Antibody-Drug Conjugates: A Precision Delivery Revolution Against Cancer

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Abstract

Antibody–drug conjugates (ADCs) represent a revolutionary targeted anticancer therapy that combines high-specificity monoclonal antibodies with potent cytotoxic agents via cleavable or non-cleavable linkers, achieving precision drug delivery akin to Paul Ehrlich's "magic bullet" concept [1]. This review systematically traces the evolution of ADC technology across three generations: from first-generation agents (e.g., gemtuzumab ozogamicin) that encountered setbacks due to immunogenicity and linker instability, through second-generation agents (e.g., brentuximab vedotin) that achieved clinical success via humanized antibodies, more stable linkers, and more potent payloads, to third-generation agents (e.g., trastuzumab deruxtecan) that leverage site-specific conjugation, novel payloads (e.g., pyrrolobenzodiazepine dimers), and bystander killing effects to achieve breakthroughs in efficacy and indications. The review further analyzes clinical challenges including tumor heterogeneity-driven drug resistance and on-target/off-tumor toxicity, and tracks emerging technologies such as antibody–bottlebrush prodrug conjugates (ABCs) and bispecific nanobody–drug conjugates. Finally, we discuss future directions in target expansion, combination therapy, and non-oncological applications.

Key words

antibody–drug conjugates; precision therapy; targeted delivery; ADC drug generations

1. Introduction：From "Magic Bullet" to a Revolutionary Weapon in Oncology

1.1 Concept and Core Design of ADCs

Antibody–drug conjugates (ADCs) are anticancer agents composed of three structural elements: a monoclonal antibody (mAb), a highly cytotoxic payload, and a chemical linker. ADCs selectively deliver potent cytotoxic payloads to tumor cells, enabling targeted cancer therapy[1] . The design concept originated from the "magic bullet" hypothesis proposed by Paul Ehrlich in the early 20th century. Through tissue staining experiments, Ehrlich discovered that chemical dyes could selectively bind to specific cellular structures, leading him to propose the "side-

chain theory" (later the "receptor theory"), which posited that organisms possess receptors capable of binding specific toxins or antigens. He envisioned a class of drugs that could precisely recognize and act on diseased cells while sparing healthy tissues, laying the theoretical foundation for modern targeted therapy [2].

1.2 Core Components: Antibody, Linker, and Cytotoxic Payload

The three core components—antibody, linker, and cytotoxic payload—collectively determine ADC performance [3]. An ideal antibody specifically recognizes antigens (e.g., Human Epidermal Growth Factor Receptor 2 (HER2), Cluster of Differentiation 33 (CD33)) overexpressed on tumor cells with high affinity (typically Kd ≤ 10 nM) to ensure rapid and firm binding [4]. Immunoglobulin G (IgG), particularly the IgG1 subtype, is the most commonly employed format; approved ADCs such as T-DM1 and T-DXd both utilize humanized or fully human IgG1. Recent advances have introduced engineered IgG variants and bispecific antibodies [5]. The antibody serves three core functions: (1) mediating target enrichment and internalization via antigen-specific binding; (2) retaining the parent antibody's intrinsic antitumor activity for synergistic cytotoxicity; and (3) recruiting immune effector cells via the Fragment crystallizable (Fc) region, triggering Antibody-Dependent Cellular Cytotoxicity (ADCC) and Antibody-Dependent Cellular Phagocytosis (ADCP), thereby adding an immunotherapeutic dimension to ADCs [6].

The linker is the critical "bridge" connecting antibody to payload. Its core value lies in regulating the balance between stability and cleavability, directly determining ADC safety and antitumor efficacy. An ideal linker must maintain high stability in circulation while achieving efficient and specific payload release within tumor cells. Linkers are primarily classified into cleavable and non-cleavable types. Non-cleavable linkers (e.g., succinimidyl-4-(N-maleimidomethyl)cyclohexane-1-carboxylate (SMCC)) rely on lysosomal degradation of the antibody for payload release; they offer high plasma stability but lack bystander effects. Cleavable linkers respond to the tumor intracellular microenvironment and are further subdivided into chemically cleavable (hydrazone bonds, disulfide bonds) and enzymatically cleavable (Val-Cit dipeptide, β-glucuronide) subclasses. Peptide-based cleavable linkers are widely applied due to their favorable combination of high stability and efficient release [7–9].

