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BIOCONJUGATE INSIGHTS

SPOTLIGHT

From bench to bedside:
translating ADCs into the clinic

BIOCONJUGATE INSIGHTS

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BIOCONJUGATE INSIGHTS

FROM BENCH TO BEDSIDE:
TRANSLATING ADCs INTO THE CLINIC

SPOTLIGHT

Defining immune-active mechanisms of PDL1V in translational ADC development

Megan Atkins

INTERVIEW

"Our observation of synergistic antitumor activity at multiple nonclinical doses supports that PDL1V allows the functional activation and trafficking of PD-L1-positive cytotoxic immune cells within a wide therapeutic window."

Lauren Coyle (Launch Commissioning Editor, *Bioconjugate Insights*) speaks with Megan Atkins (Senior Scientist, Translational Pharmacology, Pfizer) about advancing PDL1V from non-clinical characterization to pivotal trials, and how deeper immune profiling is reshaping the future of immune-active ADCs.

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Q You have been deeply involved in advancing ADC translational pharmacology. Could you start by sharing what drew you into the field and how your current work on PDL1V fits into the broader bioconjugation field?

MA Right now, the statistics show that roughly one in two men and one in three women will develop cancer in their lifetime [1], and those numbers seem to be increasing. I am not sure that I have ever met someone who has not been impacted by cancer, either directly or indirectly. We have friends, family, and colleagues who develop cancer, and there is this irony of developing anti-cancer therapeutics and still not being impervious to it. Enabling better bench-to-bedside translation and getting cancer therapeutics to patients that work is the driving factor. For me, and probably for most of my colleagues and people in the industry, that is the primary motivation.

My current non-clinical work contributes to our understanding of the direct and indirect mechanisms of action of PDL1V that drive anti-tumor efficacy in patients. Now that PDL1V has initiated pivotal clinical trials [2], this is critical reverse translation work to identify additional responsive patient populations and inform combination approaches clinically.

Q PDL1V represents a distinctive approach to targeting PD-L1 with a vedotin. What were the key scientific questions you aimed to answer through the non-clinical characterization of PDL1V, and how did you design your studies to address them?

MA PDL1V was the first ADC specifically designed to target PD-L1 that advanced into clinical trials. It was a pioneering step in targeted immuno-oncology therapies, as there was no other PD-L1-directed ADC to serve as a benchmark.

While the PD-L1 expression profile is not significantly different from that of other tumor-associated antigens targeted by ADCs in the clinic, as a known immune checkpoint protein it has unique immunomodulatory biology.

Once the vedotin modality was chosen, the early nonclinical questions we addressed were: Can we address immune-related safety concerns and enhance the internalization and potency through validated antibody engineering? We addressed these questions by generating positive specificity, internalization, tumor-directed cytotoxicity, and Fc effector function data.

Given the heterogeneity of PD-L1 expression in patients' tumors, we also characterized the nonclinical potency of PDL1V across a broad range of PD-L1-expressing models, and its potential for the hallmark mechanisms of other clinically validated vedotin ADCs (e.g. bystander killing, immunogenic cell death).

After establishing a non-clinical data package that validated primary vedotin-driven mechanisms, we then pivoted to the safety and functional effects of PDL1V on immune cells. That is a focus of our ongoing work – building on those findings and exploring the connection that PDL1V spans between targeted cytotoxicity and its immunomodulatory anti-tumor mechanisms.

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Q Your work explores PDL1V's dual impact on immunosuppressive and immunoresponsive cells in the periphery and the TME. What were some of the most revealing findings from these investigations, and how did they expand our understanding of ADC – immune system interplay?

MA One of our primary findings was that PDL1V preferentially targets PD-L1-expressing regulatory T cells, which have been extensively implicated in dampening anti-tumor immunity in patients with solid tumors.

Targeted depletion of Tregs by PDL1V provides an additional immunomodulatory anti-tumor mechanism wherein the TME is essentially reprogrammed through targeted diminishing of immunosuppressive signaling. This non-clinical finding was particularly timely given that the 2025 Nobel Prize in Medicine was just awarded to the investigators who discovered and characterized the role of FOXP3-positive Tregs in immune tolerance.

Another key finding from our non-clinical evaluations has been the interplay between MDR1 drug efflux pumps and how integral they are to the tolerability of PD-L1-positive immune cells to PDL1V. MDR1 drug efflux has been well characterized historically as a mechanism of tumor cell resistance to ADCs. In recent years, researchers have drilled down on MDR1 expression and activity in immune cells, particularly cytotoxic T lymphocytes, showing it plays a multifaceted role. Not only is it involved in drug efflux out of the cell, whether in tumor or immune cells, but it also mediates drug sequestration inside the cell in various compartments and acts as a functional differentiation switch for immune cells such as monocyte-derived dendritic cells. We found that activated CD4 and CD8 positive T cells are highly resistant to the cytotoxic effects of PDL1V despite expressing high levels of cell-surface PD-L1. We've generated additional nonclinical data demonstrating that resistance is driven, at least in large part, by MDR1 drug efflux pump activity.

Collectively, we believe our findings position PDL1V in a new class of rationally engineered ADCs which employ not only the classical mechanisms of action (MOA) of vedotin ADCs (e.g. direct tumor debulking and immune activation through immunogenic cell death), but additional target biology-driven MOAs to reprogram a patient's tumor microenvironment by leveraging and modulating the immune compartment as well.

Q From a translational perspective, how are the mechanistic data from your non-clinical studies shaping hypotheses for clinical design – particularly dose optimization, safety margins, and combination strategies?

MA Given the solid tumor indications being evaluated clinically, the ability of PDL1V to induce immunogenic cell death preclinically, and our findings that PDL1V spares healthy T cells and antigen-presenting cells from targeted cytotoxicity, PDL1V is able to rationally combine with checkpoint inhibitors, specifically anti-PD-1s. Our nonclinical findings that PDL1V synergizes with anti-PD-1 *in vivo* gave us further confidence in clinically combining with Pembrolizumab. Our observation of synergistic antitumor activity at multiple nonclinical doses supports

"Computational modeling and systems immunology can simulate ADC–immune interactions and predict outcomes across diverse tumor microenvironments."

that PDL1V allows the functional activation and trafficking of PD-L1-positive cytotoxic immune cells within a wide therapeutic window.

Q What do your findings suggest about the importance of integrating immune profiling into ADC development pipelines more broadly? Are there specific translational approaches or analytical tools that could accelerate bench-to-bedside translation?

MA As the efficacy and MOAs of PDL1V evolve, our non-clinical investigation is increasingly focusing on the immunomodulatory interactions with the patient's immune system. Incorporating immune profiling earlier in bioconjugate development will become essential for understanding the full therapeutic potential of these molecules. It could also help improve clinical trial design.

Computational modeling and systems immunology can simulate ADC–immune interactions and predict outcomes across diverse tumor microenvironments. I think single-cell RNA sequencing can improve our understanding of immune-activating potential and should be incorporated into in vivo pharmacodynamic analyses whenever possible, as it enables high-resolution mapping of immune cell prevalence and functional states across multiple immune compartments within the model.

Spatial transcriptomics and multiplexed IHC provide a visual of cell-to-cell target expression, interactions, payload distribution, and immune infiltration within the spatial context of the TME. Many companies and labs are improving their *in vitro* and *in vivo* patient-derived tumor models by incorporating tumors with established standard-of-care drug and ADC resistance or tumors with known actionable genomic alterations. Those models should also be incorporated early whenever possible.

Q As the field moves toward increasingly immune-active ADCs, how do you envision the next phase of translational pharmacology evolving? What scientific or technological advances will most influence how we design and interpret early clinical studies?

MA Translational pharmacology is evolving to incorporate more integrated, systemic-level models that provide a deeper understanding of ADC interactions with the patient's immune system, spanning beyond antigen targeting, payload potency, and exposure alone. I can see computational modeling and AI-driven analytical models trained on multi-omic data to enable more predictive modeling of ADC behavior both non-clinically and in patients. Non-clinical functional immunoassays are also improving over time. Modeling early nonclinical learnings on immune cell localization,

activation, suppression, antigen presentation, cytokine release, etc. alongside clinical biomarker data, will only help us to continue bridging the gap between bench and bedside.

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BIOGRAPHY

Megan Atkins is a Senior Scientist at Pfizer, working within the Oncology Research and Development Unit since 2023. Before Pfizer's acquisition of Seagen in 2023, she held an R&D role at Seagen starting in 2019. Megan's earlier experience includes serving as a research technician at Fred Hutch, where she focused on hematopoiesis in non-human primates and murine models, as well as adapting gene therapies for anti-HIV biologics. She also worked at Nektar Therapeutics as an intern and research associate, where she designed immunohistochemical protocols for c-Fos biomarker detection and examined protein localization. Megan earned her Bachelor of Science in Biology from Old Dominion University, Norfolk, VA, USA, and a Master of Science in Biotechnology from Johns Hopkins University, Baltimore, MD, USA.

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FROM BENCH TO BEDSIDE:
TRANSLATING ADCs INTO THE CLINIC

SPOTLIGHT

Crossing the ADC inflection points: what separates clinical success from failure

Antoine Yver

INTERVIEW

"Drug development is not a race to be first; it is a race to win. History is full of examples where being first did not matter, but being right did."

Lauren Coyle, Launch Commissioning Editor, *Bioconjugate Insights*, speaks with Antoine Yver, Board Chair, Ona Therapeutics, with more than three and a half decades of experience shaping global cancer drug development. In this conversation, they explore what determines whether an ADC successfully crosses the critical threshold and how teams should rethink dose finding, toxicity, and what it truly takes to set a program up for long-term success in the clinic.

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"For cytotoxic ADCs, what matters is not progression-free survival, which is highly dependent on patient selection, but objective and durable tumor response."

Q You have led multiple oncology programs from discovery to approval. What do you see as the most critical translational inflection points, when looking specifically at ADCs, that determine whether a molecule successfully crosses the 'bench-to-bedside' threshold?

AY There are two major inflection points, and while they may sound obvious, the details are everything. The first is the non-clinical package. Many people still underestimate how predictive this phase can be if it is done rigorously. I described previously in my work, what became known as the seven key characteristics of ADCs, and these continue to hold true today. These include drug–antibody ratio (DAR), payload mechanism, potency, stability in serum and aggregation behavior, bystander effect, linker selectivity, and short systemic half-life of the payload.

