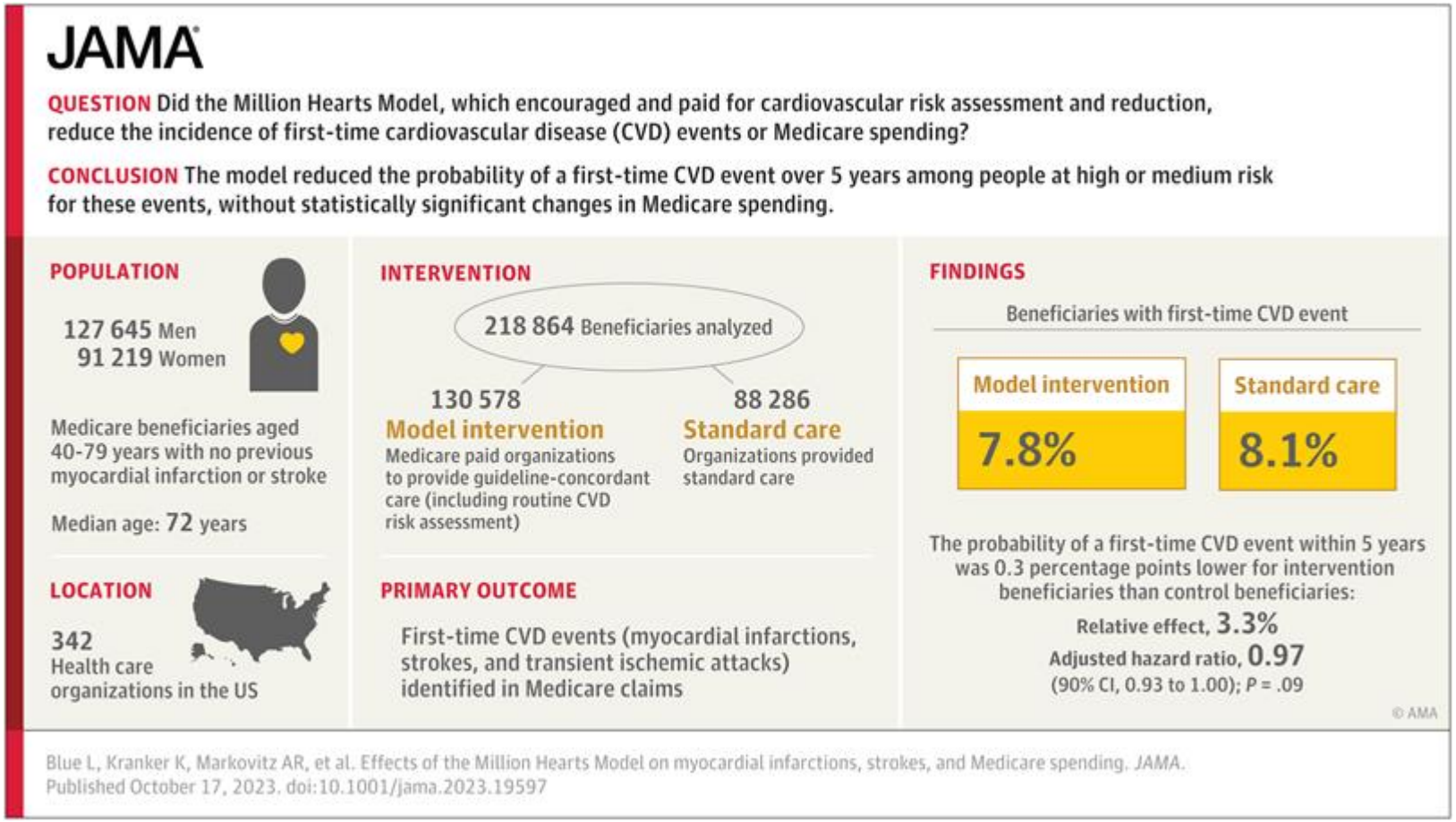
2023 outlook confirmed

Group sales growth[1]	Low single digit decline
Core EPS growth[1]	Broadly in line with sales decline
Dividend outlook	Further increase dividend in Swiss francs

Source: https://assets.roche.com/f/176343/x/e8afe51e54/irp231019-a.pdf

Effects of the Million Hearts Model on Myocardial Infarctions, Strokes, and Medicare Spending

Laura Blue et.al., JAMA, October 17, 2023



Source: https://jamanetwork.com/journals/jama/article-abstract/2810696

Research briefing

Innate immune mechanisms mediate loss of corticostriatal synapses in Huntington's disease

By analyzing human samples and multiple mouse models of Huntington's disease, we found that complement proteins and microglia mediate early and selective loss of corticostriatal synapses. Strategies that block this process can reduce synaptic loss, increase excitatory input to the striatum and prevent the development of cognitive deficits in mice.

Wilton, D. K. et al. Microglia and complement mediate early corticostriatal synapse loss and cognitive dysfunction in Huntington's disease. *Nat. Med*. (2023).

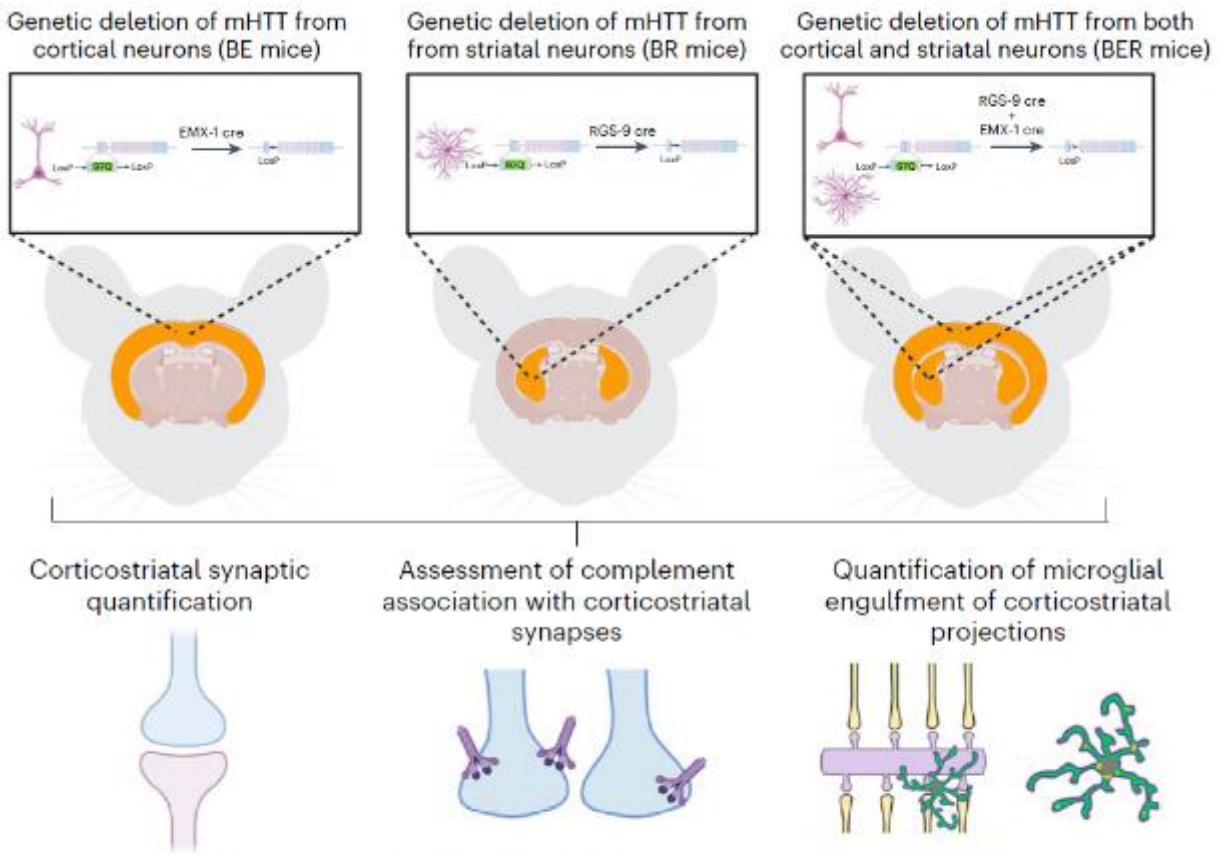
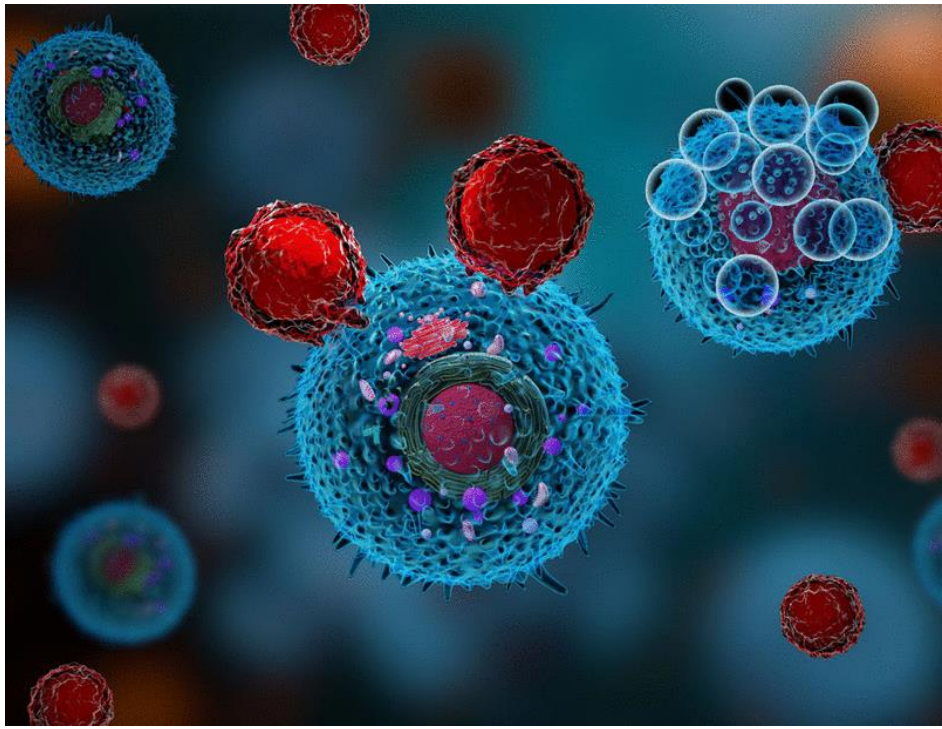


Fig. 1 | Complement and microglia mediate elimination of corticostriatal synapses in HD mice. Genetic and experimental strategies used to demonstrate that increased association of complement with corticostriatal synapses, increased microglial engulfment of corticostriatal projections and loss of corticostriatal synapses are initiated by and dependent on mHTT expression in both cortical neurons and striatal neurons. Transgenic BACHD mice express an *HTT* variant, encoded in a bacterial artificial chromosome, that carries 97 CAG repeats (97Q). BACHD mice in which *mHTT* had been selectively ablated from the cortex (through the use of EMX1 cre),

Source: https://www.nature.com/articles/s41591-023-02616-w

BCL6 Promotes a Stem-like CD8+ T Cell Program in Cancer via Antagonizing BLIMP1

Source: Sun Q, Cai D, Liu D, Zhao X, Li R, Xu W, Xie B, Gou M, Wei K, Li Y, Huang J, Chi X, Wei P, Hao J, Guo X, Pan B, Fu Y, Ni L, Dong C. BCL6 promotes a stem-like CD8⁺ T cell program in cancer via antagonizing BLIMP1. *Sci Immunol*. 2023 Oct 27;8(88):eadh1306. Epub 2023 Oct 20.



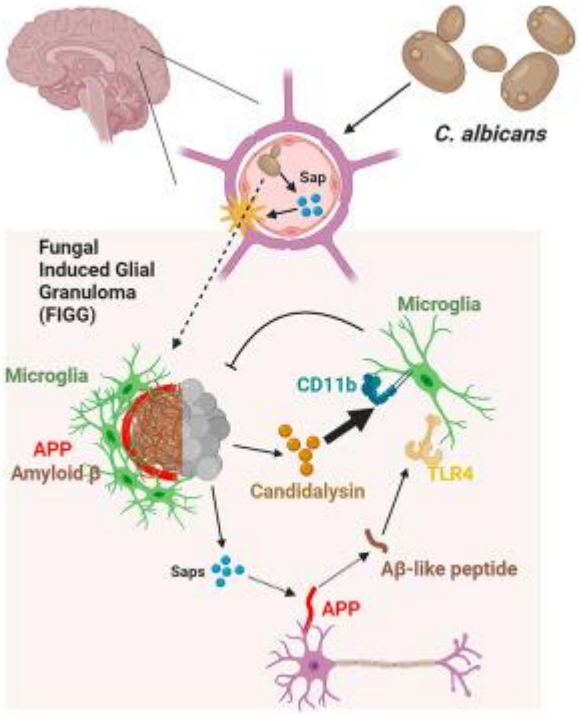
Overcoming $CD8^+$ T cell exhaustion is critical in cancer immunotherapy. Recently, an intratumor stem/progenitor-like $CD8^+$ T cell (T_{prog} cell) population that mediates the persistence of antitumor responses has been defined, which can further develop into a terminally differentiated $CD8^+$ T cell (T_{term} cell) subpopulation with potent cytotoxic functions. T_{prog} cells are the main responders to immune checkpoint blockade therapies, yet how extrinsic signals via transcription factors control T_{prog} cell generation and persistence in tumors is unclear. Here, we found that BCL6 inhibits tumor-specific T_{term} cell generation from T_{prog} cell downstream of TCF1. We show that *Bcl6* deficiency reduced the persistence of T_{prog} cells, without affecting their generation, thus abrogating long-term tumor control. High-level BCL6 expression was observed in tumor-specific T cells in draining lymph nodes (LNs) and was associated with T cell exhaustion. This was observed in TOX^+TCF1^+ T_{prog} cells in both LNs and tumors. BCL6 expression in $CD8^+$ T cells was up-regulated by TGF-β–SMAD2 signaling but down-regulated by the IL-2–STAT5 pathway. Mechanistically, BCL6 transcriptionally repressed the expression of T_{term} cell–associated genes and induced those of T_{prog} cell–related genes, in a manner antagonistic to BLIMP1. *Prdm1* deficiency also promoted the T_{prog} cell program and greatly improved the efficacy of anti–PD-1 therapy. Thus, we identified the TGF-β–BCL6 and IL-2–BLIMP1 antagonistic pathways in regulation of antitumor $CD8^+$ T cells, which may benefit the development of long-lasting and effective cancer immunotherapy.

Source: https://pubmed.ncbi.nlm.nih.gov/37862431/

Toll-like Receptor 4 and CD11b Expressed on Microglia Coordinate Eradication of Candida Albicans Cerebral Mycosis

Wu Y, Du S, Bimler LH, Mauk KE, Lortal L, Kichik N, Griffiths JS, Osicka R, Song L, Polsky K, Kasper L, Sebo P, Weatherhead J, Knight JM, Kheradmand F, Zheng H, Richardson JP, Hube B, Naglik JR, Corry DB. Toll-like receptor 4 and CD11b expressed on microglia coordinate eradication of Candida albicans cerebral mycosis. Cell Rep. 2023 Oct 10;42(10):113240.

The fungal pathogen Candida albicans is linked to chronic brain diseases such as Alzheimer's disease (AD), but the molecular basis of brain anti-Candida immunity remains unknown. We show that C. albicans enters the mouse brain from the blood and induces two neuroimmune sensing mechanisms involving secreted aspartic proteinases (Saps) and candidalysin. Saps disrupt tight junction proteins of the blood-brain barrier (BBB) to permit fungal brain invasion. Saps also hydrolyze amyloid precursor protein (APP) into amyloid β (Aβ)-like peptides that bind to Toll-like receptor 4 (TLR4) and promote fungal killing in vitro while candidalysin engages the integrin CD11b (Mac-1) on microglia. Recognition of Aβ-like peptides and candidalysin promotes fungal clearance from the brain, and disruption of candidalysin recognition through CD11b markedly prolongs C. albicans cerebral mycosis. Thus, C. albicans is cleared from the brain through innate immune mechanisms involving Saps, Aβ, candidalysin, and CD11b.



