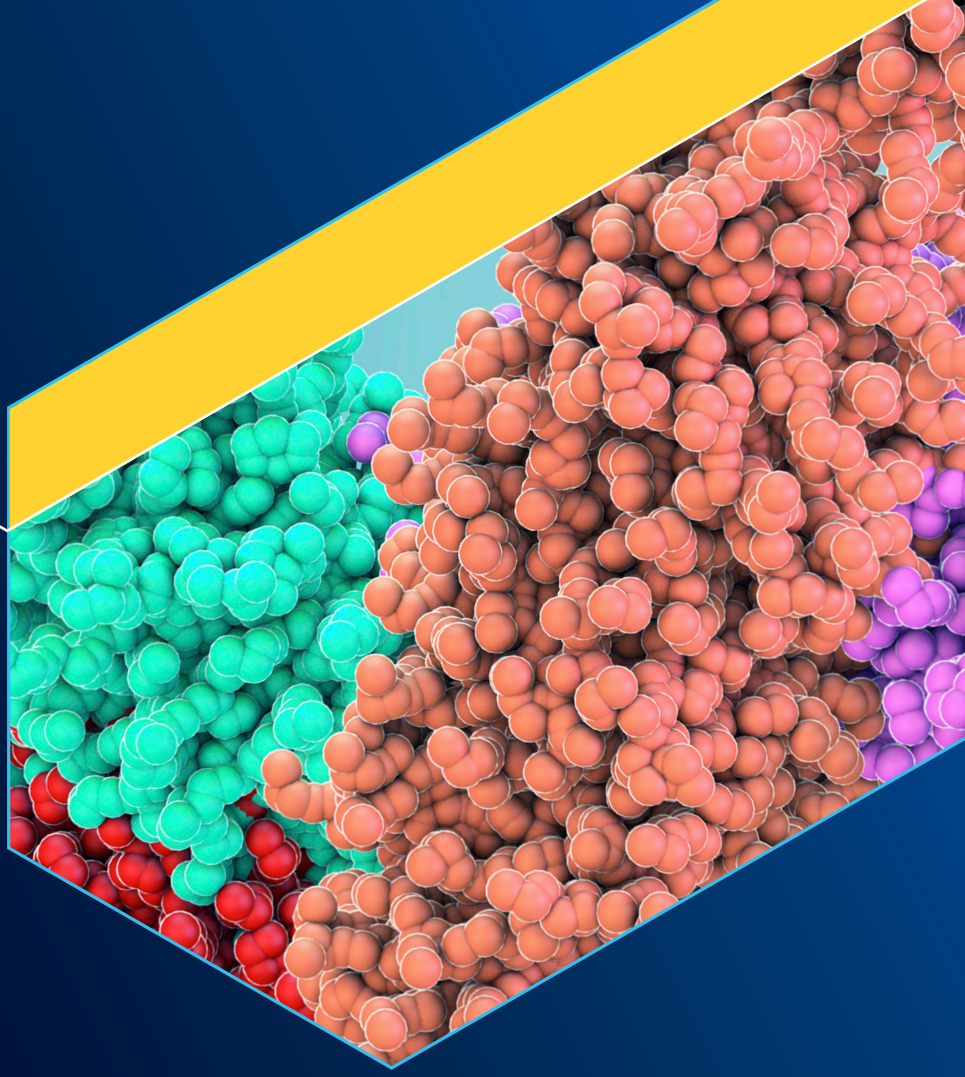


STRATEGIC INSIGHTS IN ANTIBODY-DRUG CONJUGATE DEVELOPMENT

How to navigate the evolving IP landscape

CAS
A division of the
American Chemical Society

Executive summary

As interest and investment in antibody-drug conjugates (ADCs) continues to grow, strategies that allow intellectual property (IP) analysts, search experts, lawyers, and R&D decision-makers to stay on top of the latest R&D and IP activities are vital for commercialization success.

ADCs are emerging as a revolutionary class of biopharmaceuticals, combining the precision of monoclonal antibodies with the power of small-molecule drugs.

