

human amylin. Thus, the numbering of any given residue in Formula I above, and in other formulae elsewhere in this specification, reflects the corresponding residue in human amylin when optimally aligned therewith and does not necessarily reflect its linear position in the particular sequence.

5

(It will be apparent that any of the relevant formulae presented in this specification could be written to include residues X21-X22 at the appropriate positions, wherein X21 and X22 are absent.)

10 It has surprisingly been found that simultaneous deletion of the residues at positions X21 and X22 (and even additionally at positions X19 and X20) leads to active and stable amylin analogues. Further, without wishing to be bound by any particular theory, it is believed that the deletion of these residues may enhance the chemical stability of the molecules, especially at neutral and/or alkaline pH. Fibrillation and precipitation of the  
15 compounds may also be reduced. Thus the compounds may have superior properties for formulation as compared to existing amylin analogues.

Furthermore, the compounds described here show similar or even increased activity compared to wild type amylin (e.g. agonist activity at the hAMYR3 and/or hAMYR1 and/or  
20 hCTR2 receptors), despite being methylated at the same positions as IAPP-GI (which has lower activity than wild type amylin).

In some examples of formula I it may be desirable that:

X31 is Glu;

25 X19-X20 is Ser-Ser or is absent; and/or

X37 is Hyp or Pro.

In one aspect, the present disclosure refers to an amylin analogue selected from the group consisting of: [19CD]-isoGlu-RCNTATCATQRLADFLHRSSF-Gly(Me)-A-Ile(Me)-LSSTEVGSETP-NH<sub>2</sub>.

30 In another aspect, the disclosure refers to the use of an amylin analogue, pharmaceutically acceptable salt or solvate in the preparation of a medicament: (a) for treating obesity, morbid obesity, obesity prior to surgery, obesity-linked inflammation, obesity-linked gallbladder disease, obesity-induced sleep apnea and respiratory problems, degeneration of cartilage, osteoarthritis, or reproductive health complications of obesity or overweight such as infertility; or (b) for prevention or  
35 treatment of 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, hypertension, atherogenic dyslipidemia, hepatic steatosis ("fatty liver"), kidney failure, arteriosclerosis (e.g. atherosclerosis), macrovascular disease, microvascular disease, diabetic  
40 heart (including diabetic cardiomyopathy and heart failure as a diabetic complication) coronary heart disease, peripheral artery disease or stroke, and combinations thereof.

It may be desirable that the amylin analogue contains at least one of His14, Asn14, Aad14, Gln17 and Thr17.

If X14 is Asp, then it may be desirable that X17 is Asn, Gln, Glu, Thr or Aad.

X17 is Gln may be particularly preferred.

- 5 In some circumstances, it may be desirable that X35 is not a hydrophobic residue, e.g. Phe. Such residues may increase tendency towards fibrillation in some formulations.

Z may be an amino acid sequence of formula II:

- 10 Arg-Cys-X3-Thr-Ala-Thr-Cys-Ala-Thr-X10-Arg-Leu-Ala-X14-Phe-Leu-X17-Arg-X19-X20-Phe-Gly(Me)-Ala-Ile(Me)-Leu-Ser-Ser-Thr-Glu-Val-Gly-Ser-X35-Thr-X37 (II);

wherein

X3 is selected from the group consisting of Asn, Gly and Gln;

X10 is selected from the group consisting of Gln, Asp and Glu;

X14 is selected from the group consisting of Asp, His and Aad;

- 15 X17 is selected from the group consisting of His, Asn, Gln, Glu, Lys and Aad;

X19-X20 is Ser-Ser or is absent;

X35 is selected from the group consisting of Asp, Glu, Asn, Ser, Orn, Aad, Gly and Thr; and

X37 is selected from the group consisting of Pro and Hyp;

and wherein the compound has at least one residue selected from:

- 20 X3 is Gln;

X14 is His or Aad;

X17 is Asn, Gln, Glu or Aad; and

X35 is Ser, Phe, Orn, Aad, Gly or Thr.

In some examples of formula II, X17 may be selected from His and Gln.

- 25 Z may be an amino acid sequence of formula III:

Arg-Cys-X3-Thr-Ala-Thr-Cys-Ala-Thr-X10-Arg-Leu-Ala-X14-Phe-Leu-X17-Arg-X19-X20-Phe-Gly(Me)-Ala-Ile(Me)-Leu-Ser-Ser-Thr-Glu-Val-Gly-Ser-X35-Thr-X37 (III);

wherein

X3 is selected from the group consisting of Asn, Gly and Gln;

- 30 X10 is selected from the group consisting of Gln, Asp and Glu;

Within these constraints, a drug holiday phase may have a duration of at least two days, at least a week, at least 2 weeks, at least 4 weeks, at least a month, at least 2 months, at least 3 months, at least 6 months, or more, depending on the administration pattern during the previous administration phase.

