

AMYLIN ANALOGUES FOR REDUCING CONSUMPTION OF HIGH-FAT FOOD

FIELD OF THE INVENTION

The present invention relates to the use of petrelintide to reduce consumption of high-fat
5 food.

BACKGROUND TO THE INVENTION

Obesity is a currently a significant public health issue across much of the developed world and is correlated with the development of several serious conditions, such as cardiovascular
10 disease, type 2 diabetes, sleep apnoea, and certain cancers. The standard treatment for obesity is lifestyle intervention, including the reduction of energy intake and the increase of exercise. However, while such interventions can achieve temporary success, it is often challenging for patients to sustain such lifestyle changes over a long period such that the weight loss achieved is permanent.

15 Amylin is one of a family of peptide hormones that includes amylin, calcitonin, calcitonin gene-related peptide, adrenomedullin and intermedin (intermedin also being known as AFP-6), and has been implicated in various metabolic diseases and disorders. Human amylin was first isolated, purified and characterized as the major component of amyloid deposits in the
20 islets of pancreases from type 2 diabetes patients.

Native human amylin is a 37-amino acid peptide having the sequence:

Hy-KC()₁NTATC()₂ATQRLANFLVHSSNNFGAILSSTNVGSNTY-NH₂
(SEQ ID NO: 2)

25 wherein Hy- at the N-terminus designates a hydrogen atom, corresponding to the presence of a free amino group on the N-terminal amino acid residue [i.e. the lysine (K) residue at sequence position number 1 in the sequence shown above], wherein -NH₂ at the C-terminus indicates that the C-terminal carboxyl group is in the amide form, and wherein the parentheses “()” associated with the two cysteine (C, Cys) residues at sequence positions 2
30 and 7 indicate the presence of an intramolecular disulfide bridge between the two Cys residues.

Amylin may be beneficial in treating metabolic disorders such as diabetes and/or obesity. Amylin is believed to regulate gastric emptying, and to suppress glucagon secretion and
35 food intake, thereby regulating the rate of glucose release to the circulation. Amylin appears to complement the actions of insulin. Compared to healthy adults, type 1 diabetes patients

have no circulating amylin, and type 2 diabetes patients exhibit reduced postprandial amylin concentrations.

WO 2018/046719 describes amylin analogues having, inter alia, a lactam bridge instead of a
5 disulfide bridge, N-methylated residues, and a deletion corresponding to the residues Asn21 and Asn22 of native human amylin. Such analogues have considerably lower tendency towards fibrillation than native amylin, while also having higher potency than other known amylin analogues.

10 SUMMARY OF THE INVENTION

Broadly, the present invention relates to methods of reducing consumption of high-fat food by a subject. Otherwise expressed, the invention relates to altering food preference of a subject, such that the subject preferentially consumes non-high-fat food, rather than high-fat food.

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More specifically, the invention is based on the surprising finding that administration to a subject of an long-acting amylin analogue comprising a lactam bridge results (petrelintide, compound 35) in reduced intake (i.e. consumption) of high-fat food but does not affect consumption of non-high-fat food.

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The methods and uses of the invention therefore advantageously promote effective weight loss as a subject which prefers non-high-fat food would be more likely to adhere to a dietary regimen of non-high-fat food.

25 The methods and uses of the invention also promote healthy weight loss because the subject's food preference changes to healthier, non-high-fat food.

The methods and uses of the invention may thus be useful for therapy, allowing treatment or prevention of conditions characterised by, or associated with, excess body fat, such as
30 overweight, obesity and morbid obesity, and diseases associated with overweight, obesity and morbid obesity.

Additionally, weight loss due to reduction of consumption of high fat food would be desirable for cosmetic reasons, even in subjects that do not suffer from a medical condition or disease
35 such as obesity. Thus, the invention also provides use of petrelintide in non-therapeutic methods of reducing consumption of high fat food.

Petrelintide comprises a lactam bridge between the amino acids at positions 2 and 7.

In this respect, native amylin is known to form fibrils in aqueous solution almost instantly.

The tendency for fibrillation can be reduced by incorporating N-methylated residues (as
5 mentioned above) and/or by substitution of certain amino acids at various positions. Native
amylin, and the vast majority of amylin analogues (such as pramlintide) contain a disulphide
bridge between cysteine residues at positions 2 and 7. The internal cyclisation which this
bridge provides appears to be required for full potency and activity. Compounds containing
an internal disulphide bond are frequently less chemically stable than might be desired, and
10 the presence of the bond may contribute to dimerisation and oligomerisation, e.g. via
disulphide exchange reactions.

However, lactam-based cyclisations are very compatible with amylin analogues having
deletions at positions 21 and 22, as the replacement of the disulphide bridge by a lactam
15 bridge leads to a substantial increase of stability in aqueous solution while other beneficial
properties of these amylin analogues, such as low tendency for fibrillation, high activity and
good solubility are retained.

Thus, petrelintide retains amylin receptor agonist activity (i.e. activity at the hCT-R, hAMYR1,
20 hAMYR2 and/or hAMYR3 receptors) but additionally has excellent chemical stability and
resistance to fibrillation, especially but not exclusively in the neutral pH range. This
enhanced chemical stability in aqueous solution would facilitate development of a
corresponding pharmaceutical product, potentially even in the form of a ready-to-use
formulation, e.g. at or around the neutral pH range (pH 7 – 7.4).

25 Furthermore, petrelintide is a “long-acting” amylin analogue in that it has a much longer half-
life than native amylin and other “short-acting” amylin analogues. In particular, native amylin
has a half-life of about 15 minutes in humans, and the amylin analogue pramlintide has a
half-life of about 50 minutes in humans. In contrast, petrelintide has a half-life of about 10
30 days in humans. It may not be expected that long-acting petrelintide works in the same way
as short-acting amylin receptor agonists, such as native amylin. The longer half-life of
petrelintide facilitates longer dosing intervals, such as once weekly dosing.

It has now been surprisingly shown that petrelintide causes reduced consumption of high-fat
35 food preferentially over non-high-fat food when administered to a subject.

Thus, it is now recognised for the first time that petrelintide combines the characteristics of potent amylin receptor agonist activity, the ability to reduce consumption of specifically high-fat food, excellent chemical stability and resistance to fibrillation, and long half-life. In particular, it may not be expected that petrelintide, as a long-acting amylin analogue, would affect food preference.

The invention therefore provides a method of reducing consumption of high-fat food by a subject, the method comprising administering to the subject petrelintide or a pharmaceutically acceptable salt or solvate thereof.

The invention also provides a method of treating or preventing overweight, obesity, morbid obesity or a disease associated with overweight, obesity, morbid obesity in a subject, wherein the method reduces consumption of high-fat food by the subject, the method comprising administering to the subject petrelintide or a pharmaceutically acceptable salt or solvate thereof.

The invention accordingly also provides medical uses of petrelintide or a pharmaceutically acceptable salt or solvate thereof in the methods described herein.

The amylin analogue is petrelintide, which has the following formula:

[19CD]-isoGlu-RD()GTATK()ATERLA-Aad-FLQRSSF-Gly(Me)-A-Ile(Me)-LSSTEVGSTNT-Hyp-NH₂ (SEQ ID NO: 1)

wherein

[19CD]-isoGlu is a 19-carboxynonadecanoyl group covalently attached to the alpha amino group of an iso-glutamic acid linker; an intramolecular lactam bridge is formed between the side chains of residues indicated by parentheses “()”;

Aad refers to 2-aminoadipic acid;

Gly(Me) refers to N-methylglycine;

Ile(Me) refers to N-methylisoleucine; and

Hyp refers to 4-hydroxyproline.

Petrelintide is also referred to as Compound 35 herein.

In some embodiments, the subject is following a weight loss dietary regimen. The combination of administration of petrelintide with a weight loss dietary regimen may provide

particularly effective weight loss as petrelintide improves compliance with the weight loss dietary regimen.

BRIEF DESCRIPTION OF THE FIGURES

- 5 In the Figures, “Q2D” means administration once every 2 days, “Q4D” means administration once every 4 days and “BID” means administration twice every day.

Figure 1 shows the actual (A) and relative (B) body weight change (day 1 = 100%) recorded on a daily basis for obese rats administered vehicle, petrelintide or liraglutide, as indicated.

- 10 Data are expressed as mean $\pm$ standard error of the mean (SEM) (n = 10); treatment groups were compared to the vehicle-treated group by use of a two-way ANOVA RM followed by Bonferroni’s multiple comparison tests. → indicate Q4D dosing days. *P<0.05, **P<0.01, ***P<0.001.

- 15 **Figure 2** shows the relative body weight change (day 1 = 100%) recorded on day 30 for obese rats administered vehicle, petrelintide or liraglutide, as indicated. Data are expressed as mean $\pm$ standard error of the mean (SEM) (n = 10).

- 20 **Figure 3** shows the daily intake of chow (g) per two animals in obese rats administered vehicle, petrelintide or liraglutide, as indicated. Animals were semi fasted on day 30 (50% high-fat diet; no chow offered). Data are expressed as mean $\pm$ SEM (n = 10); treatment groups were compared to the vehicle-treated group by use of a two-way ANOVA RM followed by Bonferroni’s multiple comparison tests. → indicate Q4D dosing days.

- 25 **Figure 4** shows cumulative intake of chow during the entire study period quantified as grams per two animals in obese rats administered vehicle, petrelintide or liraglutide, as indicated. Data are expressed as mean $\pm$ SEM (n = 10). Data on day 30 have been omitted due to semi fast (no chow; 50% high-fat diet).

- 30 Total cumulative chow intake (A) in the treatment groups were compared to the vehicle-treated group by use of a one-way ANOVA with Dunnett’s post-hoc test. Cumulated chow intake per day during the study period (B) in the treatment groups were compared to the vehicle-treated group by use of a two-way ANOVA RM with Bonferroni’s multiple comparison test

- 35 **Figure 5** shows high-fat diet intake recorded daily in grams per two animals in obese rats administered vehicle, petrelintide or liraglutide, as indicated. Animals were semi fasted on

day 30 (50% high-fat diet; no chow offered). Data are expressed as mean $\pm$ SEM (n = 10); treatment groups were compared to the vehicle-treated group by use of a two-way ANOVA RM followed by Bonferroni's multiple comparison tests. → indicate Q4D dosing days.

*P<0.05, **P<0.01, ***P<0.001

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Figure 6 shows cumulative intake of high-fat diet during the entire study period quantified as grams per two animals in obese rats administered vehicle, petrelintide or liraglutide, as indicated. Data are expressed as mean $\pm$ SEM (n = 10). Data on day 30 have been omitted due to semi fast (no chow; 50% high-fat diet).

10 Total cumulated high-fat diet intake (**A**) in the treatment groups were compared to the vehicle-treated group by use of a one-way ANOVA with Dunnett's post-hoc test. Cumulated high-fat diet intake per day (**B**) in the treatment groups was compared to the vehicle-treated group by use of a two-way ANOVA RM with Bonferroni's multiple comparison test. *P<0.05, **P<0.01, ***P<0.001

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DETAILED DESCRIPTION OF THE INVENTION

Unless otherwise defined herein, scientific and technical terms used in this application shall have the meanings that are commonly understood by those of ordinary skill in the art.

Generally, nomenclature used in connection with, and techniques of, chemistry, molecular
20 biology, cell and cancer biology, immunology, microbiology, pharmacology, and protein and nucleic acid chemistry, described herein, are those well-known and commonly used in the art.

All patents, published patent applications and non-patent publications referred to in this
25 application are specifically incorporated by reference herein. In case of conflict, the present specification, including its specific definitions, will control.

Each embodiment of the invention described herein may be taken alone or in combination with one or more other embodiments of the invention.

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General definitions

Unless specified otherwise, the following definitions are provided for specific terms used in the present written description. All other terms will be understood as having a meaning that is common in the art as would be attributed to them by the person skilled in the art.

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Throughout this specification, the word “comprise”, and grammatical variants thereof, such as “comprises” or “comprising”, will be understood to imply the inclusion of a stated integer or component, or group of integers or components, but not the exclusion of any other integer or component, or group of integers or components.

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The singular forms “a,” “an,” and “the” include the plurals unless the context clearly dictates otherwise.

The term “including” is used to mean “including but not limited to”. “Including” and “including but not limited to” may be used interchangeably.

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Throughout the present description and claims, in representing agonist peptides the conventional three-letter and one-letter codes for naturally occurring amino acids are used, i.e.:

15 A (Ala), G (Gly), L (Leu), I (Ile), V (Val), F (Phe), W (Trp), S (Ser), T (Thr), Y (Tyr), N (Asn), Q (Gln), D (Asp), E (Glu), K (Lys), R (Arg), H (His), M (Met), C (Cys) and P (Pro);

as well as generally accepted three-letter codes for other α -amino acids, such as 2-aminoadipic acid (e.g. (2S)-2-aminoadipic acid [also known as (2S)-2-aminohexanedioic acid]) (“Aad”),

20 4-hydroxyproline, also referred to herein as hydroxyproline (e.g. (2S,4R)-4-hydroxyproline [also denoted (4R)-4-hydroxy-L-proline]) (“Hyp” or “4Hyp”),
N-methylglycine (also known as sarcosine (Sar)) (“Gly(Me)”), and
N-methylisoleucine (“Ile(Me)”).

25 Such other α -amino acids may be shown between hyphens “- -” (e.g. “-Aad-”) when used in a general formula or sequence in the present specification, especially when the rest of the formula or sequence is shown using the single letter code.

Unless otherwise specified, amino acid residues in peptides of the invention are of the L-configuration. However, D-configuration amino acids may be incorporated. In the present
30 context, an amino acid code written with a small letter represents the D-configuration of said amino acid, e.g. “k” represents the D-configuration of lysine (K).

Among sequences disclosed herein are sequences incorporating a “Hy-” or “H-” moiety at
35 the amino terminus (N-terminus) of the sequence, and either an “-OH” moiety or an “-NH₂” moiety at the carboxy terminus (C-terminus) of the sequence. In such cases, and unless otherwise indicated, a “Hy-” or “H-” moiety at the N-terminus of the sequence in question

indicates a hydrogen atom, corresponding to the presence of a free primary or secondary amino group at the N-terminus. An “-OH” moiety at the C-terminus of the sequence indicates a hydroxy group, corresponding to the presence of a carboxy (COOH) group at the C-terminus]. An “-NH₂” moiety at the C-terminus of the sequence indicates an amino group
 5 [e.g. R² = NH₂ in the general formulas], corresponding to the presence of an amido (CONH₂) group at the C-terminus. In each sequence, a C-terminal “-OH” moiety may be substituted for a C-terminal “-NH₂” moiety, and vice-versa.

Parentheses “()” shown after the symbols for particular amino acid residues indicate
 10 residues whose side chains participate in an intramolecular lactam bridge. Thus, petrelintide has an intramolecular lactam bridge between the side chains of the residues at position 2 (aspartic acid, D) and at position 7 (lysine, K) as indicated by parentheses.

