CLAIMS

What is claimed is:

1. A peptide inhibitor according to Formula (Z'):

$$R^1\text{-X4-X5-X6-X7-X8-X9-X10-X11-X12-X13-X14-X15-}R^2 \text{ (Z')}$$

or a pharmaceutically acceptable salt thereof, wherein

X4 is Pen;

X5 is Asn;

X6 is Thr;

X7 is Trp substituted with alkyl;

X8 is Gln, alpha-MeLys, alpha-MeLeu, alpha-MeLys(Ac), beta-homoGln, Cit, Glu, Phe, Asn, Thr, Val, Aib, alpha-MeGln, alpha-MeAsn, Lys(Ac), Dab(Ac), Dap(Ac), homo-Lys(Ac), 1-Nal, 2-Nal, or Trp;

X9 is Pen;

X10 is unsubstituted Phe, or Phe substituted with halo, alkyl, haloalkyl, hydroxy, alkoxy, carboxy, carboxamido, 2-aminoethoxy, or 2-acetylaminoethoxy;

X11 is 2-Nal, Phe(2-Me), Phe(3-Me), Phe(4-Me), Phe(3,4-dimethoxy), 1-Nal, unsubstituted Trp, or Trp substituted with cyano, halo, alkyl, haloalkyl, hydroxy, or alkoxy;

X12 is 4-amino-4-carboxy-tetrahydropyran (THP), alpha-MeLys, alpha-MeLeu, alpha-MeArg, alpha-MePhe, alpha-MeLeu, alpha-MeLys, alpha-MeAsn, alpha-MeTyr, Ala, cyclohexylAla, Lys, or Aib;

X13 is Aib, Glu, Cit, Gln, Lys(Ac), alpha-MeArg, alpha-MeGlu, alpha-MeLeu, alpha-MeLys, alpha-Me-Asn, alpha-MeLys(Ac), Dab(Ac), Dap(Ac), homo-Lys(Ac), Lys, pegylated Lys, b-homoGlu, or Lys(Y2-Ac), wherein Y2 is an amino acid;

X14 is Asn, 2-Nap, Aib, Arg, Cit, Asp, Phe, Gly, Lys, Leu, Ala, (D)Ala, beta-Ala, His, Thr, n-Leu, Gln, Ser, (D)Ser, Tic, Trp, alpha-MeGln, alpha-MeAsn, alpha-MeLys(Ac), Dab(Ac), Dap(Ac), homo-Lys(Ac), or Lys(Ac);

X15 is Leu, (D)Leu, beta-Ala, Cit, or (D)Lys;

R^1 is hydrogen, a C1-C6 alkyl, a C6-C12 aryl, a C6-C12aryl-C1-C6alkyl, or a C1-C20 alkanoyl; and

R^2 is OH or NH_2;

wherein the peptide inhibitor or pharmaceutically acceptable salt or solvate thereof comprises a disulfide bond between two Pen residues;

and

wherein the peptide inhibitor or pharmaceutically acceptable salt thereof inhibits the binding of an interleukin-23 (IL-23) to an IL-23 receptor.

2. The peptide inhibitor or pharmaceutically acceptable salt thereof of claim 1, wherein X7 is Trp substituted with alkyl, and the substitution is at a 1-, 2-, or 7-position.

3. The peptide inhibitor or pharmaceutically acceptable salt thereof of claim 2, wherein X7 is Trp substituted with 1-Me, 2-Me, or 7-Me.

4. The peptide inhibitor or pharmaceutically acceptable salt thereof of claim 2, wherein X8 is Gln, alpha-Me-Lys, alpha-MeLys(Ac), or Glu.

5. The peptide inhibitor or pharmaceutically acceptable salt thereof of claim 2, wherein X8 is Gln.

6. The peptide inhibitor or pharmaceutically acceptable salt thereof of claim 2, wherein X8 is Gln, Cit, alpha-MeLys, alpha-MeLeu, Aib, or Lys(AC).

7. The peptide inhibitor or pharmaceutically acceptable salt thereof of claim 2, wherein X8 is Lys(Ac).

8. The peptide inhibitor or pharmaceutically acceptable salt thereof of claim 2, wherein X10 is Phe, Phe[4-(2-aminoethoxy)], Phe[4-(2-acetylaminoethoxy)], or Phe(4-$CONH_2$).

9. The peptide inhibitor or pharmaceutically acceptable salt thereof of claim 2, wherein X10 is Phe[4-(2-aminoethoxy)], or Phe[4-(2-acetylaminoethoxy)].

10. The peptide inhibitor or pharmaceutically acceptable salt thereof of claim 2, wherein X11 is Trp substituted with cyano, halo, alkyl, haloalkyl, hydroxy, or alkoxy.

11. The peptide inhibitor or pharmaceutically acceptable salt thereof of claim 2, wherein X11 is 2-Nal, Phe(2-Me), Phe(3-Me), Phe(4-Me), Phe(3,4-dimethoxy), or 1-Nal.

12. The peptide inhibitor or pharmaceutically acceptable salt thereof of claim 2, wherein X11 is 2-Nal or 1-Nal.

13. The peptide inhibitor or pharmaceutically acceptable salt thereof of claim 2, wherein X11 is 2-Nal.

14. The peptide inhibitor or pharmaceutically acceptable salt thereof claim 1, wherein R^1 is Ac.

15. The peptide inhibitor or pharmaceutically acceptable salt thereof of claim 1, wherein the peptide inhibitor is:
Ac-[Pen]-N-T-[W(7-Me)]-Q-[Pen]-Phe[4-(2-aminoethoxy)]-[2-Nal]-[a-MeLeu]-[Lys(Ac)]-N-[bA]-NH_2 (SEQ ID NO: 201);
Ac-[Pen]-N-T-[W(7-Me)]-[Cit]-[Pen]-Phe[4-(2-aminoethoxy)]-[2-Nal]-[a-MeLeu]-[Lys(Ac)]-N-[bA]-NH_2 (SEQ ID NO: 227);
Ac-[Pen]-N-T-[W(7-Me)]-[Lys(Ac)]-[Pen]-Phe[4-(2-aminoethoxy)]-[2-Nal]-[a-MeLys]-[Lys(Ac)]-N-[bA]-NH_2 (SEQ ID NO: 242);
Ac-[Pen]-N-T-[W(7-Me)]-[Lys(Ac)]-[Pen]-Phe[4-(2-aminoethoxy)]-[2-Nal]-[a-MeLys]-[Lys(Ac)]-N-[(D)Leu]-NH_2 (SEQ ID NO: 245);
Ac-[Pen]-N-T-[W(7-Me)]-[Lys(Ac)]-[Pen]-Phe[4-(2-aminoethoxy)]-[2-Nal]-[a-MeLys]-[Lys(Ac)]-N-[Cit]-NH_2 (SEQ ID NO: 249);

