

reduce weight gain. An alternative amylin analogue incorporating N-methylated residues and having a reduced tendency to fibrillation, designated IAPP-GI, has been described by Yan et al. (PNAS, 103(7), 2046-2051, 2006). IAPP-GI appears to have lower activity than native amylin, however. Further analogues of amylin or pramlintide are described in
5 WO2013/156594, WO2012/168430, WO2012/168431 and WO2012/168432, as well as WO2006/042745.

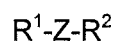
Obesity is believed to be a major causal factor in development of type 2 diabetes, which constitutes a growing and worldwide major health problem. Diseases or disorders that
10 may develop as a consequence of untreated diabetes include cardiovascular and peripheral artery disease, micro- and macrovascular complications, stroke, and certain forms of cancer, particularly hematopoietic cancers.

There is a need in the art for further amylin analogues. For example, amylin analogues
15 that show a reduced tendency for fibrillation and/or high chemical stability at or around pH 7 might allow for a formulation at or near physiological pH. Amylin analogues having high levels of agonist activity at the amylin receptor and/or appropriately long plasma elimination half lives, may also enable longer intervals between dosing than is currently possible (e.g. once weekly, or even less frequently) and hence improve patient
20 compliance.

SUMMARY

The present invention relates to compounds which are analogues of human amylin. The subject matter of the present invention is as defined in the depending claims.
25

Also described herein is an amylin analogue which is a compound having the formula:



wherein

R¹ is hydrogen, C₁₋₄ acyl, benzoyl or C₁₋₄ alkyl, or a half-life extending moiety M, wherein
30 M is optionally linked to Z via a linker moiety L;

R² is OH or NHR³, wherein R³ is hydrogen or C₁₋₃-alkyl; and

Z is an amino acid sequence of formula I:

[19CD]-isoGlu-RCGTATCATERLAHFLTRSSF-Gly(Me)-A-Ile(Me)-LSSTEVGSGT-Hyp-NH₂

[19CD]-isoGlu-RCNTATCATQRLAHFLHRF-Gly(Me)-A-Ile(Me)-LSSTEVGSETP-NH₂

[19CD]-isoGlu-RCGTATCATERLAHFLHRSSF-Gly(Me)-A-Ile(Me)-LSSTEVGSNTP-NH₂

or

- 5 [19CD]-isoGlu-RCNTATCATQRLAHFLHRSSF-Gly(Me)-A-Ile(Me)-LSSTEVGSNTP-NH₂;

(wherein [19CD] represents [19-carboxynonadecanoyl])

and pharmaceutically acceptable salts and solvates thereof;

or any such compounds comprising an intramolecular disulphide bridge formed between the cysteine residues present at positions 2 and 7 of the amino acid sequence.

- 10 In another aspect, the invention further provides a composition comprising an amylin analogue as described above. The composition may be a pharmaceutical composition, and may comprise a pharmaceutically acceptable carrier, excipient or vehicle.

- In another aspect, there is provided a device comprising an amylin analogue as described herein, 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.
- 15

- The disclosure further provides a method for the synthesis of an amylin analogue as described above. The method may comprise the steps of synthesising the peptide by solid-phase or liquid-phase methodology, and optionally isolating and/or purifying the final product. The method may further comprise the step of forming a disulphide bond between the thiol groups of the cysteine side chains at positions 2 and 7.
- 20

Also described herein is an amylin analogue as disclosed herein for use in a method of medical treatment.

- 25 The amylin analogues are useful, inter alia, in the reduction of food intake, promotion of weight loss, and inhibition or reduction of weight gain. As a result, they may be used for treatment of a variety of conditions, diseases, or disorders in a subject, including, but not limited to, obesity and various obesity-related conditions, diseases, or disorders, such as diabetes (e.g. type 2 diabetes), hypertension, dyslipidemia, sleep apnea and cardiovascular disease. The subject may be affected by obesity 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. It will be understood that the amylin analogues may thus be administered to subjects affected by conditions characterised by inadequate control of appetite or otherwise over-feeding, such as binge-
- 30

eating disorder and Prader-Willi syndrome. It will be clear that the analogues can be used for treatment of combinations of the conditions described.

Thus, the disclosure provides an amylin analogue of the invention for use in a method of treating, inhibiting or reducing weight gain, promoting weight loss and/or reducing excess
5 body weight. Treatment may be achieved, for example, by control of appetite, feeding, food intake, calorie intake and/or energy expenditure.

