

CLAIMS

1. A peptide ligand specific for EphA2, or a pharmaceutically acceptable salt or modified derivative thereof, the peptide ligand comprising a polypeptide comprising three cysteine residues, separated by two loop sequences, and a non-aromatic molecular scaffold which forms covalent bonds with the cysteine residues of the polypeptide such that two polypeptide loops are formed on the molecular scaffold, wherein the peptide ligand is a peptide ligand which comprises an amino acid selected from sequence other than:

~~———Ci(HyP)LVNPLCiLHP(D-Asp)W(HArg)Ciii (SEQ ID NO: 1), wherein HyP is hydroxyproline, HArg is homoarginine and Ci, Cii and Ciii represent first, second and third cysteine residues, respectively or a pharmaceutically acceptable salt thereof~~

(β-Ala)-Sar₁₀-A(HArg)DC(HyP)LVNPLCLHP(D-Asp)W(HArg)C (SEQ ID NO: 2);

ACMNDWWCAMGWKCA (SEQ ID NO: 3);

ACVPDRRCAYMNVCA (SEQ ID NO: 4);

ACVVDGRCAYMNVCA (SEQ ID NO: 5);

ACVDSRCAYMNVCA (SEQ ID NO: 6);

ACVPDSRCAYMNVCA (SEQ ID NO: 7);

ACYVGKECAIRNVCA (SEQ ID NO: 8);

ACYVGKECAYMNVCA (SEQ ID NO: 9);

ARDCPLVNPLCLHPGWTC (SEQ ID NO: 10);

A(HArg)DCPLVNPLCLHPGWTC (SEQ ID NO: 11);

CPLVNPLCLHPGWTCCLHG (SEQ ID NO: 12);

CPLVNPLCLHPGWTCCL(D-His)G (SEQ ID NO: 13);

CPLVNPLCLHPGWSCRGO (SEQ ID NO: 14);

CPLVNPLCLHPGWSC(HArg)GQ (SEQ ID NO: 15);

ACVPDRRCAYMNVCA (SEQ ID NO: 16);

DLRCGGDPRCAYMNVCA (SEQ ID NO: 17);

SRPCVIDSRCAYMNVCA (SEQ ID NO: 18);

ESRCSPDARCAVMNVCA (SEQ ID NO: 19);

HSGCRPDPRCAVMNVCA (SEQ ID NO: 20);

GSGCKPDSRCAYMNVCA (SEQ ID NO: 21);

ETVCLPDSRCAYMNVCA (SEQ ID NO: 22);

GQVCIVDARCAVMNVCA (SEQ ID NO: 23);

ACVPDRRCAFENVCDH (SEQ ID NO: 24);

ACVPDRRCAFMNVCEDR (SEQ ID NO: 25);

ACVPDRRCAFQDVCDHE (SEQ ID NO: 26);

ACVPDRRCAFRDVCLTG (SEQ ID NO: 27);