Petrelintide

15 Petrelintide is an acylated peptide molecule that agonises amylin receptors. Petrelintide was first described in the patent application published as WO 2018/046719 A1 (which is incorporated herein by reference), wherein petrelintide was referred to as Compound 35. Petrelintide may be referred to herein as Compound 35 or Cpd 35.

20 Petrelintide has the following formula:

[19CD]-isoGlu-RD()GTATK()ATERLA-Aad-FLQRSSF-Gly(Me)-A-Ile(Me)-LSSTEVGST-Hyp-NH₂ (SEQ ID NO: 1)

wherein

[19CD]-isoGlu is a 19-carboxynonadecanoyl group covalently attached to the alpha amino
 25 group of an iso-glutamic acid linker;
 an intramolecular lactam bridge is formed between the side chains of residues indicated by parentheses “()”;

Aad refers to 2-aminoadipic acid;

Gly(Me) refers to N-methylglycine;

30 Ile(Me) refers to N-methylisoleucine; and

Hyp refers to 4-hydroxyproline.

The formula of petrelintide may also be presented as follows:

[19CD]-isoGlu-RD(cyclo)GTATK(cyclo)ATERLA-Aad-FLQRSSF-Gly(Me)-A-Ile(Me)-
 35 LSSTEVGST-Hyp-NH₂ (SEQ ID NO: 1)

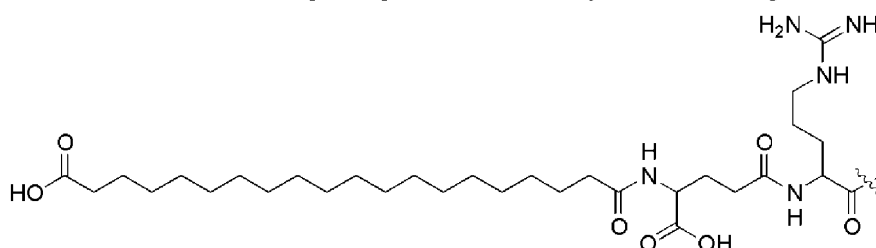
wherein

[19CD]-isoGlu is a 19-carboxynonadecanoyl group covalently attached to the alpha amino group of an iso-glutamic acid linker;

an intramolecular lactam bridge is formed between the side chains of residues followed by “(cyclo)”;

- 5 Aad refers to 2-aminoadipic acid;
 Gly(Me) refers to N-methylglycine;
 Ile(Me) refers to N-methylisoleucine; and
 Hyp refers to 4-hydroxyproline.

- 10 The chemical structure of [19CD]-isoGlu- covalently attached to arginine is shown below:



- 15 Petrelintide is an amylin receptor agonist. In other words, petrelintide is capable of binding to, and inducing signalling by, one or more receptors or receptor complexes regarded as physiological receptors for human amylin. These include the human calcitonin receptor (hCT-R), as well as complexes comprising hCT-R and at least one of the human receptor activity modifying proteins designated hRAMP1, hRAMP2 and hRAMP3. Complexes between hCT-R and hRAMP1, hRAMP2 and hRAMP3 are designated hAMYR1, hAMYR2 and hAMYR3 (i.e. human amylin receptors 1, 2 and 3) respectively. Petrelintide has agonist activity at hAMYR1, hAMYR2 and hAMYR3 as described in WO 2018/046719 A1. Binding to a suitable receptor induces intracellular signalling, e.g. cyclic AMP production. *In vivo*, petrelintide has the biological activity of (inter alia) reducing food intake, promoting weight loss, and/or inhibiting or reducing weight gain. It may be employed for various therapeutic applications as described elsewhere in this specification and in WO 2018/046719 A1.

- 25 Petrelintide may suitably be manufactured by standard synthetic methods. Thus, petrelintide may be synthesized by, e.g., methods comprising synthesizing the peptide by standard solid-phase or liquid-phase methodology, either stepwise or by fragment assembly, and optionally isolating and purifying the final peptide product. In this context, reference may be made to WO 98/11125 or, *inter alia*, Fields, G.B. et al., “Principles and Practice of Solid-Phase Peptide Synthesis”; in: *Synthetic Peptides*, Gregory A. Grant (ed.), Oxford University Press (2nd edition, 2002) and the synthesis examples herein. The method typically further

comprises the step of forming an amide bond between the side chains at positions 2 and 7, e.g. as described below. In the case of solid phase synthesis, cyclisation may be performed in situ on the solid phase (e.g. resin), i.e. before removal of the peptide from the solid phase. Synthesis of petrelintide is described in Example 1 of WO 2018/046719 A1.

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Pharmaceutically acceptable salts and solvates

Petrelintide as used in the invention may be in the form of a pharmaceutically acceptable salt or solvate, such as a pharmaceutically acceptable acid addition salt. Thus, it is to be understood that any reference herein to petrelintide encompasses pharmaceutically

10 acceptable salts and solvates thereof.

As used herein, the term “pharmaceutically acceptable salt” is intended to indicate a salt which is not harmful to a patient or subject to which the salt in question is administered. It may suitably be a salt chosen, e.g., among acid addition salts and basic salts. Suitable salts
15 formed with bases include metal salts, such as alkali metal or alkaline earth metal salts, for example sodium, potassium or magnesium salts; ammonia salts and organic amine salts, such as those formed with morpholine, thiomorpholine, piperidine, pyrrolidine, a lower mono-, di- or tri-alkylamine (e.g., ethyl-tert-butyl-, diethyl-, diisopropyl-, triethyl-, tributyl- or dimethylpropylamine), or a lower mono-, di- or tri-(hydroxyalkyl)amine (e.g., mono-, di- or
20 triethanolamine). Internal salts may also be formed. Similarly, when a compound of the present invention contains a basic moiety, salts can be formed using organic or inorganic acids. For example, salts can be formed from the following acids: formic, acetic, propionic, butyric, valeric, caproic, oxalic, lactic, citric, tartaric, succinic, fumaric, maleic, malonic, mandelic, malic, phthalic, hydrochloric, hydrobromic, phosphoric, nitric, sulphuric, benzoic,
25 carbonic, uric, methanesulphonic, naphthalenesulphonic, benzenesulphonic, toluenesulphonic, p-toluenesulphonic (i.e. 4-methylbenzene-sulphonic), camphorsulphonic, 2-aminoethanesulphonic, aminomethylphosphonic and trifluoromethanesulphonic acid (the latter also being denoted triflic acid), as well as other known pharmaceutically acceptable acids. Amino acid addition salts can also be formed with amino acids, such as lysine,
30 glycine, or phenylalanine. Other examples of pharmaceutically acceptable salts are described in “Remington’s Pharmaceutical Sciences”, 17th edition, Alfonso R. Gennaro (Ed.), Mark Publishing Company, Easton, PA, USA, 1985 (and more recent editions thereof), in the “Encyclopaedia of Pharmaceutical Technology”, 3rd edition, James Swarbrick (Ed.), Informa Healthcare USA (Inc.), NY, USA, 2007, and in *J. Pharm. Sci.* 66: 2 (1977).

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Petrelintide may be in the form of a pharmaceutically acceptable chloride salt. In some embodiments, petrelintide may have the formula

([19CD]-isoGlu-RD()GTATK()ATERLA-Aad-FLQRSSF-Gly(Me)-A-Ile(Me)-LSSTEVGSNT-Hyp-NH₂), x(Cl)

where x is 1.0-2.0.

- 5 The term “solvate” in the context of the present invention refers to a complex of defined stoichiometry formed between a solute (*in casu*, a peptide or pharmaceutically acceptable salt thereof according to the invention) and a solvent. The solvent in this connection may, for example, be water, ethanol or another pharmaceutically acceptable, typically small-molecular organic species, such as, but not limited to, acetic acid or lactic acid. When the
- 10 solvent in question is water, such a solvate is normally referred to as a hydrate.

Consumption of high-fat food

The invention provides a method of reducing consumption of high-fat food by a subject.

- 15 “Food” is a substance consumed by the subject to obtain nutrients. The term “consumption” refers to the subject eating food. “Consumption” is used interchangeably with the terms “eating” and “intake” herein.

- The term “high-fat food” refers to food that is relatively high in fat content. High-fat food may
- 20 be any food that is deemed to have a high fat content in the medical field or food industry. High-fat food may accordingly be labelled as such on its packaging in accordance with regulatory guidelines.

- The term “fat” as used herein refers to the nutrient group found in food, which encompasses
- 25 all types of molecules which may be referred to as fats (e.g. lipids, mono-, di- and triglycerides, phospholipids, free fatty acids).

- In some embodiments, high-fat food is food having a total fat content of about 5 g or more of fat per 100 g. In some embodiments, high-fat food is food having a total fat content of about
- 30 6 g or more, about 7 g or more, about 8 g or more, about 9 g or more, about 10 g or more, about 11 g or more, about 12 g or more, about 13 g or more, about 14 g or more, about 15 g or more, about 16 g or more, about 17 g or more, or about 17.5 g or more of fat per 100 g.

- Fat content of food may be measured using techniques known in the art, such as gas
- 35 chromatography and gravimetric techniques (acid hydrolysis, base hydrolysis or acid and base hydrolysis).

In the field of nutrition, fats are divided into saturated fats and unsaturated fats. The term “fat” as used herein encompasses both saturated fat and unsaturated fat. Foods high in saturated fats are regarded as unhealthy, and it is advised to restrict consumption of such foods.

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In some embodiments, high-fat food is food having a total saturated fat content of about 1 g or more of saturated fat per 100 g. In some embodiments, high-fat food is food having a total saturated fat content of about 2 g or more of saturated fat per 100 g, about 3 g or more, about 4 g or more, or about 5 g or more of saturated fat per 100 g.

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The term “non-high-fat food” is used herein to refer to any food which is not “high-fat food” (i.e. any food which does not fall within the definition of high-fat food). As such, non-high-fat food is not necessarily particularly low in fat, and indeed may have a comparatively high fat content. Non-high-fat food is simply food that is not “high-fat food” as defined herein.

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Reducing consumption of high-fat food

The methods and medical uses of the invention reduce consumption of high-fat food.

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It may be determined whether consumption of high-fat food by a subject treated with petrelintide is reduced by monitoring the amount (i.e. weight) of high-fat food and non-high-fat food consumed by the subject treated with petrelintide over time and comparing the amount of each type of food consumed by the subject to the amount of each type of food consumed by a control subject that not been administrated petrelintide.

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Thus, in some embodiments, the method reduces consumption of high-fat food by the subject over a period compared to a control subject that has not been administrated petrelintide.

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In some embodiments, the control or control subject is the same subject which has not been administered petrelintide according to the methods and uses of the invention for the same period at a different time-point (such as prior to administration of petrelintide). In other words, it can be determined whether consumption of high-fat food has been reduced by first measuring the consumption of high-fat food by the subject over a given period when the subject has not been administered petrelintide (or has been administered a vehicle), and subsequently measuring consumption of high-fat food by the subject over a period of the same length when the subject has been administered petrelintide.

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Herein, the period over which consumption of high-fat food is measured to determine whether consumption of high-fat food is reduced may be referred to as “the consumption measurement period”.

- 5 The consumption measurement period is thus the period over which consumption of high-fat food of the subject (and a control subject) is measured to determine whether consumption of high-fat food is indeed reduced. However, the total length of time over which a subject is administered petrelintide (i.e., the administration period) may be (and typically is) longer than the consumption measurement period.

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The person skilled in the art knows how to determine an appropriate length of consumption measurement period to reliably determine whether consumption of high-fat food is actually reduced. Example 1 describes an exemplary procedure for determining whether consumption of high-fat food is reduced in an animal model.

15

- In some embodiments, the period over which consumption of high-fat food by the subject is measured and compared to a control subject to determine whether consumption of high-fat food is reduced is at least about 1 day. In some embodiments, the period is at least about 2 days, at least about 3 days, at least about 4 days, at least about 5 days, at least about 6 days, at least about 30 days, at least about 1 week, at least about 2 weeks, at least about 3 weeks, at least about 4 weeks, at least about 1 month, at least about 6 months, at least about 1 year, at least about 2 years, at least about 3 years, at least about 4 years, at least about 5 years, at least about 6 years, at least about 7 years, at least about 8 years, at least about 9 years, at least about 10 years, or more than 10 years.

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- In other words, in some embodiments, the method reduces consumption of high-fat food by the subject over a period of at least about 1 day. In some embodiments, the method reduces consumption of high-fat food by the subject compared to a control subject over a period of at least about 1 day. In some embodiments, the period is at least about 2 days, at least about 3 days, at least about 4 days, at least about 5 days, at least about 6 days, at least about 30 days, at least about 1 week, at least about 2 weeks, at least about 3 weeks, at least about 4 weeks, at least about 1 month, at least about 6 months, at least about 1 year, at least about 2 years, at least about 3 years, at least about 4 years, at least about 5 years, at least about 6 years, at least about 7 years, at least about 8 years, at least about 9 years, or at least about 10 years.

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In some embodiments, the method reduces consumption of high-fat food by the subject compared to a control subject over a period of more than 10 years.

- In some embodiments, the period over which consumption of high-fat food is measured compared to a control subject to determine whether consumption of high-fat food is reduced is about 1 day. In some embodiments, the period is about 2 days, about 3 days, about 4 days, about 5 days, about 6 days, about 30 days, about 1 week, about 2 weeks, about 3 weeks, about 4 weeks, about 1 month, about 6 months, or about 1 year.
- In other words, in some embodiments, the method reduces consumption of high-fat food by the subject over a period of about 1 day. In other words, in some embodiments, the method reduces consumption of high-fat food by the subject compared to a control subject over a period of about 1 day. In some embodiments, the period is about 2 days, about 3 days, about 4 days, about 5 days, about 6 days, about 30 days, about 1 week, about 2 weeks, about 3 weeks, about 4 weeks, about 1 month, about 6 months, about 1 year, about 2 years, about 3 years, about 4 years, about 5 years, about 6 years, about 7 years, about 8 years, about 9 years, or about 10 years.

- The amount of high-fat food consumed may be expressed as total cumulative high-fat food intake over the consumption period (i.e. the total weight of high-fat food consumed between the start and end of the consumption period).

- In some embodiments, the method and use of the invention reduces consumption of high-fat food by the subject compared to a control subject by at least about 5% compared to a control. In other words, in such embodiments, the subject administered petrelintide consumes at most about 95% of the high-fat food that they would under control conditions.

- In some embodiments, the method reduces consumption of high-fat food by at least about 10%, at least about 15%, at least about 17%, at least about 20% at least about 25%, at least about 30%, at least about 33%, at least about 35%, at least about 40%, at least about 45%, at least about 50%, at least about 65%, at least about 66%, at least about 70%, at least about 75%, at least about 80%, at least about 85%, at least about 90%, at least about 95% or about 100% compared to a control. 100% reduction of consumption of high-fat food means that consumption of high-fat food is completely abolished (i.e. the subject no longer consumes any high-fat food).

In some embodiments, the method reduces consumption of high-fat food by the subject by about 5% to about 75%, such as about 10% to about 75%, about 15% to about 75%, or about 17% to about 75% compared to a control.

