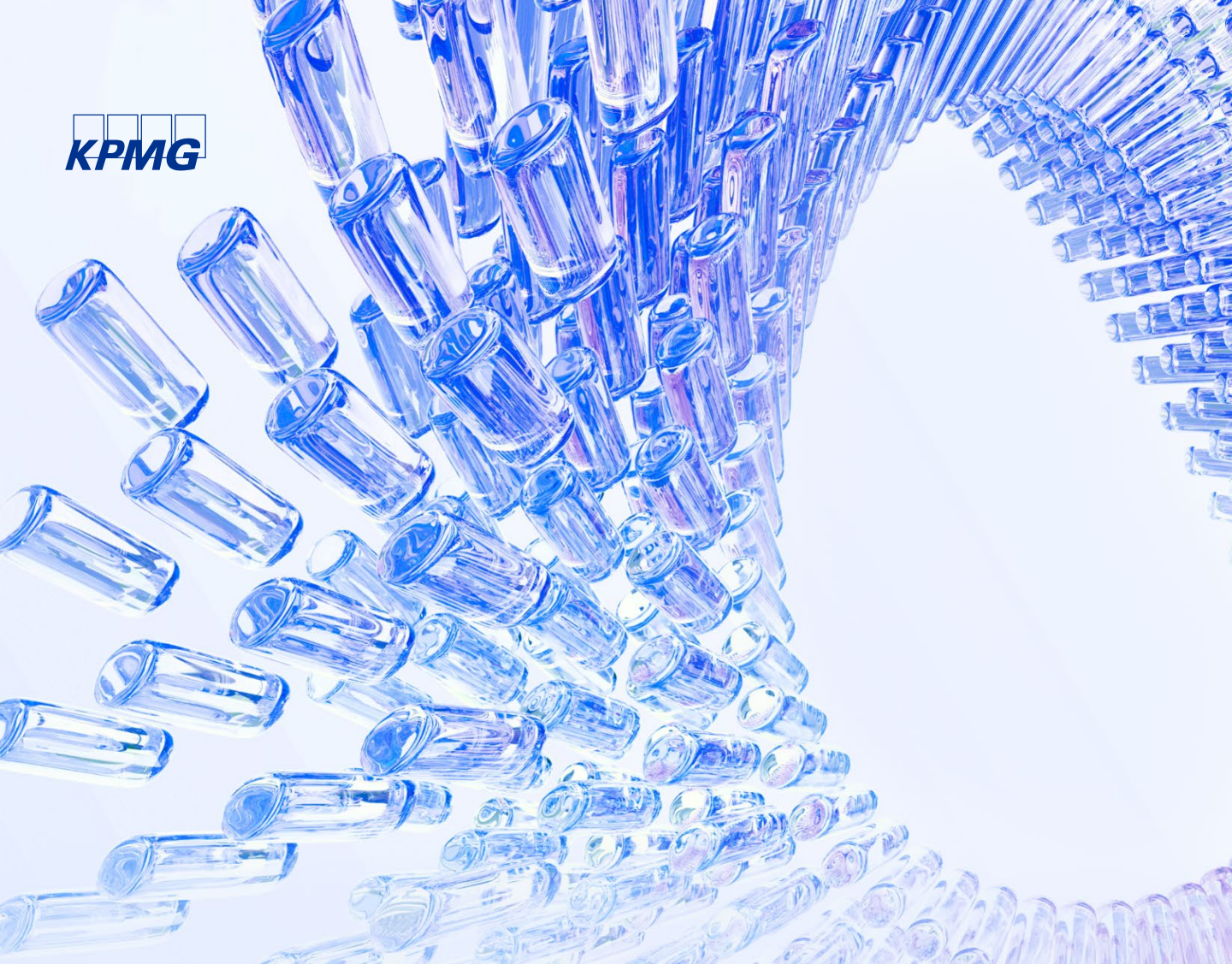


From promise to practice:

How are Antibody-drug conjugates (ADCs) changing the game?

