CLAIMS

1. A heterotandem bicyclic peptide complex or a pharmaceutically acceptable salt thereof comprising:

(a) a first peptide ligand which binds to a component present on an immune cell; wherein said component present on an immune cell is CD137, and wherein the CD137 binding bicyclic peptide ligand comprises a polypeptide comprising an amino acid sequence selected from:

C_iIEEGQYC_{ii}FADPY[Nle]C_{iii} (SEQ ID NO: 1);

C_i[tBuAla]PE[D-Ala]PYC_{ii}FADPY[Nle]C_{iii} (SEQ ID NO: 3);

C_iIEEGQYC_{ii}F[D-Ala]DPY[Nle]C_{iii} (SEQ ID NO: 4);

C_i[tBuAla]PK[D-Ala]PYC_{ii}FADPY[Nle]C_{iii} (SEQ ID NO: 5);

C_i[tBuAla]PE[D-Lys]PYC_{ii}FADPY[Nle]C_{iii} (SEQ ID NO: 6);

C_i[tBuAla]P[K(PYA)][D-Ala]PYC_{ii}FADPY[Nle]C_{iii} (SEQ ID NO: 7);

C_i[tBuAla]PE[D-Lys(PYA)]PYC_{ii}FADPY[Nle]C_{iii} (SEQ ID NO: 8);

C_iIEE[D-Lys(PYA)]QYC_{ii}FADPY(Nle)C_{iii} (SEQ ID NO: 9); and

[dC_i][dI][dE][dE][K(PYA)][dQ][dY][dC_{ii}][dF][dA][dD][dP][dY][dNle][dC_{iii}] (SEQ ID NO: 10);

or a modified derivative thereof;

conjugated via a linker to

(b) a second peptide ligand which binds to a component present on a cancer cell; wherein said component present on a cancer cell is EphA2, PD-L1, or Nectin-4, and wherein

the EphA2 binding bicyclic peptide ligand comprises a polypeptide comprising an amino acid sequence selected from:

C_i[HyP]LVNPLC_{ii}LHP[dD]W[HArg]C_{iii} (SEQ ID NO: 2); and

C_iLWDPTPC$_{ii}$ANLHL[HArg]C_{iii} (SEQ ID NO: 11);

or a modified derivative thereof;

the PD-L1 binding bicyclic peptide ligand comprises a polypeptide comprising an amino acid sequence selected from:

C_i[HArg]DWC$_{ii}$HWTFSHGHPC_{iii} (SEQ ID NO: 12);

C_iSAGWLTMC$_{ii}$QKLHLC_{iii} (SEQ ID NO: 13); and

C_iSAGWLTMC$_{ii}$Q[K(PYA)]LHLC_{iii} (SEQ ID NO: 14);

or a modified derivative thereof; and

the Nectin-4 binding bicyclic peptide ligand comprises a polypeptide comprising an amino acid sequence selected from:

$C_iP[1Nal][dD]C_{ii}M[HArg]DWSTP[HyP]WC_{iii}$ (SEQ ID NO: 15; hereinafter referred to as BCY8116);

$C_iP[1Nal][dD]C_{ii}M[HArg]D[dW]STP[HyP][dW]C_{iii}$ (SEQ ID NO: 16; hereinafter referred to as BCY11415); and

$C_iP[1Nal][dK](Sar_{10}\text{-}(B\text{-}Ala))C_{ii}M[HArg]DWSTP[HyP]WC_{iii}$ (SEQ ID NO: 17);

$C_iPFGC_{ii}M[HArg]DWSTP[HyP]WC_{iii}$ (SEQ ID NO: 18; hereinafter referred to as BCY11414);

or a modified derivative thereof;

wherein C_i, C_{ii} and C_{iii} represent first, second and third cysteine residues, respectively, Nle represents norleucine, tBuAla represents t-butyl-alanine, PYA represents 4-pentynoic acid, HyP represents hydroxyproline, dD represents aspartic acid in D-configuration, HArg represents homoarginine, 1Nal represents 1-naphthylalanine, Sar_{10} represents 10 sarcosine units, and B-Ala represents beta-alanine, or a the pharmaceutically acceptable salt thereof;

wherein each of said peptide ligands comprises a polypeptide comprising at least three cysteine residues, separated by at least two loop sequences, and a 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 each modified derivative independently comprises one or more of:

replacement of one or more amino acid residues with one or more non-natural amino acid residues;

replacement of one or more amino acid residues with one or more isosteric and/or isoelectronic amino acids; and/or

replacement of one or more L-amino acid residues with one or more D-amino acid residues.

2. The heterotandem bicyclic peptide complex or the pharmaceutically acceptable salt thereof 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+ T cells, for example CD8+ T cells; dendritic cells, follicular dendritic cells and granulocytes.

3. The heterotandem bicyclic peptide complex or the pharmaceutically acceptable salt thereof as defined in claim 1 or claim 2, wherein the component present on an immune cell is CD137.

4. The heterotandem bicyclic peptide complex or the pharmaceutically acceptable salt thereof as defined in any one of claims 1 to 3, wherein the first peptide ligand comprises a CD137 binding bicyclic peptide ligand.

5. The heterotandem bicyclic peptide complex or the pharmaceutically acceptable salt thereof as defined in any one of claims 1 to 4, wherein the CD137 binding bicyclic peptide ligand comprises N- and C-terminal modifications and comprises:

Ac-A-(SEQ ID NO: 1)-Dap (hereinafter referred to as BCY7732);

Ac-A-(SEQ ID NO: 1)-Dap(PYA) (hereinafter referred to as BCY7741);

Ac-(SEQ ID NO: 3)-Dap (hereinafter referred to as BCY9172);

Ac-(SEQ ID NO: 3)-Dap(PYA) (hereinafter referred to as BCY11014);

Ac-A-(SEQ ID NO: 4)-Dap (hereinafter referred to as BCY8045);

Ac-(SEQ ID NO: 5)-A (hereinafter referred to as BCY8919);

Ac-(SEQ ID NO: 6)-A (hereinafter referred to as BCY8920);

Ac-(SEQ ID NO: 7)-A (hereinafter referred to as BCY8927);

Ac-(SEQ ID NO: 8)-A (hereinafter referred to as BCY8928);

Ac-A-(SEQ ID NO: 9)-A (hereinafter referred to as BCY7744); and

Ac-[dA]-(SEQ ID NO: 10)-[dA]-NH_2 (hereinafter referred to as BCY11506);

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

6. The heterotandem bicyclic peptide complex or the pharmaceutically acceptable salt thereof as defined in claim 5, wherein the CD137 binding bicyclic peptide ligand comprises:

Ac-(SEQ ID NO: 8)-A (hereinafter referred to as BCY8928);

wherein Ac represents an acetyl group.

7. The heterotandem bicyclic peptide complex or the pharmaceutically acceptable salt thereof as defined in any one of claims 1 to 6, wherein the cancer cell is selected from an HT1080, SC-OV-3, PC3, H1376, NCI-H292, LnCap, MC38 and RKO tumor cell.

8. The heterotandem bicyclic peptide complex or the pharmaceutically acceptable salt thereof as defined in any one of claims 1 to 7, wherein the component present on a cancer cell is EphA2.

9. The heterotandem bicyclic peptide complex or the pharmaceutically acceptable salt thereof as defined in any one of claims 1 to 8, wherein the second peptide ligand comprises an EphA2 binding bicyclic peptide ligand.

10. The heterotandem bicyclic peptide complex or the pharmaceutically acceptable salt thereof as defined in claim 9, wherein the EphA2 binding bicyclic peptide ligand comprises N-terminal modifications and comprises:

A-HArg-D-(SEQ ID NO: 2) (hereinafter referred to as BCY9594);

[B-Ala]-[Sar_{10}]-A-[HArg]-D-(SEQ ID NO: 2) (hereinafter referred to as BCY6099);

[PYA]-[B-Ala]-[Sar_{10}]-A-[HArg]-D-(SEQ ID NO: 2) (hereinafter referred to as BCY6169); and

[PYA]-[B-Ala]-[Sar_{10}]-VGP-(SEQ ID NO: 11) (hereinafter referred to as BCY8941);

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

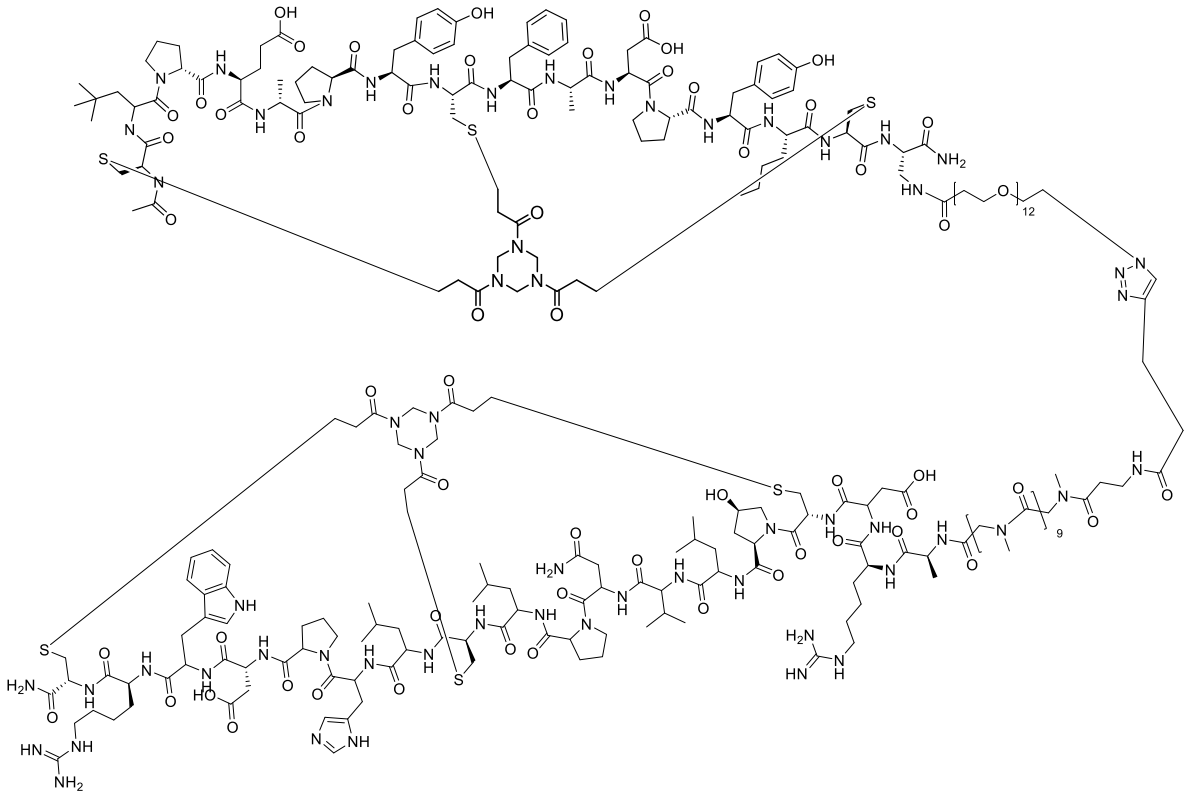
11. The heterotandem bicyclic peptide complex or the pharmaceutically acceptable salt thereof as defined in claim 9 or claim 10 which is a CD137/EphA2 complex comprising a first peptide ligand comprising a CD137 binding bicyclic peptide ligand attached to a TATA scaffold, and a second peptide ligand comprising an EphA2 binding bicyclic peptide ligand attached to a TATA scaffold, wherein said heterotandem bicyclic peptide complex comprises:

- [PYA]-[B-Ala]-[Sar_{10}]-A-[HArg]-D-(SEQ ID NO: 2) (BCY6169) and Ac-(SEQ ID NO: 3)-Dap (BCY9172), wherein the N-terminal PYA of BCY6169 is linked to the C-terminal Dap of (BCY9172) via a -PEG_{12}- linker;
- [PYA]-[B-Ala]-[Sar_{10}]-A-[HArg]-D-(SEQ ID NO: 2) (BCY6169) and Ac-A-(SEQ ID NO: 1)-Dap (BCY7732), wherein the N-terminal PYA of BCY6169 is linked to the C-terminal Dap of BCY7732 via a -PEG_{12}- linker;
- [PYA]-[B-Ala]-[Sar_{10}]-A-[HArg]-D-(SEQ ID NO: 2) (BCY6169) and Ac-A-(SEQ ID NO: 4)-Dap, (BCY8045) wherein the N-terminal PYA of BCY6169 is linked to the C-terminal Dap of BCY8045 via a -PEG_{12}- linker;
- [PYA]-[B-Ala]-[Sar_{10}]-VGP-(SEQ ID NO: 11) (BCY8941) and Ac-A-(SEQ ID NO: 1)-Dap (BCY7732), wherein the N-terminal PYA of BCY8941 is linked to the C-terminal Dap of BCY7732 via a -PEG_{12}- linker;
- [B-Ala]-[Sar_{10}]-A-[HArg]-D-(SEQ ID NO: 2) (BCY6099) and Ac-A-(SEQ ID NO: 1)-Dap(PYA) (BCY7741), wherein the N-terminus of BCY6099 is linked to the C-terminal Dap(PYA) of BCY7741 via a -PEG_{10}- linker;
- [B-Ala]-[Sar_{10}]-A-[HArg]-D-(SEQ ID NO: 2) (BCY6099) and Ac-A-(SEQ ID NO: 1)-Dap(PYA) (BCY7741), wherein the N-terminus of BCY6099 is linked to the C-terminal Dap(PYA) of BCY7741 via a -PEG_{23}- linker;

- [B-Ala]-[Sar_{10}]-A-[HArg]-D-(SEQ ID NO: 2) (BCY6099) and Ac-A-(SEQ ID NO: 1)-Dap(PYA) (BCY7741), wherein the N-terminus of BCY6099 is linked to the C-terminal Dap(PYA) of BCY7741 via a -PEG_{15}-Sar_5- linker;
- [B-Ala]-[Sar_{10}]-A-[HArg]-D-(SEQ ID NO: 2) (BCY6099) and Ac-A-(SEQ ID NO: 1)-Dap(PYA) (BCY7741), wherein the N-terminus of BCY6099 is linked to the C-terminal Dap(PYA) of BCY7741 via a -PEG_{10}-Sar_{10}- linker;
- [B-Ala]-[Sar_{10}]-A-[HArg]-D-(SEQ ID NO: 2) (BCY6099) and Ac-A-(SEQ ID NO: 1)-Dap(PYA) (BCY7741), wherein the N-terminus of BCY6099 is linked to the C-terminal Dap(PYA) of BCY7741 via a -PEG_5-Sar_{15}- linker;
- [B-Ala]-[Sar_{10}]-A-[HArg]-D-(SEQ ID NO: 2) (BCY6099) and Ac-A-(SEQ ID NO: 1)-Dap(PYA) (BCY7741), wherein the N-terminus of BCY6099 sequence is linked to the C-terminal Dap(PYA) of BCY7741 via a -PEG_5-Sar_5- linker;
- [B-Ala]-[Sar_{10}]-A-[HArg]-D-(SEQ ID NO: 2) (BCY6099) and Ac-A-(SEQ ID NO: 1)-Dap(PYA) (BCY7741), wherein the N-terminus of BCY6099 is linked to the C-terminal Dap(PYA) of BCY7741 via a -PEG_5- linker;
- [B-Ala]-[Sar_{10}]-A-[HArg]-D-(SEQ ID NO: 2) (BCY6099) and Ac-A-(SEQ ID NO: 1)-Dap (BCY7732), wherein the N-terminus of BCY6099 is linked to the C-terminal Dap of BCY7732 via a -PEG_{24}- linker;
- [PYA]-[B-Ala]-[Sar_{10}]-A-[HArg]-D-(SEQ ID NO: 2) (BCY6169) and Ac-(SEQ ID NO: 5)-A (BCY8919), wherein the N-terminal PYA of BCY6169 is linked to the Lys3 of BCY8919 via a -PEG_{12}- linker;
- [PYA]-[B-Ala]-[Sar_{10}]-A-[HArg]-D-(SEQ ID NO: 2) (BCY6169) and Ac-(SEQ ID NO: 6)-A (BCY8920), wherein the N-terminal PYA of BCY6169 is linked to the dLys4 of BCY8920 via a -PEG_{12}- linker;
- A-HArg-D-(SEQ ID NO: 2) (BCY9594) and Ac-(SEQ ID NO: 7)-A (BCY8927), wherein the N-terminus of BCY9594 is linked to the Lys(PYA)3 of BCY8927 via a -PEG_5- linker;
- A-HArg-D-(SEQ ID NO: 2) (BCY9594) and Ac-(SEQ ID NO: 8)-A (BCY8928), wherein the N-terminus of BCY9594 is linked to the dLys(PYA)4 of BCY8928 via a -PEG_5-linker;
- A-HArg-D-(SEQ ID NO: 2) (BCY9594) and Ac-(SEQ ID NO: 3)-Dap(PYA) (BCY11014), wherein the N-terminus of BCY9594 is linked to the C-terminal Dap(PYA) of BCY11014 via a -PEG_5- linker; or
- [PYA]-[B-Ala]-[Sar_{10}]-A-[HArg]-D-(SEQ ID NO: 2) (BCY6169) and Ac-(SEQ ID NO: 3)-Dap (BCY9172) wherein the N-terminus of BCY6169 is linked to the C-terminal Dap of BCY9172 via a -CH_2- linker.

12. The heterotandem bicyclic peptide complex or the pharmaceutically acceptable salt thereof as defined in any one of claims 9 to 11 which is a CD137/EphA2 complex selected from:

BCY9173



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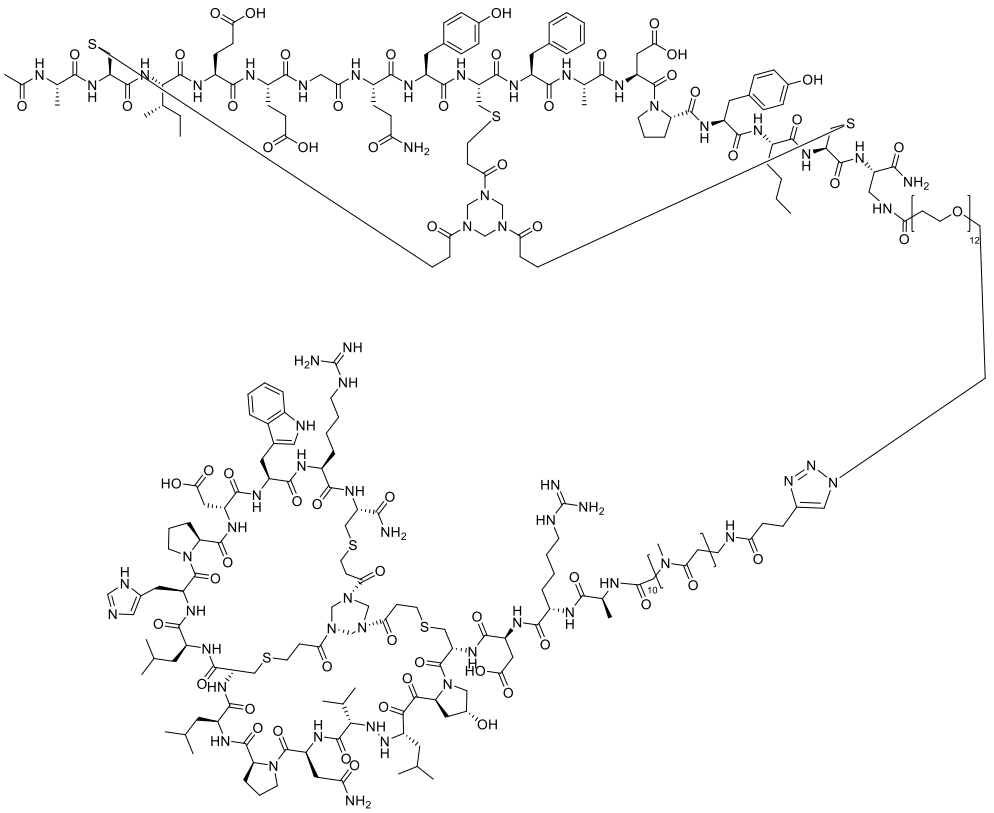

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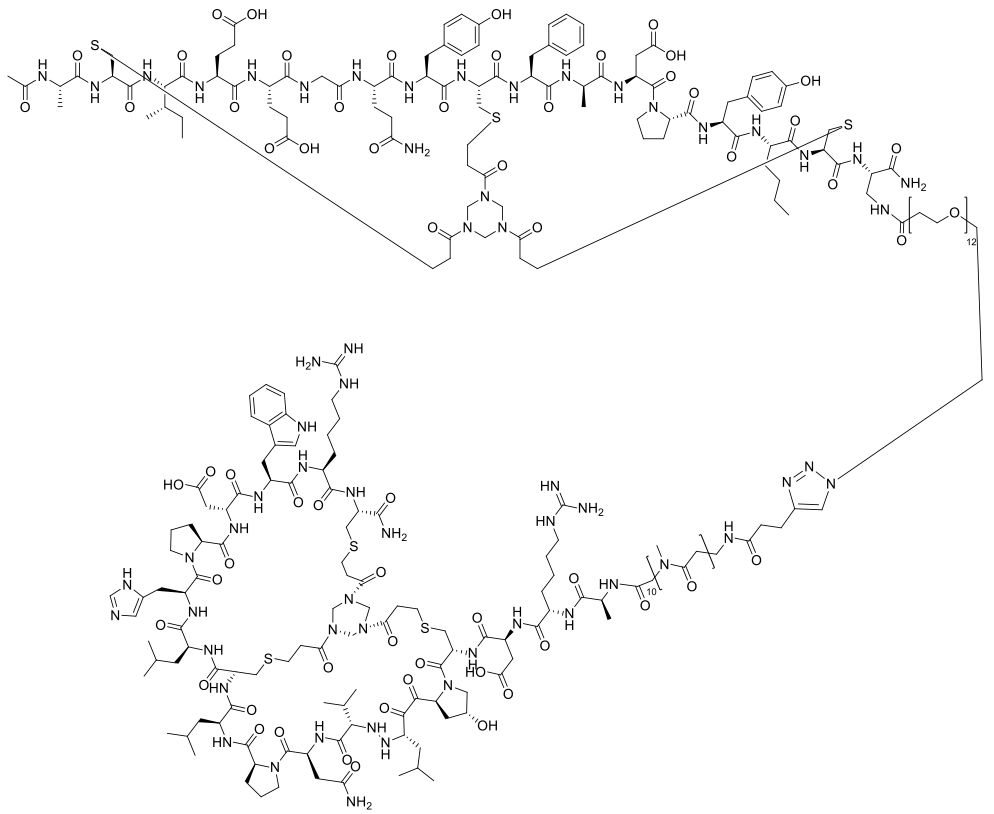

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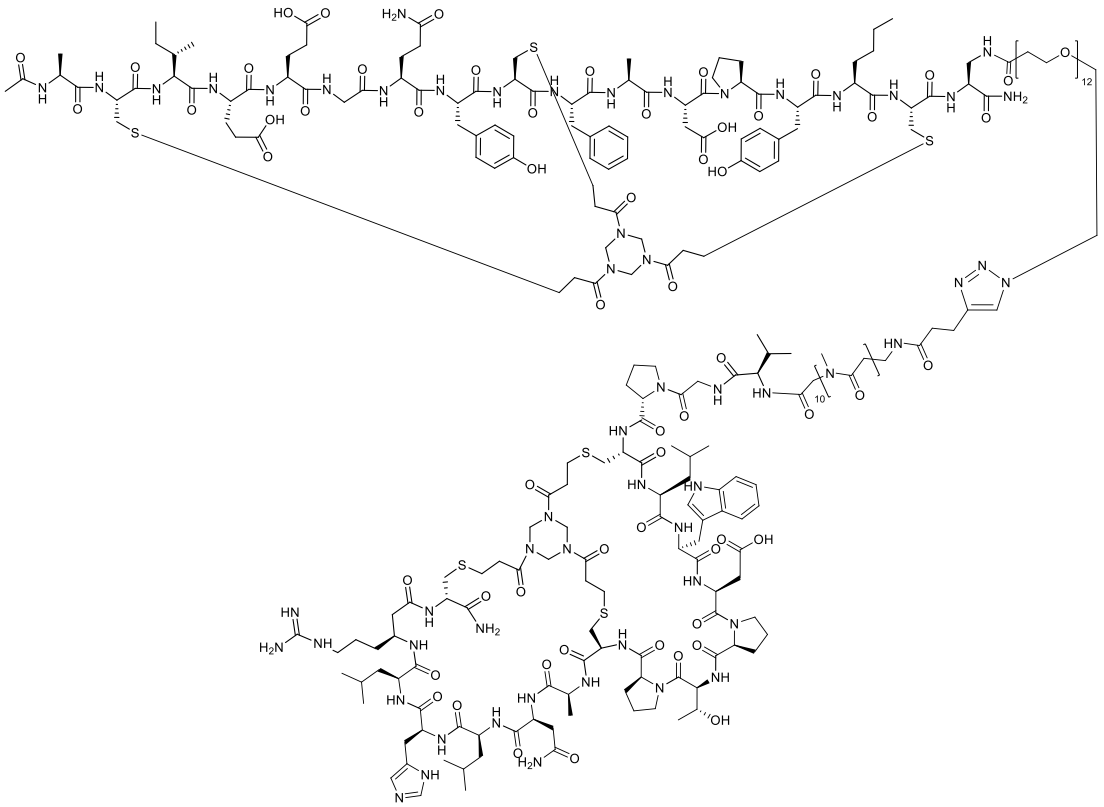