The highly cytotoxic payload is the key effector for tumor cell killing, typically exhibiting IC50 values in the nanomolar to picomolar range [10]. Current payload classes include topoisomerase I (TOP1) inhibitors, microtubule inhibitors, DNA-damaging agents, photosensitizers, and bacterial toxins. Microtubule inhibitors (e.g., auristatins, maytansinoids) are the most mature and widely used class, blocking mitosis by binding tubulin and disrupting microtubule dynamics. DNA-damaging agents (e.g., calicheamicin, duocarmycins) target nuclear DNA through alkylation, crosslinking, or direct cleavage, inducing cell death [10,11].

1.3 Mechanism of Action

The antitumor action of ADCs is a multi-step cascade: after intravenous administration, ADCs enter systemic circulation and precisely bind to target antigens (e.g., HER2, Cluster of Differentiation 30 (CD30)) overexpressed on tumor cells; the ADC–antigen complex is internalized via receptor-mediated endocytosis into early endosomes; early endosomes mature into late endosomes and fuse with lysosomes, providing the acidic environment (pH 4.5–5.0) and hydrolytic enzymes for payload release; payload release occurs according to linker type—cleavable linkers respond to lysosomal proteases, acidic pH, or reducing glutathione, while non-cleavable linkers rely on complete proteolytic degradation of the antibody within lysosomes; released payloads enter the cytoplasm, arresting the cell cycle at G2/M phase or inducing DNA damage, ultimately triggering apoptosis [1,5].

2. The Evolution of ADCs: Three Generations of Technological Iteration

Given the structural complexity of ADCs, generational classification is not a simple task. This review adopts the classification proposed by Fu et al., which accounts for the distinct properties of each component and is considered the most broadly applicable [12].

2.1 First-Generation ADCs: Arduous Exploration and Technical Lessons

Although early ADC exploration began before 1975, the field's meaningful development started with Köhler and Milstein's generation of murine monoclonal antibodies via hybridoma technology, which provided highly specific targeting tools [13]. Early ADCs employed murine mAbs, conventional chemotherapeutic payloads (e.g., doxorubicin), and predominantly non-cleavable linkers. BR96–doxorubicin (BR96-DOX), a chimeric anti-Lewis Y (LeY) mAb conjugated to doxorubicin via an acid-labile hydrazone bond, was developed for metastatic breast cancer [14]. Preclinically, BR96-DOX induced complete tumor regression in 72%–100% of xenograft models and cured 70% of mice with established metastases, whereas free doxorubicin was nearly ineffective [15]. However, clinical translation was severely limited by insufficient doxorubicin potency (requiring >100 mg/kg for cure), linker instability (systemic release half-life of only 43 h), and LeY antigen expression in normal gastrointestinal tissue. These factors resulted in limited antitumor activity in Phase I/II trials, with gastrointestinal toxicity as the dose-limiting toxicity [16].

Learning from BR96-DOX, researchers subsequently employed more potent payloads and sought antigens exclusively overexpressed in cancer cells, ultimately leading to the first FDA-approved ADC, gemtuzumab ozogamicin (Mylotarg) [13]. This ADC comprised a humanized IgG4 anti-CD33 antibody, the potent DNA-damaging agent calicheamicin, and an acid-labile hydrazone linker, with a drug-to-antibody ratio (DAR) of approximately 2–3 via random lysine conjugation [17]. In relapsed CD33-positive acute myeloid leukemia, gemtuzumab ozogamicin monotherapy produced a 30% overall response rate (16% complete remission, 13% complete remission with incomplete platelet recovery), with a median response duration of 60 days. The toxicity profile featured predictable hematologic toxicity and hepatotoxicity, with low incidences of severe infection, mucositis, and alopecia, and no cardiotoxicity [18]. However, first-generation ADCs faced fundamental limitations: (1) murine or chimeric antibodies elicited immunogenic responses, accelerating drug clearance; (2) unstable linkers (e.g., acid-labile hydrazone bonds) caused premature payload release, inducing myelosuppression and hepatotoxicity; (3) random conjugation produced highly heterogeneous DAR distributions, compromising pharmacokinetics and narrowing the therapeutic window. These deficiencies drove the development of second-generation ADCs [19].

