

## GLP-1 AND GLUCAGON DUAL AGONIST PEPTIDES WITH IMPROVED BIOLOGICAL STABILITY

### BACKGROUND OF THE INVENTION

- [0001] The incidence of obesity and diabetes have been rising in epidemic proportions. Diabetes is characterized by high levels of blood glucose resulting from defects in insulin production, insulin action, or both. Type 2 diabetes mellitus (T2DM) accounts for some 90 to 95 percent of all diagnosed cases of diabetes, and the risk of type 2 diabetes rises with increasing body weight. The prevalence of type 2 diabetes is three to seven times higher in those who are affected by obesity than in normal weight adults, and is 20 times more likely in those with a body mass index (BMI) greater than 35 kg/m<sup>2</sup>. However, weight-loss can improve control or cure type 2 diabetes.
- [0002] Glucagon and glucagon-like peptide-1 (GLP-1) derive from pre-proglucagon, a 158 amino acid precursor polypeptide that is processed in different tissues to form a number of different proglucagon-derived peptides, including glucagon, glucagon-like peptide-1 (GLP-1), glucagon-like peptide-2 (GLP-2) and oxyntomodulin (OXM), that are involved in a wide variety of physiological functions, including glucose homeostasis, insulin secretion, gastric emptying, and intestinal growth, as well as the regulation of food intake. Glucagon is a 29-amino acid peptide that corresponds to amino acids 33 through 61 of proglucagon (53 to 81 of preproglucagon), while GLP-1 is produced as a 37-amino acid peptide that corresponds to amino acids 72 through 108 of proglucagon (92 to 128 of preproglucagon). GLP-1(7-36) amide or GLP-1(7-37) acid are biologically active forms of GLP-1, that demonstrate essentially equivalent activity at the GLP-1 receptor.
- [0003] Glucagon is produced by the pancreas and interacts with the glucagon receptor ("glucR"). Glucagon acts in the liver to raise blood glucose via gluconeogenesis and glycogenolysis. When blood glucose begins to fall, glucagon signals the liver to break down glycogen and release glucose, causing blood glucose levels to rise toward a normal level.
- [0004] GLP-1 has different biological activities compared to glucagon. It is secreted from gut L cells and binds to the GLP-1 receptor. Its activities include stimulation of insulin synthesis and secretion, inhibition of glucagon secretion, and inhibition of food intake.

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- [0005] Both glucagon and GLP-1, acting as agonists at their respective receptors, have been shown to be effective in weight loss. Certain GLP-1 analogs are being sold or are in development for treatment of obesity including, *e.g.*, Liraglutide (Saxenda® from Novo Nordisk) and Semaglutide (Wegovy® from Novo Nordisk). Glucagon/GLP-1 dual agonist peptides such as cotadutide are also known and are in clinical development for treatment of diabetes, obesity, and nonalcoholic steatohepatitis (NASH). However, all of these proposed therapies involve chronic self-medication necessitating patient compliance over an extended period of time. Other peptides, *e.g.*, amylin analogues are also being considered for the treatment of obesity, excess food intake, and diabetes (WO 2018/046719).
- [0006] Accordingly, there remains a need for therapeutics that can agonize both GLP-1 and glucagon functions to *e.g.*, improve glycemic control, reduce weight, treat type 2 diabetes mellitus, (T2DM) and/or treat NASH, while minimizing burdens associated with administration to improve patient compliance and quality of life.

## BRIEF SUMMARY OF THE INVENTION

- [0007] Provided herein are GLP-1 and glucagon dual agonists with improved biological stability (*e.g.*, proteolytic stability) and duration of action. The GLP-1 and glucagon dual agonist peptides provided herein can have improved properties, *e.g.*, as compared to semaglutide H(Aib)EGTFTSDVSSYLEGQAAX20EFIAWLVRGRG-acid, wherein X20=Lys[O2Oc-O2Oc- $\gamma$ E-C18diacid] (SEQ ID NO: 539)) and/or cotadutide (HSQGTFTSDX10SEYLDSEARDFVAWLEAGG-acid, wherein X10=Lys[ $\epsilon$ - $\gamma$ E-Palmitoyl] (SEQ ID NO: 538)). Accordingly, the GLP-1 and glucagon dual agonist peptides provided herein can be administered once weekly.
- [0008] Certain aspects of the disclosure are directed to a peptide comprising the sequence: H-X2-X3-G-X5-X6-T-S-D-X10-S-X12- $\alpha$ Methyl-Phenylalanine ( $\alpha$ MePhe)-L-X15-X16-X17-X18-A-X20-X21-X22-X23-X24-X25-X26-X27-X28-X29-X30-X31-Z, wherein X2 is Aminoisobutyric acid (Aib), S, or A, X3 is Q, H, or E, X5 is T or S, X6 is F or  $\alpha$ MePhe, X10 is V, K or Y, X12 is K, E, or S, X15 is D or E, X16 is T, S, or G, X17 is K, R, E, or Q, X18 is R or A, X20 is R, K, or Q, X21 is D or E, X22 is  $\alpha$ MePhe or F, X23 is V or I, X24 is Q or A, X25 is Aib or W, X26 is L or I, X27 is L, A, E, V, or M, X28 is E, N, A, R, or K, X29 is

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Aib, T, or G, X30 is G, R, or not present, X31 is G or not present, and Z is amide or acid (SEQ ID NO: 540).

[0009] In some aspects, X2 is Aib. In some aspects, X3 is Q. In some aspects, X3 is H. In some aspects, X5 is T. In some aspects, X5 is S. In some aspects, X6 is F. In some aspects, X6 is  $\alpha$ MePhe. In some aspects, X10 is V. In some aspects, X12 is K. In some aspects, X15 is D. In some aspects, X16 is T. In some aspects, X16 is S. In some aspects, X17 is K. In some aspects, X17 is R. In some aspects, X18 is R. In some aspects, X18 is A. In some aspects, X20 is R. In some aspects, X20 is K. In some aspects, X21 is D. In some aspects, X22 is F. In some aspects, X22 is  $\alpha$ MePhe. In some aspects, X23 is V. In some aspects, X24 is Q. In some aspects, X25 is W. In some aspects, X25 is Aib. In some aspects, X26 is L. In some aspects, X26 is I. In some aspects, X27 is L. In some aspects, X27 is A. In some aspects, X28 is E. In some aspects, X28 is N. In some aspects, X29 is Aib. In some aspects, X29 is T. In some aspects, X30 is G. In some aspects, X30 is not present. In some aspects, X31 is not present. In some aspects, Z is amide. In some aspects, Z is acid.

[0010] In some aspects, X2 is Aib, X12 is K, and X24 is Q. In some aspects, X16 is T, X17 is K, X27 is L, X28, is E, and X29 is Aib. In some aspects, X3 is Q, X5 is T, X6 is F, X10 is V, X12 is K, X15 is D, X16 is T, X17 is K, X18 is R, X20 is R, X21 is D, X22 is F, X23 is V, X24 is Q, X25 is W, X26 is L, X27 is L, X28 is E, X29 is Aib, X30 is G, X31 is not present, and Z is acid. In some aspects, X3 is H, X5 is S, X6 is  $\alpha$ MePhe, X10 is V, X12 is K, X15 is D, X16 is S, X17 is R, X18 is A, X20 is K, X21 is D, X22 is  $\alpha$ MePhe, X23 is V, X24 is Q, X25 is Aib, X26 is I, X27 is A, X28 is N, X29 is T, X30 is not present, X31 is not present, and Z is amide.

[0011] In some aspects, one or more lysine residues are acylated. In some aspects, the lysine at position 17 is acylated. In some aspects, the lysine at position 20 is acylated.

[0012] In some aspects, one or more lysine residues are lipidated. In some aspects, the lysine at position 17 is lipidated. In some aspects, the lysine at position 20 is lipidated.

[0013] In some aspects, the lipid is selected from the group consisting of octadecanedioic acid (C18diacid) and icosanedioic acid (C20diacid). In some aspects, the lipid is octadecanedioic acid (C18diacid). In some aspects, the lipid is icosanedioic acid (C20diacid). In some aspects, the lipid is linked to the epsilon amino group of lysine at position 17 or 20 via a linker.

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- [0014] In some aspects, the linker is ((O2Oc)-(O2Oc)- $\gamma$ E) or ((O2Oc)-(O2Oc)- $\gamma$ E- $\gamma$ E) in the C- to N-terminal orientation. In some aspects, the linker is ((O2Oc)-(O2Oc)- $\gamma$ E) in the C- to N-terminal orientation. In some aspects, the linker is ((O2Oc)-(O2Oc)- $\gamma$ E- $\gamma$ E) in the C- to N-terminal orientation. In some aspects, the linker is linked to the epsilon amino group of the residue at position 17 or 20.
- [0015] Certain aspects of the disclosure are directed to a peptide comprising the sequence of H-Aib-Q-G-T-F-T-S-D-V-S-K- $\alpha$ MePhe-L-D-T-K-R-A-R-D-F-V-Q-W-L-L-E-Aib-G-acid (SEQ ID NO: 541).
- [0016] In some aspects, the lysine at position 17 is acylated and lipidated, the lipid is linked to the acylated lysine via its epsilon amino group to ((O2Oc)-(O2Oc)- $\gamma$ E) linker in the C to N terminal orientation, and the lipid is octadecanedioic acid (C18diacid). In some aspects, the lysine at position 17 is acylated and lipidated, the lipid is linked to the acylated lysine via its epsilon amino group to ((O2Oc)-(O2Oc)- $\gamma$ E) linker in the C to N terminal orientation, and the lipid is icosanedioic acid (C20diacid).
- [0017] Certain aspects of the disclosure are directed to a peptide comprising the sequence H-Aib-H-G-S- $\alpha$ MePhe-T-S-D-V-S-K- $\alpha$ MePhe-L-D-S-R-A-A-K( $\epsilon$ -(O2Oc)-(O2Oc)- $\gamma$ E-C18diacid)20-D- $\alpha$ MePhe-V-Q-Aib-I-A-N-T-amide (SEQ ID NO: 228).
- [0018] Certain aspects of the disclosure are directed to a peptide comprising the sequence H-Aib-H-G-S- $\alpha$ MePhe-T-S-D-V-S-K- $\alpha$ MePhe-L-D-S-R-A-A-K( $\epsilon$ -(O2Oc)-(O2Oc)- $\gamma$ E-C20diacid)20-D- $\alpha$ MePhe-V-Q-Aib-I-A-N-T-amide (SEQ ID NO: 233).
- [0019] In some aspects, the peptide binds to the GLP-1 receptor (GLP-1R), binds to the glucagon receptor (GCGR), or binds to both a GLP-1 receptor and a glucagon receptor. In some aspects, the GLP-1R is a human GLP-1R. In some aspects, the GCGR is a human GCGR.
- [0020] In some aspects, the peptide is an agonist of GLP-1 activity, an agonist of glucagon activity, or an agonist of both GLP-1 and glucagon activity. In some aspects, the peptide has increased proteolytic-resistance relative to the natural ligand of the GLP-1R and/or GCGR.
- [0021] In some aspects, the peptide is isolated.
- [0022] In some aspects, the peptide has at least 50%, at least 60%, at least 70%, at least 75%, at least 80%, at least 85%, at least 90%, at least 95, or 100% of intact peptide remaining after incubation with a protease at 37°C for 5 min, 10 min, 15 min, 30 min, 2 hr, 4 hr, or 24 hr. In

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some aspects, the protease is selected from the group consisting of neprilysin, pepsin, pancreatin, simulated gastric fluid with pepsin, and simulated intestinal fluid with pancreatin.

[0023] In some aspects, the peptide has a half-life in cynomolgus monkeys after intravenous administration of at least 45 hours, at least 50 hours, at least 60 hours, at least 70 hours, at least 80 hours, at least 90 hours, at least 100 hours, at least 110 hours, at least 120 hours, or about 130 hours. In some aspects, the peptide has an s.c. bioavailability in cynomolgus monkeys of at least 75%, at least 80%, at least 90%, or about 95%.

[0024] In some aspects, a pharmaceutical composition comprising the peptide is provided herein. In some aspects, the composition is a solid composition. In some aspects, the composition is a liquid composition.

[0025] In some aspects, provided herein is a method of treating or preventing a disease or condition caused or characterized by excess body weight, wherein the method comprises administering to a subject in need of treatment an effective amount of any peptide or composition provide herein. In some aspects, the disease or condition is obesity. In some aspects, the disease or condition is type 2 diabetes.

[0026] In some aspects, provided herein is a method of treating or preventing non-alcoholic steatohepatitis (NASH), wherein the method comprises administering to a subject in need of treatment an effective amount of any peptide or composition provide herein.

[0027] In some aspects of a method provided herein, the administration is by injection. In some aspects of a method provided herein, the administration is oral. In some aspects of a method provided herein, the administration decreases body weight of the subject, increases insulin secretion in the subject, delays gastric emptying in the subject, decreases food intake in the subject, increases mitochondria function in the subject, inhibits de novo lipogenesis in the subject, decreases HbA1c in the subject, enhances fatty oxidation in the subject, decreases hepatic mitochondrial oxidative stress in the subject, decreases steatosis in the subject, decreases fibrosis in the subject, decreases glycogen synthesis in the subject, increases gluconeogenesis in the subject, halts disease progression in the subject, reverses fibrosis in the subject, and/or reduces risk of death due to cirrhosis, hepatocellular carcinoma, and/or cardiorenal disease in the subject. In some aspects of a method provided herein, the subject is a human. In some aspects of a method provided herein, the peptide is administered about once a week.

## BRIEF DESCRIPTION OF THE DRAWINGS/FIGURES

**[0028]** **FIGs. 1A-1G** are drawings depicting the exemplary lipids icosanedioic acid (C20diacid) (**FIG. 1A**), octadecanedioic acid (C18diacid) (**FIG. 1B**), stearoyl (**FIG. 1C**), margaroyl (**FIG. 1D**), palmitoyl (**FIG. 1E**), myristoyl (**FIG. 1F**), and lauryl (**FIG. 1G**).

**[0029]** **FIGs. 2A-2F** are drawings depicting exemplary linkers attached to lipids depicted in **FIGs. 1A-1G** 2-(2-(2-aminoethoxy)ethoxy)acetic acid (O2Oc) (**FIG. 2A**), (O2Oc)-(O2Oc) (**FIG. 2B**), (O2Oc)- $\gamma$ E-(O2Oc) (**FIG. 2C**), (PEG)2-(PEG)2- $\gamma$ E- $\gamma$ E (**FIG. 2D**), (PEG)2- $\gamma$ E-(PEG)2- $\gamma$ E (**FIG. 2E**),  $\gamma$ glutamyl-L-glutamic acid ( $\gamma$ E) (**FIG. 2F**),  $\gamma$ E-(O2Oc) (**FIG. 2G**),  $\gamma$ E-(O2Oc)-(O2Oc) (**FIG. 2H**),  $\gamma$ E-(O2Oc)- $\gamma$ E-(O2Oc) (**FIG. 2I**),  $\gamma$ E-(PEG)2-(PEG)2 (**FIG. 2J**),  $\gamma$ E-(PEG)2- $\gamma$ E-(PEG)2 (**FIG. 2K**),  $\gamma$ E-(PEG)4 (**FIG. 2L**),  $\gamma$ E- $\gamma$ E (**FIG. 2M**),  $\gamma$ E- $\gamma$ E-(O2Oc) (**FIG. 2N**),  $\gamma$ E- $\gamma$ E-(O2Oc)-(O2Oc) (**FIG. 2O**),  $\gamma$ E- $\gamma$ E-(PEG)12 (**FIG. 2P**),  $\gamma$ E- $\gamma$ E-(PEG)2-(PEG)2 (**FIG. 2Q**),  $\gamma$ E- $\gamma$ E-(PEG)2- $\gamma$ E- $\gamma$ E (**FIG. 2R**),  $\gamma$ E- $\gamma$ E-(PEG)4 (**FIG. 2S**),  $\gamma$ E- $\gamma$ E-(PEG)8 (**FIG. 2T**),  $\gamma$ E- $\gamma$ E-(O2Oc)-(O2Oc)- $\gamma$ E- $\gamma$ E (**FIG. 2U**), and (PEG)2-(PEG)2- $\gamma$ E (**FIG. 2V**). All linkers shown with the N-terminal on the left and C-terminal on right.

**[0030]** **FIGs. 3A-3P** are drawings depicting the exemplary non-natural amino acids 2-amino-2-methylpropanoic acid (Aib) (**FIG. 3A**), (S)-2-amino-2-methyl-3-phenylpropanoic acid ( $\alpha$ MePhe) (**FIG. 3B**), (S)-2-amino-3-hydroxy-2-methylpropanoic acid ( $\alpha$ MeSer) (**FIG. 3C**), D-glutamine (dGln) (**FIG. 3D**),  $\beta$ -dimethylglutamine ( $\beta$ -dimethylGln) (**FIG. 3E**), (S)-2,5-diamino-2-methyl-5-oxopentanoic acid ( $\alpha$ MeGln) (**FIG. 3F**), D-serine (dSer) (**FIG. 3G**), methyl-L-glutamine (N-MeGln) (**FIG. 3H**), ((1*H*-imidazol-4-yl)methyl)glycine (NHis) (**FIG. 3I**), 1-aminocyclopropane-1-carboxylic acid (Acpr) (**FIG. 3J**), 1-aminocyclobutane-1-carboxylic acid (Acbu) (**FIG. 3K**), *N*<sup>6</sup>-acetyl-L-lysine (Ac-Lys) (**FIG. 3L**), (S)-2-amino-5-guanidino-3,3-dimethylpentanoic acid ( $\beta$ -dimethylArg) (**FIG. 3M**), (S)-2-amino-3,3-diphenylpropanoic acid (Dip) (**FIG. 3N**), (S)-2-amino-3-cyclohexylpropanoic acid (Cha) (**FIG. 3O**), (S)-2-aminohexanoic acid (Nle) (**FIG. 3P**), (S)-3-([1,1'-biphenyl]-4-yl)-2-aminopropanoic acid (Bip) (**FIG. 3Q**), 1-methyl-L-tryptophan (1-Methyl-Trp) (**FIG. 3R**), and (S)-2-amino-3-(5-bromo-1*H*-indol-3-yl)propanoic acid (5-Br-Trp) (**FIG. 3S**).

**[0031]** **FIGs. 4A-4D** are drawings depicting the structure of exemplary peptides: peptide 224 (**FIG. 4A**), peptide 229 (**FIG. 4B**), peptide 188 (**FIG. 4C**), and peptide 195 (**FIG. 4D**).

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## DETAILED DESCRIPTION OF THE INVENTION

**I. Definitions**

- [0032] Unless defined otherwise, all technical and scientific terms used herein have the same meaning as commonly understood by one of ordinary skill in the art to which this disclosure is related. For example, the Concise Dictionary of Biomedicine and Molecular Biology, Juo, Pei-Show, 2nd ed., 2002, CRC Press; The Dictionary of Cell and Molecular Biology, 3rd ed., 1999, Academic Press; and the Oxford Dictionary Of Biochemistry And Molecular Biology, Revised, 2000, Oxford University Press, provide one of skill with a general dictionary of many of the terms used in this disclosure.
- [0033] Units, prefixes, and symbols are denoted in their Système International de Unites (SI) accepted form. Numeric ranges are inclusive of the numbers defining the range. Unless otherwise indicated, amino acid sequences are written left to right in amino to carboxy orientation. The headings provided herein are not limitations of the various aspects of the disclosure, which can be had by reference to the specification as a whole. Accordingly, the terms defined immediately below are more fully defined by reference to the specification in its entirety.
- [0034] Throughout this disclosure, the term "a" or "an" entity refers to one or more of that entity; for example, "a polynucleotide," is understood to represent one or more polynucleotides. As such, the terms "a" (or "an"), "one or more," and "at least one" can be used interchangeably herein.
- [0035] Furthermore, "and/or" where used herein is to be taken as specific disclosure of each of the two specified features or components with or without the other. Thus, the term "and/or" as used in a phrase such as "A and/or B" herein is intended to include "A and B," "A or B," "A" (alone), and "B" (alone). Likewise, the term "and/or" as used in a phrase such as "A, B, and/or C" is intended to encompass each of the following aspects: A, B, and C; A, B, or C; A or C; A or B; B or C; A and C; A and B; B and C; A (alone); B (alone); and C (alone).
- [0036] As used herein, the terms "about" and "approximately," when used to modify a numeric value or numeric range, indicate that deviations of up to 10% above and down to 10% below the value or range remain within the intended meaning of the recited value or range. It is understood that wherever aspects are described herein with the language "about" or

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"approximately" a numeric value or range, otherwise analogous aspects referring to the specific numeric value or range are also provided.

[0037] It is understood that wherever aspects are described herein with the language "comprising," otherwise analogous aspects described in terms of "consisting of" and/or "consisting essentially of" are also provided. A peptide "comprising" a particular amino acid sequence refers to a peptide containing the amino acid sequence, wherein the peptide may or may not contain additional amino acids or other modifications to the amino acid sequence. A peptide "consisting of" a particular amino acid sequence refers to a peptide containing only the amino acid sequence and no additional amino acids or other modifications to the amino acid sequence. A peptide "comprising" an amino acid sequence "consisting of" a particular amino acid sequence refers to a peptide containing the amino acid sequence and no additional amino acids; however, the peptide may comprise other modifications to the amino acid sequence (e.g., an acyl moiety or a palmitoyl moiety).

[0038] As used herein, the term "amino acid" refers to naturally occurring and non-natural amino acids, as well as amino acid analogs and amino acid mimetics that function in a manner similar to the naturally occurring amino acids. Naturally encoded amino acids are the 20 common amino acids (alanine, arginine, asparagine, aspartic acid, cysteine, glutamine, glutamic acid, glycine, histidine, isoleucine, leucine, lysine, methionine, phenylalanine, proline, serine, threonine, tryptophan, tyrosine, and valine) and pyrrolysine and selenocysteine. Amino acid analogs refers to compounds that have the same basic chemical structure as a naturally occurring amino acid, *i.e.*, an  $\alpha$  carbon that is bound to a hydrogen, a carboxyl group, an amino group, and an R group, such as, homoserine, norleucine, methionine sulfoxide, and methionine methyl sulfonium. Such analogs have modified R groups (such as, norleucine) or modified peptide backbones, but retain the same basic chemical structure as a naturally occurring amino acid.

[0039] A "non-natural amino acid" refers to an amino acid that is not one of the 20 common amino acids or pyrrolysine or selenocysteine; other terms that may be used synonymously with the term "non-natural amino acid" are "non-naturally encoded amino acid," "unnatural amino acid," "non-naturally-occurring amino acid," and variously hyphenated and non-hyphenated versions thereof. The term "non-natural amino acid" includes, but is not limited to, amino acids that occur naturally by modification of a naturally encoded amino acid

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(including but not limited to, the 20 common amino acids or pyrrolysine and selenocysteine) but are not themselves incorporated into a growing polypeptide chain by the translation complex.

**[0040]** Examples of naturally-occurring amino acids that are not naturally-encoded include, but are not limited to, ((1H-imidazol-4-yl)methyl)glycine (NHis), S, 1-aminocyclobutane-1-carboxylic acid (1-aminocyclobutane-1-carboxylic acid; Acbu), 1-aminocyclopropane-1-carboxylic acid (1-aminocyclopropane-1-carboxylic acid; Acpr), Aminoisobutyric acid (2-amino-2-methylpropanoic acid; Aib), D-serine (dSer),  $\alpha$ Methyl-Serine ((S)-2-amino-3-hydroxy-2-methylpropanoic acid ( $\alpha$ MeSer);  $\alpha$ MeSer), methyl-L-glutamine (N-MeGln),  $\alpha$ Methyl-Glutamine ((S)-2,5-diamino-2-methyl-5-oxopentanoic acid;  $\alpha$ MeGln),  $\beta$ -dimethylGln,  $\alpha$ Methyl-Phenylalanine (S)-2-amino-2-methyl-3-phenylpropanoic acid;  $\alpha$ MePhe), acetylated lysine *N*<sup>6</sup>-acetyl-L-lysine (Ac-Lys), Diphenylalanine ((S)-2-amino-3,3-diphenylpropanoic acid; Dip),  $\beta$ -dimethylarginine ((S)-2-amino-5-guanidino-3,3-dimethylpentaonic acid;  $\beta$ -dimethylArg), beta-cyclohexyl-L-alanine ((S)-2-amino-3-cyclohexylpropanoic acid; Cha), norleucine ((S)-2-aminohexanoic acid; Nle), D-glutamine (dGln) (S)-3-([1,1'-biphenyl]-4-yl)-2-aminopropanoic acid (Bip), 1-methyl-L-tryptophan (1-Methyl-Trp), and (S)-2-amino-3-(5-bromo-1H-indol-3-yl)propanoic acid (5-Br-Trp).

**[0041]** Amino acids may be referred to herein by either their commonly known three letter symbols or by the one-letter symbols recommended by the IUPAC-IUB Biochemical Nomenclature Commission. Nucleotides, likewise, may be referred to by their commonly accepted single-letter codes.

**[0042]** As used herein, the term "polypeptide" is intended to encompass a singular "polypeptide" as well as plural "polypeptides," and comprises any chain or chains of two or more amino acids. Thus, as used herein, a "peptide," a "peptide subunit," a "protein," an "amino acid chain," an "amino acid sequence," or any other term used to refer to a chain or chains of two or more amino acids, are included in the definition of a "polypeptide," even though each of these terms can have a more specific meaning. The term "polypeptide" can be used instead of, or interchangeably with any of these terms. The term further includes polypeptides which have undergone post-translational or post-synthesis modifications, for example, conjugation of a palmitoyl group, glycosylation, acetylation, phosphorylation,

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amidation, derivatization by known protecting/blocking groups, proteolytic cleavage, or modification by non-naturally occurring amino acids.

**[0043]** More specifically, the term "peptide" as used herein encompasses full length peptides and fragments, variants or derivatives thereof, *e.g.*, a GLP-1/glucagon agonist peptide (*e.g.*, 29, 30, or 31 amino acids in length). A "peptide" as disclosed herein, *e.g.*, a GLP-1/glucagon agonist peptide, can be part of a fusion polypeptide comprising additional components such as, *e.g.*, an Fc domain or an albumin domain, to increase half-life. A peptide as described herein can also be derivatized in a number of different ways. A peptide described herein can comprise modifications including *e.g.*, conjugation of a lipid including a palmitoyl group, stearoyl group, lauryl group, myristoyl group, margaroyl group, octadecanedioic acid (C18diacid), or icosanedioic acid (C20diacid). Exemplary lipids are provided in FIGs. 1A-1G.

**[0044]** A peptide described herein can comprise modifications including *e.g.*, conjugation of a linker comprising 2-(2-(2-aminoethoxy)ethoxy)acetic acid (O2Oc), PEG, and/or gammaglutamic acid ( $\gamma$ E). In some aspects, a linker comprises 2-(2-(2-aminoethoxy)ethoxy)acetic acid (O2Oc), (O2Oc)-(O2Oc), (O2Oc)- $\gamma$ E-(O2Oc), 3-(2-(2-aminoethoxy)ethoxy)propanoic acid ((PEG)2), 1-amino-3,6,9,12-tetraoxapentadecan-15-oic acid ((PEG)4), 1-amino-3,6,9,12,15,18,21,14-octaoxaheptacosan-27-oic acid ((PEG)8), 1-amino-3,6,9,12,15,18,21,24,27,30,33,36-dodecaoxanonatriacontan-39-oic acid ((PEG)12), gammaglutamic acid ( $\gamma$ E), (PEG)2-(PEG)2- $\gamma$ E- $\gamma$ E, (PEG)2- $\gamma$ E-(PEG)2- $\gamma$ E,  $\gamma$ E-(O2Oc),  $\gamma$ E-(O2Oc)-(O2Oc),  $\gamma$ E-(O2Oc)- $\gamma$ E-(O2Oc),  $\gamma$ E-(PEG)2-(PEG)2,  $\gamma$ E-(PEG)2- $\gamma$ E-(PEG)2,  $\gamma$ E-(PEG)4,  $\gamma$ E- $\gamma$ E,  $\gamma$ E- $\gamma$ E-(O2Oc),  $\gamma$ E- $\gamma$ E-(O2Oc)-(O2Oc),  $\gamma$ E- $\gamma$ E-(PEG)12,  $\gamma$ E- $\gamma$ E-(PEG)2-(PEG)2,  $\gamma$ E- $\gamma$ E-(PEG)2- $\gamma$ E- $\gamma$ E,  $\gamma$ E- $\gamma$ E-(PEG)4,  $\gamma$ E- $\gamma$ E-(PEG)8,  $\gamma$ E- $\gamma$ E-(O2Oc)-(O2Oc)- $\gamma$ E- $\gamma$ E, and (PEG)2-(PEG)2- $\gamma$ E. Exemplary linkers are provided in FIGs. 2A-2V.

**[0045]** The term "isolated" refers to the state in which peptides or nucleic acids, will generally be in accordance with the present disclosure. Isolated peptides and isolated nucleic acids will be free or substantially free of material with which they are naturally associated such as other peptides or nucleic acids with which they are found in their natural environment, or the environment in which they are prepared (*e.g.* cell culture) when such preparation is by recombinant DNA technology practiced *in vitro* or *in vivo*. Peptides and nucleic acid can be formulated with diluents or adjuvants and still for practical purposes be isolated - for example the peptides will normally be mixed with gelatin or other carriers if used to coat microtitre

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plates for use in immunoassays, or will be mixed with pharmaceutically acceptable carriers or diluents when used in diagnosis or therapy.

[0046] A "recombinant" peptide refers to a peptide produced via recombinant DNA technology. Recombinantly produced peptides expressed in host cells are considered isolated for the purpose of the present disclosure, as are native or recombinant polypeptides which have been separated, fractionated, or partially or substantially purified by any suitable technique.

[0047] The terms "fragment," "analog," "derivative," or "variant" when referring to a GLP-1/glucagon agonist peptide include any peptide which retains at least some desirable activity, *e.g.*, binding to glucagon receptors and/or GLP-1 receptors. Fragments of GLP-1/glucagon agonist peptides provided herein include proteolytic fragments, deletion fragments which exhibit desirable properties during expression, purification, and or administration to a subject.

[0048] The term "variant," as used herein, refers to a peptide that differs from the recited peptide due to amino acid substitutions, deletions, insertions, and/or modifications. Variants can be produced using art-known mutagenesis techniques. Variants can also, or alternatively, contain other modifications. For example, a peptide can be conjugated or coupled, *e.g.*, fused to a heterologous amino acid sequence or other moiety, *e.g.*, for increasing half-life, solubility, or stability. Examples of moieties to be conjugated or coupled to a peptide provided herein include, but are not limited to, albumin, an immunoglobulin Fc region, polyethylene glycol (PEG), and the like. The peptide can also be conjugated or produced coupled to a linker or other sequence for ease of synthesis, purification or identification of the peptide (*e.g.*, 6-His), or to enhance binding of the polypeptide to a solid support.

[0049] The terms "composition" or "pharmaceutical composition" refer to compositions containing a GLP-1/glucagon agonist peptide provided herein, along with *e.g.*, pharmaceutically acceptable carriers, excipients, or diluents for administration to a subject in need of treatment, *e.g.*, a human subject in need of improved glycemic control, weight loss, treatment of Type 2 Diabetes Mellitus, and/or treatment of NASH.

[0050] The term "pharmaceutically acceptable" refers to compositions that are, within the scope of sound medical judgment, suitable for contact with the tissues of human beings and animals without excessive toxicity or other complications commensurate with a reasonable benefit/risk ratio.

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- [0051] An "effective amount" is that amount of an agent provided herein (e.g., a GLP-1/glucagon agonist peptide), the administration of which to a subject, either in a single dose or as part of a series, is effective for treatment, *e.g.*, for improved glycemic control, weight loss, treatment of Type 2 Diabetes Mellitus, and/or treatment of NASH.
- [0052] As used herein, the terms "subject" and "patient" are used interchangeably. The subject can be an animal. In some aspects of the present disclosure, the subject is a mammal such as a non-human animal (*e.g.*, cow, pig, horse, cat, dog, rat, mouse, monkey or other primate, etc.). In some aspects of the present disclosure, the subject is a cynomolgus monkey. In some aspects of the present disclosure, the subject is a human.
- [0053] As used herein, a "subject in need thereof" or a "patient in need thereof" refers to an individual for whom it is desirable to treat, *e.g.*, a subject in need of improved glycemic control, weight loss, treatment of Type 2 Diabetes Mellitus, and/or treatment of NASH.
- [0054] Terms such as "treating" or "treatment" or "to treat" refer to therapeutic measures that cure and/or halt progression of a diagnosed pathologic condition or disorder. Terms such as "preventing" refer to prophylactic or preventative measures that prevent and/or slow the development of a targeted pathologic condition or disorder. Thus, those in need of treatment include those already with the disease or condition. Those in need of prevention include those prone to have the disease or condition and those in whom the disease or condition is to be prevented.
- [0055] Terms such as "decreasing the severity" refer to therapeutic measures that slow down or lessen the symptoms of a diagnosed pathologic condition or disorder.
- [0056] As used herein, a "GLP-1 agonist peptide" is a peptide that is not native GLP-1 but exhibits activity at the GLP-1 receptor of about at least 1% or more relative to native GLP-1, under the conditions of the cAMP assay (see Example 2). In some aspects, a GLP-1 agonist peptide exhibits activity at the GLP-1 receptor of at least 5%, 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90%, 95%, or more relative to native GLP-1, under the conditions of the cAMP assay (see Example 2).
- [0057] As used herein, a "glucagon agonist peptide" is a peptide that is not native glucagon but exhibits activity at the glucagon receptor of at least 1%, or more relative to native glucagon, under the conditions of the cAMP assay (see Example 2). In some aspects, a glucagon agonist peptide exhibits activity at the glucagon receptor of at least 5%, 10%, 20%, 30%, 40%, 50%,

60%, 70%, 80%, 90%, 95%, or more relative to native GLP-1, under the conditions of the cAMP assay (see Example 2).

**[0058]** As used herein a "GLP-1/glucagon agonist peptide," "GLP-1/glucagon coagonist peptide," "GLP-1 and glucagon dual agonist peptide" or "GLP-1 and glucagon dual coagonist peptide" is a peptide that is not native GLP-1 and is not native glucagon that exhibits activity at the glucagon receptor of at least 1% or more relative to native glucagon and also exhibits activity at the GLP-1 receptor of about at least 1% or more relative to native GLP-1, under the conditions of the cAMP assay (see Example 2). In some aspects, a "GLP-1/glucagon agonist peptide" or a "GLP-1 and glucagon dual agonist peptide" exhibits activity at the glucagon receptor of at least 5%, 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90%, 95%, or more relative to native glucagon and also exhibits activity at the GLP-1 receptor of about at least 5%, 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, 90%, 95%, or more relative to native GLP-1, under the conditions of the cAMP assay (see Example 2).

**[0059]** As used herein, term "relative potency ratio" refers to the % GLP-1R activity relative to GLP-1 / % GlucR activity relative to glucagon.

**[0060]** As used herein the term "native glucagon" refers to naturally-occurring glucagon, *e.g.*, human glucagon, comprising the sequence of SEQ ID NO: 1. The term "native GLP-1" refers to naturally-occurring GLP-1, *e.g.*, human GLP-1, and is a generic term that encompasses, *e.g.*, GLP-1(7-36) amide (SEQ ID NO: 2), GLP-1(7-37) acid (SEQ ID NO: 3), or a mixture of those two compounds. As used herein, a general reference to "glucagon" or "GLP-1" in the absence of any further designation is intended to mean native human glucagon or native human GLP-1, respectively. Unless otherwise indicated, "glucagon" refers to human glucagon, and "GLP-1" refers to human GLP-1.

**[0061]** The term "sequence identity" as used herein refers to a relationship between two or more polynucleotide sequences or between two or more polypeptide sequences. When a position in one sequence is occupied by the same nucleic acid base or amino acid in the corresponding position of the comparator sequence, the sequences are said to be "identical" at that position. The percentage "sequence identity" is calculated by determining the number of positions at which the identical nucleic acid base or amino acid occurs in both sequences to yield the number of "identical" positions. The number of "identical" positions is then divided by the total number of positions in the comparison window and multiplied by 100 to yield the

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percentage of "sequence identity." Percentage of "sequence identity" is determined by comparing two optimally aligned sequences over a comparison window. In order to optimally align sequences for comparison, the portion of a polynucleotide or polypeptide sequence in the comparison window can comprise additions or deletions termed gaps while the reference sequence is kept constant. An optimal alignment is that alignment which, even with gaps, produces the greatest possible number of "identical" positions between the reference and comparator sequences. Percentage "sequence identity" between two sequences can be determined using the version of the program "BLAST 2 Sequences" which was available from the National Center for Biotechnology Information as of September 1, 2004, which program incorporates the programs BLASTN (for nucleotide sequence comparison) and BLASTP (for polypeptide sequence comparison), which programs are based on the algorithm of Karlin and Altschul (*Proc. Natl. Acad. Sci. USA* 90(12):5873-5877, 1993). When utilizing "BLAST 2 Sequences," parameters that were default parameters as of September 1, 2004, can be used for word size (3), open gap penalty (11), extension gap penalty (1), gap drop-off (50), expect value (10), and any other required parameter including but not limited to matrix option.

**Glucagon (SEQ ID NO: 1)**

HSQGTFTSDYSKYLDSSRAQDFVQWLMNT-acid

**GLP-1(7-36) amide (SEQ ID NO: 2)**

HAEGTFTSDVSSYLEGQAAKEFIAWLVKGR-amide

**GLP-1(7-37) acid (SEQ ID NO: 3)**

HAEGTFTSDVSSYLEGQAAKEFIAWLVKGRG-acid

**II. GLP-1/Glucagon Agonist Peptides**

[0062] Provided herein are peptides that bind both to a glucagon receptor and to a GLP-1 receptor. In some aspects, the peptides provided herein are co-agonists (dual agonists) of glucagon and GLP-1 activity. Such peptides are referred to herein as GLP-1/glucagon agonist peptides. In some aspects, GLP-1/glucagon agonist peptides as provided herein are active at the human GLP1 and human glucagon receptors.

[0063] In certain aspects, GLP-1/glucagon agonist peptides provided herein exhibit *in vitro* potencies at the GLP-1 receptor as shown by an EC<sub>50</sub> in the cAMP assay (see Example 2) of less than 10,000 pM, less than 5000 pM, less than 2500 pM, less than 1000 pM, less than 900

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pM, less than 800 pM, less than 700 pM, less than 600 pM, less than 500 pM, less than 400 pM, less than 300 pM, less than 200 pM, less than 100 pM, less than 50 pM, less than 25 pM, less than 20 pM, less than 15 pM, less than 10 pM, less than 5 pM, less than 4 pM, less than 3 pM, or less than 2 pM.

[0064] In certain aspects, GLP-1/glucagon agonist peptides provided herein exhibit *in vitro* potencies at the glucagon receptor as shown by an EC<sub>50</sub> in the cAMP assay (see Example 2) of less than 10,000 pM, less than 5000 pM, less than 2500 pM, less than 1000 pM, less than 900 pM, less than 800 pM, less than 700 pM, less than 600 pM, less than 500 pM, less than 400 pM, less than 300 pM, less than 200 pM, less than 100 pM, less than 50 pM, less than 25 pM, less than 20 pM, less than 15 pM, less than 10 pM, less than 5 pM, less than 4 pM, less than 3 pM, or less than 2 pM.

[0065] In certain aspects, GLP-1/glucagon agonist peptides provided herein have a hGLP-1R/hGCGR relative potency ratio of about 1 to about 25. In certain aspects, GLP-1/glucagon agonist peptides provided herein have a hGLP-1R/hGCGR relative potency ratio of about 1 to about 20. In certain aspects, GLP-1/glucagon agonist peptides provided herein have a hGLP-1R/hGCGR relative potency ratio of about 1 to about 15. In certain aspects, GLP-1/glucagon agonist peptides provided herein have a hGLP-1R/hGCGR relative potency ratio of about 1 to about 10.

[0066] In certain aspects, GLP-1/glucagon agonist peptides provided herein have a hGLP-1R/hGCGR relative potency ratio of about 2 to about 25. In certain aspects, GLP-1/glucagon agonist peptides provided herein have a hGLP-1R/hGCGR relative potency ratio of about 2 to about 20. In certain aspects, GLP-1/glucagon agonist peptides provided herein have a hGLP-1R/hGCGR relative potency ratio of about 2 to about 15. In certain aspects, GLP-1/glucagon agonist peptides provided herein have a hGLP-1R/hGCGR relative potency ratio of about 2 to about 10.

[0067] In certain aspects, GLP-1/glucagon agonist peptides provided herein, when administered to mice at 10 nmol/kg (as performed in Example 3) reduce 24-hour food intake by at least 10% relative to mice treated with a vehicle control. In certain aspects, GLP-1/glucagon agonist peptides provided herein, when administered to mice at 10 nmol/kg (as performed in Example 3) reduce 24-hour food intake by at least 20% relative to mice treated with a vehicle control. In certain aspects, GLP-1/glucagon agonist peptides provided herein,

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when administered to mice at 10 nmol/kg (as performed in Example 3) reduce 24-hour food intake by at least 30% relative to mice treated with a vehicle control.

**[0068]** In certain aspects, GLP-1/glucagon agonist peptides provided herein, when administered to mice at 10 nmol/kg (as performed in Example 3) reduce 24-hour food intake by at 10-70% relative to mice treated with a vehicle control. In certain aspects, GLP-1/glucagon agonist peptides provided herein, when administered to mice at 10 nmol/kg (as performed in Example 3) reduce 24-hour food intake by at least 20% or by 20-70% relative to mice treated with a vehicle control. In certain aspects, GLP-1/glucagon agonist peptides provided herein, when administered to mice at 10 nmol/kg (as performed in Example 3) reduce 24-hour food intake by at least 30% or by 30-70% relative to mice treated with a vehicle control.

**[0069]** In certain aspects, GLP-1/glucagon agonist peptides provided herein are stable. For example, in certain aspects, GLP-1/glucagon agonist peptides provided herein stable in the presence of FasSSGF (fasted state simulated gastric fluid) such that at least 25% of the GLP-1/glucagon agonist peptide remains intact after incubation with FasSSGF for 30 minutes (as performed in Example 4.) In certain aspects, GLP-1/glucagon agonist peptides provided herein stable in the presence of FasSSGF such that at least 40% of the GLP-1/glucagon agonist peptide remains intact after incubation with FasSSGF for 30 minutes (as performed in Example 4.) In certain aspects, GLP-1/glucagon agonist peptides provided herein stable in the presence of FasSSGF such that at least 50% of the GLP-1/glucagon agonist peptide remains intact after incubation with FasSSGF for 30 minutes (as performed in Example 4.) In certain aspects, GLP-1/glucagon agonist peptides provided herein stable in the presence of FasSSGF such that at least 60% of the GLP-1/glucagon agonist peptide remains intact after incubation with FasSSGF for 30 minutes (as performed in Example 4.) In certain aspects, GLP-1/glucagon agonist peptides provided herein stable in the presence of FasSSGF such that at least 70% of the GLP-1/glucagon agonist peptide remains intact after incubation with FasSSGF for 30 minutes (as performed in Example 4.)

**[0070]** In certain aspects, GLP-1/glucagon agonist peptides provided herein stable in the presence of neprilysin such that at least 55% of the GLP-1/glucagon agonist peptide remains intact after incubation with neprilysin for 24 hours (as performed in Example 5.) In certain aspects, GLP-1/glucagon agonist peptides provided herein stable in the presence of neprilysin

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such that at least 60% of the GLP-1/glucagon agonist peptide remains intact after incubation with neprilysin for 24 hours (as performed in Example 5.) In certain aspects, GLP-1/glucagon agonist peptides provided herein stable in the presence of neprilysin such that at least 65% of the GLP-1/glucagon agonist peptide remains intact after incubation with neprilysin for 24 hours (as performed in Example 5.) In certain aspects, GLP-1/glucagon agonist peptides provided herein stable in the presence of neprilysin such that at least 70% of the GLP-1/glucagon agonist peptide remains intact after incubation with neprilysin for 24 hours (as performed in Example 5.) In certain aspects, GLP-1/glucagon agonist peptides provided herein stable in the presence of neprilysin such that at least 75% of the GLP-1/glucagon agonist peptide remains intact after incubation with neprilysin for 24 hours (as performed in Example 5.) In certain aspects, GLP-1/glucagon agonist peptides provided herein stable in the presence of neprilysin such that at least 80% of the GLP-1/glucagon agonist peptide remains intact after incubation with neprilysin for 24 hours (as performed in Example 5.) In certain aspects, GLP-1/glucagon agonist peptides provided herein stable in the presence of neprilysin such that at least 85% of the GLP-1/glucagon agonist peptide remains intact after incubation with neprilysin for 24 hours (as performed in Example 5.) In certain aspects, GLP-1/glucagon agonist peptides provided herein stable in the presence of neprilysin such that at least 90% of the GLP-1/glucagon agonist peptide remains intact after incubation with neprilysin for 24 hours (as performed in Example 5.) In certain aspects, GLP-1/glucagon agonist peptides provided herein stable in the presence of neprilysin such that at least 95% of the GLP-1/glucagon agonist peptide remains intact after incubation with neprilysin for 24 hours (as performed in Example 5.)

[0071] In certain aspects, GLP-1/glucagon agonist peptides provided herein are stable. For example, in certain aspects, GLP-1/glucagon agonist peptides provided herein stable in the presence of FasSSIF (fasted state simulated intestinal fluid)/Pancreatin such that at least 10% of the GLP-1/glucagon agonist peptide remains intact after incubation with FasSSIF/Pancreatin for 30 minutes (as performed in Example 6.) In certain aspects, GLP-1/glucagon agonist peptides provided herein are stable. For example, in certain aspects, GLP-1/glucagon agonist peptides provided herein stable in the presence of FasSSIF/Pancreatin such that at least 20% of the GLP-1/glucagon agonist peptide remains intact after incubation with FasSSIF/Pancreatin for 30 minutes (as performed in Example 6.)

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In certain aspects, GLP-1/glucagon agonist peptides provided herein are stable. For example, in certain aspects, GLP-1/glucagon agonist peptides provided herein stable in the presence of FasSSIF/Pancreatin such that at least 25% of the GLP-1/glucagon agonist peptide remains intact after incubation with FasSSIF/Pancreatin for 30 minutes (as performed in Example 6.)

In certain aspects, GLP-1/glucagon agonist peptides provided herein are stable. For example, in certain aspects, GLP-1/glucagon agonist peptides provided herein stable in the presence of FaSSSIF/Pancreatin such that at least 50% of the GLP-1/glucagon agonist peptide remains intact after incubation with FasSSSIF/Pancreatin for 30 minutes (as performed in Example 6.)

In certain aspects, GLP-1/glucagon agonist peptides provided herein are stable. For example, in certain aspects, GLP-1/glucagon agonist peptides provided herein stable in the presence of FasSSIF/Pancreatin such that at least 75% of the GLP-1/glucagon agonist peptide remains intact after incubation with FasSSIF/Pancreatin for 30 minutes (as performed in Example 6.) In certain aspects, GLP-1/glucagon agonist peptides provided herein are stable. For example, in certain aspects, GLP-1/glucagon agonist peptides provided herein stable in the presence of FasSSIF/Pancreatin such that at least 80% of the GLP-1/glucagon agonist peptide remains intact after incubation with FasSSIF/Pancreatin for 30 minutes (as performed in Example 6.) In certain aspects, GLP-1/glucagon agonist peptides provided herein are stable. For example, in certain aspects, GLP-1/glucagon agonist peptides provided herein stable in the presence of FasSSIF/Pancreatin such that at least 90% of the GLP-1/glucagon agonist peptide remains intact after incubation with FasSSIF/Pancreatin for 30 minutes (as performed in Example 6.)

**[0072]** A GLP-1/glucagon agonist peptide as disclosed herein can comprise a heterologous moiety, *e.g.*, to extend half-life. The heterologous moiety can be a protein, a peptide, a protein domain, a linker, an organic polymer, an inorganic polymer, a polyethylene glycol (PEG), biotin, an albumin, a human serum albumin (HSA), a HSA FcRn binding portion, an antibody, a domain of an antibody, an antibody fragment, a single chain antibody, a domain antibody, an albumin binding domain, an enzyme, a ligand, a receptor, a binding peptide, a non-FnIII scaffold, an epitope tag, a recombinant polypeptide polymer, a cytokine, and a combination of two or more of such moieties.

**[0073]** In some aspects, a GLP-1/glucagon agonist peptide as disclosed herein binds to a GLP-1 receptor (GLP-1R), binds to a glucagon receptor (GCGR), or binds to both a GLP-1R and a

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GCGR. In some aspects, the GLP-1R is human GLP-1R. In some aspects, the GCGR is human GCGR. In some aspects, the peptide is an agonist of GLP-1 activity, an agonist of glucagon activity, or an agonist of both GLP-1 and glucagon activity.

**[0074]** In some aspects, a GLP-1/glucagon agonist peptide as disclosed herein has increased proteolytic-resistance relative to the natural ligand of the GLP-1R and/or GCGR. In some aspects, a GLP-1/glucagon agonist peptide as disclosed herein has increased proteolytic-resistance relative to cotadutide (SEQ ID NO: 358). In some aspects, a GLP-1/glucagon agonist peptide as disclosed herein has increased proteolytic-resistance relative to semaglutide (SEQ ID NO: 359). In some aspects, a GLP-1/glucagon agonist peptide as disclosed herein has increased proteolytic-resistance relative to cotadutide (SEQ ID NO: 358) and semaglutide (SEQ ID NO: 359).

**[0075]** In some aspects, a GLP-1/glucagon agonist peptide provided herein comprises the sequence: X1-X2-X3-G-X5-X6-T-S-D-X10-S-X12-X13-L-X15-X16-X17-X18-X19-X20-X21-X22-X23-X24-X25-X26-X27-X28-X29-X30-X31-Z, wherein X1 is H or NHis, X2 is S, 1-aminocyclobutane-1-carboxylic acid (Acbu), 1-aminocyclopropane-1-carboxylic acid (Acpr), Aminoisobutyric acid (Aib), D-serine (dSer), or  $\alpha$ Methyl-Serine ( $\alpha$ MeSer), X3 is Q, H, I, D-glutamine (dGln), methyl-L-glutamine (N-MeGln),  $\alpha$ -Methyl-glutamine ( $\alpha$ MeGln), or  $\beta$ -dimethylglutamine ( $\beta$ -dimethylGln), X5 is T or S, X6 is F or  $\alpha$ Methyl-Phenylalanine ( $\alpha$ MePhe), X10 is Y, K, or V, wherein the K can comprise an acyl moiety and/or can be lipidated, X12 is K, acetylated lysine (Ac-Lys), E, or R, X13 is Y, Aib,  $\alpha$ Methyl-Phenylalanine ( $\alpha$ MePhe), Diphenylalanine (Dip), I, or K, wherein the K can comprise an acyl moiety and/or can be lipidated, X15 is D or E, X16 is S, Aib, E, T, R, A, K, L, or V, X17 is R, E, K, Q, or  $\beta$ -dimethylarginine ( $\beta$ -dimethylArg), wherein the K can comprise an acyl moiety and/or can be lipidated, X18 is R, A, Aib, Q, S, or  $\beta$ -dimethylArg, X19 is A or V, X20 is Q, Aib, E, K, L, or R, wherein the K can comprise an acyl moiety and/or can be lipidated, X21 is D, E, or L, X22 is F, I, or  $\alpha$ MePhe, X23 is V or I, X24 is Q, A, E, K, L, or R, wherein the K can comprise an acyl moiety and/or can be lipidated, X25 is W, Aib, Dip, H, I, S, biphenyl-alanine (Bip), 1-methyl tryptophan (1-Methyl-Trp), 5-Bromo trptophan (5-BrTrp), or  $\alpha$ MePhe, X26 is L, beta-cyclohexyl-L-alanine (Cha), I, or V, X27 is M, A, E, I, L, norleucine (Nle), S, K, or V, X28 is N, (PEG)4, A, Aib, E, G, R, S, or not present, X29 is T, Aib, E, G, A, R, or not present, X30 is not present, E, A, Aib, K, T, or G, X31 is not present, I, or G, and Z is amide or acid (SEQ

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ID NO: 4), wherein the peptide does not comprise SEQ ID NO: 1 and does not comprise HSQGTFTSDX10SEYLDSEARDFVAWLEAGG-acid, wherein X10=Lys[ $\epsilon$ - $\gamma$ E-Palmitoyl] (SEQ ID NO: 538). In some aspects, X2 is Aib and/or X10 is V. In some aspects, X3 is Q, X15 is D, X18 is R, X20 is R, X21 is D, X23 is V, and/or X30 is G. In some aspects, X13 is  $\alpha$ MePhe, X16 is T, X17 is K, X27 is L, X28 is E, and/or X29 is Aib.

[0076] In some aspects, the residue at position 10, 13, 17, 20, or 24 is acylated. In some aspects, the residue at position 10, 13, 17, 20, or 24 is lipidated. In some aspects, the lipid is selected from the group consisting of a palmitoyl group, stearoyl group, lauryl group, myristoyl group, margaroyl group, arachidoyl group, octadecanedioic acid (C18diacid), and icosanedioic acid (C20diacid).

[0077] In some aspects, the lipid attached to the residue at position 10, 13, 17, 20, or 24 is attached via a linker. In some aspects, the linker is selected from the group consisting of (O2Oc), (O2Oc)-(O2Oc), (O2Oc)- $\gamma$ E-(O2Oc), (PEG)2-(PEG)2- $\gamma$ E- $\gamma$ E, (PEG)2- $\gamma$ E-(PEG)2- $\gamma$ E,  $\gamma$ E,  $\gamma$ E-(O2Oc),  $\gamma$ E-(O2Oc)-(O2Oc),  $\gamma$ E-(O2Oc)- $\gamma$ E-(O2Oc),  $\gamma$ E-(PEG)2-(PEG)2,  $\gamma$ E-(PEG)2- $\gamma$ E-(PEG)2,  $\gamma$ E-(PEG)4,  $\gamma$ E- $\gamma$ E,  $\gamma$ E- $\gamma$ E-(O2Oc),  $\gamma$ E- $\gamma$ E-(O2Oc)-(O2Oc),  $\gamma$ E- $\gamma$ E-(PEG)12,  $\gamma$ E- $\gamma$ E-(PEG)2-(PEG)2,  $\gamma$ E- $\gamma$ E-(PEG)2- $\gamma$ E- $\gamma$ E,  $\gamma$ E- $\gamma$ E-(PEG)4, (PEG)2-(PEG)2- $\gamma$ E,  $\gamma$ E- $\gamma$ E-(O2Oc)-(O2Oc)- $\gamma$ E- $\gamma$ E, and  $\gamma$ E- $\gamma$ E-(PEG)8.

[0078] In some aspects, the linker is linked to the epsilon amino group of the residue at position 10, 13, 17, 20, and/or 24.

[0079] In some aspects, the peptide comprises any one of SEQ ID NOs: 6-411 and 418-537. In some aspects, the peptide comprises SEQ ID NO: 99. In some aspects, the peptide comprises SEQ ID NO: 106. In some aspects, the peptide comprises SEQ ID NO: 228. In some aspects, the peptide comprises SEQ ID NO: 233.

[0080] In some aspects, the peptide comprises the sequence: H-X2-X3-G-X5-X6-T-S-D-X10-S-X12-X13-L-X15-X16-X17-X18-A-X20-D-X22-X23-X24-X25-X26-X27-X28-X29-X30-X31-Z, wherein X2 is S, Aminoisobutyric acid (Aib), or  $\alpha$ Methyl-Serine ( $\alpha$ MeSer), X3 is Q or H, X5 is T or S, X6 is F or  $\alpha$ Methyl-Phenylalanine ( $\alpha$ MePhe), X10 is Y or V, X12 is K or acetylated lysine (Ac-Lys), X13 is Y,  $\alpha$ MePhe, Aib, Diphenylalanine (Dip), or I, X15 is D or E, X16 is S, T, A, E, K, L, R, or V, X17 is R or K, wherein the K can comprise an acyl moiety and/or can be lipidated, X18 is R, A, Q, or  $\beta$ -dimethylarginine ( $\beta$ -dimethylArg), X20 is Q, R, Aib, L, or E, X22 is F, I, or  $\alpha$ MePhe, X23 is V or I, X24 is Q, E, A, L, or R, X25 is W, Aib, S,

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Dip, I, H, biphenyl-alanine (Bip), 1-methyl tryptophan (1-Methyl-Trp), 5-Bromo trptophan (5-BrTrp), or  $\alpha$ MePhe, X26 is L, I, or beta-cyclohexyl-L-alanine (Cha) or V, X27 is M, A, L, E, V, I, K, norleucine (Nle), or S, X28 is N, Aib, E, (PEG)4, A, S, or G, X29 is T, not present, Aib, G, A, R, or E, X30 is not present, G, A, Aib, K, or E, X31 is not present, and Z is amide or acid (SEQ ID NO: 5), wherein the peptide does not comprise SEQ ID NO: 1.

**[0081]** In some aspects, the residue at position 17 is acylated. In some aspects, the residue at position 17 is lipidated. In some aspects, the lipid is selected from the group consisting of a palmitoyl group, stearoyl group, lauryl group, myristoyl group, margaroyl group, arachidoyl group, octadecanedioic acid (C18diacid), and icosanedioic acid (C20diacid).

**[0082]** In some aspects, the lipid attached to the residue at position 17 is attached via a linker. In some aspects, the linker is selected from the group consisting of (O2Oc), (O2Oc)-(O2Oc), (O2Oc)- $\gamma$ E-(O2Oc), (PEG)2-(PEG)2- $\gamma$ E- $\gamma$ E, (PEG)2- $\gamma$ E-(PEG)2- $\gamma$ E,  $\gamma$ E,  $\gamma$ E-(O2Oc),  $\gamma$ E-(O2Oc)-(O2Oc),  $\gamma$ E-(O2Oc)- $\gamma$ E-(O2Oc),  $\gamma$ E-(PEG)2-(PEG)2,  $\gamma$ E-(PEG)2- $\gamma$ E-(PEG)2,  $\gamma$ E-(PEG)4,  $\gamma$ E- $\gamma$ E,  $\gamma$ E- $\gamma$ E-(O2Oc),  $\gamma$ E- $\gamma$ E-(O2Oc)-(O2Oc),  $\gamma$ E- $\gamma$ E-(PEG)12,  $\gamma$ E- $\gamma$ E-(PEG)2-(PEG)2,  $\gamma$ E- $\gamma$ E-(PEG)2- $\gamma$ E- $\gamma$ E,  $\gamma$ E- $\gamma$ E-(PEG)4, and  $\gamma$ E- $\gamma$ E-(PEG)8. In some aspects, the linker is selected from the group consisting of  $\gamma$ E- $\gamma$ E-(O2Oc)-(O2Oc)- $\gamma$ E- $\gamma$ E, (O2Oc)-(O2Oc),  $\gamma$ E,  $\gamma$ E-(O2Oc)-(O2Oc),  $\gamma$ E- $\gamma$ E-(O2Oc)-(O2Oc),  $\gamma$ E- $\gamma$ E-(PEG)4,  $\gamma$ E- $\gamma$ E-(PEG)2-(PEG)2,  $\gamma$ E- $\gamma$ E-(PEG)8,  $\gamma$ E- $\gamma$ E-(PEG)12, (PEG)2-(PEG)2- $\gamma$ E- $\gamma$ E, (PEG)2- $\gamma$ E-(PEG)2- $\gamma$ E,  $\gamma$ E-(PEG)2- $\gamma$ E-(PEG)2,  $\gamma$ E-(PEG)2-(PEG)2, (PEG)2-(PEG)2- $\gamma$ E, and  $\gamma$ E-(PEG)4.

**[0083]** In some aspects, the linker is linked to the epsilon amino group of the residue at position 17.

**[0084]** In some aspects, the peptide comprises the sequence: H-Aminoisobutyric acid (Aib)-Q-G-T-X6-T-S-D-V-S-K- $\alpha$ Methyl-Phenylalanine ( $\alpha$ MePhe)-L-X15-X16-K-X18-A-X20-X21-X22-X23-X24-W-X26-X27-X28-X29-X30-X31-Z, wherein X6 is F or  $\alpha$ Methyl-Phenylalanine ( $\alpha$ MePhe), X15 is E or D, X16 is T, S, K, E, A, L, or R, X18 is R or A, X20 is R, Q, or L, X21 is D or E, X22 is F or  $\alpha$ MePhe, X23 is V or I, X24 is R, A, Q, or L, X25 is W,  $\alpha$ MePhe biphenyl-alanine (Bip), 1-methyl tryptophan (1-Methyl-Trp), 5-Bromo trptophan (5-BrTrp), or Aib, X26 is L, I, or V, X27 is L, A, E, V, I, or K, X28 is E, S, A, Aib, not present, or R, X29 is G, Aib, R, T, E, A, or not present, X30 is G, Aib, E, A, K, or not present, X31 is I or not present, and or G, and Z is amide or acid (SEQ ID NO: 412).

