L is a linker moiety;

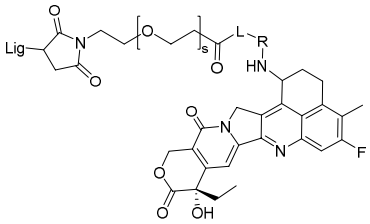
R is selected from the group consisting of -R^1, -C(O)-R^1-, -C(O)-O-R^1-, -C(O)-NH-R^1-, -C(O)-C_{0-3}alkyl-C(O)-NH-R^1-, -C(O)-(5-6 membered heteroaryl)-R^1-, -CH_2-(5-6 membered heteroaryl)-R^1-, -C(O)-(4-6 membered heterocyclyl)-, -C(O)-(4-6 membered heterocyclyl)-C(O)-R^1-, -C(O)-(4-6 membered heterocyclyl)-NH-R^1-, -C(O)-C_{3-4}cycloalkyl-R^1-, -C(S)-C_{3-4}cycloalkyl-R^1-, and -C(O)-O-phenyl-R^1-; wherein any aforementioned heteroaryl, heterocyclyl, alkyl, and cycloalkyl may optionally be substituted by one, two or three substituents each independently selected from the group consisting of halogen, hydroxyl, and oxo;

R^1 is selected from the group consisting of CH_2-CH_2O-, -CH_2-O-, -NH-, -CH_2ONH-, and -$CH(CH_3)$-NH-; and

s is 0, 1, 2, 3, 4, 5, 6, 7, or 8; and

t is 0, 1, 2, 3, 4, 5, 6, 7, or 8.

[0009a] In one aspect, the present disclosure refers to a compound represented by Formula IA:

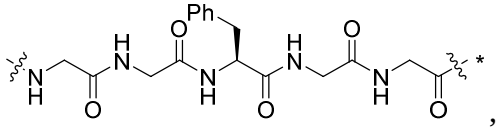


(IA);

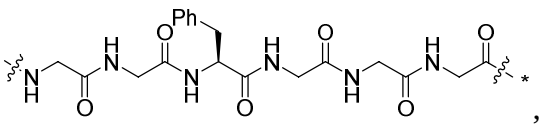
or a pharmaceutically acceptable salt or stereoisomer thereof, wherein:

Lig is a monoclonal antibody;

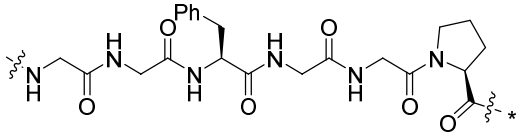
L is selected from the group consisting of:



