The antibody-drug conjugate (ADC), a humanized or human monoclonal antibody conjugated with highly cytotoxic small molecules (payloads) through chemical linkers, is a novel therapeutic format and has great potential to make a paradigm shift in cancer chemotherapy. The three components of the ADC together give rise to a powerful oncolytic agent capable of delivering normally intolerable cytotoxins directly to cancer cells, which then internalize and release the cell-destroying drugs. At present, two ADCs, Adcetris and Kadcyla, have received regulatory approval with >40 others in clinical development.

ADCs are administered intravenously in order to prevent the mAb from being destroyed by gastric acids and proteolytic enzymes. The mAb component of the ADC enables it to circulate in the bloodstream until it finds and binds to tumor-specific cell surface antigens present on target cancer cells. Linker chemistry is an important determinant of the safety, specificity, potency and activity of ADCs. Linkers are designed to be stable in the blood stream (to conform to the increased circulation time of mAbs) and labile at the cancer site to allow rapid release of the cytotoxic drug. First generation ADCs made use of early cytotoxins such as the anthracycline, doxorubicin or the anti-metabolite/antifolate agent, methotrexate. Current cytotoxins have far greater potency and can be divided into three main groups: auristatins, maytansines and calicheamicins.

The development of site-specific conjugation methodologies for constructing homogeneous ADCs is an especially promising path to improving ADC design, which will open the way for novel cancer therapeutics.

References:
Target List in Antibody-drug Conjugate/ADC Related

- ADC Cytotoxin ........................................ 3
- ADC Linker ........................................... 8
- Drug-Linker Conjugates for ADC .............. 11
- PROTAC-linker Conjugate for PAC .......... 15
Antibody-drug conjugates (ADCs) represent a novel class of cancer therapeutics. Their design involves a tumor-specific antibody, a linker and a cytotoxic payload. The payload in ADCs are highly potent cytotoxins, exerting their effects on critical cellular processes required for survival. Typically, the cytotoxins used in ADCs are a 100-1000 times more potent than regular chemotherapeutics and preferably have sub-nanomolar potency. Most compounds in current clinical testing utilize either maytansine derivatives (DM1/DM4) or auristatins (MMAE/ MMAF), which are both microtubule inhibitors. These typically induce apoptosis in cells undergoing mitosis by causing cell cycle arrest at G2/M. More recent work shows that microtubule inhibitors may also disrupt non-dividing cells in interphase. Other classes of cytotoxins used in ADCs include enediyne (Calicheamicin), duocarmycin derivatives, pyrrolobenzodiazepines (PBDs) and indolinobenzodiazepines, all of which target the minor groove of DNA, and quinoline alkaloids (SN-38), which inhibit topoisomerase. For example, the potent cytotoxic drug doxorubicin and daunorubicin may interact with DNA by intercalation.
### ADC Cytotoxin Inhibitors & Modulators