Ac-[Pen]-N--T-[W(7-Me)]-[Lys(Ac)]-[Pen]-Phe[4-(2-aminoethoxy)]-[2-Nal]-[a-MeLys]-[Lys(Ac)]-N-[(D)Lys]-NH_2 (SEQ ID NO: 252);

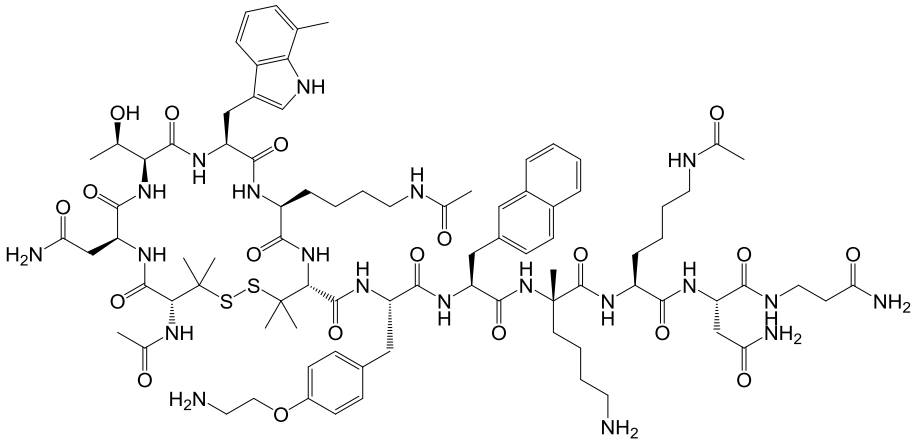
Ac-[Pen]-NT-[W(7-Me)]-Q-[Pen]-Phe[4-(2-aminoethoxy)]-[2-Nal]-[a-MeLys]-[Lys(Ac)]-N-[bA]-NH_2 (SEQ ID NO: 267);

Ac-[Pen]-N-T-[W(7-Et)]-[Lys(Ac)]-[Pen]-Phe[4-(2-aminoethoxy)]-[2-Nal]-[a-MeLys]-[Lys(Ac)]-N-[(D)Leu]-NH_2 (SEQ ID NO: 284); or

Ac-[Pen]-N-T-[W(7-n-Pr)]-[Lys(Ac)]-[Pen]-Phe[4-(2-aminoethoxy)]-[2-Nal]-[a-MeLys]-[Lys(Ac)]-N-[(D)Leu]-NH_2 (Seq. ID. NO: 285).

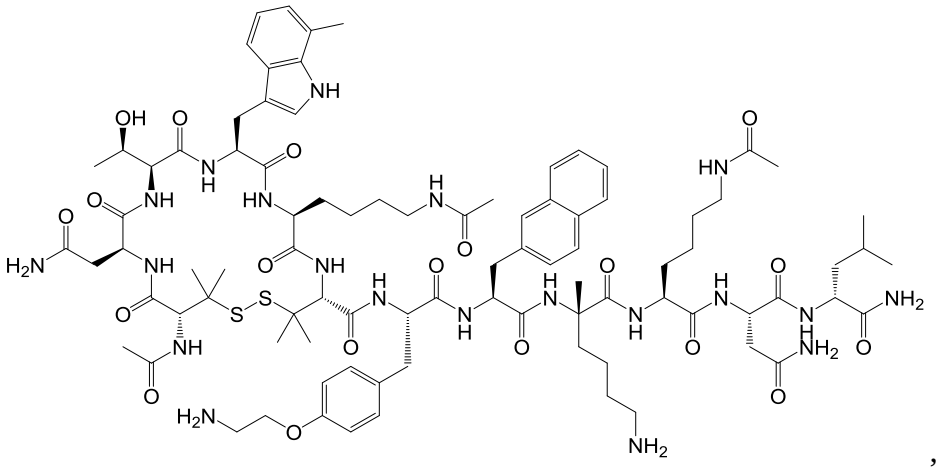
16. The peptide inhibitor or pharmaceutically acceptable salt thereof of claim 1, wherein the peptide inhibitor is:

Ac-[Pen]-N-T-[W(7-Me)]-[Lys(Ac)]-[Pen]-Phe[4-(2-aminoethoxy)]-[2-Nal]-[a-MeLys]-[Lys(Ac)]-N-[bA]-NH_2 (SEQ ID NO: 242)