ACQPSNHCAFMNYCA (SEQ ID NO: 28);
ACSPTPACAVQNLCA (SEQ ID NO: 29);
ACTSCWAYPDSFCA (SEQ ID NO: 30);
ACTKPTGFCAYPDTICA (SEQ ID NO: 31);
ACRGEWGYCAYPDTICA (SEQ ID NO: 32);
ACRNWGMYCAYPDTICA (SEQ ID NO: 33);
ACPDWGKYCAYPDTICA (SEQ ID NO: 34);
ACRVYGPYCAYPDTICA (SEQ ID NO: 35);
ACSSCWAYPDSVCA (SEQ ID NO: 36);
ACQSCWAYPDTYCA (SEQ ID NO: 37);
ACGFMGLEPCETFCA (SEQ ID NO: 38);
ACGFMGLVPCEVHCA (SEQ ID NO: 39);
ACGFMGLEPCEMVCA (SEQ ID NO: 40);
ACGFMGLEPCVTYCA (SEQ ID NO: 41);
ACGFMGLEPCELVCA (SEQ ID NO: 42);
ACGFMGLVPCNVFCA (SEQ ID NO: 43);
ACGFMGLEPCELFCA (SEQ ID NO: 44);
ACGFMGLEPCELCMPK (SEQ ID NO: 45);
ACGFMGLEPCELYCA (SEQ ID NO: 46);
ACGFMGLEPCELYCAHT (SEQ ID NO: 47);
ACGFMGLEPCEMYCA (SEQ ID NO: 48);
ACGFMGLVPCELYCADN (SEQ ID NO: 49);
ACPLVNPLCLTSGWKCA (SEQ ID NO: 50);
ACPMVNPLCLHPGWICA (SEQ ID NO: 51);
ACPLVNPLCLHPGWICA (SEQ ID NO: 52);
ACPLVNPLCLHPGWRCA (SEQ ID NO: 53);
ACPLVNPLCNLPGWTCA (SEQ ID NO: 54);
ACPLVNPLCLVPGWSCA (SEQ ID NO: 55);
ACPLVNPLCLLDGWTCA (SEQ ID NO: 56);
ACPLVNPLCLMPGWGCA (SEQ ID NO: 57);
ACPLVNPLCMIGNWTCA (SEQ ID NO: 58);
ACPLVNPLCLMTGWSCA (SEQ ID NO: 59);
ACPLVNPLCMMGGWKCA (SEQ ID NO: 60);
ACPLVNPLCLYGSWKCA (SEQ ID NO: 61);
ACPLVNPLCLHPGWTCA (SEQ ID NO: 62);
ARDCPLVNPLCLHPGWTCA (SEQ ID NO: 63);
RPACPLVNPLCLHPGWTCA (SEQ ID NO: 64);

RPPCPLVNPLCLHPGWTCA (SEQ ID NO: 65);
KHSCPLVNPLCLHPGWTCA (SEQ ID NO: 66);
ACPLVNPLCLHPGWTCLHG (SEQ ID NO: 67);
ACPLVNPLCLHPGWTCL(D-His)G (SEQ ID NO: 68);
ACPLVNPLCLHPG(2Nal)TCLHG (SEQ ID NO: 69);
RHDCPLVNPLCLLPGWTCA (SEQ ID NO: 70);
TPRCPLVNPLCLMPGWTCA (SEQ ID NO: 71);
ACPLVNPLCLAPGWTCA (SEQ ID NO: 72);
ACPLVNPLCLAPGWTCSRS (SEQ ID NO: 73);
ACPLVNPLCLEPGWTCA (SEQ ID NO: 74);
ACPLVNPLCLEPGWTCAKR (SEQ ID NO: 75);
ACPLVNPLCLHPGWSCA (SEQ ID NO: 76);
ACPLVNPLCLHPGWSCRGO (SEQ ID NO: 77);
ACPLVNPLCLHPGWSC(HArg)GQ (SEQ ID NO: 78);
ACPLVNPLCLHPG(2Nal)SCRGO (SEQ ID NO: 79);
ACPLVNPLCLTPGWTCTNT (SEQ ID NO: 80);
ACPMVNPLCLHPGWKCA (SEQ ID NO: 81);
ACPMVNPLCLTPGWICA (SEQ ID NO: 82);
ACPMVNPLCLHPGWTCA (SEQ ID NO: 83);
H(D-Asp)VT-C(Aib)(1Nal)G(Aib)F(1Nal)CP(tBuGly)N(HArg)P(D-Asp)C (SEQ ID NO: 84);
A(HArg)DC(HyP)(Hse(Me))VNPLCLHP(D-Asp)W(HArg)C (SEQ ID NO: 85);
A(HArg)DC(HyP)(Hse(Me))VNPLCLHP(D-Asp)WTC (SEQ ID NO: 86);
A(HArg)DC(HyP)LVNPLCLHP(D-Ala)WTC (SEQ ID NO: 87);
A(HArg)DCPLVNPLCLHP(D-Ala)WTC (SEQ ID NO: 88);
ARDC(HyP)LVNPLCLHPGWTC (SEQ ID NO: 89);
ARDCPLVNPLCL(D-3,3-DPA)PGWTC (SEQ ID NO: 90);
ARDCPLVNPLCLHPGWTCLH (SEQ ID NO: 91);
A(HArg)DCPLVNPLCLHP(D-Cya)WTC (SEQ ID NO: 92);
A(D-Arg)DC(HyP)LVNPLCL(D-3,3-DPA)P(D-Asp)W(HArg)C (SEQ ID NO: 93); and
CPLVNPLCLHPGWTC (SEQ ID NO: 97);