The disclosure also provides an amylin analogue of the invention for use in a method of treating obesity as well as associated diseases, disorders and health conditions, including, but not limited to, morbid obesity, obesity prior to surgery, obesity-linked inflammation,
10 obesity-linked gallbladder disease and obesity-induced sleep apnea and respiratory problems, degeneration of cartilage, osteoarthritis, and reproductive health complications of obesity or overweight such as infertility. The subject may be affected by obesity 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.

15 The disclosure also provides an amylin analogue of the invention for use in a method of 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
20 steatosis ("fatty liver"; including non-alcoholic fatty liver disease (NAFLD), which itself includes non-alcoholic steatohepatitis (NASH)), 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.

25 The disclosure also provides an amylin analogue of the invention for use in a method of lowering circulating LDL levels and/or increasing HDL/LDL ratio.

Effects of amylin analogues on these conditions may be mediated in whole or in part via an effect on body weight, or may be independent thereof.

30 Also described herein is the use of an amylin analogue of the invention in the manufacture of a medicament for treating, inhibiting or reducing weight gain, promoting weight loss and/or reducing excess body weight.

CLAIMS

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

[19CD]-isoGlu-RCNTATCATQRLAHFLHRSSF-Gly(Me)-A-Ile(Me)-LSSTEVGSETP-NH₂

5 [19CD]-isoGlu-RCNTATCATQRLANFLHRSSF-Gly(Me)-A-Ile(Me)-LSSTEVGSETP-NH₂

[19CD]-isoGlu-RCGTATCATERLAHFLNRSSF-Gly(Me)-A-Ile(Me)-LSSTEVGSNTP-Hyp-NH₂

[19CD]-isoGlu-RCGTATCATERLAHFLQRSSF-Gly(Me)-A-Ile(Me)-LSSTEVGSNTP-Hyp-NH₂

[19CD]-isoGlu-RCGTATCATERLAHFLERSSF-Gly(Me)-A-Ile(Me)-LSSTEVGSNTP-Hyp-NH₂

[19CD]-isoGlu-RCGTATCATERLAHFLTRSSF-Gly(Me)-A-Ile(Me)-LSSTEVGSSP-Hyp-NH₂

10 [19CD]-isoGlu-RCGTATCATERLAHFLTRSSF-Gly(Me)-A-Ile(Me)-LSSTEVGSP-Hyp-NH₂

[19CD]-isoGlu-RCGTATCATERLAHFLTRSSF-Gly(Me)-A-Ile(Me)-LSSTEVGSP-Orn-T-Hyp-NH₂

[19CD]-isoGlu-RCGTATCATERLAHFLTRSSF-Gly(Me)-A-Ile(Me)-LSSTEVGSP-Aad-T-Hyp-NH₂

15 [19CD]-isoGlu-RCGTATCATERLAHFLTRSSF-Gly(Me)-A-Ile(Me)-LSSTEVGSP-Hyp-NH₂