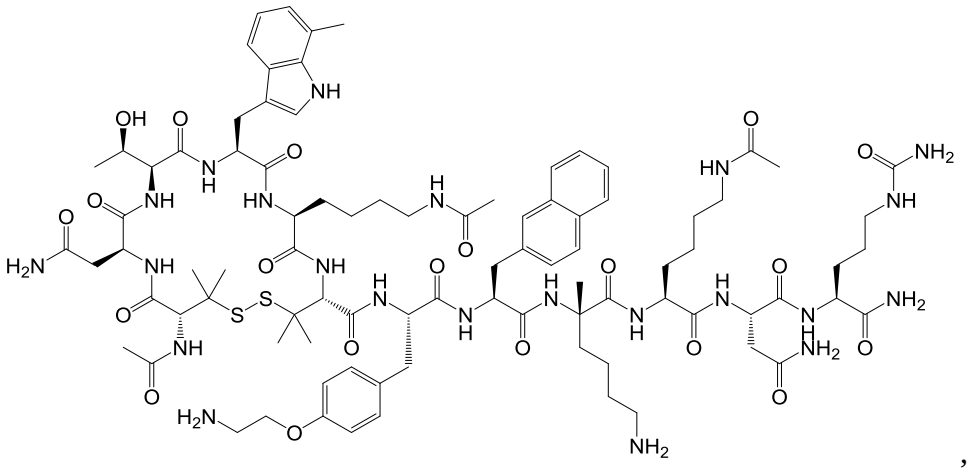


,

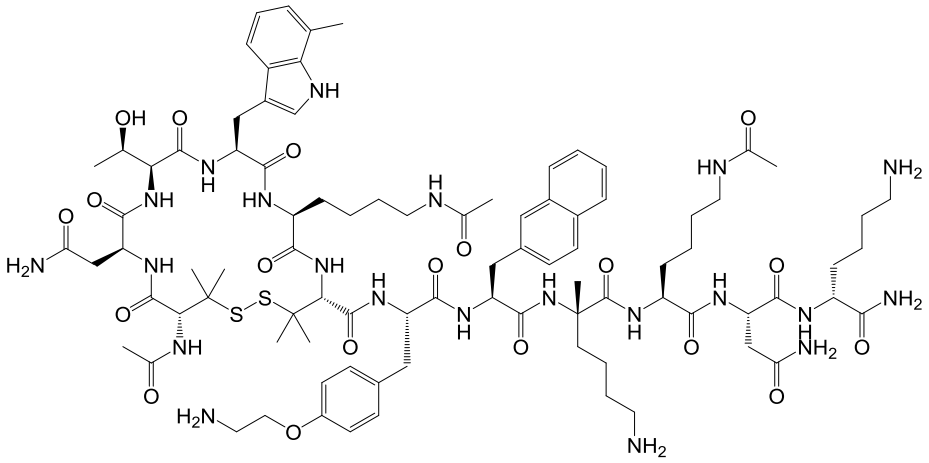
Ac-[Pen]-N-T-[W(7-Me)]-[Lys(Ac)]-[Pen]-Phe[4-(2-aminoethoxy)]-[2-Nal]-[a-MeLys]-[Lys(Ac)]-N-[(D)Leu]-NH_2 (SEQ ID NO: 245)



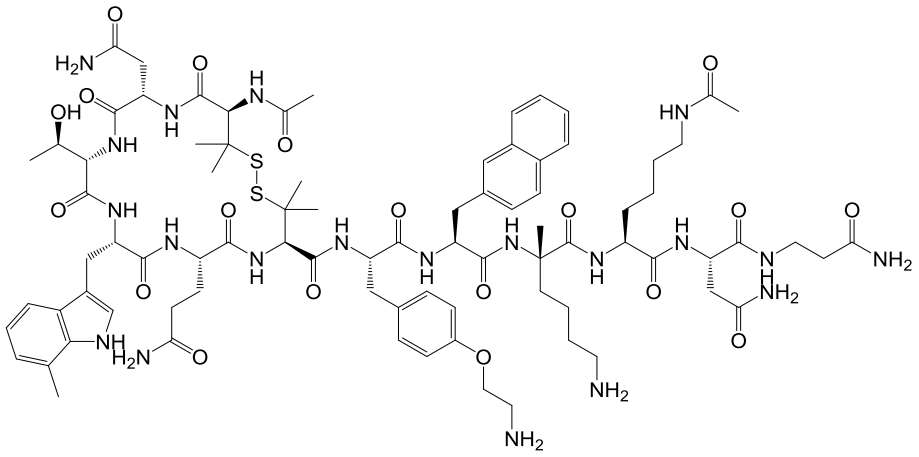
Ac-[Pen]-N-T-[W(7-Me)]-[Lys(Ac)]-[Pen]-Phe[4-(2-aminoethoxy)]-[2-Nal]-[a-MeLys]-[Lys(Ac)]-N-[Cit]-NH_2 (SEQ ID NO: 249)



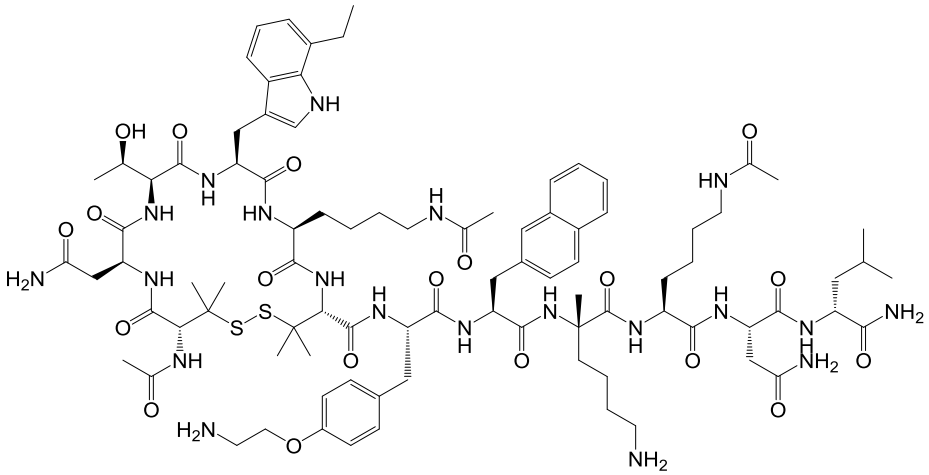
Ac-[Pen]-N-T-[W(7-Me)]-[Lys(Ac)]-[Pen]-Phe[4-(2-aminoethoxy)]-[2-Nal]-[a-MeLys]-[Lys(Ac)]-N-[(D)Lys]-NH_2 (SEQ ID NO: 252)



Ac-[Pen]-N-T-[W(7-Me)]-Q-[Pen]-Phe[4-(2-aminoethoxy)]-[2-Nal]-[a-MeLys]-[Lys(Ac)]-N-[bA]-NH_2 (SEQ ID NO: 267)

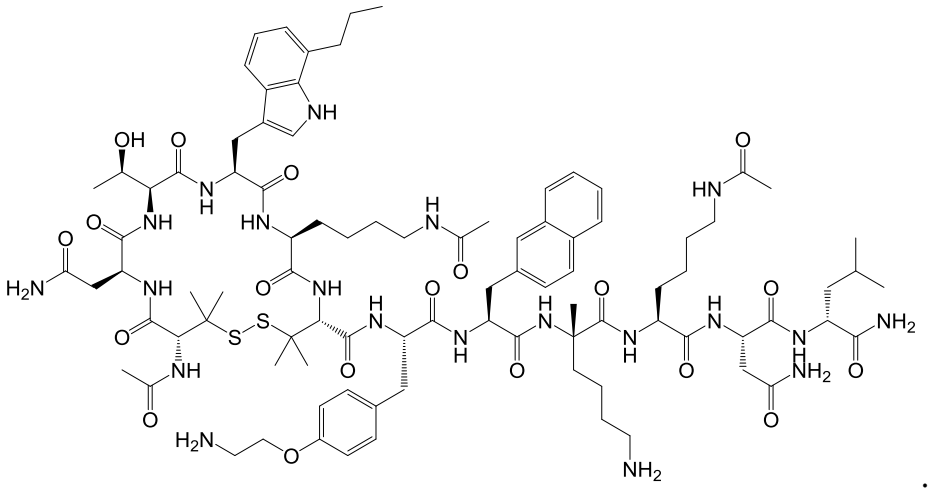


Ac-[Pen]-N-T-[W(7-Et)]-[Lys(Ac)]-[Pen]-Phe[4-(2-aminoethoxy)]-[2-Nal]-[a-MeLys]-[Lys(Ac)]-N-[(D)Leu]-NH_2 (SEQ ID NO: 284)



