

CLAIMS

1. A heterotandem bicyclic peptide complex comprising:
 - (a) a first peptide ligand, or a pharmaceutically acceptable salt thereof, which binds to a component present on a cancer cell; conjugated via a linker to
 - (b) two or more second peptide ligands, or pharmaceutically acceptable salts thereof, which bind to a component present on an immune cell;wherein each of said peptide ligands comprise a polypeptide comprising at least three reactive groups, separated by at least two loop sequences, and a 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 heterotandem bicyclic peptide complex as defined in claim 1, wherein the immune cell is selected from: white blood cells; lymphocytes (e.g. T lymphocytes or T cells, B cells or natural killer cells); CD8 or CD4; CD8; dendritic cells, follicular dendritic cells and granulocytes.
3. The heterotandem bicyclic peptide complex as defined in claim 1 or claim 2, wherein said reactive groups are selected from cysteine, 3-mercaptopropionic acid and/or cysteamine residues.
4. The heterotandem bicyclic peptide complex as defined in any one of claims 1 to 3, wherein the component present on an immune cell is CD137.
5. The heterotandem bicyclic peptide complex as defined in any one of claims 1 to 4, wherein the two or more second peptide ligands comprise a CD137 binding bicyclic peptide ligand.
6. The heterotandem bicyclic peptide complex as defined in claim 5, wherein the CD137 binding bicyclic peptide ligand comprises an amino acid sequence selected from:
 - C_iIEEGQYC_{ii}FADPY[Nle]C_{iii} (SEQ ID NO: 5);
 - C_i[tBuAla]PE[D-Ala]PYC_{ii}FADPY[Nle]C_{iii} (SEQ ID NO: 6);
 - C_iIEEGQYC_{ii}F[D-Ala]DPY[Nle]C_{iii} (SEQ ID NO: 7);
 - C_i[tBuAla]PK[D-Ala]PYC_{ii}FADPY[Nle]C_{iii} (SEQ ID NO: 8);
 - C_i[tBuAla]PE[D-Lys]PYC_{ii}FADPY[Nle]C_{iii} (SEQ ID NO: 9);
 - C_i[tBuAla]P[K(PYA)][D-Ala]PYC_{ii}FADPY[Nle]C_{iii} (SEQ ID NO: 10);
 - C_i[tBuAla]PE[D-Lys(PYA)]PYC_{ii}FADPY[Nle]C_{iii} (SEQ ID NO: 11);
 - (SEQ ID NO: 11)-A (herein referred to as BCY14601);

C_iIEE[D-Lys(PYA)]QYC_{ii}FADPY[Nle]C_{iii} (SEQ ID NO: 12);
 C_i[tBuAla]PE[dK]PYC_{ii}FADPY[Nle]C_{iii} (SEQ ID NO: 60);
 C_iIEE[dK(PYA)]QYC_{ii}FADPY[Nle]C_{iii} (SEQ ID NO: 61);
 C_i[tBuAla]EE(dK)PYC_{ii}FADPY[Nle]C_{iii} (SEQ ID NO: 62);
 C_i[tBuAla]PE[dK(PYA)]PYC_{ii}FADPY[Nle]C_{iii} (SEQ ID NO: 63);
 C_i[tBuAla]EE[dK(PYA)]PYC_{ii}FADPY[Nle]C_{iii} (SEQ ID NO: 64);
 C_i[tBuAla]PE[dK(PYA)]PYC_{ii}FANPY[Nle]C_{iii} (SEQ ID NO: 65);
 C_i[tBuAla]PE[dK(PYA)]PYC_{ii}FAEPY[Nle]C_{iii} (SEQ ID NO: 66);
 C_i[tBuAla]PE[dK(PYA)]PYC_{ii}FA[Aad]PY[Nle]C_{iii} (SEQ ID NO: 67);
 C_i[tBuAla]PE[dK(PYA)]PYC_{ii}FAQPY[Nle]C_{iii} (SEQ ID NO: 68);
 C_i[tBuAla]PE[dK(PYA)]PYC_{ii}FADPY[Nle][Cysam]_{iii} (SEQ ID NO: 69);
 [MerPro]_i[tBuAla]PE[dK(PYA)]PYC_{ii}FADPY[Nle]C_{iii} (SEQ ID NO: 70; herein referred to as BCY12353);

[MerPro]_i[tBuAla]PE[dK(PYA)]PYC_{ii}FADPY[Nle][Cysam]_{iii} (SEQ ID NO: 71; herein referred to as BCY12354);

C_i[tBuAla]PE[dK(PYA)]PYC_{ii}FADPY[Nle]C_{iii} (SEQ ID NO: 72);
 C_i[tBuAla]PE[dK(PYA)]PYC_{ii}FADPY[Nle]C_{iii} (SEQ ID NO: 73);
 C_i[tBuAla]PE[dK(PYA)]PYC_{ii}FADPY[Nle]C_{iii} (SEQ ID NO: 74; herein referred to as BCY12372);

C_i[tBuAla]PE[dK(PYA)]PYC_{ii}FAD[NMeAla]Y[Nle]C_{iii} (SEQ ID NO: 75);
 C_i[tBuAla]PE[dK(PYA)]PYC_{ii}FAD[NMeDAla]Y[Nle]C_{iii} (SEQ ID NO: 76);
 C_i[tBuAla]P[K(PYA)][dA]PYC_{ii}FADPY[Nle]C_{iii} (SEQ ID NO: 77);
 C_i[tBuAla]PE[dK(PYA)]PYC_{ii}FADPY[Nle]C_{iii} (SEQ ID NO: 78);
 C_i[tBuAla]PE[dK(Me,PYA)]PYC_{ii}FADPY[Nle]C_{iii} (SEQ ID NO: 79);
 C_i[tBuAla]PE[dK(Me,PYA)]PYC_{ii}FADPY[Nle]C_{iii} (SEQ ID NO: 80); and
 [MerPro]_i[tBuAla]EE[dK]PYC_{ii}FADPY[Nle]C_{iii} (SEQ ID NO: 81; herein referred to as BCY13137);

wherein [MerPro]_i, C_i, C_{ii}, C_{iii} and [Cysam]_{iii} represent first (i), second (ii) and third (iii) reactive groups which are selected from cysteine, MerPro and Cysam, Nle represents norleucine, tBuAla represents t-butyl-alanine, PYA represents 4-pentynoic acid, Aad represents alpha-L-amino adipic acid, MerPro represents 3-mercaptopropionic acid and Cysam represents cysteamine, NMeAla represents N-methyl-alanine, or a pharmaceutically acceptable salt thereof.