Source: https://pubmed.ncbi.nlm.nih.gov/37819761/

ESMO Update

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

Summary of Selected Lung Cancer Study Presentations at ESMO

Revolution Medicines

Advanced NSCLC

Regimen: **RMC-6236**
MOA: **Multiple RAS mutations**
Doses: **80mg to 400mg (Ph 1)**
Evaluable Subjects: **40**
Median Prior Lines of Tx: **2**
ORR: **38%** | CR's: **2.5%**
Median Survival: **NA**
Grade 3 TRAE's: **9%**
Write-Up: Link

Johnson&Johnson

PAPILLON Study

Advanced NSCLC w/EGFR Exon20 mutation

Regimen: **RYBREVANT + chemo vs chemo**
MOA: **EGFR x MET (Phase 3)**
Doses: **1400mg weekly**
ITT Subjects: **308**
Prior Lines of Tx: **0**
ORR: **73% (vs. 47% chemo)**
Median PFS: **11.4 mo vs. 6.7**
OS HR**:** 0.67
Grade 3 TRAE's: **75% (vs 54%)**
Write-Up: Link

Johnson&Johnson

MARIPOSA Study

Advanced NSCLC w/EGFR Exon19 mut

Regimen: **RYBREVANT + Lazertinib vs. Tagrisso**
MOA: **EGFR x MET + EGFR TKI vs. EGFR TKI (Phase 3)**
Doses: **NA**
Evaluable Subjects: **1,074**
Prior Lines of Tx: **0**
ORR: **NA**
Complete Response: **NA**
Grade 3 TRAE's: **NA**
Write-Up: Link

GSK

Metastatic NSCLC

Regimen: **Dostarlimab + Chemo vs. Pembrolizumab + Chemo**
MOA: **PD-1 inhibitor (Phase 3)**
Doses: **500mg (d) or 200mg (p) Q3W**
Evaluable Subjects: **243**
Prior Lines of Tx: **NA**
ORR: **45% (d) vs. 39% (p)**
Complete Response: **4.4%**
% Deaths: **49% (d) vs. 61% (p)**
Grade 3 TRAE's: **NA**
Write-Up: Link

SYSTIMMUNE

Metastatic NSCLC w/EGFR wt mut

Regimen: **BL-B01D1**
MOA: **EGFR x HER3 ADC**
Doses: **Escalating Phase 1**
Evaluable Subjects: **62**
Prior Lines of Tx: **3**
ORR: **40.3%**
Complete Response: **0%**
mDOR: **Not reached**
Grade 3 TRAE's: **61%**
Write-Up: Link

AstraZeneca

Tropion – Lung05

Advanced or Metastatic NSCLC w/mutations

Regimen: **Datopotamab DXd**
MOA: **Trop2 ADC**
Doses: **6mg/Kg (Phase 3)**
Evaluable Subjects: **137**
Prior Lines of Tx: **3**
ORR: **36%**
Complete Response: **3%**
mDOR: **7 months**
Grade 3 TRAE's: **14%**
Write-Up: Link

Roche

ALK+ Stage IB – IIIA NSCLC

Regimen: **Alectinib**
MOA: **ALK/Ret Inhibitor**
Doses: **10mg / 100mg**
ITT Subjects: **116 (Phase 3)**
Prior Lines of Tx: **NA**
Death Rate: **12% (vs. 39% w/chemo)**
Grade 3 AE's **23%**
Write-Up: Link

Lilly

RET Fusion+ Advanced NSCLC

Regimen: **Selpercatinib**
MOA: **Ret Inhibitor vs. control**
Doses: **160mg twice daily or control (chemo +/- pembro)**
ITT Subjects: **261 (Phase 3)**
ORR: **84% (vs 65% control)**
Complete Response: **7% (vs 6%)**
mDOR: **24.2 mo (vs. 11.5 w/control)**
Grade 3 AE's **70% (57% control)**
Write-Up: Link

AMGEN

Advanced SCLC

Regimen: **Tarlatamab**
MOA: **DLL T-cell engager**
Doses: **10mg / 100mg**
ITT Subjects: **188 (Phase 2)**
Prior Lines of Tx: **NA**
ORR: **40%**
Complete Response: **4.4%**
Median Survival: **10.6 mos**
Grade 3 TRAE's (100mg): **33%**
Write-Up: Link

HARPOON Therapeutics

Advanced SCLC

Regimen: **HPN328**
MOA: **DLL T-cell engager**
Doses: **1mg (priming dose)**
Evaluable Subjects: **19 (Phase 1)**
Prior Lines of Tx: **NA**
ORR: **32%**
Median Survival: **10.6 mos**
Grade 3 TRAE's (high dose): **25%**
Write-Up: Link

Summary of Other Cancer Drug Study Presentations at ESMO

AstraZeneca

BEGONIA Arm 7

First Line Metastatic TNBC

Regimen: **Datopotamab DXd + PD-L1 mAb**
MOA: **Trop2 ADC**
Doses: **6mg/Kg (Phase 3)**
Evaluable Subjects: **62**
Prior Lines of Tx: **0**
ORR: **79%**
Complete Response: **10%**
mDOR: **15.5 months**
Grade 3 TRAE's: **~30%**
Write-Up: Link

MERCK KELUN

HR+ / HER2- Breast Cancer

Regimen: **SKB264 / MK-2870**
MOA: **TROP2 ADC**
Doses: **5 mg/kg Q2W**
Evaluable Subjects: **38**
Prior Lines of Tx: **2**
ORR: **36.8%**
Complete Response: **0%**
Grade 3 TRAE's: **48.8%**
Write-Up: Link

GSK HANSOH PHARMA

TNBC

Regimen: **HS-20089**
MOA: **B7H4 ADC**
Doses: **5.8 to 7.2 mg/kg**
Evaluable Subjects: **24**
Prior Lines of Tx: **NA**
ORR: **30.3%**
Complete Response: **0%**
Grade 3 TRAE's: **> 50%**
Write-Up: Link

Gantargia

Metastatic TNBC

Regimen: **nadunolimab + chemo**
MOA: **IL1 RAP mAb + chemo**
Doses: **1 to 5 mg/kg**
Evaluable Subjects: **15**
Prior Lines of Tx: **1**
ORR: **60%**
Complete Response: **7%**
Grade 3 TRAE's: **NA**
Write-Up: Link

Daiichi-Sankyo

Heavily Pretreated Ovarian Cancer

Regimen: **Raludotatug DXd**
MOA: **CDH6 ADC**
Doses: **4.8 to 6mg**
Evaluable Subjects: **60**
Median Prior Lines of Tx: **4**
ORR: **46%** | CR's: **2%**
Median DoR: **11.2 months**
Median PFS: **7.9 months**
Grade 3 TRAE's: **52%**
Write-Up: Link

Revolution Medicines

PDAC

Regimen: **RMC-6236**
MOA: **Multiple RAS mutations**
Doses: **80mg to 400mg**
Evaluable Subjects: **46**
Median Prior Lines of Tx: **3**
ORR: **20%** | CR's: **2.5%**
Median Survival: **NA**
Grade 3 TRAE's: **9%**
Write-Up: Link

CanBas
Cancer therapy by Basic research

Metastatic PDAC

Regimen: **CBP-501**
MOA: **Calmodulin Modulator**
Doses: **25 mg/m2 + Cis/Nivo vs Cis/Nivo Alone (third line)**
Evaluable Subjects: **36**
Median Prior Lines of Tx: **2**
ORR: **22%** vs. **0%**
Median 3M PFS: **44% vs. 22%**
Grade 3 TRAE's: **NA**
Write-Up: Link

agenus

Refractory Metastatic Sarcoma

Regimen: **Botensilimab / Balstilimab**
MOA: **CTLA4 / PD1**
Doses: **1 or 2mg/kg Q6W (Bot) / 3mg/kg Q2W (Bat)**
Evaluable Subjects: **41**
Median Prior Lines of Tx: **3**
ORR: **17%** | CR's: **2.5%**
Median Survival: **NA**
Grade 3 TRAE's: **12%**
Write-Up: Link

AMBRX

Metastatic Prostate Cancer (mCRPC)

Regimen: **ARX517**
MOA: **PSMA ADC**
Doses: **Cohorts 6 to 8 (2-2.88mg/kg, Phase 1)**
Evaluable Subjects: **23**
Prior Lines of Tx: **4**
PSA50: **52%**
Complete Response: **0%**
Grade 3 TRAE's (Ch 6 to 8): **12.5%**
Write-Up: Link

AMGEN

Advanced Prostate Cancer

Regimen: **Xaluritamig**
MOA: **STEAP T-cell engager**
Doses: **> .75mg QW**
Evaluable Subjects: **37 (53% metastatic, Phase 1)**
Prior Lines of Tx: **4**
ORR: **41%**
Complete Response: **0%**
PSA50: **59%**
Grade 3 TRAE's (all doses): **55%**
Write-Up: Link

Daiichi Sankyo Presents CDH6 ADC Data in Ovarian Cancer

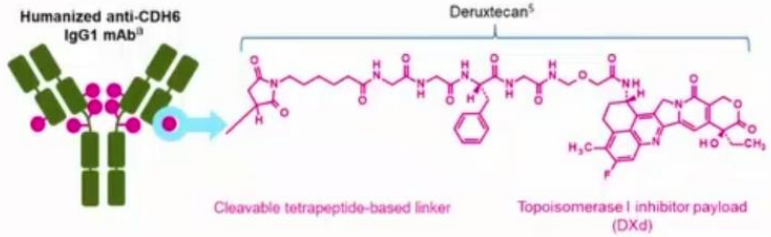
10:15 - 11:55 Mini oral session - Gynaecological cancers

CHAIRS : KOSEI HASEGAWA, ALEXANDRA LEARY, CHRISTIAN MARTH

Background

- The emergence of platinum resistance in recurrent OVC is inevitable; these patients have a clear need for novel treatments[1]
- Mirvetuximab soravtansine-gynx received accelerated approval from the FDA for the treatment of patients with platinum-resistant, FRα-positive OVC (ORR: 31.7%, median DOR: 6.9 months)[2]
- Expression of CDH6 is observed in ~65–85% of patients with OVC[3,4]
- Raludotatug deruxtecan (R-DXd; DS-6000) is a CDH6-directed ADC composed of three parts: a humanized anti-CDH6 IgG1 mAb, covalently linked to a topoisomerase I inhibitor payload via a tetrapeptide-based cleavable linker[5]

R-DXd was designed with 7 key attributes



Payload mechanism of action: topoisomerase I inhibitor[5,b]
High potency of payload[5,b]
High drug-to-antibody ratio ≈8[5,b]
Payload with short systemic half-life[6,b,c]
Stable linker-payload[5,b]
Tumor-selective cleavable linker[5,b]
Bystander antitumor effect[5,b]

[a]Image is for illustrative purposes only; actual drug positions may vary. [b]The clinical relevance of these features is under investigation. [c]Based on animal data.
ADC, antibody–drug conjugate; CDH6, cadherin 6; DOR, duration of response; DXd, deruxtecan; FDA, United States Food and Drug Administration; FRα, folate receptor alpha; IgG1, immunoglobulin G1; mAb, monoclonal antibody; ORR, objective response rate; OVC, ovarian cancer.

1. Richardson DL, et al. *JAMA Oncol*. 2023;9:851–859. 2. ELAHERE™ (mirvetuximab soravtansine-gynx) prescribing information. Accessed September 1, 2023. 3. Bartolomé RA, et al. *Mol Oncol*. 2021;15:1849–1865. 4. Shintani D, et al. *Gynecol Oncol*. 2022;166(Suppl. 1):S116. 5. Suzuki H, et al. *Ann Oncol*. 2021;32(Suppl. 5):S361–S375. 6. Nakada T, et al. *Chem Pharm Bull (Tokyo)*. 2019;67:173–185.

MADRID 2023 ESMO congress

Kathleen Moore

Kathleen Moore

Raludotatug deruxtecan (R-DXd; DS-6000) monotherapy in patients with previously treated ovarian cancer (OVC): Subgroup analysis of a first-in-human phase I study

MADRID 2023 ESMO congress

Valencia Auditorium - Hall 10

MADRID SPAIN **20-24 OCTOBER 2023**

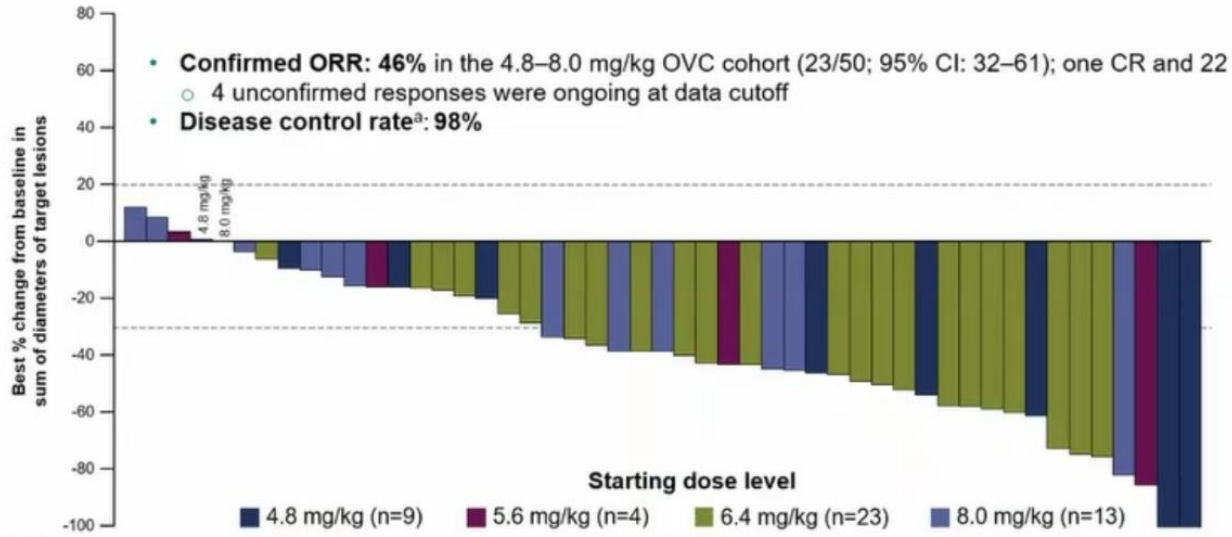
Daiichi Sankyo Presents CDH6 ADC Data in Ovarian Cancer

10:15 - 11:55 Mini oral session - Gynaecological cancers

CHAIRS : KOSEI HASEGAWA, ALEXANDRA LEARY, CHRISTIAN MARTH

Preliminary efficacy data for R-DXd are promising in pretreated OVC patients

- **Confirmed ORR: 46%** in the 4.8–8.0 mg/kg OVC cohort (23/50; 95% CI: 32–61); one CR and 22 PRs
  - 4 unconfirmed responses were ongoing at data cutoff
- **Disease control rate[a]: 98%**



Data cutoff: July 14, 2023.
[a]CR + PR + stable disease.

The efficacy evaluable population included patients who received ≥1 dose of study treatment and completed ≥1 post-baseline tumor assessment or discontinued treatment for any reason. Change from baseline in target tumor size was assessed per RECIST v1.1. Two patients with no measurable lesions at baseline and one patient who discontinued and did not have a post-baseline tumor assessment were not included in the waterfall plot.

CI, confidence interval; CR, complete response; ORR, objective response rate; OVC, ovarian cancer; PR, partial response; RECIST v1.1, Response Evaluation Criteria in Solid Tumors version 1.1.

MADRID 2023 ESMO congress

Kathleen Moore

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Raludotatug deruxtecan (R-DXd; DS-6000) monotherapy in patients with previously treated ovarian cancer (OVC): Subgroup analysis of a first-in-human phase I study

MADRID 2023 ESMO congress

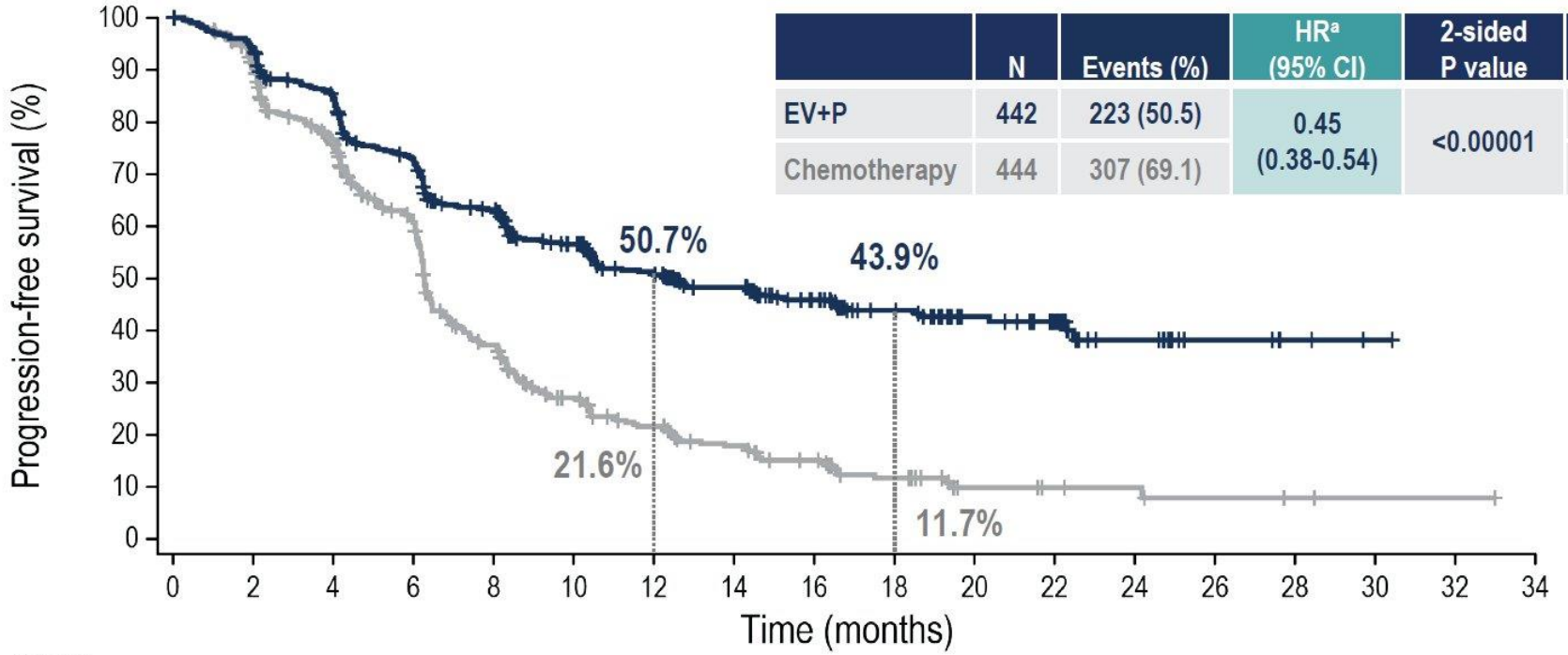
Valencia Auditorium - Hall 10

MADRID SPAIN **20-24 OCTOBER 2023**

PADCEV + Keytruda in 1L Urothelial Cancer versus Chemo

Progression-Free Survival per BICR

Risk of progression or death was reduced by 55% in patients who received EV+P



	N	Events (%)	HR[a] (95% CI)	2-sided P value	mPFS (95% CI), months
EV+P	442	223 (50.5)	0.45 (0.38-0.54)	<0.00001	12.5 (10.4-16.6)
Chemotherapy	444	307 (69.1)			6.3 (6.2-6.5)

N at risk

EV+P	442	409	361	303	253	204	167	132	102	73	45	33	17	6	3	1
Chemotherapy	444	380	297	213	124	78	56	41	30	19	8	6	5	3	2	1	1

Data cutoff: 08 Aug 2023

PFS at 12 and 18 months as estimated using Kaplan-Meier method
HR, hazard ratio; mPFS, median progression-free survival
[a]Calculated using stratified Cox proportional hazards model; a hazard ratio <1 favors the EV+P arm

MADRID 2023 ESMO congress

Powles et al.

