Under-the-radar ADC innovators

Companies to Watch 2024

Clarivate™

7 innovators changing the drug discovery and development paradigm

A look at emerging standouts in the field of antibody drug conjugates (ADCs), including:

Potential benefits of their products for patients and caregivers

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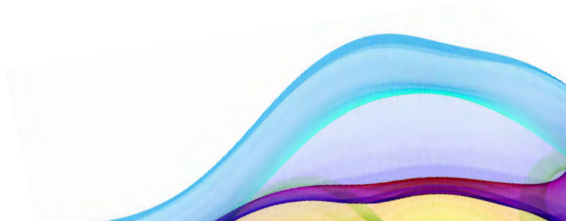
Financing, patent filings and R&D activity to date

What sets them apart from the pack and makes them Companies to Watch

Contents



Methodology

To select our ADC Companies to Watch, we weighted companies according to factors including:

- Medical, business and scientific challenges these companies are attempting to solve;
- Whether the company has demonstrated proof of concept and achieved key developmental milestones
- Positioning in clinical trials;
- Relationships with notable scientific and academic institutions;
- Patient unmet need and/or burden of disease their solutions aim to address;
- Financial positioning, including funding secured, relationships with industry and institutional investors, financial runway and prospects for future fundraising or partnerships; and
- Ownership and status of intellectual property (IP) estate.

Clarivate™ analysts assessed the changing ADC landscape with a variety of proprietary data sources:

BioWorld™ is the industry's leading suite of news services delivering actionable intelligence and the most innovative therapeutics and medical technologies in development.

Cortellis Clinical Trials Intelligence™ is a comprehensive source of detailed insights on clinical sites and trial protocols including biomarkers, targets and indications.

Cortellis Deals Intelligence™ combines the industry's largest source of deals intelligence with enhanced visualizations of the highest quality data, to quickly find the optimal deal without compromising due diligence. Cortellis Deals Intelligence™ combines a robust and comprehensive source of deals intelligence predictive analytics dashboard uses data science techniques, including a combination of automated machine learning and human intelligence, to accurately predict deal valuation and probability of success for partnered assets.

Cortellis Drug Discovery Intelligence™ is the broadest, deepest, most accurate source of R&D intelligence focusing exclusively on pharma and drug development, harmonizing and integrating essential biological, chemical and pharmacological data from disparate sources into a single platform.

OFF-X™ preclinical and clinical safety intelligence is a unique translational tool providing drug and class safety intelligence to anticipate risks and drive new competitive value.

These and other Clarivate data sources provide high-quality, curated data for our proprietary AI capabilities that form the mainstay of our intelligence solutions and services, including advanced search algorithms, bespoke consulting and predictive analytics (e.g., DTSR).

In order to ensure that our information was up to date and accurate, we reached out to the companies our analysts identified as potential Companies to Watch. The companies featured in this report responded, while some did not. This varied response rate resulted in a list skewed toward Western-based countries, not reflecting the rapid pace of innovation in Mainland China and elsewhere in the Asia-Pacific region.

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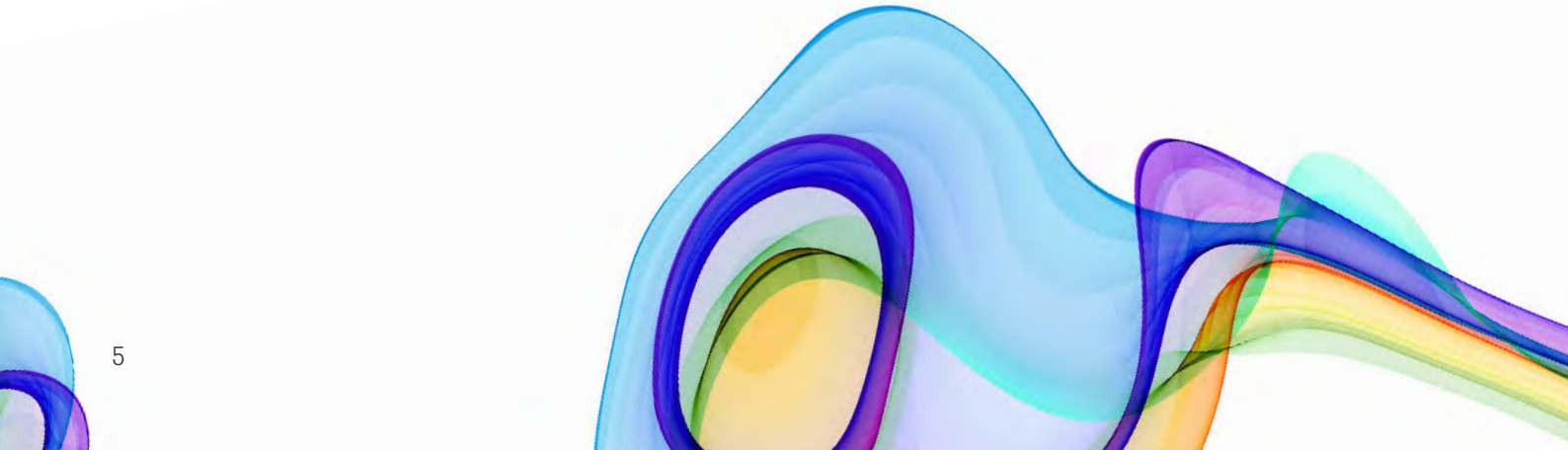


Introduction

Antibody drug conjugates (ADCs) are emerging as a powerful platform for delivering highly targeted doses of cancer treatments (and potentially other drugs) to patients with minimum side effects and toxicity. Large pharmas are anxious to partner with or acquire ADC makers to access this technology — witness Pfizer Inc's $43bn acquisition of Seagen Inc, AbbVie's $10bn acquisition of ImmunoGen and Johnson & Johnson's $2bn acquisition of Ambrx Biopharma Inc — as they seek to replenish their oncology pipelines with next-generation targeted treatments.

Through the combination of their constituent parts — the cytotoxic payload (drug), a monoclonal antibody (mAb) and a chemical linker — ADCs capitalize on the therapeutical potential of mAbs to treat a number of diseases, particularly cancer, with greater target specificity, a wider therapeutic index and fewer side effects than conventional therapies (i.e., chemotherapy and radiation). At the same time, they deliver the toxic agent, which would be unsuitable on its own due to high toxicity, directly to the target cells.

Clinical development has been slow owing to the complexities of selecting the right combination of target and each ADC constituent to provide a stable linkage, high binding specificity and affinity, low immunogenicity, an acceptable rate of internalization and payload potency. ADC technologies also present other challenges, including a potential for degradation during storage and the need to find a formulation that balances sufficient bioavailability and stability.

In addition, factors such as manufacturing infrastructure and regulatory acceptance have hampered the introduction of ADC therapies, but this is changing, with contract development and manufacturing organizations (CDMOs) lending their expertise and more than a dozen therapies approved globally.

Capitalizing on a growing acceptance of the technology and a better understanding of the ADC components, both individually and in conjugated form, as well as their effects on disease targets, the companies highlighted in this report are taking innovative approaches to ADC therapies, from pioneering platforms to identifying novel targets.

Successful innovation relies on overcoming inherent challenges with ADCs

Although the first experimental ADC design was published 60 years ago,[1] it took another 20 years for the first clinical trials[2] and 40 years for the first approval.[3] However, the first ADC was withdrawn from the market 10 years after its approval when the confirmatory trial failed to demonstrate clinical benefit and identified new safety concerns (e.g., higher rate of induction fatalities than chemotherapy alone and occurrence of hepatic veno-occlusive disease). Subsequent technological breakthroughs by innovative companies, supported by a growing understanding of the ADC mechanism of action (MoA), have since moved the field forward.

This history of ADC development highlights the challenges pharma companies face across the development and commercialization lifecycle and what they should consider when acquiring and using ADCs.

Clinical

Optimizing drug-linker chemistry
Selecting the appropriate drug-linker chemistry is crucial to achieving optimal drug payload, stability and efficacy while minimizing off-target toxicity. Developing and optimizing novel drug-linker technologies can be time-consuming and resource-intensive.

Tumor heterogeneity
The heterogeneity in tumor characteristics, such as variability in antigen expression and resistance mechanisms, can limit the effectiveness of ADCs at targeting cancer cells. Ongoing challenges in ADC development include identifying suitable biomarkers and patient populations for ADC therapies and addressing mechanisms of resistance.

Off-target toxicity
Off-target toxicity, caused by non-specific binding of ADCs to normal tissue expressing low levels of target antigens, can lead to dose-limiting side effects and adverse events. Minimizing off-target toxicity relies on balancing efficacy with safety by optimizing antibody specificity and linker stability.

Immunogenicity
ADCs can elicit immune responses against the antibody or linker components, leading to reduced efficacy and potential safety concerns. Maximizing therapeutic efficacy depends on mitigating immunogenicity through antibody engineering, linker optimization and immunosuppressive strategies.

Pharmacokinetics/pharmacodynamics
Understanding the pharmacokinetic and pharmacodynamic properties of ADCs, including drug distribution, clearance and tumor penetration, is critical for optimizing dosing regimens and treatment outcomes. Developing predictive preclinical models and biomarkers to assess ADC pharmacokinetics and pharmacodynamics in humans can facilitate clinical translation.

Clinical development
Designing and executing clinical trials for ADCs present unique challenges, including patient selection, dosing optimization and combination strategies. Addressing these challenges requires close collaboration with regulatory authorities, clinical investigators and patient advocacy groups to ensure robust clinical trial design and execution.

Regulatory

Strict oversight
Given the potential for side effects, regulators closely scrutinize the safety and efficacy data for ADCs. It is important to be familiarwith the latest guidance to meet expectations regarding pharmacokinetic, pharmacodynamic and toxicology data.

Market access

RWE/HEOR to support pricing and reimbursement negotiations
Demonstrating the value of ADCs in terms of clinical efficacy, safety and cost-effectiveness is essential for securing market access and reimbursement from payers. Generating real-world evidence and health economic data to support pricing and reimbursement negotiations will help optimize market uptake of and patient access to ADC therapies.

Manufacturing

Complex manufacturing
The manufacturing processes for ADCs require precise conjugation of cytotoxic drugs to mAbs. Ensuring consistent quality, purity and stability throughout the manufacturing process can be challenging and may require specialized expertise and infrastructure.

Manufacturing scale-up and cost
Scaling up ADC manufacturing to meet commercial demand while maintaining product quality and consistency is a significant challenge. Developing cost-effective manufacturing processes and supply chain strategies to minimize production costs and ensure product affordability for patients are important considerations for successful commercialization.

Intellectual property (IP)

Complex IP
Navigating intellectual property issues around ADCs can be challenging given that each component (antibody, linker, cytotoxic agent) could be supplied by different partners. Identifying and documenting ownership early in collaborations is necessary to avoid infringement and to protect IP.

Addressing these challenges requires interdisciplinary collaboration, innovative technologies and continuous investment in research and development to advance the field of ADCs and realize their full therapeutic potential in oncology and other disease areas.

For this expanding space, what does the data tell us?

Big pharma is rapidly adding ADCs to their portfolios by partnering with or acquiring companies innovating in the space.

ADCs are maturing into the clinical space at an accelerated rate and expanding into therapeutic areas other than cancer.

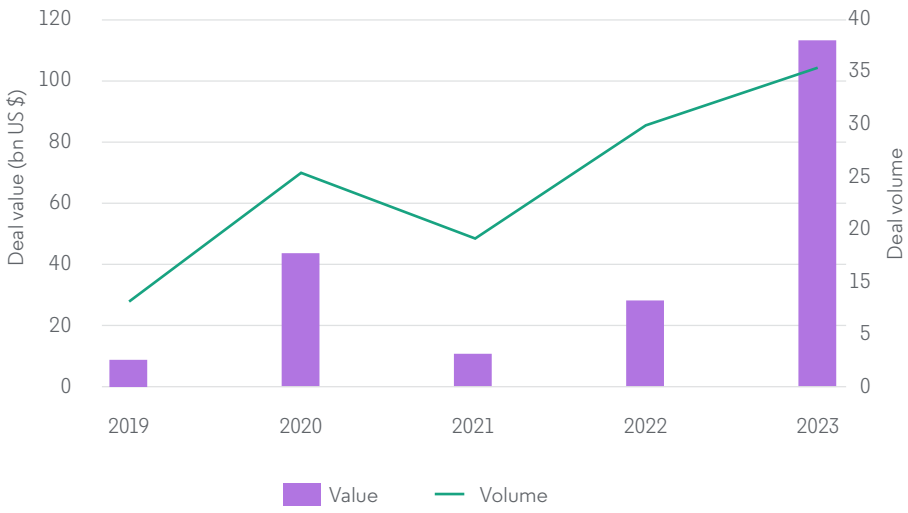
Approvals over the past five years have pushed the number of ADCs on the global market into double digits.

After a phenomenal 2023, ADC deals show no sign of slowing

As ADC technology matures, we are seeing a parallel increase in deals activity by companies seeking new opportunities — either accessing well-developed assets or purchasing entire companies to bring the technology in-house.

Many of the companies featured in this report are innovating in ways that could help big players differentiate their offerings and complement their existing portfolios. This is reflected in both the number and value of deals (Figure 1).

Figure 1: ADC-related deals have increased in both value and volume over the last 5 years



Source: Cortellis Deals Intelligence; only deals with disclosed values included

The 33 disclosed blockbuster deals (~$1bn+) in the past five years represent a significant jump in activity and valuation. The 2023 agreement between Merck & Co/MSD and Daiichi Sankyo represents the largest deal by far in the space (Table 1). Including commitments of up to $22bn, the companies will co-develop and co-commercialize three of Daiichi Sankyo's ADC therapies against solid tumors (ifinatamab deruxtecan, patritumab deruxtecan, raludotatug deruxtecan).[4] This follows Merck/MSD's 2022 license and collaboration agreement with Kelun-Biotech, a subsidiary of Sichuan Kelun-Biotech Biopharmaceutical Co, to develop seven investigational preclinical ADCs to treat cancer, which also came in at number one in terms of deal value for 2022 and in second for the last five years.