7. The heterotandem bicyclic peptide complex as defined in claim 5 or claim 6, wherein the CD137 binding bicyclic peptide ligand comprises an amino acid sequence which is:

C_i[tBuAla]PE[D-Lys(PYA)]PYC_{ii}FADPY[Nle]C_{iii} (SEQ ID NO: 11);

wherein C_i, C_{ii} and C_{iii} represent first, second and third cysteine residues, respectively, tBuAla represents t-butyl-alanine, PYA represents 4-pentynoic acid, Nle represents norleucine, or a pharmaceutically acceptable salt thereof.

8. The heterotandem bicyclic peptide complex as defined in claim 6 or claim 7, wherein the CD137 binding bicyclic peptide ligand comprises N- and C-terminal modifications and comprises:

Ac-A-(SEQ ID NO: 5)-Dap (herein referred to as BCY7732);
Ac-A-(SEQ ID NO: 5)-Dap(PYA) (herein referred to as BCY7741);
Ac-(SEQ ID NO: 6)-Dap (herein referred to as BCY9172);
Ac-(SEQ ID NO: 6)-Dap(PYA) (herein referred to as BCY11014);
Ac-A-(SEQ ID NO: 7)-Dap (herein referred to as BCY8045);
Ac-(SEQ ID NO: 8)-A (herein referred to as BCY8919);
Ac-(SEQ ID NO: 9)-A (herein referred to as BCY8920);
Ac-(SEQ ID NO: 10)-A (herein referred to as BCY8927);
Ac-(SEQ ID NO: 11)-A (herein referred to as BCY8928);
Ac-A-(SEQ ID NO: 12)-A (herein referred to as BCY7744);
Ac-(SEQ ID NO: 60)-Dap(PYA) (herein referred to as BCY11144);
Ac-A-(SEQ ID NO: 61)-K (herein referred to as BCY11613);
Ac-(SEQ ID NO: 62)-Dap(PYA) (herein referred to as BCY12023);
Ac-(SEQ ID NO: 63) (herein referred to as BCY12149);
Ac-(SEQ ID NO: 64) (herein referred to as BCY12143);
Ac-(SEQ ID NO: 65) (herein referred to as BCY12147);
Ac-(SEQ ID NO: 66) (herein referred to as BCY12145);
Ac-(SEQ ID NO: 67) (herein referred to as BCY12146);
Ac-(SEQ ID NO: 68) (herein referred to as BCY12150);
Ac-(SEQ ID NO: 69) (herein referred to as BCY12352);
Ac-(SEQ ID NO: 72)-[1,2-diaminoethane] (herein referred to as BCY12358);
[Palmitic Acid]-[yGlu]-[yGlu]-(SEQ ID NO: 73) (herein referred to as BCY12360);
Ac-(SEQ ID NO: 75) (herein referred to as BCY12381);
Ac-(SEQ ID NO: 76) (herein referred to as BCY12382);
Ac-(SEQ ID NO: 77)-K (herein referred to as BCY12357);
Ac-(SEQ ID NO: 78)-[dA] (herein referred to as BCY13095);
[Ac]-(SEQ ID NO: 78)-K (herein referred to as BCY13389);
Ac-(SEQ ID NO: 79)-[dA] (herein referred to as BCY13096); and
Ac-(SEQ ID NO: 80) (herein referred to as BCY13097);

wherein Ac represents an acetyl group, Dap represents diaminopropionic acid and PYA represents 4-pentynoic acid, or a pharmaceutically acceptable salt thereof.

9. The heterotandem bicyclic peptide complex as defined in any one of claims 6 to 8, wherein the CD137 binding bicyclic peptide ligand comprises N- and C-terminal modifications and comprises:

Ac-(SEQ ID NO: 11)-A (herein referred to as BCY8928);

wherein Ac represents an acetyl group, or a pharmaceutically acceptable salt thereof.

10. The heterotandem bicyclic peptide complex as defined in any one of claims 1 to 3, wherein the component present on an immune cell is OX40.

11. The heterotandem bicyclic peptide complex as defined in any one of claims 1 to 3 and 10, wherein the two or more second peptide ligands comprise an OX40 binding bicyclic peptide ligand.

12. The heterotandem bicyclic peptide complex as defined in claim 11, wherein the OX40 binding bicyclic peptide ligand comprises an amino acid sequence:

C_iILWC_{ii}LPEPHDEC_{iii} (SEQ ID NO: 82);
C_iA^K/S^N/E C_{ii}DPFWYQFYC_{iii} (SEQ ID NO: 83);
C_iAKNC_{ii}DPFWYQFYC_{iii} (SEQ ID NO: 84);
C_iASEC_{ii}DPFWYQFYC_{iii} (SEQ ID NO: 85);
C_iL^L/N YSPC_{ii}WHPLN^D/K C_{iii} (SEQ ID NO: 86);
C_iLYSPC_{ii}WHPLNDC_{iii} (SEQ ID NO: 87);
C_iNYSPC_{ii}WHPLNKC_{iii} (SEQ ID NO: 88);
C_iWYEYDC_{ii}NNWERC_{iii} (SEQ ID NO: 89);
C_iVIRYSPC_{ii}SHYLN C_{iii} (SEQ ID NO: 90);
C_iDYSPWWHPC_{ii}NHIC_{iii} (SEQ ID NO: 91);
C_iDAC_{ii}LYPDYYVC_{iii} (SEQ ID NO: 92);
C_iRLWC_{ii}IPAPTDDC_{iii} (SEQ ID NO: 93);
C_iTMWC_{ii}IPAKGDWC_{iii} (SEQ ID NO: 94);
C_iMLWC_{ii}LPAPTDEC_{iii} (SEQ ID NO: 95);
C_iILWC_{ii}LPEPPDEC_{iii} (SEQ ID NO: 96);
C_iLLWC_{ii}IPNPDDNC_{iii} (SEQ ID NO: 97);
C_iWLWC_{ii}VPNPDDTC_{iii} (SEQ ID NO: 98);
C_iVLWC_{ii}TPYPGDDC_{iii} (SEQ ID NO: 99);
C_iALWC_{ii}IPDPQDEC_{iii} (SEQ ID NO: 100);

