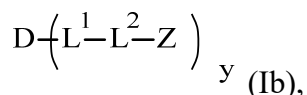
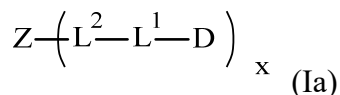


Claims

1. A conjugate or a pharmaceutically acceptable salt thereof of formula (Ia) or (Ib)



wherein

-D comprises an IL-2 protein of formula (I)

Ala – SEQ A – Cys* – SEQ B (I),

wherein

SEQ A has at least 94% sequence identity to SEQ ID NO:1;

SEQ B has at least 94% sequence identity to SEQ ID NO:2;

Ala is an alanine residue; and

Cys* is a cysteine residue;

-L¹- is a linker moiety covalently and reversibly attached to -D;

-L²- is a chemical bond or is a spacer moiety;

Z is a polymeric moiety or a substituted fatty acid moiety;

x is an integer selected from the group consisting of 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15 or 16; and

y is an integer selected from the group consisting of 2, 3, 4 and 5.

2. The conjugate or a pharmaceutically acceptable salt thereof of claim 1, wherein SEQ A is selected from the group consisting of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10 and SEQ ID NO:11.

3. The conjugate or a pharmaceutically acceptable salt thereof of claim 1 or 2, wherein SEQ A has the sequence of SEQ ID NO:1.

4. The conjugate or a pharmaceutically acceptable salt thereof of any one of claims 1 to 3, wherein SEQ B has the sequence of SEQ ID NO:2.

5. The conjugate or a pharmaceutically acceptable salt thereof of any one of claims 1 to 3, wherein SEQ B has the sequence of SEQ ID NO:12.

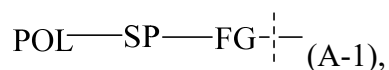
6. The conjugate or a pharmaceutically acceptable salt thereof of any one of claims 1 to 3 and 5, wherein the IL-2 protein has the sequence of SEQ ID NO:14.

7. The conjugate or a pharmaceutically acceptable salt thereof of any one of claims 1 to 6, wherein the IL-2 protein comprises a moiety M_{mod} conjugated to the cysteine marked with the asterisk in the IL-2 protein of formula (I).

8. The conjugate or a pharmaceutically acceptable salt thereof of any one of claims 1 to 7, wherein the conjugate is a biased IL-2.

9. The conjugate or a pharmaceutically acceptable salt thereof of claim 7 or 8, wherein M_{mod} is a polymeric moiety.

10. The conjugate or a pharmaceutically acceptable salt thereof of any one of claims 7 to 9, wherein M_{mod} is of formula (A-1)



wherein

-FG- is a linkage;

-SP- is a spacer moiety; and

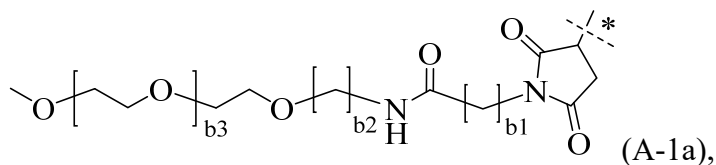
-POL is a polymer.

11. The conjugate or a pharmaceutically acceptable salt thereof of any one of claims 7 to 10, wherein M_{mod} has a molecular weight ranging from 0.5 kDa to 120 kDa.

12. The conjugate or a pharmaceutically acceptable salt thereof of any one of claims 7 to 11, wherein M_{mod} is a PEG-based polymer.

13. The conjugate or a pharmaceutically acceptable salt thereof of any one of claims 7 to 12, wherein attachment of M_{mod} to the IL-2 protein is via a stable linkage.

14. The conjugate or a pharmaceutically acceptable salt thereof of any one of claims 7 to 13, wherein M_{mod} is of formula (A-1a)



wherein

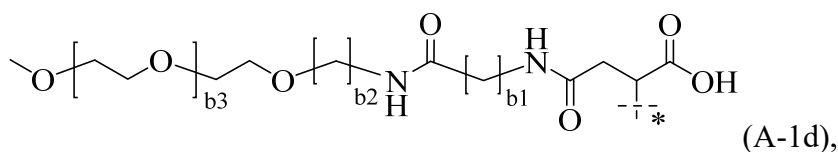
the dashed line marked with the asterisk indicates attachment to the sulfur of the cysteine marked with the asterisk in formula (I);

b_1 is an integer selected from the group consisting of 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19 and 20;

b_2 is an integer selected from the group consisting of 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19 and 20; and

b_3 is an integer ranging from 12 to 22700.

