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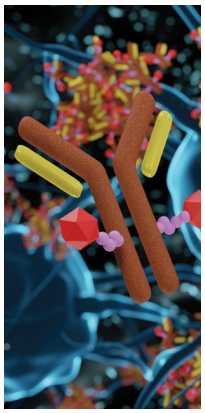

AN INDUSTRY BRIEF FROM INSTITUTE@PRECISION

25 Years of Antibody–Drug Conjugates: From Breakthroughs to Access by Design

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The Institute@Precision is part of Precision Medicine Group, an ecosystem of organizations spanning discovery to commercialization, purpose-built for precision.

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Introduction

The oncology landscape has been fundamentally reshaped over the past 25 years by antibody–drug conjugates (ADCs). By combining the precision targeting of an antibody with a potent cytotoxic payload, ADCs have evolved from early promise to established, high-impact therapies across multiple tumor types.

As we mark a quarter century since the first AD approval, the focus shifts from molecular engineering to market precision and access predictability. The next wave of ADC approvals will not be defined by efficacy alone; their success hinges on Access by Design, a strategy rooted in payer-rationalized clinical trial design that anticipates and directly addresses the financial and clinical risk concerns of national health plans.

Grounded in our collective experience advising biopharma clients on ADC launches, analog markets, and competitive access strategies worldwide, five imperatives emerge for manufacturers looking to achieve durable, payer-aligned success.

1. Prioritize Within a Broader Evidence Story

Overall survival (OS) remains the clearest signal of meaningful patient benefit, a standard reinforced by the 2025 FDA draft guidance prioritizing OS in randomized oncology trials. Yet payers increasingly evaluate OS within a wider evidence mosaic: durability of response, real-world effectiveness, and total-cost implications.

For payers, OS remains foundational, but true confidence comes when that survival signal is supported by a constellation of reinforcing endpoints. Biopharmaceutical manufacturers must demonstrate that clinical benefit is sustained and robust — unconfounded by crossover or subsequent therapy effects — and accompanied by improved time on therapy, event-free survival, and quality-of-life outcomes. Together, these metrics help payers translate efficacy into predictable, defensible value.

2. Simplify the Safety Story: Managing Financial and Clinical Risk

ADCs have advanced dramatically, yet perceived complexity in their adverse-event profiles remains a barrier to market access. Payers view manageable toxicity not only as a safety issue but as a cost-containment and compliance factor.

Clear, evidence-backed narratives that demonstrate a predictable, low-variation toxicity profile build confidence, especially for known class effects such as interstitial lung disease, neuropathy, or neutropenia. The goal is to prove that the ADC's adverse events are both anticipated and manageable within existing physician networks and treatment pathways. A simplified, transparent safety story accelerates provider confidence and reduces the cost risk associated with acute-care interventions, hospitalizations, and emergency visits tied to severe, unmanaged toxicities.

> Safety concerns, including dose selection and toxicity, can derail ADC development programs. Learn more in our white paper by Nicholas Richardson, DO, MPH, Precision for Medicine's VP of Clinical Development and former FDA Deputy Director of the Division of Hematologic Malignancies 2

3. Design Trials for Access: The Payer-Rationalized Approach

Regulatory approval is only the beginning. Payer hesitation post-approval often stems from trial designs that fail to address their most fundamental questions. Access by Design — or payer-rationalized clinical trial design — means selecting credible comparators and patient populations that reflect where the ADC will be used in practice.

This alignment is essential for achieving timely inclusion in NCCN Guidelines and other compendia, which remain the non-negotiable foundation for coverage in the U.S. Designing trials to secure such compendia status ensures that the evidence base is directly relevant to payer populations and the treatment pathways used by their provider networks. Real-world evidence can further reinforce compendia listings and close the gap between trial efficacy and real-world effectiveness.

Across payers, policy updates for ADCs frequently occur in direct response to changes in FDA labeling or National Comprehensive Cancer Network (NCCN) compendia. When evidence packages are timed so that guideline updates coincide with launch, coverage language tends to expand more rapidly and with fewer exceptions. This underscores why designing trials around credible comparators and guideline-relevant endpoints is central to Access by Design.

4. Define Place in Pathway and Sequencing Clarity

As ADCs shift into earlier lines of therapy, payers require clear, prospective sequencing models. A health plan's medical director must understand precisely where an ADC fits within the immuno-oncology or targeted-therapy landscape and, crucially, what the most cost-effective next step is when a patient progresses.

> ADCs as front-line therapies have the potential to revolutionize oncology treatment. Learn the key takeaways for moving your ADC to the front line in our white paper by Harpreet Singh, MD, Precision for Medicine's Chief Medical Officer and former Director of the FDA's Division of Oncology 2.

Thoughtful pathway modeling that integrates biomarker eligibility, anticipated resistance mechanisms, and total cost implications strengthens both coverage and clinician adoption. When sequencing is defined up front, it prevents off-pathway utilization, supports formulary placement, and aligns the ADC's role with formalized clinical pathways increasingly used by national payers.

5. Anticipate Operational and Site-of-Care Barriers

Access is operationalized within the health system, and payers remain highly sensitive to site-of-care costs. Biopharmaceutical manufacturers must account for physician preferences and the cost differential between community oncology clinics and academic centers of excellence. The value proposition should demonstrate support for treatment in the most appropriate, cost-efficient setting.

Operational readiness also means full preparedness in diagnostic testing, provider training, and supply-chain stability. Proactive investment in these enablers signals a mature, reliable partner to payers and mitigates operational risks that lead to treatment delays, denials, or appeal cycles.

Closing Takeaway

Over 25 years, ADCs have redefined how precision and potency coexist in oncology. The next era will be defined by how effectively manufacturers align innovation with payer reality. Success will depend not only on molecular precision but on market precision — delivering unconfounded overall survival, clear safety narratives, and proven operational readiness that manage payer risk and ensure every eligible patient benefits from the science that has come so far.

At Precision, we remain committed to helping biopharma partners translate breakthrough science into equitable, sustainable access, bridging innovation and impact for patients worldwide.

About the Authors

Greg Gregory, PhD: Greg is a life sciences veteran with a passion for transforming commercialization strategies. With decades of experience in pricing, market access, and patient support services, he's a trusted advisor to both start-ups and top pharmaceutical companies. Known for his expertise in rare diseases, orphan drugs, and vaccines, Greg partners with executives to turn big ideas into commercial success, driving innovation every step of the way.

Cherry Moldovan, PhD: Cherry is Director of Strategic Consulting at Precision AQ, with years of experience advising leading pharmaceutical and biotech companies. She specializes in commercial strategy and market access, with expertise across therapeutic areas including oncology, hematology, rare diseases, nephrology, autoimmune, respiratory, and cardiovascular conditions.

Cherry has guided clients through a wide range of initiatives spanning clinical development and post-approval commercialization. Her experience includes launch sequence optimization, pricing and market access strategy, value communication and messaging, payer and provider contracting, life cycle and loss-of-exclusivity planning, innovative contracting models, and clinical advisory boards for strategic program planning.