ESMO: Seagen, Astellas and Merck Knock it Out of the Park with Padcev-Keytruda Combo in Bladder Cancer

FiercePharma, October 18, 2023 (excerpt)

Four weeks ago, Seagen and Astellas made waves when they revealed that the pairing of Padcev with Merck's oncology superstar Keytruda had achieved improved outcomes over standard of care in patients with previously untreated bladder cancer.

The report was a bit of a tease, however, as the companies did not put numbers to the claim. Those highly anticipated figures are now in for the EV-302 phase 3 trial, and they lend more credence to the idea that the combo has the potential to be "practice-changing," in the words last month of Seagen R&D chief Roger Dansey, M.D.

The results have been released ahead of the European Society for Medical Oncology (ESMO) Congress, which kicks off Friday in Madrid.

In the trial of 886 bladder cancer patients who were eligible for cisplatin or carboplatin-containing chemotherapy, the Keytruda-Padcev combination reduced the risk of death by 53% over chemo, according to a late-breaking ESMO abstract.

The median overall survival (OS) result for combo regimen patients was 31.5 months, compared to 16.1 months for those on chemotherapy.

The combo produced similar success in progression-free survival (PFS), reducing the risk of disease progression or death by 55%. Patients on the combo regimen lived a median of 12.5 months without progression, versus 6.3 months for the chemo arm.

Source: https://www.fiercepharma.com/pharma/esmo-2023-seagen-astellas-merck-knock-it-out-park-padcev-keytruda-data

Agenus' Botensilimab/Balstilimab Combination Delivers Durable Responses across Multiple Sarcoma Subtypes

Agenus Press Release, October 21, 2023

LEXINGTON, Mass.--(BUSINESS WIRE)--Agenus Inc. (Nasdaq:AGEN), a leader in developing novel immunological agents to treat various cancers, today announced expanded data from the company's phase 1b study of botensilimab (BOT, multifunctional immune activator) in combination with balstilimab (BAL, anti-PD-1) in patients with advanced sarcomas. The results were presented in an oral presentation at the European Society for Medical Oncology (ESMO) Congress 2023.

Efficacy in all comers (as measured by iRECIST; n=41)
•40% 6-month PFS
•20% ORR
- 29% ORR at the BOT 2 mg/kg dose level
- 15% ORR at the 1 mg/kg dose level

•63% disease control rate (best response of a complete response + partial response + stable disease)
•Median duration of response was 19.4 months
Safety in all comers (N=50)
•No new safety signals reported, with tolerability consistent across tumor types
•Adverse events were generally manageable and reversible
•Diarrhea/colitis was the most clinically significant immune-mediated adverse event
•No grade 4 or 5 treatment-related adverse events and no related cases of irreversible events such as hypophysitis, pneumonitis, hepatitis, or myocarditis were reported

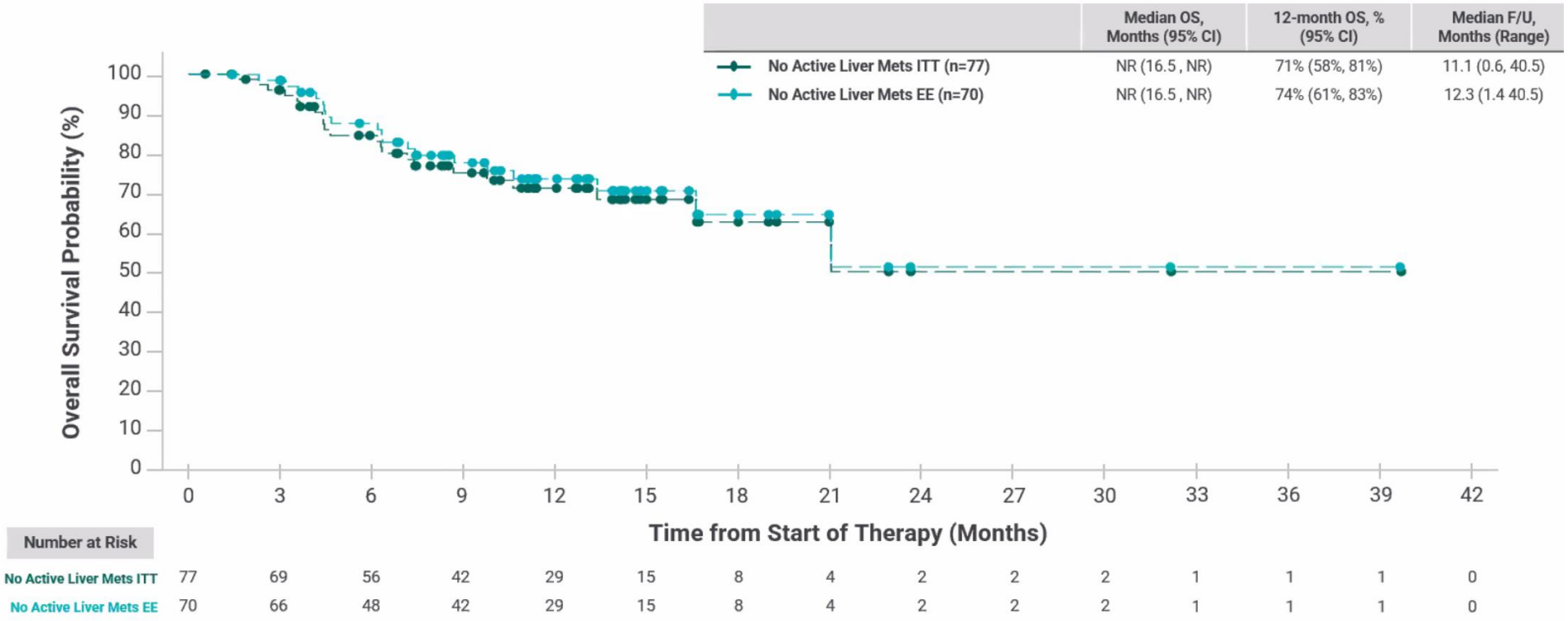
Source: https://www.businesswire.com/news/home/20231021037175/en/ESMO-2023-Agenus%E2%80%99-BotensilimabBalstilimab-Combination-Delivers-Durable-Responses-across-Multiple-Sarcoma-Subtypes

Agenus' Botensilimab Delivers Strong Survival in Colorectal Cancer

Agenus Presentation, October 22, 2023

Updated Clinical Data in Refractory MSS CRC

Confirmed ORR Rate: 24%
Median Follow-Up: 12.3 months



Source: Agenus Data (26SEPT2023); NR = Not Reached

agenus

Agenus Pursuing a Registrational Pathway in CRC

Rapid Development Pathway for BOT/BAL in 2/3L+ MSS CRC

Registration Strategy

- No active liver mets (clinical marker)
- Filing planned for midyear 2024
- Population: ~380 patients with MSS CRC
  - Ph. 1b (n~150)
  - Randomized Ph. 2 (n~230); enrollment completed
- Efficacy based on ~175 patients at each dose level (1 & 2) with reference SOC chemo and synthetic control (supportive survival)
- Results (in efficacy evaluable no active liver mets subpopulation):
  - ORR ~24% (95% CI, 15%, 36%)
  - Median OS not reached (95% CI, 16.5, not reached)
  - 12-month OS% 74% (95% CI, 61%, 83%)

Regulatory Engagement

US

- Fast Track designation **granted**
- Dose optimization **completed**
- Pediatric study plan **completed**
- FDA alignment on Phase 1L study as a confirmatory study **in progress**
- **Planned submission Midyear 2024**

Europe

- National advice from Denmark and Spain **completed**
- Pediatric study plan **in progress**
- Scientific advice from EMA **in progress**
- **Planned submission to EMA in 1H 2025**

Case Study: Recent Precedence for Accelerated Approval in Advanced mCRC

- Tucatinib & trastuzumab for HER2-positive mCRC
- Approval January 2023
- Efficacy based on 86 patients with ≥1 dose tucatinib + trastuzumab

Results:
- ORR of 38.1% (95% CI, 27.7, 49.3)
- Median DOR of 12.4 months (95% CI, 8.5, 20.5)
- OS of 24.1 months (95% CI, 20.3, 36.7)

Amgen Presents Tarlatamab Data (DLL BiTe) at ESMO

Tarlatamab Delivered an Encouraging Objective Response Rate of 40% and Median Overall Survival of 14.3 Months in Patients with Advanced SCLC

THOUSAND OAKS, Calif., Oct. 20, 2023 /PRNewswire/ -- Amgen (NASDAQ:AMGN) today announced results from the global Phase 2 DeLLphi-301 study, evaluating tarlatamab, an investigational delta-like ligand 3 (DLL3) targeting BiTE® (bispecific T-cell engager) molecule, in patients with advanced stage small cell lung cancer (SCLC) who had failed two or more prior lines of treatment. The data are being presented today at 3:20 PM CEST at a Proffered Paper session as a late-breaking oral presentation (LBA92) during the European Society for Medical Oncology (ESMO) Congress 2023 in Madrid, Spain, with publication in the New England Journal of Medicine.

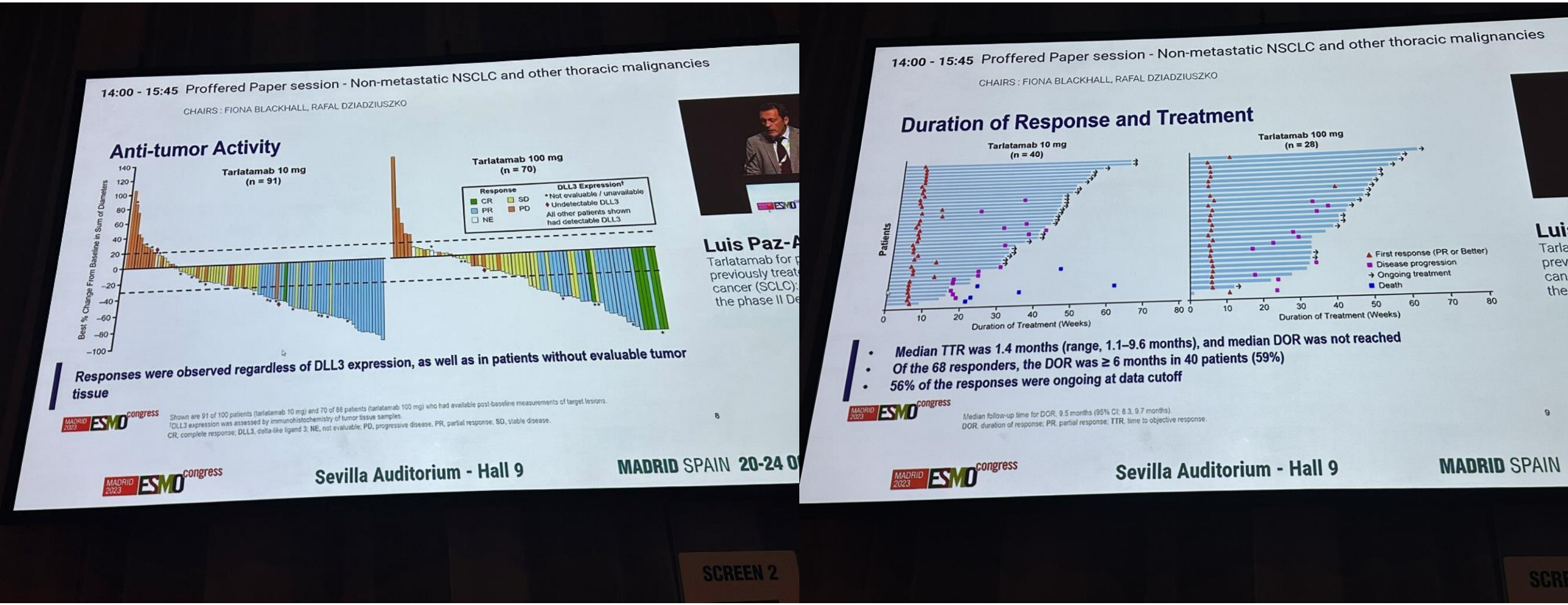
With a median follow-up of 10.6 months, an intention-to-treat analysis that included 100 patients at the selected 10 mg dose for tarlatamab demonstrated an objective response rate (ORR; primary endpoint) of 40% (97.5% Confidence Interval (CI): 29, 52). For key secondary endpoints, median progression-free survival (mPFS) was 4.9 months (95% CI: 2.9, 6.7) and median overall survival (mOS) was 14.3 months (95% CI: 10.8, NE). Median response duration was not reached. Of the patients who responded to treatment with tarlatamab at 10 mg dose, 58% experienced at least six months of response and 55% of responses were ongoing at data cutoff.

"Small cell lung cancer has represented one of the greatest challenges in cancer treatment, where there has been little progress against this deadly tumor type in decades," said David M. Reese, M.D., executive vice president of Research and Development at Amgen. "The tarlatamab results show the potential for this BiTE® molecule in a common solid tumor. We look forward to discussing these potentially registrational data with regulatory authorities."

There were no new safety signals observed compared to Phase 1 study. Discontinuations due to treatment-related adverse events (TRAEs) were infrequent (4%). The most common treatment-emergent adverse events (TEAEs) reported among patients in the tarlatamab 10 mg group, were cytokine release syndrome (CRS; 49%), pyrexia (38%), decreased appetite (25%) and dysgeusia (24%). CRS was largely confined to the first and second dose, predominantly grade 1 or 2 and were generally managed with supportive care. At the tarlatamab 10 mg dose, grade 3 CRS was low (0%) and grade 3 immune effector cell-associated neurotoxicity syndrome (ICANS) and associated neurologic events were not observed (0%). There were no reported grade 4 or 5 cases for either of these two adverse events.

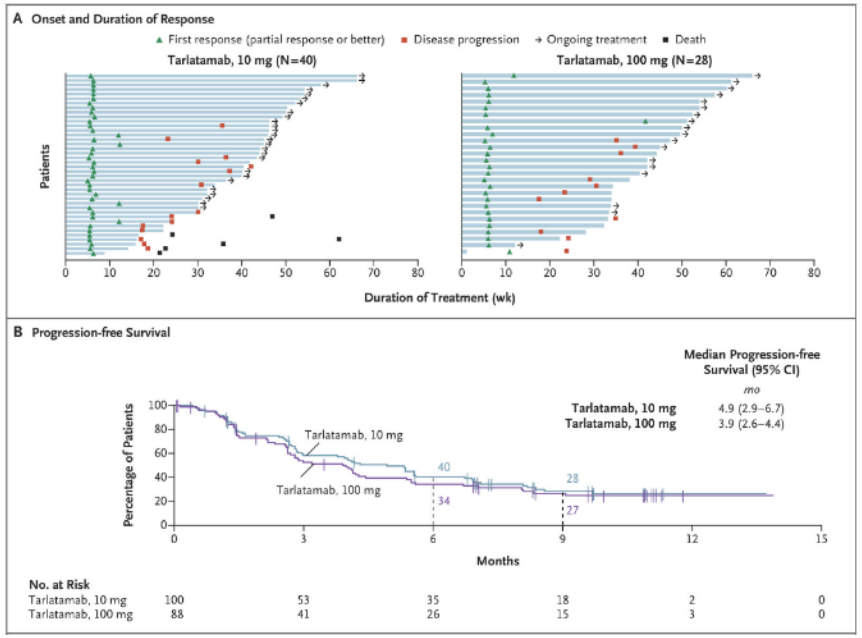
Source: https://www.amgen.com/newsroom/press-releases/2023/10/amgen-presents-new-tarlatamab-data-in-small-cell-lung-cancer

Tarlatamab Responses Deep and Durable

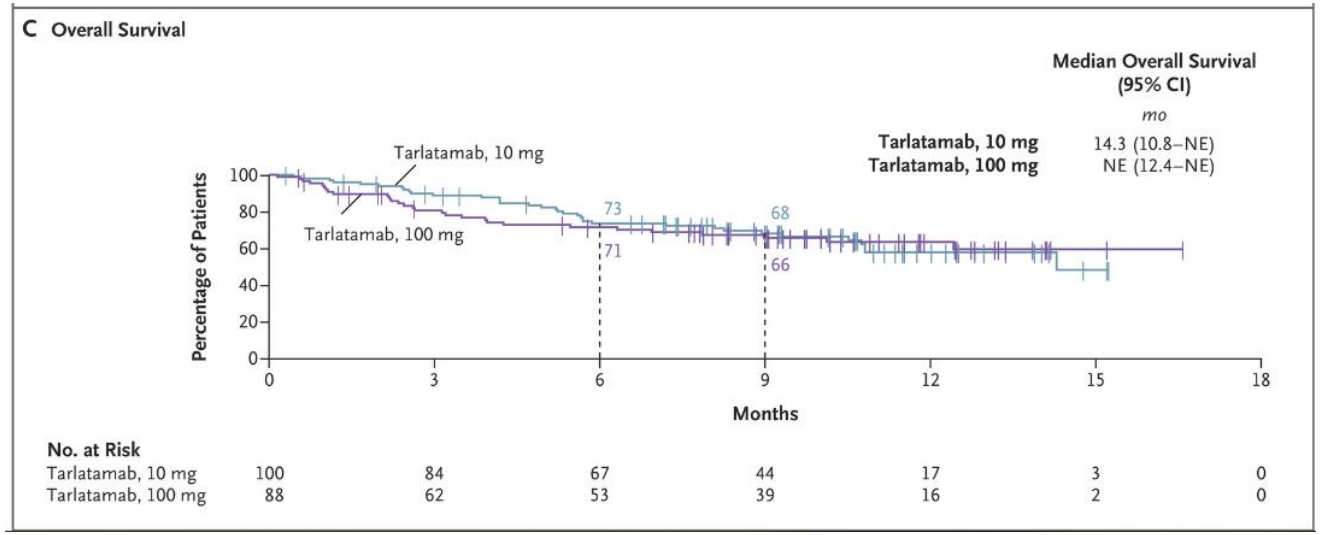


NEJM Publication: Tarlatamab for Patients with Previously Treated Small-Cell Lung Cancer

Ahn MJ, Cho BC, Felip E, Korantzis I, Ohashi K, Majem M, Juan-Vidal O, Handzhiev S, Izumi H, Lee JS, Dziadziuszko R, Wolf J, Blackhall F, Reck M, Bustamante Alvarez J, Hummel HD, Dingemans AC, Sands J, Akamatsu H, Owonikoko TK, Ramalingam SS, Borghaei H, Johnson ML, Huang S, Mukherjee S, Minocha M, Jiang T, Martinez P, Anderson ES, Paz-Ares L; DeLLphi-301 Investigators. Tarlatamab for Patients with Previously Treated Small-Cell Lung Cancer. *N Engl J Med*. 2023 Oct 20 (excerpt).