[19CD]-isoGlu-RCNTATCATQRLAHFLHRF-Gly(Me)-A-Ile(Me)-LSSTEVGSETP-NH₂

[19CD]-isoGlu-RCGTATCATERLAHFLHRSSF-Gly(Me)-A-Ile(Me)-LSSTEVGSNTP-NH₂

[19CD]-isoGlu-RCNTATCATQRLAHFLHRSSF-Gly(Me)-A-Ile(Me)-LSSTEVGSNTP-NH₂

[19CD]-isoGlu-RCGTATCATERLANFLVRSSF-Gly(Me)-A-Ile(Me)-LSSTEVGSNTP-Hyp-NH₂

20 [19CD]-isoGlu-RCGTATCATERLAHFLTRSSF-Gly(Me)-A-Ile(Me)-LSSTEVGSNTP-Hyp-NH₂

[19CD]-isoGlu-RCGTATCATERLAHFLKRSSF-Gly(Me)-A-Ile(Me)-LSSTEVGSNTP-Hyp-NH₂

[19CD]-isoGlu-RCNTATCATQRLAHFLHRVF-Gly(Me)-A-Ile(Me)-LSSTEVGSETP-NH₂

[19CD]-isoGlu-RCNTATCATQRLAHFLHRVSF-Gly(Me)-A-Ile(Me)-LSSTEVGSETP-NH₂

[19CD]-isoGlu-RCGTATCATERLAHFLVRSSF-Gly(Me)-A-Ile(Me)-LSSTEVGSETP-NH₂

- [19CD]-isoGlu-RCPTATCATDRLAHFLVRSSF-Gly(Me)-A-Ile(Me)-LSSTDVGS DTP-NH₂
- [19CD]-isoGlu-RCNTATCATQRLAHFLVRSSF-Gly(Me)-A-Ile(Me)-LSSTEVGSETP-NH₂
- [19CD]-isoGlu-RCPTATCATDRLAHFLHRSSF-Gly(Me)-A-Ile(Me)-LSSTDVGSNTP-NH₂
- [19CD]-isoGlu-RCGTATCATERLAHFLHRSSF-Gly(Me)-A-Ile(Me)-LSSTEVGSETP-NH₂
- 5 [19CD]-isoGlu-RCPTATCATDRLAHFLHRSSF-Gly(Me)-A-Ile(Me)-LSSTDVGS DTP-NH₂
- [19CD]-isoGlu-RCGTATCATERLAHFLQRSSF-Gly(Me)-A-Ile(Me)-LSSTEVGSS T-Hyp-NH₂
- [19CD]-isoGlu-RCGTATCATERLAHFLNRSSF-Gly(Me)-A-Ile(Me)-LSSTEVGSS T-Hyp-NH₂
- [19CD]-isoGlu-RCGTATCATERLAHFLHRSSF-Gly(Me)-A-Ile(Me)-LSSTEVGSS T-Hyp-NH₂
- [19CD]-isoGlu-RCGTATCATERLAHFLVRSSF-Gly(Me)-A-Ile(Me)-LSSTEVGSS T-Hyp-NH₂
- 10 [19CD]-isoGlu-RCGTATCATERLAHFLQRSSF-Gly(Me)-A-Ile(Me)-LSSTEVG SFT-Hyp-NH₂
- [19CD]-isoGlu-RCGTATCATERLAHFLNRSSF-Gly(Me)-A-Ile(Me)-LSSTEVG SFT-Hyp-NH₂
- [19CD]-isoGlu-RCGTATCATERLAHFLQRSSF-Gly(Me)-A-Ile(Me)-LSSTEVG S STP-NH₂
- [19CD]-isoGlu-RCGTATCATERLAHFLNRSSF-Gly(Me)-A-Ile(Me)-LSSTEVG S STP-NH₂
- [19CD]-isoGlu-RCGTATCATERLAHFLERSSF-Gly(Me)-A-Ile(Me)-LSSTEVG S STP-NH₂
- 15 [19CD]-isoGlu-RCGTATCATERLAHFLHRSSF-Gly(Me)-A-Ile(Me)-LSSTEVG S STP-NH₂
- [19CD]-isoGlu-RCGTATCATERLAHFLVRSSF-Gly(Me)-A-Ile(Me)-LSSTEVG S STP-NH₂
- [19CD]-isoGlu-RCGTATCATERLAHFLQRSSF-Gly(Me)-A-Ile(Me)-LSSTEVG SFTP-NH₂
- [19CD]-isoGlu-RCGTATCATERLAHFLNRSSF-Gly(Me)-A-Ile(Me)-LSSTEVG SFTP-NH₂
- [19CD]-isoGlu-RCGTATCATERLADFLTRSSF-Gly(Me)-A-Ile(Me)-LSSTEVG S S T-Hyp-NH₂
- 20 [19CD]-isoGlu-RCGTATCATERLADFLTRSSF-Gly(Me)-A-Ile(Me)-LSSTEVG SFT-Hyp-NH₂
- [19CD]-isoGlu-RCGTATCATERLA-Aad-FLTRSSF-Gly(Me)-A-Ile(Me)-LSSTEVG S S T-Hyp-NH₂