Table 1: Top deals in the previous five years (2019-2023), all for oncology except one not reported

Principal company	Partnering company	Details	Projected total value ($B)	Date
Daiichi Sankyo	MSD	Codevelop and cocommercialize patritumab deruxtecan (HER3-DXd), ifinatamab deruxtecan (I-DXd) and raludotatug deruxtecan (R-DXd) worldwide, except in Japan	22.0	10/19/2023
Kelun-Biotech	MSD	Develop seven preclinical ADCs for the treatment of cancer worldwide excluding Mainland China, Hong Kong and Macau	9.5	12/22/2022
Daiichi Sankyo	AstraZeneca	Develop and commercialize DS-8201 (trastuzumab deruxtecan) to treat cancers including breast and gastric cancer and additional development in non-small cell lung cancer (NSCLC) and colorectal cancer worldwide except Japan using DXd ADC technology	6.9	03/28/2019
Daiichi Sankyo	AstraZeneca	Develop and commercialize DS-1062 (datopotamab deruxtecan) for NSCLC and triple negative breast cancer (TNBC) worldwide excluding Japan	6.0	07/27/2020
Genmab A/S	AbbVie Inc	Codevelop and cocommercialize Genmab's next-generation bispecific antibody programs, including epcoritamab (DuoBody-CD3xCD20), DuoHexaBody-CD37 and DuoBody-CD3x5T4, for cancers worldwide excluding the U.S. and Japan	3.9	06/10/2020
Nurix Therapeutics Inc	Seagen Inc	Strategic partnership combining the Nurix Therapeutics DELigase platform, a targeted protein degradation technology with antibody-drug conjugation to develop degrader-antibody conjugates (DACs) against cancer	3.5	09/07/2023
Seagen Inc (Seattle Genetics)	MSD	Develop and commercialize ladiratuzumab vedotin against breast cancer and solid tumors worldwide	3.2	09/14/2020
Eisai Co Ltd	Bristol-Myers Squibb Co	Codevelop and cocommercialize MORAb-202 for cancers worldwide	3.1	06/17/2021
RemeGen Co Ltd	Seagen Inc	Codevelop, manufacture and commercialize disitamab vedotin (RC-48) for solid tumors including urothelial, gastric and breast cancers worldwide	2.6	08/09/2021
Bliss Biopharmaceutical Co Ltd	Eisai Co Ltd	Develop and commercialize BB-1701 against breast and various types of cancers worldwide excluding Mainland China, Hong Kong, Macau and Taiwan	2.0	05/08/2023
Synaffix B.V.	Amgen	Utilize Synaffix 's antibody conjugation technology to develop one ADC program using Synaffix B.V.'s antibody conjugation technology, with the option for exclusive research and commercial licenses for an additional four programs later	2.0	01/05/2023

Source: Cortellis Deals Intelligence

Already in 2024, 32 ADC-related deals have been announced or completed (as of April 12, 2024). The largest disclosed deals (>$500m) have been between:

- Systimmune and Bristol-Myers Squibb for a projected $8.4bn to codevelop and cocommercialize BL-B01D1 in the U.S. to treat patients with metastatic or unresectable NSCLC (completed April 17, 2024);
- Caris Discovery™ and MSD for a projected $1.4bn to identify targets and develop ADCs for cancer worldwide (announced April 4, 2024);
- MediLink Therapeutics and Roche for a projected $1bn to develop, manufacture and commercialize MediLink Therapeutics' YL-211 against solid tumors worldwide (announced January 2, 2024); and
- Sutro Biopharma Inc and Ipsen for a projected $899m to develop and commercialize STRO-003 for solid tumors (announced April 2, 2024).

Regarding M&A activity, 15 ADC-related transactions occurred in the past five years. Seven of these, or nearly 50%, occurred in 2023 alone.

Leading the way, Pfizer Inc acquired Seagen Inc for a whopping $43bn (Table 2). With the acquisition, Pfizer significantly added to its oncology pipeline, which already consisted of 24 approved innovative cancer medicines (which generated $12.1bn in 2022 revenues),[5] and strengthened its renewed focus on oncology as it pivots from waning COVID-19 sales and declining stock prices. Seagen contributed 11 new molecular entities and its four FDA-approved products to treat solid tumors and hematologic malignancies (ADCETRIS®/brentuximab vedotin, PADCEV®/enfortumab vedotin, TIVDAK®/tisotumab vedotin, all ADCs, and TUKYSA®/tucatinib, a tyrosine kinase inhibitor [TKI]), which are also under development for potential expansion into other indications. Together, these assets represent potential risk-adjusted revenues greater than $10bn in 2030.

According to Clarivate data, 3 ADC-related M&A transactions have already been announced or completed in 2024 (as of April 12, 2024) between:

- ImmunoGen and AbbVie (estimated $10.1bn; completed February 12, 2024)
- Ambrx Biopharma Inc and Johnson & Johnson (projected $2bn; completed March 7, 2024) and
- ProfoundBio (Suzhou) Co Ltd and Genmab A/S (projected $1.8bn; announced April 3, 2024).

Table 2: Top ADC-related M&A transactions in the previous five years (2019-2023), all for oncology

Target	Acquirer	Projected total value ($B)	Date
Seagen Inc	Pfizer Inc	43.0	12/14/2023
Immunomedics Inc	Gilead Sciences Inc	21.0	10/23/2020
VelosBio	MSD	2.8	12/2020
NBE-Therapeutics	Boehringer Ingelheim	1.4	12/10/2020
Synaffix B.V.	Lonza	0.2	6/2/2023

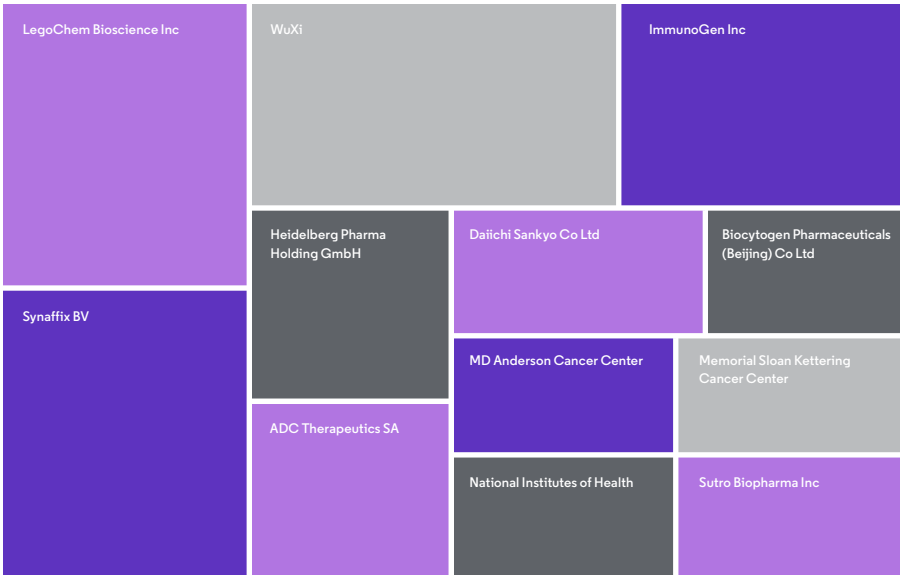
Source: Cortellis Deals Intelligence

The dealmaking environment is dominated by a few big players on both sides of the relationship, partnering to gain access to clinical trial expertise, manufacturing capabilities, or ADC components, as well as to out-license their assets to larger companies wanting to enter the space (Figures 2 and 3).

Figure 2: Most acquisitive companies (with at least five deals) in the ADC space over the last 10 years (2014-2023)

Source: Cortellis Deals Intelligence

Figure 3: Most active providers of ADC technology and assets (with at least five deals) over the last 10 years (2014-2023)

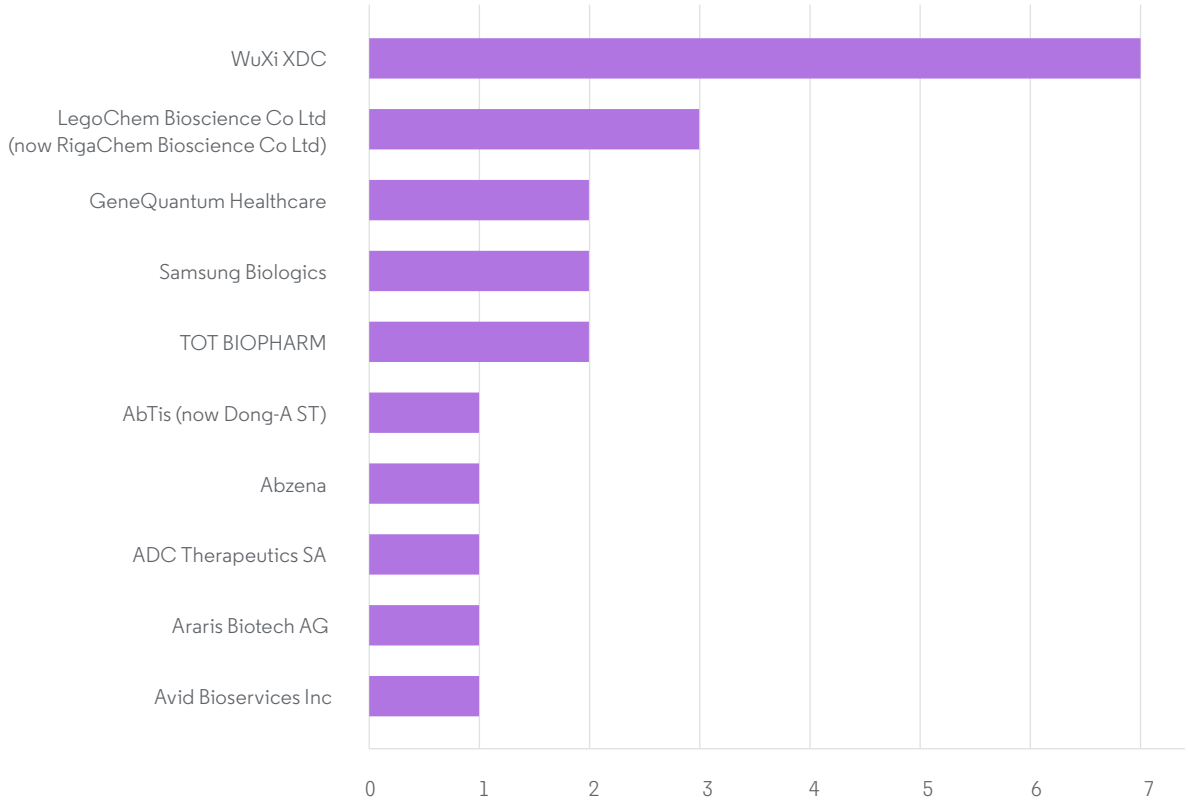


Source: Cortellis Deals Intelligence

Faced with the challenges of ADC manufacturing, many companies rely on the expertise of CDMOs. The CDMOs leading the pack in ADC service agreements hail the APAC region (Figure 4).

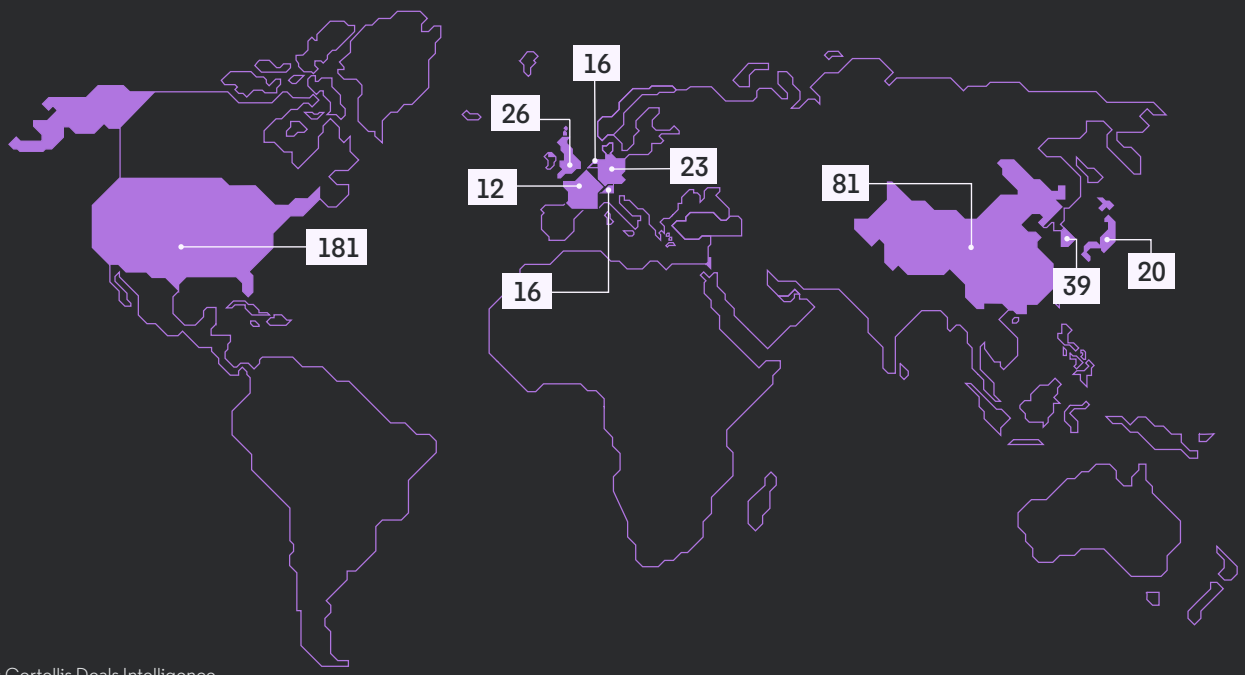
Companies in the United States, followed by those in Mainland China, account for the vast majority of ADC-related deals (Figure 5). Although the U.S. clearly dominates the space, companies in Mainland China provide a significant source of ADC technology and assets.

Figure 4: Top CDMOs with ADC service agreements



Source: Cortellis Deals Intelligence as of April 2024

Figure 5: Countries with the highest number of deals in the ADC space over the last 10 years (2014-2023)



Source: Cortellis Deals Intelligence

As the primary focus of ADC development to date, oncology assets lie at the center of the vast majority of deals to date, although the success in that area is spurring innovation and expansion into other indications, particularly infectious diseases.

Table 3: Cancer leads all ADC-related deals in both volume and value (2014-2023)

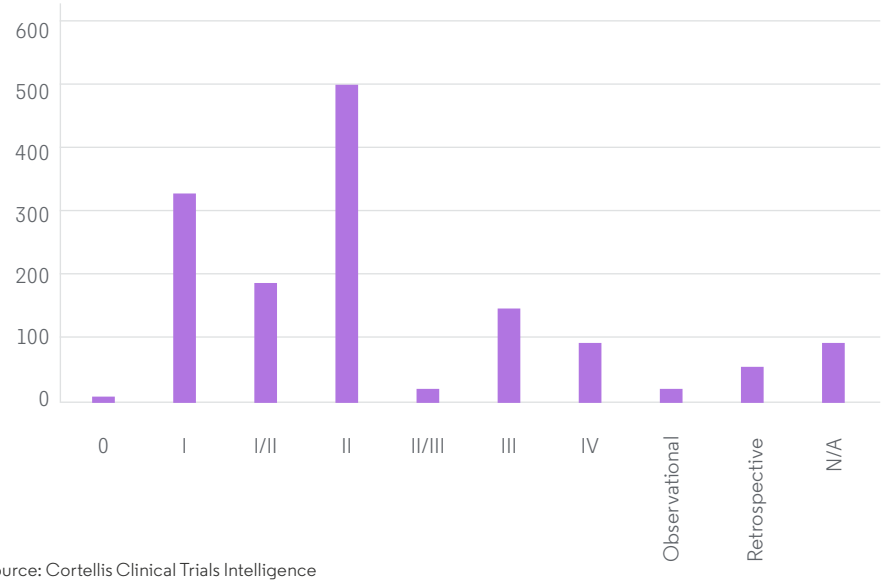
Therapeutic area	Number of deals	Projected total value (m US$)
Cancer	392	205,719.1
Infectious diseases	9	805.6
Immune	3	415.0
Gastrointestinal	1	870.0
Hematologic	1	Not specified
Musculoskeletal	1	420.0
Ocular	1	Not specified
Diversified	5	55.0
Not applicable	8	Not specified
Not specified	38	4,245.3

Source: Cortellis Deals Intelligence

Clinical trial activity reflects the growing maturity of ADC technologies

Companies innovating in this space have made great strides in understanding the most effective combinations of antigen, payload and linker for both efficacy and safety. As a result, assets are increasingly moving into the clinical stage, with more than 1200 active clinical trials for ADCs according to Clarivate data, the majority of which have begun within the last five years (Figure 6).

