Oncology Market Update

Trends, Deals, Valuations and Players in the Market

June 8, 2024 / #ASCO2024 Recap Edition

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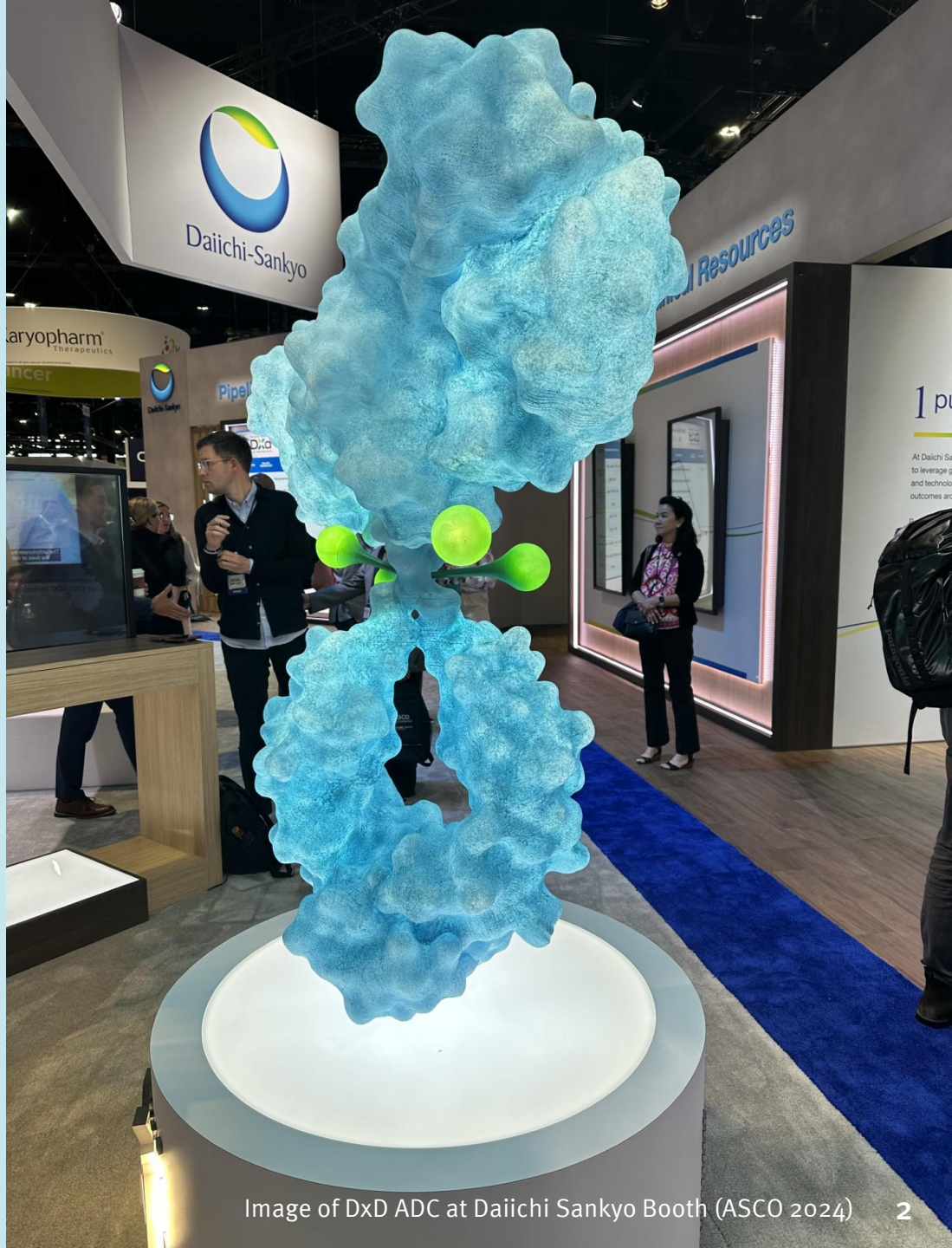

Image of DxD ADC at Daiichi Sankyo Booth (ASCO 2024)

Accessing Past Issues

If you wish to be added to mailing list for this publication, please notify Natasha Yeung (yeungn@stifel.com). Recent issues:

May 27, 2024 (IBD)
May 20, 2024 (Returning Capital)
May 13, 2024 (Brain, AlphaFold 3)
May 6, 2024 (Earnings, Obesity)
April 29, 2024 (M&A, Japan)
April 22, 2024 (Pharma Pricing)
April 15, 2024 (AI in Pharma)
April 8, 2024 (The Buyside)
April 1, 2024 (Biotech Balance Sheets)
March 25, 2024 (Women's Health)
March 18, 2024 (Inflammasome)
March 11, 2024 (IRA, Immunology)
March 4, 2024 (Biotech Employment)
Feb 26, 2024 (Biotech Strategy)
Feb 19, 2024 (Big Drugs, Autoantibodies)
Feb 12, 2024 (Fibrosis, Endometriosis)
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Jan 29, 2024 (Pharma R&D Productivity)
Jan 22, 2024 (AI in medicine)
Jan 15, 2024 (FDA Commissioner Priorities)
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Dec 18, 2023 (Expectations for Future)
Dec 11, 2023 (ASH, R&D Days)
Dec 4, 2023 (Big Pharma, CEA)
November 22, 2023 (Bullish on Biotech)
November 20, 2023 (M&A)
November 13, 2023 (AHA, Bear Market)
November 7, 2023 (Unmet Needs)
October 30, 2023 (ADCs)
October 23, 2023 (ESMO Review)
October 16, 2023 (Cancer Screening)
October 9, 2023 (Biosimilars, M&A)
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August 21, 2023 (Covid, China)
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June 12, 2023 (IRA, State of Industry)
May 29, 2023 (Oncology update)
May 22, 2023 (FTC case on Amgen/Horizon)

Stifel: A Powerhouse in Oncology Financings and Advisory

Stifel has a broad team focused on oncology equity financings and strategic advisory work.

The team has deep scientific knowledge and strong relationships with KOLs and has advised on over 75 financing and strategic transactions in oncology over the last five years.

Stifel is one of the world's most active advisors on financing and strategic transactions in oncology therapeutics.

Financings

$60,000,000 celcuity — Registered Direct Joint Bookrunning Manager *May 2024*	€19,200,000 MaSTaT — Follow-On Offering Sole Global Coordinator and Joint Bookrunner *May 2024*	$280,000,000 cullinan THERAPEUTICS — PIPE Joint Placement Agent *April 2024*	$201,250,000 nurix — Confidentially Marketed Follow-on Offering Joint Bookrunning Manager *April 2024*	$240,100,310 nkarta THERAPEUTICS — Registered Direct Joint Bookrunning Manager *March 2024*
$150,000,000 geron — Registered Direct Joint Bookrunning Manager *March 2024*	£31,100,000 Avacta — Follow-on Offering Joint Bookrunner, Joint Corporate Broker and Nomad *March 2024*	$230,000,000 Syndax — Confidentially Marketed Follow-on Offering Joint Bookrunning Manager *December 2023*	Up to $40,000,000 tem — PIPE Sole Placement Agent *July 2023*	$350,000,000 ARCELLX — At-the-Market Offering Sole Agent *Commenced May 2023*
$227,843,965 geron — Follow-on Offering Joint Bookrunning Manager *January 2023*	$115,799,748 VOR — Registered Direct & PIPE Joint Bookrunner Joint Placement Agent *December 2022*	$125,000,000 VOR — At-the-Market Offering Sole Agent *Commenced December 2022*	$80,250,000 COMPASS THERAPEUTICS — PIPE Joint Placement Agent *November 2022*	£62,000,000 Avacta — Convertible Bond & Follow-on Offering Sole Bookrunner Sole Placement Agent Sole Broker and Nomad *October 2022*
$230,000,000 nkarta THERAPEUTICS — Confidentially Marketed Follow-on Offering Joint Bookrunning Manager *April 2022*	$230,000,000 igm Biosciences, Inc. — Follow-on Offering Joint Bookrunning Manager *March 2022*	$75,000,000 geron — Confidentially Marketed Follow-on Offering Left Bookrunning Manager *March 2022*	$115,000,000 zymeworks — Confidentially Marketed Follow-on Offering Joint Bookrunning Manager *January 2022*	$52,325,000 MEI Pharma — Follow-on Offering Joint Bookrunning Manager *December 2021*
$60,000,000 eFFECTOR THERAPEUTICS — PIPE Lead Placement Agent *August 2021*	$174,560,000 IMAGO BioSciences — Initial Public Offering Joint Bookrunning Manager *July 2021*	$160,425,000 nurix — Follow-on Offering Joint Bookrunning Manager *March 2021*	$55,200,000 AVEO ONCOLOGY — Follow-on Offering Joint Bookrunning Manager *March 2021*	$50,652,000 cti BIOPHARMA — Confidentially Marketed Follow-on Offering Left Bookrunning Manager *March 2021*

Strategic Transactions

Up to $51,300,000 CSTONE PHARMACEUTICALS — Out-License of Sugemalimab in CEE Region ewopharma — Advisor to Licensor *May 2024*	$175,000,000 PROPELLA — Has Been Acquired by astellas — Advisor to Seller *December 2023*	$90,833,010 immunome — Has Merged with morphimmune — Advisor to Buyer *October 2023*	erytech — Has Merged with PHERECYDES — Advisor to Seller *June 2023*	Up to $600,000,000 LaNova 礼新医药 — Out-Licencing of LM-305 to AstraZeneca — Advisor to Licensor *May 2023*
ayala pharmaceuticals — Has Been Acquired by ADVAXIS IMMUNOTHERAPIES — Advisor to Seller *January 2023*	$290,000,000 ORION — Global Collaboration for the development and commercialization of ODM-208 with MERCK — Advisor *August 2022*	Up to $89,000,000 APOLLO THERAPEUTICS — In-Licensing of AVTX-007 from avalo THERAPEUTICS — Advisor to Licensee *August 2022*	Up to $1,200,000,000 LaNova 礼新医药 — Out-licensing of LM-302 to Turning Point Therapeutics — Advisor to Licensor *May 2022*	€26,000,000 medigene — Global Multi-target Collaboration for TCR Immunotherapies; Acquisition of PRAME TCR BIONTECH — Advisor *February 2022*
Noria Therapeutics & PSMA Therapeutics, Inc. — Has Been Acquired by BAYER — Advisor to Seller *June 2021*	BIOTHERA pharmaceuticals — Has Sold Imprime PGG to HiberCell — Advisor to Seller *June 2020*	Up to $202,000,000 ΣELLAS LIFE SCIENCES GROUP — In-License of Galinpepimut-S in Greater China by 3DMed — Advisor to Licensee *December 2020*	$1,500,000,000 Nuvation Bio — Has Been Acquired by PANACEA — Advisor to Special Committee of the Board of Directors *October 2020*	sesen bio — Out-License of Vicineum™ in Greater China Region to QILU PHARMACEUTICAL — Advisor to Licensor *July 2020*
$221,000,000 sunesis — Has Merged with viracta — Financial Advisor *February 2021*	Up to $30,000,000 oncosec IMMUNOTHERAPIES — Co-Promotion Agreement for TAVO with 远大医药 GRANDPHARMA SIRTeX — Financial Advisor *February 2020*	Up to $306,000,000 Mereo BioPharma — Out-License of Navicixzumab to Oncologie — Advisor to Licensor *January 2020*	Humanigen — Clinical Collaboration for lenzilumab with Yescarta Kite A GILEAD Company — Advisor to Humanigen, Inc. *May 2019*	SIMBEC ORION GROUP — Has Been Acquired by cbpe — Advisor to Seller *February 2019*
Up to $505,000,000 KINETA — Research Collaboration and Out-license of RIG-I Platforms to Pfizer — Advisor to Licensor *December 2018*	XOMA — Has Aquired Royalty Interest Position for 7 Assets from agenus — Advisor to Buyer *September 2018*	$31,000,000 XOMA — Out-license of Gevokizumab and IL-1 Beta IP to NOVARTIS — Advisor to Licensor *August 2017*	$22,000,000 XOMA — Royalties Have Been Acquired By HEALTHCARE ROYALTY PARTNERS — Advisor to Seller *December 2016*	XOMA — Biodefense Business Has Been Aquired by nanotherapeutics — Advisor to Seller *October 2015*

Note: As of May 31, 2024. Deal values and dates represented are as of the announcement that the definitive agreement was signed. Stifel transactions include deals completed by Stifel, Nicolaus & Company, Incorporated and its affiliated entities and Torreya Capital LLC and its affiliated entities.

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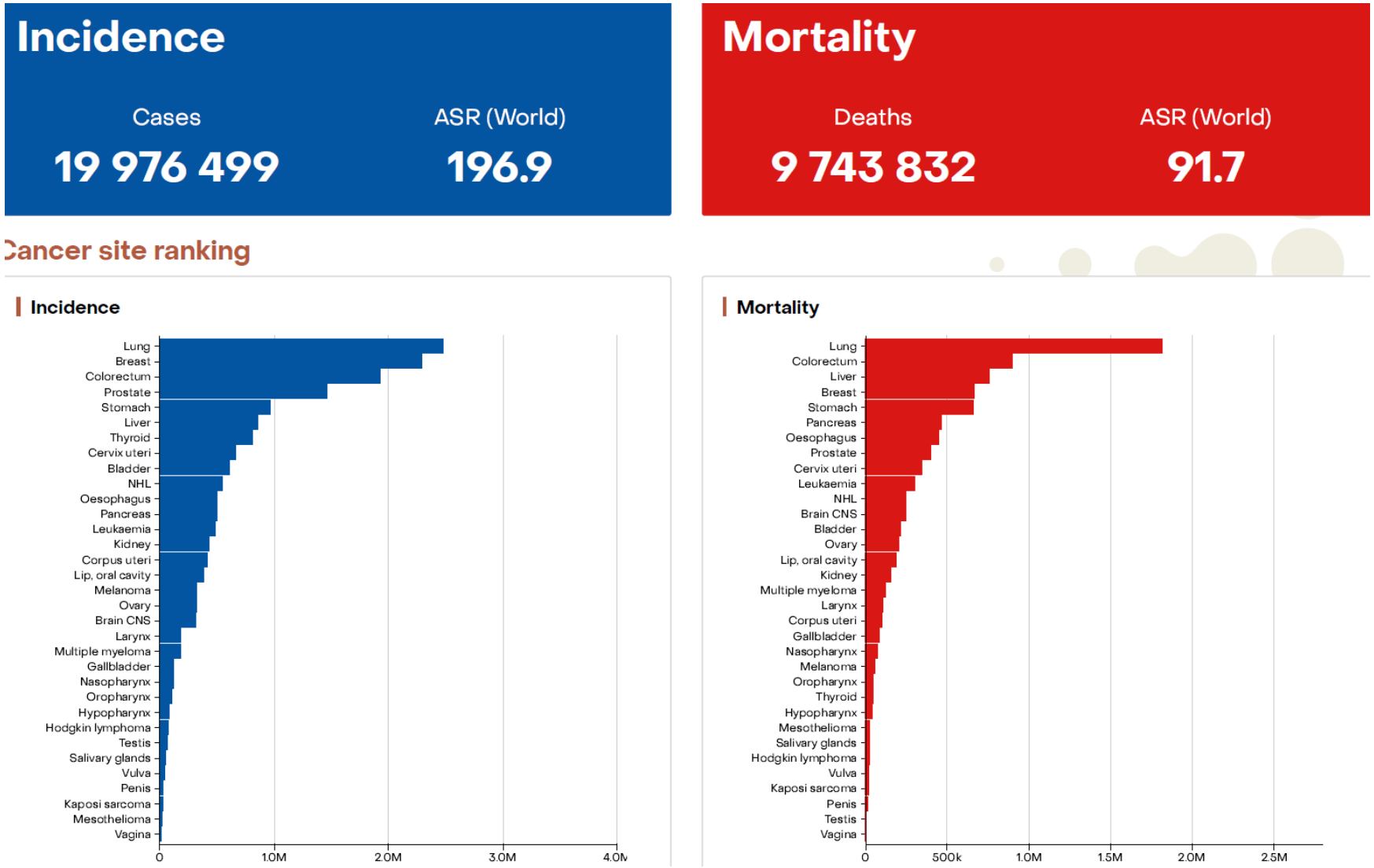
The Growing Market for Oncology Drugs

Areas of Highest Unmet Need in Cancer Care: Global Data

The disease burden data from WHO at right indicate that the areas of greatest unmet need in cancer care include lung cancer, colon cancer, pancreatic cancer and renal cancer. There is also significant death and morbidity associated with breast cancer, brain cancer and stomach cancer.



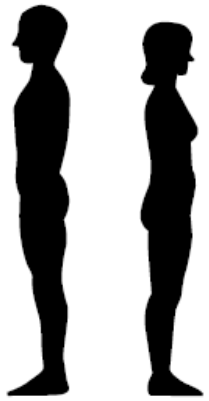
Source: https://gco.iarc.fr/today/en/fact-sheets-cancers

Cancers and Deaths by Type: U.S. Data

American Cancer Society Data

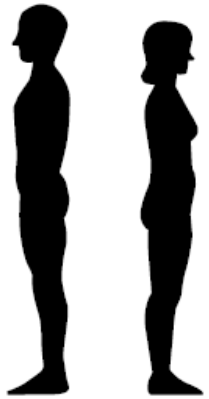
Estimated New Cases

Male			Female		
Prostate	299,010	29%	Breast	310,720	32%
Lung & bronchus	116,310	11%	Lung & bronchus	118,270	12%
Colon & rectum	81,540	8%	Colon & rectum	71,270	7%
Urinary bladder	63,070	6%	Uterine corpus	67,880	7%
Melanoma of the skin	59,170	6%	Melanoma of the skin	41,470	4%
Kidney & renal pelvis	52,380	5%	Non-Hodgkin lymphoma	36,030	4%
Non-Hodgkin lymphoma	44,590	4%	Pancreas	31,910	3%
Oral cavity & pharynx	41,510	4%	Thyroid	31,520	3%
Leukemia	36,450	4%	Kidney & renal pelvis	29,230	3%
Pancreas	34,530	3%	Leukemia	26,320	3%
All sites	**1,029,080**		**All sites**	**972,060**	



Estimated Deaths

Male			Female		
Lung & bronchus	65,790	20%	Lung & bronchus	59,280	21%
Prostate	35,250	11%	Breast	42,250	15%
Colon & rectum	28,700	9%	Pancreas	24,480	8%
Pancreas	27,270	8%	Colon & rectum	24,310	8%
Liver & intrahepatic bile duct	19,120	6%	Uterine corpus	13,250	5%
Leukemia	13,640	4%	Ovary	12,740	4%
Esophagus	12,880	4%	Liver & intrahepatic bile duct	10,720	4%
Urinary bladder	12,290	4%	Leukemia	10,030	3%
Non-Hodgkin lymphoma	11,780	4%	Non-Hodgkin lymphoma	8,360	3%
Brain & other nervous system	10,690	3%	Brain & other nervous system	8,070	3%
All sites	**322,800**		**All sites**	**288,920**	



Estimates are rounded to the nearest 10, and cases exclude basal cell and squamous cell skin cancers and in situ carcinoma except urinary bladder. Estimates do not include Puerto Rico or other US territories. Ranking is based on modeled projections and may differ from the most recent observed data.

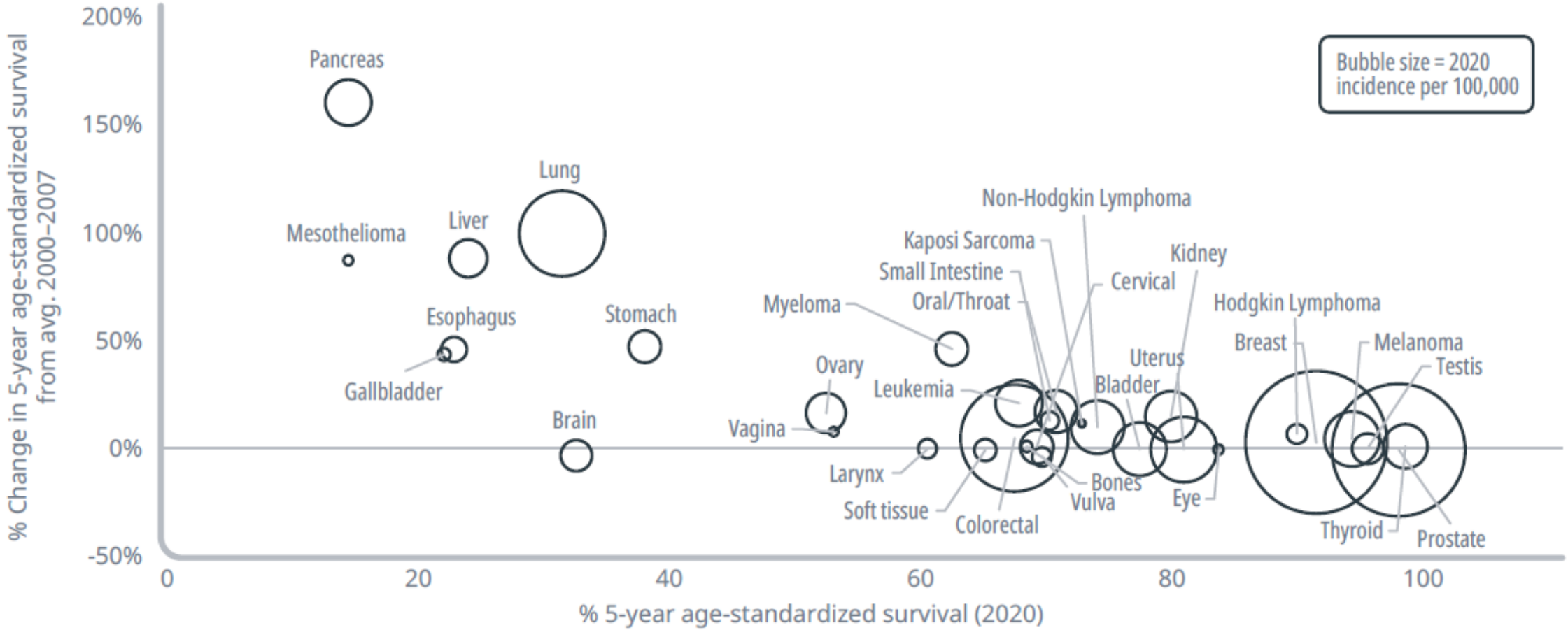
©2024, American Cancer Society, Inc., Surveillance and Health Equity Science

FIGURE 1 Ten leading cancer types for the estimated new cancer cases and deaths by sex, United States, 2024. Estimates are rounded to the nearest 10, and cases exclude basal cell and squamous cell skin cancers and in situ carcinoma except urinary bladder. Ranking is based on modeled projections and may differ from the most recent observed data.

Source: https://acsjournals.onlinelibrary.wiley.com/doi/epdf/10.3322/caac.21820

Biggest Improvements in Survival Rates Have Been in Tumor Types with Low Historical Survival

Exhibit 4: U.S. 5-year age-standardized survival in 2020 and % change from 2000–2007 average

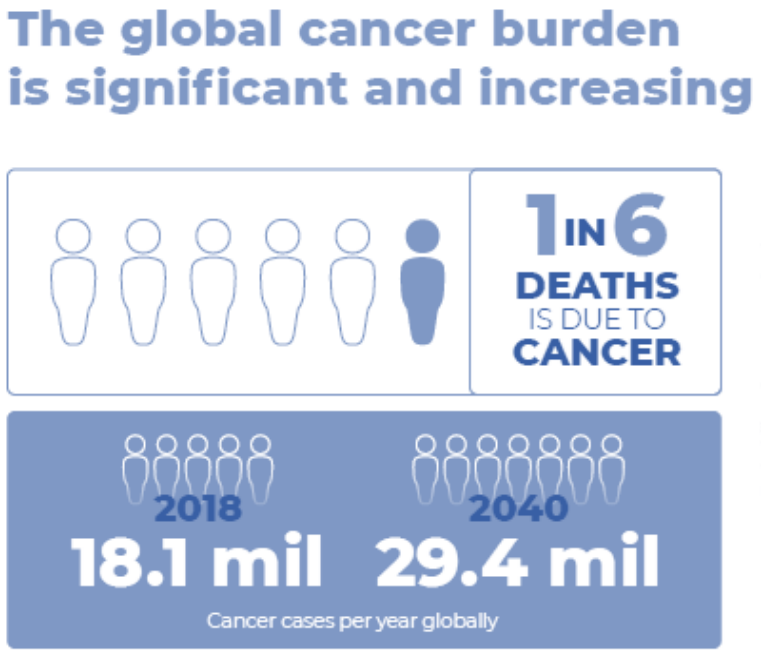


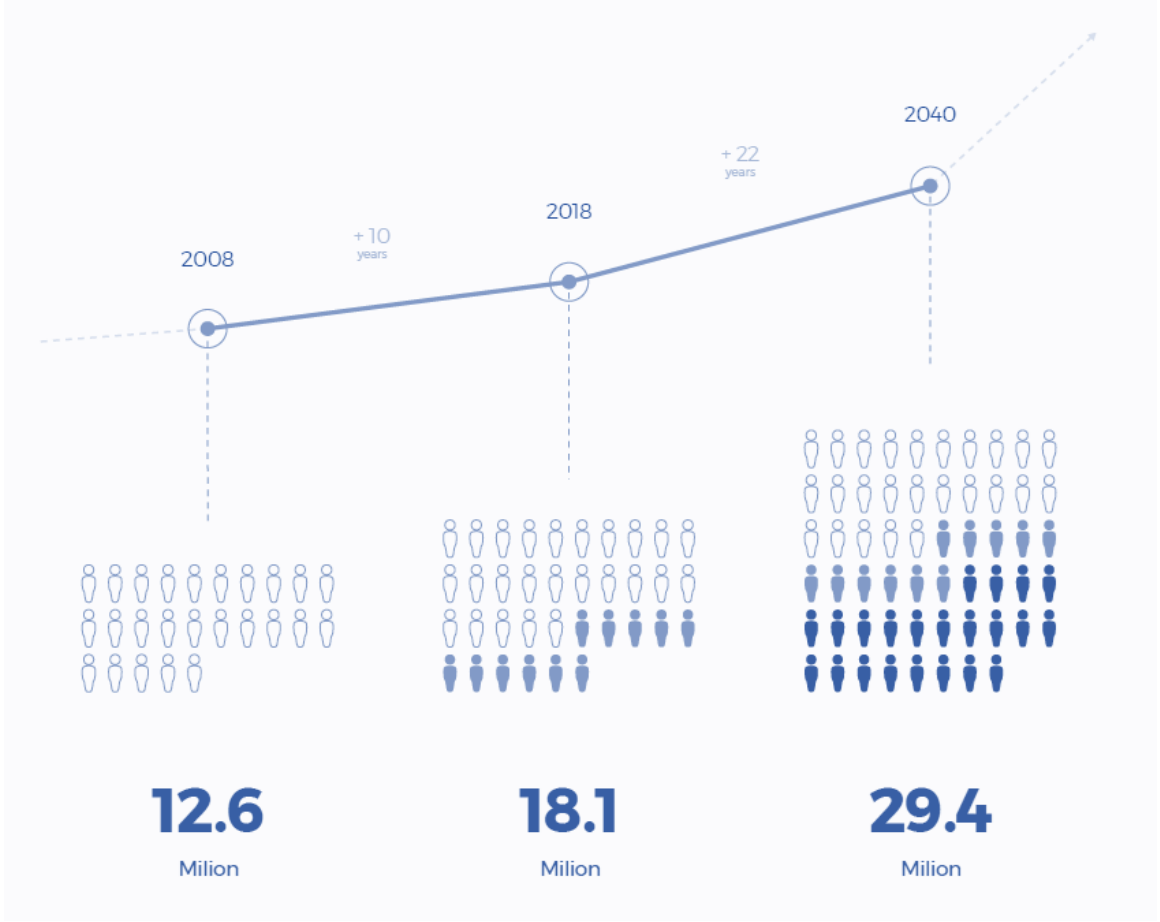
Source: U.S. SEER 5-year Survival average of 2000–2007 and projected trend to 2020, accessed 18 Apr 2024.

Sourced from: https://www.iqvia.com/insights/the-iqvia-institute/reports-and-publications/reports/global-oncology-trends-2024

World Health Organization: As We Live Longer the Probably of Getting Cancer Goes Up

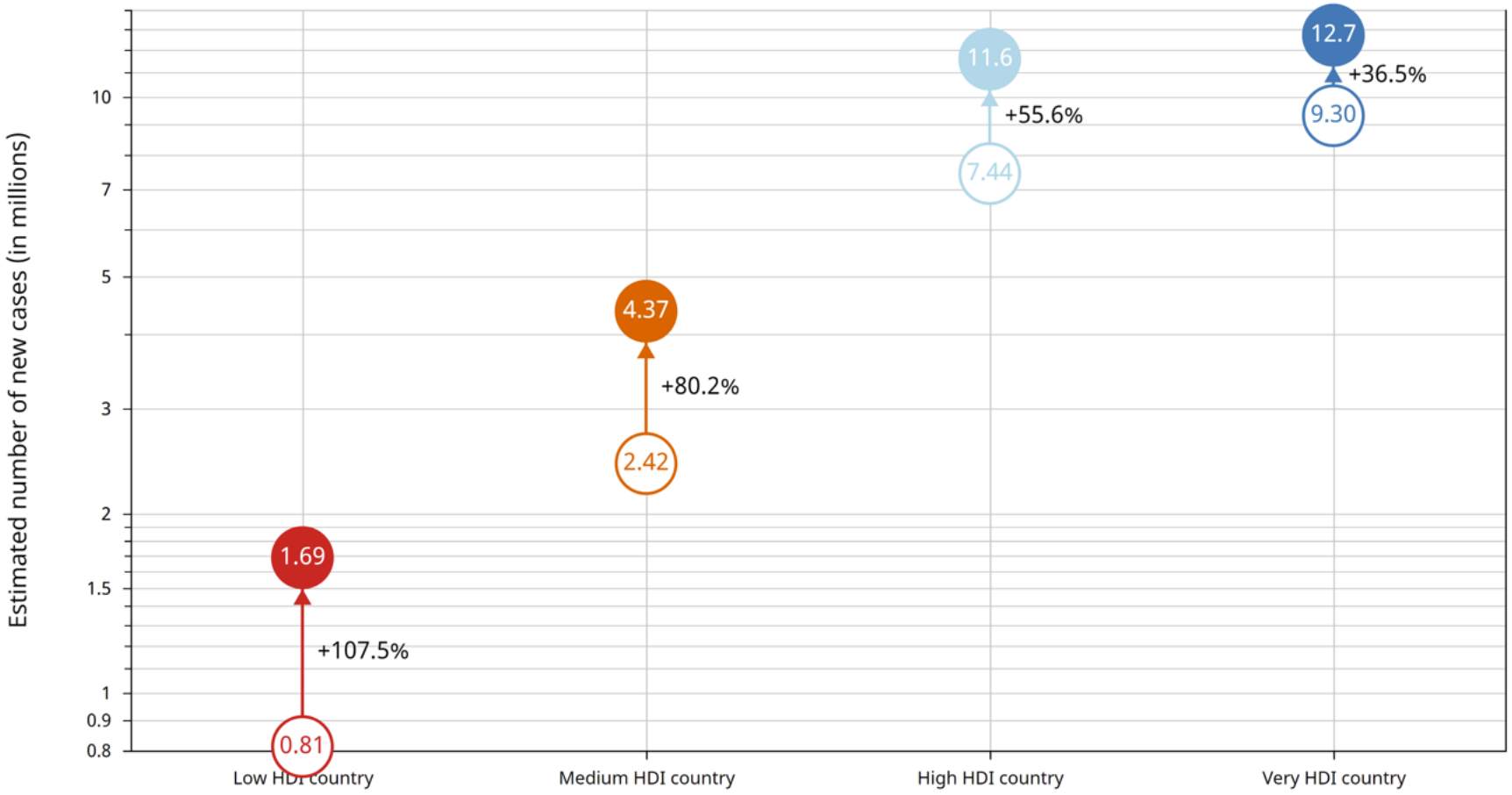
Ironically, longer human life spans make cancer more of a problem. This is because the incidence of cancer is much higher in persons over 65 years of age. As a result, the demand for cancer therapeutics is likely to rise disproportionately to overall pharma spend for at least several decades to come.