What matters is not simply optimizing these parameters in isolation but using them to define what makes an ADC uniquely capable of addressing an unmet medical need. If the molecule is slightly different without being meaningfully better, you are essentially building a 'me-too late drug'. True success comes from being either genuinely best-in-class, such as ENHERTU compared to KADCYLA, or first-in-class. In either case, the characteristics should be assessed and defined to what you are looking for. Additionally, if you have any flags that are being raised, particularly with manufacturing, it is key to have a handle on this to cross the bridge from bench-to-bedside.

The second inflection point is first-in-human. For cytotoxic ADCs, what matters is not progression-free survival, which is highly dependent on patient selection, but objective and durable tumor response. ADCs, when they work, tend to deliver deep and durable responses. At this stage, understanding exposure–response relationships, pharmacokinetics/pharmacodynamics (PK/PD), and safety modeling is essential. Once you have that first-in-human data, you are no longer guessing, you can declare whether you truly have a drug.

Q ADCs often present atypical toxicity profiles and non-linear response kinetics. How should early development teams rethink dose-finding and safety management strategies to avoid applying conventional monoclonal antibody or small-molecule paradigms that simply don't fit?

AY This is a complex question, but several core principles can guide early ADC development. The first principle is not to assume the mechanism of action (MoA) is fully understood simply because a target has been identified. A true understanding of MoA extends beyond target binding and includes intracellular trafficking, payload release, spatial and temporal drug distribution, and bystander

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effects. Extensive work from studies such as the DAISY trial and the ICARUS program demonstrated how ADCs interact with receptors, how payloads are released, and how neighboring cells are affected and play a role.

These studies explained why drugs like trastuzumab deruxtecan (Enhertu) could work in HER2-low breast cancer or HER2-mutant lung cancer, even when receptor expression is not detectable by conventional immunohistochemistry. At the same time, they also explained failures, such as when mechanisms were misunderstood, and drugs were developed based on incorrect assumptions.

Conversely, incomplete understanding of MoA can negatively impact development. For example, certain ADCs function less as classical targeted conjugates and more as depot delivery systems with sustained payload release and intermittent intratumoral boosts. When these mechanisms are not recognized early, clinical development strategies may fail to sustain efficacy across tumor types, despite promising initial assumptions. A robust and continuously evolving understanding of MoA is therefore essential.

Second, you must align pharmacology with the clinical need. A good example is the early HER2-low data with DS-8201. Based on deep pharmacologic understanding and early clinical signals, it was understood early on, with as little as 23 subjects worth of data in the first-in-human study, that this drug would be transformative, long before POC or confirmatory trials were completed, or even underway.

Third, development should focus less on traditional dose finding and more on dose justification. Dose justification is significantly more important than simply identifying a maximum tolerated dose. Dose justification continues throughout pivotal development up to submission for approval.

I often describe this through six pillars of drug development:

1. **Defining the effect:** clearly establish the therapeutic efficacy by aligning pharmacology with unmet clinical need and defining how the effect will be measured
2. **Reproducibility:** demonstrating that the observed effect can be reliably reproduced, which may enable regulatory approval even with limited datasets if robustness is clear.
3. **Safety understanding:** treat a sufficient number of patients to enable prediction of real-world safety profiles.
4. **Justifying the dose:** focus on dose justification rather than dose finding alone. Dose justification remains an ongoing process that continues alongside pivotal trials and is more critical for regulatory success than identifying a single 'optimal' dose.
5. **Experience with the product:** ensure that the final, market-intended CMC product is evaluated in humans, typically in a defined subset of patients.
6. **Building robust CMC bridges:** establish appropriate bridging between non-clinical material, early clinical versions, and the final commercial formulation.

Notably, clinical phase labels, such as Phase 1, 2, or 3, and classical dose-finding frameworks are largely irrelevant if these pillars are properly addressed. To me, the distinction between Phase 1, 2, or 3 is less important than ensuring that efficacy, safety, dose justification, and product relevance are addressed in parallel. Conventional dose-finding

"Ultimately, there is no shortcut. You must understand your mechanism, demonstrate the durability of effect, and show that your drug does something meaningfully different. That is how you de-risk development and make confident decisions."

paradigms are insufficient on their own and should not dominate early ADC development strategies.

Q As payloads diversify and mechanisms evolve, what do you consider the most appropriate early clinical endpoints to convincingly demonstrate mechanistic value and accelerate early go/no-go decisions?

AY It always comes back to selecting the right patient. Go/no-go decisions depend on how well your pharmacology aligns with a defined patient population. The construct should address a clearly defined biological context, with patient selection strategies aligned to that context. In those cases, you must acquire tissue, perform deep translational analyses, and learn along the way. TROP2 is a good example where early expression assays did not correlate clearly with clinical response. In such scenarios, it becomes especially important to collect biopsies and generate the translational evidence required to understand which features, beyond target expression, predict response.

A similar principle applies to HER3. In this setting, target engagement and receptor dynamics may vary between the first and subsequent treatment cycles, influencing apparent exposure-response relationships and clinical activity. This highlights the limitations of relying on single-timepoint expression measurements and supports the use of endpoints and biomarker strategies.

Go/no-go decisions, and the endpoints used to support them, should be grounded in pharmacology and mechanism rather than in target expression. Demonstration of effect remains necessary, but durability of effect and mechanistic plausibility are equally important, particularly when the therapeutic concept differs meaningfully from existing approaches. Early development should prioritize endpoints that enable de-risking through evidence of biological activity, clinical signal, and consistency with the proposed mechanism.

The development pathway for HER3-directed ADCs illustrates this point. Although progress initially appeared similar to that of HER2-directed programs, the timeline to market was longer, and the intended clinical positioning evolved. Non-clinical development initially emphasized breast cancer, however, the first approval was achieved in lung cancer, reflecting stronger alignment between pharmacology and disease biology, particularly the interaction with EGFR, receptor expression patterns, prior TKI use, and unmet clinical need.

Ultimately, there is no shortcut. You must understand your mechanism, demonstrate the durability of effect, and show that your drug does something meaningfully different. That is how you de-risk development and make confident decisions.

Q For modern ADCs, what level of biomarker maturity or target-expression characterization is truly required before entering first-in-human studies?

AY The level of biomarker maturity must match your understanding of pharmacology. If non-clinical work cannot fully answer the question, then human translational studies become essential. This means collecting biopsies, performing pre- and post-treatment analyses, and investing in translational science early. If you do not do this work, you risk running large trials without truly understanding what you are testing. This is one reason why so many ADC programs fail late.

Before entry into first-in-human studies, and especially before advancing beyond early clinical exploration, there is limited value in relying on target expression alone. There is simply no escape from deeply understanding your biology and aligning it with your development strategy.

Q Preparing an IND for a first-in-class ADC places enormous pressure on analytical, CMC, and scalability planning. From your experience, what defines 'IND-readiness,' and what common CMC missteps most often jeopardize smooth progression into GMP manufacturing?

AY These challenges are not specific to ADCs. When a compound is a true drug candidate, one with the potential to move quickly and achieve accelerated approval, CMC becomes the rate-limiting factor. This has been observed across multiple programs, including small molecules and biologics.

For example, in the case of a small-molecule TKI, the time from first dose in humans to US approval was two years and eight months, the fastest on record. In that program, the timing of submission and approval was entirely driven by CMC considerations, specifically scale-up and the availability of stability data. The product was launched with only three months of shelf life, showing how tightly CMC constrained timelines.

A similar situation occurred with an ADC program. At the time of joining the Daiichi Sankyo team in early 2016, only a small number of patients had been treated in the first-in-human study (n=5) , and the program was deprioritized. Other products were already in Phase 3, and the ADC was planned for submission 8 years later. At that time, industry-wide confidence in ADCs was low, with several companies reducing investment after failing to achieve meaningful breakthroughs.

Within months, however, emerging clinical data became compelling. Our ESMO late-breaking abstract was accepted based on a limited patient dataset, even after the formal submission deadline. Following this, company leadership was informed that the compound had clear drug potential and that the timing of approval would be dictated almost entirely by the ability to scale manufacturing and generate the required CMC data.

At that point, the manufacturing plan was misaligned with the new clinical reality. Production was projected to deliver a limited number of clinical-grade vials, around 90,000, several years later, which was consistent with a 'slow' development trajectory. In contrast, commercial readiness required production on the order of two million vials

at commercial grade, with a manufacturing cycle of approximately 12 months from raw materials to product release.

The critical decision was to invest decisively and early. Substantial capital was committed within a very short timeframe to enable scale-up and stability generation. This allowed the program to progress rapidly, culminating in submission less than three years after first-in-human dosing and approval shortly after. The program became one of the fastest biologics approvals on record.

The key lesson is that lack of boldness in CMC planning is the most common misstep. Failure to recognize how completely CMC drives approval timelines can critically delay development. IND readiness is not simply a technical milestone, but a strategic commitment. Significant investment and effort are required, but the lesson is simple: once you de-risk first-in-human and you know you have a drug, you must fully commit. Hesitation at this stage is what delays or kills programs.

Q Translating ADCs into the clinic increasingly requires seamless integration of discovery workflows with GMP-compatible conjugation and scale up. What operational principles or lessons learned from past programs do you believe are essential for avoiding delays at this transition point?

AY The operational principles are relatively simple and well understood, but they are often overlooked due to the pressure to move quickly. The first and most important principle is that there must be real closeness between discovery, early development, and CMC teams. This includes both physical and leadership-level proximity between discovery teams working with research-grade drug substance, early clinical teams, and CMC groups responsible for process development and scale-up. The transition cannot be managed as a handoff; you cannot throw a molecule over the fence and expect success.

Second, which is frequently underestimated, is the importance of taking the time to get the construct right. Drug development is not a race to be first; it is a race to win. History is full of examples where being first did not matter, but being right did. In the development of a leading EGFR inhibitor, competing programmes were several months ahead. However, additional time spent during drug design and early candidate development allowed elimination of a specific receptor-mediated effect that later proved critical. One competing programme experienced severe metabolic toxicity, leading to high discontinuation rates and failure to achieve approval. Similar patterns have been seen repeatedly across oncology development: being first does not guarantee success, as illustrated by multiple high-profile competitive dynamics.