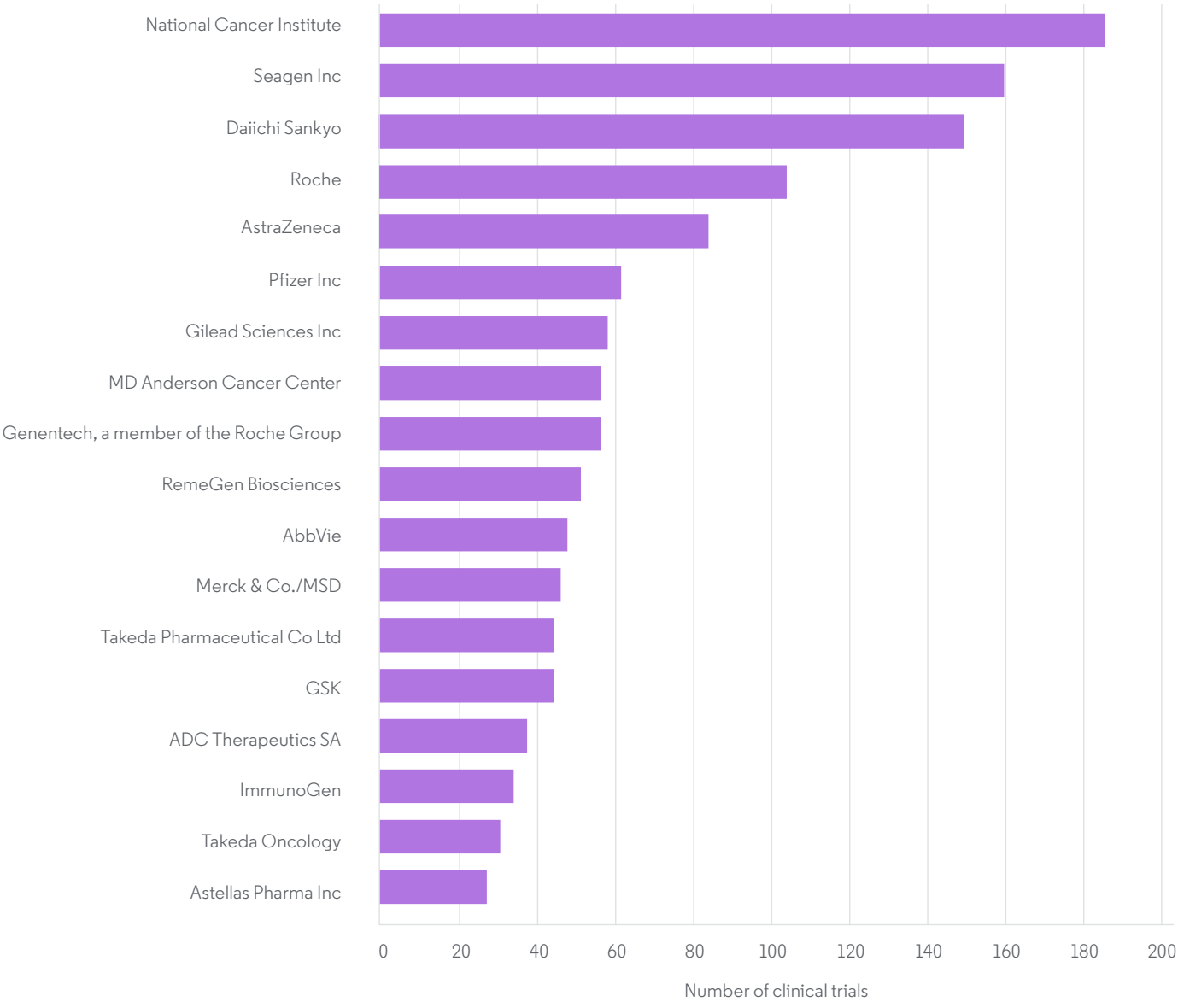
Figure 6: ADC clinical trials started in the last five years (2019-2023) by phase



Source: Cortellis Clinical Trials Intelligence

The companies conducting the most clinical trials are also those with the greatest dealmaking activity. With the recent flurry of acquisitions and licensing deals, the list of the most active companies will continue to shift to reflect those buying their way into the dominant position. For example, the recent acquisition of Seagen Inc by Pfizer Inc moves Seagen/ Pfizer to the top of the list, above the National Cancer Institute, in Figure 7.

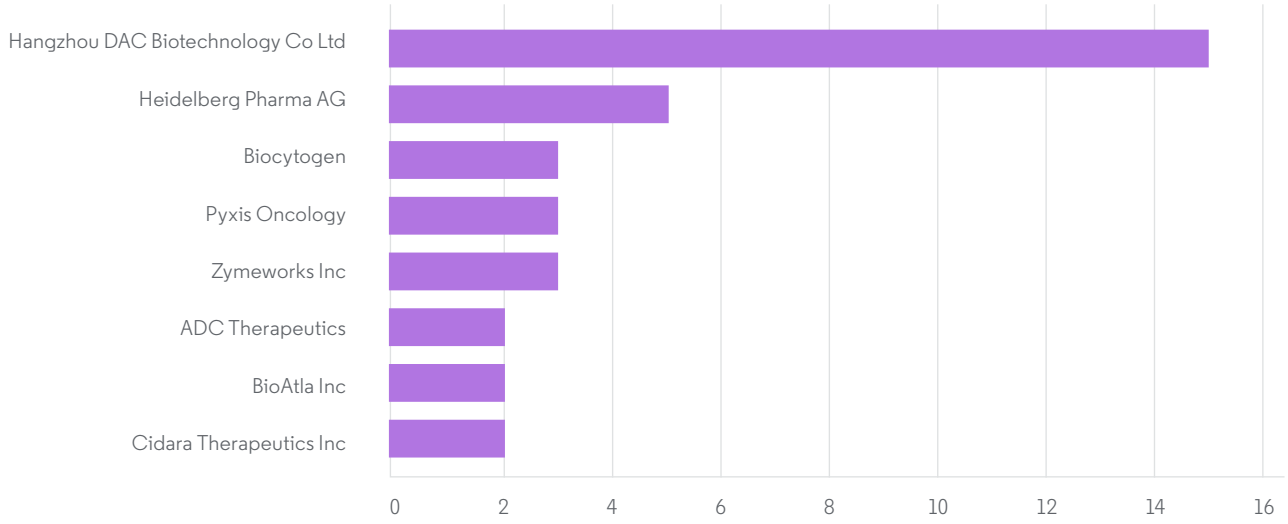
Figure 7: Most active companies/organizations with ADC assets in clinical trials



Source: Cortellis Clinical Trials Intelligence as of April 2024

A look at the companies with assets in preclinical development (Figure 8) highlights who could be moving into the clinical stage soon or who might have proven assets ready for out-licensing or acquisition.

Figure 8: Top companies with ADCs in active preclinical development



Source: Cortellis Drug Discovery Intelligence as of April 2024

Although cancer drugs have been the focus of most ADC research activity to date, 13 non-oncology ADC assets are being evaluated in clinical trials that started in the last 5 years according to Clarivate data. These trials cover the following indications: age-related macular degeneration (AMD), AL amyloidosis, Crohn's disease, diabetic macular edema, Duchenne muscular dystrophy, influenza, kidney disease, NASH, rheumatoid arthritis, scleroderma, familial amyotrophic lateral sclerosis and hepatitis B virus infection. Of these, Kodiak Sciences Inc's KSI-501 for AMD is the furthest along in development, with the phase 3 trial slated to start in June 2024.

Double-digit ADC approvals set the foundation for future regulatory decisions

With great potential to address unmet therapeutic needs, ADC therapies have gained traction.

From a slow start in the early 2010s, regulatory approvals have also accelerated over the past five years, helping to validate the promise of these therapies (Table 4). Despite being peppered with a few failures following initial accelerated approval, the regulatory environment for ADCs is looking up, with nine new approvals of drugs that remain available i.e., (have not been withdrawn) in the major markets since 2018.

Table 4: Approved ADCs across the major markets

ADC	Antigen, payload, linker, target	Company(s)	First approval date	Region(s) and country(s)	Indication(s)
MYLOTARG™ (gemtuzumab ozogamicin)	CD33, N-acetyl-γ-calicheamicin, AcButDMH (cleavable), DNA	Wyeth Pharmaceuticals LLC (acquired by Pfizer Inc in 2009)	May 2000	Australia, E.U., Japan, U.S.	Newly diagnosed and relapsed or refractory (R/R) CD33-positive acute myeloid leukemia (AML)
ADCETRIS® (brentuximab vedotin)	CD30, monomethyl auristatin E (MMAE), Mc-Val-Cit-PABC (cleavable), microtubule	Seagen Inc (acquired by Pfizer Inc in December 2023) and Millennium Pharmaceuticals Inc (acquired by Takeda Pharmaceutical Co Ltd in April 2008)	August 2011	E.U., Japan, Mainland China, U.S.	R/R Hodgkin lymphoma, systemic anaplastic large cell lymphoma (ALCL), primary cutaneous ALCL, CD30-expressing mycosis fungoides, T-cell lymphoma
KADCYLA® (ado-trastuzumab emtansine)	HER2, DM1, SMCC, microtubule	Genentech, a member of the Roche Group	February 2013	Australia, E.U., Japan, Mainland China, U.S.	Metastatic HER2-positive breast cancer
BESPONSA® (inotuzumab ozogamicin)	CD22, N-acetyl-γ-calicheamicin, AcButDMH (cleavable), DNA	Pfizer Inc	June 2017	E.U., Japan, Mainland China, U.S.	R/R acute lymphocytic leukemia (ALL)

ADC	Antigen, payload, linker, target	Company(s)	First approval date	Region(s) and country(s)	Indication(s)
LUMOXITI® (moxetumomab pasudotox)	CD22, PE38, Mc-Val-Cit-PABC (cleavable), EEF2K	AstraZeneca	September 2018	E.U., U.S. (withdrawn from both)	R/R hairy cell leukemia (HCL)
POLIVY® (polatuzumab vedotin)	CD79b, MMAE, Mc-Val-Cit-PABC (cleavable), microtubule	Genentech, a member of the Roche Group	June 2019	Australia, Canada, E.U., Japan, U.S.	R/R diffuse large B-cell lymphoma (DLBCL)
PADCEV® (enfortumab vedotin)	Nectin-4, MMAE, Mc-Val-Cit-PABC (cleavable), microtubule	Astellas Pharma Inc and Seagen Inc (now Pfizer Inc)	December 2019	E.U., Japan, U.S.	Locally advanced or metastatic urothelial cancer
ENHERTU® (fam-trastuzumab deruxtecan)	HER2, DX-8951 derivative (DXd), Mc-Gly-Gly-Phe-Gly (cleavable), DNA topoisomerase 1 (TOP1)	Daiichi Sankyo and AstraZeneca	December 2019	Australia, E.U., Japan, U.S.	Unresectable or metastatic HER2-positive and HER2-low breast cancer, unresectable or metastatic NSCLC, locally advanced or metastatic HER2-positive gastric or gastroesophageal junction adenocarcinoma
TRODELVY® (sacituzumab govitecan)	TROP2, SN-38, CL2A (cleavable), DNA TOP1	Immunomedics (acquired by Gilead Sciences Inc in September 2020)	April 2020	E.U., Mainland China, U.S.	Metastatic triple-negative breast cancer, locally advanced or metastatic urothelial cancer
BLENREP® (belantamab mafadotin)	B-cell maturation antigen (BCMA), monomethyl auristatin F (MEAF), maleimidocarpyl (not cleavable), microtubule	GSK	August 2020	E.U., U.S. (withdrawn from both)	R/R multiple myeloma
Akalux® (cetuximab sarotalocan)	EGFR, IRDye700DX, linear alkyl/alkoxy linker (not cleavable), not disclosed	Rakuten Medical Inc	September 2020	Japan	Unresectable locally advanced or recurrent head and neck cancer
ZYNLONTA® (loncastuximab tesirine)	CD19, SG3199, Mal-PEG8-Val-Ala-PABC (cleavable), DNA	ADC Therapeutics	April 2021	E.U., U.S.	R/R LBCL including DLBCL
Aidixi® (disitamab vedotin)	HER2. MMAE, Mc-Val-Cit-PABC (cleavable), microtubule	RemeGen Biosciences	June 2021	Mainland China	Locally advanced or metastatic gastric cancer
TIVDAK® (tisotumab vedotin)	Tissue factor, MMAE, Mc-Val-Cit-PABC (cleavable), microtubule	Seagen (acquired by Pfizer Inc in December 2023) and Genmab A/S	September 2021	U.S.	Recurrent or metastatic cervical cancer
ELAHERE® (mirvetuximab soravtansine)	FRα, maytansinoid DM4, sulfo-SPDB (cleavable), DNA	ImmunoGen (acquired by AbbVie in February 2024)	November 2022	U.S.	FRα-positive epithelial ovarian, fallopian tube or primary peritoneal adult cancer

Source: European Medicines Agency (EMA) website, U.S. Food & Drug Administration website, company websites

Looking to the future, new ADC candidates are currently moving through the regulatory process, with approvals expected within the next 12-18 months. Both the U.S. FDA and EMA accepted biologics license applications (BLAs) and marketing approval applications (MAAs), respectively, from Daiichi Sankyo and AstraZeneca in early 2024 for their ADC datopotamab deruxtecan (Dato-DXd).[6,7] Featured in Clarivate's Drugs to Watch 2024,[8] Data-DXd is under review for two indications: unresectable or metastatic hormone receptor (HR)-positive, HER2-negative breast cancer and locally advanced or metastatic NSCLC. The U.S. PDUFA dates are set for January 29, 2025, and December 20, 2024, respectively. Discovered by Daiichi Sankyo and jointly developed by Daiichi Sankyo and AstraZeneca, Dato-DXd could be the first TROP2-directed ADC for lung cancer and second to market, after TRODELVY, for HR-positive/ HER2-negative breast cancer. It is one of six ADCs developed with Daiichi Sankyo's DXd ADC technology and the most advanced in AstraZeneca's ADC portfolio. The regulatory applications included data from the Tropion-Breast01 and Tropion-Lung01 phase 3 trials that demonstrated significant improvements in progression-free survival (PFS) over chemotherapy.