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- [0085] In some aspects, the lysine at position 17 is acylated. In some aspects, the lysine at position 17 is lipidated. In some aspects, the lipid is selected from the group consisting of a palmitoyl group, stearoyl group, lauryl group, myristoyl group, margaroyl group, arachidoyl group, octadecanedioic acid (C18diacid), and icosanedioic acid (C20diacid). In some aspects, the lipid is selected from the group consisting of octadecanedioic acid (C18diacid) and icosanedioic acid (C20diacid). In some aspects, the lipid is an octadecanedioic acid (C18diacid). In some aspects, the lipid is an icosanedioic acid (C20diacid).
- [0086] In some aspects, the lipid is linked to the lysine at position 17 via a linker. In some aspects, the linker is selected from the group consisting of (O2Oc), (O2Oc)-(O2Oc), (O2Oc)- $\gamma$ E-(O2Oc), (PEG)2-(PEG)2- $\gamma$ E- $\gamma$ E, (PEG)2- $\gamma$ E-(PEG)2- $\gamma$ E,  $\gamma$ E,  $\gamma$ E-(O2Oc),  $\gamma$ E-(O2Oc)-(O2Oc),  $\gamma$ E-(O2Oc)- $\gamma$ E-(O2Oc),  $\gamma$ E-(PEG)2-(PEG)2,  $\gamma$ E-(PEG)2- $\gamma$ E-(PEG)2,  $\gamma$ E-(PEG)4,  $\gamma$ E- $\gamma$ E,  $\gamma$ E- $\gamma$ E-(O2Oc),  $\gamma$ E- $\gamma$ E-(O2Oc)-(O2Oc),  $\gamma$ E- $\gamma$ E-(PEG)12,  $\gamma$ E- $\gamma$ E-(PEG)2-(PEG)2,  $\gamma$ E- $\gamma$ E-(PEG)2- $\gamma$ E- $\gamma$ E,  $\gamma$ E- $\gamma$ E-(PEG)4, (PEG)2-(PEG)2- $\gamma$ E,  $\gamma$ E- $\gamma$ E-(O2Oc)-(O2Oc), and  $\gamma$ E- $\gamma$ E-(PEG)8. In some aspects, the peptide of claim X, wherein the linker is selected from the group consisting of (PEG)2-(PEG)2- $\gamma$ E, (O2Oc)-(O2Oc),  $\gamma$ E,  $\gamma$ E-(O2Oc)-(O2Oc),  $\gamma$ E- $\gamma$ E-(O2Oc)-(O2Oc), and  $\gamma$ E- $\gamma$ E-(O2Oc)-(O2Oc)- $\gamma$ E- $\gamma$ E. In some aspects, the linker is  $\gamma$ E-(O2Oc)-(O2Oc).
- [0087] In some aspects, the linker is linked to the epsilon amino group of the residue at position 17.
- [0088] In certain aspects, GLP-1/glucagon agonist peptides as disclosed have desirable potencies at the glucagon and GLP-1 receptors, and have desirable relative potencies for promoting weight loss.
- [0089] In some aspects, the peptide has the sequence of any one of SEQ ID NOs: 6-206 and 418-531. In some aspects, the peptide comprises SEQ ID NO: 99. In some aspects, the peptide comprises SEQ ID NO: 106.
- [0090] In some aspects, the peptide has the structure of any one of the structures depicted in FIGs 4C-4D. In some aspects, the peptide has the structure of FIG. 4C. In some aspects, the peptide has the structure of FIG. 4D.
- [0091] In some aspects, the peptide is any one of the peptides in **Table 1**.

**Table 1. Peptides Modified at Position 17**

| Peptide          | Sequence                                                                                                                                   | SEQ ID NO | Albumin binding moiety | Linker (described N->C term.)        | Acylation site | C-term. | Sequence modification with respect to glucagon.                                                            |
|------------------|--------------------------------------------------------------------------------------------------------------------------------------------|-----------|------------------------|--------------------------------------|----------------|---------|------------------------------------------------------------------------------------------------------------|
| <b>Peptide 1</b> | HSQGS( $\alpha$ MePhe)TSDVSK(Aib)LDSK(O2Oc-O2Oc- $\gamma$ E-C18diacid)17AAQD( $\alpha$ MePhe)VQ(Aib)IAN-amide                              | 6         | C18diacid              | $\gamma$ E-(O2Oc)-(O2Oc)             | 17             | Amide   | 5S, 6 $\alpha$ MePhe, 10V, 13Aib, 17K, 18A, 22 $\alpha$ MePhe, 25Aib, 26I, 27A, des29T                     |
| <b>Peptide 2</b> | HSQGS( $\alpha$ MePhe)TSDVSK( $\alpha$ MePhe)LDSK(O2Oc-O2Oc- $\gamma$ E-C20diacid)17AAQD( $\alpha$ MePhe)VQWIAN-amide                      | 7         | C20diacid              | $\gamma$ E-(O2Oc)-(O2Oc)             | 17             | Amide   | 5S, 6 $\alpha$ MePhe, 10V, 13 $\alpha$ MePhe, 17K, 18A, 22 $\alpha$ MePhe, 26I, 27A                        |
| <b>Peptide 3</b> | HSQGS( $\alpha$ MePhe)TSDVSK( $\alpha$ MePhe)LDSK( $\gamma$ E-C18diacid)17AAQDFVQWIAN-amide                                                | 8         | C18diacid              | $\gamma$ E                           | 17             | Amide   | 5S, 6 $\alpha$ MePhe, 10V, 13 $\alpha$ MePhe, 17K, 18A, 26I, 27A                                           |
| <b>Peptide 4</b> | HSQGS( $\alpha$ MePhe)TSDVSK( $\alpha$ MePhe)LDSK(O2Oc-O2Oc- $\gamma$ E-C18diacid)17AAQDFVQWIAN-amide                                      | 9         | C18diacid              | $\gamma$ E-(O2Oc)-(O2Oc)             | 17             | Amide   | 5S, 6 $\alpha$ MePhe, 10V, 13 $\alpha$ MePhe, 17K, 18A, 26I, 27A                                           |
| <b>Peptide 5</b> | H(Aib)QGS( $\alpha$ MePhe)TS DVSK( $\alpha$ MePhe)LDSK(O2Oc-O2Oc- $\gamma$ E- $\gamma$ E-C18diacid)17AAQD( $\alpha$ MePhe)VQ(Aib)IAN-amide | 10        | C18diacid              | $\gamma$ E- $\gamma$ E-(O2Oc)-(O2Oc) | 17             | Amide   | 2Aib, 5S, 6 $\alpha$ MePhe, 10V, 13 $\alpha$ MePhe, 17K, 18A, 22 $\alpha$ MePhe, 25Aib, 26I, 27A, des29T   |
| <b>Peptide 6</b> | H(Aib)HGS( $\alpha$ MePhe)TS DVSK( $\alpha$ MePhe)LDSK(O2Oc-O2Oc- $\gamma$ E-C18diacid)17AAQD( $\alpha$ MePhe)VEWIAN-amide                 | 11        | C18diacid              | $\gamma$ E-(O2Oc)-(O2Oc)             | 17             | Amide   | 2Aib, 3H, 5S, 6 $\alpha$ MePhe, 10V, 13 $\alpha$ MePhe, 17K, 18A, 22 $\alpha$ MePhe, 24E, 26I, 27A, des29T |

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|                   |                                                                                                                                            |    |           |                                  |    |       |                                                                                                    |
|-------------------|--------------------------------------------------------------------------------------------------------------------------------------------|----|-----------|----------------------------------|----|-------|----------------------------------------------------------------------------------------------------|
| <b>Peptide 7</b>  | H(Aib)HGS( $\alpha$ MePhe)TS<br>DVSK( $\alpha$ MePhe)LDSK( $\gamma$ E-<br>C18diacid)17AAQD( $\alpha$ MePhe)VEWANT-amide                    | 12 | C18diacid | $\gamma$ E                       | 17 | Amide | 2Aib, 3H, 5S, 6 $\alpha$ MePhe, 10V, 13 $\alpha$ MePhe, 17K, 18A, 22 $\alpha$ MePhe, 24E, 26I, 27A |
| <b>Peptide 8</b>  | H(Aib)HGS( $\alpha$ MePhe)TS<br>DVSK( $\alpha$ MePhe)LDSK(O<br>2Oc-O2Oc- $\gamma$ E-<br>C18diacid)17AAQDFVQ<br>WANT-amide                  | 13 | C18diacid | $\gamma$ E-<br>(O2Oc)-<br>(O2Oc) | 17 | Amide | 2Aib, 3H, 5S, 6 $\alpha$ MePhe, 10V, 13 $\alpha$ MePhe, 17K, 18A, 26I, 27A                         |
| <b>Peptide 9</b>  | H(Aib)HGS( $\alpha$ MePhe)TS<br>DVSK( $\alpha$ MePhe)LDSK(O<br>2Oc-O2Oc- $\gamma$ E-<br>C18diacid)17AARDFVQ<br>WANT-amide                  | 14 | C18diacid | $\gamma$ E-<br>(O2Oc)-<br>(O2Oc) | 17 | Amide | 2Aib, 3H, 5S, 6 $\alpha$ MePhe, 10V, 13 $\alpha$ MePhe, 17K, 18A, 20R, 26I, 27A                    |
| <b>Peptide 10</b> | H(Aib)HGS( $\alpha$ MePhe)TS<br>DVSK( $\alpha$ MePhe)LDSK(O<br>2Oc-O2Oc- $\gamma$ E-<br>C18diacid)17AARDFVE<br>WANT-amide                  | 15 | C18diacid | $\gamma$ E-<br>(O2Oc)-<br>(O2Oc) | 17 | Amide | 2Aib, 3H, 5S, 6 $\alpha$ MePhe, 10V, 13 $\alpha$ MePhe, 17K, 18A, 20R, 24E, 26I, 27A               |
| <b>Peptide 11</b> | H(Aib)HGS( $\alpha$ MePhe)TS<br>DVSK( $\alpha$ MePhe)LDSK(O<br>2Oc-O2Oc- $\gamma$ E-<br>C18diacid)17AAQDFVQ<br>(Aib)IANT-amide             | 16 | C18diacid | $\gamma$ E-<br>(O2Oc)-<br>(O2Oc) | 17 | Amide | 2Aib, 3H, 5S, 6 $\alpha$ MePhe, 10V, 13 $\alpha$ MePhe, 17K, 18A, 25Aib, 26I, 27A                  |
| <b>Peptide 12</b> | H(Aib)HGS( $\alpha$ MePhe)TS<br>DVSK( $\alpha$ MePhe)LDSK(O<br>2Oc-O2Oc- $\gamma$ E-<br>C18diacid)17AARDFVQ<br>(Aib)IANT-amide             | 17 | C18diacid | $\gamma$ E-<br>(O2Oc)-<br>(O2Oc) | 17 | Amide | 2Aib, 3H, 5S, 6 $\alpha$ MePhe, 10V, 13 $\alpha$ MePhe, 17K, 18A, 20R, 25Aib, 26I, 27A             |
| <b>Peptide 13</b> | H(Aib)HGS( $\alpha$ MePhe)TS<br>DVSK( $\alpha$ MePhe)LDSK(O<br>2Oc-O2Oc- $\gamma$ E-<br>C18diacid)17AARD( $\alpha$ MePhe)VQ(Aib)IANT-amide | 18 | C18diacid | $\gamma$ E-<br>(O2Oc)-<br>(O2Oc) | 17 | Amide | 2Aib, 3H, 5S, 6 $\alpha$ MePhe, 10V, 13 $\alpha$ MePhe, 17K, 18A, 20R,                             |

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|                       |                                                                                                                                                    |    |           |                                              |    |       |                                                                                                                                                |
|-----------------------|----------------------------------------------------------------------------------------------------------------------------------------------------|----|-----------|----------------------------------------------|----|-------|------------------------------------------------------------------------------------------------------------------------------------------------|
|                       |                                                                                                                                                    |    |           |                                              |    |       | 22 $\alpha$ MePhe,<br>25Aib, 26I,<br>27A                                                                                                       |
| <b>Peptide<br/>14</b> | H(Aib)HGS( $\alpha$ MePhe)TS<br>DVSK( $\alpha$ MePhe)LDSK(O<br>2Oc2- $\gamma$ E2-<br>C20diacid)17AARD( $\alpha$ M<br>ePhe)VQ(Aib)IANT-<br>amide    | 19 | C20diacid | $\gamma$ E- $\gamma$ E-<br>(O2Oc)-<br>(O2Oc) | 17 | Amide | 2Aib, 3H, 5S,<br>6 $\alpha$ MePhe,<br>10V,<br>13 $\alpha$ MePhe,<br>17K, 18A,<br>20R,<br>22 $\alpha$ MePhe,<br>25Aib, 26I,<br>27A              |
| <b>Peptide<br/>15</b> | H(Aib)HGS( $\alpha$ MePhe)TS<br>DVSK( $\alpha$ MePhe)LDSK(O<br>2Oc-O2Oc- $\gamma$ E-<br>C18diacid)17AARD( $\alpha$ M<br>ePhe)VE(Aib)IANT-<br>amide | 20 | C18diacid | $\gamma$ E-<br>(O2Oc)-<br>(O2Oc)             | 17 | Amide | 2Aib, 3H, 5S,<br>6 $\alpha$ MePhe,<br>10V,<br>13 $\alpha$ MePhe,<br>17K, 18A,<br>20R,<br>22 $\alpha$ MePhe,<br>24E, 25Aib,<br>26I, 27A         |
| <b>Peptide<br/>16</b> | H(Aib)HGS( $\alpha$ MePhe)TS<br>DVSK( $\alpha$ MePhe)LDSK(O<br>2Oc-O2Oc- $\gamma$ E-<br>C18diacid)17AARD( $\alpha$ M<br>ePhe)IA(Aib)IANT-<br>amide | 21 | C18diacid | $\gamma$ E-<br>(O2Oc)-<br>(O2Oc)             | 17 | Amide | 2Aib, 3H, 5S,<br>6 $\alpha$ MePhe,<br>10V,<br>13 $\alpha$ MePhe,<br>17K, 18A,<br>20R,<br>22 $\alpha$ MePhe,<br>23I, 24A,<br>25Aib, 26I,<br>27A |
| <b>Peptide<br/>17</b> | H(Aib)HGS( $\alpha$ MePhe)TS<br>DVSK( $\alpha$ MePhe)LDSK(O<br>2Oc-O2Oc- $\gamma$ E-<br>C18diacid)17AARD( $\alpha$ M<br>ePhe)VESIANT-amide         | 22 | C18diacid | $\gamma$ E-<br>(O2Oc)-<br>(O2Oc)             | 17 | Amide | 2Aib, 3H, 5S,<br>6 $\alpha$ MePhe,<br>10V,<br>13 $\alpha$ MePhe,<br>17K, 18A,<br>20R,<br>22 $\alpha$ MePhe,<br>24E, 25S,<br>26I, 27A           |
| <b>Peptide<br/>18</b> | H(Aib)HGS( $\alpha$ MePhe)TS<br>DVSK( $\alpha$ MePhe)LDSK(O<br>2Oc-O2Oc- $\gamma$ E-<br>C18diacid)17AARD( $\alpha$ M<br>ePhe)VQSIANT-amide         | 23 | C18diacid | $\gamma$ E-<br>(O2Oc)-<br>(O2Oc)             | 17 | Amide | 2Aib, 3H, 5S,<br>6 $\alpha$ MePhe,<br>10V,<br>13 $\alpha$ MePhe,<br>17K, 18A,<br>20R,                                                          |

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|                       |                                                                                                                                                        |    |           |                                              |    |       |                                                                                                                                        |
|-----------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------|----|-----------|----------------------------------------------|----|-------|----------------------------------------------------------------------------------------------------------------------------------------|
|                       |                                                                                                                                                        |    |           |                                              |    |       | 22 $\alpha$ MePhe,<br>25S, 26I, 27A                                                                                                    |
| <b>Peptide<br/>19</b> | H(Aib)HGS( $\alpha$ MePhe)TS<br>DVSK( $\alpha$ MePhe)LDSK(O<br>2Oc2- $\gamma$ E2-<br>C18diacid)17AARD( $\alpha$ M<br>ePhe)VQ(Aib)IANT-<br>amide        | 24 | C18diacid | $\gamma$ E- $\gamma$ E-<br>(O2Oc)-<br>(O2Oc) | 17 | Amide | 2Aib, 3H, 5S,<br>6 $\alpha$ MePhe,<br>10V,<br>13 $\alpha$ MePhe,<br>17K, 18A,<br>20R,<br>22 $\alpha$ MePhe,<br>25Aib, 26I,<br>27A      |
| <b>Peptide<br/>20</b> | H(Aib)HGS( $\alpha$ MePhe)TS<br>DVSK( $\alpha$ MePhe)LDSK(O<br>2Oc2- $\gamma$ E2-<br>C18diacid)17AARD( $\alpha$ M<br>ePhe)VE(Aib)IANT-<br>amide        | 25 | C18diacid | $\gamma$ E- $\gamma$ E-<br>(O2Oc)-<br>(O2Oc) | 17 | Amide | 2Aib, 3H, 5S,<br>6 $\alpha$ MePhe,<br>10V,<br>13 $\alpha$ MePhe,<br>17K, 18A,<br>20R,<br>22 $\alpha$ MePhe,<br>24E, 25Aib,<br>26I, 27A |
| <b>Peptide<br/>21</b> | H(Aib)HGS( $\alpha$ MePhe)TS<br>DVSK( $\alpha$ MePhe)LDSK( $\gamma$ E<br>-<br>C18diacid)17AAQD( $\alpha$ M<br>ePhe)VESIANT-amide                       | 26 | C18diacid | $\gamma$ E                                   | 17 | Amide | 2Aib, 3H, 5S,<br>6 $\alpha$ MePhe,<br>10V,<br>13 $\alpha$ MePhe,<br>17K, 18A,<br>22 $\alpha$ MePhe,<br>24E, 25S,<br>26I, 27A           |
| <b>Peptide<br/>22</b> | H(Aib)HGS( $\alpha$ MePhe)TS<br>DVSK( $\alpha$ MePhe)LDSK(O<br>2Oc-O2Oc- $\gamma$ E- $\gamma$ E-<br>C20diacid)17AAQD( $\alpha$ M<br>ePhe)VESIANT-amide | 27 | C20diacid | $\gamma$ E- $\gamma$ E-<br>(O2Oc)-<br>(O2Oc) | 17 | Amide | 2Aib, 3H, 5S,<br>6 $\alpha$ MePhe,<br>10V,<br>13 $\alpha$ MePhe,<br>17K, 18A,<br>22 $\alpha$ MePhe,<br>24E, 25S,<br>26I, 27A           |
| <b>Peptide<br/>23</b> | H(Aib)HGS( $\alpha$ MePhe)TS<br>DVSK( $\alpha$ MePhe)LDSK(O<br>2Oc-O2Oc- $\gamma$ E-<br>C18diacid)17AAQD( $\alpha$ M<br>ePhe)VESIANT-amide             | 28 | C18diacid | $\gamma$ E-<br>(O2Oc)-<br>(O2Oc)             | 17 | Amide | 2Aib, 3H, 5S,<br>6 $\alpha$ MePhe,<br>10V,<br>13 $\alpha$ MePhe,<br>17K, 18A,<br>22 $\alpha$ MePhe,<br>24E, 25S,<br>26I, 27A           |
| <b>Peptide<br/>24</b> | H(Aib)HGS( $\alpha$ MePhe)TS<br>DVSK( $\alpha$ MePhe)LDSK(O<br>2Oc-O2Oc- $\gamma$ E-                                                                   | 29 | C18diacid | $\gamma$ E-<br>(O2Oc)-<br>(O2Oc)             | 17 | Amide | 2Aib, 3H, 5S,<br>6 $\alpha$ MePhe,<br>10V,                                                                                             |

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|                   |                                                                                                                                             |    |           |                                      |    |       |                                                                                                        |
|-------------------|---------------------------------------------------------------------------------------------------------------------------------------------|----|-----------|--------------------------------------|----|-------|--------------------------------------------------------------------------------------------------------|
|                   | C18diacid)17AAQD( $\alpha$ MePhe)VQ(Aib)IANT-amide                                                                                          |    |           |                                      |    |       | 13 $\alpha$ MePhe, 17K, 18A, 22 $\alpha$ MePhe, 25Aib, 26I, 27A                                        |
| <b>Peptide 25</b> | H(Aib)HGS( $\alpha$ MePhe)TS DVSK( $\alpha$ MePhe)LDSK(O2Oc-O2Oc- $\gamma$ E- $\gamma$ E-C20diacid)17AAQD( $\alpha$ MePhe)VQ(Aib)IANT-amide | 30 | C20diacid | $\gamma$ E- $\gamma$ E-(O2Oc)-(O2Oc) | 17 | Amide | 2Aib, 3H, 5S, 6 $\alpha$ MePhe, 10V, 13 $\alpha$ MePhe, 17K, 18A, 22 $\alpha$ MePhe, 25Aib, 26I, 27A   |
| <b>Peptide 26</b> | H(Aib)QGS( $\alpha$ MePhe)TS DVSK( $\alpha$ MePhe)LDSK(O2Oc-O2Oc- $\gamma$ E-C18diacid)17AAQD( $\alpha$ MePhe)VQWIAN-amide                  | 31 | C18diacid | $\gamma$ E-(O2Oc)-(O2Oc)             | 17 | Amide | 2Aib, 5S, 6 $\alpha$ MePhe, 10V, 13 $\alpha$ MePhe, 17K, 18A, 22 $\alpha$ MePhe, 26I, 27A, des29T      |
| <b>Peptide 27</b> | H(Aib)QGS( $\alpha$ MePhe)TS DVSK( $\alpha$ MePhe)LDSK(O2Oc-O2Oc- $\gamma$ E-C18diacid)17AAQD( $\alpha$ MePhe)VEWIAN-amide                  | 32 | C18diacid | $\gamma$ E-(O2Oc)-(O2Oc)             | 17 | Amide | 2Aib, 5S, 6 $\alpha$ MePhe, 10V, 13 $\alpha$ MePhe, 17K, 18A, 22 $\alpha$ MePhe, 24E, 26I, 27A, des29T |
| <b>Peptide 28</b> | H(Aib)QGTFTSDVSK( $\alpha$ MePhe)LDSK(O2Oc-O2Oc- $\gamma$ E-C18diacid)17RAQDFVR WLL(Aib)T-acid                                              | 33 | C18diacid | $\gamma$ E-(O2Oc)-(O2Oc)             | 17 | Acid  | 2Aib, 10V, 13 $\alpha$ MePhe, 17K, 24R, 27L, 28Aib                                                     |
| <b>Peptide 29</b> | H(Aib)QGTFTSDVSK( $\alpha$ MePhe)LDSK(O2Oc-O2Oc- $\gamma$ E-C18diacid)17RA(Aib)DF VQWLL(Aib)T-acid                                          | 34 | C18diacid | $\gamma$ E-(O2Oc)-(O2Oc)             | 17 | Acid  | 2Aib, 10V, 13 $\alpha$ MePhe, 17K, 20Aib, 27L, 28Aib                                                   |
| <b>Peptide 30</b> | H(Aib)QGTFTSDVSK( $\alpha$ MePhe)LDSK(O2Oc-O2Oc- $\gamma$ E-C18diacid)17RAQDFVR WLL(Aib)TG-acid                                             | 35 | C18diacid | $\gamma$ E-(O2Oc)-(O2Oc)             | 17 | Acid  | 2Aib, 10V, 13 $\alpha$ MePhe, 17K, 24R, 27L, 28Aib, 30G                                                |
| <b>Peptide 31</b> | H(Aib)QGTFTSDVSK( $\alpha$ MePhe)LDSK(O2Oc-O2Oc- $\gamma$ E-                                                                                | 36 | C18diacid | $\gamma$ E-(O2Oc)-(O2Oc)             | 17 | Acid  | 2Aib, 10V, 13 $\alpha$ MePhe, 17K, 24R,                                                                |

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|                       |                                                                                                               |    |           |                                  |    |       |                                                                     |
|-----------------------|---------------------------------------------------------------------------------------------------------------|----|-----------|----------------------------------|----|-------|---------------------------------------------------------------------|
|                       | C18diacid)17RAQDFVR<br>WLL(Aib)G-acid                                                                         |    |           |                                  |    |       | 27L, 28E,<br>29Aib, 30G                                             |
| <b>Peptide<br/>32</b> | H(Aib)QGTFTSDVSK( $\alpha$<br>MePhe)LDSK( $\gamma$ E-<br>C18diacid)17RA(Aib)DF<br>VQWIAnt-amide               | 37 | C18diacid | $\gamma$ E                       | 17 | Amide | 2Aib, 10V,<br>13 $\alpha$ MePhe,<br>17K, 20Aib,<br>26I, 27A         |
| <b>Peptide<br/>33</b> | H(Aib)QGTFTSDVSK( $\alpha$<br>MePhe)LDSK(O2Oc-<br>O2Oc- $\gamma$ E-<br>C18diacid)17RAQDFVQ<br>WLL(Aib)T-acid  | 38 | C18diacid | $\gamma$ E-<br>(O2Oc)-<br>(O2Oc) | 17 | Acid  | 2Aib, 10V,<br>13 $\alpha$ MePhe,<br>17K, 27E,<br>28Aib              |
| <b>Peptide<br/>34</b> | H(Aib)QGTFTSDVSK( $\alpha$<br>MePhe)LDSK(O2Oc-<br>O2Oc- $\gamma$ E-<br>C18diacid)17RAQDFVQ<br>WLL(Aib)E-acid  | 39 | C18diacid | $\gamma$ E-<br>(O2Oc)-<br>(O2Oc) | 17 | Acid  | 2Aib, 10V,<br>13 $\alpha$ MePhe,<br>17K, 27L,<br>28Aib, 29E         |
| <b>Peptide<br/>35</b> | H(Aib)QGTFTSDVSK( $\alpha$<br>MePhe)LDTK(O2Oc-<br>O2Oc- $\gamma$ E-<br>C18diacid)17RAQDFVQ<br>WLL(Aib)T-acid  | 40 | C18diacid | $\gamma$ E-<br>(O2Oc)-<br>(O2Oc) | 17 | Acid  | 2Aib, 10V,<br>13 $\alpha$ MePhe,<br>16T, 17K,<br>27L, 28Aib         |
| <b>Peptide<br/>36</b> | H(Aib)QGTFTSDVSK( $\alpha$<br>MePhe)LDSK(O2Oc-<br>O2Oc- $\gamma$ E-<br>C18diacid)17RARDFVQ<br>WLL(Aib)T-acid  | 41 | C18diacid | $\gamma$ E-<br>(O2Oc)-<br>(O2Oc) | 17 | Acid  | 2Aib, 10V,<br>13 $\alpha$ MePhe,<br>17K, 20R,<br>27L, 28Aib         |
| <b>Peptide<br/>37</b> | H(Aib)QGTFTSDVSK( $\alpha$<br>MePhe)LDSK(O2Oc-<br>O2Oc- $\gamma$ E-<br>C18diacid)17RAEDFVQ<br>WLL(Aib)T-acid  | 42 | C18diacid | $\gamma$ E-<br>(O2Oc)-<br>(O2Oc) | 17 | Acid  | 2Aib, 10V,<br>13 $\alpha$ MePhe,<br>17K, 20E,<br>27L, 28Aib         |
| <b>Peptide<br/>38</b> | H(Aib)QGTFTSDVSK( $\alpha$<br>MePhe)LDSK(O2Oc-<br>O2Oc- $\gamma$ E-<br>C18diacid)17RAQDFVE<br>WLL(Aib)T-acid  | 43 | C18diacid | $\gamma$ E-<br>(O2Oc)-<br>(O2Oc) | 17 | Acid  | 2Aib, 10V,<br>13 $\alpha$ MePhe,<br>17K, 24E,<br>27L, 28Aib         |
| <b>Peptide<br/>39</b> | H(Aib)QGTFTSDVSK( $\alpha$<br>MePhe)LDSK(O2Oc-<br>O2Oc- $\gamma$ E-<br>C18diacid)17RAQDFVR<br>WLL(Aib)TE-acid | 44 | C18diacid | $\gamma$ E-<br>(O2Oc)-<br>(O2Oc) | 17 | Acid  | 2Aib, 10V,<br>13 $\alpha$ MePhe,<br>17K, 24R,<br>27L, 28Aib,<br>30E |
| <b>Peptide<br/>40</b> | H(Aib)QGTFTSDVSK( $\alpha$<br>MePhe)LDSK(O2Oc-<br>O2Oc- $\gamma$ E-<br>C18diacid)17RAQDFVQ<br>WLL(Aib)T-acid  | 45 | C18diacid | $\gamma$ E-<br>(O2Oc)-<br>(O2Oc) | 17 | Acid  | 2Aib, 10V,<br>13 $\alpha$ MePhe,<br>17K, 27L,<br>28Aib,             |

|                   |                                                                                                                                     |     |           |                                      |    |       |                                                                                                |
|-------------------|-------------------------------------------------------------------------------------------------------------------------------------|-----|-----------|--------------------------------------|----|-------|------------------------------------------------------------------------------------------------|
| <b>Peptide 41</b> | H(Aib)QGTFTSDYSK( $\alpha$ MePhe)LDSK(O2Oc-O2Oc- $\gamma$ E-C18diacid)17RAQDFVQWLV(PEG)4-amide                                      | 46  | C18diacid | $\gamma$ E-(O2Oc)-(O2Oc)             | 17 | Amide | 2Aib, 13 $\alpha$ MePhe, 17K, 27V, 28(PEG)4, des29                                             |
| <b>Peptide 42</b> | H(Aib)QGTFTSDVSK( $\alpha$ MePhe)LDSK(O2Oc-O2Oc- $\gamma$ E-C18diacid)17RAQDFVQ(Aib)LVAT-acid                                       | 47  | C18diacid | $\gamma$ E-(O2Oc)-(O2Oc)             | 17 | Acid  | 2Aib, 10V, 13 $\alpha$ MePhe, 17K, 25Aib, 27V, 28A                                             |
| <b>Peptide 43</b> | H(Aib)QGS( $\alpha$ MePhe)TS DVSK(Dip)LDSK((PEG)4- $\gamma$ E- $\gamma$ E-Palmitoyl)17RAQD( $\alpha$ MePhe)VE(Aib)LEAGG-amide       | 114 | Palmitoyl | $\gamma$ E- $\gamma$ E-(PEG)4        | 17 | Amide | 2Aib, 5S, 6 $\alpha$ MePhe, 10V, 13Dip, 17K, 22 $\alpha$ MePhe, 24E, 25Aib, 27E, 28A, 29G, 30G |
| <b>Peptide 44</b> | H(Aib)QGS( $\alpha$ MePhe)TS DVSK(Dip)LDSK((PEG)2-(PEG)2- $\gamma$ E- $\gamma$ E-Stearoyl)17AAQD( $\alpha$ MePhe)VE(Aib)LEAGG-amide | 115 | Stearoyl  | $\gamma$ E- $\gamma$ E-(PEG)2-(PEG)2 | 17 | Amide | 2Aib, 5S, 6 $\alpha$ MePhe, 10V, 13Dip, 17K, 22 $\alpha$ MePhe, 24E, 25Aib, 27E, 28A, 29G, 30G |
| <b>Peptide 45</b> | H(Aib)QGS( $\alpha$ MePhe)TS DVSK(Dip)LDSK((PEG)2-(PEG)2- $\gamma$ E- $\gamma$ E-Stearoyl)17AAQD( $\alpha$ MePhe)VE(Aib)LANT-amide  | 116 | Stearoyl  | $\gamma$ E- $\gamma$ E-(PEG)2-(PEG)2 | 17 | Amide | 2Aib, 5S, 6 $\alpha$ MePhe, 10V, 13Dip, 17K, 22 $\alpha$ MePhe, 24E, 25Aib, 27A                |
| <b>Peptide 46</b> | HSQGS( $\alpha$ MePhe)TSDVSK(Dip)LDSK((PEG)2-(PEG)2- $\gamma$ E- $\gamma$ E-Stearoyl)17AAQD( $\alpha$ MePhe)VE(Aib)LEAGG-amide      | 117 | Stearoyl  | $\gamma$ E- $\gamma$ E-(PEG)2-(PEG)2 | 17 | Amide | 5S, 6 $\alpha$ MePhe, 10V, 13Dip, 17K, 18A, 22 $\alpha$ MePhe, 24E, 25Aib, 27E, 28A, 29G, 30G  |
| <b>Peptide 47</b> | HSQGS( $\alpha$ MePhe)TSDVSK(Dip)LDSK((PEG)2-(PEG)2- $\gamma$ E- $\gamma$ E-Stearoyl)17AAQD( $\alpha$ MePhe)VE(Aib)LANT-amide       | 118 | Stearoyl  | $\gamma$ E- $\gamma$ E-(PEG)2-(PEG)2 | 17 | Amide | 5S, 6 $\alpha$ MePhe, 10V, 13Dip, 17K, 18A, 22 $\alpha$ MePhe,                                 |

|                   |                                                                                                                                  |     |          |                                      |    |       |                                                                                                    |
|-------------------|----------------------------------------------------------------------------------------------------------------------------------|-----|----------|--------------------------------------|----|-------|----------------------------------------------------------------------------------------------------|
|                   |                                                                                                                                  |     |          |                                      |    |       | 24E, 25Aib, 27A                                                                                    |
| <b>Peptide 48</b> | HSQGS( $\alpha$ MePhe)TSDVS K(Dip)LDSK((PEG)2-(PEG)2- $\gamma$ E- $\gamma$ E-Stearoyl)17AAQD( $\alpha$ MePhe)VE(Aib)LISG-amide   | 119 | Stearoyl | $\gamma$ E- $\gamma$ E-(PEG)2-(PEG)2 | 17 | Amide | 5S, 6 $\alpha$ MePhe, 10V, 13Dip, 17K, 18A, 22 $\alpha$ MePhe, 24E, 25Aib, 27I, 28S, 29G           |
| <b>Peptide 49</b> | HSQGS( $\alpha$ MePhe)TSDVS K(Dip)LDSK((PEG)2-(PEG)2- $\gamma$ E- $\gamma$ E-Stearoyl)17AAQD( $\alpha$ MePhe)VE(Aib)IANT-amide   | 120 | Stearoyl | $\gamma$ E- $\gamma$ E-(PEG)2-(PEG)2 | 17 | Amide | 5S, 6 $\alpha$ MePhe, 10V, 13Dip, 17K, 18A, 22 $\alpha$ MePhe, 24E, 25Aib, 26I, 27A                |
| <b>Peptide 50</b> | HSQGS( $\alpha$ MePhe)TSDVS K(Dip)LDSK((PEG)2-(PEG)2- $\gamma$ E- $\gamma$ E-Stearoyl)17AAQD( $\alpha$ MePhe)VE(Aib)IINT-amide   | 121 | Stearoyl | $\gamma$ E- $\gamma$ E-(PEG)2-(PEG)2 | 17 | Amide | 5S, 6 $\alpha$ MePhe, 10V, 13Dip, 17K, 18A, 22 $\alpha$ MePhe, 24E, 25Aib, 26I, 27I                |
| <b>Peptide 51</b> | HSQGS( $\alpha$ MePhe)TSDVS K(Dip)LDSK((PEG)2-(PEG)2- $\gamma$ E- $\gamma$ E-Stearoyl)17AAQD( $\alpha$ MePhe)VE(Aib)LLNT-amide   | 122 | Stearoyl | $\gamma$ E- $\gamma$ E-(PEG)2-(PEG)2 | 17 | Amide | 5S, 6 $\alpha$ MePhe, 10V, 13Dip, 17K, 18A, 22 $\alpha$ MePhe, 24E, 25Aib, 27L                     |
| <b>Peptide 52</b> | HSQGS( $\alpha$ MePhe)TSDVS K(Dip)LDSK((PEG)2-(PEG)2- $\gamma$ E- $\gamma$ E-Stearoyl)17AAQD( $\alpha$ MePhe)VE(Aib)ChaANT-amide | 123 | Stearoyl | $\gamma$ E- $\gamma$ E-(PEG)2-(PEG)2 | 17 | Amide | 5S, 6 $\alpha$ MePhe, 10V, 13Dip, 17K, 18A, 22 $\alpha$ MePhe, 24E, 25Aib, 26Cha, 27A              |
| <b>Peptide 53</b> | HSQGS( $\alpha$ MePhe)TSDVS K(Dip)LDSK((PEG)2-(PEG)2- $\gamma$ E- $\gamma$ E-Stearoyl)17AAQD( $\alpha$ MePhe)VE(Aib)VVEGG-amide  | 124 | Stearoyl | $\gamma$ E- $\gamma$ E-(PEG)2-(PEG)2 | 17 | Amide | 5S, 6 $\alpha$ MePhe, 10V, 13Dip, 17K, 18A, 22 $\alpha$ MePhe, 24E, 25Aib, 26V, 27V, 28E, 29G, 30G |

|                   |                                                                                                                                               |     |          |                                                 |    |       |                                                                                                          |
|-------------------|-----------------------------------------------------------------------------------------------------------------------------------------------|-----|----------|-------------------------------------------------|----|-------|----------------------------------------------------------------------------------------------------------|
| <b>Peptide 54</b> | HSQGS( $\alpha$ MePhe)TSDVS<br>K(Dip)LDSK((PEG)2-<br>(PEG)2- $\gamma$ E- $\gamma$ E-<br>Stearoyl)17AAQD( $\alpha$ Me<br>Phe)VQ(Aib)IAN-amide  | 125 | Stearoyl | $\gamma$ E- $\gamma$ E-<br>(PEG)2-<br>(PEG)2    | 17 | Amide | 5S,<br>6 $\alpha$ MePhe,<br>10V, 13Dip,<br>17K, 18A,<br>22 $\alpha$ MePhe,<br>25Aib, 26I,<br>27A, des29T |
| <b>Peptide 55</b> | HSQGS( $\alpha$ MePhe)TSDVS<br>K(Dip)LDSK((PEG)2-<br>(PEG)2- $\gamma$ E- $\gamma$ E-<br>Stearoyl)17AAQD( $\alpha$ Me<br>Phe)VQ(Dip)LEA-amide  | 126 | Stearoyl | $\gamma$ E- $\gamma$ E-<br>(PEG)2-<br>(PEG)2    | 17 | Amide | 5S,<br>6 $\alpha$ MePhe,<br>10V, 13Dip,<br>17K, 18A,<br>22 $\alpha$ MePhe,<br>25Dip, 27E,<br>28A, des29T |
| <b>Peptide 56</b> | HSQGS( $\alpha$ MePhe)TSDVS<br>K(Dip)LDSK((PEG)4- $\gamma$ E-<br>$\gamma$ E-<br>Stearoyl)17AAQD( $\alpha$ Me<br>Phe)VE(Aib)IINT-amide         | 127 | Stearoyl | $\gamma$ E- $\gamma$ E-<br>(PEG)4               | 17 | Amide | 5S,<br>6 $\alpha$ MePhe,<br>10V, 13Dip,<br>17K, 18A,<br>22 $\alpha$ MePhe,<br>24E, 25Aib,<br>26I, 27I    |
| <b>Peptide 57</b> | HSQGS( $\alpha$ MePhe)TSDVS<br>K(Dip)LDSK((PEG)8- $\gamma$ E-<br>$\gamma$ E-<br>Stearoyl)17AAQD( $\alpha$ Me<br>Phe)VE(Aib)IINT-amide         | 128 | Stearoyl | $\gamma$ E- $\gamma$ E-<br>(PEG)8               | 17 | Amide | 5S,<br>6 $\alpha$ MePhe,<br>10V, 13Dip,<br>17K, 18A,<br>22 $\alpha$ MePhe,<br>24E, 25Aib,<br>26I, 27I    |
| <b>Peptide 58</b> | HSQGS( $\alpha$ MePhe)TSDVS<br>K(Dip)LDSK((PEG)12-<br>$\gamma$ E- $\gamma$ E-<br>Stearoyl)17AAQD( $\alpha$ Me<br>Phe)VE(Aib)IINT-amide        | 129 | Stearoyl | $\gamma$ E- $\gamma$ E-<br>(PEG)12              | 17 | Amide | 5S,<br>6 $\alpha$ MePhe,<br>10V, 13Dip,<br>17K, 18A,<br>22 $\alpha$ MePhe,<br>24E, 25Aib,<br>26I, 27I    |
| <b>Peptide 59</b> | HSQGS( $\alpha$ MePhe)TSDVS<br>K(Dip)LDSK( $\gamma$ E- $\gamma$ E-<br>(PEG)2-(PEG)2-<br>Stearoyl)17AAQD( $\alpha$ Me<br>Phe)VE(Aib)IINT-amide | 130 | Stearoyl | (PEG)2-<br>(PEG)2-<br>$\gamma$ E- $\gamma$ E    | 17 | Amide | 5S,<br>6 $\alpha$ MePhe,<br>10V, 13Dip,<br>17K, 18A,<br>22 $\alpha$ MePhe,<br>24E, 25Aib,<br>26I, 27I    |
| <b>Peptide 60</b> | HSQGS( $\alpha$ MePhe)TSDVS<br>K(Dip)LDSK( $\gamma$ E-(PEG)2-<br>$\gamma$ E-(PEG)2-<br>Stearoyl)17AAQD( $\alpha$ Me<br>Phe)VE(Aib)IINT-amide  | 131 | Stearoyl | (PEG)2-<br>$\gamma$ E-<br>(PEG)2-<br>$\gamma$ E | 17 | Amide | 5S,<br>6 $\alpha$ MePhe,<br>10V, 13Dip,<br>17K, 18A,<br>22 $\alpha$ MePhe,                               |

|                   |                                                                                                                                                               |     |           |                                                 |    |       |                                                                                                                |
|-------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------|-----|-----------|-------------------------------------------------|----|-------|----------------------------------------------------------------------------------------------------------------|
|                   |                                                                                                                                                               |     |           |                                                 |    |       | 24E, 25Aib, 26I, 27I                                                                                           |
| <b>Peptide 61</b> | HSQGS( $\alpha$ MePhe)TSDVS<br>K(Dip)LDSK((PEG)2- $\gamma$ E-<br>(PEG)2- $\gamma$ E-<br>Stearoyl)17AAQD( $\alpha$ Me<br>Phe)VE(Aib)IINT-amide                 | 132 | Stearoyl  | $\gamma$ E-<br>(PEG)2-<br>$\gamma$ E-<br>(PEG)2 | 17 | Amide | 5S,<br>6 $\alpha$ MePhe,<br>10V, 13Dip,<br>17K, 18A,<br>22 $\alpha$ MePhe,<br>24E, 25Aib,<br>26I, 27I          |
| <b>Peptide 62</b> | HSQGS( $\alpha$ MePhe)TSDVS<br>K(Dip)LDSK((PEG)2-<br>(PEG)2- $\gamma$ E- $\gamma$ E-<br>Lauryl)17AAQD( $\alpha$ MePh<br>e)VE(Aib)IINT-amide                   | 133 | Lauryl    | $\gamma$ E- $\gamma$ E-<br>(PEG)2-<br>(PEG)2    | 17 | Amide | 5S,<br>6 $\alpha$ MePhe,<br>10V, 13Dip,<br>17K, 18A,<br>22 $\alpha$ MePhe,<br>24E, 25Aib,<br>26I, 27I          |
| <b>Peptide 63</b> | HSQGS( $\alpha$ MePhe)TSDVS<br>K(Dip)LDSK((PEG)2-<br>(PEG)2- $\gamma$ E- $\gamma$ E-<br>Myristoyl)17AAQD( $\alpha$ Me<br>Phe)VE(Aib)IINT-amide                | 134 | Myristoyl | $\gamma$ E- $\gamma$ E-<br>(PEG)2-<br>(PEG)2    | 17 | Amide | 5S,<br>6 $\alpha$ MePhe,<br>10V, 13Dip,<br>17K, 18A,<br>22 $\alpha$ MePhe,<br>24E, 25Aib,<br>26I, 27I          |
| <b>Peptide 64</b> | HSQGS( $\alpha$ MePhe)TSDVS<br>K(Dip)LDSK((PEG)2-<br>(PEG)2- $\gamma$ E- $\gamma$ E-<br>Palmitoyl)17AAQD( $\alpha$ M<br>ePhe)VE(Aib)IINT-<br>amide            | 135 | Palmitoyl | $\gamma$ E- $\gamma$ E-<br>(PEG)2-<br>(PEG)2    | 17 | Amide | 5S,<br>6 $\alpha$ MePhe,<br>10V, 13Dip,<br>17K, 18A,<br>22 $\alpha$ MePhe,<br>24E, 25Aib,<br>26I, 27I          |
| <b>Peptide 65</b> | HSQGS( $\alpha$ MePhe)TSDVS<br>K(Dip)LDSK((PEG)2-<br>(PEG)2- $\gamma$ E- $\gamma$ E-<br>C18diacid)17AAQD( $\alpha$ M<br>ePhe)VE(Aib)IINT-<br>amide            | 136 | Stearoyl  | $\gamma$ E- $\gamma$ E-<br>(PEG)2-<br>(PEG)2    | 17 | Amide | 5S,<br>6 $\alpha$ MePhe,<br>10V, 13Dip,<br>17K, 18A,<br>22 $\alpha$ MePhe,<br>24E, 25Aib,<br>26I, 27I          |
| <b>Peptide 66</b> | H(Aib)QGS( $\alpha$ MePhe)TS<br>DVSK(Dip)LDSK( $\epsilon$ -<br>((PEG)2-(PEG)2- $\gamma$ E- $\gamma$ E-<br>Stearyl)17AAQD( $\alpha$ MeP<br>he)VQ(Aib)IAN-amide | 137 | Stearoyl  | $\gamma$ E- $\gamma$ E-<br>(PEG)2-<br>(PEG)2    | 17 | Amide | 2Aib, 5S,<br>6 $\alpha$ MePhe,<br>10V, 13Dip,<br>17K, 18A,<br>22 $\alpha$ MePhe,<br>25Aib, 26I,<br>27A, des29T |

|                   |                                                                                                                                           |     |           |                                      |    |       |                                                                                                                 |
|-------------------|-------------------------------------------------------------------------------------------------------------------------------------------|-----|-----------|--------------------------------------|----|-------|-----------------------------------------------------------------------------------------------------------------|
| <b>Peptide 67</b> | H(Aib)QGS( $\alpha$ MePhe)TS DVSK(Dip)LDSK( $\epsilon$ -((PEG)2-(PEG)2- $\gamma$ E-Palmitoyl)17AAQD( $\alpha$ MePhe)VQ(Aib)IAN-amide      | 138 | Palmitoyl | $\gamma$ E-(PEG)2-(PEG)2             | 17 | Amide | 2Aib, 5S, 6 $\alpha$ MePhe, 10V, 13Dip, 17K, 18A, 22 $\alpha$ MePhe, 25Aib, 26I, 27A, des29T                    |
| <b>Peptide 68</b> | H(Aib)QGTFTSDVSK( $\alpha$ MePhe)LDVK((PEG)4- $\gamma$ E-Palmitoyl)17RAQD( $\alpha$ MePhe)VE(Aib)LNleET-amide                             | 139 | Palmitoyl | $\gamma$ E-(PEG)4                    | 17 | Amide | 2Aib, 10V, 13 $\alpha$ MePhe, 16V, 17K, 22 $\alpha$ MePhe, 24E, 25Aib, 27Nle, 28E                               |
| <b>Peptide 69</b> | H(Aib)QGTFTSDVSK( $\alpha$ MePhe)LDSK((PEG)2-(PEG)2- $\gamma$ E- $\gamma$ E-Stearoyl)17RAQD( $\alpha$ MePhe)VQ(Aib)LNleET-amide           | 140 | Stearoyl  | $\gamma$ E- $\gamma$ E-(PEG)2-(PEG)2 | 17 | Amide | 2Aib, 10V, 13 $\alpha$ MePhe, 16V, 17K, 22 $\alpha$ MePhe, 24E, 25Aib, 27Nle, 28E                               |
| <b>Peptide 70</b> | H(Aib)QGS( $\alpha$ MePhe)TS DVSK( $\alpha$ MePhe)LDSK((PEG)4- $\gamma$ E- $\gamma$ E-Stearoyl)17RAQD( $\alpha$ MePhe)VE(Aib)LEAGG-amide  | 141 | Stearoyl  | $\gamma$ E- $\gamma$ E-(PEG)4        | 17 | Amide | 2Aib, 5S, 6 $\alpha$ MePhe, 10V, 13 $\alpha$ MePhe, 17K, 22 $\alpha$ MePhe, 24E, 25Aib, 27E, 28A, 29G, 30G      |
| <b>Peptide 71</b> | H(Aib)QGS( $\alpha$ MePhe)TS DVSK( $\alpha$ MePhe)LDSK((PEG)4- $\gamma$ E- $\gamma$ E-Stearoyl)17AAQD( $\alpha$ MePhe)VE(Aib)LEAGG-amide  | 142 | Stearoyl  | $\gamma$ E- $\gamma$ E-(PEG)4        | 17 | Amide | 2Aib, 5S, 6 $\alpha$ MePhe, 10V, 13 $\alpha$ MePhe, 17K, 18A, 22 $\alpha$ MePhe, 24E, 25Aib, 27E, 28A, 29G, 30G |
| <b>Peptide 72</b> | H(Aib)QGS( $\alpha$ MePhe)TS DVSK( $\alpha$ MePhe)LDSK((PEG)4- $\gamma$ E- $\gamma$ E-Palmitoyl)17AAQD( $\alpha$ MePhe)VE(Aib)LEAGG-amide | 143 | Palmitoyl | $\gamma$ E- $\gamma$ E-(PEG)4        | 17 | Amide | 2Aib, 5S, 6 $\alpha$ MePhe, 10V, 13 $\alpha$ MePhe, 17K, 18A, 22 $\alpha$ MePhe, 24E, 25Aib, 27E, 28A, 29G, 30G |

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|                   |                                                                                                                                                                                              |     |           |                                              |    |       |                                                                                                                                                                |
|-------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----|-----------|----------------------------------------------|----|-------|----------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <b>Peptide 73</b> | H(Aib)QGS( $\alpha$ MePhe)TS<br>DVSK( $\alpha$ MePhe)LDSK((P<br>EG)2-(PEG)2- $\gamma$ E- $\gamma$ E-<br>Palmitoyl)17AAQD( $\alpha$ M<br>ePhe)VQ(Aib)IAN-<br>amide                            | 144 | Palmitoyl | $\gamma$ E- $\gamma$ E-<br>(PEG)2-<br>(PEG)2 | 17 | Amide | 2Aib, 5S,<br>6 $\alpha$ MePhe,<br>10V,<br>13 $\alpha$ MePhe,<br>17K, 18A,<br>22 $\alpha$ MePhe,<br>25Aib, 26I,<br>27A, des29T                                  |
| <b>Peptide 74</b> | H(Aib)QGS( $\alpha$ MePhe)TS<br>DVSK( $\alpha$ MePhe)LDSK((P<br>EG)2-(PEG)2- $\gamma$ E- $\gamma$ E-<br>Stearoyl)17( $\beta$ -<br>dimethylGln)AQD( $\alpha$ Me<br>Phe)VE(Aib)LEAGG-<br>amide | 145 | Stearoyl  | $\gamma$ E- $\gamma$ E-<br>(PEG)2-<br>(PEG)2 | 17 | Amide | 2Aib, 5S,<br>6 $\alpha$ MePhe,<br>10V,<br>13 $\alpha$ MePhe,<br>17K, 18 $\beta$ -<br>dimethyl-R,<br>22 $\alpha$ MePhe,<br>24E, 25Aib,<br>27E, 28A,<br>29G, 30G |
| <b>Peptide 75</b> | H(Aib)QGS( $\alpha$ MePhe)TS<br>DVSK( $\alpha$ MePhe)LDSK((P<br>EG)2-(PEG)2- $\gamma$ E- $\gamma$ E-<br>Palmitoyl)17AAQDIVQII<br>AN-amide                                                    | 146 | Palmitoyl | $\gamma$ E- $\gamma$ E-<br>(PEG)2-<br>(PEG)2 | 17 | Amide | 2Aib, 5S,<br>6 $\alpha$ MePhe,<br>10V,<br>13 $\alpha$ MePhe,<br>17K, 18A,<br>22I, 25I, 26I,<br>27A, des29T                                                     |
| <b>Peptide 76</b> | H(Aib)QGS( $\alpha$ MePhe)TS<br>DVSK( $\alpha$ MePhe)LDSK((P<br>EG)2-(PEG)2- $\gamma$ E- $\gamma$ E-<br>Stearoyl)17AAQD( $\alpha$ Me<br>Phe)VQ(Aib)VVEGG-<br>amide                           | 147 | Stearoyl  | $\gamma$ E- $\gamma$ E-<br>(PEG)2-<br>(PEG)2 | 17 | Amide | 2Aib, 5S,<br>6 $\alpha$ MePhe,<br>10V,<br>13 $\alpha$ MePhe,<br>17K, 18A,<br>22 $\alpha$ MePhe,<br>25Aib, 26V,<br>27V, 28E,<br>29G, 30G                        |
| <b>Peptide 77</b> | H(Aib)QGS( $\alpha$ MePhe)TS<br>DVSK( $\alpha$ MePhe)LDSK((P<br>EG)2-(PEG)2- $\gamma$ E- $\gamma$ E-<br>Stearoyl)17AAQD( $\alpha$ Me<br>Phe)VQ(Aib)LISG-<br>amide                            | 148 | Stearoyl  | $\gamma$ E- $\gamma$ E-<br>(PEG)2-<br>(PEG)2 | 17 | Amide | 2Aib, 5S,<br>6 $\alpha$ MePhe,<br>10V,<br>13 $\alpha$ MePhe,<br>17K, 18A,<br>22 $\alpha$ MePhe,<br>25Aib, 27I,<br>28S, 29G                                     |
| <b>Peptide 78</b> | HSQGS( $\alpha$ MePhe)TSDVS<br>K( $\alpha$ MePhe)LDSK((PEG)<br>2-(PEG)2- $\gamma$ E- $\gamma$ E-<br>Stearoyl)17AAQD( $\alpha$ Me                                                             | 149 | Stearoyl  | $\gamma$ E- $\gamma$ E-<br>(PEG)2-<br>(PEG)2 | 17 | Amide | 5S,<br>6 $\alpha$ MePhe,<br>10V,<br>13 $\alpha$ MePhe,<br>17K, 18A,                                                                                            |