If you take the time early to build the right molecule and de-risk it properly, you can move extremely fast later. Cutting corners early almost always slows you down in the end.

"The first and most important principal is that there must be real closeness between discovery, early development, and CMC teams"

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Q What single innovation, whether technical, biological, or regulatory, would most profoundly improve the success rates of ADCs entering the clinic over the next decade?

AY Rather than naming a specific technology, I would focus on principles. Only pursue programs that are truly best in class or meaningfully first-in-class. Being different is not enough. Innovation must be clinically relevant.

Second, maintain a laser focus on what makes your drug unique. Do not chase big market numbers; they are almost always wrong. The most successful drugs were often underestimated early on.

Success rates improve when teams are disciplined, focused, and honest about what truly differentiates their molecule. That focus, more than any single innovation, is what drives long-term success.

BIOGRAPHY

Antoine Yver is an accomplished oncology leader and physician–scientist with more than three decades of experience shaping global cancer drug development. Over his career, he has led or contributed to the approval of multiple transformative therapies, including osimertinib and trastuzumab deruxtecan (ENHERTU®), and has been instrumental in building some of the most successful oncology portfolios in the industry. Formerly Head of Global Oncology R&D at Daiichi Sankyo and senior executive at AstraZeneca, Dr Yver has a track record of driving innovation, forging landmark ADC partnerships, and delivering life-changing treatments to patients. Today, he serves on several boards and scientific committees, including Sanofi, Duality Biologics, D3 Bio, and Ona Therapeutics, where he continues to mentor and guide the next generation of biotech innovators. Trained as a pediatric oncologist and immunologist in Paris, he combines deep medical expertise with strategic vision and an unwavering commitment to improving patient outcomes.

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You can also listen to the recorded podcast here:

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INNOVATOR INSIGHT

Regulatory and CMC considerations for next-generation antibody drug conjugates

Nathan C Ihle and Rakesh Dixit

PANEL

"The next generation of ADC success will depend not only on innovative payloads and linkers, but also on robust, science-driven development strategies..."

ADCs are undergoing rapid diversification. While highly potent cytotoxic payloads largely define ADCs, the field is now expanding to include immune agonists, metabolic modulators, radio-conjugates, and other non-cytotoxic modalities. This evolution is opening new therapeutic opportunities, but it is also exposing gaps in existing regulatory frameworks and CMC strategies that were largely built around classical cytotoxic conjugates.

In this expert Q&A, *Bioconjugate Insights* brings together perspectives from industry leaders to explore whether current global regulatory guidance remains fit for purpose, how sponsors can navigate ambiguity across development and submission, and what lessons from earlier ADC generations should inform the next wave of innovation.

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Q As ADC technology diversifies beyond traditional cytotoxic payloads, are current regulatory frameworks fit for purpose?

RD Despite some of the gaps that are becoming increasingly apparent, the current regulatory framework is reasonably fit for purpose, provided it is applied with a strong mechanistic and risk-based justification. Existing guidance, including ICH quality guidelines and nonclinical frameworks for ADCs and combination products, offers a solid starting point.

However, these frameworks were primarily developed with cytotoxic ADCs in consideration and do not sufficiently address non-cytotoxic modalities, such as immune-stimulating conjugates, enzyme-modulating payloads, cytokine fusions, metabolic modulators, small interfering RNA (siRNA) conjugates, or radioconjugates. These emerging platforms rely heavily on immune modulation rather than direct cytotoxicity, and that distinction has profound implications for both safety assessment and dose selection.

From my perspective, there is a clear need for either a new regulatory framework or meaningful adaptations to existing guidance to better address non-cytotoxic ADCs. We have already seen serious consequences when cytotoxic paradigms were applied inappropriately, including a fatal outcome in a first-in-human study of an immune agonist ADC. That case demonstrated that dose-selection principles developed for cytotoxic payloads simply do not translate to potent immune agonists.

NCI I agree that these emerging modalities introduce fundamentally different risk profiles. The more developers and regulators can focus on the underlying science of each specific modality, the better positioned we will be to identify the true areas of highest risk. Relying solely on tools and assumptions developed for cytotoxic ADCs is unlikely to be sufficient.

From a manufacturing perspective, new modalities also introduce differences in chemistry, conjugation, and facility requirements. Some non-cytotoxic ADCs may allow relaxation of certain containment expectations that were driven by highly potent cytotoxins. That said, for immune-stimulatory conjugates, product carryover and impurity control remain critical, and complacency would be dangerous.

Q How can companies best engage regulators early to clarify expectations for linker, payload, and biologic control strategies?

NCI Early regulatory interaction is critical, particularly when developing novel ADC modalities. Traditional pre-IND interactions can be valuable, but they are often high-stakes and time-limited, which can make deep scientific discussion challenging.

One effective approach has been engagement through scientific conferences and workshops that involve both industry and regulators. These settings allow for open, science-driven dialogue and real-time feedback. Unfortunately, regulator participation in such forums has become more limited in recent years, which is a missed opportunity for the field.

Another important mechanism is the development of industry-led scientific white papers and position papers that articulate emerging best practices. While these typically

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"Ultimately, regulators expect sponsors to own the scientific understanding of their molecule and to propose solutions..."

appear later in a technology's lifecycle, they can play an important role in harmonizing both industry approaches and global regulatory expectations.

RD From my experience, having worked extensively with regulatory agencies, early scientific advice meetings can be extremely valuable, whether with the US FDA or the EMA. However, sponsors must approach these interactions with a clear and focused strategy.

It is important to note that regulators are not consultants. Interactive meetings allow only a limited scope of discussion, so companies must come prepared with a strong understanding of their molecule, its mechanism of action, and a proposed control strategy. It is essential to clearly articulate which component of the ADC is driving efficacy and which elements contribute most significantly to safety risk.

For example, free payload and process-related impurities require careful justification, particularly when dealing with genotoxic compounds. While genotoxic payloads may be acceptable in oncology settings, the same assumptions may not apply in non-oncology indications. Sponsors should present a draft impurity control strategy, supported by genotoxic risk assessment and mechanistic rationale.

Well-prepared sponsors who ask targeted questions tend to receive far more useful feedback than those who present long lists of unfocused queries. Ultimately, regulators expect sponsors to own the scientific understanding of their molecule and to propose solutions, rather than asking agencies to define them.

Q What are the most common CMC challenges across the ADC lifecycle, and how can teams proactively design robust processes?

RD One of the most persistent challenges is conjugation variability, particularly heterogeneity in drug-antibody ratio (DAR). This is sometimes treated as a secondary issue in early development, but it often becomes a major problem during scale-up. High-resolution analytical methods and early exposure–response modeling are essential to understanding and controlling DAR distribution from the outset.

Another common weakness is insufficient characterization of linker–payload stability. Platform linkers are often reused without fully understanding how they interact with a specific payload or antibody. This can lead to unexpected instability or off-target release later in development.

Process robustness should also be taken into consideration. Conditions such as pH, temperature, and molar ratios must be well understood and controlled, particularly as programs move from gram-scale material for early studies to large-scale GMP production. Analytical methods must be fit for purpose and capable of detecting subtle but clinically meaningful changes in product quality.

NCI A deep understanding of critical quality attributes is fundamental. Average DAR, DAR distribution, and conjugation consistency are all central to

"Benefit–risk for the patient must remain the guiding principle..."

product performance. Classical process characterization studies remain the most effective way to build this understanding.

Importantly, this knowledge develops over time. Early-phase manufacturing will not provide complete insight, but data must be collected continuously throughout development. Teams that delay process understanding until late stages often struggle during validation and commercialization. As understanding improves, some early control assumptions may prove overly conservative. This can allow rational simplification of control strategies, which is beneficial as programs move toward commercial manufacturing.

Q Are lessons from first-generation ADCs still relevant for next-generation platforms?

NCI Many foundational principles remain relevant, but they must be applied with flexibility. Cytotoxic ADCs established a framework, but immune-stimulating conjugates and other novel payloads require evaluation through a different lens. Developers must continuously reassess assumptions based on the mechanism of action, linker chemistry, and payload class.

There is no universal solution. Benefit–risk for the patient must remain the guiding principle, and developers must critically evaluate whether a given technology genuinely improves that balance or simply adds complexity.

RD Looking back over the evolution of ADCs, early-generation products underperformed largely as conjugation and linker technologies had not yet been optimized. Subsequent advances demonstrated that linker stability and payload selection are decisive factors in clinical success.

Comparisons between earlier and more recent HER2-targeted ADCs clearly illustrate how improvements in linker–payload design and DAR optimization can dramatically enhance therapeutic outcomes. These lessons remain highly relevant, but they must be adapted to the specific risks of newer payload classes.

Different payloads demand different strategies. Radioconjugates, immune agonists, and moderately potent cytotoxins each require tailored linker design, dosing strategies, and toxicity mitigation plans. There is no justification for assuming that one conjugation approach will suit all modalities.

Q How do regional regulatory differences affect global ADC development strategies?

RD Global development requires a truly global regulatory strategy. Although international guidelines exist, their interpretation can vary significantly between regions. Differences in nonclinical expectations, impurity tolerance, and study design requirements can create substantial challenges.

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Sponsors must understand these regional nuances early and plan accordingly. A conservative approach that meets the highest regulatory bar may increase upfront cost and time, but it often prevents far more serious delays later, such as clinical holds or rejected submissions.

NCI While global harmonization has improved, differences in interpretation remain inevitable. One practical approach is to develop to the strictest applicable guideline, even if that means exceeding requirements in some regions.

Industry-wide sharing of best practices through publications and collaborative initiatives can also help. Educating reviewers, particularly those early in their careers, is essential for fostering consistency in regulatory decision-making.

CLOSING REMARKS

As ADC technologies continue to evolve, the field is moving beyond the regulatory and CMC paradigms that shaped first-generation cytotoxic conjugates. Non-cytotoxic and immune-modulating ADCs offer significant promise, but they also demand deeper scientific understanding, more nuanced risk assessment, and earlier, more strategic engagement with regulators.

The next generation of ADC success will depend not only on innovative payloads and linkers, but also on robust, science-driven development strategies that align regulatory expectations with the true biology of these complex therapeutics.