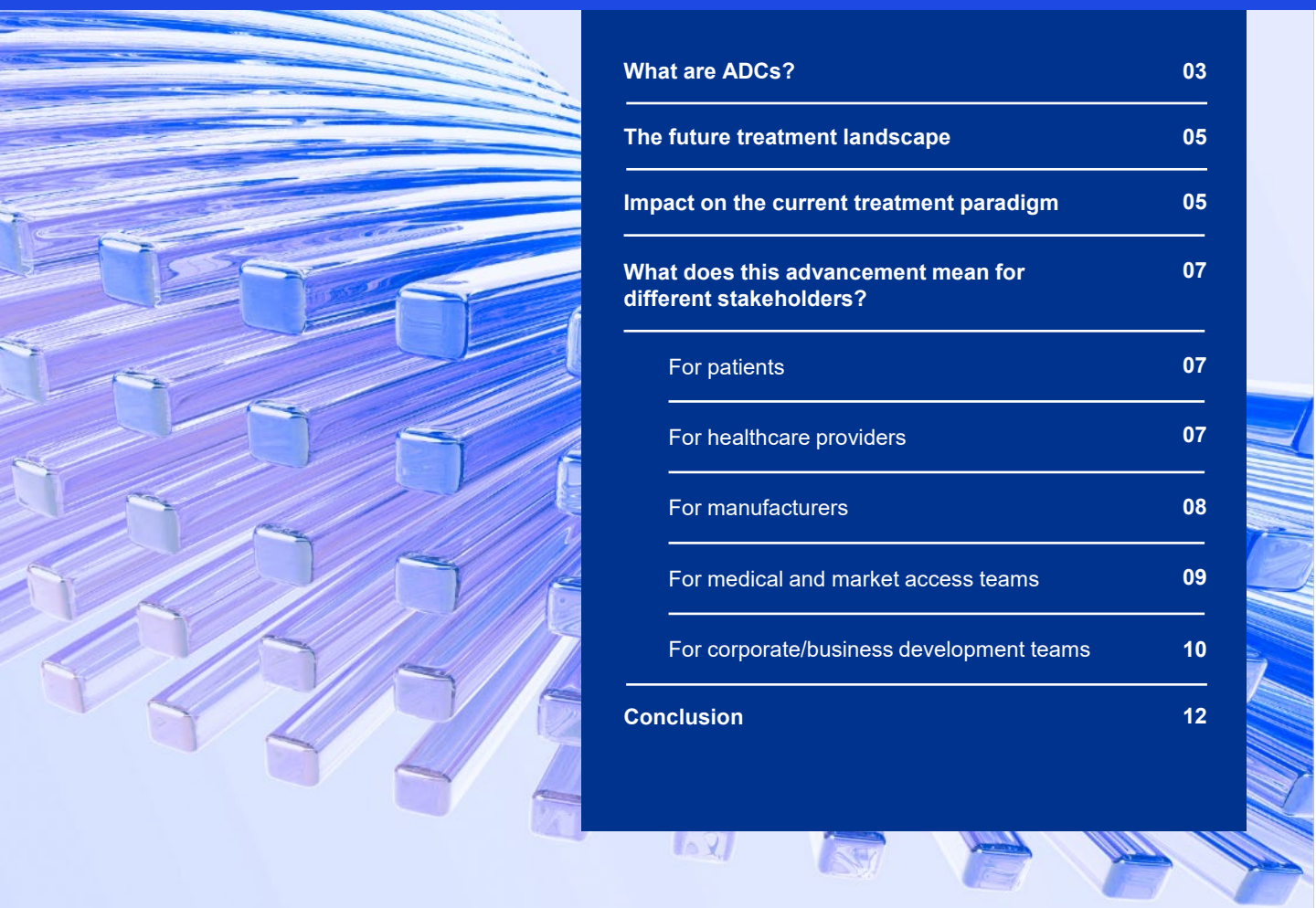
—

July 2025

Introduction

Antibody-drug conjugates (ADCs) represent a groundbreaking innovation in the pharmaceutical industry. Whilst other modalities such as cell and gene therapy have previously gained significant attention, ADCs are emerging as a pivotal area of interest with the potential to revolutionise cancer treatment and extend to other therapeutic areas. This piece aims to explore key drivers for their growth, with a particular focus on innovation across the components, and how this is reshaping the landscape for various stakeholders including individuals, healthcare professionals, and pharmaceutical companies.

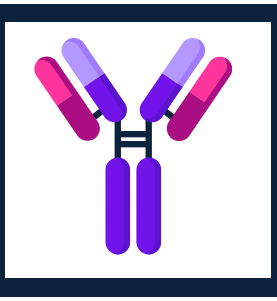
Contents



What are ADCs?