C_iTLWC_{ii}IPDASDSC_{iii} (SEQ ID NO: 101);
 C_iQLWC_{ii}IPDADDDC_{iii} (SEQ ID NO: 102);
 C_iQLWC_{ii}VPEPGDSC_{iii} (SEQ ID NO: 103);
 C_iALWC_{ii}IPEESDDC_{iii} (SEQ ID NO: 104);
 C_iVLWC_{ii}IPEPQDKC_{iii} (SEQ ID NO: 105);
 C_iTLWC_{ii}IPDPDDSC_{iii} (SEQ ID NO: 106);
 C_iRLWC_{ii}VPKAEDYC_{iii} (SEQ ID NO: 107);
 C_iTKPC_{ii}IAYYNQSC_{iii} (SEQ ID NO: 108);
 C_iMNPC_{ii}IAYYQQEC_{iii} (SEQ ID NO: 109);
 C_iTNAC_{ii}VAYYHQAC_{iii} (SEQ ID NO: 110);
 C_iSDPC_{ii}ISYYNQAC_{iii} (SEQ ID NO: 111);
 C_iDPPC_{ii}DPFWYAFYC_{iii} (SEQ ID NO: 112);
 C_iPDDC_{ii}DPFWYNFYC_{iii} (SEQ ID NO: 113);
 C_iRYSPC_{ii}YHPHNC_{iii} (SEQ ID NO: 114);
 C_iLYSPC_{ii}NHPLNSC_{iii} (SEQ ID NO: 115);
 C_iEDNYC_{ii}FMWTPYC_{iii} (SEQ ID NO: 116);
 C_iLDSPC_{ii}WHPLNDC_{iii} (SEQ ID NO: 117);
 C_iRFSPC_{ii}SHPLNQC_{iii} (SEQ ID NO: 118);
 C_iKYSPC_{ii}WHPLNLC_{iii} (SEQ ID NO: 119);
 C_iRYSPC_{ii}WHPLNNC_{iii} (SEQ ID NO: 120);
 C_iEWISC_{ii}PGEPHRWWC_{iii} (SEQ ID NO: 121);
 C_iVWEAC_{ii}PEHPDQWWC_{iii} (SEQ ID NO: 122);
 C_iSTWHC_{ii}FWNLQEGKC_{iii} (SEQ ID NO: 123);
 C_iEWKAC_{ii}EHDRERWWC_{iii} (SEQ ID NO: 124);
 C_iRTWQC_{ii}FYEWQNGHC_{iii} (SEQ ID NO: 125);
 C_iKTWDC_{ii}FWASQVSEC_{iii} (SEQ ID NO: 126);
 C_iSTWQC_{ii}FYDLQEGHC_{iii} (SEQ ID NO: 127);
 C_iTTWEC_{ii}FYDLQEGHC_{iii} (SEQ ID NO: 128);
 C_iETWEC_{ii}FWRLQAGEC_{iii} (SEQ ID NO: 129);
 C_iRTWQC_{ii}FWDLQEGLC_{iii} (SEQ ID NO: 130);
 C_iSTWQC_{ii}FWDSQLGAC_{iii} (SEQ ID NO: 131);
 C_iETWEC_{ii}FEWQVGSC_{iii} (SEQ ID NO: 132);
 C_iTTWEC_{ii}FWDLQEGLC_{iii} (SEQ ID NO: 133);
 C_iHTWDC_{ii}FYQWQDGHC_{iii} (SEQ ID NO: 134);
 C_iTTWEC_{ii}FYSLQDGHC_{iii} (SEQ ID NO: 135);
 C_iNEDMYC_{ii}FMWMEC_{iii} (SEQ ID NO: 136);
 C_iLYEYDC_{ii}YTWRRRC_{iii} (SEQ ID NO: 137);

C_iRYEYDC_{ii}HTWQRC_{iii} (SEQ ID NO: 138);
 C_iWYEYDC_{ii}TTWERC_{iii} (SEQ ID NO: 139);
 C_iWYEYDC_{ii}RTWTRC_{iii} (SEQ ID NO: 140);
 C_iLYEYDC_{ii}HTWTRC_{iii} (SEQ ID NO: 141);
 C_iWYEYDC_{ii}RTWTFC_{iii} (SEQ ID NO: 142);
 C_iHGGVWC_{ii}IPNINDSC_{iii} (SEQ ID NO: 143);
 C_iDSPVRC_{ii}YWNTQKGC_{iii} (SEQ ID NO: 144);
 C_iGSPVPC_{ii}YWNTRKGC_{iii} (SEQ ID NO: 145);
 C_iAPFEFNC_{ii}YTWRPC_{iii} (SEQ ID NO: 146);
 C_iRVLYSPC_{ii}YHWLNC_{iii} (SEQ ID NO: 147);
 C_iSIMYSPC_{ii}EHPHNHC_{iii} (SEQ ID NO: 148);
 C_iDKWEPDHL C_{ii}YWWC_{iii} (SEQ ID NO: 149);
 C_iDAWPETHVC_{ii}YWWC_{iii} (SEQ ID NO: 150);
 C_iDEYTPEHLC_{ii}YWWC_{iii} (SEQ ID NO: 151);
 C_iWINYSISPC_{ii}YVGEC_{iii} (SEQ ID NO: 152); and
 C_iRYEYPEHLC_{ii}YTWQC_{iii} (SEQ ID NO: 153);

such as:

C_iLYSPC_{ii}WHPLNDC_{iii} (SEQ ID NO: 87);

wherein C_i, C_{ii} and C_{iii} represent first, second and third cysteine residues, respectively, or a modified derivative, or a pharmaceutically acceptable salt thereof.

13. The heterotandem bicyclic peptide complex as defined in claim 12, wherein the OX40 binding bicyclic peptide ligand additionally comprises N- and/or C-terminal modifications and comprises an amino acid sequence selected from:

A-(SEQ ID NO: 82)-A-[Sar6]-[Kbiot] (herein referred to as BCY10551);
 A-(SEQ ID NO: 82)-A (herein referred to as BCY10371);
 A-(SEQ ID NO: 84)-A-[Sar6]-[Kbiot] (herein referred to as BCY10552);
 [Biot]-G-[Sar5]-A-(SEQ ID NO: 84)-A (herein referred to as BCY10479);
 A-(SEQ ID NO: 84)-A (herein referred to as BCY10378);
 [Biot]-G-[Sar5]-A-(SEQ ID NO: 85)-A (herein referred to as BCY11371);
 A-(SEQ ID NO: 85)-A (herein referred to as BCY10743);
 [Biot]-G-[Sar5]-A-(SEQ ID NO: 87)-A (herein referred to as BCY10482);
 A-(SEQ ID NO: 87)-A-[Sar6]-[Kbiot] (herein referred to as BCY10549);
 A-(SEQ ID NO: 87)-A-K(Pya) (herein referred to as BCY11607);
 Ac-A-(SEQ ID NO: 87)-A-K(Pya) (herein referred to as BCY12708);
 A-(SEQ ID NO: 87)-A (herein referred to as BCY10351);
 A-(SEQ ID NO: 88)-A-[Sar6]-[Kbiot] (herein referred to as BCY11501);