The promise of ADC technology is marked by a significant increase in R&D investment as companies search for more effective, tailored treatments for difficult-to-treat diseases such as breast cancer, lymphoma, leukemia, autoimmune disease, inflammatory disorders, and complex bacterial infections.

The volume of scientific and patent data related to ADCs is rising exponentially, with explosive growth since the first FDA-approved ADC in 2000.

An analysis of the CAS Content Collection™ shows a 33% increase in patent publications alone from 2020 to 2022, demonstrating sustained, rapid growth and an intensified focus on these emerging therapeutics.

This rapid growth and the complexities that come with innovation in leading-edge domains introduce inevitable challenges for companies when navigating a complex and competitive IP and scientific landscape.

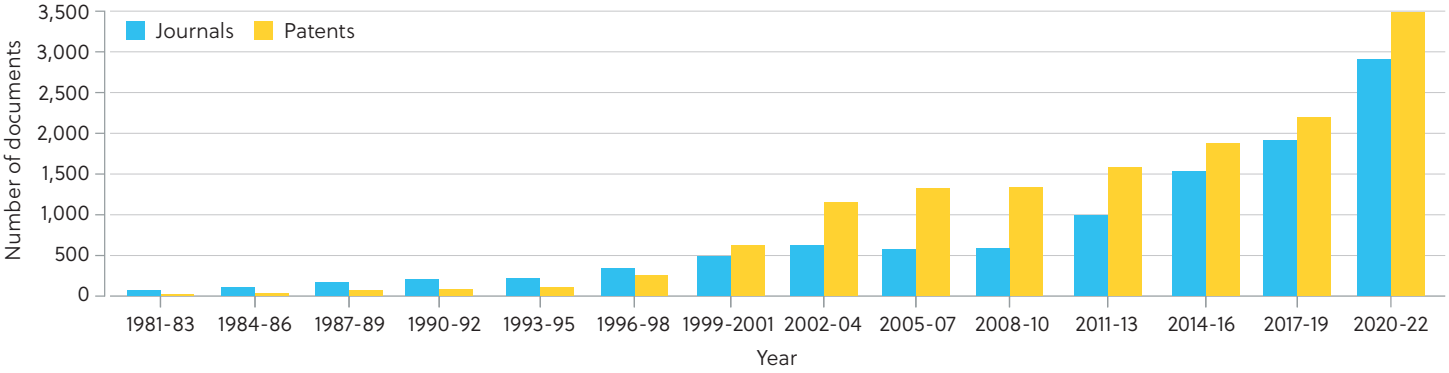
How can IP professionals optimize their searches to generate better insights, inform decision-making, protect innovations, and maximize ROI in the complex and dynamic ADC landscape?

This white paper explores the unique challenges that ADC innovation presents, providing actionable insights and opportunities that impact innovation, commercialization, and IP protection.

Entering the fast-moving world of ADCs

We are seeing rapid growth in a crowded landscape

The number of ADC-related patents continues to grow year-over-year, with data showing a 50-fold increase since the 1990s. Between 2020 and 2022 alone, the 33% increase in patents, despite the global COVID-19 pandemic, illustrates the rapid pace of innovation in the R&D space.



ADCs represent a transformative frontier in disease therapy, delivering high-impact drugs directly to specific cells and limiting off-target adverse effects. This motivation to innovate is evidenced by the continuously evolving patent environment associated with ADCs, with targets for breast cancer and myeloma seeing the highest growth rate in the last five years.

The ADC publication environment is continually evolving, with more than 160 ADC preclinical candidates being researched worldwide.

Analysis of private investments in this sector illustrates the global increase in capital investments in recent years. With the sustained interest amounting to a capital investment of >$600 million since its dramatic rise in 2018, commercial interest is driving further innovation and contributing to the boom of ADC-related IP.