15. The conjugate or a pharmaceutically acceptable salt thereof of any one of claims 7 to 13, wherein M_{mod} is of formula (A-1d)



wherein

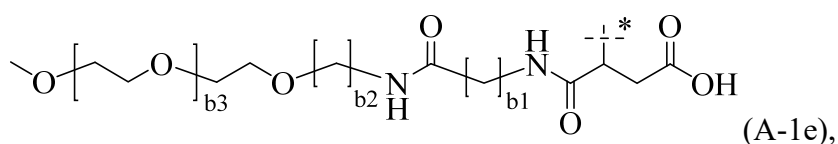
the dashed line marked with the asterisk indicates attachment to the sulfur of the cysteine marked with the asterisk in formula (I);

b_1 is an integer selected from the group consisting of 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19 and 20;

b_2 is an integer selected from the group consisting of 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19 and 20; and

b_3 is an integer ranging from 12 to 22700.

16. The conjugate or a pharmaceutically acceptable salt thereof of any one of claims 7 to 13, wherein M_{mod} is of formula (A-1e)



wherein

the dashed line marked with the asterisk indicates attachment to the sulfur of the cysteine marked with the asterisk in formula (I);

b1 is an integer selected from the group consisting of 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19 and 20;

5 b2 is an integer selected from the group consisting of 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19 and 20; and

b3 is an integer ranging from 12 to 22700.

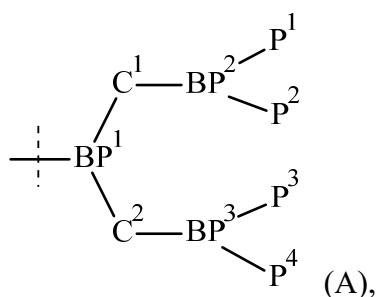
10 17. The conjugate or a pharmaceutically acceptable salt thereof of any one of claims 7 to 13, wherein in a plurality of conjugates M_{mod} comprises a mixture of formula (A-1d) and formula (A-1e).

18. The conjugate or a pharmaceutically acceptable salt thereof of any one of claims 1 to 17, wherein -Z is a polymeric moiety.

15 19. The conjugate or a pharmaceutically acceptable salt thereof of any one of claims 1 to 18, wherein -Z is a polymeric moiety having a molecular weight ranging from 1 kDa to 1000 kDa.

20 20. The conjugate or a pharmaceutically acceptable salt thereof of any one of claims 1 to 19, wherein -Z is a PEG-based polymeric moiety.

21. The conjugate or a pharmaceutically acceptable salt thereof of any one of claims 1 to 20, wherein -Z comprises a moiety of formula (A)



wherein

-BP¹<, -BP²<, -BP³< are independently of each other selected from the group consisting of -N< and -C(R⁸)<;

R^8 is selected from the group consisting of H, C_{1-6} alkyl, C_{2-6} alkenyl and C_{2-6} alkynyl;

$-P^1$, $-P^2$, $-P^3$, $-P^4$ are independently of each other a PEG-based chain comprising at least 40% PEG and having a molecular weight ranging from 3 to 40 kDa;

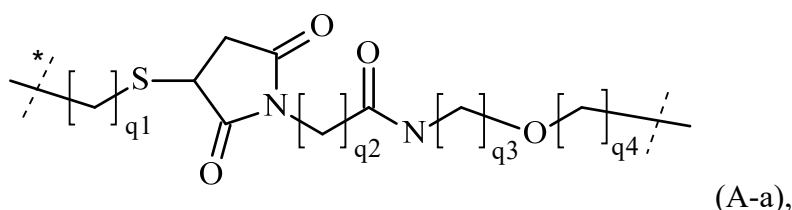
$-C^1$ -, $-C^2$ - are independently of each other selected from the group consisting of C_{1-50} alkyl, C_{2-50} alkenyl, and C_{2-50} alkynyl; wherein C_{1-50} alkyl, C_{2-50} alkenyl, and C_{2-50} alkynyl are optionally substituted with one or more R^9 , which are the same or different and wherein C_{1-50} alkyl, C_{2-50} alkenyl, and C_{2-50} alkynyl are optionally interrupted by one or more groups selected from the group consisting of $-T$ -, $-C(O)O$ -, $-O$ -, $-C(O)$ -, $-C(O)N(R^{10})$ -, $-S(O)_2N(R^{10})$ -, $-S(O)N(R^{10})$ -, $-S(O)_2$ -, $-S(O)$ -, $-N(R^{10})S(O)_2N(R^{10a})$ -, $-S$ -, $-N(R^{10})$ -, $-OC(OR^{10})(R^{10a})$ -, $-N(R^{10})C(O)N(R^{10a})$ -, and $-OC(O)N(R^{10})$ -;