A-(SEQ ID NO: 88)-A (herein referred to as BCY10729);
A-(SEQ ID NO: 89)-A-[Sar6]-[KBiot] (herein referred to as BCY10550);
A-(SEQ ID NO: 89)-A (herein referred to as BCY10361);
A-(SEQ ID NO: 90)-A-[Sar6]-[KBiot] (herein referred to as BCY10794);
A-(SEQ ID NO: 90)-A (herein referred to as BCY10349);
[Biot]-G-[Sar5]-A-(SEQ ID NO: 91)-A (herein referred to as BCY11369);
A-(SEQ ID NO: 91)-A (herein referred to as BCY10331);
A-(SEQ ID NO: 92)-A (herein referred to as BCY10375);
A-(SEQ ID NO: 93)-A (herein referred to as BCY10364);
A-(SEQ ID NO: 94)-A (herein referred to as BCY10365);
A-(SEQ ID NO: 95)-A (herein referred to as BCY10366);
A-(SEQ ID NO: 96)-A (herein referred to as BCY10367);
A-(SEQ ID NO: 97)-A (herein referred to as BCY10368);
A-(SEQ ID NO: 98)-A (herein referred to as BCY10369);
A-(SEQ ID NO: 99)-A (herein referred to as BCY10374);
A-(SEQ ID NO: 100)-A (herein referred to as BCY10376);
A-(SEQ ID NO: 101)-A (herein referred to as BCY10737);
A-(SEQ ID NO: 102)-A (herein referred to as BCY10738);
A-(SEQ ID NO: 103)-A (herein referred to as BCY10739);
A-(SEQ ID NO: 104)-A (herein referred to as BCY10740);
A-(SEQ ID NO: 105)-A (herein referred to as BCY10741);
A-(SEQ ID NO: 106)-A (herein referred to as BCY10742);
A-(SEQ ID NO: 107)-A (herein referred to as BCY10380);
A-(SEQ ID NO: 108)-A (herein referred to as BCY10370);
A-(SEQ ID NO: 109)-A (herein referred to as BCY10372);
A-(SEQ ID NO: 110)-A (herein referred to as BCY10373);
A-(SEQ ID NO: 111)-A (herein referred to as BCY10379);
A-(SEQ ID NO: 112)-A (herein referred to as BCY10377);
A-(SEQ ID NO: 113)-A (herein referred to as BCY10744);
A-(SEQ ID NO: 114)-A (herein referred to as BCY10343);
A-(SEQ ID NO: 115)-A (herein referred to as BCY10350);
A-(SEQ ID NO: 116)-A (herein referred to as BCY10352);
A-(SEQ ID NO: 117)-A (herein referred to as BCY10353);
A-(SEQ ID NO: 118)-A (herein referred to as BCY10354);
A-(SEQ ID NO: 119)-A (herein referred to as BCY10730);
A-(SEQ ID NO: 120)-A (herein referred to as BCY10731);
A-(SEQ ID NO: 121)-A (herein referred to as BCY10339);

A-(SEQ ID NO: 122)-A (herein referred to as BCY10340);
A-(SEQ ID NO: 123)-A (herein referred to as BCY10342);
A-(SEQ ID NO: 124)-A (herein referred to as BCY10345);
A-(SEQ ID NO: 125)-A (herein referred to as BCY10347);
A-(SEQ ID NO: 126)-A (herein referred to as BCY10348);
A-(SEQ ID NO: 127)-A (herein referred to as BCY10720);
A-(SEQ ID NO: 128)-A (herein referred to as BCY10721);
A-(SEQ ID NO: 129)-A (herein referred to as BCY10722);
A-(SEQ ID NO: 130)-A (herein referred to as BCY10723);
A-(SEQ ID NO: 131)-A (herein referred to as BCY10724);
A-(SEQ ID NO: 132)-A (herein referred to as BCY10725);
A-(SEQ ID NO: 133)-A (herein referred to as BCY10726);
A-(SEQ ID NO: 134)-A (herein referred to as BCY10727);
A-(SEQ ID NO: 135)-A (herein referred to as BCY10728);
A-(SEQ ID NO: 136)-A (herein referred to as BCY10360);
A-(SEQ ID NO: 137)-A (herein referred to as BCY10363);
A-(SEQ ID NO: 138)-A (herein referred to as BCY10732);
A-(SEQ ID NO: 139)-A (herein referred to as BCY10733);
A-(SEQ ID NO: 140)-A (herein referred to as BCY10734);
A-(SEQ ID NO: 141)-A (herein referred to as BCY10735);
A-(SEQ ID NO: 142)-A (herein referred to as BCY10736);
A-(SEQ ID NO: 143)-A (herein referred to as BCY10336);
A-(SEQ ID NO: 144)-A (herein referred to as BCY10337);
A-(SEQ ID NO: 145)-A (herein referred to as BCY10338);
A-(SEQ ID NO: 146)-A (herein referred to as BCY10346);
A-(SEQ ID NO: 147)-A (herein referred to as BCY10357);
A-(SEQ ID NO: 148)-A (herein referred to as BCY10362);
A-(SEQ ID NO: 149)-A (herein referred to as BCY10332);
A-(SEQ ID NO: 150)-A (herein referred to as BCY10717);
A-(SEQ ID NO: 151)-A (herein referred to as BCY10718);
A-(SEQ ID NO: 152)-A (herein referred to as BCY10334); and
A-(SEQ ID NO: 153)-A (herein referred to as BCY10719);

such as:

A-(SEQ ID NO: 87)-A-K(Pya) (herein referred to as BCY11607);

wherein Pya represents 4-pentynoyl moiety.

14. The heterotandem bicyclic peptide complex as defined in any one of claims 1 to 13, wherein the cancer cell is selected from an HT1080, A549, SC-OV-3, PC3, HT1376, NCI-H292, LnCap, MC38, MC38 #13, 4T1-D02, H322, HT29, T47D and RKO tumor cell.

15. The heterotandem bicyclic peptide complex as defined in any one of claims 1 to 14, wherein the component present on a cancer cell is Nectin-4.

16. The heterotandem bicyclic peptide complex as defined in any one of claims 1 to 15, wherein the first peptide ligand comprises a Nectin-4 binding bicyclic peptide ligand.