An administration regime entailing the use of drug holiday comprises at least 2 administration phases. Consecutive administration phases are separated by respective drug holiday phases. Thus the administration regime may comprise at least 3, at least 4, at least 5, at least 10, at least 15, at least 20, at least 25, or at least 30 administration phases, or more, each separated by respective drug holiday phases.

Consecutive administration phases may utilise the same administration pattern, although this may not always be desirable or necessary. However, if other drugs or active agents are administered in combination with a peptide of the invention, then typically the same combination of drugs or active agents is given in consecutive administration phases. In certain embodiments, the recipient subject is a human.

#### Combination therapy

An amylin analogue of the invention may be administered as part of a combination therapy together with another active agent for the treatment of the disease or disorder in question, e.g. an anti-diabetic agent, an anti-obesity agent, an agent for treatment of metabolic syndrome, an anti-dyslipidemia agent, an anti-hypertensive agent, a proton pump inhibitor, or an anti-inflammatory agent. In such cases, the two active agents may be given together or separately, e.g. as constituents in the same pharmaceutical composition or formulation, or as separate formulations.

Thus a peptide of the invention may have some benefit if administered in combination with an anti-diabetic agent of known type, including, but not limited to, metformin, a sulfonylurea, a glinide, a dipeptidyl peptidase IV (DPP-IV) inhibitor, a glitazone, a Glucagon-like peptide-1 (GLP-1) receptor agonist (including GLP-1 or a GLP-1 analogue, an exendin-4 or an exendin-4 analogue, any other GLP-1 receptor agonist including liraglutide (Saxenda™, Victoza™), Dulaglutide or Albiglutide or a glucagon-GLP-1 dual agonist, e.g. as described in WO2008/101017, WO2008/152403, WO2010/070252, WO2010/070253, WO2010/070255, WO2010/070251, WO2011/006497, WO2011/160630, WO2011/160633, WO2013/092703, WO2014/041195), an Sodium-glucose co-transporter-2 (SGLT2) inhibitor (i.e. an inhibitor of sodium-glucose transport,

e.g. a gliflozin such as empagliflozin, canagliflozin, dapagliflozin or ipragliflozin), a G-protein coupled receptor 40 (GPR40) agonist (FFAR1/FFA1 agonist, e.g. fasiglifam), or an insulin or an insulin analogue. Examples of appropriate insulin analogues include, but are not limited to, Lantus™, Novorapid™, Humalog™, Novomix™, Actraphane™ HM, 5 Levemir™, Degludec™ and Apidra™. Other relevant anti-diabetic agents in this connection include GLP-1 receptor agonists, such as exenatide (Byetta™ and Bydureon™, exendin-4) and Byetta LAR™, lixisenatide (Lyxumia™) and liraglutide (Victoza™).

Moreover, a peptide of the invention may be used in combination with an anti-obesity 10 agent of known type, including, but not limited to, peptide YY or an analogue thereof, neuropeptide Y (NPY) or an analogue thereof, a cannabinoid receptor 1 antagonist, a lipase inhibitor, Human proinsulin Peptide (HIP), a melanocortin receptor 4 agonist, a GLP-1 receptor agonist (including GLP-1 or a GLP-1 analogue, an exendin-4 or an exendin-4 analogue, any other GLP-1 receptor agonist including liraglutide (Saxenda™, Victoza™), 15 Dulaglutide or Albiglutide or a glucagon-GLP-1 dual agonist, e.g. as described in WO2008/101017, WO2008/152403, WO2010/070252, WO2010/070253, WO2010/070255, WO2010/070251, WO2011/006497, WO2011/160630, WO2011/160633, WO2013/092703, WO2014/041195), Orlistat™, Sibutramine™, phentermine, a melanin concentrating hormone receptor 1 antagonist, Cholecystokinin 20 (CCK), amylin, pramlintide and leptin, as well as analogues thereof.

A peptide of the invention may further be used in combination with an anti-hypertension agent of a known type, including, but not limited to, an angiotensin-converting enzyme inhibitor, an angiotensin II receptor blocker, a diuretic, a beta-blocker and a calcium channel blocker.

25 A peptide of the invention may still further be used in combination with an anti-dyslipidemia agent of known type, including, but not limited to, a statin, a fibrate, a niacin, a PCSK9 (Proprotein convertase subtilisin/kexin type 9) inhibitor, and a cholesterol absorption inhibitor.