each T is independently selected from the group consisting of phenyl, naphthyl, indenyl, indanyl, tetralinyl, C_{3-10} cycloalkyl, 3- to 10-membered heterocyclyl, 8- to 11-membered heterobicycyl, 8-to 30-membered carbopolycyclyl, and 8- to 30-membered heteropolycyclyl; wherein each T is independently optionally substituted with one or more R^9 , which are the same or different;

each R^9 is independently selected from the group consisting of halogen, $-CN$, oxo ($=O$), $-COOR^{11}$, $-OR^{11}$, $-C(O)R^{11}$, $-C(O)N(R^{11}R^{11a})$, $-S(O)_2N(R^{11}R^{11a})$, $-S(O)N(R^{11}R^{11a})$, $-S(O)_2R^{11}$, $-S(O)R^{11}$, $-N(R^{11})S(O)_2N(R^{11a}R^{11b})$, $-SR^{11}$, $-N(R^{11}R^{11a})$, $-NO_2$, $-OC(O)R^{11}$, $-N(R^{11})C(O)R^{11a}$, $-N(R^{11})S(O)_2R^{11a}$, $-N(R^{11})S(O)R^{11a}$, $-N(R^{11})C(O)OR^{11a}$, $-N(R^{11})C(O)N(R^{11a}R^{11b})$, $-OC(O)N(R^{11}R^{11a})$, and C_{1-6} alkyl; wherein C_{1-6} alkyl is optionally substituted with one or more halogen, which are the same or different; and

each R^{10} , R^{10a} , R^{11} , R^{11a} and R^{11b} is independently selected from the group consisting of $-H$, and C_{1-6} alkyl, wherein C_{1-6} alkyl is optionally substituted with one or more halogen, which are the same or different.

22. The conjugate or a pharmaceutically acceptable salt thereof of claim 21, wherein C^1 and C^2 are of formula (A-a)



wherein

the dashed line marked with the asterisk indicates attachment to BP¹;

the unmarked dashed line indicates attachment to BP² or BP³, respectively;

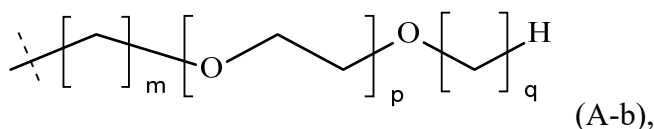
q₁ is selected from the group consisting of 1, 2, 3, 4, 5, 6, 7 and 8;

5 q₂ is selected from the group consisting of 1, 2, 3, 4, and 5;

q₃ is selected from the group consisting of 1, 2, 3, 4, 5, 6, 7 and 8; and

q₄ is selected from the group consisting of 1, 2 and 3.

- 10 23. The conjugate or a pharmaceutically acceptable salt thereof of claim 21 or 22, wherein P¹, P², P³ and P⁴ are independently of each other of formula (A-b)



wherein

the dashed line indicates attachment to the remainder of -Z;

m is 0 or 1;

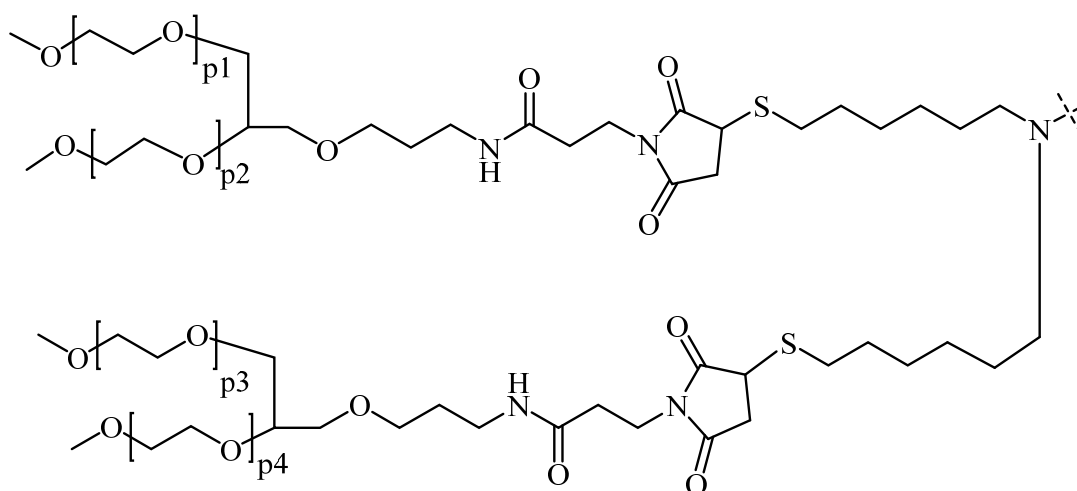
15 p is an integer ranging from 70 to 900; and

q is selected from the group consisting of 1, 2, 3, 4, 5, and 6.