17. The heterotandem bicyclic peptide complex as defined in claim 16, wherein the Nectin-4 binding bicyclic peptide ligand comprises an amino acid sequence selected from:

C_iP[1Nal][dD]C_{ii}M[HArg]DWSTP[HyP]WC_{iii} (SEQ ID NO: 1; herein referred to as BCY8116);

C_iP[1Nal][dK](Sar₁₀-(B-Ala))C_{ii}M[HArg]DWSTP[HyP]WC_{iii} (SEQ ID NO: 3);

C_iPFGC_{ii}M[HArg]DWSTP[HyP]WC_{iii} (SEQ ID NO: 4; herein referred to as BCY11414);

C_iP[1Nal][dK]C_{ii}M[HArg]DWSTP[HyP]WC_{iii} (SEQ ID NO: 14);

[MerPro]_iP[1Nal][dK]C_{ii}M[HArg]DWSTP[HyP]WC_{iii} (SEQ ID NO: 15; herein referred to as BCY12363);

C_iP[1Nal][dK]C_{ii}M[HArg]DWSTP[HyP]W[Cysam]_{iii} (SEQ ID NO: 16);

[MerPro]_iP[1Nal][dK]C_{ii}M[HArg]DWSTP[HyP]W[Cysam]_{iii} (SEQ ID NO: 17; herein referred to as BCY12365);

C_iP[1Nal][dK]C_{ii}M[HArg]HWSTP[HyP]WC_{iii} (SEQ ID NO: 18);

C_iP[1Nal][dK]C_{ii}M[HArg]EWSTP[HyP]WC_{iii} (SEQ ID NO: 19);

C_iP[1Nal][dE]C_{ii}M[HArg]DWSTP[HyP]WC_{iii} (SEQ ID NO: 20; herein referred to as BCY12368);

C_iP[1Nal][dA]C_{ii}M[HArg]DWSTP[HyP]WC_{iii} (SEQ ID NO: 21; herein referred to as BCY12369);

C_iP[1Nal][dE]C_{ii}L[HArg]DWSTP[HyP]WC_{iii} (SEQ ID NO: 22; herein referred to as BCY12370); and

C_iP[1Nal][dE]C_{ii}M[HArg]EWSTP[HyP]WC_{iii} (SEQ ID NO: 23; herein referred to as BCY12384);

wherein [MerPro]_i, C_i, C_{ii}, C_{iii} and [Cysam]_{iii} represent first (i), second (ii) and third (iii) reactive groups which are selected from cysteine, MerPro and Cysam, 1Nal represents 1-naphthylalanine, HArg represents homoarginine, HyP represents trans-4-hydroxy-L-proline, Sar₁₀ represents 10 sarcosine units, B-Ala represents beta-alanine, MerPro represents 3-

mercaptopropionic acid and Cysam represents cysteamine, or a pharmaceutically acceptable salt thereof.

18. The heterotandem bicyclic peptide complex as defined in claim 17, wherein the Nectin-4 binding bicyclic peptide ligand optionally comprises N-terminal modifications and comprises:

SEQ ID NO: 1 (herein referred to as BCY8116);
[PYA]-[B-Ala]-[Sar₁₀]- (SEQ ID NO: 1) (herein referred to as BCY8846);
[PYA]- (SEQ ID NO: 1) (herein referred to as BCY11015);
[PYA]-[B-Ala]- (SEQ ID NO: 1) (herein referred to as BCY11016);
[PYA]-[B-Ala]-[Sar₁₀]- (SEQ ID NO: 2) (herein referred to as BCY11942);
Ac- (SEQ ID NO: 3) (herein referred to as BCY8831);
SEQ ID NO: 4 (herein referred to as BCY11414);
[PYA]-[B-Ala]- (SEQ ID NO: 14) (herein referred to as BCY11143);
Palmitic-yGlu-yGlu- (SEQ ID NO: 14) (herein referred to as BCY12371);
Ac- (SEQ ID NO: 14) (herein referred to as BCY12024);
Ac- (SEQ ID NO: 16) (herein referred to as BCY12364);
Ac- (SEQ ID NO: 18) (herein referred to as BCY12366); and
Ac- (SEQ ID NO: 19) (herein referred to as BCY12367);

wherein PYA represents 4-pentynoic acid, B-Ala represents beta-alanine, Sar₁₀ represents 10 sarcosine units, or a pharmaceutically acceptable salt thereof.

19. The heterotandem bicyclic peptide complex as defined in claim 17 or claim 18, wherein the Nectin-4 binding bicyclic peptide ligand comprises SEQ ID NO: 1 (herein referred to as BCY8116).

20. The heterotandem bicyclic peptide complex as defined in any one of claims 15 to 19, which is selected from any one of the complexes listed in Tables A and B, such as BCY11027, BCY11863 and BCY11864.

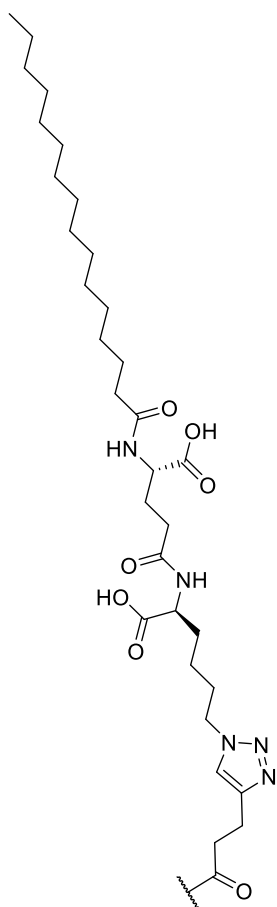
21. The heterotandem bicyclic peptide complex as defined in any one of claims 15 to 19, which is selected from any one of the complexes listed in Table E, such as BCY12967.

22. The heterotandem bicyclic peptide complex as defined in any one of claims 1 to 14, wherein the component present on a cancer cell is EphA2.

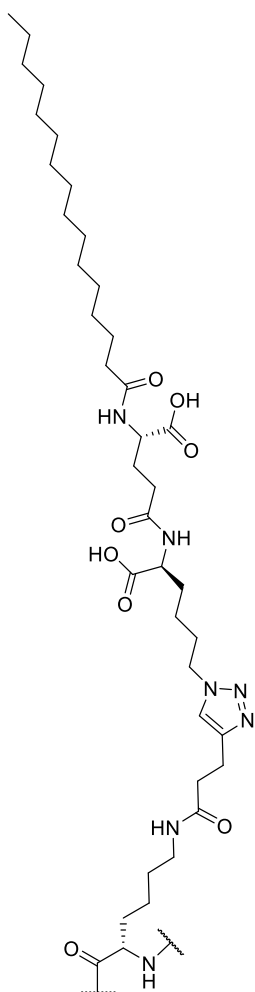
23. The heterotandem bicyclic peptide complex as defined in claim 22, wherein the EphA2 binding bicyclic peptide ligand comprises an amino acid sequence selected from:

C_i[HyP]LVNPLC_{ii}LHP[dD]W[HArg]C_{iii} (SEQ ID NO: 24);
 C_iLWDPTPC_{ii}ANLHL[HArg]C_{iii} (SEQ ID NO: 25);
 C_i[HyP]LVNPLC_{ii}L[K(PYA)]P[dD]W[HArg]C_{iii} (SEQ ID NO: 26);
 C_i[HyP][K(PYA)]VNPLC_{ii}LHP[dD]W[HArg]C_{iii} (SEQ ID NO: 27);
 C_i[HyP]LVNPLC_{ii}[K(PYA)]HP[dD]W[HArg]C_{iii} (SEQ ID NO: 28);
 C_i[HyP]LVNPLC_{ii}LKP[dD]W[HArg]C_{iii} (SEQ ID NO: 29);
 C_i[HyP]KVNPLC_{ii}LHP[dD]W[HArg]C_{iii} (SEQ ID NO: 30);
 C_i[HyP]LVNPLC_{ii}KHP[dD]W[HArg]C_{iii} (SEQ ID NO: 31);
 C_i[HyP]LVNPLC_{ii}LHP[dE]W[HArg]C_{iii} (SEQ ID NO: 32);
 C_i[HyP]LVNPLC_{ii}LEP[dD]W[HArg]C_{iii} (SEQ ID NO: 33);
 C_i[HyP]LVNPLC_{ii}LHP[dD]WTC_{iii} (SEQ ID NO: 34);
 C_i[HyP]LVNPLC_{ii}LEP[dD]WTC_{iii} (SEQ ID NO: 35);
 C_i[HyP]LVNPLC_{ii}LEP[dA]WTC_{iii} (SEQ ID NO: 36);
 C_i[HyP]LVNPLC_{ii}L[3,3-DPA]P[dD]WTC_{iii} (SEQ ID NO: 37; herein referred to as BCY12860);
 C_i[HyP][Cba]VNPLC_{ii}LHP[dD]W[HArg]C_{iii} (SEQ ID NO: 38);
 C_i[HyP][Cba]VNPLC_{ii}LEP[dD]WTC_{iii} (SEQ ID NO: 39);
 C_i[HyP][Cba]VNPLC_{ii}L[3,3-DPA]P[dD]WTC_{iii} (SEQ ID NO: 40);
 C_i[HyP]LVNPLC_{ii}L[3,3-DPA]P[dD]W[HArg]C_{iii} (SEQ ID NO: 41);
 C_i[HyP]LVNPLC_{ii}LHP[d1NaI]W[HArg]C_{iii} (SEQ ID NO: 42);
 C_i[HyP]LVNPLC_{ii}L[1NaI]P[dD]W[HArg]C_{iii} (SEQ ID NO: 43);
 C_i[HyP]LVNPLC_{ii}LEP[d1NaI]WTC_{iii} (SEQ ID NO: 44);
 C_i[HyP]LVNPLC_{ii}L[1NaI]P[dD]WTC_{iii} (SEQ ID NO: 45; herein referred to as BCY13119);
 C_i[HyP][Cba]VNPLC_{ii}LEP[dA]WTC_{iii} (SEQ ID NO: 46);
 C_i[HyP][hGlu]VNPLC_{ii}LHP[dD]W[HArg]C_{iii} (SEQ ID NO: 47);
 C_i[HyP]LVNPLC_{ii}[hGlu]HP[dD]W[HArg]C_{iii} (SEQ ID NO: 48);
 C_i[HyP]LVNPLC_{ii}L[hGlu]P[dD]W[HArg]C_{iii} (SEQ ID NO: 49);
 C_i[HyP]LVNPLC_{ii}LHP[dNle]W[HArg]C_{iii} (SEQ ID NO: 50);
 C_i[HyP]LVNPLC_{ii}L[Nle]P[dD]W[HArg]C_{iii} (SEQ ID NO: 51);
 [MerPro]_i[HyP]LVNPLC_{ii}L[3,3-DPA]P[dD]WTC_{iii} (SEQ ID NO: 154);
 C_i[HyP]LVNPLC_{ii}LHP[dD]W[HArg][Cysam]_{iii} (SEQ ID NO: 155);
 C_i[HyP]LVNPLC_{ii}L[His3Me]P[dD]W[HArg]C_{iii} (SEQ ID NO: 156);
 C_i[HyP]LVNPLC_{ii}L[His1Me]P[dD]W[HArg]C_{iii} (SEQ ID NO: 157);
 C_i[HyP]LVNPLC_{ii}L[4ThiAz]P[dD]W[HArg]C_{iii} (SEQ ID NO: 158);
 C_i[HyP]LVNPLC_{ii}LFP[dD]W[HArg]C_{iii} (SEQ ID NO: 159);
 C_i[HyP]LVNPLC_{ii}L[Thi]P[dD]W[HArg]C_{iii} (SEQ ID NO: 160);
 C_i[HyP]LVNPLC_{ii}L[3Thi]P[dD]W[HArg]C_{iii} (SEQ ID NO: 161);
 C_i[HyP]LVNPLC_{ii}LNP[dD]W[HArg]C_{iii} (SEQ ID NO: 162);

C_i[HyP]LVNPLC_{ii}LQP[dD]W[HArg]C_{iii} (SEQ ID NO: 163); and
 C_i[HyP]LVNPLC_{ii}L[K(PYA-(Palmitoyl-Glu-LysN₃))]P[dD]W[HArg]C_{iii} (SEQ ID NO: 164);
 wherein [MerPro]_i, C_i, C_{ii}, C_{iii} and [Cysam]_{iii} represent first (i), second (ii) and third (iii) reactive groups which are selected from cysteine, MerPro and Cysam, HyP represents trans-4-hydroxy-L-proline, HArg represents homoarginine, PYA represents 4-pentynoic acid, 3,3-DPA represents 3,3-diphenylalanine, Cba represents β-cyclobutylalanine, 1Nal represents 1-naphthylalanine, hGlu represents homoglutamic acid, Thi represents thienyl-alanine, 4ThiAz represents beta-(4-thiazolyl)-alanine, His1Me represents N1-methyl-L-histidine, His3Me represents N3-methyl-L-histidine, 3Thi represents , Palmitoyl-Glu-LysN₃[PYA] represents:



(Palmitoyl-Glu-LysN₃)[PYA] , [K(PYA-(Palmitoyl-Glu-LysN₃))] represents:



[K(PYA(Palmitoyl-Glu-LysN3))], Nle represents norleucine, MerPro represents 3-mercaptopropionic acid and Cysam represents cysteamine, or a pharmaceutically acceptable salt thereof.

24. The heterotandem bicyclic peptide complex as defined in claim 23, wherein the EphA2 binding bicyclic peptide ligand comprises an amino acid sequence which is:

C_i [HyP]LVNPLC_{ii}LHP[dD]W[HArg]C_{iii} (SEQ ID NO: 24);

wherein C_i , C_{ii} , C_{iii} and represent first (i), second (ii) and third (iii) cysteine groups, HyP represents trans-4-hydroxy-L-proline, HArg represents homoarginine, or a pharmaceutically acceptable salt thereof.

