

for treating diabetes, obesity, obesity-related comorbidities. These GGG tri-receptor agonists exhibit a prolonged activity and thus appear suitable for once-weekly administration.

[006] There are, however, potential problems associated with administration of products with prolonged activity at each of the GCG, GLP-1 and GIP receptors. For instance, it is well-known that GLP-1 single agonist treatments are associated with nausea, vomiting, and/or diarrhea. For example, one study reported that all GLP-1 receptor agonist dosing regimens significantly increased the incidence of gastrointestinal adverse events. *Diabetes Technol Ther.* 2015 Jan;17(1):35-42. Clinical trials of GIP/GLP-1 and GLP-1/GCG dual agonist compounds have also indicated that tolerability at high doses is limited by gastrointestinal adverse events. See e.g. Schmitt, C. *et al.*, *Diabetes Obes. Metab.* 2017;19:1436-1445; Portron, A. *et al.*, 2390-PUB, A624, ADA-2017; Portron, A. *et al.*, *Diabetes Obes. Metab.* 2017;19:1446-1453; Ambery P. D. *et al.*, *British Journal of Clinical Pharmacology*, 2018 Oct;84(10):2325-2335; Alba M. *et al.*, *Clinical Obesity*, 2021 Apr;11(2):e12432). Thus, development of effective doses and dosing regimen for a triple agonist that has activity at all three GCG, GLP-1 and GIP receptors remains an unpredictable and challenging task. The dose limitation associated with gastrointestinal adverse events may prevent dosing to the desired effective dose, may compromise patient compliance with treatment, and may limit the effectiveness of the treatment regimen. In addition, administration of a compound having prolonged activity once-weekly may require multiple weeks to reach a steady state of activity, especially balanced activity, resulting in sub-optimal control in the interim.

[007] Therefore, there is a need for optimized doses and dosing regimens of GGG tri-receptor agonists that provide effective glycemic control and/or effective weight management in an individual in need of such treatment, while also preserving an overall acceptable profile of safety and adverse events and tolerability to the individual.

BRIEF SUMMARY

[007a] In a first aspect of the present disclosure, there is provided a use of a glucose-dependent insulintropic polypeptide (GIP), glucagon-like peptide-1 (GLP-1) and glucagon (GCG) (GGG) tri-receptor agonist comprising SEQ ID NO:1 in the manufacture of a medicament for improving glycemic control in an individual, wherein a first once

weekly dose of the GGG tri-receptor agonist is to be administered to the individual for at least 1 week, and wherein the first once weekly dose is from about 0.5 mg to about 4.0 mg. [007b] In another aspect of the present disclosure, there is provided a use of a glucose-dependent insulintropic polypeptide (GIP), glucagon-like peptide-1 (GLP-1) and glucagon (GCG) (GGG) tri-receptor agonist comprising SEQ ID NO:1 in the manufacture of a medicament for improving glycemic control in an individual, wherein a first once weekly dose of the GGG tri-receptor agonist is from about 0.5 mg to about 4.0 mg and is to be administered to the individual for at least 1 week, and wherein the first once weekly dose is increased by increments of about 1.0 mg to about 4.0 mg to a once weekly dose of ≤ 12.0 mg, and wherein each increased once weekly dose is to be administered to the individual for at least 1 week.

[007c] In yet another aspect of the present disclosure, there is provided a use of a glucose-dependent insulintropic polypeptide (GIP), glucagon-like peptide-1 (GLP-1) and glucagon (GCG) (GGG) tri-receptor agonist comprising SEQ ID NO:1 suitable for once-weekly dosing in the manufacture of a medicament for improving glycemic control in an individual, wherein a dose of the GGG tri-receptor agonist from about 0.5 mg to about 4.0 mg is to be administered to the individual for at least 1 week, followed by a dose of the GGG tri-receptor agonist from about 2.0 mg to about 8.0 mg for at least 1 week, followed by a dose of the GGG tri-receptor agonist from about 8.0 mg to about 12.0 mg for at least 1 week.