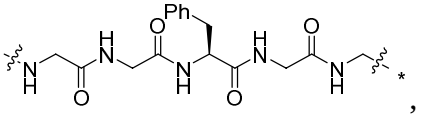
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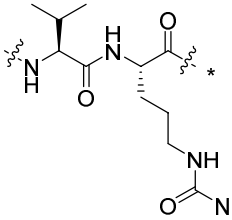
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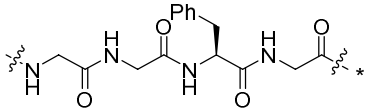
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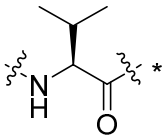
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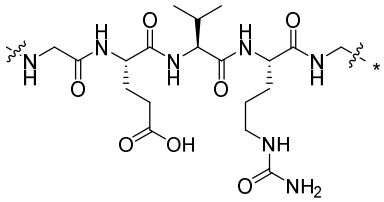
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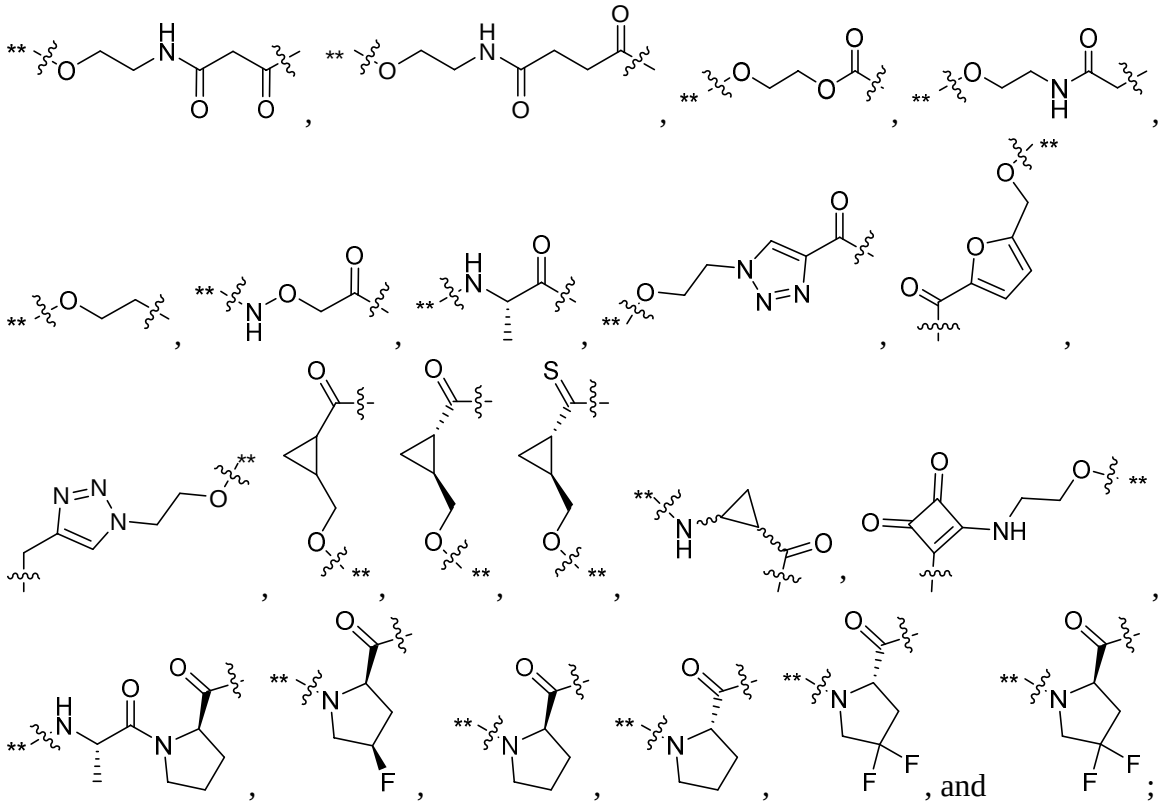
, and



;

wherein * denotes the point of attachment to R;

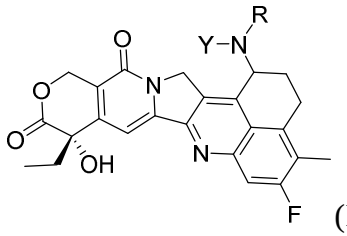
R is selected from the group consisting of:



wherein ** denotes the point of attachment to L; and

s is 0, 1, 2, 3, 4, 5, 6, 7, or 8.

[0010] Also disclosed herein is a therapeutic payload represented by Formula II:



(II);

or a pharmaceutically acceptable salt or stereoisomer thereof, wherein:

Y is hydrogen or -$C_{1\text{-}3}$alkyl;

R is selected from the group consisting of -C(O)-C_3alkyl, -C(O)-C_3cycloalkyl, -C(O)-C_4cycloalkyl, -C_1alkyl, -C(O)-(pyrrolidinyl), and -C(O)-CH_2ONH-C(O)-(pyrrolidinyl);

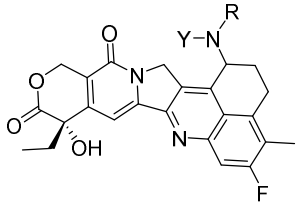
wherein:

-C(O)-C_3alkyl, -C(O)-C_3cycloalkyl, -C(O)-C_4cycloalkyl or -C_1alkyl is substituted by one or two substituents each independently selected from the group consisting of hydroxyl, -NH_2, -CHO, and -COOH;

-C(O)-(pyrrolidinyl) and -C(O)-CH_2ONH-C(O)-(pyrrolidinyl) may optionally be substituted on an available pyrrolidinyl carbon atom by one or two substituents each independently selected from the group consisting of halogen and hydroxyl, or two R^1 join together to form oxo; and

-C(O)-(pyrrolidinyl) may optionally be substituted on an available pyrrolidinyl nitrogen atom by -CHO, -C(O)CH_3, or -C(O)CH_2NH_2.