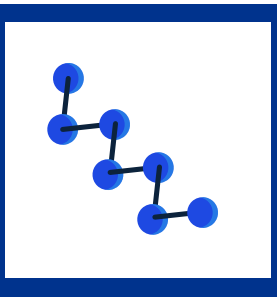
ADCs are typically composed of a monoclonal antibody covalently attached to a cytotoxic drug (or payload) via a chemical linker. This structure is designed to increase specificity and efficacy of therapy, whilst reducing harm to healthy cells, over standard chemotherapy agents.

Figure 1: Basic structure of an antibody drug conjugate



Antibody

- Component responsible for recognising and binding to an antigen (this is targeted to a tumour-associated antigen).
- The binding affinity impacts the rate of internalisation of the ADCs into the targets cells.



Linker

- A bridge connecting the antibody with the cytotoxic payload; a key component impacting the stability of the ADC, and the release profile of the payload.
- The linker ensures that the payload is only released once the ADC has been internalised into the target cell.

Payload

- Exerts cytotoxicity, destroying the cells upon internalisation of the ADC into the target cells.
- High potency (maximum cytotoxicity at a minimal concentration) is required for a payload.

1. Zhiwen Fu et al., Antibody drug conjugate: the “biological missile” for targeted cancer therapy. 2022.
2. Candice Maria Mckertish, Veysel Kayser. Advances and Limitations of Antibody Drug Conjugates for Cancer. 2021.
3. Ricarda M Hoffman et al., Antibody structure and engineering considerations for the design and function of Antibody Drug Conjugates (ADCs). 2017.

What are ADCs? (cont.)

The first ADC launched was Mylotarg (Gemtuzumab ozogamicin) back in 2000, but this was withdrawn entirely in 2010 due to toxicity and a lack of demonstrated clinical benefit[4]. Following a new dosing regimen, Mylotarg received reapproval in 2017. In 2011, the second approved ADC was launched in the UK and EU, which was Adcetris (Brentuximab vedotin).

As of 2022, there were **13 EMA approved ADCs**, all indications being within oncology. The advancement of technology across the three components has helped to improve therapeutic outcomes while minimising adverse effects and allowing a wider range of patients to undergo treatment.

Table 1: 13 EMA approved ADCs

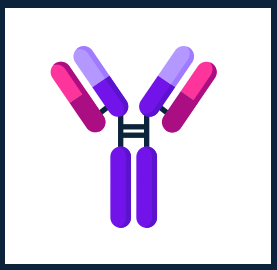
Drug	Trade name	Company	Approved countries	1st approval date	Target	Linker	Payload	Indication
Gemtuzumab ozogamicin	Mylotarg®	Pfizer	FDA/EMA	May 2000	CD33	cleavable	Calichea-micin	Acute Myeloid Leukemia (AML)
Brentuximab vedotin	Adcetris®	Seagen/ Takeda	FDA/EMA/PMDA/ NMPA	Aug 2011	CD30	cleavable	MMAE	HL;sALCL;MF; DLBCL
Trastuzumab emtansine	Kadcyla®	Roche	FDA/EMA/PMDA/ NMPA	Feb 2013	HER2	non-cleavable	DM1	HER2+ BC
Inotuzumab ozogamicin	Besponsa®	Pfizer	FDA/EMA/PMDA/ NMPA	Jun 2017	CD22	cleavable	Calichea-micin	ALL
Polatuzumab vedotin	Polivy®	Roche	FDA/EMA/PMDA/ NMPA	Jun 2019	CD79b	cleavable	MMAE	DLBCL
Enfortumab vedotin	Padcev®	Astellas/ Seagen	FDA/EMA/PMDA/ NMPA	Dec 2019	Nectin-4	cleavable	MMAE	UC
Trastuzumab deruxtecan	Enhertu®	Daiichi Sankyo	FDA/EMA/PMDA/ NMPA	Dec 2019	HER2	cleavable	Dxd	HER2+ BC, HER2-Low/Ultralow MBC, HER2+ GC, NSCLC
Sacituzumab govitecan	Trodelvy®	Gilead	FDA/EMA/PMDA/ NMPA	Apr 2022	TROP2	cleavable	SN-38	HR+/HER2- MBC, TNBC
Belantamab mafodotin	Blenrep®	GSK	EMA/PMDA	Aug 2020	BCMA	non-cleavable	MMAF	MM
Loncastuximab tesirine	Zynlonta®	ADC Therapeutics	FDA/EMA/NMPA	Apr 2021	CD19	cleavable	PBD SG3199	DLBCL
Tisotumab vedotin	Tivdak®	Seagen	FDA/PMDA/EMA	Sept 2021	TF	cleavable	MMAE	Cervical Cancer
Mirvetuximab soravtansine	ELAHERE ™	ImmunoGen	FDA/EMA	Nov 2022	FRα	cleavable	DM4	Ovarian Cancer
Datopotamab Deruxtecan	Datroway	AstraZeneca/ Daiichi Sankyo	PMDA/FDA/EMA	Dec 2024	Trop-2	cleavable	Dxd	HR+/HER2– BC

