SK pharmteco

White Paper

# Advancing Antibody Drug Conjugates (ADCs) with Expertise in Payloads and Linkers

Antibody Drug Conjugates (ADCs) represent one of the most exciting and rapidly expanding classes of targeted cancer therapies. By combining the specificity of antibodies with the potency of cytotoxic drugs, ADCs offer the promise of delivering powerful treatments directly to diseased cells while sparing healthy tissue. However, their development and manufacturing pose significant challenges.

Customers consistently seek optimized capacity, deep expertise in complex chemistry, and world-class chromatography proficiency. Meeting these demands requires not only specialized facilities but also a proven track record of developing robust, scalable, and compliant processes.

# Introduction

SK pharmteco's ADC payload and linker solutions combine scale, safety, and scientific depth to meet the most demanding program needs. Our right-sized, specialized facilities are designed with advanced containment strategies to ensure both operator protection and regulatory compliance across every stage of development and manufacturing. Backed by more than two decades of high-potency API expertise and over a decade of proven success supplying commercial linkers for ADCs, our team has the knowledge to navigate complex, multi-step synthesis with precision. Adding to this foundation is our world-class chromatography capability, enabling us to consistently deliver payloads and linkers of exceptional purity. Together, these strengths position SK pharmteco as a trusted partner for advancing ADC therapeutics from concept through commercialization.

This white paper explores best practices for ADC payloads and linkers development, illustrated by two case studies where SK pharmteco's global team successfully optimized complex linker-payload processes and built new routes to accelerate delivery



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## Best Practices for ADC Development Capacity and Safety in Manufacturing

ADCs require highly potent payloads that can only be safely handled in facilities designed with advanced containment strategies. Specialized production capacity ensures projects progress from toxicology material through GMP batches without delay, while containment measures protect both staff and the product.

### Complex Chemistry and Multi-Step Synthesis

The multi-step nature of ADC linker and payload chemistry requires experience across diverse chemical reactions, scale-up strategies, and process intensification. Understanding impurity profiles and developing efficient purging strategies are critical to meeting purity requirements and regulatory expectations.

### Chromatography and Downstream Purification

Chromatography plays a central role in downstream purification of payloads and linkers, particularly when intermediates present difficult impurities or unstable profiles. Developing robust purification strategies for drug linkers enhances yields and ensures high-purity material. Combining isolation and drying technologies like lyophilization and Tangential Flow Filtration (TFF), facilitates scalability and improves isolation cycle times.

# Case Study 1:

## Optimization of a Complex Multi-Step Linker Payload

### The Challenge

A customer required rapid development of a complex multi-step process involving a highly potent payload linker. From the outset, all steps were classified as OEL < 10 ng/m³, requiring strict containment and expertise in HPAPI handling. The project also faced significant scientific and technical hurdles, including poorly characterized intermediates with minimal purge data, problematic solubility and unfavorable physical characteristics (sticky solids, oils, and precipitation), and a purity profile vulnerable to oxidation, hydrolysis, and side reactions.

### The Solution

To meet the tight timeline, SK pharmteco employed a cross-site collaboration model. The Ireland site developed steps 1–5 and shipped crude intermediates to the USA site, where purification of step 5 and the remaining steps (6–10) were completed. This seamless handoff leveraged expertise across both regions while maintaining project momentum.

In parallel, the team refined purification strategies by conducting purging studies, which improved chromatography efficiency across multiple steps. Coupling conditions were optimized and steps were telescoped, which reduced the number of unit operations and improved overall yields. A deeper understanding of impurity formation and degradation pathways allowed for revised chromatography parameters, leading to better impurity clearance. Finally, Tangential Flow Filtration (TFF) was adopted to intensify the downstream process, replacing three chromatography steps with a streamlined, more efficient workflow.

## The Result

The optimized process delivered toxicology material exceeding required purity standards, scaling from 1 g to 150 g while achieving 95% purity. The throughput gains and purification improvements provided a foundation for GMP manufacturing. A GMP batch of 190 g at 92% purity was successfully delivered, representing a fourfold scale-up from the tox batch while meeting all in-process controls and specifications. All unit operations performed as expected, supporting clinical supply and providing a basis for future R&D intensification.