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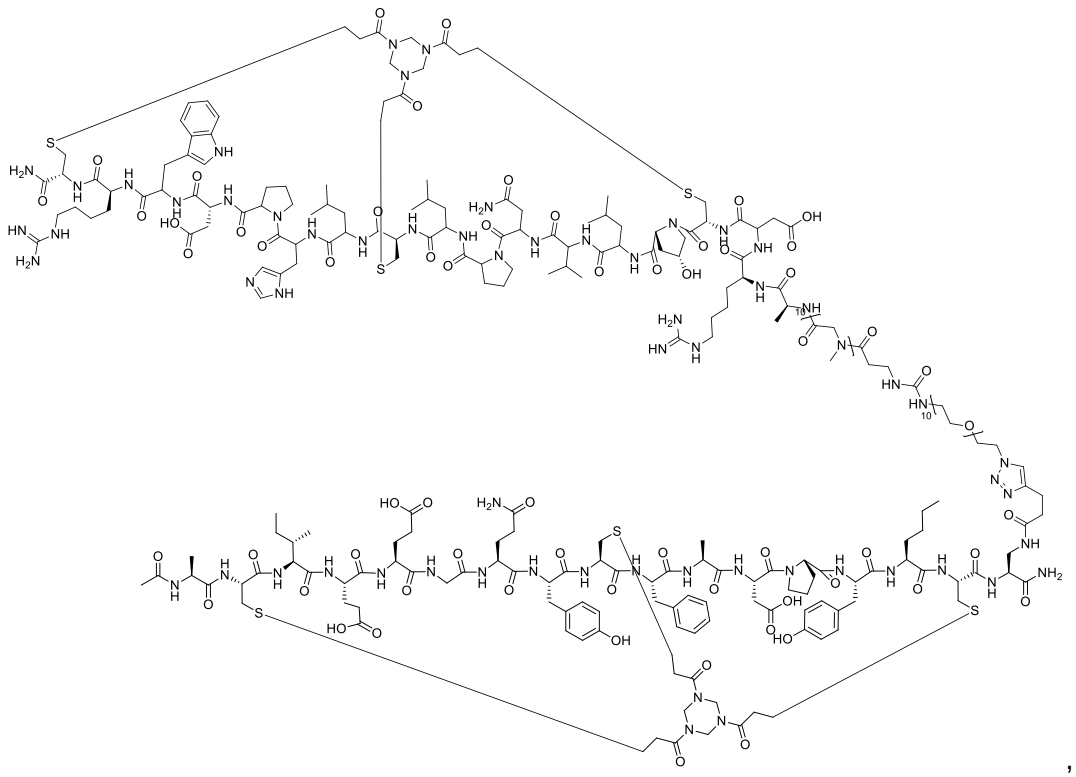

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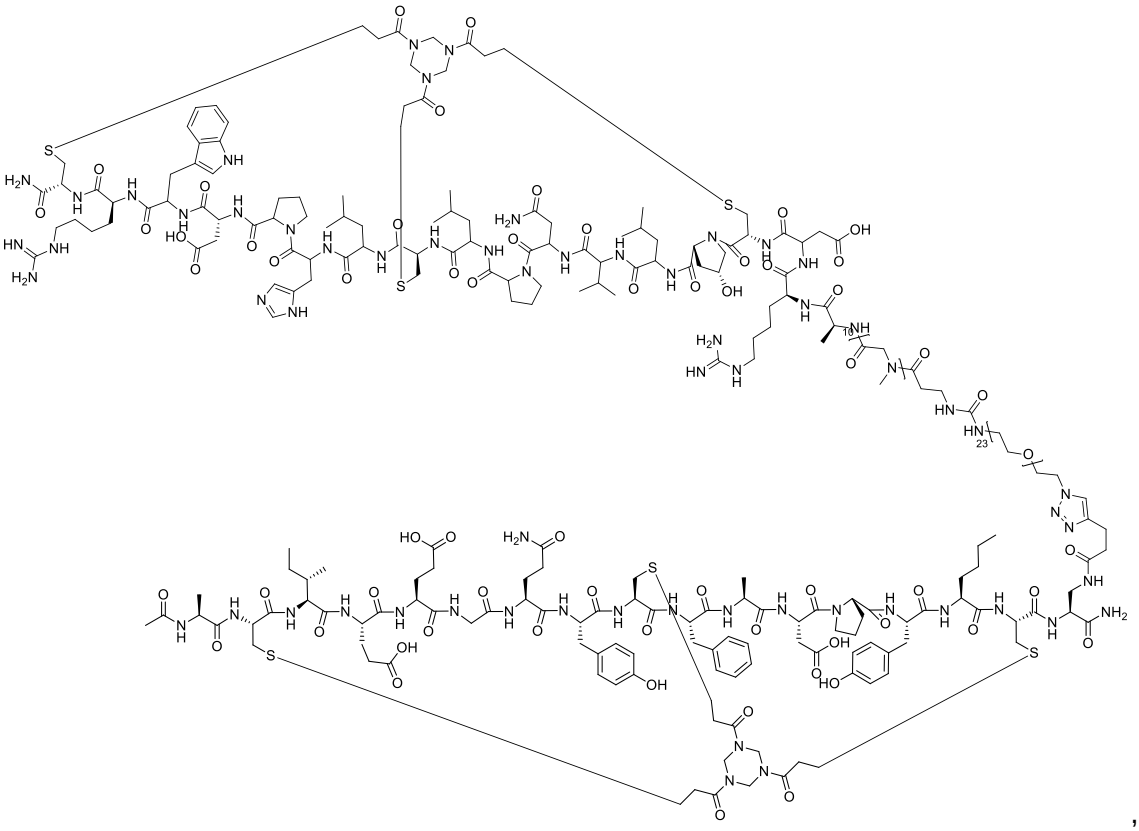

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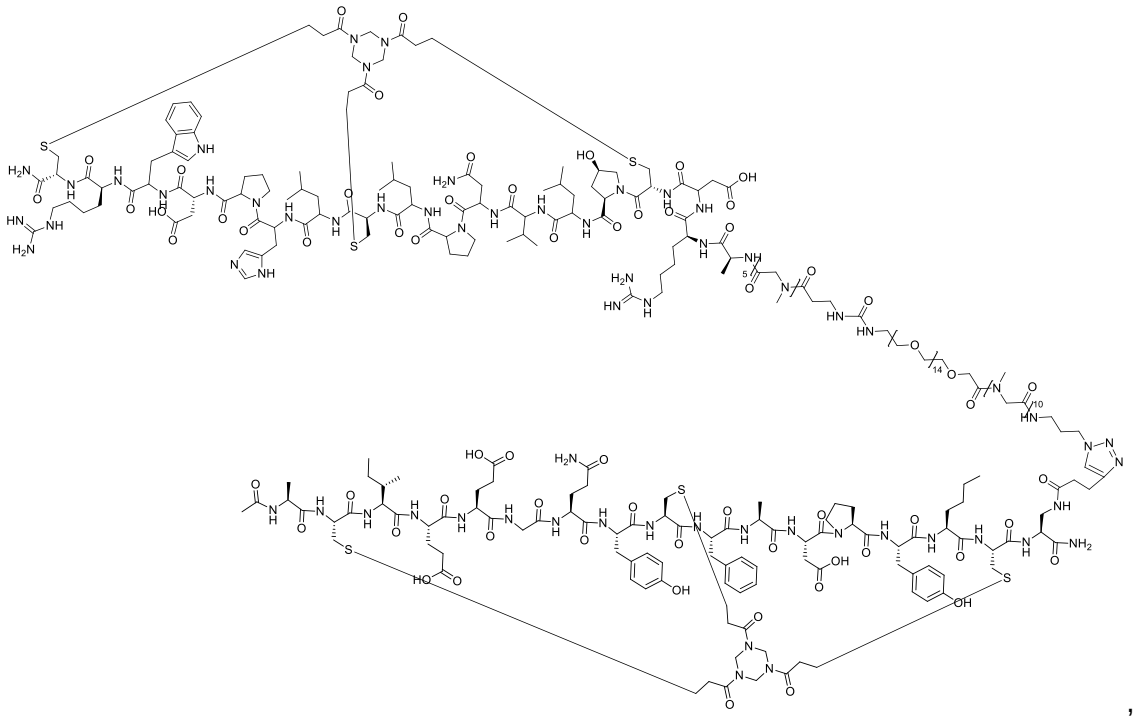

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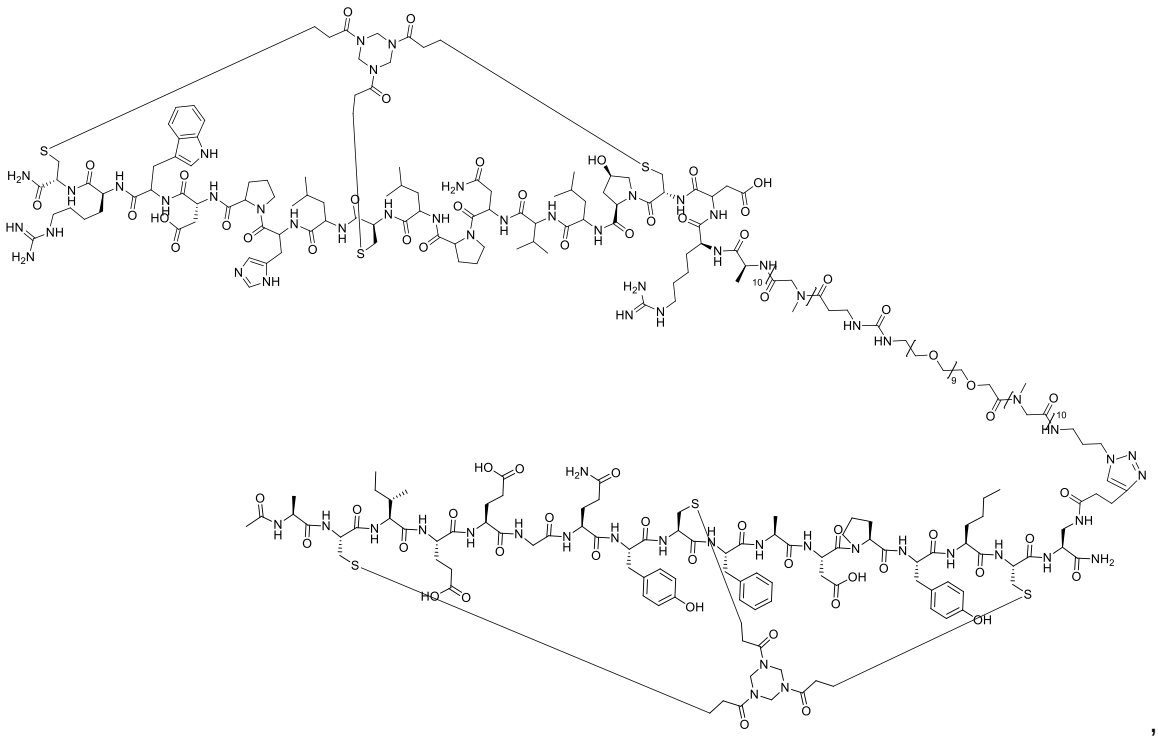

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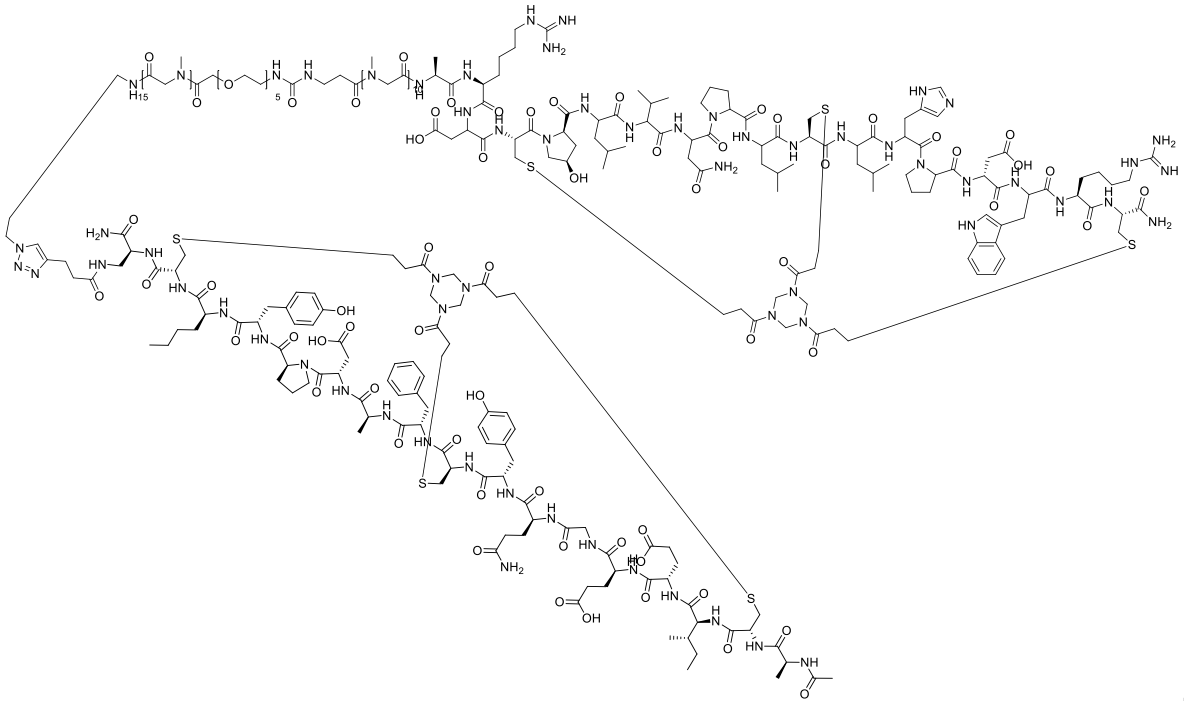

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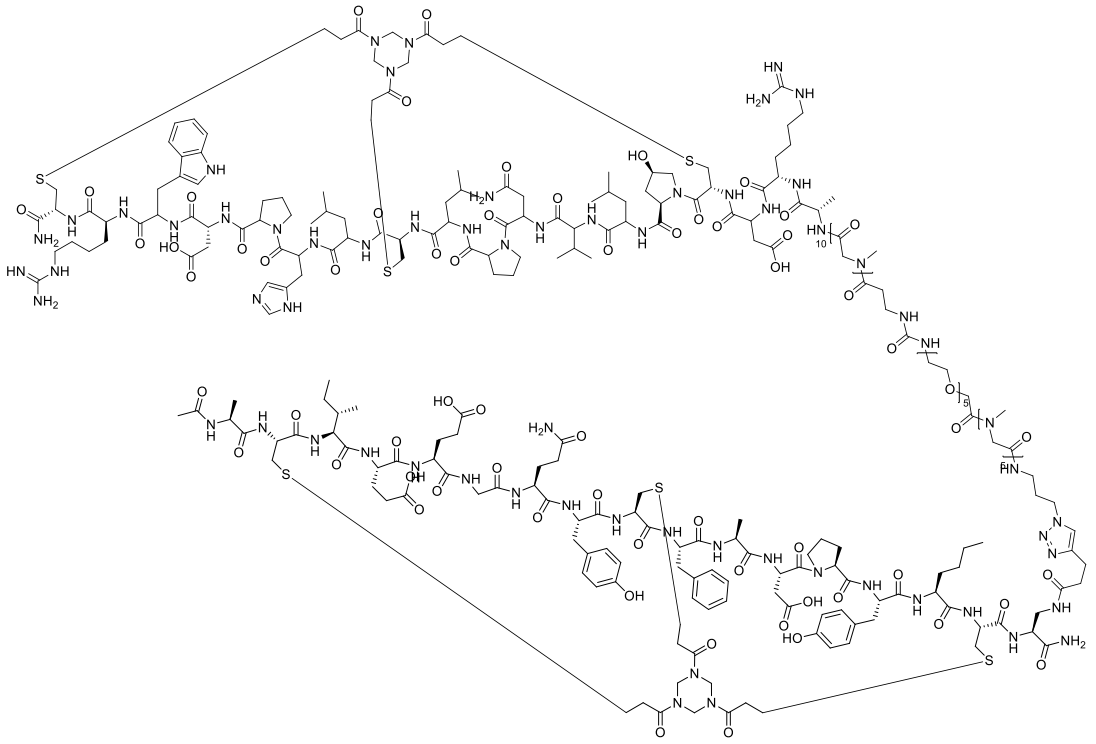

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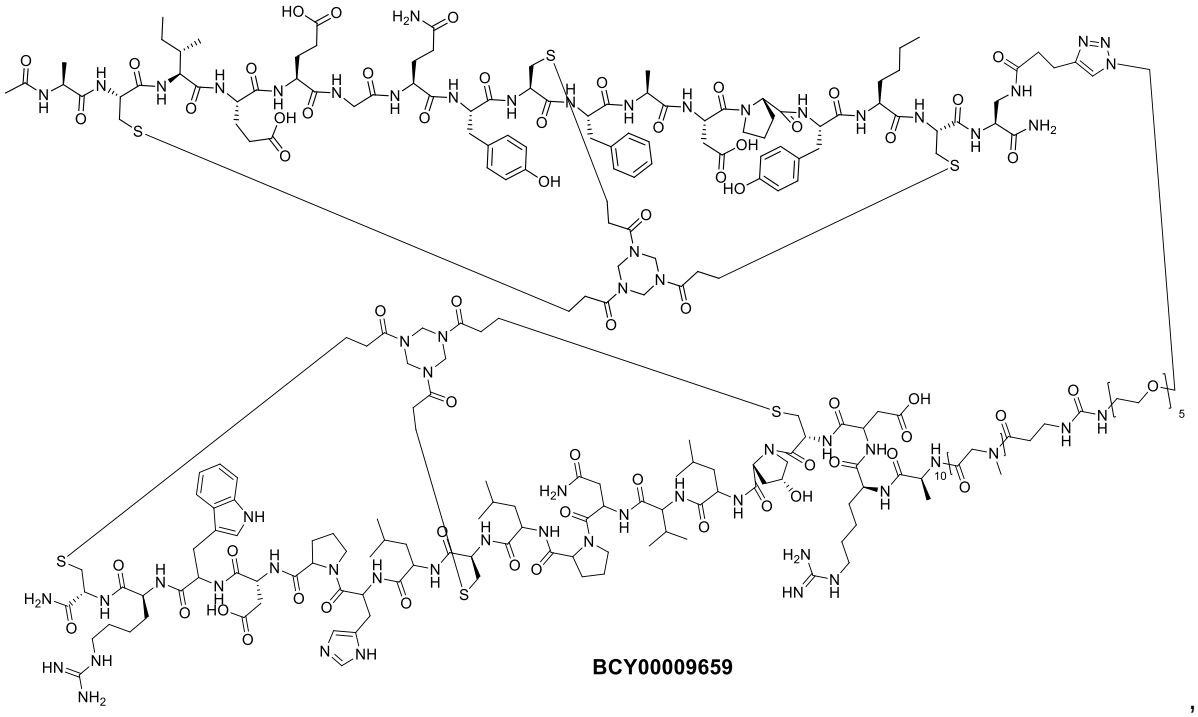

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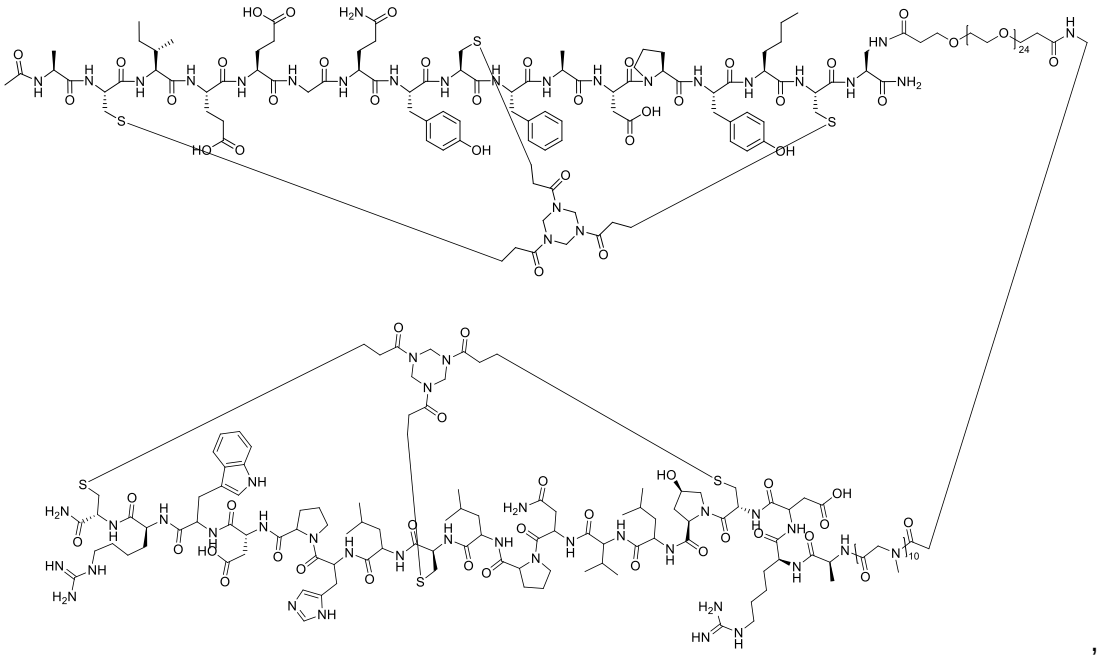

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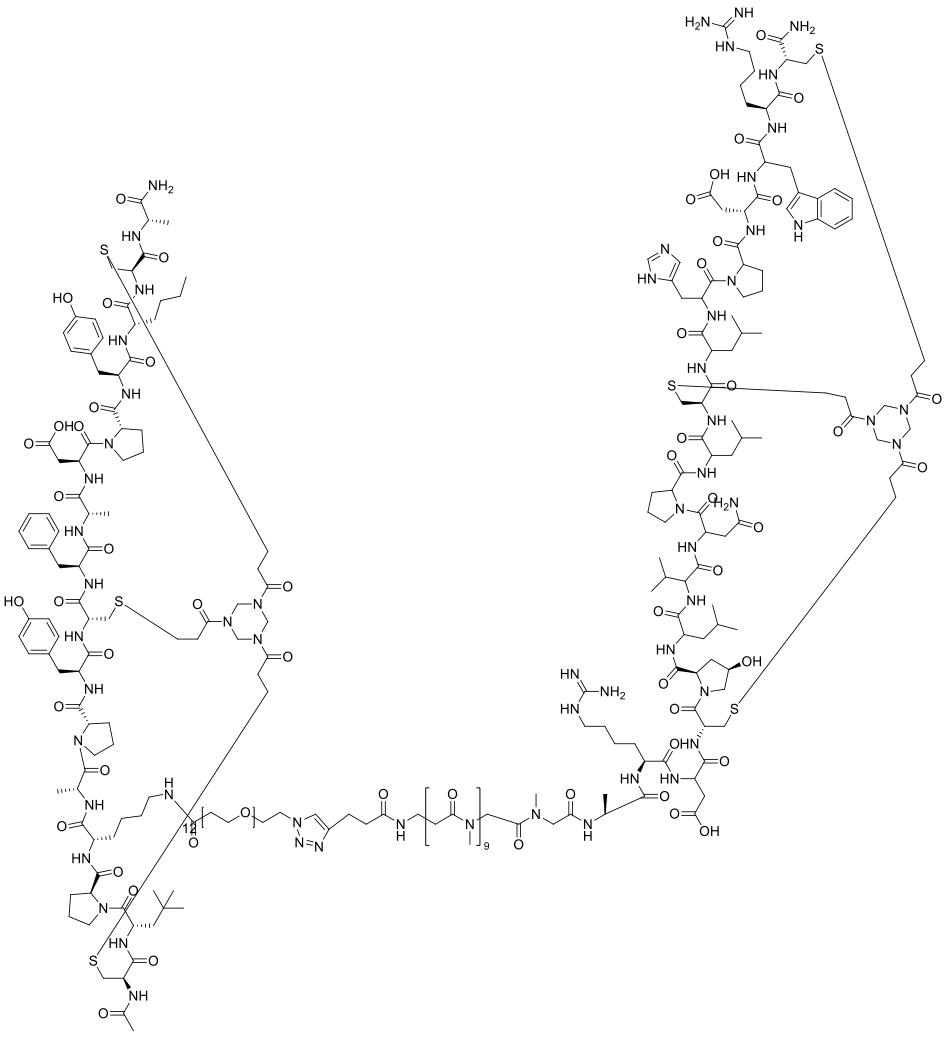

