**Introduction**

The warhead of an antibody-drug conjugate (ADC) is comprised of a cytotoxic payload drug and a molecular linker that covalently bridges the antibody and the payload. With an extensive library of payload drugs and linkers, plus years of experience in synthetic and conjugation chemistry, Creative Biolabs is dedicated to helping our clients design and prepare highly customized linker and drug-linker complexes for the creation of ADCs using our featured “DrugLink” services. From conventional payload-linkers bearing auristatin or maytansinoid derivatives to more innovated warheads such as topoisomerase inhibitors, we have created many unique compounds tailored to clients’ special projects.

Presented here is a case study for the synthesis of two customized payload-linker complexes via the “DrugLink” organic synthesis service. SN38 is the payload of choice and two cleavable linkers are used to formulate the SN38-linker complexes. For the protection of custom IP, the reaction conditions, catalysts, as well as solvents are omitted from the synthesis routes.

**SN38: a novel payload for ADC development**

**Case 1: Mc-vc-PAB-SN38**

**Compound specifics:**
1. Chemical formula: C51H58N8O13
2. MW: 1497.7
3. Elemental analysis: C-60.08; H-6.63; N-11.31; O-21.01

**Synthesis route design:**
Based on the structure of Mc-vc-PAB-SN38, a 3-step synthesis route was designed.

**Case 2: CL2A-SN38**

**Compound specifics:**
1. Chemical formula: C51H58N8O13
2. MW: 1497.7
3. Elemental analysis: C-60.08; H-6.63; N-11.31; O-21.01

**CL2A-SN38 structure breakdown:**

**Synthesis of CL2A-SN38:**
1. Reactions for each step were carried out in optimized conditions with suitable solvents and catalysts, if necessary.
2. The yields of each step were recorded and reported, and the products from each step were characterized by LC-MS to ensure the correct MW.
3. The final product: CL2A-SN38 was characterized by both LC-MS and 1HNMR to assess purity and validate structure.
4. Synthesis lead time was 10 weeks.

**Results**
CL2A-SN38 was successfully synthesized in 10 weeks. Final product is characterized as:

1. Purity: > 95% by LC-MS

**References**