### CHALLENGES

- HPAPI Handling
- Poor solubility
- Difficult intermediates

### SOLUTIONS

- Cross-site collaboration
- Improved chromatography
- TFF integration

### RESULTS

- 150x scale-up
- GMP batch delivered
- 3 chromatography steps removed

Optimization of a Complex Multi-Step Linker Payload

# Case Study 2:

## Global Approach to Payload Development

### The Challenge

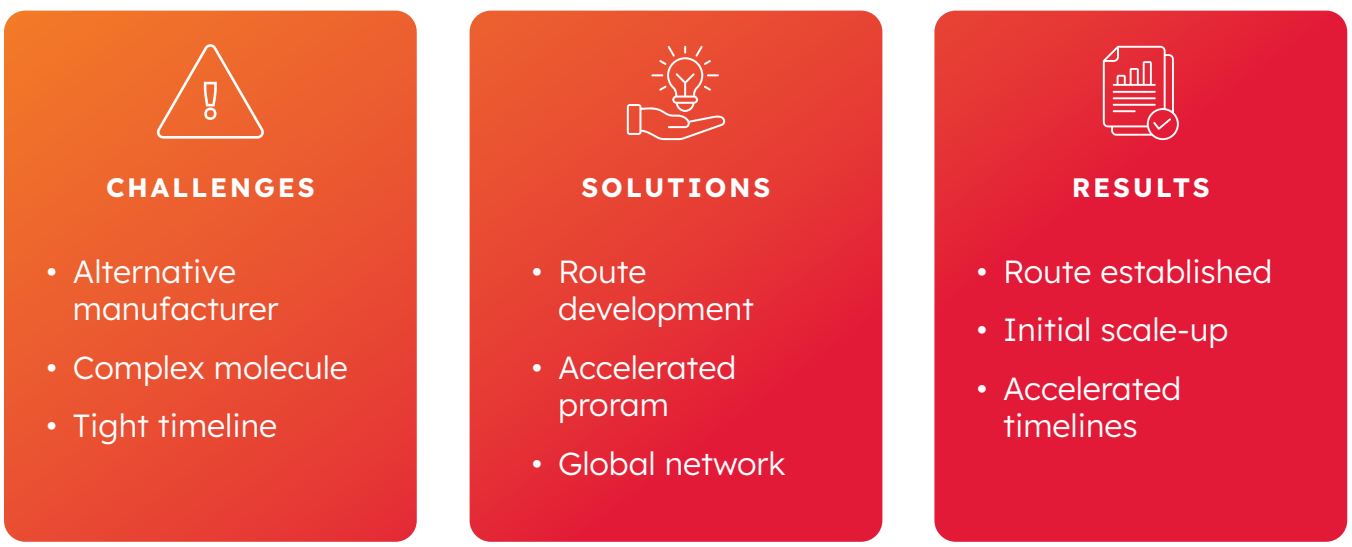
A large biopharma customer sought an alternative Western-based manufacturer for a well-known payload-linker (xx-MMAE). The project required rapid development of a complex multi-step molecule without any transferred process knowledge. In addition, the customer required a transparent manufacturing process that would support regulatory filings and align with accelerated timelines.

### The Solution

SK pharmteco designed a novel synthetic route with freedom to operate, ensuring the customer could proceed without licensing restrictions. To accelerate development, activities were distributed across SK pharmteco's global network and trusted partner organizations, enabling multiple tasks to be carried out in parallel. The project was fully aligned with the customer's needs through regular communication and transparent updates, ensuring regulatory and technical requirements were consistently met.

## The Result

A new manufacturing route was established, and initial lab-scale process development was successfully completed. The accelerated approach allowed the customer to meet their demanding timelines while establishing a robust path forward for future development and scale-up. By designing a process from scratch, SK pharmteco provided both technical freedom and confidence for regulatory filings, positioning the customer for commercial success.




Global Approach to Payload Development

## Bringing It All Together:

# How SK pharmteco Delivers What Customers Need

### Across the ADC landscape, customers consistently look for:

- Optimized Capacity to ensure programs advance seamlessly from clinical to commercial scale.
- Complex Chemistry Experience to manage highly potent, multi-step payloads and linkers.
- Chromatography Expertise to purify and deliver high-quality intermediates.
- High Potency containment and expertise

### SK pharmteco delivers on these needs with:

- Right-sized, specialized facilities with advanced containment to OEL < 10 ng/m³.
- 20+ years of HPAPI expertise and over a decade of commercial linker supply experience.
- Industry-leading chromatography capabilities and in-house analytical testing.
- A single dedicated project manager to ensure smooth communication and project delivery.

This combination of capacity, experience, and expertise allows SK pharmteco to provide customers with confidence, scalability, and accelerated time-to-market in the competitive ADC space.

## About SK pharmteco

SK pharmteco is a global contract development and manufacturing organization (CDMO) serving the pharmaceutical and biopharmaceutical industries. With CGMP manufacturing sites, research and development facilities, and analytical laboratories across the United States, Europe, and South Korea, the company provides integrated services spanning Active Pharmaceutical Ingredients (APIs), advanced intermediates, registered starting materials, viral vectors for gene therapy, and analytical capabilities in support of client programs.

SK pharmteco partners with companies of all sizes to enable the development and delivery of transformative therapies worldwide. The company is a subsidiary of SK Inc. (KRX: 034730), the strategic investment arm of SK Group, South Korea's second-largest conglomerate.

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