[007d] In a further aspect of the present disclosure, there is provided a use of a glucose-dependent insulintropic polypeptide (GIP), glucagon-like peptide-1 (GLP-1) and glucagon (GCG) (GGG) tri-receptor agonist comprising SEQ ID NO:1 in the manufacture of a medicament for providing chronic weight management in an individual, wherein a first once weekly dose of the GGG tri-receptor agonist is to be administered to the individual for at least 1 week and wherein the first once weekly dose is from about 0.5 mg to 4.0 mg.

[007e] In another aspect of the present disclosure, there is provided a use of a glucose-dependent insulintropic polypeptide (GIP), glucagon-like peptide-1 (GLP-1) and glucagon (GCG) (GGG) tri-receptor agonist comprising SEQ ID NO:1 in the manufacture of a medicament for providing chronic weight management in an individual, wherein a first once weekly dose of the GGG tri-receptor agonist is from about 0.5 mg to about 4.0 mg

and is to be administered to the individual for at least 1 week, and wherein the first once weekly dose is increased by increments of about 1.0 to about 4.0 mg to a once weekly dose of ≤ 12.0 mg, and wherein each increased once weekly dose is to be administered to the individual for at least 1 week.

[007f] In yet another aspect of the present disclosure, there is provided a use of a glucose-dependent insulintropic polypeptide (GIP), glucagon-like peptide-1 (GLP-1) and glucagon (GCG) (GGG) tri-receptor agonist comprising SEQ ID NO:1 suitable for once-weekly dosing in the manufacture of a medicament for providing chronic weight management in an individual, wherein a dose of the GGG tri-receptor agonist from about 0.5 mg to about 4.0 mg is to be administered to the individual for at least 1 week, followed by a dose of the GGG tri-receptor agonist from about 2.0 mg to about 8.0 mg for at least 1 week, followed by a dose of the GGG tri-receptor agonist from about 8.0 mg to about 12.0 mg for at least 1 week.

[008] To address this need, the disclosure describes doses of a GGG tri-receptor agonist having a structure of SEQ ID NO:1, where such doses can be from about 0.5 mg to about 12.0. In some instances, the dose is from about 0.5 mg to about 4.0 mg, from about 2.0 mg

to about 8.0 mg, or from about 4.0 mg to about 12.0 mg. In other instances, the dose is ≤ 12.0 mg.

[009] The disclosure also describes pharmaceutical formulations that include a GGG tri-receptor agonist having a structure of SEQ ID NO:1 at a dose of about 0.5 mg to about 12.0 mg.

[0010] The disclosure also describes methods of improving glycemic control in an individual, providing chronic weight management in an overweight or obese individual, as well as methods of treating diabetes mellitus (especially T2DM), dyslipidemia, metabolic syndrome, NAFLD, NASH and/or obesity, obstructive sleep apnea, osteoarthritis, polycystic ovary syndrome and/or chronic kidney disease.

[0011] In one example, the disclosure describes methods of improving glycemic control in an individual, where such methods include administering to the individual a first once weekly dose of a GGG tri-receptor agonist comprising SEQ ID NO:1 for at least about 1 week, where the first once weekly dose is from about 0.5 mg to about 4.0 mg.

[0012] In some instances, the methods also include administering to the individual a second once weekly dose of the GGG tri-receptor agonist for at least 1 week. In some instances, the second once weekly dose can be less than the first once weekly dose. Alternatively, the second once weekly dose can be the same as the first once weekly dose. Alternatively, the second once weekly dose can be greater than the first once weekly dose. In some instances, the second once weekly dose is from about 2.0 mg to about 8.0 mg.

[0013] In some instances, the methods also include administering to the individual a third once weekly dose of the GGG tri-receptor agonist for at least 1 week. In some instances, the third once weekly dose can be less than the second once weekly dose. Alternatively, the third once weekly dose can be the same as the second once weekly dose. Alternatively, the third once weekly dose can be greater than the second once weekly dose. In some instances, the third once weekly dose is from about 4.0 mg to about 12.0 mg.