- 20 24. The conjugate or a pharmaceutically acceptable salt thereof of any one of claims 21 to 23, wherein BP¹ is -N<..

25. The conjugate or a pharmaceutically acceptable salt thereof of any one of claims 21 to 24, wherein BP² and BP² are both -CH<.

- 25 26. The conjugate or a pharmaceutically acceptable salt thereof of any one of claims 1 to 25, wherein -Z comprises a moiety of formula (A-c):

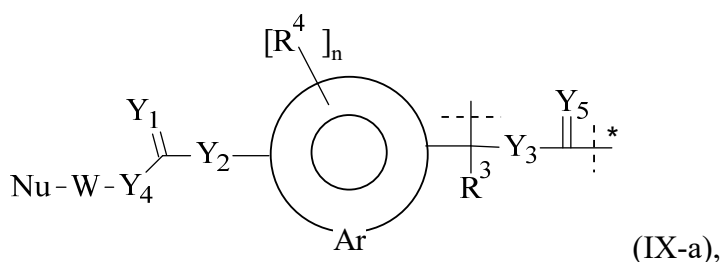


(A-c),

wherein

5 p1, p2, p3, p4 are independently of each other an integer ranging from 70 to 900.

27. The conjugate or a pharmaceutically acceptable salt thereof of any one of claims 1 to 26, wherein -L¹- is of formula (IX-a):



10 wherein

the dashed line marked with the asterisk indicates attachment to a nitrogen of -D and the unmarked dashed line indicates attachment to -L²-Z;

n is 0, 1, 2, 3, or 4;

=Y₁, is selected from the group consisting of =O and =S;

15 -Y₂- is selected from the group consisting of -O- and -S-;

-Y₃- is selected from the group consisting of -O- and -S-;

-Y₄- is selected from the group consisting of -O-, -NR⁵- and -C(R⁶R^{6a})-;

=Y₅ is selected from the group consisting of =O and =S;

20 -R³, -R⁵, -R⁶, -R^{6a} are independently of each other selected from the group consisting of -H, methyl, ethyl, n-propyl, isopropyl, n-butyl, isobutyl, sec-butyl, tert-butyl, n-pentyl, 2-methylbutyl, 2,2-dimethylpropyl, n-

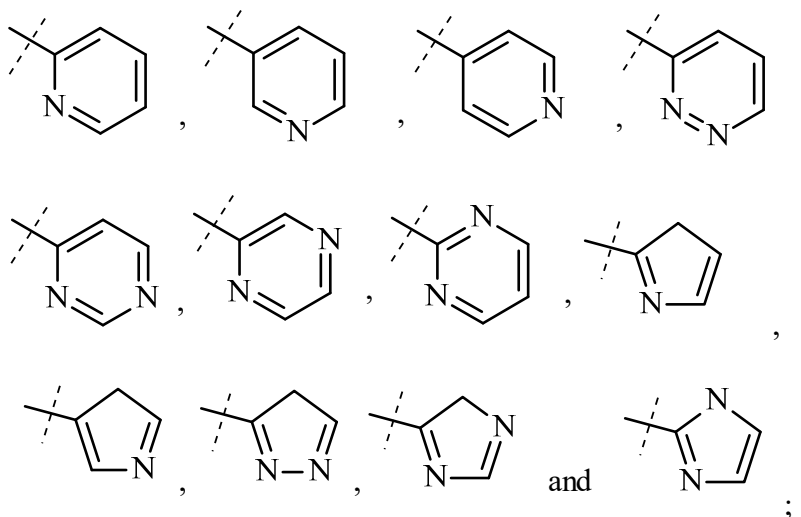
hexyl, 2-methylpentyl, 3-methylpentyl, 2,2-dimethylbutyl, 2,3-dimethylbutyl and 3,3-dimethylpropyl;

