

CLAIMS

1. A peptide ligand specific for Nectin-4 comprising a polypeptide comprising at least three cysteine residues, separated by at least two loop sequences, and a molecular scaffold
5 which forms covalent bonds with the cysteine residues of the polypeptide such that at least two polypeptide loops are formed on the molecular scaffold, wherein the peptide ligand comprises the amino acid sequence:
$$C_iP[1NaI][dD]C_{ii}M[HArg]DWSTP[HyP]WC_{iii}$$
 (SEQ ID NO: 1);
wherein 1NaI represents 1-naphthylalanine, HArg represents homoarginine, HyP represents
10 hydroxyproline and C_i , C_{ii} and C_{iii} represent first, second and third cysteine residues, respectively or a pharmaceutically acceptable salt thereof.
2. The peptide ligand according to claim 1, which comprises an amino acid sequence selected from:
15 [B-Ala][Sar10]-(SEQ ID NO: 1) (hereinafter referred to as BCY8234);
Ac-[B-Ala][Sar₅]- (SEQ ID NO: 1) (hereinafter referred to as BCY8122);
Ac-(SEQ ID NO: 1) (hereinafter referred to as BCY8126);
(SEQ ID NO: 1) (hereinafter referred to as BCY8116);
Fluorescein-(SEQ ID NO: 1) (hereinafter referred to as BCY8205); and
20 [PYA][B-Ala][Sar10]-(SEQ ID NO: 1) (hereinafter referred to as BCY8846).
3. The peptide ligand according to claim 1 or claim 2, which comprises an amino acid sequence selected from:
[B-Ala][Sar10]-(SEQ ID NO: 1) (hereinafter referred to as BCY8234);
25 Ac-[B-Ala][Sar₅]- (SEQ ID NO: 1) (hereinafter referred to as BCY8122);
Ac-(SEQ ID NO: 1) (hereinafter referred to as BCY8126);
(SEQ ID NO: 1) (hereinafter referred to as BCY8116); and
Fluorescein-(SEQ ID NO: 1) (hereinafter referred to as BCY8205).
- 30 4. The peptide ligand according to any one of claims 1 to 3, which comprises an amino acid sequence selected from:
Ac-[B-Ala][Sar₅]- (SEQ ID NO: 1) (hereinafter referred to as BCY8122);
Ac-(SEQ ID NO: 1) (hereinafter referred to as BCY8126); and
(SEQ ID NO: 1) (hereinafter referred to as BCY8116).

5. The peptide ligand according to any one of claims 1 to 4, which comprises an amino acid sequence selected from:

Ac-[B-Ala][Sar₅]- (SEQ ID NO: 1) (hereinafter referred to as BCY8122); and

Ac- (SEQ ID NO: 1) (hereinafter referred to as BCY8126).

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6. The peptide ligand according to any one of claims 1 to 3, which comprises an amino acid sequence selected from:

[B-Ala][Sar₁₀]- (SEQ ID NO: 1) (hereinafter referred to as BCY8234).

10 7. The peptide ligand according to any one of claims 1 to 6, wherein the molecular scaffold is selected from 1,1',1''-(1,3,5-triazinane-1,3,5-triyl)triprop-2-en-1-one (TATA).

8. The peptide ligand according to any one of claims 1 to 7, wherein the pharmaceutically acceptable salt is selected from the free acid or the sodium, potassium, calcium, ammonium salt.

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9. The peptide ligand according to any one of claims 1 to 8, wherein the Nectin-4 is human Nectin-4.

20 10. A drug conjugate comprising a peptide ligand as defined in any one of claims 1 to 9, conjugated to one or more effector and/or functional groups.

11. The drug conjugate as defined in claim 10, conjugated to one or more cytotoxic agents.

25 12. The drug conjugate as defined in claim 11, wherein said cytotoxic agent is selected from MMAE or DM1, in particular MMAE.

13. The drug conjugate as defined in claim 12, wherein the cytotoxic agent is MMAE and said conjugate additionally comprises a linker selected from: -PABC-Cit-Val-Glutaryl- or -PABC-cyclobutyl-Ala-Cit-βAla-, such as -PABC-Cit-Val-Glutaryl-, wherein PABC represents p-aminobenzylcarbamate.

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14. The drug conjugate as defined in claim 13, wherein the cytotoxic agent is DM1 and said conjugate additionally comprises a linker which is -SPDB-(SO₃H)-, wherein SPDB represents N-succinimidyl 3-(2-pyridyldithio)propionate.

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15. The drug conjugate as defined in any one of claims 10 to 14, which is selected from: BCY8245 or BCY8549, in particular BCY8245.

16. A pharmaceutical composition which comprises the peptide ligand of any one of
5 claims 1 to 9 or the drug conjugate of any one of claims 10 to 15, in combination with one or more pharmaceutically acceptable excipients.

17. The pharmaceutical composition as defined in claim 16, which additionally comprises one or more therapeutic agents.

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18. The drug conjugate as defined in any one of claims 10 to 15, for use in preventing, suppressing or treating a disease or disorder mediated by Nectin-4.

19. A method of preventing, suppressing or treating cancer, which comprises
15 administering to a patient in need thereof the drug conjugate as defined in any one of claims 10 to 15, wherein said patient is identified as having an increased copy number variation (CNV) of Nectin-4.