Source: https://www.who.int/publications/i/item/9789240001299

Highest Growth in Cancer from 2022 to 2045 Will be in Low Human Development Index (HDI) Countries



Cancer is mostly a disease of old age. Importantly, as life expectancies grow, there will be more cancer to deal with as a global society.

Source: IARC Global Cancer Observatory https://gco.iarc.who.int/tomorrow/en/

High Expected Growth in Oncology Drugs Reflects Unmet Need Among Patients

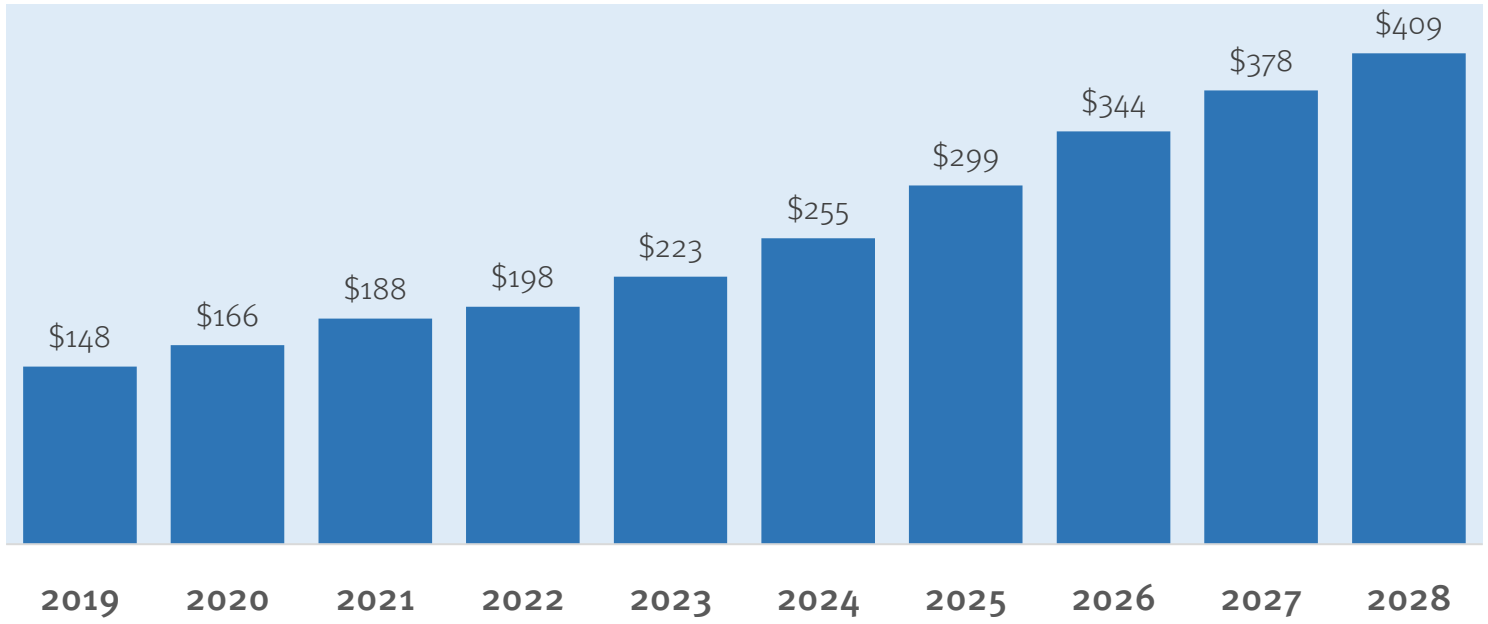
CAGR 2024–2028

9.9%

+$154BN

NET NEW GROWTH IN NEXT FIVE YEARS

Global Spending on Oncology Pharmaceuticals, 2019 to 2028 ($Billions)



ONCOLOGY DRUGS EXPECTED TO HAVE MOST DOLLAR GROWTH BETWEEN 2024 AND 2028 BY ANALYSTS

DARZALEX® +$6.1BN

ENHERTU® trastuzumab deruxtecan ▼ +$6.1BN

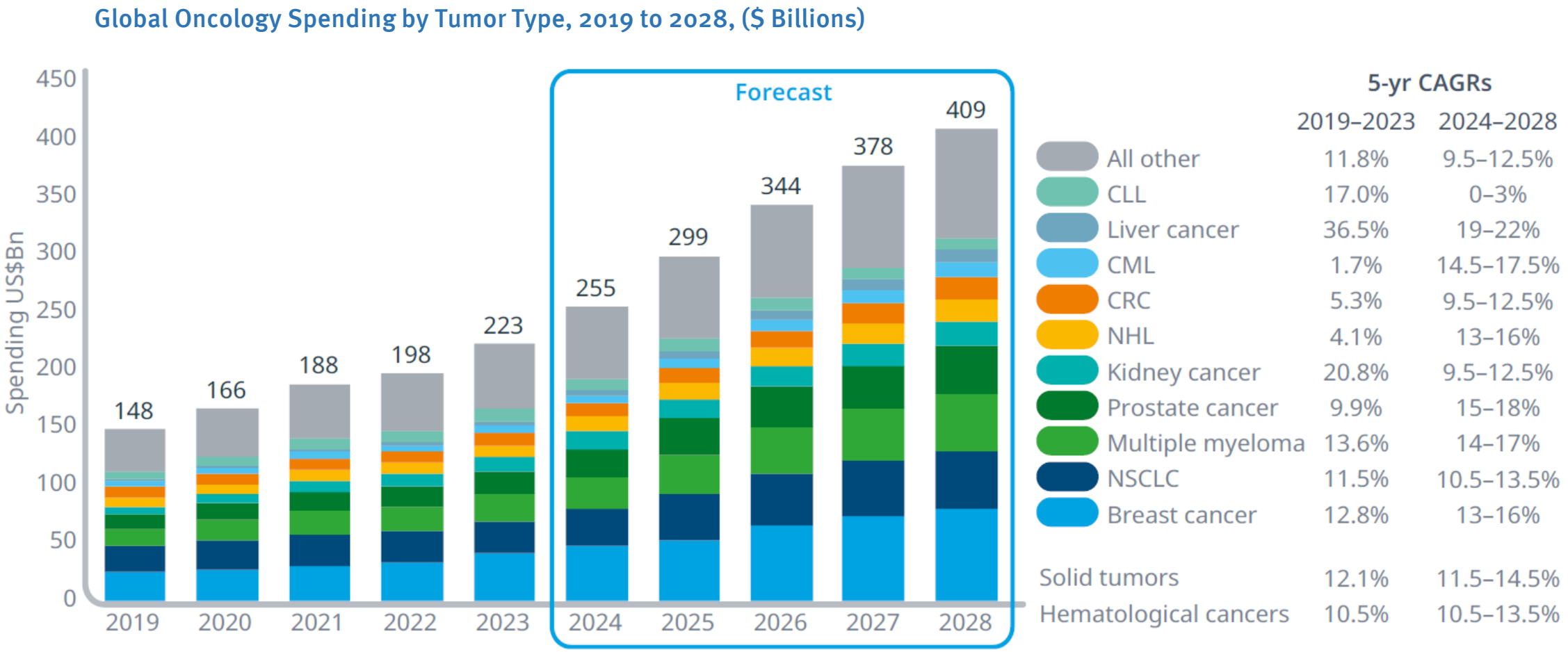
KEYTRUDA® (pembrolizumab) Injection 100 mg +$4.1BN

KISQALI® ribociclib +$3.8BN

CARVYKTI™ (ciltacabtagene autoleucel) Suspension for IV Infusion +$3.7BN

Source: IQVIA Institute, May 2024 (https://www.iqvia.com/insights/the-iqvia-institute/reports-and-publications/reports/global-oncology-trends-2024)

IQVIA Institute: Most Top Tumor Types Will See Double Digit Spending Growth From 2024 to 2028

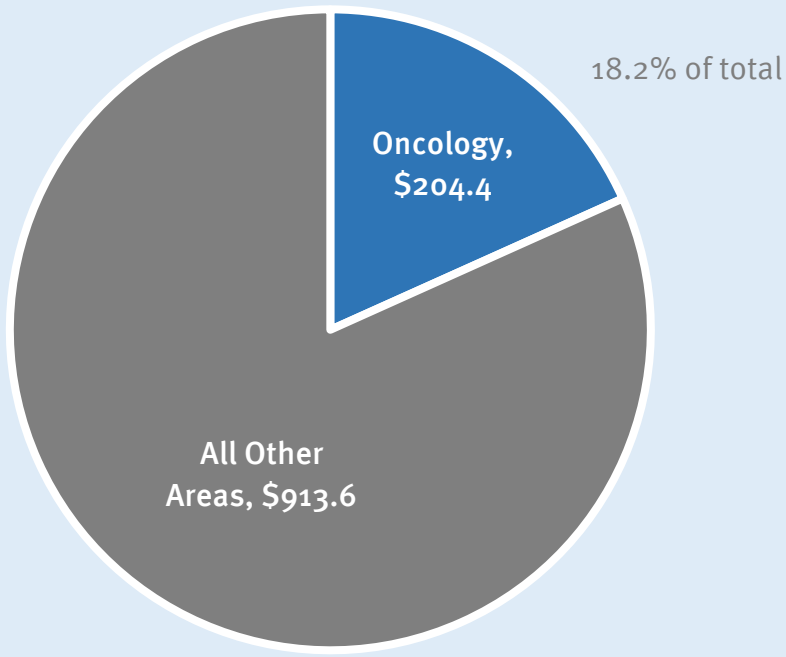


Sourced from: https://www.iqvia.com/insights/the-iqvia-institute/reports-and-publications/reports/global-oncology-trends-2024

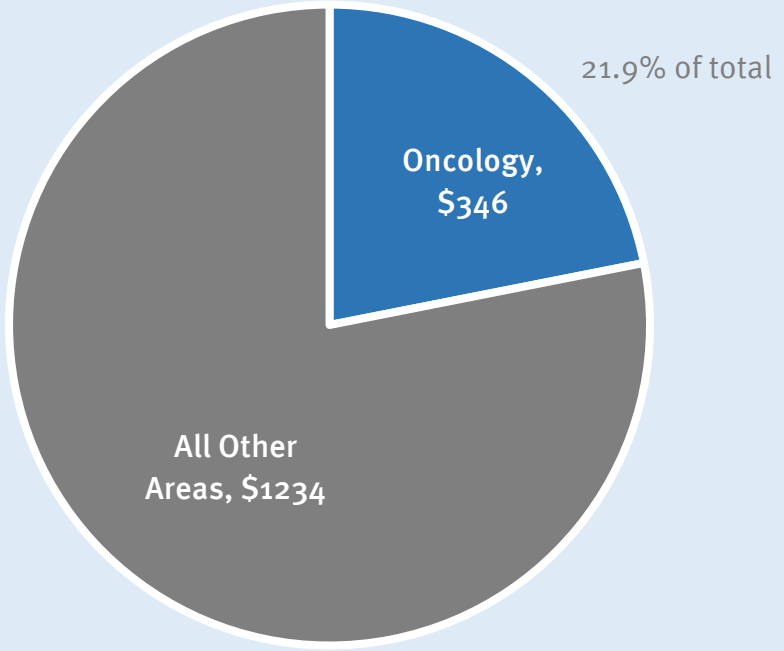
Evaluate Pharma: Oncology is the Largest Therapeutic Area by Total Revenue (2023 and 2028)

Cancer drugs make up by far the largest share of the global pharmaceuticals market (around 17%). Because of the high remaining areas of unmet need in cancer care, Evaluate Pharma forecasts that oncology drugs as a category are due to grow quite rapidly in the five years ahead.

Total Worldwide Pharma Sales, 2023 ($ Billions)



Total Worldwide Pharma Sales, 2028 ($ Billions)



Evaluate Pharma reports that 37.4% of pharma R&D is spent on oncology projects.

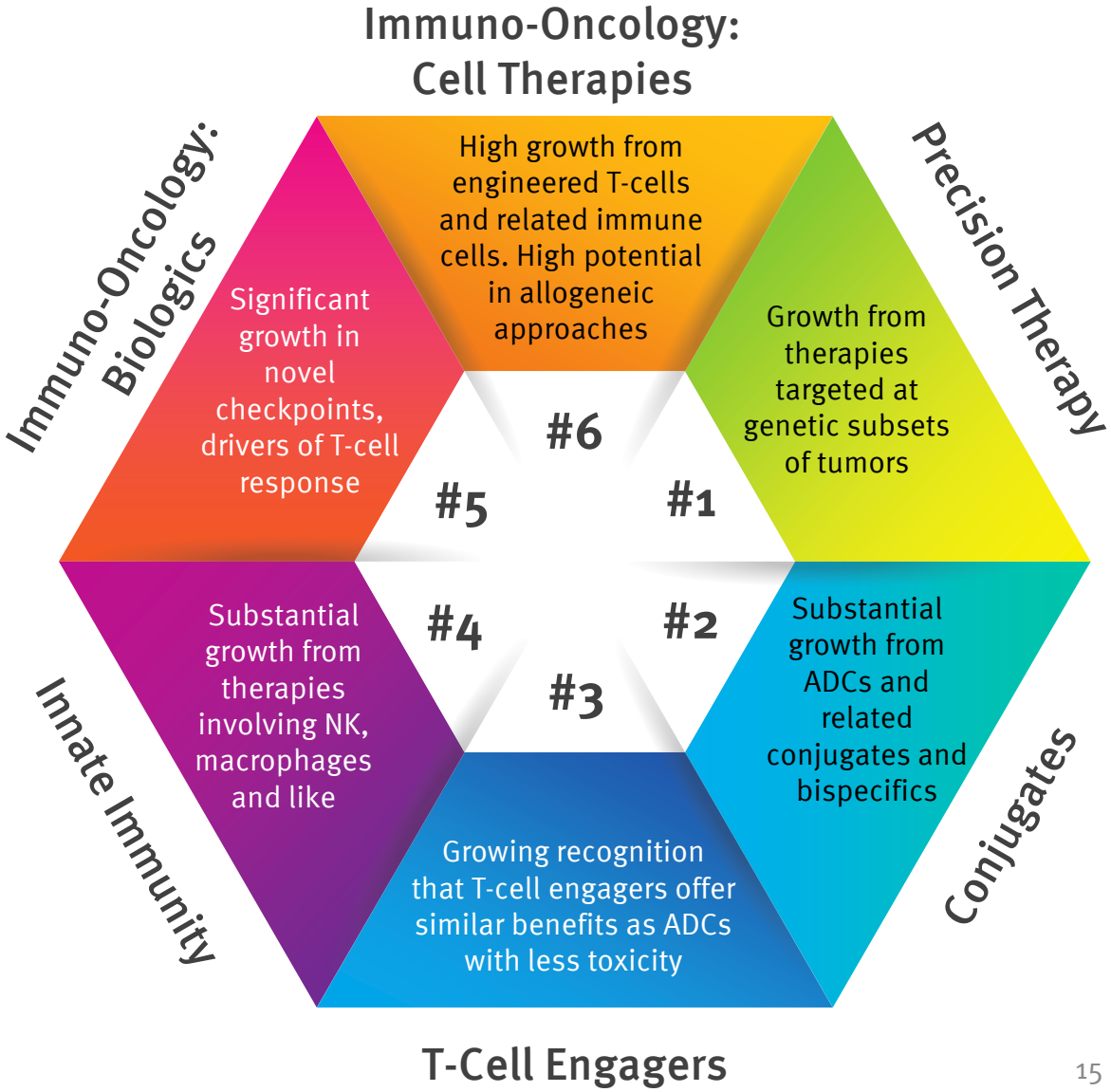
Sources: Evaluate Pharma data on oncology spend and *Evaluate Pharma World Preview 2023*.

Growth Areas in Oncology Therapeutics

The level of scientific focus and engagement on novel approaches to oncology is unprecedented.

Oncologists are rapidly embracing novel and improved ways to treat cancer. While legacy cytoxics and targeted therapies will be with us for many decades yet, the interest is particularly high in several new areas which include:

- precision therapies which offer the potential for very high efficacy, if even curative potential in genetically selected subsets of tumors;
- enhanced targeted therapies leveraging breakthroughs in understanding how to drug hard targets and to exploit synthetic lethality in drug design;
- antibody drug conjugates such as Enhertu® and PADCEV® and the many emerging variations on conjugate engineering;
- T-cell engagers which have the promise of ADC's but instead use the immune system to ablate tumorigenic cells;
- innate immune approaches including NK's and the inflammasome;
- antibodies against checkpoints that stretch well beyond PD-1 and CTLA-4 and
- cell therapies such as YESCARTA® and CARVYKTI®. The innovation in engineered TCR's, and CAR-T's has been impressive.



Top Ten Global Pharma Marketers of Innovative Oncology Drugs by 2023 Revenue ($ Billions)

Company	Lead Drug Today	Key Focus Area Today	Revenue Rank 2023	Oncology Revenue 2023 ($billion)	Revenue Rank 2025	Oncology Revenue 2025 ($billion)	Revenue Rank 2030	Oncology Revenue 2030 ($billion)
MERCK	Keytruda®	Immuno-Oncology	1	$27.90	1	$31.10	4	$25.10
Bristol Myers Squibb	Opdivo®	Immuno-Oncology	2	$26.50	4	$23.20	7	$17.30
Roche	Perjeta®	Targeted Oncology	3	$25.40	2	$26.67	3	$27.40
Johnson&Johnson	Darzalex®	B-Cell Targets	4	$17.70	3	$23.70	1	$36.80
AstraZeneca	Tagrisso®	Targeted Oncology	5	$17.20	5	$21.60	2	$29.50
Pfizer	Ibrance®	Targeted Oncology	6	$14.60	6	$19.56	5	$20.59
NOVARTIS	Kisqali®	Targeted Oncology	7	$14.40	7	$16.56	8	$15.30
AMGEN	Kyprolis®	Targeted Oncology	8	$8.10	8	$9.23	10	$9.40
Lilly	Verzenio®	Targeted Oncology	9	$6.50	9	$8.90	9	$12.80
abbvie	Imbruvica®	B-Cell Targets	10	$5.90	11	$6.10	11	$8.70

Note: Revenue estimate in oncology for 2023 taken from Pharmasights and each company's annual reports and earnings statements (sometimes data are not fully transparent, and we have had to make estimates). Revenue estimates for 2025 and 20230 are obtained from securities analyst reports for each company as tabulated by Evaluate Pharma.

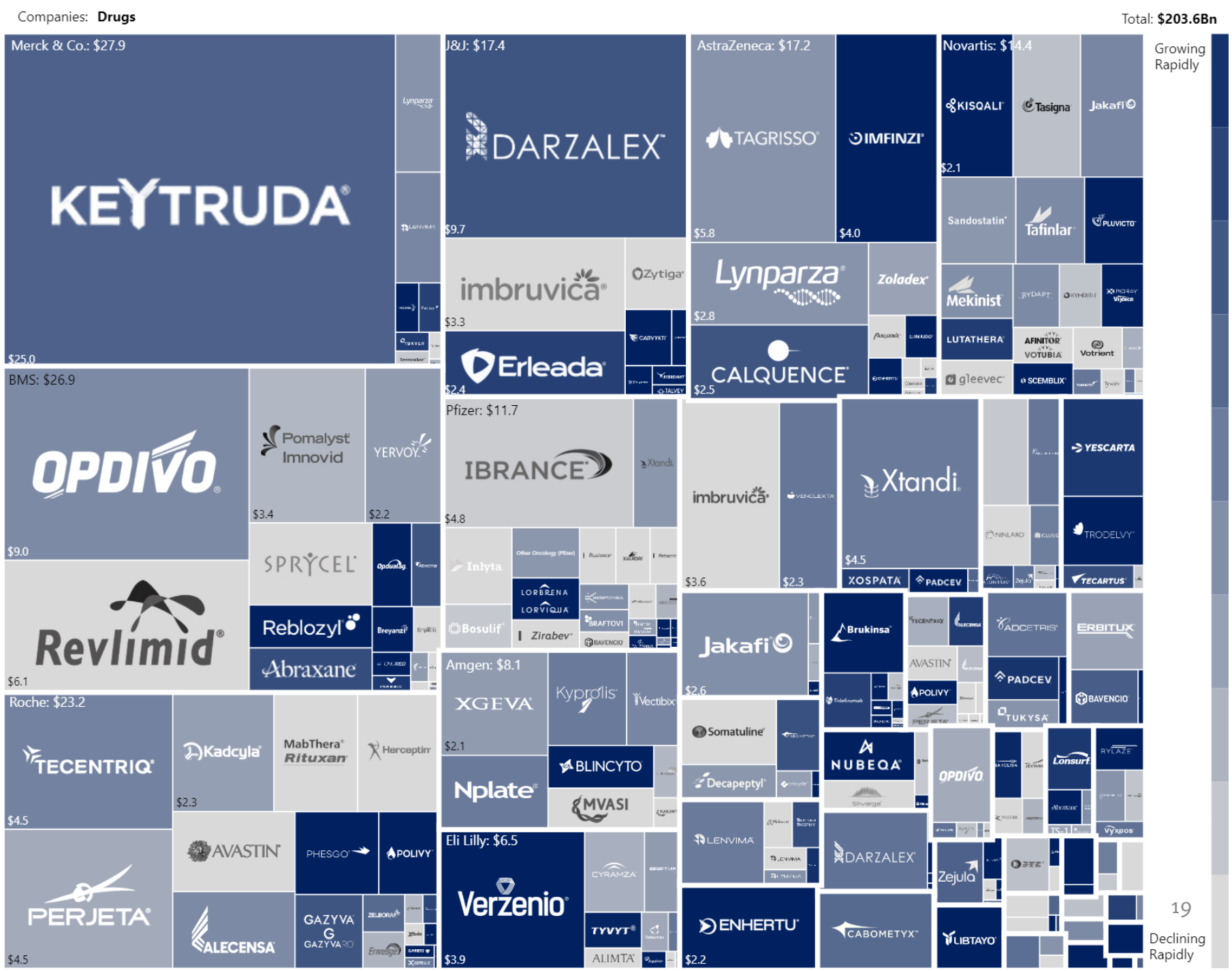
Next Ten Global Pharma Marketers of Innovative Oncology Drugs by 2023 Revenue ($ Billions)

Company	Lead Drug Today	Key Focus Area Today	Revenue Rank 2023	Oncology Revenue 2023 ($billion)	Revenue Rank 2025	Oncology Revenue 2025 ($billion)	Revenue Rank 2030	Oncology Revenue 2030 ($billion)
astellas	XTANDI®	Androgen Deprivation	11	$5.80	10	$6.20	15	$4.30
Takeda	Velcade®	Targeted Oncology	12	$3.90	17	$3.10	19	$2.85
Daiichi-Sankyo	Enhertu®	Targeted Oncology	13	$2.90	12	$6.00	6	$17.80
GILEAD	Trodelvy®	Targeted Oncology	14	$2.90	14	$4.40	12	$8.50
Incyte	Jakafi®	Targeted Oncology	15	$2.80	16	$3.30	25	$1.40
齐鲁制药 QILU PHARMACEUTICAL	Yiruike	Targeted Oncology	16	$2.70	13	$4.70	14	$4.70
IPSEN	Somatuline®	Targeted Oncology	17	$2.60	24	$1.70	24	$1.50
Eisai	Lenvima®	Targeted Oncology	18	$2.40	19	$2.40	27	$1.30
BeiGene	Brukinsa®	B-Cell Targets	19	$2.00	15	$3.50	13	$8.00
BAYER	Stivarga®	Targeted Oncology	20	$2.00	18	$3.00	16	$3.80

Note: Revenue estimate in oncology for 2023 taken from Pharmasights and each company's annual reports and earnings statements (sometimes data are not fully transparent, and we have had to make estimates). Revenue estimates for 2025 and 20230 are obtained from securities analyst reports for each company as tabulated by Evaluate Pharma.

Other Significant Commercial Players in Oncology Drugs

Oncology Market Map 2023



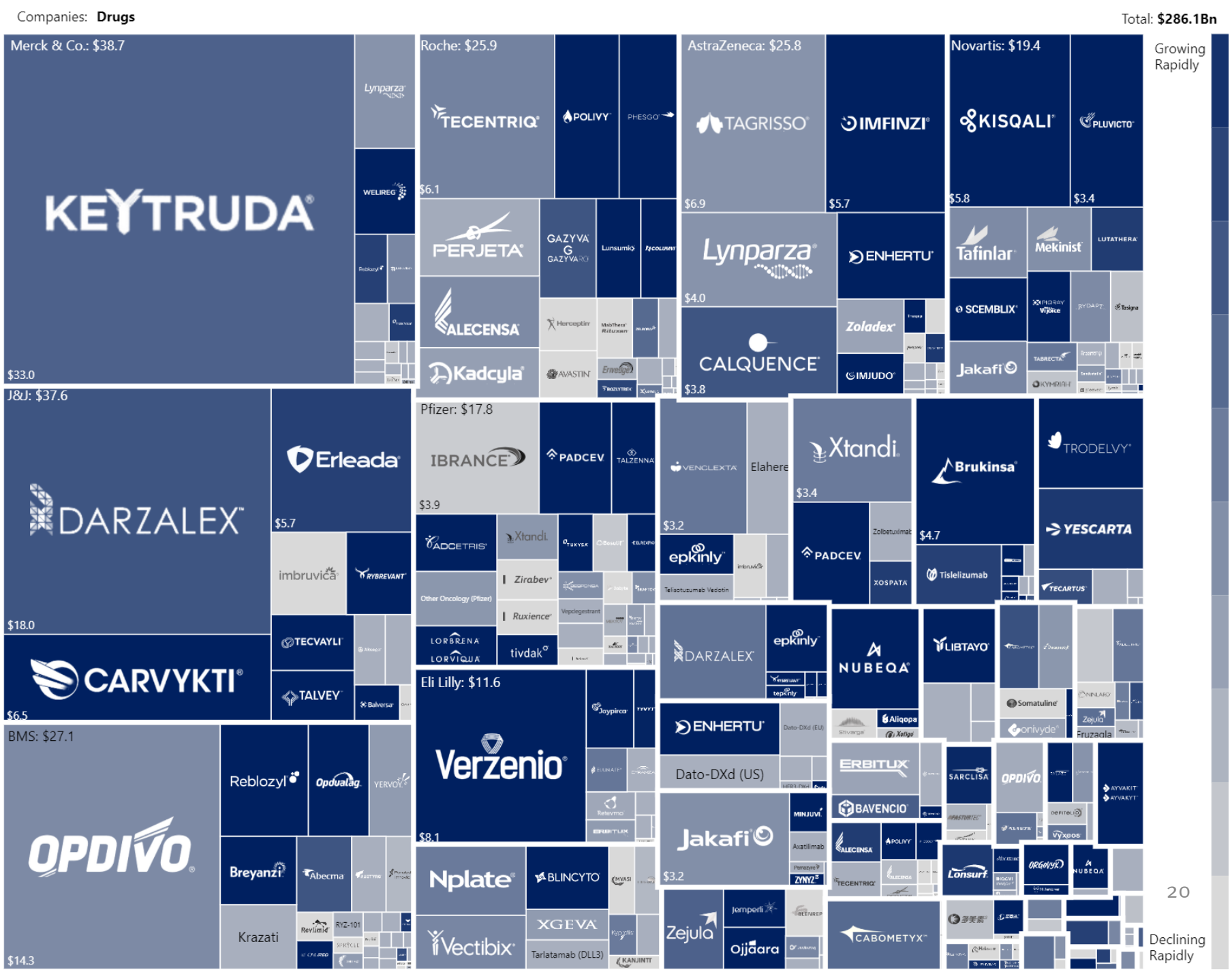
Source: Pharmasights

Oncology Market Map 2028

Merck still rules with $38.7bn in sales but Darzalex is gaining fast.

J&J moves into #2 slot (from #4) and Pfizer remains in #5 slot.

