# NON-NATURALLY OCCURRING MELANOCORTIN ANALOGS AND USES THEREOF FOR TREATING SUBSTANCE USE DISORDERS

## CROSS-REFERENCE TO RELATED APPLICATION(S)

**[0001]** This application claims the benefit of U.S. Provisional Patent Application No. 63/607,500, filed December 7, 2023, U.S. Provisional Patent Application No. 63/618,843, filed January 8, 2024, U.S. Provisional Patent Application No. 63/557,385, filed February 23, 2024, U.S. Provisional Patent Application No. 63/573,429, filed April 2, 2024, of U.S. Provisional Patent Application No. 63/650,705, filed May 22, 2024, U.S. Provisional Patent Application No. 63/656,583, filed June 5, 2025, and U.S. Provisional Patent Application No. 63/663,648, filed June 24, 2024, all of which applications are incorporated herein by reference in their entirety.

## INCORPORATION BY REFERENCE OF SEQUENCE LISTING

**[0002]** This application contains an ST.26 compliant Sequence Listing, which is submitted concurrently in xml format and hereby incorporated by reference in its entirety. The .xml copy, created on December 9, 2024, is titled "146316_8017_WO02_SL.xml" and is 1,472,360 bytes in size.

## BACKGROUND

**[0003]** Opioid receptors (e.g., mu opioid receptor, delta opioid receptor) are major molecular targets for pain management. The vast majority of clinically prescribed pain medications are opioid receptor ligands (i.e., opioid drugs) that are structurally similar to or derived from morphine or other opiates. While these medications serve as effective painkillers, usage can result in several unwanted adverse side effects, including increased tolerance, addiction, overdose, respiratory distress and constipation.

**[0004]** Opioid and other substance addictions, for example, alcohol and nicotine addictions, contribute to millions of premature deaths each year. Although current therapies aimed at treating addiction can be effective, many substance users are unable to overcome their addiction, despite having a desire to quit.

**[0005]** Even after recent advances in pain medication development, there remains considerable need for new medications to manage pain with improved therapeutic profiles (e.g., robust therapeutic activity and reduced unwanted adverse side effects) compared to conventional opioid drugs. There is also a growing demand for new therapies to treat opioid use disorders (i.e., opioid addictions) and other addictions (e.g., alcohol use disorder, and nicotine addiction).

## SUMMARY

**[0006]** The present technology comprises methods of reducing substance use disorders and/or pain in subjects in need thereof, comprising administering to the subject, a non-naturally occurring melanocortin analog.

**[0007]** In some embodiments, the present technology comprises a method of reducing a pain level in a subject in need thereof relative to a control, including administering to the subject a non-naturally occurring melanocortin analog of Formula (I): X1-X2-X3-R1-R2-R3-R4-R5-R6-R7-R8-Y1-Y2-Y3-Y4-Y5-Y6-Y7 (I), wherein: X1 is absent or is selected from the group consisting of norleucine (Nle), arginine (Arg), D-arginine (dArg), alanine (Ala), lysine (Lys), D-lysine (dLys), histidine (His), and D-histidine (dHis); X2 is absent, phenylalanine (Phe), or Nle; X3 is absent, Phe, or Nle; R1 is selected from the group consisting of Nle, D-norleucine (dNle), Ala, D-alanine (dAla), Arg, dArg, Lys, dLys, His, dHis, ornithine (Orn), D-ornithine (dOrn), D-leucine (dLeu), D-tyrosine (dTyr), phenylalanine (Phe), D-phenylalanine (dPhe), tryptophan (Trp), D-tryptophan (dTrp), aspartic acid (Asp), cysteine (Cys), and D-cysteine (dCys); R2 is selected from the group consisting of Asp, proline (Pro), D-aspartic acid (dAsp), Cys, dCys, D-penicillamine (dPen), Ala, dAla, Trp, Phe, dPhe, His, dHis, Tyr, and dTyr; R3 is absent or is selected from the group consisting of His, Ala, Pro, hydroxyproline (Hyp), leucine (Leu), D-glutamine (dGln), Phe, dPhe, Trp, dTrp, Tyr, dTyr, 4-amino-1,2,4,5-tetrahydro-2-benzazepin-3-one (Aba), 7-amino-7,8-dihydro-4H-[1,2,3]triazolo-[1,5-a][1,4]diazepin-6(5H)-one (Ata), 4-amino-1,4,5,6-tetrahydroazepino[4,3-b]indol-3(2H)-one (Aia), 2-aminotetraline-2-carboxylic acid (Atc), 1-amino-4-phenylcyclohexane-carboxylic acid (APC), 4-aminophenylpiperidine-4-carboxylic acid (APPC), octohydroindole-2-carboxylic acid (Oic), 1-amino-1-cyclohexanecarboxylic acid (Che), tetrahydro-isoquinoline-3-carboxylic acid (Tic), indoline-2-carboxylic acid (Ioc), 1-

amino-1-cyclopentane carboxylic (Cpe), and biphenylalanine (Bip); R4 is selected from the group consisting of Phe, dPhe, 2'-D-naphthylalanine (dNal(2')), para-chloro-D-phenylalanine (p(Cl)dPhe), para-bromo-D-phenylalanine (p(Br)dPhe), and para-fluoro-D-phenylalanine (p(F)dPhe); R5 is selected from the group consisting of Arg, His, cisPro(guan), and transPro(guan); R6 is selected from the group consisting of Trp, dTrp, Phe, Aia, Aba, Ata, dNal(2'), 2'-naphthylalanine (Nal(2')), and 1'-naphthylalanine (Nal(1')); R7 is selected from the group consisting of Gly, Pro, Lys, dLys, Cys, dCys, penicillamine (Pen), dPen, and Orn; R8 is absent or Lys; Y1 is absent or is selected from the group consisting of valine (Val), D-valine (dVal), b2-valine (b2-Val), b3-valine (b3-Val), Pro, D-proline (dPro), b-proline (b-Pro), Hyp, D-hydroxyproline (dHyp), D-tert-leucine (dTle), dLeu, Trp, Arg, dArg, Lys, dLys, Gly, Ala, dAla, Asp, dAsp, asparagine (Asn), D-asparagine (dAsn), and D-threonine (dThr); Y2 is absent or is selected from the group consisting of Val, dVal, b2-Val, b3-Val, Pro, dPro, b-Pro, Hyp, dHyp, dTle, Arg, dArg, Gly, Ala, dAla, Asp, and dAsn; Y3 is absent or is selected from the group consisting of Val, dVal, Pro, dPro, dThr, Lys, and dLys; Y4 is absent or is selected from the group consisting of dVal, dPro, Asp, and dAsp; Y5 is absent or dVal; Y6 is absent or dVal; Y7 is absent or dPro; and the non-naturally occurring melanocortin analog is cyclized through a moiety selected from the group consisting of: a disulfide bond between R1 or R2 and R7 when each of R1 or R2 and R7 are independently selected from the group consisting of Cys, dCys, and dPen; a disulfide bond between R2 and R7 when R2 is Cys, R7 is Pen, and R3 is absent; a lactam bridge between R1 or R2 and R7 or R8 when R1 or R2 is Asp and R7 or R8 is Lys or Orn; and a lactam bridge between R2 and R7 when R2 is dAsp and R7 is dLys; provided that: when R4 is dNal(2'), then R3 is His and R7 is Pro; when R4 is p(F)dPhe, then (i) R3 is selected from Pro, dGln, dTyr, R6 is Trp, and the non-naturally occurring melanocortin analog is not cyclized between Cys at R2 and Cys at R7 or (ii) R3 is His and either R6 is Nal(2') or the non-naturally occurring melanocortin analog is cyclized through a disulfide bond between R2 and R7; when R4 is p(Br)dPhe, then the non-naturally occurring melanocortin analog is cyclized through a disulfide bond between dCys at R2 and Cys or dCys at R7; when R4 is dPhe, then (i) R3 is not His, Pro, or absent, (ii) R3 is His and either R2 is Phe or dAla or R2 is Ala and X1 is Arg or dArg, (iii) R3 is Pro and (a) R2 is Trp, and R5 is not His or R6 is not Phe or (b) R2 is not Trp or Pro, and either R5 is not dNal(2') or Nal(2') or X1 and Y3 are not both present, or (iv) R3 is absent and R2 and R7 are not

both dPen; when R4 is p(Cl)dPhe, then (i) R3 is selected from Aba, Aia, and Ata or (ii) R3 is His, R1 is not Ala, and (a) if R1 is Nle and Y1Y2 is dVal-dPro, then X1 is absent and the non-naturally occurring melanocortin analog is cyclized through a disulfide bond between dCys at R2 and dCys at R7, or (b) if R1 is Nle, and Y1Y2 is not dVal-dPro, then either X1 or Y3 is present; and when R2 is dAla, then R4 is dPhe and Y1-Y7 are absent.

**[0008]** In some embodiments, the present technology comprises a use of a non-naturally occurring melanocortin analog for reducing a pain level in a subject in need thereof relative to a control, the non-naturally occurring melanocortin analog including a sequence of Formula (I).

**[0009]** In some embodiments, the present technology comprises a method of treating, preventing, or reducing an addiction in a subject relative to a control, including administering to the subject a non-naturally occurring melanocortin analog including a sequence of Formula (I).

**[0010]** In some embodiments, the present technology comprises a use of a non-naturally occurring melanocortin analog for treating, preventing, or reducing an addiction in a subject relative to a control, the non-naturally occurring melanocortin analog including a sequence of Formula (I).

**[0011]** In some embodiments, the present technology comprises a method of preventing or reducing a use of or dependence on an addictive substance in a subject relative to a control, including administering to the subject a non-naturally occurring melanocortin analog including a sequence of Formula (I).

**[0012]** In some embodiments, the present technology comprises a use of a non-naturally occurring melanocortin analog for treating, preventing, or reducing a use of or dependence on an addictive substance in a subject relative to a control, the non-naturally occurring melanocortin analog including a sequence of Formula (I).

**[0013]** In some embodiments, the present technology comprises a method of treating or preventing an opioid use disorder (OUD) in a subject in need thereof relative to a control, including administering to the subject a non-naturally occurring melanocortin analog including a sequence of Formula (I).

**[0014]** In some embodiments, the present technology comprises a use of a non-naturally occurring melanocortin analog for treating or preventing an OUD in a subject in need thereof relative to a control, the non-naturally occurring melanocortin analog including a sequence of Formula (I).

**[0015]** In some embodiments, the present technology comprises a method of treating or preventing an alcohol use disorder (AUD) in a subject in need thereof relative to a control, including administering to the subject a non-naturally occurring melanocortin analog including a sequence of Formula (I).

**[0016]** In some embodiments, the present technology comprises a use of a non-naturally occurring melanocortin analog for treating or preventing an AUD in a subject in need thereof relative to a control, the non-naturally occurring melanocortin analog including a sequence of Formula (I).

**[0017]** In some embodiments, the method or the use includes reducing a dose used or consumed of an addictive substance, relative to a control.

**[0018]** In some embodiments, the method or the use includes reducing a dependency on an addictive substance, relative to a control.

**[0019]** In some embodiments, the method or the use includes reducing a frequency of an addictive substance use, relative to a control.

**[0020]** In some embodiments, the method or the use includes reducing a dose or dosage of a conventional medication used to treat an addiction, relative to a control.

**[0021]** In some embodiments, the present technology comprises a method of augmenting an effect of a conventional medication used to treat an addiction in a subject in need thereof, relative to a control, including administering to the subject a non-naturally occurring melanocortin analog including a sequence of Formula (I).

**[0022]** In some embodiments, the present technology comprises a use of a non-naturally occurring melanocortin analog for augmenting an effect of a conventional medication used to treat an addiction in a subject in need thereof, the non-naturally occurring melanocortin analog including a sequence of Formula (I).

**[0023]** In some embodiments, the present technology comprises a method of reducing or eliminating a need for a conventional medication used to treat an addiction in a subject in need thereof, relative to a control, including administering to the subject a non-naturally occurring melanocortin analog including a sequence of Formula (I).

**[0024]** In some embodiments, the present technology comprises a use of a non-naturally occurring melanocortin analog for reducing or eliminating a need for a conventional medication used to treat an addiction in a subject in need thereof, the non-naturally occurring melanocortin analog including a sequence of Formula (I).

**[0025]** In some embodiments, the treatment of the addiction is improved during or after administration of the non-naturally occurring melanocortin analog relative to treatment of the addiction using the conventional medication to treat the addiction alone.

**[0026]** In some embodiments, the conventional medication to treat the addiction is selected from the group consisting of buprenorphine, naltrexone, acamprosate, methadone, naloxone, nalmefene, xycodone, levo-alpha-acetylmethadol (LAAM), codeine, lofexidine, and a slow-release morphine.

**[0027]** In some embodiments, the present technology comprises a method of reducing a need for a hospitalization or rehabilitation associated with addiction or use of an addictive substance, relative to a control, including administering to the subject a non-naturally occurring melanocortin analog including a sequence of Formula (I).

**[0028]** In some embodiments, the present technology comprises a use of a non-naturally occurring melanocortin analog for reducing a need for a hospitalization or rehabilitation associated with addiction or use of an addictive substance, relative to a control, the non-naturally occurring melanocortin analog including a sequence of Formula (I).

**[0029]** In some embodiments, the present technology comprises a method of preventing or reducing a withdrawal from an addictive substance in a subject, including administering to the subject a non-naturally occurring melanocortin analog including a sequence of Formula (I).

**[0030]** In some embodiments, the present technology comprises a use of a non-naturally occurring melanocortin analog for preventing or reducing a withdrawal from an

addictive substance in a subject, relative to a control, the non-naturally occurring melanocortin analog including a sequence of Formula (I).

**[0031]** In some embodiments, the present technology comprises a method of preventing or reducing a symptom associated with withdrawal from an addictive substance in a subject relative to a control, including administering to the subject a non-naturally occurring melanocortin analog including a sequence of Formula (I).

**[0032]** In some embodiments, the present technology comprises a use of a non-naturally occurring melanocortin analog for preventing or reducing a symptom associated with withdrawal from an addictive substance in a subject, relative to a control, the non-naturally occurring melanocortin analog including a sequence of Formula (I).

**[0033]** In some embodiments, the symptom associated with withdrawal from an addictive substance is selected from the group consisting of pain, anxiety, depression, diarrhea, dizziness, fatigue, muscle aches, nausea, sleep problems, suicidal ideation, tremors, and visual disturbances.

**[0034]** In some embodiments, the subject has an addiction to an addictive substance or is susceptible to an addiction to an addictive substance.

**[0035]** In some embodiments, the subject has used or is using one or more addictive substances.

**[0036]** In some embodiments, the present technology comprises a method or the use wherein the addictive substance includes a prescription medication, a substance in an over-the-counter medication, a recreational substance, or an illegal substance.

**[0037]** In some embodiments, the addictive substance is selected from the group consisting of an opioid, a painkiller, a stimulant, a narcotic, an alcohol, a sedative, marijuana, a cannabis, a tetrahydrocannabinol (THC), a cannabidiol (CBD), and an inhalant.

**[0038]** In some embodiments, the opioid is selected from the group consisting of morphine, heroin, codeine, oxycodone, hydrocodone, and fentanyl.

**[0039]** In some embodiments, the stimulant is selected from the group consisting of caffeine, nicotine, methamphetamines, cocaine, and amphetamines.

**[0040]** In some embodiments, the sedative includes a barbiturate or a benzodiazepine.

**[0041]** In some embodiments, the barbiturate is selected from the group consisting of phenobarbital, methohexital, butalbital, pentobarbital, primidone, and amobarbital.

**[0042]** In some embodiments, the benzodiazepine is selected from the group consisting of alprazolam, lorazepam, clonazepam, diazepam, and temazepam.

**[0043]** In some embodiments, the sedative is selected from the group consisting of tranquilizers, xylazine, eszopiclone, zaleplon, zolpidem, and zopiclone.

**[0044]** In some embodiments, the inhalant is selected from the group consisting of aerosols, butanes, freon, helium, nitrous oxide, propane, and nitrites.

**[0045]** In some embodiments, the nicotine includes a tobacco chew, a nicotine pouch, or a smoking device.

**[0046]** In some embodiments, the smoking device is selected from the group consisting of cigarettes, electronic cigarettes, cigars, and vape products.

**[0047]** In some embodiments, the control includes the subject before administration of the non-naturally occurring melanocortin analog.

**[0048]** In some embodiments, the control includes the subject at baseline.

**[0049]** In some embodiments, the non-naturally occurring melanocortin analog is a melanocortin 4 receptor (MC4R) agonist.

**[0050]** In some embodiments, the MC4R agonist is a full MC4R agonist.

**[0051]** In some embodiments, the MC4R agonist is a partial MC4R agonist.

**[0052]** In some embodiments, the non-naturally occurring melanocortin analog is a MC3R antagonist.

**[0053]** In some embodiments, the MC3R antagonist is a full MC3R antagonist.

**[0054]** In some embodiments, the MC3R antagonist is a partial MC3R antagonist.

**[0055]** In some embodiments, the non-naturally occurring melanocortin analog does not have MC3R activity.

**[0056]** In some embodiments, the non-naturally occurring melanocortin analog includes a sequence according to Formula (I), wherein: X1 is absent or is selected from the group consisting of norleucine (Nle), arginine (Arg), D-arginine (dArg), alanine (Ala), lysine (Lys), D-lysine (dLys), histidine (His), and D-histidine (dHis); X2 is absent, phenylalanine (Phe), or Nle; X3 is absent, Phe, or Nle; R1 is selected from the group consisting of Nle, D-norleucine (dNle), Ala, D-alanine (dAla), Arg, dArg, Lys, dLys, His, dHis, ornithine (Orn), D-ornithine (dOrn), D-leucine (dLeu), D-tyrosine (dTyr), phenylalanine (Phe), D-phenylalanine (dPhe), tryptophan (Trp), D-tryptophan (dTrp), aspartic acid (Asp), cysteine (Cys), and D-cysteine (dCys); R2 is selected from the group consisting of Asp, proline (Pro), D-aspartic acid (dAsp), Cys, dCys, D-penicillamine (dPen), Ala, dAla, Trp, Phe, dPhe, His, dHis, Tyr, and dTyr; R3 is absent or is selected from the group consisting of His, Ala, Pro, hydroxyproline (Hyp), leucine (Leu), D-glutamine (dGln), Phe, dPhe, Trp, dTrp, Tyr, dTyr, 4-amino-1,2,4,5-tetrahydro-2-benzazepin-3-one (Aba), 7-amino-7,8-dihydro-4H-[1,2,3]triazolo-[1,5-a][1,4]diazepin-6(5H)-one (Ata), 4-amino-1,4,5,6-tetrahydroazepino[4,3-b]indol-3(2H)-one (Aia), 2-aminotetraline-2-carboxylic acid (Atc), 1-amino-4-phenylcyclohexane-carboxylic acid (APC), 4-aminophenylpiperidine-4-carboxylic acid (APPC), octohydroindole-2-carboxylic acid (Oic), 1-amino-1-cyclohexanecarboxylic acid (Che), tetrahydro-isoquinoline-3-carboxylic acid (Tic), indoline-2-carboxylic acid (Ioc), 1-amino-1-cyclopentane carboxylic (Cpe), and biphenylalanine (Bip); R4 is selected from the group consisting of Phe, dPhe, 2'-D-naphthylalanine (dNal(2')), para-chloro-D-phenylalanine (p(Cl)dPhe), para-bromo-D-phenylalanine (p(Br)dPhe), and para-fluoro-D-phenylalanine (p(F)dPhe); R5 is selected from the group consisting of Arg, His, cisPro(guan), and transPro(guan); R6 is selected from the group consisting of Trp, dTrp, Phe, Aia, Aba, Ata, dNal(2'), 2'-naphthylalanine (Nal(2')), and 1'-naphthylalanine (Nal(1')); R7 is selected from the group consisting of Gly, Pro, Lys, dLys, Cys, dCys, penicillamine (Pen), dPen, and Orn; R8 is absent or Lys; Y1 is absent or is selected from the group consisting of valine (Val), D-valine (dVal), b2-valine (b2-Val), b3-valine (b3-Val), Pro, D-proline (dPro), b-proline (b-Pro), Hyp, D-hydroxyproline (dHyp), D-tert-leucine (dTle), dLeu, Trp, Arg, dArg, Lys, dLys, Gly, Ala, dAla, Asp, dAsp, asparagine (Asn), D-asparagine (dAsn), and D-threonine (dThr); Y2 is absent or is selected from the group consisting of Val, dVal, b2-Val, b3-Val, Pro, dPro, b-Pro, Hyp, dHyp, dTle, Arg, dArg, Gly, Ala, dAla, Asp, and dAsn; Y3 is absent or is selected

from the group consisting of Val, dVal, Pro, dPro, dThr, Lys, and dLys; Y4 is absent or is selected from the group consisting of dVal, dPro, Asp, and dAsp; Y5 is absent or dVal; Y6 is absent or dVal; Y7 is absent or dPro; and the non-naturally occurring melanocortin analog is cyclized through a moiety selected from the group consisting of: a disulfide bond between R1 or R2 and R7 or R8 when each of R1 or R2 and R7 or R8 are independently selected from the group consisting of Cys, dCys, and dPen; a disulfide bond between R2 and R7 when R2 is Cys, R7 is Pen, and R3 is absent; a lactam bridge between R1 or R2 and R7 or R8 when R1 or R2 is Asp and R7 or R8 is Lys or Orn; and a lactam bridge between R2 and R7 when R2 is dAsp and R7 is dLys; provided that the non-naturally occurring melanocortin analog does not include a sequence selected from the group consisting of: Ac-Nle-c[Asp-Pro-Pro-dNal(2')-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 194); Ac-Nle-c[Asp-Pro-His-dNal(2')-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 5); Ac-Nle-c[Asp-Pro-His-dNal(2')-Arg-Trp-Lys]-dPro-dVal-NH2 (SEQ ID NO: 10); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dVal-dPro (SEQ ID NO: 2); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 3); Ac-Nle-c[Asp-Hyp-dNal(2')-Arg-Trp-Pro-Lys]-dVal-dPro-NH2 (SEQ ID NO: 4); Ac-Nle-c[Asp-Phe-His-dNal(2')-Arg-Trp-Lys]-dLeu-dPro-NH2 (SEQ ID NO: 6); Ac-Nle-c[Asp-Phe-His-dNal(2')-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 7); Ac-Nle-c[Asp-Hyp-dNal(2')-Arg-Trp-Pro-Lys]-dVal-dPro-NH2 (SEQ ID NO: 9); Ac-Nle-Phe-Phe-c[Asp-Phe-His-dNal(2')-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 12); Ac-dArg-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 15); Ac-dLeu-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 18); Ac-dAla-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 20); Ac-Ala-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 21); Ac-dNle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 24); Ac-dCys-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 28); Ac-dPhe-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 29); Ac-dTyr-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 30); dTyr-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 35); Tyr-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 36); Ac-Nle-c[Cys-Pro-dNal(2')-Arg-Trp-Cys]-dVal-dPro-NH2 (SEQ ID NO: 40); Ac-Nle-c[dCys-Pro-dNal(2')-Arg-Trp-Cys]-dVal-dPro-NH2 (SEQ ID NO: 41); Ac-Nle-c[Cys-Pro-dNal(2')-Arg-Trp-dCys]-dVal-dPro-NH2 (SEQ ID NO: 42); Ac-Nle-c[dCys-Pro-dNal(2')-Arg-Trp-dCys]-dVal-dPro-NH2 (SEQ ID NO: 43); Ac-Nle-c[Cys-Pro-dNal(2')-Arg-Trp-Pen]-dVal-dPro-NH2

(SEQ ID NO: 48); Ac-Nle-c[dPen-Pro-dNal(2')-Arg-Trp-dPen]-dVal-dPro-NH2 (SEQ ID NO: 54); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Orn]-dVal-dPro-NH2 (SEQ ID NO: 64); Ac-Nle-c[Asp-dNal(2')-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 68); Ac-Nle-c[Asp-Ala-dNal(2')-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 69); Ac-Nle-c[Asp-Leu-dNal(2')-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 76); Ac-Nle-c[Asp-Trp-dNal(2')-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 82); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-Val-Pro-NH2 (SEQ ID NO: 115); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dVal-dPro-OH (SEQ ID NO: 116); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dPro-dVal-OH (SEQ ID NO: 117); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dVal-Hyp-NH2 (SEQ ID NO: 118); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dVal-dHyp-NH2 (SEQ ID NO: 119); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-Val-Hyp-NH2 (SEQ ID NO: 120); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-Val-dHyp-NH2 (SEQ ID NO: 121); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-Hyp-dVal-NH2 (SEQ ID NO: 122); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dHyp-dVal-NH2 (SEQ ID NO: 123); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-Hyp-Val-NH2 (SEQ ID NO: 124); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dHyp-Val-NH2 (SEQ ID NO: 125); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dVal-dVal-NH2 (SEQ ID NO: 126); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dPro-dPro-NH2 (SEQ ID NO: 127); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dVal-NH2 (SEQ ID NO: 128); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dPro-NH2 (SEQ ID NO: 129); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-Val-NH2 (SEQ ID NO: 130); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-Pro-NH2 (SEQ ID NO: 131); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-Ala-NH2 (SEQ ID NO: 132); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dAla-NH2 (SEQ ID NO: 133); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dHyp-NH2 (SEQ ID NO: 134); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-Hyp-NH2 (SEQ ID NO: 135); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dAla-dAla-NH2 (SEQ ID NO: 136); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-Ala-Ala-NH2 (SEQ ID NO: 137); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-Gly-Gly-NH2 (SEQ ID NO: 138); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dVal-Asp-NH2 (SEQ ID NO: 139); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dVal-Arg-NH2 (SEQ ID NO: 140); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dVal-dArg-NH2 (SEQ ID NO: 143); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dVal-dAsn-NH2 (SEQ ID NO: 144); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-Asp-dPro-NH2 (SEQ ID NO: 145); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-Arg-dPro-NH2 (SEQ ID NO: 146); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-Asn-dPro-NH2 (SEQ ID NO: 147); Ac-Nle-c[Asp-Pro-

dNal(2')-Arg-Trp-Lys]-dAsp-dPro-NH2 (SEQ ID NO: 148); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dArg-dPro-NH2 (SEQ ID NO: 149); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dAsn-dPro-NH2 (SEQ ID NO: 150); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-Asp-NH2 (SEQ ID NO: 151); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-Arg-NH2 (SEQ ID NO: 152); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-Asn-NH2 (SEQ ID NO: 153); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dAsp-NH2 (SEQ ID NO: 154); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dArg-NH2 (SEQ ID NO: 155); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dAsn-NH2 (SEQ ID NO: 156); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-Lys-Pro-Val-NH2 (SEQ ID NO: 157); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-Lys-dPro-dVal-NH2 (SEQ ID NO: 158); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dLys-dPro-dVal-NH2 (SEQ ID NO: 159); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-Lys-dPro-NH2 (SEQ ID NO: 160); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dLys-dPro-NH2 (SEQ ID NO: 161); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-Lys-Val-Pro-NH2 (SEQ ID NO: 162); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-Lys-dVal-dPro-NH2 (SEQ ID NO: 164); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dLys-dVal-dPro-NH2 (SEQ ID NO: 164); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-Arg-Pro-Val-NH2 (SEQ ID NO: 165); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-Arg-dPro-dVal-NH2 (SEQ ID NO: 166); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dArg-dPro-dVal-NH2 (SEQ ID NO: 167); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-Arg-Val-Pro-NH2 (SEQ ID NO: 168); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-Arg-dVal-dPro-NH2 (SEQ ID NO: 169); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dArg-dVal-dPro-NH2 (SEQ ID NO: 170); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dTle-dVal-dPro-NH2 (SEQ ID NO: 171); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 172); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dTle-dVal-NH2 (SEQ ID NO: 173); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dTle-dTle-NH2 (SEQ ID NO: 174); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dTle-dTle-dPro-NH2 (SEQ ID NO: 175); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dTle-dTle-dVal-NH2 (SEQ ID NO: 176); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dPro-dTle-NH2 (SEQ ID NO: 177); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dVal-dTle-NH2 (SEQ ID NO: 178); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dVal-dVal-dPro-NH2 (SEQ ID NO: 179); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dPro-dVal-dPro-NH2 (SEQ ID NO: 180); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dVal-dVal-dVal-dPro-NH2 (SEQ ID NO: 181); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dVal-dPro-dVal-dPro-NH2 (SEQ ID NO: 182); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dVal-dVal-dVal-dVal-dVal-dVal-dPro-NH2 (SEQ ID

NO: 183); Ac-Nle-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 184); Ac-Nle-Nle-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 185); Ac-Nle-Nle-Nle-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 186); Ac-Nle-c[Asp-Trp-Pro-dNal(2')-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 195); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-dTrp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 196); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-Trp-NH2 (SEQ ID NO: 203); Ac-Nle-c[Asp-Aba-dNal(2')-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 204); Ac-Nle-c[Asp-Aia-dNal(2')-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 205); Ac-Nle-c[Asp-Ata-dNal(2')-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 206); Ac-Nle-c[Asp-Cpe-dNal(2')-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 240); Ac-Nle-c[Asp-Che-dNal(2')-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 241); Ac-Nle-c[Asp-Oic-dNal(2')-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 242); Ac-Nle-c[Asp-Tic-dNal(2')-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 244); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Pro-Lys]-dVal-dPro-NH2 (SEQ ID NO: 245); Ac-Nle-c[Asp-His-dNal(2')-transPro(guan)-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 247); Ac-Nle-c[Asp-His-dNal(2')-cisPro(guan)-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 248); Ac-Nle-c[Asp-Pro-dNal(2')-transPro(guan)-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 250); Ac-Nle-c[Asp-Pro-dNal(2')-cisPro(guan)Pro-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 251); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Aba-Lys]-dVal-dPro-NH2 (SEQ ID NO: 253); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Ata-Lys]-dVal-dPro-NH2 (SEQ ID NO: 254); Ac-Nle-c[Asp-Glu-dNal(2')-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 255); Ac-Nle-c[Asp-Glu-dNal(2')-Arg-Trp-Gly-Lys]-dVal-dPro-NH2 (SEQ ID NO: 256); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Gly-Lys]-dVal-dPro-NH2 (SEQ ID NO: 259); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Gly-Lys]-dPro-dPro-Lys-Asp-NH2 (SEQ ID NO: 260); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Gly-Lys]-dPro-dPro-dLys-dAsp-NH2 (SEQ ID NO: 261); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dPro-dPro-dLys-dAsp-NH2 (SEQ ID NO: 263); Ac-Nle-c[Asp-Ala-His-dNal(2')-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 273); Ac-Arg-c[Asp-Ala-His-dNal(2')-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 274); Ac-dArg-c[Asp-Ala-His-dNal(2')-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 275); Ac-dLeu-c[dPen-Pro-dNal(2')-Arg-Trp-dPen]-dVal-dPro-NH2 (SEQ ID NO: 327); Ac-dNle-c[dPen-Pro-dNal(2')-Arg-Trp-dPen]-dVal-dPro-NH2 (SEQ ID NO: 328); Ac-dArg-c[dPen-Pro-dNal(2')-Arg-Trp-dPen]-dVal-dPro-NH2 (SEQ ID NO: 329); Ac-Arg-c[dPen-Pro-dNal(2')-Arg-Trp-dPen]-dVal-dPro-NH2 (SEQ ID NO: 330); Ac-dPhe-c[dPen-Pro-dNal(2')-Arg-Trp-dPen]-dVal-dPro-NH2 (SEQ ID NO: 331); Ac-dTyr-c[dPen-Pro-dNal(2')-Arg-Trp-

dPen]-dVal-dPro-NH2 (SEQ ID NO: 332); Ac-Ala-c[dPen-Pro-dNal(2')-Arg-Trp-dPen]-dVal-dPro-NH2 (SEQ ID NO: 333); Ac-dHis-c[dPen-Pro-dNal(2')-Arg-Trp-dPen]-dVal-dPro-NH2 (SEQ ID NO: 334); Ac-His-c[dPen-Pro-dNal(2')-Arg-Trp-dPen]-dVal-dPro-NH2 (SEQ ID NO: 335); Ac-dLys-c[dPen-Pro-dNal(2')-Arg-Trp-dPen]-dVal-dPro-NH2 (SEQ ID NO: 336); Ac-Lys-c[dPen-Pro-dNal(2')-Arg-Trp-dPen]-dVal-dPro-NH2 (SEQ ID NO: 337); Ac-Nle-c[dPen-Pro-dNal(2')-Arg-Trp-dPen]-dArg-dVal-dPro-NH2 (SEQ ID NO: 344); Ac-Nle-c[dPen-Pro-dNal(2')-Arg-Trp-dPen]-dLys-dVal-dPro-NH2 (SEQ ID NO: 345); Ac-Nle-c[dPen-Pro-dNal(2')-Arg-Trp-dPen]-dArg-dPro-NH2 (SEQ ID NO: 346); Ac-Nle-c[dPen-Pro-dNal(2')-Arg-Trp-dPen]-dLys-dPro-NH2 (SEQ ID NO: 347); Ac-Nle-c[dPen-Pro-dNal(2')-Arg-Trp-dPen]-dVal-dHyp-NH2 (SEQ ID NO: 348); Ac-Nle-c[dPen-Pro-dNal(2')-Arg-Trp-dPen]-dTle-dPro-NH2 (SEQ ID NO: 349); Ac-Nle-c[dPen-Pro-dNal(2')-Arg-Trp-Gly-dPen]-dVal-dPro-NH2 (SEQ ID NO: 350); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Aia-Lys]-dVal-dPro-NH2 (SEQ ID NO: 103); Ac-Nle-c[Asp-Ioc-dNal(2')-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 243); Ac-Nle-c[Cys-dNal(2')-Arg-Trp-Cys]-dVal-dPro-NH2 (SEQ ID NO: 44); Ac-Nle-c[dCys-dNal(2')-Arg-Trp-Cys]-dVal-dPro-NH2 (SEQ ID NO: 45); Ac-Nle-c[Cys-dNal(2')-Arg-Trp-dCys]-dVal-dPro-NH2 (SEQ ID NO: 46); Ac-Nle-c[dCys-dNal(2')-Arg-Trp-dCys]-dVal-dPro-NH2 (SEQ ID NO: 47); Ac-Nle-c[Cys-dNal(2')-Arg-Trp-Pen]-dVal-dPro-NH2 (SEQ ID NO: 56); Ac-Nle-c[dPen-dNal(2')-Arg-Trp-dPen]-dVal-dPro-NH2 (SEQ ID NO: 62); Ac-Nle-c[Asp-dTrp-dNal(2')-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 83); Ac-Nle-c[dPen-Ala-dNal(2')-Arg-Trp-dPen]-dVal-dPro-NH2 (SEQ ID NO: 338); Ac-Nle-c[dPen-Leu-dNal(2')-Arg-Trp-dPen]-dVal-dPro-NH2 (SEQ ID NO: 339); Ac-Nle-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 223); Ac-Arg-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 464); Ac-Lys-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 465); Ac-dLys-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 466); Ac-His-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 467); Ac-dHis-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 468); Ac-Nle-Nle-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 469); Ac-Nle-c[Asp-His-p(F)dPhe-His-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 470); Ac-Nle-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dVal-dVal-dVal-dPro-NH2 (SEQ ID NO: 474); Ac-Nle-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dPro-dVal-dPro-NH2 (SEQ ID NO: 475); Ac-Nle-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 476); Ac-Nle-Nle-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID

NO: 477); Ac-Nle-Nle-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dPro-dVal-dPro-NH2 (SEQ ID NO: 478); Ac-Arg-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 481); Ac-Lys-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 482); Ac-dLys-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 483); Ac-His-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 484); Ac-dHis-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 485); Ac-dArg-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 463); Ac-Ala-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 462); Ac-Ala-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 479); Ac-Nle-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dTle-dTle-dVal-NH2 (SEQ ID NO: 473); Ac-dArg-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 480); Ac-Nle-c[Asp-Gln-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 491); Ac-Nle-c[Asp-Bip-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 489); Ac-Nle-c[Asp-Trp-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 493); Ac-Nle-c[Asp-Pro-p(F)dPhe-Arg-dNal(2')-Lys]-dVal-dPro-NH2 (SEQ ID NO: 444); Ac-Nle-c[Asp-Pro-p(F)dPhe-Arg-Nal(2')-Lys]-dVal-dPro-NH2 (SEQ ID NO: 445); Ac-Nle-c[Asp-Tyr-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 495); Ac-Nle-c[Asp-Phe-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 487); Ac-Nle-c[Asp-dPhe-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 488); Ac-Nle-c[Asp-dTrp-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 494); Ac-Nle-c[Asp-His-p(F)dPhe-Arg-dNal(2')-Lys]-dVal-dPro-NH2 (SEQ ID NO: 471); Ac-Nle-c[Cys-Pro-p(F)dPhe-Arg-Trp-Cys]-dVal-dPro-NH2 (SEQ ID NO: 432); Ac-Nle-c[Asp-Pro-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 217); Ac-Nle-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 222); Ac-Nle-c[Cys-His-p(Br)dPhe-Arg-Trp-Cys]-dVal-dPro-NH2 (SEQ ID NO: 535); Ac-Ala-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 538); Ac-Nle-Nle-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 545); Ac-Nle-c[Asp-His-p(Br)dPhe-His-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 546); Ac-Nle-c[Asp-His-p(Br)dPhe-Arg-dNal(2')-Lys]-dVal-dPro-NH2 (SEQ ID NO: 547); Ac-Nle-c[Asp-His-p(Br)dPhe-Arg-Nal(2')-Lys]-dVal-dPro-NH2 (SEQ ID NO: 548); Ac-Nle-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dTle-dTle-dVal-NH2 (SEQ ID NO: 549); Ac-Nle-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dPro-dVal-dPro-NH2 (SEQ ID NO: 551); Ac-Nle-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 552); Ac-Nle-Nle-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 553); Ac-Ala-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO:

555); Ac-Nle-c[Asp-dHis-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 562); Ac-Nle-c[Asp-Phe-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 563); Ac-Nle-c[Asp-dPhe-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 564); Ac-Nle-c[Asp-Bip-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 565); Ac-Nle-c[Asp-dGln-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 568); Ac-Nle-c[Asp-Trp-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 569); Ac-Nle-c[Asp-dTrp-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 570); Ac-Nle-c[Asp-Tyr-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 571); Ac-Nle-c[Asp-dTyr-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 572); Ac-dArg-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 539); Ac-dHis-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 544); Ac-dHis-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 561); Ac-dArg-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 556); Ac-dLys-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 542); Ac-His-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 560); Ac-His-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 543); Ac-dLys-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 559); Ac-Arg-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 557); Ac-Lys-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 541); Ac-Nle-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dVal-dVal-dVal-dPro-NH2 (SEQ ID NO: 550); Ac-Lys-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 558); Ac-Arg-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 540); Ac-Nle-Nle-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dPro-dVal-dPro-NH2 (SEQ ID NO: 554); Ac-Nle-c[Asp-His-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 363); Ac-Nle-c[Asp-His-dPhe-Arg-Trp-Pro-Lys]-dVal-dPro-NH2 (SEQ ID NO: 418); Ac-Nle-c[Asp-His-dPhe-Arg-Trp-Lys]-dPro-dVal-NH2 (SEQ ID NO: 621); Ac-Nle-c[Asp-His-dPhe-transPro(guan)-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 228); Ac-Nle-c[Asp-His-dPhe-cisPro(guan)-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 229); Ac-Nle-c[Asp-Ala-His-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 380); Ac-Nle-c[Asp-Trp-Pro-dPhe-His-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 398); Ac-Nle-c[Asp-Trp-Pro-dPhe-Arg-Phe-Lys]-dVal-dPro-NH2 (SEQ ID NO: 401); Ac-Nle-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dPro-dVal-dPro-NH2 (SEQ ID NO: 639); Ac-Nle-c[Asp-Pro-dPhe-Arg-dNal(2')-Lys]-dVal-dPro-NH2 (SEQ ID NO: 430); Ac-Nle-c[Asp-Pro-dPhe-Arg-Nal(2')-Lys]-dVal-dPro-NH2 (SEQ ID NO: 431); Ac-Nle-c[Asp-Pro-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2

(SEQ ID NO: 225); Ac-Nle-c[dPen-dPhe-Arg-Trp-dPen]-dVal-dPro-NH2 (SEQ ID NO: 326); Ac-Nle-c[Asp-Pro-His-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 297); Ac-Nle-c[Asp-Pro-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 215); Ac-Nle-c[Asp-Phe-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 525); Ac-Nle-c[Asp-dPhe-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 526); Ac-Nle-c[Asp-Bip-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 527); Ac-Nle-c[Asp-Trp-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 531); Ac-Nle-c[Asp-Tyr-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 533); Ac-Nle-c[Asp-dTyr-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 534); Ac-Nle-c[Asp-dTrp-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 532); Ac-Nle-c[dCys-His-p(Cl)dPhe-Arg-Trp-Cys]-dVal-dPro-NH2 (SEQ ID NO: 498); Ac-Nle-c[Cys-His-p(Cl)dPhe-Arg-Trp-Cys]-dVal-dPro-NH2 (SEQ ID NO: 497); Ac-Nle-c[Asp-His-p(Cl)dPhe-Arg-dNal(2')-Lys]-dVal-dPro-NH2 (SEQ ID NO: 509); Ac-Nle-c[Asp-His-p(Cl)dPhe-Arg-Nal(2')-Lys]-dVal-dPro-NH2 (SEQ ID NO: 510); Ac-Nle-c[Asp-His-p(Cl)dPhe-His-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 508); Ac-Nle-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 220); Ac-Nle-Nle-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 507); Ac-Ala-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 517); Ac-Ala-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 500); Ac-Nle-Nle-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dPro-dVal-dPro-NH2 (SEQ ID NO: 516); Ac-Nle-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 514); Ac-Nle-c[Asp-dGln-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 530); Ac-Arg-c[Asp-dAla-His-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 268); Ac-Nle-c[Asp-dAla-His-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 378); Ac-dArg-c[Asp-dAla-His-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 379); Ac-Nle-c[Asp-dAla-His-dNal(2')-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 266); Ac-Arg-c[Asp-dAla-His-dNal(2')-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 267); Ac-Arg-c[Cys-dAla-His-dNal(2')-Arg-Trp-Cys]-dVal-dPro-NH2 (SEQ ID NO: 269); Ac-dArg-c[Asp-dAla-His-dNal(2')-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 270); Ac-Arg-c[Cys-dAla-His-dNal(2')-Arg-Trp-Cys]-NH2 (SEQ ID NO: 282); and Ac-Arg-c[Asp-dAla-His-dNal(2')-Arg-Trp-Lys]-NH2 (SEQ ID NO: 283).

**[0057]** In some embodiments, the present technology comprises a method or use, wherein the non-naturally occurring melanocortin analog includes a sequence according to Formula (IA): X1-X2-X3-R1-R2-R3-R4-R5-R6-R7-R8-Y1-Y2-Y3-Y4 (IA), wherein: X1 is

absent or is selected from the group consisting of norleucine (Nle), arginine (Arg), D-arginine (dArg), alanine (Ala), lysine (Lys), D-lysine (dLys), histidine (His), D-histidine (dHis); X2 is absent, phenylalanine (Phe), or Nle; X3 is absent, Phe, or Nle; R1 is selected from the group consisting of Nle, D-norleucine (dNle), Ala, D-alanine (dAla), Arg, dArg, Lys, dLys, His, dHis, ornithine (Orn), D-ornithine (dOrn), D-leucine (dLeu), D-tyrosine (dTyr), phenylalanine (Phe), D-phenylalanine (dPhe), tryptophan (Trp), D-tryptophan (dTrp), aspartic acid (Asp), cysteine (Cys), and D-cysteine (dCys); R2 is selected from the group consisting of Asp, D-aspartic acid (dAsp), Cys, dCys, D-penicillamine (dPen), Ala, Trp, Phe, dPhe, His, dHis, Tyr, and dTyr; R3 is absent or is selected from the group consisting of His, Ala, proline (Pro), hydroxyproline (Hyp), leucine (Leu), D-glutamine (dGln), Phe, dPhe, Trp, dTrp, Tyr, dTyr, 2-aminotetraline-2-carboxylic acid (Atc), octohydroindole-2-carboxylic acid (Oic), 1-amino-1-cyclohexanecarboxylic acid (Che), tetrahydro-isoquinoline-3-carboxylic acid (Tic), 1-amino-1-cyclopentane carboxylic (Cpe), and biphenylalanine (Bip); R4 is selected from the group consisting of dPhe, para-chloro-D-phenylalanine (p(Cl)dPhe), para-bromo-D-phenylalanine (p(Br)dPhe), and para-fluoro-D-phenylalanine (p(F)dPhe); R5 is Arg or His; R6 is selected from the group consisting of Trp, dTrp, Phe, dNal(2'), 2'-naphthylalanine (Nal(2')), and 1'-naphthylalanine (Nal(1')); R7 is selected from the group consisting of Gly, Pro, Lys, dLys, Cys, dCys, penicillamine (Pen), dPen, and Orn; R8 is absent or Lys; Y1 is selected from the group consisting of valine (Val), D-valine (dVal), b2-valine (b2-Val), b3-valine (b3-Val), Pro, D-proline (dPro), b-proline (b-Pro), Hyp, D-hydroxyproline (dHyp), D-tert-leucine (dTle), dLeu, Trp, Arg, dArg, Lys, dLys, Gly, Ala, dAla, Asp, dAsp, asparagine (Asn), D-asparagine (dAsn), and D-threonine (dThr); Y2 is absent or is selected from the group consisting of Val, dVal, b2-Val, b3-Val, Pro, dPro, b-Pro, Hyp, dHyp, dTle, Arg, dArg, Gly, Ala, dAla, Asp, and dAsn; Y3 is absent or is selected from the group consisting of Val, dVal, Pro, dPro, dThr, Lys, and dLys; Y4 is absent or is selected from the group consisting of dVal, dPro, Asp, and dAsp; and the non-naturally occurring melanocortin analog is cyclized through a moiety selected from the group consisting of: a disulfide bond between R1 or R2 and R7 or R8 when each of R1 or R2 and R7 or R8 are independently selected from the group consisting of Cys, dCys, and dPen; a disulfide bond between R2 and R7 when R2 is Cys,R7 is Pen, and R3 is absent; a lactam bridge between R1 or R2 and R7 or R8 when R1 or R2 is Asp and R7 or R8 is Lys or Orn; and a lactam bridge between R2 and R7 when R2 is dAsp and

R7 is dLys; provided that: when R4 is p(F)dPhe, then (i) R3 is selected from Pro, dGln, dTyr, R6 is Trp, and the non-naturally occurring melanocortin analog is not cyclized between Cys at R2 and Cys at R7 or (ii) R3 is His and either R6 is Nal(2') or the non-naturally occurring melanocortin analog is cyclized through a disulfide bond between R2 and R7, where R2 and R7 are the same; when R4 is p(Br)dPhe, then the non-naturally occurring melanocortin analog is cyclized through a disulfide bond between dCys at R2 and Cys or dCys at R7; when R4 is dPhe, then (i) R3 is not His, Pro, or absent, (ii) R3 is His and either R2 is Phe or dAla or R2 is Ala and X1 is Arg or dArg, (iii) R3 is Pro and (a) R2 is Trp, and R5 is not His or R6 is not Phe or (b) R2 is not Trp or Pro, and either R5 is not dNal(2') or Nal(2') or X1 and Y3 are not both present, or (iv) R3 is absent and R2 and R7 are not both dPen; and when R4 is p(Cl)dPhe, then (i) R3 is selected from Aba, Aia, and Ata or (ii) R3 is His, R1 is not Ala, and (a) if R1 is Nle and Y1Y2 is dVal-dPro, then X1 is absent and the non-naturally occurring melanocortin analog is cyclized through a disulfide bond between dCys at R2 and dCys at R7, or (b) if R1 is Nle, and Y1Y2 is not dVal-dPro, then either X1 or Y3 is present.

**[0058]** In some embodiments, the non-naturally occurring melanocortin analog includes a sequence according to Formula (IA), wherein: X1 is absent or is selected from the group consisting of norleucine (Nle), arginine (Arg), D-arginine (dArg), alanine (Ala), lysine (Lys), D-lysine (dLys), histidine (His), D-histidine (dHis); X2 is absent, phenylalanine (Phe), or Nle; X3 is absent, Phe, or Nle; R1 is selected from the group consisting of Nle, D-norleucine (dNle), Ala, D-alanine (dAla), Arg, dArg, Lys, dLys, His, dHis, ornithine (Orn), D-ornithine (dOrn), D-leucine (dLeu), D-tyrosine (dTyr), phenylalanine (Phe), D-phenylalanine (dPhe), tryptophan (Trp), D-tryptophan (dTrp), aspartic acid (Asp), cysteine (Cys), and D-cysteine (dCys); R2 is selected from the group consisting of Asp, D-aspartic acid (dAsp), Cys, dCys, D-penicillamine (dPen), Ala, Trp, Phe, dPhe, His, dHis, Tyr, and dTyr; R3 is absent or is selected from the group consisting of His, Ala, proline (Pro), hydroxyproline (Hyp), leucine (Leu), D-glutamine (dGln), Phe, dPhe, Trp, dTrp, Tyr, dTyr, 2-aminotetraline-2-carboxylic acid (Atc), octohydroindole-2-carboxylic acid (Oic), 1-amino-1-cyclohexanecarboxylic acid (Che), tetrahydro-isoquinoline-3-carboxylic acid (Tic), 1-amino-1-cyclopentane carboxylic (Cpe), and biphenylalanine (Bip); R4 is selected from the group consisting of dPhe, para-chloro-D-phenylalanine (p(Cl)dPhe), para-bromo-D-phenylalanine (p(Br)dPhe), and para-fluoro-D-phenylalanine (p(F)dPhe); R5 is Arg or His; R6 is selected

from the group consisting of Trp, dTrp, Phe, dNal(2'), 2'-naphthylalanine (Nal(2')), and 1'-naphthylalanine (Nal(1')); R7 is selected from the group consisting of Gly, Pro, Lys, dLys, Cys, dCys, penicillamine (Pen), dPen, and Orn; R8 is absent or Lys; Y1 is selected from the group consisting of valine (Val), D-valine (dVal), b2-valine (b2-Val), b3-valine (b3-Val), Pro, D-proline (dPro), b-proline (b-Pro), Hyp, D-hydroxyproline (dHyp), D-tert-leucine (dTle), dLeu, Trp, Arg, dArg, Lys, dLys, Gly, Ala, dAla, Asp, dAsp, asparagine (Asn), D-asparagine (dAsn), and D-threonine (dThr); Y2 is absent or is selected from the group consisting of Val, dVal, b2-Val, b3-Val, Pro, dPro, b-Pro, Hyp, dHyp, dTle, Arg, dArg, Gly, Ala, dAla, Asp, and dAsn; Y3 is absent or is selected from the group consisting of Val, dVal, Pro, dPro, dThr, Lys, and dLys; Y4 is absent or is selected from the group consisting of dVal, dPro, Asp, and dAsp; and the non-naturally occurring melanocortin analog is cyclized through a moiety selected from the group consisting of: a disulfide bond between R1 or R2 and R7 or R8 when each of R1 or R2 and R7 or R8 are independently selected from the group consisting of Cys, dCys, and dPen; a disulfide bond between R2 and R7 when R2 is Cys, R7 is Pen, and R3 is absent; a lactam bridge between R1 or R2 and R7 or R8 when R1 or R2 is Asp and R7 or R8 is Lys or Orn; and a lactam bridge between R2 and R7 when R2 is dAsp and R7 is dLys; provided that the non-naturally occurring melanocortin analog does not include a sequence selected from the group consisting of: Ac-Nle-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 223); Ac-Arg-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 464); Ac-Lys-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 465); Ac-dLys-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 466); Ac-His-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 467); Ac-dHis-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 468); Ac-Nle-Nle-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 469); Ac-Nle-c[Asp-His-p(F)dPhe-His-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 470); Ac-Nle-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dVal-dVal-dVal-dPro-NH2 (SEQ ID NO: 474); Ac-Nle-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dPro-dVal-dPro-NH2 (SEQ ID NO: 475); Ac-Nle-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 476); Ac-Nle-Nle-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 477); Ac-Nle-Nle-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dPro-dVal-dPro-NH2 (SEQ ID NO: 478); Ac-Arg-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 481); Ac-Lys-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 482); Ac-dLys-c[Asp-

His-p(F)dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 483); Ac-His-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 484); Ac-dHis-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 485); Ac-dArg-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 463); Ac-Ala-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 462); Ac-Ala-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 479); Ac-Nle-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dTle-dTle-dVal-NH2 (SEQ ID NO: 473); Ac-dArg-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 480); Ac-Nle-c[Asp-Bip-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 489); Ac-Nle-c[Asp-Trp-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 493); Ac-Nle-c[Asp-Pro-p(F)dPhe-Arg-dNal(2')-Lys]-dVal-dPro-NH2 (SEQ ID NO: 444); Ac-Nle-c[Asp-Pro-p(F)dPhe-Arg-Nal(2')-Lys]-dVal-dPro-NH2 (SEQ ID NO: 445); Ac-Nle-c[Asp-Tyr-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 495); Ac-Nle-c[Asp-Phe-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 487); Ac-Nle-c[Asp-dPhe-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 488); Ac-Nle-c[Asp-dTrp-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 494); Ac-Nle-c[Asp-His-p(F)dPhe-Arg-dNal(2')-Lys]-dVal-dPro-NH2 (SEQ ID NO: 471); Ac-Nle-c[Cys-Pro-p(F)dPhe-Arg-Trp-Cys]-dVal-dPro-NH2 (SEQ ID NO: 432); Ac-Nle-c[dCys-His-p(F)dPhe-Arg-Trp-Cys]-dVal-dPro-NH2 (SEQ ID NO: 460); Ac-Nle-c[Asp-Pro-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 217); Ac-Nle-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 222); Ac-Nle-c[Cys-His-p(Br)dPhe-Arg-Trp-Cys]-dVal-dPro-NH2 (SEQ ID NO: 535); Ac-Ala-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 538); Ac-Nle-Nle-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 545); Ac-Nle-c[Asp-His-p(Br)dPhe-His-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 546); Ac-Nle-c[Asp-His-p(Br)dPhe-Arg-dNal(2')-Lys]-dVal-dPro-NH2 (SEQ ID NO: 547); Ac-Nle-c[Asp-His-p(Br)dPhe-Arg-Nal(2')-Lys]-dVal-dPro-NH2 (SEQ ID NO: 548); Ac-Nle-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dTle-dTle-dVal-NH2 (SEQ ID NO: 549); Ac-Nle-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dPro-dVal-dPro-NH2 (SEQ ID NO: 551); Ac-Nle-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 552); Ac-Nle-Nle-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 553); Ac-Ala-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 555); Ac-Nle-c[Asp-Phe-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 563); Ac-Nle-c[Asp-dPhe-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 564); Ac-Nle-c[Asp-Bip-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2

(SEQ ID NO: 565); Ac-Nle-c[Asp-dGln-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 568); Ac-Nle-c[Asp-Trp-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 569); Ac-Nle-c[Asp-dTrp-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 570); Ac-Nle-c[Asp-Tyr-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 571); Ac-Nle-c[Asp-dTyr-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 572); Ac-dArg-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 539); Ac-dHis-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 544); Ac-dHis-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 561); Ac-dArg-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 556); Ac-dLys-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 542); Ac-His-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 560); Ac-His-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 543); Ac-dLys-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 559); Ac-Arg-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 557); Ac-Lys-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 541); Ac-Nle-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dVal-dVal-dVal-dPro-NH2 (SEQ ID NO: 550); Ac-Lys-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 558); Ac-Arg-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 540); Ac-Nle-Nle-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dPro-dVal-dPro-NH2 (SEQ ID NO: 554); Ac-Nle-c[Asp-His-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 363); Ac-Nle-c[Asp-His-dPhe-Arg-Trp-Pro-Lys]-dVal-dPro-NH2 (SEQ ID NO: 418); Ac-Nle-c[Asp-His-dPhe-Arg-Trp-Lys]-dPro-dVal-NH2 (SEQ ID NO: 621); Ac-Nle-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dPro-dVal-dPro-NH2 (SEQ ID NO: 639); Ac-Nle-c[dPen-dPhe-Arg-Trp-dPen]-dVal-dPro-NH2 (SEQ ID NO: 326); Ac-Nle-c[Asp-Trp-Pro-dPhe-His-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 398); Ac-Nle-c[Asp-Trp-Pro-dPhe-Arg-Phe-Lys]-dVal-dPro-NH2 (SEQ ID NO: 401); Ac-Nle-c[Asp-Pro-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 225); Ac-Nle-c[Asp-Pro-dPhe-Arg-dNal(2')-Lys]-dVal-dPro-NH2 (SEQ ID NO: 430); Ac-Nle-c[Asp-Pro-dPhe-Arg-Nal(2')-Lys]-dVal-dPro-NH2 (SEQ ID NO: 431); Ac-Nle-c[Asp-Ala-His-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 380); Ac-Nle-c[Asp-Pro-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 215); Ac-Nle-c[Asp-Phe-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 525); Ac-Nle-c[Asp-dPhe-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 526); Ac-Nle-c[Asp-Bip-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 527); Ac-Nle-c[Asp-Trp-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 531); Ac-

Nle-c[Asp-Tyr-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 533); Ac-Nle-c[Asp-dTyr-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 534); Ac-Nle-c[Asp-dTrp-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 532); Ac-Nle-c[dCys-His-p(Cl)dPhe-Arg-Trp-Cys]-dVal-dPro-NH2 (SEQ ID NO: 498); Ac-Nle-c[Cys-His-p(Cl)dPhe-Arg-Trp-Cys]-dVal-dPro-NH2 (SEQ ID NO: 497); Ac-Nle-c[Asp-His-p(Cl)dPhe-Arg-dNal(2')-Lys]-dVal-dPro-NH2 (SEQ ID NO: 509); Ac-Nle-c[Asp-His-p(Cl)dPhe-Arg-Nal(2')-Lys]-dVal-dPro-NH2 (SEQ ID NO: 510); Ac-Nle-c[Asp-His-p(Cl)dPhe-His-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 508); Ac-Nle-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 220); Ac-Nle-Nle-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 507); Ac-Ala-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 517); Ac-Ala-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 500); Ac-Nle-Nle-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dPro-dVal-dPro-NH2 (SEQ ID NO: 516); and Ac-Nle-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 514).

**[0059]** In some embodiments, the present technology comprises a method or use, wherein the non-naturally occurring melanocortin analog includes a sequence of Formula (IB): X1-X2-X3-R1-R2-Pro-R4-R5-R6-R7-R8-Y1-Y2-Y3-Y4-Y5-Y6-Y7 (IB), wherein: X1 is absent or norleucine (Nle); X2 is absent or Nle; X3 is absent or Nle; R1 is selected from the group consisting of Nle, D-norleucine (dNle), alanine (Ala), D-alanine (dAla), arginine (Arg), D-arginine (dArg), lysine (Lys), D-lysine (dLys), histidine (His), D-histidine (dHis), ornithine (Orn), D-ornithine (dOrn), D-leucine (dLeu), D-tyrosine (dTyr), phenylalanine (Phe), D-phenylalanine (dPhe), tryptophan (Trp), and D-tryptophan (dTrp); R2 is selected from the group consisting of aspartic acid (Asp), D-aspartic acid (dAsp), cysteine (Cys), D-cysteine (dCys), and D-penicillamine (dPen); R4 is dPhe or para-fluoro-D-phenylalanine (p(F)dPhe); R5 is selected from the group consisting of Arg, His, cisPro(guan), and transPro(guan); R6 is selected from the group consisting of Trp, dTrp, Phe, Aia, Aba, Ata, and 1'-naphthylalanine (Nal(1')); R7 is selected from the group consisting of Gly, Lys, dLys, Cys, dCys, dPen, and Orn; R8 is absent or Lys; Y1 is absent or is selected from the group consisting of valine (Val), D-valine (dVal), b2-valine (b2-Val), b3-valine (b3-Val), Pro, D-proline (dPro), b-proline (b-Pro), Hyp, D-hydroxyproline (dHyp), D-tert-leucine (dTle), dLeu, Trp, Arg, dArg, Lys, dLys, Gly, Ala, dAla, Asp, dAsp, asparagine (Asn), D-asparagine (dAsn), and D-threonine (dThr); Y2 is absent or is selected from the group consisting of Val, dVal, b2-Val, b3-Val, Pro, dPro,

b-Pro, Hyp, dHyp, dTle, Arg, dArg, Gly, Ala, dAla, Asp, and dAsn; Y3 is absent or is selected from the group consisting of Val, dVal, Pro, dPro, dThr, Lys, and dLys; Y4 is absent or is selected from the group consisting of dVal, dPro, Asp, and dAsp; Y5 is absent or dVal; Y6 is absent or dVal; Y7 is absent or dPro; and the non-naturally occurring melanocortin analog is cyclized through a moiety selected from the group consisting of: a disulfide bond between R2 and R7 when each of R2 and R7 are independently selected from the group consisting of Cys, dCys, and dPen; and a lactam bridge between R2 and R7 when R2 is Asp or dAsp and R7 is Lys, dLys, or Orn; provided that: when R4 is p(F)dPhe, then the non-naturally occurring melanocortin analog is not cyclized between Cys at R2 and Cys at R7; and when R4 is dPhe and one or more of X1, X2, and X3 is present, then Y3-Y7 are absent.

**[0060]** In some embodiments, the present technology comprises a method or use, wherein the non-naturally occurring melanocortin analog includes a sequence of Formula (IB), wherein: X1-X2-X3-R1-R2-Pro-R4-R5-R6-R7-R8-Y1-Y2-Y3-Y4-Y5-Y6-Y7 (IB), wherein: X1 is absent or norleucine (Nle); X2 is absent or Nle; X3 is absent or Nle; R1 is selected from the group consisting of Nle, D-norleucine (dNle), alanine (Ala), D-alanine (dAla), arginine (Arg), D-arginine (dArg), lysine (Lys), D-lysine (dLys), histidine (His), D-histidine (dHis), ornithine (Orn), D-ornithine (dOrn), D-leucine (dLeu), D-tyrosine (dTyr), phenylalanine (Phe), D-phenylalanine (dPhe), tryptophan (Trp), and D-tryptophan (dTrp); R2 is selected from the group consisting of aspartic acid (Asp), D-aspartic acid (dAsp), cysteine (Cys), D-cysteine (dCys), and D-penicillamine (dPen); R4 is dPhe or para-fluoro-D-phenylalanine (p(F)dPhe); R5 is selected from the group consisting of Arg, His, cisPro(guan), and transPro(guan); R6 is selected from the group consisting of Trp, dTrp, Phe, Aia, Aba, Ata, and 1'-naphthylalanine (Nal(1')); R7 is selected from the group consisting of Gly, Lys, dLys, Cys, dCys, dPen, and Orn; R8 is absent or Lys; Y1 is absent or is selected from the group consisting of valine (Val), D-valine (dVal), b2-valine (b2-Val), b3-valine (b3-Val), Pro, D-proline (dPro), b-proline (b-Pro), Hyp, D-hydroxyproline (dHyp), D-tert-leucine (dTle), dLeu, Trp, Arg, dArg, Lys, dLys, Gly, Ala, dAla, Asp, dAsp, asparagine (Asn), D-asparagine (dAsn), and D-threonine (dThr); Y2 is absent or is selected from the group consisting of Val, dVal, b2-Val, b3-Val, Pro, dPro, b-Pro, Hyp, dHyp, dTle, Arg, dArg, Gly, Ala, dAla, Asp, and dAsn; Y3 is absent or is selected from the group consisting of Val, dVal, Pro, dPro, dThr, Lys, and dLys; Y4 is absent or is selected from the group consisting of dVal,

dPro, Asp, and dAsp; Y5 is absent or dVal; Y6 is absent or dVal; Y7 is absent or dPro; and the non-naturally occurring melanocortin analog is cyclized through a moiety selected from the group consisting of: a disulfide bond between R2 and R7 when each of R2 and R7 are independently selected from the group consisting of Cys, dCys, and dPen; and a lactam bridge between R2 and R7 when R2 is Asp or dAsp and R7 is Lys, dLys, or Orn; provided that the non-naturally occurring melanocortin analog does not include a sequence of: Ac-Nle-c[Cys-Pro-p(F)dPhe-Arg-Trp-Cys]-dVal-dPro-NH2 (SEQ ID NO: 432); or Ac-Nle-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dPro-dVal-dPro-NH2 (SEQ ID NO: 639).

**[0061]** In some embodiments, the present technology comprises a method or use, wherein the non-naturally occurring melanocortin analog includes a sequence of Formula (IC): X1-X2-R1-R2-Pro-dPhe-R5-R6-R7-Y1-Y2-Y3-Y4 (IC), wherein: X1 is selected from the group consisting of norleucine (Nle), arginine (Arg), D-arginine (dArg), alanine (Ala), lysine (Lys), D-lysine (dLys), histidine (His), D-histidine (dHis); X2 is absent or Nle; R1 is selected from the group consisting of aspartic acid (Asp), cysteine (Cys), and D-cysteine (dCys); R2 is selected from the group consisting of tryptophan (Trp), phenylalanine (Phe), D-phenylalanine (dPhe), histidine (His), D-histidine (dHis), tyrosine (Tyr), and D-tyrosine (dTyr); R5 is Arg; R6 is selected from the group consisting of Trp, 2'-D-naphthylalanine (dNal(2')), 2'-naphthylalanine (Nal(2')), and 1'-naphthylalanine (Nal(1')); R7 is selected from the group consisting of Lys, Cys, and dCys; Y1 is absent or is selected from the group consisting of D-valine (dVal), D-tert-leucine (dTle), dArg, and dLys; Y2 is absent or is selected from the group consisting of dVal, dPro, and D-hydroxyproline (dHyp); Y3 is absent, dVal, or dPro; Y4 is absent or dPro; and the non-naturally occurring melanocortin analog is cyclized through a moiety selected from the group consisting of: a disulfide bond between R1 and R7 when both of R1 and R7 are independently selected from the group consisting of Cys, dCys, and dPen; and a lactam bridge between R1 and R7 when R1 is Asp and R7 is Lys;

**[0062]** In some embodiments, the present technology comprises a method or use, wherein the non-naturally occurring melanocortin analog includes a sequence of Formula (ID): X1-R1-R2-R3-p(Cl)dPhe-Arg-Trp-R7-Y1-Y2-Y3-Y4 (ID), wherein: X1 is absent or norleucine (Nle); R1 is selected from the group consisting of Nle, arginine (Arg), D-arginine

(dArg), lysine (Lys), D-lysine (dLys), histidine (His), and D-histidine (dHis); R2 is aspartic acid (Asp) or D-cysteine (dCys); R3 is selected from the group consisting of His, 4-amino-1,2,4,5-tetrahydro-2-benzazepin-3-one (Aba), 7-amino-7,8-dihydro-4H-[1,2,3]triazolo-[1,5-a][1,4]diazepin-6(5H)-one (Ata), and 4-amino-1,4,5,6-tetrahydroazepino[4,3-b]indol-3(2H)-one (Aia); R7 is Lys or dCys; Y1 is selected from the group consisting of D-valine (dVal), D-proline (dPro), and D-tert-leucine (dTle); Y2 is absent or is selected from the group consisting of dVal, dPro, and dTle; Y3 is absent, dVal, or dPro; Y4 is absent or dPro; and the non-naturally occurring melanocortin analog is cyclized through a moiety selected from the group consisting of: a disulfide bond between R2 and R7 when both of R2 and R7 are dCys; and a lactam bridge between R2 and R7 when R2 is Asp and R7 is Lys; provided that when R3 is His and R1 is Nle, then (i) Y1Y2 is dVal-dPro, X1 is absent, and the non-naturally occurring melanocortin analog is cyclized through a disulfide bond, or (b) Y1Y2 is not dVal-dPro and either X1 or Y3 is present.

**[0063]** In some embodiments, the present technology comprises a method or use, wherein the non-naturally occurring melanocortin analog includes a sequence of Formula (ID), wherein: X1 is absent or norleucine (Nle); R1 is selected from the group consisting of Nle, arginine (Arg), D-arginine (dArg), lysine (Lys), D-lysine (dLys), histidine (His), and D-histidine (dHis); R2 is aspartic acid (Asp) or D-cysteine (dCys); R3 is selected from the group consisting of His, 4-amino-1,2,4,5-tetrahydro-2-benzazepin-3-one (Aba), 7-amino-7,8-dihydro-4H-[1,2,3]triazolo-[1,5-a][1,4]diazepin-6(5H)-one (Ata), and 4-amino-1,4,5,6-tetrahydroazepino[4,3-b]indol-3(2H)-one (Aia); R7 is Lys or dCys; Y1 is selected from the group consisting of D-valine (dVal), D-proline (dPro), and D-tert-leucine (dTle); Y2 is absent or is selected from the group consisting of dVal, dPro, and dTle; Y3 is absent, dVal, or dPro; Y4 is absent or dPro; and the non-naturally occurring melanocortin analog is cyclized through a moiety selected from the group consisting of: a disulfide bond between R2 and R7 when both of R2 and R7 are dCys; and a lactam bridge between R2 and R7 when R2 is Asp and R7 is Lys; provided that the non-naturally occurring melanocortin analog does not include a sequence selected from the group consisting of: Ac-Nle-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 220); Ac-Nle-Nle-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 507); Ac-Nle-Nle-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dPro-

dVal-dPro-NH2 (SEQ ID NO: 516); Ac-Nle-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 514); and.

**[0064]** In some embodiments, an N-terminus of the non-naturally occurring melanocortin analog is modified by an acyl group.

**[0065]** In some embodiments, the acyl group is an acetyl group.

**[0066]** In some embodiments, an N-terminus of the non-naturally occurring melanocortin analog is not modified.

**[0067]** In some embodiments, a C-terminus of the non-naturally occurring melanocortin analog is modified by an amide group.

**[0068]** In some embodiments, a C-terminus of the non-naturally occurring melanocortin analog is not modified.

**[0069]** In some embodiments, Y1-Y2 are present and Y3- Y8 are absent.

**[0070]** In some embodiments, Y1 is D-valine and Y2 is D-proline.

**[0071]** In some embodiments, the present technology comprises a method or a use, w wherein Y1 is D-tert-leucine and Y2 is D-proline.

**[0072]** In some embodiments, R4 is dNal(2').

**[0073]** In some embodiments, the sequence of Formula (I) is: Ac-Nle-c[Asp-His-dNal(2')-Arg-Trp-Pro-Lys]-dVal-dPro-NH2 (SEQ ID NO: 8), wherein c represents cyclization through R2 and R8 via a lactam bond.

**[0074]** In some embodiments, R4 is Phe or dPhe.

**[0075]** In some embodiments, the sequence of any one of Formulae (I)-(ID) is selected from the group consisting of: Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-OH (SEQ ID NO: 291); Ac-Nle-c[Asp-Pro-Phe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 294); Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 295; E2); and Ac-Nle-c[Asp-Pro-His-Phe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 296). wherein c represents cyclization through R2 and R7 via a lactam bond.

**[0076]** In some embodiments, the sequence of any one of Formulae (I)-(ID) is selected from the group consisting of: Ac-dLeu-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO:298); Ac-dAla-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 299); Ac-Ala-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro- NH2 (SEQ ID NO: 300); Ac-dNle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 301); Ac-dArg-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 302); Ac-dPhe-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 303); Ac-dTyr-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 304); Phe-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 305); His-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 306); Trp-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 307); dPhe-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 308); dHis-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 309); dTrp-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 310); Ac-Arg-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 311); Ac-dLys-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 312); Ac-Lys-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 313); Ac-His-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 314); Ac-dHis-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 315); Ac-Orn-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 316); and Ac-dOrn-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 317), wherein c represents cyclization through R2 and R7 via a lactam bond.

**[0077]** In some embodiments, the sequence of any one of Formulae (I)-(ID) is selected from the group consisting of: Ac-Nle-c[Cys-Pro-dPhe-Arg-Trp-Cys]-dVal-dPro-NH2 (SEQ ID NO: 318); Ac-Nle-c[dCys-Pro-dPhe-Arg-Trp-Cys]-dVal-dPro-NH2 (SEQ ID NO: 319); Ac-Nle-c[dPen-Pro-dPhe-Arg-Trp-dPen]-dVal-dPro-NH2 (SEQ ID NO: 320); Ac-Nle-c[dCys-Pro-dPhe-Arg-Trp-dCys]-dVal-dPro-NH2 (SEQ ID NO: 321); Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Orn]-dVal-dPro-NH2 (SEQ ID NO: 322); and Ac-Nle-c[Cys-dPhe-Arg-Trp-Pen]-dVal-dPro-NH2 (SEQ ID NO: 324), wherein c represents cyclization through R2 and R7 via a disulfide bond.

**[0078]** In some embodiments, the sequence of any one of Formulae (I)-(ID) is selected from the group consisting of: Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Gly-Lys]-dVal-dPro-NH2 (SEQ ID NO: 351); Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Gly-Lys]-dPro-dPro-Lys-Asp-NH2

(SEQ ID NO: 352); and Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Gly-Lys]-dPro-dPro-dLys-dAsp-NH2 (SEQ ID NO: 353), wherein c represents cyclization through R2 and R8 via a lactam bond.

**[0079]** In some embodiments, the sequence of any one of Formulae (I)-(ID) is selected from the group consisting of: Ac-Nle-c[Asp-Ala-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 354); Ac-Nle-c[Asp-Leu-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 355); Ac-Nle-c[Asp-Cpe-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 358); Ac-Nle-c[Asp-Che-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 359); Ac-Nle-c[Asp-Oic-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 360); Ac-Nle-c[Asp-Ioc-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 361); Ac-Nle-c[Asp-Tic-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 362); Ac-Nle-c[Asp-Hyp-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 364); Ac-Nle-c[Asp-Phe-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 366); Ac-Nle-c[Asp-dPhe-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 367); Ac-Nle-c[Asp-Bip-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 368); Ac-Nle-c[Asp-dGln-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 371); Ac-Nle-c[Asp-Trp-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 372); Ac-Nle-c[Asp-dTrp-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 373); Ac-Nle-c[Asp-Tyr-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 374); Ac-Nle-c[Asp-dTyr-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 375); Ac-Nle-c[Asp-Aba-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 198); Ac-Nle-c[Asp-Aia-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 207); Ac-Nle-c[Asp-Ata-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 208); Ac-Nle-c[Asp-Atc-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 212); Ac-Nle-c[Asp-APC-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 213); and Ac-Nle-c[Asp-APPC-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 214), wherein c represents cyclization through R2 and R7 via a lactam bond.

**[0080]** In some embodiments, the sequence of any one of Formulae (I)-(ID) is selected from the group consisting of: Ac-Arg-c[Asp-dAla-His-dPhe-Arg-Trp-Lys]-NH2 (SEQ ID NO: 281); Ac-Arg-c[Asp-Ala-His-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 381); and Ac-dArg-c[Asp-Ala-His-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 382), wherein c represents cyclization through R1 and R7 via a lactam bond.

**[0081]** In some embodiments, the sequence of any one of Formulae (I)-(ID) is selected from the group consisting of: Ac-Nle-c[Asp-Trp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 226); Ac-Nle-c[Cys-Trp-Pro-dPhe-Arg-Trp-Cys]-dVal-dPro-NH2 (SEQ ID NO: 383); Ac-Nle-c[dCys-Trp-Pro-dPhe-Arg-Trp-Cys]-dVal-dPro-NH2 (SEQ ID NO: 384); Ac-Nle-c[dCys-Trp-Pro-dPhe-Arg-Trp-dCys]-dVal-dPro-NH2 (SEQ ID NO: 385); Ac-Ala-c[Asp-Trp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 386); Ac-Lys-c[Asp-Trp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 387); Ac-dLys-c[Asp-Trp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 388); Ac-Arg-c[Asp-Trp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 389); Ac-dArg-c[Asp-Trp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 390); Ac-dHis-c[Asp-Trp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 391); Ac-His-c[Asp-Trp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 392); Ac-Nle-Nle-c[Asp-Trp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 393); Ac-Nle-c[Asp-Trp-Ala-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 394); Ac-Nle-c[Asp-Trp-Leu-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 395); Ac-Nle-c[Asp-Trp-Pro-dPhe-Arg-Nal(1']-Lys]-dVal-dPro-NH2 (SEQ ID NO: 399); Ac-Nle-c[Asp-Trp-Pro-dPhe-Arg-dNal(2')-Lys]-dVal-dPro-NH2 (SEQ ID NO: 403); Ac-Nle-c[Asp-Trp-Pro-dPhe-Arg-Nal(2')-Lys]-dVal-dPro-NH2 (SEQ ID NO: 404); Ac-Nle-c[Asp-Trp-Pro-dPhe-Arg-Trp-Lys]-dArg-dVal-dPro-NH2 (SEQ ID NO: 405); Ac-Nle-c[Asp-Trp-Pro-dPhe-Arg-Trp-Lys]-dLys-dVal-dPro-NH2 (SEQ ID NO: 406); Ac-Nle-c[Asp-Trp-Pro-dPhe-Arg-Trp-Lys]-dArg-dPro-NH2 (SEQ ID NO: 407); Ac-Nle-c[Asp-Trp-Pro-dPhe-Arg-Trp-Lys]-dLys-dPro-NH2 (SEQ ID NO: 408); Ac-Nle-c[Asp-Trp-Pro-dPhe-Arg-Trp-Lys]-dVal-dHyp-NH2 (SEQ ID NO: 409); Ac-Nle-c[Asp-Trp-Pro-dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 410); Ac-Nle-c[Asp-Trp-Pro-dPhe-Arg-Trp-Lys]-dVal-dVal-dVal-dPro-NH2 (SEQ ID NO: 411); Ac-Nle-c[Asp-Phe-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 412); Ac-Nle-c[Asp-His-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 413); Ac-Nle-c[Asp-Tyr-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 414); Ac-Nle-c[Asp-dPhe-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 415); Ac-Nle-c[Asp-dHis-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 416); and Ac-Nle-c[Asp-dTyr-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 417), wherein c represents cyclization through R1 and R7 via a lactam bond or a disulfide bond.

**[0082]** In some embodiments, the sequence of any one of Formulae (I)-(ID) is: Ac-Nle-c[Asp-Hyp-dPhe-Arg-Trp-Pro-Lys]-dVal-dPro-NH2 (SEQ ID NO: 419), wherein c represents cyclization through R2 and R8 via a lactam bond.

**[0083]** In some embodiments, the sequence of any one of Formulae (I)-(ID) is selected from the group consisting of: Ac-Nle-Phe-Phe-c[Asp-Phe-His-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 421); Ac-Nle-c[Asp-Phe-His-dPhe-Arg-Trp-Lys]-dLeu-dPro-NH2 (SEQ ID NO: 422); Ac-Nle-c[Asp-Phe-His-dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 423); and Ac-Nle-c[Asp-Phe-His-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 424), wherein c represents cyclization through R1 and R7 via a lactam bond.

**[0084]** In some embodiments, the sequence of any one of Formulae (I)-(ID) is selected from the group consisting of: Ac-Nle-c[Asp-Pro-dPhe-Arg-dTrp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 187); Ac-Nle-c[Asp-Pro-dPhe-Arg-Aia-Lys]-dVal-dPro-NH2 (SEQ ID NO: 233); Ac-Nle-c[Asp-Pro-dPhe-Arg-Aba-Lys]-dVal-dPro-NH2 (SEQ ID NO: 234); Ac-Nle-c[Asp-Pro-dPhe-Arg-Ata-Lys]-dVal-dPro-NH2 (SEQ ID NO: 235); Ac-Nle-c[Asp-Pro-dPhe-Arg-Nal(1')-Lys]-dVal-dPro-NH2 (SEQ ID NO: 427); and Ac-Nle-c[Asp-Pro-dPhe-Arg-Phe-Lys]-dVal-dPro-NH2 (SEQ ID NO: 429), wherein c represents cyclization through R2 and R7 via a lactam bond.

**[0085]** In some embodiments, the sequence of any one of Formulae (I)-(ID) is selected from the group consisting of: Ac-Nle-c[Asp-Pro-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 218); Ac-Nle-c[dCys-Pro-p(F)dPhe-Arg-Trp-Cys]-dVal-dPro-NH2 (SEQ ID NO: 433); Ac-Nle-c[dCys-Pro-p(F)dPhe-Arg-Trp-dCys]-dVal-dPro-NH2 (SEQ ID NO: 434); Ac-Ala-c[Asp-Pro-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 435); Ac-dArg-c[Asp-Pro-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 436); Ac-Arg-c[Asp-Pro-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 437); Ac-Lys-c[Asp-Pro-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 438); Ac-dLys-c[Asp-Pro-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 439); Ac-His-c[Asp-Pro-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 440); Ac-dHis-c[Asp-Pro-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 441); Ac-Nle-Nle-c[Asp-Pro-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 442); Ac-Nle-c[Asp-Pro-p(F)dPhe-His-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 443); Ac-Nle-c[Asp-Pro-p(F)dPhe-Arg-Trp-Lys]-dTle-dTle-dVal-NH2 (SEQ ID NO: 446); Ac-Nle-

c[Asp-Pro-p(F)dPhe-Arg-Trp-Lys]-dVal-dVal-dVal-dPro-NH2 (SEQ ID NO: 447); Ac-Nle-c[Asp-Pro-p(F)dPhe-Arg-Trp-Lys]-dPro-dVal-dPro-NH2 (SEQ ID NO: 448); Ac-Nle-c[Asp-Pro-p(F)dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 449); Ac-Nle-Nle-c[Asp-Pro-p(F)dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 450); Ac-Nle-Nle-c[Asp-Pro-p(F)dPhe-Arg-Trp-Lys]-dPro-dVal-dPro-NH2 (SEQ ID NO: 451); Ac-Ala-c[Asp-Pro-p(F)dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 452); Ac-dArg-c[Asp-Pro-p(F)dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 453); Ac-Arg-c[Asp-Pro-p(F)dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 454); Ac-Lys-c[Asp-Pro-p(F)dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 455); Ac-dLys-c[Asp-Pro-p(F)dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 456); Ac-His-c[Asp-Pro-p(F)dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 457); Ac-dHis-c[Asp-Pro-p(F)dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 458); Ac-Nle-c[Cys-His-p(F)dPhe-Arg-Trp-Cys]-dVal-dPro-NH2 (SEQ ID NO: 459); Ac-Nle-c[dCys-His-p(F)dPhe-Arg-Trp-Cys]-dVal-dPro-NH2 (SEQ ID NO: 460); Ac-Nle-c[dCys-His-p(F)dPhe-Arg-Trp-dCys]-dVal-dPro-NH2 (SEQ ID NO: 461); Ac-Nle-c[Asp-His-p(F)dPhe-Arg-Nal(2')-Lys]-dVal-dPro-NH2 (SEQ ID NO: 472); Ac-Nle-c[Asp-dGln-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 492); and Ac-Nle-c[Asp-dTyr-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 496), wherein c represents cyclization through R2 and R7 via a lactam bond or a disulfide bond.

**[0086]** In some embodiments, the sequence of any one of Formulae (I)-(ID) is selected from the group consisting of: Ac-Nle-c[Asp-Aba-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 209); Ac-Nle-c[Asp-Aia-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 210); Ac-Nle-c[Asp-Ata-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 211); Ac-Nle-c[dCys-His-p(Cl)dPhe-Arg-Trp-dCys]-dVal-dPro-NH2 (SEQ ID NO: 499); Ac-dArg-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 501); Ac-Arg-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 502); Ac-Lys-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 503); Ac-dLys-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 504); Ac-His-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 505); Ac-dHis-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 506); Ac-Nle-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dTle-dTle-dVal-NH2 (SEQ ID NO: 511); Ac-Nle-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dVal-dVal-dPro-NH2 (SEQ ID NO: 512); Ac-Nle-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dPro-dVal-dPro-NH2 (SEQ ID NO: 513); Ac-Nle-Nle-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 515); Ac-

dArg-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 518); Ac-Arg-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 519); Ac-Lys-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 520); Ac-dLys-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 521); Ac-His-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 522); and Ac-dHis-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 523), wherein c represents cyclization through R2 and R7 via a lactam bond or a disulfide bond.

**[0087]** In some embodiments, the sequence of any one of Formulae (I)-(ID) is selected from the group consisting of: Ac-Nle-c[dCys-His-p(Br)dPhe-Arg-Trp-Cys]-dVal-dPro-NH2 (SEQ ID NO: 536); or Ac-Nle-c[dCys-His-p(Br)dPhe-Arg-Trp-dCys]-dVal-dPro-NH2 (SEQ ID NO: 537), wherein c represents cyclization through R2 and R7 via a disulfide bond.

**[0088]** In some embodiments, the sequence of any one of Formulae (I)-(ID) is selected from the group consisting of: Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-Val-Pro-NH2 (SEQ ID NO: 573); Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-Hyp-NH2 (SEQ ID NO: 574); Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dHyp-NH2 (SEQ ID NO: 575); Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-Val-NH2 (SEQ ID NO: 576); Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-Pro-NH2 (SEQ ID NO: 577); Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-Arg-NH2 (SEQ ID NO: 578); Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dArg-NH2 (SEQ ID NO: 579); Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dArg-dPro-NH2 (SEQ ID NO: 580); Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-Arg-NH2 (SEQ ID NO: 581); Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dArg-NH2 (SEQ ID NO: 582); Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-Lys-Pro-Val-NH2 (SEQ ID NO: 583); Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dLys-dPro-NH2 (SEQ ID NO: 584); Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-Lys-Val-Pro-NH2 (SEQ ID NO: 585); Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-Lys-dVal-dPro-NH2 (SEQ ID NO: 586); Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dLys-dVal-dPro-NH2 (SEQ ID NO: 587); Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-Arg-Pro-Val-NH2 (SEQ ID NO: 588); Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-Arg-Val-Pro-NH2 (SEQ ID NO: 589); Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dArg-dVal-dPro-NH2 (SEQ ID NO: 590); Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 591); Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dTle-dTle-dPro-NH2 (SEQ ID NO: 592); Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dTle-dTle-dVal-NH2 (SEQ ID NO: 593); Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-

dVal-dTle-NH2 (SEQ ID NO: 594); Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dVal-dPro-NH2 (SEQ ID NO: 595); Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dPro-dVal-dPro-NH2 (SEQ ID NO: 596); Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dVal-dVal-dPro-NH2 (SEQ ID NO: 597); Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-dVal-dPro-NH2 (SEQ ID NO: 598); Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dVal-dVal-dVal-dVal-dVal-dPro-NH2 (SEQ ID NO: 599); Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-Trp-NH2 (SEQ ID NO: 600); Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-Lys-dPro-dVal-NH2 (SEQ ID NO: 601); Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dAla-dAla-NH2 (SEQ ID NO: 602); Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-Asp-NH2 (SEQ ID NO: 603); Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dHyp-NH2 (SEQ ID NO: 604); Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dAsn-NH2 (SEQ ID NO: 605); Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-Asp-NH2 (SEQ ID NO: 606); Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-Asn-dPro-NH2 (SEQ ID NO: 607); Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-Hyp-NH2 (SEQ ID NO: 608); Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-Ala-Ala-NH2 (SEQ ID NO: 609); Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-Gly-Gly-NH2 (SEQ ID NO: 610); Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-Asp-dPro-NH2 (SEQ ID NO: 611); Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dAsn-dPro-NH2 (SEQ ID NO: 612); Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-Asn-NH2 (SEQ ID NO: 613); Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dAsp-NH2 (SEQ ID NO: 614); Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dAsn-NH2 (SEQ ID NO: 615); Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-Lys-dPro-NH2 (SEQ ID NO: 616); Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dPro-dVal-OH (SEQ ID NO: 617); Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dThr-dPro-dThr-NH2 (SEQ ID NO: 618); Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dThr-dPro-dThr-OH (SEQ ID NO: 619); Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dPro-dVal-NH2 (SEQ ID NO: 620); Ac-Nle-c[dAsp-Pro-dPhe-Arg-Trp-dLys]-dPro-dVal-NH2 (SEQ ID NO: 622); Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-βPro-β2Val-NH2 (SEQ ID NO: 623); Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-βPro-β3Val-NH2 (SEQ ID NO: 624); Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-β2Val-βPro-NH2 (SEQ ID NO: 625); Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-β3Val-βPro-NH2 (SEQ ID NO: 626); and Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-βPro-βPro-NH2 (SEQ ID NO: 627), wherein c represents cyclization through R2 and R7 via a lactam bond.

**[0089]** In some embodiments, the sequence of any one of Formulae (I)-(ID) is selected from the group consisting of: Ac-Nle-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 628); Ac-Nle-Nle-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID

NO: 629); and Ac-Nle-Nle-Nle-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 630), wherein c represents cyclization through R2 and R7 via a lactam bond.

**[0090]** In some embodiments, the sequence of any one of Formulae (I)-(ID) is selected from the group consisting of: Ac-Arg-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dArg-dVal-dPro-NH2 (SEQ ID NO: 631); Ac-dLys-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dLys-dVal-dPro-NH2 (SEQ ID NO: 632); Ac-Lys-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dArg-dPro-NH2 (SEQ ID NO: 633); Ac-His-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dLys-dPro-NH2 (SEQ ID NO: 634); Ac-dHis-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dHyp-NH2 (SEQ ID NO: 635); Ac-Orn-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 636); Ac-dOrn-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dVal-dVal-dPro-NH2 (SEQ ID NO: 637); Ac-Nle-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 638); Ac-Ala-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 640); Ac-dArg-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 641); Ac-Arg-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 642); Ac-Lys-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 643); Ac-dLys-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 644); Ac-His-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 645); and Ac-dHis-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 646), wherein c represents cyclization through R2 and R7 via a lactam bond.

**[0091]** In some embodiments, the non-naturally occurring melanocortin analog includes any one of SEQ ID NOs: 8, 187, 198, 207-218, 226, 231-235, 281, 291, 294-296, 298-322, 324, 351-355, 358-362, 364, 366-368, 371-375, 381-395, 399, 403-417, 419, 421-425, 427, 429, 433-443, 446-461, 472, 492, 496, 499-506, 511-513, 515, 518-523, 536-537, 573-599, 600-620, 622-646.

**[0092]** In some embodiments, the non-naturally occurring melanocortin analog includes any one of the sequences of SEQ ID NOs: 187, 212, 218, 226, 291, 295, 298-322, 324, 351-355, 358-360, 362, 364, 366-368, 371-375, 381-395, 399, 403-417, 419, 421-425, 427, 429, 433-443, 446-461, 472, 492, 496, 499-506, 511-513, 515, 518-523, 536-537, 573-598, 600-646.

**[0093]** In some embodiments, the non-naturally occurring melanocortin analog includes any one of the sequences of SEQ ID NOs: 187, 218, 231-235, 291, 295, 298-322, 351-353, 425, 427, 429, 433-443, 446-458, 573-599, 600-620, 622-646.

**[0094]** In some embodiments, the non-naturally occurring melanocortin analog includes any one of the sequences of SEQ ID NOs: 226, 383-393, 399, 403-417.

**[0095]** In some embodiments, the non-naturally occurring melanocortin analog includes any one of the sequences of SEQ ID NOs: 209-211, 499, 501-506, 511-513, 515, 518-523.

**[0096]** In some embodiments, the non-naturally occurring melanocortin analog is present in a pharmaceutical composition.

**[0097]** In some embodiments, the pharmaceutical composition includes one or more pharmaceutically acceptable excipients and/or carriers.

**[0098]** In some embodiments, the one or more pharmaceutically acceptable excipients and/or carriers of the pharmaceutical composition include water.

**[0099]** In some embodiments, the non-naturally occurring melanocortin analog is administered (i) at a first dose of about 5 mg/kg to about 20 mg/kg administered once a day for about 5 days to about 10 days; (ii) at a second dose of about 10 mg/kg to about 40 mg/kg administered once a day after administration of the first dose for about 5 days to about 10 days; (iii) at a third dose of about 5 mg/kg to about 30 mg/kg administered twice a day after administration of the second dose for at least about 5 days to about 10 days.

**[0100]** In some embodiments, the non-naturally occurring melanocortin analog is administered (i) at a first dose of about 5 mg/kg administered once a day for about 7 days; (ii) at a second dose of about 15 mg/kg administered once a day after administration of the first dose for about 7 days; (iii) at a third dose of about 10 mg/kg administered twice a day after administration of the second dose for at least about 7 days.

**[0101]** In some embodiments, the non-naturally occurring melanocortin analog is administered (i) at a first dose of about 10 mg/kg administered once a day for about 7 days; (ii) at a second dose of about 20 mg/kg administered once a day after administration of the first dose for about 7 days; (iii) at a third dose of about 15 mg/kg administered twice a day after administration of the second dose for at least about 7 days.

**[0102]** In some embodiments, the present technology comprises a method or the use wherein the non-naturally occurring melanocortin analog is administered (i) at a first dose of about 15 mg/kg administered once a day for about 7 days; (ii) at a second dose of about 25 mg/kg administered once a day after administration of the first dose for about 7 days; (iii) at a third dose of about 20 mg/kg administered twice a day after administration of the second dose for at least about 7 days.

**[0103]** In some embodiments, the non-naturally occurring melanocortin analog is administered at a dose of about 0.5 mg/kg to about 10 mg/kg per body weight of the subject once daily.

**[0104]** In some embodiments, the non-naturally occurring melanocortin analog is administered at a dose of about 1 mg/kg or 3 mg/kg per body weight of the subject once daily.

**[0105]** In some embodiments, the non-naturally occurring melanocortin analog is administered at a dose of about 0.1 mg to about 100 mg once daily.

**[0106]** In some embodiments, the non-naturally occurring melanocortin analog is administered at a dose of about 10 mg or about 50 mg once daily.

**[0107]** In some embodiments, the non-naturally occurring melanocortin analog is administered via intraperitoneal, intravenous, parenteral, subcutaneous, intramuscular, intracerebroventricular, intranasal, or oral administration.

**[0108]** In some embodiments, the non-naturally occurring melanocortin analog crosses a blood-brain-barrier of a subject.

**[0109]** In some embodiments, the non-naturally occurring melanocortin analog includes any one of the sequences of SEQ ID NOs: 8, 187, 198, 207-218, 226, 231-235, 281, 291, 294-296, 298-322, 324, 351-355, 358-362, 364, 366-368, 371-375, 381-395, 399, 403-417, 419, 421-425, 427, 429, 433-443, 446-461, 472, 492, 496, 499-506, 511-513, 515, 518-523, 536-537, 573-599, 600-620, 622-646 and is administered at least once daily in an amount ranging from 0.001 mg/kg to 25 mg/kg per body weight of the subject.

**[0110]** In some embodiments, the non-naturally occurring melanocortin analog includes any one of the sequences of SEQ ID NOs: 8, 187, 198, 207-218, 226, 231-235, 281, 291, 294-296, 298-322, 324, 351-355, 358-362, 364, 366-368, 371-375, 381-395, 399, 403-417, 419, 421-425, 427, 429, 433-443, 446-461, 472, 492, 496, 499-506, 511-513, 515, 518-523, 536-537, 573-599, 600-620, 622-646 and is administered at least once daily in an amount ranging from 0.5 mg/kg to 10 mg/kg per body weight of the subject.

**[0111]** In some embodiments, the non-naturally occurring melanocortin analog is administered to a subject for at least 1 day, 1 week, 1 month, 3 months, 6 months, 1 year, or 5 years.

**[0112]** In some embodiments, the non-naturally occurring melanocortin analog is administered to a subject for 1 day, 5 days, 7 days, 14 days, 21 days, 28 days, 35 days, 40 days, 45 days, 50 days, 60 days, 75 days, 90 days, 100 days, 110 days, or 120 days.

**[0113]** In some embodiments, the present technology comprises a method of reducing a pain level in a subject in need thereof relative to a control, including administering to the subject a non-naturally occurring melanocortin analog of Formula (I): X1-X2-X3-R1-R2-R3-R4-R5-R6-R7-R8-Y1-Y2-Y3-Y4-Y5-Y6-Y7 (I), wherein: X1 is absent or is selected from the group consisting of norleucine (Nle), arginine (Arg), D-arginine (dArg), alanine (Ala), lysine (Lys), D-lysine (dLys), histidine (His), and D-histidine (dHis); X2 is absent, phenylalanine (Phe), or Nle; X3 is absent, Phe, or Nle; R1 is selected from the group consisting of Nle, D-norleucine (dNle), Ala, D-alanine (dAla), Arg, dArg, Lys, dLys, His, dHis, ornithine (Orn), D-ornithine (dOrn), D-leucine (dLeu), D-tyrosine (dTyr), phenylalanine (Phe), D-phenylalanine (dPhe), tryptophan (Trp), D-tryptophan (dTrp), aspartic acid (Asp), cysteine (Cys), and D-cysteine (dCys); R2 is selected from the group consisting of Asp, proline (Pro), D-aspartic acid (dAsp), Cys, dCys, D-penicillamine (dPen), Ala, dAla, Trp, Phe, dPhe, His, dHis, Tyr, and dTyr; R3 is absent or is selected from the group consisting of His, Ala, Pro, hydroxyproline (Hyp), leucine (Leu), D-glutamine (dGln), Phe, dPhe, Trp, dTrp, Tyr, dTyr, 4-amino-1,2,4,5-tetrahydro-2-benzazepin-3-one (Aba), 7-amino-7,8-dihydro-4H-[1,2,3]triazolo-[1,5-a][1,4]diazepin-6(5H)-one (Ata), 4-amino-1,4,5,6-tetrahydroazepino[4,3-b]indol-3(2H)-one (Aia), 2-aminotetraline-2-carboxylic acid (Atc), 1-amino-4-phenylcyclohexane-carboxylic acid (APC), 4-aminophenylpiperidine-4-carboxylic acid

(APPC), octohydroindole-2-carboxylic acid (Oic), 1-amino-1-cyclohexanecarboxylic acid (Che), tetrahydro-isoquinoline-3-carboxylic acid (Tic), indoline-2-carboxylic acid (Ioc), 1-amino-1-cyclopentane carboxylic (Cpe), and biphenylalanine (Bip); R4 is selected from the group consisting of Phe, dPhe, 2'-D-naphthylalanine (dNal(2')), para-chloro-D-phenylalanine (p(Cl)dPhe), para-bromo-D-phenylalanine (p(Br)dPhe), and para-fluoro-D-phenylalanine (p(F)dPhe); R5 is selected from the group consisting of Arg, His, cisPro(guan), and transPro(guan); R6 is selected from the group consisting of Trp, dTrp, Phe, Aia, Aba, Ata, dNal(2'), 2'-naphthylalanine (Nal(2')), and 1'-naphthylalanine (Nal(1')); R7 is selected from the group consisting of Gly, Pro, Lys, dLys, Cys, dCys, penicillamine (Pen), dPen, and Orn; R8 is absent or Lys; Y1 is absent or is selected from the group consisting of valine (Val), D-valine (dVal), b2-valine (b2-Val), b3-valine (b3-Val), Pro, D-proline (dPro), b-proline (b-Pro), Hyp, D-hydroxyproline (dHyp), D-tert-leucine (dTle), dLeu, Trp, Arg, dArg, Lys, dLys, Gly, Ala, dAla, Asp, dAsp, asparagine (Asn), D-asparagine (dAsn), and D-threonine (dThr); Y2 is absent or is selected from the group consisting of Val, dVal, b2-Val, b3-Val, Pro, dPro, b-Pro, Hyp, dHyp, dTle, Arg, dArg, Gly, Ala, dAla, Asp, and dAsn; Y3 is absent or is selected from the group consisting of Val, dVal, Pro, dPro, dThr, Lys, and dLys; Y4 is absent or is selected from the group consisting of dVal, dPro, Asp, and dAsp; Y5 is absent or dVal; Y6 is absent or dVal; Y7 is absent or dPro; and the non-naturally occurring melanocortin analog is cyclized through a moiety selected from the group consisting of: a disulfide bond between R1 or R2 and R7 when each of R1 or R2 and R7 are independently selected from the group consisting of Cys, dCys, and dPen; a disulfide bond between R2 and R7 when R2 is Cys, R7 is Pen, and R3 is absent; a lactam bridge between R1 or R2 and R7 or R8 when R1 or R2 is Asp and R7 or R8 is Lys or Orn; and a lactam bridge between R2 and R7 when R2 is dAsp and R7 is dLys; provided that: when R4 is dNal(2'), then R3 is His and R7 is Pro; when R4 is p(F)dPhe, then (i) R3 is selected from Pro, dGln, dTyr, R6 is Trp, and the non-naturally occurring melanocortin analog is not cyclized between Cys at R2 and Cys at R7 or (ii) R3 is His and either R6 is Nal(2') or the non-naturally occurring melanocortin analog is cyclized through a disulfide bond between R2 and R7; when R4 is p(Br)dPhe, then the non-naturally occurring melanocortin analog is cyclized through a disulfide bond between dCys at R2 and Cys or dCys at R7; when R4 is dPhe, then (i) R3 is not His, Pro, or absent, (ii) R3 is His and either R2 is Phe or dAla or R2 is Ala and X1 is Arg or dArg, (iii) R3 is Pro and (a) R2 is Trp,

and R5 is not His or R6 is not Phe or (b) R2 is not Trp or Pro, and either R5 is not dNal(2') or Nal(2') or X1 and Y3 are not both present, or (iv) R3 is absent and R2 and R7 are not both dPen; when R4 is p(Cl)dPhe, then (i) R3 is selected from Aba, Aia, and Ata or (ii) R3 is His, R1 is not Ala, and (a) if R1 is Nle and Y1Y2 is dVal-dPro, then X1 is absent and the non-naturally occurring melanocortin analog is cyclized through a disulfide bond between dCys at R2 and dCys at R7, or (b) if R1 is Nle, and Y1Y2 is not dVal-dPro, then either X1 or Y3 is present; and when R2 is dAla, then R4 is dPhe and Y1-Y7 are absent.

**[0114]** In some embodiments, the present technology comprises use of a non-naturally occurring melanocortin analog for reducing a pain level in a subject in need thereof relative to a control, the non-naturally occurring melanocortin analog including a sequence of Formula (I).

**[0115]** In some embodiments, the present technology comprises a method of treating, preventing, or reducing an addiction in a subject relative to a control, including administering to the subject a non-naturally occurring melanocortin analog including a sequence of Formula (I).

**[0116]** In some embodiments, the present technology comprises use of a non-naturally occurring melanocortin analog for treating, preventing, or reducing an addiction in a subject relative to a control, the non-naturally occurring melanocortin analog including a sequence of Formula (I).

**[0117]** In some embodiments, the present technology comprises a method of preventing or reducing a use of or dependence on an addictive substance in a subject relative to a control, including administering to the subject a non-naturally occurring melanocortin analog including a sequence of Formula (I).

**[0118]** In some embodiments, the present technology comprises use of a non-naturally occurring melanocortin analog for treating, preventing, or reducing a use of or dependence on an addictive substance in a subject relative to a control, the non-naturally occurring melanocortin analog including a sequence of Formula (I).

**[0119]** In some embodiments, the present technology comprises a method of treating or preventing an opioid use disorder (OUD) in a subject in need thereof relative to a control,

including administering to the subject a non-naturally occurring melanocortin analog including a sequence of Formula (I).

**[0120]** In some embodiments, the present technology comprises use of a non-naturally occurring melanocortin analog for treating or preventing an OUD in a subject in need thereof relative to a control, the non-naturally occurring melanocortin analog including a sequence of Formula (I).

**[0121]** In some embodiments, the present technology comprises a method of treating or preventing an alcohol use disorder (AUD) in a subject in need thereof relative to a control, including administering to the subject a non-naturally occurring melanocortin analog including a sequence of Formula (I).

**[0122]** In some embodiments, the present technology comprises use of a non-naturally occurring melanocortin analog for treating or preventing an AUD in a subject in need thereof relative to a control, the non-naturally occurring melanocortin analog including a sequence of Formula (I).

**[0123]** In some embodiments, the method or the use includes reducing a dose used or consumed of an addictive substance, relative to a control.

**[0124]** In some embodiments, the method or the use includes reducing a dependency on an addictive substance, relative to a control.

**[0125]** In some embodiments, the method or the use includes reducing a frequency of an addictive substance use, relative to a control.

**[0126]** In some embodiments, the method or the use includes reducing a dose or dosage of a conventional medication used to treat an addiction, relative to a control.

**[0127]** In some embodiments, the present technology comprises a method of augmenting an effect of a conventional medication used to treat an addiction in a subject in need thereof, relative to a control, including administering to the subject a non-naturally occurring melanocortin analog including a sequence of Formula (I).

**[0128]** In some embodiments, the present technology comprises use of a non-naturally occurring melanocortin analog for augmenting an effect of a conventional medication used

to treat an addiction in a subject in need thereof, the non-naturally occurring melanocortin analog including a sequence of Formula (I).

**[0129]** In some embodiments, the present technology comprises a method of reducing or eliminating a need for a conventional medication used to treat an addiction in a subject in need thereof, relative to a control, including administering to the subject a non-naturally occurring melanocortin analog including a sequence of Formula (I).

**[0130]** In some embodiments, the present technology comprises use of a non-naturally occurring melanocortin analog for reducing or eliminating a need for a conventional medication used to treat an addiction in a subject in need thereof, the non-naturally occurring melanocortin analog including a sequence of Formula (I).

**[0131]** In some embodiments, the treatment of the addiction is improved during or after administration of the non-naturally occurring melanocortin analog relative to treatment of the addiction using the conventional medication to treat the addiction alone.

**[0132]** In some embodiments, the conventional medication to treat the addiction is selected from the group consisting of buprenorphine, naltrexone, acamprosate, methadone, naloxone, nalmefene, xycodone, levo-alpha-acetylmethadol (LAAM), codeine, lofexidine, and a slow-release morphine.

**[0133]** In some embodiments, the present technology comprises a method of reducing a need for a hospitalization or rehabilitation associated with addiction or use of an addictive substance, relative to a control, including administering to the subject a non-naturally occurring melanocortin analog including a sequence of Formula (I).

**[0134]** In some embodiments, the present technology comprises use of a non-naturally occurring melanocortin analog for reducing a need for a hospitalization or rehabilitation associated with addiction or use of an addictive substance, relative to a control, the non-naturally occurring melanocortin analog including a sequence of Formula (I).

**[0135]** In some embodiments, the present technology comprises a method of preventing or reducing a withdrawal from an addictive substance in a subject, including administering to the subject a non-naturally occurring melanocortin analog including a sequence of Formula (I).

**[0136]** In some embodiments, the present technology comprises use of a non-naturally occurring melanocortin analog for preventing or reducing a withdrawal from an addictive substance in a subject, relative to a control, the non-naturally occurring melanocortin analog including a sequence of Formula (I).

**[0137]** In some embodiments, the present technology comprises a method of preventing or reducing a symptom associated with withdrawal from an addictive substance in a subject relative to a control, including administering to the subject a non-naturally occurring melanocortin analog including a sequence of Formula (I).

**[0138]** In some embodiments, the present technology comprises use of a non-naturally occurring melanocortin analog for preventing or reducing a symptom associated with withdrawal from an addictive substance in a subject, relative to a control, the non-naturally occurring melanocortin analog including a sequence of Formula (I).

**[0139]** In some embodiments, the symptom associated with withdrawal from an addictive substance is selected from the group consisting of pain, anxiety, depression, diarrhea, dizziness, fatigue, muscle aches, nausea, sleep problems, suicidal ideation, tremors, and visual disturbances.

**[0140]** In some embodiments, the subject has an addiction to an addictive substance or is susceptible to an addiction to an addictive substance.

**[0141]** In some embodiments, the subject has used or is using one or more addictive substances.

**[0142]** In some embodiments, the present technology comprises a method or the use wherein the addictive substance includes a prescription medication, a substance in an over-the-counter medication, a recreational substance, or an illegal substance.

**[0143]** In some embodiments, the addictive substance is selected from the group consisting of an opioid, a painkiller, a stimulant, a narcotic, an alcohol, a sedative, marijuana, a cannabis, a tetrahydrocannabinol (THC), a cannabidiol (CBD), and an inhalant.

**[0144]** In some embodiments, the opioid is selected from the group consisting of morphine, heroin, codeine, oxycodone, hydrocodone, and fentanyl.

**[0145]** In some embodiments, the stimulant is selected from the group consisting of caffeine, nicotine, methamphetamines, cocaine, and amphetamines.

**[0146]** In some embodiments, the sedative includes a barbiturate or a benzodiazepine.

**[0147]** In some embodiments, the barbiturate is selected from the group consisting of phenobarbital, methohexital, butalbital, pentobarbital, primidone, and amobarbital.

**[0148]** In some embodiments, the benzodiazepine is selected from the group consisting of alprazolam, lorazepam, clonazepam, diazepam, and temazepam.

**[0149]** In some embodiments, the sedative is selected from the group consisting of tranquilizers, xylazine, eszopiclone, zaleplon, zolpidem, and zopiclone.

**[0150]** In some embodiments, the inhalant is selected from the group consisting of aerosols, butanes, freon, helium, nitrous oxide, propane, and nitrites.

**[0151]** In some embodiments, the nicotine includes a tobacco chew, a nicotine pouch, or a smoking device.

**[0152]** In some embodiments, the smoking device is selected from the group consisting of cigarettes, electronic cigarettes, cigars, and vape products.

**[0153]** In some embodiments, the control includes the subject before administration of the non-naturally occurring melanocortin analog.

**[0154]** In some embodiments, the control includes the subject at baseline.

**[0155]** In some embodiments, the non-naturally occurring melanocortin analog is a melanocortin 4 receptor (MC4R) agonist.