wherein HyP is hydroxyproline, HArg is homoarginine, Sar is sarcosine, HArg is
homoarginine, D-Asp is D-aspartic acid, 2Nal is 2-naphthylalanine, 1Nal is 1-
naphthylalanine, Aib is 2-aminoisobutyric acid, tBuGly is tert-leucine, hSerMe is
homoserine(methyl), D-Ala is D-alanine, D-3,3-DPA is 3,3-diphenyl-D-alanine, D-Cya is D-
cysteic acid, D-Arg is D-arginine, HPhe is homophenylalanine, and D-His is D-histidine.

~~2. The peptide ligand as defined in claim 1, wherein said loop sequences comprise 2, 3, 5, 6 or 7 amino acid acids.~~

~~3. The peptide ligand as defined in claim 1 or claim 2, wherein said loop sequences comprise three cysteine residues separated by two loop sequences one of which consists of 2 amino acids and the other of which consists of 7 amino acids (such as those listed in Table 4).~~

~~4. The peptide ligand as defined in claim 1 or claim 2, wherein said loop sequences comprise three cysteine residues separated by two loop sequences both of which consist of 5 amino acids (such as those listed in Tables 3 and 4).~~

~~5. The peptide ligand as defined in claim 1 or claim 2, wherein said loop sequences comprise three cysteine residues separated by two loop sequences both of which consist of 6 amino acids (such as those listed in Tables 3 to 5 and 10).~~

~~6. The peptide ligand as defined in claim 1 or claim 2, wherein said loop sequences comprise three cysteine residues separated by two loop sequences one of which consists of 7 amino acids and the other of which consists of 3 amino acids (such as those listed in Table 4).~~

~~7. The peptide ligand as defined in claim 1 or claim 2, wherein said loop sequences comprise three cysteine residues separated by two loop sequences one of which consists of 6 amino acids and the other of which consists of 7 amino acids (such as those listed in Table 5).~~

~~8. The peptide ligand as defined in any one of claims 1 to 7, wherein the peptide ligand comprises an amino acid sequence selected from:~~

~~—C_i-X₁-C_{ii}-X₂-C_{iii}—~~

~~wherein X₁ and X₂ represent the amino acid residues between the cysteine residues listed in Tables 3 to 5 and 10 and C_i, C_{ii} and C_{iii} represent first, second and third cysteine residues, respectively or a pharmaceutically acceptable salt thereof.~~

~~9. The peptide ligand as defined in any one of claims 1 to 8, wherein the peptide ligand comprises a peptide ligand selected from Tables 3 to 5 and 10.~~

~~10. The peptide ligand as defined in any one of claims 1 to 8, wherein said loop sequences comprise three cysteine residues separated by two loop sequences both of which consist of 6 amino acids and the peptide ligand has the following amino acid sequence:~~

~~C_iPLVNPLC_{ii}LHPGWTC_{iii} (SEQ ID NO: 97);~~

~~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.~~

~~11. The peptide ligand as defined in claim 10, wherein said loop sequences comprise three cysteine residues separated by two loop sequences both of which consist of 6 amino acids and the peptide ligand has the following amino acid sequence:~~

~~((β-Ala)-Sar₁₀-A(HArg)D-C_iPLVNPLC_{ii}LHPGWTC_{iii}((β-Ala)-Sar₁₀-(SEQ ID NO: 11)) (BCY6014; Compound 67);~~

~~wherein Sar is sarcosine, HArg is homoarginine and HyP is hydroxyproline.~~

~~12. The peptide ligand as defined in any one of claims 1 to 11, wherein the molecular scaffold is selected from 1,1',1''-(1,3,5-triazinane-1,3,5-triyl)triprop-2-en-1-one (TATA) and the peptide ligand is selected from any one of the peptide ligands listed in Tables 3, 4, 5 and 10.~~

