

CLAIMS

1. A drug conjugate comprising at least two peptide ligands, which may be the same or different, each of which comprises a polypeptide comprising at least three reactive groups,
5 separated by at least two loop sequences, and a non-aromatic molecular scaffold which forms covalent bonds with the reactive groups of the polypeptide such that at least two polypeptide loops are formed on the molecular scaffold.
2. The drug conjugate as defined in claim 1, wherein said peptide ligands are specific for
10 the same or different targets.
3. The drug conjugate as defined in claim 1 or claim 2, wherein at least one of said peptide ligands is specific for an epitope present on a cancer cell.
- 15 4. The drug conjugate as defined in any one of claims 1 to 3, which comprises two peptide ligands, both of which are specific for the same target.
5. The drug conjugate as defined in any one of claims 1 to 4, wherein at least one of said peptide ligands is specific for Nectin-4.
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6. The drug conjugate as defined in claim 5, which comprises two peptide ligands, both of which are specific for Nectin-4.
7. The drug conjugate as defined in claim 5 or claim 6, which comprises two peptide
25 ligands, both of which are specific for Nectin-4 and both of which comprise the same peptide sequence.
8. The drug conjugate as defined in any one of claims 5 to 7, wherein said loop sequences comprise 3 or 9 amino acid acids.
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9. The drug conjugate as defined in any one of claims 5 to 8, wherein said loop sequences comprise three cysteine residues separated by two loop sequences one of which consists of 3 amino acids and the other of which consists of 9 amino acids.
- 35 10. The drug conjugate as defined in any one of claims 5 to 9, wherein the at least one of said peptide ligand specific for Nectin-4 has a core sequence of:

CP[1NaI][dD]CMKDWSTP[HyP]WC (SEQ ID NO: 1).

11. The drug conjugate as defined in any one of claims 5 to 10, wherein the at least one
5 of said peptide ligand specific for Nectin-4 has the full sequence of:

(β -Ala)-Sar₁₀-CP[1NaI][dD]CMKDWSTP[HyP]WC (SEQ ID NO: 2).

12. The drug conjugate as defined in any one of claims 1 to 11, wherein said reactive
10 groups comprise cysteine.

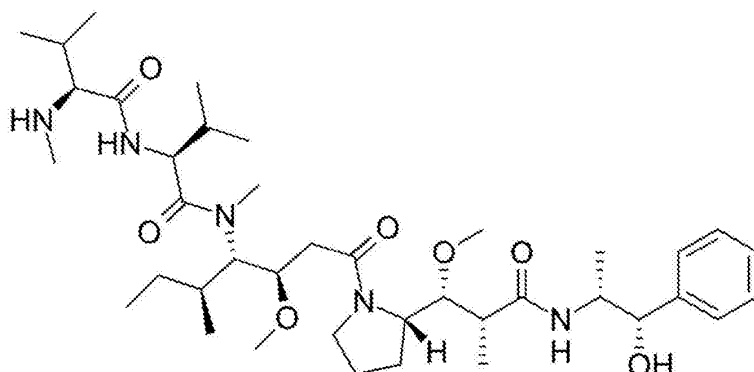
13. The drug conjugate as defined in any one of claims 1 to 12, wherein the non-
aromatic molecular scaffold is selected from 1,1',1''-(1,3,5-triazine-1,3,5-triyl)triprop-2-en-
1-one (TATA).

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14. The drug conjugate as defined in any one of claims 1 to 13, which is conjugated to
one or more active agents, such as small molecules, inhibitors, agonists, antagonists, partial
agonists and antagonists, inverse agonists and antagonists and cytotoxic agents.

- 20 15. The drug conjugate as defined in any one of claims 1 to 14, which is conjugated to
one or more cytotoxic agents.