[0014] In some instances, the methods also include administering to the individual a fourth once weekly dose of the GGG tri-receptor agonist for at least 1 week. In some instances, the fourth once weekly dose can be less than the third once weekly dose. Alternatively, the fourth once weekly dose can be the same as the third once weekly dose. Alternatively, the fourth once weekly dose can be greater than the third once weekly dose. In some instances, the fourth once weekly dose is from about 6.0 mg to about 12.0 mg.

[0015] In some instances, the methods also include a step of administering to the individual a fifth once weekly dose of the GGG tri-receptor agonist for at least 1 week. In some instances, the fifth once weekly dose can be less than the fourth once weekly dose. Alternatively, the fifth once weekly dose can be the same as the fourth once weekly dose. Alternatively, the fifth once weekly dose can be greater than the fourth once weekly dose. In some instances, the fifth once weekly dose is from about 8.0 mg to about 12.0 mg.

[0016] In some instances, each once weekly dose (the first once weekly dose and the subsequent once weekly doses) is administered for at least about two weeks. In some instances, each once weekly dose is administered for at least about four weeks.

[0017] In one example, the first once weekly dose is 2.0 mg, the second once weekly dose is 4.0 mg, the third once weekly dose is 8.0 mg, and the fourth once weekly dose is 12.0 mg. In another example, the first once weekly dose is 2.0 mg, the second once weekly dose is 4.0 mg, the third once weekly dose is 6.0 mg, the fourth once weekly dose is 9.0 mg, and the fifth once weekly dose is 12.0 mg.

[0018] In another example, the disclosure describes methods of improving glycemic control in an individual where such methods include administering to the individual a first once weekly dose of a GGG tri-receptor agonist comprising SEQ ID NO:1, where the first once weekly dose is from about 0.5 mg to about 4.0 mg and is administered for at least 1 week. The methods further include increasing the first once weekly dose by increments of about 1.0 to about 4.0 mg to a once weekly dose of ≤ 12.0 mg, wherein each increased once weekly dose is administered for at least 1 week.

[0019] In some instances, the first once weekly dose and each increased once weekly dose are administered for at least about two weeks. In some instances, the first once weekly dose and each increased once weekly dose are administered for at least about four weeks.

[0020] In some instances, the first once weekly dose is ≥ 1.0 mg and is increased at 4-week intervals by about 1.0, 2.0, 3.0 or 4.0 mg increments until achieving a dose of about 8.0 mg or about 9.0 mg or about 10.0 mg or about 11.0 mg or about 12.0 mg.

[0021] In some instances, the first once weekly dose is selected from 1.0 or 2.0 mg and the increased once weekly doses are selected from 2.0, 3.0, 4.0, 6.0, 8.0, 9.0, 10.0 or 12.0 mg.

[0022] In one example, the first once weekly dose is 2.0 mg, and the increased once weekly doses are 4.0, 8.0 and 12.0 mg. In another example, the first once weekly dose is 2.0 mg, and the increased once weekly doses are 4.0, 6.0, 9.0 and 12.0 mg.

[0023] In another example, the disclosure describes methods of improving glycemic control in an individual, where such methods include a step (a) of administering to the individual from about 0.5 mg to about 4.0 mg of a GGG tri-receptor agonist comprising a structure of SEQ ID NO:1 suitable for once-weekly dosing for at least 1 week. The methods also include a step (b) of administering to the individual from about 2.0 mg to about 8.0 mg of the GGG tri-receptor agonist once weekly for at least 1 week. The methods also include a step (c) of administering to the individual from about 8.0 mg to about 12.0 mg of the GGG tri-receptor agonist once weekly for at least 1 week.

[0024] In another example, the disclosure describes methods of providing chronic weight management in an individual, where such methods include administering to the individual a first once weekly dose of a GGG tri-receptor agonist comprising SEQ ID NO:1 for at least about 1 week, where the first once weekly dose is from about 0.5 mg to about 4.0 mg.