- 5 In some embodiments, the method reduces consumption of high-fat food by the subject by about 5% to about 70%, such as about 5% to about 66%, about 5% to about 65%, about 5% to about 60%, about 5% to about 55%, about 5% to about 50%, about 5% to about 45%, about 5% to about 40%, about 5% to about 35%, or about 5% to about 33% compared to a control.

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In some embodiments, the method reduces consumption of high-fat food by the subject by about 17% to about 66%, or about 17% to about 33% compared to a control.

- 15 In some embodiments, the method reduces consumption of high-fat food by the subject by at least about 5% compared to a control over a period of about 1 day. In some embodiments, the method reduces consumption of high-fat food by the subject by at least about 5% compared to a control over a period of about 2 days, about 3 days, about 4 days, about 5 days, about 6 days, about 30 days, about 1 week, about 2 weeks, about 3 weeks, about 4 weeks, about 1 month, about 6 months, about 1 year, about 2 years, about 3 years, about 4 years, about 5 years, about 6 years, about 7 years, about 8 years, about 9 years, or about 10 years.

- 25 In some embodiments, the method reduces consumption of high-fat food by the subject by at least about 10%, at least about 15%, at least about 17%, at least about 20% at least about 25%, at least about 30%, at least about 33%, at least about 35%, at least about 40%, at least about 45%, at least about 50%, at least about 65%, at least about 66%, at least about 70%, at least about 75%, at least about 80%, at least about 85%, at least about 90%, at least about 95% or about 100% compared to a control over a period of about 1 day. In some embodiments, the method reduces consumption of high-fat food by the subject by at least about 10%, at least about 15%, at least about 17%, at least about 20% at least about 25%, at least about 30%, at least about 33%, at least about 35%, at least about 40%, at least about 45%, at least about 50%, at least about 65%, at least about 66%, at least about 70%, at least about 75%, at least about 80%, at least about 85%, at least about 90%, at least about 95% or about 100% compared to a control over a period of about 2 days, about 3 days, about 4 days, about 5 days, about 6 days, about 30 days, about 1 week, about 2 weeks, about 3 weeks, about 4 weeks, about 1 month, about 6 months, about 1 year, about

2 years, about 3 years, about 4 years, about 5 years, about 6 years, about 7 years, about 8 years, about 9 years, or about 10 years.

Increasing consumption of non-high-fat food

- 5 In some embodiments, consumption of non-high-fat food by the subject does not change compared to a control. "Does not change" means that consumption of non-high-fat food by the subject increases or decreases by less than 1% compared to a control (i.e. the amount of non-high-fat food consumed is less than a 1% decrease or a less than 1% increase relative to control).

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In some embodiments, consumption of non-high-fat food by the subject increases compared to a control. In some embodiments, consumption of non-high-fat food by the subject does not change or increases compared to a control.

- 15 Whether the amount of non-high fat food consumed by a subject has changed may be determined in the same manner as described herein for high-fat food, namely by measuring the amount (i.e. weight) of non-high-fat food consumed by the subject to which petrelintide has been administered over a consumption period and comparing this to a control. In some embodiments, the control is the amount of non-high-fat food consumed by the same subject
20 over a period of the same length without having being administered petrelintide (or having been administered vehicle instead).

- In some embodiments, consumption of non-high-fat food by the subject increases by at least about 1% compared to a control. In some embodiments, consumption of non-high-fat food
25 by the subject increases by at least about 2%, at least about 3%, at least about 4%, at least about 5%, or at least about 10% compared to a control.

- In some embodiments, the period over which consumption of non-high-fat food by the subject is measured and compared to a control subject to determine whether there is a
30 change in consumption of non-high-fat food (the consumption period) is at least about 1 day. In some embodiments, the period is at least about 2 days, at least about 3 days, at least about 4 days, at least about 5 days, at least about 6 days, at least about 30 days, at least about 1 week, at least about 2 weeks, at least about 3 weeks, at least about 4 weeks, at least about 1 month, at least about 6 months, at least about 1 year, at least about 2 years, at
35 least about 3 years, at least about 4 years, at least about 5 years, at least about 6 years, at least about 7 years, at least about 8 years, at least about 9 years, or at least about 10 years.

In some embodiments, the period over which consumption of non-high-fat food by the subject is measured and compared to a control subject to determine whether there is a change in consumption of non-high-fat food (the consumption period) is more than 10 years.

- 5 In other words, in some embodiments, there is no change or an increase in consumption of non-high-fat food by the subject over a period of at least about 1 day. In some embodiments, there is no change or an increase in consumption of non-high-fat food by the subject compared to a control subject over a period of at least about 1 day. In some embodiments, the period is at least about 2 days, at least about 3 days, at least about 4 days, at least
10 about 5 days, at least about 6 days, at least about 30 days, at least about 1 week, at least about 2 weeks, at least about 3 weeks, at least about 4 weeks, at least about 1 month, at least about 6 months, at least about 1 year, at least about 2 years, at least about 3 years, at least about 4 years, at least about 5 years, at least about 6 years, at least about 7 years, at least about 8 years, at least about 9 years, or at least about 10 years.

15

In some embodiments, there is no change or an increase in consumption of non-high-fat food by the subject over a period of more than 10 years.

- In some embodiments, the consumption period is about 1 day. In some embodiments, the
20 period is about 2 days, about 3 days, about 4 days, about 5 days, about 6 days, about 30 days, about 1 week, about 2 weeks, about 3 weeks, about 4 weeks, about 1 month, about 6 months, about 1 year, about 2 years, about 3 years, about 4 years, about 5 years, about 6 years, about 7 years, about 8 years, about 9 years, or about 10 years.

- 25 In other words, in some embodiments, there is no change or an increase in consumption of non-high-fat food by the subject over a period of about 1 day. In some embodiments, the period is about 2 days, about 3 days, about 4 days, about 5 days, about 6 days, about 30 days, about 1 week, about 2 weeks, about 3 weeks, about 4 weeks, about 1 month, about 6 months, about 1 year, about 2 years, about 3 years, about 4 years, about 5 years, about 6
30 years, about 7 years, about 8 years, about 9 years, or about 10 years.

- In some embodiments, consumption of non-high-fat food by the subject increases by at least about 1% compared to a control over a period of about 1 day. In some embodiments, the
35 period is about 2 days, about 3 days, about 4 days, about 5 days, about 6 days, about 30 days, about 1 week, about 2 weeks, about 3 weeks, about 4 weeks, about 1 month, about 6 months, about 1 year, about 2 years, about 3 years, about 4 years, about 5 years, about 6 years, about 7 years, about 8 years, about 9 years, or about 10 years.

- In some embodiments, consumption of non-high-fat food by the subject increases by at least about 2%, at least about 3%, at least about 4%, at least about 5%, or at least about 10% compared to a control over a period of about 1 day. In some embodiments, the period is
- 5 about 2 days, about 3 days, about 4 days, about 5 days, about 6 days, about 30 days, about 1 week, about 2 weeks, about 3 weeks, about 4 weeks, about 1 month, about 6 months, about 1 year, about 2 years, about 3 years, about 4 years, about 5 years, about 6 years, about 7 years, about 8 years, about 9 years, or about 10 years.
- 10 The consumption measurement period (i.e. the period over which change in food consumption is measured) may be the same for determining change in consumption of high-fat food and determining change in consumption of non-high-fat food by the subject.

Altering food preference

- 15 As shown herein, a subject administered petrelintide consumes less high-fat food, and thus derives more of their calories from non-high-fat food. Thus, petrelintide may be described as altering the food preference of the subject.

- Accordingly, the invention provides a method of altering food preference of a subject, the
- 20 method comprising administering to the subject petrelintide or a pharmaceutically acceptable salt or solvate thereof.

- The invention also provides a method of altering food preference of a subject, such that the subject preferentially consumes non-high-fat food, rather than high-fat food, the method
- 25 comprising administering to the subject petrelintide or a pharmaceutically acceptable salt or solvate thereof.

- The invention also provides a method of altering food preference of a subject, such that the subject prefers non-high-fat food to high-fat food, the method comprising administering to the
- 30 subject petrelintide or a pharmaceutically acceptable salt or solvate thereof.

- Whether the food preference of a subject has altered can be measured by determining whether the amount of high-fat food the consumes is reduced compared to a control subject using the methods described herein.
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Effects on body weight

The invention provides petrelintide herein for use in a method of inhibiting weight gain and/or reducing body weight in a subject.

- 5 In other words, the methods and uses of the invention may be expressed as methods and uses of inhibiting weight gain and/or reducing body weight in the subject.

Thus, the invention provides a method of inhibiting weight gain and/or reducing body weight in a subject, wherein the method comprises administering to the subject petrelintide or a
10 pharmaceutically acceptable salt or solvate thereof.

The invention provides a method of inhibiting weight gain and/or reducing body weight in a subject by reducing consumption of high-fat food by the subject, wherein the method comprises administering to the subject petrelintide or a pharmaceutically acceptable salt or
15 solvate thereof.

The invention provides a method of inhibiting weight gain and/or reducing body weight in a subject by altering food preference of the subject, wherein the method comprises administering to the subject petrelintide or a pharmaceutically acceptable salt or solvate
20 thereof.

“Inhibiting weight gain” may also be referred to herein as “reducing weight gain”. “Reducing body weight” may also be referred to herein as “promoting weight loss”.

- 25 Petrelintide increases and prolongs the feeling of satiation experienced by a subject, thereby reducing the appetite of the subject, leading to reduced food intake. Thus, the invention may be expressed as petrelintide for use in a method of reducing food intake and/or reducing appetite. The invention may be expressed as petrelintide for use in a method of increasing and/or prolonging satiety. The invention may be expressed as petrelintide for use in a
30 method of increasing satiety. The invention may be expressed as petrelintide for use in a method of prolonging satiety.

In some embodiments, the method of the invention is a method of reducing food intake.

In some embodiments, the method of the invention is a method of reducing appetite.

- 35 In some embodiments, the method of the invention is a method of increasing satiety.

The effects of the compounds described above may be mediated in whole or in part via an effect on body weight, or may be independent thereof. Independently of their effect on body weight, the compounds of the invention may have a beneficial effect on glucose tolerance and/or glucose control.

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Methods and uses of the present invention are carried out *in vivo*.

Suppression of glucagon secretion and food intake associated with petrelintide, and in particular reduction of consumption of high-fat food, may promote weight loss, or at least
10 slow (i.e. reduce or inhibit) weight gain. Thus, the method of the invention may be expressed as a method of inhibiting or reducing weight gain, a method of promoting weight loss, a method of reducing food intake, and/or a method of reducing body weight in a subject, wherein lean mass is preserved in the subject.

15 Accordingly, the invention provides a method of reducing body mass (i.e. body weight) in a subject by reducing consumption of high-fat food by the subject, the method comprising administering to the subject petrelintide or a pharmaceutically acceptable salt or solvate thereof.

20 The invention also provides a method of inhibiting weight gain in a subject by reducing consumption of high-fat food by the subject, the method comprising administering to the subject petrelintide or a pharmaceutically acceptable salt or solvate thereof.

The invention also provides a method of inhibiting gain of body fat in a subject by reducing
25 consumption of high-fat food by the subject, the method comprising administering to the subject petrelintide or a pharmaceutically acceptable salt or solvate thereof.

The invention also provides a method of reducing body fat in a subject by reducing
30 consumption of high-fat food by the subject, the method comprising administering to the subject petrelintide or a pharmaceutically acceptable salt or solvate thereof.

The invention also provides a method of promoting weight loss in a subject by reducing
consumption of high-fat food by the subject, the method comprising administering to the
subject petrelintide or a pharmaceutically acceptable salt or solvate thereof.

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The terms "inhibiting weight gain" and "inhibiting gain of body fat" are used interchangeably herein.

The terms “body weight” and “body mass” are used interchangeably herein.

5 The term “body fat” refers to adipose tissue, which is the type of tissue which stores fat in the body. Body fat includes so-called “brown fat”, “beige fat” “white fat” and “pink fat”. Body fat includes particularly subcutaneous adipose tissue that stores excess fat, such as in the belly, thighs and hips of human subjects.

10 The amount of body fat in a given subject may be determined by methods known in the art. Such methods include skinfold tests, bioelectrical impedance analysis, hydrostatic weighing, dual-energy X-ray absorptiometry (DEXA), quantitative magnetic resonance (QMR) and air-displacement plethysmography (ADP). Examples of use of DEXA and QMR in animal models are described in, for example, Miller et al. *Physiol Behav* 2011 103(1) 117-121. EchoMRI™ is a commercially available type of QMR. ADP is described, for example, in the review article Fields et al. *Nutr Clin Pract* 2015 30(2) 219-226. The BOD POD® (COSMED, 15 Rome, Italy) is a commercially available measurement system for performing ADP.

In some embodiments, the subject exhibits a reduction in body weight upon administration of petrelintide. In some embodiments, the subject exhibits a reduction in body weight of at least 20 1%, such as at least 5%, at least 10%, at least 15%, at least 20%, at least 22.5% or at least 25%, compared to their body weight before administration of petrelintide. In some embodiments, the subject exhibits a reduction in body weight of at least 0.5% per month (i.e. 0.5% reduction in body weight at the end of each month compared to body weight at the start of the month), such as at least 0.75% per month, at least 1% per month, at least 1.25% 25 per month or at least 1.3% per month. In some embodiments, the subject exhibits a reduction in body weight of 0.5% per month, 0.75% per month, 1% per month, 1.25% per month or 1.3% per month.

To determine whether and by how much body weight of the subject has been reduced by the 30 methods of the invention, body weight of the subject is measured over time. In other words, in some embodiments, as a result of the method of the invention, the body weight of the subject is reduced by a given amount over a given period (i.e. the body weight of the subject at the end of the period differs from the body weight of the subject at the start of the period by a given amount).

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In some embodiments, a reduction in body weight is measured over a period of at least about 1 week. In some embodiments, a reduction in body weight is measured over a period

of at least about 2 weeks, at least about 3 weeks, at least about 4 weeks, at least about 30 days, at least about 1 month, at least about 2 months, at least about 6 months, at least about 1 year, at least about 2 years, at least about 3 years, at least about 4 years, at least about 5 years, at least about 6 years, at least about 7 years, at least about 8 years, at least about 9 years, or at least about 10 years.

In some embodiments, a reduction in body weight is measured over a period of more than 10 years.

In some embodiments, the body weight of the subject is reduced by at least about 1% over a period of about 1 week. In some embodiments, the body weight of the subject is reduced by at least about 1% over a period of about 30 days. In some embodiments, the body weight of the subject is reduced by at least about 1% over a period of about 1 month. In some embodiments, the body weight of the subject is reduced by at least about 1% over a period of about 6 months. In some embodiments, the body weight of the subject is reduced by at least about 1% over a period of about 1 year.

In some embodiments, the body weight of the subject is reduced by at least about 2% over a period of about 1 week. In some embodiments, the body weight of the subject is reduced by at least about 2% over a period of about 30 days. In some embodiments, the body weight of the subject is reduced by at least about 2% over a period of about 1 month. In some embodiments, the body weight of the subject is reduced by at least about 2% over a period of about 6 months. In some embodiments, the body weight of the subject is reduced by at least about 2% over a period of about 1 year.