2.2 Second-Generation ADCs: Technical Improvements and Clinical Success

Representative second-generation ADCs are brentuximab vedotin (FDA-approved 2011) and ado-trastuzumab emtansine (T-DM1; FDA-approved 2013). Both employ more stable linkers (protease-cleavable peptide and non-cleavable thioether, respectively) and higher DAR values (3.5–4), improving efficacy and safety [17].

Brentuximab vedotin comprises a chimeric anti-CD30 mAb (chimeric anti-CD30 monoclonal antibody (cAC10)), a protease-cleavable valine-citrulline linker, and the potent microtubule inhibitor Monomethyl Auristatin E (MMAE). Pivotal Phase II trials demonstrated objective response rates (ORR) of 75% in relapsed/refractory classic Hodgkin lymphoma and 86% in systemic anaplastic large cell lymphoma, with complete response rates of 34% and 57%, respectively, leading to accelerated FDA approval in 2011. Common adverse events include fatigue, nausea, and dose-dependent peripheral neuropathy (predominantly sensory and largely reversible); concomitant use with bleomycin is contraindicated due to risk of fatal pulmonary toxicity [20].

T-DM1 employs the high-affinity anti-HER2 mAb trastuzumab conjugated via a stable non-cleavable SMCC linker to the maytansinoid DM1 (DAR ~3.5). The landmark Phase III EMILIA trial demonstrated that T-DM1 significantly prolonged progression-free survival (PFS: 9.6 vs. 6.4 months) and overall survival (OS: 30.9 vs. 25.1 months) compared with lapatinib plus capecitabine in HER2-positive metastatic breast cancer patients previously treated with trastuzumab and a taxane. The TH3RESA study further confirmed T-DM1's efficacy in heavily pretreated patients [21].

Despite these successes, second-generation ADCs still faced challenges: limited therapeutic windows due to off-target toxicity, and when DAR exceeded 6, enhanced hydrophobicity led to aggregation, accelerated clearance, and reduced antitumor potency.

Third-generation ADC development therefore focused on two strategies: precise DAR control via site-specific conjugation, and systematic optimization of mAbs, linkers, and payloads, aiming to balance circulatory stability with efficient intratumoral payload release [19].

2.3 Third-Generation ADCs: Paradigm Shift and Efficacy Breakthroughs

Representative third-generation ADCs include polatuzumab vedotin, enfortumab vedotin, and fam-trastuzumab deruxtecan (T-DXd). Their success stems largely from site-specific conjugation technologies. To overcome the DAR ceiling, researchers developed the Fleximer polymer (PHF), a hydrophilic multivalent scaffold capable of carrying numerous hydrophobic drug molecules while maintaining solubility. This platform achieves DAR values up to 20:1 while preserving favorable pharmacokinetics [22]. Third-generation ADCs employ fully human antibodies or Fragment antigen-binding (Fab) fragments, reducing immunogenicity and enhancing tumor penetration [23,24]. Payload diversification now includes ultrapotent Pyrrolobenzodiazepine (PBD) dimers, tubulysins, and immunomodulators, expanding therapeutic potential [19].

The bystander effect—in which cytotoxic payload released from target cells diffuses to kill neighboring antigen-negative or antigen-low cells—has garnered significant attention. This property is critical for addressing tumor heterogeneity. Preclinical studies show that bystander-capable ADCs such as T-DXd effectively eliminate HER2-negative cells within HER2-heterogeneous tumors, whereas non-bystander ADCs such as T-DM1 kill only HER2-positive cells. This explains the remarkable efficacy of T-DXd in HER2-low breast cancer (DESTINY-Breast04) and HER2-positive gastric cancer (DESTINY-Gastric01). The bystander effect also helps overcome the "binding site barrier," whereby ADCs bound to highly expressed antigens at the tumor periphery impede deeper penetration. However, the bystander effect may also increase off-target toxicity, and its clinical benefit depends on multiple contextual factors that must be carefully weighed during drug development [25]. The evolutionary trajectory of ADC technology is summarized in Table 2-1.