<table>
<thead>
<tr>
<th>Compound</th>
<th>Cat. No.</th>
<th>Bioactivity</th>
<th>Purity</th>
<th>Clinical Data</th>
<th>Size</th>
</tr>
</thead>
<tbody>
<tr>
<td>10-Deacetyl-7-xylosyl paclitaxel</td>
<td>HY-20584</td>
<td>10-Deacetyl-7-xylosyl paclitaxel is a Paclitaxel derivative with improved pharmacological features and higher water solubility. IC50 value: Target: Microtubule inhibitor 10-Deacetyl-7-xylosyl paclitaxel induced mitotic cell cycle arrest and apoptosis as measured by flow cytometry, DNA...</td>
<td>98.0%</td>
<td>No Development Reported</td>
<td>10 mg, 50 mg</td>
</tr>
<tr>
<td>Aldoxorubicin (INNO-206; DOXO-EMCH)</td>
<td>HY-16261</td>
<td>Aldoxorubicin (INNO-206) is an albumin-binding prodrug of doxorubicin, which is released from albumin under acidic conditions. Aldoxorubicin (INNO-206) has potent antitumor activities in various cancer cell lines and in in murine tumor models.</td>
<td>95.0%</td>
<td>Phase 3</td>
<td>5 mg, 10 mg, 50 mg, 100 mg</td>
</tr>
<tr>
<td>alpha-Amanitin (α-Amanitin; α-Amatoxin)</td>
<td>HY-19610</td>
<td>alpha-Amanitin is the principal toxin of several deadly poisonous mushrooms, exerting its toxic function by inhibiting RNA-polymerase II.</td>
<td>99.79%</td>
<td>No Development Reported</td>
<td>1 mg, 2 mg, 5 mg</td>
</tr>
<tr>
<td>Ansamitocin P 3' (Antibiotic C 15003P3; Maytansinol butyrate)</td>
<td>HY-19839</td>
<td>Ansamitocin P 3' is a microtubule inhibitor. Ansamitocin P-3 is a macrocyclic antitumor antibiotic.</td>
<td>98.0%</td>
<td>No Development Reported</td>
<td>10 mM x 1 mL in DMSO, 5 mg, 10 mg, 50 mg, 100 mg</td>
</tr>
<tr>
<td>Ansamitocin P-3 (Antibiotic C 15003P3; Maytansinol butyrate; C15003P3)</td>
<td>HY-15739</td>
<td>Ansamitocin P-3' exhibits antitumour activity, is an antibody drug conjugate cytotoxin. The more information please refer to Ansamitocin P-3 (HY-15739).</td>
<td>87.63%</td>
<td>No Development Reported</td>
<td>10 mM x 1 mL in DMSO, 5 mg, 10 mg, 50 mg, 100 mg</td>
</tr>
<tr>
<td>Auristatin E</td>
<td>HY-15582</td>
<td>Auristatin E is a cytotoxic tubulin modifier with potent and selective antitumor activity; MMAE analog and cytotoxin in Antibody-drug conjugates.</td>
<td>99.36%</td>
<td>No Development Reported</td>
<td>10 mM x 1 mL in DMSO, 1 mg, 5 mg, 10 mg</td>
</tr>
<tr>
<td>Auristatin F</td>
<td>HY-15583</td>
<td>Auristatin F is a cytotoxic tubulin modifier with potent and selective antitumor activity; MMAF analog and cytotoxin in Antibody-drug conjugates.</td>
<td>98.85%</td>
<td>No Development Reported</td>
<td>10 mM x 1 mL in DMSO, 1 mg, 5 mg, 10 mg</td>
</tr>
<tr>
<td>Calicheamicin (Calicheamicin γ1)</td>
<td>HY-19609</td>
<td>Calicheamicin is a cytotoxic agent that causes double-strand DNA breaks.</td>
<td>98.44%</td>
<td>No Development Reported</td>
<td>10 mM x 1 mL in DMSO, 1 mg, 5 mg, 10 mg</td>
</tr>
<tr>
<td>Campathecin (Camptothecin; (S)-(+)-Camptothecin; CPT)</td>
<td>HY-16560</td>
<td>Campathecin is a potent DNA enzyme topoisomerase I inhibitor, with an IC50 of 679 nM.</td>
<td>98.26%</td>
<td>Phase 4</td>
<td>10 mM x 1 mL in DMSO, 100 mg, 500 mg</td>
</tr>
<tr>
<td>D8-MMAD (Demethyldolastatin 10 D8; Monomethylauristatin D 10D; Monomethyl Dolastatin 10 D8)</td>
<td>HY-15581S</td>
<td>D8-MMAD is a deuterated form of MMAD, which is a microtubule disrupting agent.</td>
<td>98.0%</td>
<td>No Development Reported</td>
<td>10 mM x 1 mL in DMSO, 1 mg, 5 mg, 10 mg</td>
</tr>
</tbody>
</table>
D8-MMAE  
(D8-Monomethyl auristatin E; D8-Vedotin)  
Cat. No.: HY-15162A

Bioactivity: D8-MMAE is a deuterated labeled MMAE, a potent mitotic inhibitor.

Purity: 98.31%  
Clinical Data: No Development Reported  
Size: 1 mg, 5 mg, 10 mg

D8-MMAF  
(Monomethylauristatin F D8)  
Cat. No.: HY-15579S

Bioactivity: D8-MMAF is a deuterated form of MMAF, which is a microtubule disrupting agent.

Purity: >98%  
Clinical Data: No Development Reported  
Size: 1 mg, 5 mg, 10 mg

D8-MMAF hydrochloride  
Cat. No.: HY-15579AS

Bioactivity: D8-MMAF hydrochloride is a deuterated form of MMAF hydrochloride, which is a microtubule disrupting agent.

Purity: 99.56%  
Clinical Data: No Development Reported  
Size: 10 mM x 1 mL in DMSO, 1 mg, 5 mg, 10 mg

Daun02  
Cat. No.: HY-13001

Bioactivity: Daun02 is a prodrug of the topoisomerase inhibitor Daunorubicin.

Purity: 98.56%  
Clinical Data: No Development Reported  
Size: 10 mM x 1 mL in DMSO, 2 mg, 5 mg, 10 mg

Daunorubicin  
(RP13057; Daunomycin; Rubidomycin)  
Cat. No.: HY-13062A

Bioactivity: Daunorubicin is a topoisomerase II inhibitor.

Purity: >98%  
Clinical Data: Launched  
Size: 10 mg, 50 mg

Daunorubicin Hydrochloride  
(RP 13057 Hydrochloride; Daunomycin; RP13057 Hydrochloride; ...)  
Cat. No.: HY-13062

Bioactivity: Daunorubicin hydrochloride is a topoisomerase II inhibitor with potent antineoplastic activities.

Purity: 99.27%  
Clinical Data: Launched  
Size: 10 mM x 1 mL in Water, 10 mg, 50 mg, 100 mg, 200 mg, 500 mg

Dolastatin 10  
(DLS 10; NSC 376128)  
Cat. No.: HY-15580

Bioactivity: Angiotensin II human is a vasoconstrictor that acts on the AT1 and the AT2 receptor.

Purity: 99.83%  
Clinical Data: Phase 2  
Size: 1 mg, 5 mg

Doxorubicin  
(Adriamycin; Hydroxydaunorubicin)  
Cat. No.: HY-15142A

Bioactivity: Doxorubicin is a cytotoxic anthracycline antibiotic for the treatment of multiple cancers. The possible mechanisms by which doxorubicin acts in the cancer cell are intercalation into DNA and disruption of topoisomerase-II-mediated DNA repair.