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|                   |                                                                                                  |     |           |                     |    |       |                                                                           |
|-------------------|--------------------------------------------------------------------------------------------------|-----|-----------|---------------------|----|-------|---------------------------------------------------------------------------|
|                   | Phe)VQ(Aib)LEAGG-amide                                                                           |     |           |                     |    |       | 22αMePhe, 25Aib, 27E, 28A, 29G, 30G                                       |
| <b>Peptide 79</b> | HSQGS(αMePhe)TSDVS K(αMePhe)LDSK((PEG) 2-(PEG)2-γE-γE-Palmitoyl)17AAQD(αMePhe)VQ(Aib)LEAGG-amide | 150 | Palmitoyl | γE-γE-(PEG)2-(PEG)2 | 17 | Amide | 5S, 6αMePhe, 10V, 13αMePhe, 17K, 18A, 22αMePhe, 25Aib, 27E, 28A, 29G, 30G |
| <b>Peptide 80</b> | HSQGS(αMePhe)TSDVS K(αMePhe)LDSK((PEG) 2-(PEG)2-γE-γE-Margaroyl)17AAQD(αMePhe)VQ(Aib)LEAGG-amide | 151 | Palmitoyl | γE-γE-(PEG)2-(PEG)2 | 17 | Amide | 5S, 6αMePhe, 10V, 13αMePhe, 17K, 18A, 22αMePhe, 25Aib, 27E, 28A, 29G, 30G |
| <b>Peptide 81</b> | HSQGS(αMePhe)TSDVS K(αMePhe)LDSK((PEG) 2-(PEG)2-γE-γE-Stearoyl)17AAQD(αMePhe)VE(Aib)LEAGG-amide  | 152 | Stearoyl  | γE-γE-(PEG)2-(PEG)2 | 17 | Amide | 5S, 6αMePhe, 10V, 13αMePhe, 17K, 18A, 22αMePhe, 25Aib, 27E, 28A, 29G, 30G |
| <b>Peptide 82</b> | HSQGS(αMePhe)TSDVS K(αMePhe)LDSK((PEG) 2-(PEG)2-γE-γE-Stearoyl)17AAQD(αMePhe)VQ(Aib)IANT-amide   | 153 | Stearoyl  | γE-γE-(PEG)2-(PEG)2 | 17 | Amide | 5S, 6αMePhe, 10V, 13αMePhe, 17K, 18A, 22αMePhe, 25Aib, 26I, 27A           |
| <b>Peptide 83</b> | HSQGS(αMePhe)TSDVS K(αMePhe)LDSK((PEG) 2-(PEG)2-γE-γE-Stearoyl)17AAQD(αMePhe)VQ(Aib)IINT-amide   | 154 | Stearoyl  | γE-γE-(PEG)2-(PEG)2 | 17 | Amide | 5S, 6αMePhe, 10V, 13αMePhe, 17K, 18A, 22αMePhe, 25Aib, 26I, 27I           |

|                   |                                                                                                                                                                |     |           |                                              |    |       |                                                                                                                                   |
|-------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------|-----|-----------|----------------------------------------------|----|-------|-----------------------------------------------------------------------------------------------------------------------------------|
| <b>Peptide 84</b> | HSQGS( $\alpha$ MePhe)TSDVS<br>K( $\alpha$ MePhe)LDSK((PEG)<br>2-(PEG)2- $\gamma$ E- $\gamma$ E-<br>Stearoyl)17AAQD( $\alpha$ Me<br>Phe)VQ(Aib)LLNT-<br>amide  | 155 | Stearoyl  | $\gamma$ E- $\gamma$ E-<br>(PEG)2-<br>(PEG)2 | 17 | Amide | 5S,<br>6 $\alpha$ MePhe,<br>10V,<br>13 $\alpha$ MePhe,<br>17K, 18A,<br>22 $\alpha$ MePhe,<br>25Aib, 27L                           |
| <b>Peptide 85</b> | HSQGS( $\alpha$ MePhe)TSDVS<br>K( $\alpha$ MePhe)LDSK((PEG)<br>2-(PEG)2- $\gamma$ E- $\gamma$ E-<br>Stearoyl)17AAQD( $\alpha$ Me<br>Phe)VQ(Aib)VVEGG-<br>amide | 156 | Stearoyl  | $\gamma$ E- $\gamma$ E-<br>(PEG)2-<br>(PEG)2 | 17 | Amide | 5S,<br>6 $\alpha$ MePhe,<br>10V,<br>13 $\alpha$ MePhe,<br>17K, 18A,<br>22 $\alpha$ MePhe,<br>25Aib, 26V,<br>27V, 28E,<br>29G, 30G |
| <b>Peptide 86</b> | HSQGS( $\alpha$ MePhe)TSDVS<br>K( $\alpha$ MePhe)LDSK((PEG)<br>2-(PEG)2- $\gamma$ E- $\gamma$ E-<br>Stearoyl)17AAQD( $\alpha$ Me<br>Phe)VQ(Aib)IAN-amide       | 157 | Stearoyl  | $\gamma$ E- $\gamma$ E-<br>(PEG)2-<br>(PEG)2 | 17 | Amide | 5S,<br>6 $\alpha$ MePhe,<br>10V,<br>13 $\alpha$ MePhe,<br>17K, 18A,<br>22 $\alpha$ MePhe,<br>25Aib, 26I,<br>27A, des29T           |
| <b>Peptide 87</b> | HSQGS( $\alpha$ MePhe)TSDVS<br>K( $\alpha$ MePhe)LDSK((PEG)<br>2-(PEG)2- $\gamma$ E- $\gamma$ E-<br>Palmitoyl)17AAQD( $\alpha$ M<br>ePhe)VQ(Aib)IAN-<br>amide  | 158 | Palmitoyl | $\gamma$ E- $\gamma$ E-<br>(PEG)2-<br>(PEG)2 | 17 | Amide | 5S,<br>6 $\alpha$ MePhe,<br>10V,<br>13 $\alpha$ MePhe,<br>17K, 18A,<br>22 $\alpha$ MePhe,<br>25Aib, 26I,<br>27A, des29T           |
| <b>Peptide 88</b> | HSQGS( $\alpha$ MePhe)TSDVS<br>K( $\alpha$ MePhe)LDSK((PEG)<br>2-(PEG)2- $\gamma$ E- $\gamma$ E-<br>Margaroyl)17AAQD( $\alpha$<br>MePhe)VQ(Aib)IAN-<br>amide   | 159 | Margaroyl | $\gamma$ E- $\gamma$ E-<br>(PEG)2-<br>(PEG)2 | 17 | Amide | 5S,<br>6 $\alpha$ MePhe,<br>10V,<br>13 $\alpha$ MePhe,<br>17K, 18A,<br>22 $\alpha$ MePhe,<br>25Aib, 26I,<br>27A, des29T           |
| <b>Peptide 89</b> | HSQGS( $\alpha$ MePhe)TSDVS<br>K( $\alpha$ MePhe)LDSK((PEG)<br>2-(PEG)2- $\gamma$ E- $\gamma$ E-<br>Palmitoyl)17AAQD( $\alpha$ M<br>ePhe)VQIAN-amide           | 160 | Palmitoyl | $\gamma$ E- $\gamma$ E-<br>(PEG)2-<br>(PEG)2 | 17 | Amide | 5S,<br>6 $\alpha$ MePhe,<br>10V,<br>13 $\alpha$ MePhe,<br>17K, 18A,<br>22 $\alpha$ MePhe,                                         |

|                   |                                                                                                                                            |     |           |                                      |    |       |                                                                                                         |
|-------------------|--------------------------------------------------------------------------------------------------------------------------------------------|-----|-----------|--------------------------------------|----|-------|---------------------------------------------------------------------------------------------------------|
|                   |                                                                                                                                            |     |           |                                      |    |       | 25Aib, 26I, 27A, des29T                                                                                 |
| <b>Peptide 90</b> | HSQGS( $\alpha$ MePhe)TSDVS K( $\alpha$ MePhe)LDSK((PEG)2-(PEG)2- $\gamma$ E- $\gamma$ E-Palmitoyl)17AAQD( $\alpha$ MePhe)VE(Aib)IAN-amide | 161 | Palmitoyl | $\gamma$ E- $\gamma$ E-(PEG)2-(PEG)2 | 17 | Amide | 5S, 6 $\alpha$ MePhe, 10V, 13 $\alpha$ MePhe, 17K, 18A, 22 $\alpha$ MePhe, 24E, 25Aib, 26I, 27A, des29T |
| <b>Peptide 91</b> | HSQGS( $\alpha$ MePhe)TSDVS K( $\alpha$ MePhe)LDSK((PEG)2-(PEG)2- $\gamma$ E- $\gamma$ E-Palmitoyl)17AAQD( $\alpha$ MePhe)VQ(Aib)IAG-amide | 162 | Palmitoyl | $\gamma$ E- $\gamma$ E-(PEG)2-(PEG)2 | 17 | Amide | 5S, 6 $\alpha$ MePhe, 10V, 13 $\alpha$ MePhe, 17K, 18A, 22 $\alpha$ MePhe, 25Aib, 26I, 27A, 28A, des29T |
| <b>Peptide 92</b> | HSQGS( $\alpha$ MePhe)TSDVS K(Aib)LDSK((PEG)2-(PEG)2- $\gamma$ E- $\gamma$ E-Stearoyl)17AAQD( $\alpha$ MePhe)VQ(Aib)LEA-amide              | 163 | Stearoyl  | $\gamma$ E- $\gamma$ E-(PEG)2-(PEG)2 | 17 | Amide | 5S, 6 $\alpha$ MePhe, 10V, 13Aib, 17K, 18A, 22 $\alpha$ MePhe, 25Aib, 27E, 28A, des29T                  |
| <b>Peptide 93</b> | HSQGS( $\alpha$ MePhe)TSDVS K(Aib)LDSK((PEG)2-(PEG)2- $\gamma$ E- $\gamma$ E-Stearoyl)17AAQD( $\alpha$ MePhe)VQ(Aib)LAN-amide              | 164 | Stearoyl  | $\gamma$ E- $\gamma$ E-(PEG)2-(PEG)2 | 17 | Amide | 5S, 6 $\alpha$ MePhe, 10V, 13Aib, 17K, 18A, 22 $\alpha$ MePhe, 25Aib, 27A, des29T                       |
| <b>Peptide 94</b> | HSQGS( $\alpha$ MePhe)TSDVS K(Aib)LDSK((PEG)2-(PEG)2- $\gamma$ E- $\gamma$ E-Stearoyl)17AAQD( $\alpha$ MePhe)VQ(Aib)LSE-amide              | 165 | Stearoyl  | $\gamma$ E- $\gamma$ E-(PEG)2-(PEG)2 | 17 | Amide | 5S, 6 $\alpha$ MePhe, 10V, 13Aib, 17K, 18A, 22 $\alpha$ MePhe, 25Aib, 27S, 28E, des29T                  |
| <b>Peptide 95</b> | HSQGS( $\alpha$ MePhe)TSDVS K(Aib)LDSK((PEG)2-(PEG)2- $\gamma$ E- $\gamma$ E-Stearoyl)17AAQD( $\alpha$ MePhe)VQ(Aib)LANT-amide             | 166 | Stearoyl  | $\gamma$ E- $\gamma$ E-(PEG)2-(PEG)2 | 17 | Amide | 5S, 6 $\alpha$ MePhe, 10V, 13Aib, 17K, 18A, 22 $\alpha$ MePhe, 25Aib, 27A                               |

|                    |                                                                                                                                                    |     |           |                                              |    |       |                                                                                                                  |
|--------------------|----------------------------------------------------------------------------------------------------------------------------------------------------|-----|-----------|----------------------------------------------|----|-------|------------------------------------------------------------------------------------------------------------------|
| <b>Peptide 96</b>  | HSQGS( $\alpha$ MePhe)TSDVS<br>K(Aib)LDSK((PEG)2-<br>(PEG)2- $\gamma$ E- $\gamma$ E-<br>Stearoyl)17AAQD( $\alpha$ Me<br>Phe)VQ(Aib)LEAGG-<br>amide | 167 | Stearoyl  | $\gamma$ E- $\gamma$ E-<br>(PEG)2-<br>(PEG)2 | 17 | Amide | 5S,<br>6 $\alpha$ MePhe,<br>10V, 13Aib,<br>17K, 18A,<br>22 $\alpha$ MePhe,<br>25Aib, 27E,<br>28A, 29G,<br>30G    |
| <b>Peptide 97</b>  | HSQGS( $\alpha$ MePhe)TSDVS<br>K(Aib)LDSK((PEG)2-<br>(PEG)2- $\gamma$ E- $\gamma$ E-<br>Stearoyl)17AAQD( $\alpha$ Me<br>Phe)VQ(Aib)IAN-amide       | 168 | Stearoyl  | $\gamma$ E- $\gamma$ E-<br>(PEG)2-<br>(PEG)2 | 17 | Amide | 5S,<br>6 $\alpha$ MePhe,<br>10V, 13Aib,<br>17K, 18A,<br>22 $\alpha$ MePhe,<br>25Aib, 26I,<br>27A, des29T         |
| <b>Peptide 98</b>  | HSQGS( $\alpha$ MePhe)TSDVS<br>K(Aib)LDSK((PEG)2-<br>(PEG)2- $\gamma$ E- $\gamma$ E-<br>Stearoyl)17AAQD( $\alpha$ Me<br>Phe)VQ(Aib)IIE-amide       | 169 | Stearoyl  | $\gamma$ E- $\gamma$ E-<br>(PEG)2-<br>(PEG)2 | 17 | Amide | 5S,<br>6 $\alpha$ MePhe,<br>10V, 13Aib,<br>17K, 18A,<br>22 $\alpha$ MePhe,<br>25Aib, 26I,<br>27I, 28E,<br>des29T |
| <b>Peptide 99</b>  | HSQGS( $\alpha$ MePhe)TSDVS<br>K(Aib)LDSK((PEG)2-<br>(PEG)2- $\gamma$ E- $\gamma$ E-<br>Palmitoyl)17AAQD( $\alpha$ M<br>ePhe)VQ(Aib)IAN-<br>amide  | 170 | Palmitoyl | $\gamma$ E- $\gamma$ E-<br>(PEG)2-<br>(PEG)2 | 17 | Amide | 5S,<br>6 $\alpha$ MePhe,<br>10V, 13Aib,<br>17K, 18A,<br>22 $\alpha$ MePhe,<br>25Aib, 26I,<br>27A, des29T         |
| <b>Peptide 100</b> | H(Aib)QGS( $\alpha$ MePhe)TS<br>DVSK(Aib)LDSK((PEG)2-<br>(PEG)2- $\gamma$ E- $\gamma$ E-<br>Stearyl)17AAQD( $\alpha$ MeP<br>he)VQ(Aib)IAN-amide    | 171 | Stearoyl  | $\gamma$ E- $\gamma$ E-<br>(PEG)2-<br>(PEG)2 | 17 | Amide | 2Aib, 5S,<br>6 $\alpha$ MePhe,<br>10V, 13Aib,<br>17K, 18A,<br>22 $\alpha$ MePhe,<br>25Aib, 26I,<br>27A, des29T   |
| <b>Peptide 101</b> | H(Aib)QGS( $\alpha$ MePhe)TS<br>DVSK(Aib)LDSK((PEG)2-<br>(PEG)2- $\gamma$ E- $\gamma$ E-<br>Stearyl)17AAQD( $\alpha$ MeP<br>he)VQ(Aib)IAN-acid     | 172 | Stearoyl  | $\gamma$ E- $\gamma$ E-<br>(PEG)2-<br>(PEG)2 | 17 | Amide | 2Aib, 5S,<br>6 $\alpha$ MePhe,<br>10V, 13Aib,<br>17K, 18A,<br>22 $\alpha$ MePhe,<br>25Aib, 26I,<br>27A, des29T   |
| <b>Peptide 102</b> | H(Aib)QGS( $\alpha$ MePhe)TS<br>DVSK(Aib)LDSK((PEG)2-<br>(PEG)2- $\gamma$ E- $\gamma$ E-                                                           | 173 | Stearoyl  | $\gamma$ E- $\gamma$ E-<br>(PEG)2-<br>(PEG)2 | 17 | Amide | 2Aib, 5S,<br>6 $\alpha$ MePhe,<br>10V, 13Aib,                                                                    |

|                    |                                                                                                                               |     |           |                                      |    |       |                                                                                            |
|--------------------|-------------------------------------------------------------------------------------------------------------------------------|-----|-----------|--------------------------------------|----|-------|--------------------------------------------------------------------------------------------|
|                    | Stearyl)17RAQD( $\alpha$ MePhe)VQ(Aib)IAN-amide                                                                               |     |           |                                      |    |       | 17K, 18R, 22 $\alpha$ MePhe, 25Aib, 26I, 27A, des29T                                       |
| <b>Peptide 103</b> | H(Aib)QGS( $\alpha$ MePhe)TS DVSK(Aib)LDSK((PEG)2-(PEG)2- $\gamma$ E- $\gamma$ E-Stearyl)17AAQD( $\alpha$ MePhe)VQWIAN-amide  | 174 | Stearoyl  | $\gamma$ E- $\gamma$ E-(PEG)2-(PEG)2 | 17 | Amide | 2Aib, 5S, 6 $\alpha$ MePhe, 10V, 13Aib, 17K, 18A, 22 $\alpha$ MePhe, 26I, 27A, des29T      |
| <b>Peptide 104</b> | HTQGS( $\alpha$ MePhe)TSDVSK(Aib)LDSK((PEG)2-(PEG)2- $\gamma$ E- $\gamma$ E-Stearyl)17AAQD( $\alpha$ MePhe)VQ(Aib)IAN-amide   | 175 | Stearoyl  | $\gamma$ E- $\gamma$ E-(PEG)2-(PEG)2 | 17 | Amide | 2T, 5S, 6 $\alpha$ MePhe, 10V, 13Aib, 17K, 18A, 22 $\alpha$ MePhe, 25Aib, 26I, 27A, des29T |
| <b>Peptide 105</b> | HSQGS( $\alpha$ MePhe)TSDVSK(Aib)LDSK((PEG)2-(PEG)2- $\gamma$ E- $\gamma$ E-Palmitoyl)17QAQD( $\alpha$ MePhe)VQ(Aib)IAN-amide | 176 | Palmitoyl | $\gamma$ E- $\gamma$ E-(PEG)2-(PEG)2 | 17 | Amide | 5S, 6 $\alpha$ MePhe, 10V, 13Aib, 17K, 18Q, 22 $\alpha$ MePhe, 25Aib, 26I, 27A, des29T     |
| <b>Peptide 106</b> | HSQGS( $\alpha$ MePhe)TSDVSK(Aib)LDSK((PEG)2-(PEG)2- $\gamma$ E- $\gamma$ E-Palmitoyl)17AAQD( $\alpha$ MePhe)VQHIAN-amide     | 177 | Palmitoyl | $\gamma$ E- $\gamma$ E-(PEG)2-(PEG)2 | 17 | Amide | 5S, 6 $\alpha$ MePhe, 10V, 13Aib, 17K, 18A, 22 $\alpha$ MePhe, 25H, 26I, 27A, des29T       |
| <b>Peptide 107</b> | HSQGS( $\alpha$ MePhe)TSDVSK(Aib)LDSK((PEG)2-(PEG)2- $\gamma$ E- $\gamma$ E-Palmitoyl)17QAQD( $\alpha$ MePhe)VQHIAN-amide     | 178 | Palmitoyl | $\gamma$ E- $\gamma$ E-(PEG)2-(PEG)2 | 17 | Amide | 5S, 6 $\alpha$ MePhe, 10V, 13Aib, 17K, 18Q, 22 $\alpha$ MePhe, 25H, 26I, 27A, des29T       |
| <b>Peptide 108</b> | HSQGS( $\alpha$ MePhe)TSDVSK(Aib)LDSK(O2Oc-O2Oc- $\gamma$ E-C18diacid)17AAQD( $\alpha$ MePhe)VQ(Aib)IAN-amide                 | 179 | C18diacid | $\gamma$ E-(O2Oc)-(O2Oc)             | 17 | Amide | 5S, 6 $\alpha$ MePhe, 10V, 13Aib, 17K, 18A, 22 $\alpha$ MePhe, 25Aib, 26I, 27A, des29T     |

|                    |                                                                                                                                     |     |           |                                      |    |       |                                                                                                  |
|--------------------|-------------------------------------------------------------------------------------------------------------------------------------|-----|-----------|--------------------------------------|----|-------|--------------------------------------------------------------------------------------------------|
| <b>Peptide 109</b> | HSQGS( $\alpha$ MePhe)TSDVS (Ac-Lys)(Aib)LDSK(O2Oc-O2Oc- $\gamma$ E-C18diacid)17AAQD( $\alpha$ MePhe)VQ(Aib)IAN-amide               | 180 | C18diacid | $\gamma$ E-(O2Oc)-(O2Oc)             | 17 | Amide | 5S, 6 $\alpha$ MePhe, 10V, 12Ac-Lys, 13Aib, 17K, 18A, 22 $\alpha$ MePhe, 25Aib, 26I, 27A, des29T |
| <b>Peptide 110</b> | HSQGS( $\alpha$ MePhe)TSDVS (Ac-Lys)(Aib)LDSK((PEG)2-(PEG)2- $\gamma$ E- $\gamma$ E-Stearyl)17AAQD( $\alpha$ MePhe)VQ(Aib)IAN-amide | 181 | Stearoyl  | $\gamma$ E- $\gamma$ E-(PEG)2-(PEG)2 | 17 | Amide | 5S, 6 $\alpha$ MePhe, 10V, 12Ac-Lys, 13Aib, 17K, 18A, 22 $\alpha$ MePhe, 25Aib, 26I, 27A, des29T |
| <b>Peptide 111</b> | HSQGS( $\alpha$ MePhe)TSDVS KILDSK((PEG)2-(PEG)2- $\gamma$ E- $\gamma$ E-Palmitoyl)17AAQD( $\alpha$ MePhe)VQ(Aib)IAN-amide          | 182 | Palmitoyl | $\gamma$ E- $\gamma$ E-(PEG)2-(PEG)2 | 17 | Amide | 5S, 6 $\alpha$ MePhe, 10V, 13I, 17K, 18A, 22 $\alpha$ MePhe, 25Aib, 26I, 27A, des29T             |
| <b>Peptide 112</b> | HSQGS( $\alpha$ MePhe)TSDVS KILDSK((PEG)2-(PEG)2- $\gamma$ E- $\gamma$ E-Palmitoyl)17AAQD( $\alpha$ MePhe)VQIIAN-amide              | 183 | Palmitoyl | $\gamma$ E- $\gamma$ E-(PEG)2-(PEG)2 | 17 | Amide | 5S, 6 $\alpha$ MePhe, 10V, 13I, 17K, 18A, 22 $\alpha$ MePhe, 25I, 26I, 27A, des29T               |
| <b>Peptide 113</b> | HSQGS( $\alpha$ MePhe)TSDVS KILDSK((PEG)2-(PEG)2- $\gamma$ E- $\gamma$ E-Palmitoyl)17AAQD( $\alpha$ MePhe)VQIIAG-amide              | 184 | Palmitoyl | $\gamma$ E- $\gamma$ E-(PEG)2-(PEG)2 | 17 | Amide | 5S, 6 $\alpha$ MePhe, 10V, 13I, 17K, 18A, 22 $\alpha$ MePhe, 25I, 26I, 27A, 28G, des29T          |
| <b>Peptide 114</b> | HSQGS( $\alpha$ MePhe)TSDVS KILDSK((PEG)2-(PEG)2- $\gamma$ E- $\gamma$ E-Palmitoyl)17AAQD( $\alpha$ MePhe)VEIIAN-amide              | 185 | Palmitoyl | $\gamma$ E- $\gamma$ E-(PEG)2-(PEG)2 | 17 | Amide | 5S, 6 $\alpha$ MePhe, 10V, 13I, 17K, 18A, 22 $\alpha$ MePhe, 24E, 25I, 26I, 27A, des29T          |
| <b>Peptide 115</b> | HSQGS( $\alpha$ MePhe)TSDVS KILDSK((PEG)2-(PEG)2- $\gamma$ E- $\gamma$ E-                                                           | 186 | Palmitoyl | $\gamma$ E- $\gamma$ E-(PEG)2-(PEG)2 | 17 | Amide | 5S, 6 $\alpha$ MePhe, 10V, 13I,                                                                  |

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|                    |                                                                                                                             |     |           |                                      |    |       |                                                                              |
|--------------------|-----------------------------------------------------------------------------------------------------------------------------|-----|-----------|--------------------------------------|----|-------|------------------------------------------------------------------------------|
|                    | Palmitoyl)17AAQD( $\alpha$ MePhe)VQ( $\alpha$ MePhe)IAN-amide                                                               |     |           |                                      |    |       | 17K, 18A, 22 $\alpha$ MePhe, 25 $\alpha$ MePhe, 26I, 27A, des29T             |
| <b>Peptide 116</b> | HSQGS( $\alpha$ MePhe)TSDVS KILDSK((PEG)2-(PEG)2- $\gamma$ E- $\gamma$ E-Palmitoyl)17AAQD( $\alpha$ MePhe)VEWIINT-amide     | 187 | Palmitoyl | $\gamma$ E- $\gamma$ E-(PEG)2-(PEG)2 | 17 | Amide | 5S, 6 $\alpha$ MePhe, 10V, 13I, 17K, 18A, 22 $\alpha$ MePhe, 24E, 26I, 27I   |
| <b>Peptide 117</b> | HSQGS( $\alpha$ MePhe)TSDVS KILDSK((PEG)2-(PEG)2- $\gamma$ E- $\gamma$ E-Stearoyl)17AAQD( $\alpha$ MePhe)VQ(Aib)IINT-amide  | 188 | Stearoyl  | $\gamma$ E- $\gamma$ E-(PEG)2-(PEG)2 | 17 | Amide | 5S, 6 $\alpha$ MePhe, 10V, 13I, 17K, 18A, 22 $\alpha$ MePhe, 25Aib, 26I, 27I |
| <b>Peptide 118</b> | HSQGS( $\alpha$ MePhe)TSDVS KILDSK((PEG)2-(PEG)2- $\gamma$ E- $\gamma$ E-Palmitoyl)17AAQD( $\alpha$ MePhe)VQ(Aib)IINT-amide | 189 | Palmitoyl | $\gamma$ E- $\gamma$ E-(PEG)2-(PEG)2 | 17 | Amide | 5S, 6 $\alpha$ MePhe, 10V, 13I, 17K, 18A, 22 $\alpha$ MePhe, 25Aib, 26I, 27I |
| <b>Peptide 119</b> | HSQGS( $\alpha$ MePhe)TSDVS KILDSK((PEG)2-(PEG)2- $\gamma$ E- $\gamma$ E-Myristoyl)17AAQD( $\alpha$ MePhe)VQ(Aib)IINT-amide | 190 | Myristoyl | $\gamma$ E- $\gamma$ E-(PEG)2-(PEG)2 | 17 | Amide | 5S, 6 $\alpha$ MePhe, 10V, 13I, 17K, 18A, 22 $\alpha$ MePhe, 25Aib, 26I, 27I |
| <b>Peptide 120</b> | HSQGS( $\alpha$ MePhe)TSDVS KILDSK((PEG)2-(PEG)2- $\gamma$ E- $\gamma$ E-Stearoyl)17AAQD( $\alpha$ MePhe)VQ(Aib)IINT-amide  | 191 | Stearoyl  | $\gamma$ E-(PEG)2-(PEG)2             | 17 | Amide | 5S, 6 $\alpha$ MePhe, 10V, 13I, 17K, 18A, 22 $\alpha$ MePhe, 25Aib, 26I, 27I |
| <b>Peptide 121</b> | HSQGS( $\alpha$ MePhe)TSDVS KILDSK((PEG)2-(PEG)2- $\gamma$ E- $\gamma$ E-Palmitoyl)17AAQD( $\alpha$ MePhe)VQ(Aib)IINT-amide | 192 | Palmitoyl | $\gamma$ E-(PEG)2-(PEG)2             | 17 | Amide | 5S, 6 $\alpha$ MePhe, 10V, 13I, 17K, 18A, 22 $\alpha$ MePhe, 25Aib, 26I, 27I |

|                    |                                                                                                                                                    |     |           |                                              |    |       |                                                                                                            |
|--------------------|----------------------------------------------------------------------------------------------------------------------------------------------------|-----|-----------|----------------------------------------------|----|-------|------------------------------------------------------------------------------------------------------------|
| <b>Peptide 122</b> | HSQGS( $\alpha$ MePhe)TSDVS<br>KILDSK((PEG)2-(PEG)2-<br>$\gamma$ E-<br>Myristoyl)17AAQD( $\alpha$ M<br>ePhe)VQ(Aib)IINT-<br>amide                  | 193 | Myristoyl | $\gamma$ E-<br>(PEG)2-<br>(PEG)2             | 17 | Amide | 5S,<br>6 $\alpha$ MePhe,<br>10V, 13I,<br>17K, 18A,<br>22 $\alpha$ MePhe,<br>25Aib, 26I,<br>27I             |
| <b>Peptide 123</b> | H(Aib)QGS( $\alpha$ MePhe)TS<br>DVSKILDSK((PEG)2-<br>(PEG)2- $\gamma$ E- $\gamma$ E-<br>Palmitoyl)17AAQD( $\alpha$ M<br>ePhe)VQIIAN-amide          | 194 | Palmitoyl | $\gamma$ E- $\gamma$ E-<br>(PEG)2-<br>(PEG)2 | 17 | Amide | 2Aib, 5S,<br>6 $\alpha$ MePhe,<br>10V, 13I,<br>17K, 18A,<br>22 $\alpha$ MePhe,<br>25I, 26I, 27A,<br>des29T |
| <b>Peptide 124</b> | H(Aib)QGS( $\alpha$ MePhe)TS<br>DVSKILDSK((PEG)2-<br>(PEG)2- $\gamma$ E- $\gamma$ E-<br>Stearoyl)17AAQD( $\alpha$ Me<br>Phe)VQ(Aib)IINT-amide      | 195 | Stearoyl  | $\gamma$ E- $\gamma$ E-<br>(PEG)2-<br>(PEG)2 | 17 | Amide | 2Aib, 5S,<br>6 $\alpha$ MePhe,<br>10V, 13I,<br>17K, 18A,<br>22 $\alpha$ MePhe,<br>25Aib, 26I,<br>27I       |
| <b>Peptide 125</b> | H(Aib)QGS( $\alpha$ MePhe)TS<br>DVSKILDSK((PEG)2-<br>(PEG)2- $\gamma$ E- $\gamma$ E-<br>Palmitoyl)17AAQD( $\alpha$ M<br>ePhe)VQ(Aib)IINT-<br>amide | 196 | Palmitoyl | $\gamma$ E- $\gamma$ E-<br>(PEG)2-<br>(PEG)2 | 17 | Amide | 2Aib, 5S,<br>6 $\alpha$ MePhe,<br>10V, 13I,<br>17K, 18A,<br>22 $\alpha$ MePhe,<br>25Aib, 26I,<br>27I       |
| <b>Peptide 126</b> | H(Aib)QGS( $\alpha$ MePhe)TS<br>DVSKILDSK((PEG)2-<br>(PEG)2- $\gamma$ E- $\gamma$ E-<br>Myristoyl)17AAQD( $\alpha$ M<br>ePhe)VQ(Aib)IINT-<br>amide | 197 | Myristoyl | $\gamma$ E- $\gamma$ E-<br>(PEG)2-<br>(PEG)2 | 17 | Amide | 2Aib, 5S,<br>6 $\alpha$ MePhe,<br>10V, 13I,<br>17K, 18A,<br>22 $\alpha$ MePhe,<br>25Aib, 26I,<br>27I       |
| <b>Peptide 127</b> | H(Aib)QGS( $\alpha$ MePhe)TS<br>DVSKILDSK((PEG)2-<br>(PEG)2- $\gamma$ E-<br>Stearoyl)17AAQD( $\alpha$ Me<br>Phe)VQ(Aib)IINT-amide                  | 198 | Stearoyl  | $\gamma$ E-<br>(PEG)2-<br>(PEG)2             | 17 | Amide | 2Aib, 5S,<br>6 $\alpha$ MePhe,<br>10V, 13I,<br>17K, 18A,<br>22 $\alpha$ MePhe,<br>25Aib, 26I,<br>27I       |
| <b>Peptide 128</b> | H(Aib)QGS( $\alpha$ MePhe)TS<br>DVSKILDSK((PEG)2-<br>(PEG)2- $\gamma$ E-<br>Palmitoyl)17AAQD( $\alpha$ M                                           | 199 | Palmitoyl | $\gamma$ E-<br>(PEG)2-<br>(PEG)2             | 17 | Amide | 2Aib, 5S,<br>6 $\alpha$ MePhe,<br>10V, 13I,<br>17K, 18A,<br>22 $\alpha$ MePhe,                             |

|                    |                                                                                                                                                                |     |           |                                              |    |       |                                                                                                                     |
|--------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------|-----|-----------|----------------------------------------------|----|-------|---------------------------------------------------------------------------------------------------------------------|
|                    | ePhe)VQ(Aib)IINT-amide                                                                                                                                         |     |           |                                              |    |       | 25Aib, 26I, 27I                                                                                                     |
| <b>Peptide 129</b> | H(Aib)QGS( $\alpha$ MePhe)TS<br>DVS <sub>K</sub> ILDSK((PEG)2-<br>(PEG)2- $\gamma$ E-<br>Myristoyl)17AAQD( $\alpha$ M<br>ePhe)VQ(Aib)IINT-<br>amide            | 200 | Myristoyl | $\gamma$ E-<br>(PEG)2-<br>(PEG)2             | 17 | Amide | 2Aib, 5S,<br>6 $\alpha$ MePhe,<br>10V, 13I,<br>17K, 18A,<br>22 $\alpha$ MePhe,<br>25Aib, 26I,<br>27I                |
| <b>Peptide 130</b> | H( $\alpha$ MeSer)QGS( $\alpha$ MePh<br>e)TSDVSKILDSK((PEG)2-<br>(PEG)2- $\gamma$ E- $\gamma$ E-<br>Stearoyl)17AAQD( $\alpha$ Me<br>Phe)VQ(Aib)IINT-amide      | 201 | Stearoyl  | $\gamma$ E- $\gamma$ E-<br>(PEG)2-<br>(PEG)2 | 17 | Amide | 2 $\alpha$ MeSer,<br>5S,<br>6 $\alpha$ MePhe,<br>10V, 13I,<br>17K, 18A,<br>22 $\alpha$ MePhe,<br>25Aib, 26I,<br>27I |
| <b>Peptide 131</b> | H( $\alpha$ MeSer)QGS( $\alpha$ MePh<br>e)TSDVSKILDSK((PEG)2-<br>(PEG)2- $\gamma$ E- $\gamma$ E-<br>Palmitoyl)17AAQD( $\alpha$ M<br>ePhe)VQ(Aib)IINT-<br>amide | 202 | Palmitoyl | $\gamma$ E- $\gamma$ E-<br>(PEG)2-<br>(PEG)2 | 17 | Amide | 2 $\alpha$ MeSer,<br>5S,<br>6 $\alpha$ MePhe,<br>10V, 13I,<br>17K, 18A,<br>22 $\alpha$ MePhe,<br>25Aib, 26I,<br>27I |
| <b>Peptide 132</b> | H( $\alpha$ MeSer)QGS( $\alpha$ MePh<br>e)TSDVSKILDSK((PEG)2-<br>(PEG)2- $\gamma$ E- $\gamma$ E-<br>Myristoyl)17AAQD( $\alpha$ M<br>ePhe)VQ(Aib)IINT-<br>amide | 203 | Myristoyl | $\gamma$ E- $\gamma$ E-<br>(PEG)2-<br>(PEG)2 | 17 | Amide | 2 $\alpha$ MeSer,<br>5S,<br>6 $\alpha$ MePhe,<br>10V, 13I,<br>17K, 18A,<br>22 $\alpha$ MePhe,<br>25Aib, 26I,<br>27I |
| <b>Peptide 133</b> | H( $\alpha$ MeSer)QGS( $\alpha$ MePh<br>e)TSDVSKILDSK((PEG)2-<br>(PEG)2- $\gamma$ E-<br>Stearoyl)17AAQD( $\alpha$ Me<br>Phe)VQ(Aib)IINT-amide                  | 204 | Stearoyl  | $\gamma$ E-<br>(PEG)2-<br>(PEG)2             | 17 | Amide | 2 $\alpha$ MeSer,<br>5S,<br>6 $\alpha$ MePhe,<br>10V, 13I,<br>17K, 18A,<br>22 $\alpha$ MePhe,<br>25Aib, 26I,<br>27I |
| <b>Peptide 134</b> | H( $\alpha$ MeSer)QGS( $\alpha$ MePh<br>e)TSDVSKILDSK((PEG)2-<br>(PEG)2- $\gamma$ E-<br>Palmitoyl)17AAQD( $\alpha$ M<br>ePhe)VQ(Aib)IINT-<br>amide             | 205 | Palmitoyl | $\gamma$ E-<br>(PEG)2-<br>(PEG)2             | 17 | Amide | 2 $\alpha$ MeSer,<br>5S,<br>6 $\alpha$ MePhe,<br>10V, 13I,<br>17K, 18A,<br>22 $\alpha$ MePhe,                       |

|                    |                                                                                                                                    |     |           |                                                              |    |       |                                                                                                |
|--------------------|------------------------------------------------------------------------------------------------------------------------------------|-----|-----------|--------------------------------------------------------------|----|-------|------------------------------------------------------------------------------------------------|
|                    |                                                                                                                                    |     |           |                                                              |    |       | 25Aib, 26I, 27I                                                                                |
| <b>Peptide 135</b> | H( $\alpha$ MeSer)QGS( $\alpha$ MePhe)TSDVSKILDSK((PEG)2-(PEG)2- $\gamma$ E-Myristoyl)17AAQD( $\alpha$ MePhe)VQ(Aib)IINT-amide     | 206 | Myristoyl | $\gamma$ E-(PEG)2-(PEG)2                                     | 17 | Amide | 2 $\alpha$ MeSer, 5S, 6 $\alpha$ MePhe, 10V, 13I, 17K, 18A, 22 $\alpha$ MePhe, 25Aib, 26I, 27I |
| <b>Peptide 136</b> | H(Aib)QGTFTSDVSK( $\alpha$ MePhe)LDSK( $\gamma$ E- $\gamma$ E-O2Oc-O2Oc- $\gamma$ E- $\gamma$ E-C18diacid)17RARDFVRWLLE(Aib)G-acid | 48  | C18diacid | $\gamma$ E- $\gamma$ E(O2Oc)- (O2Oc)- $\gamma$ E- $\gamma$ E | 17 | Acid  | 2Aib, 10V, 13 $\alpha$ MePhe, 17K, 20R, 24R, 27L, 28E, 29Aib, 30G                              |
| <b>Peptide 137</b> | H(Aib)QGTFTSDVSK( $\alpha$ MePhe)LDSK( $\gamma$ E- $\gamma$ E-O2Oc-O2Oc- $\gamma$ E- $\gamma$ E-C18diacid)17RAQDFVRWLLEG(Aib)-acid | 49  | C18diacid | $\gamma$ E- $\gamma$ E(O2Oc)- (O2Oc)- $\gamma$ E- $\gamma$ E | 17 | Acid  | 2Aib, 10V, 13 $\alpha$ MePhe, 17K, 24R, 27L, 28E, 29G, 30Aib                                   |
| <b>Peptide 138</b> | H(Aib)QGTFTSDVSK( $\alpha$ MePhe)LDSK( $\gamma$ E- $\gamma$ E-O2Oc-O2Oc- $\gamma$ E- $\gamma$ E-C18diacid)17RAQDFVRWLLE(Aib)G-acid | 50  | C18diacid | $\gamma$ E- $\gamma$ E(O2Oc)- (O2Oc)- $\gamma$ E- $\gamma$ E | 17 | Acid  | 2Aib, 10V, 13 $\alpha$ MePhe, 17K, 24R, 27L, 28E, 29Aib, 30G                                   |
| <b>Peptide 139</b> | H(Aib)QGTFTSDVSK( $\alpha$ MePhe)LDSK( $\gamma$ E- $\gamma$ E-O2Oc-O2Oc- $\gamma$ E- $\gamma$ E-C20diacid)17RAQDFVRWLLE(Aib)G-acid | 51  | C20diacid | $\gamma$ E- $\gamma$ E(O2Oc)- (O2Oc)- $\gamma$ E- $\gamma$ E | 17 | Acid  | 2Aib, 10V, 13 $\alpha$ MePhe, 17K, 24R, 27L, 28E, 29Aib, 30G                                   |
| <b>Peptide 140</b> | H(Aib)QGTFTSDVSK( $\alpha$ MePhe)LDTK(O2Oc-O2Oc- $\gamma$ E-C18diacid)17RAQDFVRWLLE(Aib)G-acid                                     | 52  | C18diacid | $\gamma$ E-(O2Oc)- (O2Oc)                                    | 17 | Acid  | 2Aib, 10V, 13 $\alpha$ MePhe, 16T, 17K, 24R, 27L, 28E, 29Aib, 30G                              |
| <b>Peptide 141</b> | H(Aib)QGTFTSDVSK( $\alpha$ MePhe)LDSK(O2Oc-O2Oc- $\gamma$ E-C18diacid)17RAQDFVWLLE(Aib)G-acid                                      | 53  | C18diacid | $\gamma$ E-(O2Oc)- (O2Oc)                                    | 17 | Acid  | 2Aib, 10V, 13 $\alpha$ MePhe, 17K, 24A, 27L, 28E, 29Aib, 30G                                   |
| <b>Peptide 142</b> | H(Aib)QGTFTSDVSK( $\alpha$ MePhe)LDSK(O2Oc-O2Oc- $\gamma$ E-C18diacid)17RARDFVWLLE(Aib)G-acid                                      | 54  | C18diacid | $\gamma$ E-(O2Oc)- (O2Oc)                                    | 17 | Acid  | 2Aib, 10V, 13 $\alpha$ MePhe, 17K, 20R, 24A, 27L,                                              |

|                    |                                                                                                                                      |    |           |                                                              |    |      |                                                                   |
|--------------------|--------------------------------------------------------------------------------------------------------------------------------------|----|-----------|--------------------------------------------------------------|----|------|-------------------------------------------------------------------|
|                    |                                                                                                                                      |    |           |                                                              |    |      | 28E, 29Aib, 30G                                                   |
| <b>Peptide 143</b> | H(Aib)QGTFTSDVSK( $\alpha$ M ePhe)LDSK(O2Oc-O2Oc- $\gamma$ E-C18diacid)17RARDFVQ WLL(EAib)G-acid                                     | 55 | C18diacid | $\gamma$ E-(O2Oc)-(O2Oc)                                     | 17 | Acid | 2Aib, 10V, 13 $\alpha$ MePhe, 17K, 20R, 27L, 28E, 29Aib, 30G      |
| <b>Peptide 144</b> | H(Aib)QGTFTSDVSK( $\alpha$ M ePhe)LDSK( $\gamma$ E- $\gamma$ E-O2Oc-O2Oc- $\gamma$ E- $\gamma$ E-C18diacid)17RARDFVR WLL(EAib)G-acid | 56 | C18diacid | $\gamma$ E- $\gamma$ E(O2Oc)- (O2Oc)- $\gamma$ E- $\gamma$ E | 17 | Acid | 2Aib, 10V, 13 $\alpha$ MePhe, 17K, 20R, 24R, 27L, 28E, 29Aib, 30G |
| <b>Peptide 145</b> | H(Aib)QGTFTSDVSK( $\alpha$ M ePhe)LDSK(O2Oc-O2Oc- $\gamma$ E-C18diacid)17RAQDFVR WLASRG(I)-acid                                      | 57 | C18diacid | $\gamma$ E-(O2Oc)-(O2Oc)                                     | 17 | Acid | 2Aib, 10V, 13 $\alpha$ MePhe, 17K, 24R, 27A, 28S, 29R, 30G, 31I   |
| <b>Peptide 146</b> | H(Aib)QGTFTSDVSK( $\alpha$ M ePhe)LDSK(O2Oc-O2Oc- $\gamma$ E-C18diacid)17RAQDFVR WLASR-acid                                          | 58 | C18diacid | $\gamma$ E-(O2Oc)-(O2Oc)                                     | 17 | Acid | 2Aib, 10V, 13 $\alpha$ MePhe, 17K, 24R, 27A, 28S, 29R             |
| <b>Peptide 147</b> | H(Aib)QGTFTSDVSK( $\alpha$ M ePhe)LDSK(O2Oc-O2Oc- $\gamma$ E-C18diacid)17RAQDFVR WLEA(Aib)G-acid                                     | 59 | C18diacid | $\gamma$ E-(O2Oc)-(O2Oc)                                     | 17 | Acid | 2Aib, 10V, 13 $\alpha$ MePhe, 17K, 24R, 27E, 28A, 29Aib, 30G      |
| <b>Peptide 148</b> | H(Aib)QGTFTSDVSK( $\alpha$ M ePhe)LDSK(O2Oc-O2Oc- $\gamma$ E-C18diacid)17RAQDFVR WIAE(Aib)G-acid                                     | 60 | C18diacid | $\gamma$ E-(O2Oc)-(O2Oc)                                     | 17 | Acid | 2Aib, 10V, 13 $\alpha$ MePhe, 17K, 24R, 26I, 27A, 28E, 29Aib, 30G |
| <b>Peptide 149</b> | H(Aib)QGTFTSDVSK( $\alpha$ M ePhe)LDSK(O2Oc-O2Oc- $\gamma$ E-C18diacid)17RAQDFVR WVVE(Aib)G-acid                                     | 61 | C18diacid | $\gamma$ E-(O2Oc)-(O2Oc)                                     | 17 | Acid | 2Aib, 10V, 13 $\alpha$ MePhe, 17K, 24R, 26V, 27V, 28E, 29Aib, 30G |
| <b>Peptide 150</b> | H(Aib)QGTFTSDVSK( $\alpha$ M ePhe)LDSK(O2Oc-O2Oc- $\gamma$ E-C18diacid)17RAQDFVQ WLL(Aib)TE-acid                                     | 62 | C18diacid | $\gamma$ E-(O2Oc)-(O2Oc)                                     | 17 | Acid | 2Aib, 10V, 13 $\alpha$ MePhe, 17K, 27L, 28Aib, 30E                |

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|                    |                                                                                                  |    |           |                          |    |      |                                                                   |
|--------------------|--------------------------------------------------------------------------------------------------|----|-----------|--------------------------|----|------|-------------------------------------------------------------------|
| <b>Peptide 151</b> | H(Aib)QGTFTSDVSK( $\alpha$ M ePhe)LDSK(O2Oc-O2Oc- $\gamma$ E-C20diacid)17RAQDFVR WLL(Aib)TE-acid | 63 | C20diacid | $\gamma$ E-(O2Oc)-(O2Oc) | 17 | Acid | 2Aib, 10V, 13 $\alpha$ MePhe, 17K, 24R, 27L, 28Aib, 30E           |
| <b>Peptide 152</b> | H(Aib)QGTFTSDVSK( $\alpha$ M ePhe)LDSK(O2Oc-O2Oc- $\gamma$ E-C18diacid)17RAQDFVR WLL(Aib)E-acid  | 64 | C18diacid | $\gamma$ E-(O2Oc)-(O2Oc) | 17 | Acid | 2Aib, 10V, 13 $\alpha$ MePhe, 17K, 24R, 27L, 28Aib, 29E           |
| <b>Peptide 153</b> | H(Aib)QGTFTSDVSK( $\alpha$ M ePhe)LDSK(O2Oc-O2Oc- $\gamma$ E-C20diacid)17RAQDFVR WLL(Aib)E-acid  | 65 | C20diacid | $\gamma$ E-(O2Oc)-(O2Oc) | 17 | Acid | 2Aib, 10V, 13 $\alpha$ MePhe, 17K, 24R, 27L, 28Aib, 29E           |
| <b>Peptide 154</b> | H(Aib)QGTFTSDVSK( $\alpha$ M ePhe)LDSK( $\gamma$ E-C18diacid)17RAQDFVQ WLL(Aib)T-acid            | 65 | C18diacid | $\gamma$ E               | 17 | Acid | 2Aib, 10V, 13 $\alpha$ MePhe, 17K, 27L, 28Aib                     |
| <b>Peptide 155</b> | H(Aib)QGTFTSDVSK( $\alpha$ M ePhe)LDSK( $\gamma$ E-C18diacid)17RAQDFVR WLL(EAib)G-acid           | 66 | C18diacid | $\gamma$ E               | 17 | Acid | 2Aib, 10V, 13 $\alpha$ MePhe, 17K, 24R, 27L, 28E, 29Aib, 30G      |
| <b>Peptide 156</b> | H(Aib)QGTFTSDVSK( $\alpha$ M ePhe)LDSK(O2Oc-O2Oc- $\gamma$ E-C18diacid)17RAQDFVR WLL(EAib)-acid  | 67 | C18diacid | $\gamma$ E-(O2Oc)-(O2Oc) | 17 | Acid | 2Aib, 10V, 13 $\alpha$ MePhe, 17K, 24R, 27L, 28E, 29G, 30Aib      |
| <b>Peptide 157</b> | H(Aib)QGTFTSDVSK( $\alpha$ M ePhe)LDSK( $\gamma$ E-C18diacid)17RAQDFVR WLL(EAib)-acid            | 68 | C18diacid | $\gamma$ E               | 17 | Acid | 2Aib, 10V, 13 $\alpha$ MePhe, 17K, 24R, 27L, 28E, 29G, 30Aib      |
| <b>Peptide 158</b> | H(Aib)QGTFTSDVSK( $\alpha$ M ePhe)LDSK(O2Oc-O2Oc- $\gamma$ E-C20diacid)17RAQDFVR WLL(EAib)G-acid | 69 | C20diacid | $\gamma$ E-(O2Oc)-(O2Oc) | 17 | Acid | 2Aib, 10V, 13 $\alpha$ MePhe, 17K, 24R, 27L, 28E, 29Aib, 30G      |
| <b>Peptide 159</b> | H(Aib)QGTFTSDVSK( $\alpha$ M ePhe)LDTK(O2Oc-O2Oc- $\gamma$ E-C20diacid)17RAQDFVR WLL(EAib)G-acid | 70 | C20diacid | $\gamma$ E-(O2Oc)-(O2Oc) | 17 | Acid | 2Aib, 10V, 13 $\alpha$ MePhe, 16T, 17K, 24R, 27L, 28E, 29Aib, 30G |

|                    |                                                                                                 |    |           |                          |    |      |                                                                             |
|--------------------|-------------------------------------------------------------------------------------------------|----|-----------|--------------------------|----|------|-----------------------------------------------------------------------------|
| <b>Peptide 160</b> | H(Aib)QGTFTSDVSK( $\alpha$ MePhe)LESK(O2Oc-O2Oc- $\gamma$ E-C18diacid)17RAQDFVRWLLE(Aib)G-acid  | 71 | C18diacid | $\gamma$ E-(O2Oc)-(O2Oc) | 17 | Acid | 2Aib, 10V, 13 $\alpha$ MePhe, 15E, 17K, 24R, 27L, 28E, 29Aib, 30G           |
| <b>Peptide 161</b> | H(Aib)QGTFTSDVSK( $\alpha$ MePhe)LEAK(O2Oc-O2Oc- $\gamma$ E-C18diacid)17RARDFVWLLE(Aib)G-acid   | 72 | C18diacid | $\gamma$ E-(O2Oc)-(O2Oc) | 17 | Acid | 2Aib, 10V, 13 $\alpha$ MePhe, 15E, 16A, 17K, 20R, 24A, 27L, 28E, 29Aib, 30G |
| <b>Peptide 162</b> | H(Aib)QGTFTSDVSK( $\alpha$ MePhe)LDSK(O2Oc-O2Oc- $\gamma$ E-C18diacid)17RAQDFVRWIA(Aib)TE-acid  | 73 | C18diacid | $\gamma$ E-(O2Oc)-(O2Oc) | 17 | Acid | 2Aib, 10V, 13 $\alpha$ MePhe, 17K, 24R, 26I, 27A, 28Aib, 30E                |
| <b>Peptide 163</b> | H(Aib)QGTFTSDVSK( $\alpha$ MePhe)LDSK(O2Oc-O2Oc- $\gamma$ E-C18diacid)17RAQDFVRWLLE(Aib)A-acid  | 74 | C18diacid | $\gamma$ E-(O2Oc)-(O2Oc) | 17 | Acid | 2Aib, 10V, 13 $\alpha$ MePhe, 17K, 24R, 27L, 28E, 29Aib, 30A                |
| <b>Peptide 164</b> | H(Aib)QGTFTSDVSK( $\alpha$ MePhe)LDSK(O2Oc-O2Oc- $\gamma$ E-C18diacid)17RAQDFVRWLLEA(Aib)-acid  | 75 | C18diacid | $\gamma$ E-(O2Oc)-(O2Oc) | 17 | Acid | 2Aib, 10V, 13 $\alpha$ MePhe, 17K, 24R, 27L, 28E, 29A, 30Aib                |
| <b>Peptide 165</b> | H(Aib)QGTFTSDVSK( $\alpha$ MePhe)LDSK(O2Oc-O2Oc- $\gamma$ E-C18diacid)17RAQDFVRWLVA(Aib)TE-acid | 76 | C18diacid | $\gamma$ E-(O2Oc)-(O2Oc) | 17 | Acid | 2Aib, 10V, 13 $\alpha$ MePhe, 17K, 24R, 27V, 28Aib, 30E                     |
| <b>Peptide 166</b> | H(Aib)QGTFTSDVSK( $\alpha$ MePhe)LDSK(O2Oc-O2Oc- $\gamma$ E-C18diacid)17RARDFVRWLL(Aib)TE-acid  | 77 | C18diacid | $\gamma$ E-(O2Oc)-(O2Oc) | 17 | Acid | 2Aib, 10V, 13 $\alpha$ MePhe, 17K, 20R, 24R, 27L, 28Aib, 30E                |
| <b>Peptide 167</b> | H(Aib)QGTFTSDVSK( $\alpha$ MePhe)LDSK(O2Oc-O2Oc- $\gamma$ E-C18diacid)17RARDFVWLL(Aib)TE-acid   | 78 | C18diacid | $\gamma$ E-(O2Oc)-(O2Oc) | 17 | Acid | 2Aib, 10V, 13 $\alpha$ MePhe, 17K, 20R, 24A, 27L, 28Aib, 30E                |
| <b>Peptide 168</b> | H(Aib)QGTFTSDVSK( $\alpha$ MePhe)LDSK(O2Oc-O2Oc- $\gamma$ E-                                    | 79 | C18diacid | $\gamma$ E-(O2Oc)-(O2Oc) | 17 | Acid | 2Aib, 10V, 13 $\alpha$ MePhe, 17K, 20L,                                     |

|                        |                                                                                                                |    |           |                                  |    |      |                                                                                  |
|------------------------|----------------------------------------------------------------------------------------------------------------|----|-----------|----------------------------------|----|------|----------------------------------------------------------------------------------|
|                        | C18diacid)17RALDFVR<br>WLL(Aib)TE-acid                                                                         |    |           |                                  |    |      | 24A, 27L,<br>28Aib, 30E                                                          |
| <b>Peptide<br/>169</b> | H(Aib)QGTFTSDVSK( $\alpha$ M<br>ePhe)LELK(O2Oc-O2Oc-<br>$\gamma$ E-<br>C18diacid)17RAQDFVR<br>WLL(Aib)TE-acid  | 80 | C18diacid | $\gamma$ E-<br>(O2Oc)-<br>(O2Oc) | 17 | Acid | 2Aib, 10V,<br>13 $\alpha$ MePhe,<br>15E, 16L,<br>17K, 24R,<br>27L, 28Aib,<br>30E |
| <b>Peptide<br/>170</b> | H(Aib)QGTFTSDVSK( $\alpha$ M<br>ePhe)LDEK(O2Oc-<br>O2Oc- $\gamma$ E-<br>C18diacid)17RAQDFVR<br>WLL(Aib)TE-acid | 81 | C18diacid | $\gamma$ E-<br>(O2Oc)-<br>(O2Oc) | 17 | Acid | 2Aib, 10V,<br>13 $\alpha$ MePhe,<br>16E, 17K,<br>24R, 27L,<br>28Aib, 30E         |
| <b>Peptide<br/>171</b> | H(Aib)QGTFTSDVSK( $\alpha$ M<br>ePhe)LDSK(O2Oc-<br>O2Oc- $\gamma$ E-<br>C18diacid)17RAQDFVR<br>WLE(Aib)TE-acid | 82 | C18diacid | $\gamma$ E-<br>(O2Oc)-<br>(O2Oc) | 17 | Acid | 2Aib, 10V,<br>13 $\alpha$ MePhe,<br>17K, 24R,<br>27E, 28Aib,<br>30E              |
| <b>Peptide<br/>172</b> | H(Aib)QGTFTSDVSK( $\alpha$ M<br>ePhe)LESK(O2Oc-O2Oc-<br>$\gamma$ E-<br>C18diacid)17RAQDFVR<br>WLL(Aib)TE-acid  | 83 | C18diacid | $\gamma$ E-<br>(O2Oc)-<br>(O2Oc) | 17 | Acid | 2Aib, 10V,<br>13 $\alpha$ MePhe,<br>15E, 17K,<br>24R, 27L,<br>28Aib, 30E         |
| <b>Peptide<br/>173</b> | H(Aib)QGTFTSDVSK( $\alpha$ M<br>ePhe)LESK(O2Oc-O2Oc-<br>$\gamma$ E-<br>C18diacid)17RAQDFVR<br>WLL(Aib)E-acid   | 84 | C18diacid | $\gamma$ E-<br>(O2Oc)-<br>(O2Oc) | 17 | Acid | 2Aib, 10V,<br>13 $\alpha$ MePhe,<br>15E, 17K,<br>24R, 27L,<br>28Aib, 29E         |
| <b>Peptide<br/>174</b> | H(Aib)QGTFTSDVSK( $\alpha$ M<br>ePhe)LDTK(O2Oc-<br>O2Oc- $\gamma$ E-<br>C18diacid)17RAQDFVR<br>WLL(Aib)TE-acid | 85 | C18diacid | $\gamma$ E-<br>(O2Oc)-<br>(O2Oc) | 17 | Acid | 2Aib, 10V,<br>13 $\alpha$ MePhe,<br>16T, 17K,<br>24R, 27L,<br>28Aib, 30E         |
| <b>Peptide<br/>175</b> | H(Aib)QGTFTSDVSK( $\alpha$ M<br>ePhe)LDSK(O2Oc-<br>O2Oc- $\gamma$ E-<br>C18diacid)17RAQDFVR<br>WLA(Aib)TE-acid | 86 | C18diacid | $\gamma$ E-<br>(O2Oc)-<br>(O2Oc) | 17 | Acid | 2Aib, 10V,<br>13 $\alpha$ MePhe,<br>17K, 24R,<br>27A, 28Aib,<br>30E              |
| <b>Peptide<br/>176</b> | H(Aib)QGTFTSDVSK( $\alpha$ M<br>ePhe)LDSK(O2Oc-<br>O2Oc- $\gamma$ E-<br>C18diacid)17RAQDFVR<br>WLL(Aib)TA-acid | 87 | C18diacid | $\gamma$ E-<br>(O2Oc)-<br>(O2Oc) | 17 | Acid | 2Aib, 10V,<br>13 $\alpha$ MePhe,<br>17K, 24R,<br>27A, 28Aib,<br>30A              |
| <b>Peptide<br/>177</b> | H(Aib)QGTFTSDVSK( $\alpha$ M<br>ePhe)LDSK(O2Oc-<br>O2Oc- $\gamma$ E-                                           | 88 | C18diacid | $\gamma$ E-<br>(O2Oc)-<br>(O2Oc) | 17 | Acid | 2Aib, 10V,<br>13 $\alpha$ MePhe,<br>17K, 24R,                                    |

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|                        |                                                                                                                 |    |           |                                  |    |       |                                                                                  |
|------------------------|-----------------------------------------------------------------------------------------------------------------|----|-----------|----------------------------------|----|-------|----------------------------------------------------------------------------------|
|                        | C18diacid)17RAQDFVR<br>WLL(Aib)TK-acid                                                                          |    |           |                                  |    |       | 27A, 28Aib,<br>30K                                                               |
| <b>Peptide<br/>178</b> | H(Aib)QGTFTSDVSK( $\alpha$ M<br>ePhe)LDKK(O2Oc-<br>O2Oc- $\gamma$ E-<br>C18diacid)17RAQDFVR<br>WLL(Aib)TE-acid  | 89 | C18diacid | $\gamma$ E-<br>(O2Oc)-<br>(O2Oc) | 17 | Acid  | 2Aib, 10V,<br>13 $\alpha$ MePhe,<br>16K, 17K,<br>24R, 27L,<br>28Aib, 30E         |
| <b>Peptide<br/>179</b> | H(Aib)QGTFTSDVSK( $\alpha$ M<br>ePhe)LDSK(O2Oc-<br>O2Oc- $\gamma$ E-<br>C18diacid)17RAQDFVR<br>WLLEAG-acid      | 90 | C18diacid | $\gamma$ E-<br>(O2Oc)-<br>(O2Oc) | 17 | Acid  | 2Aib, 10V,<br>13 $\alpha$ MePhe,<br>17K, 24R,<br>27L, 28E,<br>29A, 30G           |
| <b>Peptide<br/>180</b> | H(Aib)QGTFTSDVSK( $\alpha$ M<br>ePhe)LDSK(O2Oc-<br>O2Oc- $\gamma$ E-<br>C18diacid)17RAQDFVR<br>WLLA(Aib)G-acid  | 91 | C18diacid | $\gamma$ E-<br>(O2Oc)-<br>(O2Oc) | 17 | Acid  | 2Aib, 10V,<br>13 $\alpha$ MePhe,<br>17K, 24R,<br>27L, 28A,<br>29Aib, 30G         |
| <b>Peptide<br/>181</b> | H(Aib)QGTFTSDVSK( $\alpha$ M<br>ePhe)LDSK(O2Oc-<br>O2Oc-<br>C18diacid)17RAQDFVR<br>WLLE(Aib)G-acid              | 92 | C18diacid | (O2Oc)-<br>(O2Oc)                | 17 | Acid  | 2Aib, 10V,<br>13 $\alpha$ MePhe,<br>17K, 24R,<br>27L, 28E,<br>29Aib, 30G         |
| <b>Peptide<br/>182</b> | H(Aib)QGTFTSDVSK( $\alpha$ M<br>ePhe)LDKK(O2Oc-<br>O2Oc- $\gamma$ E-<br>C18diacid)17RAQDFVR<br>WLLE(Aib)G-acid  | 93 | C18diacid | $\gamma$ E-<br>(O2Oc)-<br>(O2Oc) | 17 | Acid  | 2Aib, 10V,<br>13 $\alpha$ MePhe,<br>16K, 17K,<br>24R, 27L,<br>28E, 29Aib,<br>30G |
| <b>Peptide<br/>183</b> | H(Aib)QGTFTSDVSK( $\alpha$ M<br>ePhe)LDSK(O2Oc-<br>O2Oc- $\gamma$ E-<br>C18diacid)17RAQDFVR<br>WLLE(Aib)K-acid  | 94 | C18diacid | $\gamma$ E-<br>(O2Oc)-<br>(O2Oc) | 17 | Acid  | 2Aib, 10V,<br>13 $\alpha$ MePhe,<br>17K, 24R,<br>27L, 28E,<br>29Aib, 30K         |
| <b>Peptide<br/>184</b> | H(Aib)QGTFTSDVSK( $\alpha$ M<br>ePhe)LDKK(O2Oc-<br>O2Oc-<br>C18diacid)17RAQDFVR<br>WLLA(Aib)K-acid              | 95 | C18diacid | (O2Oc)-<br>(O2Oc)                | 17 | Acid  | 2Aib, 10V,<br>13 $\alpha$ MePhe,<br>16K, 17K,<br>24R, 27L,<br>28A, 29Aib,<br>30K |
| <b>Peptide<br/>185</b> | H(Aib)QGTFTSDVSK( $\alpha$ M<br>ePhe)LDTK(O2Oc-<br>O2Oc- $\gamma$ E-<br>C18diacid)17RAQDFVR<br>WLLE(Aib)G-amide | 96 | C18diacid | $\gamma$ E-<br>(O2Oc)-<br>(O2Oc) | 17 | Amide | 2Aib, 10V,<br>13 $\alpha$ MePhe,<br>16T, 17K,<br>24R, 27L,<br>28E, 29Aib,<br>30G |

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|                    |                                                                                                  |     |           |                          |    |      |                                                                        |
|--------------------|--------------------------------------------------------------------------------------------------|-----|-----------|--------------------------|----|------|------------------------------------------------------------------------|
| <b>Peptide 186</b> | H(Aib)QGTFTSDVSK( $\alpha$ M ePhe)LDTK(O2Oc-O2Oc- $\gamma$ E-C18diacid)17RAQDFVR WLEAG-acid      | 97  | C18diacid | $\gamma$ E-(O2Oc)-(O2Oc) | 17 | Acid | 2Aib, 10V, 13 $\alpha$ MePhe, 16T, 17K, 24R, 27L, 28E, 29A, 30G        |
| <b>Peptide 187</b> | H(Aib)QGTFTSDVSK( $\alpha$ M ePhe)LDTK(O2Oc-O2Oc- $\gamma$ E-C18diacid)17RARDFVR WLVE(Aib)G-acid | 98  | C18diacid | $\gamma$ E-(O2Oc)-(O2Oc) | 17 | Acid | 2Aib, 10V, 13 $\alpha$ MePhe, 16T, 17K, 20R, 24R, 27V, 28E, 29Aib, 30G |
| <b>Peptide 188</b> | H(Aib)QGTFTSDVSK( $\alpha$ M ePhe)LDTK(O2Oc-O2Oc- $\gamma$ E-C18diacid)17RARDFVQ WLE(Aib)G-acid  | 99  | C18diacid | $\gamma$ E-(O2Oc)-(O2Oc) | 17 | Acid | 2Aib, 10V, 13 $\alpha$ MePhe, 16T, 17K, 20R, 27L, 28E, 29Aib, 30G      |
| <b>Peptide 189</b> | H(Aib)QGTFTSDVSK( $\alpha$ M ePhe)LDTK(O2Oc-O2Oc- $\gamma$ E-C18diacid)17RARDFVR WLE(Aib)G-acid  | 100 | C18diacid | $\gamma$ E-(O2Oc)-(O2Oc) | 17 | Acid | 2Aib, 10V, 13 $\alpha$ MePhe, 16T, 17K, 20R, 24R, 27L, 28E, 29Aib, 30G |
| <b>Peptide 190</b> | H(Aib)QGTFTSDVSK( $\alpha$ M ePhe)LDTK(O2Oc-O2Oc- $\gamma$ E-C20diacid)17RAQDFVR WLVE(Aib)G-acid | 101 | C20diacid | $\gamma$ E-(O2Oc)-(O2Oc) | 17 | Acid | 2Aib, 10V, 13 $\alpha$ MePhe, 16T, 17K, 24R, 27V, 28E, 29Aib, 30G      |
| <b>Peptide 191</b> | H(Aib)QGTFTSDVSK( $\alpha$ M ePhe)LDTK(O2Oc-O2Oc- $\gamma$ E-C18diacid)17RAQDFVR WLVE(Aib)G-acid | 102 | C18diacid | $\gamma$ E-(O2Oc)-(O2Oc) | 17 | Acid | 2Aib, 10V, 13 $\alpha$ MePhe, 16T, 17K, 24R, 27V, 28E, 29Aib, 30G      |
| <b>Peptide 192</b> | H(Aib)QGTFTSDVSK( $\alpha$ M ePhe)LDTK(O2Oc-O2Oc- $\gamma$ E-C18diacid)17RAQDFVR WLL(Aib)E-acid  | 103 | C18diacid | $\gamma$ E-(O2Oc)-(O2Oc) | 17 | Acid | 2Aib, 10V, 13 $\alpha$ MePhe, 16T, 17K, 24R, 27L, 28Aib, 29E           |
| <b>Peptide 193</b> | H(Aib)QGTFTSDVSK( $\alpha$ M ePhe)LDTK(O2Oc-O2Oc- $\gamma$ E-C20diacid)17RAQDFVR WLL(Aib)E-acid  | 104 | C20diacid | $\gamma$ E-(O2Oc)-(O2Oc) | 17 | Acid | 2Aib, 10V, 13 $\alpha$ MePhe, 16T, 17K, 24R, 27L, 28Aib, 29E           |

