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Ã¢â?¬Å?Industry needs to evolve and invest in ADC payloads with more differentiated mechanisms of actionÃ¢â?¬Â•

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Antibody drug conjugates (ADCs) are becoming highly valuable in the market, with currently 15 approved ADCs targeting 16 different indications for haematological and solid tumour malignancies. With key components of ADCs, such as mAbs, linkers, payloads, and conjugation technologies, undergoing rapid advancements, a solid foundation has been laid for future research and development in this field, particularly in North America which is the largest market shareholder for ADCs. US recently wrapped up the world's largest & definitive Antibody-Drug Conjugate event, World ADC, held in November 2025, highlighting the development of novel ADCs through key market players, and a surge in patent application filing for ADCs. Dr Allan Jordan, Vice President of Oncology Drug Discovery at Sygnature Discovery, UK spoke in detail with BioSpectrum Asia about the future outlook of ADCs.



What were the key highlights at Sygnature Discovery in 2025? Please elaborate upon the company's plans for 2026.

Despite current market challenges in terms of funding constraints and geopolitical uncertainties, we have seen many project successes. Several of our customers have had potential human therapeutics nominated for pre-clinical development. We also hit a really significant milestone, with two compounds gaining marketing approval. We're building for success, with investments in areas like high-throughput chemistry to help drive progress and rapidly explore emerging structure-reactivity relationships across all of our projects. 2025 also heralded a broadening of our offerings in other modalities, particularly with the launch of our New Path ADC platform. We believe that ADC linkers and payloads are the overlooked aspects of ADC discovery and, through bringing together our expertise in small molecule drug discovery and applying it to this setting, we can help to deliver a step change in the potency and safety of these agents.

We're positioning ourselves to help our customers, planning for growth and further scientific success. We're fully committed to enhancing our cutting-edge drug discovery solutions, across all modalities, from small molecules, through glues, degraders and other modalities, to our ADC capabilities. We remain committed to further strengthening our capabilities in the use of AI tools to generate ideas, test hypotheses and amplify the impact and delivery of our scientific teams.

Sygnature recently took part in World ADC in the US, the world's largest and longest-standing ADC-dedicated forum. What were the key takeaways from the event?

One of the key themes of the meeting was the desire to move away from the limited choice of payloads deployed in current ADCs. Almost all ADCs in pre-clinical and clinical development still depend on the delivery of drugs interfering with microtubules or with topoisomerases. While these remain clinically effective, they do also carry significant liabilities and side effects, and it's getting increasingly harder to differentiate new agents entering the clinic from established and approved therapies, making the chances of successful approval more difficult. So, the industry needs to evolve and invest in payloads with more differentiated mechanisms of action. The desire to move in this direction is clear, but the expertise to do so is running somewhat further behind. That's the specific gap that our NewPath platform and expertise is designed to address.

My other take-home was actually a topic that was not being talked about very much, in that the actual patient experience with ADCs was almost completely absent. While we talk about these agents being targeted and demonstrating reduced side effects, they are still not as kind and as gentle as we persuade ourselves to believe. It's really important that we do not lose sight of the end customer, our patients, and strive to improve these therapies to really improve patient quality of life. We also heard many stories of improvements in cancer patient's Progression Free Survival (PFS) but overlooked the fact that the key measure, Overall Survival (OS) is often little unchanged compared to untreated patients. Again, we need to make radical improvements here, and I'm optimistic that the move toward novel payloads will help to drive this forward.

AI is transforming drug discovery. How is Sygnature making use of AI-driven methods to accelerate ADC development?

There has been much talk of AI playing a deeper role in the design of more specific antibodies and delivering biomolecules with better stability, lower immunogenicity and more robust control over conjugation of the linker/payload to the antibody. There is real promise to improve the delivery vector, which in turn will help improve therapeutic profiles. We routinely embed Generative AI tools across our design-make-test-analyse cycles, alongside real-world human expertise and intelligence across many of our small molecule therapeutic projects. This combination of expert scientist and AI system is known as Human-in-the-Loop AI and we believe this is the most effective way to deploy AI tools and to amplify the expertise of our own scientific teams. We're using these models to design novel payload ideas, but also predict ADME properties most appropriate for ADC payloads, prioritising ideas for synthesis and evaluation. Equally, we can apply these tools in the pursuit of better ADC payloads, helping with idea generation and compound triage to optimise parameters such as potency, permeability, efflux and lowering systemic exposure through increased metabolic clearance.

What emerging trends, challenges & new scientific methodologies are shaping up the ADCs space currently?

We feel we're on the cusp of a revolution in the ADC space. Payload-focussed ADC discovery is becoming more common, with highly targeted therapeutics slowly replacing the more overtly cytotoxic payloads of old. But this is only the beginning of this new renaissance in ADC research. We're really excited by the potential of delivery vectors beyond antibodies, such as CNS-targeting peptides and other biomolecules as the targeting vector. And the promise of dual-payload ADCs – be they formed from dually functionalised linkers or from two separate linker/payload architectures, conjugated to different antibody residues. This yields the enticing possibility of combination therapies for disease using a single ADC moiety, with some element of control over the relative drug stoichiometries – the possibilities here are enticing!

And the ADC field is now systematically re-thinking how we can "rescue" small molecule drugs with poor PK properties or intolerable on-target mechanistic toxicity and turn these into viable therapeutics. We call these "fallen angel" payloads, and we can now start to think differently about how we can rescue that investment in compounds with real therapeutic promise, but which fell short of becoming single agent small molecule therapeutics. We can extend this further, into larger molecular weight payloads, such as heterobifunctional degraders, and protein-protein interaction inhibitors, overcoming some of the challenges in the delivery of those agents. But we're also excited about the transition of ADCs into therapeutic spaces beyond oncology, finally tapping into the potential of ADC therapies for other patient populations. These were the key themes we delved into in the panel discussion we chaired at World ADC – it was great to see the level of interest from the attendees and it was standing room only for the duration of the session, which suggests the rest of the community are equally excited.

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