Source: Pharmasights



#ASCO2024 Highlights

Selected Cancer Study Presentation Summaries from ASCO

AFFIMED

Advanced NSCLC w/EGFR mutation

Regimen: **AFM24**
MOA: **EGFR x CD16A bispecific**
Evaluable Subjects: **5**
Median Prior Lines of Tx: **3**
ORR: **33%** | CR's: **7.5%**
Median Survival: **NA**
Grade 3 TRAE's: **47%**
Write-Up: Link

Akesobio / Summit therapeutics

Harmoni-2 Study

First Line NSCLC with EGFR mutation

Regimen: **ivonescimab vs chemo**
MOA: **PD1 x VEGFA (Phase 3)**
Doses: **20mg/kg every 3 weeks**
ITT Subjects: **322**
Prior Lines of Tx: **1**
ORR: **51% (vs. 44% chemo)**
Median PFS: **7.1 mo vs. 4.8**
OS HR**:** 0.46
Grade 3 TRAE's: **62% (vs 49%)**
Write-Up: Link

Johnson&Johnson

PALOMA 2 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

Pfizer

ALK+ NSCLC

Regimen: **Lorlatinib**
MOA: **ALK inhibitor**
Doses: **100mg lorlatinib vs 250mg crizotinib**
Evaluable Subjects: **296**
Prior Lines of Tx: **0**
Median PFS: **not reached mo vs. 9.3 months crizo**
PFS HR**:** 0.28
Grade 3 TRAE's: **77% v. 57%**
Write-Up: Link

Bristol Myers Squibb

KRASG12C-mutated NSCLC (Stage III/IV)

Regimen: **Adagrasib**
MOA: **KRAS inhibitor**
Doses: **600mg bid**
Evaluable Subjects: **453**
ORR by BICR: **31.9% v. 9.2%**
Grade 3 TRAE's: 4**7% v. 45%**
Write-Up: Link

AstraZeneca

DESTINY-Breast06

Breast Cancer HER2+, HER2 Low, HER2 ultralow

Regimen: **Datopotamab DXd**
MOA: **HER2 ADC V. chemo**
Evaluable Subjects: **866**
Prior Lines of Tx: **2**
ORR: **57.3% v. 31.2%**
HR: **38%**
Complete Response: **3%**
mDOR: **14 v 8.6 months**
Write-Up: Link

AstraZeneca

LAURA Ttrial

Stage 3 unresectable NSCLC w Exon 19/21 mut

Regimen: **Tagrisso**
MOA: **EGFR**
Doses: **80mg Tagrisso or placebo**
Evaluable Subjects: **216**
ORR: **57% v. 33%**
HR of death: **26%**
Complete Response: **2%**
mDOR: **37 months v. 7 months**
Grade 3 TRAE's: **32%**
Write-Up: Link

Merus

Recurrent HNSCC

Regimen: **Petosemtamab**
MOA: **EGFR x LGR5**
Doses: **1500mg Q2W**
Evaluable Subjects: **24**
Median Prior Lines of Tx: **2**
ORR: **67%** | CR's: **2.5%**
Median Survival: **NA**
Grade 3 TRAE's: **24%**
Write-Up: Link

sanofi

First Line Multiple Myeloma

Regimen: **Isatuximab + VRd**
MOA: **CD38 mAb**
Doses: 10**mg/Kg (Phase 3)**
Evaluable Subjects: **446**
Prior Lines of Tx: **0**
PFS: **59.7 mo vs. 45.2% VRd**
ORR: **36%**
Complete Response: **75% v. 64%**
Grade 3 TRAE's: **14%**
Write-Up: Link

Pfizer

ER+HER2– Metastatic Breast Cancer

Regimen: **PF-07248144**
MOA: **KAT6 inhibitor**
Doses: 1**mg to 15mg (Phase 1)**
Evaluable Subjects: **29**
Prior Lines of Tx: **5**
ORR: **11% (combo: 38%)**
Grade 3 TRAE's: **60%**
Write-Up: Link

Stat+ on #ASCO2024

By Adam Feuerstein , Matthew Herper , and Angus Chen, *Stat+*, June 4, 2024 (excerpt)

Adam's Take: Some hits, but relatively quiet

This was a big meeting for small hazard ratios. We're talking "HRs" in the teens from targeted medicines made by AstraZeneca and Pfizer. For those not statistically inclined, that means long-term treatment benefits that reduce a patient's risk of death or tumor progression by 80% or more. Phenomenal.

I spied a KRAS conundrum. Elegant science and decades of research finally cracked the undruggable cancer target, yielding two marketed drugs: Amgen's Lumakras and Bristol Myers Squibb's Krazati. But their benefits for patients with non-small cell lung cancer, where the mutation is most prevalent, are modest at best. Krazati showed a median tumor progression benefit of just 1.6 months over chemotherapy in a confirmatory study presented here. On a more encouraging note, there were early looks at data here on combination regimens and next-generation KRAS-targeting drugs that may yield better outcomes.

AstraZeneca is the Real Madrid of ASCO. Six plenary podiums in a row.

Daiichi Sankyo had its own mini-plenary with the presentation of the Enhertu DB-06 study in hormone receptor-positive, metastatic breast cancer, including a new category of "ultra low HER2" patients. "It's not an overestimation to say that [Enhertu] is the most potent drug ever developed for breast cancer," Paolo Tarantino, a medical oncologist at the Dana-Farber Cancer Institute, told me.

It was a relatively quiet meeting for biotechs. Most of the investors I met here mentioned Merus and Immunocore, but little else stood out. Summit Therapeutics was a sideshow.

Speaking of Merus, the company exploited an ASCO-sanctioned loophole that allows companies to report "final" data before the meeting even starts. There are some limitations, but essentially, the Merus ASCO suspense ended days before anyone even flew to Chicago.

There's also some suspense for the future of CAR-T. For so long, the CAR-T field has been trying, in vain, to crack the solid tumor egg. This ASCO had a very interesting Phase 1 study from (continuing ASCO crown-winner, agreed) AstraZeneca and its partners at AbelZeta and Zhejiang University School of Medicine.

In the dose escalation trial, their CAR-T for advanced liver cancer had an overall response rate of over 50% and a response rate of 75% in the highest dose level. With ongoing responses and a reasonable safety profile, I'm definitely looking forward to seeing how the Phase 2 trial turns out. AstraZeneca is recruiting for it now.

This CAR had an interesting target in the oncofetal protein GPC3, and it also was armored against the immunosuppressive cytokine TGF-beta. If success is seen in the Phase 2, it could mean there's a future in solid tumors with these next generation CAR-Ts that include armoring or other strategies.

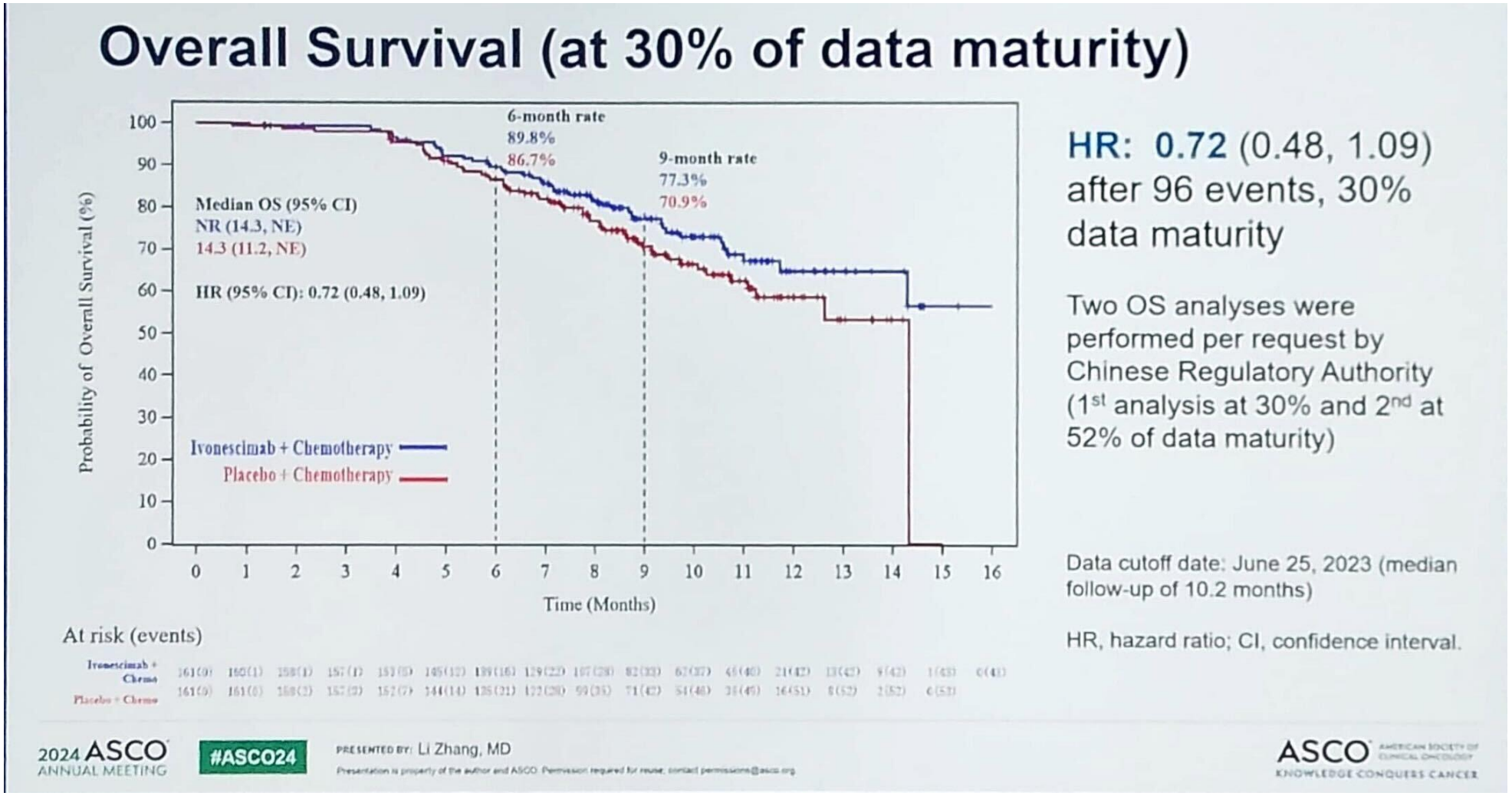
Source: https://www.statnews.com/2024/06/04/asco-takeaways-cancer-care-astrazeneca-car-t-china-data/

ASCO Kicks Off with a Jolt

“Good morning, Vietnam! Hey, this is not a test. This is rock and roll. Time to rock it from the delta to the DMZ!”

Adrian Cronauer - Good Morning, Vietnam

Promising Data from Summit / AkesoBio



JAMA®

QUESTION Among patients with non-small cell lung cancer with the epidermal growth factor receptor (EGFR) variant with resistance to EGFR tyrosine kinase inhibitor (EGFR-TKI) treatment, does the addition of ivonescimab to chemotherapy improve progression-free survival?

CONCLUSION Ivonescimab plus chemotherapy significantly improved progression-free survival, compared with placebo plus chemotherapy, with tolerable safety profile in TKI-treated non-small cell lung cancer.

© AMA

POPULATION

156 Men
166 Women

Adults 18 to 75 years with EGFR-variant non-small cell lung cancer with the with resistance to EGFR-TKI treatment

Median age: 59 years

LOCATION

55
Medical centers in China

INTERVENTION

322 Patients randomized

161

Ivonescimab

Ivonescimab plus pemetrexed and carboplatin for 4 cycles followed by ivonescimab plus pemetrexed maintenence

161

Placebo

Placebo plus pemetrexed and carboplatin for 4 cycles followed by placebo plus pemetrexed maintenence

PRIMARY OUTCOME

Progression-free survival

FINDINGS

Median progression-free survival

Ivonescimab	7.1 months (95% CI, 5.9 to 8.7)
Placebo	4.8 months (95% CI, 4.2 to 5.6)

Ivonescimab plus chemotherapy significantly improved progression-free survival:

Between-group difference, **2.3 months**

Hazard ratio, **0.46** (95% CI, 0.34 to 0.62); $P < .001$

HARMONi-A Study Investigators. Ivonescimab plus chemotherapy in non-small cell lung cancer with EGFR variant: a randomized clinical trial. *JAMA*. Published online May 31, 2024. doi:10.1001/jama.2024.10613

Ivonescimab Monotherapy Decisively Beats Pembrolizumab Monotherapy Head-to-Head, Achieves Statistically Significant Superiority in PFS in First-Line Treatment of Patients with PD-L1 Positive NSCLC in China

Miami, Florida, May 30, 2024 – Summit Therapeutics Inc. (NASDAQ: SMMT) ("Summit," "we," or the "Company") today announced that the Phase III clinical trial, HARMONi-2 or AK112-303, met its primary endpoint of progression-free survival (PFS). HARMONi-2 evaluated monotherapy ivonescimab against monotherapy pembrolizumab in patients with locally advanced or metastatic non-small cell lung cancer (NSCLC) whose tumors have positive PD-L1 expression (PD-L1 TPS ›1%). HARMONi-2 is a single region, multi-center, double-blinded Phase III study conducted in China sponsored by Akeso, Inc. (Akeso, HKEX Code: 9926.HK) with data generated and analyzed by Akeso.

At a prespecified interim analysis conducted by an independent Data Monitoring Committee, ivonescimab demonstrated a statistically significant and clinically meaningful improvement in PFS by blinded independent central radiology review committee (BICR) compared to pembrolizumab. The PFS benefit was demonstrated across clinical subgroups, including those with PD-L1 low expression (PD-L1 TPS 1-49%), PD-L1 high expression (PD-L1 TPS ›50%), squamous and non-squamous histologies, as well as other high-risk patients.

There are no known Phase III clinical trials in NSCLC which have shown a statistically significant improvement compared to pembrolizumab in a head-to-head setting.

The Phase III HARMONi-2 study, along with the approval of ivonescimab in China in combination with chemotherapy based on the results of the HARMONi-A trial, provides clear evidence supporting the purposefully-engineered, differentiated mechanism of action of ivonescimab, a PD-1 / VEGF bispecific antibody evidencing cooperative binding characteristics, and its opportunity to improve upon the existing standards of care for solid tumors.

Source: https://www.smmttx.com/pressrelease/ivonescimab-monotherapy-decisively-beats-pembrolizumab-monotherapy-head-to-head-achieves-statistically-significant-superiority-in-pfs-in-first-line-treatment-of-patients-with-pd-l1-positive-nsclc-in/

Akeso, Summit's Keytruda Win Draws 'Explosive' Interest at ASCO. But What Does Merck Think?

Angus Liu, *FiercePharma*, June 3, 2024 (excerpt)

Analysts are doing their best to sort out the financial ramifications, and biopharma insiders are eager to see the exact data. But what does Merck think?

"Good news for patients or maybe another [treatment] option," Eliav Barr, M.D., chief medical officer at Merck Research Laboratories, said in an interview with Fierce Pharma at the ASCO 2024 meeting. "The issue," Barr continued, is that "there's been a lot of data looking at VEGF inhibitors in lung cancer. And we've done, God knows, a lot of studies of VEGF inhibition with [Keytruda]. In many of our studies, PFS was positive, including in lung. But [overall survival] was a little more difficult to show." "Patients, regulators, payers [...] will focus on OS," Barr continued. "So, we'll see. It's possible that this is going to be something interesting."

Indeed, in the phase 3 LEAP-007 trial in first-line PD-L1-positive NSCLC, Merck and partner Eisai's combination of Keytruda and Lenvima led to a statistically significant 22% reduction in the risk of disease progression or death but a negative 10% trend in overall survival compared with Keytruda alone. Lenvima is a kinase inhibitor targeting VEGF receptors and many other proteins involved in cancer. As Barr indicated, an overall survival win would likely be needed for the Akeso/Summit drug to win an approval from the FDA in first-line NSCLC. Trouncing Keytruda in its home turf would be a huge deal, considering the drug's $25 billion in sales across numerous indications in 2023.

Source: https://www.fiercepharma.com/pharma/merck-cmo-akeso-summits-keytruda-head-head-win-maybe-another-option-issue

Summit's ASCO press release indicating a decisive win against Keytruda® was the biggest news at ASCO this year.

The comments at left indicate that we will need to wait to see OS data for Ivonescimab against Keytruda®.

This is fair although Summit is on track to deliver those data with the Harmoni trial – which involves a head-to-head study of ivo against pembro in squamous first-line lung cancer. The Harmoni study will be fully enrolled this year and should report out initial results in 2025.

Importantly, the design of ivo involves a tetravalent structure (four binding sites) designed to enable higher avidity in the tumor microenvironment with over 18-fold increased binding affinity to PD-1 in the presence of VEGF in vitro.

It strikes us as not unlikely that ivo will, indeed, show a survival benefit versus pembro when Harmoni reads out in the next year or two.

Ivonescimab Global Oncology Clinical Trials

Summit therapeutics

Trial	Indication	Histology/Population	Regimen	Phase III
★ HARMONi	NSCLC	EGFRm+ 2L+ Advanced or Metastatic	Combo ivonescimab + chemo vs. placebo + chemo	
★ HARMONi-3	NSCLC	Squamous 1L Metastatic	Combo ivonescimab + chemo vs. pembro + chemo	

Akesobio

Indication	Regimen	Phase I	Phase II	Phase III
★ NSCLC: 2L EGFRm+ / HARMONi-A	Randomized: Combo (chemo) vs. chemo			
NSCLC: 1L PD-L1 TPS>1% / HARMONi-2	Randomized: Monotherapy vs. pembro (PD-1)			
★ NSCLC: 1L Squamous	Randomized: Combo (chemo) vs. tislelizumab (PD-1) + chemo			
★ NSCLC: 1L Squamous	Randomized: Combo (chemo) vs. pembro (PD-1) + chemo			
Advanced Solid Tumors	Monotherapy			
NSCLC	Combo (chemo)			
NSCLC	Monotherapy			
GYN Tumors	Monotherapy			
Ovarian Cancer	Combination (PARPi)			
NSCLC	Monotherapy & Combo (chemo)			
CRC	Combo (CD47 + chemo)			
HCC	Monotherapy			
NSCLC	Combo (PD-1 / CTLA-4 bsAb + chemo)			
HNSCC	Combo (CD47)			
Advanced Solid Tumors**	Combo (CD47, CD47 + chemo, chemo)			
TNBC	Combo (chemo, CD47 + chemo)			
NSCLC	Combo (CD73 + chemo)			
Advanced Solid Tumors	Monotherapy			
ES-SCLC	Combo (chemo)			

These ivonescimab clinical trials are being conducted in China and/or Australia and are fully sponsored and managed by Akeso.

1,600+ Patients Treated with Ivonescimab

19 Clinical Trials
4 Phase III
13 Phase II
2 Phase I

7 Dedicated Trials
Outside NSCLC

NSCLC: Non-Small-cell Lung Cancer, EGFRm+: Epidermal Growth Factor Receptor mutant positives, Combo: Combination, Chemo: Chemotherapy, pembro: pembrolizumab, CRC: Colorectal Cancer, HCC: Hepatocellular Carcinoma, HNSCC: Head & Neck Squamous Cell Carcinoma, BTC: Biliary Tract Cancer, TNBC: Triple Negative Breast Cancer, ES-SCLC: Extensive Stage Small Cell Lung Cancer, PD-1: Programmed Cell Death Protein 1, PARPi: poly(ADP-ribose) polymerase inhibitors **Includes Gastric, BTC, Pancreatic, NSCLC

★★ Same Patient Population

Ivonescimab is an investigational therapy not approved by any regulatory authority other than China's National Medical Products Administration (NMPA)

Insanely Good Data in Locally Advanced Mismatch Repair Deficient CRC with Ipi / Nivo Neoadjuvant Combo

The NEW ENGLAND JOURNAL of MEDICINE
ESTABLISHED IN 1812 JUNE 6, 2024 VOL. 390 NO. 21

Neoadjuvant Immunotherapy in Locally Advanced Mismatch Repair–Deficient Colon Cancer

Myriam Chalabi, M.D., Ph.D., Yara L. Verschoor, M.D., Pedro Batista Tan, M.Sc., Sara Balduzzi, Ph.D.,

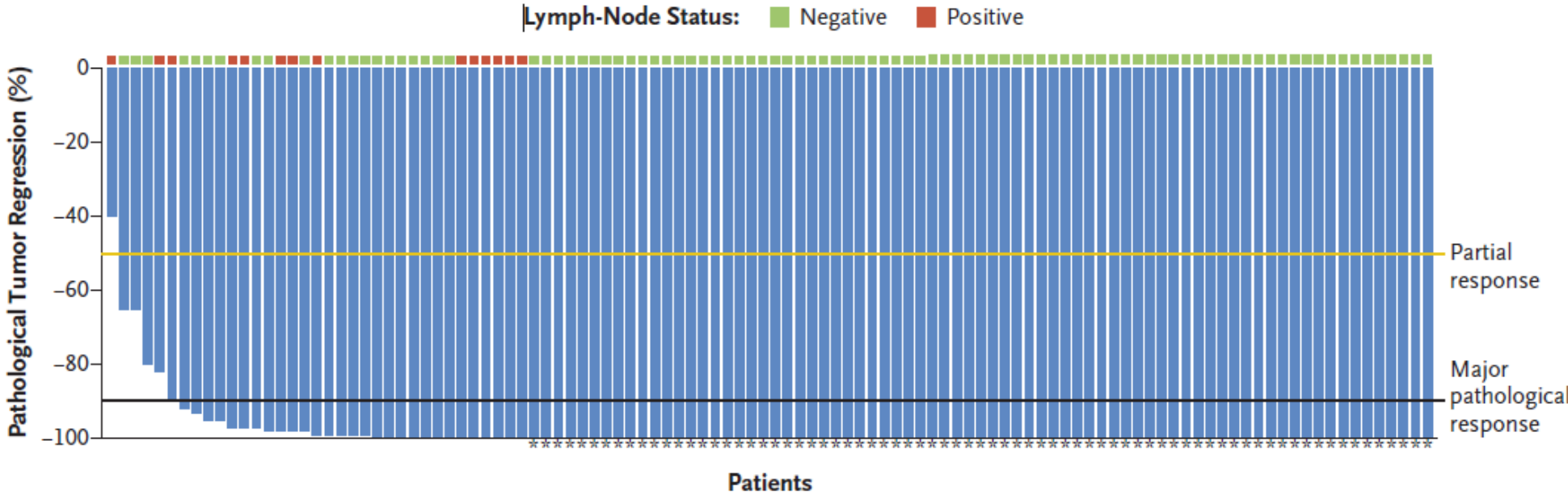


Figure 2. Pathological Responses among Patients in the Efficacy Analysis.

The waterfall plot shows the percentage of pathological tumor regression per tumor among the 110 tumors that could be evaluated for a pathological response. Boxes above each bar indicate the corresponding pathological lymph-node status. Patients with a pathological complete response in both the primary tumor and the lymph nodes are indicated by an asterisk. The black horizontal line indicates the threshold for a major pathological response, specified as at least 90% tumor regression. The yellow line indicates the threshold for a partial response, specified as at least a 50% regression.

Source: https://www.nejm.org/doi/full/10.1056/NEJMoa2400634

Jemperli® Trial Continues to Show Unprecedented Results with no Evidence of Disease in 100% of Patients with Locally Advanced Mismatch Repair Deficient (dMMR) Rectal Cancer

GSK Press Release, June 3, 2024

GSK plc (LSE/NYSE: GSK) today announced updated, longer-term results from the phase II supported collaborative study with Memorial Sloan Kettering Cancer Center (MSK) evaluating Jemperli (dostarlimab-gxly) as a first-line treatment—as an alternative to surgery—for mismatch repair deficient (dMMR) locally advanced rectal cancer. **The trial showed an unprecedented 100% clinical complete response rate (cCR) in 42 patients who completed treatment with dostarlimab-gxly, defined as complete pathologic response or no evidence of tumors as assessed by magnetic resonance imaging, endoscopy and digital rectal exam.** In the first 24 patients evaluated, a sustained clinical complete response with a median follow-up of 26.3 months (95% CI: 12.4-50.5) was observed.

These late-breaking data are being presented today at the 2024 American Society of Clinical Oncology (ASCO) Annual Meeting (May 31– June 4) in Chicago, IL as a rapid oral presentation (abstract LBA3512). The latest research presented today from the phase II trial builds on the findings initially presented in a late-breaking presentation at the 2022 ASCO Annual Meeting with simultaneous publication in The New England Journal of Medicine.

Hesham Abdullah, Senior Vice President, Global Head Oncology, R&D, GSK, said: “The data showing no evidence of disease in 42 patients is remarkable. These results bring us one step closer to understanding the potential of dostarlimab-gxly in this curative-intent setting for patients with dMMR locally advanced rectal cancer. We look forward to evaluating dostarlimab-gxly in certain colorectal cancers in our ongoing AZUR-1 and AZUR-2 registrational studies.”

Source: https://us.gsk.com/en-us/media/press-releases/jemperli-dostarlimab-gxly-trial-continues-to-show-unprecedented-results/

100% of Cancer Patients Cured Long-term in ‘Remarkable’ Human Trial

Bronwyn Thompson, *New Atlas*, June 5, 2024 (excerpt)

In what researchers have called an "unprecedented" response, a new drug that treats locally advanced rectal cancer has shown to have completely eradicated tumors in all 42 patients who took part in the Phase II trial.

The drug, Jemperli (dostarlimab-gxly), had earlier shown great potential for eliminating mismatch repair deficient (dMMR) cancers, which make up 5-10% of colorectal cancers. Following the Phase II trial, the first 24 patients assessed showed a "sustained complete clinical response" – no cancer evident – after an average of 26.3 months.

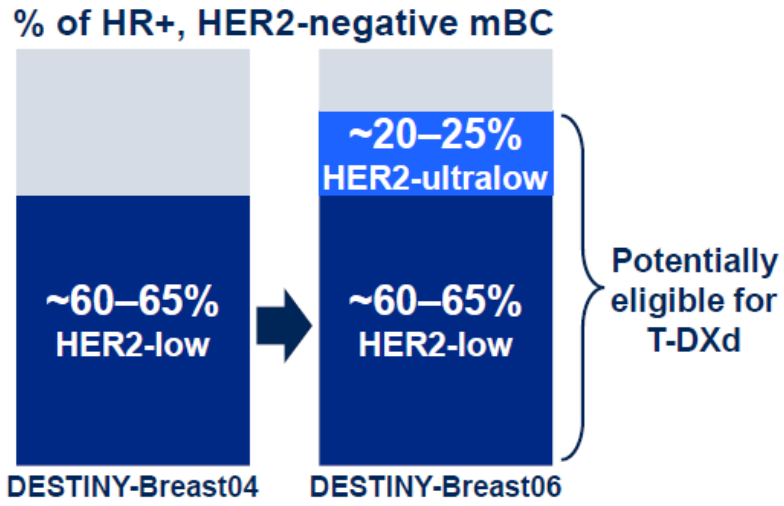
"These findings demonstrate the potential of dostarlimab-gxly as a novel approach to treating locally advanced dMMR rectal cancer that leads to durable complete tumor regression without the need for life-altering treatment," said Dr Andrea Cercek, researcher and oncologist at the Memorial Sloan Kettering Cancer Center (MSK). "As a clinician, I’ve seen firsthand the debilitating impact of standard treatment of dMMR rectal cancer and am thrilled about the potential of dostarlimab-gxly in these patients.”

The drug is a hugely promising first-line treatment option, bypassing the need for chemotherapy and radiation. Right now, while traditional treatment is effective, it's incredibly invasive and impacts long-term quality of life. And ultimately, a third of patients will see their cancer metastasize and become terminal.

Source: https://newatlas.com/medical/colorectal-cancer-dostarlimab-gxly/

DESTINY-Breasto6 Opens Up Many More Pts to Enhertu®

DESTINY-Breast06: key takeaways



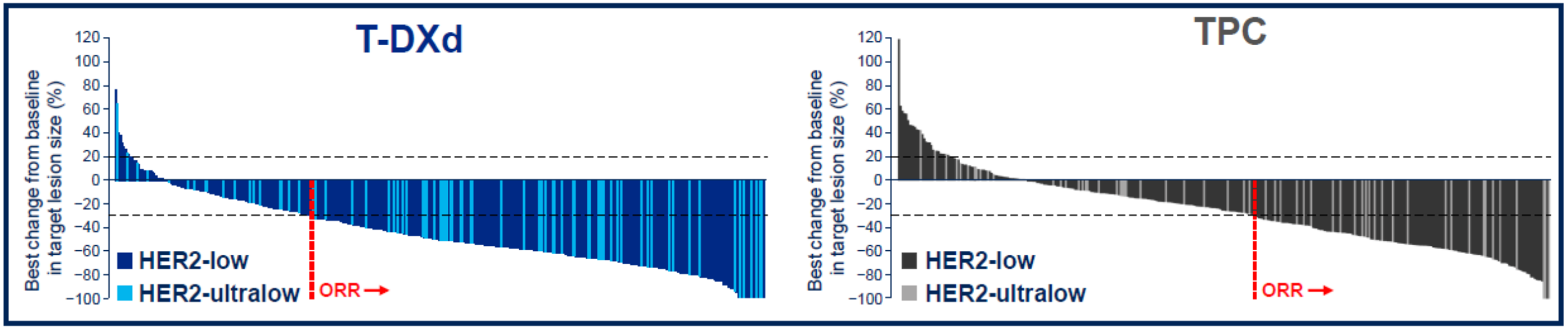
- T-DXd demonstrated efficacy in **HER2-low mBC** in an **earlier line of treatment** to DESTINY-Breast04
- Including HER2-ultralow, the proportion of patients who could benefit from T-DXd is **~85% of HR+, HER2-negative mBC** after DESTINY-Breast06

In DESTINY-Breast06, T-DXd demonstrated a statistically significant and clinically meaningful PFS benefit vs TPC (chemotherapy) in HR+, HER2-low mBC after ≥1 endocrine-based therapy, with consistent results in HER2-ultralow mBC

HER2, human epidermal growth factor receptor 2; HR+, hormone receptor–positive; mBC, metastatic breast cancer; PFS, progression-free survival; T-DXd, trastuzumab deruxtecan; TPC, chemotherapy treatment of physician's choice

Source: https://www.daiichisankyo.com/files/investors/library/materials/2024/ASCO_2024_presentation.pdf

Antitumor activity For Enhertu in DESTINY-Breasto6

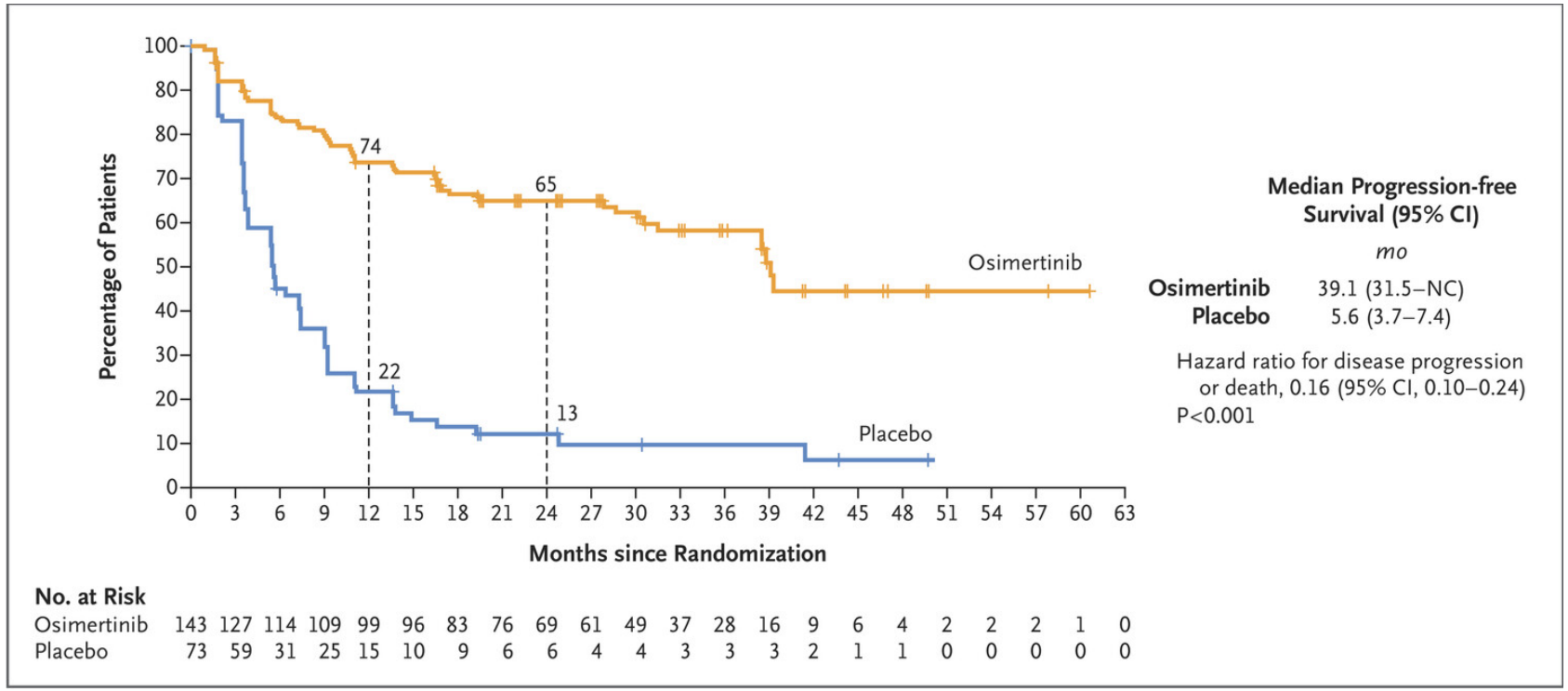


	HER2-low*		ITT		HER2-ultralow*	
	T-DXd (n=359)	TPC (n=354)	T-DXd (n=436)	TPC (n=430)	T-DXd (n=76)	TPC (n=76)
Confirmed ORR, n (%)	**203 (56.5)**	**114 (32.2)**	**250 (57.3)**	**134 (31.2)**	**47 (61.8)**	**20 (26.3)**
Best overall response, n (%)						
Complete response	9 (2.5)	0	13 (3.0)	0	4 (5.3)	0
Partial response	194 (54.0)	114 (32.2)	237 (54.4)	134 (31.2)	43 (56.6)	20 (26.3)
Stable disease	125 (34.8)	170 (48.0)	148 (33.9)	212 (49.3)	22 (28.9)	42 (55.3)
Clinical benefit rate, n (%)†	275 (76.6)	190 (53.7)	334 (76.6)	223 (51.9)	58 (76.3)	33 (43.4)
Median duration of response, mo	14.1	8.6	14.3	8.6	14.3	14.1

ORR based on RECIST v1.1; response required confirmation after 4 weeks
*HER2-low status defined at randomization per IRT data, and HER2-ultralow status defined by central laboratory testing data; †defined as complete response + partial response + stable disease at Week 24, by blinded independent central review
HER2, human epidermal growth factor receptor 2; IHC, immunohistochemistry; IRT, interactive response technology; ITT, intent-to-treat; mo, months; ORR, objective response rate; RECIST, Response Evaluation Criteria in Solid Tumors;

Source: https://www.daiichisankyo.com/files/investors/library/materials/2024/ASCO_2024_presentation.pdf

Tagrisso® Reduced the Risk of Disease Progression or Death by 84% in patients with Unresectable, Stage III EGFR-mutated Lung Cancer vs. Placebo in LAURA Phase III Trial



The figure shows Kaplan–Meier estimates of the duration of progression-free survival (assessed by blinded independent central review with the use of Response Evaluation Criteria in Solid Tumors, version 1.1). Tick marks indicate censored data, and vertical dashed lines indicate the times of landmark analyses of progression-free survival. The median duration of follow-up for progression-free survival in all patients was 22.0 months (range, <0.1 to 60.6) in the osimertinib group and 5.6 months (range, <0.1 to 49.7) in the placebo group; the median duration of follow-up for progression-free survival in patients whose data were censored was 27.7 months (range, <0.1 to 60.6) in the osimertinib group and 19.5 months (range, <0.1 to 49.7) in the placebo group. CI denotes confidence interval, and NC not calculable.