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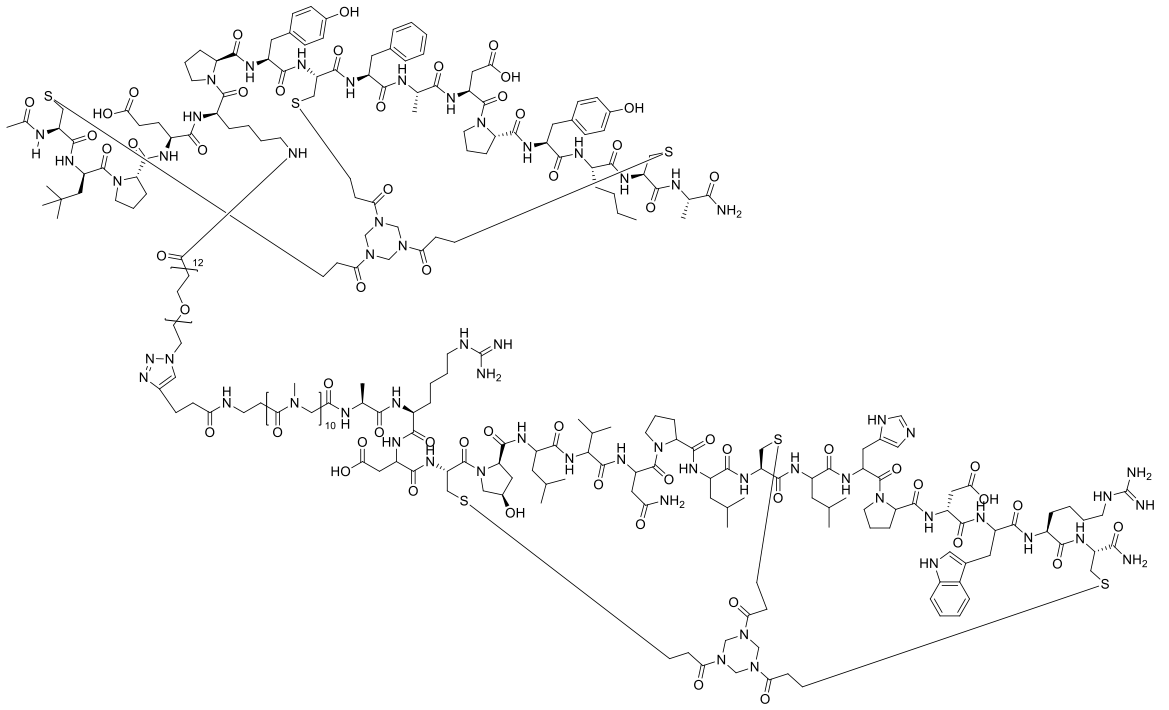

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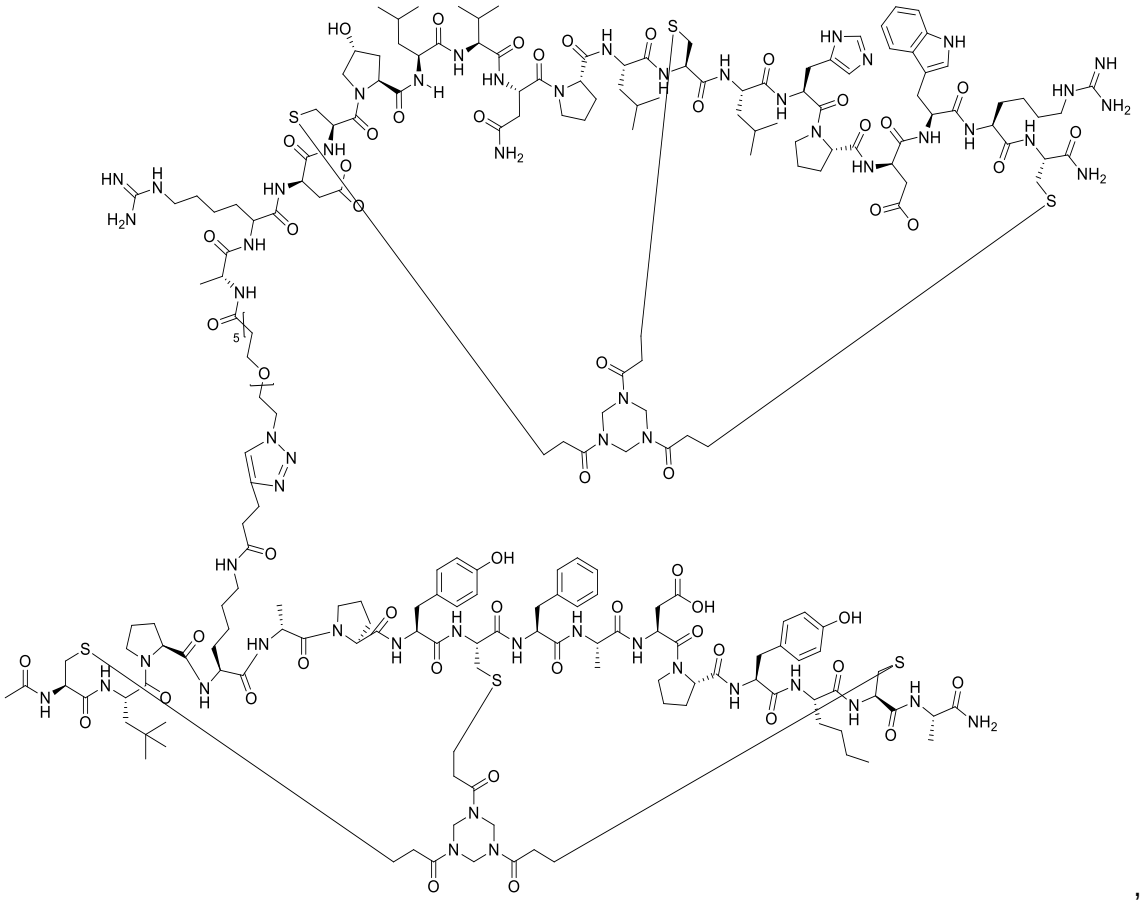

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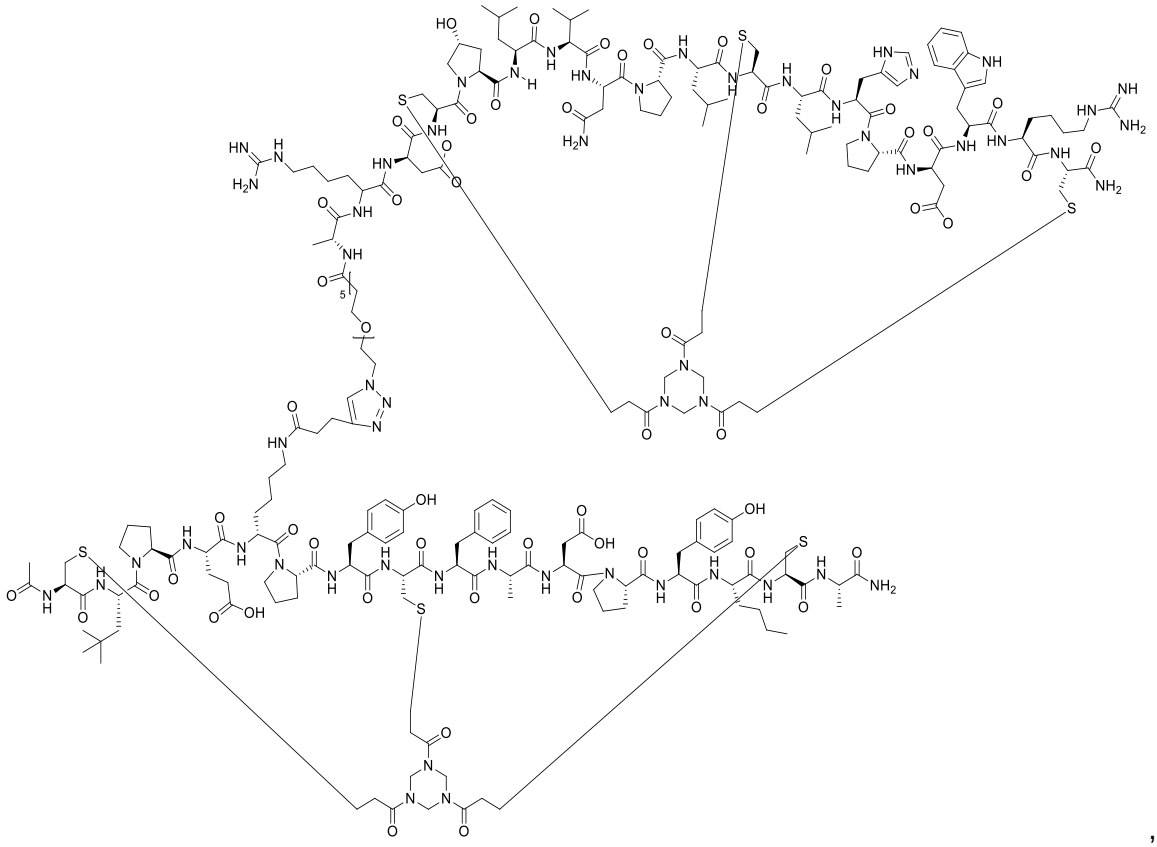

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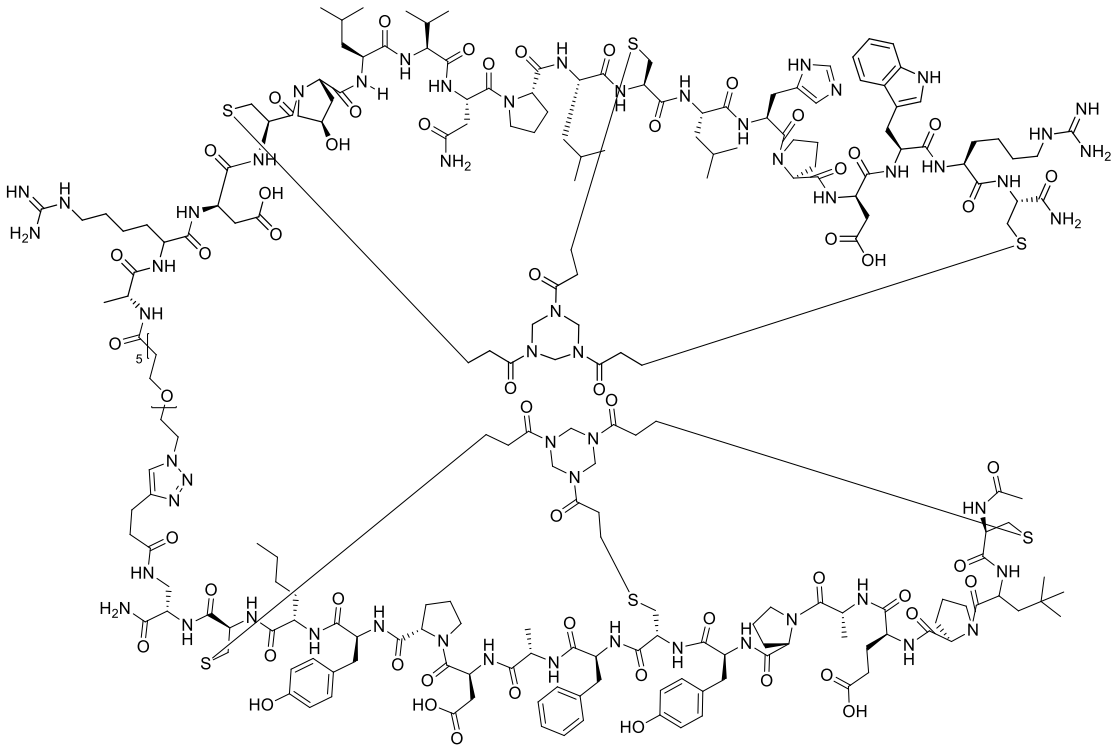

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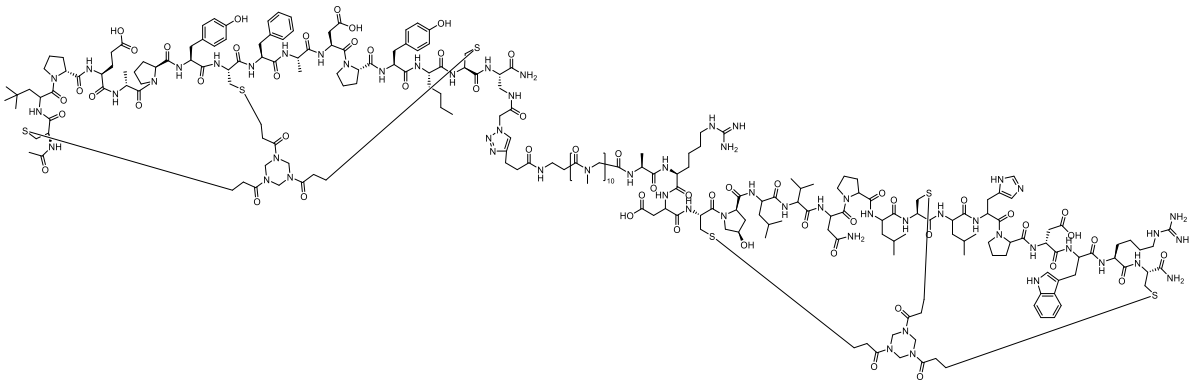

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13. The heterotandem bicyclic peptide complex or the pharmaceutically acceptable salt thereof as defined in any one of claims 1 to 7, wherein the component present on a cancer cell is PD-L1.

14. The heterotandem bicyclic peptide complex or the pharmaceutically acceptable salt thereof as defined in any one of claims 1 to 7 and 13, wherein the second peptide ligand comprises PD-L1 binding bicyclic peptide ligand.

15. The heterotandem bicyclic peptide complex or the pharmaceutically acceptable salt thereof as defined in claim 14, wherein the PD-L1 binding bicyclic peptide ligand comprises N-terminal and/or C-terminal modifications and comprises:

[PYA]-[B-Ala]-[Sar_{10}]-(SEQ ID NO: 12) (hereinafter referred to as BCY8938);

[PYA]-[B-Ala]-[Sar_{10}]-SDK-(SEQ ID NO: 13) (hereinafter referred to as BCY10043);

NH_2-SDK-(SEQ ID NO: 13)-[Sar_{10}]-[K(PYA)] (hereinafter referred to as BCY10044);

NH_2-SDK-(SEQ ID NO: 14) (hereinafter referred to as BCY10045); and

Ac-SDK-(SEQ ID NO: 14)-PSH (hereinafter referred to as BCY10861);

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

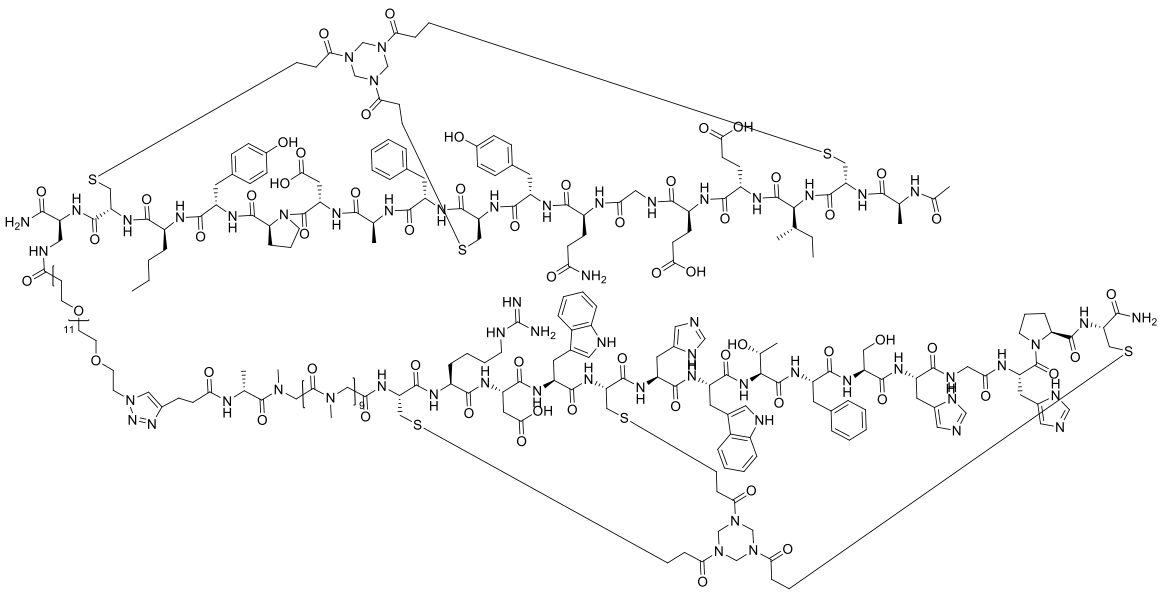
16. The heterotandem bicyclic peptide complex or the pharmaceutically acceptable salt thereof as defined in claim 14 or 15 which is a CD137/PD-L1 complex comprising a first peptide ligand comprising a PD-L1 binding bicyclic peptide ligand attached to a TATA scaffold, and a second peptide ligand comprising a PD-L1 binding bicyclic peptide ligand attached to a TATA scaffold, wherein said heterotandem bicyclic peptide complex comprises:

- [PYA]-[B-Ala]-[Sar_{10}]-(SEQ ID NO: 12) (BCY8938) and Ac-A-(SEQ ID NO: 1)-Dap (BCY7732), wherein the N-terminal PYA of BCY8938 and the C-terminal Dap of BCY7732 are linked via a -PEG_{12}- linker;
- [PYA]-[B-Ala]-[Sar_{10}]-SDK-(SEQ ID NO: 13) (BCY10043) and Ac-(SEQ ID NO: 3)-Dap (BCY9172), wherein the N-terminal PYA of BCY10043 and the C-terminal Dap of BCY9172 are linked via a -PEG_{12}- linker;
- NH_2-SDK-(SEQ ID NO: 13)-[Sar_{10}]-[K(PYA)] (BCY10044) and Ac-(SEQ ID NO: 3)-Dap (BCY9172), wherein the C-terminal Lys(PYA) of BCY10044 and the C-terminal Dap of BCY9172 are linked via a -PEG_{12}- linker;
- NH_2-SDK-(SEQ ID NO: 14) (BCY10045) and Ac-(SEQ ID NO: 3)-Dap (BCY9172), wherein the Lys(PYA)9 of BCY10044 and the C-terminal Dap of BCY9172 are linked via a -PEG_{12}- linker;
- Ac-SDK-(SEQ ID NO: 14)-PSH (BCY10861) and Ac-(SEQ ID NO: 5)-A (BCY8919), wherein the Lys(PYA)9 of BCY10861 and the Lys3 of BCY8919 are linked via a -PEG_{12}- linker;
- Ac-SDK-(SEQ ID NO: 14)-PSH (BCY10861) and Ac-(SEQ ID NO: 6)-A (BCY8920), wherein the Lys(PYA)9 of BCY10861 and the dLys4 of BCY8920 are linked via a -PEG_{12}- linker;
- Ac-SDK-(SEQ ID NO: 14)-PSH (BCY10861) and Ac-(SEQ ID NO: 3)-Dap (BCY9172), wherein the Lys(PYA)9 of BCY10861 and the C-terminal Dap of BCY9172 are linked via a -PEG_{12}- linker;
- Ac-SDK-(SEQ ID NO: 14)-PSH (BCY10861) and Ac-(SEQ ID NO: 5)-A (BCY8919), wherein the Lys(PYA)9 of BCY10861 and the Lys3 of BCY8919 are linked via a -CH_2- linker;
- Ac-SDK-(SEQ ID NO: 14)-PSH (BCY10861) and Ac-(SEQ ID NO: 6)-A (BCY8920), wherein the Lys(PYA)9 of BCY10861 and the dLys4 of BCY8920 are linked via a -CH_2- linker;
- Ac-SDK-(SEQ ID NO: 14)-PSH (BCY10861) and Ac-(SEQ ID NO: 3)-Dap (BCY9172), wherein the Lys(PYA)9 of BCY10861 and the C-terminal Dap of BCY9172 are linked via a -CH_2- linker;
- Ac-SDK-(SEQ ID NO: 14)-PSH (BCY10861) and Ac-(SEQ ID NO: 5)-A (BCY8919), wherein the Lys(PYA)9 of BCY10861 and the Lys3 of BCY8919 are linked via a -PEG_5- linker;
- Ac-SDK-(SEQ ID NO: 14)-PSH (BCY10861) and Ac-(SEQ ID NO: 6)-A (BCY8920), wherein the Lys(PYA)9 of BCY10861 and the dLys4 of BCY8920 are linked via a -PEG_5- linker; or

- Ac-SDK-(SEQ ID NO: 14)-PSH (BCY10861) and Ac-(SEQ ID NO: 3)-Dap (BCY9172), wherein the Lys(PYA)9 of BCY10861 and the C-terminal Dap of BCY9172 are linked via a -PEG_5- linker.

17. The heterotandem bicyclic peptide complex or the pharmaceutically acceptable salt thereof as defined in any one of claims 14 to 16 which is a CD137/PD-L1 complex selected from:

BCY8939



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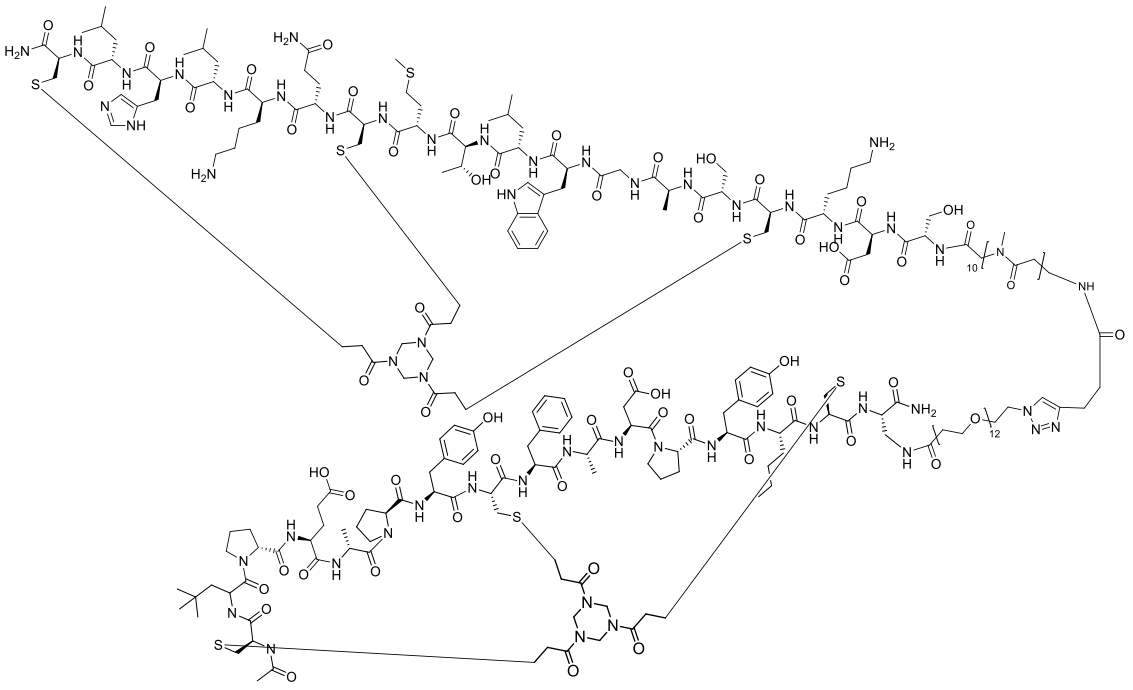

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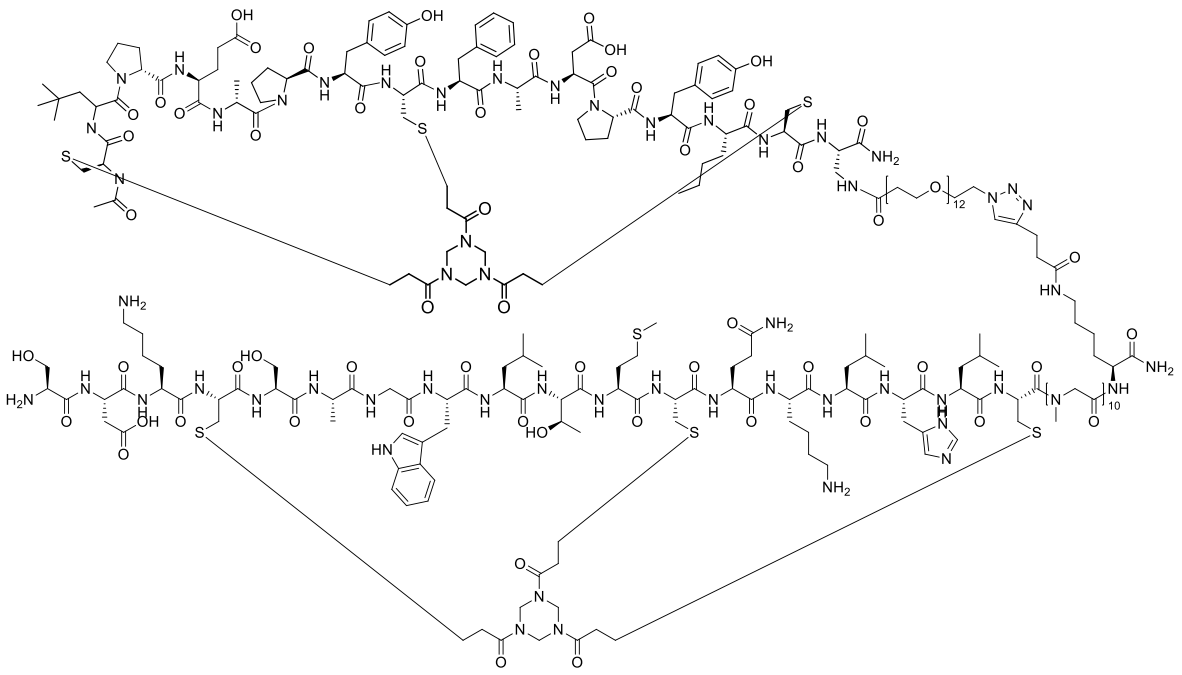

