from WNT1, WNT2, WNT2B, WNT3, WNT4, WNT5A, WNT5B, WNT6, WNT7A, WNT7B, WNT8A, WNT8B, WNT9A, WNT9B, WNT10A, WNT10B, WNT11 and WNT16.

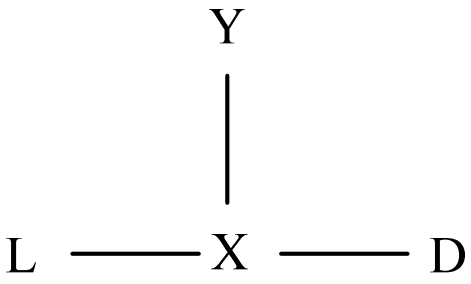
[0082] In yet another aspect, the present disclosure provides a kit for diagnosis or treatment including any of the antibodies or antibody fragments, the immunoconjugates, or the pharmaceutical compositions of the present disclosure described above.

[0083] In yet another aspect, the present disclosure provides a pharmaceutical composition that includes any of the linker, conjugate, and/or immunoconjugate, of the disclosure described above, together with a pharmaceutically acceptable carrier.

[0084] The present disclosure also provides use of a linker, conjugate, and/or immunoconjugate of any one of the embodiments described above, for the treatment of cancer.

[0085] The present disclosure further provides a kit for diagnosis or treatment, said kit comprising of a linker, conjugate, and/or immunoconjugate of any one of the embodiments of described above, and instructions for using the a linker, conjugate, and/or immunoconjugate for diagnosis or treatment of cancer.

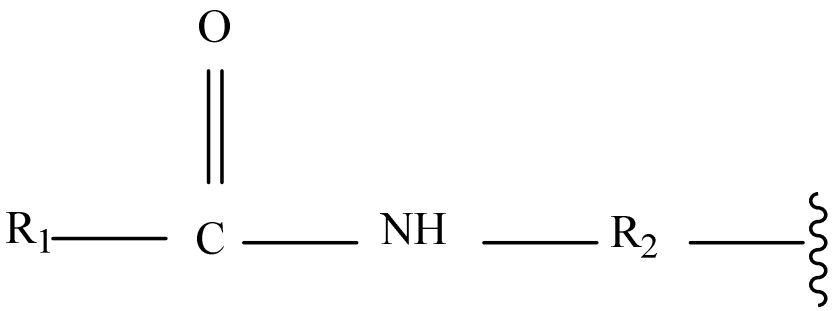
[0085a] In one aspect, the present disclosure refers to a conjugate of Formula I,



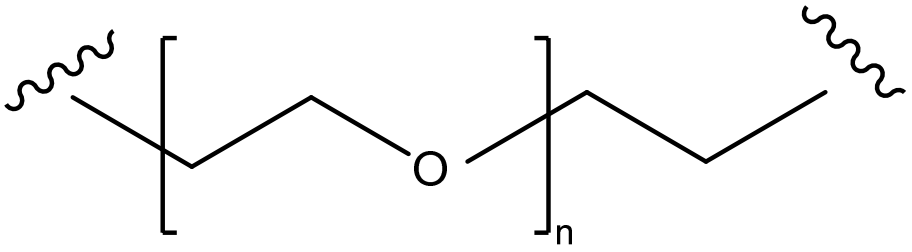
Formula I

wherein:

L is a linker represented by:

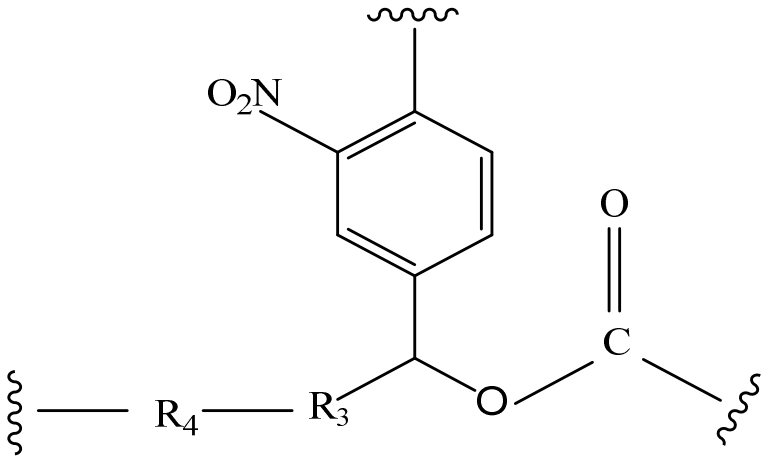


where R_1 is a nucleophilic functional group capable of coupling to an antibody, said nucleophilic functional group being selected from the group consisting of a C_1-C_{10} alkyl halide, a C_1-C_{10} alkyl alcohol, a phenol, a C_1-C_{10} alkyl thiol, and a C_1-C_{10} alkyl azide, and R_2 is a substituted or unsubstituted C_1-C_{20} alkylene, or a substituted or unsubstituted $(PEG)_n$ moiety represented by



where n is 1 to 20;