~~13. The peptide ligand as defined in any one of claims 1 or claim 2 to 11, wherein the molecular scaffold is selected from 1,1',1''-(1,3,5-triazinane-1,3,5-triyl)triprop-2-en-1-one (TATA) and the peptide ligand is~~

~~((β-Ala)-Sar₁₀-A(HArg)D-C_iPLVNPLC_{ii}LHPGWTC_{iii}((β-Ala)-Sar₁₀-(SEQ ID NO: 11)) (BCY6014; Compound 67);~~

~~wherein Sar is sarcosine, HArg is homoarginine and HyP is hydroxyproline.~~

~~14. The peptide ligand as defined in any one of claims 1 to 13, wherein said peptide ligand is selected from:~~

~~ACMNDWWCAMGWKCA-Sar6-K(FI) ((SEQ ID NO: 3)-Sar6-K(FI));~~

~~ACVPDRRCAYMNVCA-Sar6-K(FI) ((SEQ ID NO: 4)-Sar6-K(FI));~~

~~ACVVDGRCAYMNVCA-Sar6-K(FI) ((SEQ ID NO: 5)-Sar6-K(FI));~~

~~ACVDSRCAYMNVCA-Sar6-K(FI) ((SEQ ID NO: 6)-Sar6-K(FI));~~

~~ACVPDSRCAYMNVCA-Sar6-K(FI) ((SEQ ID NO: 7)-Sar6-K(FI));~~

~~ACYVGKECAIRNVCA-Sar6-K(FI) ((SEQ ID NO: 8)-Sar6-K(FI));~~

~~ACYVGKECAYMNVCA-Sar6-K(FI) ((SEQ ID NO: 9)-Sar6-K(FI));~~

FI-G-Sar5-ACYVGKECAYMNVCA (FI-G-Sar5-(SEQ ID NO: 9));
 FI-(β -Ala)-Sar10-ARDCPLVNPLCLHPGWTC (FI-(β -Ala)-Sar10-(SEQ ID NO: 10));
 FI-(β -Ala)-Sar10-A(HArg)DCPLVNPLCLHPGWTC (FI-(β -Ala)-Sar10-(SEQ ID NO: 11));
 Ac-CPLVNPLCLHPGWTCCLHG-Sar6-(D-K[FI]) (Ac-(SEQ ID NO: 12)-Sar6-(D-K[FI]));
 Ac-CPLVNPLCLHPGWTCCL(D-His)G-Sar6-(D-K[FI]) (Ac-SEQ ID NO: 13)-Sar6-(D-K[FI]));
 Ac-CPLVNPLCLHPGWSCRQG-Sar6-(D-K[FI]) (Ac-(SEQ ID NO: 14)- Sar6-(D-K[FI]));
 Ac-CPLVNPLCLHPGWSC(HArg)GQ-Sar6-(D-K[FI]) (Ac-(SEQ ID NO: 15)- Sar6-(D-K[FI]));
 ACMNDWWCAMGWKCA (SEQ ID NO: 3);
 ACVPDRRCAYMNVCA (SEQ ID NO: 4);
 (β -Ala)-Sar10-ACVPDRRCAYMNVCA ((β -Ala)-Sar10-(SEQ ID NO: 16));
 DLRCGGDPRCAYMNVCA (SEQ ID NO: 17);
 SRPCVIDSRCAYMNVCA (SEQ ID NO: 18);
 ESRCSPPDARCAVMNVCA (SEQ ID NO: 19);
 HSGCRPDPRCAYMNVCA (SEQ ID NO: 20);
 GSGCKPDSRCAYMNVCA (SEQ ID NO: 21);
 ETVCLPDSRCAYMNVCA (SEQ ID NO: 22);
 GQVCIVDARCAVMNVCA (SEQ ID NO: 23);
 ACVPDRRCAFENVCDH (SEQ ID NO: 24);
 ACVPDRRCAFMNVCEDR (SEQ ID NO: 25);
 ACVPDRRCAFQDVCDHE (SEQ ID NO: 26);
 ACVPDRRCAFRDVCLTG (SEQ ID NO: 27);
 ACYVGKECAYMNVCA (SEQ ID NO: 9);
 ACQPSNHCAFMYNYCA (SEQ ID NO: 28);
 ACSPTPACAVQNLCA (SEQ ID NO: 29);
 ACTSCWAYPDSFCA (SEQ ID NO: 30);
 ACTKPTGFCAYPDTICA (SEQ ID NO: 31);
 ACRGEWGYCAYPDTICA (SEQ ID NO: 32);
 ACRNWGMYCAYPDTICA (SEQ ID NO: 33);
 ACPDWGKYCAYPDTICA (SEQ ID NO: 34);
 ACRVYGPYCAYPDTICA (SEQ ID NO: 35);
 ACSSCWAYPDSVCA (SEQ ID NO: 36);
 ACQSCWAYPDTYCA (SEQ ID NO: 37);
 ACGFMGLEPCETFCA (SEQ ID NO: 38);
 ACGFMGLVPCEVHCA (SEQ ID NO: 39);