Table 2-1. Evolution of ADC Technology Across Three Generations

Feature	1st Generation	2nd Generation	3rd Generation
Antibody	Murine or chimeric	Humanized	Fully human or Fab fragments
Linker	Unstable (hydrazone)	Stable, cleavable & non-cleavable	Precision tumor-site release
Payload	Low potency (e.g., calicheamicin, doxorubicin)	High potency (e.g., auristatins, maytansinoids)	Ultra-high potency (e.g., PBDs, tubulysins, immunomodulators)
Conjugation	Random (lysine)	Random (lysine or cysteine)	Site-specific
DAR	Uncontrolled (0–8)	4–8	2–4 (precisely controlled)
Representatives	Gemtuzumab ozogamicin Inotuzumab ozogamicin	Brentuximab vedotin T-DM1	Polatuzumab vedotin Enfortumab vedotin T-DXd
Advantages	Specific targeting; broadened therapeutic window	Enhanced targeting; more potent payloads; lower immunogenicity	Effective against low-antigen cells; homogeneous DAR; improved PK/PD; reduced off-target toxicity
Disadvantages	Heterogeneous; low potency; narrow TI; premature release; high immunogenicity	Heterogeneous; rapid clearance at high DAR; off-target toxicity; drug resistance	Novel toxicity risks from ultrapotent payloads; interspecies metabolic differences; drug resistance

3. Current Challenges: Bottlenecks in ADC Clinical Application

In terms of drug targets, ADCs face challenges of tumor heterogeneity, insufficient internalization efficiency, and scarcity of ideal targets. Intratumoral and intertumoral genetic/phenotypic differences lead to heterogeneous antigen expression, allowing antigen-negative cells to escape ADC-mediated killing. Moreover, most targets (e.g., EGFR, TROP2) exhibit low-level expression in normal tissues, causing on-target off-tumor toxicity.

Drug resistance is a formidable problem. Target-dependent resistance involves antigen downregulation or mutation, directly impairing ADC recognition and binding, as well as reduced internalization efficiency or

aberrant trafficking to recycling rather than lysosomal degradation pathways. Payload-related resistance is equally prominent: highly hydrophobic payloads are actively effluxed by overexpressed multidrug resistance proteins (e.g., Multidrug Resistance Protein 1 (MDR1), Multidrug Resistance-associated Protein 1 (MRP1)), reducing intracellular drug concentrations, while payloads lacking bystander effects cannot eliminate antigen-negative or heterogeneous tumor cell populations, facilitating selection of resistant clones. Additionally, lysosomal dysfunction—altered pH or reduced activity of cathepsins and other key hydrolases—directly impairs cleavable linker processing. These mechanisms often intertwine, collectively driving adaptive resistance and ultimately limiting long-term ADC efficacy [26].

ADC toxicity primarily arises from cytotoxic payload exposure in non-target tissues, classified as target-independent (off-target) and target-dependent (on-target off-tumor). Target-independent toxicity, the most common dose-limiting toxicity, results from premature linker cleavage in plasma (e.g., hydrazone hydrolysis in gemtuzumab ozogamicin), passive diffusion of lipophilic payloads (e.g., MMAE) into rapidly proliferating cells in bone marrow or neurons, and non-specific endocytosis of high-DAR/hydrophobic ADCs by hepatic tissues. ADCs can also bind Fcγ receptors on immune cells (macrophages, megakaryocytes) or undergo mannose receptor-mediated uptake by liver sinusoidal endothelial cells, causing thrombocytopenia or hepatic veno-occlusive disease. Target-dependent toxicity occurs when ADCs bind low-level antigen expressed in healthy tissues—for instance, enfortumab vedotin targeting Nectin-4 in salivary glands causes dysgeusia, and anti-HER2 ADCs binding HER2 in lung and myocardium can trigger interstitial lung disease or cardiac dysfunction. Toxicity profiles correlate with payload class: microtubule inhibitors (e.g., MMAE) commonly cause neutropenia and peripheral neuropathy; DNA-damaging agents (e.g., calicheamicin, PBD dimers) cause myelosuppression and hepatotoxicity; TOP1 inhibitors (e.g., 7-ethyl-10-hydroxycamptothecin (SN-38)) mainly cause neutropenia and diarrhea. Current mitigation strategies focus on optimizing linker stability (e.g., PEGylation, tandem-cleavage linkers), developing Probody-DCs for tumor-selective activation, and co-administering anti-payload antibody fragments to neutralize free payload [27].