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|                    |                                                                                                             |     |           |                          |    |      |                                                                             |
|--------------------|-------------------------------------------------------------------------------------------------------------|-----|-----------|--------------------------|----|------|-----------------------------------------------------------------------------|
| <b>Peptide 194</b> | H(Aib)QGTFTSDVSK( $\alpha$ M ePhe)LDTK(O2Oc-O2Oc- $\gamma$ E- $\gamma$ E-C20diacid)17RAQDFVR WLL(Aib)E-acid | 105 | C20diacid | $\gamma$ E-(O2Oc)-(O2Oc) | 17 | Acid | 2Aib, 10V, 13 $\alpha$ MePhe, 16T, 17K, 24R, 27L, 28Aib, 29E                |
| <b>Peptide 195</b> | H(Aib)QGTFTSDVSK( $\alpha$ M ePhe)LDTK(O2Oc-O2Oc- $\gamma$ E-C20diacid)17RARDFVQ WLL(Aib)G-acid             | 106 | C20diacid | $\gamma$ E-(O2Oc)-(O2Oc) | 17 | Acid | 2Aib, 10V, 13 $\alpha$ MePhe, 16T, 17K, 20R, 27L, 28E, 29Aib, 30G           |
| <b>Peptide 196</b> | H(Aib)QGTFTSDVSK( $\alpha$ M ePhe)LDSK(O2Oc-O2Oc- $\gamma$ E-C18diacid)17RAQDFVR WLL(Aib)E-acid             | 107 | C18diacid | $\gamma$ E-(O2Oc)-(O2Oc) | 17 | Acid | 2Aib, 10V, 13 $\alpha$ MePhe, 17K, 24R, 27L, 28Aib, 29E                     |
| <b>Peptide 197</b> | H(Aib)QGTFTSDVSK( $\alpha$ M ePhe)LDTK(O2Oc-O2Oc- $\gamma$ E-C18diacid)17RARDFVR WLL(Aib)E-acid             | 108 | C18diacid | $\gamma$ E-(O2Oc)-(O2Oc) | 17 | Acid | 2Aib, 10V, 13 $\alpha$ MePhe, 16T, 17K, 20R, 24R, 27L, 28Aib, 29E           |
| <b>Peptide 198</b> | H(Aib)QGTFTSDVSK( $\alpha$ M ePhe)LDTK(O2Oc-O2Oc- $\gamma$ E-C18diacid)17RARDFIA WLL(Aib)E-acid             | 109 | C18diacid | $\gamma$ E-(O2Oc)-(O2Oc) | 17 | Acid | 2Aib, 10V, 13 $\alpha$ MePhe, 16T, 17K, 20R, 23I, 24A, 27L, 28Aib, 29E      |
| <b>Peptide 199</b> | H(Aib)QGTFTSDVSK( $\alpha$ M ePhe)LDTK(O2Oc-O2Oc- $\gamma$ E-C18diacid)17RARDFIA WLL(Aib)G-acid             | 110 | C18diacid | $\gamma$ E-(O2Oc)-(O2Oc) | 17 | Acid | 2Aib, 10V, 13 $\alpha$ MePhe, 16T, 17K, 20R, 23I, 24A, 27L, 28E, 29Aib, 30G |
| <b>Peptide 200</b> | H(Aib)QGTFTSDVSK( $\alpha$ M ePhe)LDTK(O2Oc-O2Oc- $\gamma$ E-C18diacid)17RARDFVA WLL(Aib)G-acid             | 111 | C18diacid | $\gamma$ E-(O2Oc)-(O2Oc) | 17 | Acid | 2Aib, 10V, 13 $\alpha$ MePhe, 16T, 17K, 20R, 24A, 27L, 28E, 29Aib, 30G      |
| <b>Peptide 201</b> | H(Aib)QGTFTSDVSK( $\alpha$ M ePhe)LDTK(O2Oc-O2Oc- $\gamma$ E-C18diacid)17RARDFVA WLEA(Aib)G-acid            | 112 | C18diacid | $\gamma$ E-(O2Oc)-(O2Oc) | 17 | Acid | 2Aib, 10V, 13 $\alpha$ MePhe, 16T, 17K, 20R, 24A, 27E, 28A, 29Aib, 30G      |

|                    |                                                                                                            |     |           |                                      |    |      |                                                                         |
|--------------------|------------------------------------------------------------------------------------------------------------|-----|-----------|--------------------------------------|----|------|-------------------------------------------------------------------------|
| <b>Peptide 202</b> | H(Aib)QGTFTSDVSK( $\alpha$ MePhe)LDTK(O2Oc-O2Oc- $\gamma$ E-C18diacid)17RARDFVQWLEA(Aib)G-acid             | 113 | C18diacid | $\gamma$ E-(O2Oc)-(O2Oc)             | 17 | Acid | 2(Aib), 10V, 13 $\alpha$ MePhe, 16T, 17K, 20R, 27E, 28A, 29Aib, 30G     |
| <b>Peptide 407</b> | H(Aib)QGTFTSDVSK( $\alpha$ MePhe)LDTK(O2Oc-O2Oc- $\gamma$ E-C20diacid)17RAQDFVRWLEA(Aib)G-acid             | 418 | C20diacid | $\gamma$ E-(O2Oc)-(O2Oc)             | 17 | Acid | 2(Aib), 10V, 13( $\alpha$ MePhe), 16T, 17K, 24R, 27E, 28A, 29(Aib), 30G |
| <b>Peptide 408</b> | H(Aib)QGTFTSDVSK( $\alpha$ MePhe)LDTK(O2Oc-O2Oc- $\gamma$ E- $\gamma$ E-C20diacid)17RAQDFVRWLEA(Aib)G-acid | 419 | C20diacid | $\gamma$ E- $\gamma$ E-(O2Oc)-(O2Oc) | 17 | Acid | 2(Aib), 10V, 13( $\alpha$ MePhe), 16T, 17K, 24R, 27E, 28A, 29(Aib), 30G |
| <b>Peptide 409</b> | H(Aib)QGTFTSDVSK( $\alpha$ MePhe)LDTK(O2Oc-O2Oc- $\gamma$ E-C18diacid)17RARDFVAWLL(Aib)TE-acid             | 420 | C18diacid | $\gamma$ E-(O2Oc)-(O2Oc)             | 17 | Acid | 2(Aib), 10V, 13( $\alpha$ MePhe), 16T, 17K, 20R, 24A, 27L, 28(Aib), 30E |
| <b>Peptide 410</b> | H(Aib)QGTFTSDVSK( $\alpha$ MePhe)LDTK(O2Oc-O2Oc- $\gamma$ E-C20diacid)17RARDFVAWLL(Aib)TE-acid             | 421 | C20diacid | $\gamma$ E-(O2Oc)-(O2Oc)             | 17 | Acid | 2(Aib), 10V, 13( $\alpha$ MePhe), 16T, 17K, 20R, 24A, 27L, 28(Aib), 30E |
| <b>Peptide 411</b> | H(Aib)QGTFTSDVSK( $\alpha$ MePhe)LDTK(O2Oc-O2Oc- $\gamma$ E-C18diacid)17RAQDFVAWLEAGG-acid                 | 422 | C18diacid | $\gamma$ E-(O2Oc)-(O2Oc)             | 17 | Acid | 2(Aib), 10V, 13( $\alpha$ MePhe), 16T, 17K, 24A, 27E, 28A, 29G, 30G     |
| <b>Peptide 412</b> | H(Aib)QGTFTSDVSK( $\alpha$ MePhe)LDTK(O2Oc-O2Oc- $\gamma$ E-C20diacid)17RAQDFVAWLEAGG-acid                 | 423 | C20diacid | $\gamma$ E-(O2Oc)-(O2Oc)             | 17 | Acid | 2(Aib), 10V, 13( $\alpha$ MePhe), 16T, 17K, 24A, 27E, 28A, 29G, 30G     |
| <b>Peptide 413</b> | H(Aib)QGTFTSDVSK( $\alpha$ MePhe)LDTK(O2Oc-O2Oc- $\gamma$ E- $\gamma$ E-C20diacid)17RAQDFVAWLEAGG-acid     | 424 | C20diacid | $\gamma$ E- $\gamma$ E-(O2Oc)-(O2Oc) | 17 | Acid | 2(Aib), 10V, 13( $\alpha$ MePhe), 16T, 17K, 24A, 27E,                   |

|                    |                                                                                                            |     |           |                                      |    |       |                                                                         |
|--------------------|------------------------------------------------------------------------------------------------------------|-----|-----------|--------------------------------------|----|-------|-------------------------------------------------------------------------|
|                    |                                                                                                            |     |           |                                      |    |       | 28A, 29G, 30G                                                           |
| <b>Peptide 414</b> | H(Aib)QGTFTSDVSK( $\alpha$ MePhe)LDKK(O2Oc-O2Oc- $\gamma$ E-C18diacid)17RARDFVRWLL(Aib)E-acid              | 425 | C18diacid | $\gamma$ E-(O2Oc)-(O2Oc)             | 17 | Acid  | 2(Aib), 10V, 13( $\alpha$ MePhe), 16K, 17K, 20R, 24R, 27L, 28(Aib), 29E |
| <b>Peptide 415</b> | H(Aib)QGTFTSDVSK( $\alpha$ MePhe)LESK(O2Oc-O2Oc- $\gamma$ E-C18diacid)17RAQDFVRWLEA(Aib)G-acid             | 426 | C18diacid | $\gamma$ E-(O2Oc)-(O2Oc)             | 17 | Acid  | 2(Aib), 10V, 13( $\alpha$ MePhe), 15E, 17K, 24R, 27E, 28A, 29(Aib), 30G |
| <b>Peptide 416</b> | H(Aib)QGTFTSDVSK( $\alpha$ MePhe)LESK(O2Oc-O2Oc- $\gamma$ E-C20diacid)17RAQDFVRWLEA(Aib)G-acid             | 427 | C20diacid | $\gamma$ E-(O2Oc)-(O2Oc)             | 17 | Acid  | 2(Aib), 10V, 13( $\alpha$ MePhe), 15E, 17K, 24R, 27E, 28A, 29(Aib), 30G |
| <b>Peptide 417</b> | H(Aib)QGTFTSDVSK( $\alpha$ MePhe)LDTK(O2Oc-O2Oc- $\gamma$ E- $\gamma$ E-C18diacid)17RAQDFVAWLEA(Aib)G-acid | 428 | C18diacid | $\gamma$ E- $\gamma$ E-(O2Oc)-(O2Oc) | 17 | Acid  | 2(Aib), 10V, 13( $\alpha$ MePhe), 16T, 17K, 24A, 27E, 28A, 29(Aib), 30G |
| <b>Peptide 418</b> | H(Aib)QGTFTSDVSK( $\alpha$ MePhe)LDTK(O2Oc-O2Oc- $\gamma$ E- $\gamma$ E-C20diacid)17RAQDFVAWLEA(Aib)G-acid | 429 | C20diacid | $\gamma$ E- $\gamma$ E-(O2Oc)-(O2Oc) | 17 | Acid  | 2(Aib), 10V, 13( $\alpha$ MePhe), 16T, 17K, 24A, 27E, 28A, 29(Aib), 30G |
| <b>Peptide 419</b> | H(Aib)QGTFTSDVSK( $\alpha$ MePhe)LDTK(O2Oc-O2Oc- $\gamma$ E-C18diacid)17RAQDFVRWLE(Aib)E-acid              | 430 | C18diacid | $\gamma$ E-(O2Oc)-(O2Oc)             | 17 | Acid  | 2(Aib), 10V, 13( $\alpha$ MePhe), 16T, 17K, 24R, 27E, 28(Aib), 29E      |
| <b>Peptide 420</b> | H(Aib)QGTFTSDVSK( $\alpha$ MePhe)LDKK(O2Oc-O2Oc- $\gamma$ E-C18diacid)17RAQDFVRWLL(Aib)E-amide             | 431 | C18diacid | $\gamma$ E-(O2Oc)-(O2Oc)             | 17 | Amide | 2(Aib), 10V, 13( $\alpha$ MePhe), 16K, 17K, 24R, 27L, 28(Aib), 29E      |
| <b>Peptide 421</b> | H(Aib)QGTFTSDVSK( $\alpha$ MePhe)LDRK(O2Oc-O2Oc- $\gamma$ E-C18diacid)17RAQDFVRWLL(Aib)TE-acid             | 432 | C18diacid | $\gamma$ E-(O2Oc)-(O2Oc)             | 17 | Acid  | 2(Aib), 10V, 13( $\alpha$ MePhe), 16R, 17K, 24R, 27L, 28(Aib), 30E      |

|                        |                                                                                                                             |     |           |                                              |    |       |                                                                                        |
|------------------------|-----------------------------------------------------------------------------------------------------------------------------|-----|-----------|----------------------------------------------|----|-------|----------------------------------------------------------------------------------------|
| <b>Peptide<br/>422</b> | H(Aib)QGTFTSDVSK( $\alpha$ M<br>ePhe)LDRK(O2Oc-<br>O2Oc- $\gamma$ E-<br>C18diacid)17RAQDFVR<br>WLL(Aib)TE-amide             | 433 | C18diacid | $\gamma$ E-<br>(O2Oc)-<br>(O2Oc)             | 17 | Amide | 2(Aib), 10V,<br>13( $\alpha$ MePhe),<br>16R, 17K,<br>24R, 27L,<br>28(Aib), 30E         |
| <b>Peptide<br/>423</b> | H(Aib)QGTFTSDVSK( $\alpha$ M<br>ePhe)LDKK(O2Oc-<br>O2Oc- $\gamma$ E-<br>C18diacid)17RAQDFVR<br>WLK(Aib)TE-acid              | 434 | C18diacid | $\gamma$ E-<br>(O2Oc)-<br>(O2Oc)             | 17 | Acid  | 2(Aib), 10V,<br>13( $\alpha$ MePhe),<br>16K, 17K,<br>24R, 27K,<br>28(Aib), 30E         |
| <b>Peptide<br/>424</b> | H(Aib)QGTFTSDVSK( $\alpha$ M<br>ePhe)LDKK(O2Oc-<br>O2Oc- $\gamma$ E-<br>C18diacid)17RAQDFVR<br>WLL(Aib)TK-acid              | 435 | C18diacid | $\gamma$ E-<br>(O2Oc)-<br>(O2Oc)             | 17 | Acid  | 2(Aib), 10V,<br>13( $\alpha$ MePhe),<br>16K, 17K,<br>24R, 27L,<br>28(Aib), 30K         |
| <b>Peptide<br/>425</b> | H(Aib)QGTFTSDVSK( $\alpha$ M<br>ePhe)LDKK(O2Oc-<br>O2Oc- $\gamma$ E-<br>C18diacid)17RAQDFVR<br>WLKA(Aib)G-acid              | 436 | C18diacid | $\gamma$ E-<br>(O2Oc)-<br>(O2Oc)             | 17 | Acid  | 2(Aib), 10V,<br>13( $\alpha$ MePhe),<br>16K, 17K,<br>24R, 27K,<br>28A, 29(Aib),<br>30G |
| <b>Peptide<br/>426</b> | H(Aib)QGTFTSDVSK( $\alpha$ M<br>ePhe)LDKK(O2Oc-<br>O2Oc- $\gamma$ E-<br>C18diacid)17RAQDFVR<br>WLLR(Aib)K-acid              | 437 | C18diacid | $\gamma$ E-<br>(O2Oc)-<br>(O2Oc)             | 17 | Acid  | 2(Aib), 10V,<br>13( $\alpha$ MePhe),<br>16K, 17K,<br>24R, 27L,<br>28R, 29(Aib),<br>30K |
| <b>Peptide<br/>427</b> | H(Aib)QGTFTSDVSK( $\alpha$ M<br>ePhe)LDTK(O2Oc-<br>O2Oc- $\gamma$ E-<br>C18diacid)17RARDFVQ<br>WLLE(Aib)G-amide             | 438 | C18diacid | $\gamma$ E-<br>(O2Oc)-<br>(O2Oc)             | 17 | Amide | 2(Aib), 10V,<br>13( $\alpha$ MePhe),<br>16T, 17K,<br>20R, 27L,<br>28E, 29(Aib),<br>30G |
| <b>Peptide<br/>428</b> | H(Aib)QGTFTSDVSK( $\alpha$ M<br>ePhe)LDTK(O2Oc-<br>O2Oc- $\gamma$ E- $\gamma$ E-<br>C18diacid)17RARDFVQ<br>WLLE(Aib)G-amide | 439 | C18diacid | $\gamma$ E- $\gamma$ E-<br>(O2Oc)-<br>(O2Oc) | 17 | Amide | 2(Aib), 10V,<br>13( $\alpha$ MePhe),<br>16T, 17K,<br>20R, 27L,<br>28E, 29(Aib),<br>30G |
| <b>Peptide<br/>429</b> | H(Aib)QGTFTSDVSK( $\alpha$ M<br>ePhe)LDSK(O2Oc-<br>O2Oc- $\gamma$ E-<br>C18diacid)17RAQDFVR<br>WLEA(Aib)G-amide             | 440 | C18diacid | $\gamma$ E-<br>(O2Oc)-<br>(O2Oc)             | 17 | Amide | 2(Aib), 10V,<br>13( $\alpha$ MePhe),<br>17K, 24R,<br>27E, 28A,<br>29(Aib), 30G         |
| <b>Peptide<br/>430</b> | H(Aib)QGTFTSDVSK( $\alpha$ M<br>ePhe)LDSK(O2Oc-<br>O2Oc- $\gamma$ E- $\gamma$ E-<br>C18diacid)17RAQDFVR<br>WLEA(Aib)G-amide | 441 | C18diacid | $\gamma$ E- $\gamma$ E-<br>(O2Oc)-<br>(O2Oc) | 17 | Amide | 2(Aib), 10V,<br>13( $\alpha$ MePhe),<br>17K, 24R,                                      |

|                        |                                                                                                                                |     |           |                                              |    |       |                                                                                                 |
|------------------------|--------------------------------------------------------------------------------------------------------------------------------|-----|-----------|----------------------------------------------|----|-------|-------------------------------------------------------------------------------------------------|
|                        | C18diacid)17RAQDFVR<br>WLEA(Aib)G-amide                                                                                        |     |           |                                              |    |       | 27E, 28A,<br>29(Aib), 30G                                                                       |
| <b>Peptide<br/>431</b> | H(Aib)QGTFTSDVSK( $\alpha$ M<br>ePhe)LDTK(O2Oc-<br>O2Oc- $\gamma$ E- $\gamma$ E-<br>C18diacid)17RAQDFVA<br>WLEA(Aib)G-amide    | 442 | C18diacid | $\gamma$ E- $\gamma$ E-<br>(O2Oc)-<br>(O2Oc) | 17 | Amide | 2(Aib), 10V,<br>13( $\alpha$ MePhe),<br>16T, 17K,<br>24A, 27E,<br>28A, 29(Aib),<br>30G          |
| <b>Peptide<br/>432</b> | H(Aib)QGTFTSDVSK( $\alpha$ M<br>ePhe)LDSK(O2Oc-<br>O2Oc- $\gamma$ E-<br>C18diacid)17RAQDFVR(<br>Bip)LL(Aib)E-acid              | 443 | C18diacid | $\gamma$ E-<br>(O2Oc)-<br>(O2Oc)             | 17 | Acid  | 2(Aib), 10V,<br>13( $\alpha$ MePhe),<br>17K, 24R,<br>25(Bip), 27L,<br>28(Aib), 29E              |
| <b>Peptide<br/>433</b> | H(Aib)QGTFTSDVSK( $\alpha$ M<br>ePhe)LDSK(O2Oc-<br>O2Oc- $\gamma$ E-<br>C18diacid)17RAQDFVR(<br>1-Methyl-Trp)LL(Aib)E-<br>acid | 444 | C18diacid | $\gamma$ E-<br>(O2Oc)-<br>(O2Oc)             | 17 | Acid  | 2(Aib), 10V,<br>13( $\alpha$ MePhe),<br>17K, 24R,<br>25(1-Methyl-<br>Trp), 27L,<br>28(Aib), 29E |
| <b>Peptide<br/>434</b> | H(Aib)QGTFTSDVSK( $\alpha$ M<br>ePhe)LDSK(O2Oc-<br>O2Oc- $\gamma$ E-<br>C18diacid)17RAQDFVR(<br>5-BrTrp)LL(Aib)E-acid          | 445 | C18diacid | $\gamma$ E-<br>(O2Oc)-<br>(O2Oc)             | 17 | Acid  | 2(Aib), 10V,<br>13( $\alpha$ MePhe),<br>17K, 24R,<br>25(5-BrTrp),<br>27L, 28(Aib),<br>29E       |
| <b>Peptide<br/>435</b> | H(Aib)QGTFTSDVSK( $\alpha$ M<br>ePhe)LDTK(O2Oc-<br>O2Oc- $\gamma$ E-<br>C18diacid)17RARDFVQ(<br>Aib)LLE(Aib)G-acid             | 446 | C18diacid | $\gamma$ E-<br>(O2Oc)-<br>(O2Oc)             | 17 | Acid  | 2(Aib), 10V,<br>13( $\alpha$ MePhe),<br>16T, 17K,<br>20R, 25(Aib),<br>27L, 28E,<br>29(Aib), 30G |
| <b>Peptide<br/>436</b> | H(Aib)QGTFTSDVSK( $\alpha$ M<br>ePhe)LDRK(O2Oc-<br>O2Oc- $\gamma$ E-<br>C18diacid)17RAQDFVR<br>WLV(Aib)E-amide                 | 447 | C18diacid | $\gamma$ E-<br>(O2Oc)-<br>(O2Oc)             | 17 | Amide | 2(Aib), 10V,<br>13( $\alpha$ MePhe),<br>16R, 17K,<br>24R, 27V,<br>28(Aib), 29E                  |
| <b>Peptide<br/>437</b> | H(Aib)QGTFTSDVSK( $\alpha$ M<br>ePhe)LDRK(O2Oc-<br>O2Oc- $\gamma$ E-<br>C20diacid)17RAQDFVR<br>WLV(Aib)E-amide                 | 448 | C20diacid | $\gamma$ E-<br>(O2Oc)-<br>(O2Oc)             | 17 | Amide | 2(Aib), 10V,<br>13( $\alpha$ MePhe),<br>16R, 17K,<br>24R, 27V,<br>28(Aib), 29E                  |
| <b>Peptide<br/>438</b> | H(Aib)QGTFTSDVSK( $\alpha$ M<br>ePhe)LDKK(O2Oc-<br>O2Oc- $\gamma$ E-<br>C18diacid)17RAQDFVR<br>WLEA(Aib)G-amide                | 449 | C18diacid | $\gamma$ E-<br>(O2Oc)-<br>(O2Oc)             | 17 | Amide | 2(Aib), 10V,<br>13( $\alpha$ MePhe),<br>16K, 17K,<br>24R, 27E,<br>28A, 29(Aib),<br>30G          |

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|                    |                                                                                                             |     |           |                                      |    |       |                                                                              |
|--------------------|-------------------------------------------------------------------------------------------------------------|-----|-----------|--------------------------------------|----|-------|------------------------------------------------------------------------------|
| <b>Peptide 439</b> | H(Aib)QGTFTSDVSK( $\alpha$ M ePhe)LDRK(O2Oc-O2Oc- $\gamma$ E-C18diacid)17RAQDFVR WLL(Aib)E-amide            | 450 | C18diacid | $\gamma$ E-(O2Oc)-(O2Oc)             | 17 | Amide | 2(Aib), 10V, 13( $\alpha$ MePhe), 16R, 17K, 24R, 27L, 28(Aib), 29E           |
| <b>Peptide 440</b> | H(Aib)QGTFTSDVSK( $\alpha$ M ePhe)LDKK(O2Oc-O2Oc- $\gamma$ E-C20diacid)17RARDFVR WLL(Aib)E-acid             | 451 | C20diacid | $\gamma$ E-(O2Oc)-(O2Oc)             | 17 | Acid  | 2(Aib), 10V, 13( $\alpha$ MePhe), 16K, 17K, 20R, 24R, 27L, 28(Aib), 29E      |
| <b>Peptide 441</b> | H(Aib)QGTFTSDVSK( $\alpha$ M ePhe)LDKK(O2Oc-O2Oc- $\gamma$ E-C20diacid)17RAQDFVR WLL(Aib)E-amide            | 452 | C20diacid | $\gamma$ E-(O2Oc)-(O2Oc)             | 17 | Amide | 2(Aib), 10V, 13( $\alpha$ MePhe), 16K, 17K, 24R, 27L, 28(Aib), 29E           |
| <b>Peptide 442</b> | H(Aib)QGTFTSDVSK( $\alpha$ M ePhe)LDKK(O2Oc-O2Oc- $\gamma$ E-C18diacid)17RAQDFVR WLL(Aib)G-amide            | 453 | C18diacid | $\gamma$ E-(O2Oc)-(O2Oc)             | 17 | Amide | 2(Aib), 10V, 13( $\alpha$ MePhe), 16K, 17K, 24R, 27L, 28E, 29(Aib), 30G      |
| <b>Peptide 443</b> | H(Aib)QGTFTSDVSK( $\alpha$ M ePhe)LDKK(O2Oc-O2Oc- $\gamma$ E-C18diacid)17RARDFVR WLL(Aib)E-amide            | 454 | C18diacid | $\gamma$ E-(O2Oc)-(O2Oc)             | 17 | Amide | 2(Aib), 10V, 13( $\alpha$ MePhe), 16K, 17K, 20R, 24R, 27L, 28(Aib), 29E      |
| <b>Peptide 444</b> | H(Aib)QGTFTSDVSK( $\alpha$ M ePhe)LETK(O2Oc-O2Oc- $\gamma$ E-C20diacid)17RARDFVQ WLL(Aib)G-acid             | 455 | C18diacid | $\gamma$ E-(O2Oc)-(O2Oc)             | 17 | Acid  | 2(Aib), 10V, 13( $\alpha$ MePhe), 15E, 16T, 17K, 20R, 27L, 28E, 29(Aib), 30G |
| <b>Peptide 445</b> | H(Aib)QGTFTSDVSK( $\alpha$ M ePhe)LETK(O2Oc-O2Oc- $\gamma$ E-C18diacid)17RARDFVQ WLL(Aib)G-acid             | 456 | C18diacid | $\gamma$ E-(O2Oc)-(O2Oc)             | 17 | Acid  | 2(Aib), 10V, 13( $\alpha$ MePhe), 15E, 16T, 17K, 20R, 27L, 28E, 29(Aib), 30G |
| <b>Peptide 446</b> | H(Aib)QGTFTSDVSK( $\alpha$ M ePhe)LDRK(O2Oc-O2Oc- $\gamma$ E- $\gamma$ E-C18diacid)17RAQDFVR WLVAib)E-amide | 457 | C18diacid | $\gamma$ E- $\gamma$ E-(O2Oc)-(O2Oc) | 17 | Amide | 2(Aib), 10V, 13( $\alpha$ MePhe), 16R, 17K, 24R, 27V, 28(Aib), 29E           |

|                        |                                                                                                                            |     |           |                                              |    |       |                                                                                        |
|------------------------|----------------------------------------------------------------------------------------------------------------------------|-----|-----------|----------------------------------------------|----|-------|----------------------------------------------------------------------------------------|
| <b>Peptide<br/>447</b> | H(Aib)QGTFTSDVSK( $\alpha$ M<br>ePhe)LDRK(O2Oc-<br>O2Oc- $\gamma$ E- $\gamma$ E-<br>C20diacid)17RAQDFVR<br>WLV(Aib)E-amide | 458 | C20diacid | $\gamma$ E- $\gamma$ E-<br>(O2Oc)-<br>(O2Oc) | 17 | Amide | 2(Aib), 10V,<br>13( $\alpha$ MePhe),<br>16R, 17K,<br>24R, 27V,<br>28(Aib), 29E         |
| <b>Peptide<br/>448</b> | H(Aib)QGTFTSDVSK( $\alpha$ M<br>ePhe)LDKK(O2Oc-<br>O2Oc- $\gamma$ E- $\gamma$ E-<br>C18diacid)17RARDFVR<br>WLL(Aib)E-acid  | 459 | C18diacid | $\gamma$ E- $\gamma$ E-<br>(O2Oc)-<br>(O2Oc) | 17 | Acid  | 2(Aib), 10V,<br>13( $\alpha$ MePhe),<br>16K, 17K,<br>20R, 24R,<br>27L, 28(Aib),<br>29E |
| <b>Peptide<br/>449</b> | H(Aib)QGTFTSDVSK( $\alpha$ M<br>ePhe)LDTK(O2Oc-<br>O2Oc- $\gamma$ E- $\gamma$ E-<br>C20diacid)17RARDFVQ<br>WLLE(Aib)G-acid | 460 | C20diacid | $\gamma$ E- $\gamma$ E-<br>(O2Oc)-<br>(O2Oc) | 17 | Acid  | 2(Aib), 10V,<br>13( $\alpha$ MePhe),<br>16T, 17K,<br>20R, 27L,<br>28E, 29(Aib),<br>30G |
| <b>Peptide<br/>450</b> | H(Aib)QGTFTSDVSK( $\alpha$ M<br>ePhe)LDKK(O2Oc-<br>O2Oc- $\gamma$ E- $\gamma$ E-<br>C18diacid)17RAQDFVR<br>WLLE(Aib)G-acid | 461 | C18diacid | $\gamma$ E- $\gamma$ E-<br>(O2Oc)-<br>(O2Oc) | 17 | Acid  | 2(Aib), 10V,<br>13( $\alpha$ MePhe),<br>16K, 17K,<br>24R, 27L,<br>28E, 29(Aib),<br>30G |
| <b>Peptide<br/>451</b> | H(Aib)QGTFTSDVSK( $\alpha$ M<br>ePhe)LDKK(O2Oc-<br>O2Oc- $\gamma$ E-<br>C20diacid)17RARDFVL<br>WLL(Aib)E-amide             | 462 | C20diacid | $\gamma$ E-<br>(O2Oc)-<br>(O2Oc)             | 17 | Amide | 2(Aib), 10V,<br>13( $\alpha$ MePhe),<br>16K, 17K,<br>20R, 24L,<br>27L, 28(Aib),<br>29E |
| <b>Peptide<br/>452</b> | H(Aib)QGTFTSDVSK( $\alpha$ M<br>ePhe)LDKK(O2Oc-<br>O2Oc- $\gamma$ E-<br>C20diacid)17RALDFVR<br>WLL(Aib)E-amide             | 463 | C20diacid | $\gamma$ E-<br>(O2Oc)-<br>(O2Oc)             | 17 | Amide | 2(Aib), 10V,<br>13( $\alpha$ MePhe),<br>16K, 17K,<br>20L, 24R,<br>27L, 28(Aib),<br>29E |
| <b>Peptide<br/>453</b> | H(Aib)QGTFTSDVSK( $\alpha$ M<br>ePhe)LDKK(O2Oc-<br>O2Oc- $\gamma$ E-<br>C20diacid)17RAQDFVR<br>WLLE(Aib)G-amide            | 464 | C20diacid | $\gamma$ E-<br>(O2Oc)-<br>(O2Oc)             | 17 | Amide | 2(Aib), 10V,<br>13( $\alpha$ MePhe),<br>16K, 17K,<br>24R, 27L,<br>28E, 29(Aib),<br>30G |
| <b>Peptide<br/>454</b> | H(Aib)QGTFTSDVSK( $\alpha$ M<br>ePhe)LDKK(O2Oc-<br>O2Oc- $\gamma$ E-<br>C20diacid)17RAQDFVR<br>WLEA(Aib)G-amide            | 465 | C20diacid | $\gamma$ E-<br>(O2Oc)-<br>(O2Oc)             | 17 | Amide | 2(Aib), 10V,<br>13( $\alpha$ MePhe),<br>16K, 17K,<br>24R, 27E,<br>28A, 29(Aib),<br>30G |

|                        |                                                                                                                             |     |           |                                              |    |       |                                                                                        |
|------------------------|-----------------------------------------------------------------------------------------------------------------------------|-----|-----------|----------------------------------------------|----|-------|----------------------------------------------------------------------------------------|
| <b>Peptide<br/>455</b> | H(Aib)QGTFTSDVSK( $\alpha$ M<br>ePhe)LDKK(O2Oc-<br>O2Oc- $\gamma$ E- $\gamma$ E-<br>C20diacid)17RAQDFVR<br>WLL(Aib)E-amide  | 466 | C20diacid | $\gamma$ E- $\gamma$ E-<br>(O2Oc)-<br>(O2Oc) | 17 | Amide | 2(Aib), 10V,<br>13( $\alpha$ MePhe),<br>16K, 17K,<br>24R, 27L,<br>28(Aib), 29E         |
| <b>Peptide<br/>456</b> | H(Aib)QGTFTSDVSK( $\alpha$ M<br>ePhe)LDRK(O2Oc-<br>O2Oc- $\gamma$ E-<br>C20diacid)17RAQDFVR<br>WLL(Aib)E-amide              | 467 | C20diacid | $\gamma$ E-<br>(O2Oc)-<br>(O2Oc)             | 17 | Amide | 2(Aib), 10V,<br>13( $\alpha$ MePhe),<br>16R, 17K,<br>24R, 27L,<br>28(Aib), 29E         |
| <b>Peptide<br/>457</b> | H(Aib)QGTFTSDVSK( $\alpha$ M<br>ePhe)LDTK(O2Oc-<br>O2Oc- $\gamma$ E-<br>C20diacid)17RARDFVQ<br>WLLE(Aib)G-amide             | 468 | C20diacid | $\gamma$ E-<br>(O2Oc)-<br>(O2Oc)             | 17 | Amide | 2(Aib), 10V,<br>13( $\alpha$ MePhe),<br>16T, 17K,<br>20R, 27L,<br>28E, 29(Aib),<br>30G |
| <b>Peptide<br/>458</b> | H(Aib)QGTFTSDVSK( $\alpha$ M<br>ePhe)LDTK(O2Oc-<br>O2Oc- $\gamma$ E- $\gamma$ E-<br>C20diacid)17RARDFVQ<br>WLLE(Aib)G-amide | 469 | C20diacid | $\gamma$ E- $\gamma$ E-<br>(O2Oc)-<br>(O2Oc) | 17 | Amide | 2(Aib), 10V,<br>13( $\alpha$ MePhe),<br>16T, 17K,<br>20R, 27L,<br>28E, 29(Aib),<br>30G |
| <b>Peptide<br/>459</b> | H(Aib)QGTFTSDVSK( $\alpha$ M<br>ePhe)LDKK(O2Oc-<br>O2Oc- $\gamma$ E-<br>C18diacid)17RAQDFVR<br>WLLAE-amide                  | 470 | C18diacid | $\gamma$ E-<br>(O2Oc)-<br>(O2Oc)             | 17 | Amide | 2(Aib), 10V,<br>13( $\alpha$ MePhe),<br>16K, 17K,<br>24R, 27L,<br>28A, 29E             |
| <b>Peptide<br/>460</b> | H(Aib)QGTFTSDVSK( $\alpha$ M<br>ePhe)LDKK(O2Oc-<br>O2Oc- $\gamma$ E-<br>C20diacid)17RAQDFVR<br>WLLAE-amide                  | 471 | C20diacid | $\gamma$ E-<br>(O2Oc)-<br>(O2Oc)             | 17 | Amide | 2(Aib), 10V,<br>13( $\alpha$ MePhe),<br>16K, 17K,<br>24R, 27L,<br>28A, 29E             |
| <b>Peptide<br/>461</b> | H(Aib)QGTFTSDVSK( $\alpha$ M<br>ePhe)LDRK(O2Oc-<br>O2Oc- $\gamma$ E-<br>C18diacid)17RAQDFVR<br>WLLAE-amide                  | 472 | C18diacid | $\gamma$ E-<br>(O2Oc)-<br>(O2Oc)             | 17 | Amide | 2(Aib), 10V,<br>13( $\alpha$ MePhe),<br>16R, 17K,<br>24R, 27L,<br>28A, 29E             |
| <b>Peptide<br/>462</b> | H(Aib)QGTFTSDVSK( $\alpha$ M<br>ePhe)LDTK(O2Oc-<br>O2Oc- $\gamma$ E-<br>C18diacid)17RARDFVQ<br>WLLEAG-acid                  | 473 | C18diacid | $\gamma$ E-<br>(O2Oc)-<br>(O2Oc)             | 17 | Acid  | 2(Aib), 10V,<br>13( $\alpha$ MePhe),<br>16T, 17K,<br>20R, 27L,<br>28E, 29A,<br>30G     |
| <b>Peptide<br/>463</b> | H(Aib)QGTFTSDVSK( $\alpha$ M<br>ePhe)LDSK(O2Oc-<br>O2Oc- $\gamma$ E- $\gamma$ E-<br>C18diacid)17RAQDFVR<br>WLLAE-amide      | 474 | C18diacid | $\gamma$ E- $\gamma$ E-<br>(O2Oc)-<br>(O2Oc) | 17 | Amide | 2(Aib), 10V,<br>13( $\alpha$ MePhe),<br>17K, 27L,<br>28(Aib)                           |

|                        |                                                                                                                            |     |           |                                              |    |       |                                                                                |
|------------------------|----------------------------------------------------------------------------------------------------------------------------|-----|-----------|----------------------------------------------|----|-------|--------------------------------------------------------------------------------|
|                        | C18diacid)17RAQDFVQ<br>WLL(Aib)T-amide                                                                                     |     |           |                                              |    |       |                                                                                |
| <b>Peptide<br/>464</b> | H(Aib)QGTFTSDVSK( $\alpha$ M<br>ePhe)LDTK(O2Oc-<br>O2Oc- $\gamma$ E-<br>C18diacid)17RAQDFVQ<br>WLL(Aib)G-acid              | 475 | C18diacid | $\gamma$ E-<br>(O2Oc)-<br>(O2Oc)             | 17 | Acid  | 2(Aib), 10V,<br>13( $\alpha$ MePhe),<br>16T, 17K,<br>27L, 28E,<br>29(Aib), 30G |
| <b>Peptide<br/>465</b> | H(Aib)QGTFTSDVSK( $\alpha$ M<br>ePhe)LDLK(O2Oc-<br>O2Oc- $\gamma$ E- $\gamma$ E-<br>C18diacid)17RAQDFVQ<br>WLL(Aib)T-acid  | 476 | C18diacid | $\gamma$ E- $\gamma$ E-<br>(O2Oc)-<br>(O2Oc) | 17 | Acid  | 2(Aib), 10V,<br>13( $\alpha$ MePhe),<br>16L, 17K,<br>27L, 28(Aib)              |
| <b>Peptide<br/>466</b> | H(Aib)QGTFTSDVSK( $\alpha$ M<br>ePhe)LDTK(O2Oc-<br>O2Oc- $\gamma$ E-<br>C18diacid)17RAQDFVQ<br>WLL(Aib)G-amide             | 477 | C18diacid | $\gamma$ E-<br>(O2Oc)-<br>(O2Oc)             | 17 | Amide | 2(Aib), 10V,<br>13( $\alpha$ MePhe),<br>16T, 17K,<br>27L, 28E,<br>29(Aib), 30G |
| <b>Peptide<br/>467</b> | H(Aib)QGTFTSDVSK( $\alpha$ M<br>ePhe)LDTK(O2Oc-<br>O2Oc- $\gamma$ E-<br>C20diacid)17RAQDFVQ<br>WLL(Aib)G-amide             | 478 | C20diacid | $\gamma$ E-<br>(O2Oc)-<br>(O2Oc)             | 17 | Amide | 2(Aib), 10V,<br>13( $\alpha$ MePhe),<br>16T, 17K,<br>27L, 28E,<br>29(Aib), 30G |
| <b>Peptide<br/>468</b> | H(Aib)QGTFTSDVSK( $\alpha$ M<br>ePhe)LDTK(O2Oc-<br>O2Oc- $\gamma$ E- $\gamma$ E-<br>C18diacid)17RAQDFVQ<br>WLL(Aib)G-amide | 479 | C18diacid | $\gamma$ E- $\gamma$ E-<br>(O2Oc)-<br>(O2Oc) | 17 | Amide | 2(Aib), 10V,<br>13( $\alpha$ MePhe),<br>16T, 17K,<br>27L, 28E,<br>29(Aib), 30G |
| <b>Peptide<br/>469</b> | H(Aib)QGTFTSDVSK( $\alpha$ M<br>ePhe)LDTK(O2Oc-<br>O2Oc- $\gamma$ E- $\gamma$ E-<br>C20diacid)17RAQDFVQ<br>WLL(Aib)G-amide | 480 | C20diacid | $\gamma$ E- $\gamma$ E-<br>(O2Oc)-<br>(O2Oc) | 17 | Amide | 2(Aib), 10V,<br>13( $\alpha$ MePhe),<br>16T, 17K,<br>27L, 28E,<br>29(Aib), 30G |
| <b>Peptide<br/>470</b> | H(Aib)QGTFTSDVSK( $\alpha$ M<br>ePhe)LDKK(O2Oc-<br>O2Oc- $\gamma$ E-<br>C20diacid)17RARDFVQ<br>WLL(Aib)E-amide             | 481 | C20diacid | $\gamma$ E-<br>(O2Oc)-<br>(O2Oc)             | 17 | Amide | 2(Aib), 10V,<br>13( $\alpha$ MePhe),<br>16K, 17K,<br>20R, 27L,<br>28(Aib), 29E |
| <b>Peptide<br/>471</b> | H(Aib)QGTFTSDVSK( $\alpha$ M<br>ePhe)LDLK(O2Oc-<br>O2Oc- $\gamma$ E-<br>C20diacid)17RARDFVQ<br>WLL(Aib)E-amide             | 482 | C20diacid | $\gamma$ E-<br>(O2Oc)-<br>(O2Oc)             | 17 | Amide | 2(Aib), 10V,<br>13( $\alpha$ MePhe),<br>16R, 17K,<br>20R, 27L,<br>28(Aib), 29E |
| <b>Peptide<br/>472</b> | H(Aib)QGTFTSDVSK( $\alpha$ M<br>ePhe)LDKK(O2Oc-<br>O2Oc- $\gamma$ E-<br>C18diacid)17RARDFVQ<br>WLL(Aib)E-amide             | 483 | C18diacid | $\gamma$ E-<br>(O2Oc)-<br>(O2Oc)             | 17 | Amide | 2(Aib), 10V,<br>13( $\alpha$ MePhe),<br>16K, 17K,<br>20R, 27L,<br>28(Aib), 29E |

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|                        |                                                                                                                 |     |           |                                  |    |       |                                                                                        |
|------------------------|-----------------------------------------------------------------------------------------------------------------|-----|-----------|----------------------------------|----|-------|----------------------------------------------------------------------------------------|
| <b>Peptide<br/>473</b> | H(Aib)QGTFTSDVSK( $\alpha$ M<br>ePhe)LDRK(O2Oc-<br>O2Oc- $\gamma$ E-<br>C18diacid)17RARDFVQ<br>WLL(Aib)E-amide  | 484 | C18diacid | $\gamma$ E-<br>(O2Oc)-<br>(O2Oc) | 17 | Amide | 2(Aib), 10V,<br>13( $\alpha$ MePhe),<br>16R, 17K,<br>20R, 27L,<br>28(Aib), 29E         |
| <b>Peptide<br/>474</b> | H(Aib)QGTFTSDVSK( $\alpha$ M<br>ePhe)LDTK(O2Oc-<br>O2Oc- $\gamma$ E-<br>C18diacid)17RARDFVQ<br>WLLA(Aib)G-amide | 485 | C18diacid | $\gamma$ E-<br>(O2Oc)-<br>(O2Oc) | 17 | Amide | 2(Aib), 10V,<br>13( $\alpha$ MePhe),<br>16T, 17K,<br>20R, 27L,<br>28A, 29(Aib),<br>30G |
| <b>Peptide<br/>475</b> | H(Aib)QGTFTSDVSK( $\alpha$ M<br>ePhe)LDTK(O2Oc-<br>O2Oc- $\gamma$ E-<br>C20diacid)17RARDFVQ<br>WLLA(Aib)G-amide | 486 | C20diacid | $\gamma$ E-<br>(O2Oc)-<br>(O2Oc) | 17 | Amide | 2(Aib), 10V,<br>13( $\alpha$ MePhe),<br>16T, 17K,<br>20R, 27L,<br>28A, 29(Aib),<br>30G |
| <b>Peptide<br/>476</b> | H(Aib)QGTFTSDVSK( $\alpha$ M<br>ePhe)LDTK(O2Oc-<br>O2Oc- $\gamma$ E-<br>C18diacid)17RAQDFVR<br>WLLA(Aib)G-amide | 487 | C18diacid | $\gamma$ E-<br>(O2Oc)-<br>(O2Oc) | 17 | Amide | 2(Aib), 10V,<br>13( $\alpha$ MePhe),<br>16T, 17K,<br>24R, 27L,<br>28A, 29(Aib),<br>30G |
| <b>Peptide<br/>477</b> | H(Aib)QGTFTSDVSK( $\alpha$ M<br>ePhe)LDTK(O2Oc-<br>O2Oc- $\gamma$ E-<br>C20diacid)17RAQDFVR<br>WLLA(Aib)G-amide | 488 | C20diacid | $\gamma$ E-<br>(O2Oc)-<br>(O2Oc) | 17 | Amide | 2(Aib), 10V,<br>13( $\alpha$ MePhe),<br>16T, 17K,<br>24R, 27L,<br>28A, 29(Aib),<br>30G |
| <b>Peptide<br/>478</b> | H(Aib)QGTFTSDVSK( $\alpha$ M<br>ePhe)LDTK(O2Oc-<br>O2Oc- $\gamma$ E-<br>C18diacid)17RAQDFVR<br>WLLE(Aib)K-amide | 489 | C18diacid | $\gamma$ E-<br>(O2Oc)-<br>(O2Oc) | 17 | Amide | 2(Aib), 10V,<br>13( $\alpha$ MePhe),<br>16T, 17K,<br>24R, 27L,<br>28E, 29(Aib),<br>30K |
| <b>Peptide<br/>479</b> | H(Aib)QGTFTSDVSK( $\alpha$ M<br>ePhe)LDTK(O2Oc-<br>O2Oc- $\gamma$ E-<br>C20diacid)17RAQDFVR<br>WLLE(Aib)K-amide | 490 | C20diacid | $\gamma$ E-<br>(O2Oc)-<br>(O2Oc) | 17 | Amide | 2(Aib), 10V,<br>13( $\alpha$ MePhe),<br>16T, 17K,<br>24R, 27L,<br>28E, 29(Aib),<br>30K |
| <b>Peptide<br/>480</b> | H(Aib)QGTFTSDVSK( $\alpha$ M<br>ePhe)LDTK(O2Oc-<br>O2Oc- $\gamma$ E-<br>C18diacid)17RARDFVQ<br>WLLE(Aib)K-amide | 491 | C18diacid | $\gamma$ E-<br>(O2Oc)-<br>(O2Oc) | 17 | Amide | 2(Aib), 10V,<br>13( $\alpha$ MePhe),<br>16T, 17K,<br>20R, 27L,<br>28E, 29(Aib),<br>30K |

|                        |                                                                                                                 |     |           |                                  |    |       |                                                                                        |
|------------------------|-----------------------------------------------------------------------------------------------------------------|-----|-----------|----------------------------------|----|-------|----------------------------------------------------------------------------------------|
| <b>Peptide<br/>481</b> | H(Aib)QGTFTSDVSK( $\alpha$ M<br>ePhe)LDTK(O2Oc-<br>O2Oc- $\gamma$ E-<br>C20diacid)17RARDFVQ<br>WLL(Aib)K-amide  | 492 | C20diacid | $\gamma$ E-<br>(O2Oc)-<br>(O2Oc) | 17 | Amide | 2(Aib), 10V,<br>13( $\alpha$ MePhe),<br>16T, 17K,<br>20R, 27L,<br>28E, 29(Aib),<br>30K |
| <b>Peptide<br/>482</b> | H(Aib)QGTFTSDVSK( $\alpha$ M<br>ePhe)LESK(O2Oc-O2Oc-<br>$\gamma$ E-<br>C18diacid)17RAQDFVQ<br>WLL(Aib)E-acid    | 493 | C18diacid | $\gamma$ E-<br>(O2Oc)-<br>(O2Oc) | 17 | Acid  | 2(Aib), 10V,<br>13( $\alpha$ MePhe),<br>15E, 17K,<br>27L, 28(Aib),<br>29E              |
| <b>Peptide<br/>483</b> | H(Aib)QGTFTSDVSK( $\alpha$ M<br>ePhe)LDTK(O2Oc-<br>O2Oc- $\gamma$ E-<br>C18diacid)17RAQDFVQ<br>WLL(Aib)E-acid   | 494 | C18diacid | $\gamma$ E-<br>(O2Oc)-<br>(O2Oc) | 17 | Acid  | 2(Aib), 10V,<br>13( $\alpha$ MePhe),<br>16T, 17K,<br>27L, 28(Aib),<br>29E              |
| <b>Peptide<br/>484</b> | H(Aib)QGTFTSDVSK( $\alpha$ M<br>ePhe)LDTK(O2Oc-<br>O2Oc- $\gamma$ E-<br>C20diacid)17RAQDFVQ<br>WLL(Aib)E-acid   | 495 | C20diacid | $\gamma$ E-<br>(O2Oc)-<br>(O2Oc) | 17 | Acid  | 2(Aib), 10V,<br>13( $\alpha$ MePhe),<br>16T, 17K,<br>27L, 28(Aib),<br>29E              |
| <b>Peptide<br/>485</b> | H(Aib)QGTFTSDVSK( $\alpha$ M<br>ePhe)LDTK(O2Oc-<br>O2Oc- $\gamma$ E-<br>C20diacid)17RAQDFVQ<br>WLL(Aib)E-amide  | 496 | C20diacid | $\gamma$ E-<br>(O2Oc)-<br>(O2Oc) | 17 | Amide | 2(Aib), 10V,<br>13( $\alpha$ MePhe),<br>16T, 17K,<br>27L, 28(Aib),<br>29E              |
| <b>Peptide<br/>486</b> | H(Aib)QGTFTSDVSK( $\alpha$ M<br>ePhe)LDLK(O2Oc-<br>O2Oc- $\gamma$ E-<br>C20diacid)17RAQDFVR<br>WLL(Aib)E-acid   | 497 | C20diacid | $\gamma$ E-<br>(O2Oc)-<br>(O2Oc) | 17 | Acid  | 2(Aib), 10V,<br>13( $\alpha$ MePhe),<br>16L, 17K,<br>24R, 27L,<br>28(Aib), 29E         |
| <b>Peptide<br/>487</b> | H(Aib)QGTFTSDVSK( $\alpha$ M<br>ePhe)LDTK(O2Oc-<br>O2Oc- $\gamma$ E-<br>C18diacid)17RARDFVQ<br>WLL(Aib)TE-acid  | 498 | C18diacid | $\gamma$ E-<br>(O2Oc)-<br>(O2Oc) | 17 | Acid  | 2(Aib), 10V,<br>13( $\alpha$ MePhe),<br>16T, 17K,<br>20R, 27L,<br>28(Aib), 30E         |
| <b>Peptide<br/>488</b> | H(Aib)QGTFTSDVSK( $\alpha$ M<br>ePhe)LDTK(O2Oc-<br>O2Oc- $\gamma$ E-<br>C20diacid)17RARDFVQ<br>WLL(Aib)TE-acid  | 499 | C20diacid | $\gamma$ E-<br>(O2Oc)-<br>(O2Oc) | 17 | Acid  | 2(Aib), 10V,<br>13( $\alpha$ MePhe),<br>16T, 17K,<br>20R, 27L,<br>28(Aib), 30E         |
| <b>Peptide<br/>489</b> | H(Aib)QGTFTSDVSK( $\alpha$ M<br>ePhe)LDTK(O2Oc-<br>O2Oc- $\gamma$ E-<br>C18diacid)17RARDFVQ<br>WLL(Aib)TE-amide | 500 | C18diacid | $\gamma$ E-<br>(O2Oc)-<br>(O2Oc) | 17 | Amide | 2(Aib), 10V,<br>13( $\alpha$ MePhe),<br>16T, 17K,<br>20R, 27L,<br>28(Aib), 30E         |

|                        |                                                                                                                 |     |           |                                  |    |       |                                                                                        |
|------------------------|-----------------------------------------------------------------------------------------------------------------|-----|-----------|----------------------------------|----|-------|----------------------------------------------------------------------------------------|
| <b>Peptide<br/>490</b> | H(Aib)QGTFTSDVSK( $\alpha$ M<br>ePhe)LDTK(O2Oc-<br>O2Oc- $\gamma$ E-<br>C20diacid)17RARDFVQ<br>WLL(Aib)TE-amide | 501 | C20diacid | $\gamma$ E-<br>(O2Oc)-<br>(O2Oc) | 17 | Amide | 2(Aib), 10V,<br>13( $\alpha$ MePhe),<br>16T, 17K,<br>20R, 27L,<br>28(Aib), 30E         |
| <b>Peptide<br/>491</b> | H(Aib)QGTFTSDVSK( $\alpha$ M<br>ePhe)LDTK(O2Oc-<br>O2Oc- $\gamma$ E-<br>C18diacid)17RARDFVR<br>WLL(Aib)TE-acid  | 502 | C18diacid | $\gamma$ E-<br>(O2Oc)-<br>(O2Oc) | 17 | Acid  | 2(Aib), 10V,<br>13( $\alpha$ MePhe),<br>16T, 17K,<br>20R, 24R,<br>27L, 28(Aib),<br>30E |
| <b>Peptide<br/>492</b> | H(Aib)QGTFTSDVSK( $\alpha$ M<br>ePhe)LDTK(O2Oc-<br>O2Oc- $\gamma$ E-<br>C20diacid)17RARDFVR<br>WLL(Aib)TE-acid  | 503 | C20diacid | $\gamma$ E-<br>(O2Oc)-<br>(O2Oc) | 17 | Acid  | 2(Aib), 10V,<br>13( $\alpha$ MePhe),<br>16T, 17K,<br>20R, 24R,<br>27L, 28(Aib),<br>30E |
| <b>Peptide<br/>493</b> | H(Aib)QGTFTSDVSK( $\alpha$ M<br>ePhe)LDTK(O2Oc-<br>O2Oc- $\gamma$ E-<br>C18diacid)17RAQDFVR<br>WLLR(Aib)K-acid  | 504 | C18diacid | $\gamma$ E-<br>(O2Oc)-<br>(O2Oc) | 17 | Acid  | 2(Aib), 10V,<br>13( $\alpha$ MePhe),<br>16T, 17K,<br>24R, 27L,<br>28R, 29(Aib),<br>30K |
| <b>Peptide<br/>494</b> | H(Aib)QGTFTSDVSK( $\alpha$ M<br>ePhe)LDTK(O2Oc-<br>O2Oc- $\gamma$ E-<br>C20diacid)17RAQDFVR<br>WLLR(Aib)K-acid  | 505 | C20diacid | $\gamma$ E-<br>(O2Oc)-<br>(O2Oc) | 17 | Acid  | 2(Aib), 10V,<br>13( $\alpha$ MePhe),<br>16T, 17K,<br>24R, 27L,<br>28R, 29(Aib),<br>30K |
| <b>Peptide<br/>495</b> | H(Aib)QGTFTSDVSK( $\alpha$ M<br>ePhe)LDTK(O2Oc-<br>O2Oc- $\gamma$ E-<br>C18diacid)17RAQDFVR<br>WLLR(Aib)K-amide | 506 | C18diacid | $\gamma$ E-<br>(O2Oc)-<br>(O2Oc) | 17 | Amide | 2(Aib), 10V,<br>13( $\alpha$ MePhe),<br>16T, 17K,<br>24R, 27L,<br>28R, 29(Aib),<br>30K |
| <b>Peptide<br/>496</b> | H(Aib)QGTFTSDVSK( $\alpha$ M<br>ePhe)LDTK(O2Oc-<br>O2Oc- $\gamma$ E-<br>C20diacid)17RAQDFVR<br>WLLR(Aib)K-amide | 507 | C20diacid | $\gamma$ E-<br>(O2Oc)-<br>(O2Oc) | 17 | Amide | 2(Aib), 10V,<br>13( $\alpha$ MePhe),<br>16T, 17K,<br>24R, 27L,<br>28R, 29(Aib),<br>30K |
| <b>Peptide<br/>497</b> | H(Aib)QGTFTSDVSK( $\alpha$ M<br>ePhe)LDTK(O2Oc-<br>O2Oc- $\gamma$ E-<br>C18diacid)17RAQDFVR<br>WLLR(Aib)A-acid  | 508 | C18diacid | $\gamma$ E-<br>(O2Oc)-<br>(O2Oc) | 17 | Acid  | 2(Aib), 10V,<br>13( $\alpha$ MePhe),<br>16T, 17K,<br>24R, 27L,<br>28R, 29(Aib),<br>30A |

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|                        |                                                                                                                 |     |           |                                  |    |       |                                                                                        |
|------------------------|-----------------------------------------------------------------------------------------------------------------|-----|-----------|----------------------------------|----|-------|----------------------------------------------------------------------------------------|
| <b>Peptide<br/>498</b> | H(Aib)QGTFTSDVSK( $\alpha$ M<br>ePhe)LDTK(O2Oc-<br>O2Oc- $\gamma$ E-<br>C20diacid)17RAQDFVR<br>WLLR(Aib)A-acid  | 509 | C20diacid | $\gamma$ E-<br>(O2Oc)-<br>(O2Oc) | 17 | Acid  | 2(Aib), 10V,<br>13( $\alpha$ MePhe),<br>16T, 17K,<br>24R, 27L,<br>28R, 29(Aib),<br>30A |
| <b>Peptide<br/>499</b> | H(Aib)QGTFTSDVSK( $\alpha$ M<br>ePhe)LDTK(O2Oc-<br>O2Oc- $\gamma$ E-<br>C18diacid)17RAQDFVQ<br>WLLR(Aib)A-acid  | 510 | C18diacid | $\gamma$ E-<br>(O2Oc)-<br>(O2Oc) | 17 | Acid  | 2(Aib), 10V,<br>13( $\alpha$ MePhe),<br>16T, 17K,<br>27L, 28R,<br>29(Aib), 30A         |
| <b>Peptide<br/>500</b> | H(Aib)QGTFTSDVSK( $\alpha$ M<br>ePhe)LDTK(O2Oc-<br>O2Oc- $\gamma$ E-<br>C20diacid)17RAQDFVQ<br>WLLR(Aib)A-acid  | 511 | C20diacid | $\gamma$ E-<br>(O2Oc)-<br>(O2Oc) | 17 | Acid  | 2(Aib), 10V,<br>13( $\alpha$ MePhe),<br>16T, 17K,<br>27L, 28R,<br>29(Aib), 30A         |
| <b>Peptide<br/>501</b> | H(Aib)QGTFTSDVSK( $\alpha$ M<br>ePhe)LDTK(O2Oc-<br>O2Oc- $\gamma$ E-<br>C18diacid)17RARDFVQ<br>WLLR(Aib)A-acid  | 512 | C18diacid | $\gamma$ E-<br>(O2Oc)-<br>(O2Oc) | 17 | Acid  | 2(Aib), 10V,<br>13( $\alpha$ MePhe),<br>16T, 17K,<br>20R, 27L,<br>28R, 29(Aib),<br>30A |
| <b>Peptide<br/>502</b> | H(Aib)QGTFTSDVSK( $\alpha$ M<br>ePhe)LDTK(O2Oc-<br>O2Oc- $\gamma$ E-<br>C20diacid)17RARDFVQ<br>WLLR(Aib)A-acid  | 513 | C20diacid | $\gamma$ E-<br>(O2Oc)-<br>(O2Oc) | 17 | Acid  | 2(Aib), 10V,<br>13( $\alpha$ MePhe),<br>16T, 17K,<br>20R, 27L,<br>28R, 29(Aib),<br>30A |
| <b>Peptide<br/>503</b> | H(Aib)QGTFTSDVSK( $\alpha$ M<br>ePhe)LDTK(O2Oc-<br>O2Oc- $\gamma$ E-<br>C20diacid)17RAQDFVR<br>WLLE(Aib)K-acid  | 514 | C20diacid | $\gamma$ E-<br>(O2Oc)-<br>(O2Oc) | 17 | Acid  | 2(Aib), 10V,<br>13( $\alpha$ MePhe),<br>16T, 17K,<br>24R, 27L,<br>28E, 29(Aib),<br>30K |
| <b>Peptide<br/>504</b> | H(Aib)QGTFTSDVSK( $\alpha$ M<br>ePhe)LESK(O2Oc-O2Oc-<br>$\gamma$ E-<br>C20diacid)17RAQDFVR<br>WLLE(Aib)K-acid   | 515 | C20diacid | $\gamma$ E-<br>(O2Oc)-<br>(O2Oc) | 17 | Acid  | 2(Aib), 10V,<br>13( $\alpha$ MePhe),<br>15E, 17K,<br>24R, 27L,<br>28E, 29(Aib),<br>30K |
| <b>Peptide<br/>505</b> | H(Aib)QGTFTSDVSK( $\alpha$ M<br>ePhe)LDTK(O2Oc-<br>O2Oc- $\gamma$ E-<br>C20diacid)17RAQDFVQ<br>WLLE(Aib)K-amide | 516 | C20diacid | $\gamma$ E-<br>(O2Oc)-<br>(O2Oc) | 17 | Amide | 2(Aib), 10V,<br>13( $\alpha$ MePhe),<br>16T, 17K,<br>27L, 28E,<br>29(Aib), 30K         |

|                    |                                                                                                                                  |     |           |                          |    |       |                                                                                                                  |
|--------------------|----------------------------------------------------------------------------------------------------------------------------------|-----|-----------|--------------------------|----|-------|------------------------------------------------------------------------------------------------------------------|
| <b>Peptide 506</b> | H(Aib)QGTFTSDVSK( $\alpha$ MePhe)LDTK(O2Oc-O2Oc- $\gamma$ E-C20diacid)17RARDFVAWLLE(Aib)G-acid                                   | 517 | C20diacid | $\gamma$ E-(O2Oc)-(O2Oc) | 17 | Acid  | 2(Aib), 10V, 13( $\alpha$ MePhe), 16T, 17K, 20R, 24A, 27L, 28E, 29(Aib), 30G                                     |
| <b>Peptide 507</b> | H(Aib)QGTFTSDVSK( $\alpha$ MePhe)LDTK(O2Oc-O2Oc- $\gamma$ E-C20diacid)17RARDFVAWLLE(Aib)G-amide                                  | 518 | C20diacid | $\gamma$ E-(O2Oc)-(O2Oc) | 17 | Amide | 2(Aib), 10V, 13( $\alpha$ MePhe), 16T, 17K, 20R, 24A, 27L, 28E, 29(Aib), 30G                                     |
| <b>Peptide 508</b> | H(Aib)QGTFTSDVSK( $\alpha$ MePhe)LESK(O2Oc-O2Oc- $\gamma$ E-C20diacid)17RAQDFVRWLVE(Aib)G-amide                                  | 519 | C20diacid | $\gamma$ E-(O2Oc)-(O2Oc) | 17 | Amide | 2(Aib), 10V, 13( $\alpha$ MePhe), 15E, 17K, 24R, 27V, 28E, 29(Aib), 30G                                          |
| <b>Peptide 509</b> | H(Aib)QGTFTSDVSK( $\alpha$ MePhe)LESK(O2Oc-O2Oc- $\gamma$ E-C20diacid)17RAQDFVRWLL(Aib)TE-acid                                   | 520 | C20diacid | $\gamma$ E-(O2Oc)-(O2Oc) | 17 | Acid  | 2(Aib), 10V, 13( $\alpha$ MePhe), 15E, 17K, 24R, 27L, 28(Aib), 30E                                               |
| <b>Peptide 510</b> | H(Aib)QGTFTSDVSK( $\alpha$ MePhe)LDTK(O2Oc-O2Oc- $\gamma$ E-C20diacid)17RARDFVRWLL(Aib)E-acid                                    | 521 | C20diacid | $\gamma$ E-(O2Oc)-(O2Oc) | 17 | Acid  | 2(Aib), 10V, 13( $\alpha$ MePhe), 16T, 17K, 20R, 24R, 27L, 28(Aib), 29E                                          |
| <b>Peptide 511</b> | H(Aib)QGTFTSDVSK( $\alpha$ MePhe)LDTK(O2Oc-O2Oc- $\gamma$ E-C20diacid)17RARDFVRWLL(Aib)E-amide                                   | 522 | C20diacid | $\gamma$ E-(O2Oc)-(O2Oc) | 17 | Amide | 2(Aib), 10V, 13( $\alpha$ MePhe), 16T, 17K, 20R, 24R, 27L, 28(Aib), 29E                                          |
| <b>Peptide 512</b> | H(Aib)QGT( $\alpha$ MePhe)TS DVSK( $\alpha$ MePhe)LDTK(O2Oc-O2Oc- $\gamma$ E-C18diacid)17RAQD( $\alpha$ MePhe)VRWLLA(Aib)G-amide | 523 | C18diacid | $\gamma$ E-(O2Oc)-(O2Oc) | 17 | Amide | 2(Aib), 6( $\alpha$ MePhe), 10V, 13( $\alpha$ MePhe), 16T, 17K, 22( $\alpha$ MePhe), 24R, 27L, 28A, 29(Aib), 30G |
| <b>Peptide 513</b> | H(Aib)QGT( $\alpha$ MePhe)TS DVSK( $\alpha$ MePhe)LDTK(O2Oc-O2Oc- $\gamma$ E-                                                    | 524 | C18diacid | $\gamma$ E-(O2Oc)-(O2Oc) | 17 | Amide | 2(Aib), 6( $\alpha$ MePhe), 10V,                                                                                 |

|                        |                                                                                                                                                   |     |           |                                                                         |    |       |                                                                                                      |
|------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------|-----|-----------|-------------------------------------------------------------------------|----|-------|------------------------------------------------------------------------------------------------------|
|                        | C18diacid)17RARD( $\alpha$ M<br>ePhe)VQWLLA(Aib)G-<br>amide                                                                                       |     |           |                                                                         |    |       | 13( $\alpha$ MePhe),<br>16T, 17K,<br>20R,<br>22( $\alpha$ MePhe),<br>27L, 28A,<br>29(Aib), 30G       |
| <b>Peptide<br/>514</b> | H(Aib)QGTFTSDVSK( $\alpha$ M<br>ePhe)LDTK(O2Oc-<br>O2Oc- $\gamma$ E-<br>C18diacid)17AARDFVQ<br>WLLE(Aib)G-amide                                   | 525 | C18diacid | $\gamma$ E-<br>(O2Oc)-<br>(O2Oc)                                        | 17 | Amide | 2(Aib), 10V,<br>13( $\alpha$ MePhe),<br>16T, 17K,<br>18A, 20R,<br>27L, 28E,<br>29(Aib), 30G          |
| <b>Peptide<br/>515</b> | H(Aib)QGTFTSDVSK( $\alpha$ M<br>ePhe)LDTK(O2Oc-<br>O2Oc- $\gamma$ E-<br>C20diacid)17AARDFVQ<br>WLLE(Aib)G-amide                                   | 526 | C20diacid | $\gamma$ E-<br>(O2Oc)-<br>(O2Oc)                                        | 17 | Amide | 2(Aib), 10V,<br>13( $\alpha$ MePhe),<br>16T, 17K,<br>18A, 20R,<br>27L, 28E,<br>29(Aib), 30G          |
| <b>Peptide<br/>516</b> | H(Aib)QGTFTSDVSK( $\alpha$ M<br>ePhe)LESK(O2Oc-O2Oc-<br>$\gamma$ E-<br>C20diacid)17RAQDFVR<br>WLLA(Aib)G-amide                                    | 527 | C20diacid | $\gamma$ E-<br>(O2Oc)-<br>(O2Oc)                                        | 17 | Amide | 2(Aib), 10V,<br>13( $\alpha$ MePhe),<br>15E, 17K,<br>24R, 27L,<br>28A, 29(Aib),<br>30G               |
| <b>Peptide<br/>517</b> | H(Aib)QGTFTSDVSK( $\alpha$ M<br>ePhe)LEAK(O2Oc-<br>O2Oc- $\gamma$ E- $\gamma$ E-<br>C18diacid)17AAREFIW<br>LLET-amide                             | 528 | C18diacid | $\gamma$ E- $\gamma$ E-<br>(O2Oc)-<br>(O2Oc)                            | 17 | Amide | 2(Aib), 10V,<br>13( $\alpha$ MePhe),<br>15E, 16A,<br>17K, 18A,<br>20R, 21E,<br>23I, 24A,<br>27L, 28E |
| <b>Peptide<br/>518</b> | H(Aib)QGTFTSDVSK( $\alpha$ M<br>ePhe)LDTK(O2Oc-<br>O2Oc- $\gamma$ E- $\gamma$ E-<br>C18diacid)17RARDVQ<br>WLLE(Aib)G-acid                         | 529 | C18diacid | $\gamma$ E- $\gamma$ E-<br>(O2Oc)-<br>(O2Oc)                            | 17 | Acid  | 2(Aib), 10V,<br>13( $\alpha$ MePhe),<br>16T, 17K,<br>20R, 27L,<br>28E, 29(Aib),<br>30G               |
| <b>Peptide<br/>519</b> | H(Aib)QGTFTSDVSK( $\alpha$ M<br>ePhe)LDTK( $\gamma$ E- $\gamma$ E-<br>O2Oc-O2Oc- $\gamma$ E- $\gamma$ E-<br>C18diacid)17RARDVQ<br>WLLE(Aib)G-acid | 530 | C18diacid | $\gamma$ E- $\gamma$ E-<br>(O2Oc)-<br>(O2Oc)-<br>$\gamma$ E- $\gamma$ E | 17 | Acid  | 2(Aib), 10V,<br>13( $\alpha$ MePhe),<br>16T, 17K,<br>20R, 27L,<br>28E, 29(Aib),<br>30G               |
| <b>Peptide<br/>520</b> | H(Aib)QGTFTSDVSK( $\alpha$ M<br>ePhe)LDTK( $\gamma$ E- $\gamma$ E-<br>O2Oc-O2Oc- $\gamma$ E- $\gamma$ E-                                          | 531 | C20diacid | $\gamma$ E- $\gamma$ E-<br>(O2Oc)-<br>(O2Oc)-<br>$\gamma$ E- $\gamma$ E | 17 | Acid  | 2(Aib), 10V,<br>13( $\alpha$ MePhe),<br>16T, 17K,<br>20R, 27L,                                       |

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|  |                                      |  |  |  |  |  |                      |
|--|--------------------------------------|--|--|--|--|--|----------------------|
|  | C20diacid)17RARDVQ<br>WLE(Aib)G-acid |  |  |  |  |  | 28E, 29(Aib),<br>30G |
|--|--------------------------------------|--|--|--|--|--|----------------------|

**[0092]** In some aspects, the peptide comprises the sequence: H-X2-X3-G-X5-X6-T-S-D-X10-S-X12-X13-L-X15-X16-X17-X18-X19-X20-X21-X22-X23-X24-X25-X26-X27-X28-X29-X30-X31-Z, wherein X2 is S, Aminoisobutyric acid (Aib),  $\alpha$ Methyl-Serine ( $\alpha$ MeS), D-serine (dSer), 1-aminocyclopropane-1-carboxylic acid (Acpr), or S, 1-aminocyclobutane-1-carboxylic acid (Acbu), X3 is Q, H,  $\alpha$ Methyl-Glutamine ( $\alpha$ MeGln), N-Methyl-Glutamine (N-MeGln), D-glutamine (dGln) or  $\beta$ -dimethylglutamine ( $\beta$ -dimethylGln), X5 is T or S, X6 is F or  $\alpha$ Methyl-Phenylalanine ( $\alpha$ MePhe), X10 is Y or V, X12 is K, E, or R, X13 is Y,  $\alpha$ MePhe, or Aib, X15 is D or E, X16 is S, T, E, or Aib, X17 is R, Q, or E, X18 is R, A, Aib, or S, X19 is A or V, X20 is Q or K, wherein the K can comprise an acyl moiety and/or can be lipidated, X21 is D or L, X22 is F or  $\alpha$ Methyl-Phenylalanine ( $\alpha$ MePhe), X23 is V or I, X24 is Q, E, A, or R, X25 is W, Aib, or S, X26 is L or I, X27 is M, A, L, E, I, or V, X28 is N, E, (PEG)4, Aib, S, or A, X29 is T, not present, E, or G, X30 is not present, E, T, or G, X31 is not present or G, and Z is amide or acid (SEQ ID NO: 413), wherein the peptide does not comprise SEQ ID NO: 1.