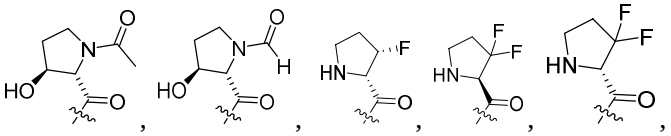
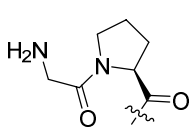
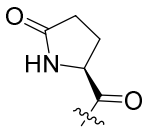
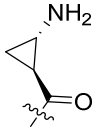
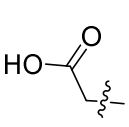
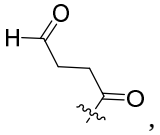
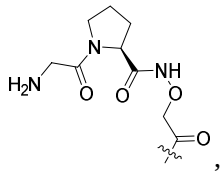
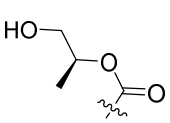
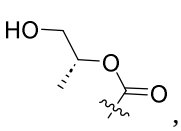
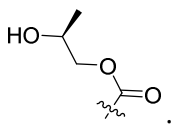
[0010a] In one aspect, the present disclosure refers to a compound represented by Formula II:



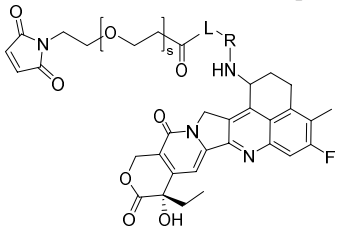
(II);

or a pharmaceutically acceptable salt or stereoisomer thereof, wherein:

Y is hydrogen or -C_{1-3}alkyl; and

R is selected from the group consisting of: , , , , , , , , , and .

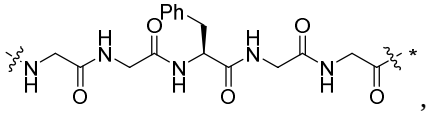
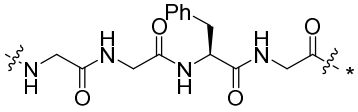
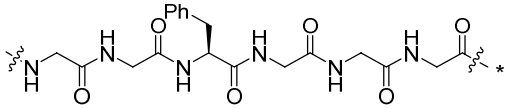
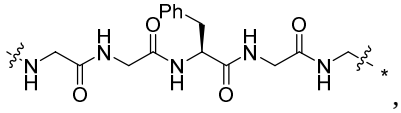
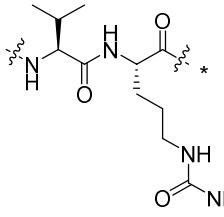
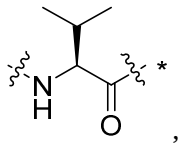
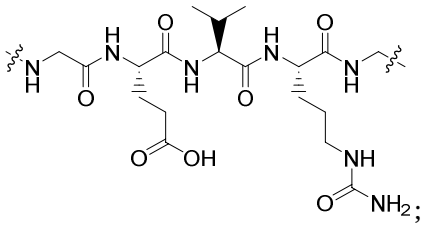
[0010b] In one aspect, the present disclosure refers to a compound represented by Formula IIIA:



(IIIA);