ACGFMGLEPCCEMVCA (SEQ ID NO: 40);
 ACGFMGLEPCVTYCA (SEQ ID NO: 41);
 ACGFMGLEPCELVCA (SEQ ID NO: 42);
 ACGFMGLVPCNVFCA (SEQ ID NO: 43);
 ACGFMGLEPCELFCA (SEQ ID NO: 44);
 ACGFMGLEPCELCMPK (SEQ ID NO: 45);
 ACGFMGLEPCELYCA (SEQ ID NO: 46);
 ACGFMGLEPCELYCAHT (SEQ ID NO: 47);
 ACGFMGLEPCEMYCA (SEQ ID NO: 48);
 ACGFMGLVPCELYCADN (SEQ ID NO: 49);
 ACPLVNPLCLTSGWKCA (SEQ ID NO: 50);
 ACPMVNPLCLHPGWICA (SEQ ID NO: 51);
 ACPLVNPLCLHPGWICA (SEQ ID NO: 52);
 ACPLVNPLCLHPGWRCA (SEQ ID NO: 53);
 ACPLVNPLCNLPGWTCA (SEQ ID NO: 54);
 ACPLVNPLCLVPGWSCA (SEQ ID NO: 55);
 ACPLVNPLCLLDGWTCA (SEQ ID NO: 56);
 ACPLVNPLCLMPGWGCA (SEQ ID NO: 57);
 ACPLVNPLCMIGNWTCA (SEQ ID NO: 58);
 ACPLVNPLCLMTGWSCA (SEQ ID NO: 59);
 ACPLVNPLCMMGGWKCA (SEQ ID NO: 60);
 ACPLVNPLCLYGSWKCA (SEQ ID NO: 61);
 ACPLVNPLCLHPGWTCA (SEQ ID NO: 62);
 ARDCPLVNPLCLHPGWTCA (SEQ ID NO: 63);
 (β -Ala)-Sar10-A(HArg)DCPLVNPLCLHPGWTCA ((β -Ala)-Sar10-(SEQ ID NO: 11);
 Ac-ARDCPLVNPLCLHPGWTCA-Sar6-(D-K) (Ac-(SEQ ID NO: 63)-Sar6-(D-K));
 Ac-A(HArg)DCPLVNPLCLHPGWTCA- Sar6-(D-K) (Ac-(SEQ ID NO: 11)-A-Sar6-(D-K));
 RPACPLVNPLCLHPGWTCA (SEQ ID NO: 64);
 RPPCPLVNPLCLHPGWTCA (SEQ ID NO: 65);
 KHSCPLVNPLCLHPGWTCA (SEQ ID NO: 66);
 ACPLVNPLCLHPGWTCLHG (SEQ ID NO: 67);
 Ac-CPLVNPLCLHPGWTCLHG (Ac-(SEQ ID NO: 12));
 (β -Ala)-Sar10-ACPLVNPLCLHPGWTCLHG ((β -Ala)-Sar10-(SEQ ID NO: 67));
 (β -Ala)-Sar10-ACPLVNPLCLHPGWTCL(D-His)G ((β -Ala)-Sar10-(SEQ ID NO: 68));
 Ac-CPLVNPLCLHPGWTCLHG-Sar6-(D-K) (Ac-(SEQ ID NO: 12)-Sar6-(D-K));
 Ac-CPLVNPLCLHPGWTCL(D-His)G-Sar6-(D-K) (Ac-(SEQ ID NO: 13)- Sar6-(D-K));