**[0093]** In some aspects, the residue at position 20 is acylated. In some aspects, the residue at position 20 is lipidated. In some aspects, the lipid is selected from the group consisting of a palmitoyl group, stearoyl group, lauryl group, myristoyl group, margaroyl group, octadecanedioic acid (C18diacid), and icosanedioic acid (C20diacid). In some aspects, the lipid is selected from the group consisting of a stearoyl group, octadecanedioic acid (C18diacid), and icosanedioic acid (C20diacid).

**[0094]** In some aspects, the lipid attached to the residue at position 20 is attached via a linker. In some aspects, the linker is selected from the group consisting of (O2Oc), (O2Oc)-(O2Oc), (O2Oc)- $\gamma$ E-(O2Oc), (PEG)2-(PEG)2- $\gamma$ E- $\gamma$ E, (PEG)2- $\gamma$ E-(PEG)2- $\gamma$ E,  $\gamma$ E,  $\gamma$ E-(O2Oc),  $\gamma$ E-(O2Oc)-(O2Oc),  $\gamma$ E-(O2Oc)- $\gamma$ E-(O2Oc),  $\gamma$ E-(PEG)2-(PEG)2,  $\gamma$ E-(PEG)2- $\gamma$ E-(PEG)2,  $\gamma$ E-(PEG)4,  $\gamma$ E- $\gamma$ E,  $\gamma$ E- $\gamma$ E-(O2Oc),  $\gamma$ E- $\gamma$ E-(O2Oc)-(O2Oc),  $\gamma$ E- $\gamma$ E-(PEG)12,  $\gamma$ E- $\gamma$ E-(PEG)2-(PEG)2,  $\gamma$ E- $\gamma$ E-(PEG)2- $\gamma$ E- $\gamma$ E,  $\gamma$ E- $\gamma$ E-(PEG)4, and  $\gamma$ E- $\gamma$ E-(PEG)8. In some aspects, the linker is selected from the group consisting of  $\gamma$ E,  $\gamma$ E- $\gamma$ E,  $\gamma$ E- $\gamma$ E-(O2Oc),  $\gamma$ E-(O2Oc)-(O2Oc),  $\gamma$ E- $\gamma$ E-(O2Oc)-(O2Oc),  $\gamma$ E-(O2Oc),  $\gamma$ E- $\gamma$ E-(PEG)2-(PEG)2,  $\gamma$ E-(O2Oc)- $\gamma$ E-(O2Oc),  $\gamma$ E-(PEG)4,  $\gamma$ E- $\gamma$ E-(PEG)4, (O2Oc)- $\gamma$ E-(O2Oc), (O2Oc)-(O2Oc), and (O2Oc).

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- [0095] In some aspects, the peptide comprises the sequence: H-Aminoisobutyric acid (Aib)-Q-G-T-F-T-S-D-X10-S-X12- $\alpha$ Methyl-Phenylalanine ( $\alpha$ MePhe)-L-D-X16-X17-X18-A-K-D-F-V-X24-W-X26-X27-X28-X29-X30-Z, wherein X10 is V or Y, X12 is K or E, X16 is S or Aib, X17 is R or E, X18 is R or A, X24 is A, R, or Q, X26 is L or I, X27 is E, L, A, or I, X28 is A, E, Aib, S, or N, X29 is G, Aib, T, or E, X30 is G, E, T, or not present, and Z is amide or acid (SEQ ID NO: 414).
- [0096] In some aspects, the lysine at position 20 is acylated. In some aspects, the lysine at position 20 is lipidated. In some aspects, the lipid is selected from the group consisting of a palmitoyl group, stearoyl group, lauryl group, myristoyl group, margaroyl group, octadecanedioic acid (C18diacid), and icosanedioic acid (C20diacid). In some aspects, the lipid is octadecanedioic acid (C18diacid).
- [0097] In some aspects, the lipid is linked to the lysine at position 20 via a linker. In some aspects, the linker is selected from the group consisting of (O2Oc), (O2Oc)-(O2Oc), (O2Oc)- $\gamma$ E-(O2Oc), (PEG)2-(PEG)2- $\gamma$ E- $\gamma$ E, (PEG)2- $\gamma$ E-(PEG)2- $\gamma$ E,  $\gamma$ E,  $\gamma$ E-(O2Oc),  $\gamma$ E-(O2Oc)-(O2Oc),  $\gamma$ E-(O2Oc)- $\gamma$ E-(O2Oc),  $\gamma$ E-(PEG)2-(PEG)2,  $\gamma$ E-(PEG)2- $\gamma$ E-(PEG)2,  $\gamma$ E-(PEG)4,  $\gamma$ E- $\gamma$ E,  $\gamma$ E- $\gamma$ E-(O2Oc),  $\gamma$ E- $\gamma$ E-(O2Oc)-(O2Oc),  $\gamma$ E- $\gamma$ E-(PEG)12,  $\gamma$ E- $\gamma$ E-(PEG)2-(PEG)2,  $\gamma$ E- $\gamma$ E-(PEG)2- $\gamma$ E- $\gamma$ E,  $\gamma$ E- $\gamma$ E-(PEG)4, and  $\gamma$ E- $\gamma$ E-(PEG)8. In some aspects, the linker is selected from the group consisting of  $\gamma$ E,  $\gamma$ E-(O2Oc)-(O2Oc), and  $\gamma$ E- $\gamma$ E-(O2Oc)-(O2Oc)- $\gamma$ E- $\gamma$ E.
- [0098] In some aspects, the peptide comprises any one of SEQ ID NOs: 207-347 and 532-537. In some aspects, the peptide comprises SEQ ID NO: 228. In some aspects, the peptide comprises SEQ ID NO: 233.
- [0099] In some aspects, the peptide has the structure of any one of the structures depicted in FIGs 4A-4B. In some aspects, the peptide has the structure of FIG. 4A. In some aspects, the peptide has the structure of FIG. 4B.
- [0100] In some aspects, the peptide is any one of the peptides in **Table 2**.

**Table 2. Peptides Modified at Position 20**

| Peptide            | Sequence                                                                                                          | SEQ ID NO | Albumin binding moiety | Linker (described N->C term) | Acylation site | C-term. | Sequence modification with respect to glucagon                                         |
|--------------------|-------------------------------------------------------------------------------------------------------------------|-----------|------------------------|------------------------------|----------------|---------|----------------------------------------------------------------------------------------|
| <b>Peptide 203</b> | H(Aib)HGS( $\alpha$ MePhe)TS DVSK( $\alpha$ MePhe)LDSQAA K(O2Oc-O2Oc- $\gamma$ E-C18diacid)20DFVQWIA NT-amide     | 207       | C18diacid              | $\gamma$ E-(O2Oc)-(O2Oc)     | 20             | Amide   | 2Aib, 3H, 5S, 6 $\alpha$ MePhe, 10V, 13 $\alpha$ MePhe, 17Q, 18A, 20K, 26I, 27A        |
| <b>Peptide 204</b> | H(Aib)QGT( $\alpha$ MePhe)TS DVSK( $\alpha$ MePhe)LDSRAA K(O2Oc-O2Oc- $\gamma$ E-C18diacid)20DFVQWIA NT-amide     | 208       | C18diacid              | $\gamma$ E-(O2Oc)-(O2Oc)     | 20             | Amide   | 2Aib, 5S, 6 $\alpha$ MePhe, 10V, 13 $\alpha$ MePhe, 18A, 20K, 26I, 27A                 |
| <b>Peptide 205</b> | H(Aib)HGS( $\alpha$ MePhe)TS DVSK( $\alpha$ MePhe)LDSRAA K(O2Oc-O2Oc- $\gamma$ E-C18diacid)20DFVQWIA NT-amide     | 209       | C18diacid              | $\gamma$ E-(O2Oc)-(O2Oc)     | 20             | Amide   | 2Aib, 3H, 5S, 6 $\alpha$ MePhe, 10V, 13 $\alpha$ MePhe, 18A, 20K, 26I, 27A             |
| <b>Peptide 206</b> | H(Aib)HGS( $\alpha$ MePhe)TS DVSK( $\alpha$ MePhe)LDSR(Aib)AK(O2Oc-O2Oc- $\gamma$ E-C18diacid)20DFVQWIA NT-amide  | 210       | C18diacid              | $\gamma$ E-(O2Oc)-(O2Oc)     | 20             | Amide   | 2Aib, 3H, 5S, 6 $\alpha$ MePhe, 10V, 13 $\alpha$ MePhe, 18Aib, 20K, 26I, 27A           |
| <b>Peptide 207</b> | H(Aib)HGS( $\alpha$ MePhe)TS DVSK( $\alpha$ MePhe)LDSQAA K(O2Oc-O2Oc- $\gamma$ E-C18diacid)20DFVQ(Aib) IANT-amide | 211       | C18diacid              | $\gamma$ E-(O2Oc)-(O2Oc)     | 20             | Amide   | 2Aib, 3H, 5S, 6 $\alpha$ MePhe, 10V, 13 $\alpha$ MePhe, 17Q, 18A, 20K, 25Aib, 26I, 27A |
| <b>Peptide 208</b> | H(Aib)QGTFTSDVSK( $\alpha$ MePhe)LDSRAAK( $\gamma$ E-C18diacid)20DFVQWIA NT-amide                                 | 212       | C18diacid              | $\gamma$ E                   | 20             | Amide   | 2Aib, 10V, 13 $\alpha$ MePhe, 18A, 20K, 26I, 27A                                       |
| <b>Peptide 209</b> | H(Aib)HGS( $\alpha$ MePhe)TS DVSK( $\alpha$ MePhe)LDSQAA K(O2Oc-O2Oc- $\gamma$ E-C18diacid)20DFVEWIA NT-amide     | 213       | C18diacid              | $\gamma$ E-(O2Oc)-(O2Oc)     | 20             | Amide   | 2Aib, 3H, 5S, 6 $\alpha$ MePhe, 10V, 13 $\alpha$ MePhe, 17Q, 18A, 20K, 24E, 26I, 27A   |

|                    |                                                                                                                                             |     |           |                                              |    |       |                                                                                                                      |
|--------------------|---------------------------------------------------------------------------------------------------------------------------------------------|-----|-----------|----------------------------------------------|----|-------|----------------------------------------------------------------------------------------------------------------------|
| <b>Peptide 210</b> | H(Aib)HGS( $\alpha$ MePhe)TS<br>DVSK( $\alpha$ MePhe)LDSQAA<br>K(O2Oc-O2Oc- $\gamma$ E- $\gamma$ E-<br>C18diacid)20DFVEWIA<br>NT-amide      | 214 | C18diacid | $\gamma$ E- $\gamma$ E-<br>(O2Oc)-<br>(O2Oc) | 20 | Amide | 2Aib, 3H, 5S,<br>6 $\alpha$ MePhe,<br>10V,<br>13 $\alpha$ MePhe,<br>17Q, 18A,<br>20K, 24E,<br>26I, 27A               |
| <b>Peptide 211</b> | H(Aib)HGS( $\alpha$ MePhe)TS<br>DVSK( $\alpha$ MePhe)LDSRAA<br>K(O2Oc-O2Oc- $\gamma$ E- $\gamma$ E-<br>C20diacid)20DFVQWIA<br>NT-amide      | 215 | C20diacid | $\gamma$ E- $\gamma$ E-<br>(O2Oc)-<br>(O2Oc) | 20 | Amide | 2Aib, 3H, 5S,<br>6 $\alpha$ MePhe,<br>10V,<br>13 $\alpha$ MePhe,<br>18A, 20K,<br>26I, 27A                            |
| <b>Peptide 212</b> | H(Aib)HGS( $\alpha$ MePhe)TS<br>DVSK( $\alpha$ MePhe)LDSRAA<br>K(O2Oc-O2Oc- $\gamma$ E-<br>C20diacid)20DFVEWIA<br>NT-amide                  | 216 | C20diacid | $\gamma$ E-<br>(O2Oc)-<br>(O2Oc)             | 20 | Amide | 2Aib, 3H, 5S,<br>6 $\alpha$ MePhe,<br>10V,<br>13 $\alpha$ MePhe,<br>18A, 20K,<br>24E, 26I, 27A                       |
| <b>Peptide 213</b> | H(Aib)HGS( $\alpha$ MePhe)TS<br>DVSK( $\alpha$ MePhe)LDSRAA<br>K(O2Oc-O2Oc- $\gamma$ E- $\gamma$ E-<br>C20diacid)20DFVEWIA<br>NT-amide      | 217 | C20diacid | $\gamma$ E- $\gamma$ E-<br>(O2Oc)-<br>(O2Oc) | 20 | Amide | 2Aib, 3H, 5S,<br>6 $\alpha$ MePhe,<br>10V,<br>13 $\alpha$ MePhe,<br>18A, 20K,<br>24E, 26I, 27A                       |
| <b>Peptide 214</b> | H(Aib)HGS( $\alpha$ MePhe)TS<br>DVSK( $\alpha$ MePhe)LDSRAA<br>K(O2Oc-O2Oc- $\gamma$ E-<br>C20diacid)20DFVQWIA<br>NT-amide                  | 218 | C20diacid | $\gamma$ E-<br>(O2Oc)-<br>(O2Oc)             | 20 | Amide | 2Aib, 3H, 5S,<br>6 $\alpha$ MePhe,<br>10V,<br>13 $\alpha$ MePhe,<br>18A, 20K,<br>26I, 27A                            |
| <b>Peptide 215</b> | H(Aib)HGS( $\alpha$ MePhe)TS<br>DVSK( $\alpha$ MePhe)LDSRAA<br>K(O2Oc-O2Oc- $\gamma$ E-<br>C20diacid)20D( $\alpha$ MePh<br>e)VQWIA NT-amide | 219 | C20diacid | $\gamma$ E-<br>(O2Oc)-<br>(O2Oc)             | 20 | Amide | 2Aib, 3H, 5S,<br>6 $\alpha$ MePhe,<br>10V,<br>13 $\alpha$ MePhe,<br>18A, 20K,<br>22 $\alpha$ MePhe,<br>26I, 27A      |
| <b>Peptide 216</b> | H(Aib)HGS( $\alpha$ MePhe)TS<br>DVSK( $\alpha$ MePhe)LDSRAA<br>K(O2Oc-O2Oc- $\gamma$ E-<br>C20diacid)20D( $\alpha$ MePh<br>e)VEWIA NT-amide | 220 | C20diacid | $\gamma$ E-<br>(O2Oc)-<br>(O2Oc)             | 20 | Amide | 2Aib, 3H, 5S,<br>6 $\alpha$ MePhe,<br>10V,<br>13 $\alpha$ MePhe,<br>18A, 20K,<br>22 $\alpha$ MePhe,<br>24E, 26I, 27A |

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|                    |                                                                                                                                                   |     |           |                                              |    |       |                                                                                                        |
|--------------------|---------------------------------------------------------------------------------------------------------------------------------------------------|-----|-----------|----------------------------------------------|----|-------|--------------------------------------------------------------------------------------------------------|
| <b>Peptide 217</b> | H(Aib)HGS( $\alpha$ MePhe)TS<br>DVSK( $\alpha$ MePhe)LDSR(Ai<br>b)AK(O2Oc-O2Oc- $\gamma$ E-<br>$\gamma$ E-<br>C20diacid)20DFVQWIA<br>NT-amide     | 221 | C20diacid | $\gamma$ E- $\gamma$ E-<br>(O2Oc)-<br>(O2Oc) | 20 | Amide | 2Aib, 3H, 5S,<br>6 $\alpha$ MePhe,<br>10V,<br>13 $\alpha$ MePhe,<br>18Aib, 20K,<br>26I, 27A            |
| <b>Peptide 218</b> | H(Aib)HGS( $\alpha$ MePhe)TS<br>DVSK( $\alpha$ MePhe)LDSRAA<br>K(O2Oc-O2Oc- $\gamma$ E- $\gamma$ E-<br>C20diacid)20DFVQWIA<br>NTG-amide           | 222 | C20diacid | $\gamma$ E- $\gamma$ E-<br>(O2Oc)-<br>(O2Oc) | 20 | Amide | 2Aib, 3H, 5S,<br>6 $\alpha$ MePhe,<br>10V,<br>13 $\alpha$ MePhe,<br>18A, 20K,<br>26I, 27A,<br>30G      |
| <b>Peptide 219</b> | H(Aib)HGS( $\alpha$ MePhe)TS<br>DVSK( $\alpha$ MePhe)LDSRAA<br>K(O2Oc-O2Oc- $\gamma$ E- $\gamma$ E-<br>C20diacid)20DFVQWIA<br>NTGG-amide          | 223 | C20diacid | $\gamma$ E- $\gamma$ E-<br>(O2Oc)-<br>(O2Oc) | 20 | Amide | 2Aib, 3H, 5S,<br>6 $\alpha$ MePhe,<br>10V,<br>13 $\alpha$ MePhe,<br>18A, 20K,<br>26I, 27A,<br>30G, 31G |
| <b>Peptide 220</b> | H(Aib)HGS( $\alpha$ MePhe)TS<br>DVSK( $\alpha$ MePhe)LDSR(Ai<br>b)AK(O2Oc-O2Oc- $\gamma$ E-<br>$\gamma$ E-<br>C20diacid)20DFVQ(Aib)<br>IANT-amide | 224 | C20diacid | $\gamma$ E- $\gamma$ E-<br>(O2Oc)-<br>(O2Oc) | 20 | Amide | 2Aib, 3H, 5S,<br>6 $\alpha$ MePhe,<br>10V,<br>13 $\alpha$ MePhe,<br>18Aib, 20K,<br>25Aib, 26I,<br>27A  |
| <b>Peptide 221</b> | H(Aib)HGS( $\alpha$ MePhe)TS<br>DVSK( $\alpha$ MePhe)LDSRAA<br>K(O2Oc-O2Oc- $\gamma$ E- $\gamma$ E-<br>C20diacid)20DFVQ(Aib)<br>IANT-amide        | 225 | C20diacid | $\gamma$ E- $\gamma$ E-<br>(O2Oc)-<br>(O2Oc) | 20 | Amide | 2Aib, 3H, 5S,<br>6 $\alpha$ MePhe,<br>10V,<br>13 $\alpha$ MePhe,<br>18A, 20K,<br>25Aib, 26I,<br>27A    |
| <b>Peptide 222</b> | H(Aib)HGS( $\alpha$ MePhe)TS<br>DVSK( $\alpha$ MePhe)LDSQAA<br>K(O2Oc-O2Oc- $\gamma$ E-<br>C18diacid)20DFVQSIAN<br>T-amide                        | 226 | C18diacid | $\gamma$ E-<br>(O2Oc)-<br>(O2Oc)             | 20 | Amide | 2Aib, 3H, 5S,<br>6 $\alpha$ MePhe,<br>10V,<br>13 $\alpha$ MePhe,<br>17Q, 18A,<br>20K, 25S,<br>26I, 27A |
| <b>Peptide 223</b> | H(Aib)HGS( $\alpha$ MePhe)TS<br>DVSK( $\alpha$ MePhe)LDSR(Ai<br>b)AK(O2Oc-O2Oc- $\gamma$ E-<br>C18diacid)20DFVQSIAN<br>T-amide                    | 227 | C18diacid | $\gamma$ E-<br>(O2Oc)-<br>(O2Oc)             | 20 | Amide | 2Aib, 3H, 5S,<br>6 $\alpha$ MePhe,<br>10V,<br>13 $\alpha$ MePhe,<br>18Aib, 20K,<br>25S, 26I, 27A       |

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|                    |                                                                                                                                                            |     |           |                                              |    |       |                                                                                                                                        |
|--------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------|-----|-----------|----------------------------------------------|----|-------|----------------------------------------------------------------------------------------------------------------------------------------|
| <b>Peptide 224</b> | H(Aib)HGS( $\alpha$ MePhe)TS<br>DVSK( $\alpha$ MePhe)LDSRAA<br>K(O2Oc-O2Oc- $\gamma$ E-<br>C18diacid)20D( $\alpha$ MePh<br>e)VQ(Aib)IANT-amide             | 228 | C18diacid | $\gamma$ E-<br>(O2Oc)-<br>(O2Oc)             | 20 | Amide | 2Aib, 3H, 5S,<br>6 $\alpha$ MePhe,<br>10V,<br>13 $\alpha$ MePhe,<br>18A, 20K,<br>22 $\alpha$ MePhe,<br>25Aib, 26I,<br>27A              |
| <b>Peptide 225</b> | H(Aib)HGS( $\alpha$ MePhe)TS<br>DVSK( $\alpha$ MePhe)LDSRAA<br>K(O2Oc-O2Oc- $\gamma$ E-<br>C18diacid)20D( $\alpha$ MePh<br>e)VQ(Aib)IANTGG-<br>amide       | 229 | C18diacid | $\gamma$ E-<br>(O2Oc)-<br>(O2Oc)             | 20 | Amide | 2Aib, 3H, 5S,<br>6 $\alpha$ MePhe,<br>10V,<br>13 $\alpha$ MePhe,<br>18A, 20K,<br>22 $\alpha$ MePhe,<br>25Aib, 26I,<br>27A, 30G,<br>31G |
| <b>Peptide 226</b> | H(Aib)HGS( $\alpha$ MePhe)TS<br>DVSK( $\alpha$ MePhe)LDSRAA<br>K(O2Oc-O2Oc- $\gamma$ E-<br>C18diacid)20D( $\alpha$ MePh<br>e)VE(Aib)IANT-amide             | 230 | C18diacid | $\gamma$ E-<br>(O2Oc)-<br>(O2Oc)             | 20 | Amide | 2Aib, 3H, 5S,<br>6 $\alpha$ MePhe,<br>10V,<br>13 $\alpha$ MePhe,<br>18A, 20K,<br>22 $\alpha$ MePhe,<br>24E, 25Aib,<br>26I, 27A         |
| <b>Peptide 227</b> | H(Aib)HGS( $\alpha$ MePhe)TS<br>DVSK( $\alpha$ MePhe)LDSRAA<br>K(O2Oc-O2Oc- $\gamma$ E-<br>C18diacid)20D( $\alpha$ MePh<br>e)IA(Aib)IANT-amide             | 231 | C18diacid | $\gamma$ E-<br>(O2Oc)-<br>(O2Oc)             | 20 | Amide | 2Aib, 3H, 5S,<br>6 $\alpha$ MePhe,<br>10V,<br>13 $\alpha$ MePhe,<br>18A, 20K,<br>22 $\alpha$ MePhe,<br>23I, 24A,<br>25Aib, 26I,<br>27A |
| <b>Peptide 228</b> | H(Aib)HGS( $\alpha$ MePhe)TS<br>DVSK( $\alpha$ MePhe)LDSRAA<br>K(O2Oc-O2Oc- $\gamma$ E- $\gamma$ E-<br>C20diacid)20D( $\alpha$ MePh<br>e)VQW IANT-amide    | 232 | C20diacid | $\gamma$ E- $\gamma$ E-<br>(O2Oc)-<br>(O2Oc) | 20 | Amide | 2Aib, 3H, 5S,<br>6 $\alpha$ MePhe,<br>10V,<br>13 $\alpha$ MePhe,<br>18A, 20K,<br>22 $\alpha$ MePhe,<br>26I, 27A                        |
| <b>Peptide 229</b> | H(Aib)HGS( $\alpha$ MePhe)TS<br>DVSK( $\alpha$ MePhe)LDSRAA<br>K(O2Oc-O2Oc- $\gamma$ E- $\gamma$ E-<br>C20diacid)20D( $\alpha$ MePh<br>e)VQ(Aib)IANT-amide | 233 | C20diacid | $\gamma$ E- $\gamma$ E-<br>(O2Oc)-<br>(O2Oc) | 20 | Amide | 2Aib, 3H, 5S,<br>6 $\alpha$ MePhe,<br>10V,<br>13 $\alpha$ MePhe,<br>18A, 20K,<br>22 $\alpha$ MePhe,                                    |

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|                    |                                                                                                                                                                  |     |           |                                              |    |       |                                                                                                                                        |
|--------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----|-----------|----------------------------------------------|----|-------|----------------------------------------------------------------------------------------------------------------------------------------|
|                    |                                                                                                                                                                  |     |           |                                              |    |       | 25Aib, 26I, 27A                                                                                                                        |
| <b>Peptide 230</b> | H(Aib)HGS( $\alpha$ MePhe)TS<br>DVSK( $\alpha$ MePhe)LDSRAA<br>K(O2Oc-O2Oc- $\gamma$ E-<br>C18diacid)20D( $\alpha$ MePh<br>e)IAWIAnt-amide                       | 234 | C18diacid | $\gamma$ E-<br>(O2Oc)-<br>(O2Oc)             | 20 | Amide | 2Aib, 3H, 5S,<br>6 $\alpha$ MePhe,<br>10V,<br>13 $\alpha$ MePhe,<br>18A, 20K,<br>22 $\alpha$ MePhe,<br>26I, 27A                        |
| <b>Peptide 231</b> | H(Aib)HGS( $\alpha$ MePhe)TS<br>DVSK( $\alpha$ MePhe)LDSRAA<br>K(O2Oc-O2Oc- $\gamma$ E- $\gamma$ E-<br>C18diacid)20D( $\alpha$ MePh<br>e)VQ(Aib)IAnt-amide       | 235 | C18diacid | $\gamma$ E- $\gamma$ E-<br>(O2Oc)-<br>(O2Oc) | 20 | Amide | 2Aib, 3H, 5S,<br>6 $\alpha$ MePhe,<br>10V,<br>13 $\alpha$ MePhe,<br>18A, 20K,<br>22 $\alpha$ MePhe,<br>25Aib, 26I,<br>27A              |
| <b>Peptide 232</b> | H(Aib)HGS( $\alpha$ MePhe)TS<br>DVSK( $\alpha$ MePhe)LDSRAA<br>K(O2Oc-O2Oc- $\gamma$ E- $\gamma$ E-<br>C20diacid)20D( $\alpha$ MePh<br>e)VQ(Aib)IAntGG-<br>amide | 236 | C20diacid | $\gamma$ E- $\gamma$ E-<br>(O2Oc)-<br>(O2Oc) | 20 | Amide | 2Aib, 3H, 5S,<br>6 $\alpha$ MePhe,<br>10V,<br>13 $\alpha$ MePhe,<br>18A, 20K,<br>22 $\alpha$ MePhe,<br>25Aib, 26I,<br>27A, 30G,<br>31G |
| <b>Peptide 233</b> | H(Aib)HGS( $\alpha$ MePhe)TS<br>DVSK( $\alpha$ MePhe)LDSRAA<br>K(O2Oc-O2Oc- $\gamma$ E- $\gamma$ E-<br>C20diacid)20D( $\alpha$ MePh<br>e)VE(Aib)IAnt-amide       | 237 | C20diacid | $\gamma$ E- $\gamma$ E-<br>(O2Oc)-<br>(O2Oc) | 20 | Amide | 2Aib, 3H, 5S,<br>6 $\alpha$ MePhe,<br>10V,<br>13 $\alpha$ MePhe,<br>18A, 20K,<br>22 $\alpha$ MePhe,<br>24E, 25Aib,<br>26I, 27A         |
| <b>Peptide 234</b> | H(Aib)HGS( $\alpha$ MePhe)TS<br>DVSK( $\alpha$ MePhe)LDSRAA<br>K(O2Oc-O2Oc- $\gamma$ E- $\gamma$ E-<br>C20diacid)20DFVQ(Aib)<br>IAntG-amide                      | 238 | C20diacid | $\gamma$ E- $\gamma$ E-<br>(O2Oc)-<br>(O2Oc) | 20 | Amide | 2Aib, 3H, 5S,<br>6 $\alpha$ MePhe,<br>10V,<br>13 $\alpha$ MePhe,<br>18A, 20K,<br>25Aib, 26I,<br>27A, 30G                               |
| <b>Peptide 235</b> | H(Aib)HGS( $\alpha$ MePhe)TS<br>DVSK( $\alpha$ MePhe)LDSRAA<br>K(O2Oc-O2Oc- $\gamma$ E- $\gamma$ E-<br>C20diacid)20DFVQ(Aib)<br>IAntGG-amide                     | 239 | C20diacid | $\gamma$ E- $\gamma$ E-<br>(O2Oc)-<br>(O2Oc) | 20 | Amide | 2Aib, 3H, 5S,<br>6 $\alpha$ MePhe,<br>10V,<br>13 $\alpha$ MePhe,<br>18A, 20K,<br>22 $\alpha$ MePhe,                                    |

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|                        |                                                                                                                                                           |     |           |                                              |    |       |                                                                                                                                        |
|------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------|-----|-----------|----------------------------------------------|----|-------|----------------------------------------------------------------------------------------------------------------------------------------|
|                        |                                                                                                                                                           |     |           |                                              |    |       | 25Aib, 26I,<br>27A, 30G,<br>31G                                                                                                        |
| <b>Peptide<br/>236</b> | H(Aib)HGS( $\alpha$ MePhe)TS<br>DVSK( $\alpha$ MePhe)LDSRAA<br>K(O2Oc-O2Oc- $\gamma$ E- $\gamma$ E-<br>C18diacid)20DFVQ(Aib)<br>IANTG-amide               | 240 | C18diacid | $\gamma$ E- $\gamma$ E-<br>(O2Oc)-<br>(O2Oc) | 20 | Amide | 2Aib, 3H, 5S,<br>6 $\alpha$ MePhe,<br>10V,<br>13 $\alpha$ MePhe,<br>18A, 20K,<br>25Aib, 26I,<br>27A, 30G                               |
| <b>Peptide<br/>237</b> | H(Aib)HGS( $\alpha$ MePhe)TS<br>DVSK( $\alpha$ MePhe)LDSRAA<br>K(O2Oc-O2Oc- $\gamma$ E- $\gamma$ E-<br>C18diacid)20DFVQ(Aib)<br>IANTGG-amide              | 241 | C18diacid | $\gamma$ E- $\gamma$ E-<br>(O2Oc)-<br>(O2Oc) | 20 | Amide | 2Aib, 3H, 5S,<br>6 $\alpha$ MePhe,<br>10V,<br>13 $\alpha$ MePhe,<br>18A, 20K,<br>22 $\alpha$ MePhe,<br>25Aib, 26I,<br>27A, 30G,<br>31G |
| <b>Peptide<br/>238</b> | H(Aib)HGS( $\alpha$ MePhe)TS<br>DVSK( $\alpha$ MePhe)LDSRAA<br>K(O2Oc-O2Oc- $\gamma$ E- $\gamma$ E-<br>C20diacid)20D( $\alpha$ MePh<br>e)VQW IANTG-amide  | 242 | C20diacid | $\gamma$ E- $\gamma$ E-<br>(O2Oc)-<br>(O2Oc) | 20 | Amide | 2Aib, 3H, 5S,<br>6 $\alpha$ MePhe,<br>10V,<br>13 $\alpha$ MePhe,<br>18A, 20K,<br>22 $\alpha$ MePhe,<br>26I, 27A,<br>30G                |
| <b>Peptide<br/>239</b> | H(Aib)HGS( $\alpha$ MePhe)TS<br>DVSK( $\alpha$ MePhe)LDSRAA<br>K(O2Oc-O2Oc- $\gamma$ E- $\gamma$ E-<br>C20diacid)20D( $\alpha$ MePh<br>e)VQW IANTGG-amide | 243 | C20diacid | $\gamma$ E- $\gamma$ E-<br>(O2Oc)-<br>(O2Oc) | 20 | Amide | 2Aib, 3H, 5S,<br>6 $\alpha$ MePhe,<br>10V,<br>13 $\alpha$ MePhe,<br>18A, 20K,<br>22 $\alpha$ MePhe,<br>26I, 27A,<br>30G, 31G           |
| <b>Peptide<br/>240</b> | H(Aib)HGS( $\alpha$ MePhe)TS<br>DVSK( $\alpha$ MePhe)LDSRAA<br>K(O2Oc-O2Oc- $\gamma$ E- $\gamma$ E-<br>C18diacid)20D( $\alpha$ MePh<br>e)VQW IANTG-amide  | 244 | C18diacid | $\gamma$ E- $\gamma$ E-<br>(O2Oc)-<br>(O2Oc) | 20 | Amide | 2Aib, 3H, 5S,<br>6 $\alpha$ MePhe,<br>10V,<br>13 $\alpha$ MePhe,<br>18A, 20K,<br>22 $\alpha$ MePhe,<br>26I, 27A,<br>30G                |
| <b>Peptide<br/>241</b> | H(Aib)HGS( $\alpha$ MePhe)TS<br>DVSK( $\alpha$ MePhe)LDSRAA<br>K(O2Oc-O2Oc- $\gamma$ E- $\gamma$ E-                                                       | 245 | C18diacid | $\gamma$ E- $\gamma$ E-<br>(O2Oc)-<br>(O2Oc) | 20 | Amide | 2Aib, 3H, 5S,<br>6 $\alpha$ MePhe,<br>10V,<br>13 $\alpha$ MePhe,                                                                       |

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|                    |                                                                                                                                          |     |           |                                      |    |       |                                                                                                         |
|--------------------|------------------------------------------------------------------------------------------------------------------------------------------|-----|-----------|--------------------------------------|----|-------|---------------------------------------------------------------------------------------------------------|
|                    | C18diacid)20D( $\alpha$ MePhe)VQWIA NTGG-amide                                                                                           |     |           |                                      |    |       | 18A, 20K, 22 $\alpha$ MePhe, 26I, 27A, 30G, 31G                                                         |
| <b>Peptide 242</b> | H(Aib)HGS( $\alpha$ MePhe)TS DVSK( $\alpha$ MePhe)LDSR(Aib)AK(O2Oc-O2Oc- $\gamma$ E- $\gamma$ E-C20diacid)20DFVQSIANT-amide              | 246 | C20diacid | $\gamma$ E- $\gamma$ E-(O2Oc)-(O2Oc) | 20 | Amide | 2Aib, 3H, 5S, 6 $\alpha$ MePhe, 10V, 13 $\alpha$ MePhe, 18Aib, 20K, 25S, 26I, 27A                       |
| <b>Peptide 243</b> | H(Aib)HGS( $\alpha$ MePhe)TS DVSK( $\alpha$ MePhe)LDSRAAK(O2Oc-O2Oc- $\gamma$ E-C18diacid)20D( $\alpha$ MePhe)VQSIANT-amide              | 247 | C18diacid | $\gamma$ E-(O2Oc)-(O2Oc)             | 20 | Amide | 2Aib, 3H, 5S, 6 $\alpha$ MePhe, 10V, 13 $\alpha$ MePhe, 18A, 20K, 22 $\alpha$ MePhe, 25S, 26I, 27A      |
| <b>Peptide 244</b> | H(Aib)HGS( $\alpha$ MePhe)TS DVSK( $\alpha$ MePhe)LDSRAAK(O2Oc-O2Oc- $\gamma$ E- $\gamma$ E-C20diacid)20D( $\alpha$ MePhe)VQSIANT-amide  | 248 | C20diacid | $\gamma$ E- $\gamma$ E-(O2Oc)-(O2Oc) | 20 | Amide | 2Aib, 3H, 5S, 6 $\alpha$ MePhe, 10V, 13 $\alpha$ MePhe, 18A, 20K, 22 $\alpha$ MePhe, 25S, 26I, 27A      |
| <b>Peptide 245</b> | H(Aib)HGS( $\alpha$ MePhe)TS DVSK( $\alpha$ MePhe)LDSRAAK(O2Oc-O2Oc- $\gamma$ E-C18diacid)20D( $\alpha$ MePhe)VESIANT-amide              | 249 | C18diacid | $\gamma$ E-(O2Oc)-(O2Oc)             | 20 | Amide | 2Aib, 3H, 5S, 6 $\alpha$ MePhe, 10V, 13 $\alpha$ MePhe, 18A, 20K, 22 $\alpha$ MePhe, 24E, 25S, 26I, 27A |
| <b>Peptide 246</b> | H(Aib)HGS( $\alpha$ MePhe)TS DVSK( $\alpha$ MePhe)LDSRAAK(O2Oc-O2Oc- $\gamma$ E- $\gamma$ E-C20diacid)20D( $\alpha$ MePhe)VESIANT-amide  | 250 | C20diacid | $\gamma$ E- $\gamma$ E-(O2Oc)-(O2Oc) | 20 | Amide | 2Aib, 3H, 5S, 6 $\alpha$ MePhe, 10V, 13 $\alpha$ MePhe, 18A, 20K, 22 $\alpha$ MePhe, 24E, 25S, 26I, 27A |
| <b>Peptide 247</b> | H(Aib)HGS( $\alpha$ MePhe)TS DVSK( $\alpha$ MePhe)LDSRAAK(O2Oc-O2Oc- $\gamma$ E- $\gamma$ E-C18diacid)20D( $\alpha$ MePhe)VQWIA NT-amide | 251 | C18diacid | $\gamma$ E- $\gamma$ E-(O2Oc)-(O2Oc) | 20 | Amide | 2Aib, 3H, 5S, 6 $\alpha$ MePhe, 10V, 13 $\alpha$ MePhe, 18A, 20K, 22 $\alpha$ MePhe, 26I, 27A           |

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|                    |                                                                                                                                            |     |           |                                      |    |       |                                                                                                           |
|--------------------|--------------------------------------------------------------------------------------------------------------------------------------------|-----|-----------|--------------------------------------|----|-------|-----------------------------------------------------------------------------------------------------------|
| <b>Peptide 248</b> | (NHis)SHGS( $\alpha$ MePhe)TSDVSK( $\alpha$ MePhe)LDSRAK(O2Oc-O2Oc- $\gamma$ E- $\gamma$ E-C20diacid)20D( $\alpha$ MePhe)VQWIAnt-amide     | 252 | C20diacid | $\gamma$ E- $\gamma$ E-(O2Oc)-(O2Oc) | 20 | Amide | 2Aib, 3H, 5S, 6 $\alpha$ MePhe, 10V, 13 $\alpha$ MePhe, 18A, 20K, 22 $\alpha$ MePhe, 26I, 27A             |
| <b>Peptide 249</b> | H(Aib)HGS( $\alpha$ MePhe)TSDVSK( $\alpha$ MePhe)LDSR(Aib)AK(O2Oc-O2Oc- $\gamma$ E- $\gamma$ E-C20diacid)20D( $\alpha$ MePhe)VESIAnt-amide | 253 | C20diacid | $\gamma$ E- $\gamma$ E-(O2Oc)-(O2Oc) | 20 | Amide | 2Aib, 3H, 5S, 6 $\alpha$ MePhe, 10V, 13 $\alpha$ MePhe, 18Aib, 20K, 22 $\alpha$ MePhe, 24E, 25S, 26I, 27A |
| <b>Peptide 250</b> | H(Aib)HGS( $\alpha$ MePhe)TSDVSK( $\alpha$ MePhe)LDSR(Aib)AK(O2Oc-O2Oc- $\gamma$ E- $\gamma$ E-C18diacid)20D( $\alpha$ MePhe)VESIAnt-amide | 254 | C18diacid | $\gamma$ E- $\gamma$ E-(O2Oc)-(O2Oc) | 20 | Amide | 2Aib, 3H, 5S, 6 $\alpha$ MePhe, 10V, 13 $\alpha$ MePhe, 18Aib, 20K, 22 $\alpha$ MePhe, 24E, 25S, 26I, 27A |
| <b>Peptide 251</b> | H(Aib)HGS( $\alpha$ MePhe)TSDVSK( $\alpha$ MePhe)LDSR(Aib)AK(O2Oc-O2Oc- $\gamma$ E-C18diacid)20DFVESIAnt-amide                             | 255 | C18diacid | $\gamma$ E-(O2Oc)-(O2Oc)             | 20 | Amide | 2Aib, 3H, 5S, 6 $\alpha$ MePhe, 10V, 13 $\alpha$ MePhe, 18Aib, 20K, 24E, 25S, 26I, 27A                    |
| <b>Peptide 252</b> | H(Aib)HGS( $\alpha$ MePhe)TSDVSK( $\alpha$ MePhe)LDSR(Aib)AK(O2Oc-O2Oc- $\gamma$ E-C20diacid)20DFVESIAnt-amide                             | 256 | C20diacid | $\gamma$ E-(O2Oc)-(O2Oc)             | 20 | Amide | 2Aib, 3H, 5S, 6 $\alpha$ MePhe, 10V, 13 $\alpha$ MePhe, 18Aib, 20K, 24E, 25S, 26I, 27A                    |
| <b>Peptide 253</b> | H(Aib)HGS( $\alpha$ MePhe)TSDVSK( $\alpha$ MePhe)LDSR(Aib)AK(O2Oc- $\gamma$ E-C18diacid)20DFVESIAnt-amide                                  | 257 | C18diacid | $\gamma$ E-(O2Oc)                    | 20 | Amide | 2Aib, 3H, 5S, 6 $\alpha$ MePhe, 10V, 13 $\alpha$ MePhe, 18Aib, 20K, 24E, 25S, 26I, 27A                    |
| <b>Peptide 254</b> | H(Aib)HGS( $\alpha$ MePhe)TSDVSK( $\alpha$ MePhe)LDSR(Aib)AK( $\gamma$ E-                                                                  | 258 | C18diacid | $\gamma$ E                           | 20 | Amide | 2Aib, 3H, 5S, 6 $\alpha$ MePhe, 10V,                                                                      |

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|                        |                                                                                                                                                                |     |           |                                              |    |       |                                                                                                                                   |
|------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------|-----|-----------|----------------------------------------------|----|-------|-----------------------------------------------------------------------------------------------------------------------------------|
|                        | C18diacid)20DFVESIAN<br>T-amide                                                                                                                                |     |           |                                              |    |       | 13 $\alpha$ MePhe,<br>18Aib, 20K,<br>24E, 25S,<br>26I, 27A                                                                        |
| <b>Peptide<br/>255</b> | H(Aib)HGS( $\alpha$ MePhe)TS<br>DVSK( $\alpha$ MePhe)LDSQAA<br>K(O2Oc-O2Oc- $\gamma$ E-<br>C18diacid)20D( $\alpha$ MePh<br>e)VQ(Aib)IANT-amide                 | 259 | C18diacid | $\gamma$ E-<br>(O2Oc)-<br>(O2Oc)             | 20 | Amide | 2Aib, 3H, 5S,<br>6 $\alpha$ MePhe,<br>10V,<br>13 $\alpha$ MePhe,<br>17Q, 18A,<br>20K,<br>22 $\alpha$ MePhe,<br>25Aib, 26I,<br>27A |
| <b>Peptide<br/>256</b> | H(Aib)HGS( $\alpha$ MePhe)TS<br>DVSK( $\alpha$ MePhe)LDSQAA<br>K(O2Oc-O2Oc- $\gamma$ E- $\gamma$ E-<br>C20diacid)20D( $\alpha$ MePh<br>e)VQ(Aib)IANT-amide     | 260 | C20diacid | $\gamma$ E- $\gamma$ E-<br>(O2Oc)-<br>(O2Oc) | 20 | Amide | 2Aib, 3H, 5S,<br>6 $\alpha$ MePhe,<br>10V,<br>13 $\alpha$ MePhe,<br>17Q, 18A,<br>20K,<br>22 $\alpha$ MePhe,<br>25Aib, 26I,<br>27A |
| <b>Peptide<br/>257</b> | H(Aib)HGS( $\alpha$ MePhe)TS<br>DVSK( $\alpha$ MePhe)LDSRAA<br>K(O2Oc-O2Oc- $\gamma$ E- $\gamma$ E-<br>Stearoyl)20D( $\alpha$ MePhe)<br>VQ(Aib)IANT-amide      | 261 | Stearoyl  | $\gamma$ E- $\gamma$ E-<br>(O2Oc)-<br>(O2Oc) | 20 | Amide | 2Aib, 3H, 5S,<br>6 $\alpha$ MePhe,<br>10V,<br>13 $\alpha$ MePhe,<br>18A, 20K,<br>22 $\alpha$ MePhe,<br>25Aib, 26I,<br>27A         |
| <b>Peptide<br/>258</b> | H(Aib)HGS( $\alpha$ MePhe)TS<br>DVSK( $\alpha$ MePhe)LDSRAA<br>K((PEG)2-(PEG)2- $\gamma$ E- $\gamma$ E-<br>C18diacid)20D( $\alpha$ MePh<br>e)VQ(Aib)IANT-amide | 262 | C18diacid | $\gamma$ E- $\gamma$ E-<br>(PEG)2-<br>(PEG)2 | 20 | Amide | 2Aib, 3H, 5S,<br>6 $\alpha$ MePhe,<br>10V,<br>13 $\alpha$ MePhe,<br>18A, 20K,<br>22 $\alpha$ MePhe,<br>25Aib, 26I,<br>27A         |
| <b>Peptide<br/>259</b> | H(Aib)HGS( $\alpha$ MePhe)TS<br>DVSK( $\alpha$ MePhe)LDSRAA<br>K(O2Oc- $\gamma$ E-O2Oc-<br>C18diacid)20D( $\alpha$ MePh<br>e)VQ(Aib)IANT-amide                 | 263 | C18diacid | (O2Oc)-<br>$\gamma$ E-<br>(O2Oc)             | 20 | Amide | 2Aib, 3H, 5S,<br>6 $\alpha$ MePhe,<br>10V,<br>13 $\alpha$ MePhe,<br>18A, 20K,<br>22 $\alpha$ MePhe,<br>25Aib, 26I,<br>27A         |

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|                    |                                                                                                                                                                |     |           |                                                 |    |       |                                                                                                                           |
|--------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------|-----|-----------|-------------------------------------------------|----|-------|---------------------------------------------------------------------------------------------------------------------------|
| <b>Peptide 260</b> | H(Aib)HGS( $\alpha$ MePhe)TS<br>DVSK( $\alpha$ MePhe)LDSRAA<br>K(O2Oc- $\gamma$ E-O2Oc- $\gamma$ E-<br>C18diacid)20D( $\alpha$ MePh<br>e)VQ(Aib)IANT-amide     | 264 | C18diacid | $\gamma$ E-<br>(O2Oc)-<br>$\gamma$ E-<br>(O2Oc) | 20 | Amide | 2Aib, 3H, 5S,<br>6 $\alpha$ MePhe,<br>10V,<br>13 $\alpha$ MePhe,<br>18A, 20K,<br>22 $\alpha$ MePhe,<br>25Aib, 26I,<br>27A |
| <b>Peptide 261</b> | H(Aib)HGS( $\alpha$ MePhe)TS<br>DVSK( $\alpha$ MePhe)LDSRAA<br>K((PEG)4- $\gamma$ E-<br>C18diacid)20D( $\alpha$ MePh<br>e)VQ(Aib)IANT-amide                    | 265 | C18diacid | $\gamma$ E-<br>(PEG)4                           | 20 | Amide | 2Aib, 3H, 5S,<br>6 $\alpha$ MePhe,<br>10V,<br>13 $\alpha$ MePhe,<br>18A, 20K,<br>22 $\alpha$ MePhe,<br>25Aib, 26I,<br>27A |
| <b>Peptide 262</b> | H(Aib)HGS( $\alpha$ MePhe)TS<br>DVSK( $\alpha$ MePhe)LDSRAA<br>K(O2Oc- $\gamma$ E-<br>C18diacid)20D( $\alpha$ MePh<br>e)VQ(Aib)IANT-amide                      | 266 | C18diacid | $\gamma$ E-<br>(O2Oc)                           | 20 | Amide | 2Aib, 3H, 5S,<br>6 $\alpha$ MePhe,<br>10V,<br>13 $\alpha$ MePhe,<br>18A, 20K,<br>22 $\alpha$ MePhe,<br>25Aib, 26I,<br>27A |
| <b>Peptide 263</b> | H(Aib)HGS( $\alpha$ MePhe)TS<br>DVSK( $\alpha$ MePhe)LDSRAA<br>K((PEG)4- $\gamma$ E- $\gamma$ E-<br>C18diacid)20D( $\alpha$ MePh<br>e)VQ(Aib)IANT-amide        | 267 | C18diacid | $\gamma$ E- $\gamma$ E-<br>(PEG)4               | 20 | Amide | 2Aib, 3H, 5S,<br>6 $\alpha$ MePhe,<br>10V,<br>13 $\alpha$ MePhe,<br>18A, 20K,<br>22 $\alpha$ MePhe,<br>25Aib, 26I,<br>27A |
| <b>Peptide 264</b> | H(Aib)HGS( $\alpha$ MePhe)TS<br>DVSK( $\alpha$ MePhe)LDSRAA<br>K((PEG)2-(PEG)2- $\gamma$ E- $\gamma$ E-<br>C20diacid)20D( $\alpha$ MePh<br>e)VQ(Aib)IANT-amide | 268 | C20diacid | $\gamma$ E- $\gamma$ E-<br>(PEG)2-<br>(PEG)2    | 20 | Amide | 2Aib, 3H, 5S,<br>6 $\alpha$ MePhe,<br>10V,<br>13 $\alpha$ MePhe,<br>18A, 20K,<br>22 $\alpha$ MePhe,<br>25Aib, 26I,<br>27A |
| <b>Peptide 265</b> | H(Aib)HGS( $\alpha$ MePhe)TS<br>DVSK( $\alpha$ MePhe)LDSRAA<br>K(O2Oc- $\gamma$ E-O2Oc-<br>C20diacid)20D( $\alpha$ MePh<br>e)VQ(Aib)IANT-amide                 | 269 | C20diacid | (O2Oc)-<br>$\gamma$ E-<br>(O2Oc)                | 20 | Amide | 2Aib, 3H, 5S,<br>6 $\alpha$ MePhe,<br>10V,<br>13 $\alpha$ MePhe,<br>18A, 20K,<br>22 $\alpha$ MePhe,                       |

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|                    |                                                                                                                                             |     |           |                                      |    |       |                                                                                                      |
|--------------------|---------------------------------------------------------------------------------------------------------------------------------------------|-----|-----------|--------------------------------------|----|-------|------------------------------------------------------------------------------------------------------|
|                    |                                                                                                                                             |     |           |                                      |    |       | 25Aib, 26I, 27A                                                                                      |
| <b>Peptide 266</b> | H(Aib)HGS( $\alpha$ MePhe)TS DVSK( $\alpha$ MePhe)LDSRAAK(O2Oc- $\gamma$ E-O2Oc- $\gamma$ E-C20diacid)20D( $\alpha$ MePhe)VQ(Aib)IANT-amide | 270 | C20diacid | $\gamma$ E-(O2Oc)- $\gamma$ E-(O2Oc) | 20 | Amide | 2Aib, 3H, 5S, 6 $\alpha$ MePhe, 10V, 13 $\alpha$ MePhe, 18A, 20K, 22 $\alpha$ MePhe, 25Aib, 26I, 27A |
| <b>Peptide 267</b> | H(Aib)HGS( $\alpha$ MePhe)TS DVSK( $\alpha$ MePhe)LDSRAAK((PEG)4- $\gamma$ E-C20diacid)20D( $\alpha$ MePhe)VQ(Aib)IANT-amide                | 271 | C20diacid | $\gamma$ E-(PEG)4                    | 20 | Amide | 2Aib, 3H, 5S, 6 $\alpha$ MePhe, 10V, 13 $\alpha$ MePhe, 18A, 20K, 22 $\alpha$ MePhe, 25Aib, 26I, 27A |
| <b>Peptide 268</b> | H(Aib)HGS( $\alpha$ MePhe)TS DVSK( $\alpha$ MePhe)LDSRAAK(O2Oc- $\gamma$ E-C20diacid)20D( $\alpha$ MePhe)VQ(Aib)IANT-amide                  | 272 | C20diacid | $\gamma$ E-(O2Oc)                    | 20 | Amide | 2Aib, 3H, 5S, 6 $\alpha$ MePhe, 10V, 13 $\alpha$ MePhe, 18A, 20K, 22 $\alpha$ MePhe, 25Aib, 26I, 27A |
| <b>Peptide 269</b> | H(Aib)HGS( $\alpha$ MePhe)TS DVSK( $\alpha$ MePhe)LDSRAAK((PEG)4- $\gamma$ E- $\gamma$ E-C20diacid)20D( $\alpha$ MePhe)VQ(Aib)IANT-amide    | 273 | C20diacid | $\gamma$ E- $\gamma$ E-(PEG)4        | 20 | Amide | 2Aib, 3H, 5S, 6 $\alpha$ MePhe, 10V, 13 $\alpha$ MePhe, 18A, 20K, 22 $\alpha$ MePhe, 25Aib, 26I, 27A |
| <b>Peptide 270</b> | H(Aib)HGS( $\alpha$ MePhe)TS DVSK( $\alpha$ MePhe)LDSRAAK( $\gamma$ E- $\gamma$ E-C18diacid)20D( $\alpha$ MePhe)VQ(Aib)IANT-amide           | 274 | C18diacid | $\gamma$ E- $\gamma$ E               | 20 | Amide | 2Aib, 3H, 5S, 6 $\alpha$ MePhe, 10V, 13 $\alpha$ MePhe, 18A, 20K, 22 $\alpha$ MePhe, 25Aib, 26I, 27A |
| <b>Peptide 271</b> | H(Aib)HGS( $\alpha$ MePhe)TS DVSK( $\alpha$ MePhe)LDSRAAK( $\gamma$ E-C18diacid)20D( $\alpha$ MePhe)VQ(Aib)IANT-amide                       | 275 | C18diacid | $\gamma$ E                           | 20 | Amide | 2Aib, 3H, 5S, 6 $\alpha$ MePhe, 10V, 13 $\alpha$ MePhe, 18A, 20K,                                    |