The BLA for the ADC patritumab deruxtecan, which was also developed by Daiichi Sankyo, was accepted by the U.S. FDA for priority review with a PDUFA date of June 26, 2024, as announced Daiichi Sankyo and its development and commercialization partner MSD in December 2023.[9] The FDA previously granted Breakthrough Therapy Designation in December 2021. The companies submitted the BLA for the HER3-directed DXd ADC to treat locally advanced or metastatic EGFR-mutated NSCLC based on results from the pivotal phase 2 HERTHENA-Lung01 trial.

On another note, after failing to meet the dual primary endpoint of PFS compared with docetaxel in the phase 3 Carmen-LC03 trial,[10] Sanofi ended its program for the ADC tusamitamab ravtansine. This is despite the trend for improved overall survival (OS), the other primary endpoint. The drug was being evaluated as monotherapy in second-line treatment of metastatic NSCLC, and the company had anticipated submitting marketing applications in 2024 but will continue exploring the potential of other tusamitimab-based ADCs.

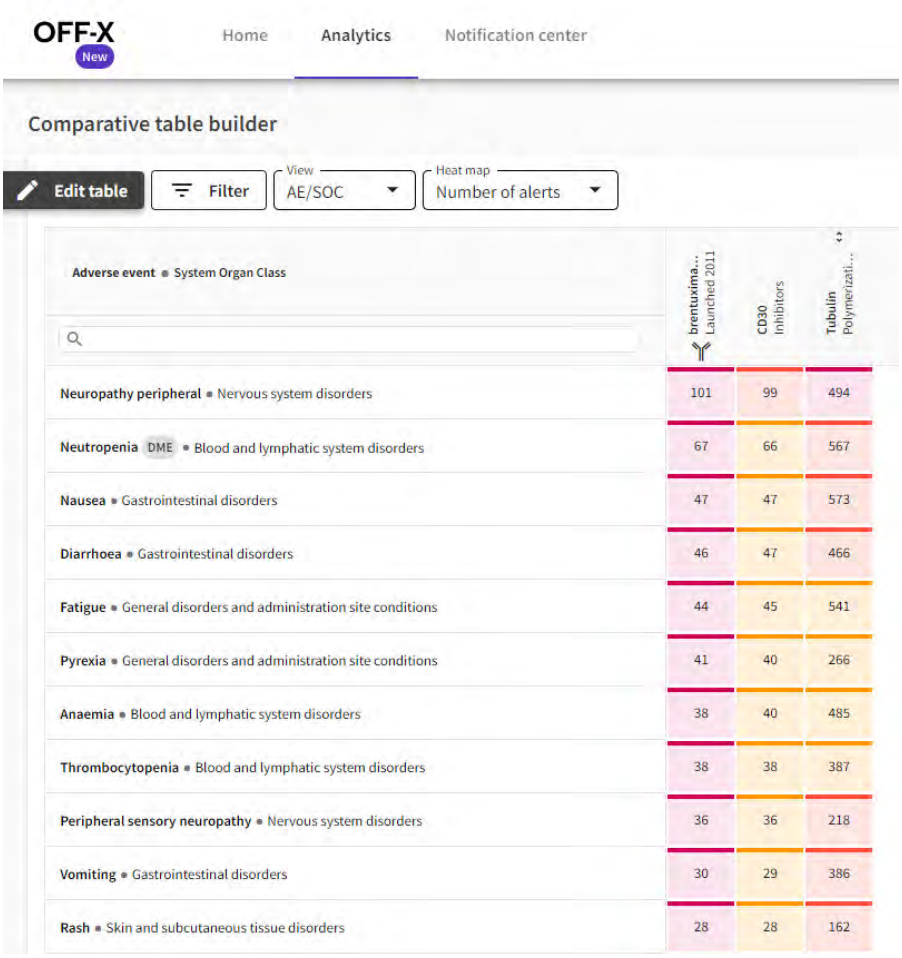
As more companies enter the fray of ADC development, regulatory agencies have taken notice.

As more companies enter the fray of ADC development, regulatory agencies have taken notice and have developed recommendations using their previous experience approving, and withdrawing approval for, ADCs. The U.S. FDA issued its guidance on clinical pharmacology considerations for ADCs with a small molecule payload in March 2024.[11] The document emphasizes the importance of considering the independent impact of an ADC's constituent parts on safety and efficacy, with a particular focus on bioanalytical methods, dosing strategies, dose- and exposure-response analyses, intrinsic factors, QTc assessments, immunogenicity and drug-drug interactions. Importantly, the agency recommends early planning in preclinical development, from which data could inform study design in later stages, particularly around specific safety monitoring needs.

Gathering intelligence about previous ADCs, both successful and failed, early in a program facilitates appropriate planning (Figures 9 and 10), by helping to:

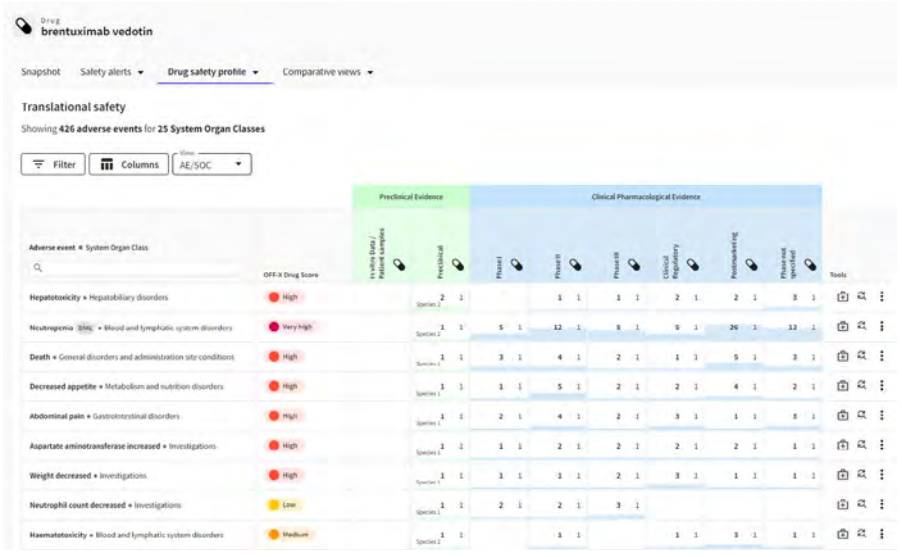
- Identify the toxicities that could be associated specifically with the antibody and specifically with the payload,
- Benchmark the candidate ADC's safety against other antibodies (bispecific, polyspecific, ADCs),
- Anticipate the safety of a novel ADC based on the target and payload,
- Predict the candidate ADC's safety when administered in combination with other drugs and
- Assess the correlations between preclinical findings with clinical findings.

Figure 9: Comparison of ADC-related adverse events within a system organ class



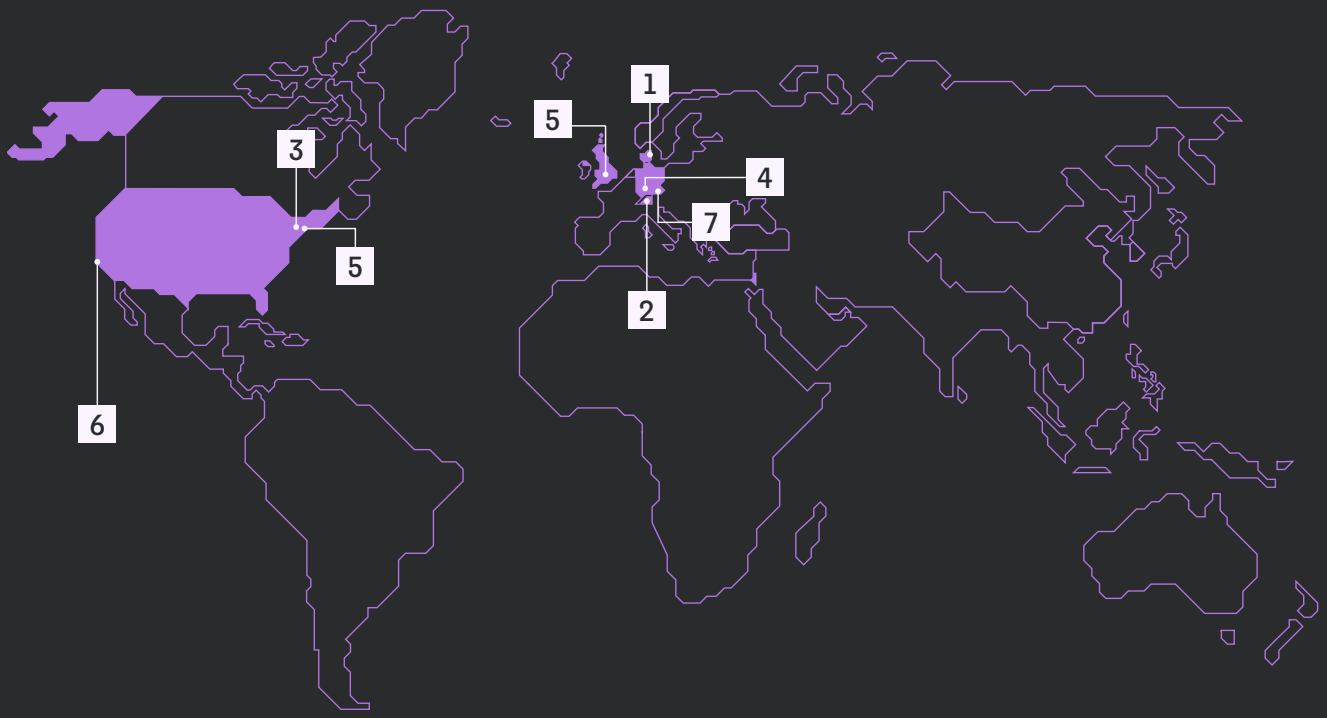
Source: OFF-X™

Figure 10: Evaluating the safety profile of a candidate ADC



Source: OFF-X™

Companies to watch



1. Adcendo ApS
Copenhagen, Denmark
Niels Behrendt, Lars Engelholm, Christoffer Nielsen, Henrik Stage

2.Araris Biotech AG
Zurich, Switzerland
Dragan Grabulovski, Philipp Spycher, Isabella Attinger-Toller, Martin Behe, Roger Schibli

3. GO Therapeutics
Cambridge, MA
Constantine Theodoropulos, Hans Wandall

4. Heidelberg Pharma AG
Ladenburg, Germany
Emerged from two companies

5. Pheon Therapeutics
London, UK; Boston, MA
David Thurston, Paul Jackson

6. Tallac Therapeutics Inc
Burlingame, CA
Hong Wan, Corey Goodman, Jaume Pons, Curt Bradshaw

7. Tubulis
Planegg-Martinsried, Germany
Dominik Schumacher, Jonas Helma-Smets, Ingo Lehrke, Christian Hackenberger, Heinrich Leonardt

Adcendo ApS

Adcendo ApS was established as a spin-out of The Finsen Laboratory at University of Copenhagen and Rigshospitalet in Copenhagen, Denmark, then incubated at the BioInnovation Institute (BII) before closing its series A in 2021.

The company aims to develop breakthrough ADCs to treat underserved cancers. The first-in-class (FIC) lead program targets the uPARAP receptor, which is overexpressed by several mesenchymal cancers, including soft tissue sarcoma (STS), bone sarcoma, gastrointestinal stromal tumors (GIST) and mesothelioma. The uPARAP receptor is also highly expressed by certain cells of the stromal component of many epithelial cancers, potentially broadening the application of uPARAP-targeted ADCs.

Company profile

Founded: **2017**

Founders: **Niels Behrendt, Lars Engelholm, Christoffer Nielsen, Henrik Stage**

Headquarters: **Copenhagen, Denmark**

Investors

- Gilde Healthcare
- HealthCap
- Novo Holdings
- Pontifax Venture Capital
- RA Capital Management
- Ysios Capital

Partners

Academic

Finsen Laboratory, Rigshospitalet, University of Copenhagen
Joint research on the expression of the ADC target uPARAP and the in vitro and in vivo activity of a uPARAP-targeting ADC in various indications

Laboratory of Experimental Oncology at KU Leuven/Leuven Cancer Institute
Joint research on the expression of the novel ADC target uPARAP in STS and bone sarcoma

Corporate

Duality Biologics
License agreement for Adcendo to use Duality Biologics' proprietary DITAC (Duality Immune Toxin Antibody Conjugates) linker/payload platform for its lead uPARAP-ADC program in mesenchymal cancers and nominate ADCs against additional novel ADC targets

What makes this company stand out?

- The company has attracted an international, highly experienced management team and a first-tier investor syndicate, allowing it to move its lead candidate forward and further build out its ADC pipeline focusing on FIC targets and assets.
- The company has partnered with leading next-gen ADC technology providers to enable optimal composition of its development candidate ADCs.
- STS is the target of the lead program, which is expected to have first patient dosed by the end of 2024.
- A second pipeline asset will move to candidate nomination and pre-IND work in mid-2024, and additional assets are at the research stage.

How will the company's platform benefit patients and their caregivers?

- Adcendo aims to become a powerhouse at developing FIC ADCs that address cancer indications with high unmet needs.
- The company's vision is to ultimately replace conventional chemotherapy with a targeted, personalized treatment strategy that has fewer side effects.

Funding and grants

April 2023: Series A extension funding (€31m), led by Pontifax Venture Capital, Novo Holdings and Ysios Capital, with participation by RA Capital Management, HealthCap and Gilde Healthcare

April 2021: Series A funding (€51m), led by Novo Seeds, the early-stage investment and company creation team of Novo Holdings, and Ysios Capital, with participation by Glide Healthcare, HealthCap and RA Capital Management

IP status and patent filings

- Non-disclosed

R&D activity

- In vivo proof-of-concept data have been generated with the company's lead uPARAP ADC asset in multiple target indications with multiple payload (MoA), counting both CDX as well as PDX models. The program is currently at the IND submission stage.
- The company aims to initiate its first clinical study with a uPARAP-targeted ADC in STS by the end of 2024.
- The company also plans to nominate a development candidate in their second program targeting an FIC target in epithelial cancers by mid-2024.
- Additional FIC ADC targets and assets are in non-clinical development.