Purity: >98%  
Clinical Data: Launched  
Size: 50 mg, 100 mg, 200 mg, 500 mg

Doxorubicin hydrochloride  
(Adriamycin; Hydroxydaunorubicin hydrochloride)  
Cat. No.: HY-15142

Bioactivity: Doxorubicin hydrochloride is a cytotoxic anthracycline antibiotic for the treatment of multiple cancers. The possible mechanisms by which doxorubicin acts in the cancer cell are intercalation into DNA and disruption of topoisomerase-II-mediated DNA repair.

Purity: 99.47%  
Clinical Data: Launched  
Size: 10 mM x 1 mL in DMSO, 50 mg, 100 mg, 200 mg, 500 mg, 1 g

Duocarmycin TM  
Cat. No.: HY-107769

Bioactivity: Duocarmycin TM is an exceptionally potent antitumor antibiotic.

Purity: 98.99%  
Clinical Data: No Development Reported  
Size: 10 mM x 1 mL in DMSO, 5 mg, 10 mg, 25 mg, 50 mg, 100 mg
**Dxd**  
(Exatecan derivative)  
Cat. No.: HY-13631D

**Bioactivity:** Dxd is a potent DNA topoisomerase I inhibitor, with an IC$_{50}$ of 0.31 μM, used as a conjugated drug of HER2-targeting ADC (DS-8201a).

**Purity:** 98.20%

**Clinical Data:** No Development Reported

**Size:** 10mM x 1mL in DMSO,
1 mg, 5 mg, 10 mg

---

**Maytansinol**  
(Ansamitocin P-0)  
Cat. No.: HY-19474

**Bioactivity:** Maytansinol inhibits microtubule assembly and induces microtubule disassembly in vitro. Target: Microtubule/Tubulin in vitro. Maytansinol disrupts the mitotic spindle and prevents mitotic exit in Drosophila. Maytansinol reduces the growth and/or survival of HCT116 cells in a dose-dependent...

**Purity:** 98.15%

**Clinical Data:** No Development Reported

**Size:** 10mM x 1mL in DMSO,
5 mg, 10 mg, 50 mg

---

**MC-DOXHZN**  
(Doxorubicin(6-maleimidocaproyl)hydrazone)  
Cat. No.: HY-16261A

**Bioactivity:** DOXO-EMCH is a 6-maleimidocaproyl hydrazone derivative of Doxorubicin, is an albumin binding prodrug.

**Purity:** >98%

**Clinical Data:** Phase 3

**Size:** 5 mg, 10 mg, 50 mg, 100 mg

---

**Methotrexate**  
(Anmethopterin; CL14377; WR19039)  
Cat. No.: HY-14519

**Bioactivity:** Methotrexate is a folate antagonist, with median IC$_{50}$ of 78 nM in vitro assay.

**Purity:** 99.75%

**Clinical Data:** No Development Reported

**Size:** 10mM x 1mL in DMSO,
100 mg, 500 mg

---

**Mitomycin C**  
(Ametycine)  
Cat. No.: HY-13316

**Bioactivity:** Mitomycin C is an antitumor drug and antibiotic that shows extraordinary ability to inhibit DNA synthesis.

**Purity:** 98.89%

**Clinical Data:** Launched

**Size:** 10mM x 1mL in DMSO,
5 mg, 10 mg, 50 mg, 100 mg, 200 mg, 500 mg

---

**MMAD**  
(Demethyldolastatin 10; Monomethylauristatin D; Monomethyl Dolastatin 10)  
Cat. No.: HY-15581

**Bioactivity:** MMAD is a potent tubulin inhibitor, is a toxin payload in antibody drug conjugates (ADCs).

**Purity:** 99.92%

**Clinical Data:** No Development Reported

**Size:** 10mM x 1mL in DMSO,
5 mg, 10 mg, 50 mg, 100 mg

---

**MMAF**  
(Monomethylauristatin F)  
Cat. No.: HY-15579

**Bioactivity:** MMAF (Monomethylauristatin F) is an antitubulin agent that inhibit cell division; inhibits H3397 cell growth with an IC$_{50}$ of 105 nM.

**Purity:** >98%

**Clinical Data:** No Development Reported

**Size:** 2 mg, 5 mg, 10 mg

---

**MMAF Hydrochloride**  
(Monomethylauristatin F Hydrochloride)  
Cat. No.: HY-15579A

**Bioactivity:** MMAF hydrochloride is an antitubulin agent that inhibit cell division; inhibits H3397 cell growth with an IC$_{50}$ of 105 nM.

**Purity:** 98.96%

**Clinical Data:** No Development Reported

**Size:** 10mM x 1mL in DMSO,
2 mg, 5 mg, 10 mg

---

**MMAF-OMe**  
(Monomethyl auristatin F methyl ester)  
Cat. No.: HY-79256

**Bioactivity:** MMAF-OMe belongs to ADC, and inhibits several tumor cell lines with IC$_{50}$s of 0.056 nM, 0.166 nM, 0.183 nM, and 0.449 nM for MDAMB435/S74, MDAMB361DYT2, MDAMB468, and Raji (ST4) cell lines, respectively.