-R⁴ is selected from the group consisting of methyl, ethyl, n-propyl, isopropyl,

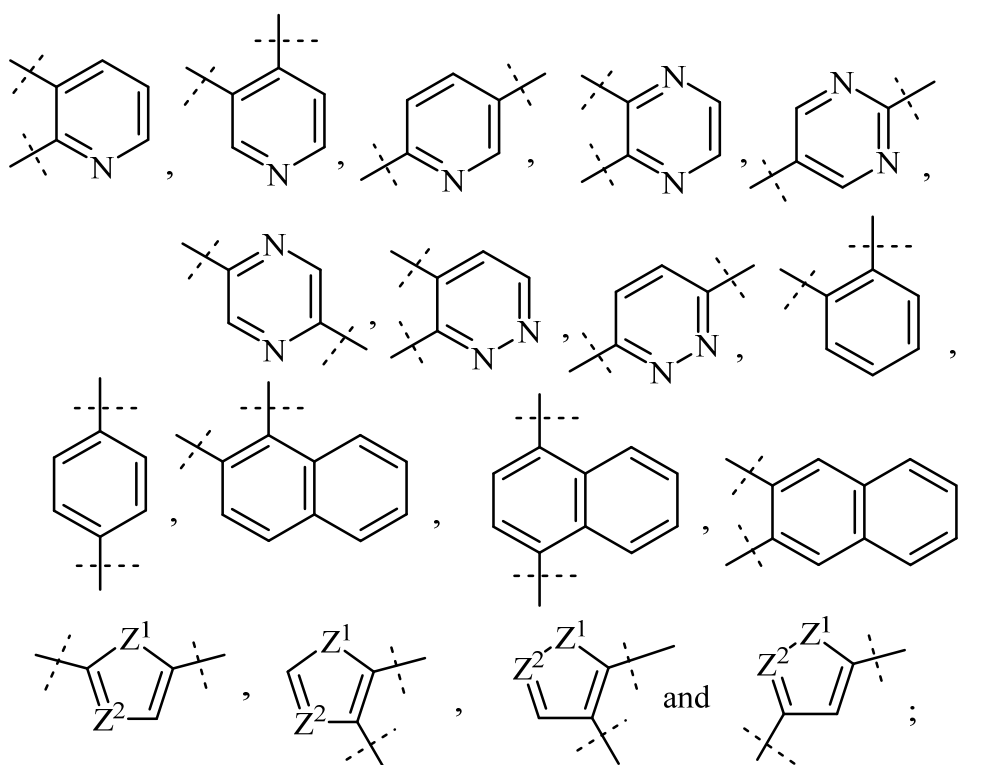
5 n-butyl, isobutyl, sec-butyl, tert-butyl, n-pentyl, 2-methylbutyl, 2,2-dimethylpropyl, n-hexyl, 2-methylpentyl, 3-methylpentyl, 2,2-dimethylbutyl, 2,3-dimethylbutyl and 3,3-dimethylpropyl;

10 -W- is selected from the group consisting of C₁₋₂₀ alkyl optionally interrupted by one or more groups selected from the group consisting of C₃₋₁₀ cycloalkyl, 8- to 30-membered carbopolycyclyl, 3- to 10-membered heterocyclyl, -C(O)-, -C(O)N(R⁷)-, -O-, -S- and -N(R⁷)-;

-Nu is a nucleophile selected from the group consisting of -N(R⁷R^{7a}), -N(R⁷OH), -N(R⁷)-N(R^{7a}R^{7b}), -S(R⁷), -COOH,



15 -Ar- is selected from the group consisting of



wherein

dashed lines indicate attachment to the remainder of $-L^1-$,

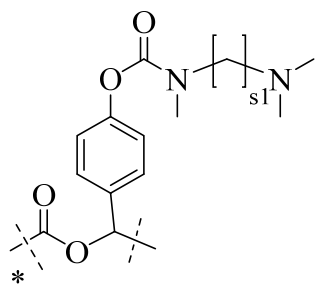
$-Z^1-$ is selected from the group consisting of $-O-$, $-S-$ and $-N(R^7)-$, and

$-Z^2-$ is $-N(R^7)-$; and

$-R^7$, $-R^{7a}$, $-R^{7b}$ are independently of each other selected from the group consisting of $-H$, C_{1-6} alkyl, C_{2-6} alkenyl and C_{2-6} alkynyl;

wherein $-L^1-$ is optionally further substituted.

28. The conjugate or a pharmaceutically acceptable salt thereof of any one of claims 1 to 27, wherein $-L^1-$ is of formula (IX-c)



(IX-c),

wherein

the dashed line marked with the asterisk indicates attachment to a nitrogen of $-D$;

the unmarked dashed line indicates attachment to $-L^2-Z$; and

s1 is an integer selected from the group consisting of 1, 2, 3, 4, 5, 6, 7, 8, 9 and 10.