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|                        |                                                                                                          |     |           |                   |    |       |                                                                                                |
|------------------------|----------------------------------------------------------------------------------------------------------|-----|-----------|-------------------|----|-------|------------------------------------------------------------------------------------------------|
|                        |                                                                                                          |     |           |                   |    |       | 22αMePhe,<br>25Aib, 26I,<br>27A                                                                |
| <b>Peptide<br/>272</b> | H(Aib)HGS(αMePhe)TS<br>DVSK(αMePhe)LDSRAA<br>K(O2Oc-O2Oc-<br>C18diacid)20D(αMePh<br>e)VQ(Aib)IANT-amide  | 276 | C18diacid | (O2Oc)-<br>(O2Oc) | 20 | Amide | 2Aib, 3H, 5S,<br>6αMePhe,<br>10V,<br>13αMePhe,<br>18A, 20K,<br>22αMePhe,<br>25Aib, 26I,<br>27A |
| <b>Peptide<br/>273</b> | H(Aib)HGS(αMePhe)TS<br>DVSK(αMePhe)LDSRAA<br>K(O2Oc-<br>C18diacid)20D(αMePh<br>e)VQ(Aib)IANT-amide       | 277 | C18diacid | (O2Oc)            | 20 | Amide | 2Aib, 3H, 5S,<br>6αMePhe,<br>10V,<br>13αMePhe,<br>18A, 20K,<br>22αMePhe,<br>25Aib, 26I,<br>27A |
| <b>Peptide<br/>274</b> | H(Aib)HGS(αMePhe)TS<br>DVSK(αMePhe)LDSRAA<br>K(O2Oc-γE-γE-<br>C18diacid)20D(αMePh<br>e)VQ(Aib)IANT-amide | 278 | C18diacid | γE-γE-<br>(O2Oc)  | 20 | Amide | 2Aib, 3H, 5S,<br>6αMePhe,<br>10V,<br>13αMePhe,<br>18A, 20K,<br>22αMePhe,<br>25Aib, 26I,<br>27A |
| <b>Peptide<br/>275</b> | H(Aib)HGS(αMePhe)TS<br>DVSK(αMePhe)LDSRAA<br>K(γE-γE-<br>C20diacid)20D(αMePh<br>e)VQ(Aib)IANT-amide      | 279 | C20diacid | γE-γE             | 20 | Amide | 2Aib, 3H, 5S,<br>6αMePhe,<br>10V,<br>13αMePhe,<br>18A, 20K,<br>22αMePhe,<br>25Aib, 26I,<br>27A |
| <b>Peptide<br/>276</b> | H(Aib)HGS(αMePhe)TS<br>DVSK(αMePhe)LDSRAA<br>K(γE-<br>C20diacid)20D(αMePh<br>e)VQ(Aib)IANT-amide         | 280 | C20diacid | γE                | 20 | Amide | 2Aib, 3H, 5S,<br>6αMePhe,<br>10V,<br>13αMePhe,<br>18A, 20K,<br>22αMePhe,<br>25Aib, 26I,<br>27A |
| <b>Peptide<br/>277</b> | H(Aib)HGS(αMePhe)TS<br>DVSK(αMePhe)LDSRAA<br>K(O2Oc-O2Oc-                                                | 281 | C20diacid | (O2Oc)-<br>(O2Oc) | 20 | Amide | 2Aib, 3H, 5S,<br>6αMePhe,<br>10V,<br>13αMePhe,                                                 |

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|                    |                                                                                                                                        |     |           |                                      |    |       |                                                                                                      |
|--------------------|----------------------------------------------------------------------------------------------------------------------------------------|-----|-----------|--------------------------------------|----|-------|------------------------------------------------------------------------------------------------------|
|                    | C20diacid)20D( $\alpha$ MePhe)VQ(Aib)IANT-amide                                                                                        |     |           |                                      |    |       | 18A, 20K, 22 $\alpha$ MePhe, 25Aib, 26I, 27A                                                         |
| <b>Peptide 278</b> | H(Aib)HGS( $\alpha$ MePhe)TS DVSK( $\alpha$ MePhe)LDSRAAK(O2Oc-C20diacid)20D( $\alpha$ MePhe)VQ(Aib)IANT-amide                         | 282 | C20diacid | (O2Oc)                               | 20 | Amide | 2Aib, 3H, 5S, 6 $\alpha$ MePhe, 10V, 13 $\alpha$ MePhe, 18A, 20K, 22 $\alpha$ MePhe, 25Aib, 26I, 27A |
| <b>Peptide 279</b> | H(Aib)HGS( $\alpha$ MePhe)TS DVSK( $\alpha$ MePhe)LDSRAAK(O2Oc- $\gamma$ E- $\gamma$ E-C20diacid)20D( $\alpha$ MePhe)VQ(Aib)IANT-amide | 283 | C20diacid | $\gamma$ E- $\gamma$ E-(O2Oc)        | 20 | Amide | 2Aib, 3H, 5S, 6 $\alpha$ MePhe, 10V, 13 $\alpha$ MePhe, 18A, 20K, 22 $\alpha$ MePhe, 25Aib, 26I, 27A |
| <b>Peptide 280</b> | H(Aib)HGS( $\alpha$ MePhe)TS DVSK( $\alpha$ MePhe)LDSRAAK(O2Oc-O2Oc- $\gamma$ E-C20diacid)20D( $\alpha$ MePhe)VQ(Aib)IANT-amide        | 284 | C20diacid | $\gamma$ E-(O2Oc)-(O2Oc)             | 20 | Amide | 2Aib, 3H, 5S, 6 $\alpha$ MePhe, 10V, 13 $\alpha$ MePhe, 18A, 20K, 22 $\alpha$ MePhe, 25Aib, 26I, 27A |
| <b>Peptide 281</b> | HSHGS( $\alpha$ MePhe)TSDVSK( $\alpha$ MePhe)LDSRAAK(O2Oc-O2Oc- $\gamma$ E- $\gamma$ E-C20diacid)20D( $\alpha$ MePhe)VQ(Aib)IANT-amide | 285 | C20diacid | $\gamma$ E- $\gamma$ E-(O2Oc)-(O2Oc) | 20 | Amide | 3H, 5S, 6 $\alpha$ MePhe, 10V, 13 $\alpha$ MePhe, 18A, 20K, 22 $\alpha$ MePhe, 25Aib, 26I, 27A       |
| <b>Peptide 282</b> | H(Aib)HGSFTSDVSK( $\alpha$ MePhe)LDSRAAK(O2Oc-O2Oc- $\gamma$ E- $\gamma$ E-C20diacid)20D( $\alpha$ MePhe)VQ(Aib)IANT-amide             | 286 | C20diacid | $\gamma$ E- $\gamma$ E-(O2Oc)-(O2Oc) | 20 | Amide | 2Aib, 3H, 5S, 10V, 13 $\alpha$ MePhe, 18A, 20K, 22 $\alpha$ MePhe, 25Aib, 26I, 27A                   |
| <b>Peptide 283</b> | H(Aib)HGS( $\alpha$ MePhe)TS DVSKYLDSTRAAK(O2Oc-O2Oc- $\gamma$ E- $\gamma$ E-                                                          | 287 | C20diacid | $\gamma$ E- $\gamma$ E-(O2Oc)-(O2Oc) | 20 | Amide | 2Aib, 3H, 5S, 6 $\alpha$ MePhe, 10V, 18A, 20K,                                                       |

|                    |                                                                                                                            |     |           |                                      |    |       |                                                                                                |
|--------------------|----------------------------------------------------------------------------------------------------------------------------|-----|-----------|--------------------------------------|----|-------|------------------------------------------------------------------------------------------------|
|                    | C20diacid)20D( $\alpha$ MePhe)VQ(Aib)IANT-amide                                                                            |     |           |                                      |    |       | 22 $\alpha$ MePhe, 25Aib, 26I, 27A                                                             |
| <b>Peptide 284</b> | HSHGS( $\alpha$ MePhe)TSDVSK( $\alpha$ MePhe)LDSRAAK(O2Oc-O2Oc- $\gamma$ E-C18diacid)20D( $\alpha$ MePhe)VQ(Aib)IANT-amide | 288 | C18diacid | $\gamma$ E-(O2Oc)-(O2Oc)             | 20 | Amide | 3H, 5S, 6 $\alpha$ MePhe, 10V, 13 $\alpha$ MePhe, 18A, 20K, 22 $\alpha$ MePhe, 25Aib, 26I, 27A |
| <b>Peptide 285</b> | H(Aib)HGSFTSDVSK( $\alpha$ MePhe)LDSRAAK(O2Oc-O2Oc- $\gamma$ E-C18diacid)20D( $\alpha$ MePhe)VQ(Aib)IANT-amide             | 289 | C18diacid | $\gamma$ E-(O2Oc)-(O2Oc)             | 20 | Amide | 2Aib, 3H, 5S, 10V, 13 $\alpha$ MePhe, 18A, 20K, 22 $\alpha$ MePhe, 25Aib, 26I, 27A             |
| <b>Peptide 286</b> | H(Aib)HGS( $\alpha$ MePhe)TSDVSKYLDSRAAK(O2Oc-O2Oc- $\gamma$ E-C18diacid)20D( $\alpha$ MePhe)VQ(Aib)IANT-amide             | 290 | C18diacid | $\gamma$ E-(O2Oc)-(O2Oc)             | 20 | Amide | 2Aib, 3H, 5S, 6 $\alpha$ MePhe, 10V, 18A, 20K, 22 $\alpha$ MePhe, 25Aib, 26I, 27A              |
| <b>Peptide 287</b> | H(Aib)HGS( $\alpha$ MePhe)TSDVSK( $\alpha$ MePhe)LDSRAAK(O2Oc-O2Oc- $\gamma$ E-C18diacid)20DFVQ(Aib)IANT-amide             | 291 | C18diacid | $\gamma$ E-(O2Oc)-(O2Oc)             | 20 | Amide | 2Aib, 3H, 5S, 6 $\alpha$ MePhe, 10V, 13 $\alpha$ MePhe, 18A, 20K, 25Aib, 26I, 27A              |
| <b>Peptide 288</b> | H(Aib)HGS( $\alpha$ MePhe)TSDVSK( $\alpha$ MePhe)LDSRAAK(O2Oc-O2Oc- $\gamma$ E-C18diacid)20D( $\alpha$ MePhe)VQWIANT-amide | 292 | C18diacid | $\gamma$ E-(O2Oc)-(O2Oc)             | 20 | Amide | 2Aib, 3H, 5S, 6 $\alpha$ MePhe, 10V, 13 $\alpha$ MePhe, 18A, 20K, 22 $\alpha$ MePhe, 26I, 27A  |
| <b>Peptide 289</b> | H(Aib)HGS( $\alpha$ MePhe)TSDVSKYLDSRAAK(O2Oc-O2Oc- $\gamma$ E- $\gamma$ E-C20diacid)20DFVQWIA NT-amide                    | 293 | C20diacid | $\gamma$ E- $\gamma$ E-(O2Oc)-(O2Oc) | 20 | Amide | 2Aib, 3H, 5S, 6 $\alpha$ MePhe, 10V, 18A, 20K, 26I, 27A                                        |
| <b>Peptide 290</b> | H(Aib)HGSFTSDVSK( $\alpha$ MePhe)LDSRAAK(O2Oc-O2Oc- $\gamma$ E- $\gamma$ E-                                                | 294 | C20diacid | $\gamma$ E- $\gamma$ E-(O2Oc)-(O2Oc) | 20 | Amide | 2Aib, 3H, 5S, 10V, 13 $\alpha$ MePhe,                                                          |

|                        |                                                                                                            |     |           |                             |    |       |                                                                                                     |
|------------------------|------------------------------------------------------------------------------------------------------------|-----|-----------|-----------------------------|----|-------|-----------------------------------------------------------------------------------------------------|
|                        | C20diacid)20DFVQWIA<br>NT-amide                                                                            |     |           |                             |    |       | 18A, 20K,<br>26I, 27A                                                                               |
| <b>Peptide<br/>291</b> | H(Aib)HGSFTSDVSKYLD<br>SRAAK(O2Oc-O2Oc-γE-<br>γE-<br>C20diacid)20D(αMePh<br>e)VQWIA NT-amide               | 295 | C20diacid | γE-γE-<br>(O2Oc)-<br>(O2Oc) | 20 | Amide | 2Aib, 3H, 5S,<br>10V, 18A,<br>20K,<br>22αMePhe,<br>26I, 27A                                         |
| <b>Peptide<br/>292</b> | H(Aib)HGS(αMePhe)TS<br>DVSKYLD SRAAK(O2Oc-<br>O2Oc-γE-<br>C18diacid)20DFVQWIA<br>NT-amide                  | 296 | C18diacid | γE-<br>(O2Oc)-<br>(O2Oc)    | 20 | Amide | 2Aib, 3H, 5S,<br>6αMePhe,<br>10V, 18A,<br>20K, 26I, 27A                                             |
| <b>Peptide<br/>293</b> | H(Aib)HGSFTSDVSK(αM<br>ePhe)LDSRAAK(O2Oc-<br>O2Oc-γE-<br>C18diacid)20DFVQWIA<br>NT-amide                   | 297 | C18diacid | γE-<br>(O2Oc)-<br>(O2Oc)    | 20 | Amide | 2Aib, 3H, 5S,<br>10V,<br>13αMePhe,<br>18A, 20K,<br>26I, 27A                                         |
| <b>Peptide<br/>294</b> | H(Aib)HGSFTSDVSKYLD<br>SRAAK(O2Oc-O2Oc-γE-<br>C18diacid)20D(αMePh<br>e)VQWIA NT-amide                      | 298 | C18diacid | γE-<br>(O2Oc)-<br>(O2Oc)    | 20 | Amide | 2Aib, 3H, 5S,<br>10V, 18A,<br>20K,<br>22αMePhe,<br>26I, 27A                                         |
| <b>Peptide<br/>295</b> | H(Aib)HGS(αMePhe)TS<br>DVSK(Aib)LDSRAAK(O2<br>Oc-O2Oc-γE-γE-<br>C20diacid)20D(αMePh<br>e)VQ(Aib)IANT-amide | 299 | C20diacid | γE-γE-<br>(O2Oc)-<br>(O2Oc) | 20 | Amide | 2Aib, 3H, 5S,<br>6αMePhe,<br>10V, 13Aib,<br>18A, 20K,<br>22αMePhe,<br>25Aib, 26I,<br>27A            |
| <b>Peptide<br/>296</b> | H(Aib)HGS(αMePhe)TS<br>DVSK(Aib)LDSRAAK(O2<br>Oc-O2Oc-γE-<br>C18diacid)20D(αMePh<br>e)VQ(Aib)IANT-amide    | 300 | C18diacid | γE-<br>(O2Oc)-<br>(O2Oc)    | 20 | Amide | 2Aib, 3H, 5S,<br>6αMePhe,<br>10V, 13Aib,<br>18A, 20K,<br>22αMePhe,<br>25Aib, 26I,<br>27A            |
| <b>Peptide<br/>297</b> | H(Aib)HGS(αMePhe)TS<br>DVSR(αMePhe)LDSRAA<br>K(O2Oc-O2Oc-γE-<br>C18diacid)20D(αMePh<br>e)VQ(Aib)IANT-amide | 301 | C18diacid | γE-<br>(O2Oc)-<br>(O2Oc)    | 20 | Amide | 2Aib, 3H, 5S,<br>6αMePhe,<br>10V, 12R,<br>13αMePhe,<br>18A, 20K,<br>22αMePhe,<br>25Aib, 26I,<br>27A |
| <b>Peptide<br/>298</b> | H(Aib)HGS(αMePhe)TS<br>DVSR(αMePhe)LDSRAA<br>K(O2Oc-O2Oc-γE-γE-                                            | 302 | C20diacid | γE-γE-<br>(O2Oc)-<br>(O2Oc) | 20 | Amide | 2Aib, 3H, 5S,<br>6αMePhe,<br>10V, 12R,                                                              |

|                    |                                                                                                                                             |     |           |                                      |    |       |                                                                                                                     |
|--------------------|---------------------------------------------------------------------------------------------------------------------------------------------|-----|-----------|--------------------------------------|----|-------|---------------------------------------------------------------------------------------------------------------------|
|                    | C20diacid)20D( $\alpha$ MePhe)VQ(Aib)IAET-amide                                                                                             |     |           |                                      |    |       | 13 $\alpha$ MePhe, 18A, 20K, 22 $\alpha$ MePhe, 25Aib, 26I, 27A                                                     |
| <b>Peptide 299</b> | H(Aib)HGS( $\alpha$ MePhe)TS DVSK( $\alpha$ MePhe)LDSRAAK(O2Oc-O2Oc- $\gamma$ E- $\gamma$ E-C20diacid)20D( $\alpha$ MePhe)VQ(Aib)IAET-amide | 303 | C20diacid | $\gamma$ E- $\gamma$ E-(O2Oc)-(O2Oc) | 20 | Amide | 2Aib, 3H, 5S, 6 $\alpha$ MePhe, 10V, 13 $\alpha$ MePhe, 18A, 20K, 22 $\alpha$ MePhe, 25Aib, 26I, 27A, 28E           |
| <b>Peptide 300</b> | H(Aib)HGS( $\alpha$ MePhe)TS DVSK( $\alpha$ MePhe)LDSRAAK(O2Oc-O2Oc- $\gamma$ E-C18diacid)20D( $\alpha$ MePhe)VQ(Aib)IAET-amide             | 304 | C18diacid | $\gamma$ E-(O2Oc)-(O2Oc)             | 20 | Amide | 2Aib, 3H, 5S, 6 $\alpha$ MePhe, 10V, 13 $\alpha$ MePhe, 18A, 20K, 22 $\alpha$ MePhe, 25Aib, 26I, 27A, 28E           |
| <b>Peptide 301</b> | H(Aib)HGS( $\alpha$ MePhe)TS DVSK( $\alpha$ MePhe)LDSRAAK(O2Oc-O2Oc- $\gamma$ E-C18diacid)20D( $\alpha$ MePhe)IA(Aib)IAET-amide             | 305 | C18diacid | $\gamma$ E-(O2Oc)-(O2Oc)             | 20 | Amide | 2Aib, 3H, 5S, 6 $\alpha$ MePhe, 10V, 13 $\alpha$ MePhe, 18A, 20K, 22 $\alpha$ MePhe, 23I, 24A, 25Aib, 26I, 27A, 28E |
| <b>Peptide 302</b> | H(Aib)HGS( $\alpha$ MePhe)TS DVSK( $\alpha$ MePhe)LDSRAAK(O2Oc-O2Oc- $\gamma$ E- $\gamma$ E-C20diacid)20D( $\alpha$ MePhe)IA(Aib)IAET-amide | 306 | C20diacid | $\gamma$ E- $\gamma$ E-(O2Oc)-(O2Oc) | 20 | Amide | 2Aib, 3H, 5S, 6 $\alpha$ MePhe, 10V, 13 $\alpha$ MePhe, 18A, 20K, 22 $\alpha$ MePhe, 23I, 24A, 25Aib, 26I, 27A, 28E |
| <b>Peptide 303</b> | H(Aib)HGS( $\alpha$ MePhe)TS DVSK( $\alpha$ MePhe)LDSRAAK(O2Oc-O2Oc- $\gamma$ E-C18diacid)20D( $\alpha$ MePhe)VQ(Aib)IAET-acid              | 307 | C18diacid | $\gamma$ E-(O2Oc)-(O2Oc)             | 20 | Acid  | 2Aib, 3H, 5S, 6 $\alpha$ MePhe, 10V, 13 $\alpha$ MePhe, 18A, 20K, 22 $\alpha$ MePhe, 25Aib, 26I, 27A                |

|                    |                                                                                                                                                           |     |           |                                              |    |       |                                                                                                                           |
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| <b>Peptide 304</b> | H(Aib)HGS( $\alpha$ MePhe)TS<br>DVSK( $\alpha$ MePhe)LDSRAA<br>K(O2Oc-O2Oc- $\gamma$ E- $\gamma$ E-<br>C20diacid)20D( $\alpha$ MePh<br>e)VQ(Aib)IANT-acid | 308 | C20diacid | $\gamma$ E- $\gamma$ E-<br>(O2Oc)-<br>(O2Oc) | 20 | Acid  | 2Aib, 3H, 5S,<br>6 $\alpha$ MePhe,<br>10V,<br>13 $\alpha$ MePhe,<br>18A, 20K,<br>22 $\alpha$ MePhe,<br>25Aib, 26I,<br>27A |
| <b>Peptide 305</b> | H(Aib)HGTFTSDVSK( $\alpha$<br>MePhe)LDSRAAK(O2Oc<br>-O2Oc- $\gamma$ E- $\gamma$ E-<br>C20diacid)20DFVQWIA<br>NT-amide                                     | 309 | C20diacid | $\gamma$ E- $\gamma$ E-<br>(O2Oc)-<br>(O2Oc) | 20 | Amide | 2Aib, 3H,<br>10V,<br>13 $\alpha$ MePhe,<br>18A, 20K,<br>26I, 27A                                                          |
| <b>Peptide 306</b> | H(Aib)QGTFTSDVSK( $\alpha$<br>MePhe)LDSRAAK(O2Oc<br>-O2Oc- $\gamma$ E-<br>C18diacid)20DFVEWIA<br>NT-amide                                                 | 310 | C18diacid | $\gamma$ E-<br>(O2Oc)-<br>(O2Oc)             | 20 | Amide | 2Aib, 10V,<br>13 $\alpha$ MePhe,<br>18A, 20K,<br>24E, 26I, 27A                                                            |
| <b>Peptide 307</b> | H(Aib)QGTFTSDVSK( $\alpha$<br>MePhe)LDSRAAK(O2Oc<br>-O2Oc- $\gamma$ E-<br>C18diacid)20DFVRWIA<br>NT-amide                                                 | 311 | C18diacid | $\gamma$ E-<br>(O2Oc)-<br>(O2Oc)             | 20 | Amide | 2Aib, 10V,<br>13 $\alpha$ MePhe,<br>18A, 20K,<br>24R, 26I,<br>27A                                                         |
| <b>Peptide 308</b> | H(Aib)QGTFTSDVSK( $\alpha$<br>MePhe)LDTRAAK(O2Oc<br>-O2Oc- $\gamma$ E-<br>C18diacid)20DFVQWIA<br>NT-amide                                                 | 312 | C18diacid | $\gamma$ E-<br>(O2Oc)-<br>(O2Oc)             | 20 | Amide | 2Aib, 10V,<br>13 $\alpha$ MePhe,<br>16T, 18A,<br>20K, 26I, 27A                                                            |
| <b>Peptide 309</b> | H(Aib)QGTFTSDVSK( $\alpha$<br>MePhe)LDERRAAK(O2Oc<br>-O2Oc- $\gamma$ E-<br>C18diacid)20DFVQWIA<br>NT-amide                                                | 313 | C18diacid | $\gamma$ E-<br>(O2Oc)-<br>(O2Oc)             | 20 | Amide | 2Aib, 10V,<br>13 $\alpha$ MePhe,<br>16E, 18A,<br>20K, 26I, 27A                                                            |
| <b>Peptide 310</b> | H(Aib)QGTFTSDVSK( $\alpha$<br>MePhe)LDSRAAK(O2Oc<br>-O2Oc- $\gamma$ E-<br>C18diacid)20DFVQWLE<br>AGG-amide                                                | 314 | C18diacid | $\gamma$ E-<br>(O2Oc)-<br>(O2Oc)             | 20 | Amide | 2Aib, 10V,<br>13 $\alpha$ MePhe,<br>18A, 20K,<br>27E, 28A,<br>29G, 30G                                                    |
| <b>Peptide 311</b> | H(Aib)QGTFTSDVSK( $\alpha$<br>MePhe)LDSRAAK(O2Oc<br>-O2Oc- $\gamma$ E-<br>C18diacid)20DFVQWLV<br>ET-amide                                                 | 315 | C18diacid | $\gamma$ E-<br>(O2Oc)-<br>(O2Oc)             | 20 | Amide | 2Aib, 10V,<br>13 $\alpha$ MePhe,<br>18A, 20K,<br>27V, 28E                                                                 |
| <b>Peptide 312</b> | H(Aib)QGTFTSDYSK( $\alpha$ M<br>ePhe)LDSRRRAK(O2Oc-<br>O2Oc- $\gamma$ E-                                                                                  | 316 | C18diacid | $\gamma$ E-<br>(O2Oc)-<br>(O2Oc)             | 20 | Amide | 2Aib, 10V,<br>13 $\alpha$ MePhe,<br>18A, 20K,<br>27V,                                                                     |

|                        |                                                                                                                                                |     |           |                                  |    |       |                                                                            |
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|                        | C18diacid)20DFVQWLV<br>((PEG)4)-amide                                                                                                          |     |           |                                  |    |       | 28(PEG)4,<br>des29                                                         |
| <b>Peptide<br/>313</b> | H(Aib)QGTFTSDVSK( $\alpha$<br>MePhe)LDSR(Aib)AK(O<br>2Oc-O2Oc- $\gamma$ E-<br>C18diacid)20DFVQWLL<br>NT-acid                                   | 317 | C18diacid | $\gamma$ E-<br>(O2Oc)-<br>(O2Oc) | 20 | Acid  | 2Aib, 10V,<br>13 $\alpha$ MePhe,<br>18Aib, 20K,<br>27L                     |
| <b>Peptide<br/>314</b> | H(Aib)QGTFTSDVSK( $\alpha$<br>MePhe)LDSR(Aib)AK(O<br>2Oc-O2Oc- $\gamma$ E-<br>C18diacid)20DFVQ(Aib)<br>LVAT-amide                              | 318 | C18diacid | $\gamma$ E-<br>(O2Oc)-<br>(O2Oc) | 20 | Amide | 2Aib, 10V,<br>13 $\alpha$ MePhe,<br>18Aib, 20K,<br>25Aib, 27V,<br>28A      |
| <b>Peptide<br/>315</b> | H(Aib)QGTFTSDVSK( $\alpha$<br>MePhe)LDSRAAK(O2Oc<br>-O2Oc- $\gamma$ E-<br>C18diacid)20DFVQ(Aib)<br>LVAT-amide                                  | 319 | C18diacid | $\gamma$ E-<br>(O2Oc)-<br>(O2Oc) | 20 | Amide | 2Aib, 10V,<br>13 $\alpha$ MePhe,<br>18A, 20K,<br>25Aib, 27V,<br>28A        |
| <b>Peptide<br/>316</b> | HSQGTFTSDYSK( $\alpha$ MeP<br>he)LEEEAVK(O2Oc-<br>O2Oc- $\gamma$ E-<br>stearOOH)20LFIRWLM<br>NT-amide                                          | 320 | C18diacid | $\gamma$ E-<br>(O2Oc)-<br>(O2Oc) | 20 | Amide | 13 $\alpha$ MeF,<br>15E, 16E,<br>17E, 18A,<br>19V, 20K,<br>21L, 23I, 24R   |
| <b>Peptide<br/>317</b> | H(Aib)QGTFTSDVSK( $\alpha$<br>MePhe)LD(Aib)RAAK(O<br>2Oc-O2Oc- $\gamma$ E-<br>C18diacid)20DFVQWIA<br>NT-amide                                  | 321 | C18diacid | $\gamma$ E-<br>(O2Oc)-<br>(O2Oc) | 20 | Amide | 2Aib, 10V,<br>13 $\alpha$ MePhe,<br>16Aib, 18A,<br>20K, 25Aib,<br>26I, 27A |
| <b>Peptide<br/>318</b> | H( $\alpha$ MeSer)QGTFTSDVS<br>K( $\alpha$ MePhe)LDSRAAK(O<br>2Oc-O2Oc- $\gamma$ E-<br>C18diacid)20DFVQWIA<br>NT-amide                         | 322 | C18diacid | $\gamma$ E-<br>(O2Oc)-<br>(O2Oc) | 20 | Amide | 2 $\alpha$ MeSer,<br>10V,<br>13 $\alpha$ MePhe,<br>18A, 20K,<br>26I, 27A   |
| <b>Peptide<br/>319</b> | HS( $\alpha$ MeGln)GTFTSDVS<br>K( $\alpha$ MePhe)LDSRAAK(O<br>2Oc-O2Oc- $\gamma$ E-<br>C18diacid)20DFVQWIA<br>NT-amide                         | 323 | C18diacid | $\gamma$ E-<br>(O2Oc)-<br>(O2Oc) | 20 | Amide | 3 $\alpha$ MeGln,<br>10V,<br>13 $\alpha$ MePhe,<br>18A, 20K,<br>26I, 27A   |
| <b>Peptide<br/>320</b> | H(DSer)QGTFTSDVSK( $\alpha$<br>MePhe)LDSRAAK(O2Oc<br>-O2Oc- $\gamma$ E-<br>C18diacid)20DFVQWIA<br>NT-amide                                     | 324 | C18diacid | $\gamma$ E-<br>(O2Oc)-<br>(O2Oc) | 20 | Amide | 2dS, 10V,<br>13 $\alpha$ MePhe,<br>18A, 20K,<br>26I, 27A                   |
| <b>Peptide<br/>321</b> | H(Aib)QGS( $\alpha$ MePhe)TS<br>DVSK( $\alpha$ MePhe)LDSRAA<br>K(O2Oc-O2Oc- $\gamma$ E-<br>C18diacid)20D( $\alpha$ MePh<br>e)VQ(Aib)IANT-amide | 325 | C18diacid | $\gamma$ E-<br>(O2Oc)-<br>(O2Oc) | 20 | Amide | 2Aib, 5S,<br>6 $\alpha$ MePhe,<br>10V,<br>13 $\alpha$ MePhe,<br>18A, 20K,  |

|                        |                                                                                                                          |     |           |                          |    |       |                                                                                                             |
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|                        |                                                                                                                          |     |           |                          |    |       | 22αMePhe,<br>25Aib, 26I,<br>27A                                                                             |
| <b>Peptide<br/>322</b> | H(Aib)QGS(αMePhe)TS<br>DVSK(αMePhe)LDSRAA<br>K(O2Oc-O2Oc-γE-γE-<br>C20diacid)20D(αMePh<br>e)VQ(Aib)IANT-amide            | 326 | C20diacid | γE-<br>(O2Oc)-<br>(O2Oc) | 20 | Amide | 2Aib, 5S,<br>6αMePhe,<br>10V,<br>13αMePhe,<br>18A, 20K,<br>22αMePhe,<br>25Aib, 26I,<br>27A                  |
| <b>Peptide<br/>323</b> | HS(αMeGln)GS(αMePh<br>e)TSDVSK(αMePhe)LDS<br>RAAK(O2Oc-O2Oc-γE-<br>C18diacid)20D(αMePh<br>e)VQ(Aib)IANT-amide            | 327 | C18diacid | γE-<br>(O2Oc)-<br>(O2Oc) | 20 | Amide | 3αMeGln,<br>5S,<br>6αMePhe,<br>10V,<br>13αMePhe,<br>18A, 20K,<br>22αMePhe,<br>25Aib, 26I,<br>27A            |
| <b>Peptide<br/>324</b> | HS(β-<br>dimethylGln)GS(αMeP<br>he)TSDVSK(αMePhe)LD<br>SRAAK(O2Oc-O2Oc-γE-<br>C18diacid)20D(αMePh<br>e)VQ(Aib)IANT-amide | 328 | C18diacid | γE-<br>(O2Oc)-<br>(O2Oc) | 20 | Amide | 3β-<br>dimethylGln,<br>5S,<br>6αMePhe,<br>10V,<br>13αMePhe,<br>18A, 20K,<br>22αMePhe,<br>25Aib, 26I,<br>27A |
| <b>Peptide<br/>325</b> | HS(N-<br>MeGln)GS(αMePhe)TS<br>DVSK(αMePhe)LDSRAA<br>K(O2Oc-O2Oc-γE-<br>C18diacid)20D(αMePh<br>e)VQ(Aib)IANT-amide       | 329 | C18diacid | γE-<br>(O2Oc)-<br>(O2Oc) | 20 | Amide | 3N-MeGln,<br>5S,<br>6αMePhe,<br>10V,<br>13αMePhe,<br>18A, 20K,<br>22αMePhe,<br>25Aib, 26I,<br>27A           |
| <b>Peptide<br/>326</b> | HS(dGln)GS(αMePhe)T<br>SDVSK(αMePhe)LDSRA<br>AK(O2Oc-O2Oc-γE-<br>C18diacid)20D(αMePh<br>e)VQ(Aib)IANT-amide              | 330 | C18diacid | γE-<br>(O2Oc)-<br>(O2Oc) | 20 | Amide | 3dGln, 5S,<br>6αMePhe,<br>10V,<br>13αMePhe,<br>18A, 20K,<br>22αMePhe,<br>25Aib, 26I,<br>27A                 |

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|                    |                                                                                                                                            |     |           |                          |    |       |                                                                                                              |
|--------------------|--------------------------------------------------------------------------------------------------------------------------------------------|-----|-----------|--------------------------|----|-------|--------------------------------------------------------------------------------------------------------------|
| <b>Peptide 327</b> | H(Acpr)QGS( $\alpha$ MePhe)TSDVSK( $\alpha$ MePhe)LDSRAAK(O2Oc-O2Oc- $\gamma$ E-C18diacid)20D( $\alpha$ MePhe)VQ(Aib)IANT-amide            | 331 | C18diacid | $\gamma$ E-(O2Oc)-(O2Oc) | 20 | Amide | 2Acpr, 5S, 6 $\alpha$ MePhe, 10V, 13 $\alpha$ MePhe, 18A, 20K, 22 $\alpha$ MePhe, 25Aib, 26I, 27A            |
| <b>Peptide 328</b> | H(Acbu)QGS( $\alpha$ MePhe)TSDVSK( $\alpha$ MePhe)LDSRAAK(O2Oc-O2Oc- $\gamma$ E-C18diacid)20D( $\alpha$ MePhe)VQ(Aib)IANT-amide            | 332 | C18diacid | $\gamma$ E-(O2Oc)-(O2Oc) | 20 | Amide | 2Acbu, 5S, 6 $\alpha$ MePhe, 10V, 13 $\alpha$ MePhe, 18A, 20K, 22 $\alpha$ MePhe, 25Aib, 26I, 27A            |
| <b>Peptide 329</b> | H( $\alpha$ MeSer)QGS( $\alpha$ MePhe)TSDVSK( $\alpha$ MePhe)LDSRAAK(O2Oc-O2Oc- $\gamma$ E-C18diacid)20D( $\alpha$ MePhe)VQ(Aib)IANT-amide | 333 | C18diacid | $\gamma$ E-(O2Oc)-(O2Oc) | 20 | Amide | 2 $\alpha$ MeSer, 5S, 6 $\alpha$ MePhe, 10V, 13 $\alpha$ MePhe, 18A, 20K, 22 $\alpha$ MePhe, 25Aib, 26I, 27A |
| <b>Peptide 330</b> | H(dSer)QGS( $\alpha$ MePhe)TSDVSK( $\alpha$ MePhe)LDSRAAK(O2Oc-O2Oc- $\gamma$ E-C18diacid)20D( $\alpha$ MePhe)VQ(Aib)IANT-amide            | 334 | C18diacid | $\gamma$ E-(O2Oc)-(O2Oc) | 20 | Amide | 2dSer, 5S, 6 $\alpha$ MePhe, 10V, 13 $\alpha$ MePhe, 18A, 20K, 22 $\alpha$ MePhe, 25Aib, 26I, 27A            |
| <b>Peptide 331</b> | H(Aib)QGTFTSDVSK( $\alpha$ MePhe)LDSRRRAK(O2Oc-O2Oc- $\gamma$ E-C18diacid)20DFVRWLL E(Aib)G-acid                                           | 335 | C18diacid | $\gamma$ E-(O2Oc)-(O2Oc) | 20 | Acid  | 2Aib, 10V, 13 $\alpha$ MePhe, 20K, 24R, 27L, 28E, 29Aib, 30G                                                 |
| <b>Peptide 332</b> | H(Aib)QGTFTSDVSK( $\alpha$ MePhe)LDSRRRAK(O2Oc-O2Oc- $\gamma$ E-C18diacid)20DFVQWLL E(Aib)G-acid                                           | 336 | C18diacid | $\gamma$ E-(O2Oc)-(O2Oc) | 20 | Acid  | 2Aib, 10V, 13 $\alpha$ MePhe, 20K, 27L, 28E, 29Aib, 30G                                                      |
| <b>Peptide 333</b> | H(Aib)QGTFTSDVSK( $\alpha$ MePhe)LDSRRRAK(O2Oc-O2Oc- $\gamma$ E-                                                                           | 337 | C18diacid | $\gamma$ E-(O2Oc)-(O2Oc) | 20 | Acid  | 2Aib, 10V, 13 $\alpha$ MePhe, 20K, 27L, 28Aib, 30E                                                           |

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|                    |                                                                                                                                 |     |           |                                                                 |    |       |                                                    |
|--------------------|---------------------------------------------------------------------------------------------------------------------------------|-----|-----------|-----------------------------------------------------------------|----|-------|----------------------------------------------------|
|                    | C18diacid)20DFVQWLL(Aib)TE-acid                                                                                                 |     |           |                                                                 |    |       |                                                    |
| <b>Peptide 334</b> | H(Aib)QGTFTSDYSK( $\alpha$ MePhe)LDSRRAK( $\gamma$ E-C18diacid)20DFVQWLA(Aib)E-acid                                             | 338 | C18diacid | $\gamma$ E                                                      | 20 | Acid  | 2Aib, 13 $\alpha$ MePhe, 20K, 27A, 28Aib, 30E      |
| <b>Peptide 335</b> | H(Aib)QGTFTSDYSK( $\alpha$ MePhe)LDSRRAK( $\gamma$ E-C18diacid)20DFVQWLL E(Aib)G-acid                                           | 339 | C18diacid | $\gamma$ E                                                      | 20 | Acid  | 2Aib, 13 $\alpha$ MePhe, 20K, 27L, 28E, 29Aib, 30G |
| <b>Peptide 336</b> | H(Aib)QGTFTSDYSK( $\alpha$ MePhe)LDSRRAK( $\gamma$ E-C18diacid)20DFVQWLIS E-acid                                                | 340 | C18diacid | $\gamma$ E                                                      | 20 | Acid  | 2Aib, 13 $\alpha$ MePhe, 20K, 27L, 28S, 29E        |
| <b>Peptide 337</b> | H(Aib)QGTFTSDYSK( $\alpha$ MePhe)LDSRRAK( $\gamma$ E-C18diacid)20DFVQWLL(Aib)T-acid                                             | 341 | C18diacid | $\gamma$ E                                                      | 20 | Acid  | 2Aib, 13 $\alpha$ MePhe, 20K, 27L, 28Aib           |
| <b>Peptide 338</b> | H(Aib)QGTFTSDYSK( $\alpha$ MePhe)LD(Aib)RRAK( $\gamma$ E-C18diacid)20DFVQWLL(Aib)T-acid                                         | 342 | C18diacid | $\gamma$ E                                                      | 20 | Acid  | 2Aib, 13 $\alpha$ MePhe, 16Aib, 20K, 27L, 28Aib    |
| <b>Peptide 339</b> | H(Aib)QGTFTSDYSK( $\alpha$ MePhe)LDSRRAK( $\gamma$ E-C18diacid)20DFVQWLL(Aib)E-acid                                             | 343 | C18diacid | $\gamma$ E                                                      | 20 | Acid  | 2Aib, 13 $\alpha$ MePhe, 20K, 27L, 28Aib, 29E      |
| <b>Peptide 340</b> | H(Aib)QGTFTSDYSK( $\alpha$ MePhe)LDSRRAK( $\gamma$ E-C18diacid)20DFVQWLL(Aib)TE-acid                                            | 344 | C18diacid | $\gamma$ E                                                      | 20 | Acid  | 2Aib, 13 $\alpha$ MePhe, 20K, 27L, 28Aib, 30E      |
| <b>Peptide 341</b> | H(Aib)QGTFTSDYSK( $\alpha$ MePhe)LDSRRAK( $\gamma$ E-C18diacid)20DFVQWLL E(Aib)T-acid                                           | 345 | C18diacid | $\gamma$ E                                                      | 20 | Acid  | 2Aib, 13 $\alpha$ MePhe, 20K, 27L, 28E, 29Aib, 30T |
| <b>Peptide 342</b> | H(Aib)QGTFTSDVSK( $\alpha$ MePhe)LDSRAAK( $\gamma$ E-C18diacid)20DFVQWIA NT-acid                                                | 346 | C18diacid | $\gamma$ E                                                      | 20 | Acid  | 2Aib, 10V, 13 $\alpha$ MePhe, 18A, 20K, 26I, 27A   |
| <b>Peptide 343</b> | H(Aib)QGTFTSDVSK( $\alpha$ MePhe)LDSRAAK( $\gamma$ E- $\gamma$ E-O2Oc-O2Oc- $\gamma$ E- $\gamma$ E-C18diacid)20DFVQWIA NT-amide | 347 | C18diacid | $\gamma$ E- $\gamma$ E(O2Oc)-<br>(O2Oc)- $\gamma$ E- $\gamma$ E | 20 | Amide | 2Aib, 10V, 13 $\alpha$ MePhe, 18A, 20K, 26I, 27A   |

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|                    |                                                                                                 |     |           |                          |    |      |                                                                      |
|--------------------|-------------------------------------------------------------------------------------------------|-----|-----------|--------------------------|----|------|----------------------------------------------------------------------|
| <b>Peptide 521</b> | H(Aib)QGTFTSDVSK( $\alpha$ MePhe)LDSERAK(O2Oc-O2Oc- $\gamma$ E-C18diacid)20DFVQWLE AGG-acid     | 532 | C18diacid | $\gamma$ E-(O2Oc)-(O2Oc) | 20 | Acid | 2Aib, 10V, 13 $\alpha$ MePhe, 17E, 20K, 27E, 28A, 29G, 30G           |
| <b>Peptide 522</b> | H(Aib)QGTFTSDVSK( $\alpha$ MePhe)LDSERAK(O2Oc-O2Oc- $\gamma$ E-C18diacid)20DFVAWLE AGG-acid     | 533 | C18diacid | $\gamma$ E-(O2Oc)-(O2Oc) | 20 | Acid | 2Aib, 10V, 13 $\alpha$ MePhe, 17E, 20K, 24A, 27E, 28A, 29G, 30G      |
| <b>Peptide 523</b> | H(Aib)QGTFTSDVSK( $\alpha$ MePhe)LDSERAK(O2Oc-O2Oc- $\gamma$ E-C20diacid)20DFVAWLE AGG-acid     | 534 | C20diacid | $\gamma$ E-(O2Oc)-(O2Oc) | 20 | Acid | 2Aib, 10V, 13 $\alpha$ MePhe, 17E, 20K, 24A, 27E, 28A, 29G, 30G      |
| <b>Peptide 524</b> | H(Aib)QGTFTSDVSE( $\alpha$ MePhe)LDSERAK(O2Oc-O2Oc- $\gamma$ E-C18diacid)20DFVRWLE AGG-acid     | 535 | C18diacid | $\gamma$ E-(O2Oc)-(O2Oc) | 20 | Acid | 2Aib, 10V, 12E, 13 $\alpha$ MePhe, 17E, 20K, 24R, 27E, 28A, 29G, 30G |
| <b>Peptide 525</b> | H(Aib)QGTFTSDVSK( $\alpha$ MePhe)LDSERAK(O2Oc-O2Oc- $\gamma$ E-C18diacid)20DFVQWLE A(Aib)G-acid | 536 | C18diacid | $\gamma$ E-(O2Oc)-(O2Oc) | 20 | Acid | 2Aib, 10V, 13 $\alpha$ MePhe, 17E, 20K, 27E, 28A, 29Aib, 30G         |
| <b>Peptide 526</b> | H(Aib)QGTFTSDVSK( $\alpha$ MePhe)LDSERAK(O2Oc-O2Oc- $\gamma$ E-C18diacid)20DFVAWLE A(Aib)G-acid | 537 | C18diacid | $\gamma$ E-(O2Oc)-(O2Oc) | 20 | Acid | 2Aib, 10V, 13 $\alpha$ MePhe, 17E, 20K, 24A, 27E, 28A, 29Aib, 30G    |

[0101] In some aspects, the peptide comprises the sequence: X1-X2-X3-G-X5-X6-T-S-D-X10-S-K-X13-L-X15-X16-X17-X18-X19-X20-X21-X22-X23-X24-X25-X26-X27-X28-X29-X30-X31-Z, wherein X1 is H or ((1H-imidazol-4-yl)methyl)glycine (NHis), X2 is S or Aminoisobutyric acid (Aib), X3 is Q, H, or I, X5 is T or S, X6 is F or  $\alpha$ Methyl-Phenylalanine ( $\alpha$ MePhe), X10 is Y or V, X13 is Y,  $\alpha$ MePhe, Aib, or Diphenylalanine (Dip), X15 is D or E, X16 is S, E, or L, X17 is R, Q, or E, X18 is R, A, or Aib, X19 is A or V, X20 is Q or R, X21 is D or L, X22 is F or  $\alpha$ MePhe, X23 is V or I, X24 is Q or K, wherein the K can comprise an

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acyl moiety and/or can be lipidated, X25 is W, Aib, or S, X26 is L or I, X27 is M, V, L, or A, X28 is N, E, or Aib, X29 is T, Aib, G, or not present, X30 is not present, Aib, or G, X31 is not present or G, and Z is amide or acid (SEQ ID NO: 415), wherein the peptide does not comprise SEQ ID NO: 1.

**[0102]** In some aspects, the residue at position 24 is acylated. In some aspects, the residue at position 24 is lipidated. In some aspects, the lipid is selected from the group consisting of a palmitoyl group, stearoyl group, lauryl group, myristoyl group, margaroyl group, octadecanedioic acid (C18diacid), and icosanedioic acid (C20diacid). In some aspects, the lipid is selected from the group consisting of an octadecanedioic acid (C18diacid), and icosanedioic acid (C20diacid).

**[0103]** In some aspects, the lipid attached to the residue at position 24 is attached via a linker. In some aspects, the linker is selected from the group consisting of (O2Oc), (O2Oc)-(O2Oc), (O2Oc)- $\gamma$ E-(O2Oc), (PEG)2-(PEG)2- $\gamma$ E- $\gamma$ E, (PEG)2- $\gamma$ E-(PEG)2- $\gamma$ E,  $\gamma$ E,  $\gamma$ E-(O2Oc),  $\gamma$ E-(O2Oc)-(O2Oc),  $\gamma$ E-(O2Oc)- $\gamma$ E-(O2Oc),  $\gamma$ E-(PEG)2-(PEG)2,  $\gamma$ E-(PEG)2- $\gamma$ E-(PEG)2,  $\gamma$ E-(PEG)4,  $\gamma$ E- $\gamma$ E,  $\gamma$ E- $\gamma$ E-(O2Oc),  $\gamma$ E- $\gamma$ E-(O2Oc)-(O2Oc),  $\gamma$ E- $\gamma$ E-(PEG)12,  $\gamma$ E- $\gamma$ E-(PEG)2-(PEG)2,  $\gamma$ E- $\gamma$ E-(PEG)2- $\gamma$ E- $\gamma$ E,  $\gamma$ E- $\gamma$ E-(PEG)4, and  $\gamma$ E- $\gamma$ E-(PEG)8. In some aspects, linker is selected from the group consisting of  $\gamma$ E,  $\gamma$ E-(O2Oc)-(O2Oc),  $\gamma$ E- $\gamma$ E-(PEG)2-(PEG)2,  $\gamma$ E- $\gamma$ E-(PEG)2- $\gamma$ E- $\gamma$ E, and  $\gamma$ E- $\gamma$ E-(O2Oc)-(O2Oc).

**[0104]** In some aspects, the peptide comprises the sequence: H-Aminoisobutyric acid (Aib)-Q-G-T-F-T-S-D-V-S-K- $\alpha$ Methyl-Phenylalanine ( $\alpha$ MePhe)-L-X15-X16-R-R-A-Q-D-F-V-K-W-L-X27-X28-X29-X30-Z, wherein X15 is D or E, X16 is S or L, X27 is V or L, X28 is E or Aib, X29 is T, Aib or G, X30 is G or Aib or not present, Z is amide or acid (SEQ ID NO: 416).

**[0105]** In some aspects, the lysine at position 24 is acylated. In some aspects, the lipid is selected from the group consisting of a palmitoyl group, stearoyl group, lauryl group, myristoyl group, margaroyl group, octadecanedioic acid (C18diacid), and icosanedioic acid (C20diacid). In some aspects, the lysine at position 24 is lipidated. In some aspects, the lipid is octadecanedioic acid (C18diacid).

**[0106]** In some aspects, the lipid is linked to the lysine at position 24 via a linker. In some aspects, the linker is selected from the group consisting of (O2Oc), (O2Oc)-(O2Oc), (O2Oc)- $\gamma$ E-(O2Oc), (PEG)2-(PEG)2- $\gamma$ E- $\gamma$ E, (PEG)2- $\gamma$ E-(PEG)2- $\gamma$ E,  $\gamma$ E,  $\gamma$ E-(O2Oc),  $\gamma$ E-(O2Oc)-

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(O2Oc),  $\gamma$ E-(O2Oc)- $\gamma$ E-(O2Oc),  $\gamma$ E-(PEG)2-(PEG)2,  $\gamma$ E-(PEG)2- $\gamma$ E-(PEG)2,  $\gamma$ E-(PEG)4,  $\gamma$ E- $\gamma$ E,  $\gamma$ E- $\gamma$ E-(O2Oc),  $\gamma$ E- $\gamma$ E-(O2Oc)-(O2Oc),  $\gamma$ E- $\gamma$ E-(PEG)12,  $\gamma$ E- $\gamma$ E-(PEG)2-(PEG)2,  $\gamma$ E- $\gamma$ E-(PEG)2- $\gamma$ E- $\gamma$ E,  $\gamma$ E- $\gamma$ E-(PEG)4, and  $\gamma$ E- $\gamma$ E-(PEG)8. In some aspects, the linker is  $\gamma$ E-(O2Oc)-(O2Oc).

[0107] In certain aspects, GLP-1/glucagon agonist peptides as disclosed have desirable potencies at the glucagon and GLP-1 receptors.

[0108] In some aspects, the peptide comprises any one of SEQ ID NOs: 348-395.

[0109] In some aspects, the peptide is any one any of the peptides in **Table 3**.

**Table 3. Peptides Modified at Position 24**

| Peptide            | Sequence                                                                                                      |     | Albumin binding moiety | Linker (described N->C term) | Acylation site | C-term. | Sequence modification with respect to glucagon                                         |
|--------------------|---------------------------------------------------------------------------------------------------------------|-----|------------------------|------------------------------|----------------|---------|----------------------------------------------------------------------------------------|
| <b>Peptide 343</b> | H(Aib)QGSFTSDVSK(Dip)LDsRAAQDFVK( $\gamma$ E-C18diacid)24WIAnt-amide                                          | 348 | C18diacid              | $\gamma$ E                   | 24             | Amide   | 2Aib, 5S, 10V, 13Dip, 18A, 24K, 26I, 27A                                               |
| <b>Peptide 344</b> | HSQGS( $\alpha$ MePhe)TSDVSK(Aib)LDsRAAQD( $\alpha$ MePhe)VK(O2OC-O2OC- $\gamma$ E-C18diacid)24(Aib)IAn-amide | 349 | C18diacid              | $\gamma$ E-(O2Oc)-(O2Oc)     | 24             | Amide   | 5S, 6 $\alpha$ MePhe, 10V, 13Aib, 18A, 22 $\alpha$ MePhe, 24K, 25Aib, 26I, 27A, des29T |
| <b>Peptide 345</b> | H(Aib)HGTFTSDVSK( $\alpha$ MePhe)LDsQAAQDFVK(O2Oc-O2Oc- $\gamma$ E-C18diacid)24WIAnt-amide                    | 350 | C18diacid              | $\gamma$ E-(O2Oc)-(O2Oc)     | 24             | Amide   | 2Aib, 3H, 10V, 13 $\alpha$ MePhe, 17Q, 18A, 24K, 26I, 27A                              |
| <b>Peptide 346</b> | H(Aib)HGTFTSDVSK( $\alpha$ MePhe)LDsQAAQDFVK( $\gamma$ E-C18diacid)24WIAnt-amide                              | 351 | C18diacid              | $\gamma$ E                   | 24             | Amide   | 2Aib, 3H, 10V, 13 $\alpha$ MePhe, 17Q, 18A, 24K, 26I, 27A                              |
| <b>Peptide 347</b> | H(Aib)HGTFTSDVSK( $\alpha$ MePhe)LDsQAAQDFVK( $\gamma$ E-C20diacid)24WIAnt-amide                              | 352 | C20diacid              | $\gamma$ E                   | 24             | Amide   | 2Aib, 3H, 10V, 13 $\alpha$ MePhe, 17Q, 18A, 24K, 26I, 27A                              |

|                    |                                                                                                                                                                |     |           |                                                              |    |       |                                                                                                             |
|--------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------|-----|-----------|--------------------------------------------------------------|----|-------|-------------------------------------------------------------------------------------------------------------|
| <b>Peptide 348</b> | H(Aib)QGS( $\alpha$ MePhe)TS<br>DVSK( $\alpha$ MePhe)LDSQAA<br>QDFVK(O2Oc-O2Oc- $\gamma$ E-<br>C18diacid)24WIAnt-<br>amide                                     | 353 | C18diacid | $\gamma$ E-<br>(O2Oc)-<br>(O2Oc)                             | 24 | Amide | 2Aib, 5S,<br>6 $\alpha$ MePhe,<br>10V,<br>13 $\alpha$ MePhe,<br>17Q, 18A,<br>24K, 26I, 27A                  |
| <b>Peptide 349</b> | H(Aib)HGS( $\alpha$ MePhe)TS<br>DVSK( $\alpha$ MePhe)LDSQAA<br>QDFVK(O2Oc-O2Oc- $\gamma$ E-<br>C18diacid)24WIAnt-<br>amide                                     | 354 | C18diacid | $\gamma$ E-<br>(O2Oc)-<br>(O2Oc)                             | 24 | Amide | 2Aib, 3H, 5S,<br>6 $\alpha$ MePhe,<br>10V,<br>13 $\alpha$ MePhe,<br>17Q, 18A,<br>24K, 26I, 27A              |
| <b>Peptide 350</b> | H(Aib)HGS( $\alpha$ MePhe)TS<br>DVSK( $\alpha$ MePhe)LDSQAA<br>QDFVK(O2Oc-O2Oc- $\gamma$ E-<br>C18diacid)24WIAntGG-<br>-amide                                  | 355 | C18diacid | $\gamma$ E-<br>(O2Oc)-<br>(O2Oc)                             | 24 | Amide | 2Aib, 3H, 5S,<br>6 $\alpha$ MePhe,<br>10V,<br>13 $\alpha$ MePhe,<br>17Q, 18A,<br>24K, 26I, 27A,<br>30G, 31G |
| <b>Peptide 351</b> | H(Aib)HGS( $\alpha$ MePhe)TS<br>DVSK( $\alpha$ MePhe)LDSQAA<br>QDFVK( $\gamma$ E-<br>C18diacid)24WIAnt-<br>amide                                               | 356 | C18diacid | $\gamma$ E                                                   | 24 | Amide | 2Aib, 3H, 5S,<br>6 $\alpha$ MePhe,<br>10V,<br>13 $\alpha$ MePhe,<br>17Q, 18A,<br>24K, 26I, 27A              |
| <b>Peptide 352</b> | H(Aib)HGS( $\alpha$ MePhe)TS<br>DVSK( $\alpha$ MePhe)LDSQAA<br>QDFVK((PEG)2-(PEG)2-<br>$\gamma$ E- $\gamma$ E-<br>C18diacid)24WIAnt-<br>amide                  | 357 | C18diacid | $\gamma$ E- $\gamma$ E-<br>(PEG)2-<br>(PEG)2                 | 24 | Amide | 2Aib, 3H, 5S,<br>6 $\alpha$ MePhe,<br>10V,<br>13 $\alpha$ MePhe,<br>17Q, 18A,<br>24K, 26I, 27A              |
| <b>Peptide 353</b> | H(Aib)HGS( $\alpha$ MePhe)TS<br>DVSK( $\alpha$ MePhe)LDSQAA<br>QDFVK( $\gamma$ E- $\gamma$ E-(PEG)2-<br>$\gamma$ E- $\gamma$ E-<br>C18diacid)24WIAnt-<br>amide | 358 | C18diacid | $\gamma$ E- $\gamma$ E-<br>(PEG)2-<br>$\gamma$ E- $\gamma$ E | 24 | Amide | 2Aib, 3H, 5S,<br>6 $\alpha$ MePhe,<br>10V,<br>13 $\alpha$ MePhe,<br>17Q, 18A,<br>24K, 26I, 27A              |
| <b>Peptide 354</b> | H(Aib)HGS( $\alpha$ MePhe)TS<br>DVSK( $\alpha$ MePhe)LDSQAA<br>QDFVK( $\gamma$ E-<br>C20diacid)24WIAnt-<br>amide                                               | 359 | C20diacid | $\gamma$ E                                                   | 24 | Amide | 2Aib, 3H, 5S,<br>6 $\alpha$ MePhe,<br>10V,<br>13 $\alpha$ MePhe,<br>17Q, 18A,<br>24K, 26I, 27A              |
| <b>Peptide 355</b> | H(Aib)HGS( $\alpha$ MePhe)TS<br>DVSK( $\alpha$ MePhe)LDSQAA<br>QDFVK((PEG)2-(PEG)2-<br>$\gamma$ E- $\gamma$ E-                                                 | 360 | C20diacid | $\gamma$ E- $\gamma$ E-<br>(PEG)2-<br>(PEG)2                 | 24 | Amide | 2Aib, 3H, 5S,<br>6 $\alpha$ MePhe,<br>10V,<br>13 $\alpha$ MePhe,                                            |

|                    |                                                                                                                                               |     |           |                                                       |    |       |                                                                                 |
|--------------------|-----------------------------------------------------------------------------------------------------------------------------------------------|-----|-----------|-------------------------------------------------------|----|-------|---------------------------------------------------------------------------------|
|                    | C20diacid)24WIANT-amide                                                                                                                       |     |           |                                                       |    |       | 17Q, 18A, 24K, 26I, 27A                                                         |
| <b>Peptide 356</b> | H(Aib)HGS( $\alpha$ MePhe)TS DVSK( $\alpha$ MePhe)LDSQAA QDFVK(O2OC-O2OC- $\gamma$ E-C20diacid)24WIANT-amide                                  | 361 | C20diacid | $\gamma$ E-(O2Oc)-(O2Oc)                              | 24 | Amide | 2Aib, 3H, 5S, 6 $\alpha$ MePhe, 10V, 13 $\alpha$ MePhe, 17Q, 18A, 24K, 26I, 27A |
| <b>Peptide 357</b> | H(Aib)HGS( $\alpha$ MePhe)TS DVSK( $\alpha$ MePhe)LDSQAA QDFVK( $\gamma$ E- $\gamma$ E-(PEG)2- $\gamma$ E- $\gamma$ E-C20diacid)24WIANT-amide | 362 | C20diacid | $\gamma$ E- $\gamma$ E-(PEG)2- $\gamma$ E- $\gamma$ E | 24 | Amide | 2Aib, 3H, 5S, 6 $\alpha$ MePhe, 10V, 13 $\alpha$ MePhe, 17Q, 18A, 24K, 26I, 27A |
| <b>Peptide 358</b> | H(Aib)IGS( $\alpha$ MePhe)TSD VSK( $\alpha$ MePhe)LDSQAA QDFVK(O2Oc-O2Oc- $\gamma$ E-C18diacid)24WIANT-amide                                  | 363 | C18diacid | $\gamma$ E-(O2Oc)-(O2Oc)                              | 24 | Amide | 2Aib, 3I, 5S, 6 $\alpha$ MePhe, 10V, 13 $\alpha$ MePhe, 17Q, 18A, 24K, 26I, 27A |
| <b>Peptide 359</b> | H(Aib)IGS( $\alpha$ MePhe)TSD VSK( $\alpha$ MePhe)LDSRAAQ DFVK(O2Oc-O2Oc- $\gamma$ E-C18diacid)24WIANT-amide                                  | 364 | C18diacid | $\gamma$ E-(O2Oc)-(O2Oc)                              | 24 | Amide | 2Aib, 3I, 5S, 6 $\alpha$ MePhe, 10V, 13 $\alpha$ MePhe, 18A, 24K, 26I, 27A      |
| <b>Peptide 360</b> | H(Aib)IGS( $\alpha$ MePhe)TSD VSK( $\alpha$ MePhe)LDSRAAQ DFVK(O2OC-O2OC- $\gamma$ E-C20diacid)24WIANT-amide                                  | 365 | C20diacid | $\gamma$ E-(O2Oc)-(O2Oc)                              | 24 | Amide | 2Aib, 3I, 5S, 6 $\alpha$ MePhe, 10V, 13 $\alpha$ MePhe, 18A, 24K, 26I, 27A      |
| <b>Peptide 361</b> | H(Aib)HGS( $\alpha$ MePhe)TS DVSK( $\alpha$ MePhe)LDSRAA QDFVK(O2Oc-O2Oc- $\gamma$ E-C18diacid)24WIANT-amide                                  | 366 | C18diacid | $\gamma$ E-(O2Oc)-(O2Oc)                              | 24 | Amide | 2Aib, 3H, 5S, 6 $\alpha$ MePhe, 10V, 13 $\alpha$ MePhe, 18A, 24K, 26I, 27A      |
| <b>Peptide 362</b> | H(Aib)HGS( $\alpha$ MePhe)TS DVSK( $\alpha$ MePhe)LDSRAA QDFVK(O2OC-O2OC- $\gamma$ E- $\gamma$ E-C18diacid)24WIANT-amide                      | 367 | C18diacid | $\gamma$ E- $\gamma$ E-(O2Oc)-(O2Oc)                  | 24 | Amide | 2Aib, 3H, 5S, 6 $\alpha$ MePhe, 10V, 13 $\alpha$ MePhe, 18A, 24K, 26I, 27A      |
| <b>Peptide 363</b> | H(Aib)HGS( $\alpha$ MePhe)TS DVSK( $\alpha$ MePhe)LDSRAA QDFVK(O2OC-O2OC-                                                                     | 368 | C18diacid | $\gamma$ E- $\gamma$ E-(O2Oc)-(O2Oc)                  | 24 | Amide | 2Aib, 3H, 5S, 6 $\alpha$ MePhe, 10V,                                            |