**Purity:** 96.88%

**Clinical Data:** No Development Reported

**Size:** 10mM x 1mL in DMSO,
2 mg, 5 mg, 10 mg

---

**Monomethyl auristatin E**  
(Vedotin; MMAE)  
Cat. No.: HY-15162

**Bioactivity:** Monomethyl auristatin E (MMAE) is a synthetic derivative of dolastatin 10 and functions as a potent mitotic inhibitor by inhibiting tubulin polymerization. MMAE is widely used as a cytotoxic component of antibody-drug conjugates (ADCs) to treat several different cancer types.

**Purity:** 99.94%

**Clinical Data:** Phase 4

**Size:** 10mM x 1mL in DMSO,
1 mg, 5 mg, 10 mg, 50 mg, 100 mg, 500 mg, 1 g
Paclitaxel  
(Taxol)  
Cat. No.: HY-80015

**Bioactivity:** Paclitaxel (Taxol) is a potent anticancer medication which can promote microtubule (MT) assembly, inhibit MT depolymerization, and change MT dynamics required for mitosis and cell proliferation.

**Purity:** >98%

**Clinical Data:** No Development Reported

**Size:** 1 mg, 50 mg, 100 mg, 500 mg

---

PF-06380101  
Cat. No.: HY-12522

**Bioactivity:** PF-06380101 is a novel cytotoxic Dolastatin 10 analogue, with excellent potencies in tumor cell proliferation assays and differential ADME properties when compared to other synthetic auristatin analogues that are used in the preparation of ADCs.

**IC50 value:** ~0.2 nM(G150 in BT474, MDA-MB-361-DYT2 and N87...

**Purity:** 99.68%

**Clinical Data:** No Development Reported

**Size:** 10mM x 1mL in DMSO, 1 mg, 5 mg, 10 mg

---

PNU-159682  
Cat. No.: HY-16700

**Bioactivity:** PNU-159682, a highly potent metabolite of the anthracycline nemorubicin with outstanding cytotoxicity, is a potent ADCs cytotoxin.

**Purity:** 96.84%

**Clinical Data:** No Development Reported

**Size:** 10mM x 1mL in DMSO, 1 mg, 5 mg, 10 mg, 50 mg

---

Taltobulin  
(HTI-286, SPA-110)  
Cat. No.: HY-15584

**Bioactivity:** Taltobulin (HTI-286; SPA-110) is an analogue of Hemiasterlin; potent tubulin inhibitor; ADCs cytotoxin. IC50 value: Target: tubulin in vitro: HTI-286 significantly inhibited proliferation of all three hepatic tumor cell lines (mean IC50 = 2 nmol/L +/- 1 nmol/L) in vitro. Interestingly, no decrease...

**Purity:** 99.90%

**Clinical Data:** No Development Reported

**Size:** 10mM x 1mL in DMSO, 5 mg, 10 mg, 50 mg

---

Taltobulin hydrochloride  
(HTI-286 hydrochloride; SPA-110 hydrochloride)  
Cat. No.: HY-15584B

**Bioactivity:** Taltobulin hydrochloride is an analogue of Hemiasterlin; potent tubulin inhibitor; ADCs cytotoxin. IC50 value: Target: tubulin in vitro: HTI-286 significantly inhibits proliferation of all three hepatic tumor cell lines (mean IC50 = 2 nmol/L +/- 1 nmol/L). Interestingly, no decrease in viable primary...

**Purity:** 99.05%

**Clinical Data:** No Development Reported

**Size:** 10mM x 1mL in DMSO, 5 mg, 10 mg, 50 mg

---

Taltobulin trifluoroacetate  
(HTI-286 trifluoroacetate; SPA-110 trifluoroacetate)  
Cat. No.: HY-15584A

**Bioactivity:** Taltobulin trifluoroacetate (HTI-286; SPA-110) is an analogue of Hemiasterlin; potent tubulin inhibitor; ADCs cytotoxin. IC50 value: Target: tubulin in vitro: HTI-286 significantly inhibited proliferation of all three hepatic tumor cell lines (mean IC50 = 2 nmol/L +/- 1 nmol/L) in vitro. Interestingly,...

**Purity:** 99.96%

**Clinical Data:** No Development Reported

**Size:** 10mM x 1mL in DMSO, 5 mg, 10 mg, 50 mg

---

Tubulysin A  
(TubA)  
Cat. No.: HY-15995

**Bioactivity:** Tubulysin A(TubA) is a myxobacterial product that can function as an antiangiogenic agent in many in vitro assays; anti-microtubule, anti-mitotic, an apoptosis inducer, anticancer, anti-angiogenic, and antiproliferative. IC50 value: Target: microtubule Tubulysin A is a novel antibiotic,...

**Purity:** >98%

**Clinical Data:** No Development Reported

**Size:** 1 mg
Antibody-drug conjugates (ADCs) consist of a desirable monoclonal antibody, an active cytotoxic drug and an appropriate linker. An appropriate linker between the antibody and the cytotoxic drug provides a specific bridge, and thus helps the antibody to selectively deliver the cytotoxic drug to tumor cells and accurately releases the cytotoxic drug at tumor sites. In addition to conjugation, the linkers maintain ADCs’ stability during the preparation and storage stages of the ADCs and during the systemic circulation period.