**[0156]** In some embodiments, the MC4R agonist is a full MC4R agonist.

**[0157]** In some embodiments, the MC4R agonist is a partial MC4R agonist.

**[0158]** In some embodiments, the non-naturally occurring melanocortin analog is a MC3R antagonist.

**[0159]** In some embodiments, the MC3R antagonist is a full MC3R antagonist.

**[0160]** In some embodiments, the MC3R antagonist is a partial MC3R antagonist.

**[0161]** In some embodiments, the non-naturally occurring melanocortin analog does not have MC3R activity.

**[0162]** In some embodiments, the non-naturally occurring melanocortin analog includes a sequence according to Formula (I), wherein: X1 is absent or is selected from the group consisting of norleucine (Nle), arginine (Arg), D-arginine (dArg), alanine (Ala), lysine (Lys), D-lysine (dLys), histidine (His), and D-histidine (dHis); X2 is absent, phenylalanine (Phe), or Nle; X3 is absent, Phe, or Nle; R1 is selected from the group consisting of Nle, D-norleucine (dNle), Ala, D-alanine (dAla), Arg, dArg, Lys, dLys, His, dHis, ornithine (Orn), D-ornithine (dOrn), D-leucine (dLeu), D-tyrosine (dTyr), phenylalanine (Phe), D-phenylalanine (dPhe), tryptophan (Trp), D-tryptophan (dTrp), aspartic acid (Asp), cysteine (Cys), and D-cysteine (dCys); R2 is selected from the group consisting of Asp, proline (Pro), D-aspartic acid (dAsp), Cys, dCys, D-penicillamine (dPen), Ala, dAla, Trp, Phe, dPhe, His, dHis, Tyr, and dTyr; R3 is absent or is selected from the group consisting of His, Ala, Pro, hydroxyproline (Hyp), leucine (Leu), D-glutamine (dGln), Phe, dPhe, Trp, dTrp, Tyr, dTyr, 4-amino-1,2,4,5-tetrahydro-2-benzazepin-3-one (Aba), 7-amino-7,8-dihydro-4H-[1,2,3]triazolo-[1,5-a][1,4]diazepin-6(5H)-one (Ata), 4-amino-1,4,5,6-tetrahydroazepino[4,3-b]indol-3(2H)-one (Aia), 2-aminotetraline-2-carboxylic acid (Atc), 1-amino-4-phenylcyclohexane-carboxylic acid (APC), 4-aminophenylpiperidine-4-carboxylic acid (APPC), octohydroindole-2-carboxylic acid (Oic), 1-amino-1-cyclohexanecarboxylic acid (Che), tetrahydro-isoquinoline-3-carboxylic acid (Tic), indoline-2-carboxylic acid (Ioc), 1-amino-1-cyclopentane carboxylic (Cpe), and biphenylalanine (Bip); R4 is selected from the group consisting of Phe, dPhe, 2'-D-naphthylalanine (dNal(2')), para-chloro-D-phenylalanine (p(Cl)dPhe), para-bromo-D-phenylalanine (p(Br)dPhe), and para-fluoro-D-phenylalanine (p(F)dPhe); R5 is selected from the group consisting of Arg, His, cisPro(guan), and transPro(guan); R6 is selected from the group consisting of Trp, dTrp, Phe, Aia, Aba, Ata, dNal(2'), 2'-naphthylalanine (Nal(2')), and 1'-naphthylalanine (Nal(1')); R7 is selected from the group consisting of Gly, Pro, Lys, dLys, Cys, dCys, penicillamine (Pen), dPen, and Orn; R8 is absent or Lys; Y1 is absent or is selected from the group consisting of valine (Val), D-valine (dVal), b2-valine (b2-Val), b3-valine (b3-Val), Pro, D-proline (dPro), b-proline (b-Pro), Hyp, D-hydroxyproline (dHyp), D-tert-leucine (dTle), dLeu, Trp, Arg, dArg, Lys, dLys, Gly, Ala, dAla, Asp, dAsp, asparagine (Asn), D-asparagine (dAsn), and D-threonine (dThr); Y2

is absent or is selected from the group consisting of Val, dVal, b2-Val, b3-Val, Pro, dPro, b-Pro, Hyp, dHyp, dTle, Arg, dArg, Gly, Ala, dAla, Asp, and dAsn; Y3 is absent or is selected from the group consisting of Val, dVal, Pro, dPro, dThr, Lys, and dLys; Y4 is absent or is selected from the group consisting of dVal, dPro, Asp, and dAsp; Y5 is absent or dVal; Y6 is absent or dVal; Y7 is absent or dPro; and the non-naturally occurring melanocortin analog is cyclized through a moiety selected from the group consisting of: a disulfide bond between R1 or R2 and R7 or R8 when each of R1 or R2 and R7 or R8 are independently selected from the group consisting of Cys, dCys, and dPen; a disulfide bond between R2 and R7 when R2 is Cys, R7 is Pen, and R3 is absent; a lactam bridge between R1 or R2 and R7 or R8 when R1 or R2 is Asp and R7 or R8 is Lys or Orn; and a lactam bridge between R2 and R7 when R2 is dAsp and R7 is dLys; provided that the non-naturally occurring melanocortin analog does not include a sequence selected from the group consisting of: Ac-Nle-c[Asp-Pro-Pro-dNal(2')-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 194); Ac-Nle-c[Asp-Pro-His-dNal(2')-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 5); Ac-Nle-c[Asp-Pro-His-dNal(2')-Arg-Trp-Lys]-dPro-dVal-NH2 (SEQ ID NO: 10); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dVal-dPro (SEQ ID NO: 2); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 3); Ac-Nle-c[Asp-Hyp-dNal(2')-Arg-Trp-Pro-Lys]-dVal-dPro-NH2 (SEQ ID NO: 4); Ac-Nle-c[Asp-Phe-His-dNal(2')-Arg-Trp-Lys]-dLeu-dPro-NH2 (SEQ ID NO: 6); Ac-Nle-c[Asp-Phe-His-dNal(2')-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 7); Ac-Nle-c[Asp-Hyp-dNal(2')-Arg-Trp-Pro-Lys]-dVal-dPro-NH2 (SEQ ID NO: 9); Ac-Nle-Phe-Phe-c[Asp-Phe-His-dNal(2')-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 12); Ac-dArg-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 15); Ac-dLeu-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 18); Ac-dAla-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 20); Ac-Ala-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 21); Ac-dNle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 24); Ac-dCys-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 28); Ac-dPhe-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 29); Ac-dTyr-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 30); dTyr-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 35); Tyr-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 36); Ac-Nle-c[Cys-Pro-dNal(2')-Arg-Trp-Cys]-dVal-dPro-NH2 (SEQ ID NO: 40); Ac-Nle-c[dCys-Pro-dNal(2')-Arg-Trp-Cys]-dVal-dPro-NH2 (SEQ ID NO: 41); Ac-Nle-c[Cys-Pro-dNal(2')-Arg-

Trp-dCys]-dVal-dPro-NH2 (SEQ ID NO: 42); Ac-Nle-c[dCys-Pro-dNal(2')-Arg-Trp-dCys]-dVal-dPro-NH2 (SEQ ID NO: 43); Ac-Nle-c[Cys-Pro-dNal(2')-Arg-Trp-Pen]-dVal-dPro-NH2 (SEQ ID NO: 48); Ac-Nle-c[dPen-Pro-dNal(2')-Arg-Trp-dPen]-dVal-dPro-NH2 (SEQ ID NO: 54); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Orn]-dVal-dPro-NH2 (SEQ ID NO: 64); Ac-Nle-c[Asp-dNal(2')-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 68); Ac-Nle-c[Asp-Ala-dNal(2')-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 69); Ac-Nle-c[Asp-Leu-dNal(2')-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 76); Ac-Nle-c[Asp-Trp-dNal(2')-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 82); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-Val-Pro-NH2 (SEQ ID NO: 115); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dVal-dPro-OH (SEQ ID NO: 116); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dPro-dVal-OH (SEQ ID NO: 117); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dVal-Hyp-NH2 (SEQ ID NO: 118); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dVal-dHyp-NH2 (SEQ ID NO: 119); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-Val-Hyp-NH2 (SEQ ID NO: 120); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-Val-dHyp-NH2 (SEQ ID NO: 121); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-Hyp-dVal-NH2 (SEQ ID NO: 122); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dHyp-dVal-NH2 (SEQ ID NO: 123); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-Hyp-Val-NH2 (SEQ ID NO: 124); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dHyp-Val-NH2 (SEQ ID NO: 125); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dVal-dVal-NH2 (SEQ ID NO: 126); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dPro-dPro-NH2 (SEQ ID NO: 127); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dVal-NH2 (SEQ ID NO: 128); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dPro-NH2 (SEQ ID NO: 129); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-Val-NH2 (SEQ ID NO: 130); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-Pro-NH2 (SEQ ID NO: 131); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-Ala-NH2 (SEQ ID NO: 132); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dAla-NH2 (SEQ ID NO: 133); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dHyp-NH2 (SEQ ID NO: 134); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-Hyp-NH2 (SEQ ID NO: 135); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dAla-dAla-NH2 (SEQ ID NO: 136); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-Ala-Ala-NH2 (SEQ ID NO: 137); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-Gly-Gly-NH2 (SEQ ID NO: 138); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dVal-Asp-NH2 (SEQ ID NO: 139); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dVal-Arg-NH2 (SEQ ID NO: 140); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dVal-dArg-NH2 (SEQ ID NO: 143); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dVal-dAsn-NH2 (SEQ ID NO: 144); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-Asp-dPro-NH2 (SEQ ID NO:

145); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-Arg-dPro-NH2 (SEQ ID NO: 146); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-Asn-dPro-NH2 (SEQ ID NO: 147); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dAsp-dPro-NH2 (SEQ ID NO: 148); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dArg-dPro-NH2 (SEQ ID NO: 149); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dAsn-dPro-NH2 (SEQ ID NO: 150); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-Asp-NH2 (SEQ ID NO: 151); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-Arg-NH2 (SEQ ID NO: 152); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-Asn-NH2 (SEQ ID NO: 153); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dAsp-NH2 (SEQ ID NO: 154); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dArg-NH2 (SEQ ID NO: 155); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dAsn-NH2 (SEQ ID NO: 156); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-Lys-Pro-Val-NH2 (SEQ ID NO: 157); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-Lys-dPro-dVal-NH2 (SEQ ID NO: 158); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dLys-dPro-dVal-NH2 (SEQ ID NO: 159); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-Lys-dPro-NH2 (SEQ ID NO: 160); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dLys-dPro-NH2 (SEQ ID NO: 161); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-Lys-Val-Pro-NH2 (SEQ ID NO: 162); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-Lys-dVal-dPro-NH2 (SEQ ID NO: 164); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dLys-dVal-dPro-NH2 (SEQ ID NO: 164); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-Arg-Pro-Val-NH2 (SEQ ID NO: 165); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-Arg-dPro-dVal-NH2 (SEQ ID NO: 166); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dArg-dPro-dVal-NH2 (SEQ ID NO: 167); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-Arg-Val-Pro-NH2 (SEQ ID NO: 168); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-Arg-dVal-dPro-NH2 (SEQ ID NO: 169); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dArg-dVal-dPro-NH2 (SEQ ID NO: 170); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dTle-dVal-dPro-NH2 (SEQ ID NO: 171); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 172); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dTle-dVal-NH2 (SEQ ID NO: 173); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dTle-dTle-NH2 (SEQ ID NO: 174); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dTle-dTle-dPro-NH2 (SEQ ID NO: 175); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dTle-dTle-dVal-NH2 (SEQ ID NO: 176); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dPro-dTle-NH2 (SEQ ID NO: 177); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dVal-dTle-NH2 (SEQ ID NO: 178); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dVal-dVal-dPro-NH2 (SEQ ID NO: 179); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dPro-dVal-dPro-NH2 (SEQ ID NO: 180); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dVal-dVal-dVal-dPro-NH2 (SEQ ID NO: 181);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dVal-dPro-dVal-dPro-NH2 (SEQ ID NO: 182); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dVal-dVal-dVal-dVal-dVal-dVal-dPro-NH2 (SEQ ID NO: 183); Ac-Nle-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 184); Ac-Nle-Nle-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 185); Ac-Nle-Nle-Nle-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 186); Ac-Nle-c[Asp-Trp-Pro-dNal(2')-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 195); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-dTrp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 196); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-Trp-NH2 (SEQ ID NO: 203); Ac-Nle-c[Asp-Aba-dNal(2')-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 204); Ac-Nle-c[Asp-Aia-dNal(2')-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 205); Ac-Nle-c[Asp-Ata-dNal(2')-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 206); Ac-Nle-c[Asp-Cpe-dNal(2')-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 240); Ac-Nle-c[Asp-Che-dNal(2')-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 241); Ac-Nle-c[Asp-Oic-dNal(2')-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 242); Ac-Nle-c[Asp-Tic-dNal(2')-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 244); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Pro-Lys]-dVal-dPro-NH2 (SEQ ID NO: 245); Ac-Nle-c[Asp-His-dNal(2')-transPro(guan)-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 247); Ac-Nle-c[Asp-His-dNal(2')-cisPro(guan)-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 248); Ac-Nle-c[Asp-Pro-dNal(2')-transPro(guan)-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 250); Ac-Nle-c[Asp-Pro-dNal(2')-cisPro(guan)Pro-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 251); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Aba-Lys]-dVal-dPro-NH2 (SEQ ID NO: 253); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Ata-Lys]-dVal-dPro-NH2 (SEQ ID NO: 254); Ac-Nle-c[Asp-Glu-dNal(2')-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 255); Ac-Nle-c[Asp-Glu-dNal(2')-Arg-Trp-Gly-Lys]-dVal-dPro-NH2 (SEQ ID NO: 256); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Gly-Lys]-dVal-dPro-NH2 (SEQ ID NO: 259); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Gly-Lys]-dPro-dPro-Lys-Asp-NH2 (SEQ ID NO: 260); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Gly-Lys]-dPro-dPro-dLys-dAsp-NH2 (SEQ ID NO: 261); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dPro-dPro-dLys-dAsp-NH2 (SEQ ID NO: 263); Ac-Nle-c[Asp-Ala-His-dNal(2')-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 273); Ac-Arg-c[Asp-Ala-His-dNal(2')-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 274); Ac-dArg-c[Asp-Ala-His-dNal(2')-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 275); Ac-dLeu-c[dPen-Pro-dNal(2')-Arg-Trp-dPen]-dVal-dPro-NH2 (SEQ ID NO: 327); Ac-dNle-c[dPen-Pro-dNal(2')-Arg-Trp-dPen]-dVal-dPro-NH2 (SEQ ID NO: 328); Ac-dArg-c[dPen-Pro-dNal(2')-Arg-Trp-dPen]-dVal-dPro-NH2 (SEQ ID NO: 329); Ac-Arg-c[dPen-Pro-

dNal(2')-Arg-Trp-dPen]-dVal-dPro-NH2 (SEQ ID NO: 330); Ac-dPhe-c[dPen-Pro-dNal(2')-Arg-Trp-dPen]-dVal-dPro-NH2 (SEQ ID NO: 331); Ac-dTyr-c[dPen-Pro-dNal(2')-Arg-Trp-dPen]-dVal-dPro-NH2 (SEQ ID NO: 332); Ac-Ala-c[dPen-Pro-dNal(2')-Arg-Trp-dPen]-dVal-dPro-NH2 (SEQ ID NO: 333); Ac-dHis-c[dPen-Pro-dNal(2')-Arg-Trp-dPen]-dVal-dPro-NH2 (SEQ ID NO: 334); Ac-His-c[dPen-Pro-dNal(2')-Arg-Trp-dPen]-dVal-dPro-NH2 (SEQ ID NO: 335); Ac-dLys-c[dPen-Pro-dNal(2')-Arg-Trp-dPen]-dVal-dPro-NH2 (SEQ ID NO: 336); Ac-Lys-c[dPen-Pro-dNal(2')-Arg-Trp-dPen]-dVal-dPro-NH2 (SEQ ID NO: 337); Ac-Nle-c[dPen-Pro-dNal(2')-Arg-Trp-dPen]-dArg-dVal-dPro-NH2 (SEQ ID NO: 344); Ac-Nle-c[dPen-Pro-dNal(2')-Arg-Trp-dPen]-dLys-dVal-dPro-NH2 (SEQ ID NO: 345); Ac-Nle-c[dPen-Pro-dNal(2')-Arg-Trp-dPen]-dArg-dPro-NH2 (SEQ ID NO: 346); Ac-Nle-c[dPen-Pro-dNal(2')-Arg-Trp-dPen]-dLys-dPro-NH2 (SEQ ID NO: 347); Ac-Nle-c[dPen-Pro-dNal(2')-Arg-Trp-dPen]-dVal-dHyp-NH2 (SEQ ID NO: 348); Ac-Nle-c[dPen-Pro-dNal(2')-Arg-Trp-dPen]-dTle-dPro-NH2 (SEQ ID NO: 349); Ac-Nle-c[dPen-Pro-dNal(2')-Arg-Trp-Gly-dPen]-dVal-dPro-NH2 (SEQ ID NO: 350); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Aia-Lys]-dVal-dPro-NH2 (SEQ ID NO: 103); Ac-Nle-c[Asp-Ioc-dNal(2')-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 243); Ac-Nle-c[Cys-dNal(2')-Arg-Trp-Cys]-dVal-dPro-NH2 (SEQ ID NO: 44); Ac-Nle-c[dCys-dNal(2')-Arg-Trp-Cys]-dVal-dPro-NH2 (SEQ ID NO: 45); Ac-Nle-c[Cys-dNal(2')-Arg-Trp-dCys]-dVal-dPro-NH2 (SEQ ID NO: 46); Ac-Nle-c[dCys-dNal(2')-Arg-Trp-dCys]-dVal-dPro-NH2 (SEQ ID NO: 47); Ac-Nle-c[Cys-dNal(2')-Arg-Trp-Pen]-dVal-dPro-NH2 (SEQ ID NO: 56); Ac-Nle-c[dPen-dNal(2')-Arg-Trp-dPen]-dVal-dPro-NH2 (SEQ ID NO: 62); Ac-Nle-c[Asp-dTrp-dNal(2')-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 83); Ac-Nle-c[dPen-Ala-dNal(2')-Arg-Trp-dPen]-dVal-dPro-NH2 (SEQ ID NO: 338); Ac-Nle-c[dPen-Leu-dNal(2')-Arg-Trp-dPen]-dVal-dPro-NH2 (SEQ ID NO: 339); Ac-Nle-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 223); Ac-Arg-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 464); Ac-Lys-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 465); Ac-dLys-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 466); Ac-His-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 467); Ac-dHis-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 468); Ac-Nle-Nle-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 469); Ac-Nle-c[Asp-His-p(F)dPhe-His-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 470); Ac-Nle-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dVal-dVal-dVal-dPro-NH2 (SEQ ID NO: 474); Ac-Nle-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dPro-dVal-

dPro-NH2 (SEQ ID NO: 475); Ac-Nle-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 476); Ac-Nle-Nle-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 477); Ac-Nle-Nle-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dPro-dVal-dPro-NH2 (SEQ ID NO: 478); Ac-Arg-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 481); Ac-Lys-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 482); Ac-dLys-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 483); Ac-His-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 484); Ac-dHis-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 485); Ac-dArg-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 463); Ac-Ala-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 462); Ac-Ala-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 479); Ac-Nle-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dTle-dTle-dVal-NH2 (SEQ ID NO: 473); Ac-dArg-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 480); Ac-Nle-c[Asp-Gln-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 491); Ac-Nle-c[Asp-Bip-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 489); Ac-Nle-c[Asp-Trp-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 493); Ac-Nle-c[Asp-Pro-p(F)dPhe-Arg-dNal(2')-Lys]-dVal-dPro-NH2 (SEQ ID NO: 444); Ac-Nle-c[Asp-Pro-p(F)dPhe-Arg-Nal(2')-Lys]-dVal-dPro-NH2 (SEQ ID NO: 445); Ac-Nle-c[Asp-Tyr-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 495); Ac-Nle-c[Asp-Phe-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 487); Ac-Nle-c[Asp-dPhe-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 488); Ac-Nle-c[Asp-dTrp-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 494); Ac-Nle-c[Asp-His-p(F)dPhe-Arg-dNal(2')-Lys]-dVal-dPro-NH2 (SEQ ID NO: 471); Ac-Nle-c[Cys-Pro-p(F)dPhe-Arg-Trp-Cys]-dVal-dPro-NH2 (SEQ ID NO: 432); Ac-Nle-c[Asp-Pro-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 217); Ac-Nle-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 222); Ac-Nle-c[Cys-His-p(Br)dPhe-Arg-Trp-Cys]-dVal-dPro-NH2 (SEQ ID NO: 535); Ac-Ala-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 538); Ac-Nle-Nle-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 545); Ac-Nle-c[Asp-His-p(Br)dPhe-His-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 546); Ac-Nle-c[Asp-His-p(Br)dPhe-Arg-dNal(2')-Lys]-dVal-dPro-NH2 (SEQ ID NO: 547); Ac-Nle-c[Asp-His-p(Br)dPhe-Arg-Nal(2')-Lys]-dVal-dPro-NH2 (SEQ ID NO: 548); Ac-Nle-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dTle-dTle-dVal-NH2 (SEQ ID NO: 549); Ac-Nle-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dPro-dVal-dPro-NH2 (SEQ ID NO: 551); Ac-Nle-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dTle-dPro-

NH2 (SEQ ID NO: 552); Ac-Nle-Nle-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 553); Ac-Ala-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 555); Ac-Nle-c[Asp-dHis-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 562); Ac-Nle-c[Asp-Phe-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 563); Ac-Nle-c[Asp-dPhe-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 564); Ac-Nle-c[Asp-Bip-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 565); Ac-Nle-c[Asp-dGln-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 568); Ac-Nle-c[Asp-Trp-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 569); Ac-Nle-c[Asp-dTrp-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 570); Ac-Nle-c[Asp-Tyr-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 571); Ac-Nle-c[Asp-dTyr-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 572); Ac-dArg-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 539); Ac-dHis-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 544); Ac-dHis-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 561); Ac-dArg-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 556); Ac-dLys-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 542); Ac-His-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 560); Ac-His-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 543); Ac-dLys-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 559); Ac-Arg-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 557); Ac-Lys-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 541); Ac-Nle-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dVal-dVal-dVal-dPro-NH2 (SEQ ID NO: 550); Ac-Lys-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 558); Ac-Arg-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 540); Ac-Nle-Nle-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dPro-dVal-dPro-NH2 (SEQ ID NO: 554); Ac-Nle-c[Asp-His-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 363); Ac-Nle-c[Asp-His-dPhe-Arg-Trp-Pro-Lys]-dVal-dPro-NH2 (SEQ ID NO: 418); Ac-Nle-c[Asp-His-dPhe-Arg-Trp-Lys]-dPro-dVal-NH2 (SEQ ID NO: 621); Ac-Nle-c[Asp-His-dPhe-transPro(guan)-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 228); Ac-Nle-c[Asp-His-dPhe-cisPro(guan)-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 229); Ac-Nle-c[Asp-Ala-His-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 380); Ac-Nle-c[Asp-Trp-Pro-dPhe-His-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 398); Ac-Nle-c[Asp-Trp-Pro-dPhe-Arg-Phe-Lys]-dVal-dPro-NH2 (SEQ ID NO: 401); Ac-Nle-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dPro-dVal-dPro-NH2 (SEQ ID NO: 639); Ac-Nle-c[Asp-Pro-dPhe-Arg-dNal(2')-

Lys]-dVal-dPro-NH2 (SEQ ID NO: 430); Ac-Nle-c[Asp-Pro-dPhe-Arg-Nal(2')-Lys]-dVal-dPro-NH2 (SEQ ID NO: 431); Ac-Nle-c[Asp-Pro-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 225); Ac-Nle-c[dPen-dPhe-Arg-Trp-dPen]-dVal-dPro-NH2 (SEQ ID NO: 326); Ac-Nle-c[Asp-Pro-His-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 297); Ac-Nle-c[Asp-Pro-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 215); Ac-Nle-c[Asp-Phe-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 525); Ac-Nle-c[Asp-dPhe-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 526); Ac-Nle-c[Asp-Bip-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 527); Ac-Nle-c[Asp-Trp-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 531); Ac-Nle-c[Asp-Tyr-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 533); Ac-Nle-c[Asp-dTyr-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 534); Ac-Nle-c[Asp-dTrp-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 532); Ac-Nle-c[dCys-His-p(Cl)dPhe-Arg-Trp-Cys]-dVal-dPro-NH2 (SEQ ID NO: 498); Ac-Nle-c[Cys-His-p(Cl)dPhe-Arg-Trp-Cys]-dVal-dPro-NH2 (SEQ ID NO: 497); Ac-Nle-c[Asp-His-p(Cl)dPhe-Arg-dNal(2')-Lys]-dVal-dPro-NH2 (SEQ ID NO: 509); Ac-Nle-c[Asp-His-p(Cl)dPhe-Arg-Nal(2')-Lys]-dVal-dPro-NH2 (SEQ ID NO: 510); Ac-Nle-c[Asp-His-p(Cl)dPhe-His-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 508); Ac-Nle-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 220); Ac-Nle-Nle-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 507); Ac-Ala-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 517); Ac-Ala-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 500); Ac-Nle-Nle-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dPro-dVal-dPro-NH2 (SEQ ID NO: 516); Ac-Nle-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 514); Ac-Nle-c[Asp-dGln-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 530); Ac-Arg-c[Asp-dAla-His-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 268); Ac-Nle-c[Asp-dAla-His-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 378); Ac-dArg-c[Asp-dAla-His-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 379); Ac-Nle-c[Asp-dAla-His-dNal(2')-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 266); Ac-Arg-c[Asp-dAla-His-dNal(2')-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 267); Ac-Arg-c[Cys-dAla-His-dNal(2')-Arg-Trp-Cys]-dVal-dPro-NH2 (SEQ ID NO: 269); Ac-dArg-c[Asp-dAla-His-dNal(2')-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 270); Ac-Arg-c[Cys-dAla-His-dNal(2')-Arg-Trp-Cys]-NH2 (SEQ ID NO: 282); and Ac-Arg-c[Asp-dAla-His-dNal(2')-Arg-Trp-Lys]-NH2 (SEQ ID NO: 283).

**[0163]** In some embodiments, the present technology comprises a method or use, wherein the non-naturally occurring melanocortin analog includes a sequence according to Formula (IA): X1-X2-X3-R1-R2-R3-R4-R5-R6-R7-R8-Y1-Y2-Y3-Y4 (IA), wherein: X1 is absent or is selected from the group consisting of norleucine (Nle), arginine (Arg), D-arginine (dArg), alanine (Ala), lysine (Lys), D-lysine (dLys), histidine (His), D-histidine (dHis); X2 is absent, phenylalanine (Phe), or Nle; X3 is absent, Phe, or Nle; R1 is selected from the group consisting of Nle, D-norleucine (dNle), Ala, D-alanine (dAla), Arg, dArg, Lys, dLys, His, dHis, ornithine (Orn), D-ornithine (dOrn), D-leucine (dLeu), D-tyrosine (dTyr), phenylalanine (Phe), D-phenylalanine (dPhe), tryptophan (Trp), D-tryptophan (dTrp), aspartic acid (Asp), cysteine (Cys), and D-cysteine (dCys); R2 is selected from the group consisting of Asp, D-aspartic acid (dAsp), Cys, dCys, D-penicillamine (dPen), Ala, Trp, Phe, dPhe, His, dHis, Tyr, and dTyr; R3 is absent or is selected from the group consisting of His, Ala, proline (Pro), hydroxyproline (Hyp), leucine (Leu), D-glutamine (dGln), Phe, dPhe, Trp, dTrp, Tyr, dTyr, 2-aminotetraline-2-carboxylic acid (Atc), octohydroindole-2-carboxylic acid (Oic), 1-amino-1-cyclohexanecarboxylic acid (Che), tetrahydro-isoquinoline-3-carboxylic acid (Tic), 1-amino-1-cyclopentane carboxylic (Cpe), and biphenylalanine (Bip); R4 is selected from the group consisting of dPhe, para-chloro-D-phenylalanine (p(Cl)dPhe), para-bromo-D-phenylalanine (p(Br)dPhe), and para-fluoro-D-phenylalanine (p(F)dPhe); R5 is Arg or His; R6 is selected from the group consisting of Trp, dTrp, Phe, dNal(2'), 2'-naphthylalanine (Nal(2')), and 1'-naphthylalanine (Nal(1')); R7 is selected from the group consisting of Gly, Pro, Lys, dLys, Cys, dCys, penicillamine (Pen), dPen, and Orn; R8 is absent or Lys; Y1 is selected from the group consisting of valine (Val), D-valine (dVal), b2-valine (b2-Val), b3-valine (b3-Val), Pro, D-proline (dPro), b-proline (b-Pro), Hyp, D-hydroxyproline (dHyp), D-tert-leucine (dTle), dLeu, Trp, Arg, dArg, Lys, dLys, Gly, Ala, dAla, Asp, dAsp, asparagine (Asn), D-asparagine (dAsn), and D-threonine (dThr); Y2 is absent or is selected from the group consisting of Val, dVal, b2-Val, b3-Val, Pro, dPro, b-Pro, Hyp, dHyp, dTle, Arg, dArg, Gly, Ala, dAla, Asp, and dAsn; Y3 is absent or is selected from the group consisting of Val, dVal, Pro, dPro, dThr, Lys, and dLys; Y4 is absent or is selected from the group consisting of dVal, dPro, Asp, and dAsp; and the non-naturally occurring melanocortin analog is cyclized through a moiety selected from the group consisting of: a disulfide bond between R1 or R2 and R7 or R8 when each of R1 or R2 and R7 or R8 are independently selected from the group consisting

of Cys, dCys, and dPen; a disulfide bond between R2 and R7 when R2 is Cys,R7 is Pen, and R3 is absent; a lactam bridge between R1 or R2 and R7 or R8 when R1 or R2 is Asp and R7 or R8 is Lys or Orn; and a lactam bridge between R2 and R7 when R2 is dAsp and R7 is dLys; provided that: when R4 is p(F)dPhe, then (i) R3 is selected from Pro, dGln, dTyr, R6 is Trp, and the non-naturally occurring melanocortin analog is not cyclized between Cys at R2 and Cys at R7 or (ii) R3 is His and either R6 is Nal(2') or the non-naturally occurring melanocortin analog is cyclized through a disulfide bond between R2 and R7, where R2 and R7 are the same; when R4 is p(Br)dPhe, then the non-naturally occurring melanocortin analog is cyclized through a disulfide bond between dCys at R2 and Cys or dCys at R7; when R4 is dPhe, then (i) R3 is not His, Pro, or absent, (ii) R3 is His and either R2 is Phe or dAla or R2 is Ala and X1 is Arg or dArg, (iii) R3 is Pro and (a) R2 is Trp, and R5 is not His or R6 is not Phe or (b) R2 is not Trp or Pro, and either R5 is not dNal(2') or Nal(2') or X1 and Y3 are not both present, or (iv) R3 is absent and R2 and R7 are not both dPen; and when R4 is p(Cl)dPhe, then (i) R3 is selected from Aba, Aia, and Ata or (ii) R3 is His, R1 is not Ala, and (a) if R1 is Nle and Y1Y2 is dVal-dPro, then X1 is absent and the non-naturally occurring melanocortin analog is cyclized through a disulfide bond between dCys at R2 and dCys at R7, or (b) if R1 is Nle, and Y1Y2 is not dVal-dPro, then either X1 or Y3 is present.

**[0164]** In some embodiments, the non-naturally occurring melanocortin analog includes a sequence according to Formula (IA), wherein: X1 is absent or is selected from the group consisting of norleucine (Nle), arginine (Arg), D-arginine (dArg), alanine (Ala), lysine (Lys), D-lysine (dLys), histidine (His), D-histidine (dHis); X2 is absent, phenylalanine (Phe), or Nle; X3 is absent, Phe, or Nle; R1 is selected from the group consisting of Nle, D-norleucine (dNle), Ala, D-alanine (dAla), Arg, dArg, Lys, dLys, His, dHis, ornithine (Orn), D-ornithine (dOrn), D-leucine (dLeu), D-tyrosine (dTyr), phenylalanine (Phe), D-phenylalanine (dPhe), tryptophan (Trp), D-tryptophan (dTrp), aspartic acid (Asp), cysteine (Cys), and D-cysteine (dCys); R2 is selected from the group consisting of Asp, D-aspartic acid (dAsp), Cys, dCys, D-penicillamine (dPen), Ala, Trp, Phe, dPhe, His, dHis, Tyr, and dTyr; R3 is absent or is selected from the group consisting of His, Ala, proline (Pro), hydroxyproline (Hyp), leucine (Leu), D-glutamine (dGln), Phe, dPhe, Trp, dTrp, Tyr, dTyr, 2-aminotetraline-2-carboxylic acid (Atc), octohydroindole-2-carboxylic acid (Oic), 1-amino-1-cyclohexanecarboxylic acid (Che), tetrahydro-isoquinoline-3-carboxylic acid (Tic), 1-amino-

1-cyclopentane carboxylic (Cpe), and biphenylalanine (Bip); R4 is selected from the group consisting of dPhe, para-chloro-D-phenylalanine (p(Cl)dPhe), para-bromo-D-phenylalanine (p(Br)dPhe), and para-fluoro-D-phenylalanine (p(F)dPhe); R5 is Arg or His; R6 is selected from the group consisting of Trp, dTrp, Phe, dNal(2'), 2'-naphthylalanine (Nal(2')), and 1'-naphthylalanine (Nal(1')); R7 is selected from the group consisting of Gly, Pro, Lys, dLys, Cys, dCys, penicillamine (Pen), dPen, and Orn; R8 is absent or Lys; Y1 is selected from the group consisting of valine (Val), D-valine (dVal), b2-valine (b2-Val), b3-valine (b3-Val), Pro, D-proline (dPro), b-proline (b-Pro), Hyp, D-hydroxyproline (dHyp), D-tert-leucine (dTle), dLeu, Trp, Arg, dArg, Lys, dLys, Gly, Ala, dAla, Asp, dAsp, asparagine (Asn), D-asparagine (dAsn), and D-threonine (dThr); Y2 is absent or is selected from the group consisting of Val, dVal, b2-Val, b3-Val, Pro, dPro, b-Pro, Hyp, dHyp, dTle, Arg, dArg, Gly, Ala, dAla, Asp, and dAsn; Y3 is absent or is selected from the group consisting of Val, dVal, Pro, dPro, dThr, Lys, and dLys; Y4 is absent or is selected from the group consisting of dVal, dPro, Asp, and dAsp; and the non-naturally occurring melanocortin analog is cyclized through a moiety selected from the group consisting of: a disulfide bond between R1 or R2 and R7 or R8 when each of R1 or R2 and R7 or R8 are independently selected from the group consisting of Cys, dCys, and dPen; a disulfide bond between R2 and R7 when R2 is Cys, R7 is Pen, and R3 is absent; a lactam bridge between R1 or R2 and R7 or R8 when R1 or R2 is Asp and R7 or R8 is Lys or Orn; and a lactam bridge between R2 and R7 when R2 is dAsp and R7 is dLys; provided that the non-naturally occurring melanocortin analog does not include a sequence selected from the group consisting of: Ac-Nle-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 223); Ac-Arg-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 464); Ac-Lys-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 465); Ac-dLys-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 466); Ac-His-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 467); Ac-dHis-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 468); Ac-Nle-Nle-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 469); Ac-Nle-c[Asp-His-p(F)dPhe-His-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 470); Ac-Nle-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dVal-dVal-dVal-dPro-NH2 (SEQ ID NO: 474); Ac-Nle-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dPro-dVal-dPro-NH2 (SEQ ID NO: 475); Ac-Nle-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 476); Ac-Nle-Nle-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ

ID NO: 477); Ac-Nle-Nle-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dPro-dVal-dPro-NH2 (SEQ ID NO: 478); Ac-Arg-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 481); Ac-Lys-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 482); Ac-dLys-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 483); Ac-His-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 484); Ac-dHis-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 485); Ac-dArg-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 463); Ac-Ala-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 462); Ac-Ala-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 479); Ac-Nle-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dTle-dTle-dVal-NH2 (SEQ ID NO: 473); Ac-dArg-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 480); Ac-Nle-c[Asp-Bip-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 489); Ac-Nle-c[Asp-Trp-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 493); Ac-Nle-c[Asp-Pro-p(F)dPhe-Arg-dNal(2')-Lys]-dVal-dPro-NH2 (SEQ ID NO: 444); Ac-Nle-c[Asp-Pro-p(F)dPhe-Arg-Nal(2')-Lys]-dVal-dPro-NH2 (SEQ ID NO: 445); Ac-Nle-c[Asp-Tyr-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 495); Ac-Nle-c[Asp-Phe-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 487); Ac-Nle-c[Asp-dPhe-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 488); Ac-Nle-c[Asp-dTrp-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 494); Ac-Nle-c[Asp-His-p(F)dPhe-Arg-dNal(2')-Lys]-dVal-dPro-NH2 (SEQ ID NO: 471); Ac-Nle-c[Cys-Pro-p(F)dPhe-Arg-Trp-Cys]-dVal-dPro-NH2 (SEQ ID NO: 432); Ac-Nle-c[dCys-His-p(F)dPhe-Arg-Trp-Cys]-dVal-dPro-NH2 (SEQ ID NO: 460); Ac-Nle-c[Asp-Pro-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 217); Ac-Nle-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 222); Ac-Nle-c[Cys-His-p(Br)dPhe-Arg-Trp-Cys]-dVal-dPro-NH2 (SEQ ID NO: 535); Ac-Ala-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 538); Ac-Nle-Nle-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 545); Ac-Nle-c[Asp-His-p(Br)dPhe-His-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 546); Ac-Nle-c[Asp-His-p(Br)dPhe-Arg-dNal(2')-Lys]-dVal-dPro-NH2 (SEQ ID NO: 547); Ac-Nle-c[Asp-His-p(Br)dPhe-Arg-Nal(2')-Lys]-dVal-dPro-NH2 (SEQ ID NO: 548); Ac-Nle-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dTle-dTle-dVal-NH2 (SEQ ID NO: 549); Ac-Nle-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dPro-dVal-dPro-NH2 (SEQ ID NO: 551); Ac-Nle-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 552); Ac-Nle-Nle-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 553); Ac-Ala-c[Asp-His-p(Br)dPhe-

Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 555); Ac-Nle-c[Asp-Phe-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 563); Ac-Nle-c[Asp-dPhe-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 564); Ac-Nle-c[Asp-Bip-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 565); Ac-Nle-c[Asp-dGln-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 568); Ac-Nle-c[Asp-Trp-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 569); Ac-Nle-c[Asp-dTrp-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 570); Ac-Nle-c[Asp-Tyr-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 571); Ac-Nle-c[Asp-dTyr-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 572); Ac-dArg-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 539); Ac-dHis-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 544); Ac-dHis-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 561); Ac-dArg-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 556); Ac-dLys-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 542); Ac-His-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 560); Ac-His-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 543); Ac-dLys-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 559); Ac-Arg-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 557); Ac-Lys-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 541); Ac-Nle-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dVal-dVal-dVal-dPro-NH2 (SEQ ID NO: 550); Ac-Lys-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 558); Ac-Arg-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 540); Ac-Nle-Nle-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dPro-dVal-dPro-NH2 (SEQ ID NO: 554); Ac-Nle-c[Asp-His-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 363); Ac-Nle-c[Asp-His-dPhe-Arg-Trp-Pro-Lys]-dVal-dPro-NH2 (SEQ ID NO: 418); Ac-Nle-c[Asp-His-dPhe-Arg-Trp-Lys]-dPro-dVal-NH2 (SEQ ID NO: 621); Ac-Nle-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dPro-dVal-dPro-NH2 (SEQ ID NO: 639); Ac-Nle-c[dPen-dPhe-Arg-Trp-dPen]-dVal-dPro-NH2 (SEQ ID NO: 326); Ac-Nle-c[Asp-Trp-Pro-dPhe-His-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 398); Ac-Nle-c[Asp-Trp-Pro-dPhe-Arg-Phe-Lys]-dVal-dPro-NH2 (SEQ ID NO: 401); Ac-Nle-c[Asp-Pro-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 225); Ac-Nle-c[Asp-Pro-dPhe-Arg-dNal(2')-Lys]-dVal-dPro-NH2 (SEQ ID NO: 430); Ac-Nle-c[Asp-Pro-dPhe-Arg-Nal(2')-Lys]-dVal-dPro-NH2 (SEQ ID NO: 431); Ac-Nle-c[Asp-Ala-His-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 380); Ac-Nle-c[Asp-Pro-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 215); Ac-Nle-c[Asp-Phe-p(Cl)dPhe-Arg-Trp-Lys]-

dVal-dPro-NH2 (SEQ ID NO: 525); Ac-Nle-c[Asp-dPhe-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 526); Ac-Nle-c[Asp-Bip-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 527); Ac-Nle-c[Asp-Trp-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 531); Ac-Nle-c[Asp-Tyr-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 533); Ac-Nle-c[Asp-dTyr-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 534); Ac-Nle-c[Asp-dTrp-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 532); Ac-Nle-c[dCys-His-p(Cl)dPhe-Arg-Trp-Cys]-dVal-dPro-NH2 (SEQ ID NO: 498); Ac-Nle-c[Cys-His-p(Cl)dPhe-Arg-Trp-Cys]-dVal-dPro-NH2 (SEQ ID NO: 497); Ac-Nle-c[Asp-His-p(Cl)dPhe-Arg-dNal(2')-Lys]-dVal-dPro-NH2 (SEQ ID NO: 509); Ac-Nle-c[Asp-His-p(Cl)dPhe-Arg-Nal(2')-Lys]-dVal-dPro-NH2 (SEQ ID NO: 510); Ac-Nle-c[Asp-His-p(Cl)dPhe-His-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 508); Ac-Nle-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 220); Ac-Nle-Nle-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 507); Ac-Ala-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 517); Ac-Ala-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 500); Ac-Nle-Nle-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dPro-dVal-dPro-NH2 (SEQ ID NO: 516); and Ac-Nle-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 514).

**[0165]** In some embodiments, the present technology comprises a method or use, wherein the non-naturally occurring melanocortin analog includes a sequence of Formula (IB): X1-X2-X3-R1-R2-Pro-R4-R5-R6-R7-R8-Y1-Y2-Y3-Y4-Y5-Y6-Y7 (IB), wherein: X1 is absent or norleucine (Nle); X2 is absent or Nle; X3 is absent or Nle; R1 is selected from the group consisting of Nle, D-norleucine (dNle), alanine (Ala), D-alanine (dAla), arginine (Arg), D-arginine (dArg), lysine (Lys), D-lysine (dLys), histidine (His), D-histidine (dHis), ornithine (Orn), D-ornithine (dOrn), D-leucine (dLeu), D-tyrosine (dTyr), phenylalanine (Phe), D-phenylalanine (dPhe), tryptophan (Trp), and D-tryptophan (dTrp); R2 is selected from the group consisting of aspartic acid (Asp), D-aspartic acid (dAsp), cysteine (Cys), D-cysteine (dCys), and D-penicillamine (dPen); R4 is dPhe or para-fluoro-D-phenylalanine (p(F)dPhe); R5 is selected from the group consisting of Arg, His, cisPro(guan), and transPro(guan); R6 is selected from the group consisting of Trp, dTrp, Phe, Aia, Aba, Ata, and 1'-naphthylalanine (Nal(1')); R7 is selected from the group consisting of Gly, Lys, dLys, Cys, dCys, dPen, and Orn; R8 is absent or Lys; Y1 is absent or is selected from the group consisting of valine (Val), D-valine (dVal), b2-valine (b2-Val), b3-valine (b3-Val), Pro, D-proline (dPro), b-proline

(b-Pro), Hyp, D-hydroxyproline (dHyp), D-tert-leucine (dTle), dLeu, Trp, Arg, dArg, Lys, dLys, Gly, Ala, dAla, Asp, dAsp, asparagine (Asn), D-asparagine (dAsn), and D-threonine (dThr); Y2 is absent or is selected from the group consisting of Val, dVal, b2-Val, b3-Val, Pro, dPro, b-Pro, Hyp, dHyp, dTle, Arg, dArg, Gly, Ala, dAla, Asp, and dAsn; Y3 is absent or is selected from the group consisting of Val, dVal, Pro, dPro, dThr, Lys, and dLys; Y4 is absent or is selected from the group consisting of dVal, dPro, Asp, and dAsp; Y5 is absent or dVal; Y6 is absent or dVal; Y7 is absent or dPro; and the non-naturally occurring melanocortin analog is cyclized through a moiety selected from the group consisting of: a disulfide bond between R2 and R7 when each of R2 and R7 are independently selected from the group consisting of Cys, dCys, and dPen; and a lactam bridge between R2 and R7 when R2 is Asp or dAsp and R7 is Lys, dLys, or Orn; provided that: when R4 is p(F)dPhe, then the non-naturally occurring melanocortin analog is not cyclized between Cys at R2 and Cys at R7; and when R4 is dPhe and one or more of X1, X2, and X3 is present, then Y3-Y7 are absent.

**[0166]** In some embodiments, the present technology comprises a method or use, wherein the non-naturally occurring melanocortin analog includes a sequence of Formula (IB), wherein: X1-X2-X3-R1-R2-Pro-R4-R5-R6-R7-R8-Y1-Y2-Y3-Y4-Y5-Y6-Y7 (IB), wherein: X1 is absent or norleucine (Nle); X2 is absent or Nle; X3 is absent or Nle; R1 is selected from the group consisting of Nle, D-norleucine (dNle), alanine (Ala), D-alanine (dAla), arginine (Arg), D-arginine (dArg), lysine (Lys), D-lysine (dLys), histidine (His), D-histidine (dHis), ornithine (Orn), D-ornithine (dOrn), D-leucine (dLeu), D-tyrosine (dTyr), phenylalanine (Phe), D-phenylalanine (dPhe), tryptophan (Trp), and D-tryptophan (dTrp); R2 is selected from the group consisting of aspartic acid (Asp), D-aspartic acid (dAsp), cysteine (Cys), D-cysteine (dCys), and D-penicillamine (dPen); R4 is dPhe or para-fluoro-D-phenylalanine (p(F)dPhe); R5 is selected from the group consisting of Arg, His, cisPro(guan), and transPro(guan); R6 is selected from the group consisting of Trp, dTrp, Phe, Aia, Aba, Ata, and 1'-naphthylalanine (Nal(1')); R7 is selected from the group consisting of Gly, Lys, dLys, Cys, dCys, dPen, and Orn; R8 is absent or Lys; Y1 is absent or is selected from the group consisting of valine (Val), D-valine (dVal), b2-valine (b2-Val), b3-valine (b3-Val), Pro, D-proline (dPro), b-proline (b-Pro), Hyp, D-hydroxyproline (dHyp), D-tert-leucine (dTle), dLeu, Trp, Arg, dArg, Lys, dLys, Gly, Ala, dAla, Asp, dAsp, asparagine (Asn), D-asparagine (dAsn), and D-threonine (dThr); Y2 is absent or is selected from the group

consisting of Val, dVal, b2-Val, b3-Val, Pro, dPro, b-Pro, Hyp, dHyp, dTle, Arg, dArg, Gly, Ala, dAla, Asp, and dAsn; Y3 is absent or is selected from the group consisting of Val, dVal, Pro, dPro, dThr, Lys, and dLys; Y4 is absent or is selected from the group consisting of dVal, dPro, Asp, and dAsp; Y5 is absent or dVal; Y6 is absent or dVal; Y7 is absent or dPro; and the non-naturally occurring melanocortin analog is cyclized through a moiety selected from the group consisting of: a disulfide bond between R2 and R7 when each of R2 and R7 are independently selected from the group consisting of Cys, dCys, and dPen; and a lactam bridge between R2 and R7 when R2 is Asp or dAsp and R7 is Lys, dLys, or Orn; provided that the non-naturally occurring melanocortin analog does not include a sequence of: Ac-Nle-c[Cys-Pro-p(F)dPhe-Arg-Trp-Cys]-dVal-dPro-NH2 (SEQ ID NO: 432); or Ac-Nle-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dPro-dVal-dPro-NH2 (SEQ ID NO: 639).

**[0167]** In some embodiments, the present technology comprises a method or use, wherein the non-naturally occurring melanocortin analog includes a sequence of Formula (IC): X1-X2-R1-R2-Pro-dPhe-R5-R6-R7-Y1-Y2-Y3-Y4 (IC), wherein: X1 is selected from the group consisting of norleucine (Nle), arginine (Arg), D-arginine (dArg), alanine (Ala), lysine (Lys), D-lysine (dLys), histidine (His), D-histidine (dHis); X2 is absent or Nle; R1 is selected from the group consisting of aspartic acid (Asp), cysteine (Cys), and D-cysteine (dCys); R2 is selected from the group consisting of tryptophan (Trp), phenylalanine (Phe), D-phenylalanine (dPhe), histidine (His), D-histidine (dHis), tyrosine (Tyr), and D-tyrosine (dTyr); R5 is Arg; R6 is selected from the group consisting of Trp, 2'-D-naphthylalanine (dNal(2')), 2'-naphthylalanine (Nal(2')), and 1'-naphthylalanine (Nal(1')); R7 is selected from the group consisting of Lys, Cys, and dCys; Y1 is absent or is selected from the group consisting of D-valine (dVal), D-tert-leucine (dTle), dArg, and dLys; Y2 is absent or is selected from the group consisting of dVal, dPro, and D-hydroxyproline (dHyp); Y3 is absent, dVal, or dPro; Y4 is absent or dPro; and the non-naturally occurring melanocortin analog is cyclized through a moiety selected from the group consisting of: a disulfide bond between R1 and R7 when both of R1 and R7 are independently selected from the group consisting of Cys, dCys, and dPen; and a lactam bridge between R1 and R7 when R1 is Asp and R7 is Lys;

**[0168]** In some embodiments, the present technology comprises a method or use, wherein the non-naturally occurring melanocortin analog includes a sequence of Formula (ID): X1-R1-R2-R3-p(Cl)dPhe-Arg-Trp-R7-Y1-Y2-Y3-Y4 (ID), wherein: X1 is absent or norleucine (Nle); R1 is selected from the group consisting of Nle, arginine (Arg), D-arginine (dArg), lysine (Lys), D-lysine (dLys), histidine (His), and D-histidine (dHis); R2 is aspartic acid (Asp) or D-cysteine (dCys); R3 is selected from the group consisting of His, 4-amino-1,2,4,5-tetrahydro-2-benzazepin-3-one (Aba), 7-amino-7,8-dihydro-4H-[1,2,3]triazolo-[1,5-a][1,4]diazepin-6(5H)-one (Ata), and 4-amino-1,4,5,6-tetrahydroazepino[4,3-b]indol-3(2H)-one (Aia); R7 is Lys or dCys; Y1 is selected from the group consisting of D-valine (dVal), D-proline (dPro), and D-tert-leucine (dTle); Y2 is absent or is selected from the group consisting of dVal, dPro, and dTle; Y3 is absent, dVal, or dPro; Y4 is absent or dPro; and the non-naturally occurring melanocortin analog is cyclized through a moiety selected from the group consisting of: a disulfide bond between R2 and R7 when both of R2 and R7 are dCys; and a lactam bridge between R2 and R7 when R2 is Asp and R7 is Lys; provided that when R3 is His and R1 is Nle, then (i) Y1Y2 is dVal-dPro, X1 is absent, and the non-naturally occurring melanocortin analog is cyclized through a disulfide bond, or (b) Y1Y2 is not dVal-dPro and either X1 or Y3 is present.

**[0169]** In some embodiments, the present technology comprises a method or use, wherein the non-naturally occurring melanocortin analog includes a sequence of Formula (ID), wherein: X1 is absent or norleucine (Nle); R1 is selected from the group consisting of Nle, arginine (Arg), D-arginine (dArg), lysine (Lys), D-lysine (dLys), histidine (His), and D-histidine (dHis); R2 is aspartic acid (Asp) or D-cysteine (dCys); R3 is selected from the group consisting of His, 4-amino-1,2,4,5-tetrahydro-2-benzazepin-3-one (Aba), 7-amino-7,8-dihydro-4H-[1,2,3]triazolo-[1,5-a][1,4]diazepin-6(5H)-one (Ata), and 4-amino-1,4,5,6-tetrahydroazepino[4,3-b]indol-3(2H)-one (Aia); R7 is Lys or dCys; Y1 is selected from the group consisting of D-valine (dVal), D-proline (dPro), and D-tert-leucine (dTle); Y2 is absent or is selected from the group consisting of dVal, dPro, and dTle; Y3 is absent, dVal, or dPro; Y4 is absent or dPro; and the non-naturally occurring melanocortin analog is cyclized through a moiety selected from the group consisting of: a disulfide bond between R2 and R7 when both of R2 and R7 are dCys; and a lactam bridge between R2 and R7 when R2 is Asp and R7 is Lys; provided that the non-naturally occurring melanocortin analog does not

include a sequence selected from the group consisting of: Ac-Nle-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 220); Ac-Nle-Nle-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 507); Ac-Nle-Nle-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dPro-dVal-dPro-NH2 (SEQ ID NO: 516); Ac-Nle-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 514); and.

**[0170]** In some embodiments, an N-terminus of the non-naturally occurring melanocortin analog is modified by an acyl group.

**[0171]** In some embodiments, the acyl group is an acetyl group.

**[0172]** In some embodiments, an N-terminus of the non-naturally occurring melanocortin analog is not modified.

**[0173]** In some embodiments, a C-terminus of the non-naturally occurring melanocortin analog is modified by an amide group.

**[0174]** In some embodiments, a C-terminus of the non-naturally occurring melanocortin analog is not modified.

**[0175]** In some embodiments, Y1-Y2 are present and Y3- Y8 are absent.

**[0176]** In some embodiments, Y1 is D-valine and Y2 is D-proline.

**[0177]** In some embodiments, the present technology comprises a method or a use, w wherein Y1 is D-tert-leucine and Y2 is D-proline.

**[0178]** In some embodiments, R4 is dNal(2').

**[0179]** In some embodiments, the sequence of Formula (I) is: Ac-Nle-c[Asp-His-dNal(2')-Arg-Trp-Pro-Lys]-dVal-dPro-NH2 (SEQ ID NO: 8), wherein c represents cyclization through R2 and R8 via a lactam bond.

**[0180]** In some embodiments, R4 is Phe or dPhe.

**[0181]** In some embodiments, the sequence of any one of Formulae (I)-(ID) is selected from the group consisting of: Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-OH (SEQ ID NO: 291); Ac-Nle-c[Asp-Pro-Phe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 294); Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 295; E2); and Ac-Nle-c[Asp-

Pro-His-Phe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 296). wherein c represents cyclization through R2 and R7 via a lactam bond.

**[0182]** In some embodiments, the sequence of any one of Formulae (I)-(ID) is selected from the group consisting of: Ac-dLeu-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO:298); Ac-dAla-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 299); Ac-Ala-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro- NH2 (SEQ ID NO: 300); Ac-dNle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 301); Ac-dArg-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 302); Ac-dPhe-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 303); Ac-dTyr-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 304); Phe-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 305); His-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 306); Trp-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 307); dPhe-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 308); dHis-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 309); dTrp-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 310); Ac-Arg-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 311); Ac-dLys-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 312); Ac-Lys-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 313); Ac-His-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 314); Ac-dHis-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 315); Ac-Orn-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 316); and Ac-dOrn-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 317), wherein c represents cyclization through R2 and R7 via a lactam bond.

**[0183]** In some embodiments, the sequence of any one of Formulae (I)-(ID) is selected from the group consisting of: Ac-Nle-c[Cys-Pro-dPhe-Arg-Trp-Cys]-dVal-dPro-NH2 (SEQ ID NO: 318); Ac-Nle-c[dCys-Pro-dPhe-Arg-Trp-Cys]-dVal-dPro-NH2 (SEQ ID NO: 319); Ac-Nle-c[dPen-Pro-dPhe-Arg-Trp-dPen]-dVal-dPro-NH2 (SEQ ID NO: 320); Ac-Nle-c[dCys-Pro-dPhe-Arg-Trp-dCys]-dVal-dPro-NH2 (SEQ ID NO: 321); Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Orn]-dVal-dPro-NH2 (SEQ ID NO: 322); and Ac-Nle-c[Cys-dPhe-Arg-Trp-Pen]-dVal-dPro-NH2 (SEQ ID NO: 324), wherein c represents cyclization through R2 and R7 via a disulfide bond.

**[0184]** In some embodiments, the sequence of any one of Formulae (I)-(ID) is selected from the group consisting of: Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Gly-Lys]-dVal-dPro-NH2 (SEQ ID NO: 351); Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Gly-Lys]-dPro-dPro-Lys-Asp-NH2 (SEQ ID NO: 352); and Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Gly-Lys]-dPro-dPro-dLys-dAsp-NH2 (SEQ ID NO: 353), wherein c represents cyclization through R2 and R8 via a lactam bond.

**[0185]** In some embodiments, the sequence of any one of Formulae (I)-(ID) is selected from the group consisting of: Ac-Nle-c[Asp-Ala-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 354); Ac-Nle-c[Asp-Leu-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 355); Ac-Nle-c[Asp-Cpe-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 358); Ac-Nle-c[Asp-Che-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 359); Ac-Nle-c[Asp-Oic-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 360); Ac-Nle-c[Asp-Ioc-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 361); Ac-Nle-c[Asp-Tic-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 362); Ac-Nle-c[Asp-Hyp-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 364); Ac-Nle-c[Asp-Phe-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 366); Ac-Nle-c[Asp-dPhe-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 367); Ac-Nle-c[Asp-Bip-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 368); Ac-Nle-c[Asp-dGln-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 371); Ac-Nle-c[Asp-Trp-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 372); Ac-Nle-c[Asp-dTrp-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 373); Ac-Nle-c[Asp-Tyr-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 374); Ac-Nle-c[Asp-dTyr-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 375); Ac-Nle-c[Asp-Aba-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 198); Ac-Nle-c[Asp-Aia-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 207); Ac-Nle-c[Asp-Ata-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 208); Ac-Nle-c[Asp-Atc-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 212); Ac-Nle-c[Asp-APC-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 213); and Ac-Nle-c[Asp-APPC-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 214), wherein c represents cyclization through R2 and R7 via a lactam bond.

**[0186]** In some embodiments, the sequence of any one of Formulae (I)-(ID) is selected from the group consisting of: Ac-Arg-c[Asp-dAla-His-dPhe-Arg-Trp-Lys]-NH2 (SEQ ID NO: 281); Ac-Arg-c[Asp-Ala-His-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 381); and Ac-

dArg-c[Asp-Ala-His-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 382), wherein c represents cyclization through R1 and R7 via a lactam bond.

**[0187]** In some embodiments, the sequence of any one of Formulae (I)-(ID) is selected from the group consisting of: Ac-Nle-c[Asp-Trp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 226); Ac-Nle-c[Cys-Trp-Pro-dPhe-Arg-Trp-Cys]-dVal-dPro-NH2 (SEQ ID NO: 383); Ac-Nle-c[dCys-Trp-Pro-dPhe-Arg-Trp-Cys]-dVal-dPro-NH2 (SEQ ID NO: 384); Ac-Nle-c[dCys-Trp-Pro-dPhe-Arg-Trp-dCys]-dVal-dPro-NH2 (SEQ ID NO: 385); Ac-Ala-c[Asp-Trp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 386); Ac-Lys-c[Asp-Trp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 387); Ac-dLys-c[Asp-Trp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 388); Ac-Arg-c[Asp-Trp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 389); Ac-dArg-c[Asp-Trp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 390); Ac-dHis-c[Asp-Trp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 391); Ac-His-c[Asp-Trp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 392); Ac-Nle-Nle-c[Asp-Trp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 393); Ac-Nle-c[Asp-Trp-Ala-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 394); Ac-Nle-c[Asp-Trp-Leu-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 395); Ac-Nle-c[Asp-Trp-Pro-dPhe-Arg-Nal(1']-Lys]-dVal-dPro-NH2 (SEQ ID NO: 399); Ac-Nle-c[Asp-Trp-Pro-dPhe-Arg-dNal(2')-Lys]-dVal-dPro-NH2 (SEQ ID NO: 403); Ac-Nle-c[Asp-Trp-Pro-dPhe-Arg-Nal(2')-Lys]-dVal-dPro-NH2 (SEQ ID NO: 404); Ac-Nle-c[Asp-Trp-Pro-dPhe-Arg-Trp-Lys]-dArg-dVal-dPro-NH2 (SEQ ID NO: 405); Ac-Nle-c[Asp-Trp-Pro-dPhe-Arg-Trp-Lys]-dLys-dVal-dPro-NH2 (SEQ ID NO: 406); Ac-Nle-c[Asp-Trp-Pro-dPhe-Arg-Trp-Lys]-dArg-dPro-NH2 (SEQ ID NO: 407); Ac-Nle-c[Asp-Trp-Pro-dPhe-Arg-Trp-Lys]-dLys-dPro-NH2 (SEQ ID NO: 408); Ac-Nle-c[Asp-Trp-Pro-dPhe-Arg-Trp-Lys]-dVal-dHyp-NH2 (SEQ ID NO: 409); Ac-Nle-c[Asp-Trp-Pro-dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 410); Ac-Nle-c[Asp-Trp-Pro-dPhe-Arg-Trp-Lys]-dVal-dVal-dVal-dPro-NH2 (SEQ ID NO: 411); Ac-Nle-c[Asp-Phe-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 412); Ac-Nle-c[Asp-His-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 413); Ac-Nle-c[Asp-Tyr-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 414); Ac-Nle-c[Asp-dPhe-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 415); Ac-Nle-c[Asp-dHis-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 416); and Ac-Nle-c[Asp-dTyr-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 417), wherein c represents cyclization through R1 and R7 via a lactam bond or a disulfide bond.

**[0188]** In some embodiments, the sequence of any one of Formulae (I)-(ID) is: Ac-Nle-c[Asp-Hyp-dPhe-Arg-Trp-Pro-Lys]-dVal-dPro-NH2 (SEQ ID NO: 419), wherein c represents cyclization through R2 and R8 via a lactam bond.

**[0189]** In some embodiments, the sequence of any one of Formulae (I)-(ID) is selected from the group consisting of: Ac-Nle-Phe-Phe-c[Asp-Phe-His-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 421); Ac-Nle-c[Asp-Phe-His-dPhe-Arg-Trp-Lys]-dLeu-dPro-NH2 (SEQ ID NO: 422); Ac-Nle-c[Asp-Phe-His-dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 423); and Ac-Nle-c[Asp-Phe-His-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 424), wherein c represents cyclization through R1 and R7 via a lactam bond.

**[0190]** In some embodiments, the sequence of any one of Formulae (I)-(ID) is selected from the group consisting of: Ac-Nle-c[Asp-Pro-dPhe-Arg-dTrp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 187); Ac-Nle-c[Asp-Pro-dPhe-Arg-Aia-Lys]-dVal-dPro-NH2 (SEQ ID NO: 233); Ac-Nle-c[Asp-Pro-dPhe-Arg-Aba-Lys]-dVal-dPro-NH2 (SEQ ID NO: 234); Ac-Nle-c[Asp-Pro-dPhe-Arg-Ata-Lys]-dVal-dPro-NH2 (SEQ ID NO: 235); Ac-Nle-c[Asp-Pro-dPhe-Arg-Nal(1')-Lys]-dVal-dPro-NH2 (SEQ ID NO: 427); and Ac-Nle-c[Asp-Pro-dPhe-Arg-Phe-Lys]-dVal-dPro-NH2 (SEQ ID NO: 429), wherein c represents cyclization through R2 and R7 via a lactam bond.

**[0191]** In some embodiments, the sequence of any one of Formulae (I)-(ID) is selected from the group consisting of: Ac-Nle-c[Asp-Pro-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 218); Ac-Nle-c[dCys-Pro-p(F)dPhe-Arg-Trp-Cys]-dVal-dPro-NH2 (SEQ ID NO: 433); Ac-Nle-c[dCys-Pro-p(F)dPhe-Arg-Trp-dCys]-dVal-dPro-NH2 (SEQ ID NO: 434); Ac-Ala-c[Asp-Pro-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 435); Ac-dArg-c[Asp-Pro-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 436); Ac-Arg-c[Asp-Pro-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 437); Ac-Lys-c[Asp-Pro-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 438); Ac-dLys-c[Asp-Pro-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 439); Ac-His-c[Asp-Pro-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 440); Ac-dHis-c[Asp-Pro-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 441); Ac-Nle-Nle-c[Asp-Pro-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 442); Ac-Nle-c[Asp-Pro-p(F)dPhe-His-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 443); Ac-Nle-c[Asp-Pro-p(F)dPhe-Arg-Trp-Lys]-dTle-dTle-dVal-NH2 (SEQ ID NO: 446); Ac-Nle-

c[Asp-Pro-p(F)dPhe-Arg-Trp-Lys]-dVal-dVal-dVal-dPro-NH2 (SEQ ID NO: 447); Ac-Nle-c[Asp-Pro-p(F)dPhe-Arg-Trp-Lys]-dPro-dVal-dPro-NH2 (SEQ ID NO: 448); Ac-Nle-c[Asp-Pro-p(F)dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 449); Ac-Nle-Nle-c[Asp-Pro-p(F)dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 450); Ac-Nle-Nle-c[Asp-Pro-p(F)dPhe-Arg-Trp-Lys]-dPro-dVal-dPro-NH2 (SEQ ID NO: 451); Ac-Ala-c[Asp-Pro-p(F)dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 452); Ac-dArg-c[Asp-Pro-p(F)dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 453); Ac-Arg-c[Asp-Pro-p(F)dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 454); Ac-Lys-c[Asp-Pro-p(F)dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 455); Ac-dLys-c[Asp-Pro-p(F)dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 456); Ac-His-c[Asp-Pro-p(F)dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 457); Ac-dHis-c[Asp-Pro-p(F)dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 458); Ac-Nle-c[Cys-His-p(F)dPhe-Arg-Trp-Cys]-dVal-dPro-NH2 (SEQ ID NO: 459); Ac-Nle-c[dCys-His-p(F)dPhe-Arg-Trp-Cys]-dVal-dPro-NH2 (SEQ ID NO: 460); Ac-Nle-c[dCys-His-p(F)dPhe-Arg-Trp-dCys]-dVal-dPro-NH2 (SEQ ID NO: 461); Ac-Nle-c[Asp-His-p(F)dPhe-Arg-Nal(2')-Lys]-dVal-dPro-NH2 (SEQ ID NO: 472); Ac-Nle-c[Asp-dGln-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 492); and Ac-Nle-c[Asp-dTyr-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 496), wherein c represents cyclization through R2 and R7 via a lactam bond or a disulfide bond.

**[0192]** In some embodiments, the sequence of any one of Formulae (I)-(ID) is selected from the group consisting of: Ac-Nle-c[Asp-Aba-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 209); Ac-Nle-c[Asp-Aia-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 210); Ac-Nle-c[Asp-Ata-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 211); Ac-Nle-c[dCys-His-p(Cl)dPhe-Arg-Trp-dCys]-dVal-dPro-NH2 (SEQ ID NO: 499); Ac-dArg-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 501); Ac-Arg-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 502); Ac-Lys-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 503); Ac-dLys-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 504); Ac-His-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 505); Ac-dHis-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 506); Ac-Nle-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dTle-dTle-dVal-NH2 (SEQ ID NO: 511); Ac-Nle-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dVal-dVal-dPro-NH2 (SEQ ID NO: 512); Ac-Nle-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dPro-dVal-dPro-NH2 (SEQ ID NO: 513); Ac-Nle-Nle-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 515); Ac-

dArg-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 518); Ac-Arg-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 519); Ac-Lys-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 520); Ac-dLys-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 521); Ac-His-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 522); and Ac-dHis-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 523), wherein c represents cyclization through R2 and R7 via a lactam bond or a disulfide bond.

**[0193]** In some embodiments, the sequence of any one of Formulae (I)-(ID) is selected from the group consisting of: Ac-Nle-c[dCys-His-p(Br)dPhe-Arg-Trp-Cys]-dVal-dPro-NH2 (SEQ ID NO: 536); or Ac-Nle-c[dCys-His-p(Br)dPhe-Arg-Trp-dCys]-dVal-dPro-NH2 (SEQ ID NO: 537), wherein c represents cyclization through R2 and R7 via a disulfide bond.

**[0194]** In some embodiments, the sequence of any one of Formulae (I)-(ID) is selected from the group consisting of: Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-Val-Pro-NH2 (SEQ ID NO: 573); Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-Hyp-NH2 (SEQ ID NO: 574); Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dHyp-NH2 (SEQ ID NO: 575); Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-Val-NH2 (SEQ ID NO: 576); Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-Pro-NH2 (SEQ ID NO: 577); Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-Arg-NH2 (SEQ ID NO: 578); Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dArg-NH2 (SEQ ID NO: 579); Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dArg-dPro-NH2 (SEQ ID NO: 580); Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-Arg-NH2 (SEQ ID NO: 581); Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dArg-NH2 (SEQ ID NO: 582); Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-Lys-Pro-Val-NH2 (SEQ ID NO: 583); Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dLys-dPro-NH2 (SEQ ID NO: 584); Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-Lys-Val-Pro-NH2 (SEQ ID NO: 585); Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-Lys-dVal-dPro-NH2 (SEQ ID NO: 586); Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dLys-dVal-dPro-NH2 (SEQ ID NO: 587); Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-Arg-Pro-Val-NH2 (SEQ ID NO: 588); Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-Arg-Val-Pro-NH2 (SEQ ID NO: 589); Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dArg-dVal-dPro-NH2 (SEQ ID NO: 590); Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 591); Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dTle-dTle-dPro-NH2 (SEQ ID NO: 592); Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dTle-dTle-dVal-NH2 (SEQ ID NO: 593); Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-

dVal-dTle-NH2 (SEQ ID NO: 594); Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dVal-dPro-NH2 (SEQ ID NO: 595); Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dPro-dVal-dPro-NH2 (SEQ ID NO: 596); Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dVal-dVal-dPro-NH2 (SEQ ID NO: 597); Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-dVal-dPro-NH2 (SEQ ID NO: 598); Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dVal-dVal-dVal-dVal-dVal-dPro-NH2 (SEQ ID NO: 599); Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-Trp-NH2 (SEQ ID NO: 600); Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-Lys-dPro-dVal-NH2 (SEQ ID NO: 601); Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dAla-dAla-NH2 (SEQ ID NO: 602); Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-Asp-NH2 (SEQ ID NO: 603); Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dHyp-NH2 (SEQ ID NO: 604); Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dAsn-NH2 (SEQ ID NO: 605); Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-Asp-NH2 (SEQ ID NO: 606); Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-Asn-dPro-NH2 (SEQ ID NO: 607); Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-Hyp-NH2 (SEQ ID NO: 608); Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-Ala-Ala-NH2 (SEQ ID NO: 609); Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-Gly-Gly-NH2 (SEQ ID NO: 610); Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-Asp-dPro-NH2 (SEQ ID NO: 611); Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dAsn-dPro-NH2 (SEQ ID NO: 612); Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-Asn-NH2 (SEQ ID NO: 613); Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dAsp-NH2 (SEQ ID NO: 614); Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dAsn-NH2 (SEQ ID NO: 615); Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-Lys-dPro-NH2 (SEQ ID NO: 616); Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dPro-dVal-OH (SEQ ID NO: 617); Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dThr-dPro-dThr-NH2 (SEQ ID NO: 618); Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dThr-dPro-dThr-OH (SEQ ID NO: 619); Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dPro-dVal-NH2 (SEQ ID NO: 620); Ac-Nle-c[dAsp-Pro-dPhe-Arg-Trp-dLys]-dPro-dVal-NH2 (SEQ ID NO: 622); Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-βPro-β2Val-NH2 (SEQ ID NO: 623); Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-βPro-β3Val-NH2 (SEQ ID NO: 624); Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-β2Val-βPro-NH2 (SEQ ID NO: 625); Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-β3Val-βPro-NH2 (SEQ ID NO: 626); and Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-βPro-βPro-NH2 (SEQ ID NO: 627), wherein c represents cyclization through R2 and R7 via a lactam bond.

**[0195]** In some embodiments, the sequence of any one of Formulae (I)-(ID) is selected from the group consisting of: Ac-Nle-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 628); Ac-Nle-Nle-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID

NO: 629); and Ac-Nle-Nle-Nle-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 630), wherein c represents cyclization through R2 and R7 via a lactam bond.

**[0196]** In some embodiments, the sequence of any one of Formulae (I)-(ID) is selected from the group consisting of: Ac-Arg-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dArg-dVal-dPro-NH2 (SEQ ID NO: 631); Ac-dLys-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dLys-dVal-dPro-NH2 (SEQ ID NO: 632); Ac-Lys-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dArg-dPro-NH2 (SEQ ID NO: 633); Ac-His-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dLys-dPro-NH2 (SEQ ID NO: 634); Ac-dHis-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dHyp-NH2 (SEQ ID NO: 635); Ac-Orn-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 636); Ac-dOrn-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dVal-dVal-dPro-NH2 (SEQ ID NO: 637); Ac-Nle-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 638); Ac-Ala-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 640); Ac-dArg-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 641); Ac-Arg-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 642); Ac-Lys-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 643); Ac-dLys-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 644); Ac-His-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 645); and Ac-dHis-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 646), wherein c represents cyclization through R2 and R7 via a lactam bond.

**[0197]** In some embodiments, the non-naturally occurring melanocortin analog includes any one of SEQ ID NOs: 8, 187, 198, 207-218, 226, 231-235, 281, 291, 294-296, 298-322, 324, 351-355, 358-362, 364, 366-368, 371-375, 381-395, 399, 403-417, 419, 421-425, 427, 429, 433-443, 446-461, 472, 492, 496, 499-506, 511-513, 515, 518-523, 536-537, 573-599, 600-620, 622-646.

**[0198]** In some embodiments, the non-naturally occurring melanocortin analog includes any one of the sequences of SEQ ID NOs: 187, 212, 218, 226, 291, 295, 298-322, 324, 351-355, 358-360, 362, 364, 366-368, 371-375, 381-395, 399, 403-417, 419, 421-425, 427, 429, 433-443, 446-461, 472, 492, 496, 499-506, 511-513, 515, 518-523, 536-537, 573-598, 600-646.

**[0199]** In some embodiments, the non-naturally occurring melanocortin analog includes any one of the sequences of SEQ ID NOs: 187, 218, 231-235, 291, 295, 298-322, 351-353, 425, 427, 429, 433-443, 446-458, 573-599, 600-620, 622-646.

**[0200]** In some embodiments, the non-naturally occurring melanocortin analog includes any one of the sequences of SEQ ID NOs: 226, 383-393, 399, 403-417.

**[0201]** In some embodiments, the non-naturally occurring melanocortin analog includes any one of the sequences of SEQ ID NOs: 209-211, 499, 501-506, 511-513, 515, 518-523.

**[0202]** In some embodiments, the non-naturally occurring melanocortin analog is present in a pharmaceutical composition.

**[0203]** In some embodiments, the pharmaceutical composition includes one or more pharmaceutically acceptable excipients and/or carriers.

**[0204]** In some embodiments, the one or more pharmaceutically acceptable excipients and/or carriers of the pharmaceutical composition include water.

**[0205]** In some embodiments, the non-naturally occurring melanocortin analog is administered (i) at a first dose of about 5 mg/kg to about 20 mg/kg administered once a day for about 5 days to about 10 days; (ii) at a second dose of about 10 mg/kg to about 40 mg/kg administered once a day after administration of the first dose for about 5 days to about 10 days; (iii) at a third dose of about 5 mg/kg to about 30 mg/kg administered twice a day after administration of the second dose for at least about 5 days to about 10 days.

**[0206]** In some embodiments, the non-naturally occurring melanocortin analog is administered (i) at a first dose of about 5 mg/kg administered once a day for about 7 days; (ii) at a second dose of about 15 mg/kg administered once a day after administration of the first dose for about 7 days; (iii) at a third dose of about 10 mg/kg administered twice a day after administration of the second dose for at least about 7 days.

**[0207]** In some embodiments, the non-naturally occurring melanocortin analog is administered (i) at a first dose of about 10 mg/kg administered once a day for about 7 days; (ii) at a second dose of about 20 mg/kg administered once a day after administration of the first dose for about 7 days; (iii) at a third dose of about 15 mg/kg administered twice a day after administration of the second dose for at least about 7 days.

**[0208]** In some embodiments, the present technology comprises a method or the use wherein the non-naturally occurring melanocortin analog is administered (i) at a first dose of about 15 mg/kg administered once a day for about 7 days; (ii) at a second dose of about 25 mg/kg administered once a day after administration of the first dose for about 7 days; (iii) at a third dose of about 20 mg/kg administered twice a day after administration of the second dose for at least about 7 days.

**[0209]** In some embodiments, the non-naturally occurring melanocortin analog is administered at a dose of about 0.5 mg/kg to about 10 mg/kg per body weight of the subject once daily.

**[0210]** In some embodiments, the non-naturally occurring melanocortin analog is administered at a dose of about 1 mg/kg or 3 mg/kg per body weight of the subject once daily.

**[0211]** In some embodiments, the non-naturally occurring melanocortin analog is administered at a dose of about 0.1 mg to about 100 mg once daily.

**[0212]** In some embodiments, the non-naturally occurring melanocortin analog is administered at a dose of about 10 mg or about 50 mg once daily.

**[0213]** In some embodiments, the non-naturally occurring melanocortin analog is administered via intraperitoneal, intravenous, parenteral, subcutaneous, intramuscular, intracerebroventricular, intranasal, or oral administration.

**[0214]** In some embodiments, the non-naturally occurring melanocortin analog crosses a blood-brain-barrier of a subject.

**[0215]** In some embodiments, the non-naturally occurring melanocortin analog includes any one of the sequences of SEQ ID NOs: 8, 187, 198, 207-218, 226, 231-235, 281, 291, 294-296, 298-322, 324, 351-355, 358-362, 364, 366-368, 371-375, 381-395, 399, 403-417, 419, 421-425, 427, 429, 433-443, 446-461, 472, 492, 496, 499-506, 511-513, 515, 518-523, 536-537, 573-599, 600-620, 622-646 and is administered at least once daily in an amount ranging from 0.001 mg/kg to 25 mg/kg per body weight of the subject.

**[0216]** In some embodiments, the non-naturally occurring melanocortin analog includes any one of the sequences of SEQ ID NOs: 8, 187, 198, 207-218, 226, 231-235, 281, 291, 294-296, 298-322, 324, 351-355, 358-362, 364, 366-368, 371-375, 381-395, 399, 403-417, 419, 421-425, 427, 429, 433-443, 446-461, 472, 492, 496, 499-506, 511-513, 515, 518-523, 536-537, 573-599, 600-620, 622-646 and is administered at least once daily in an amount ranging from 0.5 mg/kg to 10 mg/kg per body weight of the subject.

**[0217]** In some embodiments, the non-naturally occurring melanocortin analog is administered to a subject for at least 1 day, 1 week, 1 month, 3 months, 6 months, 1 year, or 5 years.

**[0218]** In some embodiments, the non-naturally occurring melanocortin analog is administered to a subject for 1 day, 5 days, 7 days, 14 days, 21 days, 28 days, 35 days, 40 days, 45 days, 50 days, 60 days, 75 days, 90 days, 100 days, 110 days, or 120 days.In some embodiments, the present technology comprises a method of reducing a pain level in a subject in need thereof relative to a control, including administering to the subject a non-naturally occurring melanocortin analog of Formula (I): X1-X2-X3-R1-R2-R3-R4-R5-R6-R7-R8-Y1-Y2-Y3-Y4-Y5-Y6-Y7 (I), wherein: X1 is absent or is selected from the group consisting of norleucine (Nle), arginine (Arg), D-arginine (dArg), alanine (Ala), lysine (Lys), D-lysine (dLys), histidine (His), and D-histidine (dHis); X2 is absent, phenylalanine (Phe), or Nle; X3 is absent, Phe, or Nle; R1 is selected from the group consisting of Nle, D-norleucine (dNle), Ala, D-alanine (dAla), Arg, dArg, Lys, dLys, His, dHis, ornithine (Orn), D-ornithine (dOrn), D-leucine (dLeu), D-tyrosine (dTyr), phenylalanine (Phe), D-phenylalanine (dPhe), tryptophan (Trp), D-tryptophan (dTrp), aspartic acid (Asp), cysteine (Cys), and D-cysteine (dCys); R2 is selected from the group consisting of Asp, proline (Pro), D-aspartic acid (dAsp), Cys, dCys, D-penicillamine (dPen), Ala, dAla, Trp, Phe, dPhe, His, dHis, Tyr, and dTyr; R3 is absent or is selected from the group consisting of His, Ala, Pro, hydroxyproline (Hyp), leucine (Leu), D-glutamine (dGln), Phe, dPhe, Trp, dTrp, Tyr, dTyr, 4-amino-1,2,4,5-tetrahydro-2-benzazepin-3-one (Aba), 7-amino-7,8-dihydro-4H-[1,2,3]triazolo-[1,5-a][1,4]diazepin-6(5H)-one (Ata), 4-amino-1,4,5,6-tetrahydroazepino[4,3-b]indol-3(2H)-one (Aia), 2-aminotetraline-2-carboxylic acid (Atc), 1-amino-4-phenylcyclohexane-carboxylic acid (APC), 4-aminophenylpiperidine-4-carboxylic acid (APPC), octohydroindole-2-

carboxylic acid (Oic), 1-amino-1-cyclohexanecarboxylic acid (Che), tetrahydro-isoquinoline-3-carboxylic acid (Tic), indoline-2-carboxylic acid (Ioc), 1-amino-1-cyclopentane carboxylic (Cpe), and biphenylalanine (Bip); R4 is selected from the group consisting of Phe, dPhe, 2'-D-naphthylalanine (dNal(2')), para-chloro-D-phenylalanine (p(Cl)dPhe), para-bromo-D-phenylalanine (p(Br)dPhe), and para-fluoro-D-phenylalanine (p(F)dPhe); R5 is selected from the group consisting of Arg, His, cisPro(guan), and transPro(guan); R6 is selected from the group consisting of Trp, dTrp, Phe, Aia, Aba, Ata, dNal(2'), 2'-naphthylalanine (Nal(2')), and 1'-naphthylalanine (Nal(1')); R7 is selected from the group consisting of Gly, Pro, Lys, dLys, Cys, dCys, penicillamine (Pen), dPen, and Orn; R8 is absent or Lys; Y1 is absent or is selected from the group consisting of valine (Val), D-valine (dVal), b2-valine (b2-Val), b3-valine (b3-Val), Pro, D-proline (dPro), b-proline (b-Pro), Hyp, D-hydroxyproline (dHyp), D-tert-leucine (dTle), dLeu, Trp, Arg, dArg, Lys, dLys, Gly, Ala, dAla, Asp, dAsp, asparagine (Asn), D-asparagine (dAsn), and D-threonine (dThr); Y2 is absent or is selected from the group consisting of Val, dVal, b2-Val, b3-Val, Pro, dPro, b-Pro, Hyp, dHyp, dTle, Arg, dArg, Gly, Ala, dAla, Asp, and dAsn; Y3 is absent or is selected from the group consisting of Val, dVal, Pro, dPro, dThr, Lys, and dLys; Y4 is absent or is selected from the group consisting of dVal, dPro, Asp, and dAsp; Y5 is absent or dVal; Y6 is absent or dVal; Y7 is absent or dPro; and the non-naturally occurring melanocortin analog is cyclized through a moiety selected from the group consisting of: a disulfide bond between R1 or R2 and R7 when each of R1 or R2 and R7 are independently selected from the group consisting of Cys, dCys, and dPen; a disulfide bond between R2 and R7 when R2 is Cys, R7 is Pen, and R3 is absent; a lactam bridge between R1 or R2 and R7 or R8 when R1 or R2 is Asp and R7 or R8 is Lys or Orn; and a lactam bridge between R2 and R7 when R2 is dAsp and R7 is dLys; provided that: when R4 is dNal(2'), then R3 is His and R7 is Pro; when R4 is p(F)dPhe, then (i) R3 is selected from Pro, dGln, dTyr, R6 is Trp, and the non-naturally occurring melanocortin analog is not cyclized between Cys at R2 and Cys at R7 or (ii) R3 is His and either R6 is Nal(2') or the non-naturally occurring melanocortin analog is cyclized through a disulfide bond between R2 and R7; when R4 is p(Br)dPhe, then the non-naturally occurring melanocortin analog is cyclized through a disulfide bond between dCys at R2 and Cys or dCys at R7; when R4 is dPhe, then (i) R3 is not His, Pro, or absent, (ii) R3 is His and either R2 is Phe or dAla or R2 is Ala and X1 is Arg or dArg, (iii) R3 is Pro and (a) R2 is Trp, and

R5 is not His or R6 is not Phe or (b) R2 is not Trp or Pro, and either R5 is not dNal(2') or Nal(2') or X1 and Y3 are not both present, or (iv) R3 is absent and R2 and R7 are not both dPen; when R4 is p(Cl)dPhe, then (i) R3 is selected from Aba, Aia, and Ata or (ii) R3 is His, R1 is not Ala, and (a) if R1 is Nle and Y1Y2 is dVal-dPro, then X1 is absent and the non-naturally occurring melanocortin analog is cyclized through a disulfide bond between dCys at R2 and dCys at R7, or (b) if R1 is Nle, and Y1Y2 is not dVal-dPro, then either X1 or Y3 is present; and when R2 is dAla, then R4 is dPhe and Y1-Y7 are absent.

**[0219]** In some embodiments, the present technology comprises use of a non-naturally occurring melanocortin analog for reducing a pain level in a subject in need thereof relative to a control, the non-naturally occurring melanocortin analog including a sequence of Formula (I).

**[0220]** In some embodiments, the present technology comprises a method of treating, preventing, or reducing an addiction in a subject relative to a control, including administering to the subject a non-naturally occurring melanocortin analog including a sequence of Formula (I).

**[0221]** In some embodiments, the present technology comprises use of a non-naturally occurring melanocortin analog for treating, preventing, or reducing an addiction in a subject relative to a control, the non-naturally occurring melanocortin analog including a sequence of Formula (I).

**[0222]** In some embodiments, the present technology comprises a method of preventing or reducing a use of or dependence on an addictive substance in a subject relative to a control, including administering to the subject a non-naturally occurring melanocortin analog including a sequence of Formula (I).

**[0223]** In some embodiments, the present technology comprises use of a non-naturally occurring melanocortin analog for treating, preventing, or reducing a use of or dependence on an addictive substance in a subject relative to a control, the non-naturally occurring melanocortin analog including a sequence of Formula (I).

**[0224]** In some embodiments, the present technology comprises a method of treating or preventing an opioid use disorder (OUD) in a subject in need thereof relative to a control,

including administering to the subject a non-naturally occurring melanocortin analog including a sequence of Formula (I).

**[0225]** In some embodiments, the present technology comprises use of a non-naturally occurring melanocortin analog for treating or preventing an OUD in a subject in need thereof relative to a control, the non-naturally occurring melanocortin analog including a sequence of Formula (I).

**[0226]** In some embodiments, the present technology comprises a method of treating or preventing an alcohol use disorder (AUD) in a subject in need thereof relative to a control, including administering to the subject a non-naturally occurring melanocortin analog including a sequence of Formula (I).

**[0227]** In some embodiments, the present technology comprises use of a non-naturally occurring melanocortin analog for treating or preventing an AUD in a subject in need thereof relative to a control, the non-naturally occurring melanocortin analog including a sequence of Formula (I).

**[0228]** In some embodiments, the method or the use includes reducing a dose used or consumed of an addictive substance, relative to a control.

**[0229]** In some embodiments, the method or the use includes reducing a dependency on an addictive substance, relative to a control.

**[0230]** In some embodiments, the method or the use includes reducing a frequency of an addictive substance use, relative to a control.

**[0231]** In some embodiments, the method or the use includes reducing a dose or dosage of a conventional medication used to treat an addiction, relative to a control.

**[0232]** In some embodiments, the present technology comprises a method of augmenting an effect of a conventional medication used to treat an addiction in a subject in need thereof, relative to a control, including administering to the subject a non-naturally occurring melanocortin analog including a sequence of Formula (I).

**[0233]** In some embodiments, the present technology comprises use of a non-naturally occurring melanocortin analog for augmenting an effect of a conventional medication used

to treat an addiction in a subject in need thereof, the non-naturally occurring melanocortin analog including a sequence of Formula (I).

**[0234]** In some embodiments, the present technology comprises a method of reducing or eliminating a need for a conventional medication used to treat an addiction in a subject in need thereof, relative to a control, including administering to the subject a non-naturally occurring melanocortin analog including a sequence of Formula (I).

**[0235]** In some embodiments, the present technology comprises use of a non-naturally occurring melanocortin analog for reducing or eliminating a need for a conventional medication used to treat an addiction in a subject in need thereof, the non-naturally occurring melanocortin analog including a sequence of Formula (I).

**[0236]** In some embodiments, the treatment of the addiction is improved during or after administration of the non-naturally occurring melanocortin analog relative to treatment of the addiction using the conventional medication to treat the addiction alone.

**[0237]** In some embodiments, the conventional medication to treat the addiction is selected from the group consisting of buprenorphine, naltrexone, acamprosate, methadone, naloxone, nalmefene, xycodone, levo-alpha-acetylmethadol (LAAM), codeine, lofexidine, and a slow-release morphine.

**[0238]** In some embodiments, the present technology comprises a method of reducing a need for a hospitalization or rehabilitation associated with addiction or use of an addictive substance, relative to a control, including administering to the subject a non-naturally occurring melanocortin analog including a sequence of Formula (I).

**[0239]** In some embodiments, the present technology comprises use of a non-naturally occurring melanocortin analog for reducing a need for a hospitalization or rehabilitation associated with addiction or use of an addictive substance, relative to a control, the non-naturally occurring melanocortin analog including a sequence of Formula (I).

**[0240]** In some embodiments, the present technology comprises a method of preventing or reducing a withdrawal from an addictive substance in a subject, including administering to the subject a non-naturally occurring melanocortin analog including a sequence of Formula (I).

**[0241]** In some embodiments, the present technology comprises use of a non-naturally occurring melanocortin analog for preventing or reducing a withdrawal from an addictive substance in a subject, relative to a control, the non-naturally occurring melanocortin analog including a sequence of Formula (I).

**[0242]** In some embodiments, the present technology comprises a method of preventing or reducing a symptom associated with withdrawal from an addictive substance in a subject relative to a control, including administering to the subject a non-naturally occurring melanocortin analog including a sequence of Formula (I).

**[0243]** In some embodiments, the present technology comprises use of a non-naturally occurring melanocortin analog for preventing or reducing a symptom associated with withdrawal from an addictive substance in a subject, relative to a control, the non-naturally occurring melanocortin analog including a sequence of Formula (I).

**[0244]** In some embodiments, the symptom associated with withdrawal from an addictive substance is selected from the group consisting of pain, anxiety, depression, diarrhea, dizziness, fatigue, muscle aches, nausea, sleep problems, suicidal ideation, tremors, and visual disturbances.

**[0245]** In some embodiments, the subject has an addiction to an addictive substance or is susceptible to an addiction to an addictive substance.

**[0246]** In some embodiments, the subject has used or is using one or more addictive substances.

**[0247]** In some embodiments, the present technology comprises a method or the use wherein the addictive substance includes a prescription medication, a substance in an over-the-counter medication, a recreational substance, or an illegal substance.

**[0248]** In some embodiments, the addictive substance is selected from the group consisting of an opioid, a painkiller, a stimulant, a narcotic, an alcohol, a sedative, marijuana, a cannabis, a tetrahydrocannabinol (THC), a cannabidiol (CBD), and an inhalant.

**[0249]** In some embodiments, the opioid is selected from the group consisting of morphine, heroin, codeine, oxycodone, hydrocodone, and fentanyl.

**[0250]** In some embodiments, the stimulant is selected from the group consisting of caffeine, nicotine, methamphetamines, cocaine, and amphetamines.

**[0251]** In some embodiments, the sedative includes a barbiturate or a benzodiazepine.

**[0252]** In some embodiments, the barbiturate is selected from the group consisting of phenobarbital, methohexital, butalbital, pentobarbital, primidone, and amobarbital.

**[0253]** In some embodiments, the benzodiazepine is selected from the group consisting of alprazolam, lorazepam, clonazepam, diazepam, and temazepam.

**[0254]** In some embodiments, the sedative is selected from the group consisting of tranquilizers, xylazine, eszopiclone, zaleplon, zolpidem, and zopiclone.

**[0255]** In some embodiments, the inhalant is selected from the group consisting of aerosols, butanes, freon, helium, nitrous oxide, propane, and nitrites.

**[0256]** In some embodiments, the nicotine includes a tobacco chew, a nicotine pouch, or a smoking device.

**[0257]** In some embodiments, the smoking device is selected from the group consisting of cigarettes, electronic cigarettes, cigars, and vape products.

**[0258]** In some embodiments, the control includes the subject before administration of the non-naturally occurring melanocortin analog.

**[0259]** In some embodiments, the control includes the subject at baseline.

**[0260]** In some embodiments, the non-naturally occurring melanocortin analog is a melanocortin 4 receptor (MC4R) agonist.

**[0261]** In some embodiments, the MC4R agonist is a full MC4R agonist.

**[0262]** In some embodiments, the MC4R agonist is a partial MC4R agonist.

**[0263]** In some embodiments, the non-naturally occurring melanocortin analog is a MC3R antagonist.

**[0264]** In some embodiments, the MC3R antagonist is a full MC3R antagonist.

**[0265]** In some embodiments, the MC3R antagonist is a partial MC3R antagonist.

**[0266]** In some embodiments, the non-naturally occurring melanocortin analog does not have MC3R activity.

**[0267]** In some embodiments, the non-naturally occurring melanocortin analog includes a sequence according to Formula (I), wherein: X1 is absent or is selected from the group consisting of norleucine (Nle), arginine (Arg), D-arginine (dArg), alanine (Ala), lysine (Lys), D-lysine (dLys), histidine (His), and D-histidine (dHis); X2 is absent, phenylalanine (Phe), or Nle; X3 is absent, Phe, or Nle; R1 is selected from the group consisting of Nle, D-norleucine (dNle), Ala, D-alanine (dAla), Arg, dArg, Lys, dLys, His, dHis, ornithine (Orn), D-ornithine (dOrn), D-leucine (dLeu), D-tyrosine (dTyr), phenylalanine (Phe), D-phenylalanine (dPhe), tryptophan (Trp), D-tryptophan (dTrp), aspartic acid (Asp), cysteine (Cys), and D-cysteine (dCys); R2 is selected from the group consisting of Asp, proline (Pro), D-aspartic acid (dAsp), Cys, dCys, D-penicillamine (dPen), Ala, dAla, Trp, Phe, dPhe, His, dHis, Tyr, and dTyr; R3 is absent or is selected from the group consisting of His, Ala, Pro, hydroxyproline (Hyp), leucine (Leu), D-glutamine (dGln), Phe, dPhe, Trp, dTrp, Tyr, dTyr, 4-amino-1,2,4,5-tetrahydro-2-benzazepin-3-one (Aba), 7-amino-7,8-dihydro-4H-[1,2,3]triazolo-[1,5-a][1,4]diazepin-6(5H)-one (Ata), 4-amino-1,4,5,6-tetrahydroazepino[4,3-b]indol-3(2H)-one (Aia), 2-aminotetraline-2-carboxylic acid (Atc), 1-amino-4-phenylcyclohexane-carboxylic acid (APC), 4-aminophenylpiperidine-4-carboxylic acid (APPC), octohydroindole-2-carboxylic acid (Oic), 1-amino-1-cyclohexanecarboxylic acid (Che), tetrahydro-isoquinoline-3-carboxylic acid (Tic), indoline-2-carboxylic acid (Ioc), 1-amino-1-cyclopentane carboxylic (Cpe), and biphenylalanine (Bip); R4 is selected from the group consisting of Phe, dPhe, 2'-D-naphthylalanine (dNal(2')), para-chloro-D-phenylalanine (p(Cl)dPhe), para-bromo-D-phenylalanine (p(Br)dPhe), and para-fluoro-D-phenylalanine (p(F)dPhe); R5 is selected from the group consisting of Arg, His, cisPro(guan), and transPro(guan); R6 is selected from the group consisting of Trp, dTrp, Phe, Aia, Aba, Ata, dNal(2'), 2'-naphthylalanine (Nal(2')), and 1'-naphthylalanine (Nal(1')); R7 is selected from the group consisting of Gly, Pro, Lys, dLys, Cys, dCys, penicillamine (Pen), dPen, and Orn; R8 is absent or Lys; Y1 is absent or is selected from the group consisting of valine (Val), D-valine (dVal), b2-valine (b2-Val), b3-valine (b3-Val), Pro, D-proline (dPro), b-proline (b-Pro), Hyp, D-hydroxyproline (dHyp), D-tert-leucine (dTle), dLeu, Trp, Arg, dArg, Lys, dLys, Gly, Ala, dAla, Asp, dAsp, asparagine (Asn), D-asparagine (dAsn), and D-threonine (dThr); Y2

is absent or is selected from the group consisting of Val, dVal, b2-Val, b3-Val, Pro, dPro, b-Pro, Hyp, dHyp, dTle, Arg, dArg, Gly, Ala, dAla, Asp, and dAsn; Y3 is absent or is selected from the group consisting of Val, dVal, Pro, dPro, dThr, Lys, and dLys; Y4 is absent or is selected from the group consisting of dVal, dPro, Asp, and dAsp; Y5 is absent or dVal; Y6 is absent or dVal; Y7 is absent or dPro; and the non-naturally occurring melanocortin analog is cyclized through a moiety selected from the group consisting of: a disulfide bond between R1 or R2 and R7 or R8 when each of R1 or R2 and R7 or R8 are independently selected from the group consisting of Cys, dCys, and dPen; a disulfide bond between R2 and R7 when R2 is Cys, R7 is Pen, and R3 is absent; a lactam bridge between R1 or R2 and R7 or R8 when R1 or R2 is Asp and R7 or R8 is Lys or Orn; and a lactam bridge between R2 and R7 when R2 is dAsp and R7 is dLys; provided that the non-naturally occurring melanocortin analog does not include a sequence selected from the group consisting of: Ac-Nle-c[Asp-Pro-Pro-dNal(2')-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 194); Ac-Nle-c[Asp-Pro-His-dNal(2')-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 5); Ac-Nle-c[Asp-Pro-His-dNal(2')-Arg-Trp-Lys]-dPro-dVal-NH2 (SEQ ID NO: 10); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dVal-dPro (SEQ ID NO: 2); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 3); Ac-Nle-c[Asp-Hyp-dNal(2')-Arg-Trp-Pro-Lys]-dVal-dPro-NH2 (SEQ ID NO: 4); Ac-Nle-c[Asp-Phe-His-dNal(2')-Arg-Trp-Lys]-dLeu-dPro-NH2 (SEQ ID NO: 6); Ac-Nle-c[Asp-Phe-His-dNal(2')-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 7); Ac-Nle-c[Asp-Hyp-dNal(2')-Arg-Trp-Pro-Lys]-dVal-dPro-NH2 (SEQ ID NO: 9); Ac-Nle-Phe-Phe-c[Asp-Phe-His-dNal(2')-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 12); Ac-dArg-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 15); Ac-dLeu-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 18); Ac-dAla-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 20); Ac-Ala-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 21); Ac-dNle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 24); Ac-dCys-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 28); Ac-dPhe-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 29); Ac-dTyr-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 30); dTyr-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 35); Tyr-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 36); Ac-Nle-c[Cys-Pro-dNal(2')-Arg-Trp-Cys]-dVal-dPro-NH2 (SEQ ID NO: 40); Ac-Nle-c[dCys-Pro-dNal(2')-Arg-Trp-Cys]-dVal-dPro-NH2 (SEQ ID NO: 41); Ac-Nle-c[Cys-Pro-dNal(2')-Arg-

Trp-dCys]-dVal-dPro-NH2 (SEQ ID NO: 42); Ac-Nle-c[dCys-Pro-dNal(2')-Arg-Trp-dCys]-dVal-dPro-NH2 (SEQ ID NO: 43); Ac-Nle-c[Cys-Pro-dNal(2')-Arg-Trp-Pen]-dVal-dPro-NH2 (SEQ ID NO: 48); Ac-Nle-c[dPen-Pro-dNal(2')-Arg-Trp-dPen]-dVal-dPro-NH2 (SEQ ID NO: 54); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Orn]-dVal-dPro-NH2 (SEQ ID NO: 64); Ac-Nle-c[Asp-dNal(2')-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 68); Ac-Nle-c[Asp-Ala-dNal(2')-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 69); Ac-Nle-c[Asp-Leu-dNal(2')-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 76); Ac-Nle-c[Asp-Trp-dNal(2')-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 82); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-Val-Pro-NH2 (SEQ ID NO: 115); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dVal-dPro-OH (SEQ ID NO: 116); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dPro-dVal-OH (SEQ ID NO: 117); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dVal-Hyp-NH2 (SEQ ID NO: 118); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dVal-dHyp-NH2 (SEQ ID NO: 119); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-Val-Hyp-NH2 (SEQ ID NO: 120); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-Val-dHyp-NH2 (SEQ ID NO: 121); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-Hyp-dVal-NH2 (SEQ ID NO: 122); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dHyp-dVal-NH2 (SEQ ID NO: 123); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-Hyp-Val-NH2 (SEQ ID NO: 124); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dHyp-Val-NH2 (SEQ ID NO: 125); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dVal-dVal-NH2 (SEQ ID NO: 126); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dPro-dPro-NH2 (SEQ ID NO: 127); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dVal-NH2 (SEQ ID NO: 128); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dPro-NH2 (SEQ ID NO: 129); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-Val-NH2 (SEQ ID NO: 130); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-Pro-NH2 (SEQ ID NO: 131); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-Ala-NH2 (SEQ ID NO: 132); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dAla-NH2 (SEQ ID NO: 133); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dHyp-NH2 (SEQ ID NO: 134); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-Hyp-NH2 (SEQ ID NO: 135); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dAla-dAla-NH2 (SEQ ID NO: 136); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-Ala-Ala-NH2 (SEQ ID NO: 137); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-Gly-Gly-NH2 (SEQ ID NO: 138); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dVal-Asp-NH2 (SEQ ID NO: 139); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dVal-Arg-NH2 (SEQ ID NO: 140); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dVal-dArg-NH2 (SEQ ID NO: 143); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dVal-dAsn-NH2 (SEQ ID NO: 144); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-Asp-dPro-NH2 (SEQ ID NO:

145); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-Arg-dPro-NH2 (SEQ ID NO: 146); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-Asn-dPro-NH2 (SEQ ID NO: 147); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dAsp-dPro-NH2 (SEQ ID NO: 148); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dArg-dPro-NH2 (SEQ ID NO: 149); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dAsn-dPro-NH2 (SEQ ID NO: 150); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-Asp-NH2 (SEQ ID NO: 151); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-Arg-NH2 (SEQ ID NO: 152); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-Asn-NH2 (SEQ ID NO: 153); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dAsp-NH2 (SEQ ID NO: 154); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dArg-NH2 (SEQ ID NO: 155); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dAsn-NH2 (SEQ ID NO: 156); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-Lys-Pro-Val-NH2 (SEQ ID NO: 157); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-Lys-dPro-dVal-NH2 (SEQ ID NO: 158); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dLys-dPro-dVal-NH2 (SEQ ID NO: 159); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-Lys-dPro-NH2 (SEQ ID NO: 160); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dLys-dPro-NH2 (SEQ ID NO: 161); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-Lys-Val-Pro-NH2 (SEQ ID NO: 162); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-Lys-dVal-dPro-NH2 (SEQ ID NO: 164); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dLys-dVal-dPro-NH2 (SEQ ID NO: 164); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-Arg-Pro-Val-NH2 (SEQ ID NO: 165); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-Arg-dPro-dVal-NH2 (SEQ ID NO: 166); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dArg-dPro-dVal-NH2 (SEQ ID NO: 167); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-Arg-Val-Pro-NH2 (SEQ ID NO: 168); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-Arg-dVal-dPro-NH2 (SEQ ID NO: 169); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dArg-dVal-dPro-NH2 (SEQ ID NO: 170); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dTle-dVal-dPro-NH2 (SEQ ID NO: 171); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 172); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dTle-dVal-NH2 (SEQ ID NO: 173); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dTle-dTle-NH2 (SEQ ID NO: 174); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dTle-dTle-dPro-NH2 (SEQ ID NO: 175); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dTle-dTle-dVal-NH2 (SEQ ID NO: 176); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dPro-dTle-NH2 (SEQ ID NO: 177); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dVal-dTle-NH2 (SEQ ID NO: 178); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dVal-dVal-dPro-NH2 (SEQ ID NO: 179); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dPro-dVal-dPro-NH2 (SEQ ID NO: 180); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dVal-dVal-dVal-dPro-NH2 (SEQ ID NO: 181);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dVal-dPro-dVal-dPro-NH2 (SEQ ID NO: 182); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dVal-dVal-dVal-dVal-dVal-dVal-dPro-NH2 (SEQ ID NO: 183); Ac-Nle-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 184); Ac-Nle-Nle-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 185); Ac-Nle-Nle-Nle-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 186); Ac-Nle-c[Asp-Trp-Pro-dNal(2')-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 195); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-dTrp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 196); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-Trp-NH2 (SEQ ID NO: 203); Ac-Nle-c[Asp-Aba-dNal(2')-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 204); Ac-Nle-c[Asp-Aia-dNal(2')-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 205); Ac-Nle-c[Asp-Ata-dNal(2')-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 206); Ac-Nle-c[Asp-Cpe-dNal(2')-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 240); Ac-Nle-c[Asp-Che-dNal(2')-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 241); Ac-Nle-c[Asp-Oic-dNal(2')-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 242); Ac-Nle-c[Asp-Tic-dNal(2')-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 244); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Pro-Lys]-dVal-dPro-NH2 (SEQ ID NO: 245); Ac-Nle-c[Asp-His-dNal(2')-transPro(guan)-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 247); Ac-Nle-c[Asp-His-dNal(2')-cisPro(guan)-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 248); Ac-Nle-c[Asp-Pro-dNal(2')-transPro(guan)-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 250); Ac-Nle-c[Asp-Pro-dNal(2')-cisPro(guan)Pro-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 251); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Aba-Lys]-dVal-dPro-NH2 (SEQ ID NO: 253); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Ata-Lys]-dVal-dPro-NH2 (SEQ ID NO: 254); Ac-Nle-c[Asp-Glu-dNal(2')-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 255); Ac-Nle-c[Asp-Glu-dNal(2')-Arg-Trp-Gly-Lys]-dVal-dPro-NH2 (SEQ ID NO: 256); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Gly-Lys]-dVal-dPro-NH2 (SEQ ID NO: 259); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Gly-Lys]-dPro-dPro-Lys-Asp-NH2 (SEQ ID NO: 260); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Gly-Lys]-dPro-dPro-dLys-dAsp-NH2 (SEQ ID NO: 261); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dPro-dPro-dLys-dAsp-NH2 (SEQ ID NO: 263); Ac-Nle-c[Asp-Ala-His-dNal(2')-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 273); Ac-Arg-c[Asp-Ala-His-dNal(2')-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 274); Ac-dArg-c[Asp-Ala-His-dNal(2')-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 275); Ac-dLeu-c[dPen-Pro-dNal(2')-Arg-Trp-dPen]-dVal-dPro-NH2 (SEQ ID NO: 327); Ac-dNle-c[dPen-Pro-dNal(2')-Arg-Trp-dPen]-dVal-dPro-NH2 (SEQ ID NO: 328); Ac-dArg-c[dPen-Pro-dNal(2')-Arg-Trp-dPen]-dVal-dPro-NH2 (SEQ ID NO: 329); Ac-Arg-c[dPen-Pro-

dNal(2')-Arg-Trp-dPen]-dVal-dPro-NH2 (SEQ ID NO: 330); Ac-dPhe-c[dPen-Pro-dNal(2')-Arg-Trp-dPen]-dVal-dPro-NH2 (SEQ ID NO: 331); Ac-dTyr-c[dPen-Pro-dNal(2')-Arg-Trp-dPen]-dVal-dPro-NH2 (SEQ ID NO: 332); Ac-Ala-c[dPen-Pro-dNal(2')-Arg-Trp-dPen]-dVal-dPro-NH2 (SEQ ID NO: 333); Ac-dHis-c[dPen-Pro-dNal(2')-Arg-Trp-dPen]-dVal-dPro-NH2 (SEQ ID NO: 334); Ac-His-c[dPen-Pro-dNal(2')-Arg-Trp-dPen]-dVal-dPro-NH2 (SEQ ID NO: 335); Ac-dLys-c[dPen-Pro-dNal(2')-Arg-Trp-dPen]-dVal-dPro-NH2 (SEQ ID NO: 336); Ac-Lys-c[dPen-Pro-dNal(2')-Arg-Trp-dPen]-dVal-dPro-NH2 (SEQ ID NO: 337); Ac-Nle-c[dPen-Pro-dNal(2')-Arg-Trp-dPen]-dArg-dVal-dPro-NH2 (SEQ ID NO: 344); Ac-Nle-c[dPen-Pro-dNal(2')-Arg-Trp-dPen]-dLys-dVal-dPro-NH2 (SEQ ID NO: 345); Ac-Nle-c[dPen-Pro-dNal(2')-Arg-Trp-dPen]-dArg-dPro-NH2 (SEQ ID NO: 346); Ac-Nle-c[dPen-Pro-dNal(2')-Arg-Trp-dPen]-dLys-dPro-NH2 (SEQ ID NO: 347); Ac-Nle-c[dPen-Pro-dNal(2')-Arg-Trp-dPen]-dVal-dHyp-NH2 (SEQ ID NO: 348); Ac-Nle-c[dPen-Pro-dNal(2')-Arg-Trp-dPen]-dTle-dPro-NH2 (SEQ ID NO: 349); Ac-Nle-c[dPen-Pro-dNal(2')-Arg-Trp-Gly-dPen]-dVal-dPro-NH2 (SEQ ID NO: 350); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Aia-Lys]-dVal-dPro-NH2 (SEQ ID NO: 103); Ac-Nle-c[Asp-Ioc-dNal(2')-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 243); Ac-Nle-c[Cys-dNal(2')-Arg-Trp-Cys]-dVal-dPro-NH2 (SEQ ID NO: 44); Ac-Nle-c[dCys-dNal(2')-Arg-Trp-Cys]-dVal-dPro-NH2 (SEQ ID NO: 45); Ac-Nle-c[Cys-dNal(2')-Arg-Trp-dCys]-dVal-dPro-NH2 (SEQ ID NO: 46); Ac-Nle-c[dCys-dNal(2')-Arg-Trp-dCys]-dVal-dPro-NH2 (SEQ ID NO: 47); Ac-Nle-c[Cys-dNal(2')-Arg-Trp-Pen]-dVal-dPro-NH2 (SEQ ID NO: 56); Ac-Nle-c[dPen-dNal(2')-Arg-Trp-dPen]-dVal-dPro-NH2 (SEQ ID NO: 62); Ac-Nle-c[Asp-dTrp-dNal(2')-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 83); Ac-Nle-c[dPen-Ala-dNal(2')-Arg-Trp-dPen]-dVal-dPro-NH2 (SEQ ID NO: 338); Ac-Nle-c[dPen-Leu-dNal(2')-Arg-Trp-dPen]-dVal-dPro-NH2 (SEQ ID NO: 339); Ac-Nle-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 223); Ac-Arg-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 464); Ac-Lys-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 465); Ac-dLys-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 466); Ac-His-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 467); Ac-dHis-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 468); Ac-Nle-Nle-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 469); Ac-Nle-c[Asp-His-p(F)dPhe-His-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 470); Ac-Nle-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dVal-dVal-dVal-dPro-NH2 (SEQ ID NO: 474); Ac-Nle-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dPro-dVal-

dPro-NH2 (SEQ ID NO: 475); Ac-Nle-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 476); Ac-Nle-Nle-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 477); Ac-Nle-Nle-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dPro-dVal-dPro-NH2 (SEQ ID NO: 478); Ac-Arg-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 481); Ac-Lys-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 482); Ac-dLys-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 483); Ac-His-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 484); Ac-dHis-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 485); Ac-dArg-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 463); Ac-Ala-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 462); Ac-Ala-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 479); Ac-Nle-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dTle-dTle-dVal-NH2 (SEQ ID NO: 473); Ac-dArg-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 480); Ac-Nle-c[Asp-Gln-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 491); Ac-Nle-c[Asp-Bip-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 489); Ac-Nle-c[Asp-Trp-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 493); Ac-Nle-c[Asp-Pro-p(F)dPhe-Arg-dNal(2')-Lys]-dVal-dPro-NH2 (SEQ ID NO: 444); Ac-Nle-c[Asp-Pro-p(F)dPhe-Arg-Nal(2')-Lys]-dVal-dPro-NH2 (SEQ ID NO: 445); Ac-Nle-c[Asp-Tyr-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 495); Ac-Nle-c[Asp-Phe-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 487); Ac-Nle-c[Asp-dPhe-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 488); Ac-Nle-c[Asp-dTrp-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 494); Ac-Nle-c[Asp-His-p(F)dPhe-Arg-dNal(2')-Lys]-dVal-dPro-NH2 (SEQ ID NO: 471); Ac-Nle-c[Cys-Pro-p(F)dPhe-Arg-Trp-Cys]-dVal-dPro-NH2 (SEQ ID NO: 432); Ac-Nle-c[Asp-Pro-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 217); Ac-Nle-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 222); Ac-Nle-c[Cys-His-p(Br)dPhe-Arg-Trp-Cys]-dVal-dPro-NH2 (SEQ ID NO: 535); Ac-Ala-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 538); Ac-Nle-Nle-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 545); Ac-Nle-c[Asp-His-p(Br)dPhe-His-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 546); Ac-Nle-c[Asp-His-p(Br)dPhe-Arg-dNal(2')-Lys]-dVal-dPro-NH2 (SEQ ID NO: 547); Ac-Nle-c[Asp-His-p(Br)dPhe-Arg-Nal(2')-Lys]-dVal-dPro-NH2 (SEQ ID NO: 548); Ac-Nle-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dTle-dTle-dVal-NH2 (SEQ ID NO: 549); Ac-Nle-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dPro-dVal-dPro-NH2 (SEQ ID NO: 551); Ac-Nle-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dTle-dPro-

NH2 (SEQ ID NO: 552); Ac-Nle-Nle-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 553); Ac-Ala-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 555); Ac-Nle-c[Asp-dHis-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 562); Ac-Nle-c[Asp-Phe-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 563); Ac-Nle-c[Asp-dPhe-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 564); Ac-Nle-c[Asp-Bip-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 565); Ac-Nle-c[Asp-dGln-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 568); Ac-Nle-c[Asp-Trp-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 569); Ac-Nle-c[Asp-dTrp-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 570); Ac-Nle-c[Asp-Tyr-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 571); Ac-Nle-c[Asp-dTyr-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 572); Ac-dArg-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 539); Ac-dHis-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 544); Ac-dHis-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 561); Ac-dArg-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 556); Ac-dLys-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 542); Ac-His-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 560); Ac-His-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 543); Ac-dLys-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 559); Ac-Arg-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 557); Ac-Lys-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 541); Ac-Nle-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dVal-dVal-dVal-dPro-NH2 (SEQ ID NO: 550); Ac-Lys-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 558); Ac-Arg-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 540); Ac-Nle-Nle-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dPro-dVal-dPro-NH2 (SEQ ID NO: 554); Ac-Nle-c[Asp-His-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 363); Ac-Nle-c[Asp-His-dPhe-Arg-Trp-Pro-Lys]-dVal-dPro-NH2 (SEQ ID NO: 418); Ac-Nle-c[Asp-His-dPhe-Arg-Trp-Lys]-dPro-dVal-NH2 (SEQ ID NO: 621); Ac-Nle-c[Asp-His-dPhe-transPro(guan)-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 228); Ac-Nle-c[Asp-His-dPhe-cisPro(guan)-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 229); Ac-Nle-c[Asp-Ala-His-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 380); Ac-Nle-c[Asp-Trp-Pro-dPhe-His-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 398); Ac-Nle-c[Asp-Trp-Pro-dPhe-Arg-Phe-Lys]-dVal-dPro-NH2 (SEQ ID NO: 401); Ac-Nle-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dPro-dVal-dPro-NH2 (SEQ ID NO: 639); Ac-Nle-c[Asp-Pro-dPhe-Arg-dNal(2')-

Lys]-dVal-dPro-NH2 (SEQ ID NO: 430); Ac-Nle-c[Asp-Pro-dPhe-Arg-Nal(2')-Lys]-dVal-dPro-NH2 (SEQ ID NO: 431); Ac-Nle-c[Asp-Pro-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 225); Ac-Nle-c[dPen-dPhe-Arg-Trp-dPen]-dVal-dPro-NH2 (SEQ ID NO: 326); Ac-Nle-c[Asp-Pro-His-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 297); Ac-Nle-c[Asp-Pro-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 215); Ac-Nle-c[Asp-Phe-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 525); Ac-Nle-c[Asp-dPhe-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 526); Ac-Nle-c[Asp-Bip-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 527); Ac-Nle-c[Asp-Trp-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 531); Ac-Nle-c[Asp-Tyr-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 533); Ac-Nle-c[Asp-dTyr-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 534); Ac-Nle-c[Asp-dTrp-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 532); Ac-Nle-c[dCys-His-p(Cl)dPhe-Arg-Trp-Cys]-dVal-dPro-NH2 (SEQ ID NO: 498); Ac-Nle-c[Cys-His-p(Cl)dPhe-Arg-Trp-Cys]-dVal-dPro-NH2 (SEQ ID NO: 497); Ac-Nle-c[Asp-His-p(Cl)dPhe-Arg-dNal(2')-Lys]-dVal-dPro-NH2 (SEQ ID NO: 509); Ac-Nle-c[Asp-His-p(Cl)dPhe-Arg-Nal(2')-Lys]-dVal-dPro-NH2 (SEQ ID NO: 510); Ac-Nle-c[Asp-His-p(Cl)dPhe-His-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 508); Ac-Nle-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 220); Ac-Nle-Nle-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 507); Ac-Ala-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 517); Ac-Ala-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 500); Ac-Nle-Nle-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dPro-dVal-dPro-NH2 (SEQ ID NO: 516); Ac-Nle-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 514); Ac-Nle-c[Asp-dGln-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 530); Ac-Arg-c[Asp-dAla-His-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 268); Ac-Nle-c[Asp-dAla-His-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 378); Ac-dArg-c[Asp-dAla-His-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 379); Ac-Nle-c[Asp-dAla-His-dNal(2')-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 266); Ac-Arg-c[Asp-dAla-His-dNal(2')-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 267); Ac-Arg-c[Cys-dAla-His-dNal(2')-Arg-Trp-Cys]-dVal-dPro-NH2 (SEQ ID NO: 269); Ac-dArg-c[Asp-dAla-His-dNal(2')-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 270); Ac-Arg-c[Cys-dAla-His-dNal(2')-Arg-Trp-Cys]-NH2 (SEQ ID NO: 282); and Ac-Arg-c[Asp-dAla-His-dNal(2')-Arg-Trp-Lys]-NH2 (SEQ ID NO: 283).

**[0268]** In some embodiments, the present technology comprises a method or use, wherein the non-naturally occurring melanocortin analog includes a sequence according to Formula (IA): X1-X2-X3-R1-R2-R3-R4-R5-R6-R7-R8-Y1-Y2-Y3-Y4 (IA), wherein: X1 is absent or is selected from the group consisting of norleucine (Nle), arginine (Arg), D-arginine (dArg), alanine (Ala), lysine (Lys), D-lysine (dLys), histidine (His), D-histidine (dHis); X2 is absent, phenylalanine (Phe), or Nle; X3 is absent, Phe, or Nle; R1 is selected from the group consisting of Nle, D-norleucine (dNle), Ala, D-alanine (dAla), Arg, dArg, Lys, dLys, His, dHis, ornithine (Orn), D-ornithine (dOrn), D-leucine (dLeu), D-tyrosine (dTyr), phenylalanine (Phe), D-phenylalanine (dPhe), tryptophan (Trp), D-tryptophan (dTrp), aspartic acid (Asp), cysteine (Cys), and D-cysteine (dCys); R2 is selected from the group consisting of Asp, D-aspartic acid (dAsp), Cys, dCys, D-penicillamine (dPen), Ala, Trp, Phe, dPhe, His, dHis, Tyr, and dTyr; R3 is absent or is selected from the group consisting of His, Ala, proline (Pro), hydroxyproline (Hyp), leucine (Leu), D-glutamine (dGln), Phe, dPhe, Trp, dTrp, Tyr, dTyr, 2-aminotetraline-2-carboxylic acid (Atc), octohydroindole-2-carboxylic acid (Oic), 1-amino-1-cyclohexanecarboxylic acid (Che), tetrahydro-isoquinoline-3-carboxylic acid (Tic), 1-amino-1-cyclopentane carboxylic (Cpe), and biphenylalanine (Bip); R4 is selected from the group consisting of dPhe, para-chloro-D-phenylalanine (p(Cl)dPhe), para-bromo-D-phenylalanine (p(Br)dPhe), and para-fluoro-D-phenylalanine (p(F)dPhe); R5 is Arg or His; R6 is selected from the group consisting of Trp, dTrp, Phe, dNal(2'), 2'-naphthylalanine (Nal(2')), and 1'-naphthylalanine (Nal(1')); R7 is selected from the group consisting of Gly, Pro, Lys, dLys, Cys, dCys, penicillamine (Pen), dPen, and Orn; R8 is absent or Lys; Y1 is selected from the group consisting of valine (Val), D-valine (dVal), b2-valine (b2-Val), b3-valine (b3-Val), Pro, D-proline (dPro), b-proline (b-Pro), Hyp, D-hydroxyproline (dHyp), D-tert-leucine (dTle), dLeu, Trp, Arg, dArg, Lys, dLys, Gly, Ala, dAla, Asp, dAsp, asparagine (Asn), D-asparagine (dAsn), and D-threonine (dThr); Y2 is absent or is selected from the group consisting of Val, dVal, b2-Val, b3-Val, Pro, dPro, b-Pro, Hyp, dHyp, dTle, Arg, dArg, Gly, Ala, dAla, Asp, and dAsn; Y3 is absent or is selected from the group consisting of Val, dVal, Pro, dPro, dThr, Lys, and dLys; Y4 is absent or is selected from the group consisting of dVal, dPro, Asp, and dAsp; and the non-naturally occurring melanocortin analog is cyclized through a moiety selected from the group consisting of: a disulfide bond between R1 or R2 and R7 or R8 when each of R1 or R2 and R7 or R8 are independently selected from the group consisting

of Cys, dCys, and dPen; a disulfide bond between R2 and R7 when R2 is Cys,R7 is Pen, and R3 is absent; a lactam bridge between R1 or R2 and R7 or R8 when R1 or R2 is Asp and R7 or R8 is Lys or Orn; and a lactam bridge between R2 and R7 when R2 is dAsp and R7 is dLys; provided that: when R4 is p(F)dPhe, then (i) R3 is selected from Pro, dGln, dTyr, R6 is Trp, and the non-naturally occurring melanocortin analog is not cyclized between Cys at R2 and Cys at R7 or (ii) R3 is His and either R6 is Nal(2') or the non-naturally occurring melanocortin analog is cyclized through a disulfide bond between R2 and R7, where R2 and R7 are the same; when R4 is p(Br)dPhe, then the non-naturally occurring melanocortin analog is cyclized through a disulfide bond between dCys at R2 and Cys or dCys at R7; when R4 is dPhe, then (i) R3 is not His, Pro, or absent, (ii) R3 is His and either R2 is Phe or dAla or R2 is Ala and X1 is Arg or dArg, (iii) R3 is Pro and (a) R2 is Trp, and R5 is not His or R6 is not Phe or (b) R2 is not Trp or Pro, and either R5 is not dNal(2') or Nal(2') or X1 and Y3 are not both present, or (iv) R3 is absent and R2 and R7 are not both dPen; and when R4 is p(Cl)dPhe, then (i) R3 is selected from Aba, Aia, and Ata or (ii) R3 is His, R1 is not Ala, and (a) if R1 is Nle and Y1Y2 is dVal-dPro, then X1 is absent and the non-naturally occurring melanocortin analog is cyclized through a disulfide bond between dCys at R2 and dCys at R7, or (b) if R1 is Nle, and Y1Y2 is not dVal-dPro, then either X1 or Y3 is present.