, or

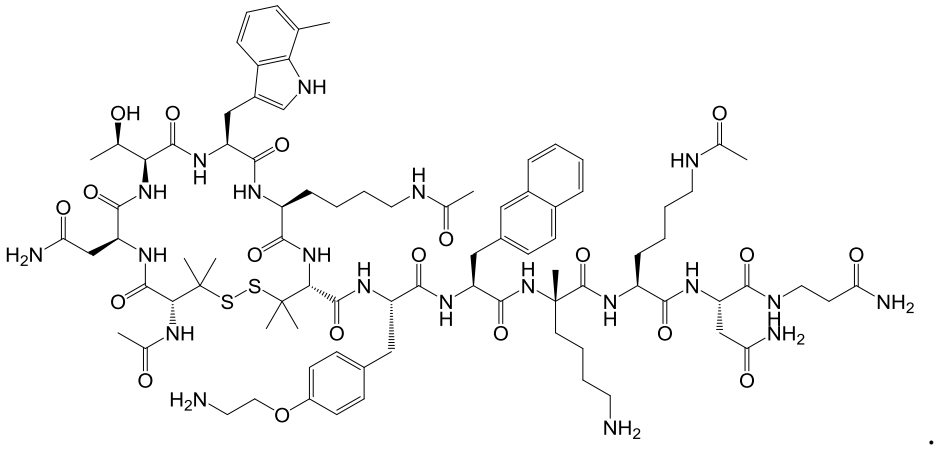
Ac-[Pen]-N-T-[W(7-n-Pr)]-[Lys(Ac)]-[Pen]-Phe[4-(2-aminoethoxy)]-[2-Nal]-[a-MeLys]-[Lys(Ac)]-N-[(D)Leu]-NH_2 (Seq. ID. NO: 285)



.

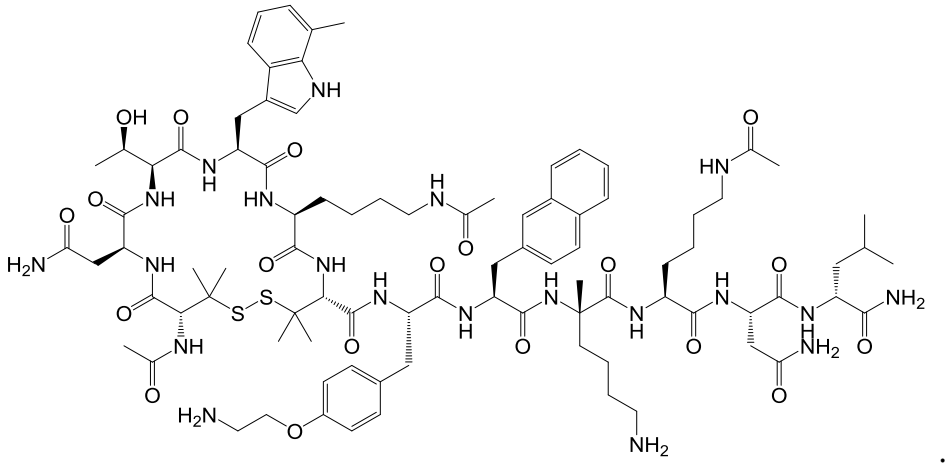
17. The peptide inhibitor or pharmaceutically acceptable salt thereof of claim 1, wherein the peptide inhibitor is:

Ac-[Pen]-N-T-[W(7-Me)]-[Lys(Ac)]-[Pen]-Phe[4-(2-aminoethoxy)]-[2-Nal]-[a-MeLys]-[Lys(Ac)]-N-[bA]-NH_2 (SEQ ID NO: 242)



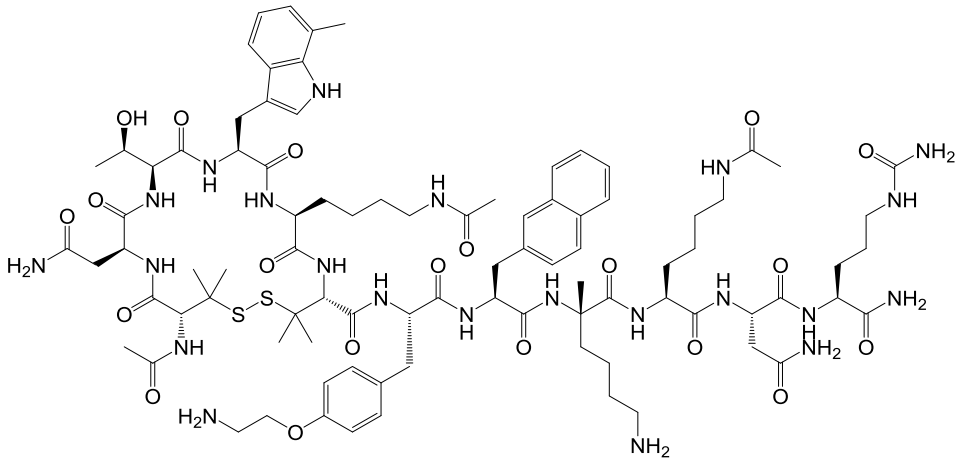
18. The peptide inhibitor or pharmaceutically acceptable salt thereof of claim 1, wherein the peptide inhibitor is:

Ac-[Pen]-N-T-[W(7-Me)]-[Lys(Ac)]-[Pen]-Phe[4-(2-aminoethoxy)]-[2-Nal]-[a-MeLys]-[Lys(Ac)]-N-[(D)Leu]-NH_2 (SEQ ID NO: 245)