In some embodiments, the body weight of the subject is reduced by at least about 5% over a period of about 6 months. In some embodiments, the body weight of the subject is reduced by at least about 5% over a period of about 1 year.

In some embodiments, the body weight of the subject is reduced by at least about 10% over a period of about 1 year.

In some embodiments, the body weight of the subject is reduced by at least about 1% over a period selected from about 1 week, about 2 weeks, about 3 weeks, about 4 weeks, about 30 days, about 1 month, about 2 months, about 6 months, about 1 year, about 2 years, about 5 years or about 10 years.

In some embodiments, the body weight of the subject is reduced by at least about 2% over a period selected from about 1 week, about 2 weeks, about 3 weeks, about 4 weeks, about 30 days, about 1 month, about 2 months, about 6 months, about 1 year, about 2 years, about 5 years or about 10 years.

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In some embodiments, the body weight of the subject is reduced by at least about 3% over a period selected from about 1 week, about 2 weeks, about 3 weeks, about 4 weeks, about 30 days, about 1 month, about 2 months, about 6 months, about 1 year, about 2 years, about 5 years or about 10 years.

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In some embodiments, the body weight of the subject is reduced by at least about 4% over a period selected from about 1 week, about 2 weeks, about 3 weeks, about 4 weeks, about 30 days, about 1 month, about 2 months, about 6 months, about 1 year, about 2 years, about 5 years or about 10 years.

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In some embodiments, the body weight of the subject is reduced by at least about 5% over a period selected from about 1 week, about 2 weeks, about 3 weeks, about 4 weeks, about 30 days, about 1 month, about 2 months, about 6 months, about 1 year, about 2 years, about 5 years or about 10 years.

20

In some embodiments, the body weight of the subject is reduced by at least about 6% over a period selected from about 1 week, about 2 weeks, about 3 weeks, about 4 weeks, about 30 days, about 1 month, about 2 months, about 6 months, about 1 year, about 2 years, about 5 years or about 10 years.

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In some embodiments, the body weight of the subject is reduced by at least about 7% over a period selected from about 1 week, about 2 weeks, about 3 weeks, about 4 weeks, about 30 days, about 1 month, about 2 months, about 6 months, about 1 year, about 2 years, about 5 years or about 10 years.

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In some embodiments, the body weight of the subject is reduced by at least about 8% over a period selected from about 1 week, about 2 weeks, about 3 weeks, about 4 weeks, about 30 days, about 1 month, about 2 months, about 6 months, about 1 year, about 2 years, about 5 years or about 10 years.

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In some embodiments, the body weight of the subject is reduced by at least about 9% over a period selected from about 1 week, about 2 weeks, about 3 weeks, about 4 weeks, about 30

days, about 1 month, about 2 months, about 6 months, about 1 year, about 2 years, about 5 years or about 10 years.

- 5 In some embodiments, the body weight of the subject is reduced by at least about 10% over a period selected from about 1 week, about 2 weeks, about 3 weeks, about 4 weeks, about 30 days, about 1 month, about 2 months, about 6 months, about 1 year, about 2 years, about 5 years or about 10 years.

Subject

- 10 The terms "patient", "subject", "participant" and "individual" are used interchangeably herein and refer to either a human or a non-human animal. These terms include mammals such as humans, non-human primates (e.g. great apes, Old World monkeys and New World monkeys), livestock animals (e.g. bovines and porcines), companion animals (e.g. canines and felines) and rodents (e.g. mice and rats). Preferably, the subject is human.

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In some embodiments of the methods of treatment and medical uses of the invention, the subject is of a healthy weight. In other words, in some embodiments, the subject is not overweight, not obese and not morbidly obese.

- 20 In some embodiments, the subject has a Body Mass Index (BMI) of 18.5 to 24.9 corresponding to healthy weight.

BMI is calculated for human subjects by dividing the weight of the subject in kilograms by the square of the height of the subject in metres.

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In some embodiments of the methods of treatment and medical uses of the invention, wherein the subject is overweight, obese or morbidly obese.

In some embodiments, the subject is overweight.

In some embodiments, the subject is obese.

- 30 In some embodiments, the subject is morbidly obese.

In some embodiments of the methods of treatment and medical uses of the invention, the subject has a BMI of 25.0 to 29.9 corresponding to overweight, a BMI of 30.0 to 39.9 corresponding to obese, or a BMI of 40.0 or higher corresponding to morbidly obese.

- 35 In some embodiments, the subject has a BMI of 25.0 to 29.9 corresponding to overweight. In some embodiments, the subject has a BMI of 30.0 to 39.9 corresponding to obese.

In some embodiments, the subject has a BMI of 40.0 or higher corresponding to morbidly obese.

Non-therapeutic uses

5 The methods of reducing consumption of high-fat food of the invention may be non-therapeutic methods. In other words, petrelintide may be used for non-therapeutic purposes. In this respect, it may be desirable for a subject to reduce high-fat food intake so as to lose weight (or inhibit weight gain), and thereby reduce body fat, despite the subject not being obese, diabetic or suffering from any other weight-related disease, such as for cosmetic reasons. Administration of petrelintide may achieve these desired effects (reduced food intake, weight loss and/or inhibited weight gain). In such embodiments, administration of petrelintide would not be therapeutic as no disease or disorder is being treated by petrelintide.

15 Petrelintide may be used for therapeutic or cosmetic purposes. Thus, the inhibition of weight gain or reduction of body weight of the subject may be cosmetic (i.e. non-therapeutic). Effects of the compounds of the invention on body weight may be therapeutic or cosmetic.

The invention further relates to petrelintide for use in methods that are not directed towards treating disease *per se*. Such uses and methods may be considered preventative of disease in so far as they may be utilised prior to the onset of disease (e.g. pre diagnosis) e.g. to ameliorate unwanted physiological characteristics or alter certain physiological parameters. Furthermore, such uses or methods may be considered cosmetic.

25 Thus, in some embodiments, the method of the invention is a non-therapeutic method.

The invention therefore provides a non-therapeutic method of reducing consumption of high-fat food by a subject, the method comprising administering to the subject petrelintide or a pharmaceutically acceptable salt or solvate thereof.

30 The non-therapeutic nature of certain methods of the invention is particularly pertinent when the subject is of healthy weight or overweight (i.e. a subject that is not obese or morbidly obese). Administration of petrelintide to a subject that is a healthy weight or that is overweight, for which there are no therapeutic reasons to reduce body fat, is a cosmetic (non-therapeutic) method.

The invention therefore provides a non-therapeutic method of reducing consumption of high-fat food by a subject of healthy weight, the method comprising administering to the subject an amylin analogue or a pharmaceutically acceptable salt or solvate thereof, wherein the amylin analogue is as defined herein.

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Body weight is defined in the medical field by body mass index (BMI). BMI is calculated for human subjects by dividing the weight of the subject in kilograms by the square of the height of the subject in metres. A BMI of 18.5 to 24.9 corresponds to healthy weight. A BMI of 25.0 to 29.9 corresponds to overweight. Thus, in some embodiments of the non-therapeutic (i.e.,
10 cosmetic) methods of the invention, the subject has a Body Mass Index (BMI) of 18.5 to 24.9 corresponding to healthy weight. In some embodiments of the non-therapeutic (i.e., cosmetic) methods of the invention, the subject has a BMI of 25.0 to 29.9 corresponding to overweight.

15 In other words, the subject of a non-therapeutic method of the invention of reducing consumption of high-fat food need not be obese or morbidly obese.

The invention therefore provides a non-therapeutic method of reducing consumption of high-fat food by a subject, the method comprising administering to the subject petrelintide or a
20 pharmaceutically acceptable salt or solvate thereof, wherein the subject is a healthy weight or is overweight.

The invention also provides a non-therapeutic method of altering food preference of a subject, the method comprising administering to the subject petrelintide or a
25 pharmaceutically acceptable salt or solvate thereof, wherein the subject is a healthy weight or is overweight.

Considerations regarding petrelintide as outlined herein apply equally when petrelintide is used for therapeutic and non-therapeutic purposes.

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Therapeutic uses

In accordance with the surprising finding that petrelintide reduces consumption of high-fat food, petrelintide has utility in a number of therapeutic settings. Petrelintide is useful in the treatment or prevention of disease.

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More specifically, petrelintide is useful, *inter alia*, in the reduction of food intake, promotion of weight loss, and inhibition or reduction of weight gain. Petrelintide may therefore provide an

attractive treatment option for, *inter alia*, obesity and metabolic diseases caused, characterized by, or associated with, excess body weight. Treatment may be achieved, for example, by control of appetite, feeding, food intake, calorie intake and/or energy expenditure.

5

The term "treatment" (as well as "treating" and other grammatical variants thereof) as employed in the context of the invention refers to an approach for obtaining beneficial or desired clinical results. For the purposes of the present invention, beneficial or desired clinical results include, but are not limited to, alleviation of symptoms, diminishment of extent of disease, stabilization of (i.e. not worsening of) state of disease, delay or slowing of disease progression, amelioration or palliation of disease state, and remission (whether partial or total), whether detectable or undetectable. "Treatment" may also refer to prolongation of survival compared to expected survival in the absence of treatment. "Treatment" is an intervention performed with the intention of preventing the development of, or altering the pathology of, a disorder. Accordingly, "treatment" refers both to therapeutic treatment and to prophylactic or preventative measures. As used in the context of prophylactic or preventative measures, the amylin analogue or concomitant agent need not completely prevent the development of the disease or disorder. Those in need of treatment include those already suffering from the disorder, as well as those in which development of the disorder is to be prevented. "Treatment" also means inhibition or reduction of an increase in pathology or symptoms (e.g. weight gain or hypoglycaemia) compared to the absence of treatment, and is not necessarily meant to imply complete cessation or cure of the relevant condition. The term "prevention" (as well as "preventing" and other grammatical variants thereof) refers to prophylaxis of disease, such as by reducing symptoms of disease.

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The terms "prevention" and grammatical variants thereof (e.g., "prevented", "preventing", "prevent") as employed in the present context refer to an approach for hindering or preventing the development of, or altering the pathology of, a condition, disease or disorder. Accordingly, "prevention" may refer to prophylactic or preventive measures. For the purposes of this invention, beneficial or desired clinical results include, but are not limited to, prevention or slowing of symptoms, progression or development of a disease, whether detectable or undetectable. A subject (e.g. a human) in need of "prevention" may thus be a subject not yet afflicted with the disease or disorder in question. The term "prevention" thus includes inhibiting or slowing the onset of disease relative to the absence of treatment, and is not necessarily meant to imply permanent prevention of the relevant disease, disorder or condition. In some embodiments, "prevention" or "prophylaxis" in the context of the present

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invention may mean prevention of weight gain (i.e. inhibiting weight gain). In some embodiments, "prevention" or "prophylaxis" may mean prevention of gain of body fat.

Methods of treatment

- 5 Therapeutic methods (i.e. methods of treating or preventing disease) are within the scope of the methods of reducing consumption of high-fat food of the invention, as described herein.

Thus, the invention provides a therapeutic method of reducing consumption of high-fat food by a subject, wherein the method treats or prevents a disease in the subject, the method
10 comprising administering to the subject petrelintide or a pharmaceutically acceptable salt or solvate thereof.

Furthermore, the invention provides a method of treating or preventing overweight, obesity, morbid obesity or a disease associated with overweight, obesity or morbid obesity in a
15 subject, wherein the method reduces consumption of high-fat food by the subject, the method comprising administering to the subject petrelintide or a pharmaceutically acceptable salt or solvate thereof.

Thus, the methods of the invention, when applied to a subject that is overweight, obese, morbidly obese or suffers from a disease associated with overweight, obesity or morbid
20 obesity, may be considered therapeutic methods.

However, for a method of the invention to be therapeutic it is not required that the subject is overweight, obese or morbidly obese. It will be understood in particular that in a method of
25 the invention of inhibiting weight gain, the subject need not be overweight, obese or morbidly obese. Such a method may be prophylactic in that it prevents (i.e. inhibits) weight gain as part of treatment of the disease from which the subject suffers.

The invention provides a method of treating overweight, obesity, morbid obesity or a disease associated with overweight, obesity or morbid obesity in a subject, wherein the method
30 reduces consumption of high-fat food by the subject, the method comprising administering to the subject petrelintide or a pharmaceutically acceptable salt or solvate thereof.

The invention provides a method of preventing overweight, obesity, morbid obesity or a disease associated with overweight, obesity or morbid obesity in a subject, wherein the
35 method reduces consumption of high-fat food by the subject, the method comprising

administering to the subject petrelintide or a pharmaceutically acceptable salt or solvate thereof.

5 The invention provides a method of treating or preventing overweight, obesity or morbid obesity in a subject, or preventing a disease associated with overweight, obesity or morbid obesity, in a subject, wherein the method reduces consumption of high-fat food by the subject, the method comprising administering to the subject petrelintide or a pharmaceutically acceptable salt or solvate thereof.

10 Furthermore, the invention provides a method of treating or preventing obesity, morbid obesity or a disease associated with obesity or morbid obesity in a subject, wherein the method reduces consumption of high-fat food by the subject, the method comprising administering to the subject petrelintide or a pharmaceutically acceptable salt or solvate thereof.

15 The invention provides a method of treating obesity, morbid obesity or a disease associated with obesity or morbid obesity in a subject, wherein the method reduces consumption of high-fat food by the subject, the method comprising administering to the subject petrelintide or a pharmaceutically acceptable salt or solvate thereof.

20 The invention provides a method of preventing obesity, morbid obesity or a disease associated with obesity or morbid obesity in a subject, wherein the method reduces consumption of high-fat food by the subject, the method comprising administering to the subject petrelintide or a pharmaceutically acceptable salt or solvate thereof.

25 The invention provides a method of treating or preventing obesity or morbid obesity in a subject, or preventing a disease associated with obesity or morbid obesity in a subject, wherein the method reduces consumption of high-fat food by the subject, the method comprising administering to the subject petrelintide or a pharmaceutically acceptable salt or solvate thereof.

30 Furthermore, the invention provides a method of treating or preventing obesity or morbid obesity in a subject, wherein the method reduces consumption of high-fat food by the subject, the method comprising administering to the subject petrelintide or a pharmaceutically acceptable salt or solvate thereof.

35 In some embodiments, the method is a method of treating or preventing overweight.
In some embodiments, the method is a method of treating overweight.

In some embodiments, the method is a method of preventing overweight.

In some embodiments, the method is a method of treating or preventing obesity.

In some embodiments, the method is a method of treating obesity.

5 In some embodiments, the method is a method of preventing obesity.

In some embodiments, the method is a method of treating or preventing morbid obesity.

In some embodiments, the method is a method of treating morbid obesity.

In some embodiments, the method is a method of preventing morbid obesity.

10

Medical uses

The methods of the invention described herein may also be expressed as medical uses of petrelintide.

15 Accordingly, the invention provides petrelintide or a pharmaceutically acceptable salt or solvate thereof for use in a method of reducing consumption of high-fat food by a subject, the method comprising administering to the subject petrelintide or pharmaceutically acceptable salt or solvate thereof.