A peptide of the invention may also be used in combination with a proton pump inhibitor 30 (i.e. a pharmaceutical agent possessing pharmacological activity as an inhibitor of H<sup>+</sup>/K<sup>+</sup>-ATPase) of known type, including, but not limited to, an agent of the benzimidazole derivative type or of the imidazopyridine derivative type, such as Omeprazole™, Lansoprazole™, Dexlansoprazole™, Esomeprazole™, Pantoprazole™, Rabeprazole™, Zolpidem™, Alpidem™, Saripidem™ or Necopidem™.

In addition, with regard to anti-inflammatory treatment, a peptide of the invention may be beneficial if administered in combination with an anti-inflammatory agent of known type, including, but not limited to:

- steroids and corticosteroids, such as beclomethasone, methylprednisolone,  
5 betamethasone, prednisone, dexamethasone, and hydrocortisone;
- non-steroidal anti-inflammatory agents (NSAIDs), such as propionic acid derivatives (e.g. alminoprofen, benoxaprofen, bucloxic acid, carprofen, fenbufen, fenoprofen, fluprofen, flurbiprofen, ibuprofen, indoprofen, ketoprofen, mioprofen, naproxen, oxaprozin, pirprofen, pranoprofen, suprofen, tiaprofenic acid and tioxaprofen); acetic acid derivatives  
10 (e.g. indomethacin, acemetacin, alclofenac, clidanac, diclofenac, fenclofenac, fenclozic acid, fentiazac, furofenac, ibufenac, isoxepac, oxpinac, sulindac, tiopinac, tolmetin, zidometacin and zomepirac); fenamic acid derivatives (e.g. flufenamic acid, meclofenamic acid, mefenamic acid, niflumic acid and tolfenamic acid); biphenylcarboxylic acid derivatives (e.g. diflunisal and flufenisal); oxicams (e.g. isoxicam, piroxicam, sudoxicam  
15 and tenoxicam); salicylates (e.g. acetylsalicylic acid and sulfasalazine); and pyrazolones (e.g. apazone, bezpiperylon, feprazone, mofebutazone, oxyphenbutazone and phenylbutazone);
- Cyclooxygenase-II (COX II) inhibitors, such as rofecoxib and celecoxib; preparations of  
20 interferon beta (e.g. interferon beta-1a or interferon beta-1b);
- and certain other compounds, such as 5-aminosalicylic acid and prodrugs and pharmaceutically acceptable salts thereof.
- 25 Metformin has also been demonstrated to have anti-inflammatory properties (see, e.g., Haffner et al., *Diabetes* 54: 1566-1572 (2005)) and as such may also be useful in combination with compounds (peptides) of the invention.

#### Devices and kits

- 30 In some embodiments, the invention relates to a device comprising an amylin analogue or pharmaceutical composition of the invention, for delivery of the analogue to a subject. Via such devices, amylin analogues can be administered to a patient via a variety of delivery methods, including: intravenous, subcutaneous, intramuscular or intraperitoneal injection; oral administration; transdermal administration; pulmonary or transmucosal administration;

## CLAIMS

1. An amylin analogue selected from the group consisting of:

[19CD]-isoGlu-RCNTATCATQRLAHFLHRSSF-Gly(Me)-A-Ile(Me)-LSSTEVGSETP-NH<sub>2</sub>

5 [19CD]-isoGlu-RCNTATCATQRLANFLHRSSF-Gly(Me)-A-Ile(Me)-LSSTEVGSETP-NH<sub>2</sub>

[19CD]-isoGlu-RCGTATCATERLAHFLNRSSF-Gly(Me)-A-Ile(Me)-LSSTEVGSNTP-Hyp-NH<sub>2</sub>

[19CD]-isoGlu-RCGTATCATERLAHFLQRSSF-Gly(Me)-A-Ile(Me)-LSSTEVGSNTP-Hyp-NH<sub>2</sub>

[19CD]-isoGlu-RCGTATCATERLAHFLERSSF-Gly(Me)-A-Ile(Me)-LSSTEVGSNTP-Hyp-NH<sub>2</sub>

[19CD]-isoGlu-RCGTATCATERLAHFLTRSSF-Gly(Me)-A-Ile(Me)-LSSTEVGSSP-Hyp-NH<sub>2</sub>

10 [19CD]-isoGlu-RCGTATCATERLAHFLTRSSF-Gly(Me)-A-Ile(Me)-LSSTEVGSP-Hyp-NH<sub>2</sub>

[19CD]-isoGlu-RCGTATCATERLAHFLTRSSF-Gly(Me)-A-Ile(Me)-LSSTEVGSP-Orn-T-Hyp-NH<sub>2</sub>

[19CD]-isoGlu-RCGTATCATERLAHFLTRSSF-Gly(Me)-A-Ile(Me)-LSSTEVGSP-Aad-T-Hyp-NH<sub>2</sub>