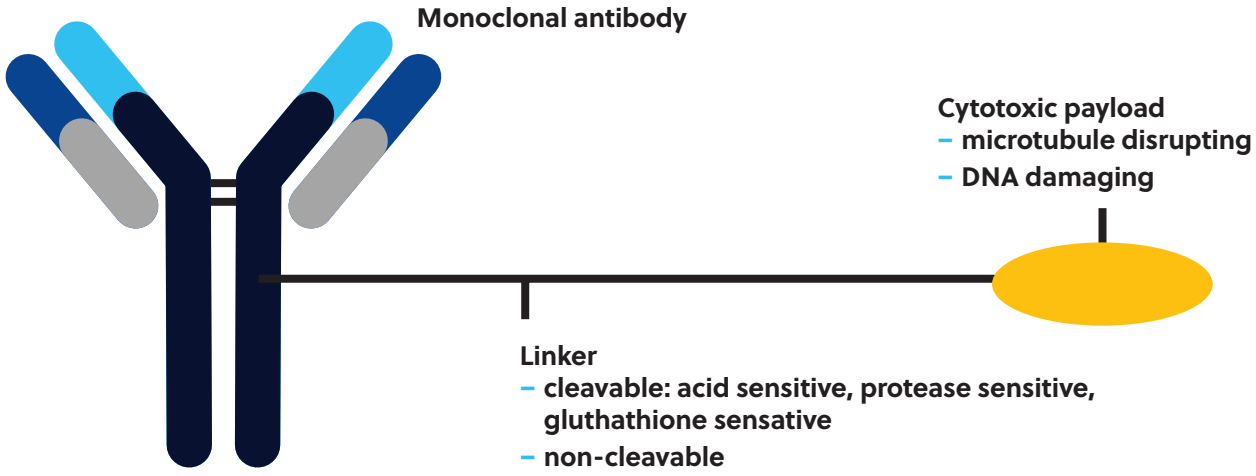
The ADC IP landscape is evolving

ADCs consist of three main components: a monoclonal antibody, a cytotoxic payload drug, and a stable linker molecule, enabling the potent and targeted treatment of cancers and other conditions. This complexity impacts IP considerations. IP analysis must include not only the ADC, but each of these individual components.

Emerging ADCs may include components that are already known or protected (i.e., reuse of a monoclonal antibody that is a known therapeutic agent). However, the unique combination of a known component and target may provide a patentable product that does not infringe on third-party IP rights.

Significant advancements in ADC payload technology have pioneered an expanding number of new classes of compounds being explored as potential chemotherapeutic agents. With the fastest yearly growth from STING agonists, glucocorticoid receptor modulators, and topoisomerase I inhibitors.

Despite 80% of all ADC documents relating to oncology medicine, the evolving clinical applicability of ADCs has led to the expansion of the disease portfolio that ADCs can target and treat. This layered IP landscape creates multidimensional complexities that must be considered and navigated through an ongoing comprehensive search.



ADC complexity requires a multi-faceted search strategy

Embarking on a thorough search for ADCs transcends mere name searches. It necessitates a layered strategy, involving distinct searches for each component, synthesizing these findings, and deriving conclusive insights.

For antibodies, sequence searches are paramount. Innovations may call for analyses of full antibody sequences or fragments. Commonly, a complementarity-determining region (CDR) search is employed. When delving into antibody genetic variants and derivatives, the search must extend to chemical modifications and rare residues, as a single alteration can significantly affect functionality. Thus, pinpointing sequences unambiguously is essential.

In exploring linkers and payloads, chemical structure searches are crucial. Given that some linkers are peptide-based, sequence analysis is applicable here as well. Moreover, ADCs often involve generic formulas, making a Markush search indispensable for investigating payloads, linkers, spacers, and their combinations.

Incorporating traditional keyword searches into your analysis is also vital, given the ambiguous and rapidly evolving nature of patent language and scientific terminology in this field. Navigating through this complexity requires a keen eye for valid terms and a reliance on controlled terminology and indexing to refine your search strategy.

In essence, conducting a comprehensive ADC search is inherently multi-faceted, demanding a broad spectrum of search techniques and approaches to capture the full breadth of innovation within these complex entities.

Maximize ADC success through strategic IP monitoring—early and often

IP monitoring keeps a pulse on competitor's activities and market opportunities

Staying abreast of the latest trends, terminologies, and scientific breakthroughs is essential for ADC IP analysts. This vigilance in tracking R&D developments, such as emerging antibody varieties and the expansion of payload options, is a cornerstone of strategic IP management, which in turn, plays a pivotal role in the success of R&D initiatives.