The ADCs currently undergoing clinical evaluation contain linkers are mostly classified into two categories: cleavable and noncleavable. Cleavable linkers rely on processes inside the cell to liberate the toxin, such as reduction in the cytoplasm, exposure to acidic conditions in the lysosome, or cleavage by specific proteases within the cell. Noncleavable linkers require proteolytic degradation of the antibody portion of the ADC for release of the cytotoxic molecule, which will retain the linker and the amino acid by which it was attached to the antibody.

The selection of linker is target dependent, based on the knowledge of the internalization and degradation of the antibody-target antigen complex, and a preclinical in vitro and in vivo activity comparison of conjugates. Moreover, the choice of a linker is also influenced by which cytotoxin is used, as each molecule has different chemical constraints, and frequently the drug structure lends itself to a specific linker.
ADC Linker Inhibitors & Modulators

(Ac)Phe-Lys(Alloc)-PABC-PNP  
Cat. No.: HY-20560

Bioactivity: (Ac)Phe-Lys(Alloc)-PABC-PNP is a useful chemical linker in antibody drug conjugates.

Purity: >98%
Clinical Data: No Development Reported
Size: 5 mg, 10 mg, 50 mg, 100 mg

6-Maleimidohexanoic acid N-hydroxysuccinimide ester (EMCS)  
Cat. No.: HY-78961

Bioactivity: 6-Maleimidohexanoic acid N-hydroxysuccinimide ester (EMCS) is a useful protective group in antibody drug conjugates.

Purity: 99.96%
Clinical Data: No Development Reported
Size: 50 mg, 100 mg, 300 mg

6-Quinoxalinecarboxylic acid, 2,3-bis(bromomethyl)-  
Cat. No.: HY-21210

Bioactivity: 6-Quinoxalinecarboxylic acid, 2,3-bis(bromomethyl)- is an useful linker for antibody-drug-conjugations (ADCs), extracted from [Bioorg Chem. 2012 Apr-Jun;41-42:1-5.] compound 1i.

Purity: >98%
Clinical Data: No Development Reported
Size: 1 g

DC1  
Cat. No.: HY-112899

Bioactivity: DC1, an analogue of the minor groove-binding DNA alkylator CC-1065, is an antibody conjugate of cytotoxic DNA alkylators for the targeted treatment of cancer.

Purity: >98%
Clinical Data: No Development Reported
Size: 5 mg, 10 mg, 25 mg, 50 mg, 100 mg

DC1-SMe  
Cat. No.: HY-112898

Bioactivity: DC1-Sme is an antibody conjugate of phosphate prodrug of cytotoxic DNA alkylators for the targeted treatment of cancer.

Purity: >98%
Clinical Data: No Development Reported
Size: 5 mg, 10 mg, 25 mg, 50 mg, 100 mg

Fmoc-Phe-Lys(Boc)-PAB-PNP  
Cat. No.: HY-114430

Bioactivity: Fmoc-Phe-Lys(Boc)-PAB-PNP is an ADC linker used in the synthesis of antibody-drug conjugates (ADCs).

Purity: >98%
Clinical Data: No Development Reported
Size: 50 mg

Fmoc-Val-Cit-PAB  
Cat. No.: HY-19318

Bioactivity: Fmoc-Val-Cit-PAB is a linker for antibody-drug-conjugation (ADC).

Purity: 98.13%
Clinical Data: No Development Reported
Size: 10 mg, 50 mg, 100 mg, 500 mg

Fmoc-Val-Cit-PAB-PNP  
Cat. No.: HY-41189

Bioactivity: Fmoc-Val-Cit-PAB-PNP is a peptide prodrug linker, is a linker for antibody-drug-conjugation (ADC).

Purity: 96.13%
Clinical Data: No Development Reported
Size: 50 mg

MC-Val-Cit-PAB  
Cat. No.: HY-78738

Bioactivity: MC-Val-Cit-PAB is a cathepsin cleavable ADC linker that is used for making antibody-drug conjugate. FDA approved drugs such as brentuximab vedotin use this linker.

Purity: 99.66%
Clinical Data: No Development Reported
Size: 1 g

Mc-Val-Cit-PABC-PNP  
Cat. No.: HY-20336

Bioactivity: Mc-Val-Cit-PABC-PNP is a cathepsin cleavable ADC linker used in the synthesis of antibody-drug conjugates (ADCs).