15 [19CD]-isoGlu-RCGTATCATERLAHFLTRSSF-Gly(Me)-A-Ile(Me)-LSSTEVGSGP-Hyp-NH<sub>2</sub>

[19CD]-isoGlu-RCNTATCATQRLAHFLHRF-Gly(Me)-A-Ile(Me)-LSSTEVGSETP-NH<sub>2</sub>

[19CD]-isoGlu-RCGTATCATERLAHFLHRSSF-Gly(Me)-A-Ile(Me)-LSSTEVGSNTP-NH<sub>2</sub>

[19CD]-isoGlu-RCNTATCATQRLAHFLHRSSF-Gly(Me)-A-Ile(Me)-LSSTEVGSNTP-NH<sub>2</sub>

[19CD]-isoGlu-RCGTATCATERLANFLVRSSF-Gly(Me)-A-Ile(Me)-LSSTEVGSNTP-Hyp-NH<sub>2</sub>

20 [19CD]-isoGlu-RCGTATCATERLAHFLTRSSF-Gly(Me)-A-Ile(Me)-LSSTEVGSNTP-Hyp-NH<sub>2</sub>

[19CD]-isoGlu-RCGTATCATERLAHFLKRSSF-Gly(Me)-A-Ile(Me)-LSSTEVGSNTP-Hyp-NH<sub>2</sub>

[19CD]-isoGlu-RCNTATCATQRLAHFLHRVSF-Gly(Me)-A-Ile(Me)-LSSTEVGSETP-NH<sub>2</sub>

[19CD]-isoGlu-RCNTATCATQRLAHFLHRVSF-Gly(Me)-A-Ile(Me)-LSSTEVGSETP-NH<sub>2</sub>

[19CD]-isoGlu-RCGTATCATERLAHFLVRSSF-Gly(Me)-A-Ile(Me)-LSSTEVGSETP-NH<sub>2</sub>

- [19CD]-isoGlu-RCPTATCATDRLAHFLVRSSF-Gly(Me)-A-Ile(Me)-LSSTDVGS DTP-NH<sub>2</sub>
- [19CD]-isoGlu-RCNTATCATQRLAHFLVRSSF-Gly(Me)-A-Ile(Me)-LSSTEVGSETP-NH<sub>2</sub>
- [19CD]-isoGlu-RCPTATCATDRLAHFLHRSSF-Gly(Me)-A-Ile(Me)-LSSTDVGSNTP-NH<sub>2</sub>
- [19CD]-isoGlu-RCGTATCATERLAHFLHRSSF-Gly(Me)-A-Ile(Me)-LSSTEVGSETP-NH<sub>2</sub>
- 5 [19CD]-isoGlu-RCPTATCATDRLAHFLHRSSF-Gly(Me)-A-Ile(Me)-LSSTDVGS DTP-NH<sub>2</sub>
- [19CD]-isoGlu-RCGTATCATERLAHFLQRSSF-Gly(Me)-A-Ile(Me)-LSSTEVGSSST-Hyp-NH<sub>2</sub>
- [19CD]-isoGlu-RCGTATCATERLAHFLNRSSF-Gly(Me)-A-Ile(Me)-LSSTEVGSSST-Hyp-NH<sub>2</sub>
- [19CD]-isoGlu-RCGTATCATERLAHFLHRSSF-Gly(Me)-A-Ile(Me)-LSSTEVGSSST-Hyp-NH<sub>2</sub>
- [19CD]-isoGlu-RCGTATCATERLAHFLVRSSF-Gly(Me)-A-Ile(Me)-LSSTEVGSSST-Hyp-NH<sub>2</sub>
- 10 [19CD]-isoGlu-RCGTATCATERLAHFLQRSSF-Gly(Me)-A-Ile(Me)-LSSTEVG SFT-Hyp-NH<sub>2</sub>
- [19CD]-isoGlu-RCGTATCATERLAHFLNRSSF-Gly(Me)-A-Ile(Me)-LSSTEVG SFT-Hyp-NH<sub>2</sub>
- [19CD]-isoGlu-RCGTATCATERLAHFLQRSSF-Gly(Me)-A-Ile(Me)-LSSTEVG SSTP-NH<sub>2</sub>
- [19CD]-isoGlu-RCGTATCATERLAHFLNRSSF-Gly(Me)-A-Ile(Me)-LSSTEVG SSTP-NH<sub>2</sub>
- [19CD]-isoGlu-RCGTATCATERLAHF LERSSF-Gly(Me)-A-Ile(Me)-LSSTEVG SSTP-NH<sub>2</sub>
- 15 [19CD]-isoGlu-RCGTATCATERLAHFLHRSSF-Gly(Me)-A-Ile(Me)-LSSTEVG SSTP-NH<sub>2</sub>
- [19CD]-isoGlu-RCGTATCATERLAHFLVRSSF-Gly(Me)-A-Ile(Me)-LSSTEVG SSTP-NH<sub>2</sub>
- [19CD]-isoGlu-RCGTATCATERLAHFLQRSSF-Gly(Me)-A-Ile(Me)-LSSTEVG SFTP-NH<sub>2</sub>
- [19CD]-isoGlu-RCGTATCATERLAHFLNRSSF-Gly(Me)-A-Ile(Me)-LSSTEVG SFTP-NH<sub>2</sub>
- [19CD]-isoGlu-RCGTATCATERLADFLTRSSF-Gly(Me)-A-Ile(Me)-LSSTEVG SST-Hyp-NH<sub>2</sub>
- 20 [19CD]-isoGlu-RCGTATCATERLADFLTRSSF-Gly(Me)-A-Ile(Me)-LSSTEVG SFT-Hyp-NH<sub>2</sub>
- [19CD]-isoGlu-RCGTATCATERLA-Aad-FLTRSSF-Gly(Me)-A-Ile(Me)-LSSTEVG SST-Hyp-NH<sub>2</sub>

