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Rise of ADCs: Expanding Applications and the Road to Commercialisation

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The development of antibody-drug conjugates (ADCs) has advanced significantly in the biopharmaceutical sector;in the last five years, eight of the 14 ADCs that are currently approved have obtained regulatory approval. The quantity of pre-clinical to commercial ADC compounds in the innovative modality pipeline increased by more than 25 per cent year over year, according to a market trend. ADCs have the potential to transform targeted medicine and give patients everywhere new hope with further development and wise funding.

Over the past decade, interest in Antibody-Drug Conjugates (ADCs) has surged, driven by their promise for patients, advancements in research, clinical adoption, and market expansion. It is estimated that the global market for ADCs could reach upwards of more than €24 billion by 2030, according to a Grand View Research report.

While initially focused on oncology, ADC development is now extending into non-cancerous diseases, such as cardiovascular and inflammatory diseases, marking a significant milestone for the biopharmaceutical industry and an opportunity for further growth of the modality. A year-over-year market trend reveals that the number of pre-clinical to commercial ADC molecules in the novel modality pipeline grew more than 25 per cent.

Because of their unique structure and mechanism of action, ADCs require special regulatory considerations when compared to biologics and small molecule drugs. Still, developers are finding success amidst this complex regulatory landscape, underscoring the growing potential of these bioconjugates. A significant portion of ADC projects are outsourced to contract development and manufacturing organisations (CDMOs) and with the continued expansion of pipelines, this trend is likely to continue.

Growing Impact of ADCs

ADCs represent a transformative approach to oncology, enabling targeted therapies that minimise damage to healthy tissues. They consist of a monoclonal antibody, a chemotherapy drug (payload), and a chemical linker that ensures precise drug release within target cells. This approach enhances efficacy while minimising off-target toxicity, making ADCs a more precise alternative to traditional chemotherapy. As the market for this novel modality grows and the medical community adopts them as first-line treatments, it may mean that fewer patients need invasive treatments like chemotherapy and radiation that cause significant side effects.

The biopharmaceutical industry has witnessed remarkable growth in ADC development, with eight of the 14 currently approved ADCs receiving regulatory approval in the past five years. Our Life Science business at Merck KGaA, Darmstadt, Germany, enables customers with comprehensive solutions along the entire journey from molecule to medicine with more than 15 years of experience in ADC supply, contributing to the production of nearly 50 per cent of the commercially available ADCs today. Our expertise extends to commercial-scale production of linker payloads, as well as biologics manufacturing.

Navigating Global Regulatory Landscape

ADCs combine the complexity of biologics manufacturing with the environmental controls required for highly potent compounds. This combination necessitates a holistic view of ADC manufacturing and controls to build a detailed roadmap for commercialisation.

ADCs must also comply with stringent regulatory requirements from national-level regulatory agencies, like the US Food and Drug Administration (FDA), European Medicines Agency (EMA), and Health Sciences Authority (HSA), which demand high levels of characterisation, impurity profiling, and adherence to good manufacturing practices (GMP). Robust analytical methods are required to assess purity, potency, and stability, adding complexity to manufacturing—particularly at a commercial scale.

As more ADCs advance to market, there is an increasing need for CDMOs with expertise in executing late-stage studies to support regulatory filings. CDMOs investing in commercial-scale ADC manufacturing must establish efficient supply chains and implement advanced facility and process controls to ensure product quality, security, and scalability.

Ensuring Robust ADC Manufacturing

To start the journey of commercialisation, determining what is required and expected for commercial ADC manufacturing includes control strategies, risk assessment, process characterisation and validation. Extensive preparation leads to getting the approval to manufacture commercial batches.

Before these therapies can reach patients, the world’s leading researchers and therapeutic manufacturers must have access to state-of-the-art tools, services and expertise to develop these novel modalities. A strong control strategy, defined as a comprehensive plan that ensures the consistent quality and safety of the final product throughout its lifecycle, is essential for ADC commercialisation, from process development to regulatory approval.

Key considerations in ADC process control include:

- **Microbial Control:** Manufacturing a biologic requires a well-defined control strategy for endotoxins and bioburden. Consider an approach that involves setting in-process endotoxin acceptance criteria based on the worst-case raw material input and historical process data.
- **Quality by Design (QbD):** Once downstream conjugation and purification are optimised and scaled, quality by design (QbD) is used to gain a deep understanding of the inputs and outputs of the process and establish controls to ensure critical quality attributes (CQAs). A step attribute matrix (SAM) is the first formal step in understanding how material inputs and unit operations of the process may affect product quality attributes.
- **Process Characterisation:** A key aspect of process characterisation is qualifying the scale-down model. This model ensures that the bench-scale model is predictive of the GMP scale; if it isn't, the full-scale process can't be scientifically supported with data generated at the small scale.
- **Commercial Control Strategy:** As part of the validation master plan scoping, additional risk assessments needed for commercial manufacture should be identified, along with existing risk assessments which should be reviewed and updated to support additional controls for commercial manufacture.
- **Regulatory Readiness:** Subject matter expert-led inspections focus on control strategies and facility robustness. Walk-throughs and mock audits are invaluable for helping subject matter experts become comfortable with the audit process and know what to expect.

A well-defined control strategy—spanning microbial control, risk assessments, and process validation—lays the foundation for successful commercialisation, ensuring efficient, high-quality production of life-saving therapies.

Future Outlook for ADCs

The future of ADCs is marked by continuous innovation, expanded clinical applications, and improved manufacturing scalability. Advances in linker technologies and novel payloads are enhancing precision and efficacy, making ADCs more effective against resistant cancers. Beyond oncology, researchers are exploring ADCs for autoimmune and infectious diseases, broadening their therapeutic potential. Additionally, the integration of ADCs with immunotherapies is showing promise in improving patient outcomes.

As demand grows, improvements in manufacturing processes and scalability will be critical to ensuring broader accessibility and commercial success. With continued advancements and strategic investments, ADCs are poised to revolutionise targeted therapy, offering new hope for patients worldwide.

To navigate the increasingly complex regulatory landscape, partnering with an experienced CDMO that understands evolving compliance requirements is essential. Collaborating with a trusted partner early in development can streamline regulatory approvals, optimize production and mitigate risks, ultimately accelerating the path to commercialisation and expanding access to patients in need.

Benjamin Hein, Head of Life Science Services, Merck KGaA