Source: https://www.nejm.org/doi/full/10.1056/NEJMoa2402614

Merus Phase 2 Study in First Line Recurrent Head and Neck Cancer

Phase 2 study (NCT03526835)

1L petosemtamab in combination with pembrolizumab

Key HNSCC inclusion criteria

- 1L r/m PD-L1+ HNSCC*
- ECOG PS 0-1
- Measurable disease

Treatment plan

- Petosemtamab 1500 mg IV, Q2W (28-day cycle) with pembrolizumab 400 mg IV Q6W
- Until PD or toxicity
- Tumor assessment Q8W

Follow-up

- Survival follow-up for up to 3 years

Objectives

- **Primary objectives:** ORR using RECIST 1.1 per investigator, and safety and tolerability
- **Secondary objectives:** DOR and PFS (per investigator and central review), ORR (per central review), OS, PK, immunogenicity, and biomarkers
- **Efficacy evaluable population:** Patients treated as of the abstract cutoff date (who had the opportunity for ≥4 months follow-up), with ≥2 treatment cycles and ≥1 post-baseline tumor assessment, or who discontinued early due to disease progression or death

Enrollment and analysis

Data cutoff date
06-Mar-2024

Enrollment
45 patients

Efficacy evaluable population
24 patients

- 19 patients enrolled after abstract cutoff date
- 2 patients were excluded per protocol:
  - 1 patient withdrew consent prior to first tumor assessment
  - 1 patient discontinued due to toxicity with <2 cycles of treatment

**PD-L1+ is defined as a patient with a PD-L1 CPS ≥1.*
CPS, combined positive score; DOR, duration of response; ECOG PS, Eastern Cooperative Oncology Group performance status; IV, intravenous; OS, overall survival; PD, progressive disease; PD-L1, programmed cell death-ligand 1; PFS, progression-free survival; PK, pharmacokinetics; Q2W, every 2 weeks; Q6W, every 6 weeks; Q8W, every 8 weeks; RECIST, response evaluation criteria in solid tumors.

4

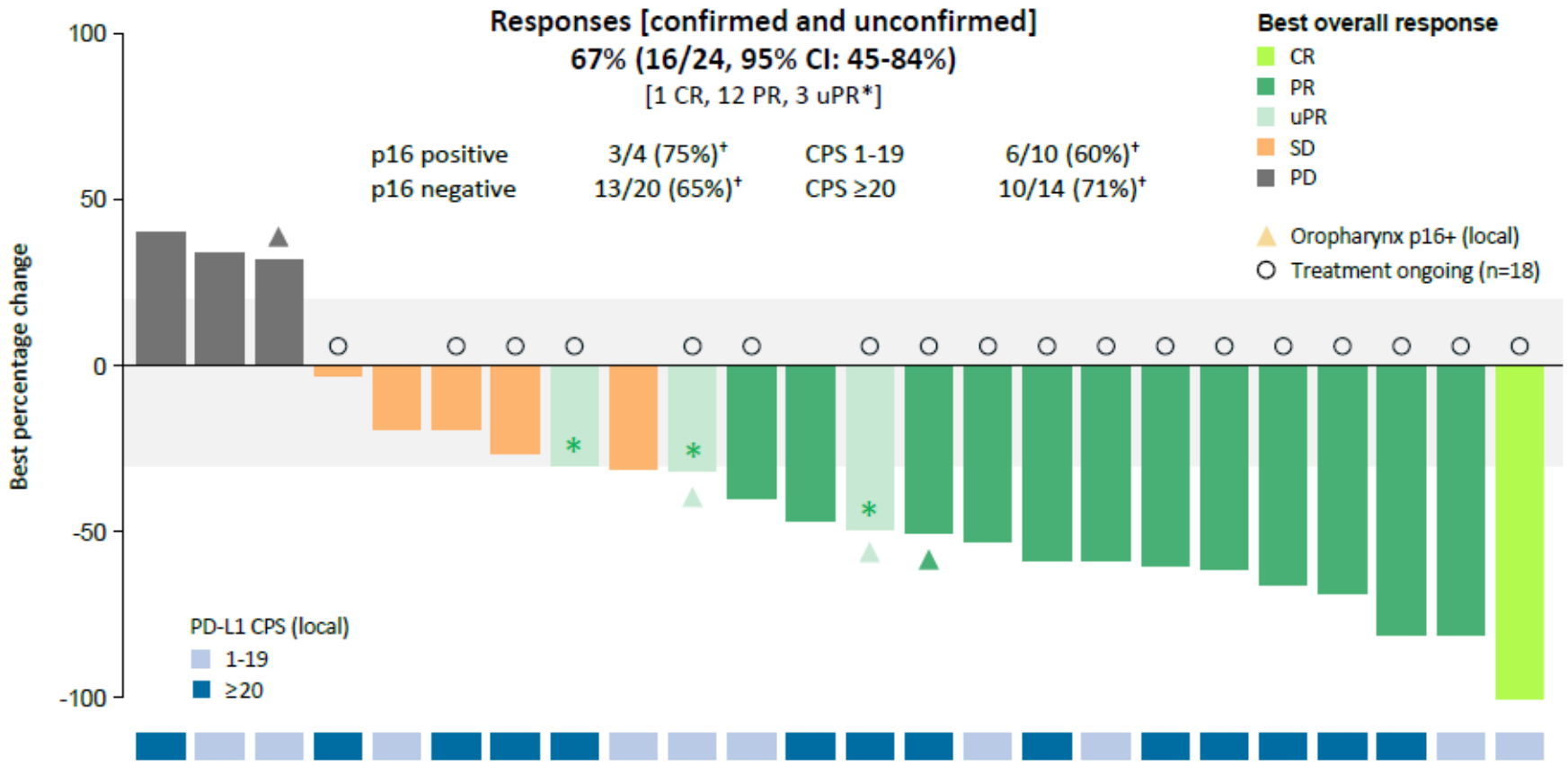
PRESENTED BY: Dr. Jérôme Fayette

Merus

Source: https://merus.nl/wp-content/uploads/2024/06/MCLA-158-oral-ASCO2024-FINAL.pdf

Overall response rate (RECIST 1.1, per investigator)

Best percent change in sum of target lesions from baseline (n=24)



**All 3 uPR were confirmed as PR after data cutoff date; †Response values for p16 and PD-L1 CPS subgroups include CR, PR, and uPR.*
CI, confidence interval; CR, complete response; PR, partial response; SD, stable disease; uPR, unconfirmed partial response.

PRESENTED BY: Dr. Jérôme Fayette

Merus

Source: https://merus.nl/wp-content/uploads/2024/06/MCLA-158-oral-ASCO2024-FINAL.pdf

AbelZeta Announces Clinical Data Showing Preliminary Anti-tumor Activity for C-CAR031, an Armored Autologous GPC3 CAR-T, in Advanced HCC

ROCKVILLE, Md., June 4, 2024 /PRNewswire/ -- AbelZeta Pharma, Inc. ("AbelZeta" or the "Company"), a global clinical-stage biopharmaceutical company focused on the discovery and development of innovative and proprietary cell-based therapeutic products, today announced preliminary safety and efficacy results from its first time in human investigator-initiated trial (IIT) of C-CAR031 in connection with the Company's oral presentation at the 2024 American Society of Clinical Oncology (ASCO) Annual Meeting. The presentation shared data indicating a manageable safety profile and encouraging anti-tumor activity of C-CAR031 in patients with heavily pretreated advanced hepatocellular carcinoma (HCC) (1-6 lines of prior therapy). C-CAR031 is based on a novel GPC3-targeting CAR-T designed by AstraZeneca (LSE/STO/Nasdaq: AZN) and is manufactured by AbelZeta. C-CAR031 is being co-developed in China by AbelZeta and AstraZeneca.

As of March 14, 2024, 23 of 24 patients on the study were eligible for efficacy assessment**. Tumor reductions were observed in 91.3% patients, in both intrahepatic and extrahepatic lesions, with a median reduction of 42.2% (range, -28.1% 94.4%).** The disease control rate was 91.3% and the **ORR was 56.5% for patients across all DLs.** In DL4, the ORR was 75.0%. With 9.03-month median follow-up, Kaplan-Meier estimation of median overall survival (mOS) is 11.14 months (95% CI, 7.56-NE).

Source: https://www.prnewswire.com/news-releases/abelzeta-announces-clinical-data-showing-preliminary-anti-tumor-activity-for-c-car031-an-armored-autologous-gpc3-car-t-in-patients-with-advanced-hepatocellular-carcinoma-at-asco-annual-meeting-2024-302162941.html

AstraZeneca's GPC3 Secret Sauce

Jacob Plieth, *Oncology Pipeline*, June 3, 2024 (excerpt)

A Car-T therapy to which Astra has rights has wowed in a solid tumour after others had disappointed. The intrigue surrounding AbelZeta's solid tumour Car-T breakthrough went up a notch today with the revelation that a more recent cut of the liver cancer trial of this project, C-CAR031, has seen the confirmed response rate climb from 50% to 57%.

The 50% ORR, relating to a January cutoff described in the abstract, had already impressed, given that patients had progressed on a median 3.5 prior therapy lines. With AstraZeneca's AZD5851 using the same construct – the two companies have a cross-licensing arrangement – investors and other Car-T players in this space will want to know why C-CAR031 has shown promise where others failed.

This divergence has been thrown into focus by the failure of Noile-Immune's similarly acting Car-T therapy NIB102 to yield a single response at ASCO, and being discontinued by partner Takeda. Other players working on anti-GPC3 Cars include Sotio, Legend and the private US biotech Eureka Therapeutics.

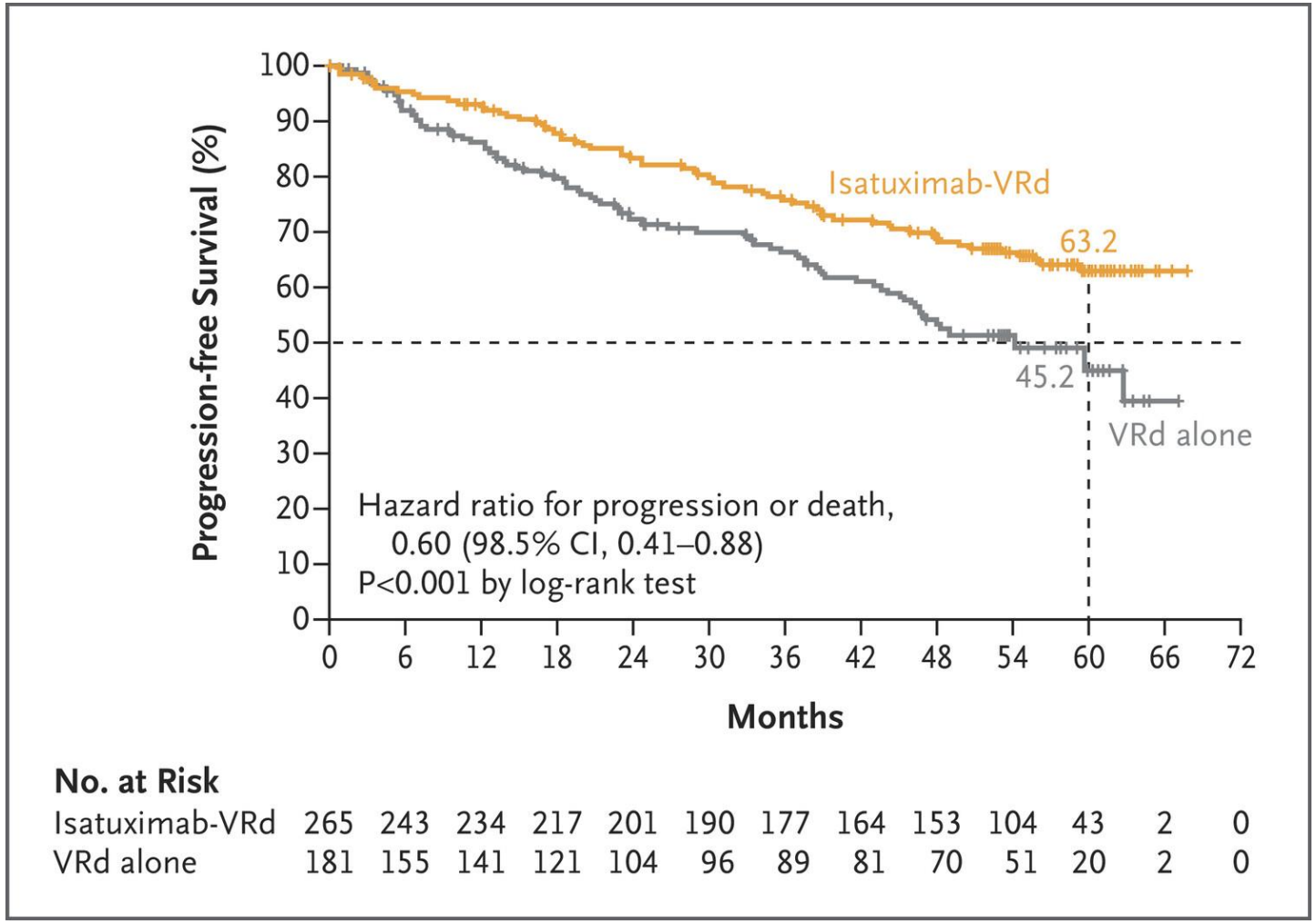
One possible reason for AbelZeta's success is the construct C-CAR031 uses, suggesting that simply targeting the GPC3 protein without additional bells and whistles isn't enough.

At today's ASCO presentation Dr Qi Zhang, from Zhejiang University School of Medicine, revealed that C-CAR031 used an affinity-tuned antibody-derived binding domain that he suggested might enhance safety.

Meanwhile, an "armouring" element on C-CAR031 comprises a co-expressed dominant-negative TGFβ receptor that's been truncated, so it lacks an intracellular domain necessary for downstream signalling. This feature is designed to protect the Car-T cells from TGFβ-driven immunosuppression.

Source: https://www.oncologypipeline.com/apexonco/asco-2024-astrazenecas-gpc3-secret-sauce

ASCO: Impressive Results with Sanofi CD38 Mab in First Line Multiple Myeloma



Shown are Kaplan–Meier estimates of progression-free survival among patients in the intention-to-treat population (defined as all the patients who underwent randomization). The interim analysis of progression-free survival was performed after 162 events of disease progression or death had occurred (which was 73% of the 222 events specified for the planned final analysis). The median progression-free survival was not reached (95% CI, not reached to not reached) in the isatuximab-VRd group (in which patients received isatuximab plus a regimen of bortezomib, lenalidomide, and dexamethasone) and 54.3 months (95% CI, 45.2 to not reached) in the VRd group (in which patients received bortezomib, lenalidomide, and dexamethasone). Tick marks indicate censored data.

Source: https://www.nejm.org/doi/full/10.1056/NEJMoa2400712

ASCO: Strong Signal Seen with Pfizer KAT6A/B Inhibitor

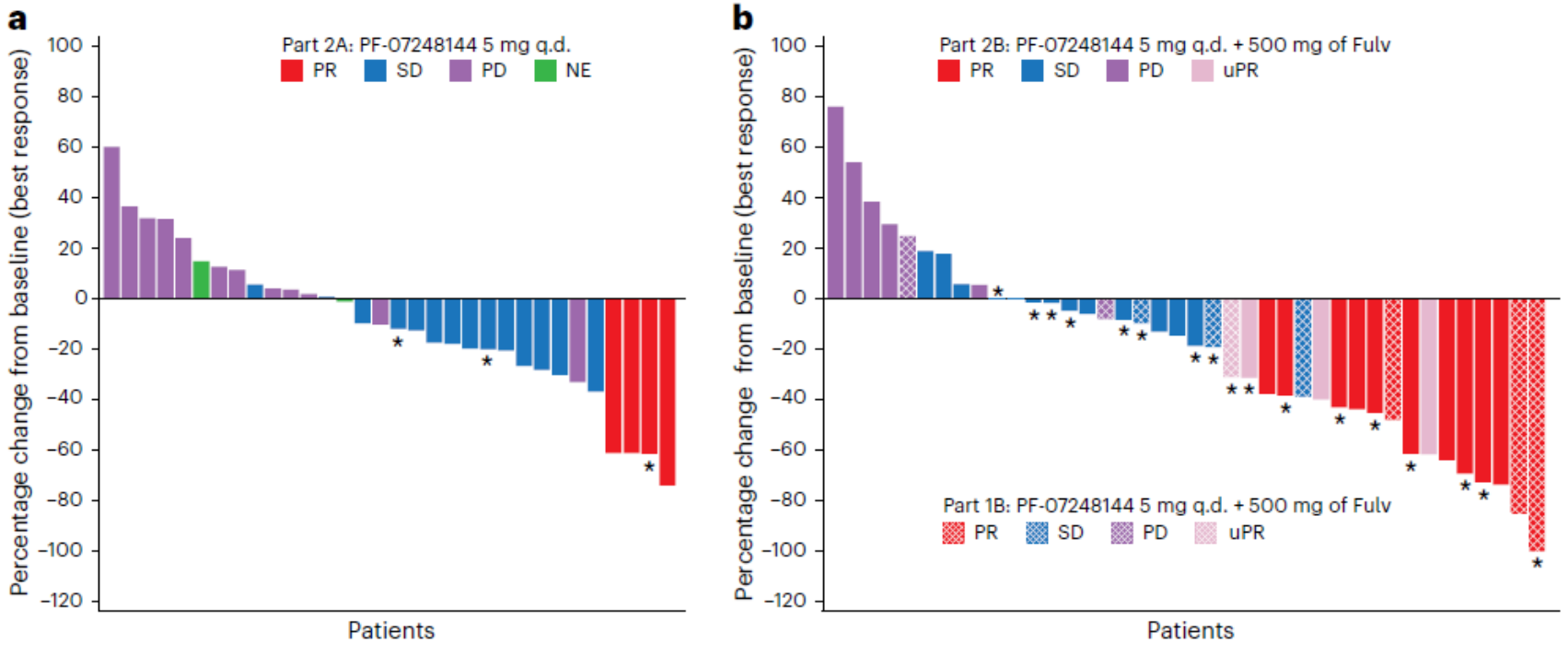
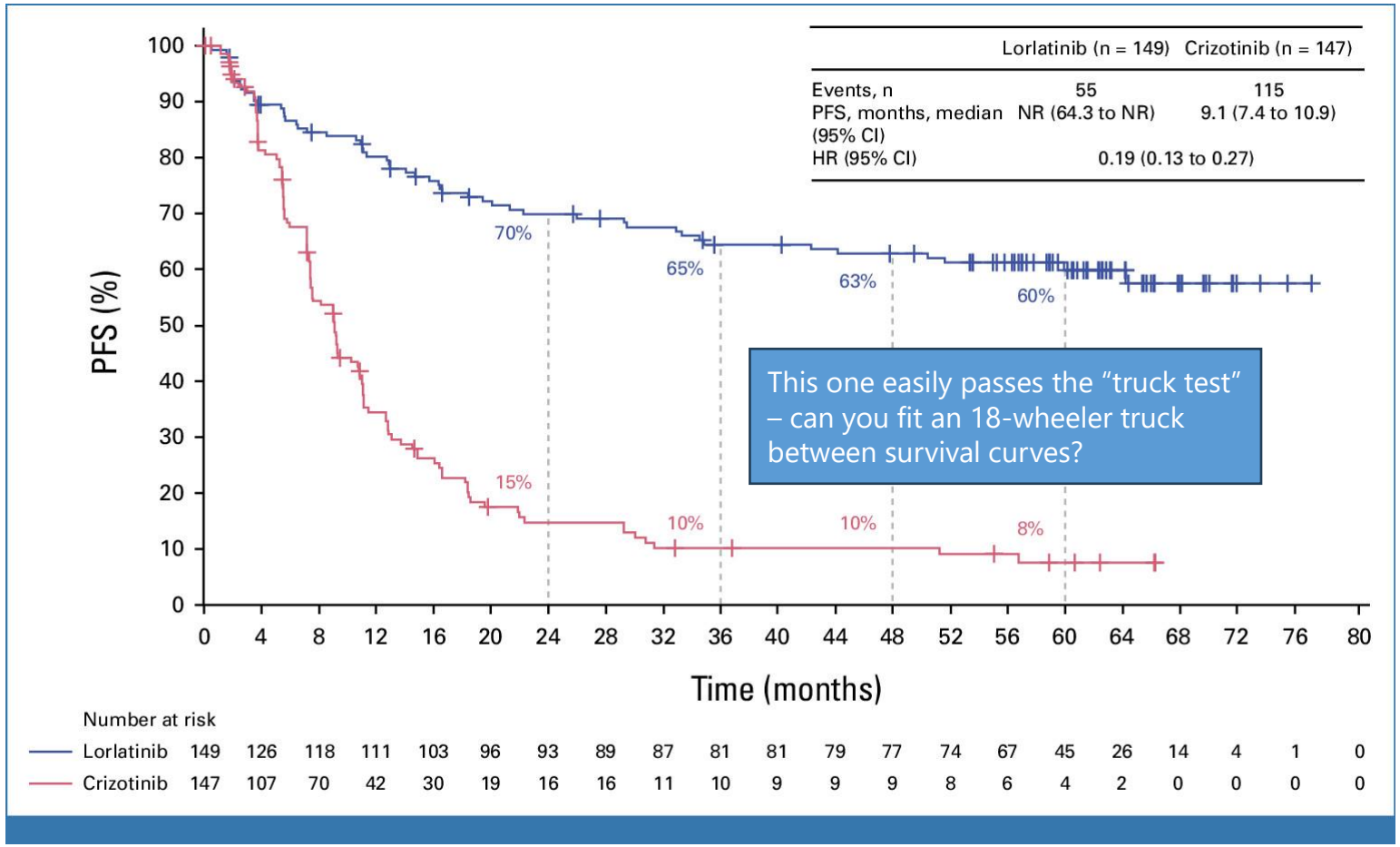


Fig. 2 | Waterfall plot of tumor size change from baseline. a, Waterfall plot of patients in part 2A (PF-07248144 5 mg q.d.). **b**, Waterfall plot of patients in parts 1B and 2B (PF-07248144 5 mg q.d. + fulvestrant 500 mg). Largest decrease or smallest increase represents the best response to treatment. uPR, unconfirmed PR (considered as SD in Table 3). * indicates ongoing.

Source: https://www.nature.com/articles/s41591-024-03060-0

ASCO: Strong Signal Seen with Pfizer ALK Inhibitor, Lorlatinib, in ALK+ NSCLC



After 5 years of follow-up, median PFS has yet to be reached in the lorlatinib group, corresponding to the longest PFS ever reported with any single-agent molecular targeted treatment in advanced NSCLC and across all metastatic solid tumors. These results coupled with prolonged intracranial efficacy and absence of new safety signals represent an unprecedented outcome for patients with advanced *ALK*-positive NSCLC and set a new benchmark for targeted therapies in cancer.

Source: https://ascopubs.org/doi/10.1200/JCO.24.00581

Lung Cancer Was a Death Sentence. Now Drugs Are Saving Lives

Brianna Abbott, *Wall Street Journal*, June 2, 2024 (excerpt)

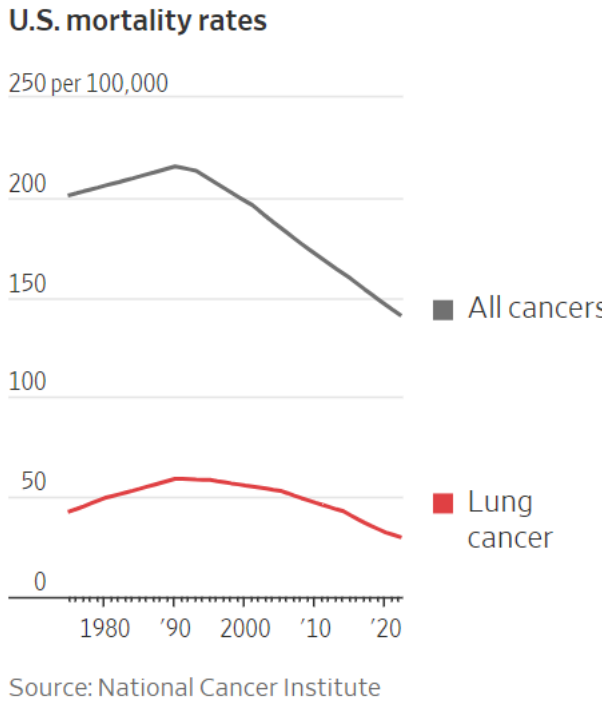
There is more hope than ever for people diagnosed with the deadliest cancer.

Declines in smoking and the advent of screening and newer drugs have transformed the outlook for patients with lung cancer, once considered a death sentence. Progress against the disease has propelled the drop in overall cancer deaths in the U.S. over the past three decades.

And there is more to gain. More patients can fend off the disease for months or years with targeted or immune-boosting drugs, results released this weekend at a top cancer conference showed. That includes patients with forms of the disease that are notoriously tough to treat. AstraZeneca's drug Tagrisso can contain lung cancer nearly three years longer than chemotherapy and radiation alone for some stage-three patients, one study released Sunday showed. Another found that some patients with aggressive disease survived nearly two years longer with the company's immunotherapy drug Imfinzi, the first advance for that lung-cancer subtype in decades.

Another study presented at the American Society of Clinical Oncology conference in Chicago found that 60% of advanced patients were alive without their disease advancing at five years after taking Pfizer's Lorbrena, a drug that targeted a genetic mutation in their tumors. That compares with just 8% of patients on an older drug with the same target. "These results are really outstanding," said Dr. David Spigel, chief scientific officer at Sarah Cannon Research Institute in Tennessee, lead researcher on the Imfinzi trial. "A really major step forward in lung-cancer care."

Lorbrena has kept Matt Hiznay's stage-four lung cancer at bay for nine years. Hiznay, who never smoked, was diagnosed in 2011 after a persistent cough at 24 years old.



Source: https://www.wsj.com/health/healthcare/lung-cancer-treatment-deaths-5cfeb6fd

Safety and Efficacy of IBI389 (Claudin18.2 T-Cell Engager) in Patients with Advanced Pancreatic Ductal Adenocarcinoma: Preliminary Results from the Phase I Study

Dr. Hui Zhou, Senior Vice President of Innovent Biologics, stated, "We are excited to share the latest clinical development progress of IBI389 at ASCO. Different from monoclonal antibodies, IBI389 redirects T cells to tumor cells by binding both CLDN18.2 expressed on tumor cells and CD3 on T cells, inducing T cell-mediated cell killing. Preclinical results showed that IBI389 could bind to tumor cells and exhibit significant anti-tumor effects even in cell lines with low CLDN18.2 expression. In the presented clinical data, IBI389 has shown promising efficacy in advanced G/GEJ tumors and PDAC, including those subjects with low and moderate CLDN18.2 expression. Notably, IBI389 is the world's first bispecific antibody targeting CLDN18.2/CD3 to show encouraging efficacy signal in PDAC, representing a breakthrough for innovative treatments in difficult-to-treat cancers. We will continue to advance the clinical development of IBI389 for the benefit of more cancer patients."

