CYTOTOXIC COMPOUNDS AND CONJUGATES THEREOF

CROSS REFERENCE TO RELATED APPLICATIONS

[0001] This patent application claims the priority benefit of U.S. Provisional Application No. 63/397,776, filed on August 12, 2022, and EP Application No. 22202077.8, filed on October 18, 2022, the contents of each of which are incorporated herein by reference in their entirety.

REFERENCE TO AN ELECTRONIC SEQUENCE LISTING

[0002] The contents of the electronic sequence listing (761682007641SEQLIST.xml; Size: 966,947 bytes; and Date of Creation: August 10, 2023) are herein incorporated by reference in their entirety.

BACKGROUND OF THE INVENTION

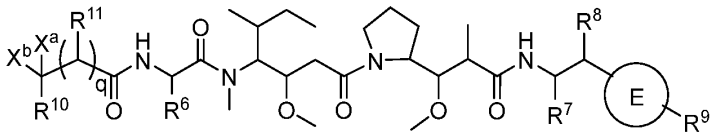
[0003] A variety of ligands have been investigated for the targeted delivery of cytotoxic agents to tumor cells, including oligopeptides, antibodies, and other proteins. While various drug classes have been evaluated for targeted delivery by these ligands, only a few drug classes have proved sufficiently active as Ligand-Drug Conjugates, while having a suitable toxicity profile and other pharmacological properties, to warrant clinical development. There is thus a need for additional cytotoxic agents with improved toxicity profile and other pharmacological properties.

[0004] The techniques and procedures described or referenced herein are generally well understood and commonly employed using conventional methodology by those skilled in the art, such as, for example, the widely utilized methodologies described in Sambrook *et al.*, *Molecular Cloning: A Laboratory Manual* 4th edition (2012) Cold Spring Harbor Laboratory Press, Cold Spring Harbor N.Y.; Current Protocols In Molecular Biology (F. M. Ausubel, *et al. eds*., (2003)); the series METHODS IN ENZYMOLOGY (Academic Press, Inc.); PCR 2: A Practical Approach (M. J. MacPherson, B. D. Hames and G. R. Taylor *eds*. (1995)); Greenfield, *ed*. (2013) Antibodies, A Laboratory Manual, 2nd edition, Cold Spring Harbor Laboratory Press; Oligonucleotide Synthesis (M. J. Gait, *ed*., 1984); Methods in Molecular Biology, Humana Press; Cell Biology: A Laboratory Notebook (J. E. Cellis, *ed*., 1998) Academic Press; Animal Cell Culture (R. I. Freshney), *ed*., 1987); Introduction to Cell and Tissue Culture (J. P. Mather and P. E. Roberts, 1998) Plenum Press; Cell and Tissue Culture

Laboratory Procedures (A. Doyle, J. B. Griffiths, and D. G. Newell, eds., 1993-8) J. Wiley and Sons; Handbook of Experimental Immunology (D. M. Weir and C. C. Blackwell, *eds.*); Gene Transfer Vectors for Mammalian Cells (J. M. Miller and M. P. Calos, *eds.*, 1987); PCR: The Polymerase Chain Reaction, (Mullis *et al.*, *eds.*, 1994); Current Protocols in Immunology (J. E. Coligan *et al.*, *eds.*, 1991); Short Protocols in Molecular Biology (Wiley and Sons, 1999); Immunobiology (C. A. Janeway and P. Travers, 1997); Antibodies (P. Finch, 1997); Antibodies: A Practical Approach (D. Catty., *ed.*, IRL Press, 1988-1989); Monoclonal Antibodies: A Practical Approach (P. Shepherd and C. Dean, *eds.*, Oxford University Press, 2000); Using Antibodies: A Laboratory Manual (E. Harlow and D. Lane (Cold Spring Harbor Laboratory Press, 1999); The Antibodies (M. Zanetti and J. D. Capra, *eds.*, Harwood Academic Publishers, 1995); Cancer: Principles and Practice of Oncology (V. T. DeVita *et al.*, *eds.*, J.B. Lippincott Company, 1993); and updated versions thereof. Each of the foregoing references in this paragraph is incorporated herein by reference in its entirety.

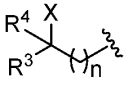
BRIEF SUMMARY OF THE INVENTION

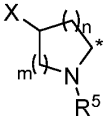
[0005] Provided herein is a compound of Formula (I):



(I)

or a salt thereof, wherein

X^b is $-NR^1R^2$; and X^a is  ; or

X^a and X^b are taken together with the carbon atom to which they are attached to form  , wherein the asterisk denotes the carbon atom of Formula (I) that bears the X^a and X^b groups;

R^1, R^2, R^3, R^4, R^a, R^b, R^5, and R^{10} are each independently H or C_1-C_4 alkyl;

X is H, OH, $-C(O)NR^aR^b$, $-S(O)_2R^a$, $-S(O)-R^a$ $-S(O)_2NR^aR^b$, $-NHS(O)_2R^a$, or $-NHC(O)R^a$;

R^6 is C_1-C_4 alkyl optionally substituted with OH;

R^7 is H, C_1-C_4 alkyl optionally substituted with one or two OH moieties, or 5-6 membered heteroaryl;

E is phenyl or 5-6 membered heteroaryl;

R^8, R^9, and R^{11} are each independently H or OH;

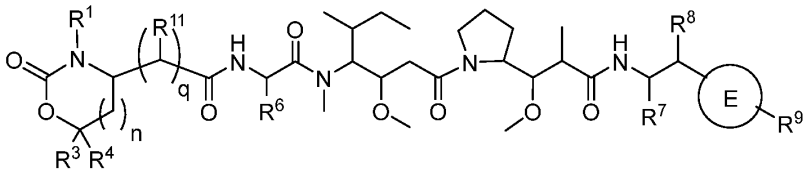
n is 0, 1, 2, or 3;

m is 1, 2, 3, or 4; and

q is 0 or 1,

wherein when X is H, at least two of R^7, R^8, R^9, and R^{11} comprise an OH moiety.

[0006] Also provided herein is a compound of Formula (II):



(II)

or a salt thereof, wherein

R^1, R^3, and R^4 are independently H or C_1-C_4 alkyl;

R^6 is C_1-C_4 alkyl optionally substituted with OH;

R^7 is H, C_1-C_4 alkyl optionally substituted with one or two OH moieties, or 5-6 membered heteroaryl;

E is phenyl or 5-6 membered heteroaryl;

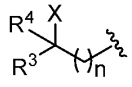
R^8, R^9, and R^{11} are each independently H or OH;

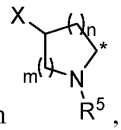
n is 0, 1, or 2; and

q is 0 or 1.

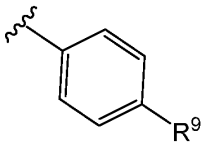
[0007] In some embodiments of Formula (I) and (II), q is 0. In some embodiments, q is 1. In some embodiments, R^{11} is H. In some embodiments, R^{11} is OH.

[0008] In some embodiments of Formula (I), X is OH. In some embodiments, X is $-C(O)NR^aR^b$, $-S(O)_2R^a$, $-S(O)-R^a$ $-S(O)_2NR^aR^b$, $-NHS(O)_2R^a$, or $-NHC(O)R^a$. In some embodiments, X^b is

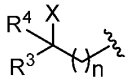
$-NR^1R^2$ and X^a is . In some embodiments, R^3 is H. In some embodiments, R^4 is H. In some embodiments, n is 0 or 1. In some embodiments, X^a and X^b are taken together with

the carbon atom to which they are attached to form , wherein the asterisk denotes the carbon atom of Formula (I) that bears the X^a and X^b groups. In some embodiments, m is 2 or 3.

[0009] In some embodiments of Formula (I) or (II), R^1 is H. In some embodiments, R^1 is C_1-C_4 alkyl. In some embodiments, R^1 is methyl. In some embodiments, R^2 is methyl. In some embodiments, R^{10} is H. In some embodiments, R^{10} is methyl. In some embodiments, R^6 is unsubstituted C_1-C_4 alkyl. In some embodiments, R^6 is isopropyl. In some embodiments, R^6 is C_1-C_4 alkyl substituted with OH. In some embodiments, R^7 C_1-C_4 alkyl substituted with OH. In some embodiments, R^7 is -CH_2OH. In some embodiments, R^7 is H. In some embodiments, R^7 is unsubstituted C_1-C_4 alkyl. In some embodiments, R^7 is methyl. In some embodiments, R^7 is 5-6 membered heteroaryl. In some embodiments, R^8 is H. In some embodiments, R^8 is OH. In some embodiments, E is phenyl. In some embodiments, E-R^9 is

, wherein the wavy line indicates the point of attachment of E to the rest of the compound. In some embodiments, E is 5-6 membered heteroaryl. In some embodiments, R^9 is H. In some embodiments, R^9 is OH.

[0010] In some embodiments of Formula (I),

X^a is ;

X^b is -NR^1R^2;

R^1 is H or methyl;

R^2 is methyl;

X is OH;

R^3 and R^4 are H;

R^6 is isopropyl;

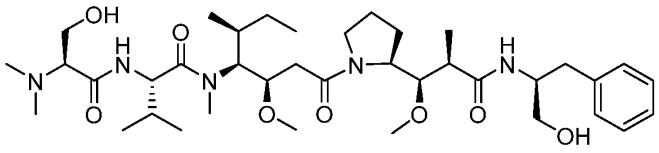
R^7 is -CH_2OH;

R^8 is H;

E is phenyl; and

R^9 is H.

[0011] In some embodiments of Formula (I), the compound is



or a salt thereof.

[0012] In some embodiments, the compound is a compound of Table 1.

[0013] Also provided herein is a Drug-Linker compound of the following formula:

Q-D,

or a salt thereof, wherein

Q is a Linker Unit selected from the group consisting of:

(i) Z'-A-RL-,

(ii) Z'-A-RL-Y-,

(iii) Z'-A-S*-RL-,

(iv) Z'-A-S*-RL-Y-,

(v) Z'-A-B(S*)-RL-,

(vi) Z'-A-B(S*)-RL-Y-,

(vii) Z'-A-,

(viii) Z'-A-S*-W-,

(ix) Z'-A-B(S*)-W-,

(x) Z'-A-S*-W-RL-, and

(xi) Z'-A-B(S*)-W-RL-;

Z' is a Stretcher Unit precursor;

A is a bond or a Connector Unit;

B is a Parallel Connector Unit;

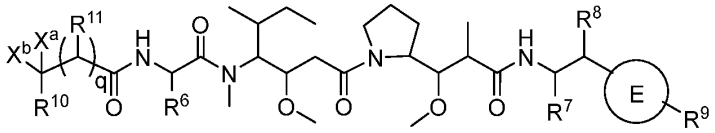
S* is a Partitioning Agent;

RL is a Releasable Linker;

W is an Amino Acid Unit;

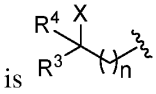
Y is a Spacer Unit; and

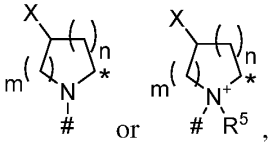
D is a Drug Unit of Formula (I'):



(I')

wherein

X^b is $-NR^{2}-^{\#}$ or $-N^{+}R^{1}R^{5}-^{\#}$, wherein the # denotes the point of attachment to Q, and X^a is ; or

X^a and X^b are taken together with the carbon atom to which they are attached to form  or , wherein the asterisk denotes the carbon atom of Formula (I) that bears the X^a and X^b groups, and the # denotes the point of attachment to Q;

R^1 and R^5 are independently C_1-C_4 alkyl;

X is H, OH, $-C(O)NR^aR^b$, $-S(O)_2R^a$, $-S(O)-R^a$ $-S(O)_2NR^aR^b$, $-NHS(O)_2R^a$, or $-NHC(O)R^a$;

R^2, R^3, R^4, R^{10}, R^a, and R^b are each independently H or C_1-C_4 alkyl;

R^6 is C_1-C_4 alkyl optionally substituted with OH;

R^7 is H, C_1-C_4 alkyl optionally substituted with one or two OH moieties, or 5-6 membered heteroaryl;

E is phenyl or 5-6 membered heteroaryl;

R^8, R^9, and R^{11} are each independently H or OH;

n is 0, 1, 2, or 3;

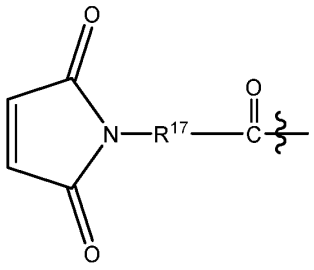
m is 1, 2, 3, or 4;

q is 0 or 1; and

wherein when X is H, at least two of R^7, R^8, R^9, and R^{11} comprise an OH moiety.

[0014] In some embodiments, the Linker Unit Q is of formula (i), (ii), (iii), (iv), (x), or (xi). In some embodiments, the Linker Unit Q is of formula (v), (vi), (ix), or (xi). In some embodiments, the Linker Unit Q is of formula (viii), (ix), (x), or (xi).

[0015] In some embodimemts, the Stretcher Unit Z' is



wherein

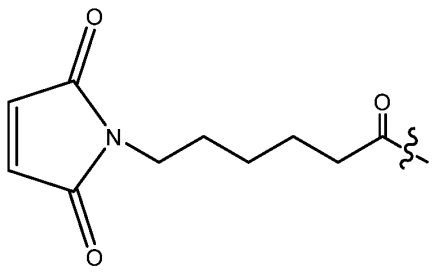
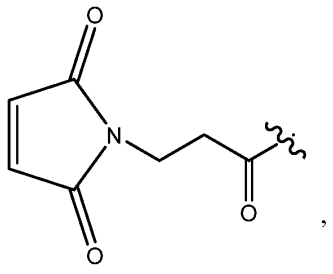
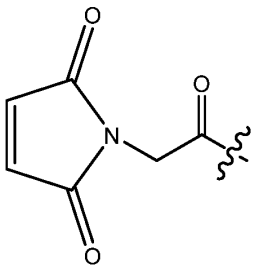
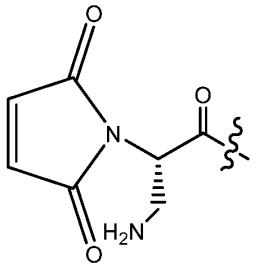
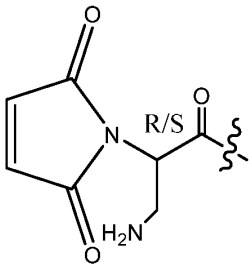
R^{17} is $–CH_2CH_2(OCH_2CH_2)_k–$, -C_1-C_{10} alkylene-, C_1-C_{10} heteroalkylene-, -C_3-C_8 carbocyclo-, -O-(C_1-C_8 alkylene)-, -arylene-, -C_1-C_{10} alkylene-arylene-, -arylene-C_1-C_{10} alkylene-, -C_1-C_{10} alkylene-(C_3-C_8 carbocyclo)-, -(C_3-C_8 carbocyclo)-C_1-C_{10} alkylene-, -C_3-C_8 heterocyclo-, -C_1-C_{10} alkylene-(C_3-C_8 heterocyclo)-, -(C_3-C_8 heterocyclo)-C_1-C_{10} alkylene-, -C_1-C_{10} alkylene-C(=O)-, C_1-C_{10} heteroalkylene-C(=O)-, -C_3-C_8 carbocyclo-C(=O)-, -O-(C_1-C_8 alkylene)-C(=O)-, -arylene-C(=O)-, -C_1-C_{10} alkylene-arylene-C(=O)-, -arylene-C_1-C_{10} alkylene-C(=O)-, -C_1-C_{10} alkylene-(C_3-C_8 carbocyclo)-C(=O)-,-(C_3-C_8 carbocyclo)-C_1-C_{10} alkylene-C(=O)-, -C_3-C_8 heterocyclo-C(=O)-, -C_1-C_{10} alkylene-(C_3-C_8 heterocyclo)-C(=O)-, -(C_3-C_8 heterocyclo)-C_1-C_{10} alkylene-C(=O)-, -C_1-C_{10} alkylene-NH-, C_1-C_{10} heteroalkylene-NH-, -C_3-C_8 carbocyclo-NH-, -O-(C_1-C_8 alkylene)-NH-, -arylene-NH-, -C_1-C_{10} alkylene-arylene-NH-, -arylene-C_1-C_{10} alkylene-NH-, -C_1-C_{10} alkylene-(C_3-C_8 carbocyclo)-NH-, -(C_3-C_8 carbocyclo)-C_1-C_{10} alkylene-NH-, -C_3-C_8 heterocyclo-NH-, -C_1-C_{10} alkylene-(C_3-C_8 heterocyclo)-NH-, -(C_3-C_8 heterocyclo)-C_1-C_{10} alkylene-NH-, -C_1-C_{10} alkylene-S-, C_1-C_{10} heteroalkylene-S -, -C_3-C_8 carbocyclo-S -, -O-(C_1-C_8 alkylene)-S -, -arylene-S-, -C_1-C_{10} alkylene-arylene-S-, -arylene-C_1-C_{10} alkylene-S-, -C_1-C_{10} alkylene-(C_3-C_8 carbocyclo)-S-, -(C_3-C_8 carbocyclo)-C_1-C_{10} alkylene-S-, -C_3-C_8 heterocyclo-S-, -C_1-C_{10} alkylene-(C_3-C_8 heterocyclo)-S-, or -(C_3-C_8 heterocyclo)-C_1-C_{10} alkylene-S-;

subscript k is an integer ranging from 1 to 36;

R^{17} is optionally substituted by a Basic Unit (BU) such as an aminoalkyl moiety, e.g. $–(CH_2)_xNH_2$, $–(CH_2)_xNHR^a$, and $–(CH_2)_xNR^a{}_2$, wherein x is an integer of from 1-4 and each R^a is independently selected from the group consisting of C_{1-6} alkyl and C_{1-6} haloalkyl, or two R^a groups are combined with the nitrogen to which they are attached to form an azetidinyl, pyrrolidinyl or piperidinyl group; and

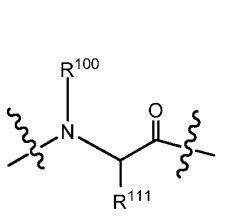
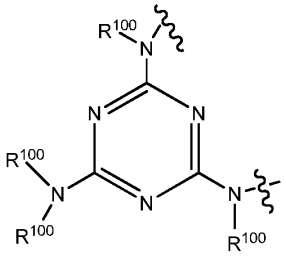
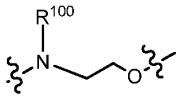
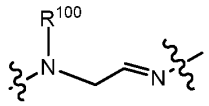
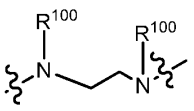
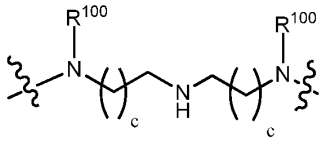
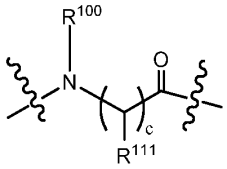
the wavy line indicates the point of covalent attachment to the rest of the Drug-Linker compound.

[0016] In some embodiments, the Stretcher Unit Z' is


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, or


wherein the wavy lines indicate the point of covalent attachment to the rest of the Drug-Linker compound.

[0017] In some embodiments, the Connector Unit A is

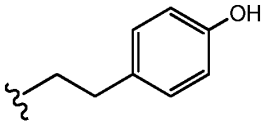

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or


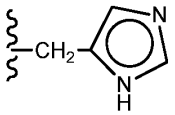
wherein

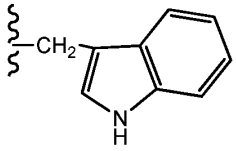
each R^{100} is independently selected from hydrogen or -C_1-C_3 alkyl;

R^{111} is independently selected from the group consisting of hydrogen, *p*-hydroxybenzyl, methyl, isopropyl, isobutyl, *sec*-butyl, -CH_2OH, -$CH(OH)CH_3$, -

$CH_2CH_2SCH_3$, $-CH_2CONH_2$, $-CH_2COOH$, $-CH_2CH_2CONH_2$, $-CH_2CH_2COOH$, $-(CH_2)_3NHC(=NH)NH_2$, $-(CH_2)_3NH_2$, $-(CH_2)_3NHCOCH_3$, $-(CH_2)_3NHCHO$, $-(CH_2)_4NHC(=NH)NH_2$, $-(CH_2)_4NH_2$, $-(CH_2)_4NHCOCH_3$, $-(CH_2)_4NHCHO$, $-(CH_2)_3NHCONH_2$, $-(CH_2)_4NHCONH_2$, $-CH_2CH_2CH(OH)CH_2NH_2$, 2-pyridylmethyl-, 3-pyridylmethyl-, 4-pyridylmethyl-,



,


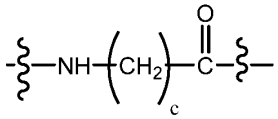
, and


;

each subscript c is an independently selected integer from 1 to 10; and

the wavy lines indicate attachment of the Connector Unit to the rest of the Drug-Linker compound.

[0018] In some embodiments, the Connector Unit A is

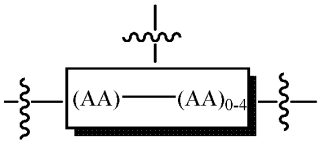


;

c is an integer ranging from 1 to 6; and

the wavy lines indicate the site of attachment to the rest of the Drug-Linker compound or salt thereof.

[0019] In some embodiments, A is a bond.

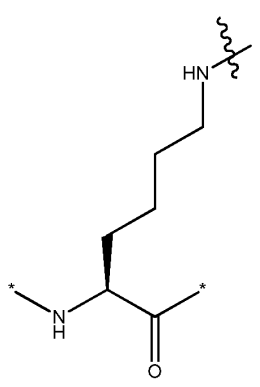
[0020] In some embodiments, B is 

;

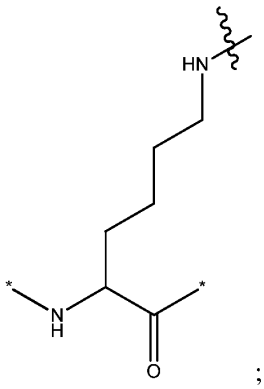
each AA is independently a proteinogenic or non-proteinogenic amino acid; and

the wavy lines indicate points of attachment to the rest of the Drug-Linker compound or salt thereof.

[0021] In some embodiments, B is an amino acid. In some embodiments, B is



or

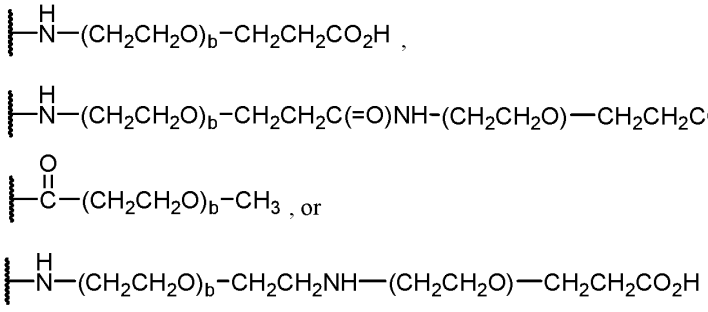


;

the wavy line indicates the point of attachement to the Partitioning Agent S*; and

the asterisks indicate points of attachment to the rest of the Drug-Linker structure.

[0022] In some embodiments, the Partitioning Agent S^* is a polyethylene glycol (PEG) unit, cyclodextrin unit, polyamide, hydrophilic peptide, polysaccharide, or dendrimer. In some embodiments, Partitioning Agent S^* is a PEG Unit comprising from 4 to 72 (CH_2CH_2O) subunits. In some embodiments, the PEG Unit is



;

b is selected from the group consisting of 4 to 36; and

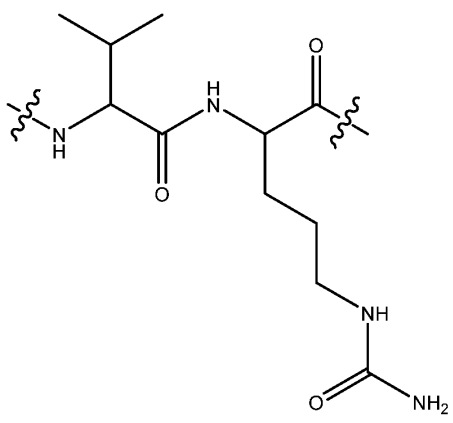
the wavy lines indicate the site of attachment to the rest of the Drug-Linker compound or salt thereof.

[0023] In some embodiments, the Releasable Linker RL is

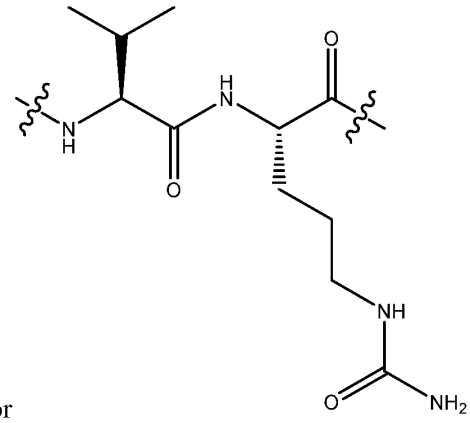
$–(AA)_{1-12}–$; and

each AA is independently a proteinogenic or non-proteinogenic amino acid.

[0024] In some embodiments, the Releasable Linker RL is $–AA_1\text{-}AA_2–$ or $–AA_1\text{-}AA_2\text{-}AA_3–$, wherein AA_1 is attached to the Stretcher Unit Z' or the Connector Unit A. In some embodiments, the Releasable Linker RL is



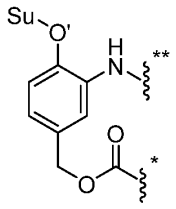
or



; and

the wavy line adjacent to the -NH- group indicates attachment to the Stretcher Unit Z' or the Connector Unit A and the wavy line adjacent to the -C(=O)- group indicates attachment to the Spacer Unit Y or the Drug Unit D.

[0025] In some embodiments, the Releasable Linker RL is a glycoside. In some embodiments, the Releasable Linker RL is



wherein

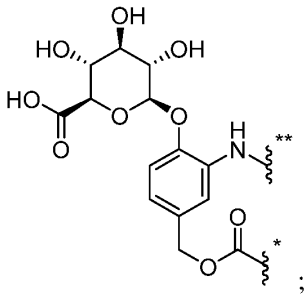
Su is a hexose form a monosaccharide;

O' represents the oxygen atom of a glycosidic bond that is capable of cleavage by a glycosidase;

the wavy line marked with a single asterisk (*) indicates the site of covalent attachment to D; and

the wavy line marked with a double asterisk (**) indicates the site of covalent attachment to the remainder of Q.

[0026] In some embodiments, the Releasable Linker RL is

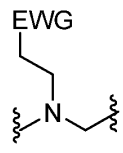


;

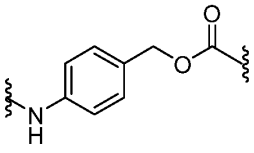
the wavy line marked with a single asterisk (*) indicates the site of covalent attachment to D; and

the wavy line marked with a double asterisk (**) indicates the site of covalent attachment to the remainder of Q.

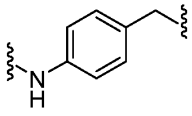
[0027] In some embodiments, the Spacer Unit Y is



,



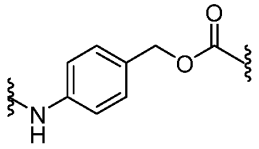
, or



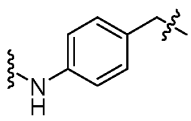
wherein EWG is an electron-withdrawing group; and

the wavy lines indicate the site of attachment to the rest of the Drug-Linker compound or salt thereof.

[0028] In some embodiments, the Spacer Unit Y is



or

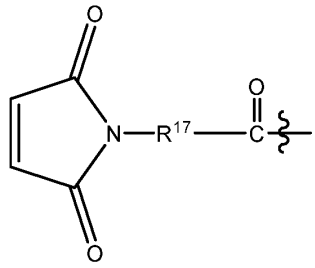


; and

the wavy lines indicate the site of attachment to the rest of the Drug-Linker compound or salt thereof.

[0029] In some embodiments,

Z' is



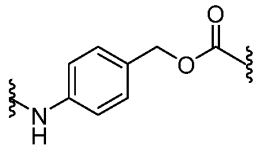
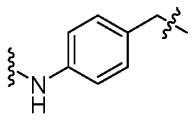
;

R^{17} is C_1-C_{10} alkylene;

A is a bond;

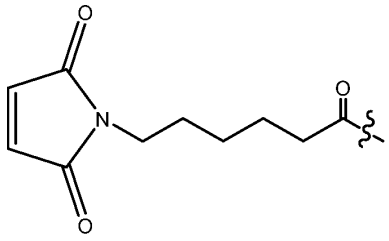
RL is –AA_1-AA_2–;

AA_1 and AA_2 are each independently a proteinogenic amino acid;

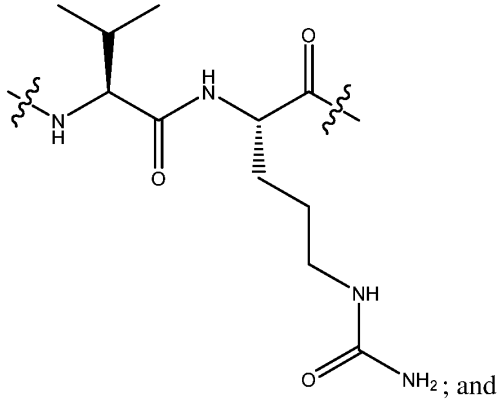
Y is  or  ; and

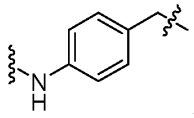
the wavy lines indicate the site of attachment to the rest of the Drug-Linker compound or salt thereof.

[0030] In some embodiments,

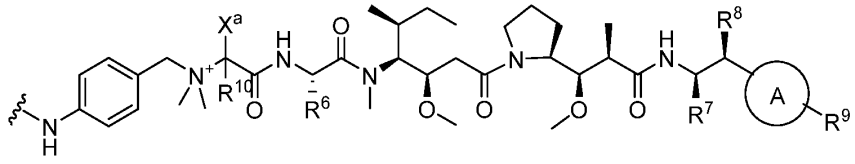
Z' is  ;

A is a bond;

RL is  ; and

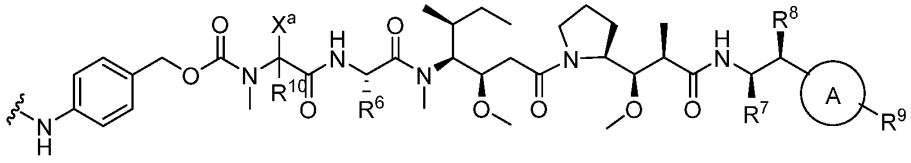
Y is  .

[0031] In some embodiments, Y-D is

 ; and

the wavy line indicates the site of attachment to the rest of the Drug-Linker compound or salt thereof.

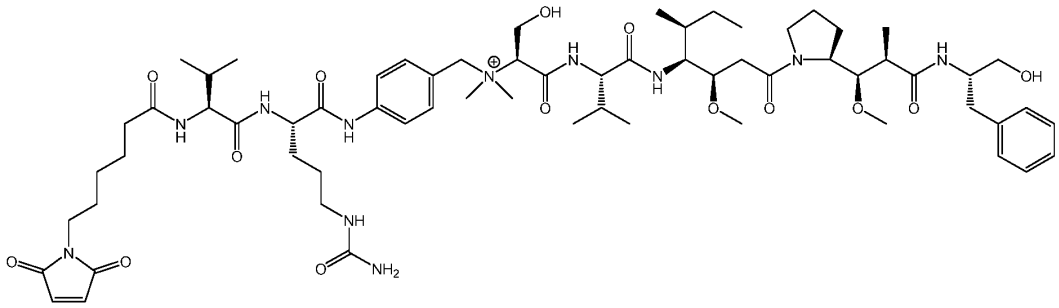
[0032] In some embodiments, Y-D is



; and

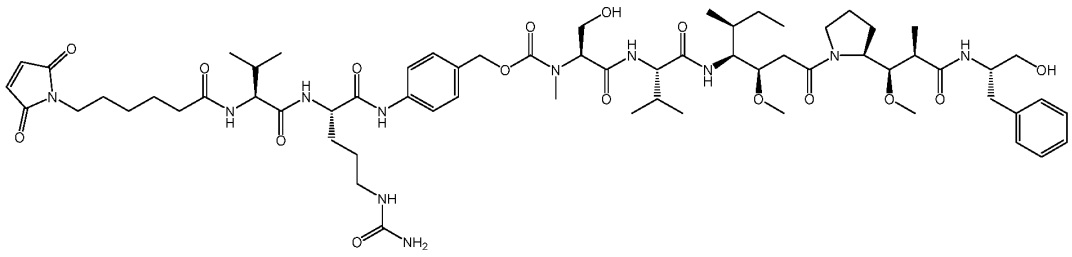
the wavy line indicates the site of attachment to the rest of the Drug-Linker compound or salt thereof.

[0033] In some embodiments, the compound is

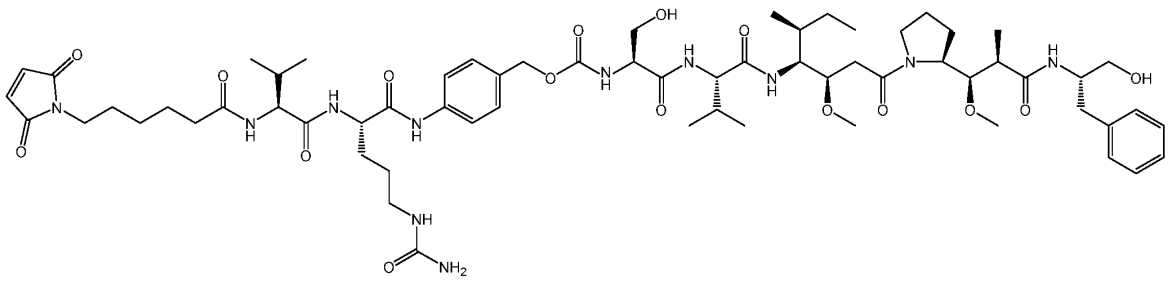


or a salt thereof.

[0034] In some embodiments, the compound is



or



or a salt thereof.

[0035] In some embodiments, the Drug-Linker compound is a compound of Table 2.

[0036] Also provided herein is a Ligand-Drug Conjugate compound of the formula:

$$L\text{-}(Q\text{-}D)_p$$

or a pharmaceutically acceptable salt thereof, wherein

L is a Ligand Unit;

Q is a Linker Unit selected from the group consisting of:

(i) Z'-A-RL-,

(ii) Z'-A-RL-Y-,

(iii) Z'-A-S*-RL-,

(iv) Z'-A-S*-RL-Y-,

(v) Z'-A-B(S*)-RL-,

(vi) Z'-A-B(S*)-RL-Y-,

(vii) Z'-A-,

(viii) Z'-A-S*-W-,

(ix) Z'-A-B(S*)-W-,

(x) Z'-A-S*-W-RL-, and

(xi) Z'-A-B(S*)-W-RL-;

Z' is a Stretcher Unit precursor;

A is a bond or a Connector Unit;

B is a Parallel Connector Unit;

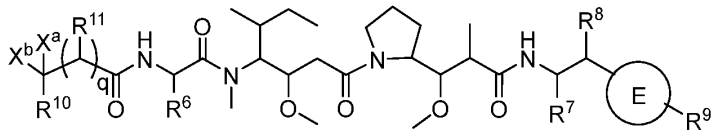
S* is a Partitioning Agent;

RL is a Releasable Linker;

W is a Amino Acid Unit;

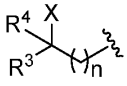
Y is a Spacer Unit; and

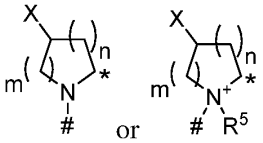
D is a Drug Unit of Formula (I'):



(I')

wherein

X^b is $-NR^{2}-^{\#}$ or $-N^+R^1R^5-^{\#}$, wherein the # denotes the point of attachment to Q, and X^a is  ; or

X^a and X^b are taken together with the carbon atom to which they are attached to form  , wherein the asterisk denotes the carbon atom of Formula (I) that bears the X^a and X^b groups, and the # denotes the point of attachment to Q;

R^1 and R^5 are independently C_1-C_4 alkyl;

X is H, OH, $-C(O)NR^aR^b$, $-S(O)_2R^a$, $-S(O)-R^a$ $-S(O)_2NR^aR^b$, $-NHS(O)_2R^a$, or $-NHC(O)R^a$;

R^2, R^3, R^4, R^{10}, R^a, and R^b are each independently H or C_1-C_4 alkyl;

R^6 is C_1-C_4 alkyl optionally substituted with OH;

R^7 is H, C_1-C_4 alkyl optionally substituted with one or two OH moieties, or 5-6 membered heteroaryl;

E is phenyl or 5-6 membered heteroaryl;

R^8, R^9, and R^{11} are each independently H or OH;

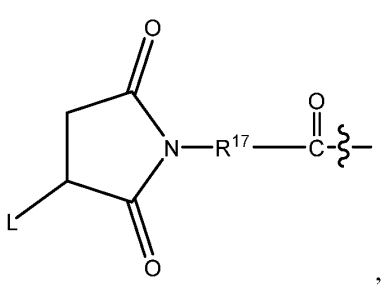
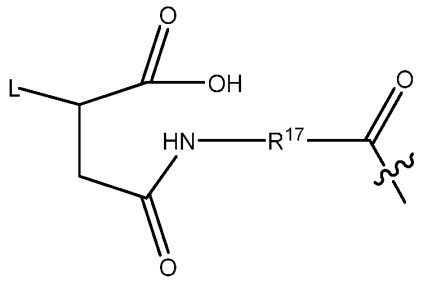
n is 0, 1, 2, or 3;

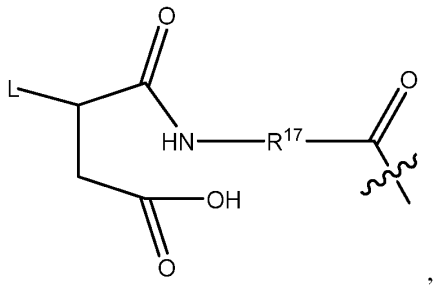
m is 1, 2, 3, or 4;

q is 0 or 1; and

wherein when X is H, at least two of R^7, R^8, R^9, and R^{11} comprise an OH moiety.

[0037] In some embodiments, the Linker Unit Q is of formula (i), (ii), (iii), (iv), (x), or (xi). In some embodiments, the Linker Unit Q is of formula (v), (vi), (ix), or (xi). In some embodiments, the Linker Unit Q is of formula (viii), (ix), (x), or (xi).

[0038] In some embodiments, the Ligand Unit L and the Stretcher Unit Z together are  ,  , or



,

wherein

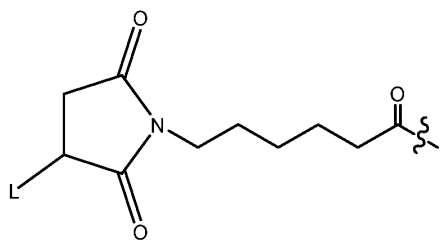
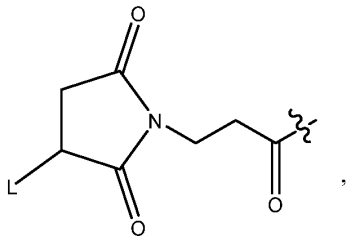
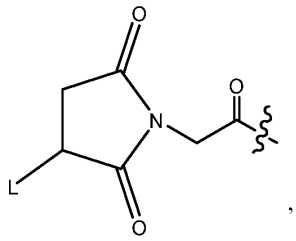
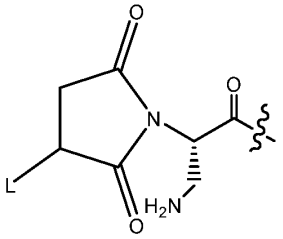
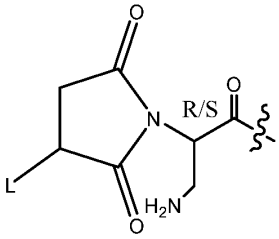
R^{17} is $–CH_2CH_2(OCH_2CH_2)_k–$, -C_1-C_{10} alkylene-, C_1-C_{10} heteroalkylene-, -C_3-C_8 carbocyclo-, -O-(C_1-C_8 alkylene)-, -arylene-, -C_1-C_{10} alkylene-arylene-, -arylene-C_1-C_{10} alkylene-, -C_1-C_{10} alkylene-(C_3-C_8 carbocyclo)-, -(C_3-C_8 carbocyclo)-C_1-C_{10} alkylene-, -C_3-C_8 heterocyclo-, -C_1-C_{10} alkylene-(C_3-C_8 heterocyclo)-, -(C_3-C_8 heterocyclo)-C_1-C_{10} alkylene-, -C_1-C_{10} alkylene-C(=O)-, C_1-C_{10} heteroalkylene-C(=O)-, -C_3-C_8 carbocyclo-C(=O)-, -O-(C_1-C_8 alkylene)-C(=O)-, -arylene-C(=O)-, -C_1-C_{10} alkylene-arylene-C(=O)-, -arylene-C_1-C_{10} alkylene-C(=O)-, -C_1-C_{10} alkylene-(C_3-C_8 carbocyclo)-C(=O)-,-(C_3-C_8 carbocyclo)-C_1-C_{10} alkylene-C(=O)-, -C_3-C_8 heterocyclo-C(=O)-, -C_1-C_{10} alkylene-(C_3-C_8 heterocyclo)-C(=O)-, -(C_3-C_8 heterocyclo)-C_1-C_{10} alkylene-C(=O)-, -C_1-C_{10} alkylene-NH-, C_1-C_{10} heteroalkylene-NH-, -C_3-C_8 carbocyclo-NH-, -O-(C_1-C_8 alkylene)-NH-, -arylene-NH-, -C_1-C_{10} alkylene-arylene-NH-, -arylene-C_1-C_{10} alkylene-NH-, -C_1-C_{10} alkylene-(C_3-C_8 carbocyclo)-NH-, -(C_3-C_8 carbocyclo)-C_1-C_{10} alkylene-NH-, -C_3-C_8 heterocyclo-NH-, -C_1-C_{10} alkylene-(C_3-C_8 heterocyclo)-NH-, -(C_3-C_8 heterocyclo)-C_1-C_{10} alkylene-NH-, -C_1-C_{10} alkylene-S-, C_1-C_{10} heteroalkylene-S -, -C_3-C_8 carbocyclo-S -, -O-(C_1-C_8 alkylene)-S -, -arylene-S-, -C_1-C_{10} alkylene-arylene-S-, -arylene-C_1-C_{10} alkylene-S-, -C_1-C_{10} alkylene-(C_3-C_8 carbocyclo)-S-, -(C_3-C_8 carbocyclo)-C_1-C_{10} alkylene-S-, -C_3-C_8 heterocyclo-S-, -C_1-C_{10} alkylene-(C_3-C_8 heterocyclo)-S-, or -(C_3-C_8 heterocyclo)-C_1-C_{10} alkylene-S-;

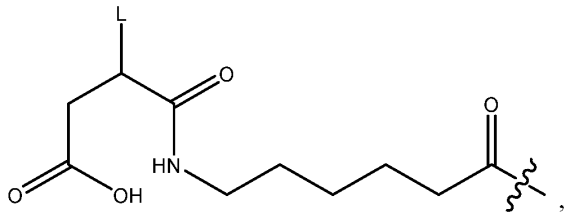
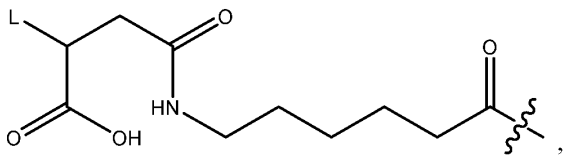
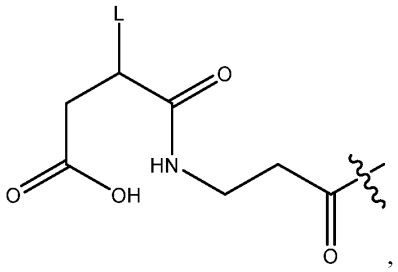
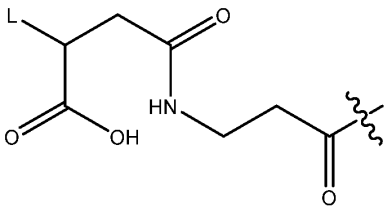
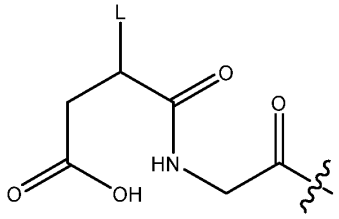
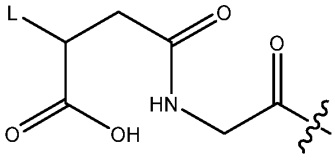
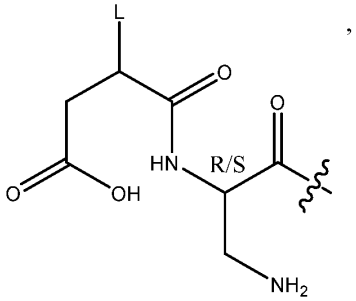
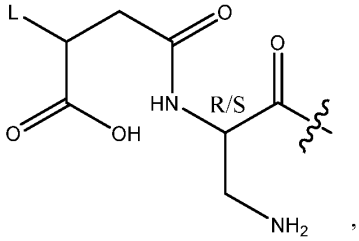
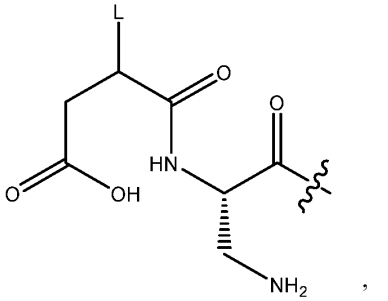
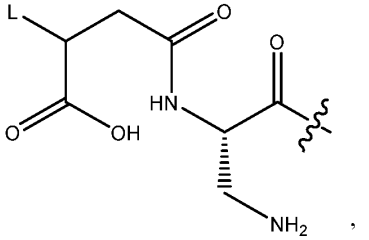
subscript k is an integer ranging from 1 to 36;

R^{17} is optionally substituted by a Basic Unit (BU) such as an aminoalkyl moiety, e.g. $–(CH_2)_xNH_2$, $–(CH_2)_xNHR^a$, and $–(CH_2)_xNR^a{}_2$, wherein x is an integer of from 1-4 and each R^a is independently selected from the group consisting of C_{1-6} alkyl and C_{1-6} haloalkyl, or two R^a groups are combined with the nitrogen to which they are attached to form an azetidinyl, pyrrolidinyl or piperidinyl group; and

the wavy line indicates the point of covalent attachment to the rest of the Ligand-Drug Conjugate compound.

[0039] In some embodiments, the Ligand Unit L and the Stretcher Unit Z together are

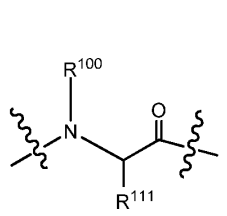
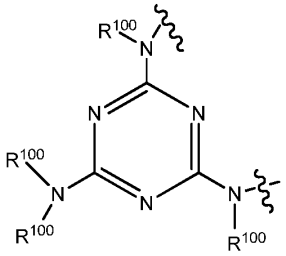
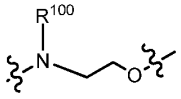
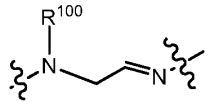
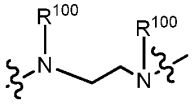
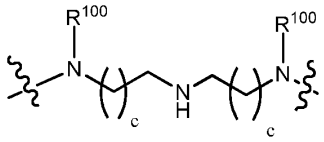
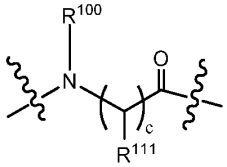

,

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,

,

,

or

wherein the wavy lines indicate the point of covalent attachment to the rest of the Ligand-Drug Conjugate compound.

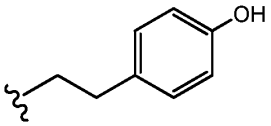
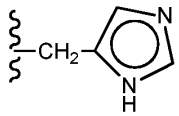
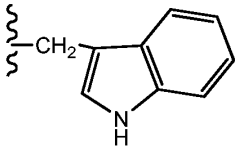
[0040] In some embodiments, the Connector Unit A is


,

,

,

,

,

or


wherein

each R^{100} is independently selected from hydrogen or -C_1-C_3 alkyl;

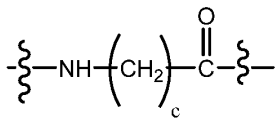
R^{111} is independently selected from the group consisting of hydrogen, *p*-hydroxybenzyl, methyl, isopropyl, isobutyl, *sec*-butyl, -CH_2OH, -$CH(OH)CH_3$, -$CH_2CH_2SCH_3$, -CH_2CONH_2, -CH_2COOH, -$CH_2CH_2CONH_2$, -CH_2CH_2COOH, -$(CH_2)_3NHC(=NH)NH_2$, -$(CH_2)_3NH_2$, -$(CH_2)_3NHCOCH_3$, -$(CH_2)_3NHCHO$, -$(CH_2)_4NHC(=NH)NH_2$, -$(CH_2)_4NH_2$, -$(CH_2)_4NHCOCH_3$, -$(CH_2)_4NHCHO$, -$(CH_2)_3NHCONH_2$, -$(CH_2)_4NHCONH_2$, -$CH_2CH_2CH(OH)CH_2NH_2$, 2-pyridylmethyl-, 3-pyridylmethyl-, 4-pyridylmethyl-,


,

, and

;

each subscript c is an independently selected integer from 1 to 10; and

the wavy lines indicate attachment of the Connector Unit to the rest of the Ligand-Drug Conjugate compound or pharmaceutically acceptable salt thereof.

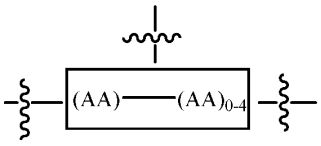
[0041] In some embodiments, the Connector Unit A is


;

c is an integer ranging from 1 to 6; and

the wavy lines indicate the site of attachment to the rest of the Ligand-Drug Conjugate compound or pharmaceutically acceptable salt thereof.

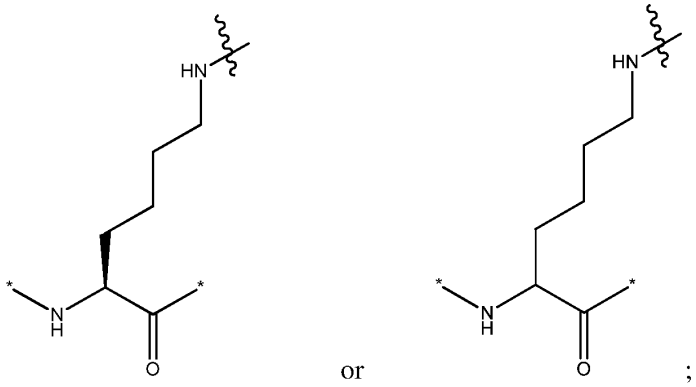
[0042] In some embodiments, A is a bond.

[0043] In some embodiments, B is ;

each AA is independently a proteinogenic or non-proteinogenic amino acid; and

the wavy lines indicate points of attachment to the rest of the Ligand-Drug Conjugate compound or pharmaceutically acceptable salt thereof.

[0044] In some embodiments, B is an amino acid. In some embodiments, B is

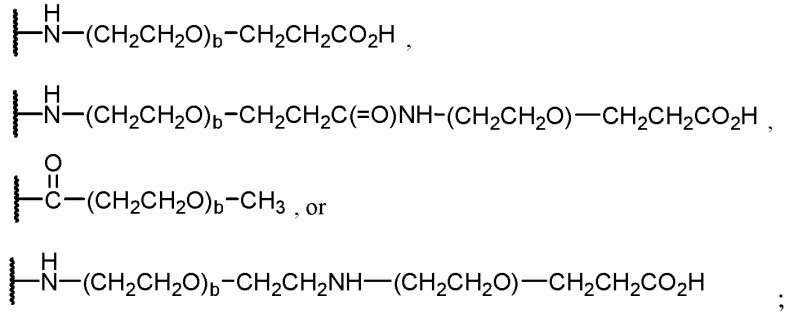


or ;

the wavy line indicates the point of attachement to the Partitioning Agent S*; and

the asterisks indicate points of attachment to the rest of the Ligand-Drug Conjugate compound or pharmaceutically acceptable salt thereof.

[0045] In some embodiments, the Partitioning Agent S^* is a polyethylene glycol (PEG) unit, cyclodextrin unit, polyamide, hydrophilic peptide, polysaccharide, or dendrimer. In some embodiments, the Partitioning Agent S^* is a PEG Unit comprising from 4 to 72 (CH_2CH_2O) subunits. In some embodiments, the PEG Unit is



b is selected from the group consisting of 4 to 36; and

the wavy lines indicate the site of attachment to the rest of the Ligand-Drug Conjugate compound or pharmaceutically acceptable salt thereof.

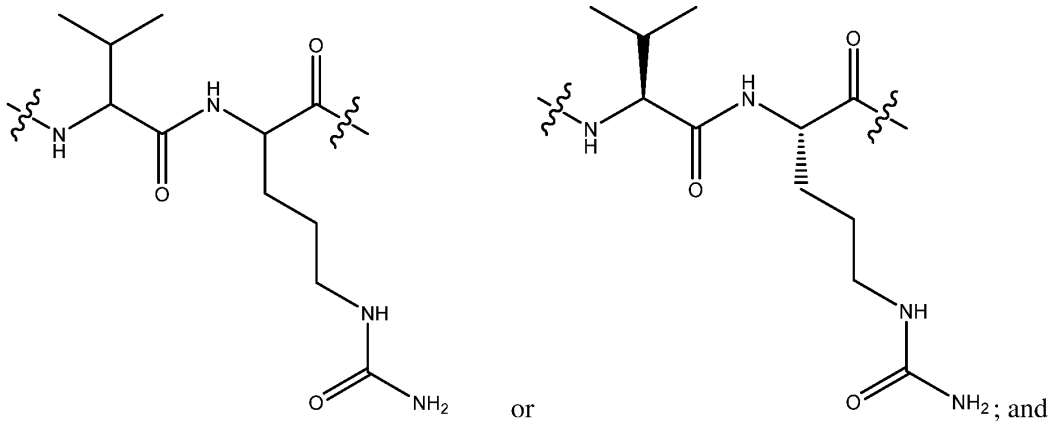
[0046] In some embodiments, the Releasable Linker RL is

$-(AA)_{1-12}-$; and

each AA is independently a proteinogenic or non-proteinogenic amino acid.

[0047] In some embodiments, the Releasable Linker RL is $-AA_1\text{-}AA_2-$ or $-AA_1\text{-}AA_2\text{-}AA_3-$, wherein AA_1 is attached to the Stretcher Unit Z or the Connector Unit A.

[0048] In some embodiments, the Releasable Linker RL is



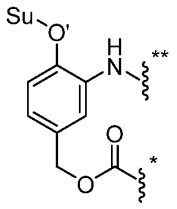
or

; and

the wavy line adjacent to the -NH- group indicates attachment to the Stretcher Unit Z or the Connector Unit A and the wavy line adjacent to the -C(=O)- group indicates attachment to the Spacer Unit Y or the Drug Unit D.

[0049] In some embodiments, the Releasable Linker RL is a glycoside.

[0050] In some embodiments, the Releasable Linker RL is



wherein

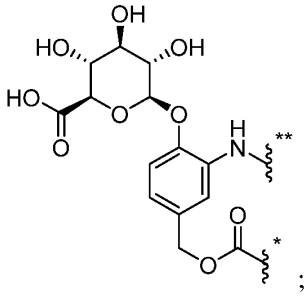
Su is a hexose form a monosaccharide;

O' represents the oxygen atom of a glycosidic bond that is capable of cleavage by a glycosidase;

the wavy line marked with a single asterisk (*) indicates the site of covalent attachment to D; and

the wavy line marked with a double asterisk (**) indicates the site of covalent attachment to the remainder of Q.

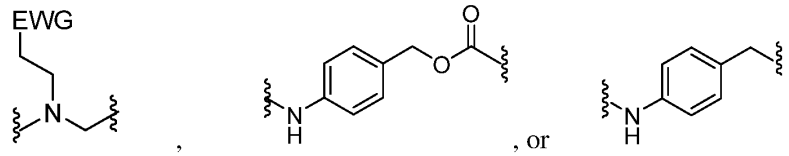
[0051] In some embodiments, the Releasable Linker RL is


;

the wavy line marked with a single asterisk (*) indicates the site of covalent attachment to D; and

the wavy line marked with a double asterisk (**) indicates the site of covalent attachment to the remainder of Q.

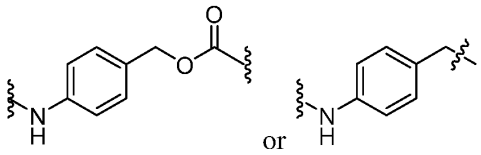
[0052] In some embodiments, the Spacer Unit Y is


, , or

wherein EWG is an electron-withdrawing group; and

the wavy lines indicate the site of attachment to the rest of the Ligand-Drug Conjugate compound or pharmaceutically acceptable salt thereof.

[0053] In some embodiments, the Spacer Unit Y is


or ; and

the wavy lines indicate the site of attachment to the rest of the Ligand-Drug Conjugate compound or pharmaceutically acceptable salt thereof.

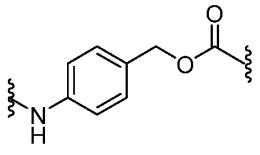
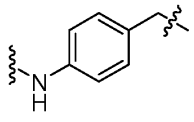
[0054] In some embodiments,

R^{17} is C_1-C_{10} alkylene;

A is a bond;

RL is –AA_1-AA_2–;

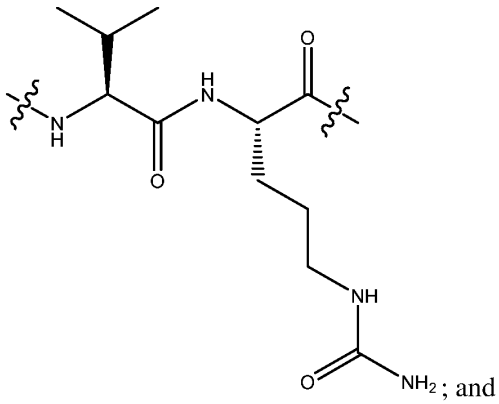
AA_1 and AA_2 are each independently a proteinogenic amino acid;

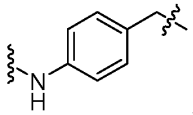
Y is  or  ; and

the wavy lines indicate the site of attachment to the rest of the Ligand-Drug Conjugate compound or pharmaceutically acceptable salt thereof.

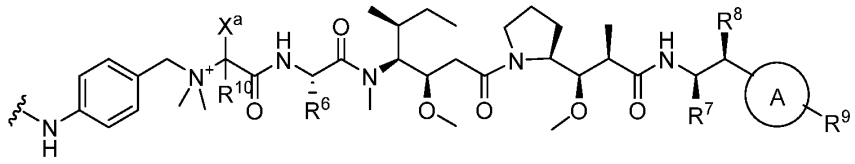
[0055] In some embodiments,

A is a bond;

RL is  ; and

Y is  .

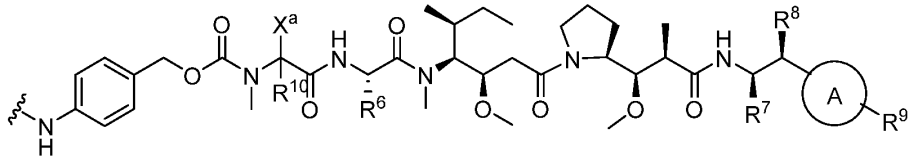
[0056] In some embodiments, Y-D is



; and

the wavy line indicates the site of attachment to the rest of the Ligand-Drug Conjugate compound or pharmaceutically acceptable salt thereof.

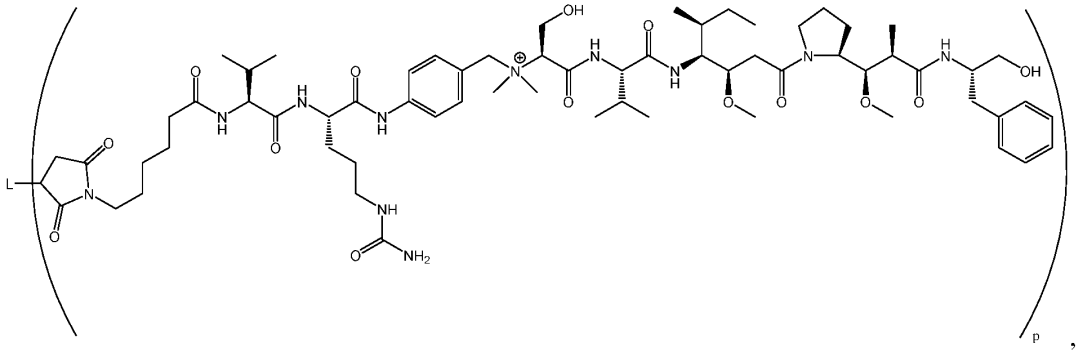
[0057] In some embodiments, Y-D is



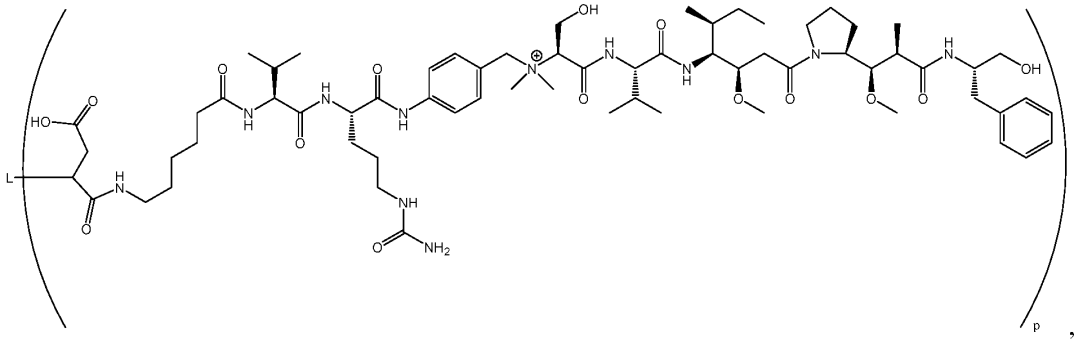
; and

the wavy line indicates the site of attachment to the rest of the Ligand-Drug Conjugate compound or pharmaceutically acceptable salt thereof.

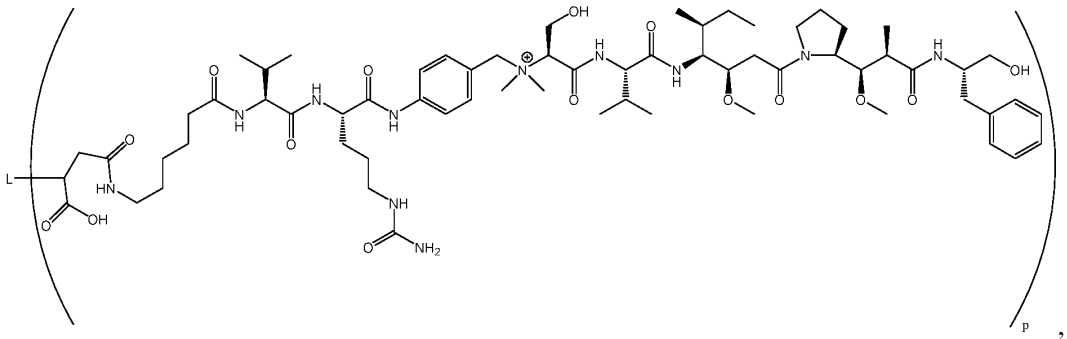
[0058] In some embodiments, the compound is



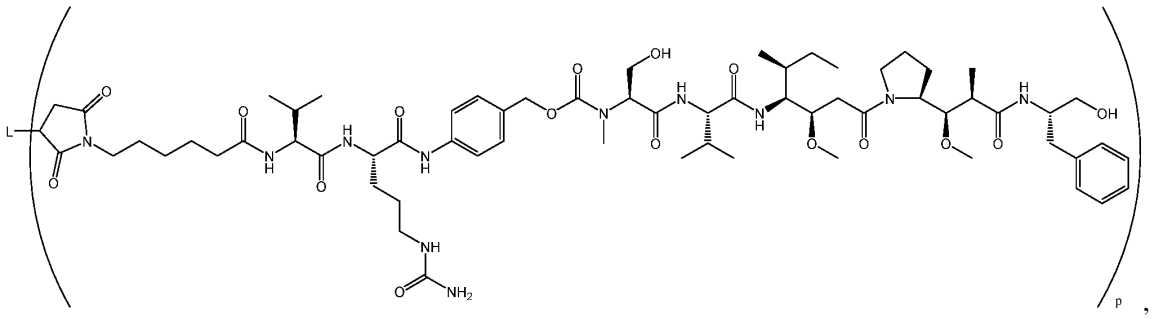
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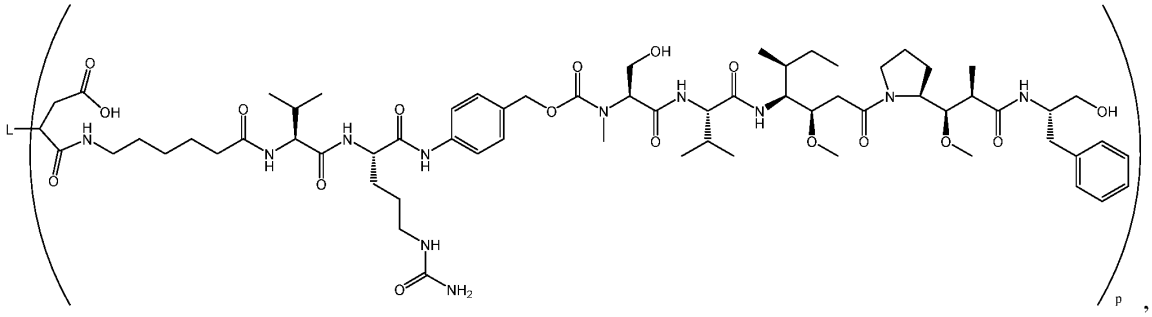
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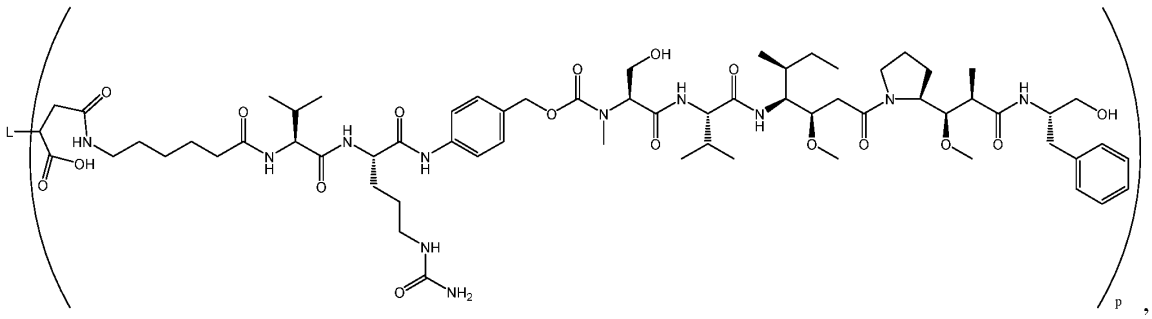
p ,



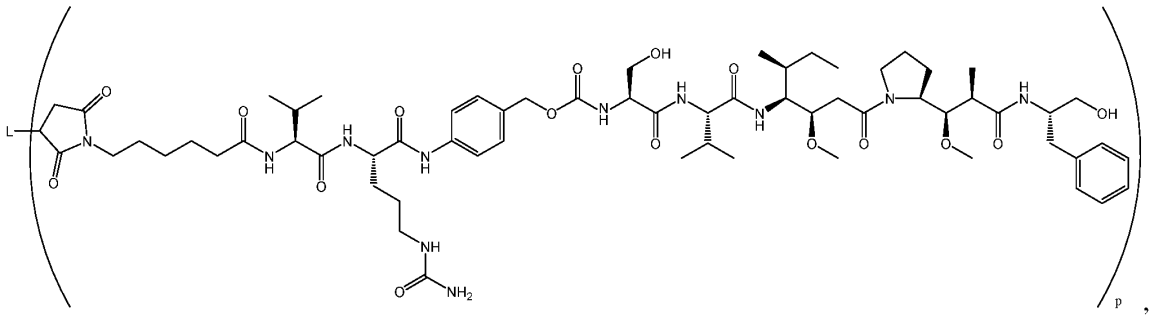
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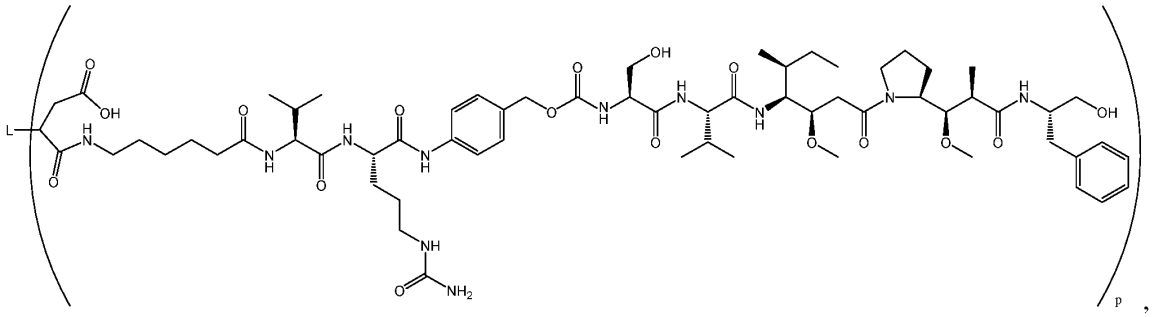


p ,

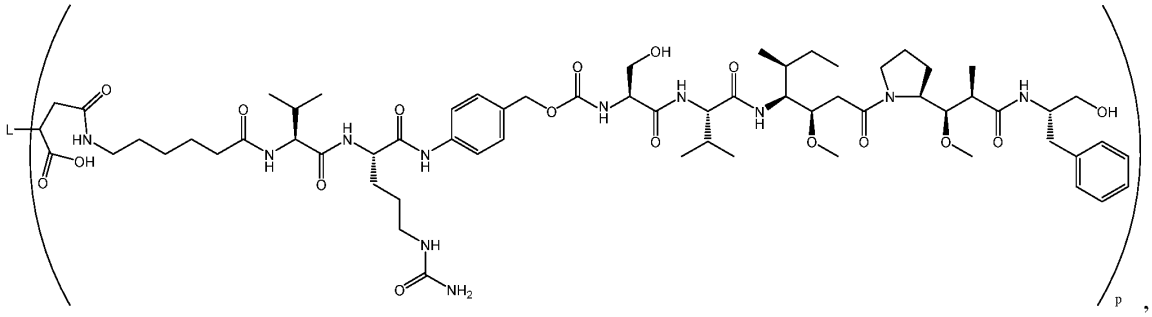


p ,





or



or a pharmaceutically acceptable salt thereof.

[0059] In some embodiments, the Ligand-Drug Conjugate compound is a compound of Table 3.

[0060] In some embodiments, p is an integer ranging from 2 to 6. In some embodiments, p is 4.

[0061] Also provided herein is a pharmaceutical composition comprising a Ligand-Drug Conjguate compound as described herein and a pharmaceutically acceptable excipient. In some embodiments, the composition comprises a plurlaity of Ligand-Drug Conjugate compounds with an average drug loading from 2 to 8. In some embodiments, the average drug loading is about 4. In some embodiments, the average drug loading is from 3.5 to 4.5.

[0062] Also provided herein is a method of treating cancer comprising administering a therapeutically effective amount of the Ligand-Drug Conjugate compound of any one of claims 66-96, or a pharmaceutically acceptable salt thereof, to a subject in need thereof. In some embodiments, the subject tolerates treatment with the Ligand-Drug Conjugate compound better than treatment with another Ligand-Drug Conjugate compound in therapeutically effective doses. In some embodiments, the another Ligand-Drug Conjugate compound comprises a monomethyl auristatin E or monomethyl auristatin F Drug Unit.

BRIEF DISCRIPTION OF THE FIGURES

[0063] **FIG 1.** Illustrates the *in vivo* mean tumor volume data for various Ag1 ADCs in the A2058 melanoma xenograft model.

[0064] **FIG 2.** Illustrates the *in vivo* mean tumor volume data for various h2A2 ADCs in the Detroit562 pharyngeal cancer xenograft model.

[0065] **FIG 3.** Illustrates the *in vivo* median tumor volume data for various cAC10 ADCs in the Karpas/KarpasBVR admixed Hodgkin lymphoma xenograft model.

[0066] **FIG 4.** Illustrates the *in vivo* mean tumor volume data for various cAC10 ADCs in the Karpas Hodgkin lymphoma xenograft model.

[0067] **FIG 5.** Illustrates the *in vivo* mean tumor volume data for various cAC10 ADCs in the Karpas Hodgkin lymphoma xenograft model.

[0068] **FIG 6.** Summarizes plasma neutrophil levels at day 5 and day 8 following administration by non-binding ADCs to rats.

[0069] **FIG 7.** Summarizes reticulocyte levels at day 5 and day 8 following administration by non-binding ADCs to rats.

[0070] **FIG 8.** Summarizes platelet levels at day 5 and day 8 following administration by non-binding ADCs to rats.

[0071] **FIG 9.** Summarizes aspartate transaminase (AST) levels at day 8 following administration by non-binding ADCs to rats.

[0072] **FIG 10.** Illustrates the efficacy of a variety of hCR011 ADCs and a non-binding control ADC as measured in the WM2664 melanoma xenograft model.

[0073] **FIG 11.** Illustrates the efficacy of a variety of hCR011 ADCs and non-binding control ADCs as measured in the SKMEL5 melanoma xenograft model.

[0074] **FIG 12.** Illustrates the efficacy of non-binding, Ag2, and hCR011 ADCs as measured in the PDX_1 melanoma xenograft model.

[0075] **FIG 13.** Illustrates the efficacy of non-binding, Ag2 and hCR011 ADCs as measured in the PDX_4 melanoma xenograft model.

[0076] **FIG 14.** Illustrates the efficacy of non-binding, Ag2 and hCR011 ADCs as measured in the PDX_3 NSCLC xenograft model.

[0077] **FIG 15.** Illustrates the efficacy of non-binding, Ag2 and hCR011 ADCs as measured in the PDX_2 NSCLC xenograft model.

[0078] **FIG 16.** Summarizes the anti-tumor activity of 6 hCR011 ADCs using AUC.3.

[0079] **FIG 17.** Summarizes plasma neutrophil levels at baseline, day 4, day 15, and day 29 following administration of hCR011 ADCs to cynomologous monkeys.

[0080] **FIG 18.** Summarizes reticulocyte levels at baseline, day 4, day 15, and day 29 following administration of hCR011 ADCs to cynomologous monkeys.

[0081] **FIG 19.** Summarizes platelet levels at baseline, day 4, day 15, and day 29 following administration of hCR011 ADCs to cynomologous monkeys.

[0082] **FIG 20.** Summarizes aspartate transaminase levels at baseline and day 8 following administration of hCR011 ADCs to cynomologous monkeys.

[0083] **FIG 21.** shows neutrophil counts from blood samples taken prior to dosing and post-dose on Day 8.

DETAILED DESCRIPTION OF THE INVENTION

[0084] One drug class of interest for use in Ligand-Drug Conjguates is auristatins. Auristatins have been shown to be effective payloads in some Ligand-Drug Conjugates (LDCs), but it is believed that their hydrophobicity can contribute to off-target toxicity due to increased permeability and high bystander activity of the free auristatin. Additionally, hydrophobic payloads, such as auristatins, may increase the hydrophobicity of the LDC, resulting in rapid clearance of the LDC from the body of a subject. Therefore, there is a need for auristain conjugates engineered to have optimized cell permeability, pharmacokinetics, and toxicity profile.

[0085] Without being bound by theory, it is believed that the hydrophilic groups of the auristatin compounds provided herein influence the properties of the compounds and of

resulting conjugates (*e.g.*, Ligand-Drug Conjugates). The hydrophilic groups are believed to increase the effectiveness of the resulting conjugates in two ways. Conjugates comprising a hydrophilic auristatin group may improve tumor exposure to the Drug Unit due to decreased plasma clearance, and they may simultaneously demonstrate reduced off-target toxicity due to decreased cell permeability of the free drug after it is released from the conjugate.

I. Definitions

[0086] Unless stated otherwise, the following terms and phrases as used herein are intended to have the following meanings. When trade names are used herein, the trade name includes the product formulation, the generic drug, and the active pharmaceutical ingredient(s) of the trade name product, unless otherwise indicated by context.

[0087] Unless defined otherwise, all technical and scientific terms used herein have the same meaning as commonly understood by one of ordinary skill in the art to which this disclosure is related. For example, the Concise Dictionary of Biomedicine and Molecular Biology, Juo, Pei-Show, 2nd ed., 2002, CRC Press; The Dictionary of Cell and Molecular Biology, 5th ed., 2013, Academic Press; and the Oxford Dictionary Of Biochemistry And Molecular Biology, 2nd ed., 2006, Oxford University Press, provide one of skill with a general dictionary of many of the terms used in this disclosure.

[0088] Unless otherwise required by context or expressly indicated, singular terms shall include pluralities and plural terms shall include the singular.

[0089] It is understood that aspect and embodiments of the invention described herein include "comprising," "consisting," and/or "consisting essentially of" aspects and embodiments.

[0090] As used herein, the singular form "a", "an", and "the" should be understood to refer to "one or more" of any recited or enumerated component unless indicated otherwise.

[0091] The term "about" refers to a value or composition that is within an acceptable error range for the particular value or composition as determined by one of ordinary skill in the art, which will depend in part on how the value or composition is measured or determined, *i.e.*, the limitations of the measurement system. As is understood by one skilled in the art, reference to "about" a value or parameter herein includes (and describes) embodiments that are directed to that value or parameter per se. For example, description referring to "about X" includes description of "X".

[0092] As described herein, any concentration range, percentage range, ratio range, or integer range is to be understood to include the value of any integer within the recited range and, when appropriate, fractions thereof (such as one tenth and one hundredth of an integer), unless otherwise indicated.

[0093] When a trade name is used herein, reference to the trade name also refers to the product formulation, the generic drug, and the active pharmaceutical ingredient(s) of the trade name product, unless otherwise indicated by context.

[0094] The term "and/or" where used herein is to be taken as specific disclosure of each of the two specified features or components with or without the other. Thus, the term "and/or" as used in a phrase such as "A and/or B" herein is intended to include "A and B," "A or B," "A" (alone), and "B" (alone). Likewise, the term "and/or" as used in a phrase such as "A, B, and/or C" is intended to encompass each of the following aspects: A, B, and C; A, B, or C; A or C; A or B; B or C; A and C; A and B; B and C; A (alone); B (alone); and C (alone).

[0095] The term “antibody” as used herein is used in the broadest sense and specifically covers intact monoclonal antibodies, polyclonal antibodies, monospecific antibodies, multispecific antibodies (*e.g.,* bispecific antibodies), and antibody fragments (i.e., antigen-binding fragments) that retain, at least in part, one or more of the the desired biological activities of the full-length antibody, for example, affinity for its cognate antigen. The native form of an antibody is a tetramer and consists of two identical pairs of immunoglobulin chains, each pair having one light chain and one heavy chain. In each pair, the light and heavy chain variable regions (V_L and V_H) are together primarily responsible for binding to an antigen. The light chain and heavy chain variable domains consist of a framework region interrupted by three hypervariable regions, also called “complementarity determining regions” or “CDRs.” In some aspects, the constant regions are recognized by and interact with the immune system (*see, e.g.*, Janeway *et al.*, 2001, *Immunol. Biology, 5th Ed.*, Garland Publishing, New York). The antibodies herein are of any type (*e.g.*, IgG, IgE, IgM, IgD, and IgA), class (*e.g.,* IgG_1, IgG_2, IgG_3, IgG_4, IgA_1 and IgA_2), or subclass thereof. In some aspects, the antibody is derived from a suitable species. In some embodiments, the antibody is of human or murine origin. In some aspects, the antibody is human, humanized, or chimeric. An antibody can be human, humanized, chimeric and/or affinity matured, as well as an antibody from other species, for example, mouse and rabbit, *etc.* The term “antibody” thus includes, for instance, a polypeptide product of B cells within the immunoglobulin class of

polypeptides that is able to bind to a specific molecular antigen and is composed of two identical pairs of polypeptide chains, wherein each pair has one heavy chain (about 50-70 kDa) and one light chain (about 25 kDa), each amino-terminal portion of each chain includes a variable region of about 100 to about 130 or more amino acids, and each carboxy-terminal portion of each chain includes a constant region. *See, e.g.*, Antibody Engineering (Borrebaeck ed., 2d ed. 1995); and Kuby, Immunology (3d ed. 1997). The term "antibody" also includes, but is not limited to, synthetic antibodies, recombinantly produced antibodies, camelized antibodies, intrabodies, anti-idiotypic (anti-Id) antibodies, and functional fragments (*e.g.*, antigen-binding fragments) of any of the above, which refers to a portion of an antibody heavy and/or light chain polypeptide that retains some or all of the binding activity of the antibody from which the fragment was derived. Non-limiting examples of functional fragments (*e.g.*, antigen-binding fragments) include single-chain Fvs (scFv) (*e.g.*, including monospecific, bispecific, *etc.*), Fab fragments, F(ab') fragments, $F(ab)_2$ fragments, $F(ab')_2$ fragments, disulfide-linked Fvs (dsFv), Fd fragments, Fv fragments, diabody, triabodies, tetrabodies, and minibodies. In particular, antibodies provided herein include immunoglobulin molecules and immunologically active portions of immunoglobulin molecules, for example, antigen-binding domains or molecules that contain an antigen-binding site that binds to an antigen (*e.g.*, one or more CDRs of an antibody). Such antibody fragments can be found in, for example, Harlow and Lane, Antibodies: A Laboratory Manual (1989); Mol. Biology and Biotechnology: A Comprehensive Desk Reference (Myers ed., 1995); Huston *et al.*, 1993, Cell Biophysics 22:189-224; Plückthun and Skerra, 1989, Meth. Enzymol. 178:497-515; and Day, Advanced Immunochemistry (2d ed. 1990). The antibodies provided herein can be of any class (*e.g.*, IgG, IgE, IgM, IgD, and IgA) or any subclass (*e.g.*, IgG1, IgG2, IgG3, IgG4, IgA1, and IgA2) of immunoglobulin molecule.

[0096] The term "monoclonal antibody" as used herein refers to an antibody obtained from a population of substantially homogeneous antibodies, *i.e.,* the individual antibodies comprising the population are identical except for possible naturally occurring mutations that are present, in some aspects, in minor amounts. Monoclonal antibodies are highly specific, being directed against a single antigenic site. The modifier "monoclonal" indicates the character of the antibody as being obtained from a substantially homogeneous population of antibodies and is not to be construed as requiring production of the antibody by any particular method.

[0097] An "intact antibody" is one which comprises an antigen-binding variable region as well as a light chain constant domain (C_L) and heavy chain constant domains, C_H1, C_H2, C_H3, and C_H4, as appropriate for the antibody class. In some aspects the constant domains are native sequence constant domains (*e.g.,* human native sequence constant domains) and in other aspects are amino acid sequence variants thereof.

[0098] An "antibody fragment" comprises a portion of an intact antibody, comprising the antigen-binding or variable region thereof. Examples of antibody fragments include Fab, Fab', F(ab')$_2$, and Fv fragments, diabodies, triabodies, tetrabodies, linear antibodies, single-chain antibody molecules, scFv, scFv-Fc, multispecific antibody fragments formed from antibody fragment(s), a fragment(s) produced by a Fab expression library, or an epitope-binding fragments of any of the above which immunospecifically bind to a target antigen (*e.g.*, a cancer cell antigen, a viral antigen or a microbial antigen).

[0099] An "antigen-binding fragment" (or simply "fragment") or "antigen-binding domain", of an antigen binding protein (e.g., an antibody) as used herein refers to one or more fragments of an antigen binding protein (e.g., an antibody), regardless of how obtained or synthesized, that retain the ability to specifically bind to the antigen bound by the whole antigen binding protein. Examples of antibody fragments include, but are not limited to, Fv; Fab; Fab'; Fab'-SH; F(ab')$_2$; diabodies; linear antibodies; single-chain antibody molecules (*e.g.* scFv); and multispecific antibodies formed from antibody fragments. A "Fv" fragment includes a non-covalently-linked dimer of one heavy chain variable domain and one light chain variable domain. A "Fab" fragment includes, the constant domain of the light chain and the first constant domain (C_{H1}) of the heavy chain, in addition to the heavy and light chain variable domains of the Fv fragment. A "F(ab')$_2$" fragment includes two Fab fragments joined, near the hinge region, by disulfide bonds.

[0100] An "antigen" is an entity to which an antibody specifically binds.

[0101] The terms "specific binding" and "specifically binds" mean that the antibody or antibody derivative will bind, in a highly selective manner, with its corresponding epitope of a target antigen and not with the multitude of other antigens. Typically, the antibody or antibody derivative binds with an affinity of at least about $1x10^{-7}$ M, and preferably 10^{-8} M to 10^{-9} M, 10^{-10} M, 10^{-11} M, or 10^{-12} M and binds to the predetermined antigen with an affinity that is at least two-fold greater than its affinity for binding to a non-specific antigen (*e.g.*, BSA, casein) other than the predetermined antigen or a closely-related antigen.

[0102] The term "inhibits" or "inhibition of" means to reduce by a measurable amount, or to prevent entirely.

[0103] The term "therapeutically effective amount" refers to an amount of a conjugate effective to treat a disease or disorder in a mammal. In the case of cancer, the therapeutically effective amount of the conjugate may reduce the number of cancer cells; reduce the tumor size; inhibit (*i.e.,* slow to some extent and preferably stop) cancer cell infiltration into peripheral organs; inhibit (*i.e.,* slow to some extent and preferably stop) tumor metastasis; inhibit, to some extent, tumor growth; and/or relieve to some extent one or more of the symptoms associated with the cancer. In some aspects, the drug inhibits growth and/or kills existing cancer cell. In some aspects, the drug is cytostatic and/or cytotoxic. For cancer therapy, efficacy is measured by commonly available tools. In some aspects, efficacy is measured by assessing the time to disease progression (TTP) and/or determining the response rate (RR).

[0104] As used herein, "Percent (%) amino acid sequence identity" and "homology" with respect to a peptide, polypeptide or antigen binding protein (e.g., antibody) sequence are defined as the percentage of amino acid residues in a candidate sequence that are identical with the amino acid residues in the specific peptide or polypeptide sequence, after aligning the sequences and introducing gaps, if necessary, to achieve the maximum percent sequence identity, and not considering any conservative substitutions as part of the sequence identity. Alignment for purposes of determining percent amino acid sequence identity can be achieved in various ways that are within the skill in the art, for instance, using publicly available computer software such as BLAST, BLAST-2, ALIGN or MEGALIGN™ (DNASTAR) software. Those skilled in the art can determine appropriate parameters for measuring alignment, including any algorithms needed to achieve maximal alignment over the full length of the sequences being compared. For example, the % sequence identity of a given amino acid sequence A to, with, or against a given amino acid sequence B (which can alternatively be phrased as a given amino acid sequence A that has or comprises a certain % sequence identity to, with, or against a given amino acid sequence B) is calculated as follows:

100 times the fraction X/Y

where X is the number of amino acid residues scored as identical matches by the sequence in that program's alignment of A and B, and where Y is the total number of amino acid residues in B. Unless specifically stated otherwise, all % amino acid sequence identity values used

herein are calculated according to this formula using the ALIGN-2 computer program. It will be appreciated that where the length of amino acid sequence A is not equal to the length of amino acid sequence B, the % sequence identity of A to B will not equal the % sequence identity of B to A.

[0105] The term "substantial" or "substantially" refers to a majority, *i.e.* >50% of a population, of a mixture or a sample, preferably more than 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97 %, 98%, or 99% of a population.

[0106] The term "cytotoxic activity" refers to a cell-killing effect of a drug or Ligand-Drug Conjugate compound or an intracellular metabolite of a Ligand-Drug Conjugate compound. In some aspects, cytotoxic activity is expressed as the IC_{50} value, which is the concentration (molar or mass) per unit volume at which half the cells survive.

[0107] The term "cytostatic activity" refers to an anti-proliferative effect of a drug or Ligand-Drug Conjugate compound or an intracellular metabolite of a Ligand-Drug Conjugate compound.

[0108] The term "cytotoxic agent" as used herein refers to a substance that has cytotoxic activity and causes destruction of cells. The term is intended to include chemotherapeutic agents, and toxins such as small molecule toxins or enzymatically active toxins of bacterial, fungal, plant or animal origin, including synthetic analogs and derivatives thereof.

[0109] The term "cytostatic agent" as used herein refers to a substance that inhibits a function of cells, including cell growth or multiplication. Cytostatic agents include inhibitors such as protein inhibitors, e.g., enzyme inhibitors. Cytostatic agents have cytostatic activity.

[0110] The terms "cancer" and "cancerous" refer to or describe the physiological condition or disorder in mammals that is typically characterized by unregulated cell growth. A "tumor" comprises one or more cancerous cells.

[0111] The term "immunoglobulin" refers to a class of structurally related glycoproteins consisting of two pairs of polypeptide chains, one pair of light (L) low molecular weight chains and one pair of heavy (H) chains, all four inter-connected by disulfide bonds. The structure of immunoglobulins has been well characterized. See, for instance, Fundamental Immunology (Paul, W., ed., 7th ed. Raven Press, N .Y. (2013)). Briefly, each heavy chain typically is comprised of a heavy chain variable region (abbreviated herein as V_H or VH) and a heavy chain constant region (C_H or CH). The heavy chain constant region typically is comprised of three domains, C_H1, C_H2, and C_H3. The heavy chains are generally inter-

connected via disulfide bonds in the so-called "hinge region." Each light chain typically is comprised of a light chain variable region (abbreviated herein as V_L or VL) and a light chain constant region (C_L or CL). The light chain constant region typically is comprised of one domain, C_L. The CL can be of κ (kappa) or λ (lambda) isotype. The terms "constant domain" and "constant region" are used interchangeably herein. An immunoglobulin can derive from any of the commonly known isotypes, including but not limited to IgA, secretory IgA, IgG, and IgM. IgG subclasses are also well known to those in the art and include but are not limited to human IgG1, IgG2, IgG3 and IgG4. "Isotype" refers to the antibody class or subclass (*e.g.*, IgM or IgG1) that is encoded by the heavy chain constant region genes.

[0112] The term "hypervariable region" or "HVR," as used herein, refers to each of the regions of an antibody variable domain which are hypervariable in sequence. HVRs can form structurally defined loops ("hypervariable loops"). Generally, native four-chain antibodies comprise six HVRs; three in the VH (H1, H2, H3), and three in the VL (L1, L2, L3). In native antibodies, H3 and L3 display the most diversity of the six HVRs, and H3 in particular is believed to play a unique role in conferring fine specificity to antibodies. See, e.g., Xu et al., Immunity 13:37-45 (2000); Johnson and Wu, in Methods in Molecular Biology 248:1 -25 (Lo, ed., Human Press, Totowa, NJ, 2003). Indeed, naturally-occurring camelid antibodies consisting of a heavy chain only are functional and stable in the absence of light chain. See, e.g., Hamers-Casterman et al., Nature 363:446-448 (1993); Sheriff et al., Nature Struct. Biol. 3:733-736 (1996).

[0113] HVRs generally comprise amino acid residues from the hypervariable loops and/or from the "complementary determining regions" (CDRs), CDRs being of highest sequence variability and/or involved in antigen recognition. A variety of schemes for defining the boundaries of a given CDR are known in the art. For example, the Kabat Complementarity Determining Regions (CDRs) are based on sequence variability and are the most commonly used (Kabat et at., Sequences of Proteins of Immunological Interest, 5th Ed. Public Health Service, National Institutes of Health, Bethesda, MD. (1991)). Chothia refers instead to the location of the structural loops (Chothia and Lesk, J. Mol. Biol. 196:901-917 (1987)). The AbM CDRs represent a compromise between the Kabat CDRs and Chothia structural loops and are used by Oxford Molecular's AbM antibody modeling software. The "contact" CDRs are based on an analysis of the available complex crystal structures. Additional details on the foregoing schemes as well as other numbering conventions are provided in the following references: Al-Lazikani et al., (1997) J. Mol. Biol. 273: 927-948

("Chothia" numbering scheme); MacCallum et al., (1996) J. Mol. Biol. 262:732-745 (1996), (Contact" numbering scheme); Lefranc M-P., et al., (2003) Dev. Comp. Immunol. 27:55-77 ("IMGT" numbering scheme); and Honegger A. & Pluckthun A. (2001) J. Mol/ Biol. 309:657-70, (AHo numbering scheme).

[0114] In some embodiments, the HVR regions and associated sequences are the same as the CDR regions and associated sequences based upon one of the foregoing numbering conventions. As such, residues for exemplary HVRs and/or CDRs are summarized in the Table D1 below.

Table D1: Summary of Different CDR Numbering Schemes.

Loop	IMGT	Kabat	AbM	Chothia	Contact
CDR-H1	27-38	31-35	26-35	26-32	30-35
CDR-H2	56-65	50-65	50-58	52-56	47-58
CDR-H3	105-117	95-102	95-102	95-102	93-101
CDR-L1	27-38	24-34	24-34	24-34	30-36
CDR-L2	56-65	50-56	50-56	50-56	46-55
CDR-L3	105-117	89-97	89-97	89-97	89-96

[0115] In some embodiments, HVRs can comprise extended HVRs as follows: 24-36 or 24-34 (L1), 46-56 or 50-56 (L2) and 89-97 or 89-96 (L3) in the VL and 26-35 (H1), 50-65 or 49-65 (H2) and 93-102, 94-102, or 95-102 (H3) in the VH. The variable domain residues are numbered according to Kabat et at., supra, for each of these definitions.

[0116] Unless otherwise specified, the terms "CDR" and "complementary determining region" of a given antibody or region thereof, such as a variable region, as well as individual CDRs (*e.g.*, "CDR-H1, CDR-H2) of the antibody or region thereof, should be understood to encompass the complementary determining region as defined by any of the known schemes described herein above. In some instances, the scheme for identification of a particular CDR or CDRs is specified, such as the CDR as defined by the IMGT, Kabat, AbM, Chothia, or Contact method. In other instances, the particular amino acid sequence of a CDR is given.

[0117] Thus, in some embodiments, the antigen binding protein comprises CDRs and/or HVRs as defined by the IMGT system. In other embodiments, the antigen binding protein

comprises CDRs or HVRs as defined by the Kabat system. In still other embodiments, the antigen binding protein comprises CDRs or HVRs as defined by the AbM system. In further embodiments, the antigen binding protein comprises CDRs or HVRs as defined by the Chothia system. In yet other embodiments, the antigen binding protein comprises CDRs or HVRs as defined by the IMGT system.

[0118] The term "variable region" or "variable domain" refers to the domain of an antigen binding protein (e.g., an antibody) heavy or light chain that is involved in binding the antigen binding protein (e.g., antibody) to antigen. The variable regions or domains of the heavy chain and light chain (VH and VL, respectively) of an antigen binding protein such as an antibody can be further subdivided into regions of hypervariability (or hypervariable regions, which may be hypervariable in sequence and/or form of structurally defined loops), such as hypervariable regions (HVRs) or complementarity-determining regions (CDRs), interspersed with regions that are more conserved, termed framework regions (FRs). In general, there are three HVRs (HVR-H1, HVR-H2, HVR-H3) or CDRs (CDR-H1, CDR-H2, CDR-H3) in each heavy chain variable region, and three HVRs (HVR-L1, HVR-L2, HVR-L3) or CDRs in (CDR-L1, CDR-L2, CDR-L3) in each light chain variable region. "Framework regions" and "FR" are known in the art to refer to the non-HVR or non-CDR portions of the variable regions of the heavy and light chains. In general, there are four FRs in each full-length heavy chain variable region (FR-H1, FR-H2, FR-H3, and FR-H4), and four FRs in each full-length light chain variable region (FR-L1, FR-L2, FR-L3, and FR-L4). Within each VH and VL, three HVRs or CDRs and four FRs are typically arranged from amino-terminus to carboxy-terminus in the following order: FR1, HVR1, FR2, HVR2, FR3, HVR3, FR4 in the case of HVRs, or FR1, CDR1, FR2, CDR2, FR3, CDR3, FR4 in the case of CDRs (*See* also Chothia and Lesk *J. Mot. Biol.*, 195, 901-917 (1987)). A single VH or VL domain can be sufficient to confer antigen-binding specificity. In addition, antibodies that bind a particular antigen can be isolated using a VH or VL domain from an antibody that binds the antigen to screen a library of complementary VL or VH domains, respectively. See, e.g., Portolano et al. J. Immunol. 150:880-887 (1993); Clarkson et al., Nature 352:624-628 (1991).

[0119] The term "heavy chain variable region" (VH) as used herein refers to a region comprising heavy chain HVR-H1, FR-H2, HVR-H2, FR-H3, and HVR-H3. For example, a heavy chain variable region may comprise heavy chain CDR-H1, FR-H2, CDR-H2, FR-H3,

and CDR-H3. In some embodiments, a heavy chain variable region also comprises at least a portion of an FR-H1 and/or at least a portion of an FR-H4.

[0120] The term "heavy chain constant region" as used herein refers to a region comprising at least three heavy chain constant domains, C_H1, C_H2, and C_H3. Nonlimiting exemplary heavy chain constant regions include γ, δ, and α. Nonlimiting exemplary heavy chain constant regions also include ε and μ. Each heavy constant region corresponds to an antibody isotype. For example, an antibody comprising a γ constant region is an IgG antibody, an antibody comprising a δ constant region is an IgD antibody, and an antibody comprising an α constant region is an IgA antibody. Further, an antibody comprising a μ constant region is an IgM antibody, and an antibody comprising an ε constant region is an IgE antibody. Certain isotypes can be further subdivided into subclasses. For example, IgG antibodies include, but are not limited to, IgG1 (comprising a γ_1 constant region), IgG2 (comprising a γ_2 constant region), IgG3 (comprising a γ_3 constant region), and IgG4 (comprising a γ_4 constant region) antibodies; IgA antibodies include, but are not limited to, IgA1 (comprising an α_1 constant region) and IgA2 (comprising an α_2 constant region) antibodies; and IgM antibodies include, but are not limited to, IgM1 and IgM2.

[0121] The term "heavy chain" (HC) as used herein refers to a polypeptide comprising at least a heavy chain variable region, with or without a leader sequence. In some embodiments, a heavy chain comprises at least a portion of a heavy chain constant region. The term "full-length heavy chain" as used herein refers to a polypeptide comprising a heavy chain variable region and a heavy chain constant region, with or without a leader sequence.

[0122] The term "light chain variable region" (VL) as used herein refers to a region comprising light chain HVR-L1, FR-L2, HVR-L2, FR-L3, and HVR-L3. In some embodiments, the light chain variable region comprises light chain CDR-L1, FR-L2, CDR-L2, FR-L3, and CDR-L3. In some embodiments, a light chain variable region also comprises an FR-L1 and/or an FR-L4.

[0123] The term "light chain constant region" as used herein refers to a region comprising a light chain constant domain, C_L. Nonlimiting exemplary light chain constant regions include λ and κ.

[0124] The term "light chain" (LC) as used herein refers to a polypeptide comprising at least a light chain variable region, with or without a leader sequence. In some embodiments, a light chain comprises at least a portion of a light chain constant region. The term "full-length

light chain" as used herein refers to a polypeptide comprising a light chain variable region and a light chain constant region, with or without a leader sequence.

[0125] The "EU numbering system" or "EU index" is generally used when referring to a residue in an immunoglobulin heavy chain constant region (e.g., the EU index reported in Kabat et al., Sequences of Proteins of Immunological Interest, 5th Ed. Public Health Service, National Institutes of Health, Bethesda, Md., 1991). The "EU index as in Kabat" refers to the residue numbering of the human IgG1 EU antibody. Unless stated otherwise herein, references to residue numbers in the constant domain of antibodies means residue numbering by the EU numbering system.

[0126] The term "derivative" refers to a molecule (e.g., an antigen binding protein such as an antibody or fragment thereof) that includes a chemical modification other than an insertion, deletion, or substitution of amino acids (or nucleic acids). In certain embodiments, derivatives comprise covalent modifications, including, but not limited to, chemical bonding with polymers, lipids, or other organic or inorganic moieties. In certain embodiments, a derivative of a particular antigen binding protein can have a greater circulating half-life than an antigen binding protein that is not chemically modified. In certain embodiments, a derivative can have improved targeting capacity for desired cells, tissues, and/or organs. In some embodiments, a derivative of an antigen binding protein is covalently modified to include one or more polymers, including, but not limited to, monomethoxy-polyethylene glycol, dextran, cellulose, or other carbohydrate based polymers, poly-(N-vinyl pyrrolidone)-polyethylene glycol, propylene glycol homopolymers, a polypropylene oxide/ethylene oxide co-polymer, polyoxyethylated polyols (e.g., glycerol) and polyvinyl alcohol, as well as mixtures of such polymers. See, e.g., U.S. Pat. Nos. 4,640,835, 4,496,689, 4,301,144, 4,670,417, 4,791,192 and 4,179,337.

[0127] The term "compete" when used in the context of antigen binding proteins (*e.g.*, antibodies or fragments thereof) that compete for the same epitope means competition between antigen binding proteins as determined by an assay in which the antigen binding protein (*e.g.*, an antibody or fragment thereof) being tested (e.g., a test antibody) prevents or inhibits (partially or completely) specific binding of a reference antigen binding protein (*e.g.*, a reference antibody) to a common antigen (*e.g.*, gpNMB or a fragment thereof). Numerous types of competitive binding assays can be used to determine if one antigen binding protein competes with another, including various label-free biosensor approaches such as surface plasmon resonance (SPR) analysis (see, *e.g.*, Abdiche, *et al.*, 2009, *Anal. Biochem.* 386:172-

180; Abdiche, *et al.*, 2012, *J. Immunol Methods* 382:101-116; and Abdiche, *et al.*, 2014 *PLoS One* 9:e92451. Other assays that can be used include: solid phase direct or indirect radioimmunoassay (RIA), solid phase direct or indirect enzyme immunoassay (EIA), sandwich competition assay (see, *e.g.*, Stahli et al., 1983, *Methods in Enzymology* 9:242-253); solid phase direct biotin-avidin EIA (see, *e.g.*, Kirkland et al., 1986, *J. Immunol.* 137:3614-3619) solid phase direct labeled assay, solid phase direct labeled sandwich assay (see, *e.g.*, Harlow and Lane, 1988, *Antibodies, A Laboratory Manual*, Cold Spring Harbor Press); solid phase direct label RIA using I-125 label (see, *e.g.*, Morel *et al.*, 1988, *Mol. Immunol.* 25:7-15); solid phase direct biotin-avidin EIA (see, *e.g.*, Cheung, *et al.*, 1990, *Virology* 176:546-552); direct labeled RIA (Moldenhauer *et al.*, 1990, *Scand. J. Immunol.* 32:77-82). Typically, the test antigen binding protein is present in excess (e.g., at least 2x, 5x, 10x, 20x or 100x). Usually, when a competing antigen binding protein is present in excess, it will inhibit specific binding of a reference antigen binding protein to a common antigen by at least 40%, 50%, 60%, 70%, 80%, 90%, 95% or 100%. In instances in in which each antigen binding protein (e.g., an antibody or fragment thereof) detectably inhibits the binding of the other antigen binding protein with its cognate epitope, whether to the same, greater, or lesser extent, the antigen binding proteins are said to "cross-compete" with each other for binding of their respective epitope(s) or to "cross-block" one another. Typically, such cross-competition studies are done using the conditions and methods described above for competition studies and the extent of blocking is at least 30%, at least 40%, or at least 50% each way.

[0128] An "affinity matured" antibody refers to an antibody with one or more alterations in one or more hypervariable regions (HVRs) compared to a parent antibody which does not possess such alterations, such alterations resulting in an improvement in the affinity of the antibody for antigen. In some examples, an affinity matured antibody refers to an antibody with one or more alterations in one or more complementarity determining regions (CDRs) compared to a parent antibody which does not possess such alterations, such alterations resulting in an improvement in the affinity of the antibody for antigen.

[0129] As used herein, the term "specifically binds", "binding" or simply "binds" or other related terms in the context of the binding of an antigen binding protein to its target antigen means that the antigen binding protein exhibits essentially background binding to non-target molecules. An antigen binding protein that specifically binds a target antigen (e.g.,

gpNMB) may, however, cross-react with the corresponding protein (such as gpNMB) from different species.

[0130] The term "K_D" (M), as used herein, refers to the dissociation equilibrium constant of a particular antigen binding protein-antigen interaction (e.g., antibody-antigen interaction). Affinity, as used herein, and K_D are inversely related, such that higher affinity is intended to refer to lower K_D, and lower affinity is intended to refer to higher K_D.

[0131] An "antibody-drug-conjugate" or simply "ADC" refers to an antibody conjugated to a cytotoxic agent or cytostatic agent. An antibody-drug-conjugate typically binds to the target antigen (e.g., gpNMB) on a cell surface followed by internalization of the antibody-drug-conjugate into the cell where the drug is released.

[0132] A "cytotoxic effect" refers to the depletion, elimination and/or killing of a target cell.

[0133] A "cytotoxic agent" refers to an agent that has a cytotoxic effect on a cell.

[0134] A "cytostatic effect" refers to the inhibition of cell proliferation.

[0135] A "cytostatic agent" refers to an agent that has a cytostatic effect on a cell, thereby inhibiting the growth of and/or expansion of a specific subset of cells. Cytostatic agents can be conjugated to an antibody or administered in combination with an antibody.

[0136] The term "Fc region" herein is used to define a C-terminal region of an immunoglobulin heavy chain that contains at least a portion of the constant region. The term includes native sequence Fc regions and variant Fc regions. In one embodiment, a human IgG heavy chain Fc region extends from Cys226, or from Pro230, to the carboxyl-terminus of the heavy chain. However, the C-terminal lysine (Lys447) of the Fc region may or may not be present. Unless otherwise specified herein, numbering of amino acid residues in the Fc region or constant region is according to the EU numbering system, also called the EU index, as described in Kabat et al., Sequences of Proteins of Immunological Interest, 5th Ed. Public Health Service, National Institutes of Health, Bethesda, Md., 1991.

[0137] A "functional Fc region" possesses an "effector function" of a native sequence Fc region. Exemplary "effector functions" include Fc receptor binding; C1q binding; complement dependent cytotoxicity (CDC); antibody-dependent cell-mediated cytotoxicity (ADCC); antibody-dependent cellular phagocytosis (ADCP); down regulation of cell surface receptors (*e.g.* B cell receptor; BCR), *etc.* Such effector functions generally require the Fc

region to be combined with a binding domain (*e.g.*, an antibody variable domain) and can be assessed using various assays.

[0138] A "native sequence Fc region" comprises an amino acid sequence identical to the amino acid sequence of an Fc region found in nature. Native sequence human Fc regions include a native sequence human IgG1 Fc region (non-A and A allotypes); native sequence human IgG2 Fc region; native sequence human IgG3 Fc region; and native sequence human IgG4 Fc region as well as naturally occurring variants thereof.

[0139] A "variant Fc region" comprises an amino acid sequence which differs from that of a native sequence Fc region by virtue of at least one amino acid modification.

[0140] "Fc receptor" or "FcR" describes a receptor that binds to the Fc region of an antibody. In some embodiments, an FcγR is a native human FcR. In some embodiments, an FcR is one which binds an IgG antibody (a gamma receptor) and includes receptors of the FcγRI, FcγRII, and FcγRIII subclasses, including allelic variants and alternatively spliced forms of those receptors. FcγRII receptors include FcγRIIA (an "activating receptor") and FcγRIIB (an "inhibiting receptor"), which have similar amino acid sequences that differ primarily in the cytoplasmic domains thereof. Activating receptor FcγRIIA contains an immunoreceptor tyrosine-based activation motif (ITAM) in its cytoplasmic domain Inhibiting receptor FcγRIIB contains an immunoreceptor tyrosine-based inhibition motif (ITIM) in its cytoplasmic domain. (see, *e.g.*, Daeron, *Annu. Rev. Immunol.* 15:203-234 (1997)). FcRs are reviewed, for example, in Ravetch and Kinet, *Annu. Rev. Immunol* 9:457-92 (1991); Capel *et al.*, *Immunomethods* 4:25-34 (1994); and de Haas *et al.*, *J. Lab. Clin. Med.* 126:330-41 (1995). Other FcRs, including those to be identified in the future, are encompassed by the term "FcR" herein. The term "Fc receptor" or "FcR" also includes the neonatal receptor, FcRn, which is responsible for the transfer of maternal IgGs to the fetus (Guyer *et al.*, *J. Immunol.* 117:587 (1976) and Kim *et al.*, *J. Immunol.* 24:249 (1994)) and regulation of homeostasis of immunoglobulins. Methods of measuring binding to FcRn are known (see, *e.g.*, Ghetie and Ward., *Immunol. Today* 18(12):592-598 (1997); Ghetie *et al.*, *Nature Biotechnology*, 15(7):637-640 (1997); Hinton *et al.*, *J. Biol. Chem.* 279(8):6213-6216 (2004); WO 2004/92219 (Hinton *et al.*).

[0141] "Effector functions" refer to biological activities attributable to the Fc region of an antibody, which vary with the antibody isotype. Examples of antibody effector functions include: Clq binding and complement dependent cytotoxicity (CDC); Fc receptor binding;

antibody-dependent cell-mediated cytotoxicity (ADCC); antibody-dependent cellular phagocytosis (ADCP); down regulation of cell surface receptors (*e.g.* B cell receptor); and B cell activation. Such functions can be affected by, for example, binding of an Fc effector domain(s) to an Fc receptor on an immune cell with phagocytic or lytic activity or by binding of an Fc effector domain(s) to components of the complement system. Typically, the effect(s) mediated by the Fc-binding cells or complement components result in inhibition and/or depletion of the CD33 targeted cell. Fc regions of antibodies can recruit Fc receptor (FcR)-expressing cells and juxtapose them with antibody-coated target cells. Cells expressing surface FcR for IgGs including FcγRIII (CD16), FcγRII (CD32) and FcγRIII (CD64) can act as effector cells for the destruction of IgG-coated cells. Such effector cells include monocytes, macrophages, natural killer (NK) cells, neutrophils and eosinophils. Engagement of FcγR by IgG activates antibody-dependent cellular cytotoxicity (ADCC) or antibody-dependent cellular phagocytosis (ADCP). ADCC is mediated by $CD16^+$ effector cells through the secretion of membrane pore-forming proteins and proteases, while phagocytosis is mediated by $CD32^+$ and $CD64^+$ effector cells (see, *e.g.*, *Fundamental Immunology*, 4^{th} ed., Paul ed., Lippincott-Raven, N.Y., 1997, Chapters 3, 17 and 30; Uchida *et al.*, 2004, *J. Exp. Med.* 199:1659-69; Akewanlop *et al.*, 2001, *Cancer Res.* 61:4061-65; Watanabe *et al.*, 1999, *Breast Cancer Res. Treat.* 53:199-207.

[0142] "Human effector cells" are leukocytes which express one or more FcRs and perform effector functions. In certain embodiments, the cells express at least FcγRIII and perform ADCC effector function(s). Examples of human leukocytes which mediate ADCC include peripheral blood mononuclear cells (PBMC), natural killer (NK) cells, monocytes, cytotoxic T cells, and neutrophils. The effector cells may be isolated from a native source, *e.g.*, from blood.

[0143] "Antibody-dependent cell-mediated cytotoxicity" or "ADCC" refers to a mechanism of cytotoxicity in which the Fc region of antibodies bound to antigen on the cell surface of target cells interact with Fc receptors (FcRs) present on certain cytotoxic effector cells (*e.g.* NK cells, neutrophils, and macrophages). This interaction enables these cytotoxic effector cells to subsequently kill the target cell with cytotoxins. The primary cells for mediating ADCC, NK cells, express FcγRIII only, whereas monocytes express FcγRI, FcγRII, and FcγRIII. FcR expression on hematopoietic cells is summarized in Table 3 on page 464 of Ravetch and Kinet, *Annu. Rev. Immunol* 9:457-92 (1991). To assess ADCC activity of a molecule of interest, an in vitro ADCC assay, such as that described in US Pat.

Nos. 5,500,362 or 5,821,337 or U.S. Pat. No. 6,737,056 (Presta), can be performed. Useful effector cells for such assays include PBMC and NK cells. ADCC activity of the molecule of interest can also be assessed in vivo, *e.g.*, in an animal model such as that disclosed in Clynes *et al. Proc. Natl. Acad. Sci. (USA)* 95:652-656 (1998). Additional polypeptide variants with altered Fc region amino acid sequences (polypeptides with a variant Fc region) and increased or decreased ADCC activity are described, *e.g.*, in U.S. Pat. No. 7,923,538, and U.S. Pat. No. 7,994,290.

[0144] "Complement dependent cytotoxicity" or "CDC" refers to the lysis of a target cell in the presence of complement. Activation of the classical complement pathway is initiated by the binding of the first component of the complement system (C1q) to the Fc region of antibodies (of the appropriate subclass), which are bound to their cognate antigen on a target cell. This binding activates a series of enzymatic reactions culminating in the formation of holes in the target cell membrane and subsequent cell death. Activation of complement may also result in deposition of complement components on the target cell surface that facilitate ADCC by binding complement receptors (e.g., CR3) on leukocytes. To assess complement activation, a CDC assay, *e.g.*, as described in Gazzano-Santoro *et al.*, *J. Immunol. Methods* 202:163 (1996), can be performed. Polypeptide variants with altered Fc region amino acid sequences (polypeptides such as an antibody with a variant Fc region) and increased or decreased C1q binding capability are described, *e.g.*, in U.S. Pat. No. 6,194,551 B1, U.S. Pat. No. 7,923,538, U.S. Pat. No. 7,994,290 and WO 1999/51642. See also, *e.g.*, Idusogie *et al.*, *J. Immunol.* 164: 4178-4184 (2000).

[0145] The term "antibody-dependent cellular phagocytosis", or simply "ADCP", refers to the process by which antibody-coated cells are internalized, either in whole or in part, by phagocytic immune cells (*e.g.*, macrophages, neutrophils and dendritic cells) that bind to an Fc region of Ig.

[0146] A polypeptide variant with "altered" FcR binding affinity or ADCC activity (*e.g.*, an antibody) is one which has either enhanced or diminished FcR binding activity and/or ADCC activity compared to a parent polypeptide or to a polypeptide comprising a native sequence Fc region. The polypeptide variant which "displays increased binding" to an FcR binds at least one FcR with better affinity than the parent polypeptide. The polypeptide variant which "displays decreased binding" to an FcR, binds at least one FcR with lower affinity than a parent polypeptide. In some embodiments, such variants which display

decreased binding to an FcR may possess little or no appreciable binding to an FcR, *e.g.*, 0-20% binding to the FcR compared to a native sequence IgG Fc region.

[0147] The term "substantially similar" or "substantially the same," as used herein, denotes a sufficiently high degree of similarity between two or more numeric values such that one of skill in the art would consider the difference between the two or more values to be of little or no biological and/or statistical significance within the context of the biological characteristic measured by said value. In some embodiments the two or more substantially similar values differ by no more than about any one of 5%, 10%, 15%, 20%, 25%, or 50%.

[0148] "Affinity" refers to the strength of the sum total of noncovalent interactions between a single binding site of a molecule (*e.g.*, an antibody) and its binding partner (*e.g.*, an antigen). The affinity of a molecule X for its partner Y can generally be represented by the dissociation constant (K_d). Affinity can be measured by common methods known in the art, including those described herein.

[0149] An "autoimmune disease" as used herein refers to a disease or disorder arising from and directed against an individual's own tissues or proteins.

[0150] "Patient" as used herein refers to a subject to whom is administered a Ligand-Drug Conjugate compound of the present invention. Patient includes, but are not limited to, a human, rat, mouse, guinea pig, non-human primate, pig, goat, cow, horse, dog, cat, bird and fowl. Typically, the patient is a rat, mouse, dog, human or non-human primate, more typically a human.

[0151] The terms "treat" or "treatment," unless otherwise indicated by context, refer to therapeutic treatment and prophylactic wherein the object is to inhibit or slow down (lessen) an undesired physiological change or disorder, such as the development or spread of cancer. For purposes of this invention, beneficial or desired clinical results include, but are not limited to, alleviation of symptoms, diminishment of extent of disease, stabilized (*i.e.,* not worsening) state of disease, delay or slowing of disease progression, amelioration or palliation of the disease state, and remission (whether partial or total), whether detectable or undetectable. "Treatment" can also mean prolonging survival as compared to expected survival if not receiving treatment. Those in need of treatment include those already with the condition or disorder as well as those prone to have the condition or disorder.

[0152] In the context of cancer, the term "treating" includes any or all of: killing tumor cells; inhibiting growth of tumor cells, cancer cells, or of a tumor; inhibiting replication of

tumor cells or cancer cells, lessening of overall tumor burden or decreasing the number of cancerous cells, and ameliorating one or more symptoms associated with the disease.

[0153] In the context of an autoimmune disease, the term "treating" includes any or all of: inhibiting replication of cells associated with an autoimmune disease state including, but not limited to, cells that produce an autoimmune antibody, lessening the autoimmune-antibody burden and ameliorating one or more symptoms of an autoimmune disease.

[0154] "Compound" as the term is used herein, refers to and encompasses the chemical compound itself, either named or represented by structure, and salt form(s) thereof, whether explicitly stated or not, unless context makes clear that such salt forms are to be excluded. The term "compound" further encompasses solvate forms of the compound, in which solvent is noncovalently associated with the compound or is reversibly associated covalently with the compound, as when a carbonyl group of the compound is hydrated to form a gem-diol. Solvate forms include those of the compound itself and its salt form(s) and are inclusive of hemisolvates, monosolvates, disolvates, including hydrates; when a compound is associated with two or more solvent molecules, the two or more solvent molecules are the same or different.

[0155] In some instances, a compound of the invention will include an explicit reference to one or more of the above forms, e.g., salts and solvates, which does not imply any solid state form of the compound; however, this reference is for emphasis only, and is not to be construed as excluding any other of the forms as identified above. Furthermore, when explicit reference to a salt and/or solvate form of a compound or a Ligand Drug Conjugate composition is not made, that omission is not to be construed as excluding the salt and/or solvate form(s) of the compound or Conjugate unless context make clear that such salt and/or solvate forms are to be excluded.

[0156] The phrase "salt thereof" as the phrase is used herein, refers to a salt form of a compound (e.g., a Drug, a Drug-Linker compound or a Ligand-Drug Conjugate compound). A salt form of a compound is of one or more internal salt forms and/or involves the inclusion of another molecule such as an acetate ion, a succinate ion or other counterion. The counterion in a salt form of a compound is typically an organic or inorganic moiety that stabilizes the charge on the parent compound. A salt form of a compound has one or more than one charged atom in its structure. In instances where multiple charged atoms are part of the salt form, multiple counter ions and/or multiple charged counter ions are present. Hence,

a salt form of a compound typically has one or more charged atoms corresponding to those of the non-salt form of the compound and one or more counterions. In some aspects, the non-salt form of a compound contains at least one amino group or other basic moeity, and accordingly in the presence of an acid, an acid addition salt with the basic moiety is obtained. In other aspects, the non-salt form of a compound contains at least one carboxylic acid group or other acidic moiety, and accordingly in the presence of a base, a carboxylate or other anionic moiety is obtained. Exemplary salts include, but are not limited to, sulfate, trifluoroacetate, citrate, acetate, oxalate, chloride, bromide, iodide, nitrate, bisulfate, phosphate, acid phosphate, isonicotinate, lactate, salicylate, acid citrate, tartrate, oleate, tannate, pantothenate, bitartrate, ascorbate, succinate, maleate, gentisinate, fumarate, gluconate, glucuronate, saccharate, formate, benzoate, glutamate, methanesulfonate, ethanesulfonate, benzenesulfonate, *p*-toluenesulfonate, and pamoate (*i.e.*, 1,1'-methylene-bis-(2-hydroxy-3-naphthoate)) salts.

[0157] A pharmaceutically acceptable salt is a salt form of a compound that is suitable for administration to a subject as described herein and in some aspects includes countercations or counteranions as described by P. H. Stahl and C. G. Wermuth, editors, Handbook of Pharmaceutical Salts: Properties, Selection and Use, Weinheim/Zürich:Wiley-VCH/VHCA, 2002.

[0158] A "Linker Unit" as used herein is a bifunctional moiety that connects or is capable of connecting a Drug Unit to a Ligand Unit in a Ligand-Drug Conjugate compound. The Linker Units of the present invention comprise two or more components selected from the group consisting of a Stretcher Unit which in some embodiments will have a Basic Unit; a Connector Unit; a Parallel Connector Unit; a Releasable Linker; and a Spacer Unit.

[0159] "PEG", "PEG Unit" or "polyethylene glycol" as used herein is an organic moiety comprising repeating ethylene-oxy subunits and is polydisperse, monodisperse, or discrete (i.e., having discrete number of ethylene-oxy subunits). Polydisperse PEGs are a heterogeneous mixture of sizes and molecular weights whereas monodisperse PEGs are typically purified from heterogeneous mixtures and are therefore provide a single chain length and molecular weight. Preferred PEG Units are discrete PEGs, compounds that are synthesized in stepwise fashion and not via a polymerization process. Discrete PEGs provide a single molecule with defined and specified chain length.

[0160] The PEG Unit provided herein comprises one or multiple polyethylene glycol chains, each comprising one or more ethyleneoxy subunits, covalently attached to each other. The polyethylene glycol chains are linked together in any pattern (*e.g.*, in a linear, branched, or star shaped configuration). Typically, at least one of the polyethylene glycol chains prior to incorporation into a Ligand-Drug Conjugate compound is derivitized at one end with an alkyl moiety substituted with an electrophilic group for covalent attachment to the carbamate nitrogen of a methylene carbamate unit (i.e., represents an instance of R). Typically, the terminal ethyleneoxy subunit in each polyethylene glycol chains not involved in covalent attachment to the remainder of the Linker Unit is modified with a PEG Capping Unit, typically H or an optionally substituted alkyl such as $–CH_3$, $-CH_2CH_3$ or $-CH_2CH_2CO_2H$. A preferred PEG Unit has a single polyethylene glycol chain with 4 to 24 $–CH_2CH_2O-$ subunits covalently attached in series and terminated at one end with a PEG Capping Unit.

[0161] "Halogen" as the term is used herein by itself or in combination with another term, unless otherwise stated or implied by context, refers to fluorine, chlorine, bromine or iodine and is typically -F or -Cl.

[0162] Unless otherwise indicated, the term "alkyl" by itself or as part of another term refers to a straight chain or branched, saturated hydrocarbon having the indicated number of carbon atoms (*e.g.*, "$-C_1$-C_4 alkyl," "$-C_1$-C_8 alkyl," or "$-C_1$-C_{10}" alkyl refer to an alkyl group having from 1 to 4, 1 to 8, or 1 to 10 carbon atoms, respectively). When the number of carbon atoms is not indicated, the alkyl group has from 1 to 8 carbon atoms. Representative straight chain "$-C_1$-C_8 alkyl" groups include, but are not limited to, -methyl, -ethyl, -n-propyl, -n-butyl, -n-pentyl, -n-hexyl, -n-heptyl and -n-octyl; while branched $–C_3$-C_8 alkyls include, but are not limited to, -isopropyl, -*sec*-butyl, -isobutyl, -*tert*-butyl, -isopentyl, and -2-methylbutyl.

[0163] Unless otherwise indicated, "alkylene," by itself of as part of another term, refers to a saturated, branched or straight chain or cyclic hydrocarbon radical of the stated number of carbon atoms, typically 1-4, 1-8, or 1-10 carbon atoms, and having two monovalent radical centers derived by the removal of two hydrogen atoms from the same or two different carbon atoms of a parent alkane. Typical alkylene radicals include, but are not limited to: methylene ($-CH_2-$), 1,2-ethylene ($-CH_2CH_2-$), 1,3-propylene ($-CH_2CH_2CH_2-$), 1,4-butylene ($-CH_2CH_2CH_2CH_2-$), and the like. In preferred aspects, an alkylene is a branched or straight chain hydrocarbon (i.e., it is not a cyclic hydrocarbon).

[0164] "Alkenyl" as the term is used herein, by itself or as part of another term, unless otherwise stated or implied by context, refers to an organic moiety, substituent or group that comprises one or more double bond functional groups (e.g., a -CH=CH- moiety) or 1, 2, 3, 4, 5 or 6 or more, typically 1, 2 or 3 of such functional groups, more typically one such functional group, and in some aspects may contain non-aromatic linked normal, secondary, tertiary or cyclic carbon atoms, i.e., linear, branched, cyclic or any combination thereof as part of the base moiety unless the alkenyl substituent, moiety or group is a vinyl moiety (e.g., a -CH=CH_2 moiety). An alkenyl moiety, group or substituent having multiple double bonds may have the double bonds arranged contiguously (i.e., a 1,3-butadienyl moiety) or non-contiguously with one or more intervening saturated carbon atoms or a combination thereof, provided that a cyclic, contiguous arrangement of double bonds do not form a cyclic conjugated system of 4n + 2 electrons (i.e., is not aromatic).

[0165] An alkenyl moiety, group or substituent contains at least one sp^2 carbon atom in which that carbon atom is divalent and is doubly bonded to another organic moiety or Markush structure to which it is associated, or contains at least two sp^2 carbon atoms in conjugation to each other in which one of the sp^2 carbon atoms is monovalent and is singly bonded to another organic moiety or Markush structure to which it is associated. Typically, when alkenyl is used as a Markush group (i.e., is a substituent) the alkenyl is singly bonded to a Markush formula or another organic moiety with which it is associated through a sp^2 carbon of an alkene functional group of the alkenyl moiety. In some aspects, when an alkenyl moiety is specified, species encompasses those corresponding to any of the optionally substituted alkyl or carbocyclyl, groups moieties or substituents described herein that has one or more *endo* double bonds in which a sp^2 carbon atom thereof is monovalent and monovalent moieties derived from removal of a hydrogen atom from a sp^2 carbon of a parent alkene compound. Such monovalent moieties are exemplified without limitation by vinyl (-CH=CH_2), allyl, 1-methylvinyl, butenyl, iso-butenyl, 3-methyl-2-butenyl, 1-pentenyl, cyclopentenyl, 1-methyl-cyclopentenyl, 1-hexenyl, 3-hexenyl, and cyclohexenyl. In some aspects, the term alkenyl encompasses those and/or other linear, cyclic and branched chained, all carbon-containing moieties containing at least one double bond functional group in which one of the sp^2 carbon atoms is monovalent.

[0166] The number of carbon atoms in an alkenyl moiety is defined by the number of sp^2 carbon atoms of the alkene functional group(s) that defines it as an alkenyl substituent and the total number of contiguous non-aromatic carbon atoms appended to each of these sp^2

carbons not including any carbon atom of the other moiety or Markush structure for which the alkenyl moiety is a variable group and carbon atoms from any optional substituent to the alkenyl moiety. That number ranges from 1 to 50 or 1 to 30, typically 1 to 20 or 1 to 12, more typically, 1 to 8, 1 to 6 or 1 to 4 carbon atoms when the double bond functional group is doubly bonded to a Markush structure (e.g. $=CH_2$), or ranges from 2 to 50, typically 2 to 30, 2 to 20 or 2 to 12, more typically 2 to 8, 2 to 6 or 2 to 4 carbon atoms, when the double bond functional group is singly bonded to the Markush structure (e.g., $-CH=CH_2$). For example, C_2-C_8 alkenyl or C2-C8 alkenyl means an alkenyl moiety containing 2, 3, 4, 5, 6, 7 or 8 carbon atoms in which at least two are sp^2 carbon atoms in conjugation with each other with one of these carbon atoms being monovalent, and C_2-C_6 alkenyl or C2-C6 alkenyl means an alkenyl moiety containing 2, 3, 4, 5 or 6 carbon atoms in which at least two are sp^2 carbons that are in conjugation with each other with one of these carbon atoms being monovalent. In some aspects, an alkenyl substituent or group is a C_2-C_6 or C_2-C_4 alkenyl moiety having only two sp^2 carbons that are in conjugation with each other with one of these carbon atoms being monovalent. Typically, an alkenyl substituent is a C_2-C_6 or C_2-C_4 alkenyl moiety having only two sp^2 carbons that are in conjugation with each other. When the number of carbon atoms is not indicated, an alkenyl moiety has from 2 to 8 carbon atoms.

[0167] "Alkenylene" as the term is used herein, by itself of as part of another term, unless otherwise stated or implied by context, refers to an organic moiety, substituent or group that comprises one or more double bond moieties, as previously described for alkenyl, of the stated number of carbon atoms and has two radical centers derived by the removal of two hydrogen atoms from the same or two different sp^2 carbon atoms of an alkene functional group or removal of two hydrogen atoms from two separate alkene functional groups in a parent alkene. In some aspects, an alkenylene moiety is that of an alkenyl radical as described herein in which a hydrogen atom has been removed from the same or different sp^2 carbon atom of a double bond functional group of the alkenyl radical, or from a sp^2 carbon from a different double bonded moiety to provide a diradical. Typically, alkenylene moieties encompass diradicals containing the structure of –C=C- or –C=C-X^1-C=C- wherein X^1 is absent or is an alkylene as defined herein, which is typically a C_1-C_6 alkylene. The number of carbon atoms in an alkenylene moiety is defined by the number of sp^2 carbon atoms of its alkene functional group(s) that defines it as an alkenylene moiety and the total number of contiguous non-aromatic carbon atoms appended to each of its sp^2 carbons not including any carbon atoms of the other moiety or Markush structure in which the alkenyl moiety is a

present as a variable group. That number, unless otherwise specified, ranges from 2 to 50 or 2 to 30, typically from 2 to 20 or 2 to 12, more typically from 2 to 8, 2 to 6 or 2 to 4 carbon atoms. For example, C_2-C_8 alkenylene or C2-C8 alkenylene means an alkenylene moiety containing 2, 3, 4, 5, 6, 7 or 8 carbon atoms, in which at least two are sp^2 carbons in which one is divalent or both are monovalent, that are in conjugation with each other and C_2-C_6 alkenylene or C2-C6 alkenylene means an alkenyl moiety containing 2, 3, 4, 5 or 6 carbon atoms in which at least two are sp^2 carbons, in which at least two are sp^2 carbons in which one is divalent or both are monovalent, that are in conjugation with each other. In some aspects, an alkenylene moiety is a C_2-C_6 or C_2-C_4 alkenylene having two sp^2 carbons that are in conjugation with each other in which both sp^2 carbon atoms are monovalent. When the number of carbon atoms is not indicated, an alkenylene moiety has from 2 to 8 carbon atoms.

[0168] "Alkynyl" as the term is used herein, by itself or as part of another term, unless otherwise stated or implied by context, refers to an organic moiety, substituent or group that comprises one or more triple bond functional groups (e.g., a -C≡C- moiety) or 1, 2, 3, 4, 5, or 6 or more, typically 1, 2, or 3 of such functional groups, more typically one such functional group. An alkynyl moiety, group or substituent having multiple triple bonds may have the triple bonds arranged contiguously or non-contiguously with one or more intervening saturated or unsaturated carbon atoms or a combination thereof, provided that a cyclic, contiguous arrangement of triple bonds do not form a cyclic conjugated system of 4n + 2 electrons (i.e., is not aromatic).

[0169] An alkynyl moiety, group or substituent contains at least two sp carbon atom in which the carbon atoms are conjugation to each other and in which one of the sp carbon atoms is singly bonded, to another organic moiety or Markush structure to which it is associated. When alkynyl is used as a Markush group (i.e., is a substituent) the alkynyl is singly bonded to a Markush formula or another organic moiety with which it is associated through a triple-bonded carbon (i.e., a sp carbon) of a terminal alkyne functional group. In some aspects when an alkynyl moiety, group or substituent is specified, species encompasses are any of the alkyl or carbocyclyl, groups moieties or substituents described herein that has one or more *endo* triple bonds and monovalent moieties derived from removal of a hydrogen atom from a sp carbon of a parent alkyne compound. Such monovalent moieties are exemplified without limitation by -C≡CH, and -C≡C-CH_3, and -C≡C-Ph.

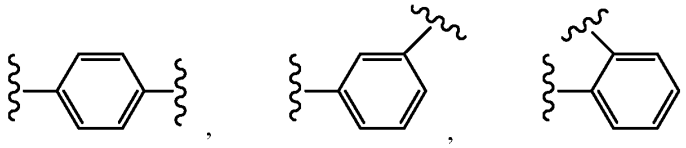
[0170] The number of carbon atoms in an alkynyl substituent is defined by the number of sp carbon atoms of the alkene functional group that defines it as an alkynyl substituent and

the total number of contiguous non-aromatic carbon atoms appended to each of these sp carbons not including any carbon atom of the other moiety or Markush structure for which the alkenyl moiety is a variable group. That number can vary ranging from 2 to 50, typically 2 to 30, 2 to 20, or 2 to 12, more typically 2 to 8, 2 to 6, or 2 to 4 carbon atoms, when the triple bond functional group is singly bonded to the Markush structure (e.g., -CH≡CH). For example, C_2-C_8 alkynyl or C2-C8 alkynyl means an alkynyl moiety containing 2, 3, 4, 5, 6, 7, or 8 carbon atoms in which at least two are sp carbon atoms in conjugation with each other with one of these carbon atoms being monovalent, and C_2-C_6 alkynyl or C2-C6 alkynyl means an alkynyl moiety containing 2, 3, 4, 5, or 6 carbon atoms in which at least two are sp carbons that are in conjugation with each other with one of these carbon atoms being monovalent. In some aspects, an alkynyl substituent or group is a C_2-C_6 or C_2-C_4 alkynyl moiety having two sp carbons that are in conjugation with each other with one of these carbon atoms being monovalent. When the number of carbon atoms is not indicated, an alkynyl moiety, group or substituent has from 2 to 8 carbon atoms.

[0171] The term “Prodrug” as used herein refers to a less biologically active or inactive compound which is transformed within the body into a more biologically active compound via a chemical or biological process (i.e., a chemical reaction or an enzymatic biotransformation). Typically, a biologically active compound is rendered less biologically active (i.e., is converted to a prodrug) by chemically modifying the compound with a prodrug moiety. In some aspects, the prodrug is a Type II prodrug, which are bioactivated outside cells, e.g., in digestive fluids, or in the body's circulation system, e.g., in blood. Exemplary prodrugs are esters and β-D-glucopyranosides.

[0172] Unless otherwise indicated, "aryl," by itself or as part of another term, means amonovalent carbocyclic aromatic hydrocarbon radical of the stated number of carbon atoms, typically 6-20 carbon atoms, derived by the removal of one hydrogen atom from a single carbon atom of a parent aromatic ring system. Some aryl groups are represented in the exemplary structures as “Ar”. Typical aryl groups include, but are not limited to, radicals derived from benzene, naphthalene, anthracene, biphenyl, and the like. An exemplary aryl group is a phenyl group.

[0173] Unless otherwise indicated, an “arylene,” by itself or as part of another term, is an aryl group as defined above which has two covalent bonds (i.e., it is divalent) and is in the ortho, meta, or para orientations as shown in the following structures, with phenyl as the exemplary group:



[0174] Unless otherwise indicated, a "C_3-C_8 heterocycle," by itself or as part of another term, refers to a monovalentaromatic or non-aromatic monocyclic or bicyclic ring system having from 3 to 8 carbon atoms (also referred to as ring members) and one to four heteroatom ring members independently selected from N, O, P or S, and derived by removal of one hydrogen atom from a ring atom of a parent ring system. In some aspects, one or more N, C or S atoms in the heterocycle is/are oxidized. In some aspects, the ring that includes the heteroatom is aromatic or nonaromatic. Heterocycles in which all the ring atoms are involved in aromaticity are referred to as heteroaryls and otherwise are referred to heterocarbocycles.

[0175] Unless otherwise noted, the heterocycle is attached to its pendant group at any heteroatom or carbon atom that results in a stable structure. In some aspects, a heteroaryl is bonded through an aromatic carbon of its aromatic ring system, referred to as a C-linked heteroaryl. In other aspects, a heteroaryl is bonded through a non-double-bonded N atom (i.e., not =N-) in its aromatic ring system, which is referred to as an N-linked heteroaryl. Thus, nitrogen-containing heterocycles are C-linked or N-linked and include pyrrole moieties, such as pyrrol-1-yl (N-linked) and pyrrol-3-yl (C-linked), and imidazole moieties such as imidazol-1-yl and imidazol-3-yl (both N-linked), and imidazol-2-yl, imidazol-4-yl and imidazol-5-yl moieties (all of which are C-linked).

[0176] Unless otherwise indicated, a"C_3-C_8 heteroaryl," is an aromatic C_3-C_8 heterocycle in which the subscript denotes the total number of carbons of the cyclic ring system of the heterocycle or the total number of aromatic carbons of the aromatic ring system of the heteroaryl and does not implicate the size of the ring system or the presence or absence of ring fusion. Representative examples of a C_3-C_8 heterocycle include, but are not limited to, pyrrolidinyl, azetidinyl, piperidinyl, morpholinyl, tetrahydrofuranyl, tetrahydropyranyl, benzofuranyl, benzothiophene, indolyl, benzopyrazolyl, pyrrolyl, thiophenyl (thiophene), furanyl, thiazolyl, imidazolyl, pyrazolyl, pyrimidinyl, pyridinyl, pyrazinyl, pyridazinyl, isothiazolyl, and isoxazolyl.

[0177] When explicitly given, the size of the ring system of a heterocycle or heteroaryl is indicated by the total number of atoms in the ring. For example, designation as a 5- or 6-

membered heteroaryl indicates the total number of aromatic atoms (i.e., 5 or 6) in the heteroaromatic ring system of the heteroaryl but does not imply the number of aromatic heteroatoms or the number of aromatic carbon atoms in that ring system. Fused heteroaryls are explicitly stated or implied by context as such and are typically indicated by the number of aromatic atoms in each aromatic ring that are fused together to make up the fused heteroaromatic ring system. For example, a 5,6-membered heteroaryl is an aromatic 5-membered ring fused to an aromatic 6-membered ring in which one or both rings have aromatic heteroatom(s) or where a heteroatom is shared between the two rings.

[0178] A heterocycle fused to an aryl or heteroaryl such that the heterocycle remains non-aromatic and is part of a larger structure through attachment with the non-aromatic portion of the fused ring system is an example of a heterocycle in which the heterocycle is substituted by ring fusion with the aryl or heteroaryl. Likewise, an aryl or heteroaryl fused to heterocycle or carbocycle that is part of a larger structure through attachment with the aromatic portion of the fused ring system is an example of an aryl or heterocycle in which the aryl or heterocycle is substituted by ring fusion with the heterocycle or carbocycle.

[0179] Unless otherwise indicated, "C_3-C_8 heterocyclo," by itself or as part of another term, refers to a C_3-C_8 heterocyclic defined above wherein one of the hydrogen atoms of the heterocycle is replaced with a bond (i.e., it is divalent). Unless otherwise indicated, a "C_3-C_8 heteroarylene," by itself or as part of another term, refers to a C_3-C_8 heteroaryl group defined above wherein one of the heteroaryl group's hydrogen atoms is replaced with a bond (i.e., it is divalent). When explicitly given, the size of the ring system of a heteroarylene is indicated by the total number of atoms in the ring. For example, designation as a 5- or 6-membered heteroarylene indicates the total number of atoms (i.e., 5 or 6) in the heterocyclic ring system of the heterocycle, but does not imply the number of heteroatoms or the number of carbon atoms in that ring system.