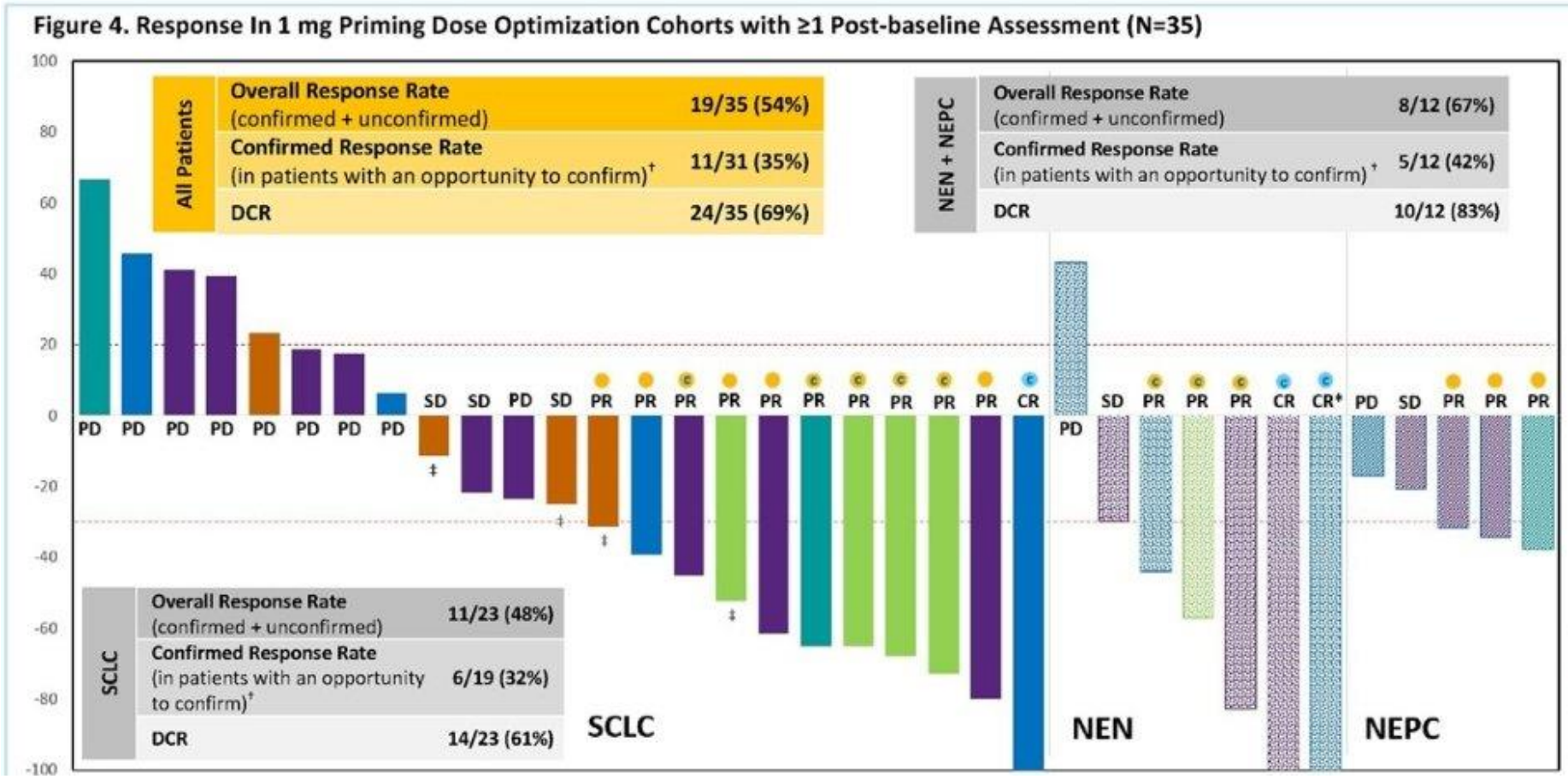


In this phase 2 DeLLphi-301 trial, tarlatamab had durable antitumor activity in patients with heavily pretreated small-cell lung cancer. The trial was designed to compare two active doses, which is consistent with the Food and Drug Administration Project Optimus initiative to reform the dose-optimization and dose-selection paradigm in the development of oncologic drugs. The 10-mg dose was selected for subsequent tarlatamab trials because it had a more favorable benefit-to-risk profile than the 100-mg dose, with an objective response in 40% of the patients and a median overall survival of 14.3 months (the median duration of response was not evaluable). The objective response of 40% far exceeded the historical control benchmark of 15% for the primary end point.



Source: https://pubmed.ncbi.nlm.nih.gov/37861218/

Harpoon Also Has DLL3 T-Cell Engager Data at ESMO



Confirmed ORR of 32% in SCLC with Harpoon's HPN328 is a little lower than the 40% we saw with the 10mg dose of Amgen's T-cell engager tarlatamab

Revolution Medicines Presents Promising Clinical Activity and Safety Data from Phase 1/1b Trial of RMC-6236 (Multi RAS Inhibitor)

REDWOOD CITY, Calif., Oct. 22, 2023 (GLOBE NEWSWIRE) -- Revolution Medicines, Inc. (Nasdaq: RVMD), a clinical-stage oncology company developing targeted therapies for RAS-addicted cancers, today announced promising anti-tumor and safety data for RMC-6236, its RASMULTI(ON) Inhibitor, in patients with previously treated non-small cell lung cancer (NSCLC) and pancreatic ductal adenocarcinoma (PDAC) across several dose levels and KRASG12X genotypes, including common KRAS-mutant genotypes G12D and G12V. These initial results were presented during a Proffered Paper session at the European Society for Medical Oncology (ESMO) Congress in Madrid, October 20-24, 2023.

The RMC-6236-001 Phase 1/1b trial is a multicenter, open-label, dose-escalation and dose-expansion study designed to evaluate RMC-6236 as monotherapy in patients with advanced solid tumors harboring KRASG12X mutations. As of an October 12, 2023 data extraction, a total of 111 patients with NSCLC (n=46) or PDAC (n=65) were treated at dose levels administered once daily (QD) ranging from 80 mg to 400 mg. Common KRAS mutations in patients evaluated included G12D, G12V, G12R, G12A and G12S; patients with KRASG12C mutations were excluded from the study due to the availability of currently approved KRASG12C(OFF) inhibitors. All patients had previously been treated with standard of care appropriate for tumor type and stage. Patients with NSCLC had received a median of two prior lines of therapy (range 1–6) while patients with PDAC had received a median of three prior lines of therapy (range 1–7).

RMC-6236 demonstrated preliminary evidence of clinical activity and an acceptable safety profile that was generally well tolerated across the dose levels analyzed. Clinical activity was evaluated in patients who had received the first dose of RMC-6236 at least eight weeks prior to the data extraction date (n=86). **Among the 40 efficacy evaluable NSCLC patients, the objective response rate was 38 percent, with one patient achieving a complete response (CR) as a best response and 14 patients achieving a partial response (PR) (including three unconfirmed PRs).** The disease control rate (DCR) in this NSCLC population was 85 percent. **Among the 46-efficacy evaluable PDAC patients, the objective response rate was 20 percent, with nine patients achieving a PR (including four unconfirmed PRs) as a best response.** The DCR in this PDAC population was 87 percent. Confirmed objective responses included tumors harboring KRAS mutations G12D, G12V or G12R, and disease control was observed across all KRAS mutations, including G12A and G12S.

The most common treatment-related adverse events (TRAEs) were rash and GI-related toxicities that were primarily Grade 1 or 2 in severity. The reported Grade 3 TRAEs were rash (6%), stomatitis (2%), and diarrhea (1%). One previously reported Grade 4 TRAE occurred in a patient with PDAC at the 80 mg QD dose level who had a large intestine perforation at the site of an invasive tumor that reduced in size while on treatment, which resulted in treatment discontinuation. No safety signals were observed that indicated an elevated risk of hepatotoxicity, which has been reported for some KRASG12C(OFF) inhibitors.

Source: https://ir.revmed.com/news-releases/news-release-details/revolution-medicines-presents-promising-clinical-activity-and

GSK Jemperli® (Dostarlimab) Shines in Head to Head Study in NSCLC vs. Keytruda®

GSK Press Release, October 17, 2023

GSK will share updates from the PERLA trial evaluating dostarlimab plus chemotherapy versus pembrolizumab plus chemotherapy in the first-line treatment of metastatic non-squamous NSCLC. Expanding upon the primary data presented at the ESMO Immuno-Oncology Congress 2022, late-breaking results at ESMO 2023 (LBA64) will highlight a positive numerical trend in OS outcomes, favouring dostarlimab plus chemotherapy vs. pembrolizumab plus chemotherapy. The PERLA phase II trial is a randomised, double-blind trial of 243 patients and is the largest global head-to-head trial of programmed death receptor-1 (PD-1) inhibitors in this patient population.

In the PERLA trial, the median OS for patients receiving dostarlimab plus chemotherapy was 19.4 months (95% CI: 14.5-NR) versus 15.9 months (95% CI: 11.6-19.3) for patients receiving pembrolizumab plus chemotherapy, after a median follow-up of 20.7 months (17.3-24.0) and 21.6 months (18.3-24.1), respectively (HR: 0.75: [95% CI: 0.53-1.05]). An additional analysis with greater OS maturity is planned and will be reported at a later date. Safety profiles in this secondary analysis were similar and consistent with those previously reported in the primary analysis for the PERLA trial.

Data from PERLA supports the company's ambition for dostarlimab to become its backbone immuno-oncology therapy when used alone and in combination with standard of care and future novel cancer therapies.

Source: https://www.gsk.com/en-gb/media/press-releases/gsk-highlights-new-data-in-non-small-cell-lung-cancer-and-endometrial-cancer-at-esmo/

Ambrx PSMA ADC (ARX517): Impressive Data in Prostate Cancer at ESMO

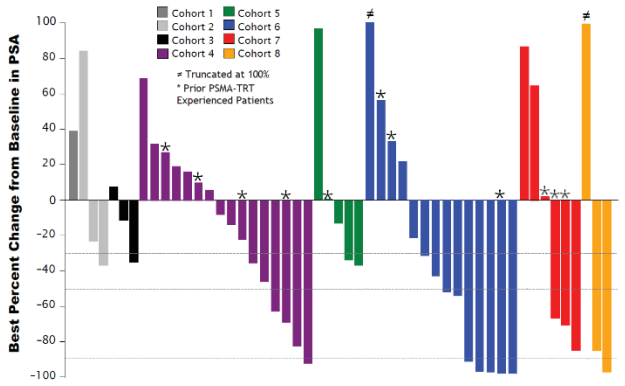
Updated Safety, Efficacy and PK Data from On-going Phase 1 / 2 Trial APEX-01 (NCT04662580)

2023 European Society for Medical Oncology

October 22, 2023

AMBRX

PSA Reductions Deepened as Dose Levels Increased, Demonstrating a Dose-Dependent PSA Reduction



25% of patients (4/16) at 1.4 mg/kg (Cohort 4) experienced a >50% PSA reduction

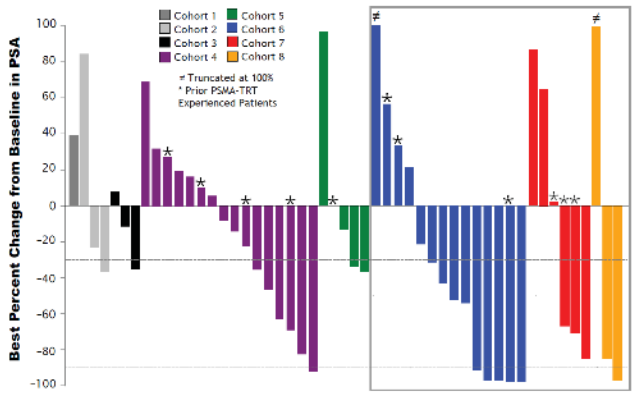
50% of patients (7/14) at 2.0 mg/kg (Cohort 6) experienced a >50% PSA reduction

On going and next steps:
Expansion of Cohort 8 (2.88 mg/kg)
Escalate to next higher dose Cohort 9 (3.4 mg/kg)

AMBRX

PSA waterfall includes patients with at least two on-treatment PSA assessments or discontinued before the second assessment. Prior to reaching MTD, two dose cohorts (4 and 6) were expanded based on three criteria: 1) PSA decline of ≥50% 2) no treatment-related SAEs 3) target lesion reduction or RECIST v1.1 response.

PSA Reduction Observed in Patients with Prior PSMA-Targeted Radionuclide Therapy (PSMA-TRT) – 50% (3/6) at doses ≥2.0 mg/kg



"Patients with late stage mCRPC have few effective systemic therapy options; the data from APEX-01 study show very promising PSA declines as well as ctDNA reductions, all pointing in the right direction. Based on the safety and preliminary efficacy data presented in the poster, I believe this drug is worthy of further development."

Dr. Oliver Sartor, medical oncologist and translational researcher with a special focus on prostate cancer over the past 33 years

*Prior PSMA-TRT Experienced Patients

PSA 50% reduction achieved in patients who had prior PSMA-TRT:

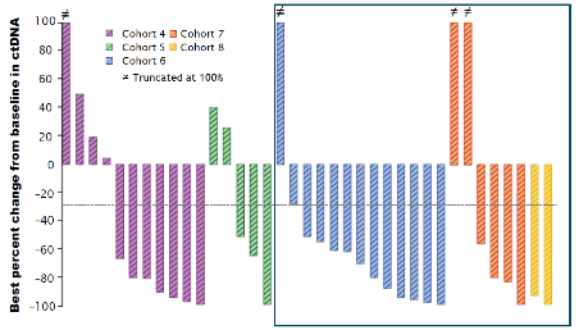
- 37% (4/11) at doses ≥1.4 mg/kg
- 50% (3/6) at doses ≥2.0 mg/kg

AMBRX

PSA waterfall includes patients with at least two on-treatment PSA assessments or discontinued before the second assessment. Prior to reaching MTD, two dose cohorts (4 and 6) were expanded based on three criteria: 1) PSA decline of >50% 2) no treatment-related SAEs 3) target lesion reduction or RECIST v1.1 response.

81% (17/21) of Patients Experienced ≥50% PSA Reduction in Circulating Tumor DNA (ctDNA)

On treatment changes in ctDNA have been shown to predict time to progression and survival [1,2]



Circulating tumor DNA (ctDNA) decline correlates with PSA reduction
Both biomarkers have been associated with longer PFS and OS

Serial plasma samples were collected at baseline, C3D1, C4D1 and EOT. ctDNA was measured using GuardantINFINITY test (Guardant Health) with a specificity of 99.9%, a sensitivity of 91.3% and a reported lower limit of detection 0.08%. Samples were processed after passing multiple quality control measurements encompassing DNA yield, QC loss, methylation loss, diversity, and contamination checks. ctDNA changes compared with its baseline level were measured based on aggregated tumor-specific methylation signal scores.

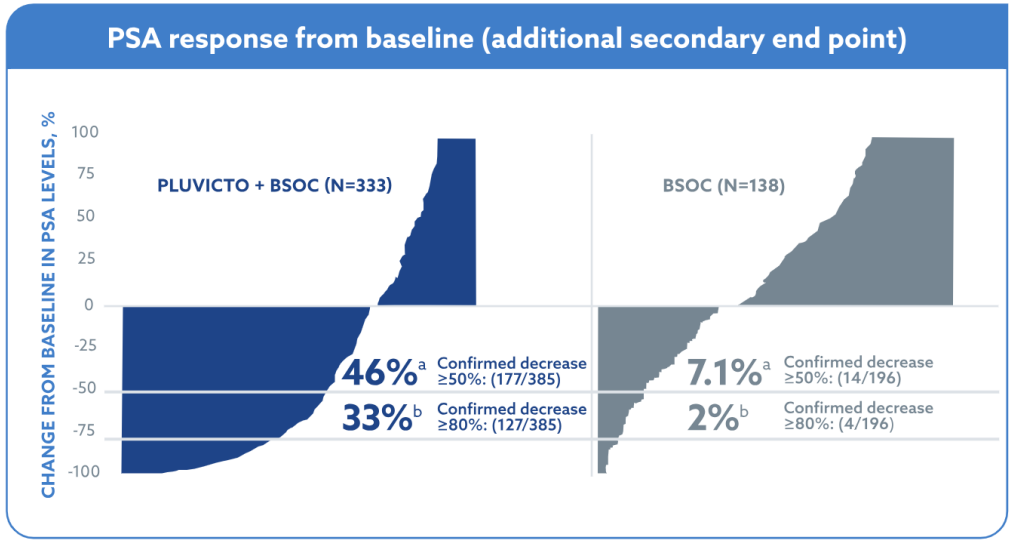
1. Tolmeijer SH et al. Clin Cancer Res. 2023 Aug 1;29(15):2835-2844. doi: 10.1158/1078-0432.CCR-22-2908.
2. Sartor O. Clin Cancer Res. 2023 Aug 1;29(15):2745-2747. doi: 10.1158/1078-0432.CCR-23-1043.

AMBRX

Ambrx ARX517 Appears Competitive with Novartis' PLUVICTO®

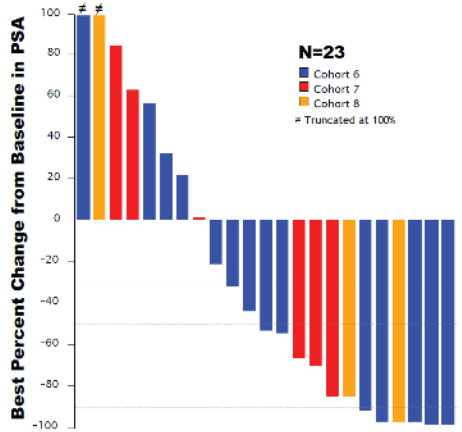
The Ambrx ADC approach avoids the need for generating and supplying radionucleotide and is potentially far more easily accessed by community oncologists.