As of March 11, 2024, a total of 72 subjects with advanced unresectable or metastatic pancreatic ductal adenocarcinoma have received IBI389 monotherapy. All subjects had received at least one prior systemic treatment, and 55.6% of the subjects had received two or more prior lines of systemic therapy.
The results showed that:

- In subjects with CLDN18.2 IHC 2/3+≥10%, signs of efficacy were observed when treated with 100 μg/kg.
- **The recommended phase 2 dose (RP2D) 600 μg/kg group shows superior efficacy. 27 subjects have performed at least one post-baseline tumor evaluation, the objective response rate (ORR) was 29.6% (95%CI: 13.8-50.2), the confirmed objective response rate (cORR) was 25.9% (95%CI：1-46.3), and the disease control rate (DCR) was 70.4% (95%CI：49.8-86.2). Among the 18 subjects with CLDN18.2 IHC 2/3+≥40%, the cORR was 38.9% (95%CI：17.3-64.3).**
- As of May 1, 2024, the median progression-free survival (PFS) follow-up time was 4 months, and the median PFS was not yet mature, with a 3-month PFS rate of 57.1%.
- Safety was similar to that of the overall population, and no new safety signals were observed.

Source: https://www.innoventbio.com/InvestorsAndMedia/PressReleaseDetail?key=456

ASCO: After CAR-T's Stellar Showing, GSK Pads ADC Blenrep's Case in Multiple Myeloma

Angus Liu, *FierceBiotech*, June 2, 2024 (excerpt)

Armed with two positive phase 3 trial readouts and the hope that at least one will show a significant patient survival benefit, GSK thinks it has the data to convince doctors and the FDA that the once-failed antibody-drug conjugate (ADC) Blenrep can work in multiple myeloma.

In a second phase 3 win, Blenrep cut the risk of cancer progression or death by 48% compared with Takeda's Velcade (V) in their respective combinations with Bristol Myers Squibb's Pomalyst (P) and the steroid dexamethasone (d). The results came from the DREAMM-8 trial conducted in multiple myeloma patients who had tried at least one prior line of therapy and were shared at the American Society of Clinical Oncology 2024 annual meeting.

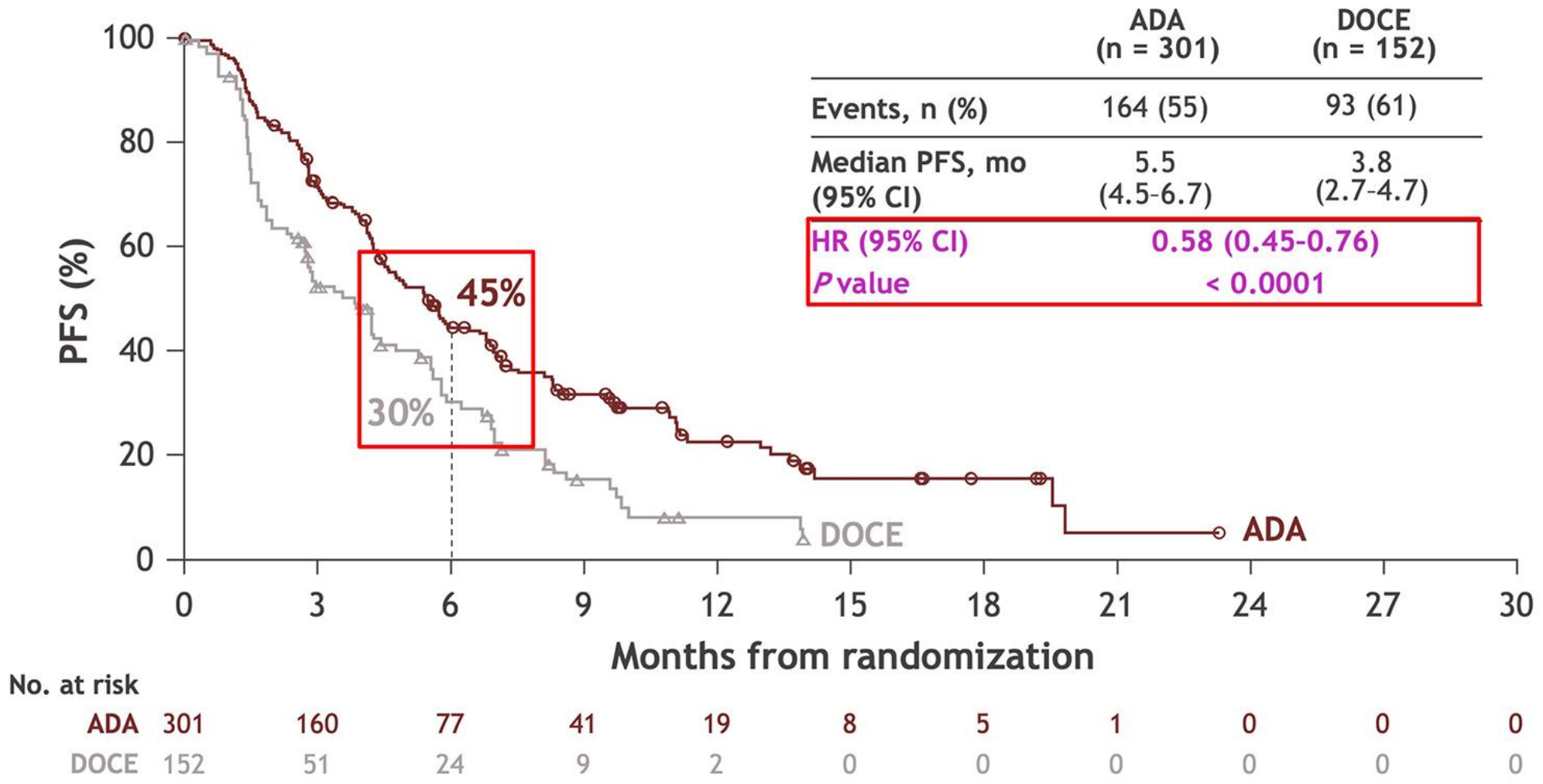
After a median follow-up of 21.8 months, the median progression-free survival (PFS) was still not reached for the Blenrep arm, versus 12.7 months for control.

The latest data set follows a recent readout from the DREAMM-7 trial, in which Blenrep beat Johnson & Johnson's Darzalex (D) by 59% on PFS in their respective pairings with Vd. That study also tested the regimens in the second line or later.

With the two positive trials, GSK plans to file Blenrep with the FDA in the second half of this year, Hesham Abdullah, M.D., GSK's head of oncology R&D, told Fierce Pharma. The company hopes to reintroduce Blenrep in the U.S. following a market withdrawal in the late-line setting, which was triggered by the drug's phase 3 flop as a monotherapy.

Source: https://www.fiercepharma.com/pharma/asco-despite-car-ts-stellar-showing-gsk-pads-adc-blenreps-case-multiple-myeloma

BMS Adagrasib Delivers Against Docetaxel in Phase 3 Trial in Advanced Kras-Positive NSCLC

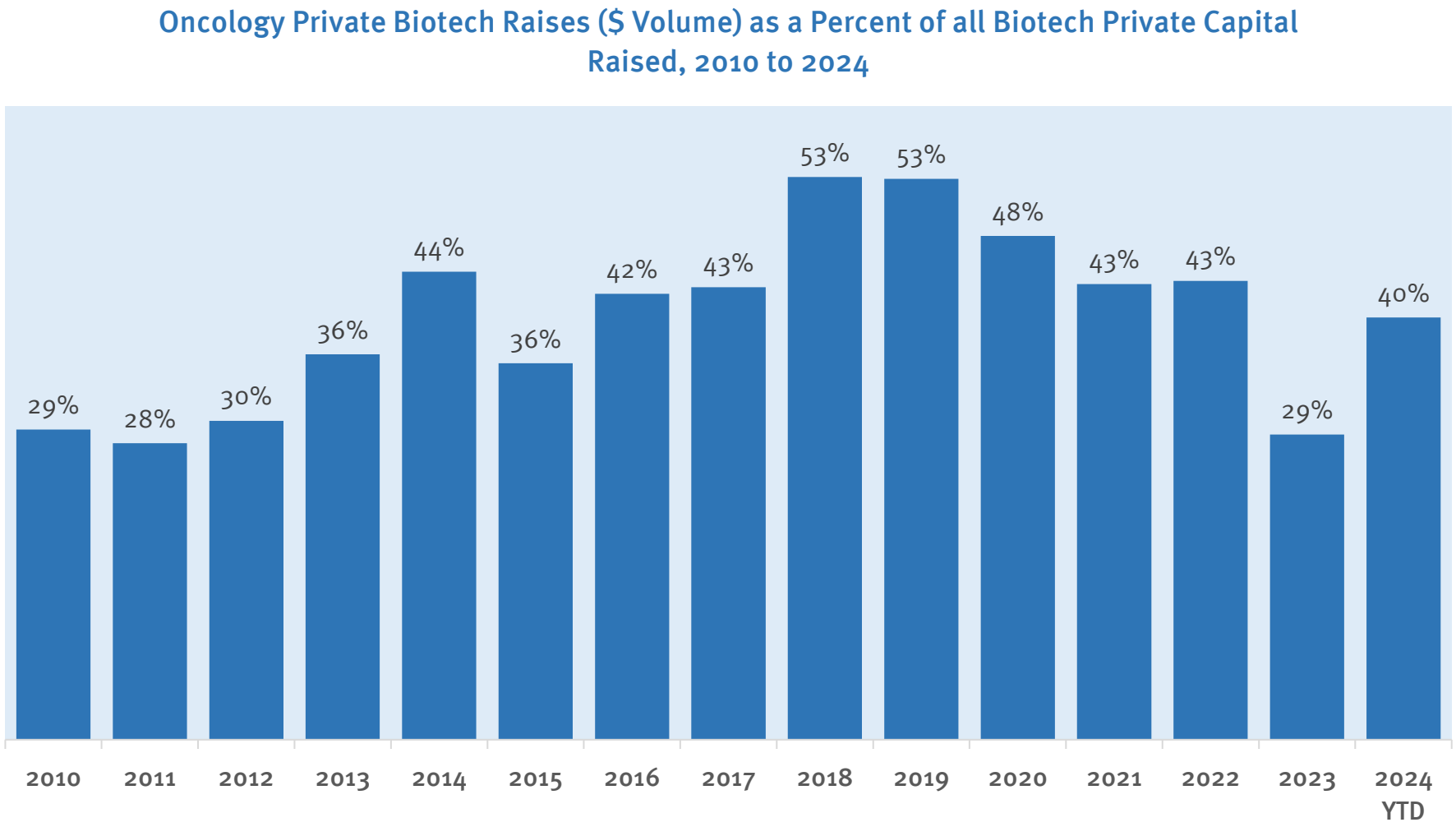


	ADA (n = 301)	DOCE (n = 152)
Events, n (%)	164 (55)	93 (61)
Median PFS, mo (95% CI)	5.5 (4.5-6.7)	3.8 (2.7-4.7)
HR (95% CI)	0.58 (0.45-0.76)	
P value	< 0.0001	

Source: https://dailynews.ascopubs.org/do/krystal-12-shows-pfs-benefit-adagrasib-over-docetaxel-previously-treated-advanced-kras

Oncology Pharmaceuticals Environment and Deals

Importance of Oncology as a Focus of Private Venture Capital Formation Shrinking Since 2019



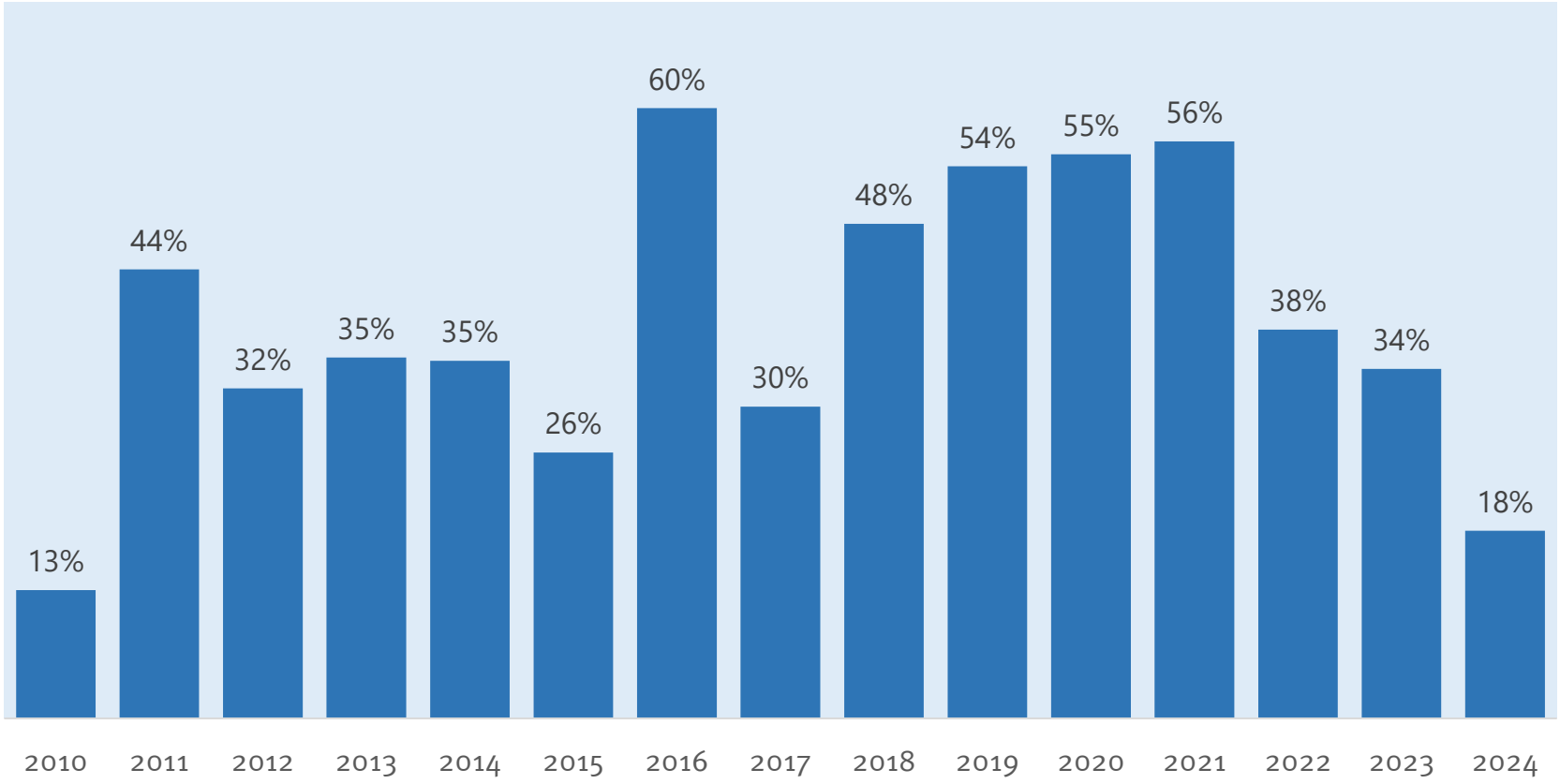
Forty-percent of venture dollars invested in therapeutics companies so far this year have gone into oncology biotechs.

This is down from peak levels over 50% prior to the Pandemic.

Source: DealForma and Stifel Research.

Importance of Oncology as a Focus of Biotech IPOs Also Shrinking Since 2019

Oncology Biotech IPO Dollars Raised ($ Volume) as a Percent of all Biotech Dollars Raised, 2010 to 2024



The oncology therapeutics field accounts for only 18% of all private capital raised in IPO's in 2024. This is down from peak levels over 50% as recently as 2021. Other areas such as I&I and cardiometabolic have risen in relative popularity with investors.

Source: DealForma and Stifel Research.

Most Active Oncology Dealmakers, Jan 2015 to May 2024

BMS and Pfizer has been heavy spenders in oncology business development activity. BMS, Roche and Merck lead in terms of the sheer number of deals over the last decade. Interestingly, BMS' market cap now is below the amount it has spent on oncology deals.

Company	Total Deal Count	Total Deal Spend (upfront $mm)	M&A Deal Count	M&A Total Spend Upfront ($mm)	Asset Sale Count	Asset Sale Total Spend Upfront ($mm)	Global Licensing Deal Count (upfront > $3mm only)	Licensing Total Spend Upfront ($mm)
Bristol-Myers Squibb	43	$108,332	11	$100,916	1	$0	31	$7,416
Pfizer	17	$74,197	4	$71,864	0	$0	13	$2,333
Gilead	21	$39,601	5	$37,134	0	$0	16	$2,467
AbbVie	12	$37,571	4	$36,489	0	$0	8	$1,082
Merck	23	$18,866	11	$10,455	0	$0	12	$8,411
AstraZeneca	21	$16,147	5	$7,768	1	$5,100	15	$3,279
Celgene	10	$12,441	4	$11,205	0	$0	6	$1,236
Eli Lilly	12	$12,016	7	$11,620	0	$0	5	$396
Novartis	17	$11,078	6	$10,483	0	$0	11	$595
GSK	11	$8,763	2	7398.12	0	$0	9	$1,365
Takeda	13	$7,163	3	$5,925	0	$0	10	$1,238
Sanofi	16	$4,309	2	$2,832	0	$0	14	$1,477
Roche	28	$4,040	4	$2,270	1	$42	23	$1,728
Amgen	7	$3,163	3	$3,008	0	$0	4	$155
J&J	14	$2,858	3	$2,075	0	$0	11	$783
Grand Total	**265**	**$360,546**	**74**	**$321,442**	**3**	**$5,142**	**188**	**$33,961**

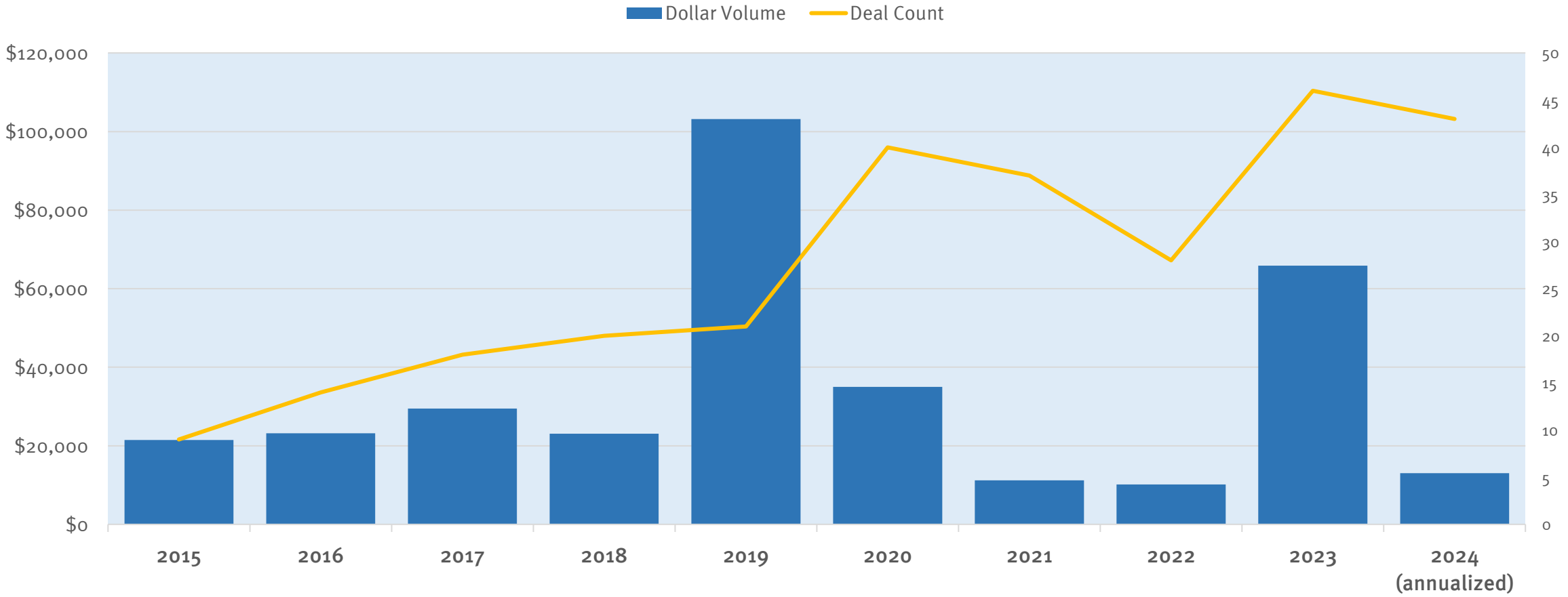
Source: DealForma and Stifel Research.

Oncology Biopharma Dealmaking Activity

Oncology M&A Activity Light in 2024 vs. Most Previous Years

It's an election year with Democrats in power and a vigilant FTC. As a result, M&A this year has been quite light in the oncology field. Actually, as shown on the next page, M&A dollar volume has been light across the board in 2024. Notably, deal count in 2024 is near an all-time high level. Deals, on average, are smaller right now than in past years.

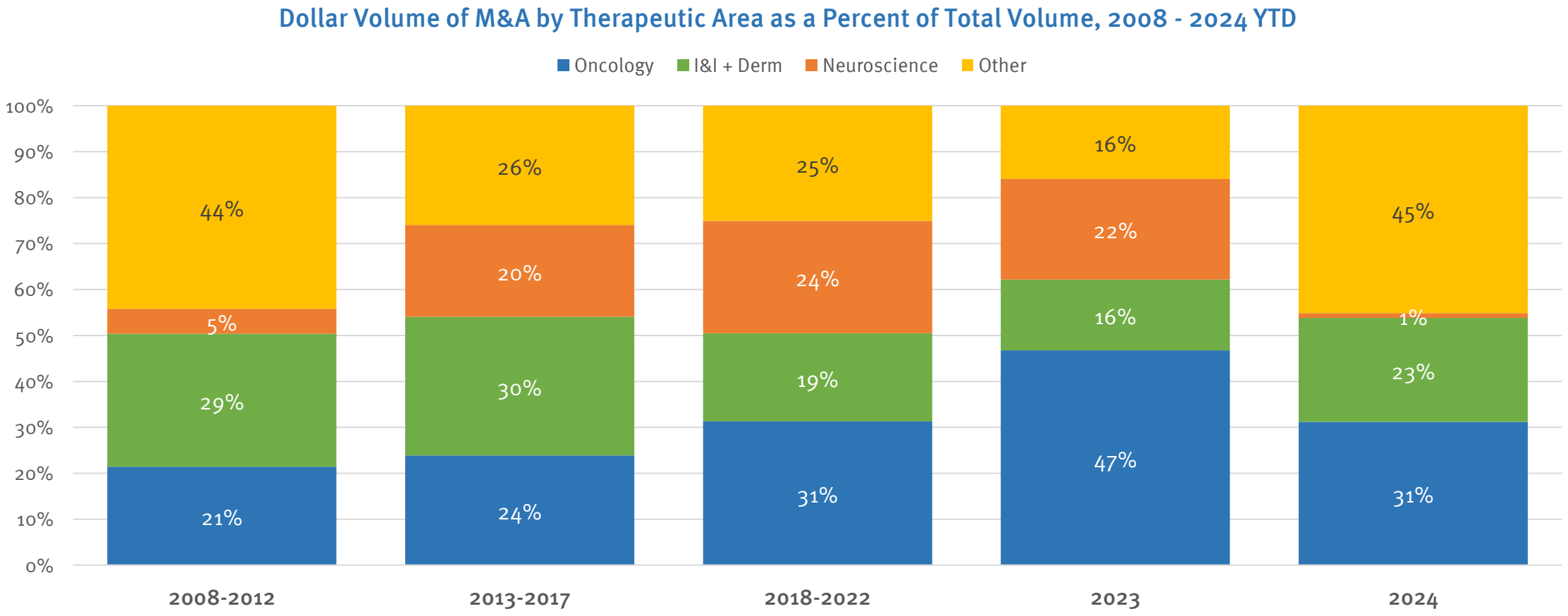
Total M&A Dollar Volume in Oncology Therapeutics, Jan 2015 – May 30, 2024 ($Millions)



Source: DealForma and Stifel Research. We count cash and equity upfront payments as dollar volume and do not include contingent deal payments.

Oncology Volume as a Percent of Total M&A in 2024 In Line with Past Years

Thirty-one percent of all therapeutics M&A dollars spent in the first five months of 2024 were for oncology targets. This is not out of line with previous periods. We saw the most spend for a year in 2023 when Seagen was done in an otherwise light year and the least done in the 2008 to 2012 period when oncology was less important as an overall part of the bioeconomy.

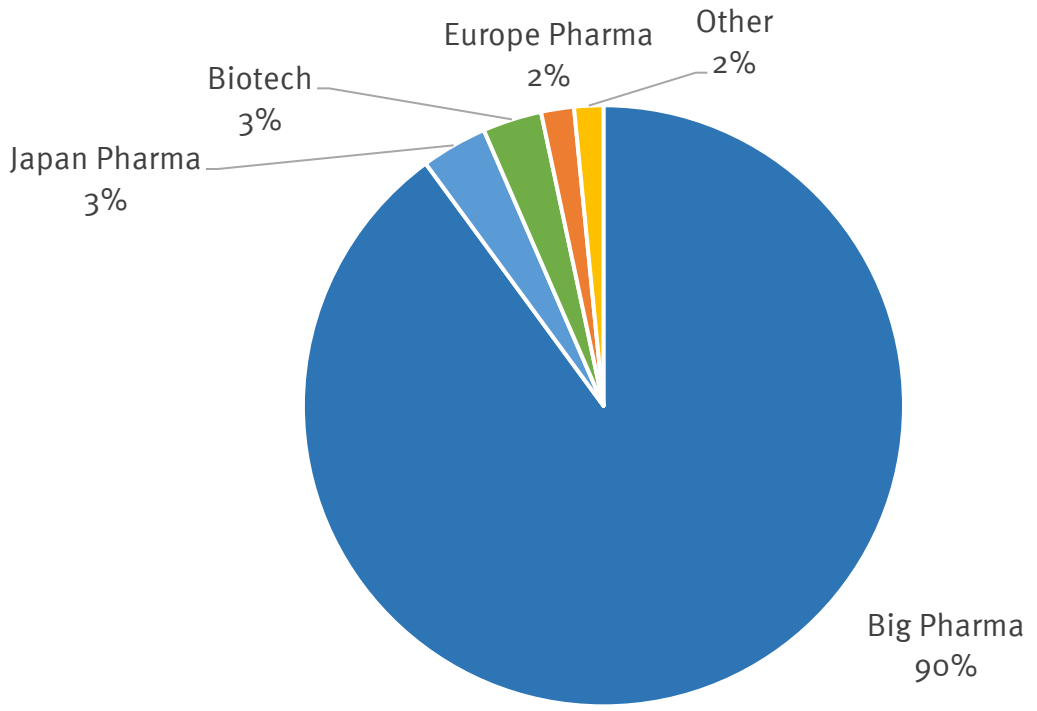


Source: DealForma and Stifel Research

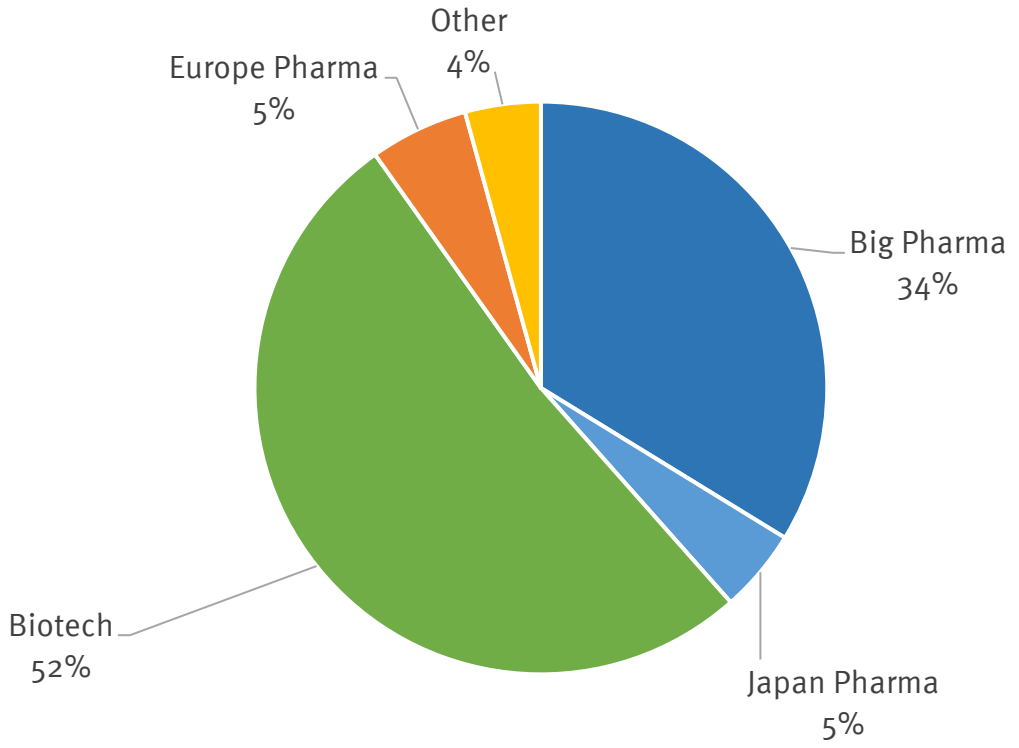
Who Are The M&A Buyers in Oncology?

From a dollar perspective, the buyers in oncology are big pharma. But from a deal count perspective, smaller biotech companies comprise over half of the deals.