|                    |                                                                                           |     |           |                     |    |       |                                                                 |
|--------------------|-------------------------------------------------------------------------------------------|-----|-----------|---------------------|----|-------|-----------------------------------------------------------------|
|                    | γE-γE-C18diacid)24W IANTG-amide                                                           |     |           |                     |    |       | 13αMePhe, 18A, 24K, 26I, 27A, 30G                               |
| <b>Peptide 364</b> | H(Aib)HGS(αMePhe)TS DVSK(αMePhe)LDSRAA QDFVK(O2OC-O2OC-γE-γE-C18diacid)24W IANTGG-amide   | 369 | C18diacid | γE-γE-(O2Oc)-(O2Oc) | 24 | Amide | 2Aib, 3H, 5S, 6αMePhe, 10V, 13αMePhe, 18A, 24K, 26I, 27A, 31G   |
| <b>Peptide 365</b> | H(Aib)HGS(αMePhe)TS DVSK(αMePhe)LDSR(Ai b)AQDFVK(O2OC-O2Oc-γE-C18diacid)24W IANT-amide    | 370 | C18diacid | γE-(O2Oc)-(O2Oc)    | 24 | Amide | 2Aib, 3H, 5S, 6αMePhe, 10V, 13αMePhe, 18Aib, 24K, 26I, 27A      |
| <b>Peptide 366</b> | H(Aib)HGS(αMePhe)TS DVSK(αMePhe)LDSRAA QDFVK(O2Oc-O2OC-γE-C18diacid)24(Aib)IANT-amide     | 371 | C18diacid | γE-(O2Oc)-(O2Oc)    | 24 | Amide | 2Aib, 3H, 5S, 6αMePhe, 10V, 13αMePhe, 18A, 24K, 25Aib, 26I, 27A |
| <b>Peptide 367</b> | H(Aib)HGS(αMePhe)TS DVSK(αMePhe)LDSRAA QDFVK(O2OC-O2OC-γE-C20diacid)24W IANT-amide        | 372 | C20diacid | γE-(O2Oc)-(O2Oc)    | 24 | Amide | 2Aib, 3H, 5S, 6αMePhe, 10V, 13αMePhe, 18A, 24K, 26I, 27A        |
| <b>Peptide 368</b> | H(Aib)HGS(αMePhe)TS DVSK(αMePhe)LDSR(Ai b)AQDFVK(O2OC-O2OC-γE-C20diacid)24W IANT-amide    | 373 | C20diacid | γE-(O2Oc)-(O2Oc)    | 24 | Amide | 2Aib, 3H, 5S, 6αMePhe, 10V, 13αMePhe, 18Aib, 24K, 26I, 27A      |
| <b>Peptide 369</b> | H(Aib)HGS(αMePhe)TS DVSK(αMePhe)LDSRAA QDFVK(O2OC-O2OC-γE-C20diacid)24(Aib)IANT-amide     | 374 | C20diacid | γE-(O2Oc)-(O2Oc)    | 24 | Amide | 2Aib, 3H, 5S, 6αMePhe, 10V, 13αMePhe, 18A, 24K, 25Aib, 26I, 27A |
| <b>Peptide 370</b> | H(Aib)HGS(αMePhe)TS DVSK(αMePhe)LDSQAA QD(αMePhe)VK(O2OC-O2Oc-γE-C18diacid)24W IANT-amide | 375 | C18diacid | γE-(O2Oc)-(O2Oc)    | 24 | Amide | 2Aib, 3H, 5S, 6αMePhe, 10V, 13αMePhe, 17Q, 18A,                 |

|                        |                                                                                                                                                                                       |     |           |                                                                        |    |       |                                                                                                                                        |
|------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----|-----------|------------------------------------------------------------------------|----|-------|----------------------------------------------------------------------------------------------------------------------------------------|
|                        |                                                                                                                                                                                       |     |           |                                                                        |    |       | 22 $\alpha$ MePhe,<br>24K, 26I, 27A                                                                                                    |
| <b>Peptide<br/>371</b> | H(Aib)HGS( $\alpha$ MePhe)TS<br>DVSK( $\alpha$ MePhe)LDSRAA<br>QD( $\alpha$ MePhe)VK(O <sub>2</sub> OC <sub>2</sub><br>- $\gamma$ E- $\gamma$ E-<br>C18diacid)24W ANT-<br>amide       | 376 | C18diacid | $\gamma$ E- $\gamma$ E-<br>(O <sub>2</sub> Oc)-<br>(O <sub>2</sub> Oc) | 24 | Amide | 2Aib, 3H, 5S,<br>6 $\alpha$ MePhe,<br>10V,<br>13 $\alpha$ MePhe,<br>18A,<br>22 $\alpha$ MePhe,<br>24K, 26I, 27A                        |
| <b>Peptide<br/>372</b> | H(Aib)HGS( $\alpha$ MePhe)TS<br>DVSK( $\alpha$ MePhe)LDSRAA<br>QD( $\alpha$ MePhe)VK(O <sub>2</sub> OC <sub>2</sub><br>- $\gamma$ E- $\gamma$ E-<br>C18diacid)24(Aib) ANT-<br>amide   | 377 | C18diacid | $\gamma$ E- $\gamma$ E-<br>(O <sub>2</sub> Oc)-<br>(O <sub>2</sub> Oc) | 24 | Amide | 2Aib, 3H, 5S,<br>6 $\alpha$ MePhe,<br>10V,<br>13 $\alpha$ MePhe,<br>18A,<br>22 $\alpha$ MePhe,<br>24K, 25Aib,<br>26I, 27A              |
| <b>Peptide<br/>373</b> | H(Aib)HGS( $\alpha$ MePhe)TS<br>DVSK( $\alpha$ MePhe)LDSRAA<br>QD( $\alpha$ MePhe)VK(O <sub>2</sub> OC <sub>2</sub><br>- $\gamma$ E- $\gamma$ E-<br>C18diacid)24(Aib) ANT<br>GG-amide | 378 | C18diacid | $\gamma$ E- $\gamma$ E-<br>(O <sub>2</sub> Oc)-<br>(O <sub>2</sub> Oc) | 24 | Amide | 2Aib, 3H, 5S,<br>6 $\alpha$ MePhe,<br>10V,<br>13 $\alpha$ MePhe,<br>18A,<br>22 $\alpha$ MePhe,<br>24K, 25Aib,<br>26I, 27A,<br>30G, 31G |
| <b>Peptide<br/>374</b> | H(Aib)HGS( $\alpha$ MePhe)TS<br>DVSK( $\alpha$ MePhe)LDSRAA<br>QD( $\alpha$ MePhe)VK(O <sub>2</sub> OC <sub>2</sub><br>- $\gamma$ E- $\gamma$ E-<br>C20diacid)24W ANT-<br>amide       | 379 | C20diacid | $\gamma$ E- $\gamma$ E-<br>(O <sub>2</sub> Oc)-<br>(O <sub>2</sub> Oc) | 24 | Amide | 2Aib, 3H, 5S,<br>6 $\alpha$ MePhe,<br>10V,<br>13 $\alpha$ MePhe,<br>18A,<br>22 $\alpha$ MePhe,<br>24K, 26I, 27A                        |
| <b>Peptide<br/>375</b> | H(Aib)HGS( $\alpha$ MePhe)TS<br>DVSK( $\alpha$ MePhe)LDSRAA<br>QD( $\alpha$ MePhe)VK(O <sub>2</sub> OC <sub>2</sub><br>- $\gamma$ E- $\gamma$ E-<br>C20diacid)24(Aib) ANT-<br>amide   | 380 | C20diacid | $\gamma$ E- $\gamma$ E-<br>(O <sub>2</sub> Oc)-<br>(O <sub>2</sub> Oc) | 24 | Amide | 2Aib, 3H, 5S,<br>6 $\alpha$ MePhe,<br>10V,<br>13 $\alpha$ MePhe,<br>18A,<br>22 $\alpha$ MePhe,<br>24K, 25Aib,<br>26I, 27A              |
| <b>Peptide<br/>376</b> | H(Aib)HGS( $\alpha$ MePhe)TS<br>DVSK( $\alpha$ MePhe)LDSRAA<br>QD( $\alpha$ MePhe)VK(O <sub>2</sub> OC <sub>2</sub><br>- $\gamma$ E- $\gamma$ E-<br>C20diacid)24(Aib) ANT<br>GG-amide | 381 | C20diacid | $\gamma$ E- $\gamma$ E-<br>(O <sub>2</sub> Oc)-<br>(O <sub>2</sub> Oc) | 24 | Amide | 2Aib, 3H, 5S,<br>6 $\alpha$ MePhe,<br>10V,<br>13 $\alpha$ MePhe,<br>18A,<br>22 $\alpha$ MePhe,                                         |

|                        |                                                                                                                                                                                 |     |           |                                                                        |    |       |                                                                                                                         |
|------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----|-----------|------------------------------------------------------------------------|----|-------|-------------------------------------------------------------------------------------------------------------------------|
|                        |                                                                                                                                                                                 |     |           |                                                                        |    |       | 24K, 25Aib,<br>26I, 27A,<br>30G, 31G                                                                                    |
| <b>Peptide<br/>377</b> | H(Aib)HGS( $\alpha$ MePhe)TS<br>DVSK( $\alpha$ MePhe)LDSRAA<br>QDFVK(O <sub>2</sub> OC <sub>2</sub> - $\gamma$ E- $\gamma$ E-<br>C20diacid)24WIAANT-<br>amide                   | 382 | C20diacid | $\gamma$ E- $\gamma$ E-<br>(O <sub>2</sub> Oc)-<br>(O <sub>2</sub> Oc) | 24 | Amide | 2Aib, 3H, 5S,<br>6 $\alpha$ MePhe,<br>10V,<br>13 $\alpha$ MePhe,<br>18A, 24K, 26I,<br>27A                               |
| <b>Peptide<br/>378</b> | H(Aib)HGS( $\alpha$ MePhe)TS<br>DVSK( $\alpha$ MePhe)LDSRAA<br>QD( $\alpha$ MePhe)VK(O <sub>2</sub> OC <sub>2</sub><br>- $\gamma$ E- $\gamma$ E-<br>C18diacid)24SIANT-<br>amide | 383 | C18diacid | $\gamma$ E- $\gamma$ E-<br>(O <sub>2</sub> Oc)-<br>(O <sub>2</sub> Oc) | 24 | Amide | 2Aib, 3H, 5S,<br>6 $\alpha$ MePhe,<br>10V,<br>13 $\alpha$ MePhe,<br>18A,<br>22 $\alpha$ MePhe,<br>24K, 25S, 26I,<br>27A |
| <b>Peptide<br/>379</b> | H(Aib)HGS( $\alpha$ MePhe)TS<br>DVSK( $\alpha$ MePhe)LDSRAA<br>QD( $\alpha$ MePhe)VK(O <sub>2</sub> OC <sub>2</sub><br>- $\gamma$ E-C18diacid)24SIANT-<br>amide                 | 384 | C18diacid | $\gamma$ E- $\gamma$ E-<br>(O <sub>2</sub> Oc)-<br>(O <sub>2</sub> Oc) | 24 | Amide | 2Aib, 3H, 5S,<br>6 $\alpha$ MePhe,<br>10V,<br>13 $\alpha$ MePhe,<br>18A,<br>22 $\alpha$ MePhe,<br>24K, 25S, 26I,<br>27A |
| <b>Peptide<br/>380</b> | (NHis)SHGS( $\alpha$ MePhe)T<br>SDVSK( $\alpha$ MePhe)LDSRA<br>AQDFVK(O <sub>2</sub> OC <sub>2</sub> - $\gamma$ E- $\gamma$ E-<br>C20diacid)24WIAANT-<br>amide                  | 385 | C20diacid | $\gamma$ E- $\gamma$ E-<br>(O <sub>2</sub> Oc)-<br>(O <sub>2</sub> Oc) | 24 | Amide | 1NHis, 3H,<br>5S,<br>6 $\alpha$ MePhe,<br>10V,<br>13 $\alpha$ MePhe,<br>18A, 24K, 26I,<br>27A                           |
| <b>Peptide<br/>381</b> | H(Aib)HGS( $\alpha$ MePhe)TS<br>DVSK( $\alpha$ MePhe)LDSRAA<br>QDFVK(O <sub>2</sub> OC-O <sub>2</sub> OC-<br>$\gamma$ E- $\gamma$ E-<br>C18diacid)24SIANTGG-<br>amide           | 386 | C18diacid | $\gamma$ E- $\gamma$ E-<br>(O <sub>2</sub> Oc)-<br>(O <sub>2</sub> Oc) | 24 | Amide | 2Aib, 3H, 5S,<br>6 $\alpha$ MePhe,<br>10V,<br>13 $\alpha$ MePhe,<br>18A, 24K,<br>25S, 26I, 27A,<br>30G, 31G             |
| <b>Peptide<br/>382</b> | H(Aib)HGS( $\alpha$ MePhe)TS<br>DVSK( $\alpha$ MePhe)LDSR(Ai<br>b)AQDFVK(O <sub>2</sub> OC-<br>O <sub>2</sub> OC- $\gamma$ E- $\gamma$ E-<br>C18diacid)24SIANTGG-<br>amide      | 387 | C18diacid | $\gamma$ E- $\gamma$ E-<br>(O <sub>2</sub> Oc)-<br>(O <sub>2</sub> Oc) | 24 | Amide | 2Aib, 3H, 5S,<br>6 $\alpha$ MePhe,<br>10V,<br>13 $\alpha$ MePhe,<br>18Aib, 24K,<br>25S, 26I, 27A,<br>30G, 31G           |

|                    |                                                                                                                                                                |     |           |                                              |    |       |                                                                                                                                |
|--------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------|-----|-----------|----------------------------------------------|----|-------|--------------------------------------------------------------------------------------------------------------------------------|
| <b>Peptide 383</b> | H(Aib)HGS( $\alpha$ MePhe)TS<br>DVSK( $\alpha$ MePhe)LDSQAA<br>QD( $\alpha$ MePhe)VK(O2Oc-<br>O2Oc- $\gamma$ E-<br>C18diacid)24(Aib)IANT-<br>amide             | 388 | C18diacid | $\gamma$ E-<br>(O2Oc)-<br>(O2Oc)             | 24 | Amide | 2Aib, 3H, 5S,<br>6 $\alpha$ MePhe,<br>10V,<br>13 $\alpha$ MePhe,<br>17Q, 18A,<br>22 $\alpha$ MePhe,<br>24K, 25Aib,<br>26I, 27A |
| <b>Peptide 384</b> | H(Aib)HGS( $\alpha$ MePhe)TS<br>DVSK( $\alpha$ MePhe)LDSQAA<br>QD( $\alpha$ MePhe)VK(O2OC-<br>O2OC- $\gamma$ E- $\gamma$ E-<br>C20diacid)24(Aib)IANT-<br>amide | 389 | C20diacid | $\gamma$ E- $\gamma$ E-<br>(O2Oc)-<br>(O2Oc) | 24 | Amide | 2Aib, 3H, 5S,<br>6 $\alpha$ MePhe,<br>10V,<br>13 $\alpha$ MePhe,<br>17Q, 18A,<br>22 $\alpha$ MePhe,<br>24K, 25Aib,<br>26I, 27A |
| <b>Peptide 385</b> | HSQGTFTSDYSK( $\alpha$ MePhe)<br>LEEEAVRLFVK(O2OC-<br>O2OC- $\gamma$ E-<br>stearOOH)24WLMNT-<br>amide                                                          | 390 | C18diacid | $\gamma$ E-<br>(O2Oc)-<br>(O2Oc)             | 24 | Amide | 13 $\alpha$ MePhe,<br>15E, 16E,<br>17E, 18A,<br>19V, 20R,<br>21L, 23I, 24K,                                                    |
| <b>Peptide 386</b> | H(Aib)QGTFTSDVSK( $\alpha$<br>MePhe)LDSRRAQDFVK(<br>O2OC-O2OC- $\gamma$ E-<br>C18diacid)24WLVE(Aib)<br>G-acid                                                  | 391 | C18diacid | $\gamma$ E-<br>(O2Oc)-<br>(O2Oc)             | 24 | Acid  | 2Aib, 10V,<br>13 $\alpha$ MePhe,<br>24K, 25Aib,<br>27V, 28E,<br>29Aib, 30G                                                     |
| <b>Peptide 387</b> | H(Aib)QGTFTSDVSK( $\alpha$<br>MePhe)LESRRAQDFVK(<br>O2OC-O2OC- $\gamma$ E-<br>C18diacid)24WLVE(Aib)<br>G-acid                                                  | 392 | C18diacid | $\gamma$ E-<br>(O2Oc)-<br>(O2Oc)             | 24 | Acid  | 2Aib, 10V,<br>13 $\alpha$ MePhe,<br>15E, 24K,<br>25Aib, 27V,<br>28E, 29Aib,<br>30G                                             |
| <b>Peptide 388</b> | H(Aib)QGTFTSDVSK( $\alpha$<br>MePhe)LDLRAQDFVK(<br>O2OC-O2OC- $\gamma$ E-<br>C18diacid)24WLVE(Aib)<br>G-acid                                                   | 393 | C18diacid | $\gamma$ E-<br>(O2Oc)-<br>(O2Oc)             | 24 | Acid  | 2Aib, 10V,<br>13 $\alpha$ MePhe,<br>16L, 24K,<br>25Aib, 27V,<br>28E, 29Aib,<br>30G                                             |
| <b>Peptide 389</b> | H(Aib)QGTFTSDVSK( $\alpha$<br>MePhe)LDSRRAQDFVK(<br>O2OC-O2OC- $\gamma$ E-<br>C18diacid)24WLL(Aib)T-<br>acid                                                   | 394 | C18diacid | $\gamma$ E-<br>(O2Oc)-<br>(O2Oc)             | 24 | Acid  | 2Aib, 10V,<br>13 $\alpha$ MePhe,<br>24K, 25Aib,<br>27L, 28Aib                                                                  |
| <b>Peptide 390</b> | H(Aib)QGTFTSDVSK( $\alpha$<br>MePhe)LDSRRAQDFVK(<br>O2OC-O2OC- $\gamma$ E-                                                                                     | 395 | C18diacid | $\gamma$ E-<br>(O2Oc)-<br>(O2Oc)             | 24 | Acid  | 2Aib, 10V,<br>13 $\alpha$ MePhe,<br>24K, 25Aib,                                                                                |

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|  |                             |  |  |  |  |  |                      |
|--|-----------------------------|--|--|--|--|--|----------------------|
|  | C18diacid)24WLVEG(Aib)-acid |  |  |  |  |  | 27V, 28E, 29G, 30Aib |
|--|-----------------------------|--|--|--|--|--|----------------------|

- [0110] In some aspects, the peptide comprises the sequence: H-X2-X3-G-X5-X6-T-S-D-X10-S-K-X13-L-D-S-X17-X18-A-Q-D-X22-V-X24-X25-X26-X27-N-T-X(30)-X(31)-Z, wherein X2 is S or Aminoisobutyric acid (Aib), X3 is Q or H, X5 is T or S, X6 is F or  $\alpha$ -methylphenylalanine ( $\alpha$ MePhe), X10 is Y, V, or K, wherein the K can comprise an acyl moiety and/or can be lipidated, X13 is Y,  $\alpha$ MePhe, I, or Diphenylalanine (Dip), or K wherein the K can comprise an acyl moiety and/or can be lipidated, X17 is R, Q, or  $\beta$ -dimethylarginine ( $\beta$ -diMeArg), X18 is R or A, X22 is F or  $\alpha$ MePhe, X24 is Q or E, X25 is W, Aib, or H, X26 is L or I, X27 is M or A, X(30) is not present, X(31) is not present, and Z is amide or acid (SEQ ID NO: 417), wherein the peptide does not comprise SEQ ID NO: 1.
- [0111] In some aspects, the residue at position 10 or 13 is acylated. In some aspects, the residue at position 10 or 13 is lipidated. In some aspects, the lipid is selected from the group consisting of a palmitoyl group, stearoyl group, lauryl group, myristoyl group, margaroyl group, octadecanedioic acid (C18diacid), and icosanedioic acid (C20diacid). In some aspects, the lipid is selected from the group consisting of an octadecanedioic acid (C18diacid), and icosanedioic acid (C20diacid), stearoyl group, and palmitoyl group.
- [0112] In some aspects, the lipid attached to the residue at position 10 or 13 is attached via a linker. In some aspects, the linker is selected from the group consisting of (O2Oc), (O2Oc)-(O2Oc), (O2Oc)- $\gamma$ E-(O2Oc), (PEG)2-(PEG)2- $\gamma$ E- $\gamma$ E, (PEG)2- $\gamma$ E-(PEG)2- $\gamma$ E,  $\gamma$ E,  $\gamma$ E-(O2Oc),  $\gamma$ E-(O2Oc)-(O2Oc),  $\gamma$ E-(O2Oc)- $\gamma$ E-(O2Oc),  $\gamma$ E-(PEG)2-(PEG)2,  $\gamma$ E-(PEG)2- $\gamma$ E-(PEG)2,  $\gamma$ E-(PEG)4,  $\gamma$ E- $\gamma$ E,  $\gamma$ E- $\gamma$ E-(O2Oc),  $\gamma$ E- $\gamma$ E-(O2Oc)-(O2Oc),  $\gamma$ E- $\gamma$ E-(PEG)12,  $\gamma$ E- $\gamma$ E-(PEG)2-(PEG)2,  $\gamma$ E- $\gamma$ E-(PEG)2- $\gamma$ E- $\gamma$ E,  $\gamma$ E- $\gamma$ E-(PEG)4, and  $\gamma$ E- $\gamma$ E-(PEG)8. In some aspects, the linker is selected from the group consisting of  $\gamma$ E- $\gamma$ E-(O2Oc)-(O2Oc),  $\gamma$ E-(O2Oc)-(O2Oc),  $\gamma$ E- $\gamma$ E-(PEG)2-(PEG)2, and  $\gamma$ E-(PEG)2-(PEG)2.
- [0113] In some aspects, the peptide comprises any one of SEQ ID NOs: 396-411.
- [0114] In some aspects, the peptide is any one of the peptides in **Table 4** or **Table 5**.

**Table 4. Peptides Modified at Position 10**

| Peptide            | Sequence                                                                                                                                                                                          | SEQ ID NO | Albumin binding moiety | Linker (described N->C)                                                | Acylation site | C-term. | Sequence modification with respect to glucagon                                                                            |
|--------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------|------------------------|------------------------------------------------------------------------|----------------|---------|---------------------------------------------------------------------------------------------------------------------------|
| <b>Peptide 390</b> | H(Aib)HGS( $\alpha$ MePhe)TS<br>DK(O <sub>2</sub> OC-O <sub>2</sub> OC- $\gamma$ E- $\gamma$ E-<br>C <sub>20</sub> diacid)10SK( $\alpha$ MePh<br>e)LDSRAAQD( $\alpha$ MePhe)<br>VQ(Aib)IANT-amide | 396       | C <sub>20</sub> diacid | $\gamma$ E- $\gamma$ E-<br>(O <sub>2</sub> Oc)-<br>(O <sub>2</sub> Oc) | 10             | Amide   | 2Aib, 3H, 5S,<br>6 $\alpha$ MePhe,<br>10K,<br>13 $\alpha$ MePhe,<br>18A,<br>22 $\alpha$ MePhe,<br>25Aib, 26I,<br>27A      |
| <b>Peptide 391</b> | H(Aib)HGS( $\alpha$ MePhe)TS<br>DK(O <sub>2</sub> OC-O <sub>2</sub> OC- $\gamma$ E-<br>C <sub>18</sub> diacid)10SK( $\alpha$ MePh<br>e)LDSRAAQD( $\alpha$ MePhe)<br>VQ(Aib)IANT-amide             | 397       | C <sub>18</sub> diacid | $\gamma$ E-<br>(O <sub>2</sub> Oc)-<br>(O <sub>2</sub> Oc)             | 10             | Amide   | 2Aib, 3H, 5S,<br>6 $\alpha$ MePhe,<br>10K,<br>13 $\alpha$ MePhe,<br>18A,<br>22 $\alpha$ MePhe,<br>25Aib, 26I,<br>27A      |
| <b>Peptide 392</b> | HSQGS( $\alpha$ MePhe)TSDK(<br>(PEG)2-(PEG)2- $\gamma$ E- $\gamma$ E-<br>Stearoyl)10SK(Dip)LDS(<br>$\beta$ -<br>dimethylArg)AAQD( $\alpha$ M<br>ePhe)VE(Aib)IANT-<br>amide                        | 398       | Stearoyl               | $\gamma$ E- $\gamma$ E-<br>(PEG)2-<br>(PEG)2                           | 10             | Amide   | 5S,<br>6 $\alpha$ MePhe,<br>10K, 13Dip,<br>17 $\beta$ -<br>dimethylR,<br>18A,<br>22 $\alpha$ MePhe,<br>24E, 25Aib,<br>27A |
| <b>Peptide 393</b> | HSQGS( $\alpha$ MePhe)TSDK(<br>(PEG)2-(PEG)2- $\gamma$ E- $\gamma$ E-<br>Palmitoyl)10SK(Dip)LDS<br>( $\beta$ -<br>dimethylArg)AAQD( $\alpha$ M<br>ePhe)VE(Aib)IANT-<br>amide                      | 399       | Palmitoyl              | $\gamma$ E- $\gamma$ E-<br>(PEG)2-<br>(PEG)2                           | 10             | Amide   | 5S,<br>6 $\alpha$ MePhe,<br>10K, 13Dip,<br>17 $\beta$ -<br>dimethylR,<br>18A,<br>22 $\alpha$ MePhe,<br>24E, 25Aib,<br>27A |
| <b>Peptide 394</b> | H(Aib)QGSFTSDK((PEG)<br>2-(PEG)2- $\gamma$ E-<br>Palmitoyl)10SKILDSRAA<br>QDFVEWIANIANT-amide                                                                                                     | 400       | Palmitoyl              | $\gamma$ E-<br>(PEG)2-<br>(PEG)2                                       | 10             | Amide   | 2Aib, 5S,<br>10K, 13I,<br>18A, 24E,<br>26I, 27A                                                                           |
| <b>Peptide 395</b> | H(Aib)QGS( $\alpha$ MePhe)TS<br>DK((PEG)2-(PEG)2- $\gamma$ E-<br>Palmitoyl)10SKILDSRAA                                                                                                            | 401       | Palmitoyl              | $\gamma$ E-<br>(PEG)2-<br>(PEG)2                                       | 10             | Amide   | 2Aib, 5S,<br>6 $\alpha$ MePhe,<br>10K, 13I,<br>18A,                                                                       |

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|                    |                                                                                                                                                 |     |          |                                      |    |       |                                                                                                |
|--------------------|-------------------------------------------------------------------------------------------------------------------------------------------------|-----|----------|--------------------------------------|----|-------|------------------------------------------------------------------------------------------------|
|                    | QD( $\alpha$ MePhe)VEWIAANT-amide                                                                                                               |     |          |                                      |    |       | 22 $\alpha$ MePhe, 24E, 26I, 27A                                                               |
| <b>Peptide 396</b> | HSQGS( $\alpha$ MePhe)TSDK((PEG)2-(PEG)2- $\gamma$ E- $\gamma$ E-Stearoyl)10SK(Dip)LDS QAAQD( $\alpha$ MePhe)VE(Aib)LANT-amide                  | 402 | Stearoyl | $\gamma$ E- $\gamma$ E-(PEG)2-(PEG)2 | 10 | Amide | 5S, 6 $\alpha$ MePhe, 10K, 13Dip, 17Q, 18A, 22 $\alpha$ MePhe, 24E, 25Aib, 27A                 |
| <b>Peptide 397</b> | HSQGS( $\alpha$ MePhe)TSDK((PEG)2-(PEG)2- $\gamma$ E- $\gamma$ E-Stearoyl)10SK(Dip)LDS( $\beta$ -dimethylArg)AAQD( $\alpha$ MePhe)VEHLANT-amide | 403 | Stearoyl | $\gamma$ E- $\gamma$ E-(PEG)2-(PEG)2 | 10 | Amide | 5S, 6 $\alpha$ MePhe, 10K, 13Dip, 17 $\beta$ -dimethylR, 18A, 22 $\alpha$ MePhe, 24E, 25H, 27A |

**Table 5. Peptides Modified at Position 13**

| Peptide            | Sequence                                                                                                                                         | SEQ ID NO | Albumin binding moiety | Linker (described N->C term.)        | Acylation site | C-term. | Sequence modification with respect to glucagon                                                 |
|--------------------|--------------------------------------------------------------------------------------------------------------------------------------------------|-----------|------------------------|--------------------------------------|----------------|---------|------------------------------------------------------------------------------------------------|
| <b>Peptide 398</b> | HSQGS( $\alpha$ MePhe)TSDVSKK((PEG)2-(PEG)2- $\gamma$ E- $\gamma$ E-Stearoyl)13LDS( $\beta$ -dimethylArg)AAQD( $\alpha$ MePhe)VE(Aib)LANT-amide  | 404       | Stearoyl               | $\gamma$ E- $\gamma$ E-(PEG)2-(PEG)2 | 13             | Amide   | 5S, 6 $\alpha$ MePhe, 10V, 13K, 17 $\beta$ -dimethylR, 18A, 22 $\alpha$ MePhe, 24E, 25Aib, 27A |
| <b>Peptide 399</b> | HSQGS( $\alpha$ MePhe)TSDVSKK((PEG)2-(PEG)2- $\gamma$ E- $\gamma$ E-Palmitoyl)13LDS( $\beta$ -dimethylArg)AAQD( $\alpha$ MePhe)VE(Aib)LANT-amide | 405       | Palmitoyl              | $\gamma$ E- $\gamma$ E-(PEG)2-(PEG)2 | 13             | Amide   | 5S, 6 $\alpha$ MePhe, 10V, 13K, 17 $\beta$ -dimethylR, 18A, 22 $\alpha$ MePhe, 24E, 25Aib, 27A |
| <b>Peptide 340</b> | H(Aib)QGS( $\alpha$ MePhe)TSDVSKK((PEG)2-(PEG)2- $\gamma$ E-Palmitoyl)13LDSRAAQ                                                                  | 406       | Palmitoyl              | $\gamma$ E-(PEG)2-(PEG)2             | 13             | Amide   | 2Aib, 5S, 6 $\alpha$ MePhe, 10V, 13K, 18A,                                                     |

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|                    |                                                                                                                                 |     |           |                                      |    |       |                                                                                              |
|--------------------|---------------------------------------------------------------------------------------------------------------------------------|-----|-----------|--------------------------------------|----|-------|----------------------------------------------------------------------------------------------|
|                    | D( $\alpha$ MePhe)VEWIAANT-amide                                                                                                |     |           |                                      |    |       | 22 $\alpha$ MePhe, 24E, 26I, 27A                                                             |
| <b>Peptide 341</b> | H(Aib)QGSFTSDVSKK((PEG)2-(PEG)2- $\gamma$ E-Palmitoyl)13LDSRAAQDFVEWIAANT-amide                                                 | 407 | Palmitoyl | $\gamma$ E-(PEG)2-(PEG)2             | 13 | Amide | 2Aib, 5S, 10V, 13K, 18A, 24E, 26I, 27A                                                       |
| <b>Peptide 342</b> | HSQGS( $\alpha$ MePhe)TSDVSKK((PEG)2-(PEG)2- $\gamma$ E-Stearoyl)13LDSQAAQD( $\alpha$ MePhe)VE(Aib)LANT-amide                   | 408 | Stearoyl  | $\gamma$ E- $\gamma$ E-(PEG)2-(PEG)2 | 13 | Amide | 5S, 6 $\alpha$ MePhe, 10V, 13K, 17Q, 18A, 22 $\alpha$ MePhe, 24E, 25Aib, 27A                 |
| <b>Peptide 343</b> | HSQGS( $\alpha$ MePhe)TSDVSKK((PEG)2-(PEG)2- $\gamma$ E-Stearoyl)13LDS( $\beta$ -dimethylArg)AAQD( $\alpha$ MePhe)VEHLANT-amide | 409 | Stearoyl  | $\gamma$ E- $\gamma$ E-(PEG)2-(PEG)2 | 13 | Amide | 5S, 6 $\alpha$ MePhe, 10V, 13K, 17 $\beta$ -dimethylR, 18A, 22 $\alpha$ MePhe, 24E, 25H, 27A |
| <b>Peptide 344</b> | H(Aib)HGS( $\alpha$ MePhe)TSDVSKK(O2OC-O2OC- $\gamma$ E-C20diacid)13LDSRAAQD( $\alpha$ MePhe)VQ(Aib)IANT-amide                  | 410 | C20diacid | $\gamma$ E- $\gamma$ E-(O2Oc)-(O2Oc) | 13 | Amide | 2Aib, 3H, 5S, 6 $\alpha$ MePhe, 10V, 13K, 18A, 22 $\alpha$ MePhe, 25Aib, 26I, 27A            |
| <b>Peptide 345</b> | H(Aib)HGS( $\alpha$ MePhe)TSDVSKK(O2OC-O2OC- $\gamma$ E-C18diacid)13LDSRAAQD( $\alpha$ MePhe)VQ(Aib)IANT-amide                  | 411 | C18diacid | $\gamma$ E-(O2Oc)-(O2Oc)             | 13 | Amide | 2Aib, 3H, 5S, 6 $\alpha$ MePhe, 10V, 13K, 18A, 22 $\alpha$ MePhe, 25Aib, 26I, 27A            |

[0115] In some aspects, the peptide comprises the sequence: H-X2-X3-G-X5-X6-T-S-D-X10-S-X12- $\alpha$ Methyl-Phenylalanine ( $\alpha$ MePhe)-L-X15-X16-X17-X18-A-X20-X21-X22-X23-X24-X25-X26-X27-X28-X29-X30-X31-Z, wherein X2 is Aminoisobutyric acid (Aib), S, or A, X3 is Q, H, or E, X5 is T or S, X6 is F or  $\alpha$ MePhe, X10 is V, K or Y, X11 is S, X12 is K, E, or S, X15 is D or E, X16 is T, S, or G, X17 is K, R, E, or Q, X18 is R or A, X20 is R, K, or Q, X21 is D or E, X22 is  $\alpha$ MePhe or F, X23 is V or I, X24 is Q or A, X25 is Aib or W, X26 is L or I, X27 is L, A, E, V, or M, X28 is E, N, A, R, or K, X29 is Aib, T, or

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G, X30 is G, R, or not present, X31 is G or not present, and Z is amide or acid (SEQ ID NO: 540).

[0116] In some aspects, X2 is Aib. In some aspects, X3 is Q. In some aspects, X3 is H. In some aspects, X5 is T. In some aspects, X5 is S. In some aspects, X6 is F. In some aspects, X6 is  $\alpha$ MePhe. In some aspects, X10 is V. In some aspects, X12 is K. In some aspects, X15 is D. In some aspects, X16 is T. In some aspects, X16 is S. In some aspects, X17 is K. In some aspects, X17 is R. In some aspects, X18 is R. In some aspects, X18 is A. In some aspects, X20 is R. In some aspects, X20 is K. In some aspects, X21 is D. In some aspects, X22 is F. In some aspects, X22 is  $\alpha$ MePhe. In some aspects, X23 is V. In some aspects, X24 is Q. In some aspects, X25 is W. In some aspects, X25 is Aib. In some aspects, X26 is L. In some aspects, X26 is I. In some aspects, X27 is L. In some aspects, X27 is A. In some aspects, X28 is E. In some aspects, X28 is N. In some aspects, X29 is Aib. In some aspects, X29 is T. In some aspects, X30 is G. In some aspects, X30 is not present. In some aspects, X31 is not present. In some aspects, Z is amide. In some aspects, Z is acid.

[0117] In some aspects, X2 is Aib, X12 is K, and X24 is Q. In some aspects, X16 is T, X17 is K, X27 is L, X28, is E, and X29 is Aib.

[0118] In some aspects, X3 is Q, X5 is T, X6 is F, X10 is V, X12 is K, X15 is D, X16 is T, X17 is K, X18 is R, X20 is R, X21 is D, X22 is F, X23 is V, X24 is Q, X25 is W, X26 is L, X27 is L, X28 is E, X29 is Aib, X30 is G, and X31 is not present.

[0119] In some aspects, X3 is H, X5 is S, X6 is  $\alpha$ MePhe, X10 is V, X12 is K, X15 is D, X16 is S, X17 is R, X18 is A, X20 is K, X21 is D, X22 is  $\alpha$ MePhe, X23 is V, X24 is Q, X25 is Aib, X26 is I, X27 is A, X28 is N, X29 is T, X30 is not present, and X31 is not present.

[0120] In some aspects, one or more lysine residues are acylated. In some aspects, the lysine at position 17 is acylated. In some aspects, the lysine at position 20 is acylated.

[0121] In some aspects, one or more lysine residues are lipidated. In some aspects, the lysine at position 17 is lipidated. In some aspects, the lysine at position 20 is lipidated.

[0122] In some aspects, the lipid is selected from the group consisting of octadecanedioic acid (C18diacid) and icosanedioic acid (C20diacid). In some aspects, the lipid is octadecanedioic acid (C18diacid). In some aspects, the lipid is icosanedioic acid (C20diacid).

[0123] In some aspects, the lipid is linked to the residue at position 17 or 20 via a linker. In some aspects, the linker is  $\gamma$ E-(O2Oc)-(O2Oc) or  $\gamma$ E- $\gamma$ E-(O2Oc)-(O2Oc). In some aspects,

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the linker is  $\gamma$ E-(O2Oc)-(O2Oc). In some aspects, the linker is  $\gamma$ E- $\gamma$ E-(O2Oc)-(O2Oc). In some aspects, the linker is linked to the epsilon amino group of the residue at position 17 or 20.

- [0124] Certain aspects of the disclosure are directed to a peptide comprising the sequence of H-Aib-Q-G-T-F-T-S-D-V-S-K- $\alpha$ MePhe-L-D-T-K-R-A-R-D-F-V-Q-W-LL-E-Aib-G-acid (SEQ ID NO: 541).
- [0125] In some aspects, the lysine at position 17 is acylated and lipidated, the lipid is linked to the acylated lysine via a ( $\epsilon$ -(O2Oc)-(O2Oc)- $\gamma$ E-C18diacid).
- [0126] In some aspects, the lysine at position 17 is acylated and lipidated, the lipid is linked to the acylated lysine at position 17 via a ( $\epsilon$ -(O2Oc)-(O2Oc)- $\gamma$ E-C20diacid).
- [0127] Certain aspects of the disclosure are directed to a peptide comprising the sequence H-Aib-H-G-S- $\alpha$ MePhe-T-S-D-V-S-K- $\alpha$ MePhe-L-D-S-R-A-A-K( $\epsilon$ -(O2Oc)-(O2Oc)- $\gamma$ E-C18diacid)20-D- $\alpha$ MePhe-V-Q-Aib-I-A-N-T-amide (SEQ ID NO: 228).
- [0128] Certain aspects of the disclosure are directed to a peptide comprising the sequence H-Aib-H-G-S- $\alpha$ MePhe-T-S-D-V-S-K- $\alpha$ MePhe-L-D-S-R-A-A-K( $\epsilon$ -(O2Oc)-(O2Oc)- $\gamma$ E- $\gamma$ E-C20diacid)20-D- $\alpha$ MePhe-V-Q-Aib-I-A-N-T-amide (SEQ ID NO: 233).
- [0129] In some aspects, the peptide binds to the GLP-1 receptor (GLP-1R), binds to the glucagon receptor (GCGR), or binds to both a GLP-1 receptor and a glucagon receptor. In some aspects, the GLP-1R is a human GLP-1R. In some aspects, the GCGR is a human GCGR. In some aspects, the peptide is an agonist of GLP-1 activity, an agonist of glucagon activity, or an agonist of both GLP-1 and glucagon activity.
- [0130] In some aspects, the peptide has increased proteolytic-resistance relative to the natural ligand of the GLP-1R and/or GCGR.
- [0131] In some aspects, the peptide is isolated.
- [0132] In some aspects, the peptide has at least 50%, at least 60%, at least 70%, at least 75%, at least 80%, at least 85%, at least 90%, at least 95, or 100% of intact peptide remaining after incubation with a protease at 37°C for 5min, 10min, 15min, 30min, 2hr, 4hr or 24hr. In some aspects, the protease is selected from the group consisting of neprilysin, pepsin, pancreatin, simulated gastric fluid with pepsin, and simulated intestinal fluid with pancreatin.
- [0133] In some aspects, the peptide has a half-life in cynomolgus monkeys after intravenous administration of at least 45 hours, at least 50 hours, at least 60 hours, at least 70 hours, at

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least 80 hours, at least 90 hours, at least 100 hours, at least 110 hours, at least 120 hours, or about 130 hours.

[0134] In some aspects, the peptide has an s.c. bioavailability in cynomolgus monkeys of at least 75%, at least 80%, at least 90%, or about 95%.

### **III. Methods of Making GLP-1/Glucagon Agonist Peptides**

[0135] GLP-1/glucagon agonist peptides for uses provided herein can be made by any suitable method. For example, in some aspects provided herein, the GLP-1/glucagon agonist peptides for uses provided herein are chemically synthesized by methods well known to those of ordinary skill in the art, *e.g.*, by solid phase synthesis as described by Merrifield (1963, *J. Am. Chem. Soc.* 85:2149-2154). Solid phase peptide synthesis can be accomplished, *e.g.*, by using automated synthesizers, using standard reagents, *e.g.*, as explained in Example 1 of WO 2014/091316, which is herein incorporated by reference in its entirety.

[0136] Alternatively, GLP-1/glucagon agonist peptides for uses provided herein can be produced recombinantly using a convenient vector/host cell combination as would be well known to the person of ordinary skill in the art. A variety of methods are available for recombinantly producing GLP-1/glucagon agonist peptides. Generally, a polynucleotide sequence encoding the GLP-1/glucagon agonist peptide is inserted into an appropriate expression vehicle, *e.g.*, a vector which contains the necessary elements for the transcription and translation of the inserted coding sequence. The nucleic acid encoding the GLP-1/glucagon agonist peptide is inserted into the vector in proper reading frame. The expression vector is then transfected into a suitable host cell which will express the GLP-1/glucagon agonist peptide. Suitable host cells include without limitation bacteria, yeast, or mammalian cells. A variety of commercially-available host-expression vector systems can be utilized to express the GLP-1/glucagon agonist peptides described herein.

### ***Pharmaceutical Compositions***

[0137] Further provided are compositions, *e.g.*, pharmaceutical compositions, that contain an effective amount of a GLP-1/glucagon agonist peptide as provided herein, formulated for the treatment of metabolic diseases, *e.g.*, obesity, type 2 diabetes, and/or NASH.

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- [0138] Compositions of the disclosure can be formulated according to known methods. Suitable preparation methods are described, for example, in *Remington's Pharmaceutical Sciences*, 19th Edition, A.R. Gennaro, ed., Mack Publishing Co., Easton, PA (1995), which is incorporated herein by reference in its entirety. Composition can be in a variety of forms, including, but not limited to an aqueous solution, an emulsion, a gel, a suspension, lyophilized form, or any other form known in the art. In addition, the composition can contain pharmaceutically acceptable additives including, for example, diluents, binders, stabilizers, and preservatives. Once formulated, compositions of the invention can be administered directly to the subject.
- [0139] In some aspects, the pharmaceutical composition is a solid composition. In some aspects, the pharmaceutical composition is a liquid composition.

#### **IV. Methods of Using GLP-1/Glucacon Agonist Peptides**

- [0140] As provided herein, GLP-1/glucagon agonist peptides can be used to improve glycemic control, reduce weight, type 2 diabetes mellitus (T2DM), and/or treat or prevent non-alcoholic steatohepatitis (NASH).
- [0141] In some aspects, administration of the GLP-1/glucagon agonist peptides decreases body weight of the subject, increases insulin secretion in the subject, delays gastric emptying in the subject, decreases food intake in the subject, increases mitochondria function in the subject, inhibits de novo lipogenesis in the subject, decreases HbA1c in the subject, enhances fatty oxidation in the subject, decreases hepatic mitochondrial oxidative stress in the subject, decreases steatosis in the subject, decreases fibrosis in the subject, decreases glycogen synthesis in the subject, increases gluconeogenesis in the subject, halts disease progression in the subject, reverses fibrosis in the subject, and/or reduces risk of death due to cirrhosis, hepatocellular carcinoma, and/or cardiorenal disease in the subject.
- [0142] As provided herein a method of improving glycemic control or reduce weight in a human subject with T2DM and/or NASH can comprise administering to the subject a GLP-1/glucagon agonist peptide.
- [0143] This disclosure also provides a GLP-1/glucagon agonist peptide for use in the manufacture of a medicament for improving glycemic control or reduce weight in a human subject with T2DM and/or NASH.

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- [0144] In some aspects, the peptide is administered about once a week.
- [0145] In some aspects, the GLP-1/glucagon agonist peptide is administered to treat or prevent a disease or condition cause or characterized by excess body weight. In some aspects, the disease or condition is obesity. In some aspects, the disease or condition is type 2 diabetes.
- [0146] In some aspects, the GLP-1/glucagon agonist peptide is administered to treat or non-alcoholic steatohepatitis (NASH). In some aspects, the GLP-1/glucagon agonist peptide is administered by injection. In some aspects, the GLP-1/glucagon agonist peptide is administered orally. In some aspects, administration of the GLP-1/glucagon agonist peptide decreases body weight of the subject, increases insulin secretion in the subject, delays gastric emptying in the subject, decreases food intake in the subject, increases mitochondria function in the subject, inhibits de novo lipogenesis in the subject, decreases HbA1c in the subject, enhances fatty oxidation in the subject, decreases hepatic mitochondrial oxidative stress in the subject, decreases steatosis in the subject, decreases fibrosis in the subject, decreases glycogen synthesis in the subject, increases gluconeogenesis in the subject, halts disease progression in the subject, reverses fibrosis in the subject, and/or reduces risk of death due to cirrhosis, hepatocellular carcinoma, and/or cardiorenal disease in the subject. In some aspects, the subject is a human. In some aspects, the peptide is administered about once a week.

## Examples

### Example 1: Lipidated-GLP-1/Glucagon Dual Agonist Peptide Analogue Preparation

- [0147] Lipidated-GLP-1R/GCGR dual agonist peptides were synthesized as C-terminal corboxamides or carboxylic acids using rink amide MBHA resin (100 – 200 mesh) or Wang resin (100 – 200 mesh). All peptides were prepared by automated synthesis using a PTI Prelude solid phase peptide synthesizer using the 9-fluorenylmethoxycarbonyl (Fmoc)/*tert*-butyl (<sup>t</sup>Bu) protocol. Manufacturer-supplied protocols were applied for coupling of amino acids in *N,N*-dimethylformamide (DMF) and deprotection of Fmoc protecting group using piperidine in DMF (20% v/v). Asparagine (Asn), glutamine (Gln) and histidine (His) were incorporated as their sidechain triphenylmethyl, trityl (Trt) derivatives. Lysine (Lys) was incorporated as the sidechain *tert*-butyloxycarbonyl (Boc) derivative. Serine (Ser), threonine (Thr) and tyrosine (Tyr) were incorporated as sidechain <sup>t</sup>Bu ethers, and aspartate (Asp) and glutamate (Glu) as their sidechain O<sup>t</sup>Bu esters. Arginine (Arg) was incorporated as the

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sidechain 2,2,4,6,7-pentamethyldihydrobenzofuran-5-sulfonyl (Pbf) derivative. Other amino acids were incorporated with an appropriate sidechain protection.

**[0148]** Lys(Mmt) was incorporated when a subsequent chemical modification of the lysine side chain was required. Upon completion of the peptide chain elongation, Mmt side chain protection was removed by treatment of the resin with selective deprotection cocktail (1% trifluoroacetic acid (TFA), 5% TIPS in dichloromethane (DCM)) at 100 mL/mmol for 1 min, and repeated at least 10 times until Mmt group deprotection was completed. The reaction was quenched with 10% *N,N*-diisopropylethylamine (DIPEA)/NMP. Subsequent coupling of a albumin binding moiety, such as a lipid and linker, was performed manually using 1-[Bis(dimethylamino)methylene]-1H-1,2,3-triazolo[4,5-b]pyridinium 3-oxid hexafluorophosphate (HATU) as a coupling reagent in the presence of DIPEA.

**[0149]** Peptides were cleaved from the solid support by treatment with a mixture of TFA: triisopropylsilane (TIS):water (92.5.5:2.5v/v) for 4 h with agitation at room temperature. Thereafter, the cleavage mixtures were filtered, concentrated in vacuo, precipitated and washed with diethyl ether and solids were isolated by centrifugation. The crude peptides were dried under a flow of nitrogen and dissolved in 20% acetonitrile (MeCN)/water (v/v) and filtered. The crude peptides were purified using a preparative reversed-phase high-performance liquid chromatography (RP-HPLC) on a Varian SD-1 Prep Star binary pump system, monitoring by ultraviolet (UV) absorption at 210 nm using an Xbridge C18-A stationary phase (19.0 x 250 mm, 5 micron) column eluting a linear solvent gradient of 25 – 70% MeCN (0.1% TFA v/v) in water (0.1% TFA v/v) over 25 min. The purified fractions were pooled, frozen and lyophilised.

**[0150]** Liquid chromatography / mass spectrometry (LC/MS) characterization of purified peptides were performed on a Waters MassLynx 3100 platform using a XBridge C18 stationary phase (4.6 x 100 mm, 3 micron) eluting a linear binary gradient of 10 – 90% MeCN (0.1% TFA v/v) in water (0.1% TFA v/v) over 10 minutes at 1.5 mL/min at ambient temperature. Analytes were detected by both UV absorption at 210 nm and ionization using a Waters 3100 mass detector (electrospray ionisation (ESI)+ mode). Analytical RP-HPLC characterization was performed on an Agilent 1260 Infinity system using an Agilent Polaris C8-A stationary phase (4.6 x 100 mm, 3 micron) eluting a linear binary gradient of 10 – 90% MeCN (0.1% TFA v/v) in water (0.1% TFA v/v) at 1.5 mL/min over 15 minutes at 40 °C.

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**Example 2: GLP-1 Receptor and Glucagon Receptor *In Vitro* Functional Assay**

- [0151] The functional activities of lipidated-GLP-1R/GCGR peptides, such as cAMP production, were tested in CHO cell line with stable recombinant expression of human GLP-1 receptor (hGLP-1R) or human glucagon receptor (hGCGR).
- [0152] Cryopreserved cell stocks were thawed rapidly in a water-bath, suspended in assay buffer (0.1% BSA (Sigma # A3059) in HBSS (Sigma # H8264) with 25mM HEPES, pH 7.4 and containing 0.5mM IBMX (Sigma# 17018)) and centrifuged at 240xg for 5 minutes. Cells were re-suspended in assay buffer at a batch-dependent optimized concentration (typically hGLP-1R cells at  $1 \times 10^5$  cells/mL, hGCGR cells at  $2 \times 10^5$  cells/mL).
- [0153] The test peptide stock was prepared in DMSO and serially diluted in assay buffer to prepare 11-point concentration response curves, in duplicate, in 384-well low volume microtiter assay plates (Corning # 4514) using a non-contact liquid dispenser (ECHO™, LabCyte). Cells were added to the assay plate using a multidrop dispenser and incubated at room temperature for 30 minutes before measuring the cAMP level using a cAMP dynamic 2 homogeneous time resolved Fluorescence (HTRF) kit (Cisbio Bioassays # 62AM4PEJ) following the two-step protocol as per manufacturer's recommendations. In brief, anti-cAMP cryptate (donor fluorophore) and cAMP-d2 (acceptor fluorophore) were made up separately by diluting each 1 in 20 in conjugate and lysis buffer provided in the kit. Anti-cAMP cryptate was added to all wells of the assay plate, followed by cAMP-d2 added to all wells except non-specific binding (NSB) wells (to which conjugate and lysis buffer was added). Plates were incubated at room temperature for one hour and then read on an Envision (Perkin Elmer) using an excitation wavelength of 320nm and emission wavelengths of 620nm & 665nm.
- [0154] Data was transformed to % Delta F as described in the manufacturer's guidelines and analyzed by 4-parameter logistic fit to determine EC<sub>50</sub> values. The selectivity ratio of a peptide to hGLP-1R vs hGCGR is defined as: % Relative Potency Ratio = % GLP-1R activity relative to GLP-1 / % GlucR activity relative to glucagon. Data is shown as the geometric mean EC<sub>50</sub> (pM) from > n = 2 independent experiments.
- [0155] The relative potency ratios of peptides is listed in **Tables 6-10**.

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**Table 6. Potency of Peptides with Modification on Amino Acid at Position 17**

| <b>Peptide</b>           | <b>hGLP-1R EC<sub>50</sub> (pM)</b> | <b>hGluc-R EC<sub>50</sub> (pM)</b> | <b>% Relative Potency Ratio</b> |
|--------------------------|-------------------------------------|-------------------------------------|---------------------------------|
| <b>GLP-1(7-36) amide</b> | 2.196                               | -                                   | -                               |
| <b>Glucagon</b>          | -                                   | 1.110                               | -                               |
| <b>1</b>                 | 3197.264                            | >27100                              | -                               |
| <b>2</b>                 | 1281.484                            | 4192.851                            | 6.5                             |
| <b>3</b>                 | 69.013                              | 149.198                             | 4.3                             |
| <b>4</b>                 | 240.004                             | 1167.129                            | 9.6                             |
| <b>5</b>                 | 282.756                             | 7137.899                            | 49.9                            |
| <b>6</b>                 | 567.937                             | 516.038                             | 1.8                             |
| <b>7</b>                 | 84.551                              | 30.666                              | 0.7                             |
| <b>8</b>                 | 87.845                              | 53.635                              | 1.2                             |
| <b>9</b>                 | 241.876                             | 278.726                             | 2.3                             |
| <b>10</b>                | 657.981                             | 376.720                             | 1.1                             |
| <b>11</b>                | 156.625                             | 117.572                             | 1.5                             |
| <b>12</b>                | 14.531                              | 47.666                              | 6.5                             |
| <b>13</b>                | 15.895                              | 44.043                              | 5.5                             |
| <b>14</b>                | 93.788                              | 462.195                             | 9.7                             |
| <b>15</b>                | 33.122                              | 61.419                              | 3.7                             |
| <b>16</b>                | 32.959                              | 104.788                             | 6.3                             |
| <b>17</b>                | 44.976                              | 134.979                             | 5.9                             |
| <b>18</b>                | 20.493                              | 121.569                             | 11.7                            |
| <b>19</b>                | 38.345                              | 133.477                             | 6.9                             |
| <b>20</b>                | 152.448                             | 135.633                             | 1.8                             |
| <b>21</b>                | 377.683                             | 68.754                              | 0.4                             |
| <b>22</b>                | 1226.703                            | 2724.463                            | 4.4                             |
| <b>23</b>                | 266.349                             | 321.178                             | 2.4                             |
| <b>24</b>                | 82.803                              | 101.130                             | 2.4                             |
| <b>25</b>                | 725.678                             | 1311.347                            | 3.6                             |
| <b>26</b>                | 80.600                              | 8904.381                            | 218.5                           |
| <b>27</b>                | 18.189                              | 1438.437                            | 156.4                           |
| <b>28</b>                | 129.321                             | 259.647                             | 4.0                             |
| <b>29</b>                | 106.638                             | 629.359                             | 11.7                            |
| <b>30</b>                | 52.683                              | 234.982                             | 8.8                             |
| <b>31</b>                | 41.292                              | 56.793                              | 2.7                             |
| <b>40</b>                | 29.909                              | 123.325                             | 8.2                             |
| <b>41</b>                | 662.690                             | 5737.086                            | 17.1                            |
| <b>42</b>                | 665.048                             | 8189.848                            | 24.4                            |
| <b>136</b>               | 45.196                              | 509.273                             | 22.3                            |
| <b>137</b>               | 143.435                             | 267.783                             | 3.7                             |
| <b>138</b>               | 104.274                             | 183.767                             | 3.5                             |
| <b>139</b>               | 630.031                             | 983.762                             | 3.1                             |
| <b>140</b>               | 22.725                              | 46.408                              | 4.0                             |

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|     |          |          |       |
|-----|----------|----------|-------|
| 141 | 263.906  | 392.259  | 2.9   |
| 142 | 59.361   | 107.506  | 3.6   |
| 143 | 19.134   | 32.638   | 3.4   |
| 144 | 45.230   | 702.417  | 30.7  |
| 145 | 22.618   | 4587.203 | 401.2 |
| 146 | 24.628   | 1634.605 | 131.3 |
| 147 | 15.328   | 43.496   | 5.6   |
| 148 | 40.233   | 567.838  | 27.9  |
| 149 | 8.707    | 2653.203 | 602.8 |
| 150 | 166.473  | 355.432  | 4.2   |
| 151 | 111.202  | 178.430  | 3.2   |
| 152 | 11.912   | 20.350   | 3.4   |
| 153 | 41.161   | 99.002   | 4.8   |
| 158 | 303.611  | 332.670  | 2.2   |
| 159 | 145.208  | 144.564  | 2.0   |
| 160 | 55.178   | 416.851  | 14.9  |
| 162 | 59.567   | 1027.507 | 34.1  |
| 161 | 50.942   | 1030.580 | 40.0  |
| 166 | 48.005   | 269.638  | 11.1  |
| 167 | 76.814   | 310.656  | 8.0   |
| 43  | 1.894    | 5.520    | 5.8   |
| 44  | 2.117    | 18.235   | 17.0  |
| 45  | 2.028    | 14.943   | 14.6  |
| 46  | 3.395    | 5.914    | 3.4   |
| 47  | 1.715    | 2.381    | 2.7   |
| 48  | 19.862   | 43.244   | 4.3   |
| 49  | 1.738    | 1.728    | 2.0   |
| 50  | 4.903    | 8.738    | 3.5   |
| 51  | 18.101   | 41.930   | 4.6   |
| 52  | 22.733   | 6.646    | 0.6   |
| 53  | 3.025    | 18.850   | 12.3  |
| 54  | 2.810    | 2.588    | 1.8   |
| 55  | 18.800   | 19.085   | 2.0   |
| 56  | 4.860    | 10.909   | 4.4   |
| 57  | 9.093    | 16.912   | 3.7   |
| 58  | 3.900    | 11.329   | 5.7   |
| 59  | 6.181    | 28.350   | 9.1   |
| 60  | 5.161    | 21.118   | 8.1   |
| 61  | 4.125    | 9.554    | 4.6   |
| 62  | 10.098   | 15.204   | 3.0   |
| 63  | 3.139    | 2.488    | 1.6   |
| 64  | 2.574    | 3.065    | 2.4   |
| 65  | 1230.000 | 2060.580 | 3.3   |
| 66  | 1.524    | 6.426    | 8.3   |
| 67  | 2.432    | 9.488    | 7.7   |
| 68  | 1.095    | 4.670    | 8.4   |

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|     |          |            |       |
|-----|----------|------------|-------|
| 69  | 1.145    | 6.442      | 11.1  |
| 70  | 1.550    | 30.865     | 39.4  |
| 71  | 2.174    | 53.722     | 48.9  |
| 72  | 3.418    | 73.660     | 42.6  |
| 73  | 0.275    | 21.956     | 157.9 |
| 74  | 1.831    | 10.893     | 11.8  |
| 75  | 18.897   | 2803.488   | 293.5 |
| 76  | 1.776    | 339.882    | 378.6 |
| 77  | 8.682    | 243.406    | 55.5  |
| 78  | 1.135    | 8.972      | 15.6  |
| 79  | 1.733    | 10.679     | 12.2  |
| 80  | 1.033    | 9.179      | 17.6  |
| 81  | 1.188    | 13.543     | 22.6  |
| 82  | 0.839    | 7.774      | 18.3  |
| 83  | 1.043    | 15.604     | 29.6  |
| 84  | 2.798    | 44.887     | 31.7  |
| 85  | 1.038    | 47.687     | 90.9  |
| 86  | 0.772    | 6.459      | 16.6  |
| 87  | 1.289    | 8.465      | 13.0  |
| 88  | 1.040    | 6.467      | 12.3  |
| 89  | 3.769    | 15.282     | 8.0   |
| 90  | 1.866    | 6.606      | 7.0   |
| 91  | 1.570    | 7.797      | 9.8   |
| 92  | 0.895    | 10.899     | 24.1  |
| 93  | 0.472    | 8.920      | 37.4  |
| 94  | 0.515    | 5.397      | 20.7  |
| 95  | 0.608    | 12.464     | 40.6  |
| 96  | 0.851    | 30.053     | 69.9  |
| 97  | 1.055    | 12.962     | 24.3  |
| 98  | 2.442    | 54.125     | 43.8  |
| 99  | 2.212    | 33.196     | 29.7  |
| 100 | 0.258    | 40.473     | 310.3 |
| 101 | 0.713    | 119.000    | 330.1 |
| 102 | 0.231    | 26.508     | 227.0 |
| 103 | 0.532    | 59.381     | 220.8 |
| 104 | 246.670  | 45.636     | 0.4   |
| 105 | 64.817   | 121.121    | 3.7   |
| 106 | 6.819    | 36.794     | 10.7  |
| 107 | 65.867   | 99.074     | 3.0   |
| 108 | 3197.264 | >27100.000 | -     |
| 109 | 697.596  | >26800.000 | -     |
| 110 | 0.627    | 48.465     | 152.9 |
| 111 | 1.918    | 2.090      | 2.2   |
| 112 | 3.364    | 2.689      | 1.6   |
| 113 | 1.613    | 4.603      | 5.6   |
| 114 | 3.647    | 2.648      | 1.4   |

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|     |         |          |       |
|-----|---------|----------|-------|
| 117 | 15.615  | 2.990    | 0.4   |
| 116 | 24.329  | 10.308   | 0.8   |
| 117 | 1.398   | 1.848    | 2.6   |
| 118 | 1.068   | 1.201    | 2.2   |
| 119 | 1.392   | 1.700    | 2.4   |
| 120 | 1.810   | 2.616    | 2.9   |
| 121 | 1.502   | 1.200    | 1.6   |
| 122 | 1.417   | 0.857    | 1.2   |
| 123 | 0.496   | 12.883   | 51.4  |
| 124 | 1.274   | 9.790    | 15.2  |
| 125 | 0.575   | 6.676    | 23.0  |
| 128 | 0.594   | 10.997   | 36.6  |
| 127 | 0.998   | 12.649   | 25.1  |
| 128 | 0.788   | 4.695    | 11.8  |
| 129 | 0.462   | 4.100    | 17.6  |
| 130 | 1.087   | 32.889   | 59.9  |
| 131 | 0.511   | 17.811   | 68.9  |
| 132 | 0.949   | 34.315   | 71.5  |
| 133 | 1.060   | 29.964   | 55.9  |
| 134 | 0.592   | 15.008   | 50.1  |
| 135 | 0.407   | 14.984   | 72.8  |
| 407 | 208.719 | 462.060  | 4.4   |
| 408 | 370.323 | 828.459  | 4.4   |
| 409 | 22.673  | 203.000  | 17.7  |
| 410 | 78.013  | 455.043  | 11.5  |
| 411 | 98.122  | 377.956  | 7.6   |
| 412 | 185.707 | 397.402  | 4.2   |
| 413 | 406.086 | 1023.554 | 5.0   |
| 414 | 32.273  | 26.904   | 1.6   |
| 415 | 14.693  | 301.237  | 40.6  |
| 416 | 67.741  | 581.428  | 17.0  |
| 417 | 33.876  | 16.440   | 1.0   |
| 418 | 88.091  | 221.794  | 5.0   |
| 419 | 96.888  | 264.191  | 5.4   |
| 420 | 23.104  | 36.906   | 3.2   |
| 421 | 87.299  | 179.876  | 4.1   |
| 422 | 27.559  | 123.460  | 8.9   |
| 423 | 26.123  | 2219.743 | 168.1 |
| 424 | 15.540  | 129.497  | 16.5  |
| 425 | 11.490  | 826.662  | 142.3 |
| 426 | 7.303   | 61.169   | 16.6  |
| 427 | 12.433  | 47.225   | 7.5   |
| 428 | 33.081  | 10.501   | 0.6   |
| 429 | 15.013  | 144.446  | 19.0  |
| 430 | 24.421  | 160.262  | 13.0  |
| 431 | 44.587  | 193.903  | 8.6   |