PLUVICTO®
lutetium Lu 177 vipivotide tetraxetan
INJECTION FOR INTRAVENOUS USE



vs.

52% (12/23) of Patients Experienced ≥50% PSA reduction at 2.0 – 2.88 mg/kg in Patients Who Have Exhausted Available and Appropriate Treatment Options



	Cohort 6 (n = 14)	Cohort 7 (n = 6)	Cohort 8 (n = 3)	Cohorts 6-8 (n=23)
≥30% PSA	64%	50%	67%	61%
≥50% PSA	50%	50%	67%	52%
≥90% PSA	36%	0	33%	26%

"The PSA results are very encouraging, especially in this heavily pre-treated patient population where eligible patients would have exhausted most available and appropriate treatment options prior to enrolling in this study."

Dr. John Shen, medical oncologist and investigator on APEX-01

AMBRX | ESMO Congress 2023 9

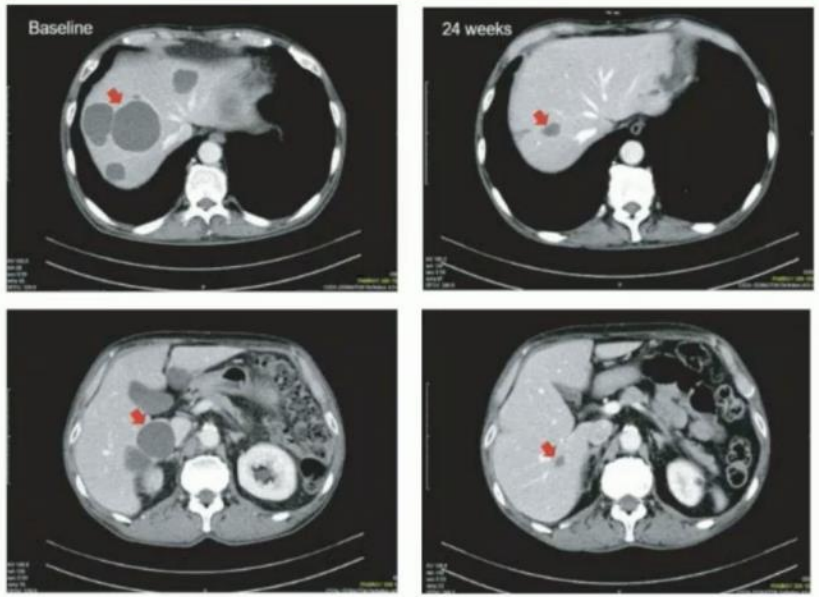
Sources: https://ir.ambrx.com/news/news-details/2023/ESMO-2023-Posters-and-ARX517-Slide-Deck-Available-Here/default.aspx, https://www.hcp.novartis.com/products/pluvicto/psma-positive-mcrpc/efficacy/

Amgen Shares Impressive Early Prostate Cancer Data for Xaluritamig, a STEAP T-Cell Engager

Anti-tumor activity has been observed against both soft tissue and bone disease

CT Scan

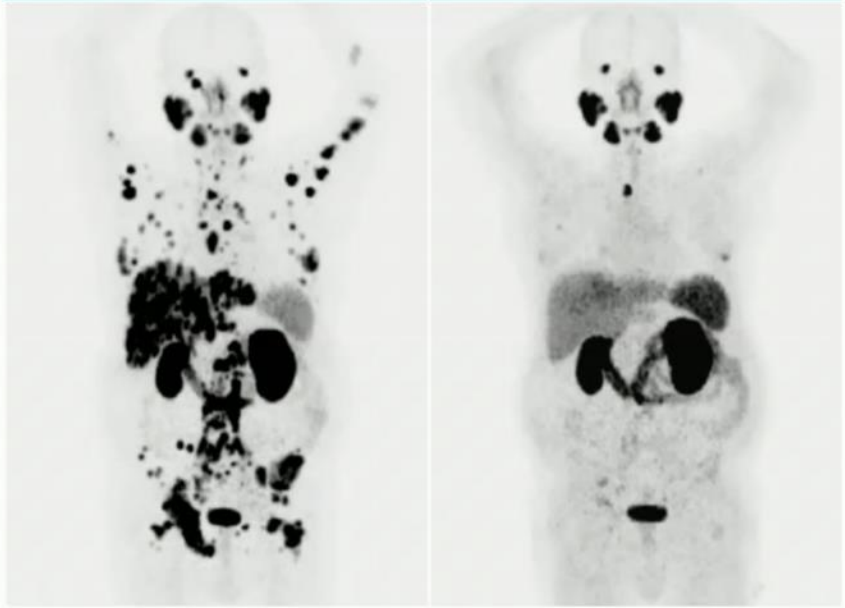
Baseline	Week 24



65-year-old heavily pre-treated patient with mCRPC. Patient was enrolled in cohort 11 and achieved a confirmed RECIST and PSA90 response.

PSMA PET Imaging

Baseline	Week 12



56-year-old heavily pre-treated patient with mCRPC. Patient was enrolled in cohort 12 and achieved a confirmed PSA90 response (not RECIST evaluable).

MADRID 2023 ESMO congress

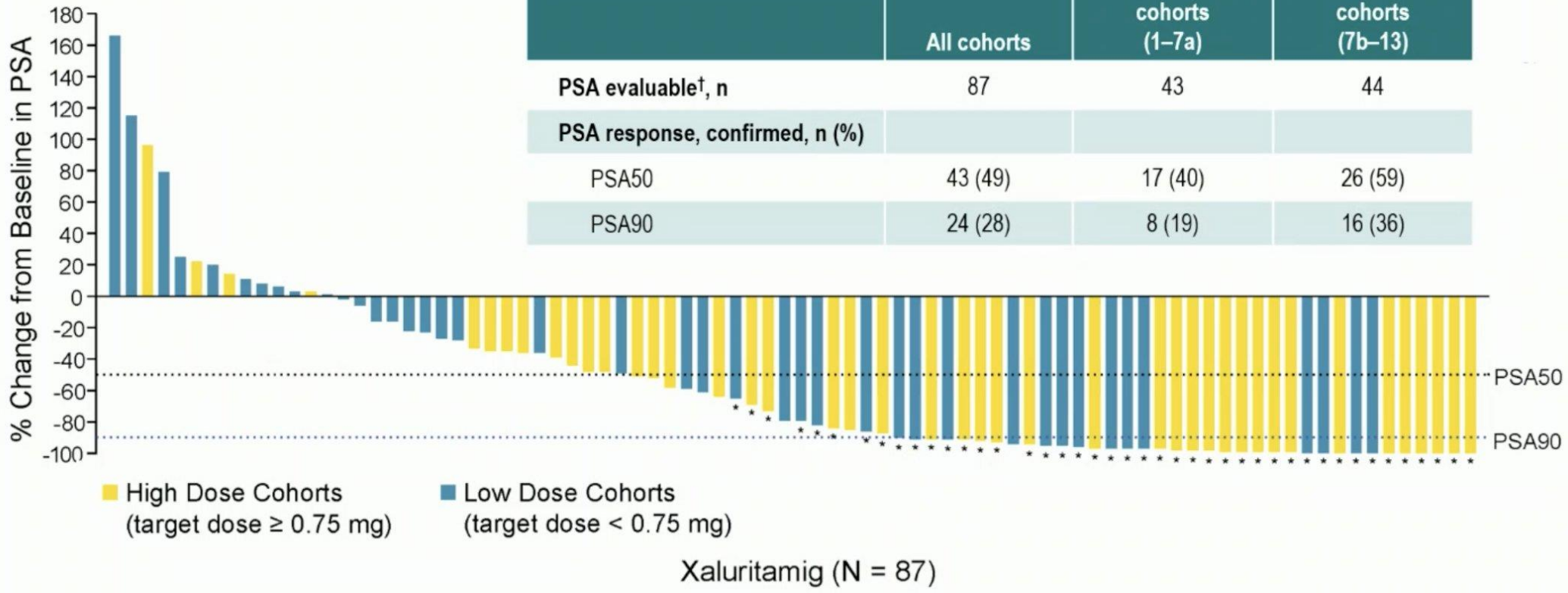
CT, computerized tomography; mCRPC, metastatic castration-resistant prostate cancer; PSA, prostate specific antigen; PSMA PET, prostate-specific membrane antigen positron emission tomography scan; RECIST, Response Evaluation Criteria in Solid Tumors.

At ESMO, Dr. William Kelly presented the results of a phase 1 trial with AMG-509 (xaluritamig), a new STEAP-CD3 engager immunotherapy for heavily pre-treated metastatic prostate cancer patients.

Amgen Xaluritamig, a STEAP T-Cell Engager, Achieves PSA50 49% of Time

Confirmed PSA responses were observed across cohorts

	All cohorts	Low dose cohorts (1–7a)	High dose cohorts (7b–13)
PSA evaluable†, n	87	43	44
PSA response, confirmed, n (%)			
PSA50	43 (49)	17 (40)	26 (59)
PSA90	24 (28)	8 (19)	16 (36)



MADRID 2023 ESMO congress

*Confirmed PSA responders of PSA50 or better.
†10 patients were not PSA evaluable: 6 patients were missing baseline PSA values, and 4 patients did not have sufficient follow-up duration.
PSA, prostate specific antigen.

Amivantamab Plus Lazertinib vs Osimertinib as First-line Treatment in Patients with EGFR-mutated, Advanced Non-small Cell Lung cancer (NSCLC): Primary Results From MARIPOSA, a Phase III, Global, Randomized, Controlled Trial

Apar Kishar Ganti, MD, *ESMO 2023 Preview*, Oct 19, 2023 (excerpt)

Apar Ganti, Univ. Nebraska

"The most exciting abstract in my mind is the [one on the] MARIPOSA trial, which is looking at a combination of amivantamab, which is currently approved for EGFR exon 20 insertion mutations, and lazertinib," Ganti said. "This combination is being compared with the current standard-of-care [SOC] for first-line patients with EGFR-mutated lung cancer, osimertinib. The results of that are exciting because if the combination is shown to be better than osimertinib, then that could very well become the new SOC for [these] patients."

The open-label, randomized, phase 3 MARIPOSA trial (NCT04487080) enrolled patients with locally advanced or metastatic non–small cell lung cancer (NSCLC) harboring EGFR mutations and randomized them to 1 of 3 arms. In arm A, patients received 1050 mg of intravenous (IV) amivantamab-vmjw (Rybrevant; for those with a bodyweight <80 kg) or 1400 mg of IV amivantamab (for those with a bodyweight ≥ 80 kg) once weekly in cycle 1 with a split dose on days 1 and 2, followed by once every 2 weeks in subsequent cycles, plus 240 mg of oral lazertinib (Leclaza) once per day. In the control group (arm B), patients received 80 mg of oral osimertinib once per day plus a matching lazertinib placebo once per day. In the other experimental group (arm C), patients received 240 mg of lazertinib once per day plus a matching osimertinib placebo once per day.

The doublet was found to significantly improve progression-free survival (PFS) vs osimertinib (Tagrisso) in this population, and the planned interim analysis showed an overall survival (OS) trend favoring amivantamab plus lazertinib.1 Detailed data, including secondary end point findings, will be presented at the meeting.

"[MARIPOSA] is also potentially practice-changing for [patients with] EGFR-mutated NSCLC patients who have progressed on osimertinib," Wakelee said.

Sources: https://www.onclive.com/view/esmo-2023-experts-preview-anticipated-data-spanning-tumor-types, https://www.prnewswire.com/news-releases/landmark-phase-3-mariposa-study-meets-primary-endpoint-resulting-in-statistically-significant-and-clinically-meaningful-improvement-in-progression-free-survival-for-rybrevant-amivantamab-vmjw-plus-lazertinib-versus-osimertinib--301941646.html

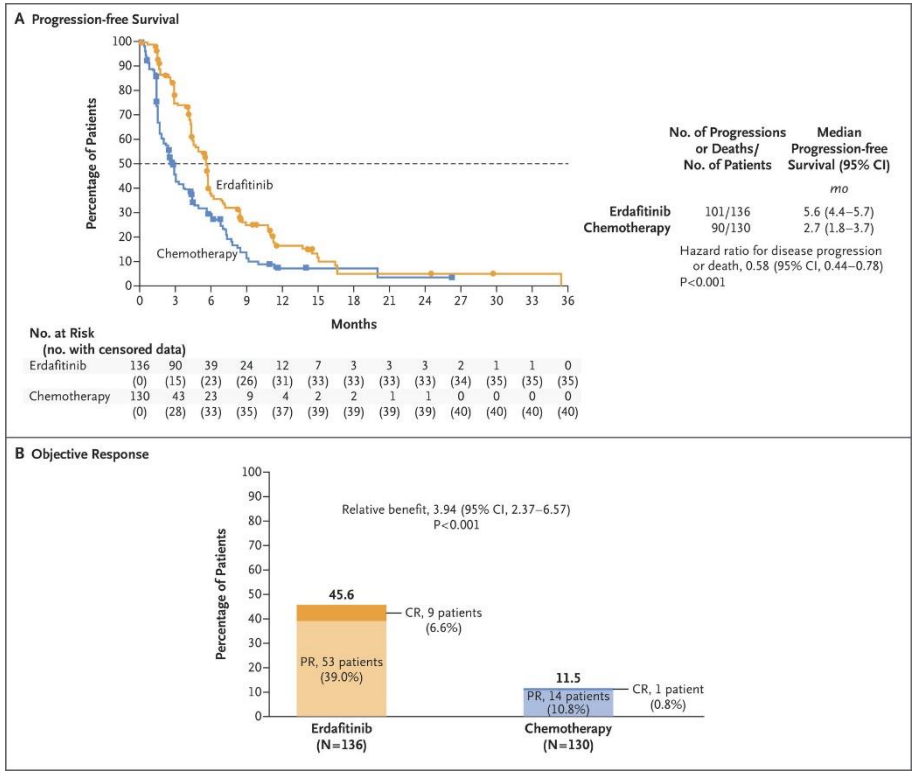
Erdafitinib or Chemotherapy in Advanced or Metastatic Urothelial Carcinoma

Loriot et.al., *N Engl J Med. Oct 21, 2023*

Erdafitinib is a pan–fibroblast growth factor receptor (FGFR) inhibitor approved for the treatment of locally advanced or metastatic urothelial carcinoma in adults with susceptible FGFR3/2 alterations who have progression after platinum-containing chemotherapy. The effects of erdafitinib in patients with FGFR-altered metastatic urothelial carcinoma who have progression during or after treatment with checkpoint inhibitors (anti–programmed cell death protein 1 [PD-1] or anti–programmed death ligand 1 [PD-L1] agents) are unclear.

We conducted a global phase 3 trial of erdafitinib as compared with chemotherapy in patients with metastatic urothelial carcinoma with susceptible FGFR3/2 alterations who had progression after one or two previous treatments that included an anti–PD-1 or anti–PD-L1. Patients were randomly assigned in a 1:1 ratio to receive erdafitinib or the investigator's choice of chemotherapy (docetaxel or vinflunine). The primary end point was overall survival.

A total of 266 patients underwent randomization: 136 to the erdafitinib group and 130 to the chemotherapy group. The median follow-up was 15.9 months. The median overall survival was significantly longer with erdafitinib than with chemotherapy (12.1 months vs. 7.8 months; hazard ratio for death, 0.64; 95% confidence interval [CI], 0.47 to 0.88; P=0.005). **The median progression-free survival was also longer with erdafitinib than with chemotherapy (5.6 months vs. 2.7 months; hazard ratio for progression or death, 0.58; 95% CI, 0.44 to 0.78; P<0.001).** The incidence of grade 3 or 4 treatment-related adverse events was similar in the two groups (45.9% in the erdafitinib group and 46.4% in the chemotherapy group). Treatment-related adverse events that led to death were less common with erdafitinib than with chemotherapy (in 0.7% vs. 5.4% of patients).



Source: https://www.nejm.org/doi/full/10.1056/NEJMoa2308849

Exact Sciences Advances Early Cancer Detection and Precision Oncology Programs With Data Presentations at ESMO

MADISON, Wis., October 20, 2023 – Exact Sciences Corp. (NASDAQ: EXAS), a leading provider of cancer screening and diagnostic tests, today announced it will present new data supporting the company's research in early cancer detection, genomic testing, and treatment guidance at the 2023 European Society for Medical Oncology (ESMO) Congress, October 20-24, in Madrid, Spain.

Exact Sciences will feature studies from across its multi-cancer early detection (MCED) and precision oncology portfolios, highlighting:

1. Two trials evaluating the company's blood-based, MCED program
2. OncoExTra™ data showing the frequency of the detection of actionable fusions, signals of some cancers, in nearly 8,000 people with solid tumors, helping inform treatment decisions by using next-generation sequencing (NGS) to assess a tumor's RNA and DNA

"At Exact Sciences, we are driving paradigm shifts in the early detection and treatment of cancer," said Jorge Garces, Ph.D., chief science officer, Exact Sciences. "With continued advances in understanding tumor biology and the precise identification of actionable biomarkers, our screening and diagnostic tools are improving the lives of people living with or at risk for cancer today – and are poised to transform the cancer landscape in the future."

Cancerguard™

Exact Sciences is taking a robust and rigorous approach to developing an MCED test, and today unveiled its brand name, Cancerguard. Building upon decades of research, Exact Sciences is designing the Cancerguard test to harness the additive sensitivity of multiple biomarker classes to detect more early-stage cancers. The Cancerguard test will utilize a streamlined and standardized imaging-based diagnostic pathway, resulting in fewer follow-up procedures. The test is being developed to provide high specificity to help minimize false positives, while detecting multiple cancers, including those with the biggest impact on human health.