[19CD]-isoGlu-RCGTATCATERLA-Aad-FLTRSSF-Gly(Me)-A-Ile(Me)-LSSTEVGGS-Orn-T-Hyp-NH<sub>2</sub>

[19CD]-isoGlu-RCGTATCATERLAHFLTRSSF-Gly(Me)-A-Ile(Me)-LSSTEVGSSST-Apr-NH<sub>2</sub>

[19CD]-isoGlu-RCGTATCATERLAHFLTRSSF-Gly(Me)-A-Ile(Me)-LSSTEVGSSSTP-NH<sub>2</sub>

5 [19CD]-isoGlu-RCGTATCATERLAHFLTRSSF-Gly(Me)-A-Ile(Me)-LSSTEVGGS-Orn-TP-NH<sub>2</sub>

[19CD]-isoGlu-RCGTATCATERLAHFLTRSSF-Gly(Me)-A-Ile(Me)-LSSTEVGSTT-Hyp-NH<sub>2</sub>

[19CD]-isoGlu-RCNTATCATQRLADFLQRSSF-Gly(Me)-A-Ile(Me)-LSSTEVGGSNT-Hyp-NH<sub>2</sub>

[19CD]-isoGlu-RCNTATCATQRLAHFL-Aad-RSSF-Gly(Me)-A-Ile(Me)-LSSTEVGGSNT-Hyp-NH<sub>2</sub>

10 [19CD]-isoGlu-RCGTATCATERLAHFLQRSSF-Gly(Me)-A-Ile(Me)-LSSTEVGGS-Orn-T-Hyp-NH<sub>2</sub>

[19CD]-isoGlu-RCGTATCATERLAHFLQRSSF-Gly(Me)-A-Ile(Me)-LSSTEVGSGT-Hyp-NH<sub>2</sub>

[19CD]-isoGlu-RCGTATCATERLAHFLQRSSF-Gly(Me)-A-Ile(Me)-LSSTEVGGS-Aad-T-Hyp-NH<sub>2</sub>

15 [19CD]-isoGlu-RCGTATCATERLADFLQRSSF-Gly(Me)-A-Ile(Me)-LSSTEVGGSNT-Hyp-NH<sub>2</sub>

[19CD]-isoGlu-RCGTATCATERLA-Aad-FLQRSSF-Gly(Me)-A-Ile(Me)-LSSTEVGGSNT-Hyp-NH<sub>2</sub>

[19CD]-isoGlu-RCNTATCATERLAHFLQRSSF-Gly(Me)-A-Ile(Me)-LSSTEVGGSNT-Hyp-NH<sub>2</sub>

[19CD]-isoGlu-RCQTATCATERLAHFLQRSSF-Gly(Me)-A-Ile(Me)-LSSTEVGGSNT-Hyp-NH<sub>2</sub>

20 [19CD]-isoGlu-RCNTATCATQRLAHFLQRSSF-Gly(Me)-A-Ile(Me)-LSSTEVGGSNT-Hyp-NH<sub>2</sub>

[19CD]-isoGlu-RCPTATCATDRLAHFLQRSSF-Gly(Me)-A-Ile(Me)-LSSTDVGSNT-Hyp-NH<sub>2</sub>

[19CD]-isoGlu-RCNTATCATERLAHFLQRSSF-Gly(Me)-A-Ile(Me)-LSSTEVGSDT-Hyp-NH<sub>2</sub>