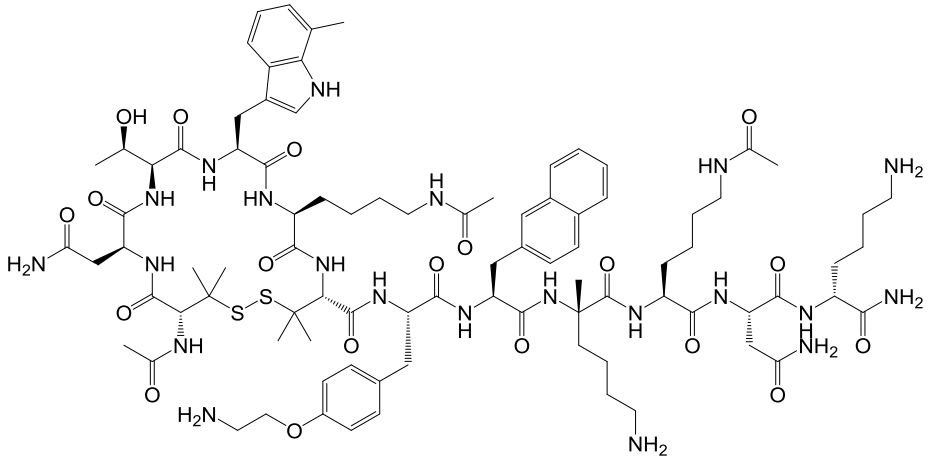
19. The peptide inhibitor or pharmaceutically acceptable salt thereof of claim 1, wherein the peptide inhibitor is:

Ac-[Pen]-N-T-[W(7-Me)]-[Lys(Ac)]-[Pen]-Phe[4-(2-aminoethoxy)]-[2-Nal]-[a-MeLys]-[Lys(Ac)]-N-[Cit]-NH_2 (SEQ ID NO: 249)



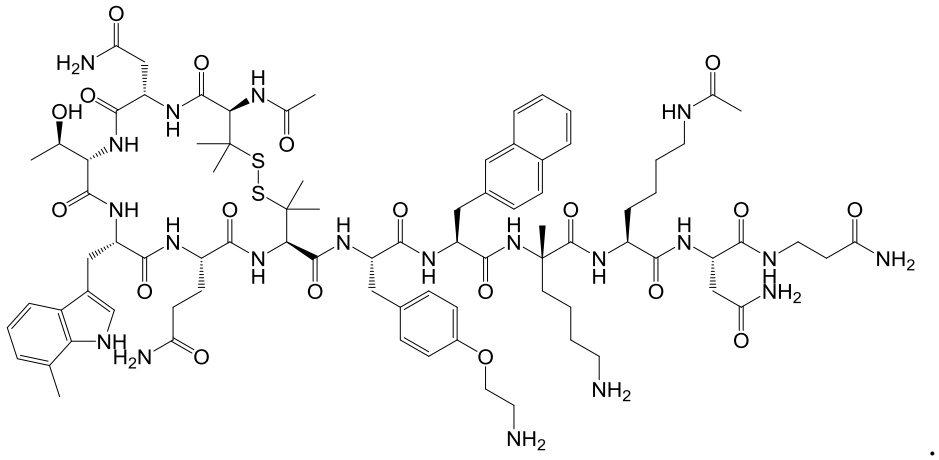
20. The peptide inhibitor or pharmaceutically acceptable salt thereof of claim 1, wherein the peptide inhibitor is

Ac-[Pen]-N-T-[W(7-Me)]-[Lys(Ac)]-[Pen]-Phe[4-(2-aminoethoxy)]-[2-Nal]-[a-MeLys]-[Lys(Ac)]-N-[(D)Lys]-NH_2 (SEQ ID NO: 252)



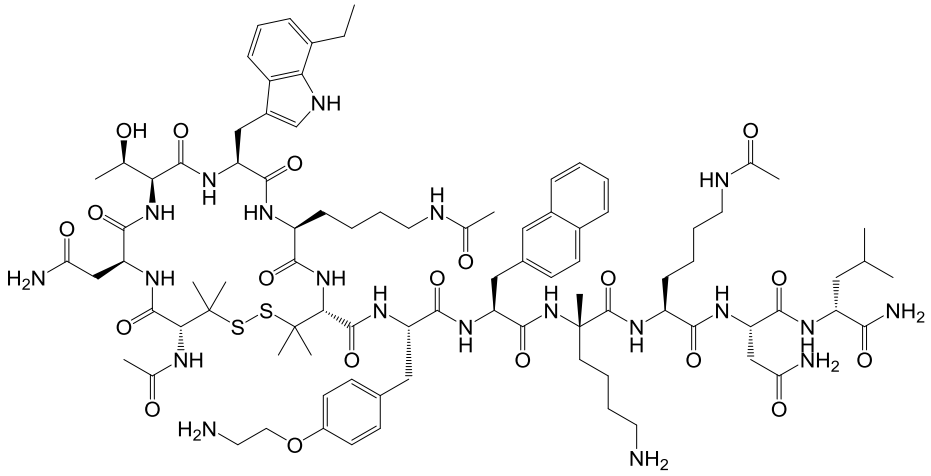
21. The peptide inhibitor or pharmaceutically acceptable salt thereof of claim 1, wherein the peptide inhibitor is:

Ac-[Pen]-N-T-[W(7-Me)]-Q-[Pen]-Phe[4-(2-aminoethoxy)]-[2-Nal]-[a-MeLys]-[Lys(Ac)]-N-[bA]-NH_2 (SEQ IS NO: 267)



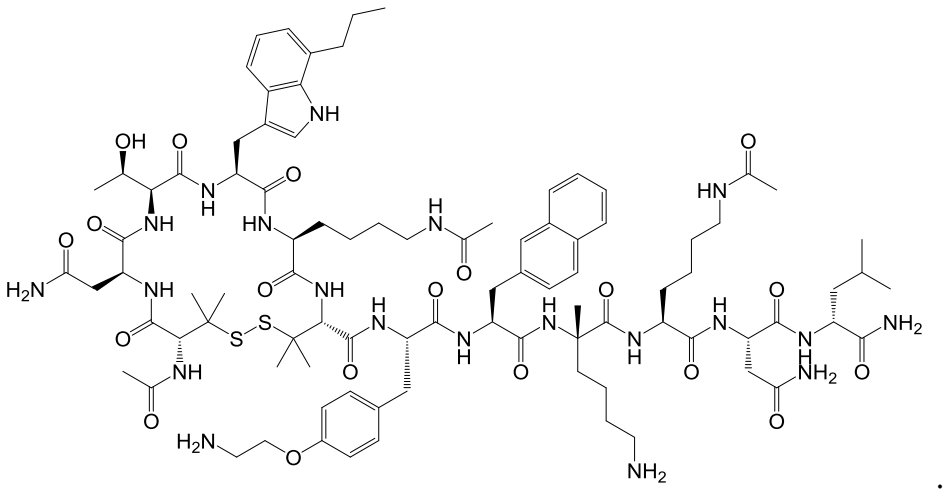
22. The peptide inhibitor or pharmaceutically acceptable salt thereof of claim 1, wherein the peptide inhibitor is:

Ac-[Pen]-N-T-[W(7-Et)]-[Lys(Ac)]-[Pen]-Phe[4-(2-aminoethoxy)]-[2-Nal]-[a-MeLys]-[Lys(Ac)]-N-[(D)Leu]-NH_2 (SEQ ID NO: 284)



23. The peptide inhibitor or pharmaceutically acceptable salt thereof of claim 1, wherein the peptide inhibitor is:

Ac-[Pen]-N-T-[W(7-n-Pr)]-[Lys(Ac)]-[Pen]-Phe[4-(2-aminoethoxy)]-[2-Nal]-[a-MeLys]-[Lys(Ac)]-N-[(D)Leu]-NH_2 (Seq. ID. NO: 285)



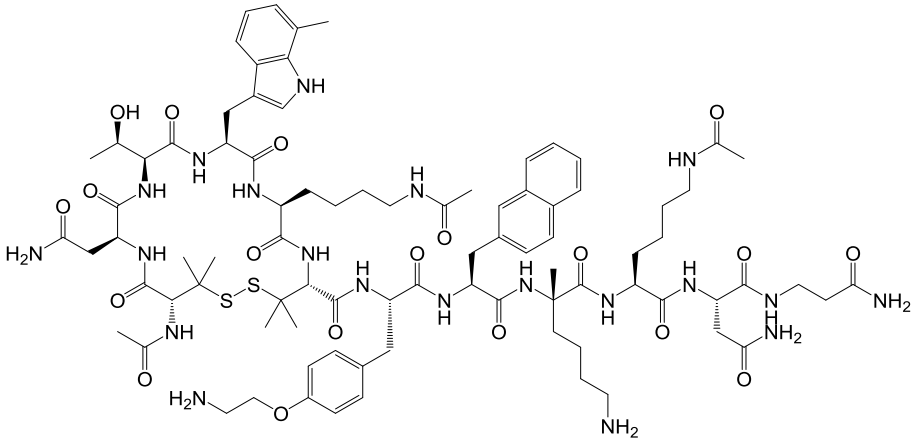
24. A pharmaceutical composition comprising the peptide inhibitor or pharmaceutically acceptable salt thereof of claim 1, and a pharmaceutically acceptable carrier, excipient, or diluent.

25. The pharmaceutical composition of claim 24, wherein the peptide inhibitor is:
Ac-[Pen]-N-T-[W(7-Me)]-Q-[Pen]-Phe[4-(2-aminoethoxy)]-[2-Nal]-[a-MeLeu]-[Lys(Ac)]-N-[bA]-NH_2 (SEQ ID NO: 201);
Ac-[Pen]-N-T-[W(7-Me)]-[Cit]-[Pen]-Phe[4-(2-aminoethoxy)]-[2-Nal]-[a-MeLeu]-[Lys(Ac)]-N-[bA]-NH_2 (SEQ ID NO: 227);
Ac-[Pen]-N-T-[W(7-Me)]-[Lys(Ac)]-[Pen]-Phe[4-(2-aminoethoxy)]-[2-Nal]-[a-MeLys]-[Lys(Ac)]-N-[bA]-NH_2 (SEQ ID NO: 242);
Ac-[Pen]-N-T-[W(7-Me)]-[Lys(Ac)]-[Pen]-Phe[4-(2-aminoethoxy)]-[2-Nal]-[a-MeLys]-[Lys(Ac)]-N-[(D)Leu]-NH_2 (SEQ ID NO: 245);
Ac-[Pen]-N-T-[W(7-Me)]-[Lys(Ac)]-[Pen]-Phe[4-(2-aminoethoxy)]-[2-Nal]-[a-MeLys]-[Lys(Ac)]-N-[Cit]-NH_2 (SEQ ID NO: 249);
Ac-[Pen]-N--T-[W(7-Me)]-[Lys(Ac)]-[Pen]-Phe[4-(2-aminoethoxy)]-[2-Nal]-[a-MeLys]-[Lys(Ac)]-N-[(D)Lys]-NH_2 (SEQ ID NO: 252);
Ac-[Pen]-NT-[W(7-Me)]-Q-[Pen]-Phe[4-(2-aminoethoxy)]-[2-Nal]-[a-MeLys]-[Lys(Ac)]-N-[bA]-NH_2 (SEQ ID NO: 267);

Ac-[Pen]-N-T-[W(7-Et)]-[Lys(Ac)]-[Pen]-Phe[4-(2-aminoethoxy)]-[2-Nal]-[a-MeLys]-[Lys(Ac)]-N-[(D)Leu]-NH_2 (SEQ ID NO: 284); or
Ac-[Pen]-N-T-[W(7-n-Pr)]-[Lys(Ac)]-[Pen]-Phe[4-(2-aminoethoxy)]-[2-Nal]-[a-MeLys]-[Lys(Ac)]-N-[(D)Leu]-NH_2 (Seq. ID. No. 285).

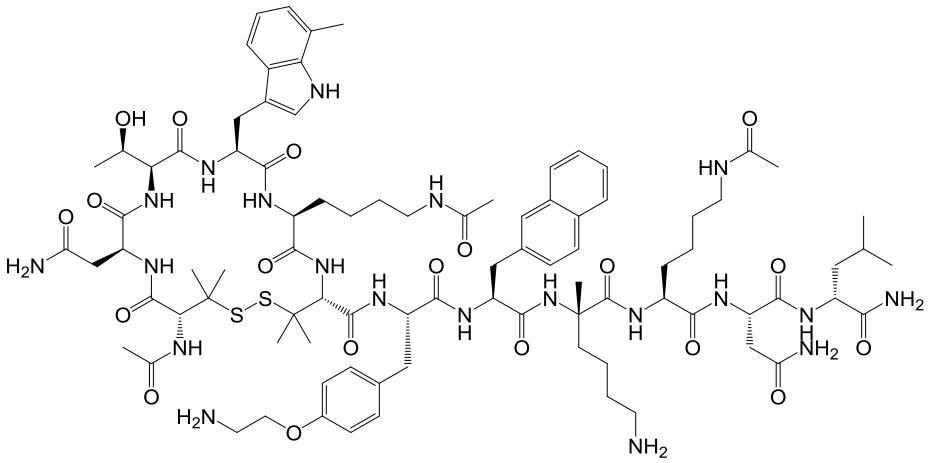
26. The pharmaceutical composition of claim 24, wherein the peptide inhibitor is:

Ac-[Pen]-N-T-[W(7-Me)]-[Lys(Ac)]-[Pen]-Phe[4-(2-aminoethoxy)]-[2-Nal]-[a-MeLys]-[Lys(Ac)]-N-[bA]-NH_2 (SEQ ID NO: 242)



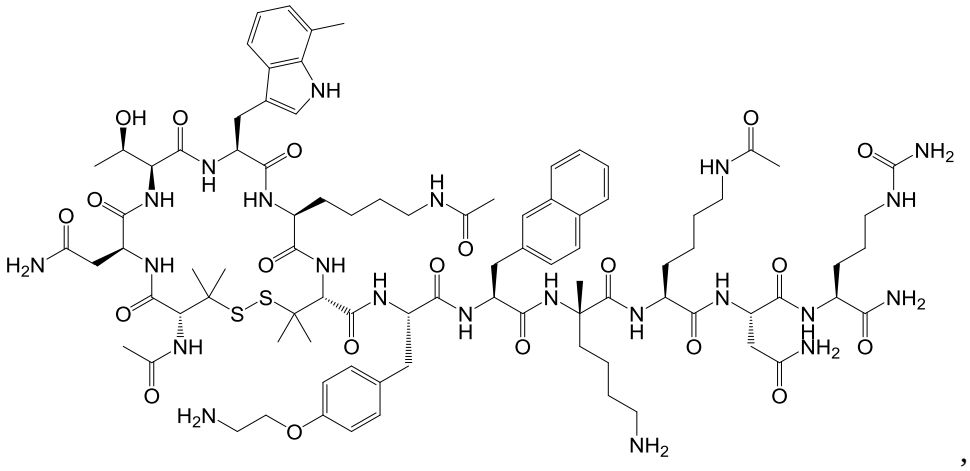
,

Ac-[Pen]-N-T-[W(7-Me)]-[Lys(Ac)]-[Pen]-Phe[4-(2-aminoethoxy)]-[2-Nal]-[a-MeLys]-[Lys(Ac)]-N-[(D)Leu]-NH_2 (SEQ ID NO: 245)



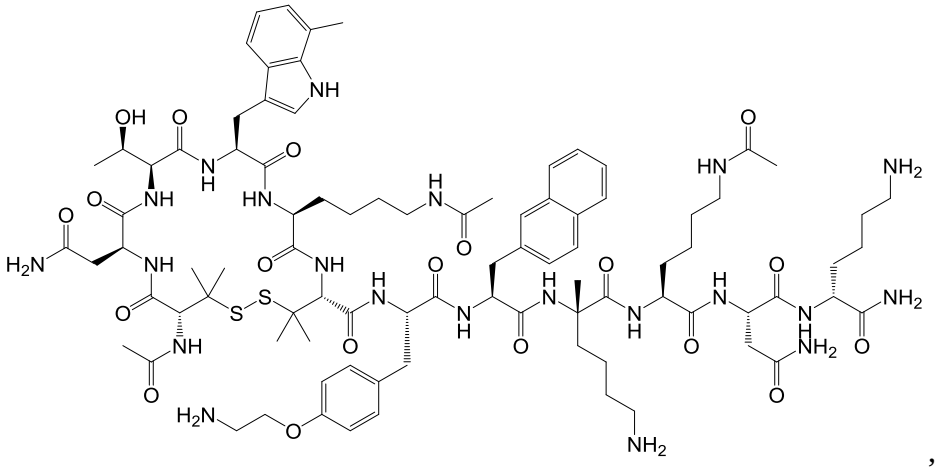
,

Ac-[Pen]-N-T-[W(7-Me)]-[Lys(Ac)]-[Pen]-Phe[4-(2-aminoethoxy)]-[2-Nal]-[a-MeLys]-[Lys(Ac)]-N-[Cit]-NH_2 (SEQ ID NO: 249)



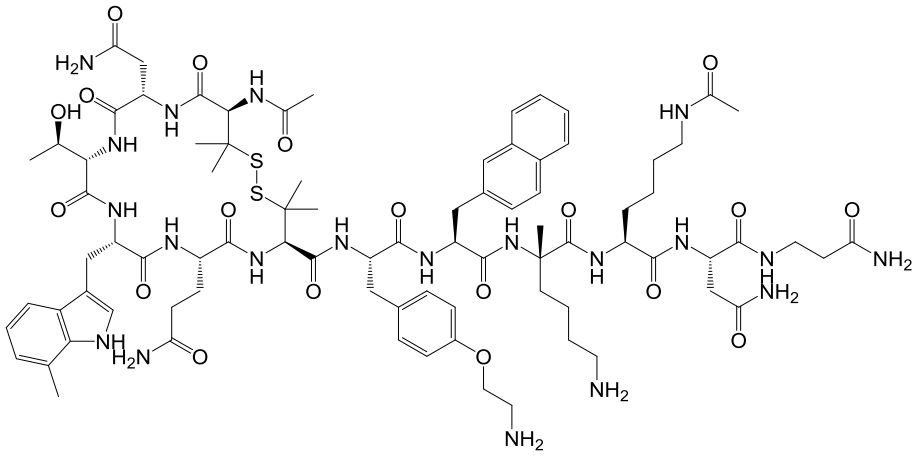
,

Ac-[Pen]-N-T-[W(7-Me)]-[Lys(Ac)]-[Pen]-Phe[4-(2-aminoethoxy)]-[2-Nal]-[a-MeLys]-[Lys(Ac)]-N-[(D)Lys]-NH_2 (SEQ ID NO: 252)