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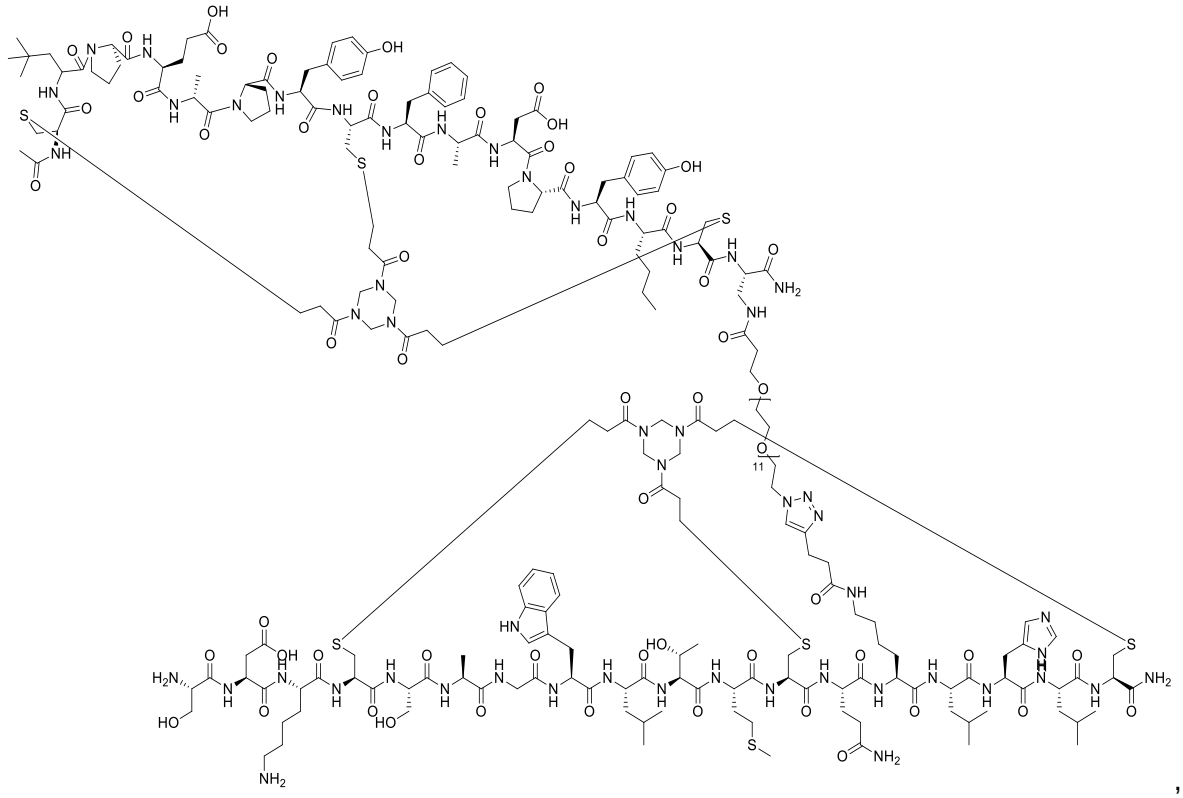

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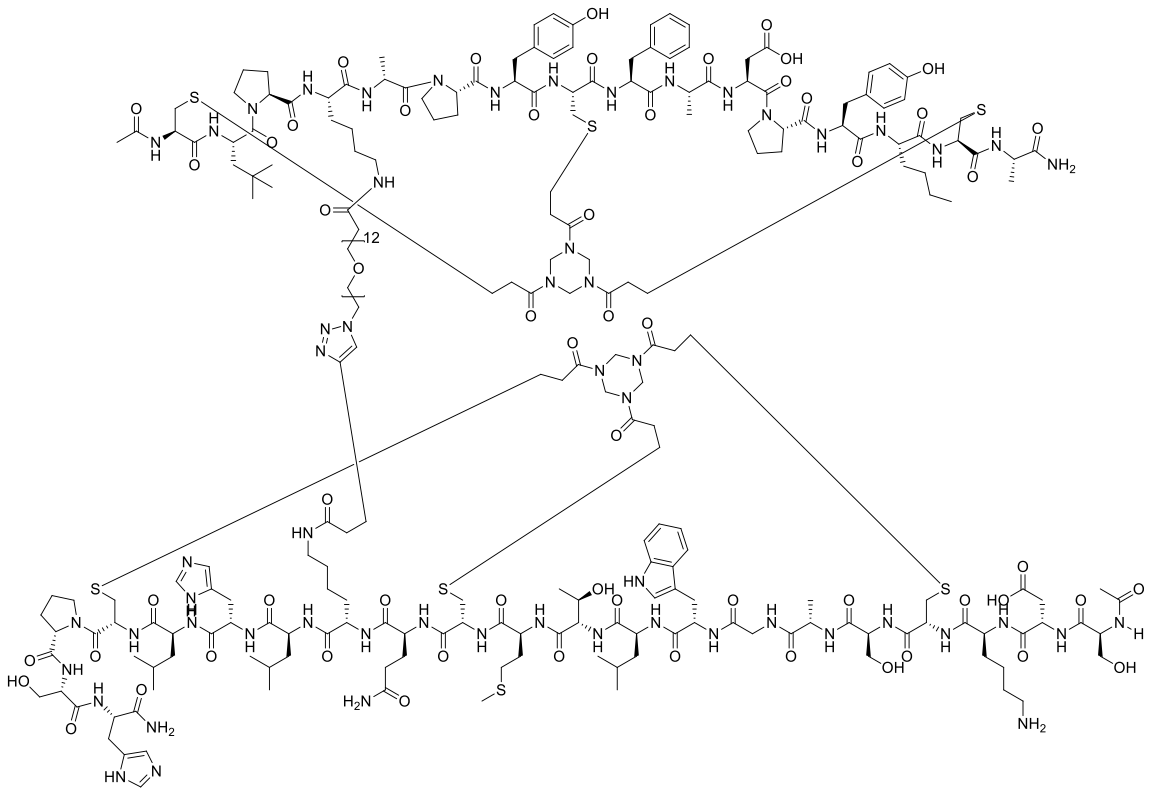

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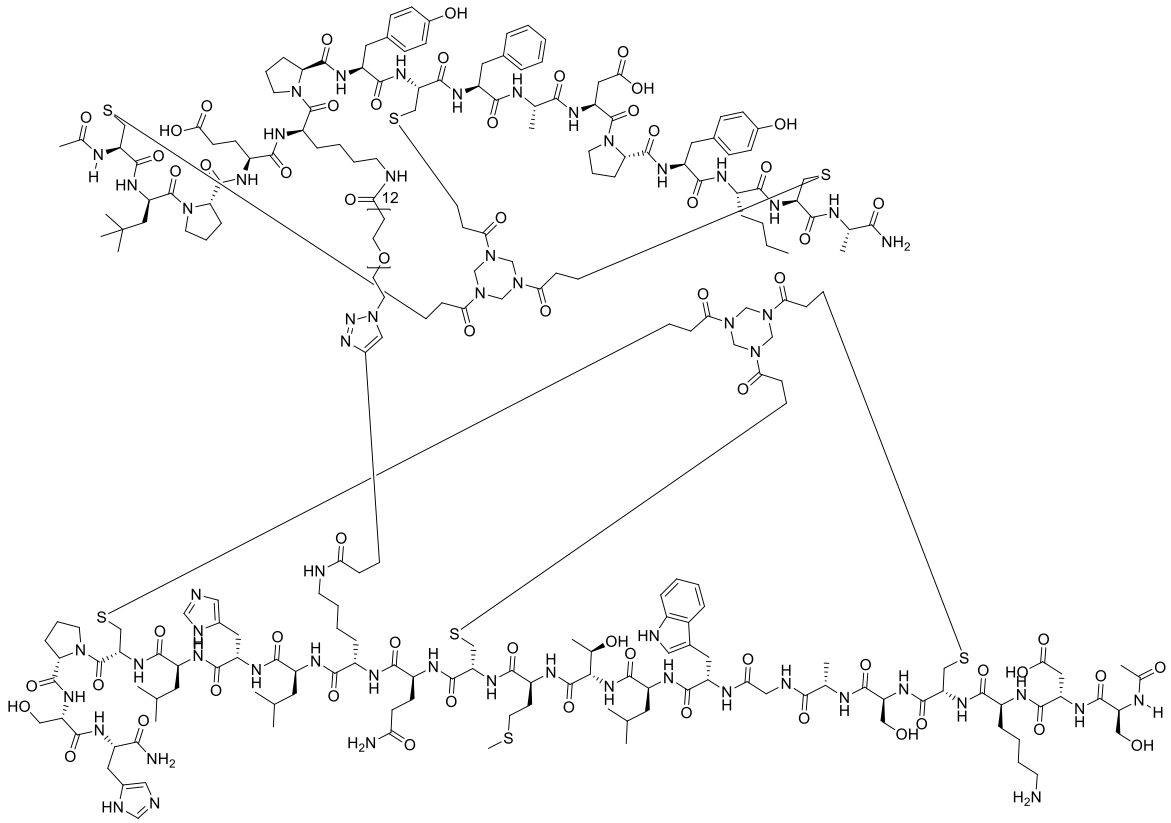

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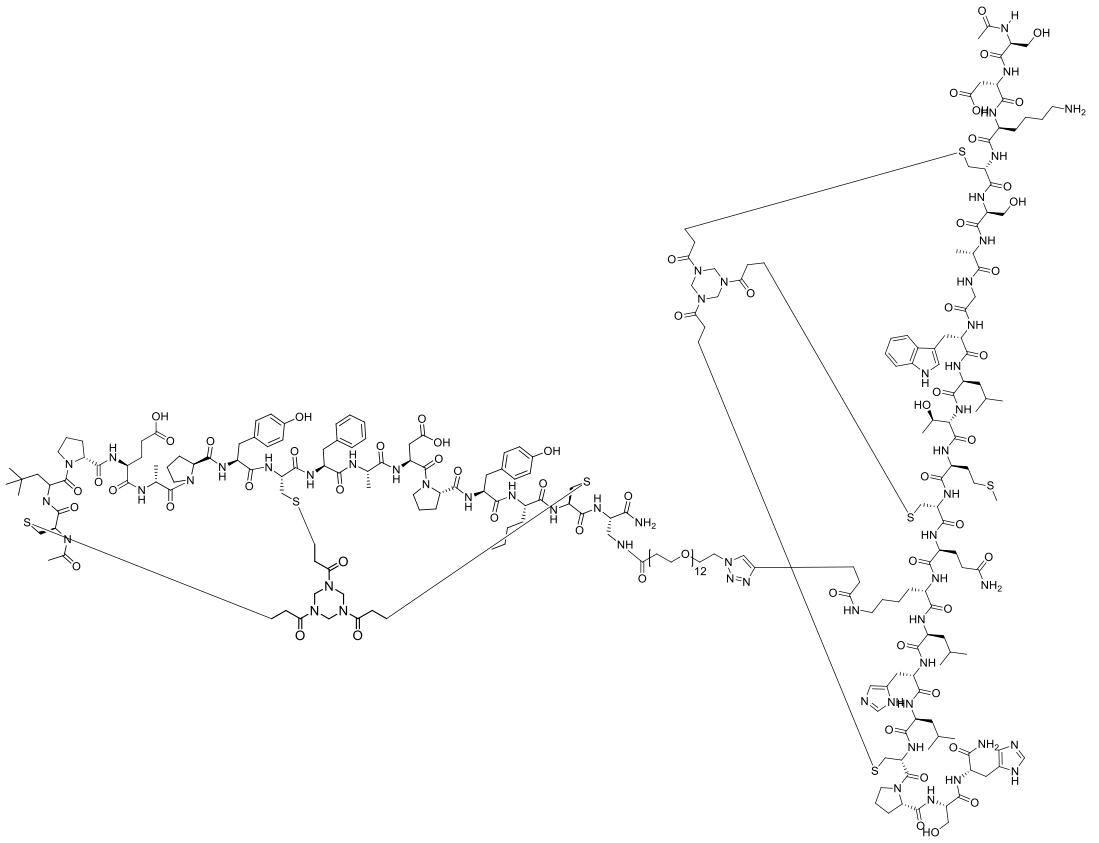

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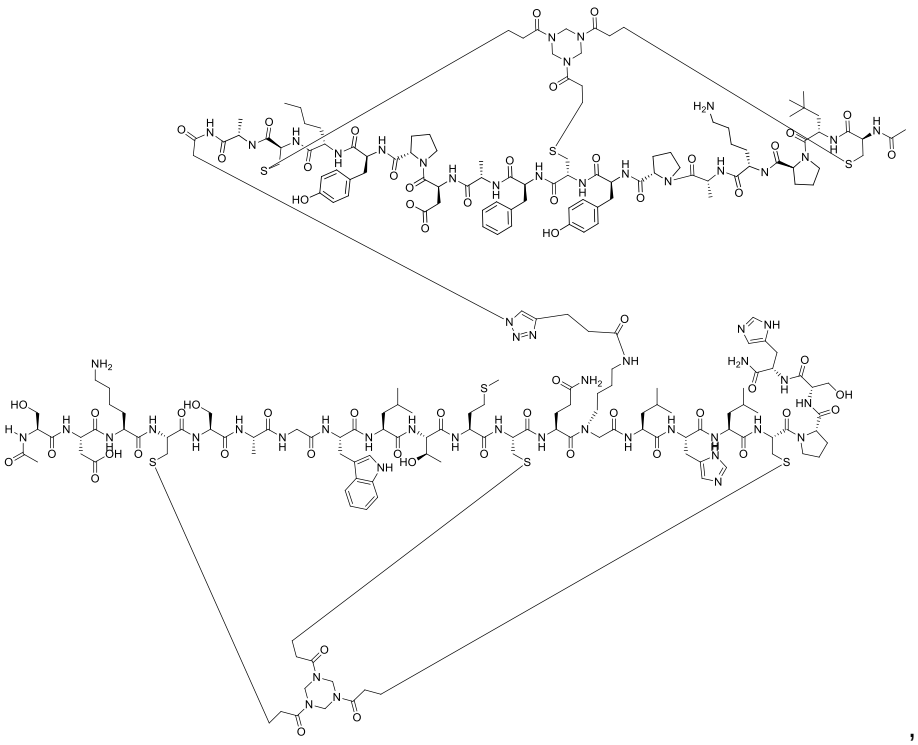

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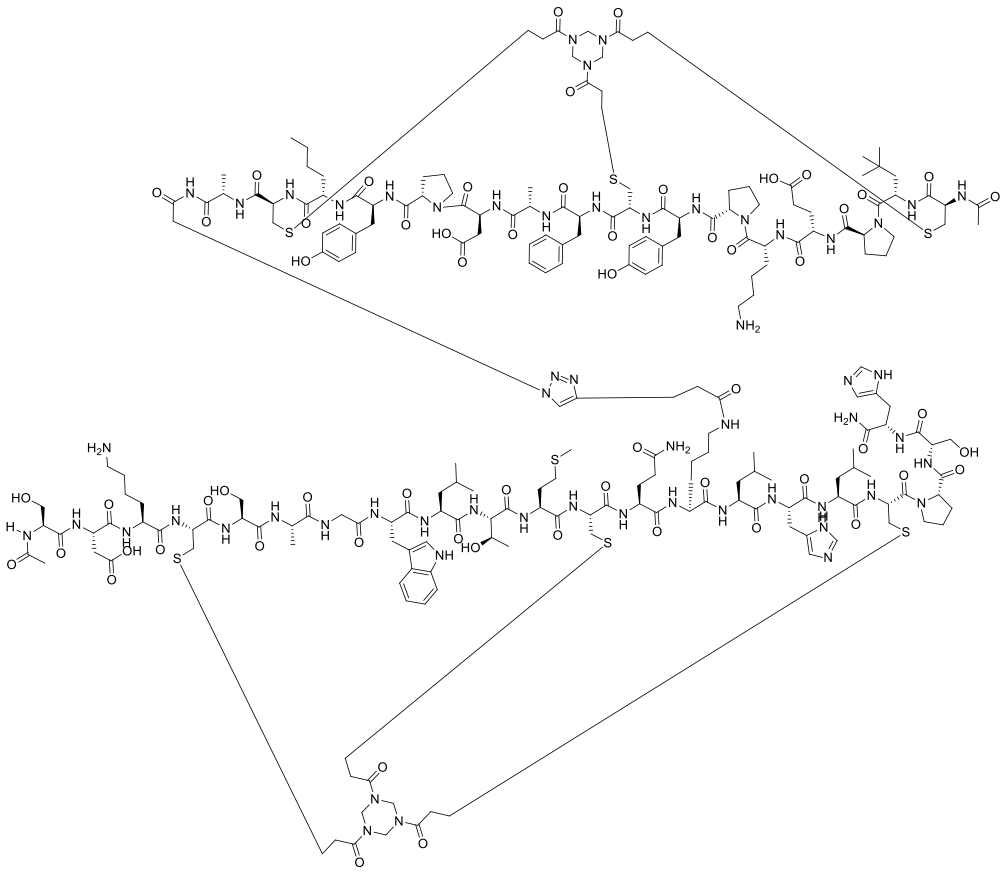

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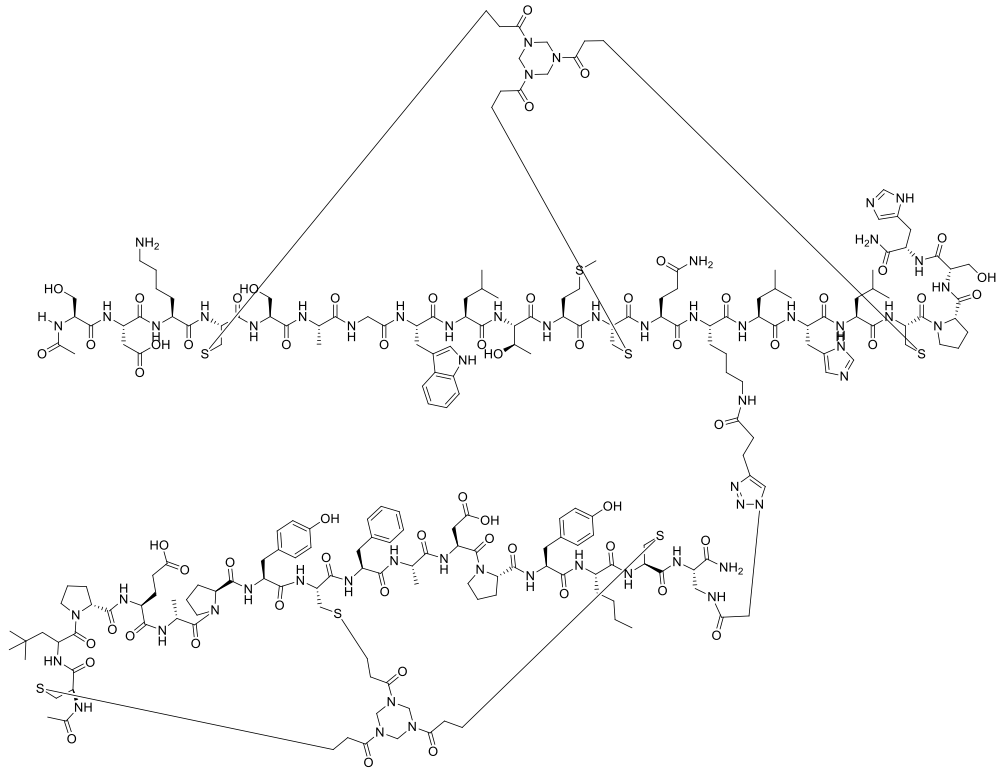

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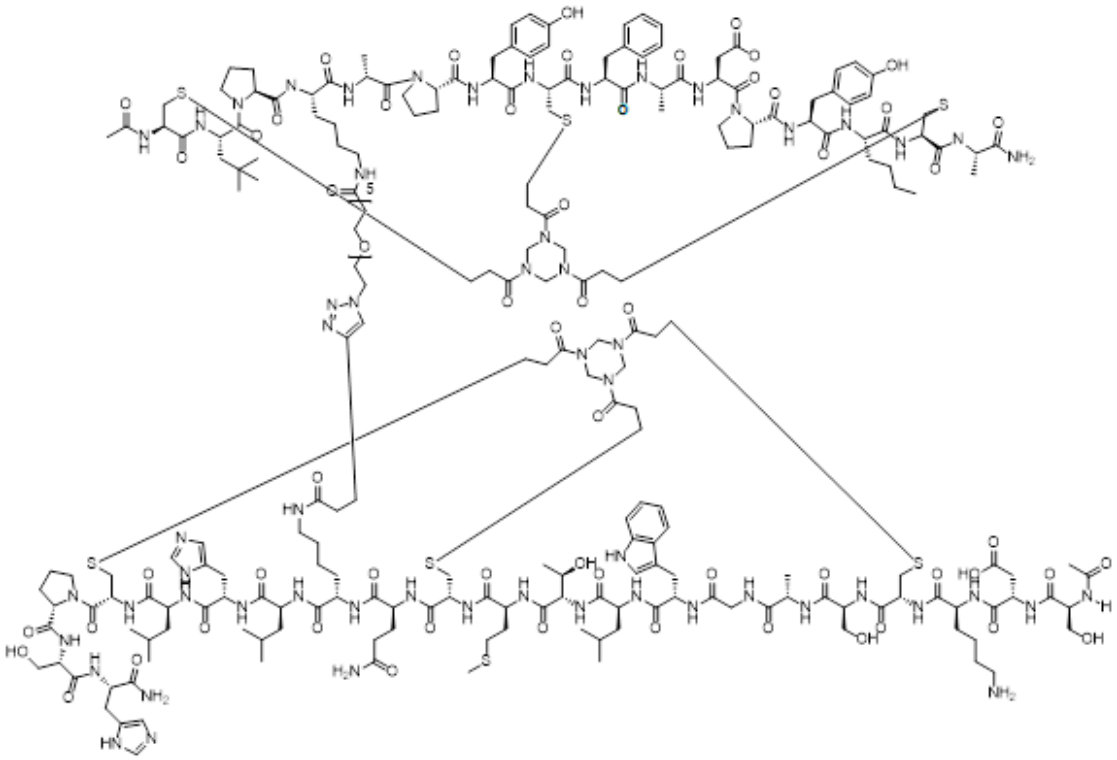

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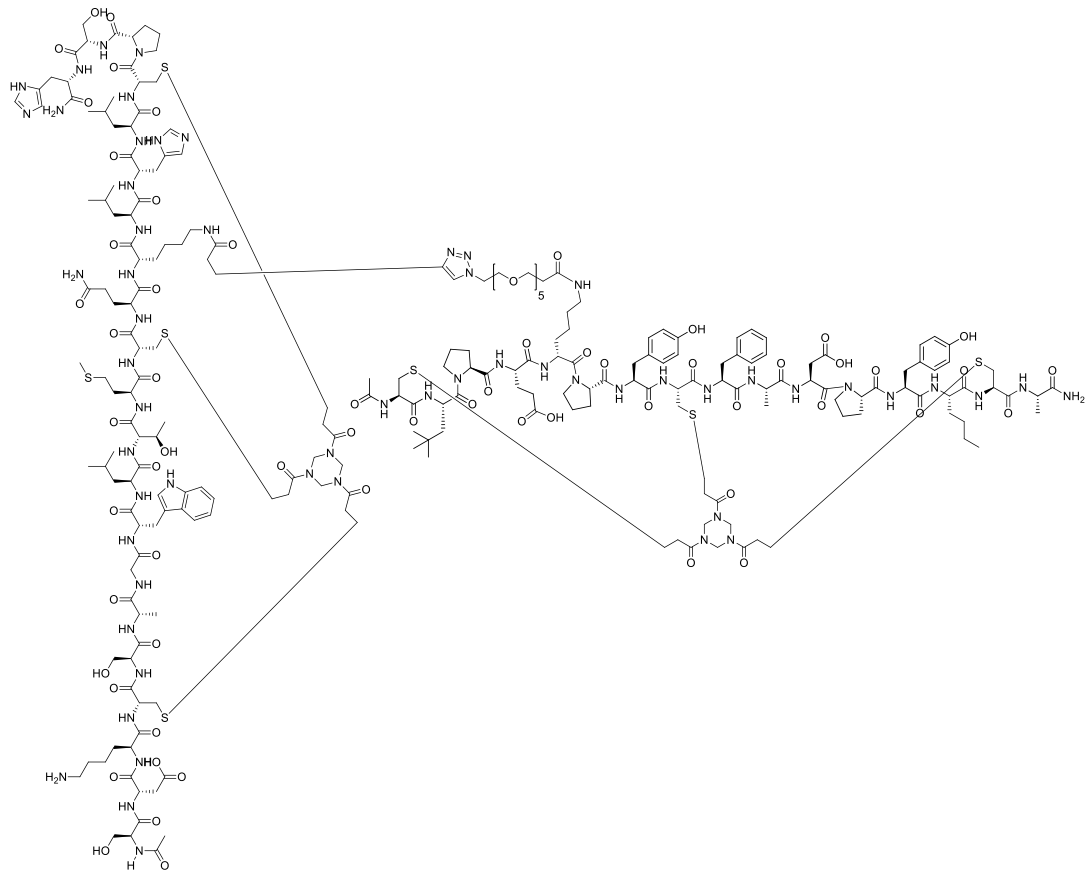