IP insights are invaluable across all stages of the development cycle. While IP, especially patents, has traditionally been viewed as a means of safeguarding innovation at the commercialization stage, the path to commercialization is anything but straightforward. IP needs arise at various stages, not just at the culmination. Beyond patentability and freedom-to-operate searches, innovators must identify unexplored areas early on, protect their IP portfolio, navigate legal hurdles, and seize emerging business opportunities. Thus, IP insights are indispensable from start to finish.

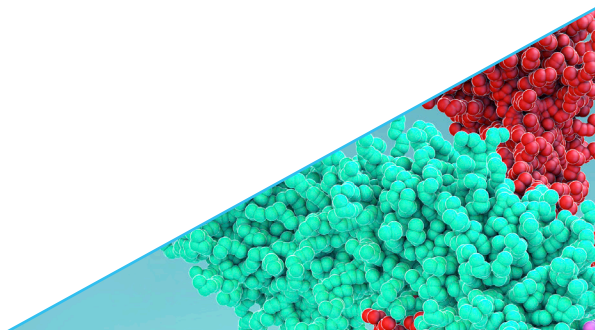
> **Industry Insight:** Regarding target antigens, HER2 and EGFR have been the primary focus for solid tumors, and CD19, CD22, CD30, and CD33 for hematological malignancies, as evidenced by a significant volume of published research and patents. However, the landscape has shifted in the past five years. In solid tumors, Trop-2 and Nectin-4 antigens have seen a surge in popularity, a trend highlighted by an increase in journal articles and patents, especially in the last three years. For hematological malignancies, CD79B has experienced the most rapid growth in research output over the same period. Leveraging such detailed insights enables developers to prioritize projects that align with current gaps in the market or present new avenues for future IP protection.

By recognizing changes in the ADC development arena, innovators can swiftly pinpoint new targets and opportunities, guiding strategic decisions on where to allocate research efforts and resources for optimal return on investment.

Cross-discipline search is necessary to protect IP and investments

The necessity of a cross-disciplinary approach in safeguarding intellectual property (IP) and investments in the realm of ADC research and development cannot be overstated. Given the complexity and the specialized nature of ADCs, which marry immunotherapy with small-molecule drug delivery, the IP landscape for ADCs is notably intricate. This complexity is compounded by the fact that ADCs, as multi-component entities, might necessitate multiple patents to fully cover their compositions—including the antibody, the cytotoxic (cancer-killing) payload, and the linker that connects them. This proliferation of patents, coupled with the swift expansion of the IP field, presents significant hurdles. It makes the task of pinpointing new investment avenues challenging and places innovators at risk of resource depletion, potential patent infringement, and licensing issues.

The integration of cross-disciplinary insights into the formulation and execution of a comprehensive IP strategy introduces considerable obstacles. A recent survey among innovators and IP professionals highlights the depth of these challenges: approximately half of the participants noted the identification of key players in the field and the development of an all-encompassing search methodology as the most daunting tasks in navigating the ADC IP terrain. These challenges underscore the importance of a meticulous and informed approach to ADC IP management, emphasizing the need for dynamic strategies.



Collect strategic IP insights in ADC innovation early and often

Gathering strategic intellectual property (IP) insights early and frequently is paramount in steering ADC innovation toward success. Developing and refining search strategies to gather these insights ensures that research directions and market entry plans are well-aligned. By proactively monitoring R&D trends from the outset, companies can stay ahead of the competition and significantly reduce the risk of infringing on existing patents.

The journey from initial exploration to commercial success encompasses several critical stages, each requiring a distinct set of IP considerations. In the exploration phase, conducting thorough landscape and competitive analyses is crucial for identifying potential leads and opportunities. During the design and synthesis phase, assessing novelty, recognizing prior art, and planning the path to commercialization are key. As projects move into testing, validation, and scaling, considerations shift toward developing a robust IP portfolio strategy and preparing for potential opposition.