[0180] Unless otherwise indicated, a "C_3-C_8 carbocycle," by itself or as part of another term, is a 3-, 4-, 5-, 6-, 7- or 8-membered monovalent,saturated or unsaturated non-aromatic monocyclic or bicyclic carbocyclic ring derived by the removal of one hydrogen atom from a ring atom of a parent ring system. Representative -C_3-C_8 carbocycles include, but are not limited to, cyclopropyl, cyclobutyl, cyclopentyl, cyclopentadienyl, cyclohexyl, cyclohexenyl, 1,3-cyclohexadienyl, 1,4-cyclohexadienyl, cycloheptyl, 1,3-cycloheptadienyl, 1,3,5-cycloheptatrienyl, cyclooctyl, and cyclooctadienyl.

[0181] Unless otherwise indicated, a "C_3-C_8 carbocyclo," by itself or as part of another term, refers to a C_3-C_8 carbocycle group defined above wherein another one of the carbocycle group's hydrogen atoms is replaced with a bond (i.e., it is divalent).

[0182] Unless otherwise indicated, the term "heteroalkyl," by itself or in combination with another term, means, unless otherwise stated, a stable straight or branched chain hydrocarbon, or combinations thereof, fully saturated or containing from 1 to 3 degrees of unsaturation, consisting of the stated number of carbon atoms and from one to ten, preferably one to three, heteroatoms selected from the group consisting of O, N, Si and S, and wherein the nitrogen and sulfur atoms are optionally oxidized and the nitrogen heteroatom is optionally quaternized. The heteroatom(s) O, N and S are placed at any interior position of the heteroalkyl group or at the position at which the alkyl group is attached to the remainder of the molecule. The heteroatom Si is placed at any position of the heteroalkyl group, including the position at which the alkyl group is attached to the remainder of the molecule. When explicitly given, the number of atoms in a heteroalkyl or heteroarylene is indicated by the total number of atoms in the group. For example, designation as a C_1-C_2 heteroalkyl indicates the total number of atoms (i.e., 1 or 2) in the heteroalkyl group, but does not imply the number of heteroatoms or the number of carbon atoms in that group.

[0183] Examples include $–CH_2$-CH_2-O-CH_3, -CH_2-CH_2-NH-CH_3, -CH_2-CH_2-N(CH_3)-CH_3, -CH_2-S-CH_2-CH_3, -CH_2-CH_2-S(O)-CH_3, -NH-CH_2-CH_2-NH-C(O)-CH_2-CH_3, -CH_2-CH_2-S(O)$_2$-CH_3, -CH=CH-O-CH_3, -Si(CH_3)$_3$, -CH_2-CH=N-O-CH_3, and –CH=CH-N(CH_3)-CH_3. In some aspects, two heteroatoms are consecutive, such as, for example, -CH_2-NH-OCH_3 and –CH_2-O-Si(CH_3)$_3$. Typically, a C_1 to C_4 heteroalkyl or heteroalkylene has 1 to 4 carbon atoms and 1 or 2 heteroatoms and a C_1 to C_3 heteroalkyl or heteroalkylene has 1 to 3 carbon atoms and 1 or 2 heteroatoms. In some aspects, a heteroalkyl or heteroalkylene is saturated.

[0184] Unless otherwise indicated, the term "heteroalkylene" by itself or in combination with another term means a divalent group derived from heteroalkyl (as discussed above), as exemplified by –CH_2-CH_2-S-CH_2-CH_2- and –CH_2-S-CH_2-CH_2-NH-CH_2-. For heteroalkylene groups, heteroatoms can also occupy either or both of the chain termini. Still further, for alkylene and heteroalkylene linking groups, no orientation of the linking group is implied.

[0185] Unless otherwise indicated, "aminoalkyl" by itself or in combination with another term means a heteroalkyl wherein an alkyl moiety as defined herein is substituted with an

amino, alkylamino, dialkylamino or cycloalkylamino group. Exemplary non-limiting aminoalkyls are $–CH_2NH_2$, $-CH_2CH_2NH_2$, $-CH_2CH_2NHCH_3$ and $-CH_2CH_2N(CH_3)_2$ and further includes branched species such as $–CH(CH_3)NH_2$ and $-C(CH_3)CH_2NH_2$ in the (R)- or (S)- configuration. Alternatively, an aminoalkyl is an alkyl moiety, group, or substituent as defined herein wherein a sp^3 carbon other than the radical carbon atom of the alkyl moiety has been replaced with an amino or alkylamino moiety wherein its sp^3 nitrogen atom replaces the sp^3 carbon of the alkyl moiety provided that at least one sp^3 carbon atom of the alkyl moiety remains. When referring to an aminoalkyl moiety as a substituent to a larger structure or another moiety the aminoalkyl is covalently attached to the structure or moiety through the carbon radical of the alkyl moiety of the aminoalkyl.

[0186] "Hydroxyalkyl" as the term is used herein by itself or in combination with another term, unless otherwise stated or implied by context, refers to an alkyl moiety, group, or substituent having a hydroxyl radical in place of one or more hydrogen atoms of the alkyl moiety, group, or substituent. In some aspects, one or two hydrogen atoms are each replaced with a hydroxyl substituent in a hydroxyalkyl group. A hydroxyalkyl is typically denoted by the number of contiguous carbon atoms of its alkyl or alkylene moiety. Thus, a C_1 hydroxyalkyl is exemplified without limitation by $–CH_2OH$, and a C_2 hydroxyalkyl is exemplified without limitation by $–CH_2CH_2OH$ or $–CH_2(OH)CH_3$.

[0187] "Haloalkyl" as the term is used herein by itself or in combination with another term, unless otherwise stated or implied by context, referes to an alkyl moiety, group, or substituent having a halogen in place of one or more hydrogen atoms of the alkyl moiety, group, or substituent. In some aspects, one or two hydrogen atoms are each replaced with a halogen in a haloalkyl group. A haloalkyl is typically denoted by the number of contiguous carbon atoms of its alkyl or alkylene moiety. Thus, a C_1 haloalkyl is exemplified without limitation by $–CH_2F$, $–CH_2Cl$, $–CH_2Br$, or $–CH_2I$, and a C_2 haloalkyl is exemplified without limitation by $–CH_2CH_2F$, $–CH_2CH_2Cl$, $–CH_2CH_2Br$, $–CH_2CH_2I$, $–CH_2(F)CH_3$, $–CH_2(Cl)CH_3$, $–CH_2(Br)CH_3$, or $–CH_2(I)CH_3$. In some embodiments, the term "haloalkyl" refers to an alkyl moiety, group, or substituent having halogens in place of two or more hydrogen atoms. For example, a C_1 haloalkyl is also exemplified without limitation by $–CHF_2$, $–CHCl_2$, $–CHBr_2$, or $–CHI_2$, and a C_2 haloalkyl is exemplified without limitation by $–CH_2CHF_2$, $–CH_2CHCl_2$, $–CH_2CHBr_2$, $–CH_2CHI_2$, $–CH(F)_2CH_3$, $–CH(Cl)_2CH_3$, $–CH(Br)_2CH_3$, or $–CH(I)_2CH_3$. In some aspects, the term "haloalkyl" refers to an alkyl moiety, group, or substituent having halogens in place of all hydrogen atoms. Thus, in some aspects, the term "haloalkyl" encompasses

fully halogenated alkyl moieties, groups, or substituents. For example, a C_1 haloalkyl is also exemplified without limitation by $–CF_3$, $–CCl_3$, $–CBr_3$, or $–CI_3$.

[0188] Unless otherwise indicated "alkylamino" and "cycloalkylamino" by itself or in combination with another term means an alkyl or cycloalkyl radical, as described herein, wherein the radical carbon atom of the alkyl or cycloalkyl radical has been replaced with a nitrogen radical, provided that at least one sp^3 carbon atom of the alkyl or cycloalkyl radical remains. In those instances where the alkylamino is substituted at its nitrogen with another alkyl moiety the resulting substituted radical is sometimes referred to as a dialkylamino moiety, group or substituent wherein the alkyl moieties substituting nitrogen are independently selected.

[0189] Exemplary and non-limiting amino, alkylamino and dialkylamino substituents, include those having the structure of $–N(R')_2$, wherein R' in these examples are independently hydrogen or C_{1-6} alkyl, typically hydrogen or methyl, whereas in cycloalkyl amines, which are included in heterocycloalkyls, both R' together with the nitrogen to which they are attached define a heterocyclic ring. When both R' are hydrogen or alkyl, the moiety is sometimes described as a primary amino group and a tertiary amine group, respectively. When one R' is hydrogen and the other is alkyl, then the moiety is sometimes described as a secondary amino group. Primary and secondary alkylamino moieties are typically more reactive as nucleophiles towards carbonyl-containing electrophilic centers whereas tertiary amines are typically more basic.

[0190] The term "substituted" means that the specified group or moiety bears one or more substituents. Typical substituents include, but are not limited to a -X, -R", -OH, -OR", -SR", , $-N(R")_2$, $-N(R")_3$, =NR", $-CX_3$, -CN, $-NO_2$, -NR"C(=O)R", -C(=O)R", $-C(=O)N(R")_2$, $-S(=O)_2R"$, $-S(=O)_2NR"$, -S(=O)R", $-OP(=O)(OR")_2$, $-P(=O)(OR")_2$, $-PO_3^=$, PO_3H_2, -C(=O)R", -C(=S)R", $-CO_2R"$, $-CO_2^-$, -C(=S)OR", -C(=O)SR", -C(=S)SR", $-C(=O)N(R")_2$, $-C(=S)N(R")_2$, and $-C(=NR)N(R")_2$, where each X is independently selected from the group consisting of a halogen: -F, -Cl, -Br, and -I; and wherein each R" is independently selected from the group consisting of -H, $-C_1$-C_{20} alkyl, $-C_6$-C_{20} aryl, $-C_3$-C_{14} heterocycle, a protecting group, and a prodrug moiety.

[0191] More typically substituents are selected from the group consisting of -X, -R", -OH, -OR", -SR", $-N(R")_2$, $-N(R")_3$, =NR", -NR"C(=O)R", -C(=O)R", $-C(=O)N(R")_2$, $-S(=O)_2R"$, $-S(=O)_2NR"$, -S(=O)R", -C(=O)R", -C(=S)R", $-C(=O)N(R")_2$, -

$C(=S)N(R")_2$, and $-C(=NR)N(R")_2$, wherein each X is independently selected from the group consisting of –F and -Cl, or are selected from the group consisting of -X, -R", -OH, -OR", $-N(R")_2$, $-N(R")_3$, -NR"C(=O)R", $-C(=O)N(R")_2$, $-S(=O)_2R"$, $-S(=O)_2NR"$, -S(=O)R", -C(=O)R", $-C(=O)N(R")_2$, $-C(=NR)N(R")_2$, a protecting group, and a prodrug moiety, wherein each X is –F; and wherein each R' is independently selected from the group consisting of hydrogen, $-C_1$-C_{20} alkyl, $-C_6$-C_{20} aryl, $-C_3$-C_{14} heterocycle, a protecting group, and a prodrug moiety.

[0192] In some aspects, a substituent on an alkyl, alkenyl, or alkynyl is selected from the group consisting $-N(R")_2$, $-N(R")_3$ and $-C(=NR)N(R")_2$, wherein R" is selected from the group consisting of hydrogen and $-C_1$-C_{20} alkyl. In other aspects, alkyl, alkenyl, or alkynyl is substituted with a series of ethyleneoxy moieties to define a PEG Unit as described herein. In some embodiments, alkylene, carbocycle, carbocyclo, arylene, heteroalkyl, heteroalkylene, heterocycle, heterocyclo, heteroaryl, and heteroarylene groups as described above are similarly substituted.

[0193] The term "unsubstituted" means that the specified group bears no substituents. Where the term "substituted is used to described a structural system, the substitution is meant to occur at any valency-allowed position on the system. When a group or moiety bears more than one substituent, it is understood that the substituents may be the same or different from one another. In some embodiments a substituted group or moiety bears from one to five substituents. In some embodiments a substituted group or moiety bears one substituent. In some embodiments a substituted group or moiety bears two substituents. In some embodiments a substituted group or moiety bears three substituents. In some embodiments a substituted group or moiety bears four substituents. In some embodiments a substituted group or moiety bears five substituents.

[0194] By "optional" or "optionally" is meant that the subsequently described event or circumstance may or may not occur, and that the description includes instances where the event or circumstance occurs and instances in which it does not. For example, "optionally substituted alkyl" encompasses both "alkyl" and "substituted alkyl" as defined herein. It will be understood by those skilled in the art, with respect to any group containing one or more substituents, that such groups are not intended to introduce any substitution or substitution patterns that are sterically impractical, synthetically non-feasible, and/or inherently unstable. It will also be understood that where a group or moiety is optionally substituted, the

disclosure includes both embodiments in which the group or moiety is substituted and embodiments in which the group or moiety is unsubstituted.

[0195] "Protecting group" as used here means a moiety that prevents or reduces the ability of the atom or functional group to which it is linked from participating in unwanted reactions. Typical protecting groups for atoms or functional groups are given in Greene (1999), "PROTECTIVE GROUPS IN ORGANIC SYNTHESIS, 3RD ED.", Wiley Interscience, which is incorporated by reference herein. Protecting groups for heteroatoms such as oxygen, sulfur and nitrogen are used in some instances to minimize or avoid unwanted their reactions with electrophilic compounds. In other instances, the protecting group is used to reduce or eliminate the nucleophilicity and/or basicity of the unprotected heteroatom. Non-limiting examples of protected oxygen are given by $-OR^{PR}$, wherein R^{PR} is a protecting group for hydroxyl, wherein hydroxyl is typically protected as an ester (e.g. acetate, propionate or benzoate). Other protecting groups for hydroxyl avoid interfering with the nucleophilicity of organometallic reagents or other highly basic reagents, where hydroxyl is typically protected as an ether, including alkyl or heterocycloalkyl ethers, (e.g., methyl or tetrahydropyranyl ethers), alkoxymethyl ethers (e.g., methoxymethyl or ethoxymethyl ethers), optionally substituted aryl ethers, and silyl ethers (e.g., trimethylsilyl (TMS), triethylsilyl (TES), tert-butyldiphenylsilyl (TBDPS), tert-butyldimethylsilyl (TBS/TBDMS), triisopropylsilyl (TIPS) and [2-(trimethylsilyl)ethoxy]-methylsilyl (SEM)). Nitrogen protecting groups include those for primary or secondary amines as in $-NHR^{PR}$ or $-N(R^{PR})_2-$, wherein least one of R^{PR} is a nitrogen atom protecting group or both R^{PR} together comprise a protecting group.

[0196] A protecting group is suitable when it is capable of preventing or avoiding unwanted side-reactions or premature loss of the protecting group under reaction conditions required to effect desired chemical transformation elsewhere in the molecule and during purification of the newly formed molecule when desired, and are removable under conditions that do not adversely affect the structure or stereochemical integrity of that newly formed molecule. By way of example and not limitation, a suitable protecting group includes those previously described for protecting otherwise reactive functional groups. A suitable protecting group is sometimes a protecting group used in peptide coupling reactions.

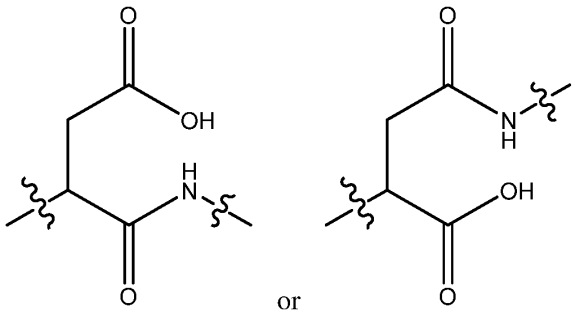
[0197] "Electron withdrawing group" as used herein means a functional group or electronegative atom that draws electron density away from an atom to which it is bonded either inductively and/or through resonance, whichever is more dominant (i.e., in some aspects, a functional group or atom is electron withdrawing inductively but is overall electron

donating through resonance) and tends to stabilize anions or electron-rich moieties. The electron withdrawing effect is typically transmitted inductively, albeit in attenuated form, to other atoms attached to the bonded atom that has been made electron deficient by the electron withdrawing group (EWG), thus affecting the electrophilicity of a more remote reactive center. Exemplary electron withdrawing groups include, but are not limited to -C(=O), -CN, $-NO_2$, $-CX_3$, -X, $-C(=O)OR'$, $-C(=O)N(R')_2$, $-C(=O)R'$, -C(=O)X, $-S(=O)_2R'$, $-S(=O)_2OR'$, $-S(=O)_2NHR'$, $-S(=O)_2N(R')_2$, $-P(=O)(OR')_2$, $-P(=O)(CH_3)NHR'$, -NO, $-N(R')_3^+$, wherein X is -F, -Br, -Cl, or -I, and R' in some aspects is, at each occurrence, independently selected from the group consisting of hydrogen and C_{1-6} alkyl, and certain O-linked moieties as described herein such as acyloxy.

[0198] Exemplary EWGs can also include aryl groups (e.g., phenyl) depending on substitution of its aromatic ring and certain heteroaryl groups (e.g., pyridine). Thus, the term "electron withdrawing groups" also includes aryls or heteroaryls that are further substituted with electron withdrawing groups. Typically, electron withdrawing groups on aryls or heteroaryls are -C(=O), -CN, $-NO_2$, $-CX_3$, and –X, wherein X independently selected is halogen, typically –F or -Cl. Depending on their substituents, an alkyl moiety may also be an electron withdrawing group.

[0199] "Succinimide moiety" as used herein refers to an organic moiety comprising a succinimide ring system, which is present in one type of Stretcher Unit (Z) that typically further comprises an alkylene-containing moiety bonded to the imide nitrogen of that ring system. A succinimide moiety typically results from Michael addition of a sulfhydryl group of a Ligand Unit to the maleimide ring system of a Stretcher Unit precursor (Z') in a Drug Linker compound or maleimide-containing intermediate thereof. A succinimide moiety therefore comprises a thio-substituted succinimide ring system and when present in a Ligand-Drug Conjugate compound has its imide nitrogen substituted with the remainder of the Linker Unit of the Ligand-Drug Conjugate compound and is optionally substituted with substituent(s) that were present on the maleimide ring system of Z'.

[0200] "Succinic acid-amide moiety" as used herein refers to a succinic acid moiety wherein one of the two carboxylic acid groups is replaced with an amide substituent that results from the thio-substituted succinimide ring system of a succinimide moiety as defined herein having undergone breakage of one of its carbonyl-nitrogen bonds by hydrolysis. In some aspects, the succinic acid-amide moiety has the structure:



or

wherein the wavy line on the left indicates attachment to a Ligand Unit or hydrogen atom and the wavy line on the right indicates attachment to the remainder of a Ligand-Drug Conjugate compound, Drug-Linker compound, intermediate, or fragment thereof. Hydrolysis resulting in a succinic acid-amide moiety provides a Linker Unit less likely to suffer premature loss of the Ligand Unit to which it is bonded through elimination of the antibody-thio substituent. Hydrolysis of the succinimide ring system of the thio-substituted succinimide moiety is expected to provide regiochemical isomers of acid-amide moieties that are due to differences in reactivity of the two carbonyl carbons of the succinimide ring system attributable at least in part to any substituent present in the maleimide ring system of the Stretcher Unit precursor and to the thio substituent introduced by the targeting ligand, which is a precursor to the Ligand Unit.

[0201] In many instances, the assembly of the conjugates, linkers and components described herein will refer to reactive groups. A "reactive group" or RG is a group that contains a reactive site (RS) capable of forming a bond with either the components of the Linker Unit Q or the Drug Unit D. RS is the reactive site within a Reactive Group (RG). Reactive groups include sulfhydryl groups to form disulfide bonds or thioether bonds, aldehyde, ketone, or hydrazine groups to form hydrazone bonds, carboxylic or amino groups to form peptide bonds, carboxylic or hydroxy groups to form ester bonds, sulfonic acids to form sulfonamide bonds, alcohols to form carbamate bonds, and amines to form sulfonamide bonds or carbamate bonds.

[0202] The following table is illustrative of Reactive Groups, Reactive Sites, and exemplary functional groups capable of forming after reaction of the reactive site. The table is not limiting. One of skill in the art will appreciate that the noted R^* and R^{**} portions in the table are effectively any organic moiety (e.g., an alkyl group, aryl group, heteroaryl group, or substituted alkyl, aryl, or heteroaryl, group) that is compatible with the bond formation provided in converting RG to one of the Exemplary Functional Groups. It will also be

appreciated that, as applied to the various aspects of the present invention, R^* represents one or more components of the self-stabilizing linker or optional secondary linker, and R^{**} represents one or more components of the optional secondary linker, Drug Unit, stabilizing unit, or detection unit.

RG	RS	Exemplary Functional Groups
1) R^*-SH	-S-	R^*-S-R^{**}, R^*-S-S-R^{**}
2) R^*-C(=O)OH	-C(=O)-	R^*-C(=O)NH-R^{**}
3) R^*-C(=O)ONHS	-C(=O)-	R^*-C(=O)NH-R^{**}
4) $R^*S(=O)_2$-OH	-$S(=O)_2$-	$R^*S(=O)_2NH$-R^{**}
5) R^*-CH_2-X (X is Br, I, Cl)	-CH_2-	R^*-CH_2-S-R^{**}
6) R^*-NH_2	-N-	R^*-NHC(=O)R^{**}

II. Embodiments

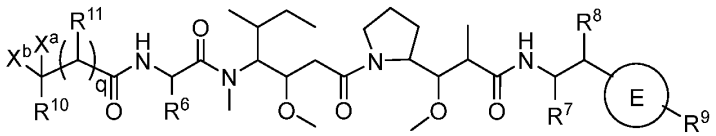
Auristatin Compounds

[0203] The present application is based, in part, on the surprising discovery that it is possible to improve the properties of auristatin-containing Ligand-Drug Conjugate compounds by tuning the hydrophilicity of auristatin drugs with polar moieities, *e.g.*, hydroxyl groups. The hydrophobicity of auristatin drugs is a known barrier to their implementation in pharmaceuticals, including Ligand-Drug Conjugates, due to the potential for off-target toxicity due to high bystander activity and rapid clearance of the drug from the body of subjects. The compounds of the present application attenuate the hydphobicity of the Drug Unit, which in turn attentuates the off-target toxicity and rapid clearance of the drugs. The use of Drug Units with polar moieities in certain locations on the auristatin backbone leads to decreased permeability and on-cell potency of the free drug, and thus fewer off-target effects during treatment, without sacrificing efficacy of intact Ligand-Drug Conjugate compounds that incorporate the Drug Units.

[0204] In some embodiments herein, provided are auristatin compounds comprising at least one polar moiety on the auristatin backbone. In some embodiments, provided herein are Drug-Linker compounds comprising an auristatin moiety, as described herein. In some embodiments, provided herein are Ligand-Drug Conjugate compounds comprising an auristatin moiety, as described herein. In some embodiments, provided herein are methods of treating cancer using the Ligand-Drug Conjugate compounds described herein. In some embodiments, provided are methods of making auristatin compounds comprising at least one

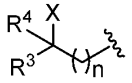
hydrophilic moiety, Drug-Linkers thereof and their intermediates, and Ligand-Drug Conjugate compounds thereof. In some embodiments, the polar moiety is a polar moiety other than carboxylate. In some embodiments, the polar moiety is a hydroxyl group.

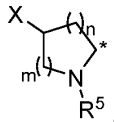
[0205] In some embodiments, provided is a compound of formula (I):



(I)

or a salt thereof, wherein

X^b is $-NR^1R^2$; and X^a is  ; or

X^a and X^b are taken together with the carbon atom to which they are attached to form  , wherein the asterisk denotes the carbon atom of Formula (I) that bears the X^a and X^b groups;

R^1, R^2, R^3, R^4, R^a, R^b, R^5, and R^{10} are each independently H or C_1-C_4 alkyl;

X is H, OH, $-C(O)NR^aR^b$, $-S(O)_2R^a$, $-S(O)-R^a$ $-S(O)_2NR^aR^b$, $-NHS(O)_2R^a$, or $-NHC(O)R^a$;

R^6 is C_1-C_4 alkyl optionally substituted with OH;

R^7 is H, C_1-C_4 alkyl optionally substituted with one or two OH moieties, or 5-6 membered heteroaryl;

E is phenyl or 5-6 membered heteroaryl;

R^8, R^9, and R^{11} are each independently H or OH;

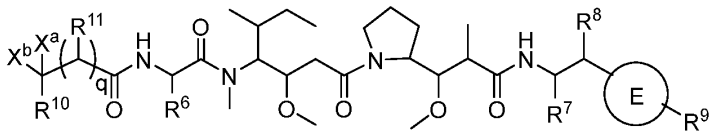
n is 0, 1, 2, or 3;

m is 1, 2, 3, or 4; and

q is 0 or 1,

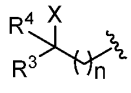
wherein when X is H, at least two of R^7, R^8, R^9, and R^{11} comprise an OH moiety.

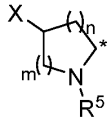
[0206] In some embodiments, provided is a compound of formula (Iz):



(Iz)

or a salt thereof, wherein

X^b is $-NR^1R^2$; and X^a is  ; or

X^a and X^b are taken together with the carbon atom to which they are attached to form  , wherein the asterisk denotes the carbon atom of Formula (I) that bears the X^a and X^b groups;

R^1, R^2, R^3, R^4, R^a, R^b, R^5, and R^{10} are each independently H or C_1-C_4 alkyl;

X is OH, $-C(O)NR^aR^b$, $-S(O)_2R^a$, $-S(O)-R^a$ $-S(O)_2NR^aR^b$, $-NHS(O)_2R^a$, or $-NHC(O)R^a$;

R^6 is C_1-C_4 alkyl optionally substituted with OH;

R^7 is H, C_1-C_4 alkyl optionally substituted with one or two OH moieties, or 5-6 membered heteroaryl;

E is phenyl or 5-6 membered heteroaryl;

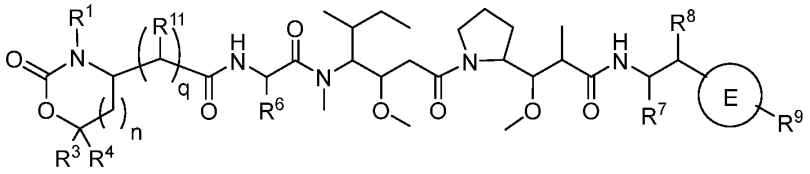
R^8, R^9, and R^{11} are each independently H or OH;

n is 0, 1, 2, or 3;

m is 1, 2, 3, or 4; and

q is 0 or 1.

[0207] In some embodiments, provided is compound of Formula (II):



(II)

or a salt thereof, wherein

R^1, R^3, and R^4 are independently H or C_1-C_4 alkyl;

R^6 is C_1-C_4 alkyl optionally substituted with OH;

R^7 is H, C_1-C_4 alkyl optionally substituted with one or two OH moieties, or 5-6 membered heteroaryl;

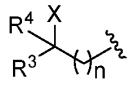
E is phenyl or 5-6 membered heteroaryl;

R^8, R^9, and R^{11} are each independently H or OH;

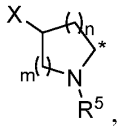
n is 0, 1, or 2; and

q is 0 or 1.

[0208] In some embodiments of Formula (I), q is 0. In some embodiments of Formula (I), q is 1. In some embodiments of Formula (II), q is 0. In some embodiments of Formula (II), q is 1.

[0209] In some embodiments of Formula (I) or (Iz), X^b is $-NR^1R^2$ is and X^a is . In some embodiments, R^1 and R^2 are each independently C_1-C_4 alkyl. In some embodiments, R^1 and R^2 are both H. In some embodiments, R^1 and R^2 are each independently n-propyl, isopropyl, ethyl, or methyl. In some embodiments, R^1 and R^2 are each independently ethyl or methyl. In some embodiments, R^1 and R^2 are both methyl. In some embodiments, R^1 is H and R^2 is C_1-C_4 alkyl. In some embodiments, R^1 is H and R^2 is n-propyl, isopropyl, ethyl, or methyl. In some embodiments, R^1 is H and R^2 is ethyl or methyl. In some embodiments, R^1 is H and R^2 is methyl. In some emodiments, R^3 and R^4 are each independently C_1-C_4 alkyl. In some embodiments, R^3 is H and R^4 is C_1-C_4 alkyl. In some embodiments, R^3 and R^4 are H. In some embodiments, R^3 is H and R^4 is methyl. In some embodiments, n is 0, 1, 2, or 3. In some embodiments, n is 0, 1, or 2. In some embodiments, n is 0 or 1. In some embodiments, n is 1. In some embodiments, n is 0. In some embodiments, R^1 is H, R^2 is methyl, R^3 is H, R^4 is H, and n is 0. In some embodiments, R^1 is methyl, R^2 is methyl, R^3 is H, R^4 is H, and n is 0.

[0210] In some embodiments of Formula (I) or (Iz), X^a and X^b are taken together with the carbon atom to which they are attached to form

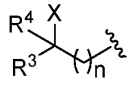
,

wherein the asterisk denotes the carbon atom of Formula (I) that bears the X^a and X^b groups. In some embodiments, R^5 is H, n-propyl, isopropyl, ethyl, or methyl. In some embodiments, R^5 is H, ethyl, or methyl. In some embodiments, R^5 is H or methyl. In some embodiments, R^5 is ethyl or methyl. In some embodiments, R^5 is H. In some embodiments, R^5 is ethyl. In some embodiments, R^5 is methyl. In some embodiments, m is 1, 2, or 3. In some embodiments, m is 1 or 2. In some embodiments, m is 2 or 3. In some embodiments, m is 2. In some embodiments, n is 0, 1, or 2. In some embodiments, n is 0 or 1. In some

embodiments, n is 0 or 1 and m is 0, 1, or 2. In some embodiments, n is 0 and m is 2. In some embodiments, n is 1 and m is 1. In some embodiments, m is 2 and n is 1. In some embodiments, X is H or OH. In some embodiments, X is H. In some embodiments, X is OH.

[0211] In some embodiments of Formula (I), X is H, OH, $-C(O)NR^aR^b$, $-S(O)_2R^a$, $-S(O)-R^a$, $-S(O)_2NR^aR^b$, $-NHS(O)_2R^a$, or $-NHC(O)R^a$. In some embodiments, X is OH, $-S(O)_2R^a$, $-S(O)-R^a$, $-S(O)_2NR^aR^b$, $-NHS(O)_2R^a$, or $-NHC(O)R^a$. In some embodiments, X is H or OH. In some embodiments, X is OH. In some embodiments, X is OH, $-NHS(O)_2R^a$, or $-NHC(O)R^a$. In some embodiments, X is OH, $-S(O)_2R^a$, $-S(O)-R^a$, or $-S(O)_2NR^aR^b$. In some embodiments, X is $-NHS(O)_2R^a$, or $-NHC(O)R^a$. In some embodiments, X is $-S(O)_2R^a$, $-S(O)-R^a$, or $-S(O)_2NR^aR^b$. In some embodiments, X is H, OH, $-NHS(O)_2R^a$, or $-NHC(O)R^a$. In some embodiments, X is H, OH, $-S(O)_2R^a$, $-S(O)-R^a$, or $-S(O)_2NR^aR^b$. In some embodiments, X is H, $-NHS(O)_2R^a$, or $-NHC(O)R^a$. In some embodiments, X is H, $-S(O)_2R^a$, $-S(O)-R^a$, or $-S(O)_2NR^aR^b$. In some embodiments, X is H, OH, or $-C(O)NR^aR^b$. In some embodiments, X is OH or $-C(O)NR^aR^b$. In some embodiments, X is H or $-C(O)NR^aR^b$. In some embodiments, R^a and R^b are independently H, n-propyl, isopropyl, ethyl, or methyl. In some embodiments, R^a and R^b are independently H, ethyl, or methyl. In some embodiments, R^a and R^b are independently H or methyl. In some embodiments, R^a is H and R^b is n-propyl, isopropyl, ethyl, or methyl. In some embodiments, R^a is H and R^b is methyl.

[0212] In some embodiments of Formula (Iz), X is OH, $-C(O)NR^aR^b$, $-S(O)_2R^a$, $-S(O)-R^a$, $-S(O)_2NR^aR^b$, $-NHS(O)_2R^a$, or $-NHC(O)R^a$. In some embodiments, X is OH. In some embodiments, X is OH, $-NHS(O)_2R^a$, or $-NHC(O)R^a$. In some embodiments, X is OH, $-S(O)_2R^a$, $-S(O)-R^a$, or $-S(O)_2NR^aR^b$. In some embodiments, X is $-NHS(O)_2R^a$, or $-NHC(O)R^a$. In some embodiments, X is $-S(O)_2R^a$, $-S(O)-R^a$, or $-S(O)_2NR^aR^b$. In some embodiments, X is OH or $-C(O)NR^aR^b$. In some embodiments, X is $-C(O)NR^aR^b$. In some embodiments, R^a and R^b are independently H, n-propyl, isopropyl, ethyl, or methyl. In some embodiments, R^a and R^b are independently H, ethyl, or methyl. In some embodiments, R^a and R^b are independently H or methyl. In some embodiments, R^a is H and R^b is n-propyl, isopropyl, ethyl, or methyl. In some embodiments, R^a is H and R^b is methyl.

[0213] In some embodiments of Formula (I) or (Iz), X^b is $-NR^1R^2$ is and X^a is , X is OH, R^1 is H or methyl, R^2 is methyl, R^3 is H, R^4 is H, and n is 0. In some

embodiments, X is OH, R^1 is methyl, R^2 is methyl, R^3 is H, R^4 is H, and n is 0. In some embodiments, X is OH, R^1 is H, R^2 is methyl, R^3 is H, R^4 is H, and n is 0. In some embodiments, X is OH, R^3 and R^4 are H, and n is 0. In some embodiments, X is OH, R^1 is H, R^2 is H, R^3 is H, R^4 is H, and n is 0.

[0214] In some embodiments of Formula (II), R^1 is H, n-propyl, isopropyl, ethyl, or methyl. In some embodiments, R^1 is H, ethyl, or methyl. In some embodiments, R^1 is H or methyl. In some embodiments, R^1 is ethyl. In some embodiments, R^1 is methyl. In some embodiments, R^1 is H. In some embodiments, n is 0 or 1. In some embodiments, n is 1. In some embodiments, n is 0.

[0215] In some embodiments of Formula (II), R^3 and R^4 are H. In some embodiments, R^3 and R^4 are methyl. In some embodiments, R^3 is H and R^4 is methyl.

[0216] In some embodiments or Formula (I), (Iz), or (II), R^6 is n-propyl, isopropyl, ethyl, or methyl. In some embodiments, R^6 is ethyl or methyl. In some embodiments, R^6 is isopropyl. In some embodiments, R^6 is n-propyl, isopropyl, ethyl, or methyl, each of which is substituted with OH. In some embodiments, R^6 is isopropyl substituted with OH. In some embodiments, R^6 is ethyl substituted with OH. In some embodiments, R^6 is methyl substituted with OH.

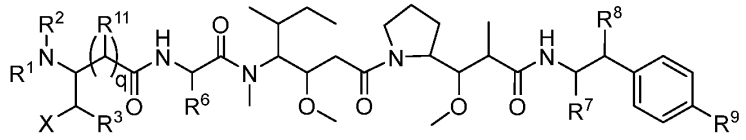
[0217] In some embodiments of Formula (I), (Iz), or (II), R^7 is C_1-C_4 alkyl substituted with OH. In some embodiments, R^7 is C_1-C_4 alkyl subsituted by two OH moieties. In some embodiments, R^7 is n-propyl, isopropyl, ethyl, or methyl, each of which is substituted with OH. In some embodiments, $R^7$is C_1-C_4 alkyl. In some embodiments, R^7 is n-propyl, isopropyl, ethyl, or methyl. In some embodiments, R^7 is methyl. In some embodiments, R^7 is $-CH_2CH_2OH$ or CH_2OH. In some embodiments, R^7 is $-CH_2OH$. In some embodiments, R^7 is 5-6 membered heteroaryl. In some embodiments, R^7 is 5-membered heteroaryl. In some embodiments, R^7 is thiazolyl.

[0218] In some embodiments of Formula (I), (Iz), or (II), R^8, R^9, and R^{11} are H. In some embodiments, R^8 is OH, R^9 is H, and R^{11} is H. In some embodiments, R^8 and R^9 are each OH and R^{11} is H. In some embodiments, R^8 is OH, R^9 is H, and R^{11} is OH. In some embodiments, R^8 is H, R^9 is H, and R^{11} is OH.

[0219] In some embodiments of Formula (I), (Iz), or (II), E is a 6-membered ring. In some embodiments, E is pyridine or phenyl. In some embodiments, E is phenyl.

[0220] In some embodiments of Formula (I), (Iz), or (II), R^7 is -CH_2OH, R^8 is H, R^9 is H, and E is phenyl.

[0221] In some embodiments, provided is a compound of Formula (Ia):



(Ia)

or a salt thereof, wherein

R^1, R^2, R^3, R^4, R^a, and R^b are each independently H or C_1-C_4 alkyl;

X is H, OH, -$C(O)NR^aR^b$, -$S(O)_2R^a$, -S(O)-R^a -$S(O)_2NR^aR^b$, -$NHS(O)_2R^a$, or -$NHC(O)R^a$;

R^6 is C_1-C_4 alkyl;

R^7 is H, C_1-C_4 alkyl optionally substituted with one or two OH moieties, or 5-6 membered heteroaryl;

R^8, R^9, and R^{11} are each independently H or OH;

q is 0 or 1; and

wherein when X is H, at least two of R^7, R^8, R^9, and R^{11} comprise an OH moiety.

[0222] In some embodiments of Formula (Ia), q is 0. In some embodiments, q is 1.

[0223] In some embodiments of Formula (Ia), R^1 is H and R^2 is C_1-C_4-alkyl. In some embodiments, R^1 is H and R^2 is n-propyl, isopropyl, ethyl, or methyl. In some embodiments, R^1 is H and R^2 is ethyl or methyl. In some embodiments, R^1 is H and R^2 is methyl. In some embodiments, R^1 and R^2 are each independently C_1-C_4 alkyl. In some embodiments, R^1 and R^2 are each independently n-propyl, isopropyl, ethyl, or methyl. In some embodiments, R^1 and R^2 are each independently ethyl or methyl. In some embodiments, R^1 and R^2 are methyl. In some embodiments, R^1 and R^2 are both H.

[0224] In some embodiments of Formula (Ia), X is H, OH, -$C(O)NR^aR^b$, -$S(O)_2R^a$, -S(O)-R^a, -$S(O)_2NR^aR^b$, -$NHS(O)_2R^a$, or -$NHC(O)R^a$. In some embodiments, X is OH, -$S(O)_2R^a$, -S(O)-R^a, -$S(O)_2NR^aR^b$, -$NHS(O)_2R^a$, or -$NHC(O)R^a$. In some embodiments, X is H or OH. In some embodiments, X is OH. In some embodiments, X is OH, -$NHS(O)_2R^a$, or -$NHC(O)R^a$. In some embodiments, X is OH, -$S(O)_2R^a$, -S(O)-R^a, or -$S(O)_2NR^aR^b$. In some embodiments, X is -$NHS(O)_2R^a$, or -$NHC(O)R^a$. In some embodiments, X is -$S(O)_2R^a$, -S(O)-R^a, or -$S(O)_2NR^aR^b$. In some embodiments, X is H, OH, -$NHS(O)_2R^a$, or -$NHC(O)R^a$. In some embodiments, X is H, OH, -$S(O)_2R^a$, -S(O)-R^a, or -$S(O)_2NR^aR^b$. In some

embodiments, X is H, -$NHS(O)_2R^a$, or -$NHC(O)R^a$. In some embodiments, X is H, -$S(O)_2R^a$, -$S(O)$-R^a, or -$S(O)_2NR^aR^b$. In some embodiments, X is H, OH, or -$C(O)NR^aR^b$. In some embodiments, X is OH or -$C(O)NR^aR^b$. In some embodiments, X is H or -$C(O)NR^aR^b$. In some embodiments, R^a and R^b are independently H, n-propyl, isopropyl, ethyl, or methyl. In some embodiments, R^a and R^b are independently H, ethyl, or methyl. In some embodiments, R^a and R^b are independently H or methyl. In some embodiments, R^a is H and R^b is n-propyl, isopropyl, ethyl, or methyl. In some embodiments, R^a is H and R^b is methyl.

[0225] In some embodiments of Formula (Ia), X is OH, -$C(O)NR^aR^b$, -$S(O)_2R^a$, -$S(O)$-R^a, -$S(O)_2NR^aR^b$, -$NHS(O)_2R^a$, or -$NHC(O)R^a$. In some embodiments, X is OH. In some embodiments, X is OH, -$NHS(O)_2R^a$, or -$NHC(O)R^a$. In some embodiments, X is OH, -$S(O)_2R^a$, -$S(O)$-R^a, or -$S(O)_2NR^aR^b$. In some embodiments, X is -$NHS(O)_2R^a$, or -$NHC(O)R^a$. In some embodiments, X is -$S(O)_2R^a$, -$S(O)$-R^a, or -$S(O)_2NR^aR^b$. In some embodiments, X is OH or -$C(O)NR^aR^b$. In some embodiments, X is -$C(O)NR^aR^b$. In some embodiments, R^a and R^b are independently H, n-propyl, isopropyl, ethyl, or methyl. In some embodiments, R^a and R^b are independently H, ethyl, or methyl. In some embodiments, R^a and R^b are independently H or methyl. In some embodiments, R^a is H and R^b is n-propyl, isopropyl, ethyl, or methyl. In some embodiments, R^a is H and R^b is methyl.

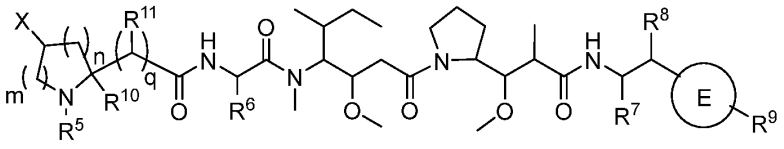
[0226] In some embodiments of Formula (Ia), R^6 is n-propyl, isopropyl, ethyl, or methyl. In some embodiments, R^6 is ethyl or methyl. In some embodiments, R^6 is isopropyl. In some embodiments, R^6 is n-propyl, isopropyl, ethyl, or methyl, each of which is substituted with OH. In some embodiments, R^6 is isopropyl substituted with OH. In some embodiments, R^6 is ethyl substituted with OH. In some embodiments, R^6 is methyl substituted with OH.

[0227] In some embodiments of Formula (Ia), R^7 is C_1-C_4 alkyl substituted with OH. In some embodiments, R^7 is n-propyl, isopropyl, ethyl, or methyl, each of which is substituted with OH. In some embodiments, R^7 is -CH_2CH_2OH or CH_2OH. In some embodiments, R^7 is -CH_2OH. In some embodiments, R^7 is C_1-C_4 alkyl. In some embodiments, R^7 is n-propyl, isopropyl, ethyl, or methyl. In some embodiments, R^7 is methyl. In some embodiments, R^7 is 5-6 membered heteroaryl. In some embodiments, R^7 is 5-membered heteroaryl. In some embodiments, R^7 is thiazolyl.

[0228] In some embodiments of Formula (Ia), R^8, R^9, and R^{11} are H. In some embodiments, R^8 is OH, R^9 is H, and R^{11} is H. In some embodiments, R^8 and R^9 are each OH and R^{11} is H. In some embodiments, R^8 is OH, R^9 is H, and R^{11} is OH.

[0229] In some embodiments of Formula (Ia), X is OH, R^3 is H or methyl, R^1 is H or C_1-C_4 alkyl, R^2 is C_1-C_4 alkyl, R_6 is C_1-C_4 alkyl, R^7 is C_1-C_4 alkyl optionally substituted with OH, R^8 is H or C_1-C_4 alkyl, R^9 is H, and q is 0. In some embodiments, X is OH, R^3 is H, R^1 is H or methyl, R^2 is methyl, R^6 is isopropyl, R^7 is CH_2OH, R^8 is H, R^9 is H, and q is 0.

[0230] In some embodiments, provided is a compound of Formula (Ib):



(Ib)

or a salt thereof, wherein the variables are as defined for Formula (I).

[0231] In some embodiments of Formula (Ib), X is H. In some embodiments, X is H or OH. In some embodiments, R^5 is H or methyl. In some embodiments, R^5 is H. In some embodiments, m is 1 or 2. In some embodiments, m is 2. In some embodiments, n is 2. In some embodiments, n is 0 or 1. In some embodiments, n is 1. In some embodiments, n is 0. In some embodiments, m is 2 and n is 0. In some embodiments, m is 1 and n is 1.

[0232] In some embodiments or Formula (Ib), R^6 is n-propyl, isopropyl, ethyl, or methyl. In some embodiments, R^6 is ethyl or methyl. In some embodiments, R^6 is isopropyl. In some embodiments, R^6 is n-propyl, isopropyl, ethyl, or methyl, each of which is substituted with OH. In some embodiments, R^6 is isopropyl substituted with OH. In some embodiments, R^6 is ethyl substituted with OH. In some embodiments, R^6 is methyl substituted with OH.

[0233] In some embodiments of Formula (Ib), R^7 is C_1-C_4 alkyl substituted with OH. In some embodiments, R^7 is n-propyl, isopropyl, ethyl, or methyl, each of which substituted with OH. In some embodiments, $R^7$is C_1-C_4 alkyl. In some embodiments, R^7 is n-propyl, isopropyl, ethyl, or methyl. In some embodiments, R^7 is methyl. In some embodiments, R^7 is -CH_2CH_2OH or CH_2OH. In some embodiments, R^7 is -CH_2OH. In some embodiments, R^7 is 5-6 membered heteroaryl. In some embodiments, R^7 is 5-membered heteroaryl. In some embodiments, R^7 is thiazolyl.

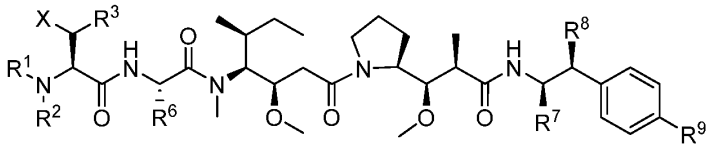
[0234] In some embodiments of Formula (Ib), R^8, R^9, and R^{11} are each H. In some embodiments, R^8 is OH, R^9 is H, and R^{11} is H. In some embodiments, R^8 and R^9 are each OH and R^{11} is H. In some embodiments, R^8 is OH, R^9 is H, and R^{11} is OH. In some embodiments, R^8 is H, R^9 is H, and R^{11} is OH.

[0235] In some embodiments of Formula (Ib), E is a 6-membered ring. In some embodiments, E is pyridine or phenyl. In some embodiments, E is phenyl.

[0236] In some embodiments of Formula (Ib), R^7 is -CH_2OH, R^8 is H, R^9 is H, and E is phenyl.

[0237] In some embodiments of Formula (Ib), R^7 is -CH_2OH, R^8 is H, and R^9 is H. In some embodiments, m is 2, n is 0, X is H, R^{10} is methyl, R^6 is isopropyl, R^7 is H, R^8 is OH, and R^9 is OH. In some embodiments, m is 1, n is 1, X is H, R^{10} is methyl, R^6 is isopropyl, R^7 is H, R^8 is OH, and R^9 is OH. In some embodiments, m is 2, n is 1, X is H, R^{10} is methyl, R^6 is isopropyl, R^7 is H, R^8 is OH, and R^9 is OH.

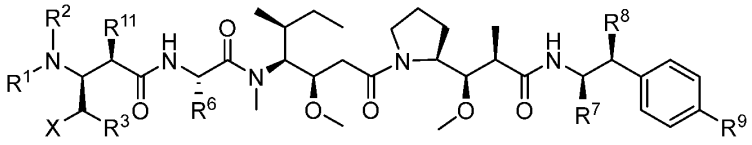
[0238] In some embodiments, provided is a compound of Formula (Ic):



(Ic)

or a salt thereof, wherein the variables are as defined for Formula (I), (Iz), or (Ia).

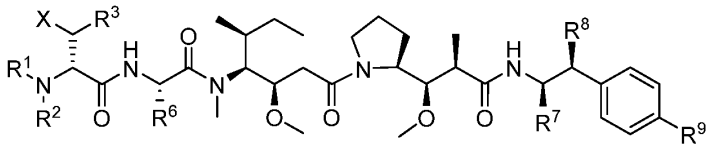
[0239] In some embodiments, provided is a compound of Formula (Id):



(Id)

or a salt thereof, wherein the variables are as defined for Formula (I), (Iz), or (Ia).

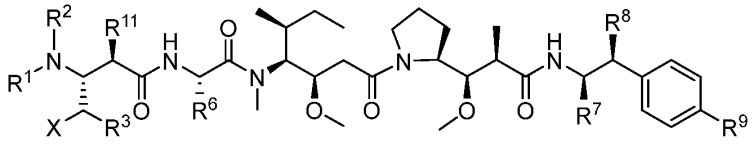
[0240] In some embodiments, provided is a compound of Formula (Ie):



(Ie)

or a salt thereof, wherein the variables are as defined for Formula (I), (Iz), or (Ia).

[0241] In some embodiments, provided is a compound of Formula (Id):



(If)

or a salt thereof, wherein the variables are as defined for Formula (I), (Iz), or (Ia).

[0242] In some embodiments of Formula (Ic), (Id), (Ie), or (If), R^1 and R^1 are both H. R^1 is H and R^2 is C_1-C_4-alkyl. In some embodiments, R^1 is H and R^2 is n-propyl, isopropyl, ethyl, or methyl. In some embodiments, R^1 is H and R^2 is ethyl or methyl. In some embodiments, R^1 is H and R^2 is methyl. In some embodiments, R^1 and R^2 are each independently C_1-C_4 alkyl. In some embodiments, R^1 and R^2 are each independently n-propyl, isopropyl, ethyl, or methyl. In some embodiments, R^1 and R^2 are each independently ethyl or methyl. In some embodiments, R^1 and R^2 are methyl.

[0243] In some embodiments of Formula (Ic), (Id), (Ie), or (If), X is H, OH, $-C(O)NR^aR^b$, or $-NHC(O)R^a$. In some embodiments, X is H, OH, $-C(O)NR^aR^b$, or $-NHC(O)R^a$. In some embodiments, X is H or OH. In some embodiments, X is OH. In some embodiments, R^3 is H or C_1-C_4 alkyl. In some embodiments, R^3 is H, n-propyl, isopropyl, ethyl, or methyl. In some embodiments, R^3 is H, ethyl, or methyl. In some embodiments, X is H or OH and R^3 is H or methyl. In some embodiments, X is OH and R^3 is H. In some embodiments, X is OH and R^3 is methyl. In some embodiments, R^a is ethyl or methyl. In some embodiments, R^a is methyl.

[0244] In some embodiments of Formula (Ic), (Id), (Ie), or (If), R^6 is n-propyl, isopropyl, ethyl, or methyl. In some embodiments, R^6 is ethyl or methyl. In some embodiments, R^6 is isopropyl. In some embodiments, R^6 is n-propyl, isopropyl, ethyl, or methyl, each of which is substituted with OH. In some embodiments, R^6 is isopropyl substituted with OH. In some embodiments, R^6 is ethyl substituted with OH. In some embodiments, R^6 is methyl substituted with OH.

[0245] In some embodiments of Formula (Ic), (Id), (Ie), or (If), R^7 is C_1-C_4 alkyl substituted with OH. In some embodiments, R^7 is C_1-C_4 alkyl subsituted by two OH moieties. In some embodiments, R^7 is n-propyl, isopropyl, ethyl, or methyl, each of which is substituted with OH. In some embodiments, R^7 is $-CH_2CH_2OH$ or CH_2OH. In some embodiments, R^7 is $-CH_2OH$. In some embodiments, $R^7$is C_1-C_4 alkyl. In some embodiments, R^7 is n-propyl, isopropyl, ethyl, or methyl. In some embodiments, R^7 is

methyl. In some embodiments, R^7 is 5-6 membered heteroaryl. In some embodiments, R^7 is 5-membered heteroaryl. In some embodiments, R^7 is thiazolyl.

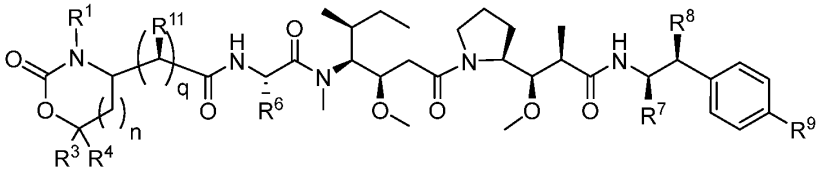
[0246] In some embodiments of Formula (Ic) or (Ie), R^8 and R^9 are H. In some embodiments, R^8 is OH and R^9 is H. In some embodiments, R^8 and R^9 are each OH.

[0247] In some embodiments of Formaul (Id) or (If), R^8, R^9, and R^{11} are H. In some embodiments, R^8 is OH, R^9 is H, and R^{11} is H. In some embodiments, R^8 and R^9 are each OH and R^{11} is H. In some embodiments, R^8 is OH, R^9 is H, and R^{11} is OH. In some embodiments, R^8 is H, R^9 is H, and R^{11} is OH.

[0248] In some embodiments of Formula (Ic), (Id), (Ie), or (If), X is OH, R^3 is H or methyl, R^1 is H or C_1-C_4 alkyl, R^2 is C_1-C_4 alkyl, R_6 is C_1-C_4 alkyl, R^7 is C_1-C_4 alkyl optionally substituted with OH, R^8 is H or C_1-C_4 alkyl, and R^9 is H. In some embodiments, X is OH, R^3 is H, R^1 is H or methyl, R^2 is methyl, R^6 is isopropyl, R^7 is CH_2OH, R^8 is H, and R^9 is H.

[0249] In some embodiments of Formula (Ic), R^7 is -CH_2OH, R^8 is H, and R^9 is H.

[0250] In some embodiments, provided is a compound of Formula (IIa):



(IIa)

or a salt thereof, wherein the variables are as defined for Formula (II).

[0251] In some embodiments of Formula (IIa), q is 0. In some embodiments, q is 1.

[0252] In some embodiments of Formula (IIa), R^1 is H, n-propyl, isopropyl, ethyl, or methyl. In some embodiments, R^1 is H, ethyl, or methyl. In some embodiments, R^1 is H or methyl. In some embodiments, R^1 is ethyl. In some embodiments, R^1 is methyl. In some embodiments, R^1 is H. In some embodiments, n is 0 or 1. In some embodiments, n is 1. In some embodiments, n is 0.

[0253] In some embodiments or Formula (IIa), R^6 is n-propyl, isopropyl, ethyl, or methyl. In some embodiments, R^6 is ethyl or methyl. In some embodiments, R^6 is isopropyl. In some embodiments, R^6 is n-propyl, isopropyl, ethyl, or methyl, each of which is substituted with

OH. In some embodiments, R^6 is isopropyl substituted with OH. In some embodiments, R^6 is ethyl substituted with OH. In some embodiments, R^6 is methyl substituted with OH.

[0254] In some embodiments of Formula (IIa), R^7 is C_1-C_4 alkyl substituted with OH. In some embodiments, R^7 is C_1-C_4 alkyl subsituted by two OH moieties. In some embodiments, R^7 is n-propyl, isopropyl, ethyl, or methyl, each of which is substituted with OH. In some embodiments, $R^7$is C_1-C_4 alkyl. In some embodiments, R^7 is n-propyl, isopropyl, ethyl, or methyl. In some embodiments, R^7 is methyl. In some embodiments, R^7 is $-CH_2CH_2OH$ or CH_2OH. In some embodiments, R^7 is $-CH_2OH$. In some embodiments, R^7 is 5-6 membered heteroaryl. In some embodiments, R^7 is 5-membered heteroaryl. In some embodiments, R^7 is thiazolyl.

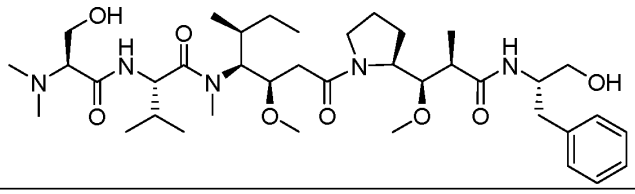
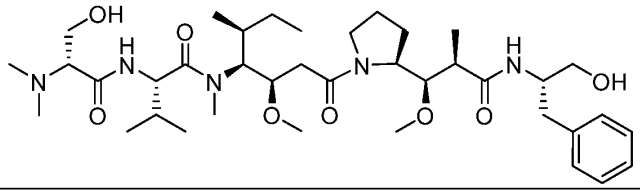
[0255] In some embodiments of Formula (IIa), R^8, R^9, and R^{11} are H. In some embodiments, R^8 is OH, R^9 is H, and R^{11} is H. In some embodiments, R^8 and R^9 are each OH and R^{11} is H. In some embodiments, R^8 is OH, R^9 is H, and R^{11} is OH. In some embodiments, R^8 is H, R^9 is H, and R^{11} is OH.

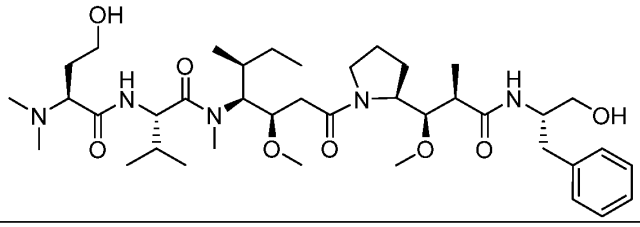
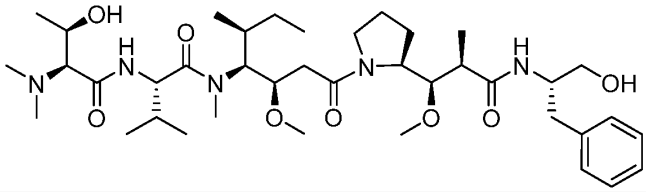
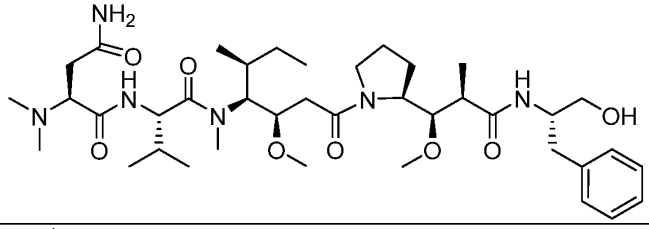
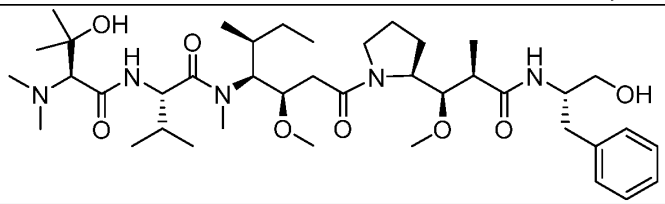
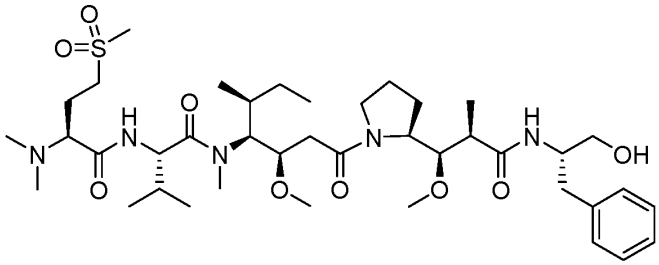
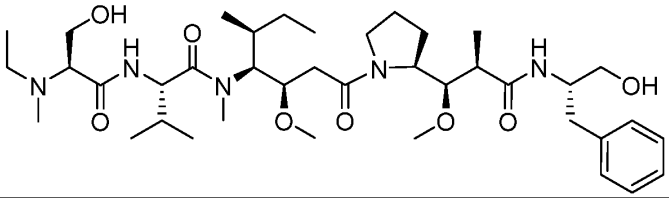
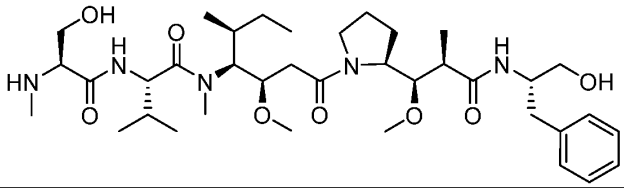
[0256] In some embodiments of Formula (IIa), E is a 6-membered ring. In some embodiments, E is pyridine or phenyl. In some embodiments, E is phenyl.

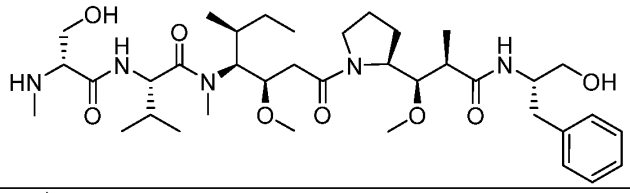
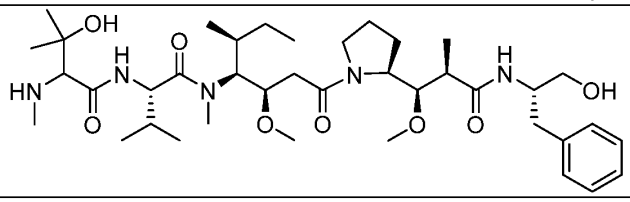
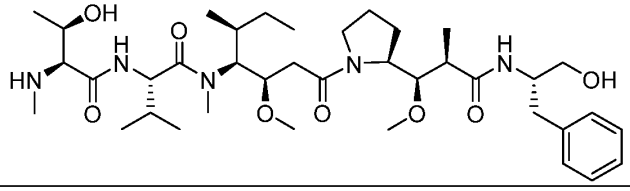
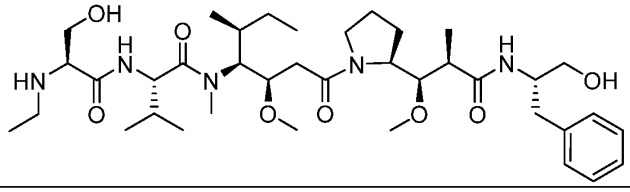
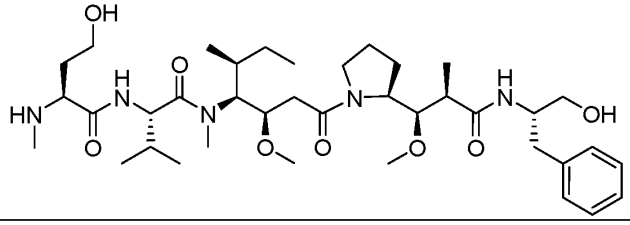
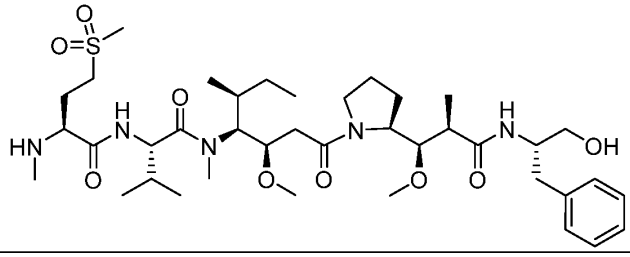
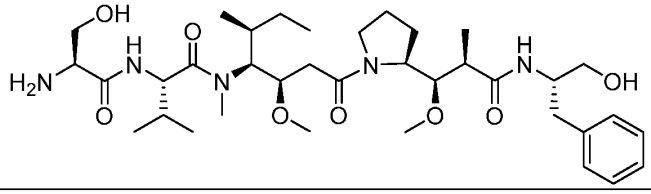
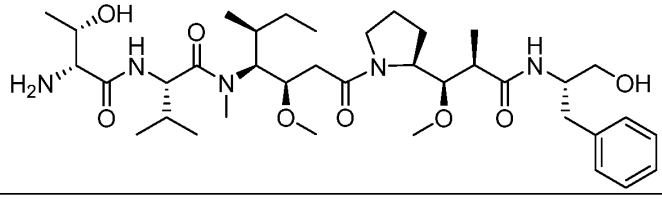
[0257] In some embodiments of Formula (IIa), R^7 is $-CH_2OH$, R^8 is H, R^9 is H, and R^{11} is H.

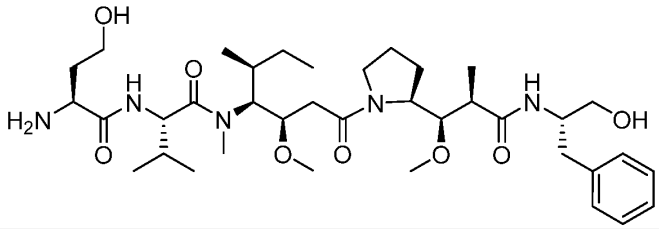
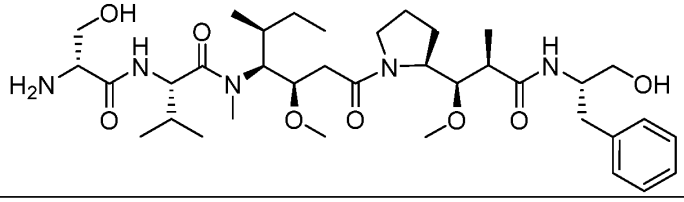
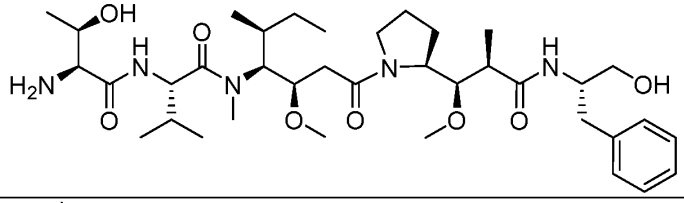
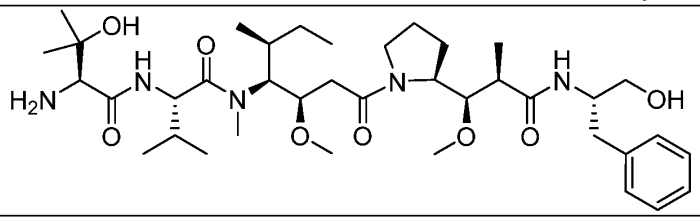
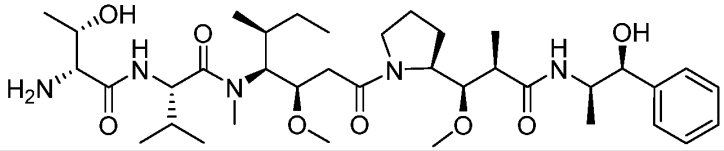
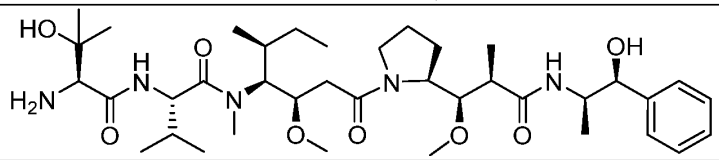
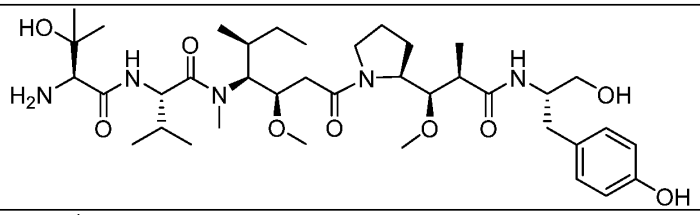
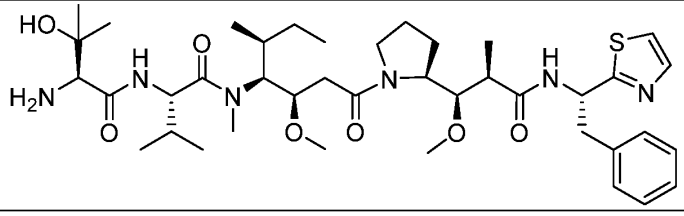
[0258] In some embodiments, provided is a compound of Table 1, or a salt thereof (e.g., a pharmaceutically acceptable salt).

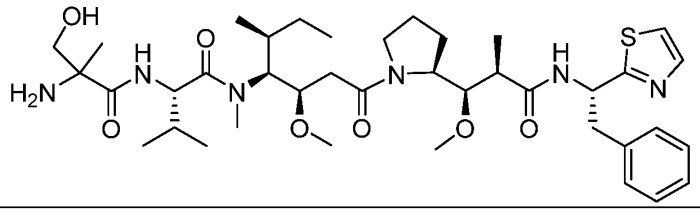
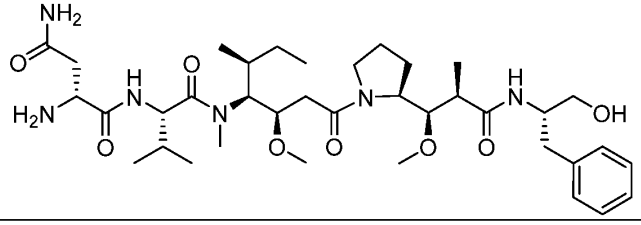
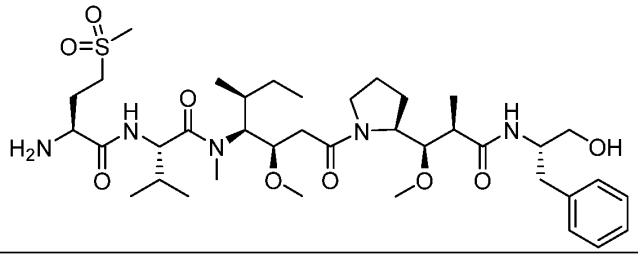
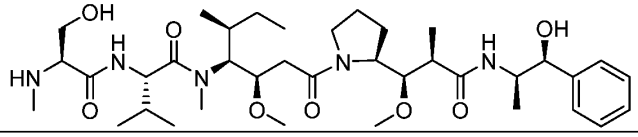
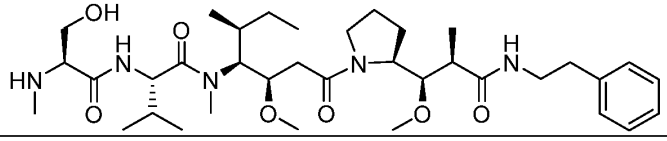
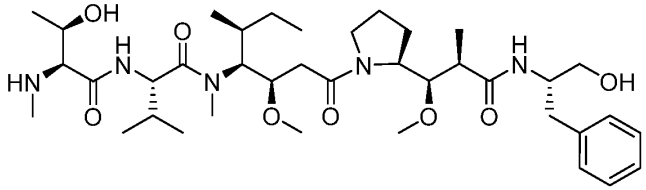
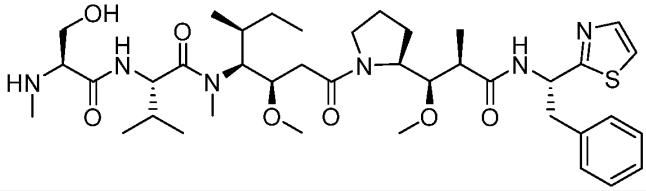
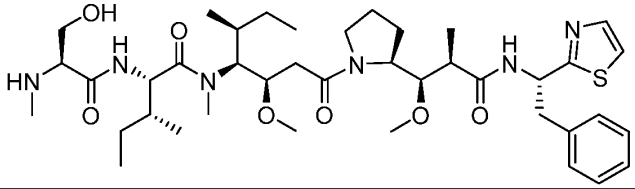
Table 1. Hydrophilic auristatin compounds

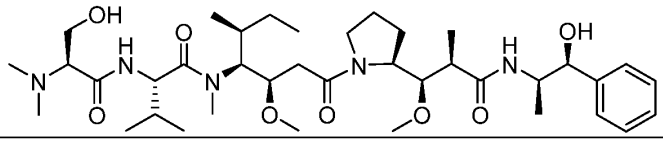
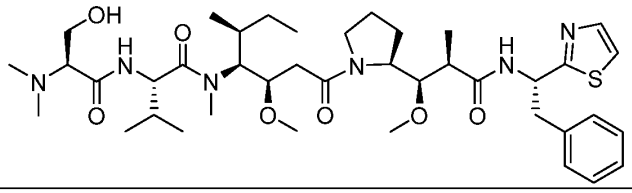
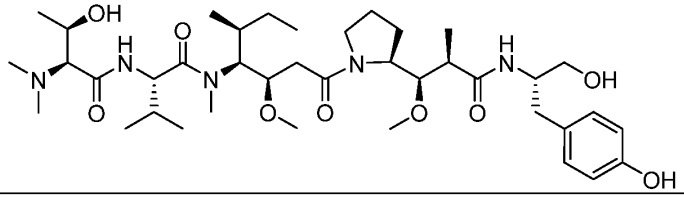
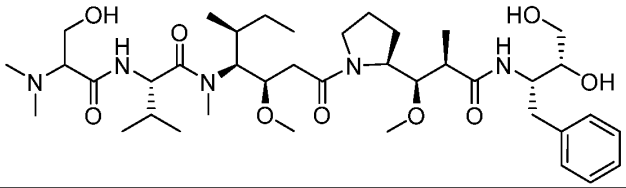
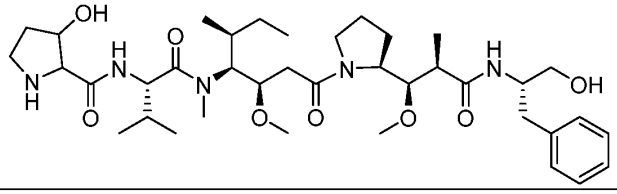
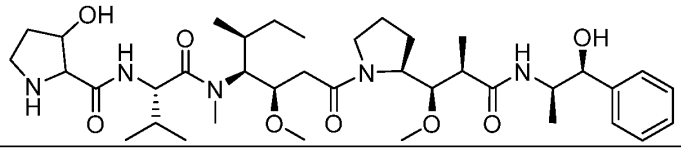
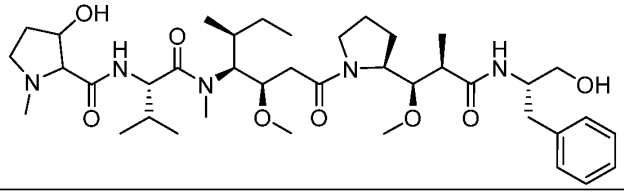
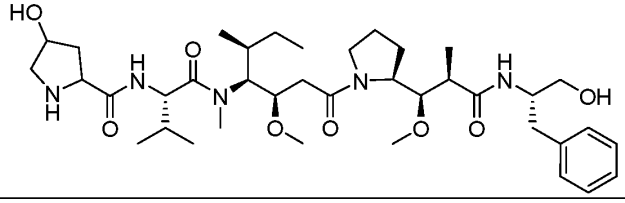
Compound #	Compound Structure
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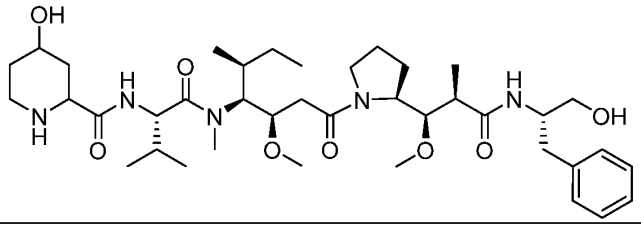
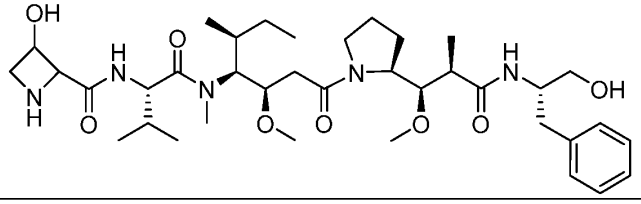
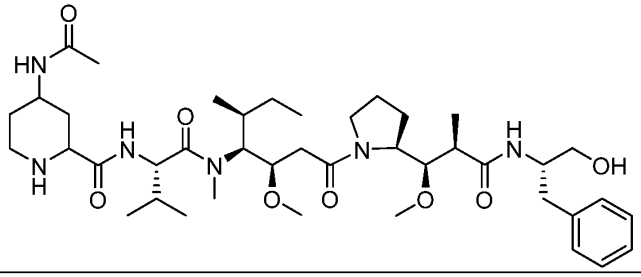
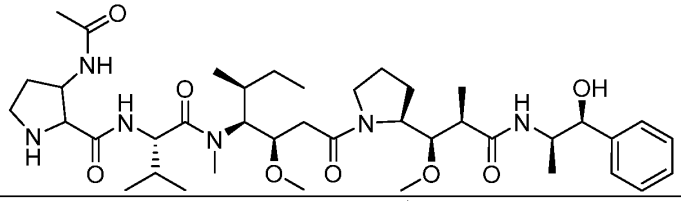
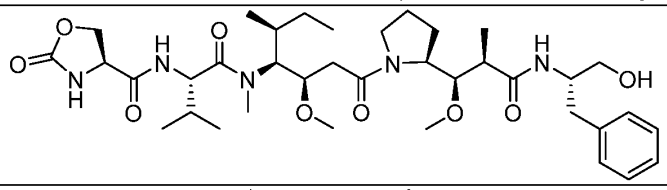
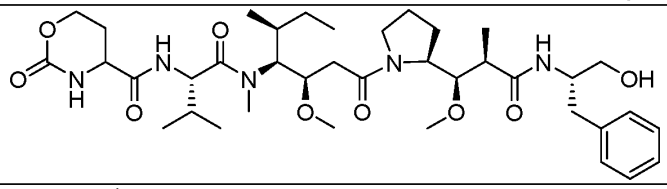
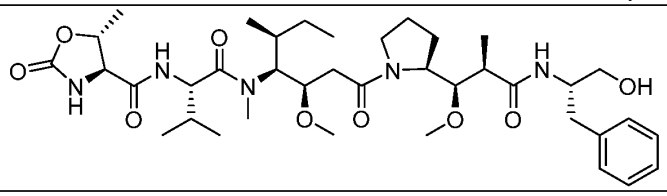
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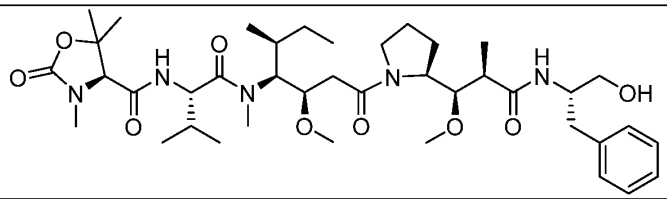
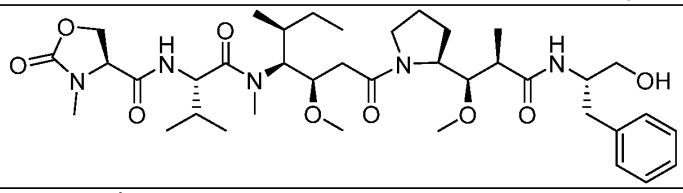
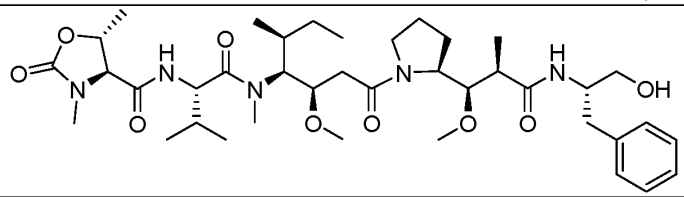
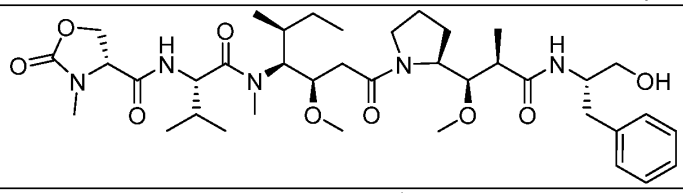
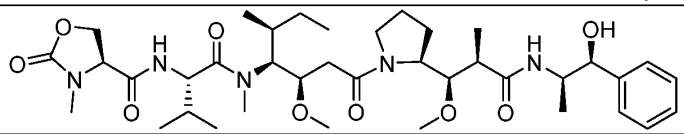
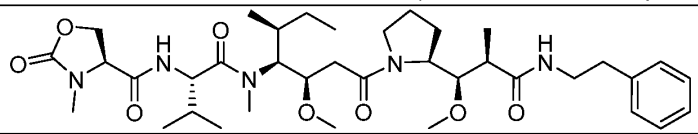
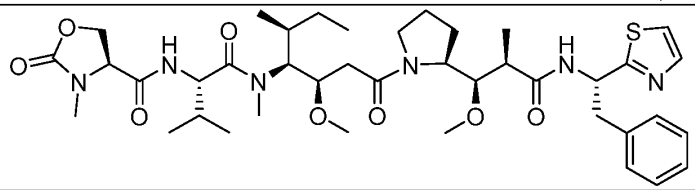
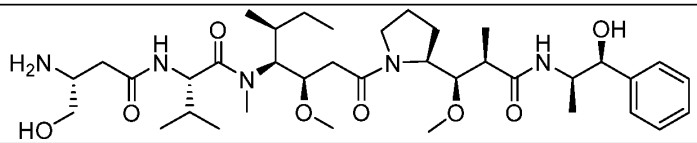
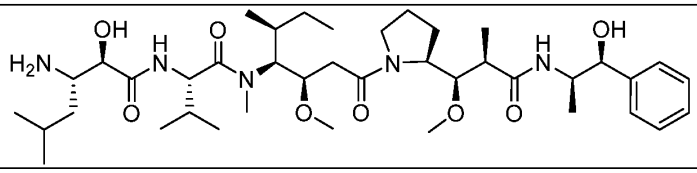
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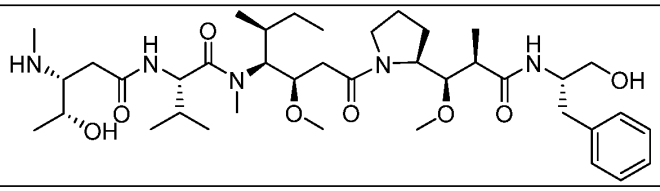
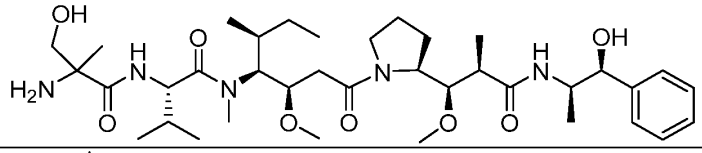
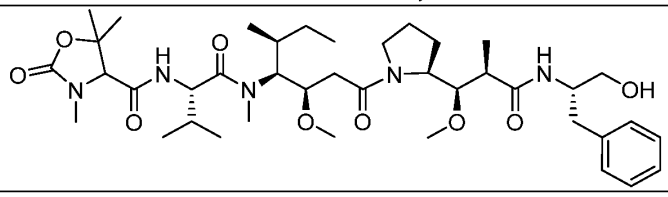
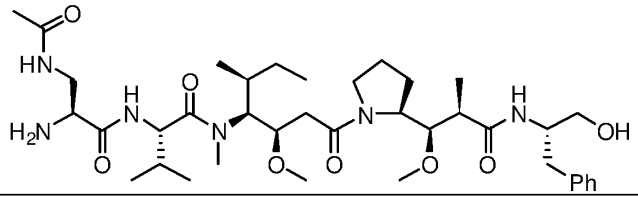
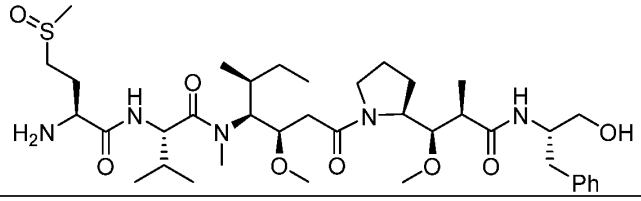
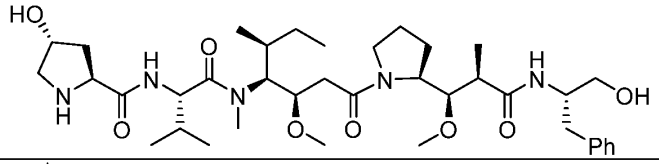
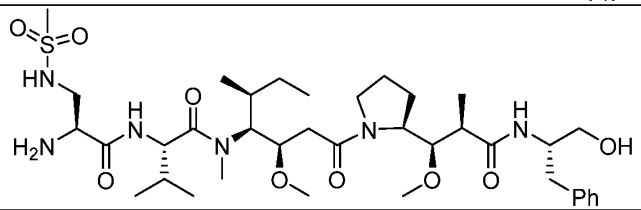
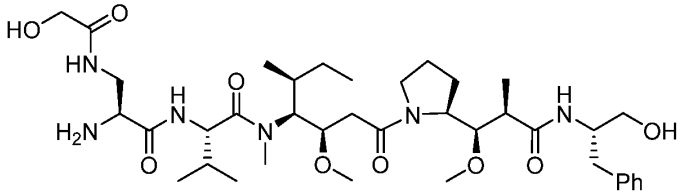
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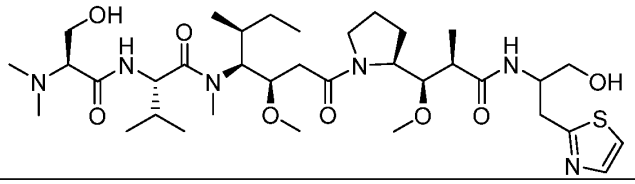
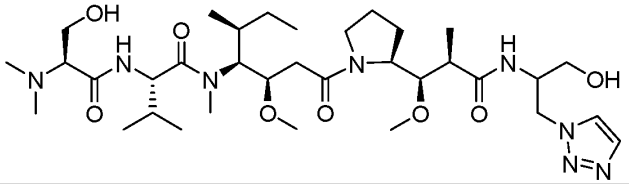
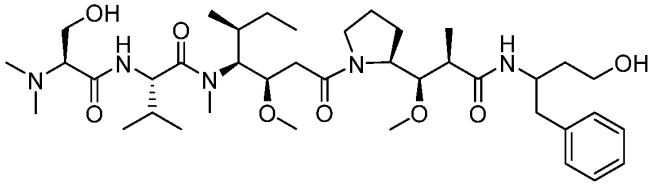
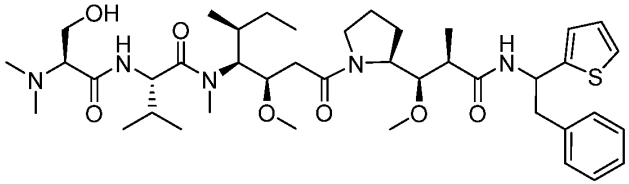
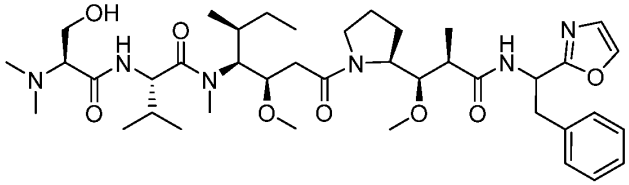
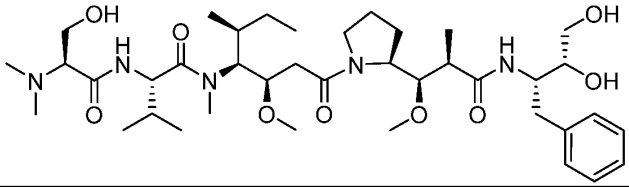
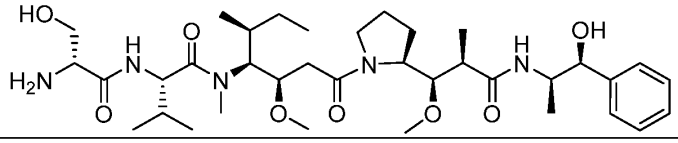
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Drug-Linker Compounds

[0259] In some embodiments, when preparing Ligand-Drug Conjugate compounds described herein, it will be desirable to synthesize the full Drug-Linker compound prior to conjugation to a targeting agent, which becomes the Ligand Unit of the Ligand-Drug conjugate compound. In such embodiments, Drug-Linker compounds as described herein, are intermediate compounds. In those embodiments, the Stretcher Unit in a Drug-Linker

compound is not yet covalently attached to the Ligand Unit (*i.e.*, is a Stretcher Unit precursor, Z'), and therefore has a functional group for conjugation to a targeting agent. In one embodiment, a Drug-Linker compound comprises an auristatin moiety (shown herein as Formulae (I) and (II), or any subformula thereof) or, and a Linker Unit (Q) through which the Ligand Unit is connected to the Drug Unit.

[0260] In another embodiment, a Drug-Linker compound comprises an auristatin compound of Formula (I), or any subformula thereof, as a Drug Unit and a Linker Unit (Q) comprising a Releasable Linker (RL) that is other than a Glycoside (e.g., Glucuronide) Unit through which the Ligand Unit is connected to the conjugated auristatin compound. The Linker Unit comprises, in addition to RL, a Stretcher Unit precursor (Z') comprising a functional group for conjugation to a targeting agent that is the precursor to the Ligand Unit and thus is capable of (directly or indirectly) connecting the RL to the Ligand Unit. In some of those embodiments a Parallel Connector Unit (B) is present when it is desired to add a Partitioning Agent (S^*) as a side chain appendage. In any one of those embodiments, a Connector Unit (A) is present when it is desirable to add more distance between the Stretcher Unit and RL.

[0261] In one group of embodiments, a Drug-Linker compound comprises an auristatin compound of Formula (I), or any subformula thereof, and a Linker Unit (Q), wherein Q comprises a Releasable Linker (RL) that is a Glycoside (e.g., Glucuronide) Unit, directly attached to a Stretcher Unit precursor (Z') or indirectly to Z' through attachment to intervening component(s) of the Drug-Linker compound's Linker Unit (i.e., A, S^* and/or $B(S^*)$), wherein Z' comprises a functional group capable of forming a covalent bond to a targeting agent.

[0262] In another group of embodiments, a Drug-Linker compound comprises an auristatin of Formula (I), or any subformula thereof, and a Linker Unit (Q), wherein Q comprises a Releasable Linker (RL) that is other than a Glycoside (e.g., Glucuronide) Unit (RL), directly attached to a Stretcher Unit precursor (Z') or indirectly to Z' through attachment to intervening component(s) of the Drug-Linker compound's Linker Unit (i.e., A, S^* and/or $B(S^*)$), wherein Z' comprises a functional group capable of forming a covalent bond to a targeting agent.

[0263] In some embodiments, the Drug-Linker compound has the formula:

Q-D,

or a salt thereof, wherein

Q is a Linker Unit selected from the group consisting of:

(i) Z'-A-RL-,

(ii) Z'-A-RL-Y-,

(iii) Z'-A-S*-RL-,

(iv) Z'-A-S*-RL-Y-,

(v) Z'-A-B(S*)-RL-,

(vi) Z'-A-B(S*)-RL-Y-,

(vii) Z'-A-,

(viii) Z'-A-S*-W-,

(ix) Z'-A-B(S*)-W-,

(x) Z'-A-S*-W-RL-, and

(xi) Z'-A-B(S*)-W-RL-;

Z' is a Stretcher Unit precursor;

A is a bond or a Connector Unit;

B is a Parallel Connector Unit;

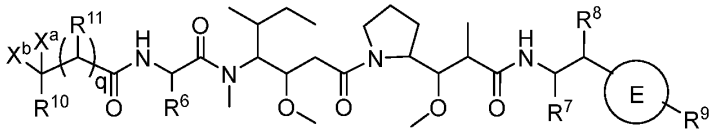
S* is a Partitioning Agent;

RL is a Releasable Linker;

W is a Amino Acid Unit;

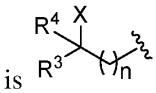
Y is a Spacer Unit; and

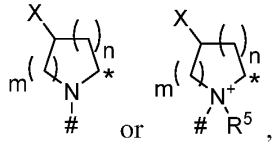
D is a Drug Unit of Formula (I'):



(I')

wherein

X^b is $-NR^{2}-^{\#}$ or $-N^{+}R^{1}R^{5}-^{\#}$, wherein the # denotes the point of attachment to Q, and X^a is ; or

X^a and X^b are taken together with the carbon atom to which they are attached to form  or , wherein the asterisk denotes the carbon atom of Formula (I) that bears the X^a and X^b groups, and the # denotes the point of attachment to Q;

R^1 and R^5 are independently C_1-C_4 alkyl;

X is H, OH, $-C(O)NR^aR^b$, $-S(O)_2R^a$, $-S(O)-R^a$ $-S(O)_2NR^aR^b$, $-NHS(O)_2R^a$, or $-NHC(O)R^a$;

R^2, R^3, R^4, R^{10}, R^a, and R^b are each independently H or C_1-C_4 alkyl;

R^6 is C_1-C_4 alkyl optionally substituted with OH;

R^7 is H, C_1-C_4 alkyl optionally substituted with one or two OH moieties, or 5-6 membered heteroaryl;

E is phenyl or 5-6 membered heteroaryl;

R^8, R^9, and R^{11} are each independently H or OH;

n is 0, 1, 2, or 3;

m is 1, 2, 3, or 4;

q is 0 or 1; and

wherein when X is H, at least two of R^7, R^8, R^9, and R^{11} comprise an OH moiety.

[0264] In the context of the Drug-Linker Compounds – the assembly is best described in terms of its component groups. While some procedures for the preparation of Drug-Linker compounds are described herein, the order of assembly and the general conditions to prepare the compounds will be well understood by one of skill in the art in view of the teachings of the application.

Component groups

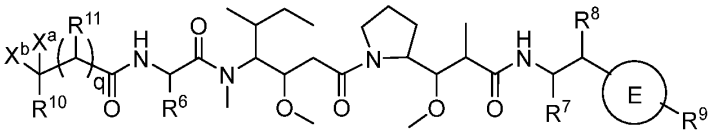
1. Drug Unit D

[0265] The Drug Units of the Drug-Linker compounds, or Ligand-Drug Conjugate thereof, provided herein are auristatin moieities of the compounds disclosed herein and are referred to herein as Drug Units.

[0266] In some embodiments, the Drug Unit D has Formula (I'), as described above.

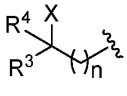
[0267] In some embodiments of Formula (I'), q is 0. In some embodiments, q is 1.

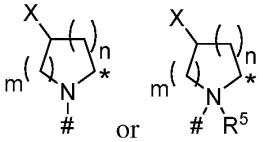
[0268] In some embodiments, the Drug Unit D has Formula (Iz'):



(Iz')

wherein

X^b is $-NR^2-^{\#}$ or $-N^+R^1R^5-^{\#}$, wherein the # denotes the point of attachment to Q, and X^a is  ; or

X^a and X^b are taken together with the carbon atom to which they are attached to form  , wherein the asterisk denotes the carbon atom of Formula (I) that bears the X^a and X^b groups, and the # denotes the point of attachment to Q;

R^1 and R^5 are independently C_1-C_4 alkyl;

X is OH, $-C(O)NR^aR^b$, $-S(O)_2R^a$, -S(O)-R^a $-S(O)_2NR^aR^b$, $-NHS(O)_2R^a$, or $-NHC(O)R^a$;

R^2, R^3, R^4, R^{10}, R^a, and R^b are each independently H or C_1-C_4 alkyl;

R^6 is C_1-C_4 alkyl optionally substituted with OH;

R^7 is H, C_1-C_4 alkyl optionally substituted with one or two OH moieties, or 5-6 membered heteroaryl;

E is phenyl or 5-6 membered heteroaryl;

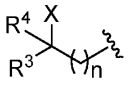
R^8, R^9, and R^{11} are each independently H or OH;

n is 0, 1, 2, or 3;

m is 1, 2, 3, or 4; and

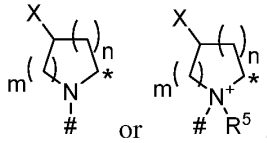
q is 0 or 1.

[0269] In some embodiments of Formula (I') or (Iz'), q is 0. In some embodiments, q is 1.

[0270] In some embodiments, of Formula (I') or (Iz'), X^b is $-NR^2-^{\#}$ or $-N^+R^1R^5-^{\#}$, wherein the # denotes the point of attachment to Q, and X^a is  . In some embodiments, R^1 and R^2 are each independently C_1-C_4 alkyl. In some embodiments, R^1 and R^5 are each independently n-propyl, isopropyl, ethyl, or methyl. In some embodiments, R^1 and R^5 are each independently ethyl or methyl. In some embodiments, R^1 and R^5 are methyl. In some

emodiments, R^3 and R^4 are each independently C_1-C_4 alkyl. In some embodiments, R^3 is H and R^4 is C_1-C_4 alkyl. In some embodiments, R^3 and R^4 are H. In some embodiments, R^3 is H and R^4 is methyl. In some embodiments, n is 0, 1, 2, or 3. In some embodiments, n is 0, 1, or 2. In some embodiments, n is 0 or 1. In some embodiments, n is 1. In some embodiments, n is 0. In some embodiments, R^1 is methyl, R^5 is methyl, R^3 is H, R^4 is H, and n is 0. In some embodiments, R^2 is n-propyl, isopropyl, ethyl or methyl. In some embodiments, R^2 is ethyl or methyl. In some embodiments, R^2 is methyl. In some embodiments, R^2 is H.

[0271] In some embodiments of Formula (I') or (Iz'), X^a and X^b are taken together with the carbon atom to which they are attached to form

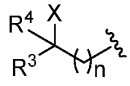


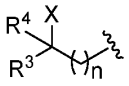
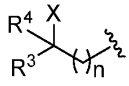
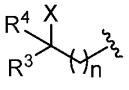
wherein the asterisk denotes the carbon atom of Formula (I) that bears the X^a and X^b groups, and the # denotes the point of attachment to Q. In some embodiments, R^5 is n-propyl, isopropyl, ethyl, or methyl. In some embodiments, R^5 is ethyl or methyl. In some embodiments, R^5 is ethyl. In some embodiments, R^5 is methyl. In some embodiments, m is 1, 2, or 3. In some embodiments, m is 1 or 2. In some embodiments, m is 2 or 3. In some embodiments, m is 2. In some embodiments, n is 0, 1, or 2. In some embodiments, n is 0 or 1. In some embodiments, m is 1 or 2 and n is 0 or 1.

[0272] In some embodiments of Formula (I'), X is H, OH, $-C(O)NR^aR^b$, $-S(O)_2R^a$, $-S(O)-R^a$, $-S(O)_2NR^aR^b$, $-NHS(O)_2R^a$, or $-NHC(O)R^a$. In some embodiments, X is OH, $-S(O)_2R^a$, $-S(O)-R^a$, $-S(O)_2NR^aR^b$, $-NHS(O)_2R^a$, or $-NHC(O)R^a$. In some embodiments, X is H or OH. In some embodiments, X is OH. In some embodiments, X is OH, $-NHS(O)_2R^a$, or $-NHC(O)R^a$. In some embodiments, X is OH, $-S(O)_2R^a$, $-S(O)-R^a$, or $-S(O)_2NR^aR^b$. In some embodiments, X is $-NHS(O)_2R^a$, or $-NHC(O)R^a$. In some embodiments, X is $-S(O)_2R^a$, $-S(O)-R^a$, or $-S(O)_2NR^aR^b$. In some embodiments, X is H, OH, $-NHS(O)_2R^a$, or $-NHC(O)R^a$. In some embodiments, X is H, OH, $-S(O)_2R^a$, $-S(O)-R^a$, or $-S(O)_2NR^aR^b$. In some embodiments, X is H, $-NHS(O)_2R^a$, or $-NHC(O)R^a$. In some embodiments, X is H, $-S(O)_2R^a$, $-S(O)-R^a$, or $-S(O)_2NR^aR^b$. In some embodiments, X is H, OH, or $-C(O)NR^aR^b$. In some embodiments, X is OH or $-C(O)NR^aR^b$. In some embodiments, X is H or $-C(O)NR^aR^b$. In some embodiments, R^a and R^b are independently H, n-propyl, isopropyl, ethyl, or methyl. In some embodiments, R^a and R^b are independently H, ethyl, or methyl. In some embodiments,

R^a and R^b are independently H or methyl. In some embodiments, R^a is H and R^b is n-propyl, isopropyl, ethyl, or methyl. In some embodiments, R^a is H and R^b is methyl.

[0273] In some embodiments of Formula (Iz'), X is OH, $-C(O)NR^aR^b$, $-S(O)_2R^a$, $-S(O)-R^a$, $-S(O)_2NR^aR^b$, $-NHS(O)_2R^a$, or $-NHC(O)R^a$. In some embodiments, X is OH. In some embodiments, X is OH, $-NHS(O)_2R^a$, or $-NHC(O)R^a$. In some embodiments, X is OH, $-S(O)_2R^a$, $-S(O)-R^a$, or $-S(O)_2NR^aR^b$. In some embodiments, X is $-NHS(O)_2R^a$, or $-NHC(O)R^a$. In some embodiments, X is $-S(O)_2R^a$, $-S(O)-R^a$, or $-S(O)_2NR^aR^b$. In some embodiments, X is OH or $-C(O)NR^aR^b$. In some embodiments, X is $-C(O)NR^aR^b$. In some embodiments, R^a and R^b are independently H, n-propyl, isopropyl, ethyl, or methyl. In some embodiments, R^a and R^b are independently H, ethyl, or methyl. In some embodiments, R^a and R^b are independently H or methyl. In some embodiments, R^a is H and R^b is n-propyl, isopropyl, ethyl, or methyl. In some embodiments, R^a is H and R^b is methyl.

[0274] In some embodiments of Formula (I') or (Iz'), X^b is $-N^+R^1R^5-^{\#}$ and X^a is , X is OH, R^1 is methyl or methyl, R^5 is methyl, R^3 is H, R^4 is H, and n is 0. In some embodiments, X is OH, R^1 is methyl, R^5 is methyl, R^3 is H, R^4 is H, and n is 0. In some embodiments, X is OH, R^3 and R^4 are H, and n is 0.

[0275] In some embodiments of Formula (I') or (Iz'), X^b is $-NR^2-^{\#}$, X^a is , X is OH, and R^2 is H or C_1-C_4 alkyl. In some embodiments, X^b is $-NR^2-^{\#}$ and X^a is , X is OH, and R^2 is H. In some embodiments, X^b is $-NR^2-^{\#}$ and X^a is , X is OH, and R^2 is C_1-C_4 alkyl.

[0276] In some embodiments or Formula (I') or (Iz'), R^6 is n-propyl, isopropyl, ethyl, or methyl. In some embodiments, R^6 is ethyl or methyl. In some embodiments, R^6 is isopropyl. In some embodiments, R^6 is n-propyl, isopropyl, ethyl, or methyl, each of which is substituted with OH. In some embodiments, R^6 is isopropyl substituted with OH. In some embodiments, R^6 is ethyl substituted with OH. In some embodiments, R^6 is methyl substituted with OH.

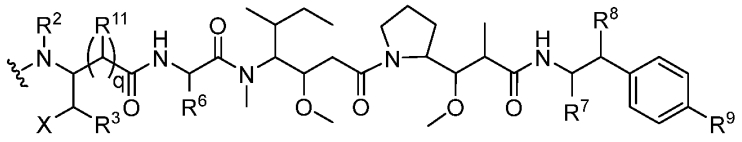
[0277] In some embodiments of Formula (I') or (Iz'), R^7 is C_1-C_4 alkyl substituted with OH. In some embodiments, R^7 is C_1-C_4 alkyl substituted by two OH moieties. In some embodiments, R^7 is n-propyl, isopropyl, ethyl, or methyl, each of which is substituted with OH. In some embodiments, $R^7$is C_1-C_4 alkyl. In some embodiments, R^7 is n-propyl, isopropyl, ethyl, or methyl. In some embodiments, R^7 is methyl. In some embodiments, R^7 is $-CH_2CH_2OH$ or CH_2OH. In some embodiments, R^7 is $-CH_2OH$. In some embodiments, R^7 is 5-6 membered heteroaryl. In some embodiments, R^7 is 5-membered heteroaryl. In some embodiments, R^7 is thiazolyl.

[0278] In some embodiments of Formula (I') or (Iz'), R^8, R^9, and R^{11} are H. In some embodiments, R^8 is OH, R^9 is H, and R^{11} is H. In some embodiments, R^8 and R^9 are each OH and R^{11} is H. In some embodiments, R^8 is OH, R^9 is H, and R^{11} is OH. In some embodiments, R^8 is H, R^9 is H, and R^{11} is OH.

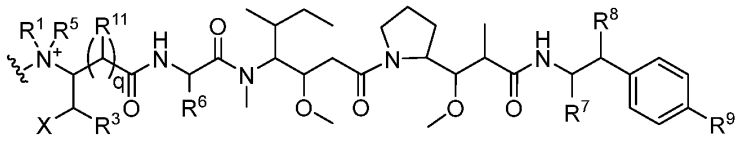
[0279] In some embodiments of Formula (I') or (Iz'), E is an optionally substituted 6-membered ring. In some embodiments, E is pyridine or phenyl, each of which is optionally substituted. In some embodiments, E is optionally substituted phenyl. In some embodiments, E is optionally substituted 5-6 membered heteroaryl. In some embodiments, E is optionally substituted 5-membered heteroaryl. In some embodiments, E is pyridine or phenyl, each of which is unsubstituted. In some embodiments, E is unsubstituted phenyl. In some embodiments, E is unsubstituted 5-6 membered heteroaryl. In some embodiments, E is unsubstituted 5-membered heteroaryl.

[0280] In some embodiments of Formula (I') or (Iz'), R^7 is $-CH_2OH$, R^8 is H, R^9 is H, and E is phenyl.

[0281] In some embodiments, the Drug Unit D has Formula (Ia') or (Ia''):



(Ia')



(Ia'')

or a salt thereof, wherein

R^1 and R^5 are independently C_1-C_4 alkyl;

X is H, OH, $-C(O)NR^aR^b$, $-S(O)_2R^a$, -S(O)-R^a $-S(O)_2NR^aR^b$, $-NHS(O)_2R^a$, or $-NHC(O)R^a$;

R^2, R^3, R^a, and R^b are each independently H or C_1-C_4 alkyl;

R^6 is C_1-C_4 alkyl;

R^7 is H, C_1-C_4 alkyl optionally substituted with OH, or 5-6 membered heteroaryl;

R^8, R^9, and R^{11} are each independently H or OH;

q is 0 or 1; and

the wavy line is the site of attachment to the rest of the Drug-Linker compound.

[0282] In some embodiments of Formula (Ia') and (Ia"), q is 0. In some embodiments, q is 1.

[0283] In some embodiments of Formula (Ia'), R^2 is C_1-C_4-alkyl. In some embodiments, R^2 is n-propyl, isopropyl, ethyl, or methyl. R^2 is ethyl or methyl. R^2 is methyl. In some embodiments, R^2 is H. In some embodiments, R^2 is ethyl, methyl, or H. In some embodiments, R^2 is methyl or H.

[0284] In some embodiments of Formula (Ia"), R^1 and R^5 are each independently n-propyl, isopropyl, ethyl, or methyl. In some embodiments, R^1 and R^5 are each independently ethyl or methyl. In some embodiments, R^1 and R^5 are each methyl. In some embodiments, R^1 is methyl and R^5 is n-propyl, isopropyl, ethyl, or methyl. In some embodiments, R^1 is methyl and R^5 is ethyl or methyl. In some embodiments, R^1 and R^5 are methyl.

[0285] In some embodiments of Formula (Ia') and (Ia"), X is H, OH, $-C(O)NR^aR^b$, $-S(O)_2R^a$, -S(O)-R^a, $-S(O)_2NR^aR^b$, $-NHS(O)_2R^a$, or $-NHC(O)R^a$. In some embodiments, X is OH, $-S(O)_2R^a$, -S(O)-R^a, $-S(O)_2NR^aR^b$, $-NHS(O)_2R^a$, or $-NHC(O)R^a$. In some embodiments, X is H or OH. In some embodiments, X is OH. In some embodiments, X is OH, $-NHS(O)_2R^a$, or $-NHC(O)R^a$. In some embodiments, X is OH, $-S(O)_2R^a$, -S(O)-R^a, or $-S(O)_2NR^aR^b$. In some embodiments, X is $-NHS(O)_2R^a$, or $-NHC(O)R^a$. In some embodiments, X is $-S(O)_2R^a$, -S(O)-R^a, or $-S(O)_2NR^aR^b$. In some embodiments, X is H, OH, $-NHS(O)_2R^a$, or $-NHC(O)R^a$. In some embodiments, X is H, OH, $-S(O)_2R^a$, -S(O)-R^a, or $-S(O)_2NR^aR^b$. In some embodiments, X is H, $-NHS(O)_2R^a$, or $-NHC(O)R^a$. In some embodiments, X is H, $-S(O)_2R^a$, -S(O)-R^a, or $-S(O)_2NR^aR^b$. In some embodiments, X is H, OH, or $-C(O)NR^aR^b$. In some embodiments, X is OH or $-C(O)NR^aR^b$. In some embodiments, X is H or $-C(O)NR^aR^b$. In some embodiments, R^a and R^b are independently H, n-propyl, isopropyl, ethyl, or methyl. In some embodiments, R^a and R^b are independently H,

ethyl, or methyl. In some embodiments, R^a and R^b are independently H or methyl. In some embodiments, R^a is H and R^b is n-propyl, isopropyl, ethyl, or methyl. In some embodiments, R^a is H and R^b is methyl.

[0286] In some embodiments of Formula (Ia') and (Ia"), R^3 is H or methyl. In some embodiments, R^3 is H. In some embodiments, R^3 is methyl.

[0287] In some embodiments of Formula (Ia') and (Ia"), R^6 is n-propyl, isopropyl, ethyl, or methyl. In some embodiments, R^6 is ethyl or methyl. In some embodiments, R^6 is isopropyl. In some embodiments, R^6 is n-propyl, isopropyl, ethyl, or methyl, each of which is substituted with OH. In some embodiments, R^6 is isopropyl substituted with OH. In some embodiments, R^6 is ethyl substituted with OH. In some embodiments, R^6 is methyl substituted with OH.

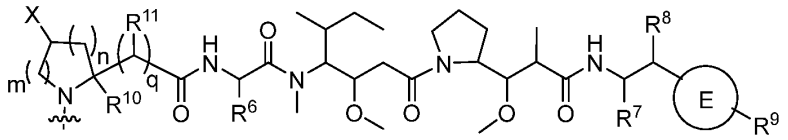
[0288] In some embodiments of Formula (Ia') and (Ia"), R^7 is C_1-C_4 alkyl substituted with OH. In some embodiments, R^7 is n-propyl, isopropyl, ethyl, or methyl, each of which is substituted with OH. In some embodiments, R^7 is $-CH_2CH_2OH$ or CH_2OH. In some embodiments, R^7 is $-CH_2OH$. In some embodiments, R^7 is C_1-C_4 alkyl. In some embodiments, R^7 is n-propyl, isopropyl, ethyl, or methyl. In some embodiments, R^7 is methyl. In some embodiments, R^7 is 5-6 membered heteroaryl. In some embodiments, R^7 is 5-membered heteroaryl. In some embodiments, R^7 is thiazolyl.

[0289] In some embodiments of Formula (Ia') and (Ia"), R^8, R^9, and R^{11} are H. In some embodiments, R^8 is OH, R^9 is H, and R^{11} is H. In some embodiments, R^8 and R^9 are each OH and R^{11} is H. In some embodiments, R^8 is OH, R^9 is H, and R^{11} is OH. In some embodiments, R^8 is H, R^9 is H, and R^{11} is OH.

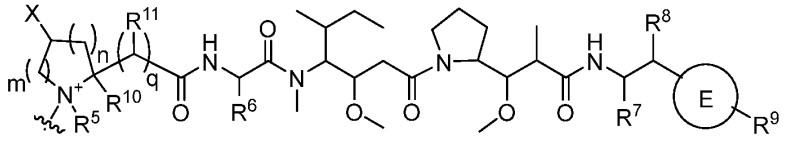
[0290] In some embodiments of Formula (Ia'), X is OH, R^3 is H or methyl, R^2 is C_1-C_4 alkyl, R_6 is C_1-C_4 alkyl, R^7 is C_1-C_4 alkyl optionally substituted with OH, R^8 is H or C_1-C_4 alkyl, and R^9 is H. In some embodiments, q is 0, X is OH, R^3 is H or methyl, R^2 is C_1-C_4 alkyl, R_6 is C_1-C_4 alkyl, R^7 is C_1-C_4 alkyl optionally substituted with OH, R^8 is H or C_1-C_4 alkyl, and R^9 is H.

[0291] In some embodiments of Formula (Ia"), X is OH, R^3 is H or methyl, R^1 C_1-C_4 alkyl, R^5 is C_1-C_4 alkyl, R_6 is C_1-C_4 alkyl, R^7 is C_1-C_4 alkyl optionally substituted with OH, R^8 is H or C_1-C_4 alkyl, and R^9 is H. In some embodiments, q is 0, X is OH, R^3 is H or methyl, R^1 C_1-C_4 alkyl, R^5 is C_1-C_4 alkyl, R_6 is C_1-C_4 alkyl, R^7 is C_1-C_4 alkyl optionally substituted with OH, R^8 is H or C_1-C_4 alkyl, and R^9 is H.

[0292] In some embodiments, of the Drug Unit D has Formula (Ib') or (Ib''):



(Ib')

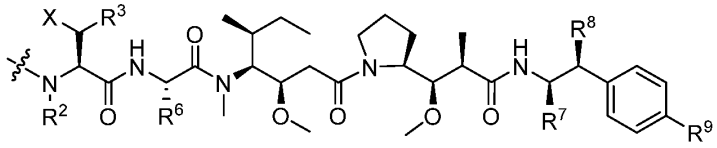


(Ib'')

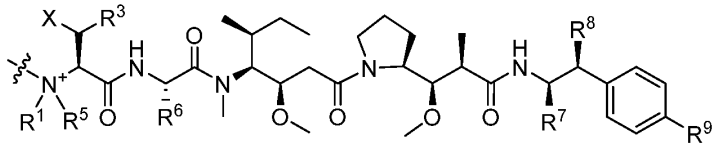
wherein the variables are as defined for Formula (Ib) and the wavy line is the site of attachment to the rest of the Drug-Linker compound.

[0293] In some embodiments of Formula (Ib') and (Ib''), R^7 is -CH_2OH, R^8 is H, and R^9 is H.

[0294] In some embodiments, the Drug Unit D has Formula (Ic') or (Ic''):



(Ic')

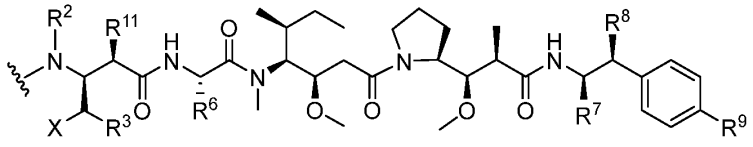


(Ic'')

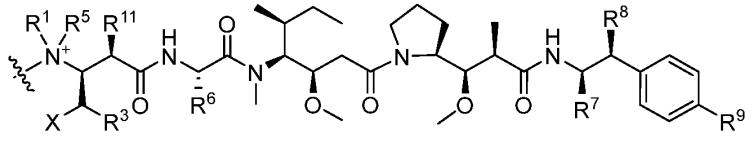
wherein the variables are as defined for Formula (Ic) and the wavy line is the site of attachment to the rest of the Drug-Linker compound.

[0295] In some embodiments of Formula (Ic') or (Ic''), X is OH and R^3 is H. In some embodiments, R^7 is -CH_2OH, R^8 is H, and R^9 is H. In some embodiments, X is OH, R^7 is -CH_2OH, R^8 is H, and R^9 is H. In some embodiments, X is OH, R^3 is H, R^7 is -CH_2OH, R^8 is H, and R^9 is H.

[0296] In some embodiments, the Drug Unit D has the Formula (Id') or (Id''):



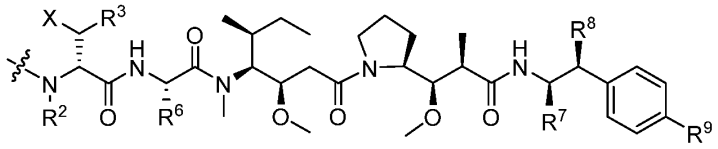
(Id')



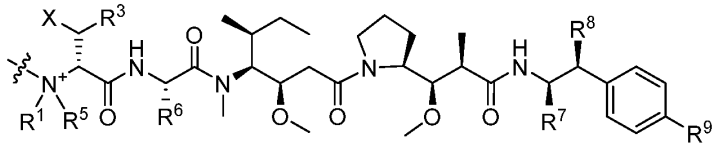
(Id")

wherein the variables are as defined for Formula (Id) and the wavy line is the site of attachement to the rest of the Drug-Linker compound.

[0297] In some embodiments, the Drug Unit D has Formula (Ie') or (Ie"):



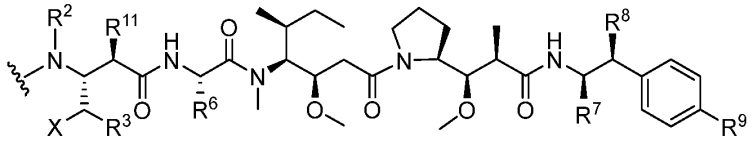
(Ie')



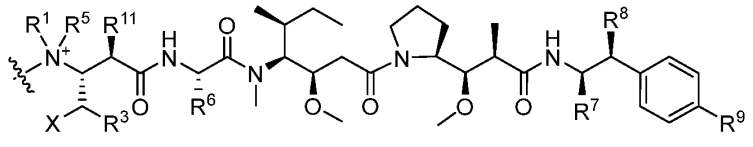
(Ie")

wherein the variables are as defined for Formula (Ie) and the wavy line is the site of attachment to the rest of the Drug-Linker compound.

[0298] In some embodiments, the Drug Unit D has the Formula (Id') or (Id"):



(If')



(If")

wherein the variables are as defined for Formula (If) and the wavy line is the site of attachement to the rest of the Drug-Linker compound.

[0299] In some embodiments of Formula (Id'), (Id''), (If'), or (If''), X is OH and R^3 is H. In some embodiments, R^7 is $-CH_2OH$, R^8 is H, and R^9 is H. In some embodiments, X is OH, R^7 is $-CH_2OH$, R^8 is H, and R^9 is H. In some embodiments, X is OH, R^3 is H, R^7 is $-CH_2OH$, R^8 is H, and R^9 is H.

[0300] In some embodiments of Formula (Ia''), (Ic''), (Id''), (Ie''), or (If'') the quaternized nitrogen atom prevents cyclization of the Drug Unit. In some embodiments, the quaternized nitrogen atom prevents premature release of the Drug Unit from the Drug-Linker compound or moiety (*e.g.*, in a Ligand-Drug Conjugate compound). In some embodiments, the quaternized nitrogen atom prevents cyclization and premature release of the Drug Unit from the Drug-Linker compound or moiety (*e.g.*, in a Ligand-Drug Conjugate compound).

2. Linker Unit Q

[0301] As noted above, is some embodiments, the Linker Unit Q has a formula selected from the group consisting of:

(i) Z'-A-RL-,
(ii) Z'-A-RL-Y-,
(iii) Z'-A-S^*-RL-,
(iv) Z'-A-S^*-RL-Y-,
(v) Z'-A-B(S^*)-RL-,
(vi) Z'-A-B(S^*)-RL-Y-,
(vii) Z'-A-,
(viii) Z'-A-S*-W-,
(ix) Z'-A-B(S*)-W-,
(x) Z'-A-S*-W-RL-, and
(xi) Z'-A-B(S*)-W-RL-;

wherein Z' is a Stretcher Unit; A is a bond or a Connector Unit; B is a Parallel Connector Unit; S^* is a Partitioning Agent; RL is Releasable Linker; W is an Amino Acid Unit; and Y is a Spacer Unit.

[0302] In other embodiments, the Linker Unit Q has a formula selected from the group consisting of:

(i) Z'-A-RL-,

(ii) Z'-A-RL-Y-,

(iii) Z'-A-S*-RL-,

(iv) Z'-A-S*-RL-Y-,

(x) Z'-A-S*-W-RL-, and

(xi) Z'-A-B(S*)-W-RL-.

[0303] In some embodiments, the Linker Unit Q has a formula selected from the group consisting of:

(v) Z'-A-B(S*)-RL-,

(vi) Z'-A-B(S*)-RL-Y-,

(ix) Z'-A-B(S*)-W-, and

(xi) Z'-A-B(S*)-W-RL-.

[0304] In some embodiments, the Linker Unit Q has a formula selected from the group consisting of:

(iii) Z'-A-S*-RL-,

(iv) Z'-A-S*-RL-Y-,

(v) Z'-A-B(S*)-RL-,

(vi) Z'-A-B(S*)-RL-Y-,

(viii) Z'-A-S*-W-,

(ix) Z'-A-B(S*)-W-,

(x) Z'-A-S*-W-RL-, and

(xi) Z'-A-B(S*)-W-RL-.

[0305] In some embodiments, the Linker Unit Q has a formula selected from the group consisting of:

(viii) Z'-A-S*-W-,

(ix) Z'-A-B(S*)-W-,

(x) Z'-A-S*-W-RL-, and

(xi) Z'-A-B(S*)-W-RL-.

3. Stretcher Unit Z'

[0306] A Stretcher Unit (Z) is a component of a Ligand-Drug Conjugate that acts to connect the Ligand Unit to the remainder of the conjugate. A Stretcher Unit precursor (Z') is

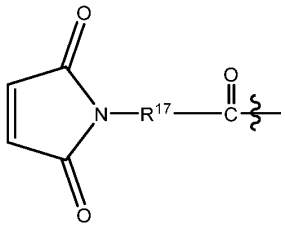
a component of a Drug-Linker compound or intermediate thereof has a functional group that can form a bond with a functional group of a targeting ligand to form a Stretcher Unit (Z).

[0307] In some embodiments, a Stretcher Unit precursor (Z') has an electrophilic group that is capable of interacting with a reactive nucleophilic group present on a Ligand Unit (e.g., an antibody) to provide a covalent bond between a Ligand Unit and the Stretcher Unit of a Linker Unit. Nucleophilic groups on an antibody having that capability include but are not limited to, sulfhydryl, hydroxyl and amino functional groups. In some aspects, the heteroatom of the nucleophilic group of an antibody is reactive to an electrophilic group on a Stretcher Unit precursor and can provide a covalent bond between the Ligand Unit and Stretcher Unit of a Linker Unit or Drug-Linker moiety. Useful electrophilic groups for that purpose include, but are not limited to, maleimide, haloacetamide groups, and NHS esters. The electrophilic group provides a convenient site for antibody attachment to form a Ligand-Drug Conjugate compound or Ligand Unit-Linker intermediate compound.

[0308] In other embodiments, a Stretcher Unit precursor has a reactive site which has a nucleophilic group that is reactive to an electrophilic group present on a Ligand Unit (e.g., an antibody). Useful electrophilic groups on an antibody for that purpose include, but are not limited to, aldehyde and ketone carbonyl groups. The heteroatom of a nucleophilic group of a Stretcher Unit precursor can react with an electrophilic group on an antibody and form a covalent bond to the antibody. Useful nucleophilic groups on a Stretcher Unit precursor for that purpose include, but are not limited to, hydrazide, hydroxylamine, amino, hydrazine, thiosemicarbazone, hydrazine carboxylate, and arylhydrazide. The electrophilic group on an antibody provides a convenient site for antibody attachment to form a Ligand-Drug Conjugate compound or Ligand Unit-Linker intermediate compound.

[0309] In some embodiments, a sulfur atom of a Ligand Unit is bound to a succinimide ring system of a Stretcher Unit formed by reaction of a thiol functional group of a targeting ligand with a maleimide moiety of the corresponding Stretcher Unit precursor. In other embodiments, a thiol functional group of a Ligand Unit reacts with an alpha haloacetamide moiety to provide a sulfur-bonded Stretcher Unit by nucleophilic displacement of its halogen substituent.

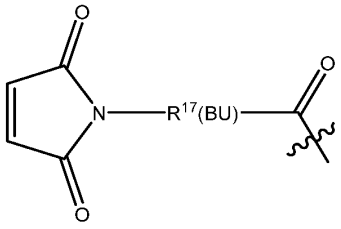
[0310] Illustrative Stretcher Units prior to conjugation to the Ligand Unit (i.e., Stretcher Unit precursors) comprise a maleimide moiety and are represented by structures including that of formula Z'a



(Z'a),

wherein the wavy line adjacent the carbonyl carbon atom indicates attachment to B, A, or S^*, in the formulae above, depending on the presence or absence of A and/or B, R^{17} is $–(CH_2)_{1\text{-}5}–$ or $–CH_2CH_2(OCH_2CH_2)_{1\text{-}36}–$. In some embodiments, R^{17} is $-CH_2-$, $-(CH_2)_2-$, $-(CH_2)_3-$, $-(CH_2)_4-$, $-(CH_2)_5-$, $–CH_2CH_2OCH_2CH_2-$, $–CH_2CH_2(OCH_2CH_2)_2–$, $–CH_2CH_2(OCH_2CH_2)_3–$, $–CH_2CH_2(OCH_2CH_2)_4–$, $–CH_2CH_2(OCH_2CH_2)_5–$, $–CH_2CH_2(OCH_2CH_2)_6–$, $–CH_2CH_2(OCH_2CH_2)_7–$, $–CH_2CH_2(OCH_2CH_2)_8–$, $–CH_2CH_2(OCH_2CH_2)_{10}–$, $–CH_2CH_2(OCH_2CH_2)_{12}–$, $–CH_2CH_2(OCH_2CH_2)_{14}–$, $–CH_2CH_2(OCH_2CH_2)_{16}–$, $–CH_2CH_2(OCH_2CH_2)_{18}–$, $–CH_2CH_2(OCH_2CH_2)_{20}–$, $–CH_2CH_2(OCH_2CH_2)_{24}–$, $–CH_2CH_2(OCH_2CH_2)_{28}–$, $–CH_2CH_2(OCH_2CH_2)_{32}–$, or $–CH_2CH_2(OCH_2CH_2)_{36}–$.

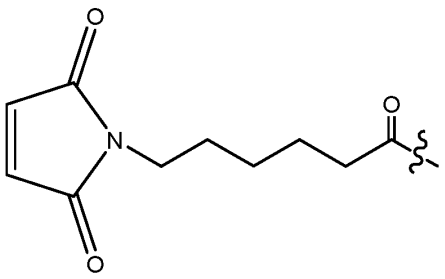
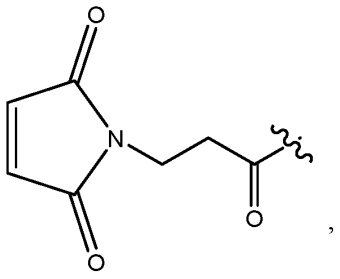
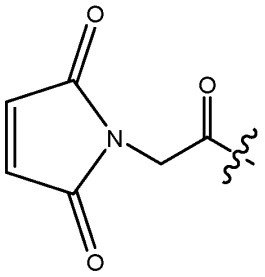
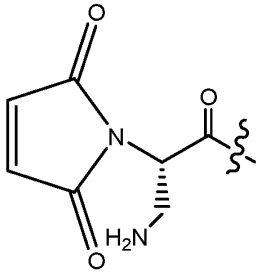
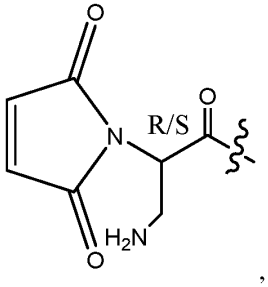
[0311] Other illustrative Stretcher Units prior to conjugation to the Ligand Unit (i.e., Stretcher Unit precursors) comprises a maleimide moiety and are represented by structures including that of formula Z'a-BU



(Z'a-BU),

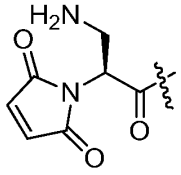
wherein the wavy line adjacent the carbonyl carbon atom indicates attachment to B, A, or S^*, in the formulae above, depending on the presence or absence of A and/or B, R^{17} is R^{17} is $–(CH_2)_{1\text{-}5}–$ or $–CH_2CH_2(OCH_2CH_2)_{1\text{-}5}–$, substituted with a Basic Unit (BU), such as an optionally substituted aminoalkyl, e.g., $–(CH_2)_xNH_2$, $–(CH_2)_xNHR^a$, and $–(CH_2)_xN(R^a)_2$, wherein subscript x is an integer of from 1-4, preferably R^{17} is $-CH_2-$ or $-CH_2CH_2-$ and subscript x is 1 or 2, and each R^a is independently selected from the group consisting of $C_{1\text{-}6}$ alkyl and $C_{1\text{-}6}$ haloalkyl, or two R^a groups are combined with the nitrogen to which they are attached to form an azetidinyl, pyrrolidinyl or piperidinyl group.

[0312] In some embodiments of formula Z'a, a Stretcher Unit precursor (Z') is represented by one of the following structures:


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, or

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wherein the wavy line adjacent to the carbonyl is as defined for Z'a or Z'a-BU.

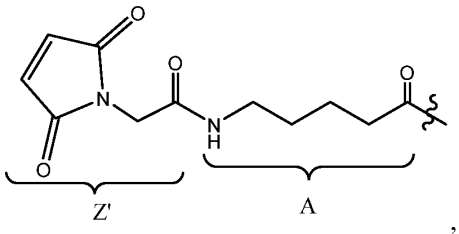
[0313] In other embodiments the Stretcher unit precursor (Z') comprises a maleimide moiety and is represented by the structure of:


,

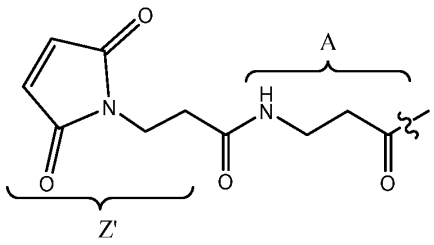
wherein the wavy line adjacent to the carbonyl is as defined for Z'a and the amino group is optional protonated or protected by an amino protecting group.

[0314] In Stretcher Units having a BU moiety, it will be understood that the amino functional group of that moiety is typically protected by an amino protecting group during synthesis, e.g., an acid labile protecting group (e.g., BOC).

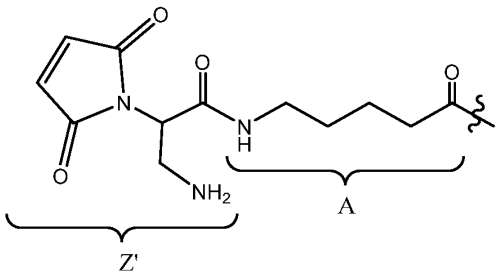
[0315] Illustrative Stretcher Unit precursors covalently attached to a Connector Unit that comprise the structure of Z'a or Z'a-BU in which $–R^{17}-$ or $–R^{17}(BU)-$ is $–CH_2-$, $-CH_2CH_2-$ or $–CH(CH_2NH_2)-$ have the following structures:



,



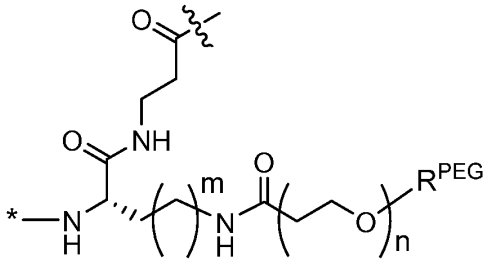
,



,

wherein the wavy line adjacent to the carbonyl is as defined for Z'a or Z'a-BU.

[0316] Other Stretcher Unit precursors bonded a Connector Unit (A) have the structures above wherein A in any one of the above Z'-A- and Z'(BU)-A- structures is replaced by a Parallel Connector Unit and Partitioning Agent (-B(S*)-) having the structure of



,

wherein subscript m ranges from 1 to 6; n ranges from 8 to 24; R^{PEG} is a PEG Capping Unit , preferably H, $–CH_3$, or $–CH_2CH_2CO_2H$, the asterisk (*) indicates covalent attachment to the Stretcher Unit precursor corresponding in structure to formula Z'a and the wavy line indicates covalent attachment to RL. In instances such as those shown here, the shown PEG group is meant to be exemplary of a variety of Partitioning Agents including PEG groups of different

lengths and other Partitioning Agents that are directly attached or modified for attachment to the Parallel Connector Unit.

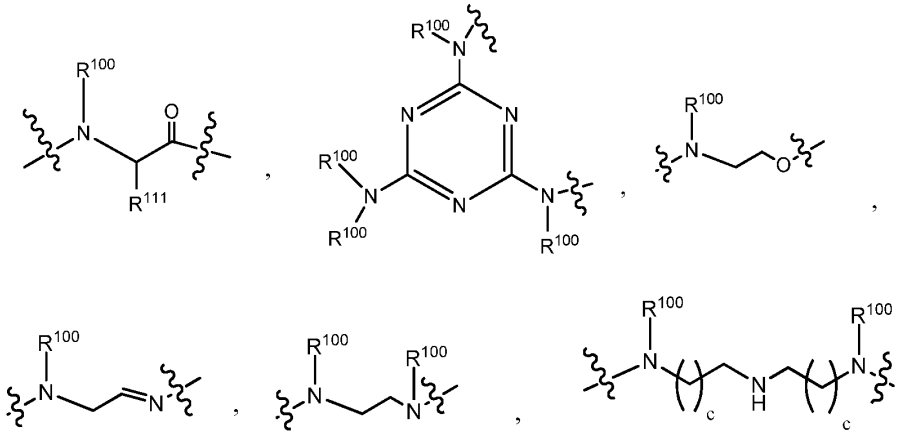
[0317] In some aspects of the prevent invention the Stretcher Unit has a mass of no more than about 1000 daltons, no more than about 500 daltons, no more than about 200 daltons, from about 30, 50 or 100 daltons to about 1000 daltons, from about 30, 50 or 100 daltons to about 500 daltons, or from about 30, 50 or 100 daltons to about 200 daltons.

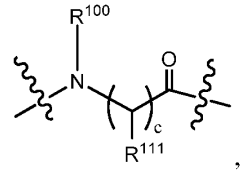
4. Connector Unit (A)

[0318] In some embodiments, a Connector Unit (A), is included in a Drug-Linker Compound in instances where it is desirable to add additional distance between the Stretcher Unit precursor (Z') and the Releasable Linker. In some embodiments, the extra distance will aid with activation within RL. Accordingly, the Connector Unit (A), when present, extends the framework of the Linker Unit. In that regard, a Connector Unit (A) is covalently bonded with the Stretcher Unit (or its precursor) at one terminus and is covalently bonded to the optional Parallel Connector Unit or the Partitioning Agent (S^*) at its other terminus.

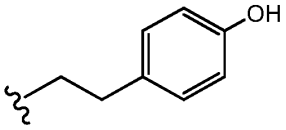
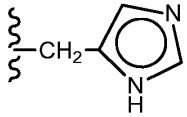
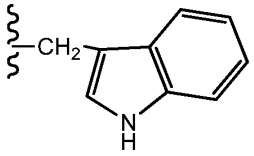
[0319] The skilled artisan will appreciate that the Connector Unit is any group that serves to provide for attachment of the Releasable Linker to the remainder of the Linker Unit (Q). The Connector Unit can, for example, comprise one or more (e.g., 1-10, preferably, 1, 2, 3, or 4) proteinogenic or non-proteinogenic amino acid, amino alcohol, amino aldehyde, diamino residues. In some embodiments, the Connector Unit is a single proteinogenic or non-proteinogenic amino acid, amino alcohol, amino aldehyde, or diamino residue. An exemplary amino acid capable of acting as Connector units is β-alanine.

[0320] In some of those embodiments, the Connector Unit has the formula denoted below:



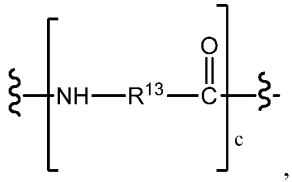
or ,

wherein the wavy lines indicate attachment of the Connector Unit within the Drug-Linker Compound; and wherein R^{111} is independently selected from the group consisting of hydrogen, *p*-hydroxybenzyl, methyl, isopropyl, isobutyl, *sec*-butyl, -CH_2OH, -$CH(OH)CH_3$, -$CH_2CH_2SCH_3$, -CH_2CONH_2, -CH_2COOH, -$CH_2CH_2CONH_2$, -CH_2CH_2COOH, -$(CH_2)_3NHC(=NH)NH_2$, -$(CH_2)_3NH_2$, -$(CH_2)_3NHCOCH_3$, -$(CH_2)_3NHCHO$, -$(CH_2)_4NHC(=NH)NH_2$, -$(CH_2)_4NH_2$, -$(CH_2)_4NHCOCH_3$, -$(CH_2)_4NHCHO$, -$(CH_2)_3NHCONH_2$, -$(CH_2)_4NHCONH_2$, -$CH_2CH_2CH(OH)CH_2NH_2$, 2-pyridylmethyl-, 3-pyridylmethyl-, 4-pyridylmethyl-,

, , and ,

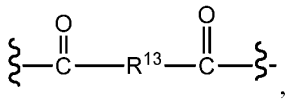
and each R^{100} is independently selected from hydrogen or -C_1-C_3 alkyl, preferably hydrogen or CH_3; and subscript c is an independently selected integer from 1 to 10, preferably 1 to 3.

[0321] A representative Connector Unit having a carbonyl group for attachment to the Partitioning Agent (S^*) or to –$B(S^*)$- is as follows:

,

wherein in each instance R^{13} is independently selected from the group consisting of –$CH_2CH_2(OCH_2CH_2)_k$–, -C_1-C_6 alkylene-, -C_3-C_8carbocyclo-, -arylene-, -C_1-C_{10} heteroalkylene-, -C_3-C_8heterocyclo-, -C_1-C_{10}alkylene-arylene-, -arylene-C_1-C_{10}alkylene-, -C_1-C_{10}alkylene-(C_3-C_8carbocyclo)-, -(C_3-C_8carbocyclo)-C_1-C_{10}alkylene-, -C_1-C_{10}alkylene-(C_3-C_8 heterocyclo)-, and -(C_3-C_8 heterocyclo)-C_1-C_{10} alkylene-, wherein subscript k is an integer ranging from 1 to 36 and the subscript c is an integer ranging from 1 to 4. In some embodiments R^{13} is -C_1-C_6 alkylene and c is 1.

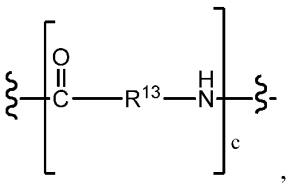
[0322] Another representative Connector Unit having a carbonyl group for attachment to Partitioning Agent (S^*) or to –B(S^*)- is as follows:



wherein R^{13} is

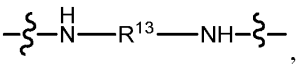
$–CH_2CH_2(OCH_2CH_2)_k–$, -C_1-C_6 alkylene-, -C_3-C_8carbocyclo-, -arylene-, -C_1-C_{10} heteroalkylene-, -C_3-C_8heterocyclo-, -C_1-C_{10}alkylene-arylene-, -arylene-C_1-C_{10}alkylene-, -C_1-C_{10}alkylene-(C_3-C_8carbocyclo)-, -(C_3-C_8carbocyclo)-C_1-C_{10}alkylene-, -C_1-C_{10}alkylene-(C_3-C_8 heterocyclo)-, or -(C_3-C_8 heterocyclo)-C_1-C_{10} alkylene-, wherein subscript k is an integer ranging from 1 to 36. In some embodiments R^{13} is -C_1-C_6 alkylene.