29. The conjugate or a pharmaceutically acceptable salt thereof of claim 28, wherein s1 is 3.

30. The conjugate or a pharmaceutically acceptable salt thereof of any one of claims 1 to 29, wherein -L²- is a spacer.

31. The conjugate or a pharmaceutically acceptable salt thereof of any one of claims 1 to 30, wherein -L²- is selected from the group consisting of -T-, -C(O)O-, -O-, -C(O)-, -C(O)N(R^{y1})-, -S(O)₂N(R^{y1})-, -S(O)N(R^{y1})-, -S(O)₂-, -S(O)-, -N(R^{y1})S(O)₂N(R^{y1a})-, -S-, -N(R^{y1})-, -OC(OR^{y1})(R^{y1a})-, -N(R^{y1})C(O)N(R^{y1a})-, -OC(O)N(R^{y1})-, C₁₋₅₀ alkyl, C₂₋₅₀ alkenyl, and C₂₋₅₀ alkynyl; wherein -T-, C₁₋₅₀ alkyl, C₂₋₅₀ alkenyl, and C₂₋₅₀ alkynyl are optionally substituted with one or more -R^{y2}, which are the same or different and wherein C₁₋₅₀ alkyl, C₂₋₅₀ alkenyl, and C₂₋₅₀ alkynyl are optionally interrupted by one or more groups selected from the group consisting of -T-, -C(O)O-, -O-, -C(O)-, -C(O)N(R^{y3})-, -S(O)₂N(R^{y3})-, -S(O)N(R^{y3})-, -S(O)₂-, -S(O)-, -N(R^{y3})S(O)₂N(R^{y3a})-, -S-, -N(R^{y3})-, -OC(OR^{y3})(R^{y3a})-, -N(R^{y3})C(O)N(R^{y3a})-, and -OC(O)N(R^{y3})-;

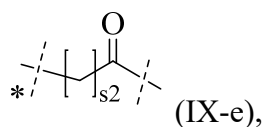
-R^{y1} and -R^{y1a} are independently of each other selected from the group consisting of -H-, -T-, C₁₋₅₀ alkyl, C₂₋₅₀ alkenyl, and C₂₋₅₀ alkynyl; wherein -T-, C₁₋₅₀ alkyl, C₂₋₅₀ alkenyl, and C₂₋₅₀ alkynyl are optionally substituted with one or more -R^{y2}, which are the same or different, and wherein C₁₋₅₀ alkyl, C₂₋₅₀ alkenyl, and C₂₋₅₀ alkynyl are optionally interrupted by one or more groups selected from the group consisting of -T-, -C(O)O-, -O-, -C(O)-, -C(O)N(R^{y4})-, -S(O)₂N(R^{y4})-, -S(O)N(R^{y4})-, -S(O)₂-, -S(O)-, -N(R^{y4})S(O)₂N(R^{y4a})-, -S-, -N(R^{y4})-, -OC(OR^{y4})(R^{y4a})-, -N(R^{y4})C(O)N(R^{y4a})-, and -OC(O)N(R^{y4})-;

each T is independently selected from the group consisting of phenyl, naphthyl, indenyl, indanyl, tetralinyl, C₃₋₁₀ cycloalkyl, 3- to 10-membered heterocyclyl, 8- to 11-membered heterobicycyl, 8- to 30-membered carbopolycyclyl, and 8- to 30-membered heteropolycyclyl; wherein each T is independently optionally substituted with one or more -R^{y2}, which are the same or different;

each $-R^{y2}$ is independently selected from the group consisting of halogen, $-CN$, oxo ($=O$), $-COOR^{y5}$, $-OR^{y5}$, $-C(O)R^{y5}$, $-C(O)N(R^{y5}R^{y5a})$, $-S(O)_2N(R^{y5}R^{y5a})$, $-S(O)N(R^{y5}R^{y5a})$, $-S(O)_2R^{y5}$, $-S(O)R^{y5}$, $-N(R^{y5})S(O)_2N(R^{y5a}R^{y5b})$, $-SR^{y5}$, $-N(R^{y5}R^{y5a})$, $-NO_2$, $-OC(O)R^{y5}$, $-N(R^{y5})C(O)R^{y5a}$, $-N(R^{y5})S(O)_2R^{y5a}$, $-N(R^{y5})S(O)R^{y5a}$, $-N(R^{y5})C(O)OR^{y5a}$, $-N(R^{y5})C(O)N(R^{y5a}R^{y5b})$, $-OC(O)N(R^{y5}R^{y5a})$, and C_{1-6} alkyl; wherein C_{1-6} alkyl is optionally substituted with one or more halogen, which are the same or different; and each $-R^{y3}$, $-R^{y3a}$, $-R^{y4}$, $-R^{y4a}$, $-R^{y5}$, $-R^{y5a}$ and $-R^{y5b}$ is independently selected from the group consisting of $-H$, and C_{1-6} alkyl, wherein C_{1-6} alkyl is optionally substituted with one or more halogen, which are the same or different.