Consider external IP and technical expertise to access unseen information and fuel future ADCs

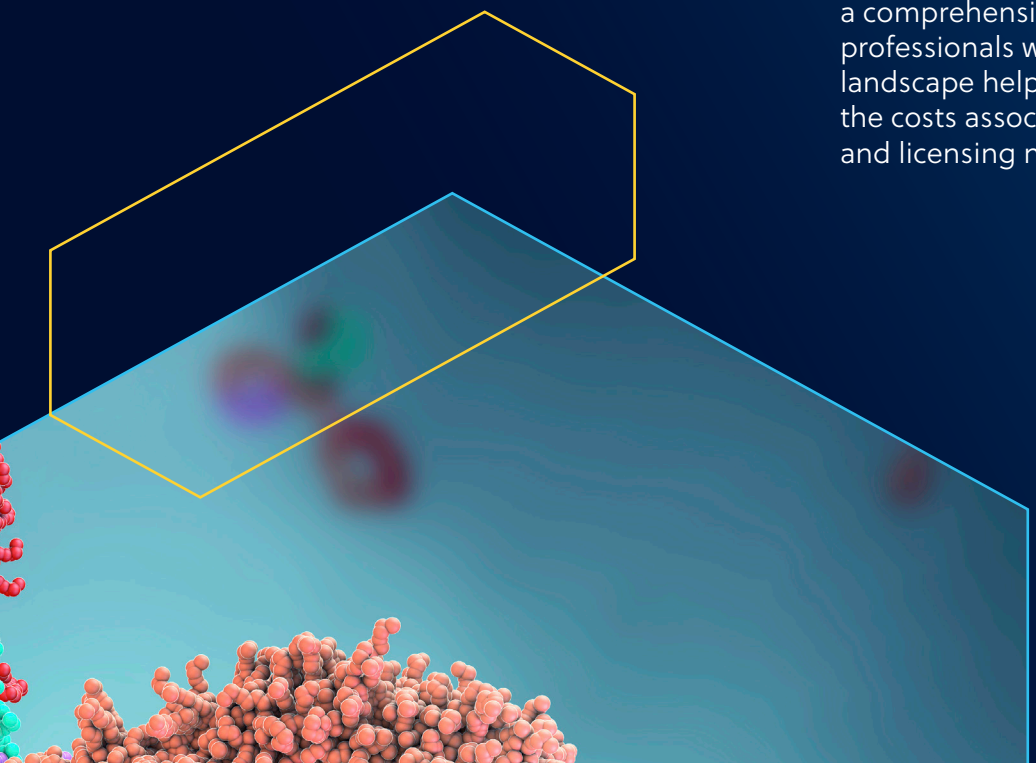
By design, ADCs exist at the intersection of biology and chemistry, with their synthesis and application relying on expertise across antibody discovery, protein bioengineering, linker and payload chemistry, pharmacokinetics, and clinical R&D, making investing in robust, multi-faceted IP analyses essential.

Assessing if you have the IP experts and search technology that help identify reliable opportunities early and navigate potential challenges efficiently is the first step toward commercial success.

Working with experts can streamline the process of keeping current with existing patents and prior art while circumventing potential IP infringements. Even in the evolving ADC landscape, collaborative efforts within the industry and between disciplines are the best way to derisk and safely navigate the complex environment.

In addition to industry and IP search expertise, look for partners and technology that help unite the R&D, IP, and legal teams. When done well, this ensures close alignment on strategy, scope, and next steps.

As the ADC R&D environment becomes more complex, so do the requirements for a comprehensive search. Working with IP professionals who can adapt to the rapidly changing landscape helps reduce resource burden, keeping the costs associated with patent filings, litigation, and licensing negotiations low.



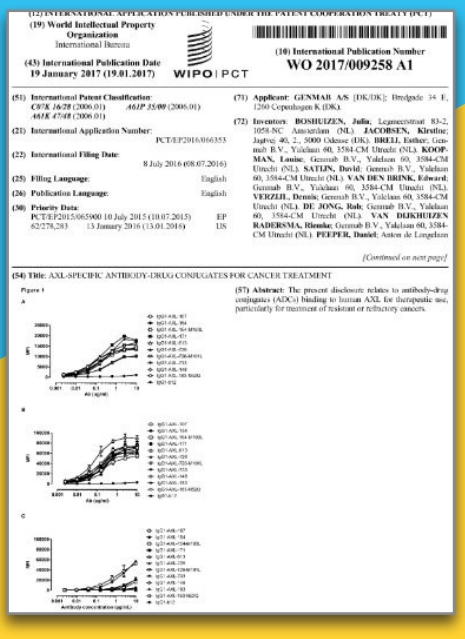
Case study: CAS maximizes patent information extraction

The challenge

IP search in the ADC innovation sphere is complex, owing to the multi-component nature of ADCs and the potential for overlapping patent estates. Paired with the exponential increase in related scientific data and patent filings, maintaining a clear and comprehensive understanding of the field is a demanding and resource-draining task.