- [19CD]-isoGlu-RCGTATCATERLA-Aad-FLTRSSF-Gly(Me)-A-Ile(Me)-LSSTEVGGS-Orn-T-Hyp-NH₂
- [19CD]-isoGlu-RCGTATCATERLAHFLTRSSF-Gly(Me)-A-Ile(Me)-LSSTEVGGSST-Apr-NH₂
- [19CD]-isoGlu-RCGTATCATERLAHFLTRSSF-Gly(Me)-A-Ile(Me)-LSSTEVGGSSTP-NH₂
- 5 [19CD]-isoGlu-RCGTATCATERLAHFLTRSSF-Gly(Me)-A-Ile(Me)-LSSTEVGGS-Orn-TP-NH₂
- [19CD]-isoGlu-RCGTATCATERLAHFLTRSSF-Gly(Me)-A-Ile(Me)-LSSTEVGSTT-Hyp-NH₂
- [19CD]-isoGlu-RCNTATCATQRLADFLQRSSF-Gly(Me)-A-Ile(Me)-LSSTEVGGSNT-Hyp-NH₂
- [19CD]-isoGlu-RCNTATCATQRLAHFL-Aad-RSSF-Gly(Me)-A-Ile(Me)-LSSTEVGGSNT-Hyp-NH₂
- 10 [19CD]-isoGlu-RCGTATCATERLAHFLQRSSF-Gly(Me)-A-Ile(Me)-LSSTEVGGS-Orn-T-Hyp-NH₂
- [19CD]-isoGlu-RCGTATCATERLAHFLQRSSF-Gly(Me)-A-Ile(Me)-LSSTEVGSGT-Hyp-NH₂
- [19CD]-isoGlu-RCGTATCATERLAHFLQRSSF-Gly(Me)-A-Ile(Me)-LSSTEVGGS-Aad-T-Hyp-NH₂
- 15 [19CD]-isoGlu-RCGTATCATERLADFLQRSSF-Gly(Me)-A-Ile(Me)-LSSTEVGGSNT-Hyp-NH₂
- [19CD]-isoGlu-RCGTATCATERLA-Aad-FLQRSSF-Gly(Me)-A-Ile(Me)-LSSTEVGGSNT-Hyp-NH₂
- [19CD]-isoGlu-RCNTATCATERLAHFLQRSSF-Gly(Me)-A-Ile(Me)-LSSTEVGGSNT-Hyp-NH₂
- [19CD]-isoGlu-RCQTATCATERLAHFLQRSSF-Gly(Me)-A-Ile(Me)-LSSTEVGGSNT-Hyp-NH₂
- 20 [19CD]-isoGlu-RCNTATCATQRLAHFLQRSSF-Gly(Me)-A-Ile(Me)-LSSTEVGGSNT-Hyp-NH₂
- [19CD]-isoGlu-RCPTATCATDRLAHFLQRSSF-Gly(Me)-A-Ile(Me)-LSSTDVGSNT-Hyp-NH₂
- [19CD]-isoGlu-RCNTATCATERLAHFLQRSSF-Gly(Me)-A-Ile(Me)-LSSTEVGSDT-Hyp-NH₂
- [19CD]-isoGlu-RCNTATCATQRLAHFLQRSSF-Gly(Me)-A-Ile(Me)-LSSTEVGSNTP-NH₂
- [19CD]-isoGlu-RCNTATCATERLAHFLQRSSF-Gly(Me)-A-Ile(Me)-LSSTEVGSNTP-NH₂
- 25 [19CD]-isoGlu-RCPTATCATERLAHFLQRSSF-Gly(Me)-A-Ile(Me)-LSSTEVGGSNT-Hyp-NH₂