4. Pfizer press release, Pfizer Prepares For Voluntary Withdrawal Of U.S. New Drug Application And For Discontinuation Of Commercial Availability Of Mylotarg®, 2010.
5. Juliana T W Tong et al., An Insight into FDA Approved Antibody-Drug Conjugates for Cancer Therapy. 2021.
6. Biochempeg. Antibody-drug Conjugates (ADCs) - Approvals by FDA/EMA/NMPA/PMDA. Access here.

The future treatment landscape

The ADC market is poised for significant growth, projected to expand at a compound annual growth rate (CAGR) of **28.4% from 2024 to 2029**. The rising incidence of cancer worldwide is driving demand for newer technologies and innovations across all three components of an ADC – antibody, linker, and drug – is a key contributor driving ADC's growth.

Figure 2: Future improvements in the ADC space



Antibody

- The use of bispecific antibody technology is one example of innovation, improving antibody internalisation and tumour specificity. One example of this is Zanidatamab, a bispecific antibody targeting two domains of HER2 in the treatment of HER2-positive breast and gastric or gastro-oesophageal junction cancer.
- Another strategy is to replace the traditional structure of the antibody, and instead to couple the payload to the polypeptide fragment or single chain variable region of the antibody. This aims to reduce the molecular weight of the ADC, and in turn improve the penetration efficiency and payload delivery to the target cells.

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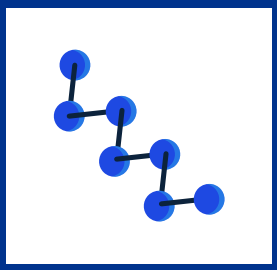

Linker

- Advancements in linker technology include the development of novel chemical triggers to improve the selective cleavage of the linkers and reduce the non-specific release of the payloads. One example is Brentuximab vedotin, which uses a capthesin B-cleavable link to target CD30 positive cancers.
- Hydrophilic linkers are another development in linker technology, aiming to reduce aggregation of the ADCs and improve stability and solubility. One example is Loncastuximab tesirine which uses a PEG hydrophilic linker.

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Payload

- Novel classes of cytotoxic agent such as Pyrrolobenzo-diazepines (PBDs), tubulysin and immunomodulators aim to increase efficacy against more traditional agents - Loncastuximab tesirine is currently the only ADC in clinical use that employs PBD as the payload.
- Dual-payload ADCs employ two distinct cytotoxic agents within a single ADC and aims to reduce the likelihood of drug resistance - KH18 is due to start a Phase 1 trial in April 2025, which will make it the first dual-payload ADC.