ACPLVNPLCLHPG(2NaI)TCLHG (SEQ ID NO: 69);
 RHDCPLVNPLCLLPGWTC (SEQ ID NO: 70);
 TPRCPLVNPLCLMPGWTC (SEQ ID NO: 71);
 ACPLVNPLCLAPGWTC (SEQ ID NO: 72);
 ACPLVNPLCLAPGWTCRS (SEQ ID NO: 73);
 ACPLVNPLCLEPGWTC (SEQ ID NO: 74);
 ACPLVNPLCLEPGWTCAR (SEQ ID NO: 75);
 ACPLVNPLCLHPGWSCA (SEQ ID NO: 76);
 ACPLVNPLCLHPGWSCRQ (SEQ ID NO: 77);
 Ac-CPLVNPLCLHPGWSCRQ (Ac-(SEQ ID NO: 14));
 ((β -Ala)-Sar10-ACPLVNPLCLHPGWSCRQ ((β -Ala)-Sar10-(SEQ ID NO: 77);
 ((β -Ala)-Sar10-ACPLVNPLCLHPGWSC(HArg)GQ ((β -Ala)-Sar10-(SEQ ID NO: 78));
 Ac-CPLVNPLCLHPGWSCRQ-Sar6-(D-K) (Ac-(SEQ ID NO: 14)-Sar6-(D-K));
 Ac-CPLVNPLCLHPGWSC(HArg)GQ-Sar6-(D-K) (Ac-(SEQ ID NO: 15) -Sar6-(D-K));
 ACPLVNPLCLHPG(2NaI)SCRQ (SEQ ID NO: 79);
 ACPLVNPLCLTPGWTCNT (SEQ ID NO: 80);
 ACPMVNPLCLHPGWKCA (SEQ ID NO: 81);
 ACPMVNPLCLTPGWICA (SEQ ID NO: 82);
 ACPMVNPLCLHPGWTC (SEQ ID NO: 83);
 ((β -Ala)-Sar10-H(D-Asp)VT-C(Aib)(1NaI)G(Aib)F(1NaI)CP(tBuGly)N(HArg)P(D-Asp)C
 ((β -Ala)-Sar10-(SEQ ID NO: 84));
 ((β -Ala)-Sar10-A(HArg)DC(HyP)(Hse(Me))VNPLCLHP(D-Asp)W(HArg)C ((β -Ala)-
 Sar10-(SEQ ID NO: 85));
 ((β -Ala)-Sar10-A(HArg)DC(HyP)(Hse(Me))VNPLCLHP(D-Asp)WTC ((β -Ala)-Sar10-
 (SEQ ID NO: 86));
 ((β -Ala)-Sar10-A(HArg)DC(HyP)LVNPLCLHP(D-Ala)WTC ((β -Ala)-Sar10-(SEQ ID
 NO: 87));
 ((β -Ala)-Sar10-A(HArg)DCPLVNPLCLHP(D-Ala)WTC ((β -Ala)-Sar10-(SEQ ID NO:
 88));
 ((β -Ala)-Sar10-ARDC(HyP)LVNPLCLHPGWTC ((β -Ala)-Sar10-(SEQ ID NO: 89));
 ((β -Ala)-Sar10-ARDCPLVNPLCL(D-3,3-DPA)PGWTC ((β -Ala)-Sar10-(SEQ ID NO:
 90));
 ((β -Ala)-Sar10-ARDCPLVNPLCLHPGWTC (LH ((β -Ala)-Sar10-(SEQ ID NO: 91))
 Ac-(SEQ ID NO: 12)-Sar6-(D-K[Ac]);
 ((β -AlaSO₃H)-Sar4-(Cya)-Sar4-(Cya)-A(HArg)DCPLVNPLCLHP(D-Cya)WTC ((β -
 AlaSO₃H)-Sar4-(Cya)-Sar4-(Cya)-(SEQ ID NO: 92));
 ((β -Ala)-Sar10-ARDCPLVNPLCLHPGWTC ((β -Ala)-Sar10-(SEQ ID NO: 10));

A(HArg)DCPLVNPLCLHPGWTC (SEQ ID NO: 11);
 (β-Ala)-Sar5-(SEQ ID NO: 11);
 (β-AlaSO₃H)-Sar10-(SEQ ID NO: 11);
 (β-Ala)-Sar10-A(D-Arg)DC(HyP)LVNPLCL(D-3,3-DPA)P(D-Asp)W(HArg)C ((β-Ala)-Sar10-(SEQ ID NO: 93)); and
 (β-AlaSO₃H)-Sar5-(SEQ ID NO: 11);
 or a pharmaceutically acceptable salt thereof.