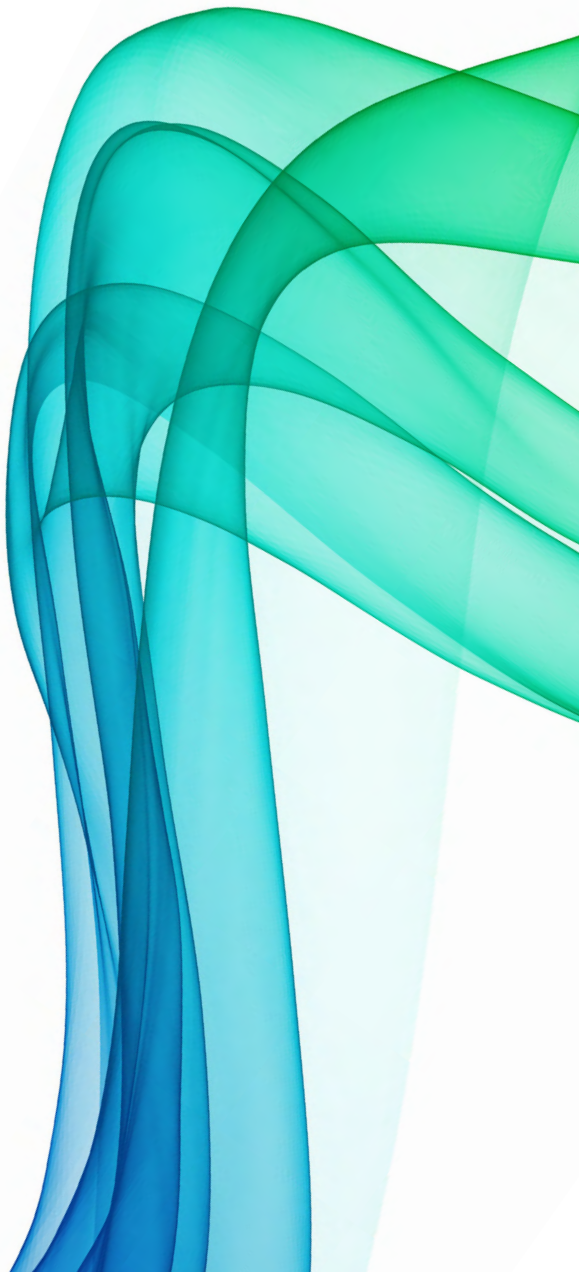
"We believe ADCs are at the forefront of innovation in the oncology space and that we will be looking at a change in treatment paradigms as next-gen ADC technologies and assets continue to advance through clinical testing phases. Adcendo seeks to fuel and be part of this change by developing first-in-class ADCs, providing cancer patients in high unmet need indications with novel and better treatment options."

Michael Pehl,
Adcendo ApS CEO.

Araris Biotech AG

Founded as a spin-out from ETH Zurich and the Paul-Scherrer-Institute, Araris Biotech uses its proprietary conjugation technology and linker-payload platforms to efficiently develop and advance next-generation ADCs, with a focus on cancers.

With its proprietary ADC linker technology, Araris' drug attachment is simple (i.e., one step), is site-specific and has the potential to stably accommodate various drug-load combinations without altering the pharmacokinetic profile of the antibody, resulting in ADCs with a high therapeutic window. The company is interested in partnering with pharma companies to use its conjugation technology and linker-payload platforms to generate novel, next-generation ADCs against partner-provided targets.



Company profile

Founded: **2019**

Founders: **Dragan Grabulovski, Philipp Spycher, Isabella Attinger-Toller, Martin Behe, Roger Schibli**

Headquarters: **Au (ZH), Zurich, Switzerland**

Investors

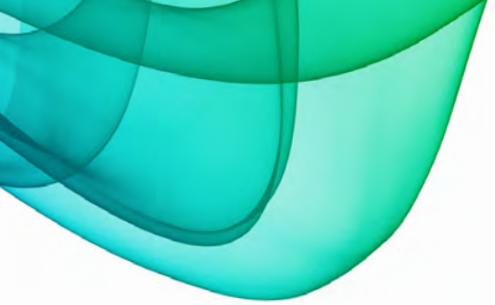
- 4BIO Capital
- Pureos Bioventures
- VI Partners
- Redalpine
- Samsung Ventures
- Schroder Adveq
- btov Partners
- Institute for Follicular Lymphoma Innovation
- Wille Finance

Partners

Academic	Corporate
ETH Zurich	Taiho Pharmaceutical Co Collaboration for Araris to use its proprietary linker-conjugation platform to generate novel ADCs against undisclosed targets provided by Taiho Pharmaceutical Co
Paul-Scherrer-Institute	
Ongoing relationship after the company was spun out	

What makes this company stand out?

- Araris' ADC technology for ready-to-use antibodies enables a one-step, easy-to-use method to efficiently conjugate payloads to any off-the-shelf antibody in a site-specific manner, without the need to engineer the antibody, at drug-to-antibody ratios (DARs) of up to 8 without the use of solubility-enhancing moieties like polyethylene glycol (PEG).
- Araris is pioneering the development of ADCs carrying dual or triple payloads with different MoAs to overcome cancer resistance and heterogeneity.
- In preclinical studies to date, Araris' ADCs have demonstrated excellent stability and biophysical properties, with no payload loss, linker cleavage or deconjugation in the blood stream, helping to maximize payload delivery to tumors.
- In head-to-head animal model studies against multiple ADCs, the next-generation ADCs created using Araris' ADC technology demonstrated improved efficacy, even at low doses, as well as excellent tolerability, resulting in a significant improvement in therapeutic index.



How will the company's platform benefit patients and their caregivers?

- Araris' technology allows the company to generate ADCs that have the potential to be more efficacious with less toxicity than current ADC treatments for patients with various cancers.

Funding and grants

May 2023: Accelerator grant funding (CHF 2.5m) from Innosuisse

April 2023: Independent funding (non-disclosed amount) via the Samsung Life Science Fund, jointly created by Samsung Biologics and Samsung C&T and managed by Samsung Venture Investment Corporation

October 2022: Series A funding (U.S. $24m) led by 4BIO Capital and Pureos Bioventures, with participation from Redalpine, Schroder Adveq, VI Partners, btov Partners, the Institute for Follicular Lymphoma Innovation and Wille AG

October 2020: Completion of seed funding (CHF 12.7m), led by Pureos Bioventures with participation from 4BIO Capital, btov Partners, Redalpine, Schroder Adveq and VI Partners

August 2019: Seed funding (CHF 2.5m), with participation by Redalpine, Schroder Adveq and VI Partners

June 2019: Venture Kick award (CHF 130,000)

IP status and patent filings

- Araris Biotech has filed several patents broadly covering the technology and ADC assets.
- Several patents have been granted in key markets.

R&D activity

- The company's pipeline of ADCs is currently in preclinical studies.
- Several ADCs have been characterized up to non-human primates (NHPs).
- Preclinical data were presented by the company in Q1 2023 on a novel ADC targeting nectin-4 with MMAE as the payload and in Q1 2024 on two novel dual TOP inhibitor (TOP1i) ADCs generated using two TOP1i payloads targeting HER2 and NaPi2b.

"We believe we're at the forefront of unlocking the full potential of ADCs and their impact on patients with a variety of cancers. Our ADC conjugation technology and linker-payload platforms have allowed us to efficiently generate ADCs that have demonstrated significantly improved efficacy and safety compared to multiple FDA-approved ADCs in preclinical studies to date. We look forward to continuing to advance our pipeline of next-generation ADCs that can deliver multiple drug payloads against solid tumors."

Philipp Spycher, PhD;
Araris Biotech CSO and founder.

GO Therapeutics

Using new advances in glycoproteomics, GO Therapeutics uses a platform-based approach to developing antibody-based therapies against clean glycoprotein cancer targets.

With this approach, the company is developing novel, multimodal FIC cancer therapeutics against intractable targets.

Company profile

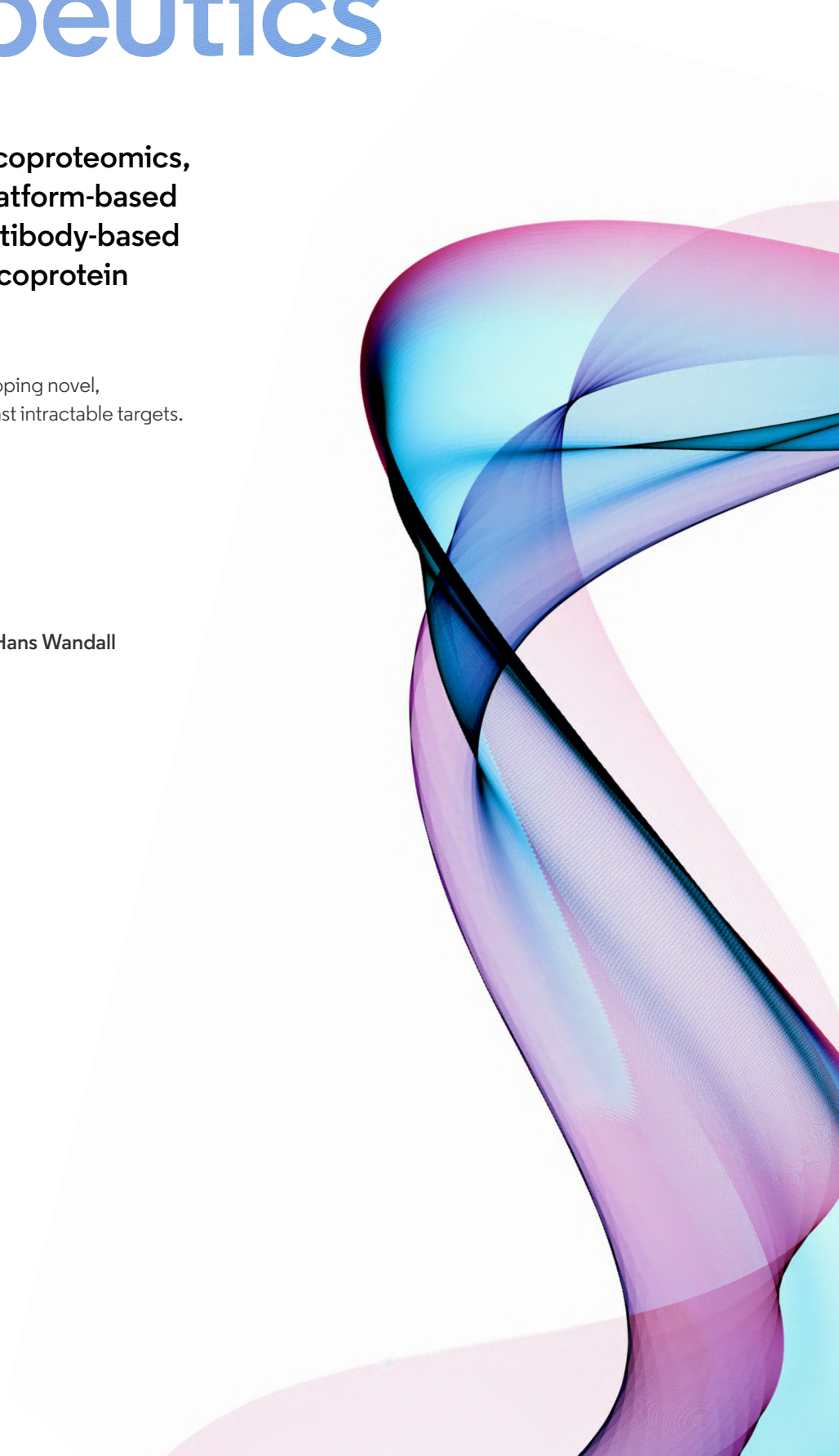
Founded: **2014**

Founders: **Constantine Theodoropulos, Hans Wandall**

Headquarters: **Cambridge, MA**

Investors

- Salubris Pharmaceutical Limited



Partners

Academic

University of Copenhagen

University of Pennsylvania

Joint research of a CAR-T targeting a cancer-specific glycoprotein on CD44v6 expressed on multiple solid tumors

Corporate

Xyphos Biosciences Inc, subsidiary of Astellas Pharma Inc
Strategic research collaboration and license agreement to develop novel immuno-oncology therapeutics with high affinity to two different glycoprotein targets and apply these antibodies to a range of therapeutic modalities

Roche
License agreement to develop and commercialize a new glyco-targeting bispecific antibody

What makes this company stand out?

- O-glycoproteins with truncated O-glycans are absent from normal tissues but are present in 60-80% of human epithelial cancers, which makes them viable therapeutic targets.
- The company has mapped the expression of truncated O-glycans in >700 tissue cores representing healthy and tumor tissues, showing that surface expression of truncated O-glycans is limited to cancers of epithelial origin, making the cancer-associated truncated O-glycans Tn and STn attractive immunological targets to treat human carcinomas.
- Based on this information, GO Therapeutics is developing a new class of cancer-specific, potent, broad-spectrum therapies, both wholly owned and in collaboration with biopharma partners.
- The company's pipeline includes the ADCs GO-13C3, GO-8H3, GO-STn and GO-C15 against solid tumors and the ECM, as well as multiple early-stage T-cell bispecific (TCB), CAR-T cell and immunokine therapies for solid tumors.

How will the company's platform benefit patients and their caregivers?

- The company's 'super clean' tumor targets have the potential to produce cancer treatments with a greater therapeutic index, increasing the efficacy of immunotherapies with less damage to healthy tissues.
- Selectively targeting O-glycoproteins could deliver more treatments for patients with many different types of cancer.
- GO Therapeutics pursues partnerships that utilize its platform approach to get treatments to patients faster.

Funding and grants

September 2017: Independent funding (U.S.$5m) from Salubris Pharmaceutical Limited

IP status and patent filings

- GO Therapeutics wholly owns eight patent families that have counterparts in at least the United States, Europe, Japan, Mainland China, South Korea, Australia and Canada.
- The company co-owns an, as yet, unpublished patent family.

R&D activity

- GO Therapeutics continues to discover novel glycoprotein targets/antibodies that are the framework for novel ADCs and cell therapies, five of which are in IND-enabling studies as of the start of 2024.

"The frustrating clinical reality is that the possibility of potent and potentially curative cancer therapies is being held back by a lack of suitable targets. GO is mining a rich domain of glycoprotein targets for super clean, novel targets that will unleash the next wave of cancer therapies. GO-based ADCs have the potential to achieve complete responses without debilitating on- and off-target toxicities."

Constantine Theodoropulos,
GO Therapeutics CEO and co-founder.

Heidelberg Pharma AG

Heidelberg Pharma uses its proprietary ADC payload technology (ATAC® technology) to develop ADCs called ATACs that have amanitin-based compounds as the payload.

The company is the first worldwide to make amanitin (a member of the amatoxin group of natural poisons occurring in the death cap mushroom *[Amanita phalloides]*) available for cancer therapy. Amanitin has a unique biological MoA that works by inhibiting RNA polymerase II, which results in apoptosis.