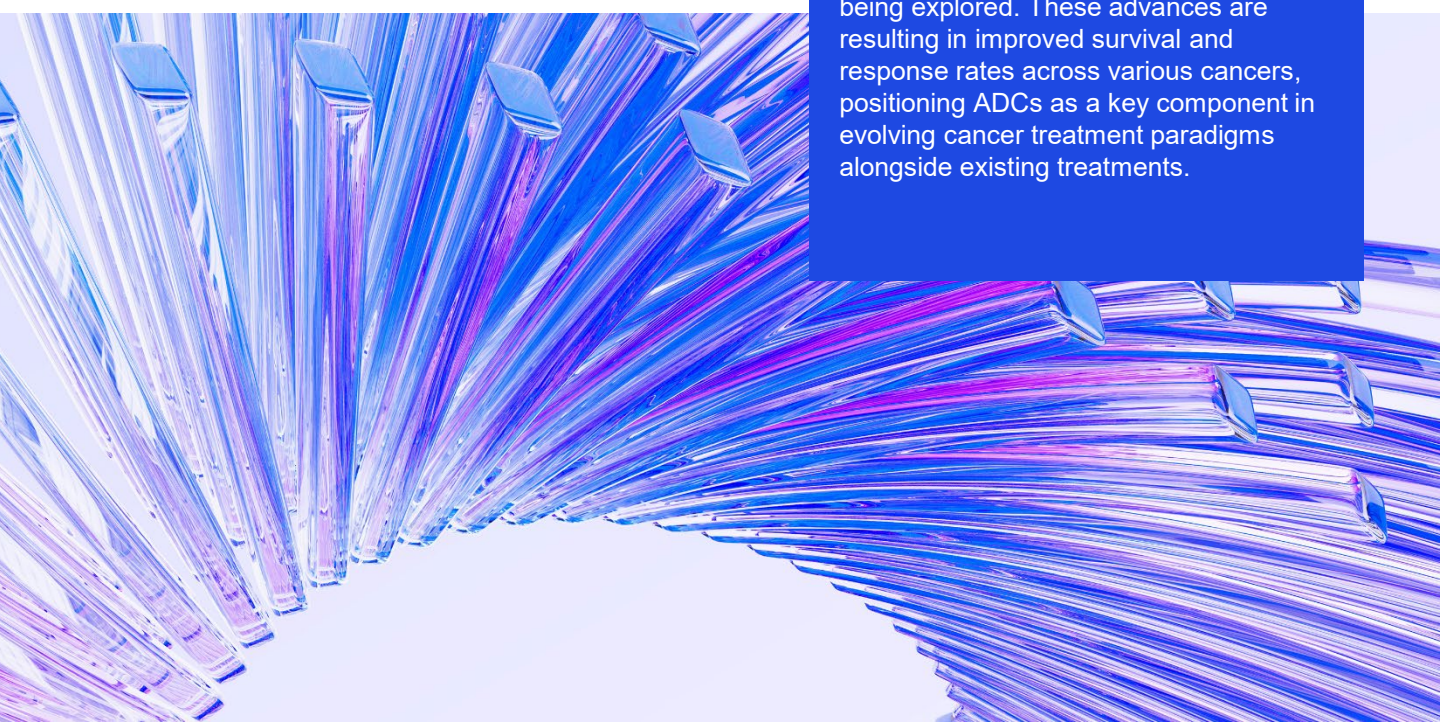
7. PR Newswire, Antibody-Drug Conjugates Market to Grow at 28.4% CAGR from 2024 to 2029. 2021.
8. Zhiwen Fu et al., Antibody drug conjugate: the "biological missile" for targeted cancer therapy. 2022.
9. Funda Meric-Bernstam et al., Zanidatamab, a novel bispecific antibody, for the treatment of locally advanced or metastatic HER2-expressing or HER2-amplified cancers: a phase 9. 1, dose-escalation and expansion study. 2022.
10. Zheng Su et al., Antibody–drug conjugates: Recent advances in linker chemistry. 2021.
11. Seetharamsing Balamkundu, Chuan-Fa Liu. Lysosomal-Cleavable Peptide Linkers in Antibody–Drug Conjugates. 2023.
12. BroadPharm, Zynlonta (loncastuximab tesirine-lpyl). 2021.
13. ApexOnco, Oncology Pipeline. AACR 2025 preview – a surge in dual-payload conjugates. 2025.

The future treatment landscape (cont.)

Whilst these innovations present opportunities for differentiation, they also pose challenges. The increased complexity in development leads to higher R&D costs, and regulatory pathways are uncertain – especially in non-oncology applications. Whilst ADCs can be tailored to specific patient populations by leveraging genetic markers, the patient segmentation that this causes can lead to smaller target populations, potentially limiting more widespread adoption for the new ADCs.

Impact on the current treatment paradigm

ADCs are having a significant impact on the current cancer treatment paradigm by providing targeted delivery of cytotoxic agents. Compared to traditional chemotherapy, ADCs offer increased efficacy whilst reducing systemic toxicity. Preclinical studies show that ADCs can be combined with radiotherapy to further enhance tumour control. Additionally, combinations with other modalities, such as immune checkpoint inhibitors, are also being explored. These advances are resulting in improved survival and response rates across various cancers, positioning ADCs as a key component in evolving cancer treatment paradigms alongside existing treatments.



14. TheMedicineMaker, ADC Innovation: The Road Ahead. 2025.
15. Allegra Gerharz et al., Multimodal cancer therapy consisting of antibody-drug conjugates and radiotherapy in cancer treatment. Published in Cancer Research April 2025.
16. Yuzhen Zhou et al., Activity of antibody-drug conjugates with radiation in preclinical bladder cancer models. Published in Clinical Cancer Research January 2025.
17. Richard L. Kendall et al., Next generation antibody drug conjugates targeting HER2 and TROP2: Multi-Payload ConjugatesTM targeting orthogonal mechanisms of cell killing. Published in Cancer Research 21 April 2025.