**[0269]** In some embodiments, the non-naturally occurring melanocortin analog includes a sequence according to Formula (IA), wherein: X1 is absent or is selected from the group consisting of norleucine (Nle), arginine (Arg), D-arginine (dArg), alanine (Ala), lysine (Lys), D-lysine (dLys), histidine (His), D-histidine (dHis); X2 is absent, phenylalanine (Phe), or Nle; X3 is absent, Phe, or Nle; R1 is selected from the group consisting of Nle, D-norleucine (dNle), Ala, D-alanine (dAla), Arg, dArg, Lys, dLys, His, dHis, ornithine (Orn), D-ornithine (dOrn), D-leucine (dLeu), D-tyrosine (dTyr), phenylalanine (Phe), D-phenylalanine (dPhe), tryptophan (Trp), D-tryptophan (dTrp), aspartic acid (Asp), cysteine (Cys), and D-cysteine (dCys); R2 is selected from the group consisting of Asp, D-aspartic acid (dAsp), Cys, dCys, D-penicillamine (dPen), Ala, Trp, Phe, dPhe, His, dHis, Tyr, and dTyr; R3 is absent or is selected from the group consisting of His, Ala, proline (Pro), hydroxyproline (Hyp), leucine (Leu), D-glutamine (dGln), Phe, dPhe, Trp, dTrp, Tyr, dTyr, 2-aminotetraline-2-carboxylic acid (Atc), octohydroindole-2-carboxylic acid (Oic), 1-amino-1-cyclohexanecarboxylic acid (Che), tetrahydro-isoquinoline-3-carboxylic acid (Tic), 1-amino-

1-cyclopentane carboxylic (Cpe), and biphenylalanine (Bip); R4 is selected from the group consisting of dPhe, para-chloro-D-phenylalanine (p(Cl)dPhe), para-bromo-D-phenylalanine (p(Br)dPhe), and para-fluoro-D-phenylalanine (p(F)dPhe); R5 is Arg or His; R6 is selected from the group consisting of Trp, dTrp, Phe, dNal(2'), 2'-naphthylalanine (Nal(2')), and 1'-naphthylalanine (Nal(1')); R7 is selected from the group consisting of Gly, Pro, Lys, dLys, Cys, dCys, penicillamine (Pen), dPen, and Orn; R8 is absent or Lys; Y1 is selected from the group consisting of valine (Val), D-valine (dVal), b2-valine (b2-Val), b3-valine (b3-Val), Pro, D-proline (dPro), b-proline (b-Pro), Hyp, D-hydroxyproline (dHyp), D-tert-leucine (dTle), dLeu, Trp, Arg, dArg, Lys, dLys, Gly, Ala, dAla, Asp, dAsp, asparagine (Asn), D-asparagine (dAsn), and D-threonine (dThr); Y2 is absent or is selected from the group consisting of Val, dVal, b2-Val, b3-Val, Pro, dPro, b-Pro, Hyp, dHyp, dTle, Arg, dArg, Gly, Ala, dAla, Asp, and dAsn; Y3 is absent or is selected from the group consisting of Val, dVal, Pro, dPro, dThr, Lys, and dLys; Y4 is absent or is selected from the group consisting of dVal, dPro, Asp, and dAsp; and the non-naturally occurring melanocortin analog is cyclized through a moiety selected from the group consisting of: a disulfide bond between R1 or R2 and R7 or R8 when each of R1 or R2 and R7 or R8 are independently selected from the group consisting of Cys, dCys, and dPen; a disulfide bond between R2 and R7 when R2 is Cys, R7 is Pen, and R3 is absent; a lactam bridge between R1 or R2 and R7 or R8 when R1 or R2 is Asp and R7 or R8 is Lys or Orn; and a lactam bridge between R2 and R7 when R2 is dAsp and R7 is dLys; provided that the non-naturally occurring melanocortin analog does not include a sequence selected from the group consisting of: Ac-Nle-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 223); Ac-Arg-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 464); Ac-Lys-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 465); Ac-dLys-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 466); Ac-His-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 467); Ac-dHis-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 468); Ac-Nle-Nle-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 469); Ac-Nle-c[Asp-His-p(F)dPhe-His-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 470); Ac-Nle-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dVal-dVal-dVal-dPro-NH2 (SEQ ID NO: 474); Ac-Nle-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dPro-dVal-dPro-NH2 (SEQ ID NO: 475); Ac-Nle-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 476); Ac-Nle-Nle-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ

ID NO: 477); Ac-Nle-Nle-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dPro-dVal-dPro-NH2 (SEQ ID NO: 478); Ac-Arg-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 481); Ac-Lys-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 482); Ac-dLys-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 483); Ac-His-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 484); Ac-dHis-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 485); Ac-dArg-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 463); Ac-Ala-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 462); Ac-Ala-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 479); Ac-Nle-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dTle-dTle-dVal-NH2 (SEQ ID NO: 473); Ac-dArg-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 480); Ac-Nle-c[Asp-Bip-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 489); Ac-Nle-c[Asp-Trp-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 493); Ac-Nle-c[Asp-Pro-p(F)dPhe-Arg-dNal(2')-Lys]-dVal-dPro-NH2 (SEQ ID NO: 444); Ac-Nle-c[Asp-Pro-p(F)dPhe-Arg-Nal(2')-Lys]-dVal-dPro-NH2 (SEQ ID NO: 445); Ac-Nle-c[Asp-Tyr-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 495); Ac-Nle-c[Asp-Phe-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 487); Ac-Nle-c[Asp-dPhe-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 488); Ac-Nle-c[Asp-dTrp-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 494); Ac-Nle-c[Asp-His-p(F)dPhe-Arg-dNal(2')-Lys]-dVal-dPro-NH2 (SEQ ID NO: 471); Ac-Nle-c[Cys-Pro-p(F)dPhe-Arg-Trp-Cys]-dVal-dPro-NH2 (SEQ ID NO: 432); Ac-Nle-c[dCys-His-p(F)dPhe-Arg-Trp-Cys]-dVal-dPro-NH2 (SEQ ID NO: 460); Ac-Nle-c[Asp-Pro-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 217); Ac-Nle-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 222); Ac-Nle-c[Cys-His-p(Br)dPhe-Arg-Trp-Cys]-dVal-dPro-NH2 (SEQ ID NO: 535); Ac-Ala-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 538); Ac-Nle-Nle-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 545); Ac-Nle-c[Asp-His-p(Br)dPhe-His-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 546); Ac-Nle-c[Asp-His-p(Br)dPhe-Arg-dNal(2')-Lys]-dVal-dPro-NH2 (SEQ ID NO: 547); Ac-Nle-c[Asp-His-p(Br)dPhe-Arg-Nal(2')-Lys]-dVal-dPro-NH2 (SEQ ID NO: 548); Ac-Nle-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dTle-dTle-dVal-NH2 (SEQ ID NO: 549); Ac-Nle-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dPro-dVal-dPro-NH2 (SEQ ID NO: 551); Ac-Nle-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 552); Ac-Nle-Nle-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 553); Ac-Ala-c[Asp-His-p(Br)dPhe-

Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 555); Ac-Nle-c[Asp-Phe-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 563); Ac-Nle-c[Asp-dPhe-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 564); Ac-Nle-c[Asp-Bip-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 565); Ac-Nle-c[Asp-dGln-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 568); Ac-Nle-c[Asp-Trp-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 569); Ac-Nle-c[Asp-dTrp-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 570); Ac-Nle-c[Asp-Tyr-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 571); Ac-Nle-c[Asp-dTyr-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 572); Ac-dArg-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 539); Ac-dHis-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 544); Ac-dHis-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 561); Ac-dArg-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 556); Ac-dLys-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 542); Ac-His-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 560); Ac-His-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 543); Ac-dLys-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 559); Ac-Arg-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 557); Ac-Lys-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 541); Ac-Nle-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dVal-dVal-dVal-dPro-NH2 (SEQ ID NO: 550); Ac-Lys-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 558); Ac-Arg-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 540); Ac-Nle-Nle-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dPro-dVal-dPro-NH2 (SEQ ID NO: 554); Ac-Nle-c[Asp-His-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 363); Ac-Nle-c[Asp-His-dPhe-Arg-Trp-Pro-Lys]-dVal-dPro-NH2 (SEQ ID NO: 418); Ac-Nle-c[Asp-His-dPhe-Arg-Trp-Lys]-dPro-dVal-NH2 (SEQ ID NO: 621); Ac-Nle-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dPro-dVal-dPro-NH2 (SEQ ID NO: 639); Ac-Nle-c[dPen-dPhe-Arg-Trp-dPen]-dVal-dPro-NH2 (SEQ ID NO: 326); Ac-Nle-c[Asp-Trp-Pro-dPhe-His-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 398); Ac-Nle-c[Asp-Trp-Pro-dPhe-Arg-Phe-Lys]-dVal-dPro-NH2 (SEQ ID NO: 401); Ac-Nle-c[Asp-Pro-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 225); Ac-Nle-c[Asp-Pro-dPhe-Arg-dNal(2')-Lys]-dVal-dPro-NH2 (SEQ ID NO: 430); Ac-Nle-c[Asp-Pro-dPhe-Arg-Nal(2')-Lys]-dVal-dPro-NH2 (SEQ ID NO: 431); Ac-Nle-c[Asp-Ala-His-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 380); Ac-Nle-c[Asp-Pro-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 215); Ac-Nle-c[Asp-Phe-p(Cl)dPhe-Arg-Trp-Lys]-

dVal-dPro-NH2 (SEQ ID NO: 525); Ac-Nle-c[Asp-dPhe-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 526); Ac-Nle-c[Asp-Bip-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 527); Ac-Nle-c[Asp-Trp-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 531); Ac-Nle-c[Asp-Tyr-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 533); Ac-Nle-c[Asp-dTyr-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 534); Ac-Nle-c[Asp-dTrp-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 532); Ac-Nle-c[dCys-His-p(Cl)dPhe-Arg-Trp-Cys]-dVal-dPro-NH2 (SEQ ID NO: 498); Ac-Nle-c[Cys-His-p(Cl)dPhe-Arg-Trp-Cys]-dVal-dPro-NH2 (SEQ ID NO: 497); Ac-Nle-c[Asp-His-p(Cl)dPhe-Arg-dNal(2')-Lys]-dVal-dPro-NH2 (SEQ ID NO: 509); Ac-Nle-c[Asp-His-p(Cl)dPhe-Arg-Nal(2')-Lys]-dVal-dPro-NH2 (SEQ ID NO: 510); Ac-Nle-c[Asp-His-p(Cl)dPhe-His-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 508); Ac-Nle-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 220); Ac-Nle-Nle-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 507); Ac-Ala-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 517); Ac-Ala-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 500); Ac-Nle-Nle-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dPro-dVal-dPro-NH2 (SEQ ID NO: 516); and Ac-Nle-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 514).

**[0270]** In some embodiments, the present technology comprises a method or use, wherein the non-naturally occurring melanocortin analog includes a sequence of Formula (IB): X1-X2-X3-R1-R2-Pro-R4-R5-R6-R7-R8-Y1-Y2-Y3-Y4-Y5-Y6-Y7 (IB), wherein: X1 is absent or norleucine (Nle); X2 is absent or Nle; X3 is absent or Nle; R1 is selected from the group consisting of Nle, D-norleucine (dNle), alanine (Ala), D-alanine (dAla), arginine (Arg), D-arginine (dArg), lysine (Lys), D-lysine (dLys), histidine (His), D-histidine (dHis), ornithine (Orn), D-ornithine (dOrn), D-leucine (dLeu), D-tyrosine (dTyr), phenylalanine (Phe), D-phenylalanine (dPhe), tryptophan (Trp), and D-tryptophan (dTrp); R2 is selected from the group consisting of aspartic acid (Asp), D-aspartic acid (dAsp), cysteine (Cys), D-cysteine (dCys), and D-penicillamine (dPen); R4 is dPhe or para-fluoro-D-phenylalanine (p(F)dPhe); R5 is selected from the group consisting of Arg, His, cisPro(guan), and transPro(guan); R6 is selected from the group consisting of Trp, dTrp, Phe, Aia, Aba, Ata, and 1'-naphthylalanine (Nal(1')); R7 is selected from the group consisting of Gly, Lys, dLys, Cys, dCys, dPen, and Orn; R8 is absent or Lys; Y1 is absent or is selected from the group consisting of valine (Val), D-valine (dVal), b2-valine (b2-Val), b3-valine (b3-Val), Pro, D-proline (dPro), b-proline

(b-Pro), Hyp, D-hydroxyproline (dHyp), D-tert-leucine (dTle), dLeu, Trp, Arg, dArg, Lys, dLys, Gly, Ala, dAla, Asp, dAsp, asparagine (Asn), D-asparagine (dAsn), and D-threonine (dThr); Y2 is absent or is selected from the group consisting of Val, dVal, b2-Val, b3-Val, Pro, dPro, b-Pro, Hyp, dHyp, dTle, Arg, dArg, Gly, Ala, dAla, Asp, and dAsn; Y3 is absent or is selected from the group consisting of Val, dVal, Pro, dPro, dThr, Lys, and dLys; Y4 is absent or is selected from the group consisting of dVal, dPro, Asp, and dAsp; Y5 is absent or dVal; Y6 is absent or dVal; Y7 is absent or dPro; and the non-naturally occurring melanocortin analog is cyclized through a moiety selected from the group consisting of: a disulfide bond between R2 and R7 when each of R2 and R7 are independently selected from the group consisting of Cys, dCys, and dPen; and a lactam bridge between R2 and R7 when R2 is Asp or dAsp and R7 is Lys, dLys, or Orn; provided that: when R4 is p(F)dPhe, then the non-naturally occurring melanocortin analog is not cyclized between Cys at R2 and Cys at R7; and when R4 is dPhe and one or more of X1, X2, and X3 is present, then Y3-Y7 are absent.

**[0271]** In some embodiments, the present technology comprises a method or use, wherein the non-naturally occurring melanocortin analog includes a sequence of Formula (IB), wherein: X1-X2-X3-R1-R2-Pro-R4-R5-R6-R7-R8-Y1-Y2-Y3-Y4-Y5-Y6-Y7 (IB), wherein: X1 is absent or norleucine (Nle); X2 is absent or Nle; X3 is absent or Nle; R1 is selected from the group consisting of Nle, D-norleucine (dNle), alanine (Ala), D-alanine (dAla), arginine (Arg), D-arginine (dArg), lysine (Lys), D-lysine (dLys), histidine (His), D-histidine (dHis), ornithine (Orn), D-ornithine (dOrn), D-leucine (dLeu), D-tyrosine (dTyr), phenylalanine (Phe), D-phenylalanine (dPhe), tryptophan (Trp), and D-tryptophan (dTrp); R2 is selected from the group consisting of aspartic acid (Asp), D-aspartic acid (dAsp), cysteine (Cys), D-cysteine (dCys), and D-penicillamine (dPen); R4 is dPhe or para-fluoro-D-phenylalanine (p(F)dPhe); R5 is selected from the group consisting of Arg, His, cisPro(guan), and transPro(guan); R6 is selected from the group consisting of Trp, dTrp, Phe, Aia, Aba, Ata, and 1'-naphthylalanine (Nal(1')); R7 is selected from the group consisting of Gly, Lys, dLys, Cys, dCys, dPen, and Orn; R8 is absent or Lys; Y1 is absent or is selected from the group consisting of valine (Val), D-valine (dVal), b2-valine (b2-Val), b3-valine (b3-Val), Pro, D-proline (dPro), b-proline (b-Pro), Hyp, D-hydroxyproline (dHyp), D-tert-leucine (dTle), dLeu, Trp, Arg, dArg, Lys, dLys, Gly, Ala, dAla, Asp, dAsp, asparagine (Asn), D-asparagine (dAsn), and D-threonine (dThr); Y2 is absent or is selected from the group

consisting of Val, dVal, b2-Val, b3-Val, Pro, dPro, b-Pro, Hyp, dHyp, dTle, Arg, dArg, Gly, Ala, dAla, Asp, and dAsn; Y3 is absent or is selected from the group consisting of Val, dVal, Pro, dPro, dThr, Lys, and dLys; Y4 is absent or is selected from the group consisting of dVal, dPro, Asp, and dAsp; Y5 is absent or dVal; Y6 is absent or dVal; Y7 is absent or dPro; and the non-naturally occurring melanocortin analog is cyclized through a moiety selected from the group consisting of: a disulfide bond between R2 and R7 when each of R2 and R7 are independently selected from the group consisting of Cys, dCys, and dPen; and a lactam bridge between R2 and R7 when R2 is Asp or dAsp and R7 is Lys, dLys, or Orn; provided that the non-naturally occurring melanocortin analog does not include a sequence of: Ac-Nle-c[Cys-Pro-p(F)dPhe-Arg-Trp-Cys]-dVal-dPro-NH2 (SEQ ID NO: 432); or Ac-Nle-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dPro-dVal-dPro-NH2 (SEQ ID NO: 639).

**[0272]** In some embodiments, the present technology comprises a method or use, wherein the non-naturally occurring melanocortin analog includes a sequence of Formula (IC): X1-X2-R1-R2-Pro-dPhe-R5-R6-R7-Y1-Y2-Y3-Y4 (IC), wherein: X1 is selected from the group consisting of norleucine (Nle), arginine (Arg), D-arginine (dArg), alanine (Ala), lysine (Lys), D-lysine (dLys), histidine (His), D-histidine (dHis); X2 is absent or Nle; R1 is selected from the group consisting of aspartic acid (Asp), cysteine (Cys), and D-cysteine (dCys); R2 is selected from the group consisting of tryptophan (Trp), phenylalanine (Phe), D-phenylalanine (dPhe), histidine (His), D-histidine (dHis), tyrosine (Tyr), and D-tyrosine (dTyr); R5 is Arg; R6 is selected from the group consisting of Trp, 2'-D-naphthylalanine (dNal(2')), 2'-naphthylalanine (Nal(2')), and 1'-naphthylalanine (Nal(1')); R7 is selected from the group consisting of Lys, Cys, and dCys; Y1 is absent or is selected from the group consisting of D-valine (dVal), D-tert-leucine (dTle), dArg, and dLys; Y2 is absent or is selected from the group consisting of dVal, dPro, and D-hydroxyproline (dHyp); Y3 is absent, dVal, or dPro; Y4 is absent or dPro; and the non-naturally occurring melanocortin analog is cyclized through a moiety selected from the group consisting of: a disulfide bond between R1 and R7 when both of R1 and R7 are independently selected from the group consisting of Cys, dCys, and dPen; and a lactam bridge between R1 and R7 when R1 is Asp and R7 is Lys;

**[0273]** In some embodiments, the present technology comprises a method or use, wherein the non-naturally occurring melanocortin analog includes a sequence of Formula (ID): X1-R1-R2-R3-p(Cl)dPhe-Arg-Trp-R7-Y1-Y2-Y3-Y4 (ID), wherein: X1 is absent or norleucine (Nle); R1 is selected from the group consisting of Nle, arginine (Arg), D-arginine (dArg), lysine (Lys), D-lysine (dLys), histidine (His), and D-histidine (dHis); R2 is aspartic acid (Asp) or D-cysteine (dCys); R3 is selected from the group consisting of His, 4-amino-1,2,4,5-tetrahydro-2-benzazepin-3-one (Aba), 7-amino-7,8-dihydro-4H-[1,2,3]triazolo-[1,5-a][1,4]diazepin-6(5H)-one (Ata), and 4-amino-1,4,5,6-tetrahydroazepino[4,3-b]indol-3(2H)-one (Aia); R7 is Lys or dCys; Y1 is selected from the group consisting of D-valine (dVal), D-proline (dPro), and D-tert-leucine (dTle); Y2 is absent or is selected from the group consisting of dVal, dPro, and dTle; Y3 is absent, dVal, or dPro; Y4 is absent or dPro; and the non-naturally occurring melanocortin analog is cyclized through a moiety selected from the group consisting of: a disulfide bond between R2 and R7 when both of R2 and R7 are dCys; and a lactam bridge between R2 and R7 when R2 is Asp and R7 is Lys; provided that when R3 is His and R1 is Nle, then (i) Y1Y2 is dVal-dPro, X1 is absent, and the non-naturally occurring melanocortin analog is cyclized through a disulfide bond, or (b) Y1Y2 is not dVal-dPro and either X1 or Y3 is present.

**[0274]** In some embodiments, the present technology comprises a method or use, wherein the non-naturally occurring melanocortin analog includes a sequence of Formula (ID), wherein: X1 is absent or norleucine (Nle); R1 is selected from the group consisting of Nle, arginine (Arg), D-arginine (dArg), lysine (Lys), D-lysine (dLys), histidine (His), and D-histidine (dHis); R2 is aspartic acid (Asp) or D-cysteine (dCys); R3 is selected from the group consisting of His, 4-amino-1,2,4,5-tetrahydro-2-benzazepin-3-one (Aba), 7-amino-7,8-dihydro-4H-[1,2,3]triazolo-[1,5-a][1,4]diazepin-6(5H)-one (Ata), and 4-amino-1,4,5,6-tetrahydroazepino[4,3-b]indol-3(2H)-one (Aia); R7 is Lys or dCys; Y1 is selected from the group consisting of D-valine (dVal), D-proline (dPro), and D-tert-leucine (dTle); Y2 is absent or is selected from the group consisting of dVal, dPro, and dTle; Y3 is absent, dVal, or dPro; Y4 is absent or dPro; and the non-naturally occurring melanocortin analog is cyclized through a moiety selected from the group consisting of: a disulfide bond between R2 and R7 when both of R2 and R7 are dCys; and a lactam bridge between R2 and R7 when R2 is Asp and R7 is Lys; provided that the non-naturally occurring melanocortin analog does not

include a sequence selected from the group consisting of: Ac-Nle-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 220); Ac-Nle-Nle-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 507); Ac-Nle-Nle-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dPro-dVal-dPro-NH2 (SEQ ID NO: 516); Ac-Nle-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 514); and.

**[0275]** In some embodiments, an N-terminus of the non-naturally occurring melanocortin analog is modified by an acyl group.

**[0276]** In some embodiments, the acyl group is an acetyl group.

**[0277]** In some embodiments, an N-terminus of the non-naturally occurring melanocortin analog is not modified.

**[0278]** In some embodiments, a C-terminus of the non-naturally occurring melanocortin analog is modified by an amide group.

**[0279]** In some embodiments, a C-terminus of the non-naturally occurring melanocortin analog is not modified.

**[0280]** In some embodiments, Y1-Y2 are present and Y3- Y8 are absent.

**[0281]** In some embodiments, Y1 is D-valine and Y2 is D-proline.

**[0282]** In some embodiments, the present technology comprises a method or a use, w wherein Y1 is D-tert-leucine and Y2 is D-proline.

**[0283]** In some embodiments, R4 is dNal(2').

**[0284]** In some embodiments, the sequence of Formula (I) is: Ac-Nle-c[Asp-His-dNal(2')-Arg-Trp-Pro-Lys]-dVal-dPro-NH2 (SEQ ID NO: 8), wherein c represents cyclization through R2 and R8 via a lactam bond.

**[0285]** In some embodiments, R4 is Phe or dPhe.

**[0286]** In some embodiments, the sequence of any one of Formulae (I)-(ID) is selected from the group consisting of: Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-OH (SEQ ID NO: 291); Ac-Nle-c[Asp-Pro-Phe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 294); Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 295; E2); and Ac-Nle-c[Asp-

Pro-His-Phe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 296). wherein c represents cyclization through R2 and R7 via a lactam bond.

**[0287]** In some embodiments, the sequence of any one of Formulae (I)-(ID) is selected from the group consisting of: Ac-dLeu-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO:298); Ac-dAla-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 299); Ac-Ala-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro- NH2 (SEQ ID NO: 300); Ac-dNle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 301); Ac-dArg-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 302); Ac-dPhe-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 303); Ac-dTyr-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 304); Phe-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 305); His-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 306); Trp-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 307); dPhe-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 308); dHis-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 309); dTrp-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 310); Ac-Arg-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 311); Ac-dLys-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 312); Ac-Lys-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 313); Ac-His-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 314); Ac-dHis-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 315); Ac-Orn-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 316); and Ac-dOrn-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 317), wherein c represents cyclization through R2 and R7 via a lactam bond.

**[0288]** In some embodiments, the sequence of any one of Formulae (I)-(ID) is selected from the group consisting of: Ac-Nle-c[Cys-Pro-dPhe-Arg-Trp-Cys]-dVal-dPro-NH2 (SEQ ID NO: 318); Ac-Nle-c[dCys-Pro-dPhe-Arg-Trp-Cys]-dVal-dPro-NH2 (SEQ ID NO: 319); Ac-Nle-c[dPen-Pro-dPhe-Arg-Trp-dPen]-dVal-dPro-NH2 (SEQ ID NO: 320); Ac-Nle-c[dCys-Pro-dPhe-Arg-Trp-dCys]-dVal-dPro-NH2 (SEQ ID NO: 321); Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Orn]-dVal-dPro-NH2 (SEQ ID NO: 322); and Ac-Nle-c[Cys-dPhe-Arg-Trp-Pen]-dVal-dPro-NH2 (SEQ ID NO: 324), wherein c represents cyclization through R2 and R7 via a disulfide bond.

**[0289]** In some embodiments, the sequence of any one of Formulae (I)-(ID) is selected from the group consisting of: Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Gly-Lys]-dVal-dPro-NH2 (SEQ ID NO: 351); Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Gly-Lys]-dPro-dPro-Lys-Asp-NH2 (SEQ ID NO: 352); and Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Gly-Lys]-dPro-dPro-dLys-dAsp-NH2 (SEQ ID NO: 353), wherein c represents cyclization through R2 and R8 via a lactam bond.

**[0290]** In some embodiments, the sequence of any one of Formulae (I)-(ID) is selected from the group consisting of: Ac-Nle-c[Asp-Ala-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 354); Ac-Nle-c[Asp-Leu-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 355); Ac-Nle-c[Asp-Cpe-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 358); Ac-Nle-c[Asp-Che-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 359); Ac-Nle-c[Asp-Oic-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 360); Ac-Nle-c[Asp-Ioc-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 361); Ac-Nle-c[Asp-Tic-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 362); Ac-Nle-c[Asp-Hyp-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 364); Ac-Nle-c[Asp-Phe-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 366); Ac-Nle-c[Asp-dPhe-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 367); Ac-Nle-c[Asp-Bip-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 368); Ac-Nle-c[Asp-dGln-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 371); Ac-Nle-c[Asp-Trp-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 372); Ac-Nle-c[Asp-dTrp-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 373); Ac-Nle-c[Asp-Tyr-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 374); Ac-Nle-c[Asp-dTyr-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 375); Ac-Nle-c[Asp-Aba-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 198); Ac-Nle-c[Asp-Aia-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 207); Ac-Nle-c[Asp-Ata-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 208); Ac-Nle-c[Asp-Atc-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 212); Ac-Nle-c[Asp-APC-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 213); and Ac-Nle-c[Asp-APPC-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 214), wherein c represents cyclization through R2 and R7 via a lactam bond.

**[0291]** In some embodiments, the sequence of any one of Formulae (I)-(ID) is selected from the group consisting of: Ac-Arg-c[Asp-dAla-His-dPhe-Arg-Trp-Lys]-NH2 (SEQ ID NO: 281); Ac-Arg-c[Asp-Ala-His-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 381); and Ac-

dArg-c[Asp-Ala-His-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 382), wherein c represents cyclization through R1 and R7 via a lactam bond.

**[0292]** In some embodiments, the sequence of any one of Formulae (I)-(ID) is selected from the group consisting of: Ac-Nle-c[Asp-Trp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 226); Ac-Nle-c[Cys-Trp-Pro-dPhe-Arg-Trp-Cys]-dVal-dPro-NH2 (SEQ ID NO: 383); Ac-Nle-c[dCys-Trp-Pro-dPhe-Arg-Trp-Cys]-dVal-dPro-NH2 (SEQ ID NO: 384); Ac-Nle-c[dCys-Trp-Pro-dPhe-Arg-Trp-dCys]-dVal-dPro-NH2 (SEQ ID NO: 385); Ac-Ala-c[Asp-Trp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 386); Ac-Lys-c[Asp-Trp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 387); Ac-dLys-c[Asp-Trp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 388); Ac-Arg-c[Asp-Trp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 389); Ac-dArg-c[Asp-Trp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 390); Ac-dHis-c[Asp-Trp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 391); Ac-His-c[Asp-Trp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 392); Ac-Nle-Nle-c[Asp-Trp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 393); Ac-Nle-c[Asp-Trp-Ala-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 394); Ac-Nle-c[Asp-Trp-Leu-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 395); Ac-Nle-c[Asp-Trp-Pro-dPhe-Arg-Nal(1']-Lys]-dVal-dPro-NH2 (SEQ ID NO: 399); Ac-Nle-c[Asp-Trp-Pro-dPhe-Arg-dNal(2')-Lys]-dVal-dPro-NH2 (SEQ ID NO: 403); Ac-Nle-c[Asp-Trp-Pro-dPhe-Arg-Nal(2')-Lys]-dVal-dPro-NH2 (SEQ ID NO: 404); Ac-Nle-c[Asp-Trp-Pro-dPhe-Arg-Trp-Lys]-dArg-dVal-dPro-NH2 (SEQ ID NO: 405); Ac-Nle-c[Asp-Trp-Pro-dPhe-Arg-Trp-Lys]-dLys-dVal-dPro-NH2 (SEQ ID NO: 406); Ac-Nle-c[Asp-Trp-Pro-dPhe-Arg-Trp-Lys]-dArg-dPro-NH2 (SEQ ID NO: 407); Ac-Nle-c[Asp-Trp-Pro-dPhe-Arg-Trp-Lys]-dLys-dPro-NH2 (SEQ ID NO: 408); Ac-Nle-c[Asp-Trp-Pro-dPhe-Arg-Trp-Lys]-dVal-dHyp-NH2 (SEQ ID NO: 409); Ac-Nle-c[Asp-Trp-Pro-dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 410); Ac-Nle-c[Asp-Trp-Pro-dPhe-Arg-Trp-Lys]-dVal-dVal-dVal-dPro-NH2 (SEQ ID NO: 411); Ac-Nle-c[Asp-Phe-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 412); Ac-Nle-c[Asp-His-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 413); Ac-Nle-c[Asp-Tyr-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 414); Ac-Nle-c[Asp-dPhe-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 415); Ac-Nle-c[Asp-dHis-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 416); and Ac-Nle-c[Asp-dTyr-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 417), wherein c represents cyclization through R1 and R7 via a lactam bond or a disulfide bond.

**[0293]** In some embodiments, the sequence of any one of Formulae (I)-(ID) is: Ac-Nle-c[Asp-Hyp-dPhe-Arg-Trp-Pro-Lys]-dVal-dPro-NH2 (SEQ ID NO: 419), wherein c represents cyclization through R2 and R8 via a lactam bond.

**[0294]** In some embodiments, the sequence of any one of Formulae (I)-(ID) is selected from the group consisting of: Ac-Nle-Phe-Phe-c[Asp-Phe-His-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 421); Ac-Nle-c[Asp-Phe-His-dPhe-Arg-Trp-Lys]-dLeu-dPro-NH2 (SEQ ID NO: 422); Ac-Nle-c[Asp-Phe-His-dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 423); and Ac-Nle-c[Asp-Phe-His-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 424), wherein c represents cyclization through R1 and R7 via a lactam bond.

**[0295]** In some embodiments, the sequence of any one of Formulae (I)-(ID) is selected from the group consisting of: Ac-Nle-c[Asp-Pro-dPhe-Arg-dTrp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 187); Ac-Nle-c[Asp-Pro-dPhe-Arg-Aia-Lys]-dVal-dPro-NH2 (SEQ ID NO: 233); Ac-Nle-c[Asp-Pro-dPhe-Arg-Aba-Lys]-dVal-dPro-NH2 (SEQ ID NO: 234); Ac-Nle-c[Asp-Pro-dPhe-Arg-Ata-Lys]-dVal-dPro-NH2 (SEQ ID NO: 235); Ac-Nle-c[Asp-Pro-dPhe-Arg-Nal(1')-Lys]-dVal-dPro-NH2 (SEQ ID NO: 427); and Ac-Nle-c[Asp-Pro-dPhe-Arg-Phe-Lys]-dVal-dPro-NH2 (SEQ ID NO: 429), wherein c represents cyclization through R2 and R7 via a lactam bond.

**[0296]** In some embodiments, the sequence of any one of Formulae (I)-(ID) is selected from the group consisting of: Ac-Nle-c[Asp-Pro-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 218); Ac-Nle-c[dCys-Pro-p(F)dPhe-Arg-Trp-Cys]-dVal-dPro-NH2 (SEQ ID NO: 433); Ac-Nle-c[dCys-Pro-p(F)dPhe-Arg-Trp-dCys]-dVal-dPro-NH2 (SEQ ID NO: 434); Ac-Ala-c[Asp-Pro-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 435); Ac-dArg-c[Asp-Pro-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 436); Ac-Arg-c[Asp-Pro-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 437); Ac-Lys-c[Asp-Pro-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 438); Ac-dLys-c[Asp-Pro-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 439); Ac-His-c[Asp-Pro-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 440); Ac-dHis-c[Asp-Pro-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 441); Ac-Nle-Nle-c[Asp-Pro-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 442); Ac-Nle-c[Asp-Pro-p(F)dPhe-His-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 443); Ac-Nle-c[Asp-Pro-p(F)dPhe-Arg-Trp-Lys]-dTle-dTle-dVal-NH2 (SEQ ID NO: 446); Ac-Nle-

c[Asp-Pro-p(F)dPhe-Arg-Trp-Lys]-dVal-dVal-dVal-dPro-NH2 (SEQ ID NO: 447); Ac-Nle-c[Asp-Pro-p(F)dPhe-Arg-Trp-Lys]-dPro-dVal-dPro-NH2 (SEQ ID NO: 448); Ac-Nle-c[Asp-Pro-p(F)dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 449); Ac-Nle-Nle-c[Asp-Pro-p(F)dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 450); Ac-Nle-Nle-c[Asp-Pro-p(F)dPhe-Arg-Trp-Lys]-dPro-dVal-dPro-NH2 (SEQ ID NO: 451); Ac-Ala-c[Asp-Pro-p(F)dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 452); Ac-dArg-c[Asp-Pro-p(F)dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 453); Ac-Arg-c[Asp-Pro-p(F)dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 454); Ac-Lys-c[Asp-Pro-p(F)dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 455); Ac-dLys-c[Asp-Pro-p(F)dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 456); Ac-His-c[Asp-Pro-p(F)dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 457); Ac-dHis-c[Asp-Pro-p(F)dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 458); Ac-Nle-c[Cys-His-p(F)dPhe-Arg-Trp-Cys]-dVal-dPro-NH2 (SEQ ID NO: 459); Ac-Nle-c[dCys-His-p(F)dPhe-Arg-Trp-Cys]-dVal-dPro-NH2 (SEQ ID NO: 460); Ac-Nle-c[dCys-His-p(F)dPhe-Arg-Trp-dCys]-dVal-dPro-NH2 (SEQ ID NO: 461); Ac-Nle-c[Asp-His-p(F)dPhe-Arg-Nal(2')-Lys]-dVal-dPro-NH2 (SEQ ID NO: 472); Ac-Nle-c[Asp-dGln-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 492); and Ac-Nle-c[Asp-dTyr-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 496), wherein c represents cyclization through R2 and R7 via a lactam bond or a disulfide bond.

**[0297]** In some embodiments, the sequence of any one of Formulae (I)-(ID) is selected from the group consisting of: Ac-Nle-c[Asp-Aba-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 209); Ac-Nle-c[Asp-Aia-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 210); Ac-Nle-c[Asp-Ata-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 211); Ac-Nle-c[dCys-His-p(Cl)dPhe-Arg-Trp-dCys]-dVal-dPro-NH2 (SEQ ID NO: 499); Ac-dArg-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 501); Ac-Arg-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 502); Ac-Lys-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 503); Ac-dLys-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 504); Ac-His-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 505); Ac-dHis-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 506); Ac-Nle-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dTle-dTle-dVal-NH2 (SEQ ID NO: 511); Ac-Nle-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dVal-dVal-dPro-NH2 (SEQ ID NO: 512); Ac-Nle-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dPro-dVal-dPro-NH2 (SEQ ID NO: 513); Ac-Nle-Nle-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 515); Ac-

dArg-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 518); Ac-Arg-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 519); Ac-Lys-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 520); Ac-dLys-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 521); Ac-His-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 522); and Ac-dHis-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 523), wherein c represents cyclization through R2 and R7 via a lactam bond or a disulfide bond.

**[0298]** In some embodiments, the sequence of any one of Formulae (I)-(ID) is selected from the group consisting of: Ac-Nle-c[dCys-His-p(Br)dPhe-Arg-Trp-Cys]-dVal-dPro-NH2 (SEQ ID NO: 536); or Ac-Nle-c[dCys-His-p(Br)dPhe-Arg-Trp-dCys]-dVal-dPro-NH2 (SEQ ID NO: 537), wherein c represents cyclization through R2 and R7 via a disulfide bond.

**[0299]** In some embodiments, the sequence of any one of Formulae (I)-(ID) is selected from the group consisting of: Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-Val-Pro-NH2 (SEQ ID NO: 573); Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-Hyp-NH2 (SEQ ID NO: 574); Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dHyp-NH2 (SEQ ID NO: 575); Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-Val-NH2 (SEQ ID NO: 576); Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-Pro-NH2 (SEQ ID NO: 577); Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-Arg-NH2 (SEQ ID NO: 578); Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dArg-NH2 (SEQ ID NO: 579); Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dArg-dPro-NH2 (SEQ ID NO: 580); Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-Arg-NH2 (SEQ ID NO: 581); Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dArg-NH2 (SEQ ID NO: 582); Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-Lys-Pro-Val-NH2 (SEQ ID NO: 583); Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dLys-dPro-NH2 (SEQ ID NO: 584); Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-Lys-Val-Pro-NH2 (SEQ ID NO: 585); Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-Lys-dVal-dPro-NH2 (SEQ ID NO: 586); Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dLys-dVal-dPro-NH2 (SEQ ID NO: 587); Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-Arg-Pro-Val-NH2 (SEQ ID NO: 588); Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-Arg-Val-Pro-NH2 (SEQ ID NO: 589); Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dArg-dVal-dPro-NH2 (SEQ ID NO: 590); Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 591); Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dTle-dTle-dPro-NH2 (SEQ ID NO: 592); Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dTle-dTle-dVal-NH2 (SEQ ID NO: 593); Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-

dVal-dTle-NH2 (SEQ ID NO: 594); Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dVal-dPro-NH2 (SEQ ID NO: 595); Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dPro-dVal-dPro-NH2 (SEQ ID NO: 596); Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dVal-dVal-dPro-NH2 (SEQ ID NO: 597); Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-dVal-dPro-NH2 (SEQ ID NO: 598); Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dVal-dVal-dVal-dVal-dVal-dPro-NH2 (SEQ ID NO: 599); Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-Trp-NH2 (SEQ ID NO: 600); Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-Lys-dPro-dVal-NH2 (SEQ ID NO: 601); Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dAla-dAla-NH2 (SEQ ID NO: 602); Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-Asp-NH2 (SEQ ID NO: 603); Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dHyp-NH2 (SEQ ID NO: 604); Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dAsn-NH2 (SEQ ID NO: 605); Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-Asp-NH2 (SEQ ID NO: 606); Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-Asn-dPro-NH2 (SEQ ID NO: 607); Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-Hyp-NH2 (SEQ ID NO: 608); Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-Ala-Ala-NH2 (SEQ ID NO: 609); Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-Gly-Gly-NH2 (SEQ ID NO: 610); Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-Asp-dPro-NH2 (SEQ ID NO: 611); Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dAsn-dPro-NH2 (SEQ ID NO: 612); Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-Asn-NH2 (SEQ ID NO: 613); Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dAsp-NH2 (SEQ ID NO: 614); Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dAsn-NH2 (SEQ ID NO: 615); Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-Lys-dPro-NH2 (SEQ ID NO: 616); Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dPro-dVal-OH (SEQ ID NO: 617); Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dThr-dPro-dThr-NH2 (SEQ ID NO: 618); Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dThr-dPro-dThr-OH (SEQ ID NO: 619); Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dPro-dVal-NH2 (SEQ ID NO: 620); Ac-Nle-c[dAsp-Pro-dPhe-Arg-Trp-dLys]-dPro-dVal-NH2 (SEQ ID NO: 622); Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-βPro-β2Val-NH2 (SEQ ID NO: 623); Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-βPro-β3Val-NH2 (SEQ ID NO: 624); Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-β2Val-βPro-NH2 (SEQ ID NO: 625); Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-β3Val-βPro-NH2 (SEQ ID NO: 626); and Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-βPro-βPro-NH2 (SEQ ID NO: 627), wherein c represents cyclization through R2 and R7 via a lactam bond.

**[0300]** In some embodiments, the sequence of any one of Formulae (I)-(ID) is selected from the group consisting of: Ac-Nle-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 628); Ac-Nle-Nle-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID

NO: 629); and Ac-Nle-Nle-Nle-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 630), wherein c represents cyclization through R2 and R7 via a lactam bond.

**[0301]** In some embodiments, the sequence of any one of Formulae (I)-(ID) is selected from the group consisting of: Ac-Arg-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dArg-dVal-dPro-NH2 (SEQ ID NO: 631); Ac-dLys-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dLys-dVal-dPro-NH2 (SEQ ID NO: 632); Ac-Lys-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dArg-dPro-NH2 (SEQ ID NO: 633); Ac-His-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dLys-dPro-NH2 (SEQ ID NO: 634); Ac-dHis-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dHyp-NH2 (SEQ ID NO: 635); Ac-Orn-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 636); Ac-dOrn-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dVal-dVal-dPro-NH2 (SEQ ID NO: 637); Ac-Nle-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 638); Ac-Ala-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 640); Ac-dArg-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 641); Ac-Arg-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 642); Ac-Lys-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 643); Ac-dLys-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 644); Ac-His-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 645); and Ac-dHis-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 646), wherein c represents cyclization through R2 and R7 via a lactam bond.

**[0302]** In some embodiments, the non-naturally occurring melanocortin analog includes any one of SEQ ID NOs: 8, 187, 198, 207-218, 226, 231-235, 281, 291, 294-296, 298-322, 324, 351-355, 358-362, 364, 366-368, 371-375, 381-395, 399, 403-417, 419, 421-425, 427, 429, 433-443, 446-461, 472, 492, 496, 499-506, 511-513, 515, 518-523, 536-537, 573-599, 600-620, 622-646.

**[0303]** In some embodiments, the non-naturally occurring melanocortin analog includes any one of the sequences of SEQ ID NOs: 187, 212, 218, 226, 291, 295, 298-322, 324, 351-355, 358-360, 362, 364, 366-368, 371-375, 381-395, 399, 403-417, 419, 421-425, 427, 429, 433-443, 446-461, 472, 492, 496, 499-506, 511-513, 515, 518-523, 536-537, 573-598, 600-646.

**[0304]** In some embodiments, the non-naturally occurring melanocortin analog includes any one of the sequences of SEQ ID NOs: 187, 218, 231-235, 291, 295, 298-322, 351-353, 425, 427, 429, 433-443, 446-458, 573-599, 600-620, 622-646.

**[0305]** In some embodiments, the non-naturally occurring melanocortin analog includes any one of the sequences of SEQ ID NOs: 226, 383-393, 399, 403-417.

**[0306]** In some embodiments, the non-naturally occurring melanocortin analog includes any one of the sequences of SEQ ID NOs: 209-211, 499, 501-506, 511-513, 515, 518-523.

**[0307]** In some embodiments, the non-naturally occurring melanocortin analog is present in a pharmaceutical composition.

**[0308]** In some embodiments, the pharmaceutical composition includes one or more pharmaceutically acceptable excipients and/or carriers.

**[0309]** In some embodiments, the one or more pharmaceutically acceptable excipients and/or carriers of the pharmaceutical composition include water.

**[0310]** In some embodiments, the non-naturally occurring melanocortin analog is administered (i) at a first dose of about 5 mg/kg to about 20 mg/kg administered once a day for about 5 days to about 10 days; (ii) at a second dose of about 10 mg/kg to about 40 mg/kg administered once a day after administration of the first dose for about 5 days to about 10 days; (iii) at a third dose of about 5 mg/kg to about 30 mg/kg administered twice a day after administration of the second dose for at least about 5 days to about 10 days.

**[0311]** In some embodiments, the non-naturally occurring melanocortin analog is administered (i) at a first dose of about 5 mg/kg administered once a day for about 7 days; (ii) at a second dose of about 15 mg/kg administered once a day after administration of the first dose for about 7 days; (iii) at a third dose of about 10 mg/kg administered twice a day after administration of the second dose for at least about 7 days.

**[0312]** In some embodiments, the non-naturally occurring melanocortin analog is administered (i) at a first dose of about 10 mg/kg administered once a day for about 7 days; (ii) at a second dose of about 20 mg/kg administered once a day after administration of the first dose for about 7 days; (iii) at a third dose of about 15 mg/kg administered twice a day after administration of the second dose for at least about 7 days.

**[0313]** In some embodiments, the present technology comprises a method or the use wherein the non-naturally occurring melanocortin analog is administered (i) at a first dose of about 15 mg/kg administered once a day for about 7 days; (ii) at a second dose of about 25 mg/kg administered once a day after administration of the first dose for about 7 days; (iii) at a third dose of about 20 mg/kg administered twice a day after administration of the second dose for at least about 7 days.

**[0314]** In some embodiments, the non-naturally occurring melanocortin analog is administered at a dose of about 0.5 mg/kg to about 10 mg/kg per body weight of the subject once daily.

**[0315]** In some embodiments, the non-naturally occurring melanocortin analog is administered at a dose of about 1 mg/kg or 3 mg/kg per body weight of the subject once daily.

**[0316]** In some embodiments, the non-naturally occurring melanocortin analog is administered at a dose of about 0.1 mg to about 100 mg once daily.

**[0317]** In some embodiments, the non-naturally occurring melanocortin analog is administered at a dose of about 10 mg or about 50 mg once daily.

**[0318]** In some embodiments, the non-naturally occurring melanocortin analog is administered via intraperitoneal, intravenous, parenteral, subcutaneous, intramuscular, intracerebroventricular, intranasal, or oral administration.

**[0319]** In some embodiments, the non-naturally occurring melanocortin analog crosses a blood-brain-barrier of a subject.

**[0320]** In some embodiments, the non-naturally occurring melanocortin analog includes any one of the sequences of SEQ ID NOs: 8, 187, 198, 207-218, 226, 231-235, 281, 291, 294-296, 298-322, 324, 351-355, 358-362, 364, 366-368, 371-375, 381-395, 399, 403-417, 419, 421-425, 427, 429, 433-443, 446-461, 472, 492, 496, 499-506, 511-513, 515, 518-523, 536-537, 573-599, 600-620, 622-646 and is administered at least once daily in an amount ranging from 0.001 mg/kg to 25 mg/kg per body weight of the subject.

**[0321]** In some embodiments, the non-naturally occurring melanocortin analog includes any one of the sequences of SEQ ID NOs: 8, 187, 198, 207-218, 226, 231-235, 281, 291, 294-296, 298-322, 324, 351-355, 358-362, 364, 366-368, 371-375, 381-395, 399, 403-417, 419, 421-425, 427, 429, 433-443, 446-461, 472, 492, 496, 499-506, 511-513, 515, 518-523, 536-537, 573-599, 600-620, 622-646 and is administered at least once daily in an amount ranging from 0.5 mg/kg to 10 mg/kg per body weight of the subject.

**[0322]** In some embodiments, the non-naturally occurring melanocortin analog is administered to a subject for at least 1 day, 1 week, 1 month, 3 months, 6 months, 1 year, or 5 years.

**[0323]** In some embodiments, the non-naturally occurring melanocortin analog is administered to a subject for 1 day, 5 days, 7 days, 14 days, 21 days, 28 days, 35 days, 40 days, 45 days, 50 days, 60 days, 75 days, 90 days, 100 days, 110 days, or 120 days.In some embodiments, the present technology comprises a method of reducing a pain level in a subject in need thereof relative to a control, including administering to the subject a non-naturally occurring melanocortin analog of Formula (I): X1-X2-X3-R1-R2-R3-R4-R5-R6-R7-R8-Y1-Y2-Y3-Y4-Y5-Y6-Y7 (I), wherein: X1 is absent or is selected from the group consisting of norleucine (Nle), arginine (Arg), D-arginine (dArg), alanine (Ala), lysine (Lys), D-lysine (dLys), histidine (His), and D-histidine (dHis); X2 is absent, phenylalanine (Phe), or Nle; X3 is absent, Phe, or Nle; R1 is selected from the group consisting of Nle, D-norleucine (dNle), Ala, D-alanine (dAla), Arg, dArg, Lys, dLys, His, dHis, ornithine (Orn), D-ornithine (dOrn), D-leucine (dLeu), D-tyrosine (dTyr), phenylalanine (Phe), D-phenylalanine (dPhe), tryptophan (Trp), D-tryptophan (dTrp), aspartic acid (Asp), cysteine (Cys), and D-cysteine (dCys); R2 is selected from the group consisting of Asp, proline (Pro), D-aspartic acid (dAsp), Cys, dCys, D-penicillamine (dPen), Ala, dAla, Trp, Phe, dPhe, His, dHis, Tyr, and dTyr; R3 is absent or is selected from the group consisting of His, Ala, Pro, hydroxyproline (Hyp), leucine (Leu), D-glutamine (dGln), Phe, dPhe, Trp, dTrp, Tyr, dTyr, 4-amino-1,2,4,5-tetrahydro-2-benzazepin-3-one (Aba), 7-amino-7,8-dihydro-4H-[1,2,3]triazolo-[1,5-a][1,4]diazepin-6(5H)-one (Ata), 4-amino-1,4,5,6-tetrahydroazepino[4,3-b]indol-3(2H)-one (Aia), 2-aminotetraline-2-carboxylic acid (Atc), 1-amino-4-phenylcyclohexane-carboxylic acid (APC), 4-aminophenylpiperidine-4-carboxylic acid (APPC), octohydroindole-2-

carboxylic acid (Oic), 1-amino-1-cyclohexanecarboxylic acid (Che), tetrahydro-isoquinoline-3-carboxylic acid (Tic), indoline-2-carboxylic acid (Ioc), 1-amino-1-cyclopentane carboxylic (Cpe), and biphenylalanine (Bip); R4 is selected from the group consisting of Phe, dPhe, 2'-D-naphthylalanine (dNal(2')), para-chloro-D-phenylalanine (p(Cl)dPhe), para-bromo-D-phenylalanine (p(Br)dPhe), and para-fluoro-D-phenylalanine (p(F)dPhe); R5 is selected from the group consisting of Arg, His, cisPro(guan), and transPro(guan); R6 is selected from the group consisting of Trp, dTrp, Phe, Aia, Aba, Ata, dNal(2'), 2'-naphthylalanine (Nal(2')), and 1'-naphthylalanine (Nal(1')); R7 is selected from the group consisting of Gly, Pro, Lys, dLys, Cys, dCys, penicillamine (Pen), dPen, and Orn; R8 is absent or Lys; Y1 is absent or is selected from the group consisting of valine (Val), D-valine (dVal), b2-valine (b2-Val), b3-valine (b3-Val), Pro, D-proline (dPro), b-proline (b-Pro), Hyp, D-hydroxyproline (dHyp), D-tert-leucine (dTle), dLeu, Trp, Arg, dArg, Lys, dLys, Gly, Ala, dAla, Asp, dAsp, asparagine (Asn), D-asparagine (dAsn), and D-threonine (dThr); Y2 is absent or is selected from the group consisting of Val, dVal, b2-Val, b3-Val, Pro, dPro, b-Pro, Hyp, dHyp, dTle, Arg, dArg, Gly, Ala, dAla, Asp, and dAsn; Y3 is absent or is selected from the group consisting of Val, dVal, Pro, dPro, dThr, Lys, and dLys; Y4 is absent or is selected from the group consisting of dVal, dPro, Asp, and dAsp; Y5 is absent or dVal; Y6 is absent or dVal; Y7 is absent or dPro; and the non-naturally occurring melanocortin analog is cyclized through a moiety selected from the group consisting of: a disulfide bond between R1 or R2 and R7 when each of R1 or R2 and R7 are independently selected from the group consisting of Cys, dCys, and dPen; a disulfide bond between R2 and R7 when R2 is Cys, R7 is Pen, and R3 is absent; a lactam bridge between R1 or R2 and R7 or R8 when R1 or R2 is Asp and R7 or R8 is Lys or Orn; and a lactam bridge between R2 and R7 when R2 is dAsp and R7 is dLys; provided that: when R4 is dNal(2'), then R3 is His and R7 is Pro; when R4 is p(F)dPhe, then (i) R3 is selected from Pro, dGln, dTyr, R6 is Trp, and the non-naturally occurring melanocortin analog is not cyclized between Cys at R2 and Cys at R7 or (ii) R3 is His and either R6 is Nal(2') or the non-naturally occurring melanocortin analog is cyclized through a disulfide bond between R2 and R7; when R4 is p(Br)dPhe, then the non-naturally occurring melanocortin analog is cyclized through a disulfide bond between dCys at R2 and Cys or dCys at R7; when R4 is dPhe, then (i) R3 is not His, Pro, or absent, (ii) R3 is His and either R2 is Phe or dAla or R2 is Ala and X1 is Arg or dArg, (iii) R3 is Pro and (a) R2 is Trp, and

R5 is not His or R6 is not Phe or (b) R2 is not Trp or Pro, and either R5 is not dNal(2') or Nal(2') or X1 and Y3 are not both present, or (iv) R3 is absent and R2 and R7 are not both dPen; when R4 is p(Cl)dPhe, then (i) R3 is selected from Aba, Aia, and Ata or (ii) R3 is His, R1 is not Ala, and (a) if R1 is Nle and Y1Y2 is dVal-dPro, then X1 is absent and the non-naturally occurring melanocortin analog is cyclized through a disulfide bond between dCys at R2 and dCys at R7, or (b) if R1 is Nle, and Y1Y2 is not dVal-dPro, then either X1 or Y3 is present; and when R2 is dAla, then R4 is dPhe and Y1-Y7 are absent.

**[0324]** In some embodiments, the present technology comprises use of a non-naturally occurring melanocortin analog for reducing a pain level in a subject in need thereof relative to a control, the non-naturally occurring melanocortin analog including a sequence of Formula (I).

**[0325]** In some embodiments, the present technology comprises a method of treating, preventing, or reducing an addiction in a subject relative to a control, including administering to the subject a non-naturally occurring melanocortin analog including a sequence of Formula (I).

**[0326]** In some embodiments, the present technology comprises use of a non-naturally occurring melanocortin analog for treating, preventing, or reducing an addiction in a subject relative to a control, the non-naturally occurring melanocortin analog including a sequence of Formula (I).

**[0327]** In some embodiments, the present technology comprises a method of preventing or reducing a use of or dependence on an addictive substance in a subject relative to a control, including administering to the subject a non-naturally occurring melanocortin analog including a sequence of Formula (I).

**[0328]** In some embodiments, the present technology comprises use of a non-naturally occurring melanocortin analog for treating, preventing, or reducing a use of or dependence on an addictive substance in a subject relative to a control, the non-naturally occurring melanocortin analog including a sequence of Formula (I).

**[0329]** In some embodiments, the present technology comprises a method of treating or preventing an opioid use disorder (OUD) in a subject in need thereof relative to a control,

including administering to the subject a non-naturally occurring melanocortin analog including a sequence of Formula (I).

**[0330]** In some embodiments, the present technology comprises use of a non-naturally occurring melanocortin analog for treating or preventing an OUD in a subject in need thereof relative to a control, the non-naturally occurring melanocortin analog including a sequence of Formula (I).

**[0331]** In some embodiments, the present technology comprises a method of treating or preventing an alcohol use disorder (AUD) in a subject in need thereof relative to a control, including administering to the subject a non-naturally occurring melanocortin analog including a sequence of Formula (I).

**[0332]** In some embodiments, the present technology comprises use of a non-naturally occurring melanocortin analog for treating or preventing an AUD in a subject in need thereof relative to a control, the non-naturally occurring melanocortin analog including a sequence of Formula (I).

**[0333]** In some embodiments, the method or the use includes reducing a dose used or consumed of an addictive substance, relative to a control.

**[0334]** In some embodiments, the method or the use includes reducing a dependency on an addictive substance, relative to a control.

**[0335]** In some embodiments, the method or the use includes reducing a frequency of an addictive substance use, relative to a control.

**[0336]** In some embodiments, the method or the use includes reducing a dose or dosage of a conventional medication used to treat an addiction, relative to a control.

**[0337]** In some embodiments, the present technology comprises a method of augmenting an effect of a conventional medication used to treat an addiction in a subject in need thereof, relative to a control, including administering to the subject a non-naturally occurring melanocortin analog including a sequence of Formula (I).

**[0338]** In some embodiments, the present technology comprises use of a non-naturally occurring melanocortin analog for augmenting an effect of a conventional medication used

to treat an addiction in a subject in need thereof, the non-naturally occurring melanocortin analog including a sequence of Formula (I).

**[0339]** In some embodiments, the present technology comprises a method of reducing or eliminating a need for a conventional medication used to treat an addiction in a subject in need thereof, relative to a control, including administering to the subject a non-naturally occurring melanocortin analog including a sequence of Formula (I).

**[0340]** In some embodiments, the present technology comprises use of a non-naturally occurring melanocortin analog for reducing or eliminating a need for a conventional medication used to treat an addiction in a subject in need thereof, the non-naturally occurring melanocortin analog including a sequence of Formula (I).

**[0341]** In some embodiments, the treatment of the addiction is improved during or after administration of the non-naturally occurring melanocortin analog relative to treatment of the addiction using the conventional medication to treat the addiction alone.

**[0342]** In some embodiments, the conventional medication to treat the addiction is selected from the group consisting of buprenorphine, naltrexone, acamprosate, methadone, naloxone, nalmefene, xycodone, levo-alpha-acetylmethadol (LAAM), codeine, lofexidine, and a slow-release morphine.

**[0343]** In some embodiments, the present technology comprises a method of reducing a need for a hospitalization or rehabilitation associated with addiction or use of an addictive substance, relative to a control, including administering to the subject a non-naturally occurring melanocortin analog including a sequence of Formula (I).

**[0344]** In some embodiments, the present technology comprises use of a non-naturally occurring melanocortin analog for reducing a need for a hospitalization or rehabilitation associated with addiction or use of an addictive substance, relative to a control, the non-naturally occurring melanocortin analog including a sequence of Formula (I).

**[0345]** In some embodiments, the present technology comprises a method of preventing or reducing a withdrawal from an addictive substance in a subject, including administering to the subject a non-naturally occurring melanocortin analog including a sequence of Formula (I).

**[0346]** In some embodiments, the present technology comprises use of a non-naturally occurring melanocortin analog for preventing or reducing a withdrawal from an addictive substance in a subject, relative to a control, the non-naturally occurring melanocortin analog including a sequence of Formula (I).

**[0347]** In some embodiments, the present technology comprises a method of preventing or reducing a symptom associated with withdrawal from an addictive substance in a subject relative to a control, including administering to the subject a non-naturally occurring melanocortin analog including a sequence of Formula (I).

**[0348]** In some embodiments, the present technology comprises use of a non-naturally occurring melanocortin analog for preventing or reducing a symptom associated with withdrawal from an addictive substance in a subject, relative to a control, the non-naturally occurring melanocortin analog including a sequence of Formula (I).

**[0349]** In some embodiments, the symptom associated with withdrawal from an addictive substance is selected from the group consisting of pain, anxiety, depression, diarrhea, dizziness, fatigue, muscle aches, nausea, sleep problems, suicidal ideation, tremors, and visual disturbances.

**[0350]** In some embodiments, the subject has an addiction to an addictive substance or is susceptible to an addiction to an addictive substance.

**[0351]** In some embodiments, the subject has used or is using one or more addictive substances.

**[0352]** In some embodiments, the present technology comprises a method or the use wherein the addictive substance includes a prescription medication, a substance in an over-the-counter medication, a recreational substance, or an illegal substance.

**[0353]** In some embodiments, the addictive substance is selected from the group consisting of an opioid, a painkiller, a stimulant, a narcotic, an alcohol, a sedative, marijuana, a cannabis, a tetrahydrocannabinol (THC), a cannabidiol (CBD), and an inhalant.

**[0354]** In some embodiments, the opioid is selected from the group consisting of morphine, heroin, codeine, oxycodone, hydrocodone, and fentanyl.

**[0355]** In some embodiments, the stimulant is selected from the group consisting of caffeine, nicotine, methamphetamines, cocaine, and amphetamines.

**[0356]** In some embodiments, the sedative includes a barbiturate or a benzodiazepine.

**[0357]** In some embodiments, the barbiturate is selected from the group consisting of phenobarbital, methohexital, butalbital, pentobarbital, primidone, and amobarbital.

**[0358]** In some embodiments, the benzodiazepine is selected from the group consisting of alprazolam, lorazepam, clonazepam, diazepam, and temazepam.

**[0359]** In some embodiments, the sedative is selected from the group consisting of tranquilizers, xylazine, eszopiclone, zaleplon, zolpidem, and zopiclone.

**[0360]** In some embodiments, the inhalant is selected from the group consisting of aerosols, butanes, freon, helium, nitrous oxide, propane, and nitrites.

**[0361]** In some embodiments, the nicotine includes a tobacco chew, a nicotine pouch, or a smoking device.

**[0362]** In some embodiments, the smoking device is selected from the group consisting of cigarettes, electronic cigarettes, cigars, and vape products.

**[0363]** In some embodiments, the control includes the subject before administration of the non-naturally occurring melanocortin analog.

**[0364]** In some embodiments, the control includes the subject at baseline.

**[0365]** In some embodiments, the non-naturally occurring melanocortin analog is a melanocortin 4 receptor (MC4R) agonist.

**[0366]** In some embodiments, the MC4R agonist is a full MC4R agonist.

**[0367]** In some embodiments, the MC4R agonist is a partial MC4R agonist.

**[0368]** In some embodiments, the non-naturally occurring melanocortin analog is a MC3R antagonist.

**[0369]** In some embodiments, the MC3R antagonist is a full MC3R antagonist.

**[0370]** In some embodiments, the MC3R antagonist is a partial MC3R antagonist.

**[0371]** In some embodiments, the non-naturally occurring melanocortin analog does not have MC3R activity.

**[0372]** In some embodiments, the non-naturally occurring melanocortin analog includes a sequence according to Formula (I), wherein: X1 is absent or is selected from the group consisting of norleucine (Nle), arginine (Arg), D-arginine (dArg), alanine (Ala), lysine (Lys), D-lysine (dLys), histidine (His), and D-histidine (dHis); X2 is absent, phenylalanine (Phe), or Nle; X3 is absent, Phe, or Nle; R1 is selected from the group consisting of Nle, D-norleucine (dNle), Ala, D-alanine (dAla), Arg, dArg, Lys, dLys, His, dHis, ornithine (Orn), D-ornithine (dOrn), D-leucine (dLeu), D-tyrosine (dTyr), phenylalanine (Phe), D-phenylalanine (dPhe), tryptophan (Trp), D-tryptophan (dTrp), aspartic acid (Asp), cysteine (Cys), and D-cysteine (dCys); R2 is selected from the group consisting of Asp, proline (Pro), D-aspartic acid (dAsp), Cys, dCys, D-penicillamine (dPen), Ala, dAla, Trp, Phe, dPhe, His, dHis, Tyr, and dTyr; R3 is absent or is selected from the group consisting of His, Ala, Pro, hydroxyproline (Hyp), leucine (Leu), D-glutamine (dGln), Phe, dPhe, Trp, dTrp, Tyr, dTyr, 4-amino-1,2,4,5-tetrahydro-2-benzazepin-3-one (Aba), 7-amino-7,8-dihydro-4H-[1,2,3]triazolo-[1,5-a][1,4]diazepin-6(5H)-one (Ata), 4-amino-1,4,5,6-tetrahydroazepino[4,3-b]indol-3(2H)-one (Aia), 2-aminotetraline-2-carboxylic acid (Atc), 1-amino-4-phenylcyclohexane-carboxylic acid (APC), 4-aminophenylpiperidine-4-carboxylic acid (APPC), octohydroindole-2-carboxylic acid (Oic), 1-amino-1-cyclohexanecarboxylic acid (Che), tetrahydro-isoquinoline-3-carboxylic acid (Tic), indoline-2-carboxylic acid (Ioc), 1-amino-1-cyclopentane carboxylic (Cpe), and biphenylalanine (Bip); R4 is selected from the group consisting of Phe, dPhe, 2'-D-naphthylalanine (dNal(2')), para-chloro-D-phenylalanine (p(Cl)dPhe), para-bromo-D-phenylalanine (p(Br)dPhe), and para-fluoro-D-phenylalanine (p(F)dPhe); R5 is selected from the group consisting of Arg, His, cisPro(guan), and transPro(guan); R6 is selected from the group consisting of Trp, dTrp, Phe, Aia, Aba, Ata, dNal(2'), 2'-naphthylalanine (Nal(2')), and 1'-naphthylalanine (Nal(1')); R7 is selected from the group consisting of Gly, Pro, Lys, dLys, Cys, dCys, penicillamine (Pen), dPen, and Orn; R8 is absent or Lys; Y1 is absent or is selected from the group consisting of valine (Val), D-valine (dVal), b2-valine (b2-Val), b3-valine (b3-Val), Pro, D-proline (dPro), b-proline (b-Pro), Hyp, D-hydroxyproline (dHyp), D-tert-leucine (dTle), dLeu, Trp, Arg, dArg, Lys, dLys, Gly, Ala, dAla, Asp, dAsp, asparagine (Asn), D-asparagine (dAsn), and D-threonine (dThr); Y2

is absent or is selected from the group consisting of Val, dVal, b2-Val, b3-Val, Pro, dPro, b-Pro, Hyp, dHyp, dTle, Arg, dArg, Gly, Ala, dAla, Asp, and dAsn; Y3 is absent or is selected from the group consisting of Val, dVal, Pro, dPro, dThr, Lys, and dLys; Y4 is absent or is selected from the group consisting of dVal, dPro, Asp, and dAsp; Y5 is absent or dVal; Y6 is absent or dVal; Y7 is absent or dPro; and the non-naturally occurring melanocortin analog is cyclized through a moiety selected from the group consisting of: a disulfide bond between R1 or R2 and R7 or R8 when each of R1 or R2 and R7 or R8 are independently selected from the group consisting of Cys, dCys, and dPen; a disulfide bond between R2 and R7 when R2 is Cys, R7 is Pen, and R3 is absent; a lactam bridge between R1 or R2 and R7 or R8 when R1 or R2 is Asp and R7 or R8 is Lys or Orn; and a lactam bridge between R2 and R7 when R2 is dAsp and R7 is dLys; provided that the non-naturally occurring melanocortin analog does not include a sequence selected from the group consisting of: Ac-Nle-c[Asp-Pro-Pro-dNal(2')-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 194); Ac-Nle-c[Asp-Pro-His-dNal(2')-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 5); Ac-Nle-c[Asp-Pro-His-dNal(2')-Arg-Trp-Lys]-dPro-dVal-NH2 (SEQ ID NO: 10); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dVal-dPro (SEQ ID NO: 2); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 3); Ac-Nle-c[Asp-Hyp-dNal(2')-Arg-Trp-Pro-Lys]-dVal-dPro-NH2 (SEQ ID NO: 4); Ac-Nle-c[Asp-Phe-His-dNal(2')-Arg-Trp-Lys]-dLeu-dPro-NH2 (SEQ ID NO: 6); Ac-Nle-c[Asp-Phe-His-dNal(2')-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 7); Ac-Nle-c[Asp-Hyp-dNal(2')-Arg-Trp-Pro-Lys]-dVal-dPro-NH2 (SEQ ID NO: 9); Ac-Nle-Phe-Phe-c[Asp-Phe-His-dNal(2')-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 12); Ac-dArg-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 15); Ac-dLeu-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 18); Ac-dAla-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 20); Ac-Ala-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 21); Ac-dNle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 24); Ac-dCys-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 28); Ac-dPhe-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 29); Ac-dTyr-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 30); dTyr-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 35); Tyr-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 36); Ac-Nle-c[Cys-Pro-dNal(2')-Arg-Trp-Cys]-dVal-dPro-NH2 (SEQ ID NO: 40); Ac-Nle-c[dCys-Pro-dNal(2')-Arg-Trp-Cys]-dVal-dPro-NH2 (SEQ ID NO: 41); Ac-Nle-c[Cys-Pro-dNal(2')-Arg-

Trp-dCys]-dVal-dPro-NH2 (SEQ ID NO: 42); Ac-Nle-c[dCys-Pro-dNal(2')-Arg-Trp-dCys]-dVal-dPro-NH2 (SEQ ID NO: 43); Ac-Nle-c[Cys-Pro-dNal(2')-Arg-Trp-Pen]-dVal-dPro-NH2 (SEQ ID NO: 48); Ac-Nle-c[dPen-Pro-dNal(2')-Arg-Trp-dPen]-dVal-dPro-NH2 (SEQ ID NO: 54); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Orn]-dVal-dPro-NH2 (SEQ ID NO: 64); Ac-Nle-c[Asp-dNal(2')-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 68); Ac-Nle-c[Asp-Ala-dNal(2')-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 69); Ac-Nle-c[Asp-Leu-dNal(2')-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 76); Ac-Nle-c[Asp-Trp-dNal(2')-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 82); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-Val-Pro-NH2 (SEQ ID NO: 115); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dVal-dPro-OH (SEQ ID NO: 116); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dPro-dVal-OH (SEQ ID NO: 117); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dVal-Hyp-NH2 (SEQ ID NO: 118); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dVal-dHyp-NH2 (SEQ ID NO: 119); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-Val-Hyp-NH2 (SEQ ID NO: 120); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-Val-dHyp-NH2 (SEQ ID NO: 121); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-Hyp-dVal-NH2 (SEQ ID NO: 122); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dHyp-dVal-NH2 (SEQ ID NO: 123); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-Hyp-Val-NH2 (SEQ ID NO: 124); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dHyp-Val-NH2 (SEQ ID NO: 125); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dVal-dVal-NH2 (SEQ ID NO: 126); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dPro-dPro-NH2 (SEQ ID NO: 127); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dVal-NH2 (SEQ ID NO: 128); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dPro-NH2 (SEQ ID NO: 129); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-Val-NH2 (SEQ ID NO: 130); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-Pro-NH2 (SEQ ID NO: 131); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-Ala-NH2 (SEQ ID NO: 132); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dAla-NH2 (SEQ ID NO: 133); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dHyp-NH2 (SEQ ID NO: 134); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-Hyp-NH2 (SEQ ID NO: 135); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dAla-dAla-NH2 (SEQ ID NO: 136); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-Ala-Ala-NH2 (SEQ ID NO: 137); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-Gly-Gly-NH2 (SEQ ID NO: 138); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dVal-Asp-NH2 (SEQ ID NO: 139); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dVal-Arg-NH2 (SEQ ID NO: 140); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dVal-dArg-NH2 (SEQ ID NO: 143); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dVal-dAsn-NH2 (SEQ ID NO: 144); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-Asp-dPro-NH2 (SEQ ID NO:

145); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-Arg-dPro-NH2 (SEQ ID NO: 146); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-Asn-dPro-NH2 (SEQ ID NO: 147); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dAsp-dPro-NH2 (SEQ ID NO: 148); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dArg-dPro-NH2 (SEQ ID NO: 149); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dAsn-dPro-NH2 (SEQ ID NO: 150); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-Asp-NH2 (SEQ ID NO: 151); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-Arg-NH2 (SEQ ID NO: 152); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-Asn-NH2 (SEQ ID NO: 153); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dAsp-NH2 (SEQ ID NO: 154); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dArg-NH2 (SEQ ID NO: 155); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dAsn-NH2 (SEQ ID NO: 156); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-Lys-Pro-Val-NH2 (SEQ ID NO: 157); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-Lys-dPro-dVal-NH2 (SEQ ID NO: 158); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dLys-dPro-dVal-NH2 (SEQ ID NO: 159); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-Lys-dPro-NH2 (SEQ ID NO: 160); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dLys-dPro-NH2 (SEQ ID NO: 161); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-Lys-Val-Pro-NH2 (SEQ ID NO: 162); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-Lys-dVal-dPro-NH2 (SEQ ID NO: 164); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dLys-dVal-dPro-NH2 (SEQ ID NO: 164); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-Arg-Pro-Val-NH2 (SEQ ID NO: 165); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-Arg-dPro-dVal-NH2 (SEQ ID NO: 166); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dArg-dPro-dVal-NH2 (SEQ ID NO: 167); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-Arg-Val-Pro-NH2 (SEQ ID NO: 168); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-Arg-dVal-dPro-NH2 (SEQ ID NO: 169); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dArg-dVal-dPro-NH2 (SEQ ID NO: 170); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dTle-dVal-dPro-NH2 (SEQ ID NO: 171); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 172); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dTle-dVal-NH2 (SEQ ID NO: 173); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dTle-dTle-NH2 (SEQ ID NO: 174); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dTle-dTle-dPro-NH2 (SEQ ID NO: 175); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dTle-dTle-dVal-NH2 (SEQ ID NO: 176); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dPro-dTle-NH2 (SEQ ID NO: 177); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dVal-dTle-NH2 (SEQ ID NO: 178); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dVal-dVal-dPro-NH2 (SEQ ID NO: 179); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dPro-dVal-dPro-NH2 (SEQ ID NO: 180); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dVal-dVal-dVal-dPro-NH2 (SEQ ID NO: 181);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dVal-dPro-dVal-dPro-NH2 (SEQ ID NO: 182); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dVal-dVal-dVal-dVal-dVal-dVal-dPro-NH2 (SEQ ID NO: 183); Ac-Nle-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 184); Ac-Nle-Nle-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 185); Ac-Nle-Nle-Nle-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 186); Ac-Nle-c[Asp-Trp-Pro-dNal(2')-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 195); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-dTrp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 196); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-Trp-NH2 (SEQ ID NO: 203); Ac-Nle-c[Asp-Aba-dNal(2')-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 204); Ac-Nle-c[Asp-Aia-dNal(2')-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 205); Ac-Nle-c[Asp-Ata-dNal(2')-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 206); Ac-Nle-c[Asp-Cpe-dNal(2')-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 240); Ac-Nle-c[Asp-Che-dNal(2')-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 241); Ac-Nle-c[Asp-Oic-dNal(2')-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 242); Ac-Nle-c[Asp-Tic-dNal(2')-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 244); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Pro-Lys]-dVal-dPro-NH2 (SEQ ID NO: 245); Ac-Nle-c[Asp-His-dNal(2')-transPro(guan)-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 247); Ac-Nle-c[Asp-His-dNal(2')-cisPro(guan)-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 248); Ac-Nle-c[Asp-Pro-dNal(2')-transPro(guan)-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 250); Ac-Nle-c[Asp-Pro-dNal(2')-cisPro(guan)Pro-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 251); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Aba-Lys]-dVal-dPro-NH2 (SEQ ID NO: 253); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Ata-Lys]-dVal-dPro-NH2 (SEQ ID NO: 254); Ac-Nle-c[Asp-Glu-dNal(2')-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 255); Ac-Nle-c[Asp-Glu-dNal(2')-Arg-Trp-Gly-Lys]-dVal-dPro-NH2 (SEQ ID NO: 256); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Gly-Lys]-dVal-dPro-NH2 (SEQ ID NO: 259); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Gly-Lys]-dPro-dPro-Lys-Asp-NH2 (SEQ ID NO: 260); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Gly-Lys]-dPro-dPro-dLys-dAsp-NH2 (SEQ ID NO: 261); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dPro-dPro-dLys-dAsp-NH2 (SEQ ID NO: 263); Ac-Nle-c[Asp-Ala-His-dNal(2')-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 273); Ac-Arg-c[Asp-Ala-His-dNal(2')-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 274); Ac-dArg-c[Asp-Ala-His-dNal(2')-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 275); Ac-dLeu-c[dPen-Pro-dNal(2')-Arg-Trp-dPen]-dVal-dPro-NH2 (SEQ ID NO: 327); Ac-dNle-c[dPen-Pro-dNal(2')-Arg-Trp-dPen]-dVal-dPro-NH2 (SEQ ID NO: 328); Ac-dArg-c[dPen-Pro-dNal(2')-Arg-Trp-dPen]-dVal-dPro-NH2 (SEQ ID NO: 329); Ac-Arg-c[dPen-Pro-

dNal(2')-Arg-Trp-dPen]-dVal-dPro-NH2 (SEQ ID NO: 330); Ac-dPhe-c[dPen-Pro-dNal(2')-Arg-Trp-dPen]-dVal-dPro-NH2 (SEQ ID NO: 331); Ac-dTyr-c[dPen-Pro-dNal(2')-Arg-Trp-dPen]-dVal-dPro-NH2 (SEQ ID NO: 332); Ac-Ala-c[dPen-Pro-dNal(2')-Arg-Trp-dPen]-dVal-dPro-NH2 (SEQ ID NO: 333); Ac-dHis-c[dPen-Pro-dNal(2')-Arg-Trp-dPen]-dVal-dPro-NH2 (SEQ ID NO: 334); Ac-His-c[dPen-Pro-dNal(2')-Arg-Trp-dPen]-dVal-dPro-NH2 (SEQ ID NO: 335); Ac-dLys-c[dPen-Pro-dNal(2')-Arg-Trp-dPen]-dVal-dPro-NH2 (SEQ ID NO: 336); Ac-Lys-c[dPen-Pro-dNal(2')-Arg-Trp-dPen]-dVal-dPro-NH2 (SEQ ID NO: 337); Ac-Nle-c[dPen-Pro-dNal(2')-Arg-Trp-dPen]-dArg-dVal-dPro-NH2 (SEQ ID NO: 344); Ac-Nle-c[dPen-Pro-dNal(2')-Arg-Trp-dPen]-dLys-dVal-dPro-NH2 (SEQ ID NO: 345); Ac-Nle-c[dPen-Pro-dNal(2')-Arg-Trp-dPen]-dArg-dPro-NH2 (SEQ ID NO: 346); Ac-Nle-c[dPen-Pro-dNal(2')-Arg-Trp-dPen]-dLys-dPro-NH2 (SEQ ID NO: 347); Ac-Nle-c[dPen-Pro-dNal(2')-Arg-Trp-dPen]-dVal-dHyp-NH2 (SEQ ID NO: 348); Ac-Nle-c[dPen-Pro-dNal(2')-Arg-Trp-dPen]-dTle-dPro-NH2 (SEQ ID NO: 349); Ac-Nle-c[dPen-Pro-dNal(2')-Arg-Trp-Gly-dPen]-dVal-dPro-NH2 (SEQ ID NO: 350); Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Aia-Lys]-dVal-dPro-NH2 (SEQ ID NO: 103); Ac-Nle-c[Asp-Ioc-dNal(2')-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 243); Ac-Nle-c[Cys-dNal(2')-Arg-Trp-Cys]-dVal-dPro-NH2 (SEQ ID NO: 44); Ac-Nle-c[dCys-dNal(2')-Arg-Trp-Cys]-dVal-dPro-NH2 (SEQ ID NO: 45); Ac-Nle-c[Cys-dNal(2')-Arg-Trp-dCys]-dVal-dPro-NH2 (SEQ ID NO: 46); Ac-Nle-c[dCys-dNal(2')-Arg-Trp-dCys]-dVal-dPro-NH2 (SEQ ID NO: 47); Ac-Nle-c[Cys-dNal(2')-Arg-Trp-Pen]-dVal-dPro-NH2 (SEQ ID NO: 56); Ac-Nle-c[dPen-dNal(2')-Arg-Trp-dPen]-dVal-dPro-NH2 (SEQ ID NO: 62); Ac-Nle-c[Asp-dTrp-dNal(2')-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 83); Ac-Nle-c[dPen-Ala-dNal(2')-Arg-Trp-dPen]-dVal-dPro-NH2 (SEQ ID NO: 338); Ac-Nle-c[dPen-Leu-dNal(2')-Arg-Trp-dPen]-dVal-dPro-NH2 (SEQ ID NO: 339); Ac-Nle-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 223); Ac-Arg-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 464); Ac-Lys-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 465); Ac-dLys-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 466); Ac-His-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 467); Ac-dHis-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 468); Ac-Nle-Nle-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 469); Ac-Nle-c[Asp-His-p(F)dPhe-His-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 470); Ac-Nle-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dVal-dVal-dVal-dPro-NH2 (SEQ ID NO: 474); Ac-Nle-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dPro-dVal-

dPro-NH2 (SEQ ID NO: 475); Ac-Nle-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 476); Ac-Nle-Nle-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 477); Ac-Nle-Nle-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dPro-dVal-dPro-NH2 (SEQ ID NO: 478); Ac-Arg-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 481); Ac-Lys-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 482); Ac-dLys-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 483); Ac-His-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 484); Ac-dHis-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 485); Ac-dArg-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 463); Ac-Ala-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 462); Ac-Ala-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 479); Ac-Nle-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dTle-dTle-dVal-NH2 (SEQ ID NO: 473); Ac-dArg-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 480); Ac-Nle-c[Asp-Gln-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 491); Ac-Nle-c[Asp-Bip-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 489); Ac-Nle-c[Asp-Trp-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 493); Ac-Nle-c[Asp-Pro-p(F)dPhe-Arg-dNal(2')-Lys]-dVal-dPro-NH2 (SEQ ID NO: 444); Ac-Nle-c[Asp-Pro-p(F)dPhe-Arg-Nal(2')-Lys]-dVal-dPro-NH2 (SEQ ID NO: 445); Ac-Nle-c[Asp-Tyr-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 495); Ac-Nle-c[Asp-Phe-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 487); Ac-Nle-c[Asp-dPhe-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 488); Ac-Nle-c[Asp-dTrp-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 494); Ac-Nle-c[Asp-His-p(F)dPhe-Arg-dNal(2')-Lys]-dVal-dPro-NH2 (SEQ ID NO: 471); Ac-Nle-c[Cys-Pro-p(F)dPhe-Arg-Trp-Cys]-dVal-dPro-NH2 (SEQ ID NO: 432); Ac-Nle-c[Asp-Pro-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 217); Ac-Nle-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 222); Ac-Nle-c[Cys-His-p(Br)dPhe-Arg-Trp-Cys]-dVal-dPro-NH2 (SEQ ID NO: 535); Ac-Ala-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 538); Ac-Nle-Nle-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 545); Ac-Nle-c[Asp-His-p(Br)dPhe-His-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 546); Ac-Nle-c[Asp-His-p(Br)dPhe-Arg-dNal(2')-Lys]-dVal-dPro-NH2 (SEQ ID NO: 547); Ac-Nle-c[Asp-His-p(Br)dPhe-Arg-Nal(2')-Lys]-dVal-dPro-NH2 (SEQ ID NO: 548); Ac-Nle-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dTle-dTle-dVal-NH2 (SEQ ID NO: 549); Ac-Nle-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dPro-dVal-dPro-NH2 (SEQ ID NO: 551); Ac-Nle-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dTle-dPro-

NH2 (SEQ ID NO: 552); Ac-Nle-Nle-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 553); Ac-Ala-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 555); Ac-Nle-c[Asp-dHis-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 562); Ac-Nle-c[Asp-Phe-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 563); Ac-Nle-c[Asp-dPhe-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 564); Ac-Nle-c[Asp-Bip-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 565); Ac-Nle-c[Asp-dGln-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 568); Ac-Nle-c[Asp-Trp-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 569); Ac-Nle-c[Asp-dTrp-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 570); Ac-Nle-c[Asp-Tyr-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 571); Ac-Nle-c[Asp-dTyr-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 572); Ac-dArg-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 539); Ac-dHis-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 544); Ac-dHis-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 561); Ac-dArg-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 556); Ac-dLys-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 542); Ac-His-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 560); Ac-His-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 543); Ac-dLys-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 559); Ac-Arg-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 557); Ac-Lys-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 541); Ac-Nle-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dVal-dVal-dVal-dPro-NH2 (SEQ ID NO: 550); Ac-Lys-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 558); Ac-Arg-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 540); Ac-Nle-Nle-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dPro-dVal-dPro-NH2 (SEQ ID NO: 554); Ac-Nle-c[Asp-His-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 363); Ac-Nle-c[Asp-His-dPhe-Arg-Trp-Pro-Lys]-dVal-dPro-NH2 (SEQ ID NO: 418); Ac-Nle-c[Asp-His-dPhe-Arg-Trp-Lys]-dPro-dVal-NH2 (SEQ ID NO: 621); Ac-Nle-c[Asp-His-dPhe-transPro(guan)-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 228); Ac-Nle-c[Asp-His-dPhe-cisPro(guan)-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 229); Ac-Nle-c[Asp-Ala-His-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 380); Ac-Nle-c[Asp-Trp-Pro-dPhe-His-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 398); Ac-Nle-c[Asp-Trp-Pro-dPhe-Arg-Phe-Lys]-dVal-dPro-NH2 (SEQ ID NO: 401); Ac-Nle-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dPro-dVal-dPro-NH2 (SEQ ID NO: 639); Ac-Nle-c[Asp-Pro-dPhe-Arg-dNal(2')-

Lys]-dVal-dPro-NH2 (SEQ ID NO: 430); Ac-Nle-c[Asp-Pro-dPhe-Arg-Nal(2')-Lys]-dVal-dPro-NH2 (SEQ ID NO: 431); Ac-Nle-c[Asp-Pro-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 225); Ac-Nle-c[dPen-dPhe-Arg-Trp-dPen]-dVal-dPro-NH2 (SEQ ID NO: 326); Ac-Nle-c[Asp-Pro-His-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 297); Ac-Nle-c[Asp-Pro-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 215); Ac-Nle-c[Asp-Phe-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 525); Ac-Nle-c[Asp-dPhe-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 526); Ac-Nle-c[Asp-Bip-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 527); Ac-Nle-c[Asp-Trp-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 531); Ac-Nle-c[Asp-Tyr-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 533); Ac-Nle-c[Asp-dTyr-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 534); Ac-Nle-c[Asp-dTrp-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 532); Ac-Nle-c[dCys-His-p(Cl)dPhe-Arg-Trp-Cys]-dVal-dPro-NH2 (SEQ ID NO: 498); Ac-Nle-c[Cys-His-p(Cl)dPhe-Arg-Trp-Cys]-dVal-dPro-NH2 (SEQ ID NO: 497); Ac-Nle-c[Asp-His-p(Cl)dPhe-Arg-dNal(2')-Lys]-dVal-dPro-NH2 (SEQ ID NO: 509); Ac-Nle-c[Asp-His-p(Cl)dPhe-Arg-Nal(2')-Lys]-dVal-dPro-NH2 (SEQ ID NO: 510); Ac-Nle-c[Asp-His-p(Cl)dPhe-His-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 508); Ac-Nle-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 220); Ac-Nle-Nle-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 507); Ac-Ala-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 517); Ac-Ala-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 500); Ac-Nle-Nle-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dPro-dVal-dPro-NH2 (SEQ ID NO: 516); Ac-Nle-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 514); Ac-Nle-c[Asp-dGln-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 530); Ac-Arg-c[Asp-dAla-His-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 268); Ac-Nle-c[Asp-dAla-His-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 378); Ac-dArg-c[Asp-dAla-His-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 379); Ac-Nle-c[Asp-dAla-His-dNal(2')-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 266); Ac-Arg-c[Asp-dAla-His-dNal(2')-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 267); Ac-Arg-c[Cys-dAla-His-dNal(2')-Arg-Trp-Cys]-dVal-dPro-NH2 (SEQ ID NO: 269); Ac-dArg-c[Asp-dAla-His-dNal(2')-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 270); Ac-Arg-c[Cys-dAla-His-dNal(2')-Arg-Trp-Cys]-NH2 (SEQ ID NO: 282); and Ac-Arg-c[Asp-dAla-His-dNal(2')-Arg-Trp-Lys]-NH2 (SEQ ID NO: 283).

**[0373]** In some embodiments, the present technology comprises a method or use, wherein the non-naturally occurring melanocortin analog includes a sequence according to Formula (IA): X1-X2-X3-R1-R2-R3-R4-R5-R6-R7-R8-Y1-Y2-Y3-Y4 (IA), wherein: X1 is absent or is selected from the group consisting of norleucine (Nle), arginine (Arg), D-arginine (dArg), alanine (Ala), lysine (Lys), D-lysine (dLys), histidine (His), D-histidine (dHis); X2 is absent, phenylalanine (Phe), or Nle; X3 is absent, Phe, or Nle; R1 is selected from the group consisting of Nle, D-norleucine (dNle), Ala, D-alanine (dAla), Arg, dArg, Lys, dLys, His, dHis, ornithine (Orn), D-ornithine (dOrn), D-leucine (dLeu), D-tyrosine (dTyr), phenylalanine (Phe), D-phenylalanine (dPhe), tryptophan (Trp), D-tryptophan (dTrp), aspartic acid (Asp), cysteine (Cys), and D-cysteine (dCys); R2 is selected from the group consisting of Asp, D-aspartic acid (dAsp), Cys, dCys, D-penicillamine (dPen), Ala, Trp, Phe, dPhe, His, dHis, Tyr, and dTyr; R3 is absent or is selected from the group consisting of His, Ala, proline (Pro), hydroxyproline (Hyp), leucine (Leu), D-glutamine (dGln), Phe, dPhe, Trp, dTrp, Tyr, dTyr, 2-aminotetraline-2-carboxylic acid (Atc), octohydroindole-2-carboxylic acid (Oic), 1-amino-1-cyclohexanecarboxylic acid (Che), tetrahydro-isoquinoline-3-carboxylic acid (Tic), 1-amino-1-cyclopentane carboxylic (Cpe), and biphenylalanine (Bip); R4 is selected from the group consisting of dPhe, para-chloro-D-phenylalanine (p(Cl)dPhe), para-bromo-D-phenylalanine (p(Br)dPhe), and para-fluoro-D-phenylalanine (p(F)dPhe); R5 is Arg or His; R6 is selected from the group consisting of Trp, dTrp, Phe, dNal(2'), 2'-naphthylalanine (Nal(2')), and 1'-naphthylalanine (Nal(1')); R7 is selected from the group consisting of Gly, Pro, Lys, dLys, Cys, dCys, penicillamine (Pen), dPen, and Orn; R8 is absent or Lys; Y1 is selected from the group consisting of valine (Val), D-valine (dVal), b2-valine (b2-Val), b3-valine (b3-Val), Pro, D-proline (dPro), b-proline (b-Pro), Hyp, D-hydroxyproline (dHyp), D-tert-leucine (dTle), dLeu, Trp, Arg, dArg, Lys, dLys, Gly, Ala, dAla, Asp, dAsp, asparagine (Asn), D-asparagine (dAsn), and D-threonine (dThr); Y2 is absent or is selected from the group consisting of Val, dVal, b2-Val, b3-Val, Pro, dPro, b-Pro, Hyp, dHyp, dTle, Arg, dArg, Gly, Ala, dAla, Asp, and dAsn; Y3 is absent or is selected from the group consisting of Val, dVal, Pro, dPro, dThr, Lys, and dLys; Y4 is absent or is selected from the group consisting of dVal, dPro, Asp, and dAsp; and the non-naturally occurring melanocortin analog is cyclized through a moiety selected from the group consisting of: a disulfide bond between R1 or R2 and R7 or R8 when each of R1 or R2 and R7 or R8 are independently selected from the group consisting

of Cys, dCys, and dPen; a disulfide bond between R2 and R7 when R2 is Cys,R7 is Pen, and R3 is absent; a lactam bridge between R1 or R2 and R7 or R8 when R1 or R2 is Asp and R7 or R8 is Lys or Orn; and a lactam bridge between R2 and R7 when R2 is dAsp and R7 is dLys; provided that: when R4 is p(F)dPhe, then (i) R3 is selected from Pro, dGln, dTyr, R6 is Trp, and the non-naturally occurring melanocortin analog is not cyclized between Cys at R2 and Cys at R7 or (ii) R3 is His and either R6 is Nal(2') or the non-naturally occurring melanocortin analog is cyclized through a disulfide bond between R2 and R7, where R2 and R7 are the same; when R4 is p(Br)dPhe, then the non-naturally occurring melanocortin analog is cyclized through a disulfide bond between dCys at R2 and Cys or dCys at R7; when R4 is dPhe, then (i) R3 is not His, Pro, or absent, (ii) R3 is His and either R2 is Phe or dAla or R2 is Ala and X1 is Arg or dArg, (iii) R3 is Pro and (a) R2 is Trp, and R5 is not His or R6 is not Phe or (b) R2 is not Trp or Pro, and either R5 is not dNal(2') or Nal(2') or X1 and Y3 are not both present, or (iv) R3 is absent and R2 and R7 are not both dPen; and when R4 is p(Cl)dPhe, then (i) R3 is selected from Aba, Aia, and Ata or (ii) R3 is His, R1 is not Ala, and (a) if R1 is Nle and Y1Y2 is dVal-dPro, then X1 is absent and the non-naturally occurring melanocortin analog is cyclized through a disulfide bond between dCys at R2 and dCys at R7, or (b) if R1 is Nle, and Y1Y2 is not dVal-dPro, then either X1 or Y3 is present.

**[0374]** In some embodiments, the non-naturally occurring melanocortin analog includes a sequence according to Formula (IA), wherein: X1 is absent or is selected from the group consisting of norleucine (Nle), arginine (Arg), D-arginine (dArg), alanine (Ala), lysine (Lys), D-lysine (dLys), histidine (His), D-histidine (dHis); X2 is absent, phenylalanine (Phe), or Nle; X3 is absent, Phe, or Nle; R1 is selected from the group consisting of Nle, D-norleucine (dNle), Ala, D-alanine (dAla), Arg, dArg, Lys, dLys, His, dHis, ornithine (Orn), D-ornithine (dOrn), D-leucine (dLeu), D-tyrosine (dTyr), phenylalanine (Phe), D-phenylalanine (dPhe), tryptophan (Trp), D-tryptophan (dTrp), aspartic acid (Asp), cysteine (Cys), and D-cysteine (dCys); R2 is selected from the group consisting of Asp, D-aspartic acid (dAsp), Cys, dCys, D-penicillamine (dPen), Ala, Trp, Phe, dPhe, His, dHis, Tyr, and dTyr; R3 is absent or is selected from the group consisting of His, Ala, proline (Pro), hydroxyproline (Hyp), leucine (Leu), D-glutamine (dGln), Phe, dPhe, Trp, dTrp, Tyr, dTyr, 2-aminotetraline-2-carboxylic acid (Atc), octohydroindole-2-carboxylic acid (Oic), 1-amino-1-cyclohexanecarboxylic acid (Che), tetrahydro-isoquinoline-3-carboxylic acid (Tic), 1-amino-

1-cyclopentane carboxylic (Cpe), and biphenylalanine (Bip); R4 is selected from the group consisting of dPhe, para-chloro-D-phenylalanine (p(Cl)dPhe), para-bromo-D-phenylalanine (p(Br)dPhe), and para-fluoro-D-phenylalanine (p(F)dPhe); R5 is Arg or His; R6 is selected from the group consisting of Trp, dTrp, Phe, dNal(2'), 2'-naphthylalanine (Nal(2')), and 1'-naphthylalanine (Nal(1')); R7 is selected from the group consisting of Gly, Pro, Lys, dLys, Cys, dCys, penicillamine (Pen), dPen, and Orn; R8 is absent or Lys; Y1 is selected from the group consisting of valine (Val), D-valine (dVal), b2-valine (b2-Val), b3-valine (b3-Val), Pro, D-proline (dPro), b-proline (b-Pro), Hyp, D-hydroxyproline (dHyp), D-tert-leucine (dTle), dLeu, Trp, Arg, dArg, Lys, dLys, Gly, Ala, dAla, Asp, dAsp, asparagine (Asn), D-asparagine (dAsn), and D-threonine (dThr); Y2 is absent or is selected from the group consisting of Val, dVal, b2-Val, b3-Val, Pro, dPro, b-Pro, Hyp, dHyp, dTle, Arg, dArg, Gly, Ala, dAla, Asp, and dAsn; Y3 is absent or is selected from the group consisting of Val, dVal, Pro, dPro, dThr, Lys, and dLys; Y4 is absent or is selected from the group consisting of dVal, dPro, Asp, and dAsp; and the non-naturally occurring melanocortin analog is cyclized through a moiety selected from the group consisting of: a disulfide bond between R1 or R2 and R7 or R8 when each of R1 or R2 and R7 or R8 are independently selected from the group consisting of Cys, dCys, and dPen; a disulfide bond between R2 and R7 when R2 is Cys, R7 is Pen, and R3 is absent; a lactam bridge between R1 or R2 and R7 or R8 when R1 or R2 is Asp and R7 or R8 is Lys or Orn; and a lactam bridge between R2 and R7 when R2 is dAsp and R7 is dLys; provided that the non-naturally occurring melanocortin analog does not include a sequence selected from the group consisting of: Ac-Nle-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 223); Ac-Arg-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 464); Ac-Lys-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 465); Ac-dLys-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 466); Ac-His-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 467); Ac-dHis-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 468); Ac-Nle-Nle-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 469); Ac-Nle-c[Asp-His-p(F)dPhe-His-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 470); Ac-Nle-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dVal-dVal-dVal-dPro-NH2 (SEQ ID NO: 474); Ac-Nle-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dPro-dVal-dPro-NH2 (SEQ ID NO: 475); Ac-Nle-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 476); Ac-Nle-Nle-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ

ID NO: 477); Ac-Nle-Nle-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dPro-dVal-dPro-NH2 (SEQ ID NO: 478); Ac-Arg-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 481); Ac-Lys-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 482); Ac-dLys-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 483); Ac-His-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 484); Ac-dHis-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 485); Ac-dArg-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 463); Ac-Ala-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 462); Ac-Ala-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 479); Ac-Nle-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dTle-dTle-dVal-NH2 (SEQ ID NO: 473); Ac-dArg-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 480); Ac-Nle-c[Asp-Bip-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 489); Ac-Nle-c[Asp-Trp-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 493); Ac-Nle-c[Asp-Pro-p(F)dPhe-Arg-dNal(2')-Lys]-dVal-dPro-NH2 (SEQ ID NO: 444); Ac-Nle-c[Asp-Pro-p(F)dPhe-Arg-Nal(2')-Lys]-dVal-dPro-NH2 (SEQ ID NO: 445); Ac-Nle-c[Asp-Tyr-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 495); Ac-Nle-c[Asp-Phe-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 487); Ac-Nle-c[Asp-dPhe-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 488); Ac-Nle-c[Asp-dTrp-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 494); Ac-Nle-c[Asp-His-p(F)dPhe-Arg-dNal(2')-Lys]-dVal-dPro-NH2 (SEQ ID NO: 471); Ac-Nle-c[Cys-Pro-p(F)dPhe-Arg-Trp-Cys]-dVal-dPro-NH2 (SEQ ID NO: 432); Ac-Nle-c[dCys-His-p(F)dPhe-Arg-Trp-Cys]-dVal-dPro-NH2 (SEQ ID NO: 460); Ac-Nle-c[Asp-Pro-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 217); Ac-Nle-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 222); Ac-Nle-c[Cys-His-p(Br)dPhe-Arg-Trp-Cys]-dVal-dPro-NH2 (SEQ ID NO: 535); Ac-Ala-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 538); Ac-Nle-Nle-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 545); Ac-Nle-c[Asp-His-p(Br)dPhe-His-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 546); Ac-Nle-c[Asp-His-p(Br)dPhe-Arg-dNal(2')-Lys]-dVal-dPro-NH2 (SEQ ID NO: 547); Ac-Nle-c[Asp-His-p(Br)dPhe-Arg-Nal(2')-Lys]-dVal-dPro-NH2 (SEQ ID NO: 548); Ac-Nle-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dTle-dTle-dVal-NH2 (SEQ ID NO: 549); Ac-Nle-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dPro-dVal-dPro-NH2 (SEQ ID NO: 551); Ac-Nle-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 552); Ac-Nle-Nle-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 553); Ac-Ala-c[Asp-His-p(Br)dPhe-

Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 555); Ac-Nle-c[Asp-Phe-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 563); Ac-Nle-c[Asp-dPhe-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 564); Ac-Nle-c[Asp-Bip-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 565); Ac-Nle-c[Asp-dGln-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 568); Ac-Nle-c[Asp-Trp-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 569); Ac-Nle-c[Asp-dTrp-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 570); Ac-Nle-c[Asp-Tyr-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 571); Ac-Nle-c[Asp-dTyr-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 572); Ac-dArg-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 539); Ac-dHis-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 544); Ac-dHis-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 561); Ac-dArg-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 556); Ac-dLys-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 542); Ac-His-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 560); Ac-His-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 543); Ac-dLys-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 559); Ac-Arg-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 557); Ac-Lys-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 541); Ac-Nle-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dVal-dVal-dVal-dPro-NH2 (SEQ ID NO: 550); Ac-Lys-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 558); Ac-Arg-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 540); Ac-Nle-Nle-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dPro-dVal-dPro-NH2 (SEQ ID NO: 554); Ac-Nle-c[Asp-His-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 363); Ac-Nle-c[Asp-His-dPhe-Arg-Trp-Pro-Lys]-dVal-dPro-NH2 (SEQ ID NO: 418); Ac-Nle-c[Asp-His-dPhe-Arg-Trp-Lys]-dPro-dVal-NH2 (SEQ ID NO: 621); Ac-Nle-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dPro-dVal-dPro-NH2 (SEQ ID NO: 639); Ac-Nle-c[dPen-dPhe-Arg-Trp-dPen]-dVal-dPro-NH2 (SEQ ID NO: 326); Ac-Nle-c[Asp-Trp-Pro-dPhe-His-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 398); Ac-Nle-c[Asp-Trp-Pro-dPhe-Arg-Phe-Lys]-dVal-dPro-NH2 (SEQ ID NO: 401); Ac-Nle-c[Asp-Pro-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 225); Ac-Nle-c[Asp-Pro-dPhe-Arg-dNal(2')-Lys]-dVal-dPro-NH2 (SEQ ID NO: 430); Ac-Nle-c[Asp-Pro-dPhe-Arg-Nal(2')-Lys]-dVal-dPro-NH2 (SEQ ID NO: 431); Ac-Nle-c[Asp-Ala-His-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 380); Ac-Nle-c[Asp-Pro-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 215); Ac-Nle-c[Asp-Phe-p(Cl)dPhe-Arg-Trp-Lys]-

dVal-dPro-NH2 (SEQ ID NO: 525); Ac-Nle-c[Asp-dPhe-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 526); Ac-Nle-c[Asp-Bip-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 527); Ac-Nle-c[Asp-Trp-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 531); Ac-Nle-c[Asp-Tyr-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 533); Ac-Nle-c[Asp-dTyr-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 534); Ac-Nle-c[Asp-dTrp-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 532); Ac-Nle-c[dCys-His-p(Cl)dPhe-Arg-Trp-Cys]-dVal-dPro-NH2 (SEQ ID NO: 498); Ac-Nle-c[Cys-His-p(Cl)dPhe-Arg-Trp-Cys]-dVal-dPro-NH2 (SEQ ID NO: 497); Ac-Nle-c[Asp-His-p(Cl)dPhe-Arg-dNal(2')-Lys]-dVal-dPro-NH2 (SEQ ID NO: 509); Ac-Nle-c[Asp-His-p(Cl)dPhe-Arg-Nal(2')-Lys]-dVal-dPro-NH2 (SEQ ID NO: 510); Ac-Nle-c[Asp-His-p(Cl)dPhe-His-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 508); Ac-Nle-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 220); Ac-Nle-Nle-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 507); Ac-Ala-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 517); Ac-Ala-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 500); Ac-Nle-Nle-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dPro-dVal-dPro-NH2 (SEQ ID NO: 516); and Ac-Nle-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 514).

**[0375]** In some embodiments, the present technology comprises a method or use, wherein the non-naturally occurring melanocortin analog includes a sequence of Formula (IB): X1-X2-X3-R1-R2-Pro-R4-R5-R6-R7-R8-Y1-Y2-Y3-Y4-Y5-Y6-Y7 (IB), wherein: X1 is absent or norleucine (Nle); X2 is absent or Nle; X3 is absent or Nle; R1 is selected from the group consisting of Nle, D-norleucine (dNle), alanine (Ala), D-alanine (dAla), arginine (Arg), D-arginine (dArg), lysine (Lys), D-lysine (dLys), histidine (His), D-histidine (dHis), ornithine (Orn), D-ornithine (dOrn), D-leucine (dLeu), D-tyrosine (dTyr), phenylalanine (Phe), D-phenylalanine (dPhe), tryptophan (Trp), and D-tryptophan (dTrp); R2 is selected from the group consisting of aspartic acid (Asp), D-aspartic acid (dAsp), cysteine (Cys), D-cysteine (dCys), and D-penicillamine (dPen); R4 is dPhe or para-fluoro-D-phenylalanine (p(F)dPhe); R5 is selected from the group consisting of Arg, His, cisPro(guan), and transPro(guan); R6 is selected from the group consisting of Trp, dTrp, Phe, Aia, Aba, Ata, and 1'-naphthylalanine (Nal(1')); R7 is selected from the group consisting of Gly, Lys, dLys, Cys, dCys, dPen, and Orn; R8 is absent or Lys; Y1 is absent or is selected from the group consisting of valine (Val), D-valine (dVal), b2-valine (b2-Val), b3-valine (b3-Val), Pro, D-proline (dPro), b-proline

(b-Pro), Hyp, D-hydroxyproline (dHyp), D-tert-leucine (dTle), dLeu, Trp, Arg, dArg, Lys, dLys, Gly, Ala, dAla, Asp, dAsp, asparagine (Asn), D-asparagine (dAsn), and D-threonine (dThr); Y2 is absent or is selected from the group consisting of Val, dVal, b2-Val, b3-Val, Pro, dPro, b-Pro, Hyp, dHyp, dTle, Arg, dArg, Gly, Ala, dAla, Asp, and dAsn; Y3 is absent or is selected from the group consisting of Val, dVal, Pro, dPro, dThr, Lys, and dLys; Y4 is absent or is selected from the group consisting of dVal, dPro, Asp, and dAsp; Y5 is absent or dVal; Y6 is absent or dVal; Y7 is absent or dPro; and the non-naturally occurring melanocortin analog is cyclized through a moiety selected from the group consisting of: a disulfide bond between R2 and R7 when each of R2 and R7 are independently selected from the group consisting of Cys, dCys, and dPen; and a lactam bridge between R2 and R7 when R2 is Asp or dAsp and R7 is Lys, dLys, or Orn; provided that: when R4 is p(F)dPhe, then the non-naturally occurring melanocortin analog is not cyclized between Cys at R2 and Cys at R7; and when R4 is dPhe and one or more of X1, X2, and X3 is present, then Y3-Y7 are absent.

**[0376]** In some embodiments, the present technology comprises a method or use, wherein the non-naturally occurring melanocortin analog includes a sequence of Formula (IB), wherein: X1-X2-X3-R1-R2-Pro-R4-R5-R6-R7-R8-Y1-Y2-Y3-Y4-Y5-Y6-Y7 (IB), wherein: X1 is absent or norleucine (Nle); X2 is absent or Nle; X3 is absent or Nle; R1 is selected from the group consisting of Nle, D-norleucine (dNle), alanine (Ala), D-alanine (dAla), arginine (Arg), D-arginine (dArg), lysine (Lys), D-lysine (dLys), histidine (His), D-histidine (dHis), ornithine (Orn), D-ornithine (dOrn), D-leucine (dLeu), D-tyrosine (dTyr), phenylalanine (Phe), D-phenylalanine (dPhe), tryptophan (Trp), and D-tryptophan (dTrp); R2 is selected from the group consisting of aspartic acid (Asp), D-aspartic acid (dAsp), cysteine (Cys), D-cysteine (dCys), and D-penicillamine (dPen); R4 is dPhe or para-fluoro-D-phenylalanine (p(F)dPhe); R5 is selected from the group consisting of Arg, His, cisPro(guan), and transPro(guan); R6 is selected from the group consisting of Trp, dTrp, Phe, Aia, Aba, Ata, and 1'-naphthylalanine (Nal(1')); R7 is selected from the group consisting of Gly, Lys, dLys, Cys, dCys, dPen, and Orn; R8 is absent or Lys; Y1 is absent or is selected from the group consisting of valine (Val), D-valine (dVal), b2-valine (b2-Val), b3-valine (b3-Val), Pro, D-proline (dPro), b-proline (b-Pro), Hyp, D-hydroxyproline (dHyp), D-tert-leucine (dTle), dLeu, Trp, Arg, dArg, Lys, dLys, Gly, Ala, dAla, Asp, dAsp, asparagine (Asn), D-asparagine (dAsn), and D-threonine (dThr); Y2 is absent or is selected from the group

consisting of Val, dVal, b2-Val, b3-Val, Pro, dPro, b-Pro, Hyp, dHyp, dTle, Arg, dArg, Gly, Ala, dAla, Asp, and dAsn; Y3 is absent or is selected from the group consisting of Val, dVal, Pro, dPro, dThr, Lys, and dLys; Y4 is absent or is selected from the group consisting of dVal, dPro, Asp, and dAsp; Y5 is absent or dVal; Y6 is absent or dVal; Y7 is absent or dPro; and the non-naturally occurring melanocortin analog is cyclized through a moiety selected from the group consisting of: a disulfide bond between R2 and R7 when each of R2 and R7 are independently selected from the group consisting of Cys, dCys, and dPen; and a lactam bridge between R2 and R7 when R2 is Asp or dAsp and R7 is Lys, dLys, or Orn; provided that the non-naturally occurring melanocortin analog does not include a sequence of: Ac-Nle-c[Cys-Pro-p(F)dPhe-Arg-Trp-Cys]-dVal-dPro-NH2 (SEQ ID NO: 432); or Ac-Nle-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dPro-dVal-dPro-NH2 (SEQ ID NO: 639).

**[0377]** In some embodiments, the present technology comprises a method or use, wherein the non-naturally occurring melanocortin analog includes a sequence of Formula (IC): X1-X2-R1-R2-Pro-dPhe-R5-R6-R7-Y1-Y2-Y3-Y4 (IC), wherein: X1 is selected from the group consisting of norleucine (Nle), arginine (Arg), D-arginine (dArg), alanine (Ala), lysine (Lys), D-lysine (dLys), histidine (His), D-histidine (dHis); X2 is absent or Nle; R1 is selected from the group consisting of aspartic acid (Asp), cysteine (Cys), and D-cysteine (dCys); R2 is selected from the group consisting of tryptophan (Trp), phenylalanine (Phe), D-phenylalanine (dPhe), histidine (His), D-histidine (dHis), tyrosine (Tyr), and D-tyrosine (dTyr); R5 is Arg; R6 is selected from the group consisting of Trp, 2'-D-naphthylalanine (dNal(2')), 2'-naphthylalanine (Nal(2')), and 1'-naphthylalanine (Nal(1')); R7 is selected from the group consisting of Lys, Cys, and dCys; Y1 is absent or is selected from the group consisting of D-valine (dVal), D-tert-leucine (dTle), dArg, and dLys; Y2 is absent or is selected from the group consisting of dVal, dPro, and D-hydroxyproline (dHyp); Y3 is absent, dVal, or dPro; Y4 is absent or dPro; and the non-naturally occurring melanocortin analog is cyclized through a moiety selected from the group consisting of: a disulfide bond between R1 and R7 when both of R1 and R7 are independently selected from the group consisting of Cys, dCys, and dPen; and a lactam bridge between R1 and R7 when R1 is Asp and R7 is Lys;

**[0378]** In some embodiments, the present technology comprises a method or use, wherein the non-naturally occurring melanocortin analog includes a sequence of Formula (ID): X1-R1-R2-R3-p(Cl)dPhe-Arg-Trp-R7-Y1-Y2-Y3-Y4 (ID), wherein: X1 is absent or norleucine (Nle); R1 is selected from the group consisting of Nle, arginine (Arg), D-arginine (dArg), lysine (Lys), D-lysine (dLys), histidine (His), and D-histidine (dHis); R2 is aspartic acid (Asp) or D-cysteine (dCys); R3 is selected from the group consisting of His, 4-amino-1,2,4,5-tetrahydro-2-benzazepin-3-one (Aba), 7-amino-7,8-dihydro-4H-[1,2,3]triazolo-[1,5-a][1,4]diazepin-6(5H)-one (Ata), and 4-amino-1,4,5,6-tetrahydroazepino[4,3-b]indol-3(2H)-one (Aia); R7 is Lys or dCys; Y1 is selected from the group consisting of D-valine (dVal), D-proline (dPro), and D-tert-leucine (dTle); Y2 is absent or is selected from the group consisting of dVal, dPro, and dTle; Y3 is absent, dVal, or dPro; Y4 is absent or dPro; and the non-naturally occurring melanocortin analog is cyclized through a moiety selected from the group consisting of: a disulfide bond between R2 and R7 when both of R2 and R7 are dCys; and a lactam bridge between R2 and R7 when R2 is Asp and R7 is Lys; provided that when R3 is His and R1 is Nle, then (i) Y1Y2 is dVal-dPro, X1 is absent, and the non-naturally occurring melanocortin analog is cyclized through a disulfide bond, or (b) Y1Y2 is not dVal-dPro and either X1 or Y3 is present.

**[0379]** In some embodiments, the present technology comprises a method or use, wherein the non-naturally occurring melanocortin analog includes a sequence of Formula (ID), wherein: X1 is absent or norleucine (Nle); R1 is selected from the group consisting of Nle, arginine (Arg), D-arginine (dArg), lysine (Lys), D-lysine (dLys), histidine (His), and D-histidine (dHis); R2 is aspartic acid (Asp) or D-cysteine (dCys); R3 is selected from the group consisting of His, 4-amino-1,2,4,5-tetrahydro-2-benzazepin-3-one (Aba), 7-amino-7,8-dihydro-4H-[1,2,3]triazolo-[1,5-a][1,4]diazepin-6(5H)-one (Ata), and 4-amino-1,4,5,6-tetrahydroazepino[4,3-b]indol-3(2H)-one (Aia); R7 is Lys or dCys; Y1 is selected from the group consisting of D-valine (dVal), D-proline (dPro), and D-tert-leucine (dTle); Y2 is absent or is selected from the group consisting of dVal, dPro, and dTle; Y3 is absent, dVal, or dPro; Y4 is absent or dPro; and the non-naturally occurring melanocortin analog is cyclized through a moiety selected from the group consisting of: a disulfide bond between R2 and R7 when both of R2 and R7 are dCys; and a lactam bridge between R2 and R7 when R2 is Asp and R7 is Lys; provided that the non-naturally occurring melanocortin analog does not

include a sequence selected from the group consisting of: Ac-Nle-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 220); Ac-Nle-Nle-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 507); Ac-Nle-Nle-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dPro-dVal-dPro-NH2 (SEQ ID NO: 516); Ac-Nle-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 514); and.

**[0380]** In some embodiments, an N-terminus of the non-naturally occurring melanocortin analog is modified by an acyl group.

**[0381]** In some embodiments, the acyl group is an acetyl group.

**[0382]** In some embodiments, an N-terminus of the non-naturally occurring melanocortin analog is not modified.

**[0383]** In some embodiments, a C-terminus of the non-naturally occurring melanocortin analog is modified by an amide group.

**[0384]** In some embodiments, a C-terminus of the non-naturally occurring melanocortin analog is not modified.

**[0385]** In some embodiments, Y1-Y2 are present and Y3- Y8 are absent.

**[0386]** In some embodiments, Y1 is D-valine and Y2 is D-proline.

**[0387]** In some embodiments, the present technology comprises a method or a use, w wherein Y1 is D-tert-leucine and Y2 is D-proline.

**[0388]** In some embodiments, R4 is dNal(2').

**[0389]** In some embodiments, the sequence of Formula (I) is: Ac-Nle-c[Asp-His-dNal(2')-Arg-Trp-Pro-Lys]-dVal-dPro-NH2 (SEQ ID NO: 8), wherein c represents cyclization through R2 and R8 via a lactam bond.

**[0390]** In some embodiments, R4 is Phe or dPhe.

**[0391]** In some embodiments, the sequence of any one of Formulae (I)-(ID) is selected from the group consisting of: Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-OH (SEQ ID NO: 291); Ac-Nle-c[Asp-Pro-Phe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 294); Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 295; E2); and Ac-Nle-c[Asp-

Pro-His-Phe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 296). wherein c represents cyclization through R2 and R7 via a lactam bond.

**[0392]** In some embodiments, the sequence of any one of Formulae (I)-(ID) is selected from the group consisting of: Ac-dLeu-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO:298); Ac-dAla-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 299); Ac-Ala-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro- NH2 (SEQ ID NO: 300); Ac-dNle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 301); Ac-dArg-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 302); Ac-dPhe-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 303); Ac-dTyr-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 304); Phe-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 305); His-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 306); Trp-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 307); dPhe-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 308); dHis-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 309); dTrp-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 310); Ac-Arg-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 311); Ac-dLys-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 312); Ac-Lys-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 313); Ac-His-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 314); Ac-dHis-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 315); Ac-Orn-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 316); and Ac-dOrn-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 317), wherein c represents cyclization through R2 and R7 via a lactam bond.

**[0393]** In some embodiments, the sequence of any one of Formulae (I)-(ID) is selected from the group consisting of: Ac-Nle-c[Cys-Pro-dPhe-Arg-Trp-Cys]-dVal-dPro-NH2 (SEQ ID NO: 318); Ac-Nle-c[dCys-Pro-dPhe-Arg-Trp-Cys]-dVal-dPro-NH2 (SEQ ID NO: 319); Ac-Nle-c[dPen-Pro-dPhe-Arg-Trp-dPen]-dVal-dPro-NH2 (SEQ ID NO: 320); Ac-Nle-c[dCys-Pro-dPhe-Arg-Trp-dCys]-dVal-dPro-NH2 (SEQ ID NO: 321); Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Orn]-dVal-dPro-NH2 (SEQ ID NO: 322); and Ac-Nle-c[Cys-dPhe-Arg-Trp-Pen]-dVal-dPro-NH2 (SEQ ID NO: 324), wherein c represents cyclization through R2 and R7 via a disulfide bond.

**[0394]** In some embodiments, the sequence of any one of Formulae (I)-(ID) is selected from the group consisting of: Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Gly-Lys]-dVal-dPro-NH2 (SEQ ID NO: 351); Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Gly-Lys]-dPro-dPro-Lys-Asp-NH2 (SEQ ID NO: 352); and Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Gly-Lys]-dPro-dPro-dLys-dAsp-NH2 (SEQ ID NO: 353), wherein c represents cyclization through R2 and R8 via a lactam bond.

**[0395]** In some embodiments, the sequence of any one of Formulae (I)-(ID) is selected from the group consisting of: Ac-Nle-c[Asp-Ala-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 354); Ac-Nle-c[Asp-Leu-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 355); Ac-Nle-c[Asp-Cpe-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 358); Ac-Nle-c[Asp-Che-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 359); Ac-Nle-c[Asp-Oic-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 360); Ac-Nle-c[Asp-Ioc-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 361); Ac-Nle-c[Asp-Tic-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 362); Ac-Nle-c[Asp-Hyp-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 364); Ac-Nle-c[Asp-Phe-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 366); Ac-Nle-c[Asp-dPhe-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 367); Ac-Nle-c[Asp-Bip-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 368); Ac-Nle-c[Asp-dGln-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 371); Ac-Nle-c[Asp-Trp-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 372); Ac-Nle-c[Asp-dTrp-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 373); Ac-Nle-c[Asp-Tyr-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 374); Ac-Nle-c[Asp-dTyr-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 375); Ac-Nle-c[Asp-Aba-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 198); Ac-Nle-c[Asp-Aia-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 207); Ac-Nle-c[Asp-Ata-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 208); Ac-Nle-c[Asp-Atc-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 212); Ac-Nle-c[Asp-APC-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 213); and Ac-Nle-c[Asp-APPC-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 214), wherein c represents cyclization through R2 and R7 via a lactam bond.

**[0396]** In some embodiments, the sequence of any one of Formulae (I)-(ID) is selected from the group consisting of: Ac-Arg-c[Asp-dAla-His-dPhe-Arg-Trp-Lys]-NH2 (SEQ ID NO: 281); Ac-Arg-c[Asp-Ala-His-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 381); and Ac-

dArg-c[Asp-Ala-His-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 382), wherein c represents cyclization through R1 and R7 via a lactam bond.