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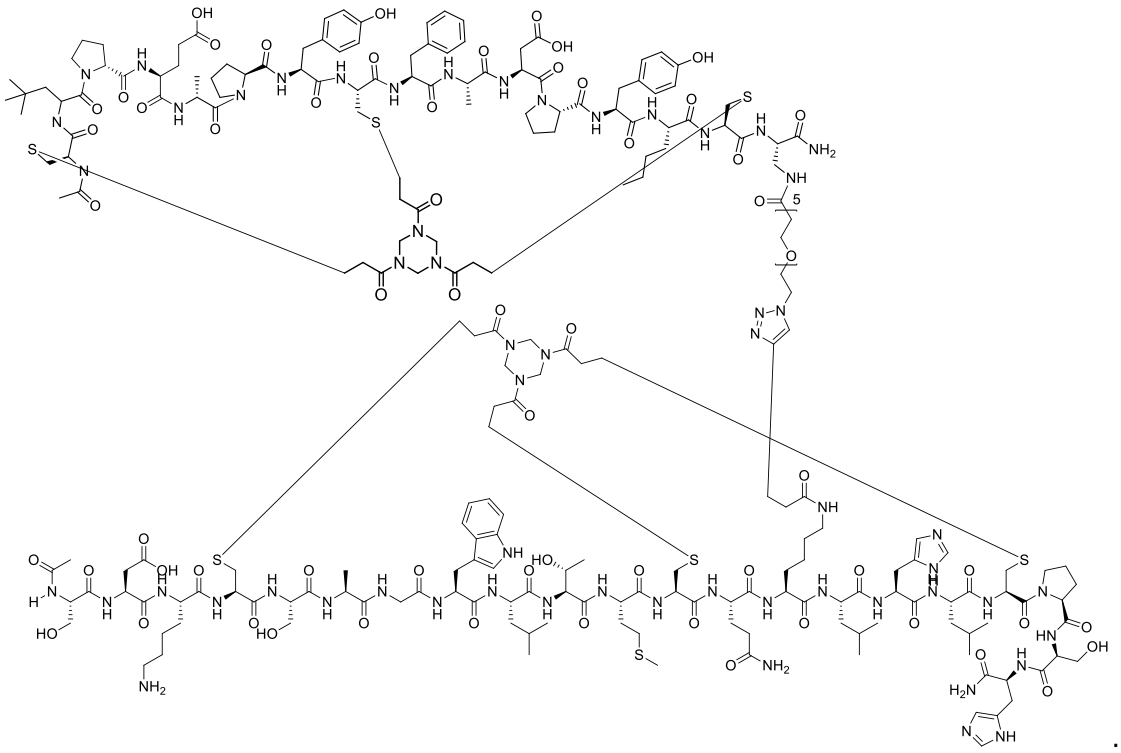

18. The heterotandem bicyclic peptide complex or the pharmaceutically acceptable salt thereof as defined in any one of claims 1 to 7, wherein the component present on a cancer cell is Nectin-4.

19. The heterotandem bicyclic peptide complex or the pharmaceutically acceptable salt thereof as defined in any one of claims 1 to 7 and 18, wherein the second peptide ligand comprises Nectin-4 binding bicyclic peptide ligand.

20. The heterotandem bicyclic peptide complex or the pharmaceutically acceptable salt thereof as defined in claim 19, wherein the Nectin-4 binding bicyclic peptide ligand optionally comprises N-terminal modifications and comprises:

SEQ ID NO: 15 (hereinafter referred to as BCY8116);

[PYA]-[B-Ala]-[Sar_{10}]-(SEQ ID NO: 15) (hereinafter referred to as BCY8846);

SEQ ID NO: 16 (hereinafter referred to as BCY11415);

[PYA]-[B-Ala]-[Sar_{10}]-(SEQ ID NO: 16) (hereinafter referred to as BCY11942);

Ac-(SEQ ID NO: 17) (hereinafter referred to as BCY8831); and

SEQ ID NO: 18 (hereinafter referred to as BCY11414);

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

21. The heterotandem bicyclic peptide complex or the pharmaceutically acceptable salt thereof as defined in claim 19 or 20, wherein the Nectin-4 binding bicyclic peptide ligand comprises:

SEQ ID NO: 15 (hereinafter referred to as BCY8116).

22. The heterotandem bicyclic peptide complex or the pharmaceutically acceptable salt thereof as defined in any one of claims 19 to 21 which is a CD137/Nectin-4 complex comprising a first peptide ligand comprising a CD137 binding bicyclic peptide ligand attached to a TATA scaffold, and a second peptide ligand comprising an Nectin-4 binding bicyclic peptide ligand attached to a TATA scaffold, wherein said heterotandem bicyclic peptide complex comprises:

- [PYA]-[B-Ala]-[Sar_{10}]-(SEQ ID NO: 15) (BCY8846) and Ac-A-(SEQ ID NO: 1)-Dap (BCY7732), wherein the N-terminal PYA of BCY8846 is linked to the C-terminal Dap of BCY7732 via a -PEG_{12}- linker;
- [PYA]-[B-Ala]-[Sar_{10}]-(SEQ ID NO: 16) (BCY11942) and Ac-A-(SEQ ID NO: 1)-Dap (BCY7732), wherein the N-terminal PYA of BCY11942 is linked to the C-terminal Dap of BCY7732 via a -PEG_{12}- linker;
- [PYA]-[B-Ala]-[Sar_{10}]-(SEQ ID NO: 15) (BCY8846) and Ac-A-(SEQ ID NO: 4)-Dap (BCY8045), wherein the N-terminal PYA of BCY8846 is linked to the C-terminal Dap of BCY8045 via a -PEG_{12}- linker;
- SEQ ID NO: 15 (BCY8116) and Ac-A-(SEQ ID NO: 1)-Dap(PYA) (BCY7741), wherein the N-terminus of BCY8116 is linked to the C-terminal Dap(PYA) of BCY7741 via a -PEG_{10}- linker;
- SEQ ID NO: 15 (BCY8116) and Ac-A-(SEQ ID NO: 1)-Dap(PYA) (BCY7741), wherein the N-terminus of BCY8116 is linked to the C-terminal Dap(PYA) of BCY7741 via a -PEG_{23}- linker;
- SEQ ID NO: 15 (BCY8116) and Ac-A-(SEQ ID NO: 1)-Dap(PYA) (BCY7741), wherein the N-terminus of BCY8116 is linked to the C-terminal Dap(PYA) of BCY7741 via a -B-Ala-Sar_{20}- linker;
- SEQ ID NO: 15 (BCY8116) and Ac-A-(SEQ ID NO: 1)-Dap(PYA) (BCY7741), wherein the N-terminus of BCY8116 is linked to the C-terminal Dap(PYA) of BCY7741 via a -B-Ala-Sar_{10}-PEG_{10}- linker;
- SEQ ID NO: 15 (BCY8116) and Ac-A-(SEQ ID NO: 1)-Dap(PYA) (BCY7741), wherein the N-terminus of BCY8116 is linked to the C-terminal Dap(PYA) of BCY7741 via a -B-Ala-Sar_5-PEG_{15}- linker;

- SEQ ID NO: 15 (BCY8116) and Ac-A-(SEQ ID NO: 1)-Dap(PYA) (BCY7741), wherein the N-terminus of BCY8116 is linked to the C-terminal Dap(PYA) of BCY7741 via a -B-Ala-Sar_5-PEG_5- linker;
- SEQ ID NO: 15 (BCY8116) and Ac-A-(SEQ ID NO: 1)-Dap(PYA) (BCY7741), wherein the N-terminus of BCY8116 is linked to the C-terminal Dap(PYA) of BCY7741 via a -PEG_{15}-Sar_5- linker;
- SEQ ID NO: 15 (BCY8116) and Ac-A-(SEQ ID NO: 1)-Dap(PYA) (BCY7741), wherein the N-terminus of BCY8116 is linked to the C-terminal Dap(PYA) of BCY7741 via a -PEG_{10}-Sar_{10}- linker;
- SEQ ID NO: 15 (BCY8116) and Ac-A-(SEQ ID NO: 1)-Dap(PYA) (BCY7741), wherein the N-terminus of BCY8116 is linked to the C-terminal Dap(PYA) of BCY7741 via a -PEG_5-Sar_{15} linker;
- SEQ ID NO: 15 (BCY8116) and Ac-A-(SEQ ID NO: 1)-Dap(PYA) (BCY7741), wherein the N-terminus of BCY8116 is linked to the C-terminal Dap(PYA) of BCY7741 via a -PEG_5-Sar_5- linker;
- SEQ ID NO: 15 (BCY8116) and Ac-A-(SEQ ID NO: 1)-Dap(PYA) (BCY7741), wherein the N-terminus of BCY8116 is linked to the C-terminal Dap(PYA) of BCY7741 via a -PEG_5- linker;
- SEQ ID NO: 15 (BCY8116) and Ac-A-(SEQ ID NO: 1)-Dap (BCY7732), wherein the N-terminus of BCY8116 is linked to the C-terminal Dap of BCY7732 via -PEG_{24}- linker;
- [PYA]-[B-Ala]-[Sar_{10}]-(SEQ ID NO: 15) (BCY8846) and Ac-(SEQ ID NO: 3)-Dap (BCY9172), wherein the N-terminal PYA of BCY8846 and the C-terminal Dap of BCY9172 are linked via a -PEG_{12}- linker;
- [PYA]-[B-Ala]-[Sar_{10}]-(SEQ ID NO: 15) (BCY8846) and Ac-(SEQ ID NO: 5)-A (BCY8919), wherein the N-terminal PYA of BCY8846 and the Lys3 of BCY8919 are linked via a -PEG_{12}- linker;
- [PYA]-[B-Ala]-[Sar_{10}]-(SEQ ID NO: 15) (BCY8846) and Ac-(SEQ ID NO: 6)-A (BCY8920), wherein the N-terminal PYA of BCY8846 and the dLys4 of BCY8920 are linked via a -PEG_{12}- linker;
- SEQ ID NO: 15 (BCY8116) and Ac-(SEQ ID NO: 7)-A (BCY8927), wherein the N-terminus of BCY8116 and the Lys(PYA)3 of BCY8927 are linked via a -PEG_5 linker;
- SEQ ID NO: 15 (BCY8116) and Ac-(SEQ ID NO: 8)-A (BCY8928), wherein the N-terminus of BCY8116 and the dLys(PYA)4 of BCY8928 are linked via a -PEG_5- linker;
- SEQ ID NO: 15 (BCY8116) and Ac-(SEQ ID NO: 3)-Dap(PYA) (BCY11014), wherein the N-terminus of BCY8116 and the C-terminal Dap(PYA) of BCY11014 are linked via a -PEG_5- linker;

- [PYA]-[B-Ala]-[Sar_{10}]-(SEQ ID NO: 15) (BCY8846) and Ac-(SEQ ID NO: 3)-Dap (BCY9172), wherein the N-terminal PYA of BCY8846 and the C-terminal Dap of BCY9172 are linked via a -CH_2- linker;
- Ac-(SEQ ID NO: 17) (BCY8831) and Ac-(SEQ ID NO: 3)-Dap(PYA) (BCY11014), wherein the dLys(Sar_{10})-(B-Ala))4 of BCY8831 and the C-terminal Dap(PYA) of BCY11014 are linked via a -PEG_{12}- linker;
- Ac-(SEQ ID NO: 17) (BCY8831) and Ac-(SEQ ID NO: 3)-Dap(PYA) (BCY11014), wherein the dLys(Sar_{10})-(B-Ala))4 of BCY8831 and the C-terminal Dap(PYA) of BCY11014 are linked via a -PEG_5- linker;
- SEQ ID NO: 15 (BCY8116) and Ac-(SEQ ID NO: 7)-A (BCY8927), wherein the N-terminus of BCY8116 and the Lys(PYA)3 of BCY8927 are linked via a -CH_2- linker;
- SEQ ID NO: 15 (BCY8116) and Ac-(SEQ ID NO: 8)-A (BCY8928), wherein the N-terminus of BCY8116 and the dLys(PYA)4 of BCY8928 are linked via a -CH_2- linker;
- SEQ ID NO: 15 (BCY8116) and Ac-(SEQ ID NO: 3)-Dap(PYA) (BCY11014), wherein the N-terminus of BCY8116 and the C-terminal Dap(PYA) of BCY11014 are linked via a -CH_2- linker;
- SEQ ID NO: 15 (BCY8116) and Ac-A-(SEQ ID NO: 9)-A (BCY7744), wherein the N-terminus of BCY8116 and the dLys (PYA)4 of BCY7744 are linked via a -PEG_5- linker;
- SEQ ID NO: 15 (BCY8116) and Ac-[dA]-(SEQ ID NO: 10)-[dA]-NH_2 (BCY11506), wherein the N-terminus of BCY8116 and the Lys(PYA)4 of BCY11506 are linked via a -PEG_5- linker;
- SEQ ID NO: 18 (BCY11414) and Ac-A-(SEQ ID NO: 9)-A (BCY7744), wherein the N-terminus of BCY11414 and the dLys(PYA)4 of BCY7744 are linked via a -PEG_5- linker;
- SEQ ID NO: 18 (BCY11414) and Ac-(SEQ ID NO: 8)-A (BCY8928), wherein the N-terminus of BCY11414 and the dLys(PYA)4 of BCY8928 are linked via a -PEG_5- linker; or
- SEQ ID NO: 16 (BCY11415) and Ac-(SEQ ID NO: 8)-A (BCY8928), and wherein the N-terminus of BCY11415 and the dLys(PYA)4 of BCY8928 are linked via a -PEG_5- linker.

23. The heterotandem bicyclic peptide complex or the pharmaceutically acceptable salt thereof as defined in any one of claims 19 to 22 which is a CD137/Nectin-4 complex selected from:

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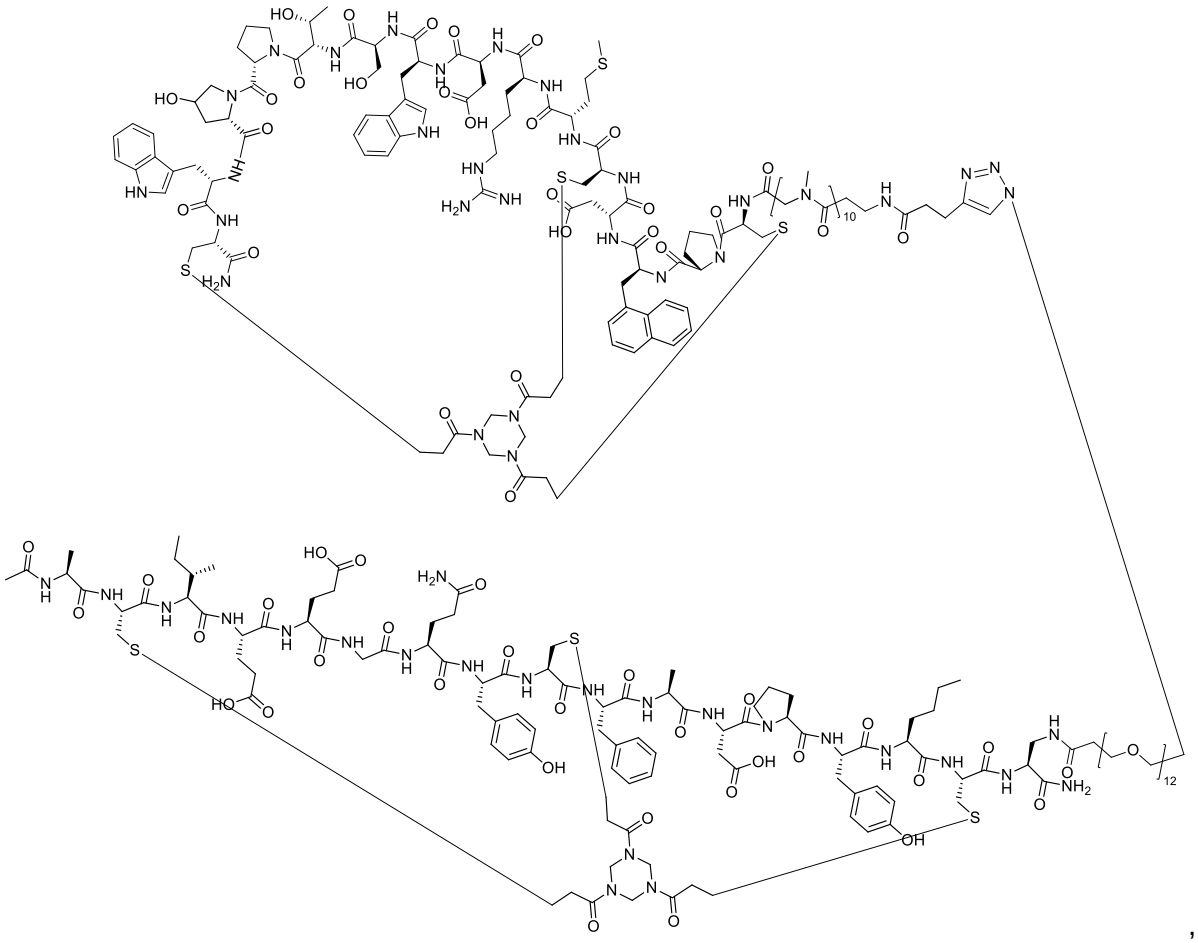

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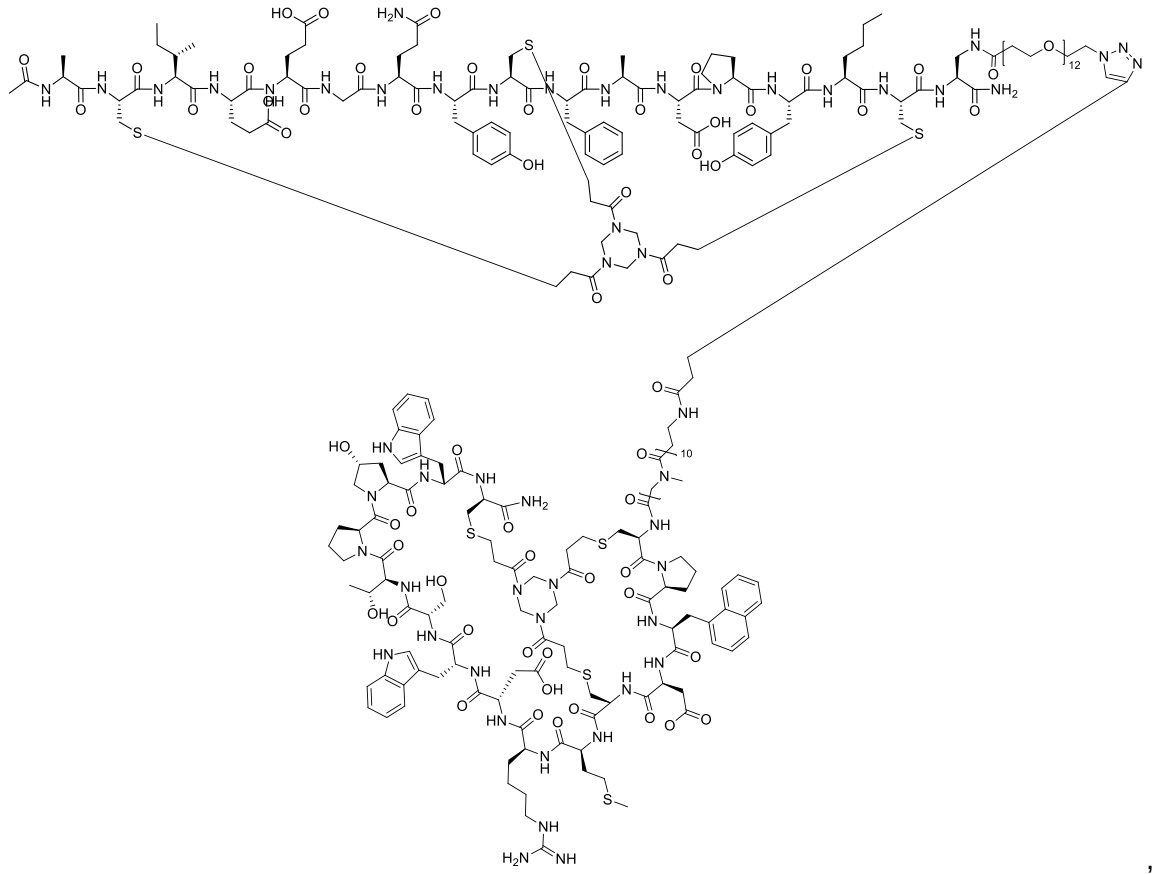

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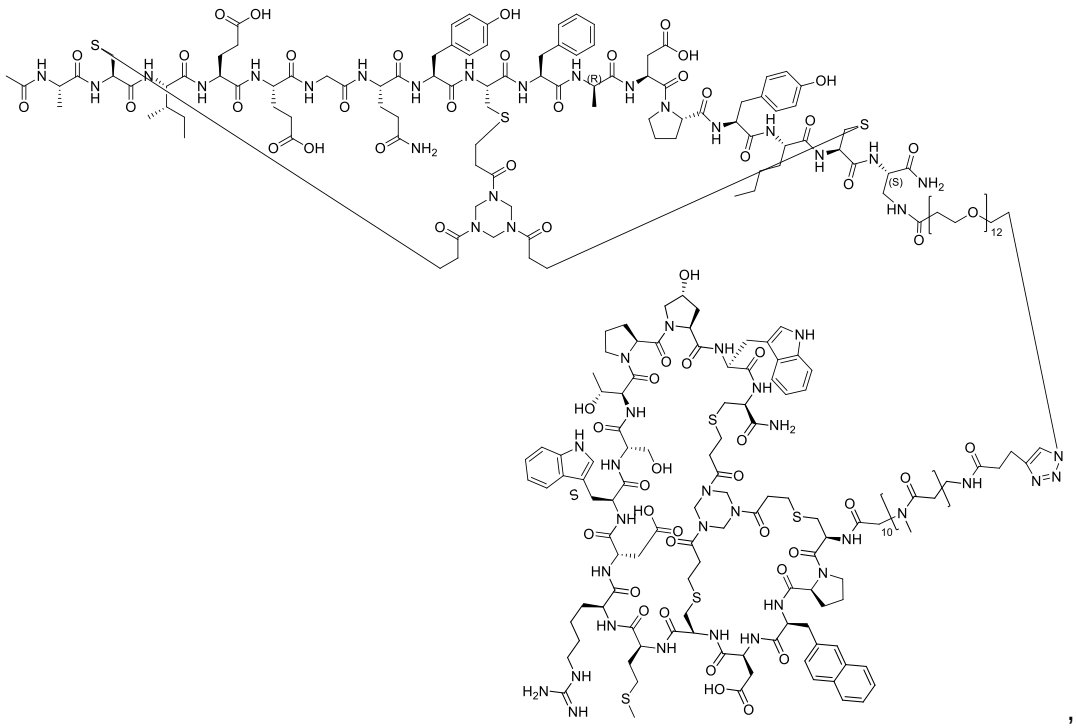