[19CD]-isoGlu-RCNTATCATQRLAHFLQRSSF-Gly(Me)-A-Ile(Me)-LSSTEVGSNTP-NH<sub>2</sub>

[19CD]-isoGlu-RCNTATCATERLAHFLQRSSF-Gly(Me)-A-Ile(Me)-LSSTEVGSNTP-NH<sub>2</sub>

25 [19CD]-isoGlu-RCPTATCATERLAHFLQRSSF-Gly(Me)-A-Ile(Me)-LSSTEVGGSNT-Hyp-NH<sub>2</sub>

[19CD]-isoGlu-RCPTATCATQRLAHFLQRSSF-Gly(Me)-A-Ile(Me)-LSSTEVGSNTP-Hyp-NH<sub>2</sub>

[19CD]-isoGlu-RCNTATCATQRLADFLQRSSF-Gly(Me)-A-Ile(Me)-LSSTEVGSNTP-NH<sub>2</sub>

[19CD]-isoGlu-RCNTATCATERLADFLQRSSF-Gly(Me)-A-Ile(Me)-LSSTEVGSNTP-NH<sub>2</sub>

[19CD]-isoGlu-RCPTATCATERLADFLQRSSF-Gly(Me)-A-Ile(Me)-LSSTEVGSNTP-NH<sub>2</sub>

5 [19CD]-isoGlu-RCNTATCATERLADFLQRSSF-Gly(Me)-A-Ile(Me)-LSSTEVGSNTP-Hyp-NH<sub>2</sub>

[19CD]-isoGlu-RCNTATCATQRLAHFLQRSSF-Gly(Me)-A-Ile(Me)-LSSTEVGSSST-Hyp-NH<sub>2</sub>

[19CD]-isoGlu-RCPTATCATERLAHFLQRSSF-Gly(Me)-A-Ile(Me)-LSSTEVGSSST-Hyp-NH<sub>2</sub>

[19CD]-isoGlu-RCNTATCATQRLAHFLQRSSF-Gly(Me)-A-Ile(Me)-LSSTEVGSGT-Hyp-NH<sub>2</sub>

[19CD]-isoGlu-RCPTATCATERLAHFLQRSSF-Gly(Me)-A-Ile(Me)-LSSTEVGSGT-Hyp-NH<sub>2</sub>

10 [19CD]-isoGlu-RCNTATCATQRLAHFLQRSSF-Gly(Me)-A-Ile(Me)-LSSTEVGSTT-Hyp-NH<sub>2</sub>

[19CD]-isoGlu-RCPTATCATERLAHFLQRSSF-Gly(Me)-A-Ile(Me)-LSSTEVGSTT-Hyp-NH<sub>2</sub>

[19CD]-isoGlu-RCNTATCATQRLAHFLQRSSF-Gly(Me)-A-Ile(Me)-LSSTEVGSAad-T-Hyp-NH<sub>2</sub>

[19CD]-isoGlu-RCPTATCATERLAHFLQRSSF-Gly(Me)-A-Ile(Me)-LSSTEVGSAad-T-Hyp-NH<sub>2</sub>

15 [19CD]-isoGlu-RCGTATCATERLAHFLQRF-Gly(Me)-A-Ile(Me)-LSSTEVGSNTP-Hyp-NH<sub>2</sub>

[19CD]-isoGlu-RCGTATCATERLAHFLQRSSF-Gly(Me)-A-Ile(Me)-LSSTEVGSNTP-NH<sub>2</sub>

[19CD]-isoGlu-RCNTATCATQRLAHFLQRF-Gly(Me)-A-Ile(Me)-LSSTEVGSGT-Hyp-NH<sub>2</sub>

[19CD]-isoGlu-RCNTATCATQRLADFLQRSSF-Gly(Me)-A-Ile(Me)-LSSTEVGSGTP-NH<sub>2</sub>

20 [19CD]-isoGlu-RCNTATCATQRLADFLQRSSF-Gly(Me)-A-Ile(Me)-LSSTEVGSGT-Hyp-NH<sub>2</sub>

[19CD]-isoGlu-RCNTATCATQRLADFLQRSSF-Gly(Me)-A-Ile(Me)-LSSTEVGSTTP-NH<sub>2</sub>

[19CD]-isoGlu-RCNTATCATQRLADFLQRSSF-Gly(Me)-A-Ile(Me)-LSSTEVGSTT-Hyp-NH<sub>2</sub>

[19CD]-isoGlu-RCNTATCATQRLAHFLERSSF-Gly(Me)-A-Ile(Me)-LSSTEVGSSSTP-NH<sub>2</sub>

[19CD]-isoGlu-RCNTATCATQRLAHFLQRSSF-Gly(Me)-A-Ile(Me)-LSSTEVGSSSTP-NH<sub>2</sub>