**[0397]** In some embodiments, the sequence of any one of Formulae (I)-(ID) is selected from the group consisting of: Ac-Nle-c[Asp-Trp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 226); Ac-Nle-c[Cys-Trp-Pro-dPhe-Arg-Trp-Cys]-dVal-dPro-NH2 (SEQ ID NO: 383); Ac-Nle-c[dCys-Trp-Pro-dPhe-Arg-Trp-Cys]-dVal-dPro-NH2 (SEQ ID NO: 384); Ac-Nle-c[dCys-Trp-Pro-dPhe-Arg-Trp-dCys]-dVal-dPro-NH2 (SEQ ID NO: 385); Ac-Ala-c[Asp-Trp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 386); Ac-Lys-c[Asp-Trp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 387); Ac-dLys-c[Asp-Trp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 388); Ac-Arg-c[Asp-Trp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 389); Ac-dArg-c[Asp-Trp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 390); Ac-dHis-c[Asp-Trp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 391); Ac-His-c[Asp-Trp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 392); Ac-Nle-Nle-c[Asp-Trp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 393); Ac-Nle-c[Asp-Trp-Ala-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 394); Ac-Nle-c[Asp-Trp-Leu-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 395); Ac-Nle-c[Asp-Trp-Pro-dPhe-Arg-Nal(1']-Lys]-dVal-dPro-NH2 (SEQ ID NO: 399); Ac-Nle-c[Asp-Trp-Pro-dPhe-Arg-dNal(2')-Lys]-dVal-dPro-NH2 (SEQ ID NO: 403); Ac-Nle-c[Asp-Trp-Pro-dPhe-Arg-Nal(2')-Lys]-dVal-dPro-NH2 (SEQ ID NO: 404); Ac-Nle-c[Asp-Trp-Pro-dPhe-Arg-Trp-Lys]-dArg-dVal-dPro-NH2 (SEQ ID NO: 405); Ac-Nle-c[Asp-Trp-Pro-dPhe-Arg-Trp-Lys]-dLys-dVal-dPro-NH2 (SEQ ID NO: 406); Ac-Nle-c[Asp-Trp-Pro-dPhe-Arg-Trp-Lys]-dArg-dPro-NH2 (SEQ ID NO: 407); Ac-Nle-c[Asp-Trp-Pro-dPhe-Arg-Trp-Lys]-dLys-dPro-NH2 (SEQ ID NO: 408); Ac-Nle-c[Asp-Trp-Pro-dPhe-Arg-Trp-Lys]-dVal-dHyp-NH2 (SEQ ID NO: 409); Ac-Nle-c[Asp-Trp-Pro-dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 410); Ac-Nle-c[Asp-Trp-Pro-dPhe-Arg-Trp-Lys]-dVal-dVal-dVal-dPro-NH2 (SEQ ID NO: 411); Ac-Nle-c[Asp-Phe-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 412); Ac-Nle-c[Asp-His-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 413); Ac-Nle-c[Asp-Tyr-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 414); Ac-Nle-c[Asp-dPhe-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 415); Ac-Nle-c[Asp-dHis-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 416); and Ac-Nle-c[Asp-dTyr-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 417), wherein c represents cyclization through R1 and R7 via a lactam bond or a disulfide bond.

**[0398]** In some embodiments, the sequence of any one of Formulae (I)-(ID) is: Ac-Nle-c[Asp-Hyp-dPhe-Arg-Trp-Pro-Lys]-dVal-dPro-NH2 (SEQ ID NO: 419), wherein c represents cyclization through R2 and R8 via a lactam bond.

**[0399]** In some embodiments, the sequence of any one of Formulae (I)-(ID) is selected from the group consisting of: Ac-Nle-Phe-Phe-c[Asp-Phe-His-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 421); Ac-Nle-c[Asp-Phe-His-dPhe-Arg-Trp-Lys]-dLeu-dPro-NH2 (SEQ ID NO: 422); Ac-Nle-c[Asp-Phe-His-dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 423); and Ac-Nle-c[Asp-Phe-His-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 424), wherein c represents cyclization through R1 and R7 via a lactam bond.

**[0400]** In some embodiments, the sequence of any one of Formulae (I)-(ID) is selected from the group consisting of: Ac-Nle-c[Asp-Pro-dPhe-Arg-dTrp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 187); Ac-Nle-c[Asp-Pro-dPhe-Arg-Aia-Lys]-dVal-dPro-NH2 (SEQ ID NO: 233); Ac-Nle-c[Asp-Pro-dPhe-Arg-Aba-Lys]-dVal-dPro-NH2 (SEQ ID NO: 234); Ac-Nle-c[Asp-Pro-dPhe-Arg-Ata-Lys]-dVal-dPro-NH2 (SEQ ID NO: 235); Ac-Nle-c[Asp-Pro-dPhe-Arg-Nal(1')-Lys]-dVal-dPro-NH2 (SEQ ID NO: 427); and Ac-Nle-c[Asp-Pro-dPhe-Arg-Phe-Lys]-dVal-dPro-NH2 (SEQ ID NO: 429), wherein c represents cyclization through R2 and R7 via a lactam bond.

**[0401]** In some embodiments, the sequence of any one of Formulae (I)-(ID) is selected from the group consisting of: Ac-Nle-c[Asp-Pro-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 218); Ac-Nle-c[dCys-Pro-p(F)dPhe-Arg-Trp-Cys]-dVal-dPro-NH2 (SEQ ID NO: 433); Ac-Nle-c[dCys-Pro-p(F)dPhe-Arg-Trp-dCys]-dVal-dPro-NH2 (SEQ ID NO: 434); Ac-Ala-c[Asp-Pro-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 435); Ac-dArg-c[Asp-Pro-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 436); Ac-Arg-c[Asp-Pro-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 437); Ac-Lys-c[Asp-Pro-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 438); Ac-dLys-c[Asp-Pro-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 439); Ac-His-c[Asp-Pro-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 440); Ac-dHis-c[Asp-Pro-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 441); Ac-Nle-Nle-c[Asp-Pro-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 442); Ac-Nle-c[Asp-Pro-p(F)dPhe-His-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 443); Ac-Nle-c[Asp-Pro-p(F)dPhe-Arg-Trp-Lys]-dTle-dTle-dVal-NH2 (SEQ ID NO: 446); Ac-Nle-

c[Asp-Pro-p(F)dPhe-Arg-Trp-Lys]-dVal-dVal-dVal-dPro-NH2 (SEQ ID NO: 447); Ac-Nle-c[Asp-Pro-p(F)dPhe-Arg-Trp-Lys]-dPro-dVal-dPro-NH2 (SEQ ID NO: 448); Ac-Nle-c[Asp-Pro-p(F)dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 449); Ac-Nle-Nle-c[Asp-Pro-p(F)dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 450); Ac-Nle-Nle-c[Asp-Pro-p(F)dPhe-Arg-Trp-Lys]-dPro-dVal-dPro-NH2 (SEQ ID NO: 451); Ac-Ala-c[Asp-Pro-p(F)dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 452); Ac-dArg-c[Asp-Pro-p(F)dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 453); Ac-Arg-c[Asp-Pro-p(F)dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 454); Ac-Lys-c[Asp-Pro-p(F)dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 455); Ac-dLys-c[Asp-Pro-p(F)dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 456); Ac-His-c[Asp-Pro-p(F)dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 457); Ac-dHis-c[Asp-Pro-p(F)dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 458); Ac-Nle-c[Cys-His-p(F)dPhe-Arg-Trp-Cys]-dVal-dPro-NH2 (SEQ ID NO: 459); Ac-Nle-c[dCys-His-p(F)dPhe-Arg-Trp-Cys]-dVal-dPro-NH2 (SEQ ID NO: 460); Ac-Nle-c[dCys-His-p(F)dPhe-Arg-Trp-dCys]-dVal-dPro-NH2 (SEQ ID NO: 461); Ac-Nle-c[Asp-His-p(F)dPhe-Arg-Nal(2')-Lys]-dVal-dPro-NH2 (SEQ ID NO: 472); Ac-Nle-c[Asp-dGln-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 492); and Ac-Nle-c[Asp-dTyr-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 496), wherein c represents cyclization through R2 and R7 via a lactam bond or a disulfide bond.

**[0402]** In some embodiments, the sequence of any one of Formulae (I)-(ID) is selected from the group consisting of: Ac-Nle-c[Asp-Aba-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 209); Ac-Nle-c[Asp-Aia-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 210); Ac-Nle-c[Asp-Ata-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 211); Ac-Nle-c[dCys-His-p(Cl)dPhe-Arg-Trp-dCys]-dVal-dPro-NH2 (SEQ ID NO: 499); Ac-dArg-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 501); Ac-Arg-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 502); Ac-Lys-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 503); Ac-dLys-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 504); Ac-His-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 505); Ac-dHis-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 506); Ac-Nle-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dTle-dTle-dVal-NH2 (SEQ ID NO: 511); Ac-Nle-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dVal-dVal-dPro-NH2 (SEQ ID NO: 512); Ac-Nle-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dPro-dVal-dPro-NH2 (SEQ ID NO: 513); Ac-Nle-Nle-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 515); Ac-

dArg-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 518); Ac-Arg-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 519); Ac-Lys-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 520); Ac-dLys-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 521); Ac-His-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 522); and Ac-dHis-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 523), wherein c represents cyclization through R2 and R7 via a lactam bond or a disulfide bond.

**[0403]** In some embodiments, the sequence of any one of Formulae (I)-(ID) is selected from the group consisting of: Ac-Nle-c[dCys-His-p(Br)dPhe-Arg-Trp-Cys]-dVal-dPro-NH2 (SEQ ID NO: 536); or Ac-Nle-c[dCys-His-p(Br)dPhe-Arg-Trp-dCys]-dVal-dPro-NH2 (SEQ ID NO: 537), wherein c represents cyclization through R2 and R7 via a disulfide bond.

**[0404]** In some embodiments, the sequence of any one of Formulae (I)-(ID) is selected from the group consisting of: Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-Val-Pro-NH2 (SEQ ID NO: 573); Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-Hyp-NH2 (SEQ ID NO: 574); Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dHyp-NH2 (SEQ ID NO: 575); Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-Val-NH2 (SEQ ID NO: 576); Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-Pro-NH2 (SEQ ID NO: 577); Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-Arg-NH2 (SEQ ID NO: 578); Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dArg-NH2 (SEQ ID NO: 579); Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dArg-dPro-NH2 (SEQ ID NO: 580); Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-Arg-NH2 (SEQ ID NO: 581); Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dArg-NH2 (SEQ ID NO: 582); Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-Lys-Pro-Val-NH2 (SEQ ID NO: 583); Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dLys-dPro-NH2 (SEQ ID NO: 584); Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-Lys-Val-Pro-NH2 (SEQ ID NO: 585); Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-Lys-dVal-dPro-NH2 (SEQ ID NO: 586); Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dLys-dVal-dPro-NH2 (SEQ ID NO: 587); Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-Arg-Pro-Val-NH2 (SEQ ID NO: 588); Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-Arg-Val-Pro-NH2 (SEQ ID NO: 589); Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dArg-dVal-dPro-NH2 (SEQ ID NO: 590); Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 591); Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dTle-dTle-dPro-NH2 (SEQ ID NO: 592); Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dTle-dTle-dVal-NH2 (SEQ ID NO: 593); Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-

dVal-dTle-NH2 (SEQ ID NO: 594); Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dVal-dPro-NH2 (SEQ ID NO: 595); Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dPro-dVal-dPro-NH2 (SEQ ID NO: 596); Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dVal-dVal-dPro-NH2 (SEQ ID NO: 597); Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-dVal-dPro-NH2 (SEQ ID NO: 598); Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dVal-dVal-dVal-dVal-dVal-dPro-NH2 (SEQ ID NO: 599); Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-Trp-NH2 (SEQ ID NO: 600); Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-Lys-dPro-dVal-NH2 (SEQ ID NO: 601); Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dAla-dAla-NH2 (SEQ ID NO: 602); Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-Asp-NH2 (SEQ ID NO: 603); Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dHyp-NH2 (SEQ ID NO: 604); Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dAsn-NH2 (SEQ ID NO: 605); Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-Asp-NH2 (SEQ ID NO: 606); Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-Asn-dPro-NH2 (SEQ ID NO: 607); Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-Hyp-NH2 (SEQ ID NO: 608); Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-Ala-Ala-NH2 (SEQ ID NO: 609); Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-Gly-Gly-NH2 (SEQ ID NO: 610); Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-Asp-dPro-NH2 (SEQ ID NO: 611); Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dAsn-dPro-NH2 (SEQ ID NO: 612); Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-Asn-NH2 (SEQ ID NO: 613); Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dAsp-NH2 (SEQ ID NO: 614); Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dAsn-NH2 (SEQ ID NO: 615); Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-Lys-dPro-NH2 (SEQ ID NO: 616); Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dPro-dVal-OH (SEQ ID NO: 617); Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dThr-dPro-dThr-NH2 (SEQ ID NO: 618); Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dThr-dPro-dThr-OH (SEQ ID NO: 619); Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dPro-dVal-NH2 (SEQ ID NO: 620); Ac-Nle-c[dAsp-Pro-dPhe-Arg-Trp-dLys]-dPro-dVal-NH2 (SEQ ID NO: 622); Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-βPro-β2Val-NH2 (SEQ ID NO: 623); Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-βPro-β3Val-NH2 (SEQ ID NO: 624); Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-β2Val-βPro-NH2 (SEQ ID NO: 625); Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-β3Val-βPro-NH2 (SEQ ID NO: 626); and Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-βPro-βPro-NH2 (SEQ ID NO: 627), wherein c represents cyclization through R2 and R7 via a lactam bond.

**[0405]** In some embodiments, the sequence of any one of Formulae (I)-(ID) is selected from the group consisting of: Ac-Nle-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 628); Ac-Nle-Nle-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID

NO: 629); and Ac-Nle-Nle-Nle-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-NH2 (SEQ ID NO: 630), wherein c represents cyclization through R2 and R7 via a lactam bond.

**[0406]** In some embodiments, the sequence of any one of Formulae (I)-(ID) is selected from the group consisting of: Ac-Arg-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dArg-dVal-dPro-NH2 (SEQ ID NO: 631); Ac-dLys-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dLys-dVal-dPro-NH2 (SEQ ID NO: 632); Ac-Lys-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dArg-dPro-NH2 (SEQ ID NO: 633); Ac-His-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dLys-dPro-NH2 (SEQ ID NO: 634); Ac-dHis-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dHyp-NH2 (SEQ ID NO: 635); Ac-Orn-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 636); Ac-dOrn-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dVal-dVal-dPro-NH2 (SEQ ID NO: 637); Ac-Nle-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 638); Ac-Ala-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 640); Ac-dArg-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 641); Ac-Arg-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 642); Ac-Lys-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 643); Ac-dLys-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 644); Ac-His-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 645); and Ac-dHis-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dTle-dPro-NH2 (SEQ ID NO: 646), wherein c represents cyclization through R2 and R7 via a lactam bond.

**[0407]** In some embodiments, the non-naturally occurring melanocortin analog includes any one of SEQ ID NOs: 8, 187, 198, 207-218, 226, 231-235, 281, 291, 294-296, 298-322, 324, 351-355, 358-362, 364, 366-368, 371-375, 381-395, 399, 403-417, 419, 421-425, 427, 429, 433-443, 446-461, 472, 492, 496, 499-506, 511-513, 515, 518-523, 536-537, 573-599, 600-620, 622-646.

**[0408]** In some embodiments, the non-naturally occurring melanocortin analog includes any one of the sequences of SEQ ID NOs: 187, 212, 218, 226, 291, 295, 298-322, 324, 351-355, 358-360, 362, 364, 366-368, 371-375, 381-395, 399, 403-417, 419, 421-425, 427, 429, 433-443, 446-461, 472, 492, 496, 499-506, 511-513, 515, 518-523, 536-537, 573-598, 600-646.

**[0409]** In some embodiments, the non-naturally occurring melanocortin analog includes any one of the sequences of SEQ ID NOs: 187, 218, 231-235, 291, 295, 298-322, 351-353, 425, 427, 429, 433-443, 446-458, 573-599, 600-620, 622-646.

**[0410]** In some embodiments, the non-naturally occurring melanocortin analog includes any one of the sequences of SEQ ID NOs: 226, 383-393, 399, 403-417.

**[0411]** In some embodiments, the non-naturally occurring melanocortin analog includes any one of the sequences of SEQ ID NOs: 209-211, 499, 501-506, 511-513, 515, 518-523.

**[0412]** In some embodiments, the non-naturally occurring melanocortin analog is present in a pharmaceutical composition.

**[0413]** In some embodiments, the pharmaceutical composition includes one or more pharmaceutically acceptable excipients and/or carriers.

**[0414]** In some embodiments, the one or more pharmaceutically acceptable excipients and/or carriers of the pharmaceutical composition include water.

**[0415]** In some embodiments, the non-naturally occurring melanocortin analog is administered (i) at a first dose of about 5 mg/kg to about 20 mg/kg administered once a day for about 5 days to about 10 days; (ii) at a second dose of about 10 mg/kg to about 40 mg/kg administered once a day after administration of the first dose for about 5 days to about 10 days; (iii) at a third dose of about 5 mg/kg to about 30 mg/kg administered twice a day after administration of the second dose for at least about 5 days to about 10 days.

**[0416]** In some embodiments, the non-naturally occurring melanocortin analog is administered (i) at a first dose of about 5 mg/kg administered once a day for about 7 days; (ii) at a second dose of about 15 mg/kg administered once a day after administration of the first dose for about 7 days; (iii) at a third dose of about 10 mg/kg administered twice a day after administration of the second dose for at least about 7 days.

**[0417]** In some embodiments, the non-naturally occurring melanocortin analog is administered (i) at a first dose of about 10 mg/kg administered once a day for about 7 days; (ii) at a second dose of about 20 mg/kg administered once a day after administration of the first dose for about 7 days; (iii) at a third dose of about 15 mg/kg administered twice a day after administration of the second dose for at least about 7 days.

**[0418]** In some embodiments, the present technology comprises a method or the use wherein the non-naturally occurring melanocortin analog is administered (i) at a first dose of about 15 mg/kg administered once a day for about 7 days; (ii) at a second dose of about 25 mg/kg administered once a day after administration of the first dose for about 7 days; (iii) at a third dose of about 20 mg/kg administered twice a day after administration of the second dose for at least about 7 days.

**[0419]** In some embodiments, the non-naturally occurring melanocortin analog is administered at a dose of about 0.5 mg/kg to about 10 mg/kg per body weight of the subject once daily.

**[0420]** In some embodiments, the non-naturally occurring melanocortin analog is administered at a dose of about 1 mg/kg or 3 mg/kg per body weight of the subject once daily.

**[0421]** In some embodiments, the non-naturally occurring melanocortin analog is administered at a dose of about 0.1 mg to about 100 mg once daily.

**[0422]** In some embodiments, the non-naturally occurring melanocortin analog is administered at a dose of about 10 mg or about 50 mg once daily.

**[0423]** In some embodiments, the non-naturally occurring melanocortin analog is administered via intraperitoneal, intravenous, parenteral, subcutaneous, intramuscular, intracerebroventricular, intranasal, or oral administration.

**[0424]** In some embodiments, the non-naturally occurring melanocortin analog crosses a blood-brain-barrier of a subject.

**[0425]** In some embodiments, the non-naturally occurring melanocortin analog includes any one of the sequences of SEQ ID NOs: 8, 187, 198, 207-218, 226, 231-235, 281, 291, 294-296, 298-322, 324, 351-355, 358-362, 364, 366-368, 371-375, 381-395, 399, 403-417, 419, 421-425, 427, 429, 433-443, 446-461, 472, 492, 496, 499-506, 511-513, 515, 518-523, 536-537, 573-599, 600-620, 622-646 and is administered at least once daily in an amount ranging from 0.001 mg/kg to 25 mg/kg per body weight of the subject.

**[0426]** In some embodiments, the non-naturally occurring melanocortin analog includes any one of the sequences of SEQ ID NOs: 8, 187, 198, 207-218, 226, 231-235, 281, 291, 294-296, 298-322, 324, 351-355, 358-362, 364, 366-368, 371-375, 381-395, 399, 403-417, 419, 421-425, 427, 429, 433-443, 446-461, 472, 492, 496, 499-506, 511-513, 515, 518-523, 536-537, 573-599, 600-620, 622-646 and is administered at least once daily in an amount ranging from 0.5 mg/kg to 10 mg/kg per body weight of the subject.

**[0427]** In some embodiments, the non-naturally occurring melanocortin analog is administered to a subject for at least 1 day, 1 week, 1 month, 3 months, 6 months, 1 year, or 5 years.

**[0428]** In some embodiments, the non-naturally occurring melanocortin analog is administered to a subject for 1 day, 5 days, 7 days, 14 days, 21 days, 28 days, 35 days, 40 days, 45 days, 50 days, 60 days, 75 days, 90 days, 100 days, 110 days, or 120 days.

## BRIEF DESCRIPTION OF THE DRAWINGS

**[0429]** FIGS. 1A-1C show the cardiac data for melanocortin agonist A07D ("E2"; SEQ ID NO: 295) up to 180 minutes after subcutaneous injection.

**[0430]** FIGS. 2A-2D show the plasma and cerebrospinal fluid (CSF) concentration of A07D ("E2"; SEQ ID NO: 295) in rats over time following subcutaneous administration.

**[0431]** FIG. 3 shows plasma concentration of A07D administered at 1mg/kg intravenously, 10 mg/kg orally, or 30 mg/kg orally to fasted male cynomolgus monkeys.

**[0432]** FIGS. 4A and 4B show results of a morphine conditioned placed preference (CPP) study in rats administered vehicle and saline, vehicle and morphine, or A07D and morphine. FIG 4A illustrates the experimental timeline. FIG 4B illustrates CPP scores in each group before and after each test.

## DETAILED DESCRIPTION

**[0433]** The present technology comprises methods of treating, preventing, reducing, or otherwise ameliorating one or more symptoms or conditions associated with pain, addiction, addictive agent use, or withdrawal from an addictive substance using a non-naturally occurring melanocortin analog. In some emfbodiments, the non-naturally occurring

melanocortin analog is administered orally. In some embodiments, the non-naturally occurring melanocortin analog is a melanocortin receptor agonist and/or an opioid receptor agonist. In some embodiments, the method comprises preventing, stabilizing, or reducing one or more of a dose used or consumed of an addictive substance, a dependency on an addictive substance, an amount/frequency of an addictive substance, use (e.g., dose or dosage) of an opioid reversal agent, relapse associated with use of an addictive substance, use (e.g., frequency/amount) of a conventional medication used to treat an addiction, an incidence of or need for hospitalization associated with use of an addictive substance, or an incidence in or a need for rehabilitation from an addiction. In some embodiments, the methods promote or increase cessation of an addictive substance.

**[0434]** The following description is merely exemplary in nature and is not intended to limit the present technology, its applications, or its uses. It should be understood that throughout the drawings, corresponding reference numerals indicate like or corresponding parts and features. The description of specific examples indicated in various embodiments of the present technology are intended for purposes of illustration only and are not intended to limit the scope of the present technology disclosed herein. Moreover, recitation of multiple embodiments having stated features is not intended to exclude other embodiments having additional features or other embodiments incorporating different combinations of the stated features.

**[0435]** The following description is merely exemplary in nature and is not intended to limit the present technology, its applications, or its uses. It should be understood that throughout the drawings, corresponding reference numerals indicate like or corresponding parts and features. The description of specific examples indicated in various embodiments of the present technology are intended for purposes of illustration only and are not intended to limit the scope of the present technology disclosed herein. Moreover, recitation of multiple embodiments having stated features is not intended to exclude other embodiments having additional features or other embodiments incorporating different combinations of the stated features.

**[0436]** While the embodiments are described in sufficient detail to enable those skilled in the art to practice the present technology, it should be understood that other embodiments

may be realized, and that logical changes may be made without departing from the spirit and scope of the present technology. Thus, the detailed description herein is presented for purposes of illustration only and not of limitation. For example, steps recited in any method or process, may be executed in any order and are not limited to the order presented. Moreover, any of the steps thereof may be outsourced to or performed by one or more third parties.

***finitions***

**[0437]** Unless defined otherwise, all technical and scientific terms used herein have the same meaning as commonly understood by those of ordinary skill in the art to which the present technology belongs. For the purposes of the present technology, the following terms are defined below.

**[0438]** The articles "a" and "an" are used herein to refer to one or to more than one (i.e., to at least one) of the grammatical object of the article. By way of example, "an element" means one element or more than one element. Likewise, any reference to singular includes plural embodiments, and any reference to more than one component may include a singular embodiment.

**[0439]** e term "about" means a quantity, level, value, number, frequency, percentage, dimension, size, amount, weight or length that varies by acceptable levels in the art. Typically, such variation may be as much 10% above and below a reference quantity, level, value, number, frequency, percentage, dimension, size, amount, weight or length and such variation may be influenced by standard applicable measurement practices. When the term "about" is used in conjunction with a numerical range, it modifies that range by extending the boundaries above and below the numerical values set forth.

**[0440]** The terms "administering" or "administer" include delivery of therapies (e.g., non-naturally occurring melanocortin analogs (also referred to herein as peptides)) of the present technology to a subject either by local or systemic administration. Administration may be topical (including ophthalmic and to mucous membranes including vaginal and rectal delivery), pulmonary (e.g., by inhalation or insufflation of powders or aerosols, including by nebulizer), intratracheal, intranasal, epidermal and transdermal, oral or parenteral.

Parenteral administration includes intravenous, intraarterial, subcutaneous, intraperitoneal or intramuscular injection or infusion; or intracranial, e.g., intrathecal or intraventricular, administration.

**[0441]** The terms "active ingredient" and "active compound" refer to a biologically active substance, whether naturally or non-naturally occurring, that is the main component of the pharmaceutical composition which elicits the intended effect of an administered therapeutic. This may be any component that drives the pharmacological activity or direct effect in the diagnosis, cure, mitigation, treatment, or prevention of the conditions associated with the present technology, such as but not limited to, substance use disorders.

**[0442]** As used herein, a "composition" or a "pharmaceutical composition" refers to a mixture of the active ingredient with other chemical components, such as pharmaceutically acceptable carriers and/or excipients.

**[0443]** As used herein, a "pharmaceutically acceptable carrier" of the pharmaceutical composition refers to a carrier or diluent that does not cause significant irritation to an organism, does not abrogate the biological activity and properties of the administered active ingredient, and/or does not interact in a deleterious manner with the other components of the composition in which it is contained. The term "carrier" encompasses any excipient, binder, diluent, filler, salt, buffer, solubilizer, lipid, stabilizer, or other material well known in the art for use in pharmaceutical formulations. The choice of a carrier for use in a composition will depend upon the intended route of administration for the composition. The preparation of pharmaceutically acceptable carriers and formulations containing these materials is described in, e.g., Remington's Pharmaceutical Sciences, 21st Edition, ed. University of the Sciences in Philadelphia, Lippincott, Williams & Wilkins, Philadelphia Pa., 2005, which is incorporated herein by reference in its entirety). Some examples of physiologically acceptable carriers include antioxidants including ascorbic acid; low molecular weight (less than about 10 residues) polypeptides; proteins, such as serum albumin, gelatin, or immunoglobulins; hydrophilic polymers such as polyvinylpyrrolidone; amino acids such as glycine, glutamine, asparagine, arginine or lysine; monosaccharides, disaccharides, and other carbohydrates including glucose, mannose, or dextrins; chelating agents such as EDTA; sugar alcohols such as mannitol or sorbitol; salt-forming counterions

such as sodium; and/or nonionic surfactants such as TWEEN® (ICI, Inc.; Bridgewater, N.J.), polyethylene glycol (PEG), and PLURONICS™ (BASF; Florham Park, N.J.). An "excipient" of the first or the pharmaceutical composition refers to an inert substance added to a composition to further facilitate administration of a compound. Examples, without limitation, of excipients include calcium carbonate, calcium phosphate, various sugars and types of starch, cellulose derivatives, gelatin, vegetable oils, and polyethylene glycols.

**[0444]** The terms "treat", "treatment", and "treating" may also refer to the reduction or inhibition of the progression and/or duration of a disease (e.g., addiction), the reduction or amelioration of the severity of the disease, and/or the amelioration of one or more symptoms thereof resulting from the administration of one or more therapies. Specifically, these terms may refer to: (1) a stabilization or reduction (e.g. by more than 10%, 20%, 30%, 40%, 50%, or more than 60% of the baseline of addiction before administration) in an addiction, (2) a stabilization or reduction (e.g. by more than 10%, 20%, 30%, 40%, 50%, or more than 60% of the baseline of symptom before administration) in a symptom associated with use or reliance on an addictive substance, (3) inhibiting or reducing rate of addiction increase, (4) relieving to some extent (or, preferably, eliminating) one or more symptoms associated with a pathology related to or caused in part by addiction, (5) an increase in disease-free, relapse-free, progression-free, and/or overall survival, duration, or rate, (6) a decrease in hospitalization rate, (7) a decrease in hospitalization length, (8) an increase in the response rate, the durability of response, or number of patients who respond, (8) a reduction in a withdrawal symptom associated with use of an addictive substance (e.g. by more than 10%, 20%, 30%, 40%, 50%, or more than 60% of the baseline withdrawal symptom associated with use of an addictive substance), (9) a decrease in the need for an opioid reversal agent (e.g. naloxone or other opioid antagonists), and (10) stabilizing, preventing, or reducing (e.g. by more than 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90% or 100% of the baseline use) use of an addictive substance. The terms "treat", "treatment", and "treating" include prophylactic and/or therapeutic treatments. If it is administered prior to clinical manifestation of a condition, the treatment is considered prophylactic. Therapeutic treatment includes, e.g., ameliorating or reducing the severity of a disease, or shortening the length or frequency of the disease.

**[0445]** As used herein, the terms "effective amount" or "therapeutically effective amount," refer to that amount of the active ingredient being administered which will relieve to some extent one or more of the symptoms of the disease or disorder being treated. The result may be a reduction and/or alleviation of the signs, symptoms, or causes of a disease or disorder, or any other desired alteration of a biological system. An appropriate "effective amount" may differ from one individual to another. An appropriate "effective amount" in any individual case may be determined using techniques, such as a dose escalation study.

**[0446]** The term "after administration" refers to any duration of time after the non-naturally occurring melanocortin analog or pharmaceutical composition thereof has been administered to a subject. "After administration" may also refer to the duration of time after one dose has been completed or after more than one dose has been completed, such as two doses, three doses, four doses, and the like. In some embodiments, "after administration" refers to completion of dosing regimen that includes one or more doses. Likewise, the term "prior to" refers to any duration of time before the non-naturally occurring melanocortin analog or pharmaceutical composition thereof has been administered to a subject. Unless otherwise specified, durations of time encompassed by "after administration" or "prior to administration" may include seconds, minutes, hours, days, weeks, months, and years.

**[0447]** The terms "subject" and "patient" refer to anyone being evaluated for disease, disorder, or condition or being administered a therapeutic or pharmaceutical composition. This includes people without diagnosed or confirmed disease or condition. This also includes people with diagnosed or confirmed disease or condition, such as an alcohol use disorder or an opioid use disorder.

**[0448]** The term "control subject," as used herein, refers to any subject used as a basis for comparison to the subject (e.g., test subject). A control subject includes, but is not limited to, any subject who has not been administered the therapeutic or pharmaceutical composition (e.g., the non-naturally occurring melanocortin analog, a therapeutically effective amount of the non-naturally occurring melanocortin analog or a pharmaceutical composition thereof) or administered a placebo.

**[0449]** Melanocortin analogs," "non-naturally occurring melanocortin analogs," "melanocortin peptides," "melanocortin receptor peptides," or "melanocortins," are used interchangeably and refer to melanocortin-receptor ligands, which are macromolecules containing at least one melanocortin pharmacophore. Melanocortin analogs are typically peptides that bind melanocortin receptors under physiological conditions. Melanocortin analogs include naturally occurring non-naturally occurring melanocortin analogs (i.e., "synthetic peptides" or "synthetic analogs") and truncated and/or modified versions of melanocortin full-length protein or peptides. For example, the full-length pro-opiomelanocortin protein (POMC), prior to proteolytic cleavage of "sub-peptides," consists of 241 amino acids. Tissue-specific proteolytic cleavage of POMC yields peptides ranging in size from 13 amino acids to 76 amino acids. See Bicknell and Lawry, Encyclopedia of Stress, vol. 3, 257-265, Academic Press (2000). Synthesized, non-naturally occurring melanocortin analogs having increased melanocortin receptor activity as discussed herein are approximately 7-12 amino acids in size. Melanocortin analogs exhibit binding functionality with melanocortin receptors. In addition to peptides, the non-naturally occurring melanocortin analogs include small molecule analogs of melanocortin or portions thereof comprised of organic compounds, inorganic compounds, or combinations of peptide and small molecule—i.e., peptide mimetics, or various combinations thereof. "Non-naturally occurring melanocortin analogs" may be structurally similar and/or functionally similar to biological melanocortin proteins in their ability to bind melanocortin receptors. Further, the melanocortin analogs generally contain the pharmacophore: His-Phe-Arg-Trp (SEQ ID NO: 1) or a modified version thereof, or a structural or functional peptide mimetic thereof.

**[0450]** A "pharmacophore" is the minimum set of amino acid residues necessary to achieve a physiological effect; or a small molecule that is (with respect to a receptor) a structural mimic of the amino acid residues required for binding to and activation of a receptor. His-Phe-Arg-Trp (SEQ ID NO: 1) and their analogs are the pharmacophore of melanocortin for the regulated physiological effect. Therefore, non-naturally occurring melanocortin pharmacophore analogs may be small peptides or organic molecules designed to mimic the appearance or function (including activation or deactivation of receptor activity) of the melanocortin pharmacophore core sequence peptide.

**[0451]** A melanocortin receptor "agonist" is a naturally occurring substance or manufactured drug substance or composition that may interact with a melanocortin receptor and initiate a pharmacological response characteristic of the melanocortin receptor.

**[0452]** A melanocortin receptor "antagonist" is a naturally occurring substance or manufactured drug substance or composition that opposes the melanocortin receptor-associated responses normally induced by a melanocortin receptor agonist agent.

**[0453]** "Potentiated therapeutic activity" refers to an increase in melanocortin activity in a non-naturally occurring melanocortin analog that has undergone derivatization at the N- and/or C-terminus. Such derivatizations do not necessarily involve the pharmacophore, but do imply a relative increase in in vivo biological half-life.

**[0454]** The terms "bind," "binding," "complex," and "complexing," refer to all types of physical and chemical binding, reactions, complexing, attraction, chelating and the like.

**[0455]** The "peptides" of the present technology may be (a) naturally-occurring, (b) produced by chemical synthesis, (c) produced by recombinant DNA technology, (d) produced by biochemical or enzymatic fragmentation of larger molecules, (e) produced by methods resulting from a combination of methods (a) through (d) listed above, or (f) produced by any other means for producing peptides.

**[0456]** The term "peptide" as used herein includes any structure comprised of two or more amino acids, including chemical modifications and derivatives of amino acids. The amino acids forming all or a part of a peptide may be naturally occurring amino acids, stereoisomers and modifications of such amino acids, non-protein amino acids, post-translationally modified amino acids, enzymatically modified amino acids, constructs or structures designed to mimic amino acids, and the like, so that the term "peptide" includes pseudopeptides and peptidomimetics, including structures which have a non-peptidic backbone. The term "peptide" also includes dimers or multimers of peptides. A "manufactured" peptide includes a peptide produced by chemical synthesis, recombinant DNA technology, biochemical, or enzymatic fragmentation of larger molecules, combinations of the foregoing or, in general, made by any other method. The term "peptide" includes peptides containing a variable number of amino acid residues, optionally with non-

amino acid residue groups at the N- and C-termini, such groups including acyl, acetyl, alkenyl, alkyl, N-alkyl, amine, or amide groups, among others.

**[0457]** By employing chemical synthesis, a useful means of production, it is possible to introduce various amino acids which do not naturally occur along the chain, modify the N- or C-terminus, and the like, thereby providing for improved stability and formulation, resistance to protease degradation, and the like.

**[0458]** "Amino acids" are molecules containing an amine group, a carboxylic acid group, and a side-chain that is specific to each amino acid. The key elements of an amino acid are carbon, hydrogen, oxygen, and nitrogen and have the generic formula $H_2N$—CHR—COOH, wherein R represents a side chain group. The various α-amino acids differ in the side-chain moiety that is attached to the α-carbon. The "amino acids" of the present technology include the known naturally occurring protein amino acids, which are referred to by both their common three letter abbreviation and single letter abbreviation. See generally *Synthetic Peptides: A User's Guide*, G. A. Grant, editor, W.H. Freeman & Co., New York (1992), the teachings of which are incorporated herein by reference, including the text and table set forth at pages 11 through 24. As set forth above, the term "amino acid" also includes stereoisomers and modifications of naturally occurring protein amino acids, non-protein amino acids, post-translationally modified amino acids, enzymatically synthesized amino acids, derivatized amino acids, constructs or structures designed to mimic amino acids, and the like. Modified and unusual amino acids are described generally in *Synthetic Peptides: A User's Guide*, supra; Hruby et al., *Biochem. J.* 268:249-262 (1990); and Toniolo, *Int. J. Peptide Protein Res.* 35:287-300 (1990); the teachings of all of which are incorporated herein by reference.

**[0459]** The phrase "amino acid side chain moiety" used herein, including as used in the specification and claims, includes any side chain of any amino acid, as the term "amino acid" is defined herein. This thus includes the side chain moiety present in naturally occurring amino acids. It further includes side chain moieties in modified naturally occurring amino acids, such as glycosylated amino acids. It further includes side chain moieties in stereoisomers and modifications of naturally occurring protein amino acids, non-protein amino acids, post-translationally modified amino acids, enzymatically synthesized amino

acids, derivatized amino acids, constructs, or structures designed to mimic amino acids, and the like. For example, the side chain moiety of any amino acid of the present technology is included within the definition. A "derivative" of an amino acid side chain moiety is included within the definition of an amino acid side chain moiety.

**[0460]** The "derivative" of an amino acid side chain moiety includes any modification to or variation in any amino acid side chain moieties, including a modification of naturally occurring amino acid side chain moieties. By way of example, derivatives of amino acid side chain moieties include straight chain or branched, cyclic or noncyclic, substituted or unsubstituted, saturated or unsaturated, alkyl, aryl or aralkyl moieties.

**[0461]** In the peptides of the present technology, conventional amino acid residues have their conventional meaning as given in Chapter 2400, of the *Manual of Patent Examining Procedure,* 8th Ed. Thus, "Ala" is alanine; "Arg" is arginine; "Asn" is asparagine; "Asp" is aspartic acid; "Cys" is cysteine; "Gln" is glutamine; "Glu" is glutamic acid; "His" is histidine; "Ile" is isoleucine; "Leu" is leucine; "Lys" is lysine; "Met" is methionine; "Phe" is phenylalanine; "Pro" is proline; "Ser" is serine; "Thr" is threonine; "Trp" is tryptophan; "Tyr" is tryosine; and "Val" is valine. Unless otherwise indicated, all amino acids abbreviations represent either isomer, i.e., the L-isomer, the D-isomer, or combinations thereof may be used. Thus, for example, "L-Phe" is L-phenylalanine; "D-Phe" is D-phenylalanine; "D-/L-Phe" is D-phenylalanine, L-phenylalanine, or combinations thereof; "Phe" is also D-phenylalanine, L-phenylalanine, or combinations thereof, and so on. Non-standard amino acids are "Nle" is norleucine; "Nal" is naphthylalanine; "D-Nal" is D-naphthylalanine; D-Nal(2′) is D-2′-naphthylalanine; L-Nal(2') is L-2′-naphthylalanine; L-Nal(1') is L-1′-naphthylalanine; D-Nal(1') is D-1′-naphthylalanine; Tle is tert-Leucine; Nva is norvaline; Orn is ornithine; Bip is biphenylalanine; and so on.

**[0462]** An alpha (α)-amino acid has the generic formula $H_2N—C_\alpha HR—COOH$, where R is a side chain moiety and the amino group is attached to the carbon atom immediately adjacent to the carboxylate group (i.e., the α-carbon). Other types of amino acids exist when the amino group is attached to a different carbon atom. For example, beta (β)-amino acids, the carbon atom to which the amino group is attached is separated from the carboxylate group by one carbon atom, $C_\beta$.

**[0463]** When β-amino acids are incorporated into peptides, two main types of β-peptides exist: those with the side chain residue, R, on the carbon next to the amine are called $\beta^3$ peptides and those with the side chain residue on the carbon next to the carbonyl group are called $\beta^2$ amino acids.

**[0464]** Gamma (γ)-amino acids are amino acids with the carbon atom to which the amino group attaches is separated from the carboxylate moiety by two carbon atoms.

**[0465]** For additional modified and unusual amino acids, see §2422 of the MPEP, particularly Table 4 at 2400-24. Additionally, "Ac" indicates N-acetyl and "cyclo" refers to a cyclic structure, which is also shown as "c." "$NH_2$" indicates an amine group, typically added on the C-terminus of a polypeptide. Accordingly, as used herein, an —$NH_2$ moiety on the C-terminus of a peptide indicates an amide, i.e., —CO—$NH_2$.

**[0466]** Additional abbreviations are used as follows: Nle is norleucine; Nal(2') is 2′-naphthylalanine; Nal(1') is 1′-naphthylalanine; Tle is tert-leucine; Nva is norvaline; Orn is ornithine; Bip is biphenylalanine; Hyp is hydroxyproline; Mamb is 3-aminomethyl-benzoic acid; Pen is Penicillamine; Tic is 1,2,3,4-tetrahydroisoquinoline-3-carboxylic Acid; Aba is 4-amino-1,2,4,5-tetra-hydro-2-benzazepin-3-one; Oic is octohydroindole-2-carboxylic acid; Atc is 2-aminotetraline-2-carboxylic acid; APC is 1-amino-4-phenylcyclohexane-carboxylic acid; APPC is 4-aminophenylpiperidine-4-carboxylic acid; Acpc is 1-aminocyclo-propane-1-carboxylic acid; Aic is 2-aminoindone-2-carboxylic acid; Ata is 7-amino-7,8-dihydro-4H-[1,2,3]triazolo-[1,5-a][1,4]diazepin-6(5H)-one; Aia is 4-amino-1,4,5,6-tetrahydroazepino[4,3-*b*]indol-3(*2H*)-one; Che is 1-amino-1-cyclohexanecarboxylic acid Ioc is indoline-2-carboxylic acid, Aic is 2-aminoindone-2-carboxylic acid; Cpe is 1-amino-1-cyclopentane carboxylic; and p(Cl)dPhe is para-chloro-phenylalanine (I – iodo, F – fluoro, Br – bromo, $CF_3$ – trifluoromethyl).

**[0467]** The term "acyl" includes a group RCO—, where R is an organic group. An example is the acetyl group $CH_3CO$—, referred to herein as "Ac."

**[0468]** A peptide or aliphatic moiety is "acylated" when an alkyl or substituted alkyl group as defined above is bonded through one or more carbonyl {—(C═O)—} groups. A peptide is most usually acylated at the N-terminus.

**[0469]** An "amine" includes compounds that contain an amine group (—$NH_2$).

**[0470]** An "amide" includes compounds that have a trivalent nitrogen attached to a carbonyl group (i.e., —CO—$NH_2$), such as for example methylamide, ethylamide, propylamide, and the like. A peptide is most usually amidated at the C-terminus by the addition of an amine (—$NH_2$) moiety to the C-terminal carboxyl group.

**[0471]** Amino acids, including stereoisomers and modifications of naturally occurring amino acids, protein amino acids, non-protein amino acids, post-translationally modified amino acids, enzymatically synthesized amino acids, derivatized amino acids, constructs, or structures designed to mimic amino acids (peptide mimetics), and the like, including all of the foregoing, are sometimes referred to herein as "residues."

**[0472]** "Substantial degradation" refers to the degradation of the N-terminal extension, the C-terminal extension, both N- and C-terminal degradation or degradation to other regions of the non-naturally occurring melanocortin analog by physiological enzymes and other factors, in such a manner or to a degree that side effects appear. According to one aspect, a non-naturally occurring melanocortin analog having a C-terminal extension that resists substantial degradation is one where no more than 50% of the administered peptide causes side effects and/or displays a low half-life. In some aspects, no more than 25% of the administered peptide causes side effects and/or displays a low half-life. More preferably, in some aspects, less than 10% of the administered peptide causes side effects and/or displays a low half-life, as compared to a non-naturally occurring melanocortin analog that lacks a C-terminal extension.

**[0473]** The disclosure of all publications, patents, and published patent applications listed herein are hereby incorporated by reference in their entireties, including but not limited to U.S. Patent Nos. [redacted]41,545 and 9,534,018.

***Non-naturally Occurring Melanocortin Analogs***

**[0474]** The non-naturally occurring melanocortin analogs of the present technology may comprise a non-naturally occurring melanocortin analog or a pharmaceutically acceptable salt, solvate, or stereoisomer thereof. Non-naturally occurring melanocortin analogs of the present technology may be selective for the melanocortin 4 receptor (MC4R)

and/or melanocortin 3 receptor (MC3R) over other melanocortin receptors, i.e., the melanocortin 1 receptor (MC1R), the melanocortin 2 receptor (MC2R), and the melanocortin 5 receptor (MC5R). Some of the non-naturally occurring melanocortin analogs may bind only the MC3R or the MC4R. Alternatively, some of the non-naturally occurring melanocortin analogs may bind the MC3R with greater affinity than the MC4R, whereas other melanocortin analogs may bind the MC4R with greater affinity than the MC3R. Certain melanocortin analogs may bind the MC3R with the same or generally similar affinity as the MC4R.

**[0475]** The non-naturally occurring melanocortin analogs of the present technology may be full agonists or full antagonists for one or more melanocortin receptors. A full agonist may comprise a non-naturally occurring melanocortin analog having a maximum effect ($E_{max}$) agonist value of greater than or equal to 85%. Similarly, a full antagonist may comprise a non-naturally occurring melanocortin analog having an $E_{max}$ antagonist value of greater than or equal to 85%.

**[0476]** The non-naturally occurring melanocortin analogs of the present technology may be partial agonists or partial antagonists. A partial agonist may comprise a non-naturally occurring melanocortin analog having a maximum effect $E_{max}$ agonist value of less than 85%. Similarly, a partial antagonist may comprise a non-naturally occurring melanocortin analog having an $E_{max}$ antagonist value of less than 85%.

**[0477]** If a non-naturally occurring melanocortin analog's $E_{max}$ agonist value is greater than it's $E_{max}$ antagonist value, then the non-naturally occurring melanocortin analog may be classified as an agonist (e.g., a full agonist or a partial agonist).

**[0478]** If a non-naturally occurring melanocortin analog's $E_{max}$ antagonist value is greater than it's $E_{max}$ agonist value, then the non-naturally occurring melanocortin analog may be classified as an antagonist (e.g., a full antagonist or a partial antagonist).

**[0479]** The non-naturally occurring melanocortin analogs of the present technology may be one or more of (i) a full MC4R agonist and a full MC3R antagonist; (ii) a full MC4R agonist and a partial MC3R antagonist; and (iii) a full MC4R agonist having no MC3R activity.

**[0480]** The non-naturally occurring melanocortin analogs of the present technology may avoid cardiac activation typically seen in conventional melanocortin peptide and small molecule agonists. For example, a subject may maintain a stable heart rate, systolic blood pressure, and/or diastolic blood pressure following administration of a melanocortin analog of the present technology.

**[0481]** The non-naturally occurring melanocortin analogs in accordance with the present technology may have certain structural features that impart specific properties on the analogs, such as, for example, degradation resistance, enhanced epithelial, gastrointestinal, and/or blood brain barrier transport, and binding affinity for the melanocortin 4 receptor and/or melanocortin 3 receptor. Accordingly, in some embodiments, the non-naturally occurring melanocortin analogs have one or more beta hairpin (β-hairpin) and/or beta turn (β-turn) structures. The presence of amino acids that are structurally rigid, such as, for example, Aia, Aba, Ata, Hyp, dHyp, Pro, dPro, *trans*Pro(guan), and *cis*Pro(guan), may lead to formation of β-hairpin and/or β-turn structures in the non-naturally occurring melanocortin analog. Additionally, dMet and disulfide bridges (e.g., cyclization via disulfide bond), as well as Pro-Gly and Gly-Gly linkers may induce and/or stabilize beta-turn structures of the non-naturally occurring melanocortin analogs. In general, cyclization may stabilize beta-turns, and D-amino acids may induce and/or stabilize beta-turns. Further, in some embodiments, melanocortin analogs include D-valine-D-proline (dVal-dPrp) chain as their C-terminus, which may provide enhanced transport and resistance to degradation.

**[0482]** In some embodiments, the non-naturally occurring melanocortin analog comprises a sequence of Formula (I),

$$X^1\text{-}X^2\text{-}X^3\text{-}R^1\text{-}R^2\text{-}R^3\text{-}R^4\text{-}R^5\text{-}R^6\text{-}R^7\text{-}R^8\text{-}Y^1\text{-}Y^2\text{-}Y^3\text{-}Y^4\text{-}Y^5\text{-}Y^6\text{-}Y^7 \quad (I),$$

wherein:

$X^1$ is absent or is selected from the group consisting of norleucine (Nle), arginine (Arg), D-arginine (dArg), alanine (Ala), lysine (Lys), D-lysine (dLys), histidine (His), and D-histidine (dHis);

$X^2$ is absent, phenylalanine (Phe), or Nle;

$X^3$ is absent, Phe, or Nle;

$R^1$ is selected from the group consisting of Nle, D-norleucine (dNle), Ala, D-alanine (dAla), Arg, dArg, Lys, dLys, His, dHis, ornithine (Orn), D-ornithine (dOrn), D-leucine (dLeu), D-tyrosine (dTyr), phenylalanine (Phe), D-phenylalanine (dPhe), tryptophan (Trp), D-tryptophan (dTrp), aspartic acid (Asp), cysteine (Cys), and D-cysteine (dCys);

$R^2$ is selected from the group consisting of Asp, proline (Pro), D-aspartic acid (dAsp), Cys, dCys, D-penicillamine (dPen), Ala, dAla, Trp, Phe, dPhe, His, dHis, Tyr, and dTyr;

$R^3$ is absent or is selected from the group consisting of His, Ala, Pro, hydroxyproline (Hyp), leucine (Leu), D-glutamine (dGln), Phe, dPhe, Trp, dTrp, Tyr, dTyr, 4-amino-1,2,4,5-tetrahydro-2-benzazepin-3-one (Aba), 7-amino-7,8-dihydro-4H-[1,2,3]triazolo-[1,5-a][1,4]diazepin-6(5H)-one (Ata), 4-amino-1,4,5,6-tetrahydroazepino[4,3-*b*]indol-3(*2H*)-one (Aia), 2-aminotetraline-2-carboxylic acid (Atc), 1-amino-4-phenylcyclohexane-carboxylic acid (APC), 4-aminophenylpiperidine-4-carboxylic acid (APPC), octohydroindole-2-carboxylic acid (Oic), 1-amino-1-cyclohexanecarboxylic acid (Che), tetrahydro-isoquinoline-3-carboxylic acid (Tic), indoline-2-carboxylic acid (Ioc), 1-amino-1-cyclopentane carboxylic (Cpe), and biphenylalanine (Bip);

$R^4$ is selected from the group consisting of Phe, dPhe, 2'-D-naphthylalanine (dNal(2')), para-chloro-D-phenylalanine (p(Cl)dPhe), para-bromo-D-phenylalanine (p(Br)dPhe), and para-fluoro-D-phenylalanine (p(F)dPhe);

$R^5$ is selected from the group consisting of Arg, His, *cis*Pro(guan), and *trans*Pro(guan);

$R^6$ is selected from the group consisting of Trp, dTrp, Phe, Aia, Aba, Ata, dNal(2'), 2'-naphthylalanine (Nal(2')), and 1'-naphthylalanine (Nal(1'));

$R^7$ is selected from the group consisting of Gly, Pro, Lys, dLys, Cys, dCys, penicillamine (Pen), dPen, and Orn;

$R^8$ is absent or Lys;

$Y^1$ is absent or is selected from the group consisting of valine (Val), D-valine (dVal), $\beta^2$-valine ($\beta^2$-Val), $\beta^3$-valine ($\beta^3$-Val), Pro, D-proline (dPro), β-proline (β-Pro), Hyp, D-

hydroxyproline (dHyp), D-tert-leucine (dTle), dLeu, Trp, Arg, dArg, Lys, dLys, Gly, Ala, dAla, Asp, dAsp, asparagine (Asn), D-asparagine (dAsn), and D-threonine (dThr);

$Y^2$ is absent or is selected from the group consisting of Val, dVal, $\beta^2$-Val, $\beta^3$-Val, Pro, dPro, β-Pro, Hyp, dHyp, dTle, Arg, dArg, Gly, Ala, dAla, Asp, and dAsn;

$Y^3$ is absent or is selected from the group consisting of Val, dVal, Pro, dPro, dThr, Lys, and dLys;

$Y^4$ is absent or is selected from the group consisting of dVal, dPro, Asp, and dAsp;

$Y^5$ is absent or dVal;

$Y^6$ is absent or dVal;

$Y^7$ is absent or dPro; and

the non-naturally occurring melanocortin analog is cyclized through a moiety selected from the group consisting of:

a disulfide bond between $R^1$ or $R^2$ and $R^7$ when each of $R^1$ or $R^2$ and $R^7$ are independently selected from the group consisting of Cys, dCys, and dPen;

a disulfide bond between $R^2$ and $R^7$ when $R^2$ is Cys, $R^7$ is Pen, and $R^3$ is absent;

a lactam bridge between $R^1$ or $R^2$ and $R^7$ or $R^8$ when $R^1$ or $R^2$ is Asp and $R^7$ or $R^8$ is Lys or Orn; and

a lactam bridge between $R^2$ and $R^7$ when $R^2$ is dAsp and $R^7$ is dLys;

provided that:

when $R^4$ is dNal(2'), then $R^3$ is His and $R^7$ is Pro;

when $R^4$ is p(F)dPhe, then (i) $R^3$ is selected from Pro, dGln, dTyr, $R^6$ is Trp, and the non-naturally occurring melanocortin analog is not cyclized between Cys at $R^2$ and Cys at $R^7$ or (ii) $R^3$ is His and either $R^6$ is Nal(2') or the non-naturally occurring melanocortin analog is cyclized through a disulfide bond between $R^2$ and $R^7$;

when $R^4$ is p(Br)dPhe, then the non-naturally occurring melanocortin analog is cyclized through a disulfide bond between dCys at $R^2$ and Cys or dCys at $R^7$;

when $R^4$ is dPhe, then (i) $R^3$ is not His, Pro, or absent, (ii) $R^3$ is His and either $R^2$ is Phe or dAla or $R^2$ is Ala and $X^1$ is Arg or dArg, (iii) $R^3$ is Pro and (a) $R^2$ is Trp, and $R^5$ is not His or $R^6$ is not Phe or (b) $R^2$ is not Trp or Pro, and either $R^5$ is not dNal(2') or Nal(2') or $X^1$ and $Y^3$ are not both present, or (iv) $R^3$ is absent and $R^2$ and $R^7$ are not both dPen;

when $R^4$ is p(Cl)dPhe, then (i) $R^3$ is selected from Aba, Aia, and Ata or (ii) $R^3$ is His, $R^1$ is not Ala, and (a) if $R^1$ is Nle and $Y^1Y^2$ is dVal-dPro, then $X^1$ is absent and the non-naturally occurring melanocortin analog is cyclized through a disulfide bond between dCys at $R^2$ and dCys at $R^7$, or (b) if $R^1$ is Nle, and $Y^1Y^2$ is not dVal-dPro, then either $X^1$ or $Y^3$ is present; and

when $R^2$ is dAla, then $R^4$ is dPhe and $Y^1$-$Y^7$ are absent.

**[0483]** In some embodiments, the non-naturally occurring melanocortin analog comprises a sequence of Formula (I), wherein:
$X^1$ is absent or is selected from the group consisting of norleucine (Nle), arginine (Arg), D-arginine (dArg), alanine (Ala), lysine (Lys), D-lysine (dLys), histidine (His), and D-histidine (dHis);

$X^2$ is absent, phenylalanine (Phe), or Nle;

$X^3$ is absent, Phe, or Nle;

$R^1$ is selected from the group consisting of Nle, D-norleucine (dNle), Ala, D-alanine (dAla), Arg, dArg, Lys, dLys, His, dHis, ornithine (Orn), D-ornithine (dOrn), D-leucine (dLeu), D-tyrosine (dTyr), phenylalanine (Phe), D-phenylalanine (dPhe), tryptophan (Trp), D-tryptophan (dTrp), aspartic acid (Asp), cysteine (Cys), and D-cysteine (dCys);

$R^2$ is selected from the group consisting of Asp, proline (Pro), D-aspartic acid (dAsp), Cys, dCys, D-penicillamine (dPen), Ala, dAla, Trp, Phe, dPhe, His, dHis, Tyr, and dTyr;

$R^3$ is absent or is selected from the group consisting of His, Ala, Pro, hydroxyproline (Hyp), leucine (Leu), D-glutamine (dGln), Phe, dPhe, Trp, dTrp, Tyr, dTyr, 4-amino-1,2,4,5-tetrahydro-2-benzazepin-3-one (Aba), 7-amino-7,8-dihydro-4H-[1,2,3]triazolo-[1,5-

a][1,4]diazepin-6(5H)-one (Ata), 4-amino-1,4,5,6-tetrahydroazepino[4,3-*b*]indol-3(*2H*)-one (Aia), 2-aminotetraline-2-carboxylic acid (Atc), 1-amino-4-phenylcyclohexane-carboxylic acid (APC), 4-aminophenylpiperidine-4-carboxylic acid (APPC), octohydroindole-2-carboxylic acid (Oic), 1-amino-1-cyclohexanecarboxylic acid (Che), tetrahydro-isoquinoline-3-carboxylic acid (Tic), indoline-2-carboxylic acid (Ioc), 1-amino-1-cyclopentane carboxylic (Cpe), and biphenylalanine (Bip);

$R^4$ is selected from the group consisting of Phe, dPhe, 2'-D-naphthylalanine (dNal(2')), para-chloro-D-phenylalanine (p(Cl)dPhe), para-bromo-D-phenylalanine (p(Br)dPhe), and para-fluoro-D-phenylalanine (p(F)dPhe);

$R^5$ is selected from the group consisting of Arg, His, *cis*Pro(guan), and *trans*Pro(guan);

$R^6$ is selected from the group consisting of Trp, dTrp, Phe, Aia, Aba, Ata, dNal(2'), 2'-naphthylalanine (Nal(2')), and 1'-naphthylalanine (Nal(1'));

$R^7$ is selected from the group consisting of Gly, Pro, Lys, dLys, Cys, dCys, penicillamine (Pen), dPen, and Orn;

$R^8$ is absent or Lys;

$Y^1$ is absent or is selected from the group consisting of valine (Val), D-valine (dVal), $\beta^2$-valine ($\beta^2$-Val), $\beta^3$-valine ($\beta^3$-Val), Pro, D-proline (dPro), β-proline (β-Pro), Hyp, D-hydroxyproline (dHyp), D-tert-leucine (dTle), dLeu, Trp, Arg, dArg, Lys, dLys, Gly, Ala, dAla, Asp, dAsp, asparagine (Asn), D-asparagine (dAsn), and D-threonine (dThr);

$Y^2$ is absent or is selected from the group consisting of Val, dVal, $\beta^2$-Val, $\beta^3$-Val, Pro, dPro, β-Pro, Hyp, dHyp, dTle, Arg, dArg, Gly, Ala, dAla, Asp, and dAsn;

$Y^3$ is absent or is selected from the group consisting of Val, dVal, Pro, dPro, dThr, Lys, and dLys;

$Y^4$ is absent or is selected from the group consisting of dVal, dPro, Asp, and dAsp;

$Y^5$ is absent or dVal;

$Y^6$ is absent or dVal;

$Y^7$ is absent or dPro; and

the non-naturally occurring melanocortin analog is cyclized through a moiety selected from the group consisting of:

a disulfide bond between $R^1$ or $R^2$ and $R^7$ or $R^8$ when each of $R^1$ or $R^2$ and $R^7$ or $R^8$ are independently selected from the group consisting of Cys, dCys, and dPen;

a disulfide bond between $R^2$ and $R^7$ when $R^2$ is Cys, $R^7$ is Pen, and $R^3$ is absent;

a lactam bridge between $R^1$ or $R^2$ and $R^7$ or $R^8$ when $R^1$ or $R^2$ is Asp and $R^7$ or $R^8$ is Lys or Orn; and

a lactam bridge between $R^2$ and $R^7$ when $R^2$ is dAsp and $R^7$ is dLys;

provided that the non-naturally occurring melanocortin analog does not comprise a sequence selected from the group consisting of:

Ac-Nle-c[Asp-Pro-Pro-dNal(2')-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 194);

Ac-Nle-c[Asp-Pro-His-dNal(2')-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 5);

Ac-Nle-c[Asp-Pro-His-dNal(2')-Arg-Trp-Lys]-dPro-dVal-$NH_2$ (SEQ ID NO: 10);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dVal-dPro (SEQ ID NO: 2);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 3);

Ac-Nle-c[Asp-Hyp-dNal(2')-Arg-Trp-Pro-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 4);

Ac-Nle-c[Asp-Phe-His-dNal(2')-Arg-Trp-Lys]-dLeu-dPro-$NH_2$ (SEQ ID NO: 6);

Ac-Nle-c[Asp-Phe-His-dNal(2')-Arg-Trp-Lys]-dTle-dPro-$NH_2$ (SEQ ID NO: 7);

Ac-Nle-c[Asp-Hyp-dNal(2')-Arg-Trp-Pro-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 9);

Ac-Nle-Phe-Phe-c[Asp-Phe-His-dNal(2')-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 12);

Ac-dArg-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 15);

Ac-dLeu-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 18);

Ac-dAla-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 20);

Ac-Ala-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 21);

Ac-dNle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 24);

Ac-dCys-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 28);

Ac-dPhe-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 29);

Ac-dTyr-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 30);

dTyr-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 35);

Tyr-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 36);

Ac-Nle-c[Cys-Pro-dNal(2')-Arg-Trp-Cys]-dVal-dPro-$NH_2$ (SEQ ID NO: 40);

Ac-Nle-c[dCys-Pro-dNal(2')-Arg-Trp-Cys]-dVal-dPro-$NH_2$ (SEQ ID NO: 41);

Ac-Nle-c[Cys-Pro-dNal(2')-Arg-Trp-dCys]-dVal-dPro-$NH_2$ (SEQ ID NO: 42);

Ac-Nle-c[dCys-Pro-dNal(2')-Arg-Trp-dCys]-dVal-dPro-$NH_2$ (SEQ ID NO: 43);

Ac-Nle-c[Cys-Pro-dNal(2')-Arg-Trp-Pen]-dVal-dPro-$NH_2$ (SEQ ID NO: 48);

Ac-Nle-c[dPen-Pro-dNal(2')-Arg-Trp-dPen]-dVal-dPro-$NH_2$ (SEQ ID NO: 54);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Orn]-dVal-dPro-$NH_2$ (SEQ ID NO: 64);

Ac-Nle-c[Asp-dNal(2')-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 68);

Ac-Nle-c[Asp-Ala-dNal(2')-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 69);

Ac-Nle-c[Asp-Leu-dNal(2')-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 76);

Ac-Nle-c[Asp-Trp-dNal(2')-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 82);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-Val-Pro-$NH_2$ (SEQ ID NO: 115);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dVal-dPro-OH (SEQ ID NO: 116);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dPro-dVal-OH (SEQ ID NO: 117);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dVal-Hyp-$NH_2$ (SEQ ID NO: 118);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dVal-dHyp-$NH_2$ (SEQ ID NO: 119);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-Val-Hyp-$NH_2$ (SEQ ID NO: 120);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-Val-dHyp-$NH_2$ (SEQ ID NO: 121);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-Hyp-dVal-$NH_2$ (SEQ ID NO: 122);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dHyp-dVal-$NH_2$ (SEQ ID NO: 123);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-Hyp-Val-$NH_2$ (SEQ ID NO: 124);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dHyp-Val-$NH_2$ (SEQ ID NO: 125);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dVal-dVal-$NH_2$ (SEQ ID NO: 126);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dPro-dPro-$NH_2$ (SEQ ID NO: 127);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dVal-$NH_2$ (SEQ ID NO: 128);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dPro-$NH_2$ (SEQ ID NO: 129);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-Val-$NH_2$ (SEQ ID NO: 130);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-Pro-$NH_2$ (SEQ ID NO: 131);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-Ala-$NH_2$ (SEQ ID NO: 132);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dAla-$NH_2$ (SEQ ID NO: 133);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dHyp-$NH_2$ (SEQ ID NO: 134);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-Hyp-$NH_2$ (SEQ ID NO: 135);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dAla-dAla-$NH_2$ (SEQ ID NO: 136);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-Ala-Ala-$NH_2$ (SEQ ID NO: 137);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-Gly-Gly-$NH_2$ (SEQ ID NO: 138);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dVal-Asp-$NH_2$ (SEQ ID NO: 139);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dVal-Arg-$NH_2$ (SEQ ID NO: 140);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dVal-dArg-$NH_2$ (SEQ ID NO: 143);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dVal-dAsn-$NH_2$ (SEQ ID NO: 144);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-Asp-dPro-$NH_2$ (SEQ ID NO: 145);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-Arg-dPro-$NH_2$ (SEQ ID NO: 146);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-Asn-dPro-$NH_2$ (SEQ ID NO: 147);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dAsp-dPro-$NH_2$ (SEQ ID NO: 148);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dArg-dPro-$NH_2$ (SEQ ID NO: 149);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dAsn-dPro-$NH_2$ (SEQ ID NO: 150);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-Asp-$NH_2$ (SEQ ID NO: 151);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-Arg-$NH_2$ (SEQ ID NO: 152);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-Asn-$NH_2$ (SEQ ID NO: 153);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dAsp-$NH_2$ (SEQ ID NO: 154);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dArg-$NH_2$ (SEQ ID NO: 155);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dAsn-$NH_2$ (SEQ ID NO: 156);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-Lys-Pro-Val-$NH_2$ (SEQ ID NO: 157);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-Lys-dPro-dVal-$NH_2$ (SEQ ID NO: 158);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dLys-dPro-dVal-$NH_2$ (SEQ ID NO: 159);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-Lys-dPro-$NH_2$ (SEQ ID NO: 160);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dLys-dPro-$NH_2$ (SEQ ID NO: 161);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-Lys-Val-Pro-$NH_2$ (SEQ ID NO: 162);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-Lys-dVal-dPro-$NH_2$ (SEQ ID NO: 164);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dLys-dVal-dPro-$NH_2$ (SEQ ID NO: 164);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-Arg-Pro-Val-$NH_2$ (SEQ ID NO: 165);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-Arg-dPro-dVal-$NH_2$ (SEQ ID NO: 166);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dArg-dPro-dVal-$NH_2$ (SEQ ID NO: 167);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-Arg-Val-Pro-$NH_2$ (SEQ ID NO: 168);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-Arg-dVal-dPro-$NH_2$ (SEQ ID NO: 169);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dArg-dVal-dPro-$NH_2$ (SEQ ID NO: 170);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dTle-dVal-dPro-$NH_2$ (SEQ ID NO: 171);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dTle-dPro-$NH_2$ (SEQ ID NO: 172);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dTle-dVal-$NH_2$ (SEQ ID NO: 173);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dTle-dTle-$NH_2$ (SEQ ID NO: 174);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dTle-dTle-dPro-$NH_2$ (SEQ ID NO: 175);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dTle-dTle-dVal-$NH_2$ (SEQ ID NO: 176);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dPro-dTle-$NH_2$ (SEQ ID NO: 177);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dVal-dTle-$NH_2$ (SEQ ID NO: 178);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dVal-dVal-dPro-$NH_2$ (SEQ ID NO: 179);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dPro-dVal-dPro-$NH_2$ (SEQ ID NO: 180);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dVal-dVal-dVal-dPro-$NH_2$ (SEQ ID NO: 181);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dVal-dPro-dVal-dPro-$NH_2$ (SEQ ID NO: 182);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dVal-dVal-dVal-dVal-dVal-dVal-dPro-$NH_2$ (SEQ ID NO: 183);

Ac-Nle-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 184);

Ac-Nle-Nle-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 185);

Ac-Nle-Nle-Nle-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 186);

Ac-Nle-c[Asp-Trp-Pro-dNal(2')-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 195);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-dTrp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 196);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-Trp-$NH_2$ (SEQ ID NO: 203);

Ac-Nle-c[Asp-Aba-dNal(2')-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 204);

Ac-Nle-c[Asp-Aia-dNal(2')-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 205);

Ac-Nle-c[Asp-Ata-dNal(2')-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 206);

Ac-Nle-c[Asp-Cpe-dNal(2')-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 240);

Ac-Nle-c[Asp-Che-dNal(2')-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 241);

Ac-Nle-c[Asp-Oic-dNal(2')-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 242);

Ac-Nle-c[Asp-Tic-dNal(2')-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 244);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Pro-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 245);

Ac-Nle-c[Asp-His-dNal(2')-transPro(guan)-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 247);

Ac-Nle-c[Asp-His-dNal(2')-cisPro(guan)-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 248);

Ac-Nle-c[Asp-Pro-dNal(2')-transPro(guan)-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 250);

Ac-Nle-c[Asp-Pro-dNal(2')-cisPro(guan)Pro-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 251);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Aba-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 253);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Ata-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 254);

Ac-Nle-c[Asp-Glu-dNal(2')-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 255);

Ac-Nle-c[Asp-Glu-dNal(2')-Arg-Trp-Gly-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 256);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Gly-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 259);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Gly-Lys]-dPro-dPro-Lys-Asp-$NH_2$ (SEQ ID NO: 260);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Gly-Lys]-dPro-dPro-dLys-dAsp-$NH_2$ (SEQ ID NO: 261);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dPro-dPro-dLys-dAsp-$NH_2$ (SEQ ID NO: 263);

Ac-Nle-c[Asp-Ala-His-dNal(2')-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 273);

Ac-Arg-c[Asp-Ala-His-dNal(2')-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 274);

Ac-dArg-c[Asp-Ala-His-dNal(2')-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 275);

Ac-dLeu-c[dPen-Pro-dNal(2')-Arg-Trp-dPen]-dVal-dPro-$NH_2$ (SEQ ID NO: 327);

Ac-dNle-c[dPen-Pro-dNal(2')-Arg-Trp-dPen]-dVal-dPro-$NH_2$ (SEQ ID NO: 328);

Ac-dArg-c[dPen-Pro-dNal(2')-Arg-Trp-dPen]-dVal-dPro-$NH_2$ (SEQ ID NO: 329);

Ac-Arg-c[dPen-Pro-dNal(2')-Arg-Trp-dPen]-dVal-dPro-$NH_2$ (SEQ ID NO: 330);

Ac-dPhe-c[dPen-Pro-dNal(2')-Arg-Trp-dPen]-dVal-dPro-$NH_2$ (SEQ ID NO: 331);

Ac-dTyr-c[dPen-Pro-dNal(2')-Arg-Trp-dPen]-dVal-dPro-$NH_2$ (SEQ ID NO: 332);

Ac-Ala-c[dPen-Pro-dNal(2')-Arg-Trp-dPen]-dVal-dPro-$NH_2$ (SEQ ID NO: 333);

Ac-dHis-c[dPen-Pro-dNal(2')-Arg-Trp-dPen]-dVal-dPro-$NH_2$ (SEQ ID NO: 334);

Ac-His-c[dPen-Pro-dNal(2')-Arg-Trp-dPen]-dVal-dPro-$NH_2$ (SEQ ID NO: 335);

Ac-dLys-c[dPen-Pro-dNal(2')-Arg-Trp-dPen]-dVal-dPro-$NH_2$ (SEQ ID NO: 336);

Ac-Lys-c[dPen-Pro-dNal(2')-Arg-Trp-dPen]-dVal-dPro-$NH_2$ (SEQ ID NO: 337);

Ac-Nle-c[dPen-Pro-dNal(2')-Arg-Trp-dPen]-dArg-dVal-dPro-$NH_2$ (SEQ ID NO: 344);

Ac-Nle-c[dPen-Pro-dNal(2')-Arg-Trp-dPen]-dLys-dVal-dPro-$NH_2$ (SEQ ID NO: 345);

Ac-Nle-c[dPen-Pro-dNal(2')-Arg-Trp-dPen]-dArg-dPro-$NH_2$ (SEQ ID NO: 346);

Ac-Nle-c[dPen-Pro-dNal(2')-Arg-Trp-dPen]-dLys-dPro-$NH_2$ (SEQ ID NO: 347);

Ac-Nle-c[dPen-Pro-dNal(2')-Arg-Trp-dPen]-dVal-dHyp-$NH_2$ (SEQ ID NO: 348);

Ac-Nle-c[dPen-Pro-dNal(2')-Arg-Trp-dPen]-dTle-dPro-$NH_2$ (SEQ ID NO: 349);

Ac-Nle-c[dPen-Pro-dNal(2')-Arg-Trp-Gly-dPen]-dVal-dPro-$NH_2$ (SEQ ID NO: 350);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Aia-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 103);

Ac-Nle-c[Asp-Ioc-dNal(2')-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 243);

Ac-Nle-c[Cys-dNal(2')-Arg-Trp-Cys]-dVal-dPro-$NH_2$ (SEQ ID NO: 44);

Ac-Nle-c[dCys-dNal(2')-Arg-Trp-Cys]-dVal-dPro-$NH_2$ (SEQ ID NO: 45);

Ac-Nle-c[Cys-dNal(2')-Arg-Trp-dCys]-dVal-dPro-$NH_2$ (SEQ ID NO: 46);

Ac-Nle-c[dCys-dNal(2')-Arg-Trp-dCys]-dVal-dPro-$NH_2$ (SEQ ID NO: 47);

Ac-Nle-c[Cys-dNal(2')-Arg-Trp-Pen]-dVal-dPro-$NH_2$ (SEQ ID NO: 56);

Ac-Nle-c[dPen-dNal(2')-Arg-Trp-dPen]-dVal-dPro-$NH_2$ (SEQ ID NO: 62);

Ac-Nle-c[Asp-dTrp-dNal(2')-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 83);

Ac-Nle-c[dPen-Ala-dNal(2')-Arg-Trp-dPen]-dVal-dPro-$NH_2$ (SEQ ID NO: 338);

Ac-Nle-c[dPen-Leu-dNal(2')-Arg-Trp-dPen]-dVal-dPro-$NH_2$ (SEQ ID NO: 339);

Ac-Nle-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 223);

Ac-Arg-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 464);

Ac-Lys-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 465);

Ac-dLys-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 466);

Ac-His-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 467);

Ac-dHis-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 468);

Ac-Nle-Nle-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 469); Ac-Nle-c[Asp-His-p(F)dPhe-His-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 470);

Ac-Nle-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dVal-dVal-dVal-dPro-$NH_2$ (SEQ ID NO: 474);

Ac-Nle-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dPro-dVal-dPro-$NH_2$ (SEQ ID NO: 475);

Ac-Nle-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dTle-dPro-$NH_2$ (SEQ ID NO: 476);

Ac-Nle-Nle-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dTle-dPro-$NH_2$ (SEQ ID NO: 477);

Ac-Nle-Nle-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dPro-dVal-dPro-$NH_2$ (SEQ ID NO: 478);

Ac-Arg-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dTle-dPro-$NH_2$ (SEQ ID NO: 481);

Ac-Lys-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dTle-dPro-$NH_2$ (SEQ ID NO: 482);

Ac-dLys-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dTle-dPro-$NH_2$ (SEQ ID NO: 483);

Ac-His-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dTle-dPro-$NH_2$ (SEQ ID NO: 484);

Ac-dHis-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dTle-dPro-$NH_2$ (SEQ ID NO: 485);

Ac-dArg-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 463);

Ac-Ala-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 462);

Ac-Ala-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dTle-dPro-$NH_2$ (SEQ ID NO: 479);

Ac-Nle-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dTle-dTle-dVal-$NH_2$ (SEQ ID NO: 473);

Ac-dArg-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dTle-dPro-$NH_2$ (SEQ ID NO: 480);

Ac-Nle-c[Asp-Gln-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 491);

Ac-Nle-c[Asp-Bip-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 489);

Ac-Nle-c[Asp-Trp-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 493);

Ac-Nle-c[Asp-Pro-p(F)dPhe-Arg-dNal(2')-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 444);

Ac-Nle-c[Asp-Pro-p(F)dPhe-Arg-Nal(2')-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 445);

Ac-Nle-c[Asp-Tyr-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 495);

Ac-Nle-c[Asp-Phe-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 487);

Ac-Nle-c[Asp-dPhe-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 488);

Ac-Nle-c[Asp-dTrp-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 494);

Ac-Nle-c[Asp-His-p(F)dPhe-Arg-dNal(2')-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 471);

Ac-Nle-c[Cys-Pro-p(F)dPhe-Arg-Trp-Cys]-dVal-dPro-$NH_2$ (SEQ ID NO: 432);

Ac-Nle-c[Asp-Pro-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 217);

Ac-Nle-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 222);

Ac-Nle-c[Cys-His-p(Br)dPhe-Arg-Trp-Cys]-dVal-dPro-$NH_2$ (SEQ ID NO: 535);

Ac-Ala-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 538);

Ac-Nle-Nle-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 545);

Ac-Nle-c[Asp-His-p(Br)dPhe-His-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 546);

Ac-Nle-c[Asp-His-p(Br)dPhe-Arg-dNal(2')-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 547);

Ac-Nle-c[Asp-His-p(Br)dPhe-Arg-Nal(2')-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 548);

Ac-Nle-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dTle-dTle-dVal-$NH_2$ (SEQ ID NO: 549);

Ac-Nle-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dPro-dVal-dPro-$NH_2$ (SEQ ID NO: 551);

Ac-Nle-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dTle-dPro-$NH_2$ (SEQ ID NO: 552);

Ac-Nle-Nle-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dTle-dPro-$NH_2$ (SEQ ID NO: 553);

Ac-Ala-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dTle-dPro-$NH_2$ (SEQ ID NO: 555);

Ac-Nle-c[Asp-dHis-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 562);

Ac-Nle-c[Asp-Phe-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 563);

Ac-Nle-c[Asp-dPhe-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 564);

Ac-Nle-c[Asp-Bip-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 565);

Ac-Nle-c[Asp-dGln-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 568);

Ac-Nle-c[Asp-Trp-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 569);

Ac-Nle-c[Asp-dTrp-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 570);

Ac-Nle-c[Asp-Tyr-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 571);

Ac-Nle-c[Asp-dTyr-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 572);

Ac-dArg-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 539);

Ac-dHis-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 544);

Ac-dHis-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dTle-dPro-$NH_2$ (SEQ ID NO: 561);

Ac-dArg-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dTle-dPro-$NH_2$ (SEQ ID NO: 556);

Ac-dLys-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 542);

Ac-His-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dTle-dPro-$NH_2$ (SEQ ID NO: 560);

Ac-His-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 543);

Ac-dLys-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dTle-dPro-$NH_2$ (SEQ ID NO: 559);

Ac-Arg-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dTle-dPro-$NH_2$ (SEQ ID NO: 557);

Ac-Lys-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 541);

Ac-Nle-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dVal-dVal-dVal-dPro-$NH_2$ (SEQ ID NO: 550);

Ac-Lys-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dTle-dPro-$NH_2$ (SEQ ID NO: 558);

Ac-Arg-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 540);

Ac-Nle-Nle-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dPro-dVal-dPro-$NH_2$ (SEQ ID NO: 554);

Ac-Nle-c[Asp-His-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 363);

Ac-Nle-c[Asp-His-dPhe-Arg-Trp-Pro-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 418);

Ac-Nle-c[Asp-His-dPhe-Arg-Trp-Lys]-dPro-dVal-$NH_2$ (SEQ ID NO: 621);

Ac-Nle-c[Asp-His-dPhe-transPro(guan)-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 228);

Ac-Nle-c[Asp-His-dPhe-cisPro(guan)-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 229);

Ac-Nle-c[Asp-Ala-His-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 380);

Ac-Nle-c[Asp-Trp-Pro-dPhe-His-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 398);

Ac-Nle-c[Asp-Trp-Pro-dPhe-Arg-Phe-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 401);

Ac-Nle-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dPro-dVal-dPro-$NH_2$ (SEQ ID NO: 639);

Ac-Nle-c[Asp-Pro-dPhe-Arg-dNal(2')-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 430);

Ac-Nle-c[Asp-Pro-dPhe-Arg-Nal(2')-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 431);

Ac-Nle-c[Asp-Pro-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 225);

Ac-Nle-c[dPen-dPhe-Arg-Trp-dPen]-dVal-dPro-$NH_2$ (SEQ ID NO: 326);

Ac-Nle-c[Asp-Pro-His-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 297);

Ac-Nle-c[Asp-Pro-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 215);

Ac-Nle-c[Asp-Phe-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 525);

Ac-Nle-c[Asp-dPhe-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 526);

Ac-Nle-c[Asp-Bip-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 527);

Ac-Nle-c[Asp-Trp-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 531);

Ac-Nle-c[Asp-Tyr-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 533);

Ac-Nle-c[Asp-dTyr-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 534);

Ac-Nle-c[Asp-dTrp-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 532);

Ac-Nle-c[dCys-His-p(Cl)dPhe-Arg-Trp-Cys]-dVal-dPro-$NH_2$ (SEQ ID NO: 498);

Ac-Nle-c[Cys-His-p(Cl)dPhe-Arg-Trp-Cys]-dVal-dPro-$NH_2$ (SEQ ID NO: 497);

Ac-Nle-c[Asp-His-p(Cl)dPhe-Arg-dNal(2')-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 509);

Ac-Nle-c[Asp-His-p(Cl)dPhe-Arg-Nal(2')-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 510);

Ac-Nle-c[Asp-His-p(Cl)dPhe-His-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 508);

Ac-Nle-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 220);

Ac-Nle-Nle-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 507);

Ac-Ala-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dTle-dPro-$NH_2$ (SEQ ID NO: 517);

Ac-Ala-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 500);

Ac-Nle-Nle-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dPro-dVal-dPro-$NH_2$ (SEQ ID NO: 516);

Ac-Nle-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dTle-dPro-$NH_2$ (SEQ ID NO: 514);

Ac-Nle-c[Asp-dGln-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 530);

Ac-Arg-c[Asp-dAla-His-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 268);

Ac-Nle-c[Asp-dAla-His-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 378);

Ac-dArg-c[Asp-dAla-His-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 379);

Ac-Nle-c[Asp-dAla-His-dNal(2')-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 266);

Ac-Arg-c[Asp-dAla-His-dNal(2')-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 267);

Ac-Arg-c[Cys-dAla-His-dNal(2')-Arg-Trp-Cys]-dVal-dPro-$NH_2$ (SEQ ID NO: 269);

Ac-dArg-c[Asp-dAla-His-dNal(2')-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 270);

Ac-Arg-c[Cys-dAla-His-dNal(2')-Arg-Trp-Cys]-$NH_2$ (SEQ ID NO: 282); and

Ac-Arg-c[Asp-dAla-His-dNal(2')-Arg-Trp-Lys]-$NH_2$ (SEQ ID NO: 283).

**[0484]** In some embodiments, $R^4$ is not dNal(2'). In further embodiments, $Y^1$ is present and $Y^5$-$Y^7$ are absent. In some embodiments, the non-naturally occurring melanocortin analog comprises a sequence of Formula (IA):

$$X^1\text{-}X^2\text{-}X^3\text{-}R^1\text{-}R^2\text{-}R^3\text{-}R^4\text{-}R^5\text{-}R^6\text{-}R^7\text{-}R^8\text{-}Y^1\text{-}Y^2\text{-}Y^3\text{-}Y^4 \text{ (IA)},$$

wherein:

$X^1$ is absent or is selected from the group consisting of norleucine (Nle), arginine (Arg), D-arginine (dArg), alanine (Ala), lysine (Lys), D-lysine (dLys), histidine (His), D-histidine (dHis);

$X^2$ is absent, phenylalanine (Phe), or Nle;

$X^3$ is absent, Phe, or Nle;

$R^1$ is selected from the group consisting of Nle, D-norleucine (dNle), Ala, D-alanine (dAla), Arg, dArg, Lys, dLys, His, dHis, ornithine (Orn), D-ornithine (dOrn), D-leucine (dLeu), D-tyrosine (dTyr), phenylalanine (Phe), D-phenylalanine (dPhe), tryptophan (Trp), D-tryptophan (dTrp), aspartic acid (Asp), cysteine (Cys), and D-cysteine (dCys);

$R^2$ is selected from the group consisting of Asp, D-aspartic acid (dAsp), Cys, dCys, D-penicillamine (dPen), Ala, Trp, Phe, dPhe, His, dHis, Tyr, and dTyr;

$R^3$ is absent or is selected from the group consisting of His, Ala, proline (Pro), hydroxyproline (Hyp), leucine (Leu), D-glutamine (dGln), Phe, dPhe, Trp, dTrp, Tyr, dTyr, 2-aminotetraline-2-carboxylic acid (Atc), octohydroindole-2-carboxylic acid (Oic), 1-amino-1-cyclohexanecarboxylic acid (Che), tetrahydro-isoquinoline-3-carboxylic acid (Tic), 1-amino-1-cyclopentane carboxylic (Cpe), and biphenylalanine (Bip);

$R^4$ is selected from the group consisting of dPhe, para-chloro-D-phenylalanine (p(Cl)dPhe), para-bromo-D-phenylalanine (p(Br)dPhe), and para-fluoro-D-phenylalanine (p(F)dPhe);

$R^5$ is Arg or His;

$R^6$ is selected from the group consisting of Trp, dTrp, Phe, dNal(2'), 2'-naphthylalanine (Nal(2')), and 1'-naphthylalanine (Nal(1'));

$R^7$ is selected from the group consisting of Gly, Pro, Lys, dLys, Cys, dCys, penicillamine (Pen), dPen, and Orn;

$R^8$ is absent or Lys;

$Y^1$ is selected from the group consisting of valine (Val), D-valine (dVal), $\beta^2$-valine ($\beta^2$-Val), $\beta^3$-valine ($\beta^3$-Val), Pro, D-proline (dPro), β-proline (β-Pro), Hyp, D-hydroxyproline

(dHyp), D-tert-leucine (dTle), dLeu, Trp, Arg, dArg, Lys, dLys, Gly, Ala, dAla, Asp, dAsp, asparagine (Asn), D-asparagine (dAsn), and D-threonine (dThr);

$Y^2$ is absent or is selected from the group consisting of Val, dVal, $\beta^2$-Val, $\beta^3$-Val, Pro, dPro, β-Pro, Hyp, dHyp, dTle, Arg, dArg, Gly, Ala, dAla, Asp, and dAsn;

$Y^3$ is absent or is selected from the group consisting of Val, dVal, Pro, dPro, dThr, Lys, and dLys;

$Y^4$ is absent or is selected from the group consisting of dVal, dPro, Asp, and dAsp; and

the non-naturally occurring melanocortin analog is cyclized through a moiety selected from the group consisting of:

a disulfide bond between $R^1$ or $R^2$ and $R^7$ or $R^8$ when each of $R^1$ or $R^2$ and $R^7$ or $R^8$ are independently selected from the group consisting of Cys, dCys, and dPen;

a disulfide bond between $R^2$ and $R^7$ when $R^2$ is Cys,$R^7$ is Pen, and $R^3$ is absent;

a lactam bridge between $R^1$ or $R^2$ and $R^7$ or $R^8$ when $R^1$ or $R^2$ is Asp and $R^7$ or $R^8$ is Lys or Orn; and

a lactam bridge between $R^2$ and $R^7$ when $R^2$ is dAsp and $R^7$ is dLys;

provided that:

when $R^4$ is p(F)dPhe, then (i) $R^3$ is selected from Pro, dGln, dTyr, $R^6$ is Trp, and the non-naturally occurring melanocortin analog is not cyclized between Cys at $R^2$ and Cys at $R^7$ or (ii) $R^3$ is His and either $R^6$ is Nal(2') or the non-naturally occurring melanocortin analog is cyclized through a disulfide bond between $R^2$ and $R^7$, where $R^2$ and $R^7$ are the same;

when $R^4$ is p(Br)dPhe, then the non-naturally occurring melanocortin analog is cyclized through a disulfide bond between dCys at $R^2$ and Cys or dCys at $R^7$;

when $R^4$ is dPhe, then (i) $R^3$ is not His, Pro, or absent, (ii) $R^3$ is His and either $R^2$ is Phe or dAla or $R^2$ is Ala and $X^1$ is Arg or dArg, (iii) $R^3$ is Pro and (a) $R^2$ is Trp, and $R^5$ is not

His or $R^6$ is not Phe or (b) $R^2$ is not Trp or Pro, and either $R^5$ is not dNal(2') or Nal(2') or $X^1$ and $Y^3$ are not both present, or (iv) $R^3$ is absent and $R^2$ and $R^7$ are not both dPen; and

when $R^4$ is p(Cl)dPhe, then (i) $R^3$ is selected from Aba, Aia, and Ata or (ii) $R^3$ is His, $R^1$ is not Ala, and (a) if $R^1$ is Nle and $Y^1Y^2$ is dVal-dPro, then $X^1$ is absent and the non-naturally occurring melanocortin analog is cyclized through a disulfide bond between dCys at $R^2$ and dCys at $R^7$, or (b) if $R^1$ is Nle, and $Y^1Y^2$ is not dVal-dPro, then either $X^1$ or $Y^3$ is present.

**[0485]** In some embodiments, the non-naturally occurring melanocortin analog comprises a sequence of Formula (IA), wherein:
$X^1$ is absent or is selected from the group consisting of norleucine (Nle), arginine (Arg), D-arginine (dArg), alanine (Ala), lysine (Lys), D-lysine (dLys), histidine (His), D-histidine (dHis);

$X^2$ is absent, phenylalanine (Phe), or Nle;

$X^3$ is absent, Phe, or Nle;

$R^1$ is selected from the group consisting of Nle, D-norleucine (dNle), Ala, D-alanine (dAla), Arg, dArg, Lys, dLys, His, dHis, ornithine (Orn), D-ornithine (dOrn), D-leucine (dLeu), D-tyrosine (dTyr), phenylalanine (Phe), D-phenylalanine (dPhe), tryptophan (Trp), D-tryptophan (dTrp), aspartic acid (Asp), cysteine (Cys), and D-cysteine (dCys);

$R^2$ is selected from the group consisting of Asp, D-aspartic acid (dAsp), Cys, dCys, D-penicillamine (dPen), Ala, Trp, Phe, dPhe, His, dHis, Tyr, and dTyr;

$R^3$ is absent or is selected from the group consisting of His, Ala, proline (Pro), hydroxyproline (Hyp), leucine (Leu), D-glutamine (dGln), Phe, dPhe, Trp, dTrp, Tyr, dTyr, 2-aminotetraline-2-carboxylic acid (Atc), octohydroindole-2-carboxylic acid (Oic), 1-amino-1-cyclohexanecarboxylic acid (Che), tetrahydro-isoquinoline-3-carboxylic acid (Tic), 1-amino-1-cyclopentane carboxylic (Cpe), and biphenylalanine (Bip);

$R^4$ is selected from the group consisting of dPhe, para-chloro-D-phenylalanine (p(Cl)dPhe), para-bromo-D-phenylalanine (p(Br)dPhe), and para-fluoro-D-phenylalanine (p(F)dPhe);

$R^5$ is Arg or His;

$R^6$ is selected from the group consisting of Trp, dTrp, Phe, dNal(2'), 2'-naphthylalanine (Nal(2')), and 1'-naphthylalanine (Nal(1'));

$R^7$ is selected from the group consisting of Gly, Pro, Lys, dLys, Cys, dCys, penicillamine (Pen), dPen, and Orn;

$R^8$ is absent or Lys;

$Y^1$ is selected from the group consisting of valine (Val), D-valine (dVal), $\beta^2$-valine ($\beta^2$-Val), $\beta^3$-valine ($\beta^3$-Val), Pro, D-proline (dPro), β-proline (β-Pro), Hyp, D-hydroxyproline (dHyp), D-tert-leucine (dTle), dLeu, Trp, Arg, dArg, Lys, dLys, Gly, Ala, dAla, Asp, dAsp, asparagine (Asn), D-asparagine (dAsn), and D-threonine (dThr);

$Y^2$ is absent or is selected from the group consisting of Val, dVal, $\beta^2$-Val, $\beta^3$-Val, Pro, dPro, β-Pro, Hyp, dHyp, dTle, Arg, dArg, Gly, Ala, dAla, Asp, and dAsn;

$Y^3$ is absent or is selected from the group consisting of Val, dVal, Pro, dPro, dThr, Lys, and dLys;

$Y^4$ is absent or is selected from the group consisting of dVal, dPro, Asp, and dAsp; and

the non-naturally occurring melanocortin analog is cyclized through a moiety selected from the group consisting of:

a disulfide bond between $R^1$ or $R^2$ and $R^7$ or $R^8$ when each of $R^1$ or $R^2$ and $R^7$ or $R^8$ are independently selected from the group consisting of Cys, dCys, and dPen;

a disulfide bond between $R^2$ and $R^7$ when $R^2$ is Cys, $R^7$ is Pen, and $R^3$ is absent;

a lactam bridge between $R^1$ or $R^2$ and $R^7$ or $R^8$ when $R^1$ or $R^2$ is Asp and $R^7$ or $R^8$ is Lys or Orn; and

a lactam bridge between $R^2$ and $R^7$ when $R^2$ is dAsp and $R^7$ is dLys;

provided that the non-naturally occurring melanocortin analog does not comprise a sequence selected from the group consisting of:
Ac-Nle-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 223);

Ac-Arg-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 464);

Ac-Lys-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 465);

Ac-dLys-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 466);

Ac-His-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 467);

Ac-dHis-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 468);

Ac-Nle-Nle-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 469);

Ac-Nle-c[Asp-His-p(F)dPhe-His-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 470);

Ac-Nle-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dVal-dVal-dVal-dPro-$NH_2$ (SEQ ID NO: 474);

Ac-Nle-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dPro-dVal-dPro-$NH_2$ (SEQ ID NO: 475);

Ac-Nle-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dTle-dPro-$NH_2$ (SEQ ID NO: 476);

Ac-Nle-Nle-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dTle-dPro-$NH_2$ (SEQ ID NO: 477);

Ac-Nle-Nle-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dPro-dVal-dPro-$NH_2$ (SEQ ID NO: 478);

Ac-Arg-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dTle-dPro-$NH_2$ (SEQ ID NO: 481);

Ac-Lys-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dTle-dPro-$NH_2$ (SEQ ID NO: 482);

Ac-dLys-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dTle-dPro-$NH_2$ (SEQ ID NO: 483);

Ac-His-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dTle-dPro-$NH_2$ (SEQ ID NO: 484);

Ac-dHis-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dTle-dPro-$NH_2$ (SEQ ID NO: 485);

Ac-dArg-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 463);

Ac-Ala-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 462);

Ac-Ala-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dTle-dPro-$NH_2$ (SEQ ID NO: 479);

Ac-Nle-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dTle-dTle-dVal-$NH_2$ (SEQ ID NO: 473);

Ac-dArg-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dTle-dPro-$NH_2$ (SEQ ID NO: 480);

Ac-Nle-c[Asp-Bip-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 489);

Ac-Nle-c[Asp-Trp-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 493);

Ac-Nle-c[Asp-Pro-p(F)dPhe-Arg-dNal(2')-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 444);

Ac-Nle-c[Asp-Pro-p(F)dPhe-Arg-Nal(2')-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 445);

Ac-Nle-c[Asp-Tyr-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 495);

Ac-Nle-c[Asp-Phe-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 487);

Ac-Nle-c[Asp-dPhe-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 488);

Ac-Nle-c[Asp-dTrp-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 494);

Ac-Nle-c[Asp-His-p(F)dPhe-Arg-dNal(2')-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 471);

Ac-Nle-c[Cys-Pro-p(F)dPhe-Arg-Trp-Cys]-dVal-dPro-$NH_2$ (SEQ ID NO: 432);

Ac-Nle-c[dCys-His-p(F)dPhe-Arg-Trp-Cys]-dVal-dPro-$NH_2$ (SEQ ID NO: 460);

Ac-Nle-c[Asp-Pro-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 217);

Ac-Nle-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 222);

Ac-Nle-c[Cys-His-p(Br)dPhe-Arg-Trp-Cys]-dVal-dPro-$NH_2$ (SEQ ID NO: 535);

Ac-Ala-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 538);

Ac-Nle-Nle-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 545);

Ac-Nle-c[Asp-His-p(Br)dPhe-His-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 546);

Ac-Nle-c[Asp-His-p(Br)dPhe-Arg-dNal(2')-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 547);

Ac-Nle-c[Asp-His-p(Br)dPhe-Arg-Nal(2')-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 548);

Ac-Nle-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dTle-dTle-dVal-$NH_2$ (SEQ ID NO: 549);

Ac-Nle-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dPro-dVal-dPro-$NH_2$ (SEQ ID NO: 551);

Ac-Nle-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dTle-dPro-$NH_2$ (SEQ ID NO: 552);

Ac-Nle-Nle-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dTle-dPro-$NH_2$ (SEQ ID NO: 553);

Ac-Ala-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dTle-dPro-$NH_2$ (SEQ ID NO: 555);

Ac-Nle-c[Asp-Phe-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 563);

Ac-Nle-c[Asp-dPhe-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 564);

Ac-Nle-c[Asp-Bip-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 565);

Ac-Nle-c[Asp-dGln-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 568);

Ac-Nle-c[Asp-Trp-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 569);

Ac-Nle-c[Asp-dTrp-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 570);

Ac-Nle-c[Asp-Tyr-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 571);

Ac-Nle-c[Asp-dTyr-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 572);

Ac-dArg-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 539);

Ac-dHis-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 544);

Ac-dHis-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dTle-dPro-$NH_2$ (SEQ ID NO: 561);

Ac-dArg-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dTle-dPro-$NH_2$ (SEQ ID NO: 556);

Ac-dLys-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 542);

Ac-His-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dTle-dPro-$NH_2$ (SEQ ID NO: 560);

Ac-His-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 543);

Ac-dLys-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dTle-dPro-$NH_2$ (SEQ ID NO: 559);

Ac-Arg-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dTle-dPro-$NH_2$ (SEQ ID NO: 557);

Ac-Lys-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 541);

Ac-Nle-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dVal-dVal-dVal-dPro-$NH_2$ (SEQ ID NO: 550);

Ac-Lys-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dTle-dPro-$NH_2$ (SEQ ID NO: 558);

Ac-Arg-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 540);

Ac-Nle-Nle-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dPro-dVal-dPro-$NH_2$ (SEQ ID NO: 554);

Ac-Nle-c[Asp-His-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 363);

Ac-Nle-c[Asp-His-dPhe-Arg-Trp-Pro-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 418);

Ac-Nle-c[Asp-His-dPhe-Arg-Trp-Lys]-dPro-dVal-$NH_2$ (SEQ ID NO: 621);

Ac-Nle-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dPro-dVal-dPro-$NH_2$ (SEQ ID NO: 639);

Ac-Nle-c[dPen-dPhe-Arg-Trp-dPen]-dVal-dPro-$NH_2$ (SEQ ID NO: 326);

Ac-Nle-c[Asp-Trp-Pro-dPhe-His-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 398);

Ac-Nle-c[Asp-Trp-Pro-dPhe-Arg-Phe-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 401);

Ac-Nle-c[Asp-Pro-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 225);

Ac-Nle-c[Asp-Pro-dPhe-Arg-dNal(2')-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 430);

Ac-Nle-c[Asp-Pro-dPhe-Arg-Nal(2')-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 431);

Ac-Nle-c[Asp-Ala-His-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 380);

Ac-Nle-c[Asp-Pro-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 215);

Ac-Nle-c[Asp-Phe-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 525);

Ac-Nle-c[Asp-dPhe-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 526);

Ac-Nle-c[Asp-Bip-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 527);

Ac-Nle-c[Asp-Trp-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 531);

Ac-Nle-c[Asp-Tyr-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 533);

Ac-Nle-c[Asp-dTyr-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 534);

Ac-Nle-c[Asp-dTrp-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 532);

Ac-Nle-c[dCys-His-p(Cl)dPhe-Arg-Trp-Cys]-dVal-dPro-$NH_2$ (SEQ ID NO: 498);

Ac-Nle-c[Cys-His-p(Cl)dPhe-Arg-Trp-Cys]-dVal-dPro-$NH_2$ (SEQ ID NO: 497);

Ac-Nle-c[Asp-His-p(Cl)dPhe-Arg-dNal(2')-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 509);

Ac-Nle-c[Asp-His-p(Cl)dPhe-Arg-Nal(2')-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 510);

Ac-Nle-c[Asp-His-p(Cl)dPhe-His-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 508);

Ac-Nle-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 220);

Ac-Nle-Nle-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 507);

Ac-Ala-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dTle-dPro-$NH_2$ (SEQ ID NO: 517);

Ac-Ala-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 500);

Ac-Nle-Nle-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dPro-dVal-dPro-$NH_2$ (SEQ ID NO: 516); and Ac-Nle-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dTle-dPro-$NH_2$ (SEQ ID NO: 514).

**[0486]** In some embodiments, $R^3$ is Pro. In further embodiments, $R^4$ is dPhe or p(F)dPhe. In some embodiments, the non-naturally occurring melanocortin analog comprises a sequence of Formula (IB):

$$X^1\text{-}X^2\text{-}X^3\text{-}R^1\text{-}R^2\text{-Pro-}R^4\text{-}R^5\text{-}R^6\text{-}R^7\text{-}R^8\text{-}Y^1\text{-}Y^2\text{-}Y^3\text{-}Y^4\text{-}Y^5\text{-}Y^6\text{-}Y^7 \text{ (IB)},$$

wherein:

$X^1$ is absent or norleucine (Nle);

$X^2$ is absent or Nle;

$X^3$ is absent or Nle;

$R^1$ is selected from the group consisting of Nle, D-norleucine (dNle), alanine (Ala), D-alanine (dAla), arginine (Arg), D-arginine (dArg), lysine (Lys), D-lysine (dLys), histidine (His), D-histidine (dHis), ornithine (Orn), D-ornithine (dOrn), D-leucine (dLeu), D-tyrosine (dTyr), phenylalanine (Phe), D-phenylalanine (dPhe), tryptophan (Trp), and D-tryptophan (dTrp);

$R^2$ is selected from the group consisting of aspartic acid (Asp), D-aspartic acid (dAsp), cysteine (Cys), D-cysteine (dCys), and D-penicillamine (dPen);

$R^4$ is dPhe or para-fluoro-D-phenylalanine (p(F)dPhe);

$R^5$ is selected from the group consisting of Arg, His, *cis*Pro(guan), and *trans*Pro(guan);

$R^6$ is selected from the group consisting of Trp, dTrp, Phe, Aia, Aba, Ata, and 1'-naphthylalanine (Nal(1')));

$R^7$ is selected from the group consisting of Gly, Lys, dLys, Cys, dCys, dPen, and Orn;

$R^8$ is absent or Lys;

$Y^1$ is absent or is selected from the group consisting of valine (Val), D-valine (dVal), $\beta^2$-valine ($\beta^2$-Val), $\beta^3$-valine ($\beta^3$-Val), Pro, D-proline (dPro), β-proline (β-Pro), Hyp, D-hydroxyproline (dHyp), D-tert-leucine (dTle), dLeu, Trp, Arg, dArg, Lys, dLys, Gly, Ala, dAla, Asp, dAsp, asparagine (Asn), D-asparagine (dAsn), and D-threonine (dThr);

$Y^2$ is absent or is selected from the group consisting of Val, dVal, $\beta^2$-Val, $\beta^3$-Val, Pro, dPro, β-Pro, Hyp, dHyp, dTle, Arg, dArg, Gly, Ala, dAla, Asp, and dAsn;

$Y^3$ is absent or is selected from the group consisting of Val, dVal, Pro, dPro, dThr, Lys, and dLys;

$Y^4$ is absent or is selected from the group consisting of dVal, dPro, Asp, and dAsp;

$Y^5$ is absent or dVal;

$Y^6$ is absent or dVal;

$Y^7$ is absent or dPro; and

the non-naturally occurring melanocortin analog is cyclized through a moiety selected from the group consisting of:

a disulfide bond between $R^2$ and $R^7$ when each of $R^2$ and $R^7$ are independently selected from the group consisting of Cys, dCys, and dPen; and

a lactam bridge between $R^2$ and $R^7$ when $R^2$ is Asp or dAsp and $R^7$ is Lys, dLys, or Orn;

provided that:

when $R^4$ is p(F)dPhe, then the non-naturally occurring melanocortin analog is not cyclized between Cys at $R^2$ and Cys at $R^7$; and

when $R^4$ is dPhe and one or more of $X^1$, $X^2$, and $X^3$ is present, then $Y^3$-$Y^7$ are absent.

**[0487]** In some embodiments, the non-naturally occurring melanocortin analog comprises a sequence of Formula (IB), wherein:
$X^1$ is absent or norleucine (Nle);

$X^2$ is absent or Nle;

$X^3$ is absent or Nle;

$R^1$ is selected from the group consisting of Nle, D-norleucine (dNle), alanine (Ala), D-alanine (dAla), arginine (Arg), D-arginine (dArg), lysine (Lys), D-lysine (dLys), histidine (His),

D-histidine (dHis), ornithine (Orn), D-ornithine (dOrn), D-leucine (dLeu), D-tyrosine (dTyr), phenylalanine (Phe), D-phenylalanine (dPhe), tryptophan (Trp), and D-tryptophan (dTrp);

$R^2$ is selected from the group consisting of aspartic acid (Asp), D-aspartic acid (dAsp), cysteine (Cys), D-cysteine (dCys), and D-penicillamine (dPen);

$R^4$ is dPhe or para-fluoro-D-phenylalanine (p(F)dPhe);

$R^5$ is selected from the group consisting of Arg, His, *cis*Pro(guan), and *trans*Pro(guan);

$R^6$ is selected from the group consisting of Trp, dTrp, Phe, Aia, Aba, Ata, and 1'-naphthylalanine (Nal(1')));

$R^7$ is selected from the group consisting of Gly, Lys, dLys, Cys, dCys, dPen, and Orn;

$R^8$ is absent or Lys;

$Y^1$ is absent or is selected from the group consisting of valine (Val), D-valine (dVal), $\beta^2$-valine ($\beta^2$-Val), $\beta^3$-valine ($\beta^3$-Val), Pro, D-proline (dPro), β-proline (β-Pro), Hyp, D-hydroxyproline (dHyp), D-tert-leucine (dTle), dLeu, Trp, Arg, dArg, Lys, dLys, Gly, Ala, dAla, Asp, dAsp, asparagine (Asn), D-asparagine (dAsn), and D-threonine (dThr);

$Y^2$ is absent or is selected from the group consisting of Val, dVal, $\beta^2$-Val, $\beta^3$-Val, Pro, dPro, β-Pro, Hyp, dHyp, dTle, Arg, dArg, Gly, Ala, dAla, Asp, and dAsn;

$Y^3$ is absent or is selected from the group consisting of Val, dVal, Pro, dPro, dThr, Lys, and dLys;

$Y^4$ is absent or is selected from the group consisting of dVal, dPro, Asp, and dAsp;

$Y^5$ is absent or dVal;

$Y^6$ is absent or dVal;

$Y^7$ is absent or dPro; and

the non-naturally occurring melanocortin analog is cyclized through a moiety selected from the group consisting of:

a disulfide bond between $R^2$ and $R^7$ when each of $R^2$ and $R^7$ are independently selected from the group consisting of Cys, dCys, and dPen; and

a lactam bridge between $R^2$ and $R^7$ when $R^2$ is Asp or dAsp and $R^7$ is Lys, dLys, or Orn;

provided that the non-naturally occurring melanocortin analog does not comprise a sequence of:

Ac-Nle-c[Cys-Pro-p(F)dPhe-Arg-Trp-Cys]-dVal-dPro-$NH_2$ (SEQ ID NO: 432); or

Ac-Nle-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dPro-dVal-dPro-$NH_2$ (SEQ ID NO: 639).

**[0488]** In some embodiments, $R^2$ is an aromatic amino acid and $R^3$ is Pro. In some embodiments, $R^2$ is Trp, Phe, dPhe, His, dHis, Tyr, or dTyr, and $R^3$ is Pro. In further embodiments, $R^2$ is Trp and $R^3$ is Pro. In still further embodiments, $R^4$ is dPhe. In some embodiments, the non-naturally occurring melanocortin analog comprises a sequence of Formula (IC):

$$X^1\text{-}X^2\text{-}R^1\text{-}R^2\text{-Pro-dPhe-}R^5\text{-}R^6\text{-}R^7\text{-}Y^1\text{-}Y^2\text{-}Y^3\text{-}Y^4 \text{ (IC)},$$

wherein:

$X^1$ is selected from the group consisting of norleucine (Nle), arginine (Arg), D-arginine (dArg), alanine (Ala), lysine (Lys), D-lysine (dLys), histidine (His), D-histidine (dHis);

$X^2$ is absent or Nle;

$R^1$ is selected from the group consisting of aspartic acid (Asp), cysteine (Cys), and D-cysteine (dCys);

$R^2$ is selected from the group consisting of tryptophan (Trp), phenylalanine (Phe), D-phenylalanine (dPhe), histidine (His), D-histidine (dHis), tyrosine (Tyr), and D-tyrosine (dTyr);

$R^5$ is Arg;

$R^6$ is selected from the group consisting of Trp, 2'-D-naphthylalanine (dNal(2')), 2'-naphthylalanine (Nal(2')), and 1'-naphthylalanine (Nal(1'));

$R^7$ is selected from the group consisting of Lys, Cys, and dCys;

$Y^1$ is absent or is selected from the group consisting of D-valine (dVal), D-tert-leucine (dTle), dArg, and dLys;

$Y^2$ is absent or is selected from the group consisting of dVal, dPro, and D-hydroxyproline (dHyp);

$Y^3$ is absent, dVal, or dPro;

$Y^4$ is absent or dPro; and

the non-naturally occurring melanocortin analog is cyclized through a moiety selected from the group consisting of:

a disulfide bond between $R^1$ and $R^7$ when both of $R^1$ and $R^7$ are independently selected from the group consisting of Cys, dCys, and dPen; and

a lactam bridge between $R^1$ and $R^7$ when $R^1$ is Asp and $R^7$ is Lys;

**[0489]** In some embodiments, $R^4$ is p(Cl)dPhe. In further embodiments, $R^3$ is His, Aba, Ata, or Aia. In still further embodiments, $R^3$ is His and $R^4$ is p(Cl)dPhe. In some embodiments, the non-naturally occurring melanocortin analog comprises a sequence of Formula (ID):

$$X^1\text{-}R^1\text{-}R^2\text{-}R^3\text{-p(Cl)dPhe-Arg-Trp-}R^7\text{-}Y^1\text{-}Y^2\text{-}Y^3\text{-}Y^4 \text{ (ID)},$$

wherein:

$X^1$ is absent or norleucine (Nle);

$R^1$ is selected from the group consisting of Nle, arginine (Arg), D-arginine (dArg), lysine (Lys), D-lysine (dLys), histidine (His), and D-histidine (dHis);

$R^2$ is aspartic acid (Asp) or D-cysteine (dCys);

$R^3$ is selected from the group consisting of His, 4-amino-1,2,4,5-tetrahydro-2-benzazepin-3-one (Aba), 7-amino-7,8-dihydro-4H-[1,2,3]triazolo-[1,5-a][1,4]diazepin-6(5H)-one (Ata), and 4-amino-1,4,5,6-tetrahydroazepino[4,3-*b*]indol-3(*2H*)-one (Aia);

$R^7$ is Lys or dCys;

$Y^1$ is selected from the group consisting of D-valine (dVal), D-proline (dPro), and D-tert-leucine (dTle);

$Y^2$ is absent or is selected from the group consisting of dVal, dPro, and dTle;

$Y^3$ is absent, dVal, or dPro;

$Y^4$ is absent or dPro; and

the non-naturally occurring melanocortin analog is cyclized through a moiety selected from the group consisting of:

a disulfide bond between $R^2$ and $R^7$ when both of $R^2$ and $R^7$ are dCys; and

a lactam bridge between $R^2$ and $R^7$ when $R^2$ is Asp and $R^7$ is Lys;

provided that when $R^3$ is His and $R^1$ is Nle, then (i) $Y^1Y^2$ is dVal-dPro, $X^1$ is absent, and the non-naturally occurring melanocortin analog is cyclized through a disulfide bond, or (b) $Y^1Y^2$ is not dVal-dPro and either $X^1$ or $Y^3$ is present.

**[0490]** In some embodiments, the non-naturally occurring melanocortin analog comprises a sequence of Formula (ID), wherein:
$X^1$ is absent or norleucine (Nle);

$R^1$ is selected from the group consisting of Nle, arginine (Arg), D-arginine (dArg), lysine (Lys), D-lysine (dLys), histidine (His), and D-histidine (dHis);

$R^2$ is aspartic acid (Asp) or D-cysteine (dCys);

$R^3$ is selected from the group consisting of His, 4-amino-1,2,4,5-tetrahydro-2-benzazepin-3-one (Aba), 7-amino-7,8-dihydro-4H-[1,2,3]triazolo-[1,5-a][1,4]diazepin-6(5H)-one (Ata), and 4-amino-1,4,5,6-tetrahydroazepino[4,3-*b*]indol-3(*2H*)-one (Aia);

$R^7$ is Lys or dCys;

$Y^1$ is selected from the group consisting of D-valine (dVal), D-proline (dPro), and D-tert-leucine (dTle);

$Y^2$ is absent or is selected from the group consisting of dVal, dPro, and dTle;

$Y^3$ is absent, dVal, or dPro;

$Y^4$ is absent or dPro; and

the non-naturally occurring melanocortin analog is cyclized through a moiety selected from the group consisting of:

a disulfide bond between $R^2$ and $R^7$ when both of $R^2$ and $R^7$ are dCys;

a lactam bridge between $R^2$ and $R^7$ when $R^2$ is Asp and $R^7$ is Lys; and

provided that the non-naturally occurring melanocortin analog does not comprise a sequence selected from the group consisting of:

Ac-Nle-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 220);

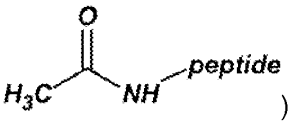
Ac-Nle-Nle-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 507);

Ac-Nle-Nle-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dPro-dVal-dPro-$NH_2$ (SEQ ID NO: 516); and

Ac-Nle-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dTle-dPro-$NH_2$ (SEQ ID NO: 514).

**[0491]** In some embodiments, the non-naturally occurring melanocortin analog has one or more beta hairpin (β-hairpin) and/or beta turn (β-turn) structures. In some embodiments, the presence of Pro, dPro, Hyp, dHyp, *trans*Pro(guan), and/or *cis*Pro(guan), provides the β-hairpin and/or β-turn structures of the non-naturally occurring melanocortin analog. In some embodiments, the disulfide bond of the sequence according to Formula (I), if present, provides the β-hairpin and/or β-turn structures of the non-naturally occurring melanocortin analog.

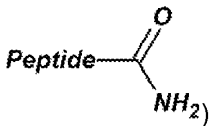
**[0492]**  will be appreciated by the skilled artisan, non-naturally occurring melanocortin analogs comprising a sequence of any one of Formulae (I)-(ID), have an N-terminus and a C-terminus. The melanocortin analogs of the present technology are written beginning with the N-terminus at the left-most amino acid residue and ending with the C-terminus at the right most residue. Accordingly, the N-terminus of a non-naturally melanocortin analog comprising a sequence of any one of Formulae (I)-(ID) may be at any of $X^1$, $X^2$, $X^3$, and $R^1$. Analogously, the C-terminus of a non-naturally occurring melanocortin analog comprising a sequence of any one of Formulae (I)-(ID) may be at any of $R^7$, $R^8$, $Y^1$, $Y^2$, $Y^3$, $Y^4$, $Y^5$, $Y^6$, and $Y^7$.

**[0493]** In some embodiments, the N-terminus of the non-naturally occurring melanocortin analog is modified by an acyl group. In some embodiments, the acyl group is acetyl group (e.g., 

).

**[0494]** In some embodiments, the N-terminus of the non-naturally occurring melanocortin analog is not modified.

**[0495]** As discussed above, $Y^1Y^2Y^3Y^4Y^5Y^6Y^7$ represents a C-terminus of the non-naturally occurring melanocortin analog. In some embodiments, $Y^1$-$Y^7$ are absent. In some embodiments, $Y^1$ is present and $Y^2$-$Y^7$ are absent. In some embodiments, $Y^1$ and $Y^2$ are present and $Y^3$-$Y^7$ are absent. In some embodiments, $Y^1$-$Y^3$ are present and $Y^4$-$Y^7$ are absent. In some embodiments, $Y^1$-$Y^4$ are present and $Y^5$-$Y^7$ are absent. In some embodiments, $Y^1$-$Y^5$ are present and $Y^6$-$Y^7$ are absent. In some embodiments, $Y^1$-$Y^6$ are present and $Y^7$ is absent. In some embodiments, $Y^1$-$Y^7$ are present.

**[0496]** In some embodiments, the C-terminus of the non-naturally occurring melanocortin analog is modified by an amide group (e.g., 

). In the sequence of any one of Formulae (I)-(ID), a non-naturally occurring melanocortin analog with a C-terminus modified by an amide may be represented by a terminal -$NH_2$.

**[0497]** In some embodiments, the C-terminus of the non-naturally occurring melanocortin analog is not modified. In the sequence of any one of Formulae (I)-(ID), a non-naturally occurring melanocortin analog with an unmodified C-terminus may be represented by -OH.

**[0498]** Non-naturally occurring melanocortin analogs comprising a sequence of any one of Formulae (I)-(ID) are cyclized. For example, the non-naturally occurring melanocortin analog may be cyclized through a moiety selected from the group consisting of: a disulfide bond between $R^2$ and $R^7$ when $R^2$ is Cys, $R^7$ is Pen, and $R^3$ is absent; a lactam bridge between $R^1$ or $R^2$ and $R^7$ or $R^8$ when $R^1$ or $R^2$ is Asp and $R^7$ or $R^8$ is Lys or Orn; and a lactam bridge between $R^2$ and $R^7$ when $R^2$ is dAsp and $R^7$ is dLys.