15. The peptide ligand as defined in any one of claims 1 to 13, wherein said peptide ligand is (β-Ala)-Sar10-A(HArg)DCPLVNPLCLHPGWTC ((β-Ala)-Sar10-(SEQ ID NO: 11) or a pharmaceutically acceptable salt thereof.

16. The peptide ligand as defined in any one of claims 1 to 15, wherein the pharmaceutically acceptable salt is selected from a free acid or a sodium, potassium, calcium, ammonium salt.

17. The peptide ligand as defined in any one of claims 1 to 16, wherein the EphA2 is human EphA2.

18. A drug conjugate comprising a peptide ligand as defined in any one of claims 1 to 17, conjugated to one or more effector and/or functional groups.

19. The drug conjugate as defined in claim 18, wherein said functional group is a cytotoxic agent selected from DM1 or monomethyl auristatin E (MMAE).

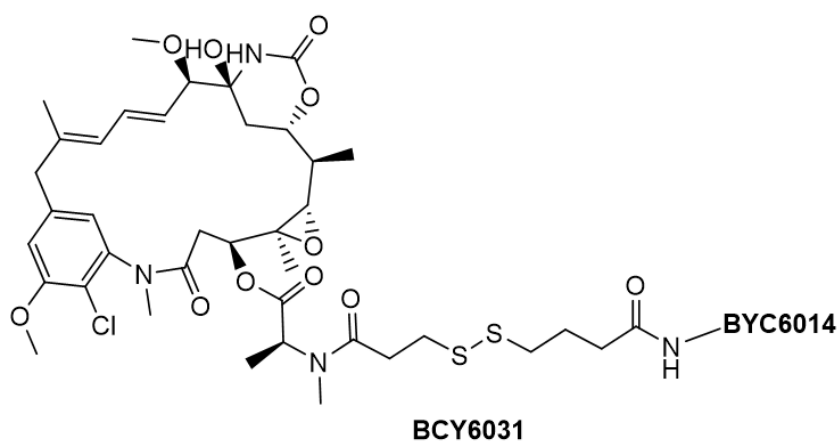
~~1020~~ 20. The drug conjugate as defined in claim 18 or claim 19, which additionally comprises a linker between said peptide ligand and said cytotoxic agent.

~~1121~~ 21. The drug conjugate as defined in claim 20, wherein said cytotoxic agent is MMAE and 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: 98).

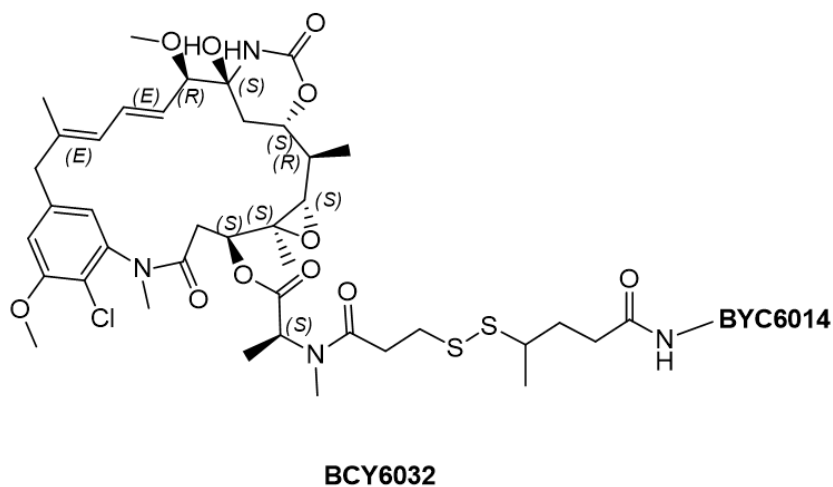
~~1222~~ 22. The drug conjugate as defined in claim 21, wherein said cytotoxic agent is MMAE and the linker is -Val-Cit-.