32. The conjugate or a pharmaceutically acceptable salt thereof of any one of claims 1 to 31, wherein $-L^2-$ is a C_{1-20} alkyl chain, which is optionally interrupted by one or more groups independently selected from $-O-$, $-T-$ and $-C(O)N(R^{y1})-$; and which C_{1-20} alkyl chain is optionally substituted with one or more groups independently selected from $-OH$, $-T$ and $-C(O)N(R^{y6}R^{y6a})$; wherein $-R^{y1}$, $-R^{y6}$, $-R^{y6a}$ are independently selected from the group consisting of H and C_{1-4} alkyl and wherein T is selected from the group consisting of phenyl, naphthyl, indenyl, indanyl, tetralinyl, C_{3-10} cycloalkyl, 3- to 10-membered heterocyclyl, 8- to 11-membered heterobicyclyl, 8- to 30-membered carbopolycyclyl, and 8- to 30-membered heteropolycyclyl.

33. The conjugate or a pharmaceutically acceptable salt thereof of any one of claims 1 to 32, wherein $-L^2-$ is of formula (IX-e)



wherein

the dashed line marked with the asterisk indicates attachment to $-L^1-$;

the unmarked dashed line indicates attachment to $-Z$; and

s_2 is an integer selected from the group consisting of 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19 and 20.

34. The conjugate or a pharmaceutically acceptable salt thereof of claim 33, wherein s_2 is 3.

35. A pharmaceutical composition comprising at least one conjugate or the pharmaceutically acceptable salt thereof of any one of claims 1 to 34 and at least one excipient.

36. The conjugate or a pharmaceutically acceptable salt thereof of any one of claims 1 to 34 or the pharmaceutical composition of claim 35 for use in ~~therapya method of treating cancer.~~

~~37. The conjugate or a pharmaceutically acceptable salt thereof or the pharmaceutical composition for use of claim 36, wherein the cancer is selected from the group consisting of sarcoma, chordoma, colon cancer, rectal cancer, colorectal cancer, pancreatic cancer, breast cancer, ovarian cancer, prostate cancer, squamous cell cancer, basal cell cancer, adenocarcinoma, sweat gland cancer, sebaceous gland cancer, papillary cancer, papillary adenocarcinomas, cystadenocarcinoma, medullary cancer, bronchogenic cancer, renal cell cancer, hepatoma, bile duct cancer, choriocarcinoma, seminoma, embryonal cancer, Wilms' tumor, cervical cancer, testicular cancer, gastric cancer, non-small cell lung cancer, small cell lung cancer, bladder cancer, renal cell carcinoma, urothelial cancer, epithelial cancer, glioma, astrocytoma, medulloblastoma, craniopharyngioma, ependymoma, pinealoma, hemangioblastoma, acoustic neuroma, oligodendroglioma, meningioma, melanoma, neuroblastoma, retinoblastoma, non-Hodgkin's lymphoma, cutaneous T-cell lymphoma, acute myeloid leukemia and leukemias.~~

~~38. The conjugate or a pharmaceutically acceptable salt thereof or the pharmaceutical composition for use of claim 36 or 37, wherein the conjugate or a pharmaceutically acceptable salt thereof or the pharmaceutical composition is administered to the patient prior to, simultaneously with, or after administration of one or more additional drug.~~

~~39. The conjugate or a pharmaceutically acceptable salt thereof or the pharmaceutical composition for use of claim 38, wherein the one or more additional drug is selected from the group consisting of pattern recognition receptor agonists (PRRA), cytotoxic/chemotherapeutic agents, immune checkpoint inhibitors or antagonists, immune checkpoint agonists, immune activating receptor agonists, multi-specific drugs, antibody drug conjugates (ADC), antibody adjuvant conjugates (AAC),~~