Purity: 98.68%
Clinical Data: No Development Reported
Size: 10 mg, 50 mg, 100 mg, 200 mg
<table>
<thead>
<tr>
<th><strong>UAA crosslinker 1</strong></th>
<th><strong>Val-cit-PAB-OH</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Bioactivity:</strong></td>
<td>Bioactivity:</td>
</tr>
<tr>
<td>UAA crosslinker 1 act as substrates for pylRS/tRNA pair that enable its incorporation into a target protein.</td>
<td>Val-cit-PAB-OH is a peptide prodrug linker.</td>
</tr>
<tr>
<td><strong>Purity:</strong></td>
<td><strong>Purity:</strong></td>
</tr>
<tr>
<td>&gt;98%</td>
<td>99.64%</td>
</tr>
<tr>
<td><strong>Clinical Data:</strong></td>
<td><strong>Clinical Data:</strong></td>
</tr>
<tr>
<td>No Development Reported</td>
<td>No Development Reported</td>
</tr>
<tr>
<td><strong>Size:</strong></td>
<td><strong>Size:</strong></td>
</tr>
<tr>
<td>250 mg, 500 mg</td>
<td>100 mg, 500 mg, 1 g</td>
</tr>
<tr>
<td>Cat. No.: HY-111434</td>
<td>Cat. No.: HY-12362</td>
</tr>
</tbody>
</table>

Tel: 609-228-6898    Fax: 609-228-5909    Email: sales@MedChemExpress.com
Antibody Drug Conjugates (ADC) are a rapidly expanding area in the pharmaceutical industry. They comprise of a desirable monoclonal antibody, an active cytotoxic drug and an appropriate linker. There are over 30 ADCs currently in pre-clinical or clinical development, and further improvements may be required to enhance the therapeutic potential of these ADCs. Monoclonal antibodies (mAbs) are of great use in many applications ranging from basic research to treatment of disease. The Drug-Linker Conjugates can expand the utility of mAbs and improve their potency and effectiveness; the antibodies are thus used as a means to target and delivery a toxic payload to the selected diseased tissue. The site-specific conjugations of Drug-Linker to an antibody may involve genetic engineering of the mAb to introduce discrete, available cysteines or non-natural amino acids with an orthogonally-reactive functional group handle such as an aldehyde, ketone, azido, or alkynyl tag. These site-specific approaches not only increase the homogeneity of ADCs but also enable novel bio-orthogonal chemistries that utilize reactive moieties other than thiol or amine. The cytotoxic drug, monomethyl auristatin E (MMAE), is conjugated to the three trastuzumab variants using a protease cleavable linker and shows in vivo therapeutic efficacy. The linker-MMAE conjugate is used in the U.S. FDA approved ADC, Brentuximab vedotin. There are also ADCs adopting linker-MMAE conjugate under clinical trials, such as Enfortumab vedotin and Glembatumumab vedotin.
## Drug-Linker Conjugates for ADC Inhibitors & Modulators

<table>
<thead>
<tr>
<th>Drug Name</th>
<th>Cat. No.</th>
<th>Bioactivity</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Acetylene-linker-Val-Cit-PABC-MMAE</strong> (LCB14-0602)</td>
<td>HY-19812</td>
<td>Acetylene-linker-Val-Cit-PABC-MMAE consists the ADCs linker (Acetylene-linker-Val-Cit-PABC) and potent tubulin inhibitor (MMAE), Acetylene-linker-Val-Cit-PABC-MMAE is an antibody drug conjugate.</td>
</tr>
<tr>
<td><strong>AcLys-PABC-VC-Aur0101</strong></td>
<td>HY-111554</td>
<td>AcLys-PABC-VC-Aur0101 is a cleavable anti-CXCR4 drug-linker conjugates for ADC.</td>
</tr>
<tr>
<td><strong>AmPEG6C2-Aur0131</strong></td>
<td>HY-111555</td>
<td>AmPEG6C2-Aur0131 is a non-cleavable anti-CXCR4 drug-linker conjugates for ADC.</td>
</tr>
<tr>
<td><strong>DBCO-(PEG)3-VC-PAB-MMAE</strong></td>
<td>HY-111012</td>
<td>DBCO-(PEG)3-VC-PAB-MMAE is made by MMAE conjugated to DBCO-(PEG)3-vc-PAB linker. Monomethyl auristatin E (MMAE), a potent tubulin inhibitor, is a toxin payload in antibody drug conjugate.</td>
</tr>
<tr>
<td><strong>Deruxtecan analog</strong></td>
<td>HY-13631E</td>
<td>Deruxtecan analog is a drug-linker conjugate for antibody-drug conjugate (ADC) extracted from patent WO2017002776A1, compound 1.</td>
</tr>
<tr>
<td><strong>Fmoc-Val-Cit-PAB-MMAE</strong></td>
<td>HY-19811</td>
<td>Fmoc-Val-Cit-PAB-MMAE consists the ADCs linker (Fmoc-Val-Cit-PAB) and potent tubulin inhibitor (MMAE), Fmoc-Val-Cit-PAB-MMAE is an antibody drug conjugate.</td>
</tr>
<tr>
<td><strong>MAL-di-EG-Val-Cit-PAB-MMAE</strong></td>
<td>HY-100567</td>
<td>MAL-di-EG-Val-Cit-PAB-MMAE consists the ADCs linker (MAL-di-EG-Val-Cit-PAB) and potent tubulin inhibitor (MMAE), MAL-di-EG-Val-Cit-PAB-MMAE is an antibody drug conjugate.</td>
</tr>
<tr>
<td><strong>Mc-MMAD</strong></td>
<td>HY-15740</td>
<td>Monomethyl auristatin D (MMAD), a potent tubulin inhibitor, is a toxin payload in antibody drug conjugate; Mc-MMAD is a protective group (maleimidocaproyl)-conjugated MMAD. IC50 Value: N/A Target: tubulin; ADCs For comparison purposes, the ADC A1-mc-MMAD and/or A1-vc-MMAD were used. The linker payload, mc-MMAD (6-maleimidocaproyl-monomethylauristatin-D) was...</td>
</tr>
<tr>
<td><strong>Mc-MMAE</strong></td>
<td>HY-15741</td>
<td>Mc-MMAE is a protective group (maleimidocaproyl)-conjugated monomethyl auristatin E (MMAE), which is a potent tubulin inhibitor, is a toxin payload in antibody drug conjugate (ADC).</td>
</tr>
</tbody>
</table>