[19CD]-isoGlu-RCNTATCATQRLA-Aad-FLQRSSF-Gly(Me)-A-Ile(Me)-LSSTEVGSNTP-Hyp-NH<sub>2</sub>

[19CD]-isoGlu-RCNTATCATQRLA-Aad-FLQRSSF-Gly(Me)-A-Ile(Me)-LSSTEVGSSST-Hyp-NH<sub>2</sub>

[19CD]-isoGlu-RCQTATCATDRLAHFLQRSSF-Gly(Me)-A-Ile(Me)-LSSTEVGSNTP-Hyp-NH<sub>2</sub>

[19CD]-isoGlu-RCQTATCATDRLA-Aad-FLQRSSF-Gly(Me)-A-Ile(Me)-LSSTEVGSNTP-Hyp-NH<sub>2</sub>

[19CD]-isoGlu-RCQTATCATERLAHFLQRSSF-Gly(Me)-A-Ile(Me)-LSSTEVGSGT-Hyp-NH<sub>2</sub>

[19CD]-isoGlu-RCQTATCATDRLAHFLQRSSF-Gly(Me)-A-Ile(Me)-LSSTEVGSGT-Hyp-NH<sub>2</sub>

[19CD]-isoGlu-RCQTATCATDRLAHFLQRSSF-Gly(Me)-A-Ile(Me)-LSSTEVGSNTP-NH<sub>2</sub>

[19CD]-isoGlu-RCQTATCATERLA-Aad-FLQRSSF-Gly(Me)-A-Ile(Me)-LSSTEVGSNTP-NH<sub>2</sub>

[19CD]-isoGlu-RCQTATCATERLA-Aad-FLQRSSF-Gly(Me)-A-Ile(Me)-LSSTEVGSGTP-NH<sub>2</sub>

[19CD]-isoGlu-RCQTATCATDRLA-Aad-FLQRF-Gly(Me)-A-Ile(Me)-LSSTEVGSNTP-Hyp-NH<sub>2</sub>

[19CD]-isoGlu-RCQTATCATERLAHFLQRF-Gly(Me)-A-Ile(Me)-LSSTEVGSNTP-NH<sub>2</sub>

wherein [19CD] represents [19-carboxynonadecanoyl];

or a pharmaceutically acceptable salt or solvate thereof.

2. An amylin analogue selected from the group consisting of:

[19CD]-isoGlu-RCNTATCATQRLADFLHRSSF-Gly(Me)-A-Ile(Me)-LSSTEVGSETP-NH<sub>2</sub>;

or a pharmaceutically acceptable salt or solvate thereof.

3. The amylin analogue:

[19CD]-isoGlu-R-C()-GTAT-C()-ATERLAHFLNRSSF-Gly(Me)-A-Ile(Me)-LSSTEVGSNTP-Hyp-NH<sub>2</sub> (Compd. 6).

4. The amylin analogue:

[19CD]-isoGlu-R-C()-GTAT-C()-ATERLAHFLQRSSF-Gly(Me)-A-Ile(Me)-LSSTEVGSTNT-Hyp-NH<sub>2</sub> (Compd. 7).

5. The amylin analogue:

5 [19CD]-isoGlu-R-C()-GTAT-C()-ATERLAHFLTRSSF-Gly(Me)-A-Ile(Me)-LSSTEVGSGT-Hyp-NH<sub>2</sub> (Compd. 13).

6. The amylin analogue:

10 [19CD]-isoGlu-R-C()-GTAT-C()-ATERLAHFLHRSSF-Gly(Me)-A-Ile(Me)-LSSTEVGSTNTP-NH<sub>2</sub> (Compd. 15).

7. The amylin analogue:

15 [19CD]-isoGlu-R-C()-NTAT-C()-ATQRLADFLQRSSF-Gly(Me)-A-Ile(Me)-LSSTEVGSTNT-Hyp-NH<sub>2</sub> (Compd. 49).

8. The amylin analogue:

[19CD]-isoGlu-R-C()-GTAT-C()-ATERLA-Aad-FLQRSSF-Gly(Me)-A-Ile(Me)-LSSTEVGSTNT-Hyp-NH<sub>2</sub> (Compd. 55).

20 9. The amylin analogue:

[19CD]-isoGlu-R-C()-NTAT-C()-ATERLAHFLQRSSF-Gly(Me)-A-Ile(Me)-LSSTEVGSTNT-Hyp-NH<sub>2</sub> (Compd. 56).

10. The amylin analogue:

25 [19CD]-isoGlu-R-C()-QTAT-C()-ATERLAHFLQRSSF-Gly(Me)-A-Ile(Me)-LSSTEVGSTNT-Hyp-NH<sub>2</sub> (Compd. 57).