~~23~~13. The drug conjugate as defined in claim ~~20~~10, 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-.

~~24~~14. The drug conjugate as defined in any one of claims 18 to ~~23~~13, which is selected from any one of BCY6031:

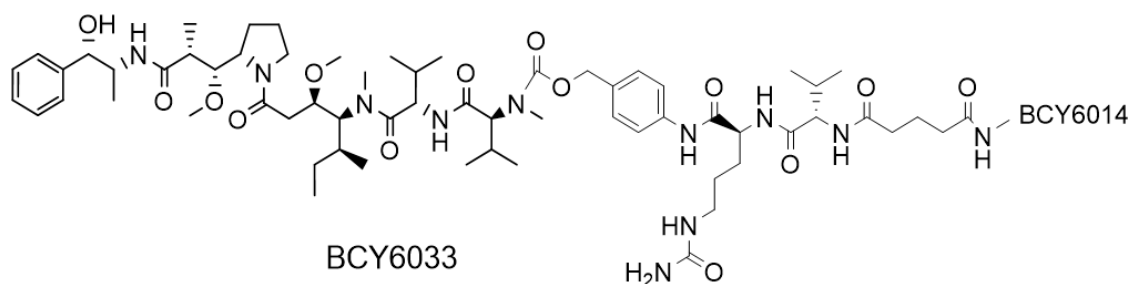


and BCY6032:

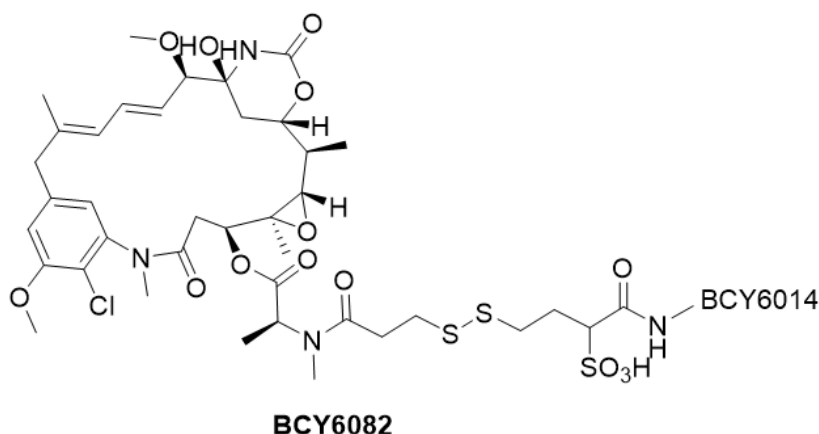


the Bicycle drug conjugates (BDCs) listed in Tables 11 or 13; or

BCY6033:



and BCY6082:



wherein BCY6014 is (β-Ala)-Sar₁₀-A(HArg)D-CiPLVNPLC_{ii}LHPGWTC_{iii} ((β-Ala)-Sar₁₀-(SEQ ID NO: 11)).

2515. The drug conjugate as defined in claim **2414**, which is selected from any one of: BCY6031, BCY6033, and BCY6082.

2616. A pharmaceutical composition which comprises the peptide ligand of any one of claims 1 to 17 or the drug conjugate of any one of claims 18 to **2515**, in combination with one or more pharmaceutically acceptable excipients.

2717. The drug conjugate as defined in any one of claims 18 to **2515**, for use in suppressing or treating a disease or disorder characterised by overexpression of EphA2 in diseased tissue.

2818. The drug conjugate as defined in any one of claims 18 to **2515**, for use in suppressing or treating cancer.

2919. The drug conjugate for use as defined in claim **2818**, 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.

3020. Use of a drug conjugate as defined in any one of claims 18 to 25-15 in the manufacture of a medicament for suppressing or treating cancer in a patient in need thereof, wherein said patient is identified as having an increased copy number variation (CNV) of EphA2.