What does this advancement mean for different stakeholders?

For patients

For patients, the increased precision of ADCs offers hope for improved survival and quality of life. Many ADCs are developed for cancers with limited treatment options, increasing access to novel therapies in areas of high unmet need. However, ADCs are inherently more complex than traditional chemotherapy which may necessitate more targeted education and support for patients to understand how treatment works and what to expect.

Patient advocacy groups (PAGs) appear to approach ADCs with a balanced but generally optimistic perspective. PAGs are emphasising the importance of involving patients in decisions related to their care, for patients to express their treatment goals, and views on the adverse events they are willing to tolerate. However, there is concern regarding the high cost of novel ADCs, especially in lower income countries and healthcare systems with strict reimbursement criteria. PAGs are increasingly advocating for greater diversity in clinical trials involving ADCs to reflect real-world populations, and enhanced transparency in trial results. Additionally, PAGs are promoting inclusion of Patient Reported Outcomes in clinical trial design, to better capture patient perspectives into dosing strategies.

For healthcare providers

For healthcare providers, ADCs are viewed as an exciting advancement. However, their complex mechanisms, evolving safety profiles and unique toxicities (e.g., ocular, pulmonary) necessitate ongoing medical education, monitoring, and coordination of care across multidisciplinary teams. Introducing ADCs in routine clinical care requires updated infusion protocols, and staffing requirements, which can further strain resources. As ADCs expand into earlier lines of therapy, there is growing need for clearer guidelines, biomarker driven patient selection and real-world evidence to inform optimal treatment mix and maximise patient outcomes.

18. MD Linx, We're witnessing an ADC-led therapeutic shift. 2025.
19. Healio, Antibody-drug conjugates 'the next pillar of cancer therapeutics'. 2023.
20. OncLive, Peer-Exchange. Antibody-Drug Conjugates in Cancer Treatment.

What does this advancement mean for different stakeholders? (cont.)

For manufacturers

The high precision of ADCs comes with increased development and production costs. The complexity involved in developing and manufacturing ADCs necessitates specialised expertise, leading many pharmaceutical companies to rely on Contract Development and Manufacturing Organisations (CDMOs).

This trend has significant implications:

Increased Demand: The rise in ADC development has escalated demand for CDMO services.

Specialised Expertise Required: CDMOs must invest in talent skilled in antibody engineering and conjugation chemistry.

Investment in Technologies: Adoption of advanced technologies such as microfluidics is crucial for maintaining competitiveness.

The rapid pace of innovation in the ADC space has helped CDMOs who can offer a complete solution to their clients thrive.

For medical and market access teams

The rise of ADCs will continue to shape the role of medical teams within pharmaceutical companies. The complex nature of ADCs requires more advanced and sophisticated scientific communication. There is an increased need for more targeted HCP education, not only on ADC's mechanism of action and evolving clinical trial data, but also on patient selection, biomarker testing, management of unique adverse events and optimal treatment sequencing. Generating real-world evidence and conducting post-marketing surveillance studies will be needed to support broader use of ADCs, particularly as new indications emerge.

Market access teams are also facing new challenges with the emergence of ADCs. Stronger value propositions, supported by health economics and outcomes research, is required to address payer challenges and justify premium prices compared with traditional chemotherapy. Data should emphasise not only improved efficacy but also improved safety profiles and quality-of-life benefits. For those ADCs linked to specific biomarkers, access strategies will need to incorporate biomarker testing infrastructure, associated reimbursement and education on biomarker-driven testing pathways. Finally, given the limited long-term safety data, complexity and high cost, ADCs are expected to undergo more rigorous HTA reviews. Proactive evidence planning and early engagement with HTA bodies will be needed to support favourable outcomes.

21. BioProcess International, Antibody–Drug Conjugate Manufacturing Challenges
22. GlobeNewsWire, Antibody Drug Conjugates
23. Medical Affairs Professional Society, Measuring Value and Impact in Medical Affairs. 2024.
24. Mingming Yu et al., Post-marketing drug safety surveillance of enfortumab vedotin. 2024.
25. Parexel, Identifying Optimal Targets for Antibody Drug Conjugates (ADCs).

What does this advancement mean for different stakeholders? (cont.)

For corporate/business development teams

Pharmaceutical companies are increasingly investing in ADCs, which has led to a surge in deal activity.

Pfizer/Seagen

$43 billion
for several approved ADCs and promising pipeline candidates.