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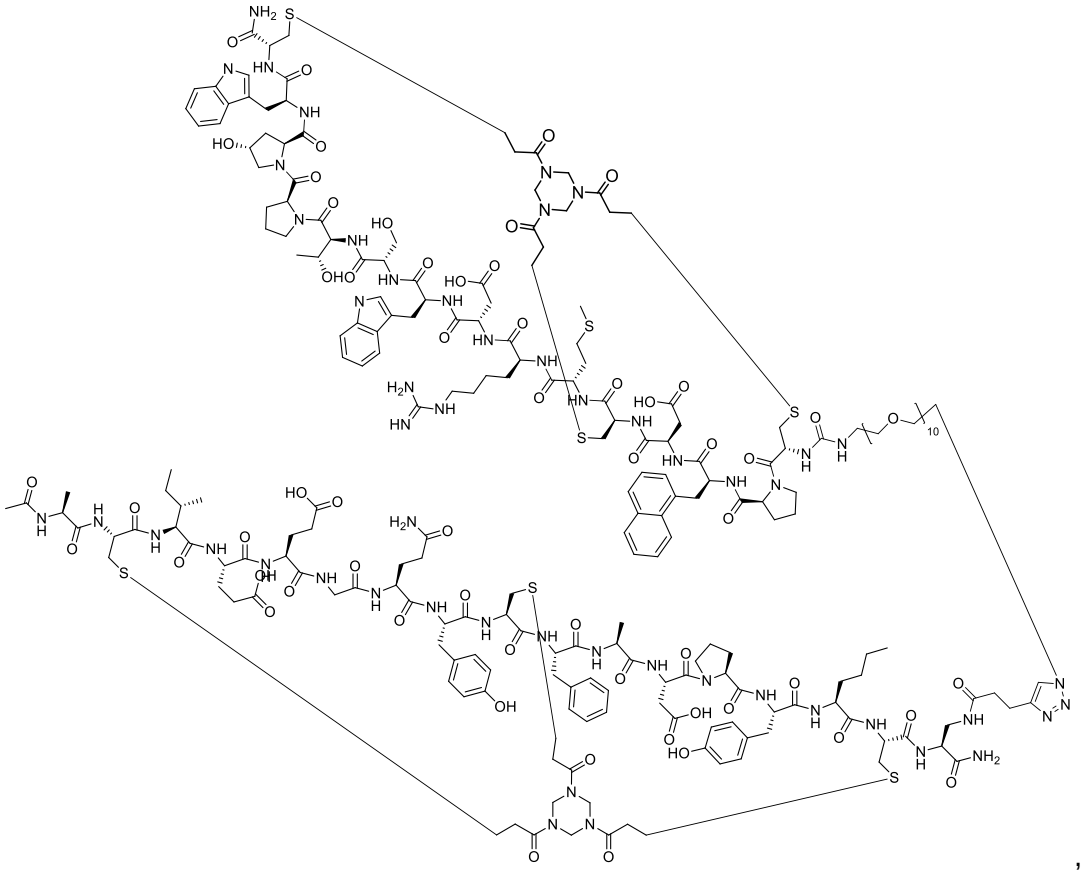

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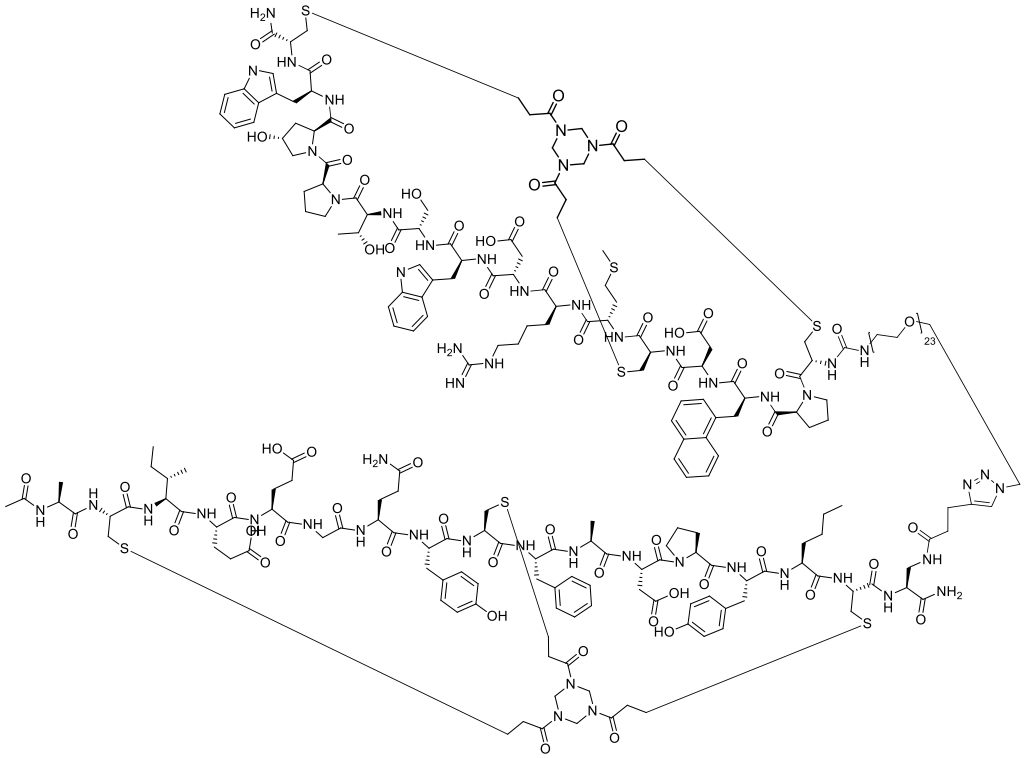

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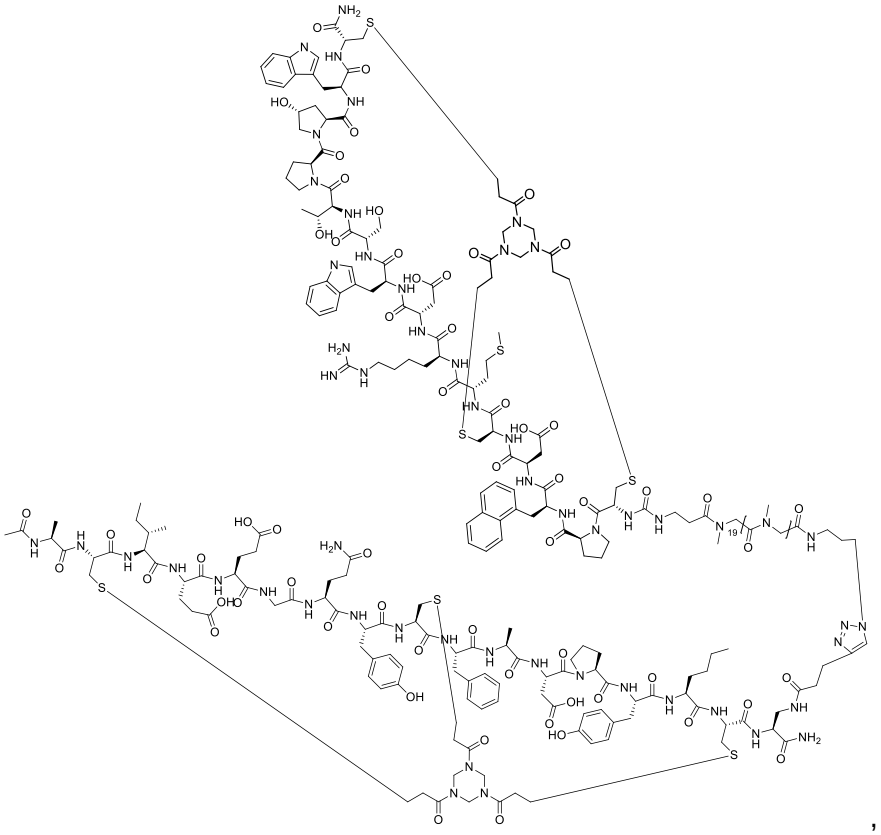

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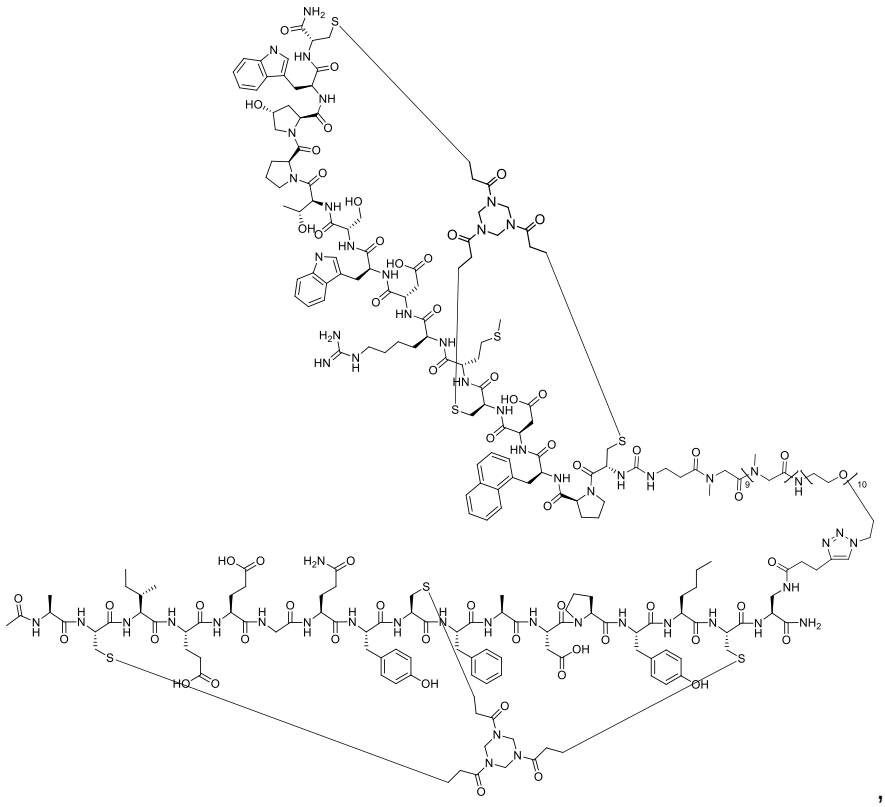

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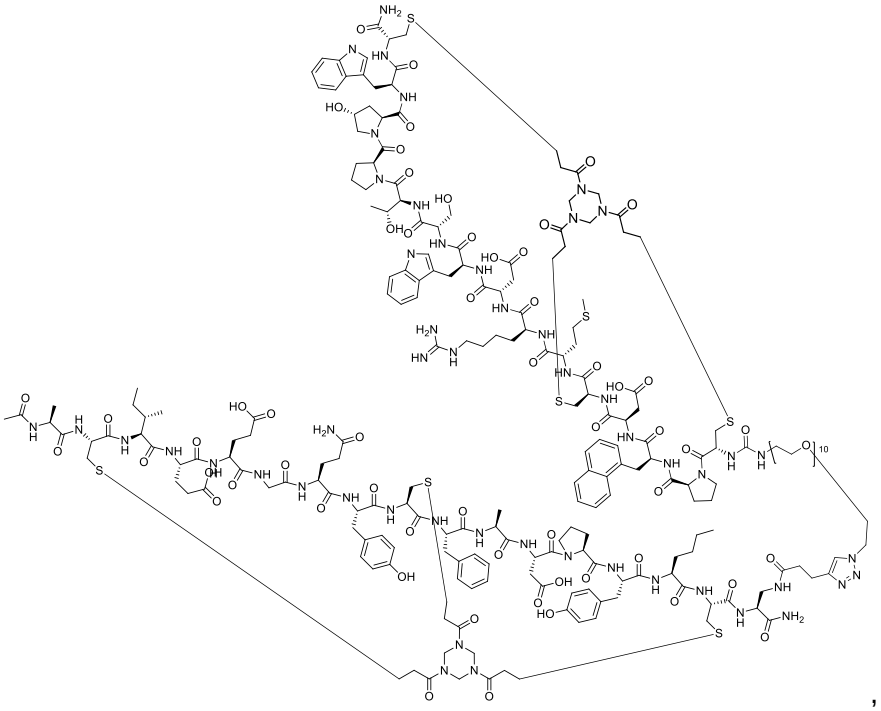

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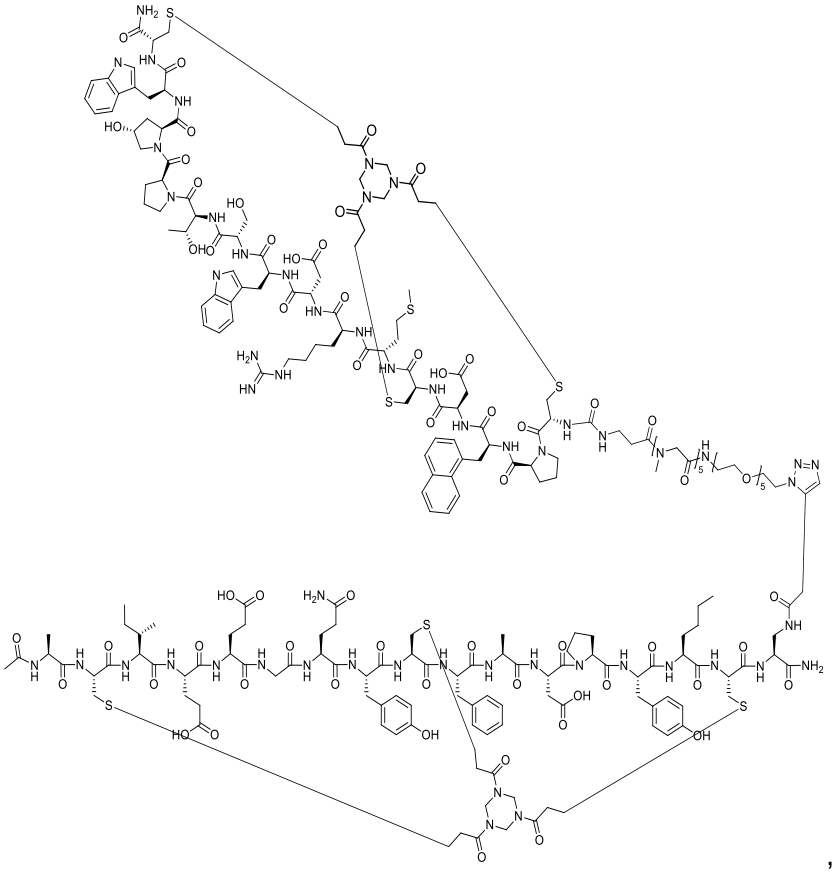

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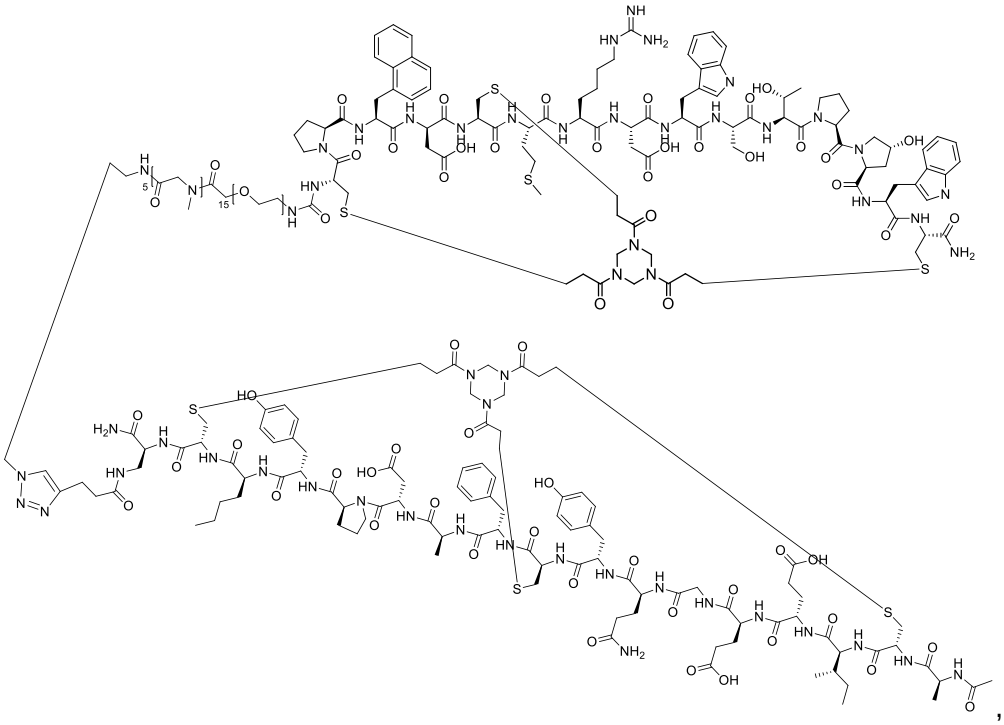

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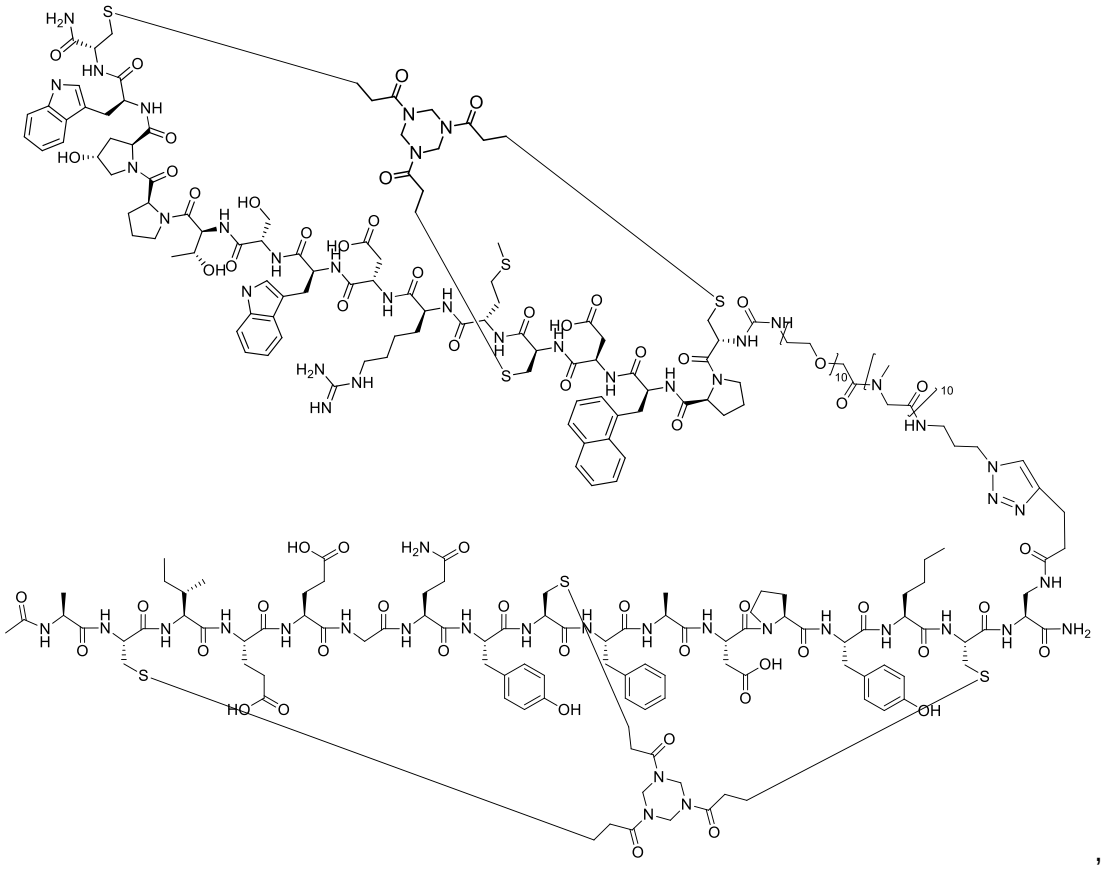

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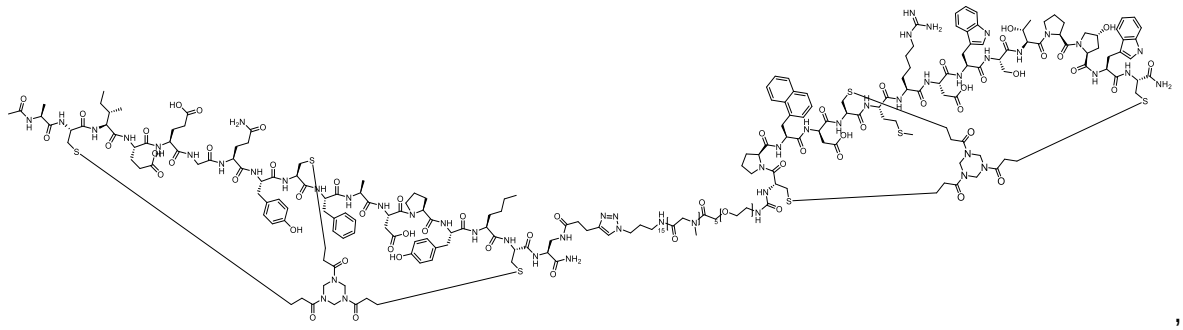

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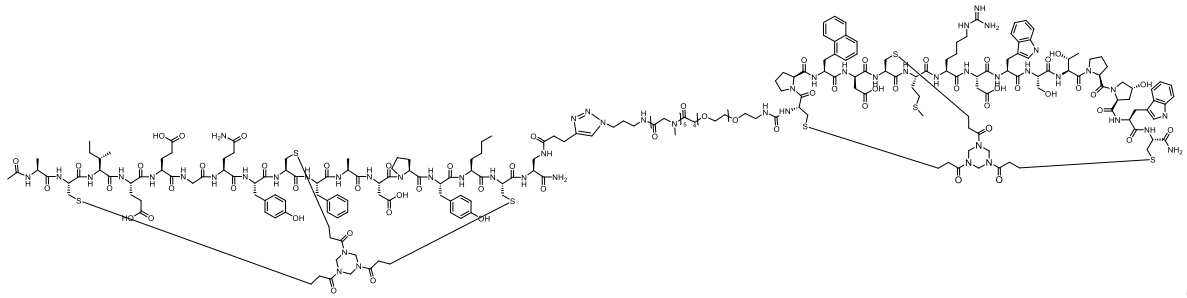

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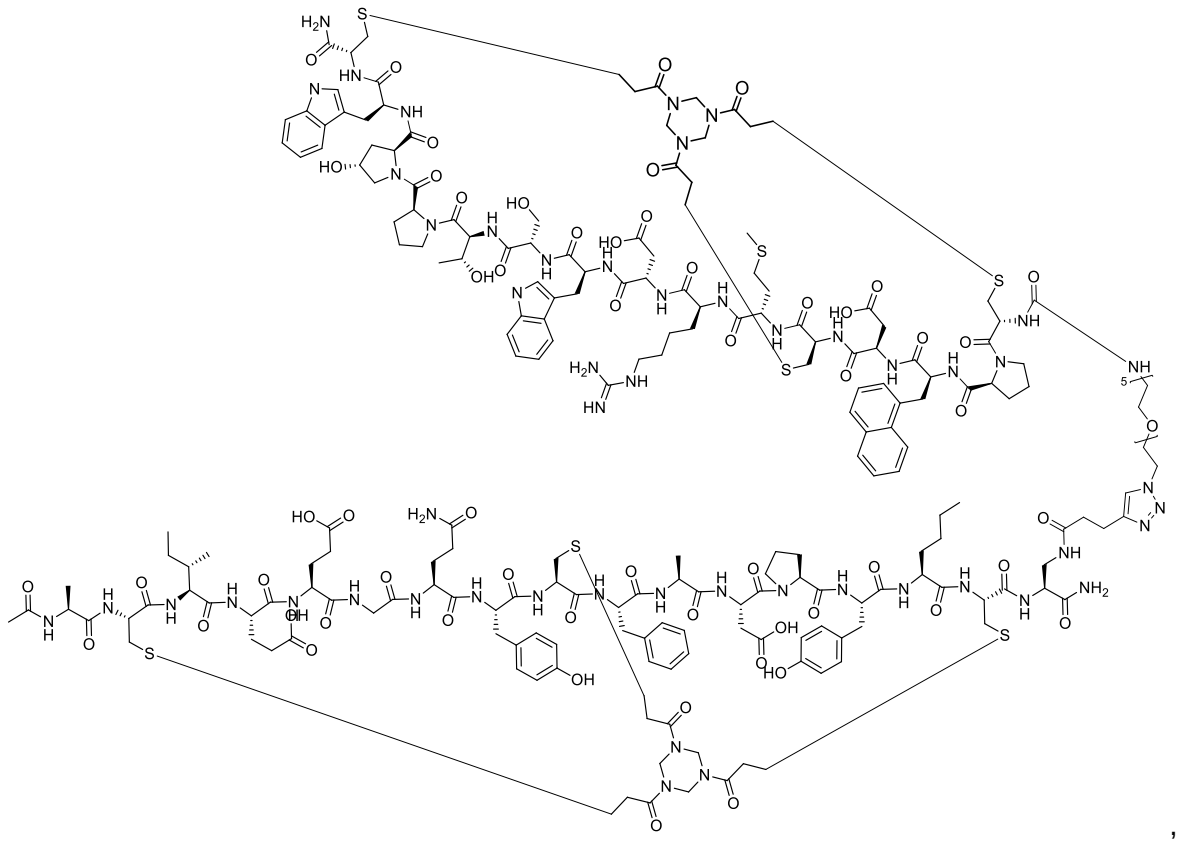