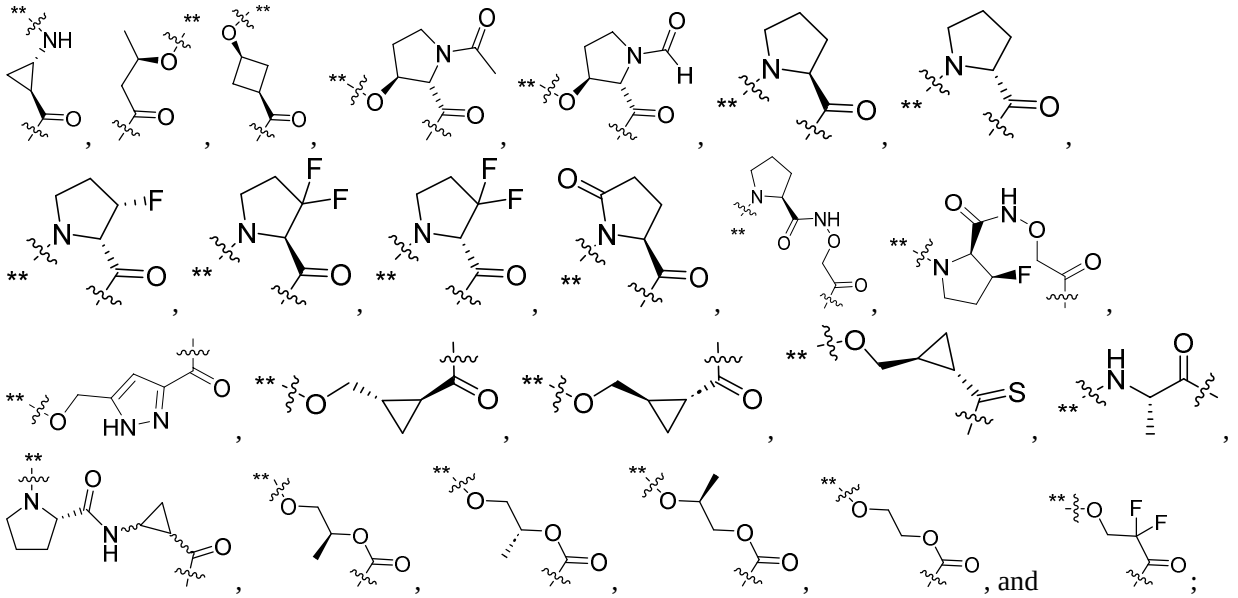
or a pharmaceutically acceptable salt or stereoisomer thereof, wherein:

L is selected from the group consisting of:

, , , , , , and ;

wherein * denotes the point of attachment to R;

R is selected from the group consisting of:


, and ;

wherein ** denotes the point of attachment to L; and

s is 0, 1, 2, 3, 4, 5, 6, 7, or 8.

[0011] Methods of treating cancer are contemplated herein, comprising administering to a patient in need thereof an effective amount of a disclosed compound. For example, provided herein is a method of treating cancer in patient in need thereof, comprising administering to the patient an effective amount of a disclosed therapeutic payload, a disclosed linker-payload construct, or a disclosed drug conjugate.

[0011a] In one aspect, the present disclosure refers to use of the compound disclosed herein, in the manufacture of a medicament for treating a cancer in a patient in need thereof.

[0012] Pharmaceutical compositions comprising at least one disclosed compound and a pharmaceutically acceptable carrier are additionally described herein. For example, provided herein is a pharmaceutically acceptable composition comprising a disclosed compound, e.g., a disclosed therapeutic payload, a disclosed linker-payload construct, or a disclosed drug conjugate and a pharmaceutically acceptable excipient.

[0012a] In one aspect, the present disclosure refers to a pharmaceutical composition comprising the compound disclosed herein, and a pharmaceutically acceptable excipient.

BRIEF DESCRIPTION OF THE DRAWINGS

[0013] FIG. 1A, FIG. 1B, and FIG. 1C show tumor suppression effect of antibody drug conjugates 3031, 3036, and 3038 on lung carcinoma cell line NCI-H292 derived xenograft in athymic nude mice. Compounds exemplified here exhibit tumor suppression greater than control.

[0014] FIG. 2A and FIG. 2B show tumor suppression effect of antibody drug conjugates 3058A and 3053B on human throat cancer cell line FaDu derived xenograft in athymic nude mice. Compounds exemplified here exhibit tumor suppression greater than control.

[0015] FIG. 3A, FIG. 3B, FIG. 3C, and FIG. 3D show tumor suppression effect of antibody drug conjugates 3058A, 3058B, 3102, and 3053B on human lung cancer cell line H1975 derived xenograft in athymic nude mice. Compounds exemplified here exhibit tumor suppression greater than control.

[0016] FIG. 4A, FIG. 4B, and FIG. 4C show tumor suppression effect of antibody drug conjugates 3053B, 3058A, and 3102 on human breast cancer cell line MDA-MB-468 derived xenograft in NOD-SCID mice. Compounds exemplified here exhibit tumor suppression greater than control.