Dollar Volume (upfronts) in Oncology M&A, 2015 to May 2024 (by Buyer Type)



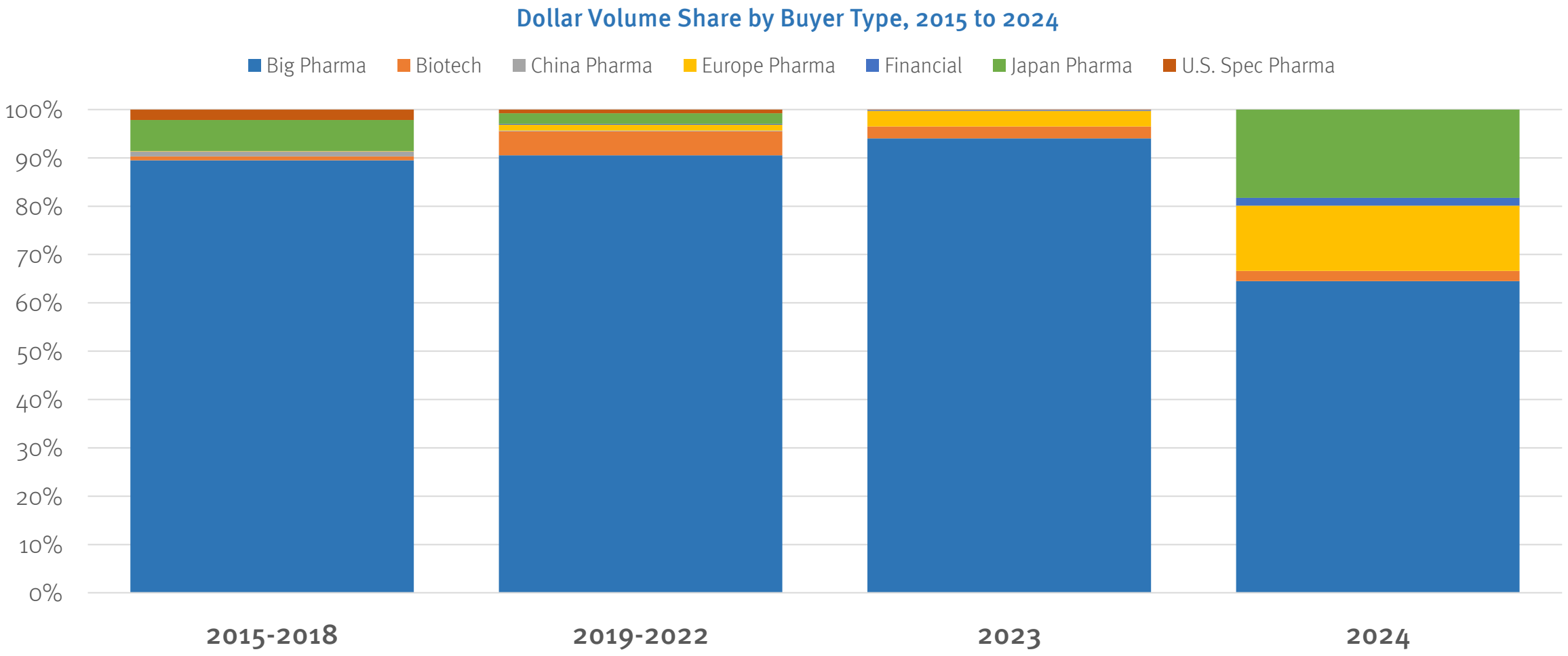
Deal Count in Oncology M&A Deals, 2015 to May 2024 (by Buyer Type)



Source: DealForma and Stifel Research

Big Pharma Less Dominant in Oncology M&A in 2024

Through the end of May 2024, big pharma has spent $8.5bn in oncology M&A. This is far less than usual while mid-sized pharma (such as Genmab) have been active. As a result, big pharma buyers account for about 65% of total volume versus 90%+ in previous years.

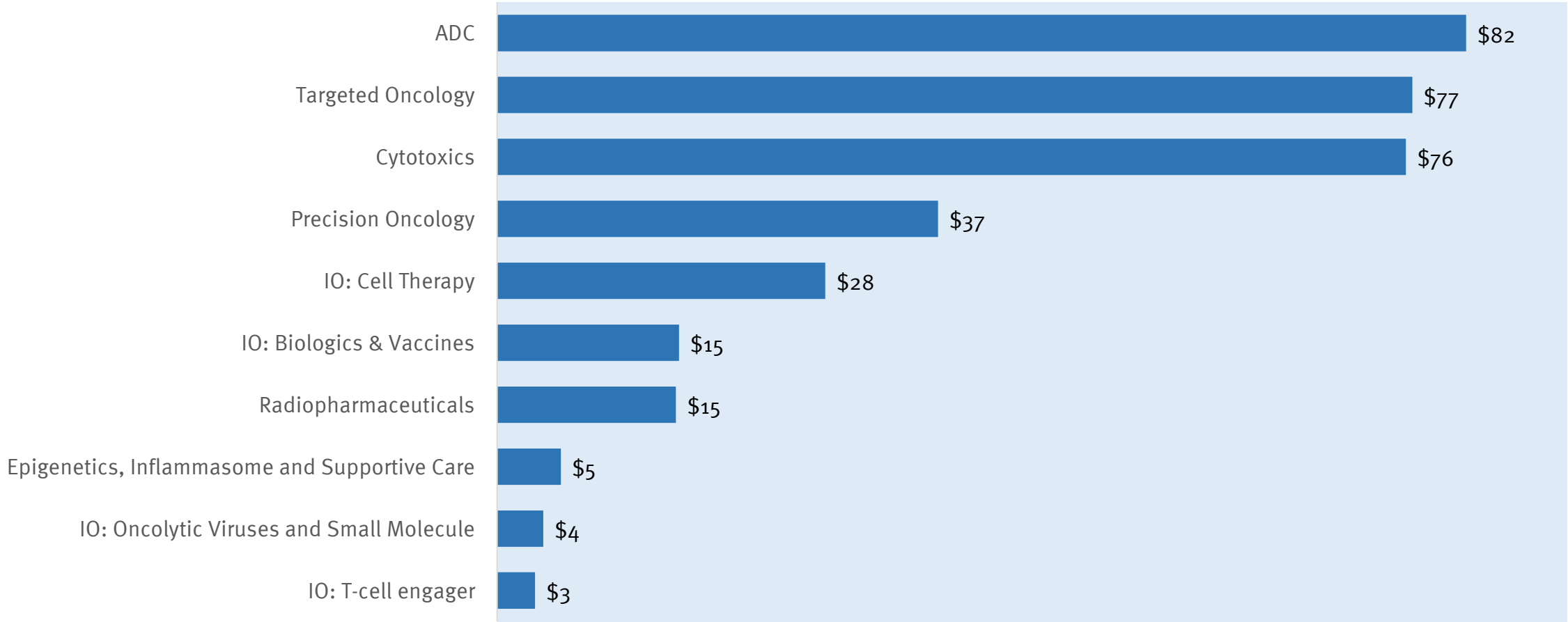


Source: DealForma and Stifel Research

M&A Dollar Volume by Mode of Action of Lead Drug

ADC's and targeted therapies (largely built around kinase inhibitors) have dominated M&A over the last decade. The high volume of cytotoxics is largely reflective of Celgene's focus on this approach with Revlimid.

Oncology M&A Deal Volume Stratified by Mode of Action of Target Firm's Lead Drug, 2015 to 2024 ($ Billions)

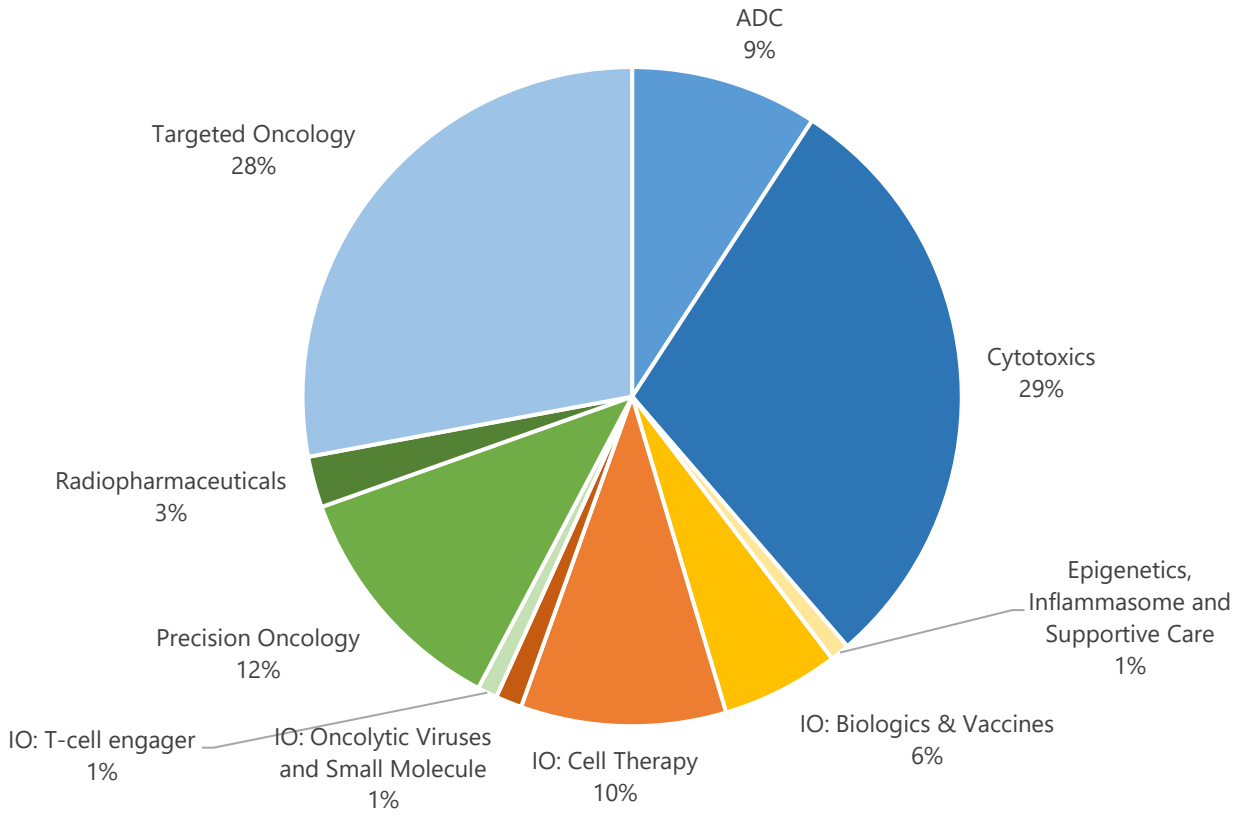


Source: Stifel oncology transaction database and DealForma.

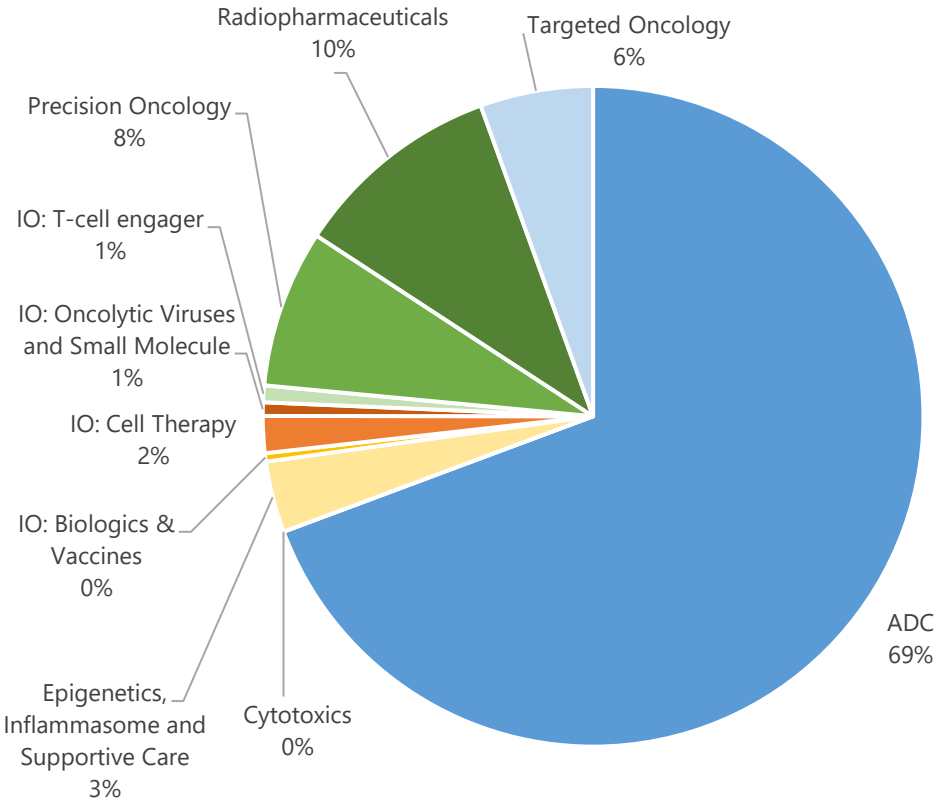
M&A Interest Has Shifted Towards ADCs and Radiopharma

M&A interests have shifted dramatically in the last two years – away from cytotoxics and targeted oncology and towards ADC's, radiopharma and T-cell engagers. Interest in precision oncology remains robust.

Oncology M&A Deal Activity Stratified by Mode of Action of Target Firm's Lead Drug ($ billions), 2015 to 2022



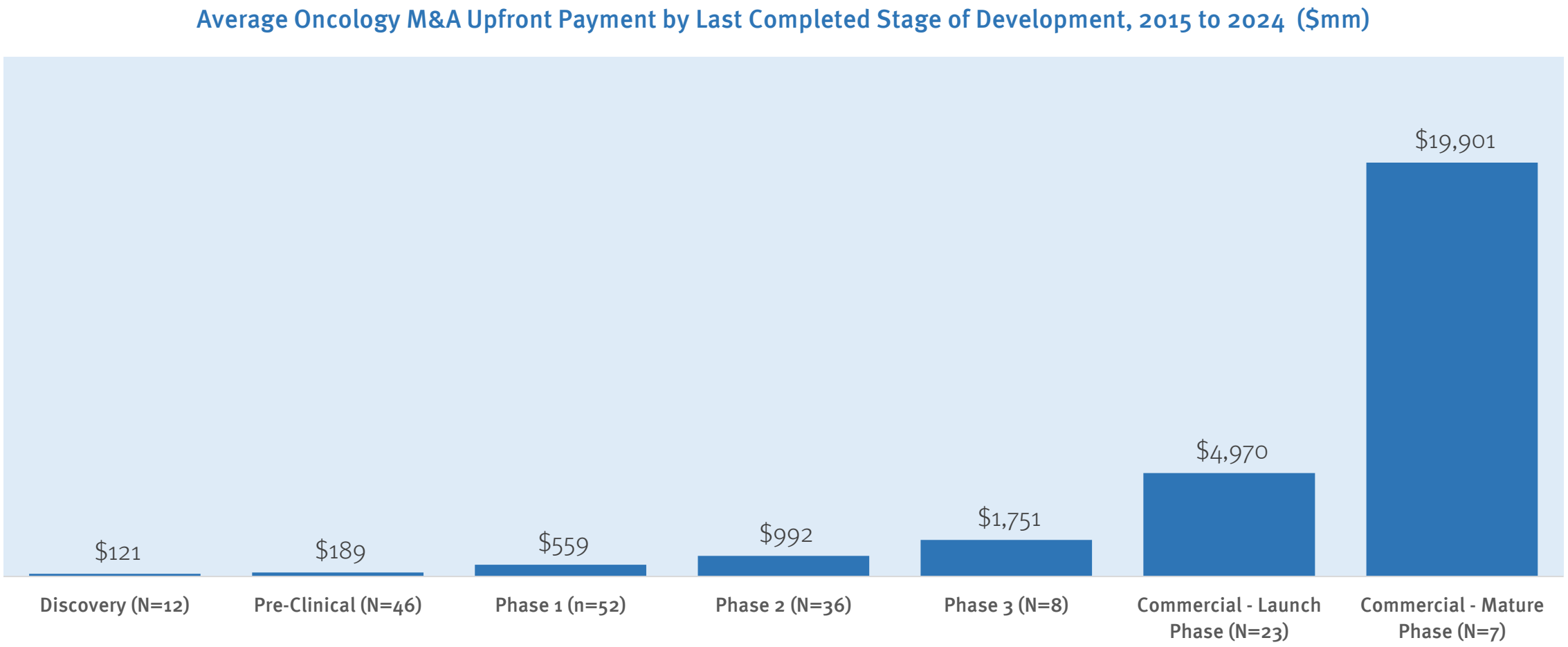
Oncology M&A Deal Activity Stratified by Mode of Action of Target Firm's Lead Drug ($ billions), 2023 to 2024



Source: Stifel oncology transaction database and DealForma. We count upfront cash and equity payments as dollar volume.

Average M&A Payments by Stage of Development

The average payment rises exponentially as drug candidates approach commercialization. There is a huge payoff for sellers to allowing their drug candidates to be de-risked and mature.

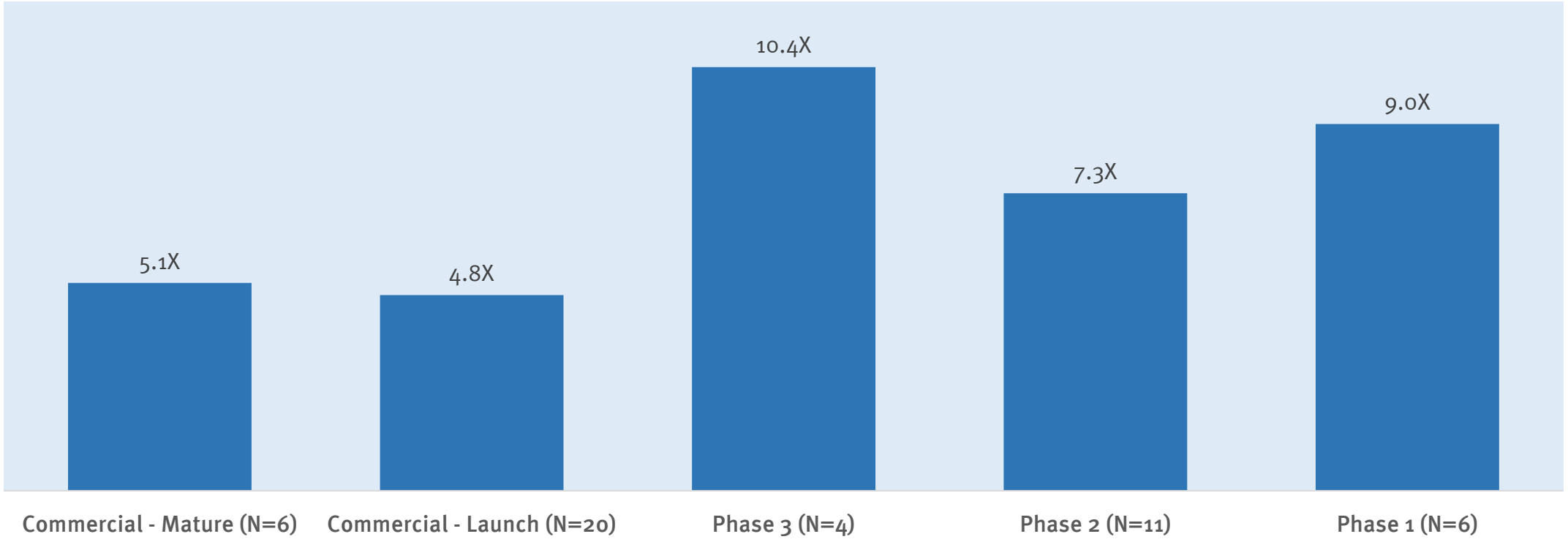


Notes: Data sourced from DealForma and Stifel oncology transaction database. Phases of development are *completed* stages of development rather than those which are ongoing.

Average Forward Revenue Multiple by Stage of Development in Oncology M&A

As companies go up the revenue curve the forward multiples paid for assets go down. Clinical stage assets are, to a significant degree, being bought at relatively high multiples versus potential revenue. It's striking that Phase 3 programs tend to draw the highest prices in the clinical sphere.

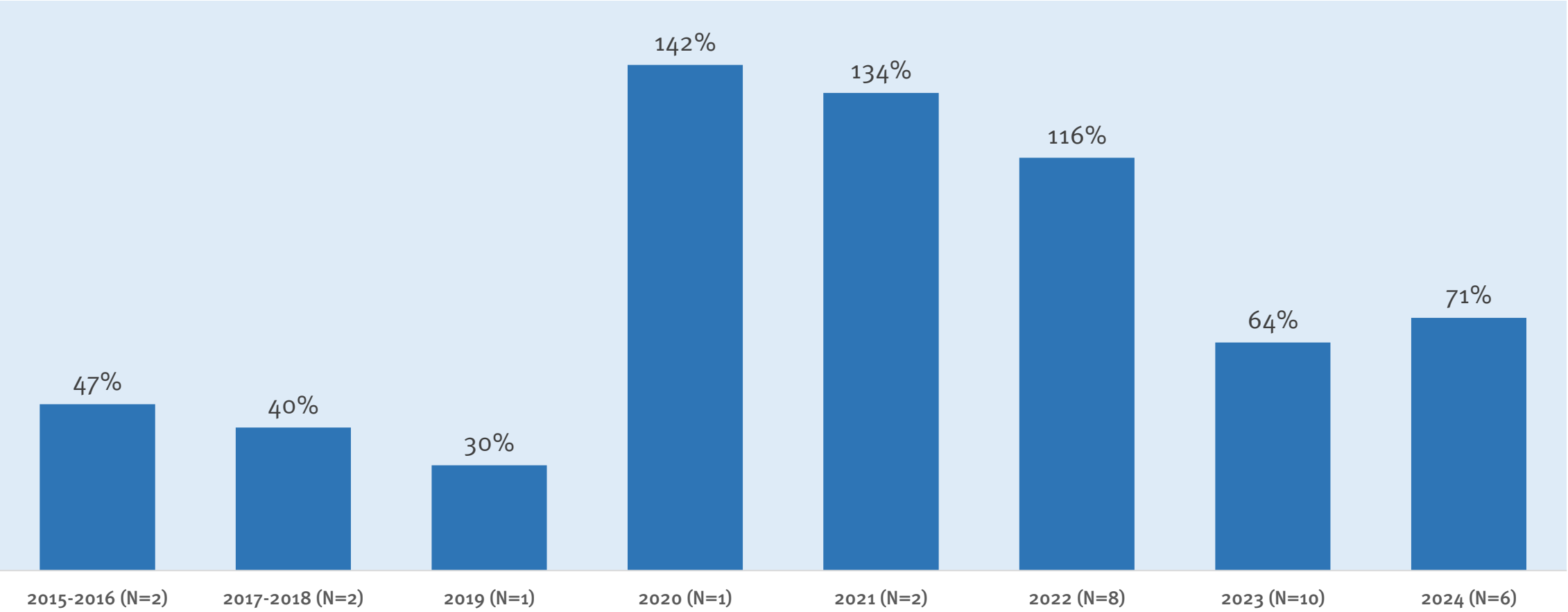
Average Multiple of Revenue Enterprise Value Paid for Target Versus Revenue Forecast in Five Years, by Development Stage, Public Oncology M&A Deals, 2015 to 2024



Source: Stifel oncology transaction database. Revenue estimates are based on consensus analyst estimates of revenue three or five years out from acquisition announcement. These estimates are sourced either from CapitalIQ, merger proxies or analyst reports from the time that are themselves sourced from CapitalIQ.

Control Premia Paid on Public Oncology M&A Have Dropped Since Market Recovery in 2023 …

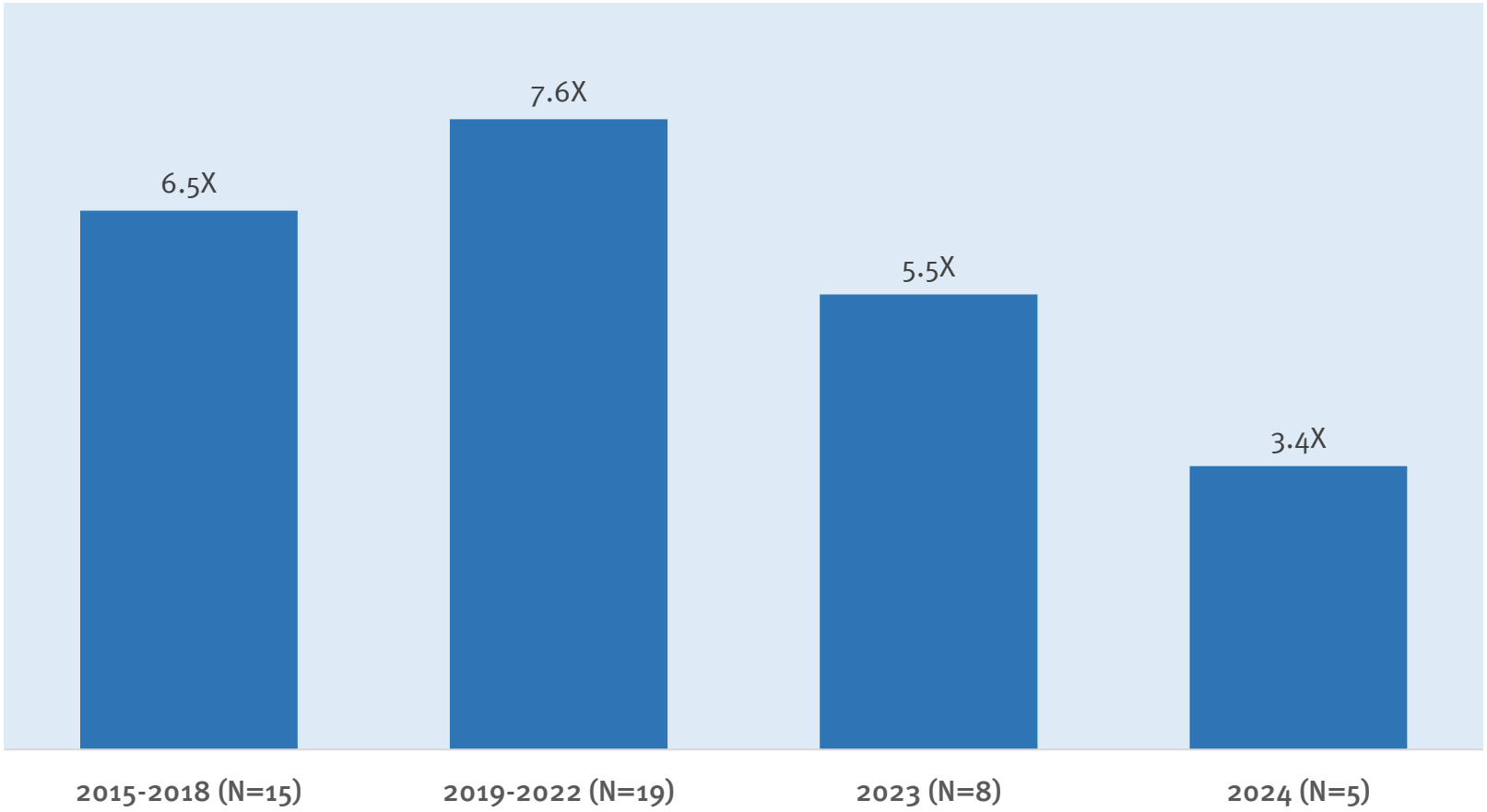
Average Control Premium (day after announcement compared to value at close day before deal announcement)
Public Oncology M&A Deals, 2015 to 2024



Source: Stifel oncology transaction database, DealForma and S&P CapIQ.

. . . While Forward Revenue Multiples on Oncology M&A Deals Has Declined Since 2022

Average Multiple of Revenue Enterprise Value Paid for Target Versus Revenue Forecast in Five Years, Public Oncology M&A Deals, 2015 to 2024



There is a clear pattern in the data on oncology M&A.

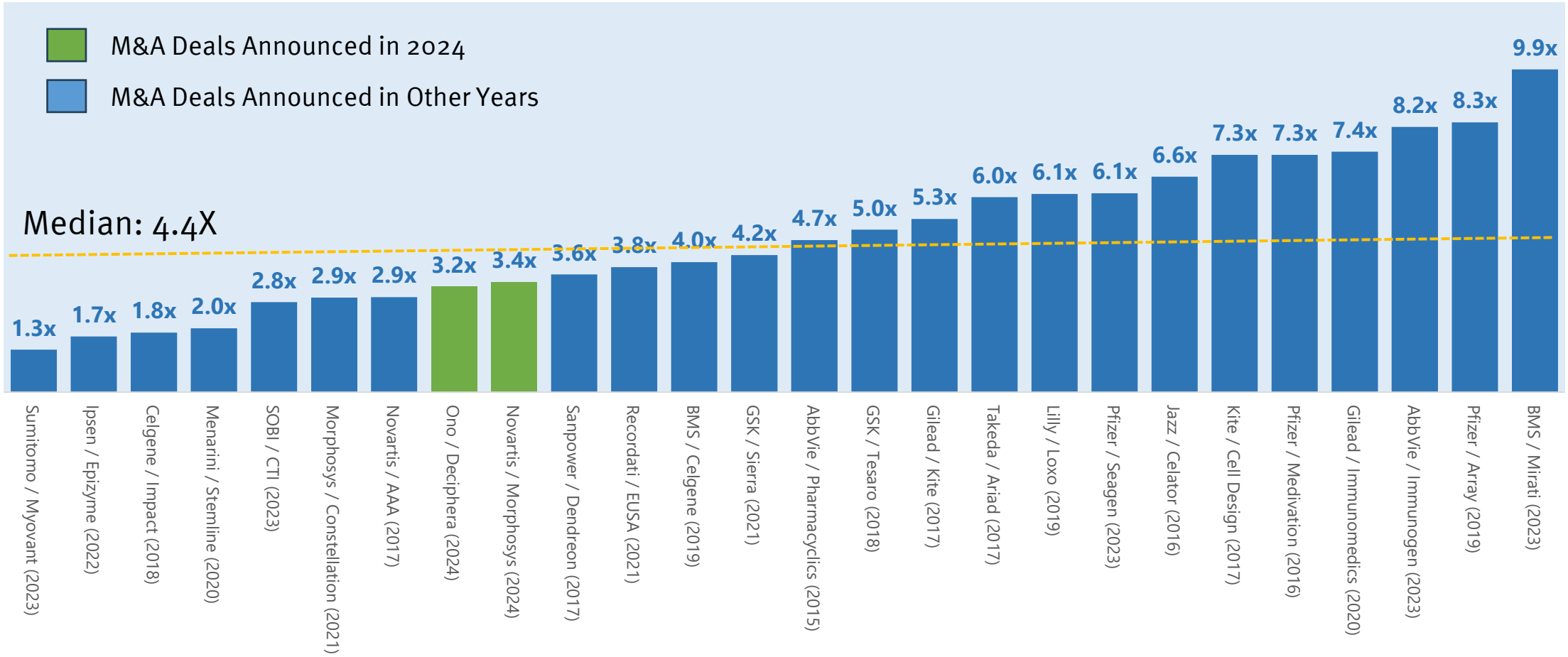
Oncology M&A deals are getting done at lower fundamental values (assuming EV multiple to five-year forward expected revenue is a reasonable proxy for fundamental value).

We think this is a reflection of several factors: (1) prices have come down substantially since the Pandemic and (2) after passage of the IRA, buyers are simply not willing to pay as much for assets.