BIOGRAPHIES

Nathan C Ihle is a leading expert in antibody-drug conjugate (ADC) research and development. His work centers on advancing targeted therapies, focusing on the design, optimization, and development of novel ADCs. With over 20 years of experience with ADCs, Dr Ihle has played a key leadership role in the development of six approved and numerous clinical-stage ADCs from discovery through commercialization. He is widely recognized for his scientific rigor, cross-functional collaboration, and strategic insight in biologics R&D. Currently, he serves as Founder and Principal Consultant at Ihle CMC Solutions, supporting the next generation of bioconjugates and novel therapeutics.

Nathan C Ihle, Founder and Principal Consultant, Ihle CMC Solutions

Rakesh Dixit is Cofounder, President, and CSO of Regio Biosciences, a spin-off of AstraZeneca, focused on developing therapies to reduce plaque burden and reverse cardiovascular disease. He is also President and CEO of BIONAVIGEN, a virtual drug development company. Previously, he was VP of Biologics Safety Assessment at AstraZeneca and held leadership roles at Merck, Johnson & Johnson, and MedImmune. Dixit played a pivotal role in developing ten marketed biopharmaceuticals and contributed to over 100 INDs and 15 BLA/NDA approvals. A recognized expert in bioconjugates, he has led the development of multiple ADC therapies, successfully filing INDs for over 10 ADC drugs. He has published 80+ papers, delivered 130+ global presentations, and received PharmaVoice's 100 Most Inspiring People award and the prestigious Long-Standing Contribution to ADCs award.

Rakesh Dixit, Cofounder, President, and CSO, Regio Biosciences; and CEO, BIONAVIGEN

AUTHORSHIP & CONFLICT OF INTEREST

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EVENT PREVIEW

Event preview of the 16th World ADC London Summit

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As ADCs continue to mature into established oncology modalities, the field faces a new set of scientific and translational challenges. Clinical saturation around established payload classes, emerging resistance mechanisms, and unmet medical needs are placing renewed emphasis on payload innovation, molecular design, and smarter clinical positioning to continue to deliver patient impact.

Returning in February 2026, the 16th World ADC London Summit convenes the global ADC community to address these challenges head-on, bringing together more than 110 speakers from Europe, North America, and Asia to explore how next-generation ADCs can be optimized for durability, tolerability, and earlier-line use. Spanning 4 days of scientific programming, seminars, and workshops, the meeting offers five parallel tracks covering discovery, preclinical and translational development, clinical lessons, process and analytical development, and manufacturing and supply chain.

DIFFERENTIATED PAYLOADS & ADC DESIGN FRONT & CENTER

As resistance to commonly used payload classes such as topoisomerase I inhibitors and tubulin agents becomes more apparent, the 2026 program places strong emphasis on differentiated payload mechanisms and novel ADC architectures. Sessions across the discovery and preclinical tracks explore non-cytotoxic payloads, dual payload conjugates, bispecific and biparatopic ADCs, and emerging non-antibody conjugate formats designed to widen therapeutic index and expand clinical utility.

Among the highlighted presentations, Ya-Chi Chen (Chief Scientific Officer, OBI Pharma) will discuss the development of bispecific, dual payload ADCs designed to deliver complementary mechanisms of action within a single molecule, to overcome tumor heterogeneity and resistance. Zhenwei Miao (Founder and Chairman, Adcoris Biopharma) will present on the rationale and preclinical development of dual payload ADCs targeting distinct resistance pathways, while Sam Murphy (Chief Executive Officer, Salubris Bio) will outline the translational development and early

clinical dose escalation of a biparatopic ADC targeting 5T4.

Additional sessions examine conditional activation technologies, novel linker-payload strategies, and emerging conjugation approaches aimed at improving safety and therapeutic index, reinforcing the meeting's focus on moving beyond incremental ADC optimization toward more fundamentally differentiated designs.

FIRST-TIME PRESENTING COMPANIES BRINGING FRESH PERSPECTIVES

The 16th World ADC London Summit also places deliberate emphasis on introducing new voices to the program. For the first time, companies including Adcoris Biopharma, ALX Oncology, Helix Biopharma, Radiance Biopharma, and Salubris Bio will present data and development strategies on the World ADC London stage. These contributions reflect the organizers' commitment to spotlighting emerging ADC programs and alternative development philosophies alongside more established pipelines.

Presentations from these first-time contributors span payload innovation, novel targeting strategies, and translational lessons learned from advancing differentiated ADCs toward the clinic. By integrating these perspectives into the broader scientific narrative, the conference aims to foster critical discussion around how smaller and mid-sized companies are navigating differentiation, capital efficiency, and clinical risk in an increasingly competitive ADC landscape.

EXPANDING THE ADC ECOSYSTEM: REGULATORS, CLINICIANS, & INVESTORS

In recognition of the increasingly interconnected nature of ADC development, the 2026 agenda broadens its speaker ecosystem to include greater representation from regulatory agencies, clinical experts, and the investment community. Regulatory perspectives are highlighted through sessions led by Christian Merz (Assessor, Non-Clinical and Quality, Antibody Therapeutics, Paul Ehrlich Institute), who

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will outline regulator expectations for ADC characterization, control strategies, and CMC submissions as conjugates grow more complex.

Clinical strategy is addressed through contributions from Paolo Tarantino (Clinical Research Fellow, Dana-Farber Cancer Institute), who will examine emerging real-world and clinical data on ADC sequencing and combination strategies, with a focus on optimizing patient outcomes as ADCs move into earlier treatment lines. Complementing these scientific discussions, the ADC Licensing, Partnering, and Investment session brings together investors and business development leaders to explore how differentiation, risk, and data maturity are shaping ADC deal-making in 2026 and beyond.

THE FUTURE OF ADC DEVELOPMENT

As ADCs transition from niche targeted therapies toward broader standards of care, the 16th World ADC London 2026 Summit provides a timely forum to assess how the field must evolve to sustain innovation. By combining deep technical discussions on payloads, design, and manufacturing with clinical, regulatory, and commercial perspectives, the meeting reflects the multidisciplinary reality of modern ADC development.

With its globally diverse faculty, strong emphasis on differentiated ADC innovation, and expanded stakeholder engagement, the 16th World ADC London 2026 Summit is positioned as a key gathering for scientists and strategists seeking to navigate the next phase of ADC maturation and unlock the full therapeutic potential of this rapidly advancing modality.

As a reader of *Bioconjugate Insights*, you're entitled to a 10% discount on delegate tickets – just use the discount code **BIOCXADC10**! You can find out more about the event **here**.

Want to know more about the journal or discuss a potential contribution? Come and chat to our editor, Lauren, who will be attending the summit, or drop an email to **lauren.coyle@insights.bio**.

INDUSTRY INSIGHTS • JANUARY 2026

Converging modalities drive the next wave of bioconjugate therapies

Lauren Coyle

As an editor with extensive experience in bioconjugation (i.e., ADCs, conjugate chemistry, diagnostics and imaging, bi/multi-specifics, targeted delivery, and theranostics), Lauren's focus is on advancing the field by facilitating and disseminating high-impact research on conjugation technologies and their applications. Lauren works closely with researchers, scientists, and industry professionals to publish cutting-edge studies exploring the latest advances in conjugation chemistry, drug delivery systems, and the development and delivery of targeted therapeutics. In addition to her editorial responsibilities, she maintains a strong network within the biopharma industry, staying up to date with emerging trends and breakthroughs in bioconjugation.

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SUMMARY

This month's updates highlighted continued momentum across ADCs, radioconjugates, and emerging conjugate modalities, underpinned by strategic partnerships, regulatory progress, and continued capital deployment.

Collaborations remained a central theme, as companies prioritized access to differentiated targets, payloads, and supply chains. Strategic alliances around radionuclide-drug conjugates and long-term isotope sourcing highlighted growing confidence in targeted radiotherapy and theranostics, while multiple ADC discovery and licensing deals emphasized bispecific formats, novel payloads, and tumor-penetrant designs.

Regulatory momentum was notable across the globe, with China advancing several next-generation ADC programs with IND clearances, while the US FDA supported innovation through Fast Track and Orphan Drug designations and continued rollout of its National Priority Voucher pilot. A major clinical inflection point came with the FDA's approval of trastuzumab deruxtecan plus pertuzumab as a first-line regimen in HER2-positive metastatic breast cancer, reinforcing ADCs as frontline standards. RNA interference also progressed, with multi-target GalNAc–siRNAs entering early clinical evaluation for cardiometabolic disease.

Market activity reflected sustained investor appetite for conjugate technologies.

Financing rounds supported DAC, surfaceome-driven ADC pipelines, and late-stage registrational studies, complemented by creative funding structures such as single-asset SPVs. Corporate rebranding, leadership appointments, and platform-focused pivots further signaled long-term commitment to conjugate-based innovation.

Clinically, the field saw a steady cadence of first-patient dosing and expansion decisions across HER2, HER3, ROR2, and Trop2 programs, alongside encouraging early efficacy signals in hard-to-treat solid tumors. Late-stage data continued to validate ADC–IO combinations, while preclinical research highlighted advances in tumor-activated delivery, precision radioconjugates, and selective targeting strategies. Collectively, these developments point to a rapidly diversifying and increasingly integrated bioconjugation ecosystem entering 2026.

COLLABORATION AND PARTNERSHIPS

Harbour BioMed entered strategic collaboration with Lannacheng to develop radionuclide drug conjugates [1]

Harbour BioMed announced a long-term strategic collaboration with Yantai Lannacheng Biotechnology to jointly advance the development of next-generation radionuclide-drug conjugates for oncology. The partnership combines Harbour BioMed's fully human antibody discovery capabilities, including its Harbour Mice® platform and heavy chain-only antibody technology, with Lannacheng's expertise in radiopharmaceutical research, radioisotope supply, linker design, and GMP manufacturing. The collaboration aims to develop targeted radiotherapies with potential theranostic applications, leveraging tumor-specific delivery of radionuclides to improve efficacy while limiting off-target toxicity. Lannacheng's integrated platform and infrastructure are expected to support scalable development and commercialization of radionuclide-drug conjugates candidates emerging from the collaboration.