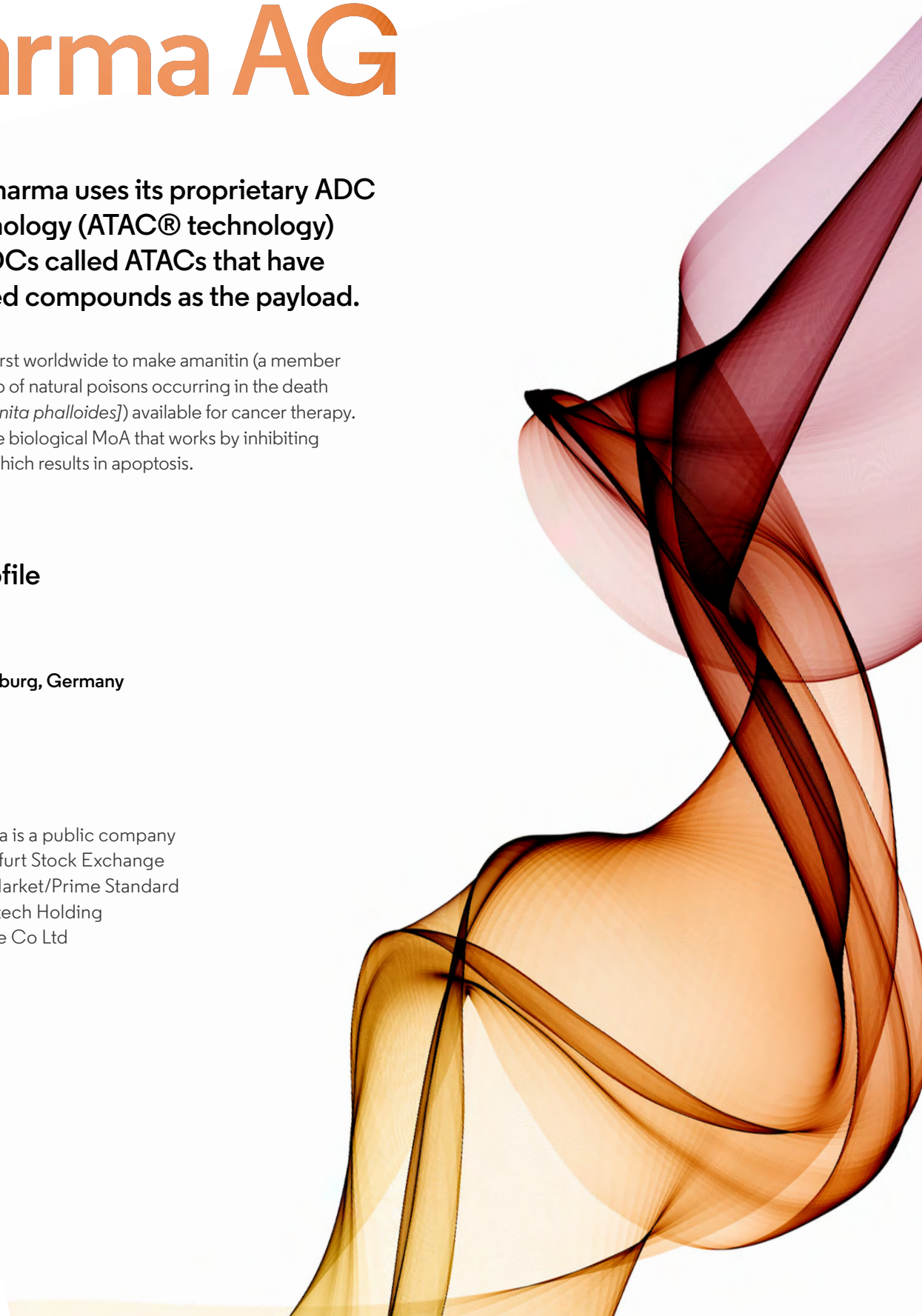
Company profile

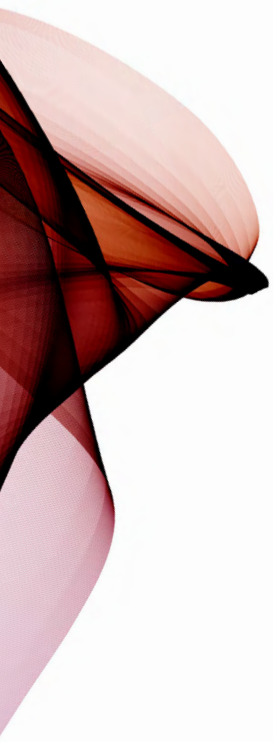
Founded: **2014**

Headquarters: **Ladenburg, Germany**

Investors

- Heidelberg Pharma is a public company listed on the Frankfurt Stock Exchange in the Regulated Market/Prime Standard
- Dietmar Hopp Biotech Holding
- Huadong Medicine Co Ltd
- Freefloat





Partners

Academic

Université de Strasbourg
EU-funded TACT project, a research program designed to train 11 early-stage researchers in the field of anti-cancer therapeutics, specifically ADCs, creating a new generation of experts

University of Münster
pHioniC program, an innovative training network on the role of pH and ion transport proteins in pancreatic cancer

Universita Degli Studi di Genova
NTEGRATA consortium, which aims to develop new NAD biosynthesis and NAD/nucleotide signaling inhibitors, assess pharmacology and toxicity of new therapeutics in preclinical models and develop a proof-of-concept of newly generated agents in relevant in vivo cancer models

Binghamton University, State University of New York
Research and exclusive option agreement related to a novel, proprietary immunostimulatory technology platform that includes potent novel immunostimulatory compounds and ADC technology for the specific delivery of these compounds to tumor tissue

Max Delbrück Center for Molecular Medicine in the Helmholtz Association
Option agreement covering various BCMA antibodies

Freiburg University
Licensing agreement for several prostate-specific membrane antigen (PSMA)-specific antibodies from the university

School of Medicine at Indiana University

Heidelberg University Hospital

MD Anderson Cancer Center at the University of Texas

Joint preclinical research of amanitin against tumors with a 17p deletion

Corporate

HealthCare Royalty
Royalty purchase agreement (HCRx) for the sale of a portion of future royalties from global sales of Zircaix® (TLX250-CDx, 89Zr-DFO-girentuximab), a radiopharmaceutical positron emission tomography (PET) imaging agent to diagnose and manage clear cell carcinomas

Huadong Medicine Co Ltd
Exclusive licensing agreement to develop and commercialize HDP-101 and HDP-103 in several Asian countries (excluding Japan) plus exclusive opt-in rights for two more pipeline candidates

Takeda Pharmaceutical Company Ltd
Exclusive research agreement to develop ADCs that use amanitin as payload using antibodies from Takeda Pharmaceutical's proprietary portfolio

RedHill Biopharma Ltd
License agreement for upamostat (RHB-107), an oral uPA/serine protease inhibitor against tumors, for the rest of the world

Telix Pharmaceuticals Limited
License agreement for the diagnostic antibody TLX250-CDx, a radiolabeled form of the antibody girentuximab, for renal cell carcinoma (Zircaix)

License agreement for the therapeutic radioimmunoconjugate (177Lu-DOTA-girentuximab, TLX250) program based on the lutetium-177-labeled girentuximab antibody

What makes this company stand out?

- Heidelberg Pharma AG, in its current form as an ADC developer, emerged in 2014 from WILEX AG and Heidelberg Pharma Research GmbH. WILEX AG was a biopharma company focused on oncology and antibodies, while Heidelberg Pharma Research GmbH focused on the development of ADC technologies.

- Years of development have resulted in Heidelberg Pharma's proprietary ATAC technology, from which it produces its ATAC ADCs with amanitin as the payload.

- Compared with amanitin, which acts to ultimately induce apoptosis, chemotherapy drugs, including other ADCs, developed to date either function as 'spindle poisons' (tubulin inhibitors) or via binding to DNA, which makes them dependent on cell division. RNA polymerase II inhibition makes it possible to break through drug resistance and kill both dividing and dormant tumor cells. The latter cells are typically not affected by current chemotherapy drugs nor ADCs and are known to drive tumor re-growth and metastasis.

- The company's proprietary ATACs include its lead clinical candidate HDP-101, a BCMA-ATAC for R/R multiple myeloma; HDP-102, a CD37-targeting ATAC for non-Hodgkin lymphoma; and HDP-103, an ATAC for prostate cancer.

- Investigations into the effects of the route of administration (subcutaneous [SC] versus intravenous) on the pharmacokinetics, tolerability and efficacy of different ATACs have shown that SC dosing not only refined the pharmacokinetic profile of ATACs but also could improve the therapeutic index. ATACs appear to be the only ADCs with the potential for SC administration due to the unique physicochemical properties of amanitin; other ADCs based on currently available payloads lead to severe local reactions that limit the use of SC administration.

- Preclinical testing of ATACs has shown high efficacy, even against quiescent tumor cells, and the ability to overcome frequently encountered resistance mechanisms.

- The company develops candidates within its own development portfolio up to early clinical phases to demonstrate their applicability and efficacy in patients.

- HDP-101 is one of the molecules produced, optimized and preclinically validated by the company based on a license with Max Delbrück Center for Molecular Medicine in the Helmholtz Association (MDC) for BCMA-specific antibodies.

- When Heidelberg Pharma licenses its technology platform to other pharmaceutical companies to develop their own ATACs, the partner provides specific antibodies to couple with amanitin and conducts the entire preclinical and clinical ATAC development.

- The company has demonstrated its ability to take a candidate into clinical testing, after which licensing partners can successfully reach regulatory submission and approval.

- Heidelberg Pharma is also working with another ADC technology platform using the payload exatecan, a TOPO1i.

- The company expects 2024 to be a transformative year following its successful business performance in 2023 and progression of its lead product candidate, HDP-101, in a first-in-human (FIH) phase 1/2a clinical trial for the treatment of R/R multiple myeloma.

How will the company's platform benefit patients and their caregivers?

- Heidelberg Pharma's ADC technology offers treatment options with a more favorable therapeutic index and potentially fewer side effects.
- Multiple myeloma, the target of the company's lead candidate, is the most common type of bone and bone marrow cancer and has a major unmet need for effective, safe therapies.
- The better pharmacokinetic distribution and improved therapeutic index of ATACs via SC dosing (compared with intravenous dosing) could provide patients with a less burdensome mode of administration than currently marketed ADCs.

Funding and grants

February 2022: Equity funding (€80m) from Huadong Medicine Co Ltd

June 2021: Capital increase (€20m)

April 2020: Capital increase (€14.4m)

September 2019: Research grant from the E.U. for the European Training Network (ETN) MAGICBULLET project

IP status and patent filings

The company has >500 granted and pending patents, including those covering:

- Site-specific ATAC conjugates comprising a genetically engineered antibody to which Heidelberg Pharma's proprietary amatoxin payloads can be coupled via specific linkers (E.U., U.S.)
- Diagnosis and treatment of patients with RNA polymerase II deletion exclusively in-licensed from the University of Texas System, on behalf of MD Anderson Cancer Center (U.S.)
- Chemical synthesis of an important synthetic building block of alpha-amanitin and amanitin derivatives (E.U.)

R&D activity

- Heidelberg Pharma's ongoing phase 1/2a clinical trial of HDP-101 is progressing into Cohort 6.
- HDP-101 was granted orphan drug designation by the FDA for the treatment of R/R multiple myeloma in March 2024.
- HDP-102 and HDP-103 are in the preclinical stage.
- The company also has a research program underway: HDP-201 targeting gastrointestinal tumors.
- Preclinical testing has shown the following:
  - Synergy when combining ATACs with immune checkpoint inhibitors
  - ATAC-induced immunogenic cell death, leading to activation of the immune system
  - Superior activity and complete remission of the tumor after a low single-dose administration in a comparison of HER2-ATAC against the ADC ENHERTU
  - Better tolerability without compromising efficacy after repeated treatment with ATACs, which could indicate an optimized treatment regimen in real-world use and support the clinical success of ATACs
  - High effectiveness of amanitin against tumors with a 17p deletion

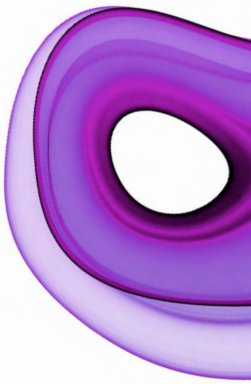
"Our payload is different. It has a mode of action never used in cancer therapy, and it works in a truly cell-cycle independent manner, meaning it is equally potent against both dividing and dormant tumor cells. We aim to not only debulk the tumor but also kill the cancer stem cells that largely evade current therapies and are known to drive tumor relapse and metastasis. This approach has the potential to achieve deeper and more durable responses in the clinic, and hopefully even complete cures."

Professor Andreas Pahl,
CEO Heidelberg Pharma.

Pheon Therapeutics

Pheon Therapeutics aims to extend the benefit of ADCs to more patients through novel oncology targets and proprietary linker-payload technologies.

The company's methodical approach to ADC development leverages its suite of in-house and in-licensed technology platforms to generate ADC constructs that are optimized for safety and efficacy for each target to treat a wide range of hard-to-treat cancers. Backed by robust preclinical data, its lead program for solid tumors, PHN-010, will enter the clinical stage in 2024.

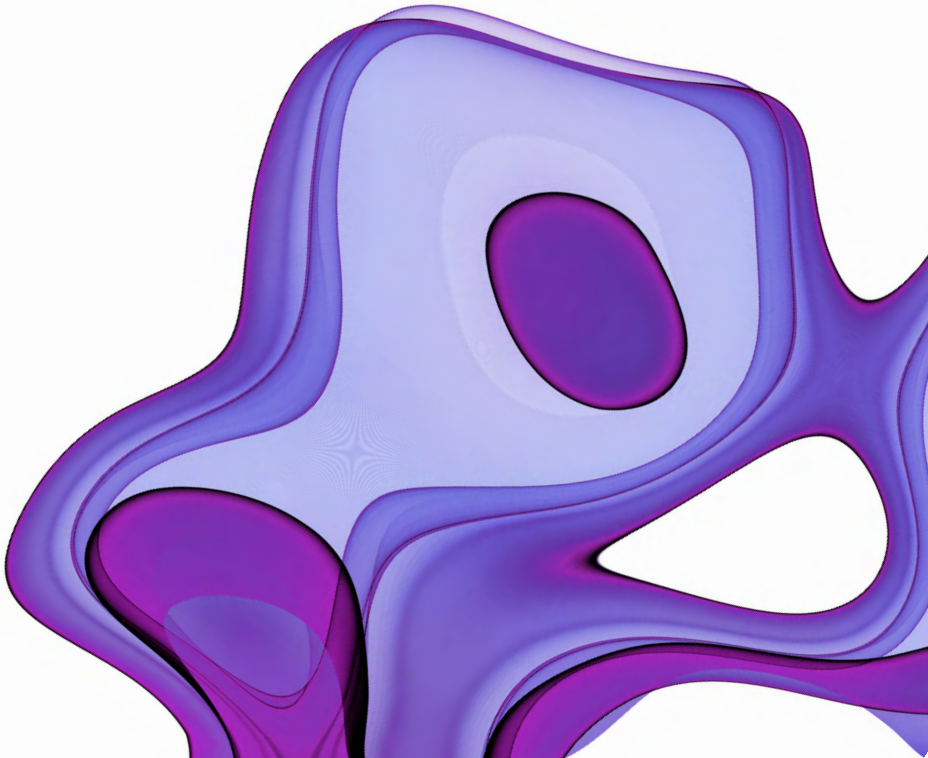


Company profile

Founded: **2015**

Founders: **David Thurston, Paul Jackson**

Headquarters: **London, UK and Boston, MA**



Investors

- Atlas Venture
- Brandon Capital
- Forbion
- Research Corporation Technologies (RCT)

Partners

Academic	Corporate
Non-disclosed	**Biocytogen Pharmaceuticals (Beijing) Co Ltd** Partnership agreement in which Pheon will develop and commercialize an ADC based on an antibody developed using Biocytogen Pharmaceutials' proprietary RenMice™ platform

What makes this company stand out?