The solution

Forming close partnerships with IP experts who use smart, collaborative approaches to their patent analysis and strategy enables companies to increase the value of their patent searches. Innovative tools, research discovery applications, and technology services that provide access to a comprehensive database of scientific information, including journal articles, patents, chemical substances, and reactions, form the basis of a detailed IP search. Together, these technologies and expert, tailored services provide reliable data sources and ensure legal compliance, enabling the directing of resources into high-potential R&D efforts.



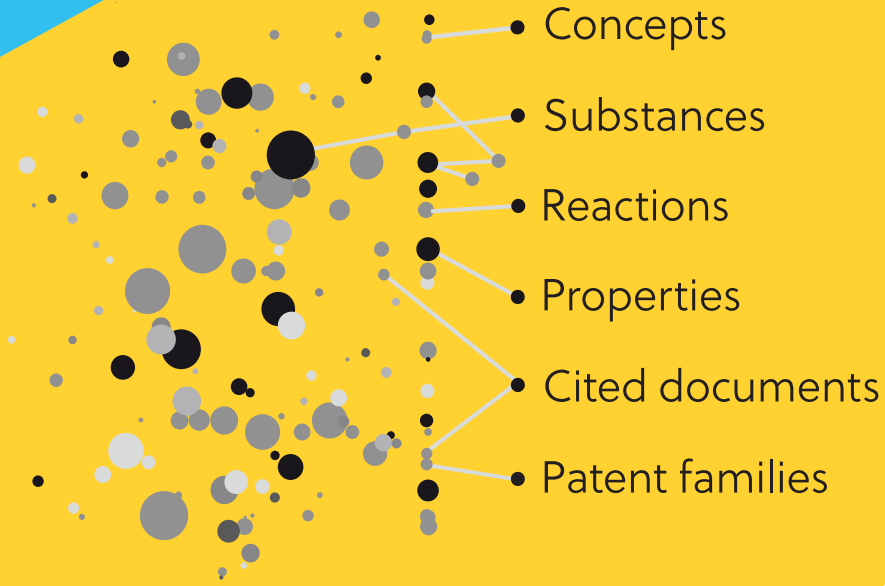
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(54) Title: AXL-SPECIFIC ANTIBODY-DRUG CONJUGATES FOR CANCER TREATMENT



The outcome

Working with trusted professionals at CAS enables unseen connections and insights to be revealed, increasing the value of patent data. Through access to comprehensive resources and tools from CAS, IP experts maximize knowledge extraction from a diverse collection of scientific literature, chemical structures, properties, reactions, and patents.

In the patent example, AXL ADC for cancer treatments, CAS experts could curate 55 concepts, 129 substances, 26 reactions, 76 patent family members, and 5 cited documents, as well as the connections between this knowledge from one patent.

As interest in ADCs continues to evolve, strategies that allow companies' legal counsels to maximize data extraction, keep up with the latest R&D trends, and optimize their ADC IP search will ensure the early identification of new opportunities and evidential success in ADC development.

Learn more about how CAS can optimize your IP search at cas.org.



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1. Sasso JM, Tenchov R, Bird R, Iyer KA, Ralhan K, Rodriguez Y, Zhou QA. The Evolving Landscape of Antibody–Drug Conjugates: In Depth Analysis of Recent Research Progress. Bioconjug Chem. 2023;34(11):1951-2000. doi:10.1021/acs.bioconjchem.3c00374

2. Webinar lives at: https://www.cas.org/resources/webinar/antibody-drug-conjugates-using-ip-and-rd-trends-inform-innovation

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