**[0499]** In some embodiments, $R^4$ is dNal(2'). In further embodiments, the non-naturally occurring melanocortin analog is cyclized through a lactam bond between $R^2$ and $R^8$. In some embodiments, the sequence of Formula (I) is: Ac-Nle-$_c$[Asp-His-dNal(2')-Arg-Trp-Pro-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 8), wherein c represents cyclization through $R^2$ and $R^8$ via a lactam bond.

**[0500]** In some embodiments of the sequence of any one of Formulae (I)-(ID), $R^4$ is dPhe or Phe. In further embodiments, $X^1$ is absent or Nle, $R^2$ is Nle or Asp, $R^2$ is Asp or Pro, $R^3$ is Pro or His, $R^5$ is Arg, $R^6$ is Trp, and $R^7$ is Lys. In some embodiments, $Y^1$ is dVal and $Y^2$ is dPro. In some embodiments, the sequence of any one of Formulae (I)-(ID) is selected from the group consisting of:

Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-OH (SEQ ID NO: 291);

Ac-Nle-c[Asp-Pro-Phe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 294);

Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 295; E2); and

Ac-Nle-c[Asp-Pro-His-Phe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 296).

wherein c represents cyclization through $R^2$ and $R^7$ via a lactam bond.

**[0501]** In some embodiments of the sequence of any one of Formulae (I)-(ID), $R^1$ is Nle. Alternatively, in some embodiments, $R^1$ is an amino acid other than Nle. In some embodiments, when $R^1$ is an amino acid other than Nle, $R^1$ is selected from Ac-dLeu, Ac-dAla, Ac-Ala, Ac-dArg, Ac-Arg, Ac-dNle, Ac-dPhe, Ac-dTyr, Ac-dLys, Ac-Lys, Ac-dHis, Ac-His, Ac-dOrn, and Ac-Orn. In some embodiments, $R^1$ is an amino acid that is not acetylated. In some embodiments, when $R^1$ is an amino acid that is not acetylated, $R^1$ is selected from Phe, dPhe, His, dHis, Trp, and dTrp. In some embodiments, when $R^1$ is an amino acid other than acetylated norleucine, $R^2$ is Asp, $R^3$ is Pro, $R^4$ is dPhe, $R^5$ is Arg, $R^6$ is Trp, $R^7$ is Lys, and $Y^1$ and $Y^2$ are each independently dVal or dPro. In some embodiments, the sequence of Formula (IB) is selected from the group consisting of:

Ac-dLeu-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO:298);

Ac-dAla-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 299);

Ac-Ala-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro- $NH_2$ (SEQ ID NO: 300);

Ac-dNle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 301);

Ac-dArg-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 302);

Ac-dPhe-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 303);

Ac-dTyr-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 304);

Phe-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 305);

His-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 306);

Trp-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 307);

dPhe-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 308);

dHis-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 309);

dTrp-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 310);

Ac-Arg-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 311);

Ac-dLys-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 312);

Ac-Lys-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 313);

Ac-His-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 314);

Ac-dHis-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 315);

Ac-Orn-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 316); and

Ac-dOrn-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 317),

wherein c represents cyclization through $R^2$ and $R^7$ via a lactam bond.

**[0502]** In some embodiments, the sequence of any one of Formulae (I)-(ID) is cyclized through $R^2$ and $R^7$. In some embodiments, when the sequence of any one of Formulae (I)-(ID) is cyclized through $R^2$ and $R^7$, $R^2$ is Asp and $R^7$ is Lys. Alternatively, in some embodiments, when the sequence of any one of Formulae (I)-(ID) is cyclized through $R^2$ and $R^7$, $R^2$ is an amino acid capable of forming a linkage to the residue at $R^7$ other than Asp and/or $R^7$ is an amino acid capable of forming a linkage to the residue at $R^2$ other than Lys. For example, when $R^2$ is an amino acid other than Asp and/or $R^7$ is an amino acid other than Lys, the residue at $R^2$ may be capable of forming a linkage such as a lactam bond or a

disulfide bond with the residue at $R^7$. In some embodiments, $R^2$ and $R^7$ are each independently Cys, dCys, Pen, or dPen, and the peptide is cyclized through $R^2$ and $R^7$ via a disulfide bond. In some embodiments, $R^2$ is Asp and $R^7$ is Orn, and the peptide is cyclized through $R^2$ and $R^7$ via a lactam bond. In some embodiments, when $R^2$ is an amino acid other than Asp and/or $R^7$ is an amino acid other than Lys, the peptide is cyclized through $R^2$ and $R^7$, $R^1$ is Ac-Nle, $R^3$ is Pro or absent, $R^4$ is dPhe, $R^5$ is Arg, $R^6$ is Trp and $Y^1$ and $Y^2$ are each independently dVal or dPro. In some embodiments, the sequence of any one of Formulae (I)-(ID) is selected from the group consisting of:

Ac-Nle-c[Cys-Pro-dPhe-Arg-Trp-Cys]-dVal-dPro-$NH_2$ (SEQ ID NO: 318);

Ac-Nle-c[dCys-Pro-dPhe-Arg-Trp-Cys]-dVal-dPro-$NH_2$ (SEQ ID NO: 319);

Ac-Nle-c[dPen-Pro-dPhe-Arg-Trp-dPen]-dVal-dPro-$NH_2$ (SEQ ID NO: 320);

Ac-Nle-c[dCys-Pro-dPhe-Arg-Trp-dCys]-dVal-dPro-$NH_2$ (SEQ ID NO: 321);

Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Orn]-dVal-dPro-$NH_2$ (SEQ ID NO: 322); and

Ac-Nle-c[Cys-dPhe-Arg-Trp-Pen]-dVal-dPro-$NH_2$ (SEQ ID NO: 324),

wherein c represents cyclization through $R^2$ and $R^7$ via a disulfide bond.

**[0503]** In some embodiments, the sequence of any one of Formulae (I)-(ID)is cyclized through $R^2$ and $R^8$. In some embodiments, when the sequence of any one of Formulae (I)-(ID)is cyclized through $R^2$ and $R^8$, then $R^2$ is Asp and $R^8$ is Lys. In some embodiments, $R^1$ is Ac-Nle, $R^3$ is Pro, $R^4$ is dPhe, $R^5$ is Arg, $R^6$ is Trp, and $R^7$ is Gly. In some embodiments, the sequence of any one of Formulae (I)-(ID)is selected from the group consisting of:

Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Gly-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 351);

Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Gly-Lys]-dPro-dPro-Lys-Asp-$NH_2$ (SEQ ID NO: 352); and

Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Gly-Lys]-dPro-dPro-dLys-dAsp-$NH_2$ (SEQ ID NO: 353),

wherein c represents cyclization through $R^2$ and $R^8$ via a lactam bond.

**[0504]** In some embodiments of the sequence of any one of Formulae (I)-(ID), $R^3$ is Pro. Alternatively, in some embodiments, $R^3$ is absent or an amino acid other than Pro. For example, when $R^3$ is an amino acid other than Pro, $R^3$ may be Ala, Leu, dIle, dVal, Cpe,

Che, Oic, Ioc, Tic, His, Hyp, dHis, Phe, dPhe, Bip, dBip, Gln, dGln, Trp, dTrp, Tyr, dTyr, Aba, Aia, Ata, Atc, APC, or APPC. In some embodiments, $R^1$ is Ac-Nle, $R^2$ is Asp, $R^3$ is an amino acid other than Pro, $R^4$ is dPhe, $R^5$ is Arg, $R^6$ is Trp, $R^7$ is Lys, and $Y^1$ and $Y^2$ are each independently dVal or dPro. In some embodiments, the sequence of any one of Formulae (I)-(ID)is selected from the group consisting of:

Ac-Nle-c[Asp-Ala-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 354);

Ac-Nle-c[Asp-Leu-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 355);

Ac-Nle-c[Asp-Cpe-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 358);

Ac-Nle-c[Asp-Che-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 359);

Ac-Nle-c[Asp-Oic-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 360);

Ac-Nle-c[Asp-Ioc-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 361);

Ac-Nle-c[Asp-Tic-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 362);

Ac-Nle-c[Asp-Hyp-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 364);

Ac-Nle-c[Asp-Phe-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 366);

Ac-Nle-c[Asp-dPhe-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 367);

Ac-Nle-c[Asp-Bip-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 368);

Ac-Nle-c[Asp-dGln-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 371);

Ac-Nle-c[Asp-Trp-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 372);

Ac-Nle-c[Asp-dTrp-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 373);

Ac-Nle-c[Asp-Tyr-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 374);

Ac-Nle-c[Asp-dTyr-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 375);

Ac-Nle-c[Asp-Aba-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 198);

Ac-Nle-c[Asp-Aia-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 207);

Ac-Nle-c[Asp-Ata-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 208);

Ac-Nle-c[Asp-Atc-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 212);

Ac-Nle-c[Asp-APC-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 213); and

Ac-Nle-c[Asp-APPC-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 214)

wherein c represents cyclization through $R^2$ and $R^7$ via a lactam bond.

**[0505]** In some embodiments, the sequence is cyclized through $R^1$ and $R^7$ via a lactam bond. In some embodiments, $R^2$ is Ala or dAla, $R^3$ is His. In further embodiments, $X^1$ is Nle, Arg, or dArg, $R^4$ is dPhe, $R^6$ is Arg, $R^7$ is Trp, and $R^7$ is Lys. In some embodiments, the sequence of any one of Formulae (I)-(ID) is selected from the group consisting of:

Ac-Arg-c[Asp-dAla-His-dPhe-Arg-Trp-Lys]-$NH_2$ (SEQ ID NO: 281);

Ac-Arg-c[Asp-Ala-His-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 381); and

Ac-dArg-c[Asp-Ala-His-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 382),

wherein c represents cyclization through $R^1$ and $R^7$ via a lactam bond.

**[0506]** In other embodiments, when the sequence is cyclized through $R^1$ and $R^7$ via a lactam bond, $R^2$ is Trp, Phe, dPhe, His, dHis, Tyr, or dTyr, and $R^3$ is Pro Ala, or Leu. In further embodiments, $X^1$ is Nle, Ala, Lys, dLys, His, or dHis, $R^4$ is dPhe, $R^6$ is Arg, $R^7$ is Trp, Nal(1'), Nal(2'), or dNal(2'), and $R^7$ is Lys. In some embodiments, the sequence of any one of Formulae (I)-(ID) is selected from the group consisting of:

Ac-Nle-c[Asp-Trp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 226);

Ac-Nle-c[Cys-Trp-Pro-dPhe-Arg-Trp-Cys]-dVal-dPro-$NH_2$ (SEQ ID NO: 383);

Ac-Nle-c[dCys-Trp-Pro-dPhe-Arg-Trp-Cys]-dVal-dPro-$NH_2$ (SEQ ID NO: 384);

Ac-Nle-c[dCys-Trp-Pro-dPhe-Arg-Trp-dCys]-dVal-dPro-$NH_2$ (SEQ ID NO: 385);

Ac-Ala-c[Asp-Trp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 386);

Ac-Lys-c[Asp-Trp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 387);

Ac-dLys-c[Asp-Trp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 388);

Ac-Arg-c[Asp-Trp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 389);

Ac-dArg-c[Asp-Trp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 390);

Ac-dHis-c[Asp-Trp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 391);

Ac-His-c[Asp-Trp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 392);

Ac-Nle-Nle-c[Asp-Trp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 393);

Ac-Nle-c[Asp-Trp-Ala-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 394);

Ac-Nle-c[Asp-Trp-Leu-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 395);

Ac-Nle-c[Asp-Trp-Pro-dPhe-Arg-Nal(1']-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 399);

Ac-Nle-c[Asp-Trp-Pro-dPhe-Arg-dNal(2')-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 403);

Ac-Nle-c[Asp-Trp-Pro-dPhe-Arg-Nal(2')-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 404);

Ac-Nle-c[Asp-Trp-Pro-dPhe-Arg-Trp-Lys]-dArg-dVal-dPro-$NH_2$ (SEQ ID NO: 405);

Ac-Nle-c[Asp-Trp-Pro-dPhe-Arg-Trp-Lys]-dLys-dVal-dPro-$NH_2$ (SEQ ID NO: 406);

Ac-Nle-c[Asp-Trp-Pro-dPhe-Arg-Trp-Lys]-dArg-dPro-$NH_2$ (SEQ ID NO: 407);

Ac-Nle-c[Asp-Trp-Pro-dPhe-Arg-Trp-Lys]-dLys-dPro-$NH_2$ (SEQ ID NO: 408);

Ac-Nle-c[Asp-Trp-Pro-dPhe-Arg-Trp-Lys]-dVal-dHyp-$NH_2$ (SEQ ID NO: 409);

Ac-Nle-c[Asp-Trp-Pro-dPhe-Arg-Trp-Lys]-dTle-dPro-$NH_2$ (SEQ ID NO: 410);

Ac-Nle-c[Asp-Trp-Pro-dPhe-Arg-Trp-Lys]-dVal-dVal-dVal-dPro-$NH_2$ (SEQ ID NO: 411);

Ac-Nle-c[Asp-Phe-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 412);

Ac-Nle-c[Asp-His-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 413);

Ac-Nle-c[Asp-Tyr-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 414);

Ac-Nle-c[Asp-dPhe-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 415);

Ac-Nle-c[Asp-dHis-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 416); and

Ac-Nle-c[Asp-dTyr-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 417),

wherein c represents cyclization through $R^1$ and $R^7$ via a lactam bond or a disulfide bond.

**[0507]** In some embodiments, the sequence is cyclized through $R^2$ and $R^8$ via a lactam bond. some, when $R^3$ is Hyp, $R^4$ is dPhe, $R^5$ is Arg, $R^6$ is Trp, $R^7$ is Pro, and the peptide is cyclized through $R^2$ and $R^8$ via a lactam bond. In some embodiments, the sequence of any

one of Formulae (I)-(ID) is: Ac-Nle-c[Asp-Hyp-dPhe-Arg-Trp-Pro-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 419), wherein c represents cyclization through $R^2$ and $R^8$ via a lactam bond.

**[0508]** In still other embodiments, when the sequence is cyclized through $R^1$ and $R^7$ via a lactam bond, then $R^2$ is Phe and $R^3$ is His. In some embodiments, the sequence of any one of Formulae (I)-(ID) is selected from the group consisting of:

Ac-Nle-Phe-Phe-c[Asp-Phe-His-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 421);

Ac-Nle-c[Asp-Phe-His-dPhe-Arg-Trp-Lys]-dLeu-dPro-$NH_2$ (SEQ ID NO: 422);

Ac-Nle-c[Asp-Phe-His-dPhe-Arg-Trp-Lys]-dTle-dPro-$NH_2$ (SEQ ID NO: 423); and

Ac-Nle-c[Asp-Phe-His-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 424),

wherein c represents cyclization through $R^2$ and any one of $R^8$-$R^{10}$ via a lactam bond or a disulfide bond.

**[0509]** In some embodiments of the sequence of any one of Formulae (I)-(ID), $R^5$ is Arg. Alternatively, in some embodiments, $R^5$ is absent or an amino acid other than Arg. For example, when $R^5$ is an amino acid other than Arg, $R^5$ is *cis*Pro(guan), *trans*Pro(guan), or His. In some embodiments, $R^1$ is Ac-Nle, $R^2$ is Asp, $R^3$ is Pro, $R^4$ is dPhe, $R^5$ is an amino acid other than Arg, $R^6$ is Trp, $R^7$ is Lys and $Y^1$ and $Y^2$ are each independently dVal or dPro. In some embodiments, the sequence of any one of Formulae (I)-(ID) is selected from the group consisting of:

Ac-Nle-c[Asp-Pro-dPhe-transPro(guan)-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 231);

Ac-Nle-c[Asp-Pro-dPhe-cisPro(guan)-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 232);

Ac-Nle-c[Asp-Pro-dPhe-His-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 425),

wherein c represents cyclization through $R^2$ and $R^7$ via a lactam bond.

**[0510]** In some embodiments of the sequence of any one of Formulae (I)-(ID), $R^6$ is Trp. Alternatively, in some embodiments, $R^6$ is absent or an amino acid other than Trp. In some embodiments, when $R^6$ is an amino acid other than Trp, $R^6$ is selected from dTrp, Aia, Aba, Ata, Nal(1'), and Phe. In some embodiments, $R^1$ is Ac-Nle, $R^2$ is Asp, $R^3$ is Pro, $R^4$ is dPhe, $R^5$ is Arg, $R^6$ is an amino acid other than Trp, $R^7$ is Lys, and $Y^1$ and $Y^2$ are each

independently dVal or dPro. In some embodiments, the sequence of any one of Formulae (I)-(ID) is selected from the group consisting of:

Ac-Nle-c[Asp-Pro-dPhe-Arg-dTrp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 187);

Ac-Nle-c[Asp-Pro-dPhe-Arg-Aia-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 233);

Ac-Nle-c[Asp-Pro-dPhe-Arg-Aba-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 234);

Ac-Nle-c[Asp-Pro-dPhe-Arg-Ata-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 235);

Ac-Nle-c[Asp-Pro-dPhe-Arg-Nal(1')-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 427); and

Ac-Nle-c[Asp-Pro-dPhe-Arg-Phe-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 429),

wherein c represents cyclization through $R^2$ and $R^7$ via a lactam bond.

**[0511]** In some embodiments of the sequence of any one of Formulae (I)-(ID), $R^4$ is dPhe. In some embodiments, $R^4$ is a derivative of dPhe. In some embodiments, when $R^4$ is a derivative of dPhe, $R^4$ is p(Cl)dPhe p(Br)dPhe, or p(F)dPhe.

**[0512]** In some embodiments, $R^4$ is p(F)dPhe. In some embodiments, $R^1$ is Ac-Nle, $R^2$ is Cys, dCys, or Asp, $R^3$ is Pro, His, dGln, or dTyr, $R^4$ is p(F)dPhe, $R^5$ is Arg or His, $R^6$ is Trp or Nal(2'), and $R^7$ is Cys, dCys, or Lys. In some embodiments, $R^3$ is Pro, $R^4$ is p(F)dPhe, $R^5$ is Arg or His, and $R^6$ is Trp. In some embodiments, $Y^1$ and $Y^2$ are each independently selected from dVal, dTle, and dPro; $Y^3$ is absent, dVal, or dPro; and $Y^4$ is absent or is dPro. In some embodiments, the sequence of any one of Formulae (I)-(ID) is selected from the group consisting of:

Ac-Nle-c[Asp-Pro-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 218);

Ac-Nle-c[dCys-Pro-p(F)dPhe-Arg-Trp-Cys]-dVal-dPro-$NH_2$ (SEQ ID NO: 433);

Ac-Nle-c[dCys-Pro-p(F)dPhe-Arg-Trp-dCys]-dVal-dPro-$NH_2$ (SEQ ID NO: 434);

Ac-Ala-c[Asp-Pro-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 435);

Ac-dArg-c[Asp-Pro-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 436);

Ac-Arg-c[Asp-Pro-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 437);

Ac-Lys-c[Asp-Pro-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 438);

Ac-dLys-c[Asp-Pro-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 439);

Ac-His-c[Asp-Pro-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 440);

Ac-dHis-c[Asp-Pro-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 441);

Ac-Nle-Nle-c[Asp-Pro-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 442);

Ac-Nle-c[Asp-Pro-p(F)dPhe-His-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 443);

Ac-Nle-c[Asp-Pro-p(F)dPhe-Arg-Trp-Lys]-dTle-dTle-dVal-$NH_2$ (SEQ ID NO: 446);

Ac-Nle-c[Asp-Pro-p(F)dPhe-Arg-Trp-Lys]-dVal-dVal-dVal-dPro-$NH_2$ (SEQ ID NO: 447);

Ac-Nle-c[Asp-Pro-p(F)dPhe-Arg-Trp-Lys]-dPro-dVal-dPro-$NH_2$ (SEQ ID NO: 448);

Ac-Nle-c[Asp-Pro-p(F)dPhe-Arg-Trp-Lys]-dTle-dPro-$NH_2$ (SEQ ID NO: 449);

Ac-Nle-Nle-c[Asp-Pro-p(F)dPhe-Arg-Trp-Lys]-dTle-dPro-$NH_2$ (SEQ ID NO: 450);

Ac-Nle-Nle-c[Asp-Pro-p(F)dPhe-Arg-Trp-Lys]-dPro-dVal-dPro-$NH_2$ (SEQ ID NO: 451);

Ac-Ala-c[Asp-Pro-p(F)dPhe-Arg-Trp-Lys]-dTle-dPro-$NH_2$ (SEQ ID NO: 452);

Ac-dArg-c[Asp-Pro-p(F)dPhe-Arg-Trp-Lys]-dTle-dPro-$NH_2$ (SEQ ID NO: 453);

Ac-Arg-c[Asp-Pro-p(F)dPhe-Arg-Trp-Lys]-dTle-dPro-$NH_2$ (SEQ ID NO: 454);

Ac-Lys-c[Asp-Pro-p(F)dPhe-Arg-Trp-Lys]-dTle-dPro-$NH_2$ (SEQ ID NO: 455);

Ac-dLys-c[Asp-Pro-p(F)dPhe-Arg-Trp-Lys]-dTle-dPro-$NH_2$ (SEQ ID NO: 456);

Ac-His-c[Asp-Pro-p(F)dPhe-Arg-Trp-Lys]-dTle-dPro-$NH_2$ (SEQ ID NO: 457);

Ac-dHis-c[Asp-Pro-p(F)dPhe-Arg-Trp-Lys]-dTle-dPro-$NH_2$ (SEQ ID NO: 458);

Ac-Nle-c[Cys-His-p(F)dPhe-Arg-Trp-Cys]-dVal-dPro-$NH_2$ (SEQ ID NO: 459);

Ac-Nle-c[dCys-His-p(F)dPhe-Arg-Trp-Cys]-dVal-dPro-$NH_2$ (SEQ ID NO: 460);

Ac-Nle-c[dCys-His-p(F)dPhe-Arg-Trp-dCys]-dVal-dPro-$NH_2$ (SEQ ID NO: 461);

Ac-Nle-c[Asp-His-p(F)dPhe-Arg-Nal(2')-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 472);

Ac-Nle-c[Asp-dGln-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 492); and

Ac-Nle-c[Asp-dTyr-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 496),

wherein c represents cyclization through $R^2$ and $R^7$ via a lactam bond or a disulfide bond.

**[0513]** In some embodiments, $R^4$ is p(Cl)dPhe. In some embodiments, $R^2$ is dCys or Asp, $R^3$ is His, Aba, Aia, or Ata, $R^4$ is p(Cl)dPhe, $R^5$ is Arg, $R^6$ is Trp, and $R^7$ is dCys or Lys. In some embodiments, $R^1$ is Ac-Nle, Ac-dArg, Ac-Lys, Ac-dLys, Ac-His, Ac-dHis, or Nle. In some embodiments, $Y^1$ and $Y^2$ are each independently selected from dVal, dTle, and dPro; $Y^3$ is absent, dVal, or dPro; and $Y^4$ is absent or is dPro. In some embodiments, the sequence of any one of Formulae (I)-(ID) is selected from the group consisting of:

Ac-Nle-c[Asp-Aba-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 209);

Ac-Nle-c[Asp-Aia-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 210);

Ac-Nle-c[Asp-Ata-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 211);

Ac-Nle-c[dCys-His-p(Cl)dPhe-Arg-Trp-dCys]-dVal-dPro-$NH_2$ (SEQ ID NO: 499);

Ac-dArg-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 501);

Ac-Arg-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 502);

Ac-Lys-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 503);

Ac-dLys-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 504);

Ac-His-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 505);

Ac-dHis-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 506);

Ac-Nle-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dTle-dTle-dVal-$NH_2$ (SEQ ID NO: 511);

Ac-Nle-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dVal-dVal-dPro-$NH_2$ (SEQ ID NO: 512);

Ac-Nle-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dPro-dVal-dPro-$NH_2$ (SEQ ID NO: 513);

Ac-Nle-Nle-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dTle-dPro-$NH_2$ (SEQ ID NO: 515);

Ac-dArg-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dTle-dPro-$NH_2$ (SEQ ID NO: 518);

Ac-Arg-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dTle-dPro-$NH_2$ (SEQ ID NO: 519);

Ac-Lys-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dTle-dPro-$NH_2$ (SEQ ID NO: 520);

Ac-dLys-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dTle-dPro-$NH_2$ (SEQ ID NO: 521);

Ac-His-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dTle-dPro-$NH_2$ (SEQ ID NO: 522); and

Ac-dHis-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dTle-dPro-$NH_2$ (SEQ ID NO: 523),

wherein c represents cyclization through $R^2$ and $R^7$ via a lactam bond or a disulfide bond.

**[0514]** In some embodiments, $R^4$ is p(Br)dPhe. In some embodiments, $R^1$ is Ac-Nle, and the sequence is cyclized through a disulfide bond between $R^2$ and $R^7$. In some embodiments, the sequence of any one of Formulae (I)-(ID) is:

Ac-Nle-c[dCys-His-p(Br)dPhe-Arg-Trp-Cys]-dVal-dPro-$NH_2$ (SEQ ID NO: 536); or

Ac-Nle-c[dCys-His-p(Br)dPhe-Arg-Trp-dCys]-dVal-dPro-$NH_2$ (SEQ ID NO: 537),

wherein c represents cyclization through $R^2$ and $R^7$ via a disulfide bond.

**[0515]** In some embodiments of the sequence of any one of Formulae (I)-(ID), $Y^1$ is dVal and $Y^2$ is dPro. Alternatively, in some embodiments, $Y^1$ is an amino acid other than dVal and $Y^2$ is an amino acid other than dPro. In some embodiments, $Y^1$ is dVal and $Y^2$ is an amino acid other than dPro. In some embodiments, $Y^1$ is an amino acid other than dVal and $Y^2$ is dPro.

**[0516]** In some embodiments of the sequence of any one of Formulae (I)-(ID), $Y^1$ is dVal, $Y^2$ is dPro, and the C-terminus is modified by $NH_2$. In some embodiments, Y1 is an amino acid other than dVal, $Y^2$ is an amino acid other than dPro, and the C-terminus is modified by $NH_2$. In some embodiments, $Y^1$ is dVal, $Y^2$ is an amino acid other than dPro, and the C-terminus is modified by $NH_2$. In some embodiments, $Y^1$ is an amino acid other than dVal, $Y^2$ is dPro, and the C-terminus is modified by $NH_2$. In some embodiments, $Y^1$ is dVal, $Y^2$ is dPro, and the C-terminus is unmodified.

**[0517]** In embodiments of any one of Formulae (I)-(ID) when $Y^1$ is an amino acid other than dVal, then $Y^1$ is selected from dThr, dPro, Val, β-Val, Hyp, dHyp, Pro, β-Pro, Ala, dAla, Gly, Asp, Arg, Asn, dAsp, dArg, dAsn, Lys, dLys, and dTle. In embodiments of Formula (IB) when $Y^2$ is an amino acid other than dPro, then $Y^2$ is selected from dThr, dVal, Val, β-Val, Hyp, dHyp, Pro, β-Pro, Ala, dAla, Gly, Asp, Arg, Asn, dAsp, dArg, dAsn, and dTle.

**[0518]** In some embodiments of the sequence of any one of Formulae (I)-(ID) when $Y^3$ is present and $Y^4$-$Y^8$ are absent, then each of $Y^1$, $Y^2$, and $Y^3$ are independently selected from

dThr, dArg, Arg, dLys, Lys, Val, Pro, dVal, and dPro. In some embodiments of the sequence of Formula (IB) when $Y^3$ and $Y^4$ are present and $Y^5$-$Y^8$ are absent, then each of $Y^1$, $Y^2$, $Y^3$, and $Y^4$ are independently selected from dLys, Lys, Asp, dAsp, dVal, and dPro. In some embodiments of the sequence of any one of Formulae (I)-(ID) when $Y^3$-$Y^5$ are present and $Y^6$-$Y^8$ are absent, then each of $Y^1$-$Y^5$ are independently selected from dVal and dPro. In some embodiments of the sequence of any one of Formulae (I)-(ID) when $Y^3$-$Y^6$ are present and $Y^7$-$Y^8$ are absent, then each of $Y^1$-$Y^6$ are independently selected from dVal and dPro. In some embodiments of the sequence of any one of Formulae (I)-(ID) when $Y^3$-$Y^7$ are present and $Y^8$ is absent, then each of $Y^1$-$Y^7$ are independently selected from dVal and dPro. In some embodiments of the sequence of any one of Formulae (I)-(ID) when $Y^3$-$Y^7$ are present, then each of $Y^1$-$Y^7$ are independently selected from dVal and dPro.

**[0519]** Inclusion of one or more C-terminal residues, e.g., $Y^1$-$Y^7$, in the non-naturally occurring melanocortin analog of the present technology may enhance transport across the epithelium, the blood-brain barrier, and or the gastrointestinal tract. For example, peptides comprising a C-terminus of dVal-dPro may have enhanced transport across the blood-brain barrier, relative to the same peptide without the dVal-dPro terminus. Accordingly, various C-terminal residue combinations provide enhanced deliverability and bioavailability of the present melanocortin analogs. In some embodiments, the C-terminus is dVal-dPro. Alternatively, in some embodiments, the C-terminus is not dVal-dPro. In some embodiments, $R^1$ is Ac-Nle, $R^2$ is Asp, $R^3$ is Pro, $R^4$ is dPhe, $R^5$ is Arg, $R^6$ is Trp, $R^7$ is Lys, and the C-terminus is not dVal-dPro. In some embodiments, the sequence of Formula (IB) is selected from the group consisting of:

Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-Val-Pro-$NH_2$ (SEQ ID NO: 573);

Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-Hyp-$NH_2$ (SEQ ID NO: 574);

Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dHyp-$NH_2$ (SEQ ID NO: 575);

Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-Val-$NH_2$ (SEQ ID NO: 576);

Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-Pro-$NH_2$ (SEQ ID NO: 577);

Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-Arg-$NH_2$ (SEQ ID NO: 578);

Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dArg-$NH_2$ (SEQ ID NO: 579);

Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dArg-dPro-$NH_2$ (SEQ ID NO: 580);

Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-Arg-$NH_2$ (SEQ ID NO: 581);

Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dArg-$NH_2$ (SEQ ID NO: 582);

Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-Lys-Pro-Val-$NH_2$ (SEQ ID NO: 583);

Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dLys-dPro-$NH_2$ (SEQ ID NO: 584);

Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-Lys-Val-Pro-$NH_2$ (SEQ ID NO: 585);

Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-Lys-dVal-dPro-$NH_2$ (SEQ ID NO: 586);

Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dLys-dVal-dPro-$NH_2$ (SEQ ID NO: 587);

Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-Arg-Pro-Val-$NH_2$ (SEQ ID NO: 588);

Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-Arg-Val-Pro-$NH_2$ (SEQ ID NO: 589);

Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dArg-dVal-dPro-$NH_2$ (SEQ ID NO: 590);

Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dTle-dPro-$NH_2$ (SEQ ID NO: 591);

Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dTle-dTle-dPro-$NH_2$ (SEQ ID NO: 592);

Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dTle-dTle-dVal-$NH_2$ (SEQ ID NO: 593);

Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dTle-$NH_2$ (SEQ ID NO: 594);

Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dVal-dPro-$NH_2$ (SEQ ID NO: 595);

Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dPro-dVal-dPro-$NH_2$ (SEQ ID NO: 596);

Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dVal-dVal-dPro-$NH_2$ (SEQ ID NO: 597);

Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-dVal-dPro-$NH_2$ (SEQ ID NO: 598);

Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dVal-dVal-dVal-dVal-dVal-dPro-$NH_2$ (SEQ ID NO: 599);

Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-Trp-$NH_2$ (SEQ ID NO: 600);

Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-Lys-dPro-dVal-$NH_2$ (SEQ ID NO: 601);

Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dAla-dAla-$NH_2$ (SEQ ID NO: 602);

Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-Asp-$NH_2$ (SEQ ID NO: 603);

Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dHyp-$NH_2$ (SEQ ID NO: 604);

Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dAsn-$NH_2$ (SEQ ID NO: 605);

Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-Asp-$NH_2$ (SEQ ID NO: 606);

Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-Asn-dPro-$NH_2$ (SEQ ID NO: 607);

Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-Hyp-$NH_2$ (SEQ ID NO: 608);

Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-Ala-Ala-$NH_2$ (SEQ ID NO: 609);

Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-Gly-Gly-$NH_2$ (SEQ ID NO: 610);

Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-Asp-dPro-$NH_2$ (SEQ ID NO: 611);

Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dAsn-dPro-$NH_2$ (SEQ ID NO: 612);

Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-Asn-$NH_2$ (SEQ ID NO: 613);

Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dAsp-$NH_2$ (SEQ ID NO: 614);

Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dAsn-$NH_2$ (SEQ ID NO: 615);

Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-Lys-dPro-$NH_2$ (SEQ ID NO: 616);

Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dPro-dVal-OH (SEQ ID NO: 617);

Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dThr-dPro-dThr-$NH_2$ (SEQ ID NO: 618);

Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dThr-dPro-dThr-OH (SEQ ID NO: 619);

Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dPro-dVal-$NH_2$ (SEQ ID NO: 620);

Ac-Nle-c[dAsp-Pro-dPhe-Arg-Trp-dLys]-dPro-dVal-$NH_2$ (SEQ ID NO: 622);

Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-βPro-$\beta^2$Val-$NH_2$ (SEQ ID NO: 623);

Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-βPro-$\beta^3$Val-$NH_2$ (SEQ ID NO: 624);

Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-$\beta^2$Val-βPro-$NH_2$ (SEQ ID NO: 625);

Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-$\beta^3$Val-βPro-$NH_2$ (SEQ ID NO: 626); and

Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-βPro-βPro-$NH_2$ (SEQ ID NO: 627),

wherein c represents cyclization through $R^2$ and $R^7$ via a lactam bond.

**[0520]** In some embodiments of the sequence of any one of Formulae (I)-(ID), $X^1$ is present and is Ac-Nle and $R^1$ is present and is Nle. In some embodiments, $X^2$ is present and is Nle. In some embodiments, $X^3$ is present and is Nle. In some embodiments, when one or more of $X^1$-$X^3$ is present, $R^1$ is Nle, $R^2$ is Asp, $R^3$ is Pro, $R^4$ is dPhe, $R^5$ is Arg, $R^6$ is Trp, and $R^7$ is Lys. In some embodiments, the sequence of any one of Formulae (I)-(ID) is selected from the group consisting of:

Ac-Nle-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 628);

Ac-Nle-Nle-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 629); and

Ac-Nle-Nle-Nle-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 630),

**[0521]** wherein c represents cyclization through $R^2$ and $R^7$ via a lactam bond.

**[0522]** In some embodiments, $R^1$ is an amino acid other than Ac-Nle and the C-terminus is not dVal-dPro. In such embodiments, $R^2$ is Asp, $R^3$ is Pro, $R^4$ is dPhe, $R^5$ is Arg, $R^6$ is Trp, and $R^7$ is Lys. In some embodiments, $X^1$ is present and is Nle. In other embodiments, $X^1$ is absent. In some embodiments, the C-terminus comprises $Y^1$ and $Y^2$, where $Y^1$ is selected from dArg, dLys, dTle, and dVal and $Y^2$ is selected from dPro and dHyp. In other embodiments, the C-terminus comprises $Y^1$-$Y^3$, where $Y^1$-$Y^3$ are each independently selected from dArg, dLys, dPro, and dVal. In still other embodiments, the C-terminus comprises $Y^1$-$Y^4$, where $Y^1$-$Y^4$ are each independently dVal or dPro. In some embodiments, the sequence of Formula (I) is selected from the group consisting of:

Ac-Arg-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dArg-dVal-dPro-$NH_2$ (SEQ ID NO: 631);

Ac-dLys-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dLys-dVal-dPro-$NH_2$ (SEQ ID NO: 632);

Ac-Lys-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dArg-dPro-$NH_2$ (SEQ ID NO: 633);

Ac-His-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dLys-dPro-$NH_2$ (SEQ ID NO: 634);

Ac-dHis-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dHyp-$NH_2$ (SEQ ID NO: 635);

Ac-Orn-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dTle-dPro-$NH_2$ (SEQ ID NO: 636);

Ac-dOrn-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dVal-dVal-dPro-$NH_2$ (SEQ ID NO: 637);

Ac-Nle-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dTle-dPro-$NH_2$ (SEQ ID NO: 638);

Ac-Ala-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dTle-dPro-$NH_2$ (SEQ ID NO: 640);

Ac-dArg-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dTle-dPro-$NH_2$ (SEQ ID NO: 641);

Ac-Arg-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dTle-dPro-$NH_2$ (SEQ ID NO: 642);

Ac-Lys-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dTle-dPro-$NH_2$ (SEQ ID NO: 643);

Ac-dLys-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dTle-dPro-$NH_2$ (SEQ ID NO: 644);

Ac-His-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dTle-dPro-$NH_2$ (SEQ ID NO: 645); and

Ac-dHis-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dTle-dPro-$NH_2$ (SEQ ID NO: 646),

wherein c represents cyclization through $R^2$ and $R^7$ via a lactam bond.

**[0523]** In some embodiments, the non-naturally occurring melanocortin analog comprises a sequence of Formula (I). In some embodiments, the non-naturally occurring melanocortin analog comprises any one of the sequences of SEQ ID NOs: 8, 187, 198, 207-218, 226, 231-235, 281, 291, 294-296, 298-322, 324, 351-355, 358-362, 364, 366-368, 371-375, 381-395, 399, 403-417, 419, 421-425, 427, 429, 433-443, 446-461, 472, 492, 496, 499-506, 511-513, 515, 518-523, 536-537, 573-599, 600-620, 622-646.

**[0524]** In some embodiments, the non-naturally occurring melanocortin analog comprises a sequence of Formula (IA). In some embodiments, the non-naturally occurring melanocortin analog comprises any one of the sequences of SEQ ID NOs: 187, 212, 218, 226, 291, 295, 298-322, 324, 351-355, 358-360, 362, 364, 366-368, 371-375, 381-395, 399, 403-417, 419, 421-425, 427, 429, 433-443, 446-461, 472, 492, 496, 499-506, 511-513, 515, 518-523, 536-537, 573-598, 600-646.

**[0525]** In some embodiments, the non-naturally occurring melanocortin analog comprises a sequence of Formula (IB). In some embodiments, the non-naturally occurring melanocortin analog comprises any one of the sequences of SEQ ID NOs: 187, 218, 231-235, 291, 295, 298-322, 351-353, 425, 427, 429, 433-443, 446-458, 573-599, 600-620, 622-646.

**[0526]** In some embodiments, the non-naturally occurring melanocortin analog comprises a sequence of Formula (IC). In some embodiments, the non-naturally occurring melanocortin analog comprises any one of the sequences of SEQ ID NOs: 226, 383-393, 399, 403-417.

**[0527]** In some embodiments, the non-naturally occurring melanocortin analog comprises a sequence of Formula (ID). In some embodiments, the non-naturally occurring melanocortin analog comprises any one of the sequences of SEQ ID NOs: 209-211, 499, 501-506, 511-513, 515, 518-523.

**[0528]** The non-naturally occurring melanocortin analogs of any one of Formulae (I)-(ID) may be an agonist on one melanocortin receptor and an antagonist on another melanocortin receptor. For example, a non-naturally occurring melanocortin analog of any one of Formulae (I)-(ID) may be an agonist on the melanocortin 4 receptor and an antagonist on the melanocortin 3 receptor. In some embodiments the non-naturally occurring melanocortin analog of any one of Formulae (I)-(ID) and is full agonist on the melanocortin 4 receptor and a full antagonist on the melanocortin 3 receptor. In other embodiments the non-naturally occurring melanocortin analog of any one of Formulae (I)-(ID) and is full agonist on the melanocortin 4 receptor and a partial antagonist on the melanocortin 3 receptor. In still other embodiments the non-naturally occurring melanocortin analog of any one of Formulae (I)-(ID) and is full agonist on the melanocortin 4 receptor and has no activity on the melanocortin 3 receptor.

*Non-Naturally Occurring Melanocortin Analog Synthesis*

**[0529]** The non-naturally occurring melanocortin analogs of the present technology may be readily synthesized by any known conventional procedure for the formation of a peptide linkage between amino acids. Such conventional procedures include, for example, any solution phase procedure permitting a condensation between the free alpha amino group of an amino acid or residue thereof having the carboxyl group or other reactive groups protected and the free primary carboxyl group of another amino acid or residue thereof having the amino group or other reactive groups protected. In an exemplary procedure, the peptides of the present technology may be synthesized by solid-phase synthesis and purified according to methods known in the art. Any of a number of well-known procedures

utilizing a variety of resins and reagents may be used to prepare the peptides of the present technology.

**[0530]** The process for synthesizing the peptides may be carried out by a procedure whereby each amino acid in the desired sequence is added one at a time in succession to another amino acid or residue thereof or by a procedure whereby peptide fragments with the desired amino acid sequence are first synthesized conventionally and then condensed to provide the desired peptide. The resulting peptide is then cyclized to yield a cyclic peptide.

**[0531]** Solid phase peptide synthesis methods are well known and practiced in the art. In such methods, the synthesis of peptides may be carried out by sequentially incorporating the desired amino acid residues one at a time into the growing peptide chain according to the general principles of solid phase methods. These methods are disclosed in numerous references, including Merrifield, Angew Chem. 24:799-810 (1985) and Barany et al., The Peptides, Analysis, Synthesis and Biology, Vol. 2, Gross E. and Meienhofer J., Eds. Academic Press 1-284 (1980).

**[0532]** In chemical syntheses of peptides, reactive side chain groups of the various amino acid residues are protected with suitable protecting groups, which prevent a chemical reaction from occurring at that site until the protecting group is removed. Also common is the protection of the alpha amino group of an amino acid residue or fragment while that entity reacts at the carboxyl group, followed by the selective removal of the alpha amino protecting group to allow a subsequent reaction to take place at that site. Specific protecting for solid phase synthesis methods and solution phase synthesis methods groups are known to those having ordinary skill in the art.

**[0533]** Alpha amino groups may be protected by a suitable protecting group, including a urethane-type protecting group, such as benzyloxycarbonyl (Z) and substituted benzyloxycarbonyl, such as p-chlorobenzyloxycarbonyl, p-nitrobenzyloxycarbonyl, p-bromobenzyloxycarbonyl, p-biphenyl-isopropoxycarbonyl, 9-fluorenylmethoxycarbonyl (Fmoc) and p-methoxybenzyloxycarbonyl (Moz); aliphatic urethane-type protecting groups, such as t-butyloxycarbonyl (Boc), diisopropylmethoxycarbonyl, isopropoxycarbonyl, and allyloxycarbonyl. Fmoc is useful for alpha amino protection.

**[0534]** Guanidino groups may be protected by a suitable protecting group, such as nitro, p-toluenesulfonyl (Tosyl), Z, pentamethylchromanesulfonyl (Pmc), adamantyloxycarbonyl, pentamethyldihydrobenzofuran-5-sulfonyl (Pbf) and Boc. Pmc is a useful protecting group for Arg.

**[0535]** Solid phase synthesis is commenced from the C-terminal end of the peptide by coupling a protected alpha amino acid to a suitable resin. Such starting material is prepared by attaching an alpha amino-protected amino acid by an ester linkage to a p-benzyloxybenzyl alcohol (Wang) resin or a 2-chlorotrityl chloride resin, by an amide bond between an Fmoc-Linker, such as p-[(R,S)-α-[1-(9H-fluor-en-9-yl)-methoxyformamido]-2,4-dimethyloxybenzyl]-phenoxyacetic acid (Rink linker) to a benzhydrylamine (BHA) resin, or by other means well known in the art. Fmoc-Linker-BHA resin supports are commercially available and generally used when feasible. The resins are carried through repetitive cycles as necessary to add amino acids sequentially. The alpha amino Fmoc protecting groups are removed under basic conditions. Piperidine, piperazine, diethylamine, or morpholine (20-40% v/v) in N,N-dimethylformamide (DMF) may be used for this purpose.

**[0536]** Following removal of the alpha amino protecting group, the subsequent protected amino acids are coupled stepwise in the desired order to obtain an intermediate, protected peptide-resin. The activating reagents used for coupling of the amino acids in the solid phase synthesis of the peptides are well known in the art. After the peptide is synthesized, if desired, the orthogonally protected side chain protecting groups may be removed using methods well known in the art for further derivatization of the peptide.

**[0537]** Reactive groups in a peptide may be selectively modified, either during solid phase synthesis or after removal from the resin. For example, peptides may be modified to obtain N-terminus modifications, such as acetylation, while on resin, or may be removed from the resin by use of a cleaving reagent and then modified. Methods for N-terminus modification, such as acetylation, and for C-terminus modification, such as amidation, are known in the art. Similarly, methods for modifying side chains of amino acids are well known to those skilled in the art of peptide synthesis. The choice of modifications made to reactive groups present on the peptide will be determined, in part, by the characteristics that are desired in the peptide.

**[0538]** The peptide may be cyclized prior to cleavage from the peptide resin. For cyclization through reactive side chain moieties, the desired side chains are deprotected, and the peptide suspended in a suitable solvent and a cyclic coupling agent added. Suitable solvents include, for example DMF, dichloromethane (DCM) or 1-methyl-2-pyrrolidone (NMP). Suitable cyclic coupling reagents include, for example, 2-(1H-benzotriazol-1-yl)-1,1,3,3-tetramethyluronium tetrafluoroborate (TBTU), 2-(1H-benzotriazol-1-yl)-1,1,3,3-tetramethyluronium hexafluorophosphate (HBTU), benzotriazole-1-yl-oxy-tris(dimethylamino)phosphoniumhexafluorophosphate (BOP), benzotriazole-1-yl-oxy-tris(pyrrolidino)phosphoniumhexafluorophosphate (PyBOP), 2-(7-aza-1H-benzotriazol-1-yl)-1,1,3,3-tetramethyluronium tetrafluoroborate (TATU), 2-(2-oxo-1 (2H)-pyridyl)-1,1,3,3-tetramethyluronium tetrafluoroborate (TPTU) or N,N′-dicyclohexylcarbodiimide/1-hydroxybenzotriazole (DCCI/HOBt). Coupling is convention initiated by use of a suitable base, such as N,N-diispropylethylamine (DIPEA), sym-collidine or N-methylmorpholine (NMM).

**[0539]** Following cleavage of peptides from the solid phase following their synthesis, the peptide may be purified by any number of methods, such as reverse phase high performance liquid chromatography (RP-HPLC), using a suitable column, such as a C18 column. Other methods of separation or purification, such as methods based on the size or charge of the peptide, may also be employed. Once purified, the peptide may be characterized by any number of methods, such as high-performance liquid chromatograph (HPLC), amino acid analysis, mass spectrometry, and the like.

*Salt Forms of Non-Naturally Occurring Melanocortin Analogs*

**[0540]** The non-naturally occurring melanocortin analog peptides of the present technology may be in the form of any salt. The term “pharmaceutically acceptable salts” refers to salts prepared from non-toxic bases or acids including inorganic or organic bases and inorganic or organic acids. Salts derived from inorganic bases include aluminum, ammonium, calcium, copper, ferric, ferrous, lithium, magnesium, manganic salts, manganous, potassium, sodium, zinc, and the like. Exemplary salts are the ammonium, calcium, lithium, magnesium, potassium, and sodium salts. Salts derived from organic non-toxic bases include salts of primary, secondary, and tertiary amines, substituted amines

including naturally occurring substituted amines, cyclic amines, and basic ion exchange resins, such as arginine, betaine, caffeine, choline, N,N′-dibenzylethylenediamine, diethylamine, 2-diethylaminoethanol, 2-dimethylaminoethanol, ethanolamine, ethylenediamine, N-ethyl-morpholine, N-ethylpiperidine, glucamine, glucosamine, histidine, hydrabamine, isopropylamine, lysine, methylglucamine, morpholine, piperazine, piperidine, polyamine resins, procaine, purines, theobromine, triethylamine, trimethylamine, tripropylamine, tromethamine, and the like.

**[0541]** When the peptides of the present technology are basic, acid addition salts may be prepared from non-toxic acids, including inorganic and organic acids. Such acids include acetic, benzenesulfonic, benzoic, camphorsulfonic, carboxylic, citric, ethanesulfonic, formic, fumaric, gluconic, glutamic, hydrobromic, hydrochloric, isethionic, lactic, maleic, malic, mandelic, methanesulfonic, malonic, mucic, nitric, pamoic, pantothenic, phosphoric, propionic, succinic, sulfuric, tartaric, p-toluenesulfonic acid, trifluoroacetic acid, and the like. Acid addition salts of the peptides of the present technology are prepared in a suitable solvent from the peptide and an excess of an acid, such as hydrochloric, hydrobromic, sulfuric, phosphoric, acetic, trifluoroacetic, citric, tartaric, maleic, succinic or methanesulfonic acid. The acetate salt form is especially useful. Where the peptides of the present technology include an acidic moiety, suitable salts may include alkali metal salts, such as sodium or potassium salts, or alkaline earth metal salts, such as calcium or magnesium salts.

***armaceutical Compositions, Formulations, and Administration***

**[0542]** The non-naturally occurring melanocortin analogs of the present technology may be present in a pharmaceutical composition.

**[0543]** In some embodiments, the non-naturally occurring melanocortin analog is present in the pharmaceutical composition in a concentration of 0.1 mg/mL to 50 mg/mL, relative to a total volume of the pharmaceutical composition. In some embodiments, the non-naturally occurring melanocortin analog is present in the pharmaceutical composition in a concentration of 0.1 mg/mL to 50 mg/mL, 0.5 mg/mL to 40 mg/mL, 1 mg/mL to 30 mg/mL, 2.5 mg/mL to 20 mg/mL, 5 mg/mL to 15 mg/mL, or 5 mg/mL to 10 mg/mL, relative to a total volume of the pharmaceutical composition. In some embodiments, the non-naturally

occurring melanocortin analog is present in the pharmaceutical composition in a concentration of 10 mg/mL, relative to a total volume of the pharmaceutical composition.

**[0544]** In some embodiments, the non-naturally occurring melanocortin analog is present in the pharmaceutical composition in a concentration of about 0.1 mg/mL to about 50 mg/mL, relative to a total volume of the pharmaceutical composition. In some embodiments, the non-naturally occurring melanocortin analog is present in the pharmaceutical composition in a concentration of about 0.1 mg/mL to about 50 mg/mL, about 0.5 mg/mL to about 40 mg/mL, about 1 mg/mL to about 30 mg/mL, about 2.5 mg/mL to about 20 mg/mL, about 5 mg/mL to about 15 mg/mL, or about 5 mg/mL to about 10 mg/mL, relative to a total volume of the pharmaceutical composition. In some embodiments, the non-naturally occurring melanocortin analog is present in the pharmaceutical composition in a concentration of about 10 mg/mL, relative to a total volume of the pharmaceutical composition.

**[0545]** In some embodiments, the non-naturally occurring melanocortin analog is present in the pharmaceutical composition in a concentration of at least 0.1 mg/mL to at least 50 mg/mL, relative to a total volume of the pharmaceutical composition. In some embodiments, the non-naturally occurring melanocortin analog is present in the pharmaceutical composition in a concentration of at least 0.1 mg/mL to at least 50 mg/mL, at least 0.5 mg/mL to at least 40 mg/mL, at least 1 mg/mL to at least 30 mg/mL, at least 2.5 mg/mL to at least 20 mg/mL, at least 5 mg/mL to at least 15 mg/mL, or at least 5 mg/mL to at least 10 mg/mL, relative to a total volume of the pharmaceutical composition. In some embodiments, the non-naturally occurring melanocortin analog is present in the pharmaceutical composition in a concentration of at least 10 mg/mL, relative to a total volume of the pharmaceutical composition.

**[0546]** In some embodiments, the non-naturally occurring melanocortin analog is present in the pharmaceutical composition in a concentration of at least about 0.1 mg/mL to at least about 50 mg/mL, relative to a total volume of the pharmaceutical composition. In some embodiments, the non-naturally occurring melanocortin analog is present in the pharmaceutical composition in a concentration of at least about 0.1 mg/mL to at least about 50 mg/mL, at least about 0.5 mg/mL to at least about 40 mg/mL, at least about 1 mg/mL to

at least about 30 mg/mL, at least about 2.5 mg/mL to at least about 20 mg/mL, at least about 5 mg/mL to at least about 15 mg/mL, or at least about 5 mg/mL to at least about 10 mg/mL, relative to a total volume of the pharmaceutical composition. In some embodiments, the non-naturally occurring melanocortin analog is present in the pharmaceutical composition in a concentration of at least about 10 mg/mL, relative to a total volume of the pharmaceutical composition.

*Formulations*

**[0547]** The pharmaceutical composition comprising the non-naturally occurring melanocortin analog may be formulated for intraperitoneal, intravenous, parenteral, depot, subcutaneous, intramuscular, intracerebroventricular, intranasal, or oral administration. In some embodiments, the pharmaceutical composition comprising the non-naturally occurring melanocortin analog is formulated for subcutaneous administration. In some embodiments, the pharmaceutical composition comprising the non-naturally occurring melanocortin analog is formulated for oral administration. In some embodiments, the pharmaceutical composition comprising the non-naturally occurring melanocortin analog is formulated for depot administration.

**[0548]** In some embodiments, the pharmaceutical composition further comprises a pharmaceutical salt. Any pharmaceutical salt known in the art may be included in the pharmaceutical composition.

**[0549]** Pharmaceutical compositions comprising the non-naturally occurring melanocortin analog may be administered using any means known in the art, including orally, rectally, vaginally, ocularly, intranasally, topically, parenterally, or by injection. If administered by injection, the injection may be intravenous (IV), subcutaneous (SC), intramuscular (IM), intraperitoneal (IP), intracerebroventricular (ICV), or other means known in the art. Compositions administered by injection may be formulated for depot injection. Pharmaceutical compositions may be formulated by any means known in the art, including but not limited to formulation as tablets, capsules, caplets, suspensions, powders, lyophilized preparations, suppositories, pessaries, ocular drops, skin patches, orally soluble formulations, enteric formulations, solutions sprays, aerosols and the like, and may be mixed and formulated with buffers, binders, excipients, stabilizers, lubricants, oils, adjuvants,

antioxidants and other agents known in the art. In general, any route of administration by which the compositions are introduced across an epidermal layer of cells may be employed. Administration includes topical delivery. Administration includes delivery across the epithelium. Administration includes delivery through the gastrointestinal tract. Administration includes delivery across the blood brain barrier. Administration includes delivery through mucous membranes, buccal administration, ophthalmic administration, oral administration, dermal administration, inhalation administration, nasal administration, urethral administration, vaginal administration, rectal administration, and the like.

**[0550]** In order to facilitate delivery of the active ingredients, to enhance dispersion, solubility, and stability of the active ingredients, and/or to reduce adverse injection site reactions, the pharmaceutical composition may further comprise one or more pharmaceutically acceptable carriers and/or excipients.

**[0551]** The pharmaceutical composition may comprise one or more pharmaceutically acceptable carriers and/or excipients such as, for example, buffers, binders, excipients, stabilizers, lubricants, oils, adjuvants, and antioxidants. For example, when the pharmaceutical composition is formulated for subcutaneous administration, the one or more pharmaceutically acceptable carriers and/or excipients may comprise water.

**[0552]** In some embodiments, the pharmaceutical composition contains 0.1 to 99.9999 wt.%, 1 to 99.999 wt.%, 5 to 99.99 wt.%, 10 to 99.9 wt.%, 15 to 99 wt.%, 20 to 90 wt.%, 30 to 85 wt.%, 40 to 80 wt.%, 50 to 75 wt.%, or 60 to 70 wt.% of the one or more pharmaceutically acceptable carriers and/or excipients relative to a total weight of the pharmaceutical composition.

**[0553]** In some embodiments, the pharmaceutical composition contains 0.1 to 99.9999 wt.%, 1 to 99.999 wt.%, 5 to 99.99 wt.%, 10 to 99.9 wt.%, 15 to 99 wt.%, 20 to 90 wt.%, 30 to 85 wt.%, 40 to 80 wt.%, 50 to 75 wt.%, or 60 to 70 wt.% of the one or more pharmaceutically acceptable carriers and/or excipients relative to a total weight of the pharmaceutical composition.

**[0554]** In some embodiments, the pharmaceutical composition contains at least 0.1 to at least 99.9999 wt.%, at least 1 to at least 99.999 wt.%, at least 5 to at least 99.99 wt.%, at

least 10 to at least 99.9 wt.%, at least 15 to at least 99 wt.%, at least 20 to at least 90 wt.%, at least 30 to at least 85 wt.%, at least 40 to at least 80 wt.%, at least 50 to at least 75 wt.%, or at least 60 to at least 70 wt.% of the one or more pharmaceutically acceptable carriers and/or excipients relative to a total weight of the pharmaceutical composition.

**[0555]** In some embodiments, the pharmaceutical composition contains at least about 0.1 to at least about 99.9999 wt.%, at least about 1 to at least about 99.999 wt.%, at least about 5 to at least about 99.99 wt.%, at least about 10 to at least about 99.9 wt.%, at least about 15 to at least about 99 wt.%, at least about 20 to at least about 90 wt.%, at least about 30 to at least about 85 wt.%, at least about 40 to at least about 80 wt.%, at least about 50 to at least about 75 wt.%, or at least about 60 to at least about 70 wt.% of the one or more pharmaceutically acceptable carriers and/or excipients relative to a total weight of the pharmaceutical composition.

**[0556]** Any pharmaceutically acceptable carriers and/or excipients known in the art may be included in the pharmaceutical composition. Non-limiting examples of pharmaceutically acceptable carriers and/or excipients include buffers, binders, excipients, stabilizers, lubricants, oils, adjuvants, preservatives, lipids, and antioxidants. The pharmaceutical composition may comprise any combination of the one or more pharmaceutically acceptable carriers and/or excipients previously described in relation to the first and pharmaceutical compositions. In some embodiments, the one or more pharmaceutically acceptable carriers and/or excipients comprise water.

**[0557]** To facilitate delivery of the non-naturally occurring melanocortin analog, the pharmaceutical composition may comprise one or more pharmaceutically acceptable carriers and/or excipients. Other pharmaceutically acceptable carriers and/or excipients may be included in the pharmaceutical composition to enhance dispersion, solubility, and stability of the non-naturally occurring melanocortin analog, and to reduce adverse injection site reactions.

**[0558]** In some embodiments, the one or more pharmaceutically acceptable carriers and/or excipients are isotonic.

**[0559]** In some embodiments, the salt is present in the pharmaceutical composition in a concentration of about 0.1 mg/mL to about 50 mg/mL, about 1 mg/mL to about 25 mg/mL, or about 5 mg/mL to about 10 mg/mL, relative to a total volume of the composition.

**[0560]** In some embodiments, the salt is present in the pharmaceutical composition in a concentration of at least 0.1 mg/mL to at least 50 mg/mL, at least 1 mg/mL to at least 25 mg/mL, or at least 5 mg/mL to at least 10 mg/mL, relative to a total volume of the composition

**[0561]** In order to achieve a desirable tonicity, the pharmaceutical composition may further include a salt such as sodium chloride, sodium succinate, sodium sulfate, potassium chloride, magnesium chloride, magnesium sulfate, and calcium chloride.

**[0562]** In some embodiments, the salt is present in the pharmaceutical composition in a concentration of at least about 0.1 mg/mL to at least about 50 mg/mL, at least about 1 mg/mL to at least about 25 mg/mL, or at least about 5 mg/mL to at least about 10 mg/mL, relative to a total volume of the composition.

**[0563]** Pharmaceutically acceptable carriers and/or excipients that may be included in the pharmaceutical composition generally include a pH buffered aqueous solution comprising one or more of the following components: (a) sodium acetate, (b) Tris, and (c) water. In some embodiments, all components are compatible with the non-naturally occurring melanocortin analog (i.e., do not react or cause the non-naturally occurring melanocortin analog to react) and are homogeneously dispersed or dissolved uniformly in the composition.

**[0564]** In the pH buffered solution of the pharmaceutical composition, the water may act as a diluent and include, without limitation, water for injection (WFI), sterile water, bacteriostatic water for injection (BWFI), distilled water, bidistilled water, deionized water, deionized distilled water, and reverse osmosis water. In some embodiments, the water present in the pH buffered aqueous solution is water for injection.

**[0565]** In some embodiments, the pharmaceutical composition includes water in an amount of about 1 wt% to about 90 wt%, about 10 wt% to about 75 wt%, or about 25 wt% to about 50 wt%, relative to a total weight of the composition.

**[0566]** In some embodiments, the pharmaceutical composition includes water in an amount of at least 1 wt% to at least 90 wt%, at least 10 wt% to at least 75 wt%, or at least 25 wt% to at least 50 wt%, relative to a total weight of the composition.

**[0567]** In some embodiments, the pharmaceutical composition includes water in an amount of at least about 1 wt% to at least about 90 wt%, at least about 10 wt% to at least about 75 wt%, or at least about 25 wt% to at least about 50 wt%, relative to a total weight of the composition. In some embodiments, sodium acetate is present in the pharmaceutical composition in a concentration of 0.5 mg/mL to 50 mg/mL, relative to a total volume of the composition. For example, sodium acetate may be present in the pharmaceutical composition in a concentration of 0.5 mg/mL to 50 mg/mL, 1 mg/mL to 40 mg/mL, 2 mg/mL to 30 mg/mL, 4 mg/mL to 20 mg/mL, 5 mg/mL to 15 mg/mL, 6 mg/mL to 12 mg/mL, or 8 mg/mL to 10 mg/mL, relative to a total volume of the composition.

**[0568]** In some embodiments, sodium acetate is present in the pharmaceutical composition in a concentration of about 6 mg/mL to about 8 mg/mL, relative to a total volume of the composition. For example, sodium acetate may be present in the pharmaceutical composition in a concentration of 6 mg/mL, 6.5 mg/mL, 7 mg/mL, 7.1 mg/mL, 7.5 mg/mL, or 8 mg/mL, relative to a total volume of the composition.

**[0569]** In some embodiments, sodium acetate is present in the pharmaceutical composition in a molar concentration of 5 mM to 700 mM, relative to a total volume of the composition. For example, sodium acetate may be present in the pharmaceutical composition in a molar concentration of 5 mM to 700 mM, 10 mM to 600 mM, 20 mM to 500 mM, 30 mM to 400 mM, 40 mM to 300 mM, 50 mM to 200 mM, 60 mM to 100 mM, or 70 mM to 80 mM, relative to a total volume of the composition.

**[0570]** In some embodiments, sodium acetate is present in the pharmaceutical composition in a molar concentration of about 80 mM to about 100 mM, relative to a total volume of the composition. For example, sodium acetate may be present in the pharmaceutical composition in a molar concentration of 80 mM, 85 mM, 87 mM, 90 mM, 95 mM, or 100 mM, relative to a total volume of the composition.

**[0571]** The term "Tris" refers to tris(hydroxymethyl)aminomethane, which is also known as Tris buffer, Tris base, TRIS, tromethamine, tromethamine buffer, Trizma®, Trisamine, Trometamol, Tromethane, Trisaminol, or THAM. In some embodiments, Tris is present in the pharmaceutical composition in a concentration of 0.5 mg/mL to 50 mg/mL, relative to a total volume of the composition. For example, Tris may be present in the pharmaceutical composition in a concentration of 0.5 mg/mL to 50 mg/mL, 1 mg/mL to 40 mg/mL, 2 mg/mL to 30 mg/mL, 4 mg/mL to 20 mg/mL, 5 mg/mL to 15 mg/mL, 6 mg/mL to 12 mg/mL, or 8 mg/mL to 10 mg/mL, relative to a total volume of the composition.

**[0572]** In some embodiments, Tris is present in the pharmaceutical composition in a concentration of about 6 mg/mL to about 8 mg/mL, relative to a total volume of the composition. For example, Tris may be present in the pharmaceutical composition in a concentration of 6 mg/mL, 6.5 mg/mL, 7 mg/mL, 7.3 mg/mL, 7.6 mg/mL, or 8 mg/mL, relative to a total volume of the composition.

**[0573]** In some embodiments, Tris is present in the pharmaceutical composition in a molar concentration of 2 mM to 500 mM, relative to a total volume of the composition. For example, Tris may be present in the pharmaceutical composition in a molar concentration of 2 mM to 500 mM, 5 mM to 400 mM, 10 mM to 300 mM, 20 mM to 200 mM, 30 mM to 150 mM, 40 mM to 100 mM, 50 mM to 80 mM, or 60 mM to 70 mM, relative to a total volume of the composition.

**[0574]** In some embodiments, Tris is present in the pharmaceutical composition in a molar concentration of about 50 mM to about 70 mM, relative to a total volume of the composition. For example, Tris may be present in the pharmaceutical composition in a molar concentration of 50 mM, 55 mM, 60 mM, 65 mM, or 70 mM, relative to a total volume of the composition.

**[0575]** In some embodiments, the pH buffered aqueous solution provides the pharmaceutical composition with a pH equivalent or close to the physiological pH levels. This may reduce adverse injection site reactions and also provide the non-naturally occurring melanocortin analog with enhanced stability and resistance to aggregation and degradation.

**[0576]** In some embodiments, a weight ratio of sodium acetate to Tris is about 1:4 to about 4:1, about 2:7 to about 7:2, about 1:3 to about 3:1, about 2:5 to about 5:2, about 1:2 to about 2:1, about 2:3 to about 3:2, or about 1:1. In some embodiments, the weight ratio of sodium acetate to Tris is about 1:1.

**[0577]** In some embodiments, a weight ratio of the non-naturally occurring melanocortin analog to sodium acetate is about 1:1 to about 20:1, about 3:2 to about 15:1, about 2:1 to about 12:1, about 3:1 to about 10:1, about 4:1 to about 9:1, about 5:1 to about 8:1, or about 6:1 to about 7:1. In some embodiments, the weight ratio of the non-naturally occurring melanocortin analog to sodium acetate is about 7:1.

**[0578]** In some embodiments, a weight ratio of the non-naturally occurring melanocortin analog to Tris is about 1:1 to about 20:1, about 3:2 to about 15:1, about 2:1 to about 12:1, about 3:1 to about 10:1, about 4:1 to about 9:1, about 5:1 to about 8:1, or about 6:1 to about 7:1. In some embodiments, the weight ratio of the non-naturally occurring melanocortin analog to Tris is about 7:1.

**[0579]** In addition to sodium acetate and Tris, the pharmaceutical composition may include other buffering agents. Non-limiting examples of additional buffering agents include saline, phosphate, phosphoric acid, citrate, succinate, gluconate, histidine, acetic acid, ascorbate, tartartic acid, maleic acid, glycine, lactate, lactic acid, ascorbic acid, imidazole, bicarbonate, carbonic acid, succinic acid, sodium benzoate, benzoic acid, gluconate, edetate, malate, imidazole, and mixtures thereof. In some embodiments, the pharmaceutical composition comprises acetic acid as an additional buffering agent.

**[0580]** The pharmaceutical composition may further comprise one or more chelating agents. Suitable chelating agents include, but are not limited to edetate disodium dihydrate, calcium disodium edetate, sodium edetate, calcium versetamide sodium, calteridol, and diethylenetriaminepentaacetic acid. In some embodiments, the pharmaceutical composition further comprises edetate disodium dihydrate.

**[0581]** The pharmaceutical composition may further comprise a preservative agent. Exemplary preservative agents include, but are not limited to, ascorbic acid, cysteine hydrochloride, sodium bisulfate, sodium metabisulfite, sodium sulfite, ascorbyl palmitate,

butylated hydroxyanisole (BHA), butylated hydroxytoluene (BHT), lecithin, propyl gallate, phenol, m-cresol, benzyl alcohol, alpha-tocopherol, citric acid, ethylenediamine tetraacetic acid (EDTA), sorbitol, tartaric acid, phosphoric acid, benzalkonium chloride, phenoxyethanol, and methyl paraben. In some embodiments, when the pharmaceutical composition comprises a preservative agent, the preservative agent is phenol, benzyl alcohol, or a combination thereof.

**[0582]** If present in the pharmaceutical composition, the concentration of the preservative agent may range from 0.001 mg/mL to 50 mg/mL, 0.01 mg/mL to 25 mg/mL, 0.1 mg/mL to 10 mg/mL, or 1 mg/mL to 5 mg/mL, relative to a total volume of the composition.

**[0583]** The pharmaceutical composition may further comprise an emulsifier. Non-limiting examples of emulsifiers that may be included in the pharmaceutical composition include sodium carboxymethylcellulose, cetyl alcohol, glycerol monostearate, methylcellulose, and stearic acid. In some embodiments, when the pharmaceutical composition comprises an emulsifier, the emulsifier is sodium carboxymethylcellulose.

**[0584]** The pharmaceutical composition may further comprise a lipid. Lipids may enhance solubility and/or improve permeability of the non-naturally occurring melanocortin analog. In some embodiments, the lipid is a phospholipid. Non-limiting examples of phospholipids that may be included in the pharmaceutical composition include egg phosphatidylcholine, hydrogenated soybean phoshphaditylcholine, glycerophosphocholine, lecithin, and N-(carbonyl-methoxypolyethylene glycol 2000)-1,2-distearoyl-glycero-3-phosphoethanolamine sodium salt. In some embodiments, when the pharmaceutical composition comprises a lipid, the lipid is N-(carbonyl-methoxypolyethylene glycol 2000)-1,2-distearoyl-glycero-3-phosphoethanolamine sodium salt.

**[0585]** The pharmaceutical composition may further comprise a bulking agent. Inclusion of a bulking agent may increase the stability of the pharmaceutical composition. Non-limiting examples of bulking agents that may be included in the pharmaceutical composition include sucrose, lactose, trehalose, mannitol, sorbitol, glucose, raffinose, glycine, histidine, and polyvinyl pyrrolidone. In some embodiments, when the pharmaceutical composition comprises a bulking agent, the bulking agent is mannitol.

**[0586]** In some embodiments, the pharmaceutical composition is in the form of an aqueous solution or a suspension. In some embodiments, the pharmaceutical composition is in the form of an emulsion. In some embodiments, the pharmaceutical composition is in the form of an aqueous solution. In some embodiments, the pharmaceutical composition is in the form of an aqueous solution which is clear, colorless, and/or free of visible foreign matter.

**[0587]** In some embodiments, the pharmaceutical composition has a pH ranging from about 6.5 to about 8.5. In some embodiments, the pharmaceutical composition has a pH of about 6.5, 6.6, 6.7, 6.8, 6.9, 7.0, 7.1, 7.2, 7.3, 7.4, 7.5, 7.6, 7.7, 7.8, 7.9, 8.0, 8.1, 8.2, 8.3, 8.4, or 8.5.

**[0588]** In some embodiments, the pharmaceutical composition is basic and has a pH of about 7.1, 7.2, 7.3, 7.4, 7.5, 7.6, 7.7, 7.8, 7.9, 8.0, 8.1, 8.2, 8.3, 8.4, or 8.5. In some embodiments, the pharmaceutical composition has a pH ranging from about 7.3 to about 7.4. In some embodiments, the pharmaceutical composition has a pH of 7.3 or 7.4.

**[0589]** In some embodiments, the pharmaceutical composition has an osmolality ranging from 250 mOsm/kg to 350 mOsm/kg. For example, the pharmaceutical composition may have an osmolality ranging from 250 mOsm/kg to 360 mOsm/kg, 260 mOsm/kg to 340 mOsm/kg, 270 mOsm/kg to 330 mOsm/kg, 280 mOsm/kg to 320 mOsm/kg, 290 mOsm/kg to 310 mOsm/kg, or about 300 mOsm/kg. In some embodiments, the pharmaceutical composition has an osmolarity of about 250 mOsm/kg, about 260 mOsm/kg, about 270 mOsm/kg, about 280 mOsm/kg, about 290 mOsm/kg, about 300 mOsm/kg, about 310 mOsm/kg, about 320 mOsm/kg, about 330 mOsm/kg, about 340 mOsm/kg, about 350 mOsm/kg, or about 360 mOsm/kg. In some embodiments, the pharmaceutical composition has an osmolality ranging from about 275 mOsm/kg to about 330 mOsm/kg. In some embodiments, the pharmaceutical composition has an osmolality of about 279 mOsm/kg, about 314 mOsm/kg, or about 329 mOsm/kg.

**[0590]** In some embodiments, the pharmaceutical composition has a viscosity ranging from about 0.5 cP to about 5 cP. For example, the pharmaceutical composition may have a viscosity ranging from about 0.5 cP to about 5 cP, about 0.75 cP to about 4.5 cP, about 1.0 cP to about 4 cP, about 1.2 cP to about 3.5 cP, about 1.3 cP to about 3 cP, about 1.4 cP to

about 2.5 cP, about 1.5 cP to about 2 cP, or about 1.6 cP to about 1.8 cP. In some embodiments, the pharmaceutical composition has a viscosity of about 0.5 cP, 0.6 cP, 0.7 cP, 0.8 cP, 0.9 cP, 1.0 cP, 1.1 cP, 1.2 cP, 1.3 cP, 1.4 cP, 1.5 cP, 1.6 cP, 1.7 cP, 1.8 cP, 1.9 cP, or 2.0 cP. In some embodiments, the pharmaceutical composition has a viscosity of about 1.4 cP or about 1.6 cP.

**[0591]** In some embodiments, the pharmaceutical composition disclosed is formulated for parenteral administration, such as, for example, in the form of aqueous or non-aqueous isotonic sterile injection solutions or suspensions. The term "parenteral," as used herein, includes subcutaneous, intravenous, intraperitoneal, intramuscular, and intralesional, or infusion techniques.

**[0592]** When the pharmaceutical composition is formulated for parenteral administration (e.g., subcutaneous administration), the active ingredient(s) (e.g., the non-naturally occurring melanocortin analog) may be dissolved or suspended in the aforementioned carrier and/or excipient. Additional aqueous or non-aqueous carriers that may facilitate dissolution of the active ingredient include, but are not limited to, ethanol, benzyl alcohol, DMSO, polyethylene glycol, propylene glycol, corn oil, cottonseed oil, peanut oil, sesame oil, and/or various buffers.

**[0593]** In some embodiments, the pharmaceutical composition is formulated for parenteral administration (e.g., subcutaneous administration) and comprises a non-naturally occurring melanocortin analog in a concentration of about 0.001 nmol, 0.005 nmol, 0.01 nmol, 0.02 nmol, 0.05 nmol, 0.1 nmol, 0.25 nmol, 0.5 nmol, 1 nmol, 2.5 nmol, 5 nmol, 10 nmol, 20 nmol, 25 nmol, 50 nmol, 100 nmol, 250 nmol, 500 nmol, or 1000 nmol, or even more, depending on the specific peptide selected, the desired therapeutic response, the route of administration, the formulation and other factors known to those of skill in the art.

**[0594]** In some embodiments, the pharmaceutical composition is formulated for parenteral administration (e.g., subcutaneous administration) and comprises sodium acetate in a concentration of about 5 mM, 10 mM, 15 mM, 20 mM, 25 mM, 30 mM, 35 mM, 40 mM, 45 mM, 50 mM, 55 mM, 60 mM, 65 mM, 70 mM, 75 mM, 76 mM, 77 mM, 78 mM, 79 mM, 80 mM, 81 mM, 82 mM, 83 mM, 84 mM, 85 mM, 86 mM, 87 mM, 88 mM, 89 mM, 90 mM, 91 mM, 92 mM, 93 mM, 94 mM, 95 mM, 96 mM, 97 mM, 98 mM, 99 mM, 100 mM, 105 mM,

110 mM, 120 mM, 130 mM, 140 mM, 150 mM, 160 mM, 170 mM, 180 mM, 190 mM, or 200 mM.

**[0595]** In some embodiments, the pharmaceutical composition is formulated for parenteral administration (e.g., subcutaneous administration) and comprises Tris in a concentration of about 5 mM, 10 mM, 15 mM, 20 mM, 25 mM, 30 mM, 3 5mM, 40 mM, 45 mM, 50 mM, 55 mM, 60 mM, 65 mM, 70 mM, 75 mM, 80 mM, 85 mM, 90 mM, 95 mM, 100 mM, 105 mM, 110 mM, or 120 mM.

**[0596]** Alternatively, in some embodiments, the pharmaceutical composition is formulated for intranasal administration. When the pharmaceutical composition is formulated for intranasal administration, the composition may comprise one or more pharmaceutically acceptable carriers and/or excipients to facilitate delivery and enhance dispersion, solubility, and stability of the non-naturally occurring melanocortin analog.

**[0597]** The pharmaceutical composition may be formulated to be delivered by nose drop, spray device, or topical solution. In some embodiments, the pharmaceutical composition may be formulated as an aerosol, atomizer, inhalation, insufflation, metered-dose inhaler, or nebulizer. In some embodiments, the composition includes a propellant, such as hydrofluoroalkane.

**[0598]** When the pharmaceutical composition is formulated for intranasal administration, the active ingredient(s) (e.g., the non-naturally occurring melanocortin analog) may be dissolved or suspended in the one or more pharmaceutically acceptable carriers and/or excipients. Additional aqueous or non-aqueous carriers that may facilitate dissolution of the active ingredient include, but are not limited to, ethanol, benzyl alcohol, DMSO, polyethylene glycol, propylene glycol, corn oil, cottonseed oil, peanut oil, sesame oil, and/or various buffers.

**[0599]** In some embodiments, the pharmaceutical composition is formulated for intranasal administration and comprises the non-naturally occurring melanocortin analog in a concentration of about 0.001 nmol, 0.005 nmol, 0.01 nmol, 0.02 nmol, 0.05 nmol, 0.1 nmol, 0.25 nmol, 0.5 nmol, 1 nmol, 2.5 nmol, 5 nmol, 10 nmol, 20 nmol, 25 nmol, 50 nmol, 100 nmol, 250 nmol, 500 nmol, or 1000 nmol, or even more, depending on the specific peptide

selected, the desired therapeutic response, the route of administration, the formulation and other factors known to those of skill in the art.

**[0600]** In some embodiments, the pharmaceutical composition is formulated for intranasal administration and is configured to be administered using a spray device or nasal inhaler. The spray device or nasal inhaler may be configured to deliver about 1mg to about 100mg per spray. In some embodiments, the spray device or nasal inhaler is configured to deliver 1mg to 100mg, 5mg to 90mg, 10mg to 80mg, 15mg to 70mg, 20mg to 60mg, 25mg, to 50mg, or 30mg to 40mg per spray.

**[0601]** In some embodiments, the pharmaceutical composition is formulated for intranasal administration and has a pH approximating the normal pH range of the nasal fluid. Accordingly, in some embodiments, the pharmaceutical composition has a pH ranging from about 5.5 to about 6.5. In some embodiments, the pharmaceutical composition has a pH of about 5.5, 5.6, 5.7, 5.8, 5.9, 6.0, 6.1, 6.2, 6.3, 6.4, or 6.5.

**[0602]** Pharmaceutically acceptable carriers and/or excipients that may be included in the pharmaceutical composition formulated for intranasal administration may generally include (i) one or more antioxidants, (ii) one or more preservatives, (iii) one or more buffers, (iv) one or more tonicity adjustors, (v) one or more surfactants, (vi) flavor, (vii) propellants, and/or (viii) a vehicle or solvent. In some embodiments, all components are compatible with the non-naturally occurring melanocortin analog (i.e., do not react or cause the non-naturally occurring melanocortin analog to react) and are homogeneously dispersed or dissolved uniformly in the composition.

**[0603]** In some embodiments, the pharmaceutically acceptable carriers and/or excipients are isotonic to nasal fluids.

**[0604]** In order to achieve a desirable tonicity, the pharmaceutical composition formulated for intranasal administration may further include a salt such as sodium chloride, sodium succinate, sodium sulfate, potassium chloride, magnesium chloride, magnesium sulfate, and calcium chloride. In some embodiments, the salt is present in the pharmaceutical composition in a concentration of 0.1 mg/mL to 50 mg/mL, 1 mg/mL to 25 mg/mL, or 5 mg/mL to 10 mg/mL, relative to a total volume of the composition. In some

embodiments, the salt is sodium chloride and is present in a concentration of 0.9% by weight.

**[0605]** When the pharmaceutical composition is formulated for intranasal administration, the composition may comprise a pH buffered aqueous solution as previously described.

**[0606]** In some embodiments, the pharmaceutical composition is formulated for intranasal administration and comprises sodium acetate in a concentration of about 80 mM to about 100 mM. For example, sodium acetate may be present in the pharmaceutical composition in a molar concentration of 80 mM, 81 mM, 82 mM, 83 mM, 84 mM, 85 mM, 86 mM, 87 mM, 88 mM, 89 mM, 90 mM, 91 mM, 92 mM, 93 mM, 94 mM, 95 mM, 96 mM, 97 mM, 98 mM, 99 mM, or 100 mM.

**[0607]** In some embodiments, the pharmaceutical composition is formulated for intranasal administration and comprises Tris in a concentration of about 5 mM, 10 mM, 15 mM, 20 mM, 25 mM, 30 mM, 3 5mM, 40 mM, 45 mM, 50 mM, 55 mM, 60 mM, 65 mM, 70 mM, 75 mM, 80 mM, 85 mM, 90 mM, 95 mM, 100 mM, 105 mM, 110 mM, or 120 mM.

**[0608]** Additionally, when the pharmaceutical composition is formulated for intranasal administration, the composition may further comprise a phosphate, e.g., sodium phosphate. In some embodiments, the pharmaceutical composition is formulated for intranasal administration and comprises sodium phosphate in a molar concentration of about 5 mM to about 700 mM, relative to a total volume of the composition. For example, sodium phosphate may be present in the pharmaceutical composition in a molar concentration of 5 mM to 700 mM, 10 mM to 600 mM, 20 mM to 500 mM, 30 mM to 400 mM, 40 mM to 300 mM, 50 mM to 200 mM, 60 mM to 100 mM, or 70 mM to 80 mM, relative to a total volume of the composition.

**[0609]** In some embodiments, the pharmaceutical composition comprises one or more antioxidants. For example, the pharmaceutical composition may comprise ascorbic acid, cysteine, sodium metabisulfite, propyl gallate, butylated hydroxytoluene, and/or butylated hydroxyanisole.

**[0610]** In some embodiments, the pharmaceutical composition comprises a surfactant, such as a sorbitan ester.

**[0611]** In some embodiments, the pharmaceutical composition comprises a flavoring or scent, such as an aromatic oil.

**[0612]** In some embodiments, the non-naturally occurring melanocortin analog is solubilized or suspended in a solvent or vehicle. The solvent or vehicle may be purified water, ethyl alcohol, and/or propylene glycol. In some embodiments, the pharmaceutical composition comprises between 0.03 wt% and 1 wt% melanocortin analog solubilized or suspended in a solvent or vehicle. For example, the pharmaceutical composition may comprise the non-naturally occurring melanocortin analog in an amount of about 0.03 wt%, about 0.05 wt%, about 0.1 wt%, about 0.15 wt%, about 0.2 wt%, about 0.25 wt%, about 0.3 wt%, about 0.35 wt%, about 0.4 wt%, about 0.45 wt%, about 0.5 wt%, about 0.55 wt%, about 0.6 wt%, about 0.65 wt%, about 0.7 wt%, about 0.75 wt%, about 0.8 wt%, about 0.85 wt%, about 0.9 wt%, about 0.95 wt%, or about 1 wt%.

**[0613]** In some embodiments, the non-naturally occurring melanocortin analog is present in the pharmaceutical composition in a concentration of about 0.1 mg/mL to about 50 mg/mL, relative to a total volume of the composition. In some embodiments, the non-naturally occurring melanocortin analog is present in the pharmaceutical composition in a concentration of 0.1 mg/mL to 50 mg/mL, 0.5 mg/mL to 40 mg/mL, 1 mg/mL to 30 mg/mL, 2.5 mg/mL to 20 mg/mL, 5 g/mL to 15 mg/mL, or 5 mg/mL to 10 mg/mL, relative to a total volume of the pharmaceutical composition. Any of the non-naturally occurring melanocortin analogs and corresponding concentrations described previously with reference to the pharmaceutical composition may be present in the pharmaceutical composition at the same or substantially similar concentrations.

*Administration*

**[0614]** The pharmaceutical compositions of the present technology may be administered once monthly, once every three weeks, once every two weeks, once per week, twice per week, 3 times per week, 4 times per week, 5 times per week, once per day, twice per day, 3 times per day, 4 times per day, 5 times per day, or 10 times per day.

**[0615]** In some embodiments, the non-naturally occurring melanocortin analog is present in the pharmaceutical composition at a dose of about 5 mg to about 500 mg in a dose volume of about 1 mL to 20 mL, and wherein the administration is performed once monthly, once every three weeks, once every two weeks, once per week, twice per week, 3 times per week, 4 times per week, 5 times per week, once per day, twice per day, 3 times per day, 4 times per day, 5 times per day, or 10 times per day.

**[0616]** In some embodiments, the non-naturally occurring melanocortin analog is present in the pharmaceutical composition at a dose of about 50 mg to about 100 mg in a dose volume of about 2 mL to 10 mL, and wherein the administration is performed once monthly, once every three weeks, once every two weeks, once per week, twice per week, 3 times per week, 4 times per week, 5 times per week, once per day, twice per day, 3 times per day, 4 times per day, 5 times per day, or 10 times per day. In some embodiments, the non-naturally occurring melanocortin analog is present in the pharmaceutical composition at a dose of about 75 mg in a dose volume of about 5 mL, and wherein the administration is performed once monthly, once every three weeks, once every two weeks, once per week, twice per week, 3 times per week, 4 times per week, 5 times per week, once per day, twice per day, 3 times per day, 4 times per day, 5 times per day, or 10 times per day. In some embodiments, the non-naturally occurring melanocortin analog is present in the pharmaceutical composition at a dose of about 10 mg in a dose volume of about 1 mL, and wherein the administration is performed once monthly, once every three weeks, once every two weeks, once per week, twice per week, 3 times per week, 4 times per week, 5 times per week, once per day, twice per day, 3 times per day, 4 times per day, 5 times per day, or 10 times per day. In some embodiments, the administration is performed once per day. In other embodiments, the administration is performed once weekly. In some embodiments, the administration is performed once monthly.

**[0617]** In some embodiments, the non-naturally occurring melanocortin analog is any one of SEQ ID NOs: 8, 187, 198, 207-218, 226, 231-235, 281, 291, 294-296, 298-322, 324, 351-355, 358-362, 364, 366-368, 371-375, 381-395, 399, 403-417, 419, 421-425, 427, 429, 433-443, 446-461, 472, 492, 496, 499-506, 511-513, 515, 518-523, 536-537, 573-599, 600-620, 622-646 and is present in the pharmaceutical composition at a dose of about 5 mg to

about 500 mg in a dose volume of about 1 mL to 20 mL, and wherein the administration is performed once monthly, once every three weeks, once every two weeks, once per week, twice per week, 3 times per week, 4 times per week, 5 times per week, once per day, twice per day, 3 times per day, 4 times per day, 5 times per day, or 10 times per day. In some embodiments, any one of SEQ ID NOs: 8, 187, 198, 207-218, 226, 231-235, 281, 291, 294-296, 298-322, 324, 351-355, 358-362, 364, 366-368, 371-375, 381-395, 399, 403-417, 419, 421-425, 427, 429, 433-443, 446-461, 472, 492, 496, 499-506, 511-513, 515, 518-523, 536-537, 573-599, 600-620, 622-646 is present in the pharmaceutical composition at a dose of about 50 mg to about 100 mg in a dose volume of about 2 mL to 10 mL, and wherein the administration is performed once monthly, once every three weeks, once every two weeks, once per week, twice per week, 3 times per week, 4 times per week, 5 times per week, once per day, twice per day, 3 times per day, 4 times per day, 5 times per day, or 10 times per day. In some embodiments, any one of SEQ ID NOs: 8, 187, 198, 207-218, 226, 231-235, 281, 291, 294-296, 298-322, 324, 351-355, 358-362, 364, 366-368, 371-375, 381-395, 399, 403-417, 419, 421-425, 427, 429, 433-443, 446-461, 472, 492, 496, 499-506, 511-513, 515, 518-523, 536-537, 573-599, 600-620, 622-646 is present in the pharmaceutical composition at a dose of about 75 mg in a dose volume of about 5 mL, and wherein the administration is performed once monthly, once every three weeks, once every two weeks, once per week, twice per week, 3 times per week, 4 times per week, 5 times per week, once per day, twice per day, 3 times per day, 4 times per day, 5 times per day, or 10 times per day. In some embodiments, any one of SEQ ID NOs: 8, 187, 198, 207-218, 226, 231-235, 281, 291, 294-296, 298-322, 324, 351-355, 358-362, 364, 366-368, 371-375, 381-395, 399, 403-417, 419, 421-425, 427, 429, 433-443, 446-461, 472, 492, 496, 499-506, 511-513, 515, 518-523, 536-537, 573-599, 600-620, 622-646 is present in the pharmaceutical composition at a dose of about 10 mg in a dose volume of about 1 mL, and wherein the administration is performed once monthly, once every three weeks, once every two weeks, once per week, twice per week, 3 times per week, 4 times per week, 5 times per week, once per day, twice per day, 3 times per day, 4 times per day, 5 times per day, or 10 times per day. In some embodiments, the administration is performed once per day. In other embodiments, the administration is performed once weekly. In still other embodiments, the administration is performed once monthly.

**[0618]** In some embodiments, the non-naturally occurring melanocortin analog is any one of SEQ ID NOs: 187, 212, 218, 226, 291, 295, 298-322, 324, 351-355, 358-360, 362, 364, 366-368, 371-375, 381-395, 399, 403-417, 419, 421-425, 427, 429, 433-443, 446-461, 472, 492, 496, 499-506, 511-513, 515, 518-523, 536-537, 573-598, 600-646and is present in the pharmaceutical composition at a dose of about 5 mg to about 500 mg in a dose volume of about 1 mL to 20 mL, and wherein the administration is performed once monthly, once every three weeks, once every two weeks, once per week, twice per week, 3 times per week, 4 times per week, 5 times per week, once per day, twice per day, 3 times per day, 4 times per day, 5 times per day, or 10 times per day. In some embodiments, any one of SEQ ID NOs: 187, 212, 218, 226, 291, 295, 298-322, 324, 351-355, 358-360, 362, 364, 366-368, 371-375, 381-395, 399, 403-417, 419, 421-425, 427, 429, 433-443, 446-461, 472, 492, 496, 499-506, 511-513, 515, 518-523, 536-537, 573-598, 600-646 is present in the pharmaceutical composition at a dose of about 50 mg to about 100 mg in a dose volume of about 2 mL to 10 mL, and wherein the administration is performed once monthly, once every three weeks, once every two weeks, once per week, twice per week, 3 times per week, 4 times per week, 5 times per week, once per day, twice per day, 3 times per day, 4 times per day, 5 times per day, or 10 times per day. In some embodiments, any one of SEQ ID NOs: 187, 212, 218, 226, 291, 295, 298-322, 324, 351-355, 358-360, 362, 364, 366-368, 371-375, 381-395, 399, 403-417, 419, 421-425, 427, 429, 433-443, 446-461, 472, 492, 496, 499-506, 511-513, 515, 518-523, 536-537, 573-598, 600-646 is present in the pharmaceutical composition at a dose of about 75 mg in a dose volume of about 5 mL, and wherein the administration is performed once monthly, once every three weeks, once every two weeks, once per week, twice per week, 3 times per week, 4 times per week, 5 times per week, once per day, twice per day, 3 times per day, 4 times per day, 5 times per day, or 10 times per day. In some embodiments, any one of SEQ ID NOs: 187, 212, 218, 226, 291, 295, 298-322, 324, 351-355, 358-360, 362, 364, 366-368, 371-375, 381-395, 399, 403-417, 419, 421-425, 427, 429, 433-443, 446-461, 472, 492, 496, 499-506, 511-513, 515, 518-523, 536-537, 573-598, 600-646 is present in the pharmaceutical composition at a dose of about 10 mg in a dose volume of about 1 mL, and wherein the administration is performed once monthly, once every three weeks, once every two weeks, once per week, twice per week, 3 times per week, 4 times per week, 5 times per week, once per day, twice per day, 3 times per day, 4

times per day, 5 times per day, or 10 times per day. In some embodiments, the administration is performed once per day. In other embodiments, the administration is performed once weekly. In still other embodiments, the administration is performed once monthly.

**[0619]** In some embodiments, the non-naturally occurring melanocortin analog is any one of SEQ ID NOs: 187, 218, 231-235, 291, 295, 298-322, 351-353, 425, 427, 429, 433-443, 446-458, 573-599, 600-620, 622-646and is present in the pharmaceutical composition at a dose of about 5 mg to about 500 mg in a dose volume of about 1 mL to 20 mL, and wherein the administration is performed once monthly, once every three weeks, once every two weeks, once per week, twice per week, 3 times per week, 4 times per week, 5 times per week, once per day, twice per day, 3 times per day, 4 times per day, 5 times per day, or 10 times per day. In some embodiments, any one of SEQ ID NOs: 187, 218, 231-235, 291, 295, 298-322, 351-353, 425, 427, 429, 433-443, 446-458, 573-599, 600-620, 622-646is present in the pharmaceutical composition at a dose of about 50 mg to about 100 mg in a dose volume of about 2 mL to 10 mL, and wherein the administration is performed once monthly, once every three weeks, once every two weeks, once per week, twice per week, 3 times per week, 4 times per week, 5 times per week, once per day, twice per day, 3 times per day, 4 times per day, 5 times per day, or 10 times per day. In some embodiments, any one of SEQ ID NOs: 187, 218, 231-235, 291, 295, 298-322, 351-353, 425, 427, 429, 433-443, 446-458, 573-599, 600-620, 622-646 is present in the pharmaceutical composition at a dose of about 75 mg in a dose volume of about 5 mL, and wherein the administration is performed once monthly, once every three weeks, once every two weeks, once per week, twice per week, 3 times per week, 4 times per week, 5 times per week, once per day, twice per day, 3 times per day, 4 times per day, 5 times per day, or 10 times per day. In some embodiments, any one of SEQ ID NOs: 187, 218, 231-235, 291, 295, 298-322, 351-353, 425, 427, 429, 433-443, 446-458, 573-599, 600-620, 622-646is present in the pharmaceutical composition at a dose of about 10 mg in a dose volume of about 1 mL, and wherein the administration is performed once monthly, once every three weeks, once every two weeks, once per week, twice per week, 3 times per week, 4 times per week, 5 times per week, once per day, twice per day, 3 times per day, 4 times per day, 5 times per day, or 10 times per day. In some embodiments, the administration is performed once per day. In other embodiments, the

administration is performed once weekly. In still other embodiments, the administration is performed once monthly.

**[0620]** In some embodiments, the non-naturally occurring melanocortin analog is any one of SEQ ID NOs: 226, 383-393, 399, 403-417and is present in the pharmaceutical composition at a dose of about 5 mg to about 500 mg in a dose volume of about 1 mL to 20 mL, and wherein the administration is performed once monthly, once every three weeks, once every two weeks, once per week, twice per week, 3 times per week, 4 times per week, 5 times per week, once per day, twice per day, 3 times per day, 4 times per day, 5 times per day, or 10 times per day. In some embodiments, any one of SEQ ID NOs: 226, 383-393, 399, 403-417is present in the pharmaceutical composition at a dose of about 50 mg to about 100 mg in a dose volume of about 2 mL to 10 mL, and wherein the administration is performed once monthly, once every three weeks, once every two weeks, once per week, twice per week, 3 times per week, 4 times per week, 5 times per week, once per day, twice per day, 3 times per day, 4 times per day, 5 times per day, or 10 times per day. In some embodiments, any one of SEQ ID NOs: 226, 383-393, 399, 403-417is present in the pharmaceutical composition at a dose of about 75 mg in a dose volume of about 5 mL, and wherein the administration is performed once monthly, once every three weeks, once every two weeks, once per week, twice per week, 3 times per week, 4 times per week, 5 times per week, once per day, twice per day, 3 times per day, 4 times per day, 5 times per day, or 10 times per day. In some embodiments, any one of SEQ ID NOs: 226, 383-393, 399, 403-417is present in the pharmaceutical composition at a dose of about 10 mg in a dose volume of about 1 mL, and wherein the administration is performed once monthly, once every three weeks, once every two weeks, once per week, twice per week, 3 times per week, 4 times per week, 5 times per week, once per day, twice per day, 3 times per day, 4 times per day, 5 times per day, or 10 times per day. In some embodiments, the administration is performed once per day. In other embodiments, the administration is performed once weekly. In still other embodiments, the administration is performed once monthly.

**[0621]** In some embodiments, the non-naturally occurring melanocortin analog is any one of SEQ ID NOs: 209-211, 499, 501-506, 511-513, 515, 518-523and is present in the pharmaceutical composition at a dose of about 5 mg to about 500 mg in a dose volume of

about 1 mL to 20 mL, and wherein the administration is once monthly, once every three weeks, once every two weeks, once per week, twice per week, 3 times per week, 4 times per week, 5 times per week, once per day, twice per day, 3 times per day, 4 times per day, 5 times per day, or 10 times per day. In some embodiments, any one of SEQ ID NOs: 209-211, 499, 501-506, 511-513, 515, 518-523 is present in the pharmaceutical composition at a dose of about 50 mg to about 100 mg in a dose volume of about 2 mL to 10 mL, and wherein the administration is performed once monthly, once every three weeks, once every two weeks, once per week, twice per week, 3 times per week, 4 times per week, 5 times per week, once per day, twice per day, 3 times per day, 4 times per day, 5 times per day, or 10 times per day. In some embodiments, any one of SEQ ID NOs: 209-211, 499, 501-506, 511-513, 515, 518-523 is present in the pharmaceutical composition at a dose of about 75 mg in a dose volume of about 5 mL, and wherein the administration is performed once monthly, once every three weeks, once every two weeks, once per week, twice per week, 3 times per week, 4 times per week, 5 times per week, once per day, twice per day, 3 times per day, 4 times per day, 5 times per day, or 10 times per day. In some embodiments, any one of SEQ ID NOs: 209-211, 499, 501-506, 511-513, 515, 518-523 is present in the pharmaceutical composition at a dose of about 10 mg in a dose volume of about 1 mL, and wherein the administration is performed once monthly, once every three weeks, once every two weeks, once per week, twice per week, 3 times per week, 4 times per week, 5 times per week, once per day, twice per day, 3 times per day, 4 times per day, 5 times per day, or 10 times per day. In some embodiments, the administration is performed once per day. In other embodiments, the administration is performed once weekly. In still other embodiments, the administration is performed once monthly.

**[0622]** In some embodiments, the non-naturally occurring melanocortin analog or a pharmaceutical composition thereof is administered hourly (such as every hour, every 2 hours, every 4 hours, every 8 hours, etc.), once a day, or twice a day. In some embodiments, the non-naturally occurring melanocortin analog is administered every morning, every evening, or every afternoon. In some embodiments, the non-naturally occurring melanocortin analog is administered before a meal, after a meal, or with a meal.

**[0623]** In some embodiments, the non-naturally occurring melanocortin analog or pharmaceutical composition thereof may be administered as a dosing regimen comprising once, twice, or three times daily administration on a (i) weekly; (ii) every other week; (iii) one week of therapy followed by two, three or four weeks off; (iv) two weeks of therapy followed by one, two, three or four weeks off; (v) three weeks of therapy followed by one, two, three, four or five week off; (vi) four weeks of therapy followed by one, two, three, four or five week off; (vii) five weeks of therapy followed by one, two, three, four or five week off; or (viii) monthly schedule. The (i)-(viii) schedules may be repeated 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, or 12 times or more. In some embodiments, the non-naturally occurring melanocortin analog or pharmaceutical composition thereof is administered at various dosages during the dosing regimen (e.g., a first dose with an effective amount of 10 mg/kg and a second dose with an effective amount of 5 mg/kg).

**[0624]** In some embodiments, the non-naturally occurring melanocortin analog or pharmaceutical composition thereof is administered once every other day, once every 2 or 3 days, once every third day, once per week, once every other week, once every third week, once every month, once every six weeks, once every other month, once every three months, once every six months, or once per year. Administration of the non-naturally occurring melanocortin analog or pharmaceutical composition thereof at any of the dosing frequencies of the present technology may be repeated for a total of at least 2 dosages, at least 3 dosages, at least 4 dosages, at least 5 dosages, at least 10 dosages, at least 15 dosages, at least 20 dosages, at least 30 dosages, at least 40 dosages, at least 50 dosages or more. In some embodiments, the frequency of dosages of the non-naturally occurring melanocortin analog or pharmaceutical composition thereof is the same during a treatment regimen. In other embodiments, the frequency of dosages of the non-naturally occurring melanocortin analog or pharmaceutical composition thereof is different during a treatment regimen. The non-naturally occurring melanocortin analog or the pharmaceutical composition thereof may be administered even less frequently. Alternatively, the dosage regimen may be decreased or increased from an initial dosing regimen for days, weeks, months, or years. In some embodiments, the dosing regimen is repeated at other intervals.

***Dosing***

**[0625]** In some embodiments, the pharmaceutical compositions of the present technology are formulated to provide a dose of about 1 mg, about 2 mg, about 3 mg, about 5 mg, about 10 mg, about 15 mg, about 20 mg, about 25 mg, about 30 mg, about 40 mg, about 50 mg, about 60 mg, about 75 mg, about 100 mg, about 125 mg, about 150 mg, about 175 mg, about 200 mg, about 225 mg, about 250 mg, about 275 mg, about 300 mg, about 325 mg, about 350 mg, about 375 mg, about 400 mg, about 425 mg, about 450 mg, about 475 mg, or about 500 mg of the non-naturally occurring melanocortin analog to the subject in need thereof.

**[0626]** In some embodiments, the pharmaceutical compositions of the present technology are formulated to provide a dose of at least 1 mg, at least 2 mg, at least 3 mg, at least 5 mg, at least 10 mg, at least 15 mg, at least 20 mg, at least 25 mg, at least 30 mg, at least 40 mg, at least 50 mg, at least 60 mg, at least 75 mg, at least 100 mg, at least 125 mg, at least 150 mg, at least 175 mg, at least 200 mg, at least 225 mg, at least 250 mg, at least 275 mg, at least 300 mg, at least 325 mg, at least 350 mg, at least 375 mg, at least 400 mg, at least 425 mg, at least 450 mg, at least 475 mg, or at least 500 mg of the non-naturally occurring melanocortin analog to the subject in need thereof.

**[0627]** In some embodiments, the pharmaceutical compositions of the present technology are formulated to provide a dose of at least about 1 mg, at least about 2 mg, at least about 3 mg, at least about 5 mg, at least about 10 mg, at least about 15 mg, at least about 20 mg, at least about 25 mg, at least about 30 mg, at least about 40 mg, at least about 50 mg, at least about 60 mg, at least about 75 mg, at least about 100 mg, at least about 125 mg, at least about 150 mg, at least about 175 mg, at least about 200 mg, at least about 225 mg, at least about 250 mg, at least about 275 mg, at least about 300 mg, at least about 325 mg, at least about 350 mg, at least about 375 mg, at least about 400 mg, at least about 425 mg, at least about 450 mg, at least about 475 mg, or at least about 500 mg of the non-naturally occurring melanocortin analog to the subject in need thereof.

**[0628]** In some embodiments, the compositions of the present technology are administered to the subject at a dose that is based on the subject's BMI. In some embodiments, two or more doses of the compositions of the present technology are

administered to the subject, wherein the two or more doses are titrated (e.g., inversely titrated) based on the subject's BMI at the time of each administration.

**[0629]** In some embodiments, the pharmaceutical compositions of the present technology are formulated to provide a dose of about 0.001 mg/kg, about 0.005 mg/kg, about 0.01 mg/kg, about 0.05 mg/kg, about 0.10 mg/kg, about 0.5 mg/kg, about 1 mg/kg, about 2 mg/kg, about 3 mg/kg, about 5 mg/kg, about 10 mg/kg, about 15 mg/kg, about 20 mg/kg, about 25 mg/kg, about 30 mg/kg, about 40 mg/kg, about 50 mg/kg, about 60 mg/kg, about 75 mg/kg, about 100 mg/kg, about 125 mg/kg, about 150 mg/kg, about 175 mg/kg, about 200 mg/kg, about 225 mg/kg, about 250 mg/kg, about 275 mg/kg, about 300 mg/kg, about 325 mg/kg, about 350 mg/kg, about 375 mg/kg, about 400 mg/kg, about 425 mg/kg, about 450 mg/kg, about 475 mg/kg, or about 500 mg/kg of the non-naturally occurring melanocortin analog to the subject in need thereof.

**[0630]** In some embodiments, the pharmaceutical compositions of the present technology are formulated to provide a dose of at least 0.001 mg/kg, at least 0.005 mg/kg, at least 0.01 mg/kg, at least 0.05 mg/kg, at least 0.10 mg/kg, at least 0.5 mg/kg, at least 1 mg/kg, at least 2 mg/kg, at least 3 mg/kg, at least 5 mg/kg, at least 10 mg/kg, at least 15 mg/kg, at least 20 mg/kg, at least 25 mg/kg, at least 30 mg/kg, at least 40 mg/kg, at least 50 mg/kg, at least 60 mg/kg, at least 75 mg/kg, at least 100 mg/kg, at least 125 mg/kg, at least 150 mg/kg, at least 175 mg/kg, at least 200 mg/kg, at least 225 mg/kg, at least 250 mg/kg, at least 275 mg/kg, at least 300 mg/kg, at least 325 mg/kg, at least 350 mg/kg, at least 375 mg/kg, at least 400 mg/kg, at least 425 mg/kg, at least 450 mg/kg, at least 475 mg/kg, or at least 500 mg/kg of the non-naturally occurring melanocortin analog to the subject in need thereof.

In some embodiments, the pharmaceutical compositions of the present technology are formulated to provide a dose of at least about 0.001 mg/kg, at least about 0.005 mg/kg, at least about 0.01 mg/kg, at least about 0.05 mg/kg, at least about 0.10 mg/kg, at least about 0.5 mg/kg, at least about 1 mg/kg, at least about 2 mg/kg, at least about 3 mg/kg, at least about 5 mg/kg, at least about 10 mg/kg, at least about 15 mg/kg, at least about 20 mg/kg, at least about 25 mg/kg, at least about 30 mg/kg, at least about 40 mg/kg, at least about 50 mg/kg, at least about 60 mg/kg, at least about 75 mg/kg, at least about 100 mg/kg, at least

about 125 mg/kg, at least about 150 mg/kg, at least about 175 mg/kg, at least about 200 mg/kg, at least about 225 mg/kg, at least about 250 mg/kg, at least about 275 mg/kg, at least about 300 mg/kg, at least about 325 mg/kg, at least about 350 mg/kg, at least about 375 mg/kg, at least about 400 mg/kg, at least about 425 mg/kg, at least about 450 mg/kg, at least about 475 mg/kg, or at least about 500 mg/kg of the non-naturally occurring melanocortin analog to the subject in need thereof.

**[0631]** In some embodiments, the non-naturally occurring melanocortin analog is administered at a dose of about 5 mg/kg to about 500 mg/kg per body weight of the subject once daily. In some embodiments, the non-naturally occurring melanocortin analog is administered at a dose of about 10 mg/kg to about 250 mg/kg per body weight of the subject once daily. In some embodiments, non-naturally occurring melanocortin analog is administered at a dose of about 15 mg/kg to about 100 mg/kg per body weight of the subject once daily. In some embodiments, the non-naturally occurring melanocortin analog is administered at a dose of about 20 mg/kg to about 75 mg/kg per body weight of the subject once daily. In some embodiments, the non-naturally occurring melanocortin analog is administered at a dose of about 30 mg/kg or 60 mg/kg per body weight of the subject once daily.

**[0632]** In some embodiments, the non-naturally occurring melanocortin analog is administered at a dose of at least 5 mg/kg to at least 500 mg/kg per body weight of the subject once daily. In some embodiments, the non-naturally occurring melanocortin analog is administered at a dose of at least 10 mg/kg to at least 250 mg/kg per body weight of the subject once daily. In some embodiments, non-naturally occurring melanocortin analog is administered at a dose of at least 15 mg/kg to at least 100 mg/kg per body weight of the subject once daily. In some embodiments, the non-naturally occurring melanocortin analog is administered at a dose of at least 20 mg/kg to at least 75 mg/kg per body weight of the subject once daily. In some embodiments, the non-naturally occurring melanocortin analog is administered at a dose of at least 30 mg/kg or 60 mg/kg per body weight of the subject once daily.

**[0633]** In some embodiments, the non-naturally occurring melanocortin analog is administered at a dose of at least about 5 mg/kg to at least about 500 mg/kg per body weight

of the subject once daily. In some embodiments, the non-naturally occurring melanocortin analog is administered at a dose of at least about 10 mg/kg to at least about 250 mg/kg per body weight of the subject once daily. In some embodiments, non-naturally occurring melanocortin analog is administered at a dose of at least about 15 mg/kg to at least about 100 mg/kg per body weight of the subject once daily. In some embodiments, the non-naturally occurring melanocortin analog is administered at a dose of at least about 20 mg/kg to at least about 75 mg/kg per body weight of the subject once daily. In some embodiments, the non-naturally occurring melanocortin analog is administered at a dose of at least about 30 mg/kg or 60 mg/kg per body weight of the subject once daily.

**[0634]** In some embodiments, the non-naturally occurring melanocortin analog is administered at least once daily in an amount ranging from 0.001 mg/kg to 25 mg/kg, 0.01 mg/kg to 20 mg/kg, 0.05 mg/kg to 15 mg/kg, 0.075 mg/kg to 10 mg/kg, 0.1 mg/kg to 8 mg/kg, 0.2 mg/kg to 6 mg/kg, 0.3 mg/kg to 4 mg/kg, 0.4 mg/kg to 2 mg/kg, or 0.5 mg/kg to 1 mg/kg per body weight of the subject.

**[0635]** In some embodiments, the non-naturally occurring melanocortin analog is administered at least once daily in an amount ranging from about 0.5 mg/kg to about 10 mg/kg, about 1 mg/kg to about 7.5 mg/kg, or about 2.5 mg/kg to about 5 mg/kg per body weight of the subject.

**[0636]** In some embodiments, the non-naturally occurring melanocortin analog is administered at least once daily in an amount ranging from at least 0.5 mg/kg to at least 10 mg/kg, at least 1 mg/kg to at least 7.5 mg/kg, or at least 2.5 mg/kg to at least 5 mg/kg per body weight of the subject.

**[0637]** In some embodiments, the non-naturally occurring melanocortin analog is administered about once daily in an amount ranging from about 0.5 mg/kg to about 10 mg/kg, about 1 mg/kg to about 7.5 mg/kg, or about 2.5 mg/kg to about 5 mg/kg per body weight of the subject.

**[0638]** In some embodiments, the non-naturally occurring melanocortin analog is administered at a dose of about 5 mg/kg, about 10 mg/kg, about 15 mg/kg, about 20 mg/kg, about 25 mg/kg, about 30 mg/kg, about 35 mg/kg , about 40 mg/kg, about 50 mg/kg, about

65 mg/kg, about 70 mg/kg, about 75 mg/kg, about 80 mg/kg, about 85 mg/kg, about 90 mg/kg, about 95 mg/kg, about 100 mg/kg, about 125 mg/kg, about 150 mg/kg, about 175 mg/kg, about 200 mg/kg, about 250 mg/kg, about 300 mg/kg, about 350 mg/kg, about 400 mg/kg, about 450 mg/kg, or about 500 mg/kg per body weight of the subject once daily.

**[0639]** In some embodiments, the non-naturally occurring melanocortin analog is administered at a dose of at least 5 mg/kg, at least 10 mg/kg, at least 15 mg/kg, at least 20 mg/kg, at least 25 mg/kg, at least 30 mg/kg, at least 35 mg/kg , at least 40 mg/kg, at least 50 mg/kg, at least 65 mg/kg, at least 70 mg/kg, at least 75 mg/kg, at least 80 mg/kg, at least 85 mg/kg, at least 90 mg/kg, at least 95 mg/kg, at least 100 mg/kg, at least 125 mg/kg, at least 150 mg/kg, at least 175 mg/kg, at least 200 mg/kg, at least 250 mg/kg, at least 300 mg/kg, at least 350 mg/kg, at least 400 mg/kg, at least 450 mg/kg, or at least 500 mg/kg per body weight of the subject once daily.

**[0640]** In some embodiments, the non-naturally occurring melanocortin analog is administered at a dose of at least about 5 mg/kg, at least about 10 mg/kg, at least about 15 mg/kg, at least about 20 mg/kg, at least about 25 mg/kg, at least about 30 mg/kg, at least about 35 mg/kg , at least about 40 mg/kg, at least about 50 mg/kg, at least about 65 mg/kg, at least about 70 mg/kg, at least about 75 mg/kg, at least about 80 mg/kg, at least about 85 mg/kg, at least about 90 mg/kg, at least about 95 mg/kg, at least about 100 mg/kg, at least about 125 mg/kg, at least about 150 mg/kg, at least about 175 mg/kg, at least about 200 mg/kg, at least about 250 mg/kg, at least about 300 mg/kg, at least about 350 mg/kg, at least about 400 mg/kg, at least about 450 mg/kg, or at least about 500 mg/kg per body weight of the subject once daily.

**[0641]** In some embodiments, the non-naturally occurring melanocortin analog is administered at a dose of about 5 mg/kg per body weight of the subject once daily.

**[0642]** In some embodiments, the non-naturally occurring melanocortin analog is administered at a dose of at least 5 mg/kg per body weight of the subject once daily.

**[0643]** In some embodiments, the non-naturally occurring melanocortin analog is administered at a dose of at least about 5 mg/kg per body weight of the subject once daily.

**[0644]** In some embodiments, the non-naturally occurring melanocortin analog is administered at a dose of about 10 mg/kg per body weight of the subject once daily.

**[0645]** In some embodiments, the non-naturally occurring melanocortin analog is administered at a dose of at least 10 mg/kg per body weight of the subject once daily.

**[0646]** In some embodiments, the non-naturally occurring melanocortin analog is administered at a dose of at least about 10 mg/kg per body weight of the subject once daily.

**[0647]** In some embodiments, the non-naturally occurring melanocortin analog is administered at a dose of about 15 mg/kg per body weight of the subject once daily.

**[0648]** In some embodiments, the non-naturally occurring melanocortin analog is administered at a dose of at least 15 mg/kg per body weight of the subject once daily.

**[0649]** In some embodiments, the non-naturally occurring melanocortin analog is administered at a dose of at least about 15 mg/kg per body weight of the subject once daily.

**[0650]** In some embodiments, the non-naturally occurring melanocortin analog is administered at a dose of about 20 mg/kg per body weight of the subject once daily.

**[0651]** In some embodiments, the non-naturally occurring melanocortin analog is administered at a dose of at least 20 mg/kg per body weight of the subject once daily.

**[0652]** In some embodiments, the non-naturally occurring melanocortin analog is administered at a dose of at least about 20 mg/kg per body weight of the subject once daily.

**[0653]** In some embodiments, the non-naturally occurring melanocortin analog is administered at a dose of about 25 mg/kg per body weight of the subject once daily.

**[0654]** In some embodiments, the non-naturally occurring melanocortin analog is administered at a dose of at least 25 mg/kg per body weight of the subject once daily.

**[0655]** In some embodiments, the non-naturally occurring melanocortin analog is administered at a dose of at least about 25 mg/kg per body weight of the subject once daily.

**[0656]** In some embodiments, the non-naturally occurring melanocortin analog is administered at a dose of about 30 mg/kg per body weight of the subject once daily.

**[0657]** In some embodiments, the non-naturally occurring melanocortin analog is administered at a dose of at least 30 mg/kg per body weight of the subject once daily.

**[0658]** In some embodiments, the non-naturally occurring melanocortin analog is administered at a dose of at least about 30 mg/kg per body weight of the subject once daily.

**[0659]** In some embodiments, the non-naturally occurring melanocortin analog is administered at a dose of about 35 mg/kg per body weight of the subject once daily.

**[0660]** In some embodiments, the non-naturally occurring melanocortin analog is administered at a dose of at least 35 mg/kg per body weight of the subject once daily.

**[0661]** In some embodiments, the non-naturally occurring melanocortin analog is administered at a dose of at least about 35 mg/kg per body weight of the subject once daily.

**[0662]** In some embodiments, the non-naturally occurring melanocortin analog is administered at a dose of about 40 mg/kg per body weight of the subject once daily.

**[0663]** In some embodiments, the non-naturally occurring melanocortin analog is administered at a dose of at least 40 mg/kg per body weight of the subject once daily.

In some embodiments, the non-naturally occurring melanocortin analog is administered at a dose of at least about 40 mg/kg per body weight of the subject once daily.

**[0664]** In some embodiments, the non-naturally occurring melanocortin analog is administered at a dose of about 50 mg/kg per body weight of the subject once daily.

**[0665]** In some embodiments, the non-naturally occurring melanocortin analog is administered at a dose of at least 50 mg/kg per body weight of the subject once daily.

**[0666]** In some embodiments, the non-naturally occurring melanocortin analog is administered at a dose of at least about 50 mg/kg per body weight of the subject once daily.

**[0667]** In some embodiments, the non-naturally occurring melanocortin analog is administered at a dose of about 5 mg/kg, about 10 mg/kg, about 15 mg/kg, about 20 mg/kg, about 25 mg/kg, about 30 mg/kg, about 35 mg/kg , about 40 mg/kg, about 50 mg/kg, about 65 mg/kg, about 70 mg/kg, about 75 mg/kg, about 80 mg/kg, about 85 mg/kg, about 90 mg/kg, about 95 mg/kg, about 100 mg/kg, about 125 mg/kg, about 150 mg/kg, about 175

mg/kg, about 200 mg/kg, about 250 mg/kg, about 300 mg/kg, about 350 mg/kg, about 400 mg/kg, about 450 mg/kg, or about 500 mg/kg per body weight of the subject twice daily.

**[0668]** In some embodiments, the non-naturally occurring melanocortin analog is administered at a dose of at least 5 mg/kg, at least 10 mg/kg, at least 15 mg/kg, at least 20 mg/kg, at least 25 mg/kg, at least 30 mg/kg, at least 35 mg/kg , at least 40 mg/kg, at least 50 mg/kg, at least 65 mg/kg, at least 70 mg/kg, at least 75 mg/kg, at least 80 mg/kg, at least 85 mg/kg, at least 90 mg/kg, at least 95 mg/kg, at least 100 mg/kg, at least 125 mg/kg, at least 150 mg/kg, at least 175 mg/kg, at least 200 mg/kg, at least 250 mg/kg, at least 300 mg/kg, at least 350 mg/kg, at least 400 mg/kg, at least 450 mg/kg, or at least 500 mg/kg per body weight of the subject twice daily.