- The company expects 2024 to be a transformative year as it becomes a clinical-stage company.
- Its ADC constructs use both novel and clinically validated mAbs in combination with payloads from its proprietary platform or off-the-shelf linker-payloads.
- The company's first three programs are based on a novel target that is broadly overexpressed in multiple solid tumor types.
- PHN-010, its lead candidate entering clinical trials in 2024, is based on this exceptional, novel pan-tumor target and a proprietary DAR8 TOP1i linker-payload with an unprecedented preclinical therapeutic index.

How will the company's platform benefit patients and their caregivers?

- The company's approach to ADC development, including pairing of novel oncology targets and proprietary linker-payload technologies, has the potential to provide treatment options with better efficacy and tolerability for patients with solid tumors.

Funding and grants

May 2024: Series B funding (U.S.$120m), led by TCGX with participation from BVF Partners, Lightspeed, Perceptive Advisors, Atlas Venture, Brandon Capital, Forbion and Research Corporation Technologies (RCT)

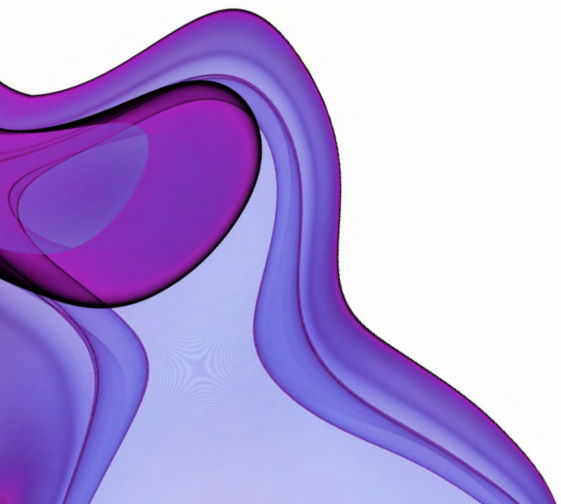
September 2022: Series A funding (U.S.$68m), led by Brandon Capital, Forbion and Atlas Venture, with participation from RCT

IP status and patent filings

- Pheon's broad suite of intellectual property covers its foundational technology platforms as well as whole ADCs and their components.

R&D activity

- Preclinical data for the company's lead program, PHN-010, have demonstrated in vivo efficacy, NHP safety and extensive expression profiling of the target in tumors and healthy tissue.
- Additional programs for solid tumors are undergoing preclinical evaluation.



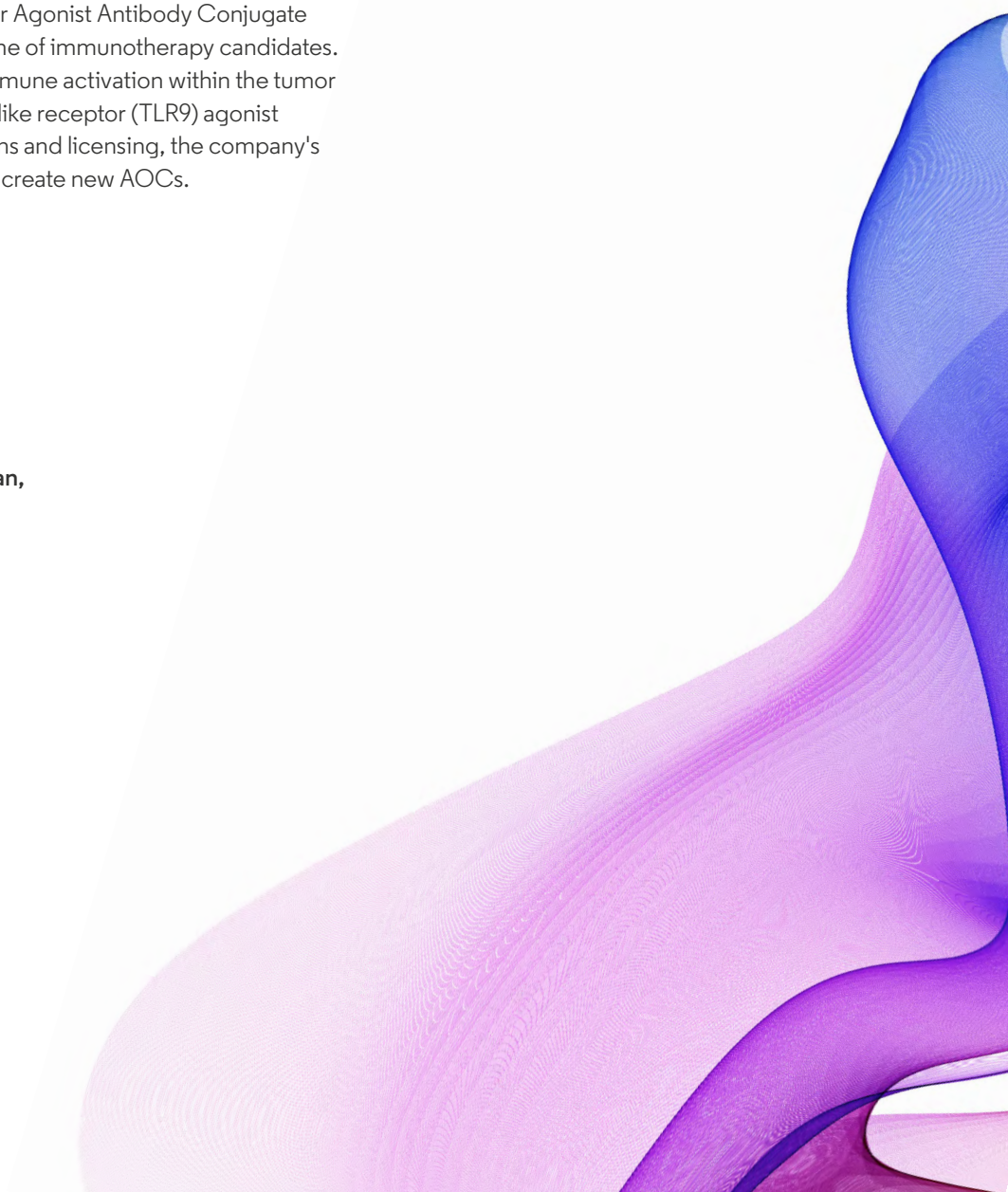
"Pheon is well poised to make unique contributions to the increasingly important field of antibody-drug conjugates for the treatment of solid tumors. We believe innovation drives differentiation. We are not looking for marginal improvements in patient outcomes, but rather leaps in efficacy and safety that are deeply meaningful for patients and their loved ones."

Cyrus Mozayeni, MD;
Pheon Therapeutics CEO.

Tallac Therapeutics Inc

Tallac Therapeutics' next-generation ADC technology uses novel oligonucleotide payloads to create antibody-oligonucleotide conjugates (AOCs) that extend the therapeutic mechanism beyond cytotoxic agents.

The company's novel Toll-like Receptor Agonist Antibody Conjugate (TRAAC) platform underpins its pipeline of immunotherapy candidates. These candidates provide targeted immune activation within the tumor microenvironment using a potent Toll-like receptor (TLR9) agonist (T-CpG). Open to clinical collaborations and licensing, the company's platform is also available to partners to create new AOCs.



Company profile

Founded: **2020**

Founders: **Hong Wan, Corey Goodman, Jaume Pons, Curt Bradshaw**

Headquarters: **Burlingame, CA**

Investors

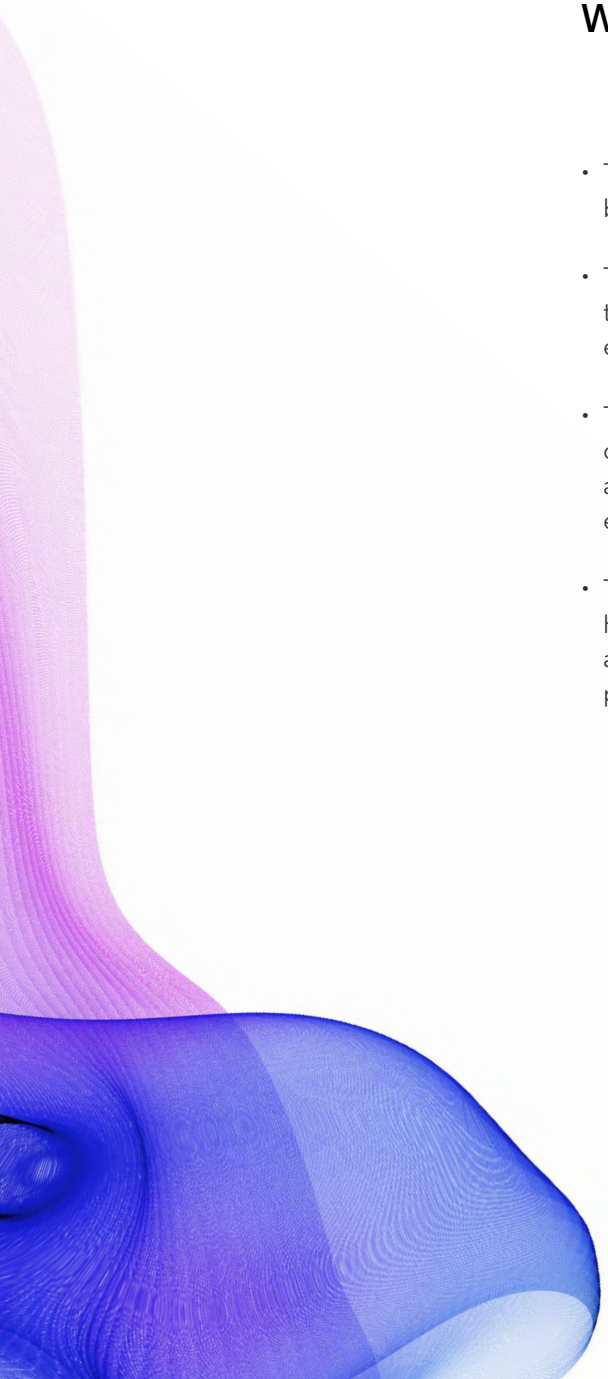
- Lightstone Ventures
- Matrix Partners China
- Merck
- Morningside Venture
- venBio Partners

Partners

Academic	Corporate
Non-disclosed	ALX Oncology Co-developing Tallac Therapeutics' second program, ALTA-002 (SIRPα TRAAC), against solid tumors

What makes this company stand out?

- The company's founders and team have significant biologics discovery and development expertise.
- Tallac Therapeutics is one of a few companies to successfully develop AOCs and is the first to enter the clinic with an AOC for oncology.
- The company's TRAAC platform utilizes site-specific conjugation, allowing precise control of the positioning and number of conjugated T-CpG molecules and enabling fine tuning of the conjugate activity.
- The company's most advanced program, TAC-001, has demonstrated immune cell activation, single-agent activity and a generally well-tolerated safety profile in the phase 1 study for solid tumors.



How will the company's platform benefit patients and their caregivers?

- Tallac's AOC molecules, with an immune agonist payload, could provide precision medicines with less toxicity and a more durable therapeutic profile in the oncology setting.
- The demonstrated single-agent clinical activity of TAC-001 for patients with melanoma that is resistant to or who have relapsed with standard of care therapies (PD-1 and CTLA inhibitors) could signal significant clinical benefit for these patients who have limited treatment options.

Funding and grants

December 2020: Series A funding (U.S. $62m), with participation from venBio Partners, Morningside Venture, Lightstone Ventures, Matrix Partners China and MRL Ventures Fund

IP status and patent filings

- The company has established and pending patents covering each aspect of its core technology platform (linker/site-specific conjugation and novel oligonucleotide payloads), as well as COM for the product candidates derived from the platform.

R&D activity

- TAC-001 (B cell activation via CD22 TLR9 agonist) is currently in phase 1 for solid tumors.
- Preclinical data have demonstrated that TAC-001, in combination with cancer vaccines, greatly improves anti-tumor vaccine efficacy.
- ALTA-002 (targeting tumors and dendritic cells via SIRPα TLR9 agonist), the company's second program, will be entering FIH studies in 2024.
- TAC-003 is at the IND-enabling stage for solid tumors. Preclinical data indicate that TAC-003 induces robust immune cell activation, leading to innate and adaptive immunity against Nectin-4-positive cancers and potent single-agent anti-tumor activity.
- There are additional programs in the discovery stage.

"At Tallac, we see a need to innovate beyond the traditional ADC approach to develop medicines with safer and more durable therapeutic profile. Tallac's next-gen ADC technology expands beyond the cytotoxic agents and allows selective delivery of oligonucleotide payloads to the cells and tumor sites of interest to safely drive potent, on-target, therapeutic effects. We are excited to see early clinical data of our immune agonist ADC and continue to advance our pipelines."

Hong Wan,
President and Chief Executive Officer of Tallac Therapeutics.

Tubulis

Tubulis was spun out from the Leibniz Research Institute in Berlin and the Ludwig Maximilians University (LMU) in Munich with the aim of bringing the true therapeutic value of ADCs to patients.

The company combines disease-specific insight with its novel proprietary technologies, including the Tub-tag® and P5 conjugation platforms, to deliver a diverse range of targeting molecules and innovative payloads in ADCs developed in house as well as by partners.

Company profile

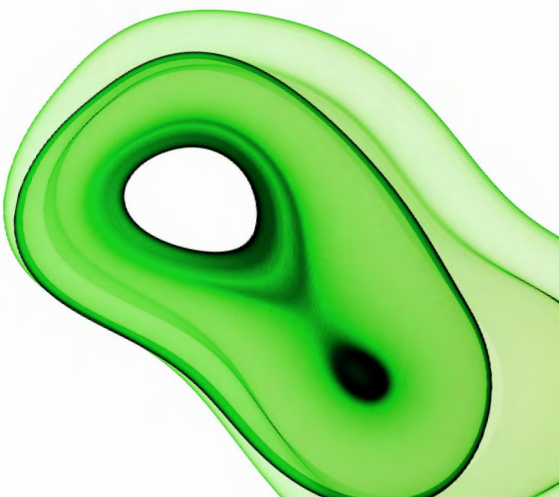
Founded: **2019**

Founders: **Dominik Schumacher, Jonas Helma-Smets, Ingo Lehrke, Christian Hackenberger, Heinrich Leonardt**

Headquarters: **Planegg-Martinsried, Germany**

Investors

- Andera Partners
- Bayern Kapital
- BioMed Partners
- coparion
- Deep Track Capital
- EQT Life Sciences
- Evotec
- Frazier Life Sciences
- Fund+
- High-Tech Gründerfonds (HGTF)
- Nextech Invest Ltd
- OCCIDENT
- Seventure Partners



Partners

Academic

Leibniz Research Institute (FMP) in Berlin

Ludwig Maximilians University (LMU) in Munich

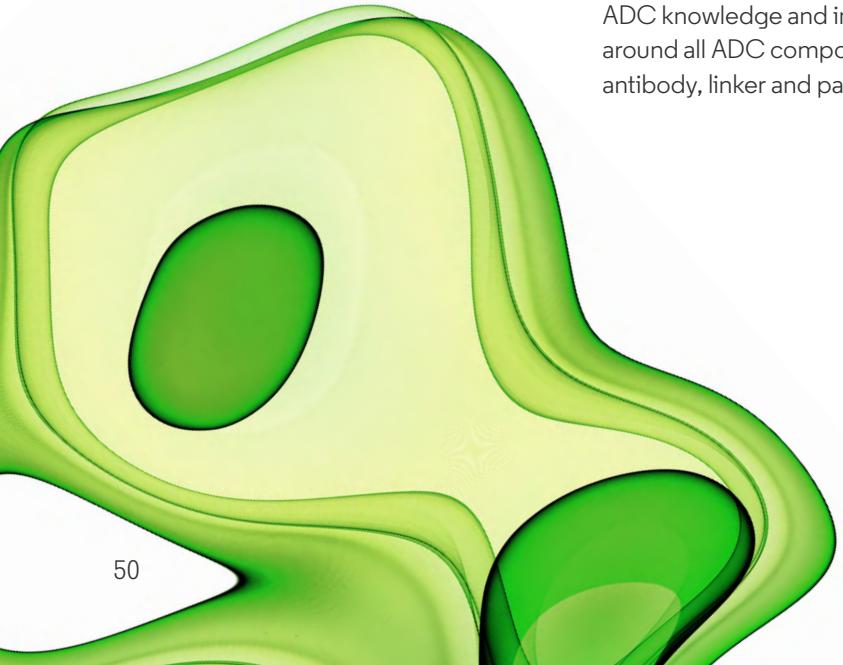
Ongoing relationship after the company was spun out

Corporate

Bristol Myers Squibb
Strategic license agreement providing Bristol Myers Squibb with rights to access Tubulis' Tubutecan payloads in combination with Tubulis' proprietary P5 conjugation platform to develop a select number of highly differentiated ADCs to treat solid tumors

Oncoteq AQ
Licensing agreement for Tubulis' potential best-in-class ADC TUB-010 (now TEQ102) for the treatment of patients with CD30-positive lymphomas, including T-cell and Hodgkin's lymphomas

What makes this company stand out?