Source: Stifel oncology transaction database and S&P CapIQ.

Commercial Stage Deals Done in 2024 Have Been at Below Median Forward Revenue Multiples

Enterprise Value / Revenue Estimate Five Years Later on Commercial Stage Oncology M&A Deals with a Public Target, 2017 to 2023



Source: Stifel oncology transaction database and S&P CapIQ.

Global Licensing Activity in Oncology

Total Cash in Upfronts Received by Global Licensor:

Oncology Licensing Deals, Jan 2008 to May 2024

Licensor	Deal Count	Upfronts from Licensing ($mm)
Daiichi Sankyo	8	$6,350
BeiGene	9	$4,163
AstraZeneca	17	$2,489
Seagen	20	$1,991
Nektar Therapeutics	3	$1,870
Sanofi	5	$1,207
Merck KGaA	12	$1,201
Arvinas LLC	2	$1,150
MorphoSys AG	9	$1,116
Juno Therapeutics	3	$1,000
Blueprint Medicines	5	$900
Genmab A/S	6	$890
Dragonfly Therapeutics Inc.	5	$832
Eisai Co.	19	$815
SystImmune Inc.	1	$800
Arcus Biosciences	3	$765
Myovant Sciences	2	$700
Regeneron Pharma	3	$670
iTeos Therapeutics	2	$654
Exelixis	6	$585

Licensor	Deal Count	Upfronts from Licensing ($mm)
Immatics N.V.	10	$576
MacroGenics Inc.	13	$575
Argenx N.V.	2	$540
Agenus	10	$530
Xencor Inc.	9	$505
Akeso Biopharma Inc.	3	$500
Jounce Therapeutics	3	$497
Loxo Oncology	2	$460
Five Prime Therapeutics	8	$453
CytomX Therapeutics	8	$450
Innate Pharma	6	$431
Alnylam Pharmaceuticals	5	$416
Novartis AG	17	$405
Autolus Therapeutics	2	$400
HUTCHMED	1	$400
Cellectis S.A.	7	$399
Foghorn Therapeutics	2	$380
CStone Pharmaceuticals	4	$358
Immunomedics	4	$330
Potenza Therapeutics	2	$329

Source: DealForma

Total Cash in Upfronts Received by Global Licensor:

Oncology Licensing Deals, Jan 2020 to May 2024

Licensor	Deal Count	Upfronts from Licensing ($mm)
Daiichi Sankyo Co. Ltd.	4	$5,000
Seagen	4	$1,755
Sanofi	2	$1,207
Arvinas	2	$1,150
BeiGene	4	$950
MorphoSys	3	$940
Blueprint Medicines	3	$815
SystImmune Inc.	1	$800
Dragonfly Therapeutics	2	$775
Genmab A/S	2	$750
Arcus Biosciences	1	$730
Myovant Sciences	2	$700
iTeos Therapeutics	1	$625
Akeso Biopharma Inc.	2	$500
Eisai Co.	2	$450
Autolus Therapeutics	2	$400
HUTCHMED	1	$400
Foghorn Therapeutics	2	$380
Immatics N.V.	5	$380
CStone Pharmaceuticals	4	$358

Licensor	Deal Count	Upfronts from Licensing ($mm)
Arcellx	1	$325
Agenus	5	$310
Cullinan Oncology	3	$295
Hanso Pharma	2	$270
Henlius Biotech	3	$261
POINT Biopharma	1	$260
IGM Biosciences	1	$250
Nykode Therapeutics	2	$250
AbelZeta Pharma	2	$245
Cellectis S.A.	2	$245
Innovent Biologics	4	$245
Debiopharm	4	$227
Orion	1	$221
Junshi Biosciences	7	$210
Kelun-Biotech	2	$210
Poseida Therapeutics	3	$210
OncoC4	1	$200
RemeGen	1	$200
Repare Therapeutics	2	$190
Jounce Therapeutics	1	$187

Source: DealForma

Total Cash Paid in Upfronts by Global Licensee:

Oncology Licensing Deals, Jan 2020 to May 2024

Licensor	Deal Count	Upfronts from Licensing ($mm)
Merck	20	$6,431
Bristol Myers Squibb	21	$2,738
Roche	23	$2,138
Pfizer	10	$1,978
Gilead Sciences	12	$1,767
Novartis	9	$1,520
AstraZeneca	21	$1,519
GSK	11	$1,365
AbbVie	10	$1,127
Regeneron Pharmaceuticals	5	$1,080
Incyte	6	$952
Sanofi	12	$876
Takeda Pharmaceutical	13	$835
BioNTech	10	$833
J&J	20	$810
Merck KGaA	15	$762
Eli Lilly	6	$730
Summit Therapeutics	1	$500
Astellas Pharma	12	$348
Innovent Biologics	7	$344

Licensor	Deal Count	Upfronts from Licensing ($mm)
Gilead Sciences	7	$325
Lantheus Holdings Inc.	2	$321
Pfizer	4	$315
Exelixis Inc.	11	$285
Huadong Medicine	5	$283
Zai Lab Ltd.	11	$275
Taiho Pharmaceutical	1	$275
Moderna Inc.	3	$200
Coherus	3	$195
EQRx	4	$170
Fosun Pharma	3	$158
Blackstone Life Sciences	1	$150
Pierre Fabre	6	$126
Erasca Inc.	3	$123
Bayer	7	$115
Menarini Pharmaceutical	3	$105
Syncromune	2	$100
Fujifilm KK Biologics	1	$100
Jazz Pharmaceuticals	5	$85
Kyowa Kirin	1	$83

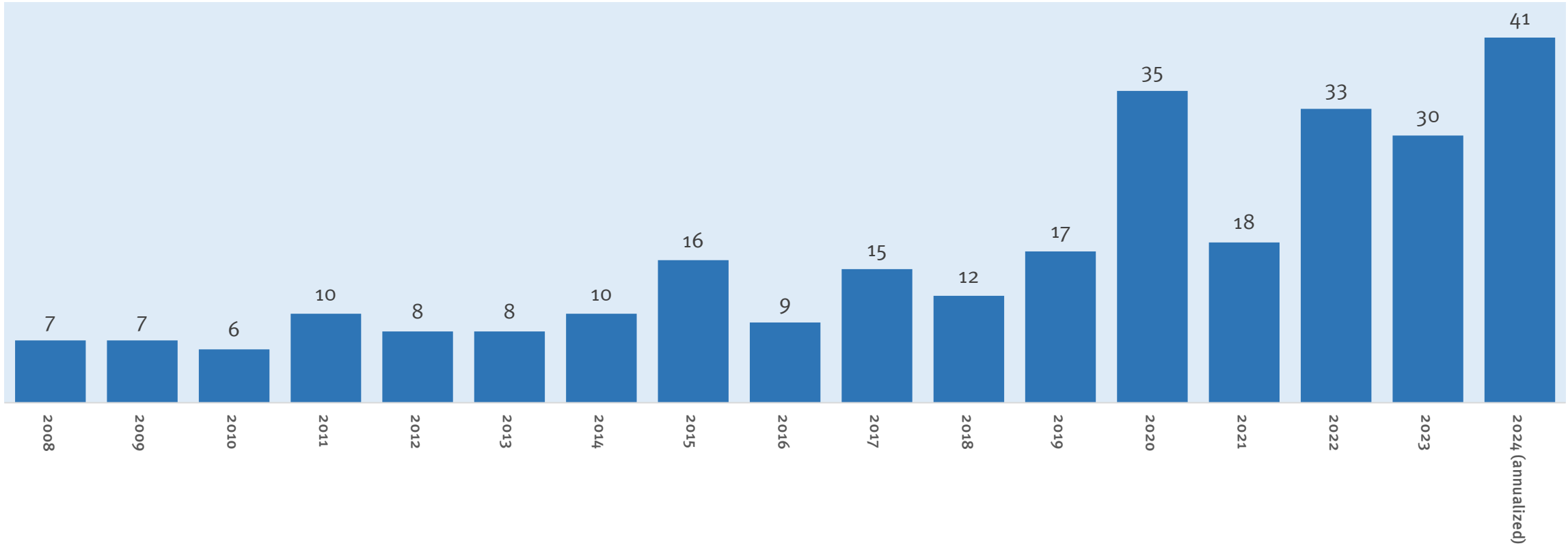
Source: DealForma

Oncology Global License Deal Count Up in 2024…

The total number of oncology licensing deals in the first half of 2024 (annualized) would equal or exceed the previous record year of 2020.

Oncology Licensing Deal Count by Year, 2015-2024

(Transactions with $3mm or more upfront and Global / US Rights Involved)



Source: DealForma

… But Upfront Global Licensing Dollars in 2024 are Down from Recent Years

Total licensing dollars paid upfront paid (even after being annualized) are lower in 2024 than in. 2020 and 2024. Last year's volume was particularly strong due to the Merck / Daiichi ADC deal.

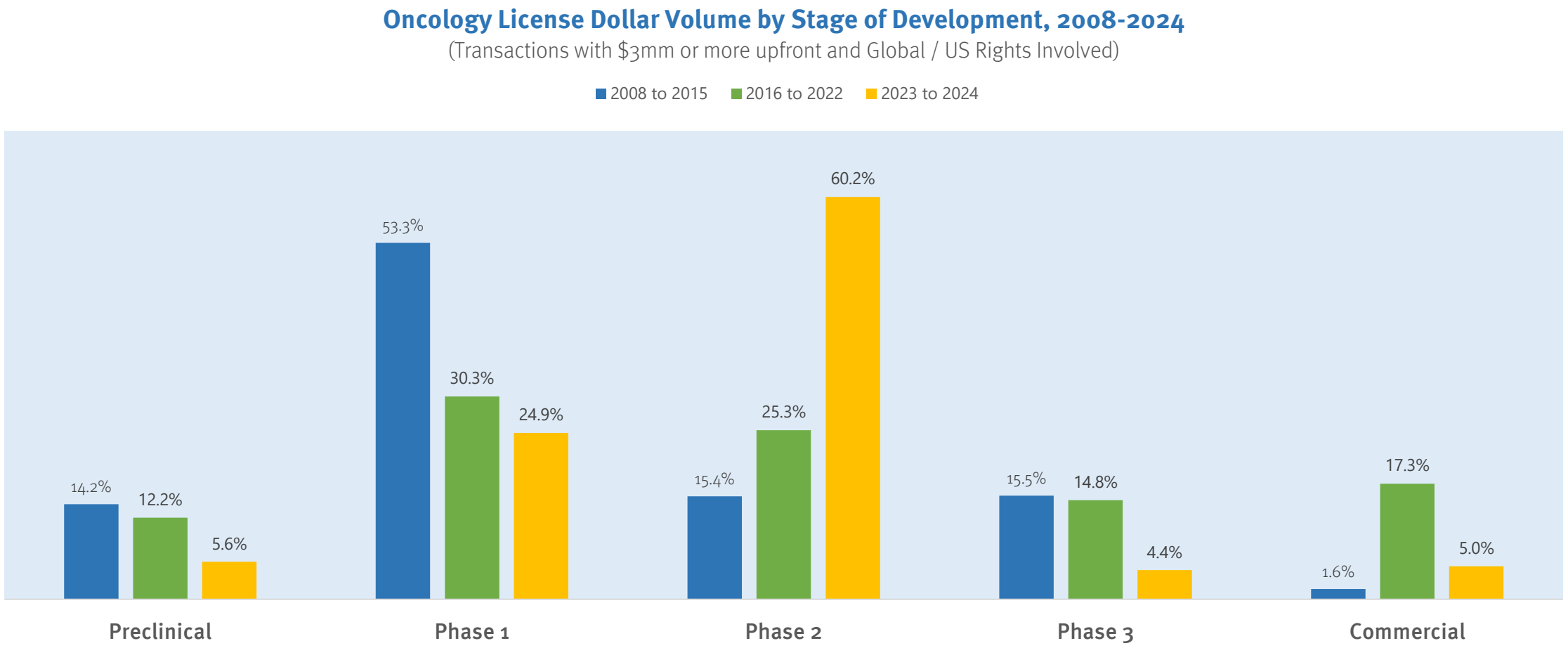
Oncology Licensing Deal Upfront Dollar Volume by Year, 2015-2024

($ Millions, Transactions with $3mm or more upfront and Global / US Rights Involved)

Source: DealForma

More Early Deals in the 2008 to 2015 Time Period. In 2023/2024 We are Seeing More Dollars at Phase 2 Point

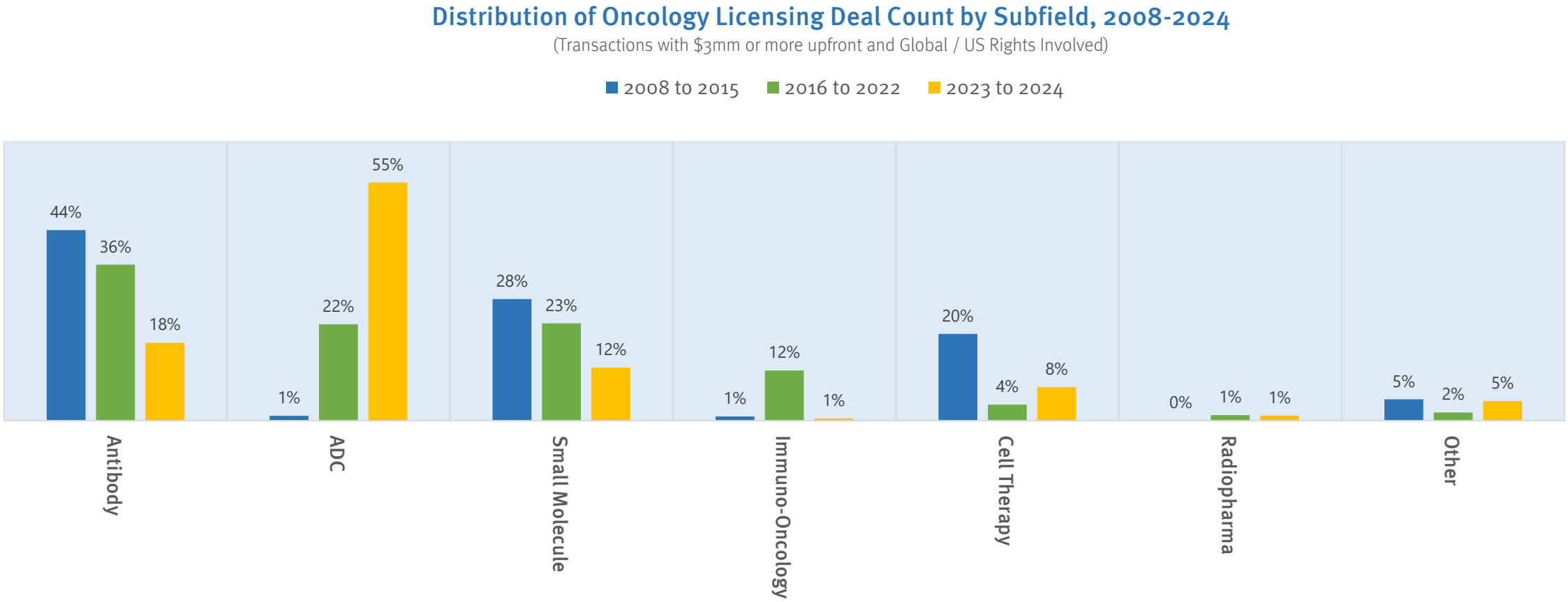
The total dollar volume (by upfront payments) of oncology licensing deals in the Phase 2 stage has risen on a relative basis in the last two years.



Source: DealForma

Increased Focus on ADC's and Less on Antibodies and Small Molecules in Oncology Licensing

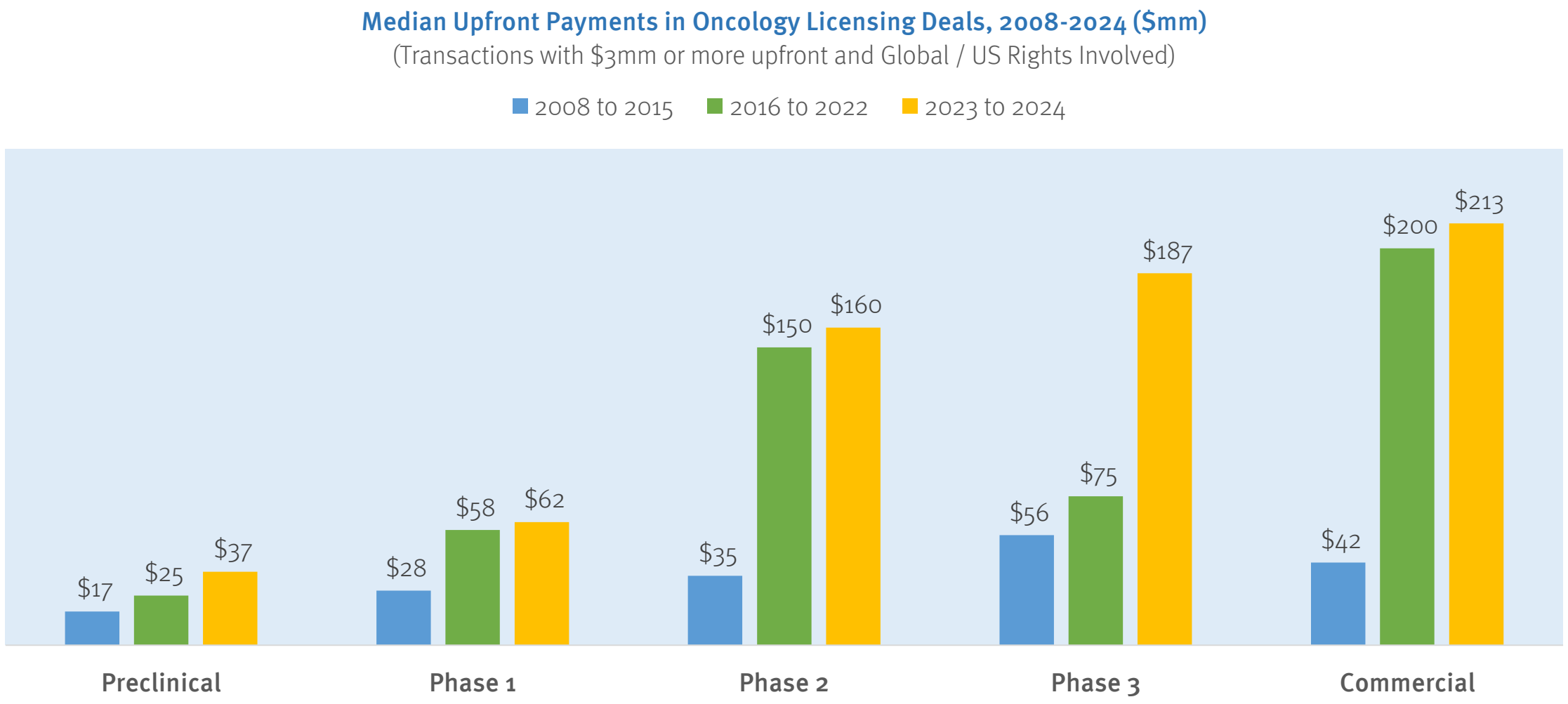
Licensees are increasing shopping within asset classes that are seen as less risky including antibody-drug conjugates, related conjugate structures, T-cell engagers and genetically-driven targets (precision oncology). There is declining interest in cell therapy and traditional targeted oncology (TKI's, cell surface targets etc.). Interest in immuno-oncology has fallen off a cliff after the 2022 time period.



Notes: Data sourced from Stifel oncology transaction database and DealForma. Phases of development are *completed* stages of development rather than those which are ongoing.

Typical Upfronts in Global Oncology License Deals

Upfronts have risen in recent years and go up substantially once assets hit the Phase 2 point.



Notes: DealForma. The Merck/Daiichi deal was excluded in this analysis.

What Pharma Buyers are Looking for in Oncology Deals

Merck, Pfizer and Takeda: Oncology Search Priorities at ASCO

Gabrielle Masson, *FierceBiotech*, June 5, 2024 (excerpt)

It's a similar story at Pfizer, a Big Pharma that has also announced hundreds of layoffs this year, including reductions and role changes at recently acquired Seagen sites.

The company has prioritized three modalities after the $43 billion Seagen buyout: ADCs, small molecules and bispecific antibodies. The strategy is to leverage strengths from ADC-focused Seagen and Pfizer's medicinal chemistry and bispecifics expertise, Megan O'Meara, M.D., Pfizer's senior vice president and head of early development for oncology, said.

The combined companies embody "the nimble mindset of a biotech and the resources of a large pharma," O'Meara said. "We really want to focus on the things that we already have the infrastructure to do really well."

"We've intentionally avoided more niche areas of therapeutic modality for now, such as cellular therapies or radioligands," O'Meara said.

"Let me put it this way: We're not actively pursuing radioligands or autologous cell therapy," Takeda's Bitetti said in a separate interview. "But I would never say 'no.'"

Astellas CMO Tadaaki Taniguchi, M.D., Ph.D., cited both cost and complications, such as short half-lives and complex chemistry, manufacturing and controls protocols, as reasons not to pursue radioligands.

"For us, we're seeking more the ADC, hybrid approach, or thinking about bispecifics and target-based drug discovery," Taniguchi said.

For Merck, combining new assets with already approved meds is an important strategy used to engineer new paradigms, according to Barr. Though Merck hasn't recently undergone widespread layoffs like many other pharmas, the company's patent for blockbuster Keytruda is set to expire in 2028. Before that happens, the company is working to build out a multimodality, diverse pipeline.

"There has to be a multifaceted approach to address patients with broad categories of disease," Barr said."To try to find a completely new way of attacking the cancer is a more high-risk endeavor and one that's just a little more difficult. But if you can try to create synergies, or … learn why patients did or didn't respond for as long as you'd like to your therapy, then you have an opportunity to target therapies to different tumors."

One of these synergistic approaches is the Merck-Moderna cancer vaccine mRNA-4157 being studied in combination with anti-PD-1 Keytruda. During ASCO, the companies presented three-year data from a phase 2b trial for resected melanoma, finding that mRNA-4157 and Keytruda reduced the risk of recurrence or death by 49% compared to Keytruda by itself.

Source: https://www.fiercebiotech.com/biotech/asco-big-pharmas-double-down-past-wins-future-success-and-steer-clear-radioligands-and-cell

What Big Pharma Buyers are Looking For in Oncology

1. We have met with over a dozen pharma buyers in oncology in recent weeks with a spate of meetings at ASCO and BIO.
2. First and foremost, the interest is highest in mid and late-stage assets in tumors where there is an unmet need, particularly, lung, breast, CRC and liver.
3. Buyers are looking for efficacy in late-stage assets that would differentiate from the standard of care.
4. Pharma's view is that biotech has been heavily picked over for good assets and that the most attractive assets are quite expensive for what they offer. Investors are seen as too enthusiastic about many leading companies.
5. Pharma sees most biotechs as focused on tumor types that don't serve enough patients.
6. A minority of companies are interested mainly in high science approaches that are pre-clinical. There is particular interest in novel targets for ADC's and engagers.

Photo: ASCO 2024 source: Stifel

Photo: Bayer and Ipsen booths at ASCO 2024, Source: Stifel

What Big Pharma Buyers are Looking For in Oncology (cont)

7. Buyers are spending much more time than before scrubbing Chinese biotechs for interesting assets – particularly those that are first-in-class or late stage. Buyers are also scrutinizing Japanese and European biotech pipelines.

8. Buyers are concerned about “target modality hopscotching”. You get a great radiopharma FAP and then someone comes along with much more agile ADC for the same target, for example. This happened last year with PSMA radiopharmaceuticals (Ambrx over Pluvicto) and we heard substantial concerns about modality competition.

9. In terms of modality, there is a strong preference for antibodies, ADCs and T-cell engagers. The focus on ADCs, might not quite be at the fever pitch level of last year and the interest in engagers is rising fast.

10. The engager space is of particular interest right now in solid tumors. Following Merck’s acquisition of Harpoon we have seen a number of groups with promising engager data including Cytomx, Janux, Merus and Xencor.

11. Several groups mentioned the “tumor maps” released recently by AZ as quite interesting.

Photo: Merck sign at ASCO 2024, source: Stifel

What Big Pharma Buyers are Looking For in Oncology (cont)

12. Interest in radiopharma remains really high. Buyers talked about the scarcity of manufacturing, interest in copper/lead platforms and a relentless search for novel radio targets.

13. There remains serious interest in targeted oncology stories. Most frequently mentioned targets were KRAS isoforms, CDK selective isoforms (particularly CDK2) and cMYC. There is a lot going on in stealth right now in MYC – an area of perennial interest.

14. There is remarkably little interest in cell therapies despite success of drugs like Yescarta®. Several companies noted that sales of these drugs have flattened out. Quiet sneers about talk of being able to deliver these drugs for less. A sense that CAR-t is just too expensive for payors.

15. In ADC's far more discernment over payloads and linkers rather than just new targets. A tangible sense through ASCO halls that ADC's are really transforming medicine.

16. Widespread chatter and nerves about Summit Therapeutics and what their emerging data will mean.

Dealmaking Asset Supply / Demand Imbalance Analysis

The pendulum has swung quite significantly in the last three years towards approaches involving new modalities and against immuno-oncology in general. Overwhelmingly, industry's interest is in finding therapeutics that have high prospective efficacy with potential to cure a cancer type. There is high focus on biology, chemistry and protein engineering. The interest in conjugates remains robust with quite a few companies looking for T-cell engagers, ADC's and radio conjugates. A consistent theme from recent discussions with pharma is the need to find late-stage drugs with good efficacy data. There is very high interest in drugs for large markets such as lung cancer, breast cancer, prostate cancer and colorectal cancer. There is remarkably little interest in novel ways of delivering traditional cytotoxics, supportive care, cancer vaccines and tumor metabolism stories.

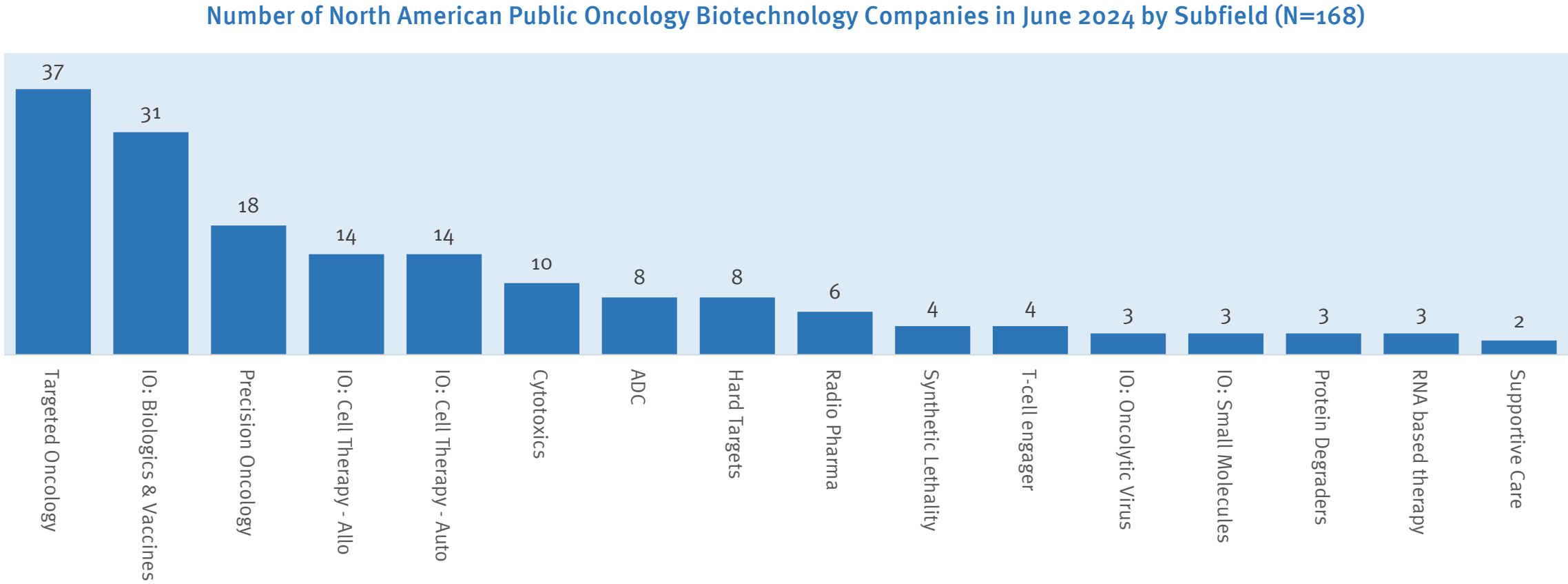
Sellers Market	**Balanced Mix of Buyers and Sellers**	**Buyers Market**
Radio conjugates	Protein Degraders & New SM Modalities	Cytotoxic Therapeutics
Late-stage Drugs w / Good Data & High Need	Immuno-Oncology: NK Engagers	Supportive Care
Drugs Versus Undruggable Targets	Immuno-Oncology: Allogeneic Cell Therapies	Tumor Metabolism / Cancer Stem Cells
T-cell Engagers	Immuno-Oncology: T-Cell Exhaustion Targets	Cancer Vaccines
Antibody Drug Conjugates	China territory assets	Oncolytic Virus
Synthetic Lethality	DNA Damage Response	Immuno-Oncology: Autologous Cell Tx
Precision Oncology	Epigenetic Targets	Immuno-Oncology: Antibodies
China Territory Candidates	TCR cell therapies	Crowded fields like HER2 / PSMA

Source: Stifel meetings with various players at ASCO and BIO, reviews of ASCO presentations, partnering presentations and web site discussions of partnering/M&A interest.