[19CD]-isoGlu-RCPTATCATQRLAHFLQRSSF-Gly(Me)-A-Ile(Me)-LSSTEVGSNTP-Hyp-NH₂

[19CD]-isoGlu-RCNTATCATQRLADFLQRSSF-Gly(Me)-A-Ile(Me)-LSSTEVGSNTP-Hyp-NH₂

[19CD]-isoGlu-RCNTATCATERLADFLQRSSF-Gly(Me)-A-Ile(Me)-LSSTEVGSNTP-Hyp-NH₂

[19CD]-isoGlu-RCPTATCATERLADFLQRSSF-Gly(Me)-A-Ile(Me)-LSSTEVGSNTP-Hyp-NH₂

5 [19CD]-isoGlu-RCNTATCATERLADFLQRSSF-Gly(Me)-A-Ile(Me)-LSSTEVGSNTP-Hyp-NH₂

[19CD]-isoGlu-RCNTATCATQRLAHFLQRSSF-Gly(Me)-A-Ile(Me)-LSSTEVGSSST-Hyp-NH₂

[19CD]-isoGlu-RCPTATCATERLAHFLQRSSF-Gly(Me)-A-Ile(Me)-LSSTEVGSSST-Hyp-NH₂

[19CD]-isoGlu-RCNTATCATQRLAHFLQRSSF-Gly(Me)-A-Ile(Me)-LSSTEVGSGT-Hyp-NH₂

[19CD]-isoGlu-RCPTATCATERLAHFLQRSSF-Gly(Me)-A-Ile(Me)-LSSTEVGSGT-Hyp-NH₂

10 [19CD]-isoGlu-RCNTATCATQRLAHFLQRSSF-Gly(Me)-A-Ile(Me)-LSSTEVGSTT-Hyp-NH₂

[19CD]-isoGlu-RCPTATCATERLAHFLQRSSF-Gly(Me)-A-Ile(Me)-LSSTEVGSTT-Hyp-NH₂

[19CD]-isoGlu-RCNTATCATQRLAHFLQRSSF-Gly(Me)-A-Ile(Me)-LSSTEVGSAad-T-Hyp-NH₂

[19CD]-isoGlu-RCPTATCATERLAHFLQRSSF-Gly(Me)-A-Ile(Me)-LSSTEVGSAad-T-Hyp-NH₂

15 [19CD]-isoGlu-RCGTATCATERLAHFLQRF-Gly(Me)-A-Ile(Me)-LSSTEVGSNTP-Hyp-NH₂

[19CD]-isoGlu-RCGTATCATERLAHFLQRSSF-Gly(Me)-A-Ile(Me)-LSSTEVGSNTP-Hyp-NH₂

[19CD]-isoGlu-RCNTATCATQRLAHFLQRF-Gly(Me)-A-Ile(Me)-LSSTEVGSGT-Hyp-NH₂

[19CD]-isoGlu-RCNTATCATQRLADFLQRSSF-Gly(Me)-A-Ile(Me)-LSSTEVGSGTP-Hyp-NH₂

20 [19CD]-isoGlu-RCNTATCATQRLADFLQRSSF-Gly(Me)-A-Ile(Me)-LSSTEVGSGT-Hyp-NH₂

[19CD]-isoGlu-RCNTATCATQRLADFLQRSSF-Gly(Me)-A-Ile(Me)-LSSTEVGSTTP-Hyp-NH₂

[19CD]-isoGlu-RCNTATCATQRLADFLQRSSF-Gly(Me)-A-Ile(Me)-LSSTEVGSTT-Hyp-NH₂

[19CD]-isoGlu-RCNTATCATQRLAHFLERSSSF-Gly(Me)-A-Ile(Me)-LSSTEVGSSSTP-Hyp-NH₂

[19CD]-isoGlu-RCNTATCATQRLAHFLQRSSF-Gly(Me)-A-Ile(Me)-LSSTEVGSSSTP-NH₂

[19CD]-isoGlu-RCNTATCATQRLA-Aad-FLQRSSF-Gly(Me)-A-Ile(Me)-LSSTEVGSNTP-Hyp-NH₂

5 [19CD]-isoGlu-RCNTATCATQRLA-Aad-FLQRSSF-Gly(Me)-A-Ile(Me)-LSSTEVGSSST-Hyp-NH₂

[19CD]-isoGlu-RCQTATCATDRLAHFLQRSSF-Gly(Me)-A-Ile(Me)-LSSTEVGSNTP-Hyp-NH₂

[19CD]-isoGlu-RCQTATCATDRLA-Aad-FLQRSSF-Gly(Me)-A-Ile(Me)-LSSTEVGSNTP-Hyp-NH₂

[19CD]-isoGlu-RCQTATCATERLAHFLQRSSF-Gly(Me)-A-Ile(Me)-LSSTEVGSGT-Hyp-NH₂

10 [19CD]-isoGlu-RCQTATCATDRLAHFLQRSSF-Gly(Me)-A-Ile(Me)-LSSTEVGSGT-Hyp-NH₂

[19CD]-isoGlu-RCQTATCATDRLAHFLQRSSF-Gly(Me)-A-Ile(Me)-LSSTEVGSNTP-NH₂

[19CD]-isoGlu-RCQTATCATERLA-Aad-FLQRSSF-Gly(Me)-A-Ile(Me)-LSSTEVGSNTP-NH₂

[19CD]-isoGlu-RCQTATCATERLA-Aad-FLQRSSF-Gly(Me)-A-Ile(Me)-LSSTEVGSGTP-NH₂

[19CD]-isoGlu-RCQTATCATDRLA-Aad-FLQRF-Gly(Me)-A-Ile(Me)-LSSTEVGSNTP-Hyp-NH₂

15 [19CD]-isoGlu-RCQTATCATERLAHFLQRF-Gly(Me)-A-Ile(Me)-LSSTEVGSNTP-NH₂

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

or a pharmaceutically acceptable salt or solvate thereof.