- Tubulis' two proprietary ADC technologies are based on scientific discoveries made in the research groups of its co-founders Professor Christian Hackenberger (FMP), Professor Heinrich Leonhardt (LMU) and Dr. Jonas Helma-Smets.
- Based on the deep understanding of the technology by the experienced team, the company is uniquely positioned to consolidate the last 20 years of ADC knowledge and innovate around all ADC components: antibody, linker and payload.
- Tubulis' differentiated suite of platform technologies addresses the main bottlenecks of ADC stability and payload-driven toxicity and allows the company to tailor each component of the ADC to its respective indication.
    - The Tub-tag conjugation platform adds stability to the ADCs and minimizes unwanted immune reactions.
    - The P5 conjugation platform offers unprecedented linker stability and chemical flexibility, enabling rapid lead identification.
- Tubulis' ability to go beyond traditional payload classes and expand antibody conjugation options through novel chemical groups results in stable, high drug-to-antibody ratios.
- Tubulis plans to use recent funding to increase its corporate footprint by establishing a U.S. subsidiary.

How will the company's platform benefit patients and their caregivers?

- The company's approach to ADCs provides the ability to deliver specific anti-cancer agents to the tumor site and avoid offsite toxicities, potentially enabling longer treatment duration and extended survival.
- Tubulis and its partners are targeting hard-to-treat solid tumors that often have few treatment choices and relatively poor long-term outcomes.
- The company's lead candidates include TUB-040, which addresses tumor-antigen Napi2b, a well-characterized target in ovarian and lung cancers, and TUB-030, which targets 5T4, an antigen often overexpressed in solid tumors. Gaps in treatment for these cancer types include safe, effective options that improve clinical outcomes as well as quality of life.

Funding and grants

March 2024: Upsized series B2 funding (US$138.8m), co-led by EQT Life Sciences and Nextech Invest Ltd, on behalf of one or more funds managed by it, with participation from Frazier Life Sciences, Deep Track Capital, Andera Partners, BioMedPartners, Fund+, Bayern Kapital (with ScaleUp-Fonds Bayern), Evotec, coparion, Seventure Partners, OCCIDENT and HTGF

May 2022: Series B funding (US$63m) led by Andera Partners, with participation from Evotec, Fund+, Bayern Kapital (with Wachstumsfonds Bayern 2), BioMedPartners, coparion, HTGF, OCCIDENT and Seventure Partners

July 2020: Series A funding (€10.7m) co-led by BioMedPartners and HTGF, with participation by Seventure Partners, coparion, Bayern Kapital, OCCIDENT, private individual funds and the founders

IP status and patent filings

- The company has several proprietary platforms and programs protected by broad intellectual property rights.

R&D activity

- Preclinical proof-of-concept data for the company's lead candidates, TUB-040 and TUB-030, showed their ability to create effective, durable responses even in low target-expressing tumor mouse models.
- The company expects to begin phase 1/2 clinical trials, including dose escalation and dose optimization cohorts, in 2024.
- Additional programs (TUB-050 and TUB-060) are in the discovery stage.

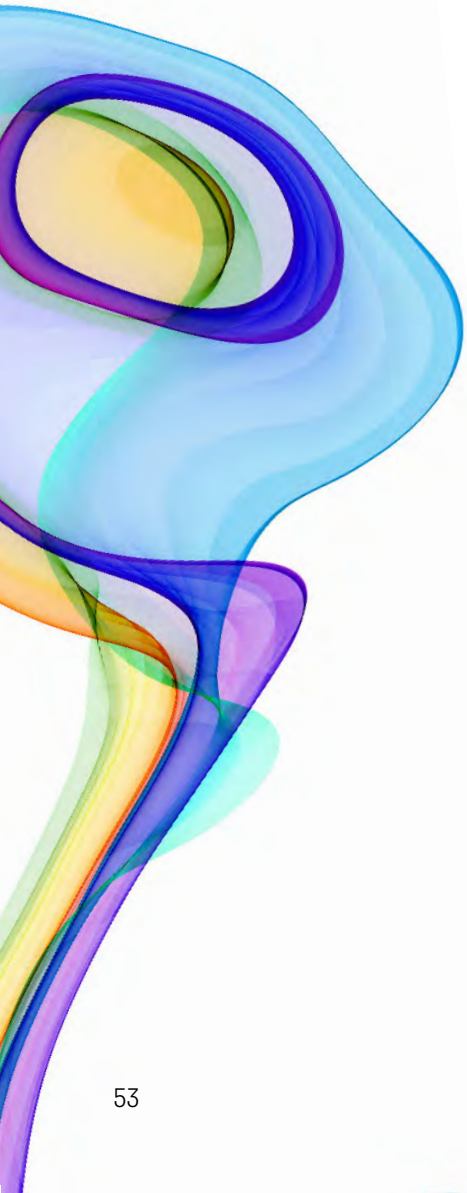
"Our proprietary platform technologies and internal know-how are the foundation for our pipeline of truly differentiated protein-drug conjugates. Our goal is to establish Tubulis as a global ADC leader as we transition into a clinical-stage company and harness the full power of ADCs to bring their therapeutic value to patients with solid tumors."

Dominik Schumacher, PhD;
Tubulis CEO and co-founder.

Key takeaways

The flurry of clinical research and deal-making around ADCs, particularly in the past five years, represents the growing acknowledgment of the potential of this technology to change the treatment paradigm for previously undruggable cancers as well as other hard-to-treat conditions.

Strategic partnerships and savvy acquisitions will help move this technology forward for both patient benefit and commercial success:



ADC companies must set themselves apart from others in an increasingly crowded market. To capture the attention of investors and partners, ADC companies will need to demonstrate the unique impact of their platform and/or assets on the therapeutic and competitive landscape.

Life science companies need to perform due diligence when evaluating assets. Awareness of the strengths and limitations of potential partners' platforms, differentiating characteristics and early preclinical data is essential to gain confidence that the platform and/or asset can pass regulatory scrutiny and be accepted by patients and physicians in the market.

A flexible, multitargeted ADC platform could springboard multiple opportunities. Rather than focusing on a single cancer type, ADC platforms that involve multiple targets or a target present in multiple cancers could provide greater value across several patient populations.

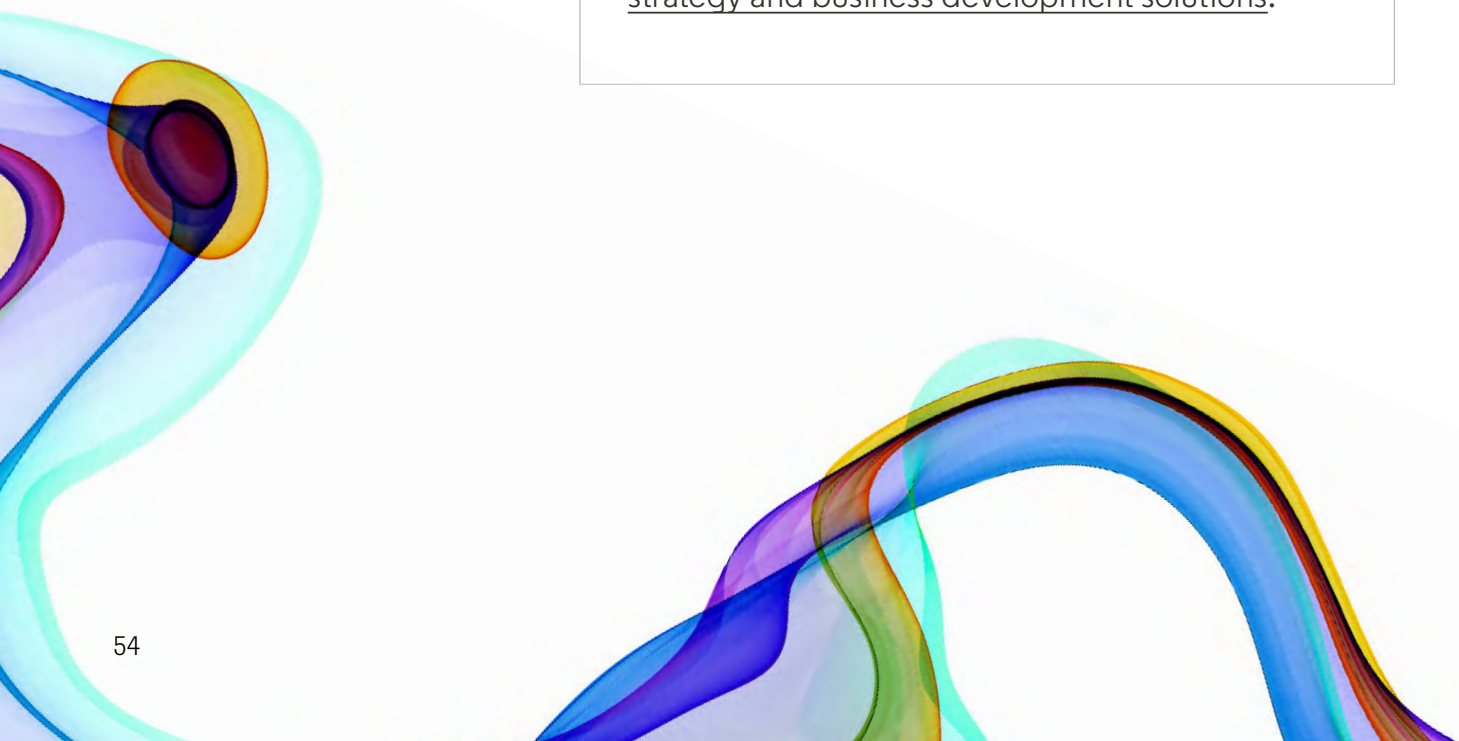
How can Clarivate help?

Navigating the global healthcare landscape is increasingly complex, and discovering, developing, funding and commercializing successful treatments that change patient lives is a monumental task.

Clarivate supports life science companies around the world with the development and commercialization of life-saving treatments. The top deal makers and innovators across pharma, biotech and medtech trust our intelligence to inform their portfolio and investment strategies. For more information on how Clarivate can support both sides of the negotiation table make informed decisions, see Clarivate portfolio strategy and business development solutions.

Learn more

For more information on how Clarivate can support both sides of the negotiation table make informed decisions, see Clarivate portfolio strategy and business development solutions.



References

1. DeCarvalho S, Rand HJ, Lewis A. Coupling of cyclic chemotherapeutic compounds to immune gamma-globulins. Nature 1964;202:255-8. doi: 10.1038/202255a0

2. Ford CH, Newman CE, Johnson JR, et al. Localisation and toxicity study of a vindesine-anti-CEA conjugate in patients with advanced cancer. Br J Cancer 1983;47:35-42.

3. Norsworthy KJ, Ko CW, Lee JE, Let al. FDA approval summary: Mylotarg for treatment of patients with relapsed or refractory CD33-positive acute myeloid leukemia. Oncologist. 2018;23(9):1103-1108. doi: 10.1634/theoncologist.2017-0604.

4. BioWorld, October 24, 2023. Merck agrees to pay Daiichi up to $22B in record ADC agreement. [Online] Available at: www.bioworld.com/articles/702163-merck-greesto-pay-daiichi-up-to-22b-in-record-adcagreement [Accessed March 22, 2024]

5. BioWorld, March 13, 2023. Pfizer to buy Seagen for $43B. [Online] Available at: www.bioworld.com/articles/695053-pfizer-to-buy-seagen-for-43b [Accessed March 19, 2024]

6. BioWorld, April 3, 2024. FDA accepts Daiichi/Astrazeneca's BLA for Trop2 breast cancer drug. [Online] Available at: www.bioworld.com/articles/707240-fda-accepts-daiichi-astrazenecas-bla-for-trop2-breast-cancer-drug [Accessed May 3, 2024]

7. BioWorld, March 4, 2024. EMA validates two filings for Daiichi-Astrazeneca's ADC. [Online] Available at: www.bioworld.com/articles/706191-ema-validates-two-filings-for-daiichi-astrazenecas-adc [Accessed May 3, 2024]

8. Clarivate. Drugs to Watch. [Online] Available at: clarivate.com/drugs-to-watch/ [Accessed May 3, 2024]

9. MSD, December 22, 2023. Patritumab Deruxtecan Granted Priority Review in the U.S. for Certain Patients with Previously Treated Locally Advanced or Metastatic EGFR-Mutated Non-Small Cell Lung Cancer. [Online] Available at: www.merck.com/news/patritumab-deruxtecan-granted-priority-review-in-the-u-s-for-certain-patients-with-previously-treated-locally-advanced-or-metastatic-egfr-mutated-non-small-cell-lung-cancer/ [Accessed May 3, 2024]

10. BioWorld, December 22, 2023. Antibody-drug tusamitamab ravtansine fails in phase III; Sanofi bows out. [Online] Available at: www.bioworld.com/articles/704110-antibody-drug-tusamitamab-ravtansine-fails-in-phase-iii-sanofi-bows-out [Accessed May 3, 2024]

11. FDA, March 2024. Clinical Pharmacology Considerations for Antibody-Drug Conjugates: Guidance for Industry. [Online] Available at: www.fda.gov/media/155997/download [Accessed May 2, 2024]

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