### Property Details

<table>
<thead>
<tr>
<th>Property</th>
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<tr>
<td><strong>Purity</strong></td>
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<td><strong>Clinical Data</strong></td>
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<td><strong>Size</strong></td>
<td>10mM x 1mL in DMSO, 1 mg, 5 mg, 10 mg</td>
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<tr>
<td><strong>Purity</strong></td>
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<tr>
<td><strong>Purity</strong></td>
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<td><strong>Clinical Data</strong></td>
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<td><strong>Purity</strong></td>
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<tr>
<td><strong>Clinical Data</strong></td>
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<td><strong>Purity</strong></td>
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<td><strong>Clinical Data</strong></td>
<td>No Development Reported</td>
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<td><strong>Size</strong></td>
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</table>
### McMMAF (Maleimidocaproyl monomethylauristatin F)  
**Cat. No.:** HY-15578  
**Bioactivity:** McMMAF is a protective group-conjugated MMAF. MMAF is a more potent drug than Monomethyl auristatin E (MMAE), but it is charged and relatively membrane-impermeable, so it is a toxin payload in antibody drug conjugate. Target: MMAF is a new auristatin derivative with a...  
**Purity:** 99.58%  
**Clinical Data:** No Development Reported  
**Size:** 10mM x 1mL in DMSO, 1 mg, 5 mg, 10 mg

### mDPR-Val-Cit-PAB-MMAE  
**Cat. No.:** HY-19813  
**Bioactivity:** mDPR-Val-Cit-PAB-MMAE consists the ADCs linker (mDPR-Val-Cit-PAB) and potent tubulin inhibitor (MMAE), mDPR-Val-Cit-PAB-MMAE is an antibody drug conjugate.  
**Purity:** >98%  
**Clinical Data:** No Development Reported  
**Size:** 1 mg, 5 mg, 10 mg

### Mertansine (DM1; Maytansinoid DM1)  
**Cat. No.:** HY-19792  
**Bioactivity:** Mertansine (DM1) is a microtubulin inhibitor which binds at the tips of microtubules and suppresses the dynamics of microtubules. Mertansine is an antibody-conjugatable maytansinoid that was developed to overcome systemic toxicity associated with maytansine and to enhance tumor-specific...  
**Purity:** 98.74%  
**Clinical Data:** Phase 2  
**Size:** 2 mg, 5 mg, 10 mg, 25 mg, 50 mg, 100 mg

### N3-PEG3-vc-PAB-MMAE  
**Cat. No.:** HY-100874  
**Bioactivity:** N3-PEG3-vc-PAB-MMAE is a drug-linker conjugate for ADC with potent antitumor activity by using the anti-mitotic agent, monomethyl auristatin E (MMAE), linked via the peptide N3-PEG3-vc-PAB.  
**Purity:** 99.18%  
**Clinical Data:** No Development Reported  
**Size:** 10mM x 1mL in DMSO, 1 mg, 5 mg, 10 mg

### NAMPT inhibitor-linker 1  
**Cat. No.:** HY-112615  
**Bioactivity:** NAMPT inhibitor-linker 1 is a drug-linker conjugates for ADC, composed of an NAMPT inhibitor as a payload, and a linker. ADC-3 consists of an NAMPT inhibitor-linker 1 and an anti-c-Kit monoclonal antibody, exhibits potent activity against c-Kit expressing cell lines such as GIST-T1 and...  
**Purity:** >98%  
**Clinical Data:** No Development Reported  
**Size:**

### NAMPT inhibitor-linker 2  
**Cat. No.:** HY-112616  
**Bioactivity:** NAMPT inhibitor-linker 2 is a drug-linker conjugates for ADC, composed of an NAMPT inhibitor as a payload, and a linker. ADC-4 consists of an NAMPT inhibitor-linker 2 and an anti-c-Kit monoclonal antibody, exhibits potent activity against c-Kit expressing cell lines such as GIST-T1 and...  
**Purity:** >98%  
**Clinical Data:** No Development Reported  
**Size:**

### SMCC-DM1 (DM1-SMCC)  
**Cat. No.:** HY-101070  
**Bioactivity:** SMCC-DM1 is DM1 with a reactive linker SMCC to make antibody drug conjugate. DM1 (mertansine), a thiol-containing maytansinoid, is a potent microtubule-disrupting agent.  
**Purity:** 99.54%  
**Clinical Data:** No Development Reported  
**Size:** 10mM x 1mL in DMSO, 1 mg, 5 mg, 10 mg, 25 mg, 50 mg, 100 mg