Akari Therapeutics initiated GMP manufacturing for lead ADC AKTX-101 [2]

Akari Therapeutics announced the initiation of GMP manufacturing activities to support IND-enabling development of AKTX-101, its lead ADC program. The company selected WuXi XDC as its contract development and manufacturing organization to produce GMP-grade material for upcoming clinical studies. AKTX-101 incorporates Akari's proprietary PH1 payload, which is designed to modulate RNA splicing and provide combined cytotoxic and immuno-oncology (I-O) activity. The manufacturing campaign is intended to support a planned Phase 1 first-in-human trial, which Akari expects to initiate in late 2026 or early 2027, pending regulatory clearance. The collaboration establishes a strategic partnership between Akari and WuXi XDC for current and potential future ADC programs.

Ipsen licensed LRRC15-targeted ADC rights from Simcere Zaiming [3]

Ipsen announced a licensing agreement with Simcere Zaiming for rights outside Greater China to SIM0613, an investigational ADC targeting LRRC15. Under the terms of the deal, Simcere Zaiming is eligible to receive up to $1.06 billion in upfront,

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development, regulatory, and commercial milestone payments, along with tiered royalties on net sales. SIM0613 is designed to target LRRC15, a protein highly expressed on multiple tumor types and cancer-associated fibroblasts, with limited expression on normal tissues, and is engineered for enhanced tumor penetration. Ipsen will assume responsibility for manufacturing, clinical development, and regulatory activities outside Greater China. SIM0613 is expected to enter Phase 1 development in the second half of 2026.

Nona Biosciences and Valink Therapeutics formed bispecific antibody and ADC discovery alliance [4]

Nona Biosciences and Valink Therapeutics announced a strategic biologics discovery alliance to accelerate the development of bispecific antibodies and bispecific ADCs. The collaboration, branded 'Biology to Bispecific' (B2B)™, combines Nona's Harbour Mice® fully human antibody platforms, including heavy chain-only antibodies, with Valink's LiliumX™ discovery and screening technology. The alliance will initially focus on generating bispecific ADC candidates for solid tumors, with plans to expand Valink's internal pipeline and support future co-development and licensing opportunities. By integrating complementary antibody repertoires and high-throughput functional screening, the collaboration aims to enable rapid identification of novel target combinations and differentiated complex biologics.

Cellectar Biosciences entered multi-year radioisotope supply agreement with Ionetix [5]

Cellectar Biosciences announced a multi-year supply agreement with Ionetix Corporation to secure clinical- and commercial-scale supplies of the alpha-emitting radioisotopes actinium-225 and astatine-211. Under the agreement, Ionetix will provide cGMP-grade isotopes to support Cellectar's targeted alpha therapy programs through clinical development and potential commercialization. The supply will support expansion of Cellectar's radiotherapeutic pipeline, including its proprietary Phospholipid Drug Conjugate™ delivery platform, and advancement of CLR-225 into clinical trials for solid tumors such as pancreatic cancer.

Bicycle Therapeutics entered long-term agreements to secure lead-212 supply for radioconjugate development [6]

Bicycle Therapeutics announced a 15-year agreement with the UK Nuclear Decommissioning Authority for access to up to 400 tonnes of reprocessed uranium to support production of lead-212 for its radioconjugate programs. The company also entered a collaboration with the UK National Nuclear Laboratory to extract thorium-228 from the material, which will be further processed into radium-224 and used to generate lead-212 via a bespoke generator being developed with SpectronRx. The arrangements are intended to enable end-to-end discovery, development, and commercial supply of Bicycle® Radioconjugates incorporating lead-212 as a targeted alpha therapy

payload. Bicycle is advancing a radioconjugate pipeline including programs targeting EphA2 and MT1-MMP.

Oxford BioTherapeutics entered a strategic oncology target discovery collaboration with GSK [7]

Oxford BioTherapeutics (OBT) announced a multi-year, multi-target strategic collaboration with GSK focused on discovering novel antibody-based therapeutics for cancer. The collaboration will leverage OBT's proprietary OGAP®-Verify platform to identify and validate oncology targets, with joint research activities supporting target validation. Subsequent research, development, and commercialization efforts will be led by GSK. Under the terms of the agreement, OBT will receive an undisclosed upfront payment and is eligible for downstream milestone payments and royalties on net sales of resulting products. OBT's pipeline includes I-O programs and ADCs, and the agreement represents the company's second major pharmaceutical collaboration announced this year.

GV20 Therapeutics reported milestone payment under ADC collaboration with Mitsubishi Tanabe Pharma [8]

GV20 Therapeutics announced receipt of a milestone payment from Mitsubishi Tanabe Pharma Corporation under a collaboration agreement established in early 2025. The collaboration focuses on the development of ADCs using GV20's antibodies directed against novel tumor antigens identified through its proprietary STEAD AI platform. Under the terms of the agreement, GV20 received an upfront payment and is eligible for additional milestone payments, while Mitsubishi Tanabe Pharma holds an exclusive right to negotiate a license to the antibodies during the collaboration period. The partnership aims to generate potentially first-in-class ADC candidates for oncology applications.

REGULATORY CHANGES AND UPDATES

Kelun-Biotech received China IND approval for ITGB6-targeted ADC [9]

Kelun-Biotech announced that China's National Medical Products Administration has approved the IND application for SKB105 (CR-003), an integrin beta-6 (ITGB6)–targeted ADC, for the treatment of advanced solid tumors. SKB105 features a fully human anti-ITGB6 IgG1 antibody conjugated to a topoisomerase I inhibitor payload using the company's proprietary Kthiol® irreversible conjugation technology. ITGB6 is highly expressed across multiple solid tumors with limited expression in normal tissues, supporting a differentiated safety profile. The approval follows Kelun-Biotech's recent strategic collaboration with Crescent Biopharma, under which Crescent holds ex-China rights to SKB105 while Kelun-Biotech retains development and commercialization rights in Greater China.

US FDA awarded national priority vouchers to TROP2 ADC and oral PCSK9 inhibitor [10]

The US FDA announced the award of Commissioner's National Priority Vouchers under its pilot program to two investigational products, citing their potential to improve patient access through affordability. The awarded products were enlicitide decanoate, an oral PCSK9 inhibitor for lowering LDL cholesterol, and sacituzumab

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tirumotecan, a TROP2-directed ADC. The voucher program, launched in June 2025, is intended to incentivize development of therapies that may enhance access to care while enabling expedited FDA review timelines. With these awards, a total of 18 products have received vouchers under the pilot program. The FDA recently reported its first completed review under the program, noting substantial time savings compared with standard review processes.

Rona Therapeutics submitted bi-valent GalNAc–siRNA RN5681 for Phase 1 clinical evaluation [11]

Rona Therapeutics announced the submission of RN5681 to the Australian Human Research Ethics Committee, advancing its first bi-valent small interfering RNA (siRNA) into clinical development, with Phase 1 dosing expected to begin in Q1 2026. RN5681 is a GalNAc-conjugated, dual-targeting siRNA designed to simultaneously silence *PCSK9* and *LPA*, two genetically validated drivers of atherosclerotic cardiovascular disease. The unimolecular design aims to achieve durable reductions in LDL cholesterol and lipoprotein(a) with infrequent dosing. The submission represents the first clinical program derived from Rona's bi- and multi-target siRNA platform and marks a regulatory milestone for the company's cardiovascular RNA interference pipeline.

US FDA expanded label for Enhertu plus pertuzumab in first-line HER2-positive metastatic breast cancer [12]

The US FDA approved a label expansion for fam-trastuzumab deruxtecan-nxki (Enhertu), a HER2-targeted ADC, in combination with pertuzumab for the first-line treatment of adults with unresectable or metastatic HER2-positive breast cancer. The decision was based on Phase 3 DESTINY-Breast09 data showing that Enhertu plus pertuzumab significantly improved progression-free survival compared with standard-of-care taxane, trastuzumab, and pertuzumab therapy. Median progression-free survival was 40.7 months for the combination versus 26.9 months for standard therapy, with a 44% reduction in the risk of disease progression or death. Overall survival data were immature at the time of approval.

Avenzo Therapeutics reported Fast Track designation for AVZO-103 in urothelial cancer [13]

Avenzo Therapeutics announced that the US FDA granted Fast Track designation to AVZO-103, a Nectin4/TROP2 bispecific ADC, for the treatment of adult patients with locally advanced or metastatic urothelial cancer who have previously been treated with enfortumab vedotin. The company stated that there are currently no approved ADCs for this patient population. AVZO-103 is being evaluated in a Phase 1/2 first-in-human, open-label study assessing safety, tolerability, and preliminary clinical activity as both a monotherapy and in combination regimens in patients with advanced solid tumors. The Fast Track designation enables increased regulatory interaction and potential eligibility for expedited review pathways.

GSK reported US FDA Orphan Drug Designation for B7-H3-targeted ADC risvutatug rezetecan in small-cell lung cancer [14]

GSK announced that risvutatug rezetecan, a B7-H3-targeted ADC, received Orphan Drug Designation from the US FDA for the treatment of small-cell lung cancer (SCLC). The designation was supported by preliminary clinical data from the Phase 1 ARTEMIS-001 study showing durable responses in patients with

extensive-stage SCLC. Risvutatug rezetecan comprises a fully human anti-B7-H3 monoclonal antibody linked to a topoisomerase inhibitor payload. The program has previously received multiple regulatory designations in the USA and Europe across several indications. A global Phase 3 trial evaluating risvutatug rezetecan in relapsed extensive-stage SCLC was initiated in August 2025.