4. Latest Technological Advances

Traditional ADCs are constrained by low DAR (DAR ≤ 8), necessitating ultra-potent payloads that limit payload diversity, narrow therapeutic windows, and increase toxicity. Antibody–bottlebrush prodrug conjugates (Antibody-Bottlebrush Prodrug Conjugate (ABC)) resolve this fundamental contradiction through architectural innovation. ABCs conjugate a mAb with a structurally defined bottlebrush prodrug (BPD) module—a nanoscale polymer featuring hydrophilic PEG side chains and drug units attached via cleavable linkers, connected to the antibody through bioorthogonal click chemistry. This design achieves ultra-high DAR values (up to 135), representing a one-to-two-order-of-magnitude increase over conventional ADCs, while the bottlebrush architecture effectively shields hydrophobic payloads, ensuring excellent solubility and stability. Functionally, ABCs extend the therapeutic payload repertoire from moderate/low-potency chemotherapeutics (e.g., SN-38, doxorubicin) to novel modalities such as Proteolysis Targeting Chimera (PROTAC). Preclinical studies demonstrate that ABCs achieve efficacy comparable or superior to approved ADCs in multiple tumor models, with particularly pronounced effects in low-antigen-expression settings and favorable pharmacokinetics and safety profiles [28]. Similarly, CD38-targeted polymer antibody–drug conjugates (Polymer Antibody-Drug Conjugate (PADC)) with ultra-high DAR (~30) significantly delayed tumor progression and prolonged survival in multiple myeloma models, with superior pharmacokinetics compared to naked antibody [29].

The Fc fragment of conventional IgG-based ADCs mediates non-specific tissue uptake and Neonatal Fc Receptor (FcRn) binding, prolonging half-life but increasing healthy tissue exposure to cytotoxins, while large size limits tumor penetration. To address this, researchers developed an Fc-free bispecific nanobody–drug conjugate simultaneously targeting Nectin-4 and Trop2, both highly expressed in various solid tumors. High-affinity nanobodies were generated through alpaca immunization and yeast display screening, followed by Complementarity-Determining Region (CDR) grafting for humanization. Anti-Nectin-4 and

anti-TROP2 nanobodies were connected via a [G4S]3 linker to create a monovalent bispecific construct, enhancing internalization and overcoming tumor heterogeneity. C18 fatty acid modification via Michael addition to an N-terminal cysteine significantly extended half-life by mitigating rapid renal clearance. Payload loading employed a Sortase A-mediated enzyme-click chemistry cascade: transpeptidation at the C-terminal LPETG sequence inserted a bis-azide linker, followed by copper-free click chemistry with Dibenzocyclooctyne (DBCO)-functionalized GGFG-eribulin, yielding homogeneous conjugates with DAR of 2. This modular design optimizes tissue penetration, plasma stability, and targeting efficiency, offering a new paradigm for solid tumor therapy [30].

Site-specific conjugation technologies have matured considerably. Enzyme-mediated conjugation (e.g., microbial transglutaminase, Sortase A) achieves precise, efficient site-specific coupling by recognizing specific peptide sequences (e.g., Q295, LPXTG), yielding highly homogeneous products with excellent process reproducibility. Click chemistry strategies—including copper-catalyzed azide-alkyne cycloaddition and Diels-Alder cycloaddition—exploit bioorthogonal reactions under mild conditions for efficient, specific conjugation, especially when combined with genetically encoded non-canonical amino acids (e.g., p-acetylphenylalanine), enabling precise control over conjugation sites. Engineered cysteine residues (e.g., Thiomab technology) achieve controlled DAR via maleimide chemistry, improving pharmacokinetic properties [31].

Linker chemistry remains a key focus. Nearly half of approved ADCs (9/19) employ peptide-based cleavable linkers, including dipeptide (Val-Cit/Val-Ala) and tetrapeptide (Gly-Gly-Phe-Gly) motifs. However, traditional peptide linkers face limitations: susceptibility to premature cleavage by plasma carboxylesterase 1C, hydrophobicity-driven aggregation, and reliance on cathepsin B alone, which may be inefficient in heterogeneous tumors. Recent advances include novel enzyme-cleavage sequences (e.g., Ala-Ala-Asn, D-Val-Leu-Lys) responsive to tumor microenvironment enzymes such as asparaginyl endopeptidase and plasmin; incorporation of PEG or cyclodextrin modules to reduce hydrophobicity and support high-DAR constructs; quaternary ammonium salt linkers that enhance solubility via positive charges; and dual self-immolative strategies to optimize release kinetics. The Gly-Gly-Phe-Gly tetrapeptide linker has demonstrated excellent clinical efficacy and safety (e.g., Enhertu), collectively driving ADCs toward broader therapeutic windows and greater programmability [32].