**[0669]** In some embodiments, the non-naturally occurring melanocortin analog is administered at a dose of at least about 5 mg/kg, at least about 10 mg/kg, at least about 15 mg/kg, at least about 20 mg/kg, at least about 25 mg/kg, at least about 30 mg/kg, at least about 35 mg/kg , at least about 40 mg/kg, at least about 50 mg/kg, at least about 65 mg/kg, at least about 70 mg/kg, at least about 75 mg/kg, at least about 80 mg/kg, at least about 85 mg/kg, at least about 90 mg/kg, at least about 95 mg/kg, at least about 100 mg/kg, at least about 125 mg/kg, at least about 150 mg/kg, at least about 175 mg/kg, at least about 200 mg/kg, at least about 250 mg/kg, at least about 300 mg/kg, at least about 350 mg/kg, at least about 400 mg/kg, at least about 450 mg/kg, or at least about 500 mg/kg per body weight of the subject twice daily.

**[0670]** In some embodiments, the non-naturally occurring melanocortin analog is administered at a dose of about 5 mg/kg per body weight of the subject twice daily.

**[0671]** In some embodiments, the non-naturally occurring melanocortin analog is administered at a dose of about 10 mg/kg per body weight of the subject twice daily.

**[0672]** In some embodiments, the non-naturally occurring melanocortin analog is administered at a dose of about 15 mg/kg per body weight of the subject twice daily.

**[0673]** In some embodiments, the non-naturally occurring melanocortin analog is administered at a dose of about 20 mg/kg per body weight of the subject twice daily.

**[0674]** In some embodiments, the non-naturally occurring melanocortin analog is administered at a dose of about 25 mg/kg per body weight of the subject twice daily.

**[0675]** In some embodiments, the non-naturally occurring melanocortin analog is administered at a dose of about 30 mg/kg per body weight of the subject twice daily.

**[0676]** In some embodiments, the non-naturally occurring melanocortin analog is administered at a dose of about 35 mg/kg per body weight of the subject twice daily.

**[0677]** In some embodiments, the non-naturally occurring melanocortin analog is administered at a dose of about 40 mg/kg per body weight of the subject twice daily.

**[0678]** In some embodiments, the non-naturally occurring melanocortin analog is administered at a dose of about 50 mg/kg per body weight of the subject twice daily.

**[0679]** In some embodiments, the non-naturally occurring melanocortin analog is administered at a dose of about 5 mg/kg per body weight of the subject twice daily.

**[0680]** In some embodiments, the non-naturally occurring melanocortin analog is administered at a dose of about 10 mg/kg per body weight of the subject twice daily.

**[0681]** In some embodiments, the non-naturally occurring melanocortin analog is administered at a dose of about 15 mg/kg per body weight of the subject twice daily.

**[0682]** In some embodiments, the non-naturally occurring melanocortin analog is administered at a dose of about 20 mg/kg per body weight of the subject twice daily.

**[0683]** In some embodiments, the non-naturally occurring melanocortin analog is administered at a dose of about 25 mg/kg per body weight of the subject twice daily.

**[0684]** In some embodiments, the non-naturally occurring melanocortin analog is administered at a dose of about 30 mg/kg per body weight of the subject twice daily.

**[0685]** In some embodiments, the non-naturally occurring melanocortin analog is administered at a dose of about 35 mg/kg per body weight of the subject twice daily.

**[0686]** In some embodiments, the non-naturally occurring melanocortin analog is administered at a dose of about 40 mg/kg per body weight of the subject twice daily.

**[0687]** In some embodiments, the non-naturally occurring melanocortin analog is administered at a dose of about 50 mg/kg per body weight of the subject twice daily.

**[0688]** In some embodiments, the non-naturally occurring melanocortin analog is administered at a dose of at least about 5 mg/kg per body weight of the subject twice daily.

**[0689]** In some embodiments, the non-naturally occurring melanocortin analog is administered at a dose of at least about 10 mg/kg per body weight of the subject twice daily.

**[0690]** In some embodiments, the non-naturally occurring melanocortin analog is administered at a dose of at least about 15 mg/kg per body weight of the subject twice daily.

**[0691]** In some embodiments, the non-naturally occurring melanocortin analog is administered at a dose of at least about 20 mg/kg per body weight of the subject twice daily.

**[0692]** In some embodiments, the non-naturally occurring melanocortin analog is administered at a dose of at least about 25 mg/kg per body weight of the subject twice daily.

**[0693]** In some embodiments, the non-naturally occurring melanocortin analog is administered at a dose of at least about 30 mg/kg per body weight of the subject twice daily.

**[0694]** In some embodiments, the non-naturally occurring melanocortin analog is administered at a dose of at least about 35 mg/kg per body weight of the subject twice daily.

**[0695]** In some embodiments, the non-naturally occurring melanocortin analog is administered at a dose of at least about 40 mg/kg per body weight of the subject twice daily.

**[0696]** In some embodiments, the non-naturally occurring melanocortin analog is administered at a dose of at least about 50 mg/kg per body weight of the subject twice daily.

**[0697]** In some embodiments, the non-naturally occurring melanocortin analog is administered at one or more doses. In some embodiments, the non-naturally occurring melanocortin analog is administered at two or more doses.

**[0698]** In some embodiments, the non-naturally occurring melanocortin analog is administered at a first dose once daily or twice daily. In some embodiments, the non-naturally occurring melanocortin analog is administered at a second dose once daily or twice daily.

**[0699]** In some embodiments, the non-naturally occurring melanocortin analog is administered at a first dose once daily for about 5 days to about 10 days. In some embodiments, the non-naturally occurring melanocortin analog is administered at a second dose once daily for about 5 days to about 10 days, after administration of the first dose. In some embodiments, the non-naturally occurring melanocortin analog is administered at a third dose twice daily for about 7 days to about 21 days, after administration of the second dose. In some embodiments, the second dose is greater than the first dose. In some embodiments, the third dose comprises a cumulative dose that is greater than the second dose.

**[0700]** In some embodiments, the non-naturally occurring melanocortin analog is administered (i) at a first dose of about 5 mg/kg to about 20 mg/kg administered once a day for about 5 days to about 10 days; (ii) at a second dose of about 10 mg/kg to about 40 mg/kg administered once a day after administration of the first dose for about 5 days to about 10 days; (iii) at a third dose of about 5 mg/kg to about 30 mg/kg administered twice a day after administration of the second dose for at least about 5 days to about 10 days. In some embodiments, the third dose is administered twice a day for at least about 7 days or more.

**[0701]** In some embodiments, the non-naturally occurring melanocortin analog is administered (i) at a first dose of about 5 mg/kg, about 10 mg/kg, about 15 mg/kg, or about 20 mg/kg administered once a day for about 5 days, about 6 days, about 7 days, about 8 days, about 9 days, or about 10 days; (ii) at a second dose of about 10 mg/kg, about 15 mg/kg, about 20 mg/kg, about 25 mg/kg, about 30 mg/kg, about 35 mg/kg, or about 40 mg/kg administered once a day after administration of the first dose about 5 days, about 6 days, about 7 days, about 8 days, about 9 days, or about 10 days; (iii) at a third dose of about 5 mg/kg, about 10 mg/kg, about 15 mg/kg, about 20 mg/kg, about 25 mg/kg, or about 30 mg/kg administered twice a day after administration of the second dose for at least about 5 days, about, 6 days, about 7 days, about 8 days, about 9 days, or about 10 days. In some embodiments, the third dose is administered twice a day for at least about 7 days, about 8 days, about 9 days, about 10 days, about 11 days, about 12 days, about 13 days, or about 14 days or more.

**[0702]** In some embodiments, the non-naturally occurring melanocortin analog is administered (i) at a first dose of about 5 mg/kg administered once a day for about 7 days; (ii) at a second dose of about 15 mg/kg administered once a day after administration of the first dose for about 7 days; (iii) at a third dose of about 10 mg/kg administered twice a day after administration of the second dose for at least about 7 days. In some embodiments, the third dose is administered twice a day for at least about 14 days or more.

**[0703]** In some embodiments, the non-naturally occurring melanocortin analog is administered (i) at a first dose of about 10 mg/kg administered once a day for about 7 days; (ii) at a second dose of about 20 mg/kg administered once a day after administration of the first dose for about 7 days; (iii) at a third dose of about 15 mg/kg administered twice a day after administration of the second dose for at least about 7 days. In some embodiments, the third dose is administered twice a day for at least about 14 days or more.

**[0704]** In some embodiments, the non-naturally occurring melanocortin analog is administered (i) at a first dose of about 15 mg/kg administered once a day for about 7 days; (ii) at a second dose of about 25 mg/kg administered once a day after administration of the first dose for about 7 days; (iii) at a third dose of about 20 mg/kg administered twice a day after administration of the second dose for at least about 7 days. In some embodiments, the third dose is administered twice a day for at least about 14 days or more.

**[0705]** In some embodiments, the non-naturally occurring melanocortin analog is any one of SEQ ID NOs: 8, 187, 198, 207-218, 226, 231-235, 281, 291, 294-296, 298-322, 324, 351-355, 358-362, 364, 366-368, 371-375, 381-395, 399, 403-417, 419, 421-425, 427, 429, 433-443, 446-461, 472, 492, 496, 499-506, 511-513, 515, 518-523, 536-537, 573-599, 600-620, 622-646 and is administered at least once daily in an amount ranging from 0.001 mg/kg to 25 mg/kg, 0.01 mg/kg to 20 mg/kg, 0.05 mg/kg to 15 mg/kg, 0.075 mg/kg to 10 mg/kg, 0.1 mg/kg to 8 mg/kg, 0.2 mg/kg to 6 mg/kg, 0.3 mg/kg to 4 mg/kg, 0.4 mg/kg to 2 mg/kg, or 0.5 mg/kg to 1 mg/kg per body weight of the subject. In some embodiments, the non-naturally occurring melanocortin analog is any one of SEQ ID NOs: 8, 187, 198, 207-218, 226, 231-235, 281, 291, 294-296, 298-322, 324, 351-355, 358-362, 364, 366-368, 371-375, 381-395, 399, 403-417, 419, 421-425, 427, 429, 433-443, 446-461, 472, 492, 496, 499-506, 511-513, 515, 518-523, 536-537, 573-599, 600-620, 622-646 and is administered at least once daily

in an amount ranging from about 0.5 mg/kg to about 10 mg/kg, about 1 mg/kg to about 7.5 mg/kg, or about 2.5 mg/kg to about 5 mg/kg per body weight of the subject.

**[0706]** In some embodiments, the non-naturally occurring melanocortin analog is any one of SEQ ID NOs: 187, 212, 218, 226, 291, 295, 298-322, 324, 351-355, 358-360, 362, 364, 366-368, 371-375, 381-395, 399, 403-417, 419, 421-425, 427, 429, 433-443, 446-461, 472, 492, 496, 499-506, 511-513, 515, 518-523, 536-537, 573-598, 600-646 and is administered at least once daily in an amount ranging from 0.001 mg/kg to 25 mg/kg, 0.01 mg/kg to 20 mg/kg, 0.05 mg/kg to 15 mg/kg, 0.075 mg/kg to 10 mg/kg, 0.1 mg/kg to 8 mg/kg, 0.2 mg/kg to 6 mg/kg, 0.3 mg/kg to 4 mg/kg, 0.4 mg/kg to 2 mg/kg, or 0.5 mg/kg to 1 mg/kg per body weight of the subject. In some embodiments, the non-naturally occurring melanocortin analog is any one of SEQ ID NOs: 187, 212, 218, 226, 291, 295, 298-322, 324, 351-355, 358-360, 362, 364, 366-368, 371-375, 381-395, 399, 403-417, 419, 421-425, 427, 429, 433-443, 446-461, 472, 492, 496, 499-506, 511-513, 515, 518-523, 536-537, 573-598, 600-646 and is administered at least once daily in an amount ranging from about 0.5 mg/kg to about 10 mg/kg, about 1 mg/kg to about 7.5 mg/kg, or about 2.5 mg/kg to about 5 mg/kg per body weight of the subject.

**[0707]** In some embodiments, the non-naturally occurring melanocortin analog is any one of SEQ ID NOs: 187, 218, 231-235, 291, 295, 298-322, 351-353, 425, 427, 429, 433-443, 446-458, 573-599, 600-620, 622-646and is administered at least once daily in an amount ranging from 0.001 mg/kg to 25 mg/kg, 0.01 mg/kg to 20 mg/kg, 0.05 mg/kg to 15 mg/kg, 0.075 mg/kg to 10 mg/kg, 0.1 mg/kg to 8 mg/kg, 0.2 mg/kg to 6 mg/kg, 0.3 mg/kg to 4 mg/kg, 0.4 mg/kg to 2 mg/kg, or 0.5 mg/kg to 1 mg/kg per body weight of the subject. In some embodiments, the non-naturally occurring melanocortin analog is any one of SEQ ID NOs: 187, 218, 231-235, 291, 295, 298-322, 351-353, 425, 427, 429, 433-443, 446-458, 573-599, 600-620, 622-646and is administered at least once daily in an amount ranging from about 0.5 mg/kg to about 10 mg/kg, about 1 mg/kg to about 7.5 mg/kg, or about 2.5 mg/kg to about 5 mg/kg per body weight of the subject.

**[0708]** In some embodiments, the non-naturally occurring melanocortin analog is any one of SEQ ID NOs: 226, 383-393, 399, 403-417 and is administered at least once daily in an amount ranging from 0.001 mg/kg to 25 mg/kg, 0.01 mg/kg to 20 mg/kg, 0.05 mg/kg to

15 mg/kg, 0.075 mg/kg to 10 mg/kg, 0.1 mg/kg to 8 mg/kg, 0.2 mg/kg to 6 mg/kg, 0.3 mg/kg to 4 mg/kg, 0.4 mg/kg to 2 mg/kg, or 0.5 mg/kg to 1 mg/kg per body weight of the subject. In some embodiments, the non-naturally occurring melanocortin analog is any one of SEQ ID NOs: 226, 383-393, 399, 403-417 and is administered at least once daily in an amount ranging from about 0.5 mg/kg to about 10 mg/kg, about 1 mg/kg to about 7.5 mg/kg, or about 2.5 mg/kg to about 5 mg/kg per body weight of the subject.

**[0709]** In some embodiments, the non-naturally occurring melanocortin analog is any one of SEQ ID NOs: 209-211, 499, 501-506, 511-513, 515, 518-523 and is administered at least once daily in an amount ranging from 0.001 mg/kg to 25 mg/kg, 0.01 mg/kg to 20 mg/kg, 0.05 mg/kg to 15 mg/kg, 0.075 mg/kg to 10 mg/kg, 0.1 mg/kg to 8 mg/kg, 0.2 mg/kg to 6 mg/kg, 0.3 mg/kg to 4 mg/kg, 0.4 mg/kg to 2 mg/kg, or 0.5 mg/kg to 1 mg/kg per body weight of the subject. In some embodiments, the non-naturally occurring melanocortin analog is any one of SEQ ID NOs: 209-211, 499, 501-506, 511-513, 515, 518-523 and is administered at least once daily in an amount ranging from about 0.5 mg/kg to about 10 mg/kg, about 1 mg/kg to about 7.5 mg/kg, or about 2.5 mg/kg to about 5 mg/kg per body weight of the subject.

**[0710]** In some embodiments, the non-naturally occurring melanocortin analog is administered at least once daily in an amount of about 0.1 mg to about 100 mg, 0.5 mg to about 50 mg, about 1 mg to about 40 mg, about 2.5 mg to about 30 mg, about 5 to about 20 mg, or about 7.5 to about 15 mg. In some embodiments, the non-naturally occurring melanocortin analog is administered once daily in an amount of about 10 mg. In some embodiments, the non-naturally occurring melanocortin analog is administered at least once daily in an amount of about 1 mg to about 100 mg, about 5 mg to about 95 mg, about 10 mg to about 90 mg, about 15 mg to about 85 mg, about 20 mg to about 80 mg, about 25 mg to about 75 mg, about 30 mg to about 70 mg, about 35 mg to about 65 mg, about 40 to about 60 mg, or about 45 to about 55 mg. In some embodiments, the non-naturally occurring melanocortin analog is administered at least once daily in an amount of about 50 mg.

**[0711]** In some embodiments, the non-naturally occurring melanocortin analog is any one of SEQ ID NOs: 8, 187, 198, 207-218, 226, 231-235, 281, 291, 294-296, 298-322, 324, 351-355, 358-362, 364, 366-368, 371-375, 381-395, 399, 403-417, 419, 421-425, 427, 429,

433-443, 446-461, 472, 492, 496, 499-506, 511-513, 515, 518-523, 536-537, 573-599, 600-620, 622-646, and is administered at least once daily in an amount of about 0.1 mg to about 100 mg, 0.5 mg to about 50 mg, about 1 mg to about 40 mg, about 2.5 mg to about 30 mg, about 5 to about 20 mg, or about 7.5 to about 15 mg. In some embodiments, the non-naturally occurring melanocortin analog is any one of SEQ ID NOs: 8, 187, 198, 207-218, 226, 231-235, 281, 291, 294-296, 298-322, 324, 351-355, 358-362, 364, 366-368, 371-375, 381-395, 399, 403-417, 419, 421-425, 427, 429, 433-443, 446-461, 472, 492, 496, 499-506, 511-513, 515, 518-523, 536-537, 573-599, 600-620, 622-646, and is administered once daily in an amount of about 10 mg. In some embodiments, the non-naturally occurring melanocortin analog is any one of SEQ ID NOs: 8, 187, 198, 207-218, 226, 231-235, 281, 291, 294-296, 298-322, 324, 351-355, 358-362, 364, 366-368, 371-375, 381-395, 399, 403-417, 419, 421-425, 427, 429, 433-443, 446-461, 472, 492, 496, 499-506, 511-513, 515, 518-523, 536-537, 573-599, 600-620, 622-646, and is administered at least once daily in an amount of about 1 mg to about 100 mg, about 5 mg to about 95 mg, about 10 mg to about 90 mg, about 15 mg to about 85 mg, about 20 mg to about 80 mg, about 25 mg to about 75 mg, about 30 mg to about 70 mg, about 35 mg to about 65 mg, about 40 to about 60 mg, or about 45 to about 55 mg. In some embodiments, the non-naturally occurring melanocortin analog is any one of SEQ ID NOs: 8, 187, 198, 207-218, 226, 231-235, 281, 291, 294-296, 298-322, 324, 351-355, 358-362, 364, 366-368, 371-375, 381-395, 399, 403-417, 419, 421-425, 427, 429, 433-443, 446-461, 472, 492, 496, 499-506, 511-513, 515, 518-523, 536-537, 573-599, 600-620, 622-646, and is administered at least once daily in an amount of about 50 mg.

**[0712]** In some embodiments, the non-naturally occurring melanocortin analog is any one of SEQ ID NOs: 187, 212, 218, 226, 291, 295, 298-322, 324, 351-355, 358-360, 362, 364, 366-368, 371-375, 381-395, 399, 403-417, 419, 421-425, 427, 429, 433-443, 446-461, 472, 492, 496, 499-506, 511-513, 515, 518-523, 536-537, 573-598, 600-646 and is administered at least once daily in an amount of about 0.1 mg to about 100 mg, 0.5 mg to about 50 mg, about 1 mg to about 40 mg, about 2.5 mg to about 30 mg, about 5 to about 20 mg, or about 7.5 to about 15 mg. In some embodiments, the non-naturally occurring melanocortin analog is any one of SEQ ID NOs: 187, 212, 218, 226, 291, 295, 298-322, 324, 351-355, 358-360, 362, 364, 366-368, 371-375, 381-395, 399, 403-417, 419, 421-425, 427,

429, 433-443, 446-461, 472, 492, 496, 499-506, 511-513, 515, 518-523, 536-537, 573-598, 600-646 and is administered once daily in an amount of about 10 mg. In some embodiments, the non-naturally occurring melanocortin analog is any one of SEQ ID NOs: 187, 212, 218, 226, 291, 295, 298-322, 324, 351-355, 358-360, 362, 364, 366-368, 371-375, 381-395, 399, 403-417, 419, 421-425, 427, 429, 433-443, 446-461, 472, 492, 496, 499-506, 511-513, 515, 518-523, 536-537, 573-598, 600-646 and is administered at least once daily in an amount of about 1 mg to about 100 mg, about 5 mg to about 95 mg, about 10 mg to about 90 mg, about 15 mg to about 85 mg, about 20 mg to about 80 mg, about 25 mg to about 75 mg, about 30 mg to about 70 mg, about 35 mg to about 65 mg, about 40 to about 60 mg, or about 45 to about 55 mg. In some embodiments, the non-naturally occurring melanocortin analog is any one of SEQ ID NOs: 187, 212, 218, 226, 291, 295, 298-322, 324, 351-355, 358-360, 362, 364, 366-368, 371-375, 381-395, 399, 403-417, 419, 421-425, 427, 429, 433-443, 446-461, 472, 492, 496, 499-506, 511-513, 515, 518-523, 536-537, 573-598, 600-646 and is administered at least once daily in an amount of about 50 mg.

**[0713]** In some embodiments, the non-naturally occurring melanocortin analog is any one of SEQ ID NOs: 187, 218, 231-235, 291, 295, 298-322, 351-353, 425, 427, 429, 433-443, 446-458, 573-599, 600-620, 622-646 and is administered at least once daily in an amount of about 0.1 mg to about 100 mg, 0.5 mg to about 50 mg, about 1 mg to about 40 mg, about 2.5 mg to about 30 mg, about 5 to about 20 mg, or about 7.5 to about 15 mg. In some embodiments, the non-naturally occurring melanocortin analog is any one of SEQ ID NOs: 187, 218, 231-235, 291, 295, 298-322, 351-353, 425, 427, 429, 433-443, 446-458, 573-599, 600-620, 622-646 and is administered once daily in an amount of about 10 mg. In some embodiments, the non-naturally occurring melanocortin analog is any one of SEQ ID NOs: 187, 218, 231-235, 291, 295, 298-322, 351-353, 425, 427, 429, 433-443, 446-458, 573-599, 600-620, 622-646 and is administered at least once daily in an amount of about 1 mg to about 100 mg, about 5 mg to about 95 mg, about 10 mg to about 90 mg, about 15 mg to about 85 mg, about 20 mg to about 80 mg, about 25 mg to about 75 mg, about 30 mg to about 70 mg, about 35 mg to about 65 mg, about 40 to about 60 mg, or about 45 to about 55 mg. In some embodiments, the non-naturally occurring melanocortin analog is any one of SEQ ID NOs: 187, 218, 231-235, 291, 295, 298-322, 351-353, 425, 427, 429, 433-443,

446-458, 573-599, 600-620, 622-646 and is administered at least once daily in an amount of about 50 mg.

**[0714]** In some embodiments, the non-naturally occurring melanocortin analog is any one of SEQ ID NOs: 226, 383-393, 399, 403-417 and is administered at least once daily in an amount of about 0.1 mg to about 100 mg, 0.5 mg to about 50 mg, about 1 mg to about 40 mg, about 2.5 mg to about 30 mg, about 5 to about 20 mg, or about 7.5 to about 15 mg. In some embodiments, the non-naturally occurring melanocortin analog is any one of SEQ ID NOs: 226, 383-393, 399, 403-417 and is administered once daily in an amount of about 10 mg. In some embodiments, the non-naturally occurring melanocortin analog is any one of SEQ ID NOs: 226, 383-393, 399, 403-417 and is administered at least once daily in an amount of about 1 mg to about 100 mg, about 5 mg to about 95 mg, about 10 mg to about 90 mg, about 15 mg to about 85 mg, about 20 mg to about 80 mg, about 25 mg to about 75 mg, about 30 mg to about 70 mg, about 35 mg to about 65 mg, about 40 to about 60 mg, or about 45 to about 55 mg. In some embodiments, the non-naturally occurring melanocortin analog is any one of SEQ ID NOs: 226, 383-393, 399, 403-417 and is administered at least once daily in an amount of about 50 mg.

**[0715]** In some embodiments, the non-naturally occurring melanocortin analog is any one of SEQ ID NOs: 209-211, 499, 501-506, 511-513, 515, 518-523 and is administered at least once daily in an amount of about 0.1 mg to about 100 mg, 0.5 mg to about 50 mg, about 1 mg to about 40 mg, about 2.5 mg to about 30 mg, about 5 to about 20 mg, or about 7.5 to about 15 mg. In some embodiments, the non-naturally occurring melanocortin analog is any one of SEQ ID NOs: 209-211, 499, 501-506, 511-513, 515, 518-523 and is administered once daily in an amount of about 10 mg. In some embodiments, the non-naturally occurring melanocortin analog is any one of SEQ ID NOs: 209-211, 499, 501-506, 511-513, 515, 518-523 and is administered at least once daily in an amount of about 1 mg to about 100 mg, about 5 mg to about 95 mg, about 10 mg to about 90 mg, about 15 mg to about 85 mg, about 20 mg to about 80 mg, about 25 mg to about 75 mg, about 30 mg to about 70 mg, about 35 mg to about 65 mg, about 40 to about 60 mg, or about 45 to about 55 mg. In some embodiments, the non-naturally occurring melanocortin analog is any one

of SEQ ID NOs: 209-211, 499, 501-506, 511-513, 515, 518-523 and is administered at least once daily in an amount of about 50 mg.

**[0716]** In some embodiments, administration of the non-naturally occurring melanocortin analog comprises delivery across the blood brain barrier. In some embodiments, administration of the non-naturally occurring melanocortin analog comprises delivery across the epithelium. In some embodiments, administration of the non-naturally occurring melanocortin analog comprises delivery across the epithelium and the blood brain barrier. In some embodiments, administration of the non-naturally occurring melanocortin analog comprises delivery through the gastrointestinal tract.

***thods***

**[0717]** The present technology comprises methods of treating, preventing, reducing, or otherwise ameliorating one or more symptoms or conditions associated with pain, addiction, addictive agent use (e.g., opioid use disorders), or withdrawal from an addictive substance by administration of a non-naturally occurring melanocortin analog. The methods of the present technology may promote reduced pain, addiction, use of and/or dependence on addictive substances, withdrawal symptoms after use of an addictive substance (e.g., pain, anxiety, depression, diarrhea, dizziness, fatigue, muscle aches, nausea, sleep problems, suicidal ideation, tremors, and visual disturbances), or any combination thereof.

**[0718]** In some embodiments, the present technology comprises methods of treating, preventing, reducing, or otherwise ameliorating an opioid use disorder (OUD). In some embodiments, the opioid use disorder is characterized by one or more of a synthetic opioid use and/or dependence or a pharmaceutical opioid use and/or dependence. In some embodiments, the opioid use disorder comprises one or more of (i) a strong desire or sense of compulsion to take opioids; (ii) difficulties in controlling opioid use; (iii) a presence of withdrawal on ceasing opioids; (iv) a development of tolerance to the effects of opioids; (v) neglecting pleasures or interests because of opioid use; and (vi) a persistent opioid use despite evidence of harmful consequences.

**[0719]** In some embodiments, the methods of the present technology comprise a prevention, stabilization, or reduction in one or more of a dose used or consumed of an

addictive substance, a dependency on an addictive substance, an amount/frequency of an addictive substance, use (e.g., dose or dosage) of an opioid reversal agent, relapse associated with use of an addictive substance, use (e.g., frequency/amount) of a conventional medication used to treat an addiction, hospitalization associated with use of an addictive substance, or a need for rehabilitation from an addiction. In some embodiments, the methods promote or increase cessation of an addictive substance.

**[0720]** The addictive substances of the present technology may comprise a substance in a prescription medication, a substance in an over-the-counter medication, a recreational substance, or an illegal substance. Nonlimiting examples of addictive substances include opioids (e.g., morphine, heroin, codeine, oxycodone, hydrocodone, fentanyl), painkillers, stimulants (e.g., caffeine, nicotine, methamphetamines, cocaine, amphetamines), narcotics, alcohol, barbiturates (e.g., phenobarbital, methohexital, butalbital, pentobarbital, primidone, and amobarbital), sedatives (e.g., tranquilizers, xylazine, eszopiclone, zaleplon, zolpidem, zopiclone), marijuana, cannabis, tetrahydrocannabinol (THC), and cannabidiol (CBD), or inhalants (e.g., aerosols, butanes, freon, helium, nitrous oxide, propane, nitrites).

**[0721]** In some embodiments, the sedative comprises barbiturates (e.g., phenobarbital, methohexital, butalbital, pentobarbital, primidone, and amobarbital) or benzodiazepines (e.g., alprazolam, lorazepam, clonazepam, diazepam, temazepam).

**[0722]** In some embodiments, the nicotine comprises nicotine in a tobacco chew, a nicotine pouch, or a smoking device (e.g., cigarettes, electronic cigarettes, cigars, vape products).

**[0723]** In some embodiments, the present technology comprises methods for augmenting the effects of or replacing a conventional medication used to treat an addiction in a subject in need thereof, comprising administering a non-naturally occurring melanocortin analog to the subject. The non-naturally occurring melanocortin analog may elicit a same or improved treatment outcome relative to the treatment outcome observed when the subject is administered the conventional medication used to treat an addiction in the absence of the non-naturally occurring melanocortin analog. The conventional medications used to treat addictions may include pharmaceutical compositions that are used in clinical settings and/or may be prescribed by a medical provider to treat one or more addictions. This may include

opioid agonists (e.g., partial or full opioid agonists), opioid antagonists, and non-opioid medications. The conventional medications do not comprise the non-naturally occurring melanocortin analogs of the present technology.

**[0724]** In some embodiments, the conventional medication used to treat an addiction comprises an opioid agonist therapy (OAT) (e.g., methadone and/or buprenorphine). In some embodiments, the conventional medication used to treat an addiction comprise an opioid reversal agent (e.g., an opioid antagonist).

**[0725]** In some embodiments, the conventional medication used to treat an addiction comprises one or more of buprenorphine, naltrexone, acamprosate, methadone, naloxone, nalmefene, xycodone, levo-alpha-acetylmethadol (LAAM), codeine, or a slow-release morphine (e.g., a slow-release oral morphine).

**[0726]** In some embodiments, the present technology comprises methods of treating, preventing, reducing, or otherwise ameliorating an alcohol use disorder (AUD) in a subject in need thereof.

**[0727]** The methods of the present technology comprise administering a non-naturally occurring melanocortin analog of the present technology to a subject in need thereof.

**[0728]** In other aspects, the present technology provides a method of suppressing pain and/or an addiction (e.g., an addiction to an addictive substance of the present technology) in a subject in need thereof. In some embodiments, the method comprises administering a non-naturally occurring melanocortin analog to the subject. The non-naturally occurring melanocortin analog may be administered prior to, during, and/or after use of an addictive substance.

**[0729]** In some embodiments, the subject of the present technology is administered a non-naturally occurring melanocortin analog at least about 30 seconds, 1 minute, 5 minutes, 30 minutes, 1 hour, 2 hours, 3 hours, 4 hours, 6 hours, 8 hours, 12 hours, 24 hours, 36 hours, 2 days, 3 days, 4 days, 5 days, 1 week, 2 weeks, 3 weeks, 4 weeks, 6 weeks, 8 weeks, 10 weeks, 15 weeks, 20 weeks, 30 weeks, 40 weeks, 1 year, or 2 years after use of an addictive substance.

**[0730]** In some embodiments, the methods comprise administering a non-naturally occurring melanocortin analog at a first dose and a second to a subject in need thereof, wherein the second dose is greater than the first dose. In some embodiments, the subject is administered a third dose that is greater than the first and the second dose.

**[0731]** In some embodiments, the methods comprise administered the non-naturally occurring melanocortin analog to the subject in increase doses or increased dosages, relative to the first dose.

*Maintenance Doses*

**[0732]** In some embodiments, a maintenance dose of the non-naturally occurring melanocortin analog is administered to the subject to maintain or enhance one or more outcomes of the methods of the present technology.

*Subjects*

**[0733]** In some embodiments, the subject has used or is using an addictive substance. In some embodiments, the subject has used or is using a medication to treat an addiction. In some embodiments, the frequency or amount of the addictive substance and/or rescue medication is reduced during or after administration of the non-naturally occurring melanocortin analog. In some embodiments, the frequency or amount of the addictive substance and/or rescue medication is reduced as the dose or dosage of the non-naturally occurring melanocortin analog increases. In some embodiments, the frequency or amount of the addictive substance and/or rescue medication comprises a downward titration during or after administration of a non-naturally occurring melanocortin analog.

**[0734]** In some embodiments, the subject is a mammal, including but not limited to a human, a non-human primate such as a chimpanzee, a domestic livestock or a farm animal such as a cow, a bison, sheep, a pig, a goat, a horse, a chicken, and a rooster, a domestic pet animal such as a dog, a cat, a rat, a mouse, and a rabbit, and a laboratory subject such as a rodent, including a rat, a mouse, and a guinea pig. In some embodiments, the subject is a human. In some embodiments, the subject is an animal such as a rat or a dog.

*Controls*

**[0735]** The controls of the present technology may comprise the subject at baseline. In some embodiments, the controls of the methods of the present technology comprise a subject that is not administered a non-naturally occurring melanocortin analog of the present technology or a subject subjected to a method lacking one or more steps of the methods of the present technology.

## EXAMPLES

**[0736]** The following examples are intended to illustrate various embodiments of the present technology. As such, the specific embodiments discussed are not to be construed as limitations on the scope of the present technology. It will be apparent to one skilled in the art that various equivalents, changes, and modifications may be made without departing from the scope of present technology, and it is understood that such equivalent embodiments, are to be included herein. Further, all references cited herein are hereby incorporated by reference in their entirety, as if fully set forth herein.

***Example 1: Peptide Synthesis-Generic***

**[0737]** The non-naturally occurring melanocortin analogs of the present technology were synthesized by conventional procedures (e.g., solution-phase procedure, solid-phase synthesis) for the formation of a peptide linkage between amino acids. The solution-phase procedure involved a condensation between the free alpha amino group of an amino acid or derivative thereof having the carboxyl group or other reactive groups protected and the free primary carboxyl group of another amino acid or derivative thereof having the amino group or other reactive groups protected. The solid-phase synthesis utilized a variety of resins and reagents and may involve additional purification steps.

**[0738]** The process for synthesizing the non-naturally occurring melanocortin analogs was generally performed by a procedure as follows. Each amino acid in the desired sequence of the non-naturally occurring melanocortin analogs was added one at a time in succession to another amino acid or derivative thereof or by a procedure whereby peptide fragments with the desired amino acid sequence were first synthesized conventionally and then condensed to provide the desired peptide. In most cases, the resulting peptide was then cyclized to yield a cyclic peptide.

**[0739]** Solid-phase peptide synthesis was carried out by sequentially incorporating the desired amino acid residues one at a time into the growing peptide chain coupled to a solid-phase support according to the general principles of solid phase methods (see Merrifield, Angew Chem. 24:799-810 (1985) and Barany et al., The Peptides, Analysis, Synthesis and Biology, Vol. 2, Gross E. and Meienhofer J., Eds. Academic Press 1-284 (1980)). An exemplary solid-phase synthesis of non-naturally occurring melanocortin analogs is provided below.

**[0740]** Initially, the C-terminal amino acid residue of the non-naturally occurring melanocortin analog was coupled to a solid-phase support, e.g., a solid-phase resin. Coupling of the C-terminal amino acid residue and the solid-phase support may be carried out according to any method know in the art. Depending on the coupling method, the alpha-amine of the C-terminal amino acid residue may or may not be protected with an amine protecting group, as described below. Likewise, the carboxyl group of the amino acid residue may or may not be activated prior to coupling to the solid-phase support in order to increase its electrophilicity. Some methods of coupling rely on the formation of an ester bond between the carboxyl group of the amino acid and a reactive handle on the solid-phase resin. For example, an amino acid residue may be coupled to a p-benzyloxybenzyl alcohol resin (Wang) or a 2-chlorotrityl chloride resin via an ester linkage. Some methods of coupling rely on the formation of an amide bond between the carboxyl group of the amino acid and a reactive handle on the solid-phase resin For example, an amino acid residue may be coupled to a benzhydrylamine (BHA) resin through an Fmoc-linker such as, for example, p-[(R,S)-α-[1-(9H-fluor-en-9-yl)-methoxyformamido]-2,4-dimethyloxybenzyl]-phenoxyacetic acid (Rink linker) via an amide linkage.

**[0741]** The non-naturally occurring melanocortin analog was then synthesized by sequential amino acid addition or combination of peptide fragments. Subsequently, the peptide was cleaved from the solid-phase support and purified by methods known in the art, such as, for example, reverse phase high performance liquid chromatography (RP-HPLC) using a suitable column, such as a C18 column. Additionally, or alternatively, other methods of separation or purification were employed, including, but not limited to, methods based on the size or charge of the peptide. Once purified, the peptide was characterized by methods

such as high-performance liquid chromatograph (HPLC), amino acid analysis, mass spectrometry, and the like.

***Example 2: Peptide Synthesis-Protecting Groups***

**[0742]** During synthesis of the non-naturally occurring melanocortin analogs, reactive side chain groups of the various amino acid residues were protected with suitable protecting groups, which prevented undesirable chemical reaction from occurring at that site until the protecting group was removed.

**[0743]** Additionally, protection of the alpha amino group of an amino acid residue or fragment was performed while that entity reacting with the carboxyl group, followed by the selective removal of the alpha amino protecting group to allow a subsequent reaction to take place at that site. Specific protecting groups for solid phase synthesis methods and solution phase synthesis methods are known to those having ordinary skill in the art. Alpha amino groups were protected by a suitable protecting group, including a urethane-type protecting group, such as benzyloxycarbonyl (Z) and substituted benzyloxycarbonyl, such as p-chlorobenzyloxycarbonyl, p-nitrobenzyloxycarbonyl, p-bromobenzyloxycarbonyl, p-biphenyl-isopropoxycarbonyl, 9-fluorenylmethoxycarbonyl (Fmoc) and p-methoxybenzyloxycarbonyl (Moz); aliphatic urethane-type protecting groups, such as t-butyloxycarbonyl (Boc), diisopropylmethoxycarbonyl, isopropoxycarbonyl, and allyloxycarbonyl. Fmoc was also used for alpha amino protection. Guanidino groups, if present, were protected by a suitable protecting group, such as nitro, p-toluenesulfonyl (Tos), Z, pentamethylchromanesulfonyl (Pmc), adamantyloxycarbonyl, pentamethyldihydrobenzofuran-5-sulfonyl (Pbf) and Boc. Pmc was used as a protecting group for Arg.

**[0744]** Alpha aminoprotecting groups may be removed under basic conditions, such as, for example, using a solution of piperidine, piperazine, diethylamine, or morpholine (20-40% v/v) in N,N-dimethylformamide (DMF). In synthesis methods in which alpha amino protecting groups were used, protecting groups were removed after synthesis of the peptide and before or after cleavage of the solid-phase support.

***Example 3: Peptide Synthesis-Additional Modifications***

**[0745]** If necessary, the peptides were further modified to obtain N-terminus modifications, such as acetylation, while on resin, or were removed from the resin by use of a cleaving reagent and then modified. Likewise, C-terminus modification (e.g., amidation), was performed if needed.

**[0746]** Additionally, the cyclized peptide structures were obtained prior to cleavage from the peptide resin. For cyclization through reactive side chain moieties, the desired side chains were deprotected, and the peptide suspended in a suitable solvent and a cyclic coupling agent added. Suitable solvents, for example DMF, dichloromethane (DCM) or 1-methyl-2-pyrrolidone (NMP), were used for the cyclization. Suitable cyclic coupling reagents (e.g., 2-(1H-benzotriazol-1-yl)-1,1,3,3-tetramethyluronium tetrafluoroborate (TBTU), 2-(1H-benzotriazol-1-yl)-1,1,3,3-tetramethyluronium hexafluorophosphate (HBTU), benzotriazole-1-yl-oxy-tris(dimethylamino)phosphoniumhexafluorophosphate (BOP), benzotriazole-1-yl-oxy-tris(pyrrolidino)phosphoniumhexafluorophosphate (PyBOP), 2-(7-aza-1H-benzotriazol-1-yl)-1,1,3,3-tetramethyluronium tetrafluoroborate (TATU), 2-(2-oxo-1 (2H)-pyridyl)-1,1,3,3-tetramethyluronium tetrafluoroborate (TPTU), N,N′-dicyclohexylcarbodiimide/1-hydroxybenzotriazole (DCCI/HOBt)) were also used for the cyclization. Coupling was initiated by a suitable base, such as N,N-diispropylethylamine (DIPEA), sym-collidine or N-methylmorpholine (NMM).

***Example 4: Biological Data***

**[0747]** The agonist and antagonist activity of exemplary non-naturally occurring melanocortin analogs at the melanocortin receptors (e.g., MC1R, MC3R, MC4R, and MC5R) were measured via cAMP accumulation assay, according to the following procedure. Experimental design and execution were conducted by Epics Therapeutics S.A. EuroscreenFast (Bruxelles, Belgium).

*Compound Handing*

**[0748]** Compounds were delivered as powder (1 mg) or 10 mM solutions (100 µl) in 100% DMSO. Powders were solubilized in 100% DMSO at a concentration of 10 mM (master solution) in a solvent volume defined. Serial dilutions were performed from master solution in 100% DMSO to obtain intermediate concentrations 200-, 300- or 400-fold higher

than the concentrations to be tested, depending on the assay. Each sample was diluted 100-fold in the assay buffer and dispensed in a test plate. Amounts, solvents, and dilutions were estimated based on standard small-molecule drugs. Cell lines used for functional assays are shown in Table 1.

**Table 1**. Cell lines

| Receptor | Accession Number | Cell Line | Reference agonist | Reference antagonist |
|---|---|---|---|---|
| MC1R | NP_002377.4 | CHO-K1 | NDP-α-MSH | N/A |
| MC3R | AAC13541.1 I81V | CHO-K1 | NDP-α-MSH | SHU9119 |
| MC4R | NP_005903.2 | CHO-K1 | NDP-α-MSH | SHU9119 |
| MC5R | NP_005904.1 | CHO-K1 | NDP-α-MSH | N/A |

*Compound Testing*

**[0749]** Compounds were tested for (i) agonist and/or antagonist activity at the human MC3 (FAST-0232C) and MC4 (FAST-0233C) receptors, (ii) agonist activity at the human MC1 (FAST-0232C) receptor, and/or (iii) agonist activity at the human MC5 (FAST-0233C) receptor at the following nanomolar concentrations, in duplicate: 0.0001, 0.001, 0.01, 0.03, 0.1, 0.3, 1, 10, 100, and 1,000.

*Testing Protocol*

**[0750]** Cyclic AMP (cAMP) Homogenous Time-Resolved Fluorescence (HTRF) assay for Gs coupled receptor:

**[0751]** CHO-K1 cells expressing recombinant human receptor grown prior to the test in media without antibiotic were detached by gentle flushing with PBS-EDTA (5 mM EDTA), recovered by centrifugation and resuspended in assay buffer (KRH: 5 mM KCl, 1.25 mM MgSO4, 124 mM NaCl, 25 mM HEPES, 13.3 mM Glucose, 1.25 mM KH2PO4, 1.45 mM CaCl2, 0.5 g/l BSA, supplemented with 1mM IBMX or 25µM Rolipram).

**[0752]** Dose response curves were performed in parallel with the reference compounds.

**[0753]** For agonist test (384well): 5 µl of cells were mixed with 5 µl of the test compound at increasing concentrations and then incubated 30 min at room temperature. After addition of the lysis buffer containing cAMP-d2 and anti-cAMP cryptate detection reagents, plates were incubated 1-hour at room temperature, and fluorescence ratios were measured according to the manufacturer specification, with the HTRF kit.

**[0754]** For antagonist test (384well): 5 µl of cells were mixed in the wells of an assay plate with 5 µl of a mix of test compound at increasing concentrations and reference agonist for a final concentration corresponding to the historical EC80. The plates were then incubated 30 min at room temperature. After addition of the lysis buffer containing cAMP-d2 and anti-cAMP cryptate detection reagents, plates were incubated 1-hour at room temperature, and fluorescence ratios were measured according to the manufacturer specification, with the HTRF kit.

*Quality Control for Compound Testing*

**[0755]** On each day of experimentation and prior to the testing of compounds, reference compounds were tested at several concentrations in duplicate (n=2) to obtain a dose-response curve and an estimated EC50 and/or IC50 values.

**[0756]** Reference values thus obtained for the test were compared to historical values obtained from the same receptor and used to validate the experimental session.

**[0757]** A session was considered as valid only if the reference value was found to be within a 0.5 logs interval from the historical value.

**[0758]** For replicate determinations, the maximum variability tolerated in the test was of +/-20% around the average of the replicates.

*Non-naturally occurring melanocortin analog grouping*

**[0759]** Non-naturally occurring melanocortin analogs were grouped based on structural similarities. Group A included non-naturally occurring melanocortin analog A1, which is a cyclic peptide comprising dNal(2') at $R^4$. The group A non-naturally occurring melanocortin analog is provided in Table 2.

**Table 2.** Group A non-naturally occurring melanocortin analog

| SEQ ID NO | Non-naturally occurring melanocortin analog | Formula |
|---|---|---|
| 8 | A1 | Ac-Nle-c[Asp-His-dNal(2')-Arg-Trp-Pro-Lys]-dVal-dPro-$NH_2$ |

**[0760]** Group B included non-naturally occurring melanocortin analogs B1-B6, all of which are cyclic peptides comprising the motif dPhe-Arg-Trp that are cyclized through a disulfide bridge. Group B non-naturally occurring melanocortin analogs are provided in Table 3.

**Table 3.** Group B non-naturally occurring melanocortin analog

| SEQ ID NO | Non-naturally occurring melanocortin analog | Formula |
|---|---|---|
| 318 | B1 | Ac-Nle-c[Cys-Pro-dPhe-Arg-Trp-Cys]-dVal-dPro-$NH_2$ |
| 319 | B2 | Ac-Nle-c[dCys-Pro-dPhe-Arg-Trp-Cys]-dVal-dPro-$NH_2$ |
| 320 | B3 | Ac-Nle-c[dPen-Pro-dPhe-Arg-Trp-dPen]-dVal-dPro-$NH_2$ |
| 321 | B4 | Ac-Nle-c[dCys-Pro-dPhe-Arg-Trp-dCys]-dVal-dPro-$NH_2$ |
| 322 | B5 | Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Orn]-dVal-dPro-$NH_2$ |
| 324 | B6 | Ac-Nle-c[Cys-dPhe-Arg-Trp-Pen]-dVal-dPro-$NH_2$ |

**[0761]** Group C included non-naturally occurring melanocortin analogs C1-C16, all of which are cyclic peptides comprising the motif $R^3$-dPhe-Arg-Trp, where $R^3$ is not Pro. Group C non-naturally occurring melanocortin analogs are provided in Table 3.

**Table 3.** Group C non-naturally occurring melanocortin analog

| SEQ ID NO | Non-naturally occurring melanocortin analog | Formula |
|---|---|---|
| 212 | C1 | Ac-Nle-c[Asp-Atc-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ |

| | | |
|---|---|---|
| 354 | C2 | Ac-Nle-c[Asp-Ala-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ |
| 355 | C3 | Ac-Nle-c[Asp-Leu-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ |
| 358 | C4 | Ac-Nle-c[Asp-Cpe-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ |
| 359 | C5 | Ac-Nle-c[Asp-Che-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ |
| 360 | C6 | Ac-Nle-c[Asp-Oic-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ |
| 362 | C7 | Ac-Nle-c[Asp-Tic-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ |
| 364 | C8 | Ac-Nle-c[Asp-Hyp-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ |
| 366 | C9 | Ac-Nle-c[Asp-Phe-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ |
| 367 | C10 | Ac-Nle-c[Asp-dPhe-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ |
| 368 | C11 | Ac-Nle-c[Asp-Bip-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ |
| 371 | C12 | Ac-Nle-c[Asp-dGln-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ |
| 372 | C13 | Ac-Nle-c[Asp-Trp-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ |
| 373 | C14 | Ac-Nle-c[Asp-dTrp-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ |
| 374 | C15 | Ac-Nle-c[Asp-Tyr-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ |
| 375 | C16 | Ac-Nle-c[Asp-dTyr-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ |

**[0762]** Group D included non-naturally occurring melanocortin analogs D1-D30, all of which are cyclic peptides with the motif Trp-Pro-dPhe, or a derivative thereof. Group D non-naturally occurring melanocortin analogs are provided in Table 3.

**Table 4.** Group D non-naturally occurring melanocortin analog

| **SEQ ID NO** | **Non-naturally occurring melanocortin analog** | **Formula** |
|---|---|---|
| 226 | D1 | Ac-Nle-c[Asp-Trp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ |
| 383 | D2 | Ac-Nle-c[Cys-Trp-Pro-dPhe-Arg-Trp-Cys]-dVal-dPro-$NH_2$ |
| 384 | D3 | Ac-Nle-c[dCys-Trp-Pro-dPhe-Arg-Trp-Cys]-dVal-dPro-$NH_2$ |
| 385 | D4 | Ac-Nle-c[dCys-Trp-Pro-dPhe-Arg-Trp-dCys]-dVal-dPro-$NH_2$ |
| 386 | D5 | Ac-Ala-c[Asp-Trp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ |
| 387 | D6 | Ac-Lys-c[Asp-Trp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ |

| | | |
|---|---|---|
| 388 | D7 | Ac-dLys-c[Asp-Trp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ |
| 389 | D8 | Ac-Arg-c[Asp-Trp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ |
| 390 | D9 | Ac-dArg-c[Asp-Trp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ |
| 391 | D10 | Ac-dHis-c[Asp-Trp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ |
| 392 | D11 | Ac-His-c[Asp-Trp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ |
| 393 | D12 | Ac-Nle-Nle-c[Asp-Trp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ |
| 394 | D13 | Ac-Nle-c[Asp-Trp-Ala-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ |
| 395 | D14 | Ac-Nle-c[Asp-Trp-Leu-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ |
| 399 | D15 | Ac-Nle-c[Asp-Trp-Pro-dPhe-Arg-Nal(1')-Lys]-dVal-dPro-$NH_2$ |
| 403 | D16 | Ac-Nle-c[Asp-Trp-Pro-dPhe-Arg-dNal(2')-Lys]-dVal-dPro-$NH_2$ |
| 404 | D17 | Ac-Nle-c[Asp-Trp-Pro-dPhe-Arg-Nal(2')-Lys]-dVal-dPro-$NH_2$ |
| 405 | D18 | Ac-Nle-c[Asp-Trp-Pro-dPhe-Arg-Trp-Lys]-dArg-dVal-dPro-$NH_2$ |
| 406 | D19 | Ac-Nle-c[Asp-Trp-Pro-dPhe-Arg-Trp-Lys]-dLys-dVal-dPro-$NH_2$ |
| 407 | D20 | Ac-Nle-c[Asp-Trp-Pro-dPhe-Arg-Trp-Lys]-dArg-dPro-$NH_2$ |
| 408 | D21 | Ac-Nle-c[Asp-Trp-Pro-dPhe-Arg-Trp-Lys]-dLys-dPro-$NH_2$ |
| 409 | D22 | Ac-Nle-c[Asp-Trp-Pro-dPhe-Arg-Trp-Lys]-dVal-dHyp-$NH_2$ |
| 410 | D23 | Ac-Nle-c[Asp-Trp-Pro-dPhe-Arg-Trp-Lys]-dTle-dPro-$NH_2$ |
| 411 | D24 | Ac-Nle-c[Asp-Trp-Pro-dPhe-Arg-Trp-Lys]-dVal-dVal-dVal-dPro-$NH_2$ |
| 412 | D25 | Ac-Nle-c[Asp-Phe-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ |
| 413 | D26 | Ac-Nle-c[Asp-His-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ |
| 414 | D27 | Ac-Nle-c[Asp-Tyr-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ |
| 415 | D28 | Ac-Nle-c[Asp-dPhe-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ |
| 416 | D29 | Ac-Nle-c[Asp-dHis-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ |
| 417 | D30 | Ac-Nle-c[Asp-dTyr-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ |

**[0763]** Group E included non-naturally occurring melanocortin analogs E1 to E4, all of which are cyclic peptides comprising the motif Pro-dPhe-Arg-Trp, cyclized through a lactam bond between Asp and Lys, and a C-terminal dVal-dPro moiety. Group E non-naturally occurring melanocortin analogs are provided in Table 6.

**Table 5.** Group E non-naturally occurring melanocortin analogs

| SEQ ID NO | Non-naturally occurring melanocortin analog | Formula |
|---|---|---|
| 291 | E1 | Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-OH |
| 295 | E2 | Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ |
| 298 | E3 | Ac-dLeu-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ |
| 299 | E4 | Ac-dAla-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ |
| 300 | E5 | Ac-Ala-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ |
| 301 | E6 | Ac-dNle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ |
| 302 | E7 | Ac-dArg-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ |
| 303 | E8 | Ac-dPhe-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ |
| 304 | E9 | Ac-dTyr-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ |
| 305 | E10 | Phe-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ |
| 306 | E11 | His-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ |
| 307 | E12 | Trp-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ |
| 308 | E13 | dPhe-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ |
| 309 | E14 | dHis-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ |
| 310 | E15 | dTrp-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ |
| 311 | E16 | Ac-Arg-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ |
| 312 | E17 | Ac-dLys-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ |
| 313 | E18 | Ac-Lys-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ |
| 314 | E19 | Ac-His-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ |
| 315 | E20 | Ac-dHis-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ |
| 316 | E21 | Ac-Orn-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ |

| | | |
|---|---|---|
| 317 | E22 | Ac-dOrn-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ |

**[0764]** Group F included non-naturally occurring melanocortin analogs F1 to F29, all of which are cyclic peptides comprising the motif Pro-p(F)Phe-Arg-Trp or a derivative thereof. Group F non-naturally occurring melanocortin analogs are provided in Table 6.

**Table 6.** Group F non-naturally occurring melanocortin analogs

| SEQ ID NO | Non-naturally occurring melanocortin analog | Formula |
|---|---|---|
| 433 | F1 | Ac-Nle-c[dCys-Pro-p(F)dPhe-Arg-Trp-Cys]-dVal-dPro-$NH_2$ |
| 434 | F2 | Ac-Nle-c[dCys-Pro-p(F)dPhe-Arg-Trp-dCys]-dVal-dPro-$NH_2$ |
| 435 | F3 | Ac-Ala-c[Asp-Pro-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ |
| 436 | F4 | Ac-dArg-c[Asp-Pro-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ |
| 437 | F5 | Ac-Arg-c[Asp-Pro-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ |
| 438 | F6 | Ac-Lys-c[Asp-Pro-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ |
| 439 | F7 | Ac-dLys-c[Asp-Pro-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ |
| 440 | F8 | Ac-His-c[Asp-Pro-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ |
| 441 | F9 | Ac-dHis-c[Asp-Pro-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ |
| 442 | F10 | Ac-Nle-Nle-c[Asp-Pro-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ |

| | | |
|---|---|---|
| 443 | F11 | Ac-Nle-c[Asp-Pro-p(F)dPhe-His-Trp-Lys]-dVal-dPro-$NH_2$ |
| 446 | F12 | Ac-Nle-c[Asp-Pro-p(F)dPhe-Arg-Trp-Lys]-dTle-dTle-dVal-$NH_2$ |
| 447 | F13 | Ac-Nle-c[Asp-Pro-p(F)dPhe-Arg-Trp-Lys]-dVal-dVal-dVal-dPro-$NH_2$ |
| 448 | F14 | Ac-Nle-c[Asp-Pro-p(F)dPhe-Arg-Trp-Lys]-dPro-dVal-dPro-$NH_2$ |
| 449 | F15 | Ac-Nle-c[Asp-Pro-p(F)dPhe-Arg-Trp-Lys]-dTle-dPro-$NH_2$ |
| 450 | F16 | Ac-Nle-Nle-c[Asp-Pro-p(F)dPhe-Arg-Trp-Lys]-dTle-dPro-$NH_2$ |
| 451 | F17 | Ac-Nle-Nle-c[Asp-Pro-p(F)dPhe-Arg-Trp-Lys]-dPro-dVal-dPro-$NH_2$ |
| 452 | F18 | Ac-Ala-c[Asp-Pro-p(F)dPhe-Arg-Trp-Lys]-dTle-dPro-$NH_2$ |
| 453 | F19 | Ac-dArg-c[Asp-Pro-p(F)dPhe-Arg-Trp-Lys]-dTle-dPro-$NH_2$ |
| 454 | F20 | Ac-Arg-c[Asp-Pro-p(F)dPhe-Arg-Trp-Lys]-dTle-dPro-$NH_2$ |
| 455 | F21 | Ac-Lys-c[Asp-Pro-p(F)dPhe-Arg-Trp-Lys]-dTle-dPro-$NH_2$ |
| 456 | F22 | Ac-dLys-c[Asp-Pro-p(F)dPhe-Arg-Trp-Lys]-dTle-dPro-$NH_2$ |
| 457 | F23 | Ac-His-c[Asp-Pro-p(F)dPhe-Arg-Trp-Lys]-dTle-dPro-$NH_2$ |
| 458 | F24 | Ac-dHis-c[Asp-Pro-p(F)dPhe-Arg-Trp-Lys]-dTle-dPro-$NH_2$ |
| 459 | F25 | Ac-Nle-c[Cys-His-p(F)dPhe-Arg-Trp-Cys]-dVal-dPro-$NH_2$ |

| | | |
|---|---|---|
| 461 | F26 | Ac-Nle-c[dCys-His-p(F)dPhe-Arg-Trp-dCys]-dVal-dPro-$NH_2$ |
| 472 | F27 | Ac-Nle-c[Asp-His-p(F)dPhe-Arg-Nal(2')-Lys]-dVal-dPro-$NH_2$ |
| 492 | F28 | Ac-Nle-c[Asp-dGln-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ |
| 496 | F29 | Ac-Nle-c[Asp-dTyr-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ |

**[0765]** Group G included non-naturally occurring melanocortin analogs G1 to G17, all of which are cyclic peptides comprising the motif His-p(Cl)Phe-Arg-Trp or a derivative thereof. Group G non-naturally occurring melanocortin analogs are provided in Table 7.

**Table 7.** Group G non-naturally occurring melanocortin analogs

| **SEQ ID NO** | **Non-naturally occurring melanocortin analog** | **Formula** |
|---|---|---|
| 499 | G1 | Ac-Nle-c[dCys-His-p(Cl)dPhe-Arg-Trp-dCys]-dVal-dPro-$NH_2$ |
| 501 | G2 | Ac-dArg-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ |
| 502 | G3 | Ac-Arg-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ |
| 503 | G4 | Ac-Lys-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ |
| 504 | G5 | Ac-dLys-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ |
| 505 | G6 | Ac-His-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ |
| 506 | G7 | Ac-dHis-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ |

| | | |
|---|---|---|
| 511 | G8 | Ac-Nle-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dTle-dTle-dVal-$NH_2$ |
| 512 | G9 | Ac-Nle-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dVal-dVal-dPro-$NH_2$ |
| 513 | G10 | Ac-Nle-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dPro-dVal-dPro-$NH_2$ |
| 515 | G11 | Ac-Nle-Nle-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dTle-dPro-$NH_2$ |
| 518 | G12 | Ac-dArg-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dTle-dPro-$NH_2$ |
| 519 | G13 | Ac-Arg-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dTle-dPro-$NH_2$ |
| 520 | G14 | Ac-Lys-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dTle-dPro-$NH_2$ |
| 521 | G15 | Ac-dLys-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dTle-dPro-$NH_2$ |
| 522 | G16 | Ac-His-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dTle-dPro-$NH_2$ |
| 523 | G17 | Ac-dHis-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dTle-dPro-$NH_2$ |

**[0766]** Group H included non-naturally occurring melanocortin analogs H1-H2, both of which are cyclic peptides comprising the motif His-p(Br)Phe-Arg-Trp. Group H non-naturally occurring melanocortin analog is provided in Table 8.

**Table 8.** Group H non-naturally occurring melanocortin analogs

| **SEQ ID NO** | **Non-naturally occurring melanocortin analog** | **Formula** |
|---|---|---|
| 536 | H1 | Ac-Nle-c[dCys-His-p(Br)dPhe-Arg-Trp-Cys]-dVal-dPro-$NH_2$ |

| | | |
|---|---|---|
| 537 | H2 | Ac-Nle-c[dCys-His-p(Br)dPhe-Arg-Trp-dCys]-dVal-dPro-$NH_2$ |

**[0767]** Group I included non-naturally occurring melanocortin analogs I1 to I52, all of which are cyclic peptides comprising the motif Pro-dPhe-Arg-Trp, cyclized through a lactam bond between Asp and Lys, and a C-terminus other than dVal-dPro-$NH_2$. Group I non-naturally occurring melanocortin analogs are provided in Table 9.

**Table 9.** Group I non-naturally occurring melanocortin analogs

| SEQ ID NO | Non-naturally occurring melanocortin analog | Formula |
|---|---|---|
| 573 | I1 | Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-Val-Pro-NH2 |
| 574 | I2 | Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-Hyp-NH2 |
| 575 | I3 | Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dHyp-$NH_2$ |
| 576 | I4 | Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-Val-$NH_2$ |
| 577 | I5 | Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-Pro-$NH_2$ |
| 578 | I6 | Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-Arg-$NH_2$ |
| 579 | I7 | Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dArg-$NH_2$ |
| 580 | I8 | Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dArg-dPro-$NH_2$ |
| 581 | I9 | Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-Arg-$NH_2$ |
| 582 | I10 | Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dArg-$NH_2$ |
| 583 | I11 | Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-Lys-Pro-Val-$NH_2$ |
| 584 | I12 | Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dLys-dPro-$NH_2$ |

| | | |
|---|---|---|
| 585 | I13 | Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-Lys-Val-Pro-$NH_2$ |
| 586 | I14 | Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-Lys-dVal-dPro-$NH_2$ |
| 587 | I15 | Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dLys-dVal-dPro-$NH_2$ |
| 588 | I16 | Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-Arg-Pro-Val-$NH_2$ |
| 589 | I17 | Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-Arg-Val-Pro-$NH_2$ |
| 590 | I18 | Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dArg-dVal-dPro-$NH_2$ |
| 591 | I19 | Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dTle-dPro-$NH_2$ |
| 592 | I20 | Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dTle-dTle-dPro-$NH_2$ |
| 593 | I21 | Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dTle-dTle-dVal-$NH_2$ |
| 594 | I22 | Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dTle-$NH_2$ |
| 595 | I53 | Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dVal-dPro-$NH_2$ |
| 596 | I23 | Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dPro-dVal-dPro-$NH_2$ |
| 597 | I24 | Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dVal-dVal-dPro-$NH_2$ |
| 598 | I25 | Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-dVal-dPro-$NH_2$ |
| 600 | I26 | Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-Trp-$NH_2$ |

| | | |
|---|---|---|
| 601 | I27 | Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-Lys-dPro-dVal-$NH_2$ |
| 602 | I28 | Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dAla-dAla-$NH_2$ |
| 603 | I29 | Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-Asp-$NH_2$ |
| 604 | I30 | Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dHyp-$NH_2$ |
| 605 | I31 | Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dAsn-$NH_2$ |
| 606 | I32 | Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-Asp-$NH_2$ |
| 607 | I33 | Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-Asn-dPro-$NH_2$ |
| 608 | I34 | Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-Hyp-$NH_2$ |
| 609 | I35 | Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-Ala-Ala-$NH_2$ |
| 610 | I36 | Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-Gly-Gly-$NH_2$ |
| 611 | I37 | Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-Asp-dPro-$NH_2$ |
| 612 | I38 | Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dAsn-dPro-$NH_2$ |
| 613 | I39 | Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-Asn-$NH_2$ |
| 614 | I40 | Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dAsp-$NH_2$ |
| 615 | I41 | Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dAsn-$NH_2$ |
| 616 | I42 | Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-Lys-dPro-$NH_2$ |
| 617 | I43 | Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dPro-dVal-OH |
| 618 | I44 | Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dThr-dPro-dThr-$NH_2$ |
| 619 | I45 | Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dThr-dPro-dThr-OH |
| 620 | I46 | Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dPro-dVal-$NH_2$ |
| 622 | I47 | Ac-Nle-c[dAsp-Pro-dPhe-Arg-Trp-dLys]-dPro-dVal-$NH_2$ |

| | | |
|---|---|---|
| 623 | I48 | Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-βPro-β2Val-$NH_2$ |
| 624 | I49 | Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-βPro-β3Val-$NH_2$ |
| 625 | I50 | Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-β2Val-βPro-$NH_2$ |
| 626 | I51 | Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-β3Val-βPro-$NH_2$ |
| 627 | I52 | Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-βPro-βPro-$NH_2$ |

**[0768]** Group J included non-naturally occurring melanocortin analogs J1 to J3, all of which are cyclic peptides comprising the motif Pro-dPhe-Arg-Trp, cyclized through a lactam bond between Asp and Lys, and an expanded N-terminus. Group J non-naturally occurring melanocortin analogs are provided in Table 10.

**Table 10.** Group J non-naturally occurring melanocortin analogs

| **SEQ ID NO** | **Non-naturally occurring melanocortin analog** | **Formula** |
|---|---|---|
| 628 | J1 | Ac-Nle-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ |
| 629 | J2 | Ac-Nle-Nle-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ |
| 630 | J3 | Ac-Nle-Nle-Nle-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ |

**[0769]** Group K included non-naturally occurring melanocortin analogs K1 to K3, which are cyclic peptides comprising the motif dPhe-Arg-Trp-Gly, or a derivative thereof. Group K non-naturally occurring melanocortin analogs are provided in Table 11.

**Table 11.** Group K non-naturally occurring melanocortin analogs

| SEQ ID NO | Non-naturally occurring melanocortin analog | Formula |
|---|---|---|
| 351 | K1 | Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Gly-Lys]-dVal-dPro-$NH_2$ |
| 352 | K2 | Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Gly-Lys]-dPro-dPro-Lys-Asp-$NH_2$ |
| 353 | K3 | Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Gly-Lys]-dPro-dPro-dLys-dAsp-$NH_2$ |
| 419 | K4 | Ac-Nle-c[Asp-Hyp-dPhe-Arg-Trp-Pro-Lys]-dVal-dPro-$NH_2$ |

**[0770]** Group L included non-naturally occurring melanocortin analogs L1 to L4, which are cyclic peptides comprising the motif Phe-His-dPhe-Arg, or a derivative thereof. Group L non-naturally occurring melanocortin analogs are provided in Table 12.

**Table 12.** Group K non-naturally occurring melanocortin analogs

| SEQ ID NO | Non-naturally occurring melanocortin analog | Formula |
|---|---|---|
| 421 | L1 | Ac-Nle-Phe-Phe-c[Asp-Phe-His-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ |
| 422 | L2 | Ac-Nle-c[Asp-Phe-His-dPhe-Arg-Trp-Lys]-dLeu-dPro-$NH_2$ |
| 423 | L3 | Ac-Nle-c[Asp-Phe-His-dPhe-Arg-Trp-Lys]-dTle-dPro-$NH_2$ |
| 424 | L4 | Ac-Nle-c[Asp-Phe-His-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ |

**[0771]** Group L included non-naturally occurring melanocortin analogs M1 to M15, which are cyclic peptides comprising the motif Pro-dPhe-Arg-Trp, cyclized through a lactam

bond between Asp and Lys, an N-terminus other than Ac-Nle, and a C-terminus other than dVal-dPro-$NH_2$. Group L non-naturally occurring melanocortin analogs are provided in Table 13.

**Table 13.** Group L non-naturally occurring melanocortin analogs

| SEQ ID NO | Non-naturally occurring melanocortin analog | Formula |
|---|---|---|
| 631 | M1 | Ac-Arg-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dArg-dVal-dPro-$NH_2$ |
| 632 | M2 | Ac-dLys-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dLys-dVal-dPro-$NH_2$ |
| 633 | M3 | Ac-Lys-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dArg-dPro-$NH_2$ |
| 634 | M4 | Ac-His-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dLys-dPro-$NH_2$ |
| 635 | M5 | Ac-dHis-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dHyp-$NH_2$ |
| 636 | M6 | Ac-Orn-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dTle-dPro-$NH_2$ |
| 637 | M7 | Ac-dOrn-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dVal-dVal-dPro-$NH_2$ |
| 638 | M8 | Ac-Nle-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dTle-dPro-$NH_2$ |
| 640 | M9 | Ac-Ala-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dTle-dPro-$NH_2$ |
| 641 | M10 | Ac-dArg-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dTle-dPro-$NH_2$ |
| 642 | M11 | Ac-Arg-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dTle-dPro-$NH_2$ |

| | | |
|---|---|---|
| 643 | M12 | Ac-Lys-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dTle-dPro-$NH_2$ |
| 644 | M13 | Ac-dLys-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dTle-dPro-$NH_2$ |
| 645 | M14 | Ac-His-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dTle-dPro-$NH_2$ |
| 646 | M15 | Ac-dHis-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dTle-dPro-$NH_2$ |

**[0772]** Group N included non-naturally occurring melanocortin analogs N1 and N2, both of which are cyclic peptides comprising the motif Ala-His-dPhe. Group N non-naturally occurring melanocortin analogs are provided in Table 15.

**Table 15.** Group M non-naturally occurring melanocortin analogs

| **SEQ ID NO** | **Non-naturally occurring melanocortin analog** | **Formula** |
|---|---|---|
| 381 | N1 | Ac-Arg-c[Asp-Ala-His-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ |
| 382 | N2 | Ac-dArg-c[Asp-Ala-His-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ |

**[0773]** Group O included non-naturally occurring melanocortin analogs O1 to O3, both of which are cyclic peptides comprising a derivative of the motif Pro-dPhe-Arg-Trp, where either Arg is substituted for another basic amino acid or Trp is substituted for another aromatic amino acid. Group O non-naturally occurring melanocortin analogs are provided in Table 16.

**Table 16.** Group O non-naturally occurring melanocortin analogs

| **SEQ ID NO** | **Non-naturally occurring** | **Formula** |
|---|---|---|

| | melanocortin analog | |
|---|---|---|
| 425 | O1 | Ac-Nle-c[Asp-Pro-dPhe-His-Trp-Lys]-dVal-dPro-$NH_2$ |
| 427 | O2 | Ac-Nle-c[Asp-Pro-dPhe-Arg-Nal(1')-Lys]-dVal-dPro-$NH_2$ |
| 187 | O3 | Ac-Nle-c[Asp-Pro-dPhe-Arg-dTrp-Lys]-dVal-dPro-$NH_2$ |

*Agonist activity of melanocortin analogs on melanocortin 1 receptor and melanocortin 5 receptor*

**[0774]** Administration of some non-naturally occurring melanocortin analogs activated melanocortin 1 receptor (MC1R) activity and/or melanocortin 5 receptor (MC1R) activity, as measured by cAMP levels (Table 17).

**Table 17.** Dose-response results of melanocortin analogs and control against the melanocortin 1 receptor (MC1R) and melanocortin 5 receptor (MC5R)

| SEQ ID NO | Compound ID | MC1R | | MC5R | |
|---|---|---|---|---|---|
| | | EC50 (nM) | Max Activation (Emax) | EC50 (nM) | Max Activation (Emax) |
| | NDP-α-MSH | 0.039 | 101.06 | 0.12 | 101.44 |
| 8 | A1 | 0.38 | 101.26 | 3.22 | 101.59 |
| 212 | C1 | 13.48 | 99.07 | 7.55 | 104.69 |
| 226 | D1 | 4.25 | 100.95 | 33.33 | 99.53 |
| 291 | E1 | 0.07 | 101.38 | 0.45 | 101.42 |
| 299 | E3 | 6.75 | 105.70 | 7.50 | 103.05 |
| 300 | E4 | 1.66 | 101.79 | 2.74 | 102.12 |
| 301 | E5 | 0.02 | 101.39 | 0.08 | 101.90 |
| 302 | E6 | 1.88 | 100.29 | 2.69 | 103.33 |
| 303 | E7 | 0.58 | 101.44 | 1.58 | 102.54 |

| | | | | | |
|---|---|---|---|---|---|
| 304 | E8 | 8.77 | 101.34 | 51.43 | 100.24 |
| 305 | E9 | 0.11 | 100.37 | 0.24 | 105.08 |
| 306 | E10 | 3.25 | 98.64 | 11.81 | 104.41 |
| 307 | E11 | 0.19 | 103.43 | 0.63 | 104.13 |
| 308 | E12 | 0.28 | 102.54 | 1.77 | 103.35 |
| 309 | E13 | 4.93 | 104.87 | 11.43 | 103.61 |
| 310 | E14 | 0.24 | 103.25 | 1.61 | 103.27 |
| 311 | E15 | 1.31 | 102.01 | 0.69 | 104.40 |
| 312 | E16 | 4.67 | 104.03 | 4.54 | 102.85 |
| 313 | E17 | 2.56 | 104.39 | 1.57 | 103.33 |
| 314 | E18 | 6.87 | 102.37 | 6.97 | 104.63 |
| 315 | E19 | 11.47 | 100.84 | 22.23 | 103.69 |
| 316 | E20 | 4.78 | 102.51 | 4.02 | 103.38 |
| 317 | E21 | 5.53 | 102.95 | 7.68 | 103.90 |
| 318 | B1 | 0.17 | 101.44 | 0.10 | 102.07 |
| 319 | B2 | 0.02 | 100.65 | 0.01 | 102.58 |
| 320 | B3 | 18.04 | 102.68 | 78.67 | 99.36 |
| 321 | B4 | 0.01 | 102.99 | 0.01 | 101.67 |
| 322 | B5 | 0.04 | 102.33 | 0.20 | 102.38 |
| 324 | B6 | 192.92 | 100.00 | 616.59 | 100.00 |
| 351 | K1 | 0.01 | 102.11 | 0.00 | 103.30 |
| 352 | K2 | 0.01 | 102.71 | 0.01 | 105.20 |
| 353 | K3 | 0.01 | 101.74 | 0.01 | 103.65 |
| 354 | C2 | 0.05 | 102.90 | 0.61 | 101.56 |
| 355 | C3 | 0.07 | 100.60 | 0.36 | 101.34 |
| 358 | C4 | 1.25 | 100.27 | 138.39 | 112.09 |
| 359 | C5 | 0.21 | 101.61 | 59.80 | 100.26 |
| 360 | C6 | 0.74 | 96.39 | 1.19 | 100.41 |
| 362 | C7 | 0.01 | 103.06 | 0.02 | 104.44 |
| 364 | C8 | 0.03 | 100.86 | 0.28 | 100.84 |

| | | | | | |
|---|---|---|---|---|---|
| 366 | C9 | 0.02 | 101.89 | 0.05 | 104.20 |
| 367 | C10 | 3.09 | 97.55 | 14.95 | 99.27 |
| 368 | C11 | 1.23 | 104.40 | 0.22 | 104.54 |
| 371 | C12 | 22.29 | 101.68 | 101.95 | 106.50 |
| 372 | C13 | 0.07 | 101.02 | 0.07 | 102.56 |
| 373 | C14 | 21.66 | 99.44 | 57.67 | 104.43 |
| 374 | C15 | 0.01 | 102.05 | 0.03 | 101.45 |
| 375 | C16 | 12.10 | 101.41 | 98.25 | 117.39 |
| 381 | N1 | 0.15 | 102.19 | 432.03 | 100.00 |
| 382 | N2 | 0.22 | 100.80 | 181.61 | 98.22 |
| 383 | D2 | 0.49 | 107.77 | 7.59 | 104.79 |
| 384 | D3 | 1.89 | 106.79 | 25.37 | 103.05 |
| 385 | D4 | 38.25 | 100.23 | 174.89 | 97.25 |
| 386 | D5 | 12.99 | 106.71 | 45.52 | 103.83 |
| 387 | D6 | 3.01 | 105.24 | 34.35 | 96.96 |
| 388 | D7 | 6.95 | 106.61 | 53.13 | 97.06 |
| 389 | D8 | 6.44 | 104.37 | 54.26 | 97.19 |
| 390 | D9 | 18.84 | 102.22 | 448.00 | 102.49 |
| 391 | D10 | 7.33 | 104.83 | 102.30 | 100.00 |
| 392 | D11 | 5.29 | 105.71 | 104.72 | 100.87 |
| 393 | D12 | 3.77 | 108.98 | 4.55 | 101.78 |
| 394 | D13 | 12.92 | 102.68 | 195.24 | 100.00 |
| 395 | D14 | 7.76 | 103.52 | 40.93 | 100.20 |
| 399 | D15 | 261.34 | 116.55 | 1683.41 | 100.00 |
| 403 | D16 | 7.00 | 99.16 | 57.31 | 95.79 |
| 404 | D17 | 11.88 | 97.12 | 267.75 | 100.00 |
| 405 | D18 | 2.42 | 102.93 | 82.73 | 100.46 |
| 406 | D19 | 3.31 | 100.39 | 89.44 | 100.92 |
| 407 | D20 | 2.08 | 102.23 | 27.61 | 101.25 |
| 408 | D21 | 2.31 | 102.04 | 45.73 | 103.66 |

| | | | | | |
|---|---|---|---|---|---|
| 409 | D22 | 2.75 | 102.03 | 43.46 | 97.63 |
| 410 | D23 | 8.31 | 100.84 | 89.00 | 98.47 |
| 411 | D24 | 20.77 | 103.20 | 128.18 | 96.70 |
| 412 | D25 | 33.74 | 100.69 | 155.75 | 108.18 |
| 413 | D26 | 375.94 | 98.62 | 133.53 | 97.82 |
| 414 | D27 | 28.49 | 103.09 | 112.65 | 93.67 |
| 415 | D28 | 31.25 | 101.18 | 214.61 | 92.30 |
| 416 | D29 | 29.79 | 101.53 | 245.07 | 100.00 |
| 417 | D30 | 70.55 | 99.37 | 473.61 | 100.00 |
| 419 | K4 | 9.20 | 103.43 | 59.94 | 99.02 |
| 421 | L1 | 0.18 | 101.72 | 43.59 | 96.63 |
| 422 | L2 | 0.02 | 101.80 | 8.41 | 94.67 |
| 423 | L3 | 0.02 | 102.85 | 15.82 | 99.77 |
| 424 | L4 | 0.03 | 103.31 | 21.17 | 95.88 |
| 425 | O1 | 7.09 | 102.64 | 1.16 | 100.06 |
| 427 | O2 | 0.23 | 102.10 | 4.50 | 101.15 |
| 429 | O3 | 0.81 | 103.92 | 7.72 | 102.29 |
| 433 | F1 | 0.02 | 102.24 | 0.01 | 102.56 |
| 434 | F2 | 0.01 | 101.40 | 0.01 | 103.56 |
| 435 | F3 | 2.57 | 102.60 | 0.87 | 104.42 |
| 436 | F4 | 1.42 | 103.74 | 0.76 | 106.55 |
| 437 | F5 | 1.30 | 100.89 | 0.21 | 103.00 |
| 438 | F6 | 1.99 | 101.09 | 0.58 | 104.66 |
| 439 | F7 | 3.54 | 102.03 | 1.57 | 105.10 |
| 440 | F8 | 5.17 | 99.39 | 1.39 | 106.28 |
| 441 | F9 | 9.12 | 108.52 | 3.86 | 106.88 |
| 442 | F10 | 0.02 | 100.36 | 0.01 | 105.13 |
| 443 | F11 | 1.63 | 100.37 | 0.06 | 102.60 |
| 446 | F12 | 0.49 | 100.42 | 0.35 | 102.49 |
| 447 | F13 | 0.01 | 100.40 | 0.01 | 103.78 |

| | | | | | |
|---|---|---|---|---|---|
| 448 | F14 | 0.10 | 101.31 | 0.27 | 100.96 |
| 449 | F15 | 0.01 | 102.11 | 0.01 | 103.06 |
| 450 | F16 | 0.01 | 101.76 | 0.01 | 103.31 |
| 451 | F17 | 0.51 | 101.11 | 0.35 | 101.99 |
| 452 | F18 | 1.10 | 102.96 | 0.57 | 102.59 |
| 453 | F19 | 0.45 | 98.69 | 0.30 | 101.03 |
| 454 | F20 | 0.67 | 102.62 | 0.15 | 103.78 |
| 455 | F21 | 0.89 | 103.71 | 0.24 | 104.77 |
| 456 | F22 | 2.38 | 102.82 | 0.93 | 104.96 |
| 457 | F23 | 2.01 | 101.33 | 0.92 | 103.80 |
| 458 | F24 | 3.44 | 102.73 | 2.82 | 104.14 |
| 459 | F25 | 0.00 | 102.51 | 0.06 | 101.66 |
| 461 | F26 | 4.67 | 102.91 | 31.64 | 101.43 |
| 472 | F27 | 0.01 | 101.98 | 0.08 | 98.77 |
| 492 | F28 | 33.22 | 102.68 | 140.72 | 100.00 |
| 496 | F29 | 52.92 | 99.79 | 191.20 | 88.87 |
| 499 | G1 | 16.02 | 99.35 | 11.87 | 103.59 |
| 501 | G2 | 0.01 | 101.17 | 0.10 | 102.35 |
| 502 | G3 | 0.01 | 100.46 | 0.09 | 100.92 |
| 503 | G4 | 0.01 | 99.29 | 0.16 | 102.51 |
| 504 | G5 | 0.02 | 101.04 | 0.55 | 101.75 |
| 505 | G6 | 0.02 | 100.53 | 0.21 | 101.97 |
| 506 | G7 | 0.03 | 99.65 | 0.83 | 100.86 |
| 511 | G8 | 0.01 | 100.79 | 0.08 | 103.93 |
| 512 | G9 | 0.01 | 101.48 | 0.01 | 102.79 |
| 513 | G10 | 0.00 | 102.02 | 0.02 | 103.42 |
| 515 | G11 | 0.01 | 101.98 | 0.02 | 102.59 |
| 518 | G12 | 0.01 | 102.27 | 0.18 | 103.84 |
| 519 | G13 | 0.01 | 101.88 | 0.08 | 102.90 |
| 520 | G14 | 0.01 | 102.66 | 0.19 | 102.49 |

| | | | | | |
|---|---|---|---|---|---|
| 521 | G15 | 0.03 | 102.53 | 0.54 | 104.16 |
| 522 | G16 | 0.02 | 102.65 | 0.36 | 103.05 |
| 523 | G17 | 0.02 | 102.99 | 0.71 | 102.84 |
| 536 | H1 | 0.10 | 100.98 | 0.12 | 100.74 |
| 537 | H2 | 5.49 | 102.34 | 7.05 | 102.33 |
| 573 | I1 | 0.01 | 101.56 | 0.02 | 100.77 |
| 574 | I2 | 0.01 | 103.32 | 0.02 | 103.36 |
| 575 | I3 | 0.03 | 100.32 | 0.02 | 101.72 |
| 576 | I4 | 0.02 | 101.85 | 0.05 | 103.15 |
| 577 | I5 | 0.21 | 102.22 | 0.09 | 103.09 |
| 578 | I6 | 0.01 | 101.90 | 0.02 | 102.23 |
| 579 | I7 | 0.01 | 102.00 | 0.02 | 102.58 |
| 580 | I8 | 0.01 | 100.58 | 0.01 | 103.14 |
| 581 | I9 | 0.00 | 101.30 | 0.01 | 102.71 |
| 582 | I10 | 0.00 | 99.14 | 0.00 | 101.77 |
| 583 | I11 | 0.00 | 103.89 | 0.01 | 103.95 |
| 584 | I12 | 0.01 | 101.14 | 0.02 | 103.59 |
| 585 | I13 | 0.01 | 101.68 | 0.02 | 102.08 |
| 586 | I14 | 0.01 | 101.41 | 0.01 | 102.09 |
| 587 | I15 | 0.00 | 104.98 | 0.02 | 102.83 |
| 588 | I16 | 0.00 | 100.24 | 0.00 | 102.98 |
| 589 | I17 | 0.00 | 104.81 | 0.00 | 104.64 |
| 590 | I18 | 0.00 | 104.01 | 0.01 | 103.56 |
| 591 | I19 | 0.00 | 105.00 | 0.02 | 102.89 |
| 592 | I20 | 0.01 | 104.63 | 0.03 | 102.10 |
| 593 | I21 | 0.18 | 101.47 | 0.53 | 103.92 |
| 594 | I22 | 0.03 | 102.57 | 0.10 | 103.54 |
| 595 | I53 | 0.02 | 101.52 | 0.07 | 102.03 |
| 596 | I23 | 0.11 | 101.63 | 0.25 | 103.21 |
| 597 | I24 | 0.02 | 102.56 | 0.09 | 105.07 |

| | | | | | |
|---|---|---|---|---|---|
| 598 | I25 | 0.02 | 102.13 | 0.04 | 101.26 |
| 600 | I26 | 0.01 | 102.79 | 0.01 | 104.27 |
| 601 | I27 | 0.01 | 101.21 | 0.03 | 100.56 |
| 602 | I28 | 0.05 | 101.27 | 0.06 | 102.47 |
| 603 | I29 | 0.19 | 101.72 | 0.57 | 102.52 |
| 604 | I30 | 0.20 | 101.68 | 0.11 | 101.46 |
| 605 | I31 | 0.02 | 99.49 | 0.04 | 101.35 |
| 606 | I32 | 0.09 | 100.11 | 0.18 | 101.59 |
| 607 | I33 | 0.03 | 102.27 | 0.10 | 103.58 |
| 608 | I34 | 0.57 | 102.73 | 0.29 | 102.14 |
| 609 | I35 | 0.02 | 102.73 | 0.03 | 103.56 |
| 610 | I36 | 0.02 | 103.30 | 0.04 | 104.04 |
| 611 | I37 | 0.16 | 103.63 | 0.44 | 103.48 |
| 612 | I38 | 0.02 | 101.17 | 0.03 | 103.18 |
| 613 | I39 | 0.02 | 102.56 | 0.03 | 102.32 |
| 614 | I40 | 0.30 | 102.38 | 0.26 | 101.84 |
| 615 | I41 | 0.03 | 101.65 | 0.03 | 101.39 |
| 616 | I42 | 0.06 | 101.66 | 0.47 | 102.62 |
| 617 | I43 | 0.61 | 100.61 | 9.35 | 97.69 |
| 618 | I44 | 0.06 | 101.31 | 0.23 | 101.00 |
| 619 | I45 | 0.11 | 101.57 | 0.52 | 102.47 |
| 620 | I46 | 0.23 | 102.09 | 0.93 | 100.69 |
| 622 | I47 | 9.59 | 101.13 | 73.51 | 101.01 |
| 623 | I48 | 0.71 | 101.00 | 0.56 | 100.86 |
| 624 | I49 | 0.55 | 100.49 | 0.53 | 101.84 |
| 625 | I50 | 0.02 | 101.95 | 0.13 | 102.11 |
| 626 | I51 | 0.06 | 100.71 | 0.28 | 101.29 |
| 627 | I52 | 0.54 | 101.82 | 0.56 | 102.19 |
| 628 | J1 | 0.02 | 101.31 | 0.03 | 100.71 |
| 629 | J2 | 0.04 | 99.81 | 0.07 | 101.97 |

| | | | | | |
|---|---|---|---|---|---|
| 630 | J3 | 0.21 | 99.28 | 0.27 | 102.77 |
| 631 | M1 | 0.42 | 103.32 | 0.36 | 104.49 |
| 632 | M2 | 1.52 | 102.32 | 4.64 | 106.94 |
| 633 | M3 | 0.49 | 105.33 | 0.29 | 106.44 |
| 634 | M4 | 2.31 | 103.88 | 1.90 | 104.00 |
| 635 | M5 | 5.59 | 103.83 | 10.83 | 100.26 |
| 636 | M6 | 3.56 | 102.53 | 3.14 | 103.35 |
| 637 | M7 | 2.78 | 102.61 | 11.45 | 106.28 |
| 638 | M8 | 0.02 | 104.14 | 0.04 | 104.55 |
| 640 | M9 | 2.53 | 102.24 | 3.80 | 101.63 |
| 641 | M10 | 1.82 | 102.37 | 3.55 | 103.87 |
| 642 | M11 | 1.08 | 102.81 | 1.01 | 104.67 |
| 643 | M12 | 2.49 | 102.55 | 2.11 | 103.82 |
| 644 | M13 | 4.54 | 104.26 | 6.12 | 104.94 |
| 645 | M14 | 9.98 | 101.60 | 8.97 | 101.26 |
| 646 | M15 | 4.98 | 98.90 | 14.58 | 102.18 |

*Agonist activity of melanocortin analogs on melanocortin 3 receptor and melanocortin 4 receptor*

**[0775]** Administration of some non-naturally occurring melanocortin analogs activated melanocortin 3 receptor (MC3R) activity and/or melanocortin 4 receptor (MC4R) activity, as measured by cAMP levels (Table 18).

**Table 18.** Dose-response results of melanocortin analogs and control against the melanocortin 3 receptor (MC3R) and melanocortin 4 receptor (MC4R)

| SEQ ID NO | Compound ID | MC3R | | MC4R | |
|---|---|---|---|---|---|
| | | EC50 (nM) | Max Activation (Emax) | EC50 (nM) | Max Activation (Emax) |
| | NDP-α-MSH | 106.05 | 0.17 | 103.19 | 0.07 |

| | | | | | |
|---|---|---|---|---|---|
| 212 | C1 | - | - | 29.60 | 96.67 |
| 226 | D1 | - | - | 7.38 | 98.82 |
| 291 | E1 | - | - | 7.92 | 86.80 |
| 299 | E3 | - | - | 18.32 | 94.68 |
| 300 | E4 | - | - | 8.74 | 87.32 |
| 301 | E5 | - | - | 2.56 | 95.73 |
| 302 | E6 | - | - | 5.70 | 96.49 |
| 303 | E7 | - | - | 19.46 | 96.37 |
| 304 | E8 | - | - | 24.77 | 97.54 |
| 305 | E9 | 16.63 | 37.79 | 0.06 | 104.36 |
| 306 | E10 | - | - | 0.82 | 106.76 |
| 307 | E11 | 7.49 | 29.97 | 0.09 | 102.19 |
| 308 | E12 | - | - | 0.51 | 104.38 |
| 309 | E13 | 42.74 | 28.39 | 1.23 | 101.39 |
| 310 | E14 | - | - | 0.53 | 102.59 |
| 311 | E15 | 1.86 | 21.79 | 0.15 | 102.38 |
| 312 | E16 | - | - | 0.59 | 103.37 |
| 313 | E17 | 26.00 | 40.68 | 0.82 | 104.73 |
| 314 | E18 | - | - | 1.91 | 102.89 |
| 315 | E19 | - | - | 0.91 | 99.31 |
| 316 | E20 | 96.87 | 33.38 | 0.63 | 105.62 |
| 317 | E21 | 11.92 | 20.65 | 0.74 | 103.53 |
| 318 | B1 | - | - | 2.78 | 86.97 |
| 319 | B2 | 1.05 | 42.70 | 0.01 | 102.78 |
| 320 | B3 | - | - | 110.62 | 95.13 |
| 321 | B4 | - | - | 0.11 | 99.71 |
| 322 | B5 | 5.20 | 23.80 | 1.71 | 91.87 |
| 324 | B6 | - | - | 519.38 | 100.00 |
| 351 | K1 | 0.21 | 61.73 | 0.03 | 97.55 |
| 352 | K2 | 0.67 | 70.46 | 0.02 | 103.16 |

| | | | | | |
|---|---|---|---|---|---|
| 353 | K3 | 0.43 | 47.58 | 0.03 | 102.99 |
| 354 | C2 | - | - | 2.93 | 94.23 |
| 355 | C3 | 9.60 | 71.26 | 3.04 | 86.02 |
| 358 | C4 | - | - | 416.34 | 100.00 |
| 359 | C5 | - | - | 304.07 | 100.00 |
| 360 | C6 | - | - | 333.53 | 100.00 |
| 362 | C7 | 0.45 | 73.31 | 0.02 | 102.80 |
| 364 | C8 | - | - | 1.35 | 95.82 |
| 366 | C9 | 4.09 | 61.18 | 0.12 | 97.46 |
| 367 | C10 | - | - | 24.33 | 121.06 |
| 368 | C11 | 4.40 | 62.29 | 0.15 | 92.85 |
| 371 | C12 | - | - | 14.70 | 103.29 |
| 372 | C13 | 4.50 | 48.85 | 0.24 | 91.71 |
| 373 | C14 | - | - | 54.42 | 91.73 |
| 374 | C15 | 1.08 | 47.46 | 0.10 | 91.80 |
| 375 | C16 | - | - | 20.73 | 95.26 |
| 381 | N1 | - | - | 7.75 | 100.02 |
| 382 | N2 | - | - | 10.03 | 100.75 |
| 383 | D2 | - | - | 3.41 | 99.98 |
| 384 | D3 | - | - | 26.80 | 99.01 |
| 385 | D4 | - | - | 589.92 | 100.00 |
| 386 | D5 | - | - | 1.61 | 100.03 |
| 387 | D6 | - | - | 44.78 | 96.39 |
| 388 | D7 | - | - | 33.95 | 100.01 |
| 389 | D8 | - | - | 12.98 | 98.15 |
| 390 | D9 | - | - | 39.16 | 98.06 |
| 391 | D10 | - | - | 28.00 | 102.28 |
| 392 | D11 | - | - | 26.27 | 99.71 |
| 393 | D12 | - | - | 54.94 | 101.59 |
| 394 | D13 | - | - | 16.10 | 94.34 |

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|---|---|---|---|---|---|
| 395 | D14 | - | - | 39.71 | 85.73 |
| 399 | D15 | - | - | 461.80 | 96.18 |
| 403 | D16 | - | - | 125.57 | 87.87 |
| 404 | D17 | - | - | 42.06 | 98.58 |
| 405 | D18 | - | - | 4.63 | 100.71 |
| 406 | D19 | - | - | 4.13 | 99.32 |
| 407 | D20 | - | - | 1.91 | 99.42 |
| 408 | D21 | - | - | 2.82 | 100.91 |
| 409 | D22 | - | - | 9.59 | 98.38 |
| 410 | D23 | - | - | 60.58 | 100.79 |
| 411 | D24 | - | - | 45.98 | 99.76 |
| 412 | D25 | - | - | 326.11 | 87.61 |
| 413 | D26 | - | - | 475.33 | 100.00 |
| 414 | D27 | - | - | 123.60 | 97.41 |
| 415 | D28 | - | - | 169.49 | 100.00 |
| 416 | D29 | - | - | 488.54 | 100.00 |
| 417 | D30 | - | - | 163.45 | 100.00 |
| 419 | K4 | - | - | 853.10 | 100.00 |
| 421 | L1 | 20.90 | 66.90 | 0.87 | 104.37 |
| 422 | L2 | 3.31 | 67.45 | 0.03 | 103.26 |
| 423 | L3 | 4.18 | 69.29 | 0.24 | 103.06 |
| 424 | L4 | 4.42 | 62.02 | 0.27 | 100.60 |
| 425 | O1 | - | - | 19.69 | 92.69 |
| 427 | O2 | - | - | 7.39 | 86.22 |
| 429 | O3 | - | - | 133.74 | 89.11 |
| 433 | F1 | - | - | 0.05 | 100.96 |
| 434 | F2 | - | - | 0.17 | 99.46 |
| 435 | F3 | 3.39 | 22.11 | 0.10 | 98.22 |
| 436 | F4 | - | - | 0.13 | 99.98 |
| 437 | F5 | - | - | 0.10 | 103.20 |

| | | | | | |
|---|---|---|---|---|---|
| 438 | F6 | 7.26 | 26.63 | 0.19 | 101.79 |
| 439 | F7 | 21.88 | 23.10 | 0.12 | 101.62 |
| 440 | F8 | - | - | 0.17 | 102.32 |
| 441 | F9 | 9.25 | 21.62 | 0.40 | 102.39 |
| 442 | F10 | 0.78 | 41.37 | 0.10 | 99.05 |
| 443 | F11 | 2.34 | 41.54 | 0.19 | 96.76 |
| 446 | F12 | - | - | 7.26 | 88.81 |
| 447 | F13 | 2.02 | 22.14 | 0.53 | 95.74 |
| 448 | F14 | - | - | 0.90 | 93.00 |
| 449 | F15 | 3.76 | 30.97 | 0.12 | 97.24 |
| 450 | F16 | 0.40 | 38.57 | 0.08 | 98.23 |
| 451 | F17 | - | - | 1.17 | 95.47 |
| 452 | F18 | 8.23 | 22.17 | 0.14 | 96.36 |
| 453 | F19 | - | - | 0.07 | 102.74 |
| 454 | F20 | - | - | 0.10 | 102.49 |
| 455 | F21 | 63.31 | 31.98 | 0.18 | 104.46 |
| 456 | F22 | - | - | 0.15 | 101.76 |
| 457 | F23 | - | - | 0.43 | 102.66 |
| 458 | F24 | - | - | 0.22 | 103.19 |
| 459 | F25 | 1.72 | 63.73 | 0.09 | 99.98 |
| 461 | F26 | - | - | 134.09 | 89.34 |
| 472 | F27 | 1.66 | 48.65 | 0.28 | 96.77 |
| 492 | F28 | - | - | 85.13 | 99.23 |
| 496 | F29 | - | - | 984.11 | 100.00 |
| 499 | G1 | - | - | 192.88 | 100.00 |
| 501 | G2 | - | - | 0.21 | 92.87 |
| 502 | G3 | 0.21 | 34.74 | 0.17 | 91.87 |
| 503 | G4 | 0.71 | 42.05 | 0.28 | 93.53 |
| 504 | G5 | - | - | 0.42 | 95.20 |
| 505 | G6 | 3.73 | 41.53 | 0.25 | 97.28 |

| | | | | | |
|---|---|---|---|---|---|
| 506 | G7 | 10.69 | 32.44 | 0.44 | 97.19 |
| 511 | G8 | 0.58 | 42.87 | 0.99 | 85.36 |
| 512 | G9 | 0.24 | 42.08 | 0.29 | 87.89 |
| 513 | G10 | 0.23 | 57.56 | 0.12 | 89.99 |
| 515 | G11 | 1.30 | 52.48 | 0.35 | 86.04 |
| 518 | G12 | 2.07 | 31.98 | 0.02 | 99.25 |
| 519 | G13 | 0.17 | 59.05 | 0.02 | 98.79 |
| 520 | G14 | 0.18 | 69.45 | 0.01 | 99.43 |
| 521 | G15 | 0.13 | 24.79 | 0.03 | 99.42 |
| 522 | G16 | 7.87 | 63.93 | 0.02 | 101.79 |
| 523 | G17 | 1.90 | 52.37 | 0.02 | 102.43 |
| 536 | H1 | - | - | 4.78 | 90.30 |
| 537 | H2 | - | - | 272.76 | 100.00 |
| 573 | I1 | - | - | 0.87 | 93.70 |
| 574 | I2 | 0.21 | 32.39 | 0.09 | 96.76 |
| 575 | I3 | 8.85 | 57.37 | 0.09 | 98.50 |
| 576 | I4 | - | - | 1.78 | 93.61 |
| 577 | I5 | - | - | 1.06 | 95.09 |
| 578 | I6 | - | - | 0.69 | 93.12 |
| 579 | I7 | - | - | 0.27 | 96.29 |
| 580 | I8 | - | - | 0.29 | 91.59 |
| 581 | I9 | 2.41 | 23.33 | 0.31 | 93.95 |
| 582 | I10 | 4.36 | 22.74 | 0.30 | 95.22 |
| 583 | I11 | 3.34 | 21.86 | 0.29 | 94.58 |
| 584 | I12 | - | - | 0.29 | 91.69 |
| 585 | I13 | - | - | 0.38 | 91.57 |
| 586 | I14 | - | - | 0.97 | 91.88 |
| 587 | I15 | 7.57 | 51.84 | 0.03 | 100.20 |
| 588 | I16 | 3.14 | 46.33 | 0.02 | 101.37 |
| 589 | I17 | 3.14 | 33.14 | 0.03 | 99.75 |

| | | | | | |
|---|---|---|---|---|---|
| 590 | I18 | 1.15 | 47.06 | 0.03 | 102.71 |
| 591 | I19 | 4.71 | 35.17 | 0.08 | 98.38 |
| 592 | I20 | 23.57 | 36.84 | 0.23 | 100.20 |
| 593 | I21 | 4.86 | 28.27 | 0.42 | 100.45 |
| 594 | I22 | 1.35 | 43.14 | 0.05 | 100.47 |
| 595 | I53 | - | - | 0.66 | 96.62 |
| 596 | I23 | - | - | 0.93 | 101.29 |
| 597 | I24 | 3.65 | 45.43 | 0.06 | 101.01 |
| 598 | I25 | - | - | 1.20 | 90.48 |
| 600 | I26 | - | - | | |
| 601 | I27 | 0.85 | 45.60 | 0.02 | 100.93 |
| 602 | I28 | - | - | 0.55 | 94.26 |
| 603 | I29 | - | - | 0.41 | 95.61 |
| 604 | I30 | - | - | 7.13 | 88.67 |
| 605 | I31 | - | - | 0.81 | 94.70 |
| 606 | I32 | 8.99 | 22.06 | 2.73 | 93.06 |
| 607 | I33 | - | - | 5.07 | 91.77 |
| 608 | I34 | 1.35 | 21.10 | 0.80 | 94.30 |
| 609 | I35 | - | - | 1.05 | 95.26 |
| 610 | I36 | 4.20 | 21.20 | 0.76 | 92.22 |
| 611 | I37 | 2.82 | 30.43 | 0.21 | 96.81 |
| 612 | I38 | - | - | 3.61 | 94.92 |
| 613 | I39 | 2.63 | 20.84 | 0.36 | 94.81 |
| 614 | I40 | - | - | 0.52 | 91.80 |
| 615 | I41 | - | - | 3.19 | 93.90 |
| 616 | I42 | - | - | 0.72 | 94.19 |
| 617 | I43 | - | - | 1.35 | 94.18 |
| 618 | I44 | - | - | 8.66 | 93.55 |
| 619 | I45 | - | - | 1.49 | 90.06 |
| 620 | I46 | - | - | 7.08 | 85.34 |

| | | | | | |
|---|---|---|---|---|---|
| 622 | I47 | - | - | 1.89 | 95.42 |
| 623 | I48 | - | - | 37.89 | 100.84 |
| 624 | I49 | - | - | 1.92 | 95.63 |
| 625 | I50 | - | - | 1.25 | 94.65 |
| 626 | I51 | 5.12 | 23.46 | 0.74 | 94.20 |
| 627 | I52 | - | - | 2.00 | 93.74 |
| 628 | J1 | - | - | 2.04 | 97.01 |
| 629 | J2 | 3.39 | 20.71 | 1.11 | 92.35 |
| 630 | J3 | - | - | 2.15 | 92.02 |
| 631 | M1 | - | - | 9.63 | 93.74 |
| 632 | M2 | 21.28 | 31.71 | 0.01 | 104.66 |
| 633 | M3 | 610.89 | 25.90 | 0.27 | 101.93 |
| 634 | M4 | 10.88 | 45.59 | 0.09 | 102.44 |
| 635 | M5 | - | - | 0.09 | 99.76 |
| 636 | M6 | - | - | 31.74 | 99.40 |
| 637 | M7 | - | - | 3.20 | 102.76 |
| 638 | M8 | - | - | 0.27 | 102.96 |
| 640 | M9 | 6.30 | 36.37 | 0.27 | 97.54 |
| 641 | M10 | - | - | 0.42 | 94.40 |
| 642 | M11 | - | - | 0.36 | 97.33 |
| 643 | M12 | - | - | 0.37 | 100.93 |
| 644 | M13 | 24.13 | 31.62 | 0.74 | 100.93 |
| 645 | M14 | - | - | 0.84 | 101.48 |
| 646 | M15 | - | - | 1.96 | 101.47 |

*Antagonist activity of melanocortin analogs on melanocortin 3 receptor and melanocortin 4 receptor*

**[0776]** Administration of some non-naturally occurring melanocortin analogs inhibited melanocortin 3 receptor (MC3R) activity and/or melanocortin 4 receptor (MC4R) activity, as measured by cAMP levels (Table 19).

**Table 19.** Dose-response results of melanocortin analogs and control against the melanocortin 3 receptor (MC3R) and melanocortin 4 receptor (MC4R)

| SEQ ID NO | Compound ID | MC3R | | MC4R | |
|---|---|---|---|---|---|
| | | EC50 (nM) | Max Activation (Emax) | EC50 (nM) | Max Activation (Emax) |
| | NDP-α-MSH | 406.52 | 100.00 | 46.68 | 67.13 |
| 291 | E1 | 254.18 | 100.00 | - | - |
| 299 | E3 | 572.62 | 100.00 | - | - |
| 300 | E4 | 309.36 | 81.42 | - | - |
| 301 | E5 | 49.90 | 82.70 | - | - |
| 302 | E6 | 217.69 | 83.76 | - | - |
| 303 | E7 | 97.56 | 95.98 | - | - |
| 304 | E8 | 374.81 | 100.92 | - | - |
| 305 | E9 | 76.22 | 98.38 | - | - |
| 306 | E10 | 319.98 | 100.00 | - | - |
| 307 | E11 | 40.28 | 95.51 | - | - |
| 308 | E12 | 94.54 | 103.47 | - | - |
| 309 | E13 | 415.54 | 100.00 | - | - |
| 310 | E14 | 80.26 | 103.58 | - | - |
| 311 | E15 | 51.05 | 88.38 | - | - |
| 312 | E16 | 393.75 | 100.00 | - | - |
| 313 | E17 | 424.34 | 99.76 | - | - |
| 314 | E18 | 654.90 | 100.00 | - | - |
| 315 | E19 | 885.21 | 100.00 | - | - |
| 316 | E20 | 946.89 | 100.00 | - | - |
| 317 | E21 | 643.22 | 100.00 | - | - |

| | | | | | |
|---|---|---|---|---|---|
| 318 | B1 | 124.99 | 84.39 | - | - |
| 319 | B2 | 43.72 | 71.22 | - | - |
| 321 | B4 | 198.95 | 100.00 | - | - |
| 322 | B5 | 35.74 | 66.65 | - | - |
| 351 | K1 | 3.27 | 62.01 | - | - |
| 352 | K2 | 9.33 | 48.53 | - | - |
| 353 | K3 | 21.69 | 71.10 | - | - |
| 354 | C2 | 54.30 | 76.00 | - | - |
| 355 | C3 | 7.15 | 20.34 | - | - |
| 360 | C6 | 180.86 | 97.17 | - | - |
| 362 | C7 | 12.43 | 36.47 | - | - |
| 364 | C8 | 52.21 | 69.24 | - | - |
| 366 | C9 | 118.54 | 55.89 | - | - |
| 368 | C11 | 49.24 | 58.38 | - | - |
| 372 | C13 | 48.42 | 61.46 | - | - |
| 374 | C15 | 35.86 | 66.47 | - | - |
| 383 | D2 | 339.19 | 100.00 | - | - |
| 384 | D3 | 920.15 | 100.00 | - | - |
| 387 | D6 | 715.98 | 100.00 | - | - |
| 389 | D8 | 699.91 | 100.00 | - | - |
| 395 | D14 | 741.56 | 89.60 | - | - |
| 403 | D16 | 726.01 | 100.00 | - | - |
| 407 | D20 | 740.95 | 100.00 | - | - |
| 421 | L1 | 969.05 | 100.00 | - | - |
| 422 | L2 | 79.55 | 62.22 | - | - |
| 423 | L3 | 788.30 | 100.00 | - | - |
| 424 | L4 | 63.31 | 42.51 | - | - |
| 425 | O1 | 659.23 | 100.00 | - | - |
| 427 | O2 | 294.96 | 100.00 | - | - |
| 429 | O3 | 254.32 | 100.00 | - | - |

| | | | | | |
|---|---|---|---|---|---|
| 433 | F1 | 9.49 | 63.87 | - | - |
| 434 | F2 | 56.71 | 73.38 | - | - |
| 435 | F3 | 63.41 | 91.45 | - | - |
| 436 | F4 | 27.50 | 93.24 | - | - |
| 437 | F5 | 34.48 | 104.31 | - | - |
| 438 | F6 | 165.88 | 88.68 | - | - |
| 439 | F7 | 118.17 | 92.99 | - | - |
| 440 | F8 | 233.94 | 105.85 | - | - |
| 441 | F9 | 153.54 | 93.16 | - | - |
| 442 | F10 | 15.10 | 81.16 | - | - |
| 443 | F11 | 82.66 | 66.65 | - | - |
| 446 | F12 | 110.73 | 80.80 | - | - |
| 447 | F13 | 10.95 | 86.81 | - | - |
| 448 | F14 | 563.18 | 110.16 | - | - |
| 449 | F15 | 14.53 | 84.02 | - | - |
| 450 | F16 | 37.54 | 90.33 | - | - |
| 451 | F17 | 532.29 | 100.00 | - | - |
| 452 | F18 | 97.74 | 95.08 | - | - |
| 453 | F19 | 124.42 | 111.31 | - | - |
| 454 | F20 | 57.75 | 93.42 | - | - |
| 455 | F21 | 210.23 | 85.29 | - | - |
| 456 | F22 | 320.59 | 102.66 | - | - |
| 457 | F23 | 296.08 | 110.19 | - | - |
| 458 | F24 | 364.88 | 112.56 | - | - |
| 459 | F25 | 7.81 | 29.23 | - | - |
| 472 | F27 | 2.60 | 36.45 | - | - |
| 501 | G2 | 4.88 | 87.66 | - | - |
| 502 | G3 | 1.58 | 61.19 | - | - |
| 503 | G4 | 2.85 | 48.99 | - | - |
| 504 | G5 | 13.18 | 77.70 | - | - |

| | | | | | |
|---|---|---|---|---|---|
| 505 | G6 | 9.18 | 57.04 | - | - |
| 506 | G7 | 25.31 | 69.15 | - | - |
| 511 | G8 | 14.98 | 63.55 | - | - |
| 512 | G9 | 1.21 | 56.49 | - | - |
| 513 | G10 | 4.80 | 61.69 | - | - |
| 515 | G11 | 9.76 | 77.05 | 13.01 | 25.98 |
| 518 | G12 | 9.90 | 77.76 | - | - |
| 519 | G13 | 2.31 | 65.28 | - | - |
| 520 | G14 | 3.59 | 54.84 | - | - |
| 521 | G15 | 30.90 | 89.18 | - | - |
| 522 | G16 | 13.81 | 58.67 | - | - |
| 523 | G17 | 23.87 | 62.98 | - | - |
| 536 | H1 | 110.01 | 87.53 | - | - |
| 573 | I1 | 141.73 | 100.00 | - | - |
| 574 | I2 | 44.81 | 84.83 | - | - |
| 575 | I3 | 46.51 | 72.89 | - | - |
| 576 | I4 | 213.43 | 100.00 | - | - |
| 577 | I5 | 876.72 | 100.00 | - | - |
| 578 | I6 | 42.67 | 83.72 | - | - |
| 579 | I7 | 31.59 | 79.24 | - | - |
| 580 | I8 | 11.29 | 68.56 | - | - |
| 581 | I9 | 9.10 | 70.59 | - | - |
| 582 | I10 | 17.29 | 74.16 | - | - |
| 583 | I11 | 3.81 | 75.84 | - | - |
| 584 | I12 | 17.60 | 84.38 | - | - |
| 585 | I13 | 11.00 | 84.98 | - | - |
| 586 | I14 | 12.75 | 77.21 | - | - |
| 587 | I15 | 45.77 | 73.07 | - | - |
| 588 | I16 | 7.99 | 75.03 | - | - |
| 589 | I17 | 20.77 | 81.03 | - | - |

| | | | | | |
|---|---|---|---|---|---|
| 590 | I18 | 55.62 | 83.59 | - | - |
| 591 | I19 | 48.28 | 82.75 | - | - |
| 592 | I20 | 100.60 | 85.83 | - | - |
| 593 | I21 | 455.16 | 100.00 | - | - |
| 594 | I22 | 85.30 | 77.24 | - | - |
| 595 | I53 | 26.62 | 79.66 | - | - |
| 597 | I24 | 103.98 | 81.82 | - | - |
| 598 | I25 | 14.35 | 78.39 | - | - |
| 601 | I27 | 18.89 | 62.05 | - | - |
| 602 | I28 | 17.97 | 74.84 | - | - |
| 603 | I29 | 37.75 | 73.58 | - | - |
| 604 | I30 | 145.75 | 100.00 | - | - |
| 605 | I31 | 119.87 | 74.83 | - | - |
| 606 | I32 | 29.71 | 67.41 | - | - |
| 607 | I33 | 74.46 | 70.45 | - | - |
| 608 | I34 | 26.34 | 71.47 | - | - |
| 609 | I35 | 169.13 | 67.13 | - | - |
| 610 | I36 | 14.74 | 77.00 | - | - |
| 611 | I37 | 16.55 | 67.68 | - | - |
| 612 | I38 | 105.45 | 71.83 | - | - |
| 613 | I39 | 35.71 | 75.57 | - | - |
| 614 | I40 | 15.53 | 71.70 | - | - |
| 615 | I41 | 115.32 | 80.11 | - | - |
| 616 | I42 | 31.71 | 73.19 | - | - |
| 617 | I43 | 28.92 | 75.21 | - | - |
| 618 | I44 | 847.61 | 100.00 | - | - |
| 619 | I45 | 102.81 | 100.00 | - | - |
| 620 | I46 | 381.33 | 100.00 | - | - |
| 622 | I47 | 994.99 | 100.00 | - | - |
| 625 | I50 | 623.30 | 100.00 | - | - |

| | | | | | |
|---|---|---|---|---|---|
| 626 | I51 | 26.27 | 80.25 | - | - |
| 627 | I52 | 95.80 | 86.26 | - | - |
| 628 | J1 | 964.23 | 100.00 | - | - |
| 629 | J2 | 17.55 | 81.85 | - | - |
| 630 | J3 | 42.62 | 88.49 | - | - |
| 631 | M1 | 96.42 | 79.92 | - | - |
| 632 | M2 | 54.74 | 79.91 | - | - |
| 633 | M3 | 3055.93 | 100.00 | - | - |
| 634 | M4 | 605.48 | 100.00 | - | - |
| 635 | M5 | 686.80 | 100.00 | - | - |
| 636 | M6 | 560.69 | 100.00 | - | - |
| 640 | M9 | 86.13 | 72.08 | - | - |
| 641 | M10 | 141.38 | 66.80 | - | - |
| 642 | M11 | 122.01 | 72.86 | - | - |
| 643 | M12 | 224.95 | 101.22 | - | - |
| 644 | M13 | 845.19 | 100.00 | - | - |
| 645 | M14 | 838.02 | 100.00 | - | - |

***Example 5: Cardiac Activation of Melanocortin Analogs***

**[0777]** The effect of the melanocortin analogs on cardiac activation in rats was tested using E2 (SEQ ID NO:295) according to the following procedure. Baseline measurements of heart rate, systolic blood pressure, and diastolic blood pressure of rats were taken 15 minutes prior to administration of E2. The rats were then administered saline, 3 mg/kg E2, or 6 mg/kg E2 via subcutaneous injection and the heart rate, systolic blood pressure, and diastolic blood pressure were measure at the following time points post injection: 5 minutes, 15 minutes, 30 minutes, 60 minutes, 120 minutes, and 180 minutes.

**[0778]** FIGS. 1A-1C show the cardiac activation data from 15 minutes before subcutaneous injection of E2 to 180 minutes after injection of E2. As shown in FIG. 1A, the heart rate of rats administered 3 mg/kg E2 (G1) decreased directly after injection, increased

steadily from 30 minutes to 120 minutes, and then decreased again at 180 minutes to just slightly above the starting heart rate (i.e., at -15 min). Rats administered 6 mg/kg E2 (G2) maintained a steady heart rate until 120 minutes after injection when an increase in heart rate may be seen, however, the final heart rate of G2 rats was similar to that of G1 and control (G3) rats.

**[0779]** As may be seen in FIG. 1B the systolic blood pressure (SBP) of the rats in each group was similar for all time points, with a slight increase overall after injection for all three groups. The diastolic blood pressure (DBP) of rats administered 3 mg/kg E2 and 6 mg/kg E2 was higher than the diastolic blood pressure of the control rats at all time points post injection, however, no group of rats had a diastolic blood pressure above 100 at any time point (FIG. 1C).

**[0780]** This data suggests that melanocortin analogs in accordance with the present technology such as E2 avoid cardiac activation, which has been seen in earlier peptide and small molecule agonists of the melanocortin receptors.

***Example 6: Pharmacokinetic Assessment of Non-Naturally Occurring Melanocortin Analogs Following Subcutaneous Administration to Rats***

*Study Objective*

**[0781]** The objective of this study is to determine the pharmacokinetics of non-naturally occurring melanocortin analogs of the present technology following subcutaneous administration in male rats. In rats, the test article will be monitored in plasma for up to 24 hours post each dose. Study design and sample collection will be conducted as outlined in Table 20 and 21.

Table 20. Study Design

| Animal | N | Compound | Target Dose Level (mg/kg) | Target Dose Volume (mL/kg) | Target Dose Concen-tration (mg/mL) | Vehicle | Dose Route |
|---|---|---|---|---|---|---|---|
| Rat | 3 | A07D | 1 | 1 | 1 | physiological saline | SC |
| Rat | 3 | A07D | 3 | 1 | 3 | physiological saline | SC |
| Rat | 3 | A07D | 10 | 1 | 10 | physiological saline | SC |

Table 21. Sample Collections

| Group | Dosage | Sampling time points (hr.) | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | (mg/kg) | 0.083 | 0.25 | 0.5 | 1 | 2 | 4 | 6 | 8 | 24 |
| Rat | 1 | P | P | P | P | P | P | P | P | P |
| Rat | 3 | P | P | P | P | P | P | P | P | P |
| Rat | 10 | P | P | P | P | P/C | P/C | P | P | P |

E: Anticoagulant: Potassium ($K_2$) EDTA;

P: plasma

C: cerebrospinal fluid (CSF)

**[0782]** Dose Solution Analysis Samples: After each dose preparation, remove approximately 0.5 mL aliquots from the formulations, transfer the aliquots into amber HPLC vials and stored at -60°C or lower until assayed in duplicate for dose validation.