### SPDB-DM4  
**Cat. No.:** HY-12460  
**Bioactivity:** SPDB-DM4 is a drug-linker conjugate for ADC by using the maytansinebased payload (DM4) via a SPDB linker, exhibiting potent anti-tumor activity.  
**Purity:** 95.58%  
**Clinical Data:** No Development Reported  
**Size:** 10mM x 1mL in DMSO, 1 mg, 5 mg, 10 mg

### sulfo-SPDB-DM4  
**Cat. No.:** HY-101141  
**Bioactivity:** sulfo-SPDB-DM4 is a drug-linker conjugate for ADC by using the maytansinebased payload (DM4) via the sulfo-SPDB linker.  
**Purity:** >98%  
**Clinical Data:** No Development Reported  
**Size:** 1 mg, 5 mg

### SuO-Val-Cit-PAB-MMAE  
**Cat. No.:** HY-100566  
**Bioactivity:** SuO-Val-Cit-PAB-MMAE is a drug-linker conjugate for ADC by using the anti-mitotic agent, monomethyl auristatin E (MMAE), linked via the peptide SuO-Val-Cit-PAB.  
**Purity:** 97.87%  
**Clinical Data:** No Development Reported  
**Size:** 10mM x 1mL in DMSO, 1 mg, 5 mg, 10 mg
<table>
<thead>
<tr>
<th><strong>Bioactivity</strong></th>
<th><strong>Purity</strong></th>
<th><strong>Clinical Data</strong></th>
<th><strong>Size</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>SW-163D-AcLysValCit-PABC-DMAE</strong></td>
<td>&gt;98%</td>
<td>No Development Reported</td>
<td>250 mg, 500 mg</td>
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<tr>
<td><strong>Val-Cit-PAB-MMAE</strong></td>
<td>99.83%</td>
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<td><strong>Vc-MMAD</strong></td>
<td>&gt;98%</td>
<td>No Development Reported</td>
<td>10mM x 1mL in DMSO, 1 mg, 5 mg, 10 mg</td>
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<td><strong>VcMMAE (mc-vc-PAB-MMAE)</strong></td>
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<td>Phase 2</td>
<td>10mM x 1mL in DMSO, 1 mg, 5 mg, 10 mg, 50 mg, 100 mg</td>
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</tbody>
</table>

Bioactivity: **SW-163D-AcLysValCit-PABC-DMAE** is a **Drug-Linker Conjugates for ADC** which consists of a natural bis-intercalator, SW-163D, conjugated via an AcLysValCitPABC-DMAE linker \[1\].

Bioactivity: **Val-Cit-PAB-MMAE** is a **drug-linker conjugate for ADC** by using the anti-mitotic agent, monomethyl auristatin E (MMAE), linked via the peptide Val-Cit-PAB.

Bioactivity: **Vc-MMAD** consists the ADCs linker(Val-Cit) and potent tubulin inhibitor (MMAD), Vc-MMAD is an antibody drug conjugate. IC50 Valu: N/A Target: tubulin; ADCs Monomethyl auristatin D (MMAD), a potent tubulin inhibitor, is a toxin payload and antibody drug conjugate. For comparison purposes, the ADC A1...

Bioactivity: **VcMMAE** is a **drug-linker conjugate for ADC** with potent antitumor activity by using the anti-mitotic agent, monomethyl auristatin E (MMAE), linked via the lysosomally cleavable dipeptide, valine-citrulline (vc).
PROTAC-linker Conjugate for PAC

PROTAC-linker for PROTAC-antibody Conjugate

PROTAC-linker Conjugate for PAC comprises an antibody conjugated via a linker to a PROTAC. The PROTAC-Antibody Conjugate (PAC) molecules comprise an antibody conjugated via a linker (L1) to a PROTAC, wherein the PROTAC comprises an ubiquitin E3 ligase binding group (“E3LB”), a linker (“L2”) and a protein binding group (“PB”). To obtain a PAC having potent efficacy and a desirable therapeutic index, the following components are provided.

1. Antibody (Ab): The antibody portion of a PAC can target a cell that expresses an antigen whereby the antigen specific PAC is delivered intracellularly to the target cell, typically through endocytosis. While PACs that comprise an antibody directed to an antigen that is not found on the cell surface may result in less specific intracellular delivery of the PROTAC portion into the cell, the PAC may still undergo pinocytosis.

2. Linkers (L1): A “linker” (L1) is a bifunctional or multifunctional moiety that can be used to link one or more PROTAC moieties (D) to an antibody (Ab) to form a PAC. In some embodiments, PACs can be prepared using a L1 having reactive functionalities for covalently attaching to the PROTAC and to the antibody.

3. PROTAC(D).
### PROTAC-linker Conjugate for PAC Inhibitors & Modulators

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<th>PAC</th>
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<tr>
<td><strong>Bioactivity:</strong></td>
<td>PAC comprises an antibody conjugated via a linker to a PROTAC. PAC extracts from patent WO2017201449A1, compound PAC1. PAC is a more marked estrogen receptor-alpha (ERα) degrader compared to PROTAC (without Ab).</td>
</tr>
<tr>
<td>Purity:</td>
<td>&gt;98%</td>
</tr>
<tr>
<td>Clinical Data:</td>
<td>No Development Reported</td>
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<td>Size:</td>
<td>5 mg, 10 mg</td>
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