Gilead/Immunomedics

$21 billion
for ADCs including Trodelvy (for breast cancer).

AbbVie/ImmunoGen

$10 billion
for ADCs including Elahere, focusing on boosting AbbVie's capabilities in the solid tumour space.

Recent partnerships also reflect the strategic interest from major players:

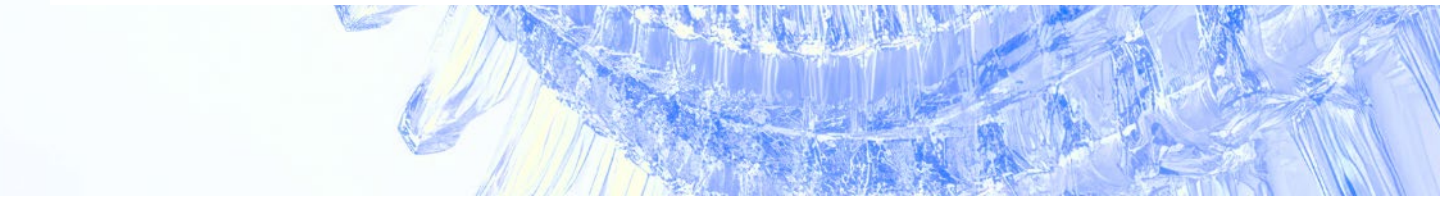
AstraZeneca/ Daiichi Sankyo

$7 billion
collaboration focused on commercialisation of Enhertu. Combined sales of $2.5 billion were generated in 2023, already showing the partnership's success.

Bristol Myers Squibb/SystImmume

$8.4 billion
to develop BL-B01D1, a bispecific ADC aiming to use new strategies in manufacturing Antibodies to drive value.

The year 2023 alone witnessed **76 ADC-related deals** including licenses and collaborations. The investment of major pharmaceutical companies in ADC technology and platforms is expected to increase as companies secure access to promising pipelines.



26. Pfizer press release - Pfizer Completes Acquisition of Seagen, 2023
27. Gilead News - Gilead Sciences Completes Acquisition of Immunomedics, 2020
28. AbbVie News Center – AbbVie to acquire ImmunoGen, 2023
29. Foley & Lardner LLP, Cancer Drugs: Deals and Licensing for Antibody-Drug Conjugates, 2024

What does this advancement mean for different stakeholders? (cont.)

For corporate/business development teams

Table 2: Deals and Licensing for ADCs

Acquirer/Licensee	Seller/Licensor	Drug	$ Value	Deal Date
Pfizer	Seagen (formerly Seattle Genetics)	brentuximab vedotin enfortumab vedotin tisotumab vedotin	$43B	2023
Merck	Daiichi Sankyo	patritumab deruxtecan (HER3-DXd); ifinatamab deruxtecan (I-DXd); raludotatug deruxtecan (R-DXd)	$16.5B	2023
AbbVie	ImmunoGen	Mirvetuximab soravtansine-gyxn	$10.1B	2024
Johnson & Johnson	Ambrx Biopharma	ARX517 ARX788 ARX305	$2B	2024
Genmab	Profound Bio	Rina-S (rinatabart sesutecan)	$1.8B	2024
BioNTech	Duality Biologics	DB-1303 and DB-1311	Up to $1.5B	2023
BMS	Tubulis	P5 conjugation platform & Tubutecan payloads (topoisomerase-1 inhibitors)	Up to $1B	2023
Ipsen	Sutro Bioscience	STRO-003	$900M	2024
Lilly	Mablink Bioscience	PSARlink platform (linker technology) MBK-103	$700M+	2023
Lilly	Emergence Therapeutics	ETx-22	$470M	2023
GSK	Hansoh Pharma	HS-20093	$185M	2023
GSK	Mersana Therapeutics	XMT-2056	$100M	
BMS	Orum Therapeutics	ORM-6151	$100M	2023
GSK	Hansoh Pharma	HS-20089	$85M+	2023
AstraZeneca	LaNova Medicines	LM-305	$55M	2023
BioNTech	MediLink Therapeutics	TMALIN ADC platform	$25M+	2023

30. Foley & Lardner LLP, Cancer Drugs: Deals and Licensing for Antibody-Drug Conjugates, 2024

Conclusion

As the field of ADCs continues to evolve, establishing viable partnerships will be essential for pharmaceutical companies looking to capitalise on this burgeoning market. Collaborations will facilitate access to cutting-edge expertise and technologies while sharing risks associated with development costs and reducing the overall time-to-market.