X is a substituted nitrophenyl represented by



where R_3 is a C_1-C_{20} alkylene, and R_4 is a triazole ring having a C=C double bond in the ring;

Y is a glycoside or glycoside derivative; and

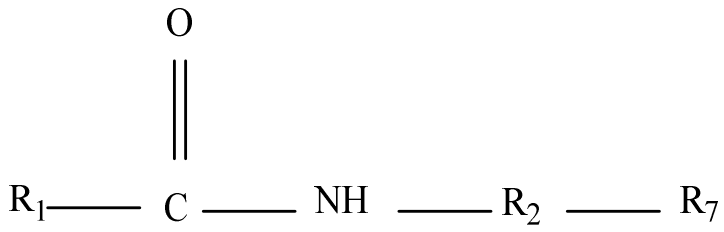
D is a drug; and

Y is bonded to X at the site of a wavy line covalent attachment on the nitrophenyl ring,

D is bonded to X at the site of a wavy line covalent attachment on the carbonyl group, and

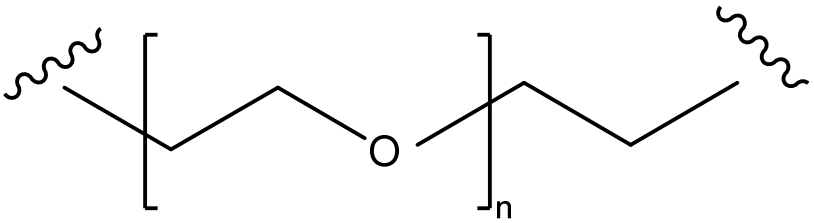
L is bonded to X via bonding of a wavy line covalent attachment between R_2 and R_4.

[0085b] In another aspect, the present disclosure refers to a linker–intermediate (L^{int}) having a formula represented by



where R_1 is a nucleophilic functional group capable of coupling to an antibody selected from the group consisting of a C_1-C_{10} alkyl halide, a C_1-C_{10} alkyl alcohol, a phenol, a C_1-C_{10} alkyl thiol, and a C_1-C_{10} alkyl azide,

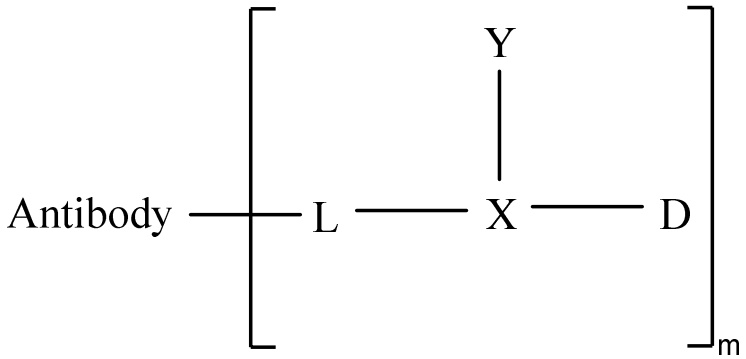
R_2 is a substituted or unsubstituted C_1-C_{20} alkylene, or a substituted or unsubstituted $(PEG)_n$ moiety represented by:



where n is 1 to 20, and

R_7 is an azide group.

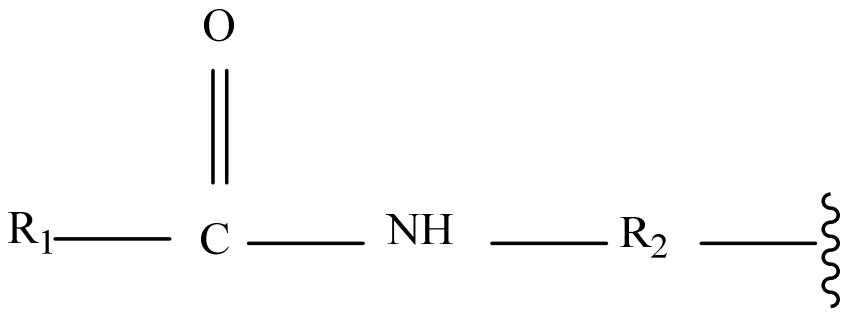
[0085c] In another aspect, the present disclosure refers to an immunoconjugate of Formula II,