[0323] A representative Connector Unit having a NH moiety that attaches to Partitioning Agent (S^*) or to –B(S^*)- is as follows:



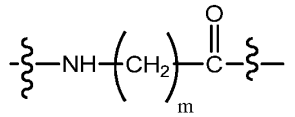
wherein in each instance, R^{13} is independently selected from the group consisting of $–CH_2CH_2(OCH_2CH_2)_k–$, -C_1-C_6 alkylene-, -C_3-C_8carbocyclo-, -arylene-, -C_1-C_{10} heteroalkylene-, -C_3-C_8heterocyclo-, -C_1-C_{10}alkylene-arylene-, -arylene-C_1-C_{10}alkylene-, -C_1-C_{10}alkylene-(C_3-C_8carbocyclo)-, -(C_3-C_8carbocyclo)-C_1-C_{10}alkylene-, -C_1-C_{10}alkylene-(C_3-C_8 heterocyclo)-, and -(C_3-C_8 heterocyclo)-C_1-C_{10} alkylene-, wherein subscript k is an integer ranging from 1 to 36 and subscript c is an integer ranging from 1 to 36. In some embodiments R^{13} is -C_1-C_6 alkylene and subscript c is 1.

[0324] Another representative Connector Unit having a NH moiety that attaches to Partitioning Agent (S^*) or to –B(S^*)- is as follows:

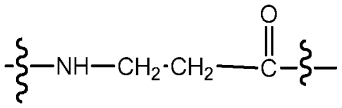


wherein R^{13} is $–CH_2CH_2(OCH_2CH_2)_k–$, -C_1-C_6 alkylene-, -C_3-C_8carbocyclo-, -arylene-, -C_1-C_{10} heteroalkylene-, -C_3-C_8heterocyclo-, -C_1-C_{10}alkylene-arylene-, -arylene-C_1-C_{10}alkylene-, -C_1-C_{10}alkylene-(C_3-C_8carbocyclo)-, -(C_3-C_8carbocyclo)-C_1-C_{10}alkylene-, -C_1-C_{10}alkylene-(C_3-C_8 heterocyclo)-, -(C_3-C_8 heterocyclo)-C_1-C_{10} alkylene-, –C(=O)C_1-C_6 alkylene- or -C_1-C_6 alkylene-C(=O)-C_1-C_6 alkylene, wherein subscript k is an integer ranging from 1 to 36.

[0325] Selected embodiments of Connector Units include those having the following structure of:



or



,

wherein the wavy line adjacent to the nitrogen indicates covalent attachment a Stretcher Unit (Z) (or its precursor Z'), and the wavy line adjacent to the carbonyl indicates covalent attachment to Partitioning Agent (S^*) or to –B(S^*)-; and m is an integer ranging from 1 to 6, preferably 2 to 6, more preferably 2 to 4.

5. Releasable Linker (RL)

[0326] The Releasable Linker (RL) is capable of linking to the Spacer Unit (Y) or the Drug Unit (D). RL comprises a cleavable bond (i.e., a reactive site) that upon action by an enzyme present within a hyper-proliferating cell or hyper-activated immune cells or characteristic of the immediate environment of these abnormal or unwanted cells, or upon non-enzymatic action due to conditions more likely experienced by hyper-proliferating cells in comparison to normal cells, releases free drug. Alternatively, RL comprises a cleavable bond that is more likely acted upon intracellularly in a hyper-proliferating cell or hyper-activated immune cell due to preferential entry into such cells in comparison to normal cells.

Peptide Releasable Linkers

[0327] In some embodiments, the Releasable Linker is a Peptide Releasable Linker. In some embodiments, the Peptide Releasable Linker (RL) will comprise one or more contiguous or non-contiguous sequences of amino acids (e.g., so that RL has 1 to no more than 12 amino acids). The Peptide Releasable Linker can comprise or consist of, for example, an amino acid, a dipeptide, tripeptide, tetrapeptide, pentapeptide, hexapeptide, heptapeptide, octapeptide, nonapeptide, decapeptide, undecapeptide or dodecapeptide unit. In some aspects, in the presence of an enzyme (e.g., a tumor-associated protease), an amide linkage between the amino acids is cleaved, which ultimately leads to release of free drug.

[0328] Each amino acid is proteinogenic or non-proteinogenic and/or a D- or L-isomer provided that RL comprises a cleavable bond that, when cleaved, initiates release of the Drug

Unit. In some embodiments, the Peptide Releasable Linker will comprise only proteinogenic amino acids. In some aspects, the Peptide Releasable Linker will have from 1 to no more than 12 amino acids in contiguous sequence.

[0329] In some embodiments, each amino acid is independently selected from the group consisting of alanine, arginine, aspartic acid, asparagine, histidine, glycine, glutamic acid, glutamine, phenylalanine, lysine, leucine, serine, tyrosine, threonine, isoleucine, proline, tryptophan, valine, cysteine, methionine, selenocysteine, ornithine, penicillamine, β-alanine, aminoalkanoic acid, aminoalkynoic acid, aminoalkanedioic acid, aminobenzoic acid, amino-heterocyclo-alkanoic acid, heterocyclo-carboxylic acid, citrulline, statine, diaminoalkanoic acid, and derivatives thereof. In some embodiments, each amino acid is independently selected from the group consisting of alanine, arginine, aspartic acid, asparagine, histidine, glycine, glutamic acid, glutamine, phenylalanine, lysine, leucine, serine, tyrosine, threonine, isoleucine, proline, tryptophan, valine, cysteine, methionine, and selenocysteine. In some embodiments, each amino acid is independently selected from the group consisting of alanine, arginine, aspartic acid, asparagine, histidine, glycine, glutamic acid, glutamine, phenylalanine, lysine, leucine, serine, tyrosine, threonine, isoleucine, proline, tryptophan, and valine. In some embodiments, each amino acid is selected from the proteinogenic or the non-proteinogenic amino acids.

[0330] In another embodiment, each amino acid is independently selected from the group consisting of the following L-(proteinogenic) amino acids: alanine, arginine, aspartic acid, asparagine, histidine, glycine, glutamic acid, glutamine, phenylalanine, lysine, leucine, serine, tyrosine, threonine, isoleucine, tryptophan and valine.

[0331] In another embodiment, each amino acid is independently selected from the group consisting of the following D-isomers of these proteinogenic amino acids: alanine, arginine, aspartic acid, asparagine, histidine, glycine, glutamic acid, glutamine, phenylalanine, lysine, leucine, serine, tyrosine, threonine, isoleucine, tryptophan and valine.

[0332] In certain embodiments, the Peptide Releasable Linker comprises only proteinogenic amino acids. In other embodiments, the Peptide Releasable Linker comprises only non-proteinogenic amino acids. In some embodiments, the Peptide Releasable Linker comprises a proteinogenic amino acid attached to a non-proteinogenic amino acid. In some embodiments, Peptide Releasable Linker comprises a proteinogenic amino acid attached to a D-isomer of a proteinogenic amino acid.

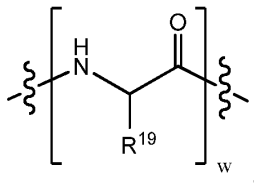
[0333] In another embodiment, each amino acid is independently selected from the group consisting of β-alanine, N-methylglycine, glycine, lysine, valine and phenylalanine.

[0334] Exemplary Peptide Releasable Linkers include dipeptides or tripeptides with-Val-Lys-Gly-, -Val-Cit-, -Phe-Lys- or –Val-Ala-.

[0335] Useful Peptide Releasable Linkers are designed and optimized in their selectivity for enzymatic cleavage by a particular enzyme, for example, a tumor-associated protease. In some embodiments, cleavage of a linkage is catalyzed by cathepsin B, C or D, or a plasmin protease.

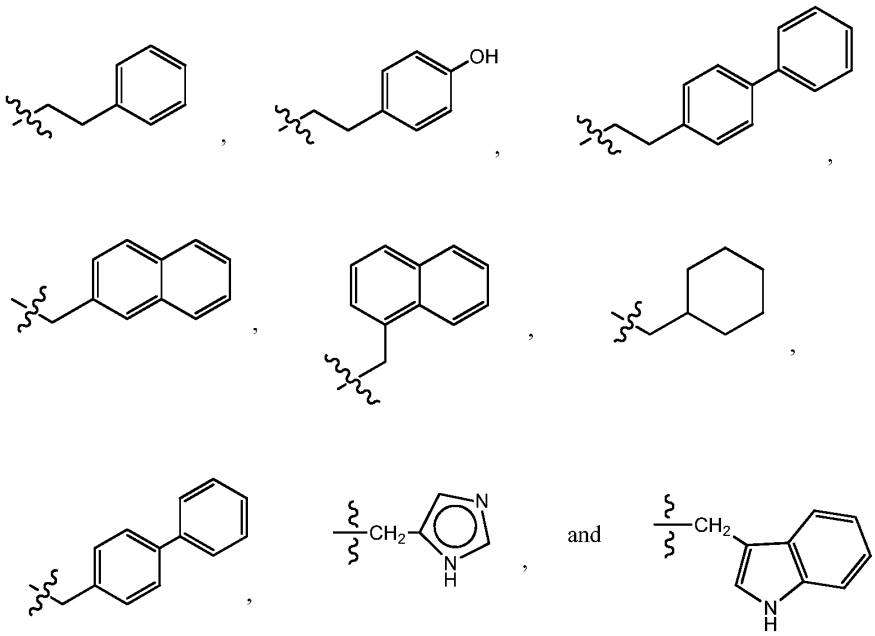
[0336] In some embodiments, the Peptide Releasable Linker (RL) will be represented by -(–AA-)$_{1\text{-}12}$-, or (–AA-AA-)$_{1\text{-}6}$ wherein AA is at each occurrence independently selected from proteinogenic or non-proteinogenic amino acids. In one aspect, AA is at each occurrence independently selected from proteinogenic amino acids. In another aspect, RL is a tripeptide having the formula: AA_1-AA_2- AA_3, wherein AA_1, AA_2 and AA_3 are each independently an amino acid and wherein AA_1 attaches to –NH- and AA_3 attaches to S*. In yet another aspect, AA_3 is gly or β-ala.

[0337] In some embodiments, the Peptide Releasable Linker has the formula denoted below in the square brackets, the subscript w is an integer ranging from 1 to 12; or w is 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, or 12; or w is 2, 3, or 4; or w is 3; or w is 4:



,

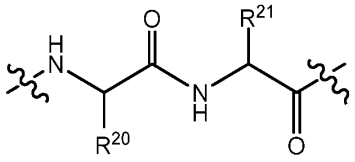
wherein R^{19} is, in each instance, independently selected from the group consisting of hydrogen, methyl, isopropyl, isobutyl, *sec*-butyl, benzyl, *p*-hydroxybenzyl, -CH_2OH, -$CH(OH)CH_3$, -$CH_2CH_2SCH_3$, -CH_2CONH_2, -CH_2COOH, -$CH_2CH_2CONH_2$, -CH_2CH_2COOH, -$(CH_2)_3NHC(=NH)NH_2$, -$(CH_2)_3NH_2$, -$(CH_2)_3NHCOCH_3$, -$(CH_2)_3NHCHO$, -$(CH_2)_4NHC(=NH)NH_2$, -$(CH_2)_4NH_2$, -$(CH_2)_4NHCOCH_3$, -$(CH_2)_4NHCHO$, -$(CH_2)_3NHCONH_2$, -$(CH_2)_4NHCONH_2$, -$CH_2CH_2CH(OH)CH_2NH_2$, 2-pyridylmethyl-, 3-pyridylmethyl-, 4-pyridylmethyl-, phenyl, cyclohexyl,



. In some aspects, the subscript w is not 3.

[0338] In some aspects, each R^{19} is independently hydrogen, methyl, isopropyl, isobutyl, *sec*-butyl, $-(CH_2)_3NH_2$, or $-(CH_2)_4NH_2$. In some aspects, each R^{19} is independently hydrogen, isopropyl, or $-(CH_2)_4NH_2$.

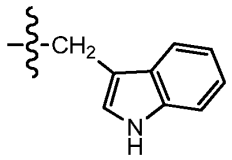
[0339] Illustrative Peptide Releasable Linkers are represented by formulae (Pa), (Pb) and (Pc):

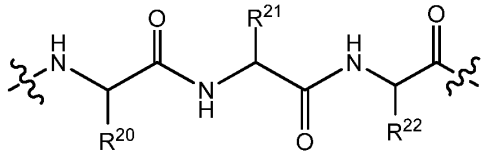


(Pa),

wherein R^{20} and R^{21} are as follows:

R^{20}	R^{21}
benzyl	$(CH_2)_4NH_2$;
methyl	$(CH_2)_4NH_2$;
isopropyl	$(CH_2)_4NH_2$;
isopropyl	$(CH_2)_3NHCONH_2$;
benzyl	$(CH_2)_3NHCONH_2$;
isobutyl	$(CH_2)_3NHCONH_2$;

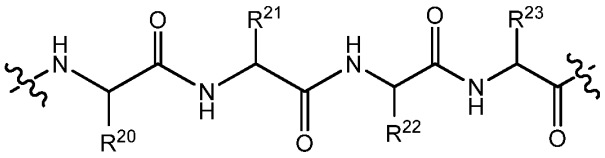
sec-butyl	$(CH_2)_3NHCONH_2$;
	$(CH_2)_3NHCONH_2$;
benzyl	methyl; and
benzyl	$(CH_2)_3NHC(=NH)NH_2$;



(Pb),

wherein R^{20}, R^{21} and R^{22} are as follows:

R^{20}	R^{21}	R^{22}
benzyl	benzyl	$-(CH_2)_4NH_2$
isopropyl	benzyl	$-(CH_2)_4NH_2$
H	Benzyl	$-(CH_2)_4NH_2$
isopropyl	$-(CH_2)_4NH_2$	-H



(Pc),

wherein R^{20}, R^{21}, R^{22} and R^{23} are as follows:

R^{20}	R^{21}	R^{22}	R^{23}
H	benzyl	isobutyl	H; and
methyl	isobutyl	methyl	isobutyl.

[0340] In some embodiments, RL comprises a peptide selected from the group consisting of gly-gly, gly-gly-gly, gly-gly-gly-gly, val-gly-gly, val-cit-gly, val-gln-gly, val-glu-gly, phe-lys-gly, leu-lys-gly, gly-val-lys-gly, val-lys-gly-gly, val-lys-gly, val-lys-ala, val-lys-leu, leu-leu-gly, gly-gly-phe-gly, gly-gly-phe-gly-gly, val-gly, and val-lys-β-ala.

[0341] In other embodiments, RL comprises a peptide selected from the group consisting of gly-gly-gly, gly-gly-gly-gly, val-gly-gly, val-cit-gly, val-gln-gly, val-glu-gly, phe-lys-gly, leu-lys-gly, gly-val-lys-gly, val-lys-gly-gly, val-lys-gly, val-lys-ala, val-lys-leu, leu-leu-gly, gly-gly-phe-gly, and val-lys-β-ala.

[0342] In still other embodiments, RL comprises a peptide selected from the group consisting of gly-gly-gly, val-gly-gly, val-cit-gly, val-gln-gly, val-glu-gly, phe-lys-gly, leu-lys-gly, val-lys-gly, val-lys-ala, val-lys-leu, leu-leu-gly and val-lys-β-ala.

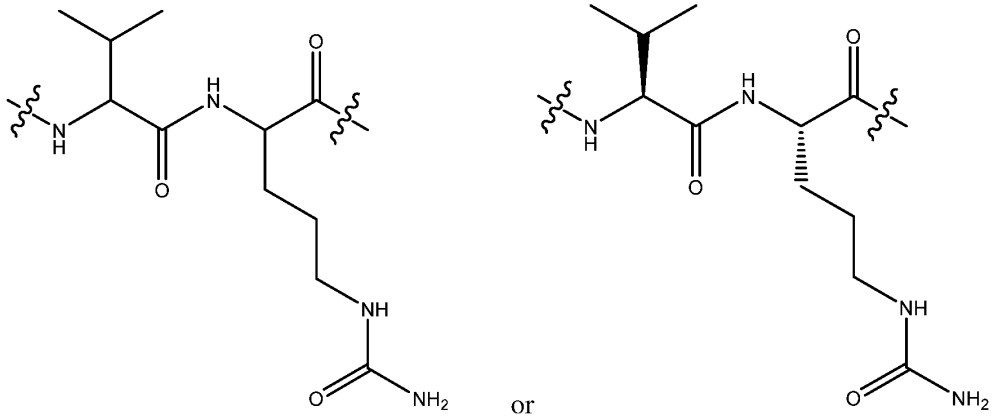
[0343] In yet other embodiments, RL comprises a peptide selected from the group consisting of gly-gly-gly-gly, gly-val-lys-gly, val-lys-gly-gly, and gly-gly-phe-gly.

[0344] In other embodiments, RL is a peptide selected from the group consisting of val-gln-gly, val-glu-gly, phe-lys-gly, leu-lys-gly, val-lys-gly, val-lys-ala, val-lys-leu, leu-leu-gly and val-lys-β-ala.

[0345] In still other embodiments, RL is val-lys-gly.

[0346] In still other embodiments, RL is val-lys-β-ala.

[0347] In some embodiments, the Releasable Linker RL is



or

wherein the wavy line adjacent to the -NH- group indicates attachment to the Stretcher Unit Z' or the Connector Unit A and the wavy line adjacent to the -C(=O)- group indicates attachment to the Spacer Unit Y or the Drug Unit D.

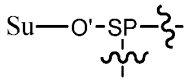
Glycoside Unit Releasable Linkers

[0348] In some embodiments, the Releasable Linker is a Glycoside (e.g., Glucuronide) Unit. In such embodiments, a self-immolation cascade is activated by operation of a glycosidase on a carbohydrate moiety of the Glycoside (e.g., Glucuronide) Unit. A number

of sugars are useful in the embodiments described herein. Particular carbohydrate moieties include those of Galactose, Glucose, Mannose, Xylose, Arabinose, Mannose-6-phosphate, Fucose, Rhamnose, Gulose, Allose, 6-deoxy-glucose, Lactose, Maltose, Cellobiose, Gentiobiose, Maltotriose, GlcNAc, GalNAc and maltohexaose.

[0349] A Glycoside (e.g., Glucuronide) Unit typically comprises a sugar moiety (Su) linked via an oxygen glycosidic bond to a self-immolative spacer. Cleavage of the oxygen glycosidic bond initiates the self-immolation reaction sequence that result in release of free drug. In some embodiments, the self-immolation sequence is activated from cleavage by β-glucuronidase of a Glycoside (e.g., Glucuronide) Unit, which is an exemplary glycoside unit. The Glycoside (e.g., Glucuronide) Unit comprises an activation unit and a self-immolative Spacer Unit. The Glycoside (e.g., Glucuronide) Unit comprises a sugar moiety (Su) linked via an oxygen glycosidic bond to a self-immolative Spacer Unit.

[0350] In some embodiments, a Glycoside (e.g., Glucuronide) Unit comprises a sugar moiety (Su) linked via an oxygen glycoside bond (-O'-) to a Self-immolative Unit (SP) of the formula:

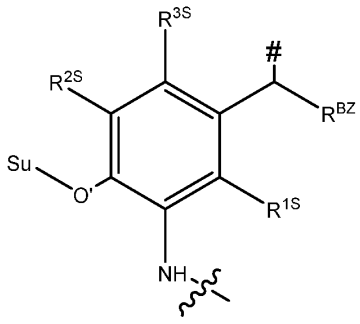


,

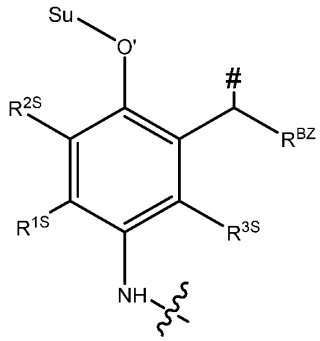
wherein the wavy lines indicate covalent attachment to the Drug Unit or to a Spacer Unit that is attached to the Drug Unit, and to the Stretcher Unit precursor (Z'), either directly or indirectly through the Connector Unit (A) or Parallel Connector Unit (B), Partitioning Agent (S^*) or combinations of the Connector Unit and Parallel Connector Unit, as the case may be.

[0351] The oxygen glycosidic bond (-O'-) is typically a β-glucuronidase-cleavage site (i.e., Su is from glucuronide), such as a glycoside bond cleavable by human, lysosomal β-glucuronidase.

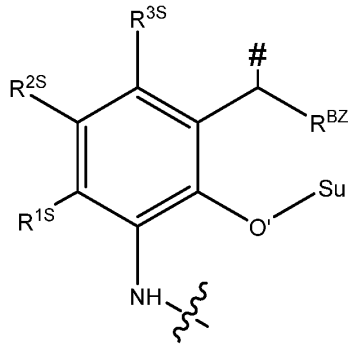
[0352] In some embodiments, the Glycoside (e.g., Glucuronide) Unit is represented by formula Ga, Gb, or Gc:



(Ga),



(Gb), or

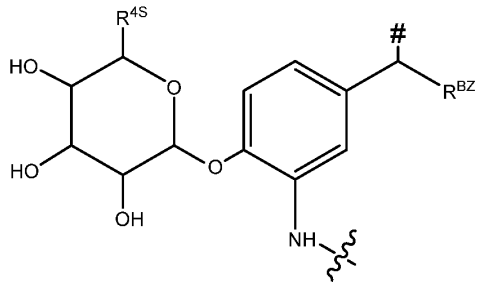


(Gc);

wherein Su is a Sugar moiety, -O'- represents an oxygen glycosidic bond; R^{1S}, R^{2S} and R^{3S} independently are hydrogen, a halogen, -CN,-NO_2, or other electron withdrawing group, or an electron donating group; R^{BZ} is selected from the group consisting of C_1-C_6 alkyl, C_1-C_6 haloalkyl, a PEG unit, a cyclodextrin unit, a polyamide, a hydrophilic peptide, a polysaccharide, and a dendrimer; and wherein the wavy line indicates attachment to a Stretcher Unit precursor (Z'), either directly or indirectly through a Connector Unit or Parallel Connector Unit or Connector unit and Parallel Connector Unit); and # indicates attachment to the Drug Unit or to a Spacer (either directly or indirectly via an intervening functional group or other moiety).

[0353] In some embodiments, R^{1S}, R^{2S}, and R^{3S} are independently selected from hydrogen, halogen, -CN, or -NO_2. In some embodiments, R^{1S}, R^{2S} and R^{3S} are each hydrogen. In some embodiments, R^{2S} is an electron withdrawing group, preferably NO_2, and R^{1S} and R^{3S} are each hydrogen.

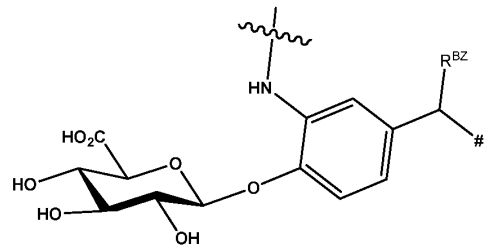
[0354] In some such aspects the activatable self-immolative group capable of glycosidase cleavage to initiate the self-immolative reaction sequence is represented by the formula Gd:



(Gd),

wherein R^{4S} is CH_2OH or $–CO_2H$, the wavy line indicates covalent attachment to a Stretcher Unit (Z) (or its precursor Z'), either directly or indirectly through a Connector Unit or Parallel Connector Unit or Connector unit and Parallel Connector Unit, and the hash mark (#) indicates covalent attachment to the methylene carbamate unit.

[0355] In some embodiments wherein the activatable self-immolative moiety comprises a Glycoside (e.g., Glucuronide) Unit, it is represented by the following formula Ge:



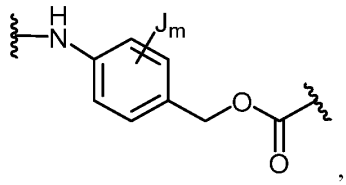
(Ge),

wherein the wavy line indicates covalent attachment to a Stretcher Unit (Z) (or its precursor Z'), either directly or indirectly through a Connector Unit or Parallel Connector Unit or Connector unit and Parallel Connector Unit and the hash mark (#) indicates covalent attachment of the benzylic carbon of a Spacer or functional group attached to the Drug Unit. In some embodiments, the structure of formula Ge is attached to the Drug Unit via a quaternized tertiary amine (N^+), wherein the nitrogen atom is from a tertiary amine functional group on the unconjugated Drug Unit.

[0356] Another type of Releasable Linker that provides a mechanism for separation of the Drug Unit from the Ligand Unit and other components of the Linker Unit through activation of a self-immolation cascade within the Linker Unit comprises a p-aminobenzyloxycarbonyl (PAB) moiety whose phenylene component is substituted with J_m wherein the subscript m indicating the number of substituents is an integer ranging from 0-4, and each J is independently -C_1-C_8 alkyl, -O-(C_1-C_8 alkyl), -halogen, -nitro or -cyano.

[0357] In some embodiments, RL is a self-immolative group capable of releasing -D without the need for a separate hydrolysis step or subsequent self-immolative event. In some embodiments, -RL- is a PAB moiety that is linked to the carbonyl of -W- via the amino nitrogen atom of the PAB group, and connected directly to -D via a carbonate group. In related embodiments, -RL- comprises a PAB moiety that is linked to the carbonyl of -A-, -S*- or –B- via the amino nitrogen atom of the PAB group, and connected directly to -D via a carbonate group. Without being bound by any particular theory or mechanism, a possible mechanism of Drug release from RL comprises a PAB moiety in which RL is attached directly to -D via a carbonate group is shown in Toki *et al.* (2002) J Org. Chem. 67:1866-1872.

[0358] In some embodiments, RL units containing a PAB moiety are represented by the formula:

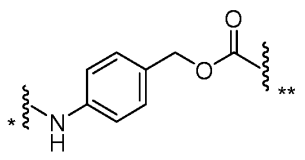


wherein subscript m is an integer ranging from 0-4, and each J is independently -C_1-C_8 alkyl, -O-(C_1-C_8 alkyl), -halogen, -nitro or –cyano.

[0359] Other examples of self-immolative groups include, but are not limited to, aromatic compounds that are electronically similar to the PAB moiety such as 2-aminoimidazol-5-methanol derivatives (Hay *et al.* (1999) Bioorg. Med. Chem. Lett. 9:2237) and ortho or para-aminobenzylacetals. Other RLs undergo cyclization upon amide bond hydrolysis, such as substituted and unsubstituted 4-aminobutyric acid amides (Rodrigues *et al.*, Chemistry Biology, 1995, 2, 223), appropriately substituted bicyclo[2.2.1] and bicyclo[2.2.2] ring systems (Storm, *et al.*, J. Amer. Chem. Soc., 1972, 94, 5815) and 2-aminophenylpropionic acid amides (Amsberry, *et al.*, J. Org. Chem., 1990, 55, 5867).

[0360] In one embodiment, RL is a branched bis(hydroxymethyl)styrene (BHMS) unit.

[0361] In some embodiments, RL has the formula:



wherein the wavy line marked with ** indicates the site of attachment to D; and the wavy line marked with * indicates the point of attachment to additional linker components of Q. In some embodiments, a PAB-containing RL is directly attached to the Drug Unit.

6. Partitioning Agent S^*

[0362] The Ligand-Drug Conjugates described herein can also include a Partitioning Agent (S^*). The Partitioning Agent portions are useful, for example, to mask the hydrophobicity of particular Drug Units or Linking Unit components.

[0363] Representative Partitioning Agents include polyethylene glycol (PEG) units, cyclodextrin units, polyamides, hydrophilic peptides, polysaccharides and dendrimers.

[0364] When the polyethylene glycol (PEG) units, cyclodextrin units, polyamides, hydrophilic peptides, polysaccharides or dendrimers are included in Q, the groups may be present as an 'in line' component or as a side chain or branched component. For those embodiments in which a branched version is present, the Linker Units can include a lysine residue (or Parallel Connector Unit, B) that provides simple functional conjugation of, for example, the PEG unit, to the remainder of the Linking Unit.

Polyethylene Glycol (PEG) Unit

[0365] When present, polydisperse PEGs, monodisperse PEGs, and discrete PEGs are used as part of the Partitioning Agents in Compounds of the present invention. Polydisperse PEGs are a heterogeneous mixture of sizes and molecular weights whereas monodisperse PEGs are typically purified from heterogeneous mixtures and are therefore provide a single chain length and molecular weight. Preferred PEG Units are discrete PEGs, compounds that are synthesized in stepwise fashion and not via a polymerization process. Discrete PEGs provide a single molecule with defined and specified chain length.

[0366] The PEG Unit provided herein can comprise one or multiple polyethylene glycol chains. A polyethylene glycol chain is composed of at least two ethylene oxide (CH_2CH_2O) subunits. In some embodiments the polyethylene glycol chains are linked together, for example, in a linear, branched or star shaped configuration. Typically, at least one of the PEG chains is derivitized at one end for covalent attachment to an appropriate site on a component of the Linker Unit (e.g. B) or is used as an in-line (e.g., bifunctional) linking group within to covalently join two of the Linker Unit components (e.g., Z-A-S^*-RL- , Z-A-S^*-RL-Y-). Exemplary attachments within the Linker Unit are by means of non-conditionally cleavable linkages or via conditionally cleavable linkages. Exemplary

attachments are via amide linkage, ether linkages, ester linkages, hydrazone linkages, oxime linkages, disulfide linkages, peptide linkages or triazole linkages. In some embodiments, attachment within the Linker Unit is by means of a non-conditionally cleavable linkage. In some embodiments, attachment within the Linker Unit is not via an ester linkage, hydrazone linkage, oxime linkage, or disulfide linkage. In some embodiments, attachment within the Linker Unit is not via a hydrazone linkage.

[0367] A conditionally cleavable linkage refers to a linkage that is not substantially sensitive to cleavage while circulating in the plasma but is sensitive to cleavage in an intracellular or intratumoral environment. A non-conditionally cleavable linkage is one that is not substantially sensitive to cleavage in any biological environment. Chemical hydrolysis of a hydrazone, reduction of a disulfide, and enzymatic cleavage of a peptide bond or glycosidic linkage are examples of conditionally cleavable linkages.

[0368] In some embodiments, the PEG Unit is directly attached to a Parallel Connector Unit B, wherein the other terminus (or termini) of the PEG Unit is free and untethered and may take the form of a methoxy, carboxylic acid, alcohol or other suitable functional group. The methoxy, carboxylic acid, alcohol or other suitable functional group acts as a cap for the terminal PEG subunit of the PEG Unit. By untethered, it is meant that the PEG Unit will not be attached at that untethered site to a Drug Unit, to an antibody, or to another linking component. The skilled artisan will understand that the PEG Unit in addition to comprising repeating ethylene glycol subunits may also contain non-PEG material (e.g., to facilitate coupling of multiple PEG chains to each other). Non-PEG material refers to the atoms in the PEG Unit that are not part of the repeating $-CH_2CH_2O-$ subunits. In some embodiments provided herein, the PEG Unit comprises two monomeric PEG chains attached to each other via non-PEG elements. In other embodiments provided herein, the PEG Unit comprises two linear PEG chains attached to a central core or Parallel Connector Unit (i.e., the PEG Unit itself is branched).

[0369] There are a number of PEG attachment methods available to those skilled in the art, [see, e.g., Goodson, et al. (1990) *Bio/Technology* **8**:343 (PEGylation of interleukin-2 at its glycosylation site after site-directed mutagenesis); EP 0 401 384 (coupling PEG to G-CSF); Malik, et al., (1992) *Exp. Hematol.* **20**:1028-1035 (PEGylation of GM-CSF using tresyl chloride); PCT Pub. No. WO 90/12874 (PEGylation of erythropoietin containing a recombinantly introduced cysteine residue using a cysteine-specific mPEG derivative); U.S. Pat. No. 5,757,078 (PEGylation of EPO peptides); U.S. Pat. No. 5,672,662 (Poly(ethylene

glycol) and related polymers monosubstituted with propionic or butanoic acids and functional derivatives thereof for biotechnical applications); U.S. Pat. No. 6,077,939 (PEGylation of an N-terminal .alpha.-carbon of a peptide); Veronese et al., (1985) *Appl. Biochem. Biotechnol* **11**:141-142 (PEGylation of an N-terminal α-carbon of a peptide with PEG-nitrophenylcarbonate ("PEG-NPC") or PEG-trichlorophenylcarbonate); and Veronese (2001) *Biomaterials* **22**:405-417 (Review article on peptide and protein PEGylation)].

[0370] For example, PEG may be covalently bound to amino acid residues via a reactive group. Reactive groups are those to which an activated PEG molecule may be bound (e.g., a free amino or carboxyl group). For example, N-terminal amino acid residues and lysine (K) residues have a free amino group; and C-terminal amino acid residues have a free carboxyl group. Thiol groups (e.g., as found on cysteine residues) can also be useful as a reactive group for attaching PEG. In addition, enzyme-assisted methods for introducing activated groups (e.g., hydrazide, aldehyde, and aromatic-amino groups) specifically at the C-terminus of a polypeptide have been described (see Schwarz, et al. (1990) *Methods Enzymol.* **184**:160; Rose, et al. (1991) *Bioconjugate Chem.* **2**:154; and Gaertner, et al. (1994) *J. Biol. Chem.* **269**:7224].

[0371] In some embodiments, PEG molecules may be attached to amino groups using methoxylated PEG ("mPEG") having different reactive moieties. Non-limiting examples of such reactive moieties include succinimidyl succinate (SS), succinimidyl carbonate (SC), mPEG-imidate, para-nitrophenylcarbonate (NPC), succinimidyl propionate (SPA), and cyanuric chloride. Non-limiting examples of such mPEGs include mPEG-succinimidyl succinate (mPEG-SS), $mPEG_2$-succinimidyl succinate ($mPEG_2$-SS); mPEG-succinimidyl carbonate (mPEG-SC), $mPEG_2$-succinimidyl carbonate ($mPEG_2$-SC); mPEG-imidate, mPEG-para-nitrophenylcarbonate (mPEG-NPC), mPEG-imidate; $mPEG_2$-para-nitrophenylcarbonate ($mPEG_2$-NPC); mPEG-succinimidyl propionate (mPEG-SPA); $mPEG_2$-succinimidyl propionate ($mPEG_2$-SPA); mPEG-N-hydroxy-succinimide (mPEG-NHS); $mPEG_2$-N-hydroxy-succinimide ($mPEG_2$-NHS); mPEG-cyanuric chloride; $mPEG_2$-cyanuric chloride; $mPEG_2$-Lysinol-NPC, and $mPEG_2$-Lys-NHS.

[0372] Generally, at least one of the PEG chains that make up the PEG Unit is functionalized so that it is capable of covalent attachment to other Linker Unit components.

[0373] Functionalization includes, for example, via an amine, thiol, NHS ester, maleimide, alkyne, azide, carbonyl, or other functional group. In some embodiments, the

PEG Unit further comprises non-PEG material (i.e., material does not comprise -CH_2CH_2O-) that provides coupling to other Linker Unit components or to facilitate coupling of two or more PEG chains.

[0374] The presence of the PEG Unit (or other Partitioning Agent) in the Linker Unit can have two potential impacts upon the pharmacokinetics of the resulting Ligand-Drug Conjugate. The desired impact is a decrease in clearance (and consequent increase in exposure) that arises from the reduction in non-specific interactions induced by the exposed hydrophobic elements of the Ligand-Drug Conjugate or to the Drug Unit itself. The second impact is undesired and is a decrease in volume and rate of distribution that sometimes arises from the increase in the molecular weight of the Ligand-Drug Conjugate.

[0375] Increasing the number of PEG subunits increases the hydrodynamic radius of a conjugate, typically resulting in decreased diffusivity. In turn, decreased diffusivity typically diminishes the ability of the Ligand-Drug Conjugate to penetrate into a tumor (Schmidt and Wittrup, *Mol Cancer Ther* 2009;8:2861-2871). Because of these two competing pharmacokinetic effects, it is desirable to use a PEG that is sufficiently large to decrease the Ligand-Drug Conjugate clearance thus increasing plasma exposure, but not so large as to greatly diminish its diffusivity, to an extent that it interferes with the ability of the Ligand-Drug Conjugate to reach the intended target cell population. See the examples (e.g., examples 1, 18, and 21) of US2016/0310612, which are incorporated by reference herein, for methodology for selecting an optimal PEG size for a particular drug-linker.

[0376] In one group of embodiments, the PEG Unit comprises one or more linear PEG chains each having at least 2 subunits, at least 3 subunits, at least 4 subunits, at least 5 subunits, at least 6 subunits, at least 7 subunits, at least 8 subunits, at least 9 subunits, at least 10 subunits, at least 11 subunits, at least 12 subunits, at least 13 subunits, at least 14 subunits, at least 15 subunits, at least 16 subunits, at least 17 subunits, at least 18 subunits, at least 19 subunits, at least 20 subunits, at least 21 subunits, at least 22 subunits, at least 23 subunits, or at least 24 subunits. In some embodiments, the PEG Unit comprises a combined total of at least 4 subunits, at least 6 subunits, at least 8 subunits, at least 10 subunits, or at least 12 subunits. In some such embodiments, the PEG Unit comprises no more than a combined total of about 72 subunits, preferably no more than a combined total of about 36 subunits.

[0377] In one group of embodiments, the PEG Unit comprises one or more linear PEG chains each having 2 subunits, 3 subunits, 4 subunits, 5 subunits, 6 subunits, 7 subunits, 8

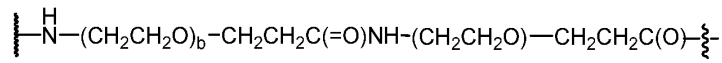
subunits, 9 subunits, 10 subunits, 11 subunits, 12 subunits, 13 subunits, 14 subunits, 15 subunits, 16 subunits, 17 subunits, 18 subunits, 19 subunits, 20 subunits, 21 subunits, 22 subunits, 23 subunits, or 24 subunits. In some embodiments, the PEG Unit comprises a combined total of 4 subunits, 6 subunits, 8 subunits, 10 subunits, or 12 subunits. In some such embodiments, the PEG Unit comprises no more than a combined total of about 72 subunits, preferably no more than a combined total of about 36 subunits.

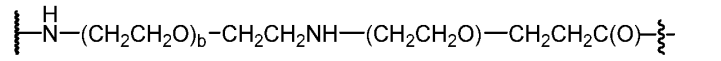
[0378] In another group of embodiments, the PEG Unit comprises a combined total of from 4 to 72, 4 to 60, 4 to 48, 4 to 36 or 4 to 24 subunits, from 5 to 72, 5 to 60, 5 to 48, 5 to 36 or 5 to 24 subunits, from 6 to 72, 6 to 60, 6 to 48, 6 to 36 or from 6 to 24 subunits, from 7 to 72, 7 to 60, 7 to 48, 7 to 36 or 7 to 24 subunits, from 8 to 72, 8 to 60, 8 to 48, 8 to 36 or 8 to 24 subunits, from 9 to 72, 9 to 60, 9 to 48, 9 to 36 or 9 to 24 subunits, from 10 to 72, 10 to 60, 10 to 48, 10 to 36 or 10 to 24 subunits, from 11 to 72, 11 to 60, 11 to 48, 11 to 36 or 11 to 24 subunits, from 12 to 72, 12 to 60, 12 to 48, 12 to 36 or 12 to 24 subunits, from 13 to 72, 13 to 60, 13 to 48, 13 to 36 or 13 to 24 subunits, from 14 to 72, 14 to 60, 14 to 48, 14 to 36 or 14 to 24 subunits, from 15 to 72, 15 to 60, 15 to 48, 15 to 36 or 15 to 24 subunits, from 16 to 72, 16 to 60, 16 to 48, 16 to 36 or 16 to 24 subunits, from 17 to 72, 17 to 60, 17 to 48, 17 to 36 or 17 to 24 subunits, from 18 to 72, 18 to 60, 18 to 48, 18 to 36 or 18 to 24 subunits, from 19 to 72, 19 to 60, 19 to 48, 19 to 36 or 19 to 24 subunits, from 20 to 72, 20 to 60, 20 to 48, 20 to 36 or 20 to 24 subunits, from 21 to 72, 21 to 60, 21 to 48, 21 to 36 or 21 to 24 subunits, from 22 to 72, 22 to 60, 22 to 48, 22 to 36 or 22 to 24 subunits, from 23 to 72, 23 to 60, 23 to 48, 23 to 36 or 23 to 24 subunits, or from 24 to 72, 24 to 60, 24 to 48, 24 to 36 or 24 subunits.

[0379] In some embodiments, the Partitioning Agent S* is a linear PEG Unit comprising from 2 to 20, or from 2 to 12, or from 4 to 12, or 4, 8, or 12 $-CH_2CH_2O-$ subunits. In some embodiments, the linear PEG Unit is connected at one end of the PEG Unit to the RL Unit and at the other end of the PEG Unit to the Stretcher/Connector Units (Z-A-). In some embodiments, the PEG Unit is connected to the RL Unit via a $-CH_2CH_2C(O)-$ group that forms an amide bond with the RL Unit (e.g., $-(CH_2CH_2O)_n-CH_2CH_2C(O)$-RL) and to the Stretcher Unit/Connector Unit (Z-A-) via an -NH- group (e.g., Z-A-NH-$(CH_2CH_2O)_n-$) that forms an amide bond with the Z-A- portion.

[0380] Illustrative embodiments for PEG Units that are connected to the RL and Stretcher/Connector Units (Z-A-) are shown below:







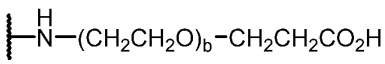
and in a particular embodiment, the PEG Unit is:

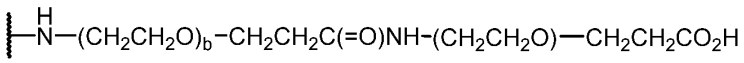


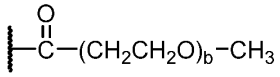
wherein the wavy line on the left indicates the site of attachment to Z-A-, the wavy line on the right indicates the site of attachment to RL, and each b is independently selected from 2 to 72, 4 to 72, 6 to 72, 8 to 72, 10 to 72, 12 to 72, 2 to 24, 4 to 24, 6 to 24, or 8 to 24, 2 to 12, 4 to 12, 6 to 12, and 8 to 12. In some embodiments, subscript b is 2, 4, 8, 12, or 24. In some embodiments, subscript b is 2. In some embodiments, subscript b is 4. In some embodiments, subscript b is 8. In some embodiments, subscript b is 12.

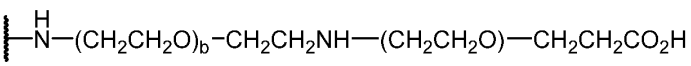
[0381] In some embodiments, the linear PEG Unit that is connected to the Parallel Connector Unit at one end and comprises a terminal cap at the other end. In some embodiments, the PEG Unit is connected to the Parallel Connector Unit via a carbonyl group that forms an amide bond with the Parallel Connector Unit lysine residue amino group (e.g., –$CH_2CH_2(OCH_2CH_2)_k$–C(O)-B-, wherein k is an integer from 1 to 36) and includes a PEG Unit terminal cap group selected from the group consisting of C_{1-4}alkyl and C_{1-4}alkyl-CO_2H. In some embodiments, the Partitioning Agent S* is a linear PEG Unit comprising 4, 8, or 12 -CH_2CH_2O- subunits and a terminal methyl cap.

[0382] Illustrative linear PEG Units that are used in any of the embodiments provided herein are as follows:

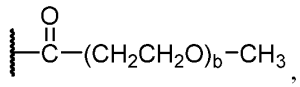








and in a particular embodiment, the PEG Unit is:



wherein the wavy line indicates site of attachment to the Parallel Connector Unit (B), and each n is independently selected from 4 to 72, 6 to 72, 8 to 72, 10 to 72, 12 to 72, 6 to 24, or 8 to 24. In some embodiments, subscript b is about 4, about 8, about 12, or about 24.

[0383] As used to herein, terms "PEG2", "PEG4", "PEG8", and "PEG12" refers to specific embodiments of PEG Unit which comprises the number of PEG subunits (i.e., the number of subscription "b"). For example, "PEG2" refers to embodiments of PEG Unit that comprises 2 PEG subunits, "PEG4" refers to embodiments of PEG Unit that comprises 4 PEG subunits, "PEG8" refers to embodiments of PEG Unit that comprises 8 PEG subunits, and "PEG12" refers to embodiments of PEG Unit that comprises 12 PEG subunits.

[0384] As described herein, the PEG unit is selected such that it improves clearance of the resultant Ligand-Drug Conjugate but does not significantly impact the ability of the Conjugate to penetrate into the tumor. In embodiments, the PEG unit to be selected for use will preferably have from 2 subunits to about 24 subunits, from 4 subunits to about 24 subunits, more preferably about 4 subunits to about 12 subunits.

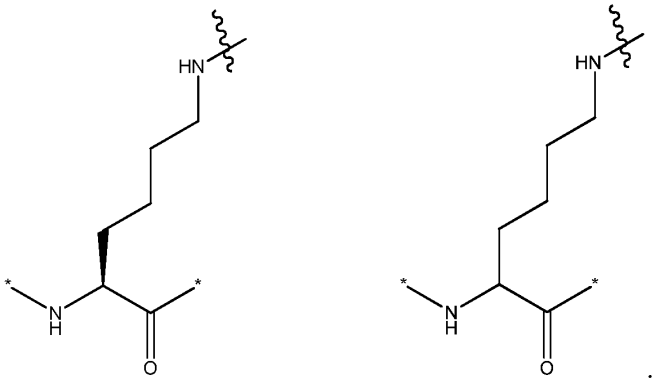
[0385] In some embodiments of the present disclosure the PEG Unit is from about 300 daltons to about 5 kilodaltons; from about 300 daltons, to about 4 kilodaltons; from about 300 daltons, to about 3 kilodaltons; from about 300 daltons, to about 2 kilodaltons; or from about 300 daltons, to about 1 kilodalton. In some such aspects, the PEG Unit has at least 6 subunits or at least 8, 10 or 12 subunits. In some such aspects, the PEG Unit has at least 6 subunits or at least 8, 10 or 12 subunits but no more than 72 subunits, preferably no more than 36 subunits.

[0386] It will be appreciated that when referring to PEG subunits, and depending on context, the number of subunits can represent an average number, e.g., when referring to a population of Ligand-Drug Conjugates or Drug-Linker Compounds, and/or using polydisperse PEGs.

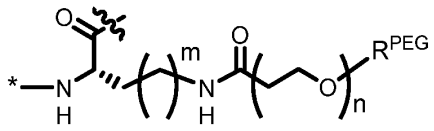
7. Parallel Connector Unit (B)

[0387] In some embodiments, the Ligand-Drug Conjugates and Drug-Linker Compounds will comprise a Parallel Connector Unit to provide a point of attachment to a Partitioning Agent (shown in the Linker Units as -B(S^*)-). In some embodiments, the PEG Unit is attached to a Parallel Connector Unit such as lysine as shown below wherein the wavy line

and asterisks indicate covalent linkage within the Linker Unit of a Ligand-Drug Conjugate or Drug-Linker Compound:



[0388] In some embodiments, the Parallel Connector Unit (B) and Partitioning Agent (S*) (together, -B(S*)-) have the structure of

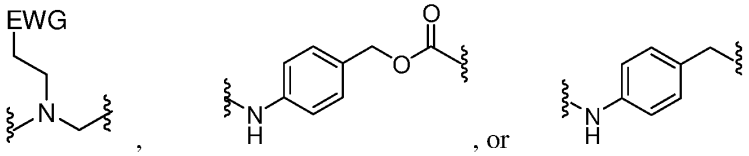


wherein m ranges from 0 to 6; n ranges from 2 to 24; R^{PEG} is a PEG Capping Unit, preferably H, $–CH_3$, or $–CH_2CH_2CO_2H$, the asterisk (*) indicates covalent attachment to a Connector Unit A corresponding in formula Za, Za', Zb' or Zc' and the wavy line indicates covalent attachment to the Releasable Linker (RL). In some embodiments, the structure is attached to a Connector Unit A in formula Za or Za'. In some embodiments, n is 2, 4, 8, or 12. In instances such as those shown here, the shown PEG group is meant to be exemplary of a variety of Partitioning Agents including PEG groups of different lengths and other Partitioning Agents that are directly attached or modified for attachment to the Parallel Connector Unit.

8. Spacer Unit (Y)

[0389] In some embodiments, the Ligand-Drug Conjugates provided herein will have a Spacer (Y) between the Releasable Linker (RL) and the Drug Unit. The Spacer Unit is a functional group to facilitate attachment of RL to the Drug Unit, or provides additional structural components to further facilitate release of the Drug Unit from the remainder of the Conjugate (e.g., a methylene carbamate unit or a self-immolative para-aminobenzyl (PAB) component).

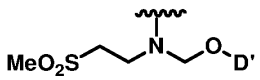
[0390] In those embodiments to further facilitate release of the Drug Unit as free drug, the Spacer Unit Y is represented by one of the following formulae:



, , or

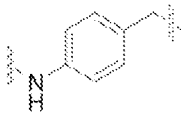
wherein EWG represents an electron-withdrawing group and the wavy lines indicate the site of attachment to the rest of the Drug-Linker compound or salt thereof. In some embodiments, EWG is selected from the group consisting of -CN, -NO_2, -CX_3, -X, -C(=O)OR', -C(=O)N(R')$_2$, -C(=O)R', -C(=O)X, -S(=O)$_2$R', -S(=O)$_2$OR', -S(=O)$_2$NHR', -S(=O)$_2$N(R')$_2$, -P(=O)(OR')$_2$, -P(=O)(CH_3)NHR', -NO, -N(R')$_3^+$, wherein X is -F, -Br, -Cl, or -I, and R' is independently selected from the group consisting of hydrogen and C_1-C_6 alkyl.

[0391] In some embodiments, the Spacer Unit-Drug Unit group (–Y-T*-D) is represented by one of the following formulae:



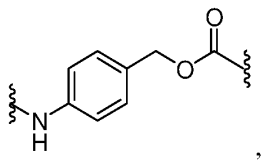
wherein the wavy line adjacent is the point of covalent attachment to RL, T* is as defined above, and D' represents the remainder of the Drug Unit, wherein T* and D' together form a Drug Unit of Formula (Ia), or any subformula thereof.

[0392] In some embodiments, the Spacer Unit is represented by the formula:



wherein the wavy line adjacent to the nitrogen atom is the point of covalent attachment to RL, as defined above, and the wavy line next to the benzylic carbon atom connects to a Drug Unit. In some embodiments, the Drug Unit is attached to the benzylic carbon atom via a quaternized tertiary amine (N+) of D.

[0393] In still other embodiments, the Spacer Unit is represented by the formula:

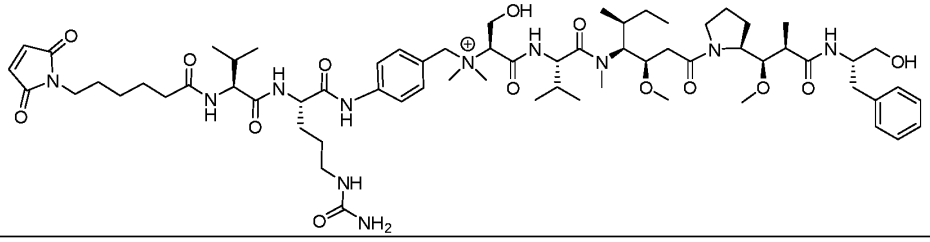
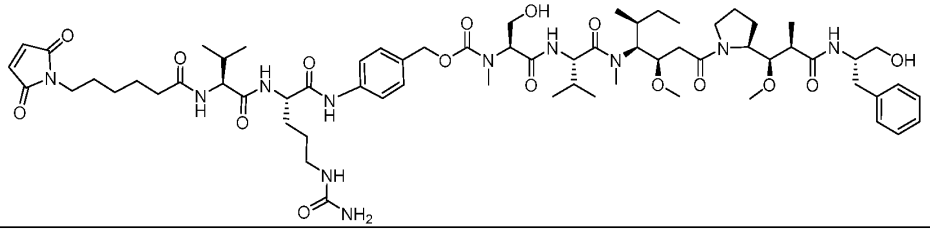
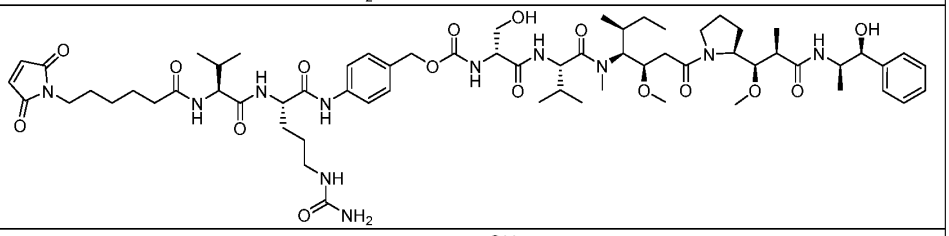
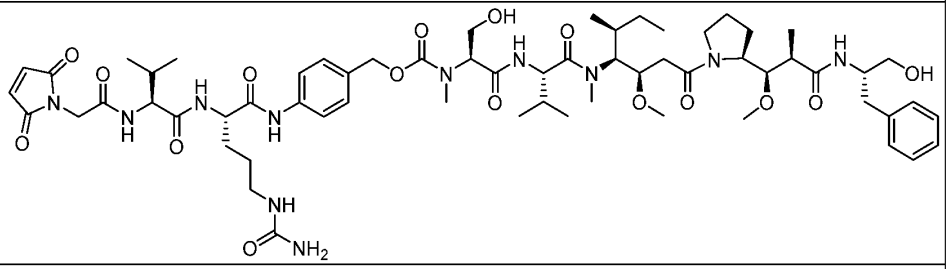
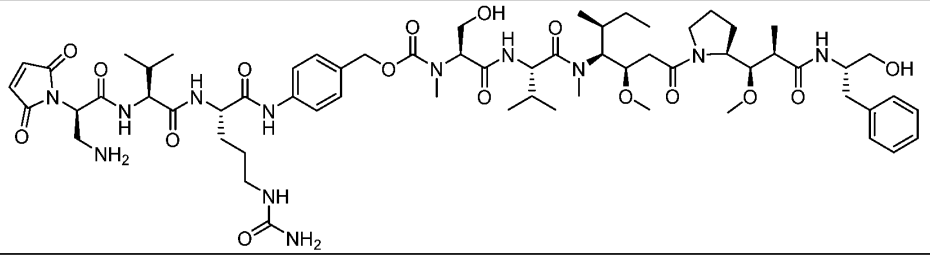


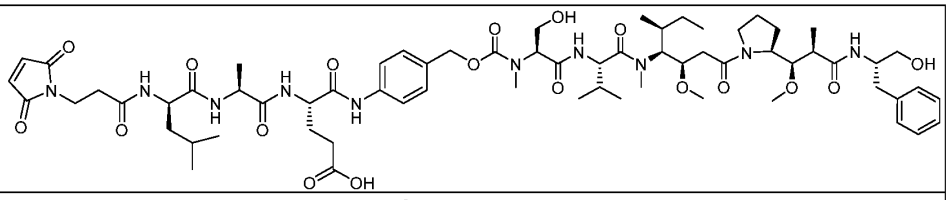
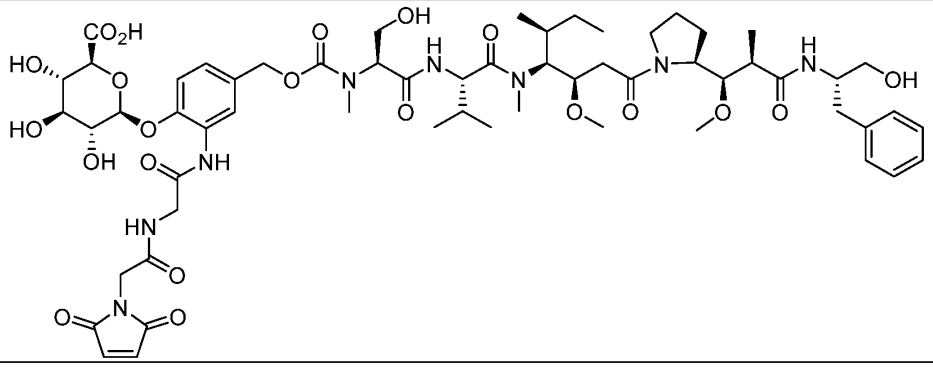
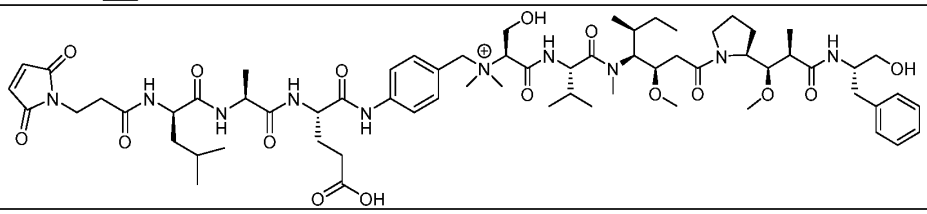
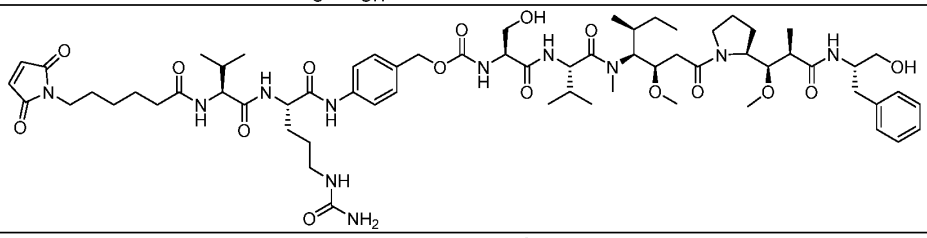
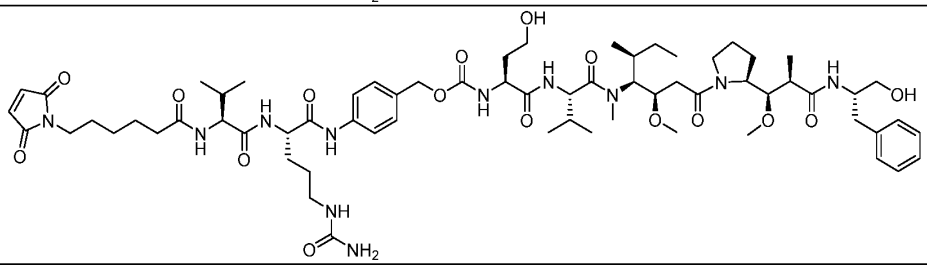
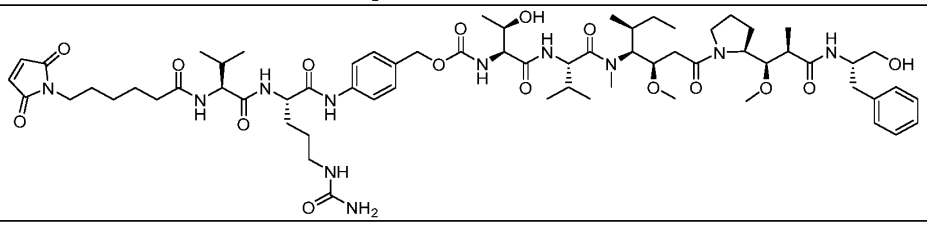
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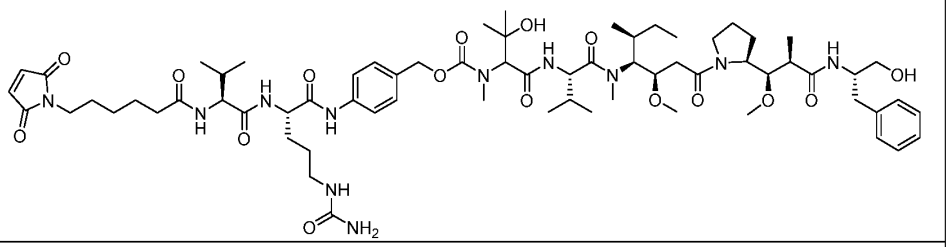
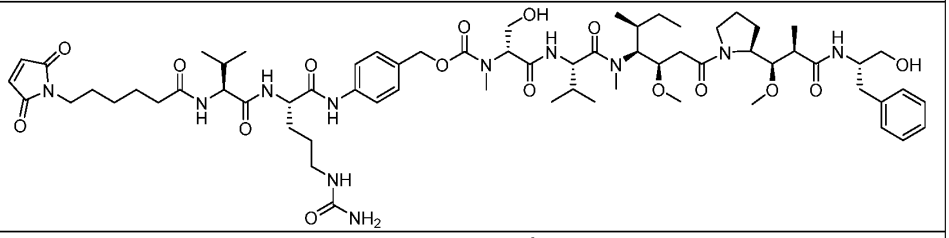
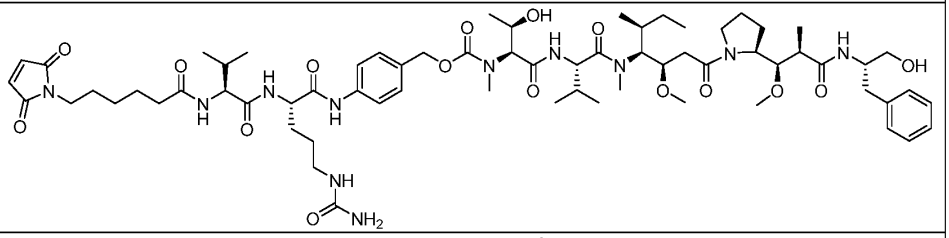
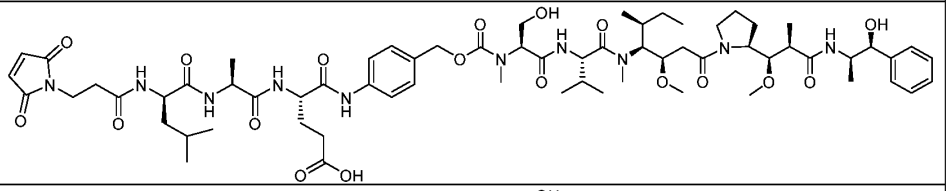
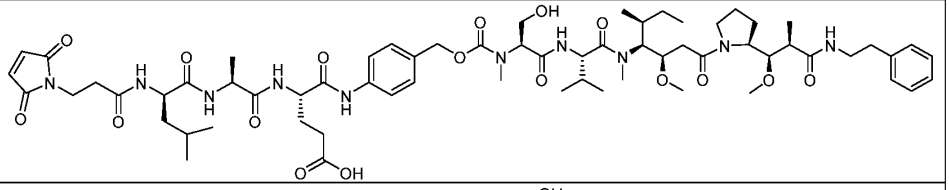
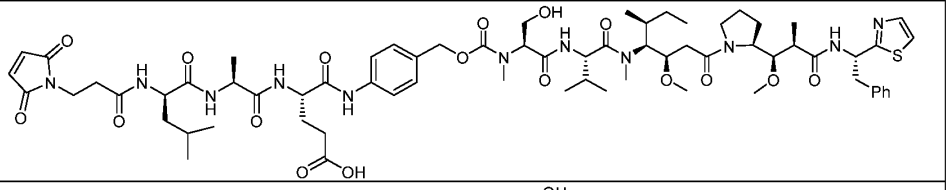
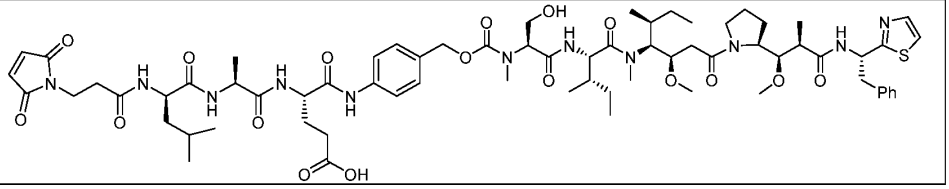
wherein the wavy line adjacent to the nitrogen atom is the point of covalent attachment to RL, as defined above, and the wavy line next to the -OC(O)- group connects to a Drug Unit. In some embodiments, the Drug Unit is attached via a primary or secondary amine.

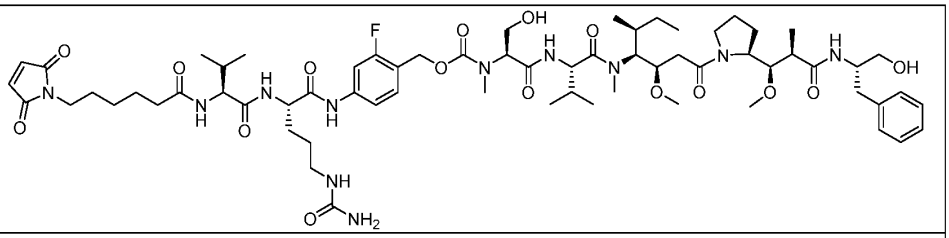
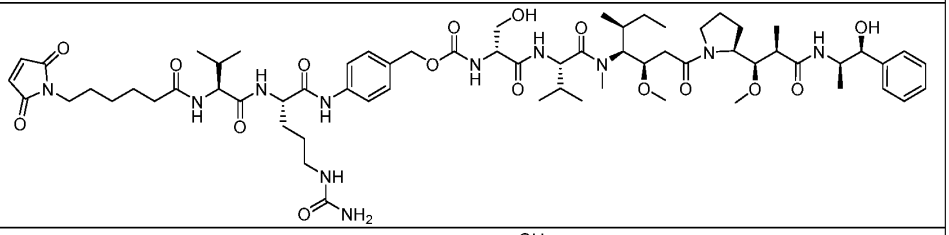
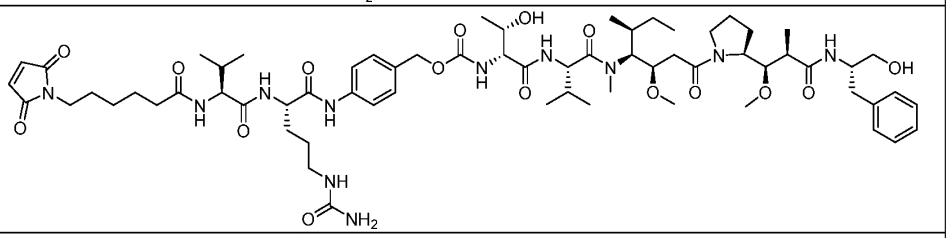
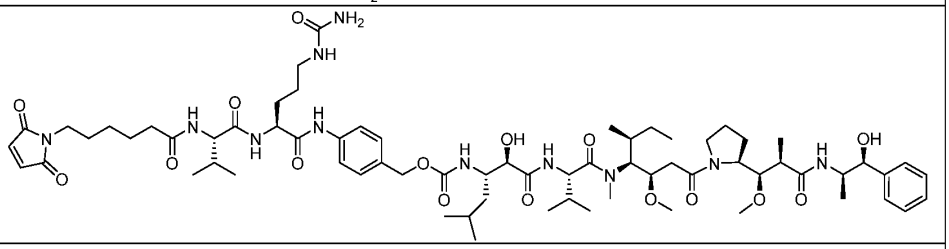
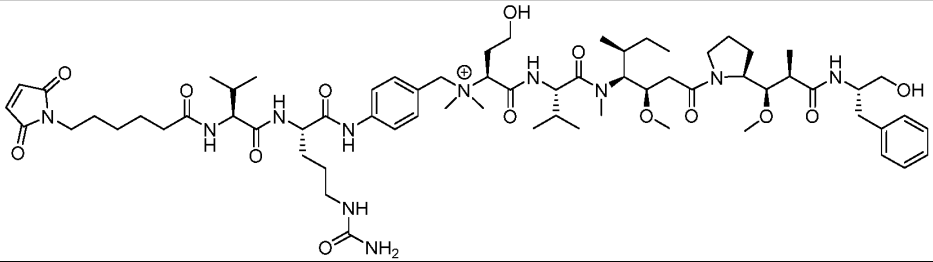
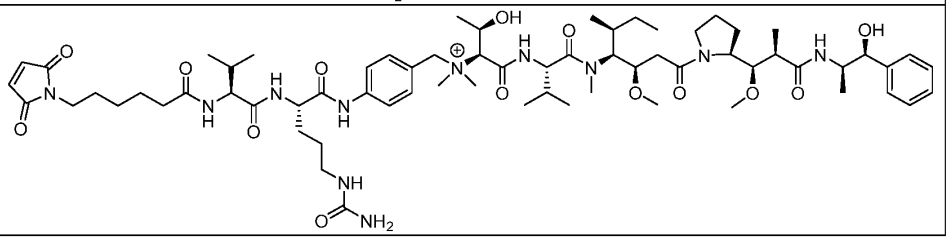
[0394] In some embodiments, provided herein is a Drug-Linker compound of Table 2, or a salt thereof.

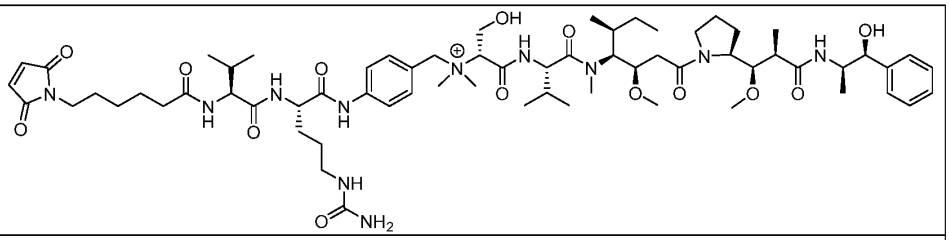
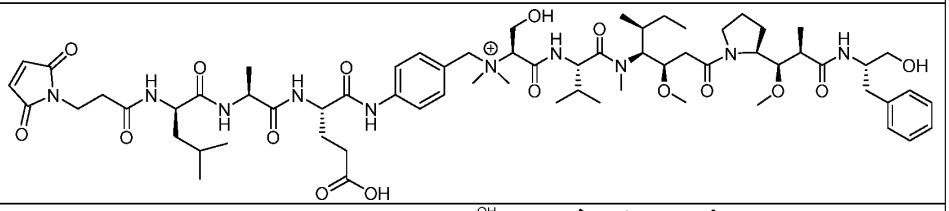
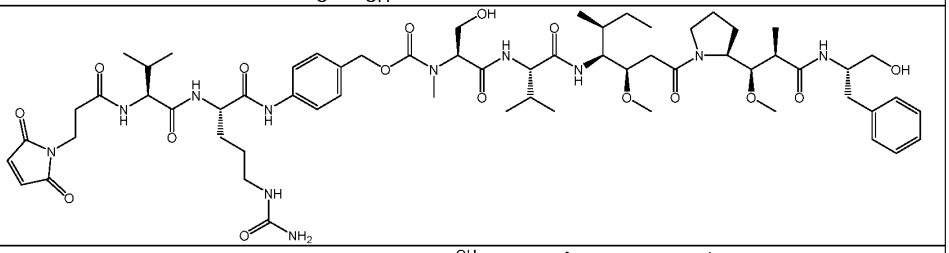
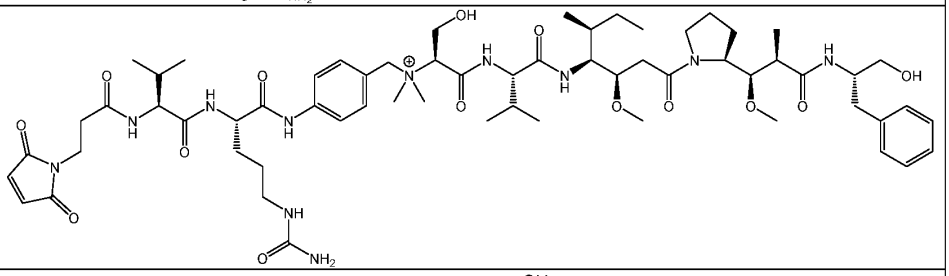
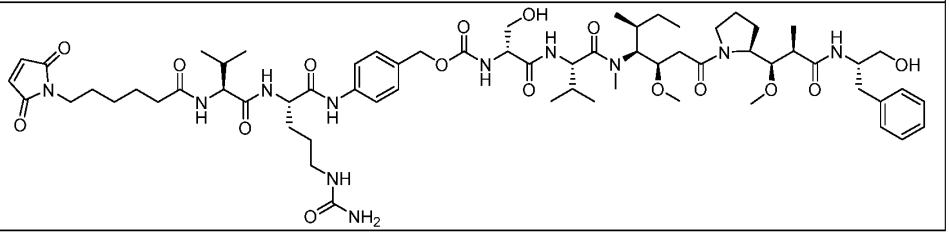
Table 2. Drug-Linker compounds

#	Drug-Linker structure
2.1	
2.2	
2.3	
2.4	
2.5	

2.6	
2.7	
2.8	
2.9	
2.10	
2.11	

2.12	
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2.26	
2.27	
2.28	
2.29	

Ligand-Drug Conjugate compounds

[0395] In context of Ligand-Drug Conjugate compounds – the assembly is described by the component groups as described for Drug-Linker compounds, with the exception of the Stretcher Unit Z and the Ligand Unit L. The Stretcher Unit Z is coordinated to the Ligand Unit L in Ligand-Drug Conjugate compounds, as described below. While some procedures for the preparation of Ligand-Drug Conjugate compounds are described herein, the order of assembly and the general conditions to prepare the compounds will be well understood by one of skill in the art.

[0396] In some embodiments, a Ligand-Drug Conjugate compound comprises an auristatin compound of Formula (I), or any subformula thereof, a Linker Unit (Q) comprising a Releasable Linker (RL) that is other than a Glycoside (e.g., Glucuronide) Unit through which the Ligand Unit is connected to the conjugated auristatin compound, and a Ligand Unit (L). The Linker Unit comprises, in addition to RL, a Stretcher Unit (Z) connected to the Ligand Unit and is capable of (directly or indirectly) connecting the RL to the Ligand Unit. In some embodiments, a Parallel Connector Unit (B) is present when it is desired to add a Partitioning Agent (S^*) as a side chain appendage. In any one of those embodiments, a Connector Unit (A) is present when it is desirable to add more distance between the Stretcher Unit and RL.

[0397] In some embodiments, a Ligand-Drug Conjugate compound comprises an auristatin compound of Formula (I), or any subformula thereof, and a Linker Unit (Q), wherein Q comprises a Releasable Linker (RL) that is a Glycoside (e.g., Glucuronide) Unit, directly attached to a Stretcher Unit (Z) or indirectly to Z through attachment to intervening component(s) of the Ligand-Drug Conjugate compound's Linker Unit (i.e., A, S^* and/or $B(S^*)$), wherein Z forms a covalent bond to a targeting agent (*e.g.*, a Ligand Unit).

[0398] In another group of embodiments, a Ligand-Drug Conjugate compound comprises an auristatin of Formula (I), or any subformula thereof, a Linker Unit (Q), wherein Q comprises a Releasable Linker (RL) that is other than a Glycoside (e.g., Glucuronide) Unit (RL), directly attached to a Stretcher Unit (Z) or indirectly to Z through attachment to intervening component(s) of the Ligand-Drug Conjugate compound's Linker Unit (i.e., A, S^* and/or $B(S^*)$), wherein Z forms a covalent bond to a targeting agent (*e.g.*, a Ligand Unit).

[0399] In some embodiments, the Ligand-Drug Conjugate compound has the formula:

$$L\text{-}(Q\text{-}D)_p$$

or a pharmaceutically acceptable salt thereof, wherein

L is a Ligand Unit;

Q is a Linker Unit selected from the group consisting of:

(i) Z'-A-RL-,

(ii) Z'-A-RL-Y-,

(iii) Z'-A-S^*-RL-,

(iv) Z'-A-S^*-RL-Y-,

(v) Z'-A-B(S^*)-RL-,

(vi) Z'-A-B(S*)-RL-Y-,

(vii) Z'-A-,

(viii) Z'-A-S*-W-,

(ix) Z'-A-B(S*)-W-,

(x) Z'-A-S*-W-RL-, and

(xi) Z'-A-B(S*)-W-RL-;

Z' is a Stretcher Unit precursor;

A is a bond or a Connector Unit;

B is a Parallel Connector Unit;

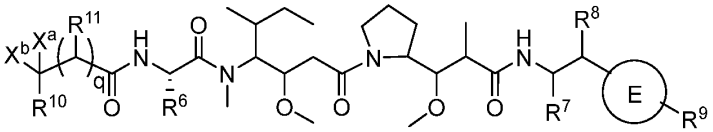
S^* is a Partitioning Agent;

RL is a Releasable Linker;

W is a Amino Acid Unit;

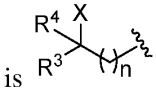
Y is a Spacer Unit; and

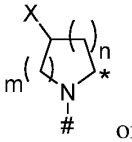
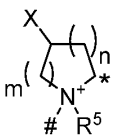
D is a Drug Unit of Formula (I'):



(I')

wherein

X^b is $-NR^{2}-^{\#}$ or $-N^+R^1R^5-^{\#}$, wherein the # denotes the point of attachment to Q, and X^a is  ; or

X^a and X^b are taken together with the carbon atom to which they are attached to form  or  , wherein the asterisk denotes the carbon atom of Formula (I) that bears the X^a and X^b groups, and the # denotes the point of attachment to Q;

R^1 and R^5 are independently C_1-C_4 alkyl;

X is H, OH, $-C(O)NR^aR^b$, $-S(O)_2R^a$, $-S(O)-R^a$ $-S(O)_2NR^aR^b$, $-NHS(O)_2R^a$, or $-NHC(O)R^a$;

R^2, R^3, R^4, R^{10}, R^a, and R^b are each independently H or C_1-C_4 alkyl;

R^6 is C_1-C_4 alkyl optionally substituted with OH;

R^7 is H, C_1-C_4 alkyl optionally substituted with OH, or 5-6 membered heteroaryl;

E is phenyl or 5-6 membered heteroaryl;

R^8, R^9, and R^{11} are each independently H or OH;

n is 0, 1, 2, or 3;

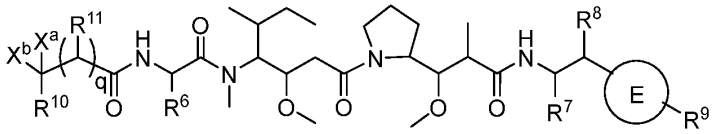
m is 1, 2, 3, or 4;

q is 0 or 1; and

p is an integer ranging from 1 to 12,

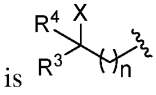
wherein when X is H, at least two of R^7, R^8, R^9, and R^{11} comprise an OH moiety.

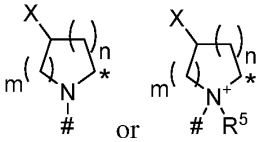
[0400] In some embodiments, provided herein are Ligand-Drug Conjugate compounds of formula L-(Q-D)$_p$, wherein the Drug Unit D has Formula (Iz*):



(Iz*)

wherein

X^b is -NR^2-$^{\#}$ or -$N^+R^1R^5$-$^{\#}$, wherein the # denotes the point of attachment to Q, and X^a is  ; or

X^a and X^b are taken together with the carbon atom to which they are attached to form  , wherein the asterisk denotes the carbon atom of Formula (I) that bears the X^a and X^b groups, and the # denotes the point of attachment to Q;

R^1 and R^5 are independently C_1-C_4 alkyl;

X is OH, -$S(O)_2R^a$, -S(O)-R^a -$S(O)_2NR^aR^b$, -$NHS(O)_2R^a$, or -$NHC(O)R^a$;

R^2, R^3, R^4, R^{10}, R^a, and R^b are each independently H or C_1-C_4 alkyl;

R^6 is C_1-C_4 alkyl optionally substituted with OH;

R^7 is H, C_1-C_4 alkyl optionally substituted with OH, or 5-6 membered heteroaryl;

E is phenyl or 5-6 membered heteroaryl;

R^8, R^9, and R^{11} are each independently H or OH;

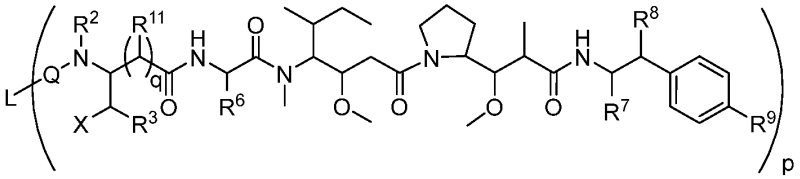
n is 0, 1, 2, or 3;

m is 1, 2, 3, or 4;

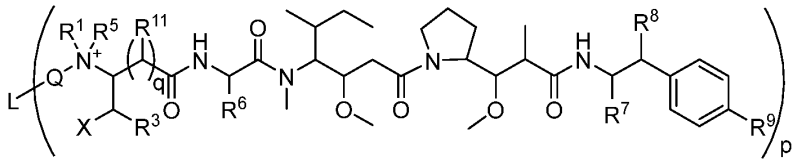
q is 0 or 1; and

p is an integer ranging from 1 to 12.

[0401] In some embodiments, the Ligand-Drug Conjugate compound has Formula (Ia*) or (Ia**):



(Ia*)



(Ia**)

or a salt thereof, wherein

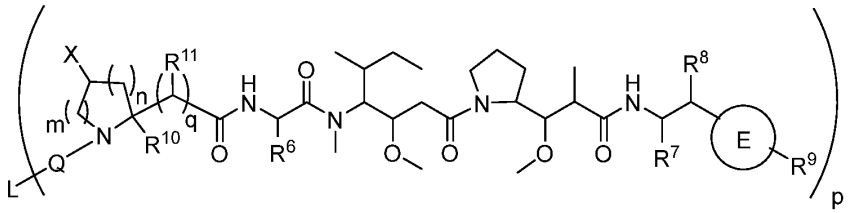
L is a Ligand Unit;

Q is a Linker Unit as described above;

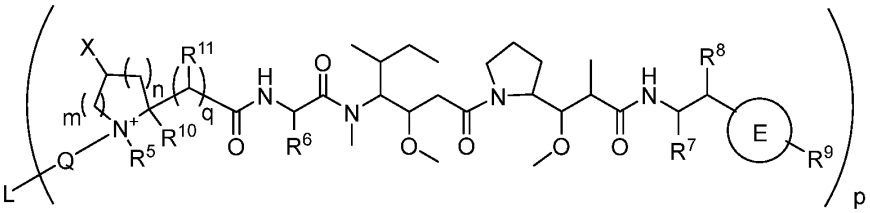
p is an integer ranging from 1 to 12; and

the remaining variables are as described for Drug-Linker moieties of Formula (Ia') or Formula (Ia") above.

[0402] In some embodiments, the Ligand-Drug Conjugate compound has Formula (Ib*) or (Ib**):



(Ib*)



(Ib**)

or a salt thereof, wherein

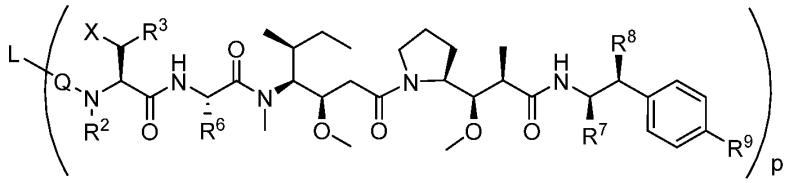
L is a Ligand Unit;

Q is a Linker Unit as described above;

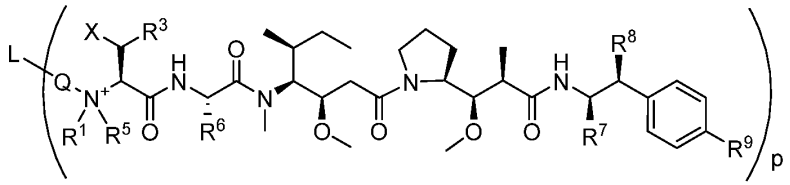
p is an integer ranging from 1 to 12; and

the remaining variables are as described for Drug-Linker moieties of Formula (Ib') or Formula (Ib") above.

[0403] In some embodiments, the Ligand-Drug Conjugate compound has Formula (Ic*) or (Ic**):



(Ic*)



(Ic**)

or a salt thereof, wherein

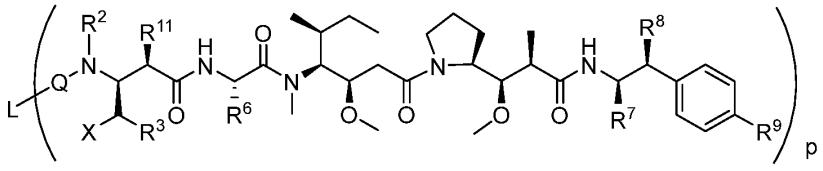
L is a Ligand Unit;

Q is a Linker Unit as described above;

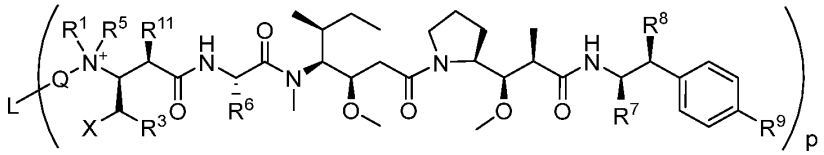
p is an integer ranging from 1 to 12; and

the remaining variables are as described for Drug-Linker moieties of Formula (Ic') or Formula (Ic") above.

[0404] In some embodiments, the Ligand-Drug Conjugate compound has Formula (Id*) or (Id**):



(Id*)



(Id**)

or a salt thereof, wherein

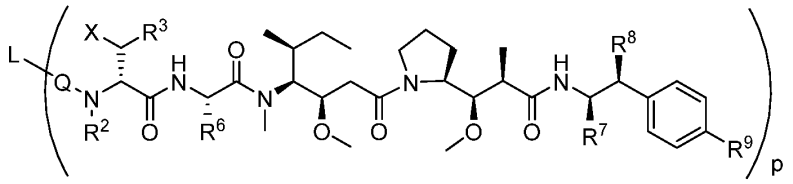
L is a Ligand Unit;

Q is a Linker Unit as described above;

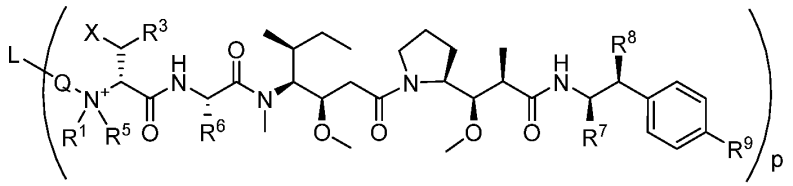
p is an integer ranging from 1 to 12; and

the remaining variables are as described for Drug-Linker moieties of Formula (Id') or Formula (Id") above.

[0405] In some embodiments, the Ligand-Drug Conjugate compound has Formula (Ie*) or (Ie**):



(Ie*)



(Ie**)

or a salt thereof, wherein

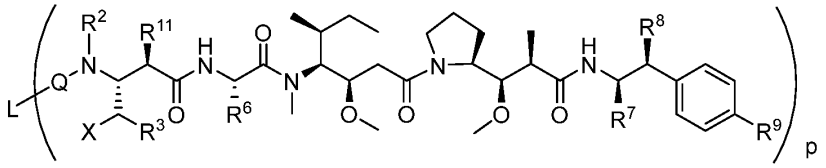
L is a Ligand Unit;

Q is a Linker Unit as described above;

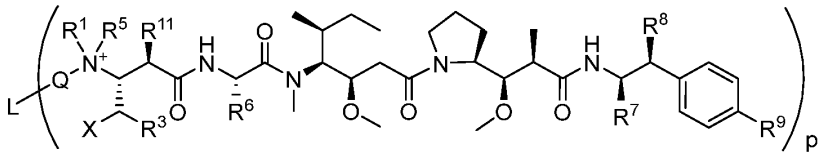
p is an integer ranging from 1 to 12; and

the remaining variables are as described for Drug-Linker moieties of Formula (Ie') or Formula (Ie") above.

[0406] In some embodiments, the Ligand-Drug Conjugate compound has Formula (If*) or (If**):



(If*)



(If**)

or a salt thereof, wherein

L is a Ligand Unit;

Q is a Linker Unit as described above;

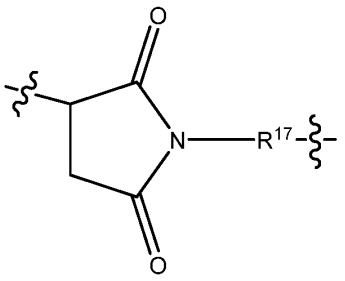
p is an integer ranging from 1 to 12; and

the remaining variables are as described for Drug-Linker moieties of Formula (If') or Formula (If'') above.

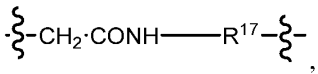
[0407] In the context of the Ligand-Drug Conjugate compounds – the assembly is best described in terms of its component groups. While some procedures for the preparation of Ligand-Drug Conjugate compounds are described herein, the order of assembly and the general conditions to prepare the compounds will be well understood by one of skill in the art. The component groups of the Ligand-Drug Conjugate compounds described are in many cases identical to the component groups for Drug-Linker compounds as described above, including A, B, S*, RL, W, Y, and D. It is to be understood that embodiments are contemplated wherein the Drug Unit D of the Ligand-Drug Conjugates described herein is conforms to the description of Formula (I'), or any subformula thereof. Other component groups are described below.

Stretcher Unit Z

[0408] Representative Stretcher Units of such embodiments include those having the structures of:



and



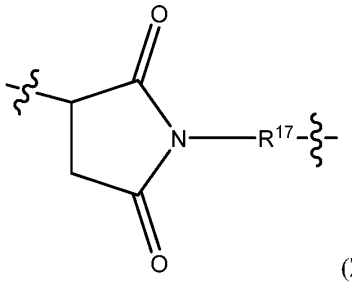
,

wherein the wavy line adjacent to R^{17} indicates attachment to the Parallel Connector Unit (B) or Connector Unit (A) if B is absent, or a Partitioning Agent (S^*), if B is absent, the other wavy line indicates covalent attachment to a sulfur atom of a Ligand Unit, and R^{17} is $–CH_2CH_2(OCH_2CH_2)_k–$, -C_1-C_{10} alkylene-, C_1-C_{10} heteroalkylene-, -C_3-C_8 carbocyclo-, -O-(C_1-C_8 alkylene)-, -arylene-, -C_1-C_{10} alkylene-arylene-, -arylene-C_1-C_{10} alkylene-, -C_1-C_{10} alkylene-(C_3-C_8 carbocyclo)-, -(C_3-C_8 carbocyclo)-C_1-C_{10} alkylene-, -C_3-C_8 heterocyclo-, -C_1-C_{10} alkylene-(C_3-C_8 heterocyclo)-, -(C_3-C_8 heterocyclo)-C_1-C_{10} alkylene-, -C_1-C_{10} alkylene-C(=O)-, C_1-C_{10} heteroalkylene-C(=O)-, -C_3-C_8 carbocyclo-C(=O)-, -O-(C_1-C_8 alkylene)-C(=O)-, -arylene-C(=O)-, -C_1-C_{10} alkylene-arylene-C(=O)-, -arylene-C_1-C_{10} alkylene-C(=O)-, -C_1-C_{10} alkylene-(C_3-C_8 carbocyclo)-C(=O)-, -(C_3-C_8 carbocyclo)-C_1-C_{10} alkylene-C(=O)-, -C_3-C_8 heterocyclo-C(=O)-, -C_1-C_{10} alkylene-(C_3-C_8 heterocyclo)-C(=O)-, -(C_3-C_8 heterocyclo)-C_1-C_{10} alkylene-C(=O)-, -C_1-C_{10} alkylene-NH-, -C_1-C_{10} heteroalkylene-NH-, -C_3-C_8 carbocyclo-NH-, -O-(C_1-C_8 alkylene)-NH-, -arylene-NH-, -C_1-C_{10} alkylene-arylene-NH-, -arylene-C_1-C_{10} alkylene-NH-, -C_1-C_{10} alkylene-(C_3-C_8 carbocyclo)-NH-, -(C_3-C_8 carbocyclo)-C_1-C_{10} alkylene-NH-, -C_3-C_8 heterocyclo-NH-, -C_1-C_{10} alkylene-(C_3-C_8 heterocyclo)-NH-, -(C_3-C_8 heterocyclo)-C_1-C_{10} alkylene-NH-, -C_1-C_{10} alkylene-S-, C_1-C_{10} heteroalkylene-S -, -C_3-C_8 carbocyclo-S -, -O-(C_1-C_8 alkylene)-S -, -arylene-S-, -C_1-C_{10} alkylene-arylene-S-, -arylene-C_1-C_{10} alkylene-S-, -C_1-C_{10} alkylene-(C_3-C_8 carbocyclo)-S-, -(C_3-C_8 carbocyclo)-C_1-C_{10} alkylene-S-, -C_3-C_8 heterocyclo-S-, -C_1-C_{10} alkylene-(C_3-C_8 heterocyclo)-S-, or -(C_3-C_8 heterocyclo)-C_1-C_{10} alkylene-S-, wherein subscript k is an integer ranging from 1 to 36.

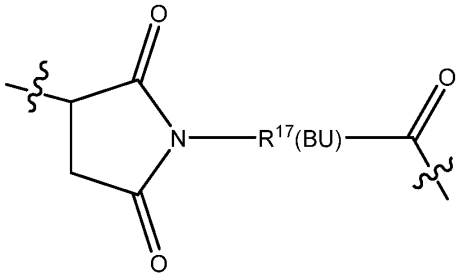
[0409] In some embodiments, the R^{17} group is optionally substituted by a Basic Unit (BU) such as an aminoalkyl moiety, e.g. $–(CH_2)_xNH_2$, $–(CH_2)_xNHR^a$, and $–(CH_2)_xNR^a_2$, wherein subscript x is an integer of from 1-4 and each R^a is independently selected from the

group consisting of C_{1-6} alkyl and C_{1-6} haloalkyl, or two R^a groups are combined with the nitrogen to which they are attached to form an azetidinyl, pyrrolidinyl or piperidinyl group.

[0410] An illustrative Stretcher Unit is that of Formula Za or Za-BU in which R^{17} is $–CH_2CH_2(OCH_2CH_2)_k–$, -C_1-C_{10} alkylene-C(=O)-, -C_1-C_{10} heteroalkylene-C(=O)-, -C_3-C_8 carbocyclo-C(=O)-, -O-(C_1-C_8 alkylene)-C(=O)-, -arylene-C(=O)-, -C_1-C_{10} alkylene-arylene-C(=O)-, -arylene-C_1-C_{10} alkylene-C(=O)-, -C_1-C_{10} alkylene-(C_3-C_8 carbocyclo)-C(=O)-,-(C_3-C_8 carbocyclo)-C_1-C_{10} alkylene-C(=O)-, -C_3-C_8 heterocyclo-C(=O)-, -C_1-C_{10} alkylene-(C_3-C_8 heterocyclo)-C(=O)-, or -(C_3-C_8 heterocyclo)-C_1-C_{10} alkylene-C(=O), wherein subscript k is an integer ranging from 1 to 36:



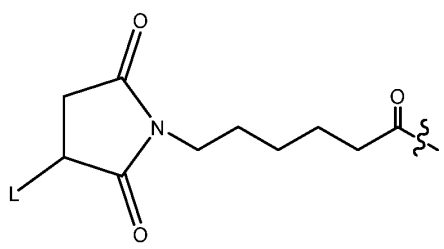
(Za),



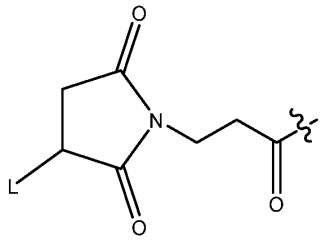
(Za-BU),

wherein the wavy line adjacent the carbonyl carbon atom indicates attachment to L^P, B, A, or S^*, in the formulae above, depending on the presence or absence of A and/or B, and the other wavy line indicates covalent bonding of the succinimide ring carbon atom to a sulfur atom of a Ligand Unit. In some aspects, the basic amino functional group of the Basic Unit (BU) is protected by a protecting group during synthesis.

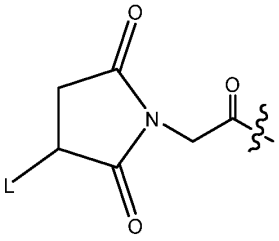
[0411] In some embodiments, Stretcher Units of formula Za and Za-BU are as follows:


O
N
L
O
O

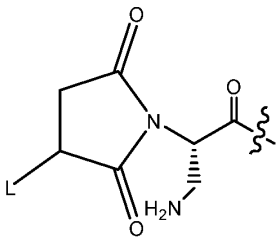
,


O
N
L
O
O

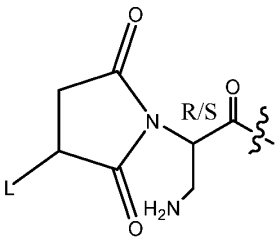
,


O
N
L
O
O

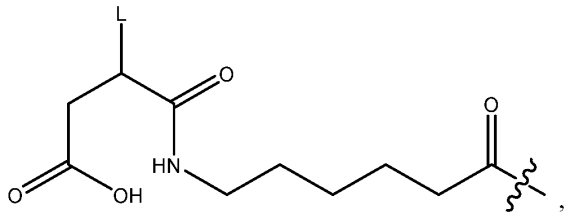
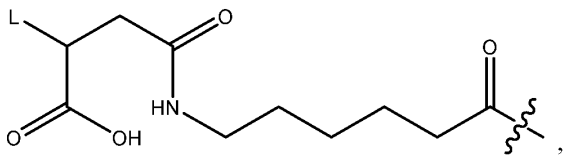
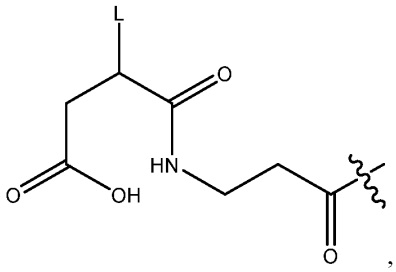
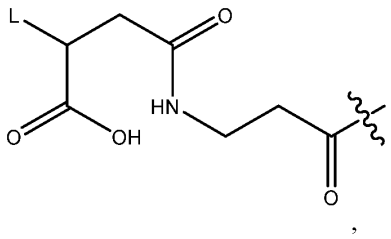
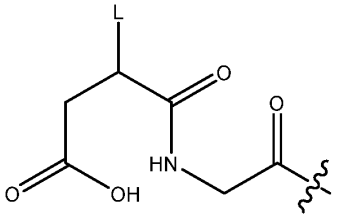
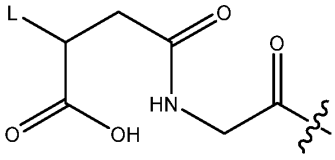
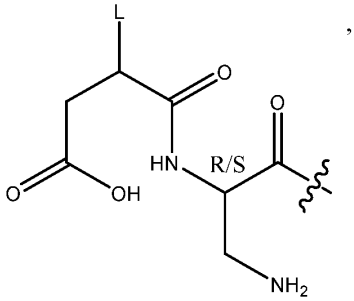
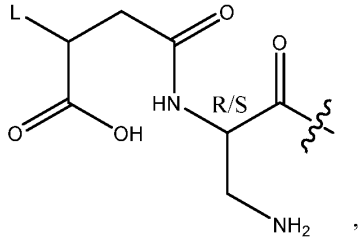
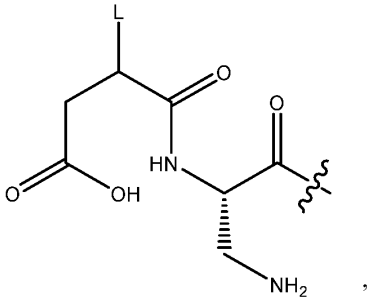
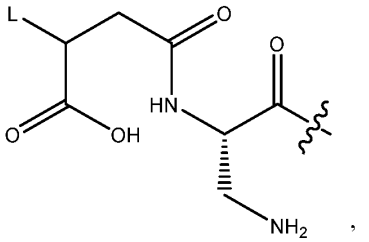
,


O
N
L
O
O
H2N

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O
N
R/S
L
O
O
H2N

,

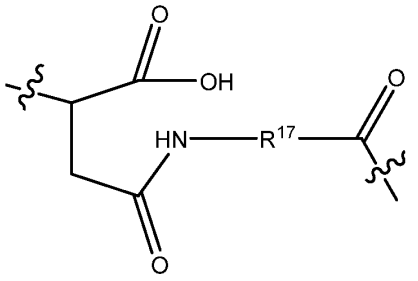

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or

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wherein the wavy line adjacent the carbonyl carbon atom indicates attachment to B, A, or S*, in the formulae above, depending on the presence or absence of A and/or B, and the other

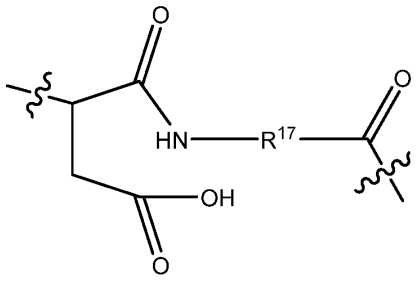
wavy line indicates covalent bonding of the succinimide ring carbon atom to a sulfur atom of a Ligand Unit.

[0412] It will be understood that a Ligand Unit-substituted succinimide may exist in hydrolyzed form(s). Those forms are exemplified below for hydrolysis of Za or Za-BU, wherein the structures representing the regioisomers from that hydrolysis have formula Zb and Zc or Zb-BU and Zc-BU.

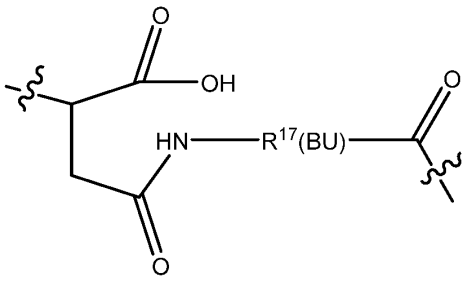
[0413] Accordingly, in some embodiments, a Stretcher unit (Z) comprises a succinic acid-amide moiety represented by the following:



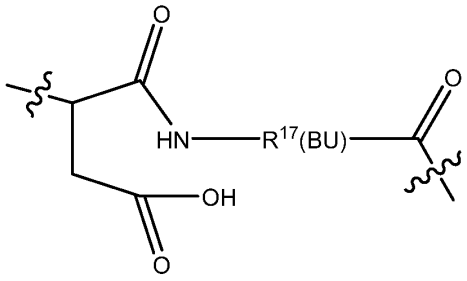
(Zb),



(Zc),



(Zb-BU),

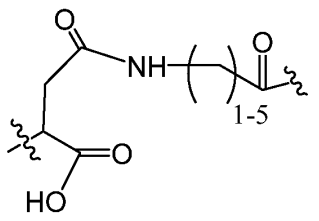


(Zc-BU),

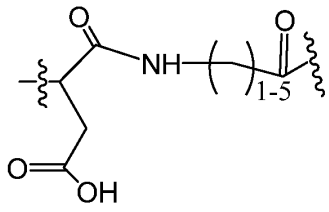
wherein the wavy line adjacent to the carbonyl carbon atom bonded to R^{17} and the wavy line adjacent to the carbon atom of the succinic acid-amide moiety is as defined for Za or Za-BU, depending on the presence or absence of A and/or B; and R^{17} is $-C_1$-C_5 alkylene-, wherein in Zb-BU and Zc-BU the alkylene is substituted by a Basic Unit (BU), wherein BU is $-(CH_2)_xNH_2$, $-(CH_2)_xNHR^a$, or $-(CH_2)_xN(R^a)_2$, wherein subscript x is an integer of from 1-4 and each R^a is independently selected from the group consisting of C_{1-6} alkyl and C_{1-6} haloalkyl, or both R^a together with the nitrogen to which they are attached define an azetidinyl, pyrrolidinyl or piperidinyl group.

[0414] In some embodiments, -Z-A- comprises a moiety derived from a maleimido-alkanoic acid moiety or an mDPR moiety. See, for example, see WO 2013/173337. In one group of embodiments, Z-A- is derived from a maleimido-propionyl moiety.

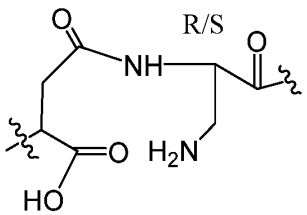
[0415] In some embodiments, a Stretcher unit (Z) comprises an succinic acid-amide moiety represented by the structure of formula Zb', Zc', (R/S)-Zb'-BU, (S)-Zb'-BU, (R/S)-Zc'-BU or (S)-Zc'-BU as follows:



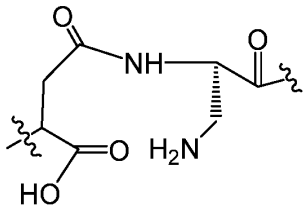
Zb'



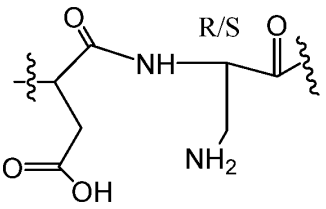
Zc'



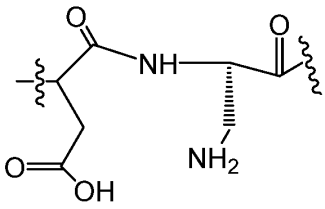
(R/S)-Zb'-BU



(S)-Zb'-BU



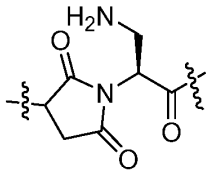
(R/S)-Zc'-BU



(S)-Zc'-BU

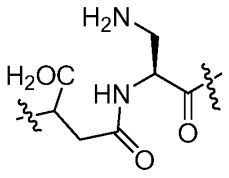
wherein the wavy lines are as defined for Za or Za-BU.

[0416] In some embodiments, a Stretcher unit (Z) comprises a succinimide moiety represented by the structure of

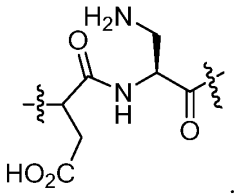


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which may be generated from a maleimido-amino-propionyl (mDPR) analog (a 3-amino-2-(2,5-dioxo-2,5-dihydro-1H-pyrrol-1-yl)propanoic acid derivative), or comprises a succinic acid-amide moiety represented by the structure of:

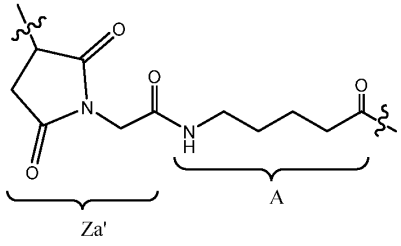


or



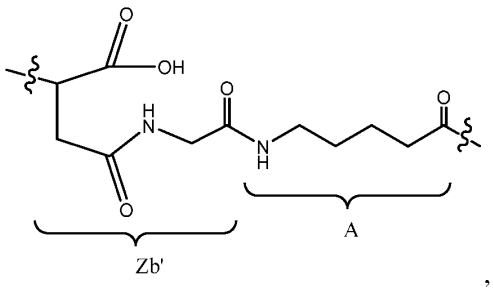
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[0417] Illustrative Stretcher Units bonded to a Connector Unit (A) which comprise Za', Zb' or Zc', in which $-R^{17}-$ of Za, Zb or Zc is $-CH_2-$ or $-CH_2CH_2-$, or comprise Za'-BU, Zb'-BU or Zc'-BU in which $-R^{17}$(BU)- of Za'-BU, Zb'-BU or Zc'-BU is $-CH(CH_2NH_2)-$, have the following structures:



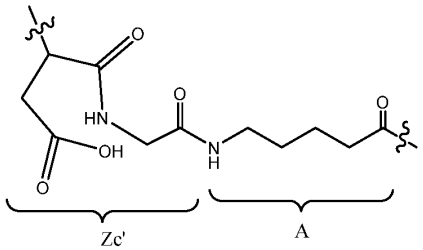
Za'

,

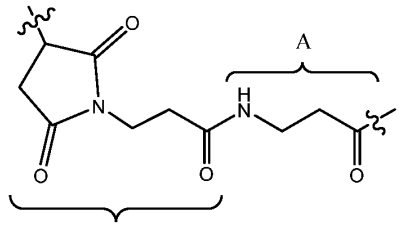


Zb'

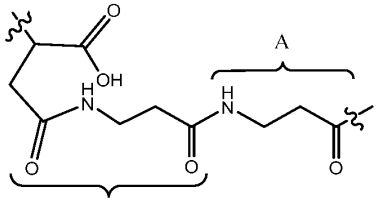
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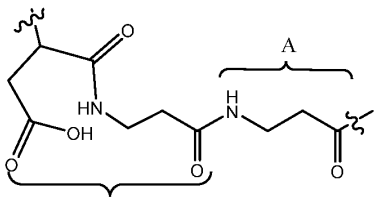
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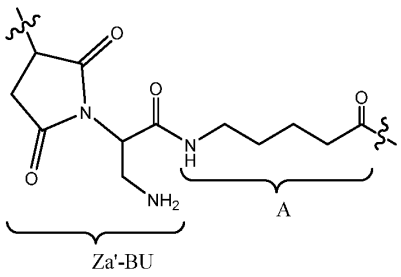


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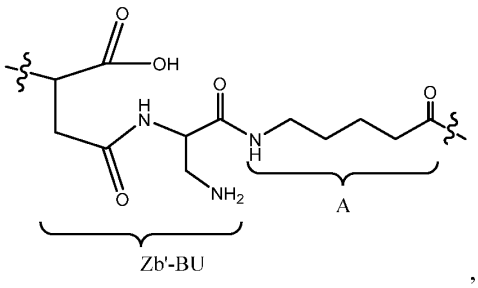


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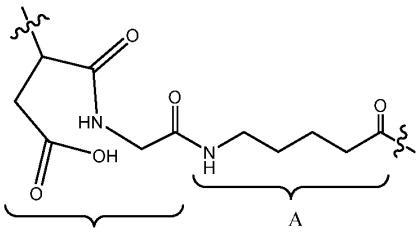




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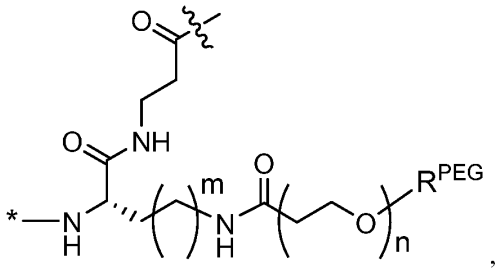
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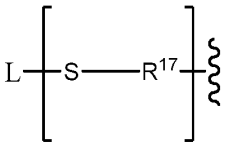
wherein the wavy lines are as defined for Za or Za-BU.

[0418] Other Stretcher Units bonded to a Ligand Unit (L) and a Connector Unit (A) have the structures above wherein A in any one of the above -Za'-A-, -Za'(BU)-A-, -Za'-A-, -Za'(BU)-A-, -Zb'-A-, -Zb'(BU)-A-, -Zb'-A-, -Zb'(BU)-, -Zc'-A- and Zc'(BU)-A- structures is replaced by a Parallel Connector Unit having the structure of:



wherein subscript m ranges from 1 to 6; n ranges from 8 to 24; R^{PEG} is a PEG Capping Unit, preferably H, $–CH_3$, or $–CH_2CH_2CO_2H$, the asterisk (*) indicates covalent attachment to a Stretcher Unit corresponding in structure to formula Za, Za', Zb' or Zc' and the wavy line indicates covalent attachment to the Releasable Linker (RL).

[0419] In another embodiment, the Stretcher Unit is attached to the Ligand Unit via a disulfide bond between a sulfur atom of the Ligand Unit and a sulfur atom of the Stretcher unit. A representative Stretcher Unit of this embodiment is depicted within the square brackets of Formula Zb:

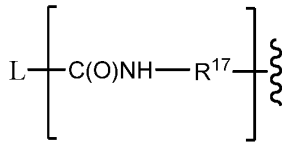


(Zb),

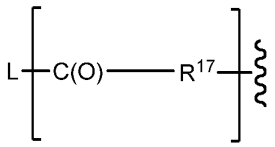
wherein the wavy line indicates attachment to the Parallel Connector Unit (B) or Connector Unit (A) if B is absent or a Partitioning Agent (S^*), if A and B are absent and R^{17} is $–CH_2CH_2(OCH_2CH_2)_k–$, -C_1-C_{10} alkylene-, C_1-C_{10} heteroalkylene-, -C_3-C_8 carbocyclo-, -O-(C_1-C_8 alkylene)-, -arylene-, -C_1-C_{10} alkylene-arylene-, -arylene-C_1-C_{10} alkylene-, -C_1-C_{10} alkylene-(C_3-C_8 carbocyclo)-, -(C_3-C_8 carbocyclo)-C_1-C_{10} alkylene-, -C_3-C_8 heterocyclo-, -C_1-C_{10} alkylene-(C_3-C_8 heterocyclo)-, -(C_3-C_8 heterocyclo)-C_1-C_{10} alkylene-, -C_1-C_{10} alkylene-C(=O)-, C_1-C_{10} heteroalkylene-C(=O)-, -C_3-C_8 carbocyclo-C(=O)-, -O-(C_1-C_8 alkylene)-C(=O)-, -arylene-C(=O)-, -C_1-C_{10} alkylene-arylene-C(=O)-, -arylene-C_1-C_{10} alkylene-C(=O)-, -C_1-C_{10} alkylene-(C_3-C_8 carbocyclo)-C(=O)-,-(C_3-C_8 carbocyclo)-C_1-C_{10} alkylene-C(=O)-, -C_3-C_8 heterocyclo-C(=O)-, -C_1-C_{10} alkylene-(C_3-C_8 heterocyclo)-C(=O)-, -(C_3-C_8 heterocyclo)-C_1-C_{10} alkylene-C(=O)-, -C_1-C_{10} alkylene-NH-, C_1-C_{10} heteroalkylene-NH-, -C_3-C_8 carbocyclo-NH-, -O-(C_1-C_8 alkylene)-NH-, -arylene-NH-, -C_1-C_{10} alkylene-arylene-NH-, -arylene-C_1-C_{10} alkylene-NH-, -C_1-C_{10} alkylene-(C_3-C_8 carbocyclo)-NH-, -(C_3-C_8 carbocyclo)-C_1-C_{10} alkylene-NH-, -C_3-C_8 heterocyclo-NH-, -C_1-C_{10} alkylene-(C_3-C_8 heterocyclo)-NH-, -(C_3-C_8 heterocyclo)-C_1-C_{10} alkylene-NH-, -C_1-C_{10} alkylene-S-, C_1-C_{10}

heteroalkylene-S -, -C_3-C_8 carbocyclo-S -, -O-(C_1-C_8 alkylene)-S -, -arylene-S-, -C_1-C_{10} alkylene-arylene-S-, -arylene-C_1-C_{10} alkylene-S-, -C_1-C_{10} alkylene-(C_3-C_8 carbocyclo)-S-, -(C_3-C_8 carbocyclo)-C_1-C_{10} alkylene-S-, -C_3-C_8 heterocyclo-S-, -C_1-C_{10} alkylene-(C_3-C_8 heterocyclo)-S-, or -(C_3-C_8 heterocyclo)-C_1-C_{10} alkylene-S-, wherein subscript k is an integer ranging from 1 to 36.

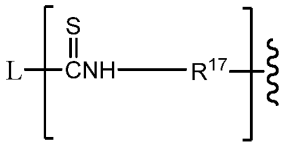
[0420] In yet another embodiment, the reactive group of a Stretcher Unit precursor contains a reactive site that can form a bond with a primary or secondary amino group of a Ligand Unit. Examples of these reactive sites include, but are not limited to, activated esters such as succinimide esters, 4-nitrophenyl esters, pentafluorophenyl esters, tetrafluorophenyl esters, anhydrides, acid chlorides, sulfonyl chlorides, isocyanates and isothiocyanates. Representative Stretcher Units of this embodiment are depicted within the square brackets of Formulas Zci, Zcii and Zciii:



(Zci),



(Zcii),

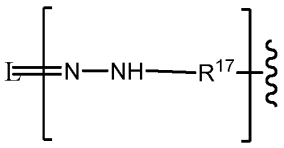


(Zciii),

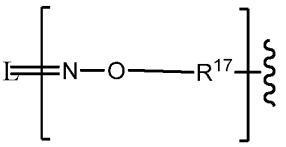
wherein the wavy line indicates attachment to the Parallel Connector Unit (B) or Connector Unit (A) if B is absent or a Partitioning Agent (S^*), if A and B are absent and R^{17} is –$CH_2CH_2(OCH_2CH_2)_k$–, -C_1-C_{10} alkylene-, C_1-C_{10} heteroalkylene-, -C_3-C_8 carbocyclo-, -O-(C_1-C_8 alkylene)-, -arylene-, -C_1-C_{10} alkylene-arylene-, -arylene-C_1-C_{10} alkylene-, -C_1-C_{10} alkylene-(C_3-C_8 carbocyclo)-, -(C_3-C_8 carbocyclo)-C_1-C_{10} alkylene-, -C_3-C_8 heterocyclo-, -C_1-C_{10} alkylene-(C_3-C_8 heterocyclo)-, -(C_3-C_8 heterocyclo)-C_1-C_{10} alkylene-, -C_1-C_{10} alkylene-C(=O)-, C_1-C_{10} heteroalkylene-C(=O)-, -C_3-C_8 carbocyclo-C(=O)-, -O-(C_1-C_8 alkylene)-C(=O)-, -arylene-C(=O)-, -C_1-C_{10} alkylene-arylene-C(=O)-, -arylene-C_1-C_{10} alkylene-C(=O)-, -C_1-C_{10} alkylene-(C_3-C_8 carbocyclo)-C(=O)-,-(C_3-C_8 carbocyclo)-C_1-C_{10}

alkylene-C(=O)-, -C_3-C_8 heterocyclo-C(=O)-, -C_1-C_{10} alkylene-(C_3-C_8 heterocyclo)-C(=O)-, -(C_3-C_8 heterocyclo)-C_1-C_{10} alkylene-C(=O)-, -C_1-C_{10} alkylene-NH-, C_1-C_{10} heteroalkylene-NH-, -C_3-C_8 carbocyclo-NH-, -O-(C_1-C_8 alkylene)-NH-, -arylene-NH-, -C_1-C_{10} alkylene-arylene-NH-, -arylene-C_1-C_{10} alkylene-NH-, -C_1-C_{10} alkylene-(C_3-C_8 carbocyclo)-NH-, -(C_3-C_8 carbocyclo)-C_1-C_{10} alkylene-NH-, -C_3-C_8 heterocyclo-NH-, -C_1-C_{10} alkylene-(C_3-C_8 heterocyclo)-NH-, -(C_3-C_8 heterocyclo)-C_1-C_{10} alkylene-NH-, -C_1-C_{10} alkylene-S-, C_1-C_{10} heteroalkylene-S -, -C_3-C_8 carbocyclo-S -, -O-(C_1-C_8 alkylene)-S -, -arylene-S-, -C_1-C_{10} alkylene-arylene-S-, -arylene-C_1-C_{10} alkylene-S-, -C_1-C_{10} alkylene-(C_3-C_8 carbocyclo)-S-, -(C_3-C_8 carbocyclo)-C_1-C_{10} alkylene-S-, -C_3-C_8 heterocyclo-S-, -C_1-C_{10} alkylene-(C_3-C_8 heterocyclo)-S-, or -(C_3-C_8 heterocyclo)-C_1-C_{10} alkylene-S-, wherein subscript k is an integer ranging from 1 to 36.

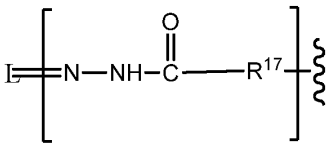
[0421] In still other embodiments, the reactive group of the Stretcher Unit precursor contains a reactive nucleophile that is capable of reacting with an electrophile present on, or introduced to, a Ligand Unit. For example, in some aspects, a carbohydrate moiety on a targeting ligand is mildly oxidized using a reagent such as sodium periodate and the resulting electrophilic functional group (-CHO) of the oxidized carbohydrate is condensed with a Stretcher Unit precursor that contains a reactive nucleophile such as a hydrazide, an oxime, a primary or secondary amine, a hydrazine, a thiosemicarbazone, a hydrazine carboxylate, or an arylhydrazide such as those described by Kaneko, T. *et al.* (1991) Bioconjugate Chem. 2:133-41. Representative Stretcher Units of this embodiment are depicted within the square brackets of Formulas Zdi, Zdii, and Zdiii:



(Zdi),



(Zdii),

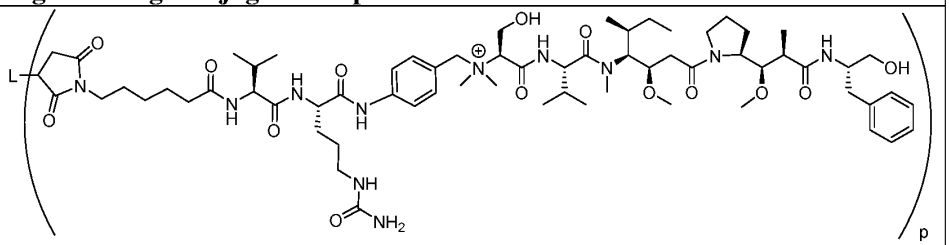


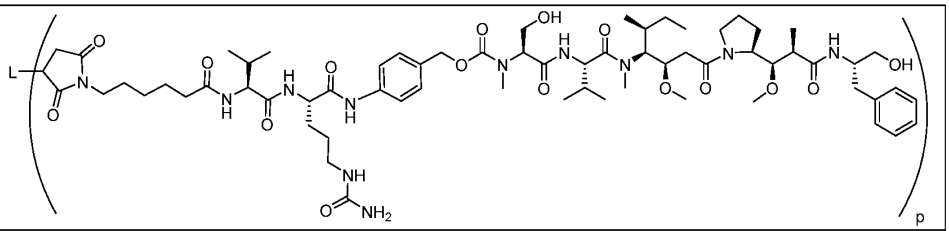
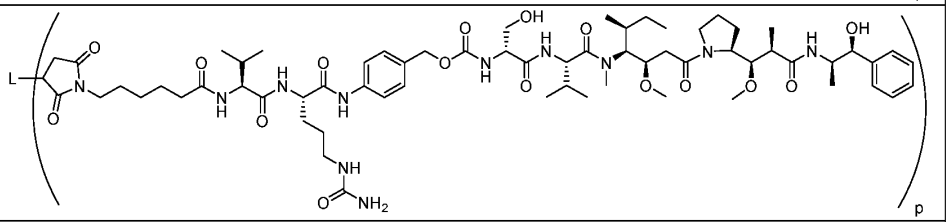
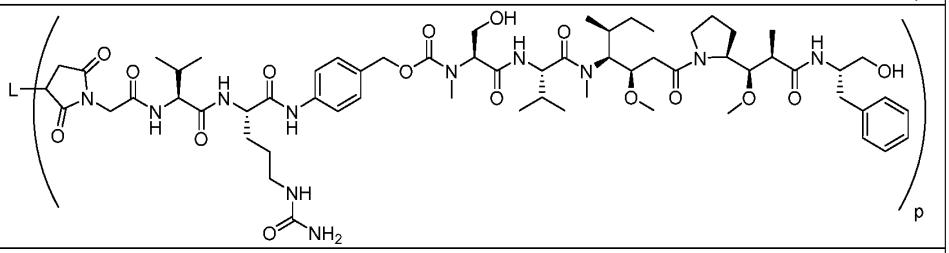
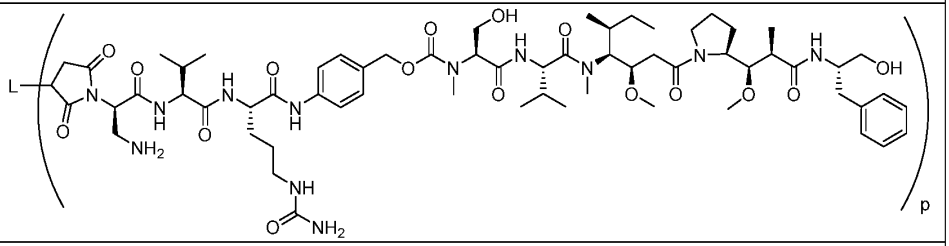
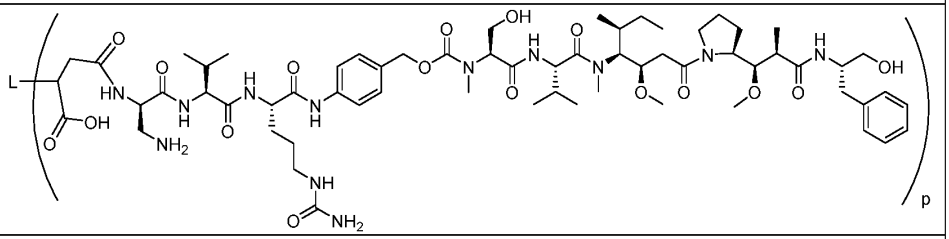
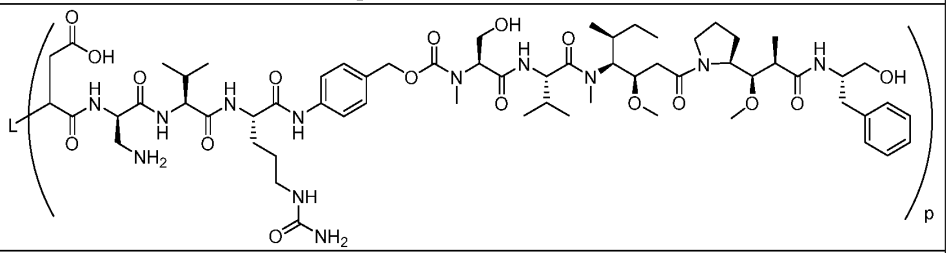
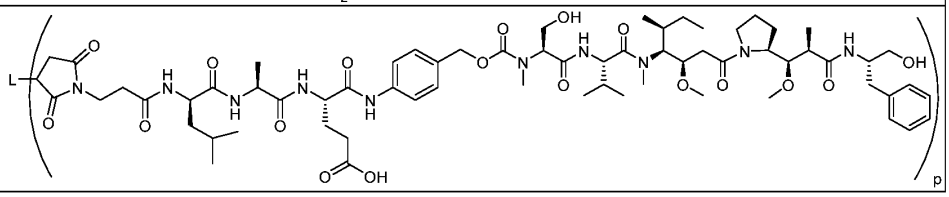
(Zdiii),

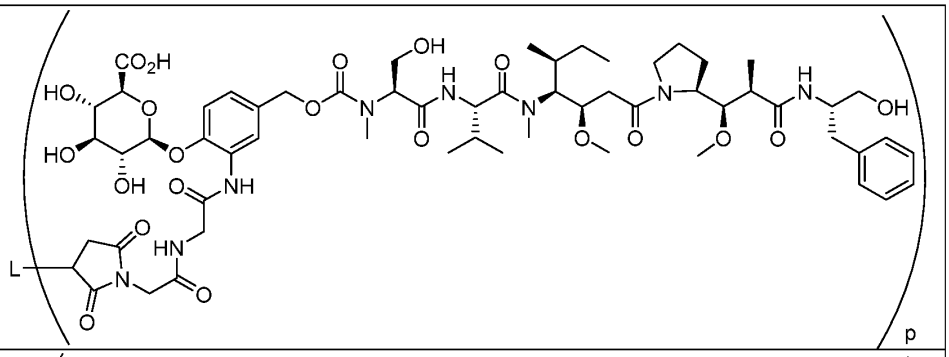
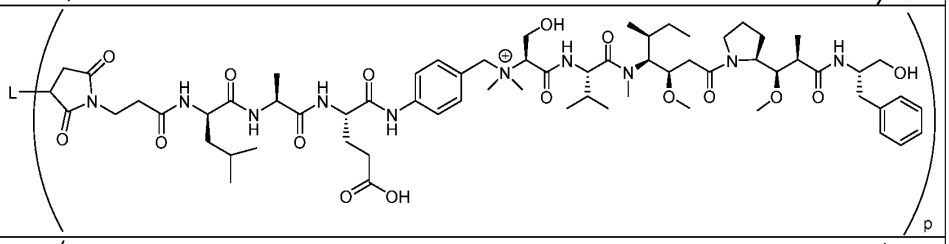
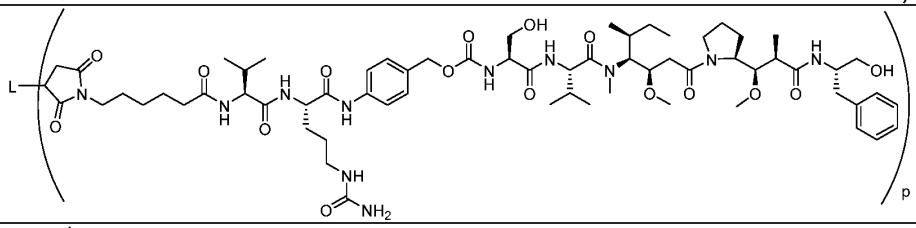
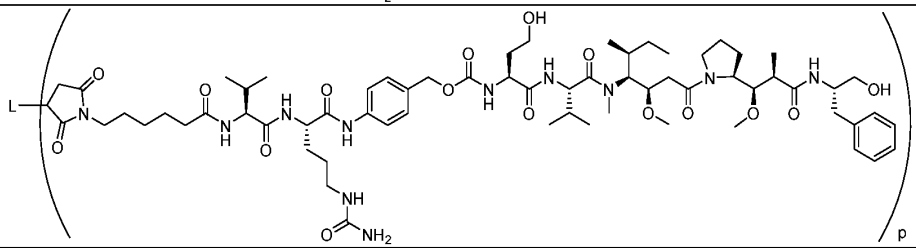
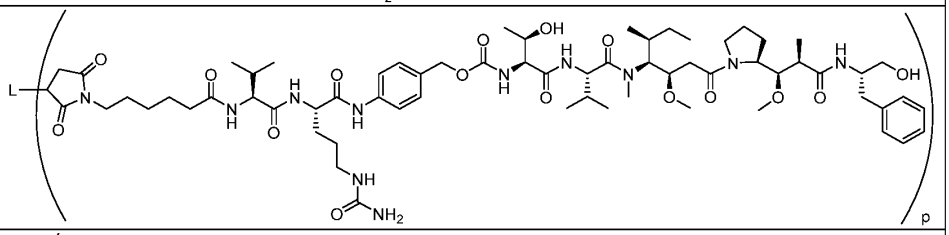
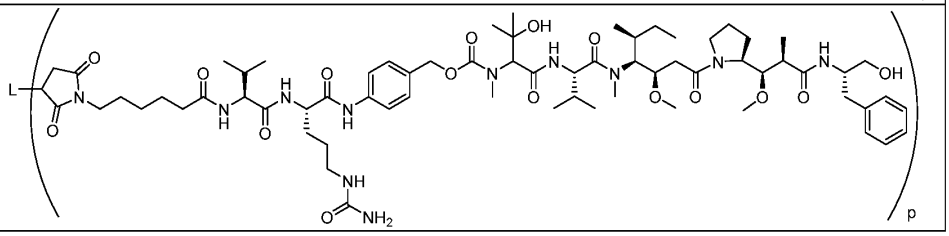
[0422] wherein the wavy line indicates attachment to the Parallel Connector Unit (B) or Connector Unit (A), or a Partitioning Agent (S^*), if A and B are absent and R^{17} is $–CH_2CH_2(OCH_2CH_2)_k–$, -C_1-C_{10} alkylene-, C_1-C_{10} heteroalkylene-, -C_3-C_8 carbocyclo-, -O-(C_1-C_8 alkylene)-, -arylene-, -C_1-C_{10} alkylene-arylene-, -arylene-C_1-C_{10} alkylene-, -C_1-C_{10} alkylene-(C_3-C_8 carbocyclo)-, -(C_3-C_8 carbocyclo)-C_1-C_{10} alkylene-, -C_3-C_8 heterocyclo-, -C_1-C_{10} alkylene-(C_3-C_8 heterocyclo)-, -(C_3-C_8 heterocyclo)-C_1-C_{10} alkylene-, -C_1-C_{10} alkylene-C(=O)-, C_1-C_{10} heteroalkylene-C(=O)-, -C_3-C_8 carbocyclo-C(=O)-, -O-(C_1-C_8 alkylene)-C(=O)-, -arylene-C(=O)-, -C_1-C_{10} alkylene-arylene-C(=O)-, -arylene-C_1-C_{10} alkylene-C(=O)-, -C_1-C_{10} alkylene-(C_3-C_8 carbocyclo)-C(=O)-,-(C_3-C_8 carbocyclo)-C_1-C_{10} alkylene-C(=O)-, -C_3-C_8 heterocyclo-C(=O)-, -C_1-C_{10} alkylene-(C_3-C_8 heterocyclo)-C(=O)-, -(C_3-C_8 heterocyclo)-C_1-C_{10} alkylene-C(=O)-, -C_1-C_{10} alkylene-NH-, C_1-C_{10} heteroalkylene-NH-, -C_3-C_8 carbocyclo-NH-, -O-(C_1-C_8 alkylene)-NH-, -arylene-NH-, -C_1-C_{10} alkylene-arylene-NH-, -arylene-C_1-C_{10} alkylene-NH-, -C_1-C_{10} alkylene-(C_3-C_8 carbocyclo)-NH-, -(C_3-C_8 carbocyclo)-C_1-C_{10} alkylene-NH-, -C_3-C_8 heterocyclo-NH-, -C_1-C_{10} alkylene-(C_3-C_8 heterocyclo)-NH-, -(C_3-C_8 heterocyclo)-C_1-C_{10} alkylene-NH-, -C_1-C_{10} alkylene-S-, C_1-C_{10} heteroalkylene-S -, -C_3-C_8 carbocyclo-S -, -O-(C_1-C_8 alkylene)-S -, -arylene-S-, -C_1-C_{10} alkylene-arylene-S-, -arylene-C_1-C_{10} alkylene-S-, -C_1-C_{10} alkylene-(C_3-C_8 carbocyclo)-S-, -(C_3-C_8 carbocyclo)-C_1-C_{10} alkylene-S-, -C_3-C_8 heterocyclo-S-, -C_1-C_{10} alkylene-(C_3-C_8 heterocyclo)-S-, or -(C_3-C_8 heterocyclo)-C_1-C_{10} alkylene-S-, wherein subscript k is an integer ranging from 1 to 36.

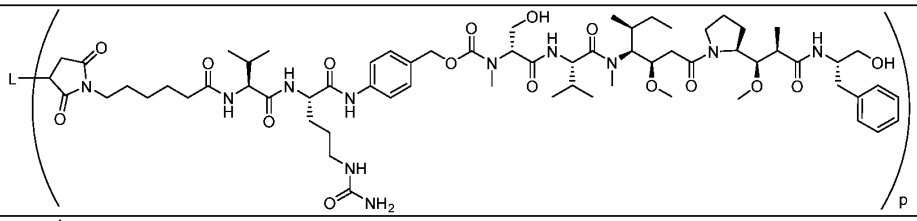
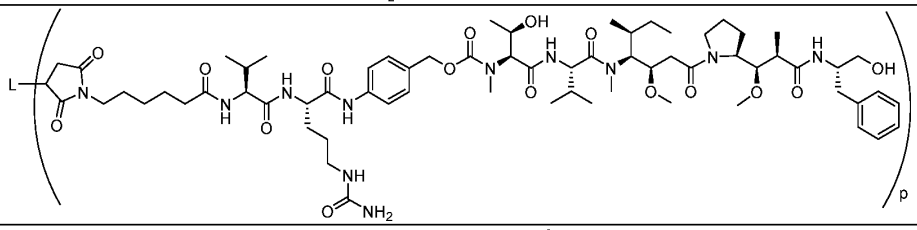
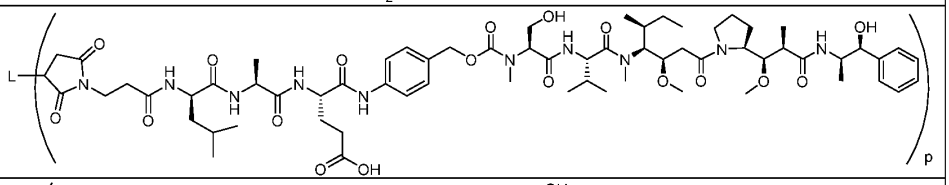
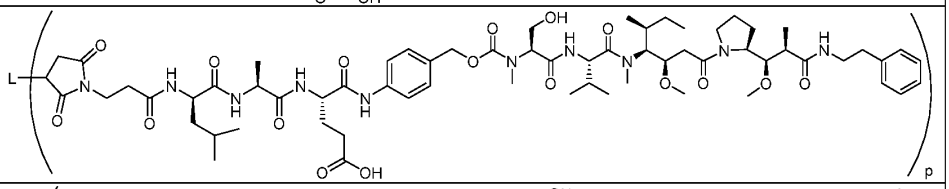
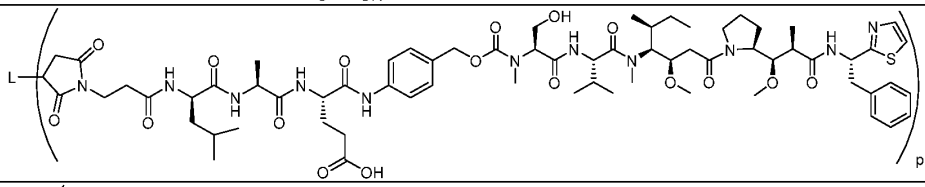
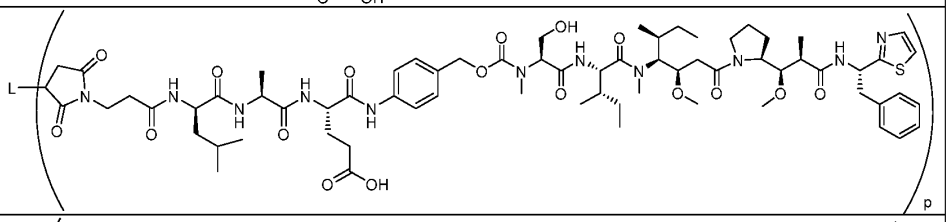
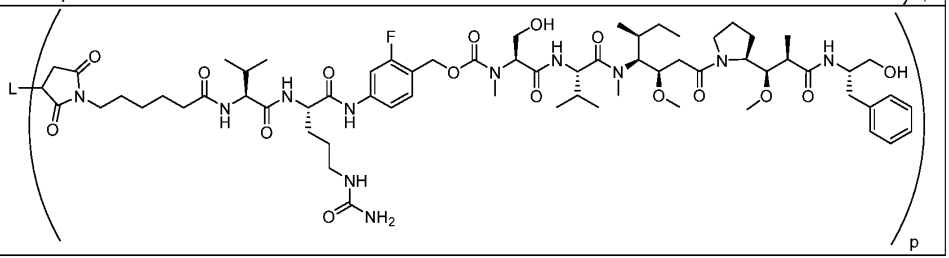
[0423] In some embodiments, provided herein is a Ligand-Drug Conjguate compound of Table 3, or a pharmaceutically acceptable salt thereof. Ligand-Drug Conjugate compounds corresponding to the compounds of Table 3 but having a succinic acid-amide moiety in place of the succinimide moiety are contemplated.