Source: https://www.exactsciences.com/newsroom/press-releases/Exact%20Sciences%20Advances%20Early%20Cancer%20Detection%20and%20Precision%20Oncology%20Programs%20with%20Data%20Presentations%20at%20ESMO%202023%20Annual%20Congress

Design and enrollment for a classifier development study for a blood-based multi-cancer early detection (MCED) test

Christopher Douville,[1] Larson Hogstrom,[2] Vladimir Gainullin,[2] Hee Jung Hwang,[2] Sudhir Chowbina,[2] Yongqiang Zhang,[2] Melissa Gray,[2] Christopher L Nobles,[2] Madhav Kumar,[2] Mael Manesse,[2] Fanglei Zhuang,[2] Vuna Fa,[2] Xi Chen,[2] Jorge Garces,[2] Abigail McElhinny,[2] Gustavo C Cerqueira,[2] Gerard A. Silvestri,[3] Seema Rego,[2] Tomasz M. Beer,[2] Frank Diehl[2]*

[1]Johns Hopkins University, Baltimore, MD, [2]Exact Sciences Corporation, Madison, WI, [3] Medical University of South Carolina, Charleston, SC

MADRID 2023 ESMO congress FPN 189P

Background

The aim of the Ascertaining Serial Cancer patients to Enable New Diagnostic 2 (ASCEND 2) study is to develop a classifier algorithm for a refined version of a multi-analyte blood-based MCED test.

Here, we report the study design, enrollment, and sample selection from the ASCEND-2 study.

Study Design

ASCEND 2 is a multi-center, prospective, case-control study of clinically characterized participants.

One hundred fifty-one sites within the US and Europe were engaged for subject enrollment.

Samples consisted of blood collected using LBgard® tubes for plasma and buffy samples.

The study population includes male and female subjects ≥50 years old with known cancer, suspicion of cancer, and controls without suspicion of cancer. All subjects provided informed consent and were assessed for study participation eligibility.

Enrollment

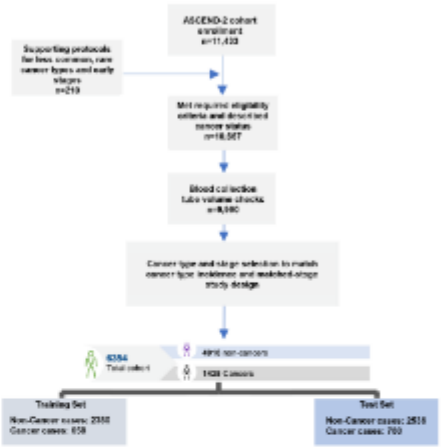
Over 11,000 subjects were enrolled in this study.

A subset of 6354 samples was selected to develop and refine a multi-analyte cancer detection classifier. The subset includes 1438 cancer subjects, from 21 organ sites (Enrollment and SEER Incidence Table) reflective of US cancer incidence by tumor type[1], and 4916 age-matched subjects without suspicion of cancer. Demographics are reported in the Demographics Table.

Relative to SEER incidence, the study enriched for lung cancers. Similarly, breast and prostate cancers were de-prioritized. These adjustments reflect cfDNA shedding rates and the expected clinical utility for MCED in these cancer types[2,3,4].

Cancer types were selected in approximately equal proportions for stage I-IV to power cancer staging performance assessment.

Study Enrollment Diagram



Allocation to training and testing sets:
The samples were partitioned into training and independent test sets. The performance of one or more locked cancer detection models developed in the training phase will be tested.
Cancer types with enrollment below incidence targets were allocated to the test set over the training set.
A subset of participants enrolled at unique sites were included in the test set but not the training set.

Demographics Table

Variable	Training Set (N=3,046)	Test Set (N=3,316)
Non-Cancer cases	2,388	2,536
Cancer Cases	658	780
Age (years)		
Mean (SD)	65.3 (8.3)	65.8 (8.4)
Sex, n (%)		
Female	1,705 (56.1%)	1,871 (56.4%)
Male	1,333 (43.9%)	1,445 (43.6%)
Race, n (%)		
White	2,467 (81.2%)	2,724 (82.1%)
Black/African American	410 (13.5%)	407 (12.3%)
Asian	110 (3.6%)	93 (2.8%)
American Indian/Alaskan Native	12 (0.4%)	17 (0.5%)
Native Hawaiian or Other Pacific Islander	3 (0.1%)	3 (0.1%)
Multiracial	4 (0.1%)	8 (0.2%)
Unknown*	32 (1.1%)	63 (1.9%)
Ethnicity, n (%)		
Hispanic/Latino	416 (13.7%)	412 (12.4%)
Not Hispanic/Latino	2,592 (85.1%)	2,893 (87.3%)
Unknown*	38 (1.2%)	51 (1.5%)
Region, n (%)		
Midwest	612 (20.1%)	576 (17.4%)
Northeast	405 (13.3%)	428 (12.9%)
South	1,328 (43.7%)	1,781 (53.7%)
West	683 (18.6%)	510 (15.4%)
Outside US	105 (3.5%)	56 (1.7%)
Unknown	23 (0.8%)	15 (0.5%)
Cigarette Smoking Status,** n (%)		
Current	29 (1.0%)	39 (1.1%)
Former	25 (0.8%)	37 (1.1%)
Never	2,978 (98.0%)	3,235 (97.8%)
Unknown*	6 (0.2%)	7 (0.2%)
Cancer Stage, n (%)		
Stage I	199 (30.2%)	197 (25.3%)
Stage II	127 (19.3%)	171 (21.9%)
Stage III	182 (27.7%)	189 (24.7%)
Stage IV	136 (20.7%)	183 (23.5%)
Unknown*	14 (2.1%)	39 (4.8%)

*Participants with missing/unknown information are grouped under Unknown category. ** Self-reported smoking status.

Training and test set demographics represented a racially, ethnically, and geographically diverse cohort

Enrollment and SEER Incidence[1]

Cancer Type	% of total (number of samples)	Normalized SEER Incidence %*
anus	1.0% (28)	0.6%
bladder and urinary	4.5% (65)	3.0%
Breast*	11.5% (165)	17.2%
cervix uteri	1.5% (22)	0.6%
colon and rectum	11.2% (161)	9.9%
esophagus	3.7% (53)	1.3%
head and neck	5.4% (78)	4.3%
kidney	5.6% (80)	4.6%
liver and bile duct	3.5% (50)	2.9%
lung and bronchus**	24.2% (340)	15.6%
multiple myeloma***	0.1% (1)	2.8%
non-Hodgkin's lymphoma***	0.6% (9)	5.0%
ovary	2.5% (37)	1.4%
pancreas	5.3% (76)	3.8%
Prostate*	4.6% (66)	17.5%
small intestine	0.8% (12)	0.7%
stomach	4.0% (58)	1.6%
testis	0.1% (2)	0.1%
thyroid	1.7% (25)	2.3%
uterus	5.6% (81)	4.2%
vulva	1.5% (21)	0.4%

* Normalized SEER proportions are adjusted to account only cancer types included in this study. Values do not account for incidence of 7 rare cancer types tracked in SEER but not this study. *Breast and prostate selection was de-prioritized due to low expected cfDNA shedding. **Lung and bronchus cancer selection was enriched because of high expected cfDNA shedding and potential clinical utility. ***Hematological cancer cases were lower than SEER incidence rates due to a lower-than-expected enrollment rate.

Target enrollment, including rare cancers, (based on SEER incidence rates) was achieved for most cancer types

The ASCEND 2 study selected cancer types in an incidence-targeted manner, including rare and common cancers and evenly distributed stages

The ASCEND-2 study represents a racially, ethnically, and geographically diverse cohort for MCED test development

*Corresponding author: fdiehl@exactsciences.com

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3. Dao J, et al. *International Journal of Molecular Sciences* 2023 Vol. 24 Issue 17 Pages 13219.
4. Shen H, et al. *BMC Medicine* 2022 Vol. 20 Issue 1 Pages 480.

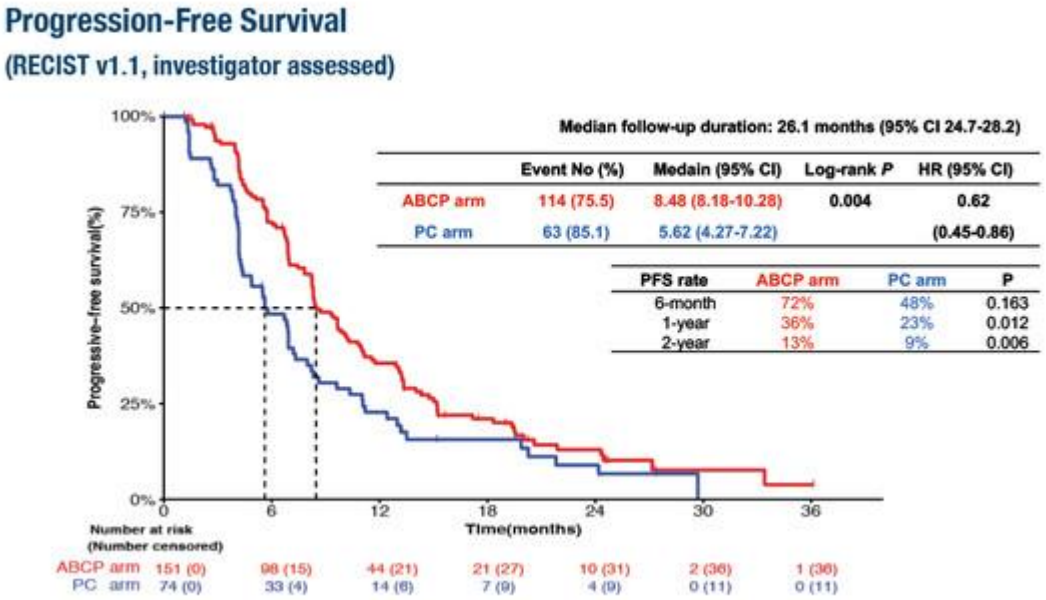
Acknowledgements: Medical writing and editorial support was provided by Carolyn Hall, PhD, and Feyza Sancar, PhD (Exact Sciences, Madison, WI).
This study was sponsored by Exact Sciences Corp., Madison, WI.

Disclosure: Christopher Douville is an inventor on some technologies. Licenses to these technologies are or will be associated with equity or royalty payments to the inventors as well as to Johns Hopkins University. CD is a consultant with Exact Sciences. The terms of these arrangements are being managed by Johns Hopkins University in accordance with its conflict-of-interest policies. He is also the founder of Belay Diagnostics.

Promising Data From the ATTLAS Phase III Study Indicate a New Approach for Treating Patients Progressing on TKIs

As presented at the ESMO Congress 2023 (Madrid, 20–24 October), ATTLAS, the first randomised phase III trial of atezolizumab, bevacizumab and chemotherapy (ABCP) in patients with non-small cell lung cancer (NSCLC) and acquired resistance to TKIs, met its primary endpoint, with significantly longer median progression-free survival (PFS) in patients treated with ABCP compared with chemotherapy alone (8.5 months versus 5.6 months, hazard ratio [HR] 0.62; 95% confidence interval 0.45–0.86; p=0.004) (LBA67).

"The ATTLAS study represents part of the ongoing research effort focused on the unmet need for novel treatments in patients who have progressed on TKIs, and these results confirm findings from previous preliminary data in subgroup analyses of the IMpower150 study," says Dr Daniel Tan from the National Cancer Centre Singapore. In the IMpower 150 study, a potential survival benefit was reported for patients with *EGFR* mutations and previous TKI therapy treated with the combination of a PD-L1 inhibitor and a VEGF inhibitor (Lancet Respir Med. 2019;75:3887–3401).



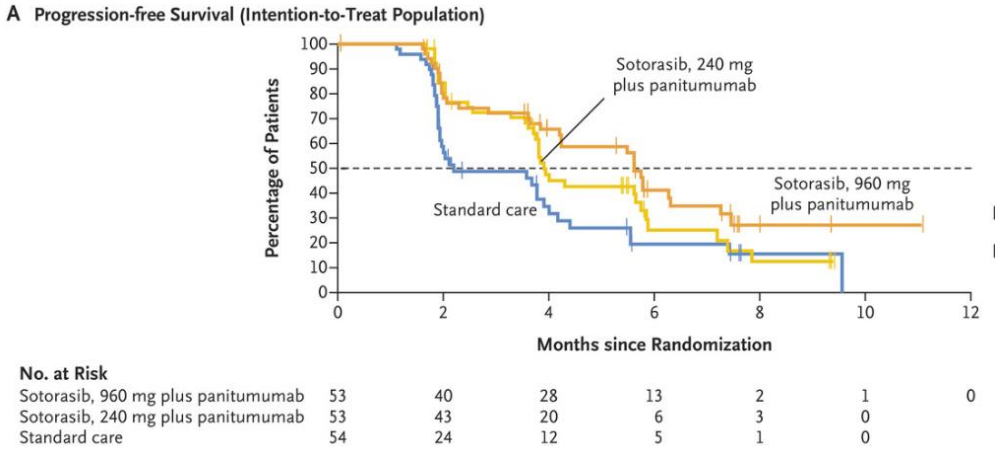
Source: https://dailyreporter.esmo.org/esmo-congress-2023/top-news/longer-pfs-reported-with-a-quadruple-treatment-regimen-in-egfr-or-alk-mutated-nsclc

Sotorasib Plus Panitumumab in Refractory Colorectal Cancer with Mutated KRAS G12C

Fakih et.al., *N Engl J Med. Oct 22, 2023*

In this phase 3, multicenter, open-label, randomized trial, we assigned patients with chemorefractory metastatic colorectal cancer with mutated KRAS G12C who had not received previous treatment with a KRAS G12C inhibitor to receive sotorasib at a dose of 960 mg once daily plus panitumumab (53 patients), sotorasib at a dose of 240 mg once daily plus panitumumab (53 patients), or the investigator's choice of trifluridine–tipiracil or regorafenib (standard care; 54 patients). The primary end point was progression-free survival as assessed by blinded independent central review according to the Response Evaluation Criteria in Solid Tumors, version 1.1. Key secondary end points were overall survival and objective response.

After a median follow-up of 7.8 months (range, 0.1 to 13.9), the median progression-free survival was 5.6 months (95% confidence interval [CI], 4.2 to 6.3) and 3.9 months (95% CI, 3.7 to 5.8) in the 960-mg sotorasib–panitumumab and 240-mg sotorasib–panitumumab groups, respectively, as compared with 2.2 months (95% CI, 1.9 to 3.9) in the standard-care group. The hazard ratio for disease progression or death in the 960-mg sotorasib–panitumumab group as compared with the standard-care group was 0.49 (95% CI, 0.30 to 0.80; P=0.006), and the hazard ratio in the 240-mg sotorasib–panitumumab group was 0.58 (95% CI, 0.36 to 0.93; P=0.03). Overall survival data are maturing. The objective response was 26.4% (95% CI, 15.3 to 40.3), 5.7% (95% CI, 1.2 to 15.7), and 0% (95% CI, 0.0 to 6.6) in the 960-mg sotorasib–panitumumab, 240-mg sotorasib–panitumumab, and standard-care groups, respectively.



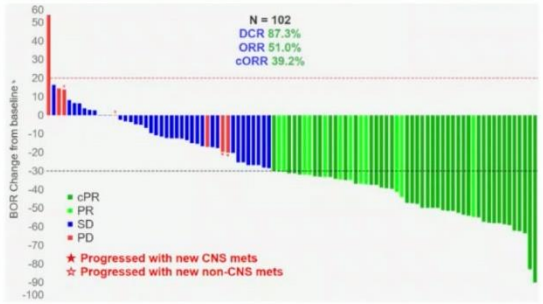
Source: https://www.nejm.org/doi/full/10.1056/NEJMoa2308795

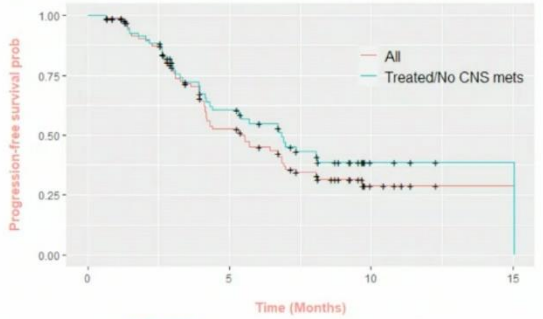
Impressive Data for BL-B01D1, a first-in-class EGFR×HER3 Bispecific ADC from Systimmune

08:30 - 10:00 Mini oral session 1 - NSCLC, metastatic

CHAIRS : LIZZA HENDRIKS, JORDI REMON MASIP, DANIEL SHAO WENG TAN, YI-LONG WU

Overall efficacy of NSCLC patients





The impact of baseline CNS metastasis

	All NSCLC	All NSCLC with treated/no CNS mets	All NSCLC with untreated CNS mets
Enrolled[1]	N = 102	N = 75	N = 27
Median Prior line	3 (1-8)	3 (1-8)	3 (1-7)
Prior TKI or ICI[2]	92% (94/102)	93% (70/75)	89% (24/27)
Prior PBC	89% (91/102)	91% (68/75)	85% (23/27)
DCR (95%CI), %	87.3 (79.2, 93.0)	86.7 (76.8, 93.4)	88.9 (70.8, 97.6)
ORR (95%CI), %	51.0 (40.9, 61.0)	52.0 (40.2, 63.7)	48.1 (28.7, 68.1)
cORR (95%CI), %	39.2 (29.7, 49.4)	41.3 (30.1, 53.3)	33.3 (16.5, 54.0)
mDOR (95%CI), mo	8.5 (5.4, NR)	12.3 (5.4, NR)	4.2 (2.2, NR)
mPFS (95%CI), mo[3]	5.6 (4.1, 6.8)	6.8 (4.3, NR)	4.1 (3.1, 5.6)

[1] Two patients (01061, 05003) were censored at their last tumor assessment before COVID-19 related delays exceeding 28 days. [2] TKI for patients with NSCLC EGFRmt, ICI for patients with NSCLC EGFRwt. [3] The mPFS, mDOR and CI were calculated based on Kaplan–Meier method and log-log transformation.