[0025] In some instances, the methods also include administering to the individual a second once weekly dose of the GGG tri-receptor agonist for at least 1 week. In some instances, the second once weekly dose can be less than the first once weekly dose. Alternatively, the second once weekly dose can be the same as the first once weekly dose. Alternatively, the second once weekly dose can be greater than the first once weekly dose. In some instances, the second once weekly dose is from about 2.0 mg to about 8.0 mg.

[0026] In some instances, the methods also include administering to the individual a third once weekly dose of the GGG tri-receptor agonist for at least 1 week. In some instances, the third once weekly dose can be less than the second once weekly dose. Alternatively, the third once weekly dose can be the same as the second once weekly dose. Alternatively, the third once weekly dose can be greater than the second once weekly dose. In some instances, the third once weekly dose is from about 4.0 mg to about 12.0 mg.

[0027] In some instances, the methods also include a step of administering to the individual a fourth once weekly dose of the GGG tri-receptor agonist for at least 1 week. In some instances, the fourth once weekly dose can be less than the third once weekly dose. Alternatively, the fourth once weekly dose can be the same as the third once weekly dose.

Alternatively, the fourth once weekly dose can be greater than the third once weekly dose. In some instances, the fourth once weekly dose is from about 6.0 mg to about 12.0 mg.

[0028] In some instances, the methods also include a step of administering to the individual a fifth once weekly dose of the GGG tri-receptor agonist for at least 1 week. In some instances, the fifth once weekly dose can be less than the fourth once weekly dose. Alternatively, the fifth once weekly dose can be the same as the fourth once weekly dose. Alternatively, the fifth once weekly dose can be greater than the fourth once weekly dose. In some instances, the fifth once weekly dose is from about 8.0 mg to about 12.0 mg.

[0029] In some instances, each once weekly dose is administered for at least about two weeks. In some instances, each once weekly dose is administered for at least about four weeks.

[0030] In one example, the first once weekly dose is 2.0 mg, the second once weekly dose is 4.0 mg, the third once weekly dose is 8.0 mg, and the fourth once weekly dose is 12.0 mg. In another example, the first once weekly dose is 2.0 mg, the second once weekly dose is 4.0 mg, the third once weekly dose is 6.0 mg, the fourth once weekly dose is 9.0 mg, and the fifth once weekly dose is 12.0 mg.

[0031] In another example, the disclosure describes methods of providing chronic weight management in an individual, where such methods include administering to the individual a first once weekly dose of a GGG tri-receptor agonist having a structure of SEQ ID NO:1, where the first once weekly dose is from about 0.5 mg to about 4.0 mg and is administered for at least 1 week. The methods include increasing the first once weekly dose by increments of about 1.0 mg to about 4.0 mg to a once weekly dose of ≤ 12.0 mg, wherein each increased once weekly dose is administered for at least 1 week.

[0032] In some instances, the first once weekly dose and each increased once weekly dose are administered for at least about two weeks. In some instances, the first once weekly dose and each increased once weekly dose are administered for at least about four weeks.

[0033] In certain instances, the first once weekly dose is ≥ 1.0 mg and is increased at 4-week intervals by about 1.0, 2.0, 3.0 or 4.0 mg increments until achieving a dose of about 8.0 mg or about 9.0 mg or about 10.0 mg or about 11.0 mg or about 12.0 mg.

[0034] In one example, the first once weekly dose is 2.0 mg, and the increased once weekly doses are 4.0, 8.0 and 12.0 mg. In another example, the first once weekly dose is 2.0 mg, and the increased once weekly doses are 4.0, 6.0, 9.0 and 12.0 mg.

[0035] In another example, the disclosure describes methods of providing chronic weight management in an individual, where such methods include a step (a) of administering to the individual from about 0.5 mg to about 4.0 mg of a GGG tri-receptor agonist having a structure of SEQ ID NO:1 suitable for once-weekly dosing for at least 1 week. The methods also include a step (b) of administering to the individual from about 2.0 mg to about 8.0 mg of the GGG tri-receptor agonist for at least 1 week. The methods also include a step (c) of administering to the individual from about 8.0 mg to about 12.0 mg of the GGG tri-receptor agonist once weekly for at least 1 week.