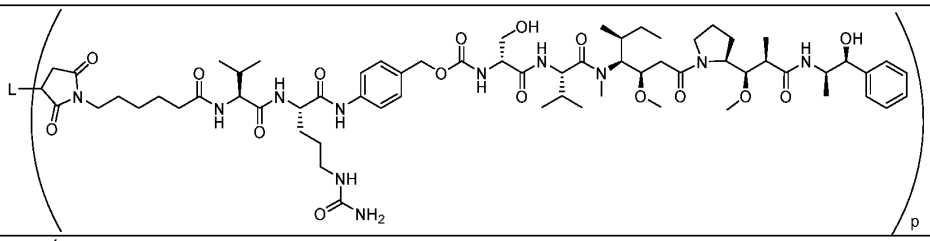
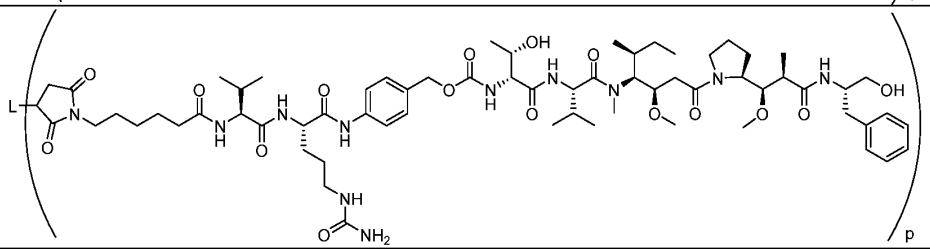
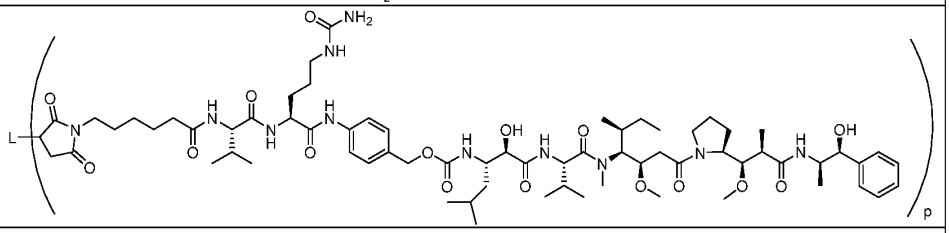
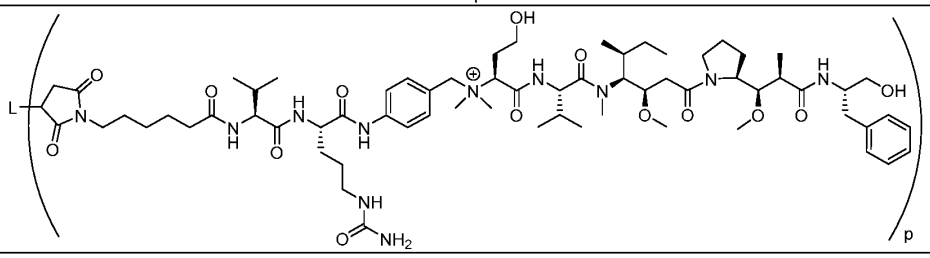
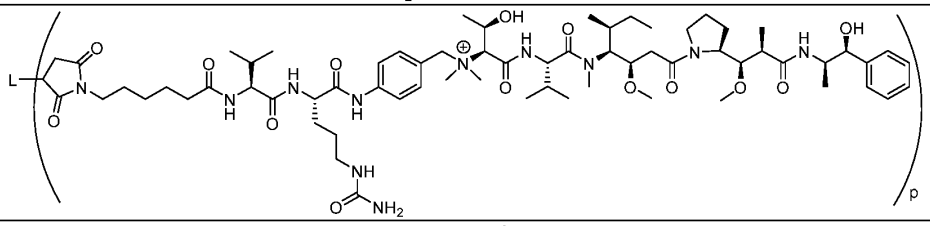
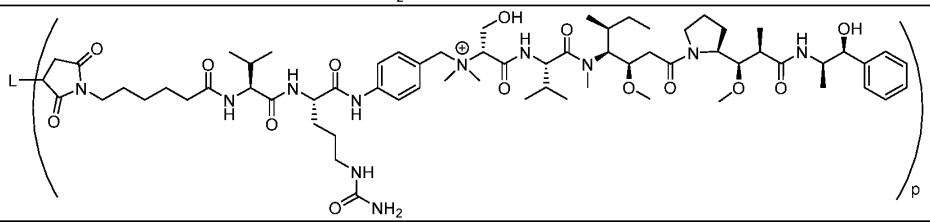
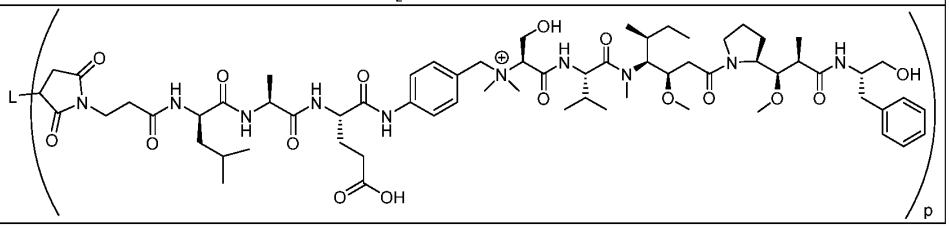
Table 3. Ligand-Drug Conjugate compounds

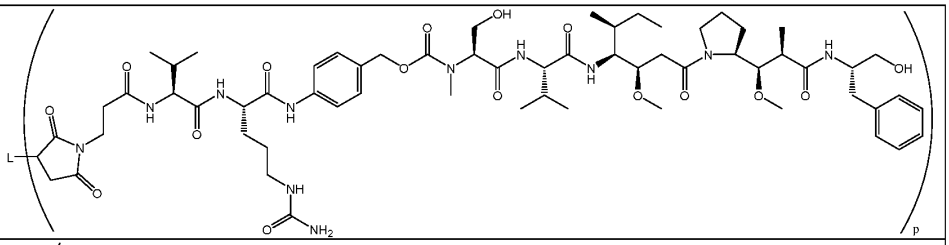
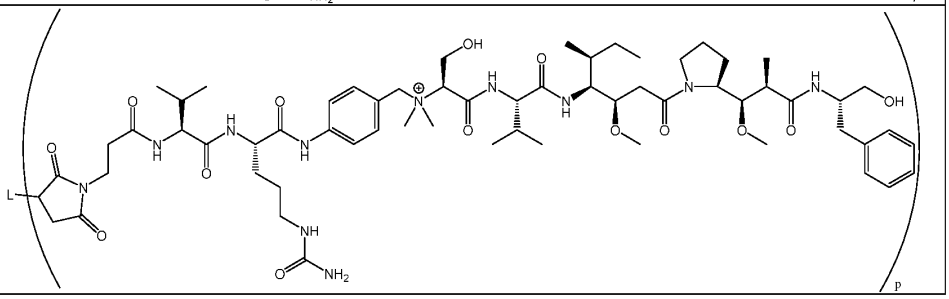
#	Ligand-Drug Conjugate compound structure
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Subscript p

[0424] Subscript p represents the number of Drug Linker moieties on a Ligand Unit of an individual Ligand-Drug Conjugate compound and is an integer ranging from 1 to 16, 1 to 12, 1 to 10, or 1 to 8. In any of the embodiments herein, there are 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, or 16 Drug Linker moieties conjugated to a Ligand Unit of an individual Ligand-Drug Conjugate compound.

[0425] In some embodiments, any of the structures and descriptions as described herein represent a population of individual Ligand-Drug Conjugate compounds substantially identical except for the number of Drug-Linker moieties bound to each Ligand Unit (i.e., a Ligand-Drug Conjugate composition) so that subscript p represents the average number of Drug-Linker moieties bound to the Ligand Units of the Ligand-Drug Conjugate composition. In that group of embodiments, subscript p is a number ranging from 1 to about 16, 1 to about 12, 1 to about 10, or 1 to about 8, from 2 to about 16, 2 to about 12, 2 to about 10, or 2 to about 8. In some aspects, p is about 2. In some aspects, p is about 4. In some aspects, p is about 8. In some aspects, p is about 16. In some aspects, p is 2. In some aspects, p is 4. In some aspects, p is 8. In some aspects, p is 16. In some embodiments, the value of subscript p refers to the average drug loading as well as the drug loading of the predominate Ligand-Drug Conjugate compound in the composition.

[0426] In some embodiments, conjugation will be via the reduced interchain disulfides and there will from 1 to about 8 Drug-Linker Compound molecules conjugated to a targeting agent that becomes a Ligand Unit. In some embodiments, conjugation will be via an

introduced cysteine residue as well as reduced interchain disulfides and there will be from 1 to 10 or 1 to 12 or 1 to 14 or 1 to 16 Drug-Linker Compound moieties conjugated to a Ligand Unit. In some embodiments, conjugation will be via an introduced cysteine residue and there will be 2 or 4 Drug-Linker Compound molecules conjugated to a Ligand Unit.

Ligand Unit L

[0427] In some embodiments of the invention, a Ligand Unit is present. The Ligand Unit (L-) is a targeting agent that specifically binds to a target moiety. In one group of embodiments, the Ligand Unit specifically and selectively binds to a cell component (a Cell Binding Agent) or to another target molecule of interest. The Ligand Unit acts to target and present the Drug Unit (such as one of Formula (I) or any subformula thereof) to the particular target cell population with which the Ligand Unit interacts due to the presence of its targeted component or molecule and allows for subsequent release of free drug within (i.e., intracellularly) or within the vicinity of the target cells (i.e., extracellularly). Ligand Units, L, include, but are not limited to, proteins, polypeptides and peptides. Suitable Ligand Units include, for example, antibodies, e.g., full-length antibodies and antigen binding fragments thereof, interferons, lymphokines, hormones, growth factors and colony-stimulating factors, vitamins, nutrient-transport molecules (such as, but not limited to, transferrin), or any other cell binding molecule or substance. In some embodiments, the Ligand Unit (L) is from an antibody or a non-antibody protein targeting agent.

[0428] In one group of embodiments a Ligand Unit is bonded to Q (a Linker Unit) which comprises a Glucuronide Releasable Linker. As noted above, in some aspects other linking components are present in the conjugates described herein to serve the purpose of providing additional space between the Drug Unit compound and the Ligand Unit (e.g., a Stretcher Unit and optionally a Connector Unit, A), or providing attributes to the composition to increases solubility (e.g., a Partitioning Agent, S^*). In some of those embodiments, the Ligand Unit is bonded to Z of the Linker Unit via a heteroatom of the Ligand Unit. Heteroatoms that may be present on a Ligand Unit for that bonding include sulfur (in one embodiment, from a sulfhydryl group of a targeting ligand), oxygen (in one embodiment, from a carboxyl or hydroxyl group of a targeting ligand) and nitrogen, optionally substituted (in one embodiment, from a primary or secondary amine functional group of a targeting ligand or in another embodiment from an optionally substituted amide nitrogen). Those heteroatoms are present on the targeting ligand in the ligand's natural state, for example in a naturally

occurring antibody, or are introduced into the targeting ligand via chemical modification or biological engineering.

[0429] In some embodiments, the Ligand Unit is an antibody.

[0430] Useful polyclonal antibodies are heterogeneous populations of antibody molecules derived from the sera of immunized animals. Useful monoclonal antibodies are homogeneous populations of antibodies to a particular antigenic determinant (e.g., a cancer or immune cell antigen, a protein, a peptide, a carbohydrate, a chemical, nucleic acid, or fragments thereof). A monoclonal antibody (mAb) to an antigen-of-interest can be prepared by using any technique known in the art which provides for the production of antibody molecules by continuous cell lines in culture.

[0431] Useful monoclonal antibodies include, but are not limited to, human monoclonal antibodies, humanized monoclonal antibodies, or chimeric human-mouse (or other species) monoclonal antibodies. The antibodies include full-length antibodies and antigen binding fragments thereof. Human monoclonal antibodies may be made by any of numerous techniques known in the art (*e.g.*, Teng *et al.*, 1983, *Proc. Natl. Acad. Sci. USA.* 80:7308-7312; Kozbor *et al.*, 1983, *Immunology Today* 4:72-79; and Olsson *et al.*, 1982, *Meth. Enzymol.* 92:3-16).

[0432] In some embodiments, an antibody includes a functionally active fragment, derivative or analog of an antibody that binds specifically to target cells (e.g., cancer cell antigens) or other antibodies bound to cancer cells or matrix. In this regard, "functionally active" means that the fragment, derivative or analog is able to bind specifically to target cells. To determine which CDR sequences bind the antigen, synthetic peptides containing the CDR sequences are typically used in binding assays with the antigen by any binding assay method known in the art (e.g., the Biacore assay) (*See*, *e.g.*, Kabat *et al.*, 1991, *Sequences of Proteins of Immunological Interest*, Fifth Edition, National Institute of Health, Bethesda, Md; Kabat E *et al.*, 1980, *J. Immunology* 125(3):961-969).

[0433] Additionally, recombinant antibodies, such as chimeric and humanized monoclonal antibodies, comprising both human and non-human portions, which are typically obtained using standard recombinant DNA techniques, are useful antibodies. A chimeric antibody is a molecule in which different portions are derived from different animal species, such as for example, those having a variable region derived from a murine monoclonal and a constant region derived from a human immunoglobulin. *See*, e.g., U.S. Patent No. 4,816,567;

and U.S. Patent No. 4,816,397, which are incorporated herein by reference in their entireties. Humanized antibodies are antibody molecules from non-human species having one or more CDRs from the non-human species and a framework region from a human immunoglobulin molecule. *See*, e.g., U.S. Patent No. 5,585,089, which is incorporated herein by reference in its entirety. Such chimeric and humanized monoclonal antibodies can be produced by recombinant DNA techniques known in the art, for example using methods described in International Publication No. WO 87/02671; European Patent Publication No. 0 184 187; European Patent Publication No. 0 171 496; European Patent Publication No. 0 173 494; International Publication No. WO 86/01533; U.S. Patent No. 4,816,567; European Patent Publication No. 012 023; Berter *et al.*, 1988, *Science* 240:1041-1043; Liu *et al.*, 1987, *Proc. Natl. Acad. Sci. USA* 84:3439-3443; Liu *et al.*, 1987, *J. Immunol.* 139:3521-3526; Sun *et al.*, 1987, *Proc. Natl. Acad. Sci. USA* 84:214-218; Nishimura *et al.*, 1987, *Cancer. Res.* 47:999-1005; Wood *et al.*, 1985, *Nature* 314:446-449; and Shaw *et al.*, 1988, *J. Natl. Cancer Inst.* 80:1553-1559; Morrison, 1985, *Science* 229:1202-1207; Oi *et al.*, 1986, *BioTechniques* 4:214; U.S. Patent No. 5,225,539; Jones *et al.*, 1986, *Nature* 321: 522-525; Verhoeyan *et al.*, 1988, *Science* 239:1534; and Beidler *et al.*, 1988, *J. Immunol.* 141:4053-4060; each of which is incorporated herein by reference in its entirety.

[0434] In some embodiments, an antibody is a completely human antibody. In some embodiments, an antibody is produced using transgenic mice that are incapable of expressing endogenous immunoglobulin heavy and light chain genes, but which are capable of expressing human heavy and light chain genes.

[0435] In some embodiments, an antibody is an intact or fully-reduced antibody. The term 'fully-reduced' is meant to refer to an antibody in which all four inter-chain disulfide linkages have been reduced to provide eight thiols that can be attached to a linker (L).

[0436] Attachment to an antibody can be via thioether linkages from native and/or engineered cysteine residues, or from an amino acid residue engineered to participate in a cycloaddition reaction (such as a click reaction) with the corresponding linker intermediate. *See,* e.g., Maerle, et al., *PLOS One* 2019: 14(1); e0209860. In some embodiments, an antibody is an intact or fully-reduced antibody, or is an antibody bearing engineered an cysteine group that is modified with a functional group that can participate in, for example, click chemistry or other cycloaddition reactions for attachment of other components of the ADC as described herein (e.g., Diels-Alder reactions or other [3+2] or [4+2] cycloadditions). *See,* e.g., Agard, et al., *J. Am. Chem. Soc.* Vol. 126, pp. 15046-15047 (2004); Laughlin, et al.,

Science, Vol. 320, pp. 664-667 (2008); Beatty, et al., *ChemBioChem*, Vol. 11, pp. 2092-2095 (2010); and Van Geel, et al., *Bioconjug. Chem.* Vol. 26, pp.2233-2242 (2015).

[0437] Antibodies that bind specifically to a cancer or immune cell antigen are available commercially or produced by any method known to one of skill in the art such as, e.g., chemical synthesis or recombinant expression techniques. The nucleotide sequences encoding antibodies that bind specifically to a cancer or immune cell antigen are obtainable, e.g., from the GenBank database or similar database, literature publications, or by routine cloning and sequencing.

[0438] In some embodiments, the antibody can be used for the treatment of a cancer (e.g., an antibody approved by the FDA and/or EMA). Antibodies that bind specifically to a cancer or immune cell antigen are available commercially or produced by any method known to one of skill in the art such as, e.g., recombinant expression techniques. The nucleotide sequences encoding antibodies that bind specifically to a cancer or immune cell antigen are obtainable, e.g., from the GenBank database or similar database, literature publications, or by routine cloning and sequencing.

[0439] In some cases, the antibody has a mutation or post-translational modification which affects non-Fab mediated uptake. Peripheral immune cells, which are highly responsive to TLR7/8 agonists can facilitate strong, systemic responses when activated through non-antigen specific, Fc-mediated uptake of the TLR7/8 antibody drug conjugate which may be harmful or otherwise undesirable. In such cases, the antibody can have an effector function-diminishing mutation, such as L234A/L235A, D265A/N297A, D270A, K322A, P329A, P329G or a combination thereof, which diminishes non-immune uptake (e.g., FcgR-mediated uptake).

[0440] In some embodiments, an antibody can be configured to bind to a surface antigen of a cell. The antibody, or a complex comprising the antibody, can be configured to internalize within a cell upon binding to the surface antigen. For example, the antibody or an ADC comprising the antibody can be configured to endocytose upon binding to a surface antigen of a cell. In some embodiments, the antibody (or an ADC comprising the antibody) is configured to internalize within a cancer cell. In some embodiments, the antibody (or an ADC comprising the antibody) is configured to internalize within an immune cell. In some embodiments, the immune cell is a tumor associated macrophage. In some embodiments, the surface antigen is a receptor or a receptor complex (e.g., expressed on lymphocytes). In some

embodiments, the receptor or receptor complex comprises an immunoglobulin gene superfamily member, a TNF receptor superfamily member, an integrin, a cytokine receptor, a chemokine receptor, a major histocompatibility protein, a lectin, or a complement control protein or other immune cell expressed surface receptor.

[0441] In some embodiments, an antibody is configured to bind specifically to a cancer cell antigen. In some embodiments, an antibody is configured to bind specifically to an immune cell antigen. In some embodiments, the immune cell antigen is a tumor associated macrophage antigen. In some embodiments, an antibody is configured to bind specifically to EphA2. It will be understood that the antibody component in an ADC is an antibody in residue form such that "Ab" in the ADC structures described herein incorporates the structure of the antibody.

[0442] Non-limiting examples of antibodies that can be used for treatment of cancer and antibodies that bind specifically to tumor associated antigens are disclosed in Franke, A. E., Sievers, E. L., and Scheinberg, D. A., "Cell surface receptor-targeted therapy of acute myeloid leukemia: a review" *Cancer Biother Radiopharm.* 2000,15, 459-76; Murray, J. L., "Monoclonal antibody treatment of solid tumors: a coming of age" *Semin Oncol.* 2000, 27, 64-70; Breitling, F., and Dubel, S., *Recombinant Antibodies*, John Wiley, and Sons, New York, 1998, each of which is hereby incorporated by reference in its entirety.

[0443] Non-limiting examples of antigens which antibodies of the present disclosure may target include ADAM12 (e.g., Catalog #14139-1-AP); ADAM9 (e.g., IMGC936); AFP (e.g., ThermoFisher Catalog #PA5-25959); AGR2 (e.g., ThermoFisher Catalog #PA5-34517); AKAP-4 (e.g., Catalog #PA5-52230); ALK (e.g., DLX521); ALPP (e.g., Catalog #MA5-15652); ALPPL2 (e.g., Catalog #PA5-22336); AMHR2 (e.g., ThermoFisher Catalog #PA5-13902); androgen receptor (e.g., ThermoFisher Catalog #MA5-13426); ANTXR1 (e.g., Catalog #MA1-91702); ANXA1 (e.g., Catalog #71-3400); ARTN (e.g., ThermoFisher Catalog #PA5-47063); ASCT2 (e.g., idactamab); Axl (e.g., BA3011; tilvestamab); B7-DC (e.g., Catalog #PA5-20344); B7-H3 (e.g., enoblituzumab, omburtamab, MGD009, MGC018, DS-7300); B7-H4 (e.g., Catalog #14-5949-82); B7-H6 (e.g., Catalog #12-6526-42); B7-H7; BAFF-R (e.g., Catalog #14-9117-82); BCMA; BCR-ABL; BMPR2; BORIS; C4.4a; CanAg; C5 complement (e.g., BCD-148; CAN106); CA-125; CA19-9 (e.g., AbGn-7; MVT-5873); CA9 (e.g., girentuximab); CALCR (*see,* e.g., International Publication No. WO 2015077826); CAMPATH-1 (e.g., alemtuzumab; ALLO-647; ANT1034); carcinoembryonic antigen (e.g., arcitumomab; cergutuzumab; amunaleukin; labetuzumab); CCNB1; CD112

(*see,* e.g., U.S. Publication No. 20100008928); CD115 (e.g., axatilimab; cabiralizumab; emactuzumab); CD123 (e.g., BAY-943; CSL360); CD137 (e.g., ADG106; CTX-471); CD138; CD142; CD166; CD147 (e.g., gavilimomab; metuzumab); CD155 (e.g., U.S. Publication No. 2018/0251548); CD19 (e.g., ALLO-501); CD20 (e.g., divozilimab; ibritumomab tiuxetan); CD24 (*see,* e.g., U.S. Patent No. 8,614,301); CD244 (e.g., R&D AF1039); CD247 (e.g., AFM15); CD27 (e.g., varlilumab); CD274 (e.g., adebrelimab; atezolizumab; garivulimab); CD3 (e.g., otelixizumab; visilizumab); CD30 (e.g., iratumumab); CD33 (e.g., lintuzumab; BI 836858; AMG 673); CD288; CD352 (e.g., SGN-CD352A); CD37 (e.g., lilotomab; GEN3009); CD38 (e.g., felzartamab; AMG 424); CD3D; CD3E (e.g., foralumab; teplizumab); CD3G; CD45 (e.g., apamistamab); CD47 (e.g., letaplimab; magrolimab); CD48 (e.g., SGN-CD48A); CD5 (e.g., MAT 304; zolimomab aritox); CD56; CD59; CD70 (e.g., cusatuzumab); CD74 (e.g., milatuzumab); CD79A (*see,* e.g., International Publication No. WO 2020252110); CD79b; CD96; CD97; CD-262 (e.g., tigatuzumab); CDCP1 (e.g., RG7287); CDH17 (*see,* e.g., International Publication No. WO 2018115231); CDH3 (e.g., PCA062); CDH6 (e.g., HKT288); CEACAM1; CEACAM5; CEACAM6; CLDN1 (e.g., INSERM anti-Claudin-1); CLDN16; CLDN18.1 (e.g., zolbetuximab); CLDN18.2 (e.g., zolbetuximab); CLDN19; CLDN2 (*see,* e.g., International Publication No. WO 2018123949); CLEC12A (e.g., tepoditamab); CS1; CLPTM1L; CSPG4 (e.g., U.S. Patent No. 10,822,427); CXCR4 (e.g., ulocuplumab); CYP1B1; c-Met; DCLK1 (*see,* e.g., International Publication No. WO 2018222675); DDR1; de2-7 EGFR (e.g., MAb 806); DLL-3; DPEP1; DPEP3; DPP4; DR4 (e.g., mapatumumab); DSG2 (*see,* e.g., U.S. Patent No. 10,836,823); EGF; EGFR; endosialin (e.g., ontuxizumab); ENPP1; EPCAM (e.g., adecatumumab); EPHA receptors; EPHA2; ERBB2 (e.g., trastuzumab); ERBB3; ERVMER34_1; ETV6-AML (e.g., Catalog #PA5-81865); FAS; FasL; Fas-related antigen 1; FBP; FGFR1 (e.g., RG7992); FGFR2 (e.g., aprutumab); FGFR3 (e.g., vofatamab); FGFR4 (e.g., MM-161); FLT3 (e.g., 4G8SDIEM); FN; FN1; FOLR1 (e.g., farletuzumab); FRa; FSHR; FucGM1 (e.g., BMS-986012); FZD5; FZD8; G250; GAGE; GCC; GD2 (e.g., dinutuximab); GD3 (e.g., mitumomab); GITR (e.g., ragifilimab); GloboH; GM2 (e.g., BIW-8962); GM3 (e.g., racotumomab); gp100; GPA33 (e.g., KRN330); GPC3 (e.g., codrituzumab); gpNMB (e.g., glembatumumab); GPR87; GUCY2C (e.g., indusatumab); HAS3; HAVCR2; HLA-E; HLA-F; HLA-G (e.g., TTX-080); HPV E6 E7; hTERT; ICAM1; IDO1; IFNAR1 (e.g., faralimomab); IFNAR2; IL13Ra2; IL1RAP (e.g., nidanilimab); IL-21R (e.g., PF-05230900); IL-5R (e.g., benralizumab); ITGAV (e.g., abituzumab); ITGB6; ITGB8; KISS1R; L1CAM (e.g., JCAR023); LAG-3 (e.g., encelimab); LAMP1; LCK; legumain;

LMP2; LY6G6D (e.g., PA5-23303); LY9 (e.g., PA5-95601); LYPD1 (e.g., ThermoFisher Catalog #PA5-26749); MAD-CT-1; MAD-CT-2; MAGEA1 (e.g., Catalog #MA5-11338); MAGEA3 (e.g., ThermoFisher Catalog #60054-1-IG); MAGEA4 (e.g., Catalog #MA5-26117); MAGEC2 (e.g., ThermoFisher Catalog #PA5-64010); MELTF (e.g., ThermoFisher Catalog #H00004241-M04A); MerTk (e.g., DS5MMER, Catalog #12-5751-82); a metalloproteinase; MFSD13A; MICA (e.g., 1E2C8, Catalog #66384-1-IG); MICB (e.g., Catalog #MA5-29422); Mincle (e.g., OTI2A8, Catalog #TA505101); MLANA (e.g., Catalog #MA5-15237); ML-IAP (e.g., 88C570, ThermoFisher Catalog #40958); MSLN (e.g., 5B2, Catalog #MA5-11918); MUC1 (e.g., MH1 (CT2), ThermoFisher Catalog #MA5-11202); MUC5AC (e.g., 45M1, Catalog #MA5-12178); MYCN (e.g., NCM-II 100, ThermoFisher Catalog #MA1-170); NA17; NCAM1 (e.g., ThermoFisher Catalog #MA5-11563); Nectin-4 (e.g., enfortumab); NOX1 (e.g., Catalog #PA5-103220); NT5E (e.g., 7G2, ThermoFisher Catalog #41-0200); NY-BR-1 (e.g., NY-BR-1 No. 2, Catalog #MA5-12645); NY-ESO-1 (e.g., E978m, Catalog #35-6200); OX40 (e.g., ABM193); OY-TES1; p53; p53mutant; PAP; PAX3 (e.g., GT1210, ThermoFisher Catalog #MA5-31583); PAX5; PDGFR-B (e.g., rinucumab); PDPN (e.g., ThermoFisher Catalog #14-5381-82); PLAVl; PMSA; polysialic acid (*see,* e.g., Watzlawik et al. J Nat Sci. 2015; 1(8):e141); PR1; PROM1 (e.g., Catalog #14-1331-82); PSA (e.g., ThermoFisher Catalog #PA1-38514; Daniels-Wells et al. *BMC Cancer* 2013; 13:195); PSCA (e.g., AGS-1C4D4); PSMA (e.g., BAY 2315497); PTK7 (e.g., cofetuzumab); PVRIG; Ras mutant (e.g., Shin et al. *Sci Adv.* 2020; 6(3):eaay2174); RET (e.g., WO2020210551); RGS5 (e.g., TF-TA503075); RhoC (e.g., ThermoFisher Catalog PA5-77866); ROR1 (e.g., cirmtuzumab); ROR2 (e.g., BA3021); ROS1 (e.g., WO 2019107671); Sarcoma translocation breakpoints; SART3 (e.g., TF 18025-1-AP); Sialyl-Thomsen-nouveau-antigen (e.g., Eavarone et al. *PLoS One.* 2018; 13(7): e0201314); Siglecs 1-16 (*see,* e.g., Angata et al. Trends *Pharmacol Sci.* 2015; 36(10): 645–660); SIRPa (e.g., Catalog #17-1729-42); SIRPg (e.g., PA5-104381); SIT1 (e.g., PA5-53825); SLAMF7 (e.g., elotuzumab); SLC10A2 (e.g., ThermoFisher Catalog #PA5-18990); SLC12A2 (e.g., ThermoFisher Catalog #13884-1-AP); SLC17A2 (e.g., ThermoFisher Catalog #PA5-106752); SLC38A1 (e.g., ThermoFisher Catalog #12039-1-AP); SLC39A5 (e.g., ThermoFisher Catalog #MA5-27260); SLC39A6 (e.g., ladiratuzumab); SLC44A4 (e.g., ASG-5ME); SLC6A15 (e.g., ThermoFisher Catalog #PA5-52586); SLC6A6 (e.g., ThermoFisher Catalog #PA5-53431); SLC7A11 (e.g., ThermoFisher Catalog #PA1-16893); SLC7A5; sLe; SLITRK6 (e.g., sirtratumab); Sperm protein 17 (e.g., BS-5754R); SSX2 (e.g., ThermoFisher Catalog #MA5-24971); survivin (e.g., PA1-16836); TACSTD2 (e.g., PA5-

47074); TAG-72 (e.g., MA1-25956); tenascin; TF (e.g., tisotumab); Tie3; TLR2/4/1 (e.g., tomaralimab); TM4SF5 (e.g., 18239-1-AP); TMEM132A (e.g., Catalog #PA5-62524); TMEM40 (e.g., PA5-60636); TMPRSS11D (e.g., PA5-30927); Tn; TNFRSF12 (e.g., BAY-356); TRAIL (e.g., Catalog #12-9927-42); TRAIL1; TRP-2 (e.g., PA5-52736); ULBP1/2/3/4/5/6 (e.g., PA5-82302); uPAR (e.g., ATN-658); UPK1B (e.g., ThermoFisher Catalog #PA5-56863); UPK2 (e.g., ThermoFisher Catalog #PA5-60318); UPK3B (e.g., ThermoFisher Catalog #PA5-52696); VEGF (e.g., GNR-011); VEGFR2 (e.g., gentuximab); VSIR (e.g., ThermoFisher Catalog #PA5-52493); WT1 (e.g., ThermoFisher Catalog #MA5-32215); and XAGE1 (e.g., ThermoFisher Catalog #PA5-46413).

[0444] Non-limiting examples of target antigens include Axl (e.g., BA3011; tilvestamab); B7-1 (e.g., galiximab); B7-2 (e.g., Catalog #12-0862-82); B7-DC (e.g., Catalog #PA5-20344); B7-H3 (e.g., enoblituzumab, omburtamab, MGD009, MGC018, DS-7300); B7-H4 (e.g., Catalog #14-5949-82); B7-H6 (e.g., Catalog #12-6526-42); B7-H7; BAFF-R (e.g., Catalog #14-9117-82); BCMA; C5 complement (e.g., BCD-148; CAN106); CCR4 (e.g., AT008; mogamulizumab-kpkc); CCR8 (e.g., JTX-1811); CD112 (*see,* e.g., U.S. Publication No. 20100008928); CD115 (e.g., axatilimab; cabiralizumab; emactuzumab); CD123 (e.g., BAY-943; CSL360); CD137 (e.g., ADG106; CTX-471); CD155 (e.g., U.S. Publication No. 2018/0251548); CD163 (e.g., TBI 304H); CD19 (e.g., ALLO-501); CD2 (e.g., BTI-322; siplizumab); CD20 (e.g., divozilimab; ibritumomab); CD24 (*see,* e.g., U.S. Patent No. 8,614,301); CD244 (e.g., R&D AF1039); CD247 (e.g., AFM15); CD25 (e.g., basiliximab); CD27 (e.g., varlilumab); CD274 (e.g., adebrelimab; atezolizumab; garivulimab); CD278 (e.g., feladilimab; vopratelimab); CD28 (e.g., REGN5668); CD3 (e.g., otelixizumab; visilizumab); CD30 (e.g., iratumumab); CD30L (*see,* e.g., U.S. Patent No. 9,926,373); CD32 (e.g., mAb 2B6); CD33 (e.g., lintuzumab; BI 836858; AMG 673); CD352 (e.g., SGN-CD352A); CD37 (e.g., lilotomab; GEN3009); CD38 (e.g., felzartamab; AMG 424); CD3D; CD3E (e.g., foralumab; teplizumab); CD3G; CD40 (e.g., dacetuzumab; lucatumumab); CD44 (e.g., RG7356); CD45 (e.g., apamistamab); CD47 (e.g., letaplimab; magrolimab); CD48 (e.g., SGN-CD48A); CD5 (e.g., MAT 304; zolimomab aritox); CD51; CD70 (e.g., cusatuzumab); CD74 (e.g., milatuzumab); CD79A (*see,* e.g., International Publication No. WO 2020252110); CD83 (e.g., CBT004); CD97; CD262 (e.g., tigatuzumab); CLEC12A (e.g., tepoditamab); CTLA4 (e.g., ipilimumab); CXCR4 (e.g., ulocuplumab); DCIR; DCSIGN (*see,* e.g., International Publication No. WO 2018134389); Dectin1 (*see,* e.g., U.S. Patent No. 9,045,542); Dectin2 (e.g., ThermoFisher Catalog #MA5-16250); DR4 (e.g., mapatumumab);

endosialin (e.g., ontuxizumab); FasL; FLT3 (e.g., 4G8SDIEM); GITR (e.g., ragifilimab); HAVCR2; HER2; HER3; HLA-DR; HLA-E; HLA-F; HLA-G (e.g., TTX-080); ICAM1; IDO1; IFNAR1 (e.g., faralimomab); IFNAR2; IGF-1R; IL1RAP (e.g., nidanilimab); IL-21R (e.g., PF-05230900); IL-5R (e.g., benralizumab); Integrin αvβ6; LAG-3 (e.g., encelimab); LAMP1; LAYN; LCK; LILRB2; LILRB4; MerTk (e.g., DS5MMER, Catalog #12-5751-82); Mesothelin; MICA (e.g., 1E2C8, Catalog #66384-1-IG); MICB (e.g., Catalog #MA5-29422); MICA; Mincle (e.g., OTI2A8, Catalog #TA505101); MRC1 (e.g., ThermoFisher Catalog #12-2061-82); MUC1; Muc16; NcaPi2B; Nectin-4; OX40 (e.g., ABM193); PD-1 (e.g., balstilimab; budigalimab; geptanolimab); PD-L1; Prolactin receptor; PTK7; PVRIG; ROR-1; Sialyl-Thomsen-nouveau-antigen (e.g., Eavarone et al. *PLoS One*, 2018; 13(7): e0201314); Siglecs 1-16 (*see,* e.g., Angata et al. Trends Pharmacol Sci. 2015; 36(10): 645–660);); SIRPa (e.g., Catalog #17-1729-42); SIRPg (e.g., PA5-104381); SIT1 (e.g., PA5-53825); SLAMF7 (e.g., elotuzumab); SLTRK6; STEAP1; TIGIT (e.g., etigilimab); TLR2/4/1 (e.g., tomaralimab); Trem2 (e.g., PY314); TROP2; Tyrol; ULBP1/2/3/4/5/6 (e.g., PA5-82302); uPAR (e.g., ATN-658); VSIR (e.g., ThermoFisher Catalog #PA5-52493); ZIP6 (Anti-Integrin αvβ6).

(i) Heavy Chain and Light Chain Variable Regions

[0445] In some cases, an antibody target is selected from the group consisting of ADAM9, ASCT2, Axl, B7-H3, B7H4, BCMA, BCMA, C4.4a, CanAg, CD123, CD138, CD142, CD166, CD19, CD20, CD228, CD25, CD30, CD33, CD352, CD38, CD48, CD56, CD59, CD70, CD74, CD79b, CDCP1, CEACAM5, Claudin-18.2, c-Met, gpNMB, CS1, DLL-3, DPEP-3, EGFR, EpCAM, EphA2, FGFR2, FRa, GCC, gpA33, GPC3, Integrin αvβ6 , h2A2, H2G12/STn, HER2, HER3, ZIP6, IGF-1R, IL1Rap, ITGav/CD51, Mesothelin, MICA, MUC-1, Muc16, NaPi2B, Nectin-4, PD-L1, Prolactin receptor, PTK7, ROR-1, SLAMF7, SLTRK6, STEAP1, TIGIT, and TROP2.

[0446] In some cases, an antibody of the present disclosure comprises a heavy chain variable region having at least 80% sequence identity to a first sequence and a light chain variable region having at least 80% sequence identity to a second sequence, and wherein: the first sequence is SEQ ID NO: 19 and the second sequence is SEQ ID NO: 20; the first sequence is SEQ ID NO: 44 and the second sequence is SEQ ID NO: 45; the first sequence is SEQ ID NO: 55 and the second sequence is SEQ ID NO: 56; the first sequence is SEQ ID NO: 69 and the second sequence is SEQ ID NO: 70; the first sequence is SEQ ID NO: 83 and the second sequence is SEQ ID NO: 84; the first sequence is SEQ ID NO: 97 and the second

sequence is SEQ ID NO: 98; the first sequence is SEQ ID NO: 105 and the second sequence is SEQ ID NO: 106; the first sequence is SEQ ID NO:113 and the second sequence is SEQ ID NO: 114; the first sequence is SEQ ID NO: 121 and the second sequence is SEQ ID NO: 122; the first sequence is SEQ ID NO: 129 and the second sequence is SEQ ID NO: 130; the first sequence is SEQ ID NO: 137 and the second sequence is SEQ ID NO: 138; the first sequence is SEQ ID NO: 153 and the second sequence is SEQ ID NO: 154; the first sequence is SEQ ID NO: 161 and the second sequence is SEQ ID NO: 162; the first sequence is SEQ ID NO: 169 and the second sequence is SEQ ID NO: 170; the first sequence is SEQ ID NO: 177 and the second sequence is SEQ ID NO: 178; the first sequence is SEQ ID NO: 185 and the second sequence is SEQ ID NO: 186; the first sequence is SEQ ID NO: 193 and the second sequence is SEQ ID NO: 194; the first sequence is SEQ ID NO: 201 and the second sequence is SEQ ID NO: 202; the first sequence is SEQ ID NO: 209 and the second sequence is SEQ ID NO: 210; the first sequence is SEQ ID NO: 217 and the second sequence is SEQ ID NO: 218; the first sequence is SEQ ID NO: 225 and the second sequence is SEQ ID NO: 226; the first sequence is SEQ ID NO: 233 and the second sequence is SEQ ID NO: 234; the first sequence is SEQ ID NO: 241 and the second sequence is SEQ ID NO: 242; the first sequence is SEQ ID NO: 249 and the second sequence is SEQ ID NO: 250; the first sequence is SEQ ID NO: 297 and the second sequence is SEQ ID NO: 298; the first sequence is SEQ ID NO: 307 and the second sequence is SEQ ID NO: 308; the first sequence is SEQ ID NO: 315 and the second sequence is SEQ ID NO: 316; the first sequence is SEQ ID NO: 323 and the second sequence is SEQ ID NO: 324; the first sequence is SEQ ID NO: 331 and the second sequence is SEQ ID NO: 332; the first sequence is SEQ ID NO: 339 and the second sequence is SEQ ID NO: 340; the first sequence is SEQ ID NO: 347 and the second sequence is SEQ ID NO: 348; the first sequence is SEQ ID NO: 355 and the second sequence is SEQ ID NO: 356; the first sequence is SEQ ID NO: 363 and the second sequence is SEQ ID NO: 364; the first sequence is SEQ ID NO: 371 and the second sequence is SEQ ID NO: 372; the first sequence is SEQ ID NO: 379 and the second sequence is SEQ ID NO: 380; the first sequence is SEQ ID NO: 387 and the second sequence is SEQ ID NO: 388; the first sequence is SEQ ID NO: 395 and the second sequence is SEQ ID NO: 396; the first sequence is SEQ ID NO: 403 and the second sequence is SEQ ID NO: 404; the first sequence is SEQ ID NO: 411 and the second sequence is SEQ ID NO: 412; the first sequence is SEQ ID NO: 419 and the second sequence is SEQ ID NO: 420; the first sequence is SEQ ID NO: 427 and the second sequence is SEQ ID NO: 428; the first sequence is SEQ ID NO: 435 and the second sequence is SEQ ID NO: 436; the first sequence is SEQ ID NO: 443 and the second sequence

is SEQ ID NO: 444; the first sequence is SEQ ID NO: 451 and the second sequence is SEQ ID NO: 452; the first sequence is SEQ ID NO: 459 and the second sequence is SEQ ID NO: 460; the first sequence is SEQ ID NO: 467 and the second sequence is SEQ ID NO: 468; the first sequence is SEQ ID NO: 475 and the second sequence is SEQ ID NO: 476; the first sequence is SEQ ID NO: 483 and the second sequence is SEQ ID NO: 484; the first sequence is SEQ ID NO: 491 and the second sequence is SEQ ID NO: 492; the first sequence is SEQ ID NO: 501 and the second sequence is SEQ ID NO: 502; the first sequence is SEQ ID NO: 509 and the second sequence is SEQ ID NO: 510; the first sequence is SEQ ID NO: 517 and the second sequence is SEQ ID NO: 518; the first sequence is SEQ ID NO: 525 and the second sequence is SEQ ID NO: 526; the first sequence is SEQ ID NO: 533 and the second sequence is SEQ ID NO: 534; the first sequence is SEQ ID NO: 541 and the second sequence is SEQ ID NO: 542; the first sequence is SEQ ID NO: 549 and the second sequence is SEQ ID NO: 550; the first sequence is SEQ ID NO: 557 and the second sequence is SEQ ID NO: 558; the first sequence is SEQ ID NO: 565 and the second sequence is SEQ ID NO: 566; the first sequence is SEQ ID NO: 574 and the second sequence is SEQ ID NO: 574; the first sequence is SEQ ID NO: 581 and the second sequence is SEQ ID NO: 582; the first sequence is SEQ ID NO: 589 and the second sequence is SEQ ID NO: 590; the first sequence is SEQ ID NO: 597 and the second sequence is SEQ ID NO: 598; the first sequence is SEQ ID NO: 605 and the second sequence is SEQ ID NO: 606; the first sequence is SEQ ID NO: 613 and the second sequence is SEQ ID NO: 614; the first sequence is SEQ ID NO: 621 and the second sequence is SEQ ID NO: 622; the first sequence is SEQ ID NO: 629 and the second sequence is SEQ ID NO: 630; the first sequence is SEQ ID NO: 637 and the second sequence is SEQ ID NO: 638; the first sequence is SEQ ID NO: 645 and the second sequence is SEQ ID NO: 646; the first sequence is SEQ ID NO: 653 and the second sequence is SEQ ID NO: 654; the first sequence is SEQ ID NO: 661 and the second sequence is SEQ ID NO: 662; the first sequence is SEQ ID NO: 669 and the second sequence is SEQ ID NO: 670; the first sequence is SEQ ID NO: 677 and the second sequence is SEQ ID NO: 678; the first sequence is SEQ ID NO: 685 and the second sequence is SEQ ID NO: 686; the first sequence is SEQ ID NO: 693 and the second sequence is SEQ ID NO: 694; the first sequence is SEQ ID NO: 701 and the second sequence is SEQ ID NO: 702; the first sequence is SEQ ID NO: 703 and the second sequence is SEQ ID NO: 704; the first sequence is SEQ ID NO: 711 and the second sequence is SEQ ID NO: 712; the first sequence is SEQ ID NO: 713 and the second sequence is SEQ ID NO: 714; the first sequence is SEQ ID NO: 715 and the second sequence is SEQ ID NO: 716; the first sequence is SEQ ID NO: 731 and the second sequence is SEQ

ID NO: 732; the first sequence is SEQ ID NO: 739 and the second sequence is SEQ ID NO: 740; the first sequence is SEQ ID NO: 747 and the second sequence is SEQ ID NO: 748; the first sequence is SEQ ID NO: 755 and the second sequence is SEQ ID NO: 756; the first sequence is SEQ ID NO: 765 and the second sequence is SEQ ID NO: 766; the first sequence is SEQ ID NO: 773 and the second sequence is SEQ ID NO: 774; the first sequence is SEQ ID NO: 781 and the second sequence is SEQ ID NO: 782; the first sequence is SEQ ID NO: 789 and the second sequence is SEQ ID NO: 790; the first sequence is SEQ ID NO: 797 and the second sequence is SEQ ID NO: 798; the first sequence is SEQ ID NO: 805 and the second sequence is SEQ ID NO: 806; the first sequence is SEQ ID NO: 813 and the second sequence is SEQ ID NO: 814; the first sequence is SEQ ID NO: 821 and the second sequence is SEQ ID NO: 822; the first sequence is SEQ ID NO: 829 and the second sequence is SEQ ID NO: 830; the first sequence is SEQ ID NO: 837 and the second sequence is SEQ ID NO: 838; the first sequence is SEQ ID NO: 845 and the second sequence is SEQ ID NO: 846; the first sequence is SEQ ID NO: 853 and the second sequence is SEQ ID NO: 854; the first sequence is SEQ ID NO: 861 and the second sequence is SEQ ID NO: 862; the first sequence is SEQ ID NO: 869 and the second sequence is SEQ ID NO: 870; the first sequence is SEQ ID NO: 877 and the second sequence is SEQ ID NO: 878; the first sequence is SEQ ID NO: 885 and the second sequence is SEQ ID NO: 886; the first sequence is SEQ ID NO: 893 and the second sequence is SEQ ID NO: 894; the first sequence is SEQ ID NO: 900 and the second sequence is SEQ ID NO: 901; the first sequence is SEQ ID NO: 909 and the second sequence is SEQ ID NO: 910; the first sequence is SEQ ID NO: 917 and the second sequence is SEQ ID NO: 918; the first sequence is SEQ ID NO: 925 and the second sequence is SEQ ID NO: 926; the first sequence is SEQ ID NO: 933 and the second sequence is SEQ ID NO: 934; the first sequence is SEQ ID NO: 941 and the second sequence is SEQ ID NO: 942; the first sequence is SEQ ID NO: 943 and the second sequence is SEQ ID NO: 944; the first sequence is SEQ ID NO: 951 and the second sequence is SEQ ID NO: 952; the first sequence is SEQ ID NO: 959 and the second sequence is SEQ ID NO: 960; the first sequence is SEQ ID NO: 967 and the second sequence is SEQ ID NO: 968; the first sequence is SEQ ID NO: 975 and the second sequence is SEQ ID NO: 976; the first sequence is SEQ ID NO: 983 and the second sequence is SEQ ID NO: 984; the first sequence is SEQ ID NO: 991 and the second sequence is SEQ ID NO: 992; the first sequence is SEQ ID NO: 993 and the second sequence is SEQ ID NO: 994; the first sequence is SEQ ID NO: 995 and the second sequence is SEQ ID NO: 996; the first sequence is SEQ ID NO: 1003 and the second sequence is SEQ ID NO: 1004; the first sequence is SEQ ID NO: 1011 and the second sequence is SEQ ID

NO: 1012; the first sequence is SEQ ID NO: 1019 and the second sequence is SEQ ID NO: 1020; the first sequence is SEQ ID NO: 1027 and the second sequence is SEQ ID NO: 1028; the first sequence is SEQ ID NO: 1035 and 1036; or the first sequence is SEQ ID NO: 1043 and the second sequence is SEQ ID NO: 1044.

[0447] In some cases, an antibody of the present disclosure targets an immune checkpoint selected from the group consisting of PDL1, B7H4, B7H3, and TIGIT. For example, in some cases, the antibody comprises a heavy chain variable region having at least 80% sequence identity to a first sequence and a light chain variable region having at least 80% sequence identity to a second sequence, wherein: the first sequence is SEQ ID NO: 19 and the second sequence is SEQ ID NO: 20; the first sequence is SEQ ID NO: 83 and the second sequence is SEQ ID NO: 84; the first sequence is SEQ ID NO: 97 and the second sequence is SEQ ID NO: 98; the first sequence is SEQ ID NO: 105 and the second sequence is SEQ ID NO: 106; the first sequence is SEQ ID NO:113 and the second sequence is SEQ ID NO: 114; the first sequence is SEQ ID NO: 121 and the second sequence is SEQ ID NO: 122; the first sequence is SEQ ID NO: 129 and the second sequence is SEQ ID NO: 130; the first sequence is SEQ ID NO: 137 and the second sequence is SEQ ID NO: 138; the first sequence is SEQ ID NO: 153 and the second sequence is SEQ ID NO: 154; the first sequence is SEQ ID NO: 161 and the second sequence is SEQ ID NO: 162; the first sequence is SEQ ID NO: 169 and the second sequence is SEQ ID NO: 170; the first sequence is SEQ ID NO: 177 and the second sequence is SEQ ID NO: 178; the first sequence is SEQ ID NO: 185 and the second sequence is SEQ ID NO: 186; the first sequence is SEQ ID NO: 193 and the second sequence is SEQ ID NO: 194; the first sequence is SEQ ID NO: 201 and the second sequence is SEQ ID NO: 202; the first sequence is SEQ ID NO: 209 and the second sequence is SEQ ID NO: 210; the first sequence is SEQ ID NO: 217 and the second sequence is SEQ ID NO: 218; the first sequence is SEQ ID NO: 225 and the second sequence is SEQ ID NO: 226; the first sequence is SEQ ID NO: 233 and the second sequence is SEQ ID NO: 234; the first sequence is SEQ ID NO: 241 and the second sequence is SEQ ID NO: 242; the first sequence is SEQ ID NO: 249 and the second sequence is SEQ ID NO: 250; the first sequence is SEQ ID NO: 629 and the second sequence is SEQ ID NO: 630; the first sequence is SEQ ID NO: 637 and the second sequence is SEQ ID NO: 638; the first sequence is SEQ ID NO: 645 and the second sequence is SEQ ID NO: 646; the first sequence is SEQ ID NO: 653 and the second sequence is SEQ ID NO: 654; the first sequence is SEQ ID NO: 661 and the second sequence is SEQ ID NO: 662; the first sequence is SEQ ID NO: 669 and the second sequence is SEQ ID NO:

670; the first sequence is SEQ ID NO: 677 and the second sequence is SEQ ID NO: 678; the first sequence is SEQ ID NO: 685 and the second sequence is SEQ ID NO: 686; the first sequence is SEQ ID NO: 693 and the second sequence is SEQ ID NO: 694; the first sequence is SEQ ID NO: 701 and the second sequence is SEQ ID NO: 702; the first sequence is SEQ ID NO: 703 and the second sequence is SEQ ID NO: 704; the first sequence is SEQ ID NO: 711 and the second sequence is SEQ ID NO: 712; the first sequence is SEQ ID NO: 713 and the second sequence is SEQ ID NO: 714; the first sequence is SEQ ID NO: 715 and the second sequence is SEQ ID NO: 716; or the first sequence is SEQ ID NO: 1027 and the second sequence is SEQ ID NO: 1028.

[0448] In some cases, an antibody of the present disclosure comprises a heavy chain variable region having at least 80% sequence identity to a first sequence and a light chain variable region having at least 80% sequence identity to a second sequence, wherein: the first sequence is SEQ ID NO: 19 and the second sequence is SEQ ID NO: 20; the first sequence is SEQ ID NO: 83 and the second sequence is SEQ ID NO: 84; the first sequence is SEQ ID NO: 97 and the second sequence is SEQ ID NO: 98; the first sequence is SEQ ID NO: 105 and the second sequence is SEQ ID NO: 106; the first sequence is SEQ ID NO: 113 and the second sequence is SEQ ID NO: 114; the first sequence is SEQ ID NO: 121 and the second sequence is SEQ ID NO: 122; the first sequence is SEQ ID NO: 129 and the second sequence is SEQ ID NO: 130; the first sequence is SEQ ID NO: 137 and the second sequence is SEQ ID NO: 138; the first sequence is SEQ ID NO: 153 and the second sequence is SEQ ID NO: 154; the first sequence is SEQ ID NO: 161 and the second sequence is SEQ ID NO: 162; the first sequence is SEQ ID NO: 169 and the second sequence is SEQ ID NO: 170; the first sequence is SEQ ID NO: 177 and the second sequence is SEQ ID NO: 178; the first sequence is SEQ ID NO: 185 and the second sequence is SEQ ID NO: 186; the first sequence is SEQ ID NO: 193 and the second sequence is SEQ ID NO: 194; the first sequence is SEQ ID NO: 201 and the second sequence is SEQ ID NO: 202; the first sequence is SEQ ID NO: 209 and the second sequence is SEQ ID NO: 210; the first sequence is SEQ ID NO: 217 and the second sequence is SEQ ID NO: 218; the first sequence is SEQ ID NO: 225 and the second sequence is SEQ ID NO: 226; the first sequence is SEQ ID NO: 233 and the second sequence is SEQ ID NO: 234; the first sequence is SEQ ID NO: 241 and the second sequence is SEQ ID NO: 242; the first sequence is SEQ ID NO: 249 and the second sequence is SEQ ID NO: 250; or the first sequence is SEQ ID NO: 1027 and the second sequence is SEQ ID NO:

1028. In some cases, the first sequence is SEQ ID NO: 19 and the second sequence is SEQ ID NO: 20.

[0449] In some cases, the heavy chain variable region has at least 85% sequence identity to the first sequence and the light chain variable region has at least 85% sequence identity to the second sequence. In some cases, the heavy chain variable region has at least 90% sequence identity to the first sequence and the light chain variable region has at least 90% sequence identity to the second sequence. In some cases, the heavy chain variable region has at least 95% sequence identity to the first sequence and the light chain variable region has at least 95% sequence identity to the second sequence. In some cases, the heavy chain variable region has at least 98% sequence identity to the first sequence and the light chain variable region has at least 98% sequence identity to the second sequence. In some cases, the heavy chain variable region has at least 99% sequence identity to the first sequence and the light chain variable region has at least 99% sequence identity to the second sequence. In some cases, the heavy chain variable region comprises the first sequence and the light chain variable region comprises the second sequence.

(ii) Heavy and Light Chains

[0450] In some cases, an antibody of the present disclosure comprises a heavy chain having at least 80% sequence identity to a first sequence and a light chain having at least 80% sequence identity to a second sequence, wherein: the first sequence is SEQ ID NO: 1 and the second sequence is SEQ ID NO: 5; the first sequence is SEQ ID NO: 2 and the second sequence is SEQ ID NO: 5; the first sequence is SEQ ID NO: 3 and the second sequence is SEQ ID NO: 5; the first sequence is SEQ ID NO: 4 and the second sequence is SEQ ID NO: 5; the first sequence is SEQ ID NO: 6 and the second sequence is SEQ ID NO: 10; the first sequence is SEQ ID NO: 7 and the second sequence is SEQ ID NO: 10; the first sequence is SEQ ID NO: 8 and the second sequence is SEQ ID NO: 10; the first sequence is SEQ ID NO: 9 and the second sequence is SEQ ID NO: 10; the first sequence is SEQ ID NO: 46 and the second sequence is SEQ ID NO: 48; the first sequence is SEQ ID NO: 47 and the second sequence is SEQ ID NO: 48; the first sequence is SEQ ID NO: 57 and the second sequence is SEQ ID NO: 59; the first sequence is SEQ ID NO: 58 and the second sequence is SEQ ID NO: 59; the first sequence is SEQ ID NO: 60 and the second sequence is SEQ ID NO: 62; the first sequence is SEQ ID NO: 61 and the second sequence is SEQ ID NO: 62; the first sequence is SEQ ID NO: 71 and the second sequence is SEQ ID NO: 73; the first sequence is SEQ ID NO: 72 and the second sequence is SEQ ID NO: 73; the first sequence is SEQ ID

NO: 74 and the second sequence is SEQ ID NO: 76; the first sequence is SEQ ID NO: 75 and the second sequence is SEQ ID NO: 76; the first sequence is SEQ ID NO: 85 and the second sequence is SEQ ID NO: 87; the first sequence is SEQ ID NO: 86 and the second sequence is SEQ ID NO: 87; the first sequence is SEQ ID NO: 88 and the second sequence is SEQ ID NO: 90; the first sequence is SEQ ID NO: 89 and the second sequence is SEQ ID NO: 90; the first sequence is SEQ ID NO: 251 and the second sequence is SEQ ID NO: 252; the first sequence is SEQ ID NO: 253 and the second sequence is SEQ ID NO: 254; the first sequence is SEQ ID NO: 255 and the second sequence is SEQ ID NO: 256; the first sequence is SEQ ID NO: 257 and the second sequence is SEQ ID NO: 258; the first sequence is SEQ ID NO: 259 and the second sequence is SEQ ID NO: 260; the first sequence is SEQ ID NO: 261 and the second sequence is SEQ ID NO: 262; the first sequence is SEQ ID NO: 263 and the second sequence is SEQ ID NO: 264; the first sequence is SEQ ID NO: 265 and the second sequence is SEQ ID NO: 266; the first sequence is SEQ ID NO: 267 and the second sequence is SEQ ID NO: 268; the first sequence is SEQ ID NO: 269 and the second sequence is SEQ ID NO: 270; the first sequence is SEQ ID NO: 271 and the second sequence is SEQ ID NO: 272; the first sequence is SEQ ID NO: 273 and the second sequence is SEQ ID NO: 274; the first sequence is SEQ ID NO: 275 and the second sequence is SEQ ID NO: 276; the first sequence is SEQ ID NO: 277 and the second sequence is SEQ ID NO: 278; the first sequence is SEQ ID NO: 279 and the second sequence is SEQ ID NO: 280; the first sequence is SEQ ID NO: 281 and the second sequence is SEQ ID NO: 282; the first sequence is SEQ ID NO: 283 and the second sequence is SEQ ID NO: 284; the first sequence is SEQ ID NO: 285 and the second sequence is SEQ ID NO: 286; the first sequence is SEQ ID NO: 287 and the second sequence is SEQ ID NO: 288; the first sequence is SEQ ID NO: 289 and the second sequence is SEQ ID NO: 290; the first sequence is SEQ ID NO: 299 and the second sequence is SEQ ID NO: 300; the first sequence is SEQ ID NO: 493 and the second sequence is SEQ ID NO: 494; the first sequence is SEQ ID NO: 717 and the second sequence is SEQ ID NO: 718; the first sequence is SEQ ID NO: 719 and the second sequence is SEQ ID NO: 720; the first sequence is SEQ ID NO: 721 and the second sequence is SEQ ID NO: 722; the first sequence is SEQ ID NO: 723 and the second sequence is SEQ ID NO: 724; or the first sequence is SEQ ID NO: 757 and the second sequence is SEQ ID NO: 758.

[0451] In some cases, an antibody of the present disclosure comprises a heavy chain having at least 80% sequence identity to a first sequence and a light chain having at least 80% sequence identity to a second sequence, wherein: the first sequence is SEQ ID NO: 1 and the

second sequence is SEQ ID NO: 5; the first sequence is SEQ ID NO: 2 and the second sequence is SEQ ID NO: 5; the first sequence is SEQ ID NO: 3 and the second sequence is SEQ ID NO: 5; the first sequence is SEQ ID NO: 4 and the second sequence is SEQ ID NO: 5; the first sequence is SEQ ID NO: 6 and the second sequence is SEQ ID NO: 10; the first sequence is SEQ ID NO: 7 and the second sequence is SEQ ID NO: 10; the first sequence is SEQ ID NO: 8 and the second sequence is SEQ ID NO: 10; the first sequence is SEQ ID NO: 9 and the second sequence is SEQ ID NO: 10; the first sequence is SEQ ID NO: 85 and the second sequence is SEQ ID NO: 87; the first sequence is SEQ ID NO: 86 and the second sequence is SEQ ID NO: 87; the first sequence is SEQ ID NO: 88 and the second sequence is SEQ ID NO: 90; the first sequence is SEQ ID NO: 89 and the second sequence is SEQ ID NO: 90; the first sequence is SEQ ID NO: 251 and the second sequence is SEQ ID NO: 252; the first sequence is SEQ ID NO: 253 and the second sequence is SEQ ID NO: 254; the first sequence is SEQ ID NO: 255 and the second sequence is SEQ ID NO: 256; the first sequence is SEQ ID NO: 257 and the second sequence is SEQ ID NO: 258; the first sequence is SEQ ID NO: 259 and the second sequence is SEQ ID NO: 260; the first sequence is SEQ ID NO: 261 and the second sequence is SEQ ID NO: 262; the first sequence is SEQ ID NO: 263 and the second sequence is SEQ ID NO: 264; the first sequence is SEQ ID NO: 265 and the second sequence is SEQ ID NO: 266; the first sequence is SEQ ID NO: 267 and the second sequence is SEQ ID NO: 268; the first sequence is SEQ ID NO: 269 and the second sequence is SEQ ID NO: 270; the first sequence is SEQ ID NO: 271 and the second sequence is SEQ ID NO: 272; the first sequence is SEQ ID NO: 273 and the second sequence is SEQ ID NO: 274; the first sequence is SEQ ID NO: 275 and the second sequence is SEQ ID NO: 276; the first sequence is SEQ ID NO: 277 and the second sequence is SEQ ID NO: 278; the first sequence is SEQ ID NO: 279 and the second sequence is SEQ ID NO: 280; the first sequence is SEQ ID NO: 281 and the second sequence is SEQ ID NO: 282; the first sequence is SEQ ID NO: 283 and the second sequence is SEQ ID NO: 284; the first sequence is SEQ ID NO: 285 and the second sequence is SEQ ID NO: 286; the first sequence is SEQ ID NO: 287 and the second sequence is SEQ ID NO: 288; the first sequence is SEQ ID NO: 289 and the second sequence is SEQ ID NO: 290; the first sequence is SEQ ID NO: 717 and the second sequence is SEQ ID NO: 718; the first sequence is SEQ ID NO: 719 and the second sequence is SEQ ID NO: 720; the first sequence is SEQ ID NO: 721 and the second sequence is SEQ ID NO: 722; or the first sequence is SEQ ID NO: 723 and the second sequence is SEQ ID NO: 724.

[0452] In some cases, an antibody of the present disclosure comprises a heavy chain having at least 80% sequence identity to a first sequence and a light chain having at least 80% sequence identity to a second sequence, wherein: the first sequence is SEQ ID NO: 1 and the second sequence is SEQ ID NO: 5; the first sequence is SEQ ID NO: 2 and the second sequence is SEQ ID NO: 5; the first sequence is SEQ ID NO: 3 and the second sequence is SEQ ID NO: 5; the first sequence is SEQ ID NO: 4 and the second sequence is SEQ ID NO: 5; the first sequence is SEQ ID NO: 6 and the second sequence is SEQ ID NO: 10; the first sequence is SEQ ID NO: 7 and the second sequence is SEQ ID NO: 10; the first sequence is SEQ ID NO: 8 and the second sequence is SEQ ID NO: 10; the first sequence is SEQ ID NO: 9 and the second sequence is SEQ ID NO: 10; the first sequence is SEQ ID NO: 85 and the second sequence is SEQ ID NO: 87; the first sequence is SEQ ID NO: 86 and the second sequence is SEQ ID NO: 87; the first sequence is SEQ ID NO: 88 and the second sequence is SEQ ID NO: 90; the first sequence is SEQ ID NO: 89 and the second sequence is SEQ ID NO: 90; the first sequence is SEQ ID NO: 251 and the second sequence is SEQ ID NO: 252; the first sequence is SEQ ID NO: 253 and the second sequence is SEQ ID NO: 254; the first sequence is SEQ ID NO: 255 and the second sequence is SEQ ID NO: 256; the first sequence is SEQ ID NO: 257 and the second sequence is SEQ ID NO: 258; the first sequence is SEQ ID NO: 259 and the second sequence is SEQ ID NO: 260; the first sequence is SEQ ID NO: 261 and the second sequence is SEQ ID NO: 262; the first sequence is SEQ ID NO: 263 and the second sequence is SEQ ID NO: 264; the first sequence is SEQ ID NO: 265 and the second sequence is SEQ ID NO: 266; the first sequence is SEQ ID NO: 267 and the second sequence is SEQ ID NO: 268; the first sequence is SEQ ID NO: 269 and the second sequence is SEQ ID NO: 270; the first sequence is SEQ ID NO: 271 and the second sequence is SEQ ID NO: 272; the first sequence is SEQ ID NO: 273 and the second sequence is SEQ ID NO: 274; the first sequence is SEQ ID NO: 275 and the second sequence is SEQ ID NO: 276; the first sequence is SEQ ID NO: 277 and the second sequence is SEQ ID NO: 278; the first sequence is SEQ ID NO: 279 and the second sequence is SEQ ID NO: 280; the first sequence is SEQ ID NO: 281 and the second sequence is SEQ ID NO: 282; the first sequence is SEQ ID NO: 283 and the second sequence is SEQ ID NO: 284; the first sequence is SEQ ID NO: 285 and the second sequence is SEQ ID NO: 286; the first sequence is SEQ ID NO: 287 and the second sequence is SEQ ID NO: 288; or the first sequence is SEQ ID NO: 289 and the second sequence is SEQ ID NO: 290.

[0453] In some cases, an antibody of the present disclosure comprises a heavy chain having at least 80% sequence identity to a first sequence and a light chain having at least 80% sequence identity to a second sequence, wherein: the first sequence is SEQ ID NO: 1 and the second sequence is SEQ ID NO: 5; the first sequence is SEQ ID NO: 2 and the second sequence is SEQ ID NO: 5; the first sequence is SEQ ID NO: 3 and the second sequence is SEQ ID NO: 5; the first sequence is SEQ ID NO: 4 and the second sequence is SEQ ID NO: 5; the first sequence is SEQ ID NO: 6 and the second sequence is SEQ ID NO: 10; the first sequence is SEQ ID NO: 7 and the second sequence is SEQ ID NO: 10; the first sequence is SEQ ID NO: 8 and the second sequence is SEQ ID NO: 10; or the first sequence is SEQ ID NO: 9 and the second sequence is SEQ ID NO: 10.

[0454] In some cases, an antibody of the present disclosure comprises a heavy chain having at least 80% sequence identity to a first sequence and a light chain having at least 80% sequence identity to a second sequence, wherein: the first sequence is SEQ ID NO: 3 or SEQ ID NO: 4 and the second sequence is SEQ ID NO: 5.

[0455] In some cases, the heavy chain has at least 85% sequence identity to the first sequence and the light chain has at least 85% sequence identity to the second sequence. In some cases, the heavy chain has at least 90% sequence identity to the first sequence and the light chain has at least 90% sequence identity to the second sequence. In some cases, the heavy chain has at least 95% sequence identity to the first sequence and the light chain has at least 95% sequence identity to the second sequence. In some cases, the heavy chain has at least 98% sequence identity to the first sequence and the light chain has at least 98% sequence identity to the second sequence. In some cases, the heavy chain has at least 99% sequence identity to the first sequence and the light chain has at least 99% sequence identity to the second sequence. In some cases, the heavy chain comprises the first sequence and the light chain comprises the second sequence.

(iii) Complementarity-Determining Regions

[0456] In some cases, an antibody of the present disclosure comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 comprising at least 80% sequence identity to: SEQ ID NO: 13, 14, 15, 16, 17, and 18, respectively (i.e., CDR-H1 has at least 80% sequence identity to SEQ ID NO: 13, CDR-H2 has at least 80% sequence identity to SEQ ID NO: 14, CDR-H3 has at least 80% sequence identity to SEQ ID NO: 15, CDR-L1 has at least 80% sequence identity to SEQ ID NO: 16, CDR-L2 has at least 80% sequence identity to SEQ ID NO: 17, and CDR-L3 has at least 80% sequence identity to SEQ ID NO: 18); SEQ ID NO:

21, 22, 23, 24, 25, and 26, respectively; SEQ ID NO: 38, 39, 40, 41, 42, and 43, respectively; SEQ ID NO: 49, 50, 51, 52, 53, and 54, respectively; SEQ ID NO: 63, 64, 65, 66, 67, and 68, respectively; SEQ ID NO: 77, 78, 79, 80, 81, and 82, , respectively; SEQ ID NO: 91, 92, 93, 94, 95, and 96, respectively; SEQ ID NO: 99, 100, 101, 102, 103, and 104, respectively; SEQ ID NO: 107, 108, 109, 110, 111, and 112, respectively; SEQ ID NO: 115, 116, 117, 118, 119, and 120, respectively; SEQ ID NO: 123, 124, 125, 126, 127, and 128, respectively; SEQ ID NO: 131, 132, 133, 134, 135, and 136, respectively; SEQ ID NO: 139, 140, 141, 142, 143, and 144, respectively; SEQ ID NO: 147, 148, 149, 150, 151, and 152, respectively; SEQ ID NO: 155, 156, 157, 158, 159, and 160, respectively; SEQ ID NO: 163, 164, 165, 166, 167, and 168, respectively; SEQ ID NO: 171, 172, 173, 174, 175, and 176, respectively; SEQ ID NO: 179, 180, 181, 182, 183, and 184, respectively; SEQ ID NO: 187, 188, 189, 190, 191, and 192, respectively; SEQ ID NO: 195, 196, 197, 198, 199, and 200, respectively; SEQ ID NO: 203, 204, 205, 206, 207 and 208, respectively; SEQ ID NO: 211, 212, 213, 214, 215, and 216, respectively; SEQ ID NO: 219, 220, 221, 222, 223, and 224, respectively; SEQ ID NO: 227, 228, 229, 230, 231, and 232, respectively; SEQ ID NO: 235, 236, 237, 238, 239, and 240, respectively; SEQ ID NO: 243, 244, 245, 246, 247, and 248, respectively; SEQ ID NO: 291, 292, 293, 294, 295, and 296, respectively; SEQ ID NO: 301, 302, 303, 304, 305, and 306, respectively; SEQ ID NO: 309, 310, 311, 312, 313, and 314, respectively; SEQ ID NO: 317, 318, 319, 320, 321, and 322, respectively; SEQ ID NO: 325, 326, 327, 328, 329, and 330, respectively; SEQ ID NO: 333, 334, 335, 336, 337, and 338, respectively; SEQ ID NO: 341, 342, 343, 344, 345, and 346, respectively; SEQ ID NO: 349, 350, 351, 352, 353, and 354, respectively; SEQ ID NO: 357, 358, 359, 360, 361, and 362, respectively; SEQ ID NO: 365, 366, 367, 368, 369, and 370, respectively; SEQ ID NO: 373, 374, 375, 376, 377, and 378, respectively; SEQ ID NO: 381, 382, 383, 384, 385, and 386, respectively; SEQ ID NO: 389, 390, 391, 392, 393, and 394, respectively; SEQ ID NO: 397, 398, 399, 400, 401, and 402, respectively; SEQ ID NO: 405, 406, 407, 408, 409, and 410, respectively; SEQ ID NO: 413, 414, 415, 416, 417, and 418, respectively; SEQ ID NO: 421, 422, 423, 424, 425, and 426, respectively; SEQ ID NO: 429, 430, 431, 432, 433, and 434, respectively; SEQ ID NO: 437, 438, 439, 440, 441, and 442, respectively; SEQ ID NO: 445, 446, 447, 448, 449, and 450, respectively; SEQ ID NO: 453, 454, 455, 456, 457, and 458, respectively; SEQ ID NO: 461, 462, 463, 464, 465, and 466, respectively; SEQ ID NO: 469, 470, 471, 472, 473, and 474, respectively; SEQ ID NO: 477, 478, 479, 480, 481, and 482, respectively; SEQ ID NO: 485, 486, 487, 488, 489, and 490, respectively; SEQ ID NO: 495, 496, 497, 498, 499, and 500, respectively; SEQ ID NO: 503, 504, 505, 506, 507, and 508, respectively; SEQ ID

NO: 511, 512, 513, 514, 515, and 516, respectively; SEQ ID NO: 519, 520, 521, 522, 523, and 524, respectively; SEQ ID NO: 527, 528, 529, 530, 531, and 532, respectively; SEQ ID NO: 535, 536, 537, 538, 539, and 540, respectively; SEQ ID NO: 543, 544, 545, 546, 547, and 548, respectively; SEQ ID NO: 551, 552, 553, 554, 555, and 556, respectively; SEQ ID NO: 559, 560, 561, 562, 563, and 564, respectively; SEQ ID NO: 567, 568, 569, 570, 571, and 572, respectively; SEQ ID NO: 575, 576, 577, 578, 579, and 580, respectively; SEQ ID NO: 583, 584, 585, 586, 587, and 588, respectively; SEQ ID NO: 591, 592, 593, 594, 595, and 596, respectively; SEQ ID NO: 599, 600, 601, 602, 603, and 604, respectively; SEQ ID NO: 607, 608, 609, 610, 611, and 612, respectively; SEQ ID NO: 615, 616, 617, 618, 619, and 620, respectively; SEQ ID NO: 623, 624, 625, 626, 627, and 628, respectively; SEQ ID NO: 631, 632, 633, 634, 635, and 636, respectively; SEQ ID NO: 639, 640, 641, 642, 643, and 644, respectively; SEQ ID NO: 647, 648, 649, 650, 651, and 652, respectively; SEQ ID NO: 655, 656, 657, 658, 659, and 660, respectively; SEQ ID NO: 663, 664, 665, 666, 667, and 668, respectively; SEQ ID NO: 671, 672, 673, 674, 675, and 676, respectively; SEQ ID NO: 679, 680, 681, 682, 683, and 684, respectively; SEQ ID NO: 687, 688, 689, 690, 691, and 692, respectively; SEQ ID NO: 695, 696, 697, 698, 699, and 700, respectively; SEQ ID NO: 705, 706, 707, 708, 709, and 710, respectively; SEQ ID NO: 725, 726, 727, 728, 729, and 730, respectively; SEQ ID NO: 733, 734, 735, 736, 737, and 738, respectively; SEQ ID NO: 741, 742, 743, 744, 745, and 746, respectively; SEQ ID NO: 749, 750, 751, 752, 753, and 754, respectively; SEQ ID NO: 759, 760, 761, 762, 763, and 764, respectively; SEQ ID NO: 767, 768, 769, 770, 771, and 772, respectively; SEQ ID NO: 775, 776, 777, 778, 779, and 780, respectively; SEQ ID NO: 783, 784, 785, 786, 787, and 788, respectively; SEQ ID NO: 791, 792, 793, 794, 795, and 796, respectively; SEQ ID NO: 799, 800, 801, 802, 803, and 804, respectively; SEQ ID NO: 807, 808, 809, 810, 811, and 812, respectively; SEQ ID NO: 815, 816, 817, 818, 819, and 820, respectively; SEQ ID NO: 823, 824, 825, 826, 827, and 828, respectively; SEQ ID NO: 831, 832, 833, 834, 835, and 836, respectively; SEQ ID NO: 839, 840, 841, 842, 843, and 844, respectively; SEQ ID NO: 847, 848, 849, 850, 851, and 852, respectively; SEQ ID NO: 855, 856, 857, 858, 859, and 860, respectively; SEQ ID NO: 863, 864, 865, 866, 867, and 868, respectively; SEQ ID NO: 871, 872, 873, 874, 875, and 876, respectively; SEQ ID NO: 879, 880, 881, 882, 883, and 884, respectively; SEQ ID NO: 887, 888, 889, 890, 891, and 892, respectively; SEQ ID NO: 895, 896, 897, 898, 899, and 900, respectively; SEQ ID NO: 903, 904, 905, 906, 907, and 908, respectively; SEQ ID NO: 911, 912, 913, 914, 915, and 916, respectively; SEQ ID NO: 919, 920, 921, 922, 923, and 924, respectively; SEQ ID NO: 927, 928, 929, 930, 931, and 932, respectively; SEQ ID

NO: 935, 936, 937, 938, 939, and 940, respectively; SEQ ID NO: 945, 946, 947, 948, 949, and 950, respectively; SEQ ID NO: 953, 954, 955, 956, 957, and 958, respectively; SEQ ID NO: 961, 962, 963, 964, 965, and 966, respectively; SEQ ID NO: 969, 970, 971, 972, 973, and 974, respectively; SEQ ID NO: 977, 978, 979, 980, 981, and 982, respectively; SEQ ID NO: 985, 986, 987, 988, 989, and 990, respectively; SEQ ID NO: 997, 998, 999, 1000, 1001, and 1002, respectively; SEQ ID NO: 1005, 1006, 1007, 1008, 1009, and 1010, respectively; SEQ ID NO: 1013, 1014, 1015, 1016, 1017, and 1018, respectively; SEQ ID NO: 1021, 1022, 1023, 1024, 1025, and 1026, respectively; SEQ ID NO: 1029, 1030, 1031, 1032, 1033, and 1034, respectively; or SEQ ID NO: 1037, 1038, 1039, 1040, 1041, and 1042, respectively.

[0457] In some cases, an antibody of the present disclosure targets an immune checkpoint selected from the group consisting of PDL1, B7H4, B7H3, and TIGIT. For example, in some cases, an antibody of the present disclosure comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 comprising at least 80% sequence identity to: SEQ ID NO: 13, 14, 15, 16, 17, and 18, respectively; SEQ ID NO: 77, 78, 79, 80, 81, and 82, , respectively; SEQ ID NO: 91, 92, 93, 94, 95, and 96, respectively; SEQ ID NO: 99, 100, 101, 102, 103, and 104, respectively; SEQ ID NO: 107, 108, 109, 110, 111, and 112, respectively; SEQ ID NO: 115, 116, 117, 118, 119, and 120, respectively; SEQ ID NO: 123, 124, 125, 126, 127, and 128, respectively; SEQ ID NO: 131, 132, 133, 134, 135, and 136, respectively; SEQ ID NO: 139, 140, 141, 142, 143, and 144, respectively; SEQ ID NO: 147, 148, 149, 150, 151, and 152, respectively; SEQ ID NO: 155, 156, 157, 158, 159, and 160, respectively; SEQ ID NO: 163, 164, 165, 166, 167, and 168, respectively; SEQ ID NO: 171, 172, 173, 174, 175, and 176, respectively; SEQ ID NO: 179, 180, 181, 182, 183, and 184, respectively; SEQ ID NO: 187, 188, 189, 190, 191, and 192, respectively; SEQ ID NO: 195, 196, 197, 198, 199, and 200, respectively; SEQ ID NO: 203, 204, 205, 206, 207 and 208, respectively; SEQ ID NO: 211, 212, 213, 214, 215, and 216, respectively; SEQ ID NO: 219, 220, 221, 222, 223, and 224, respectively; SEQ ID NO: 227, 228, 229, 230, 231, and 232, respectively; SEQ ID NO: 235, 236, 237, 238, 239, and 240, respectively; SEQ ID NO: 243, 244, 245, 246, 247, and 248, respectively; SEQ ID NO: 623, 624, 625, 626, 627, and 628, respectively; SEQ ID NO: 631, 632, 633, 634, 635, and 636, respectively; SEQ ID NO: 639, 640, 641, 642, 643, and 644, respectively; SEQ ID NO: 647, 648, 649, 650, 651, and 652, respectively; SEQ ID NO: 655, 656, 657, 658, 659, and 660, respectively; SEQ ID NO: 663, 664, 665, 666, 667, and 668, respectively; SEQ ID NO: 671, 672, 673, 674, 675, and 676, respectively; SEQ ID

NO: 679, 680, 681, 682, 683, and 684, respectively; SEQ ID NO: 687, 688, 689, 690, 691, and 692, respectively; SEQ ID NO: 695, 696, 697, 698, 699, and 700, respectively; SEQ ID NO: 705, 706, 707, 708, 709, and 710, respectively; or SEQ ID NO: 1021, 1022, 1023, 1024, 1025, and 1026, respectively.

[0458] In some cases, the CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 comprise at least 85% sequence identity to the respective 6 indicated sequences. In some cases, the CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 each comprise at least 90% sequence identity to the respective 6 indicated sequences. In some cases, the CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 each comprise at least 95% sequence identity to the respective 6 indicated sequences. In some cases, the CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 each comprise at most one mutation relative to the respective 6 indicated sequences.

(iv) Exemplary Antibodies

[0459] In some cases, an antibody provided herein binds to PDL1. PDL1 is expressed in a broad range of cancers, as well as certain immune cells, and often serves as a primary mechanism for immune suppression in tumor microenvironments. The PDL1 agonism of PD-1 can act as an immune checkpoint, diminishing lymphocyte tumor infiltration, and T-cell receptor mediated proliferation and signaling. While PDL1 antagonism can reverse immune suppression, PDL1 targeting can also localize treatments to the sites of cancers, allowing drugs to selectively target cancer cells or stimulate immune responses in the presence of tumors.

[0460] In some cases, an anti-PDL1 antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 comprising at least 80% sequence identity, at least 85% sequence identity, at least 90% sequence identity, at least 95%, at least 98%, or at least 99% sequence identity to the amino acid sequences of SEQ ID NOs: 13, 14, 15, 16, 17, and 18 respectively. In some cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 each comprising at most one mutation relative to the amino acid sequences of SEQ ID NOs: 13, 14, 15, 16, 17, and 18, respectively.

[0461] In some embodiments, the antibody comprises a heavy chain comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of any one of SEQ ID NO: 1-4 and a light chain comprising an amino acid sequence that is at least 95% at least 96%, at least 97%, at least

98%, at least 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 5. In some embodiments, the antibody comprises a heavy chain comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 1 and a light chain comprising an amino acid sequence that is at least 95% at least 96%, at least 97%, at least 98%, at least 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 5. In some embodiments, the antibody comprises a heavy chain comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 2 and a light chain comprising an amino acid sequence that is at least 95% at least 96%, at least 97%, at least 98%, at least 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 5. In some embodiments, the antibody comprises a heavy chain comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 3 and a light chain comprising an amino acid sequence that is at least 95% at least 96%, at least 97%, at least 98%, at least 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 5. In some embodiments, the antibody comprises a heavy chain comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 4 and a light chain comprising an amino acid sequence that is at least 95% at least 96%, at least 97%, at least 98%, at least 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 5.

[0462] In some embodiments, the antibody comprises a heavy chain variable region comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of any one of SEQ ID NO: 6-9 and a light chain variable region comprising an amino acid sequence that is at least 95% at least 96%, at least 97%, at least 98%, at least 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 10. In some embodiments, the antibody comprises a heavy chain variable region comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of any one of SEQ ID NO: 6 and a light chain variable region comprising an amino acid sequence that is at least 95% at least 96%, at least 97%, at least 98%, at least 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 10. In some embodiments, the antibody comprises a heavy chain variable region comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of

any one of SEQ ID NO: 7 and a light chain variable region comprising an amino acid sequence that is at least 95% at least 96%, at least 97%, at least 98%, at least 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 10. In some embodiments, the antibody comprises a heavy chain variable region comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of any one of SEQ ID NO: 8 and a light chain variable region comprising an amino acid sequence that is at least 95% at least 96%, at least 97%, at least 98%, at least 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 10. In some embodiments, the antibody comprises a heavy chain variable region comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of any one of SEQ ID NO: 9 and a light chain variable region comprising an amino acid sequence that is at least 95% at least 96%, at least 97%, at least 98%, at least 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 10.

[0463] In some embodiments, the antibody comprises a heavy chain variable region comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 19 and a light chain variable region comprising an amino acid sequence that is at least 95% at least 96%, at least 97%, at least 98%, at least 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 20.

[0464] In some embodiments, an antibody provided herein binds to EphA2. In some embodiments, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 comprising the amino acid sequences that are at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or at least 99% identical to the amino acid sequences of SEQ ID NOs: 21, 22, 23, 24, 25, and 26, respectively.

[0465] In some embodiments, the anti-EphA2 antibody comprises a heavy chain variable region comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or at least 99% identical to the amino acid sequence of SEQ ID NO: 27 and a light chain variable region comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or at least 99% identical to the amino acid sequence of SEQ ID NO: 28. In some embodiments, the anti-EphA2 antibody comprises a heavy chain comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or at least 99% identical to the amino acid sequence of SEQ

ID NO: 29 or SEQ ID NO: 30 and a light chain comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or at least 99% identical to the amino acid sequence of the amino acid sequence of SEQ ID NO: 31. In some embodiments, the anti-EphA2 antibody comprises a heavy chain comprising the amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or at least 99% identical to the amino acid sequence of SEQ ID NO: 32 or SEQ ID NO: 33 and a light chain comprising the amino acid sequence of SEQ ID NO: 34. In some embodiments, the anti-EphA2 antibody comprises a heavy chain that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or at least 99% identical to the amino acid sequence of SEQ ID NO: 35 or SEQ ID NO: 36 and a light chain comprising the amino acid sequence of SEQ ID NO: 37. In some embodiments, the antibody is h1C1 or 1C1.

[0466] In some embodiments, the anti-EphA2 antibody comprises a heavy chain variable region comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 27 and a light chain variable region comprising an amino acid sequence that is at least 80% at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 28.

[0467] In some cases, an antibody provided herein binds to CD30. In some such cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences comprising at least 80% sequence identity, at least 85% sequence identity, at least 90% sequence identity, or at least 95% sequence identity to the amino acid sequences of SEQ ID NOs: 38, 39, 40, 41, 42, and 43, respectively. In some cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences each comprising at most one mutation relative to the amino acid sequences of SEQ ID NOs: 38, 39, 40, 41, 42, and 43, respectively. In some embodiments, the anti-CD30 antibody comprises a heavy chain comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of either SEQ ID NO: 46 or 47 and a light chain comprising an amino acid sequence that is at least 80% at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 48. In some embodiments, the anti-CD30 antibody comprises a heavy chain variable region comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 44 and a light chain variable region comprising an amino acid sequence that is at least 80% at least

85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 45.

[0468] In some cases, an antibody provided herein binds to CD228. In some such cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences comprising at least 80% sequence identity, at least 85% sequence identity, at least 90% sequence identity, or at least 95% sequence identity to the amino acid sequences of SEQ ID NOs: 49, 50, 51, 52, 53, and 54, respectively. In some cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences each comprising at most one mutation relative to the amino acid sequences of SEQ ID NOs: 49, 50, 51, 52, 53, and 54, respectively. In some embodiments, the anti-CD228 antibody comprises a heavy chain variable region comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 55 and a light chain variable region comprising an amino acid sequence that is at least 80% at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 56. In some embodiments, the anti-CD228 antibody comprises a heavy chain comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of either of SEQ ID NO: 57 or 58 and a light chain comprising an amino acid sequence that is at least 80% at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 59. In some embodiments, the anti-CD228 antibody comprises a heavy chain comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of either of SEQ ID NO: 60 or 61 and a light chain comprising an amino acid sequence that is at least 80% at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 62.

[0469] In some cases, an antibody provided herein binds to avB6. In some such cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences comprising at least 80% sequence identity, at least 85% sequence identity, at least 90% sequence identity, or at least 95% sequence identity to the amino acid sequences of SEQ ID NOs: 63, 64, 65, 66, 67, and 68, respectively. In some cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences each comprising at most one mutation relative to the amino acid sequences of SEQ ID NOs: 63, 64, 65, 66, 67, and 68, respectively. In some embodiments, the anti-H2A2 antibody comprises a heavy chain

variable region comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 69 and a light chain variable region comprising an amino acid sequence that is at least 80% at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 70. In some embodiments, the anti-H2A2 antibody comprises a heavy chain comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of either SEQ ID NO: 71 or 72 and a light chain comprising an amino acid sequence that is at least 80% at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 73. In some embodiments, the anti-H2A2 antibody comprises a heavy chain comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of either SEQ ID NO: 74 or 75 and a light chain comprising an amino acid sequence that is at least 80% at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 76. In some embodiments, the anti-avB6 antibody comprises a heavy chain variable region comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 69 and a light chain variable region comprising an amino acid sequence that is at least 80% at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 70. In some embodiments, the anti-avB6 antibody comprises a heavy chain comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of either SEQ ID NO: 71 or 72 and a light chain comprising an amino acid sequence that is at least 80% at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 73. In some embodiments, the anti-avB6 antibody comprises a heavy chain comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of either SEQ ID NO: 74 or 75 and a light chain comprising an amino acid sequence that is at least 80% at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 76.

[0470] In some cases, an antibody provided herein binds to B7H4. In some cases, the antibody comprises a set of CDR sequences (CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3, respectively) of which each sequence comprises at least 80% sequence

identity, at least 85% sequence identity, at least 90% sequence identity, at least 95%, or 100% sequence identity to amino acid sequences from a set of amino acid sequences selected from the group consisting of SEQ ID NOs: 77-82, SEQ ID NOs: 91-96, SEQ ID NOs: 99-104, SEQ ID NOs: 107-112, SEQ ID NOs: 115-120, SEQ ID NOs: 123-128, SEQ ID NOs: 131-136, SEQ ID NOs: 139-144, SEQ ID NOs: 147-152, SEQ ID NOs: 155-160, SEQ ID NOs: 163-168, SEQ ID NOs: 171-176, SEQ ID NOs: 179-184, SEQ ID NOs: 187-192, SEQ ID NOs: 195-200, SEQ ID NOs: 203-208, SEQ ID NOs: 211-216, SEQ ID NOs: 219-224, SEQ ID NOs: 227-232, SEQ ID NOs: 235-240, and SEQ ID NOs: 243-248. In some cases, the antibody comprises a set of CDR sequences (CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3, respectively) each comprising at most one mutation relative to an amino acid sequence from a set of amino acid sequences selected from the group consisting of SEQ ID NOs: 77-82, SEQ ID NOs: 91-96, SEQ ID NOs: 99-104, SEQ ID NOs: 107-112, SEQ ID NOs: 115-120, SEQ ID NOs: 123-128, SEQ ID NOs: 131-136, SEQ ID NOs: 139-144, SEQ ID NOs: 147-152, SEQ ID NOs: 155-160, SEQ ID NOs: 163-168, SEQ ID NOs: 171-176, SEQ ID NOs: 179-184, SEQ ID NOs: 187-192, SEQ ID NOs: 195-200, SEQ ID NOs: 203-208, SEQ ID NOs: 211-216, SEQ ID NOs: 219-224, SEQ ID NOs: 227-232, SEQ ID NOs: 235-240, and SEQ ID NOs: 243-248. In some cases, the anti-B7H4 antibody comprises a heavy chain and a light chain comprising amino acid sequences that are at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or at least 100% identical to the amino acid sequences of SEQ ID NO: 85 and 87, SEQ ID NO: 86 and 87, SEQ ID NO: 88 and 90, SEQ ID NO: 89 and 90, SEQ ID NO: 251 and 252, , SEQ ID NO: 253 and 254, SEQ ID NO: 255 and 256, SEQ ID NO: 257 and 258, SEQ ID NO: 259 and 260, SEQ ID NO: 261 and 262, SEQ ID NO: 263 and 264, SEQ ID NO: 265 and 266, SEQ ID NO: 267 and 268, SEQ ID NO: 269 and 270, SEQ ID NO: 271 and 272, SEQ ID NO: 273 and 274, SEQ ID NO: 275 and 276, SEQ ID NO: 277 and 278, SEQ ID NO: 279 and 280, SEQ ID NO: 281 and 282, SEQ ID NO: 283 and 284, SEQ ID NO: 285 and 286, SEQ ID NO: 287 and 288, or SEQ ID NO: 289 and 290, respectively. In some embodiments, the anti-B7H4 antibody comprises a heavy chain variable region and a light chain variable region comprising amino acid sequences that are at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or at least 100% identical to the amino acid sequences of SEQ ID NO: 83 and 84, SEQ ID NO: 97 and 98, SEQ ID NO: 105 and 106, SEQ ID NO: 113 and 114, SEQ ID NO: 121 and 122, SEQ ID NO: 129 and 130, SEQ ID NO: 137 and 138, SEQ ID NO: 153 and 154, SEQ ID NO: 161 and 162, SEQ ID NO: 169 and 170, SEQ ID NO: 177 and 178, SEQ ID NO: 185 and 186, SEQ ID NO: 193 and 194, SEQ ID NO: 201 and 202, SEQ ID NO: 209

and 210, SEQ ID NO: 217 and 218, SEQ ID NO: 225 and 226, SEQ ID NO: 233 and 234, SEQ ID NO: 241 and 242, or SEQ ID NO: 249 and 250, respectively.

[0471] In some cases, an antibody provided herein binds to CD70. In some such cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences comprising at least 80% sequence identity, at least 85% sequence identity, at least 90% sequence identity, or at least 95% sequence identity to the amino acid sequences of SEQ ID NOs: 291, 292, 293, 294, 295, and 296, respectively. In some cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences each comprising at most one mutation relative to the amino acid sequences of SEQ ID NOs: 291, 292, 293, 294, 295, and 296, respectively. In some embodiments, the anti-CD70 antibody comprises a heavy chain variable region comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 297 and a light chain variable region comprising an amino acid sequence that is at least 80% at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 298. In some embodiments, the anti-CD70 antibody comprises a heavy chain comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 299 and a light chain comprising an amino acid sequence that is at least 80% at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 300.

[0472] In some cases, an antibody provided herein binds to TROP2. In some such cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences comprising at least 80% sequence identity, at least 85% sequence identity, at least 90% sequence identity, or at least 95% sequence identity to the amino acid sequences of SEQ ID NOs: 301, 302, 303, 304, 305, and 306, respectively. In some cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences each comprising at most one mutation relative to the amino acid sequences of SEQ ID NOs: 301, 302, 303, 304, 305, and 306, respectively. In some cases, an antibody provided herein binds to TROP2. In some such cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences comprising at least 80% sequence identity, at least 85% sequence identity, at least 90% sequence identity, or at least 95% sequence identity to the amino acid sequences of SEQ ID NOs: 309, 310, 311, 312, 313, and 314 respectively. In some cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and

CDR-L3 sequences each comprising at most one mutation relative to the amino acid sequences of SEQ ID NOs: 309, 310, 311, 312, 313, and 314, respectively. In some embodiments, the anti-TROP2 antibody comprises a heavy chain variable region comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 307 and a light chain variable region comprising an amino acid sequence that is at least 80% at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 308. In some embodiments, the anti-TROP2 antibody comprises a heavy chain variable region comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 315 and a light chain variable region comprising an amino acid sequence that is at least 80% at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 316.

[0473] In some cases, an antibody provided herein binds to MICA. In some such cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences comprising at least 80% sequence identity, at least 85% sequence identity, at least 90% sequence identity, or at least 95% sequence identity to the amino acid sequences of SEQ ID NOs: 317, 318, 319, 320, 321, and 322, respectively. In some cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences each comprising at most one mutation relative to the amino acid sequences of SEQ ID NOs: 317, 318, 319, 320, 321, and 322, respectively. In some cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences comprising at least 80% sequence identity, at least 85% sequence identity, at least 90% sequence identity, or at least 95% sequence identity to the amino acid sequences of SEQ ID NOs: 325, 326, 327, 328, 329, and 330, respectively. In some cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences each comprising at most one mutation relative to the amino acid sequences of SEQ ID NOs: 325, 326, 327, 328, 329, and 330, respectively. In some cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences comprising at least 80% sequence identity, at least 85% sequence identity, at least 90% sequence identity, or at least 95% sequence identity to the amino acid sequences of SEQ ID NOs: 333, 334, 335, 336, 337, and 338, respectively. In some cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences each comprising at most one mutation relative to the amino acid sequences of SEQ

ID NOs: 333, 334, 335, 336, 337, and 338, respectively. In some cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences comprising at least 80% sequence identity, at least 85% sequence identity, at least 90% sequence identity, or at least 95% sequence identity to the amino acid sequences of SEQ ID NOs: 341, 342, 343, 344, 345, and 346, respectively. In some cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences each comprising at most one mutation relative to the amino acid sequences of SEQ ID NOs: 341, 342, 343, 344, 345, and 346, respectively. In some embodiments, the anti-MICA antibody comprises a heavy chain variable region comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 323 and a light chain variable region comprising an amino acid sequence that is at least 80% at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 324. In some embodiments, the anti-MICA antibody comprises a heavy chain variable region comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 331 and a light chain variable region comprising an amino acid sequence that is at least 80% at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 332. In some embodiments, the anti-MICA antibody comprises a heavy chain variable region comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 340 and a light chain variable region comprising an amino acid sequence that is at least 80% at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 340. In some embodiments, the anti-MICA antibody comprises a heavy chain variable region comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 347 and a light chain variable region comprising an amino acid sequence that is at least 80% at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 348.

[0474] In some cases, an antibody provided herein binds to CD51. In some such cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences comprising at least 80% sequence identity, at least 85% sequence identity, at least 90% sequence identity, or at least 95% sequence identity to the amino acid sequences of SEQ

ID NOs: 349, 350, 351, 352, 353, and 354, respectively. In some cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences each comprising at most one mutation relative to the amino acid sequences of SEQ ID NOs: 349, 350, 351, 352, 353, and 354, respectively. In some cases, an antibody provided herein binds to CD51. In some such cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences comprising at least 80% sequence identity, at least 85% sequence identity, at least 90% sequence identity, or at least 95% sequence identity to the amino acid sequences of SEQ ID NOs: 357, 358, 359, 360, 361, and 362, respectively. In some cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences each comprising at most one mutation relative to the amino acid sequences of SEQ ID NOs: 357, 358, 359, 360, 361, and 362, respectively. In some embodiments, the anti-CD51 antibody comprises a heavy chain variable region comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 355 and a light chain variable region comprising an amino acid sequence that is at least 80% at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 356. In some embodiments, the anti-CD51 antibody comprises a heavy chain variable region comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 363 and a light chain variable region comprising an amino acid sequence that is at least 80% at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 364.

[0475] In some cases, an antibody provided herein binds to gpA33. In some such cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences comprising at least 80% sequence identity, at least 85% sequence identity, at least 90% sequence identity, or at least 95% sequence identity to the amino acid sequences of SEQ ID NOs: 365, 366, 367, 368, 369, and 370, respectively. In some cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences each comprising at most one mutation relative to the amino acid sequences of SEQ ID NOs: 365, 366, 367, 368, 369, and 370, respectively. In some embodiments, the anti-gpA33 antibody comprises a heavy chain variable region comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 371 and a light chain variable region comprising an amino acid

sequence that is at least 80% at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 372.

[0476] In some cases, an antibody provided herein binds to IL1Rap. In some such cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences comprising at least 80% sequence identity, at least 85% sequence identity, at least 90% sequence identity, or at least 95% sequence identity to the amino acid sequences of SEQ ID NOs: 373, 374, 375, 376, 377, and 378, respectively. In some cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences each comprising at most one mutation relative to the amino acid sequences of SEQ ID NOs: 373, 374, 375, 376, 377, and 378, respectively. In some embodiments, the anti-IL1Rap antibody comprises a heavy chain variable region comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 379 and a light chain variable region comprising an amino acid sequence that is at least 80% at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 380.

[0477] In some cases, an antibody provided herein binds to EpCAM. In some cases, the antibody comprises a set of CDR sequences (CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3, respectively) of which each sequence comprises at least 80% sequence identity, at least 85% sequence identity, at least 90% sequence identity, at least 95%, or 100% sequence identity to amino acid sequences from a set of amino acid sequences selected from the group consisting of SEQ ID NOs: 381-386, SEQ ID NOs: 389-394, SEQ ID NOs: 397-402, SEQ ID NOs: 405-410, SEQ ID NOs: 413-418, or SEQ ID NOs: 421-426. In some embodiments, the anti-EpCAM antibody comprises a heavy chain variable region and a light chain variable region comprising amino acid sequences that are at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or at least 100% identical to the amino acid sequences of SEQ ID NO: 387 and 388, SEQ ID NO: 395 and 396, SEQ ID NO: 403 and 404, SEQ ID NO: 411 and 412, SEQ ID NO: 419 and 420, or SEQ ID NO: 427 and 428, respectively.

[0478] In some cases, an antibody provided herein binds to CD352. In some such cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences comprising at least 80% sequence identity, at least 85% sequence identity, at least 90% sequence identity, or at least 95% sequence identity to the amino acid sequences of SEQ ID NOs: 429, 430, 431, 432, 433, and 434, respectively. In some cases, the antibody

comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences each comprising at most one mutation relative to the amino acid sequences of SEQ ID NOs: 429, 430, 431, 432, 433, and 434, respectively. In some embodiments, the anti-CD352 antibody comprises a heavy chain variable region comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 435 and a light chain variable region comprising an amino acid sequence that is at least 80% at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 436.

[0479] In some cases, an antibody provided herein binds to CS1. In some such cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences comprising at least 80% sequence identity, at least 85% sequence identity, at least 90% sequence identity, or at least 95% sequence identity to the amino acid sequences of SEQ ID NOs: 437, 438, 439, 440, 441, and 442, respectively. In some cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences each comprising at most one mutation relative to the amino acid sequences of SEQ ID NOs: 437, 438, 439, 440, 441, and 442, respectively. In some embodiments, the anti-CS1 antibody comprises a heavy chain variable region comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 443 and a light chain variable region comprising an amino acid sequence that is at least 80% at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 444.

[0480] In some cases, an antibody provided herein binds to CD38. In some such cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences comprising at least 80% sequence identity, at least 85% sequence identity, at least 90% sequence identity, or at least 95% sequence identity to the amino acid sequences of SEQ ID NOs: 445, 446, 447, 448, 449, and 450, respectively. In some cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences each comprising at most one mutation relative to the amino acid sequences of SEQ ID NOs: 445, 446, 447, 448, 449, and 450, respectively. In some embodiments, the anti-CD38 antibody comprises a heavy chain variable region comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 451 and a light chain variable region comprising an amino acid

sequence that is at least 80% at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 452.

[0481] In some cases, an antibody provided herein binds to CD25. In some such cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences comprising at least 80% sequence identity, at least 85% sequence identity, at least 90% sequence identity, or at least 95% sequence identity to the amino acid sequences of SEQ ID NOs: 453, 454, 455, 456, 457, and 458, respectively. In some cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences each comprising at most one mutation relative to the amino acid sequences of SEQ ID NOs: 453, 454, 455, 456, 457, and 458, respectively. In some embodiments, the anti-CD25 antibody comprises a heavy chain variable region comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 459 and a light chain variable region comprising an amino acid sequence that is at least 80% at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 460.

[0482] In some cases, an antibody provided herein binds to ADAM9. In some such cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences comprising at least 80% sequence identity, at least 85% sequence identity, at least 90% sequence identity, or at least 95% sequence identity to the amino acid sequences of SEQ ID NOs: 461, 462, 463, 464, 465, and 466, respectively. In some cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences each comprising at most one mutation relative to the amino acid sequences of SEQ ID NOs: 461, 462, 463, 464, 465, and 466, respectively. In some such cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences comprising at least 80% sequence identity, at least 85% sequence identity, at least 90% sequence identity, or at least 95% sequence identity to the amino acid sequences of SEQ ID NOs: 469, 470, 471, 472, 473, and 474, respectively. In some cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences each comprising at most one mutation relative to the amino acid sequences of SEQ ID NOs: 469, 470, 471, 472, 473, and 474, respectively. In some embodiments, the anti-ADAM9 antibody comprises a heavy chain variable region comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 467 and a light chain variable region comprising an amino acid sequence that is at least 80% at least

85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 468. In some embodiments, the anti-ADAM9 antibody comprises a heavy chain variable region comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 475 and a light chain variable region comprising an amino acid sequence that is at least 80% at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 476.

[0483] In some cases, an antibody provided herein binds to CD59. In some such cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences comprising at least 80% sequence identity, at least 85% sequence identity, at least 90% sequence identity, or at least 95% sequence identity to the amino acid sequences of SEQ ID NOs: 477, 478, 479, 480, 481, and 482, respectively. In some cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences each comprising at most one mutation relative to the amino acid sequences of SEQ ID NOs: 477, 478, 479, 480, 481, and 482, respectively. In some embodiments, the anti-CD59 antibody comprises a heavy chain variable region comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 483 and a light chain variable region comprising an amino acid sequence that is at least 80% at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 484.

[0484] In some cases, an antibody provided herein binds to CD19. In some such cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences comprising at least 80% sequence identity, at least 85% sequence identity, at least 90% sequence identity, or at least 95% sequence identity to the amino acid sequences of SEQ ID NOs: 485, 486, 487, 488, 489, and 490, respectively. In some cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences each comprising at most one mutation relative to the amino acid sequences of SEQ ID NOs: 485, 486, 487, 488, 489, and 490, respectively. In some embodiments, the anti-CD19 antibody comprises a heavy chain variable region comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 491 and a light chain variable region comprising an amino acid sequence that is at least 80% at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 492. In some embodiments, the anti-

CD19 antibody comprises a heavy chain comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 493 and a light chain comprising an amino acid sequence that is at least 80% at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 494.

[0485] In some cases, an antibody provided herein binds to CD138. In some such cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences comprising at least 80% sequence identity, at least 85% sequence identity, at least 90% sequence identity, or at least 95% sequence identity to the amino acid sequences of SEQ ID NOs: 495, 496, 497, 498, 499, and 500, respectively. In some cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences each comprising at most one mutation relative to the amino acid sequences of SEQ ID NOs: 495, 496, 497, 498, 499, and 500, respectively. In some embodiments, the anti-CD138 antibody comprises a heavy chain variable region comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 501 and a light chain variable region comprising an amino acid sequence that is at least 80% at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 502.

[0486] In some cases, an antibody provided herein binds to CD166. In some such cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences comprising at least 80% sequence identity, at least 85% sequence identity, at least 90% sequence identity, or at least 95% sequence identity to the amino acid sequences of SEQ ID NOs: 503, 504, 505, 506, 507, and 508, respectively. In some cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences each comprising at most one mutation relative to the amino acid sequences of SEQ ID NOs: 503, 504, 505, 506, 507, and 508, respectively. In some embodiments, the anti-CD166 antibody comprises a heavy chain variable region comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 509 and a light chain variable region comprising an amino acid sequence that is at least 80% at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 510.

[0487] In some cases, an antibody provided herein binds to CD56. In some such cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3

sequences comprising at least 80% sequence identity, at least 85% sequence identity, at least 90% sequence identity, or at least 95% sequence identity to the amino acid sequences of SEQ ID NOs: 511, 512, 513, 514, 515, and 516, respectively. In some cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences each comprising at most one mutation relative to the amino acid sequences of SEQ ID NOs: 511, 512, 513, 514, 515, and 516, respectively. In some embodiments, the anti-CD56 antibody comprises a heavy chain variable region comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 517 and a light chain variable region comprising an amino acid sequence that is at least 80% at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 518.

[0488] In some cases, an antibody provided herein binds to CD74. In some such cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences comprising at least 80% sequence identity, at least 85% sequence identity, at least 90% sequence identity, or at least 95% sequence identity to the amino acid sequences of SEQ ID NOs: 519, 520, 521, 522, 523, and 524, respectively. In some cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences each comprising at most one mutation relative to the amino acid sequences of SEQ ID NOs: 519, 520, 521, 522, 523, and 524, respectively. In some embodiments, the anti-CD74 antibody comprises a heavy chain variable region comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 525 and a light chain variable region comprising an amino acid sequence that is at least 80% at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 526.

[0489] In some cases, an antibody provided herein binds to CEACAM5. In some such cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences comprising at least 80% sequence identity, at least 85% sequence identity, at least 90% sequence identity, or at least 95% sequence identity to the amino acid sequences of SEQ ID NOs: 527, 528, 529, 530, 531, and 532, respectively. In some cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences each comprising at most one mutation relative to the amino acid sequences of SEQ ID NOs: 527, 528, 529, 530, 531, and 532, respectively. In some embodiments, the anti-CEACAM5 antibody comprises a heavy chain variable region comprising an amino acid sequence that is

at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 533 and a light chain variable region comprising an amino acid sequence that is at least 80% at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 534.

[0490] In some cases, an antibody provided herein binds to CanAg. In some such cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences comprising at least 80% sequence identity, at least 85% sequence identity, at least 90% sequence identity, or at least 95% sequence identity to the amino acid sequences of SEQ ID NOs: 535, 536, 537, 538, 539, and 540, respectively. In some cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences each comprising at most one mutation relative to the amino acid sequences of SEQ ID NOs: 535, 536, 537, 538, 539, and 540, respectively. In some embodiments, the anti-CanAg antibody comprises a heavy chain variable region comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 541 and a light chain variable region comprising an amino acid sequence that is at least 80% at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 542.

[0491] In some cases, an antibody provided herein binds to DLL-3. In some such cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences comprising at least 80% sequence identity, at least 85% sequence identity, at least 90% sequence identity, or at least 95% sequence identity to the amino acid sequences of SEQ ID NOs: 543, 544, 545, 546, 547, and 548, respectively. In some cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences each comprising at most one mutation relative to the amino acid sequences of SEQ ID NOs: 543, 544, 545, 546, 547, and 548, respectively. In some embodiments, the anti-DLL-3 antibody comprises a heavy chain variable region comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 549 and a light chain variable region comprising an amino acid sequence that is at least 80% at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 550.

[0492] In some cases, an antibody provided herein binds to DPEP-3. In some such cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences comprising at least 80% sequence identity, at least 85% sequence identity, at least

90% sequence identity, or at least 95% sequence identity to the amino acid sequences of SEQ ID NOs: 551, 552, 553, 554, 555, and 556, respectively. In some cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences each comprising at most one mutation relative to the amino acid sequences of SEQ ID NOs: 551, 552, 553, 554, 555, and 556, respectively. In some embodiments, the anti-DPEP-3 antibody comprises a heavy chain variable region comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 557 and a light chain variable region comprising an amino acid sequence that is at least 80% at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 558.

[0493] In some cases, an antibody provided herein binds to EGFR. In some cases, the antibody comprises a set of CDR sequences (CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3, respectively) of which each sequence comprises at least 80% sequence identity, at least 85% sequence identity, at least 90% sequence identity, at least 95%, or 100% sequence identity to amino acid sequences from a set of amino acid sequences selected from the group consisting of SEQ ID NOs: 559-564, SEQ ID NOs: 567-572, SEQ ID NOs: 575-580, and SEQ ID NOs: 895-900. In some embodiments, the anti-EGFR antibody comprises a heavy chain variable region and a light chain variable region comprising amino acid sequences that are at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or at least 100% identical to the amino acid sequences of SEQ ID NO: 565 and 566, SEQ ID NO: 573 and 574, SEQ ID NO: 581 and 582, or SEQ ID NO: 901 and 902, respectively.

[0494] In some cases, an antibody provided herein binds to FRa. In some such cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences comprising at least 80% sequence identity, at least 85% sequence identity, at least 90% sequence identity, or at least 95% sequence identity to the amino acid sequences of SEQ ID NOs: 583, 584, 585, 586, 587, and 588, respectively. In some cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences each comprising at most one mutation relative to the amino acid sequences of SEQ ID NOs: 583, 584, 585, 586, 587, and 588, respectively. In some cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences comprising at least 80% sequence identity, at least 85% sequence identity, at least 90% sequence identity, or at least 95% sequence identity to the amino acid sequences of SEQ ID NOs: 591, 592, 593, 594, 595,

and 596, respectively. In some cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences each comprising at most one mutation relative to the amino acid sequences of SEQ ID NOs: 591, 592, 593, 594, 595, and 596, respectively. In some embodiments, the anti-FRa antibody comprises a heavy chain variable region comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 589 and a light chain variable region comprising an amino acid sequence that is at least 80% at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 590. In some embodiments, the anti-FRa antibody comprises a heavy chain variable region comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 597 and a light chain variable region comprising an amino acid sequence that is at least 80% at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 598.

[0495] In some cases, an antibody provided herein binds to MUC-1. In some such cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences comprising at least 80% sequence identity, at least 85% sequence identity, at least 90% sequence identity, or at least 95% sequence identity to the amino acid sequences of SEQ ID NOs: 599, 600, 601, 602, 603, and 604, respectively. In some cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences each comprising at most one mutation relative to the amino acid sequences of SEQ ID NOs: 599, 600, 601, 602, 603, and 604, respectively. In some embodiments, the anti-MUC-1 antibody comprises a heavy chain variable region comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 605 and a light chain variable region comprising an amino acid sequence that is at least 80% at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 606.

[0496] In some cases, an antibody provided herein binds to Mesothelin. In some such cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences comprising at least 80% sequence identity, at least 85% sequence identity, at least 90% sequence identity, or at least 95% sequence identity to the amino acid sequences of SEQ ID NOs: 607, 608, 609, 610, 611, and 612, respectively. In some cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences each

comprising at most one mutation relative to the amino acid sequences of SEQ ID NOs: 607, 608, 609, 610, 611, and 612, respectively. In some embodiments, the anti-Mesothelin antibody comprises a heavy chain variable region comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 613 and a light chain variable region comprising an amino acid sequence that is at least 80% at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 614.

[0497] In some cases, an antibody provided herein binds to ROR-1. In some such cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences comprising at least 80% sequence identity, at least 85% sequence identity, at least 90% sequence identity, or at least 95% sequence identity to the amino acid sequences of SEQ ID NOs: 615, 616, 617, 618, 619, and 620, respectively. In some cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences each comprising at most one mutation relative to the amino acid sequences of SEQ ID NOs: 615, 616, 617, 618, 619, and 620, respectively. In some embodiments, the anti-ROR-1 antibody comprises a heavy chain variable region comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 621 and a light chain variable region comprising an amino acid sequence that is at least 80% at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 622.

[0498] In some cases, an antibody provided herein binds to B7H3. In some cases, the antibody comprises a set of CDR sequences (CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3, respectively) of which each sequence comprises at least 80% sequence identity, at least 85% sequence identity, at least 90% sequence identity, at least 95%, or 100% sequence identity to amino acid sequences from a set of amino acid sequences selected from the group consisting of SEQ ID NOs: 623-628, SEQ ID NOs: 631-636, SEQ ID NOs: 639-644, SEQ ID NOs: 647-652, SEQ ID NOs: 655-660, SEQ ID NOs: 663-668, SEQ ID NOs: 671-676, SEQ ID NOs: 679-684, SEQ ID NOs: 687-692, SEQ ID NOs: 695-700, and SEQ ID NOs: 705-710. In some embodiments, the anti-B7H3 antibody comprises a heavy chain variable region and a light chain variable region comprising amino acid sequences that are at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or at least 100% identical to the amino acid sequences of SEQ ID NO: 629 and 630, SEQ ID NOs: 637 and 638, SEQ ID NOs: 645 and 646, SEQ ID NOs: 653 and 654, SEQ ID NOs: 661 and 662,

SEQ ID NOs: 669 and 670, SEQ ID NOs: 677 and 678, SEQ ID NOs: 685 and 686, SEQ ID NOs: 693 and 694, SEQ ID NOs: 701 and 702, SEQ ID NOs: 703 and 704, SEQ ID NOs: 711 and 712, SEQ ID NOs: 713 and 714, and SEQ ID NOs: 715 and 716, respectively.

[0499] In some cases, an antibody provided herein binds to HER3. In some embodiments, the anti-HER3 antibody comprises a heavy chain comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 717 and a light chain comprising an amino acid sequence that is at least 80% at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 718. In some cases, an antibody provided herein binds to HER3. In some embodiments, the anti-HER3 antibody comprises a heavy chain comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 719 and a light chain comprising an amino acid sequence that is at least 80% at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 720. In some cases, an antibody provided herein binds to HER3. In some embodiments, the anti-HER3 antibody comprises a heavy chain comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 721 and a light chain comprising an amino acid sequence that is at least 80% at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 722. In some cases, an antibody provided herein binds to HER3. In some embodiments, the anti-HER3 antibody comprises a heavy chain comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 723 and a light chain comprising an amino acid sequence that is at least 80% at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 724.

[0500] In some cases, an antibody provided herein binds to PTK7. In some cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences comprising at least 80% sequence identity, at least 85% sequence identity, at least 90% sequence identity, or at least 95% sequence identity to the amino acid sequences of SEQ ID NOs: 725, 726, 727, 728, 729, and 730, respectively. In some cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences each comprising at most one mutation relative to the amino acid sequences of SEQ ID NOs: 725,

726, 727, 728, 729, and 730, respectively. In some cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences comprising at least 80% sequence identity, at least 85% sequence identity, at least 90% sequence identity, or at least 95% sequence identity to the amino acid sequences of SEQ ID NOs: 733, 734, 735, 736, 737, and 738, respectively. In some cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences each comprising at most one mutation relative to the amino acid sequences of SEQ ID NOs: 733, 734, 735, 736, 737, and 738, respectively. In some cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences comprising at least 80% sequence identity, at least 85% sequence identity, at least 90% sequence identity, or at least 95% sequence identity to the amino acid sequences of SEQ ID NOs: 741, 742, 743, 744, 745, and 746, respectively. In some cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences each comprising at most one mutation relative to the amino acid sequences of SEQ ID NOs: 741, 742, 743, 744, 745, and 746, respectively. In some cases, the anti-PTK7 antibody comprises a heavy chain comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 731 and a light chain comprising an amino acid sequence that is at least 80% at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 732. In some cases, the anti-PTK7 antibody comprises a heavy chain comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 739 and a light chain comprising an amino acid sequence that is at least 80% at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 740. In some cases, the anti-PTK7 antibody comprises a heavy chain comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 747 and a light chain comprising an amino acid sequence that is at least 80% at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 748.

[0501] In some cases, an antibody provided herein binds to ZIP6. In some cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences comprising at least 80% sequence identity, at least 85% sequence identity, at least 90% sequence identity, or at least 95% sequence identity to the amino acid sequences of SEQ ID NOs: 749, 750, 751, 752, 753, and 754, respectively. In some cases, the antibody

comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences each comprising at most one mutation relative to the amino acid sequences of SEQ ID NOs: 749, 750, 751, 752, 753, and 754, respectively. In some cases, the anti-ZIP6 antibody comprises a heavy chain variable region comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 755 and a light chain variable region comprising an amino acid sequence that is at least 80% at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 756. In some embodiments, the anti-ZIP6 antibody comprises a heavy chain comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 757 and a light chain comprising an amino acid sequence that is at least 80% at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 758.

[0502] In some cases, an antibody provided herein binds to Integrin αvβ6. In some cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences comprising at least 80% sequence identity, at least 85% sequence identity, at least 90% sequence identity, or at least 95% sequence identity to the amino acid sequences of SEQ ID NOs: 759, 760, 761, 762, 763, and 764, respectively. In some cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences each comprising at most one mutation relative to the amino acid sequences of SEQ ID NOs: 759, 760, 761, 762, 763, and 764, respectively. In some embodiments, the anti- Integrin αvβ6 antibody comprises a heavy chain variable region comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 765 and a light chain variable region comprising an amino acid sequence that is at least 80% at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 766.

[0503] In some cases, an antibody provided herein binds to CD48. In some cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences comprising at least 80% sequence identity, at least 85% sequence identity, at least 90% sequence identity, or at least 95% sequence identity to the amino acid sequences of SEQ ID NOs: 767, 768, 769, 770, 771, and 772, respectively. In some cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences each comprising at most one mutation relative to the amino acid sequences of SEQ ID NOs: 767,

768, 769, 770, 771, and 772, respectively. In some embodiments, the anti-CD48 antibody comprises a heavy chain variable region comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 773 and a light chain variable region comprising an amino acid sequence that is at least 80% at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 774.

[0504] In some cases, an antibody provided herein binds to IGF-1R. In some cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences comprising at least 80% sequence identity, at least 85% sequence identity, at least 90% sequence identity, or at least 95% sequence identity to the amino acid sequences of SEQ ID NOs: 775, 776, 777, 778, 779, and 780, respectively. In some cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences each comprising at most one mutation relative to the amino acid sequences of SEQ ID NOs: 775, 776, 777, 778, 779, and 780, respectively. In some embodiments, the anti-IGF-1R antibody comprises a heavy chain variable region comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 781 and a light chain variable region comprising an amino acid sequence that is at least 80% at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 782.

[0505] In some cases, an antibody provided herein binds to Claudin-18.2. In some cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences comprising at least 80% sequence identity, at least 85% sequence identity, at least 90% sequence identity, or at least 95% sequence identity to the amino acid sequences of SEQ ID NOs: 783, 784, 785, 786, 787, and 788, respectively. In some cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences each comprising at most one mutation relative to the amino acid sequences of SEQ ID NOs: 783, 784, 785, 786, 787, and 788, respectively. In some cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences comprising at least 80% sequence identity, at least 85% sequence identity, at least 90% sequence identity, or at least 95% sequence identity to the amino acid sequences of SEQ ID NOs: 791, 792, 793, 794, 795, and 796, respectively. In some cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences each comprising at most one mutation relative to the amino acid sequences of SEQ ID NOs: 791, 792, 793, 794, 795, and 796, respectively. In

some embodiments, the anti-Claudin-18.2 antibody comprises a heavy chain variable region comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 789 and a light chain variable region comprising an amino acid sequence that is at least 80% at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 790. In some embodiments, the anti-Claudin-18.2 antibody comprises a heavy chain variable region comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 797 and a light chain variable region comprising an amino acid sequence that is at least 80% at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 798.

[0506] In some cases, an antibody provided herein binds to Nectin-4. In some cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences comprising at least 80% sequence identity, at least 85% sequence identity, at least 90% sequence identity, or at least 95% sequence identity to the amino acid sequences of SEQ ID NOs: 799, 800, 801, 802, 803, and 804, respectively. In some cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences each comprising at most one mutation relative to the amino acid sequences of SEQ ID NOs: 799, 800, 801, 802, 803, and 804, respectively. In some embodiments, the anti-Nectin-4 antibody comprises a heavy chain variable region comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 805 and a light chain variable region comprising an amino acid sequence that is at least 80% at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 806.

[0507] In some cases, an antibody provided herein binds to SLTRK6. In some such cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences comprising at least 80% sequence identity, at least 85% sequence identity, at least 90% sequence identity, or at least 95% sequence identity to the amino acid sequences of SEQ ID NOs: 807, 808, 809, 810, 811, and 812, respectively. In some cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences each comprising at most one mutation relative to the amino acid sequences of SEQ ID NOs: 807, 808, 809, 810, 811, and 812, respectively. In some embodiments, the anti-SLTRK6 antibody comprises a heavy chain variable region comprising an amino acid sequence that is at least

80%, at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 813 and a light chain variable region comprising an amino acid sequence that is at least 80% at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 814.

[0508] In some cases, an antibody provided herein binds to CD142. In some such cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences comprising at least 80% sequence identity, at least 85% sequence identity, at least 90% sequence identity, or at least 95% sequence identity to the amino acid sequences of SEQ ID NOs: 815, 816, 817, 818, 819, and 820, respectively. In some cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences each comprising at most one mutation relative to the amino acid sequences of SEQ ID NOs: 815, 816, 817, 818, 819, and 820, respectively. In some embodiments, the anti-CD142 antibody comprises a heavy chain variable region comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 821 and a light chain variable region comprising an amino acid sequence that is at least 80% at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 822.

[0509] In some cases, an antibody provided herein binds to Sialyl-Thomsen-nouveau antigen (STn). In some such cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences comprising at least 80% sequence identity, at least 85% sequence identity, at least 90% sequence identity, or at least 95% sequence identity to the amino acid sequences of SEQ ID NOs: 823, 824, 825, 826, 827, and 828, respectively. In some cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences each comprising at most one mutation relative to the amino acid sequences of SEQ ID NOs: 823, 824, 825, 826, 827, and 828, respectively.

[0510] In some embodiments, the anti-STn antibody comprises a heavy chain variable region comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 829 and a light chain variable region comprising an amino acid sequence that is at least 80% at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 830.

[0511] In some cases, an antibody provided herein binds to CD20. In some such cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences comprising at least 80% sequence identity, at least 85% sequence identity, at least 90% sequence identity, or at least 95% sequence identity to the amino acid sequences of SEQ ID NOs: 831, 832, 833, 834, 835, and 836, respectively. In some cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences each comprising at most one mutation relative to the amino acid sequences of SEQ ID NOs: 831, 832, 833, 834, 835, and 836, respectively. In some embodiments, the anti-CD20 antibody comprises a heavy chain variable region comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 837 and a light chain variable region comprising an amino acid sequence that is at least 80% at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 838.

[0512] In some cases, an antibody provided herein binds to HER2. In some such cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences comprising at least 80% sequence identity, at least 85% sequence identity, at least 90% sequence identity, or at least 95% sequence identity to the amino acid sequences of SEQ ID NOs: 839, 840, 841, 842, 843, and 844, respectively. In some cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences each comprising at most one mutation relative to the amino acid sequences of SEQ ID NOs: 839, 840, 841, 842, 843, and 844, respectively. In some embodiments, the anti-HER2 antibody comprises a heavy chain variable region comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 845 and a light chain variable region comprising an amino acid sequence that is at least 80% at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 846.

[0513] In some cases, an antibody provided herein binds to CD79b. In some such cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences comprising at least 80% sequence identity, at least 85% sequence identity, at least 90% sequence identity, or at least 95% sequence identity to the amino acid sequences of SEQ ID NOs: 847, 848, 849, 850, 851, and 852, respectively. In some cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences each comprising at most one mutation relative to the amino acid sequences of SEQ ID NOs: 847,

848, 849, 850, 851, and 852, respectively. In some embodiments, the anti-CD79b antibody comprises a heavy chain variable region comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 853 and a light chain variable region comprising an amino acid sequence that is at least 80% at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 854.

[0514] In some cases, an antibody provided herein binds to NaPi2B. In some such cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences comprising at least 80% sequence identity, at least 85% sequence identity, at least 90% sequence identity, or at least 95% sequence identity to the amino acid sequences of SEQ ID NOs: 855, 856, 857, 858, 859, and 860, respectively. In some cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences each comprising at most one mutation relative to the amino acid sequences of SEQ ID NOs: 855, 856, 857, 858, 859, and 860, respectively. In some embodiments, the anti-NaPi2B antibody comprises a heavy chain variable region comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 861 and a light chain variable region comprising an amino acid sequence that is at least 80% at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 862.

[0515] In some cases, an antibody provided herein binds to Muc16. In some such cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences comprising at least 80% sequence identity, at least 85% sequence identity, at least 90% sequence identity, or at least 95% sequence identity to the amino acid sequences of SEQ ID NOs: 863, 864, 865, 866, 867, and 868, respectively. In some cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences each comprising at most one mutation relative to the amino acid sequences of SEQ ID NOs: 863, 864, 865, 866, 867, and 868, respectively. In some embodiments, the anti-Muc16 antibody comprises a heavy chain variable region comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 869 and a light chain variable region comprising an amino acid sequence that is at least 80% at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 870.

[0516] In some cases, an antibody provided herein binds to STEAP1. In some such cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences comprising at least 80% sequence identity, at least 85% sequence identity, at least 90% sequence identity, or at least 95% sequence identity to the amino acid sequences of SEQ ID NOs: 871, 872, 873, 874, 875, and 876, respectively. In some cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences each comprising at most one mutation relative to the amino acid sequences of SEQ ID NOs: 871, 872, 873, 874, 875, and 876, respectively. In some embodiments, the anti-STEAP1 antibody comprises a heavy chain variable region comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 877 and a light chain variable region comprising an amino acid sequence that is at least 80% at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 878.

[0517] In some cases, an antibody provided herein binds to BCMA. In some such cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences comprising at least 80% sequence identity, at least 85% sequence identity, at least 90% sequence identity, or at least 95% sequence identity to the amino acid sequences of SEQ ID NOs: 879, 880, 881, 882, 883, and 884, respectively. In some cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences each comprising at most one mutation relative to the amino acid sequences of SEQ ID NOs: 879, 880, 881, 882, 883, and 884, respectively. In some embodiments, the anti-BCMA antibody comprises a heavy chain variable region comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 885 and a light chain variable region comprising an amino acid sequence that is at least 80% at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 886.

[0518] In some cases, an antibody provided herein binds to c-Met. In some such cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences comprising at least 80% sequence identity, at least 85% sequence identity, at least 90% sequence identity, or at least 95% sequence identity to the amino acid sequences of SEQ ID NOs: 887, 888, 889, 890, 891, and 892, respectively. In some cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences each comprising at most one mutation relative to the amino acid sequences of SEQ ID NOs: 887,

888, 889, 890, 891, and 892, respectively. In some embodiments, the anti-c-Met antibody comprises a heavy chain variable region comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 893 and a light chain variable region comprising an amino acid sequence that is at least 80% at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 893.

[0519] In some cases, an antibody provided herein binds to SLAMF7. In some such cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences comprising at least 80% sequence identity, at least 85% sequence identity, at least 90% sequence identity, or at least 95% sequence identity to the amino acid sequences of SEQ ID NOs: 903, 904, 905, 906, 907, and 908, respectively. In some cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences each comprising at most one mutation relative to the amino acid sequences of SEQ ID NOs: 903, 904, 905, 906, 907, and 908, respectively. In some embodiments, the anti-SLAMF7 antibody comprises a heavy chain variable region comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 909 and a light chain variable region comprising an amino acid sequence that is at least 80% at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 910.

[0520] In some cases, an antibody provided herein binds to C4.4a. In some such cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences comprising at least 80% sequence identity, at least 85% sequence identity, at least 90% sequence identity, or at least 95% sequence identity to the amino acid sequences of SEQ ID NOs: 911, 912, 913, 914, 915, and 916, respectively. In some cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences each comprising at most one mutation relative to the amino acid sequences of SEQ ID NOs: 911, 912, 913, 914, 915, and 916, respectively. In some embodiments, the anti-C4.4a antibody comprises a heavy chain variable region comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 917 and a light chain variable region comprising an amino acid sequence that is at least 80% at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 918.

[0521] In some cases, an antibody provided herein binds to GCC. In some such cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences comprising at least 80% sequence identity, at least 85% sequence identity, at least 90% sequence identity, or at least 95% sequence identity to the amino acid sequences of SEQ ID NOs: 919, 920, 921, 922, 923, and 924, respectively. In some cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences each comprising at most one mutation relative to the amino acid sequences of SEQ ID NOs: 919, 920, 921, 922, 923, and 924, respectively. In some embodiments, the anti-GCC antibody comprises a heavy chain variable region comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 925 and a light chain variable region comprising an amino acid sequence that is at least 80% at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 926.

[0522] In some cases, an antibody provided herein binds to Axl. In some such cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences comprising at least 80% sequence identity, at least 85% sequence identity, at least 90% sequence identity, or at least 95% sequence identity to the amino acid sequences of SEQ ID NOs: 927, 928, 929, 930, 931, and 932, respectively. In some cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences each comprising at most one mutation relative to the amino acid sequences of SEQ ID NOs: 927, 928, 929, 930, 931, and 932, respectively. In some embodiments, the anti-Axl antibody comprises a heavy chain variable region comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 933 and a light chain variable region comprising an amino acid sequence that is at least 80% at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 933.

[0523] In some cases, an antibody provided herein binds to transmembrane glycoprotein NMB (gpNMB). In some such cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences comprising at least 80% sequence identity, at least 85% sequence identity, at least 90% sequence identity, or at least 95% sequence identity to the amino acid sequences of SEQ ID NOs: 935, 936, 937, 938, 939, and 940, respectively. In some cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences each comprising at most one mutation relative to the amino acid

sequences of SEQ ID NOs: 935, 936, 937, 938, 939, and 940, respectively. In some embodiments, the anti-gpNMB antibody comprises a heavy chain variable region comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 941 and a light chain variable region comprising an amino acid sequence that is at least 80% at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 942. In some embodiments, the anti-gpNMB antibody comprises a heavy chain variable region comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 943 and a light chain variable region comprising an amino acid sequence that is at least 80% at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 944.

[0524] In some cases, an antibody provided herein binds to Prolactin receptor. In some such cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences comprising at least 80% sequence identity, at least 85% sequence identity, at least 90% sequence identity, or at least 95% sequence identity to the amino acid sequences of SEQ ID NOs: 945, 946, 947, 948, 949, and 950, respectively. In some cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences each comprising at most one mutation relative to the amino acid sequences of SEQ ID NOs: 945, 946, 947, 948, 949, and 950, respectively. In some embodiments, the anti-Prolactin receptor antibody comprises a heavy chain variable region comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 951 and a light chain variable region comprising an amino acid sequence that is at least 80% at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 952.

[0525] In some cases, an antibody provided herein binds to FGFR2. In some such cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences comprising at least 80% sequence identity, at least 85% sequence identity, at least 90% sequence identity, or at least 95% sequence identity to the amino acid sequences of SEQ ID NOs: 953, 954, 955, 956, 957, and 958, respectively. In some cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences each comprising at most one mutation relative to the amino acid sequences of SEQ ID NOs: 953, 954, 955, 956, 957, and 958, respectively. In some embodiments, the anti-FGFR2 antibody

comprises a heavy chain variable region comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 959 and a light chain variable region comprising an amino acid sequence that is at least 80% at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 960.

[0526] In some cases, an antibody provided herein binds to CDCP1. In some cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences comprising at least 80% sequence identity, at least 85% sequence identity, at least 90% sequence identity, or at least 95% sequence identity to the amino acid sequences of SEQ ID NOs: 961, 962, 963, 964, 965, and 966, respectively. In some cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences each comprising at most one mutation relative to the amino acid sequences of SEQ ID NOs: 969, 970, 971, 972, 973, and 974, respectively. In some cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences comprising at least 80% sequence identity, at least 85% sequence identity, at least 90% sequence identity, or at least 95% sequence identity to the amino acid sequences of SEQ ID NOs: 961, 962, 963, 964, 965, and 966, respectively. In some cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences each comprising at most one mutation relative to the amino acid sequences of SEQ ID NOs: 969, 970, 971, 972, 973, and 974, respectively. In some cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences comprising at least 80% sequence identity, at least 85% sequence identity, at least 90% sequence identity, or at least 95% sequence identity to the amino acid sequences of SEQ ID NOs: 977, 978, 979, 980, 981, and 982, respectively. In some cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences each comprising at most one mutation relative to the amino acid sequences of SEQ ID NOs: 977, 978, 979, 980, 981, and 982, respectively. In some cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences comprising at least 80% sequence identity, at least 85% sequence identity, at least 90% sequence identity, or at least 95% sequence identity to the amino acid sequences of SEQ ID NOs: 985, 986, 987, 988, 989, and 990, respectively. In some cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences each comprising at most one mutation relative to the amino acid sequences of SEQ ID NOs: 985, 986, 987,

988, 989, and 990, respectively. In some embodiments, the anti-CDCP1 antibody comprises a heavy chain variable region comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 967 and a light chain variable region comprising an amino acid sequence that is at least 80% at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 968. In some embodiments, the anti-CDCP1 antibody comprises a heavy chain variable region comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 975 and a light chain variable region comprising an amino acid sequence that is at least 80% at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 976. In some embodiments, the anti-CDCP1 antibody comprises a heavy chain variable region comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 983 and a light chain variable region comprising an amino acid sequence that is at least 80% at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 984. In some embodiments, the anti-CDCP1 antibody comprises a heavy chain variable region comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 991 and a light chain variable region comprising an amino acid sequence that is at least 80% at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 992.

[0527] In some cases, an antibody provided herein binds to ASCT2. In some such cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences comprising at least 80% sequence identity, at least 85% sequence identity, at least 90% sequence identity, or at least 95% sequence identity to the amino acid sequences of SEQ ID NOs: 997, 998, 999, 1000, 1001, and 1002, respectively. In some cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences each comprising at most one mutation relative to the amino acid sequences of SEQ ID NOs: 997, 998, 999, 1000, 1001, and 1002, respectively. In some embodiments, the anti-ASCT2 antibody comprises a heavy chain variable region comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 993 and a light chain variable region comprising an

amino acid sequence that is at least 80% at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 994. In some embodiments, the anti-ASCT2 antibody comprises a heavy chain variable region comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 995 and a light chain variable region comprising an amino acid sequence that is at least 80% at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 996. In some embodiments, the anti-ASCT2 antibody comprises a heavy chain variable region comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 1003 and a light chain variable region comprising an amino acid sequence that is at least 80% at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 1004.

[0528] In some cases, an antibody provided herein binds to CD123. In some such cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences comprising at least 80% sequence identity, at least 85% sequence identity, at least 90% sequence identity, or at least 95% sequence identity to the amino acid sequences of SEQ ID NOs: 1005, 1006, 1007, 1008, 1009, and 1010, respectively. In some cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences each comprising at most one mutation relative to the amino acid sequences of SEQ ID NOs: 1005, 1006, 1007, 1008, 1009, and 1010, respectively. In some embodiments, the anti-CD123 antibody comprises a heavy chain variable region comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 1011 and a light chain variable region comprising an amino acid sequence that is at least 80% at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 1012.

[0529] In some cases, an antibody provided herein binds to GPC3. In some such cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences comprising at least 80% sequence identity, at least 85% sequence identity, at least 90% sequence identity, or at least 95% sequence identity to the amino acid sequences of SEQ ID NOs: 1013, 1014, 1015, 1016, 1017, and 1018 respectively. In some cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences each comprising at most one mutation relative to the amino acid sequences of SEQ ID NOs: 1013,

1014, 1015, 1016, 1017, and 1018, respectively. In some embodiments, the anti-TIGIT antibody comprises a heavy chain variable region comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 1027 and a light chain variable region comprising an amino acid sequence that is at least 80% at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 1028.

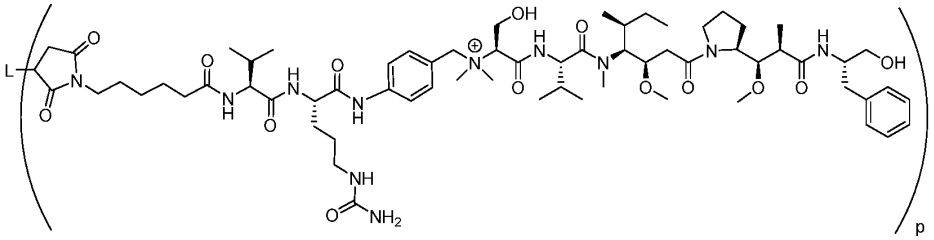
[0530] In some cases, an antibody provided herein binds to TIGIT. In some such cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences comprising at least 80% sequence identity, at least 85% sequence identity, at least 90% sequence identity, or at least 95% sequence identity to the amino acid sequences of SEQ ID NOs: 1021, 1022, 1023, 1024, 1025, and 1026, respectively. In some cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences each comprising at most one mutation relative to the amino acid sequences of SEQ ID NOs: 1021, 1022, 1023, 1024, 1025, and 1026, respectively. In some embodiments, the anti-BCMA antibody comprises a heavy chain variable region comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 1043 and a light chain variable region comprising an amino acid sequence that is at least 80% at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 1044.

[0531] In some cases, an antibody provided herein binds to CD33. In some such cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences comprising at least 80% sequence identity, at least 85% sequence identity, at least 90% sequence identity, or at least 95% sequence identity to the amino acid sequences of SEQ ID NOs: 1029, 1030, 1031, 1032, 1033, and 1034, respectively. In some cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences each comprising at most one mutation relative to the amino acid sequences of SEQ ID NOs: 1029, 1030, 1031, 1032, 1033, and 1034, respectively. In some embodiments, the anti-CD33 antibody comprises a heavy chain variable region comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 1035 and a light chain variable region comprising an amino acid sequence that is at least 80% at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 1036.

[0532] In some cases, an antibody provided herein binds to BCMA. In some such cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences comprising at least 80% sequence identity, at least 85% sequence identity, at least 90% sequence identity, or at least 95% sequence identity to the amino acid sequences of SEQ ID NOs: 1037, 1038, 1039, 1040, 1041, and 1042, respectively. In some cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences each comprising at most one mutation relative to the amino acid sequences of SEQ ID NOs: 1037, 1038, 1039, 1040, 1041, and 1042, respectively. In some embodiments, the anti-BCMA antibody comprises a heavy chain variable region comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 1043 and a light chain variable region comprising an amino acid sequence that is at least 80% at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 1044.