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

20 [19CD]-isoGlu-RCNTATCATQRLADFLHRSSF-Gly(Me)-A-Ile(Me)-LSSTEVGSETP-NH₂;

[19CD]-isoGlu-RCNTATCATQRLADFLHRSSNNF-Gly(Me)-A-Ile(Me)-LSSTNVGSNT-Apr-NH₂; and

[19CD]-isoGlu-RCNTATCATQRLAHFLHRSSNNF-Gly(Me)-A-Ile(Me)-LSSTNVGSNT-Apr-NH₂;

25 or a pharmaceutically acceptable salt or solvate thereof.

3. The amylin analogue:
[19CD]-isoGlu-R-C()-GTAT-C()-ATERLAHFLNRSSF-Gly(Me)-A-Ile(Me)-LSSTEVGSNH₂-Hyp-NH₂ (Compd. 6).
- 5 4. The amylin analogue:
[19CD]-isoGlu-R-C()-GTAT-C()-ATERLAHFLQRSSF-Gly(Me)-A-Ile(Me)-LSSTEVGSNH₂-Hyp-NH₂ (Compd. 7).
- 10 5. The amylin analogue:
[19CD]-isoGlu-R-C()-GTAT-C()-ATERLAHFLTRSSF-Gly(Me)-A-Ile(Me)-LSSTEVGSGT-Hyp-NH₂ (Compd. 13).
- 15 6. The amylin analogue:
[19CD]-isoGlu-R-C()-GTAT-C()-ATERLAHFLHRSSF-Gly(Me)-A-Ile(Me)-LSSTEVGSNTP-NH₂ (Compd. 15).
- 20 7. The amylin analogue:
[19CD]-isoGlu-R-C()-NTAT-C()-ATQRLADFLQRSSF-Gly(Me)-A-Ile(Me)-LSSTEVGSNH₂-Hyp-NH₂ (Compd. 49).
- 25 8. The amylin analogue:
[19CD]-isoGlu-R-C()-GTAT-C()-ATERLA-Aad-FLQRSSF-Gly(Me)-A-Ile(Me)-LSSTEVGSNH₂-Hyp-NH₂ (Compd. 55).
- 30 9. The amylin analogue:
[19CD]-isoGlu-R-C()-NTAT-C()-ATERLAHFLQRSSF-Gly(Me)-A-Ile(Me)-LSSTEVGSNH₂-Hyp-NH₂ (Compd. 56).
- 35 10. The amylin analogue:
[19CD]-isoGlu-R-C()-QTAT-C()-ATERLAHFLQRSSF-Gly(Me)-A-Ile(Me)-LSSTEVGSNH₂-Hyp-NH₂ (Compd. 57).
11. The amylin analogue:
[19CD]-isoGlu-R-C()-NTAT-C()-ATERLAHFLQRSSF-Gly(Me)-A-Ile(Me)-LSSTEVGSDT-Hyp-NH₂ (Compd. 60).
12. The amylin analogue:

[19CD]-isoGlu-R-C()-QTAT-C()-ATDRLAHFLQRSSF-Gly(Me)-A-Ile(Me)-LSSTEVGST-Hyp-NH₂ (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;

(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; or

5 (c) for lowering circulating LDL levels and/or increasing HDL/LDL ratio.

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.

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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.

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21. Use according to claim 20 wherein:

(a) said anti-diabetic agent is metformin, a sulfonylurea, a glinide, a DPP-IV inhibitor, a glitazone, a GLP-1 receptor agonist, an SGLT2 inhibitor, a GPR40 agonist, an insulin, or an insulin analogue;

20 (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 proleptin Peptide (HIP), a melanocortin receptor 4 agonist, a GLP-1 receptor agonist, OrlistatTM, SibutramineTM, phentermine, a melanin concentrating hormone receptor 1 antagonist, CCK, amylin, pramlintide or leptin;

25 (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;

30 (e) said proton pump inhibitor is an agent of the benzimidazole derivative type or of the imidazopyridine derivative type; or

(f) said anti-inflammatory agent is a steroid or corticosteroid, non-steroidal anti-inflammatory agent (NSAID), a COX II inhibitor, 5-aminosalicylic acid or metformin.