[0036] In some instances, the individual has diabetes, especially T2DM. In some instances, the individual is overweight or obese or has obesity. In some instances, the individual initially has a body mass index (BMI) of ≥ 27 kg/m² but < 30 kg/m² and thus is overweight. In other instances, the individual initially has a BMI ≥ 30 kg/m² and thus is obese.

[0037] In another example, methods for treating diabetes mellitus (especially T2DM), dyslipidemia, metabolic syndrome, NAFLD, NASH and/or obesity, obstructive sleep apnea, osteoarthritis, polycystic ovary syndrome and/or chronic kidney disease are also described herein.

[0038] In addition to the above methods, uses are described for a GGG tri-receptor agonist having a structure of SEQ ID NO:1 suitable for once-weekly dosing for improving glycemic control or for providing chronic weight management in an individual, where the dose of the GGG tri-receptor agonist to be administered is obtainable by one or more of the methods described herein.

[0039] Likewise, uses are described for a GGG tri-receptor agonist comprising SEQ ID NO:1 suitable for once-weekly dosing for treating diabetes mellitus (especially T2DM), dyslipidemia, metabolic syndrome, NAFLD, NASH and/or obesity, obstructive sleep apnea, osteoarthritis, polycystic ovary syndrome and/or chronic kidney disease, where the dose of the GGG tri-receptor agonist to be administered is obtainable by one or more of the methods described herein.

[0040] An advantage of the doses, regimens, methods and uses herein is that the GGG tri-receptor analog provides a longer duration of action and fewer AEs, thus requiring fewer injections than currently available incretin analogs, including as infrequently as once-weekly. Such products would have the potential to improve acceptance and compliance.

CLAIMS

The invention claimed is:

1. Use of a glucose-dependent insulintropic polypeptide (GIP), glucagon-like peptide-1 (GLP-1) and glucagon (GCG) (GGG) tri-receptor agonist comprising SEQ ID NO:1 in the manufacture of a medicament for improving glycemic control in an individual, wherein a first once weekly dose of the GGG tri-receptor agonist is to be administered to the individual for at least 1 week, and wherein the first once weekly dose is from about 0.5 mg to about 4.0 mg.
2. The use of Claim 1, wherein a second once weekly dose of the GGG tri-receptor agonist is to be administered to the individual for at least 1 week.
3. The use of Claim 2, wherein the second once weekly dose is less than the first once weekly dose.
4. The use of Claim 2, wherein the second once weekly dose is the same as the first once weekly dose.
5. The use of Claim 2, wherein the second once weekly dose is greater than the first once weekly dose.
6. The use of Claim 2, wherein the second once weekly dose is from about 2.0 mg to about 8.0 mg.
7. The use of Claim 2, wherein a third once weekly dose of the GGG tri-receptor agonist is to be administered to the individual for at least 1 week.
8. The use of Claim 7, wherein the third once weekly dose is less than the second once weekly dose.

9. The use of Claim 7, wherein the third once weekly dose is the same as the second once weekly dose.
10. The use of Claim 7, wherein the third once weekly dose is greater than the second once weekly dose.
11. The use of Claim 7, wherein the third once weekly dose is from about 4.0 mg to about 12.0 mg.
12. The use of Claim 7, wherein a fourth once weekly dose of the GGG tri-receptor agonist is to be administered to the individual for at least 1 week.
13. The use of Claim 12, wherein the fourth once weekly dose is less than the third once weekly dose.
14. The use of Claim 12, wherein the fourth once weekly dose is the same as the third once weekly dose.
15. The use of Claim 12, wherein the fourth once weekly dose is greater than the third once weekly dose.
16. The use of Claim 12, wherein the fourth once weekly dose is from about 6.0 mg to about 12.0 mg.
17. The use of Claim 12, wherein a fifth once weekly dose of the GGG tri-receptor agonist is to be administered to the individual for at least 1 week.
18. The use of Claim 17, wherein the fifth once weekly dose is less than the fourth once weekly dose.
19. The use of Claim 17, wherein the fifth once weekly dose is the same as the fourth once weekly dose.