Ligand-Drug Conjugate compounds of compound 3.1

[0533] In some embodiments, provided is a compound 3.1,



wherein L is a ligand (e.g., an antibody) that targets an antigen selected from the group consisting of ADAM12 (e.g., Catalog #14139-1-AP); ADAM9 (e.g., IMGC936); AFP (e.g., ThermoFisher Catalog #PA5-25959); AGR2 (e.g., ThermoFisher Catalog #PA5-34517); AKAP-4 (e.g., Catalog #PA5-52230); ALK (e.g., DLX521); ALPP (e.g., Catalog #MA5-15652); ALPPL2 (e.g., Catalog #PA5-22336); AMHR2 (e.g., ThermoFisher Catalog #PA5-13902); androgen receptor (e.g., ThermoFisher Catalog #MA5-13426); ANTXR1 (e.g., Catalog #MA1-91702); ANXA1 (e.g., Catalog #71-3400); ARTN (e.g., ThermoFisher Catalog #PA5-47063); ASCT2 (e.g., idactamab); Axl (e.g., BA3011; tilvestamab); B7-DC (e.g., Catalog #PA5-20344); B7-H3 (e.g., enoblituzumab, omburtamab, MGD009, MGC018, DS-7300); B7-H4 (e.g., Catalog #14-5949-82); B7-H6 (e.g., Catalog #12-6526-42); B7-H7; BAFF-R (e.g., Catalog #14-9117-82); BCMA; BCR-ABL; BMPR2; BORIS; C4.4a; CanAg; C5 complement (e.g., BCD-148; CAN106); CA-125; CA19-9 (e.g., AbGn-7; MVT-5873);

CA9 (e.g., girentuximab); CALCR (*see,* e.g., International Publication No. WO 2015077826); CAMPATH-1 (e.g., alemtuzumab; ALLO-647; ANT1034); carcinoembryonic antigen (e.g., arcitumomab; cergutuzumab; amunaleukin; labetuzumab); CCNB1; CD112 (*see,* e.g., U.S. Publication No. 20100008928); CD115 (e.g., axatilimab; cabiralizumab; emactuzumab); CD123 (e.g., BAY-943; CSL360); CD137 (e.g., ADG106; CTX-471); CD138; CD142; CD166; CD147 (e.g., gavilimomab; metuzumab); CD155 (e.g., U.S. Publication No. 2018/0251548); CD19 (e.g., ALLO-501); CD20 (e.g., divozilimab; ibritumomab tiuxetan); CD24 (*see,* e.g., U.S. Patent No. 8,614,301); CD244 (e.g., R&D AF1039); CD247 (e.g., AFM15); CD27 (e.g., varlilumab); CD274 (e.g., adebrelimab; atezolizumab; garivulimab); CD3 (e.g., otelixizumab; visilizumab); CD30 (e.g., iratumumab); CD33 (e.g., lintuzumab; BI 836858; AMG 673); CD288; CD352 (e.g., SGN-CD352A); CD37 (e.g., lilotomab; GEN3009); CD38 (e.g., felzartamab; AMG 424); CD3D; CD3E (e.g., foralumab; teplizumab); CD3G; CD45 (e.g., apamistamab); CD47 (e.g., letaplimab; magrolimab); CD48 (e.g., SGN-CD48A); CD5 (e.g., MAT 304; zolimomab aritox); CD56; CD59; CD70 (e.g., cusatuzumab); CD74 (e.g., milatuzumab); CD79A (*see,* e.g., International Publication No. WO 2020252110); CD79b; CD96; CD97; CD-262 (e.g., tigatuzumab); CDCP1 (e.g., RG7287); CDH17 (*see,* e.g., International Publication No. WO 2018115231); CDH3 (e.g., PCA062); CDH6 (e.g., HKT288); CEACAM1; CEACAM5; CEACAM6; CLDN1 (e.g., INSERM anti-Claudin-1); CLDN16; CLDN18.1 (e.g., zolbetuximab); CLDN18.2 (e.g., zolbetuximab); CLDN19; CLDN2 (*see,* e.g., International Publication No. WO 2018123949); CLEC12A (e.g., tepoditamab); CS1; CLPTM1L; CSPG4 (e.g., U.S. Patent No. 10,822,427); CXCR4 (e.g., ulocuplumab); CYP1B1; c-Met; DCLK1 (*see,* e.g., International Publication No. WO 2018222675); DDR1; de2-7 EGFR (e.g., MAb 806); DLL-3; DPEP1; DPEP3; DPP4; DR4 (e.g., mapatumumab); DSG2 (*see,* e.g., U.S. Patent No. 10,836,823); EGF; EGFR; endosialin (e.g., ontuxizumab); ENPP1; EPCAM (e.g., adecatumumab); EPHA receptors; EPHA2; ERBB2 (e.g., trastuzumab); ERBB3; ERVMER34_1; ETV6-AML (e.g., Catalog #PA5-81865); FAS; FasL; Fas-related antigen 1; FBP; FGFR1 (e.g., RG7992); FGFR2 (e.g., aprutumab); FGFR3 (e.g., vofatamab); FGFR4 (e.g., MM-161); FLT3 (e.g., 4G8SDIEM); FN; FN1; FOLR1 (e.g., farletuzumab); FRa; FSHR; FucGM1 (e.g., BMS-986012); FZD5; FZD8; G250; GAGE; GCC; GD2 (e.g., dinutuximab); GD3 (e.g., mitumomab); GITR (e.g., ragifilimab); GloboH; GM2 (e.g., BIW-8962); GM3 (e.g., racotumomab); gp100; GPA33 (e.g., KRN330); GPC3 (e.g., codrituzumab); gpNMB (e.g., glembatumumab); GPR87; GUCY2C (e.g., indusatumab); HAS3; HAVCR2; HLA-E; HLA-F; HLA-G (e.g., TTX-080); HPV E6 E7; hTERT; ICAM1;

IDO1; IFNAR1 (e.g., faralimomab); IFNAR2; IL13Ra2; IL1RAP (e.g., nidanilimab); IL-21R (e.g., PF-05230900); IL-5R (e.g., benralizumab); ITGAV (e.g., abituzumab); ITGB6; ITGB8; KISS1R; L1CAM (e.g., JCAR023); LAG-3 (e.g., encelimab); LAMP1; LCK; legumain; LMP2; LY6G6D (e.g., PA5-23303); LY9 (e.g., PA5-95601); LYPD1 (e.g., ThermoFisher Catalog #PA5-26749); MAD-CT-1; MAD-CT-2; MAGEA1 (e.g., Catalog #MA5-11338); MAGEA3 (e.g., ThermoFisher Catalog #60054-1-IG); MAGEA4 (e.g., Catalog #MA5-26117); MAGEC2 (e.g., ThermoFisher Catalog #PA5-64010); MELTF (e.g., ThermoFisher Catalog #H00004241-M04A); MerTk (e.g., DS5MMER, Catalog #12-5751-82); a metalloproteinase; MFSD13A; MICA (e.g., 1E2C8, Catalog #66384-1-IG); MICB (e.g., Catalog #MA5-29422); Mincle (e.g., OTI2A8, Catalog #TA505101); MLANA (e.g., Catalog #MA5-15237); ML-IAP (e.g., 88C570, ThermoFisher Catalog #40958); MSLN (e.g., 5B2, Catalog #MA5-11918); MUC1 (e.g., MH1 (CT2), ThermoFisher Catalog #MA5-11202); MUC5AC (e.g., 45M1, Catalog #MA5-12178); MYCN (e.g., NCM-II 100, ThermoFisher Catalog #MA1-170); NA17; NCAM1 (e.g., ThermoFisher Catalog #MA5-11563); Nectin-4 (e.g., enfortumab); NOX1 (e.g., Catalog #PA5-103220); NT5E (e.g., 7G2, ThermoFisher Catalog #41-0200); NY-BR-1 (e.g., NY-BR-1 No. 2, Catalog #MA5-12645); NY-ESO-1 (e.g., E978m, Catalog #35-6200); OX40 (e.g., ABM193); OY-TES1; p53; p53mutant; PAP; PAX3 (e.g., GT1210, ThermoFisher Catalog #MA5-31583); PAX5; PDGFR-B (e.g., rinucumab); PDPN (e.g., ThermoFisher Catalog #14-5381-82); PLAVl; PMSA; polysialic acid (*see,* e.g., Watzlawik et al. J Nat Sci. 2015; 1(8):e141); PR1; PROM1 (e.g., Catalog #14-1331-82); PSA (e.g., ThermoFisher Catalog #PA1-38514; Daniels-Wells et al. *BMC Cancer* 2013; 13:195); PSCA (e.g., AGS-1C4D4); PSMA (e.g., BAY 2315497); PTK7 (e.g., cofetuzumab); PVRIG; Ras mutant (e.g., Shin et al. *Sci Adv.* 2020; 6(3):eaay2174); RET (e.g., WO2020210551); RGS5 (e.g., TF-TA503075); RhoC (e.g., ThermoFisher Catalog PA5-77866); ROR1 (e.g., cirmtuzumab); ROR2 (e.g., BA3021); ROS1 (e.g., WO 2019107671); Sarcoma translocation breakpoints; SART3 (e.g., TF 18025-1-AP); Sialyl-Thomsen-nouveau-antigen (e.g., Eavarone et al. *PLoS One.* 2018; 13(7): e0201314); Siglecs 1-16 (*see,* e.g., Angata et al. Trends *Pharmacol Sci.* 2015; 36(10): 645–660); SIRPa (e.g., Catalog #17-1729-42); SIRPg (e.g., PA5-104381); SIT1 (e.g., PA5-53825); SLAMF7 (e.g., elotuzumab); SLC10A2 (e.g., ThermoFisher Catalog #PA5-18990); SLC12A2 (e.g., ThermoFisher Catalog #13884-1-AP); SLC17A2 (e.g., ThermoFisher Catalog #PA5-106752); SLC38A1 (e.g., ThermoFisher Catalog #12039-1-AP); SLC39A5 (e.g., ThermoFisher Catalog #MA5-27260); SLC39A6 (e.g., ladiratuzumab); SLC44A4 (e.g., ASG-5ME); SLC6A15 (e.g., ThermoFisher Catalog #PA5-52586); SLC6A6 (e.g.,

ThermoFisher Catalog #PA5-53431); SLC7A11 (e.g., ThermoFisher Catalog #PA1-16893); SLC7A5; sLe; SLITRK6 (e.g., sirtratumab); Sperm protein 17 (e.g., BS-5754R); SSX2 (e.g., ThermoFisher Catalog #MA5-24971); survivin (e.g., PA1-16836); TACSTD2 (e.g., PA5-47074); TAG-72 (e.g., MA1-25956); tenascin; TF (e.g., tisotumab); Tie3; TLR2/4/1 (e.g., tomaralimab); TM4SF5 (e.g., 18239-1-AP); TMEM132A (e.g., Catalog #PA5-62524); TMEM40 (e.g., PA5-60636); TMPRSS11D (e.g., PA5-30927); Tn; TNFRSF12 (e.g., BAY-356); TRAIL (e.g., Catalog #12-9927-42); TRAIL1; TRP-2 (e.g., PA5-52736); ULBP1/2/3/4/5/6 (e.g., PA5-82302); uPAR (e.g., ATN-658); UPK1B (e.g., ThermoFisher Catalog #PA5-56863); UPK2 (e.g., ThermoFisher Catalog #PA5-60318); UPK3B (e.g., ThermoFisher Catalog #PA5-52696); VEGF (e.g., GNR-011); VEGFR2 (e.g., gentuximab); VSIR (e.g., ThermoFisher Catalog #PA5-52493); WT1 (e.g., ThermoFisher Catalog #MA5-32215); and XAGE1 (e.g., ThermoFisher Catalog #PA5-46413).

[0534] Also provided herein is a compound 3.1, wherein L is a ligand (e.g., an antibody) that targets an antigen selected from the group consisting of Axl (e.g., BA3011; tilvestamab); B7-1 (e.g., galiximab); B7-2 (e.g., Catalog #12-0862-82); B7-DC (e.g., Catalog #PA5-20344); B7-H3 (e.g., enoblituzumab, omburtamab, MGD009, MGC018, DS-7300); B7-H4 (e.g., Catalog #14-5949-82); B7-H6 (e.g., Catalog #12-6526-42); B7-H7; BAFF-R (e.g., Catalog #14-9117-82); BCMA; C5 complement (e.g., BCD-148; CAN106); CCR4 (e.g., AT008; mogamulizumab-kpkc); CCR8 (e.g., JTX-1811); CD112 (*see,* e.g., U.S. Publication No. 20100008928); CD115 (e.g., axatilimab; cabiralizumab; emactuzumab); CD123 (e.g., BAY-943; CSL360); CD137 (e.g., ADG106; CTX-471); CD155 (e.g., U.S. Publication No. 2018/0251548); CD163 (e.g., TBI 304H); CD19 (e.g., ALLO-501); CD2 (e.g., BTI-322; siplizumab); CD20 (e.g., divozilimab; ibritumomab); CD24 (*see,* e.g., U.S. Patent No. 8,614,301); CD244 (e.g., R&D AF1039); CD247 (e.g., AFM15); CD25 (e.g., basiliximab); CD27 (e.g., varlilumab); CD274 (e.g., adebrelimab; atezolizumab; garivulimab); CD278 (e.g., feladilimab; vopratelimab); CD28 (e.g., REGN5668); CD3 (e.g., otelixizumab; visilizumab); CD30 (e.g., iratumumab); CD30L (*see,* e.g., U.S. Patent No. 9,926,373); CD32 (e.g., mAb 2B6); CD33 (e.g., lintuzumab; BI 836858; AMG 673); CD352 (e.g., SGN-CD352A); CD37 (e.g., lilotomab; GEN3009); CD38 (e.g., felzartamab; AMG 424); CD3D; CD3E (e.g., foralumab; teplizumab); CD3G; CD40 (e.g., dacetuzumab; lucatumumab); CD44 (e.g., RG7356); CD45 (e.g., apamistamab); CD47 (e.g., letaplimab; magrolimab); CD48 (e.g., SGN-CD48A); CD5 (e.g., MAT 304; zolimomab aritox); CD51; CD70 (e.g., cusatuzumab); CD74 (e.g., milatuzumab); CD79A (*see,* e.g., International Publication No. WO

2020252110); CD83 (e.g., CBT004); CD97; CD262 (e.g., tigatuzumab); CLEC12A (e.g., tepoditamab); CTLA4 (e.g., ipilimumab); CXCR4 (e.g., ulocuplumab); DCIR; DCSIGN (*see,* e.g., International Publication No. WO 2018134389); Dectin1 (*see,* e.g., U.S. Patent No. 9,045,542); Dectin2 (e.g., ThermoFisher Catalog #MA5-16250); DR4 (e.g., mapatumumab); endosialin (e.g., ontuxizumab); FasL; FLT3 (e.g., 4G8SDIEM); GITR (e.g., ragifilimab); HAVCR2; HER2; HER3; HLA-DR; HLA-E; HLA-F; HLA-G (e.g., TTX-080); ICAM1; IDO1; IFNAR1 (e.g., faralimomab); IFNAR2; IGF-1R; IL1RAP (e.g., nidanilimab); IL-21R (e.g., PF-05230900); IL-5R (e.g., benralizumab); Integrin αvβ6; LAG-3 (e.g., encelimab); LAMP1; LAYN; LCK; LILRB2; LILRB4; MerTk (e.g., DS5MMER, Catalog #12-5751-82); Mesothelin; MICA (e.g., 1E2C8, Catalog #66384-1-IG); MICB (e.g., Catalog #MA5-29422); MICA; Mincle (e.g., OTI2A8, Catalog #TA505101); MRC1 (e.g., ThermoFisher Catalog #12-2061-82); MUC1; Muc16; NcaPi2B; Nectin-4; OX40 (e.g., ABM193); PD-1 (e.g., balstilimab; budigalimab; geptanolimab); PD-L1; Prolactin receptor; PTK7; PVRIG; ROR-1; Sialyl-Thomsen-nouveau-antigen (e.g., Eavarone et al. *PLoS One*, 2018; 13(7): e0201314); Siglecs 1-16 (*see,* e.g., Angata et al. Trends Pharmacol Sci. 2015; 36(10): 645–660);); SIRPa (e.g., Catalog #17-1729-42); SIRPg (e.g., PA5-104381); SIT1 (e.g., PA5-53825); SLAMF7 (e.g., elotuzumab); SLTRK6; STEAP1; TIGIT (e.g., etigilimab); TLR2/4/1 (e.g., tomaralimab); Trem2 (e.g., PY314); TROP2; Tyrol; ULBP1/2/3/4/5/6 (e.g., PA5-82302); uPAR (e.g., ATN-658); VSIR (e.g., ThermoFisher Catalog #PA5-52493); and ZIP6 (Anti-Integrin αvβ6).

(v) Heavy Chain and Light Chain Variable Regions in a compound 3.1

[0535] In some embodiments, the L moiety of compound 3.1 is a ligand (e.g., an antibody or fragment thereof) that targets ADAM9, ASCT2, Axl, B7-H3, B7H4, BCMA, BCMA, C4.4a, CanAg, CD123, CD138, CD142, CD166, CD19, CD20, CD228, CD25, CD30, CD33, CD352, CD38, CD48, CD56, CD59, CD70, CD74, CD79b, CDCP1, CEACAM5, Claudin-18.2, c-Met, gpNMB, CS1, DLL-3, DPEP-3, EGFR, EpCAM, EphA2, FGFR2, FRa, GCC, gpA33, GPC3, Integrin αvβ6 , h2A2, H2G12/STn, HER2, HER3, ZIP6, IGF-1R, IL1Rap, ITGav/CD51, Mesothelin, MICA, MUC-1, Muc16, NaPi2B, Nectin-4, PD-L1, Prolactin receptor, PTK7, ROR-1, SLAMF7, SLTRK6, STEAP1, TIGIT, or TROP2.

[0536] In some embodiments, the L moiety of compound 3.1 comprises a heavy chain variable region having at least 80% sequence identity to a first sequence and a light chain variable region having at least 80% sequence identity to a second sequence, and wherein: the first sequence is SEQ ID NO: 19 and the second sequence is SEQ ID NO: 20; the first

sequence is SEQ ID NO: 44 and the second sequence is SEQ ID NO: 45; the first sequence is SEQ ID NO: 55 and the second sequence is SEQ ID NO: 56; the first sequence is SEQ ID NO: 69 and the second sequence is SEQ ID NO: 70; the first sequence is SEQ ID NO: 83 and the second sequence is SEQ ID NO: 84; the first sequence is SEQ ID NO: 97 and the second sequence is SEQ ID NO: 98; the first sequence is SEQ ID NO: 105 and the second sequence is SEQ ID NO: 106; the first sequence is SEQ ID NO:113 and the second sequence is SEQ ID NO: 114; the first sequence is SEQ ID NO: 121 and the second sequence is SEQ ID NO: 122; the first sequence is SEQ ID NO: 129 and the second sequence is SEQ ID NO: 130; the first sequence is SEQ ID NO: 137 and the second sequence is SEQ ID NO: 138; the first sequence is SEQ ID NO: 153 and the second sequence is SEQ ID NO: 154; the first sequence is SEQ ID NO: 161 and the second sequence is SEQ ID NO: 162; the first sequence is SEQ ID NO: 169 and the second sequence is SEQ ID NO: 170; the first sequence is SEQ ID NO: 177 and the second sequence is SEQ ID NO: 178; the first sequence is SEQ ID NO: 185 and the second sequence is SEQ ID NO: 186; the first sequence is SEQ ID NO: 193 and the second sequence is SEQ ID NO: 194; the first sequence is SEQ ID NO: 201 and the second sequence is SEQ ID NO: 202; the first sequence is SEQ ID NO: 209 and the second sequence is SEQ ID NO: 210; the first sequence is SEQ ID NO: 217 and the second sequence is SEQ ID NO: 218; the first sequence is SEQ ID NO: 225 and the second sequence is SEQ ID NO: 226; the first sequence is SEQ ID NO: 233 and the second sequence is SEQ ID NO: 234; the first sequence is SEQ ID NO: 241 and the second sequence is SEQ ID NO: 242; the first sequence is SEQ ID NO: 249 and the second sequence is SEQ ID NO: 250; the first sequence is SEQ ID NO: 297 and the second sequence is SEQ ID NO: 298; the first sequence is SEQ ID NO: 307 and the second sequence is SEQ ID NO: 308; the first sequence is SEQ ID NO: 315 and the second sequence is SEQ ID NO: 316; the first sequence is SEQ ID NO: 323 and the second sequence is SEQ ID NO: 324; the first sequence is SEQ ID NO: 331 and the second sequence is SEQ ID NO: 332; the first sequence is SEQ ID NO: 339 and the second sequence is SEQ ID NO: 340; the first sequence is SEQ ID NO: 347 and the second sequence is SEQ ID NO: 348; the first sequence is SEQ ID NO: 355 and the second sequence is SEQ ID NO: 356; the first sequence is SEQ ID NO: 363 and the second sequence is SEQ ID NO: 364; the first sequence is SEQ ID NO: 371 and the second sequence is SEQ ID NO: 372; the first sequence is SEQ ID NO: 379 and the second sequence is SEQ ID NO: 380; the first sequence is SEQ ID NO: 387 and the second sequence is SEQ ID NO: 388; the first sequence is SEQ ID NO: 395 and the second sequence is SEQ ID NO: 396; the first sequence is SEQ ID NO: 403 and the second sequence is SEQ ID NO: 404; the first sequence is SEQ ID NO:

411 and the second sequence is SEQ ID NO: 412; the first sequence is SEQ ID NO: 419 and the second sequence is SEQ ID NO: 420; the first sequence is SEQ ID NO: 427 and the second sequence is SEQ ID NO: 428; the first sequence is SEQ ID NO: 435 and the second sequence is SEQ ID NO: 436; the first sequence is SEQ ID NO: 443 and the second sequence is SEQ ID NO: 444; the first sequence is SEQ ID NO: 451 and the second sequence is SEQ ID NO: 452; the first sequence is SEQ ID NO: 459 and the second sequence is SEQ ID NO: 460; the first sequence is SEQ ID NO: 467 and the second sequence is SEQ ID NO: 468; the first sequence is SEQ ID NO: 475 and the second sequence is SEQ ID NO: 476; the first sequence is SEQ ID NO: 483 and the second sequence is SEQ ID NO: 484; the first sequence is SEQ ID NO: 491 and the second sequence is SEQ ID NO: 492; the first sequence is SEQ ID NO: 501 and the second sequence is SEQ ID NO: 502; the first sequence is SEQ ID NO: 509 and the second sequence is SEQ ID NO: 510; the first sequence is SEQ ID NO: 517 and the second sequence is SEQ ID NO: 518; the first sequence is SEQ ID NO: 525 and the second sequence is SEQ ID NO: 526; the first sequence is SEQ ID NO: 533 and the second sequence is SEQ ID NO: 534; the first sequence is SEQ ID NO: 541 and the second sequence is SEQ ID NO: 542; the first sequence is SEQ ID NO: 549 and the second sequence is SEQ ID NO: 550; the first sequence is SEQ ID NO: 557 and the second sequence is SEQ ID NO: 558; the first sequence is SEQ ID NO: 565 and the second sequence is SEQ ID NO: 566; the first sequence is SEQ ID NO: 574 and the second sequence is SEQ ID NO: 574; the first sequence is SEQ ID NO: 581 and the second sequence is SEQ ID NO: 582; the first sequence is SEQ ID NO: 589 and the second sequence is SEQ ID NO: 590; the first sequence is SEQ ID NO: 597 and the second sequence is SEQ ID NO: 598; the first sequence is SEQ ID NO: 605 and the second sequence is SEQ ID NO: 606; the first sequence is SEQ ID NO: 613 and the second sequence is SEQ ID NO: 614; the first sequence is SEQ ID NO: 621 and the second sequence is SEQ ID NO: 622; the first sequence is SEQ ID NO: 629 and the second sequence is SEQ ID NO: 630; the first sequence is SEQ ID NO: 637 and the second sequence is SEQ ID NO: 638; the first sequence is SEQ ID NO: 645 and the second sequence is SEQ ID NO: 646; the first sequence is SEQ ID NO: 653 and the second sequence is SEQ ID NO: 654; the first sequence is SEQ ID NO: 661 and the second sequence is SEQ ID NO: 662; the first sequence is SEQ ID NO: 669 and the second sequence is SEQ ID NO: 670; the first sequence is SEQ ID NO: 677 and the second sequence is SEQ ID NO: 678; the first sequence is SEQ ID NO: 685 and the second sequence is SEQ ID NO: 686; the first sequence is SEQ ID NO: 693 and the second sequence is SEQ ID NO: 694; the first sequence is SEQ ID NO: 701 and the second sequence is SEQ ID NO: 702; the first sequence is SEQ ID NO: 703 and

the second sequence is SEQ ID NO: 704; the first sequence is SEQ ID NO: 711 and the second sequence is SEQ ID NO: 712; the first sequence is SEQ ID NO: 713 and the second sequence is SEQ ID NO: 714; the first sequence is SEQ ID NO: 715 and the second sequence is SEQ ID NO: 716; the first sequence is SEQ ID NO: 731 and the second sequence is SEQ ID NO: 732; the first sequence is SEQ ID NO: 739 and the second sequence is SEQ ID NO: 740; the first sequence is SEQ ID NO: 747 and the second sequence is SEQ ID NO: 748; the first sequence is SEQ ID NO: 755 and the second sequence is SEQ ID NO: 756; the first sequence is SEQ ID NO: 765 and the second sequence is SEQ ID NO: 766; the first sequence is SEQ ID NO: 773 and the second sequence is SEQ ID NO: 774; the first sequence is SEQ ID NO: 781 and the second sequence is SEQ ID NO: 782; the first sequence is SEQ ID NO: 789 and the second sequence is SEQ ID NO: 790; the first sequence is SEQ ID NO: 797 and the second sequence is SEQ ID NO: 798; the first sequence is SEQ ID NO: 805 and the second sequence is SEQ ID NO: 806; the first sequence is SEQ ID NO: 813 and the second sequence is SEQ ID NO: 814; the first sequence is SEQ ID NO: 821 and the second sequence is SEQ ID NO: 822; the first sequence is SEQ ID NO: 829 and the second sequence is SEQ ID NO: 830; the first sequence is SEQ ID NO: 837 and the second sequence is SEQ ID NO: 838; the first sequence is SEQ ID NO: 845 and the second sequence is SEQ ID NO: 846; the first sequence is SEQ ID NO: 853 and the second sequence is SEQ ID NO: 854; the first sequence is SEQ ID NO: 861 and the second sequence is SEQ ID NO: 862; the first sequence is SEQ ID NO: 869 and the second sequence is SEQ ID NO: 870; the first sequence is SEQ ID NO: 877 and the second sequence is SEQ ID NO: 878; the first sequence is SEQ ID NO: 885 and the second sequence is SEQ ID NO: 886; the first sequence is SEQ ID NO: 893 and the second sequence is SEQ ID NO: 894; the first sequence is SEQ ID NO: 900 and the second sequence is SEQ ID NO: 901; the first sequence is SEQ ID NO: 909 and the second sequence is SEQ ID NO: 910; the first sequence is SEQ ID NO: 917 and the second sequence is SEQ ID NO: 918; the first sequence is SEQ ID NO: 925 and the second sequence is SEQ ID NO: 926; the first sequence is SEQ ID NO: 933 and the second sequence is SEQ ID NO: 934; the first sequence is SEQ ID NO: 941 and the second sequence is SEQ ID NO: 942; the first sequence is SEQ ID NO: 943 and the second sequence is SEQ ID NO: 944; the first sequence is SEQ ID NO: 951 and the second sequence is SEQ ID NO: 952; the first sequence is SEQ ID NO: 959 and the second sequence is SEQ ID NO: 960; the first sequence is SEQ ID NO: 967 and the second sequence is SEQ ID NO: 968; the first sequence is SEQ ID NO: 975 and the second sequence is SEQ ID NO: 976; the first sequence is SEQ ID NO: 983 and the second sequence is SEQ ID NO: 984; the first sequence is SEQ ID NO: 991 and the

second sequence is SEQ ID NO: 992; the first sequence is SEQ ID NO: 993 and the second sequence is SEQ ID NO: 994; the first sequence is SEQ ID NO: 995 and the second sequence is SEQ ID NO: 996; the first sequence is SEQ ID NO: 1003 and the second sequence is SEQ ID NO: 1004; the first sequence is SEQ ID NO: 1011 and the second sequence is SEQ ID NO: 1012; the first sequence is SEQ ID NO: 1019 and the second sequence is SEQ ID NO: 1020; the first sequence is SEQ ID NO: 1027 and the second sequence is SEQ ID NO: 1028; the first sequence is SEQ ID NO: 1035 and 1036; or the first sequence is SEQ ID NO: 1043 and the second sequence is SEQ ID NO: 1044.

[0537] In some embodiments, the L moiety of compound 3.1 comprises an antibody that targets an immune checkpoint selected from the group consisting of PDL1, B7H4, B7H3, and TIGIT. For example, in some cases, the antibody comprises a heavy chain variable region having at least 80% sequence identity to a first sequence and a light chain variable region having at least 80% sequence identity to a second sequence, wherein: the first sequence is SEQ ID NO: 19 and the second sequence is SEQ ID NO: 20; the first sequence is SEQ ID NO: 83 and the second sequence is SEQ ID NO: 84; the first sequence is SEQ ID NO: 97 and the second sequence is SEQ ID NO: 98; the first sequence is SEQ ID NO: 105 and the second sequence is SEQ ID NO: 106; the first sequence is SEQ ID NO:113 and the second sequence is SEQ ID NO: 114; the first sequence is SEQ ID NO: 121 and the second sequence is SEQ ID NO: 122; the first sequence is SEQ ID NO: 129 and the second sequence is SEQ ID NO: 130; the first sequence is SEQ ID NO: 137 and the second sequence is SEQ ID NO: 138; the first sequence is SEQ ID NO: 153 and the second sequence is SEQ ID NO: 154; the first sequence is SEQ ID NO: 161 and the second sequence is SEQ ID NO: 162; the first sequence is SEQ ID NO: 169 and the second sequence is SEQ ID NO: 170; the first sequence is SEQ ID NO: 177 and the second sequence is SEQ ID NO: 178; the first sequence is SEQ ID NO: 185 and the second sequence is SEQ ID NO: 186; the first sequence is SEQ ID NO: 193 and the second sequence is SEQ ID NO: 194; the first sequence is SEQ ID NO: 201 and the second sequence is SEQ ID NO: 202; the first sequence is SEQ ID NO: 209 and the second sequence is SEQ ID NO: 210; the first sequence is SEQ ID NO: 217 and the second sequence is SEQ ID NO: 218; the first sequence is SEQ ID NO: 225 and the second sequence is SEQ ID NO: 226; the first sequence is SEQ ID NO: 233 and the second sequence is SEQ ID NO: 234; the first sequence is SEQ ID NO: 241 and the second sequence is SEQ ID NO: 242; the first sequence is SEQ ID NO: 249 and the second sequence is SEQ ID NO: 250; the first sequence is SEQ ID NO: 629 and the second sequence is SEQ ID NO: 630; the first sequence

is SEQ ID NO: 637 and the second sequence is SEQ ID NO: 638; the first sequence is SEQ ID NO: 645 and the second sequence is SEQ ID NO: 646; the first sequence is SEQ ID NO: 653 and the second sequence is SEQ ID NO: 654; the first sequence is SEQ ID NO: 661 and the second sequence is SEQ ID NO: 662; the first sequence is SEQ ID NO: 669 and the second sequence is SEQ ID NO: 670; the first sequence is SEQ ID NO: 677 and the second sequence is SEQ ID NO: 678; the first sequence is SEQ ID NO: 685 and the second sequence is SEQ ID NO: 686; the first sequence is SEQ ID NO: 693 and the second sequence is SEQ ID NO: 694; the first sequence is SEQ ID NO: 701 and the second sequence is SEQ ID NO: 702; the first sequence is SEQ ID NO: 703 and the second sequence is SEQ ID NO: 704; the first sequence is SEQ ID NO: 711 and the second sequence is SEQ ID NO: 712; the first sequence is SEQ ID NO: 713 and the second sequence is SEQ ID NO: 714; the first sequence is SEQ ID NO: 715 and the second sequence is SEQ ID NO: 716; or the first sequence is SEQ ID NO: 1027 and the second sequence is SEQ ID NO: 1028.

[0538] In some embodiments, the L moiety of compound 3.1 comprises an antibody comprising a heavy chain variable region having at least 80% sequence identity to a first sequence and a light chain variable region having at least 80% sequence identity to a second sequence, wherein: the first sequence is SEQ ID NO: 19 and the second sequence is SEQ ID NO: 20; the first sequence is SEQ ID NO: 83 and the second sequence is SEQ ID NO: 84; the first sequence is SEQ ID NO: 97 and the second sequence is SEQ ID NO: 98; the first sequence is SEQ ID NO: 105 and the second sequence is SEQ ID NO: 106; the first sequence is SEQ ID NO: 113 and the second sequence is SEQ ID NO: 114; the first sequence is SEQ ID NO: 121 and the second sequence is SEQ ID NO: 122; the first sequence is SEQ ID NO: 129 and the second sequence is SEQ ID NO: 130; the first sequence is SEQ ID NO: 137 and the second sequence is SEQ ID NO: 138; the first sequence is SEQ ID NO: 153 and the second sequence is SEQ ID NO: 154; the first sequence is SEQ ID NO: 161 and the second sequence is SEQ ID NO: 162; the first sequence is SEQ ID NO: 169 and the second sequence is SEQ ID NO: 170; the first sequence is SEQ ID NO: 177 and the second sequence is SEQ ID NO: 178; the first sequence is SEQ ID NO: 185 and the second sequence is SEQ ID NO: 186; the first sequence is SEQ ID NO: 193 and the second sequence is SEQ ID NO: 194; the first sequence is SEQ ID NO: 201 and the second sequence is SEQ ID NO: 202; the first sequence is SEQ ID NO: 209 and the second sequence is SEQ ID NO: 210; the first sequence is SEQ ID NO: 217 and the second sequence is SEQ ID NO: 218; the first sequence is SEQ ID NO: 225 and the second sequence is SEQ ID NO: 226; the first sequence is SEQ ID NO:

233 and the second sequence is SEQ ID NO: 234; the first sequence is SEQ ID NO: 241 and the second sequence is SEQ ID NO: 242; the first sequence is SEQ ID NO: 249 and the second sequence is SEQ ID NO: 250; or the first sequence is SEQ ID NO: 1027 and the second sequence is SEQ ID NO: 1028. In some cases, the first sequence is SEQ ID NO: 19 and the second sequence is SEQ ID NO: 20.

[0539] In some embodiments, the heavy chain variable region of the L moiety of compound 3.1 has at least 85% sequence identity to the first sequence and the light chain variable region has at least 85% sequence identity to the second sequence. In some cases, the heavy chain variable region has at least 90% sequence identity to the first sequence and the light chain variable region has at least 90% sequence identity to the second sequence. In some cases, the heavy chain variable region has at least 95% sequence identity to the first sequence and the light chain variable region has at least 95% sequence identity to the second sequence. In some cases, the heavy chain variable region has at least 98% sequence identity to the first sequence and the light chain variable region has at least 98% sequence identity to the second sequence. In some cases, the heavy chain variable region has at least 99% sequence identity to the first sequence and the light chain variable region has at least 99% sequence identity to the second sequence. In some cases, the heavy chain variable region comprises the first sequence and the light chain variable region comprises the second sequence.

(vi) Heavy and Light Chains

[0540] In some embodiments, the L moiety of compound 3.1 comprises an antibody comprising a heavy chain having at least 80% sequence identity to a first sequence and a light chain having at least 80% sequence identity to a second sequence, wherein: the first sequence is SEQ ID NO: 1 and the second sequence is SEQ ID NO: 5; the first sequence is SEQ ID NO: 2 and the second sequence is SEQ ID NO: 5; the first sequence is SEQ ID NO: 3 and the second sequence is SEQ ID NO: 5; the first sequence is SEQ ID NO: 4 and the second sequence is SEQ ID NO: 5; the first sequence is SEQ ID NO: 6 and the second sequence is SEQ ID NO: 10; the first sequence is SEQ ID NO: 7 and the second sequence is SEQ ID NO: 10; the first sequence is SEQ ID NO: 8 and the second sequence is SEQ ID NO: 10; the first sequence is SEQ ID NO: 9 and the second sequence is SEQ ID NO: 10; the first sequence is SEQ ID NO: 46 and the second sequence is SEQ ID NO: 48; the first sequence is SEQ ID NO: 47 and the second sequence is SEQ ID NO: 48; the first sequence is SEQ ID NO: 57 and the second sequence is SEQ ID NO: 59; the first sequence is SEQ ID NO: 58 and the second sequence is SEQ ID NO: 59; the first sequence is SEQ ID NO: 60 and the second sequence is

SEQ ID NO: 62; the first sequence is SEQ ID NO: 61 and the second sequence is SEQ ID NO: 62; the first sequence is SEQ ID NO: 71 and the second sequence is SEQ ID NO: 73; the first sequence is SEQ ID NO: 72 and the second sequence is SEQ ID NO: 73; the first sequence is SEQ ID NO: 74 and the second sequence is SEQ ID NO: 76; the first sequence is SEQ ID NO: 75 and the second sequence is SEQ ID NO: 76; the first sequence is SEQ ID NO: 85 and the second sequence is SEQ ID NO: 87; the first sequence is SEQ ID NO: 86 and the second sequence is SEQ ID NO: 87; the first sequence is SEQ ID NO: 88 and the second sequence is SEQ ID NO: 90; the first sequence is SEQ ID NO: 89 and the second sequence is SEQ ID NO: 90; the first sequence is SEQ ID NO: 251 and the second sequence is SEQ ID NO: 252; the first sequence is SEQ ID NO: 253 and the second sequence is SEQ ID NO: 254; the first sequence is SEQ ID NO: 255 and the second sequence is SEQ ID NO: 256; the first sequence is SEQ ID NO: 257 and the second sequence is SEQ ID NO: 258; the first sequence is SEQ ID NO: 259 and the second sequence is SEQ ID NO: 260; the first sequence is SEQ ID NO: 261 and the second sequence is SEQ ID NO: 262; the first sequence is SEQ ID NO: 263 and the second sequence is SEQ ID NO: 264; the first sequence is SEQ ID NO: 265 and the second sequence is SEQ ID NO: 266; the first sequence is SEQ ID NO: 267 and the second sequence is SEQ ID NO: 268; the first sequence is SEQ ID NO: 269 and the second sequence is SEQ ID NO: 270; the first sequence is SEQ ID NO: 271 and the second sequence is SEQ ID NO: 272; the first sequence is SEQ ID NO: 273 and the second sequence is SEQ ID NO: 274; the first sequence is SEQ ID NO: 275 and the second sequence is SEQ ID NO: 276; the first sequence is SEQ ID NO: 277 and the second sequence is SEQ ID NO: 278; the first sequence is SEQ ID NO: 279 and the second sequence is SEQ ID NO: 280; the first sequence is SEQ ID NO: 281 and the second sequence is SEQ ID NO: 282; the first sequence is SEQ ID NO: 283 and the second sequence is SEQ ID NO: 284; the first sequence is SEQ ID NO: 285 and the second sequence is SEQ ID NO: 286; the first sequence is SEQ ID NO: 287 and the second sequence is SEQ ID NO: 288; the first sequence is SEQ ID NO: 289 and the second sequence is SEQ ID NO: 290; the first sequence is SEQ ID NO: 299 and the second sequence is SEQ ID NO: 300; the first sequence is SEQ ID NO: 493 and the second sequence is SEQ ID NO: 494; the first sequence is SEQ ID NO: 717 and the second sequence is SEQ ID NO: 718; the first sequence is SEQ ID NO: 719 and the second sequence is SEQ ID NO: 720; the first sequence is SEQ ID NO: 721 and the second sequence is SEQ ID NO: 722; the first sequence is SEQ ID NO: 723 and the second sequence is SEQ ID NO: 724; or the first sequence is SEQ ID NO: 757 and the second sequence is SEQ ID NO: 758.

[0541] In some embodiments, the L moiety of compound 3.1 comprises an antibody comprising a heavy chain having at least 80% sequence identity to a first sequence and a light chain having at least 80% sequence identity to a second sequence, wherein: the first sequence is SEQ ID NO: 1 and the second sequence is SEQ ID NO: 5; the first sequence is SEQ ID NO: 2 and the second sequence is SEQ ID NO: 5; the first sequence is SEQ ID NO: 3 and the second sequence is SEQ ID NO: 5; the first sequence is SEQ ID NO: 4 and the second sequence is SEQ ID NO: 5; the first sequence is SEQ ID NO: 6 and the second sequence is SEQ ID NO: 10; the first sequence is SEQ ID NO: 7 and the second sequence is SEQ ID NO: 10; the first sequence is SEQ ID NO: 8 and the second sequence is SEQ ID NO: 10; the first sequence is SEQ ID NO: 9 and the second sequence is SEQ ID NO: 10; the first sequence is SEQ ID NO: 85 and the second sequence is SEQ ID NO: 87; the first sequence is SEQ ID NO: 86 and the second sequence is SEQ ID NO: 87; the first sequence is SEQ ID NO: 88 and the second sequence is SEQ ID NO: 90; the first sequence is SEQ ID NO: 89 and the second sequence is SEQ ID NO: 90; the first sequence is SEQ ID NO: 251 and the second sequence is SEQ ID NO: 252; the first sequence is SEQ ID NO: 253 and the second sequence is SEQ ID NO: 254; the first sequence is SEQ ID NO: 255 and the second sequence is SEQ ID NO: 256; the first sequence is SEQ ID NO: 257 and the second sequence is SEQ ID NO: 258; the first sequence is SEQ ID NO: 259 and the second sequence is SEQ ID NO: 260; the first sequence is SEQ ID NO: 261 and the second sequence is SEQ ID NO: 262; the first sequence is SEQ ID NO: 263 and the second sequence is SEQ ID NO: 264; the first sequence is SEQ ID NO: 265 and the second sequence is SEQ ID NO: 266; the first sequence is SEQ ID NO: 267 and the second sequence is SEQ ID NO: 268; the first sequence is SEQ ID NO: 269 and the second sequence is SEQ ID NO: 270; the first sequence is SEQ ID NO: 271 and the second sequence is SEQ ID NO: 272; the first sequence is SEQ ID NO: 273 and the second sequence is SEQ ID NO: 274; the first sequence is SEQ ID NO: 275 and the second sequence is SEQ ID NO: 276; the first sequence is SEQ ID NO: 277 and the second sequence is SEQ ID NO: 278; the first sequence is SEQ ID NO: 279 and the second sequence is SEQ ID NO: 280; the first sequence is SEQ ID NO: 281 and the second sequence is SEQ ID NO: 282; the first sequence is SEQ ID NO: 283 and the second sequence is SEQ ID NO: 284; the first sequence is SEQ ID NO: 285 and the second sequence is SEQ ID NO: 286; the first sequence is SEQ ID NO: 287 and the second sequence is SEQ ID NO: 288; the first sequence is SEQ ID NO: 289 and the second sequence is SEQ ID NO: 290; the first sequence is SEQ ID NO: 717 and the second sequence is SEQ ID NO: 718; the first sequence is SEQ ID NO: 719 and the second sequence is SEQ ID NO: 720; the first sequence is SEQ ID NO: 721 and the

second sequence is SEQ ID NO: 722; or the first sequence is SEQ ID NO: 723 and the second sequence is SEQ ID NO: 724.

[0542] In some embodiments, the L moiety of compound 3.1 comprises an antibody comprising a heavy chain having at least 80% sequence identity to a first sequence and a light chain having at least 80% sequence identity to a second sequence, wherein: the first sequence is SEQ ID NO: 1 and the second sequence is SEQ ID NO: 5; the first sequence is SEQ ID NO: 2 and the second sequence is SEQ ID NO: 5; the first sequence is SEQ ID NO: 3 and the second sequence is SEQ ID NO: 5; the first sequence is SEQ ID NO: 4 and the second sequence is SEQ ID NO: 5; the first sequence is SEQ ID NO: 6 and the second sequence is SEQ ID NO: 10; the first sequence is SEQ ID NO: 7 and the second sequence is SEQ ID NO: 10; the first sequence is SEQ ID NO: 8 and the second sequence is SEQ ID NO: 10; the first sequence is SEQ ID NO: 9 and the second sequence is SEQ ID NO: 10; the first sequence is SEQ ID NO: 85 and the second sequence is SEQ ID NO: 87; the first sequence is SEQ ID NO: 86 and the second sequence is SEQ ID NO: 87; the first sequence is SEQ ID NO: 88 and the second sequence is SEQ ID NO: 90; the first sequence is SEQ ID NO: 89 and the second sequence is SEQ ID NO: 90; the first sequence is SEQ ID NO: 251 and the second sequence is SEQ ID NO: 252; the first sequence is SEQ ID NO: 253 and the second sequence is SEQ ID NO: 254; the first sequence is SEQ ID NO: 255 and the second sequence is SEQ ID NO: 256; the first sequence is SEQ ID NO: 257 and the second sequence is SEQ ID NO: 258; the first sequence is SEQ ID NO: 259 and the second sequence is SEQ ID NO: 260; the first sequence is SEQ ID NO: 261 and the second sequence is SEQ ID NO: 262; the first sequence is SEQ ID NO: 263 and the second sequence is SEQ ID NO: 264; the first sequence is SEQ ID NO: 265 and the second sequence is SEQ ID NO: 266; the first sequence is SEQ ID NO: 267 and the second sequence is SEQ ID NO: 268; the first sequence is SEQ ID NO: 269 and the second sequence is SEQ ID NO: 270; the first sequence is SEQ ID NO: 271 and the second sequence is SEQ ID NO: 272; the first sequence is SEQ ID NO: 273 and the second sequence is SEQ ID NO: 274; the first sequence is SEQ ID NO: 275 and the second sequence is SEQ ID NO: 276; the first sequence is SEQ ID NO: 277 and the second sequence is SEQ ID NO: 278; the first sequence is SEQ ID NO: 279 and the second sequence is SEQ ID NO: 280; the first sequence is SEQ ID NO: 281 and the second sequence is SEQ ID NO: 282; the first sequence is SEQ ID NO: 283 and the second sequence is SEQ ID NO: 284; the first sequence is SEQ ID NO: 285 and the second sequence is SEQ ID NO: 286; the first sequence

is SEQ ID NO: 287 and the second sequence is SEQ ID NO: 288; or the first sequence is SEQ ID NO: 289 and the second sequence is SEQ ID NO: 290.

[0543] In some embodiments, the L moiety of compound 3.1 comprises an antibody comprising a heavy chain having at least 80% sequence identity to a first sequence and a light chain having at least 80% sequence identity to a second sequence, wherein: the first sequence is SEQ ID NO: 1 and the second sequence is SEQ ID NO: 5; the first sequence is SEQ ID NO: 2 and the second sequence is SEQ ID NO: 5; the first sequence is SEQ ID NO: 3 and the second sequence is SEQ ID NO: 5; the first sequence is SEQ ID NO: 4 and the second sequence is SEQ ID NO: 5; the first sequence is SEQ ID NO: 6 and the second sequence is SEQ ID NO: 10; the first sequence is SEQ ID NO: 7 and the second sequence is SEQ ID NO: 10; the first sequence is SEQ ID NO: 8 and the second sequence is SEQ ID NO: 10; or the first sequence is SEQ ID NO: 9 and the second sequence is SEQ ID NO: 10.

[0544] In some embodiments, the L moiety of is an antibody comprising a heavy chain having at least 80% sequence identity to a first sequence and a light chain having at least 80% sequence identity to a second sequence, wherein: the first sequence is SEQ ID NO: 3 or SEQ ID NO: 4 and the second sequence is SEQ ID NO: 5.

[0545] In some embodiments, the L moiety of compound 3.1 comprises a heavy chain with at least 85% sequence identity to the first sequence and the light chain has at least 85% sequence identity to the second sequence. In some cases, the heavy chain has at least 90% sequence identity to the first sequence and the light chain has at least 90% sequence identity to the second sequence. In some cases, the heavy chain has at least 95% sequence identity to the first sequence and the light chain has at least 95% sequence identity to the second sequence. In some cases, the heavy chain has at least 98% sequence identity to the first sequence and the light chain has at least 98% sequence identity to the second sequence. In some cases, the heavy chain has at least 99% sequence identity to the first sequence and the light chain has at least 99% sequence identity to the second sequence. In some cases, the heavy chain comprises the first sequence and the light chain comprises the second sequence.

(vii) Complementarity-Determining Regions

[0546] In some embodiments, the L moiety of compound 3.1 comprises an antibody comprising CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 comprising at least 80% sequence identity to: SEQ ID NO: 13, 14, 15, 16, 17, and 18, respectively (i.e., CDR-H1 has at least 80% sequence identity to SEQ ID NO: 13, CDR-H2 has at least 80%

sequence identity to SEQ ID NO: 14, CDR-H3 has at least 80% sequence identity to SEQ ID NO: 15, CDR-L1 has at least 80% sequence identity to SEQ ID NO: 16, CDR-L2 has at least 80% sequence identity to SEQ ID NO: 17, and CDR-L3 has at least 80% sequence identity to SEQ ID NO: 18); SEQ ID NO: 21, 22, 23, 24, 25, and 26, respectively; SEQ ID NO: 38, 39, 40, 41, 42, and 43, respectively; SEQ ID NO: 49, 50, 51, 52, 53, and 54, respectively; SEQ ID NO: 63, 64, 65, 66, 67, and 68, respectively; SEQ ID NO: 77, 78, 79, 80, 81, and 82, , respectively; SEQ ID NO: 91, 92, 93, 94, 95, and 96, respectively; SEQ ID NO: 99, 100, 101, 102, 103, and 104, respectively; SEQ ID NO: 107, 108, 109, 110, 111, and 112, respectively; SEQ ID NO: 115, 116, 117, 118, 119, and 120, respectively; SEQ ID NO: 123, 124, 125, 126, 127, and 128, respectively; SEQ ID NO: 131, 132, 133, 134, 135, and 136, respectively; SEQ ID NO: 139, 140, 141, 142, 143, and 144, respectively; SEQ ID NO: 147, 148, 149, 150, 151, and 152, respectively; SEQ ID NO: 155, 156, 157, 158, 159, and 160, respectively; SEQ ID NO: 163, 164, 165, 166, 167, and 168, respectively; SEQ ID NO: 171, 172, 173, 174, 175, and 176, respectively; SEQ ID NO: 179, 180, 181, 182, 183, and 184, respectively; SEQ ID NO: 187, 188, 189, 190, 191, and 192, respectively; SEQ ID NO: 195, 196, 197, 198, 199, and 200, respectively; SEQ ID NO: 203, 204, 205, 206, 207 and 208, respectively; SEQ ID NO: 211, 212, 213, 214, 215, and 216, respectively; SEQ ID NO: 219, 220, 221, 222, 223, and 224, respectively; SEQ ID NO: 227, 228, 229, 230, 231, and 232, respectively; SEQ ID NO: 235, 236, 237, 238, 239, and 240, respectively; SEQ ID NO: 243, 244, 245, 246, 247, and 248, respectively; SEQ ID NO: 291, 292, 293, 294, 295, and 296, respectively; SEQ ID NO: 301, 302, 303, 304, 305, and 306, respectively; SEQ ID NO: 309, 310, 311, 312, 313, and 314, respectively; SEQ ID NO: 317, 318, 319, 320, 321, and 322, respectively; SEQ ID NO: 325, 326, 327, 328, 329, and 330, respectively; SEQ ID NO: 333, 334, 335, 336, 337, and 338, respectively; SEQ ID NO: 341, 342, 343, 344, 345, and 346, respectively; SEQ ID NO: 349, 350, 351, 352, 353, and 354, respectively; SEQ ID NO: 357, 358, 359, 360, 361, and 362, respectively; SEQ ID NO: 365, 366, 367, 368, 369, and 370, respectively; SEQ ID NO: 373, 374, 375, 376, 377, and 378, respectively; SEQ ID NO: 381, 382, 383, 384, 385, and 386, respectively; SEQ ID NO: 389, 390, 391, 392, 393, and 394, respectively; SEQ ID NO: 397, 398, 399, 400, 401, and 402, respectively; SEQ ID NO: 405, 406, 407, 408, 409, and 410, respectively; SEQ ID NO: 413, 414, 415, 416, 417, and 418, respectively; SEQ ID NO: 421, 422, 423, 424, 425, and 426, respectively; SEQ ID NO: 429, 430, 431, 432, 433, and 434, respectively; SEQ ID NO: 437, 438, 439, 440, 441, and 442, respectively; SEQ ID NO: 445, 446, 447, 448, 449, and 450, respectively; SEQ ID NO: 453, 454, 455, 456, 457, and 458, respectively; SEQ ID NO: 461, 462, 463, 464, 465, and 466, respectively;

SEQ ID NO: 469, 470, 471, 472, 473, and 474, respectively; SEQ ID NO: 477, 478, 479, 480, 481, and 482, respectively; SEQ ID NO: 485, 486, 487, 488, 489, and 490, respectively; SEQ ID NO: 495, 496, 497, 498, 499, and 500, respectively; SEQ ID NO: 503, 504, 505, 506, 507, and 508, respectively; SEQ ID NO: 511, 512, 513, 514, 515, and 516, respectively; SEQ ID NO: 519, 520, 521, 522, 523, and 524, respectively; SEQ ID NO: 527, 528, 529, 530, 531, and 532, respectively; SEQ ID NO: 535, 536, 537, 538, 539, and 540, respectively; SEQ ID NO: 543, 544, 545, 546, 547, and 548, respectively; SEQ ID NO: 551, 552, 553, 554, 555, and 556, respectively; SEQ ID NO: 559, 560, 561, 562, 563, and 564, respectively; SEQ ID NO: 567, 568, 569, 570, 571, and 572, respectively; SEQ ID NO: 575, 576, 577, 578, 579, and 580, respectively; SEQ ID NO: 583, 584, 585, 586, 587, and 588, respectively; SEQ ID NO: 591, 592, 593, 594, 595, and 596, respectively; SEQ ID NO: 599, 600, 601, 602, 603, and 604, respectively; SEQ ID NO: 607, 608, 609, 610, 611, and 612, respectively; SEQ ID NO: 615, 616, 617, 618, 619, and 620, respectively; SEQ ID NO: 623, 624, 625, 626, 627, and 628, respectively; SEQ ID NO: 631, 632, 633, 634, 635, and 636, respectively; SEQ ID NO: 639, 640, 641, 642, 643, and 644, respectively; SEQ ID NO: 647, 648, 649, 650, 651, and 652, respectively; SEQ ID NO: 655, 656, 657, 658, 659, and 660, respectively; SEQ ID NO: 663, 664, 665, 666, 667, and 668, respectively; SEQ ID NO: 671, 672, 673, 674, 675, and 676, respectively; SEQ ID NO: 679, 680, 681, 682, 683, and 684, respectively; SEQ ID NO: 687, 688, 689, 690, 691, and 692, respectively; SEQ ID NO: 695, 696, 697, 698, 699, and 700, respectively; SEQ ID NO: 705, 706, 707, 708, 709, and 710, respectively; SEQ ID NO: 725, 726, 727, 728, 729, and 730, respectively; SEQ ID NO: 733, 734, 735, 736, 737, and 738, respectively; SEQ ID NO: 741, 742, 743, 744, 745, and 746, respectively; SEQ ID NO: 749, 750, 751, 752, 753, and 754, respectively; SEQ ID NO: 759, 760, 761, 762, 763, and 764, respectively; SEQ ID NO: 767, 768, 769, 770, 771, and 772, respectively; SEQ ID NO: 775, 776, 777, 778, 779, and 780, respectively; SEQ ID NO: 783, 784, 785, 786, 787, and 788, respectively; SEQ ID NO: 791, 792, 793, 794, 795, and 796, respectively; SEQ ID NO: 799, 800, 801, 802, 803, and 804, respectively; SEQ ID NO: 807, 808, 809, 810, 811, and 812, respectively; SEQ ID NO: 815, 816, 817, 818, 819, and 820, respectively; SEQ ID NO: 823, 824, 825, 826, 827, and 828, respectively; SEQ ID NO: 831, 832, 833, 834, 835, and 836, respectively; SEQ ID NO: 839, 840, 841, 842, 843, and 844, respectively; SEQ ID NO: 847, 848, 849, 850, 851, and 852, respectively; SEQ ID NO: 855, 856, 857, 858, 859, and 860, respectively; SEQ ID NO: 863, 864, 865, 866, 867, and 868, respectively; SEQ ID NO: 871, 872, 873, 874, 875, and 876, respectively; SEQ ID NO: 879, 880, 881, 882, 883, and 884, respectively; SEQ ID NO: 887, 888, 889, 890, 891, and 892, respectively;

SEQ ID NO: 895, 896, 897, 898, 899, and 900, respectively; SEQ ID NO: 903, 904, 905, 906, 907, and 908, respectively; SEQ ID NO: 911, 912, 913, 914, 915, and 916, respectively; SEQ ID NO: 919, 920, 921, 922, 923, and 924, respectively; SEQ ID NO: 927, 928, 929, 930, 931, and 932, respectively; SEQ ID NO: 935, 936, 937, 938, 939, and 940, respectively; SEQ ID NO: 945, 946, 947, 948, 949, and 950, respectively; SEQ ID NO: 953, 954, 955, 956, 957, and 958, respectively; SEQ ID NO: 961, 962, 963, 964, 965, and 966, respectively; SEQ ID NO: 969, 970, 971, 972, 973, and 974, respectively; SEQ ID NO: 977, 978, 979, 980, 981, and 982, respectively; SEQ ID NO: 985, 986, 987, 988, 989, and 990, respectively; SEQ ID NO: 997, 998, 999, 1000, 1001, and 1002, respectively; SEQ ID NO: 1005, 1006, 1007, 1008, 1009, and 1010, respectively; SEQ ID NO: 1013, 1014, 1015, 1016, 1017, and 1018, respectively; SEQ ID NO: 1021, 1022, 1023, 1024, 1025, and 1026, respectively; SEQ ID NO: 1029, 1030, 1031, 1032, 1033, and 1034, respectively; or SEQ ID NO: 1037, 1038, 1039, 1040, 1041, and 1042, respectively.

[0547] In some cases, the L moiety of compound 3.1 comprises an antibody that targets an immune checkpoint selected from the group consisting of PDL1, B7H4, B7H3, and TIGIT. For example, in some cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 comprising at least 80% sequence identity to: SEQ ID NO: 13, 14, 15, 16, 17, and 18, respectively; SEQ ID NO: 77, 78, 79, 80, 81, and 82, , respectively; SEQ ID NO: 91, 92, 93, 94, 95, and 96, respectively; SEQ ID NO: 99, 100, 101, 102, 103, and 104, respectively; SEQ ID NO: 107, 108, 109, 110, 111, and 112, respectively; SEQ ID NO: 115, 116, 117, 118, 119, and 120, respectively; SEQ ID NO: 123, 124, 125, 126, 127, and 128, respectively; SEQ ID NO: 131, 132, 133, 134, 135, and 136, respectively; SEQ ID NO: 139, 140, 141, 142, 143, and 144, respectively; SEQ ID NO: 147, 148, 149, 150, 151, and 152, respectively; SEQ ID NO: 155, 156, 157, 158, 159, and 160, respectively; SEQ ID NO: 163, 164, 165, 166, 167, and 168, respectively; SEQ ID NO: 171, 172, 173, 174, 175, and 176, respectively; SEQ ID NO: 179, 180, 181, 182, 183, and 184, respectively; SEQ ID NO: 187, 188, 189, 190, 191, and 192, respectively; SEQ ID NO: 195, 196, 197, 198, 199, and 200, respectively; SEQ ID NO: 203, 204, 205, 206, 207 and 208, respectively; SEQ ID NO: 211, 212, 213, 214, 215, and 216, respectively; SEQ ID NO: 219, 220, 221, 222, 223, and 224, respectively; SEQ ID NO: 227, 228, 229, 230, 231, and 232, respectively; SEQ ID NO: 235, 236, 237, 238, 239, and 240, respectively; SEQ ID NO: 243, 244, 245, 246, 247, and 248, respectively; SEQ ID NO: 623, 624, 625, 626, 627, and 628, respectively; SEQ ID NO: 631, 632, 633, 634, 635, and 636, respectively; SEQ ID NO: 639, 640, 641,

642, 643, and 644, respectively; SEQ ID NO: 647, 648, 649, 650, 651, and 652, respectively; SEQ ID NO: 655, 656, 657, 658, 659, and 660, respectively; SEQ ID NO: 663, 664, 665, 666, 667, and 668, respectively; SEQ ID NO: 671, 672, 673, 674, 675, and 676, respectively; SEQ ID NO: 679, 680, 681, 682, 683, and 684, respectively; SEQ ID NO: 687, 688, 689, 690, 691, and 692, respectively; SEQ ID NO: 695, 696, 697, 698, 699, and 700, respectively; SEQ ID NO: 705, 706, 707, 708, 709, and 710, respectively; or SEQ ID NO: 1021, 1022, 1023, 1024, 1025, and 1026, respectively.

[0548] In some embodiments, the CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 comprise at least 85% sequence identity to the respective 6 indicated sequences. In some cases, the CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 each comprise at least 90% sequence identity to the respective 6 indicated sequences. In some cases, the CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 each comprise at least 95% sequence identity to the respective 6 indicated sequences. In some cases, the CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 each comprise at most one mutation relative to the respective 6 indicated sequences.

(viii) Exemplary Antibodies

[0549] In some cases, the L moiety of compound 3.1 comprises an antibody that binds to PDL1. PDL1 is expressed in a broad range of cancers, as well as certain immune cells, and often serves as a primary mechanism for immune suppression in tumor microenvironments. The PDL1 agonism of PD-1 can act as an immune checkpoint, diminishing lymphocyte tumor infiltration, and T-cell receptor mediated proliferation and signaling. While PDL1 antagonism can reverse immune suppression, PDL1 targeting can also localize treatments to the sites of cancers, allowing drugs to selectively target cancer cells or stimulate immune responses in the presence of tumors.

[0550] In some embodiments, the compound 3.1 comprises an anti-PDL1 antibody comprising CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 comprising at least 80% sequence identity, at least 85% sequence identity, at least 90% sequence identity, at least 95%, at least 98%, or at least 99% sequence identity to the amino acid sequences of SEQ ID NOs: 13, 14, 15, 16, 17, and 18 respectively. In some cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 each comprising at most one mutation relative to the amino acid sequences of SEQ ID NOs: 13, 14, 15, 16, 17, and 18, respectively. In some embodiments, a Ligand-Drug Conjugate corresponding to compound 3.1 in Table 3 is provided wherein L comprises any of the anti-PDL1 antibodies described

above or L comprises an amino acid sequence with at least 80% sequence identity, at least 85% sequence identity, at least 90% sequence identity, at least 95%, at least 98%, or at least 99% sequence identity an amino acid sequences of SEQ ID NOs: 13, 14, 15, 16, 17, or 18.

[0551] In some embodiments, the L moiety of compound 3.1 comprises an antibody comprising a heavy chain comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of any one of SEQ ID NO: 1-4 and a light chain comprising an amino acid sequence that is at least 95% at least 96%, at least 97%, at least 98%, at least 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 5. In some embodiments, the antibody comprises a heavy chain comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 1 and a light chain comprising an amino acid sequence that is at least 95% at least 96%, at least 97%, at least 98%, at least 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 5. In some embodiments, the antibody comprises a heavy chain comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 2 and a light chain comprising an amino acid sequence that is at least 95% at least 96%, at least 97%, at least 98%, at least 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 5. In some embodiments, the antibody comprises a heavy chain comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 3 and a light chain comprising an amino acid sequence that is at least 95% at least 96%, at least 97%, at least 98%, at least 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 5. In some embodiments, the antibody comprises a heavy chain comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 4 and a light chain comprising an amino acid sequence that is at least 95% at least 96%, at least 97%, at least 98%, at least 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 5.

[0552] In some embodiments, the L moiety of compound 3.1 comprises an antibody comprising a heavy chain variable region comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of any one of SEQ ID NO: 6-9 and a light chain variable region comprising an amino acid sequence that is at least 95% at least 96%, at least 97%, at least 98%, at least

99%, or 100% identical to the amino acid sequence of SEQ ID NO: 10. In some embodiments, the antibody comprises a heavy chain variable region comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of any one of SEQ ID NO: 6 and a light chain variable region comprising an amino acid sequence that is at least 95% at least 96%, at least 97%, at least 98%, at least 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 10. In some embodiments, the antibody comprises a heavy chain variable region comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of any one of SEQ ID NO: 7 and a light chain variable region comprising an amino acid sequence that is at least 95% at least 96%, at least 97%, at least 98%, at least 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 10. In some embodiments, the antibody comprises a heavy chain variable region comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of any one of SEQ ID NO: 8 and a light chain variable region comprising an amino acid sequence that is at least 95% at least 96%, at least 97%, at least 98%, at least 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 10. In some embodiments, the antibody comprises a heavy chain variable region comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of any one of SEQ ID NO: 9 and a light chain variable region comprising an amino acid sequence that is at least 95% at least 96%, at least 97%, at least 98%, at least 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 10.

[0553] In some embodiments, the L moiety of compound 3.1 comprises an antibody comprising a heavy chain variable region comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 19 and a light chain variable region comprising an amino acid sequence that is at least 95% at least 96%, at least 97%, at least 98%, at least 99%, or 100% identical to the amino acid sequence of SEQ ID NO: 20.

[0554] In some embodiments, the L moiety of compound 3.1 comprises an antibody that binds to EphA2. In some embodiments, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 comprising the amino acid sequences that are at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or at least 99% identical to the amino acid sequences of SEQ ID NOs: 21, 22, 23, 24, 25, and 26, respectively.

[0555] In some embodiments, the anti-EphA2 antibody comprises a heavy chain variable region comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or at least 99% identical to the amino acid sequence of SEQ ID NO: 27 and a light chain variable region comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or at least 99% identical to the amino acid sequence of SEQ ID NO: 28. In some embodiments, the anti-EphA2 antibody comprises a heavy chain comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or at least 99% identical to the amino acid sequence of SEQ ID NO: 29 or SEQ ID NO: 30 and a light chain comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or at least 99% identical to the amino acid sequence of the amino acid sequence of SEQ ID NO: 31. In some embodiments, the anti-EphA2 antibody comprises a heavy chain comprising the amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or at least 99% identical to the amino acid sequence of SEQ ID NO: 32 or SEQ ID NO: 33 and a light chain comprising the amino acid sequence of SEQ ID NO: 34. In some embodiments, the anti-EphA2 antibody comprises a heavy chain that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or at least 99% identical to the amino acid sequence of SEQ ID NO: 35 or SEQ ID NO: 36 and a light chain comprising the amino acid sequence of SEQ ID NO: 37. In some embodiments, the antibody is h1C1 or 1C1.

[0556] In some embodiments, the anti-EphA2 antibody comprises a heavy chain variable region comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 27 and a light chain variable region comprising an amino acid sequence that is at least 80% at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 28.

[0557] In some embodiments, the L moiety of compond 3.1 comprises an antibody that binds to CD30. In some such cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences comprising at least 80% sequence identity, at least 85% sequence identity, at least 90% sequence identity, or at least 95% sequence identity to the amino acid sequences of SEQ ID NOs: 38, 39, 40, 41, 42, and 43, respectively. In some cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences each comprising at most one mutation relative to the amino acid sequences of SEQ ID NOs: 38, 39, 40, 41, 42, and 43, respectively. In some embodiments, the anti-CD30

antibody comprises a heavy chain comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of either SEQ ID NO: 46 or 47 and a light chain comprising an amino acid sequence that is at least 80% at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 48. In some embodiments, the anti-CD30 antibody comprises a heavy chain variable region comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 44 and a light chain variable region comprising an amino acid sequence that is at least 80% at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 45.

[0558] In some embodiments, the L moiety of compound 3.1 comprises an antibody that binds to CD228. In some such cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences comprising at least 80% sequence identity, at least 85% sequence identity, at least 90% sequence identity, or at least 95% sequence identity to the amino acid sequences of SEQ ID NOs: 49, 50, 51, 52, 53, and 54, respectively. In some cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences each comprising at most one mutation relative to the amino acid sequences of SEQ ID NOs: 49, 50, 51, 52, 53, and 54, respectively. In some embodiments, the anti-CD228 antibody comprises a heavy chain variable region comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 55 and a light chain variable region comprising an amino acid sequence that is at least 80% at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 56. In some embodiments, the anti-CD228 antibody comprises a heavy chain comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of either of SEQ ID NO: 57 or 58 and a light chain comprising an amino acid sequence that is at least 80% at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 59. In some embodiments, the anti-CD228 antibody comprises a heavy chain comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of either of SEQ ID NO: 60 or 61 and a light chain comprising an amino acid sequence that is at least 80% at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 62.

[0559] In some embodiments, the L moiety of compound 3.1 comprises an antibody that binds to avB6. In some such cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences comprising at least 80% sequence identity, at least 85% sequence identity, at least 90% sequence identity, or at least 95% sequence identity to the amino acid sequences of SEQ ID NOs: 63, 64, 65, 66, 67, and 68, respectively. In some cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences each comprising at most one mutation relative to the amino acid sequences of SEQ ID NOs: 63, 64, 65, 66, 67, and 68, respectively. In some embodiments, the anti-H2A2 antibody comprises a heavy chain variable region comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 69 and a light chain variable region comprising an amino acid sequence that is at least 80% at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 70. In some embodiments, the anti-H2A2 antibody comprises a heavy chain comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of either SEQ ID NO: 71 or 72 and a light chain comprising an amino acid sequence that is at least 80% at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 73. In some embodiments, the anti-H2A2 antibody comprises a heavy chain comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of either SEQ ID NO: 74 or 75 and a light chain comprising an amino acid sequence that is at least 80% at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 76. In some embodiments, the anti-avB6 antibody comprises a heavy chain variable region comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 69 and a light chain variable region comprising an amino acid sequence that is at least 80% at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 70. In some embodiments, the anti-avB6 antibody comprises a heavy chain comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of either SEQ ID NO: 71 or 72 and a light chain comprising an amino acid sequence that is at least 80% at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 73. In some embodiments, the anti-avB6 antibody comprises a heavy chain comprising an amino acid sequence that is at least

80%, at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of either SEQ ID NO: 74 or 75 and a light chain comprising an amino acid sequence that is at least 80% at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 76.

[0560] In some embodiments, the L moiety of compound 3.1 comprises an antibody that binds to B7H4. In some cases, the antibody comprises a set of CDR sequences (CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3, respectively) of which each sequence comprises at least 80% sequence identity, at least 85% sequence identity, at least 90% sequence identity, at least 95%, or 100% sequence identity to amino acid sequences from a set of amino acid sequences selected from the group consisting of SEQ ID NOs: 77-82, SEQ ID NOs: 91-96, SEQ ID NOs: 99-104, SEQ ID NOs: 107-112, SEQ ID NOs: 115-120, SEQ ID NOs: 123-128, SEQ ID NOs: 131-136, SEQ ID NOs: 139-144, SEQ ID NOs: 147-152, SEQ ID NOs: 155-160, SEQ ID NOs: 163-168, SEQ ID NOs: 171-176, SEQ ID NOs: 179-184, SEQ ID NOs: 187-192, SEQ ID NOs: 195-200, SEQ ID NOs: 203-208, SEQ ID NOs: 211-216, SEQ ID NOs: 219-224, SEQ ID NOs: 227-232, SEQ ID NOs: 235-240, and SEQ ID NOs: 243-248. In some cases, the antibody comprises a set of CDR sequences (CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3, respectively) each comprising at most one mutation relative to an amino acid sequence from a set of amino acid sequences selected from the group consisting of SEQ ID NOs: 77-82, SEQ ID NOs: 91-96, SEQ ID NOs: 99-104, SEQ ID NOs: 107-112, SEQ ID NOs: 115-120, SEQ ID NOs: 123-128, SEQ ID NOs: 131-136, SEQ ID NOs: 139-144, SEQ ID NOs: 147-152, SEQ ID NOs: 155-160, SEQ ID NOs: 163-168, SEQ ID NOs: 171-176, SEQ ID NOs: 179-184, SEQ ID NOs: 187-192, SEQ ID NOs: 195-200, SEQ ID NOs: 203-208, SEQ ID NOs: 211-216, SEQ ID NOs: 219-224, SEQ ID NOs: 227-232, SEQ ID NOs: 235-240, and SEQ ID NOs: 243-248. In some cases, the anti-B7H4 antibody comprises a heavy chain and a light chain comprising amino acid sequences that are at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or at least 100% identical to the amino acid sequences of SEQ ID NO: 85 and 87, SEQ ID NO: 86 and 87, SEQ ID NO: 88 and 90, SEQ ID NO: 89 and 90, SEQ ID NO: 251 and 252, , SEQ ID NO: 253 and 254, SEQ ID NO: 255 and 256, SEQ ID NO: 257 and 258, SEQ ID NO: 259 and 260, SEQ ID NO: 261 and 262, SEQ ID NO: 263 and 264, SEQ ID NO: 265 and 266, SEQ ID NO: 267 and 268, SEQ ID NO: 269 and 270, SEQ ID NO: 271 and 272, SEQ ID NO: 273 and 274, SEQ ID NO: 275 and 276, SEQ ID NO: 277 and 278, SEQ ID NO: 279 and 280, SEQ ID NO: 281 and 282, SEQ ID NO: 283 and 284, SEQ ID NO: 285

and 286, SEQ ID NO: 287 and 288, or SEQ ID NO: 289 and 290, respectively. In some embodiments, the anti-B7H4 antibody comprises a heavy chain variable region and a light chain variable region comprising amino acid sequences that are at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or at least 100% identical to the amino acid sequences of SEQ ID NO: 83 and 84, SEQ ID NO: 97 and 98, SEQ ID NO: 105 and 106, SEQ ID NO: 113 and 114, SEQ ID NO: 121 and 122, SEQ ID NO: 129 and 130, SEQ ID NO: 137 and 138, SEQ ID NO: 153 and 154, SEQ ID NO: 161 and 162, SEQ ID NO: 169 and 170, SEQ ID NO: 177 and 178, SEQ ID NO: 185 and 186, SEQ ID NO: 193 and 194, SEQ ID NO: 201 and 202, SEQ ID NO: 209 and 210, SEQ ID NO: 217 and 218, SEQ ID NO: 225 and 226, SEQ ID NO: 233 and 234, SEQ ID NO: 241 and 242, or SEQ ID NO: 249 and 250, respectively.

[0561] In some embodiments, the L moiety of compound 3.1 comprises an antibody that binds to CD70. In some such cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences comprising at least 80% sequence identity, at least 85% sequence identity, at least 90% sequence identity, or at least 95% sequence identity to the amino acid sequences of SEQ ID NOs: 291, 292, 293, 294, 295, and 296, respectively. In some cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences each comprising at most one mutation relative to the amino acid sequences of SEQ ID NOs: 291, 292, 293, 294, 295, and 296, respectively. In some embodiments, the anti-CD70 antibody comprises a heavy chain variable region comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 297 and a light chain variable region comprising an amino acid sequence that is at least 80% at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 298. In some embodiments, the anti-CD70 antibody comprises a heavy chain comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 299 and a light chain comprising an amino acid sequence that is at least 80% at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 300.

[0562] In some embodiments, the L moiety of compound 3.1 comprises an antibody that binds to TROP2. In some such cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences comprising at least 80% sequence identity, at least 85% sequence identity, at least 90% sequence identity, or at least 95% sequence identity

to the amino acid sequences of SEQ ID NOs: 301, 302, 303, 304, 305, and 306, respectively. In some cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences each comprising at most one mutation relative to the amino acid sequences of SEQ ID NOs: 301, 302, 303, 304, 305, and 306, respectively. In some cases, an antibody provided herein binds to TROP2. In some such cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences comprising at least 80% sequence identity, at least 85% sequence identity, at least 90% sequence identity, or at least 95% sequence identity to the amino acid sequences of SEQ ID NOs: 309, 310, 311, 312, 313, and 314 respectively. In some cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences each comprising at most one mutation relative to the amino acid sequences of SEQ ID NOs: 309, 310, 311, 312, 313, and 314, respectively. In some embodiments, the anti-TROP2 antibody comprises a heavy chain variable region comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 307 and a light chain variable region comprising an amino acid sequence that is at least 80% at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 308. In some embodiments, the anti-TROP2 antibody comprises a heavy chain variable region comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 315 and a light chain variable region comprising an amino acid sequence that is at least 80% at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 316.

[0563] In some embodiments, the L moiety of compound 3.1 comprises an antibody that binds to MICA. In some such cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences comprising at least 80% sequence identity, at least 85% sequence identity, at least 90% sequence identity, or at least 95% sequence identity to the amino acid sequences of SEQ ID NOs: 317, 318, 319, 320, 321, and 322, respectively. In some cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences each comprising at most one mutation relative to the amino acid sequences of SEQ ID NOs: 317, 318, 319, 320, 321, and 322, respectively. In some cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences comprising at least 80% sequence identity, at least 85% sequence identity, at least 90% sequence identity, or at least 95% sequence identity to the amino acid sequences of SEQ

ID NOs: 325, 326, 327, 328, 329, and 330, respectively. In some cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences each comprising at most one mutation relative to the amino acid sequences of SEQ ID NOs: 325, 326, 327, 328, 329, and 330, respectively. In some cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences comprising at least 80% sequence identity, at least 85% sequence identity, at least 90% sequence identity, or at least 95% sequence identity to the amino acid sequences of SEQ ID NOs: 333, 334, 335, 336, 337, and 338, respectively. In some cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences each comprising at most one mutation relative to the amino acid sequences of SEQ ID NOs: 333, 334, 335, 336, 337, and 338, respectively. In some cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences comprising at least 80% sequence identity, at least 85% sequence identity, at least 90% sequence identity, or at least 95% sequence identity to the amino acid sequences of SEQ ID NOs: 341, 342, 343, 344, 345, and 346, respectively. In some cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences each comprising at most one mutation relative to the amino acid sequences of SEQ ID NOs: 341, 342, 343, 344, 345, and 346, respectively. In some embodiments, the anti-MICA antibody comprises a heavy chain variable region comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 323 and a light chain variable region comprising an amino acid sequence that is at least 80% at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 324. In some embodiments, the anti-MICA antibody comprises a heavy chain variable region comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 331 and a light chain variable region comprising an amino acid sequence that is at least 80% at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 332. In some embodiments, the anti-MICA antibody comprises a heavy chain variable region comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 340 and a light chain variable region comprising an amino acid sequence that is at least 80% at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 340. In some embodiments, the anti-MICA antibody comprises a heavy chain variable region comprising an amino acid sequence that is at least 80%, at least 85%, at least

90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 347 and a light chain variable region comprising an amino acid sequence that is at least 80% at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 348.

[0564] In some embodiments, the L moiety of compound 3.1 comprises an antibody that binds to CD51. In some such cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences comprising at least 80% sequence identity, at least 85% sequence identity, at least 90% sequence identity, or at least 95% sequence identity to the amino acid sequences of SEQ ID NOs: 349, 350, 351, 352, 353, and 354, respectively. In some cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences each comprising at most one mutation relative to the amino acid sequences of SEQ ID NOs: 349, 350, 351, 352, 353, and 354, respectively. In some cases, an antibody provided herein binds to CD51. In some such cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences comprising at least 80% sequence identity, at least 85% sequence identity, at least 90% sequence identity, or at least 95% sequence identity to the amino acid sequences of SEQ ID NOs: 357, 358, 359, 360, 361, and 362, respectively. In some cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences each comprising at most one mutation relative to the amino acid sequences of SEQ ID NOs: 357, 358, 359, 360, 361, and 362, respectively. In some embodiments, the anti-CD51 antibody comprises a heavy chain variable region comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 355 and a light chain variable region comprising an amino acid sequence that is at least 80% at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 356. In some embodiments, the anti-CD51 antibody comprises a heavy chain variable region comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 363 and a light chain variable region comprising an amino acid sequence that is at least 80% at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 364.

[0565] In some embodiments, the L moiety of compound 3.1 comprises an antibody that binds to gpA33. In some such cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences comprising at least 80% sequence identity, at

least 85% sequence identity, at least 90% sequence identity, or at least 95% sequence identity to the amino acid sequences of SEQ ID NOs: 365, 366, 367, 368, 369, and 370, respectively. In some cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences each comprising at most one mutation relative to the amino acid sequences of SEQ ID NOs: 365, 366, 367, 368, 369, and 370, respectively. In some embodiments, the anti-gpA33 antibody comprises a heavy chain variable region comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 371 and a light chain variable region comprising an amino acid sequence that is at least 80% at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 372.

[0566] In some embodiments, the L moiety of compound 3.1 comprises an antibody that binds to IL1Rap. In some such cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences comprising at least 80% sequence identity, at least 85% sequence identity, at least 90% sequence identity, or at least 95% sequence identity to the amino acid sequences of SEQ ID NOs: 373, 374, 375, 376, 377, and 378, respectively. In some cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences each comprising at most one mutation relative to the amino acid sequences of SEQ ID NOs: 373, 374, 375, 376, 377, and 378, respectively. In some embodiments, the anti-IL1Rap antibody comprises a heavy chain variable region comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 379 and a light chain variable region comprising an amino acid sequence that is at least 80% at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 380.

[0567] In some embodiments, the L moiety of compound 3.1 comprises an antibody that binds to EpCAM. In some cases, the antibody comprises a set of CDR sequences (CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3, respectively) of which each sequence comprises at least 80% sequence identity, at least 85% sequence identity, at least 90% sequence identity, at least 95%, or 100% sequence identity to amino acid sequences from a set of amino acid sequences selected from the group consisting of SEQ ID NOs: 381-386, SEQ ID NOs: 389-394, SEQ ID NOs: 397-402, SEQ ID NOs: 405-410, SEQ ID NOs: 413-418, or SEQ ID NOs: 421-426. In some embodiments, the anti-EpCAM antibody comprises a

heavy chain variable region and a light chain variable region comprising amino acid sequences that are at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or at least 100% identical to the amino acid sequences of SEQ ID NO: 387 and 388, SEQ ID NO: 395 and 396, SEQ ID NO: 403 and 404, SEQ ID NO: 411 and 412, SEQ ID NO: 419 and 420, or SEQ ID NO: 427 and 428, respectively.

[0568] In some embodiments, the L moiety of compound 3.1 comprises an antibody that binds to CD352. In some such cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences comprising at least 80% sequence identity, at least 85% sequence identity, at least 90% sequence identity, or at least 95% sequence identity to the amino acid sequences of SEQ ID NOs: 429, 430, 431, 432, 433, and 434, respectively. In some cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences each comprising at most one mutation relative to the amino acid sequences of SEQ ID NOs: 429, 430, 431, 432, 433, and 434, respectively. In some embodiments, the anti-CD352 antibody comprises a heavy chain variable region comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 435 and a light chain variable region comprising an amino acid sequence that is at least 80% at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 436.

[0569] In some embodiments, the L moiety of compound 3.1 comprises an antibody that binds to CS1. In some such cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences comprising at least 80% sequence identity, at least 85% sequence identity, at least 90% sequence identity, or at least 95% sequence identity to the amino acid sequences of SEQ ID NOs: 437, 438, 439, 440, 441, and 442, respectively. In some cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences each comprising at most one mutation relative to the amino acid sequences of SEQ ID NOs: 437, 438, 439, 440, 441, and 442, respectively. In some embodiments, the anti-CS1 antibody comprises a heavy chain variable region comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 443 and a light chain variable region comprising an amino acid sequence that is at least 80% at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 444.

[0570] In some embodiments, the L moiety of compound 3.1 comprises an antibody that binds to CD38. In some such cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences comprising at least 80% sequence identity, at least 85% sequence identity, at least 90% sequence identity, or at least 95% sequence identity to the amino acid sequences of SEQ ID NOs: 445, 446, 447, 448, 449, and 450, respectively. In some cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences each comprising at most one mutation relative to the amino acid sequences of SEQ ID NOs: 445, 446, 447, 448, 449, and 450, respectively. In some embodiments, the anti-CD38 antibody comprises a heavy chain variable region comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 451 and a light chain variable region comprising an amino acid sequence that is at least 80% at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 452.

[0571] In some embodiments, the L moiety of compound 3.1 comprises an antibody that binds to CD25. In some such cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences comprising at least 80% sequence identity, at least 85% sequence identity, at least 90% sequence identity, or at least 95% sequence identity to the amino acid sequences of SEQ ID NOs: 453, 454, 455, 456, 457, and 458, respectively. In some cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences each comprising at most one mutation relative to the amino acid sequences of SEQ ID NOs: 453, 454, 455, 456, 457, and 458, respectively. In some embodiments, the anti-CD25 antibody comprises a heavy chain variable region comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 459 and a light chain variable region comprising an amino acid sequence that is at least 80% at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 460.

[0572] In some embodiments, the L moiety of compound 3.1 comprises an antibody that binds to ADAM9. In some such cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences comprising at least 80% sequence identity, at least 85% sequence identity, at least 90% sequence identity, or at least 95% sequence identity to the amino acid sequences of SEQ ID NOs: 461, 462, 463, 464, 465, and 466, respectively.

In some cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences each comprising at most one mutation relative to the amino acid sequences of SEQ ID NOs: 461, 462, 463, 464, 465, and 466, respectively. In some such cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences comprising at least 80% sequence identity, at least 85% sequence identity, at least 90% sequence identity, or at least 95% sequence identity to the amino acid sequences of SEQ ID NOs: 469, 470, 471, 472, 473, and 474, respectively. In some cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences each comprising at most one mutation relative to the amino acid sequences of SEQ ID NOs: 469, 470, 471, 472, 473, and 474, respectively. In some embodiments, the anti-ADAM9 antibody comprises a heavy chain variable region comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 467 and a light chain variable region comprising an amino acid sequence that is at least 80% at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 468. In some embodiments, the anti-ADAM9 antibody comprises a heavy chain variable region comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 475 and a light chain variable region comprising an amino acid sequence that is at least 80% at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 476.

[0573] In some embodiments, the L moiety of compound 3.1 comprises an antibody that binds to CD59. In some such cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences comprising at least 80% sequence identity, at least 85% sequence identity, at least 90% sequence identity, or at least 95% sequence identity to the amino acid sequences of SEQ ID NOs: 477, 478, 479, 480, 481, and 482, respectively. In some cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences each comprising at most one mutation relative to the amino acid sequences of SEQ ID NOs: 477, 478, 479, 480, 481, and 482, respectively. In some embodiments, the anti-CD59 antibody comprises a heavy chain variable region comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 483 and a light chain variable region comprising an amino acid sequence that is at least 80% at least 85%, at least

90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 484.

[0574] In some embodiments, the L moiety of compound 3.1 comprises an antibody that binds to CD19. In some such cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences comprising at least 80% sequence identity, at least 85% sequence identity, at least 90% sequence identity, or at least 95% sequence identity to the amino acid sequences of SEQ ID NOs: 485, 486, 487, 488, 489, and 490, respectively. In some cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences each comprising at most one mutation relative to the amino acid sequences of SEQ ID NOs: 485, 486, 487, 488, 489, and 490, respectively. In some embodiments, the anti-CD19 antibody comprises a heavy chain variable region comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 491 and a light chain variable region comprising an amino acid sequence that is at least 80% at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 492. In some embodiments, the anti-CD19 antibody comprises a heavy chain comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 493 and a light chain comprising an amino acid sequence that is at least 80% at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 494.

[0575] In some embodiments, the L moiety of compond 3.1 comprises an antibody that binds to CD138. In some such cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences comprising at least 80% sequence identity, at least 85% sequence identity, at least 90% sequence identity, or at least 95% sequence identity to the amino acid sequences of SEQ ID NOs: 495, 496, 497, 498, 499, and 500, respectively. In some cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences each comprising at most one mutation relative to the amino acid sequences of SEQ ID NOs: 495, 496, 497, 498, 499, and 500, respectively. In some embodiments, the anti-CD138 antibody comprises a heavy chain variable region comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 501 and a light chain variable region comprising an amino acid sequence that is at least 80% at least 85%, at least

90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 502.

[0576] In some embodiments, the L moiety of compond 3.1 comprises an antibody that binds to CD166. In some such cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences comprising at least 80% sequence identity, at least 85% sequence identity, at least 90% sequence identity, or at least 95% sequence identity to the amino acid sequences of SEQ ID NOs: 503, 504, 505, 506, 507, and 508, respectively. In some cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences each comprising at most one mutation relative to the amino acid sequences of SEQ ID NOs: 503, 504, 505, 506, 507, and 508, respectively. In some embodiments, the anti-CD166 antibody comprises a heavy chain variable region comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 509 and a light chain variable region comprising an amino acid sequence that is at least 80% at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 510.

[0577] In some embodiments, the L moiety of compound 3.1 comprises an antibody that binds to CD56. In some such cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences comprising at least 80% sequence identity, at least 85% sequence identity, at least 90% sequence identity, or at least 95% sequence identity to the amino acid sequences of SEQ ID NOs: 511, 512, 513, 514, 515, and 516, respectively. In some cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences each comprising at most one mutation relative to the amino acid sequences of SEQ ID NOs: 511, 512, 513, 514, 515, and 516, respectively. In some embodiments, the anti-CD56 antibody comprises a heavy chain variable region comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 517 and a light chain variable region comprising an amino acid sequence that is at least 80% at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 518.

[0578] In some embodiments, the L moiety of compound 3.1 comprises an antibody that binds to CD74. In some such cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences comprising at least 80% sequence identity, at

least 85% sequence identity, at least 90% sequence identity, or at least 95% sequence identity to the amino acid sequences of SEQ ID NOs: 519, 520, 521, 522, 523, and 524, respectively. In some cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences each comprising at most one mutation relative to the amino acid sequences of SEQ ID NOs: 519, 520, 521, 522, 523, and 524, respectively. In some embodiments, the anti-CD74 antibody comprises a heavy chain variable region comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 525 and a light chain variable region comprising an amino acid sequence that is at least 80% at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 526.

[0579] In some embodiments, the L moiety of compound 3.1 comprises an antibody that binds to CEACAM5. In some such cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences comprising at least 80% sequence identity, at least 85% sequence identity, at least 90% sequence identity, or at least 95% sequence identity to the amino acid sequences of SEQ ID NOs: 527, 528, 529, 530, 531, and 532, respectively. In some cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences each comprising at most one mutation relative to the amino acid sequences of SEQ ID NOs: 527, 528, 529, 530, 531, and 532, respectively. In some embodiments, the anti-CEACAM5 antibody comprises a heavy chain variable region comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 533 and a light chain variable region comprising an amino acid sequence that is at least 80% at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 534.

[0580] In some embodiments, the L moiety of compound 3.1 comprises an antibody that binds to CanAg. In some such cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences comprising at least 80% sequence identity, at least 85% sequence identity, at least 90% sequence identity, or at least 95% sequence identity to the amino acid sequences of SEQ ID NOs: 535, 536, 537, 538, 539, and 540, respectively. In some cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences each comprising at most one mutation relative to the amino acid sequences of SEQ ID NOs: 535, 536, 537, 538, 539, and 540, respectively. In some

embodiments, the anti-CanAg antibody comprises a heavy chain variable region comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 541 and a light chain variable region comprising an amino acid sequence that is at least 80% at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 542.

[0581] In some embodiments, the L moiety of compound 3.1 comprises an antibody that binds to DLL-3. In some such cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences comprising at least 80% sequence identity, at least 85% sequence identity, at least 90% sequence identity, or at least 95% sequence identity to the amino acid sequences of SEQ ID NOs: 543, 544, 545, 546, 547, and 548, respectively. In some cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences each comprising at most one mutation relative to the amino acid sequences of SEQ ID NOs: 543, 544, 545, 546, 547, and 548, respectively. In some embodiments, the anti-DLL-3 antibody comprises a heavy chain variable region comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 549 and a light chain variable region comprising an amino acid sequence that is at least 80% at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 550.

[0582] In some embodiments, the L moiety of compound 3.1 comprises an antibody that binds to DPEP-3. In some such cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences comprising at least 80% sequence identity, at least 85% sequence identity, at least 90% sequence identity, or at least 95% sequence identity to the amino acid sequences of SEQ ID NOs: 551, 552, 553, 554, 555, and 556, respectively. In some cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences each comprising at most one mutation relative to the amino acid sequences of SEQ ID NOs: 551, 552, 553, 554, 555, and 556, respectively. In some embodiments, the anti-DPEP-3 antibody comprises a heavy chain variable region comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 557 and a light chain variable region comprising an amino acid sequence that is at least 80% at least 85%, at least

90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 558.

[0583] In some embodiments, the L moiety of compound 3.1 comprises an antibody that binds to EGFR. In some cases, the antibody comprises a set of CDR sequences (CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3, respectively) of which each sequence comprises at least 80% sequence identity, at least 85% sequence identity, at least 90% sequence identity, at least 95%, or 100% sequence identity to amino acid sequences from a set of amino acid sequences selected from the group consisting of SEQ ID NOs: 559-564, SEQ ID NOs: 567-572, SEQ ID NOs: 575-580, and SEQ ID NOs: 895-900. In some embodiments, the anti-EGFR antibody comprises a heavy chain variable region and a light chain variable region comprising amino acid sequences that are at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or at least 100% identical to the amino acid sequences of SEQ ID NO: 565 and 566, SEQ ID NO: 573 and 574, SEQ ID NO: 581 and 582, or SEQ ID NO: 901 and 902, respectively.

[0584] In some embodiments, the L moiety of compound 3.1 comprises an antibody that binds to FRa. In some such cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences comprising at least 80% sequence identity, at least 85% sequence identity, at least 90% sequence identity, or at least 95% sequence identity to the amino acid sequences of SEQ ID NOs: 583, 584, 585, 586, 587, and 588, respectively. In some cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences each comprising at most one mutation relative to the amino acid sequences of SEQ ID NOs: 583, 584, 585, 586, 587, and 588, respectively. In some cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences comprising at least 80% sequence identity, at least 85% sequence identity, at least 90% sequence identity, or at least 95% sequence identity to the amino acid sequences of SEQ ID NOs: 591, 592, 593, 594, 595, and 596, respectively. In some cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences each comprising at most one mutation relative to the amino acid sequences of SEQ ID NOs: 591, 592, 593, 594, 595, and 596, respectively. In some embodiments, the anti-FRa antibody comprises a heavy chain variable region comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 589 and a light chain variable region comprising an amino acid sequence that is at least 80% at least 85%, at least 90%, at least 95%, at least 98%, or 99%

identical to the amino acid sequence of SEQ ID NO: 590. In some embodiments, the anti-FRa antibody comprises a heavy chain variable region comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 597 and a light chain variable region comprising an amino acid sequence that is at least 80% at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 598.

[0585] In some embodiments, the L moiety of compound 3.1 comprises an antibody that binds to MUC-1. In some such cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences comprising at least 80% sequence identity, at least 85% sequence identity, at least 90% sequence identity, or at least 95% sequence identity to the amino acid sequences of SEQ ID NOs: 599, 600, 601, 602, 603, and 604, respectively. In some cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences each comprising at most one mutation relative to the amino acid sequences of SEQ ID NOs: 599, 600, 601, 602, 603, and 604, respectively. In some embodiments, the anti-MUC-1 antibody comprises a heavy chain variable region comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 605 and a light chain variable region comprising an amino acid sequence that is at least 80% at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 606.

[0586] In some embodiments, the L moiety of compound 3.1 comprises an antibody that binds to Mesothelin. In some such cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences comprising at least 80% sequence identity, at least 85% sequence identity, at least 90% sequence identity, or at least 95% sequence identity to the amino acid sequences of SEQ ID NOs: 607, 608, 609, 610, 611, and 612, respectively. In some cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences each comprising at most one mutation relative to the amino acid sequences of SEQ ID NOs: 607, 608, 609, 610, 611, and 612, respectively. In some embodiments, the anti-Mesothelin antibody comprises a heavy chain variable region comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 613 and a light chain variable region comprising an amino acid sequence that is at least 80% at least

85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 614.

[0587] In some embodiments, the L moiety of compound 3.1 comprises an antibody that binds to ROR-1. In some such cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences comprising at least 80% sequence identity, at least 85% sequence identity, at least 90% sequence identity, or at least 95% sequence identity to the amino acid sequences of SEQ ID NOs: 615, 616, 617, 618, 619, and 620, respectively. In some cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences each comprising at most one mutation relative to the amino acid sequences of SEQ ID NOs: 615, 616, 617, 618, 619, and 620, respectively. In some embodiments, the anti-ROR-1 antibody comprises a heavy chain variable region comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 621 and a light chain variable region comprising an amino acid sequence that is at least 80% at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 622.

[0588] In some embodiments, the L moiety of compound 3.1 comprises an antibody that binds to B7H3. In some cases, the antibody comprises a set of CDR sequences (CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3, respectively) of which each sequence comprises at least 80% sequence identity, at least 85% sequence identity, at least 90% sequence identity, at least 95%, or 100% sequence identity to amino acid sequences from a set of amino acid sequences selected from the group consisting of SEQ ID NOs: 623-628, SEQ ID NOs: 631-636, SEQ ID NOs: 639-644, SEQ ID NOs: 647-652, SEQ ID NOs: 655-660, SEQ ID NOs: 663-668, SEQ ID NOs: 671-676, SEQ ID NOs: 679-684, SEQ ID NOs: 687-692, SEQ ID NOs: 695-700, and SEQ ID NOs: 705-710. In some embodiments, the anti-B7H3 antibody comprises a heavy chain variable region and a light chain variable region comprising amino acid sequences that are at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, at least 99%, or at least 100% identical to the amino acid sequences of SEQ ID NO: 629 and 630, SEQ ID NOs: 637 and 638, SEQ ID NOs: 645 and 646, SEQ ID NOs: 653 and 654, SEQ ID NOs: 661 and 662, SEQ ID NOs: 669 and 670, SEQ ID NOs: 677 and 678, SEQ ID NOs: 685 and 686, SEQ ID NOs: 693 and 694, SEQ ID NOs: 701 and 702, SEQ ID NOs: 703 and 704, SEQ ID NOs: 711 and 712, SEQ ID NOs: 713 and 714, and SEQ ID NOs: 715 and 716, respectively.

[0589] In some embodiments, the L moiety of compound 3.1 comprises an antibody that binds to HER3. In some embodiments, the anti-HER3 antibody comprises a heavy chain comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 717 and a light chain comprising an amino acid sequence that is at least 80% at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 718. In some cases, an antibody provided herein binds to HER3. In some embodiments, the anti-HER3 antibody comprises a heavy chain comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 719 and a light chain comprising an amino acid sequence that is at least 80% at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 720. In some cases, an antibody provided herein binds to HER3. In some embodiments, the anti-HER3 antibody comprises a heavy chain comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 721 and a light chain comprising an amino acid sequence that is at least 80% at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 722. In some cases, an antibody provided herein binds to HER3. In some embodiments, the anti-HER3 antibody comprises a heavy chain comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 723 and a light chain comprising an amino acid sequence that is at least 80% at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 724.

[0590] In some embodiments, the L moiety of compound 3.1 comprises an antibody that binds to PTK7. In some cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences comprising at least 80% sequence identity, at least 85% sequence identity, at least 90% sequence identity, or at least 95% sequence identity to the amino acid sequences of SEQ ID NOs: 725, 726, 727, 728, 729, and 730, respectively. In some cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences each comprising at most one mutation relative to the amino acid sequences of SEQ ID NOs: 725, 726, 727, 728, 729, and 730, respectively. In some cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences comprising at least 80% sequence identity, at least 85% sequence identity, at least

90% sequence identity, or at least 95% sequence identity to the amino acid sequences of SEQ ID NOs: 733, 734, 735, 736, 737, and 738, respectively. In some cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences each comprising at most one mutation relative to the amino acid sequences of SEQ ID NOs: 733, 734, 735, 736, 737, and 738, respectively. In some cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences comprising at least 80% sequence identity, at least 85% sequence identity, at least 90% sequence identity, or at least 95% sequence identity to the amino acid sequences of SEQ ID NOs: 741, 742, 743, 744, 745, and 746, respectively. In some cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences each comprising at most one mutation relative to the amino acid sequences of SEQ ID NOs: 741, 742, 743, 744, 745, and 746, respectively. In some cases, the anti-PTK7 antibody comprises a heavy chain comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 731 and a light chain comprising an amino acid sequence that is at least 80% at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 732. In some cases, the anti-PTK7 antibody comprises a heavy chain comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 739 and a light chain comprising an amino acid sequence that is at least 80% at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 740. In some cases, the anti-PTK7 antibody comprises a heavy chain comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 747 and a light chain comprising an amino acid sequence that is at least 80% at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 748.

[0591] In some embodiments, the L moiety of compound 3.1 comprises an antibody that binds to ZIP6. In some cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences comprising at least 80% sequence identity, at least 85% sequence identity, at least 90% sequence identity, or at least 95% sequence identity to the amino acid sequences of SEQ ID NOs: 749, 750, 751, 752, 753, and 754, respectively. In some cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences each comprising at most one mutation relative to the amino acid

sequences of SEQ ID NOs: 749, 750, 751, 752, 753, and 754, respectively. In some cases, the anti-ZIP6 antibody comprises a heavy chain variable region comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 755 and a light chain variable region comprising an amino acid sequence that is at least 80% at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 756. In some embodiments, the anti-ZIP6 antibody comprises a heavy chain comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 757 and a light chain comprising an amino acid sequence that is at least 80% at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 758.

[0592] In some embodiments, the L moiety of compound 3.1 comprises an antibody that binds to Integrin αvβ6. In some cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences comprising at least 80% sequence identity, at least 85% sequence identity, at least 90% sequence identity, or at least 95% sequence identity to the amino acid sequences of SEQ ID NOs: 759, 760, 761, 762, 763, and 764, respectively. In some cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences each comprising at most one mutation relative to the amino acid sequences of SEQ ID NOs: 759, 760, 761, 762, 763, and 764, respectively. In some embodiments, the anti- Integrin αvβ6 antibody comprises a heavy chain variable region comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 765 and a light chain variable region comprising an amino acid sequence that is at least 80% at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 766.

[0593] In some embodiments, the L moiety of compound 3.1 comprises an antibody that binds to CD48. In some cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences comprising at least 80% sequence identity, at least 85% sequence identity, at least 90% sequence identity, or at least 95% sequence identity to the amino acid sequences of SEQ ID NOs: 767, 768, 769, 770, 771, and 772, respectively. In some cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences each comprising at most one mutation relative to the amino acid sequences of SEQ ID NOs: 767, 768, 769, 770, 771, and 772, respectively. In some

embodiments, the anti-CD48 antibody comprises a heavy chain variable region comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 773 and a light chain variable region comprising an amino acid sequence that is at least 80% at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 774.

[0594] In some embodiments, the L moiety of compound 3.1 comprises an antibody that binds to IGF-1R. In some cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences comprising at least 80% sequence identity, at least 85% sequence identity, at least 90% sequence identity, or at least 95% sequence identity to the amino acid sequences of SEQ ID NOs: 775, 776, 777, 778, 779, and 780, respectively. In some cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences each comprising at most one mutation relative to the amino acid sequences of SEQ ID NOs: 775, 776, 777, 778, 779, and 780, respectively. In some embodiments, the anti-IGF-1R antibody comprises a heavy chain variable region comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 781 and a light chain variable region comprising an amino acid sequence that is at least 80% at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 782.

[0595] In some embodiments, the L moiety of compound 3.1 comprises an antibody that binds to Claudin-18.2. In some cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences comprising at least 80% sequence identity, at least 85% sequence identity, at least 90% sequence identity, or at least 95% sequence identity to the amino acid sequences of SEQ ID NOs: 783, 784, 785, 786, 787, and 788, respectively. In some cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences each comprising at most one mutation relative to the amino acid sequences of SEQ ID NOs: 783, 784, 785, 786, 787, and 788, respectively. In some cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences comprising at least 80% sequence identity, at least 85% sequence identity, at least 90% sequence identity, or at least 95% sequence identity to the amino acid sequences of SEQ ID NOs: 791, 792, 793, 794, 795, and 796, respectively. In some cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences each

comprising at most one mutation relative to the amino acid sequences of SEQ ID NOs: 791, 792, 793, 794, 795, and 796, respectively. In some embodiments, the anti-Claudin-18.2 antibody comprises a heavy chain variable region comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 789 and a light chain variable region comprising an amino acid sequence that is at least 80% at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 790. In some embodiments, the anti-Claudin-18.2 antibody comprises a heavy chain variable region comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 797 and a light chain variable region comprising an amino acid sequence that is at least 80% at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 798.

[0596] In some embodiments, the L moiety of compound 3.1 comprises an antibody that binds to Nectin-4. In some cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences comprising at least 80% sequence identity, at least 85% sequence identity, at least 90% sequence identity, or at least 95% sequence identity to the amino acid sequences of SEQ ID NOs: 799, 800, 801, 802, 803, and 804, respectively. In some cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences each comprising at most one mutation relative to the amino acid sequences of SEQ ID NOs: 799, 800, 801, 802, 803, and 804, respectively. In some embodiments, the anti-Nectin-4 antibody comprises a heavy chain variable region comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 805 and a light chain variable region comprising an amino acid sequence that is at least 80% at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 806.

[0597] In some embodiments, the L moiety of compound 3.1 comprises an antibody that binds to SLTRK6. In some such cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences comprising at least 80% sequence identity, at least 85% sequence identity, at least 90% sequence identity, or at least 95% sequence identity to the amino acid sequences of SEQ ID NOs: 807, 808, 809, 810, 811, and 812, respectively. In some cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and

CDR-L3 sequences each comprising at most one mutation relative to the amino acid sequences of SEQ ID NOs: 807, 808, 809, 810, 811, and 812, respectively. In some embodiments, the anti-SLTRK6 antibody comprises a heavy chain variable region comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 813 and a light chain variable region comprising an amino acid sequence that is at least 80% at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 814.

[0598] In some embodiments, the L moiety of compound 3.1 comprises an antibody that binds to CD142. In some such cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences comprising at least 80% sequence identity, at least 85% sequence identity, at least 90% sequence identity, or at least 95% sequence identity to the amino acid sequences of SEQ ID NOs: 815, 816, 817, 818, 819, and 820, respectively. In some cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences each comprising at most one mutation relative to the amino acid sequences of SEQ ID NOs: 815, 816, 817, 818, 819, and 820, respectively. In some embodiments, the anti-CD142 antibody comprises a heavy chain variable region comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 821 and a light chain variable region comprising an amino acid sequence that is at least 80% at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 822.

[0599] In some embodiments, the L moiety of compound 3.1 comprises an antibody that binds to Sialyl-Thomsen-nouveau antigen (STn). In some such cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences comprising at least 80% sequence identity, at least 85% sequence identity, at least 90% sequence identity, or at least 95% sequence identity to the amino acid sequences of SEQ ID NOs: 823, 824, 825, 826, 827, and 828, respectively. In some cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences each comprising at most one mutation relative to the amino acid sequences of SEQ ID NOs: 823, 824, 825, 826, 827, and 828, respectively.

[0600] In some embodiments, the anti-STn antibody comprises a heavy chain variable region comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at

least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 829 and a light chain variable region comprising an amino acid sequence that is at least 80% at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 830.

[0601] In some embodiments, the L moiety of compound 3.1 comprises an antibody that binds to CD20. In some such cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences comprising at least 80% sequence identity, at least 85% sequence identity, at least 90% sequence identity, or at least 95% sequence identity to the amino acid sequences of SEQ ID NOs: 831, 832, 833, 834, 835, and 836, respectively. In some cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences each comprising at most one mutation relative to the amino acid sequences of SEQ ID NOs: 831, 832, 833, 834, 835, and 836, respectively. In some embodiments, the anti-CD20 antibody comprises a heavy chain variable region comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 837 and a light chain variable region comprising an amino acid sequence that is at least 80% at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 838.

[0602] In some embodiments, the L moiety of compound 3.1 comprises an antibody that binds to HER2. In some such cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences comprising at least 80% sequence identity, at least 85% sequence identity, at least 90% sequence identity, or at least 95% sequence identity to the amino acid sequences of SEQ ID NOs: 839, 840, 841, 842, 843, and 844, respectively. In some cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences each comprising at most one mutation relative to the amino acid sequences of SEQ ID NOs: 839, 840, 841, 842, 843, and 844, respectively. In some embodiments, the anti-HER2 antibody comprises a heavy chain variable region comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 845 and a light chain variable region comprising an amino acid sequence that is at least 80% at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 846.

[0603] In some embodiments, the L moiety of compound 3.1 comprises an antibody that binds to CD79b. In some such cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences comprising at least 80% sequence identity, at least 85% sequence identity, at least 90% sequence identity, or at least 95% sequence identity to the amino acid sequences of SEQ ID NOs: 847, 848, 849, 850, 851, and 852, respectively. In some cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences each comprising at most one mutation relative to the amino acid sequences of SEQ ID NOs: 847, 848, 849, 850, 851, and 852, respectively. In some embodiments, the anti-CD79b antibody comprises a heavy chain variable region comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 853 and a light chain variable region comprising an amino acid sequence that is at least 80% at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 854.

[0604] In some embodiments, the L moiety of compound 3.1 comprises an antibody that binds to NaPi2B. In some such cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences comprising at least 80% sequence identity, at least 85% sequence identity, at least 90% sequence identity, or at least 95% sequence identity to the amino acid sequences of SEQ ID NOs: 855, 856, 857, 858, 859, and 860, respectively. In some cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences each comprising at most one mutation relative to the amino acid sequences of SEQ ID NOs: 855, 856, 857, 858, 859, and 860, respectively. In some embodiments, the anti-NaPi2B antibody comprises a heavy chain variable region comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 861 and a light chain variable region comprising an amino acid sequence that is at least 80% at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 862.

[0605] In some embodiments, the L moiety of compound 3.1 comprises an antibody that binds to Muc16. In some such cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences comprising at least 80% sequence identity, at least 85% sequence identity, at least 90% sequence identity, or at least 95% sequence identity to the amino acid sequences of SEQ ID NOs: 863, 864, 865, 866, 867, and 868, respectively.

In some cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences each comprising at most one mutation relative to the amino acid sequences of SEQ ID NOs: 863, 864, 865, 866, 867, and 868, respectively. In some embodiments, the anti-Muc16 antibody comprises a heavy chain variable region comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 869 and a light chain variable region comprising an amino acid sequence that is at least 80% at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 870.

[0606] In some embodiments, the L moiety of compound 3.1 comprises an antibody that binds to STEAP1. In some such cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences comprising at least 80% sequence identity, at least 85% sequence identity, at least 90% sequence identity, or at least 95% sequence identity to the amino acid sequences of SEQ ID NOs: 871, 872, 873, 874, 875, and 876, respectively. In some cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences each comprising at most one mutation relative to the amino acid sequences of SEQ ID NOs: 871, 872, 873, 874, 875, and 876, respectively. In some embodiments, the anti-STEAP1 antibody comprises a heavy chain variable region comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 877 and a light chain variable region comprising an amino acid sequence that is at least 80% at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 878.

[0607] In some embodiments, the L moiety of compound 3.1 comprises an antibody that binds to BCMA. In some such cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences comprising at least 80% sequence identity, at least 85% sequence identity, at least 90% sequence identity, or at least 95% sequence identity to the amino acid sequences of SEQ ID NOs: 879, 880, 881, 882, 883, and 884, respectively. In some cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences each comprising at most one mutation relative to the amino acid sequences of SEQ ID NOs: 879, 880, 881, 882, 883, and 884, respectively. In some embodiments, the anti-BCMA antibody comprises a heavy chain variable region comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least

98%, or 99% identical to the amino acid sequence of SEQ ID NO: 885 and a light chain variable region comprising an amino acid sequence that is at least 80% at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 886.

[0608] In some embodiments, the L moiety of compound 3.1 comprises an antibody that binds to c-Met. In some such cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences comprising at least 80% sequence identity, at least 85% sequence identity, at least 90% sequence identity, or at least 95% sequence identity to the amino acid sequences of SEQ ID NOs: 887, 888, 889, 890, 891, and 892, respectively. In some cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences each comprising at most one mutation relative to the amino acid sequences of SEQ ID NOs: 887, 888, 889, 890, 891, and 892, respectively. In some embodiments, the anti-c-Met antibody comprises a heavy chain variable region comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 893 and a light chain variable region comprising an amino acid sequence that is at least 80% at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 893.

[0609] In some embodiments, the L moiety of compound comprises an antibody that binds to SLAMF7. In some such cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences comprising at least 80% sequence identity, at least 85% sequence identity, at least 90% sequence identity, or at least 95% sequence identity to the amino acid sequences of SEQ ID NOs: 903, 904, 905, 906, 907, and 908, respectively. In some cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences each comprising at most one mutation relative to the amino acid sequences of SEQ ID NOs: 903, 904, 905, 906, 907, and 908, respectively. In some embodiments, the anti-SLAMF7 antibody comprises a heavy chain variable region comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 909 and a light chain variable region comprising an amino acid sequence that is at least 80% at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 910.

[0610] In some embodiments, the L moiety of compound 3.1 comprises an antibody that binds to C4.4a. In some such cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences comprising at least 80% sequence identity, at least 85% sequence identity, at least 90% sequence identity, or at least 95% sequence identity to the amino acid sequences of SEQ ID NOs: 911, 912, 913, 914, 915, and 916, respectively. In some cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences each comprising at most one mutation relative to the amino acid sequences of SEQ ID NOs: 911, 912, 913, 914, 915, and 916, respectively. In some embodiments, the anti-C4.4a antibody comprises a heavy chain variable region comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 917 and a light chain variable region comprising an amino acid sequence that is at least 80% at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 918.

[0611] In some embodiments, the L moiety of compound 3.1 comprises an antibody that binds to GCC. In some such cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences comprising at least 80% sequence identity, at least 85% sequence identity, at least 90% sequence identity, or at least 95% sequence identity to the amino acid sequences of SEQ ID NOs: 919, 920, 921, 922, 923, and 924, respectively. In some cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences each comprising at most one mutation relative to the amino acid sequences of SEQ ID NOs: 919, 920, 921, 922, 923, and 924, respectively. In some embodiments, the anti-GCC antibody comprises a heavy chain variable region comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 925 and a light chain variable region comprising an amino acid sequence that is at least 80% at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 926.

[0612] In some embodiments, the L moiety of compound 3.1 comprises an antibody that binds to Axl. In some such cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences comprising at least 80% sequence identity, at least 85% sequence identity, at least 90% sequence identity, or at least 95% sequence identity to the amino acid sequences of SEQ ID NOs: 927, 928, 929, 930, 931, and 932, respectively.

In some cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences each comprising at most one mutation relative to the amino acid sequences of SEQ ID NOs: 927, 928, 929, 930, 931, and 932, respectively. In some embodiments, the anti-Axl antibody comprises a heavy chain variable region comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 933 and a light chain variable region comprising an amino acid sequence that is at least 80% at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 933.

[0613] In some embodiments, the L moiety of compound 3.1 comprises an antibody that binds to transmembrane glycoprotein NMB (gpNMB). In some such cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences comprising at least 80% sequence identity, at least 85% sequence identity, at least 90% sequence identity, or at least 95% sequence identity to the amino acid sequences of SEQ ID NOs: 935, 936, 937, 938, 939, and 940, respectively. In some cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences each comprising at most one mutation relative to the amino acid sequences of SEQ ID NOs: 935, 936, 937, 938, 939, and 940, respectively. In some embodiments, the anti-gpNMB antibody comprises a heavy chain variable region comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 941 and a light chain variable region comprising an amino acid sequence that is at least 80% at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 942. In some embodiments, the anti-gpNMB antibody comprises a heavy chain variable region comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 943 and a light chain variable region comprising an amino acid sequence that is at least 80% at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 944.

[0614] In some embodiments, the L moiety of compound 3.1 comprises an antibody that binds to Prolactin receptor. In some such cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences comprising at least 80% sequence identity, at least 85% sequence identity, at least 90% sequence identity, or at least 95% sequence identity to the amino acid sequences of SEQ ID NOs: 945, 946, 947, 948, 949, and

950, respectively. In some cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences each comprising at most one mutation relative to the amino acid sequences of SEQ ID NOs: 945, 946, 947, 948, 949, and 950, respectively. In some embodiments, the anti-Prolactin receptor antibody comprises a heavy chain variable region comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 951 and a light chain variable region comprising an amino acid sequence that is at least 80% at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 952.

[0615] In some embodiments, the L moiety of compound 3.1 comprises an antibody that binds to FGFR2. In some such cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences comprising at least 80% sequence identity, at least 85% sequence identity, at least 90% sequence identity, or at least 95% sequence identity to the amino acid sequences of SEQ ID NOs: 953, 954, 955, 956, 957, and 958, respectively. In some cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences each comprising at most one mutation relative to the amino acid sequences of SEQ ID NOs: 953, 954, 955, 956, 957, and 958, respectively. In some embodiments, the anti-FGFR2 antibody comprises a heavy chain variable region comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 959 and a light chain variable region comprising an amino acid sequence that is at least 80% at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 960.

[0616] In some embodiments, the L moiety of compound 3.1 comprises an antibody that binds to CDCP1. In some cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences comprising at least 80% sequence identity, at least 85% sequence identity, at least 90% sequence identity, or at least 95% sequence identity to the amino acid sequences of SEQ ID NOs: 961, 962, 963, 964, 965, and 966, respectively. In some cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences each comprising at most one mutation relative to the amino acid sequences of SEQ ID NOs: 969, 970, 971, 972, 973, and 974, respectively. In some cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences comprising at least 80% sequence identity, at least 85% sequence identity, at least

90% sequence identity, or at least 95% sequence identity to the amino acid sequences of SEQ ID NOs: 961, 962, 963, 964, 965, and 966, respectively. In some cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences each comprising at most one mutation relative to the amino acid sequences of SEQ ID NOs: 969, 970, 971, 972, 973, and 974, respectively. In some cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences comprising at least 80% sequence identity, at least 85% sequence identity, at least 90% sequence identity, or at least 95% sequence identity to the amino acid sequences of SEQ ID NOs: 977, 978, 979, 980, 981, and 982, respectively. In some cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences each comprising at most one mutation relative to the amino acid sequences of SEQ ID NOs: 977, 978, 979, 980, 981, and 982, respectively. In some cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences comprising at least 80% sequence identity, at least 85% sequence identity, at least 90% sequence identity, or at least 95% sequence identity to the amino acid sequences of SEQ ID NOs: 985, 986, 987, 988, 989, and 990, respectively. In some cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences each comprising at most one mutation relative to the amino acid sequences of SEQ ID NOs: 985, 986, 987, 988, 989, and 990, respectively. In some embodiments, the anti-CDCP1 antibody comprises a heavy chain variable region comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 967 and a light chain variable region comprising an amino acid sequence that is at least 80% at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 968. In some embodiments, the anti-CDCP1 antibody comprises a heavy chain variable region comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 975 and a light chain variable region comprising an amino acid sequence that is at least 80% at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 976. In some embodiments, the anti-CDCP1 antibody comprises a heavy chain variable region comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 983 and a light chain variable region comprising an amino acid sequence that is at least 80% at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 984. In some embodiments, the anti-CDCP1 antibody comprises a heavy chain

variable region comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 991 and a light chain variable region comprising an amino acid sequence that is at least 80% at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 992.

[0617] In some embodiments, the L moiety of compound 3.1 comprises an antibody that binds to ASCT2. In some such cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences comprising at least 80% sequence identity, at least 85% sequence identity, at least 90% sequence identity, or at least 95% sequence identity to the amino acid sequences of SEQ ID NOs: 997, 998, 999, 1000, 1001, and 1002, respectively. In some cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences each comprising at most one mutation relative to the amino acid sequences of SEQ ID NOs: 997, 998, 999, 1000, 1001, and 1002, respectively. In some embodiments, the anti-ASCT2 antibody comprises a heavy chain variable region comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 993 and a light chain variable region comprising an amino acid sequence that is at least 80% at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 994. In some embodiments, the anti-ASCT2 antibody comprises a heavy chain variable region comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 995 and a light chain variable region comprising an amino acid sequence that is at least 80% at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 996. In some embodiments, the anti-ASCT2 antibody comprises a heavy chain variable region comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 1003 and a light chain variable region comprising an amino acid sequence that is at least 80% at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 1004.

[0618] In some embodiments, the L moiety of compound 3.1 comprises an antibody that binds to CD123. In some such cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences comprising at least 80% sequence identity, at least 85% sequence identity, at least 90% sequence identity, or at least 95% sequence identity

to the amino acid sequences of SEQ ID NOs: 1005, 1006, 1007, 1008, 1009, and 1010, respectively. In some cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences each comprising at most one mutation relative to the amino acid sequences of SEQ ID NOs: 1005, 1006, 1007, 1008, 1009, and 1010, respectively. In some embodiments, the anti-CD123 antibody comprises a heavy chain variable region comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 1011 and a light chain variable region comprising an amino acid sequence that is at least 80% at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 1012.

[0619] In some embodiments, the L moiety of compound 3.1 comprises an antibody that binds to GPC3. In some such cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences comprising at least 80% sequence identity, at least 85% sequence identity, at least 90% sequence identity, or at least 95% sequence identity to the amino acid sequences of SEQ ID NOs: 1013, 1014, 1015, 1016, 1017, and 1018 respectively. In some cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences each comprising at most one mutation relative to the amino acid sequences of SEQ ID NOs: 1013, 1014, 1015, 1016, 1017, and 1018, respectively. In some embodiments, the anti-TIGIT antibody comprises a heavy chain variable region comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 1027 and a light chain variable region comprising an amino acid sequence that is at least 80% at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 1028.

[0620] In some embodiments, the L moiety of compound 3.1 comprises an antibody that binds to TIGIT. In some such cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences comprising at least 80% sequence identity, at least 85% sequence identity, at least 90% sequence identity, or at least 95% sequence identity to the amino acid sequences of SEQ ID NOs: 1021, 1022, 1023, 1024, 1025, and 1026, respectively. In some cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences each comprising at most one mutation relative to the amino acid sequences of SEQ ID NOs: 1021, 1022, 1023, 1024, 1025, and 1026, respectively. In some embodiments, the anti-BCMA antibody comprises a heavy chain variable region

comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 1043 and a light chain variable region comprising an amino acid sequence that is at least 80% at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 1044.

[0621] In some embodiments, the L moiety of compound 3.1 comprises an antibody that binds to CD33. In some such cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences comprising at least 80% sequence identity, at least 85% sequence identity, at least 90% sequence identity, or at least 95% sequence identity to the amino acid sequences of SEQ ID NOs: 1029, 1030, 1031, 1032, 1033, and 1034, respectively. In some cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences each comprising at most one mutation relative to the amino acid sequences of SEQ ID NOs: 1029, 1030, 1031, 1032, 1033, and 1034, respectively. In some embodiments, the anti-CD33 antibody comprises a heavy chain variable region comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 1035 and a light chain variable region comprising an amino acid sequence that is at least 80% at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 1036.

[0622] In some embodiments, the L moiety of compound 3.1 comprises an antibody that binds to BCMA. In some such cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences comprising at least 80% sequence identity, at least 85% sequence identity, at least 90% sequence identity, or at least 95% sequence identity to the amino acid sequences of SEQ ID NOs: 1037, 1038, 1039, 1040, 1041, and 1042, respectively. In some cases, the antibody comprises CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 sequences each comprising at most one mutation relative to the amino acid sequences of SEQ ID NOs: 1037, 1038, 1039, 1040, 1041, and 1042, respectively. In some embodiments, the anti-BCMA antibody comprises a heavy chain variable region comprising an amino acid sequence that is at least 80%, at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 1043 and a light chain variable region comprising an amino acid sequence that is at least 80% at least 85%, at least 90%, at least 95%, at least 98%, or 99% identical to the amino acid sequence of SEQ ID NO: 1044.

[0623] Throughout this application, unless the context indicates otherwise, references to a compound of Formula (I), (I'), (I*), (II), or any subformula thereof, includes all subgroups of Formula (I), (I'), (I*), (II), or any subformula thereof, defined herein, including all substructures, subgenera, preferences, embodiments, examples and particular compounds defined and/or described herein. References to a compound of Formula (I), (I'), (I*), (II), or any subformula thereof, include ionic forms, polymorphs, pseudopolymorphs, amorphous forms, solvates, co-crystals, chelates, isomers, tautomers, oxides (e.g., N-oxides, S-oxides), esters, prodrugs, isotopes and/or protected forms thereof. In some embodiments, references to a compound of Formula (I), (I'), (I*), (II), or any subformula thereof, include polymorphs, solvates, co-crystals, isomers, tautomers and/or oxides thereof. In some embodiments, references to a compound of Formula (I), (I'), (I*), (II), or any subformula thereof, include polymorphs, solvates, and/or co-crystals thereof. In some embodiments, references to a compound of Formula (I), (I'), (I*), (II), or any subformula thereof, include isomers, tautomers and/or oxides thereof. In some embodiments, references to a compound of Formula (I), (I'), (I*), (II), or any subformula thereof, include solvates thereof. Similarly, the term "salts" includes solvates of salts of compounds.

[0624] Any formula given herein, such as Formula (I), (I'), (I*), (II), or any subformula thereof, is intended to represent compounds having structures depicted by the structural formula as well as certain variations or forms. In particular, compounds of any formula given herein may have asymmetric centers and therefore exist in different enantiomeric or diastereomeric forms. All optical isomers and stereoisomers of the compounds of the general formula, and mixtures thereof in any ratio, are considered within the scope of the formula. Thus, any formula given herein is intended to represent a racemate, one or more enantiomeric forms, one or more diastereomeric forms, one or more atropisomeric forms, and mixtures thereof in any ratio. Where a compound of one of Tables 1, 2, or 3 is depicted with a particular stereochemical configuration, also provided herein is any alternative stereochemical configuration of the compound, as well as a mixture of stereoisomers of the compound in any ratio. For example, where a compound of Tables 1, 2, or 3 has a stereocenter that is in an "S" stereochemical configuration, also provided herein is enantiomer of the compound wherein that stereocenter is in an "R" stereochemical configuration. Likewise, when a compound of Tables 1, 2, or 3 has a stereocenter that is in an "R" configuration, also provided herein is enantiomer of the compound in an "S" stereochemical configuration. Also provided are mixtures of the compound with both the "S"

and the "R" stereochemical configuration. Additionally, if a compound of Tables 1, 2, or 3 has two or more stereocenters, also provided are any enantiomer or diastereomer of the compound. For example, if a compound of Tables 1, 2, or 3 contains a first stereocenter and a second stereocenter with "R" and "R" stereochemical configurations, respectively, also provided are stereoisomers of the compound having first and second stereocenters with "S" and "S" stereochemical configurations, respectively, "S" and "R" stereochemical configurations, respectively, and "R" and "S" stereochemical configurations, respectively. If a compound of Tables 1, 2, or 3 contains a first stereocenter and a second stereocenter with "S" and "S" stereochemical configurations, respectively, also provided are stereoisomers of the compound having first and second stereocenters with "R" and "R" stereochemical configurations, respectively, "S" and "R" stereochemical configurations, respectively, and "R" and "S" stereochemical configurations, respectively. If a compound of Tables 1, 2, or 3 contains a first stereocenter and a second stereocenter with "S" and "R" stereochemical configurations, respectively, also provided are stereoisomers of the compound having first and second stereocenters with "R" and "S" stereochemical configurations, respectively, "R" and "R" stereochemical configurations, respectively, and "S" and "S" stereochemical configurations, respectively. Similarly, if a compound of Tables 1, 2, or 3 contains a first stereocenter and a second stereocenter with "R" and "S" stereochemical configurations, respectively, also provided are stereoisomers of the compound having first and second stereocenters with "S" and "R" stereochemical configurations, respectively, "R" and "R" stereochemical configurations, respectively, and "S" and "S" stereochemical configurations, respectively. Furthermore, certain structures may exist as geometric isomers (i.e., *cis* and *trans* isomers), as tautomers, or as atropisomers. Additionally, any formula given herein is intended to refer also to any one of hydrates, solvates, and amorphous and polymorphic forms of such compounds, and mixtures thereof, even if such forms are not listed explicitly. In some embodiments, the solvent is water and the solvates are hydrates.

[0625] The compounds depicted herein may be present as salts even if salts are not depicted, and it is understood that the compositions and methods provided herein embrace all salts and solvates of the compounds depicted here, as well as the non-salt and non-solvate form of the compound, as is well understood by the skilled artisan. In some embodiments, the salts of the compounds provided herein are pharmaceutically acceptable salts.

[0626] Embodiments are contemplated wherein any variation or embodiment of Q, D, Z or Z', A, B, S*, RL, Y, W, L, Z^a, X^b, R^1, R^2, R^3, R^4, R^5, R^6, R^7, R^8, R^9, R^{10}, R^a, R^b, E, X,

subscript n, subscript n, subscript q, and/or subscript p provided herein is combined with every other variation or embodiment of Q, D, Z or Z', A, B, S*, RL, Y, W, L, Z^a, X^b, R^1, R^2, R^3, R^4, R^5, R^6, R^7, R^8, R^9, R^{10}, R^a, R^b, E, X, subscript n, subscript n, subscript q, and/or subscript p, as if each combination had been individually and specifically described.

[0627] In some embodiments, any of the compounds described herein, such as a compound of Formula (I), (I'), (I*), (II), or any subformula thereof, or a compound of any one of Tables 1, 2 or 3, or a salt of any of the foregoing, may be deuterated (e.g., a hydrogen atom is replaced by a deuterium atom). In some of these variations, the compound is deuterated at a single site. In other variations, the compound is deuterated at multiple sites. Deuterated compounds are sometimes prepared from deuterated starting materials in a manner similar to the preparation of the corresponding non-deuterated compounds. In some aspects, hydrogen atoms are be replaced with deuterium atoms using other methods known in the art.

[0628] Other embodiments will be apparent to those skilled in the art from the following detailed description.

[0629] As used herein, when any variable occurs more than one time in a chemical formula, its definition on each occurrence is independent of its definition at every other occurrence.

Other exemplary ligand-drug conjugates

[0630] gpNMB is a type 1 transmembrane protein that has been shown to be pro-metastatic, and high expression is correlated with worse cancer patient survival. Taya et al., Steroids, 2017, 133:102. It is expressed in many cancer indications, including melanoma, squamous non-small-cell lung cancer (sqNSCLC), Head and Neck, and esophageal cancers. An antibody-drug conjugate, glembatumumab vedotin, was in melanoma and breast cancer clinical trials, but activity was limited by off target toxicities at the MTD (Ott et al., Cancer, 2019, 125:1113). Therefore, the present inventors conceived that a gpNMB-targeted antibody-drug conjugate would pair well with a payload with an improved therapeutic index.

[0631] Thus, provided herein are ligand-drug conjugates, such as of compound 3.1, wherein the L moiety is an anti-gpNMB antibody, or antigen-binding fragment thereof.

[0632] The antibody, or antigen-binding fragment thereof, in some embodiments bind to gpNMB with an affinity (e.g., EC_{50}) of less than 10 nM, 5 nM, 2 nM, 1 nM, 500 pM, 250 pM, 100 pM, 50 pM, 25 pM, 10 pM, or 1 pM. In some embodiments, the antibody, or

antigen-binding fragment thereof, binds to gpNMB with an affinity of between 5-10 nM, 1-5 nM, 500 pM – 1 nM, 100 – 250 pM, 50 – 100 pM, 10-50 pM, or 1-10 pM.

[0633] In some embodiments, the antibody, or antigen-binding fragment thereof, comprises the CDRs, the varianble domains, and/or the heavy and light chain amino acid sequences as indicated in Table D1 and D2, below.

Table D1. Exemplary anti-gpNMB antibody CDR sequences.

SEQ ID NO	Description	Sequence
935	Anti-gpNMB CDR-H1	SFNYYWS
936	Anti-gpNMB CDR-H2	YIYYSGSTYSNPSLKS
937	Anti-gpNMB CDR-H3	GYNWNYFDY
938	Anti-gpNMB CDR-L1	RASQSVDNNLV
939	Anti-gpNMB CDR-L2	GASTRAT
940	Anti-gpNMB CDR-L3	QQYNNWPPWT

Table D2. Exemplary anti-gpNMB variable domain, light chain, and heavy chain sequences.

Description	Sequence (SEQ ID NO)
Anti-gpNMB variable heavy (VH)	QVQLQESGPGLVKPSQTLSLTCTVSGGSISSFNYYWS WIRHHPGKGLEWIGYIYYSGSTYSNPSLKSRVTISVDT SKNQFSLTLSSVTAADTAVYYCARGYNWNYFDYWG QGTLVTVSS (SEQ ID NO:941)
Anti-gpNMB variable light (VL)	EIVMTQSPATLSVSPGERATLSCRASQSVDNNLVWYQ QKPGQAPRLLIYGASTRATGIPARFSGSGSGTEFTLTIS SLQSEDFAVYYCQQYNNWPPWTFGQGTKVEIK (SEQ ID NO:942)
Anti-gpNMB heavy chain	QVQLQESGPGLVKPSQTLSLTCTVSGGSISSFNYYWS WIRHHPGKGLEWIGYIYYSGSTYSNPSLKSRVTISVDT SKNQFSLTLSSVTAADTAVYYCARGYNWNYFDYWG QGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLV KDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLS SVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSC DKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEV TCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREE QYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALP APIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTC LVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSF FLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKS LSLSPGK (SEQ ID NO:943)
Anti-gpNMB light chain	EIVMTQSPATLSVSPGERATLSCRASQSVDNNLVWYQ QKPGQAPRLLIYGASTRATGIPARFSGSGSGTEFTLTIS SLQSEDFAVYYCQQYNNWPPWTFGQGTKVEIKRTVA APSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQW KVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKAD

	YEKHKVYACEVTHQGLSSPVTKSFNRGEC (SEQ ID NO:944)

[0634] Certain of the antibodies, or antigen-binding fragments thereof, disclosed herein comprise the 6 CDRs as follows: a CDR-H1, a CDR-H2, a CDR-H3, a CDR-L1, a CDR-L2, and a CDR-L3 comprising the amino acid sequences of SEQ ID NOs:935-940, respectively.

[0635] Some of the antibodies, or antigen-binding fragments thereof, disclosed herein comprise a VH comprising the amino acid sequence of SEQ ID NO:941 and a VL comprising the amino acid sequence of SEQ ID NO:942.

[0636] Some of the antibodies, or antigen-binding fragments thereof, disclosed herein comprise a HC comprising the amino acid sequence of SEQ ID NO:943 and a LC comprising the amino acid sequence of SEQ ID NO:944.

[0637] In other embodiments, the antibody, or antigen-binding fragment thereof, that are provided include or are derived from one or more of the CDRs, variable heavy chains, variable light chains, heavy chains, and/or light chains of the antibodies listed in Tables D1 and D2, or variants or derivatives thereof.

[0638] Certain of the antibodies, or antigen-binding fragments thereof, disclosed herein comprise the 6 CDRs as follows: a CDR-H1, a CDR-H2, a CDR-H3 from the variable heavy chain sequence comprising the amino acid sequence of SEQ ID NO:941, and a CDR-L1, a CDR-L2, and a CDR-L3 from the variable light chain sequence comprising the amino acid sequence of SEQ ID NO:942, wherein the CDRs are defined by the IMGT CDR numbering scheme.

[0639] Certain of the antibodies, or antigen-binding fragments thereof, disclosed herein comprise the 6 CDRs as follows: a CDR-H1, a CDR-H2, a CDR-H3 from the variable heavy chain sequence comprising the amino acid sequence of SEQ ID NO:941, and a CDR-L1, a CDR-L2, and a CDR-L3 from the variable light chain sequence comprising the amino acid sequence of SEQ ID NO:942, wherein the CDRs are defined by the Kabat CDR numbering scheme.

[0640] Certain of the antibodies, or antigen-binding fragments thereof, disclosed herein comprise the 6 CDRs as follows: a CDR-H1, a CDR-H2, a CDR-H3 from the variable heavy chain sequence comprising the amino acid sequence of SEQ ID NO:941, and a CDR-L1, a CDR-L2, and a CDR-L3 from the variable light chain sequence comprising the amino acid

sequence of SEQ ID NO:942, wherein the CDRs are defined by the AbM CDR numbering scheme.

[0641] Certain of the antibodies, or antigen-binding fragments thereof, disclosed herein comprise the 6 CDRs as follows: a CDR-H1, a CDR-H2, a CDR-H3 from the variable heavy chain sequence comprising the amino acid sequence of SEQ ID NO:941, and a CDR-L1, a CDR-L2, and a CDR-L3 from the variable light chain sequence comprising the amino acid sequence of SEQ ID NO:942, wherein the CDRs are defined by the Chothia CDR numbering scheme.

[0642] Certain of the antibodies, or antigen-binding fragments thereof, disclosed herein comprise the 6 CDRs as follows: a CDR-H1, a CDR-H2, a CDR-H3 from the variable heavy chain sequence comprising the amino acid sequence of SEQ ID NO:941, and a CDR-L1, a CDR-L2, and a CDR-L3 from the variable light chain sequence comprising the amino acid sequence of SEQ ID NO:942, wherein the CDRs are defined by the Contact CDR numbering scheme.

[0643] Certain of the antibodies, or antigen-binding fragments thereof, disclosed herein comprise a VH comprising a CDR-H1, a CDR-H2, and a CDR-H3, wherein the CDRs of the VH collectively have at most 1, 2, 3, 4, or 5 amino acid changes relative to a corresponding CDR reference sequence, and wherein the CDR-H1 reference sequence has the amino acid sequence of SEQ ID NO:935, the CDR-H2 reference sequence has the amino acid sequence of SEQ ID NO:936, and the CDR-H3 reference sequence has the amino acid sequence of SEQ ID NO:937. In such embodiments, the amino acid changes typically are insertions, deletions and/or substitutions. In some of these embodiments, the collective number of amino acid changes are 1-3; in other embodiments, the collective number of amino acid changes are 1 or 2. In certain of the foregoing embodiments, the changes are conservative amino acid substitutions.

[0644] Certain of the antibodies, or antigen-binding fragments thereof, disclosed herein comprise a VL comprising a CDR-L1, a CDR-L2, and a CDR-L3, wherein the CDRs of the VL collectively have at most 1, 2, 3, 4, or 5 amino acid changes relative to a corresponding CDR reference sequence, and wherein the CDR-L1 reference sequence has the amino acid sequence of SEQ ID NO:938, the CDR-L2 reference sequence has the amino acid sequence of SEQ ID NO:939, and the CDR-L3 reference sequence has the amino acid sequence of SEQ ID NO:940. In such embodiments, the amino acid changes typically are insertions,

deletions and/or substitutions. In some of these embodiments, the collective number of amino acid changes are 1-3; in other embodiments, the collective number of amino acid changes are 1 or 2. In certain of the foregoing embodiments, the changes are conservative amino acid substitutions.

[0645] Certain of the antibodies, or antigen-binding fragments thereof, disclosed herein comprise a VH comprising a CDR-H1, a CDR-H2, and a CDR-H3, wherein the CDRs of the VH collectively have at most 1, 2, 3, 4, or 5 amino acid changes relative to a corresponding CDR reference sequence, and wherein the CDR-H1 reference sequence has the amino acid sequence of SEQ ID NO:935, the CDR-H2 reference sequence has the amino acid sequence of SEQ ID NO:936, and the CDR-H3 reference sequence has the amino acid sequence of SEQ ID NO:937; and a VL comprising a CDR-L1, a CDR-L2, and a CDR-L3, wherein the CDRs of the VL collectively have at most 1, 2, 3, 4, or 5 amino acid changes relative to a corresponding CDR reference sequence, and wherein the CDR-L1 reference sequence has the amino acid sequence of SEQ ID NO:938, the CDR-L2 reference sequence has the amino acid sequence of SEQ ID NO:939, and the CDR-L3 reference sequence has the amino acid sequence of SEQ ID NO:940. In such embodiments, the amino acid changes typically are insertions, deletions and/or substitutions. In some of these embodiments, the collective number of amino acid changes are 1-3; in other embodiments, the collective number of amino acid changes are 1 or 2. In certain of the foregoing embodiments, the changes are conservative amino acid substitutions.