**[0783]** Disposition of Remaining Test Article Formulations: Remaining formulations will be stored at -60°C or lower.

**[0784]** Disposition of Remaining Test Article (dry powder or solid): Remaining test article will be stored at room temperature desiccated, and protected from light until shipment or discard.

**[0785]** Animals will be fasted overnight through 4 hours post dosing.

*Vehicle and Formulation Preparation:*

**[0786]** Appropriate amount of test article will be accurately weighed and mixed with appropriate volume of vehicle to get a clear solution or suspension.

**[0787]** Formulation samples will be removed from each of the formulation solutions, transferred into 1.5 mL of polypropylene microcentrifuge tubes and run dose validation by LC/UV or LC-MS/MS.

*Animal Specifications: Rats*

**[0788]** Rat specifications are outlined in Table 22.

Table 22. Rat Specifications

| | |
|---|---|
| Species | Rat |
| Strain | SD |
| Source | Approved Vendor. |
| Gender | Male |
| Body weight | ＞200g |
| Age | 7-10 W |
| Total number of animals | 9 male rats |
| Justification | The SD rat is a standard species used in pharmacokinetic evaluations and is acceptable to regulatory agencies.<br>The number of animals used in this study is, in the judgment of the investigator involved, the minimum necessary to properly perform this plasma pharmacokinetic evaluation. |

*Observations and Examinations*

**[0789]** Clinical Observations: All animals will be observed at dosing and each scheduled collection. All abnormalities will be recorded.

**[0790]** Body Weight: All animals will be weighed on the dosing day prior to dosing to determine the dose volume to be administered.

*Sample Collection and Processing*

**[0791]** Blood Sample Collection and Process: At least 0.1 mL blood will be collected at each time point. All blood samples will be collected via jugular vein. All blood samples will be transferred into low binding EP tube with anticoagulant (0.5 M Potassium (K2) EDTA will be pre-added as a ratio of 50:1 for blood: anticoagulant), 0.05% Triton X-100 (e.g., 100uL Blood+2uL 2.5% Triton X-100) will be used for desorption the blood samples will be placed on wet ice.

**[0792]** Blood samples will be centrifuged within 1hr of collection at 3,200 g 4°C for 10 minutes. Following centrifugation, plasma samples will be transferred into their respective pre-labeled low binding EP tube and immediately frozen over dry ice. The plasma samples will be stored lower than -60°C until bioanalysis.

**[0793]** LC-MS/MS method development:

**[0794]** A LC-MS/MS method for the quantitative determination of test compound in biological matrix will be developed.

**[0795]** N in 1 cassette LC-MS/MS method can be developed for samples coming from different studies as long as these studies belong to the same sponsor.

**[0796]** Cassette administration assay could be performed if the mass difference (ΔMass) among different analytes is ≥4 Da. In this case, interference evaluation is not necessary.

**[0797]** If ΔMass among different analytes is less than 4 Da, there is a potential risk that interference would occur during LC-MS/MS analysis. If such kind of cassette assay is still requested by client, interference among analytes will not be evaluated but the LC separation of those analytes by using a generic method will be attempted.

**[0798]** Sample analysis:

**[0799]** A calibration curve with at least 6 non-zero calibration standards will be applied for each batch including LLOQ.

**[0800]** If sample number within a batch is ≤ 12, at least one set of standard curves separated with two parts through begin and end of the sequence should be included in the run and QCs are not required. The recommended injection order is C8, C6, C4, C2, study samples, C7, C5, C3, C1.

**[0801]** If sample number within a batch is > 12, one standard curve and two sets of QCs with low, middle and high concentrations will be applied for bioanalysis. Meanwhile, QCs number should be more than 5% of study sample number.

**[0802]** Samples, coming from one client with the same type of matrix in different studies, are allowed to be quantified in one analysis run by using the developed N in 1 cassette LC-MS/MS method.

**[0803]** Acceptance criteria:

**[0804]** (1) Linearity: At least 75% of the calibration standards should fall within ±20% of their nominal values for biofluid and within ±25% of their nominal values for tissue and feces samples. If the endpoints, such as LLOQ and ULOQ, on the calibration curve are eliminated, the calibration curve will be truncated. The truncated calibration curve should consist of at least 75% of the initial STDs.

**[0805]** (2) Accuracy: At least 67% of QCs should fall within ±20% of their nominal values for biofluid and within ±25% of their nominal values for tissue and feces samples. At least half of QCs at each concentration should be passed.

**[0806]** (3) Specificity: The mass response of analyte in the double blank and blank should be ≤ 50% LLOQ.

**[0807]** (4) Sensitivity: The LLOQ will be tried to target ≤ 3 ng/mL. Any adjustment of LLOQ will be informed to client in advance.

**[0808]** (5) Carryover: The mean calculated carryover peak area in the double blanks or blanks immediately after the highest standard injection should be less than that of LLOQ. If the carryover couldn't meet the criteria, the impact of the carryover on unknown samples should be re-evaluated according to the below procedure:

**[0809]** Carryover should be re-evaluated based on absolute carryover. Absolute carryover is calculated by carryover contribution multiplies carryover impact, where the carryover contribution is calculated by the area ratio of the double blank or blank with the highest carryover (Area max of carryover blank) to the ULOQ with the minimum calculated value (Area min of ULOQ), and the carryover impact is calculated by the area ratio of one injection (Area of one injection) to the following injection (Area of the following injection). The absolute carryover should be below the acceptable accuracy of the studies (e.g., 20% or 25%).

**[0810]** Carryover contribution = $Area_{max}$ of carryover blank / $Area_{min}$ of ULOQ Carryover impact = Area of one injection / Area of the following injection Absolute carryover = Carryover contribution * Carryover impact

*Data Analysis*

**[0811]** Preliminary plasma and cerebrospinal fluid (CSF) results after 24 hours of subcutaneous (SC) administration of A07D in Rats are shown in Table 23 and Table 24. Graphs of plasma concentration and CSF concentration in Rats are shown in FIGS 2A-2D.

Table 23. Concentration of A07D in plasma and CSF of Rats over time

| **Comp. Name** | **Dose (mg/kg)** | **Plasma Concentration (ng/mL) over Time** | | | | | | | | **CSF Concentration (ng/mL) over Time** | | **Plasma/CSF ratio** | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | **0.25h** | **0.5 h** | **1 h** | **2 h** | 4 h | **6 h** | **8 h** | **24 h** | **2 h** | **4 h** | **2h** | **4 h** |
| A07D | 1 | 228 | 253 | 319 | 249 | 122 | 17.1 | 1.47 | ND | - | - | - | - |
| A07D | 3 | 303 | 369 | 570 | 620 | 431 | 267 | 93.9 | ND | - | - | - | - |
| A07D | 10 | 274 | 364 | 747 | 1169 | 1139 | 844 | 575 | 7.23 | 8.60 | 15.9 | 0.00749 | 0.0141 |

ND = not determined

Table 24. Plasma Pharmacokinetic Results of A07D in Rats after 24 hours

| Comp. Name | Dose (mg/kg) | Cmax (ng/mL) | Tmax (h) | Tfinal | T1/2 (h) | $AUC_{0\text{-last}}$ (ng.h/mL) | $AUC_{0\text{-inf}}$ (ng.h/mL) | $MRT_{0\text{-last}}$ (h) | $MRT_{0\text{-inf}}$ (h) | $AUC_{EX}$ (%) | $AUMC_{EX}$ (%) | Bioavailability (%) |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| A07D | 1 | 319 | 1.00 | 8h-24h | 2.58 | 1066 | 1106 | 3.02 | 3.87 | 3.02 | 14.0 | 95.1 |
| A07D | 3 | 647 | 1.67 | 8h | 1.85 | 2986 | 3305 | 3.23 | 3.94 | 8.97 | 22.3 | 94.7 |
| A07D | 10 | 1324 | 2.67 | 24h | 2.50 | 9002 | 9032 | 5.65 | 5.72 | 0.319 | 1.50 | 77.7 |

**[0812]** Dose proportionality of A07D in male rats following a single subcutaneous administration in Rats is shown in Table 25.

Table 25. Dose Proportionality of A07D in Rats after a single SC administration

| Compound Name | Compare Doses (mg/kg) | | | Dose Ratio | Cmax Values | Cmax Ratio | $AUC_{0\text{-last}}$ Values | $AUC_{0\text{-last}}$ Ratio |
|---|---|---|---|---|---|---|---|---|
| D | 3.00 | Over | 1.00 | 3.00 | 647/319 | 2.03 | 2986/1066 | 2.80 |
| D | 10.0 | Over | 1.00 | 3.33 | 1324/647 | 2.05 | 9002/298 | 3.01 |
| D | 10.0 | Over | 3.00 | 10.0 | 13824/319 | 4.15 | 9002/1066 | 8.44 |

***Example 7: Residue Impact on Bioavailability***

**[0813]** To assess the impact of non-naturally occurring melanocortin analogs on bioavailability, various pharmacokinetic parameters were assessed in the plasma of male cynomolgus monkeys fasted prior to dosing A07D at 1 mg/kg intravenously, 10 mg/kg orally, or 30 mg/kg orally. Results are shown in Table 26 and FIG 3.

Table 26: A07D Results

| **IV bolus1 (1 mg/kg)** | | | | | | | |
|---|---|---|---|---|---|---|---|
| Time (h) | C1001 | C1002 | C1003 | Mean | | SD | CV (%) |
| -- | Plasma Concentration (ng/mL) | | | | | | |
| 0.083 | 9594 | 5458 | 5566 | 6873 | ± | 2357 | 34.3 |
| 0.25 | 6334 | 3905 | 3783 | 4674 | ± | 1439 | 30.8 |
| 0.5 | 5668 | 3474 | 3125 | 4089 | ± | 1379 | 33.7 |
| 1 | 4917 | 2312 | 2499 | 3243 | ± | 1453 | 44.8 |
| 2 | 3191 | 1673 | 1687 | 2184 | ± | 872 | 40.0 |
| 4 | 1869 | 868 | 830 | 1189 | ± | 589 | 49.6 |
| 6 | 1249 | 602 | 465 | 772 | ± | 419 | 54.2 |
| 8 | 871 | 324 | 238 | 478 | ± | 343 | 71.9 |
| 24 | 82.4 | 17.3 | 12.6 | 37.4 | ± | 39.0 | 104 |
| PK Parameters | C1001 | C1002 | C1003 | Mean | | SD | CV (%) |
| Rsq_adj | 0.999 | 0.995 | 0.989 | -- | ± | -- | -- |
| No. points used for $T_{1/2}$ | 3.00 | 4.00 | 3.00 | ND | ± | -- | -- |
| $C_0$ (ng/mL) | 11793 | 6446 | 6744 | 8328 | ± | 3005 | 36.1 |
| $T_{1/2}$ (h) | 4.63 | 3.57 | 3.57 | 3.92 | ± | 0.612 | 15.6 |
| $Vd_{ss}$ (L/kg) | 0.201 | 0.328 | 0.313 | 0.281 | ± | 0.0694 | 24.7 |
| Cl(mL/min/kg) | 0.633 | 1.37 | 1.48 | 1.16 | ± | 0.461 | 39.7 |
| $T_{last}$ (h) | 24.0 | 24.0 | 24.0 | 24.0 | ± | -- | -- |
| $AUC_{0\text{-}last}$ (ng.h/mL) | 25795 | 12071 | 11189 | 16352 | ± | 8190 | 50.1 |
| $AUC_{0\text{-}inf}$ (ng.h/mL) | 26346 | 12160 | 11254 | 16587 | ± | 8464 | 51.0 |
| $MRT_{0\text{-}last}$ (h) | 4.76 | 3.81 | 3.37 | 3.98 | ± | 0.710 | 17.8 |
| $MRT_{0\text{-}inf}$ (h) | 5.31 | 3.99 | 3.52 | 4.27 | ± | 0.928 | 21.7 |
| $AUC_{Extra}$ (%) | 2.09 | 0.733 | 0.577 | 1.13 | ± | 0.832 | 73.4 |
| $AUMC_{Extra}$ (%) | 12.1 | 5.35 | 4.78 | 7.41 | ± | 4.07 | 54.9 |

| **PO2 (10 mg/kg)** | | | | | | | |
|---|---|---|---|---|---|---|---|
| Time (h) | C2001 | C2002 | C2003 | Mean | | SD | CV (%) |
| -- | Plasma Concentration (ng/mL) | | | | | | |
| 0.083 | 2.85 | 3.83 | 8.58 | 5.09 | ± | 3.06 | 60.3 |
| 0.25 | 20.2 | 101 | 23.2 | 48.1 | ± | 45.8 | 95.2 |
| 0.5 | 67.0 | 418 | 74.9 | 187 | ± | 200 | 107 |
| 1 | 85.1 | 450 | 111 | 215 | ± | 204 | 94.5 |
| 2 | 174 | 408 | 79.6 | 221 | ± | 169 | 76.7 |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| 4 | 136 | 240 | 59.8 | 145 | ± | 90.5 | 62.3 |
| 6 | 90.9 | 171 | 45.3 | 102 | ± | 63.6 | 62.1 |
| 8 | 53.7 | 71.5 | 23.2 | 49.5 | ± | 24.4 | 49.4 |
| 24 | 8.75 | 7.42 | 2.45 | 6.21 | ± | 3.32 | 53.5 |
| PK Parameters | C2001 | C2002 | C2003 | Mean | | SD | CV (%) |
| Rsq_adj | 0.974 | 0.963 | 0.987 | -- | ± | -- | -- |
| No. points used for $T_{1/2}$ | 3.00 | 5.00 | 5.00 | ND | ± | -- | -- |
| $C_{max}$ (ng/mL) | 174 | 450 | 111 | 245 | ± | 180 | 73.6 |
| $T_{max}$ (h) | 2.00 | 1.00 | 1.00 | 1.33 | ± | 0.577 | 43.3 |
| $T_{1/2}$ (h) | 5.61 | 3.93 | 4.37 | 4.64 | ± | 0.871 | 18.8 |
| $T_{last}$ (h) | 24.0 | 24.0 | 24.0 | 24.0 | ± | -- | -- |
| $AUC_{0\text{-}last}$ (ng.h/mL) | 1251 | 2441 | 613 | 1435 | ± | 928 | 64.7 |
| $AUC_{0\text{-}inf}$ (ng.h/mL) | 1321 | 2483 | 628 | 1477 | ± | 937 | 63.4 |
| $MRT_{0\text{-}last}$ (h) | 6.94 | 5.01 | 5.74 | 5.90 | ± | 0.974 | 16.5 |
| $MRT_{0\text{-}inf}$ (h) | 8.29 | 5.43 | 6.34 | 6.69 | ± | 1.46 | 21.9 |
| $AUC_{Extra}$ (%) | 5.36 | 1.69 | 2.46 | 3.17 | ± | 1.94 | 61.0 |
| $AUMC_{Extra}$ (%) | 20.7 | 9.24 | 11.7 | 13.9 | ± | 6.03 | 43.5 |
| Bioavailability (%)[a] | - | - | - | 0.890 | -- | -- | -- |

| **PO3 (30 mg/kg)** | | | | | | | |
|---|---|---|---|---|---|---|---|
| Time (h) | C3001 | C3002 | C3003 | Mean | | SD | CV (%) |
| -- | Plasma Concentration (ng/mL) | | | | | | |
| 0.083 | 17.0 | 10.4 | 33.8 | 20.4 | ± | 12.1 | 59.1 |
| 0.25 | 108 | 24.0 | 97.6 | 76.5 | ± | 45.8 | 59.8 |
| 0.5 | 431 | 37.3 | 171 | 213 | ± | 200 | 93.9 |
| 1 | 504 | 122 | 236 | 287 | ± | 196 | 68.3 |
| 2 | 502 | 427 | 326 | 418 | ± | 88.3 | 21.1 |
| 4 | 332 | 320 | 244 | 299 | ± | 47.7 | 16.0 |
| 6 | 220 | 190 | 180 | 197 | ± | 20.8 | 10.6 |
| 8 | 120 | 124 | 163 | 136 | ± | 23.8 | 17.5 |
| 24 | 57.7 | 19.1 | 39.6 | 38.8 | ± | 19.3 | 49.8 |
| PK Parameters | C3001 | C3002 | C3003 | Mean | | SD | CV (%) |
| Rsq_adj | 0.785 | 0.989 | 0.996 | -- | ± | -- | -- |
| No. points used for $T_{1/2}$ | 5.00 | 3.00 | 3.00 | ND | ± | -- | -- |
| $C_{max}$ (ng/mL) | 504 | 427 | 326 | 419 | ± | 89.3 | 21.3 |
| $T_{max}$ (h) | 1.00 | 2.00 | 2.00 | 1.67 | ± | 0.577 | 34.6 |
| $T_{1/2}$ (h) | 7.80 | 5.61 | 8.08 | 7.16 | ± | 1.35 | 18.9 |
| $T_{last}$ (h) | 24.0 | 24.0 | 24.0 | 24.0 | ± | -- | -- |
| $AUC_{0\text{-}last}$ (ng.h/mL) | 3873 | 2772 | 3154 | 3266 | ± | 559 | 17.1 |
| $AUC_{0\text{-}inf}$ (ng.h/mL) | 4522 | 2927 | 3615 | 3688 | ± | 800 | 21.7 |
| $MRT_{0\text{-}last}$ (h) | 7.44 | 7.05 | 8.39 | 7.63 | ± | 0.689 | 9.04 |
| $MRT_{0\text{-}inf}$ (h) | 11.4 | 8.37 | 11.9 | 10.6 | ± | 1.91 | 18.1 |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| $AUC_{Extra}$ (%) | 14.4 | 5.28 | 12.8 | 10.8 | ± | 4.87 | 45.0 |
| $AUMC_{Extra}$ (%) | 44.3 | 20.2 | 38.4 | 34.3 | ± | 12.6 | 36.6 |
| Bioavailability (%)[a] | - | - | - | 0.741 | -- | -- | -- |

**[0814]** ND = Not determined (Parameters not determined due to inadequately defined terminal elimination phase).

**[0815]** BQL = Below the lower limit of quantitation (LLOQ).

**[0816]** If the adjusted rsq (linear regression coefficient of the concentration value on the terminal phase) is less than 0.9, $T_{1/2}$ might not be accurately estimated.

**[0817]** If the % $AUC_{Extra}$ > 20%, $AUC_{0\text{-}inf}$, Cl, $MRT_{0\text{-}inf}$ and $Vd_{ss}$ might not be accurately estimated.

**[0818]** If the % $AUMC_{Extra}$ > 20%, $MRT_{0\text{-}inf}$ and $Vd_{ss}$ might not be accurately estimated.

**[0819]** The adjusted linear regression coefficient of the concentration value on the terminal phase is less than 0.9, $T_{1/2}$ might not be accurately estimated.

**[0820]** a: Bioavailability (%) was calculated using $AUC_{0\text{-}inf}$ (if all $AUC_{Extra}$ ≤ 20%) or $AUC_{0\text{-}last}$ (if one or more $AUC_{Extra}$ > 20%) with Nominal Dose.

***Example 8: Effects of A07D in the Expression of Morphine Conditioned Place Preference (CPP)***

**[0821]** Effects of A07D on morphine preference was assessed in rats using a CPP assay (FIG. 4A). Rats were habituated in animal facility for 7 days and were handled for 1-2 minutes per day for 3 days before pre-test.

**[0822]** For pre-testing, rats were allowed to freely explore both sides of the box for 15 min to rule out a preference for either side (rats with a CPP score ≥+150 or ≤ -150 were excluded from the study). After pre-test, group assignment was conducted within each group according to the pre-test results such that morphine was paired with the less-preferred compartment.

**[0823]** Following the pretest phase, rats underwent place conditioning for 8 days, with alternating treatment-compartment pairings. For a conditioning session, saline (2 mL/kg,

intraperitoneal injection (i.p)) or morphine (10 mg/kg, i.p.) was administered, and rats were confined to the paired compartment for 45 minutes.

**[0824]** For post-testing, one day later, rats were randomly placed into one compartment and have access to both compartments during the 15-minute test period, and the time spend in each compartment was recorded. Animals that with a CPP score ≥ 100 in the morphine group were included for the further tests.

**[0825]** In the Expression test 1, A07D at 3 mg/kg and vehicle were administered subcutaneously (s.c) once 2 hours before the CPP expression test. The CPP score was defined as the time (in seconds) spent in the morphine-paired compartment minus the time spent in the saline-paired compartment during the CPP test. Groups included group 1 (vehicle + saline administration), group 2 (vehicle + morphine administration), and group 3 (A07D + morphine administration) (N = 10 rats per group).

**[0826]** For the Expression test 2, 24 hours later, A07D at 3 mg/kg was administered (s.c) once 1 hour before the CPP expression test. The CPP score was defined as the time (in seconds) spent in the morphine-paired compartment minus the time spent in the saline-paired compartment during the CPP test.

**[0827]** Data were analyzed by the two-way ANOVA followed by Bonferroni's pos hoc analysis.

*Results*

**[0828]** There was no difference in the pre-test for all groups (FIG. 4B). In the post-test, morphine-conditioned groups showed significant increased CPP score compared with saline-conditioned group ($p<0.0001$). There was no difference between vehicle + morphine group and A07D + morphine group in the post-test ($p>0.9999$). In the Expression test 1, A07D at the dose of 3 mg/kg almost significantly reduced the morphine CPP score when administered 2 hours prior to the test ($p = 0.08$). In the Expression test 2, A07D at the dose of 3 mg/kg significantly reduced the morphine CPP score when administered 1 hour prior to the test ($p = 0.01$). Results are further detailed in Tables 27 and 28.

**[0829]** A07D significantly decreased the expression of morphine CPP in rats, indicating a potential effect of A07D in attenuating morphine addiction-related behaviors.

Table 27: Summary Statistics for CPP Scores (N=10 per group)

| Group | Measurement | Pre-test | Post-test | Test1 | Test2 |
|---|---|---|---|---|---|
| Vehicle+saline | Mean | -69.420 | -70.610 | -79.000 | -57.060 |
| | SEM | 15.840 | 43.013 | 54.855 | 74.686 |
| Vehicle+morphine | Mean | -55.550 | 246.370 | 199.250 | 199.600 |
| | SEM | 14.304 | 28.173 | 29.830 | 34.138 |
| A07D+morphine | Mean | -64.620 | 200.980 | 84.280 | 47.080 |
| | SEM | 14.650 | 20.689 | 26.341 | 34.188 |

Table 28: Individual CPP Scores

| Treatment Group | Animal No. | Drug-paired Side | Pre-test | Post-test | Test 1 | Test 2 |
|---|---|---|---|---|---|---|
| Vehicle+saline | 1 | A | -25.5 | -302.3 | -329.2 | -318.2 |
| | 2 | A | -120.9 | -90.9 | -59.5 | 194.7 |
| | 3 | A | -20.3 | -53.5 | 274.4 | 217.1 |
| | 4 | B | -115.9 | -102.5 | -143.1 | 204.5 |
| | 5 | B | -49.6 | -5.7 | -391.3 | 124.1 |
| | 6 | B | -35.0 | -179.7 | -69.3 | -31.1 |
| | 7 | A | -17.5 | -89 | -33.6 | 259.9 |
| | 8 | B | -147.4 | 222.6 | -237.3 | 4.7 |
| | 9 | A | -43.6 | -66.6 | -64.4 | 193.9 |
| | 10 | A | -118.5 | -95.5 | -54.3 | 43.1 |
| Vehicle+morphine | 1 | A | -36.4 | -102.5 | -175.3 | 132.2 |
| | 2 | B | -83.0 | -5.7 | 107.9 | 58.8 |
| | 3 | A | 360.4 | -179.7 | 293.3 | -- |
| | 4 | B | 89.0 | 274.0 | -- | -- |
| | 5 | B | -113.5 | -222.6 | 112.6 | -- |
| | 6 | B | 258.5 | -277.6 | 317.8 | -- |
| | 7 | B | -35.1 | -278.8 | 219.2 | -- |
| | 8 | A | 66.6 | 142.8 | -- | -- |
| | 9 | B | -138.5 | 95.5 | 48.5 | -- |
| | 10 | A | -135.2 | 87.6 | 145.5 | -- |
| A07D+morphine | 1 | B | -97.7 | 174.6 | 276.6 | -- |
| | 2 | B | -97.4 | 159.1 | 329.3 | -- |
| | 3 | A | 177.9 | 164.1 | 279.7 | -- |
| | 4 | B | -21.1 | 302.5 | 126.2 | -- |

| Treatment Group | Animal No. | Drug-paired Side | Pre-test | Post-test | Test 1 | Test 2 |
|---|---|---|---|---|---|---|
| | 5 | A | 350.0 | 274.2 | -- | -- |
| | 6 | B | -125.0 | 170.5 | 332.7 | -- |
| | 7 | B | -54.2 | 57.5 | 106.5 | -- |
| | 8 | B | 29.3 | 143.2 | -- | -- |
| | 9 | B | -25.0 | 233.0 | 149.0 | -- |
| | 10 | B | 120.4 | 32.1 | -- | -- |
| Saline | 1 | A | -25.5 | -302.3 | -329.2 | -318.2 |
| | 2 | A | -120.9 | -90.9 | -59.5 | 194.7 |
| | 3 | A | -20.3 | -53.5 | 274.4 | 217.1 |
| | 4 | B | -115.9 | -102.5 | -143.1 | -391.3 |
| | 5 | B | -49.6 | -5.7 | -69.3 | 204.5 |
| | 6 | B | -35 | -179.7 | -33.6 | -237.3 |
| | 7 | A | -17.5 | 89 | -64.4 | -54.3 |
| | 8 | B | -147.4 | -222.6 | -277.6 | -278.8 |
| | 9 | A | -43.6 | 66.6 | -175.3 | 124.1 |
| | 10 | A | -118.5 | 95.5 | 87.6 | -31.1 |
| Vehicle-Morphine | 1 | A | -36.4 | 174.6 | 107.9 | 259.9 |
| | 2 | B | -72.8 | 159.1 | 293.3 | 4.7 |
| | 3 | A | -6.5 | 312.1 | 274 | 193.9 |
| | 4 | B | -83 | 360.4 | 112.6 | 317.8 |
| | 5 | A | -25 | 276.2 | 219.2 | 142.8 |
| | 6 | B | -42.3 | 106.2 | 48.5 | 145.5 |
| | 7 | B | -113.5 | 258.5 | 276.6 | 329.3 |
| | 8 | B | -35.1 | 164.1 | 279.7 | 126.2 |
| | 9 | A | -2.4 | 302.5 | 274.2 | 332.7 |
| | 10 | B | -138.5 | 350 | 106.5 | 143.2 |
| A07D-Morphine | 1 | A | -135.2 | 170.5 | 57.5 | 29.3 |
| | 2 | B | -97.7 | 233 | 149 | 32.1 |
| | 3 | B | -97.4 | 177.9 | -72.8 | -104.5 |
| | 4 | B | -21.1 | 120.4 | 142.6 | 58.3 |
| | 5 | A | -23.2 | 289.4 | 37.4 | 280.4 |
| | 6 | B | -8 | 327.4 | 98.2 | -92.7 |
| | 7 | B | -125 | 156.7 | 203.7 | 33.8 |
| | 8 | B | -54.2 | -157.4 | -15.6 | 43.1 |
| | 9 | B | -59.4 | 160.5 | 127.7 | 132.2 |

| Treatment Group | Animal No. | Drug-paired Side | Pre-test | Post-test | Test 1 | Test 2 |
|---|---|---|---|---|---|---|
| | 10 | B | -25 | 216.6 | 115.1 | 58.8 |

***Additional Embodiments***

**[0830]** Various embodiments of the present technology are set forth below in paragraphs [0839] to [0948]:

**[0831]** 1. A method of reducing a pain level in a subject in need thereof relative to a control, comprising administering to the subject a non-naturally occurring melanocortin analog of Formula (I):

$X^1$-$X^2$-$X^3$-$R^1$-$R^2$-$R^3$-$R^4$-$R^5$-$R^6$-$R^7$-$R^8$-$Y^1$-$Y^2$-$Y^3$-$Y^4$-$Y^5$-$Y^6$-$Y^7$ (I),

wherein:

$X^1$ is absent or is selected from the group consisting of norleucine (Nle), arginine (Arg), D-arginine (dArg), alanine (Ala), lysine (Lys), D-lysine (dLys), histidine (His), and D-histidine (dHis);

$X^2$ is absent, phenylalanine (Phe), or Nle;

$X^3$ is absent, Phe, or Nle;

$R^1$ is selected from the group consisting of Nle, D-norleucine (dNle), Ala, D-alanine (dAla), Arg, dArg, Lys, dLys, His, dHis, ornithine (Orn), D-ornithine (dOrn), D-leucine (dLeu), D-tyrosine (dTyr), phenylalanine (Phe), D-phenylalanine (dPhe), tryptophan (Trp), D-tryptophan (dTrp), aspartic acid (Asp), cysteine (Cys), and D-cysteine (dCys);

$R^2$ is selected from the group consisting of Asp, proline (Pro), D-aspartic acid (dAsp), Cys, dCys, D-penicillamine (dPen), Ala, dAla, Trp, Phe, dPhe, His, dHis, Tyr, and dTyr;

$R^3$ is absent or is selected from the group consisting of His, Ala, Pro, hydroxyproline (Hyp), leucine (Leu), D-glutamine (dGln), Phe, dPhe, Trp, dTrp, Tyr, dTyr, 4-amino-1,2,4,5-tetrahydro-2-benzazepin-3-one (Aba), 7-amino-7,8-dihydro-4H-[1,2,3]triazolo-[1,5-a][1,4]diazepin-6(5H)-one (Ata), 4-amino-1,4,5,6-tetrahydroazepino[4,3-*b*]indol-3(*2H*)-one (Aia), 2-aminotetraline-2-carboxylic acid (Atc), 1-amino-4-phenylcyclohexane-carboxylic

acid (APC), 4-aminophenylpiperidine-4-carboxylic acid (APPC), octohydroindole-2-carboxylic acid (Oic), 1-amino-1-cyclohexanecarboxylic acid (Che), tetrahydro-isoquinoline-3-carboxylic acid (Tic), indoline-2-carboxylic acid (Ioc), 1-amino-1-cyclopentane carboxylic (Cpe), and biphenylalanine (Bip);

$R^4$ is selected from the group consisting of Phe, dPhe, 2'-D-naphthylalanine (dNal(2')), para-chloro-D-phenylalanine (p(Cl)dPhe), para-bromo-D-phenylalanine (p(Br)dPhe), and para-fluoro-D-phenylalanine (p(F)dPhe);

$R^5$ is selected from the group consisting of Arg, His, *cis*Pro(guan), and *trans*Pro(guan);

$R^6$ is selected from the group consisting of Trp, dTrp, Phe, Aia, Aba, Ata, dNal(2'), 2'-naphthylalanine (Nal(2')), and 1'-naphthylalanine (Nal(1'));

$R^7$ is selected from the group consisting of Gly, Pro, Lys, dLys, Cys, dCys, penicillamine (Pen), dPen, and Orn;

$R^8$ is absent or Lys;

$Y^1$ is absent or is selected from the group consisting of valine (Val), D-valine (dVal), $b^2$-valine ($b^2$-Val), $b^3$-valine ($b^3$-Val), Pro, D-proline (dPro), b-proline (b-Pro), Hyp, D-hydroxyproline (dHyp), D-tert-leucine (dTle), dLeu, Trp, Arg, dArg, Lys, dLys, Gly, Ala, dAla, Asp, dAsp, asparagine (Asn), D-asparagine (dAsn), and D-threonine (dThr);

$Y^2$ is absent or is selected from the group consisting of Val, dVal, $b^2$-Val, $b^3$-Val, Pro, dPro, b-Pro, Hyp, dHyp, dTle, Arg, dArg, Gly, Ala, dAla, Asp, and dAsn;

$Y^3$ is absent or is selected from the group consisting of Val, dVal, Pro, dPro, dThr, Lys, and dLys;

$Y^4$ is absent or is selected from the group consisting of dVal, dPro, Asp, and dAsp;

$Y^5$ is absent or dVal;

$Y^6$ is absent or dVal;

$Y^7$ is absent or dPro; and

the non-naturally occurring melanocortin analog is cyclized through a moiety selected from the group consisting of:

a disulfide bond between $R^1$ or $R^2$ and $R^7$ when each of $R^1$ or $R^2$ and $R^7$ are independently selected from the group consisting of Cys, dCys, and dPen;

a disulfide bond between $R^2$ and $R^7$ when $R^2$ is Cys, $R^7$ is Pen, and $R^3$ is absent;

a lactam bridge between $R^1$ or $R^2$ and $R^7$ or $R^8$ when $R^1$ or $R^2$ is Asp and $R^7$ or $R^8$ is Lys or Orn; and

a lactam bridge between $R^2$ and $R^7$ when $R^2$ is dAsp and $R^7$ is dLys;

provided that:

when $R^4$ is dNal(2'), then $R^3$ is His and $R^7$ is Pro;

when $R^4$ is p(F)dPhe, then (i) $R^3$ is selected from Pro, dGln, dTyr, $R^6$ is Trp, and the non-naturally occurring melanocortin analog is not cyclized between Cys at $R^2$ and Cys at $R^7$ or (ii) $R^3$ is His and either $R^6$ is Nal(2') or the non-naturally occurring melanocortin analog is cyclized through a disulfide bond between $R^2$ and $R^7$;

when $R^4$ is p(Br)dPhe, then the non-naturally occurring melanocortin analog is cyclized through a disulfide bond between dCys at $R^2$ and Cys or dCys at $R^7$;

when $R^4$ is dPhe, then (i) $R^3$ is not His, Pro, or absent, (ii) $R^3$ is His and either $R^2$ is Phe or dAla or $R^2$ is Ala and $X^1$ is Arg or dArg, (iii) $R^3$ is Pro and (a) $R^2$ is Trp, and $R^5$ is not His or $R^6$ is not Phe or (b) $R^2$ is not Trp or Pro, and either $R^5$ is not dNal(2') or Nal(2') or $X^1$ and $Y^3$ are not both present, or (iv) $R^3$ is absent and $R^2$ and $R^7$ are not both dPen;

when $R^4$ is p(Cl)dPhe, then (i) $R^3$ is selected from Aba, Aia, and Ata or (ii) $R^3$ is His, $R^1$ is not Ala, and (a) if $R^1$ is Nle and $Y^1Y^2$ is dVal-dPro, then $X^1$ is absent and the non-naturally occurring melanocortin analog is cyclized through a disulfide bond between dCys at $R^2$ and dCys at $R^7$, or (b) if $R^1$ is Nle, and $Y^1Y^2$ is not dVal-dPro, then either $X^1$ or $Y^3$ is present; and

when $R^2$ is dAla, then $R^4$ is dPhe and $Y^1$-$Y^7$ are absent.

**[0832]** 2. Use of a non-naturally occurring melanocortin analog for reducing a pain level in a subject in need thereof relative to a control, the non-naturally occurring melanocortin analog comprising a sequence of Formula (I).

**[0833]** 3. A method of treating, preventing, or reducing an addiction in a subject relative to a control, comprising administering to the subject a non-naturally occurring melanocortin analog comprising a sequence of Formula (I).

**[0834]** 4. Use of a non-naturally occurring melanocortin analog for treating, preventing, or reducing an addiction in a subject relative to a control, the non-naturally occurring melanocortin analog comprising a sequence of Formula (I).

**[0835]** 5. A method of preventing or reducing a use of or dependence on an addictive substance in a subject relative to a control, comprising administering to the subject a non-naturally occurring melanocortin analog comprising a sequence of Formula (I).

**[0836]** 6. Use of a non-naturally occurring melanocortin analog for treating, preventing, or reducing a use of or dependence on an addictive substance in a subject relative to a control, the non-naturally occurring melanocortin analog comprising a sequence of Formula (I).

**[0837]** 7. A method of treating or preventing an opioid use disorder (OUD) in a subject in need thereof relative to a control, comprising administering to the subject a non-naturally occurring melanocortin analog comprising a sequence of Formula (I).

**[0838]** 8. Use of a non-naturally occurring melanocortin analog for treating or preventing an OUD in a subject in need thereof relative to a control, the non-naturally occurring melanocortin analog comprising a sequence of Formula (I).

**[0839]** 9. A method of treating or preventing an alcohol use disorder (AUD) in a subject in need thereof relative to a control, comprising administering to the subject a non-naturally occurring melanocortin analog comprising a sequence of Formula (I).

**[0840]** 10. Use of a non-naturally occurring melanocortin analog for treating or preventing an AUD in a subject in need thereof relative to a control, the non-naturally occurring melanocortin analog comprising a sequence of Formula (I).

**[0841]** 11. The method or the use of any one of embodiments 3-9, wherein the method or the use comprises reducing a dose used or consumed of an addictive substance, relative to a control.

**[0842]** 12. The method or the use of any one of embodiments 3-11, wherein the method or the use comprises reducing a dependency on an addictive substance, relative to a control.

**[0843]** 13. The method or the use of any one of embodiments 3-12, wherein the method or the use comprises reducing a frequency of an addictive substance use, relative to a control.

**[0844]** 14. The method or the use of any one of embodiments 3-13, wherein the method or the use comprises reducing a dose or dosage of a conventional medication used to treat an addiction, relative to a control.

**[0845]** 15. A method of augmenting an effect of a conventional medication used to treat an addiction in a subject in need thereof, relative to a control, comprising administering to the subject a non-naturally occurring melanocortin analog comprising a sequence of Formula (I).

**[0846]** 16. Use of a non-naturally occurring melanocortin analog for augmenting an effect of a conventional medication used to treat an addiction in a subject in need thereof, the non-naturally occurring melanocortin analog comprising a sequence of Formula (I).

**[0847]** 17. A method of reducing or eliminating a need for a conventional medication used to treat an addiction in a subject in need thereof, relative to a control, comprising administering to the subject a non-naturally occurring melanocortin analog comprising a sequence of Formula (I).

**[0848]** 18. Use of a non-naturally occurring melanocortin analog for reducing or eliminating a need for a conventional medication used to treat an addiction in a subject in need thereof, the non-naturally occurring melanocortin analog comprising a sequence of Formula (I).

**[0849]** 19. The method or the use of embodiment 17 or 18, wherein the treatment of the addiction is improved during or after administration of the non-naturally occurring melanocortin analog relative to treatment of the addiction using the conventional medication to treat the addiction alone.

**[0850]** 20. The method or the use of any one of embodiments 14-19, wherein the conventional medication to treat the addiction is selected from the group consisting of buprenorphine, naltrexone, acamprosate, methadone, naloxone, nalmefene, xycodone, levo-alpha-acetylmethadol (LAAM), codeine, lofexidine, and a slow-release morphine.

**[0851]** 21. A method of reducing a need for a hospitalization or rehabilitation associated with addiction or use of an addictive substance, relative to a control, comprising

administering to the subject a non-naturally occurring melanocortin analog comprising a sequence of Formula (I).

**[0852]** 22. Use of a non-naturally occurring melanocortin analog for reducing a need for a hospitalization or rehabilitation associated with addiction or use of an addictive substance, relative to a control, the non-naturally occurring melanocortin analog comprising a sequence of Formula (I).

**[0853]** 23. A method of preventing or reducing a withdrawal from an addictive substance in a subject, comprising administering to the subject a non-naturally occurring melanocortin analog comprising a sequence of Formula (I).

**[0854]** 24. Use of a non-naturally occurring melanocortin analog for preventing or reducing a withdrawal from an addictive substance in a subject, relative to a control, the non-naturally occurring melanocortin analog comprising a sequence of Formula (I).

**[0855]** 25. A method of preventing or reducing a symptom associated with withdrawal from an addictive substance in a subject relative to a control, comprising administering to the subject a non-naturally occurring melanocortin analog comprising a sequence of Formula (I).

**[0856]** 26. Use of a non-naturally occurring melanocortin analog for preventing or reducing a symptom associated with withdrawal from an addictive substance in a subject, relative to a control, the non-naturally occurring melanocortin analog comprising a sequence of Formula (I).

**[0857]** 27. The method or the use of embodiment 25 or 26, wherein the symptom associated with withdrawal from an addictive substance is selected from the group consisting of pain, anxiety, depression, diarrhea, dizziness, fatigue, muscle aches, nausea, sleep problems, suicidal ideation, tremors, and visual disturbances.

**[0858]** 28. The method or the use of any one of embodiments 1-27, wherein the subject has an addiction to an addictive substance or is susceptible to an addiction to an addictive substance.

**[0859]** 29. The method or the use of any one of embodiments 1-28, wherein the subject has used or is using one or more addictive substances.

**[0860]** 30. The method or the use of any one of embodiments 5-29 wherein the addictive substance comprises a prescription medication, a substance in an over-the-counter medication, a recreational substance, or an illegal substance.

**[0861]** 31. The method or the use of any one of embodiments 5-30, wherein the addictive substance is selected from the group consisting of an opioid, a painkiller, a stimulant, a narcotic, an alcohol, a sedative, marijuana, a cannabis, a tetrahydrocannabinol (THC), a cannabidiol (CBD), and an inhalant.

**[0862]** 32. The method or the use of embodiment 31, wherein the opioid is selected from the group consisting of morphine, heroin, codeine, oxycodone, hydrocodone, and fentanyl.

**[0863]** 33. The method or the use of embodiment 31, wherein the stimulant is selected from the group consisting of caffeine, nicotine, methamphetamines, cocaine, and amphetamines.

**[0864]** 34. The method or the use of embodiment 31, wherein the sedative comprises a barbiturate or a benzodiazepine.

**[0865]** 35. The method or the use of embodiment 34, wherein the barbiturate is selected from the group consisting of phenobarbital, methohexital, butalbital, pentobarbital, primidone, and amobarbital.

**[0866]** 36. The method or the use of embodiment 34, wherein the benzodiazepine is selected from the group consisting of alprazolam, lorazepam, clonazepam, diazepam, and temazepam.

**[0867]** 37. The method or the use of embodiment 31, wherein the sedative is selected from the group consisting of tranquilizers, xylazine, eszopiclone, zaleplon, zolpidem, and zopiclone.

**[0868]** 38. The method or the use of embodiment 31, wherein the inhalant is selected from the group consisting of aerosols, butanes, freon, helium, nitrous oxide, propane, and nitrites.

**[0869]** 39. The method or the use of embodiment 33, wherein the nicotine comprises a tobacco chew, a nicotine pouch, or a smoking device.

**[0870]** 40. The method or the use of embodiment 39, wherein the smoking device is selected from the group consisting of cigarettes, electronic cigarettes, cigars, and vape

products.

41. The method or the use of any one of embodiments 1-40, wherein the control comprises the subject before administration of the non-naturally occurring melanocortin analog.

**[0871]** 42. The method or the use of any one of embodiments 1-41, wherein the control comprises the subject at baseline.

**[0872]** 43. The method or the use of any one of embodiments 1-42, wherein the non-naturally occurring melanocortin analog is a melanocortin 4 receptor (MC4R) agonist.

**[0873]** 44. The method or the use of embodiment 43, wherein the MC4R agonist is a full MC4R agonist.

**[0874]** 45. The method or the use of embodiment 43, wherein the MC4R agonist is a partial MC4R agonist.

**[0875]** 46. The method or the use of any one of embodiments 1-45, wherein the non-naturally occurring melanocortin analog is a MC3R antagonist.

**[0876]** 47. The method or the use of embodiment 46, wherein the MC3R antagonist is a full MC3R antagonist.

**[0877]** 48. The method or the use of embodiment 46, wherein the MC3R antagonist is a partial MC3R antagonist.

**[0878]** 49. The method or the use of any one of embodiments 1-45, wherein the non-naturally occurring melanocortin analog does not have MC3R activity.

**[0879]** 50. The method or the use of any one of embodiments 1-49, wherein the non-naturally occurring melanocortin analog comprises a sequence according to Formula (I), wherein:

$X^1$ is absent or is selected from the group consisting of norleucine (Nle), arginine (Arg), D-arginine (dArg), alanine (Ala), lysine (Lys), D-lysine (dLys), histidine (His), and D-histidine (dHis);

$X^2$ is absent, phenylalanine (Phe), or Nle;

$X^3$ is absent, Phe, or Nle;

$R^1$ is selected from the group consisting of Nle, D-norleucine (dNle), Ala, D-alanine (dAla), Arg, dArg, Lys, dLys, His, dHis, ornithine (Orn), D-ornithine (dOrn), D-leucine (dLeu), D-

tyrosine (dTyr), phenylalanine (Phe), D-phenylalanine (dPhe), tryptophan (Trp), D-tryptophan (dTrp), aspartic acid (Asp), cysteine (Cys), and D-cysteine (dCys);

**[0880]** $R^2$ is selected from the group consisting of Asp, proline (Pro), D-aspartic acid (dAsp), Cys, dCys, D-penicillamine (dPen), Ala, dAla, Trp, Phe, dPhe, His, dHis, Tyr, and dTyr;

$R^3$ is absent or is selected from the group consisting of His, Ala, Pro, hydroxyproline (Hyp), leucine (Leu), D-glutamine (dGln), Phe, dPhe, Trp, dTrp, Tyr, dTyr, 4-amino-1,2,4,5-tetrahydro-2-benzazepin-3-one (Aba), 7-amino-7,8-dihydro-4H-[1,2,3]triazolo-[1,5-a][1,4]diazepin-6(5H)-one (Ata), 4-amino-1,4,5,6-tetrahydroazepino[4,3-*b*]indol-3(*2H*)-one (Aia), 2-aminotetraline-2-carboxylic acid (Atc), 1-amino-4-phenylcyclohexane-carboxylic acid (APC), 4-aminophenylpiperidine-4-carboxylic acid (APPC), octohydroindole-2-carboxylic acid (Oic), 1-amino-1-cyclohexanecarboxylic acid (Che), tetrahydro-isoquinoline-3-carboxylic acid (Tic), indoline-2-carboxylic acid (Ioc), 1-amino-1-cyclopentane carboxylic (Cpe), and biphenylalanine (Bip);

$R^4$ is selected from the group consisting of Phe, dPhe, 2'-D-naphthylalanine (dNal(2')), para-chloro-D-phenylalanine (p(Cl)dPhe), para-bromo-D-phenylalanine (p(Br)dPhe), and para-fluoro-D-phenylalanine (p(F)dPhe);

$R^5$ is selected from the group consisting of Arg, His, *cis*Pro(guan), and *trans*Pro(guan);

$R^6$ is selected from the group consisting of Trp, dTrp, Phe, Aia, Aba, Ata, dNal(2'), 2'-naphthylalanine (Nal(2')), and 1'-naphthylalanine (Nal(1'));

$R^7$ is selected from the group consisting of Gly, Pro, Lys, dLys, Cys, dCys, penicillamine (Pen), dPen, and Orn;

$R^8$ is absent or Lys;

$Y^1$ is absent or is selected from the group consisting of valine (Val), D-valine (dVal), $b^2$-valine ($b^2$-Val), $b^3$-valine ($b^3$-Val), Pro, D-proline (dPro), b-proline (b-Pro), Hyp, D-hydroxyproline (dHyp), D-tert-leucine (dTle), dLeu, Trp, Arg, dArg, Lys, dLys, Gly, Ala, dAla, Asp, dAsp, asparagine (Asn), D-asparagine (dAsn), and D-threonine (dThr);

$Y^2$ is absent or is selected from the group consisting of Val, dVal, $b^2$-Val, $b^3$-Val, Pro, dPro, b-Pro, Hyp, dHyp, dTle, Arg, dArg, Gly, Ala, dAla, Asp, and dAsn;

$Y^3$ is absent or is selected from the group consisting of Val, dVal, Pro, dPro, dThr, Lys, and dLys;

$Y^4$ is absent or is selected from the group consisting of dVal, dPro, Asp, and dAsp;

$Y^5$ is absent or dVal;

$Y^6$ is absent or dVal;

$Y^7$ is absent or dPro; and

the non-naturally occurring melanocortin analog is cyclized through a moiety selected from the group consisting of:

a disulfide bond between $R^1$ or $R^2$ and $R^7$ or $R^8$ when each of $R^1$ or $R^2$ and $R^7$ or $R^8$ are independently selected from the group consisting of Cys, dCys, and dPen;

a disulfide bond between $R^2$ and $R^7$ when $R^2$ is Cys, $R^7$ is Pen, and $R^3$ is absent;

a lactam bridge between $R^1$ or $R^2$ and $R^7$ or $R^8$ when $R^1$ or $R^2$ is Asp and $R^7$ or $R^8$ is Lys or Orn; and

a lactam bridge between $R^2$ and $R^7$ when $R^2$ is dAsp and $R^7$ is dLys;

provided that the non-naturally occurring melanocortin analog does not comprise a sequence selected from the group consisting of:

Ac-Nle-c[Asp-Pro-Pro-dNal(2')-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 194);

Ac-Nle-c[Asp-Pro-His-dNal(2')-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 5);

Ac-Nle-c[Asp-Pro-His-dNal(2')-Arg-Trp-Lys]-dPro-dVal-$NH_2$ (SEQ ID NO: 10);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dVal-dPro (SEQ ID NO: 2);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 3);

Ac-Nle-c[Asp-Hyp-dNal(2')-Arg-Trp-Pro-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 4);

Ac-Nle-c[Asp-Phe-His-dNal(2')-Arg-Trp-Lys]-dLeu-dPro-$NH_2$ (SEQ ID NO: 6);

Ac-Nle-c[Asp-Phe-His-dNal(2')-Arg-Trp-Lys]-dTle-dPro-$NH_2$ (SEQ ID NO: 7);

Ac-Nle-c[Asp-Hyp-dNal(2')-Arg-Trp-Pro-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 9);

Ac-Nle-Phe-Phe-c[Asp-Phe-His-dNal(2')-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 12);

Ac-dArg-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 15);

Ac-dLeu-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 18);

Ac-dAla-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 20);

Ac-Ala-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 21);

Ac-dNle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 24);

Ac-dCys-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 28);

Ac-dPhe-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 29);

Ac-dTyr-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 30);

dTyr-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 35);

Tyr-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 36);

Ac-Nle-c[Cys-Pro-dNal(2')-Arg-Trp-Cys]-dVal-dPro-$NH_2$ (SEQ ID NO: 40);

Ac-Nle-c[dCys-Pro-dNal(2')-Arg-Trp-Cys]-dVal-dPro-$NH_2$ (SEQ ID NO: 41);

Ac-Nle-c[Cys-Pro-dNal(2')-Arg-Trp-dCys]-dVal-dPro-$NH_2$ (SEQ ID NO: 42);

Ac-Nle-c[dCys-Pro-dNal(2')-Arg-Trp-dCys]-dVal-dPro-$NH_2$ (SEQ ID NO: 43);

Ac-Nle-c[Cys-Pro-dNal(2')-Arg-Trp-Pen]-dVal-dPro-$NH_2$ (SEQ ID NO: 48);

Ac-Nle-c[dPen-Pro-dNal(2')-Arg-Trp-dPen]-dVal-dPro-$NH_2$ (SEQ ID NO: 54);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Orn]-dVal-dPro-$NH_2$ (SEQ ID NO: 64);

Ac-Nle-c[Asp-dNal(2')-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 68);

Ac-Nle-c[Asp-Ala-dNal(2')-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 69);

Ac-Nle-c[Asp-Leu-dNal(2')-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 76);

Ac-Nle-c[Asp-Trp-dNal(2')-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 82);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-Val-Pro-$NH_2$ (SEQ ID NO: 115);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dVal-dPro-OH (SEQ ID NO: 116);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dPro-dVal-OH (SEQ ID NO: 117);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dVal-Hyp-$NH_2$ (SEQ ID NO: 118);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dVal-dHyp-$NH_2$ (SEQ ID NO: 119);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-Val-Hyp-$NH_2$ (SEQ ID NO: 120);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-Val-dHyp-$NH_2$ (SEQ ID NO: 121);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-Hyp-dVal-$NH_2$ (SEQ ID NO: 122);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dHyp-dVal-$NH_2$ (SEQ ID NO: 123);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-Hyp-Val-$NH_2$ (SEQ ID NO: 124);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dHyp-Val-$NH_2$ (SEQ ID NO: 125);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dVal-dVal-$NH_2$ (SEQ ID NO: 126);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dPro-dPro-$NH_2$ (SEQ ID NO: 127);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dVal-$NH_2$ (SEQ ID NO: 128);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dPro-$NH_2$ (SEQ ID NO: 129);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-Val-$NH_2$ (SEQ ID NO: 130);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-Pro-$NH_2$ (SEQ ID NO: 131);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-Ala-$NH_2$ (SEQ ID NO: 132);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dAla-$NH_2$ (SEQ ID NO: 133);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dHyp-$NH_2$ (SEQ ID NO: 134);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-Hyp-$NH_2$ (SEQ ID NO: 135);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dAla-dAla-$NH_2$ (SEQ ID NO: 136);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-Ala-Ala-$NH_2$ (SEQ ID NO: 137);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-Gly-Gly-$NH_2$ (SEQ ID NO: 138);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dVal-Asp-$NH_2$ (SEQ ID NO: 139);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dVal-Arg-$NH_2$ (SEQ ID NO: 140);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dVal-dArg-$NH_2$ (SEQ ID NO: 143);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dVal-dAsn-$NH_2$ (SEQ ID NO: 144);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-Asp-dPro-$NH_2$ (SEQ ID NO: 145);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-Arg-dPro-$NH_2$ (SEQ ID NO: 146);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-Asn-dPro-$NH_2$ (SEQ ID NO: 147);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dAsp-dPro-$NH_2$ (SEQ ID NO: 148);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dArg-dPro-$NH_2$ (SEQ ID NO: 149);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dAsn-dPro-$NH_2$ (SEQ ID NO: 150);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-Asp-$NH_2$ (SEQ ID NO: 151);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-Arg-$NH_2$ (SEQ ID NO: 152);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-Asn-$NH_2$ (SEQ ID NO: 153);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dAsp-$NH_2$ (SEQ ID NO: 154);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dArg-$NH_2$ (SEQ ID NO: 155);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dAsn-$NH_2$ (SEQ ID NO: 156);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-Lys-Pro-Val-$NH_2$ (SEQ ID NO: 157);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-Lys-dPro-dVal-$NH_2$ (SEQ ID NO: 158);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dLys-dPro-dVal-$NH_2$ (SEQ ID NO: 159);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-Lys-dPro-$NH_2$ (SEQ ID NO: 160);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dLys-dPro-$NH_2$ (SEQ ID NO: 161);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-Lys-Val-Pro-$NH_2$ (SEQ ID NO: 162);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-Lys-dVal-dPro-$NH_2$ (SEQ ID NO: 164);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dLys-dVal-dPro-$NH_2$ (SEQ ID NO: 164);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-Arg-Pro-Val-$NH_2$ (SEQ ID NO: 165);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-Arg-dPro-dVal-$NH_2$ (SEQ ID NO: 166);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dArg-dPro-dVal-$NH_2$ (SEQ ID NO: 167);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-Arg-Val-Pro-$NH_2$ (SEQ ID NO: 168);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-Arg-dVal-dPro-$NH_2$ (SEQ ID NO: 169);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dArg-dVal-dPro-$NH_2$ (SEQ ID NO: 170);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dTle-dVal-dPro-$NH_2$ (SEQ ID NO: 171);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dTle-dPro-$NH_2$ (SEQ ID NO: 172);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dTle-dVal-$NH_2$ (SEQ ID NO: 173);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dTle-dTle-$NH_2$ (SEQ ID NO: 174);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dTle-dTle-dPro-$NH_2$ (SEQ ID NO: 175);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dTle-dTle-dVal-$NH_2$ (SEQ ID NO: 176);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dPro-dTle-$NH_2$ (SEQ ID NO: 177);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dVal-dTle-$NH_2$ (SEQ ID NO: 178);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dVal-dVal-dPro-$NH_2$ (SEQ ID NO: 179);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dPro-dVal-dPro-$NH_2$ (SEQ ID NO: 180);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dVal-dVal-dVal-dPro-$NH_2$ (SEQ ID NO: 181);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dVal-dPro-dVal-dPro-$NH_2$ (SEQ ID NO: 182);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dVal-dVal-dVal-dVal-dVal-dVal-dPro-$NH_2$ (SEQ ID NO: 183);

Ac-Nle-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 184);

Ac-Nle-Nle-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 185);

Ac-Nle-Nle-Nle-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 186);

Ac-Nle-c[Asp-Trp-Pro-dNal(2')-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 195);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-dTrp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 196);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-Trp-$NH_2$ (SEQ ID NO: 203);

Ac-Nle-c[Asp-Aba-dNal(2')-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 204);

Ac-Nle-c[Asp-Aia-dNal(2')-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 205);

Ac-Nle-c[Asp-Ata-dNal(2')-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 206);

Ac-Nle-c[Asp-Cpe-dNal(2')-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 240);

Ac-Nle-c[Asp-Che-dNal(2')-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 241);

Ac-Nle-c[Asp-Oic-dNal(2')-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 242);

Ac-Nle-c[Asp-Tic-dNal(2')-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 244);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Pro-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 245);

Ac-Nle-c[Asp-His-dNal(2')-transPro(guan)-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 247);

Ac-Nle-c[Asp-His-dNal(2')-cisPro(guan)-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 248);

Ac-Nle-c[Asp-Pro-dNal(2')-transPro(guan)-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 250);

Ac-Nle-c[Asp-Pro-dNal(2')-cisPro(guan)Pro-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 251);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Aba-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 253);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Ata-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 254);

Ac-Nle-c[Asp-Glu-dNal(2')-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 255);

Ac-Nle-c[Asp-Glu-dNal(2')-Arg-Trp-Gly-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 256);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Gly-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 259);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Gly-Lys]-dPro-dPro-Lys-Asp-$NH_2$ (SEQ ID NO: 260);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Gly-Lys]-dPro-dPro-dLys-dAsp-$NH_2$ (SEQ ID NO: 261);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dPro-dPro-dLys-dAsp-$NH_2$ (SEQ ID NO: 263);

Ac-Nle-c[Asp-Ala-His-dNal(2')-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 273);

Ac-Arg-c[Asp-Ala-His-dNal(2')-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 274);

Ac-dArg-c[Asp-Ala-His-dNal(2')-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 275);

Ac-dLeu-c[dPen-Pro-dNal(2')-Arg-Trp-dPen]-dVal-dPro-$NH_2$ (SEQ ID NO: 327);

Ac-dNle-c[dPen-Pro-dNal(2')-Arg-Trp-dPen]-dVal-dPro-$NH_2$ (SEQ ID NO: 328);

Ac-dArg-c[dPen-Pro-dNal(2')-Arg-Trp-dPen]-dVal-dPro-$NH_2$ (SEQ ID NO: 329);

Ac-Arg-c[dPen-Pro-dNal(2')-Arg-Trp-dPen]-dVal-dPro-$NH_2$ (SEQ ID NO: 330);

Ac-dPhe-c[dPen-Pro-dNal(2')-Arg-Trp-dPen]-dVal-dPro-$NH_2$ (SEQ ID NO: 331);

Ac-dTyr-c[dPen-Pro-dNal(2')-Arg-Trp-dPen]-dVal-dPro-$NH_2$ (SEQ ID NO: 332);

Ac-Ala-c[dPen-Pro-dNal(2')-Arg-Trp-dPen]-dVal-dPro-$NH_2$ (SEQ ID NO: 333);

Ac-dHis-c[dPen-Pro-dNal(2')-Arg-Trp-dPen]-dVal-dPro-$NH_2$ (SEQ ID NO: 334);

Ac-His-c[dPen-Pro-dNal(2')-Arg-Trp-dPen]-dVal-dPro-$NH_2$ (SEQ ID NO: 335);

Ac-dLys-c[dPen-Pro-dNal(2')-Arg-Trp-dPen]-dVal-dPro-$NH_2$ (SEQ ID NO: 336);

Ac-Lys-c[dPen-Pro-dNal(2')-Arg-Trp-dPen]-dVal-dPro-$NH_2$ (SEQ ID NO: 337);

Ac-Nle-c[dPen-Pro-dNal(2')-Arg-Trp-dPen]-dArg-dVal-dPro-$NH_2$ (SEQ ID NO: 344);

Ac-Nle-c[dPen-Pro-dNal(2')-Arg-Trp-dPen]-dLys-dVal-dPro-$NH_2$ (SEQ ID NO: 345);

Ac-Nle-c[dPen-Pro-dNal(2')-Arg-Trp-dPen]-dArg-dPro-$NH_2$ (SEQ ID NO: 346);

Ac-Nle-c[dPen-Pro-dNal(2')-Arg-Trp-dPen]-dLys-dPro-$NH_2$ (SEQ ID NO: 347);

Ac-Nle-c[dPen-Pro-dNal(2')-Arg-Trp-dPen]-dVal-dHyp-$NH_2$ (SEQ ID NO: 348);

Ac-Nle-c[dPen-Pro-dNal(2')-Arg-Trp-dPen]-dTle-dPro-$NH_2$ (SEQ ID NO: 349);

Ac-Nle-c[dPen-Pro-dNal(2')-Arg-Trp-Gly-dPen]-dVal-dPro-$NH_2$ (SEQ ID NO: 350);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Aia-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 103);

Ac-Nle-c[Asp-Ioc-dNal(2')-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 243);

Ac-Nle-c[Cys-dNal(2')-Arg-Trp-Cys]-dVal-dPro-$NH_2$ (SEQ ID NO: 44);

Ac-Nle-c[dCys-dNal(2')-Arg-Trp-Cys]-dVal-dPro-$NH_2$ (SEQ ID NO: 45);

Ac-Nle-c[Cys-dNal(2')-Arg-Trp-dCys]-dVal-dPro-$NH_2$ (SEQ ID NO: 46);

Ac-Nle-c[dCys-dNal(2')-Arg-Trp-dCys]-dVal-dPro-$NH_2$ (SEQ ID NO: 47);

Ac-Nle-c[Cys-dNal(2')-Arg-Trp-Pen]-dVal-dPro-$NH_2$ (SEQ ID NO: 56);

Ac-Nle-c[dPen-dNal(2')-Arg-Trp-dPen]-dVal-dPro-$NH_2$ (SEQ ID NO: 62);

Ac-Nle-c[Asp-dTrp-dNal(2')-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 83);

Ac-Nle-c[dPen-Ala-dNal(2')-Arg-Trp-dPen]-dVal-dPro-$NH_2$ (SEQ ID NO: 338);

Ac-Nle-c[dPen-Leu-dNal(2')-Arg-Trp-dPen]-dVal-dPro-$NH_2$ (SEQ ID NO: 339);

Ac-Nle-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 223);

Ac-Arg-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 464);

Ac-Lys-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 465);

Ac-dLys-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 466);

Ac-His-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 467);

Ac-dHis-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 468);

Ac-Nle-Nle-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 469);

Ac-Nle-c[Asp-His-p(F)dPhe-His-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 470);

Ac-Nle-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dVal-dVal-dVal-dPro-$NH_2$ (SEQ ID NO: 474);

Ac-Nle-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dPro-dVal-dPro-$NH_2$ (SEQ ID NO: 475);

Ac-Nle-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dTle-dPro-$NH_2$ (SEQ ID NO: 476);

Ac-Nle-Nle-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dTle-dPro-$NH_2$ (SEQ ID NO: 477);

Ac-Nle-Nle-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dPro-dVal-dPro-$NH_2$ (SEQ ID NO: 478);

Ac-Arg-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dTle-dPro-$NH_2$ (SEQ ID NO: 481);

Ac-Lys-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dTle-dPro-$NH_2$ (SEQ ID NO: 482);

Ac-dLys-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dTle-dPro-$NH_2$ (SEQ ID NO: 483);

Ac-His-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dTle-dPro-$NH_2$ (SEQ ID NO: 484);

Ac-dHis-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dTle-dPro-$NH_2$ (SEQ ID NO: 485);

Ac-dArg-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 463);

Ac-Ala-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 462);

Ac-Ala-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dTle-dPro-$NH_2$ (SEQ ID NO: 479);

Ac-Nle-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dTle-dTle-dVal-$NH_2$ (SEQ ID NO: 473);

Ac-dArg-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dTle-dPro-$NH_2$ (SEQ ID NO: 480);

Ac-Nle-c[Asp-Gln-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 491);

Ac-Nle-c[Asp-Bip-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 489);

Ac-Nle-c[Asp-Trp-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 493);

Ac-Nle-c[Asp-Pro-p(F)dPhe-Arg-dNal(2')-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 444);

Ac-Nle-c[Asp-Pro-p(F)dPhe-Arg-Nal(2')-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 445);

Ac-Nle-c[Asp-Tyr-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 495);

Ac-Nle-c[Asp-Phe-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 487);

Ac-Nle-c[Asp-dPhe-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 488);

Ac-Nle-c[Asp-dTrp-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 494);

Ac-Nle-c[Asp-His-p(F)dPhe-Arg-dNal(2')-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 471);

Ac-Nle-c[Cys-Pro-p(F)dPhe-Arg-Trp-Cys]-dVal-dPro-$NH_2$ (SEQ ID NO: 432);

Ac-Nle-c[Asp-Pro-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 217);

Ac-Nle-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 222);

Ac-Nle-c[Cys-His-p(Br)dPhe-Arg-Trp-Cys]-dVal-dPro-$NH_2$ (SEQ ID NO: 535);

Ac-Ala-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 538);

Ac-Nle-Nle-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 545);

Ac-Nle-c[Asp-His-p(Br)dPhe-His-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 546);

Ac-Nle-c[Asp-His-p(Br)dPhe-Arg-dNal(2')-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 547);

Ac-Nle-c[Asp-His-p(Br)dPhe-Arg-Nal(2')-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 548);

Ac-Nle-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dTle-dTle-dVal-$NH_2$ (SEQ ID NO: 549);

Ac-Nle-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dPro-dVal-dPro-$NH_2$ (SEQ ID NO: 551);

Ac-Nle-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dTle-dPro-$NH_2$ (SEQ ID NO: 552);

Ac-Nle-Nle-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dTle-dPro-$NH_2$ (SEQ ID NO: 553);

Ac-Ala-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dTle-dPro-$NH_2$ (SEQ ID NO: 555);

Ac-Nle-c[Asp-dHis-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 562);

Ac-Nle-c[Asp-Phe-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 563);

Ac-Nle-c[Asp-dPhe-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 564);

Ac-Nle-c[Asp-Bip-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 565);

Ac-Nle-c[Asp-dGln-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 568);

Ac-Nle-c[Asp-Trp-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 569);

Ac-Nle-c[Asp-dTrp-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 570);

Ac-Nle-c[Asp-Tyr-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 571);

Ac-Nle-c[Asp-dTyr-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 572);

Ac-dArg-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 539);

Ac-dHis-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 544);

Ac-dHis-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dTle-dPro-$NH_2$ (SEQ ID NO: 561);

Ac-dArg-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dTle-dPro-$NH_2$ (SEQ ID NO: 556);

Ac-dLys-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 542);

Ac-His-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dTle-dPro-$NH_2$ (SEQ ID NO: 560);

Ac-His-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 543);

Ac-dLys-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dTle-dPro-$NH_2$ (SEQ ID NO: 559);

Ac-Arg-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dTle-dPro-$NH_2$ (SEQ ID NO: 557);

Ac-Lys-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 541);

Ac-Nle-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dVal-dVal-dVal-dPro-$NH_2$ (SEQ ID NO: 550);

Ac-Lys-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dTle-dPro-$NH_2$ (SEQ ID NO: 558);

Ac-Arg-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 540);

Ac-Nle-Nle-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dPro-dVal-dPro-$NH_2$ (SEQ ID NO: 554);

Ac-Nle-c[Asp-His-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 363);

Ac-Nle-c[Asp-His-dPhe-Arg-Trp-Pro-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 418);

Ac-Nle-c[Asp-His-dPhe-Arg-Trp-Lys]-dPro-dVal-$NH_2$ (SEQ ID NO: 621);

Ac-Nle-c[Asp-His-dPhe-transPro(guan)-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 228);

Ac-Nle-c[Asp-His-dPhe-cisPro(guan)-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 229);

Ac-Nle-c[Asp-Ala-His-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 380);

Ac-Nle-c[Asp-Trp-Pro-dPhe-His-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 398);

Ac-Nle-c[Asp-Trp-Pro-dPhe-Arg-Phe-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 401);

Ac-Nle-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dPro-dVal-dPro-$NH_2$ (SEQ ID NO: 639);

Ac-Nle-c[Asp-Pro-dPhe-Arg-dNal(2')-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 430);

Ac-Nle-c[Asp-Pro-dPhe-Arg-Nal(2')-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 431);

Ac-Nle-c[Asp-Pro-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 225);

Ac-Nle-c[dPen-dPhe-Arg-Trp-dPen]-dVal-dPro-$NH_2$ (SEQ ID NO: 326);

Ac-Nle-c[Asp-Pro-His-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 297);

Ac-Nle-c[Asp-Pro-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 215);

Ac-Nle-c[Asp-Phe-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 525);

Ac-Nle-c[Asp-dPhe-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 526);

Ac-Nle-c[Asp-Bip-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 527);

Ac-Nle-c[Asp-Trp-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 531);

Ac-Nle-c[Asp-Tyr-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 533);

Ac-Nle-c[Asp-dTyr-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 534);

Ac-Nle-c[Asp-dTrp-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 532);

Ac-Nle-c[dCys-His-p(Cl)dPhe-Arg-Trp-Cys]-dVal-dPro-$NH_2$ (SEQ ID NO: 498);

Ac-Nle-c[Cys-His-p(Cl)dPhe-Arg-Trp-Cys]-dVal-dPro-$NH_2$ (SEQ ID NO: 497);

Ac-Nle-c[Asp-His-p(Cl)dPhe-Arg-dNal(2')-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 509);

Ac-Nle-c[Asp-His-p(Cl)dPhe-Arg-Nal(2')-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 510);

Ac-Nle-c[Asp-His-p(Cl)dPhe-His-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 508);

Ac-Nle-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 220);

Ac-Nle-Nle-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 507);

Ac-Ala-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dTle-dPro-$NH_2$ (SEQ ID NO: 517);

Ac-Ala-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 500);

Ac-Nle-Nle-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dPro-dVal-dPro-$NH_2$ (SEQ ID NO: 516);

Ac-Nle-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dTle-dPro-$NH_2$ (SEQ ID NO: 514);

Ac-Nle-c[Asp-dGln-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 530);

Ac-Arg-c[Asp-dAla-His-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 268);

Ac-Nle-c[Asp-dAla-His-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 378);

Ac-dArg-c[Asp-dAla-His-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 379);

Ac-Nle-c[Asp-dAla-His-dNal(2')-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 266);

Ac-Arg-c[Asp-dAla-His-dNal(2')-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 267);

Ac-Arg-c[Cys-dAla-His-dNal(2')-Arg-Trp-Cys]-dVal-dPro-$NH_2$ (SEQ ID NO: 269);

Ac-dArg-c[Asp-dAla-His-dNal(2')-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 270);

Ac-Arg-c[Cys-dAla-His-dNal(2')-Arg-Trp-Cys]-$NH_2$ (SEQ ID NO: 282); and

Ac-Arg-c[Asp-dAla-His-dNal(2')-Arg-Trp-Lys]-$NH_2$ (SEQ ID NO: 283).

**[0881]** 51. The method or use of any one of embodiments 1-49, wherein the non-naturally occurring melanocortin analog comprises a sequence according to Formula (IA):

$X^1$-$X^2$-$X^3$-$R^1$-$R^2$-$R^3$-$R^4$-$R^5$-$R^6$-$R^7$-$R^8$-$Y^1$-$Y^2$-$Y^3$-$Y^4$ (IA),

wherein:

$X^1$ is absent or is selected from the group consisting of norleucine (Nle), arginine (Arg), D-arginine (dArg), alanine (Ala), lysine (Lys), D-lysine (dLys), histidine (His), D-histidine (dHis);

$X^2$ is absent, phenylalanine (Phe), or Nle;

$X^3$ is absent, Phe, or Nle;

$R^1$ is selected from the group consisting of Nle, D-norleucine (dNle), Ala, D-alanine (dAla), Arg, dArg, Lys, dLys, His, dHis, ornithine (Orn), D-ornithine (dOrn), D-leucine (dLeu), D-tyrosine (dTyr), phenylalanine (Phe), D-phenylalanine (dPhe), tryptophan (Trp), D-tryptophan (dTrp), aspartic acid (Asp), cysteine (Cys), and D-cysteine (dCys);

$R^2$ is selected from the group consisting of Asp, D-aspartic acid (dAsp), Cys, dCys, D-penicillamine (dPen), Ala, Trp, Phe, dPhe, His, dHis, Tyr, and dTyr;

$R^3$ is absent or is selected from the group consisting of His, Ala, proline (Pro), hydroxyproline (Hyp), leucine (Leu), D-glutamine (dGln), Phe, dPhe, Trp, dTrp, Tyr, dTyr, 2-aminotetraline-2-carboxylic acid (Atc), octohydroindole-2-carboxylic acid (Oic), 1-amino-1-cyclohexanecarboxylic acid (Che), tetrahydro-isoquinoline-3-carboxylic acid (Tic), 1-amino-1-cyclopentane carboxylic (Cpe), and biphenylalanine (Bip);

$R^4$ is selected from the group consisting of dPhe, para-chloro-D-phenylalanine (p(Cl)dPhe), para-bromo-D-phenylalanine (p(Br)dPhe), and para-fluoro-D-phenylalanine (p(F)dPhe);

$R^5$ is Arg or His;

$R^6$ is selected from the group consisting of Trp, dTrp, Phe, dNal(2'), 2'-naphthylalanine (Nal(2')), and 1'-naphthylalanine (Nal(1'));

$R^7$ is selected from the group consisting of Gly, Pro, Lys, dLys, Cys, dCys, penicillamine (Pen), dPen, and Orn;

$R^8$ is absent or Lys;

$Y^1$ is selected from the group consisting of valine (Val), D-valine (dVal), $b^2$-valine ($b^2$-Val), $b^3$-valine ($b^3$-Val), Pro, D-proline (dPro), b-proline (b-Pro), Hyp, D-hydroxyproline (dHyp), D-tert-leucine (dTle), dLeu, Trp, Arg, dArg, Lys, dLys, Gly, Ala, dAla, Asp, dAsp, asparagine (Asn), D-asparagine (dAsn), and D-threonine (dThr);

$Y^2$ is absent or is selected from the group consisting of Val, dVal, $b^2$-Val, $b^3$-Val, Pro, dPro, b-Pro, Hyp, dHyp, dTle, Arg, dArg, Gly, Ala, dAla, Asp, and dAsn;

$Y^3$ is absent or is selected from the group consisting of Val, dVal, Pro, dPro, dThr, Lys, and dLys;

$Y^4$ is absent or is selected from the group consisting of dVal, dPro, Asp, and dAsp; and

the non-naturally occurring melanocortin analog is cyclized through a moiety selected from the group consisting of:

a disulfide bond between $R^1$ or $R^2$ and $R^7$ or $R^8$ when each of $R^1$ or $R^2$ and $R^7$ or $R^8$ are independently selected from the group consisting of Cys, dCys, and dPen;

a disulfide bond between $R^2$ and $R^7$ when $R^2$ is Cys,$R^7$ is Pen, and $R^3$ is absent;

a lactam bridge between $R^1$ or $R^2$ and $R^7$ or $R^8$ when $R^1$ or $R^2$ is Asp and $R^7$ or $R^8$ is Lys or Orn; and

a lactam bridge between $R^2$ and $R^7$ when $R^2$ is dAsp and $R^7$ is dLys;

provided that:

when $R^4$ is p(F)dPhe, then (i) $R^3$ is selected from Pro, dGln, dTyr, $R^6$ is Trp, and the non-naturally occurring melanocortin analog is not cyclized between Cys at $R^2$ and Cys at $R^7$ or (ii) $R^3$ is His and either $R^6$ is Nal(2') or the non-naturally occurring melanocortin analog is cyclized through a disulfide bond between $R^2$ and $R^7$, where $R^2$ and $R^7$ are the same;

when $R^4$ is p(Br)dPhe, then the non-naturally occurring melanocortin analog is cyclized through a disulfide bond between dCys at $R^2$ and Cys or dCys at $R^7$;

when $R^4$ is dPhe, then (i) $R^3$ is not His, Pro, or absent, (ii) $R^3$ is His and either $R^2$ is Phe or dAla or $R^2$ is Ala and $X^1$ is Arg or dArg, (iii) $R^3$ is Pro and (a) $R^2$ is Trp, and $R^5$ is not His or

$R^6$ is not Phe or (b) $R^2$ is not Trp or Pro, and either $R^5$ is not dNal(2') or Nal(2') or $X^1$ and $Y^3$ are not both present, or (iv) $R^3$ is absent and $R^2$ and $R^7$ are not both dPen; and

when $R^4$ is p(Cl)dPhe, then (i) $R^3$ is selected from Aba, Aia, and Ata or (ii) $R^3$ is His, $R^1$ is not Ala, and (a) if $R^1$ is Nle and $Y^1Y^2$ is dVal-dPro, then $X^1$ is absent and the non-naturally occurring melanocortin analog is cyclized through a disulfide bond between dCys at $R^2$ and dCys at $R^7$, or (b) if $R^1$ is Nle, and $Y^1Y^2$ is not dVal-dPro, then either $X^1$ or $Y^3$ is present.

**[0882]** 52. The method or the use of any one of embodiments 1-50, wherein the non-naturally occurring melanocortin analog comprises a sequence according to Formula (IA), wherein:

$X^1$ is absent or is selected from the group consisting of norleucine (Nle), arginine (Arg), D-arginine (dArg), alanine (Ala), lysine (Lys), D-lysine (dLys), histidine (His), D-histidine (dHis);

$X^2$ is absent, phenylalanine (Phe), or Nle;

$X^3$ is absent, Phe, or Nle;

$R^1$ is selected from the group consisting of Nle, D-norleucine (dNle), Ala, D-alanine (dAla), Arg, dArg, Lys, dLys, His, dHis, ornithine (Orn), D-ornithine (dOrn), D-leucine (dLeu), D-tyrosine (dTyr), phenylalanine (Phe), D-phenylalanine (dPhe), tryptophan (Trp), D-tryptophan (dTrp), aspartic acid (Asp), cysteine (Cys), and D-cysteine (dCys);

$R^2$ is selected from the group consisting of Asp, D-aspartic acid (dAsp), Cys, dCys, D-penicillamine (dPen), Ala, Trp, Phe, dPhe, His, dHis, Tyr, and dTyr;

$R^3$ is absent or is selected from the group consisting of His, Ala, proline (Pro), hydroxyproline (Hyp), leucine (Leu), D-glutamine (dGln), Phe, dPhe, Trp, dTrp, Tyr, dTyr, 2-aminotetraline-2-carboxylic acid (Atc), octohydroindole-2-carboxylic acid (Oic), 1-amino-1-cyclohexanecarboxylic acid (Che), tetrahydro-isoquinoline-3-carboxylic acid (Tic), 1-amino-1-cyclopentane carboxylic (Cpe), and biphenylalanine (Bip);

$R^4$ is selected from the group consisting of dPhe, para-chloro-D-phenylalanine (p(Cl)dPhe), para-bromo-D-phenylalanine (p(Br)dPhe), and para-fluoro-D-phenylalanine (p(F)dPhe);

$R^5$ is Arg or His;

$R^6$ is selected from the group consisting of Trp, dTrp, Phe, dNal(2'), 2'-naphthylalanine (Nal(2')), and 1'-naphthylalanine (Nal(1'));

$R^7$ is selected from the group consisting of Gly, Pro, Lys, dLys, Cys, dCys, penicillamine (Pen), dPen, and Orn;

$R^8$ is absent or Lys;

$Y^1$ is selected from the group consisting of valine (Val), D-valine (dVal), $b^2$-valine ($b^2$-Val), $b^3$-valine ($b^3$-Val), Pro, D-proline (dPro), b-proline (b-Pro), Hyp, D-hydroxyproline (dHyp), D-tert-leucine (dTle), dLeu, Trp, Arg, dArg, Lys, dLys, Gly, Ala, dAla, Asp, dAsp, asparagine (Asn), D-asparagine (dAsn), and D-threonine (dThr);

$Y^2$ is absent or is selected from the group consisting of Val, dVal, $b^2$-Val, $b^3$-Val, Pro, dPro, b-Pro, Hyp, dHyp, dTle, Arg, dArg, Gly, Ala, dAla, Asp, and dAsn;

$Y^3$ is absent or is selected from the group consisting of Val, dVal, Pro, dPro, dThr, Lys, and dLys;

$Y^4$ is absent or is selected from the group consisting of dVal, dPro, Asp, and dAsp; and

the non-naturally occurring melanocortin analog is cyclized through a moiety selected from the group consisting of:

a disulfide bond between $R^1$ or $R^2$ and $R^7$ or $R^8$ when each of $R^1$ or $R^2$ and $R^7$ or $R^8$ are independently selected from the group consisting of Cys, dCys, and dPen;

a disulfide bond between $R^2$ and $R^7$ when $R^2$ is Cys, $R^7$ is Pen, and $R^3$ is absent;

a lactam bridge between $R^1$ or $R^2$ and $R^7$ or $R^8$ when $R^1$ or $R^2$ is Asp and $R^7$ or $R^8$ is Lys or Orn; and

a lactam bridge between $R^2$ and $R^7$ when $R^2$ is dAsp and $R^7$ is dLys;

provided that the non-naturally occurring melanocortin analog does not comprise a sequence selected from the group consisting of:

Ac-Nle-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 223);

Ac-Arg-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 464);

Ac-Lys-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 465);

Ac-dLys-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 466);

Ac-His-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 467);

Ac-dHis-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 468);

Ac-Nle-Nle-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 469);

Ac-Nle-c[Asp-His-p(F)dPhe-His-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 470);

Ac-Nle-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dVal-dVal-dVal-dPro-$NH_2$ (SEQ ID NO: 474);

Ac-Nle-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dPro-dVal-dPro-$NH_2$ (SEQ ID NO: 475);

Ac-Nle-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dTle-dPro-$NH_2$ (SEQ ID NO: 476);

Ac-Nle-Nle-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dTle-dPro-$NH_2$ (SEQ ID NO: 477);

Ac-Nle-Nle-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dPro-dVal-dPro-$NH_2$ (SEQ ID NO: 478);

Ac-Arg-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dTle-dPro-$NH_2$ (SEQ ID NO: 481);

Ac-Lys-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dTle-dPro-$NH_2$ (SEQ ID NO: 482);

Ac-dLys-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dTle-dPro-$NH_2$ (SEQ ID NO: 483);

Ac-His-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dTle-dPro-$NH_2$ (SEQ ID NO: 484);

Ac-dHis-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dTle-dPro-$NH_2$ (SEQ ID NO: 485);

Ac-dArg-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 463);

Ac-Ala-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 462);

Ac-Ala-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dTle-dPro-$NH_2$ (SEQ ID NO: 479);

Ac-Nle-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dTle-dTle-dVal-$NH_2$ (SEQ ID NO: 473);

Ac-dArg-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dTle-dPro-$NH_2$ (SEQ ID NO: 480);

Ac-Nle-c[Asp-Bip-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 489);

Ac-Nle-c[Asp-Trp-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 493);

Ac-Nle-c[Asp-Pro-p(F)dPhe-Arg-dNal(2')-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 444);

Ac-Nle-c[Asp-Pro-p(F)dPhe-Arg-Nal(2')-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 445);

Ac-Nle-c[Asp-Tyr-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 495);

Ac-Nle-c[Asp-Phe-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 487);

Ac-Nle-c[Asp-dPhe-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 488);

Ac-Nle-c[Asp-dTrp-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 494);

Ac-Nle-c[Asp-His-p(F)dPhe-Arg-dNal(2')-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 471);

Ac-Nle-c[Cys-Pro-p(F)dPhe-Arg-Trp-Cys]-dVal-dPro-$NH_2$ (SEQ ID NO: 432);

Ac-Nle-c[dCys-His-p(F)dPhe-Arg-Trp-Cys]-dVal-dPro-$NH_2$ (SEQ ID NO: 460);

Ac-Nle-c[Asp-Pro-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 217);

Ac-Nle-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 222);

Ac-Nle-c[Cys-His-p(Br)dPhe-Arg-Trp-Cys]-dVal-dPro-$NH_2$ (SEQ ID NO: 535);

Ac-Ala-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 538);

Ac-Nle-Nle-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 545);

Ac-Nle-c[Asp-His-p(Br)dPhe-His-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 546);

Ac-Nle-c[Asp-His-p(Br)dPhe-Arg-dNal(2')-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 547);

Ac-Nle-c[Asp-His-p(Br)dPhe-Arg-Nal(2')-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 548);

Ac-Nle-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dTle-dTle-dVal-$NH_2$ (SEQ ID NO: 549);

Ac-Nle-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dPro-dVal-dPro-$NH_2$ (SEQ ID NO: 551);

Ac-Nle-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dTle-dPro-$NH_2$ (SEQ ID NO: 552);

Ac-Nle-Nle-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dTle-dPro-$NH_2$ (SEQ ID NO: 553);

Ac-Ala-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dTle-dPro-$NH_2$ (SEQ ID NO: 555);

Ac-Nle-c[Asp-Phe-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 563);

Ac-Nle-c[Asp-dPhe-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 564);

Ac-Nle-c[Asp-Bip-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 565);

Ac-Nle-c[Asp-dGln-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 568);

Ac-Nle-c[Asp-Trp-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 569);

Ac-Nle-c[Asp-dTrp-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 570);

Ac-Nle-c[Asp-Tyr-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 571);

Ac-Nle-c[Asp-dTyr-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 572);

Ac-dArg-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 539);

Ac-dHis-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 544);

Ac-dHis-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dTle-dPro-$NH_2$ (SEQ ID NO: 561);

Ac-dArg-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dTle-dPro-$NH_2$ (SEQ ID NO: 556);

Ac-dLys-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 542);

Ac-His-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dTle-dPro-$NH_2$ (SEQ ID NO: 560);

Ac-His-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 543);

Ac-dLys-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dTle-dPro-$NH_2$ (SEQ ID NO: 559);

Ac-Arg-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dTle-dPro-$NH_2$ (SEQ ID NO: 557);

Ac-Lys-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 541);

Ac-Nle-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dVal-dVal-dVal-dPro-$NH_2$ (SEQ ID NO: 550);

Ac-Lys-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dTle-dPro-$NH_2$ (SEQ ID NO: 558);

Ac-Arg-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 540);

Ac-Nle-Nle-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dPro-dVal-dPro-$NH_2$ (SEQ ID NO: 554);

Ac-Nle-c[Asp-His-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 363);

Ac-Nle-c[Asp-His-dPhe-Arg-Trp-Pro-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 418);

Ac-Nle-c[Asp-His-dPhe-Arg-Trp-Lys]-dPro-dVal-$NH_2$ (SEQ ID NO: 621);

Ac-Nle-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dPro-dVal-dPro-$NH_2$ (SEQ ID NO: 639);

Ac-Nle-c[dPen-dPhe-Arg-Trp-dPen]-dVal-dPro-$NH_2$ (SEQ ID NO: 326);

Ac-Nle-c[Asp-Trp-Pro-dPhe-His-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 398);

Ac-Nle-c[Asp-Trp-Pro-dPhe-Arg-Phe-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 401);

Ac-Nle-c[Asp-Pro-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 225);

Ac-Nle-c[Asp-Pro-dPhe-Arg-dNal(2')-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 430);

Ac-Nle-c[Asp-Pro-dPhe-Arg-Nal(2')-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 431);

Ac-Nle-c[Asp-Ala-His-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 380);

Ac-Nle-c[Asp-Pro-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 215);

Ac-Nle-c[Asp-Phe-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 525);

Ac-Nle-c[Asp-dPhe-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 526);

Ac-Nle-c[Asp-Bip-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 527);

Ac-Nle-c[Asp-Trp-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 531);

Ac-Nle-c[Asp-Tyr-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 533);

Ac-Nle-c[Asp-dTyr-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 534);

Ac-Nle-c[Asp-dTrp-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 532);

Ac-Nle-c[dCys-His-p(Cl)dPhe-Arg-Trp-Cys]-dVal-dPro-$NH_2$ (SEQ ID NO: 498);

Ac-Nle-c[Cys-His-p(Cl)dPhe-Arg-Trp-Cys]-dVal-dPro-$NH_2$ (SEQ ID NO: 497);

Ac-Nle-c[Asp-His-p(Cl)dPhe-Arg-dNal(2')-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 509);

Ac-Nle-c[Asp-His-p(Cl)dPhe-Arg-Nal(2')-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 510);

Ac-Nle-c[Asp-His-p(Cl)dPhe-His-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 508);

Ac-Nle-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 220);

Ac-Nle-Nle-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 507);

Ac-Ala-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dTle-dPro-$NH_2$ (SEQ ID NO: 517);

Ac-Ala-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 500);

Ac-Nle-Nle-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dPro-dVal-dPro-$NH_2$ (SEQ ID NO: 516); and

Ac-Nle-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dTle-dPro-$NH_2$ (SEQ ID NO: 514).

**[0883]** 53. The method or use of any one of embodiments 1-49, wherein the non-naturally occurring melanocortin analog comprises a sequence of Formula (IB):

$X^1$-$X^2$-$X^3$-$R^1$-$R^2$-Pro-$R^4$-$R^5$-$R^6$-$R^7$-$R^8$-$Y^1$-$Y^2$-$Y^3$-$Y^4$-$Y^5$-$Y^6$-$Y^7$ (IB),

wherein:

$X^1$ is absent or norleucine (Nle);

$X^2$ is absent or Nle;

$X^3$ is absent or Nle;

$R^1$ is selected from the group consisting of Nle, D-norleucine (dNle), alanine (Ala), D-alanine (dAla), arginine (Arg), D-arginine (dArg), lysine (Lys), D-lysine (dLys), histidine (His), D-histidine (dHis), ornithine (Orn), D-ornithine (dOrn), D-leucine (dLeu), D-tyrosine (dTyr), phenylalanine (Phe), D-phenylalanine (dPhe), tryptophan (Trp), and D-tryptophan (dTrp);

$R^2$ is selected from the group consisting of aspartic acid (Asp), D-aspartic acid (dAsp), cysteine (Cys), D-cysteine (dCys), and D-penicillamine (dPen);

$R^4$ is dPhe or para-fluoro-D-phenylalanine (p(F)dPhe);

$R^5$ is selected from the group consisting of Arg, His, *cis*Pro(guan), and *trans*Pro(guan);

$R^6$ is selected from the group consisting of Trp, dTrp, Phe, Aia, Aba, Ata, and 1'-naphthylalanine (Nal(1'));

$R^7$ is selected from the group consisting of Gly, Lys, dLys, Cys, dCys, dPen, and Orn;

$R^8$ is absent or Lys;

$Y^1$ is absent or is selected from the group consisting of valine (Val), D-valine (dVal), $b^2$-valine ($b^2$-Val), $b^3$-valine ($b^3$-Val), Pro, D-proline (dPro), b-proline (b-Pro), Hyp, D-hydroxyproline (dHyp), D-tert-leucine (dTle), dLeu, Trp, Arg, dArg, Lys, dLys, Gly, Ala, dAla, Asp, dAsp, asparagine (Asn), D-asparagine (dAsn), and D-threonine (dThr);

$Y^2$ is absent or is selected from the group consisting of Val, dVal, $b^2$-Val, $b^3$-Val, Pro, dPro, b-Pro, Hyp, dHyp, dTle, Arg, dArg, Gly, Ala, dAla, Asp, and dAsn;

$Y^3$ is absent or is selected from the group consisting of Val, dVal, Pro, dPro, dThr, Lys, and dLys;

$Y^4$ is absent or is selected from the group consisting of dVal, dPro, Asp, and dAsp;

$Y^5$ is absent or dVal;

$Y^6$ is absent or dVal;

$Y^7$ is absent or dPro; and

the non-naturally occurring melanocortin analog is cyclized through a moiety selected from the group consisting of:

a disulfide bond between $R^2$ and $R^7$ when each of $R^2$ and $R^7$ are independently selected from the group consisting of Cys, dCys, and dPen; and

a lactam bridge between $R^2$ and $R^7$ when $R^2$ is Asp or dAsp and $R^7$ is Lys, dLys, or Orn;

provided that:

when $R^4$ is p(F)dPhe, then the non-naturally occurring melanocortin analog is not cyclized between Cys at $R^2$ and Cys at $R^7$; and

when $R^4$ is dPhe and one or more of $X^1$, $X^2$, and $X^3$ is present, then $Y^3$-$Y^7$ are absent.

**[0884]** 54. The method or use of any one of embodiments 1-50, wherein the non-naturally occurring melanocortin analog comprises a sequence of Formula (IB), wherein:

$X^1$-$X^2$-$X^3$-$R^1$-$R^2$-Pro-$R^4$-$R^5$-$R^6$-$R^7$-$R^8$-$Y^1$-$Y^2$-$Y^3$-$Y^4$-$Y^5$-$Y^6$-$Y^7$ (IB),

wherein:

$X^1$ is absent or norleucine (Nle);

$X^2$ is absent or Nle;

$X^3$ is absent or Nle;

$R^1$ is selected from the group consisting of Nle, D-norleucine (dNle), alanine (Ala), D-alanine (dAla), arginine (Arg), D-arginine (dArg), lysine (Lys), D-lysine (dLys), histidine (His), D-

histidine (dHis), ornithine (Orn), D-ornithine (dOrn), D-leucine (dLeu), D-tyrosine (dTyr), phenylalanine (Phe), D-phenylalanine (dPhe), tryptophan (Trp), and D-tryptophan (dTrp);

$R^2$ is selected from the group consisting of aspartic acid (Asp), D-aspartic acid (dAsp), cysteine (Cys), D-cysteine (dCys), and D-penicillamine (dPen);

$R^4$ is dPhe or para-fluoro-D-phenylalanine (p(F)dPhe);

$R^5$ is selected from the group consisting of Arg, His, *cis*Pro(guan), and *trans*Pro(guan);

$R^6$ is selected from the group consisting of Trp, dTrp, Phe, Aia, Aba, Ata, and 1'-naphthylalanine (Nal(1')));

$R^7$ is selected from the group consisting of Gly, Lys, dLys, Cys, dCys, dPen, and Orn;

$R^8$ is absent or Lys;

$Y^1$ is absent or is selected from the group consisting of valine (Val), D-valine (dVal), $b^2$-valine ($b^2$-Val), $b^3$-valine ($b^3$-Val), Pro, D-proline (dPro), b-proline (b-Pro), Hyp, D-hydroxyproline (dHyp), D-tert-leucine (dTle), dLeu, Trp, Arg, dArg, Lys, dLys, Gly, Ala, dAla, Asp, dAsp, asparagine (Asn), D-asparagine (dAsn), and D-threonine (dThr);

$Y^2$ is absent or is selected from the group consisting of Val, dVal, $b^2$-Val, $b^3$-Val, Pro, dPro, b-Pro, Hyp, dHyp, dTle, Arg, dArg, Gly, Ala, dAla, Asp, and dAsn;

$Y^3$ is absent or is selected from the group consisting of Val, dVal, Pro, dPro, dThr, Lys, and dLys;

$Y^4$ is absent or is selected from the group consisting of dVal, dPro, Asp, and dAsp;

$Y^5$ is absent or dVal;

$Y^6$ is absent or dVal;

$Y^7$ is absent or dPro; and

the non-naturally occurring melanocortin analog is cyclized through a moiety selected from the group consisting of:

a disulfide bond between $R^2$ and $R^7$ when each of $R^2$ and $R^7$ are independently selected from the group consisting of Cys, dCys, and dPen; and

a lactam bridge between $R^2$ and $R^7$ when $R^2$ is Asp or dAsp and $R^7$ is Lys, dLys, or Orn;

provided that the non-naturally occurring melanocortin analog does not comprise a sequence of:

Ac-Nle-c[Cys-Pro-p(F)dPhe-Arg-Trp-Cys]-dVal-dPro-$NH_2$ (SEQ ID NO: 432); or

Ac-Nle-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dPro-dVal-dPro-$NH_2$ (SEQ ID NO: 639).

**[0885]** 55. The method or use of any one of embodiments 1-49, wherein the non-naturally occurring melanocortin analog comprises a sequence of Formula (IC):

$X^1$-$X^2$-$R^1$-$R^2$-Pro-dPhe-$R^5$-$R^6$-$R^7$-$Y^1$-$Y^2$-$Y^3$-$Y^4$ (IC),

wherein:

$X^1$ is selected from the group consisting of norleucine (Nle), arginine (Arg), D-arginine (dArg), alanine (Ala), lysine (Lys), D-lysine (dLys), histidine (His), D-histidine (dHis);

$X^2$ is absent or Nle;

$R^1$ is selected from the group consisting of aspartic acid (Asp), cysteine (Cys), and D-cysteine (dCys);

$R^2$ is selected from the group consisting of tryptophan (Trp), phenylalanine (Phe), D-phenylalanine (dPhe), histidine (His), D-histidine (dHis), tyrosine (Tyr), and D-tyrosine (dTyr);

$R^5$ is Arg;

$R^6$ is selected from the group consisting of Trp, 2'-D-naphthylalanine (dNal(2')), 2'-naphthylalanine (Nal(2')), and 1'-naphthylalanine (Nal(1'));

$R^7$ is selected from the group consisting of Lys, Cys, and dCys;

$Y^1$ is absent or is selected from the group consisting of D-valine (dVal), D-tert-leucine (dTle), dArg, and dLys;

$Y^2$ is absent or is selected from the group consisting of dVal, dPro, and D-hydroxyproline (dHyp);

$Y^3$ is absent, dVal, or dPro;

$Y^4$ is absent or dPro; and

the non-naturally occurring melanocortin analog is cyclized through a moiety selected from the group consisting of:

a disulfide bond between $R^1$ and $R^7$ when both of $R^1$ and $R^7$ are independently selected from the group consisting of Cys, dCys, and dPen; and

a lactam bridge between $R^1$ and $R^7$ when $R^1$ is Asp and $R^7$ is Lys.

**[0886]** 56. The method or use of any one of embodiments 1-49, wherein the non-naturally occurring melanocortin analog comprises a sequence of Formula (ID):

$X^1$-$R^1$-$R^2$-$R^3$-p(Cl)dPhe-Arg-Trp-$R^7$-$Y^1$-$Y^2$-$Y^3$-$Y^4$ (ID),

wherein:

$X^1$ is absent or norleucine (Nle);

$R^1$ is selected from the group consisting of Nle, arginine (Arg), D-arginine (dArg), lysine (Lys), D-lysine (dLys), histidine (His), and D-histidine (dHis);

$R^2$ is aspartic acid (Asp) or D-cysteine (dCys);

$R^3$ is selected from the group consisting of His, 4-amino-1,2,4,5-tetrahydro-2-benzazepin-3-one (Aba), 7-amino-7,8-dihydro-4H-[1,2,3]triazolo-[1,5-a][1,4]diazepin-6(5H)-one (Ata), and 4-amino-1,4,5,6-tetrahydroazepino[4,3-*b*]indol-3(*2H*)-one (Aia);

$R^7$ is Lys or dCys;

$Y^1$ is selected from the group consisting of D-valine (dVal), D-proline (dPro), and D-tert-leucine (dTle);

$Y^2$ is absent or is selected from the group consisting of dVal, dPro, and dTle;

$Y^3$ is absent, dVal, or dPro;

$Y^4$ is absent or dPro; and

the non-naturally occurring melanocortin analog is cyclized through a moiety selected from the group consisting of:

a disulfide bond between $R^2$ and $R^7$ when both of $R^2$ and $R^7$ are dCys; and

a lactam bridge between $R^2$ and $R^7$ when $R^2$ is Asp and $R^7$ is Lys;

provided that when $R^3$ is His and $R^1$ is Nle, then (i) $Y^1Y^2$ is dVal-dPro, $X^1$ is absent, and the non-naturally occurring melanocortin analog is cyclized through a disulfide bond, or (b) $Y^1Y^2$ is not dVal-dPro and either $X^1$ or $Y^3$ is present.

**[0887]** 57. The method or use of any one of embodiments 1-49, wherein the non-naturally occurring melanocortin analog comprises a sequence of Formula (ID), wherein:

$X^1$ is absent or norleucine (Nle);

$R^1$ is selected from the group consisting of Nle, arginine (Arg), D-arginine (dArg), lysine (Lys), D-lysine (dLys), histidine (His), and D-histidine (dHis);

$R^2$ is aspartic acid (Asp) or D-cysteine (dCys);

$R^3$ is selected from the group consisting of His, 4-amino-1,2,4,5-tetrahydro-2-benzazepin-3-one (Aba), 7-amino-7,8-dihydro-4H-[1,2,3]triazolo-[1,5-a][1,4]diazepin-6(5H)-one (Ata), and 4-amino-1,4,5,6-tetrahydroazepino[4,3-*b*]indol-3(*2H*)-one (Aia);

$R^7$ is Lys or dCys;

$Y^1$ is selected from the group consisting of D-valine (dVal), D-proline (dPro), and D-tert-leucine (dTle);

$Y^2$ is absent or is selected from the group consisting of dVal, dPro, and dTle;

$Y^3$ is absent, dVal, or dPro;

$Y^4$ is absent or dPro; and

the non-naturally occurring melanocortin analog is cyclized through a moiety selected from the group consisting of:

a disulfide bond between $R^2$ and $R^7$ when both of $R^2$ and $R^7$ are dCys; and

a lactam bridge between $R^2$ and $R^7$ when $R^2$ is Asp and $R^7$ is Lys;

provided that the non-naturally occurring melanocortin analog does not comprise a sequence selected from the group consisting of:

Ac-Nle-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 220);

Ac-Nle-Nle-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 507);

Ac-Nle-Nle-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dPro-dVal-dPro-$NH_2$ (SEQ ID NO: 516);

Ac-Nle-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dTle-dPro-$NH_2$ (SEQ ID NO: 514); and.

**[0888]** 58. The method or the use of any one of embodiments 1-57, wherein an N-terminus of the non-naturally occurring melanocortin analog is modified by an acyl group.

**[0889]** 59. The method or the use of embodiment 58, wherein the acyl group is an acetyl group.

**[0890]** 60. The method or the use of any one of embodiments 1-57, wherein an N-terminus of the non-naturally occurring melanocortin analog is not modified.

**[0891]** 61. The method or the use of any one of embodiments 1-60, wherein a C-terminus of the non-naturally occurring melanocortin analog is modified by an amide group.

**[0892]** 62. The method or the use of any one of embodiments 1-60, wherein a C-terminus of the non-naturally occurring melanocortin analog is not modified.

**[0893]** 63. The method or the use of any one of embodiments 1-62, wherein $Y^1$-$Y^2$ are present and $Y^3$- $Y^8$ are absent.

**[0894]** 64. The method or the use of any one of embodiments 1-63, wherein $Y^1$ is D-valine and $Y^2$ is D-proline.

**[0895]** 65. The method or the use of any one of embodiments 1-63, w wherein $Y^1$ is D-tert-leucine and $Y^2$ is D-proline.

**[0896]** 66. The method or the use of any one of embodiments 1-65, wherein $R^4$ is dNal(2').

**[0897]** 67. The method or the use of embodiment 66, wherein the sequence of Formula (I) is: Ac-Nle-$_c$[Asp-His-dNal(2')-Arg-Trp-Pro-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 8), wherein c represents cyclization through $R^2$ and $R^8$ via a lactam bond.

**[0898]** 68. The method or the use of any one of embodiments 1-65, wherein $R^4$ is Phe or dPhe.

**[0899]** 69. The method or the use of embodiment 68, wherein the sequence of any one of Formulae (I)-(ID) is selected from the group consisting of:

Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-OH (SEQ ID NO: 291);

Ac-Nle-c[Asp-Pro-Phe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 294);

Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 295; E2); and

Ac-Nle-c[Asp-Pro-His-Phe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 296).

wherein c represents cyclization through $R^2$ and $R^7$ via a lactam bond.

**[0900]** 70. The method or the use of any one of embodiments 1-62, wherein the sequence of any one of Formulae (I)-(ID) is selected from the group consisting of:
Ac-dLeu-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO:298);
Ac-dAla-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 299);
Ac-Ala-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro- $NH_2$ (SEQ ID NO: 300);
Ac-dNle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 301);
Ac-dArg-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 302);
Ac-dPhe-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 303);
Ac-dTyr-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 304);
Phe-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 305);
His-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 306);
Trp-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 307);
dPhe-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 308);
dHis-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 309);
dTrp-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 310);
Ac-Arg-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 311);
Ac-dLys-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 312);
Ac-Lys-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 313);
Ac-His-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 314);
Ac-dHis-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 315);
Ac-Orn-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 316); and

Ac-dOrn-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 317),
wherein c represents cyclization through $R^2$ and $R^7$ via a lactam bond.

**[0901]** 71. The method or the use of any one of embodiments 1-62, wherein the sequence of any one of Formulae (I)-(ID) is selected from the group consisting of:

Ac-Nle-c[Cys-Pro-dPhe-Arg-Trp-Cys]-dVal-dPro-$NH_2$ (SEQ ID NO: 318);

Ac-Nle-c[dCys-Pro-dPhe-Arg-Trp-Cys]-dVal-dPro-$NH_2$ (SEQ ID NO: 319);

Ac-Nle-c[dPen-Pro-dPhe-Arg-Trp-dPen]-dVal-dPro-$NH_2$ (SEQ ID NO: 320);

Ac-Nle-c[dCys-Pro-dPhe-Arg-Trp-dCys]-dVal-dPro-$NH_2$ (SEQ ID NO: 321);

Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Orn]-dVal-dPro-$NH_2$ (SEQ ID NO: 322); and

Ac-Nle-c[Cys-dPhe-Arg-Trp-Pen]-dVal-dPro-$NH_2$ (SEQ ID NO: 324),

wherein c represents cyclization through $R^2$ and $R^7$ via a disulfide bond.

**[0902]** 72. The method or the use of any one of embodiments 1-62, wherein the sequence of any one of Formulae (I)-(ID) is selected from the group consisting of:

Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Gly-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 351);

Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Gly-Lys]-dPro-dPro-Lys-Asp-$NH_2$ (SEQ ID NO: 352); and

Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Gly-Lys]-dPro-dPro-dLys-dAsp-$NH_2$ (SEQ ID NO: 353),

wherein c represents cyclization through $R^2$ and $R^8$ via a lactam bond.

**[0903]** 73. The method or the use of any one of embodiments 1-62, wherein the sequence of any one of Formulae (I)-(ID) is selected from the group consisting of:

Ac-Nle-c[Asp-Ala-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 354);

Ac-Nle-c[Asp-Leu-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 355);

Ac-Nle-c[Asp-Cpe-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 358);

Ac-Nle-c[Asp-Che-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 359);

Ac-Nle-c[Asp-Oic-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 360);

Ac-Nle-c[Asp-Ioc-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 361);

Ac-Nle-c[Asp-Tic-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 362);

Ac-Nle-c[Asp-Hyp-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 364);

Ac-Nle-c[Asp-Phe-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 366);

Ac-Nle-c[Asp-dPhe-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 367);

Ac-Nle-c[Asp-Bip-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 368);

Ac-Nle-c[Asp-dGln-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 371);

Ac-Nle-c[Asp-Trp-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 372);

Ac-Nle-c[Asp-dTrp-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 373);

Ac-Nle-c[Asp-Tyr-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 374);

Ac-Nle-c[Asp-dTyr-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 375);

Ac-Nle-c[Asp-Aba-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 198);

Ac-Nle-c[Asp-Aia-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 207);

Ac-Nle-c[Asp-Ata-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 208);

Ac-Nle-c[Asp-Atc-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 212);

Ac-Nle-c[Asp-APC-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 213); and

Ac-Nle-c[Asp-APPC-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 214),

wherein c represents cyclization through $R^2$ and $R^7$ via a lactam bond.

**[0904]** 74. The method or the use of any one of embodiments 1-62, wherein the sequence of any one of Formulae (I)-(ID) is selected from the group consisting of:

Ac-Arg-c[Asp-dAla-His-dPhe-Arg-Trp-Lys]-$NH_2$ (SEQ ID NO: 281);

Ac-Arg-c[Asp-Ala-His-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 381); and

Ac-dArg-c[Asp-Ala-His-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 382),

wherein c represents cyclization through $R^1$ and $R^7$ via a lactam bond.

**[0905]** 75. The method or the use of any one of embodiments 1-62, wherein the sequence of any one of Formulae (I)-(ID) is selected from the group consisting of:

Ac-Nle-c[Asp-Trp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 226);

Ac-Nle-c[Cys-Trp-Pro-dPhe-Arg-Trp-Cys]-dVal-dPro-$NH_2$ (SEQ ID NO: 383);

Ac-Nle-c[dCys-Trp-Pro-dPhe-Arg-Trp-Cys]-dVal-dPro-$NH_2$ (SEQ ID NO: 384);

Ac-Nle-c[dCys-Trp-Pro-dPhe-Arg-Trp-dCys]-dVal-dPro-$NH_2$ (SEQ ID NO: 385);

Ac-Ala-c[Asp-Trp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 386);

Ac-Lys-c[Asp-Trp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 387);

Ac-dLys-c[Asp-Trp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 388);

Ac-Arg-c[Asp-Trp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 389);

Ac-dArg-c[Asp-Trp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 390);

Ac-dHis-c[Asp-Trp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 391);

Ac-His-c[Asp-Trp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 392);

Ac-Nle-Nle-c[Asp-Trp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 393);

Ac-Nle-c[Asp-Trp-Ala-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 394);

Ac-Nle-c[Asp-Trp-Leu-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 395);

Ac-Nle-c[Asp-Trp-Pro-dPhe-Arg-Nal(1']-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 399);

Ac-Nle-c[Asp-Trp-Pro-dPhe-Arg-dNal(2')-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 403);

Ac-Nle-c[Asp-Trp-Pro-dPhe-Arg-Nal(2')-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 404);

Ac-Nle-c[Asp-Trp-Pro-dPhe-Arg-Trp-Lys]-dArg-dVal-dPro-$NH_2$ (SEQ ID NO: 405);

Ac-Nle-c[Asp-Trp-Pro-dPhe-Arg-Trp-Lys]-dLys-dVal-dPro-$NH_2$ (SEQ ID NO: 406);

Ac-Nle-c[Asp-Trp-Pro-dPhe-Arg-Trp-Lys]-dArg-dPro-$NH_2$ (SEQ ID NO: 407);

Ac-Nle-c[Asp-Trp-Pro-dPhe-Arg-Trp-Lys]-dLys-dPro-$NH_2$ (SEQ ID NO: 408);

Ac-Nle-c[Asp-Trp-Pro-dPhe-Arg-Trp-Lys]-dVal-dHyp-$NH_2$ (SEQ ID NO: 409);

Ac-Nle-c[Asp-Trp-Pro-dPhe-Arg-Trp-Lys]-dTle-dPro-$NH_2$ (SEQ ID NO: 410);

Ac-Nle-c[Asp-Trp-Pro-dPhe-Arg-Trp-Lys]-dVal-dVal-dVal-dPro-$NH_2$ (SEQ ID NO: 411);

Ac-Nle-c[Asp-Phe-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 412);

Ac-Nle-c[Asp-His-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 413);

Ac-Nle-c[Asp-Tyr-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 414);

Ac-Nle-c[Asp-dPhe-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 415);

Ac-Nle-c[Asp-dHis-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 416); and

Ac-Nle-c[Asp-dTyr-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 417),

wherein c represents cyclization through $R^1$ and $R^7$ via a lactam bond or a disulfide bond.

**[0906]** 76. The method or the use of any one of embodiments 1-62, wherein the sequence of any one of Formulae (I)-(ID) is: Ac-Nle-c[Asp-Hyp-dPhe-Arg-Trp-Pro-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 419), wherein c represents cyclization through $R^2$ and $R^8$ via a lactam bond.

**[0907]** 77. The method or the use of any one of embodiments 1-62, wherein the sequence of any one of Formulae (I)-(ID) is selected from the group consisting of:

Ac-Nle-Phe-Phe-c[Asp-Phe-His-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 421);

Ac-Nle-c[Asp-Phe-His-dPhe-Arg-Trp-Lys]-dLeu-dPro-$NH_2$ (SEQ ID NO: 422);

Ac-Nle-c[Asp-Phe-His-dPhe-Arg-Trp-Lys]-dTle-dPro-$NH_2$ (SEQ ID NO: 423); and

Ac-Nle-c[Asp-Phe-His-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 424),

wherein c represents cyclization through $R^1$ and $R^7$ via a lactam bond.

**[0908]** 78. The method or the use of any one of embodiments 1-62, wherein the sequence of any one of Formulae (I)-(ID) is selected from the group consisting of:

Ac-Nle-c[Asp-Pro-dPhe-Arg-dTrp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 187);

Ac-Nle-c[Asp-Pro-dPhe-Arg-Aia-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 233);

Ac-Nle-c[Asp-Pro-dPhe-Arg-Aba-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 234);

Ac-Nle-c[Asp-Pro-dPhe-Arg-Ata-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 235);

Ac-Nle-c[Asp-Pro-dPhe-Arg-Nal(1')-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 427); and

Ac-Nle-c[Asp-Pro-dPhe-Arg-Phe-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 429),

wherein c represents cyclization through $R^2$ and $R^7$ via a lactam bond.

**[0909]** 79. The method or the use of any one of embodiments 1-62, wherein the sequence of any one of Formulae (I)-(ID) is selected from the group consisting of:

Ac-Nle-c[Asp-Pro-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 218);

Ac-Nle-c[dCys-Pro-p(F)dPhe-Arg-Trp-Cys]-dVal-dPro-$NH_2$ (SEQ ID NO: 433);

Ac-Nle-c[dCys-Pro-p(F)dPhe-Arg-Trp-dCys]-dVal-dPro-$NH_2$ (SEQ ID NO: 434);

Ac-Ala-c[Asp-Pro-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 435);

Ac-dArg-c[Asp-Pro-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 436);

Ac-Arg-c[Asp-Pro-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 437);

Ac-Lys-c[Asp-Pro-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 438);

Ac-dLys-c[Asp-Pro-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 439);

Ac-His-c[Asp-Pro-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 440);

Ac-dHis-c[Asp-Pro-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 441);

Ac-Nle-Nle-c[Asp-Pro-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 442);

Ac-Nle-c[Asp-Pro-p(F)dPhe-His-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 443);

Ac-Nle-c[Asp-Pro-p(F)dPhe-Arg-Trp-Lys]-dTle-dTle-dVal-$NH_2$ (SEQ ID NO: 446);

Ac-Nle-c[Asp-Pro-p(F)dPhe-Arg-Trp-Lys]-dVal-dVal-dVal-dPro-$NH_2$ (SEQ ID NO: 447);

Ac-Nle-c[Asp-Pro-p(F)dPhe-Arg-Trp-Lys]-dPro-dVal-dPro-$NH_2$ (SEQ ID NO: 448);

Ac-Nle-c[Asp-Pro-p(F)dPhe-Arg-Trp-Lys]-dTle-dPro-$NH_2$ (SEQ ID NO: 449);

Ac-Nle-Nle-c[Asp-Pro-p(F)dPhe-Arg-Trp-Lys]-dTle-dPro-$NH_2$ (SEQ ID NO: 450);

Ac-Nle-Nle-c[Asp-Pro-p(F)dPhe-Arg-Trp-Lys]-dPro-dVal-dPro-$NH_2$ (SEQ ID NO: 451);

Ac-Ala-c[Asp-Pro-p(F)dPhe-Arg-Trp-Lys]-dTle-dPro-$NH_2$ (SEQ ID NO: 452);

Ac-dArg-c[Asp-Pro-p(F)dPhe-Arg-Trp-Lys]-dTle-dPro-$NH_2$ (SEQ ID NO: 453);

Ac-Arg-c[Asp-Pro-p(F)dPhe-Arg-Trp-Lys]-dTle-dPro-$NH_2$ (SEQ ID NO: 454);

Ac-Lys-c[Asp-Pro-p(F)dPhe-Arg-Trp-Lys]-dTle-dPro-$NH_2$ (SEQ ID NO: 455);

Ac-dLys-c[Asp-Pro-p(F)dPhe-Arg-Trp-Lys]-dTle-dPro-$NH_2$ (SEQ ID NO: 456);

Ac-His-c[Asp-Pro-p(F)dPhe-Arg-Trp-Lys]-dTle-dPro-$NH_2$ (SEQ ID NO: 457);

Ac-dHis-c[Asp-Pro-p(F)dPhe-Arg-Trp-Lys]-dTle-dPro-$NH_2$ (SEQ ID NO: 458);

Ac-Nle-c[Cys-His-p(F)dPhe-Arg-Trp-Cys]-dVal-dPro-$NH_2$ (SEQ ID NO: 459);

Ac-Nle-c[dCys-His-p(F)dPhe-Arg-Trp-Cys]-dVal-dPro-$NH_2$ (SEQ ID NO: 460);

Ac-Nle-c[dCys-His-p(F)dPhe-Arg-Trp-dCys]-dVal-dPro-$NH_2$ (SEQ ID NO: 461);

Ac-Nle-c[Asp-His-p(F)dPhe-Arg-Nal(2')-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 472);

Ac-Nle-c[Asp-dGln-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 492); and

Ac-Nle-c[Asp-dTyr-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 496),

wherein c represents cyclization through $R^2$ and $R^7$ via a lactam bond or a disulfide bond.

**[0910]** 80. The method or the use of any one of embodiments 1-62, wherein the sequence of any one of Formulae (I)-(ID) is selected from the group consisting of:

Ac-Nle-c[Asp-Aba-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 209);

Ac-Nle-c[Asp-Aia-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 210);

Ac-Nle-c[Asp-Ata-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 211);

Ac-Nle-c[dCys-His-p(Cl)dPhe-Arg-Trp-dCys]-dVal-dPro-$NH_2$ (SEQ ID NO: 499);

Ac-dArg-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 501);

Ac-Arg-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 502);

Ac-Lys-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 503);

Ac-dLys-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 504);

Ac-His-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 505);

Ac-dHis-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 506);

Ac-Nle-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dTle-dTle-dVal-$NH_2$ (SEQ ID NO: 511);

Ac-Nle-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dVal-dVal-dPro-$NH_2$ (SEQ ID NO: 512);

Ac-Nle-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dPro-dVal-dPro-$NH_2$ (SEQ ID NO: 513);

Ac-Nle-Nle-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dTle-dPro-$NH_2$ (SEQ ID NO: 515);

Ac-dArg-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dTle-dPro-$NH_2$ (SEQ ID NO: 518);

Ac-Arg-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dTle-dPro-$NH_2$ (SEQ ID NO: 519);

Ac-Lys-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dTle-dPro-$NH_2$ (SEQ ID NO: 520);

Ac-dLys-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dTle-dPro-$NH_2$ (SEQ ID NO: 521);

Ac-His-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dTle-dPro-$NH_2$ (SEQ ID NO: 522); and

Ac-dHis-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dTle-dPro-$NH_2$ (SEQ ID NO: 523),

wherein c represents cyclization through $R^2$ and $R^7$ via a lactam bond or a disulfide bond.