16. The drug conjugate as defined in claim 15, wherein the cytotoxic agent is (S)-N-
((3R,4S,5S)-1-((S)-2-((1R,2R)-3-(((1S,2R)-1-hydroxy-1-phenylpropan-2-yl)amino)-1-
25 methoxy-2-methyl-3-oxopropyl)pyrrolidin-1-yl)-3-methoxy-5-methyl-1-oxoheptan-4-yl)-N,3-
dimethyl-2-((S)-3-methyl-2-(methylamino)butanamido)butanamide) (monomethyl auristatin E;
MMAE):



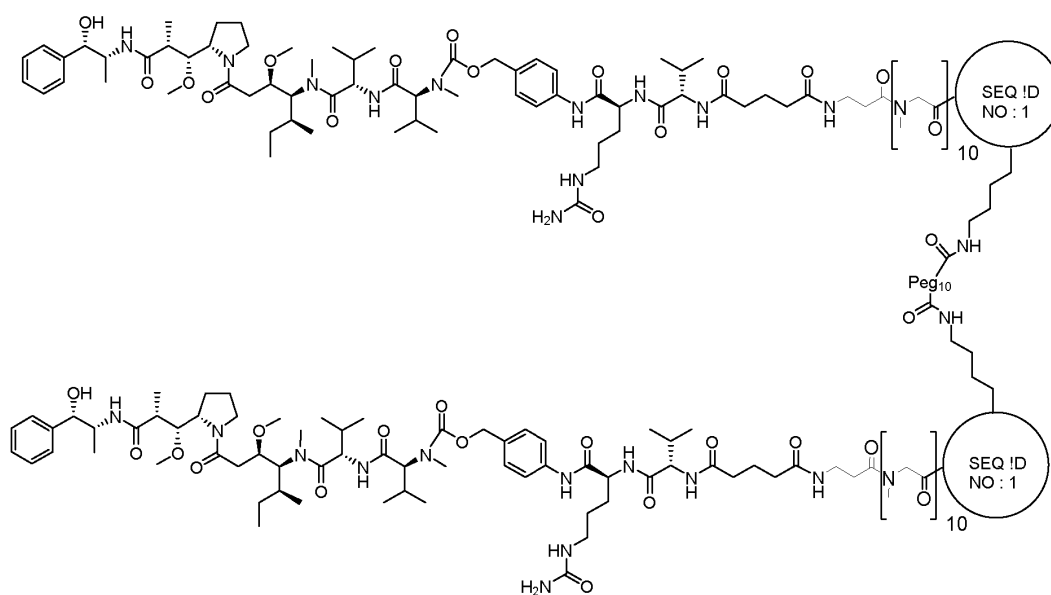
17. The drug conjugate as defined in claim 15 or claim 16, which additionally comprises a linker between said peptide ligand and each of said cytotoxic agents.

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18. The drug conjugate as defined in claim 17, wherein said linker is selected from one or more of: Val-Cit, β -Ala, p-aminobenzylcarbamate (PABC), Glu and one or more (e.g. 10) sarcosine (Sar) residues, such as a -PABC-Val-Cit-Glu- β Ala-Sar₁₀- linker, wherein said bicyclic peptides are joined at both lysine residues via a PEG10 moiety (i.e. the resultant bicyclic peptide drug conjugate comprises a (MMAE-PABC-Val-Cit-Glu- β Ala-Sar₁₀-Bicyclic peptide)-PEG₁₀-(Bicyclic peptide-Sar₁₀- β Ala-Glu-Cit-Val-PABC-MMAE) moiety).

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19. The drug conjugate as defined in any one of claims 15 to 18, which is a compound of formula (A):



BCY00008244

(A)

20. A pharmaceutical composition which comprises the drug conjugate of any one of
5 claims 1 to 19, in combination with one or more pharmaceutically acceptable excipients.
21. The drug conjugate as defined in any one of claims 1 to 19, for use in preventing,
suppressing or treating diseases.
- 10 22. The drug conjugate for use as defined in claim 21, wherein said disease is one which
may be alleviated by cell death
23. The drug conjugate for use as defined in claim 22, wherein said disease is selected
15 from diseases characterised by defective cell types, proliferative disorders such as cancer
and autoimmune disorders such as rheumatoid arthritis.