MARKET TRENDS

BioAtla and GATC Health formed special purpose vehicle to advance ROR2-targeted ADC into Phase 3 [15]

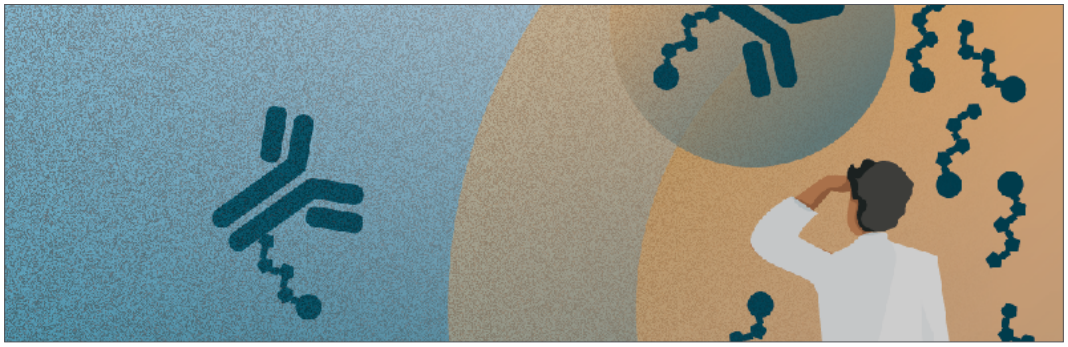
BioAtla announced a special purpose vehicle (SPV) transaction with GATC Health to advance ozuriftamab vedotin (Oz-V), a ROR2-targeted conditionally active ADC, into a Phase 3 trial for second-line or later oropharyngeal squamous cell carcinoma. Under the agreement, BioAtla will receive up to $40 million to support clinical development, beginning with an initial $5 million payment, with additional funding expected in Q1 2026. Following the transaction, BioAtla will retain 65% ownership of Oz-V across solid tumor indications, while Inversagen AI will hold 35%. Oz-V has received FDA Fast Track designation and is being developed for patients previously treated with PD-1/L1 inhibitors.

Salarius Pharmaceuticals announced a planned name and ticker change [16]

Salarius Pharmaceuticals announced plans to change its corporate name to Decoy Therapeutics Inc. and its Nasdaq ticker symbol to DCOY following its recent combination with Decoy Therapeutics. The changes are expected to become effective in early January 2026, with the company continuing to trade under the SLRX symbol until that time. The rebranding reflects the company's transition into a platform-focused biotechnology company centered on peptide-conjugate therapeutics for viral diseases and oncology. The name and ticker change will not affect operations, governance, or the company's transfer agent, and stockholder approval was not required. The combined company will be led by Decoy's senior management team alongside Salarius's finance leadership.

Orum Therapeutics secured $100 million financing to advance degrader–antibody conjugate pipeline [17]

Orum Therapeutics announced an approximately $100 million financing round to advance its degrader–antibody conjugate



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(DAC) pipeline. The round was led by returning investor KB Investment, with participation from existing investors and new backers including Weiss Asset Management and Korea Investment Partners. Proceeds will support development of Orum's lead internal program, ORM-1153, an anti-CD123 GSPT1 DAC being developed for acute myeloid leukemia and other hematologic malignancies, with an IND filing planned for the second half of 2026. Funding will also be used to advance additional programs and expand payload classes beyond GSPT1, leveraging the company's dual-precision targeted protein degradation platform.

Akari Therapeutics announces $5 million financing to support ADC payload platform development [18]

Akari Therapeutics announced definitive agreements for a registered direct offering and concurrent private placement expected to generate approximately $5 million in gross proceeds. The financing included the issuance of American Depositary Shares and unregistered warrants, with participation from directors, officers, executive management, and institutional investors. In addition, certain noteholders agreed to convert approximately $2.5 million of outstanding debt into equity-linked instruments, reducing company liabilities. Ladenburg Thalmann & Co. acted as the exclusive placement agent. Akari stated that net proceeds will be used to support continued research and development of its oncology ADC payload platform, as well as for working capital and general corporate purposes.

Immunome announces plans for $400 million underwritten public offering [19]

Immunome announced plans to commence an underwritten public offering of $400 million of its common stock, with an option for underwriters to purchase up to an additional $60 million of shares. The offering is subject to market and other conditions and will be conducted in accordance with a previously filed shelf registration statement with the US Securities and Exchange Commission. Leerink Partners, JP Morgan, TD Cowen, Goldman Sachs & Co. LLC, and Guggenheim Securities are serving as joint bookrunning managers. Immunome is a clinical-stage oncology company advancing a portfolio of targeted cancer therapies, including ADCs and radiotherapeutics, with programs spanning late-clinical to early-stage development.

Serina Therapeutics appoints Joshua Thomas as Vice President and Head of Chemistry [20]

Serina Therapeutics announced the appointment of Joshua Thomas, PhD, as Vice President and Head of Chemistry, where he will lead internal and external chemistry activities supporting the company's POZ Platform™ drug optimization technology. Thomas will oversee chemistry efforts spanning discovery through development, including optimization of POZ-based candidates. He previously held senior scientific leadership roles at Mersana Therapeutics, where he contributed to the development of ADC platforms, including work on the development of cytotoxic payloads and linker chemistries.

TuHURA Bioscience reported portfolio updates following recent financing [21]

TuHURA Biosciences provided a portfolio update highlighting clinical, scientific, and financing milestones across its I-O programs. The company reported progress in its Phase 3 study of IFx-2.0 as an adjunct to pembrolizumab in first-line Merkel cell carcinoma, conducted under a Special

Protocol Assessment with the US FDA, with enrollment targeted for completion in Q4 2026. TuHURA also summarized data presented at the 57th ASH Annual Meeting, supporting the delta opioid receptor as a target for its bi-functional ADC platform, as well as discussions from a December 2025 mini-symposium on VISTA targeting in acute myeloid leukemia. The company also announced a $15.6 million equity financing to support upcoming development milestones.

DISCO Pharmaceuticals appointed new CEO and closed €36 million seed financing to advance ADC pipeline [22]

DISCO Pharmaceuticals announced the appointment of Mark Manfredi PhD, as Chief Executive Officer and the final close of a €36 million seed financing round. The financing was co-led by Ackermans & van Haaren and NRW.Bank, with participation from Sofinnova Partners, AbbVie Ventures, M Ventures, and Panakes Partners. Proceeds will be used to advance multiple surfaceome-targeted ADC programs in SCLC and microsatellite-stable colorectal cancer toward IND-enabling studies and to expand the company's pipeline. Manfredi succeeds founder Roman Thomas MD, who will continue to support DISCO as a strategic advisor. DISCO is developing bispecific ADCs and T-cell engagers based on its proprietary surfaceome-mapping platform.

Samsung Life Science Fund announced equity investment in Phrontline Biopharma [23]

Samsung Life Science Fund announced an equity investment in Phrontline Biopharma, a clinical-stage biotechnology company developing ADCs for solid tumors. The fund is jointly established by Samsung C&T, Samsung Biologics, and Samsung Bioepis, and is managed by Samsung Ventures. Phrontline Biopharma is advancing ADCs based on proprietary bispecific antibody and dual-linker payload platforms designed to enable simultaneous delivery of two payloads with complementary mechanisms of action through a branched-linker architecture. The company aims to address limitations associated with single-payload, single-target ADCs, including resistance, tumor heterogeneity, and durability of response. The investment expands Samsung Life Science Fund's portfolio of ADC-focused companies.

Ankyra Therapeutics appoints Sailaja Battula as Chief Scientific Officer [24]

Ankyra Therapeutics announced the appointment of Sailaja Battula PhD, as chief scientific officer. Battula brings experience across I-O, drug discovery, inflammation, and autoimmunity, with prior leadership roles at Immuneering Corporation, Bicycle Therapeutics, Forma Therapeutics, and Applied Immunology. She will lead Ankyra's scientific strategy and pipeline development, including its anchored drug conjugate platform. Ankyra's lead program, tolododekin alfa (ANK-101), is an interleukin-12–based anchored drug conjugate designed for localized delivery within the TME. ANK-101 is being evaluated in first-in-human clinical studies as monotherapy and in combination with anti-PD-1 therapy, including trials in advanced solid tumors and metastatic NSCLC.

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RESEARCH AND DEVELOPMENT HIGHLIGHTS

Avacta Therapeutics reported new preclinical pharmacology data for FAP-Exd peptide drug conjugate [25]

Avacta Therapeutics announced new preclinical pharmacology data for FAP-Exd (AVA6103), its second asset derived from the pre|CISION® tumor-activated delivery platform, which is expected to enter Phase 1 testing in Q1 2026. FAP-Exd is a fibroblast activation protein–cleavable peptide-drug linking a proprietary peptide to a topoisomerase I inhibitor payload. The data demonstrated tumor-specific cytotoxicity, sustained intratumoral release of active exatecan with limited systemic exposure, and robust antitumor activity across multiple patient-derived xenograft models. Avacta also reported that artificial intelligence–guided analysis was used to prioritize clinical indications based on co-expression of FAP and SLFN11.

CLINICAL TRIALS AND RESEARCH

Hummingbird Bioscience dosed first patient in Phase 1 trial of HER3 ADC [26]

Hummingbird Bioscience announced that the first patient has been dosed in a Phase 1 clinical trial evaluating HMBD-501, a next-generation HER3-targeted ADC, in patients with advanced HER3-expressing solid tumors. The multicenter, open-label study is being conducted at sites across the USA and is designed to assess safety, tolerability, and preliminary clinical activity. HMBD-501 incorporates an exatecan payload and has been engineered to optimize efficacy while improving safety relative to earlier HER3 ADC approaches. Initial data from the dose-escalation portion of the trial are expected in the second half of 2026.

Alphamab Oncology received IND clearance in China for Phase 2 study of subcutaneous ADC–PD-L1 co-formulation in cervical cancer [27]

Alphamab Oncology announced that China's National Medical Products Administration has accepted the IND application for a Phase 2 clinical trial of JSKN033 as a first-line treatment for advanced cervical cancer. JSKN033 is a high-concentration subcutaneous co-formulation combining a HER2 bispecific ADC with a PD-L1 immune checkpoint inhibitor. The open-label, multicenter study will evaluate JSKN033 in combination with platinum-based chemotherapy, with or without bevacizumab, assessing safety, efficacy, and PK/PD outcomes. JSKN033 integrates targeted cytotoxic delivery with immune modulation and is designed to improve treatment convenience and outcomes in a setting with significant unmet clinical need.

Senhwa initiated Phase Ib study combining CX-5461 with trastuzumab deruxtecan [28]

Senhwa Biosciences announced that its first-in-class investigational agent pidnarulex (CX-5461) will be evaluated in

combination with Enhertu in a Phase 1b clinical trial for patients with HER2-positive solid tumors and breast cancer, including HER2-low and metastatic disease. The study is supported by the US National Cancer Institute's NExT program and marks CX-5461's first clinical entry into combination strategies with ADCs. CX-5461 is a G-quadruplex stabilizer designed to disrupt cancer-specific transcriptional stress pathways, while Enhertu is a HER2-directed ADC delivering a topoisomerase I inhibitor payload. The combination aims to explore synergistic efficacy in difficult-to-treat HER2-expressing tumors.