20. The use of Claim 17, wherein the fifth once weekly dose is greater than the fourth once weekly dose.
21. The use of Claim 17, wherein the fifth once weekly dose is from about 8.0 mg to about 12.0 mg.
22. The use of Claim 12, wherein the first once weekly dose is selected from about 1.0 mg to about 2.0 mg, the second once weekly dose is selected from about 2.0 mg to about 4.0 mg, the third once weekly dose is selected from about 4.0 mg to about 8.0 mg, and the fourth once weekly dose is selected from about 6.0 to about 12.0 mg.
23. The use of Claim 17, wherein the first once weekly dose is selected from about 1.0 mg to about 2.0 mg, the second once weekly dose is selected from about 2.0 mg to about 4.0 mg, the third once weekly dose is selected from about 4.0 mg to about 8.0 mg, the fourth once weekly dose is selected from about 6.0 mg to about 12.0 mg, and the fifth once weekly dose is selected from about 8.0 mg to about 12.0 mg.
24. The use of Claim 22 or 23, wherein the first once weekly dose is selected from 1.0 or 2.0 mg.
25. The use of Claim 22 or 23, wherein the second once weekly dose is selected from 2.0, 3.0 or 4.0 mg.
26. The use of Claim 22 or 23, wherein the third once weekly dose is selected from 4.0, 6.0 or 8.0 mg.
27. The use of Claim 22 or 23, wherein the fourth once weekly dose is selected from 6.0, 8.0, 9.0, 10.0 or 12.0 mg.
28. The use of Claim 23, wherein the fifth once weekly dose is selected from 8.0, 10.0 or 12.0 mg.

29. The use of claim 22, wherein the first once weekly dose is 2.0 mg, the second once weekly dose is 4.0 mg, the third once weekly dose is 8.0 mg, and the fourth once weekly dose is 12.0 mg.

30. The use of claim 23, wherein the first once weekly dose is 2.0 mg, the second once weekly dose is 4.0 mg, the third once weekly dose is 6.0 mg, the fourth once weekly dose is 9.0 mg, and the fifth once weekly dose is 12.0 mg.

31. The use of any one of claims 1 to 30, wherein each once weekly dose is to be administered to the individual for at least about 2 weeks.

32. The use of any one of claims 1 to 30, wherein each once weekly dose is to be administered to the individual for at least about 4 weeks.

33. Use of a glucose-dependent insulintropic polypeptide (GIP), glucagon-like peptide-1 (GLP-1) and glucagon (GCG) (GGG) tri-receptor agonist comprising SEQ ID NO:1 in the manufacture of a medicament for improving glycemic control in an individual, wherein a first once weekly dose of the GGG tri-receptor agonist is from about 0.5 mg to about 4.0 mg and is to be administered to the individual for at least 1 week, and wherein the first once weekly dose is increased by increments of about 1.0 mg to about 4.0 mg to a once weekly dose of ≤ 12.0 mg, and wherein each increased once weekly dose is to be administered to the individual for at least 1 week.

34. The use of Claim 33, wherein the first once weekly dose and each increased once weekly dose are to be administered to the individual for at least about two weeks.

35. The use of Claim 33, wherein the first once weekly dose and each increased once weekly dose are to be administered to the individual for at least about four weeks.