25. The heterotandem bicyclic peptide complex as defined in claim 23, wherein the EphA2 binding bicyclic peptide ligand comprises an amino acid sequence which is:

C_i [HyP]LVNPLC_{ii}LEP[d1NaI]WTC_{iii} (SEQ ID NO: 44);

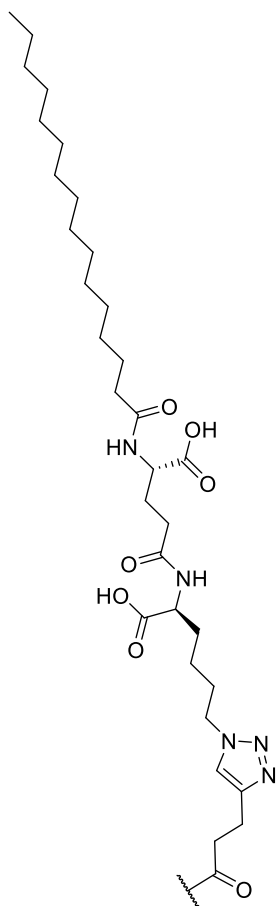
wherein C_i, C_{ii}, C_{iii} and represent first (i), second (ii) and third (iii) cysteine groups, HyP represents trans-4-hydroxy-L-proline, 1Nal represents 1-naphthylalanine, or a pharmaceutically acceptable salt thereof.

26. The heterotandem bicyclic peptide complex as defined in any one of claims 23 to 25, wherein the EphA2 binding bicyclic peptide ligand optionally comprises N-terminal modifications and comprises:

A-[HArg]-D-(SEQ ID NO: 24) (herein referred to as BCY9594);
[B-Ala]-[Sar₁₀]-A-[HArg]-D-(SEQ ID NO: 24) (herein referred to as BCY6099);
[PYA]-A-[HArg]-D-(SEQ NO: 24) (herein referred to as BCY11813);
Ac-A-[HArg]-D-(SEQ ID NO: 24)-[K(PYA)] (herein referred to as BCY11814);
Ac-A-[HArg]-D-(SEQ ID NO: 24)-K (herein referred to as BCY12734);
[NMeAla]-[HArg]-D-(SEQ ID NO: 24) (herein referred to as BCY13121);
[Ac]-(SEQ ID NO: 24)-L[dH]G[dK] (herein referred to as BCY13125);
[PYA]-[B-Ala]-[Sar₁₀]-VGP-(SEQ ID NO: 25) (herein referred to as BCY8941);
Ac-A-[HArg]-D-(SEQ ID NO: 26) (herein referred to as BCY11815);
Ac-A-[HArg]-D-(SEQ ID NO: 27) (herein referred to as BCY11816);
Ac-A-[HArg]-D-(SEQ ID NO: 28) (herein referred to as BCY11817);
Ac-A-[HArg]-D-(SEQ ID NO: 29) (herein referred to as BCY12735);
(Palmitoyl-Glu-LysN₃)[PYA]A[HArg]D-(SEQ ID NO: 29) (hereinafter known as BCY14327);
Ac-A-[HArg]-D-(SEQ ID NO: 30) (herein referred to as BCY12736);
Ac-A-[HArg]-D-(SEQ ID NO: 31) (herein referred to as BCY12737);
A-[HArg]-D-(SEQ ID NO: 32) (herein referred to as BCY12738);
A-[HArg]-E-(SEQ ID NO: 32) (herein referred to as BCY12739);
A-[HArg]-D-(SEQ ID NO: 33) (herein referred to as BCY12854);
A-[HArg]-D-(SEQ ID NO: 34) (herein referred to as BCY12855);
A-[HArg]-D-(SEQ ID NO: 35) (herein referred to as BCY12856);
A-[HArg]-D-(SEQ ID NO: 35)-[dA] (herein referred to as BCY12857);
(SEQ ID NO: 35)-[dA] (herein referred to as BCY12861);
[NMeAla]-[HArg]-D-(SEQ ID NO: 35) (herein referred to as BCY13122);
[dA]-ED-(SEQ ID NO: 35) (herein referred to as BCY13126);
[dA]-[dA]-D-(SEQ ID NO: 35) (herein referred to as BCY13127);
AD-(SEQ ID NO: 35) (herein referred to as BCY13128);
A-[HArg]-D-(SEQ ID NO: 36) (herein referred to as BCY12858);
A-[HArg]-D-(SEQ ID NO: 37) (herein referred to as BCY12859);
Ac-(SEQ ID NO: 37)-[dK] (herein referred to as BCY13120);

A-[HArg]-D-(SEQ ID NO: 38) (herein referred to as BCY12862);
 A-[HArg]-D-(SEQ ID NO: 39) (herein referred to as BCY12863);
 [dA]-[HArg]-D-(SEQ ID NO: 39)-[dA] (herein referred to as BCY12864);
 (SEQ ID NO: 40)-[dA] (herein referred to as BCY12865);
 A-[HArg]-D-(SEQ ID NO: 41) (herein referred to as BCY12866);
 A-[HArg]-D-(SEQ ID NO: 42) (herein referred to as BCY13116);
 A-[HArg]-D-(SEQ ID NO: 43) (herein referred to as BCY13117);
 A-[HArg]-D-(SEQ ID NO: 44) (herein referred to as BCY13118);
 [dA]-[HArg]-D-(SEQ ID NO: 46)-[dA] (herein referred to as BCY13123);
 [d1Nal]-[HArg]-D-(SEQ ID NO: 46)-[dA] (herein referred to as BCY13124);
 A-[HArg]-D-(SEQ ID NO: 47) (herein referred to as BCY13130);
 A-[HArg]-D-(SEQ ID NO: 48) (herein referred to as BCY13131);
 A-[HArg]-D-(SEQ ID NO: 49) (herein referred to as BCY13132);
 A-[HArg]-D-(SEQ ID NO: 50) (herein referred to as BCY13134);
 A-[HArg]-D-(SEQ ID NO: 51) (herein referred to as BCY13135);
 (SEQ ID NO: 154)-[dK] (herein referred to as BCY13129);
 A[HArg]D-(SEQ ID NO: 155) (herein referred to as BCY13133);
 A[HArg]D-(SEQ ID NO: 156) (herein referred to as BCY13917);
 A[HArg]D-(SEQ ID NO: 157) (herein referred to as BCY13918);
 A[HArg]D-(SEQ ID NO: 158) (herein referred to as BCY13919);
 A[HArg]D-(SEQ ID NO: 159) (herein referred to as BCY13920);
 A[HArg]D-(SEQ ID NO: 160) (herein referred to as BCY13922);
 A[HArg]D-(SEQ ID NO: 161) (herein referred to as BCY13923);
 A[HArg]D-(SEQ ID NO: 162) (herein referred to as BCY14047);
 A[HArg]D-(SEQ ID NO: 163) (herein referred to as BCY14048); and
 A[HArg]D-(SEQ ID NO: 164) (herein referred to as BCY14313);

wherein PYA represents 4-pentynoic acid, B-Ala represents beta-alanine, Sar₁₀ represents 10 sarcosine units, HArg represents homoarginine, NMeAla represents N-methyl-alanine, 1Nal represents 1-naphthylalanine, Palmitoyl-Glu-LysN₃[PYA] represents:



(Palmitoyl-Glu-LysN3)[PYA] , or a pharmaceutically acceptable salt thereof.