20 The invention also provides petrelintide or a pharmaceutically acceptable salt or solvate thereof for use in a method of treating or preventing overweight, obesity, morbid obesity or a disease associated with overweight, obesity or morbid obesity in a subject, wherein the method reduces consumption of high-fat food by the subject.

25 The invention also provides petrelintide or a pharmaceutically acceptable salt or solvate thereof for use in a method of treating or preventing obesity, morbid obesity or a disease associated with obesity or morbid obesity in a subject, wherein the method reduces consumption of high-fat food by the subject.

30 The invention also provides petrelintide or a pharmaceutically acceptable salt or solvate thereof for use in a method of treating or preventing obesity or morbid obesity in a subject, wherein the method reduces consumption of high-fat food by the subject.

The invention also provides use of petrelintide or a pharmaceutically acceptable salt or
35 solvate thereof in preparation of a medicament for a method of reducing consumption of high-fat food by a subject.

The invention also provides use of petrelintide or a pharmaceutically acceptable salt or solvate thereof in preparation of a medicament for a method of treating or preventing overweight, obesity, morbid obesity or a disease associated with overweight, obesity or morbid obesity in a subject, wherein the method reduces consumption of high-fat food by the subject.

The invention also provides use of petrelintide or a pharmaceutically acceptable salt or solvate thereof in preparation of a medicament for a method of treating or preventing obesity, morbid obesity or a disease associated with obesity or morbid obesity in a subject, wherein the method reduces consumption of high-fat food by the subject.

The invention also provides use of petrelintide or a pharmaceutically acceptable salt or solvate thereof in preparation of a medicament for a method of treating or preventing obesity or morbid obesity in a subject, wherein the method reduces consumption of high-fat food by the subject.

All features described herein in the context of "methods of the invention" apply equally to petrelintide for use according to the invention and the use of petrelintide in preparation of a medicament according to the invention.

20

Obesity and diseases associated with obesity

The terms "disease", "disorder" and "condition" are synonymous and are used interchangeably herein to refer to a state of malfunction of the body. The term "disease" thus encompasses "disorder" and "condition".

25

The term "obesity" may be used herein to refer to overweight, obesity and morbid obesity together (i.e. "obesity" may mean any or all of overweight, obesity and morbid obesity).

Petrelintide for use in the methods and medical uses of the present invention reduces consumption of high-fat food. Petrelintide may therefore provide an attractive treatment option for, *inter alia*, obesity and metabolic diseases caused, characterised by, or associated with, excess body weight.

Accordingly, the invention provides methods and medical uses of treating or preventing overweight, obesity, morbid obesity or a disease associated with overweight, obesity or morbid obesity in a subject.

In some embodiments, the methods of the invention is a method of treating or preventing a disease associated with overweight, obesity or morbid obesity.

In some embodiments, the methods of the invention is a method of treating a disease associated with overweight, obesity or morbid obesity.

- 5 In some embodiments, the methods of the invention is a method preventing a disease associated with overweight, obesity or morbid obesity.

A disease associated with overweight, obesity or morbid obesity may also be referred to herein as a disease associated with obesity or morbid obesity.

- 10 Thus, in some embodiments, the methods of the invention is a method of treating or preventing a disease associated with obesity or morbid obesity.

In some embodiments, the methods of the invention is a method of treating a disease associated with obesity or morbid obesity.

- 15 In some embodiments, the methods of the invention is a method preventing a disease associated with obesity or morbid obesity.

- In some embodiments, the disease associated with overweight, obesity or morbid obesity is selected from the group consisting of hypertension, dyslipidemia, sleep apnea, cardiovascular disease, binge-eating disorder, Prader-Willi syndrome, obesity prior to surgery, obesity-linked inflammation, obesity-linked gallbladder disease, respiratory problems, degeneration of cartilage, osteoarthritis, reproductive health complications such as infertility, Alzheimer's disease, diabetes, pre-diabetes, insulin resistance syndrome, impaired glucose tolerance (IGT), disease states associated with elevated blood glucose levels, metabolic disease including metabolic syndrome, hyperglycemia, atherogenic dyslipidemia, hepatic steatosis ("fatty liver"), kidney failure, arteriosclerosis, macrovascular disease, microvascular disease, diabetic heart disease, coronary heart disease, peripheral artery disease or stroke, and combinations thereof.
- 20
25

- 30 In some embodiments, the disease associated with overweight, obesity or morbid obesity is hypertension.

In some embodiments, the disease associated with overweight, obesity or morbid obesity is dyslipidemia.

In some embodiments, the disease associated with overweight, obesity or morbid obesity is sleep apnea.

- 35 In some embodiments, the disease associated with overweight, obesity or morbid obesity is cardiovascular disease.

In some embodiments, the disease associated with overweight, obesity or morbid obesity is binge-eating disorder.

In some embodiments, the disease associated with overweight, obesity or morbid obesity is Prader-Willi syndrome.

- 5 In some embodiments, the disease associated with overweight, obesity or morbid obesity is obesity prior to surgery.

In some embodiments, the disease associated with overweight, obesity or morbid obesity is obesity-linked inflammation.

- 10 In some embodiments, the disease associated with overweight, obesity or morbid obesity is obesity-linked gallbladder disease.

In some embodiments, the disease associated with overweight, obesity or morbid obesity is respiratory problems.

In some embodiments, the disease associated with overweight, obesity or morbid obesity is degeneration of cartilage.

- 15 In some embodiments, the disease associated with overweight, obesity or morbid obesity is osteoarthritis.

In some embodiments, the disease associated with overweight, obesity or morbid obesity is reproductive health complications. In some embodiments, the disease associated with overweight, obesity or morbid obesity is infertility.

- 20 In some embodiments, the disease associated with overweight, obesity or morbid obesity is Alzheimer's disease.

In some embodiments, the disease associated with overweight, obesity or morbid obesity is diabetes. In some embodiments, the diabetes is type 1 diabetes. In some embodiments, the diabetes is type 2 diabetes.

25

In some embodiments, the disease associated with overweight, obesity or morbid obesity is pre-diabetes.

In some embodiments, the disease associated with overweight, obesity or morbid obesity is insulin resistance syndrome.

- 30 In some embodiments, the disease associated with overweight, obesity or morbid obesity is impaired glucose tolerance (IGT).

In some embodiments, the disease associated with overweight, obesity or morbid obesity is a disease state associated with elevated blood glucose levels

- 35 In some embodiments, the disease associated with overweight, obesity or morbid obesity is metabolic disease. In some embodiments, the disease associated with overweight, obesity or morbid obesity is metabolic syndrome.

In some embodiments, the disease associated with overweight, obesity or morbid obesity is hyperglycemia.

In some embodiments, the disease associated with overweight, obesity or morbid obesity is atherogenic dyslipidemia.

- 5 In some embodiments, the disease associated with overweight, obesity or morbid obesity is hepatic steatosis ("fatty liver"). In some embodiments, the hepatic steatosis is non-alcoholic fatty liver disease (NAFLD). In some embodiments, the NAFLD is non-alcoholic steatohepatitis (NASH).

- 10 In some embodiments, the hepatic steatosis is Metabolic Dysfunction-Associated Steatotic Liver Disease (MASLD). In some embodiments, the hepatic steatosis is Metabolic (dysfunction) associated fatty liver disease (MAFLD). In some embodiments, the hepatic steatosis is Metabolic dysfunction-associated steatohepatitis (MASH).

- 15 In some embodiments, the disease associated with overweight, obesity or morbid obesity is kidney failure.

In some embodiments, the disease associated with overweight, obesity or morbid obesity is arteriosclerosis. In some embodiments, the arteriosclerosis is atherosclerosis.

- 20 In some embodiments, the disease associated with overweight, obesity or morbid obesity is macrovascular disease.

In some embodiments, the disease associated with overweight, obesity or morbid obesity is microvascular disease.

- 25 In some embodiments, the disease associated with overweight, obesity or morbid obesity is diabetic heart disease. In some embodiments, the diabetic heart disease is diabetic cardiomyopathy. In some embodiments, the diabetic heart disease is heart failure as a diabetic complication.

In some embodiments, the disease associated with overweight, obesity or morbid obesity is coronary heart disease.

- 30 In some embodiments, the disease associated with overweight, obesity or morbid obesity is peripheral artery disease.

In some embodiments, the disease associated with overweight, obesity or morbid obesity is stroke.

- 35 The invention also provides methods and medical uses of reducing consumption of high-fat food by a subject, wherein the subject suffers from a disease. In such embodiments of the invention, the reduction of consumption of high-fat food treats or prevents the disease.

In some embodiments, the subject suffers from a disease selected from the group consisting of hypertension, dyslipidemia, sleep apnea, cardiovascular disease, binge-eating disorder, Prader-Willi syndrome, obesity prior to surgery, obesity-linked inflammation, obesity-linked gallbladder disease, respiratory problems, degeneration of cartilage, osteoarthritis, reproductive health complications such as infertility, Alzheimer's disease, diabetes, pre-diabetes, insulin resistance syndrome, impaired glucose tolerance (IGT), disease states associated with elevated blood glucose levels, metabolic disease including metabolic syndrome, hyperglycemia, atherogenic dyslipidemia, hepatic steatosis ("fatty liver"), kidney failure, arteriosclerosis, macrovascular disease, microvascular disease, diabetic heart disease, coronary heart disease, peripheral artery disease or stroke, and combinations thereof. The reduction of body fat, inhibition of weight gain or inhibition of gain of body fat treats or prevents the disease(s).

The diabetes may be type 1 diabetes or type 2 diabetes.
The arteriosclerosis may be atherosclerosis.
The hepatic steatosis may be non-alcoholic fatty liver disease (NAFLD). The NAFLD may which be non-alcoholic steatohepatitis (NASH).
In some embodiments, the hepatic steatosis is Metabolic Dysfunction-Associated Steatotic Liver Disease (MASLD). In some embodiments, the hepatic steatosis is Metabolic (dysfunction) associated fatty liver disease (MAFLD). In some embodiments, the hepatic steatosis is metabolic dysfunction-associated steatohepatitis (MASH).

The diabetic heart diseases may be diabetic cardiomyopathy or heart failure as a diabetic complication.

Petrelinide is useful, inter alia, in the reduction of food intake, promotion of weight loss, and inhibition or reduction of weight gain. Thus, petrelinide may be used in methods of treating, inhibiting or reducing weight gain, promoting weight loss and/or reducing excess body weight.

Petrelinide may also be used to lower circulating LDL levels and/or increase HDL/LDL ratio.

In some embodiments, the subject suffers from metabolic syndrome. Metabolic syndrome is characterized by a group of metabolic risk factors in one person. They include abdominal obesity (excessive fat tissue around the abdominal internal organs), atherogenic dyslipidemia (blood fat disorders including high triglycerides, low HDL cholesterol and/or

high LDL cholesterol, which foster plaque buildup in artery walls), elevated blood pressure (hypertension), insulin resistance and glucose intolerance, prothrombotic state (e.g. high fibrinogen or plasminogen activator inhibitor–1 in the blood), and proinflammatory state (e.g., elevated C-reactive protein in the blood). Individuals with metabolic syndrome are at
5 increased risk of coronary heart disease and other diseases related to other manifestations of arteriosclerosis (e.g. stroke and peripheral vascular disease). The dominant underlying risk factor for this syndrome appears to be abdominal obesity.

In some embodiments, the subject has diabetes. In some embodiments, the subject has a
10 disease linked to obesity or to diabetes. In some embodiments, the disease is overweight. In some embodiments, the disease is obesity. In some embodiments, the disease is morbid obesity. In some embodiments, the disease is diabetes. In some embodiments, the disease is type 1 diabetes. In some embodiments, the disease is type 2 diabetes. In some embodiments, the disease is a disease linked to obesity or to diabetes.

15 Effects of petrelintide on these conditions may be mediated in whole or in part via an effect on body weight, or may be independent thereof. Treatment may be achieved, for example, by control of appetite, feeding, food intake, calorie intake and/or energy expenditure.

20 **Weight loss dietary regime**

In some embodiments of the methods and uses of the invention, the subject is following a dietary regimen.

A “dietary regimen” refers to a course of food to which the subject is restricted (a “diet” in
25 colloquial terms, i.e., the subject is on a diet).

In some embodiments, the dietary regimen is a weight loss dietary regimen, which means a dietary regimen designed to induce weight loss. In some embodiments, the dietary regimen is one wherein the consumption of high-fat food is restricted (i.e. it is intended that the
30 subject does not consume high-fat food).

In other words, the invention encompasses combining treatment with petrelintide as described herein with a dietary regimen. Such a combination may be particularly effective in promoting weight loss (or avoiding weight gain) as petrelintide assists adherence to the
35 dietary regimen by causing the subject to prefer non-high-fat food.

Administration of petrelintide

“Administering” petrelintide to the subject means providing petrelintide to the subject such that petrelintide will have its physiological effect. Petrelintide may be administered to the subject in any suitable manner or by any suitable means known in the art.

5

The term “administration event” is used herein to refer to a single act of administering petrelintide to the subject (which may be one of many such administration events).

Dose

10 The term “dose” refers to the quantity of petrelintide administered to a subject at each administration event. The term “dosage” refers to both the quantity and frequency at which a given compound is administered to a subject.

Petrelintide is administered to the subject in a therapeutically effective amount (i.e. a
15 therapeutically effective dose). The term “therapeutically effective amount” as used herein refers to an amount that is sufficient to cure, ameliorate, alleviate or partially arrest the clinical manifestations of the particular disease, disorder or condition that is the object of the treatment or other therapeutic intervention in question e.g. as measured by established clinical endpoints or other biomarkers (established or experimental). A therapeutically
20 relevant amount may be determined empirically by one skilled in the art based on the indication being treated or prevented and the subject to whom the therapeutically relevant amount is being administered. For example, the skilled worker may measure one or more of the clinically relevant indicators of bioactivity described herein, e.g. plasma lipid levels, blood glucose levels or insulin release. The skilled worker may determine a clinically relevant
25 amount through *in vitro* or *in vivo* measurements. Other exemplary measures include weight gain, weight loss, and change in blood pressure.

An amount adequate to accomplish any or all of these effects is defined as a therapeutically effective amount. The administered amount and the method of administration can be tailored
30 to achieve optimal efficacy. An amount effective for a given purpose will depend, *inter alia*, on the severity of the disease, disorder or condition that is the object of the particular treatment or other therapeutic intervention, on the body weight and general condition of the subject in question, on diet, on possible concurrent medication, and on other factors well known to those skilled in the medical arts. Determination of an appropriate dosage size and
35 dosing regimen most appropriate for administration of a peptide or pharmaceutically acceptable salt or solvate thereof according to the invention to a human may be guided by the results obtained by the present invention, and may be confirmed in properly designed

clinical trials. An effective dosage and treatment protocol may be determined by conventional means, starting with a low dose in laboratory animals and then increasing the dosage while monitoring the effects, and systematically varying the dosage regimen as well. Numerous factors may be taken into consideration by a clinician when determining an
5 optimal dosage for a given subject. Such considerations are well known to the skilled person.

The dose of petrelintide may be independently selected at each administration event.