The future landscape of cancer treatment is being reshaped by innovations in ADC technology, promising not only improved patient outcomes but also new avenues for commercial success within the pharmaceutical industry.

Going forward, we should expect to see ADCs expanding in scope and impacting other therapeutic areas, so engaging with this dynamic field will be crucial for companies aiming to stay ahead in an increasingly competitive environment.

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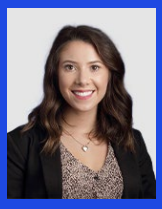

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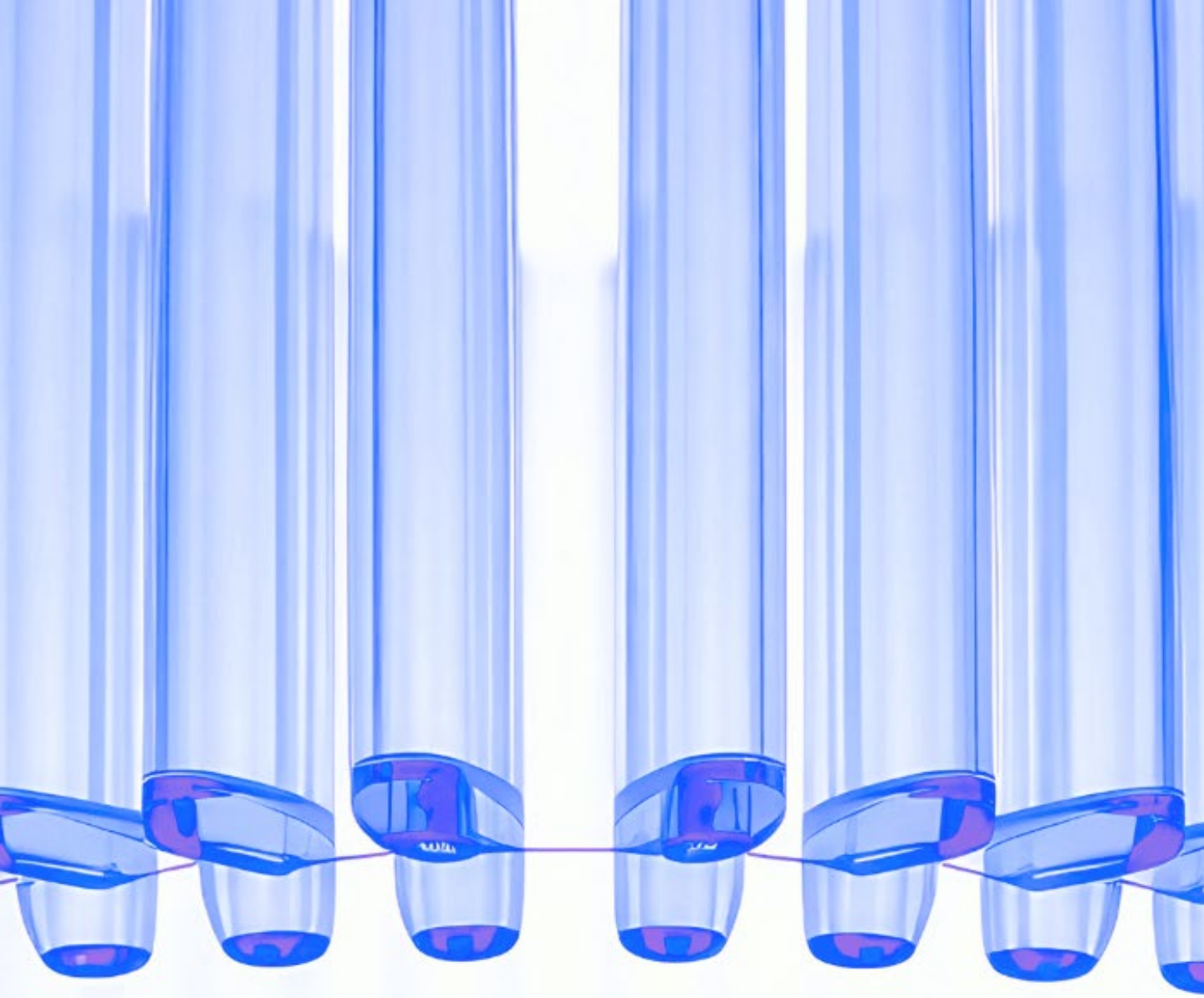

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