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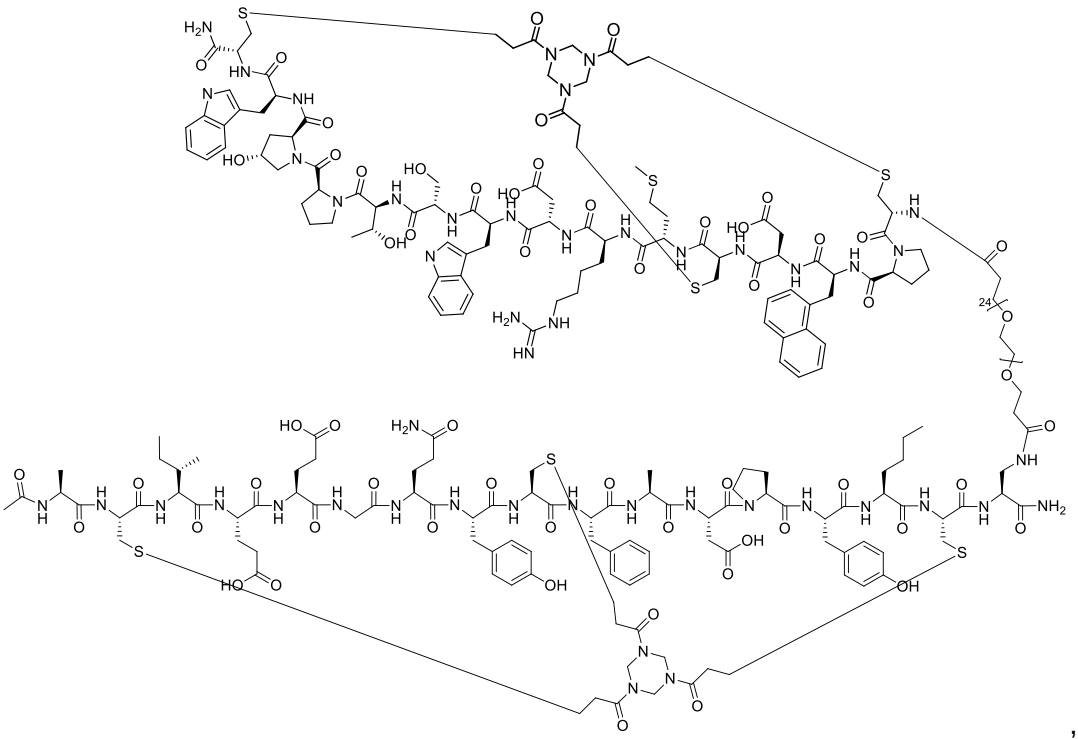

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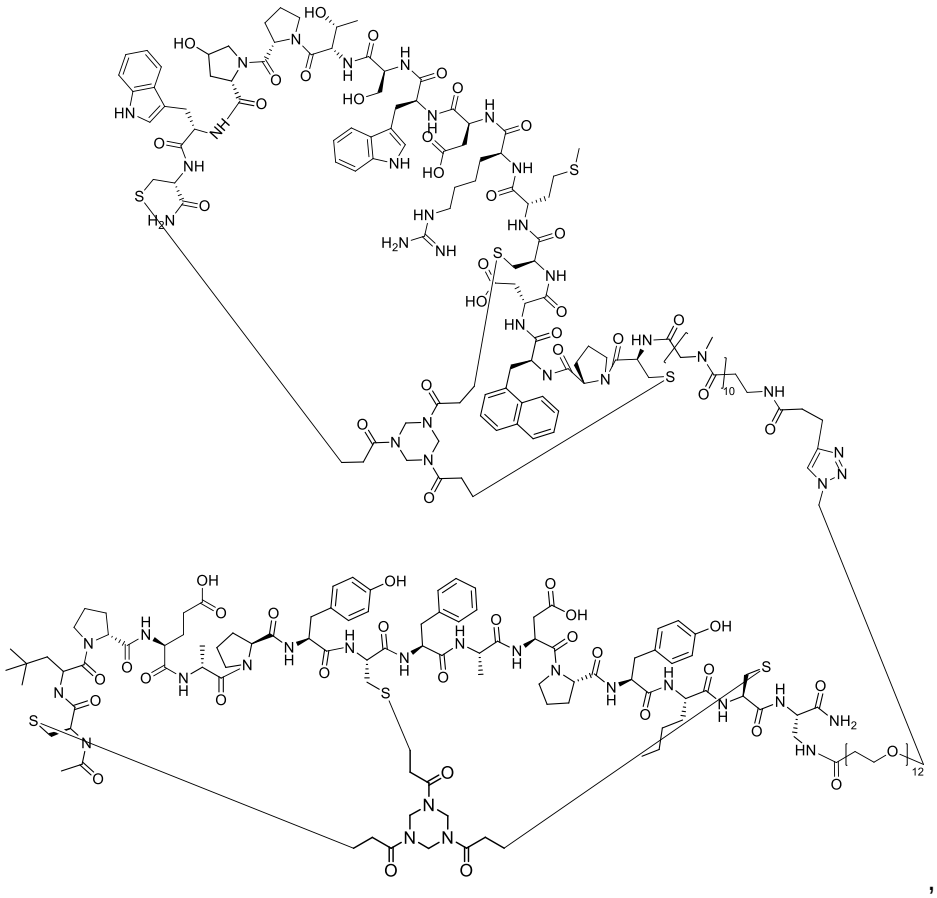

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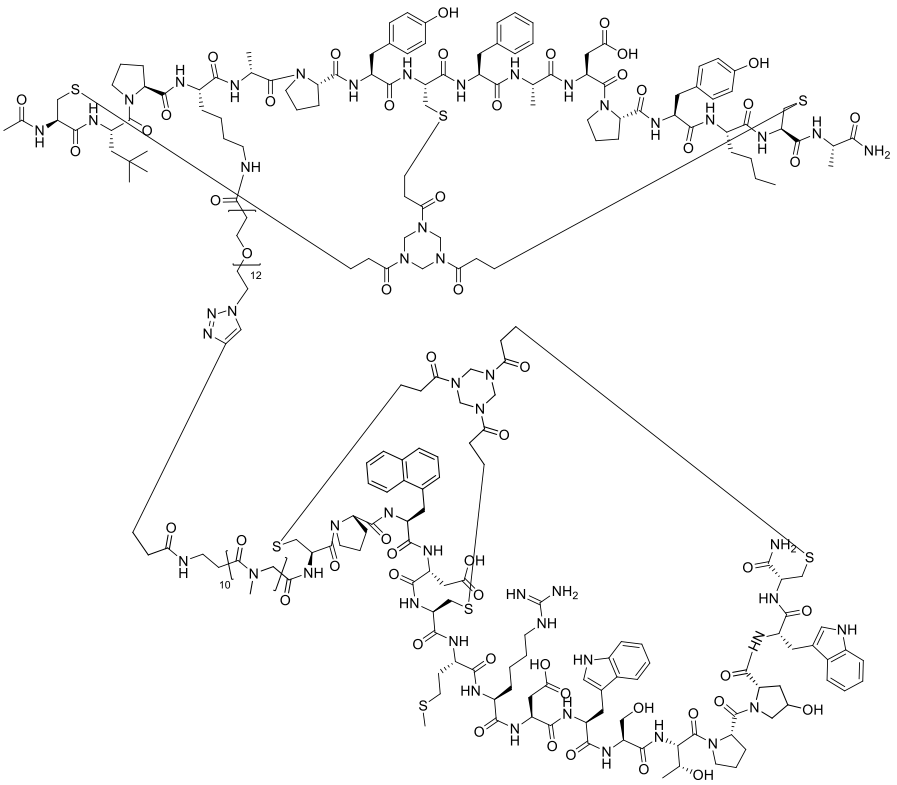

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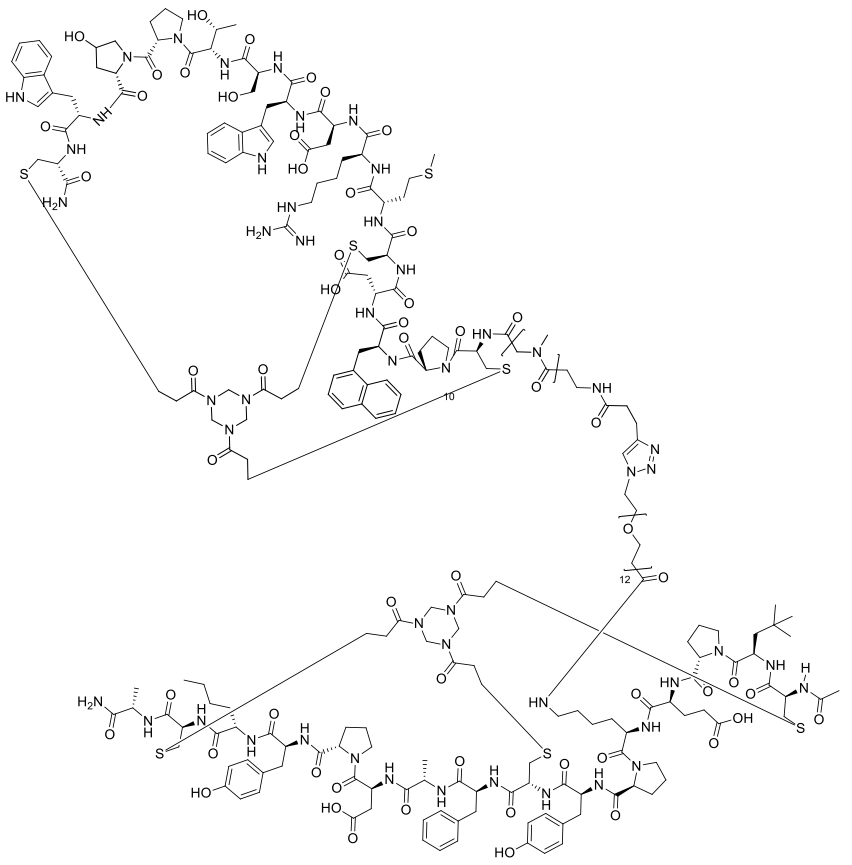

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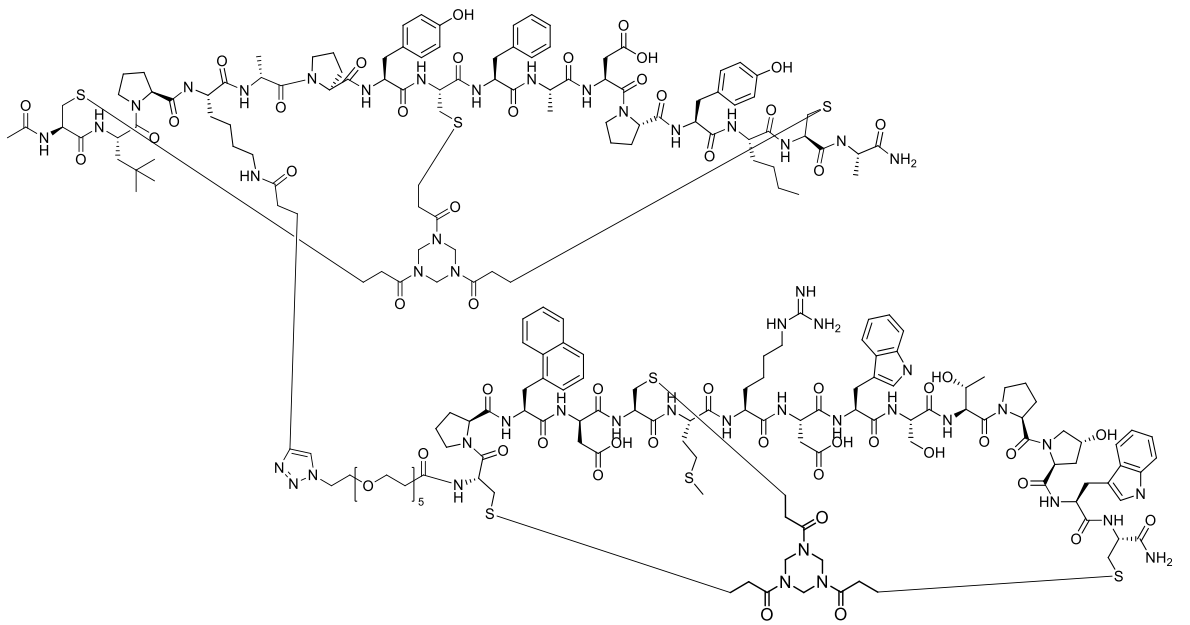

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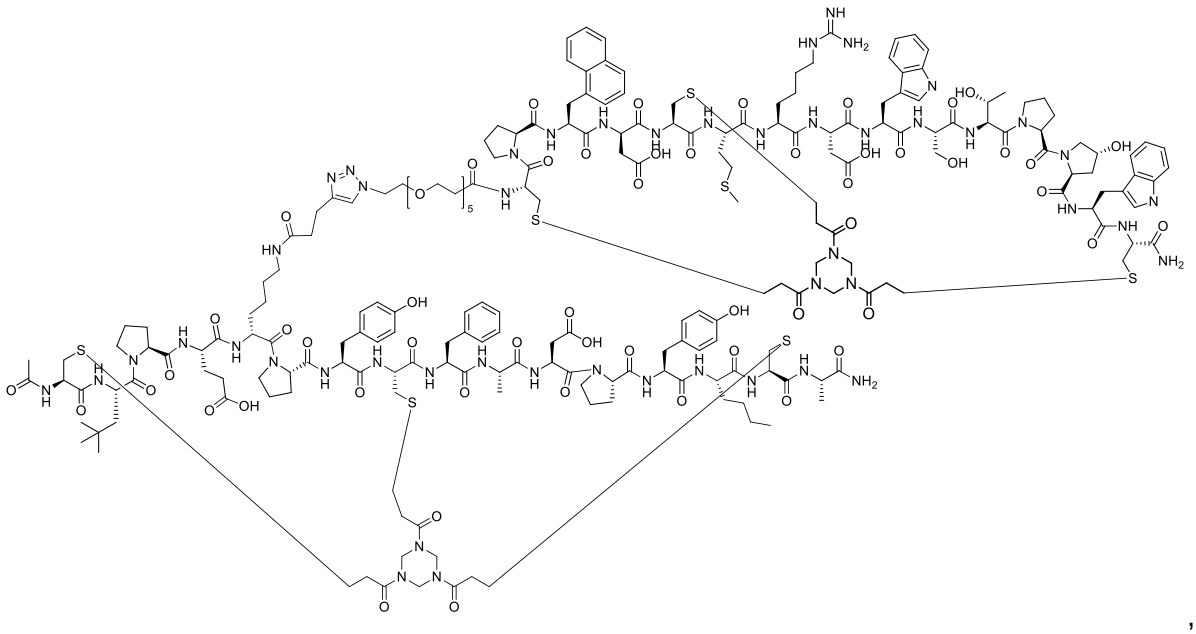

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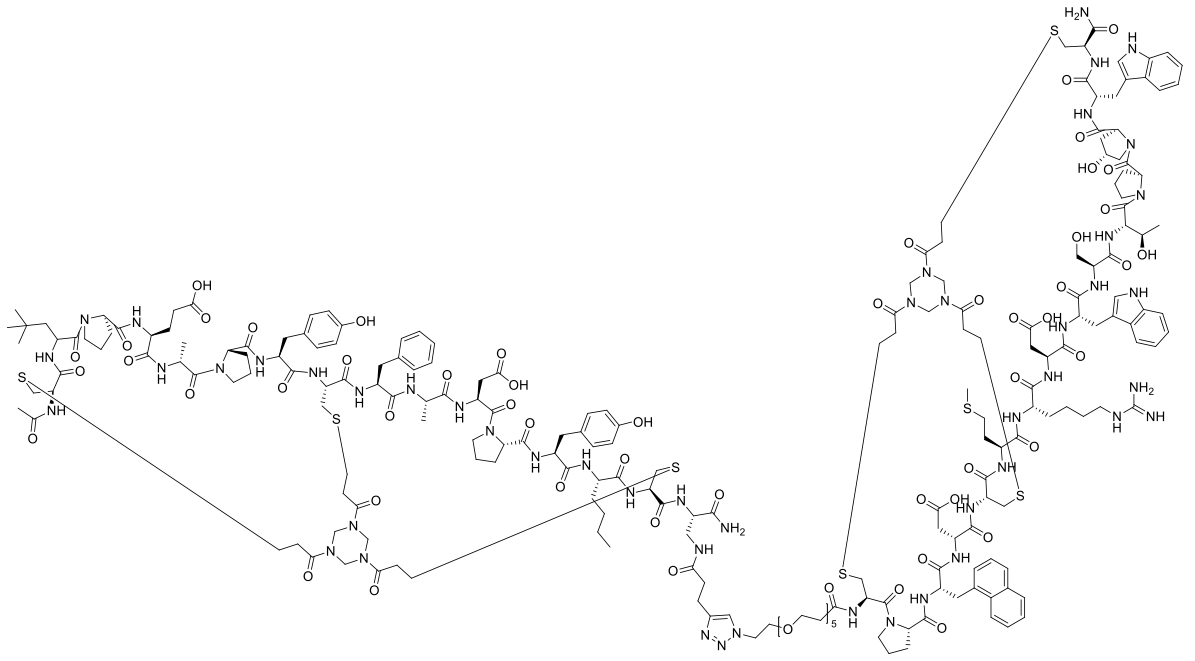

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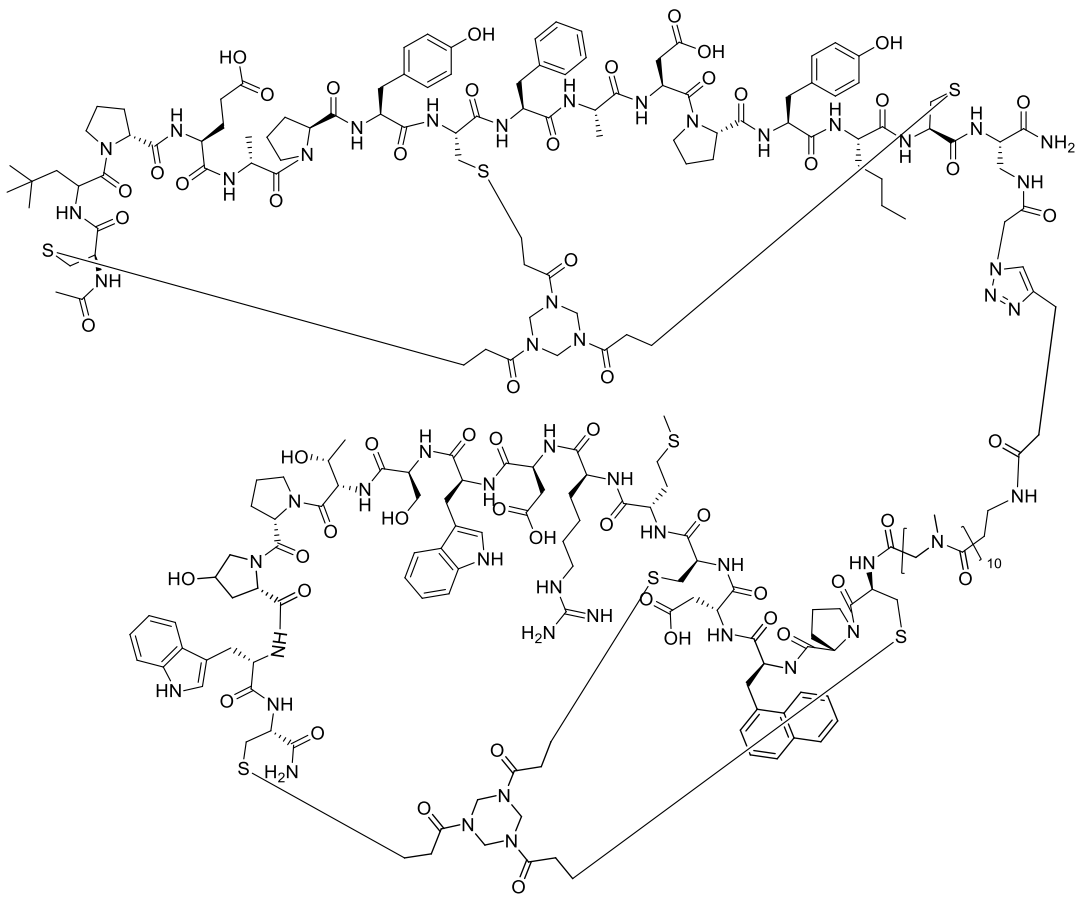

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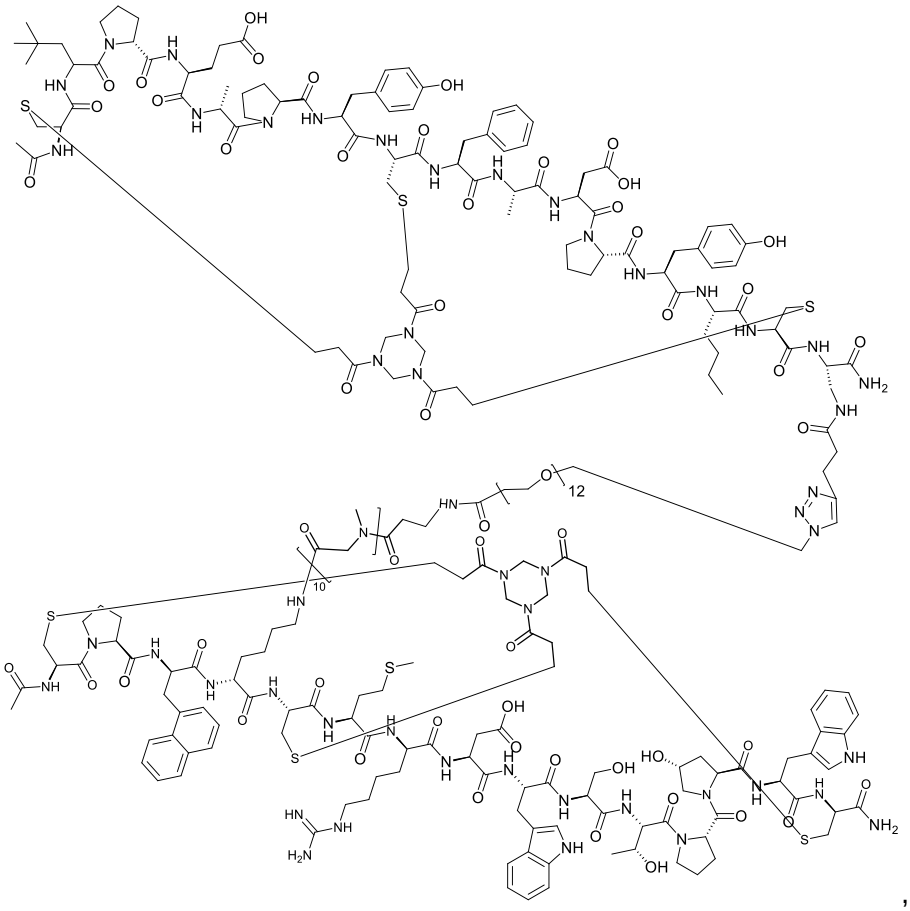

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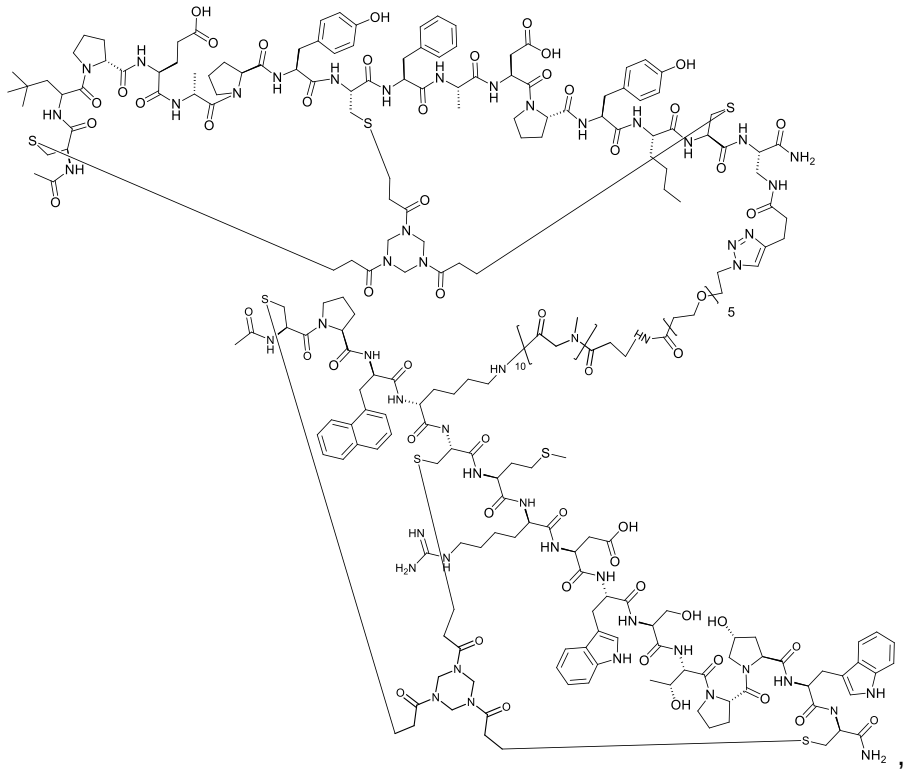