10 In some embodiments, petrelintide is administered to the subject at a dose of about 0.0001 to about 100 mg/kg body weight per day, such as about 0.0005 to about 50 mg/kg body weight per day, such as about 0.001 to about 10 mg/kg body weight per day, such as about 0.01 to about 1 mg/kg body weight per day.

15 In some embodiments, petrelintide is administered to the subject at a dose of about 0.0007 to about 700 mg/kg body weight per week, such as about 0.0035 to about 350 mg/kg body weight per week, such as about 0.007 to about 70 mg/kg body weight per week.

In some embodiments, petrelintide is administered to the subject at a dose of about 0.05 to
20 about 50,000 mg per week, such as about 0.25 to about 25,000 mg per week, such as about 0.5 to about 5,000 mg per week.

In some embodiments, the weekly dose is more than 2.4 mg up to 10.0 mg. In other words, in some embodiments, the weekly dose is higher than 2.4 mg, up to at most 10.0 mg. In
25 some embodiments, the dose is more than 3.6 mg up to 10.0 mg, more than 4.0 mg up to 10.0 mg, more than 4.8 mg up to 10.0 mg, more than 6.0 mg up to 10.0 mg, or more than 7.5 mg up to 10.0 mg.

In some embodiments, petrelintide is administered to the subject at a dose of about 2
30 nmol/kg body weight or about 10 nmol/kg body weight.

Timing of administration

Petrelintide may be administered to the subject a certain number of times “daily” or a certain number of times “a day.” “A day” is intended to mean approximately 24 hours, for example,
35 approximately 20, 21, 22, 23, 24, 25, 26, 27 or 28 hours.

In some embodiments, reference to "day" may mean 24 hours $\pm$ 8 hours. That is to say the administration may take place either up to and including about eight hours before, or up to and including about eight hours after the stated time.

5 Petrelintide may be administered to the subject a certain number of times "weekly" a certain number of times "a week". A "week" is intended to mean approximately 7 days, for example, approximately 5, 5.5, 6, 6.5, 7, 7.5, 8, 8.5 or 9 days with each "day" being counted as approximately a 24 hour period.

10 In some embodiments, reference to "week" may mean 7 days $\pm$ 2 days. That is to say the administration may take place either up to and including about two days before, or up to and including about two days after the stated day. As such, the administration may take place about 2 days or about 1 day before, or about 1 day or about 2 days after, the stated day. Hence, the administration may take place 2 days or 1 day before, or 1 day or 2 days after,
15 the stated day.

In some embodiments, petrelintide is administered to the subject once daily, twice daily, once every two, three, four, five or six days, once weekly, twice weekly, once monthly or twice monthly. In some embodiments, petrelintide is administered to the subject once or
20 twice weekly. Preferably, petrelintide is administered to the subject once weekly.

In some embodiments, petrelintide is administered to the subject twice daily, once every two days or once every four days.

25 As will be appreciated in the art, the time between doses may be varied to some extent so that each and every dose is not separated by precisely the same time (i.e. not precisely a day or precisely a week). This will often be directed under the discretion of the physician. Thus, doses may be separated in time by a clinically acceptable range of times.

30 ***Route of administration***

The administration to a subject of petrelintide described herein may be by any mode of administration common or standard in the art. In some embodiments, petrelintide is administered to the subject by injection, such as by subcutaneous (sc), intramuscular (im) or intravenous (iv) injection. In preferred embodiments, administration is by subcutaneous
35 injection. Preferably, petrelintide is in a form suitable for subcutaneous (s/c or s.c.) administration to a subject.

Administration period

The term “administration period” may be used herein to refer to the total period in which petrelintide is administered to the subject. In other words, the administration period is the period starting with the first administration event (i.e. the first time the compound is administered to the subject) and ending with the final administration event (i.e. the final time the compound is administered to the subject). Alternatively expressed, the administration period is the period in which subject is treated with the compound.

In some embodiments, petrelintide is administered to the subject for at least one month (i.e. the administration period for the amylin analogue is at least one month). In some embodiments, petrelintide is administered to the subject for at least two months, at least three months, at least four months, at least five months, at least six months, at least seven months, at least eight months, at least nine months, at least ten months, at least eleven months, or at least twelve months.

In some embodiments, petrelintide is administered to the subject for at least one year (i.e. the administration period for the amylin analogue is at least one year). In some embodiments, petrelintide is administered to the subject for at least two years, at least three years, at least four years, at least five years, at least six years, at least seven years, at least eight years, at least nine years, or at least ten years.

Petrelintide is a chronic treatment. In some embodiments, petrelintide is administered to the subject for more than ten years. In some embodiments, petrelintide is administered to the subject indefinitely. In some embodiments, petrelintide is administered to the subject for the rest of the subject's life.

Pharmaceutical compositions

Petrelintide as described herein may be formulated as a pharmaceutical composition. The terms “pharmaceutical composition”, “composition” and “formulation” are used interchangeably herein. As with all aspects of the invention, it is to be understood that reference to an amylin analogue or petrelintide encompasses reference to pharmaceutically acceptable salts and solvates.

Thus, the invention also provides a methods as described herein comprising administering to a subject a pharmaceutical composition comprising petrelintide as described herein or a pharmaceutically acceptable salt or solvate thereof.

The invention also provides a pharmaceutical composition comprising petrelintide as described herein, or a pharmaceutically acceptable salt or solvate thereof, for use in a method as described herein.

- 5 In some embodiments, the composition comprises a pharmaceutically acceptable carrier, excipient or vehicle.

- Petrelintide may be formulated as a pharmaceutical composition which is suited for administration with or without storage, and which typically comprise a therapeutically
10 effective amount of petrelintide, together with a pharmaceutically acceptable carrier, excipient or vehicle.

- The term "pharmaceutically acceptable carrier" includes any of the standard pharmaceutical carriers. Pharmaceutically acceptable carriers for therapeutic use are well known in the
15 pharmaceutical art and are described, for example, in "Remington's Pharmaceutical Sciences", 17th edition, Alfonso R. Gennaro (Ed.), Mark Publishing Company, Easton, PA, USA, 1985. For example, sterile saline and phosphate-buffered saline at slightly acidic or physiological pH may be used. Suitable pH-buffering agents may, e.g., be phosphate, citrate, acetate, tris(hydroxymethyl)aminomethane (TRIS), N-tris(hydroxymethyl)methyl-3-
20 aminopropanesulfonic acid (TAPS), ammonium bicarbonate, diethanolamine, histidine, arginine, lysine or acetate (e.g. as sodium acetate), or mixtures thereof. The term further encompasses any carrier agents listed in the US Pharmacopeia for use in animals, including humans.

- 25 In some embodiments, the pharmaceutical composition is a stable aqueous liquid pharmaceutical composition (i.e. a stable aqueous liquid formulation).

- Preferably the formulations of the present invention substantially do not include organic solvent. In particular preferred embodiments, water is the sole solvent used to make the
30 aqueous liquid formulation.

- The formulations of the invention are aqueous liquid formulations, i.e. formulations comprising water, in the form of an aqueous solution. In the context of the invention the term "aqueous formulation" will normally refer to a formulation comprising at least 50 % by weight
35 (50 % w/w) of water as a solvent, more preferably at least 75% w/w of water, more preferably at least 80% w/w of water, more preferably at least 85% w/w of water, more preferably at least 90% w/w of water, most preferably at least 95% w/w of water. In certain

embodiments, aqueous formulations of the present invention substantially do not include organic solvents, such as aprotic polar solvents such as dimethyl sulfoxide (DMSO).

- “Substantially” in this sense means that the aqueous formulations include less than 5% by volume organic solvent, more preferably less than 2% by volume (v/v) organic solvent and
5 even more preferably less than 1% by volume (v/v) organic solvent. In preferred embodiments, no organic solvent is present. Thus, typically, water is the sole solvent used to make the aqueous liquid formulations.

Petrelintide concentration

- 10 In some embodiments, petrelintide is present in the composition at a concentration of from about 0.4 mg/ml to about 25 mg/ml.

- In some embodiments, petrelintide is present in the composition at a concentration of at least about 0.4 mg/ml, at least about 0.5 mg/ml, at least about 0.6 mg/ml, at least about 1.2
15 mg/ml, or at least about 2.5 mg/ml.

- In some embodiments, petrelintide is present in the composition at a concentration of up to about 25 mg/ml, up to about 20 mg/ml, up to about 15 mg/ml, or up to about 10 mg/ml.
- 20 In some embodiments, petrelintide is present in the composition at a concentration of about 3 mg/ml to about 12 mg/ml, e.g. about 3 mg/ml to about 7 mg/ml or about 8 mg/ml to about 12 mg/ml, e.g. about 5 mg/ml or about 10 mg/ml.

Buffer

- 25 The term “buffer” as used herein denotes a pharmaceutically acceptable agent which stabilizes the pH of a pharmaceutical formulation. Suitable buffers are well known in the art and can be found in the literature.

- Any suitable buffer may be used, including a phosphate buffer, histidine buffer, TRIS
30 (tris(hydroxymethyl)aminomethane) buffer, acetate buffer, arginine buffer, citrate buffer, bicarbonate buffer, diethanolamine buffer, lysine buffer and TAPS ([tris(hydroxymethyl)methylamino]propanesulfonic acid) buffer. Particularly preferred buffers include phosphate buffer, histidine buffer, citrate buffer and TRIS buffer, especially phosphate buffer, histidine buffer and citrate buffer.

- 35 In some embodiments, the buffer is present at a concentration of about 0.5 mM to about 25 mM.

In some embodiments, the buffer is present at a concentration of about 0.5 mM to about 20 mM, about 0.5 mM to about 15 mM, about 1 mM to about 15 mM, about 1 mM to about 12 mM, about 3 mM to about 7 mM, about 8 mM to about 12 mM, or about 5 mM or about 10 mM, e.g. about 5 mM or about 10 mM particularly (but not exclusively) when the buffer is phosphate, histidine or citrate.

In some embodiments, the buffer is phosphate, histidine or citrate.

- For TRIS buffer, it may be preferred to be present at about 15 mM to about 25 mM, e.g. about 17 mM to about 23 mM, e.g. about 20 mM, since the buffering capacity of TRIS is lower than that of other buffers such as (e.g.) phosphate and histidine in the relevant pH range.
- It may be possible for the formulation to contain more than one buffer, e.g. two buffers, or even more. In such cases, the quoted concentration may represent the sum of the concentrations of the individual buffers. For example, a formulation containing 2.5 mM phosphate buffer and 2.5 mM histidine buffer may be considered to contain 5 mM buffer overall.

20

pH

- The pH of the formulation was also found to be significant for stability. Chemical stability was increased at lower pH values and physical stability was maintained. Thus, in some embodiments, the formulation has a pH of about 5.8 to about 6.9, and may, for example, have a pH of about 6.2 to about 6.8, e.g. about 6.4 to about 6.6, e.g. about 6.5. For the avoidance of doubt, pH is measured at 25°C.

25

Tonicity modifier

In some embodiments, the composition comprises a tonicity modifier.

30

- The term "tonicity modifier" as used herein denotes pharmaceutically acceptable tonicity agents that are used to modulate the tonicity of the formulation. The terms "tonicity modifier" and "tonicity agent" may be used interchangeably. The formulations of the present invention are preferably isosmotic, that is they have an osmotic pressure that is substantially the same as human blood serum, e.g. about 300+/-80 mOsm, e.g., e.g. 300+/-60 mOsm, as measured by an osmometer.

35

The tonicity modifier may be ionic or non-ionic. Suitable ionic tonicity modifiers include alkali metal salts (e.g. halides) and earth metal salts (e.g. halides), such as NaCl, NaBr, NaI, KCl, KBr, KI, LiCl, CaCl₂ and Na₂SO₄. Non-ionic tonicity modifiers include mannitol (e.g. D-mannitol), propylene glycol, sucrose, glycerol, sorbitol and trehalose. In some embodiments, mannitol (e.g. D-mannitol), propylene glycol and NaCl may be preferred as tonicity modifiers, especially mannitol and propylene glycol.

Where the tonicity modifier is a chloride salt, such as NaCl, it may be desirable that the tonicity modifier is only added to the formulation once the pH has been adjusted to the desired value. This may particularly be the case where petrelintide is itself provided in the form of a chloride salt, since the presence of chloride ions above a certain level may promote precipitation or fibrillation of the amylin analogue at pH values around the pI of the peptide (pI = 4.36).

It will be understood that the concentration of the tonicity modifier will be dependent on the concentration of other components of the formulation, especially where the formulation is intended to be isosmotic. The skilled person is capable of establishing the appropriate concentration for any given agent, in the context of a specific formulation.

For example, it may be appropriate to employ mannitol in a concentration of 200–300 mM, e.g. 230-260 mM; it may be appropriate to employ propylene glycol in a concentration of 200-250 mM, e.g. 224 mM; it may be appropriate to employ NaCl in a concentration of 100-150mM, e.g. 118-137mM.

Preservative

In some embodiments, the composition comprises a preservative, especially when it is provided in a multi-use format. Alternatively, and especially when provided in single-use format, the formulation may contain no or substantially no preservative. When a preservative is present, it will be employed in an amount effective to kill a range of bacterial types as required for regulatory approval. Suitable preservatives include meta-cresol, phenol, methylparaben, ethylparaben, propylparaben, butylparaben, chlorobutanol, benzyl alcohol, phenylmercuric nitrate, thimerosal, sorbic acid, potassium sorbate, benzoic acid, chlorocresol and benzalkonium chloride. The preservative will be present in an amount effective to kill a range of bacterial types as required for regulatory approval.

35

Stability

The aqueous liquid formulation is typically stable for at least 6 months, e.g. at least 12

months, at least 18 months or at least 24 months, at 2-8°C (e.g. at 5°C). Preferably it is stable for at least 18 months, e.g. at least 24 months, at 2-8°C (e.g. at 5°C).

For example, the formulation may display substantially no changes indicative of reduced physical stability (e.g. as demonstrated by turbidity of the solution, or of aggregation, fibrillation or gelling of the amylin analogue) after it has been stored at 2-8°C (e.g. at 5°C) for at least 6 months, at least 12 months, at least 18 months, or at least 24 months. Preferably, the formulation displays substantially no such changes after it has been stored at 2-8°C (e.g. at 5°C) for at least 18 months, e.g. at least 24 months. It will be understood that accelerated conditions may also be employed as a proxy for assessing longer term physical stability as set out in more detail below.

Additionally, or alternatively, at least 80%, more preferably at least 85%, at least 90%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% of the petrelintide remains in intact monomeric form in the formulation after it has been stored at 2-8°C (e.g. at 5°C) for at least 6 months, at least 12 months, at least 18 months, or at least 24 months. Preferably, at least 90%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% of the petrelintide remains in intact monomeric form after it has been stored at 2-8°C (e.g. at 5°C) for at least 6 months, at least 12 months, at least 18 months, or at least 24 months. More preferably, at least 90%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% of the petrelintide remains in intact monomeric form in the formulation after it has been stored at 2-8°C (e.g. at 5°C) for at least 18 months, e.g. at least 24 months.