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Li Zhang

Li Zhang

BL-B01D1, a first-in-class EGFRxHER3 bispecific antibody-drug conjugate, in patients with non-small cell lung cancer: Updated results from first-in-human phase I study

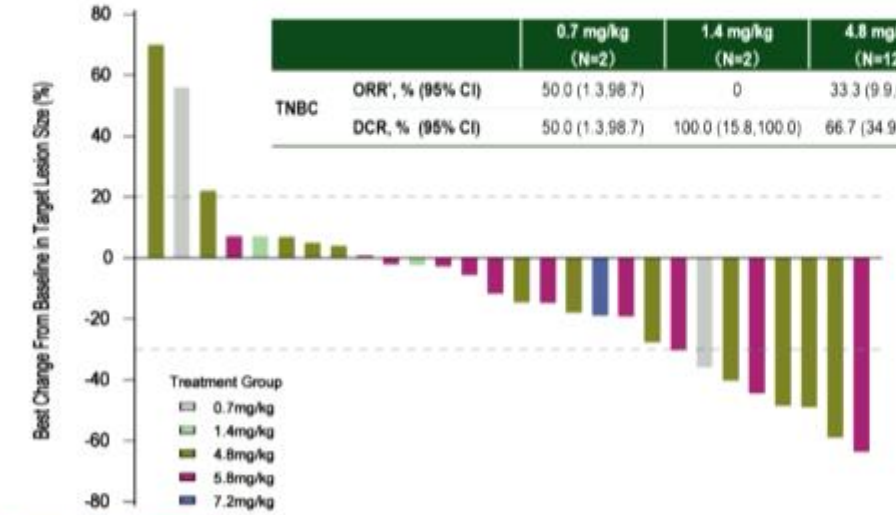
MADRID 2023 ESMO congress Granada Auditorium - Hall 3 MADRID SPAIN 20-24 OCTOBER 2023

HS-20089, a B7-H4 targeted antibody-drug conjugate, Shows Promising Results in TNBC

Efficacy - TNBC

- HS-20089 showed promising anti-tumor activity in triple-negative breast cancer (TNBC).
- At potential target therapeutic doses of 4.8 and 5.8 mg/kg, the ORR were 33.3% and 27.3%, respectively.

Figure 5. Best Percent Change of Target Lesions in TNBC



		0.7 mg/kg (N=2)	1.4 mg/kg (N=2)	4.8 mg/kg (N=12)	5.8 mg/kg (N=11)	7.2 mg/kg (N=1)	Total (N=28)
TNBC	ORR*, % (95% CI)	50.0 (1.3,98.7)	0	33.3 (9.9,65.1)	27.3† (6.0,61.0)	0	28.6 (13.2,48.7)
	DCR, % (95% CI)	50.0 (1.3,98.7)	100.0 (15.8,100.0)	66.7 (34.9,90.1)	81.8 (48.2,97.7)	100.0 (2.5,100.0)	75.0 (55.1,89.3)

*Assessed according to RECIST 1.1 by investigators.
†Including 1 confirmed PR and 2 PRs awaiting confirmation. Others were confirmed PRs.
ORR: Objective response rate.
DCR: Disease control rate.
PR: Partial response.

Clinical cutoff: August 17, 2023

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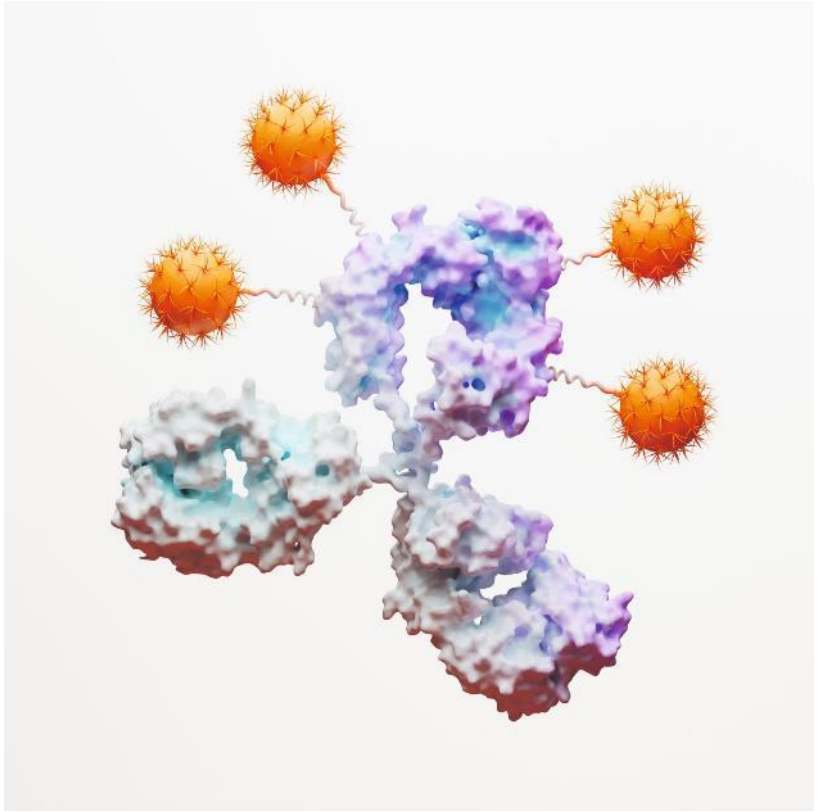
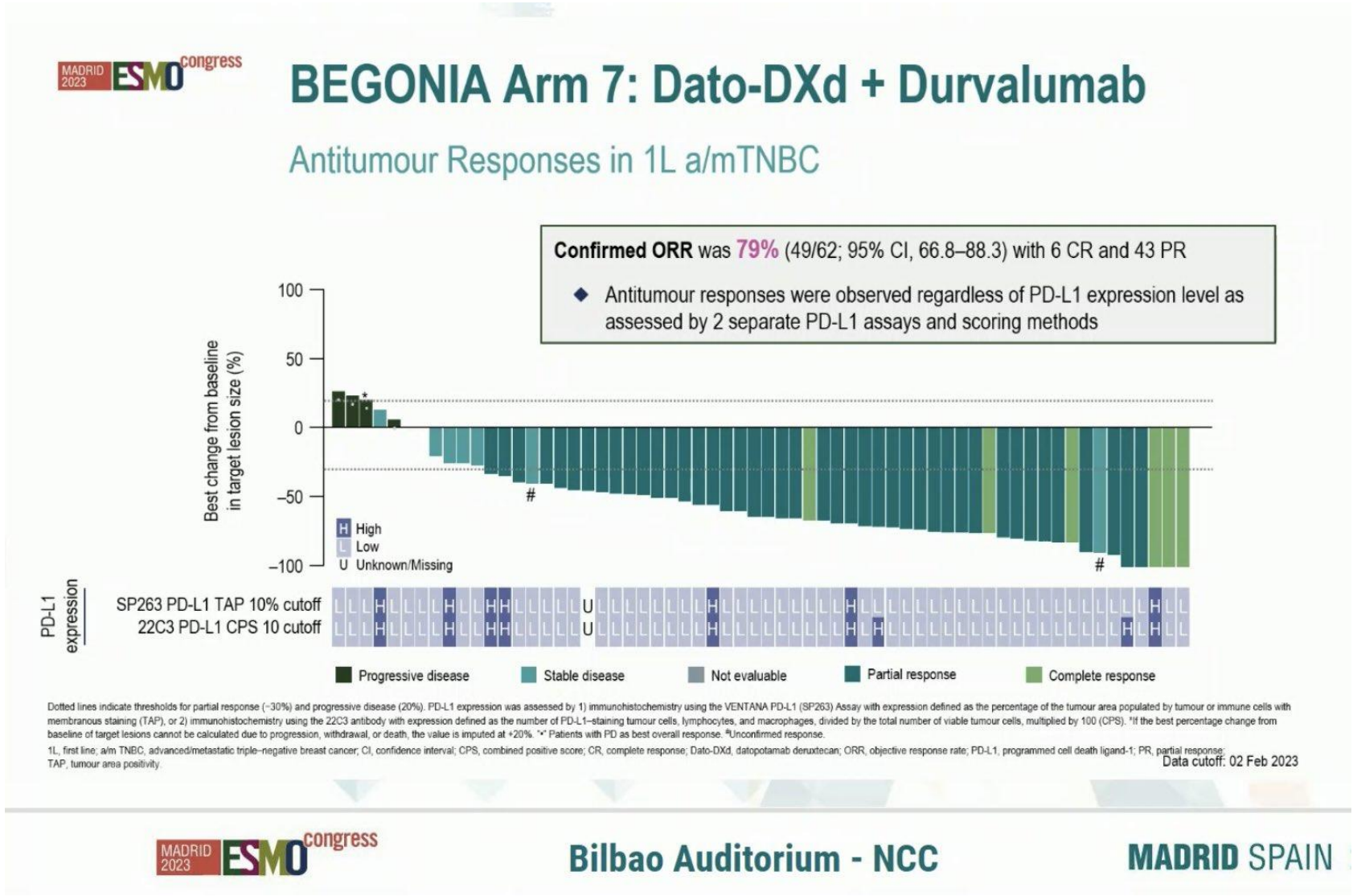
It's not hard to see why GSK paid $85mm upfront to access this ADC from Hansoh Pharma.



Dapo + Durva – BEGONIA Arm 7



Cantargia's Nadunolimab Hits 64% ORR in Metastatic TNBC

Phase Ib safety and efficacy of nadunolimab/gemcitabine/carboplatin (NadGC) in metastatic triple negative breast cancer (mTNBC)

Sara López-Tarruella[1,2,3]; Agostina Stradella[4,3]; Pablo Tolosa[5,3]; Silvia Antolin[6,3]; Marta Santisteban[7,8,3]; Javier García-Corbacho[9,3]; Angel Luis Guerrero-Zotano[10,3]; Manuel Ruiz-Borrego[11,3]; María M Caffarel[12,13,3]; Nedjad Losic[14]; Elin Jaensson Gyllenbäck[14]; Petter Skoog[14]; Helén Johansen Blanco[14]; Juan José Soto-Castillo[4]; Manuel Alva[5]; Cristina Reboredo[6]; Maribel Casas[3]; Nuria Caparroso[3]; Susana Bezares[3]; Ignacio García-Ribas[14]

[1]Medical Oncology Service, Hospital General Universitario Gregorio Marañón, Madrid, Spain; [2]Instituto de Investigación Sanitaria Gregorio Marañón (IISGM), Madrid, Spain; [3]GEICAM Spanish Breast Cancer Group, Madrid, Spain; [4]Institut Catala D'Oncologia-Duran y Reynals (ICO L'Hospitalet), Barcelona, Spain; [5]Hospital Universitario 12 de Octubre, Madrid, Spain; [6]Complejo Hospitalario Universitario A Coruña, A Coruña, Spain; [7]Clínica Universidad de Navarra, Pamplona, Spain; [8]Instituto de Investigación Sanitaria de Navarra (IdiSNA), Pamplona, Spain; [9]UGCI Oncología Médica, Hospitales Universitarios Regional y Virgen de la Victoria, Málaga, Spain; [10]Instituto Valenciano de Oncología (IVO), Valencia, Spain; [11]Hospital Universitario Virgen del Rocío, Sevilla, Spain; [12] Biodonostia Health Research Institute, San Sebastián, Spain; [13]IKERBASQUE, Basque Foundation for Science, Bilbao, Spain; [14]Cantargia AB, Lund, Sweden

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Background

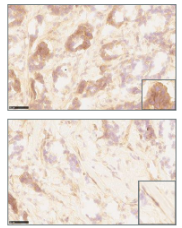


Figure 1: Immunohistochemistry staining of IL1RAP on tumor cells (top) and fibroblasts (bottom) in TNBC tumor biopsies

- Interleukin-1 Receptor Accessory Protein (IL1RAP) is expressed on cancer, stromal and infiltrating immune cells of many solid tumors. Among breast cancer subtypes, triple-negative breast cancer (TNBC) has the highest IL1RAP expression. IL-1α and IL-1β modulate tumor-promoting factors via IL-1 receptor type 1 (IL-1R1), which requires IL1RAP.
- Chemotherapy leads to upregulation of IL-1α which stimulates IL-1β release by stromal cells[1-3]. IL-1α/IL-1β contribute to tumor growth, chemoresistance and immune suppression[4-5]. Blockade of both IL-1α/IL-1β in combination with chemotherapy thus constitutes an attractive approach for cancer treatment.
- Nadunolimab (CAN04) is a fully humanized monoclonal IgG1 antibody targeting IL1RAP. It inhibits tumor-promoting and chemoresistance signals mediated by IL-1α and IL-1β and induces antibody-dependent cellular cytotoxicity of IL1RAP-expressing cells.

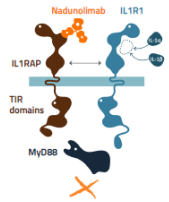
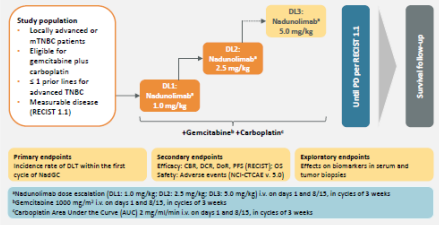


Figure 2: Mode-of-action of nadunolimab

- Interim results for nadunolimab combination with chemotherapy in pancreatic cancer and non-small cell lung cancer patients from the phase I/IIa trial CANFOUR (NCT03267316) showed acceptable safety and promising efficacy compared to historical data. In pancreatic cancer, the strongest clinical benefit was observed in patients with high tumor baseline expression of IL1RAP[6].
- TRIFOUR (NCT05181462) is a phase Ib/non-comparative randomized phase II trial to evaluate nadunolimab + gemcitabine + carboplatin (NadGC) combination in patients with metastatic TNBC (mTNBC). **Herein, preliminary safety and efficacy from the phase Ib dose escalation are presented.**

Study design



- A total of 15 patients were included; three dosed at DL1 and 12 at DL2. Patients were allowed to continue on nadunolimab monotherapy at the investigator's discretion.
- To mitigate Grade 3/4 neutropenia and reduce febrile neutropenia, all patients received prophylactic G-CSF, compulsory in Cycle 1 and left to the investigator's discretion from Cycle 2 onwards.

Results

Patient characteristics

Table 1: Baseline characteristics

	All patients (n=15)
Age (years); median (range)	50 (32-69)
Body mass index; median (range)	25 (17-32)
Menopausal status; n (%)	
Postmenopausal	10 (67)
Pre-/per-menopausal	5 (33)
ECOG performance status; n (%)	
0	12 (80)
1	3 (20)
Disease-free interval (years); median (range); n=14	1.9 (0.2-13.5)
Triple-negative; n (%)	15 (100)
Ki67 (%); median (range)	68 (10-90)
BRCA; n (%)	
Positive	0
Negative	6 (40)
Not available	9 (60)
Visceral lesions; n (%)	14 (93)
Metastatic locations; n (%)	
≤ 3	10 (67)
> 3	5 (33)
Prior lines of therapy for metastatic disease; n (%)	
None	5 (33)
1	10 (67)
Prior ICI in first line therapy for metastatic disease; n (%)	5 (33)
Prior platinum agent in (neo)adjuvant treatment; n (%)	4 (27)

- Most frequent metastatic lesions were lymph node (67%), lung (60%), liver (47%) and bone (27%).

Safety

Table 2: Grade 3 or higher treatment-emergent adverse events (TEAEs); n (%)

	All patients (n=15)	
	Grade ≥3	All grades
Neutropenia	8 (53)	10 (67)
Thrombocytopenia	4 (27)	6 (40)
Anaemia	3 (20)	6 (40)
Febrile neutropenia	2 (13)	2 (13)
COVID-19	1 (7)	1 (7)
Device-related infection	1 (7)	1 (7)
Diarrhoea	1 (7)	4 (27)
Hypocalcaemia	1 (7)	1 (7)
Hypomagnesaemia	1 (7)	2 (13)
Procedural pneumothorax	1 (7)	1 (7)

- Dose escalation was not continued beyond DL2 based on observed safety and results from other trials of nadunolimab with chemotherapy. MTD was not formally achieved; 2.5 mg/kg was the maximal administered dose of nadunolimab.
- TEAEs of Grade ≥3 were reported in 12 (80%) patients, leading to treatment discontinuation in one (7%) patient. Five (33%) patients had serious adverse events (SAEs): febrile neutropenia* (13%), hypocalcaemia* (7%), hypomagnesaemia* (7%), procedural pneumothorax (7%), device-related infection (7%) and COVID-19 (7%). SAEs marked with * were considered related.
- One infusion-related reaction (IRR) of grade 2 was reported at DL2.
- Two DLTs were reported at DL2: Grade 3 neutropenia causing a delay of >7 days in Cycle 2 and Grade 3 febrile neutropenia.
- Mean (range) number of treatment cycles with nadunolimab: 8 (2-17), gemcitabine: 7 (2-14), carboplatin: 7 (2-14). Ten (67%) patients received ≥5 treatment cycles. Fourteen (93%) patients had any dose modifications.
- Ten (67%) patients, three in DL1 and seven in DL2, received subsequent therapy.

Efficacy

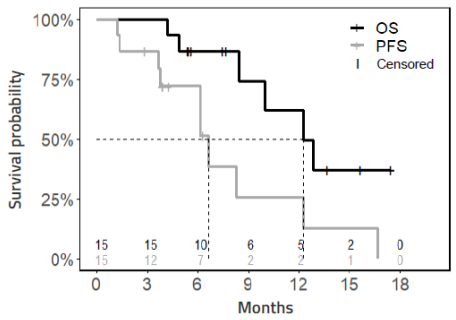


Figure 3: Kaplan-Meier curves for survival analysis (OS and PFS; n=15)

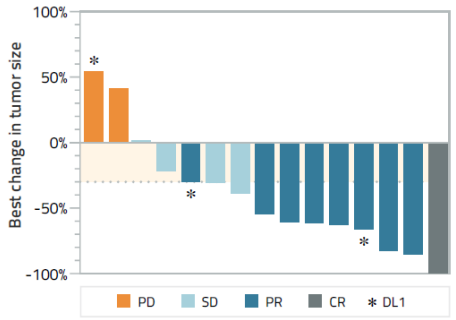


Figure 4: Waterfall plot of the best percent change in target lesion size (n=15)

- At data cut-off (17 July 2023), two (13%) patients were on treatment and six (40%) had died. The cause of death was breast cancer.
- Preliminary ORR was 60%, including one confirmed complete response (CR) and eight confirmed partial responses (PR).
- Preliminary median OS was 12.3 months (95% CI: 8.5-NE) and preliminary median PFS was 6.6 months (95% CI: 3.7-12.3).