[0646] In some embodiments, the antibody, or antigen-binding fragment thereof, comprises a VH domain, wherein the VH domain sequence has at least 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% sequence identity to the amino acid sequence of SEQ ID NO:941, provided the antibody, or antigen-binding fragment thereof, retains the ability to bind to gpNMB. In certain embodiments, such an antibody, or antigen-binding fragment thereof, contains substitutions (*e.g.*, conservative substitutions), insertions, and/or deletions relative to the reference sequence (*i.e.*, SEQ ID NO:941), provided that such an antibody, or antigen-binding fragment thereof, retains the ability to bind to gpNMB. In certain embodiments, 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 amino acids have been substituted, inserted and/or deleted in SEQ ID NO:941. In some embodiments, 1-5 or 1-3 amino acids have been substituted, inserted and/or deleted in the VH sequence. In certain of these embodiments, such substitutions, insertions, or deletions occur in regions outside the CDRs (*i.e.*, in the framework regions).

[0647] In some embodiments, the antibody, or antigen-binding fragment thereof, comprises a VL domain, wherein the VL domain sequence has at least 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% sequence identity to the amino acid sequence of SEQ ID NO:942, provided the antibody, or antigen-binding fragment thereof, retains the ability to bind to gpNMB. In certain embodiments, such an antibody, or antigen-binding fragment thereof, contains substitutions (*e.g.*, conservative substitutions), insertions, and/or deletions relative to the reference sequence (*i.e.*, SEQ ID NO:942), provided that such an antibody, or antigen-binding fragment thereof, retains the ability to bind to gpNMB. In certain embodiments, 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 amino acids have been substituted, inserted and/or deleted in SEQ ID NO:942. In some embodiments, 1-5 or 1-3 amino acids have been substituted, inserted and/or deleted in the VL sequence. In certain of these embodiments, such substitutions, insertions, or deletions occur in regions outside the CDRs (*i.e.*, in the framework regions).

[0648] In some embodiments, the antibody, or antigen-binding fragment thereof, comprises: a VH domain, wherein the VH domain sequence has at least 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% sequence identity to the amino acid sequence of SEQ ID NO:941, provided the antibody, or antigen-binding fragment thereof, retains the ability to bind to gpNMB; and a VL domain, wherein the VL domain sequence has at least 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% sequence identity to the amino acid sequence of SEQ ID NO:942, provided the antibody, or antigen-binding fragment thereof, retains the ability to bind to gpNMB. In certain embodiments, such an antibody, or antigen-binding fragment thereof, contains substitutions (*e.g.*, conservative substitutions), insertions, and/or deletions relative to the reference sequence (*i.e.*, SEQ ID NO:941 for the VH domain and SEQ ID NO:942 for the VL domain), provided that such an antibody, or antigen-binding fragment thereof, retains the ability to bind to gpNMB. In certain embodiments, 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 amino acids have been substituted, inserted and/or deleted in the VH and/or the VL sequence. In some embodiments, 1-5 or 1-3 amino acids have been substituted, inserted and/or deleted in the VH and/or VL sequence. In other embodiments, 1-5 or 1-3 amino acids have been substituted, inserted and/or deleted in the VH and VL sequence collectively. In certain of these embodiments, such substitutions, insertions, or deletions occur in regions outside the CDRs (*i.e.*, in the FRs).

[0649] In a further embodiment, an antibody, or antigen-binding fragment thereof, comprises an HC comprising the amino acid sequence of SEQ ID NO:943, and a LC comprising the amino acid sequence of SEQ ID NO:944.

[0650] The antibody, or antigen-binding fragment thereof, as described herein can be an antibody in any form. As such, the antibody, or antigen-binding fragment thereof, described in any of the above embodiments can be monoclonal, and may be multispecific, human, humanized or chimeric antibodies, single chain antibodies, Fab fragments, F(ab') fragments, fragments produced by a Fab expression library, and gpNMB-binding fragments of any of the above. The antibodies can be of any immunoglobulin isotype (*e.g.*, IgG, IgE, IgM, IgD, IgA and IgY), class (e.g., IgG1, IgG2, IgG3, IgG4, IgA1 and IgA2) or subclass.

[0651] In certain embodiments, an antibody, or antigen-binding fragment thereof, with the CDRs and/or variable domain sequences described herein is an antigen-binding fragment (*e.g.*, human antigen-binding fragments) including, but are not limited to, Fab, Fab' and $F(ab')_2$, Fd, single-chain Fvs (scFv), single-chain antibodies, disulfide-linked Fvs (sdFv) and fragments comprising either a VL or VH domain.

[0652] The antibody, or antigen-binding fragment thereof, can be monospecific or part of a bispecific or trispecific antibody, or antigen-binding fragments thereof, or part of an antibody, or antigen-binding fragment thereof, of greater multi-specificity. Multispecific antibodies can be specific for different epitopes of gpNMB or may be specific for both gpNMB and a heterologous protein.

[0653] The antibodies, or antigen-binding fragments thereof, in any of the foregoing embodiments can be an antibody in any form. As such, the antibody, or antigen-binding fragment thereof, described in any of the above embodiments can be, for example, a monoclonal antibody, a multispecific antibody, a human, humanized or chimeric antibody, and gpNMB binding fragments of any of the above, such as a single chain antibody, an Fab fragment, an F(ab') fragment, or a fragment produced by a Fab expression library. The antibodies can be of any immunoglobulin isotype (*e.g.*, IgG, IgE, IgM, IgD, IgA and IgY), class (e.g., IgG1, IgG2, IgG3, IgG4, IgA1 and IgA2) or subclass.

[0654] In certain embodiments, a antibody, or antigen-binding fragment thereof, with the CDR and/or variable domain sequences described herein is an antigen-binding fragment (*e.g.*, human antigen-binding fragments) and include, but are not limited to, Fab, Fab' and F(ab')2, Fd, single-chain Fvs (scFv), single-chain antibodies, disulfide-linked Fvs (sdFv) and

fragments comprising either a VL or VH domain. Antigen-binding fragments, including single-chain antibodies, may comprise the variable region(s) alone or in combination with the entirety or a portion of the following: hinge region, CH1, CH2, CH3 and CL domains. Also included in the present disclosure are antigen-binding fragments comprising any combination of variable region(s) with a hinge region, CH1, CH2, CH3 and CL domains.

[0655] The antibody, or antigen-binding fragment thereof, can be monospecific, bispecific, trispecific or of greater multi specificity. Multispecific antibodies can be specific for different epitopes of gpNMB or may be specific for both gpNMB as well as for a heterologous protein. See, *e.g.*, PCT publications WO 93/17715; WO 92/08802; WO 91/00360; WO 92/05793; Tutt, et al., 1991, *J. Immunol.* 147:60 69; U.S. Pat. Nos. 4,474,893; 4,714,681; 4,925,648; 5,573,920; 5,601,819; and Kostelny et al., 1992, J. Immunol. 148:1547 1553.

[0656] In any of the embodiments described herein, one or several amino acids (*e.g.*, 1, 2, 3 or 4) at the amino or carboxy terminus of the light and/or heavy chain, such as the C-terminal lysine of the heavy chain, may be missing or derivitized in some or all of the molecules in a composition. One specific example of such a modification, is an antibody, or antigen-binding fragment thereof, in which the carboxy terminal lysine of the heavy chain is missing (*e.g.*, as part of a post-translational modification). Furthermore, it should be understood that any of the sequences described herein include post-translational modifications to the specified sequence during expression of the antibody, or antigen-binding fragment thereof, in cell culture (*e.g.*, a CHO cell culture).

[0657] In other embodiments, the moiety L of compound 3.1 is not an antibody or antigen-binding fragment thereof but instead comprises a non-antibody scaffold into which one or more CDRs (*e.g.*, 1, 2, 3, 4, 5 or 6) and/or one or more variable domains as described herein is grafted, inserted, and/or joined.

Chimeric Antibody, or an Antigen-Binding Fragment thereof

[0658] In certain embodiments, the antibody, or antigen-binding fragment thereof, such as the antibody, or antigen-binding fragment thereof, which is the L moiety of compound 3.1, provided herein is a chimeric antibody. In some embodiments, a chimeric antibody comprises a non-human variable region (*e.g.*, a variable region derived from a mouse, rat, hamster, rabbit, or non-human primate, such as a monkey) and a human constant region. In a further example, a chimeric antibody is a "class switched" antibody in which the class or

subclass has been changed from that of the parent antibody. Certain chimeric antibodies are described, *e.g.*, in U.S. Patent No. 4,816,567; and Morrison *et al.*, (1984) *Proc. Natl. Acad. Sci. USA*, 81 :6851-6855 (1984)). Chimeric antibodies include antigen-binding fragments thereof. Nonlimiting exemplary chimeric antibodies include chimeric antibodies comprising any of the heavy and/or light chain variable regions as described herein. Additional nonlimiting exemplary chimeric antibodies include chimeric antibodies comprising heavy chain CDR sequences or portions thereof, and/or light chain CDR sequences as provided herein.

Humanized Antibody, or antigen-binding fragment thereof

[0659] In certain embodiments, the antibody, or antigen-binding fragment thereof, is a humanized antibody, or antigen-binding fragment thereof, that binds gpNMB. Typically, a non-human antibody is humanized to reduce immunogenicity to humans, while retaining the specificity and affinity of the parental non-human antibody. A humanized antibody is a genetically engineered antibody in which the CDRs or portions thereof from a non-human "donor" antibody are grafted into human "acceptor" antibody sequences (see, e.g., Queen, US 5,530,101 and 5,585,089; Winter, US 5,225,539; Carter, US 6,407,213; Adair, US 5,859,205; and Foote, US 6,881,557).

[0660] The acceptor antibody sequences can be, for example, a mature human antibody sequence, a composite of such sequences, a consensus sequence of human antibody sequences, or a germline region sequence. Human acceptor sequences can be selected for a high degree of sequence identity in the variable region frameworks with donor sequences to match canonical forms between acceptor and donor CDRs among other criteria. Thus, a humanized antibody is an antibody having CDRs entirely or substantially from a donor antibody and variable region framework sequences and constant regions, if present, entirely or substantially from human antibody sequences. Similarly, a humanized heavy chain typically has all three CDRs entirely or substantially from a donor antibody heavy chain, and a heavy chain variable region framework sequence and heavy chain constant region, if present, substantially from human heavy chain variable region framework and constant region sequences. Likewise, a humanized light chain usually has all three CDRs entirely or substantially from a donor antibody light chain, and a light chain variable region framework sequence and light chain constant region, if present, substantially from human light chain variable region framework and constant region sequences. A CDR in a humanized antibody is substantially from a corresponding CDR in a non-human antibody when at least 80%, 85%,

90%, 95% or 100% of corresponding residues (such as defined by Kabat) are identical between the respective CDRs. The variable region framework sequences of an antibody chain or the constant region of an antibody chain are substantially from a human variable region framework sequence or human constant region respectively when at least 80%, 85%, 90%, 95% or 100% of corresponding residues, such as defined by Kabat, are identical.

[0661] For example, when an amino acid differs between a murine variable region framework residue and a selected human variable region framework residue, the human framework amino acid can be substituted by the equivalent framework amino acid from the mouse antibody when it is reasonably expected that the amino acid:

(1) noncovalently binds antigen directly,

(2) is adjacent to a CDR region,

(3) otherwise interacts with a CDR region (e.g., is within about 6 Å of such a region);

(4) mediates interaction between the heavy and light chains, or

(5) is the result of somatic mutation in the mouse chain.

(6) is a site of glycosylation.

[0662] Framework residues from classes (1)-(3) are sometimes alternately referred to as canonical and vernier residues. Canonical residues refer to framework residues defining the canonical class of the donor CDR loops determining the conformation of a CDR loop (Chothia and Lesk, J. Mol. Biol. 196, 901-917 (1987), Thornton & Martin, J. Mol. Biol., 263, 800-815, 1996). Vernier residues refer to a layer of framework residues that support antigen-binding loop conformations and play a role in fine-tuning the fit of an antibody to antigen (Foote & Winter, 1992, J Mol Bio. 224, 487-499).

[0663] Humanized antibodies and methods of making them are reviewed, *e.g.*, in Almagro and Fransson, (2008) *Front. Biosci.* 13: 1619-1633, and are further described, *e.g.*, in Riechmann *et al.*, (1988) *Nature* 332:323-329; Queen *et al.*, (1989) *Proc. Natl Acad. Sci. USA* 86: 10029-10033; US Patent Nos. 5, 821,337, 7,527,791, 6,982,321, and 7,087,409; Kashmiri *et al.*, (2005) *Methods* 36:25-34 (describing specificity determining region (SDR) grafting); Padlan, (1991) *Mol. Immunol.* 28:489-498 (describing "resurfacing"); Dall'Acqua *et al.*, (2005) *Methods* 36:43-60 (describing "FR shuffling"); and Osbourn *et al.*, (2005)

Methods 36:61-68 and Klimka *et al.*, (2000) *Br. J. Cancer*, 83:252-260 (describing the "guided selection" approach to FR shuffling).

[0664] Human framework regions that may be used for humanization include but are not limited to: framework regions selected using the "best-fit" method (see, *e.g.*, Sims *et al.* (1993) *J. Immunol.* 151 :2296); framework regions derived from the consensus sequence of human antibodies of a particular subgroup of light or heavy chain variable regions (see, *e.g.*, Carter *et al.* (1992) *Proc. Natl. Acad. Sci. USA*, 89:4285; and Presta *et al.* (1993) *J. Immunol*, 151:2623); human mature (somatically mutated) framework regions or human germline framework regions (see, *e.g.*, Almagro and Fransson, (2008) *Front. Biosci.* 13:1619-1633); and framework regions derived from screening FR libraries (see, *e.g.*, Baca *et al.*, (1997) *J. Biol. Chem.* 272: 10678-10684 and Rosok *et al.*, (1996) *J. Biol. Chem.* 271 :22611-22618).

[0665] Non-limiting exemplary chimeric antibodies include chimeric antibodies comprising or derived from any of the CDR and/or heavy chain variable region and/or light chain variable regions as disclosed herein. .

[0666] Although humanized antibodies often incorporate all six HVRs (e.g., CDRs, preferably as defined by Kabat) from a mouse antibody, they can also be made with less than all HVRs or CDRs (*e.g.*, at least 3, 4, or 5) HVRs or CDRs from a mouse antibody (*e.g.*, Pascalis *et al.*, J. Immunol. 169:3076, 2002; Vajdos et al., Journal of Molecular Biology, 320: 415-428, 2002; Iwahashi *et al.*, Mol. Immunol. 36:1079-1091, 1999; and Tamura et al, Journal of Immunology, 164:1432-1441, 2000).

[0667] Certain amino acids from the human variable region framework residues can be selected for substitution based on their possible influence on HVR (e.g,.CDR) conformation and/or binding to antigen. Investigation of such possible influences is by modeling, examination of the characteristics of the amino acids at particular locations, or empirical observation of the effects of substitution or mutagenesis of particular amino acids.

Exemplary Antibody Constant Regions

[0668] In some embodiments, the heavy and light chain variable regions of antibodies, or antigen-binding fragments thereof, described herein can be linked to at least a portion of a human constant region. In some embodiments, the human heavy chain constant region is of an isotype selected from IgA, IgG, and IgD. In some embodiments, the human light chain constant region is of an isotype selected from κ and λ. In some embodiments, an antibody described herein comprises a human IgG constant region. In some embodiments, an antibody

described herein comprises a human IgG4 heavy chain constant region. In some of these embodiments, an antibody described herein comprises an S241P mutation in the human IgG4 constant region. In some embodiments, an antibody described herein comprises a human IgG4 constant region and a human κ light chain.

[0669] Throughout the present specification and claims unless explicitly stated or known to one skilled in the art, the numbering of the residues in an immunoglobulin heavy chain is that of the EU index as in Kabat *et al.*, *Sequences of Proteins of Immunological Interest*, 5th Ed. Public Health Service, National Institutes of Health, Bethesda, Md. (1991), expressly incorporated herein by reference. The "EU index as in Kabat" refers to the residue numbering of the human IgG1 EU antibody.

[0670] Human constant regions show allotypic variation and isoallotypic variation between different individuals, that is, the constant regions can differ in different individuals at one or more polymorphic positions. Isoallotypes differ from allotypes in that sera recognizing an isoallotype binds to a non-polymorphic region of a one or more other isotypes. Reference to a human constant region includes a constant region with any natural allotype or any permutation of residues occupying polymorphic positions in natural allotypes. Also, up to 1, 2, 5, or 10 mutations may be present relative to a natural human constant region, such as those indicated above to reduce Fcγ receptor binding or increase binding to FcRn.

[0671] In some embodiments, one or several amino acids at the amino or carboxy terminus of the light and/or heavy chain, such as the C-terminal lysine of the heavy chain, may be missing or derivatized in a proportion or all of the molecules.

[0672] The choice of constant region depends, in part, whether antibody-dependent cell-mediated cytotoxicity, antibody dependent cellular phagocytosis and/or complement dependent cytotoxicity are desired. For example, human isotopes IgG1 and IgG3 have strong complement-dependent cytotoxicity, human isotype IgG2 weak complement-dependent cytotoxicity and human IgG4 lacks complement-dependent cytotoxicity. Human IgG1 and IgG3 also induce stronger cell-mediated effector functions than human IgG2 and IgG4. Light chain constant regions can be lambda or kappa.

[0673] Furthermore, as described in greater detail below, substitutions can be made in the constant regions to reduce or increase effector function such as complement-mediated cytotoxicity or ADCC (see, e.g., Winter et al., US Patent No. 5,624,821; Tso et al., US Patent

No. 5,834,597; and Lazar et al., Proc. Natl. Acad. Sci. USA 103:4005, 2006), or to prolong half-life in humans (see, e.g., Hinton et al., J. Biol. Chem. 279:6213, 2004).

Variant Antibody or Antigen-Binding Fragments thereof

[0674] The antibodies, or antigen-binding fragments thereof, provided herein also include amino acid sequence variants of the antibody, or antigen-binding fragment thereof, provided herein such as those described in Table D1 and D2. As an example, variants with improved binding affinity and/or other biological properties of the antibody can be prepared. Amino acid sequence variants of an antigen binding protein can be prepared by introducing appropriate modifications into the nucleotide sequence encoding the antigen binding protein, or by peptide synthesis. Such modifications include, for example, deletions from, and/or insertions into and/or substitutions of residues within the amino acid sequences of the antigen binding protein. Any combination of deletion, insertion, and substitution can be made to arrive at the final construct, provided that the final construct possesses the desired characteristics, e.g., antigen-binding.

[0675] Substitution, insertion, and deletion variants. In some embodiments, an antibody, or antigen-binding fragment thereof, is a variant in that it has one or more amino acid substitutions, deletions and/or insertions relative to an antibody, or antigen-binding fragment thereof, as described herein (e.g., an antibody, or antigen-binding fragment thereof, having the amino acid sequences as described in Tables D1 and D2. In certain such embodiments, the variant has one or more amino acid substitutions. In further such embodiments, the substitutions are conservative amino acid substitutions.

[0676] An amino acid substitution can include but are not limited to the replacement of one amino acid in a polypeptide with another amino acid. Conservative amino acid substitutions can encompass non-naturally occurring amino acid residues, which are typically incorporated by chemical peptide synthesis rather than by synthesis in biological systems. Naturally occurring residues can be divided into classes based on common side chain properties.

(1) hydrophobic: Norleucine, Met, Ala, Val, Leu, Ile;

(2) neutral hydrophilic: Cys, Ser, Thr, Asn, Gln;

(3) acidic: Asp, Glu;

(4) basic: His, Lys, Arg;

(5) residues that influence chain orientation: Gly, Pro;

(6) aromatic: Trp, Tyr, Phe.

[0677] Sites of interest for substitutional mutagenesis include the CDRs and framework regions. Conservative substitutions are shown in Table D3, below, under the heading of "Preferred Substitutions." More substantial changes are provided in Table D3 under the heading of "Exemplary Substitutions," and as further described below in reference to amino acid side chain classes. Amino acid substitutions may be introduced into an antibody of interest and the products screened for a desired activity, e.g., retained/improved antigen binding, decreased immunogenicity, or improved ADCC or CDC.

Table D3. Conservative and Exemplary Amino Acid Substitutions.

Original Residue	Exemplary Substitutions	Preferred Substitutions
Ala	Val; Leu; Ile	Val
Arg	Lys; Gln; Asn	Lys
Asn	Gln; His; Asp; Lys; Arg	Gln
Asp	Glu; Asn	Glu
Cys	Ser; Ala	Ser
Gln	Asn; Glu	Asn
Glu	Asp; Gln	Asp
Gly	Pro; Ala	Ala
His	Asn; Gln; Lys; Arg	Arg
Ile	Leu; Val; Met; Ala; Phe; Norleucine	Leu
Leu	Norleucine; Ile; Val; Met; Ala; Phe	Ile
Lys	Arg; Gln; Asn	Arg
Met	Leu; Phe; Ile	Leu
Phe	Trp; Leu; Val; Ile; Ala; Tyr	Leu
Pro	Ala	Ala
Ser	Thr; Ala; Cys	Thr

Thr	Val; Ser	Ser
Trp	Tyr; Phe	Tyr
Tyr	Trp; Phe; Thr; Ser	Phe
Val	Ile; Leu; Met; Phe; Ala; Norleucine	Leu

[0678] Non-conservative substitutions involve exchanging a member of one of these classes for another class.

[0679] In altering the amino acid sequence of the antigen binding protein (e.g,. anti-gpNMB antibody or antigen-binding fragments thereof), in some embodiments the hydropathic index of amino acids can be considered. Each amino acid has been assigned a hydropathic index on the basis of its hydrophobicity and charge characteristics as follows: isoleucine (+4.5); valine (+4.2); leucine (+3.8); phenylalanine (+2.8); cysteine/cystine (+2.5); methionine (+1.9); alanine (+1.8); glycine (-0.4); threonine (-0.7); serine (-0.8); tryptophan (-0.9); tyrosine (-1.3); proline (-1.6); histidine (-3.2); glutamate (-3.5); glutamine (-3.5); aspartate (-3.5); asparagine (-3.5); lysine (-3.9); and arginine (-4.5).

[0680] The importance of the hydropathic amino acid index in conferring interactive biological function on a protein is understood in the art. Kyte *et al*., 1982, *J. Mol. Biol*., 157:105-131. It is known that certain amino acids can be substituted for other amino acids having a similar hydropathic index or score and still retain a similar biological activity. In making changes based upon the hydropathic index, in certain embodiments, the substitution of amino acids whose hydropathic indices are within ± 2 is included. In certain embodiments, those which are within ± 1 are included, and in certain embodiments, those within ± 0.5 are included.

[0681] It is also understood in the art that the substitution of like amino acids can be made effectively on the basis of hydrophilicity, particularly where the biologically functional protein or peptide (*e.g*., antibody) thus created is intended for use in immunological embodiments, as in the present case. In certain embodiments, the greatest local average hydrophilicity of a protein, as governed by the hydrophilicity of its adjacent amino acids, correlates with its immunogenicity and antigenicity, *i.e*., with a biological property of the protein.

[0682] The following hydrophilicity values have been assigned to these amino acid residues: arginine (+3.0); lysine (+3.0 ±1); aspartate (+3.0 ±1); glutamate (+3.0 ±1); serine (+0.3); asparagine (+0.2); glutamine (+0.2); glycine (0); threonine (-0.4); proline (-0.5 ±1); alanine (-0.5); histidine (-0.5); cysteine (-1.0); methionine (-1.3); valine (-1.5); leucine (-1.8); isoleucine (-1.8); tyrosine (-2.3); phenylalanine (-2.5) and tryptophan (-3.4). In making changes based upon similar hydrophilicity values, in certain embodiments, the substitution of amino acids whose hydrophilicity values are within ± 2 is included, in certain embodiments, those which are within ± 1 are included, and in certain embodiments, those within ± 0.5 are included. One can also identify epitopes from primary amino acid sequences on the basis of hydrophilicity. These regions are also referred to as "epitopic core regions."

[0683] Alterations (e.g., substitutions) can be made in CDRs, e.g., to improve antibody affinity. Such alterations can be made in CDR "hotspots," i.e., residues encoded by codons that undergo mutation at high frequency during the somatic maturation process (see, e.g., Chowdhury, Methods Mol. Biol. 207:179-196 (2008)), and/or residues that contact antigen, with the resulting variant VH or VL being tested for binding affinity. Affinity maturation by constructing and reselecting from secondary libraries has been described, e.g., in Hoogenboom et al. in Methods in Molecular Biology 178:1-37 (O'Brien et al., ed., Human Press, Totowa, N.J., (2001).) In some embodiments of affinity maturation, diversity is introduced into the variable genes chosen for maturation by any of a variety of methods (e.g., error-prone PCR, chain shuffling, or oligonucleotide-directed mutagenesis). A secondary library is then created. The library is then screened to identify any antibody variants with the desired affinity. Another method to introduce diversity involves hypervariable region (HVR)-directed approaches, in which several HVR residues (e.g., 4-6 residues at a time) are randomized. HVR residues involved in antigen binding may be specifically identified, e.g., using alanine scanning mutagenesis or modeling. CDR-H3 and CDR-L3 in particular are often targeted.

[0684] In certain embodiments, substitutions, insertions, or deletions can occur within one or more CDRs so long as such alterations do not substantially reduce the ability of the antibody to bind antigen. For example, conservative alterations (e.g., conservative substitutions as provided herein) that do not substantially reduce binding affinity may be made in CDRs. Such alterations may, for example, be outside of antigen contacting residues in the CDRs. In certain embodiments of the variant VH and VL sequences provided above,

each CDR either is unaltered, or contains no more than one, two or three amino acid substitutions.

[0685] A useful method for identification of residues or regions of an antibody that may be targeted for mutagenesis is called "alanine scanning mutagenesis" as described by Cunningham and Wells (1989) Science, 244:1081-1085. In this method, a residue or group of target residues (e.g., charged residues such as arg, asp, his, lys, and glu) are identified and replaced by a neutral or negatively charged amino acid (e.g., alanine or polyalanine) to determine whether the interaction of the antibody with antigen is affected. Further substitutions may be introduced at the amino acid locations demonstrating functional sensitivity to the initial substitutions. Alternatively, or additionally, a crystal structure of an antigen-antibody complex to identify contact points between the antibody and antigen. Such contact residues and neighboring residues may be targeted or eliminated as candidates for substitution. Variants may be screened to determine whether they contain the desired properties.

[0686] Amino acid sequence insertions include amino- and/or carboxyl-terminal fusions ranging in length from one residue to polypeptides containing a hundred or more residues, as well as intrasequence insertions of single or multiple amino acid residues. Examples of terminal insertions include an antibody with an N-terminal methionyl residue. Other insertional variants of the antibody molecule include the fusion to the N- or C-terminus of the antibody to an enzyme (e.g. for ADEPT) or a polypeptide which increases the serum half-life of the antibody.

Variants with Modified Fc Region

[0687] Antibodies with reduced effector function include those with substitution of one or more of Fc region residues 238, 265, 269, 270, 297, 327 and 329 (U.S. Pat. No. 6,737,056). Such Fc mutants include Fc mutants with substitutions at two or more of amino acid positions 265, 269, 270, 297 and 327, including the so-called "DANA" Fc mutant with substitution of residues 265 and 297 to alanine (U.S. Pat. No. 7,332,581).

[0688] In certain embodiments, an antibody variant is prepared that has improved or diminished binding to FcRs are described. (See, e.g., U.S. Pat. No. 6,737,056; WO 2004/056312, and Shields et al., J. Biol. Chem. 9(2): 6591-6604 (2001).) In some embodiments, an antibody variant comprises an Fc region with one or more amino acid substitutions which improve ADCC, e.g., substitutions at positions 298, 333, and/or 334 of

the Fc region (EU numbering of residues). For instance, a systemic substitution of solvent-exposed amino acids of human IgG1 Fc region has generated IgG variants with altered FcγR binding affinities (Shields *et al.*, 2001, *J. Biol. Chem.* 276:6591-604). When compared to parental IgG1, a subset of these variants involving substitutions at Thr256/Ser298, Ser298/Glu333, Ser298/Lys334, or Ser298/Glu333/Lys334 to Ala demonstrate increased in both binding affinity toward FcγR and ADCC activity (Shields *et al.*, 2001, *J. Biol. Chem.* 276:6591-604; Okazaki *et al.*, 2004, *J. Mol. Biol.* 336:1239-49).

[0689] In some embodiments, alterations are made in the Fc region to alter (i.e., either improved or diminished) Clq binding and/or Complement Dependent Cytotoxicity (CDC), e.g., as described in U.S. Pat. No. 6,194,551, WO 99/51642, and Idusogie et al. J. Immunol. 164: 4178-4184 (2000). For instance, complement fixation activity of antibodies (both C1q binding and CDC activity) can be improved by substitutions at Lys326 and Glu333 (Idusogie *et al.*, 2001, *J. Immunol.* 166:2571-2575). The same substitutions on a human IgG2 backbone can convert an antibody isotype that binds poorly to C1q and is severely deficient in complement activation activity to one that can both bind C1q and mediate CDC (Idusogie *et al.*, 2001, *J. Immunol.* 166:2571-75). Several other methods have also been applied to improve complement fixation activity of antibodies. For example, the grafting of an 18-amino acid carboxyl-terminal tail piece of IgM to the carboxyl-termini of IgG greatly enhances their CDC activity. This is observed even with IgG4, which normally has no detectable CDC activity (Smith *et al.*, 1995, *J. Immunol.* 154:2226-36). Also, substituting Ser444 located close to the carboxy-terminal of IgG1 heavy chain with Cys induced tail-to-tail dimerization of IgG1 with a 200-fold increase of CDC activity over monomeric IgG1 (Shopes *et al.*, 1992, *J. Immunol.* 148:2918-22). In addition, a bispecific diabody construct with specificity for C1q also confers CDC activity (Kontermann *et al.*, 1997, *Nat. Biotech.* 15:629-31).

[0690] Complement activity can be reduced by mutating at least one of the amino acid residues 318, 320, and 322 of the heavy chain to a residue having a different side chain, such as Ala. Other alkyl-substituted non-ionic residues, such as Gly, Ile, Leu, or Val, or such aromatic non-polar residues as Phe, Tyr, Trp and Pro in place of any one of the three residues also reduce or abolish C1q binding. Ser, Thr, Cys, and Met can be used at residues 320 and 322, but not 318, to reduce or abolish C1q binding activity. Replacement of the 318 (Glu) residue by a polar residue may modify but not abolish C1q binding activity. Replacing residue 297 (Asn) with Ala results in removal of lytic activity but only slightly reduces (about

three fold weaker) affinity for C1q. This alteration destroys the glycosylation site and the presence of carbohydrate that is required for complement activation. Any other substitution at this site also destroys the glycosylation site. The following mutations and any combination thereof also reduce C1q binding: D270A, K322A, P329A, and P311S (see WO 06/036291).

[0691] The half-life of an antibody as provided herein can be increased or decreased to modify its therapeutic activities. FcRn is a receptor that is structurally similar to MHC Class I antigen that non-covalently associates with β2-microglobulin. FcRn regulates the catabolism of IgGs and their transcytosis across tissues (Ghetie and Ward, 2000, *Annu. Rev. Immunol.* 18:739-766; Ghetie and Ward, 2002, *Immunol. Res.* 25:97-113). The IgG-FcRn interaction takes place at pH 6.0 (pH of intracellular vesicles) but not at pH 7.4 (pH of blood); this interaction enables IgGs to be recycled back to the circulation (Ghetie and Ward, 2000, *Ann. Rev. Immunol.* 18:739-766; Ghetie and Ward, 2002, *Immunol. Res.* 25:97-113). The region on human IgG_1 involved in FcRn binding has been mapped (Shields *et al.,* 2001, *J. Biol. Chem.* 276:6591-604). Alanine substitutions at positions Pro238, Thr256, Thr307, Gln311, Asp312, Glu380, Glu382, or Asn434 of human IgG1 enhance FcRn binding (Shields *et al.,* 2001, *J. Biol. Chem.* 276:6591-604). IgG1 molecules harboring these substitutions have longer serum half-lives. Consequently, these modified IgG_1 molecules may be able to carry out their effector functions, and hence exert their therapeutic efficacies, over a longer period of time compared to unmodified IgG_1. Other exemplary substitutions for increasing binding to FcRn include a Gln at position 250 and/or a Leu at position 428. Other studies have shown that binding of the Fc region to FcRn can be improved by introducing one or more substitutions at one or more the following Fc region residues: 238, 256, 265, 272, 286, 303, 305, 307, 311, 312, 317, 340, 356, 360, 362, 376, 378, 380, 382, 413, 424 or 434, e.g., substitution of Fc region residue 434 (see, e.g., U.S. Pat. No. 7,371,826; and US 7,361,740).

Antibody Variants with Modified Glycosylation

[0692] In certain embodiments, an antibody, or antigen-binding fragment thereof, as provided herein includes one or more modifications so as to increase or decrease the extent to which the antibody is glycosylated. Addition or deletion of glycosylation sites to an antibody can be conveniently accomplished by altering the amino acid sequence such that one or more glycosylation sites is created or removed.

[0693] Where the antibody comprises an Fc region, the carbohydrate attached thereto may be altered. Native antibodies produced by mammalian cells typically comprise a

branched, biantennary oligosaccharide that is generally attached by an N-linkage to Asn297 of the CH2 domain of the Fc region. See, e.g., Wright et al. TIBTECH 15:26-32 (1997). The oligosaccharide may include various carbohydrates, e.g., mannose, N-acetyl glucosamine (GlcNAc), galactose, and sialic acid, as well as a fucose attached to a GlcNAc in the "stem" of the biantennary oligosaccharide structure.

[0694] Engineering of this glycoform on IgG can significantly improve IgG-mediated ADCC. Addition of bisecting N-acetylglucosamine modifications (Umana *et al.*, 1999, *Nat. Biotechnol.* 17:176-180; Davies *et al.*, 2001, *Biotech. Bioeng.* 74:288-94) to this glycoform or removal of fucose (Shields *et al.*, 2002, *J. Biol. Chem.* 277:26733-40; Shinkawa *et al.*, 2003, *J. Biol. Chem.* 278:6591-604; Niwa *et al.*, 2004, *Cancer Res.* 64:2127-33) from this glycoform are two examples of IgG Fc engineering that improves the binding between IgG Fc and FcγR, thereby enhancing Ig-mediated ADCC activity. Antibodies including such substitutions or engineering are included in some of the embodiments provided herein.

[0695] In certain embodiments, antibodies are provided having a carbohydrate structure that lacks fucose attached (directly or indirectly) to an Fc region. For example, the amount of fucose in such antibody may be from 1% to 80%, from 1% to 65%, from 5% to 65% or from 20% to 40%. The amount of fucose is determined by calculating the average amount of fucose within the sugar chain at Asn297, relative to the sum of all glycostructures attached to Asn 297 (*e.g.*, complex, hybrid and high mannose structures) as measured by MALDI-TOF mass spectrometry, as described in WO 2008/077546, for example. Asn297 refers to the asparagine residue located at about position 297 in the Fc region (EU numbering of Fc region residues); however, Asn297 may also be located about ± 3 amino acids upstream or downstream of position 297, *i.e.*, between positions 294 and 300, due to minor sequence variations in antibodies. Such fucosylation variants may have improved ADCC function. See, *e.g.*, US Patent Publication Nos. US 2003/0157108 (Presta, L.); US 2004/0093621 (Kyowa Hakko Kogyo Co., Ltd). Examples of publications related to "defucosylated" or "fucose-deficient" antibody variants include: US 2003/0157108; WO 2000/61739; WO 2001/29246; US 2003/0115614; US 2002/0164328; US 2004/0093621; US 2004/0132140; US 2004/0110704; US 2004/0110282; US 2004/0109865; WO 2003/085119; WO 2003/084570; WO 2005/035586; WO 2005/035778; WO2005/053742; WO2002/031140; Okazaki *et al. J. Mol. Biol.* 336:1239-1249 (2004); Yamane-Ohnuki *et al. Biotech. Bioeng.* 87: 614 (2004). Examples of cell lines capable of producing defucosylated antibodies include Lec13 CHO cells deficient in protein fucosylation (Ripka *et al. Arch. Biochem. Biophys.*

249:533-545 (1986); US Patent Application No. US 2003/0157108 A1, Presta, L; and WO 2004/056312 A1, Adams *et al.*, especially at Example 11), and knockout cell lines, such as alpha-1,6-fucosyltransferase gene, FUT8, knockout CHO cells (see, e.g., Yamane-Ohnuki *et al. Biotech. Bioeng.* 87: 614 (2004); Kanda, Y. *et al., Biotechnol. Bioeng.*, 94(4):680-688 (2006); and WO2003/085107).

[0696] Other antibodies are further provided which contain bisected oligosaccharides, *e.g.*, in which a biantennary oligosaccharide attached to the Fc region of the antibody is bisected by GlcNAc. Such antibodies may have reduced fucosylation and/or improved ADCC function. Examples of such antibodies are described, *e.g.*, in WO 2003/011878 (Jean-Mairet *et al.*); US Patent No. 6,602,684 (Umana *et al.*); and US 2005/0123546 (Umana *et al.*). Antibodies with at least one galactose residue in the oligosaccharide attached to the Fc region are also provided. Such antibody variants may have improved CDC function. Such antibody variants are described, *e.g.*, in WO 1997/30087 (Patel *et al.*); WO 1998/58964 (Raju, S.); and WO 1999/22764 (Raju, S.).

Cysteine Engineered Antibody Variants

[0697] In some embodiments, an antibody variant as provided herein includes a substitution of the native amino acid to a cysteine residue at amino acid position 234, 235, 237, 239, 267, 298, 299, 326, 330, or 332, preferably an S239C mutation (substitutions of the constant regions are according to the EU index) in a human IgG1 isotype. The presence of an additional cysteine residue allows interchain disulfide bond formation. Such interchain disulfide bond formation can cause steric hindrance, thereby reducing the affinity of the Fc region-FcγR binding interaction. The cysteine residue(s) introduced in or in proximity to the Fc region of an IgG constant region can also serve as sites for conjugation to therapeutic agents (e.g., coupling cytotoxic drugs using thiol specific reagents such as maleimide derivatives of drugs). The presence of a therapeutic agent causes steric hindrance, thereby further reducing the affinity of the Fc region-FcγR binding interaction. Other substitutions at any of positions 234, 235, 236 and/or 237 reduce affinity for Fcγ receptors, particularly FcγRI receptor (*see*, *e.g.*, US 6,624,821, US 5,624,821.)

[0698] In other cysteine engineered antibody variants, one or more reactive thiol groups are positioned at accessible sites of the antibody and can be used to conjugate the antibody to other moieties, such as drug moieties or linker-drug moieties, to create an immunoconjugate, as described further herein. In certain embodiments, any one or more of the following

residues may be substituted with cysteine: V205 (Kabat numbering) of the light chain; A118 (EU numbering) of the heavy chain; and 5400 (EU numbering) of the heavy chain Fc region. Generating of cysteine engineered antibodies are described, e.g., in U.S. Pat. No. 7,521,541.

Competing Antibody, or Antigen-Binding Fragments thereof

[0699] The antibodies, or antigen-binding fragments thereof, provided herein include those that compete with one of the exemplified antibodies, or antigen-binding fragment thereof, for specific binding, such as to gpNMB, such as human gpNMB. In some of these embodiments, the test and reference antibody, or antigen-binding fragment thereof, cross-compete with one another. Such an antibody, or antigen-binding fragments thereof, may bind to the same epitope as one of the antibodies, or antigen-binding fragments thereof, described herein, or to an overlapping epitope. Antibodies, or antigen-binding fragments thereof, are expected to show similar functional properties (*e.g.*, one or more of the activities described above). The exemplified antibody, or antigen-binding fragment thereof, include those described above, including those with: 1) the heavy and/or light chains, 2) VHs and/or VLs, and/or 3) that comprise one or more of the CDRs included in Tables D1 and D2.

[0700] Thus, in some embodiments, the antibody, or antigen-binding fragment thereof, that are provided include those that compete with an antibody having: (a) all 6 of the CDRs listed for the antibody described in Table D1; (b) a VH and a VL listed for the antibody described in Table D2; or (c) the light chain and heavy chain as specified for the antibody described in Table D2.

[0701] In some embodiments, competition or cross-competition is determined by surface plasmon resonance analysis (e.g., BIACORE®) (see, *e.g.*, Abdiche, *et al.*, 2009, *Anal. Biochem.* 386:172-180; Abdiche, *et al.*, 2012, *J. Immunol Methods* 382:101-116; and Abdiche, *et al.*, 2014 *PLoS One* 9:e92451.

Ligand-Drug Conjugate Mixtures and Compositions

[0702] The present invention provides Ligand-Drug Conjugate mixtures and pharmaceutical compositions comprising any of the Ligand-Drug Conjugates described herein. The mixtures and pharmaceutical compositions comprise a plurality of conjugates. In some embodiments, each of the conjugates in the mixture or composition is identical or substantially identical, however, the distribution of drug-linkers on the ligands in the mixture or compositions may vary as well as the drug loading. For example, the conjugation technology used to conjugate drug-linkers to antibodies as the targeting agent in some embodiments results in a composition or mixture that is heterogeneous with respect to the

distribution of Drug-Linker compounds on the antibody (Ligand Unit) within the mixture and/or composition. In some of those embodiments, the loading of Drug-Linker compounds on each of the antibody molecules in a mixture or composition of such molecules is an integer that ranges from 1 to 16.

[0703] In those embodiments, when referring to the composition as a whole, the loading of drug-linkers is a number ranging from 1 to about 16. Within the composition or mixture, there sometimes is a small percentage of unconjugated antibodies. The average number of drug-linkers per Ligand Unit in the mixture or composition (i.e., average drug-load) is an important attribute as it determines the maximum amount of drug that is delivered to the target cell. Typically, the average drug load is 1, 2 or about 2, 3 or about 3, 4 or about 4, 5 or about 5, 6 or about 6, 7 or about 7, 8 or about 8, 9 or about 9, 10 or about 10, 11 or about 11, 12 or about 12, 13 or about 13, 14 or about 14, 15 or about 15, 16 or about 16. In some embodiments, the average drug loading is from about 1 to about 16, from about 2 to about 12, from about 3 to about 8, or about 4. In some embodiments, the average drug loading is from about 3 to about 5, from about 3.5 to about 4.5, from about 3.7 to about 4.3, from about 3.9 to about 4.3, or about 4.

[0704] In some embodiments, the mixtures and pharmaceutical compositions comprise a plurality (i.e., population) of conjugates, however, the conjugates are identical or substantially identical and are substantially homogenous with respect to the distribution of drug-linkers on the ligand molecules within the mixture and/or composition and with respect to loading of drug-linkers on the ligand molecules within the mixture and/or composition. In some such embodiments, the loading of drug-linkers on an antibody Ligand Unit is 2 or 4. Within the composition or mixture, there may also be a small percentage of unconjugated antibodies. The average drug load in such embodiments is about 2 or about 4. Typically, such compositions and mixtures result from the use of site-specific conjugation techniques and conjugation is due to an introduced cysteine residue.

[0705] The average number of Drug Units or Drug-Linker compounds per Ligand Unit in a preparation from a conjugation reaction may be characterized by conventional means such as mass spectrometry, ELISA assay, HPLC (e.g., HIC). In those instances, the quantitative distribution of Ligand-Drug Conjugates in terms of subscript p may also be determined. In other instances, separation, purification, and characterization of homogeneous Ligand-Drug Conjugates may be achieved by conventional means such as reverse phase HPLC or electrophoresis.

[0706] In some embodiments, the compositions are pharmaceutical compositions comprising the Ligand-Drug Conjugates described herein and a pharmaceutically acceptable carrier. In some of those embodiments, the pharmaceutical composition is in liquid form. In some embodiments, the pharmaceutical composition is a solid. In other of those embodiments, the pharmaceutical composition is a lyophilized powder.

[0707] The compositions, including pharmaceutical compositions, are provided in purified form. As used herein, "purified" means that when isolated, the isolate contains at least 95%, and in other embodiments at least 98%, of Conjugate by weight of the isolate.

Methods of Use

Treatment of Cancer

[0708] The Ligand-Drug Conjugates are useful for inhibiting the multiplication of a tumor cell or cancer cell, causing apoptosis in a tumor or cancer cell, or for treating a cancer in a patient. The Ligand-Drug Conjugates are used accordingly in a variety of settings for the treatment of cancers. The Ligand-Drug Conjugates are intended to deliver a drug to a tumor cell or cancer cell. Without being bound by theory, in one embodiment, the Ligand Unit of a Ligand-Drug Conjugate binds to or associates with a cancer-cell or a tumor-cell-associated antigen, and the Ligand-Drug Conjugate is taken up (internalized) inside the tumor cell or cancer cell through receptor-mediated endocytosis or other internalization mechanism. In some embodiments, the antigen is attached to a tumor cell or cancer cell or is an extracellular matrix protein associated with the tumor cell or cancer cell. Once inside the cell, via activation of the Activation Unit, the drug is released within the cell. In an alternative embodiment, the free drug is released from the Ligand-Drug Conjugate outside the tumor cell or cancer cell, and the free drug subsequently penetrates the cell.

[0709] In one embodiment, the Ligand Unit binds to the tumor cell or cancer cell.

[0710] In another embodiment, the Ligand Unit binds to a tumor cell or cancer cell antigen which is on the surface of the tumor cell or cancer cell.

[0711] In another embodiment, the Ligand Unit binds to a tumor cell or cancer cell antigen that is an extracellular matrix protein associated with the tumor cell or cancer cell.

[0712] The specificity of the Ligand Unit for a particular tumor cell or cancer cell is an important consideration for determining the tumors or cancers that are most effectively treated. For example, Ligand-Drug Conjugates that target a cancer cell antigen present on hematopoietic cancers are useful treating hematologic malignancies (e.g., anti-CD30, anti-

CD70, anti-CD19, anti-CD33 binding Ligand Unit (e.g., antibody) are useful for treating hematologic malignancies). Ligand-Drug Conjugates that target a cancer cell antigen present on solid tumors in some embodiments are useful treating such solid tumors.

[0713] Cancers that are intended to be treated with a Drug-Linker Conjugate include, but are not limited to, hematopoietic cancers such as, for example, lymphomas (Hodgkin Lymphoma and Non-Hodgkin Lymphomas) and leukemias and solid tumors. Examples of hematopoietic cancers include, follicular lymphoma, anaplastic large cell lymphoma, mantle cell lymphoma, acute myeloblastic leukemia, chronic myelocytic leukemia, chronic lymphocytic leukemia, diffuse large B cell lymphoma, and multiple myeloma. Examples of solid tumors include fibrosarcoma, myxosarcoma, liposarcoma, chondrosarcoma, osteogenic sarcoma, chordoma, angiosarcoma, endotheliosarcoma, lymphangiosarcoma, lymphangioendotheliosarcoma, synovioma, mesothelioma, Ewing's tumor, leiomyosarcoma, rhabdomyosarcoma, colon cancer, colorectal cancer, kidney cancer, pancreatic cancer, bone cancer, breast cancer, ovarian cancer, prostate cancer, esophageal cancer, stomach cancer, oral cancer, nasal cancer, throat cancer, squamous cell carcinoma, basal cell carcinoma, adenocarcinoma, sweat gland carcinoma, sebaceous gland carcinoma, papillary carcinoma, papillary adenocarcinomas, cystadenocarcinoma, medullary carcinoma, bronchogenic carcinoma, renal cell carcinoma, hepatoma, bile duct carcinoma, choriocarcinoma, seminoma, embryonal carcinoma, Wilms' tumor, cervical cancer, uterine cancer, testicular cancer, small cell lung carcinoma, bladder carcinoma, lung cancer, epithelial carcinoma, glioma, glioblastoma multiforme, astrocytoma, medulloblastoma, craniopharyngioma, ependymoma, pinealoma, hemangioblastoma, acoustic neuroma, oligodendroglioma, meningioma, neuroblastoma, and retinoblastoma.

[0714] In some embodiments, the treated cancer is any one of the above-listed lymphomas and leukemias.

Multi-Modality Therapy for Cancer

[0715] Cancers, including, but not limited to, a tumor, metastasis, or other disease or disorder characterized by uncontrolled cell growth are intended to be treated or inhibited by administration of an effective amount of a Ligand-Drug Conjugate.

[0716] In one group of embodiments, methods for treating cancer are provided, including administering to a patient in need thereof an effective amount of a Ligand-Drug Conjugate and a chemotherapeutic agent. In one embodiment the chemotherapeutic agent is one in

which treatment of the cancer has not been found to be refractory to that agent. In another embodiment, the chemotherapeutic agent one in which the treatment of cancer has been found to be refractory to that agent.

[0717] In another group of embodiments, the Ligand-Drug Conjugates is administered to a patient that has also undergone surgery as treatment for the cancer. In such embodiments a chemotherapeutic agent is typically administered over a series of sessions, or one or a combination of the chemotherapeutic agents, such a standard of care chemotherapeutic agent(s), is administered.

[0718] In either group of embodiments, the patient also receives an additional treatment, such as radiation therapy. In a specific embodiment, the Ligand-Drug Conjugate is administered concurrently with the chemotherapeutic agent or with radiation therapy. In another specific embodiment, the chemotherapeutic agent or radiation therapy is administered prior or subsequent to administration of a Ligand-Drug Conjugate.

[0719] Additionally, methods of treatment of cancer with a Ligand-Drug Conjugate are provided as an alternative to chemotherapy or radiation therapy where the chemotherapy or the radiation therapy has proven or can prove too toxic, *e.g.*, results in unacceptable or unbearable side effects, for the subject being treated. The patient being treated is optionally treated with another cancer treatment such as surgery, radiation therapy or chemotherapy, depending on which treatment is found to be acceptable or bearable.

Treatment of Autoimmune Diseases

[0720] The Ligand-Drug Conjugates are intended to be useful for killing or inhibiting the unwanted replication of cells that produce an autoimmune disease or for treating an autoimmune disease.

[0721] The Ligand-Drug Conjugates are used accordingly in a variety of settings for the treatment of an autoimmune disease in a patient. The Ligand-Drug Conjugates are typically used to deliver a Drug Unit to a target cell. Without being bound by theory, in one embodiment, the Ligand-Drug Conjugate associates with an antigen on the surface of a pro-inflammatory or inappropriately stimulated immune cell, and the Ligand-Drug Conjugate is then taken up inside the targeted cell through receptor-mediated endocytosis. Once inside the cell, the Linker Unit is cleaved, resulting in release of the Drug Unit as free drug. The free drug is then able to migrate within the cytosol and induce a cytotoxic or cytostatic activity. In an alternative embodiment, the Drug Unit is cleaved from the Ligand-Drug Conjugate

outside the target cell, and the free drug resulting from that release subsequently penetrates the cell.

[0722] In one embodiment, the Ligand Unit binds to an autoimmune antigen. In one such embodiment, the antigen is on the surface of a cell involved in an autoimmune condition.

[0723] In one embodiment, the Ligand Unit binds to activated lymphocytes that are associated with the autoimmune disease state.

[0724] In a further embodiment, the Ligand-Drug Conjugate kills or inhibits the multiplication of cells that produce an autoimmune antibody associated with a particular autoimmune disease.

[0725] Particular types of autoimmune diseases intended to be treated with the Ligand-Drug Conjugates include, but are not limited to, Th2 lymphocyte related disorders (*e.g.*, atopic dermatitis, atopic asthma, rhinoconjunctivitis, allergic rhinitis, Omenn's syndrome, systemic sclerosis, and graft versus host disease); Th1 lymphocyte-related disorders (*e.g.*, rheumatoid arthritis, multiple sclerosis, psoriasis, Sjorgren's syndrome, Hashimoto's thyroiditis, Grave's disease, primary biliary cirrhosis, Wegener's granulomatosis, and tuberculosis); and activated B lymphocyte-related disorders (*e.g.*, systemic lupus erythematosus, Goodpasture's syndrome, rheumatoid arthritis, and type I diabetes).

Multi-Drug Therapy of Autoimmune Diseases

[0726] Methods for treating an autoimmune disease are also disclosed including administering to a patient in need thereof an effective amount of a Ligand-Drug Conjugate and another therapeutic agent known for the treatment of an autoimmune disease.

For any of the methods of treatment described herein, the Ligand-Drug Conjugate compound may be administered to a subject who is unable to tolerate another Ligand-Drug Conjugate compound in therapeutically effective doses. In some embodiments, the other Ligand-Drug Conjugate compound comprises monomethyl auristain E (MMAE) or monomethyl auristatin F (MMAF). In some embodiments, the patient has greater tolerance for a Ligand-Drug Conjugate compound provided herein as compared to another Ligand-Drug Conjugate compound (e.g., a Ligand-Drug Conjugate compound comprising MMAE or MMAF). Tolerability may be determined using known methods or any of the methods decribed herein.

Compositions and Methods of Administration

[0727] The present invention provides pharmaceutical compositions comprising the Ligand-Drug Conjugates described herein and at least one pharmaceutically acceptable

carrier. The pharmaceutical composition is in any form that allows the compound to be administered to a patient for treatment of a disorder associated with expression of the antigen to which the Ligand unit binds. For example, the conjugates are in the form of a liquid or solid. The preferred route of administration is parenteral. Parenteral administration includes subcutaneous injections, intravenous, intramuscular, intrasternal injection or infusion techniques. In one embodiment, the pharmaceutical compositions is administered parenterally. In one embodiment, the conjugates are administered intravenously. Administration is by any convenient route, for example by infusion or bolus injection.

[0728] Pharmaceutical compositions are formulated to allow a Ligand-Drug Conjugate to be bioavailable upon administration of the composition to a patient. Compositions sometimes take the form of one or more dosage units.

[0729] Materials used in preparing the pharmaceutical compositions are preferably non-toxic in the amounts used. It will be evident to those of ordinary skill in the art that the optimal dosage of the active ingredient(s) in the pharmaceutical composition will depend on a variety of factors. Relevant factors include, without limitation, the type of animal (*e.g.*, human), the particular form of the compound, the manner of administration, and the composition employed.

[0730] The composition in some embodiments is in the form of a liquid. The liquid in some of those embodiments is useful for delivery by injection. In some embodiments a composition for administration by injection, in addition to the Ligand-Drug Conjugate, contains one or more excipients selected from the group consisting of a surfactant, preservative, wetting agent, dispersing agent, suspending agent, buffer, stabilizer and isotonic agent.

[0731] The liquid compositions, whether they are solutions, suspensions or other like form, in some embodiments include one or more of the following: sterile diluents such as water for injection, saline solution, preferably physiological saline, Ringer's solution, isotonic sodium chloride, fixed oils such as synthetic mono or digylcerides which can serve as the solvent or suspending medium, polyethylene glycols, glycerin, cyclodextrin, propylene glycol or other solvents; antibacterial agents such as benzyl alcohol or methyl paraben; antioxidants such as ascorbic acid or sodium bisulfite; chelating agents such as ethylenediaminetetraacetic acid; buffers such as amino acids, acetates, citrates or phosphates; detergents, such as nonionic surfactants, polyols; and agents for the adjustment of tonicity such as sodium

chloride or dextrose. A parenteral composition is sometimes enclosed in ampoule, a disposable syringe or a multiple-dose vial made of glass, plastic or other material. Physiological saline is an exemplary adjuvant. An injectable composition is preferably sterile.

[0732] The amount of the conjugate that is effective in the treatment of a particular disorder or condition will depend on the nature of the disorder or condition, which in some embodiments is determined by standard clinical techniques. In addition, *in vitro* or *in vivo* assays are optionally employed to help identify optimal dosage ranges. The precise dose to be employed in the compositions will also depend on the route of administration, and the seriousness of the disease or disorder, and should be decided according to the judgment of the practitioner and each patient's circumstances.

[0733] The compositions comprise an effective amount of a Ligand-Drug Conjugate such that a suitable dosage amount will be obtained. Typically, that amount is at least about 0.01% of a compound by weight of the composition.

[0734] For intravenous administration, the pharmaceutical composition typically comprises from about 0.01 to about 100 mg of a Ligand-Drug Conjugate per kg of the animal's body weight. In one embodiment, the composition can include from about 1 to about 100 mg of a Ligand-Drug Conjugate per kg of the animal's body weight. In another aspect, the amount administered will be in the range from about 0.1 to about 25 mg/kg of body weight of a compound. In some aspects, depending on the drug used, the dosage is even lower, for example, 1.0 μg/kg to 5.0 mg/kg, 4.0 mg/kg, 3.0 mg/kg, 2.0 mg/kg or 1.0 mg/kg, or 1.0 μg/kg to 500.0 μg/kg of the subject's body weight.

[0735] Generally, the dosage of a conjugate administered to a patient is typically about 0.01 mg/kg to about 100 mg/kg of the subject's body weight or from 1.0 μg/kg to 5.0 mg/kg of the subject's body weight. In some embodiments, the dosage administered to a patient is between about 0.01 mg/kg to about 15 mg/kg of the subject's body weight. In some embodiments, the dosage administered to a patient is between about 0.1 mg/kg and about 15 mg/kg of the subject's body weight. In some embodiments, the dosage administered to a patient is between about 0.1 mg/kg and about 20 mg/kg of the subject's body weight. In some embodiments, the dosage administered is between about 0.1 mg/kg to about 5 mg/kg or about 0.1 mg/kg to about 10 mg/kg of the subject's body weight. In some embodiments, the dosage administered is between about 1 mg/kg to about 15 mg/kg of the subject's body

weight. In some embodiments, the dosage administered is between about 1 mg/kg to about 10 mg/kg of the subject's body weight. In some embodiments, the dosage administered is between about 0.1 to 4 mg/kg, even more preferably 0.1 to 3.2 mg/kg, or even more preferably 0.1 to 2.7 mg/kg of the subject's body weight over a treatment cycle.

[0736] The term "carrier" refers to a diluent, adjuvant or excipient, with which a compound is administered. Such pharmaceutical carriers in some embodiments is a liquid, such as water and oils, including those of petroleum, animal, vegetable or synthetic origin, such as peanut oil, soybean oil, mineral oil, sesame oil. Other carriers include saline, gum acacia, gelatin, starch paste, talc, keratin, colloidal silica, urea. In addition, auxiliary, stabilizing, thickening, lubricating and coloring agents are sometimes used. In one embodiment, when administered to a patient, the Ligand-Drug Conjugate or compositions thereof and pharmaceutically acceptable carriers are sterile.

[0737] Water is an exemplary carrier when the compounds are administered intravenously. Saline solutions and aqueous dextrose and glycerol solutions are often employed as liquid carriers, particularly for injectable solutions. Suitable pharmaceutical carriers also include excipients such as starch, glucose, lactose, sucrose, gelatin, malt, rice, flour, chalk, silica gel, sodium stearate, glycerol monostearate, talc, sodium chloride, dried skim milk, glycerol, propylene, glycol, water, ethanol. The present compositions, if desired, also contain minor amounts of wetting or emulsifying agents, or pH buffering agents.

[0738] In an embodiment, the conjugates are formulated in accordance with routine procedures as a pharmaceutical composition adapted for intravenous administration to animals, particularly human beings. Typically, the carriers or vehicles for intravenous administration are sterile isotonic aqueous buffer solutions. Where necessary, the compositions include a solubilizing agent. Compositions for intravenous administration optionally comprise a local anesthetic such as lignocaine to ease pain at the site of the injection. Generally, the ingredients are supplied either separately or mixed together in unit dosage form, for example, as a dry lyophilized powder or water free concentrate in a hermetically sealed container such as an ampoule or sachets indicating the quantity of active agent. Where a conjugate is to be administered by infusion, it is typically dispensed, for example, with an infusion bottle containing sterile pharmaceutical grade water or saline. In some aspects, where the conjugate is administered by injection, an ampoule of sterile water for injection or saline is sometimes provided and the ingredients are mixed prior to administration.

[0739] The pharmaceutical compositions are generally formulated as sterile, substantially isotonic and in full compliance with all Good Manufacturing Practice (GMP) regulations of the U.S. Food and Drug Administration.

Methods of Preparing Drug-Linker compounds and Ligand-Drug Conjugate compounds

[0740] Provided herein are methods for preparing Drug-Linker compounds from the auristatin compounds provided herein. In addition to the methods recited below, method of preparing Drug-Linker compounds from auristatin compounds will be well known to a person of skill in the art.

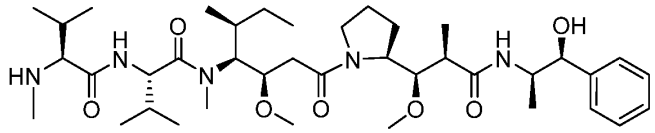
[0741] Provided herein are methods for preparing Ligand-Drug Conjugate compounds from the auristatin compounds and Drug-Linker compounds provided herein. Methods for preparing the Ligand-Drug Conjugate compounds will be well known to a person of skill in the art.

EXAMPLES

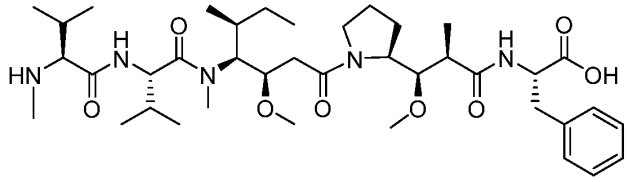
[0742] **General Information Chemical Synthesis.** All commercially available anhydrous solvents and reagents were used without further purification. UPLC-MS system 1 consisted of a Waters SQ mass detector 2 interfaced to an Acquity Ultra Performance LC equipped with a CORTECS UPLC C18 2.1 x 50 mm, 1.6 μm reverse phase column. The acidic mobile phase (0.1% formic acid) consisted of a gradient of 3% acetonitrile/97% water to 100% acetonitrile (flow rate = 0.5 mL/min). Preparative HPLC was carried out on a Waters 2545 Binary Gradient Module with a Waters 2998 Photodiode Array Detector. Products were purified over a C12 Phenomenex Synergi 250 x 10.0 mm, 4 μm, 80 Å reverse phase column (<10 mg scale) or a C12 Phenomenex Synergi 250 x 50 mm, 10 μm, 80 Å reverse phase column (10-100 mg scale) eluting with 0.1% trifluoroacetic acid in water (solvent A) and 0.1% trifluoroacetic acid in acetonitrile (solvent B). The purification methods generally consisted of linear gradients of solvent A to solvent B, ramping from 90% aqueous solvent A to 5% solvent A. The flow rate was 4.6 mL/min with monitoring at 220 nm. NMR spectral data were collected on a Varian Mercury 400 MHz spectrometer. Coupling constants (*J*) are reported in hertz.

[0743] Throughout the Examples, reference is made to the following structures:

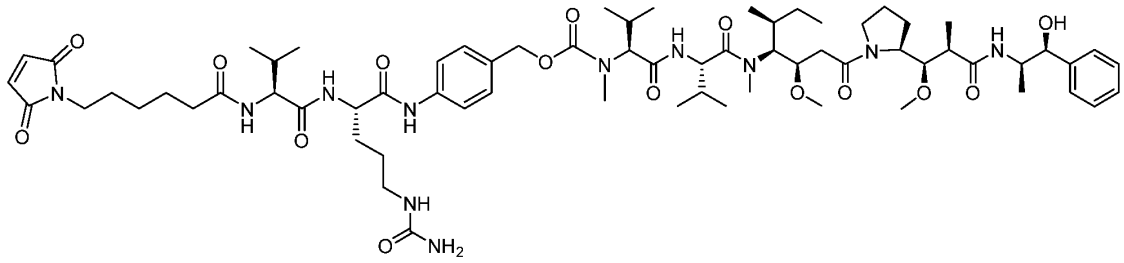
MMAE:



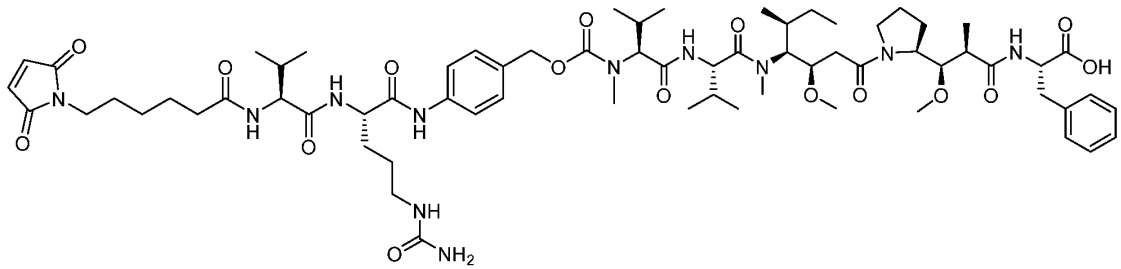
MMAF:



MC-VC-MMAE:

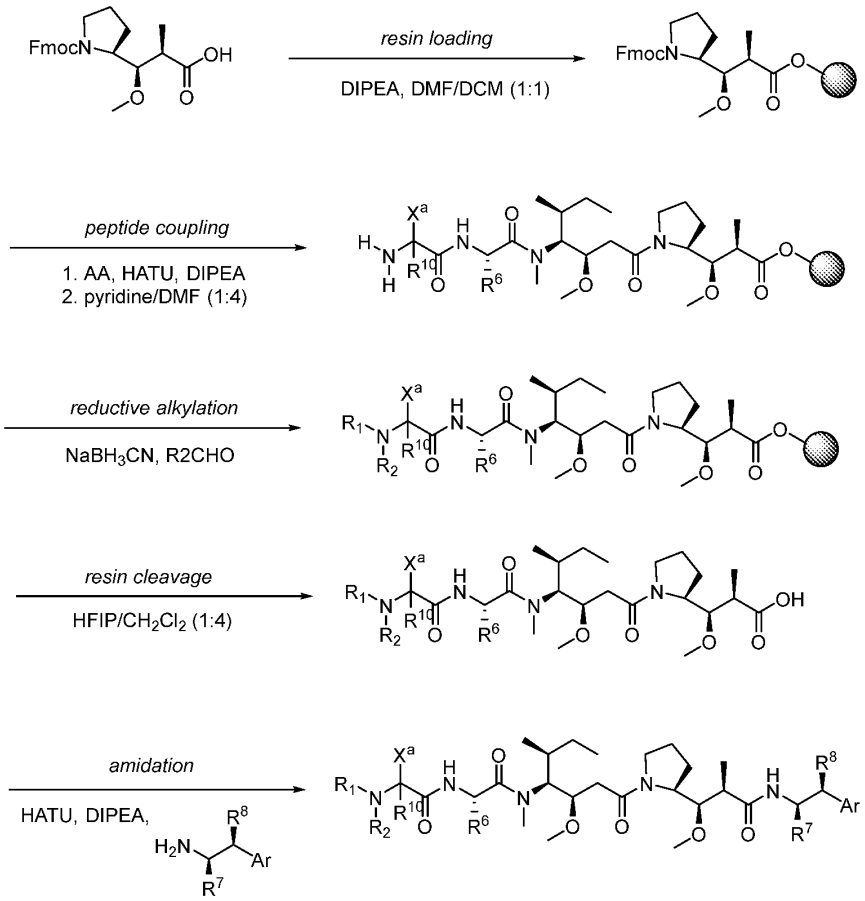


MC-VC-MMAF:



Example 1. General procedure for solid-phase/solution-phase synthesis of auristatins

[0744] A similar procedure for Fmoc deprotection, amide coupling, alkylation and resin cleavage has been published (Moquist, P. N. et al. *Mol. Cancer Ther.* **2021**, *20*, 320-328).



Example 2. General Procedure for resin loading.

[0745] 2-chlorotrityl resin (100-200 mesh), 1% DVB (Millipore Sigma, 855017) was loaded into a vessel and DCM (5V) was added to swell the resin for 30 min. The solvent was removed, and the resin was treated with solution of Fmoc-Dap (1 equivalent to resin loading) in DMF and DCM (1:1, 10V) and shaken for 2 h. The solution was filtered, and the resin resin washed with DMF (3 × 3 min), DCM (3 × 3 min), and Et2O (3 × 3 min) and vacuum-dried in a desiccator.

Example 3. General procedure for Fmoc deprotection

[0746] The resin was treated with a solution of piperidine in DMF (1:4 V/V) and shaken for 30 min. The solution was removed, and the resin was resubjected three additional times to the same conditions. The solution was filtered, and the resin are washed with DMF (3 × 3 min).

Example 4. General procedure for amide coupling

[0747] Fmoc-amino acid (2 equiv) was dissolved in dry DMF (0.2 M final concentration). DIPEA (4 equiv) and HATU (1.9 equiv) were added successively, and the reaction was stirred for 5 min. The resin was treated with the solution of activated Fmoc-amino acid and shaken for 2 h. The solution was filtered, and the resin was washed with DMF (3 × 3 min).

Example 5. General procedure for resin cleavage

[0748] Prior to cleavage the resin was washed with DCM (3 × 3 min). Resin was cleaved with a solution of 20:80 (V/V) solution of HFIP/ DCM (10 min). Solution is removed in vacuo, and crude was dissolved for UPLC analysis and preparative HPLC. HPLC fraction were frozen and dried by lyophilization.

Example 6. General procedure for reductive alkylation

[0749] Aldehyde (5 equiv.) was dissolved in a 0.6 mL solution of 1% (V/V) AcOH in DMF, followed by the addition of NaBH3CN (4 equiv.). The resin was treated with the solution and shaken for 2 h. The solution was filtered, and the resin was washed with DMF (3 × 3 mL) and DCM (3 × 3 mL) and vacuum-dried in a desiccator.

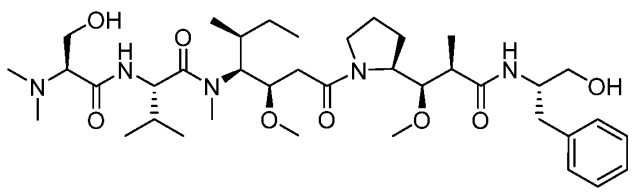
Example 7. General procedure for C-terminal amine coupling

[0750] Tetrapeptide (1 equiv) was dissolved in dry DMF (0.3 M final concentration). DIPEA (4 equiv) and HATU (0.95 equiv) were added successively, and the reaction was stirred for 15 min. The P5 amine was added to the activated ester and the reaction was stirred for 2 h. The solvent was removed in vacuo and purified by preparative HPLC. HPLC fractions were frozen and dried by lyophilization.

Auristatin compounds

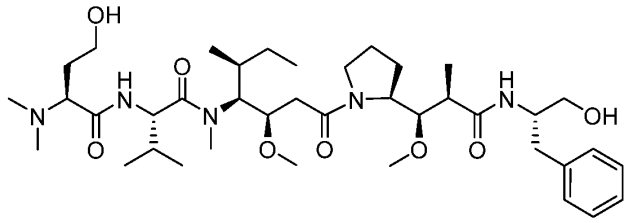
[0751] Examples 8 to 33 were synthesized according to the procedures of Examples 1 to 7.

Example 8.



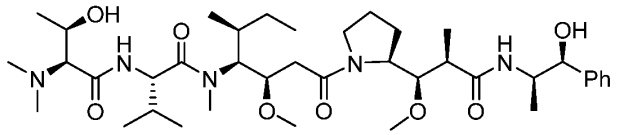
[0752] Compound 1.1 was prepared by dimethylation of tetrapeptide and amide coupling of tetrapeptide with L-phenylalaninol. Analytical UPLC-MS: $t_R = 1.33$ min, *m/z* (ES+) 720.49 $(M+H)^+$, found 720.85.

Example 9.



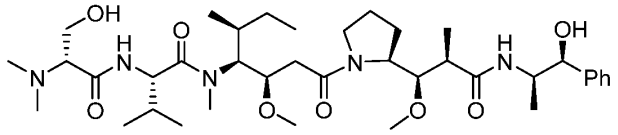
[0753] Compound 1.3 was prepared by dimethylation of tetrapeptide and amide coupling of tetrapeptide with L-phenylalaninol. Analytical UPLC-MS: $t_R = 1.16$ min, *m/z* (ES+) 734.50 $(M+H)^+$, found 734.49.

Example 10.



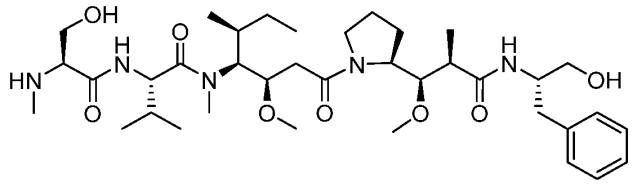
[0754] Compound 1.4 was prepared by dimethylation of tetrapeptide and amide coupling of tetrapeptide with (1*S*,2*R*)-(+)-norephedrine. Analytical UPLC-MS: $t_R = 1.29$ min, *m/z* (ES+) 734.50 $(M+H)^+$, found 734.48.

Example 11.



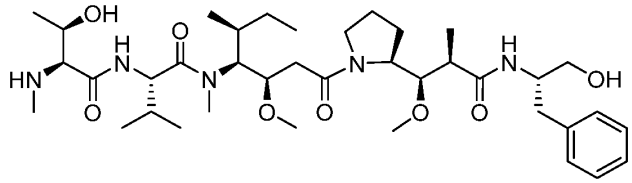
[0755] Compound 1.2 was prepared by dimethylation of tetrapeptide and amide coupling of tetrapeptide with (1*S*,2*R*)-(+)-norephedrine. Analytical UPLC-MS: $t_R = 1.26$ min, *m/z* (ES+) 720.48 $(M+H)^+$, found 720.51.

Example 12.



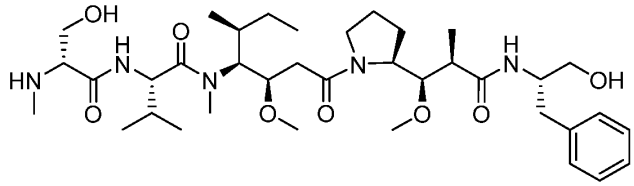
[0756] Compound 1.9 was prepared by amide coupling of tetrapeptide with L-phenylalaninol. Analytical UPLC-MS: t_R = 1.30 min, *m/z* (ES+) 706.47 $(M+H)^+$, found 707.62.

Example 13.



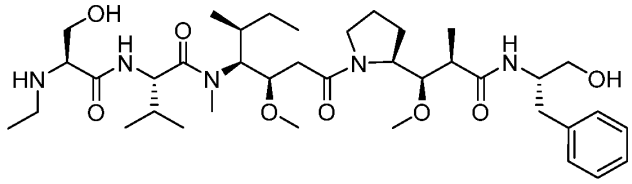
[0757] Compound 1.12 was prepared by amide coupling of tetrapeptide with L-phenylalaninol. Analytical UPLC-MS: t_R = 1.40 min, *m/z* (ES+) 719.48 $(M+H)^+$, found 720.99.

Example 14.



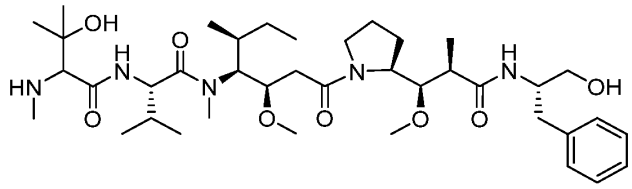
[0758] Compound 1.10 was prepared by amide coupling of tetrapeptide with L-phenylalaninol. Analytical UPLC-MS: t_R = 1.27 min, *m/z* (ES+) 706.47 $(M+H)^+$, found 706.57.

Example 15.



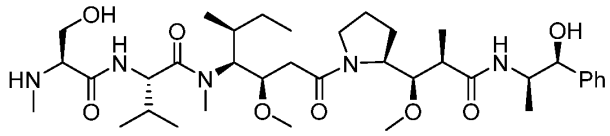
[0759] Compound 1.13 was prepared by reductive alkylation of tetrapeptide with acetaldehyde followed by amide coupling of tetrapeptide with L-phenylalaninol. Analytical UPLC-MS: $t_R = 1.21$ min, *m/z* (ES+) 720.49 $(M+H)^+$, found 720.57.

Example 16.



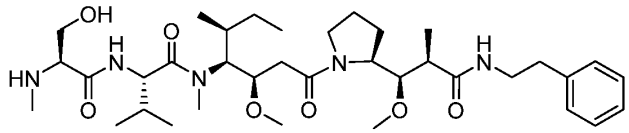
[0760] Compound 1.11 was prepared by amide coupling of tetrapeptide with L-phenylalaninol. Analytical UPLC-MS: $t_R = 1.47$ min, *m/z* (ES+) 734.51 $(M+H)^+$, found 734.85.

Example 17.



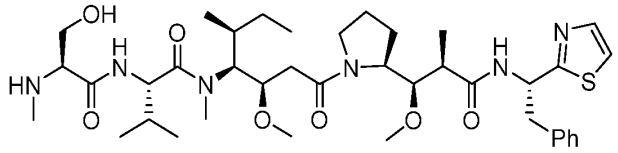
[0761] Compound 1.29 was prepared by amide coupling of tetrapeptide with (1*S*,2*R*)-(+)-norephedrine. Analytical UPLC-MS: $t_R = 1.58$ min, *m/z* (ES+) 728.46 $(M+Na)^+$, found 728.73.

Example 18.



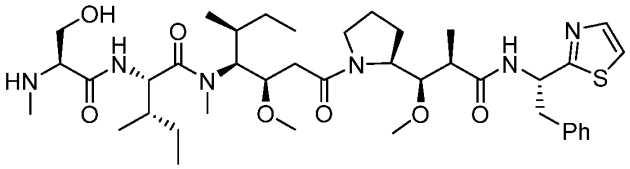
[0762] Compound 1.30 was prepared by amide coupling of tetrapeptide with phenethylamine. Analytical UPLC-MS: $t_R = 1.70$ min, *m/z* (ES+) 698.45 $(M+Na)^+$, found 698.50.

Example 19.



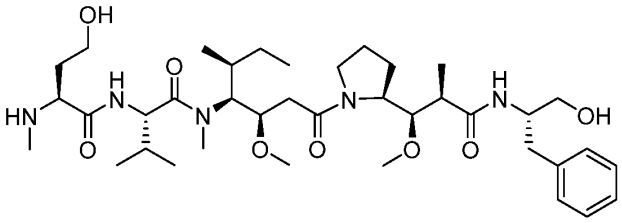
[0763] Compound 1.32 was prepared by amide coupling of tetrapeptide with *S*-dolaphenine. Analytical UPLC-MS: $t_R = 1.85$ min, *m/z* (ES+) 759.45 $(M+H)^+$, found 760.05.

Example 20.



[0764] Compound 1.33 was prepared by amide coupling of tetrapeptide with *S*-dolaphenine. Analytical UPLC-MS: $t_R = 1.89$ min, *m/z* (ES+) 773.46 $(M+H)^+$, found 773.58.

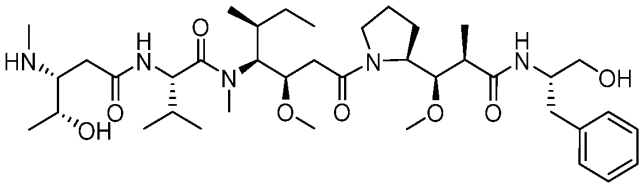
Example 21.



[0765] *N*-terminal amino acid Fmoc-(*N*-methyl)-L-h-serine was synthesized from L-h-Serine(OtBu)-OH by reaction with formaldehyde (37% aqueous, 1.5 equiv), NaH_2PO_4 (2 equiv) in water, Zn (dust, 2 equiv), and AcOH (1 equiv.) at RT overnight similar to known procedure (Da Silva, R. A. et al. *Tetrahedron Lett.* **2007**, *48*, 7680-7682). Fmoc protecting group was then installed as described in a reported procedure (Wuts, P; Green, T. "Protective Groups in Organic Synthesis" New York, **2006**).

[0766] Compound 1.14 was prepared by amide coupling of tetrapeptide with L-phenylalaninol. Analytical UPLC-MS: t_R = 1.13 min, m/z (ES+) 720.45 (M+H)+, found 720.49.

Example 22.

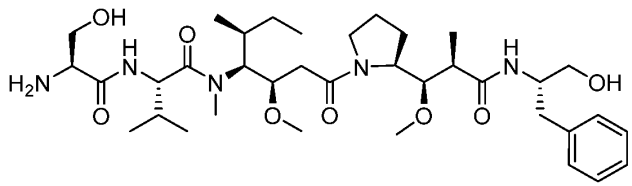


[0767] *N*-terminal amino acid Fmoc-(N-methyl)-βh-threonine was synthesized from βh-threonine-(OtBu)-OH by reaction with formaldehyde (37% aqueous, 1.5 equiv), NaH_2PO_4 (2 equiv) in water, Zn (dust, 2 equiv) and AcOH (1 equiv.) at RT overnight similar to known

procedure (Da Silva, R. A. et al. *Tetrahedron Lett.* **2007**, *48*, 7680-7682). Fmoc protecting group was then installed as described in a reported procedure (Wuts, P; Green, T. "Protective Groups in Organic Synthesis" New York, **2006**).

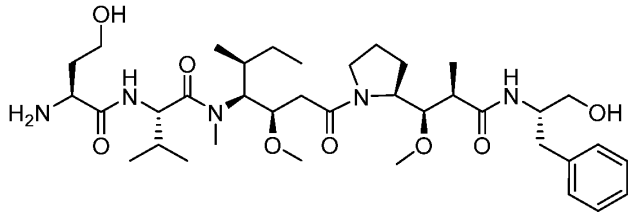
[0768] Compound 1.58 was prepared by amide coupling of tetrapeptide with L-phenylalaninol. Analytical UPLC-MS: $t_R = 1.20$ min, *m/z* (ES+) 734.50 $(M+H)^+$, found 734.52.

Example 23.



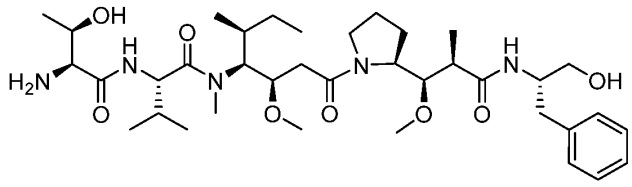
[0769] Compound 1.16 was prepared by amide coupling of tetrapeptide with L-phenylalaninol. Analytical UPLC-MS: $t_R = 1.38$ min, *m/z* (ES+) 692.46 $(M+H)^+$, found 692.93.

Example 24.



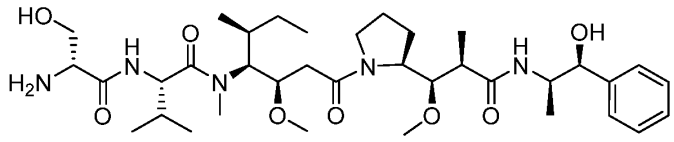
[0770] Compound 1.18 was prepared by amide coupling of tetrapeptide with L-phenylalaninol. Analytical UPLC-MS: $t_R = 1.37$ min, *m/z* (ES+) 706.47 $(M+H)^+$, found 706.55.

Example 25.



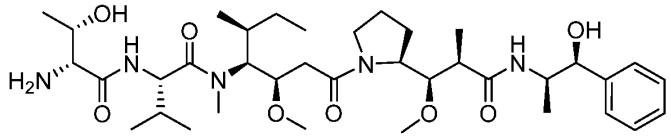
[0771] Compound 1.20 was prepared by amide coupling of tetrapeptide with L-phenylalaninol. Analytical UPLC-MS: t_R = 1.30 min, *m/z* (ES+) 706.47 $(M+H)^+$, found 706.39.

Example 26.



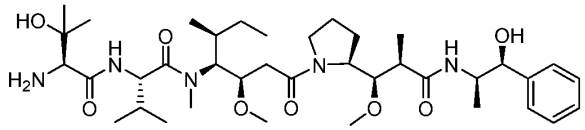
[0772] Compound 1.72 was prepared by amide coupling of tetrapeptide with (1*S*,2*R*)-(+)-norephedrine. Analytical UPLC-MS: t_R = 1.19 min, *m/z* (ES+) 692.46 $(M+H)^+$, found 692.49.

Example 27.



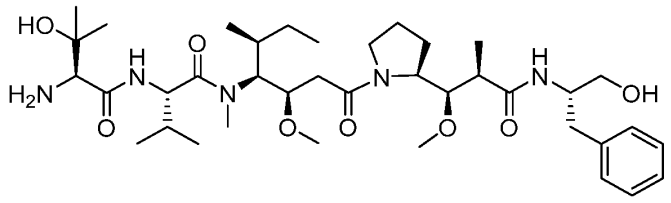
[0773] Compound 1.22 was prepared by amide coupling of tetrapeptide with (1*S*,2*R*)-(+)-norephedrine. Analytical UPLC-MS: t_R = 1.25 min, *m/z* (ES+) 706.47 $(M+H)^+$, found 706.56.

Example 28.



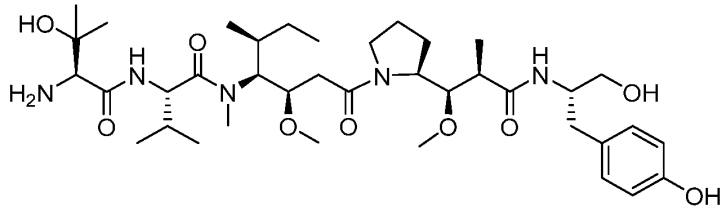
[0774] Compound 1.23repared by amide coupling of tetrapeptide with (1*S*,2*R*)-(+)-norephedrine. Analytical UPLC-MS: t_R = 1.28 min, *m/z* (ES+) 720.48 $(M+H)^+$, found 720.76.

Example 29.



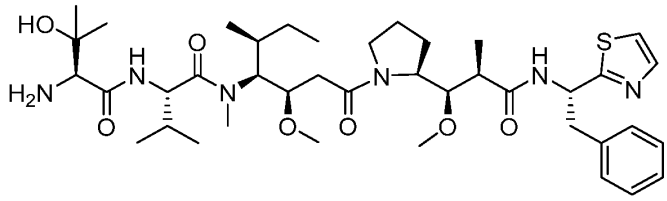
[0775] Compound 1.21 was prepared by amide coupling of tetrapeptide with L-phenylalaninol. Analytical UPLC-MS: t_R = 1.30 min, *m/z* (ES+) 720.49 $(M+H)^+$, found 720.85.

Example 30.



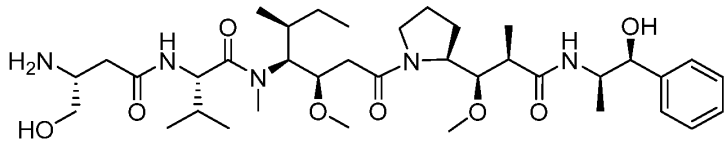
[0776] Compound 1.24 was prepared by amide coupling of tetrapeptide with L-tyrosinol. Analytical UPLC-MS: t_R = 1.15 min, *m/z* (ES+) 736.49 $(M+H)^+$, found 736.79.

Example 31.



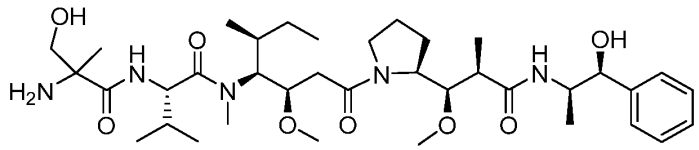
[0777] Compound 1.25 was prepared by amide coupling of tetrapeptide with S-dolaphenine. Analytical UPLC-MS: t_R = 1.49 min, *m/z* (ES+) 773.04 $(M+H)^+$, found 773.61.

Example 32.



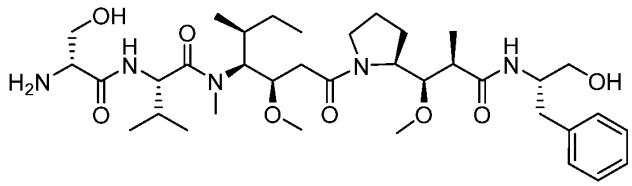
[0778] Compound 1.56 was prepared by amide coupling of tetrapeptide with (1*S*,2*R*)-(+)-norephedrine. Analytical UPLC-MS: t_R = 1.25 min, *m/z* (ES+) 706.48 $(M+H)^+$, found 706.80.

Example 33.



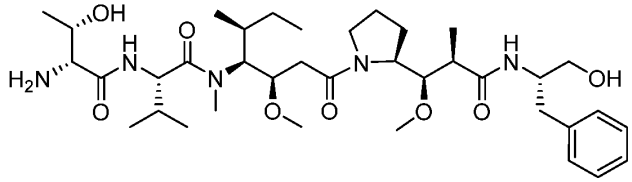
[0779] Compound 1.59 was prepared by amide coupling of tetrapeptide with (1*S*,2*R*)-(+)-norephedrine. Analytical UPLC-MS: t_R = 1.30 min, *m/z* (ES+) 706.48 $(M+H)^+$, found 706.71.

Example 34.



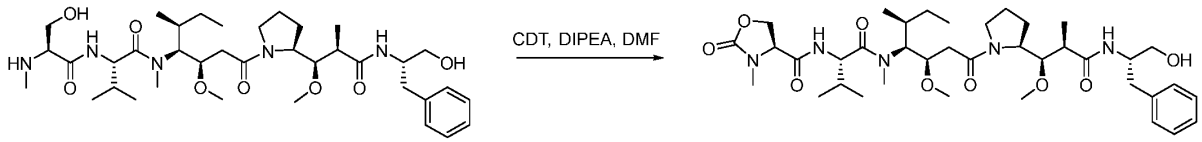
[0780] Compound 1.19 can be prepared by amide coupling of tetrapeptide with L-phenylalaninol.

Example 35.

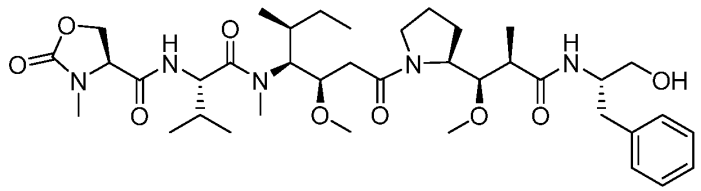


[0781] Compound 1.17 can be prepared by amide coupling of tetrapeptide with L-phenylalaninol.

Example 36. General procedure to synthesize cyclic carbamate auristatins

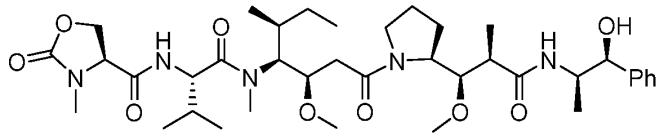


[0782] Auristatin (1 equiv) was dissolved in DMF (0.3 M final concentration). DIPEA (5 equiv) and CDI (4 equiv) were added successively, and the reaction was stirred for 2 h. Upon reaction completion, a solution of LiOH was added to hydrolyze any undesired carbonate formation. The organic lay was separated, and the solvent was removed in vacuo. The crude mixture was purified by preparative HPLC. HPLC fractions were frozen and dried by lyophilization.



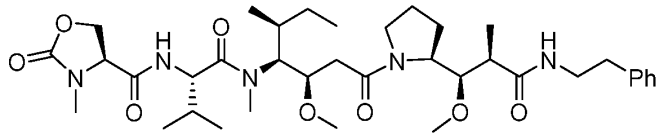
[0783] Compound 1.50. Analytical UPLC-MS: t_R = 1.67 min, *m/z* (ES+) 732.45 $(M+H)^+$, found 732.99.

Example 37.



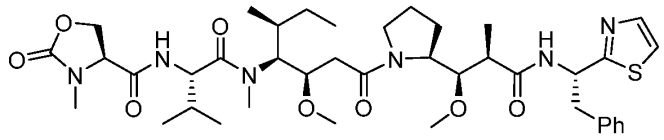
[0784] Compound 1.53. Analytical UPLC-MS: $t_R = 2.04$ min, *m/z* (ES+) 732.45 $(M+H)^+$, found 732.90.

Example 38.



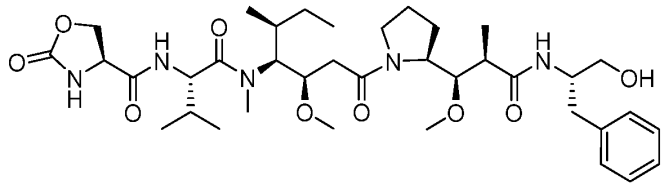
[0785] Compound 1.54. Analytical UPLC-MS: $t_R = 2.23$ min, *m/z* (ES+) 702.44 $(M+H)^+$, found 702.52.

Example 39.



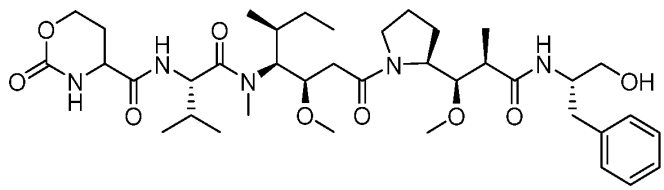
[0786] Compound 1.55. Analytical UPLC-MS: $t_R = 2.04$ min, *m/z* (ES+) 785.43 $(M+H)^+$, found 785.48.

Example 40.



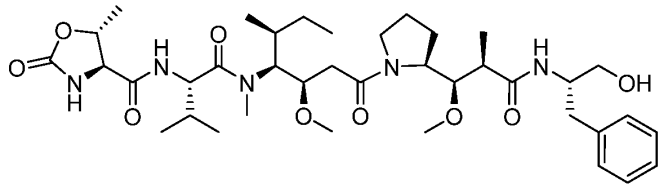
[0787] Compound 1.46. Analytical UPLC-MS: $t_R = 1.57$ min, *m/z* (ES+) 718.44 $(M+H)^+$, found 718.84.

Example 41.



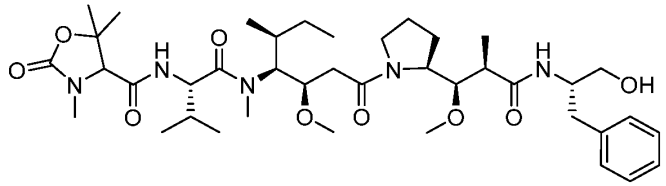
[0788] Compound 1.47. Analytical UPLC-MS: t_R = 1.58 min, *m/z* (ES+) 732.45 $(M+H)^+$, found 732.99.

Example 42.



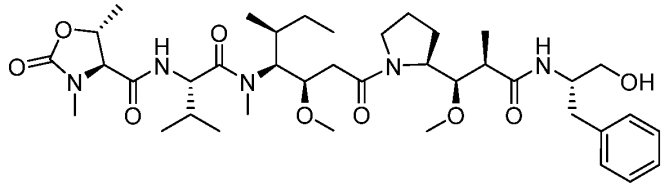
[0789] Compound 1.48. Analytical UPLC-MS: t_R = 1.70 min, *m/z* (ES+) 732.45 $(M+H)^+$, found 732.73.

Example 43.



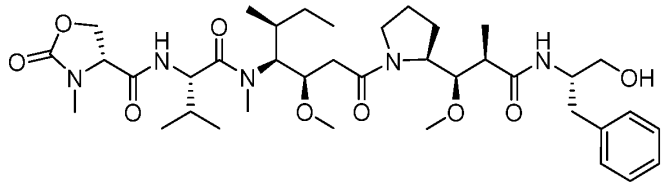
[0790] Compound 1.60. Analytical UPLC-MS: t_R = 1.78 min, *m/z* (ES+) 760.49 $(M+H)^+$, found 760.85.

Example 44.



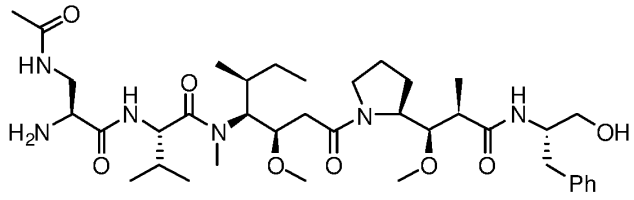
[0791] Compound 1.51. Analytical UPLC-MS: t_R = 1.70 min, *m/z* (ES+) 732.45 $(M+H)^+$, found 732.73.

Example 45.



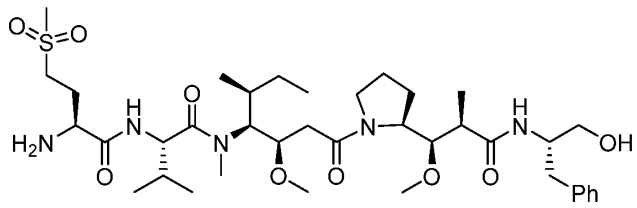
[0792] Compound 1.52. Analytical UPLC-MS: t_R = 1.61 min, *m/z* (ES+) 732.45 $(M+H)^+$, found 732.55.

Example 46.



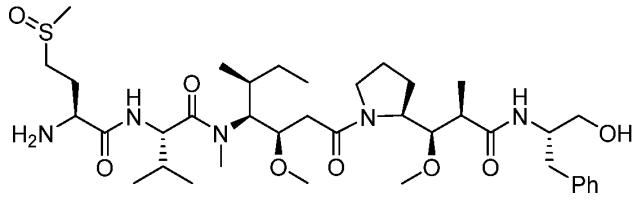
[0793] Compound 1.61 was prepared by amide coupling of tetrapeptide with L-phenylalaninol.. Analytical UPLC-MS (Method 1): $t_R = 1.25$ min, *m/z* (ES+) 733.48 $(M+H)^+$, found 733.78.

Example 47.



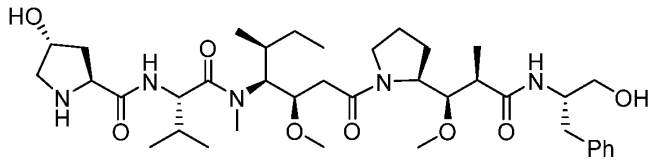
[0794] Compound 1.28 was prepared by amide coupling of tetrapeptide with L-phenylalaninol. Analytical UPLC-MS (Method 1): $t_R = 1.24$ min, *m/z* (ES+) 768.45 $(M+H)^+$, found 768.60.

Example 48.



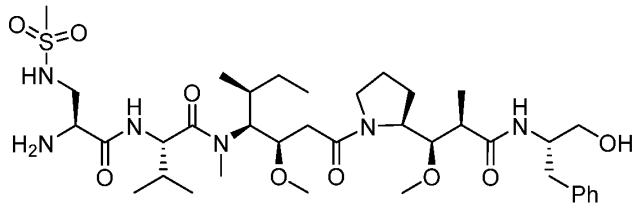
[0795] Compound 1.62 was prepared by amide coupling of tetrapeptide with L-phenylalaninol. Analytical UPLC-MS (Method 1): $t_R = 1.20$ min, *m/z* (ES+) 752.46 $(M+H)^+$, found 752.19.

Example 49.



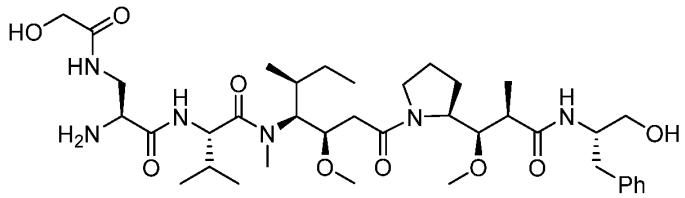
[0796] Compoud 1.41 was prepared by amide coupling of tetrapeptide with L-phenylalaninol. Analytical UPLC-MS (Method 1): $t_R = 1.21$ min, *m/z* (ES+) 718.47 $(M+H)^+$, found 718.10.

Example 50.



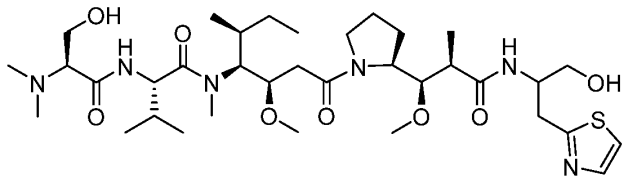
[0797] Compound 1.64 was prepared by amide coupling of tetrapeptide with L-phenylalaninol. Analytical UPLC-MS (Method 1): $t_R = 1.36$ min, *m/z* (ES+) 769.45 $(M+H)^+$, found 769.20.

Example 51.



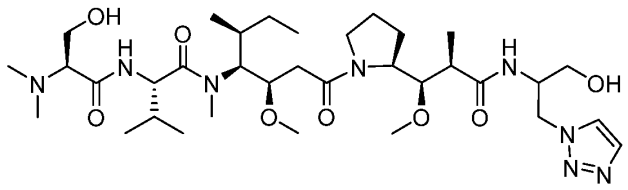
[0798] Compound 1.65 was prepared by amide coupling of tetrapeptide with L-phenylalaninol. Analytical UPLC-MS (Method 1): $t_R = 1.21$ min, *m/z* (ES+) 749.47 $(M+H)^+$, found 749.27.

Example 52.



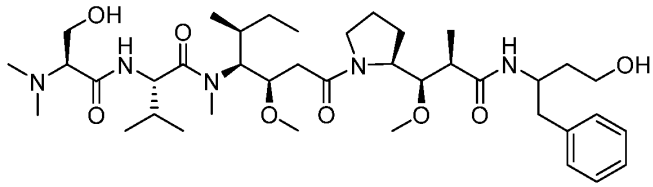
[0799] Compound 1.66 was prepared by amide coupling of tetrapeptide with L-phenylalaninol. Analytical UPLC-MS (Method 1): $t_R = 1.09$ min, *m/z* (ES+) 727.43 $(M+H)^+$, found 727.41.

Example 53.



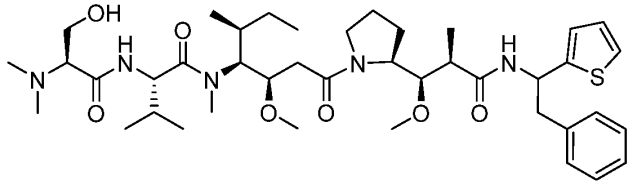
[0800] Compound 1.67 was prepared by amide coupling of tetrapeptide with 2-amino-3-(1*H*-1,2,3-triazol-1-yl)propan-1-ol.. Analytical UPLC-MS (Method 1): $t_R = 1.04$ min, *m/z* (ES+) 711.47 $(M+H)^+$, found 711.19.

Example 54.



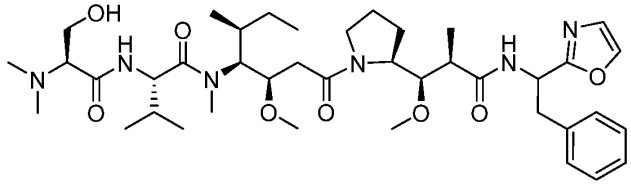
[0801] Compound 1.68 was prepared by amide coupling of tetrapeptide with 3-amino-4-phenylbutan-1-ol. Analytical UPLC-MS (Method 1): $t_R = 1.28$ min, *m/z* (ES+) 734.50 $(M+H)^+$, found 734.25.

Example 55.



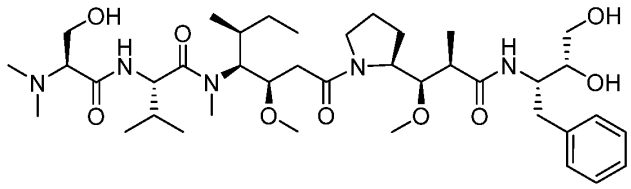
[0802] Compound 1.69 was prepared by amide coupling of tetrapeptide with 2-phenyl-1-(thiophen-2-yl)ethan-1-amine. Analytical UPLC-MS (Method 1): $t_R = 1.53$ min, *m/z* (ES+) 772.46 $(M+H)^+$, found 772.19.

Example 56.



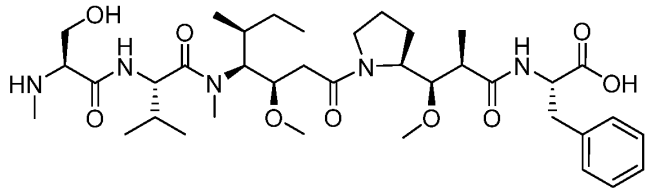
[0803] Compound 1.70 was prepared by amide coupling of tetrapeptide with 1-(oxazol-2-yl)-2-phenylethan-1-amine. Analytical UPLC-MS (Method 1): $t_R = 1.39$ min, *m/z* (ES+) 757.48 $(M+H)^+$, found 757.24.

Example 57.



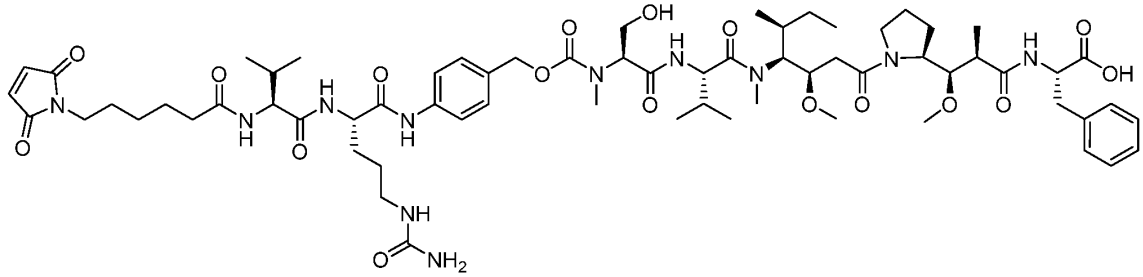
[0804] Compound 1.71 was prepared by amide coupling of tetrapeptide with (2R,3S)-3-amino-4-phenylbutane-1,2-diol. Analytical UPLC-MS (Method 1): $t_R = 1.18$ min, *m/z* (ES+) 750.49 $(M+H)^+$, found 750.20.

Comparative Example A.



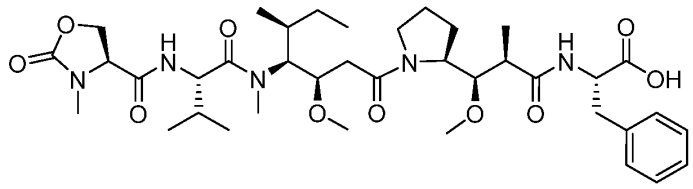
[0805] Comparative Example A was prepared by amide coupling of tetrapeptide with L-phenylalanine.. Analytical UPLC-MS (Method 1): $t_R = 1.34$ min, *m/z* (ES+) 720.45 $(M+H)^+$, found 720.38.

Comparative Example B.



[0806] Comparative Example B was prepared using method A.Analytical UPLC-MS (Method 1): $t_R = 1.79$ min, *m/z* (ES+) 1318.73 $(M+H)^+$, found 1319.21.

Comparative Example C.

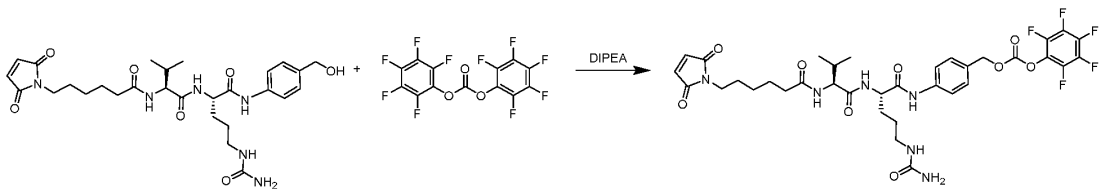


[0807] Comparative Example C was prepared in a similar fashion to Example 36.Analytical UPLC-MS (Method 1): $t_R = 1.73$ min, *m/z* (ES+) 746.43 $(M+H)^+$, found 746.76.

General procedures for solution phase synthesis of auristatins

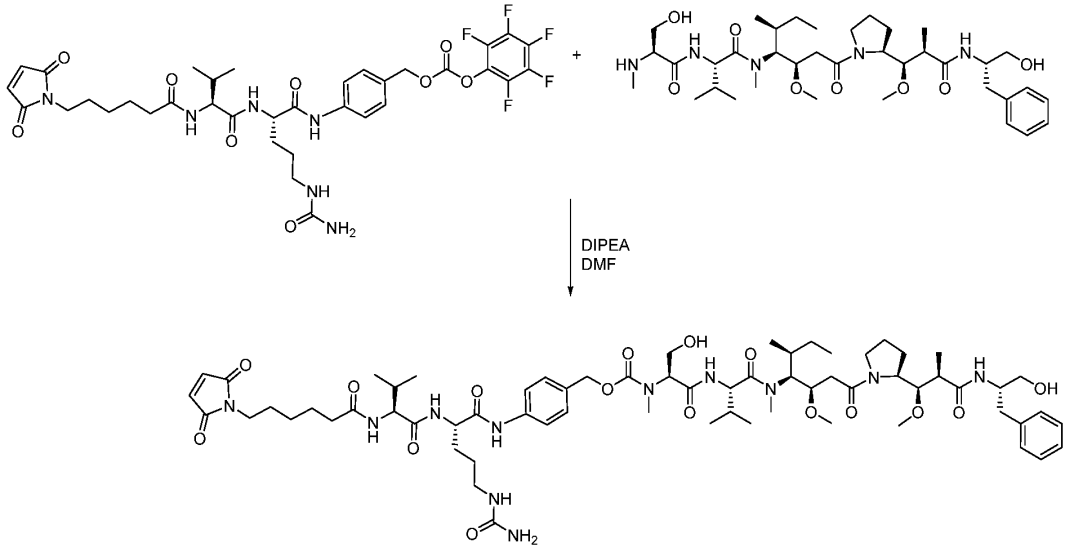
Example 58. General procedure for synthesis of dipeptide carbamate linkers (Method A)

Step 1. Synthesis of MC-VC-PAB-OPFP



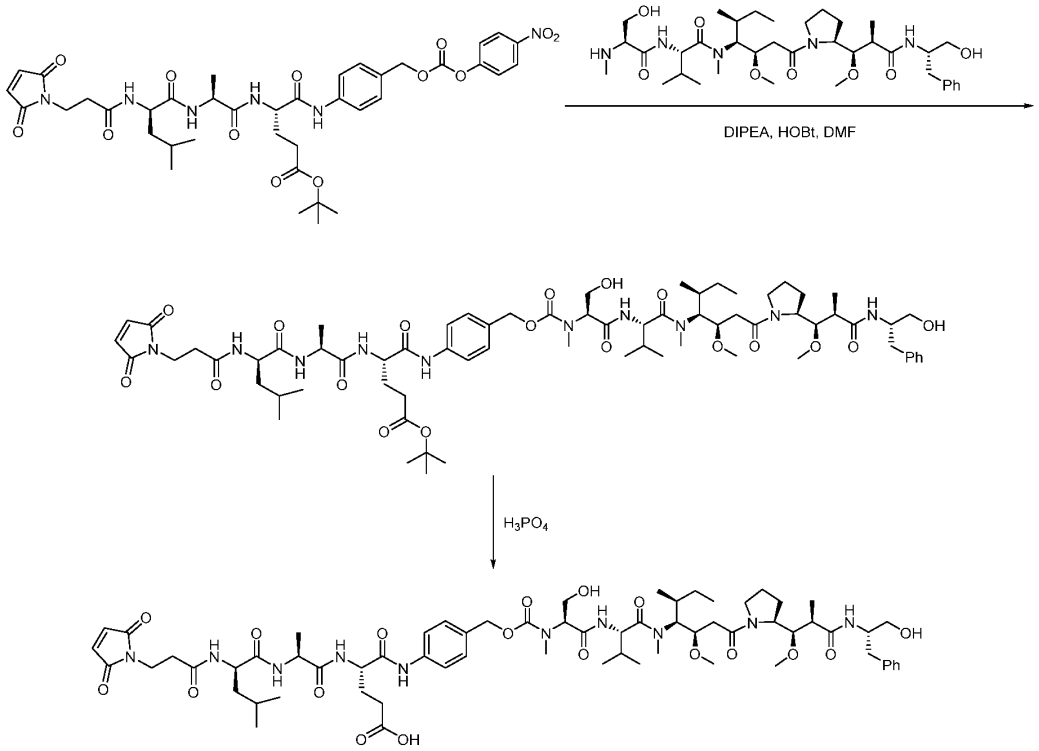
[0808] A 20 mL vial equipped with stir bar was charged with MC-VC-PABA (300 mg, 0.52 mmol), PFP carbonate (413mg, 1.04 mmol), DMF (5 mL), and DIPEA (137uL, 0.78 mmol). The mixture was stirred at RT for 3 hours. The solvent was removed in vacuo and redissolved in 20% piperidine in DMF (5 mL). The reaction was stirred for 1 hour. The solvent was removed in vacuo and was purified by Biotage reverse phase flash column chromatography with acetonitrile + 0.05% TFA and water + 0.05% TFA gradient up to 95% acetonitrile. The product fractions were lyophilized to afford 177 mg (43% yield). Analytical UPLC-MS: $t_R = 2.05$ min, *m/z* (ES+) 783.27 $(M+H)^+$, found 783.42.

Step 2. Drug-Linker formation



[0809] A 20 mL vial equipped with stir bar was charged with the compound of Example 12 (70 mg, 0.1 mmol), MC-VC-PAB-OPFP (78 mg, 0.1 mmol), DMF (5 mL), and DIPEA (26 uL, 0.15 mmol). The mixture was stirred at RT overnight. The solvent was removed in vacuo and was purified by preparative HPLC. The product fractions were lyophilized to afford 80.7 mg (62 % yield) of compound 2.2. Analytical UPLC-MS: t_{R} = 1.82 min, *m/z* (ES+) 1304.75 $(M+H)^{+}$, found 1305.54.

Example 59. General procedure for synthesis of (D)Leu-Ala-Glu tripeptide carbamate drug-linkers (Method B)



[0810] This is a modified version of a previously reported procedure. *See* WO 2021/055865.

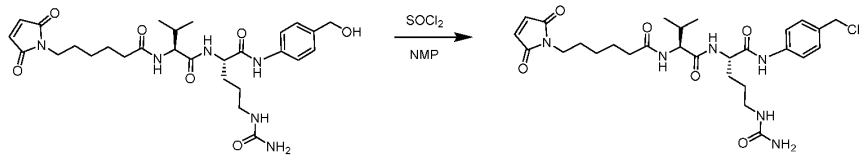
[0811] A 4 mL vial equipped with stir bar was charged with the compound from Example 12 (100 mg, 0.14 mmol), MC-(D)-Leu-Ala-Glu(OtBu)-PABA-O_pNP (114 mg, 0.14 mmol), DMF (5 mL), DIPEA (51 uL, 0.28 mmol), and HOBt (37 mg, 0.28 mmol). The mixture was stirred at RT overnight. The solvent was removed in vacuo.

[0812] The crude mixture was dissolved in propionitrile (3 mL), and H_3PO_4 (3 mL) was slowly added to the reaction mixture at RT. The reaction mixture was stirred for 2 h and priopionitrile (6 mL) was added to the mixture. The organic layer was separated, and the reaction was concentrated and purified by HPLC. The product fractions were lyophilized to afford 54 mg (26% yield) of compound 2.6.

[0813] Analytical UPLC-MS: $t_R = 1.71$ min, *m/z* (ES+) 1319.71 $(M+H)^+$, found 1320.06.

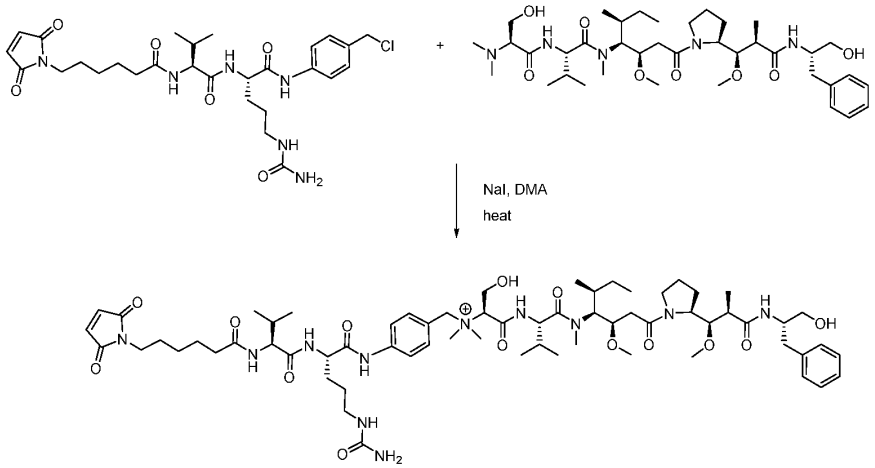
Example 60. General procedure for synthesis of quaternary linkers (Method C)

Step 1. Synthesis of MC-VC-PAB-Cl



[0814] A 20 mL vial equipped with stir bar was charged with solution of MC-Val-Cit-PAB-OH (200 mg, 349.25 umol) in N-methyl-2-pyrrolidone (NMP, 3 mL) and then cooled to 0°C. A solution of $SOCl_2$ (70.64 mg, 593.73 umol) in NMP (0.5 mL) was added dropwise. The mixture was stirred at 20°C for 30 min. TLC (ethyl acetate: methanol = 3: 1, Rf = 0.5) showed the reaction was completed. The mixture was poured into ice water and filtered, washed with acetonitrile and ethyl acetate, dried in high vacuum to give MC-Val-Cit-PAB-Cl (100 mg, yield 48.4%). Analytical UPLC-MS: t_R = 2.05 min, *m/z* (ES+) 591.27 $(M+H)^+$, found 591.42. 1H NMR: (400MHz, DMSO-d6) δ = 10.16 – 9.89 (m, 1H), 8.08 (br d, J=7.4 Hz, 1H), 7.79 (br d, J=8.6 Hz, 1H), 7.60 (br d, J=8.5 Hz, 2H), 7.36 (d, J=8.5 Hz, 2H), 7.00 (s, 2H), 5.96 (br t, J=5.4 Hz, 1H), 5.52 – 5.20 (m, 2H), 4.71 (s, 2H), 4.45 – 4.31 (m, 1H), 4.19 (br t, J=7.6 Hz, 1H), 3.45 – 3.34 (m, 2H), 3.09 – 2.85 (m, 2H), 2.14 (tq, J=7.2, 14.5 Hz, 2H), 2.03 – 1.85 (m, 1H), 1.75 – 1.55 (m, 2H), 1.54 – 1.27 (m, 6H), 1.26 – 1.10 (m, 2H), 0.83 (br dd, J=6.8, 12.9 Hz, 6H).

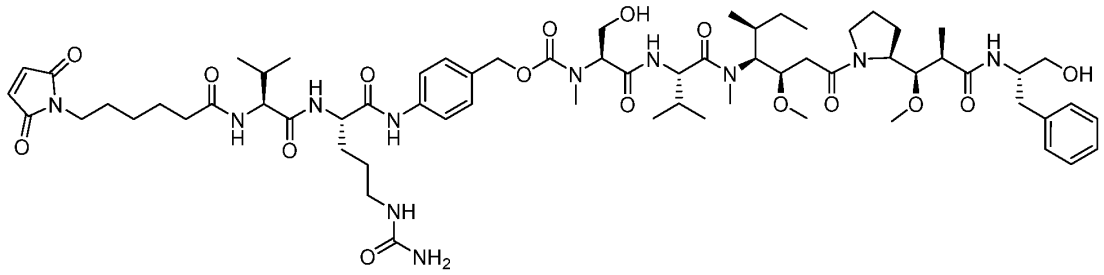
Step 2. Drug-Linker formation



[0815] A 4 mL vial equipped with stir bar was charged with the compound of Example 8 (3.3 mg, 0.004 mmol), mc-VC-PAB-Cl (4.8 mg, 0.008 mmol), DMA (0.5 mL), and NaI (1.2

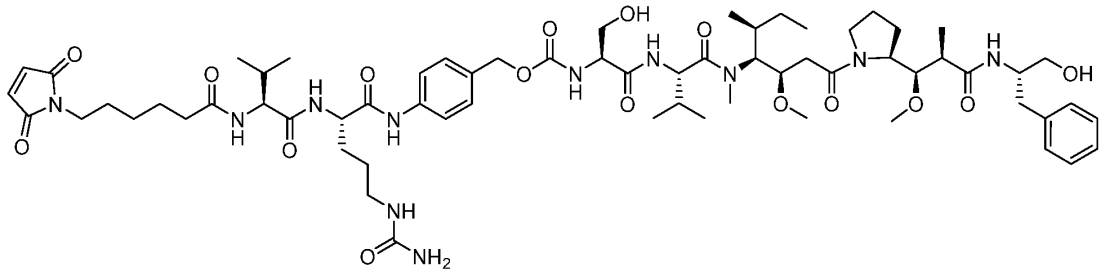
mg, 0.008 mmol). The mixture was stirred at 70° C for 4 hours. The reaction was purified by preparative HPLC. The product fractions were lyophilized to afford 3.9 mg (71% yield) of the title compound (compound 2.1). Analytical UPLC-MS : $t_R = 1.51$ min, *m/z* (ES+) 1275.62 $(M)^+$, found 1275.46.

Example 61.



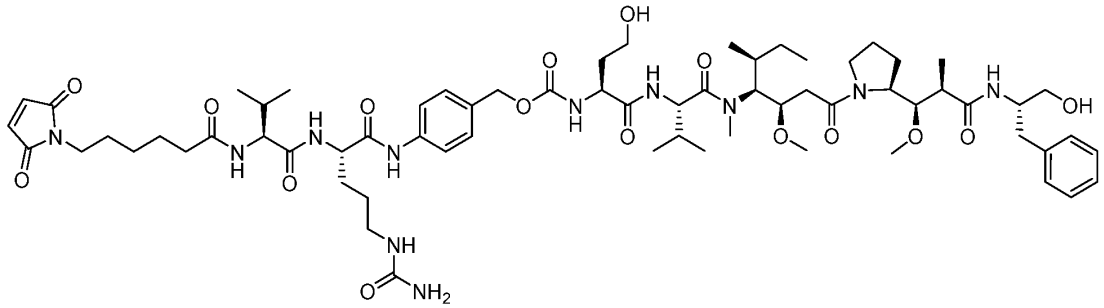
[0816] Compound 2.2 was synthesized using method A. 62% yield. Analytical UPLC-MS: $t_R = 1.82$ min, *m/z* (ES+) 1304.75 $(M+H)^+$, found 1305.54.

Example 62.



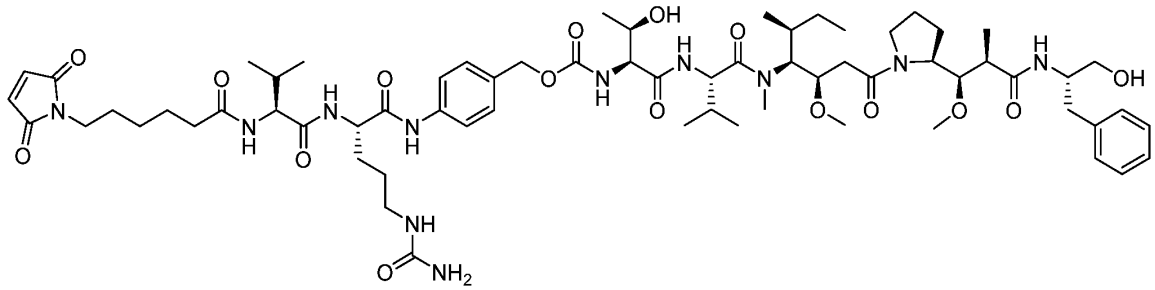
[0817] Compound 2.9 was synthesized using method A. 43% yield. Analytical UPLC-MS: $t_R = 1.72$ min, *m/z* (ES+) 1290.73 $(M+H)^+$, found 1291.59.

Example 63.



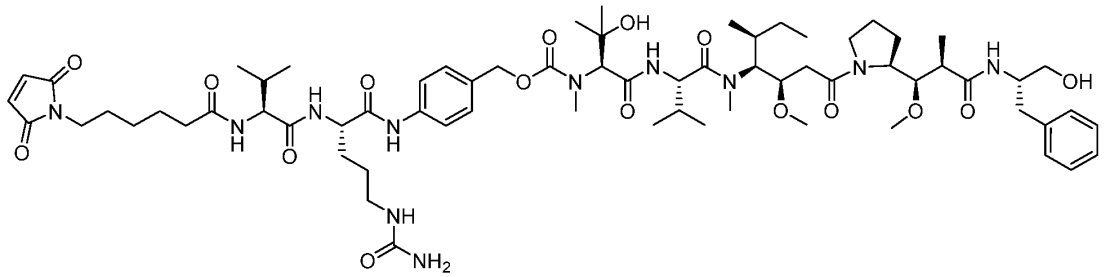
[0818] Compound 2.10 was synthesized using method A. 52% yield. Analytical UPLC-MS: $t_R = 1.74$ min, *m/z* (ES+) 1304.75 $(M+H)^+$, found 1305.28.

Example 64.



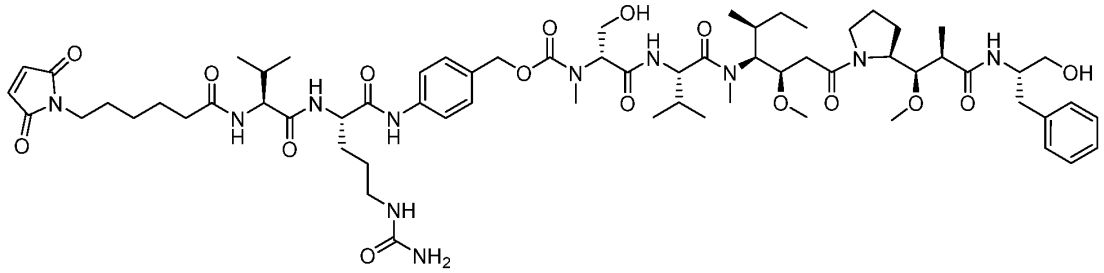
[0819] Compound 2.11 was synthesized using method A. 64% yield. Analytical UPLC-MS: t_R = 1.77 min, *m/z* (ES+) 1304.75 $(M+H)^+$, found 1304.61.

Example 65.



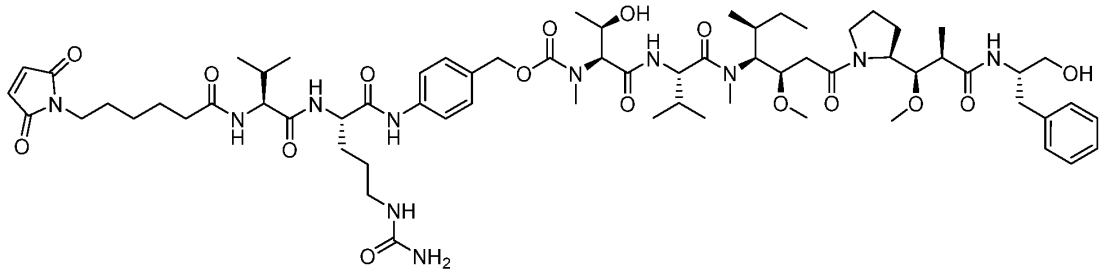
[0820] Compound 2.12 was synthesized using method A. 15% yield. Analytical UPLC-MS: t_R = 1.92 min, *m/z* (ES+) 1332.78 $(M+H)^+$, found 1333.51.

Example 66.



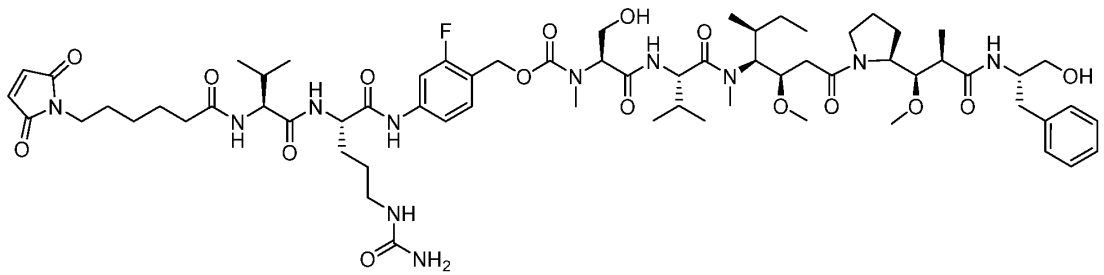
[0821] Compound 2.13 was synthesized using method A. 57% yield. Analytical UPLC-MS: t_R = 1.68 min, *m/z* (ES+) 1304.75 $(M+H)^+$, found 1305.43.

Example 67.



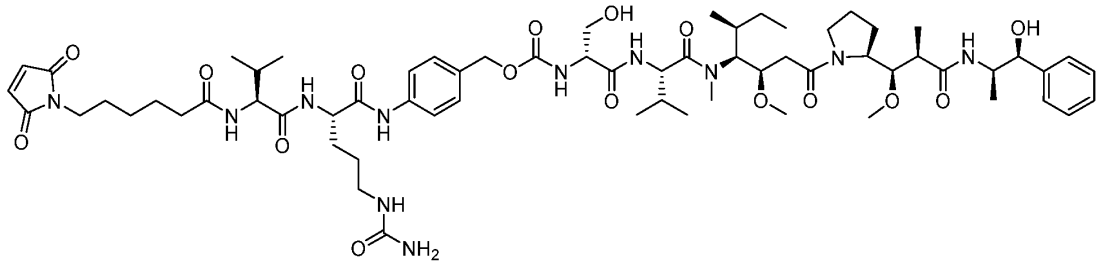
[0822] Compound 2.14 was synthesized using method A. 47% yield. Analytical UPLC-MS: $t_R = 1.72$ min, *m/z* (ES+) 1318.77 $(M+H)^+$, found 1319.31.

Example 68.



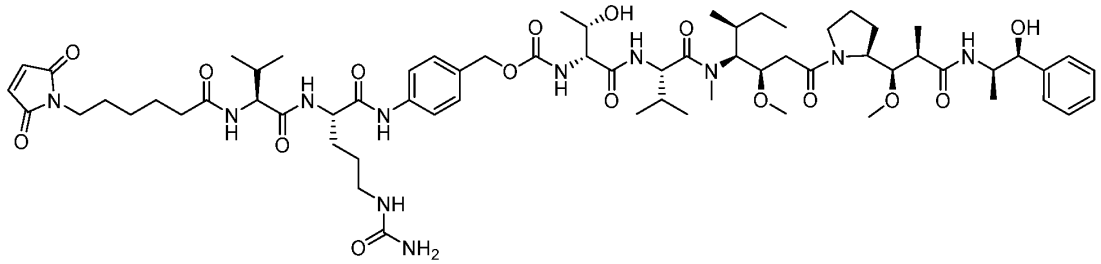
[0823] Compound 2.19 was synthesized using method A. 80% yield. Analytical UPLC-MS: $t_R = 1.75$ min, *m/z* (ES+) 1322.74 $(M+H)^+$, found 1323.30.

Example 69.



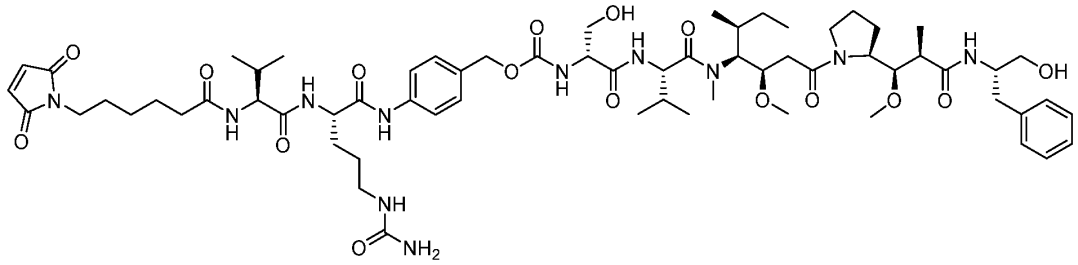
[0824] Compound 2.20 was synthesized using method A. 22% yield. Analytical UPLC-MS: $t_R = 1.67$ min, *m/z* (ES+) 1291.58 $(M+H)^+$, found 1291.42.

Example 70.



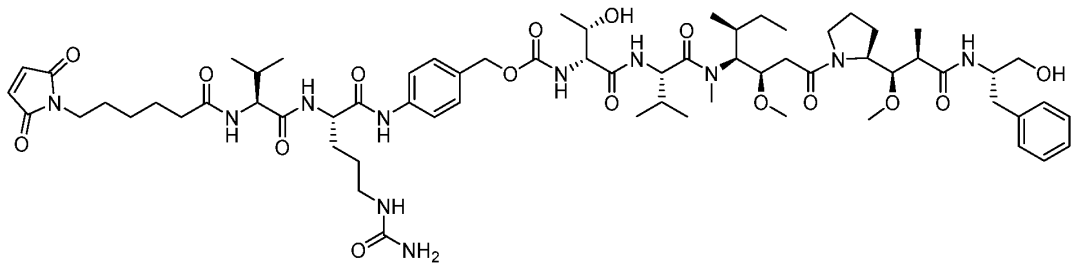
[0825] Compound 2.3 was synthesized using method A. Analytical UPLC-MS: t_R = 1.71 min, *m/z* (ES+) 1305.60 $(M+H)^+$, found 1304.91.

Example 71.



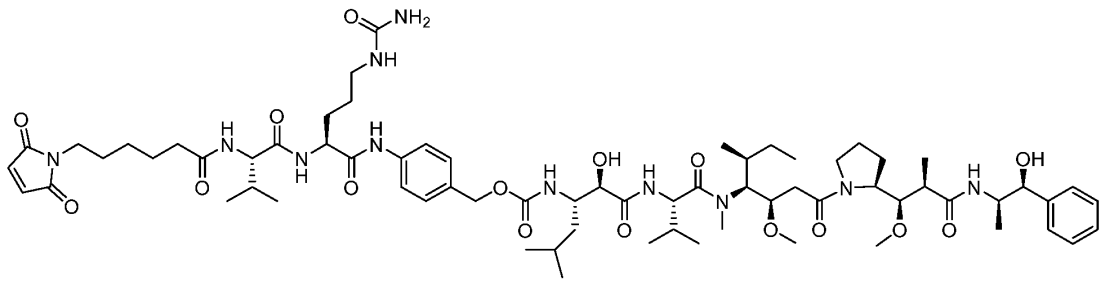
[0826] Compound 2.29 was synthesized using method A.

Example 72.



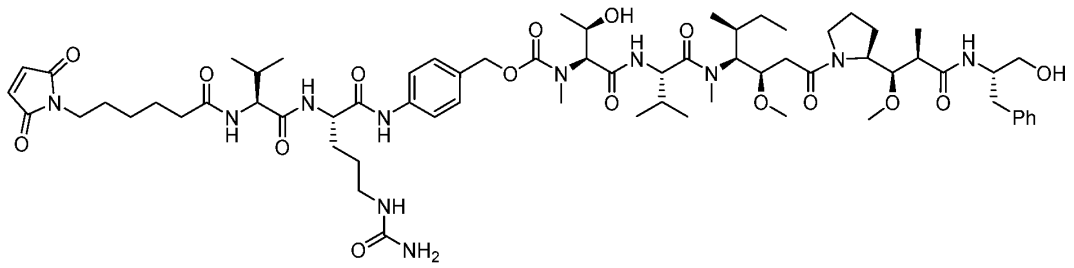
[0827] Compound 2.21 was synthesized using method A.

Example 73.



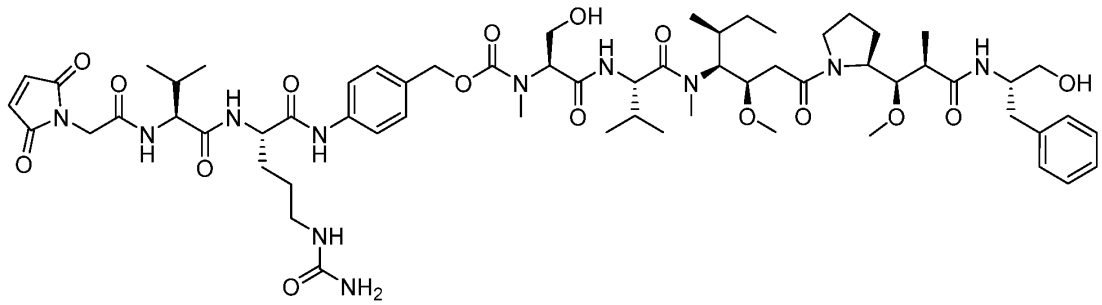
[0828] Compound 2.22 was synthesized using method A. 27% yield. Analytical UPLC-MS: t_R = 1.87 min, *m/z* (ES+) 1346.80 $(M+H)^+$, found 1347.50.

Example 74.



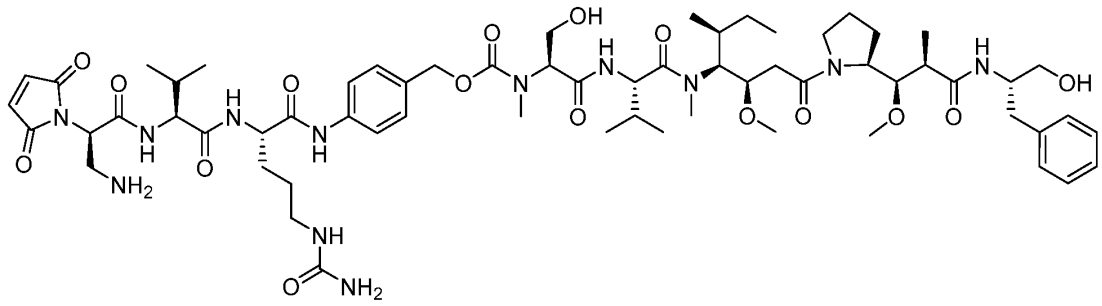
[0829] Compound 2.14 was synthesized using method A. Analytical UPLC-MS: t_R = 1.57 min, *m/z* (ES+) 1332.77 $(M+H)^+$, found 1332.81.

Example 75.



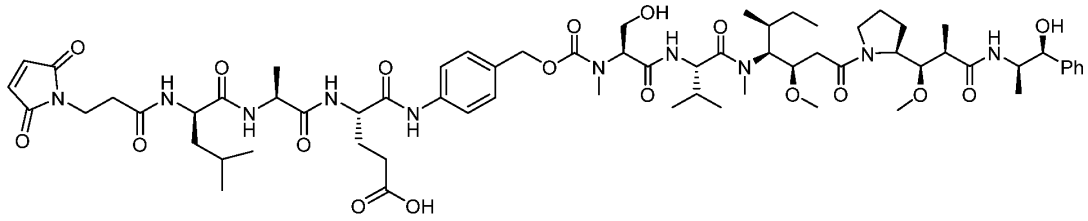
[0830] Compound 2.4 was synthesized using method A. Analytical UPLC-MS: t_R = 1.64 min, *m/z* (ES+) 1248.69 $(M+H)^+$, found 1249.42.

Example 76.



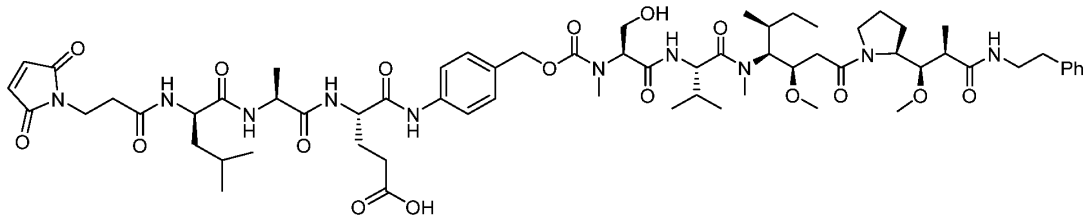
[0831] Compound 2.5 was synthesized using method A. Analytical UPLC-MS: t_R = 1.85 min, *m/z* (ES+) 1277.71 $(M+H)^+$, found 1278.21.

Example 77.