U.S. Listed Public Biotechs in Oncology

U.S. Listed Public Biotech Population by Subfield

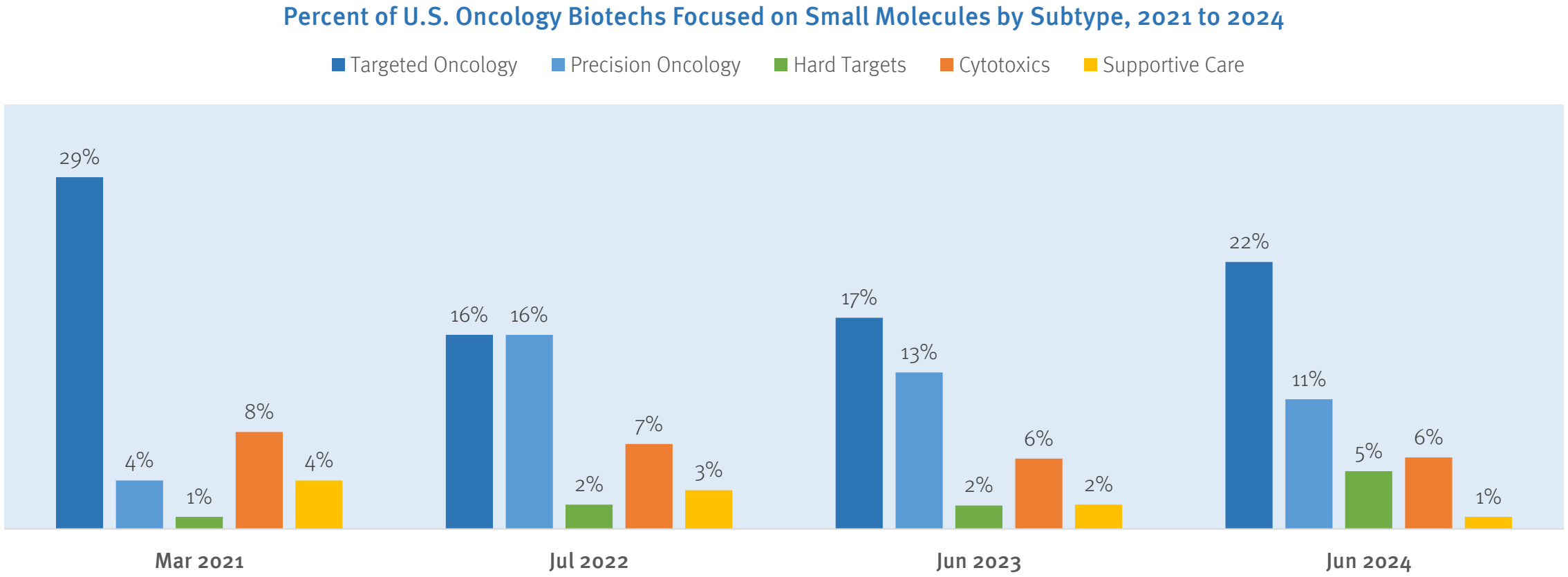
These charts show the distribution of biotechs focused on oncology by subfield today. The most common areas of interest include targeted oncology and immuno-oncology biologics. We distinguish precision oncology from targeted oncology and note that 18 public companies are focused on targets which result from somatic mutations in key cancer growth proteins (e.g., KRAS). The market has 28 companies focused on cell therapy. Even though ADC's, radiopharma and T-cell engagers are highly sought after by buyers there are relative few companies of this type.



Source: CapitalIQ and Stifel Research. Companies headquartered in US or Canada included. Biotechs defined as oncology-focused companies that do not yet have an approved product.

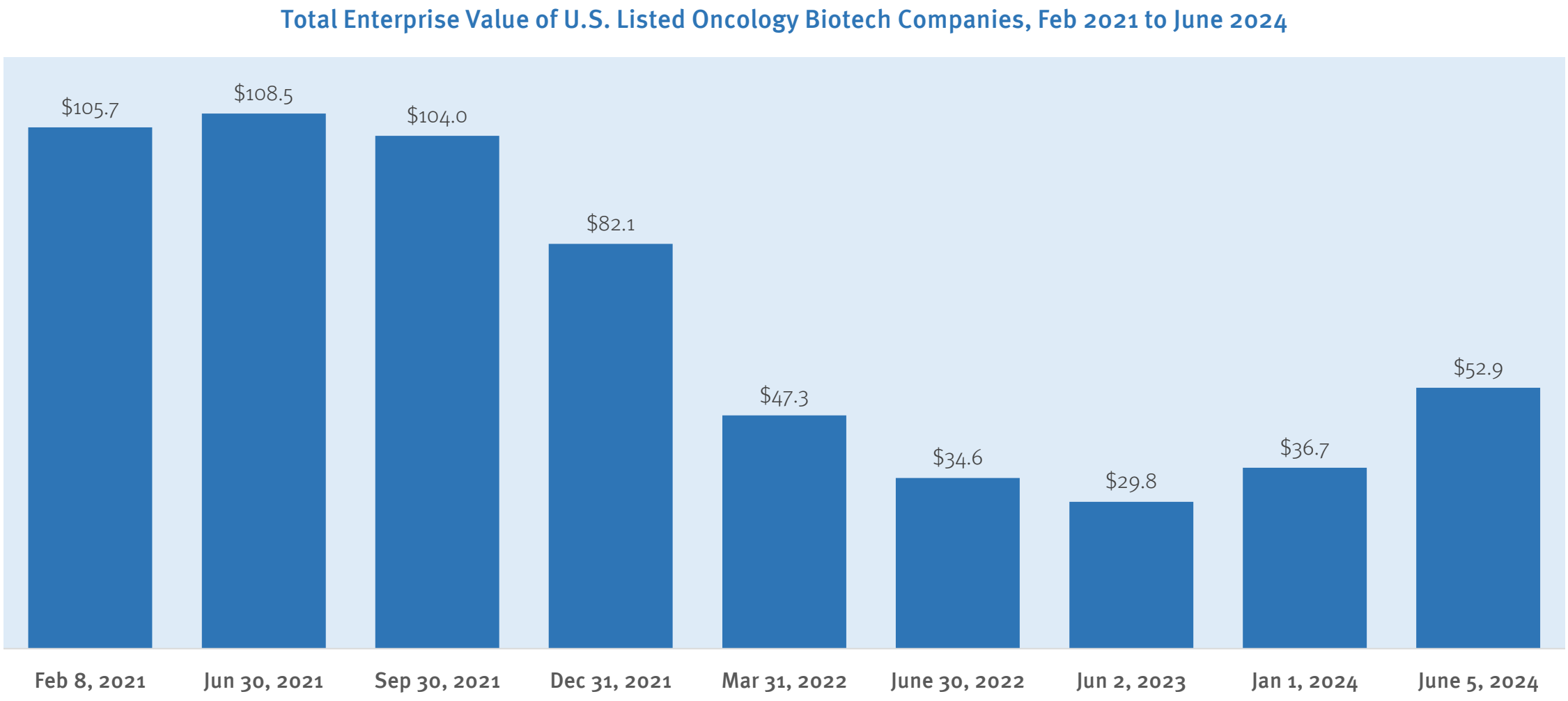
U.S. Listed Public Biotech Population by Subfield Over Time

These charts show the distribution of biotechs focused on oncology by subfield today versus the same population going back four years. The proportion of the population focused on precision oncology (somatic genetic cancer targets) jumped up in 2022 and has since shrunk while more companies today are focused on targeted oncology – a group of companies that excludes those pursuing somatic mutations. We are seeing a long-term drop in supportive care companies. The proportion of the market pursuing cytotoxics has been steady since 2022 and there are substantially more companies today than before pursuing hard targets such as KRAS or cMYC.



Source: CapitalIQ and Stifel Research

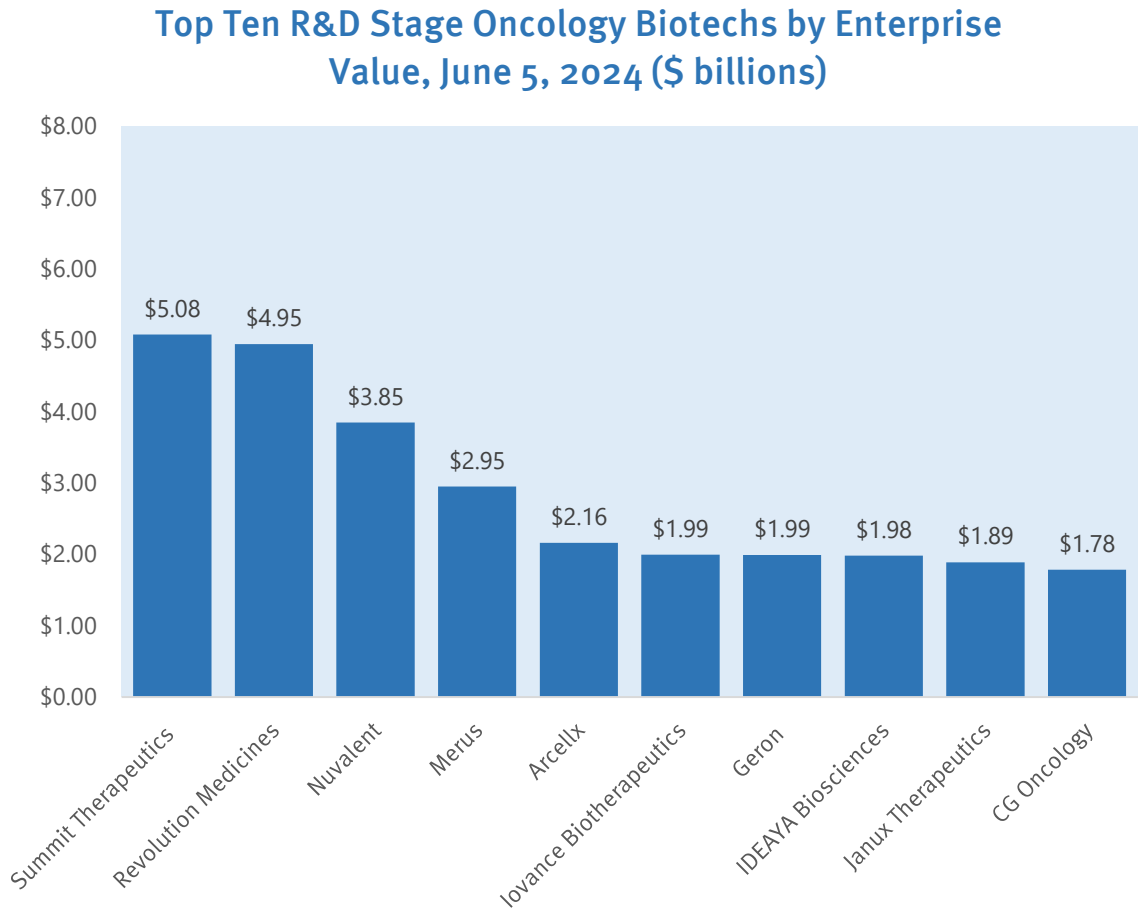
Oncology Biotech Valuations Recovered from Last Year's Nadir (Up 78%)

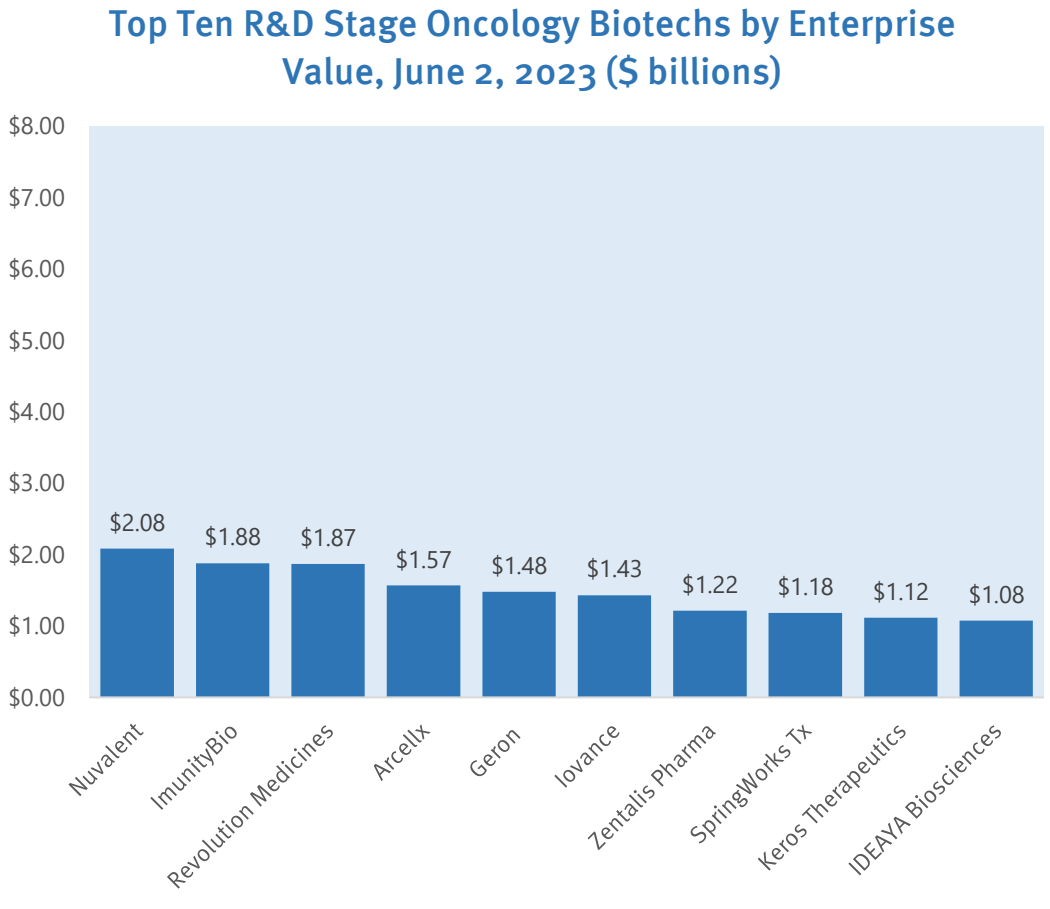


Source: CapitalIQ and Stifel Analysis.

Top of the Class: Top 10 U.S. Oncology Biotechs by Value (June 2024)

Last year's class of top 10 oncology biotech's (by enterprise value) was worth $14.9 billion. This year, the top ten group is worth $28.6 billion (almost double). Four of the companies on last year's list remain on this year's list. A number of last year's company's got drugs approved such as ImunityBio, Iovance and Springworks and thus are off this year's list.

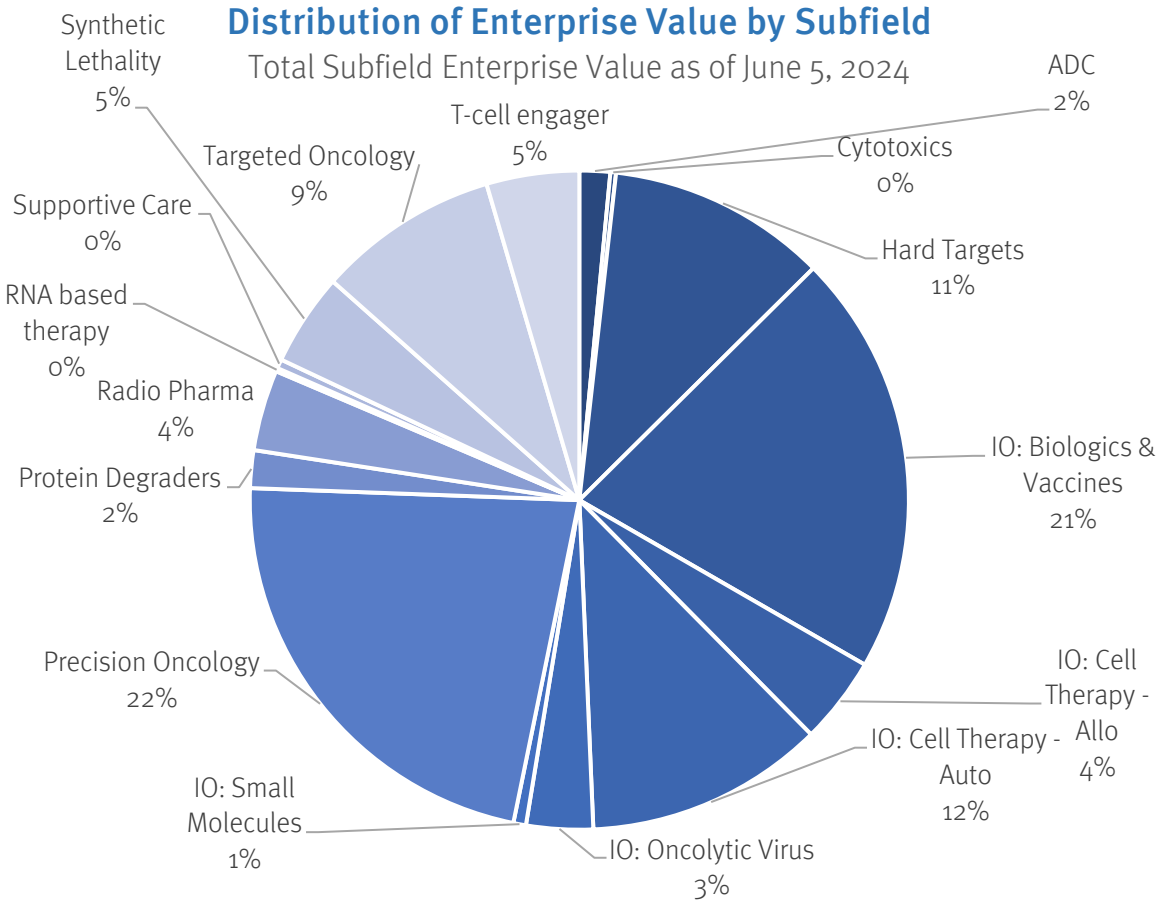


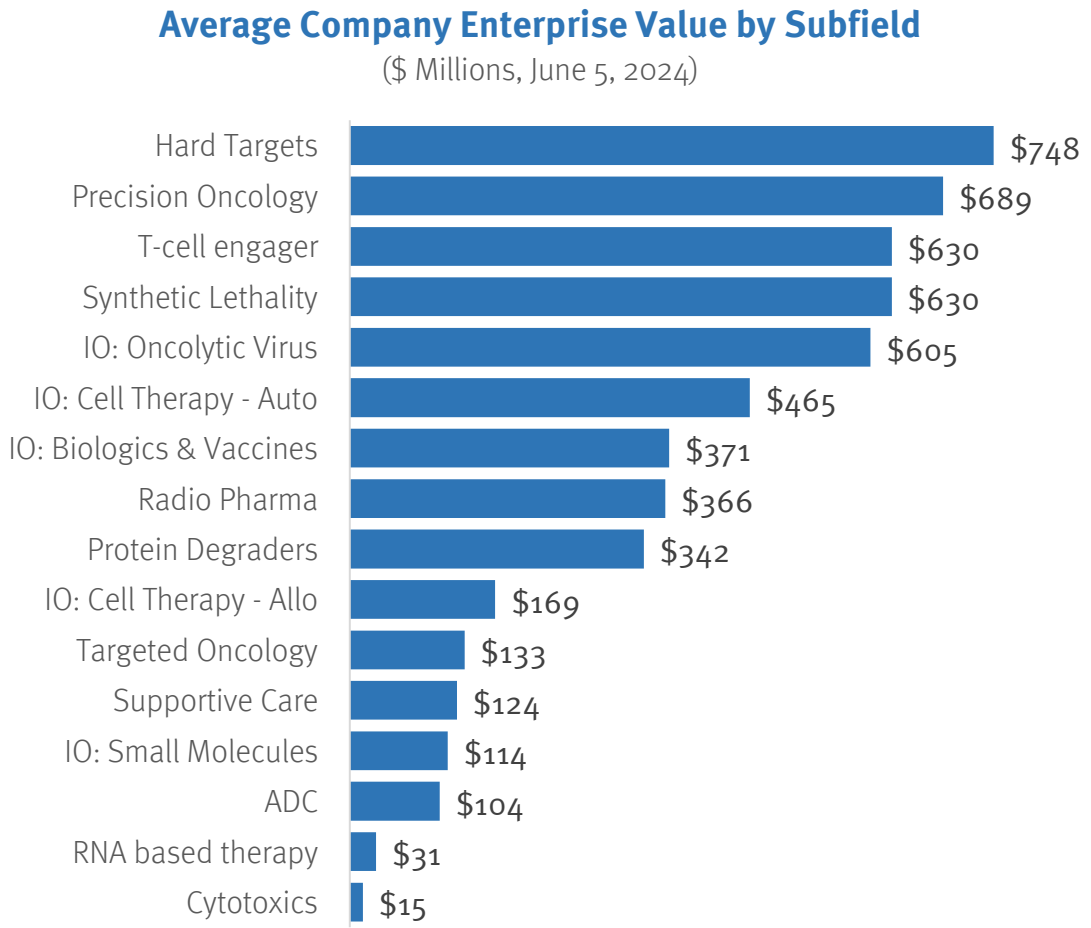


Source: CapitalIQ and Stifel Analysis.

Distribution of Value of Public Oncology Biotechs

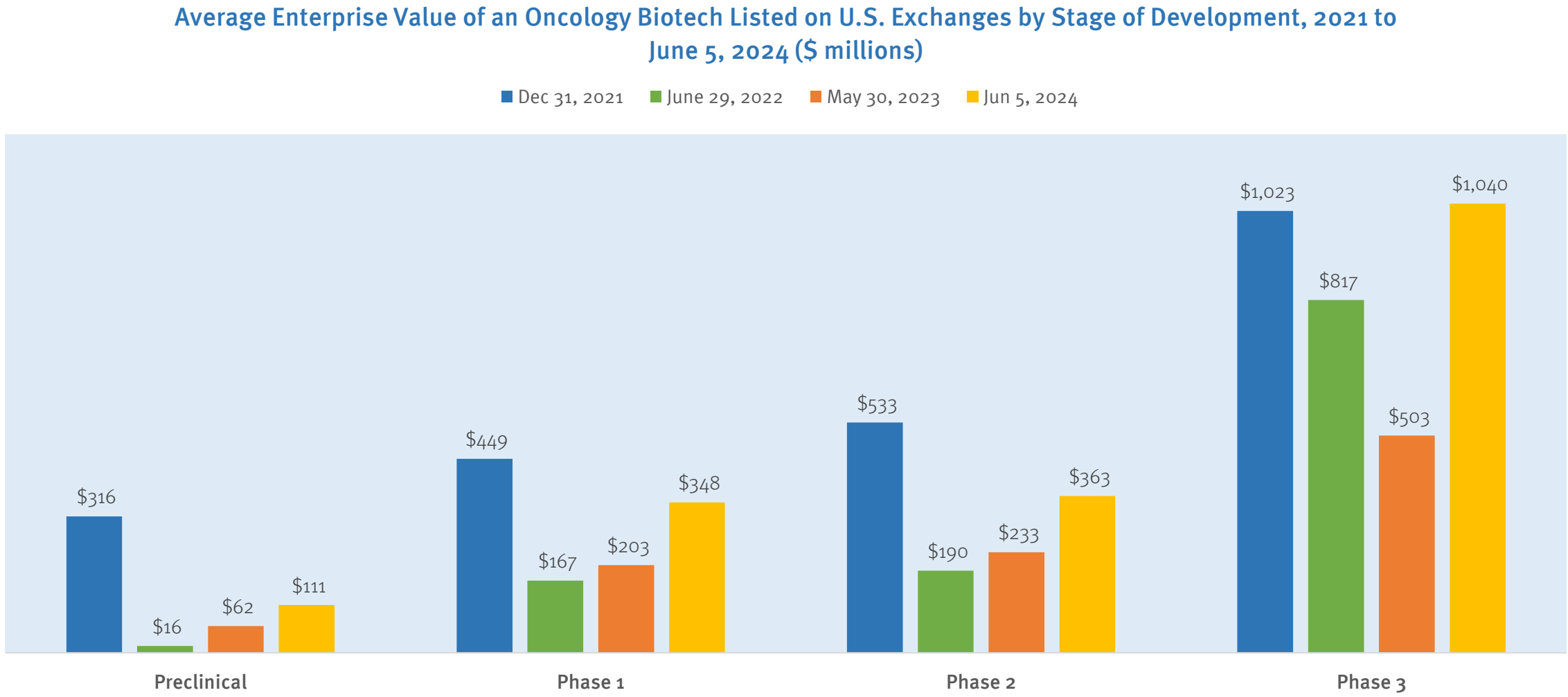
The four most valued types of oncology biotechs on the U.S. markets are those focused on hard targets, precision oncology, T-cell engagers and synthetic lethality. The least valuable are in cytotoxics and RNA therapies. Despite the high M&A interest, ADC biotechs are trading





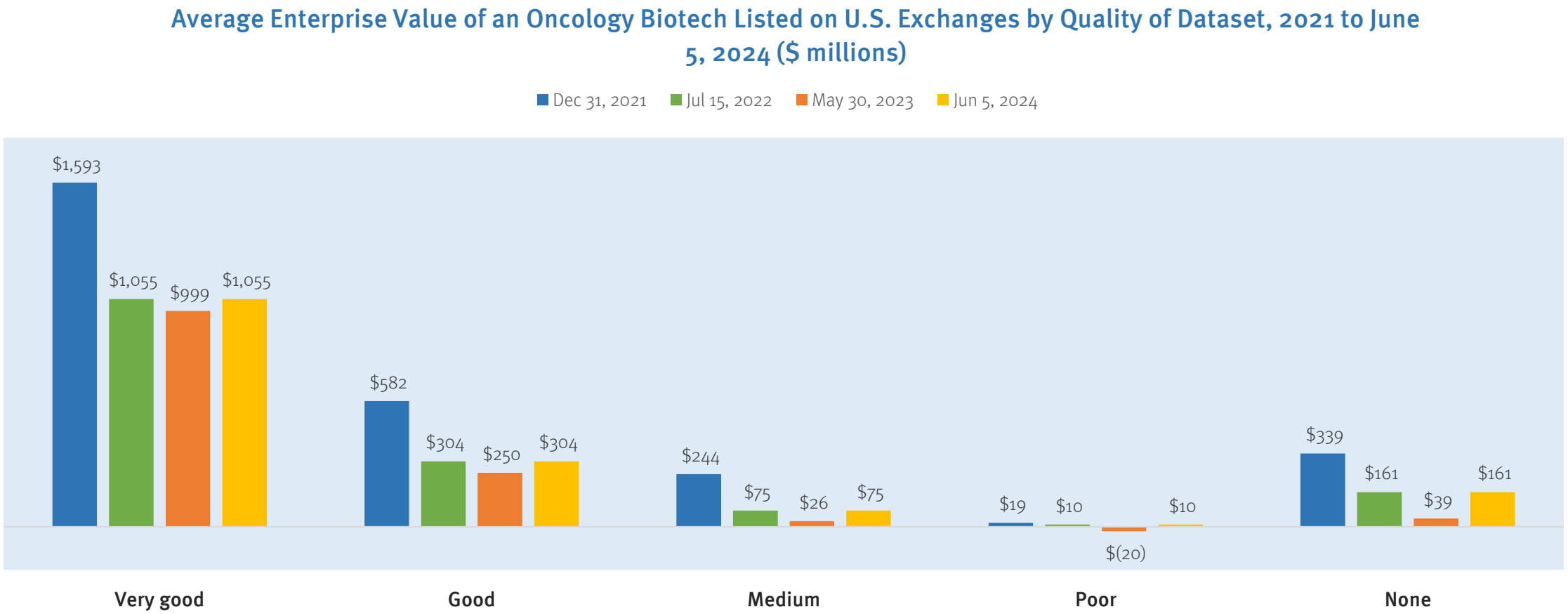
Source: CapitalIQ and Stifel Research

Later Stage Companies Holding Value While Preclinical and Phase 1 Company Values Continue Dropping



Source: CapitalIQ and Stifel Analysis.

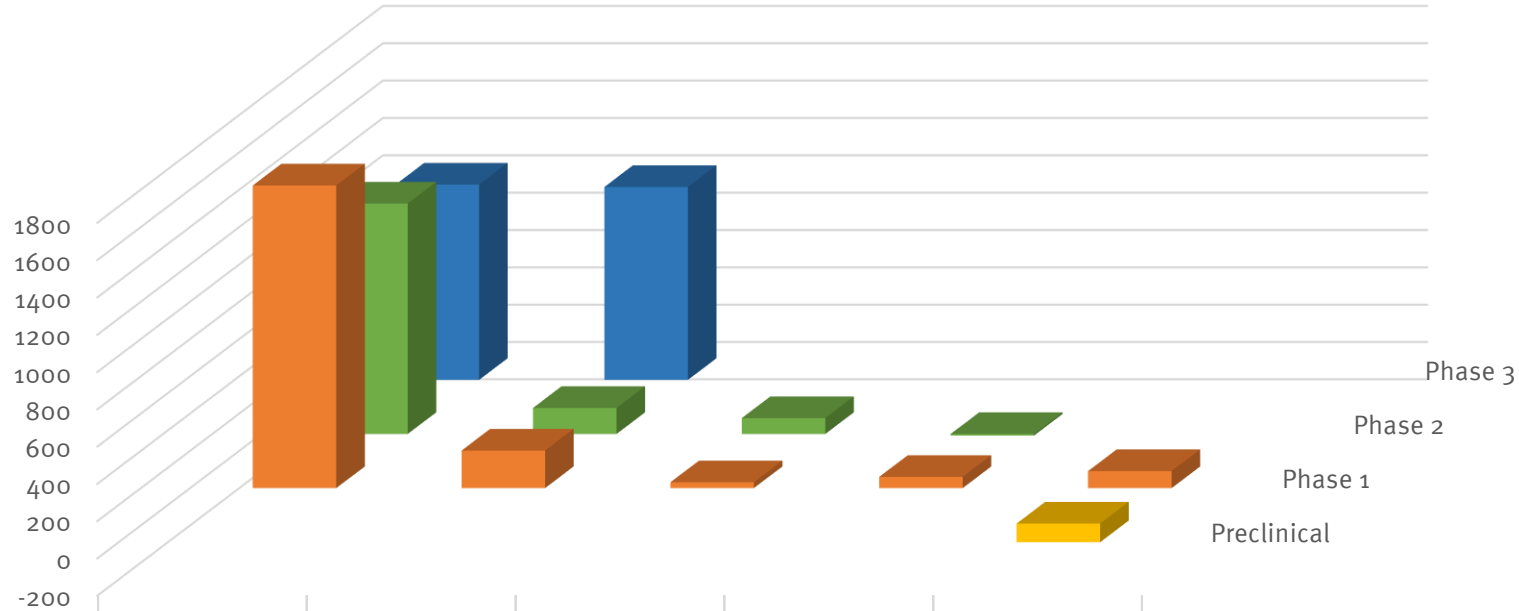
Oncology Biotechs with Very Good Data Holding Value While Those with Good, Medium or No Data Recovering Slowly from 2023 Downturn



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.

Oncology Companies with Very Good Datasets Trade at Over $1bn No Matter What Stage of Development

Average Enterprise Value of U.S. Oncology Biotechs on June 5, 2024 by Phase of Development and Data Quality ($mm)



	Very Good	Good	Medium	Poor	None
Preclinical					$100
Phase 1	$1,622	$201	$31	$60	$91
Phase 2	$1,235	$140	$85	-$8	
Phase 3	$1,046	$1,034			

Typically, a quality premium that rises as drugs get to be later stage. Today, the quality premium curve in oncology is inverted.

The reason is clear enough when one peruses the data. There are no surviving Phase 3 oncology companies with game-changing datesets for large markets. The most promising companies today in oncology are generally through Phase 1 (e.g. RevMed or Nuvalent) or have just started to produce Phase 2 data (e.g., Summit Therapeutics).

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.

Disclosure

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