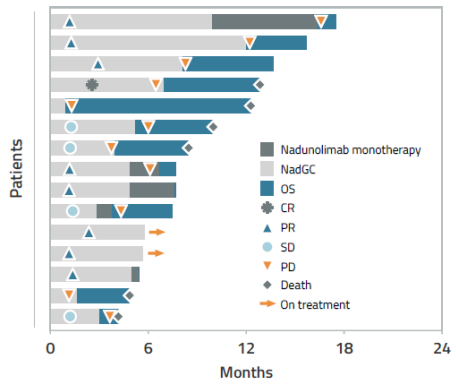


Figure 5: Treatment course for each individual patient (n=15)

Conclusions

- **Nadunolimab plus standard gemcitabine and carboplatin (NadGC) is well tolerated, and preliminary data shows promising antitumor activity in metastatic TNBC compared to historical data[7]:**
  - **ORR: 60%**
  - **Median OS: 12.3 months**
  - **Median PFS: 6.6 months**
- **The safety profile of NadGC was similar to previous reports for gemcitabine and carboplatin only**
- **The randomized phase II part of TRIFOUR is currently enrolling patients at the 2.5 mg/kg nadunolimab dose**

References

[1] Bruchard et al; Nat Med (2013)
[2] Chung et al; NPJ Breast Cancer (2022)
[3] Tjomsland et al; Neoplasia (2011)
[4] Liu et al; Cancer Res (2018)
[5] Zhang et al; Cancer Res (2018)
[6] Van Cutsem et al; Cancer Res (2023)
[7] O'Shaughnessy et al; J Clin Oncol (2014)

Acknowledgements

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Source: https://cantargia.com/assets/uploads/ESMO-2023-poster.pdf

Datopotamab Deruxtecan (Trop2 ADC) From AZ / Daiichi Sankyo Shows Promising Data in Lung and Breast Cancers

AstraZeneca Press Release, October 11, 2023

A Presidential Symposium will highlight PFS data from the TROPION-Lung01 Phase III trial evaluating datopotamab deruxtecan in patients with previously treated advanced NSCLC. In July, datopotamab deruxtecan became the first antibody drug conjugate to demonstrate a statistically significant improvement in PFS and a trend in improvement for OS compared to docetaxel, the current standard-of-care chemotherapy. Additionally, a mini-oral presentation will feature initial results from the TROPION-Lung05 Phase II trial evaluating datopotamab deruxtecan in patients with heavily pretreated advanced NSCLC with actionable genomic mutations (AGA). There are currently no TROP2-directed antibody drug conjugates approved for the treatment of patients with lung cancer.

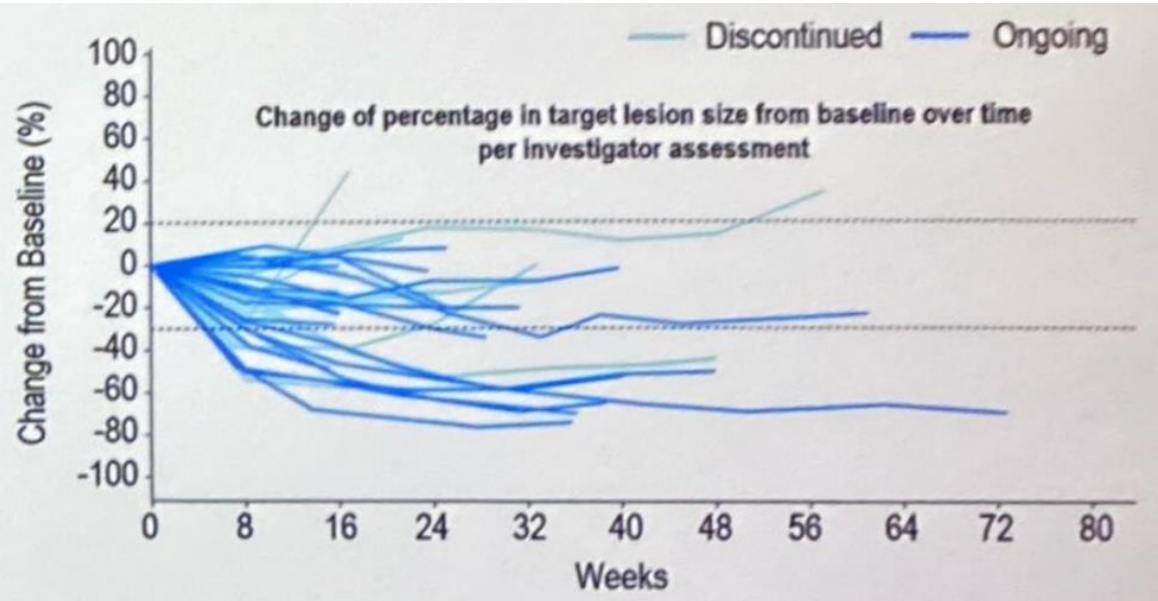
Another Presidential Symposium will showcase data from the TROPION-Breast01 Phase III trial of datopotamab deruxtecan in patients with inoperable or metastatic hormone receptor (HR)-positive, HER2-low or negative breast cancer previously treated with endocrine-based therapy and at least one systemic therapy. In September, datopotamab deruxtecan demonstrated a statistically significant and clinically meaningful improvement in PFS and a trend in improvement for OS compared to investigator's choice of chemotherapy.

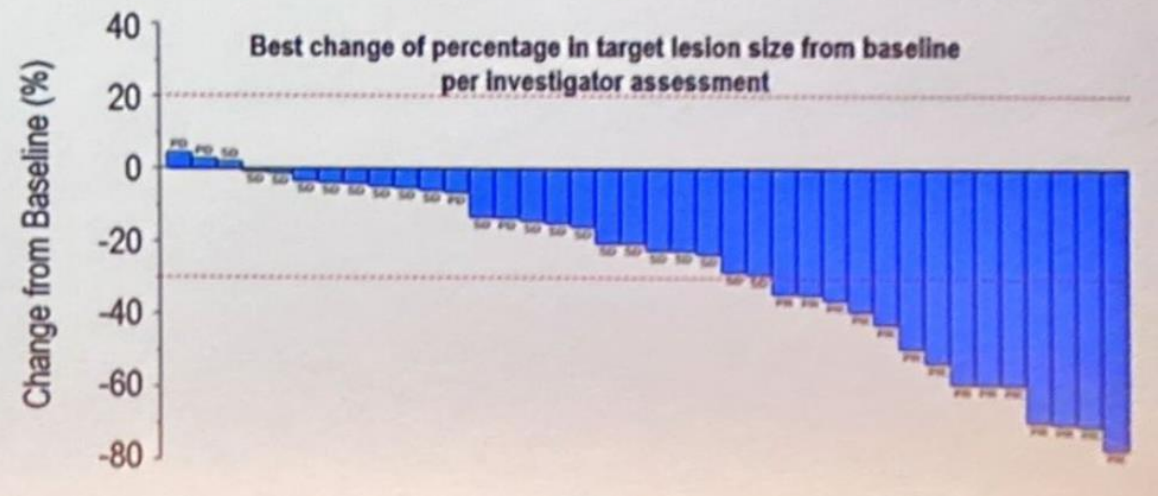
Source: https://www.astrazeneca.com/media-centre/press-releases/2023/astrazeneca-advances-scientific-leadership-across-multiple-cancers-with-first-data-from-four-pivotal-phase-iii-trials-at-esmo.html

SKB264 (Trop2 ADC) From Kelun / Merck Shows 37% ORR Rate in HR+/Her2- Breast Cancer

	All patients (N=38)[a]
ORR, n (%)	**14 (36.8)**
Confirmed PR	12
DCR, n (%)	**34 (89.5)**
DoR	
Median (Range), mo	7.4 (4.2~14.9+)
6-mon DoR rate, % (95% CI)	80.0 (40.9, 94.6)
PFS	
Median (95% CI), mo	11.1 (5.4, 13.1)
6-mon PFS rate, % (95% CI)	61.2 (41.3, 76.1)
OS	
Median (95% CI), mo	NE (10.71, NE)
9-mon OS rate (95% CI), %	81.4 (57.1, 92.7)

a. of 41 patients were enrolled, 38 patients were evaluable for response assessment (defined as ≥1 on-study scan).

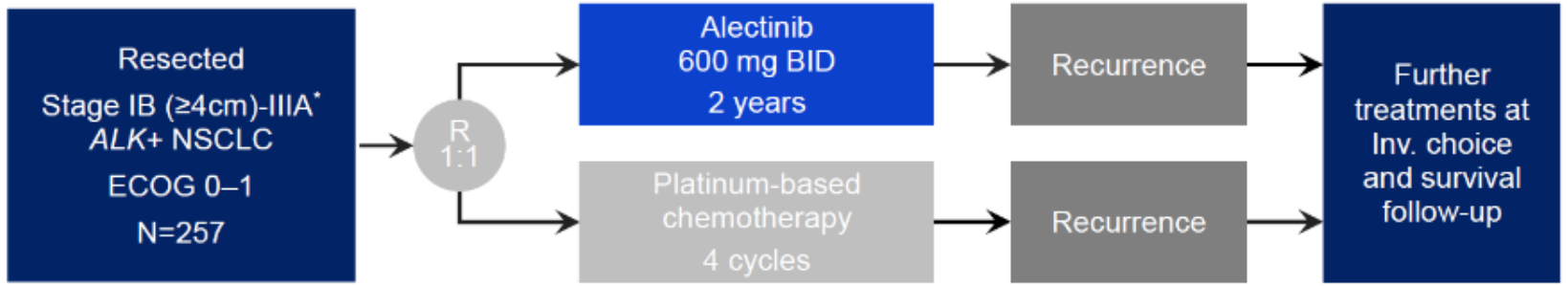




Alecensa: Unprecedented Ph III results in adjuvant ALK+ NSCLC

Risk of disease recurrence or death reduced by 76%

Ph III (ALINA) Alecensa in adjuvant ALK+ NSCLC trial design



Primary endpoint | **DFS** per investigator** | **HR=0.24** ✓

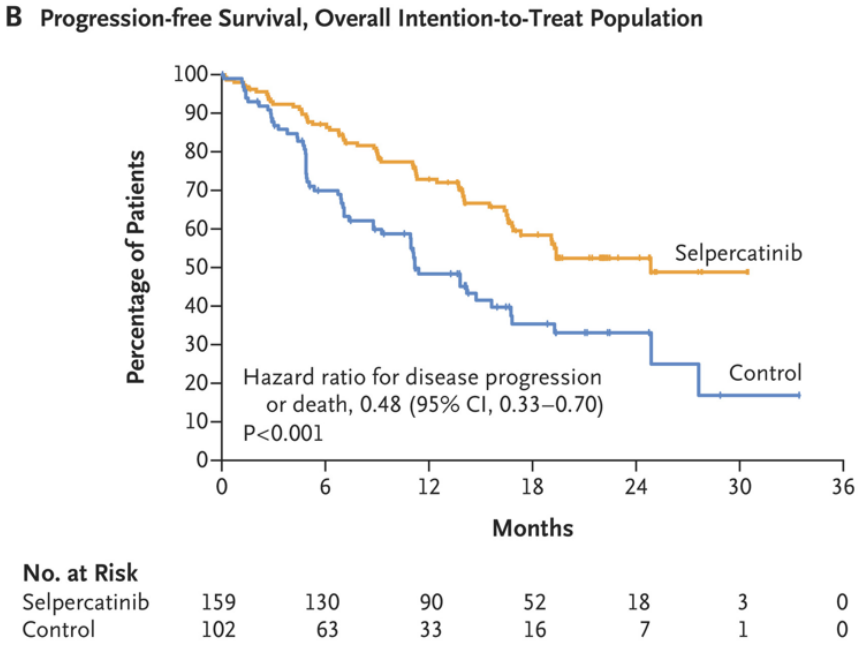
- Ph III (ALINA) met primary endpoint of DFS; risk of disease recurrence or death reduced by 76% (HR=0.24) and clinically meaningful improvement of CNS-DFS (HR=0.22) achieved
- Full results to be presented in the Presidential session 1 at ESMO 2023 on 21st October
- First-in-class global filing ongoing; US/EU launches expected in 2024
- Ph III (HORIZON-01) in unresectable NSCLC and Ph III (TAPISTRY) multi-cohort tumor-agnostic studies ongoing

Clinicaltrials.gov: NCT03456076; [1]Yano T, et al. World J Clin Oncol. 2014;5(5):1048-1054; [2]US data; ZS Primary Market Research, August 2023; *UICC/AJCC 7th edition; **Defined as the time from randomization to the first documented recurrence of disease or new primary NSCLC as determined by the investigator, or death from any cause, whichever occurs first; ALK=anaplastic lymphoma kinase; NSCLC=non-small cell lung cancer; mNSCLC=metastatic NSCLC; DFS=disease free survival; ECOG=eastern cooperative oncology group; R=randomization; BID=twice a day; CNS=central nervous system

First-Line Selpercatinib or Chemotherapy and Pembrolizumab in RET Fusion–Positive NSCLC

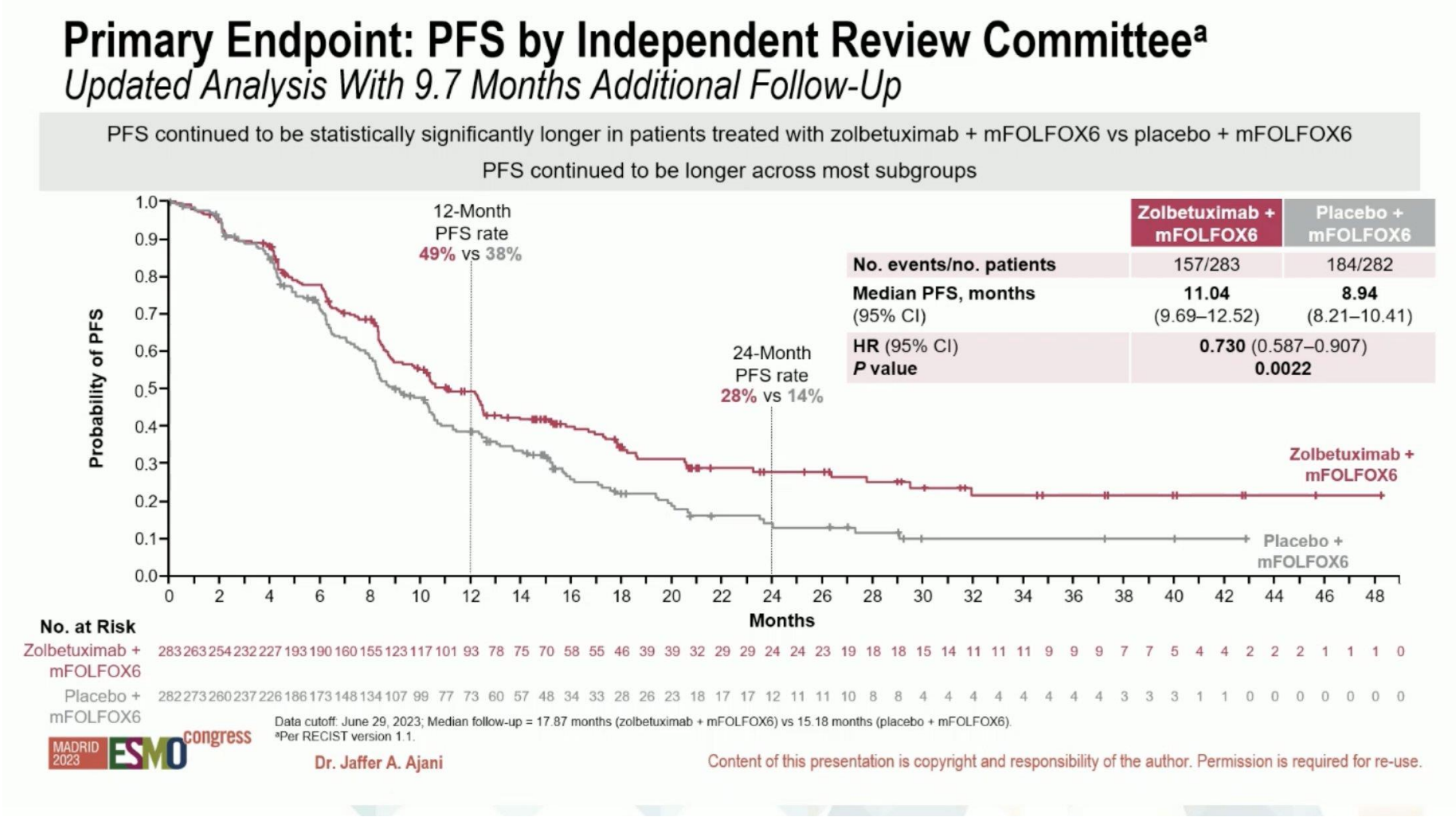
Zhou et.al., *New England Journal of Medicine*, October 21, 2023

In a randomized phase 3 trial, we evaluated the efficacy and safety of first-line selpercatinib as compared with control treatment that consisted of platinum-based chemotherapy with or without pembrolizumab at the investigator's discretion. The primary end point was progression-free survival assessed by blinded independent central review in both the intention-to-treat–pembrolizumab population (i.e., patients whose physicians had planned to treat them with pembrolizumab in the event that they were assigned to the control group) and the overall intention-to-treat population. In total, 212 patients underwent randomization in the intention-to-treat–pembrolizumab population. At the time of the preplanned interim efficacy analysis, median progression-free survival was 24.8 months (95% confidence interval [CI], 16.9 to not estimable) with selpercatinib and 11.2 months (95% CI, 8.8 to 16.8) with control treatment (hazard ratio for progression or death, 0.46; 95% CI, 0.31 to 0.70; P<0.001). The percentage of patients with an objective response was 84% (95% CI, 76 to 90) with selpercatinib and 65% (95% CI, 54 to 75) with control treatment. The cause-specific hazard ratio for the time to progression affecting the central nervous system was 0.28 (95% CI, 0.12 to 0.68). Efficacy results in the overall intention-to-treat population (261 patients) were similar to those in the intention-to-treat–pembrolizumab population. The adverse events that occurred with selpercatinib and control treatment were consistent with those previously reported.



Source: https://www.nejm.org/doi/full/10.1056/NEJMoa2309457

Astellas' Zolbetuximab + FOLFOX as 1L treatment in CLDN18.2+, HER2−, Locally Advanced Metastatic Gastric or Gastroesophageal Cancer



Source: https://www.nejm.org/doi/full/10.1056/NEJMoa2309457

Disclosure

STIFEL | Healthcare

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