First patient dosed in Phase 3 trial of trastuzumab deruxtecan in adjuvant endometrial cancer [29]

The first patient has been dosed in the global Phase 3 DESTINY-Endometrial02 trial evaluating Enhertu, a HER2-directed ADC, as adjuvant therapy in patients with HER2-expressing endometrial cancer following surgery. The randomized, open-label study is comparing Enhertu, with or without radiotherapy, versus standard-of-care chemotherapy with or without radiotherapy. Conducted in collaboration with The GOG Foundation and ENGOT, the trial will enroll ~710 treatment-naïve patients with HER2 IHC 3+ or 2+ disease across multiple regions. The primary endpoint is disease-free survival, with overall survival as a key secondary endpoint.

Phase 3 trial met primary and secondary endpoints for Keytruda plus enfortumab vedotin in muscle-invasive bladder cancer [30]

Merck reported that the Phase 3 KEYNOTE-B15/EV-304 trial evaluating perioperative pembrolizumab (Keytruda®) in combination with the nectin-4-targeted ADC (enfortumab vedotin) met its primary endpoint of event-free survival in patients with muscle-invasive bladder cancer eligible for cisplatin-based chemotherapy. The randomized study enrolled 808 patients and compared the combination plus surgery with neoadjuvant chemotherapy and surgery. The combination also met key secondary endpoints, including overall survival and pathologic complete response rates. Merck stated that the safety profile was consistent with prior studies. The companies plan to present the data at a future medical meeting and discuss the results with regulatory authorities.

HUTCHMED initiated first-in-human study of HER2-targeted antibody-targeted therapy conjugate [31]

HUTCHMED announced the initiation of a global first-in-human Phase 1/2a clinical program evaluating HMPL-A251, a first-in-class PI3K/PIKK–HER2 antibody-targeted therapy conjugate (ATTC), with the first patient dosed in December 2025. HMPL-A251 comprises a humanized anti-HER2 IgG1 antibody linked via a cleavable linker to a highly selective PI3K/PIKK inhibitor payload. The open-label, multicenter study is enrolling adults with unresectable, advanced, or metastatic HER2-expressing solid tumors and includes dose escalation and dose expansion components. Primary objectives include assessment of safety, tolerability, and dose optimization, with secondary endpoints evaluating preliminary antitumor activity, pharmacokinetics, and immunogenicity.

Rona Therapeutics completed Phase 1 of GalNAc-conjugated siRNA [32]

Rona Therapeutics announced completion of Cohort 1 dosing in its Phase 1 first-in-human clinical study of RN3161, a GalNAc-conjugated siRNA targeting INHBE for the treatment of obesity. The randomized,

double-blind, placebo-controlled study is evaluating safety, tolerability, pharmacokinetics, pharmacodynamics, and effects on body weight in adults with overweight and obesity. Cohort 1 was completed with a favorable initial safety and tolerability profile, representing the first clinical milestone for the program. RN3161 is designed to achieve deep and durable silencing of INHBE with once- or twice-yearly dosing. Additional cohorts in the Phase 1 study are planned for completion in 2026.

OKYO Pharma reported exploratory corneal nerve imaging results from Phase 2 trial [33]

OKYO Pharma announced exploratory corneal nerve imaging analyses from a randomized, placebo-controlled, double-masked Phase 2 trial evaluating urcosimod in patients with neuropathic corneal pain. Using *in vivo* confocal microscopy, patients treated with 0.05% urcosimod showed directional increases in corneal nerve fiber count and total nerve fiber length, while corresponding measures declined in the placebo group. The analyses were based on an exploratory endpoint in an 18-patient study. Urcosimod is a lipid-conjugated chemerin peptide agonist targeting the ChemR23 receptor. The company reported that the findings suggest a potential effect on corneal nerve structure in addition to previously reported pain reduction, supporting further clinical evaluation of the candidate in neuropathic corneal pain.

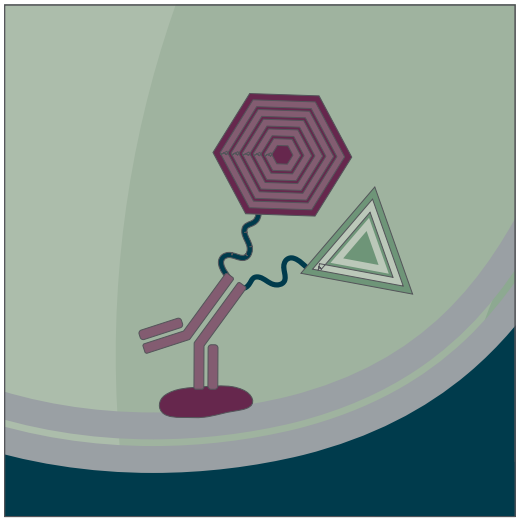
CONFERENCES, EVENTS, AND PUBLICATIONS

Iksuda presented early Phase 1 activity of HER2 ADC IKS014 in esophageal cancer [34]

Iksuda Therapeutics presented early clinical activity data from its Phase 1 study of IKS014, a HER2-directed ADC, at the 2026 ASCO Gastrointestinal Cancers Symposium. The open-label, multicenter trial is evaluating IKS014 in patients with advanced HER2-expressing solid tumors. An unplanned analysis of 10 patients with HER2-positive esophageal cancer showed encouraging antitumor activity, with five patients achieving responses, including one complete response, and three additional patients demonstrating durable stable disease beyond 6 months, resulting in an 80% clinical benefit rate. Based on these findings, the ongoing Phase 1 study will include a dedicated expansion cohort for patients with previously treated HER2-expressing esophageal adenocarcinoma.

15 years of progress in radiopharmaceutical drug conjugate research summarized in recent review article [35]

A review published in July 2025 in *Medical Journal of Peking Union Medical College Hospital* examined 15 years of progress in radiopharmaceutical drug conjugate research. Authored by researchers from Peking Union Medical College Hospital,



the review outlined current RDC classifications, including antibody-, peptide-, and small-molecule–based conjugates, and highlighted trends in clinical development and therapeutic targeting. The authors noted increasing clinical trial activity, growing interest in cyclic peptide-based RDCs due to favorable selectivity and toxicity profiles, and the impact of regulatory guidance introduced since 2020 to standardize evaluation and quality control. The review emphasized the role of radiopharmaceutical drug conjugates in theranostics and precision oncology, while identifying isotope supply, radiochemistry, and regulatory harmonization as ongoing challenges.

Johns Hopkins researchers reported TRBC2-targeted ADC for T-cell malignancies [36]

Researchers at the Johns Hopkins Kimmel Cancer Center reported the development of a TRBC2-targeted ADC for the treatment of T-cell lymphomas and leukemias, published in Nature Cancer. The ADC selectively targets the TRBC2 variant of the T-cell receptor, which is expressed in approximately half of T-cell malignancies, while sparing TRBC1-positive normal T cells. The antibody component, JX1.1, was identified using a phage-displayed antibody library and next-generation sequencing, and was conjugated to a pyrrolobenzodiazepine payload. In preclinical cell line and animal models, the ADC demonstrated selective tumor cell killing, durable tumor regression, and minimal toxicity, expanding a previously established TRBC1-based precision targeting strategy.

Actinium Pharmaceuticals presents preclinical data for radioconjugate in breast cancer [37]

Actinium Pharmaceuticals reported new preclinical data for ATNM-400, an Actinium-225-based antibody radioconjugate, at the 2025 San Antonio Breast Cancer Symposium. ATNM-400 demonstrated antitumor activity across multiple breast cancer models, including hormone receptor–positive, triple-negative, and tamoxifen- and trastuzumab-resistant disease. The target antigen was shown to be overexpressed in resistant tumors, supporting enhanced cytotoxicity. Mechanistic studies indicated alpha-particle–induced double-strand DNA damage, consistent with irreversible tumor cell killing. Favorable biodistribution with sustained tumor uptake and rapid clearance from normal tissues was reported, suggesting a differentiated tolerability profile. The data support further development of ATNM-400 as a potential pan-tumor radiotherapeutic, either as monotherapy or in combination regimens.

Biohaven presents Phase 1 combination data for Trop2 ADC at ESMO [38]

Biohaven presented Phase 1 clinical safety and efficacy data for BHV-1510, a Trop2-targeted ADC incorporating a proprietary TopoIx payload, in combination with the anti-PD-1 antibody cemiplimab at the 2025 European Society for Medical Oncology (ESMO) Congress. In heavily pretreated patients with advanced or metastatic solid

tumors, confirmed objective responses were reported in NSCLC, endometrial cancer, and urothelial cancer. At the 2.5 mg/kg Q3W dose, confirmed objective response rates included 60% in NSCLC and 100% in endometrial cancer. Across dose levels, the combination was generally well-tolerated, with low rates of hematologic and gastrointestinal toxicities and no reported cases of interstitial lung disease.

Phase 3 ASCENT-07 results showed similar PFS for sacituzumab govitecan and chemotherapy in HR-positive, HER2-negative breast cancer [39]

Results from the Phase 3 ASCENT-07 trial presented at the San Antonio Breast Cancer Symposium showed that sacituzumab govitecan-hziy, a TROP-2-targeted ADC, achieved similar progression-free survival to standard-of-care chemotherapy when used as first chemotherapy after endocrine therapy in patients with hormone receptor-positive, HER2-negative advanced breast cancer. After a median follow-up of 15.4 months, median progression-free survival was 8.3 months in both arms (hazard ratio 0.85), and the primary endpoint was not met. Objective response rates were numerically higher with sacituzumab govitecan-hziy (37% versus 33%), with a longer median duration of response. Overall survival data were immature at the time of analysis.