~~radionuclides or targeted radionuclide therapeutics, DNA damage repair inhibitors, tumor metabolism inhibitors, pattern recognition receptor agonists, protein kinase inhibitors, chemokine and chemoattractant receptor agonists, chemokine or chemokine receptor antagonists, cytokine receptor agonists, death receptor agonists, CD47 or SIRP α antagonists, oncolytic drugs, signal converter proteins, epigenetic modifiers, tumor peptides or tumor vaccines, heat shock protein (HSP) inhibitors, proteolytic enzymes, ubiquitin and proteasome inhibitors, adhesion molecule antagonists, hormones including hormone peptides and synthetic hormones, and adoptive cellular therapies such as Tumor Infiltrating Lymphocyte (TIL) therapy, Chimeric Antigen Receptor (CAR) therapy, T cell therapy, Natural Killer (NK) cell therapy, CAR T therapy, CAR NK therapy, CAR $\gamma\delta$ therapy, CAR Macrophage therapy, or any other cellular therapy with a genetically modified or genetically unmodified immune cell type.~~

~~40. The conjugate or a pharmaceutically acceptable salt thereof or the pharmaceutical composition for use of claim 36, wherein the conjugate or a pharmaceutically acceptable salt thereof or the pharmaceutical composition results in an expansion of $\gamma\delta$ T cells of at least 100-fold over baseline.~~

~~41.37. Use of the conjugate or a pharmaceutically acceptable salt thereof of any one of claims 1 to 34 or the pharmaceutical composition of claim 35 in the manufacture of a medicament for the treatment of cancer.~~

~~42.38. The use of claim 3741, wherein the cancer is selected from the group consisting of sarcoma, chordoma, colon cancer, rectal cancer, colorectal cancer, pancreatic cancer, breast cancer, ovarian cancer, prostate cancer, squamous cell cancer, basal cell cancer, adenocarcinoma, sweat gland cancer, sebaceous gland cancer, papillary cancer, papillary adenocarcinomas, cystadenocarcinoma, medullary cancer, bronchogenic cancer, renal cell cancer, hepatoma, bile duct cancer, choriocarcinoma, seminoma, embryonal cancer, Wilms' tumor, cervical cancer, testicular cancer, gastric cancer, non-small cell lung cancer, small cell lung cancer, bladder cancer, renal cell carcinoma, urothelial cancer, epithelial cancer, glioma, astrocytoma, medulloblastoma, craniopharyngioma, ependymoma, pinealoma, hemangioblastoma, acoustic neuroma, oligodendroglioma, meningioma, melanoma, neuroblastoma, retinoblastoma, non-~~

Hodgkin's lymphoma, cutaneous T-cell lymphoma, acute myeloid leukemia and leukemias.

5 ~~43.39.~~ The use of claim ~~3741~~ or ~~3842~~, wherein the conjugate or a pharmaceutically acceptable salt thereof or the pharmaceutical composition is to be administered to the patient prior to, simultaneously with, or after administration of one or more additional drug.

10 ~~44.40.~~ The use of claim ~~3943~~, wherein the one or more additional drug is selected from the group consisting of pattern recognition receptor agonists (PRRA), cytotoxic/chemotherapeutic agents, immune checkpoint inhibitors or antagonists, immune checkpoint agonists, immune activating receptor agonists, multi-specific drugs, antibody-drug conjugates (ADC), antibody-adjuvant conjugates (AAC), radionuclides or targeted radionuclide therapeutics, DNA damage repair inhibitors, tumor metabolism inhibitors, pattern recognition receptor agonists, protein kinase inhibitors, chemokine
15 and chemoattractant receptor agonists, chemokine or chemokine receptor antagonists, cytokine receptor agonists, death receptor agonists, CD47 or SIRP α antagonists, oncolytic drugs, signal converter proteins, epigenetic modifiers, tumor peptides or tumor vaccines, heat shock protein (HSP) inhibitors, proteolytic enzymes, ubiquitin and proteasome inhibitors, adhesion molecule antagonists, hormones including hormone
20 peptides and synthetic hormones, and adoptive cellular therapies such as Tumor Infiltrating Lymphocyte (TIL) therapy, Chimeric Antigen Receptor (CAR) therapy, T cell therapy, Natural Killer (NK) cell therapy, CAR-T therapy, CAR-NK therapy, CAR- $\gamma\delta$ therapy, CAR-Macrophage therapy, or any other cellular therapy with a genetically modified or genetically unmodified immune cell type.

25 ~~45. The use of claim 41, wherein the one or more additional drug is selected from the group consisting of pattern recognition receptor agonists (PRRA), cytotoxic/chemotherapeutic agents, immune checkpoint inhibitors or antagonists, immune checkpoint agonists, immune activating~~

30 ~~41. The use of claim 37 to 40, wherein the conjugate or a pharmaceutically acceptable salt thereof or the pharmaceutical composition results in an expansion of $\gamma\delta$ T cells of at least 100-fold over baseline.~~