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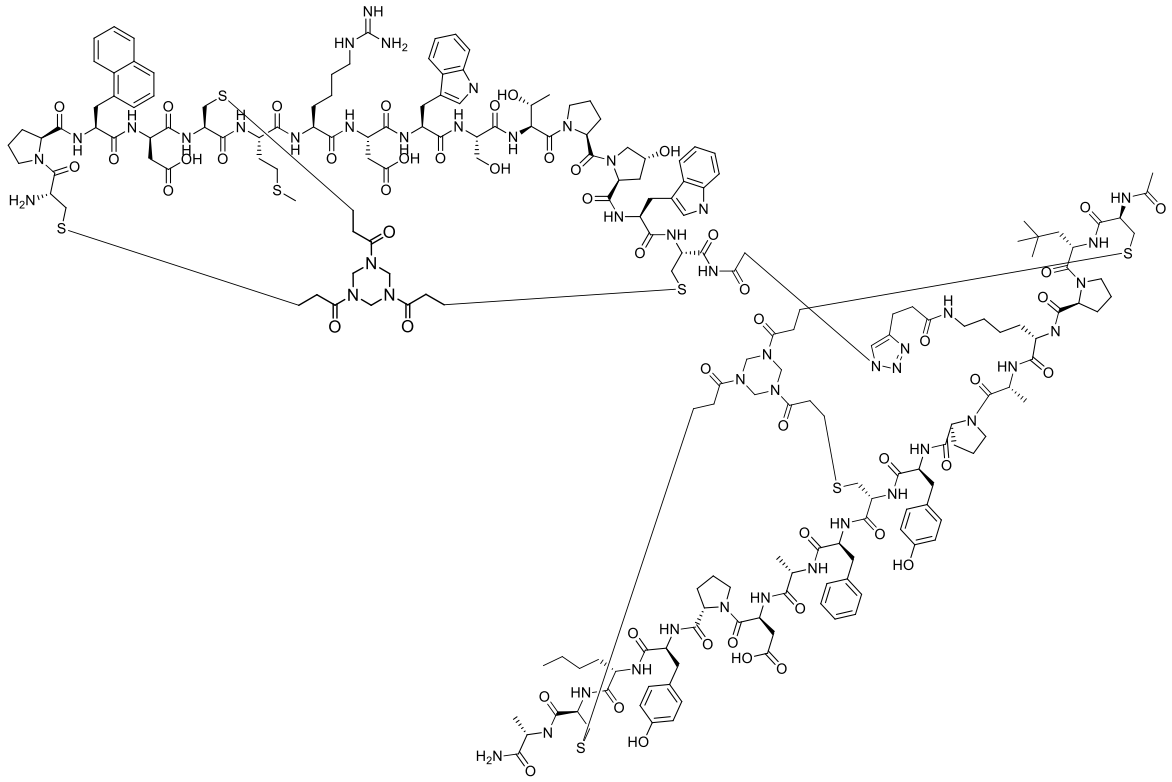

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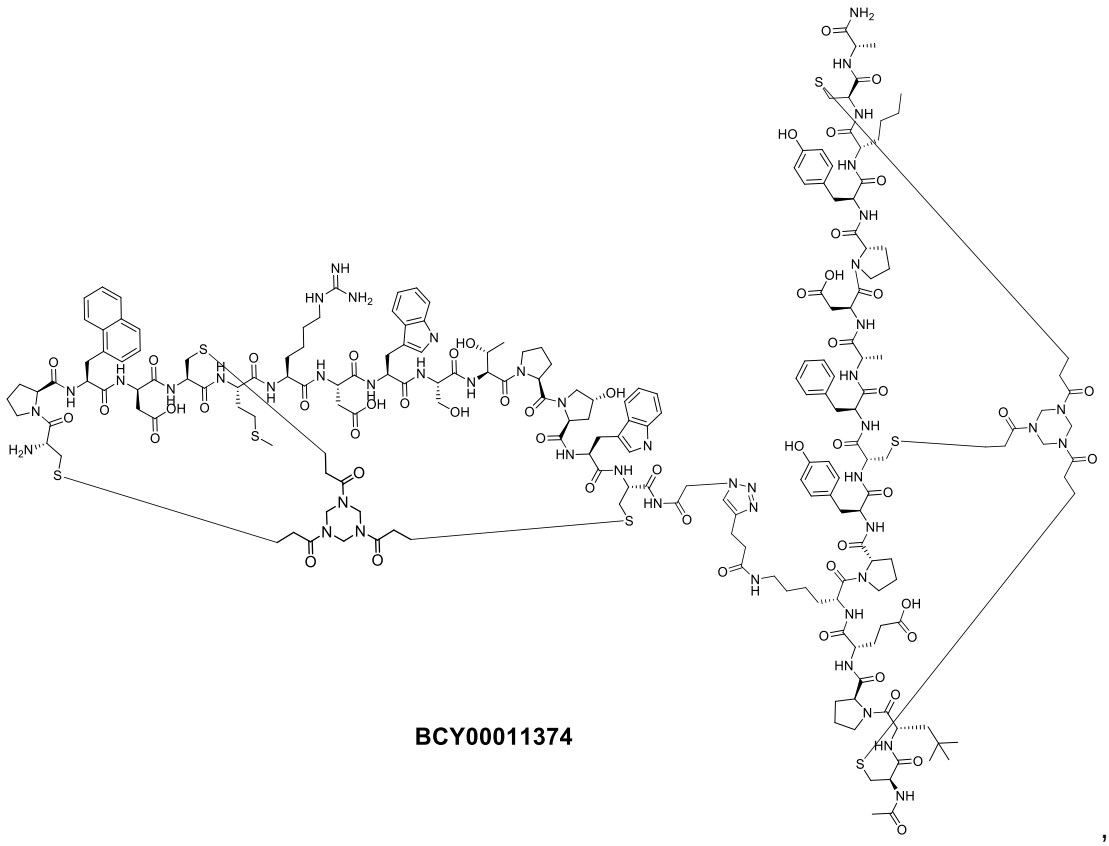

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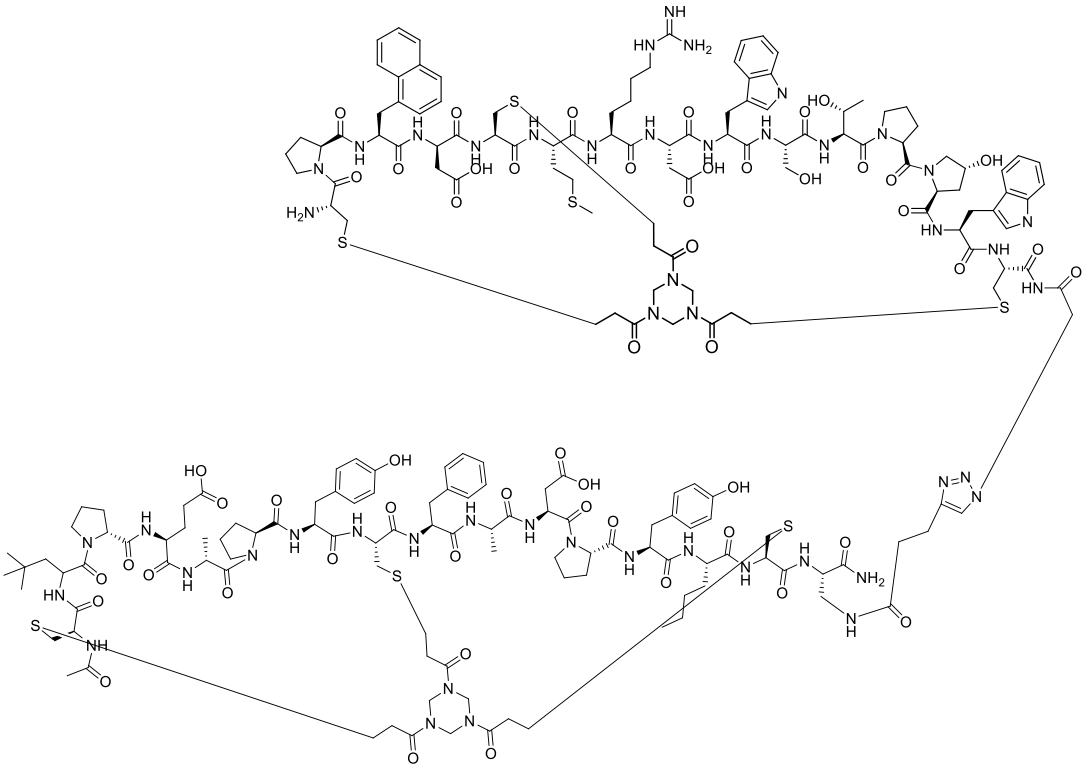

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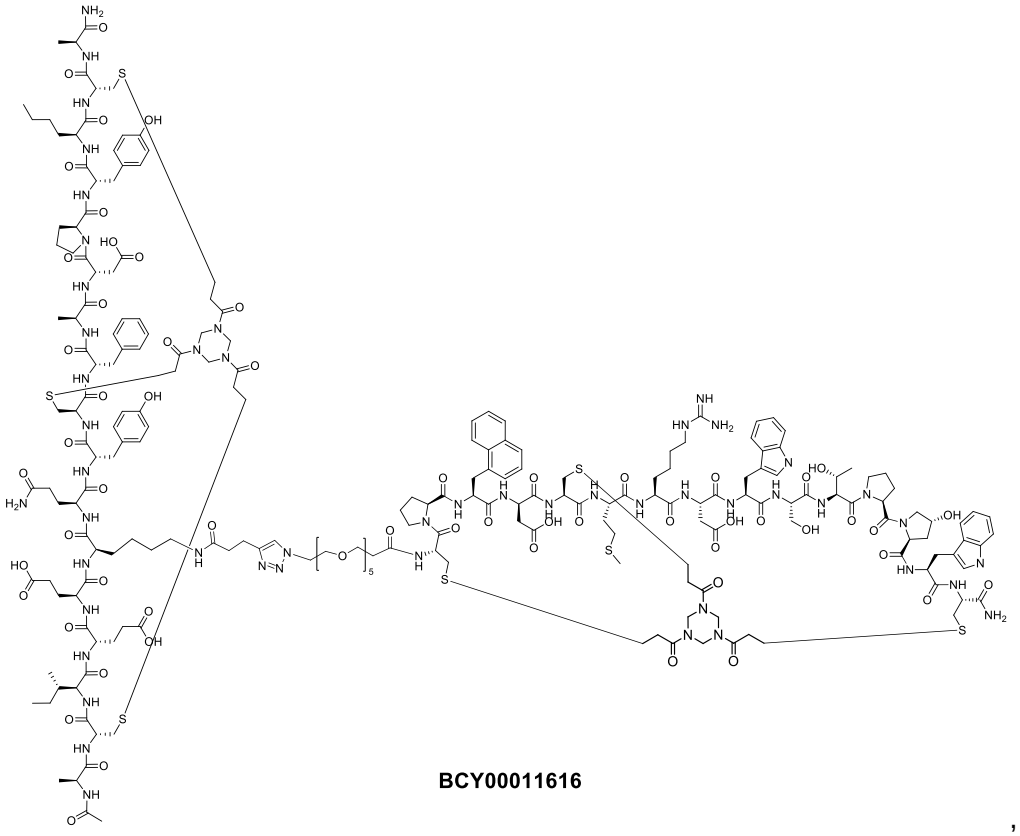

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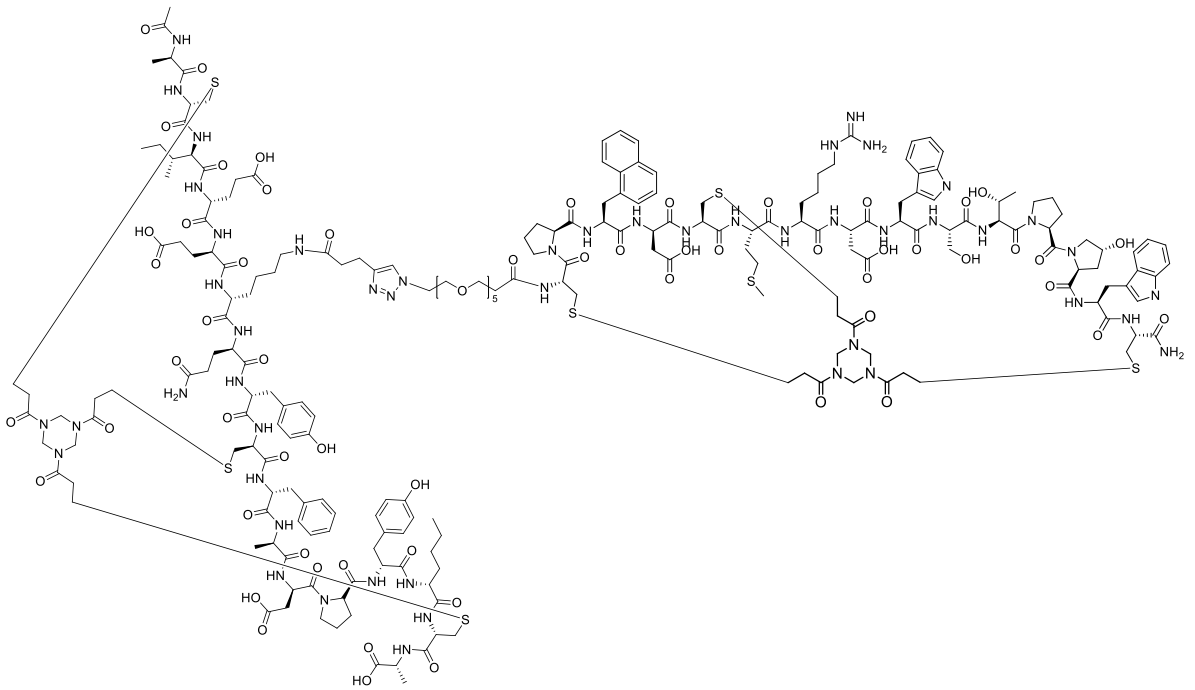

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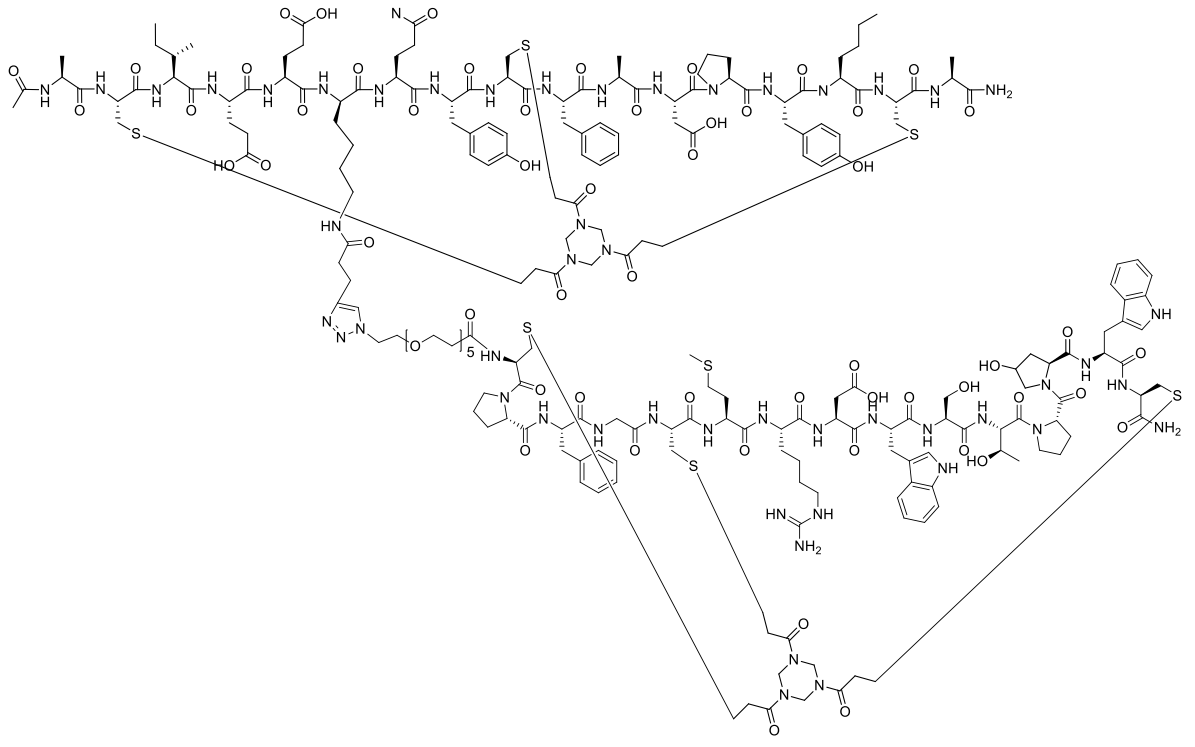

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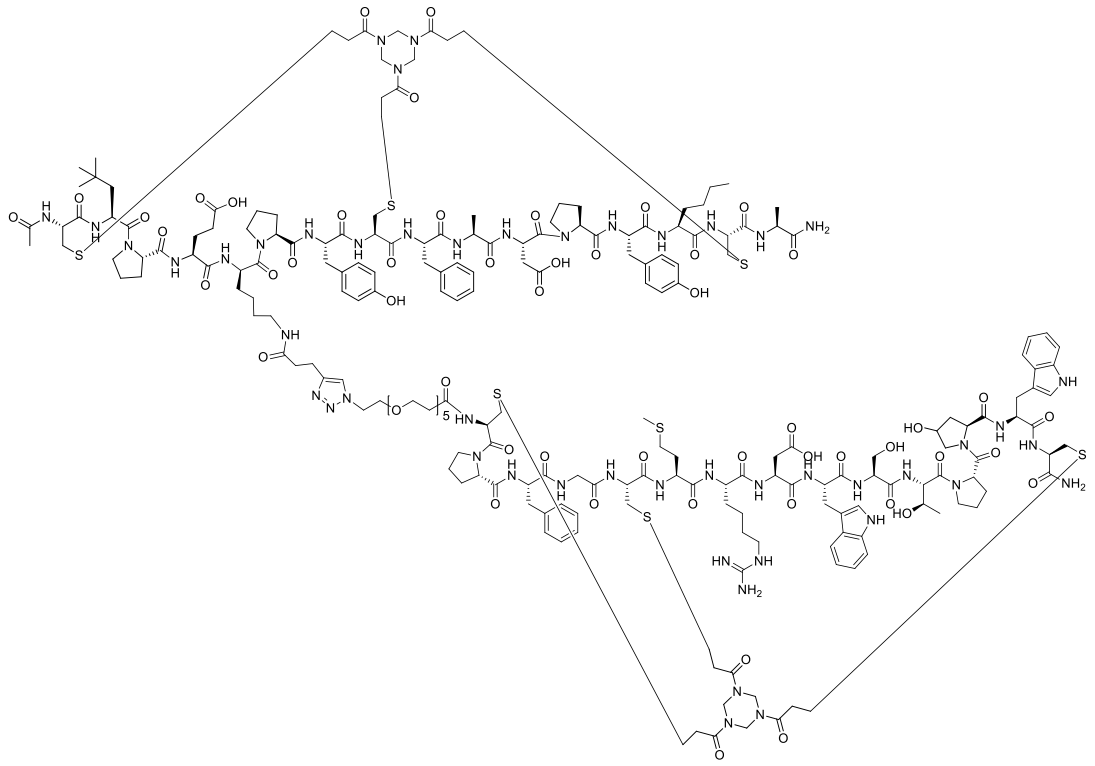

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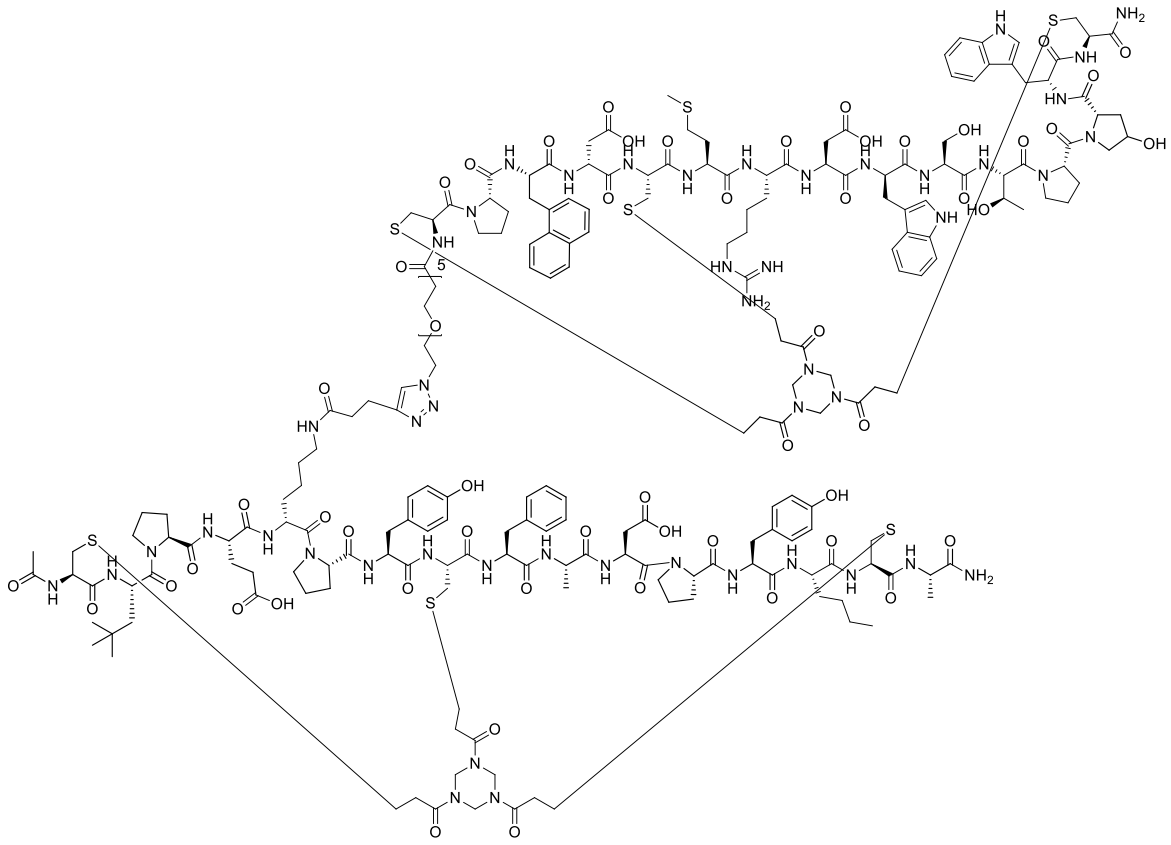

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24. The heterotandem bicyclic peptide complex or the pharmaceutically acceptable salt thereof as defined in any one of claims 1 to 23, wherein the linker is selected from: -CH_2-, -PEG_5-, -PEG_{10}-, -PEG_{12}-, -PEG_{23}-, -PEG_{24}-, -PEG_{15}-Sar_5-, -PEG_{10}-Sar_{10}-, -PEG_5-Sar_{15}-, -PEG_5-Sar_5-, -B-Ala-Sar_{20}-, -B-Ala-Sar_{10}-PEG_{10}-, -B-Ala-Sar_5-PEG_{15}- and -B-Ala-Sar_5-PEG_5-..

25. The heterotandem bicyclic peptide complex or the pharmaceutically acceptable salt thereof as defined in any one of claims 1 to 24, wherein the molecular scaffold is 1,1',1''-(1,3,5-triazinane-1,3,5-triyl)triprop-2-en-1-one (TATA).

26. The heterotandem bicyclic peptide complex or the pharmaceutically acceptable salt thereof as defined in any one of claims 1 to 25, wherein the pharmaceutically acceptable salt is selected from the free acid or the sodium, potassium, calcium, ammonium salt.

27. A pharmaceutical composition which comprises the heterotandem bicyclic peptide complex or the pharmaceutically acceptable salt thereof of any one of claims 1 to 26 in combination with one or more pharmaceutically acceptable excipients.

28. The heterotandem bicyclic peptide complex or the pharmaceutically acceptable salt thereof as defined in any one of claims 1 to 26 for use in preventing, suppressing or treating cancer wherein
(i) the second peptide ligand binds to EphA2 and the cancer is an EphA2 associated cancer;
(ii) the second peptide ligand binds to PD-L1 and the cancer is a PD-L1 associated cancer; or
(iii) the second peptide ligand binds to Nectin-4 and the cancer is a Nectin-4 associated cancer.

29. Use of the heterotandem bicyclic peptide complex or the pharmaceutically acceptable salt thereof as defined in any one of claims 1 to 26 or the pharmaceutical composition as defined in claim 27 in the manufacture of a medicament for the prevention, suppresision or treatment of cancer, wherein;
(i) the second peptide ligand binds to EphA2 and the cancer is an EphA2 associated cancer;
(ii) the second peptide ligand binds to PD-L1 and the cancer is a PD-L1 associated cancer; or
(iii) the second peptide ligand binds to Nectin-4 and the cancer is a Nectin-4 associated cancer.