Orum Therapeutics presented preclinical data for CD123-targeting DAC ORM-1153 [40]

Orum Therapeutics reported the presentation of preclinical data for ORM-1153, a CD123-targeting DAC, at the 67th American Society of Hematology Annual Meeting. ORM-1153 is designed to deliver a proprietary GSPT1-degrading payload selectively into CD123-positive cancer cells to induce targeted protein degradation. In preclinical acute myeloid leukemia models, including TP53-mutant disease, ORM-1153 demonstrated CD123-dependent internalization, efficient GSPT1 degradation, and durable antitumor activity. The compound showed approximately 1,000-fold higher potency than the unconjugated degrader payload and induced dose-dependent tumor regression in a disseminated xenograft model. Favorable tolerability and minimal effects on normal hematopoietic progenitors were also reported.

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EVENT PREVIEW

Event preview of the 5th Novel Conjugates Summit 2026

Bioconjugate Insights 2026; 1(1), 31–33 · DOI: 10.18609/bci.2026.005

Bioconjugate Insights presents a preview of the 5th Novel Conjugates Summit, taking place March 17–19, 2026, in Boston, MA, USA. The meeting will bring together discovery and early development leaders from biotech, pharma, and academia to examine how novel targeting formats and payload strategies are expanding the therapeutic reach of conjugates across oncology and beyond.

With growing interest in bispecific ADCs (BsADCs), multispecific constructs, degraders, and immune-stimulating payloads, the summit will focus on how advances in targeting logic, delivery mechanisms, and payload design are helping developers address tumor heterogeneity, resistance, and on-target off-tissue toxicity. Across 3 days, the program will explore how emerging conjugate modalities are progressing from concept to preclinical and translational validation.

5th Annual Novel Conjugates Summit

EXPANDING TARGETING LOGIC THROUGH BISPECIFIC & MULTISPECIFIC CONJUGATES

A central theme of the meeting is the evolution of targeting strategies designed to improve selectivity and functional synergy. Conditional and multispecific approaches are gaining traction as developers seek to refine payload delivery in complex disease settings.

In the session '*Conditional logic-gated bispecific ADCs: harnessing novel dual antigen fingerprints to expand efficacy and minimize on-target/off-tissue toxicity*', Tiffany Thorn (Chief Executive Officer, BiVictrix Therapeutics) will outline how logic-gated designs leverage dual antigen expression patterns to enhance tumor selectivity. The presentation will examine design principles and preclinical insights supporting the use of BsADCs in heterogeneous cancers.

Complementing this approach, '*Multispecific drug conjugates for combatting tumor heterogeneity & drug resistance*' will be presented by Caitlyn Miller (Chief Executive Officer and Co-Founder, TwoStep Therapeutics). This session will explore how multispecific targeting formats can address variability in antigen expression and overcome resistance mechanisms that limit the efficacy and safety of conventional single-target conjugates.

Together, these sessions highlight how next-generation targeting architectures are being used to expand the therapeutic window while maintaining control over safety and biodistribution.

DEGRADER & PROTAC-CONJUGATE BASED DELIVERY

The integration of targeted protein degradation into antibody-based delivery systems represents another rapidly advancing area. Degrader-antibody conjugates and PROTAC-ADCs are opening new possibilities for addressing previously intractable targets.

Andrea Geist's (Senior Scientist, PROxAb Shuttle, Merck) presentation '*Targeted PROTAC delivery: principles of crafting PROTAC-ADCs and self-assembling PROxAb shuttles*', will highlight the design and application of PROxAb Shuttle technology. The discussion will focus on how self-assembling systems have the potential to expedite the discovery of degrader-ADCs while maintaining favorable pharmacokinetic properties.

This theme will be further reinforced by Alice Chen (Chief Scientific Officer, Baylink Biosciences), who will discuss broader strategies for degrader-antibody conjugates, including linker considerations that influence efficacy and safety. These talks will provide insight into how targeted degradation is being translated into conjugate formats suitable for *in vivo* application.

DUAL-PAYLOAD & IMMUNOSTIMULATORY CONJUGATES

As resistance to single cytotoxic payloads continues to challenge ADC development, dual-payload strategies are emerging as a means of enhancing durability and immune engagement.

Garrett Gross (Director, Research Innovation and Protein Engineering, Sutro Biopharma) will present '*Dual-payload ADCs to enhance anti-tumor immune response and overcome payload resistance*'. He will explore dual-payload ADCs that demonstrate increased preclinical *in vitro* and *in vivo* efficacy, thereby overcoming acquired single-payload resistance. He will further highlight promising pharmacokinetics using a novel cell-free platform to create site-selective, high DAR, dual-payload ADCs.

By integrating immune activation with targeted cytotoxicity, these approaches reflect a broader shift toward

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multifunctional conjugates designed to modulate both tumor cells and the TME.

BROADENING CONJUGATE DESIGN & DELIVERY CONSIDERATIONS

Sujiet Puthenveetil (Director, Antibody Drug Conjugates and Radioconjugates, AstraZeneca) will contribute his perspective, along with Marc-Andre Kasper (Vice President, Chemistry and Early Development, Tubulis GmbH), on how advances in conjugation chemistry and payload integration are shaping the future of targeted therapeutics, bridging innovation across ADCs, radioconjugates, and emerging hybrid formats.

The 5th Novel Conjugates Summit will provide a focused forum for examining how novel targeting formats and payload strategies are reshaping the bioconjugate landscape. By bringing together leaders working on bispecific and multispecific ADCs, degrader-antibody conjugates, dual-payload systems, and ligand-targeted approaches, the meeting will offer a cross-modality perspective on how developers are addressing selectivity, resistance, and translational complexity.

As the field continues to move beyond traditional ADC paradigms, this summit will play an important role in clarifying where innovation is gaining traction and how emerging conjugate technologies may influence the next generation of targeted therapies.

As a reader of *Bioconjugate Insights*, you're entitled to a 10% discount on delegate tickets – just use the discount code **BI10NCS**! You can find out more about the event **here**.

Want to know more about the journal or discuss a potential contribution? Drop an email to our Editor, Lauren, at **lauren.coyle@insights.bio**.

If you are interested in other events happening in the bioconjugate space this year, you can see our 2026 Events Calendar **here**.

EVENT PREVIEW

NextGen Biomed 2026

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As part of our ongoing coverage of key gatherings in life sciences, BioInsights presents a preview of NextGen Biomed 2026. Scheduled for March 24–25, 2026, in London, UK, this event will unite the brightest scientific minds and the most disruptive innovations in biomedicine under one roof. The agenda spans advances in biologics, peptide and oligonucleotide therapeutics, immunotherapy strategies, vaccine research and development, and sustainable bioprocessing, featuring a keynote presentation from Andreas Plückthun (Professor of Biochemistry, University of Zurich), who will discuss molecular engineering for the future across therapeutic modalities, alongside contributions from a broad range of academic and industry leaders.

EXPLORING ADVANCES IN ADC ENGINEERING

The Proteins, Antibodies and ADCs program will explore topics ranging from protein and antibody engineering through to advanced bioanalytics, real-world case studies, and innovations in upstream and downstream processing. Senior leaders from pharmaceutical companies, biotechnology firms, and research institutions will share perspectives on antibody discovery, analytical development, and protein purification strategies. Charlotte Deane (Professor, University of Oxford) will examine the application of AI in protein design, while Dan Bach Kristensen (Scientific Director, Servier) will present on characterization of ADCs and next-generation biologics in biological matrices using affinity capture liquid chromatography–mass spectrometry.

OLIGONUCLEOTIDE DESIGN, CMC, & SCALE-UP STRATEGIES

Beyond ADCs, the conference will also include presentations on how computational design approaches, CMC strategies, sustainable process improvements, and advanced analytical controls are being applied to accelerate oligonucleotide-based drug development timelines. A thought leadership panel featuring Anna Perdrix (Chief Executive Officer, Sixfold Bioscience), Sritama Bose (Associate Director of Chemistry, Orfonyx Bio), and Sandor Batkai (Life Science Consultant, formerly Head of Medical Research and Intelligence, Cardior Pharmaceuticals) will explore regulatory considerations, novel technologies, and

scale-up challenges in oligonucleotide drug development.

NOVEL IMMUNOTHERAPY & IMMUNO-ONCOLOGY APPROACHES

Immunotherapy for cancer and autoimmune diseases will be another central theme, with sessions focused on biomarker-guided strategies, next-generation cellular and antibody-based approaches, and personalized treatment paradigms. Alexander Eggermont (Professor, University Medical Center Utrecht) will present on the neoadjuvant immunotherapy revolution across multiple tumor types, discussing why neoadjuvant immuno-oncology strategies may offer advantages over adjuvant approaches. Callum Scott (Senior Vice President and Head of Development, Scancell) will address the role of potency testing across the cancer vaccine development lifecycle, highlighting the intersection of technical feasibility, regulatory expectations, and commercial considerations.

INNOVATIONS IN VACCINE DESIGN & DEVELOPMENT

The vaccines program will examine advances in nucleotide-based vaccine platforms for infectious diseases, AI-driven antigen design, and emerging delivery systems. Daniel Larocque (Innovation Leader, Sanofi) will present a historical and forward-looking perspective in a session titled 'Tracing 200 years of vaccine innovation: from prophylactic to therapeutic vaccines and AI-driven vaccines'. Supriyadi Hafiz (Senior Scientist, Merck) will discuss the growing demand for responsibly sourced alternatives to animal-derived ingredients, with a focus on fermentation-derived, non-animal-origin squalene. Across the program, attendees will gain insights into adjuvant production, clinical development strategies, and translational approaches that support the progression of vaccine candidates from research to real-world application.

WOMEN IN NEXTGEN BIOMED PANEL DISCUSSION

The two-day event will also feature a Women in NextGen Biomed panel discussion. Building on the success of the previous year, this session will bring together leading female scientists and industry professionals for a discussion focused on innovation, career pathways, and addressing barriers in STEM. The panel will highlight achievements, ongoing challenges, and future opportunities for women contributing to the next generation of biomedical research and development.

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NextGen Biomed 2026 will bring together innovators across biologics, tides, and immunotherapy fields to share real-world case studies spanning novel target discovery and clinical validation, as well as biologics engineering and therapeutic development. Together, these discussions will offer a deep dive into the science and strategy behind the field's most promising breakthroughs.

You can find out more about the NextGen Biomed 2026 events **here**.

To learn about other events coming up in your field, you can find our online Events Calendars here: ***Bioconjugate Insights***, ***Nucleic Acid Insights***, and ***Vaccine Insights***.