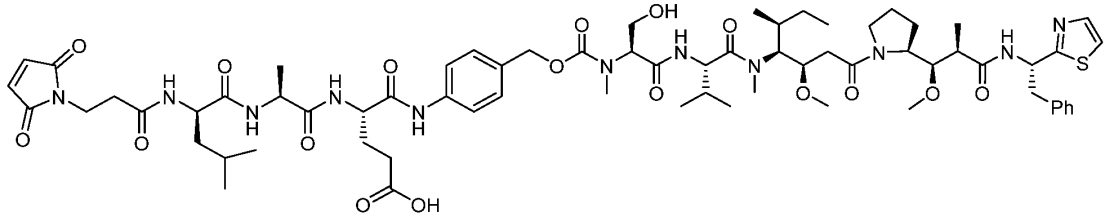
[0832] Compound 2.6 was synthesized using method B. Analytical UPLC-MS: $t_R = 1.69$ min, *m/z* (ES+) 1319.71 $(M+H)^+$, found 1319.75.

Example 78.



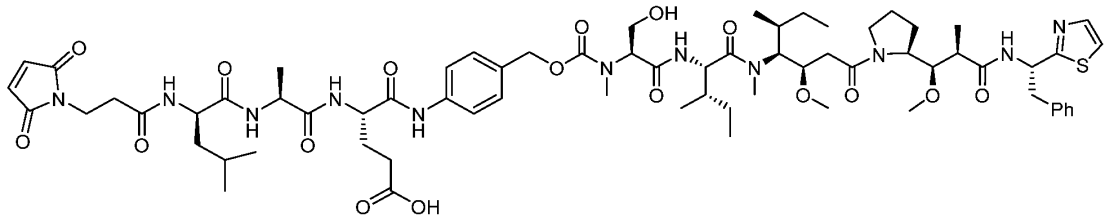
[0833] Compound 2.16 was synthesized using method B. Analytical UPLC-MS: $t_R = 1.71$ min, *m/z* (ES+) 1289.70 $(M+H)^+$, found 1289.83.

Example 79.



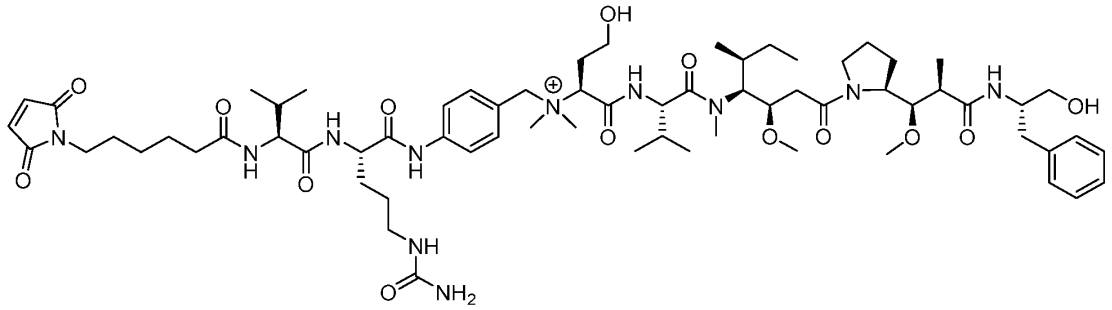
[0834] Compound 2.17 was synthesized using method B. Analytical UPLC-MS: $t_R = 1.75$ min, *m/z* (ES+) 1372.69 $(M+H)^+$, found 1372.75.

Example 80.



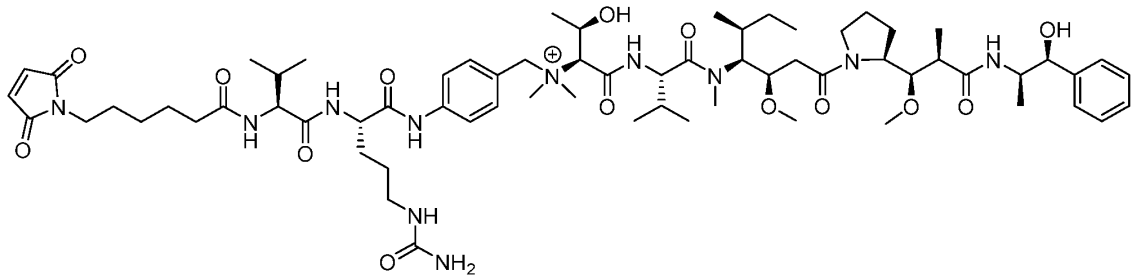
[0835] Compound 2.18 was synthesized using method B. Analytical UPLC-MS: $t_R = 1.81$ min, *m/z* (ES+) 1386.70 $(M+H)^+$, found 1386.73.

Example 81.



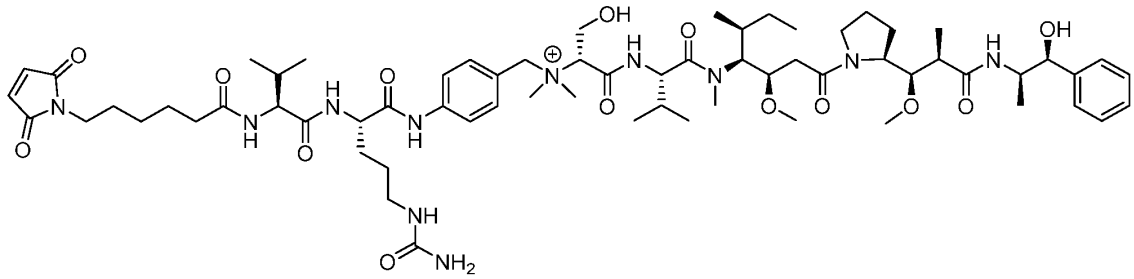
[0836] Compound 2.23 was synthesized using method C. Analytical UPLC-MS: $t_R = 1.52$ min, *m/z* (ES+) 1288.79 $(M)^+$, found 1288.88.

Example 82.



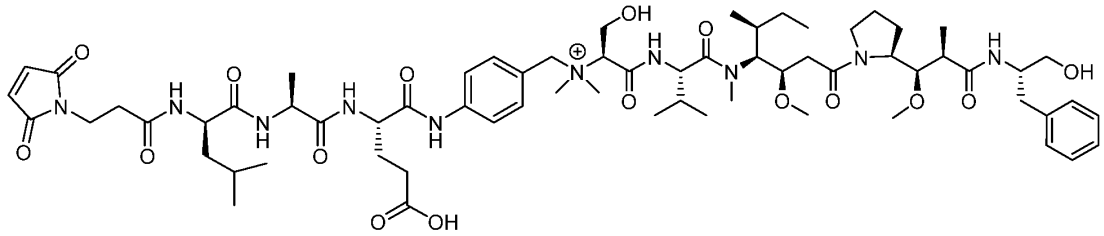
[0837] Compound 2.24 was synthesized using method C. Analytical UPLC-MS: $t_R = 1.39$ min, *m/z* (ES+) 1288.79 $(M)^+$, found 1288.82.

Example 83.



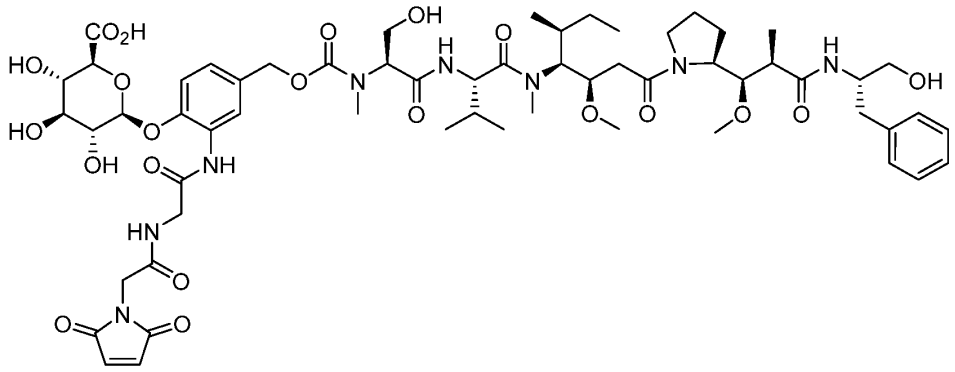
[0838] Compound 2.25 was synthesized using method C. Analytical UPLC-MS: $t_R = 1.51$ min, *m/z* (ES+) 1274.78 $(M)^+$, found 1274.88.

Example 84.



[0839] Compound 2.26 was synthesized using method C. Analytical UPLC-MS: $t_R = 1.60$ min, *m/z* (ES+) 1289.74 $(M)^+$, found 1289.92.

Example 85.



[0840] Modified – compound 2.7 synthesized according to a known procedure (Burke, P. J. et al. *Mol. Cancer Ther.* **2017**, 16, 116-123).

[0841] Analytical UPLC-MS: $t_R = 1.68$ min, *m/z* (ES+) 1241.58 $(M+H)^+$, found 1241.25.

Example 86. Measurement of LogD

[0842] The LogD (distribution coefficient) of the compounds was measured using a miniaturized 1-octanol/pH 7.4 buffer shake flask method followed by LC/MS/MS analysis. Values were determined by measuring the compound partitioned in the organic and buffered layers. Results are shown in Table 4.

Example 87. In vitro cytotoxicity

[0843] The cytotoxicity of free drugs and drug conjugates were measured by a cell proliferation assay employing the protocol described in Promega Corp. Technical Bulletin TB288; and Mendoza et al., 2002, Cancer Res. 62:5485-5488), the methods of which are specifically incorporated by reference herein. Briefly, an aliquot of 40 µl of cell culture containing about 400 cells in medium is deposited in each well of a 384-well, opaque-walled

plate. A 10 µL aliquot of free drug or drug conjugate is added to the experimental wells and incubated for 96 h and are then equilibrated to room temperature for approximately 30 minutes whereupon a volume of CellTiter-GloTM reagent equal to the volume of cell culture medium present in each well is added. The contents are mixed for 2 minutes on an orbital shaker to induce cell lysis and the plate is incubated at room temperature for 10 minutes to stabilize the luminescence signal for recordation. Results are shown in Table 4.

Table 4A. Auristatin free drug LogD values and *in vitro* IC_{50} (nM) values on cancer cell lines.

Free drug Example #	**Table 1 compound number**	DEL ALCL	Karpas299 NHL	L540cy HL	LogD
26	1.72	4.2	5	20	
32	1.56	64	56	920	0.3
12	1.9	1.1	0.3	4.8	1.2
28	1.23	7.8	9.4	28	2.0
36	1.50	6.7	27	197	
23	1.16	17	66	662	
40	1.46	12.3	60	442	
24	1.18	13	43	621	
41	1.47	15	62	457	
25	1.20	18.9	62	457	
42	1.48	16	64	481	
13	1.12	1.2	2.2	5	1.4
43	1.60	3.2	5.9	19	
17	1.29	2.5	7.6	16.2	1.1
18	1.30	0.6	2.3	16	1.9
19	1.32	0.4	0.5	2.5	2.4
37	1.53	>1000	>1000	>1000	
38	1.54	148	>1000	512	
39	1.55	512	>1000	>1000	
8	1.1	0.7	1.4	6.6	1.6
45	1.52	8.5	40.8	272	1.5
14	1.10	3.5	7.4	10	1.1
20	1.33	0.3	1	4.7	1.9
15	1.13	0.7	2.3	3.9	
22	1.58	5.8	13	16	
33	1.59	1.8	1.7	6.4	3.2
29	1.21	12.7	13.7	58	2.0
30	1.24	396	481	>1000	1.2
31	1.25	2.1	1.7	4.7	3.4
27	1.22	1.9	2.3	13	
9	1.3	0.8	0.9	4	

10	1.4	0.4	0.5	3	
11	1.2	1	1	6	
46	1.61	141	264	>1000	
47	1.28	>1000	>1000	>1000	
48	1.62	41	110	>1000	
49	1.41	32	35	76	
50	1.64	>1000	>1000	>1000	
51	1.65	93	224	>1000	
52	1.66	43	58	438	
53	1.67	>1000	>1000	>1000	
54	1.68	7	6	274	
55	1.69	0.8	1	16	
56	1.70	1	0.9	24	
57	1.71	4	3	49	
MMAE	-	0.05	0.1	0.1	1.9
MMAF	-	44	41	47	0.03

Table 4B. Auristatin free drug *in vitro* IC_{50} (nM) values on cancer cell lines.

Free Drug Example #	**Table 1 compound number**	**DEL ALCL**	**Karpas299 NHL**	**L540cy HL**
Comparative Example A		209	253	>1000
12	1.9	1.1	0.3	4.8
MMAE		0.05	0.1	0.1
MMAF		44	41	47
Comparative Example C		342	218	284
40	1.46	12.3	60	442

Example 88. Conjugation of Drug-Linker compounds to antibodies to form Ligand-Drug Conjugate compounds

[0844] Antibodies were partially reduced using the appropriate equivalents of TCEP according to the procedure, which is specifically incorporated by reference herein, of US 2005/0238649. Briefly, the antibody in phosphate buffered saline with 2 mM EDTA, pH 7.4, was treated with 2.1 eq. TCEP and then incubated at 37° C for about 45 minutes. The thiol/Ab value was checked by reacting the reduced antibody with MC-VC-MMAE and using hydrophobic interaction chromatography to determine the loading.

[0845] The auristatin drug linker compounds were conjugated to the partially reduced antibody using the method, which is specifically incorporated by reference herein, of US

2005/0238649. Briefly, Drug-Linker compound (50% excess) in DMSO, was added to the reduced antibody in PBS with EDTA along with additional DMSO for a total reaction co-solvent of 10-20%. After 30 minutes at ambient temperature, an excess of QuadraSil MPTM was added to the mixture to quench all unreacted maleimide groups. The resulting Ligand-Drug Conjugate compound was then purified, and buffer exchanged by desalting using Sephadex G25 resin into pH 6.5 histidine buffer and kept at -80° C until further use. The protein concentration of the resulting ADC composition was determined at 280 nm. The drug-antibody ratio (DAR) was confirmed by comparing predicted and observed changes in the molecular weights of heavy and light chains using PLRP-MS analysis and confirming absence of underloaded species.

Example 89. In vivo cytotoxicity of Ligand-Drug Conjugate compounds

[0846] Cancer cells were implanted into mice. Upon tumor engraftment, mice were randomized to study groups (n = 5) once the average tumor volume reached approximately 100 mm^3. ADC prepared from reduced antibody and compound was administered via an intraperitoneal or intravenous injection. Tumor volumes are calculated using the formula (0.5xLxW2) where L and W are the longer and shorter of two bidirectional measurements. Complete response (CR) is defined here as absence of measurable mass at tumor site during an experiment. Results are showin in FIGs. 1 to 5 and in Table 5 for Ligand-Drug Conjugate compounds with an average drug loading of 4 Drug-Linker moieties per antibody.

[0847] FIG. 1 shows the efficacy of a 6mg/kg dose of a variety of Ag1 ADCs as measured in the A2058 melanoma xenograft model. The data show that Ag1 ADCs comprising hydrophilic auristatin Drug Units have efficacy comparable to ADCs comprising MMAE.

[0848] FIG. 2 shows the efficacy of a 3mg/kg dose of a variety of h2A2 ADCs as measured in the Detroit 562-39 pharyngeal xenograft model. The data show that h2A2 ADCs comprising hydrophilic auristatin Drug Units have efficacy comparable to ADCs comprising MMAE.

[0849] FIG. 3 shows the efficacy of a 3 mg/kg dose of a variety of cAC10 ADCs as measured in the Karpas/KarpasBVR admixed Hodgkin lymphoma xenograft model. The data show that cAC10 ADCs with hydrophilic auristatin Drug Units have bystander activity between that of MC-VC-MMAE and MC-VC-MMAF.

[0850] FIG. 4 shows the efficacy of a 1 mg/kg dose of a variety of cAC10 ADCs in the Karpas Hodgkin lymphoma xenograft model. The data show that cAC10 ADCs comprising hydrophilic auristatin Drug Units have efficacy comparable to ADCs comprising MMAE.

[0851] FIG. 5 shows the efficacy of a 1 mg/kg dose of a variety of cAC10 ADCs in the Karpas Hodgkin xenograft model. The data show that cAC10 ADCs comprising hydrophilic auristatin Drug Units have efficacy comparable to ADCs comprising MMAE.

Example 90. Toxicity Determinations of Ligand-Drug Conjugate compounds.

[0852] *In vivo* rat safety studies were done in naive female Sprague Dawley rats (Envigo). Studies had 3 animals/group/timepoint and included a vehicle control group (1X PBS pH 7.4). Animals were administered a single dose of 15 or 80 mg/kg of an h00 ADC (DAR = 4) via intravenous injection. Blood was drawn at days 5 and day 8. Blood was sampled under isoflurane anesthesia via the jugular vein for periodic hematology analysis on the Sysmex XT-2000iV. At necropsy, blood was collected from the caudal vena cava for hematology and clinical chemistry panels. Clinical chemistry was analyzed on a Beckman Coulter AU680. Results are shown in FIGs. 6 to 9.

[0853] FIG. 6 demonstrates that neutrophil counts are higher at on Day 5 and recovery of neutrophil counts on Day 8 are higher after administering Ligand-Drug Conjugate compounds comprising hydrophilic auristatin Drug Units when compared to MMAE containing conjugates.

[0854] FIG. 7 demonstrates that recovery of reticulocytes is greatly improved after administering Ligand-Drug Conjugate compounds comprising hydrophilic auristatin Drug Units when compared to MMAE containing conjugates.

[0855] FIG. 8 shows that administering Ligand-Drug Conjugate compounds with hydrophilic auristatin Drug Units does not impact the platelet count as heavily as administering an MMAF containing conjugate. Recovery of platelets is also better after administering Ligand-Drug Conjugate compounds comprising hydrophilic auristatin Drug Units when compared to MMAE and MMAF containing conjugates.

[0856] FIG. 9 shows that aspartate transaminease (AST) levels indicating liver damage are lower 8 days after administering 80 mg/kg of Ligand-Drug Conjugate compounds comprising hydrophilic auristatin Drug Units when compared to after administering 15 mg/kg of an MMAF containing conjugates. The AST levels 8 days following administration are comparable for an 80 mg/kg dose of some Ligand-Drug Conjugate compounds comprising

hydrophilic auristatin Drug Units when compared to a 15 mg/kg dose of an MMAE conjugate.

Table 5A. *In vitro* IC_{50} (ng/mL) values of auristatin anti-CD30 ADCs on CD30-expressing cell lines using cAC10 ADCs with an average drug loading of about 4 of selected Drug-Linker compounds.

Drug-Linker moiety Example #	**Table 2 compound number**	DEL ALCL	Karpas299 NHL	L540cy HL
69	2.20	0.01	0.2	NA
71	2.29	NA	7	9
72	2.21	NA	7	15
61	2.2	0.01	0.6	6.3
59	2.6	0.1	1.2	9.3
63	2.10	12	290	>1000
62	2.9	3.8	>1000	>1000
64	2.11	22	>1000	>1000
76	2.5	NA	NA	NA
65	2.12	0.04	1.2	3.8
85	2.7	0.01	0.5	3.6
75	2.4	0.01	0.2	3.2
60	2.1	0.09	0.4	4.3
66	2.13	0.3	5.1	4.9
67	2.14	1.7	29	33
68	2.19	1	15	35
77	2.6	0.4	5.6	8.2
78	2.16	1.3	58	>1000
79	2.17	1.5	0.9	4.7
80	2.18	1.4	>1000	>1000
70	2.3	0.03	1	1.9
84	2.26	0.01	0.1	13
73	2.22	>1000	>1000	>1000
81	2.23	0.1	0.1	1
82	2.24	0.2	0.3	4
83	2.25	0.1	0.1	4
MC-VC-MMAE	-	0.4	0.6	2
MC-VC-MMAF	-	0.1	1	3

Table 5B. *In vitro* IC_{50} (ng/mL) values of auristatin anti-CD30 ADCs on CD30-expressing cell lines using cAC10 ADCs with an average drug loading of about 4 of selected Drug-Linker compounds.

Drug-Linker moiety Example #	Table 2 compound number	DEL ALCL	Karpas299 NHL	L540cy HL
Comparative Example B	-	0.01	0.01	0.1
61	2.2	0.01	0.06	6.3
MC-VC-MMAE	-	0.4	0.6	2
MC-VC-MMAF	-	0.1	1	3

Table 5C. ***In vitro*** **IC_{50} (ng/mL) values of auristatin anti-CD30 ADCs on CD30-expressing cell lines using cAC10 ADCs with an average drug loading of about 4 of selected Drug-Linker compounds.**

Drug-Linker moiety Example #	Table 2 compound number	DEL ALCL	Karpas299 NHL	L540cy HL
61	2.2	0.01	0.6	6.3
75	2.4	0.01	0.2	3.2
76	2.5	NA	NA	NA
85	2.7	0.01	0.5	3.6
59	2.6	0.1	1.2	9.3
60	2.1	0.09	0.4	4.3
84	2.26	0.01	0.1	13
MC-VC-MMAE	-	0.4	0.6	2
MC-VC-MMAF	-	0.1	1	3

Table 5D. ***In vitro*** **IC_{50} (ng/mL) values and tolerability of auristatin anti-CD30 ADCs on CD30-expressing cell lines using cAC10 ADCs with an average drug loading of about 4 of selected Drug-Linker compounds.**

Drug-Linker moiety Example #	Table 2 compund number	DEL ALCL	Karpas299 NHL	L540cy HL	Tolerated at 80 mg/kg in rats
61	2.2	0.01	0.6	6.3	Yes
78	2.16	1.3	58	>1000	Yes
79	2.17	1.5	0.9	4.7	No
80	2.18	1.4	>1000	>1000	Yes

Example 91. Comparison of compound tolerability

[0857] Tolerability of an ADC comprising the compound of Example 8 of the present application was compared to tolerability of ADCs comprising the known compounds MMAE

and MMAF. Without being bound by theory, the improvements in tolerability are believed to be related to reduced toxicities in the bone marrow and in the liver that are a result of the OH moieties on the compound of Example 8. See Table 6 below.

Table 6. Tolerability comparison of compound 1.1 to MMAE and MMAF

Compound	LogD	Avg IC50 Free drug ^ (nM)	Avg IC50 of corresponding dipeptide linked ADC^* (ng/mL)	Maximum tolerated dose** (mg/kg)	
				Based on reduced Neutrophil counts	Based on elevated AST level
MMAE	1.9	0.2	1	15	>15
Example 8 (compound 1.1)	1.6	2.9	1.5	>80	>80
MMAF	0.03	44	1.3	>15	15

^ **Average cytotoxicity of DEL, Karpas299, and L540cy cell lines**
* **anti-CD30 ADCs**
** **Dosed in Sprague-Dawley Rats**

Example 92. *In vitro* quantitative flow cytometry of cancer cell lines

[0858] Cancer cells were counted and 100,000-200,000 cells were plated in 100 µL FACS buffer in 96-well U-bottom plates (Falcon). Cells were incubated with 10 ug/mL of non-binding and targeted (hCR011) human IgG for one hour at 4°C. Cells were washed 3x before anti-IgG FITC secondary antibody and calibration beads from Human IgG Calibrator Kit (BioCytex Ref#CP101) were added for 30 minutes at 4°C. Cells were washed 2x and run on an Attune cytometer. Data was analyzed using FlowJo software (BD). Target antigen (gpNMB) copy number was determined per manufacturer's instructions; briefly, the MFI values of calibration beads were used to determine the antibody binding capacity and the specific antibody binding capacity (SABC) was determined by subtracting the non-binding IgG MFI from the targeted (hCR011) MFI. The SABC numbers for hCR011 (i.e. gpNMB copy number) are summarized in **Table 7**.

Table 7. gpNMB (hCR011) copy numbers for a panel of cancer cell lines

Cell line	SABC
WM2664	14612
SKMEL5	5035
HCC2218	13207

SKBR3	2839
SKMEL28	8671
CALU1	229
A2058	2,781

Example 93: *In vitro* cytotoxicity of Auristatin ADCs in a panel of cancer cell lines

[0859] Cancer cells were counted and plated in 40 µL complete growth media in 384-well, white-walled tissue culture treated plates (Corning). Cell plates were incubated at 37°C and with 5% CO_2 overnight to allow the cells to equilibrate. Stock solutions containing ADCs or free drugs were serially diluted in RPMI-1640 + 20% fetal bovine serum (FBS). 10 µL of each concentration were then added to each cell plate in duplicate. Cells were then incubated at 37°C and with 5% CO_2 for 96 hours, upon which, the cell plates were removed from the incubator and allowed to cool to room temperature for 30 minutes prior to analysis. CellTiter-Glo® luminescent assay reagent (Promega Corporation, Madison, WI) was prepared according to Promega's protocol. 10 µL of CellTiter-Glo® were added to assay plates using a Formulatrix Tempest liquid handler (Formulatrix) and the plates were protected from light for 30 minutes at room temperature. The luminescence of the samples was measured using an EnVision Multimode plate reader (Perkin Elmer, Waltham, MA). Raw data were analyzed in Graphpad Prism (San Diego, CA) using a nonlinear, 4-parameter curve fit model [Y=Bottom + (Top-Bottom)/(1+10^((LogEC50-X)*HillSlope))]. Results are reported as IC50 values, which are defined as the concentration of ADC or free drug required to reduce cell viability to 50%. The cytotoxic activity of auristatin free drugs and ADCs on cancer cell lines is summarized in **Tables 8** and **9**.

Table 8: Cytotoxicity of auristatin ADCs on a panel of cancer cell lines

*Cancer cell lines with > 2000 surface copy number of target antigen (determined by quantitative flow cytometry) were considered positive ("+").

	IC50 (ng/mL)				
Cell line	**Non-binding-ex. 60 (compound 3.1)**	**Non-binding-MC-VC-MMAE**	**hCR011-ex. 60 (compound 3.1)**	**hCR011-MC-VC-MMAE**	**Target expression***
A2058	>30K	>30K	19859	24300	+

CALU1	>30K	>30K	>30K	>30K	-
HCC2218	>30K	>30K	>30K	>30K	+
SKMEL5	22203	11022	1832	916	+
WM2664	>30K	>30K	1566	4468	+
SKBR3	21695	16218	5394	2690	+

Table 9: Cytotoxicity of auristatin free drugs and ADCs on a panel of cancer cell lines

*Cancer cell lines with > 2000 surface copy number of target antigen (determined by quantitative flow cytometry) were considered positive ("+").

	IC50 (ng/mL)				**IC50 (nM)**		
Cell line	**Non-binding-Ex. 60 (compound 3.1)**	**Non-binding-MC-VC-MMAE**	**hCR011-Ex. 60**	**hCR011-MC-VC-MMAE**	**Ex. 8 (compound 1.1)**	**MMAE**	**Target expression***
A2058	>30K	>30K	12858	11118	2	0.3	+
CALU1	>30K	>30K	>30K	14251	5	0.6	-
SKMEL28	>30K	>30K	6913	14020	4	0.4	+
SKMEL5	29560	13119	1513	668	2	0.2	+

Example 94: *In vivo* antitumor activity of Auristatin ADCs in WM2664 and SKMEL5 xenograft tumor models

[0860] Cancer cells were implanted into nude mice. Upon tumor engraftment, mice were randomized to study groups (n = 5) and when tumor volumes reached 100 mm^3, the mice were dosed with ADCs by intravenous injection at the indicated dose Q1Wx3 (3 weekly doses) and tumor volumes were monitored twice weekly. Tumor volumes are calculated using the formula (0.5xLxW2) where L and W are the longer and shorter of two bidirectional measurements. Complete response (CR) is defined here as absence of measurable mass at tumor site during an experiment. Results are shown in Figures 10-11 for Ligand-Drug Conjugate compounds with an average drug loading of 4 Drug-Linker moieties per antibody.

[0861] FIG. 10 shows the efficacy of a variety of hCR011 ADCs and a non-binding control ADC as measured in the WM2664 melanoma xenograft model. The data show that

hCR011 ADCs comprising hydrophilic auristatin Ex. 60 dosed at 3 mg/kg (3 weekly doses) have efficacy comparable to ADCs comprising MMAE. When hCR011-Ex. 60 ADCs are dosed at 9 mg/kg (3 weekly doses), there are 4/5 complete responses.

[0862] FIG. 11 shows the efficacy of a variety of hCR011 ADCs and non-binding control ADCs as measured in the SKMEL5 melanoma xenograft model. The data show that hCR011 ADCs comprising hydrophilic auristatin Ex. 60 dosed at 9 mg/kg (3 weekly doses) have efficacy comparable to ADCs comprising MMAE dosed at 3 mg/kg (3 weekly doses).

Example 95: Antitumor activity of Auristatin ADCs in patient-derived xenograft (PDX) models of melanoma and non-small cell lung cancer (NSCLC)

[0863] Cancer cells were implanted into Nude (Nude-*Foxn1*^{nu}) female mice. When tumors reached an average tumor volume of 150-300 mm^3 animals were matched by tumor volume into treatment or control groups and dosed with ADCs by intravenous injection at the indicated dose Q1Wx3 (3 weekly doses) and tumor volumes were monitored twice weekly. The study endpoint was when the mean tumor volume of the control group (uncensored) reached 1500 mm^3. Complete response (CR) is defined here as absence of measurable mass at tumor site during an experiment. Results are shown in Figures 12-15 for Ligand-Drug Conjugate compounds with an average drug loading of 4 Drug-Linker moieties per antibody. Ag2 refers to an antibody targeting a ubiquitous and readily internalizable antigen on cancer cells.

[0864] FIG. 12 shows the efficacy of non-binding, Ag2, and hCR011 ADCs as measured in the PDX_1 melanoma xenograft model. The data show that hCR011 ADCs comprising hydrophilic auristatin Ex. 60 (compound 3.1 wherein L is hCR011) dosed at 3 mg/kg have efficacy comparable to ADCs comprising MMAE dosed at 3 mg/kg. Ag2 and hCR011 ADCs with Ex. 60 (compound 3.1 wherein L is hCR011) dosed at 9 mg/kg elicited more robust antitumor activity.

[0865] FIG. 13 shows the efficacy of non-binding, Ag2, and hCR011 ADCs as measured in the PDX_4 melanoma xenograft model. The data show that hCR011 ADCs comprising hydrophilic auristatin Ex. 60 (compound 3.1 wherein L is hCR011) dosed at 3 mg/kg have efficacy comparable to ADCs comprising MMAE dosed at 3 mg/kg. Ag2 and hCR011 ADCs with Ex. 60 (compound 3.1 wherein L is Ag2 or hCR011, respectively) dosed at 9 mg/kg elicited more robust antitumor activity, with hCR011-Ex. 60 ADCs leading to 2/5 complete responses.

[0866] FIG. 14 shows the efficacy of non-binding, Ag2, and hCR011 ADCs as measured in the PDX_3 NSCLC xenograft model. The data show that Ag2 and hCR011 ADCs comprising hydrophilic auristatin Ex. 60 (compound 3.1 wherein L is Ag2 or hCR011, respectively) dosed at 3 and/or 9 mg/kg have efficacy comparable to ADCs comprising MMAE dosed at 3 mg/kg.

[0867] FIG. 15 shows the efficacy of non-binding, Ag2, and hCR011 ADCs as measured in the PDX_2 NSCLC xenograft model. The data show that Ag2 and hCR011 ADCs comprising hydrophilic auristatin Ex. 60 (compound 3.1 wherein L is Ag2 or hCR011, respectively) dosed as 9 mg/kg have comparable efficacy to ADCs comprising MMAE dosed at 3 mg/kg.

Example 96: Efficacy comparison of in vivo tumor models

[0868] Average Slope or AUC.3 was used to compare the anti-tumor activity of 6 different xenograft models. Tumor growth was assessed by the metric area under the curve (AUC), "AUC.3", based on Guo et al.'s best practices for reporting pre-clinical data, which

$$AUC.3 = \frac{AUC_{log2} - (log_2(Initial_Volume) * Days_on_Study)}{Days_on_Study^2}$$

reflects area under a continuous growth curve and accounts for time on study (Guo S, Jiang X, Mao B, et al. The design, analysis, and application of mouse clinical trials in oncology drug development. BMC Cancer 2019;19:718).

[0869] The data (see FIG 16) show that hCR011 ADCs comprising hydrophilic auristatin Ex. 60 (compound 3.1 wherein L is hCR011) dosed at 3 mg/kg and 9 mg/kg have comparable and enhanced efficacy, respectively, to ADCs comprising MC-VC-MMAE dosed at 3 mg/kg.

Example 97. Toxicity Determinations of Ligand-Drug Conjugate compounds

[0870] *In vivo* safety studies were done in naive cynomolgus monkeys. Studies had 1 or 2 animals/group/timepoint of hCR011-MC-VC-MMAE (DAR = 4) or hCR011-Example 60 (DAR = 4). Animals were administered four weekly doses of 3, 5, or 10 mg/kg of ADC via intravenous (slow bolus) injection. Baseline measurements for hematology and clinical chemistry parameters were taken from blood drawn at one or two time points prior to dosing, and post-dose timepoints were collected at day 8, and also on days 15 and 29 (hematology only). Results are shown in FIGs. 17 to 20.

[0871] FIG. 17 demonstrates that neutrophil counts post-administration of hydrophilic auristatin conjugate hCR011-Example 60 at 5 and 10 mg/kg were maintained at baseline levels, whereas conjugate hCR011-MC-VC-MMAE at 3 mg/kg shows a decrease relative to baseline on days 8, 15, and 29.

[0872] FIG. 18 demonstrates that loss of reticulocytes is greatly improved after administering hydrophilic auristatin conjugate hCR011-Example 60 at 5 and 10 mg/kg compared to conjugate hCR011-MC-VC-MMAE at 3 mg/kg.

[0873] FIG. 19 shows that administering hydrophilic auristatin conjugate hCR011-Example 60 does not significantly impact platelet counts at higher dose-levels of 5 and 10 mg/kg compared to conjugate hCR011-MC-VC-MMAE at 3 mg/kg.

[0874] FIG. 20 shows that administering hydrophilic auristatin conjugate hCR011-Example 60 does not significantly impact AST levels at higher dose-levels of 5 and 10 mg/kg compared to conjugate hCR011-MC-VC-MMAE at 3 mg/kg.

Example 98. Toxicity Determinations of Ligand-Drug Conjugate compounds

[0875] *In vivo* toxicology studies were done in naive cynomolgus monkeys. Studies had 2 animals/group/timepoint of hCR011-MC-VC-MMAE (DAR = 4) or hCR011-Example 60 (DAR = 4). Animals were administered four weekly doses of 5 mg/kg of ADC via intravenous (slow bolus) injection. Baseline measurements for hematology parameters were collected and results are shown in FIG. 21. The 5 mg/kg dose of hCR011-MC-VC-MMAE was not tolerated and dosing could not be completed for both animals whereas animals treated with 5 mg/kg of hCR011-Example 60 completed the study as planned.

[0876] FIG. 21 shows neutrophil counts from blood samples taken prior to dosing and post-dose on Day 8. Neutrophil counts post-administration of hydrophilic auristatin conjugate hCR011-Example 60 dosed at 5 mg/kg were maintained at baseline levels, whereas conjugate hCR011-MC-VC-MMAE at 5 mg/kg showed a decrease relative to baseline.

[0877] While the foregoing written description of the compounds, uses, and methods described herein enables one of ordinary skill to make and use the compounds, uses, and methods described herein, those of ordinary skill will understand and appreciate the existence of variations, combinations, and equivalents of the specific embodiment, method, and examples herein. The compounds, uses, and methods provided herein should therefore not be limited by the above-described embodiments, methods, or examples, but rather encompasses

all embodiments and methods within the scope and spirit of the compounds, uses, and methods provided herein.

[0878] All references disclosed herein are incorporated by reference in their entirety.

[0879] Unless otherwise indicated, all sequences and SEQ IDs referenced in the application correspond to the appropriately numbered sequence in the table below.

[0880] The Table of Sequences below provides exemplary antibody sequences consistent with the present disclosure. In this table, all targets correspond to human orthologs unless otherwise specified.

SEQ ID NO	Description	Sequence
1	Anti-PD-L1 HC	QVQLVQSGAEVKKPGSSVKVSCKTSGDTFSTAAISWVRQAPGQGLEWMGGIIPIFGKAHY AQKFQGRVTITADESTSTAYMELSSLRSEDTAVYFCARKFHFVSGSPFGMDVWGQGTTVT VSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVL QSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPEL LGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREE QYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPS RDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDK SRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK
2	Anti-PD-L1 HC v2	QVQLVQSGAEVKKPGSSVKVSCKTSGDTFSTAAISWVRQAPGQGLEWMGGIIPIFGKAHY AQKFQGRVTITADESTSTAYMELSSLRSEDTAVYFCARKFHFVSGSPFGMDVWGQGTTVT VSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVL QSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPEL LGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREE QYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPS RDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDK SRWQQGNVFSCSVMHEALHNHYTQKSLSLSPG
3	Anti-PD-L1 LALA HC	QVQLVQSGAEVKKPGSSVKVSCKTSGDTFSTAAISWVRQAPGQGLEWMGGIIPIFGKAHY AQKFQGRVTITADESTSTAYMELSSLRSEDTAVYFCARKFHFVSGSPFGMDVWGQGTTVT VSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVL QSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPEA AGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREE QYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPS RDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDK SRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK
4	Anti-PD-L1 LALA HC v2	QVQLVQSGAEVKKPGSSVKVSCKTSGDTFSTAAISWVRQAPGQGLEWMGGIIPIFGKAHY AQKFQGRVTITADESTSTAYMELSSLRSEDTAVYFCARKFHFVSGSPFGMDVWGQGTTVT VSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVL QSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPEA AGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREE QYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPS RDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDK SRWQQGNVFSCSVMHEALHNHYTQKSLSLSPG
5	Anti-PD-L1 LC	EIVLTQSPATLSLSPGERATLSCRASQSVSSYLAWYQQKPGQAPRLLIYDASNRATGIPA RFSGSGSGTDFTLTISSLEPEDFAVYYCQQRSNWPTFGQGTKVEIKRTVAAPSVFIFPPS DEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTL SKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC
6	Anti-PD-L1 (engineered cysteines) LALA HC	QVQLVQSGAEVKKPGSSVKVSCKTSGDTFSTAAISWVRQAPGQGLEWMGGIIPIFGKAHY AQKFQGRVTITADESTSTAYMELSSLRSEDTAVYFCARKFHFVSGSPFGMDVWGQGTTVT VSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVL QSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPEA AGGPCVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREE

		QYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPS RDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDK SRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK
7	Anti-PD-L1 (engineered cysteines) LALA HC v2	QVQLVQSGAEVKKPGSSVKVSCKTSGDTFSTAAISWVRQAPGQGLEWMGGIIPIFGKAHY AQKFQGRVTITADESTSTAYMELSSLRSEDTAVYFCARKFHFVSGSPFGMDVWGQGTTVT VSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVL QSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPEA AGGPCVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREE QYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPS RDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDK SRWQQGNVFSCSVMHEALHNHYTQKSLSLSPG
8	Anti-PD-L1 mIgG2a LALA HC	QVQLVQSGAEVKKPGSSVKVSCKTSGDTFSTAAISWVRQAPGQGLEWMGGIIPIFGKAHY AQKFQGRVTITADESTSTAYMELSSLRSEDTAVYFCARKFHFVSGSPFGMDVWGQGTTVT VSSAKTTAPSVYPLAPVCGDTTGSSVTLGCLVKGYFPEPVTLTWNSGSLSSGVHTFPAVL QSDLYTLSSSVTVTSSTWPSQSITCNVAHPASSTKVDKKIEPRGPTIKPCPPCKCPAPNA AGGPSVFIFPPKIKDVLMISLSPIVTCVVVDVSEDDPDVQISWFVNNVEVHTAQTQTHRE DYNSTLRVVSALPIQHQDWMSGKEFKCKVNNKDLPAPIERTISKPKGSVRAPQVYVLPPP EEEMTKKQVTLTCMVTDFMPEDIYVEWTNNGKTELNYKNTEPVLDSDGSYFMYSKLRVEK KNWVERNSYSCSVVHEGLHNHHTTKSFSRTPGK
9	Anti-PD-L1 mIgG2a LALA HC v2	QVQLVQSGAEVKKPGSSVKVSCKTSGDTFSTAAISWVRQAPGQGLEWMGGIIPIFGKAHY AQKFQGRVTITADESTSTAYMELSSLRSEDTAVYFCARKFHFVSGSPFGMDVWGQGTTVT VSSAKTTAPSVYPLAPVCGDTTGSSVTLGCLVKGYFPEPVTLTWNSGSLSSGVHTFPAVL QSDLYTLSSSVTVTSSTWPSQSITCNVAHPASSTKVDKKIEPRGPTIKPCPPCKCPAPNA AGGPSVFIFPPKIKDVLMISLSPIVTCVVVDVSEDDPDVQISWFVNNVEVHTAQTQTHRE DYNSTLRVVSALPIQHQDWMSGKEFKCKVNNKDLPAPIERTISKPKGSVRAPQVYVLPPP EEEMTKKQVTLTCMVTDFMPEDIYVEWTNNGKTELNYKNTEPVLDSDGSYFMYSKLRVEK KNWVERNSYSCSVVHEGLHNHHTTKSFSRTPG
10	Anti-PD-L1 mK LC	EIVLTQSPATLSLSPGERATLSCRASQSVSSYLAWYQQKPGQAPRLLIYDASNRATGIPA RFSGSGSGTDFTLTISSLEPEDFAVYYCQQRSNWPTFGQGTKVEIKRADAAPTVSIFPPS SEQLTSGGASVVCFLNNFYPKDINVKWKIDGSERQNGVLNSWTDQDSKDSTYSMSSTLTL TKDEYERHNSYTCEATHKTSTSPIVKSFNRNEC
11	Anti-PD-L1 mIgG2a (engineered cysteines) LALA HC	QVQLVQSGAEVKKPGSSVKVSCKTSGDTFSTAAISWVRQAPGQGLEWMGGIIPIFGKAHY AQKFQGRVTITADESTSTAYMELSSLRSEDTAVYFCARKFHFVSGSPFGMDVWGQGTTVT VSSAKTTAPSVYPLAPVCGDTTGSSVTLGCLVKGYFPEPVTLTWNSGSLSSGVHTFPAVL QSDLYTLSSSVTVTSSTWPSQSITCNVAHPASSTKVDKKIEPRGPTIKPCPPCKCPAPNA AGGPCVFIFPPKIKDVLMISLSPIVTCVVVDVSEDDPDVQISWFVNNVEVHTAQTQTHRE DYNSTLRVVSALPIQHQDWMSGKEFKCKVNNKDLPAPIERTISKPKGSVRAPQVYVLPPP EEEMTKKQVTLTCMVTDFMPEDIYVEWTNNGKTELNYKNTEPVLDSDGSYFMYSKLRVEK KNWVERNSYSCSVVHEGLHNHHTTKSFSRTPGK
12	Anti-PD-L1 mIgG2a (engineered cysteines) LALA HC v2	QVQLVQSGAEVKKPGSSVKVSCKTSGDTFSTAAISWVRQAPGQGLEWMGGIIPIFGKAHY AQKFQGRVTITADESTSTAYMELSSLRSEDTAVYFCARKFHFVSGSPFGMDVWGQGTTVT VSSAKTTAPSVYPLAPVCGDTTGSSVTLGCLVKGYFPEPVTLTWNSGSLSSGVHTFPAVL QSDLYTLSSSVTVTSSTWPSQSITCNVAHPASSTKVDKKIEPRGPTIKPCPPCKCPAPNA AGGPCVFIFPPKIKDVLMISLSPIVTCVVVDVSEDDPDVQISWFVNNVEVHTAQTQTHRE DYNSTLRVVSALPIQHQDWMSGKEFKCKVNNKDLPAPIERTISKPKGSVRAPQVYVLPPP EEEMTKKQVTLTCMVTDFMPEDIYVEWTNNGKTELNYKNTEPVLDSDGSYFMYSKLRVEK KNWVERNSYSCSVVHEGLHNHHTTKSFSRTPG
13	Anti-PD-L1 CDR-H1	TAAIS
14	Anti-PD-L1 CDR-H2	GIIPIFGKAHYAQKFQG
15	Anti-PD-L1 CDR-H3	KFHFVSGSPFGMDV
16	Anti-PD-L1 CDR-L1	RASQSVSSYLA
17	Anti-PD-L1 CDR-L2	DASNRAT
18	Anti-PD-L1 CDR-L3	QQRSNWPT
19	Anti-PD-L1	QVQLVQSGAEVKKPGSSVKVSCKTSGDTFSTAAISWVRQAPGQGLEWMGGIIPIFGKAHY

	VH	AQKFQGRVTITADESTSTAYMELSSLRSEDTAVYFCARKFHFVSGSPFGMDVWGQGTTVT VSS
20	Anti-PD-L1 VL	EIVLTQSPATLSLSPGERATLSCRASQSVSSYLAWYQQKPGQAPRLLIYDASNRATGIPA RFSGSGSGTDFTLTISSLEPEDFAVYYCQQRSNWPTFGQGTKVEIK
21	Anti-EphA2 CDR-H1	HYMMA
22	Anti-EphA2 CDR-H2	RIGPSGGPTHYADSVKG
23	Anti-EphA2 CDR-H3	YDSGYDYVAVAGPAEYFQH
24	Anti-EphA2 CDR-L1	RASQSISTWLA
25	Anti-EphA2 CDR-L2	KASNLHT
26	Anti-EphA2 CDR-L3	QQYNSYSRT
27	Anti-EphA2 VH	EVQLLESGGGLVQPGGSLRLSCAASGFTFSHYMMAWVRQAPGKGLEWVSRIGPSGGPTHY ADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAGYDSGYDYVAVAGPAEYFQHWGQ GTLVTVSS
28	Anti-EphA2 VL	DIQMTQSPSSLSASVGDRVTITCRASQSISTWLAWYQQKPGKAPKLLIYKASNLHTGVPS RFSGSGSGTEFSLTISGLQPDDFATYYCQQYNSYSRTFGQGTKVEIK
29	Anti-EphA2 HC	EVQLLESGGGLVQPGGSLRLSCAASGFTFSHYMMAWVRQAPGKGLEWVSRIGPSGGPTHY ADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAGYDSGYDYVAVAGPAEYFQHWGQ GTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHT FPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPC PAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKT KPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVY TLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSK LTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK
30	Anti-EphA2 HC v2	EVQLLESGGGLVQPGGSLRLSCAASGFTFSHYMMAWVRQAPGKGLEWVSRIGPSGGPTHY ADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAGYDSGYDYVAVAGPAEYFQHWGQ GTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHT FPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPC PAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKT KPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVY TLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSK LTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPG
31	Anti-EphA2 LC	DIQMTQSPSSLSASVGDRVTITCRASQSISTWLAWYQQKPGKAPKLLIYKASNLHTGVPS RFSGSGSGTEFSLTISGLQPDDFATYYCQQYNSYSRTFGQGTKVEIKRTVAAPSVFIFPP SDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDS KDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC
32	Anti-EphA2 mIgG2a HC	EVQLLESGGGLVQPGGSLRLSCAASGFTFSHYMMAWVRQAPGKGLEWVSRIGPSGGPTHY ADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAGYDSGYDYVAVAGPAEYFQHWGQ GTLVTVSSAKTTAPSVYPLAPVCGDTTGSSVTLGCLVKGYFPEPVTLTWNSGSLSSGVHT FPAVLQSDLYTLSSSVTVTSSTWPSQSITCNVAHPASSTKVDKKIEPRGPTIKPCPPCKC PAPNLLGGPSVFIFPPKIKDVLMISLSPIVTCVVVDVSEDDPDVQISWFVNNVEVHTAQT QTHREDYNSTLRVVSALPIQHQDWMSGKEFKCKVNNKDLPAPIERTISKPKGSVRAPQVY VLPPPEEEMTKKQVTLTCMVTDFMPEDIYVEWTNNGKTELNYKNTEPVLDSDGSYFMYSK LRVEKKNWVERNSYSCSVVHEGLHNHHTTKSFSRTPGK
33	Anti-EphA2 mIgG2a HC v2	EVQLLESGGGLVQPGGSLRLSCAASGFTFSHYMMAWVRQAPGKGLEWVSRIGPSGGPTHY ADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAGYDSGYDYVAVAGPAEYFQHWGQ GTLVTVSSAKTTAPSVYPLAPVCGDTTGSSVTLGCLVKGYFPEPVTLTWNSGSLSSGVHT FPAVLQSDLYTLSSSVTVTSSTWPSQSITCNVAHPASSTKVDKKIEPRGPTIKPCPPCKC PAPNLLGGPSVFIFPPKIKDVLMISLSPIVTCVVVDVSEDDPDVQISWFVNNVEVHTAQT QTHREDYNSTLRVVSALPIQHQDWMSGKEFKCKVNNKDLPAPIERTISKPKGSVRAPQVY VLPPPEEEMTKKQVTLTCMVTDFMPEDIYVEWTNNGKTELNYKNTEPVLDSDGSYFMYSK LRVEKKNWVERNSYSCSVVHEGLHNHHTTKSFSRTPG
34	Anti-EphA2 mIgG2a LC	DIQMTQSPSSLSASVGDRVTITCRASQSISTWLAWYQQKPGKAPKLLIYKASNLHTGVPS RFSGSGSGTEFSLTISGLQPDDFATYYCQQYNSYSRTFGQGTKVEIKRADAAPTVSIFPP SSEQLTSGGASVVCFLNNFYPKDINVKWKIDGSERQNGVLNSWTDQDSKDSTYSMSSTLT

		LTKDEYERHNSYTCEATHKTSTSPIVKSFNRNEC
35	Anti-EphA2 mIgG2a LALAPG HC	EVQLLESGGGLVQPGGSLRLSCAASGFTFSHYMMAWVRQAPGKGLEWVSRIGPSGGPTHY ADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAGYDSGYDYVAVAGPAEYFQHWGQ GTLVTVSSAKTTAPSVYPLAPVCGDTTGSSVTLGCLVKGYFPEPVTLTWNSGSLSSGVHT FPAVLQSDLYTLSSSVTVTSSTWPSQSITCNVAHPASSTKVDKKIEPRGPTIKPCPPCKC PAPNAAGGPSVFIFPPKIKDVLMISLSPIVTCVVVDVSEDDPDVQISWFVNNVEVHTAQT QTHREDYNSTLRVVSALPIQHQDWMSGKEFKCKVNNKDLGAPIERTISKPKGSVRAPQVY VLPPPEEEMTKKQVTLTCMVTDFMPEDIYVEWTNNGKTELNYKNTEPVLDSDGSYFMYSK LRVEKKNWVERNSYSCSVVHEGLHNHHTTKSFSRTPGK
36	Anti-EphA2 mIgG2a LALAPG HC v2	EVQLLESGGGLVQPGGSLRLSCAASGFTFSHYMMAWVRQAPGKGLEWVSRIGPSGGPTHY ADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAGYDSGYDYVAVAGPAEYFQHWGQ GTLVTVSSAKTTAPSVYPLAPVCGDTTGSSVTLGCLVKGYFPEPVTLTWNSGSLSSGVHT FPAVLQSDLYTLSSSVTVTSSTWPSQSITCNVAHPASSTKVDKKIEPRGPTIKPCPPCKC PAPNAAGGPSVFIFPPKIKDVLMISLSPIVTCVVVDVSEDDPDVQISWFVNNVEVHTAQT QTHREDYNSTLRVVSALPIQHQDWMSGKEFKCKVNNKDLGAPIERTISKPKGSVRAPQVY VLPPPEEEMTKKQVTLTCMVTDFMPEDIYVEWTNNGKTELNYKNTEPVLDSDGSYFMYSK LRVEKKNWVERNSYSCSVVHEGLHNHHTTKSFSRTPG
37	Anti-EphA2 mIgG2a LALAPG LC	DIQMTQSPSSLSASVGDRVTITCRASQSISTWLAWYQQKPGKAPKLLIYKASNLHTGVPS RFSGSGSGTEFSLTISGLQPDDFATYYCQQYNSYSRTFGQGTKVEIKRADAAPTVSIFPP SSEQLTSGGASVVCFLNNFYPKDINVKWKIDGSERQNGVLNSWTDQDSKDSTYSMSSTLT LTKDEYERHNSYTCEATHKTSTSPIVKSFNRNEC
38	Anti-CD30 CDR-H1	DYYIT
39	Anti-CD30 CDR-H2	WIYPGSGNTKYNEKFKG
40	Anti-CD30 CDR-H3	YGNYWFAY
41	Anti-CD30 CDR-L1	KASQSVDFDGDSYMN
42	Anti-CD30 CDR-L2	AASNLES
43	Anti-CD30 CDR-L3	QQSNEDPWT
44	Anti-CD30 VH	QIQLQQSGPEVVKPGASVKISCKASGYTFTDYYITWVKQKPGQGLEWIGWIYPGSGNTKY NEKFKGKATLTVDTSSSTAFMQLSSLTSEDTAVYFCANYGNYWFAYWGQGTQVTVSA
45	Anti-CD30 VL	DIVLTQSPASLAVSLGQRATISCKASQSVDFDGDSYMNWYQQKPGQPPKVLIYAASNLES GIPARFSGSGSGTDFTLNIHPVEEEDAATYYCQQSNEDPWTFGGGTKLEIK
46	Anti-CD30 HC	QIQLQQSGPEVVKPGASVKISCKASGYTFTDYYITWVKQKPGQGLEWIGWIYPGSGNTKY NEKFKGKATLTVDTSSSTAFMQLSSLTSEDTAVYFCANYGNYWFAYWGQGTQVTVSAAST KGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLY SLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPELLGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDELTK NQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQG NVFSCSVMHEALHNHYTQKSLSLSPGK
47	Anti-CD30 HC v2	QIQLQQSGPEVVKPGASVKISCKASGYTFTDYYITWVKQKPGQGLEWIGWIYPGSGNTKY NEKFKGKATLTVDTSSSTAFMQLSSLTSEDTAVYFCANYGNYWFAYWGQGTQVTVSAAST KGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLY SLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPELLGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDELTK NQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQG NVFSCSVMHEALHNHYTQKSLSLSPG
48	Anti-CD30 LC	DIVLTQSPASLAVSLGQRATISCKASQSVDFDGDSYMNWYQQKPGQPPKVLIYAASNLES GIPARFSGSGSGTDFTLNIHPVEEEDAATYYCQQSNEDPWTFGGGTKLEIKR TVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDS KDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC
49	Anti-CD228 CDR-H1	SGYWN
50	Anti-CD228	YISDSGITYYNPSLKS

	CDR-H2	
51	Anti-CD228 CDR-H3	RTLATYYAMDY
52	Anti-CD228 CDR-L1	RASQSLVHSDGNTYLH
53	Anti-CD228 CDR-L2	RVSNRFS
54	Anti-CD228 CDR-L3	SQSTHVPPT
55	Anti-CD228 VH	QVQLQESGPGLVKPSETLSLTCTVSGDSITSGYWNWIRQPPGKGLEYIGYISDSGITYYN PSLKSRVTISRDTSKNQYSLKLSSVTAADTAVYYCARRTLATYYAMDYWGQGTLVTVSS
56	Anti-CD228 VL	DFVMTQSPLSLPVTLGQPASISCRASQSLVHSDGNTYLHWYQQRPGQSPRLLIYRVSNRF SGVPDRFSGSGSGTDFTLKISRVEAEDVGVYYCSQSTHVPPTFGQGTKLEIK
57	Anti-CD228 HC	QVQLQESGPGLVKPSETLSLTCTVSGDSITSGYWNWIRQPPGKGLEYIGYISDSGITYYN PSLKSRVTISRDTSKNQYSLKLSSVTAADTAVYYCARRTLATYYAMDYWGQGTLVTVSSA STKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSG LYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPELLGGP SVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNS TYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDEL TKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQ QGNVFSCSVMHEALHNHYTQKSLSLSPGK
58	Anti-CD228 HC v2	QVQLQESGPGLVKPSETLSLTCTVSGDSITSGYWNWIRQPPGKGLEYIGYISDSGITYYN PSLKSRVTISRDTSKNQYSLKLSSVTAADTAVYYCARRTLATYYAMDYWGQGTLVTVSSA STKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSG LYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPELLGGP SVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNS TYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDEL TKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQ QGNVFSCSVMHEALHNHYTQKSLSLSPG
59	Anti-CD228 LC	DFVMTQSPLSLPVTLGQPASISCRASQSLVHSDGNTYLHWYQQRPGQSPRLLIYRVSNRF SGVPDRFSGSGSGTDFTLKISRVEAEDVGVYYCSQSTHVPPTFGQGTKLEIKRTVAAPSV FIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSL SSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC
60	Anti-CD228 LALAKA HC	QVQLQESGPGLVKPSETLSLTCTVSGDSITSGYWNWIRQPPGKGLEYIGYISDSGITYYN PSLKSRVTISRDTSKNQYSLKLSSVTAADTAVYYCARRTLATYYAMDYWGQGTLVTVSSA STKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSG LYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPEAAGGP SVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNS TYRVVSVLTVLHQDWLNGKEYKCAVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDEL TKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQ QGNVFSCSVMHEALHNHYTQKSLSLSPGK
61	Anti-CD228 LALAKA HC v2	QVQLQESGPGLVKPSETLSLTCTVSGDSITSGYWNWIRQPPGKGLEYIGYISDSGITYYN PSLKSRVTISRDTSKNQYSLKLSSVTAADTAVYYCARRTLATYYAMDYWGQGTLVTVSSA STKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSG LYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPEAAGGP SVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNS TYRVVSVLTVLHQDWLNGKEYKCAVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDEL TKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQ QGNVFSCSVMHEALHNHYTQKSLSLSPG
62	Anti-CD228 LALAKA LC	DFVMTQSPLSLPVTLGQPASISCRASQSLVHSDGNTYLHWYQQRPGQSPRLLIYRVSNRF SGVPDRFSGSGSGTDFTLKISRVEAEDVGVYYCSQSTHVPPTFGQGTKLEIKRTVAAPSV FIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSL SSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC
63	Anti-avB6 HC CDR-H1	DYNVN
64	Anti-AvB6 HC CDR-H2	VINPKYGTTRYNQKFKG
65	Anti-AvB6 HC CDR-H3	GLNAWDY
66	Anti-AvB6	GASENIYGALN

	LG CDR-L1	
67	Anti-AvB6 LG CDR-L2	GATNLED
68	Anti-AvB6 LG CDR-L3	QNVLTTPYT
69	Anti-AvB6 HC VH	QFQLVQSGAEVKKPGASVKVSCKASGYSFTDYNVNWVRQAPGQGLEWIGVINPKYGTTRY NQKFKGRATLTVDKSTSTAYMELSSLRSEDTAVYYCTRGLNAWDYWGQGTLVTVSS
70	Anti-AvB6 LG VL	DIQMTQSPSSLSASVGDRVTITCGASENIYGALNWYQQKPGKAPKLLIYGATNLEDGVPS RFSGSGSGRDYTFTISSLQPEDIATYYCQNVLTTPYTFGQGTKLEIK
71	Anti-AvB6 HC	QFQLVQSGAEVKKPGASVKVSCKASGYSFTDYNVNWVRQAPGQGLEWIGVINPKYGTTRY NQKFKGRATLTVDKSTSTAYMELSSLRSEDTAVYYCTRGLNAWDYWGQGTLVTVSSASTK GPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYS LSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPELLGGPSVF LFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYR VVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDELTKN QVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGN VFSCSVMHEALHNHYTQKSLSLSPGK
72	Anti-AvB6 HC v2	QFQLVQSGAEVKKPGASVKVSCKASGYSFTDYNVNWVRQAPGQGLEWIGVINPKYGTTRY NQKFKGRATLTVDKSTSTAYMELSSLRSEDTAVYYCTRGLNAWDYWGQGTLVTVSSASTK GPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYS LSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPELLGGPSVF LFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYR VVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDELTKN QVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGN VFSCSVMHEALHNHYTQKSLSLSPG
73	Anti-AvB6 LG LC	DIQMTQSPSSLSASVGDRVTITCGASENIYGALNWYQQKPGKAPKLLIYGATNLEDGVPS RFSGSGSGRDYTFTISSLQPEDIATYYCQNVLTTPYTFGQGTKLEIKRTVAAPSVFIFPP SDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLT LSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC
74	Anti-AvB6 LALAKA HC	QFQLVQSGAEVKKPGASVKVSCKASGYSFTDYNVNWVRQAPGQGLEWIGVINPKYGTTRY NQKFKGRATLTVDKSTSTAYMELSSLRSEDTAVYYCTRGLNAWDYWGQGTLVTVSSASTK GPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYS LSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPEAAGGPSVF LFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYR VVSVLTVLHQDWLNGKEYKCAVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDELTKN QVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGN VFSCSVMHEALHNHYTQKSLSLSPGK
75	Anti-AvB6 LALAKA HC v2	QFQLVQSGAEVKKPGASVKVSCKASGYSFTDYNVNWVRQAPGQGLEWIGVINPKYGTTRY NQKFKGRATLTVDKSTSTAYMELSSLRSEDTAVYYCTRGLNAWDYWGQGTLVTVSSASTK GPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYS LSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPEAAGGPSVF LFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYR VVSVLTVLHQDWLNGKEYKCAVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDELTKN QVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGN VFSCSVMHEALHNHYTQKSLSLSPG
76	Anti-AvB6 LG LALAKA LC	DIQMTQSPSSLSASVGDRVTITCGASENIYGALNWYQQKPGKAPKLLIYGATNLEDGVPS RFSGSGSGRDYTFTISSLQPEDIATYYCQNVLTTPYTFGQGTKLEIKRTVAAPSVFIFPP SDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLT LSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC
77	Anti-B7H4 CDR-H1	SGSYYWG
78	Anti-B7H4 CDR-H2	NIYYSGSTYYNPSLRS
79	Anti-B7H4 CDR-H3	EGSYPNQFDP
80	Anti-B7H4 CDR-L1	RASQSVSSNLA
81	Anti-B7H4 CDR-L2	GASTRAT
82	Anti-B7H4	QQYHSFPFT

	CDR-L3	
83	Anti-B7H4 VH	QLQLQESGPGLVKPSETLSLTCTVSGGSIKSGSYYWGWIRQPPGKGLEWIGNIYYSGSTY YNPSLRSRVTISVDTSKNQFSLKLSSVTAADTAVYYCAREGSYPNQFDPWGQGTLVTVSS
84	Anti-B7H4 VL	EIVMTQSPATLSVSPGERATLSCRASQSVSSNLAWYQQKPGQAPRLLIYGASTRATGIPA RFSGSGSGTEFTLTISSLQSEDFAVYYCQQYHSFPFTFGGGTKVEIK
85	Anti-B7H4 HC	QLQLQESGPGLVKPSETLSLTCTVSGGSIKSGSYYWGWIRQPPGKGLEWIGNIYYSGSTY YNPSLRSRVTISVDTSKNQFSLKLSSVTAADTAVYYCAREGSYPNQFDPWGQGTLVTVSS ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSS GLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPELLGG PSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYN STYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDE LTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRW QQGNVFSCSVMHEALHNHYTQKSLSLSPGK
86	Anti-B7H4 HC v2	QLQLQESGPGLVKPSETLSLTCTVSGGSIKSGSYYWGWIRQPPGKGLEWIGNIYYSGSTY YNPSLRSRVTISVDTSKNQFSLKLSSVTAADTAVYYCAREGSYPNQFDPWGQGTLVTVSS ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSS GLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPELLGG PSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYN STYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDE LTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRW QQGNVFSCSVMHEALHNHYTQKSLSLSPG
87	Anti-B7H4 LC	EIVMTQSPATLSVSPGERATLSCRASQSVSSNLAWYQQKPGQAPRLLIYGASTRATGIPA RFSGSGSGTEFTLTISSLQSEDFAVYYCQQYHSFPFTFGGGTKVEIKRTVAAPSVFIFPP SDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLT LSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC
88	Anti-B7H4 LALAKA HC	QLQLQESGPGLVKPSETLSLTCTVSGGSIKSGSYYWGWIRQPPGKGLEWIGNIYYSGSTY YNPSLRSRVTISVDTSKNQFSLKLSSVTAADTAVYYCAREGSYPNQFDPWGQGTLVTVSS ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSS GLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPEAAGG PSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYN STYRVVSVLTVLHQDWLNGKEYKCAVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDE LTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRW QQGNVFSCSVMHEALHNHYTQKSLSLSPGK
89	Anti-B7H4 LALAKA HC v2	QLQLQESGPGLVKPSETLSLTCTVSGGSIKSGSYYWGWIRQPPGKGLEWIGNIYYSGSTY YNPSLRSRVTISVDTSKNQFSLKLSSVTAADTAVYYCAREGSYPNQFDPWGQGTLVTVSS ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSS GLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPEAAGG PSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYN STYRVVSVLTVLHQDWLNGKEYKCAVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDE LTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRW QQGNVFSCSVMHEALHNHYTQKSLSLSPG
90	Anti-B7H4 LALAKA LC	EIVMTQSPATLSVSPGERATLSCRASQSVSSNLAWYQQKPGQAPRLLIYGASTRATGIPA RFSGSGSGTEFTLTISSLQSEDFAVYYCQQYHSFPFTFGGGTKVEIKRTVAAPSVFIFPP SDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLT LSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC
91	Anti-B7H4 CDR-H1	GSISSSSYYWG
92	Anti-B7H4 CDR-H2	NIYYSGSTYYNPSLKS
93	Anti-B7H4 CDR-H3	AREGSYPNWFDP
94	Anti-B7H4 CDR-L1	RASQSVSSNLA
95	Anti-B7H4 CDR-L2	GASTRAT
96	Anti-B7H4 CDR-L3	QQYHSFPFT
97	Anti-B7H4 VH	QLQLQESGPGLVKPSETLSLTCTVSGGSISSSSYYWGWIRQPPGKGLEWIGNIYYSGSTY YNPSLKSRVTISVDTSKNQFSLKLSSVTAADTAVYYCAREGSYPNWFDPWGQGTLVTVSS
98	Anti-B7H4	EIVMTQSPATLSVSPGERATLSCRASQSVSSNLAWYQQKPGQAPRLLIYGASTRATGIPA

	VL	RFSGSGSGTEFTLTISSLQSEDFAVYYCQQYHSFPFTFGGGTKVEIK
99	Anti-B7H4 CDR-H1	GSIKSGSHYWG
100	Anti-B7H4 CDR-H2	NIYYSGSTYYNPSLRS
101	Anti-B7H4 CDR-H3	AREGSYPNWFDP
102	Anti-B7H4 CDR-L1	RASQSVSSNLA
103	Anti-B7H4 CDR-L2	GASTRAT
104	Anti-B7H4 CDR-L3	QQYHSFPFT
105	Anti-B7H4 VH	QLQLQESGPGLVKPSETLSLTCTVSGGSIKSGSHYWGWIRQPPGKGLEWIGNIYYSGSTY YNPSLRSRVTISVDTSKNQFSLKLSSVTAADTAVYYCAREGSYPNWFDPWGQGTLVTVSS
106	Anti-B7H4 VL	EIVMTQSPATLSVSPGERATLSCRASQSVSSNLAWYQQKPGQAPRLLIYGASTRATGIPA RFSGSGSGTEFTLTISSLQSEDFAVYYCQQYHSFPFTFGGGTKVEIK
107	Anti-B7H4 CDR-H1	GSIKSGSHYWG
108	Anti-B7H4 CDR-H2	NIYYSGSTYYNPSLKS
109	Anti-B7H4 CDR-H3	AREGSYPNWLDP
110	Anti-B7H4 CDR-L1	RASQSVSSNLA
111	Anti-B7H4 CDR-L2	GASTRAT
112	Anti-B7H4 CDR-L3	QQYHSFPFT
113	Anti-B7H4 VH	QLQLQESGPGLVKPSETLSLTCTVSGGSIKSGSHYWGWIRQPPGKGLEWIGNIYYSGSTY YNPSLKSRVTISVDTSKNQFSLKLSSVTAADTAVYYCAREGSYPNWLDPWGQGTLVTVSS
114	Anti-B7H4 VL	EIVMTQSPATLSVSPGERATLSCRASQSVSSNLAWYQQKPGQAPRLLIYGASTRATGIPA RFSGSGSGTEFTLTISSLQSEDFAVYYCQQYHSFPFTFGGGTKVEIK
115	Anti-B7H4 CDR-H1	GSIKSGSYYWG
116	Anti-B7H4 CDR-H2	NIYYSGSTYYNPSLKS
117	Anti-B7H4 CDR-H3	AREGSYPNQFDP
118	Anti-B7H4 CDR-L1	RASQSVSSNLA
119	Anti-B7H4 CDR-L2	GASTRAT
120	Anti-B7H4 CDR-L3	QQYHSFPFT
121	Anti-B7H4 VH	QLQLQESGPGLVKPSETLSLTCTVSGGSIKSGSYYWGWIRQPPGKGLEWIGNIYYSGSTY YNPSLKSRVTISVDTSKNQFSLKLSSVTAADTAVYYCAREGSYPNQFDPWGQGILVTVSS
122	Anti-B7H4 VL	EIVMTQSPATLSVSPGERATLSCRASQSVSSNLAWYQQKPGQAPRLLIYGASTRATGIPA RFSGSGSGTEFTLTISSLQSEDFAVYYCQQYHSFPFTFGGGTKVEIK
123	Anti-B7H4 CDR-H1	GSIKSGSHYWG
124	Anti-B7H4 CDR-H2	NIYYSGSTYYNPSLKS
125	Anti-B7H4 CDR-H3	AREGSYPNWFDP
126	Anti-B7H4 CDR-L1	RASQSVSTNLA
127	Anti-B7H4 CDR-L2	DASARVT
128	Anti-B7H4	QQYHSFPFT

	CDR-L3	
129	Anti-B7H4 VH	QLQLQESGPGLVKPSETLSLTCTVSGGSIKSGSHYWGWIRQPPGKGLEWIGNIYYSGSTY YNPSLKSRVTMSVDTSKNQFSLKLSSVTAADTAVYYCAREGSYPNWFDPWGQGTLVTVSS
130	Anti-B7H4 VL	EIVMTQSPATLSVSPGERATLSCRASQSVSTNLAWYQQKPGQAPRLLIYDASARVTGIPA RFSGSGSGTEFTLTISSLQSEDFAVYYCQQYHSFPFTFGGGTKVEIK
131	Anti-B7H4 CDR-H1	GSISSSSYYWG
132	Anti-B7H4 CDR-H2	NIYYSGSTYYNPSLKS
133	Anti-B7H4 CDR-H3	AREGSYTTVLNV
134	Anti-B7H4 CDR-L1	RASQSVSSSYLA
135	Anti-B7H4 CDR-L2	GASSRAT
136	Anti-B7H4 CDR-L3	QQAASYPLT
137	Anti-B7H4 VH	QLQLQESGPGLVKPSETLSLTCTVSGGSISSSSYYWGWIRQPPGKGLEWIGNIYYSGSTY YNPSLKSRVTISVDTSKNQFSLKLSSVTAADTAVYYCAREGSYTTVLNVWGQGTMVTVSS
138	Anti-B7H4 VL	EIVLTQSPGTLSLSPGERATLSCRASQSVSSSYLAWYQQKPGQAPRLLIYGASSRATGIP DRFSGSGSGTDFTLTISRLEPEDFAVYYCQQAASYPLTFGGGTKVEIK
139	Anti-B7H4 CDR-H1	GSIGRGSYYWG
140	Anti-B7H4 CDR-H2	NIYYSGSTYYNPSLKS
141	Anti-B7H4 CDR-H3	AREGSYTTVLNV
142	Anti-B7H4 CDR-L1	RASQSVASSHLA
143	Anti-B7H4 CDR-L2	DAVSRAT
144	Anti-B7H4 CDR-L3	QQAASYPLT
145	Anti-B7H4 VH	QLQLQESGPGLVKPSETLSLTCTVSGGSIGRGSYYWGWIRQPPGKGLEWIGNIYYSGSTY YNPSLKSRVTISVDTSKNQFSLKLSSVTAADTAVYYCAREGSYTTVLNVWGQGTMVTVSS
146	Anti-B7H4 VL	EIVLTQSPGTLSLSPGERATLSCRASQSVASSHLAWYQQKPGQAPRLLIYDAVSRATGIP DRFSGSGSGTDFTLTISRLEPEDFAVYYCQQAASYPLTFGGGTKVEIK
147	Anti-B7H4 CDR-H1	GSISSGGYYWS
148	Anti-B7H4 CDR-H2	NIYYSGSTYYNPSLKS
149	Anti-B7H4 CDR-H3	ARESSTISADFDL
150	Anti-B7H4 CDR-L1	RASQGISRWLA
151	Anti-B7H4 CDR-L2	AASSLQS
152	Anti-B7H4 CDR-L3	QQAHTFPYT
153	Anti-B7H4 VH	QVQLQESGPGLVKPSQTLSLTCTVSGGSISSGGYYWSWIRQHPGKGLEWIGNIYYSGSTY YNPSLKSRVTISVDTSKNQFSLKLSSVTAADTAVYYCARESSTISADFDLWGRGTLVTVS S
154	Anti-B7H4 VL	DIQMTQSPSSVSASVGDRVTITCRASQGISRWLAWYQQKPGKAPKLLIYAASSLQSGVPS RFSGSGSGTDFTLTISSLQPEDFATYYCQQAHTFPYTFGGGTKVEIK
155	Anti-B7H4 CDR-H1	GSISHGGYYWS
156	Anti-B7H4 CDR-H2	NIYYSGSTYYNPSLKS
157	Anti-B7H4 CDR-H3	ARESSTISADFDL

158	Anti-B7H4 CDR-L1	RASQGISRWLA
159	Anti-B7H4 CDR-L2	AASSLQS
160	Anti-B7H4 CDR-L3	QQAHTFPYT
161	Anti-B7H4 VH	QLQLQESGPGLVKPSETLSLTCTASGGSISHGGYYWSWIRQHPGKGLEWIGNIYYSGSTY YNPSLKSRVTMSVDTSKNQFSLKLSSVTAADTAVYYCARESSTISADFDLWGRGTLVTVS S
162	Anti-B7H4 VL	DIQMTQSPSSVSASVGDRVTITCRASQGISRWLAWYQQKPGKAPKLLIYAASSLQSGVPS RFSGSGSGTDFTLTISSLQPEDFATYYCQQAHTFPYTFGGGTKVEIK
163	Anti-B7H4 CDR-H1	GSISSGGYYWS
164	Anti-B7H4 CDR-H2	NIYYSGSTYYNPSLKS
165	Anti-B7H4 CDR-H3	ARGLSTIDEAFDP
166	Anti-B7H4 CDR-L1	RASQSISSWLA
167	Anti-B7H4 CDR-L2	KASSLES
168	Anti-B7H4 CDR-L3	QQDNSYPYT
169	Anti-B7H4 VH	QVQLQESGPGLVKPSQTLSLTCTVSGGSISSGGYYWSWIRQHPGKGLEWIGNIYYSGSTY YNPSLKSRVTISVDTSKNQFSLKLSSVTAADTAVYYCARGLSTIDEAFDPWGQGTLVTVS S
170	Anti-B7H4 VL	DIQMTQSPSTLSASVGDRVTITCRASQSISSWLAWYQQKPGKAPKLLIYKASSLESGVPS RFSGSGSGTEFTLTISSLQPDDFATYYCQQDNSYPYTFGGGTKVEIK
171	Anti-B7H4 CDR-H1	GSISDGSYYWS
172	Anti-B7H4 CDR-H2	NIYYSGSTYYNPSLRS
173	Anti-B7H4 CDR-H3	ARGLSTIDEAFDP
174	Anti-B7H4 CDR-L1	RASQSISSWLA
175	Anti-B7H4 CDR-L2	KASSLES
176	Anti-B7H4 CDR-L3	QQDNSYPYT
177	Anti-B7H4 VH	QLQLQESGPGLVKPSETLSLTCTVSGGSISDGSYYWSWIRQHPGKGLEWIGNIYYSGSTY YNPSLRSRVTMSVDTSKNQFSLKLSSVTAADTAVYYCARGLSTIDEAFDPWGQGTLVTVS S
178	Anti-B7H4 VL	DIQMTQSPSTLSASVGDRVTITCRASQSISSWLAWYQQKPGKAPKLLIYKASSLESGVPS RFSGSGSGTEFTLTISSLQPDDFATYYCQQDNSYPYTFGGGTKVEIK
179	Anti-B7H4 CDR-H1	GSISDGSYYWS
180	Anti-B7H4 CDR-H2	NIYYSGSTYYNPSLRS
181	Anti-B7H4 CDR-H3	ARGLSTIDEAFDP
182	Anti-B7H4 CDR-L1	RASKSISSWLA
183	Anti-B7H4 CDR-L2	EASSLHS
184	Anti-B7H4 CDR-L3	QQDNSYPYT
185	Anti-B7H4 VH	QVQLQESGPGLVKPSQTLSLTCTVSGGSISDGSYYWSWIRQHPGKGLEWIGNIYYSGSTY YNPSLRSRVTMSVDTSKNQFSLKLSSVTAADTAVYYCARGLSTIDEAFDPWGQGTLVTVS S

186	Anti-B7H4 VL	DIQMTQSPSTLSASVGDRVTITCRASKSISSWLAWYQQKPGKAPKLLIYEASSLHSGVPS RFSGSGSGTEFTLTISSLQPDDFATYYCQQDNSYPYTFGGGTKVEIK
187	Anti-B7H4 CDR-H1	GSISSYYWS
188	Anti-B7H4 CDR-H2	YIYSSGSTNYNPSLKS
189	Anti-B7H4 CDR-H3	ARGSGQYAAPDYGMD
190	Anti-B7H4 CDR-L1	RASQSISSWLA
191	Anti-B7H4 CDR-L2	KASSLES
192	Anti-B7H4 CDR-L3	QQDNSFPFT
193	Anti-B7H4 VH	QVQLQESGPGLVKPSETLSLTCTVSGGSISSYYWSWIRQPPGKGLEWIGYIYSSGSTNYN PSLKSRVTISVDTSKNQFSLKLSSVTAADTAVYYCARGSGQYAAPDYGMDVWGQGTTVTV SS
194	Anti-B7H4 VL	DIQMTQSPSTLSASVGDRVTITCRASQSISSWLAWYQQKPGKAPKLLIYKASSLESGVPS RFSGSGSGTEFTLTISSLQPDDFATYYCQQDNSFPFTFGGGTKVEIK
195	Anti-B7H4 CDR-H1	GSIISYYWG
196	Anti-B7H4 CDR-H2	YIYSSGSTSYNPSLKS
197	Anti-B7H4 CDR-H3	ARGSGLYAAPDYGLDV
198	Anti-B7H4 CDR-L1	RASQSISSWLA
199	Anti-B7H4 CDR-L2	KASSLES
200	Anti-B7H4 CDR-L3	QQDNSFPFT
201	Anti-B7H4 VH	QVQLQESGPGLVKPSETLSLTCTVSGGSIISYYWGWIRQPPGKGLEWIGYIYSSGSTSYN PSLKSRVTISVDTSKNQFSLKLSSVTAADTAVYYCARGSGLYAAPDYGLDVWGQGTTVTV SS
202	Anti-B7H4 VL	DIQMTQSPSTLSASVGDRVTITCRASQSISSWLAWYQQKPGKAPKLLIYKASSLESGVPS RFSGSGSGTEFTLTISSLQPDDFATYYCQQDNSFPFTFGGGTKVEIK
203	Anti-B7H4 CDR-H1	FTFSSYAMS
204	Anti-B7H4 CDR-H2	TISGSGGSTYYADSVKG
205	Anti-B7H4 CDR-H3	ARGAGHYDLVGRY
206	Anti-B7H4 CDR-L1	RASQSISSYLN
207	Anti-B7H4 CDR-L2	AASSLQS
208	Anti-B7H4 CDR-L3	QQLYSLPPT
209	Anti-B7H4 VH	EVQLLESGGGLVQPGGSLRLSCAASGFTFSSYAMSWVRQAPGKGLEWVSTISGSGGSTYY ADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARGAGHYDLVGRYWGQGTLVTVSS
210	Anti-B7H4 VL	DIQMTQSPSSLSASVGDRVTITCRASQSISSYLNWYQQKPGKAPKLLIYAASSLQSGVPS RFSGSGSGTDFTLTISSLQPEDFATYYCQQLYSLPPTFGGGTKVEIK
211	Anti-B7H4 CDR-H1	FTFSSYAMS
212	Anti-B7H4 CDR-H2	AISGSGGSTYYADSVKG
213	Anti-B7H4 CDR-H3	ARVGFRALNY
214	Anti-B7H4 CDR-L1	RASQDISSWLA

215	Anti-B7H4 CDR-L2	AASSLQS
216	Anti-B7H4 CDR-L3	QQATSYPPWT
217	Anti-B7H4 VH	EVQLLESGGGLVQPGGSLRLSCAASGFTFSSYAMSWVRQAPGKGLEWVSAISGSGGSTYY ADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARVGFRALNYWGQGTTVTVSS
218	Anti-B7H4 VL	DIQLTQSPSSVSASVGDRVTITCRASQDISSWLAWYQQKPGKAPKLLIYAASSLQSGVPS RFSGSGSGTDFTLTISSLQPEDFATYYCQQATSYPPWTFGGGTKVEIK
219	Anti-B7H4 CDR-H1	GTFSSYAIS
220	Anti-B7H4 CDR-H2	GIIPIFGTASYAQKFQG
221	Anti-B7H4 CDR-H3	ARQQYDGRRYFGL
222	Anti-B7H4 CDR-L1	RASQSVSSNLA
223	Anti-B7H4 CDR-L2	SASTRAT
224	Anti-B7H4 CDR-L3	QQVNVWPPT
225	Anti-B7H4 VH	QVQLVQSGAEVKKPGSSVKVSCKASGGTFSSYAISWVRQAPGQGLEWMGGIIPIFGTASY AQKFQGRVTITADESTSTAYMELSSLRSEDTAVYYCARQQYDGRRYFGLWGRGTLVTVSS
226	Anti-B7H4 VL	EIVMTQSPATLSVSPGERATLSCRASQSVSSNLAWYQQKPGQAPRLLIYSASTRATGIPA RFSGSGSGTEFTLTISSLQSEDFAVYYCQQVNVWPPTFGGGTKVEIK
227	Anti-B7H4 CDR-H1	GTFSSYAIS
228	Anti-B7H4 CDR-H2	GIIPIFGTANYAQKFQG
229	Anti-B7H4 CDR-H3	ARGGPWFDP
230	Anti-B7H4 CDR-L1	RASQSISSWLA
231	Anti-B7H4 CDR-L2	KASSLES
232	Anti-B7H4 CDR-L3	QQYNSYPPFT
233	Anti-B7H4 VH	QVQLVQSGAEVKKPGSSVKVSCKASGGTFSSYAISWVRQAPGQGLEWMGGIIPIFGTANY AQKFQGRVTITADESTSTAYMELSSLRSEDTAVYYCARGGPWFDPWGQGTLVTVSS
234	Anti-B7H4 VL	DIQMTQSPSTLSASVGDRVTITCRASQSISSWLAWYQQKPGKAPKLLIYKASSLESGVPS RFSGSGSGTEFTLTISSLQPDDFATYYCQQYNSYPPFTFGGGTKVEIK
235	Anti-B7H4 CDR-H1	FTFSSYAMS
236	Anti-B7H4 CDR-H2	AISGSGGSTSYADSVKG
237	Anti-B7H4 CDR-H3	AKPSLATMLAFDI
238	Anti-B7H4 CDR-L1	RASQSISSWLA
239	Anti-B7H4 CDR-L2	DASSLES
240	Anti-B7H4 CDR-L3	QQSKSYPRT
241	Anti-B7H4 VH	EVQLLESGGGLVQPGGSLRLSCAASGFTFSSYAMSWVRQAPGKGLEWVSAISGSGGSTSY ADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAKPSLATMLAFDIWGQGTMVTVSS
242	Anti-B7H4 VL	DIQMTQSPSTLSASVGDRVTITCRASQSISSWLAWYQQKPGKAPKLLIYDASSLESGVPS RFSGSGSGTEFTLTISSLQPDDFATYYCQQSKSYPRTFGGGTKVEIK
243	Anti-B7H4 CDR-H1	GSISSSVYYWS
244	Anti-B7H4 CDR-H2	SILVSGSTYYNPSLKS

245	Anti-B7H4 CDR-H3	ARAVSFLDV
246	Anti-B7H4 CDR-L1	RASQSISSYLN
247	Anti-B7H4 CDR-L2	GASSLQS
248	Anti-B7H4 CDR-L3	QQSYDPPWT
249	Anti-B7H4 VH	QLQLQESGPGLVKPSETLSLTCTVSGGSISSSVYYWSWIRQPPGKGLEWIGSILVSGSTY YNPSLKSRVTISVDTSKNQFSLKLSSVTAADTAVYYCARAVSFLDVWGQGTMVIVSS
250	Anti-B7H4 VL	DIQMTQSPSSLSASVGDRVTITCRASQSISSYLNWYQQKPGKAPKLLIYGASSLQSGVPS RFSGSGSGTDFTLTISSLQPEDFATYYCQQSYDPPWTFGGGTKVEIK
251	Anti-B7H4 HC	QLQLQESGPGLVKPSETLSLTCTVSGGSISSSSYYWGWIRQPPGKGLEWIGNIYYSGSTY YNPSLKSRVTISVDTSKNQFSLKLSSVTAADTAVYYCAREGSYPNWFDPWGQGTLVTVSS ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSS GLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPELLGG PSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYN STYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDE LTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRW QQGNVFSCSVMHEALHNHYTQKSLSLSPGK
252	Anti-B7H4 LC	EIVMTQSPATLSVSPGERATLSCRASQSVSSNLAWYQQKPGQAPRLLIYGASTRATGIPA RFSGSGSGTEFTLTISSLQSEDFAVYYCQQYHSFPFTFGGGTKVEIKRTVAAPSVFIFPP SDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLT LSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC
253	Anti-B7H4 HC	QLQLQESGPGLVKPSETLSLTCTVSGGSIKSGSHYWGWIRQPPGKGLEWIGNIYYSGSTY YNPSLRSRVTISVDTSKNQFSLKLSSVTAADTAVYYCAREGSYPNWFDPWGQGTLVTVSS ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSS GLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPELLGG PSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYN STYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDE LTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRW QQGNVFSCSVMHEALHNHYTQKSLSLSPGK
254	Anti-B7H4 LC	EIVMTQSPATLSVSPGERATLSCRASQSVSSNLAWYQQKPGQAPRLLIYGASTRATGIPA RFSGSGSGTEFTLTISSLQSEDFAVYYCQQYHSFPFTFGGGTKVEIKRTVAAPSVFIFPP SDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLT LSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC
255	Anti-B7H4 HC	QLQLQESGPGLVKPSETLSLTCTVSGGSIKSGSHYWGWIRQPPGKGLEWIGNIYYSGSTY YNPSLKSRVTISVDTSKNQFSLKLSSVTAADTAVYYCAREGSYPNWLDPWGQGTLVTVSS ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSS GLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPELLGG PSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYN STYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDE LTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRW QQGNVFSCSVMHEALHNHYTQKSLSLSPGK
256	Anti-B7H4 LC	EIVMTQSPATLSVSPGERATLSCRASQSVSSNLAWYQQKPGQAPRLLIYGASTRATGIPA RFSGSGSGTEFTLTISSLQSEDFAVYYCQQYHSFPFTFGGGTKVEIKRTVAAPSVFIFPP SDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLT LSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC
257	Anti-B7H4 HC	QLQLQESGPGLVKPSETLSLTCTVSGGSIKSGSYYWGWIRQPPGKGLEWIGNIYYSGSTY YNPSLKSRVTISVDTSKNQFSLKLSSVTAADTAVYYCAREGSYPNQFDPWGQGILVTVSS ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSS GLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPELLGG PSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYN STYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDE LTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRW QQGNVFSCSVMHEALHNHYTQKSLSLSPGK
258	Anti-B7H4 LC	EIVMTQSPATLSVSPGERATLSCRASQSVSSNLAWYQQKPGQAPRLLIYGASTRATGIPA RFSGSGSGTEFTLTISSLQSEDFAVYYCQQYHSFPFTFGGGTKVEIKRTVAAPSVFIFPP SDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLT LSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

259	Anti-B7H4 HC	QLQLQESGPGLVKPSETLSLTCTVSGGSIKSGSHYWGWIRQPPGKGLEWIGNIYYSGSTY YNPSLKSRVTMSVDTSKNQFSLKLSSVTAADTAVYYCAREGSYPNWFDPWGQGTLVTVSS ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSS GLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPELLGG PSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYN STYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDE LTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRW QQGNVFSCSVMHEALHNHYTQKSLSLSPGK
260	Anti-B7H4 LC	EIVMTQSPATLSVSPGERATLSCRASQSVSTNLAWYQQKPGQAPRLLIYDASARVTGIPA RFSGSGSGTEFTLTISSLQSEDFAVYYCQQYHSFPFTFGGGTKVEIKRTVAAPSVFIFPP SDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLT LSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC
261	Anti-B7H4 HC	QLQLQESGPGLVKPSETLSLTCTVSGGSISSSSYYWGWIRQPPGKGLEWIGNIYYSGSTY YNPSLKSRVTISVDTSKNQFSLKLSSVTAADTAVYYCAREGSYTTVLNVWGQGTMVTVSS ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSS GLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPELLGG PSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYN STYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDE LTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRW QQGNVFSCSVMHEALHNHYTQKSLSLSPGK
262	Anti-B7H4 LC	EIVLTQSPGTLSLSPGERATLSCRASQSVSSSYLAWYQQKPGQAPRLLIYGASSRATGIP DRFSGSGSGTDFTLTISRLEPEDFAVYYCQQAASYPLTFGGGTKVEIKRTVAAPSVFIFP PSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTL TLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC
263	Anti-B7H4 HC	QLQLQESGPGLVKPSETLSLTCTVSGGSIGRGSYYWGWIRQPPGKGLEWIGNIYYSGSTY YNPSLKSRVTISVDTSKNQFSLKLSSVTAADTAVYYCAREGSYTTVLNVWGQGTMVTVSS ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSS GLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPELLGG PSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYN STYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDE LTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRW QQGNVFSCSVMHEALHNHYTQKSLSLSPGK
264	Anti-B7H4 LC	EIVLTQSPGTLSLSPGERATLSCRASQSVASSHLAWYQQKPGQAPRLLIYDAVSRATGIP DRFSGSGSGTDFTLTISRLEPEDFAVYYCQQAASYPLTFGGGTKVEIKRTVAAPSVFIFP PSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTL TLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC
265	Anti-B7H4 HC	QVQLQESGPGLVKPSQTLSLTCTVSGGSISSGGYYWSWIRQHPGKGLEWIGNIYYSGSTY YNPSLKSRVTISVDTSKNQFSLKLSSVTAADTAVYYCARESSTISADFDLWGRGTLVTVS SASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQS SGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPELLG GPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQY NSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRD ELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSR WQQGNVFSCSVMHEALHNHYTQKSLSLSPGK
266	Anti-B7H4 LC	DIQMTQSPSSVSASVGDRVTITCRASQGISRWLAWYQQKPGKAPKLLIYAASSLQSGVPS RFSGSGSGTDFTLTISSLQPEDFATYYCQQAHTFPYTFGGGTKVEIKRTVAAPSVFIFPP SDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLT LSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC
267	Anti-B7H4 HC	QLQLQESGPGLVKPSETLSLTCTASGGSISHGGYYWSWIRQHPGKGLEWIGNIYYSGSTY YNPSLKSRVTMSVDTSKNQFSLKLSSVTAADTAVYYCARESSTISADFDLWGRGTLVTVS SASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQS SGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPELLG GPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQY NSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRD ELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSR WQQGNVFSCSVMHEALHNHYTQKSLSLSPGK
268	Anti-B7H4 LC	DIQMTQSPSSVSASVGDRVTITCRASQGISRWLAWYQQKPGKAPKLLIYAASSLQSGVPS RFSGSGSGTDFTLTISSLQPEDFATYYCQQAHTFPYTFGGGTKVEIKRTVAAPSVFIFPP SDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLT LSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC
269	Anti-B7H4	QVQLQESGPGLVKPSQTLSLTCTVSGGSISSGGYYWSWIRQHPGKGLEWIGNIYYSGSTY

	HC	YNPSLKSRVTISVDTSKNQFSLKLSSVTAADTAVYYCARGLSTIDEAFDPWGQGTLVTVS SASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQS SGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPELLG GPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQY NSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRD ELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSR WQQGNVFSCSVMHEALHNHYTQKSLSLSPGK
270	Anti-B7H4 LC	DIQMTQSPSTLSASVGDRVTITCRASQSISSWLAWYQQKPGKAPKLLIYKASSLESGVPS RFSGSGSGTEFTLTISSLQPDDFATYYCQQDNSYPYTFGGGTKVEIKRTVAAPSVFIFPP SDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLT LSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC
271	Anti-B7H4 HC	QLQLQESGPGLVKPSETLSLTCTVSGGSISDGSYYWSWIRQHPGKGLEWIGNIYYSGSTY YNPSLRSRVTMSVDTSKNQFSLKLSSVTAADTAVYYCARGLSTIDEAFDPWGQGTLVTVS SASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQS SGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPELLG GPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQY NSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRD ELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSR WQQGNVFSCSVMHEALHNHYTQKSLSLSPGK
272	Anti-B7H4 LC	DIQMTQSPSTLSASVGDRVTITCRASQSISSWLAWYQQKPGKAPKLLIYKASSLESGVPS RFSGSGSGTEFTLTISSLQPDDFATYYCQQDNSYPYTFGGGTKVEIKRTVAAPSVFIFPP SDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLT LSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC
273	Anti-B7H4 HC	QVQLQESGPGLVKPSQTLSLTCTVSGGSISDGSYYWSWIRQHPGKGLEWIGNIYYSGSTY YNPSLRSRVTMSVDTSKNQFSLKLSSVTAADTAVYYCARGLSTIDEAFDPWGQGTLVTVS SASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQS SGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPELLG GPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQY NSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRD ELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSR WQQGNVFSCSVMHEALHNHYTQKSLSLSPGK
274	Anti-B7H4 LC	DIQMTQSPSTLSASVGDRVTITCRASKSISSWLAWYQQKPGKAPKLLIYEASSLHSGVPS RFSGSGSGTEFTLTISSLQPDDFATYYCQQDNSYPYTFGGGTKVEIKRTVAAPSVFIFPP SDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLT LSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC
275	Anti-B7H4 HC	QVQLQESGPGLVKPSETLSLTCTVSGGSISSYYWSWIRQPPGKGLEWIGYIYSSGSTNYN PSLKSRVTISVDTSKNQFSLKLSSVTAADTAVYYCARGSGQYAAPDYGMDVWGQGTTVTV SSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQ SSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPELL GGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQ YNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSR DELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKS RWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK
276	Anti-B7H4 LC	DIQMTQSPSTLSASVGDRVTITCRASQSISSWLAWYQQKPGKAPKLLIYKASSLESGVPS RFSGSGSGTEFTLTISSLQPDDFATYYCQQDNSFPFTFGGGTKVEIKRTVAAPSVFIFPP SDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLT LSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC
277	Anti-B7H4 HC	QVQLQESGPGLVKPSETLSLTCTVSGGSIISYYWGWIRQPPGKGLEWIGYIYSSGSTSYN PSLKSRVTISVDTSKNQFSLKLSSVTAADTAVYYCARGSGLYAAPDYGLDVWGQGTTVTV SSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQ SSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPELL GGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQ YNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSR DELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKS RWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK
278	Anti-B7H4 LC	DIQMTQSPSTLSASVGDRVTITCRASQSISSWLAWYQQKPGKAPKLLIYKASSLESGVPS RFSGSGSGTEFTLTISSLQPDDFATYYCQQDNSFPFTFGGGTKVEIKRTVAAPSVFIFPP SDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLT LSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC
279	Anti-B7H4 HC	EVQLLESGGGLVQPGGSLRLSCAASGFTFSSYAMSWVRQAPGKGLEWVSTISGSGGSTYY ADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARGAGHYDLVGRYWGQGTLVTVSS

		ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSS GLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPELLGG PSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYN STYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDE LTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRW QQGNVFSCSVMHEALHNHYTQKSLSLSPGK
280	Anti-B7H4 LC	DIQMTQSPSSLSASVGDRVTITCRASQSISSYLNWYQQKPGKAPKLLIYAASSLQSGVPS RFSGSGSGTDFTLTISSLQPEDFATYYCQQLYSLPPTFGGGTKVEIKRTVAAPSVFIFPP SDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLT LSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC
281	Anti-B7H4 HC	EVQLLESGGGLVQPGGSLRLSCAASGFTFSSYAMSWVRQAPGKGLEWVSAISGSGGSTYY ADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARVGFRALNYWGQGTTVTVSSAST KGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLY SLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPELLGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDELTK NQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQG NVFSCSVMHEALHNHYTQKSLSLSPGK
282	Anti-B7H4 LC	DIQLTQSPSSVSASVGDRVTITCRASQDISSWLAWYQQKPGKAPKLLIYAASSLQSGVPS RFSGSGSGTDFTLTISSLQPEDFATYYCQQATSYPPWTFGGGTKVEIKRTVAAPSVFIFP PSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTL TLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC
283	Anti-B7H4 HC	QVQLVQSGAEVKKPGSSVKVSCKASGGTFSSYAISWVRQAPGQGLEWMGGIIPIFGTASY AQKFQGRVTITADESTSTAYMELSSLRSEDTAVYYCARQQYDGRRYFGLWGRGTLVTVSS ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSS GLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPELLGG PSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYN STYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDE LTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRW QQGNVFSCSVMHEALHNHYTQKSLSLSPGK
284	Anti-B7H4 LC	EIVMTQSPATLSVSPGERATLSCRASQSVSSNLAWYQQKPGQAPRLLIYSASTRATGIPA RFSGSGSGTEFTLTISSLQSEDFAVYYCQQVNVWPPTFGGGTKVEIKRTVAAPSVFIFPP SDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLT LSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC
285	Anti-B7H4 HC	QVQLVQSGAEVKKPGSSVKVSCKASGGTFSSYAISWVRQAPGQGLEWMGGIIPIFGTANY AQKFQGRVTITADESTSTAYMELSSLRSEDTAVYYCARGGPWFDPWGQGTLVTVSSASTK GPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYS LSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPELLGGPSVF LFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYR VVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDELTKN QVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGN VFSCSVMHEALHNHYTQKSLSLSPGK
286	Anti-B7H4 LC	DIQMTQSPSTLSASVGDRVTITCRASQSISSWLAWYQQKPGKAPKLLIYKASSLESGVPS RFSGSGSGTEFTLTISSLQPDDFATYYCQQYNSYPPFTFGGGTKVEIKRTVAAPSVFIFP PSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTL TLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC
287	Anti-B7H4 HC	EVQLLESGGGLVQPGGSLRLSCAASGFTFSSYAMSWVRQAPGKGLEWVSAISGSGGSTSY ADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAKPSLATMLAFDIWGQGTMVTVSS ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSS GLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPELLGG PSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYN STYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDE LTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRW QQGNVFSCSVMHEALHNHYTQKSLSLSPGK
288	Anti-B7H4 LC	DIQMTQSPSTLSASVGDRVTITCRASQSISSWLAWYQQKPGKAPKLLIYDASSLESGVPS RFSGSGSGTEFTLTISSLQPDDFATYYCQQSKSYPRTFGGGTKVEIKRTVAAPSVFIFPP SDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLT LSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC
289	Anti-B7H4 HC	QLQLQESGPGLVKPSETLSLTCTVSGGSISSSVYYWSWIRQPPGKGLEWIGSILVSGSTY YNPSLKSRVTISVDTSKNQFSLKLSSVTAADTAVYYCARAVSFLDVWGQGTMVIVSSAST KGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLY

		SLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPELLGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDELTK NQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQG NVFSCSVMHEALHNHYTQKSLSLSPGK
290	Anti-B7H4 LC	DIQMTQSPSSLSASVGDRVTITCRASQSISSYLNWYQQKPGKAPKLLIYGASSLQSGVPS RFSGSGSGTDFTLTISSLQPEDFATYYCQQSYDPPWTFGGGTKVEIKRTVAAPSVFIFPP SDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLT LSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC
291	Anti-CD70 CDR-H1	NYGMN
292	Anti-CD70CDR-H2	WINTYTGEPTYADAFKG
293	Anti-CD70 CDR-H3	DYGDYGMDY
294	Anti-CD70 CDR-L1	RASKSVSTSGYSFMH
295	Anti-CD70 CDR-L2	LASNLES
296	Anti-CD70 CDR-L3	QHSREVPWT
297	Anti-CD70 VH	QVQLVQSGAEVKKPGASVKVSCKASGYTFTNYGMNWVRQAPGQGLKWMGWINTYTGEPTY ADAFKGRVTMTRDTSISTAYMELSRLRSDDTAVYYCARDYGDYGMDYWGQGTTVTVSS
298	Anti-CD70 VL	DIVMTQSPDSLAVSLGERATINCRASKSVSTSGYSFMHWYQQKPGQPPKLLIYLASNLES GVPDRFSGSGSGTDFTLTISSLQAEDVAVYYCQHSREVPWTFGQGTKVEIK
299	Anti-CD70 HC	QVQLVQSGAEVKKPGASVKVSCKASGYTFTNYGMNWVRQAPGQGLKWMGWINTYTGEPTY ADAFKGRVTMTRDTSISTAYMELSRLRSDDTAVYYCARDYGDYGMDYWGQGTTVTVSSAS TKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGL YSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPELLGGPS VFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNST YRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDELT KNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQ GNVFSCSVMHEALHNHYTQKSLSLSPGK
300	Anti-CD70 LC	DIVMTQSPDSLAVSLGERATINCRASKSVSTSGYSFMHWYQQKPGQPPKLLIYLASNLES GVPDRFSGSGSGTDFTLTISSLQAEDVAVYYCQHSREVPWTFGQGTKVEIKRTVAAPSVF IFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLS STLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC
301	Anti-TROP2 CDR-H1	NYGMN
302	Anti-TROP2 CDR-H2	WINTYTGEPTYTDDFKG
303	Anti-TROP2 CDR-H3	GGFGSSYWYFDV
304	Anti-TROP2 CDR-L1	KASQDVSIAVA
305	Anti-TROP2 CDR-L2	SASYRYT
306	Anti-TROP2 CDR-L3	QQHYITPLT
307	Anti-TROP2 VH	QVQLQQSGSELKKPGASVKVSCKASGYTFTNYGMNWVKQAPGQGLKWMGWINTYTGEPTY TDDFKGRFAFSLDTSVSTAYLQISSLKADDTAVYFCARGGFGSSYWYFDVWGQGSLVTVS S
308	Anti-TROP2 VL	DIQLTQSPSSLSASVGDRVSITCKASQDVSIAVAWYQQKPGKAPKLLIYSASYRYTGVPD RFSGSGSGTDFTLTISSLQPEDFAVYYCQQHYITPLTFGAGTKVEIK
309	Anti-TROP2 CDR-H1	TAGMQ
310	Anti-TROP2 CDR-H2	WINTHSGVPKYAEDFKG
311	Anti-TROP2 CDR-H3	SGFGSSYWYFDV

312	Anti-TROP2 CDR-L1	KASQDVSTAVA
313	Anti-TROP2 CDR-L2	SASYRYT
314	Anti-TROP2 CDR-L3	QQHYITPLT
315	Anti-TROP2 VH	QVQLVQSGAEVKKPGASVKVSCKASGYTFTTAGMQWVRQAPGQGLEWMGWINTHSGVPKY AEDFKGRVTISADTSTSTAYLQLSSLKSEDTAVYYCARSGFGSSYWYFDVWGQGTLVTVS S
316	Anti-TROP2 VL	DIQMTQSPSSLSASVGDRVTITCKASQDVSTAVAWYQQKPGKAPKLLIYSASYRYTGVPS RFSGSGSGTDFTLTISSLQPEDFAVYYCQQHYITPLTFGQGTKLEIK
317	MICA CDR-H1	SQNIY
318	MICA CDR-H2	YIEPYNVVPMYNPKFKG
319	MICA CDR-H3	SGSSNFDY
320	MICA CDR-L1	SASSSISSHYLH
321	MICA CDR-L2	RTSNLAS
322	MICA CDR-L3	QQGSSLPLT
323	Anti-MICA VH	EIQLVQSGAEVKKPGASVKVSCKASGYAFTSQNIYWVRQAPGQGLEWIGYIEPYNVVPMY NPKFKGRATLTVDKSTSTAYLELSSLRSEDTAVYYCARSGSSNFDYWGQGTLVTVSS
324	Anti-MICA VL	DIQLTQSPSSLSASVGDRVTITCSASSSISSHYLHWYQQKPGKSPKLLIYRTSNLASGVP SRFSGSGSGTDYTLTISSLQPEDFATYYCQQGSSLPLTFGQGTKVEIK
325	Anti-MICA CDR-H1	NYAMH
326	Anti-MICA CDR-H2	LIWYDGSNKFYGDSVKG
327	Anti-MICA CDR-H3	EGSGHY
328	Anti-MICA CDR-L1	RASQGISSALA
329	Anti-MICA CDR-L2	DASSLES
330	Anti-MICA CDR-L3	QQFNSYPIT
331	Anti-MICA VH	QVQLVESGGGVVQPGRSLRLSCAASGFTFSNYAMHWVRQAPGEGLEWVALIWYDGSNKFY GDSVKGRFTISRDNSKNTLYLQMNSLSAEDTAVYYCAREGSGHYWGQGTLVTVSS
332	Anti-MICA VL	AIQLTQSPSSLSASVGDRVTITCRASQGISSALAWYQQKPGKVPKSLIYDASSLESGVPS RFSGSGSGTDFTLTISSLQPEDFATYYCQQFNSYPITFGQGTRLEIK
333	Anti-MICA CDR-H1	NYAMS
334	Anti-MICA CDR-H2	YISPGGDYIYYADSVKG
335	Anti-MICA CDR-H3	DRRHYGSYAMDY
336	Anti-MICA CDR-L1	RSSKSLLHSNLNTYLY
337	Anti-MICA CDR-L2	RMSNLAS
338	Anti-MICA CDR-L3	MQHLEYPFT
339	Anti-MICA VH	QVQLVESGGGLVKPGGSLRLSCAASGFTFSNYAMSWIRQAPGKGLEWVSYISPGGDYIYY ADSVKGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCTTDRRHYGSYAMDYWGQGTLVTVS S
340	Anti-MICA VL	DIVMTQSPLSLPVTPGEPASISCRSSKSLLHSNLNTYLYWFLQKPGQSPQILIYRMSNLA SGVPDRFSGSGSGTAFTLKISRVEAEDVGVYYCMQHLEYPFTFGPGTKLEIK
341	Anti-MICA CDR-H1	TYAFH
342	Anti-MICA CDR-H2	GIVPIFGTLKYAQKFQD
343	Anti-MICA CDR-H3	AIQLEGRPFDH

344	Anti-MICA CDR-L1	RASQGITSYLA
345	Anti-MICA CDR-L2	AASALQS
346	Anti-MICA CDR-L3	QQVNRGAAIT
347	Anti-MICA VH	QVQLVQSGAEVKKPGSSVRVSCRASGGSSTTYAFHWVRQAPGQGLEWMGGIVPIFGTLKY AQKFQDRVTLTADKSTGTAYMELNSLRLDDTAVYYCARAIQLEGRPFDHWGQGTQVTVSA
348	Anti-MICA VL	DIQLTQSPSFLSASVGDRVTITCRASQGITSYLAWYQQKPGKAPKLLIYAASALQSGVPS RFSGRGSGTEFTLTISSLQPEDFATYYCQQVNRGAAITFGHGTRLDIK
349	Anti-ITGav/CD51 CDR-H1	RYTMH
350	Anti-ITGav/CD51 CDR-H2	VISFDGSNKYYVDSVKG
351	Anti-ITGav/CD51 CDR-H3	EARGSYAFDI
352	Anti-ITGav/CD51 CDR-L1	RASQSVSSYLA
353	Anti-ITGav/CD51 CDR-L2	DASNRAT
354	Anti-ITGav/CD51 CDR-L3	QQRSNWPPFT
355	Anti-ITGav/CD51 VH	QVQLVESGGGVVQPGRSRRLSCAASGFTFSRYTMHWVRQAPGKGLEWVAVISFDGSNKYY VDSVKGRFTISRDNSENTLYLQVNILRAEDTAVYYCAREARGSYAFDIWGQGTMVTVSS
356	Anti-ITGav/CD51 VL	EIVLTQSPATLSLSPGERATLSCRASQSVSSYLAWYQQKPGQAPRLLIYDASNRATGIPA RFSGSGSGTDFTLTISSLEPEDFAVYYCQQRSNWPPFTFGPGTKVDIK
357	Anti-ITGav CDR-H1	SFWMH
358	Anti-ITGav CDR-H2	YINPRSGYTEYNEIFRD
359	Anti-ITGav CDR-H3	FLGRGAMDY
360	Anti-ITGav CDR-L1	RASQDISNYLA
361	Anti-ITGav CDR-L2	YTSKIHS
362	Anti-ITGav CDR-L3	QQGNTFPYT
363	Anti-ITGav VH	QVQLQQSGGELAKPGASVKVSCKASGYTFSSFWMHWVRQAPGQGLEWIGYINPRSGYTEY NEIFRDKATMTTDTSTSTAYMELSSLRSEDTAVYYCASFLGRGAMDYWGQGTTVTVSS
364	Anti-ITGav VL	DIQMTQSPSSLSASVGDRVTITCRASQDISNYLAWYQQKPGKAPKLLIYYTSKIHSGVPS RFSGSGSGTDYTFTISSLQPEDIATYYCQQGNTFPYTFGQGTKVEIK
365	Anti-gpA33 CDR-H1	TSSYYWG
366	Anti-gpA33 CDR-H2	TIYYNGSTYYSPSLKS
367	Anti-gpA33 CDR-H3	QGYDIKINIDV
368	Anti-gpA33 CDR-L1	RASQSVSSYLA
369	Anti-gpA33 CDR-L2	VASNRAT

370	Anti-gpA33 CDR-L3	QQRSNWPLT
371	Anti-gpA33 VH	QLQLQESGPGLVKPSETLSLTCTVSGGSISTSSYYWGWIRQPPGKGLEWIGTIYYNGSTY YSPSLKSRVSISVDTSKNQFSLKLSSVTAADTSVYYCARQGYDIKINIDVWGQGTTVTVS S
372	Anti-gpA33 VL	EIVLTQSPATLSLSPGERATLSCRASQSVSSYLAWYQQKPGQAPRLLIYVASNRATGIPA RFSGSGSGTDFTLTISSLEPEDFAVYYCQQRSNWPLTFGGGTKVEIK
373	Anti-IL1Rap CDR-H1	SSWMN
374	Anti-IL1Rap CDR-H2	RIYPGDGNTHYAQKFQG
375	Anti-IL1Rap CDR-H3	GYLDPMDY
376	Anti-IL1Rap CDR-L1	QASQGINNYLN
377	Anti-IL1Rap CDR-L2	YTSGLHA
378	Anti-IL1Rap CDR-L3	QQYSILPWT
379	Anti-IL1Rap VH	QVQLVQSGAEVKKPGSSVKVSCKASGYAFTSSWMNWVRQAPGQGLEWMGRIYPGDGNTHY AQKFQGRVTLTADKSTSTAYMELSSLRSEDTAVYYCGEGYLDPMDYWGQGTLVTVSS
380	Anti-IL1Rap VL	DIQMTQSPSSLSASVGDRVTITCQASQGINNYLNWYQQKPGKAPKLLIHYTSGLHAGVPS RFSGSGSGTDYTLTISSLEPEDVATYYCQQYSILPWTFGGGTKVEIK
381	Anti-EpCAM CDR-H1	SYGMH
382	Anti-EpCAM CDR-H2	VISYDGSNKYYADSVKG
383	Anti-EpCAM CDR-H3	DMGWGSGWRPYYYYGMDV
384	Anti-EpCAM CDR-L1	RTSQSISSYLN
385	Anti-EpCAM CDR-L2	WASTRES
386	Anti-EpCAM CDR-L3	QQSYDIPYT
387	Anti-EpCAM VH	EVQLLESGGGVVQPGRSLRLSCAASGFTFSSYGMHWVRQAPGKGLEWVAVISYDGSNKYY ADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAKDMGWGSGWRPYYYYGMDVWGQG TTVTVSS
388	Anti-EpCAM VL	ELQMTQSPSSLSASVGDRVTITCRTSQSISSYLNWYQQKPGQPPKLLIYWASTRESGVPD RFSGSGSGTDFTLTISSLQPEDSATYYCQQSYDIPYTFGQGTKLEIK
389	Anti-EpCAM CDR-H1	NYWMS
390	Anti-EpCAM CDR-H2	NIKQDGSEKFYADSVKG
391	Anti-EpCAM CDR-H3	VGPSWEQDY
392	Anti-EpCAM CDR-L1	TGSSSNIGSYYGVH
393	Anti-EpCAM CDR-L2	SDTNRPS
394	Anti-EpCAM CDR-L3	QSYDKGFGHRV
395	Anti-EpCAM VH	EVQLVESGGGLVQPGGSLRLSCAASGFTFSNYWMSWVRQAPGKGLEWVANIKQDGSEKFY ADSVKGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCARVGPSWEQDYWGQGTLVTVSA
396	Anti-EpCAM VL	QSVLTQPPSVSGAPGQRVTISCTGSSSNIGSYYGVHWYQQLPGTAPKLLIYSDTNRPSGV PDRFSGSKSGTSASLAITGLQAEDEADYYCQSYDKGFGHRVFGGGTKLTVL
397	Anti-EpCAM CDR-H1	SYAIS
398	Anti-EpCAM CDR-H2	GIIPIFGTANYAQKFQG

399	Anti-EpCAM CDR-H3	GLLWNY
400	Anti-EpCAM CDR-L1	RASQSVSSNLA
401	Anti-EpCAM CDR-L2	GASTTAS
402	Anti-EpCAM CDR-L3	QQYNNWPPAYT
403	Anti-EpCAM VH	QVQLVQSGAEVKKPGSSVKVSCKASGGTFSSYAISWVRQAPGQGLEWMGGIIPIFGTANY AQKFQGRVTITADESTSTAYMELSSLRSEDTAVYYCARGLLWNYWGQGTLVTVSS
404	Anti-EpCAM VL	EIVMTQSPATLSVSPGERATLSCRASQSVSSNLAWYQQKPGQAPRLIIYGASTTASGIPA RFSASGSGTDFTLTISSLQSEDFAVYYCQQYNNWPPAYTFGQGTKLEIK
405	Anti-EpCAM CDR-H1	NYGMN
406	Anti-EpCAM CDR-H2	WINTYTGEPTYGEDFKG
407	Anti-EpCAM CDR-H3	FGNYVDY
408	Anti-EpCAM CDR-L1	RSSKNLLHSNGITYLY
409	Anti-EpCAM CDR-L2	QMSNLAS
410	Anti-EpCAM CDR-L3	AQNLEIPRT
411	Anti-EpCAM VH	QVQLVQSGPEVKKPGASVKVSCKASGYTFTNYGMNWVRQAPGQGLEWMGWINTYTGEPTY GEDFKGRFAFSLDTSASTAYMELSSLRSEDTAVYFCARFGNYVDYWGQGSLVTVSS
412	Anti-EpCAM VL	DIVMTQSPLSLPVTPGEPASISCRSSKNLLHSNGITYLYWYLQKPGQSPQLLIYQMSNLA SGVPDRFSSSGSGTDFTLKISRVEAEDVGVYYCAQNLEIPRTFGQGTKVEIK
413	Anti-EpCAM CDR-H1	KYGMN
414	Anti-EpCAM CDR-H2	WINTYTEEPTYGDDFKG
415	Anti-EpCAM CDR-H3	FGSAVDY
416	Anti-EpCAM CDR-L1	RSSKSLLHSNGITYLY
417	Anti-EpCAM CDR-L2	QMSNRAS
418	Anti-EpCAM CDR-L3	AQNLELPRT
419	Anti-EpCAM VH	QIQLVQSGPEVKKPGESVKISCKASGYTFTKYGMNWVKQAPGQGLKWMGWINTYTEEPTY GDDFKGRFTFTLDTSTSTAYLEISSLRSEDTATYFCARFGSAVDYWGQGTLVTVSS
420	Anti-EpCAM VL	DIVMTQSALSNPVTLGESGSISCRSSKSLLHSNGITYLYWYLQKPGQSPQLLIYQMSNRA SGVPDRFSSSGSGTDFTLKISRVEAEDVGVYYCAQNLELPRTFGQGTKLEMKR
421	Anti-EpCAM CDR-H1	DYSMH
422	Anti-EpCAM CDR-H2	WINTETGEPTYADDFKG
423	Anti-EpCAM CDR-H3	TAVY
424	Anti-EpCAM CDR-L1	RASQEISVSLS
425	Anti-EpCAM CDR-L2	ATSTLDS
426	Anti-EpCAM CDR-L3	LQYASYPWT
427	Anti-EpCAM VH	QVKLQESGPELKKPGETVKISCKASGYTFTDYSMHWVKQAPGKGLKWMGWINTETGEPTY ADDFKGRFAFSLETSASTAYLQINNLKNEDTATYFCARTAVYWGQGTTVTVSS
428	Anti-EpCAM VL	DIQMTQSPSSLSASLGERVSLTCRASQEISVSLSWLQQEPDGTIKRLIYATSTLDSGVPK RFSGSRSGSDYSLTISSLESEDFVDYYCLQYASYPWTFGGGTKLEIKR

429	Anti-CD352 CDR-H1	NYGMN
430	Anti-CD352 CDR-H2	WINTYSGEPRYADDFKG
431	Anti-CD352 CDR-H3	DYGRWYFDV
432	Anti-CD352 CDR-L1	RASSSVSHMH
433	Anti-CD352 CDR-L2	ATSNLAS
434	Anti-CD352 CDR-L3	QQWSSTPRT
435	Anti-CD352 VH	QIQLVQSGSELKKPGASVKVSCKASGYTFTNYGMNWVRQAPGQDLKWMGWINTYSGEPRY ADDFKGRFVFSLDKSVNTAYLQISSLKAEDTAVYYCARDYGRWYFDVWGQGTTVTVSS
436	Anti-CD352 VL	QIVLSQSPATLSLSPGERATMSCRASSSVSHMHWYQQKPGQAPRPWIYATSNLASGVPAR FSGSGSGTDYTLTISSLEPEDFAVYYCQQWSSTPRTFGGGTKVEIKR
437	Anti-CS1 CDR-H1	RYWMS
438	Anti-CS1 CDR-H2	EINPDSSTINYAPSLKD
439	Anti-CS1 CDR-H3	PDGNYWYFDV
440	Anti-CS1 CDR-L1	KASQDVGIAVA
441	Anti-CS1 CDR-L2	WASTRHT
442	Anti-CS1 CDR-L3	QQYSSYPYT
443	Anti-CS1 VH	EVQLVESGGGLVQPGGSLRLSCAASGFDFSRYWMSWVRQAPGKGLEWIGEINPDSSTINY APSLKDKFIISRDNAKNSLYLQMNSLRAEDTAVYYCARPDGNYWYFDVWGQGTLVTVSS
444	Anti-CS1 VL	DIQMTQSPSSLSASVGDRVTITCKASQDVGIAVAWYQQKPGKVPKLLIYWASTRHTGVPD RFSGSGSGTDFTLTISSLQPEDVATYYCQQYSSYPYTFGQGTKVEIKR
445	Anti-CD38 CDR-H1	SFAMS
446	Anti-CD38 CDR-H2	AISGSGGGTYYADSVKG
447	Anti-CD38 CDR-H3	DKILWFGEPVFDY
448	Anti-CD38 CDR-L1	RASQSVSSYLA
449	Anti-CD38 CDR-L2	DASNRAT
450	Anti-CD38 CDR-L3	QQRSNWPPT
451	Anti-CD38 VH	EVQLLESGGGLVQPGGSLRLSCAVSGFTFNSFAMSWVRQAPGKGLEWVSAISGSGGGTYY ADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYFCAKDKILWFGEPVFDYWGQGTLVTV SS
452	Anti-CD38 VL	EIVLTQSPATLSLSPGERATLSCRASQSVSSYLAWYQQKPGQAPRLLIYDASNRATGIPA RFSGSGSGTDFTLTISSLEPEDFAVYYCQQRSNWPPTFGQGTKVEIKR
453	Anti-CD25 CDR-H1	SYRMH
454	Anti-CD25 CDR-H2	YINPSTGYTEYNQKFKD
455	Anti-CD25 CDR-H3	GGGVFDY
456	Anti-CD25 CDR-L1	SASSSISYMH
457	Anti-CD25 CDR-L2	TTSNLAS
458	Anti-CD25	HQRSTYPLT

	CDR-L3	
459	Anti-CD25 VH	QVQLVQSGAEVKKPGSSVKVSCKASGYTFTSYRMHWVRQAPGQGLEWIGYINPSTGYTEY NQKFKDKATITADESTNTAYMELSSLRSEDTAVYYCARGGGVFDYWGQGTLVTVSS
460	Anti-CD25 VL	DIQMTQSPSTLSASVGDRVTITCSASSSISYMHWYQQKPGKAPKLLIYTTSNLASGVPAR FSGSGSGTEFTLTISSLQPDDFATYYCHQRSTYPLTFGQGTKVEVK
461	Anti-ADAM9 CDR-H1	SYWMH
462	Anti-ADAM9 CDR-H2	EIIPINGHTNYNEKFKS
463	Anti-ADAM9 CDR-H3	GGYYYYGSRDYFDY
464	Anti-ADAM9 CDR-L1	KASQSVDYDGDSYMN
465	Anti-ADAM9 CDR-L2	AASDLES
466	Anti-ADAM9 CDR-L3	QQSHEDPFT
467	Anti-ADAM9 VH	QVQLQQPGAELVKPGASVKLSCKASGYTFTSYWMHWVKQRPGQGLEWIGEIIPINGHTNY NEKFKSKATLTLDKSSSTAYMQLSSLASEDSAVYYCARGGYYYYGSRDYFDYWGQGTTLT VSS
468	Anti-ADAM9 VL	DIVLTQSPASLAVSLGQRATISCKASQSVDYDGDSYMNWYQQIPGQPPKLLIYAASDLES GIPARFSGSGSGTDFTLNIHPVEEEDAATYYCQQSHEDPFTFGGGTKLEIK
469	Anti-ADAM9 CDR-H1	SYWMH
470	Anti-ADAM9 CDR-H2	EIIPIFGHTNYNEKFKS
471	Anti-ADAM9 CDR-H3	GGYYYYPRQGFLDY
472	Anti-ADAM9 CDR-L1	KASQSVDYSGDSYMN
473	Anti-ADAM9 CDR-L2	AASDLES
474	Anti-ADAM9 CDR-L3	QQSHEDPFT
475	Anti-ADAM9 VH	EVQLVESGGGLVKPGGSLRLSCAASGFTFSSYWMHWVRQAPGKGLEWVGEIIPIFGHTNY NEKFKSRFTISLDNSKNTLYLQMGSLRAEDTAVYYCARGGYYYYPRQGFLDYWGQGTTVT VSS
476	Anti-ADAM9 VL	DIVMTQSPDSLAVSLGERATISCKASQSVDYSGDSYMNWYQQKPGQPPKLLIYAASDLES GIPARFSGSGSGTDFTLTISSLEPEDFATYYCQQSHEDPFTFGQGTKLEIK
477	Anti-CD59 CDR-H1	SYGMN
478	Anti-CD59 CDR-H2	YISSSSSTIYYADSVKG
479	Anti-CD59 CDR-H3	GPGMDV
480	Anti-CD59 CDR-L1	KSSQSVLYSSNNKNYLA
481	Anti-CD59 CDR-L2	WASTRES
482	Anti-CD59 CDR-L3	QQYYSTPQLT
483	Anti-CD59 VH	QVQLQQSGGGVVQPGRSLGLSCAASGFTFSSYGMNWVRQAPGKGLEWVSYISSSSSTIYY ADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARGPGMDVWGQGTTVTVS
484	Anti-CD59 VL	DIVLTQSPDSLAVSLGERATINCKSSQSVLYSSNNKNYLAWYQQKPGQPPKLLIYWASTR ESGVPDRFSGSGSGTDFTPAISSLQAEDVAVYYCQQYYSTPQLTFGGGTKVDIK
485	Anti-CD19 (hBU12) CDR-H1	TSGMGVG
486	Anti-CD19 (hBU12)	HIWWDDDKRYNPALKS

	CDR-H2	
487	Anti-CD19 (hBU12) CDR-H3	MELWSYYFDY
488	Anti-CD19 (hBU12) CDR-L1	SASSSVSYMH
489	Anti-CD19 (hBU12) CDR-L2	DTSKLAS
490	Anti-CD19 (hBU12) CDR-L3	FQGSVYPFT
491	Anti-CD19 (hBU12) VH	QVQLQESGPGLVKPSQTLSLTCTVSGGSISTSGMGVGWIRQHPGKGLEWIGHIWWDDDKR YNPALKSRVTISVDTSKNQFSLKLSSVTAADTAVYYCARMELWSYYFDYWGQGTLVTVSS
492	Anti-CD19 (hBU12) VL	EIVLTQSPATLSLSPGERATLSCSASSSVSYMHWYQQKPGQAPRLLIYDTSKLASGIPAR FSGSGSGTDFTLTISSLEPEDVAVYYCFQGSVYPFTFGQGTKLEIKR
493	Anti-CD19 (hBU12) HC	QVQLQESGPGLVKPSQTLSLTCTVSGGSISTSGMGVGWIRQHPGKGLEWIGHIWWDDDKR YNPALKSRVTISVDTSKNQFSLKLSSVTAADTAVYYCARMELWSYYFDYWGQGTLVTVSS ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSS GLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPELLGG PSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYN STYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDE LTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRW QQGNVFSCSVMHEALHNHYTQKSLSLSPGK
494	Anti-CD19 (hBU12) LC	EIVLTQSPATLSLSPGERATLSCSASSSVSYMHWYQQKPGQAPRLLIYDTSKLASGIPAR FSGSGSGTDFTLTISSLEPEDVAVYYCFQGSVYPFTFGQGTKLEIKRTVAAPSVFIFPPS DEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTL SKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC
495	Anti-CD138 CDR-H1	NYWIE
496	Anti-CD138 CDR-H2	EILPGTGRTIYNEKFKG
497	Anti-CD138 CDR-H3	RDYYGNFYYAMDY
498	Anti-CD138 CDR-L1	SASQGINNYLN
499	Anti-CD138 CDR-L2	YTSTLQS
500	Anti-CD138 CDR-L3	QQYSKLPRT
501	Anti-CD138 VH	QVQLQQSGSELMMPGASVKISCKATGYTFSNYWIEWVKQRPGHGLEWIGEILPGTGRTIY NEKFKGKATFTADISSNTVQMQLSSLTSEDSAVYYCARRDYYGNFYYAMDYWGQGTSVTV SS
502	Anti-CD138 VL	DIQMTQSTSSLSASLGDRVTISCSASQGINNYLNWYQQKPDGTVELLIYYTSTLQSGVPS RFSGSGSGTDYSLTISNLEPEDIGTYYCQQYSKLPRTFGGGTKLEIK
503	Anti-CD166 CDR-H1	TYGMGVG
504	Anti-CD166 CDR-H2	NIWWSEDKHYSPSLKS
505	Anti-CD166 CDR-H3	IDYGNDYAFTY
506	Anti-CD166 CDR-L1	RSSKSLLHSNGITYLY
507	Anti-CD166 CDR-L2	QMSNLAS
508	Anti-CD166 CDR-L3	AQNLELPYT
509	Anti-CD166 VH	QITLKESGPTLVKPTQTLTLTCTFSGFSLSTYGMGVGWIRQPPGKALEWLANIWWSEDKH YSPSLKSRLTITKDTSKNQVVLTITNVDPVDTATYYCVQIDYGNDYAFTYWGQGTLVTVS

		S
510	Anti-CD166 VL	DIVMTQSPLSLPVTPGEPASISCRSSKSLLHSNGITYLYWYLQKPGQSPQLLIYQMSNLA SGVPDRFSGSGSGTDFTLKISRVEAEDVGVYYCAQNLELPYTFGQGTKLEIK
511	Anti-CD56 CDR-H1	SFGMH
512	Anti-CD56 CDR-H2	YISSGSFTIYYADSVKG
513	Anti-CD56 CDR-H3	MRKGYAMDY
514	Anti-CD56 CDR-L1	RSSQIIIHSDGNTYLE
515	Anti-CD56 CDR-L2	KVSNRFS
516	Anti-CD56 CDR-L3	FQGSHVPHT
517	Anti-CD56 VH	QVQLVESGGGVVQPGRSLRLSCAASGFTFSSFGMHWVRQAPGKGLEWVAYISSGSFTIYY ADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARMRKGYAMDYWGQGTLVTVSS
518	Anti-CD56 VL	DVVMTQSPLSLPVTLGQPASISCRSSQIIIHSDGNTYLEWFQQRPGQSPRRLIYKVSNRF SGVPDRFSGSGSGTDFTLKISRVEAEDVGVYYCFQGSHVPHTFGQGTKVEIK
519	Anti-CD74 CDR-H1	NYGVN
520	Anti-CD74 CDR-H2	WINPNTGEPTFDDDFKG
521	Anti-CD74 CDR-H3	SRGKNEAWFAY
522	Anti-CD74 CDR-L1	RSSQSLVHRNGNTYLH
523	Anti-CD74 CDR-L2	TVSNRFS
524	Anti-CD74 CDR-L3	SQSSHVPPT
525	Anti-CD74 VH	QVQLQQSGSELKKPGASVKVSCKASGYTFTNYGVNWIKQAPGQGLQWMGWINPNTGEPTF DDDFKGRFAFSLDTSVSTAYLQISSLKADDTAVYFCSRSRGKNEAWFAYWGQGTLVTVSS
526	Anti-CD74 VL	DIQLTQSPLSLPVTLGQPASISCRSSQSLVHRNGNTYLHWFQQRPGQSPRLLIYTVSNRF SGVPDRFSGSGSGTDFTLKISRVEAEDVGVYFCSQSSHVPPTFGAGTRLEIK
527	Anti-CEACAM5 CDR-H1	TYWMS
528	Anti-CEACAM5 CDR-H2	EIHPDSSTINYAPSLKD
529	Anti-CEACAM5 CDR-H3	LYFGFPWFAY
530	Anti-CEACAM5 CDR-L1	KASQDVGTSVA
531	Anti-CEACAM5 CDR-L2	WTSTRHT
532	Anti-CEACAM5 CDR-L3	QQYSLYRS
533	Anti-CEACAM5 VH	EVQLVESGGGVVQPGRSLRLSCSASGFDFTTYWMSWVRQAPGKGLEWIGEIHPDSSTINY APSLKDRFTISRDNAKNTLFLQMDSLRPEDTGVYFCASLYFGFPWFAYWGQGTPVTVSS
534	Anti-CEACAM5 VL	DIQLTQSPSSLSASVGDRVTITCKASQDVGTSVAWYQQKPGKAPKLLIYWTSTRHTGVPS RFSGSGSGTDFTFTISSLQPEDIATYYCQQYSLYRSFGQGTKVEIK
535	Anti-CanAg CDR-H1	YYGMN
536	Anti-CanAg	WIDTTTGEPTYAQKFQG

	CDR-H2	
537	Anti-CanAg CDR-H3	RGPYNWYFDV
538	Anti-CanAg CDR-L1	RSSKSLLHSNGNTYLY
539	Anti-CanAg CDR-L2	RMSNLVS
540	Anti-CanAg CDR-L3	LQHLEYPFT
541	Anti-CanAg VH	QVQLVQSGAEVKKPGETVKISCKASDYTFTYYGMNWVKQAPGQGLKWMGWIDTTTGEPTY AQKFQGRIAFSLETSASTAYLQIKSLKSEDTATYFCARRGPYNWYFDVWGQGTTVTVSS
542	Anti-CanAg VL	DIVMTQSPLSVPVTPGEPVSISCRSSKSLLHSNGNTYLYWFLQRPGQSPQLLIYRMSNLV SGVPDRFSGSGSGTAFTLRISRVEAEDVGVYYCLQHLEYPFTFGPGTKLELK
543	Anti-DLL-3 CDR-H1	NYGMN
544	Anti-DLL-3 CDR-H2	WINTYTGEPTYADDFKG
545	Anti-DLL-3 CDR-H3	IGDSSPSDY
546	Anti-DLL-3 CDR-L1	KASQSVSNDVV
547	Anti-DLL-3 CDR-L2	YASNRYT
548	Anti-DLL-3 CDR-L3	QQDYTSPWT
549	Anti-DLL-3 VH	QVQLVQSGAEVKKPGASVKVSCKASGYTFTNYGMNWVRQAPGQGLEWMGWINTYTGEPTY ADDFKGRVTMTTDTSTSTAYMELRSLRSDDTAVYYCARIGDSSPSDYWGQGTLVTVSS
550	Anti-DLL-3 VL	EIVMTQSPATLSVSPGERATLSCKASQSVSNDVVWYQQKPGQAPRLLIYYASNRYTGIPA RFSGSGSGTEFTLTISSLQSEDFAVYYCQQDYTSPWTFGQGTKLEIK
551	Anti-DPEP-3 CDR-H1	SYWIE
552	Anti-DPEP-3 CDR-H2	EILPGSGNTYYNERFKD
553	Anti-DPEP-3 CDR-H3	RAAAYYSNPEWFAY
554	Anti-DPEP-3 CDR-L1	TASSSVNSFYLH
555	Anti-DPEP-3 CDR-L2	STSNLAS
556	Anti-DPEP-3 CDR-L3	HQYHRSPYT
557	Anti-DPEP-3 VH	QVQLVQSGAEVKKPGSSVKVSCKASGGTFSSYWIEWVRQAPGQGLEWMGEILPGSGNTYY NERFKDRVTITADESTSTAYMELSSLRSEDTAVYYCARRAAAYYSNPEWFAYWGQGTLVT VSS
558	Anti-DPEP-3 VL	EIVLTQSPATLSLSPGERATLSCTASSSVNSFYLHWYQQKPGLAPRLLIYSTSNLASGIP DRFSGSGSGTDFTLTISRLEPEDFAVYYCHQYHRSPYTFGQGTKLEIK
559	Anti-EGFR CDR-H1	SYWMQ
560	Anti-EGFR CDR-H2	TIYPGDGDTTYTQKFQG
561	Anti-EGFR CDR-H3	YDAPGYAMDY
562	Anti-EGFR CDR-L1	RASQDINNYLA
563	Anti-EGFR CDR-L2	YTSTLHP
564	Anti-EGFR CDR-L3	LQYDNLLYT
565	Anti-EGFR VH	QVQLVQSGAEVAKPGASVKLSCKASGYTFTSYWMQWVKQRPGQGLECIGTIYPGDGDTTY TQKFQGKATLTADKSSSTAYMQLSSLRSEDSAVYYCARYDAPGYAMDYWGQGTLVTVSS

566	Anti-EGFR VL	DIQMTQSPSSLSASVGDRVTITCRASQDINNYLAWYQHKPGKGPKLLIHYTSTLHPGIPS RFSGSGSGRDYSFSISSLEPEDIATYYCLQYDNLLYTFGQGTKLEIK
567	Anti-EGFR CDR-H1	RDFAWN
568	Anti-EGFR CDR-H2	YISYNGNTRYQPSLKS
569	Anti-EGFR CDR-H3	ASRGFPY
570	Anti-EGFR CDR-L1	HSSQDINSNIG
571	Anti-EGFR CDR-L2	HGTNLDD
572	Anti-EGFR CDR-L3	VQYAQFPWT
573	Anti-EGFR VH	EVQLQESGPGLVKPSQTLSLTCTVSGYSISRDFAWNWIRQPPGKGLEWMGYISYNGNTRY QPSLKSRITISRDTSKNQFFLKLNSVTAADTATYYCVTASRGFPYWGQGTLVTVSS
574	Anti-EGFR VL	DIQMTQSPSSMSVSVGDRVTITCHSSQDINSNIGWLQQKPGKSFKGLIYHGTNLDDGVPS RFSGSGSGTDYTLTISSLQPEDFATYYCVQYAQFPWTFGGGTKLEIK
575	Anti-EGFR CDR-H1	NYGVH
576	Anti-EGFR CDR-H2	VIWSGGNTDYNTPFTS
577	Anti-EGFR CDR-H3	ALTYYDYEFAY
578	Anti-EGFR CDR-L1	RASQSIGTNIH
579	Anti-EGFR CDR-L2	YASESIS
580	Anti-EGFR CDR-L3	QQNNNWPTT
581	Anti-EGFR VH	QVQLKQSGPGLVQPSQSLSITCTVSGFSLTNYGVHWVRQSPGKGLEWLGVIWSGGNTDYN TPFTSRLSINKDNSKSQVFFKMNSLQSNDTAIYYCARALTYYDYEFAYWGQGTLVTVSA
582	Anti-EGFR VL	DILLTQSPVILSVSPGERVSFSCRASQSIGTNIHWYQQRTNGSPRLLIKYASESISGIPS RFSGSGSGTDFTLSINSVESEDIADYYCQQNNNWPTTFGAGTKLELK
583	Anti-FRa CDR-H1	GYFMN
584	Anti-FRa CDR-H2	RIHPYDGDTFYNQKFQG
585	Anti-FRa CDR-H3	YDGSRAMDY
586	Anti-FRa CDR-L1	KASQSVSFAGTSLMH
587	Anti-FRa CDR-L2	RASNLEA
588	Anti-FRa CDR-L3	QQSREYPYT
589	Anti-FRa VH	QVQLVQSGAEVVKPGASVKISCKASGYTFTGYFMNWVKQSPGQSLEWIGRIHPYDGDTFY NQKFQGKATLTVDKSSNTAHMELLSLTSEDFAVYYCTRYDGSRAMDYWGQGTTVTVSS
590	Anti-FRa VL	DIVLTQSPLSLAVSLGQPAIISCKASQSVSFAGTSLMHWYHQKPGQQPRLLIYRASNLEA GVPDRFSGSGSKTDFTLTISPVEAEDAATYYCQQSREYPYTFGGGTKLEIK
591	Anti-FRa CDR-H1	GYGLS
592	Anti-FRa CDR-H2	MISSGGSYTYYADSVKG
593	Anti-FRa CDR-H3	HGDDPAWFAY
594	Anti-FRa CDR-L1	SVSSSISSNNLH
595	Anti-FRa CDR-L2	GTSNLAS