ADC applications have expanded beyond oncology to anti-infective and autoimmune disease indications. Antibody–antibiotic conjugates deliver antibiotics via pathogen-specific antibodies, increasing local drug concentrations while reducing systemic exposure—a promising approach against antibiotic resistance. Antibody–glucocorticoid conjugates target anti-inflammatory drugs to diseased tissues, maintaining efficacy while avoiding systemic glucocorticoid side effects. To overcome drug resistance, combination strategies are increasingly important: ADCs with distinct mechanisms (e.g., microtubule inhibitor plus DNA-damaging agent) can synergistically attack tumor cells. Particularly promising is the combination of ADCs with immune checkpoint inhibitors: ADC-induced immunogenic cell death activates the tumor immune microenvironment, while checkpoint inhibitors relieve immunosuppression, synergistically eliciting antitumor immunity. Furthermore, cleavable linker-mediated bystander effects clear antigen-negative cells, achieving localized combination killing, while non-cleavable linkers generate charged metabolites that evade efflux pumps, enhancing intratumoral drug retention [33].

Regarding payload innovation, researchers have explored using lower-potency conventional chemotherapeutics to reduce off-target toxicity. Trastuzumab–vincristine conjugates, prepared by N-alkylating vincristine with a cleavable linker and conjugating to free cysteine residues on the antibody, exhibited sub-nanomolar potency against HER2-positive cells in vitro—comparable to marketed ADCs and two orders of magnitude more potent than free vincristine. In vivo, the conjugate achieved complete tumor regression 9 days after a single dose, highlighting the untapped potential of the chemotherapeutic arsenal for novel ADC development [34].

5. Summary and Outlook

The evolution of ADC drugs represents a century-long journey from Paul Ehrlich's "magic bullet"

concept to clinical reality. This review has systematically traced the progression from arduous first-generation exploration through second-generation clinical breakthroughs to third-generation efficacy leaps. Antibodies evolved from murine to fully human, bispecific, and even nanobody formats, aiming to reduce immunogenicity and enhance tumor penetration. Linkers progressed from early acid-labile hydrazone bonds to highly stable enzymatically cleavable systems, achieving the central balance between circulatory stability and tumor-specific release. Cytotoxic payloads have undergone a qualitative leap from conventional chemotherapeutics to picomolar-potency novel toxins, alongside the emergence of immunomodulators and other novel mechanisms of action. Critically, site-specific conjugation technologies resolved the product heterogeneity challenges of random conjugation, substantially optimizing pharmacokinetics and widening therapeutic windows. Additionally, the sophisticated understanding and strategic exploitation of the bystander effect have enabled ADCs to effectively target antigenically heterogeneous tumors, demonstrating outstanding efficacy in refractory settings such as HER2-low breast cancer.

Looking ahead, the ADC field is advancing toward greater diversification, precision, and intelligence across four key fronts. First, technological platforms continue to innovate: ABC technology leverages polymer carriers to achieve ultra-high drug loading (DAR > 100), directly breaking through the payload capacity ceiling of conventional ADCs; bispecific/multispecific ADCs and nanobody–drug conjugates promise to overcome the industry-wide challenges of poor solid tumor penetration and marked heterogeneity. Second, overcoming drug resistance and managing toxicity remain core priorities. Future breakthroughs will focus on dual cleavable linkers responsive to tumor microenvironment-specific enzymes, combination regimens with immune checkpoint inhibitors, and Probody-DC technology for mitigating on-target off-tumor toxicity. Third, the application landscape continues to broaden, with ADCs now extending beyond oncology into anti-infective (antibody–antibiotic conjugates) and autoimmune disease (antibody–glucocorticoid conjugates) indications. Fourth, payload library diversification will catalyze new therapeutic breakthroughs: incorporating non-cytotoxic modalities such as PROTACs into the payload repertoire, or re-evaluating and optimizing conventional chemotherapeutics for ADC applications, both hold promise for creating safer and more effective treatment regimens.

In summary, ADCs have evolved from an innovative therapeutic concept into a cornerstone of modern cancer therapy. With deepening understanding of biological mechanisms, continuous advances in engineering technologies, and progressive accumulation of clinical experience, next-generation ADCs will undoubtedly become more precise, more intelligent, and more efficacious, ultimately bringing the promise of cure to an ever-greater number of patients.

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