36. The use of any one of Claims 33 to 35, wherein the first once weekly dose is selected from 1.0 or 2.0 mg.

37. The use of any one of Claims 33 to 36, wherein the increased once weekly doses are selected from 2.0, 3.0, 4.0, 6.0, 8.0, 9.0, 10.0 or 12.0 mg.
38. The use of any one of Claims 33 to 37, wherein the first once weekly dose is selected from 1.0 or 2.0 mg, and a first increased once weekly dose is selected from 2.0, 3.0 or 4.0 mg.
39. The use of Claim 38, wherein a second increased once weekly dose is selected from 4.0, 6.0 or 8.0 mg.
40. The use of Claim 39, wherein a third increased once weekly dose is selected from 6.0, 8.0, 9.0, 10.0 or 12.0 mg.
41. The use of Claim 40, wherein a fourth increased once weekly dose is selected from 8.0, 10.0 or 12.0 mg.
42. The use of Claim 41, wherein a fifth increased once weekly dose is selected from 10.0 or 12.0 mg.
43. The use of any one of Claims 33 to 35, wherein a sixth increased once weekly dose is 12.0 mg.
44. The use of any one of Claims 33 to 35, wherein the first once weekly dose is 2.0 mg, and the increased once weekly doses are 4.0, 8.0 and 12.0 mg.
45. The use of any one of Claims 33 to 35, wherein the first once weekly dose is 2.0 mg, and the increased once weekly doses are 4.0, 6.0, 9.0 and 12.0 mg.
46. The use of any one of Claims 33 to 35, wherein the increments are selected from 1.0, 2.0, 3.0 or 4.0 mg.

47. Use of a glucose-dependent insulintropic polypeptide (GIP), glucagon-like peptide-1 (GLP-1) and glucagon (GCG) (GGG) tri-receptor agonist comprising SEQ ID NO:1 suitable for once-weekly dosing in the manufacture of a medicament for improving glycemic control in an individual,

wherein a dose of the GGG tri-receptor agonist from about 0.5 mg to about 4.0 mg is to be administered to the individual for at least 1 week, followed by a dose of the GGG tri-receptor agonist from about 2.0 mg to about 8.0 mg for at least 1 week, followed by a dose of the GGG tri-receptor agonist from about 8.0 mg to about 12.0 mg for at least 1 week.

48. Use of a glucose-dependent insulintropic polypeptide (GIP), glucagon-like peptide-1 (GLP-1) and glucagon (GCG) (GGG) tri-receptor agonist comprising SEQ ID NO:1 in the manufacture of a medicament for providing chronic weight management in an individual, wherein a first once weekly dose of the GGG tri-receptor agonist is to be administered to the individual for at least 1 week and wherein the first once weekly dose is from about 0.5 mg to 4.0 mg.

49. Use of a glucose-dependent insulintropic polypeptide (GIP), glucagon-like peptide-1 (GLP-1) and glucagon (GCG) (GGG) tri-receptor agonist comprising SEQ ID NO:1 in the manufacture of a medicament for providing chronic weight management in an individual, wherein a first once weekly dose of the GGG tri-receptor agonist is from about 0.5 mg to about 4.0 mg and is to be administered to the individual for at least 1 week, and wherein the first once weekly dose is increased by increments of about 1.0 to about 4.0 mg to a once weekly dose of ≤ 12.0 mg, and wherein each increased once weekly dose is to be administered to the individual for at least 1 week.

50. Use of a glucose-dependent insulintropic polypeptide (GIP), glucagon-like peptide-1 (GLP-1) and glucagon (GCG) (GGG) tri-receptor agonist comprising SEQ ID NO:1 suitable for once-weekly dosing in the manufacture of a medicament for providing chronic weight management in an individual, wherein a dose of the GGG tri-receptor agonist from about 0.5 mg to about 4.0 mg is to be administered to the individual for at

least 1 week, followed by a dose of the GGG tri-receptor agonist from about 2.0 mg to about 8.0 mg for at least 1 week, followed by a dose of the GGG tri-receptor agonist from about 8.0 mg to about 12.0 mg for at least 1 week.

51. The use of any one of Claims 1 to 50, wherein the individual initially has a body mass index (BMI) of ≥ 27 kg/m² but < 30 kg/m².

52. The use of any one of Claims 1 to 50, wherein the individual initially has a body mass index (BMI) ≥ 30 kg/m².

53. The use of Claims 1 to 50, wherein the individual has type 2 diabetes.

54. The use of Claims 1 to 50, wherein the individual has obesity.