Further aspects of the compositions

In these formulations, as elsewhere, petrelintide is provided as a chloride salt, e.g. having the formula:

$[(19\text{CD})\text{-isoGlu-RD}(\text{GTATK})\text{ATERLA-Aad-FLQRSSF-Gly(Me)-A-Ile(Me)-LSSTEVGSNT-Hyp-NH}_2)_x(\text{Cl})$

where x is 1.0-2.0.

In accordance with normal pharmaceutical practice, the formulations of the present invention are sterile and/or free (or substantially free, e.g. containing no more than about 100 ppm) of reducing agent.

The formulations are suitable for parenteral administration, typically by injection. Thus administration may, for example, be by subcutaneous, intramuscular, intraperitoneal or intravenous injection, although subcutaneous administration may be preferred.

An individual dose of a formulation of the invention may be provided in any suitable volume. For example, an individual dose may have a volume of 0.1 to 1.5 ml, for example 0.3 to 1.5 ml, for example 0.3 ml to 1 ml. Examples of specific individual dose volumes include 0.5 ml and 1 ml (e.g. 1.0 ml). Individual doses may be packaged separately for single use, e.g. in individual vials, cartridges or syringes, as described in more detail below.

The formulations of the invention may be provided in a container or delivery device. In some embodiments, the container or delivery device is for single use. In other embodiments, the container or delivery device is for multi-use.

Examples include a sealed vial, a pre-filled syringe, and an injector device such as an injector pen, an adjustable dose auto-injector, a disposable auto-injector, a wearable injector, or an infusion pump.

A pharmaceutical composition of the invention may be in unit dosage form. In such form, the composition is divided into unit doses containing appropriate quantities of the active component or components.

In some embodiments, the pharmaceutical composition is as follows:

Component	Quantity/mL Drug product	Function
petrelintide	4.0 mg	Active pharmaceutical ingredient
Trometamol/Tromethamine (TRIS)	2.42 mg	Buffer
Sodium chloride	6.9 mg	Tonicity agent
1M Hydrochloric acid	q.s.	pH adjustment
0.5 M Sodium hydroxide	q.s.	pH adjustment
Water for injection	Ad 1.0 mL	Solvent

Sequence listing

SEQ ID NO: 1 – Petrelintide
SEQ ID NO: 2 – Native human amylin
SEQ ID NO: 3 – Liraglutide

EXAMPLES

The following examples are provided to illustrate preferred aspects of the invention and are not intended to limit the scope of the invention.

Example 1: Effect of peptides on food intake in obese rats

This study was performed to assess the effect of treatment with peptides on intake of food in diet-induced obese (DIO) rats.

- 5 Briefly, DIO rats were generated by feeding them a high-fat diet for 21 weeks. Then, over the course of a 30-day study period, the rats were administered vehicle (as negative control) or one of petrelintide or liraglutide.

Liraglutide, which is a derivative of GLP-1 described in Example 37 of US patent no.

- 10 6,268,343, has the formula:

Hy-HAEGTFTSDVSSYLEGQAAKEFIAWLVRGRG-OH (SEQ ID NO: 3),
wherein the side-chain amino group of the lysine at position 20 is linked to the lipophilic moiety hexadecanoyl (i.e. palmitoyl) via a γ -Glu linker.

- 15 The rats had access to high-fat food (referred to herein as "high-fat diet") and chow (non-high-fat food). Intake of chow and high-fat diet by the rats, and body weight of the rats, were measured daily throughout the study period.

- Rats administered petrelintide or liraglutide are referred to as "treatment groups" herein (in
20 contrast to the vehicle group used as control).

Administration

Vehicle was administered once every 2 days (Q2D).

- 25 Petrelintide was administered at both a lower dose (2 nmol/kg body weight) and a higher dose (10 nmol/kg body weight). The lower dose of petrelintide was administered once every 2 days (Q2D). The higher dose of petrelintide was administered once every 4 days (Q4D).

Liraglutide was administered twice daily (BID).

- 30

In these Examples, "Q2D" means administration once every 2 days, "Q4D" means administration once every 4 days and "BID" means administration twice every day.

Vehicle and peptides were all administered by subcutaneous injection (sc).

- 35

Petrelintide was formulated using 50mM histidine buffer pH 7.0 with 200 mM mannitol. For the vehicle group the same buffer without compound was used. Liraglutide was formulated using PBS with 0.1% bovine serum albumin.

- 5 The treatment groups for this study are summarised in Table 1 below:

Table 1 – Study group summary

Group name	Dose	Dosing frequency	Administration route
Vehicle	-	Once every 2 days	Subcutaneous injection (sc)
Petrelintide Q2D	2 nmol/kg / 0.0086 mg/kg	Once every 2 days	Subcutaneous injection (sc)
Petrelintide Q4D	10 nmol/kg / 0.0426 mg/kg	Once every 4 days	Subcutaneous injection (sc)
Liraglutide	5 nmol/kg / 0.02 mg/kg	Twice every day	Subcutaneous injection (sc)

Animal model

- Healthy male Sprague Dawley rats were obtained from Taconic (Denmark). The rats were 5 weeks of age at arrival. To generate DIO rats for the study, animals were fed with chow (cereal-based pellets – Altromin 1324) and high-fat diet (Gubra diet containing 60% of total energy from fat) ad libitum for 21 weeks. The Gubra diet is a highly palatable high-fat, high-sugar diet made up of a paste (1:1:1) of chocolate spread (Nutella, Ferrero, Italy), peanut butter (Sippy, Unilever, USA) and powdered regular rodent chow (Altromin 1324, Brogaarden, Denmark). Animals were housed in groups of 2, on a 12-hour light and 12-hour dark cycle (with lights on at 3am-3pm) at standard temperature and humidity conditions (19-23°C, 40-60% relative humidity) with ad libitum access to domestic quality tap water. Animals were stratified based on EchoMRI scan (fat) and bodyweight on day -1.

- 20 The high-fat diet may be referred to as “Gubra diet” herein.

Results

- Body weight of each rat was measured at the same time every day throughout the 30-day study period. **Figure 1** shows the actual (A) and relative (B) body weight change (day 1 = 100%) over the study period. Data are expressed as mean $\pm$ standard error of the mean (SEM) (n = 10); treatment groups were compared to the vehicle-treated group by use of a two-way ANOVA RM followed by Bonferroni’s multiple comparison tests. → indicate Q4D dosing days. *P<0.05, **P<0.01, ***P<0.001.
- 30 Absolute body weight appeared to decrease for all five treatment groups relative to the vehicle-treated group during the study period, though the change was not statistically significantly.

However, relative body weight decreased significantly during the study period in all five treatment groups: from day 3 and onwards in the petrelintide high dose group, and from day 7 and day 12 and onwards in the petrelintide low dose and the liraglutide groups,

5 respectively.

In particular, as shown in **Figure 2**, treatment with liraglutide and petrelintide resulted in significantly lower relative body weight compared to vehicle ($3.3 \% \pm 0.7$ vehicle, $-0.1 \% \pm 1.1$ liraglutide, $-4.1 \% \pm 0.6$ petrelintide 2 nmol/kg, $-7.8 \% \pm 0.7$ petrelintide 10 nmol/kg;

10 relative to initial body weights $\pm$ SEM).

Intake of chow and high-fat diet was measured daily throughout the study period. The results are presented in Figures 3 to 6.

15 **Figure 3** shows the daily intake of chow (g) per two animals.

Figure 4 shows total cumulative intake of chow (A) and cumulated chow intake per day (B) during the entire study period quantified as grams per two animals.

20 Daily chow intake and cumulative chow intake in the three treatment groups was not statistically significantly different from the vehicle-treated group during the study.

Figure 5 shows daily intake of high-fat diet in grams per two animals.

25 Daily intake of high-fat diet was significantly affected in all treatment groups.

As compared to the vehicle-treated group, intake of high-fat diet was significantly decreased on days 2-10; 12-13; day 15 and day 18 in the petrelintide low dose group and on days 2-4; 6-7; 10-11; 14-15; 18-19; 22-23 and day 26 in the petrelintide high dose group.

Finally, the intake of high-fat diet in the liraglutide group was significantly decreased on day

30 3 as compared to the vehicle-treated group (all $P < 0.05$).

Figure 6 shows total cumulative intake of high-fat diet (A) cumulated high-fat diet intake per day (B) during the entire study period quantified as grams per two animals.

35 Treatment with either low or high dose petrelintide significantly reduced total cumulative intake of high-fat diet in the study period.

As compared to the vehicle-treated group, intake of high-fat diet decreased significantly in the petrelintide low dose group from day 9 and onwards and in the petrelintide high dose group from day 6 and onwards (all $p < 0.05$).

- 5 In particular, treatment with petrelintide resulted in significant reduction of total cumulative intake of high fat diet compared to vehicle, in contrast to liraglutide (834 g $\pm$ 31.1 vehicle, 796 g $\pm$ 25.6 liraglutide, 646 g $\pm$ 22.3 petrelintide 2 nmol/kg, 576 g $\pm$ 17.4 petrelintide 10 nmol/kg; g $\pm$ SEM). No significant change in total cumulative intake of chow was observed in any groups compared to vehicle.

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In summary, treatment with petrelintide reduced intake of high-fat food whilst not affecting intake of non-high-fat food (chow). The treatment with petrelintide resulted in the reduction of the consumption of high-fat food by the subject and thus a preference for non-high-fat food such as e.g. healthier food, over high-fat food.

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All publications mentioned herein are herein incorporated by reference. Various modifications and variations of the described methods and system of the invention will be apparent to those skilled in the art without departing from the scope and spirit of the invention. Although the invention has been described in connection with specific preferred

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embodiments, it should be understood that the invention as claimed should not be unduly limited to such specific embodiments. Indeed, various modifications of the described modes for carrying out the invention which are obvious to those skilled in biochemistry, molecular biology or related fields are intended to be within the scope of the following aspects.

ASPECTS OF THE INVENTION

The invention is described by way of the following numbered aspects:

- 5 1. A method of reducing consumption of high-fat food by a subject, the method comprising administering to the subject petrelintide or a pharmaceutically acceptable salt or solvate thereof.
2. A method of altering food preference of a subject, the method comprising
10 administering to the subject petrelintide or a pharmaceutically acceptable salt or solvate thereof.
3. The method of aspect 1 or aspect 2, wherein the method is a non-therapeutic method.
15
4. A method of treating or preventing overweight, obesity, morbid obesity or a disease associated with overweight, obesity, morbid obesity in a subject, wherein the method reduces consumption of high-fat food by the subject, the method comprising administering to the subject petrelintide or a pharmaceutically acceptable salt or solvate thereof.
20
5. Petrelintide or a pharmaceutically acceptable salt or solvate thereof for use in a method of reducing consumption of high-fat food by a subject.
6. Petrelintide or a pharmaceutically acceptable salt or solvate thereof for use in a
25 method of altering food preference of a subject.
7. Petrelintide or a pharmaceutically acceptable salt or solvate thereof for use in a method of treating or preventing overweight, obesity, morbid obesity or a disease associated with overweight, obesity and/or morbid obesity in a subject, wherein the method reduces
30 consumption of high-fat food by the subject.
8. Use of petrelintide or a pharmaceutically acceptable salt or solvate thereof in preparation of a medicament for reducing consumption of high-fat food by a subject.
- 35 9. Use of petrelintide or a pharmaceutically acceptable salt or solvate thereof in preparation of a medicament for altering food preference of a subject.

10. Use of petrelintide or a pharmaceutically acceptable salt or solvate thereof in preparation of a medicament for a method of treating or preventing overweight, obesity, morbid obesity or a disease associated with overweight, obesity and/or morbid obesity in a subject, wherein the method reduces consumption of high-fat food by the subject.
11. The method of aspect 2, petrelintide for use of aspect 6, or the use of aspect 9, wherein the food preference of the subject is altered such that the subject prefers non-high-fat food to high-fat food.
12. The method of aspect 4, petrelintide for use of aspect 7, or the use of aspect 10, wherein the method is a method of treating overweight in the subject.
13. The method of aspect 4 or aspect 12, petrelintide for use of aspect 7 or aspect 12, or the use of aspect 10 or aspect 12, wherein the method is a method of treating obesity in the subject.
14. The method of any one of aspects 4, 12 and 13, petrelintide for use of any one of aspects 7, 12 and 13, or the use of any one of aspects 10, 12 and 13, wherein the method is a method of treating morbid obesity.
15. The method of any one of aspects 4 and 12 to 14, petrelintide for use of any one of aspects 7 and 12 to 14, or the use of any one of aspects 10 and 12 to 14, wherein the method is a method of treating a disease associated with overweight, obesity and/or morbid obesity in the subject.
16. The method of any one of aspects 4 and 12 to 14, petrelintide for use of any one of aspects 7 and 12 to 14, or the use of any one of aspects 10 and 12 to 14, wherein the method is a method of treating a disease associated with obesity and/or morbid obesity in the subject.
17. The method of any one of aspects 4 and 12 to 16, petrelintide for use of any one of aspects 7 and 12 to 16, or the use of any one of aspects 10 and 12 to 16, wherein the method is a method of preventing overweight in the subject.

18. The method of any one of aspects 4 and 12 to 17, petrelintide for use of any one of aspects 7 and 12 to 17, or the use of any one of aspects 10 and 12 to 17, wherein the method is a method of preventing obesity in the subject.

5 19. The method of any one of aspects 4 and 12 to 18, petrelintide for use of any one of aspects 7 and 12 to 18, or the use of any one of aspects 10 and 12 to 18, wherein the method is a method of preventing morbid obesity in the subject.

20. The method of any one of aspects 4 and 12 to 19, petrelintide for use of any one of
10 aspects 7 and 12 to 19, or the use of any one of aspects 10 and 12 to 19, wherein the method is a method of preventing a disease associated with overweight, obesity and/or morbid obesity in the subject.

21. The method of any one of aspects 4 and 12 to 19, petrelintide for use of any one of
15 aspects 7 and 12 to 19, or the use of any one of aspects 10 and 12 to 19, wherein the method is a method of preventing a disease associated with obesity and/or morbid obesity in the subject.

22. The method of aspect 4, petrelintide for use of aspect 7, or the use of aspect 10,
20 wherein the method is a method of treating or preventing overweight, obesity or morbid obesity or preventing a disease associated with overweight, obesity, morbid obesity in the subject.

23. The method, petrelintide for use, or the use of any one of aspects 1 to 22, wherein
25 the method is a method of inhibiting weight gain and/or reducing body weight in the subject.

24. The method, petrelintide for use, or the use of any one of aspects 1 to 23, wherein the method is a method of reducing food intake.

30 25. The method, petrelintide for use, or the use of any one of aspects 1 to 24, wherein the method is a method of reducing appetite.

26. The method, petrelintide for use, or the use of any one of aspects 1 to 25, wherein
the method is a method of increasing satiety.