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|     |            |            |      |
|-----|------------|------------|------|
| 432 | 1377.330   | 1164.734   | 1.7  |
| 433 | 4464.399   | 10463.230  | 4.6  |
| 434 | 152.763    | 293.928    | 3.8  |
| 435 | 22.659     | 240.076    | 21.0 |
| 436 | 7.427      | 68.750     | 18.3 |
| 437 | 26.892     | 96.876     | 7.1  |
| 438 | 17.923     | 68.908     | 7.6  |
| 439 | 30.650     | 57.730     | 3.7  |
| 440 | 153.518    | 81.008     | 1.0  |
| 441 | 62.730     | 72.810     | 2.3  |
| 442 | 19.052     | 35.819     | 3.7  |
| 443 | 20.559     | 22.434     | 2.2  |
| 444 | 247.415    | 1758.388   | 14.1 |
| 445 | 33.016     | 683.673    | 41.0 |
| 446 | 32.889     | 365.880    | 22.0 |
| 447 | 169.598    | 666.503    | 7.8  |
| 448 | 53.134     | 28.953     | 1.1  |
| 449 | 207.17     | 241.70     | 2.3  |
| 450 | 57.318     | 57.789     | 2.0  |
| 451 | 894.881    | 503.273    | 1.1  |
| 452 | 495.050    | 150.934    | 0.6  |
| 453 | 169.523    | 161.692    | 1.9  |
| 454 | 173.343    | 273.630    | 3.1  |
| 455 | 127.140    | 114.432    | 1.8  |
| 456 | 132.866    | 80.328     | 1.2  |
| 457 | 109.278    | 202.834    | 3.7  |
| 458 | 114.344    | 384.540    | 6.7  |
| 459 | 32.674     | 36.947     | 2.2  |
| 460 | 116.724    | 66.478     | 1.1  |
| 461 | 167.051    | Not tested | -    |
| 462 | 39.497     | 89.240     | 4.5  |
| 463 | 273.563    | Not tested | -    |
| 464 | Not tested | Not tested | -    |
| 465 | 485.020    | 436.382    | 1.8  |
| 466 | 35.571     | 131.195    | 7.3  |
| 467 | Not tested | Not tested | -    |
| 468 | 67.532     | 292.374    | 8.6  |
| 469 | 254.776    | 538.155    | 4.2  |
| 470 | 55.908     | 30.269     | 1.1  |
| 471 | 101.756    | 63.584     | 1.2  |
| 472 | 7.627      | 11.060     | 2.9  |
| 473 | 11.463     | 14.135     | 2.4  |
| 474 | 8.043      | 56.901     | 14.0 |
| 475 | 6.748      | 61.516     | 18.0 |
| 476 | 57.309     | 103.924    | 3.6  |
| 477 | 54.091     | 117.426    | 4.3  |

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|     |         |          |      |
|-----|---------|----------|------|
| 478 | 9.178   | 189.932  | 40.9 |
| 479 | 34.154  | 206.779  | 12.0 |
| 480 | 12.573  | 136.201  | 21.4 |
| 481 | 52.209  | 349.837  | 13.3 |
| 482 | 190.311 | 691.097  | 7.2  |
| 483 | 177.661 | 168.551  | 1.9  |
| 484 | 338.595 | 168.884  | 1.0  |
| 485 | 219.193 | 90.425   | 0.8  |
| 486 | 420.381 | 166.466  | 0.8  |
| 487 | 65.455  | 164.468  | 5.0  |
| 488 | 201.998 | 300.737  | 2.9  |
| 489 | 22.787  | 167.608  | 14.5 |
| 490 | 69.046  | 396.488  | 11.4 |
| 491 | 73.584  | 231.822  | 6.2  |
| 492 | 212.412 | 374.486  | 3.5  |
| 493 | 23.450  | 165.822  | 14.0 |
| 494 | 98.727  | 212.207  | 4.3  |
| 495 | 23.165  | 379.702  | 32.4 |
| 496 | 64.887  | 482.010  | 14.7 |
| 497 | 37.397  | 118.244  | 6.3  |
| 498 | 156.406 | 169.974  | 2.1  |
| 499 | 40.647  | 78.787   | 3.8  |
| 500 | 101.880 | 101.482  | 2.0  |
| 501 | 26.516  | 75.630   | 5.6  |
| 502 | 82.090  | 174.964  | 4.2  |
| 503 | 81.209  | 84.902   | 2.1  |
| 504 | 123.927 | 551.274  | 8.8  |
| 505 | 42.121  | 190.780  | 9.0  |
| 506 | 162.104 | 148.973  | 1.8  |
| 507 | 52.850  | 86.602   | 3.2  |
| 508 | 67.930  | 2802.216 | 81.6 |
| 509 | 594.123 | 3020.408 | 10.1 |
| 510 | 176.244 | 117.832  | 1.3  |
| 511 | 117.715 | 139.920  | 2.4  |
| 512 | 159.226 | 2308.999 | 28.7 |
| 513 | 93.821  | 1340.613 | 28.3 |
| 514 | 76.660  | 1373.731 | 35.4 |
| 515 | 296.991 | 2659.628 | 17.7 |
| 516 | 137.100 | 784.568  | 11.3 |
| 517 | 145.751 | 737.919  | 10.0 |
| 136 | 45.196  | 509.273  | 22.3 |
| 137 | 143.435 | 267.783  | 3.7  |
| 138 | 104.274 | 183.767  | 3.5  |
| 139 | 630.031 | 983.762  | 3.1  |
| 140 | 22.725  | 46.408   | 4.0  |
| 141 | 263.906 | 392.259  | 2.9  |

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|     |         |          |       |
|-----|---------|----------|-------|
| 142 | 59.361  | 107.506  | 3.6   |
| 143 | 19.134  | 32.638   | 3.4   |
| 144 | 45.230  | 702.417  | 30.7  |
| 145 | 22.618  | 4587.203 | 401.2 |
| 146 | 24.628  | 1634.605 | 131.3 |
| 147 | 15.328  | 43.496   | 5.6   |
| 148 | 40.233  | 567.838  | 27.9  |
| 149 | 8.707   | 2653.203 | 602.8 |
| 150 | 166.473 | 355.432  | 4.2   |
| 151 | 111.202 | 178.430  | 3.2   |
| 152 | 11.912  | 20.350   | 3.4   |
| 153 | 41.161  | 99.002   | 4.8   |
| 158 | 303.611 | 332.670  | 2.2   |
| 159 | 145.208 | 144.564  | 2.0   |
| 160 | 55.178  | 416.851  | 14.9  |
| 162 | 59.567  | 1027.507 | 34.1  |
| 165 | 50.942  | 1030.580 | 40.0  |
| 166 | 48.005  | 269.638  | 11.1  |
| 167 | 76.814  | 310.656  | 8.0   |
| 518 | 31.000  | 77.320   | 4.9   |
| 519 | 172.230 | 385.880  | 4.4   |
| 520 | 542.600 | 1616.230 | 5.9   |
| 32  | 12.953  | 240.474  | 36.7  |
| 33  | 213.123 | 548.248  | 5.1   |
| 34  | 82.377  | 160.622  | 3.9   |
| 35  | 83.697  | 334.904  | 7.9   |
| 36  | 43.060  | 277.733  | 12.8  |
| 37  | 68.620  | 2748.412 | 79.2  |
| 38  | 75.589  | 441.481  | 11.6  |
| 39  | 76.068  | 193.860  | 5.0   |
| 161 | 17.234  | 188.040  | 21.6  |
| 163 | 90.154  | 143.715  | 3.2   |
| 168 | 447.505 | 886.110  | 3.9   |
| 169 | 210.397 | 1404.311 | 13.2  |
| 170 | 147.744 | 835.556  | 11.2  |
| 171 | 106.863 | 376.304  | 7.0   |
| 172 | 213.354 | 1273.732 | 11.8  |
| 173 | 134.317 | 874.131  | 12.9  |
| 174 | 127.027 | 420.420  | 6.5   |
| 175 | 68.376  | 2018.944 | 58.4  |
| 176 | 59.942  | 480.338  | 15.9  |
| 177 | 23.777  | 306.464  | 25.5  |
| 178 | 51.770  | 104.397  | 4.0   |
| 179 | 130.928 | 203.431  | 3.1   |
| 180 | 24.377  | 71.735   | 5.8   |
| 181 | 56.000  | 33.440   | 1.2   |

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|     |         |         |      |
|-----|---------|---------|------|
| 182 | 29.060  | 22.580  | 1.5  |
| 183 | 23.730  | 81.430  | 6.8  |
| 184 | 22.040  | 29.620  | 2.7  |
| 185 | 44.113  | 229.651 | 10.3 |
| 186 | 44.923  | 100.835 | 4.4  |
| 188 | 20.847  | 34.713  | 3.3  |
| 189 | 11.315  | 44.301  | 7.7  |
| 192 | 107.568 | 227.117 | 4.2  |
| 193 | 282.849 | 476.105 | 3.3  |
| 194 | 424.799 | 592.863 | 2.8  |
| 195 | 86.016  | 94.577  | 2.2  |
| 196 | 26.953  | 240.329 | 17.6 |
| 197 | 64.040  | 111.890 | 3.5  |
| 198 | 211.810 | 302.200 | 2.8  |
| 199 | 31.604  | 180.232 | 11.3 |
| 200 | 22.687  | 97.711  | 8.5  |
| 201 | 22.724  | 182.560 | 15.9 |
| 202 | 17.824  | 242.436 | 26.9 |

**Table 7. Potency of Peptides with Modification on Amino Acid at Position 20**

| Peptide | hGLP-1R EC <sub>50</sub> (pM) | hGluc-R EC <sub>50</sub> (pM) | % Relative Potency Ratio |
|---------|-------------------------------|-------------------------------|--------------------------|
| 203     | 77.466                        | 34.112                        | 0.9                      |
| 204     | 43.306                        | 595.006                       | 27.2                     |
| 205     | 29.901                        | 8.136                         | 0.5                      |
| 206     | 70.949                        | 18.170                        | 0.5                      |
| 207     | 177.618                       | 96.175                        | 1.1                      |
| 208     | 64.412                        | 658.298                       | 20.2                     |
| 209     | 126.544                       | 42.591                        | 0.7                      |
| 210     | 156.403                       | 93.732                        | 1.2                      |
| 211     | 166.600                       | 60.904                        | 0.7                      |
| 212     | 531.595                       | 97.476                        | 0.4                      |
| 213     | 534.307                       | 140.535                       | 0.5                      |
| 214     | 2339.231                      | 809.862                       | 0.7                      |
| 215     | 7623.287                      | 2609.521                      | 0.7                      |
| 216     | 18055.470                     | 5672.548                      | 0.6                      |
| 217     | 263.939                       | 126.681                       | 0.9                      |
| 218     | 138.770                       | 422.882                       | 6.0                      |
| 219     | 94.472                        | 297.862                       | 6.2                      |
| 220     | 240.450                       | 405.230                       | 3.3                      |
| 221     | 122.449                       | 122.801                       | 2.0                      |
| 222     | 151.493                       | 243.967                       | 3.2                      |

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|     |          |           |      |
|-----|----------|-----------|------|
| 223 | 48.761   | 103.522   | 4.2  |
| 224 | 32.095   | 28.693    | 1.8  |
| 225 | 34.873   | 144.655   | 8.2  |
| 226 | 82.675   | 27.435    | 0.7  |
| 227 | 70.467   | 27.208    | 0.8  |
| 228 | 200.219  | 176.842   | 1.7  |
| 229 | 68.511   | 198.144   | 5.7  |
| 230 | 170.050  | 37.108    | 0.4  |
| 231 | 49.851   | 58.542    | 2.3  |
| 232 | 110.306  | 1023.865  | 18.4 |
| 233 | 440.364  | 407.411   | 1.8  |
| 234 | 68.020   | 1285.410  | 37.4 |
| 235 | 94.790   | 1262.350  | 26.3 |
| 236 | 22.063   | 214.558   | 19.2 |
| 237 | 26.745   | 298.747   | 22.1 |
| 238 | 154.658  | 990.172   | 12.7 |
| 239 | 105.489  | 704.613   | 13.2 |
| 240 | 57.099   | 332.464   | 11.5 |
| 241 | 35.843   | 175.226   | 9.7  |
| 242 | 248.687  | 1234.326  | 9.8  |
| 243 | 59.292   | 50.633    | 1.7  |
| 244 | 143.475  | 420.232   | 5.8  |
| 245 | 110.173  | 62.682    | 1.1  |
| 246 | 320.437  | 556.602   | 3.4  |
| 247 | 84.851   | 51.143    | 1.2  |
| 248 | 1089.266 | 13553.228 | 24.6 |
| 249 | 558.256  | 545.142   | 1.9  |
| 250 | 601.166  | 1566.333  | 5.2  |
| 251 | 79.751   | 248.071   | 6.2  |
| 252 | 119.246  | 1309.962  | 21.7 |
| 253 | 75.451   | 53.089    | 1.4  |
| 254 | 101.863  | 125.276   | 2.4  |
| 255 | 147.550  | 145.739   | 2.0  |
| 256 | 345.977  | 1306.254  | 7.5  |
| 257 | 7.348    | 1.659     | 0.4  |
| 258 | 34.046   | 93.123    | 5.4  |
| 259 | 19.118   | 34.833    | 3.6  |
| 260 | 33.080   | 76.881    | 4.6  |
| 261 | 16.152   | 29.390    | 3.6  |
| 262 | 13.017   | 11.700    | 1.8  |
| 263 | 25.386   | 64.646    | 5.0  |
| 264 | 69.537   | 297.466   | 8.5  |
| 265 | 71.223   | 130.903   | 3.6  |
| 266 | 66.478   | 293.480   | 8.7  |
| 267 | 65.581   | 127.683   | 3.9  |
| 268 | 39.521   | 29.251    | 1.5  |

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|     |          |           |       |
|-----|----------|-----------|-------|
| 269 | 51.951   | 271.143   | 10.3  |
| 270 | 24.445   | 31.318    | 2.5   |
| 271 | 54.604   | 27.999    | 1.0   |
| 272 | 15.650   | 14.309    | 1.8   |
| 273 | 22.118   | 23.336    | 2.1   |
| 274 | 27.112   | 31.277    | 2.3   |
| 275 | 110.638  | 175.236   | 3.1   |
| 276 | 143.383  | 91.395    | 1.3   |
| 277 | 49.494   | 57.270    | 2.3   |
| 278 | 78.855   | 83.493    | 2.1   |
| 279 | 86.544   | 150.224   | 3.4   |
| 280 | 78.346   | 154.623   | 3.9   |
| 281 | 155.104  | 1042.071  | 13.3  |
| 282 | 1230.958 | 1135.696  | 1.8   |
| 283 | 129.487  | 552.440   | 8.4   |
| 284 | 43.422   | 118.686   | 5.4   |
| 285 | 300.590  | 87.044    | 0.6   |
| 286 | 31.616   | 52.951    | 3.3   |
| 287 | 27.519   | 26.538    | 1.9   |
| 288 | 42.719   | 26.875    | 1.2   |
| 289 | 118.366  | 148.058   | 2.5   |
| 290 | 346.546  | 260.062   | 1.5   |
| 291 | 1509.011 | 847.167   | 1.1   |
| 292 | 28.705   | 20.397    | 1.4   |
| 293 | 91.968   | 33.473    | 0.7   |
| 294 | 510.108  | 102.417   | 0.4   |
| 295 | 312.053  | 17071.588 | 108.2 |
| 296 | 64.149   | 3253.412  | 100.3 |
| 297 | 30.440   | 103.940   | 6.8   |
| 298 | 75.450   | 572.856   | 15.0  |
| 299 | 75.820   | 193.220   | 5.0   |
| 300 | 19.742   | 18.360    | 1.8   |
| 301 | 55.339   | 31.826    | 1.1   |
| 302 | 151.070  | 270.815   | 3.5   |
| 303 | 99.136   | 99.581    | 2.0   |
| 304 | 238.821  | 687.098   | 5.7   |
| 305 | 211.193  | 154.945   | 1.5   |
| 306 | 47.214   | 775.451   | 32.5  |
| 307 | 22.180   | 1126.909  | 100.5 |
| 308 | 27.499   | 1716.004  | 123.4 |
| 309 | 70.607   | 17377.186 | 486.8 |
| 310 | 56.382   | 1836.826  | 64.4  |
| 311 | 35.100   | 468.731   | 26.4  |
| 312 | 152.183  | 2775.255  | 36.1  |
| 313 | 138.271  | 1227.004  | 17.6  |
| 314 | 30.764   | 6832.600  | 439.3 |

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|     |           |            |       |
|-----|-----------|------------|-------|
| 315 | 18.118    | 5853.796   | 639.1 |
| 318 | 55.250    | 12001.370  | 429.7 |
| 321 | 22.635    | 4402.316   | 384.7 |
| 322 | 68.302    | >24663.650 | -     |
| 323 | 11406.357 | >25553.360 | -     |
| 324 | 1329.728  | 1927.309   | 2.9   |
| 325 | 928.583   | >25546.770 | -     |
| 326 | 6741.438  | >25645.230 | -     |
| 327 | 30.097    | >25671.500 | -     |
| 328 | 15.357    | 1698.302   | 218.8 |
| 330 | 487.667   | >25645.230 | -     |
| 331 | 62.577    | 66.606     | 2.1   |
| 332 | 77.474    | 58.853     | 1.5   |
| 333 | 134.727   | 212.627    | 3.1   |
| 334 | 249.757   | 461.777    | 3.7   |
| 335 | 1060.440  | 311.556    | 0.6   |
| 336 | 631.959   | 304.533    | 1.0   |
| 337 | 400.475   | 89.638     | 0.4   |
| 338 | 307.997   | 25.677     | 0.2   |
| 339 | 311.774   | 70.289     | 0.4   |
| 340 | 312.126   | 94.738     | 0.6   |
| 341 | 362.926   | 72.771     | 0.4   |
| 342 | 220.158   | 4832.731   | 43.4  |
| 343 | 198.013   | 19629.289  | 196.1 |
| 521 | 677.458   | 10099.850  | 29.5  |
| 522 | 508.426   | 6363.603   | 24.8  |
| 523 | 615.272   | >24743.230 | -     |
| 524 | 365.830   | >24393.160 | -     |
| 525 | 177.315   | 2454.700   | 27.4  |
| 526 | 194.459   | 689.991    | 7.0   |

**Table 8. Potency of Peptides with Modification on Amino Acid at Position 24**

| Peptide | hGLP-1R EC <sub>50</sub><br>(pM) | hGluc-R EC <sub>50</sub><br>(pM) | % Relative<br>Potency Ratio |
|---------|----------------------------------|----------------------------------|-----------------------------|
| 343     | 58.553                           | 125.666                          | 4.2                         |
| 344     | 134.933                          | >26900.000                       | -                           |
| 345     | 2860.629                         | 167.753                          | 0.1                         |
| 346     | 7318.019                         | 202.791                          | 0.1                         |
| 347     | 4971.036                         | 596.962                          | 0.2                         |
| 348     | 70.074                           | 4107.919                         | 116.0                       |
| 349     | 121.061                          | 83.684                           | 1.4                         |
| 350     | 88.617                           | 383.622                          | 8.6                         |
| 351     | 605.282                          | 216.444                          | 0.7                         |
| 352     | 192.562                          | 139.241                          | 1.4                         |

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|     |          |           |       |
|-----|----------|-----------|-------|
| 353 | 311.480  | 162.628   | 1.0   |
| 354 | 1106.278 | 901.878   | 1.6   |
| 355 | 424.009  | 478.456   | 2.2   |
| 356 | 304.243  | 315.728   | 2.1   |
| 357 | 916.728  | 550.189   | 1.2   |
| 358 | 74.855   | 16049.922 | 424.1 |
| 359 | 46.101   | 5048.643  | 216.6 |
| 360 | 107.773  | 5640.213  | 103.5 |
| 361 | 35.698   | 23.565    | 1.3   |
| 362 | 54.824   | 42.799    | 1.5   |
| 363 | 18.268   | 47.517    | 5.1   |
| 364 | 23.354   | 30.435    | 2.6   |
| 365 | 51.340   | 8.774     | 0.3   |
| 366 | 31.038   | 27.411    | 1.7   |
| 367 | 139.499  | 72.449    | 1.0   |
| 368 | 186.325  | 290.003   | 3.1   |
| 369 | 103.653  | 201.633   | 3.8   |
| 370 | 323.469  | 182.253   | 1.1   |
| 371 | 190.869  | 87.178    | 0.9   |
| 372 | 71.789   | 35.094    | 1.0   |
| 373 | 66.677   | 242.458   | 7.2   |
| 374 | 434.390  | 260.160   | 1.2   |
| 375 | 225.465  | 154.858   | 1.4   |
| 376 | 155.910  | 853.499   | 10.8  |
| 377 | 149.787  | 189.515   | 2.5   |
| 378 | 158.745  | 157.793   | 2.0   |
| 379 | 71.766   | 85.739    | 2.4   |
| 380 | 871.183  | 14947.910 | 33.9  |
| 381 | 174.069  | 1308.052  | 14.9  |
| 382 | 56.012   | 329.333   | 11.6  |
| 383 | 197.271  | 231.689   | 2.3   |
| 384 | 796.819  | 1244.347  | 3.1   |
| 386 | 31.186   | 140.185   | 8.9   |
| 387 | 82.603   | 1573.075  | 37.7  |
| 388 | 52.732   | 71.929    | 2.7   |
| 389 | 224.224  | 135.698   | 1.2   |

**Table 9. Potency of Peptides with Modification on Amino Acid at Position 10**

| Peptide | hGLP-1R EC <sub>50</sub><br>(pM) | hGluc-R EC <sub>50</sub><br>(pM) | % Relative<br>Potency Ratio |
|---------|----------------------------------|----------------------------------|-----------------------------|
| 391     | 892.536                          | 22172.801                        | 49.1                        |
| 392     | 312.355                          | 6922.306                         | 43.8                        |
| 393     | 0.458                            | 2.158                            | 9.3                         |
| 394     | 0.652                            | 2.408                            | 7.3                         |
| 395     | 0.774                            | 9.554                            | 24.4                        |
| 396     | 0.583                            | 11.835                           | 40.2                        |
| 397     | 5.360                            | 10.003                           | 3.7                         |
| 398     | 3.280                            | 2.449                            | 1.5                         |

**Table 10. Potency of Peptides with Modification on Amino Acid at Position 13**

| Peptide | hGLP-1R EC <sub>50</sub><br>(pM) | hGluc-R EC <sub>50</sub><br>(pM) | % Relative<br>Potency Ratio |
|---------|----------------------------------|----------------------------------|-----------------------------|
| 399     | 0.672                            | 5.567                            | 16.4                        |
| 400     | 1.268                            | 10.714                           | 16.7                        |
| 401     | 0.585                            | 9.542                            | 32.3                        |
| 402     | 1.044                            | 18.081                           | 34.3                        |
| 404     | 5.652                            | 21.821                           | 7.6                         |
| 405     | 1041.139                         | 8585.500                         | 16.3                        |
| 406     | 457.645                          | 7308.311                         | 31.6                        |

**Example 3: Mouse Acute Food Intake Study**

[0156] Male C57Bl/6 mice obtained from Jackson Laboratories or Charles River at 8 – 9 weeks of age and were housed one per cage in BioDaq (Research Diets) cages. Mice were placed on Alpha Dri bedding, standard chow diet (Envigo, 2018) and given water pouches. Mice were allowed to acclimate for 1- 2 weeks. Body weight was measured to ensure appropriate acclimation. After acclimation, mice were sham dosed a minimum of 2 times prior to initiation of food intake study. On study day, mice were placed in clean cage bottoms, weighed, and fasted for 6 – 8 hours. Mice were sorted into groups based on average 24-hour food intake data and body weight. 1 – 2 hours prior to lights out, mice were dosed subcutaneously with one vehicle or test peptide dissolved in an appropriate vehicle at 5 mL/kg. Mice were left undisturbed and allowed access to food and water for 48 hours. Automated food intake was monitored in the BioDaq system was monitored during this time.

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Discrete food intake data was exported into MS Excel from which cumulative food intake data was generated and analyzed. Food intake at 24 hours compared to vehicle food intake (percent) is provided in **Table 11**.

**Table 11. Food Intake of Mice Administered Lipidated Peptides**

| Peptide | Dose      | 24hr % Vehicle Food Intake | Standard Error of the Mean (SEM) |
|---------|-----------|----------------------------|----------------------------------|
| 43      | 10nmol/kg | 53.2                       | 4.9                              |
| 46      | 10nmol/kg | 72.1                       | 4.3                              |
| 47      | 10nmol/kg | 51.4                       | 4.9                              |
| 49      | 10nmol/kg | 69.2                       | 9.0                              |
| 50      | 10nmol/kg | 78.5                       | 4.1                              |
| 69      | 10nmol/kg | 74.3                       | 4.6                              |
| 68      | 10nmol/kg | 74.2                       | 4.2                              |
| 96      | 10nmol/kg | 51.9                       | 5.5                              |
| 62      | 10nmol/kg | 52.7                       | 3.1                              |
| 63      | 10nmol/kg | 37.9                       | 7.0                              |
| 71      | 10nmol/kg | 80.6                       | 11.5                             |
| 45      | 10nmol/kg | 76.2                       | 4.7                              |
| 399     | 10nmol/kg | 72.3                       | 9.6                              |
| 102     | 10nmol/kg | 81.9                       | 14.6                             |
| 73      | 10nmol/kg | 63.4                       | 4.2                              |
| 7       | 10nmol/kg | 55.0                       | 4.0                              |
| 349     | 10nmol/kg | 79.9                       | 4.2                              |
| 203     | 10nmol/kg | 81.4                       | 7.3                              |
| 361     | 10nmol/kg | 78.8                       | 5.3                              |
| 364     | 10nmol/kg | 63.7                       | 5.5                              |
| 366     | 10nmol/kg | 83.5                       | 9.4                              |
| 223     | 10nmol/kg | 63.6                       | 6.3                              |
| 229     | 10nmol/kg | 54.8                       | 5.6                              |
| 224     | 10nmol/kg | 66.5                       | 7.8                              |
| 375     | 10nmol/kg | 66.0                       | 7.7                              |
| 247     | 10nmol/kg | 66.9                       | 5.5                              |
| 257     | 3nmol/kg  | 94.7                       | 6.6                              |
| 257     | 10nmol/kg | 96.5                       | 3.7                              |
| 224     | 1nmol/kg  | 91.3                       | 10.9                             |
| 224     | 3nmol/kg  | 76.6                       | 3.3                              |
| 224     | 10nmol/kg | 72.5                       | 8.3                              |
| 229     | 1nmol/kg  | 86.0                       | 4.7                              |
| 229     | 3nmol/kg  | 72.5                       | 3.6                              |
| 229     | 10nmol/kg | 50.5                       | 3.7                              |
| 289     | 3nmol/kg  | 76.1                       | 6.9                              |
| 289     | 10nmol/kg | 49.6                       | 6.7                              |
| 299     | 30nmol/kg | 43.7                       | 7.3                              |

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|     |           |       |      |
|-----|-----------|-------|------|
| 301 | 10nmol/kg | 54.9  | 7.6  |
| 300 | 10nmol/kg | 45.2  | 6.5  |
| 302 | 30nmol/kg | 46.4  | 9.5  |
| 140 | 10nmol/kg | 65.4  | 5.5  |
| 195 | 10nmol/kg | 58.2  | 8.7  |
| 188 | 10nmol/kg | 60.7  | 6.3  |
| 188 | 1nmol/kg  | 99.9  | 6.3  |
| 188 | 3nmol/kg  | 80.6  | 5.6  |
| 188 | 10nmol/kg | 49.8  | 5.1  |
| 195 | 1nmol/kg  | 102.1 | 16.9 |
| 195 | 3nmol/kg  | 84.0  | 13.3 |
| 195 | 10nmol/kg | 49.9  | 4.4  |

**Example 4: Evaluating Proteolytic-Resistance of Lipidated Peptides to Fasted State Stimulated Gastric Fluid (FasSSGF) Containing Porcine Pancreatic Pepsin**

[0157] Lyophilized porcine pancreatic pepsin (Sigma: P7012) was reconstituted to 0.5 mg/mL (~2500 units/mL) in freshly prepared FasSSGF (Biorelevant media) to give the enzyme stock solution. Peptide stock solution was prepared to a concentration of 250  $\mu$ M (~1.0 mg/mL) in FasSSGF. 200  $\mu$ L (10  $\mu$ g, ~250 units) of pepsin stock solution was added to 200  $\mu$ L of peptide solution (1.0 mg/mL, ~100  $\mu$ g of peptide, ~25 nmoles) and the mixture was co-incubated in a temperature-regulated incubator at 37°C for the duration of the experiment. 30  $\mu$ L aliquot of the peptide-enzyme mixture was periodically withdrawn (t = 0, 5, 10, 15, and 30 min) and quenched immediately by addition of 80  $\mu$ L of 0.1M ammonium bicarbonate solution in water/acetonitrile (4:1, pH 8) to arrest proteolytic activity. 30  $\mu$ L aliquot was analyzed by analytical RP-HPLC. Analytical RP-HPLC method: Agilent Polaris C8-A column (4.6 x 100 mm, 3 micron) eluted with a linear binary gradient of 10 – 90% MeCN (0.1% TFA v/v) in water (0.1% TFA v/v) over either 10 or 15 mins at 1.5 mL min<sup>-1</sup> at 40°C with detection by UV absorption at 210 nm. Manual integration (AUC) allowed estimation of remaining intact peptide over the time course of the experiment. Peptide stability data is provided in **Table 12**.

**Table 12. Stability of Lipidated Peptides Incubated with FasSSGF**

| Peptide            | % intact peptide over time (min) |     |    |     |     |
|--------------------|----------------------------------|-----|----|-----|-----|
|                    | 0                                | 5   | 10 | 15  | 30  |
| <b>Semaglutide</b> | 100                              | 15  | 13 | 12  | 14  |
| <b>7</b>           | 100                              | 81  | 60 | 35  | 18  |
| <b>229</b>         | 100                              | 100 | 97 | 91  | 79  |
| <b>15</b>          | 100                              | ND  | ND | 91  | 77  |
| <b>78</b>          | 100                              | ND  | ND | 100 | 100 |
| <b>290</b>         | 100                              | ND  | ND | 0   | 0   |
| <b>282</b>         | 100                              | ND  | ND | 83  | 76  |
| <b>283</b>         | 100                              | ND  | ND | 68  | 48  |
| <b>287</b>         | 100                              | ND  | ND | 0   | 0   |
| <b>367</b>         | 100                              | ND  | ND | 0   | 0   |

**Example 5: Evaluating Proteolytic Resistance of Peptides to Neprilysin**

**[0158]** 10.0 µg (~10 units) recombinant Neprilysin (R&D Systems: 1182-ZNC-010) was reconstituted to 100 µL (100 µg/mL, ~100 units/mL) in assay buffer (50 mM Tris, 50mM NaCl, 50mM NaHCO<sub>3</sub>, adjusted to pH 8.3) to give the enzyme stock solution. Peptide stock solutions were prepared to a concentration of ~250 µM (~1.0 mg/mL of 4 kDa peptide) in assay buffer. 100 µL (10 µg, ~10 units) of neprilysin stock solution was added to 100 µL of peptide stock solution (1.0 mg/mL, ~100 µg of peptide) and the mixture was co-incubated in a temperature regulated incubator at 37°C for the duration of the experiment. 25 µL aliquots (~ 12.5 µg initial peptide) of the peptide-enzyme mixture were periodically withdrawn (t = 0, 30 mins, 1 h, 2 h, 4 h and 24 h) and quenched immediately by addition to an equal volume (75 µL) of 10% TFA (v/v) in 1:1 water/acetonitrile to arrest proteolytic activity. The quenched aliquot centrifuged at 7800 rpm, and 30 µL of the supernatant was analyzed by analytical RP-HPLC as follows: Analytical RP-HPLC method: Agilent Polaris C8-A column (4.6 x 100 mm, 3 micron) eluted with a linear binary gradient of 10 – 90% MeCN (0.1% TFA v/v) in water (0.1% TFA v/v) over either 10 or 15 mins at 1.5 mL min<sup>-1</sup> at 40°C with detection by UV absorption at 210 nm. Manual integration (AUC) allowed estimation of remaining intact peptide over the time course of the experiment. Peptide stability data is provided in **Table 13**.

**Table 13. Stability of Lipidated Peptides Incubated with Neprilysin**

| Peptide     | % intact peptide over time |        |      |      |       |
|-------------|----------------------------|--------|------|------|-------|
|             | 0                          | 30 min | 2 hr | 4 hr | 24 hr |
| Semaglutide | 100                        | 100    | 100  | 83   | 48    |
| 7           | 100                        | 100    | 100  | 97   | 84    |
| 229         | 100                        | 100    | 100  | 100  | 100   |
| 15          | 100                        | ND     | ND   | 100  | 83    |
| 78          | 100                        | ND     | ND   | 100  | 100   |
| 290         | 100                        | ND     | ND   | 89   | 82    |
| 282         | 100                        | ND     | ND   | 100  | 97    |
| 283         | 100                        | ND     | ND   | 81   | 63    |
| 287         | 100                        | ND     | ND   | 77   | 59    |

**Example 6: Evaluating Proteolytic-Resistance of Mono-Lipidated Peptides to Fasted-State Simulated Intestinal Fluid (FasSSIF/Pancreatin)**

[0159] A fresh suspension of FasSSIF/P (Fasted-State Simulated Intestinal Fluid + USP Pancreatin®) was prepared according to that described by Galia, Nicolaides, Hörter, Löbenberg, Reppas and Dressman: Pharm. Res. 15 (1998) 698–705, and USP XL requirements. The preparation of FasSSIF/P is provided in **Table 14**. The resulting preparation was used immediately without storage.

**Table 14. Preparation of FasSSIF/Pancreatin**

| Composition                                | Conc. mM | Mol. Weight | Mass L-1 | Supplier data |
|--------------------------------------------|----------|-------------|----------|---------------|
| Sodium Taurocholate hydrate                | 3        | 537.68      | 1.61 g   | Sigma: 86339  |
| L- $\alpha$ -phosphatidylcholine (soybean) | 0.5      | av. 768     | 0.38 g   | Sigma: 44924  |
| Dibasic sodium phosphate                   | 30       | 141.96      | 4.26 g   | Sigma: S7907  |
| Sodium hydroxide                           | 10       | 40.00       | 0.40 g   | Sigma: S8045  |
| Sodium Chloride                            | 100      | 58.44       | 5.84 g   | Sigma: S7653  |
| Pancreatin (8 x USP)                       |          | -           | 1.25 g   | Sigma: P7545  |

[0160] Peptide for evaluation (1.0 mg) was dissolved in pre-warmed FasSSIF without Pancreatin® (200  $\mu$ L). To this fresh FasSSIF/Pancreatin® (100  $\mu$ L) was added to initiate potential proteolysis. Following momentary vortexing of the reaction tube the mixture was incubated at 37°C in a thermostatic water bath for the duration of the experiment. 25  $\mu$ L

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aliquot of the co-incubated peptide-enzyme mixture was periodically withdrawn ( $t = 0, 5, 10, 15$  and  $30$  min) and quenched immediately by addition to a solution of 10% TFA in 1:1 water/acetonitrile ( $75 \mu\text{L}$ ) to arrest proteolytic activity. Quenched samples were centrifuged ( $7800$  RPM,  $3$  mins) to pellet solids and  $10 \mu\text{L}$  aliquots of the supernatant solution were analyzed using analytical RP-HPLC as follows: Analytical RP-HPLC method: Agilent Polaris C8-A column ( $4.6 \times 100$  mm,  $3$  micron) eluted with a linear binary gradient of  $10 - 90\%$  MeCN ( $0.1\%$  TFA v/v) in water ( $0.1\%$  TFA v/v) over either  $10$  or  $15$  mins at  $1.5 \text{ mL min}^{-1}$  at  $40^\circ\text{C}$  with detection by UV absorption at  $210 \text{ nm}$ . Manual integration (AUC) allowed estimation of remaining intact peptide over the time course of the experiment. Peptide stability data is provided in **Table 15**.

**Table 15. Stability of Lipidated Peptides Incubated with FasSSIF.**

| Peptide     | % intact peptide over time (min) |    |    |    |    |
|-------------|----------------------------------|----|----|----|----|
|             | 0                                | 5  | 10 | 15 | 30 |
| Semaglutide | 100                              | 22 | 0  | 0  | 0  |
| 7           | 100                              | 96 | 98 | 96 | 94 |
| 229         | 100                              | 60 | 46 | 33 | 26 |
| 78          | 100                              | 83 | 76 | 69 | 58 |
| 47          | 100                              | 90 | 88 | 83 | 75 |
| 49          | 100                              | 97 | 96 | 95 | 90 |
| 117         | 100                              | 54 | 35 | 22 | 8  |
| 43          | 100                              | 83 | 33 | 29 | 19 |
| 48          | 100                              | ND | ND | ND | 94 |
| 50          | 100                              | ND | ND | ND | 98 |
| 51          | 100                              | ND | ND | ND | 91 |
| 52          | 100                              | ND | ND | ND | 90 |
| 53          | 100                              | ND | ND | ND | 92 |

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**Example 7: Glucose Levels in GLP-1R Knockout Mice Treated  
with GLP-1/Glucagon Peptides**

**[0161]** GLP-1R knockout (KO) and wildtype (WT) mice at 8-14 weeks of age were singly housed on standard chow diet (Envigo, 2918) and automatic water. They acclimated for a minimum of ~1-2 weeks, and mice were sorted into groups (n=4-8/group) based on body weight. On day of study, mice were fasted briefly for 2 hrs prior to study start. In some studies, mice were pre-treated with octreotide (BaChem, 10mg/kg) at 30 minutes prior to peptide injection. Mice were dosed by subcutaneous injection, with peptide administration at doses listed in the **Tables 16 and 17**. Glucose was measured via glucometer at various timepoints including -30 min (prior to octreotide when used in studies), 0 min (before peptide dose), 30, 60, 120, 180, 240, and 360 minutes. Since these studies are acute in nature, mice were re-used for multiple studies (no more than 3) and always allowed at least a minimum wash-out period of 1 week. Glucose changes represented as percent glucose change (at 60 or 120 min) from time 0 min are provided in **Tables 16 and 17**.

**Table 16. Glucose Change in GLP-1R KO and WT Mice Treated with GLP-1/Glucagon Peptides**

| Peptide   | Dose      | WT %<br>glucose<br>change<br>120min | WT<br>SEM | GLP-1R<br>KO%<br>glucose<br>change<br>120min | KO %<br>glucose<br>change<br>SEM | Somatostatin pretreatment? |
|-----------|-----------|-------------------------------------|-----------|----------------------------------------------|----------------------------------|----------------------------|
| Vehicle   | 5mL/kg    | 0.9                                 | 6.3       | -0.7                                         | 7.6                              | No                         |
| <b>78</b> | 3nmol/kg  | -42.0                               | 2.1       | 51.3                                         | 15.4                             | No                         |
| Vehicle   | 5mL/kg    | -19.2                               | 6.7       | -9.1                                         | 9.5                              | No                         |
| <b>69</b> | 3nmol/kg  | -27.2                               | 7.7       | 17.6                                         | 4.8                              | No                         |
| <b>43</b> | 3nmol/kg  | -56.0                               | 4.7       | 63.9                                         | 39.2                             | No                         |
| Vehicle   | 5mL/kg    | 43.3                                | 12.6      | 72.4                                         | 24.9                             | yes 30 min prior to cpd    |
| <b>49</b> | 10nmol/kg | -1.2                                | 7.2       | 193.3                                        | 16.2                             | yes 30 min prior to cpd    |
| <b>49</b> | 30nmol/kg | 16.8                                | 25.9      | 154.3                                        | 17.0                             | yes 30 min prior to cpd    |
| Vehicle   | 5mL/kg    | 28.6                                | 6.2       | 23.4                                         | 8.7                              | yes 30 min prior to cpd    |

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|                |            |       |      |       |      |                         |
|----------------|------------|-------|------|-------|------|-------------------------|
| <b>97</b>      | 10nmol/kg  | -41.9 | 3.0  | 91.1  | 25.5 | yes 30 min prior to cpd |
| <b>97</b>      | 30nmol/kg  | -14.7 | 7.8  | 150.8 | 17.3 | yes 30 min prior to cpd |
| <b>Vehicle</b> | 5mL/kg     | 25.8  | 12.9 | 14.1  | 6.9  | yes 30 min prior to cpd |
| <b>63</b>      | 10nmol/kg  | -26.4 | 5.2  | 68.2  | 10.2 | yes 30 min prior to cpd |
| <b>63</b>      | 30nmol/kg  | -23.8 | 12.1 | 113.0 | 40.1 | yes 30 min prior to cpd |
| <b>Vehicle</b> | 5mL/kg     | 30.0  | 17.4 | 29.2  | 14   | yes 30 min prior to cpd |
| <b>126</b>     | 10nmol/kg  | -26.6 | 6.1  | 76.1  | 16.6 | yes 30 min prior to cpd |
| <b>126</b>     | 30nmol/kg  | -46.2 | 3.9  | 92.4  | 30.2 | yes 30 min prior to cpd |
| <b>Vehicle</b> | 5mL/kg     | 2.2   | 5.2  | 20.5  | 7    | yes 30 min prior to cpd |
| <b>399</b>     | 10nmol/kg  | -35.4 | 3.6  | 151.0 | 52.7 | yes 30 min prior to cpd |
| <b>399</b>     | 30nmol/kg  | -45.0 | 2.9  | 121.3 | 15.6 | yes 30 min prior to cpd |
| <b>Vehicle</b> | 5mL/kg     | 11.2  | 6.5  | 12.0  | 8.7  | yes 30 min prior to cpd |
| <b>203</b>     | 10nmol/kg  | -29.5 | 4.9  | 54.6  | 17.3 | yes 30 min prior to cpd |
| <b>203</b>     | 30nmol/kg  | -36.5 | 5.1  | 106.9 | 19.5 | yes 30 min prior to cpd |
| <b>Vehicle</b> | 5mL/kg     | 14.4  | 7.0  | 49.9  | 17.7 | yes 30 min prior to cpd |
| <b>361</b>     | 10nmol/kg  | -23.0 | 10.6 | 91.5  | 14.5 | yes 30 min prior to cpd |
| <b>361</b>     | 30nmol/kg  | -38.1 | 4.7  | 93.8  | 21.1 | yes 30 min prior to cpd |
| <b>Vehicle</b> | 5mL/kg     | 10.7  | 8.9  | 31.4  | 16.6 | yes 30 min prior to cpd |
| <b>7</b>       | 1.5nmol/kg | 5.4   | 8.3  | 80.8  | 14.3 | yes 30 min prior to cpd |
| <b>7</b>       | 5nmol/kg   | -21.2 | 9.8  | 152.9 | 43.0 | yes 30 min prior to cpd |
| <b>Vehicle</b> | 5mL/kg     | 51.6  | 16.5 | 15.5  | 13.8 | yes 30 min prior to cpd |
| <b>349</b>     | 10nmol/kg  | 4.9   | 14.3 | 27.8  | 13.5 | yes 30 min prior to cpd |
| <b>349</b>     | 30nmol/kg  | -17.3 | 7.3  | 100.2 | 21.8 | yes 30 min prior to cpd |
| <b>Vehicle</b> | 5mL/kg     | 19.9  | 9.0  | 39.1  | 10.6 | yes 30 min prior to cpd |
| <b>224</b>     | 3nmol/kg   | -46.3 | 4.8  | 100.3 | 34   | yes 30 min prior to cpd |
| <b>224</b>     | 10nmol/kg  | -40.0 | 5.0  | 132.3 | 32.6 | yes 30 min prior to cpd |
| <b>Vehicle</b> | 5mL/kg     | 2.5   | 4.4  | 10.2  | 4.9  | No                      |
| <b>229</b>     | 10nmol/kg  | -36.7 | 5.2  | 14.2  | 9.0  | No                      |
| <b>229</b>     | 30nmol/kg  | -40.6 | 2.3  | 44.5  | 5.3  | No                      |
| <b>Vehicle</b> | 5mL/kg     | 7.3   | 9.2  | 19.2  | 4.1  | No                      |

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|            |           |       |     |     |     |    |
|------------|-----------|-------|-----|-----|-----|----|
| <b>289</b> | 10nmol/kg | -8.5  | 7.7 | 8.9 | 4.6 | No |
| <b>289</b> | 30nmol/kg | -16.1 | 5.9 | 7.7 | 5.6 | No |

**Table 17. Glucose Change in GLP-1R KO and WT Mice Treated with GLP-1/Glucagon Peptides**

| Peptide | Dose      | WT % glucose change 60min | WT SEM | GLP-1R KO% glucose change - 60min | KO % glucose change SEM | Somatostatin pretreatment? |
|---------|-----------|---------------------------|--------|-----------------------------------|-------------------------|----------------------------|
| Vehicle | 5mL/kg    | -4.1                      | 4.4    | 16.2                              | 7.4                     | No                         |
| 301     | 10nmol/kg | -43                       | 3.2    | 29.1                              | 16.1                    | No                         |
| 301     | 30nmol/kg | -35.7                     | 4.3    | 17.9                              | 7.7                     | No                         |
| Vehicle | 5mL/kg    | 3.7                       | 3.7    | 6.3                               | 2.1                     | No                         |
| 140     | 10nmol/kg | -32.1                     | 2.8    | 46.2                              | 6.8                     | No                         |
| 140     | 30nmol/kg | -29.0                     | 3.0    | 59.8                              | 11.4                    | No                         |
| Vehicle | 5mL/kg    | 9.9                       | 6.9    | 2.8                               | 3.4                     | No                         |
| 188     | 10nmol/kg | -23.2                     | 3.9    | 64                                | 15.6                    | No                         |
| 188     | 30nmol/kg | -31.3                     | 2.5    | 44.6                              | 11.0                    | No                         |
| Vehicle | 5mL/kg    | 10.5                      | 5.4    | 7.8                               | 4.0                     | No                         |
| 195     | 10nmol/kg | 1.4                       | 3.4    | 35.3                              | 5.4                     | No                         |
| 195     | 30nmol/kg | -17.0                     | 4.9    | 48.0                              | 15.1                    | No                         |

**Example 8: Pharmacokinetic profiling in pre-clinical species**

[0162] Selected test peptides (n=8) were profiled for pharmacokinetic (PK) properties in the mouse after single intravenous (i.v.) or subcutaneous (s.c.) dose. A subset (n=4) meeting the acceptance criteria was subsequently profiled in the dog (single i.v. dose) and non-human primate (single i.v. and s.c. dose). After administration, blood was sampled up to 48 hrs in the mouse, 120 hrs in the dog and 168 hrs in the non-human primate, at time points selected to accurately determine the full pharmacokinetic profile in each species. Low-binding plasticware containers were used during preparation and sample handling to avoid non-specific binding.

[0163] **Mouse:** PK was studied in lean male C57BL/6 (Peptide 140, Peptide 188, Peptide 195, Peptide 420, Peptide 477 and Peptide 472) or male C57BL/6 DIO pre-conditioned mice on high-fat diet (Peptide 224, Peptide 229). After dosing, PK samples were collected from the dorsal metatarsal vein. Blood of each sample was transferred into plastic micro centrifuge tubes containing EDTA-K2, inverted several times for proper mixing of contents and then placed on wet ice. The blood samples were centrifuged at 4°C to obtain plasma and stored at -75°C prior to analysis.

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- [0164] **Dog:** PK was studied in non-naïve male Beagle dogs. After dosing, PK samples were collected from the jugular vein. Blood of each sample was transferred into plastic micro centrifuge tubes containing EDTA-K2, inverted several times for proper mixing of contents and then placed on wet ice. Plasma was separated by centrifugation and stored frozen in matrix tubes at a temperature set to maintain -20°C until analysis.
- [0165] **Non-human primate:** PK was studied in non-naïve male cynomolgus monkeys. After dosing, PK samples were collected from the femoral vein. Blood of each sample was transferred into plastic micro centrifuge tubes containing EDTA-K2, inverted several times for proper mixing of contents and then placed on wet ice. The blood samples were centrifuged under refrigerated (2°C to 8°C) conditions within 30 minutes following sample collection to obtain plasma and stored at -60°C to -90°C °C prior to analysis.
- [0166] **Formulation:** Test articles were formulated in 20 mM Sodium Phosphate, 220 mM Sorbitol pH 7.5 (Peptide 224, Peptide 229, Peptide 140, Peptide 188, Peptide 195) or 20 mM sodium acetate 220 mM mannitol pH 4.5 (Peptide 420, Peptide 477, Peptide 472).
- [0167] **Samples analysis:** Samples were analyzed by LC-MS/MS. Calibration standards were injected at the beginning and end of each batch and the determined concentration for each prepared standard was used to construct a calibration curve. Plasma and dose aliquot sample concentrations were determined from the plasma calibration curve.
- [0168] **Data analysis:** Plasma concentration data was analyzed by non-compartmental analysis (NCA) using Phoenix Winnonlin v. 8.3.3.33. Linear trapezoidal rule was used for increasing values and log trapezoidal rule was used for decreasing values, applying uniform weighting for  $\lambda_z$  calculations. Subcutaneous bioavailability was calculated as the ratio  $AUC(s.c.)_{0-inf} / AUC(i.v.)_{0-inf}$ . Reported values (**Table 18**) represent the mean of the individual estimates.
- [0169] **Results:** Test peptide half-life after intravenous administration and absolute bioavailability after subcutaneous administration calculated by NCA are reported in **Table 18**. Generally, test peptides displayed pro-longed circulation half-lives in all studied pre-clinical species, and additionally a significant extension in higher order species as compared to rodent. In the mouse, estimated half-lives spanned 2.9 – 19 hrs, in the dog 86 – 71 hrs and in non-human primates 49 - 130 hrs. The bioavailability after subcutaneous administration

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was generally  $\geq 50\%$ , with comparable levels in the mice and non-human primates. Test peptides evaluated in non-human primates all displayed high bioavailability  $\geq 75\%$ .

**Table 18. Pre-clinical PK.** Half-life after intravenous administration and absolute subcutaneous bioavailability of profiled test peptides in mouse, dog and non-human primate at specified doses.

| Species | Strain        | Alias          | Dose           | Half-life i.v.<br>administration | S.c.<br>bioavailability |
|---------|---------------|----------------|----------------|----------------------------------|-------------------------|
|         |               |                | <i>nmol/kg</i> | <i>h</i>                         | <i>%</i>                |
| Mouse   | C57bl/6       | Peptide<br>140 | 10             | 6.4                              | 102                     |
|         |               | Peptide<br>188 | 10             | 7.9                              | 98                      |
|         |               | Pptide<br>195  | 10             | 11                               | 66                      |
|         |               | Peptide<br>420 | 10             | 5.7                              | 49                      |
|         |               | Peptide<br>472 | 10             | 2.9                              | 83                      |
|         |               | Peptide<br>477 | 10             | 8.9                              | 50                      |
|         | C57bl/6 (DIO) | Peptide<br>224 | 10             | 9.5                              | 109                     |
|         |               | Peptide<br>229 | 10             | 19                               | 86                      |
| Dog     | Beagle        | Peptide<br>224 | 10             | 75                               | <i>n.d.</i>             |
|         |               | Peptide<br>229 | 10             | 86                               | <i>n.d.</i>             |

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|     |            |                |    |     |             |
|-----|------------|----------------|----|-----|-------------|
|     |            | Peptide<br>188 | 10 | 71  | <i>n.d.</i> |
|     |            | Peptide<br>195 | 10 | 78  | <i>n.d.</i> |
| NHP | Cynomolgus | Peptide<br>224 | 10 | 100 | 95          |
|     |            | Peptide<br>229 | 20 | 130 | 75          |
|     |            | Peptide<br>188 | 10 | 67  | 79          |
|     |            | Peptide<br>195 | 10 | 49  | 77          |

*n.d.: not determined.*

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WHAT IS CLAIMED IS:

1. A peptide comprising the sequence: H-X2-X3-G-X5-X6-T-S-D-X10-S-X12-  $\alpha$ Methyl-Phenylalanine ( $\alpha$ MePhe)-L-X15-X16-X17-X18-A-X20-X21-X22-X23-X24-X25-X26-X27-X28-X29-X30-X31-Z, wherein

X2 is Aminoisobutyric acid (Aib), S, or A,

X3 is Q, H, or E,

X5 is T or S,

X6 is F or  $\alpha$ MePhe,

X10 is V, K or Y,

X12 is K, E, or S,

X15 is D or E,

X16 is T, S, or G,

X17 is K, R, E, or Q,

X18 is R or A,

X20 is R, K, or Q,

X21 is D or E,

X22 is  $\alpha$ MePhe or F,

X23 is V or I,

X24 is Q or A,

X25 is Aib or W,

X26 is L or I,

X27 is L, A, E, V, or M,

X28 is E, N, A, R, or K,

X29 is Aib, T, or G,

X30 is G, R, or not present,

X31 is G or not present, and

Z is amide or acid (SEQ ID NO: 540).

2. The peptide of claim 1, wherein X2 is Aib.
3. The peptide of claim 1 or 2, wherein X3 is Q.

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4. The peptide of claim 1 or 2, wherein X3 is H.
5. The peptide of any one of claims 1-4, wherein X5 is T.
6. The peptide of any one of claims 1-4, wherein X5 is S.
7. The peptide of any one of claims 1-6, wherein X6 is F.
8. The peptide of any one of claims 1-6, wherein X6 is  $\alpha$ MePhe.
9. The peptide of any one of claims 1-8, wherein X10 is V.
10. The peptide of any one of claims 1-9, wherein X12 is K.
11. The peptide of any one of claims 1-10, wherein X15 is D.
12. The peptide of any one of claims 1-11, wherein X16 is T.
13. The peptide of any one of claims 1-11, wherein X16 is S.
14. The peptide of any one of claims 1-13, wherein X17 is K.
15. The peptide of any one of claims 1-13, wherein X17 is R.
16. The peptide of any one of claims 1-15, wherein X18 is R.
17. The peptide of any one of claims 1-15, wherein X18 is A.
18. The peptide of any one of claims 1-17, wherein X20 is R.
19. The peptide of any one of claims 1-17, wherein X20 is K.
20. The peptide of any one of claims 1-19, wherein X21 is D.
21. The peptide of any one of claims 1-20, wherein X22 is F.
22. The peptide of any one of claims 1-20, wherein X22 is  $\alpha$ MePhe.
23. The peptide of any one of claims 1-22, wherein X23 is V.

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24. The peptide of any one of claims 1-23, wherein X24 is Q.
25. The peptide of any one of claims 1-24, wherein X25 is W.
26. The peptide of any one of claims 1-24, wherein X25 is Aib.
27. The peptide of any one of claims 1-26, wherein X26 is L.
28. The peptide of any one of claims 1-26, wherein X26 is I.
29. The peptide of any one of claims 1-28, wherein X27 is L.
30. The peptide of any one of claims 1-28, wherein X27 is A.
31. The peptide of any one of claims 1-30, wherein X28 is E.
32. The peptide of any one of claims 1-30, wherein X28 is N.
33. The peptide of any one of claims 1-32, wherein X29 is Aib.
34. The peptide of any one of claims 1-32, wherein X29 is T.
35. The peptide of any one of claims 1-34, wherein X30 is G.
36. The peptide of any one of claims 1-34, wherein X30 is not present.
37. The peptide of any one of claims 1-36, wherein X31 is not present.
38. The peptide of any one of claims 1-36, wherein Z is amide.
39. The peptide of any one of claims 1-36, wherein Z is acid.
40. The peptide of claim 1, wherein X2 is Aib, X12 is K, and X24 is Q.
41. The peptide of claim 1, wherein X16 is T, X17 is K, X27 is L, X28, is E, and X29 is Aib.
42. The peptide of claim 1, wherein X3 is Q, X5 is T, X6 is F, X10 is V, X12 is K, X15 is D, X16 is T, X17 is K, X18 is R, X20 is R, X21 is D, X22 is F, X23 is V, X24 is Q, X25 is W, X26 is L, X27 is L, X28 is E, X29 is Aib, X30 is G, X31 is not present, and Z is acid.

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43. The peptide of claim 1, wherein X3 is H, X5 is S, X6 is  $\alpha$ MePhe, X10 is V, X12 is K, X15 is D, X16 is S, X17 is R, X18 is A, X20 is K, X21 is D, X22 is  $\alpha$ MePhe, X23 is V, X24 is Q, X25 is Aib, X26 is I, X27 is A, X28 is N, X29 is T, X30 is not present, X31 is not present, and Z is amide.
44. The peptide of any one of claims 1-43, wherein one or more lysine residues are acylated.
45. The peptide of claim 44, wherein the lysine at position 17 is acylated.
46. The peptide of claim 44, wherein the lysine at position 20 is acylated.
47. The peptide of any one of claims 1-46, wherein one or more lysine residues are lipidated.
48. The peptide of claim 47, wherein the lysine at position 17 is lipidated.
49. The peptide of claim 47, wherein the lysine at position 20 is lipidated.
50. The peptide of any one of claims 47-49, wherein the lipid is selected from the group consisting of octadecanedioic acid (C18diacid) and icosanedioic acid (C20diacid).
51. The peptide of claim 50, wherein the lipid is octadecanedioic acid (C18diacid).
52. The peptide of claim 50, wherein the lipid is icosanedioic acid (C20diacid).
53. The peptide of any one of claims 44-52, wherein the lipid is linked to the epsilon amino group of lysine at position 17 or 20 via a linker.
54. The peptide of claim 53, wherein the linker is ((O2Oc)-(O2Oc)- $\gamma$ E) or ((O2Oc)-(O2Oc)- $\gamma$ E- $\gamma$ E) in the C- to N-terminal orientation.
55. The peptide of claim 53 or 54, wherein the linker is ((O2Oc)-(O2Oc)- $\gamma$ E) in the C- to N-terminal orientation.
56. The peptide of claim 53 or 54, wherein the linker is ((O2Oc)-(O2Oc)- $\gamma$ E- $\gamma$ E) in the C- to N-terminal orientation.

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57. The peptide of any one of claims 53-55, wherein the linker is linked to the epsilon amino group of the residue at position 17 or 20.
58. A peptide comprising the sequence of H-Aib-Q-G-T-F-T-S-D-V-S-K- $\alpha$ MePhe-L-D-T-K-R-A-R-D-F-V-Q-W-L-L-E-Aib-G-acid (SEQ ID NO: 541).
59. The peptide of claim 58, wherein the lysine at position 17 is acylated and lipidated, the lipid is linked to the acylated lysine via its epsilon amino group to ((O2Oc)-(O2Oc)- $\gamma$ E) linker in the C to N terminal orientation, and the lipid is octadecanedioic acid (C18diacid).
60. The peptide of claim 58, wherein the lysine at position 17 is acylated and lipidated, the lipid is linked to the acylated lysine via its epsilon amino group to ((O2Oc)-(O2Oc)- $\gamma$ E) linker in the C to N terminal orientation, and wherein the lipid is icosanedioic acid (C20diacid).
61. A peptide comprising the sequence H-Aib-H-G-S- $\alpha$ MePhe-T-S-D-V-S-K- $\alpha$ MePhe-L-D-S-R-A-A-K( $\epsilon$ -(O2Oc)-(O2Oc)- $\gamma$ E-C18diacid)20-D- $\alpha$ MePhe-V-Q-Aib-I-A-N-T-amide (SEQ ID NO: 228).
62. A peptide comprising the sequence H-Aib-H-G-S- $\alpha$ MePhe-T-S-D-V-S-K- $\alpha$ MePhe-L-D-S-R-A-A-K( $\epsilon$ -(O2Oc)-(O2Oc)- $\gamma$ E- $\gamma$ E-C20diacid)20-D- $\alpha$ MePhe-V-Q-Aib-I-A-N-T-amide (SEQ ID NO: 233).
63. The peptide of any one of claims 1-62, wherein the peptide binds to the GLP-1 receptor (GLP-1R), binds to the glucagon receptor (GCGR), or binds to both a GLP-1 receptor and a glucagon receptor.
64. The peptide of claim 63, wherein the GLP-1R is a human GLP-1R.
65. The peptide of claims 63 or 64, wherein the GCGR is a human GCGR.
66. The peptide of any one of claims 1-65, wherein the peptide is an agonist of GLP-1 activity, an agonist of glucagon activity, or an agonist of both GLP-1 and glucagon activity.
67. The peptide of any one of claims 1-66, wherein the peptide has increased proteolytic-resistance relative to the natural ligand of the GLP-1R and/or GCGR.

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68. The peptide of any one of claims 1-67, wherein the peptide is isolated.
69. The peptide of any one of claims 1-68, wherein the peptide has at least 50%, at least 60%, at least 70%, at least 75%, at least 80%, at least 85%, at least 90%, at least 95, or 100% of intact peptide remaining after incubation with a protease at 37°C for 5min, 10min, 15min, 30min, 2hr, 4hr or 24hr.
70. The peptide of claim 69, wherein the protease is selected from the group consisting of neprilysin, pepsin, pancreatin, simulated gastric fluid with pepsin, and simulated intestinal fluid with pancreatin.
71. The peptide of any one of claims 1-70, wherein the peptide has a half-life in cynomolgus monkeys after intravenous administration of at least 45 hours, at least 50 hours, at least 60 hours, at least 70 hours, at least 80 hours, at least 90 hours, at least 100 hours, at least 110 hours, at least 120 hours, or about 130 hours.
72. The peptide of any one of claims 1-71 wherein the peptide has an s.c. bioavailability in cynomolgus monkeys of at least 75%, at least 80%, at least 90%, or about 95%.
73. A pharmaceutical composition comprising the peptide of any one of claims 1-72.
74. The composition of claim 73, wherein the composition is a solid composition.
75. The composition of claim 73 wherein the composition is a liquid composition.