

CLAIMS

1. A peptide ligand specific for EphA2 comprising a polypeptide comprising at least three cysteine residues, separated by at least two loop sequences, and a non-aromatic molecular scaffold 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:

$$C_i(\text{HyP})\text{LVNPLC}_{ii}\text{LHP}(\text{D-Asp})\text{W}(\text{HArg})\text{C}_{iii}$$
 (SEQ ID NO: 1);
 wherein HyP is hydroxyproline, HArg is homoarginine 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 as defined in claim 1, wherein the molecular scaffold is 1,1',1''-(1,3,5-triazinane-1,3,5-triyl)triprop-2-en-1-one (TATA).
3. The peptide ligand as defined in claim 1 or claim 2, wherein the peptide ligand comprises the amino acid sequence:

$$(\beta\text{-Ala})\text{-Sar}_{10}\text{-A}(\text{HArg})\text{D-}C_i(\text{HyP})\text{LVNPLC}_{ii}\text{LHP}(\text{D-Asp})\text{W}(\text{HArg})\text{C}_{iii}$$
 (SEQ ID NO: 2) (BCY6099);
 wherein Sar is sarcosine, HArg is homoarginine and HyP is hydroxyproline.
4. The peptide ligand as defined in any one of claims 1 to 3, wherein the pharmaceutically acceptable salt is selected from the free acid or the sodium, potassium, calcium, ammonium salt.
5. The peptide ligand as defined in any one of claims 1 to 4, wherein the EphA2 is human EphA2.
6. A drug conjugate comprising a peptide ligand as defined in any one of claims 1 to 5, conjugated to one or more effector and/or functional groups, such as a cytotoxic agent.
7. The drug conjugate as defined in claim 6, wherein said cytotoxic agent is selected from DM1 or MMAE.
8. The drug conjugate as defined in claim 7, wherein said cytotoxic agent is selected from MMAE.

9. The drug conjugate as defined in any one of claims 6 to 8, which additionally comprises a linker between said peptide ligand and said cytotoxic agents.

10. The drug conjugate as defined in claim 9, wherein said cytotoxic agent is MMAE and
5 the linker is selected from: -Val-Cit-, -Trp-Cit-, -Val-Lys-, -D-Trp-Cit-, -Ala-Ala-Asn-, D-Ala-Phe-Lys- or -Glu-Pro-Cit-Gly-hPhe-Tyr-Leu- (SEQ ID NO: 3).

11. The drug conjugate as defined in claim 10, wherein said cytotoxic agent is MMAE and the linker is -Val-Cit-.

10

12. The drug conjugate as defined in claim 9, wherein said cytotoxic agent is DM1 and the linker is selected from: -S-S-, -SS(SO₃H)-, -SS-(Me)-, -(Me)-SS-(Me)-, -SS-(Me₂)- or -SS-(Me)-SO₃H-.

15 13. The drug conjugate as defined in claim 12, wherein said cytotoxic agent is DM1 and the linker is selected from: -S-S- and -SS(SO₃H)-.

14. The drug conjugate as defined in any one of claims 6 to 13, which is selected from any one of BCY6027, BCY6028, BCY61535, BCY6136, BCY6173, BCY6174 and BCY6175.

20

15. The drug conjugate as defined in claim 14, which is selected from any one of: BCY6031, BCY6033, BCY6082, BCY6135, BCY6136, BCY6173, BCY6174 and BCY6175.

16. The drug conjugate as defined in claim 14 or claim 15, which is BCY6136.

25

17. A pharmaceutical composition which comprises the peptide ligand of any one of claims 1 to 5 or the drug conjugate of any one of claims 6 to 16, in combination with one or more pharmaceutically acceptable excipients.

30 18. The drug conjugate as defined in any one of claims 6 to 16, for use in preventing, suppressing or treating a disease or disorder characterised by overexpression of EphA2 in diseased tissue.

19. The drug conjugate as defined in any one of claims 6 to 16, for use in preventing,
35 suppressing or treating cancer.

20. The drug conjugate for use as defined in claim 19, wherein the cancer is selected from: prostate cancer, lung cancer (such as non-small cell lung carcinomas (NSCLC)), breast cancer (such as triple negative breast cancer), gastric cancer, ovarian cancer, oesophageal cancer, multiple myeloma and fibrosarcoma.

5

21. A method of preventing, suppressing or treating cancer, which comprises administering to a patient in need thereof a drug conjugate as defined in any one of claims 6 to 16, wherein said patient is identified as having an increased copy number variation (CNV) of EphA2.

10