35

27. The method, petrelintide for use, or the use of any one of aspects 1 to 26, wherein high-fat food is food having a total fat content of about 5 g or more of fat per 100 g, such as

about 6 g or more, about 7 g or more, about 8 g or more, about 9 g or more, about 10 g or more, about 11 g or more, about 12 g or more, about 13 g or more, about 14 g or more, about 15 g or more, about 16 g or more, about 17 g or more, or about 17.5 g or more of fat per 100 g

5

28. The method, petrelintide for use, or the use of any one of aspects 1 to 27, wherein high-fat food is food having a total fat content of about 1 g or more of saturated fat per 100 g, such as about 2 g or more of saturated fat per 100 g, about 3 g or more, about 4 g or more, or about 5 g or more of saturated fat per 100 g.

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29. The method, petrelintide for use, or the use of any one of aspects 1 to 28, wherein the method reduces consumption of high-fat food by the subject over a period compared to a control.

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30. The method, petrelintide for use, or the use of any one of aspects 1 to 29, wherein the method reduces consumption of high-fat food by the subject by at least about 5%, such as at least about 10%, at least about 15%, at least about 17%, at least about 20% at least about 25%, at least about 30%, at least about 33%, at least about 35%, at least about 40%, at least about 45%, at least about 50%, at least about 65%, at least about 66%, at least about 70%, at least about 75%, at least about 80%, at least about 85%, at least about 90%, at least about 95% or about 100%.

20

31. The method, petrelintide for use, or the use of any one of aspects 1 to 30, wherein the method reduces consumption of high-fat food by the subject by

25

(a) about 5% to about 75%, such as about 10% to about 75%, about 15% to about 75%, or about 17% to about 75%; or

(b) about 5% to about 70%, such as about 5% to about 66%, about 5% to about 65%, about 5% to about 60%, about 5% to about 55%, about 5% to about 50%, about 5% to about 45%, about 5% to about 40%, about 5% to about 35%, or about 5% to about 33%; or

30

(c) about 17% to about 66%, or about 17% to about 33%.

32. The method, petrelintide for use, or the use of any one of aspects 1 to 31, wherein consumption of non-high-fat food by the subject does not change or increases over a period compared to a control.

35

33. The method, petrelintide for use, or the use of any one of aspects 1 to 32, wherein consumption of non-high-fat food by the subject increases by at least about 1%, such as at

least about 2%, at least about 3%, at least about 4%, at least about 5%, or at least about 10% compared to a control.

34. The method, petrelintide for use, or the use of any one of aspects 29 to 33, wherein
5 the period is at least about 1 day, at least about 2 days, at least about 3 days, at least about 4 days, at least about 5 days, at least about 6 days, at least about 30 days, at least about 1 week, at least about 2 weeks, at least about 3 weeks, at least about 4 weeks, at least about 1 month, at least about 6 months, at least about 1 year, at least about 2 years, at least about 3 years, at least about 4 years, at least about 5 years, at least about 6 years, at least about 7
10 years, at least about 8 years, at least about 9 years, at least about 10 years, or more than 10 years.

35. The method, petrelintide for use, or the use of any one of aspects 29 to 34, wherein the period is about 1 day, about 2 days, about 3 days, about 4 days, about 5 days, about 6
15 days, about 30 days, about 1 week, about 2 weeks, about 3 weeks, about 4 weeks, about 1 month, about 6 months, about 1 year, about 2 years, about 3 years, about 4 years, about 5 years, about 6 years, about 7 years, about 8 years, about 9 years, about 10 years.

36. The method, petrelintide for use, or the use of any one of aspects 1 to 35, wherein
20 the subject is of a healthy weight.

37. The method, petrelintide for use, or the use of aspect 36, wherein the subject has a Body Mass Index (BMI) of 18.5 to 24.9 corresponding to healthy weight.

25 38. The method, petrelintide for use, or the use of any one of aspects 1 to 35, wherein the subject is overweight.

39. The method, petrelintide for use, or the use of aspect 38, wherein the subject has a BMI of 25.0 to 29.9 corresponding to overweight.

30

40. The method, petrelintide for use, or the use of any one of aspects 1 to 35, wherein the subject is obese.

41. The method, petrelintide for use, or the use of aspect 40, wherein the subject has a
35 BMI of 30.0 to 39.9 corresponding to obese.

42. The method, petrelintide for use, or the use of any one of aspects 1 to 35, wherein the subject is morbidly obese.
43. The method, petrelintide for use, or the use of aspect 42, wherein the subject has a BMI of 40.0 or higher corresponding to morbidly obese.
44. The method, petrelintide for use, or the use of any one of aspects 1 to 43, wherein the subject has diabetes.
45. The method, petrelintide for use, or the use of any one of aspects 1 to 44, wherein the subject suffers from a disease associated with overweight, obesity or morbid obesity.
46. The method, petrelintide for use, or the use of aspect 45, wherein the disease associated with overweight, obesity or morbid obesity is selected from the group consisting of hypertension, dyslipidemia, sleep apnea, cardiovascular disease, binge-eating disorder, Prader-Willi syndrome, obesity prior to surgery, obesity-linked inflammation, obesity-linked gallbladder disease, respiratory problems, degeneration of cartilage, osteoarthritis, reproductive health complications such as infertility, Alzheimer's disease, diabetes, type 1 diabetes, type 2 diabetes, pre-diabetes, insulin resistance syndrome, impaired glucose tolerance (IGT), disease states associated with elevated blood glucose levels, metabolic disease including metabolic syndrome, hyperglycemia, atherogenic dyslipidemia, hepatic steatosis ("fatty liver"), non-alcoholic fatty liver disease (NAFLD), non-alcoholic steatohepatitis (NASH), metabolic dysfunction-associated steatotic liver disease (MASLD), metabolic (dysfunction) associated fatty liver disease (MAFLD), metabolic dysfunction-associated steatohepatitis (MASH), kidney failure, arteriosclerosis, atherosclerosis, macrovascular disease, microvascular disease, diabetic heart disease, diabetic cardiomyopathy, heart failure as a diabetic complication, coronary heart disease, peripheral artery disease or stroke, and combinations thereof.
47. The method, petrelintide for use, or the use of any one of aspects 1 to 46, wherein the subject is following a dietary regimen.
48. The method, petrelintide for use, or the use of any one of aspects 1 to 47, wherein petrelintide is formulated as a pharmaceutical composition.
49. The method, petrelintide for use, or the use of aspect 48, wherein the composition comprises a pharmaceutically acceptable carrier, excipient or vehicle.

50. The method, petrelintide for use, or the use of aspect 48 or aspect 49, wherein the pharmaceutical composition is a stable aqueous liquid pharmaceutical composition.

5 51. The method, petrelintide for use, or the use of any one of aspects 48 to 50, wherein petrelintide is present in the composition at a concentration of from about 0.4 mg/ml to about 25 mg/ml.

52. The method, petrelintide for use, or the use of any one of aspects 48 to 51, wherein
10 petrelintide is present in the composition at a concentration of

(a) at least about 0.4 mg/ml, at least about 0.5 mg/ml, at least about 0.6 mg/ml, at least about 1.2 mg/ml, or at least about 2.5 mg/ml; and/or

(b) up to about 25 mg/ml, up to about 20 mg/ml, up to about 15 mg/ml, or up to about 10 mg/ml; and/or

15 (c) about 3 mg/ml to about 12 mg/ml, e.g. about 3 mg/ml to about 7 mg/ml or about 8 mg/ml to about 12 mg/ml, e.g. about 5 mg/ml or about 10 mg/ml.

53. The method, petrelintide for use, or the use of any one of aspects 48 to 52, wherein the composition comprises a buffer at a concentration of about 0.5 mM to about 25 mM.

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54. The method, petrelintide for use, or the use of aspect 53, wherein the buffer is present at a concentration of about 0.5 mM to about 20 mM, about 0.5 mM to about 15 mM, about 1 mM to about 15 mM, about 1 mM to about 12 mM, about 3 mM to about 7 mM, about 8 mM to about 12 mM, or about 5 mM or about 10 mM.

25

55. The method, petrelintide for use, or the use of aspect 53 or aspect 54, wherein the buffer is phosphate, histidine or citrate.

56. The method, petrelintide for use, or the use of aspect 53, wherein the buffer is TRIS
30 buffer, and wherein the buffer is present at about 15 mM to about 25 mM, e.g. about 17 mM to about 23 mM, e.g. about 20 mM.

57. The method, petrelintide for use, or the use of any one of aspects 48 to 56, wherein the composition has a pH of about 5.8 to about 6.9.

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58. The method, petrelintide for use, or the use of aspect 57, wherein the pH is about 6.2 to about 6.8, about 6.4 to about 6.6, or about 6.5.

59. The method, petrelintide for use, or the use of any one of aspects 48 to 58, wherein the composition comprises a tonicity modifier.

5 60. The method, petrelintide for use, or the use of any one of aspects 48 to 59, wherein the composition comprises a preservative.

61. The method, petrelintide for use, or the use of aspect 60, wherein the preservative is meta-cresol, phenol, methylparaben, ethylparaben, propylparaben, butylparaben,
10 chlorobutanol, benzyl alcohol, phenylmercuric nitrate, thimerosal, sorbic acid, potassium sorbate, benzoic acid, chlorocresol or benzalkonium chloride.

62. The method, petrelintide for use, or the use of any one of aspects 1 to 61, wherein petrelintide is provided as a chloride salt.

15 63. The method, petrelintide for use, or the use of any one of aspects 1 to 62, wherein petrelintide is administered to the subject at a dose of about 0.0001 to about 100 mg/kg body weight per day, such as about 0.0005 to about 50 mg/kg body weight per day, such as about 0.001 to about 10 mg/kg body weight per day, such as about 0.01 to about 1 mg/kg body
20 weight per day.

64. The method, petrelintide for use, or the use of any one of aspects 1 to 63, wherein petrelintide is administered to the subject at a dose of about 2 nmol/kg body weight or about 10 nmol/kg body weight.

25 65. The method, petrelintide for use, or the use of any one of aspects 1 to 64, wherein petrelintide is administered to the subject once daily, twice daily, once every two, three, four, five or six days, once weekly, twice weekly, once monthly or twice monthly.

30 66. The method, petrelintide for use, or the use of aspects 65, wherein petrelintide is administered to the subject twice daily, once every two days or once every four days.

67. The method, petrelintide for use, or the use of any one of aspects 1 to 66, wherein petrelintide is administered to the subject by injection, such as by subcutaneous (sc),
35 intramuscular (im) or intravenous (iv) injection.

CLAIMS

1. A method of reducing consumption of high-fat food by a subject, the method comprising administering to the subject petrelintide or a pharmaceutically acceptable salt or solvate thereof.
- 5 2. A method of altering food preference of a subject, the method comprising administering to the subject petrelintide or a pharmaceutically acceptable salt or solvate thereof.
- 10 3. The method of claim 2, wherein the food preference of the subject is altered such that the subject prefers non-high-fat food to high-fat food.
4. A method of treating or preventing overweight, obesity, morbid obesity or a disease associated with overweight, obesity and/or morbid obesity in a subject, wherein the method
15 reduces consumption of high-fat food by the subject, the method comprising administering to the subject petrelintide or a pharmaceutically acceptable salt or solvate thereof.
5. The method of any one of claims 1 to 4, wherein the method is a method of inhibiting weight gain and/or reducing body weight in the subject.
- 20 6. The method of any one of claims 1 to 5, wherein high-fat food is food having a total fat content of about 5 g or more of fat per 100 g, such as about 6 g or more, about 7 g or more, about 8 g or more, about 9 g or more, about 10 g or more, about 11 g or more, about 12 g or more, about 13 g or more, about 14 g or more, about 15 g or more, about 16 g or
25 more, about 17 g or more, or about 17.5 g or more of fat per 100 g.
7. The method of any one of claims 1 to 6, wherein high-fat food is food having a total fat content of about 1 g or more of saturated fat per 100 g, such as about 2 g or more of saturated fat per 100 g, about 3 g or more, about 4 g or more, or about 5 g or more of
30 saturated fat per 100 g.
8. The method of any one of claims 1 to 7, wherein the method reduces consumption of high-fat food by the subject over a period compared to a control.
- 35 9. The method of any one of claims 1 to 8, wherein the method reduces consumption of high-fat food by the subject by at least about 5%, such as at least about 10%, at least about 15%, at least about 17%, at least about 20% at least about 25%, at least about 30%, at least

about 33%, at least about 35%, at least about 40%, at least about 45%, at least about 50%, at least about 65%, at least about 66%, at least about 70%, at least about 75%, at least about 80%, at least about 85%, at least about 90%, at least about 95% or about 100%.

5 10. The method of any one of claims 1 to 9, wherein consumption of non-high-fat food by the subject does not change or increases over a period compared to a control.

11. The method of any one of claims 8 to 10, wherein the period is at least about 1 day, at least about 2 days, at least about 3 days, at least about 4 days, at least about 5 days, at
10 least about 6 days, at least about 30 days, at least about 1 week, at least about 2 weeks, at least about 3 weeks, at least about 4 weeks, at least about 1 month, at least about 6 months, at least about 1 year, at least about 2 years, at least about 3 years, at least about 4 years, at least about 5 years, at least about 6 years, at least about 7 years, at least about 8 years, at least about 9 years, at least about 10 years, or more than 10 years.

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12. The method of any one of claims 1 to 11, wherein the subject is overweight, obese or morbidly obese.

13. The method of any one of claims 1 to 12, wherein the subject suffers from a disease
20 associated with overweight, obesity or morbid obesity.

14. The method of any one of claims 4 to 13, wherein the disease associated with overweight, obesity or morbid obesity is selected from the group consisting of hypertension, dyslipidemia, sleep apnea, cardiovascular disease, binge-eating disorder, Prader-Willi
25 syndrome, obesity prior to surgery, obesity-linked inflammation, obesity-linked gallbladder disease, respiratory problems, degeneration of cartilage, osteoarthritis, reproductive health complications such as infertility, Alzheimer's disease, diabetes, type 1 diabetes, type 2 diabetes, pre-diabetes, insulin resistance syndrome, impaired glucose tolerance (IGT), disease states associated with elevated blood glucose levels, metabolic disease including
30 metabolic syndrome, hyperglycemia, atherogenic dyslipidemia, hepatic steatosis ("fatty liver"), non-alcoholic fatty liver disease (NAFLD), non-alcoholic steatohepatitis (NASH), metabolic dysfunction-associated steatotic liver disease (MASLD), metabolic (dysfunction) associated fatty liver disease (MAFLD), metabolic dysfunction-associated steatohepatitis (MASH), kidney failure, arteriosclerosis, atherosclerosis, macrovascular disease,
35 microvascular disease, diabetic heart disease, diabetic cardiomyopathy, heart failure as a diabetic complication, coronary heart disease, peripheral artery disease or stroke, and combinations thereof.

15. The method of any one of claims 1 to 14, wherein the subject is following a dietary regimen.
- 5 16. The method of any one of claims 1 to 15, wherein petrelintide is formulated as a pharmaceutical composition, preferably wherein the pharmaceutical composition is a stable aqueous liquid pharmaceutical composition.
- 10 17. The method of any one of claims 1 to 3 and 5 to 16, wherein the method is a non-therapeutic method.
18. The method of claim 17, wherein the subject is of a healthy weight or is overweight.