Formula II

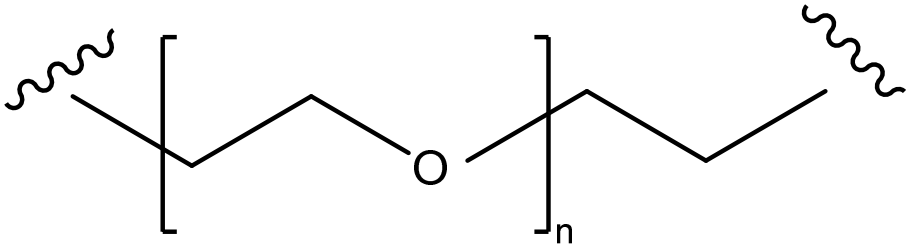
wherein:

L is represented by:



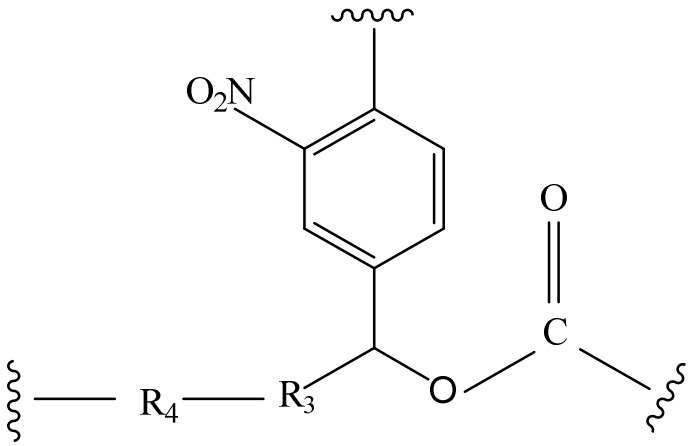
where R_1 is nucleophilic functional group capable of coupling to an antibody selected from the group consisting of a C_1-C_{10} alkyl halide, a C_1-C_{10} alkyl alcohol, a phenol, a C_1-C_{10} alkyl thiol, and a C_1-C_{10} alkyl azide,

R_2 is a substituted or unsubstituted C_1-C_{20} alkylene, or a substituted or unsubstituted $(PEG)_n$ moiety represented by



where n is 1 to 20, and

X is a substituted nitrophenyl represented by



where R_3 is a C_1-C_{20} alkylene; R_4 is a triazole ring having a C=C double bond in the ring;

Y is a glycoside or glycoside derivative;

D is a drug selected from the group consisting of an auristatin, a dolastatin, a maytansinoid, a calicheamicin, a pyrrolobenzodiazepine, an anthracycline, a ribonuclease, and a DNA endonuclease;

the wavy lines indicate a site of covalent attachment; and

m is 1 to 10,

wherein the term “antibody” in Formula II represents an antibody or antibody fragment.

[0085d] In another aspect, the present disclosure refers to pharmaceutical composition comprising: the immunoconjugate as described herein; and a pharmaceutically acceptable carrier.

[0085e] In another aspect, the present disclosure refers to use of the immunoconjugate as described herein, or the pharmaceutical composition as described herein, in the manufacture of a medicament for the treatment of cancer.

[0085f] In another aspect, the present disclosure refers to the immunoconjugate as described herein, or the pharmaceutical composition as described herein, for use in therapy.

BRIEF DESCRIPTION OF THE DRAWINGS

[0086] FIG. 1 shows the structure of SPC07, a conjugate comprising a linker of the present disclosure.

[0087] FIGS. 2A and 2B show amino acid sequences of the light chain variable regions (FIG. 2A) and the heavy chain variable regions (FIG. 2B) of a conditionally active anti-Nectin-4 antibody of the present disclosure (BA-143-01-VK and BA-143-01-VH) and of the wild type anti-Nectin-4 antibody (BAP143-00-VK and BAP143-00-VH).

[0088] FIGS. 3A and 3B show PK analysis with pH affinity ELISA of BA-143-00-MC, BA-143-00-SPC04, BA-143-00-SPC07, BA-143-00-SPC08, BA-143-01-MC, BA-143-01-SPC04, BA-143-01-SPC07, and BA-143-01-SPC08 from 0.17 h to 168 h. The results are summarized in TABLES 3 and 4.

[0089] FIGS. 4A and 4B show PK analysis with MMAE affinity ELISA of BA-143-00-MC, BA-143-00-SPC04, BA-143-00-SPC07, BA-143-00-SPC08, BA-143-01-MC, BA-143-01-SPC04, BA-143-01-SPC07, and BA-143-01-SPC08 from 0.17 h to 168 h. The results are summarized in TABLES 5 and 6.

[0090] FIG. 5A shows the mean tumor volume of Groups 1 (vehicle), 2 (BA-143-00-MC), 4 (BA-143-00-SPC07), 6 (BA-143-01-MC), 8 (BA-143-01-SPC07), 10 (BA-B12-MC), and 12 (BA-B12-SPC07) of TABLE 10-4.