**[0911]** 81. The method or the use of any one of embodiments 1-62, wherein the sequence of any one of Formulae (I)-(ID) is selected from the group consisting of:

Ac-Nle-c[dCys-His-p(Br)dPhe-Arg-Trp-Cys]-dVal-dPro-$NH_2$ (SEQ ID NO: 536); or

Ac-Nle-c[dCys-His-p(Br)dPhe-Arg-Trp-dCys]-dVal-dPro-$NH_2$ (SEQ ID NO: 537),

wherein c represents cyclization through $R^2$ and $R^7$ via a disulfide bond.

**[0912]** 82. The method or the use of any one of embodiments 1-62, wherein the sequence of any one of Formulae (I)-(ID) is selected from the group consisting of:

Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-Val-Pro-$NH_2$ (SEQ ID NO: 573);

Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-Hyp-$NH_2$ (SEQ ID NO: 574);

Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dHyp-$NH_2$ (SEQ ID NO: 575);

Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-Val-$NH_2$ (SEQ ID NO: 576);

Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-Pro-$NH_2$ (SEQ ID NO: 577);

Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-Arg-$NH_2$ (SEQ ID NO: 578);

Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dArg-$NH_2$ (SEQ ID NO: 579);

Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dArg-dPro-$NH_2$ (SEQ ID NO: 580);

Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-Arg-$NH_2$ (SEQ ID NO: 581);

Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dArg-$NH_2$ (SEQ ID NO: 582);

Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-Lys-Pro-Val-$NH_2$ (SEQ ID NO: 583);

Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dLys-dPro-$NH_2$ (SEQ ID NO: 584);

Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-Lys-Val-Pro-$NH_2$ (SEQ ID NO: 585);

Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-Lys-dVal-dPro-$NH_2$ (SEQ ID NO: 586);

Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dLys-dVal-dPro-$NH_2$ (SEQ ID NO: 587);

Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-Arg-Pro-Val-$NH_2$ (SEQ ID NO: 588);

Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-Arg-Val-Pro-$NH_2$ (SEQ ID NO: 589);

Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dArg-dVal-dPro-$NH_2$ (SEQ ID NO: 590);

Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dTle-dPro-$NH_2$ (SEQ ID NO: 591);

Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dTle-dTle-dPro-$NH_2$ (SEQ ID NO: 592);

Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dTle-dTle-dVal-$NH_2$ (SEQ ID NO: 593);

Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dTle-$NH_2$ (SEQ ID NO: 594);

Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dVal-dPro-$NH_2$ (SEQ ID NO: 595);

Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dPro-dVal-dPro-$NH_2$ (SEQ ID NO: 596);

Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dVal-dVal-dPro-$NH_2$ (SEQ ID NO: 597);

Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-dVal-dPro-$NH_2$ (SEQ ID NO: 598);

Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dVal-dVal-dVal-dVal-dVal-dPro-$NH_2$ (SEQ ID NO: 599);

Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-Trp-$NH_2$ (SEQ ID NO: 600);

Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-Lys-dPro-dVal-$NH_2$ (SEQ ID NO: 601);

Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dAla-dAla-$NH_2$ (SEQ ID NO: 602);

Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-Asp-$NH_2$ (SEQ ID NO: 603);

Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dHyp-$NH_2$ (SEQ ID NO: 604);

Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dAsn-$NH_2$ (SEQ ID NO: 605);

Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-Asp-$NH_2$ (SEQ ID NO: 606);

Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-Asn-dPro-$NH_2$ (SEQ ID NO: 607);

Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-Hyp-$NH_2$ (SEQ ID NO: 608);

Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-Ala-Ala-$NH_2$ (SEQ ID NO: 609);

Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-Gly-Gly-$NH_2$ (SEQ ID NO: 610);

Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-Asp-dPro-$NH_2$ (SEQ ID NO: 611);

Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dAsn-dPro-$NH_2$ (SEQ ID NO: 612);

Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-Asn-$NH_2$ (SEQ ID NO: 613);

Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dAsp-$NH_2$ (SEQ ID NO: 614);

Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dAsn-$NH_2$ (SEQ ID NO: 615);

Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-Lys-dPro-$NH_2$ (SEQ ID NO: 616);

Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dPro-dVal-OH (SEQ ID NO: 617);

Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dThr-dPro-dThr-$NH_2$ (SEQ ID NO: 618);

Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dThr-dPro-dThr-OH (SEQ ID NO: 619);

Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dPro-dVal-$NH_2$ (SEQ ID NO: 620);

Ac-Nle-c[dAsp-Pro-dPhe-Arg-Trp-dLys]-dPro-dVal-$NH_2$ (SEQ ID NO: 622);

Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-βPro-$\beta^2$Val-$NH_2$ (SEQ ID NO: 623);

Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-βPro-$\beta^3$Val-$NH_2$ (SEQ ID NO: 624);

Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-$\beta^2$Val-βPro-$NH_2$ (SEQ ID NO: 625);

Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-$\beta^3$Val-βPro-$NH_2$ (SEQ ID NO: 626); and

Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-βPro-βPro-$NH_2$ (SEQ ID NO: 627),

wherein c represents cyclization through $R^2$ and $R^7$ via a lactam bond.

**[0913]** 83. The method or the use of any one of embodiments 1-62, wherein the sequence of any one of Formulae (I)-(ID) is selected from the group consisting of:

Ac-Nle-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 628);

Ac-Nle-Nle-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 629); and

Ac-Nle-Nle-Nle-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 630),

wherein c represents cyclization through $R^2$ and $R^7$ via a lactam bond.

**[0914]** 84. The method or the use of any one of embodiments 1-62, wherein the sequence of any one of Formulae (I)-(ID) is selected from the group consisting of:

Ac-Arg-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dArg-dVal-dPro-$NH_2$ (SEQ ID NO: 631);

Ac-dLys-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dLys-dVal-dPro-$NH_2$ (SEQ ID NO: 632);

Ac-Lys-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dArg-dPro-$NH_2$ (SEQ ID NO: 633);

Ac-His-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dLys-dPro-$NH_2$ (SEQ ID NO: 634);

Ac-dHis-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dHyp-$NH_2$ (SEQ ID NO: 635);

Ac-Orn-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dTle-dPro-$NH_2$ (SEQ ID NO: 636);

Ac-dOrn-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dVal-dVal-dPro-$NH_2$ (SEQ ID NO: 637);

Ac-Nle-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dTle-dPro-$NH_2$ (SEQ ID NO: 638);

Ac-Ala-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dTle-dPro-$NH_2$ (SEQ ID NO: 640);

Ac-dArg-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dTle-dPro-$NH_2$ (SEQ ID NO: 641);

Ac-Arg-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dTle-dPro-$NH_2$ (SEQ ID NO: 642);

Ac-Lys-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dTle-dPro-$NH_2$ (SEQ ID NO: 643);

Ac-dLys-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dTle-dPro-$NH_2$ (SEQ ID NO: 644);

Ac-His-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dTle-dPro-$NH_2$ (SEQ ID NO: 645); and

Ac-dHis-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dTle-dPro-$NH_2$ (SEQ ID NO: 646),

wherein c represents cyclization through $R^2$ and $R^7$ via a lactam bond.

**[0915]** 85. The method or the use of any one of embodiments 1-84, wherein the non-naturally occurring melanocortin analog comprises any one of SEQ ID NOs: 8, 187, 198, 207-218, 226, 231-235, 281, 291, 294-296, 298-322, 324, 351-355, 358-362, 364, 366-368, 371-375, 381-395, 399, 403-417, 419, 421-425, 427, 429, 433-443, 446-461, 472, 492, 496, 499-506, 511-513, 515, 518-523, 536-537, 573-599, 600-620, 622-646.

**[0916]** 86. The method or the use of embodiment 85, wherein the non-naturally occurring melanocortin analog comprises any one of the sequences of SEQ ID NOs: 187, 212, 218, 226, 291, 295, 298-322, 324, 351-355, 358-360, 362, 364, 366-368, 371-375, 381-395, 399, 403-417, 419, 421-425, 427, 429, 433-443, 446-461, 472, 492, 496, 499-506, 511-513, 515, 518-523, 536-537, 573-598, 600-646.

**[0917]** 87. The method or the use of embodiment 85, wherein the non-naturally occurring melanocortin analog comprises any one of the sequences of SEQ ID NOs: 187, 218, 231-235, 291, 295, 298-322, 351-353, 425, 427, 429, 433-443, 446-458, 573-599, 600-620, 622-646.

**[0918]** 88. The method or the use of embodiment 85, wherein the non-naturally occurring melanocortin analog comprises any one of the sequences of SEQ ID NOs: 226, 383-393, 399, 403-417.

**[0919]** 89. The method or the use of embodiment 85, wherein the non-naturally occurring melanocortin analog comprises any one of the sequences of SEQ ID NOs: 209-211, 499, 501-506, 511-513, 515, 518-523.

**[0920]** 90. The method or the use of any one of embodiments 1-89, wherein the non-naturally occurring melanocortin analog is present in a pharmaceutical composition.

**[0921]** 91. The method or the use of embodiment 90, wherein the pharmaceutical composition comprises one or more pharmaceutically acceptable excipients and/or carriers.

**[0922]** 92. The method or the use of embodiment 91, wherein the one or more pharmaceutically acceptable excipients and/or carriers of the pharmaceutical composition comprise water.

**[0923]** 93. The method or the use of any one of embodiments 1-92, wherein the non-naturally occurring melanocortin analog is administered (i) at a first dose of about 5 mg/kg to about 20 mg/kg administered once a day for about 5 days to about 10 days; (ii) at

a second dose of about 10 mg/kg to about 40 mg/kg administered once a day after administration of the first dose for about 5 days to about 10 days; (iii) at a third dose of about 5 mg/kg to about 30 mg/kg administered twice a day after administration of the second dose for at least about 5 days to about 10 days.

**[0924]** 94. The method or the use of any one of embodiments 1-92, wherein the non-naturally occurring melanocortin analog is administered (i) at a first dose of about 5 mg/kg administered once a day for about 7 days; (ii) at a second dose of about 15 mg/kg administered once a day after administration of the first dose for about 7 days; (iii) at a third dose of about 10 mg/kg administered twice a day after administration of the second dose for at least about 7 days.

**[0925]** 95. The method or the use of any one of embodiments 1-92, wherein the non-naturally occurring melanocortin analog is administered (i) at a first dose of about 10 mg/kg administered once a day for about 7 days; (ii) at a second dose of about 20 mg/kg administered once a day after administration of the first dose for about 7 days; (iii) at a third dose of about 15 mg/kg administered twice a day after administration of the second dose for at least about 7 days.

**[0926]** 96. The method or the use of any one of embodiments 1-92, wherein the non-naturally occurring melanocortin analog is administered (i) at a first dose of about 15 mg/kg administered once a day for about 7 days; (ii) at a second dose of about 25 mg/kg administered once a day after administration of the first dose for about 7 days; (iii) at a third dose of about 20 mg/kg administered twice a day after administration of the second dose for at least about 7 days.

**[0927]** 97. The method or the use of any one of embodiments 1-92, wherein the non-naturally occurring melanocortin analog is administered at a dose of about 0.5 mg/kg to about 10 mg/kg per body weight of the subject once daily.

**[0928]** 98. The method or the use of embodiment 97, wherein the non-naturally occurring melanocortin analog is administered at a dose of about 1 mg/kg or 3 mg/kg per body weight of the subject once daily.

**[0929]** 99. The method or the use of any one of embodiments 1-98, wherein the non-naturally occurring melanocortin analog is administered at a dose of about 0.1 mg to about 100 mg once daily.

**[0930]** 100. The method or the use of any one of embodiments 1-92, wherein the non-naturally occurring melanocortin analog is administered at a dose of about 10 mg or about 50 mg once daily.

**[0931]** 101. The method or the use of any one of embodiments 1-100, wherein the non-naturally occurring melanocortin analog is administered via intraperitoneal, intravenous, parenteral, subcutaneous, intramuscular, intracerebroventricular, intranasal, or oral administration.

**[0932]** 102. The method or the use of any one of embodiments 1-101, wherein the non-naturally occurring melanocortin analog crosses a blood-brain-barrier of a subject.

**[0933]** 103. The method or the use of any one of embodiments 101 or 101, wherein the non-naturally occurring melanocortin analog comprises any one of the sequences of SEQ ID NOs: 8, 187, 198, 207-218, 226, 231-235, 281, 291, 294-296, 298-322, 324, 351-355, 358-362, 364, 366-368, 371-375, 381-395, 399, 403-417, 419, 421-425, 427, 429, 433-443, 446-461, 472, 492, 496, 499-506, 511-513, 515, 518-523, 536-537, 573-599, 600-620, 622-646 and is administered at least once daily in an amount ranging from 0.001 mg/kg to 25 mg/kg per body weight of the subject.

**[0934]** 104. The method or the use of embodiment 103, wherein the non-naturally occurring melanocortin analog comprises any one of the sequences of SEQ ID NOs: 8, 187, 198, 207-218, 226, 231-235, 281, 291, 294-296, 298-322, 324, 351-355, 358-362, 364, 366-368, 371-375, 381-395, 399, 403-417, 419, 421-425, 427, 429, 433-443, 446-461, 472, 492, 496, 499-506, 511-513, 515, 518-523, 536-537, 573-599, 600-620, 622-646 and is administered at least once daily in an amount ranging from 0.5 mg/kg to 10 mg/kg per body weight of the subject.

**[0935]** 105. The method or the use of any one of embodiments 1-92, wherein the non-naturally occurring melanocortin analog is administered to a subject for at least 1 day, 1 week, 1 month, 3 months, 6 months, 1 year, or 5 years.

**[0936]** 106. The method or the use of any one of embodiments 1-104, wherein the non-naturally occurring melanocortin analog is administered to a subject for 1 day, 5 days, 7 days, 14 days, 21 days, 28 days, 35 days, 40 days, 45 days, 50 days, 60 days, 75 days, 90 days, 100 days, 110 days, or 120 days.

# CLAIMS

I/We claim:

1. A method of reducing a pain level in a subject in need thereof relative to a control, comprising administering to the subject a non-naturally occurring melanocortin analog of Formula (I):

$$X^1\text{-}X^2\text{-}X^3\text{-}R^1\text{-}R^2\text{-}R^3\text{-}R^4\text{-}R^5\text{-}R^6\text{-}R^7\text{-}R^8\text{-}Y^1\text{-}Y^2\text{-}Y^3\text{-}Y^4\text{-}Y^5\text{-}Y^6\text{-}Y^7 \quad (I),$$

wherein:

$X^1$ is absent or is selected from the group consisting of norleucine (Nle), arginine (Arg), D-arginine (dArg), alanine (Ala), lysine (Lys), D-lysine (dLys), histidine (His), and D-histidine (dHis);

$X^2$ is absent, phenylalanine (Phe), or Nle;

$X^3$ is absent, Phe, or Nle;

$R^1$ is selected from the group consisting of Nle, D-norleucine (dNle), Ala, D-alanine (dAla), Arg, dArg, Lys, dLys, His, dHis, ornithine (Orn), D-ornithine (dOrn), D-leucine (dLeu), D-tyrosine (dTyr), phenylalanine (Phe), D-phenylalanine (dPhe), tryptophan (Trp), D-tryptophan (dTrp), aspartic acid (Asp), cysteine (Cys), and D-cysteine (dCys);

$R^2$ is selected from the group consisting of Asp, proline (Pro), D-aspartic acid (dAsp), Cys, dCys, D-penicillamine (dPen), Ala, dAla, Trp, Phe, dPhe, His, dHis, Tyr, and dTyr;

$R^3$ is absent or is selected from the group consisting of His, Ala, Pro, hydroxyproline (Hyp), leucine (Leu), D-glutamine (dGln), Phe, dPhe, Trp, dTrp, Tyr, dTyr, 4-amino-1,2,4,5-tetrahydro-2-benzazepin-3-one (Aba), 7-amino-7,8-dihydro-4H-[1,2,3]triazolo-[1,5-a][1,4]diazepin-6(5H)-one (Ata), 4-amino-1,4,5,6-tetrahydroazepino[4,3-*b*]indol-3(*2H*)-one (Aia), 2-aminotetraline-2-carboxylic acid (Atc), 1-amino-4-phenylcyclohexane-carboxylic acid (APC), 4-aminophenylpiperidine-4-carboxylic acid (APPC), octohydroindole-2-carboxylic acid (Oic), 1-amino-1-cyclohexanecarboxylic acid (Che), tetrahydro-isoquinoline-3-carboxylic acid (Tic), indoline-2-carboxylic acid (Ioc), 1-amino-1-cyclopentane carboxylic (Cpe), and biphenylalanine (Bip);

$R^4$ is selected from the group consisting of Phe, dPhe, 2'-D-naphthylalanine (dNal(2')), para-chloro-D-phenylalanine (p(Cl)dPhe), para-bromo-D-phenylalanine (p(Br)dPhe), and para-fluoro-D-phenylalanine (p(F)dPhe);

$R^5$ is selected from the group consisting of Arg, His, *cis*Pro(guan), and *trans*Pro(guan);

$R^6$ is selected from the group consisting of Trp, dTrp, Phe, Aia, Aba, Ata, dNal(2'), 2'-naphthylalanine (Nal(2')), and 1'-naphthylalanine (Nal(1'));

$R^7$ is selected from the group consisting of Gly, Pro, Lys, dLys, Cys, dCys, penicillamine (Pen), dPen, and Orn;

$R^8$ is absent or Lys;

$Y^1$ is absent or is selected from the group consisting of valine (Val), D-valine (dVal), $\beta^2$-valine ($\beta^2$-Val), $\beta^3$-valine ($\beta^3$-Val), Pro, D-proline (dPro), β-proline (β-Pro), Hyp, D-hydroxyproline (dHyp), D-tert-leucine (dTle), dLeu, Trp, Arg, dArg, Lys, dLys, Gly, Ala, dAla, Asp, dAsp, asparagine (Asn), D-asparagine (dAsn), and D-threonine (dThr);

$Y^2$ is absent or is selected from the group consisting of Val, dVal, $\beta^2$-Val, $\beta^3$-Val, Pro, dPro, β-Pro, Hyp, dHyp, dTle, Arg, dArg, Gly, Ala, dAla, Asp, and dAsn;

$Y^3$ is absent or is selected from the group consisting of Val, dVal, Pro, dPro, dThr, Lys, and dLys;

$Y^4$ is absent or is selected from the group consisting of dVal, dPro, Asp, and dAsp;

$Y^5$ is absent or dVal;

$Y^6$ is absent or dVal;

$Y^7$ is absent or dPro; and

the non-naturally occurring melanocortin analog is cyclized through a moiety selected from the group consisting of:

a disulfide bond between $R^1$ or $R^2$ and $R^7$ when each of $R^1$ or $R^2$ and $R^7$ are independently selected from the group consisting of Cys, dCys, and dPen;

a disulfide bond between $R^2$ and $R^7$ when $R^2$ is Cys, $R^7$ is Pen, and $R^3$ is absent;

a lactam bridge between $R^1$ or $R^2$ and $R^7$ or $R^8$ when $R^1$ or $R^2$ is Asp and $R^7$ or $R^8$ is Lys or Orn; and

a lactam bridge between $R^2$ and $R^7$ when $R^2$ is dAsp and $R^7$ is dLys;

provided that:

when $R^4$ is dNal(2'), then $R^3$ is His and $R^7$ is Pro;

when $R^4$ is p(F)dPhe, then (i) $R^3$ is selected from Pro, dGln, dTyr, $R^6$ is Trp, and the non-naturally occurring melanocortin analog is not cyclized between Cys at $R^2$ and Cys at $R^7$ or (ii) $R^3$ is His and either $R^6$ is Nal(2') or the non-naturally occurring melanocortin analog is cyclized through a disulfide bond between $R^2$ and $R^7$;

when $R^4$ is p(Br)dPhe, then the non-naturally occurring melanocortin analog is cyclized through a disulfide bond between dCys at $R^2$ and Cys or dCys at $R^7$;

when $R^4$ is dPhe, then (i) $R^3$ is not His, Pro, or absent, (ii) $R^3$ is His and either $R^2$ is Phe or dAla or $R^2$ is Ala and $X^1$ is Arg or dArg, (iii) $R^3$ is Pro and (a) $R^2$ is Trp, and $R^5$ is not His or $R^6$ is not Phe or (b) $R^2$ is not Trp or Pro, and either $R^5$ is not dNal(2') or Nal(2') or $X^1$ and $Y^3$ are not both present, or (iv) $R^3$ is absent and $R^2$ and $R^7$ are not both dPen;

when $R^4$ is p(Cl)dPhe, then (i) $R^3$ is selected from Aba, Aia, and Ata or (ii) $R^3$ is His, $R^1$ is not Ala, and (a) if $R^1$ is Nle and $Y^1Y^2$ is dVal-dPro, then $X^1$ is absent and the non-naturally occurring melanocortin analog is cyclized through a disulfide bond between dCys at $R^2$ and dCys at $R^7$, or (b) if $R^1$ is Nle, and $Y^1Y^2$ is not dVal-dPro, then either $X^1$ or $Y^3$ is present; and

when $R^2$ is dAla, then $R^4$ is dPhe and $Y^1$-$Y^7$ are absent.

2. Use of a non-naturally occurring melanocortin analog for reducing a pain level in a subject in need thereof relative to a control, the non-naturally occurring melanocortin analog comprising a sequence of Formula (I).

3. A method of treating, preventing, or reducing an addiction in a subject relative to a control, comprising administering to the subject a non-naturally occurring melanocortin analog comprising a sequence of Formula (I).

4. Use of a non-naturally occurring melanocortin analog for treating, preventing, or reducing an addiction in a subject relative to a control, the non-naturally occurring melanocortin analog comprising a sequence of Formula (I).

5. A method of preventing or reducing a use of or dependence on an addictive substance in a subject relative to a control, comprising administering to the subject a non-naturally occurring melanocortin analog comprising a sequence of Formula (I).

6. Use of a non-naturally occurring melanocortin analog for treating, preventing, or reducing a use of or dependence on an addictive substance in a subject relative to a control, the non-naturally occurring melanocortin analog comprising a sequence of Formula (I).

7. A method of treating or preventing an opioid use disorder (OUD) in a subject in need thereof relative to a control, comprising administering to the subject a non-naturally occurring melanocortin analog comprising a sequence of Formula (I).

8. Use of a non-naturally occurring melanocortin analog for treating or preventing an OUD in a subject in need thereof relative to a control, the non-naturally occurring melanocortin analog comprising a sequence of Formula (I).

9. A method of treating or preventing an alcohol use disorder (AUD) in a subject in need thereof relative to a control, comprising administering to the subject a non-naturally occurring melanocortin analog comprising a sequence of Formula (I).

10. Use of a non-naturally occurring melanocortin analog for treating or preventing an AUD in a subject in need thereof relative to a control, the non-naturally occurring melanocortin analog comprising a sequence of Formula (I).

11. The method or the use of any one of claims 3-9, wherein the method or the use comprises reducing a dose used or consumed of an addictive substance, relative to a control.

12. The method or the use of any one of claims 3-11, wherein the method or the use comprises reducing a dependency on an addictive substance, relative to a control.

13. The method or the use of any one of claims 3-12, wherein the method or the use comprises reducing a frequency of an addictive substance use, relative to a control.

14. The method or the use of any one of claims 3-13, wherein the method or the use comprises reducing a dose or dosage of a conventional medication used to treat an addiction, relative to a control.

15. A method of augmenting an effect of a conventional medication used to treat an addiction in a subject in need thereof, relative to a control, comprising administering to the subject a non-naturally occurring melanocortin analog comprising a sequence of Formula (I).

16. Use of a non-naturally occurring melanocortin analog for augmenting an effect of a conventional medication used to treat an addiction in a subject in need thereof, the non-naturally occurring melanocortin analog comprising a sequence of Formula (I).

17. A method of reducing or eliminating a need for a conventional medication used to treat an addiction in a subject in need thereof, relative to a control, comprising administering to the subject a non-naturally occurring melanocortin analog comprising a sequence of Formula (I).

18. Use of a non-naturally occurring melanocortin analog for reducing or eliminating a need for a conventional medication used to treat an addiction in a subject in need thereof, the non-naturally occurring melanocortin analog comprising a sequence of Formula (I).

19. The method or the use of claim 17 or 18, wherein the treatment of the addiction is improved during or after administration of the non-naturally occurring melanocortin analog relative to treatment of the addiction using the conventional medication to treat the addiction alone.

20. The method or the use of any one of claims 14-19, wherein the conventional medication to treat the addiction is selected from the group consisting of buprenorphine, naltrexone, acamprosate, methadone, naloxone, nalmefene, xycodone, levo-alpha-acetylmethadol (LAAM), codeine, lofexidine, and a slow-release morphine.

21. A method of reducing a need for a hospitalization or rehabilitation associated with addiction or use of an addictive substance, relative to a control, comprising administering to the subject a non-naturally occurring melanocortin analog comprising a sequence of Formula (I).

22. Use of a non-naturally occurring melanocortin analog for reducing a need for a hospitalization or rehabilitation associated with addiction or use of an addictive substance, relative to a control, the non-naturally occurring melanocortin analog comprising a sequence of Formula (I).

23. A method of preventing or reducing a withdrawal from an addictive substance in a subject, comprising administering to the subject a non-naturally occurring melanocortin analog comprising a sequence of Formula (I).

24. Use of a non-naturally occurring melanocortin analog for preventing or reducing a withdrawal from an addictive substance in a subject, relative to a control, the non-naturally occurring melanocortin analog comprising a sequence of Formula (I).

25. A method of preventing or reducing a symptom associated with withdrawal from an addictive substance in a subject relative to a control, comprising administering to the subject a non-naturally occurring melanocortin analog comprising a sequence of Formula (I).

26. Use of a non-naturally occurring melanocortin analog for preventing or reducing a symptom associated with withdrawal from an addictive substance in a subject, relative to a control, the non-naturally occurring melanocortin analog comprising a sequence of Formula (I).

27. The method or the use of claim 25 or 26, wherein the symptom associated with withdrawal from an addictive substance is selected from the group consisting of pain, anxiety, depression, diarrhea, dizziness, fatigue, muscle aches, nausea, sleep problems, suicidal ideation, tremors, and visual disturbances.

28. The method or the use of any one of claims 1-27, wherein the subject has an addiction to an addictive substance or is susceptible to an addiction to an addictive substance.

29. The method or the use of any one of claims 1-28, wherein the subject has used or is using one or more addictive substances.

30. The method or the use of any one of claims 5-29 wherein the addictive substance comprises a prescription medication, a substance in an over-the-counter medication, a recreational substance, or an illegal substance.

31. The method or the use of any one of claims 5-30, wherein the addictive substance is selected from the group consisting of an opioid, a painkiller, a stimulant, a narcotic, an alcohol, a sedative, marijuana, a cannabis, a tetrahydrocannabinol (THC), a cannabidiol (CBD), and an inhalant.

32. The method or the use of claim 31, wherein the opioid is selected from the group consisting of morphine, heroin, codeine, oxycodone, hydrocodone, and fentanyl.

33. The method or the use of claim 31, wherein the stimulant is selected from the group consisting of caffeine, nicotine, methamphetamines, cocaine, and amphetamines.

34. The method or the use of claim 31, wherein the sedative comprises a barbiturate or a benzodiazepine.

35. The method or the use of claim 34, wherein the barbiturate is selected from the group consisting of phenobarbital, methohexital, butalbital, pentobarbital, primidone, and amobarbital.

36. The method or the use of claim 34, wherein the benzodiazepine is selected from the group consisting of alprazolam, lorazepam, clonazepam, diazepam, and temazepam.

37. The method or the use of claim 31, wherein the sedative is selected from the group consisting of tranquilizers, xylazine, eszopiclone, zaleplon, zolpidem, and zopiclone.

38. The method or the use of claim 31, wherein the inhalant is selected from the group consisting of aerosols, butanes, freon, helium, nitrous oxide, propane, and nitrites.

39. The method or the use of claim 33, wherein the nicotine comprises a tobacco chew, a nicotine pouch, or a smoking device.

40. The method or the use of claim 39, wherein the smoking device is selected from the group consisting of cigarettes, electronic cigarettes, cigars, and vape products.

41. The method or the use of any one of claims 1-40, wherein the control comprises the subject before administration of the non-naturally occurring melanocortin analog.

42. The method or the use of any one of claims 1-41, wherein the control comprises the subject at baseline.

43. The method or the use of any one of claims 1-42, wherein the non-naturally occurring melanocortin analog is a melanocortin 4 receptor (MC4R) agonist.

44. The method or the use of claim 43, wherein the MC4R agonist is a full MC4R agonist.

45. The method or the use of claim 43, wherein the MC4R agonist is a partial MC4R agonist.

46. The method or the use of any one of claims 1-45, wherein the non-naturally occurring melanocortin analog is a MC3R antagonist.

47. The method or the use of claim 46, wherein the MC3R antagonist is a full MC3R antagonist.

48. The method or the use of claim 46, wherein the MC3R antagonist is a partial MC3R antagonist.

49. The method or the use of any one of claims 1-45, wherein the non-naturally occurring melanocortin analog does not have MC3R activity.

50. The method or the use of any one of claims 1-49, wherein the non-naturally occurring melanocortin analog comprises a sequence according to Formula (I), wherein:

$X^1$ is absent or is selected from the group consisting of norleucine (Nle), arginine (Arg), D-arginine (dArg), alanine (Ala), lysine (Lys), D-lysine (dLys), histidine (His), and D-histidine (dHis);

$X^2$ is absent, phenylalanine (Phe), or Nle;

$X^3$ is absent, Phe, or Nle;

$R^1$ is selected from the group consisting of Nle, D-norleucine (dNle), Ala, D-alanine (dAla), Arg, dArg, Lys, dLys, His, dHis, ornithine (Orn), D-ornithine (dOrn), D-leucine (dLeu), D-tyrosine (dTyr), phenylalanine (Phe), D-phenylalanine (dPhe), tryptophan (Trp), D-tryptophan (dTrp), aspartic acid (Asp), cysteine (Cys), and D-cysteine (dCys);

$R^2$ is selected from the group consisting of Asp, proline (Pro), D-aspartic acid (dAsp), Cys, dCys, D-penicillamine (dPen), Ala, dAla, Trp, Phe, dPhe, His, dHis, Tyr, and dTyr;

$R^3$ is absent or is selected from the group consisting of His, Ala, Pro, hydroxyproline (Hyp), leucine (Leu), D-glutamine (dGln), Phe, dPhe, Trp, dTrp, Tyr, dTyr, 4-amino-1,2,4,5-tetrahydro-2-benzazepin-3-one (Aba), 7-amino-7,8-dihydro-4H-[1,2,3]triazolo-[1,5-a][1,4]diazepin-6(5H)-one (Ata), 4-amino-1,4,5,6-tetrahydroazepino[4,3-*b*]indol-3(*2H*)-one (Aia), 2-aminotetraline-2-carboxylic acid (Atc), 1-amino-4-phenylcyclohexane-carboxylic acid (APC), 4-aminophenylpiperidine-4-carboxylic acid (APPC), octohydroindole-2-carboxylic acid (Oic), 1-amino-1-cyclohexanecarboxylic acid (Che), tetrahydro-isoquinoline-3-carboxylic acid (Tic), indoline-2-carboxylic acid (Ioc), 1-amino-1-cyclopentane carboxylic (Cpe), and biphenylalanine (Bip);

$R^4$ is selected from the group consisting of Phe, dPhe, 2'-D-naphthylalanine (dNal(2')), para-chloro-D-phenylalanine (p(Cl)dPhe), para-bromo-D-phenylalanine (p(Br)dPhe), and para-fluoro-D-phenylalanine (p(F)dPhe);

$R^5$ is selected from the group consisting of Arg, His, *cis*Pro(guan), and *trans*Pro(guan);

$R^6$ is selected from the group consisting of Trp, dTrp, Phe, Aia, Aba, Ata, dNal(2'), 2'-naphthylalanine (Nal(2')), and 1'-naphthylalanine (Nal(1'));

$R^7$ is selected from the group consisting of Gly, Pro, Lys, dLys, Cys, dCys, penicillamine (Pen), dPen, and Orn;

$R^8$ is absent or Lys;

$Y^1$ is absent or is selected from the group consisting of valine (Val), D-valine (dVal), $\beta^2$-valine ($\beta^2$-Val), $\beta^3$-valine ($\beta^3$-Val), Pro, D-proline (dPro), β-proline (β-Pro), Hyp, D-hydroxyproline (dHyp), D-tert-leucine (dTle), dLeu, Trp, Arg, dArg, Lys, dLys, Gly, Ala, dAla, Asp, dAsp, asparagine (Asn), D-asparagine (dAsn), and D-threonine (dThr);

$Y^2$ is absent or is selected from the group consisting of Val, dVal, $\beta^2$-Val, $\beta^3$-Val, Pro, dPro, β-Pro, Hyp, dHyp, dTle, Arg, dArg, Gly, Ala, dAla, Asp, and dAsn;

$Y^3$ is absent or is selected from the group consisting of Val, dVal, Pro, dPro, dThr, Lys, and dLys;

$Y^4$ is absent or is selected from the group consisting of dVal, dPro, Asp, and dAsp;

$Y^5$ is absent or dVal;

$Y^6$ is absent or dVal;

$Y^7$ is absent or dPro; and

the non-naturally occurring melanocortin analog is cyclized through a moiety selected from the group consisting of:

a disulfide bond between $R^1$ or $R^2$ and $R^7$ or $R^8$ when each of $R^1$ or $R^2$ and $R^7$ or $R^8$ are independently selected from the group consisting of Cys, dCys, and dPen;

a disulfide bond between $R^2$ and $R^7$ when $R^2$ is Cys, $R^7$ is Pen, and $R^3$ is absent;

a lactam bridge between $R^1$ or $R^2$ and $R^7$ or $R^8$ when $R^1$ or $R^2$ is Asp and $R^7$ or $R^8$ is Lys or Orn; and

a lactam bridge between $R^2$ and $R^7$ when $R^2$ is dAsp and $R^7$ is dLys;

provided that the non-naturally occurring melanocortin analog does not comprise a sequence selected from the group consisting of:

Ac-Nle-c[Asp-Pro-Pro-dNal(2')-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 194);

Ac-Nle-c[Asp-Pro-His-dNal(2')-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 5);

Ac-Nle-c[Asp-Pro-His-dNal(2')-Arg-Trp-Lys]-dPro-dVal-$NH_2$ (SEQ ID NO: 10);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dVal-dPro (SEQ ID NO: 2);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 3);

Ac-Nle-c[Asp-Hyp-dNal(2')-Arg-Trp-Pro-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 4);

Ac-Nle-c[Asp-Phe-His-dNal(2')-Arg-Trp-Lys]-dLeu-dPro-$NH_2$ (SEQ ID NO: 6);

Ac-Nle-c[Asp-Phe-His-dNal(2')-Arg-Trp-Lys]-dTle-dPro-$NH_2$ (SEQ ID NO: 7);

Ac-Nle-c[Asp-Hyp-dNal(2')-Arg-Trp-Pro-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 9);

Ac-Nle-Phe-Phe-c[Asp-Phe-His-dNal(2')-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 12);

Ac-dArg-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 15);

Ac-dLeu-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 18);

Ac-dAla-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 20);

Ac-Ala-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 21);

Ac-dNle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 24);

Ac-dCys-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 28);

Ac-dPhe-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 29);

Ac-dTyr-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 30);

dTyr-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 35);

Tyr-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 36);

Ac-Nle-c[Cys-Pro-dNal(2')-Arg-Trp-Cys]-dVal-dPro-$NH_2$ (SEQ ID NO: 40);

Ac-Nle-c[dCys-Pro-dNal(2')-Arg-Trp-Cys]-dVal-dPro-$NH_2$ (SEQ ID NO: 41);

Ac-Nle-c[Cys-Pro-dNal(2')-Arg-Trp-dCys]-dVal-dPro-$NH_2$ (SEQ ID NO: 42);

Ac-Nle-c[dCys-Pro-dNal(2')-Arg-Trp-dCys]-dVal-dPro-$NH_2$ (SEQ ID NO: 43);

Ac-Nle-c[Cys-Pro-dNal(2')-Arg-Trp-Pen]-dVal-dPro-$NH_2$ (SEQ ID NO: 48);

Ac-Nle-c[dPen-Pro-dNal(2')-Arg-Trp-dPen]-dVal-dPro-$NH_2$ (SEQ ID NO: 54);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Orn]-dVal-dPro-$NH_2$ (SEQ ID NO: 64);

Ac-Nle-c[Asp-dNal(2')-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 68);

Ac-Nle-c[Asp-Ala-dNal(2')-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 69);

Ac-Nle-c[Asp-Leu-dNal(2')-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 76);

Ac-Nle-c[Asp-Trp-dNal(2')-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 82);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-Val-Pro-$NH_2$ (SEQ ID NO: 115);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dVal-dPro-OH (SEQ ID NO: 116);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dPro-dVal-OH (SEQ ID NO: 117);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dVal-Hyp-$NH_2$ (SEQ ID NO: 118);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dVal-dHyp-$NH_2$ (SEQ ID NO: 119);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-Val-Hyp-$NH_2$ (SEQ ID NO: 120);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-Val-dHyp-$NH_2$ (SEQ ID NO: 121);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-Hyp-dVal-$NH_2$ (SEQ ID NO: 122);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dHyp-dVal-$NH_2$ (SEQ ID NO: 123);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-Hyp-Val-$NH_2$ (SEQ ID NO: 124);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dHyp-Val-$NH_2$ (SEQ ID NO: 125);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dVal-dVal-$NH_2$ (SEQ ID NO: 126);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dPro-dPro-$NH_2$ (SEQ ID NO: 127);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dVal-$NH_2$ (SEQ ID NO: 128);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dPro-$NH_2$ (SEQ ID NO: 129);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-Val-$NH_2$ (SEQ ID NO: 130);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-Pro-$NH_2$ (SEQ ID NO: 131);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-Ala-$NH_2$ (SEQ ID NO: 132);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dAla-$NH_2$ (SEQ ID NO: 133);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dHyp-$NH_2$ (SEQ ID NO: 134);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-Hyp-$NH_2$ (SEQ ID NO: 135);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dAla-dAla-$NH_2$ (SEQ ID NO: 136);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-Ala-Ala-$NH_2$ (SEQ ID NO: 137);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-Gly-Gly-$NH_2$ (SEQ ID NO: 138);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dVal-Asp-$NH_2$ (SEQ ID NO: 139);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dVal-Arg-$NH_2$ (SEQ ID NO: 140);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dVal-dArg-$NH_2$ (SEQ ID NO: 143);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dVal-dAsn-$NH_2$ (SEQ ID NO: 144);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-Asp-dPro-$NH_2$ (SEQ ID NO: 145);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-Arg-dPro-$NH_2$ (SEQ ID NO: 146);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-Asn-dPro-$NH_2$ (SEQ ID NO: 147);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dAsp-dPro-$NH_2$ (SEQ ID NO: 148);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dArg-dPro-$NH_2$ (SEQ ID NO: 149);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dAsn-dPro-$NH_2$ (SEQ ID NO: 150);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-Asp-$NH_2$ (SEQ ID NO: 151);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-Arg-$NH_2$ (SEQ ID NO: 152);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-Asn-$NH_2$ (SEQ ID NO: 153);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dAsp-$NH_2$ (SEQ ID NO: 154);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dArg-$NH_2$ (SEQ ID NO: 155);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dAsn-$NH_2$ (SEQ ID NO: 156);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-Lys-Pro-Val-$NH_2$ (SEQ ID NO: 157);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-Lys-dPro-dVal-$NH_2$ (SEQ ID NO: 158);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dLys-dPro-dVal-$NH_2$ (SEQ ID NO: 159);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-Lys-dPro-$NH_2$ (SEQ ID NO: 160);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dLys-dPro-$NH_2$ (SEQ ID NO: 161);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-Lys-Val-Pro-$NH_2$ (SEQ ID NO: 162);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-Lys-dVal-dPro-$NH_2$ (SEQ ID NO: 164);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dLys-dVal-dPro-$NH_2$ (SEQ ID NO: 164);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-Arg-Pro-Val-$NH_2$ (SEQ ID NO: 165);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-Arg-dPro-dVal-$NH_2$ (SEQ ID NO: 166);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dArg-dPro-dVal-$NH_2$ (SEQ ID NO: 167);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-Arg-Val-Pro-$NH_2$ (SEQ ID NO: 168);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-Arg-dVal-dPro-$NH_2$ (SEQ ID NO: 169);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dArg-dVal-dPro-$NH_2$ (SEQ ID NO: 170);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dTle-dVal-dPro-$NH_2$ (SEQ ID NO: 171);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dTle-dPro-$NH_2$ (SEQ ID NO: 172);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dTle-dVal-$NH_2$ (SEQ ID NO: 173);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dTle-dTle-$NH_2$ (SEQ ID NO: 174);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dTle-dTle-dPro-$NH_2$ (SEQ ID NO: 175);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dTle-dTle-dVal-$NH_2$ (SEQ ID NO: 176);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dPro-dTle-$NH_2$ (SEQ ID NO: 177);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dVal-dTle-$NH_2$ (SEQ ID NO: 178);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dVal-dVal-dPro-$NH_2$ (SEQ ID NO: 179);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dPro-dVal-dPro-$NH_2$ (SEQ ID NO: 180);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dVal-dVal-dVal-dPro-$NH_2$ (SEQ ID NO: 181);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dVal-dPro-dVal-dPro-$NH_2$ (SEQ ID NO: 182);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dVal-dVal-dVal-dVal-dVal-dVal-dPro-$NH_2$ (SEQ ID NO: 183);

Ac-Nle-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 184);

Ac-Nle-Nle-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 185);

Ac-Nle-Nle-Nle-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 186);

Ac-Nle-c[Asp-Trp-Pro-dNal(2')-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 195);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-dTrp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 196);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-Trp-$NH_2$ (SEQ ID NO: 203);

Ac-Nle-c[Asp-Aba-dNal(2')-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 204);

Ac-Nle-c[Asp-Aia-dNal(2')-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 205);

Ac-Nle-c[Asp-Ata-dNal(2')-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 206);

Ac-Nle-c[Asp-Cpe-dNal(2')-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 240);

Ac-Nle-c[Asp-Che-dNal(2')-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 241);

Ac-Nle-c[Asp-Oic-dNal(2')-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 242);

Ac-Nle-c[Asp-Tic-dNal(2')-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 244);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Pro-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 245);

Ac-Nle-c[Asp-His-dNal(2')-transPro(guan)-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 247);

Ac-Nle-c[Asp-His-dNal(2')-cisPro(guan)-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 248);

Ac-Nle-c[Asp-Pro-dNal(2')-transPro(guan)-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 250);

Ac-Nle-c[Asp-Pro-dNal(2')-cisPro(guan)Pro-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 251);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Aba-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 253);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Ata-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 254);

Ac-Nle-c[Asp-Glu-dNal(2')-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 255);

Ac-Nle-c[Asp-Glu-dNal(2')-Arg-Trp-Gly-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 256);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Gly-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 259);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Gly-Lys]-dPro-dPro-Lys-Asp-$NH_2$ (SEQ ID NO: 260);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Gly-Lys]-dPro-dPro-dLys-dAsp-$NH_2$ (SEQ ID NO: 261);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Trp-Lys]-dPro-dPro-dLys-dAsp-$NH_2$ (SEQ ID NO: 263);

Ac-Nle-c[Asp-Ala-His-dNal(2')-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 273);

Ac-Arg-c[Asp-Ala-His-dNal(2')-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 274);

Ac-dArg-c[Asp-Ala-His-dNal(2')-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 275);

Ac-dLeu-c[dPen-Pro-dNal(2')-Arg-Trp-dPen]-dVal-dPro-$NH_2$ (SEQ ID NO: 327);

Ac-dNle-c[dPen-Pro-dNal(2')-Arg-Trp-dPen]-dVal-dPro-$NH_2$ (SEQ ID NO: 328);

Ac-dArg-c[dPen-Pro-dNal(2')-Arg-Trp-dPen]-dVal-dPro-$NH_2$ (SEQ ID NO: 329);

Ac-Arg-c[dPen-Pro-dNal(2')-Arg-Trp-dPen]-dVal-dPro-$NH_2$ (SEQ ID NO: 330);

Ac-dPhe-c[dPen-Pro-dNal(2')-Arg-Trp-dPen]-dVal-dPro-$NH_2$ (SEQ ID NO: 331);

Ac-dTyr-c[dPen-Pro-dNal(2')-Arg-Trp-dPen]-dVal-dPro-$NH_2$ (SEQ ID NO: 332);

Ac-Ala-c[dPen-Pro-dNal(2')-Arg-Trp-dPen]-dVal-dPro-$NH_2$ (SEQ ID NO: 333);

Ac-dHis-c[dPen-Pro-dNal(2')-Arg-Trp-dPen]-dVal-dPro-$NH_2$ (SEQ ID NO: 334);

Ac-His-c[dPen-Pro-dNal(2')-Arg-Trp-dPen]-dVal-dPro-$NH_2$ (SEQ ID NO: 335);

Ac-dLys-c[dPen-Pro-dNal(2')-Arg-Trp-dPen]-dVal-dPro-$NH_2$ (SEQ ID NO: 336);

Ac-Lys-c[dPen-Pro-dNal(2')-Arg-Trp-dPen]-dVal-dPro-$NH_2$ (SEQ ID NO: 337);

Ac-Nle-c[dPen-Pro-dNal(2')-Arg-Trp-dPen]-dArg-dVal-dPro-$NH_2$ (SEQ ID NO: 344);

Ac-Nle-c[dPen-Pro-dNal(2')-Arg-Trp-dPen]-dLys-dVal-dPro-$NH_2$ (SEQ ID NO: 345);

Ac-Nle-c[dPen-Pro-dNal(2')-Arg-Trp-dPen]-dArg-dPro-$NH_2$ (SEQ ID NO: 346);

Ac-Nle-c[dPen-Pro-dNal(2')-Arg-Trp-dPen]-dLys-dPro-$NH_2$ (SEQ ID NO: 347);

Ac-Nle-c[dPen-Pro-dNal(2')-Arg-Trp-dPen]-dVal-dHyp-$NH_2$ (SEQ ID NO: 348);

Ac-Nle-c[dPen-Pro-dNal(2')-Arg-Trp-dPen]-dTle-dPro-$NH_2$ (SEQ ID NO: 349);

Ac-Nle-c[dPen-Pro-dNal(2')-Arg-Trp-Gly-dPen]-dVal-dPro-$NH_2$ (SEQ ID NO: 350);

Ac-Nle-c[Asp-Pro-dNal(2')-Arg-Aia-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 103);

Ac-Nle-c[Asp-Ioc-dNal(2')-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 243);

Ac-Nle-c[Cys-dNal(2')-Arg-Trp-Cys]-dVal-dPro-$NH_2$ (SEQ ID NO: 44);

Ac-Nle-c[dCys-dNal(2')-Arg-Trp-Cys]-dVal-dPro-$NH_2$ (SEQ ID NO: 45);

Ac-Nle-c[Cys-dNal(2')-Arg-Trp-dCys]-dVal-dPro-$NH_2$ (SEQ ID NO: 46);

Ac-Nle-c[dCys-dNal(2')-Arg-Trp-dCys]-dVal-dPro-$NH_2$ (SEQ ID NO: 47);

Ac-Nle-c[Cys-dNal(2')-Arg-Trp-Pen]-dVal-dPro-$NH_2$ (SEQ ID NO: 56);

Ac-Nle-c[dPen-dNal(2')-Arg-Trp-dPen]-dVal-dPro-$NH_2$ (SEQ ID NO: 62);

Ac-Nle-c[Asp-dTrp-dNal(2')-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 83);

Ac-Nle-c[dPen-Ala-dNal(2')-Arg-Trp-dPen]-dVal-dPro-$NH_2$ (SEQ ID NO: 338);

Ac-Nle-c[dPen-Leu-dNal(2')-Arg-Trp-dPen]-dVal-dPro-$NH_2$ (SEQ ID NO: 339);

Ac-Nle-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 223);

Ac-Arg-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 464);

Ac-Lys-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 465);

Ac-dLys-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 466);

Ac-His-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 467);

Ac-dHis-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 468);

Ac-Nle-Nle-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 469); Ac-Nle-c[Asp-His-p(F)dPhe-His-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 470);

Ac-Nle-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dVal-dVal-dVal-dPro-$NH_2$ (SEQ ID NO: 474);

Ac-Nle-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dPro-dVal-dPro-$NH_2$ (SEQ ID NO: 475);

Ac-Nle-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dTle-dPro-$NH_2$ (SEQ ID NO: 476);

Ac-Nle-Nle-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dTle-dPro-$NH_2$ (SEQ ID NO: 477);

Ac-Nle-Nle-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dPro-dVal-dPro-$NH_2$ (SEQ ID NO: 478);

Ac-Arg-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dTle-dPro-$NH_2$ (SEQ ID NO: 481);

Ac-Lys-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dTle-dPro-$NH_2$ (SEQ ID NO: 482);

Ac-dLys-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dTle-dPro-$NH_2$ (SEQ ID NO: 483);

Ac-His-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dTle-dPro-$NH_2$ (SEQ ID NO: 484);

Ac-dHis-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dTle-dPro-$NH_2$ (SEQ ID NO: 485);

Ac-dArg-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 463);

Ac-Ala-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 462);

Ac-Ala-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dTle-dPro-$NH_2$ (SEQ ID NO: 479);

Ac-Nle-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dTle-dTle-dVal-$NH_2$ (SEQ ID NO: 473);

Ac-dArg-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dTle-dPro-$NH_2$ (SEQ ID NO: 480);

Ac-Nle-c[Asp-Gln-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 491);

Ac-Nle-c[Asp-Bip-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 489);

Ac-Nle-c[Asp-Trp-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 493);

Ac-Nle-c[Asp-Pro-p(F)dPhe-Arg-dNal(2')-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 444);

Ac-Nle-c[Asp-Pro-p(F)dPhe-Arg-Nal(2')-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 445);

Ac-Nle-c[Asp-Tyr-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 495);

Ac-Nle-c[Asp-Phe-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 487);

Ac-Nle-c[Asp-dPhe-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 488);

Ac-Nle-c[Asp-dTrp-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 494);

Ac-Nle-c[Asp-His-p(F)dPhe-Arg-dNal(2')-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 471);

Ac-Nle-c[Cys-Pro-p(F)dPhe-Arg-Trp-Cys]-dVal-dPro-$NH_2$ (SEQ ID NO: 432);

Ac-Nle-c[Asp-Pro-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 217);

Ac-Nle-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 222);

Ac-Nle-c[Cys-His-p(Br)dPhe-Arg-Trp-Cys]-dVal-dPro-$NH_2$ (SEQ ID NO: 535);

Ac-Ala-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 538);

Ac-Nle-Nle-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 545);

Ac-Nle-c[Asp-His-p(Br)dPhe-His-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 546);

Ac-Nle-c[Asp-His-p(Br)dPhe-Arg-dNal(2')-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 547);

Ac-Nle-c[Asp-His-p(Br)dPhe-Arg-Nal(2')-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 548);

Ac-Nle-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dTle-dTle-dVal-$NH_2$ (SEQ ID NO: 549);

Ac-Nle-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dPro-dVal-dPro-$NH_2$ (SEQ ID NO: 551);

Ac-Nle-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dTle-dPro-$NH_2$ (SEQ ID NO: 552);

Ac-Nle-Nle-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dTle-dPro-$NH_2$ (SEQ ID NO: 553);

Ac-Ala-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dTle-dPro-$NH_2$ (SEQ ID NO: 555);

Ac-Nle-c[Asp-dHis-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 562);

Ac-Nle-c[Asp-Phe-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 563);

Ac-Nle-c[Asp-dPhe-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 564);

Ac-Nle-c[Asp-Bip-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 565);

Ac-Nle-c[Asp-dGln-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 568);

Ac-Nle-c[Asp-Trp-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 569);

Ac-Nle-c[Asp-dTrp-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 570);

Ac-Nle-c[Asp-Tyr-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 571);

Ac-Nle-c[Asp-dTyr-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 572);

Ac-dArg-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 539);

Ac-dHis-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 544);

Ac-dHis-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dTle-dPro-$NH_2$ (SEQ ID NO: 561);

Ac-dArg-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dTle-dPro-$NH_2$ (SEQ ID NO: 556);

Ac-dLys-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 542);

Ac-His-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dTle-dPro-$NH_2$ (SEQ ID NO: 560);

Ac-His-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 543);

Ac-dLys-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dTle-dPro-$NH_2$ (SEQ ID NO: 559);

Ac-Arg-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dTle-dPro-$NH_2$ (SEQ ID NO: 557);

Ac-Lys-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 541);

Ac-Nle-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dVal-dVal-dVal-dPro-$NH_2$ (SEQ ID NO: 550);

Ac-Lys-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dTle-dPro-$NH_2$ (SEQ ID NO: 558);

Ac-Arg-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 540);

Ac-Nle-Nle-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dPro-dVal-dPro-$NH_2$ (SEQ ID NO: 554);

Ac-Nle-c[Asp-His-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 363);

Ac-Nle-c[Asp-His-dPhe-Arg-Trp-Pro-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 418);

Ac-Nle-c[Asp-His-dPhe-Arg-Trp-Lys]-dPro-dVal-$NH_2$ (SEQ ID NO: 621);

Ac-Nle-c[Asp-His-dPhe-transPro(guan)-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 228);

Ac-Nle-c[Asp-His-dPhe-cisPro(guan)-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 229);

Ac-Nle-c[Asp-Ala-His-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 380);

Ac-Nle-c[Asp-Trp-Pro-dPhe-His-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 398);

Ac-Nle-c[Asp-Trp-Pro-dPhe-Arg-Phe-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 401);

Ac-Nle-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dPro-dVal-dPro-$NH_2$ (SEQ ID NO: 639);

Ac-Nle-c[Asp-Pro-dPhe-Arg-dNal(2')-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 430);

Ac-Nle-c[Asp-Pro-dPhe-Arg-Nal(2')-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 431);

Ac-Nle-c[Asp-Pro-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 225);

Ac-Nle-c[dPen-dPhe-Arg-Trp-dPen]-dVal-dPro-$NH_2$ (SEQ ID NO: 326);

Ac-Nle-c[Asp-Pro-His-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 297);

Ac-Nle-c[Asp-Pro-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 215);

Ac-Nle-c[Asp-Phe-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 525);

Ac-Nle-c[Asp-dPhe-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 526);

Ac-Nle-c[Asp-Bip-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 527);

Ac-Nle-c[Asp-Trp-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 531);

Ac-Nle-c[Asp-Tyr-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 533);

Ac-Nle-c[Asp-dTyr-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 534);

Ac-Nle-c[Asp-dTrp-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 532);

Ac-Nle-c[dCys-His-p(Cl)dPhe-Arg-Trp-Cys]-dVal-dPro-$NH_2$ (SEQ ID NO: 498);

Ac-Nle-c[Cys-His-p(Cl)dPhe-Arg-Trp-Cys]-dVal-dPro-$NH_2$ (SEQ ID NO: 497);

Ac-Nle-c[Asp-His-p(Cl)dPhe-Arg-dNal(2')-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 509);

Ac-Nle-c[Asp-His-p(Cl)dPhe-Arg-Nal(2')-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 510);

Ac-Nle-c[Asp-His-p(Cl)dPhe-His-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 508);

Ac-Nle-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 220);

Ac-Nle-Nle-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 507);

Ac-Ala-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dTle-dPro-$NH_2$ (SEQ ID NO: 517);

Ac-Ala-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 500);

Ac-Nle-Nle-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dPro-dVal-dPro-$NH_2$ (SEQ ID NO: 516);

Ac-Nle-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dTle-dPro-$NH_2$ (SEQ ID NO: 514);

Ac-Nle-c[Asp-dGln-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 530);

Ac-Arg-c[Asp-dAla-His-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 268);

Ac-Nle-c[Asp-dAla-His-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 378);

Ac-dArg-c[Asp-dAla-His-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 379);

Ac-Nle-c[Asp-dAla-His-dNal(2')-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 266);

Ac-Arg-c[Asp-dAla-His-dNal(2')-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 267);

Ac-Arg-c[Cys-dAla-His-dNal(2')-Arg-Trp-Cys]-dVal-dPro-$NH_2$ (SEQ ID NO: 269);

Ac-dArg-c[Asp-dAla-His-dNal(2')-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 270);

Ac-Arg-c[Cys-dAla-His-dNal(2')-Arg-Trp-Cys]-$NH_2$ (SEQ ID NO: 282); and

Ac-Arg-c[Asp-dAla-His-dNal(2')-Arg-Trp-Lys]-$NH_2$ (SEQ ID NO: 283).

51. The method or use of any one of claims 1-49, wherein the non-naturally occurring melanocortin analog comprises a sequence according to Formula (IA):

$$X^1\text{-}X^2\text{-}X^3\text{-}R^1\text{-}R^2\text{-}R^3\text{-}R^4\text{-}R^5\text{-}R^6\text{-}R^7\text{-}R^8\text{-}Y^1\text{-}Y^2\text{-}Y^3\text{-}Y^4 \text{ (IA)},$$

wherein:

$X^1$ is absent or is selected from the group consisting of norleucine (Nle), arginine (Arg), D-arginine (dArg), alanine (Ala), lysine (Lys), D-lysine (dLys), histidine (His), D-histidine (dHis);

$X^2$ is absent, phenylalanine (Phe), or Nle;

$X^3$ is absent, Phe, or Nle;

$R^1$ is selected from the group consisting of Nle, D-norleucine (dNle), Ala, D-alanine (dAla), Arg, dArg, Lys, dLys, His, dHis, ornithine (Orn), D-ornithine (dOrn), D-leucine (dLeu), D-tyrosine (dTyr), phenylalanine (Phe), D-phenylalanine (dPhe), tryptophan (Trp), D-tryptophan (dTrp), aspartic acid (Asp), cysteine (Cys), and D-cysteine (dCys);

$R^2$ is selected from the group consisting of Asp, D-aspartic acid (dAsp), Cys, dCys, D-penicillamine (dPen), Ala, Trp, Phe, dPhe, His, dHis, Tyr, and dTyr;

$R^3$ is absent or is selected from the group consisting of His, Ala, proline (Pro), hydroxyproline (Hyp), leucine (Leu), D-glutamine (dGln), Phe, dPhe, Trp, dTrp, Tyr, dTyr, 2-aminotetraline-2-carboxylic acid (Atc), octohydroindole-2-carboxylic acid (Oic), 1-amino-1-cyclohexanecarboxylic acid (Che), tetrahydro-isoquinoline-3-carboxylic acid (Tic), 1-amino-1-cyclopentane carboxylic (Cpe), and biphenylalanine (Bip);

$R^4$ is selected from the group consisting of dPhe, para-chloro-D-phenylalanine (p(Cl)dPhe), para-bromo-D-phenylalanine (p(Br)dPhe), and para-fluoro-D-phenylalanine (p(F)dPhe);

$R^5$ is Arg or His;

$R^6$ is selected from the group consisting of Trp, dTrp, Phe, dNal(2'), 2'-naphthylalanine (Nal(2')), and 1'-naphthylalanine (Nal(1'));

$R^7$ is selected from the group consisting of Gly, Pro, Lys, dLys, Cys, dCys, penicillamine (Pen), dPen, and Orn;

$R^8$ is absent or Lys;

$Y^1$ is selected from the group consisting of valine (Val), D-valine (dVal), $\beta^2$-valine ($\beta^2$-Val), $\beta^3$-valine ($\beta^3$-Val), Pro, D-proline (dPro), β-proline (β-Pro), Hyp, D-hydroxyproline (dHyp), D-tert-leucine (dTle), dLeu, Trp, Arg, dArg, Lys, dLys, Gly, Ala, dAla, Asp, dAsp, asparagine (Asn), D-asparagine (dAsn), and D-threonine (dThr);

$Y^2$ is absent or is selected from the group consisting of Val, dVal, $\beta^2$-Val, $\beta^3$-Val, Pro, dPro, β-Pro, Hyp, dHyp, dTle, Arg, dArg, Gly, Ala, dAla, Asp, and dAsn;

$Y^3$ is absent or is selected from the group consisting of Val, dVal, Pro, dPro, dThr, Lys, and dLys;

$Y^4$ is absent or is selected from the group consisting of dVal, dPro, Asp, and dAsp; and

the non-naturally occurring melanocortin analog is cyclized through a moiety selected from the group consisting of:

a disulfide bond between $R^1$ or $R^2$ and $R^7$ or $R^8$ when each of $R^1$ or $R^2$ and $R^7$ or $R^8$ are independently selected from the group consisting of Cys, dCys, and dPen;

a disulfide bond between $R^2$ and $R^7$ when $R^2$ is Cys,$R^7$ is Pen, and $R^3$ is absent;

a lactam bridge between $R^1$ or $R^2$ and $R^7$ or $R^8$ when $R^1$ or $R^2$ is Asp and $R^7$ or $R^8$ is Lys or Orn; and

a lactam bridge between $R^2$ and $R^7$ when $R^2$ is dAsp and $R^7$ is dLys;

provided that:

when $R^4$ is p(F)dPhe, then (i) $R^3$ is selected from Pro, dGln, dTyr, $R^6$ is Trp, and the non-naturally occurring melanocortin analog is not cyclized between Cys at $R^2$ and Cys at $R^7$ or (ii) $R^3$ is His and either $R^6$ is Nal(2') or the non-naturally occurring melanocortin analog is cyclized through a disulfide bond between $R^2$ and $R^7$, where $R^2$ and $R^7$ are the same;

when $R^4$ is p(Br)dPhe, then the non-naturally occurring melanocortin analog is cyclized through a disulfide bond between dCys at $R^2$ and Cys or dCys at $R^7$;

when $R^4$ is dPhe, then (i) $R^3$ is not His, Pro, or absent, (ii) $R^3$ is His and either $R^2$ is Phe or dAla or $R^2$ is Ala and $X^1$ is Arg or dArg, (iii) $R^3$ is Pro and (a) $R^2$ is Trp, and $R^5$ is not His or $R^6$ is not Phe or (b) $R^2$ is not Trp or Pro, and either $R^5$ is not dNal(2') or Nal(2') or $X^1$ and $Y^3$ are not both present, or (iv) $R^3$ is absent and $R^2$ and $R^7$ are not both dPen; and

when $R^4$ is p(Cl)dPhe, then (i) $R^3$ is selected from Aba, Aia, and Ata or (ii) $R^3$ is His, $R^1$ is not Ala, and (a) if $R^1$ is Nle and $Y^1Y^2$ is dVal-dPro, then $X^1$ is absent and the non-naturally occurring melanocortin analog is cyclized through a disulfide bond between dCys at $R^2$ and dCys at $R^7$, or (b) if $R^1$ is Nle, and $Y^1Y^2$ is not dVal-dPro, then either $X^1$ or $Y^3$ is present.

52. The method or the use of any one of claims 1-50, wherein the non-naturally occurring melanocortin analog comprises a sequence according to Formula (IA), wherein:
$X^1$ is absent or is selected from the group consisting of norleucine (Nle), arginine (Arg), D-arginine (dArg), alanine (Ala), lysine (Lys), D-lysine (dLys), histidine (His), D-histidine (dHis);

$X^2$ is absent, phenylalanine (Phe), or Nle;

$X^3$ is absent, Phe, or Nle;

$R^1$ is selected from the group consisting of Nle, D-norleucine (dNle), Ala, D-alanine (dAla), Arg, dArg, Lys, dLys, His, dHis, ornithine (Orn), D-ornithine (dOrn), D-leucine (dLeu), D-tyrosine (dTyr), phenylalanine (Phe), D-phenylalanine (dPhe), tryptophan (Trp), D-tryptophan (dTrp), aspartic acid (Asp), cysteine (Cys), and D-cysteine (dCys);

$R^2$ is selected from the group consisting of Asp, D-aspartic acid (dAsp), Cys, dCys, D-penicillamine (dPen), Ala, Trp, Phe, dPhe, His, dHis, Tyr, and dTyr;

$R^3$ is absent or is selected from the group consisting of His, Ala, proline (Pro), hydroxyproline (Hyp), leucine (Leu), D-glutamine (dGln), Phe, dPhe, Trp, dTrp, Tyr, dTyr, 2-aminotetraline-2-carboxylic acid (Atc), octohydroindole-2-carboxylic acid (Oic), 1-amino-1-cyclohexanecarboxylic acid (Che), tetrahydro-isoquinoline-3-carboxylic acid (Tic), 1-amino-1-cyclopentane carboxylic (Cpe), and biphenylalanine (Bip);

$R^4$ is selected from the group consisting of dPhe, para-chloro-D-phenylalanine (p(Cl)dPhe), para-bromo-D-phenylalanine (p(Br)dPhe), and para-fluoro-D-phenylalanine (p(F)dPhe);

$R^5$ is Arg or His;

$R^6$ is selected from the group consisting of Trp, dTrp, Phe, dNal(2'), 2'-naphthylalanine (Nal(2')), and 1'-naphthylalanine (Nal(1'));

$R^7$ is selected from the group consisting of Gly, Pro, Lys, dLys, Cys, dCys, penicillamine (Pen), dPen, and Orn;

$R^8$ is absent or Lys;

$Y^1$ is selected from the group consisting of valine (Val), D-valine (dVal), $\beta^2$-valine ($\beta^2$-Val), $\beta^3$-valine ($\beta^3$-Val), Pro, D-proline (dPro), β-proline (β-Pro), Hyp, D-hydroxyproline (dHyp), D-tert-leucine (dTle), dLeu, Trp, Arg, dArg, Lys, dLys, Gly, Ala, dAla, Asp, dAsp, asparagine (Asn), D-asparagine (dAsn), and D-threonine (dThr);

$Y^2$ is absent or is selected from the group consisting of Val, dVal, $\beta^2$-Val, $\beta^3$-Val, Pro, dPro, β-Pro, Hyp, dHyp, dTle, Arg, dArg, Gly, Ala, dAla, Asp, and dAsn;

$Y^3$ is absent or is selected from the group consisting of Val, dVal, Pro, dPro, dThr, Lys, and dLys;

$Y^4$ is absent or is selected from the group consisting of dVal, dPro, Asp, and dAsp; and

the non-naturally occurring melanocortin analog is cyclized through a moiety selected from the group consisting of:

a disulfide bond between $R^1$ or $R^2$ and $R^7$ or $R^8$ when each of $R^1$ or $R^2$ and $R^7$ or $R^8$ are independently selected from the group consisting of Cys, dCys, and dPen;

a disulfide bond between $R^2$ and $R^7$ when $R^2$ is Cys, $R^7$ is Pen, and $R^3$ is absent;

a lactam bridge between $R^1$ or $R^2$ and $R^7$ or $R^8$ when $R^1$ or $R^2$ is Asp and $R^7$ or $R^8$ is Lys or Orn; and

a lactam bridge between $R^2$ and $R^7$ when $R^2$ is dAsp and $R^7$ is dLys;

provided that the non-naturally occurring melanocortin analog does not comprise a sequence selected from the group consisting of:

Ac-Nle-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 223);

Ac-Arg-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 464);

Ac-Lys-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 465);

Ac-dLys-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 466);

Ac-His-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 467);

Ac-dHis-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 468);

Ac-Nle-Nle-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 469);

Ac-Nle-c[Asp-His-p(F)dPhe-His-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 470);

Ac-Nle-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dVal-dVal-dVal-dPro-$NH_2$ (SEQ ID NO: 474);

Ac-Nle-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dPro-dVal-dPro-$NH_2$ (SEQ ID NO: 475);

Ac-Nle-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dTle-dPro-$NH_2$ (SEQ ID NO: 476);

Ac-Nle-Nle-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dTle-dPro-$NH_2$ (SEQ ID NO: 477);

Ac-Nle-Nle-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dPro-dVal-dPro-$NH_2$ (SEQ ID NO: 478);

Ac-Arg-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dTle-dPro-$NH_2$ (SEQ ID NO: 481);

Ac-Lys-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dTle-dPro-$NH_2$ (SEQ ID NO: 482);

Ac-dLys-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dTle-dPro-$NH_2$ (SEQ ID NO: 483);

Ac-His-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dTle-dPro-$NH_2$ (SEQ ID NO: 484);

Ac-dHis-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dTle-dPro-$NH_2$ (SEQ ID NO: 485);

Ac-dArg-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 463);

Ac-Ala-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 462);

Ac-Ala-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dTle-dPro-$NH_2$ (SEQ ID NO: 479);

Ac-Nle-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dTle-dTle-dVal-$NH_2$ (SEQ ID NO: 473);

Ac-dArg-c[Asp-His-p(F)dPhe-Arg-Trp-Lys]-dTle-dPro-$NH_2$ (SEQ ID NO: 480);

Ac-Nle-c[Asp-Bip-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 489);

Ac-Nle-c[Asp-Trp-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 493);

Ac-Nle-c[Asp-Pro-p(F)dPhe-Arg-dNal(2')-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 444);

Ac-Nle-c[Asp-Pro-p(F)dPhe-Arg-Nal(2')-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 445);

Ac-Nle-c[Asp-Tyr-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 495);

Ac-Nle-c[Asp-Phe-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 487);

Ac-Nle-c[Asp-dPhe-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 488);

Ac-Nle-c[Asp-dTrp-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 494);

Ac-Nle-c[Asp-His-p(F)dPhe-Arg-dNal(2')-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 471);

Ac-Nle-c[Cys-Pro-p(F)dPhe-Arg-Trp-Cys]-dVal-dPro-$NH_2$ (SEQ ID NO: 432);

Ac-Nle-c[dCys-His-p(F)dPhe-Arg-Trp-Cys]-dVal-dPro-$NH_2$ (SEQ ID NO: 460);

Ac-Nle-c[Asp-Pro-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 217);

Ac-Nle-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 222);

Ac-Nle-c[Cys-His-p(Br)dPhe-Arg-Trp-Cys]-dVal-dPro-$NH_2$ (SEQ ID NO: 535);

Ac-Ala-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 538);

Ac-Nle-Nle-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 545);

Ac-Nle-c[Asp-His-p(Br)dPhe-His-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 546);

Ac-Nle-c[Asp-His-p(Br)dPhe-Arg-dNal(2')-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 547);

Ac-Nle-c[Asp-His-p(Br)dPhe-Arg-Nal(2')-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 548);

Ac-Nle-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dTle-dTle-dVal-$NH_2$ (SEQ ID NO: 549);

Ac-Nle-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dPro-dVal-dPro-$NH_2$ (SEQ ID NO: 551);

Ac-Nle-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dTle-dPro-$NH_2$ (SEQ ID NO: 552);

Ac-Nle-Nle-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dTle-dPro-$NH_2$ (SEQ ID NO: 553);

Ac-Ala-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dTle-dPro-$NH_2$ (SEQ ID NO: 555);

Ac-Nle-c[Asp-Phe-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 563);

Ac-Nle-c[Asp-dPhe-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 564);

Ac-Nle-c[Asp-Bip-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 565);

Ac-Nle-c[Asp-dGln-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 568);

Ac-Nle-c[Asp-Trp-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 569);

Ac-Nle-c[Asp-dTrp-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 570);

Ac-Nle-c[Asp-Tyr-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 571);

Ac-Nle-c[Asp-dTyr-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 572);

Ac-dArg-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 539);

Ac-dHis-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 544);

Ac-dHis-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dTle-dPro-$NH_2$ (SEQ ID NO: 561);

Ac-dArg-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dTle-dPro-$NH_2$ (SEQ ID NO: 556);

Ac-dLys-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 542);

Ac-His-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dTle-dPro-$NH_2$ (SEQ ID NO: 560);

Ac-His-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 543);

Ac-dLys-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dTle-dPro-$NH_2$ (SEQ ID NO: 559);

Ac-Arg-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dTle-dPro-$NH_2$ (SEQ ID NO: 557);

Ac-Lys-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 541);

Ac-Nle-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dVal-dVal-dVal-dPro-$NH_2$ (SEQ ID NO: 550);

Ac-Lys-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dTle-dPro-$NH_2$ (SEQ ID NO: 558);

Ac-Arg-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 540);

Ac-Nle-Nle-c[Asp-His-p(Br)dPhe-Arg-Trp-Lys]-dPro-dVal-dPro-$NH_2$ (SEQ ID NO: 554);

Ac-Nle-c[Asp-His-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 363);

Ac-Nle-c[Asp-His-dPhe-Arg-Trp-Pro-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 418);

Ac-Nle-c[Asp-His-dPhe-Arg-Trp-Lys]-dPro-dVal-$NH_2$ (SEQ ID NO: 621);

Ac-Nle-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dPro-dVal-dPro-$NH_2$ (SEQ ID NO: 639);

Ac-Nle-c[dPen-dPhe-Arg-Trp-dPen]-dVal-dPro-$NH_2$ (SEQ ID NO: 326);

Ac-Nle-c[Asp-Trp-Pro-dPhe-His-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 398);

Ac-Nle-c[Asp-Trp-Pro-dPhe-Arg-Phe-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 401);

Ac-Nle-c[Asp-Pro-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 225);

Ac-Nle-c[Asp-Pro-dPhe-Arg-dNal(2')-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 430);

Ac-Nle-c[Asp-Pro-dPhe-Arg-Nal(2')-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 431);

Ac-Nle-c[Asp-Ala-His-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 380);

Ac-Nle-c[Asp-Pro-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 215);

Ac-Nle-c[Asp-Phe-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 525);

Ac-Nle-c[Asp-dPhe-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 526);

Ac-Nle-c[Asp-Bip-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 527);

Ac-Nle-c[Asp-Trp-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 531);

Ac-Nle-c[Asp-Tyr-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 533);

Ac-Nle-c[Asp-dTyr-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 534);

Ac-Nle-c[Asp-dTrp-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 532);

Ac-Nle-c[dCys-His-p(Cl)dPhe-Arg-Trp-Cys]-dVal-dPro-$NH_2$ (SEQ ID NO: 498);

Ac-Nle-c[Cys-His-p(Cl)dPhe-Arg-Trp-Cys]-dVal-dPro-$NH_2$ (SEQ ID NO: 497);

Ac-Nle-c[Asp-His-p(Cl)dPhe-Arg-dNal(2')-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 509);

Ac-Nle-c[Asp-His-p(Cl)dPhe-Arg-Nal(2')-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 510);

Ac-Nle-c[Asp-His-p(Cl)dPhe-His-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 508);

Ac-Nle-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 220);

Ac-Nle-Nle-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 507);

Ac-Ala-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dTle-dPro-$NH_2$ (SEQ ID NO: 517);

Ac-Ala-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 500);

Ac-Nle-Nle-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dPro-dVal-dPro-$NH_2$ (SEQ ID NO: 516); and

Ac-Nle-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dTle-dPro-$NH_2$ (SEQ ID NO: 514).

53. The method or use of any one of claims 1-49, wherein the non-naturally occurring melanocortin analog comprises a sequence of Formula (IB):

$X^1$-$X^2$-$X^3$-$R^1$-$R^2$-Pro-$R^4$-$R^5$-$R^6$-$R^7$-$R^8$-$Y^1$-$Y^2$-$Y^3$-$Y^4$-$Y^5$-$Y^6$-$Y^7$ (IB),

wherein:

$X^1$ is absent or norleucine (Nle);

$X^2$ is absent or Nle;

$X^3$ is absent or Nle;

$R^1$ is selected from the group consisting of Nle, D-norleucine (dNle), alanine (Ala), D-alanine (dAla), arginine (Arg), D-arginine (dArg), lysine (Lys), D-lysine (dLys), histidine (His), D-histidine (dHis), ornithine (Orn), D-ornithine (dOrn), D-leucine (dLeu), D-tyrosine (dTyr), phenylalanine (Phe), D-phenylalanine (dPhe), tryptophan (Trp), and D-tryptophan (dTrp);

$R^2$ is selected from the group consisting of aspartic acid (Asp), D-aspartic acid (dAsp), cysteine (Cys), D-cysteine (dCys), and D-penicillamine (dPen);

$R^4$ is dPhe or para-fluoro-D-phenylalanine (p(F)dPhe);

$R^5$ is selected from the group consisting of Arg, His, *cis*Pro(guan), and *trans*Pro(guan);

$R^6$ is selected from the group consisting of Trp, dTrp, Phe, Aia, Aba, Ata, and 1'-naphthylalanine (Nal(1')));

$R^7$ is selected from the group consisting of Gly, Lys, dLys, Cys, dCys, dPen, and Orn;

$R^8$ is absent or Lys;

$Y^1$ is absent or is selected from the group consisting of valine (Val), D-valine (dVal), $\beta^2$-valine ($\beta^2$-Val), $\beta^3$-valine ($\beta^3$-Val), Pro, D-proline (dPro), β-proline (β-Pro), Hyp, D-hydroxyproline (dHyp), D-tert-leucine (dTle), dLeu, Trp, Arg, dArg, Lys, dLys, Gly, Ala, dAla, Asp, dAsp, asparagine (Asn), D-asparagine (dAsn), and D-threonine (dThr);

$Y^2$ is absent or is selected from the group consisting of Val, dVal, $\beta^2$-Val, $\beta^3$-Val, Pro, dPro, β-Pro, Hyp, dHyp, dTle, Arg, dArg, Gly, Ala, dAla, Asp, and dAsn;

$Y^3$ is absent or is selected from the group consisting of Val, dVal, Pro, dPro, dThr, Lys, and dLys;

$Y^4$ is absent or is selected from the group consisting of dVal, dPro, Asp, and dAsp;

$Y^5$ is absent or dVal;

$Y^6$ is absent or dVal;

$Y^7$ is absent or dPro; and

the non-naturally occurring melanocortin analog is cyclized through a moiety selected from the group consisting of:

a disulfide bond between $R^2$ and $R^7$ when each of $R^2$ and $R^7$ are independently selected from the group consisting of Cys, dCys, and dPen; and

a lactam bridge between $R^2$ and $R^7$ when $R^2$ is Asp or dAsp and $R^7$ is Lys, dLys, or Orn;

provided that:

when $R^4$ is p(F)dPhe, then the non-naturally occurring melanocortin analog is not cyclized between Cys at $R^2$ and Cys at $R^7$; and

when $R^4$ is dPhe and one or more of $X^1$, $X^2$, and $X^3$ is present, then $Y^3$-$Y^7$ are absent.

54. The method or use of any one of claims 1-50, wherein the non-naturally occurring melanocortin analog comprises a sequence of Formula (IB), wherein:

$X^1$-$X^2$-$X^3$-$R^1$-$R^2$-Pro-$R^4$-$R^5$-$R^6$-$R^7$-$R^8$-$Y^1$-$Y^2$-$Y^3$-$Y^4$-$Y^5$-$Y^6$-$Y^7$ (IB),

wherein:

$X^1$ is absent or norleucine (Nle);

$X^2$ is absent or Nle;

$X^3$ is absent or Nle;

$R^1$ is selected from the group consisting of Nle, D-norleucine (dNle), alanine (Ala), D-alanine (dAla), arginine (Arg), D-arginine (dArg), lysine (Lys), D-lysine (dLys), histidine (His), D-histidine (dHis), ornithine (Orn), D-ornithine (dOrn), D-leucine (dLeu), D-tyrosine (dTyr), phenylalanine (Phe), D-phenylalanine (dPhe), tryptophan (Trp), and D-tryptophan (dTrp);

$R^2$ is selected from the group consisting of aspartic acid (Asp), D-aspartic acid (dAsp), cysteine (Cys), D-cysteine (dCys), and D-penicillamine (dPen);

$R^4$ is dPhe or para-fluoro-D-phenylalanine (p(F)dPhe);

$R^5$ is selected from the group consisting of Arg, His, *cis*Pro(guan), and *trans*Pro(guan);

$R^6$ is selected from the group consisting of Trp, dTrp, Phe, Aia, Aba, Ata, and 1'-naphthylalanine (Nal(1'));

$R^7$ is selected from the group consisting of Gly, Lys, dLys, Cys, dCys, dPen, and Orn;

$R^8$ is absent or Lys;

$Y^1$ is absent or is selected from the group consisting of valine (Val), D-valine (dVal), $\beta^2$-valine ($\beta^2$-Val), $\beta^3$-valine ($\beta^3$-Val), Pro, D-proline (dPro), β-proline (β-Pro), Hyp, D-hydroxyproline (dHyp), D-tert-leucine (dTle), dLeu, Trp, Arg, dArg, Lys, dLys, Gly, Ala, dAla, Asp, dAsp, asparagine (Asn), D-asparagine (dAsn), and D-threonine (dThr);

$Y^2$ is absent or is selected from the group consisting of Val, dVal, $\beta^2$-Val, $\beta^3$-Val, Pro, dPro, β-Pro, Hyp, dHyp, dTle, Arg, dArg, Gly, Ala, dAla, Asp, and dAsn;

$Y^3$ is absent or is selected from the group consisting of Val, dVal, Pro, dPro, dThr, Lys, and dLys;

$Y^4$ is absent or is selected from the group consisting of dVal, dPro, Asp, and dAsp;

$Y^5$ is absent or dVal;

$Y^6$ is absent or dVal;

$Y^7$ is absent or dPro; and

the non-naturally occurring melanocortin analog is cyclized through a moiety selected from the group consisting of:

a disulfide bond between $R^2$ and $R^7$ when each of $R^2$ and $R^7$ are independently selected from the group consisting of Cys, dCys, and dPen; and

a lactam bridge between $R^2$ and $R^7$ when $R^2$ is Asp or dAsp and $R^7$ is Lys, dLys, or Orn;

provided that the non-naturally occurring melanocortin analog does not comprise a sequence of:

Ac-Nle-c[Cys-Pro-p(F)dPhe-Arg-Trp-Cys]-dVal-dPro-$NH_2$ (SEQ ID NO: 432); or

Ac-Nle-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dPro-dVal-dPro-$NH_2$ (SEQ ID NO: 639).

55. The method or use of any one of claims 1-49, wherein the non-naturally occurring melanocortin analog comprises a sequence of Formula (IC):

$X^1$-$X^2$-$R^1$-$R^2$-Pro-dPhe-$R^5$-$R^6$-$R^7$-$Y^1$-$Y^2$-$Y^3$-$Y^4$ (IC),

wherein:

$X^1$ is selected from the group consisting of norleucine (Nle), arginine (Arg), D-arginine (dArg), alanine (Ala), lysine (Lys), D-lysine (dLys), histidine (His), D-histidine (dHis);

$X^2$ is absent or Nle;

$R^1$ is selected from the group consisting of aspartic acid (Asp), cysteine (Cys), and D-cysteine (dCys);

$R^2$ is selected from the group consisting of tryptophan (Trp), phenylalanine (Phe), D-phenylalanine (dPhe), histidine (His), D-histidine (dHis), tyrosine (Tyr), and D-tyrosine (dTyr);

$R^5$ is Arg;

$R^6$ is selected from the group consisting of Trp, 2'-D-naphthylalanine (dNal(2')), 2'-naphthylalanine (Nal(2')), and 1'-naphthylalanine (Nal(1'));

$R^7$ is selected from the group consisting of Lys, Cys, and dCys;

$Y^1$ is absent or is selected from the group consisting of D-valine (dVal), D-tert-leucine (dTle), dArg, and dLys;

$Y^2$ is absent or is selected from the group consisting of dVal, dPro, and D-hydroxyproline (dHyp);

$Y^3$ is absent, dVal, or dPro;

$Y^4$ is absent or dPro; and

the non-naturally occurring melanocortin analog is cyclized through a moiety selected from the group consisting of:

a disulfide bond between $R^1$ and $R^7$ when both of $R^1$ and $R^7$ are independently selected from the group consisting of Cys, dCys, and dPen; and

a lactam bridge between $R^1$ and $R^7$ when $R^1$ is Asp and $R^7$ is Lys.

56. The method or use of any one of claims 1-49, wherein the non-naturally occurring melanocortin analog comprises a sequence of Formula (ID):

$X^1$-$R^1$-$R^2$-$R^3$-p(Cl)dPhe-Arg-Trp-$R^7$-$Y^1$-$Y^2$-$Y^3$-$Y^4$ (ID),

wherein:

$X^1$ is absent or norleucine (Nle);

$R^1$ is selected from the group consisting of Nle, arginine (Arg), D-arginine (dArg), lysine (Lys), D-lysine (dLys), histidine (His), and D-histidine (dHis);

$R^2$ is aspartic acid (Asp) or D-cysteine (dCys);

$R^3$ is selected from the group consisting of His, 4-amino-1,2,4,5-tetrahydro-2-benzazepin-3-one (Aba), 7-amino-7,8-dihydro-4H-[1,2,3]triazolo-[1,5-a][1,4]diazepin-6(5H)-one (Ata), and 4-amino-1,4,5,6-tetrahydroazepino[4,3-*b*]indol-3(*2H*)-one (Aia);

$R^7$ is Lys or dCys;

$Y^1$ is selected from the group consisting of D-valine (dVal), D-proline (dPro), and D-tert-leucine (dTle);

$Y^2$ is absent or is selected from the group consisting of dVal, dPro, and dTle;

$Y^3$ is absent, dVal, or dPro;

$Y^4$ is absent or dPro; and

the non-naturally occurring melanocortin analog is cyclized through a moiety selected from the group consisting of:

a disulfide bond between $R^2$ and $R^7$ when both of $R^2$ and $R^7$ are dCys; and

a lactam bridge between $R^2$ and $R^7$ when $R^2$ is Asp and $R^7$ is Lys;

provided that when $R^3$ is His and $R^1$ is Nle, then (i) $Y^1Y^2$ is dVal-dPro, $X^1$ is absent, and the non-naturally occurring melanocortin analog is cyclized through a disulfide bond, or (b) $Y^1Y^2$ is not dVal-dPro and either $X^1$ or $Y^3$ is present.

57. The method or use of any one of claims 1-50, wherein the non-naturally occurring melanocortin analog comprises a sequence of Formula (ID), wherein:
$X^1$ is absent or norleucine (Nle);

$R^1$ is selected from the group consisting of Nle, arginine (Arg), D-arginine (dArg), lysine (Lys), D-lysine (dLys), histidine (His), and D-histidine (dHis);

$R^2$ is aspartic acid (Asp) or D-cysteine (dCys);

$R^3$ is selected from the group consisting of His, 4-amino-1,2,4,5-tetrahydro-2-benzazepin-3-one (Aba), 7-amino-7,8-dihydro-4H-[1,2,3]triazolo-[1,5-a][1,4]diazepin-6(5H)-one (Ata), and 4-amino-1,4,5,6-tetrahydroazepino[4,3-*b*]indol-3(*2H*)-one (Aia);

$R^7$ is Lys or dCys;

$Y^1$ is selected from the group consisting of D-valine (dVal), D-proline (dPro), and D-tert-leucine (dTle);

$Y^2$ is absent or is selected from the group consisting of dVal, dPro, and dTle;

$Y^3$ is absent, dVal, or dPro;

$Y^4$ is absent or dPro; and

the non-naturally occurring melanocortin analog is cyclized through a moiety selected from the group consisting of:

a disulfide bond between $R^2$ and $R^7$ when both of $R^2$ and $R^7$ are dCys; and

a lactam bridge between $R^2$ and $R^7$ when $R^2$ is Asp and $R^7$ is Lys;

provided that the non-naturally occurring melanocortin analog does not comprise a sequence selected from the group consisting of:

Ac-Nle-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 220);

Ac-Nle-Nle-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 507);

Ac-Nle-Nle-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dPro-dVal-dPro-$NH_2$ (SEQ ID NO: 516);

Ac-Nle-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dTle-dPro-$NH_2$ (SEQ ID NO: 514); and.

58. The method or the use of any one of claims 1-57, wherein an N-terminus of the non-naturally occurring melanocortin analog is modified by an acyl group.

59. The method or the use of claim 58, wherein the acyl group is an acetyl group.

60. The method or the use of any one of claims 1-57, wherein an N-terminus of the non-naturally occurring melanocortin analog is not modified.

61. The method or the use of any one of claims 1-60, wherein a C-terminus of the non-naturally occurring melanocortin analog is modified by an amide group.

62. The method or the use of any one of claims 1-60, wherein a C-terminus of the non-naturally occurring melanocortin analog is not modified.

63. The method or the use of any one of claims 1-67, wherein $Y^1$-$Y^2$ are present and $Y^3$- $Y^8$ are absent.

64. The method or the use of any one of claims 1-63, wherein $Y^1$ is D-valine and $Y^2$ is D-proline.

65. The method or the use of any one of claims 1-63, w wherein $Y^1$ is D-tert-leucine and $Y^2$ is D-proline.

66. The method or the use of any one of claims 1-62, wherein $R^4$ is dNal(2').

67. The method or the use of claim 66, wherein the sequence of Formula (I) is: Ac-Nle-$_c$[Asp-His-dNal(2')-Arg-Trp-Pro-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 8), wherein c represents cyclization through $R^2$ and $R^8$ via a lactam bond.

68. The method or the use of any one of claims 1-62, wherein $R^4$ is Phe or dPhe.

69. The method or the use of claim 68, wherein the sequence of any one of Formulae (I)-(ID) is selected from the group consisting of:

Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-OH (SEQ ID NO: 291);

Ac-Nle-c[Asp-Pro-Phe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 294);

Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 295; E2); and

Ac-Nle-c[Asp-Pro-His-Phe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 296).

wherein c represents cyclization through $R^2$ and $R^7$ via a lactam bond.

70. The method or the use of any one of claims 1-62, wherein the sequence of any one of Formulae (I)-(ID) is selected from the group consisting of:

Ac-dLeu-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO:298);

Ac-dAla-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 299);

Ac-Ala-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro- $NH_2$ (SEQ ID NO: 300);

Ac-dNle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 301);

Ac-dArg-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 302);

Ac-dPhe-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 303);

Ac-dTyr-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 304);

Phe-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 305);

His-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 306);

Trp-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 307);

dPhe-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 308);

dHis-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 309);

dTrp-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 310);

Ac-Arg-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 311);

Ac-dLys-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 312);

Ac-Lys-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 313);

Ac-His-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 314);

Ac-dHis-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 315);

Ac-Orn-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 316); and

Ac-dOrn-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 317),

wherein c represents cyclization through $R^2$ and $R^7$ via a lactam bond.

71. The method or the use of any one of claims 1-62, wherein the sequence of any one of Formulae (I)-(ID) is selected from the group consisting of:

Ac-Nle-c[Cys-Pro-dPhe-Arg-Trp-Cys]-dVal-dPro-$NH_2$ (SEQ ID NO: 318);

Ac-Nle-c[dCys-Pro-dPhe-Arg-Trp-Cys]-dVal-dPro-$NH_2$ (SEQ ID NO: 319);

Ac-Nle-c[dPen-Pro-dPhe-Arg-Trp-dPen]-dVal-dPro-$NH_2$ (SEQ ID NO: 320);

Ac-Nle-c[dCys-Pro-dPhe-Arg-Trp-dCys]-dVal-dPro-$NH_2$ (SEQ ID NO: 321);

Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Orn]-dVal-dPro-$NH_2$ (SEQ ID NO: 322); and

Ac-Nle-c[Cys-dPhe-Arg-Trp-Pen]-dVal-dPro-$NH_2$ (SEQ ID NO: 324),

wherein c represents cyclization through $R^2$ and $R^7$ via a disulfide bond.

72. The method or the use of any one of claims 1-62, wherein the sequence of any one of Formulae (I)-(ID) is selected from the group consisting of:

Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Gly-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 351);

Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Gly-Lys]-dPro-dPro-Lys-Asp-$NH_2$ (SEQ ID NO: 352); and

Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Gly-Lys]-dPro-dPro-dLys-dAsp-$NH_2$ (SEQ ID NO: 353),

wherein c represents cyclization through $R^2$ and $R^8$ via a lactam bond.

73. The method or the use of any one of claims 1-62, wherein the sequence of any one of Formulae (I)-(ID) is selected from the group consisting of:

Ac-Nle-c[Asp-Ala-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 354);

Ac-Nle-c[Asp-Leu-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 355);

Ac-Nle-c[Asp-Cpe-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 358);

Ac-Nle-c[Asp-Che-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 359);

Ac-Nle-c[Asp-Oic-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 360);

Ac-Nle-c[Asp-Ioc-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 361);

Ac-Nle-c[Asp-Tic-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 362);

Ac-Nle-c[Asp-Hyp-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 364);

Ac-Nle-c[Asp-Phe-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 366);

Ac-Nle-c[Asp-dPhe-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 367);

Ac-Nle-c[Asp-Bip-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 368);

Ac-Nle-c[Asp-dGln-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 371);

Ac-Nle-c[Asp-Trp-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 372);

Ac-Nle-c[Asp-dTrp-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 373);

Ac-Nle-c[Asp-Tyr-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 374);

Ac-Nle-c[Asp-dTyr-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 375);

Ac-Nle-c[Asp-Aba-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 198);

Ac-Nle-c[Asp-Aia-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 207);

Ac-Nle-c[Asp-Ata-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 208);

Ac-Nle-c[Asp-Atc-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 212);

Ac-Nle-c[Asp-APC-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 213); and

Ac-Nle-c[Asp-APPC-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 214),

wherein c represents cyclization through $R^2$ and $R^7$ via a lactam bond.

74. The method or the use of any one of claims 1-62, wherein the sequence of any one of Formulae (I)-(ID) is selected from the group consisting of:

Ac-Arg-c[Asp-dAla-His-dPhe-Arg-Trp-Lys]-$NH_2$ (SEQ ID NO: 281);

Ac-Arg-c[Asp-Ala-His-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 381); and

Ac-dArg-c[Asp-Ala-His-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 382),

wherein c represents cyclization through $R^1$ and $R^7$ via a lactam bond.

75. The method or the use of any one of claims 1-62, wherein the sequence of any one of Formulae (I)-(ID) is selected from the group consisting of:

Ac-Nle-c[Asp-Trp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 226);

Ac-Nle-c[Cys-Trp-Pro-dPhe-Arg-Trp-Cys]-dVal-dPro-$NH_2$ (SEQ ID NO: 383);

Ac-Nle-c[dCys-Trp-Pro-dPhe-Arg-Trp-Cys]-dVal-dPro-$NH_2$ (SEQ ID NO: 384);

Ac-Nle-c[dCys-Trp-Pro-dPhe-Arg-Trp-dCys]-dVal-dPro-$NH_2$ (SEQ ID NO: 385);

Ac-Ala-c[Asp-Trp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 386);

Ac-Lys-c[Asp-Trp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 387);

Ac-dLys-c[Asp-Trp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 388);

Ac-Arg-c[Asp-Trp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 389);

Ac-dArg-c[Asp-Trp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 390);

Ac-dHis-c[Asp-Trp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 391);

Ac-His-c[Asp-Trp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 392);

Ac-Nle-Nle-c[Asp-Trp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 393);

Ac-Nle-c[Asp-Trp-Ala-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 394);

Ac-Nle-c[Asp-Trp-Leu-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 395);

Ac-Nle-c[Asp-Trp-Pro-dPhe-Arg-Nal(1']-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 399);

Ac-Nle-c[Asp-Trp-Pro-dPhe-Arg-dNal(2')-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 403);

Ac-Nle-c[Asp-Trp-Pro-dPhe-Arg-Nal(2')-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 404);

Ac-Nle-c[Asp-Trp-Pro-dPhe-Arg-Trp-Lys]-dArg-dVal-dPro-$NH_2$ (SEQ ID NO: 405);

Ac-Nle-c[Asp-Trp-Pro-dPhe-Arg-Trp-Lys]-dLys-dVal-dPro-$NH_2$ (SEQ ID NO: 406);

Ac-Nle-c[Asp-Trp-Pro-dPhe-Arg-Trp-Lys]-dArg-dPro-$NH_2$ (SEQ ID NO: 407);

Ac-Nle-c[Asp-Trp-Pro-dPhe-Arg-Trp-Lys]-dLys-dPro-$NH_2$ (SEQ ID NO: 408);

Ac-Nle-c[Asp-Trp-Pro-dPhe-Arg-Trp-Lys]-dVal-dHyp-$NH_2$ (SEQ ID NO: 409);

Ac-Nle-c[Asp-Trp-Pro-dPhe-Arg-Trp-Lys]-dTle-dPro-$NH_2$ (SEQ ID NO: 410);

Ac-Nle-c[Asp-Trp-Pro-dPhe-Arg-Trp-Lys]-dVal-dVal-dVal-dPro-$NH_2$ (SEQ ID NO: 411);

Ac-Nle-c[Asp-Phe-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 412);

Ac-Nle-c[Asp-His-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 413);

Ac-Nle-c[Asp-Tyr-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 414);

Ac-Nle-c[Asp-dPhe-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 415);

Ac-Nle-c[Asp-dHis-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 416); and

Ac-Nle-c[Asp-dTyr-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 417),

wherein c represents cyclization through $R^1$ and $R^7$ via a lactam bond or a disulfide bond.

76. The method or the use of any one of claims 1-62, wherein the sequence of any one of Formulae (I)-(ID) is: Ac-Nle-c[Asp-Hyp-dPhe-Arg-Trp-Pro-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 419), wherein c represents cyclization through $R^2$ and $R^8$ via a lactam bond.

77. The method or the use of any one of claims 1-62, wherein the sequence of any one of Formulae (I)-(ID) is selected from the group consisting of:

Ac-Nle-Phe-Phe-c[Asp-Phe-His-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 421);

Ac-Nle-c[Asp-Phe-His-dPhe-Arg-Trp-Lys]-dLeu-dPro-$NH_2$ (SEQ ID NO: 422);

Ac-Nle-c[Asp-Phe-His-dPhe-Arg-Trp-Lys]-dTle-dPro-$NH_2$ (SEQ ID NO: 423); and

Ac-Nle-c[Asp-Phe-His-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 424),

wherein c represents cyclization through $R^1$ and $R^7$ via a lactam bond.

78. The method or the use of any one of claims 1-62, wherein the sequence of any one of Formulae (I)-(ID) is selected from the group consisting of:

Ac-Nle-c[Asp-Pro-dPhe-Arg-dTrp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 187);

Ac-Nle-c[Asp-Pro-dPhe-Arg-Aia-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 233);

Ac-Nle-c[Asp-Pro-dPhe-Arg-Aba-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 234);

Ac-Nle-c[Asp-Pro-dPhe-Arg-Ata-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 235);

Ac-Nle-c[Asp-Pro-dPhe-Arg-Nal(1')-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 427); and

Ac-Nle-c[Asp-Pro-dPhe-Arg-Phe-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 429),

wherein c represents cyclization through $R^2$ and $R^7$ via a lactam bond.

79. The method or the use of any one of claims 1-62, wherein the sequence of any one of Formulae (I)-(ID) is selected from the group consisting of:

Ac-Nle-c[Asp-Pro-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 218);

Ac-Nle-c[dCys-Pro-p(F)dPhe-Arg-Trp-Cys]-dVal-dPro-$NH_2$ (SEQ ID NO: 433);

Ac-Nle-c[dCys-Pro-p(F)dPhe-Arg-Trp-dCys]-dVal-dPro-$NH_2$ (SEQ ID NO: 434);

Ac-Ala-c[Asp-Pro-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 435);

Ac-dArg-c[Asp-Pro-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 436);

Ac-Arg-c[Asp-Pro-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 437);

Ac-Lys-c[Asp-Pro-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 438);

Ac-dLys-c[Asp-Pro-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 439);

Ac-His-c[Asp-Pro-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 440);

Ac-dHis-c[Asp-Pro-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 441);

Ac-Nle-Nle-c[Asp-Pro-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 442);

Ac-Nle-c[Asp-Pro-p(F)dPhe-His-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 443);

Ac-Nle-c[Asp-Pro-p(F)dPhe-Arg-Trp-Lys]-dTle-dTle-dVal-$NH_2$ (SEQ ID NO: 446);

Ac-Nle-c[Asp-Pro-p(F)dPhe-Arg-Trp-Lys]-dVal-dVal-dVal-dPro-$NH_2$ (SEQ ID NO: 447);

Ac-Nle-c[Asp-Pro-p(F)dPhe-Arg-Trp-Lys]-dPro-dVal-dPro-$NH_2$ (SEQ ID NO: 448);

Ac-Nle-c[Asp-Pro-p(F)dPhe-Arg-Trp-Lys]-dTle-dPro-$NH_2$ (SEQ ID NO: 449);

Ac-Nle-Nle-c[Asp-Pro-p(F)dPhe-Arg-Trp-Lys]-dTle-dPro-$NH_2$ (SEQ ID NO: 450);

Ac-Nle-Nle-c[Asp-Pro-p(F)dPhe-Arg-Trp-Lys]-dPro-dVal-dPro-$NH_2$ (SEQ ID NO: 451);

Ac-Ala-c[Asp-Pro-p(F)dPhe-Arg-Trp-Lys]-dTle-dPro-$NH_2$ (SEQ ID NO: 452);

Ac-dArg-c[Asp-Pro-p(F)dPhe-Arg-Trp-Lys]-dTle-dPro-$NH_2$ (SEQ ID NO: 453);

Ac-Arg-c[Asp-Pro-p(F)dPhe-Arg-Trp-Lys]-dTle-dPro-$NH_2$ (SEQ ID NO: 454);

Ac-Lys-c[Asp-Pro-p(F)dPhe-Arg-Trp-Lys]-dTle-dPro-$NH_2$ (SEQ ID NO: 455);

Ac-dLys-c[Asp-Pro-p(F)dPhe-Arg-Trp-Lys]-dTle-dPro-$NH_2$ (SEQ ID NO: 456);

Ac-His-c[Asp-Pro-p(F)dPhe-Arg-Trp-Lys]-dTle-dPro-$NH_2$ (SEQ ID NO: 457);

Ac-dHis-c[Asp-Pro-p(F)dPhe-Arg-Trp-Lys]-dTle-dPro-$NH_2$ (SEQ ID NO: 458);

Ac-Nle-c[Cys-His-p(F)dPhe-Arg-Trp-Cys]-dVal-dPro-$NH_2$ (SEQ ID NO: 459);

Ac-Nle-c[dCys-His-p(F)dPhe-Arg-Trp-Cys]-dVal-dPro-$NH_2$ (SEQ ID NO: 460);

Ac-Nle-c[dCys-His-p(F)dPhe-Arg-Trp-dCys]-dVal-dPro-$NH_2$ (SEQ ID NO: 461);

Ac-Nle-c[Asp-His-p(F)dPhe-Arg-Nal(2')-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 472);

Ac-Nle-c[Asp-dGln-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 492); and

Ac-Nle-c[Asp-dTyr-p(F)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 496),

wherein c represents cyclization through $R^2$ and $R^7$ via a lactam bond or a disulfide bond.

80. The method or the use of any one of claims 1-62, wherein the sequence of any one of Formulae (I)-(ID) is selected from the group consisting of:

Ac-Nle-c[Asp-Aba-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 209);

Ac-Nle-c[Asp-Aia-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 210);

Ac-Nle-c[Asp-Ata-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 211);

Ac-Nle-c[dCys-His-p(Cl)dPhe-Arg-Trp-dCys]-dVal-dPro-$NH_2$ (SEQ ID NO: 499);

Ac-dArg-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 501);

Ac-Arg-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 502);

Ac-Lys-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 503);

Ac-dLys-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 504);

Ac-His-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 505);

Ac-dHis-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 506);

Ac-Nle-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dTle-dTle-dVal-$NH_2$ (SEQ ID NO: 511);

Ac-Nle-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dVal-dVal-dVal-dPro-$NH_2$ (SEQ ID NO: 512);

Ac-Nle-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dPro-dVal-dPro-$NH_2$ (SEQ ID NO: 513);

Ac-Nle-Nle-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dTle-dPro-$NH_2$ (SEQ ID NO: 515);

Ac-dArg-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dTle-dPro-$NH_2$ (SEQ ID NO: 518);

Ac-Arg-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dTle-dPro-$NH_2$ (SEQ ID NO: 519);

Ac-Lys-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dTle-dPro-$NH_2$ (SEQ ID NO: 520);

Ac-dLys-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dTle-dPro-$NH_2$ (SEQ ID NO: 521);

Ac-His-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dTle-dPro-$NH_2$ (SEQ ID NO: 522); and

Ac-dHis-c[Asp-His-p(Cl)dPhe-Arg-Trp-Lys]-dTle-dPro-$NH_2$ (SEQ ID NO: 523),

wherein c represents cyclization through $R^2$ and $R^7$ via a lactam bond or a disulfide bond.

81. The method or the use of any one of claims 1-62, wherein the sequence of any one of Formulae (I)-(ID) is selected from the group consisting of:

Ac-Nle-c[dCys-His-p(Br)dPhe-Arg-Trp-Cys]-dVal-dPro-$NH_2$ (SEQ ID NO: 536); or

Ac-Nle-c[dCys-His-p(Br)dPhe-Arg-Trp-dCys]-dVal-dPro-$NH_2$ (SEQ ID NO: 537),

wherein c represents cyclization through $R^2$ and $R^7$ via a disulfide bond.

82. The method or the use of any one of claims 1-62, wherein the sequence of any one of Formulae (I)-(ID) is selected from the group consisting of:

Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-Val-Pro-$NH_2$ (SEQ ID NO: 573);

Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-Hyp-$NH_2$ (SEQ ID NO: 574);

Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dHyp-$NH_2$ (SEQ ID NO: 575);

Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-Val-$NH_2$ (SEQ ID NO: 576);

Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-Pro-$NH_2$ (SEQ ID NO: 577);

Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-Arg-$NH_2$ (SEQ ID NO: 578);

Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dArg-$NH_2$ (SEQ ID NO: 579);

Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dArg-dPro-$NH_2$ (SEQ ID NO: 580);

Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-Arg-$NH_2$ (SEQ ID NO: 581);

Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dArg-$NH_2$ (SEQ ID NO: 582);

Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-Lys-Pro-Val-$NH_2$ (SEQ ID NO: 583);

Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dLys-dPro-$NH_2$ (SEQ ID NO: 584);

Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-Lys-Val-Pro-$NH_2$ (SEQ ID NO: 585);

Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-Lys-dVal-dPro-$NH_2$ (SEQ ID NO: 586);

Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dLys-dVal-dPro-$NH_2$ (SEQ ID NO: 587);

Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-Arg-Pro-Val-$NH_2$ (SEQ ID NO: 588);

Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-Arg-Val-Pro-$NH_2$ (SEQ ID NO: 589);

Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dArg-dVal-dPro-$NH_2$ (SEQ ID NO: 590);

Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dTle-dPro-$NH_2$ (SEQ ID NO: 591);

Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dTle-dTle-dPro-$NH_2$ (SEQ ID NO: 592);

Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dTle-dTle-dVal-$NH_2$ (SEQ ID NO: 593);

Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dTle-$NH_2$ (SEQ ID NO: 594);

Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dVal-dPro-$NH_2$ (SEQ ID NO: 595);

Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dPro-dVal-dPro-$NH_2$ (SEQ ID NO: 596);

Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dVal-dVal-dPro-$NH_2$ (SEQ ID NO: 597);

Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-dVal-dPro-$NH_2$ (SEQ ID NO: 598);

Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dVal-dVal-dVal-dVal-dVal-dPro-$NH_2$ (SEQ ID NO: 599);

Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-Trp-$NH_2$ (SEQ ID NO: 600);

Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-Lys-dPro-dVal-$NH_2$ (SEQ ID NO: 601);

Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dAla-dAla-$NH_2$ (SEQ ID NO: 602);

Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-Asp-$NH_2$ (SEQ ID NO: 603);

Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dHyp-$NH_2$ (SEQ ID NO: 604);

Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dAsn-$NH_2$ (SEQ ID NO: 605);

Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-Asp-$NH_2$ (SEQ ID NO: 606);

Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-Asn-dPro-$NH_2$ (SEQ ID NO: 607);

Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-Hyp-$NH_2$ (SEQ ID NO: 608);

Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-Ala-Ala-$NH_2$ (SEQ ID NO: 609);

Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-Gly-Gly-$NH_2$ (SEQ ID NO: 610);

Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-Asp-dPro-$NH_2$ (SEQ ID NO: 611);

Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dAsn-dPro-$NH_2$ (SEQ ID NO: 612);

Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-Asn-$NH_2$ (SEQ ID NO: 613);

Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dAsp-$NH_2$ (SEQ ID NO: 614);

Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dAsn-$NH_2$ (SEQ ID NO: 615);

Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-Lys-dPro-$NH_2$ (SEQ ID NO: 616);

Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dPro-dVal-OH (SEQ ID NO: 617);

Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dThr-dPro-dThr-$NH_2$ (SEQ ID NO: 618);

Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dThr-dPro-dThr-OH (SEQ ID NO: 619);

Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dPro-dVal-$NH_2$ (SEQ ID NO: 620);

Ac-Nle-c[dAsp-Pro-dPhe-Arg-Trp-dLys]-dPro-dVal-$NH_2$ (SEQ ID NO: 622);

Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-βPro-$\beta^2$Val-$NH_2$ (SEQ ID NO: 623);

Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-βPro-$\beta^3$Val-$NH_2$ (SEQ ID NO: 624);

Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-$\beta^2$Val-βPro-$NH_2$ (SEQ ID NO: 625);

Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-$\beta^3$Val-βPro-$NH_2$ (SEQ ID NO: 626); and

Ac-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-βPro-βPro-$NH_2$ (SEQ ID NO: 627),

wherein c represents cyclization through $R^2$ and $R^7$ via a lactam bond.

83. The method or the use of any one of claims 1-62, wherein the sequence of any one of Formulae (I)-(ID) is selected from the group consisting of:

Ac-Nle-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 628);

Ac-Nle-Nle-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 629); and

Ac-Nle-Nle-Nle-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dPro-$NH_2$ (SEQ ID NO: 630),

wherein c represents cyclization through $R^2$ and $R^7$ via a lactam bond.

84. The method or the use of any one of claims 1-62, wherein the sequence of any one of Formulae (I)-(ID) is selected from the group consisting of:

Ac-Arg-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dArg-dVal-dPro-$NH_2$ (SEQ ID NO: 631);

Ac-dLys-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dLys-dVal-dPro-$NH_2$ (SEQ ID NO: 632);

Ac-Lys-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dArg-dPro-$NH_2$ (SEQ ID NO: 633);

Ac-His-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dLys-dPro-$NH_2$ (SEQ ID NO: 634);

Ac-dHis-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dHyp-$NH_2$ (SEQ ID NO: 635);

Ac-Orn-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dTle-dPro-$NH_2$ (SEQ ID NO: 636);

Ac-dOrn-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dVal-dVal-dVal-dPro-$NH_2$ (SEQ ID NO: 637);

Ac-Nle-Nle-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dTle-dPro-$NH_2$ (SEQ ID NO: 638);

Ac-Ala-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dTle-dPro-$NH_2$ (SEQ ID NO: 640);

Ac-dArg-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dTle-dPro-$NH_2$ (SEQ ID NO: 641);

Ac-Arg-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dTle-dPro-$NH_2$ (SEQ ID NO: 642);

Ac-Lys-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dTle-dPro-$NH_2$ (SEQ ID NO: 643);

Ac-dLys-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dTle-dPro-$NH_2$ (SEQ ID NO: 644);

Ac-His-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dTle-dPro-$NH_2$ (SEQ ID NO: 645); and

Ac-dHis-c[Asp-Pro-dPhe-Arg-Trp-Lys]-dTle-dPro-$NH_2$ (SEQ ID NO: 646),

wherein c represents cyclization through $R^2$ and $R^7$ via a lactam bond.

85. The method or the use of any one of claims 1-57, wherein the non-naturally occurring melanocortin analog comprises any one of SEQ ID NOs: 8, 187, 198, 207-218, 226, 231-235, 281, 291, 294-296, 298-322, 324, 351-355, 358-362, 364, 366-368, 371-375, 381-395, 399, 403-417, 419, 421-425, 427, 429, 433-443, 446-461, 472, 492, 496, 499-506, 511-513, 515, 518-523, 536-537, 573-599, 600-620, 622-646.

86. The method or the use of claim 85, wherein the non-naturally occurring melanocortin analog comprises any one of the sequences of SEQ ID NOs: 187, 212, 218, 226, 291, 295, 298-322, 324, 351-355, 358-360, 362, 364, 366-368, 371-375, 381-395, 399,

403-417, 419, 421-425, 427, 429, 433-443, 446-461, 472, 492, 496, 499-506, 511-513, 515, 518-523, 536-537, 573-598, 600-646.

87. The method or the use of claim 85, wherein the non-naturally occurring melanocortin analog comprises any one of the sequences of SEQ ID NOs: 187, 218, 231-235, 291, 295, 298-322, 351-353, 425, 427, 429, 433-443, 446-458, 573-599, 600-620, 622-646.

88. The method or the use of claim 85, wherein the non-naturally occurring melanocortin analog comprises any one of the sequences of SEQ ID NOs: 226, 383-393, 399, 403-417.

89. The method or the use of claim 85, wherein the non-naturally occurring melanocortin analog comprises any one of the sequences of SEQ ID NOs: 209-211, 499, 501-506, 511-513, 515, 518-523.

90. The method or the use of any one of claims 1-89, wherein the non-naturally occurring melanocortin analog is present in a pharmaceutical composition.

91. The method or the use of claim 90, wherein the pharmaceutical composition comprises one or more pharmaceutically acceptable excipients and/or carriers.

92. The method or the use of claim 91, wherein the one or more pharmaceutically acceptable excipients and/or carriers of the pharmaceutical composition comprise water.

93. The method or the use of any one of claims 1-92, wherein the non-naturally occurring melanocortin analog is administered (i) at a first dose of about 5 mg/kg to about 20 mg/kg administered once a day for about 5 days to about 10 days; (ii) at a second dose of about 10 mg/kg to about 40 mg/kg administered once a day after administration of the first dose for about 5 days to about 10 days; (iii) at a third dose of about 5 mg/kg to about 30 mg/kg administered twice a day after administration of the second dose for at least about 5 days to about 10 days.

94. The method or the use of any one of claims 1-92, wherein the non-naturally occurring melanocortin analog is administered (i) at a first dose of about 5 mg/kg administered once a day for about 7 days; (ii) at a second dose of about 15 mg/kg administered once a day after administration of the first dose for about 7 days; (iii) at a third dose of about 10 mg/kg administered twice a day after administration of the second dose for at least about 7 days.

95. The method or the use of any one of claims 1-92, wherein the non-naturally occurring melanocortin analog is administered (i) at a first dose of about 10 mg/kg administered once a day for about 7 days; (ii) at a second dose of about 20 mg/kg administered once a day after administration of the first dose for about 7 days; (iii) at a third dose of about 15 mg/kg administered twice a day after administration of the second dose for at least about 7 days.

96. The method or the use of any one of claims 1-92 wherein the non-naturally occurring melanocortin analog is administered (i) at a first dose of about 15 mg/kg administered once a day for about 7 days; (ii) at a second dose of about 25 mg/kg administered once a day after administration of the first dose for about 7 days; (iii) at a third dose of about 20 mg/kg administered twice a day after administration of the second dose for at least about 7 days.

97. The method or the use of any one of claims 1-92, wherein the non-naturally occurring melanocortin analog is administered at a dose of about 0.5 mg/kg to about 10 mg/kg per body weight of the subject once daily.

98. The method or the use of claim 97, wherein the non-naturally occurring melanocortin analog is administered at a dose of about 1 mg/kg or 3 mg/kg per body weight of the subject once daily.

99. The method or the use of any one of claims 1-92, wherein the non-naturally

occurring melanocortin analog is administered at a dose of about 0.1 mg to about 100 mg once daily.

100. The method or the use of any one of claims 1-92, wherein the non-naturally occurring melanocortin analog is administered at a dose of about 10 mg or about 50 mg once daily.

101. The method or the use of any one of claims 1-100, wherein the non-naturally occurring melanocortin analog is administered via intraperitoneal, intravenous, parenteral, subcutaneous, intramuscular, intracerebroventricular, intranasal, or oral administration.

102. The method or the use of any one of claims 1-101, wherein the non-naturally occurring melanocortin analog crosses a blood-brain-barrier of a subject.

103. The method or the use of any one of claims 101 or 102, wherein the non-naturally occurring melanocortin analog comprises any one of the sequences of SEQ ID NOs: 8, 187, 198, 207-218, 226, 231-235, 281, 291, 294-296, 298-322, 324, 351-355, 358-362, 364, 366-368, 371-375, 381-395, 399, 403-417, 419, 421-425, 427, 429, 433-443, 446-461, 472, 492, 496, 499-506, 511-513, 515, 518-523, 536-537, 573-599, 600-620, 622-646 and is administered at least once daily in an amount ranging from 0.001 mg/kg to 25 mg/kg per body weight of the subject.

104. The method or the use of claim 103, wherein the non-naturally occurring melanocortin analog comprises any one of the sequences of SEQ ID NOs: 8, 187, 198, 207-218, 226, 231-235, 281, 291, 294-296, 298-322, 324, 351-355, 358-362, 364, 366-368, 371-375, 381-395, 399, 403-417, 419, 421-425, 427, 429, 433-443, 446-461, 472, 492, 496, 499-506, 511-513, 515, 518-523, 536-537, 573-599, 600-620, 622-646 and is administered at least once daily in an amount ranging from 0.5 mg/kg to 10 mg/kg per body weight of the subject.

105. The method or the use of any one of claims 1-92, wherein the non-naturally occurring melanocortin analog is administered to a subject for at least 1 day, 1 week, 1 month, 3 months, 6 months, 1 year, or 5 years.

106. The method or the use of any one of claims 1-104, wherein the non-naturally occurring melanocortin analog is administered to a subject for 1 day, 5 days, 7 days, 14 days, 21 days, 28 days, 35 days, 40 days, 45 days, 50 days, 60 days, 75 days, 90 days, 100 days, 110 days, or 120 days.