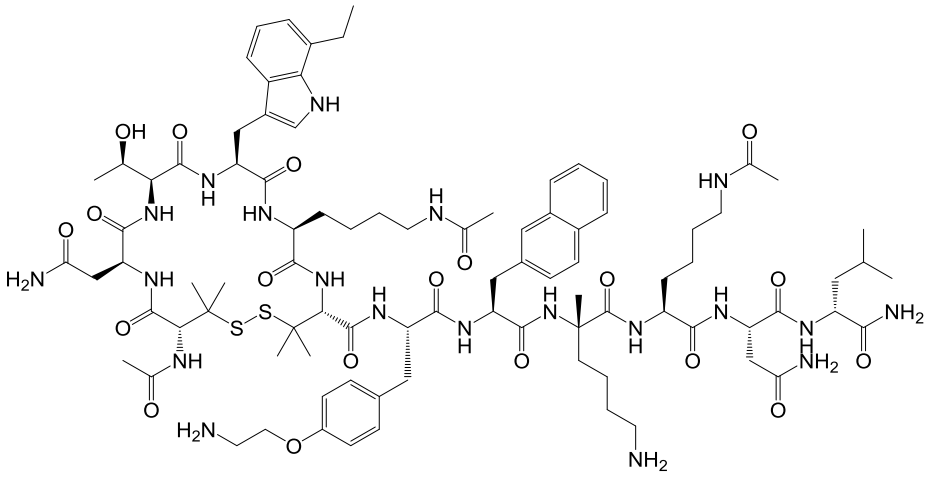


,

Ac-[Pen]-N-T-[W(7-Me)]-Q-[Pen]-Phe[4-(2-aminoethoxy)]-[2-Nal]-[a-MeLys]-[Lys(Ac)]-N-[bA]-NH_2 (SEQ ID NO: 267)

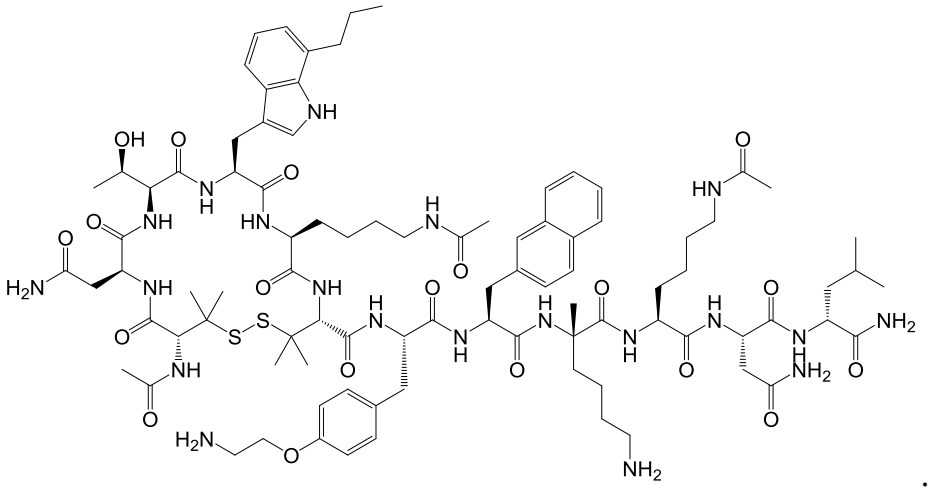


Ac-[Pen]-N-T-[W(7-Et)]-[Lys(Ac)]-[Pen]-Phe[4-(2-aminoethoxy)]-[2-Nal]-[a-MeLys]-[Lys(Ac)]-N-[(D)Leu]-NH_2 (SEQ ID NO: 284)



, or

Ac-[Pen]-N-T-[W(7-n-Pr)]-[Lys(Ac)]-[Pen]-Phe[4-(2-aminoethoxy)]-[2-Nal]-[a-MeLys]-[Lys(Ac)]-N-[(D)Leu]-NH_2 (Seq. ID. No. 285)



27. Use of a peptide inhibitor or a pharmaceutically acceptable salt thereof according to any of claims 1-23, or a pharmaceutical composition according to any of claims 24-26, in the preparation of a medicament for the treatment of a disease or disorder involving autoimmune inflammation.

28. Use of a peptide inhibitor or a pharmaceutically acceptable salt thereof according to any of claims 16-23, or a pharmaceutical composition according to claim 26, in the manufacture of a medicament for the treatment of a disease or disorder involving autoimmune inflammation.

29. The use of claim 27 or claim 28, wherein the disease or disorder is selected from the group consisting of: multiple sclerosis, asthma, rheumatoid arthritis, inflammatory bowel diseases (IBDs), juvenile IBD, adolescent IBD, Crohn's disease, sarcoidosis, Systemic Lupus Erythematosus, ankylosing spondylitis (axial spondyloarthritis), psoriatic arthritis (PsA), psoriasis (PsO), atopic dermatitis, acne ectopica, ulcerative colitis, Crohn's disease (CD), Celiac disease (nontropical Sprue), enteropathy associated with seronegative arthropathies, microscopic colitis, collagenous colitis, eosinophilic gastroenteritis/esophagitis, colitis associated with radio- or chemo-therapy, colitis associated with disorders of innate immunity as in leukocyte adhesion deficiency-1, chronic granulomatous disease, glycogen storage disease type 1b, Hermansky-Pudlak syndrome, Chediak-Higashi syndrome, Wiskott-Aldrich Syndrome, pouchitis, pouchitis

resulting after proctocolectomy and ileoanal anastomosis, gastrointestinal cancer, pancreatitis, insulin-dependent diabetes mellitus, mastitis, cholecystitis, cholangitis, primary biliary cirrhosis, viral-associated enteropathy, pericholangitis, chronic bronchitis, chronic sinusitis, asthma, uveitis, and graft versus host disease.

30. The use of claim 29, wherein the disease or disorder is selected from the group consisting of: Inflammatory Bowel Disease (IBD), Ulcerative colitis (UC), Crohn's Disease (CD), psoriasis (PsO), and psoriatic arthritis (PsA).

31. The use of claim 30, wherein the disease or disorder is Inflammatory Bowel Diseases (IBDs).

32. The use of claim 30, wherein the disease or disorder is Ulcerative colitis (UC).

33. The use of claim 30, wherein the disease or disorder is Crohn's Disease (CD).

34. The use of claim 30, wherein the disease or disorder is psoriasis (PsO).

35. The use of claim 33, wherein the psoriasis is plaque psoriasis, guttate psoriasis, inverse psoriasis, pustular psoriasis, Palmo-Plantar Pustulosis, psoriasis vulgaris, or erythrodermic psoriasis.

36. The use of claim 30, wherein the disease or disorder is psoriatic arthritis (PsA).

37. A peptide inhibitor or a pharmaceutically acceptable salt thereof according to any of claims 1-23, or a pharmaceutical composition according to any of claims 24-26, for use in the treatment of a disease or disorder involving autoimmune inflammation.

38. A peptide inhibitor or a pharmaceutically acceptable salt thereof according to any of claims 16-23, or a pharmaceutical composition according to claim 26, for use in the treatment of a disease or disorder involving autoimmune inflammation.