27. The heterotandem bicyclic peptide complex as defined in any one of claims 23 to 26, wherein the EphA2 binding bicyclic peptide ligand optionally comprises N-terminal modifications and comprises:

A-[HArg]-D-(SEQ ID NO: 24) (herein referred to as BCY9594);

wherein HArg represents homoarginine, or a pharmaceutically acceptable salt thereof.

28. The heterotandem bicyclic peptide complex as defined in any one of claims 23 to 26, wherein the EphA2 binding bicyclic peptide ligand optionally comprises N-terminal modifications and comprises:

A-[HArg]-D-(SEQ ID NO: 44) (herein referred to as BCY13118);

wherein HArg represents homoarginine, or a pharmaceutically acceptable salt thereof.

29. The heterotandem bicyclic peptide complex as defined in any one of claims 22 to 28, which is selected from any one of the complexes listed in Table C, such as BCY12491, BCY12730, BCY13048, BCY13050, BCY13053 and BCY13272.

30. The heterotandem bicyclic peptide complex as defined in claim 29, which is BCY12491.

31. The heterotandem bicyclic peptide complex as defined in claim 29, which is BCY13272.

32. The heterotandem bicyclic peptide complex as defined in any one of claims 1 to 13, wherein the component present on a cancer cell is PD-L1.

33. The heterotandem bicyclic peptide complex as defined in claim 32, wherein the PD-L1 binding bicyclic peptide ligand comprises an amino acid sequence selected from:

C_iSAGWLTMC_{ii}QKLHLC_{iii} (SEQ ID NO: 52);
C_iSAGWLTMC_{ii}Q[K(PYA)]LHLC_{iii} (SEQ ID NO: 53);
C_iSKGWLTMC_{ii}Q[K(Ac)]LHLC_{iii} (SEQ ID NO: 54);
C_iSAGWLTMC_{ii}Q[K(Ac)]LHLC_{iii} (SEQ ID NO: 55);
C_iSAGWLTMC_{ii}K[K(Ac)]LHLC_{iii} (SEQ ID NO: 56);
C_iSAGWLTMC_{ii}Q[K(Ac)]LKLC_{iii} (SEQ ID NO: 57);
C_iSAGWLTMC_{ii}Q[HArg]LHLC_{iii} (SEQ ID NO: 58); and
C_iSAGWLTMC_{ii}[HArg]QLNLC_{iii} (SEQ ID NO: 59);

wherein C_i, C_{ii} and C_{iii} represent first, second and third cysteine residues, respectively, PYA represents 4-pentynoic acid and HArg represents homoarginine, or a pharmaceutically acceptable salt thereof.

34. The heterotandem bicyclic peptide complex as defined in claim 33, wherein the PD-L1 binding bicyclic peptide ligand optionally comprises N-terminal and/or C-terminal modifications and comprises:

[PYA]-[B-Ala]-[Sar₁₀]-SDK-(SEQ ID NO: 52) (herein referred to as BCY10043);
Ac-D-[HArg]-(SEQ ID NO: 52)-PSH (herein referred to as BCY11865);
Ac-SDK-(SEQ ID NO: 53) (herein referred to as BCY11013);
Ac-SDK-(SEQ ID NO: 53)-PSH (herein referred to as BCY10861);
Ac-D-[HArg]-(SEQ ID NO: 54)-PSH (herein referred to as BCY11866);
Ac-D-[HArg]-(SEQ ID NO: 55)-PSH (herein referred to as BCY11867);
Ac-D-[HArg]-(SEQ ID NO: 56)-PSH (herein referred to as BCY11868);
Ac-D-[HArg]-(SEQ ID NO: 57)-PSH (herein referred to as BCY11869);
Ac-SD-[HArg]-(SEQ ID NO: 58)-PSHK (herein referred to as BCY12479); and
Ac-SD-[HArg]-(SEQ ID NO: 59)-PSHK (herein referred to as BCY12477);

wherein PYA represents 4-pentynoic acid, B-Ala represents beta-alanine, Sar₁₀ represents 10 sarcosine units and HArg represents homoarginine, or a pharmaceutically acceptable salt thereof.

35. The heterotandem bicyclic peptide complex as defined in any one of claims 32 to 34, which is selected from any one of the complexes listed in Table D.

36. The heterotandem bicyclic peptide complex as defined in any one of claims 1 to 5, wherein the two or more second peptide ligands comprise one CD137 binding bicyclic peptide ligand and one OX40 binding bicyclic peptide.

37. The heterotandem bicyclic peptide complex as defined in claim 36, which is the complex listed in Table F.

38. The heterotandem bicyclic peptide complex as defined in claim 1, which is selected from any one of the complexes listed in Tables G and H.

39. The heterotandem bicyclic peptide complex as defined in any one of claims 1 to 38, wherein the molecular scaffold is selected from 1,1',1''-(1,3,5-triazinane-1,3,5-triyl)triprop-2-en-1-one (TATA).

40. The heterotandem bicyclic peptide complex as defined in any one of claims 1 to 39, wherein the pharmaceutically acceptable salt is selected from the free acid or the sodium, potassium, calcium, ammonium salt.

41. A pharmaceutical composition which comprises the heterotandem bicyclic peptide complex of any one of claims 1 to 40 in combination with one or more pharmaceutically acceptable excipients.

42. The heterotandem bicyclic peptide complex as defined in any one of claims 1 to 40 for use in preventing, suppressing or treating cancer.

43. Use of a heterotandem bicyclic peptide complex as defined in any one of claims 1 to 40 in the manufacture of a medicament for treating cancer, wherein the heterotandem bicyclic peptide complex are to be administered at a dosage frequency which does not sustain plasma concentrations of said complex above the *in vitro* EC₅₀ of said complex.