11. The amylin analogue:

30 [19CD]-isoGlu-R-C()-NTAT-C()-ATERLAHFLQRSSF-Gly(Me)-A-Ile(Me)-LSSTEVGSDT-Hyp-NH<sub>2</sub> (Compd. 60).

12. The amylin analogue:

35 [19CD]-isoGlu-R-C()-QTAT-C()-ATDRLAHFLQRSSF-Gly(Me)-A-Ile(Me)-LSSTEVGSTNT-Hyp-NH<sub>2</sub> (Compd. 88).

13. A pharmaceutically acceptable salt or solvate of a compound according to any one of claims 3 to 12.

14. An amylin analogue, or pharmaceutically acceptable salt or solvate, according to any one of the preceding claims, comprising an intramolecular disulphide bridge formed between the cysteine residues present at positions 2 and 7 of the amino acid sequence.

15. A pharmaceutical composition comprising an amylin analogue, or pharmaceutically acceptable salt or solvate, according to any one of the preceding claims, in combination with a pharmaceutically acceptable carrier, excipient or vehicle.

16. A device comprising an amylin analogue, or pharmaceutically acceptable salt or solvate, according to any one of claims 1 to 14, for delivery of the amylin analogue to a subject, optionally further comprising an anti-diabetic agent, an anti-obesity agent, an agent for treatment of metabolic syndrome, an anti-dyslipidemia agent, an anti-hypertensive agent, a proton pump inhibitor, or an anti-inflammatory agent.

17. An amylin analogue, or pharmaceutically acceptable salt or solvate, according to any one of claims 1 to 14 for use in therapy.

18. Use of an amylin analogue, pharmaceutically acceptable salt or solvate according to any one of claims 1 to 14 in the preparation of a medicament:

(a) for treating obesity, morbid obesity, obesity prior to surgery, obesity-linked inflammation, obesity-linked gallbladder disease, obesity-induced sleep apnea and respiratory problems, degeneration of cartilage, osteoarthritis, or reproductive health complications of obesity or overweight such as infertility; or

(b) for prevention or treatment of 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, hypertension, atherogenic dyslipidemia, hepatic steatosis ("fatty liver"), kidney failure, arteriosclerosis (e.g. atherosclerosis), macrovascular disease, microvascular disease, diabetic heart (including diabetic cardiomyopathy and heart failure as a diabetic complication) coronary heart disease, peripheral artery disease or stroke, and combinations thereof.

19. Use according to claim 18 wherein said obesity is accompanied by at least one weight-related co-morbid condition, such as diabetes (e.g. type 2 diabetes), hypertension, dyslipidemia, sleep apnea and cardiovascular disease.
- 5 20. Use according to claim 18 or claim 19 wherein said amylin analogue is for administration in conjunction with an anti-diabetic agent, an anti-obesity agent, an agent for treatment of metabolic syndrome, an anti-dyslipidemia agent, an anti-hypertensive agent, a proton pump inhibitor, or an anti-inflammatory agent.
- 10 21. Use according to claim 20 wherein:
- (a) said anti-diabetic agent is metformin, a sulfonylurea, a glinide, a dipeptidyl peptidase IV (DPP-IV) inhibitor, a glitazone, a Glucagon-like peptide-1(GLP-1) receptor agonist, an Sodium-glucose co-transporter-2 (SGLT2) inhibitor, a G-protein coupled receptor 40 (GPR40) agonist, an insulin, or an insulin analogue;
- 15 (b) said anti-obesity agent is peptide YY or an analogue thereof, neuropeptide Y (NPY) or an analogue thereof, a cannabinoid receptor 1 antagonist, a lipase inhibitor, Human proinsulin Peptide (HIP), a melanocortin receptor 4 agonist, a GLP-1 receptor agonist, phentermine, a melanin concentrating hormone receptor 1 antagonist, Cholecystokinin (CCK), amylin, pramlintide or leptin;
- 20 (c) said anti-hypertension agent is an angiotensin-converting enzyme inhibitor, an angiotensin II receptor blocker, a diuretic, a beta-blocker or a calcium channel blocker;
- (d) said anti-dyslipidemia agent is a statin, a fibrate, a niacin, a PCSK9 (Proprotein convertase subtilisin/kexin type 9) inhibitor or a cholesterol absorption inhibitor;
- (e) said proton pump inhibitor is an agent of the benzimidazole derivative type or of the imidazopyridine derivative type; or
- 25 (f) said anti-inflammatory agent is a steroid or corticosteroid, non-steroidal anti-inflammatory agent (NSAID), a Cyclooxygenase-II (COX II) inhibitor, 5-aminosalicylic acid or metformin.