596	Anti-FRa CDR-L3	QQWSSYPYMYT
597	Anti-FRa VH	EVQLVESGGGVVQPGRSLRLSCSASGFTFSGYGLSWVRQAPGKGLEWVAMISSGGSYTYY ADSVKGRFAISRDNAKNTLFLQMDSLRPEDTGVYFCARHGDDPAWFAYWGQGTPVTVSS
598	Anti-FRa VL	DIQLTQSPSSLSASVGDRVTITCSVSSSISSNNLHWYQQKPGKAPKPWIYGTSNLASGVP SRFSGSGSGTDYTFTISSLQPEDIATYYCQQWSSYPYMYTFGQGTKVEIK
599	Anti-MUC-1 CDR-H1	NYWMN
600	Anti-MUC-1 CDR-H2	EIRLKSNNYTTHYAESVKG
601	Anti-MUC-1 CDR-H3	HYYFDY
602	Anti-MUC-1 CDR-L1	RSSKSLLHSNGITYFF
603	Anti-MUC-1 CDR-L2	QMSNLAS
604	Anti-MUC-1 CDR-L3	AQNLELPPT
605	Anti-MUC-1 VH	EVQLVESGGGLVQPGGSMRLSCVASGFPFSNYWMNWVRQAPGKGLEWVGEIRLKSNNYTT HYAESVKGRFTISRDDSKNSLYLQMNSLKTEDTAVYYCTRHYYFDYWGQGTLVTVSS
606	Anti-MUC-1 VL	DIVMTQSPLSNPVTPGEPASISCRSSKSLLHSNGITYFFWYLQKPGQSPQLLIYQMSNLA SGVPDRFSGSGSGTDFTLRISRVEAEDVGVYYCAQNLELPPTFGQGTKVEIK
607	Anti-Mesothelin CDR-H1	SYWIG
608	Anti-Mesothelin CDR-H2	IIDPGDSRTRYSPSFQG
609	Anti-Mesothelin CDR-H3	GQLYGGTYMDG
610	Anti-Mesothelin CDR-L1	TGTSSDIGGYNSVS
611	Anti-Mesothelin CDR-L2	GVNNRPS
612	Anti-Mesothelin CDR-L3	SSYDIESATPV
613	Anti-Mesothelin VH	QVELVQSGAEVKKPGESLKISCKGSGYSFTSYWIGWVRQAPGKGLEWMGIIDPGDSRTRY SPSFQGQVTISADKSISTAYLQWSSLKASDTAMYYCARGQLYGGTYMDGWGQGTLVTVSS
614	Anti-Mesothelin VL	DIALTQPASVSGSPGQSITISCTGTSSDIGGYNSVSWYQQHPGKAPKLMIYGVNNRPSGV SNRFSGSKSGNTASLTISGLQAEDEADYYCSSYDIESATPVFGGGTKLTVL
615	Anti-ROR-1 CDR-H1	AYNIH
616	Anti-ROR-1 CDR-H2	SFDPYDGGSSYNQKFKD
617	Anti-ROR-1 CDR-H3	GWYYFDY
618	Anti-ROR-1 CDR-L1	RASKSISKYLA
619	Anti-ROR-1 CDR-L2	SGSTLQS
620	Anti-ROR-1 CDR-L3	QQHDESPYT
621	Anti-ROR-1 VH	QVQLQESGPGLVKPSQTLSLTCTVSGYAFTAYNIHWVRQAPGQGLEWMGSFDPYDGGSSY NQKFKDRLTISKDTSKNQVVLTMTNMDPVDTATYYCARGWYYFDYWGHGTLVTVSS

622	Anti-ROR-1 VL	DIVMTQTPLSLPVTPGEPASISCRASKSISKYLAWYQQKPGQAPRLLIYSGSTLQSGIPP RFSGSGYGTDFTLTINNIESEDAAYYFCQQHDESPYTFGEGTKVEIK
623	Anti-B7-H3 CDR-H1	SFGMH
624	Anti-B7-H3 CDR-H2	YISSDSSAIYYADTVKG
625	Anti-B7-H3 CDR-H3	GRENIYYGSRLDY
626	Anti-B7-H3 CDR-L1	KASQNVDTNVA
627	Anti-B7-H3 CDR-L2	SASYRYS
628	Anti-B7-H3 CDR-L3	QQYNNYPFT
629	Anti-B7-H3 VH	DVQLVESGGGLVQPGGSRKLSCAASGFTFSSFGMHWVRQAPEKGLEWVAYISSDSSAIYY ADTVKGRFTISRDNPKNTLFLQMTSLRSEDTAMYYCGRGRENIYYGSRLDYWGQGTTLTV SS
630	Anti-B7-H3 VL	DIAMTQSQKFMSTSVGDRVSVTCKASQNVDTNVAWYQQKPGQSPKALIYSASYRYSGVPD RFTGSGSGTDFTLTINNVQSEDLAEYFCQQYNNYPFTFGSGTKLEIK
631	Anti-B7-H3 CDR-H1	SYGMS
632	Anti-B7-H3 CDR-H2	TINSGGSNTYYPDSLKG
633	Anti-B7-H3 CDR-H3	HDGGAMDY
634	Anti-B7-H3 CDR-L1	RASESIYSYLA
635	Anti-B7-H3 CDR-L2	NTKTLPE
636	Anti-B7-H3 CDR-L3	QHHYGTPPWT
637	Anti-B7-H3 VH	EVQLVESGGGLVKPGGSLRLSCAASGFTFSSYGMSWVRQAPGKGLEWVATINSGGSNTYY PDSLKGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCARHDGGAMDYWGQGTTVTVSS
638	Anti-B7-H3 VL	DIQMTQSPSSLSASVGDRVTITCRASESIYSYLAWYQQKPGKAPKLLVYNTKTLPEGVPS RFSGSGSGTDFTLTISSLQPEDFATYYCQHHYGTPPWTFGQGTRLEIK
639	Anti-B7-H3 CDR-H1	SFGMH
640	Anti-B7-H3 CDR-H2	YISSGSGTIYYADTVKG
641	Anti-B7-H3 CDR-H3	HGYRYEGFDY
642	Anti-B7-H3 CDR-L1	KASQNVDTNVA
643	Anti-B7-H3 CDR-L2	SASYRYS
644	Anti-B7-H3 CDR-L3	QQYNNYPFT
645	Anti-B7-H3 VH	EVQLVESGGGLVQPGGSLRLSCAASGFTFSSFGMHWVRQAPGKGLEWVAYISSGSGTIYY ADTVKGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCARHGYRYEGFDYWGQGTTVTVSS
646	Anti-B7-H3 VL	DIQMTQSPSFLSASVGDRVTITCKASQNVDTNVAWYQQKPGKAPKALIYSASYRYSGVPS RFSGSGSGTDFTLTISSLQPEDFAEYFCQQYNNYPFTFGQGTKLEIK
647	Anti-B7-H3 CDR-H1	NYVMH
648	Anti-B7-H3 CDR-H2	YINPYNDDVKYNEKFKG
649	Anti-B7-H3 CDR-H3	WGYYGSPLYYFDY
650	Anti-B7-H3 CDR-L1	RASSRLIYMH
651	Anti-B7-H3	ATSNLAS

	CDR-L2	
652	Anti-B7-H3 CDR-L3	QQWNSNPPT
653	Anti-B7-H3 VH	EVQLQQSGPELVKPGASVKMSCKASGYTFTNYVMHWVKQKPGQGLEWIGYINPYNDDVKY NEKFKGKATQTSDKSSSTAYMELSSLTSEDSAVYYCARWGYYGSPLYYFDYWGQGTTLTV SS
654	Anti-B7-H3 VL	QIVLSQSPTILSASPGEKVTMTCRASSRLIYMHWYQQKPGSSPKPWIYATSNLASGVPAR FSGSGSGTSYSLTISRVEAEDAATYYCQQWNSNPPTFGTGTKLELK
655	Anti-B7-H3 CDR-H1	NYVMH
656	Anti-B7-H3 CDR-H2	YINPYNDDVKYNEKFKG
657	Anti-B7-H3 CDR-H3	WGYYGSPLYYFDY
658	Anti-B7-H3 CDR-L1	RASSRLIYMH
659	Anti-B7-H3 CDR-L2	ATSNLAS
660	Anti-B7-H3 CDR-L3	QQWNSNPPT
661	Anti-B7-H3 VH	QVQLVQSGAEVKKPGSSVKVSCKASGYTFTNYVMHWVRQAPGQGLEWMGYINPYNDDVKY NEKFKGRVTITADESTSTAYMELSSLRSEDTAVYYCARWGYYGSPLYYFDYWGQGTLVTV SS
662	Anti-B7-H3 VL	EIVLTQSPATLSLSPGERATLSCRASSRLIYMHWYQQKPGQAPRPLIYATSNLASGIPAR FSGSGSGTDFTLTISSLEPEDFAVYYCQQWNSNPPTFGQGTKVEIK
663	Anti-B7-H3 CDR-H1	SYTIH
664	Anti-B7-H3 CDR-H2	YINPNSRNTDYAQKFQG
665	Anti-B7-H3 CDR-H3	YSGSTPYWYFDV
666	Anti-B7-H3 CDR-L1	RASSSVSYMN
667	Anti-B7-H3 CDR-L2	ATSNLAS
668	Anti-B7-H3 CDR-L3	QQWSSNPLT
669	Anti-B7-H3 VH	EVQLVQSGAEVKKPGSSVKVSCKASGYSFTSYTIHWVRQAPGQGLEWMGYINPNSRNTDY AQKFQGRVTLTADKSTSTAYMELSSLRSEDTAVYYCARYSGSTPYWYFDVWGQGTTVTVS S
670	Anti-B7-H3 VL	DIQLTQSPSFLSASVGDRVTITCRASSSVSYMNWYQQKPGKSPKPWIYATSNLASGVPSR FSVSVSGTEHTLTISSLQPEDFATYYCQQWSSNPLTFGQGTKLEIK
671	Anti-B7-H3 CDR-H1	SYWMH
672	Anti-B7-H3 CDR-H2	LIHPDSGSTNYNEMFKN
673	Anti-B7-H3 CDR-H3	GGRLYFDY
674	Anti-B7-H3 CDR-L1	RSSQSLVHSNGDTYLR
675	Anti-B7-H3 CDR-L2	KVSNRFS
676	Anti-B7-H3 CDR-L3	SQSTHVPYT
677	Anti-B7-H3 VH	EVQLVQSGAEVKKPGSSVKVSCKASGYTFSSYWMHWVRQAPGQGLEWIGLIHPDSGSTNY NEMFKNRATLTVDRSTSTAYVELSSLRSEDTAVYFCAGGGRLYFDYWGQGTTVTVSS
678	Anti-B7-H3 VL	DVVMTQSPLSLPVTPGEPASISCRSSQSLVHSNGDTYLRWYLQKPGQSPQLLIYKVSNRF SGVPDRFSGSGSGTDFTLKISRVEAEDVGVYYCSQSTHVPYTFGGGTKVEIK
679	Anti-B7-H3 CDR-H1	SYWMH

680	Anti-B7-H3 CDR-H2	LIHPESGSTNYNEMFKN
681	Anti-B7-H3 CDR-H3	GGRLYFDY
682	Anti-B7-H3 CDR-L1	RSSQSLVHSNQDTYLR
683	Anti-B7-H3 CDR-L2	KVSNRFS
684	Anti-B7-H3 CDR-L3	SQSTHVPYT
685	Anti-B7-H3 VH	EVQLVQSGAEVKKPGSSVKVSCKASGYTFSSYWMHWVRQAPGQGLEWIGLIHPESGSTNY NEMFKNRATLTVDRSTSTAYMELSSLRSEDTAVYYCAGGGRLYFDYWGQGTTVTVSS
686	Anti-B7-H3 VL	DIVMTQSPLSLPVTPGEPASISCRSSQSLVHSNQDTYLRWYLQKPGQSPQLLIYKVSNRF SGVPDRFSGSGSGTDFTLKISRVEAEDVGVYYCSQSTHVPYTFGGGTKVEIK
687	Anti-B7-H3 CDR-H1	SGYSWH
688	Anti-B7-H3 CDR-H2	YIHSSGSTNYNPSLKS
689	Anti-B7-H3 CDR-H3	YDDYFEY
690	Anti-B7-H3 CDR-L1	KASQNVGFNVAW
691	Anti-B7-H3 CDR-L2	SASYRYS
692	Anti-B7-H3 CDR-L3	QQYNWYPFT
693	Anti-B7-H3 VH	EVQLQESGPGLVKPSETLSLTCAVTGYSITSGYSWHWIRQFPGNGLEWMGYIHSSGSTNY NPSLKSRISISRDTSKNQFFLKLSSVTAADTAVYYCAGYDDYFEYWGQGTTVTVSS
694	Anti-B7-H3 VL	DIQMTQSPSSLSASVGDRVTITCKASQNVGFNVAWYQQKPGKSPKALIYSASYRYSGVPS RFSGSGSGTDFTLTISSLQPEDFAEYFCQQYNWYPFTFGQGTKLEIK
695	Anti-B7-H3 CDR-H1	NYDIN
696	Anti-B7-H3 CDR-H2	WIFPGDDSTQYNEKFKG
697	Anti-B7-H3 CDR-H3	QTTGTWFAY
698	Anti-B7-H3 CDR-L1	RASQSISDYLY
699	Anti-B7-H3 CDR-L2	YASQSIS
700	Anti-B7-H3 CDR-L3	QNGHSFPLT
701	Anti-B7-H3 VH	QVQLVQSGAEVVKPGASVKLSCKTSGYTFTNYDINWVRQRPGQGLEWIGWIFPGDDSTQY NEKFKGKATLTTDTSTSTAYMELSSLRSEDTAVYFCARQTTGTWFAYWGQGTLVTVSS
702	Anti-B7-H3 VL	EIVMTQSPATLSVSPGERVTLSCRASQSISDYLYWYQQKSHESPRLLIKYASQSISGIPA RFSGSGSGSEFTLTINSVEPEDVGVYYCQNGHSFPLTFGQGTKLELK
703	Anti-B7-H3 VH	QVQLQQSGAEVKKPGSSVKVSCKASGGTFSSYAISWVRQAPGQGLEWMGGIIPILGIANY AQKFQGRVTITADESTSTAYMELSSLRSEDTAVYYCARGGSGSYHMDVWGKGTTVTVSS
704	Anti-B7-H3 VL	EIVLTQSPATLSLSPGERATLSCRASQSVSSYLAWYQQKPGQAPRLLIYDASNRATGIPA RFSGSGSGTDFTLTISSLEPEDFAVYYCQQRSNWPPRITFGQGTRLEIK
705	Anti-B7-H3 CDR-H1	IYNVH
706	Anti-B7-H3 CDR-H2	TIFPGNGDTSYNQKFKD
707	Anti-B7-H3 CDR-H3	WDDGNVGFAH
708	Anti-B7-H3 CDR-L1	RASENINNYLT
709	Anti-B7-H3 CDR-L2	HAKTLAE

710	Anti-B7-H3 CDR-L3	QHHYGTPPT
711	Anti-B7-H3 VH	QVQLQQPGAELVKPGASVKMSCKASGYTFTIYNVHWIKQTPGQGLEWMGTIFPGNGDTSY NQKFKDKATLTTDKSSKTAYMQLNSLTSEDSAVYYCARWDDGNVGFAHWGQGTLVTVSA
712	Anti-B7-H3 VL	DIQMTQSPASLSASVGETVTITCRASENINNYLTWFQQKQGKSPQLLVYHAKTLAEGVPS RFSGSGSGTQFSLKINSLQPEDFGSYYCQHHYGTPPTFGGGTKLEIK
713	Anti-B7-H3 VH	EVQLVQSGAEVKKPGASVKVSCKASGYTFTIYNVHWVRQAPGQGLEWMGTIFPGNGDTSY NQKFKDKVTMTTDTSTSTAYMELSSLRSEDTAVYYCARWDDGNVGFAHWGQGTLVTVSS
714	Anti-B7-H3 VL	DIQMTQSPSSLSASVGDRVTITCRASENINNYLTWFQQKQGKSPQLLIYHAKTLAEGVPS RFSGSGSGTDFTLTISSLQPEDFATYYCQHHYGTPPTFGGGTKVEIK
715	Anti-B7-H3 VH	EVQLVQSGAEVKKPGASVKVSCKASGYTFTIYNVHWIRQAPGQGLEWMGTIFPGNGDTSY NQKFKDRATLTTDKSTKTAYMELRSLRSDDTAVYYCARWDDGNVGFAHWGQGTLVTVSS
716	Anti-B7-H3 VL	DIQMTQSPSSLSASVGDRVTITCRASENINNYLTWFQQKPGKAPKLLVYHAKTLAEGVPS RFSGSGSGTQFTLTISSLQPEDFATYYCQHHYGTPPTFGQGTKLEIK
717	Anti-HER3 H	QVQLQQWGAGLLKPSETLSLTCAVYGGSFSGYYWSWIRQPPGKGLEWIGEINHSGSTNYN PSLKSRVTISVETSKNQFSLKLSSVTAADTAVYYCARDKWIWYFDLWGRGTLVTVSSAST KGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLY SLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKRVEPKSCDKTHTCPPCPAPELLGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK NQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQG NVFSCSVMHEALHNHYTQKSLSLSPGK
718	Anti-HER3 L	DIEMTQSPDSLAVSLGERATINCRSSQSVLYSSSNRNYLAWYQQNPGQPPKLLIYWASTR ESGVPDRFSGSGSGTDFTLTISSLQAEDVAVYYCQQYYSTPRTFGQGTKVEIKRTVAAPS VFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYS LSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC
719	Anti-HER3 H	EVQLLESGGGLVQPGGSLRLSCAASGFTFSHYVMAWVRQAPGKGLEWVSSISSSGGWTLY ADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCTRGLKMATIFDYWGQGTLVTVSSA STKGPSVFPLAPCSRSTSESTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSG LYSLSSVVTVPSSNFGTQTYTCNVDHKPSNTKVDKTVERKCCVECPPCPAPPVAGPSVFL FPPKPKDTLMISRTPEVTCVVVDVSHEDPEVQFNWYVDGVEVHNAKTKPREEQFNSTFRV VSVLTVVHQDWLNGKEYKCKVSNKGLPAPIEKTISKTKGQPREPQVYTLPPSREEMTKNQ VSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPMLDSDGSFFLYSKLTVDKSRWQQGNV FSCSVMHEALHNHYTQKSLSLSPGK
720	Anti-HER3 L	QSALTQPASVSGSPGQSITISCTGTSSDVGSYNVVSWYQQHPGKAPKLIIYEVSQRPSGV SNRFSGSKSGNTASLTISGLQTEDEADYYCCSYAGSSIFVIFGGGTKVTVLGQPKAAPSV TLFPPSSEELQANKATLVCLVSDFYPGAVTVAWKADGSPVKVGVETTKPSKQSNNKYAAS SYLSLTPEQWKSHRSYSCRVTHEGSTVEKTVAPAECS
721	Anti-HER3 H	EVQLLESGGGLVQPGGSLRLSCAASGFTFSSYAMSWVRQAPGKGLEWVSAINSQGKSTYY ADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARWGDEGFDIWGQGTLVTVSSAST KGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLY SLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKRVEPKSCDKTHTCPPCPAPELLGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTY RVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTK NQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQG NVFSCSVMHEALHNHYTQKSLSLSPGK
722	Anti-HER3 L	DIQMTQSPSSLSASVGDRVTITCRASQGISNWLAWYQQKPGKAPKLLIYGASSLQSGVPS RFSGSGSGTDFTLTISSLQPEDFATYYCQQYSSFPTTFGQGTKVEIKRTVAAPSVFIFPP SDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLT LSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC
723	Anti-HER3 H	QVQLVQSGAEVKKPGASVKVSCKASGYTFRSSYISWVRQAPGQGLEWMGWIYAGTGSPSY NQKLQGRVTMTTDTSTSTAYMELRSLRSDDTAVYYCARHRDYYSNSLTYWGQGTLVTVSS ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSS GLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPELLGG PSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYN STYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDE LTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRW QQGNVFSCSVMHEALHNHYTQKSLSLSPG
724	Anti-HER3 L	DIVMTQSPDSLAVSLGERATINCKSSQSVLNSGNQKNYLTWYQQKPGQPPKLLIYWASTR ESGVPDRFSGSGSGTDFTLTISSLQAEDVAVYYCQSDYSYPYTFGQGTKLEIKRTVAAPS

		VFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYS LSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC
725	Anti-PTK7 CDR-H1	TSNMGVG
726	Anti-PTK7 CDR-H2	HIWWDDDKYYSPSLKS
727	Anti-PTK7 CDR-H3	SNYGYAWFAY
728	Anti-PTK7 CDR-L1	KASQDIYPYLN
729	Anti-PTK7 CDR-L2	RTNRLLD
730	Anti-PTK7 CDR-L3	LQYDEFPLT
731	Anti-PTK7 VH	QITLKESGPTLVKPTQTLTLTCTFSGFSLSTSNMGVGWIRQPPGKALEWLAHIWWDDDKY YSPSLKSRLTITKDTSKNQVVLTMTNMDPVDTATYYCVRSNYGYAWFAYWGQGTLVTVSS
732	Anti-PTK7 VL	DIQMTQSPSSLSASVGDRVTITCKASQDIYPYLNWFQQKPGKAPKTLIYRTNRLLDGVPS RFSGSGSGTDFTFTISSLQPEDIATYYCLQYDEFPLTFGAGTKLEIK
733	Anti-PTK7 CDR-H1	DYAVH
734	Anti-PTK7 CDR-H2	VISTYNDYTYNNQDFKG
735	Anti-PTK7 CDR-H3	GNSYFYALDY
736	Anti-PTK7 CDR-L1	RASESVDSYGKSFMH
737	Anti-PTK7 CDR-L2	RASNLES
738	Anti-PTK7 CDR-L3	QQSNEDPWT
739	Anti-PTK7 VH	QVQLVQSGPEVKKPGASVKVSCKASGYTFTDYAVHWVRQAPGKRLEWIGVISTYNDYTYN NQDFKGRVTMTRDTSASTAYMELSRLRSEDTAVYYCARGNSYFYALDYWGQGTSVTVSS
740	Anti-PTK7 VL	EIVLTQSPATLSLSPGERATLSCRASESVDSYGKSFMHWYQQKPGQAPRLLIYRASNLES GIPARFSGSGSGTDFTLTISSLEPEDFAVYYCQQSNEDPWTFGGGTKLEIK
741	Anti-PTK7 CDR-H1	RYWMS
742	Anti-PTK7 CDR-H2	DLNPDSSAINYVDSVKG
743	Anti-PTK7 CDR-H3	ITTLVPYTMDF
744	Anti-PTK7 CDR-L1	ITNTDIDDDMN
745	Anti-PTK7 CDR-L2	EGNGLRP
746	Anti-PTK7 CDR-L3	LQSDNLPLT
747	Anti-PTK7 VH	EVQLVESGGGLVQPGGSLRLSCAASGFDFSRYWMSWVRQAPGKGLEWIGDLNPDSSAINY VDSVKGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCTLITTLVPYTMDFWGQGTSVTVSS
748	Anti-PTK7 VL	ETTLTQSPAFMSATPGDKVNISCITNTDIDDDMNWYQQKPGEAAILLISEGNGLRPGIPP RFSGSGYGTDFTLTINNIESEDAAYYFCLQSDNLPLTFGSGTKLEIK
749	Anti-ZIP6 CDR-H1	DYYMH
750	Anti-ZIP6 CDR-H2	WIDPENGDTEYGPKFQG
751	Anti-ZIP6 CDR-H3	HNAHYGTWFAY
752	Anti-ZIP6 CDR-L1	RSSQSLLHSSGNTYLE
753	Anti-ZIP6 CDR-L2	KISTRFS

754	Anti-ZIP6 CDR-L3	FQGSHVPYT
755	Anti-ZIP6 VH	QVQLVQSGAEVKKPGASVKVSCKASGLTIEDYYMHWVRQAPGQGLEWMGWIDPENGDTEY GPKFQGRVTMTRDTSINTAYMELSRLRSDDTAVYYCAVHNAHYGTWFAYWGQGTLVTVSS
756	Anti-ZIP6 VL	DVVMTQSPLSLPVTLGQPASISCRSSQSLLHSSGNTYLEWYQQRPGQSPRPLIYKISTRF SGVPDRFSGSGSGTDFTLKISRVEAEDVGVYYCFQGSHVPYTFGGGTKVEIK
757	Anti-ZIP6 HC	QVQLVQSGAEVKKPGASVKVSCKASGLTIEDYYMHWVRQAPGQGLEWMGWIDPENGDTEY GPKFQGRVTMTRDTSINTAYMELSRLRSDDTAVYYCAVHNAHYGTWFAYWGQGTLVTVSS ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSS GLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPELLGG PSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYN STYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDE LTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRW QQGNVFSCSVMHEALHNHYTQKSLSLSPG
758	Anti-ZIP6 LC	DVVMTQSPLSLPVTLGQPASISCRSSQSLLHSSGNTYLEWYQQRPGQSPRPLIYKISTRF SGVPDRFSGSGSGTDFTLKISRVEAEDVGVYYCFQGSHVPYTFGGGTKVEIKRTVAAPSV FIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSL SSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC
759	Anti-Integrin αvβ6 CDR-H1	GYFMN
760	Anti-Integrin αvβ6 CDR-H2	LINPYNGDSFYNQKFKG
761	Anti-Integrin αvβ6 CDR-H3	GLRRDFDY
762	Anti-Integrin αvβ6 CDR-L1	KSSQSLLDSDGKTYLN
763	Anti-Integrin αvβ6 CDR-L2	LVSELDS
764	Anti-Integrin αvβ6 CDR-L3	WQGTHFPRT
765	Anti-Integrin αvβ6 VH	QVQLVQSGAEVKKPGASVKVSCKASGYSFSGYFMNWVRQAPGQGLEWMGLINPYNGDSFY NQKFKGRVTMTRQTSTSTVYMELSSLRSEDTAVYYCVRGLRRDFDYWGQGTLVTVSS
766	Anti-Integrin αvβ6 VL	DVVMTQSPLSLPVTLGQPASISCKSSQSLLDSDGKTYLNWLFQRPGQSPRRLIYLVSELD SGVPDRFSGSGSGTDFTLKISRVEAEDVGVYYCWQGTHFPRTFGGGTKLEIK
767	Anti-CD48 CDR-H1	DFGMN
768	Anti-CD48 CDR-H2	WINTFTGEPSYGNVFKG
769	Anti-CD48 CDR-H3	RHGNGNVFDS
770	Anti-CD48 CDR-L1	RASQSIGSNIH
771	Anti-CD48 CDR-L2	YTSESIS
772	Anti-CD48 CDR-L3	QQSNSWPLT
773	Anti-CD48 VH	QVQLVQSGSELKKPGASVKVSCKASGYTFTDFGMNWVRQAPGQGLEWMGWINTFTGEPSY GNVFKGRFVFSLDTSVSTAYLQISSLKAEDTAVYYCARRHGNGNVFDSWGQGTLVTVSS
774	Anti-CD48 VL	EIVLTQSPDFQSVTPKEKVTITCRASQSIGSNIHWYQQKPDQSPKLLIKYTSESISGVPS RFSGSGSGTDFTLTINSLEAEDAATYYCQQSNSWPLTFGGGTKVEIKR
775	Anti-IGF-1R CDR-H1	SYAIS

776	Anti-IGF-1R CDR-H2	GIIPIFGTANYAQKFQG
777	Anti-IGF-1R CDR-H3	APLRFLEWSTQDHYYYYYMDV
778	Anti-IGF-1R CDR-L1	QGDSLRSYYAT
779	Anti-IGF-1R CDR-L2	GENKRPS
780	Anti-IGF-1R CDR-L3	KSRDGSGQHLV
781	Anti-IGF-1R VH	EVQLVQSGAEVKKPGSSVKVSCKASGGTFSSYAISWVRQAPGQGLEWMGGIIPIFGTANY AQKFQGRVTITADKSTSTAYMELSSLRSEDTAVYYCARAPLRFLEWSTQDHYYYYYMDVW GKGTTVTVSS
782	Anti-IGF-1R VL	SSELTQDPAVSVALGQTVRITCQGDSLRSYYATWYQQKPGQAPILVIYGENKRPSGIPDR FSGSSSGNTASLTITGAQAEDEADYYCKSRDGSGQHLVFGGGTKLTVL
783	Anti-Claudin-18.2 CDR-H1	SYWIN
784	Anti-Claudin-18.2 CDR-H2	NIYPSDSYTNYNQKFKD
785	Anti-Claudin-18.2 CDR-H3	SWRGNSFDY
786	Anti-Claudin-18.2 CDR-L1	KSSQSLLNSGNQKNYLT
787	Anti-Claudin-18.2 CDR-L2	WASTRES
788	Anti-Claudin-18.2 CDR-L3	QNDYSYPFT
789	Anti-Claudin-18.2 VH	QVQLQQPGAELVRPGASVKLSCKASGYTFTSYWINWVKQRPGQGLEWIGNIYPSDSYTNY NQKFKDKATLTVDKSSSTAYMQLSSPTSEDSAVYYCTRSWRGNSFDYWGQGTTLTVSS
790	Anti-Claudin-18.2 VL	DIVMTQSPSSLTVTAGEKVTMSCKSSQSLLNSGNQKNYLTWYQQKPGQPPKLLIYWASTR ESGVPDRFTGSGSGTDFTLTISSVQAEDLAVYYCQNDYSYPFTFGSGTKLEIK
791	Anti-Claudin-18.2 CDR-H1	NYGMN
792	Anti-Claudin-18.2 CDR-H2	WINTNTGEPTYAEEFKG
793	Anti-Claudin-18.2 CDR-H3	LGFGNAMDY
794	Anti-Claudin-18.2 CDR-L1	KSSQSLLNSGNQKNYLT
795	Anti-Claudin-18.2 CDR-L2	WASTRES
796	Anti-Claudin-18.2 CDR-L3	QNDYSYPLT
797	Anti-Claudin-18.2 VH	QIQLVQSGPELKKPGETVKISCKASGYTFTNYGMNWVKQAPGKGLKWMGWINTNTGEPTY AEEFKGRFAFSLETSASTAYLQINNLKNEDTATYFCARLGFGNAMDYWGQGTSVTVSS

798	Anti-Claudin-18.2 VL	DIVMTQSPSSLTVTAGEKVTMSCKSSQSLLNSGNQKNYLTWYQQKPGQPPKLLIYWASTR ESGVPDRFTGSGSGTDFTLTISSVQAEDLAVYYCQNDYSYPLTFGAGTKLELK
799	Anti-Nectin-4 CDR-H1	SYNMN
800	Anti-Nectin-4 CDR-H2	YISSSSSTIYYADSVKG
801	Anti-Nectin-4 CDR-H3	AYYYGMDV
802	Anti-Nectin-4 CDR-L1	RASQGISGWLA
803	Anti-Nectin-4 CDR-L2	AASTLQS
804	Anti-Nectin-4 CDR-L3	QQANSFPPT
805	Anti-Nectin-4 VH	EVQLVESGGGLVQPGGSLRLSCAASGFTFSSYNMNWVRQAPGKGLEWVSYISSSSSTIYY ADSVKGRFTISRDNAKNSLSLQMNSLRDEDTAVYYCARAYYYGMDVWGQGTTVTVSS
806	Anti-Nectin-4 VL	DIQMTQSPSSVSASVGDRVTITCRASQGISGWLAWYQQKPGKAPKFLIYAASTLQSGVPS RFSGSGSGTDFTLTISSLQPEDFATYYCQQANSFPPTFGGGTKVEIK
807	Anti-SLTRK6 CDR-H1	SYGMH
808	Anti-SLTRK6 CDR-H2	VIWYDGSNQYYADSVKG
809	Anti-SLTRK6 CDR-H3	GLTSGRYGMDV
810	Anti-SLTRK6 CDR-L1	RSSQSLLLSHGFNYLD
811	Anti-SLTRK6 CDR-L2	LGSSRAS
812	Anti-SLTRK6 CDR-L3	MQPLQIPWT
813	Anti-SLTRK6 VH	QVQLVESGGGVVQPGRSLRLSCAASGFTFSSYGMHWVRQAPGKGLEWVAVIWYDGSNQYY ADSVKGRFTISRDNSKNTLFLQMHSLRAEDTAVYYCARGLTSGRYGMDVWGQGTTVTVSS
814	Anti-SLTRK6 VL	DIVMTQSPLSLPVTPGEPASISCRSSQSLLLSHGFNYLDWYLQKPGQSPQLLIYLGSSRA SGVPDRFSGSGSGTDFTLKISRVEAEDVGLYYCMQPLQIPWTFGQGTKVEIK
815	Anti-CD142 (TF) CDR-H1	NYAMS
816	Anti-CD142 (TF) CDR-H2	SISGSGDYTYYTDSVKG
817	Anti-CD142 (TF) CDR-H3	SPWGYYLDS
818	Anti-CD142 (TF) CDR-L1	RASQGISSRLA
819	Anti-CD142 (TF) CDR-L2	AASSLQS
820	Anti-CD142 (TF) CDR-L3	QQYNSYPYT
821	Anti-CD142 (TF) VH	EVQLLESGGGLVQPGGSLRLSCAASGFTFSNYAMSWVRQAPGKGLEWVSSISGSGDYTYY TDSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARSPWGYYLDSWGQGTLVTVSS
822	Anti-CD142 (TF) VL	DIQMTQSPPSLSASAGDRVTITCRASQGISSRLAWYQQKPEKAPKSLIYAASSLQSGVPS RFSGSGSGTDFTLTISSLQPEDFATYYCQQYNSYPYTFGQGTKLEIK
823	Anti-h2G12/STn CDR-H1	DHAIH

824	Anti-STn CDR-H2	YFSPGNDDIKYNEKFRG
825	Anti-STn CDR-H3	SLSTPY
826	Anti-STn CDR-L1	KSSQSLLNRGNHKNYLT
827	Anti-STn CDR-L2	WASTRES
828	Anti-STn CDR-L3	QNDYTYPYT
829	Anti-STn VH	EVQLVQSGAEVKKPGASVKVSCKASGYTFTDHAIHWVRQAPGQGLEWMGYFSPGNDDIKY NEKFRGRVTMTADKSSSTAYMELRSLRSDDTAVYFCKRSLSTPYWGQGTLVTVSS
830	Anti-STn VL	DIVMTQSPDSLAVSLGERATINCKSSQSLLNRGNHKNYLTWYQQKPGQPPKLLIYWASTR ESGVPDRFSGSGSGTDFTLTISSLQAEDVAVYYCQNDYTYPYTFGQGTKVEIK
831	Anti-CD20 CDR-H1	SYNMH
832	Anti-CD20 CDR-H2	AIYPGNGDTSYNQKFKG
833	Anti-CD20 CDR-H3	STYYGGDWYFNV
834	Anti-CD20 CDR-L1	RASSSVSYIH
835	Anti-CD20 CDR-L2	ATSNLAS
836	Anti-CD20 CDR-L3	QQWTSNPPT
837	Anti-CD20 VH	QVQLQQPGAELVKPGASVKMSCKASGYTFTSYNMHWVKQTPGRGLEWIGAIYPGNGDTSY NQKFKGKATLTADKSSSTAYMQLSSLTSEDSAVYYCARSTYYGGDWYFNVWGAGTTVTVS A
838	Anti-CD20 VL	QIVLSQSPAILSASPGEKVTMTCRASSSVSYIHWFQQKPGSSPKPWIYATSNLASGVPVR FSGSGSGTSYSLTISRVEAEDAATYYCQQWTSNPPTFGGGTKLEIK
839	Anti-HER2 CDR-H1	DTYIH
840	Anti-HER2 CDR-H2	RIYPTNGYTRYADSVKG
841	Anti-HER2 CDR-H3	WGGDGFYAMDY
842	Anti-HER2 CDR-L1	RASQDVNTAVA
843	Anti-HER2 CDR-L2	SASFLYS
844	Anti-HER2 CDR-L3	QQHYTTPPT
845	Anti-HER2 VH	EVQLVESGGGLVQPGGSLRLSCAASGFNIKDTYIHWVRQAPGKGLEWVARIYPTNGYTRY ADSVKGRFTISADTSKNTAYLQMNSLRAEDTAVYYCSRWGGDGFYAMDYWGQGTLVTVSS
846	Anti-HER2 VL	DIQMTQSPSSLSASVGDRVTITCRASQDVNTAVAWYQQKPGKAPKLLIYSASFLYSGVPS RFSGSRSGTDFTLTISSLQPEDFATYYCQQHYTTPPTFGQGTKVEIK
847	Anti-CD79b CDR-H1	SYWIE
848	Anti-CD79b CDR-H2	EILPGGGDTNYNEIFKG
849	Anti-CD79b CDR-H3	RVPIRLDY
850	Anti-CD79b CDR-L1	KASQSVDYEGDSFLN
851	Anti-CD79b CDR-L2	AASNLES
852	Anti-CD79b CDR-L3	QQSNEDPLT
853	Anti-CD79b	EVQLVESGGGLVQPGGSLRLSCAASGYTFSSYWIEWVRQAPGKGLEWIGEILPGGGDTNY

	VH	NEIFKGRATFSADTSKNTAYLQMNSLRAEDTAVYYCTRRVPIRLDYWGQGTLVTVSS
854	Anti-CD79b VL	DIQLTQSPSSLSASVGDRVTITCKASQSVDYEGDSFLNWYQQKPGKAPKLLIYAASNLES GVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQSNEDPLTFGQGTKVEIK
855	Anti-NaPi2B CDR-H1	DFAMS
856	Anti-NaPi2B CDR-H2	TIGRVAFHTYYPDSMKG
857	Anti-NaPi2B CDR-H3	HRGFDVGHFDF
858	Anti-NaPi2B CDR-L1	RSSETLVHSSGNTYLE
859	Anti-NaPi2B CDR-L2	RVSNRFS
860	Anti-NaPi2B CDR-L3	FQGSFNPLT
861	Anti-NaPi2B VH	EVQLVESGGGLVQPGGSLRLSCAASGFSFSDFAMSWVRQAPGKGLEWVATIGRVAFHTYY PDSMKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARHRGFDVGHFDFWGQGTLVTVSS
862	Anti-NaPi2B VL	DIQMTQSPSSLSASVGDRVTITCRSSETLVHSSGNTYLEWYQQKPGKAPKLLIYRVSNRF SGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCFQGSFNPLTFGQGTKVEIK
863	Anti-Muc16 CDR-H1	NDYAWN
864	Anti-Muc16 CDR-H2	YISYSGYTTYNPSLKS
865	Anti-Muc16 CDR-H3	WTSGLDY
866	Anti-Muc16 CDR-L1	KASDLIHNWLA
867	Anti-Muc16 CDR-L2	GATSLET
868	Anti-Muc16 CDR-L3	QQYWTTPFT
869	Anti-Muc16 VH	EVQLVESGGGLVQPGGSLRLSCAASGYSITNDYAWNWVRQAPGKGLEWVGYISYSGYTTY NPSLKSRFTISRDTSKNTLYLQMNSLRAEDTAVYYCARWTSGLDYWGQGTLVTVSS
870	Anti-Muc16 VL	DIQMTQSPSSLSASVGDRVTITCKASDLIHNWLAWYQQKPGKAPKLLIYGATSLETGVPS RFSGSGSGTDFTLTISSLQPEDFATYYCQQYWTTPFTFGQGTKVEIK
871	Anti-STEAP1 CDR-H1	SDYAWN
872	Anti-STEAP1 CDR-H2	YISNSGSTSYNPSLKS
873	Anti-STEAP1 CDR-H3	ERNYDYDDYYYAMDY
874	Anti-STEAP1 CDR-L1	KSSQSLLYRSNQKNYLA
875	Anti-STEAP1 CDR-L2	WASTRES
876	Anti-STEAP1 CDR-L3	QQYYNYPRT
877	Anti-STEAP1 VH	EVQLVESGGGLVQPGGSLRLSCAVSGYSITSDYAWNWVRQAPGKGLEWVGYISNSGSTSY NPSLKSRFTISRDTSKNTLYLQMNSLRAEDTAVYYCARERNYDYDDYYYAMDYWGQGTLV TVSS
878	Anti-STEAP1 VL	DIQMTQSPSSLSASVGDRVTITCKSSQSLLYRSNQKNYLAWYQQKPGKAPKLLIYWASTR ESGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQYYNYPRTFGQGTKVEIK
879	Anti-BCMA CDR-H1	NYWMH
880	Anti-BCMA CDR-H2	ATYRGHSDTYYNQKFKG
881	Anti-BCMA CDR-H3	GAIYDGYDVLDN
882	Anti-BCMA CDR-L1	SASQDISNYLN

883	Anti-BCMA CDR-L2	YTSNLHS
884	Anti-BCMA CDR-L3	QQYRKLPWT
885	Anti-BCMA VH	QVQLVQSGAEVKKPGSSVKVSCKASGGTFSNYWMHWVRQAPGQGLEWMGATYRGHSDTYY NQKFKGRVTITADKSTSTAYMELSSLRSEDTAVYYCARGAIYDGYDVLDNWGQGTLVTVS S
886	Anti-BCMA VL	DIQMTQSPSSLSASVGDRVTITCSASQDISNYLNWYQQKPGKAPKLLIYYTSNLHSGVPS RFSGSGSGTDFTLTISSLQPEDFATYYCQQYRKLPWTFGQGTKLEIK
887	Anti-c-Met CDR-H1	AYTMH
888	Anti-c-Met CDR-H2	WIKPNNGLANYAQKFQG
889	Anti-c-Met CDR-H3	SEITTEFDY
890	Anti-c-Met CDR-L1	KSSESVDSYANSFLH
891	Anti-c-Met CDR-L2	RASTRES
892	Anti-c-Met CDR-L3	QQSKEDPLT
893	Anti-c-Met VH	QVQLVQSGAEVKKPGASVKVSCKASGYIFTAYTMHWVRQAPGQGLEWMGWIKPNNGLANY AQKFQGRVTMTRDTSISTAYMELSRLRSDDTAVYYCARSEITTEFDYWGQGTLVTVSS
894	Anti-c-Met VL	DIVMTQSPDSLAVSLGERATINCKSSESVDSYANSFLHWYQQKPGQPPKLLIYRASTRES GVPDRFSGSGSGTDFTLTISSLQAEDVAVYYCQQSKEDPLTFGGGTKVEIK
895	Anti-EGFR CDR-H1	SDFAWN
896	Anti-EGFR CDR-H2	YISYSGNTRYQPSLKS
897	Anti-EGFR CDR-H3	AGRGFPY
898	Anti-EGFR CDR-L1	HSSQDINSNIG
899	Anti-EGFR CDR-L2	HGTNLDD
900	Anti-EGFR CDR-L3	VQYAQFPWT
901	Anti-EGFR VH	QVQLQESGPGLVKPSQTLSLTCTVSGYSISSDFAWNWIRQPPGKGLEWMGYISYSGNTRY QPSLKSRITISRDTSKNQFFLKLNSVTAADTATYYCVTAGRGFPYWGQGTLVTVSS
902	Anti-EGFR VL	DIQMTQSPSSMSVSVGDRVTITCHSSQDINSNIGWLQQKPGKSFKGLIYHGTNLDDGVPS RFSGSGSGTDYTLTISSLQPEDFATYYCVQYAQFPWTFGGGTKLEIK
903	Anti-SLAMF7 CDR-H1	DYYMA
904	Anti-SLAMF7 CDR-H2	SINYDGSSTYYVDSVKG
905	Anti-SLAMF7 CDR-H3	DRGYYFDY
906	Anti-SLAMF7 CDR-L1	RSSQSLVHSNGNTYLH
907	Anti-SLAMF7 CDR-L2	KVSNRFS
908	Anti-SLAMF7 CDR-L3	SQSTHVPPFT
909	Anti-SLAMF7 VH	EVQLVESGGGLVQPGGSLRLSCAASGFTFSDYYMAWVRQAPGKGLEWVASINYDGSSTYY VDSVKGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCARDRGYYFDYWGQGTTVTVSS
910	Anti-SLAMF7 VL	DVVMTQTPLSLSVTPGQPASISCRSSQSLVHSNGNTYLHWYLQKPGQSPQLLIYKVSNRF SGVPDRFSGSGSGTDFTLKISRVEAEDVGVYFCSQSTHVPPFTFGGGTKVEIK
911	Anti-C4.4a CDR-H1	NAWMS
912	Anti-C4.4a	YISSSGSTIYYADSVKG

	CDR-H2	
913	Anti-C4.4a CDR-H3	EGLWAFDY
914	Anti-C4.4a CDR-L1	TGSSSNIGAGYVVH
915	Anti-C4.4a CDR-L2	DNNKRPS
916	Anti-C4.4a CDR-L3	AAWDDRLNGPV
917	Anti-C4.4a VH	EVQLLESGGGLVQPGGSLRLSCAASGFTFSNAWMSWVRQAPGKGLEWVSYISSSGSTIYY ADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAREGLWAFDYWGQGTLVTVSS
918	Anti-C4.4a VL	ESVLTQPPSVSGAPGQRVTISCTGSSSNIGAGYVVHWYQQLPGTAPKLLIYDNNKRPSGV PDRFSGSKSGTSASLAISGLRSEDEADYYCAAWDDRLNGPVFGGGTKLTVL
919	Anti-GCC CDR-H1	GYYWS
920	Anti-GCC CDR-H2	EINHRGNTNDNPSLKS
921	Anti-GCC CDR-H3	ERGYTYGNFDH
922	Anti-GCC CDR-L1	RASQSVSRNLA
923	Anti-GCC CDR-L2	GASTRAT
924	Anti-GCC CDR-L3	QQYKTWPRT
925	Anti-GCC VH	QVQLQQWGAGLLKPSETLSLTCAVFGGSFSGYYWSWIRQPPGKGLEWIGEINHRGNTNDN PSLKSRVTISVDTSKNQFALKLSSVTAADTAVYYCARERGYTYGNFDHWGQGTLVTVSS
926	Anti-GCC VL	EIVMTQSPATLSVSPGERATLSCRASQSVSRNLAWYQQKPGQAPRLLIYGASTRATGIPA RFSGSGSGTEFTLTIGSLQSEDFAVYYCQQYKTWPRTFGQGTNVEIK
927	Anti-Axl CDR-H1	SYAMN
928	Anti-Axl CDR-H2	TTSGSGASTYYADSVKG
929	Anti-Axl CDR-H3	IWIAFDI
930	Anti-Axl CDR-L1	RASQSVSSSYLA
931	Anti-Axl CDR-L2	GASSRAT
932	Anti-Axl CDR-L3	QQYGSSPYT
933	Anti-Axl VH	EVQLLESGGGLVQPGGSLRLSCAASGFTFSSYAMNWVRQAPGKGLEWVSTTSGSGASTYY ADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCAKIWIAFDIWGQGTMVTVSS
934	Anti-Axl VL	EIVLTQSPGTLSLSPGERATLSCRASQSVSSSYLAWYQQKPGQAPRLLIYGASSRATGIP DRFSGSGSGTDFTLTISRLEPEDFAVYYCQQYGSSPYTFGQGTKLEIK
935	Anti-gpNMB CDR-H1	SFNYYWS
936	Anti-gpNMB CDR-H2	YIYYSGSTYSNPSLKS
937	Anti-gpNMB CDR-H3	GYNWNYFDY
938	Anti-gpNMB CDR-L1	RASQSVDNNLV
939	Anti-gpNMB CDR-L2	GASTRAT
940	Anti-gpNMB CDR-L3	QQYNNWPPWT
941	Anti-gpNMB VH	QVQLQESGPGLVKPSQTLSLTCTVSGGSISSFNYYWSWIRHHPGKGLEWIGYIYYSGSTY SNPSLKSRVTISVDTSKNQFSLTLSSVTAADTAVYYCARGYNWNYFDYWGQGTLVTVSS
942	Anti-gpNMB	EIVMTQSPATLSVSPGERATLSCRASQSVDNNLVWYQQKPGQAPRLLIYGASTRATGIPA

	VL	RFSGSGSGTEFTLTISSLQSEDFAVYYCQQYNNWPPWTFGQGTKVEIK
943	Anti-gpNMB HC	QVQLQESGPGLVKPSQTLSLTCTVSGGSISSFNYYWSWIRHHPGKGLEWIGYIYYSGSTY SNPSLKSRVTISVDTSKNQFSLTLSSVTAADTAVYYCARGYNWNYFDYWGQGTLVTVSSA STKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSG LYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPELLGGP SVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNS TYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDEL TKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQ QGNVFSCSVMHEALHNHYTQKSLSLSPGK
944	Anti-gpNMB LC	EIVMTQSPATLSVSPGERATLSCRASQSVDNNLVWYQQKPGQAPRLLIYGASTRATGIPA RFSGSGSGTEFTLTISSLQSEDFAVYYCQQYNNWPPWTFGQGTKVEIKRTVAAPSVFIFP PSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTL TLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC
945	Anti-Prolactin receptor CDR-H1	TYWMH
946	Anti-Prolactin receptor CDR-H2	EIDPSDSYSNYNQKFKD
947	Anti-Prolactin receptor CDR-H3	NGGLGPAWFSY
948	Anti-Prolactin receptor CDR-L1	KASQYVGTAVA
949	Anti-Prolactin receptor CDR-L2	SASNRYT
950	Anti-Prolactin receptor CDR-L3	QQYSSYPWT
951	Anti-Prolactin receptor VH	EVQLVQSGAEVKKPGSSVKVSCKASGYTFTTYWMHWVRQAPGQGLEWIGEIDPSDSYSNY NQKFKDRATLTVDKSTSTAYMELSSLRSEDTAVYYCARNGGLGPAWFSYWGQGTLVTVSS
952	Anti-Prolactin receptor VL	DIQMTQSPSSVSASVGDRVTITCKASQYVGTAVAWYQQKPGKSPKLLIYSASNRYTGVPS RFSDSGSGTDFTLTISSLQPEDFATYFCQQYSSYPWTFGGGTKVEIK
953	Anti-FGFR2 CDR-H1	SYAMS
954	Anti-FGFR2 CDR-H2	AISGSGTSTYYADSVKG
955	Anti-FGFR2 CDR-H3	VRYNWNHGDWFDP
956	Anti-FGFR2 CDR-L1	SGSSSNIGNNYVS
957	Anti-FGFR2 CDR-L2	ENYNRPA
958	Anti-FGFR2 CDR-L3	SSWDDSLNYWV
959	Anti-FGFR2 VH	EVQLLESGGGLVQPGGSLRLSCAASGFTFSSYAMSWVRQAPGKGLEWVSAISGSGTSTYY ADSVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARVRYNWNHGDWFDPWGQGTLVTV SS
960	Anti-FGFR2 VL	QSVLTQPPSASGTPGQRVTISCSGSSSNIGNNYVSWYQQLPGTAPKLLIYENYNRPAGVP DRFSGSKSGTSASLAISGLRSEDEADYYCSSWDDSLNYWVFGGGTKLTVL

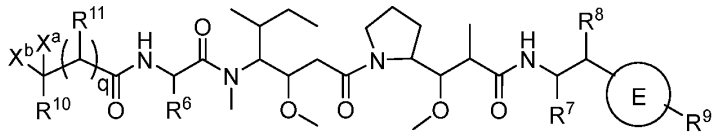
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964	Anti-CDCP1 CDR-L1	SVSSSVFYVH
965	Anti-CDCP1 CDR-L2	DTSKLAS
966	Anti-CDCP1 CDR-L3	QQWNSNPPT
967	Anti-CDCP1 VH	EVQLVESGGGLVQPGGSLRLSCAASGFTFNSYGMSWVRQAPGKGLEWVATISSGGSYKYY VDSVKGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCARHPDYDGVWFAYWGQGTLVTVSS
968	Anti-CDCP1 VL	DIQMTQSPSSLSASVGDRVTITCSVSSSVFYVHWYQQKPGKAPKLLIYDTSKLASGVPSR FSGSGSGTDFTFTISSLQPEDIATYYCQQWNSNPPTFGGGTKVEIK
969	Anti-CDCP1 CDR-H1	SYGMS
970	Anti-CDCP1 CDR-H2	TISSGGSYTYYPDSVKG
971	Anti-CDCP1 CDR-H3	HPDYDGVWFAY
972	Anti-CDCP1 CDR-L1	SVSSSVFYVH
973	Anti-CDCP1 CDR-L2	DTSKLAS
974	Anti-CDCP1 CDR-L3	QQWNSNPPT
975	Anti-CDCP1 VH	EVQLVESGGDLVKPGGSLKLSCAASGFTFNSYGMSWVRQTPDKRLEWVATISSGGSYTYY PDSVKGRFTISRDNAKNTLYLQMSSLKSEDTAMYYCARHPDYDGVWFAYWGQGTLVTVSA
976	Anti-CDCP1 VL	QIVLTQSPAIMSASPGEKVTMTCSVSSSVFYVHWYQQKSGTSPKRWIYDTSKLASGVPAR FSGSGSGTSYSLTISSMEAEDAATYYCQQWNSNPPTFGGGTKLEIK
977	Anti-CDCP1 CDR-H1	SYYMH
978	Anti-CDCP1 CDR-H2	IINPSGGSTSYAQKFQG
979	Anti-CDCP1 CDR-H3	DGVLRYFDWLLDYYYYMDV
980	Anti-CDCP1 CDR-L1	RASQSVGSYLA
981	Anti-CDCP1 CDR-L2	DASNRAT
982	Anti-CDCP1 CDR-L3	QQRANVFT
983	Anti-CDCP1 VH	EVQLVQSGAEVKKPGASVKVSCKASGYTFTSYYMHWVRQAPGQGLEWMGIINPSGGSTSY AQKFQGRVTMTRDTSTSTVYMELSSLRSEDTAVYYCARDGVLRYFDWLLDYYYYMDVWGK GTTVTVSS
984	Anti-CDCP1 VL	EIVLTQSPATLSLSPGERATLSCRASQSVGSYLAWYQQRPGQAPRLLIYDASNRATGIPA RFSGSGSGTDFTLTISSLEPEDFAVYYCQQRANVFTFGQGTKVEIK
985	Anti-CDCP1 CDR-H1	SYYMH
986	Anti-CDCP1 CDR-H2	IINPSGGSTSYAQKFQG
987	Anti-CDCP1 CDR-H3	DAELRHFDHLLDYHYYMDV
988	Anti-CDCP1 CDR-L1	RASQSVGSYLA
989	Anti-CDCP1 CDR-L2	DASNRAT
990	Anti-CDCP1	QQRAQEFT

	CDR-L3	
991	Anti-CDCP1 VH	EVQLVQSGAEVKKPGASVKVSCKASGYTFTSYYMHWVRQAPGQGLEWMGIINPSGGSTSY AQKFQGRVTMTRDTSTSTVYMELSSLRSEDTAVYYCARDAELRHFDHLLDYHYYMDVWGQ GTTVTVSS
992	Anti-CDCP1 VL	EIVMTQSPATLSLSPGERATLSCRASQSVGSYLAWYQQKPGQAPRLLIYDASNRATGIPA RFSGSGSGTDFTLTISSLQPEDFAVYYCQQRAQEFTFGQGTKVEIK
993	Anti-ASCT2 VH	QVQLVQSGSELKKPGAPVKVSCKASGYTFSTFGMSWVRQAPGQGLKWMGWIHTYAGVPIY GDDFKGRFVFSLDTSVSTAYLQISSLKAEDTAVYFCARRSDNYRYFFDYWGQGTTVTVSS
994	Anti-ASCT2 VL	DIQMTQSPSSLSASLGDRVTITCRASQDIRNYLNWYQQKPGKAPKLLIYYTSRLHSGVPS RFSGSGSGTDYTLTISSLQPEDFATYFCQQGHTLPPTFGQGTKLEIK
995	Anti-ASCT2 VH	QIQLVQSGPELKKPGAPVKISCKASGYTFTTFGMSWVKQAPGQGLKWMGWIHTYAGVPIY GDDFKGRFVFSLDTSVSTAYLQISSVKAEDTATYFCARRSDNYRYFFDYWGQGTTLTVSS
996	Anti-ASCT2 VL	DIQMTQSPSSLSASLGDRVTITCRASQDIRNYLNWYQQKPGKAPKLLIYYTSRLHSGVPS RFSGSGSGTDYTLTISSLQPEDFATYFCQQGHTLPPTFGQGTKLEIK
997	Anti-ASCT2 CDR-H1	NYYMA
998	Anti-ASCT2 CDR-H2	SITKGGGNTYYRDSVKG
999	Anti-ASCT2 CDR-H3	QVTIAAVSTSYFDS
1000	Anti-ASCT2 CDR-L1	KTNQKVDYYGNSYVY
1001	Anti-ASCT2 CDR-L2	LASNLAS
1002	Anti-ASCT2 CDR-L3	QQSRNLPYT
1003	Anti-ASCT2 VH	EVQLVESGGGLVQSGRSIRLSCAASGFSFSNYYMAWVRQAPSKGLEWVASITKGGGNTYY RDSVKGRFTFSRDNAKSTLYLQMDSLRSEDTATYYCARQVTIAAVSTSYFDSWGQGVMVT VSS
1004	Anti-ASCT2 VL	DIVLTQSPALAVSLGQRATISCKTNQKVDYYGNSYVYWYQQKPGQQPKLLIYLASNLASG IPARFSGRGSGTDFTLTIDPVEADDTATYYCQQSRNLPYTFGAGTKLELK
1005	Anti-CD123 CDR-H1	DYYMK
1006	Anti-CD123 CDR-H2	DIIPSNGATFYNQKFKG
1007	Anti-CD123 CDR-H3	SHLLRASWFAY
1008	Anti-CD123 CDR-L1	KSSQSLLNSGNQKNYLT
1009	Anti-CD123 CDR-L2	WASTRES
1010	Anti-CD123 CDR-L3	QNDYSYPYT
1011	Anti-CD123 VH	QVQLVQSGAEVKKPGASVKMSCKASGYTFTDYYMKWVKQAPGQGLEWIGDIIPSNGATFY NQKFKGKATLTVDRSISTAYMHLNRLRSDDTAVYYCTRSHLLRASWFAYWGQGTLVTVSS
1012	Anti-CD123 VL	DFVMTQSPDSLAVSLGERATINCKSSQSLLNSGNQKNYLTWYLQKPGQPPKLLIYWASTR ESGVPDRFSGSGSGTDFTLTISSLQAEDVAVYYCQNDYSYPYTFGQGTKLEIK
1013	Anti-GPC3 CDR-H1	DYEMH
1014	Anti-GPC3 CDR-H2	GIDPETGGTAYNQKFKG
1015	Anti-GPC3 CDR-H3	YYSFAY
1016	Anti-GPC3 CDR-L1	RSSQSIVHSNANTYLQ
1017	Anti-GPC3 CDR-L2	KVSNRFS
1018	Anti-GPC3 CDR-L3	FQVSHVPYT
1019	Anti-GPC3	EVQLVQSGAEVKKPGATVKISCKVSGYTFTDYEMHWVQQAPGKGLEWMGGIDPETGGTAY

	VH	NQKFKGRVTLTADKSTDTAYMELSSLRSEDTAVYYCGRYYSFAYWGQGTLVTVSS
1020	Anti-GPC3 VL	DVVMTQSPLSLPVTLGQPASISCRSSQSIVHSNANTYLQWFQQRPGQSPRLLIYKVSNRF SGVPDRFSGSGSGTDFTLKISRVEAEDVGVYYCFQVSHVPYTFGQGTKLEIK
1021	Anti-TIGIT CDR-H1	SYAIS
1022	Anti-TIGIT CDR-H2	SIIPIFGTANYAQKFQG
1023	Anti-TIGIT CDR-H3	GPSEVGAILGYVWFDP
1024	Anti-TIGIT CDR-L1	RSSQSLLHSNGYNYLD
1025	Anti-TIGIT CDR-L2	LGSNRAS
1026	Anti-TIGIT CDR-L3	MQARRIPIT
1027	Anti-TIGIT VH	QVQLVQSGAEVKKPGSSVKVSCKASGGTFSSYAISWVRQAPGQGLEWMGSIIPIFGTANY AQKFQGRVTITADESTSTAYMELSSLRSEDTAVYYCARGPSEVGAILGYVWFDPWGQGTL VTVSS
1028	Anti-TIGIT VL	DIVMTQSPLSLPVTPGEPASISCRSSQSLLHSNGYNYLDWYLQKPGQSPQLLIYLGSNRA SGVPDRFSGSGSGTDFTLKISRVEAEDVGVYYCMQARRIPITFGGGTKVEIK
1029	Anti-CD33 CDR-H1	NYDIN
1030	Anti-CD33 CDR-H2	WIYPGDGSTKYNEKFKA
1031	Anti-CD33 CDR-H3	GYEDAMDY
1032	Anti-CD33 CDR-L1	KASQDINSYLS
1033	Anti-CD33 CDR-L2	RANRLVD
1034	Anti-CD33 CDR-L3	LQYDEFPLT
1035	Anti-CD33 VH	QVQLVQSGAE VKKPGASVKV SCKASGYTFT NYDINWVRQA PGQGLEWIGW IYPGDGSTKY NEKFKAKATL TADTSTSTAY MELRSLRSDD TAVYYCASGY EDAMDYWGQG TTVTVSS
1036	Anti-CD33 VL	DIQMTQSPSSLSASVGDRVTINCKASQDINSYLSWFQQKPGKAPKTLIYRANRVDGVPSR FSGSGSGQDYTLT ISSLQPEDFATYYCLQYDEFPLTFGGGTKVEIK
1037	Anti-BCMA CDR-H1	DYYIH
1038	Anti-BCMA CDR-H2	YINPNSGYTNYAQKFQG
1039	Anti-BCMA CDR-H3	YMWERVTGFFDF
1040	Anti-BCMA CDR-L1	LASEDISDDLA
1041	Anti-BCMA CDR-L2	TTSSLQS
1042	Anti-BCMA CDR-L3	QQTYKFPPT
1043	Anti-BCMA VH	QVQLVQSGAEVKKPGASVKLSCKASGYTFTDYYIHWVRQAPGQGLEWIGYINPNSGYTNY AQKFQGRATMTADKSINTAYVELSRLRSDDTAVYFCTRYMWERVTGFFDFWGQGTMVTVS S
1044	Anti-BCMA VL	DIQMTQSPSSVSASVGDRVTITCLASEDISDDLAWYQQKPGKAPKVLVYTTSSLQSGVPS RFSGSGSGTDFTLTISSLQPEDFATYFCQQTYKFPPTFGGGTKVEIK

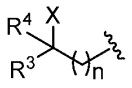
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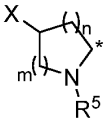
1. A compound of Formula (I):



(I)

or a salt thereof, wherein

X^b is $-NR^1R^2$; and X^a is  ; or

X^a and X^b are taken together with the carbon atom to which they are attached to form  , wherein the asterisk denotes the carbon atom of Formula (I) that bears the X^a and X^b groups;

R^1, R^2, R^3, R^4, R^a, R^b, R^5, and R^{10} are each independently H or C_1-C_4 alkyl;

X is H, OH, $-C(O)NR^aR^b$, $-S(O)_2R^a$, $-S(O)-R^a$ $-S(O)_2NR^aR^b$, $-NHS(O)_2R^a$, or $-NHC(O)R^a$;

R^6 is C_1-C_4 alkyl optionally substituted with OH;

R^7 is H, C_1-C_4 alkyl optionally substituted with one or two OH moieties, or 5-6 membered heteroaryl;

E is phenyl or 5-6 membered heteroaryl;

R^8, R^9, and R^{11} are each independently H or OH;

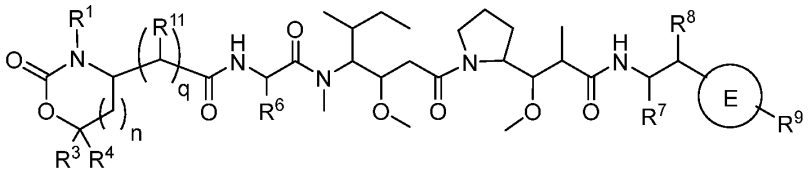
n is 0, 1, 2, or 3;

m is 1, 2, 3, or 4; and

q is 0 or 1,

wherein when X is H, at least two of R^7, R^8, R^9, and R^{11} comprise an OH moiety.

2. A compound of Formula (II):



(II)

or a salt thereof, wherein

R^1, R^3, and R^4 are independently H or C_1-C_4 alkyl;

R^6 is C_1-C_4 alkyl optionally substituted with OH;

R^7 is H, C_1-C_4 alkyl optionally substituted with one or two OH moieties, or 5-6 membered heteroaryl;

E is phenyl or 5-6 membered heteroaryl;

R^8, R^9, and R^{11} are each independently H or OH;

n is 0, 1, or 2; and

q is 0 or 1.

3. The compound of claim 1 or 2, wherein q is 0.

4. The compound of claim 1 or 2, wherein q is 1.

5. The compound of claim 1, or a salt thereof, wherein

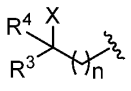
X is OH.

6. The compound of claim 1, or a salt thereof, wherein

X is $-C(O)NR^aR^b$, $-S(O)_2R^a$, $-S(O)-R^a$ $-S(O)_2NR^aR^b$, $-NHS(O)_2R^a$, or $-NHC(O)R^a$.

7. The compound of any one of claims 1 or 3-6, or a salt thereof, wherein

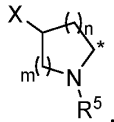
X^b is $-NR^1R^2$; and

X^a is .

8. The compound of any one of claims 1-7, or a salt thereof, wherein R^3 is H.

9. The compound of any one of claims 1-8, or a salt thereof, wherein R^4 is H.

10. The compound of any one of claims 1-9, or a salt thereof, wherein n is 0 or 1.

11. The compound of any one of claims 1 or 3-6, or a salt thereof, wherein X^a and X^b are taken together with the carbon atom to which they are attached to form , wherein the asterisk denotes the carbon atom of Formula (I) that bears the X^a and X^b groups.

12. The compound of any one of claims 1 or 3-11, wherein m is 1 or 2.

13. The compound of any one of claims 1-10, or a salt thereof, wherein R^1 is H.

14. The compound of any one of claims 1-10, or a salt thereof, wherein R^1 is C_1-C_4 alkyl.

15. The compound of any one of claims 1-10 or 14, or a salt thereof, wherein R^1 is methyl.

16. The compound of any one of claims 1, 3-10, or 13-15, or a salt thereof, wherein R^2 is methyl.

17. The compound of any one of claims 1-16, or a salt thereof, wherein R^{10} is H.

18. The compound of any one of claims 1-16, or a salt thereof, wherein R^{10} is methyl.

19. The compound of any one of claims 1-18, or a salt thereof, wherein R^6 is unsubstituted C_1-C_4 alkyl.

20. The compound of any one of claims 1-19, or a salt thereof, wherein R^6 is isopropyl.

21. The compound of any one of claims 1-18, or a salt thereof, wherein R^6 is C_1-C_4 alkyl substituted with OH.

22. The compound of any one of claims 1-21, or a salt thereof, wherein R^7 C_1-C_4 alkyl substituted with OH.

23. The compound of any one of claims 1-22, or a salt thereof, wherein R^7 is $-CH_2OH$.

24. The compound of any one of claims 1-21, or a salt thereof, wherein R^7 is H.

25. The compound of any one of claims 1-21, or a salt thereof, wherein R^7 is unsubstituted C_1-C_4 alkyl.

26. The compound of any one of claims 1-21 or 25, or a salt thereof, wherein R^7 is methyl.

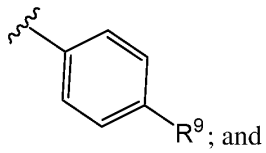
27. The compound of any one of claims 1-21, or a salt thereof, wherein R^7 is 5-6 membered heteroaryl.

28. The compound of any one of claims 1-27, or a salt thereof, wherein R^8 is H.

29. The compound of any one of claims 1-28, or a salt thereof, wherein R^8 is OH.

30. The compound of any one of claims 1-29, or a salt thereof, wherein E is phenyl.

31. The compound of any one of claims 1-30, or a salt thereof, wherein E-R^9 is



; and

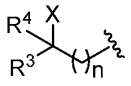
the wavy line indicates the point of attachment of E to the rest of the compound.

32. The compound of any one of claims 1-29, or a salt thereof, wherein E is 5-6 membered heteroaryl.

33. The compound of any one of claims 1-32, or a salt thereof, wherein R^9 is H.

34. The compound of any one of claims 1-33, or a salt thereof, wherein R^9 is OH.

35. The compound of claim 1, or a salt thereof, wherein

X^a is ;

X^b is $-NR^1R^2$;

R^1 is H or methyl;

R^2 is methyl;

X is OH;

R^3 and R^4 are H;

R^6 is isopropyl;

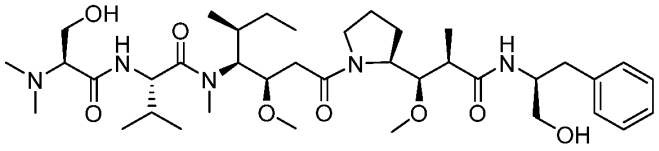
R^7 is $-CH_2OH$;

R^8 is H;

E is phenyl; and

R^9 is H.

36. The compound of claim 1, wherein the compound is

 or a salt thereof.

37. A Drug-Linker compound of the following formula:

Q-D,

or a salt thereof, wherein

Q is a Linker Unit selected from the group consisting of:

(i) Z'-A-RL-,

(ii) Z'-A-RL-Y-,

(iii) Z'-A-S^*-RL-,

(iv) Z'-A-S*-RL-Y-,

(v) Z'-A-B(S*)-RL-,

(vi) Z'-A-B(S*)-RL-Y-,

(vii) Z'-A-,

(viii) Z'-A-S*-W-,

(ix) Z'-A-B(S*)-W-,

(x) Z'-A-S*-W-RL-, and

(xi) Z'-A-B(S*)-W-RL-;

Z' is a Stretcher Unit precursor;

A is a bond or a Connector Unit;

B is a Parallel Connector Unit;

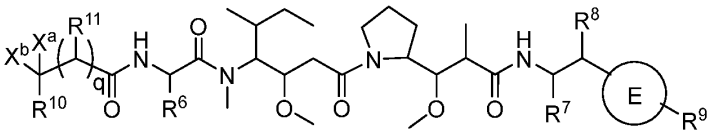
S* is a Partitioning Agent;

RL is a Releasable Linker;

W is an Amino Acid Unit;

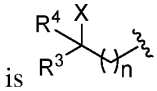
Y is a Spacer Unit; and

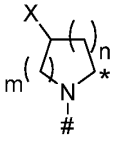
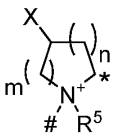
D is a Drug Unit of Formula (I'):



(I')

wherein

X^b is $-NR^2-^{\#}$ or $-N^+R^1R^5-^{\#}$, wherein the # denotes the point of attachment to Q, and X^a is  ; or

X^a and X^b are taken together with the carbon atom to which they are attached to form  or  , wherein the asterisk denotes the carbon atom of Formula (I) that bears the X^a and X^b groups, and the # denotes the point of attachment to Q;

R^1 and R^5 are independently C_1-C_4 alkyl;

X is H, OH, $-C(O)NR^aR^b$, $-S(O)_2R^a$, $-S(O)-R^a$ $-S(O)_2NR^aR^b$, $-NHS(O)_2R^a$, or $-NHC(O)R^a$;

R^2, R^3, R^4, R^{10}, R^a, and R^b are each independently H or C_1-C_4 alkyl;

R^6 is C_1-C_4 alkyl optionally substituted with OH;

R^7 is H, C_1-C_4 alkyl optionally substituted with one or two OH moieties, or 5-6 membered heteroaryl;

E is phenyl or 5-6 membered heteroaryl;

R^8, R^9, and R^{11} are each independently H or OH;

n is 0, 1, 2, or 3;

m is 1, 2, 3, or 4;

q is 0 or 1; and

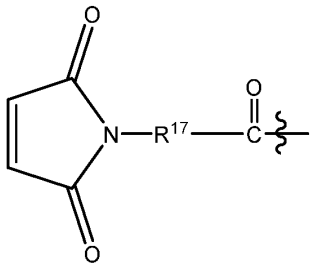
wherein when X is H, at least two of R^7, R^8, R^9, and R^{11} comprise an OH moiety.

38. The Drug-Linker compound of claim 37, or a salt thereof, wherein the Linker Unit Q is of formula (i), (ii), (iii), (iv), (x), or (xi).

39. The Drug-Linker compound of claim 37, or a salt thereof, wherein the Linker Unit Q is of formula (v), (vi), (ix), or (xi).

40. The Drug-Linker compound of claim 37, or a salt thereof, wherein the Linker Unit Q is of formula (viii), (ix), (x), or (xi).

41. The Drug-Linker compound of any one of claims 37-40, or a salt thereof, wherein the Stretcher Unit Z' is



wherein

R^{17} is $–CH_2CH_2(OCH_2CH_2)_k–$, -C_1-C_{10} alkylene-, C_1-C_{10} heteroalkylene-, -C_3-C_8 carbocyclo-, -O-(C_1-C_8 alkylene)-, -arylene-, -C_1-C_{10} alkylene-arylene-, -arylene-C_1-C_{10} alkylene-, -C_1-C_{10} alkylene-(C_3-C_8 carbocyclo)-, -(C_3-C_8 carbocyclo)-C_1-C_{10} alkylene-, -C_3-C_8 heterocyclo-, -C_1-C_{10} alkylene-(C_3-C_8 heterocyclo)-, -(C_3-C_8 heterocyclo)-C_1-C_{10} alkylene-, -C_1-C_{10} alkylene-C(=O)-, C_1-C_{10} heteroalkylene-C(=O)-, -C_3-C_8 carbocyclo-C(=O)-, -O-(C_1-C_8 alkylene)-C(=O)-, -arylene-C(=O)-, -C_1-C_{10} alkylene-arylene-C(=O)-, -arylene-C_1-C_{10}

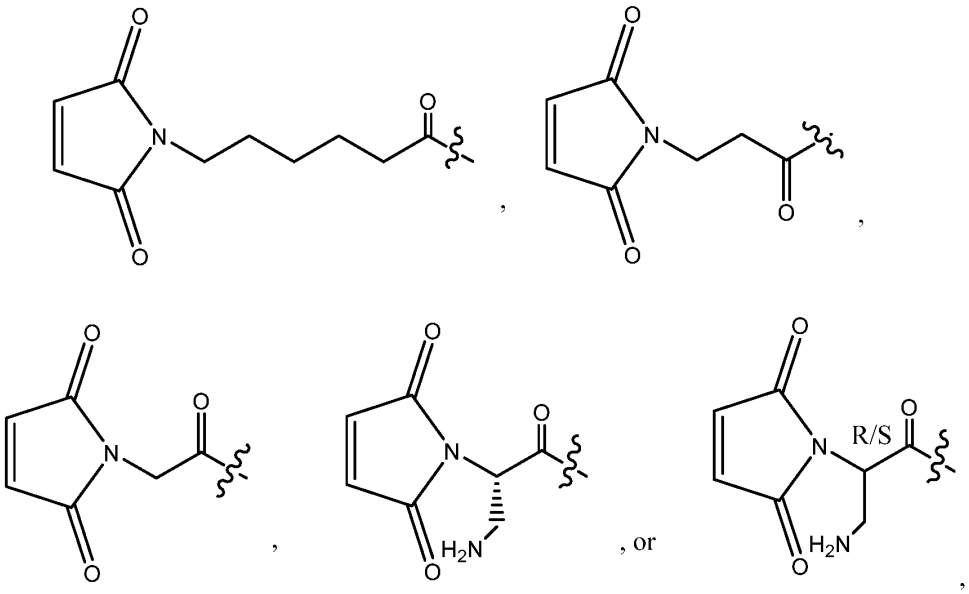
alkylene-C(=O)-, -C_1-C_{10} alkylene-(C_3-C_8 carbocyclo)-C(=O)-,-(C_3-C_8 carbocyclo)-C_1-C_{10} alkylene-C(=O)-, -C_3-C_8 heterocyclo-C(=O)-, -C_1-C_{10} alkylene-(C_3-C_8 heterocyclo)-C(=O)-, -(C_3-C_8 heterocyclo)-C_1-C_{10} alkylene-C(=O)-, -C_1-C_{10} alkylene-NH-, C_1-C_{10} heteroalkylene-NH-, -C_3-C_8 carbocyclo-NH-, -O-(C_1-C_8 alkylene)-NH-, -arylene-NH-, -C_1-C_{10} alkylene-arylene-NH-, -arylene-C_1-C_{10} alkylene-NH-, -C_1-C_{10} alkylene-(C_3-C_8 carbocyclo)-NH-, -(C_3-C_8 carbocyclo)-C_1-C_{10} alkylene-NH-, -C_3-C_8 heterocyclo-NH-, -C_1-C_{10} alkylene-(C_3-C_8 heterocyclo)-NH-, -(C_3-C_8 heterocyclo)-C_1-C_{10} alkylene-NH-, -C_1-C_{10} alkylene-S-, C_1-C_{10} heteroalkylene-S -, -C_3-C_8 carbocyclo-S -, -O-(C_1-C_8 alkylene)-S -, -arylene-S-, -C_1-C_{10} alkylene-arylene-S-, -arylene-C_1-C_{10} alkylene-S-, -C_1-C_{10} alkylene-(C_3-C_8 carbocyclo)-S-, -(C_3-C_8 carbocyclo)-C_1-C_{10} alkylene-S-, -C_3-C_8 heterocyclo-S-, -C_1-C_{10} alkylene-(C_3-C_8 heterocyclo)-S-, or -(C_3-C_8 heterocyclo)-C_1-C_{10} alkylene-S-;

subscript k is an integer ranging from 1 to 36;

R^{17} is optionally substituted by a Basic Unit (BU) such as an aminoalkyl moiety, e.g. $–(CH_2)_xNH_2$, $–(CH_2)_xNHR^a$, and $–(CH_2)_xNR^a{}_2$, wherein x is an integer of from 1-4 and each R^a is independently selected from the group consisting of C_{1-6} alkyl and C_{1-6} haloalkyl, or two R^a groups are combined with the nitrogen to which they are attached to form an azetidinyl, pyrrolidinyl or piperidinyl group; and

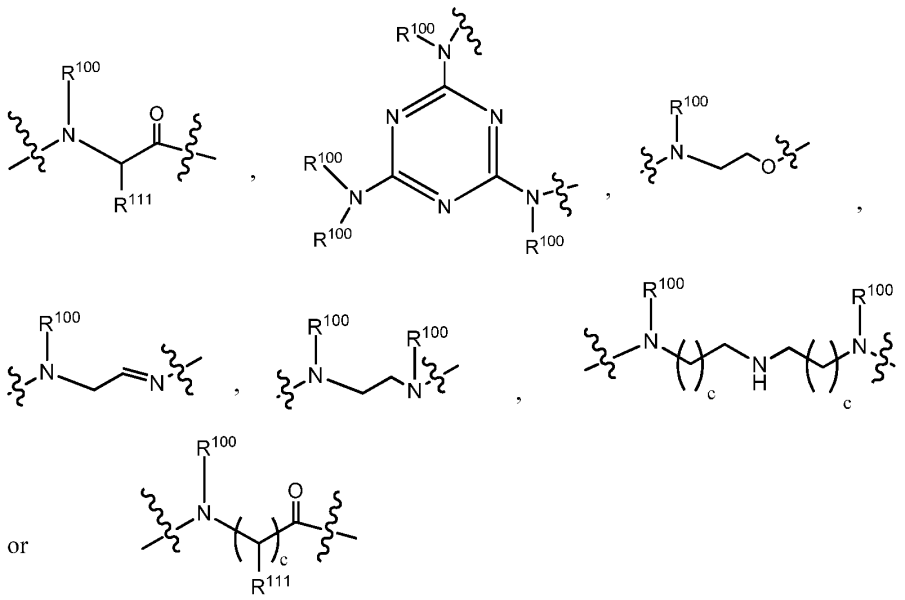
the wavy line indicates the point of covalent attachment to the rest of the Drug-Linker compound.

42. The Drug-Linker of any one of claims 37-41, or a salt thereof, wherein the Stretcher Unit Z' is



wherein the wavy lines indicate the point of covalent attachment to the rest of the Drug-Linker compound.

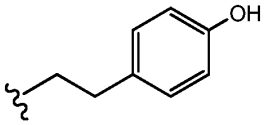
43. The Drug-Linker compound of any one of claims 37-42, or a salt thereof, wherein the Connector Unit A is



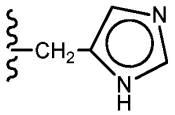
wherein

each R^{100} is independently selected from hydrogen or -C_1-C_3 alkyl;

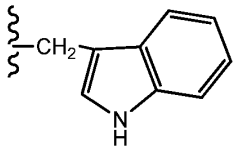
R^{111} is independently selected from the group consisting of hydrogen, *p*-hydroxybenzyl, methyl, isopropyl, isobutyl, *sec*-butyl, $-CH_2OH$, $-CH(OH)CH_3$, $-CH_2CH_2SCH_3$, $-CH_2CONH_2$, $-CH_2COOH$, $-CH_2CH_2CONH_2$, $-CH_2CH_2COOH$, $-(CH_2)_3NHC(=NH)NH_2$, $-(CH_2)_3NH_2$, $-(CH_2)_3NHCOCH_3$, $-(CH_2)_3NHCHO$, $-(CH_2)_4NHC(=NH)NH_2$, $-(CH_2)_4NH_2$, $-(CH_2)_4NHCOCH_3$, $-(CH_2)_4NHCHO$, $-(CH_2)_3NHCONH_2$, $-(CH_2)_4NHCONH_2$, $-CH_2CH_2CH(OH)CH_2NH_2$, 2-pyridylmethyl-, 3-pyridylmethyl-, 4-pyridylmethyl-,



,



, and

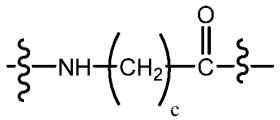


;

each subscript c is an independently selected integer from 1 to 10; and

the wavy lines indicate attachment of the Connector Unit to the rest of the Drug-Linker compound.

44. The Drug-Linker compound of any one of claims 37-43, or a salt thereof, wherein the Connector Unit A is



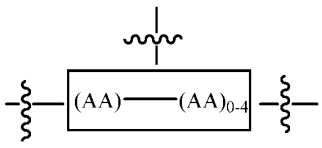
;

c is an integer ranging from 1 to 6; and

the wavy lines indicate the site of attachment to the rest of the Drug-Linker compound or salt thereof.

45. The Drug-Linker compound of any one of claims 37-42, or a salt thereof, wherein A is a bond.

46. The Drug-Linker compound of claims 37-45, or a salt thereof, wherein B is



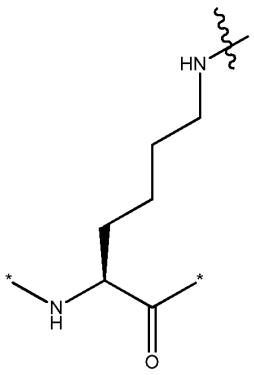
;

each AA is independently a proteinogenic or non-proteinogenic amino acid; and

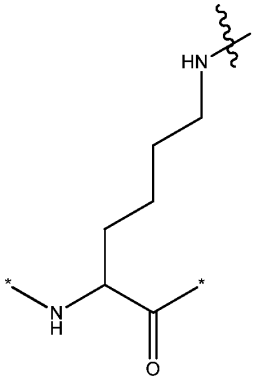
the wavy lines indicate points of attachment to the rest of the Drug-Linker compound or salt thereof.

47. The Drug-Linker compound of any one of claims 37-46, or a salt thereof, wherein B is an amino acid.

48. The Drug-Linker compound of any one of claims 37-47, or a salt thereof, wherein B is



or



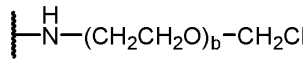
;

the wavy line indicates the point of attachement to the Partitioning Agent S*; and the asterisks indicate points of attachment to the rest of the Drug-Linker structure.

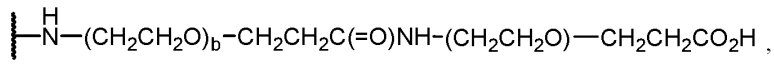
49. The Drug-Linker compound of any one of claims 37-48, or a salt thereof, wherein the Partitioning Agent S^* is a polyethylene glycol (PEG) unit, cyclodextrin unit, polyamide, hydrophilic peptide, polysaccharide, or dendrimer.

50. The Drug-Linker compound of any one of claims 37-49, or a salt thereof, wherein the Partitioning Agent S^* is a PEG Unit comprising from 4 to 72 (CH_2CH_2O) subunits.

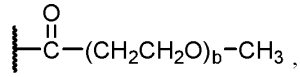
51. The Drug Linker of any one of claims 37-50, or a salt thereof, wherein the PEG Unit is



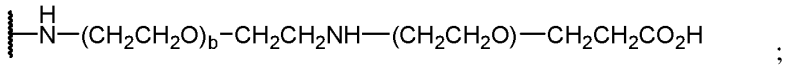
,



,



, or



;

b is selected from the group consisting of 4 to 36; and

the wavy lines indicate the site of attachment to the rest of the Drug-Linker compound or salt thereof.

52. The Drug-Linker compound of any one of claims 37-51, or a salt thereof, wherein the Releasable Linker RL is

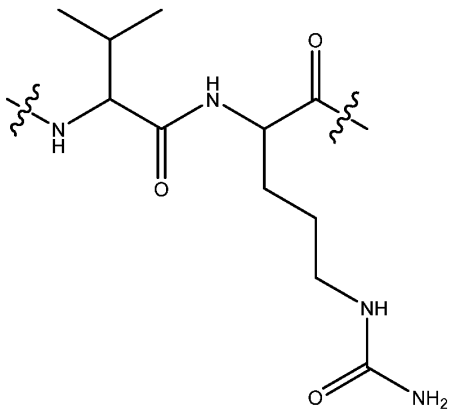
$-(AA)_{1-12}-$; and

each AA is independently a proteinogenic or non-proteinogenic amino acid.

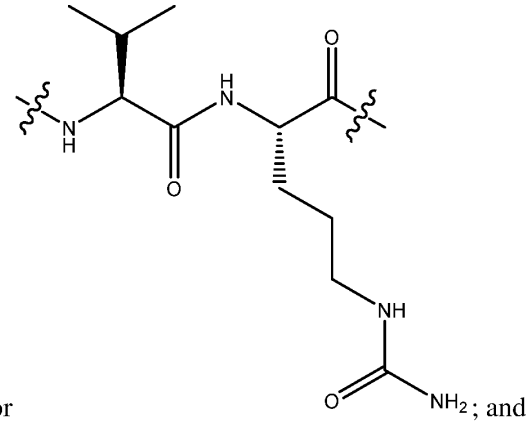
53. The Drug-Linker compound of any one of claims 37-52, or a salt thereof, wherein the Releasable Linker RL is

$-AA_1\text{-}AA_2-$ or $-AA_1\text{-}AA_2\text{-}AA_3-$, wherein AA_1 is attached to the Stretcher Unit Z' or the Connector Unit A.

54. The Drug-Linker compound of any one of claims 37-53, or a salt thereof, wherein the Releasable Linker RL is



or

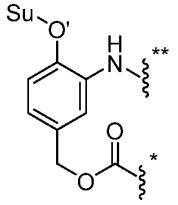


; and

the wavy line adjacent to the -NH- group indicates attachment to the Stretcher Unit Z' or the Connector Unit A and the wavy line adjacent to the -C(=O)- group indicates attachment to the Spacer Unit Y or the Drug Unit D.

55. The Drug-Linker compound of any one of claims 37-54, or a salt thereof, wherein the Releasable Linker RL is a glycoside.

56. The Drug-Linker compound of any one of claims 37-55, or a salt thereof, wherein the Releasable Linker RL is



wherein

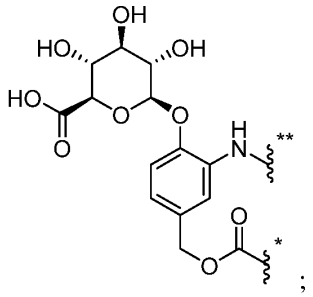
Su is a hexose form a monosaccharide;

O' represents the oxygen atom of a glycosidic bond that is capable of cleavage by a glycosidase;

the wavy line marked with a single asterisk (*) indicates the site of covalent attachment to D; and

the wavy line marked with a double asterisk (**) indicates the site of covalent attachment to the remainder of Q.

57. The Drug-Linker compound of any one of claims 37-56, or a salt thereof, wherein the Releasable Linker RL is

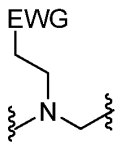


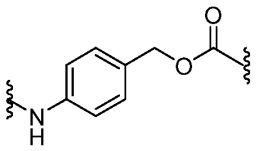
;

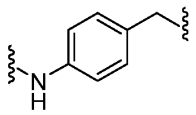
the wavy line marked with a single asterisk (*) indicates the site of covalent attachment to D; and

the wavy line marked with a double asterisk (**) indicates the site of covalent attachment to the remainder of Q.

58. The Drug-Linker compound of any one of claims 37-39 or 41-57, or a salt thereof, wherein the Spacer Unit Y is



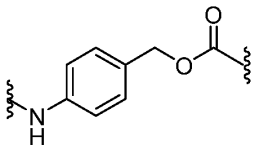
, 

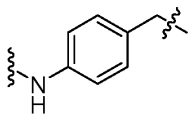
, or 

wherein EWG is an electron-withdrawing group; and

the wavy lines indicate the site of attachment to the rest of the Drug-Linker compound or salt thereof.

59. The Drug-Linker compound of any one of claims 37-39 or 41-58, or a salt thereof, wherein the Spacer Unit Y is

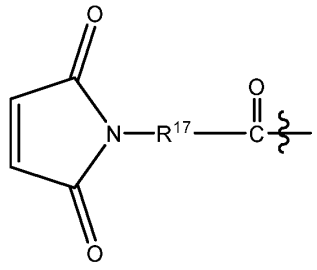


or 

; and

the wavy lines indicate the site of attachment to the rest of the Drug-Linker compound or salt thereof.

60. The Drug-Linker compound of any one of claims 37, 41-42, 45-48, 52-54, or 58-59, or a salt thereof, wherein

Z' is 

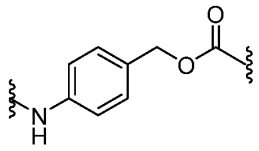
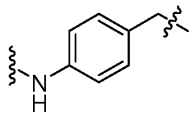
;

R^{17} is C_1-C_{10} alkylene;

A is a bond;

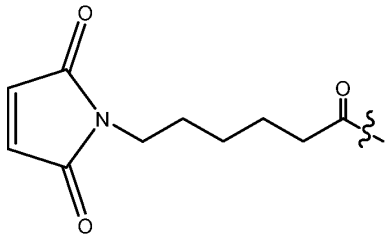
RL is $–AA_1$-$AA_2–$;

AA_1 and AA_2 are each independently a proteinogenic amino acid;

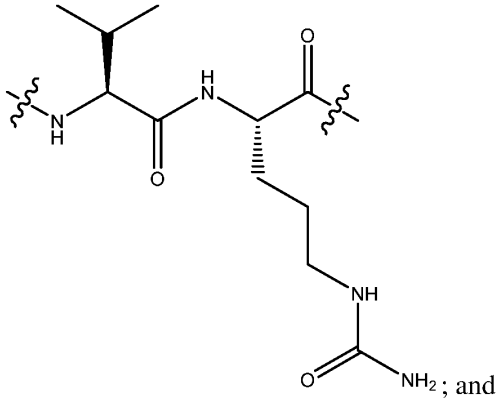
Y is  or  ; and

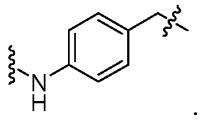
the wavy lines indicate the site of attachment to the rest of the Drug-Linker compound or salt thereof.

61. The Drug-Linker compound of any one of claims 37, 41-42, 45-48, 52-54, or 58-60, or a salt thereof, wherein

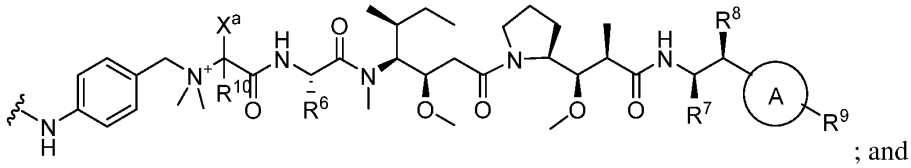
Z' is  ;

A is a bond;

RL is  ; and

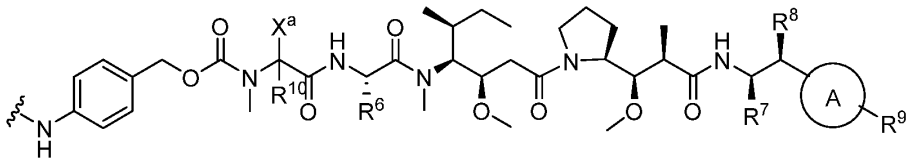
Y is  .

62. The Drug-Linker compound of any one of claims 37-38 or 41-61, wherein Y-D is

 ; and

the wavy line indicates the site of attachment to the rest of the Drug-Linker compound or salt thereof.

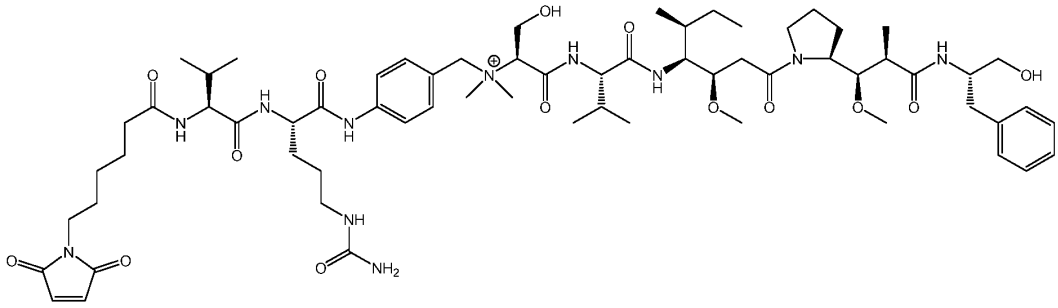
63. The Drug-Linker compound of any one of claims 37-38 or 41-61, wherein Y-D is



; and

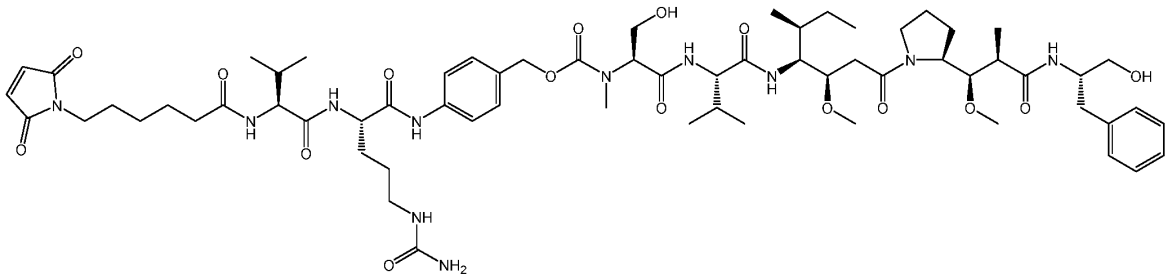
the wavy line indicates the site of attachment to the rest of the Drug-Linker compound or salt thereof.

64. The Drug-Linker compound of any one of claims 37, 41-42, 45-48, 52-54, 58-61, or 62, wherein the compound is

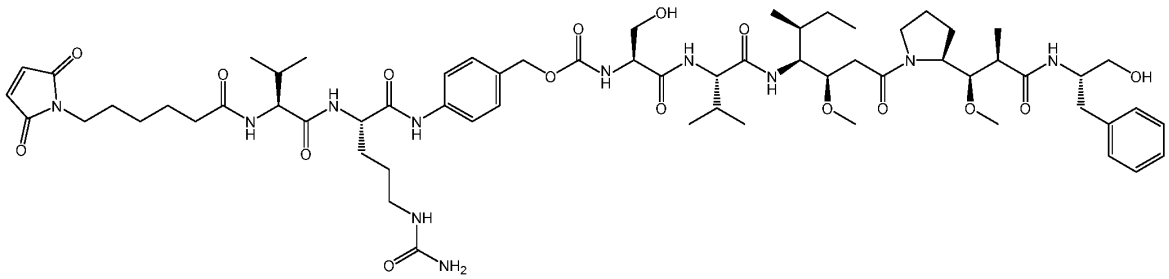


or a salt thereof.

65. The Drug-Linker compound of any one of claims 37, 41-42, 45-48, 52-54, 58-61, or 63, wherein the compound is



or



or a salt thereof.

66. A Ligand-Drug Conjugate compound of the formula:

$$L\text{-}(Q\text{-}D)_p$$

or a pharmaceutically acceptable salt thereof, wherein

L is a Ligand Unit;

Q is a Linker Unit selected from the group consisting of:

(i) Z'-A-RL-,

(ii) Z'-A-RL-Y-,

(iii) Z'-A-S*-RL-,

(iv) Z'-A-S*-RL-Y-,

(v) Z'-A-B(S*)-RL-,

(vi) Z'-A-B(S*)-RL-Y-,

(vii) Z'-A-,

(viii) Z'-A-S*-W-,

(ix) Z'-A-B(S*)-W-,

(x) Z'-A-S*-W-RL-, and

(xi) Z'-A-B(S*)-W-RL-;

Z' is a Stretcher Unit;

A is a bond or a Connector Unit;

B is a Parallel Connector Unit;

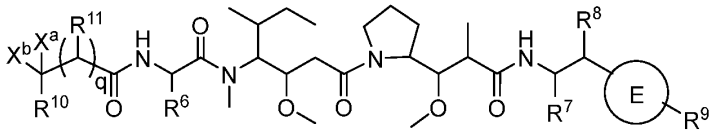
S^* is a Partitioning Agent;

RL is a Releasable Linker;

W is a Amino Acid Unit;

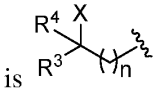
Y is a Spacer Unit; and

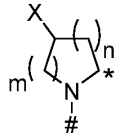
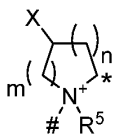
D is a Drug Unit of Formula (I'):



(I')

wherein

X^b is $-NR^2-^{\#}$ or $-N^+R^1R^5-^{\#}$, wherein the # denotes the point of attachment to Q, and X^a is  ; or

X^a and X^b are taken together with the carbon atom to which they are attached to form  or  , wherein the asterisk denotes the carbon atom of Formula (I) that bears the X^a and X^b groups, and the # denotes the point of attachment to Q;

R^1 and R^5 are independently C_1-C_4 alkyl;

X is H, OH, $-C(O)NR^aR^b$, $-S(O)_2R^a$, $-S(O)-R^a$ $-S(O)_2NR^aR^b$, $-NHS(O)_2R^a$, or $-NHC(O)R^a$;

R^2, R^3, R^4, R^{10}, R^a, and R^b are each independently H or C_1-C_4 alkyl;

R^6 is C_1-C_4 alkyl optionally substituted with OH;

R^7 is H, C_1-C_4 alkyl optionally substituted with one or two OH moieties, or 5-6 membered heteroaryl;

E is phenyl or 5-6 membered heteroaryl;

R^8, R^9, and R^{11} are each independently H or OH;

n is 0, 1, 2, or 3;

m is 1, 2, 3, or 4;

q is 0 or 1;

p is an integer ranging from 1 to 12; and

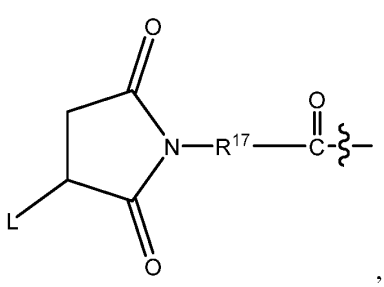
wherein when X is H, at least two of R^7, R^8, R^9, and R^{11} comprise an OH moiety.

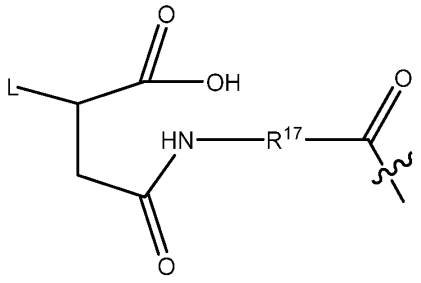
67. The Ligand-Drug Conjugate compound of claim 66, or a pharmaceutically acceptable salt thereof, wherein the Linker Unit Q is of formula (i), (ii), (iii), (iv), (x), or (xi).

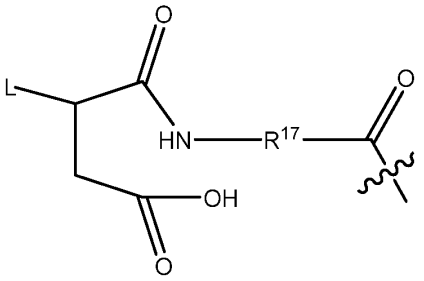
68. The Ligand-Drug Conjugate compound of claim 66, or a pharmaceutically acceptable salt thereof, wherein the Linker Unit Q is of formula (v), (vi), (ix), or (xi).

69. The Ligand-Drug Conjugate compound of claim 66, or a pharmaceutically acceptable salt thereof, wherein the Linker Unit Q is of formula (viii), (ix), (x), or (xi).

70. The Ligand-Drug Conjugate compound of any one of claims 66-69, or a pharmaceutically acceptable salt thereof, wherein the Ligand Unit L and the Stretcher Unit Z together are



,


, or


,

wherein

R^{17} is $–CH_2CH_2(OCH_2CH_2)_k–$, -C_1-C_{10} alkylene-, C_1-C_{10} heteroalkylene-, -C_3-C_8 carbocyclo-, -O-(C_1-C_8 alkylene)-, -arylene-, -C_1-C_{10} alkylene-arylene-, -arylene-C_1-C_{10} alkylene-, -C_1-C_{10} alkylene-(C_3-C_8 carbocyclo)-, -(C_3-C_8 carbocyclo)-C_1-C_{10} alkylene-, -C_3-C_8 heterocyclo-, -C_1-C_{10} alkylene-(C_3-C_8 heterocyclo)-, -(C_3-C_8 heterocyclo)-C_1-C_{10} alkylene-, -C_1-C_{10} alkylene-C(=O)-, C_1-C_{10} heteroalkylene-C(=O)-, -C_3-C_8 carbocyclo-C(=O)-, -O-(C_1-C_8 alkylene)-C(=O)-, -arylene-C(=O)-, -C_1-C_{10} alkylene-arylene-C(=O)-, -arylene-C_1-C_{10} alkylene-C(=O)-, -C_1-C_{10} alkylene-(C_3-C_8 carbocyclo)-C(=O)-,-(C_3-C_8 carbocyclo)-C_1-C_{10}

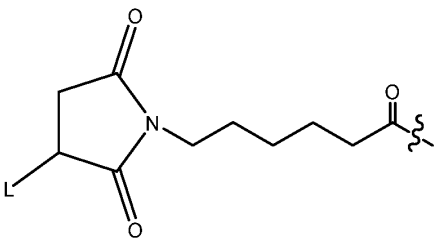
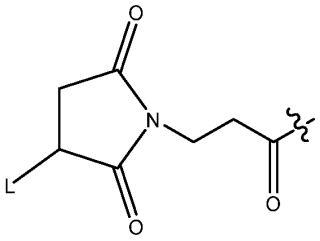
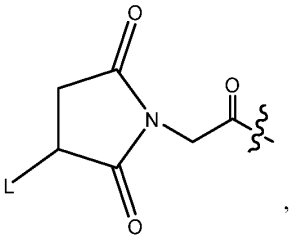
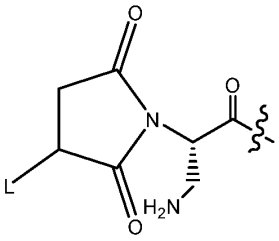
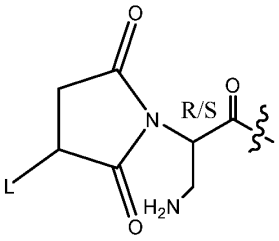
alkylene-C(=O)-, -C_3-C_8 heterocyclo-C(=O)-, -C_1-C_{10} alkylene-(C_3-C_8 heterocyclo)-C(=O)-, -(C_3-C_8 heterocyclo)-C_1-C_{10} alkylene-C(=O)-, -C_1-C_{10} alkylene-NH-, C_1-C_{10} heteroalkylene-NH-, -C_3-C_8 carbocyclo-NH-, -O-(C_1-C_8 alkylene)-NH-, -arylene-NH-, -C_1-C_{10} alkylene-arylene-NH-, -arylene-C_1-C_{10} alkylene-NH-, -C_1-C_{10} alkylene-(C_3-C_8 carbocyclo)-NH-, -(C_3-C_8 carbocyclo)-C_1-C_{10} alkylene-NH-, -C_3-C_8 heterocyclo-NH-, -C_1-C_{10} alkylene-(C_3-C_8 heterocyclo)-NH-, -(C_3-C_8 heterocyclo)-C_1-C_{10} alkylene-NH-, -C_1-C_{10} alkylene-S-, C_1-C_{10} heteroalkylene-S -, -C_3-C_8 carbocyclo-S -, -O-(C_1-C_8 alkylene)-S -, -arylene-S-, -C_1-C_{10} alkylene-arylene-S-, -arylene-C_1-C_{10} alkylene-S-, -C_1-C_{10} alkylene-(C_3-C_8 carbocyclo)-S-, -(C_3-C_8 carbocyclo)-C_1-C_{10} alkylene-S-, -C_3-C_8 heterocyclo-S-, -C_1-C_{10} alkylene-(C_3-C_8 heterocyclo)-S-, or -(C_3-C_8 heterocyclo)-C_1-C_{10} alkylene-S-;

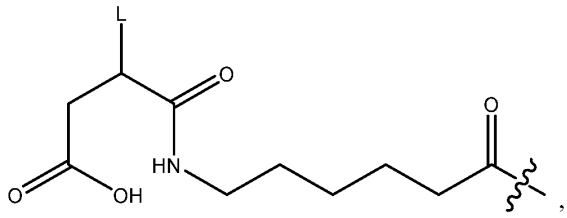
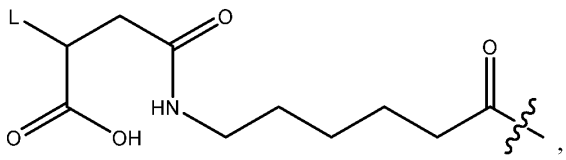
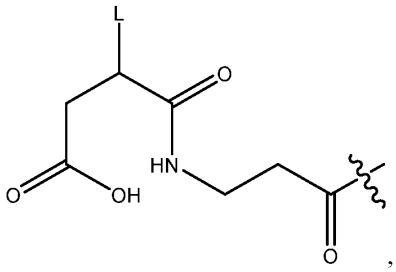
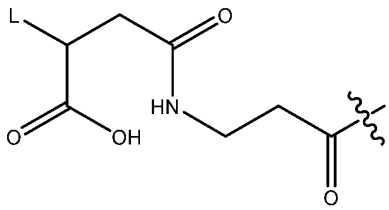
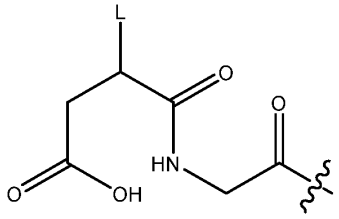
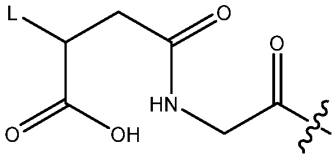
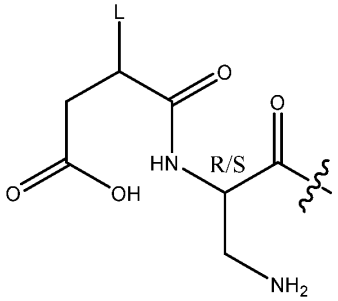
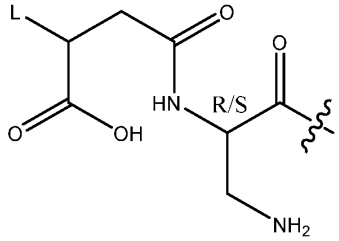
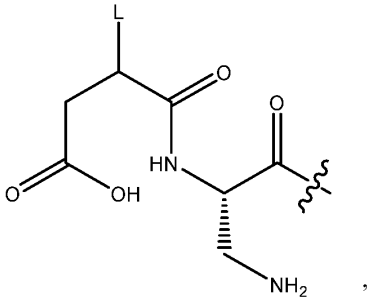
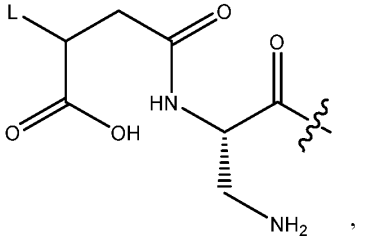
subscript k is an integer ranging from 1 to 36;

R^{17} is optionally substituted by a Basic Unit (BU) such as an aminoalkyl moiety, e.g. –$(CH_2)_xNH_2$, –$(CH_2)_xNHR^a$, and –$(CH_2)_xNR^a{}_2$, wherein x is an integer of from 1-4 and each R^a is independently selected from the group consisting of C_{1-6} alkyl and C_{1-6} haloalkyl, or two R^a groups are combined with the nitrogen to which they are attached to form an azetidinyl, pyrrolidinyl or piperidinyl group; and

the wavy line indicates the point of covalent attachment to the rest of the Ligand-Drug Conjugate compound.

71. The Ligand-Drug Conjugate compound of any one of claims 66-70, or a pharmaceutically acceptable salt thereof, wherein the Ligand Unit L and the Stretcher Unit Z together are

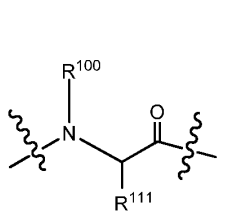
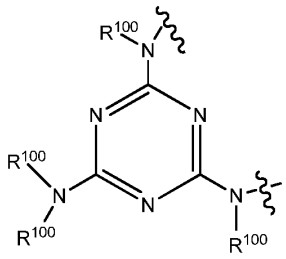
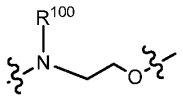
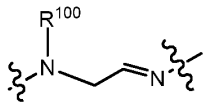
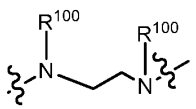
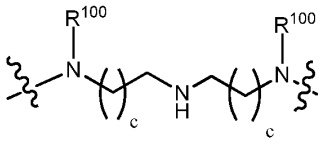
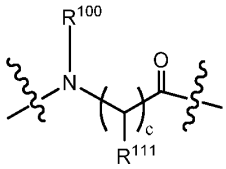

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or

wherein the wavy lines indicate the point of covalent attachment to the rest of the Ligand-Drug Conjugate compound.

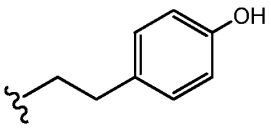
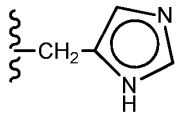
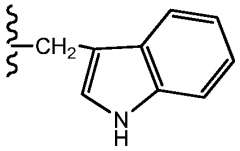
72. The Ligand-Drug Conjugate compound of any one of claims 66-71, or a pharmaceutically acceptable salt thereof, wherein the Connector Unit A is


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or


wherein

each R^{100} is independently selected from hydrogen or -C_1-C_3 alkyl;

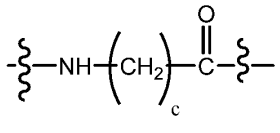
R^{111} is independently selected from the group consisting of hydrogen, *p*-hydroxybenzyl, methyl, isopropyl, isobutyl, *sec*-butyl, -CH_2OH, -$CH(OH)CH_3$, -$CH_2CH_2SCH_3$, -CH_2CONH_2, -CH_2COOH, -$CH_2CH_2CONH_2$, -CH_2CH_2COOH, -$(CH_2)_3NHC(=NH)NH_2$, -$(CH_2)_3NH_2$, -$(CH_2)_3NHCOCH_3$, -$(CH_2)_3NHCHO$, -$(CH_2)_4NHC(=NH)NH_2$, -$(CH_2)_4NH_2$, -$(CH_2)_4NHCOCH_3$, -$(CH_2)_4NHCHO$, -$(CH_2)_3NHCONH_2$, -$(CH_2)_4NHCONH_2$, -$CH_2CH_2CH(OH)CH_2NH_2$, 2-pyridylmethyl-, 3-pyridylmethyl-, 4-pyridylmethyl-,


,

, and

;

each subscript c is an independently selected integer from 1 to 10; and

the wavy lines indicate attachment of the Connector Unit to the rest of the Ligand-Drug Conjugate compound or pharmaceutically acceptable salt thereof.

73. The Ligand-Drug Conjugate compound of any one of claims 66-72, or a pharmaceutically acceptable salt thereof, wherein the Connector Unit A is



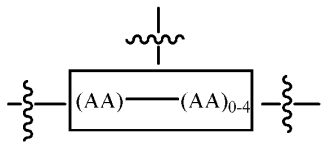
;

c is an integer ranging from 1 to 6; and

the wavy lines indicate the site of attachment to the rest of the Ligand-Drug Conjugate compound or pharmaceutically acceptable salt thereof.

74. The Ligand-Drug Conjugate compound of any one of claims 66-71, or a pharmaceutically acceptable salt thereof, wherein A is a bond.

75. The Ligand-Drug Conjugate compound of claims 66-74, or a salt thereof, wherein B is



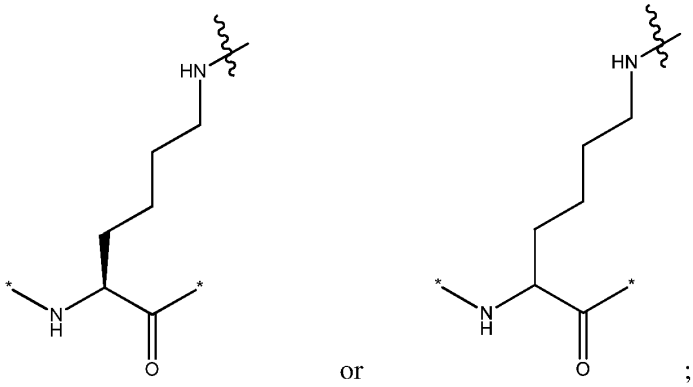
;

each AA is independently a proteinogenic or non-proteinogenic amino acid; and

the wavy lines indicate points of attachment to the rest of the Ligand-Drug Conjugate compound or pharmaceutically acceptable salt thereof.

76. The Ligand-Drug Conjugate compound of any one of claims 66-75, or a pharmaceutically acceptable salt thereof, wherein B is an amino acid.

77. The Ligand-Drug Conjugate compound of any one of claims 66-76, or a pharmaceutically acceptable salt thereof, wherein B is



;

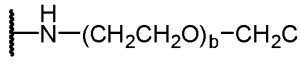
the wavy line indicates the point of attachement to the Partitioning Agent S*; and

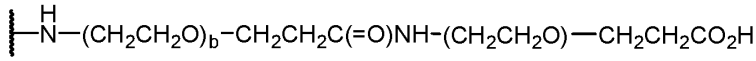
the asterisks indicate points of attachment to the rest of the Ligand-Drug Conjugate compound or pharmaceutically acceptable salt thereof.

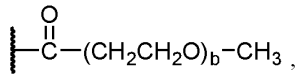
78. The Ligand-Drug Conjugate compound of any one of claims 66-77, or a pharmaceutically acceptable salt thereof, wherein the Partitioning Agent S^* is a polyethylene glycol (PEG) unit, cyclodextrin unit, polyamide, hydrophilic peptide, polysaccharide, or dendrimer.

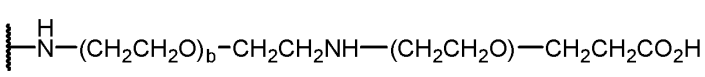
79. The Ligand-Drug Conjugate compound of any one of claims 66-78, or a pharmaceutically acceptable salt thereof, wherein the Partitioning Agent S^* is a PEG Unit comprising from 4 to 72 (CH_2CH_2O) subunits.

80. The Ligand-Drug Conjugate compound of any one of claims 66-79, or a pharmaceutically acceptable salt thereof, wherein the PEG Unit is









;

b is selected from the group consisting of 4 to 36; and

the wavy lines indicate the site of attachment to the rest of the Ligand-Drug Conjugate compound or pharmaceutically acceptable salt thereof.

81. The Ligand-Drug Conjugate compound of any one of claims 66-80, or a pharmaceutically acceptable salt thereof, wherein the Releasable Linker RL is

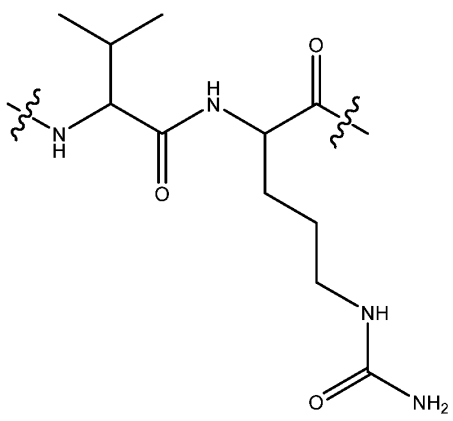
$–(AA)_{1-12}–$; and

each AA is independently a proteinogenic or non-proteinogenic amino acid.

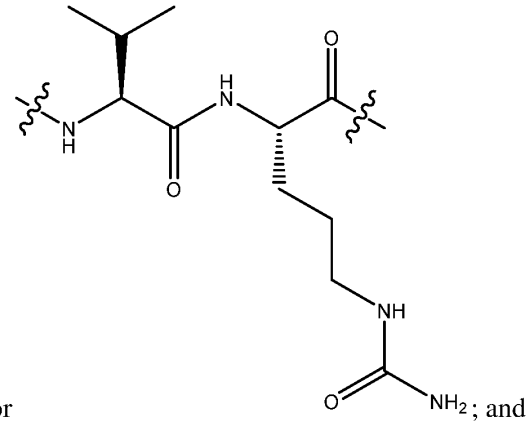
82. The Ligand-Drug Conjugate compound of any one of claims 66-81, or a pharmaceutically acceptable salt thereof, wherein the Releasable Linker RL is

$–AA_1\text{-}AA_2–$ or $–AA_1\text{-}AA_2\text{-}AA_3–$, wherein AA_1 is attached to the Stretcher Unit Z or the Connector Unit A.

83. The Ligand-Drug Conjugate compound of any one of claims 66-82, or a pharmaceutically acceptable salt thereof, wherein the Releasable Linker RL is



or

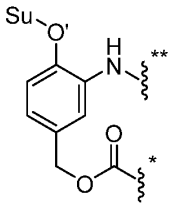


; and

the wavy line adjacent to the -NH- group indicates attachment to the Stretcher Unit Z or the Connector Unit A and the wavy line adjacent to the -C(=O)- group indicates attachment to the Spacer Unit Y or the Drug Unit D.

84. The Ligand-Drug Conjugate compound of any one of claims 66-83, or a pharmaceutically acceptable salt thereof, wherein the Releasable Linker RL is a glycoside.

85. The Ligand-Drug Conjugate compound of any one of claims 66-84, or a pharmaceutically acceptable salt thereof, wherein the Releasable Linker RL is



wherein

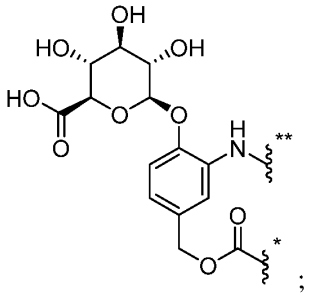
Su is a hexose form a monosaccharide;

O' represents the oxygen atom of a glycosidic bond that is capable of cleavage by a glycosidase;

the wavy line marked with a single asterisk (*) indicates the site of covalent attachment to D; and

the wavy line marked with a double asterisk (**) indicates the site of covalent attachment to the remainder of Q.

86. The Ligand-Drug Conjugate compound of any one of claims 66-85, or a pharmaceutically acceptable salt thereof, wherein the Releasable Linker RL is

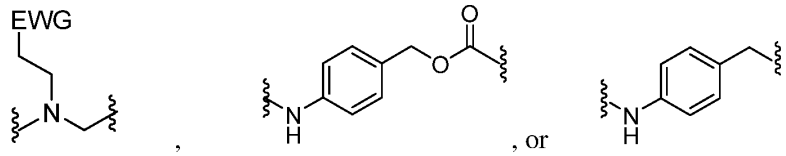


;

the wavy line marked with a single asterisk (*) indicates the site of covalent attachment to D; and

the wavy line marked with a double asterisk (**) indicates the site of covalent attachment to the remainder of Q.

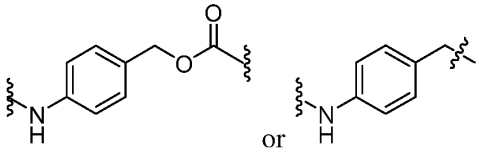
87. The Ligand-Drug Conjugate compound of any one of claims 66-68 or 70-86, or a pharmaceutically acceptable salt thereof, wherein the Spacer Unit Y is



wherein EWG is an electron-withdrawing group; and

the wavy lines indicate the site of attachment to the rest of the Ligand-Drug Conjugate compound or pharmaceutically acceptable salt thereof.

88. The Ligand-Drug Conjugate compound of any one of claims 66-68 or 70-87, or a pharmaceutically acceptable salt thereof, wherein the Spacer Unit Y is



; and

the wavy lines indicate the site of attachment to the rest of the Ligand-Drug Conjugate compound or pharmaceutically acceptable salt thereof.

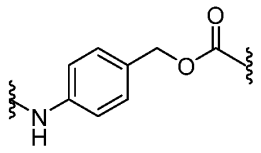
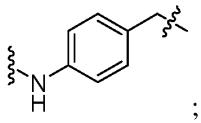
89. The Ligand-Drug Conjugate compound of any one of claims 66-67, 70-71, 74, 81-83, or 87-88, or a pharmaceutically acceptable salt thereof, wherein

R^{17} is C_1-C_{10} alkylene;

A is a bond;

RL is –AA_1-AA_2–;

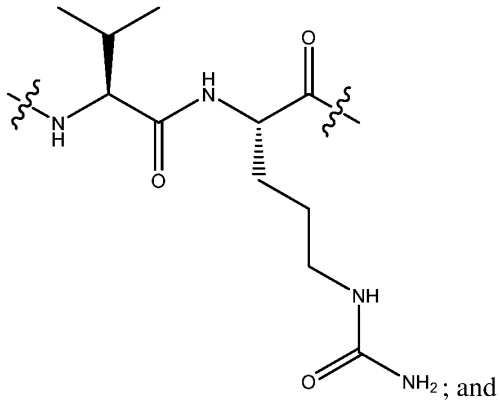
AA_1 and AA_2 are each independently a proteinogenic amino acid;

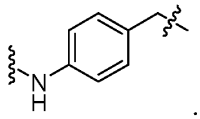
Y is  or  ; and

the wavy lines indicate the site of attachment to the rest of the Ligand-Drug Conjugate compound or pharmaceutically acceptable salt thereof.

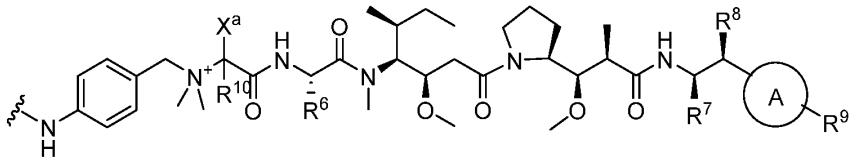
90. The Ligand-Drug Conjugate compound of any one of claims 66-67, 70-71, 74, 81-83, or 87-89, or a pharmaceutically acceptable salt thereof, wherein

A is a bond;

RL is  ; and

Y is  .

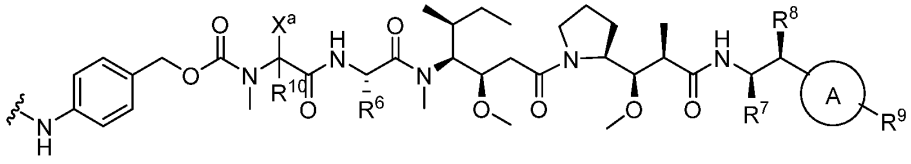
91. The Ligand-Drug Conjugate compound of any one of claims 66-67, 70-71, 74, 81-83, or 87-90, or a pharmaceutically acceptable salt thereof, wherein Y-D is



; and

the wavy line indicates the site of attachment to the rest of the Ligand-Drug Conjugate compound or pharmaceutically acceptable salt thereof.

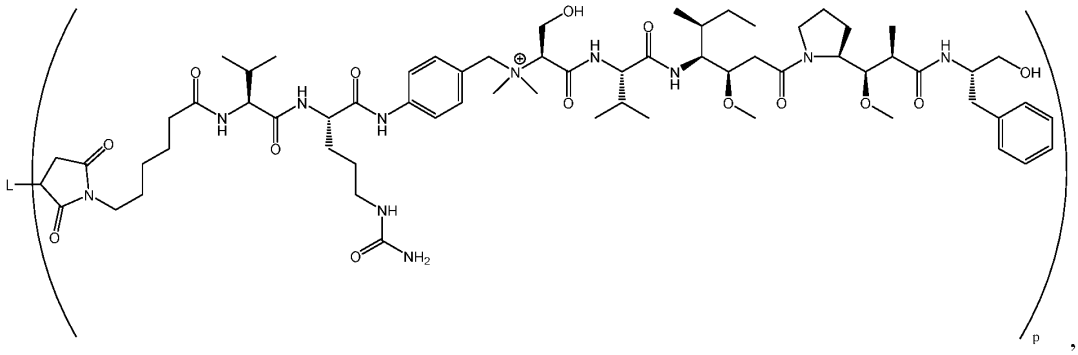
92. The Ligand-Drug Conjugate compound of any one of claims 66-67, 70-71, 74, 81-83, or 87-90, or a pharmaceutically acceptable salt thereof, wherein Y-D is



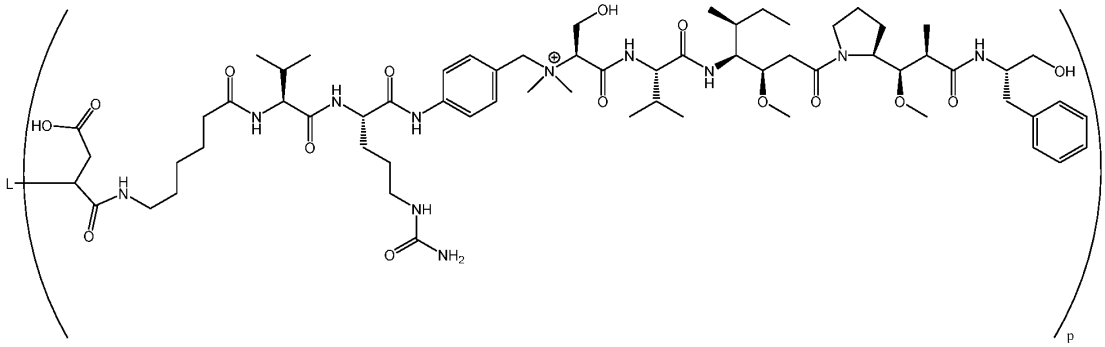
; and

the wavy line indicates the site of attachment to the rest of the Ligand-Drug Conjugate compound or pharmaceutically acceptable salt thereof.

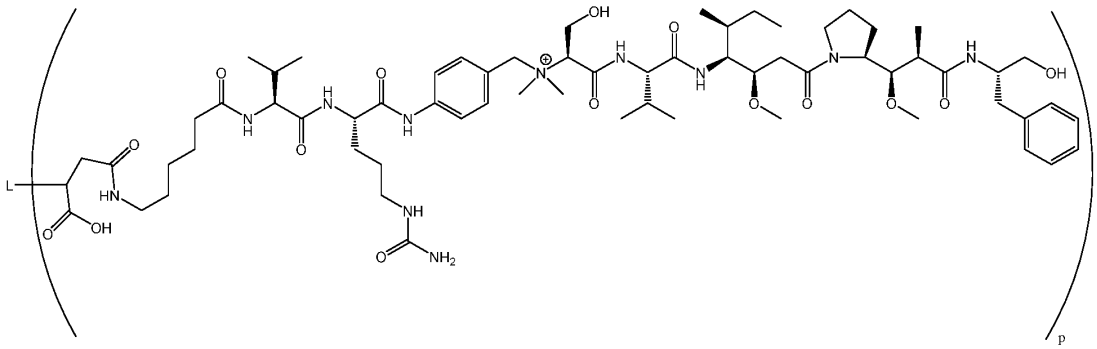
93. The Ligand-Drug Conjugate compound of any one of claims 66-67, 70-71, 74, 81-83, or 87-91, wherein the compound is



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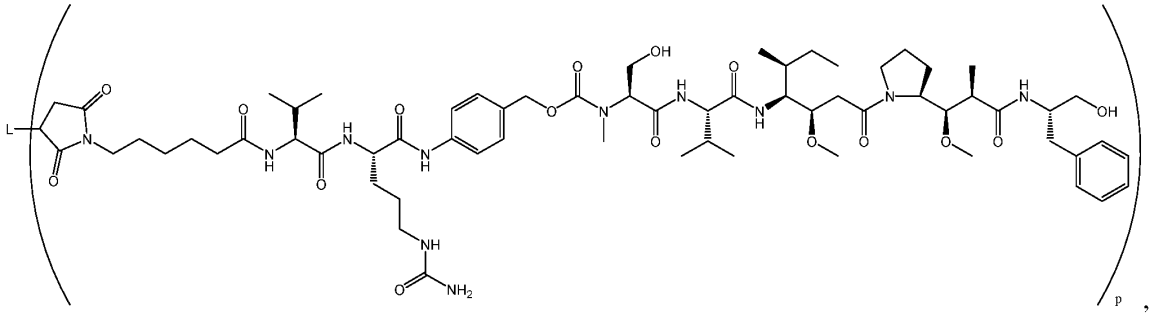


, or

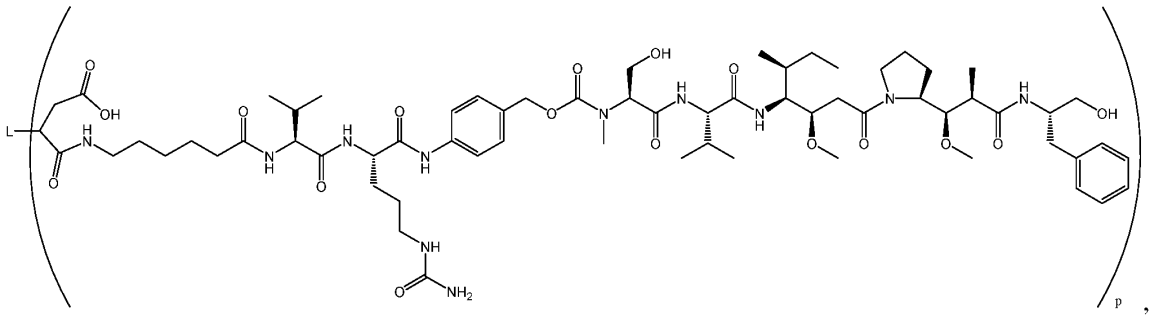


or a pharmaceutically acceptable salt thereof.

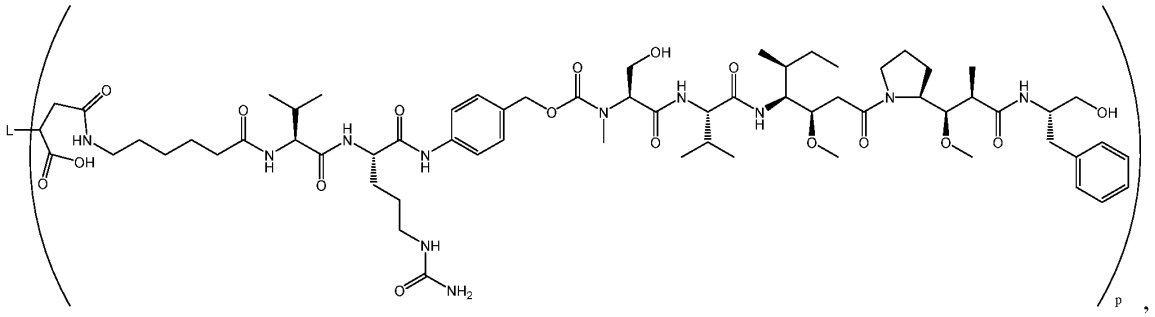
94. The Ligand-Drug Conjugate compound of any one of claims 66-67, 70-71, 74, 81-83, 87-90, or 92, wherein the compound is



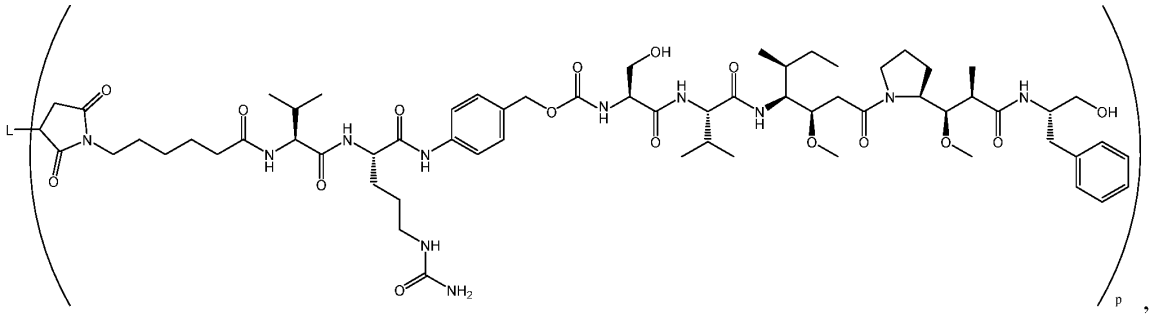
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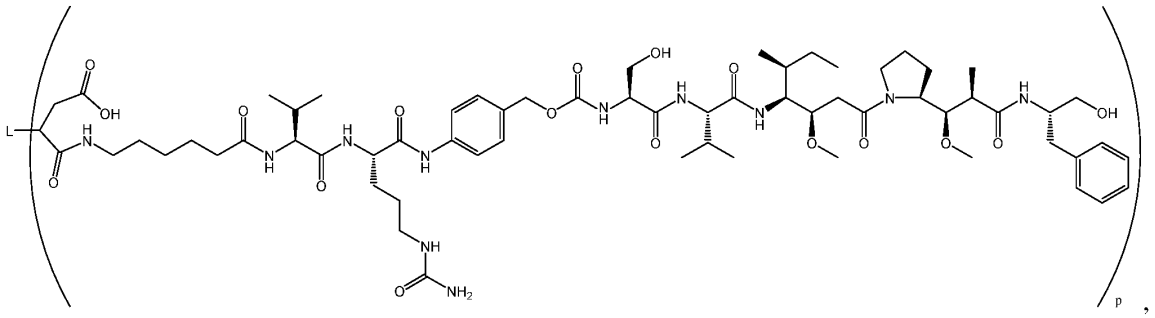
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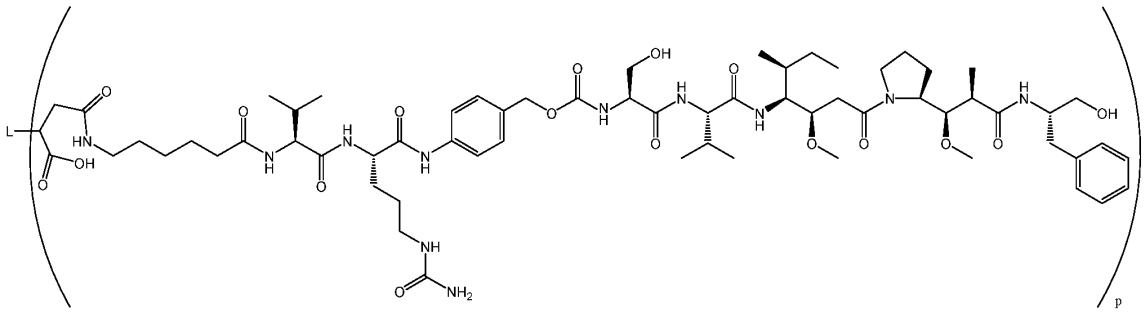


,



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or



or a pharmaceutically acceptable salt thereof.

95. The Ligand-Drug Conjugate compound of any one of claims 66-94, wherein p is an integer ranging from 2 to 8.

96. The Ligand-Drug Conjugate compound of any one of claims 66-95, wherein p is 4.

97. A pharmaceutical composition comprising the Ligand-Drug Conjugate compound of any one of claims 66-94 and a pharmaceutically acceptable excipient.

98. The pharmaceutical composition of claim 97, wherein the composition comprises a plurality of Ligand-Drug Conjugate compounds with an average drug-loading from 2 to 8.

99. The pharmaceutical composition of claim 98, wherein the average drug loading is about 4.

100. The pharmaceutical composition claim 98, wherein the average drug loading is from 3.5 to 4.5.

101. A method of treating cancer comprising administering a therapeutically effective amount of the Ligand-Drug Conjugate compound of any one of claims 66-96, or a pharmaceutically acceptable salt thereof, to a subject in need thereof.

102. The method of claim 101, wherein the subject tolerates treatment from the Ligand-Drug Conjugate compound better than another Ligand-Drug Conjugate compound in therapeutically effective doses.

103. The method of claim 102, wherein the another Ligand-Drug Conjugate compound comprises a monomethyl auristatin E or monomethyl auristatin F Drug Unit.

104. A compound, wherein the compound is selected from the group consisting of the compounds listed in Table 1 or a salt thereof.

105. A Drug-Linker compound, wherein the Drug-Linker compound is selected from the group consisting of the compounds listed in Table 2 or a salt thereof.

106. A Ligand-Drug Conjugate compound, wherein the Ligand-Drug Conjugate compound is selected from the group consisting of the compounds listed in Table 3, or a salt thereof, and p is an integer ranging from 1 to 12.

107. The Ligand-Drug Conjugate compound of any one of claims 66-96 or 106, wherein L is an antibody.

108. The Ligand-Drug Conjugate compound of any one of claims 66-96 or 106-107, wherein L comprises an amino acid sequence that is at least 80% identical to the amino acid sequence of any one of SEQ ID Nos. 1 to 1044.

109. The Ligand Drug-Conjugate of any one of claims 66-96 or 106-108, wherein L comprises an amino acid sequence that is at least 85% identical to the amino acid sequence of any one of SEQ ID Nos. 1 to 1044.

110. The Ligand Drug-Conjugate of any one of claims 66-96 or 106-109, wherein L comprises an amino acid sequence that is at least 90% identical to the amino acid sequence of any one of SEQ ID Nos. 1 to 1044.

111. The Ligand Drug-Conjugate of any one of claims 66-96 or 106-110, wherein L comprises an amino acid sequence that is at least 95% identical to the amino acid sequence of any one of SEQ ID Nos. 1 to 1044.

112. The Ligand Drug-Conjugate of any one of claims 66-96 or 106-111, wherein L comprises an amino acid sequence that is at least 98% identical to the amino acid sequence of any one of SEQ ID Nos. 1 to 1044.

113. The Ligand Drug-Conjugate of any one of claims 66-96 or 106-112, wherein L comprises an amino acid sequence that is at least 99% identical to the amino acid sequence of any one of SEQ ID Nos. 1 to 1044.

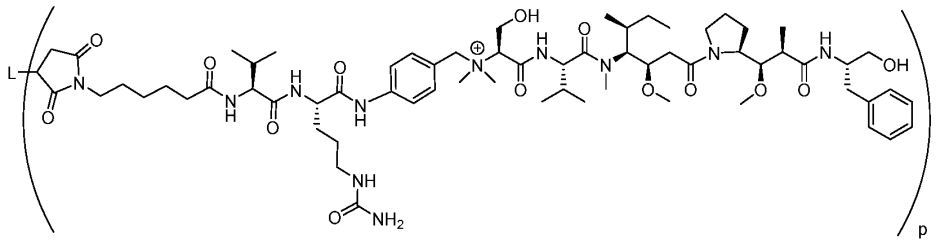
114. The Ligand-Drug Conjugate compound of any one of claims claim 66-96 or 106-113, wherein L comprises the amino acid sequence of any one of SEQ ID Nos. 1 to 1044.

115. The Ligand-Drug Conjugate compound of any one of claims 66-96 or 106-114, wherein L consists of the amino acid sequence of any one of SEQ ID Nos. 1 to 1044.

116. The Ligand-Drug Conjugate of any one of claims 66-96 or 106-115, wherein p is 8.

117. The Ligand-Drug Conjugate of any one of claims 66-96 or 106-115, wherein p is and integer from 1 to 8.

118. A Ligand-Drug Conjugate of the following formula:



wherein L is an anti-gpNMB antibody,

and p is an integer from 1 to 14, or from 1 to 8, or is 8.

119. The Ligand-Drug Conjugate of claim 118, wherein the anti-gpNMB antibody comprises an amino acid sequence that is at least 80, 85, 90, 95, 98, or 99% identical to the amino acid sequence of any one of SEQ ID Nos. 935-944.