activities. WO2013/164483 also discloses compounds stated to have GLP-1R and GIPR activities.

WO2018/181864 discloses compounds stated to have GIPR agonist activity.

There is a need for T2DM treatments capable of providing effective glucose control for a larger portion of the patients in need of such treatment. There is a further need for T2DM treatments capable of providing effective glucose control and with a favorable side effect profile. There is a need for alternate treatment options to provide therapeutic weight loss in a patient in need of such treatment, such as a patient with severe obesity. There is a desire for diabetes treatment options that may be combined with insulin therapy and/or incretin therapy to provide the patient with superior glycemic outcomes and/or more desirable side effect profiles.

Summary

In an aspect of the present disclosure, there is provided a compound, or pharmaceutically acceptable salt thereof, wherein the compound is SEQ ID NO:7 or SEQ ID NO:10.

In another aspect of the present disclosure, there is provided a pharmaceutical composition comprising the compound, or a pharmaceutically acceptable salt thereof, disclosed herein and at least one pharmaceutically acceptable carrier, diluent, or excipient.

In a further aspect of the present disclosure, there is provided a use of the compound, or a pharmaceutically acceptable salt thereof, disclosed herein, in the manufacture of a medicament for treating a condition selected from the group consisting of diabetes mellitus, obesity, and metabolic syndrome.

In another aspect of the present disclosure, there is provided a use of the compound, or a pharmaceutically acceptable salt thereof, disclosed herein, in the manufacture of a medicament for treating diabetes in a patient receiving insulin therapy.

In a further aspect of the present disclosure, there is provided a compound disclosed herein, or a pharmaceutically acceptable salt thereof, for use in therapy.

Detailed Description

Compounds with extended duration of action at the GIP receptor are desirable to allow for less frequent dosing of the compound.

Accordingly, embodiment 1 is a compound of Formula I

$Z_1X_1X_2EGTX_6ISDYSIX_{13}LDX_{16}X_{17}X_{18}QX_{20}X_{21}X_{22}VX_{24}X_{25}X_{26}L$

$X_{28}X_{29}GPSSGAPPPSZ_2$ (SEQ ID NO:4) wherein:

Z_1 is a modification of the N-terminal amino group wherein the modification is selected from the group consisting of acetyl and absent;

X_1 is selected from the group consisting of Y and D-Tyr;

X_2 is selected from the group consisting of Aib, A, and D-Ala;

X_6 is selected from the group consisting of F, αMeF, Iva, L, αMeL, and αMeF(2F);

X_{13} is selected from the group consisting of αMeL, A, L, and Aib;

X_{16} is selected from the group consisting of K, E, and Orn;

X_{17} is selected from the group consisting of I and K(2-[2-(2-amino-ethoxy)-ethoxy]- acetyl)$_2$-(γ-Glu)-CO-$(CH_2)_q$-CO_2H;

X_{18} is selected from the group consisting of H, A, and R;

X_{20} is selected from the group consisting of Aib and Q;

X_{21} is selected from the group consisting of D and E;

X_{22} is selected from the group consisting of F and αMeF;

X_{24} is selected from the group consisting of E, N, Q, and D-Glu;

WE CLAIM:

1. A compound of the formula:

$Z_1X_1X_2EGTX_6ISDYSIX_{13}LDX_{16}X_{17}X_{18}QX_{20}X_{21}X_{22}VX_{24}$

$X_{25}X_{26}L$

$X_{28}X_{29}GPSSGAPPPSZ_2$ (SEQ ID NO:4) wherein:

Z_1 is a modification of the N-terminal amino group wherein the modification is selected from the group consisting of acetyl and absent;

X_1 is selected from the group consisting of Y and D-Tyr;

X_2 is selected from the group consisting of Aib, A, and D-Ala,

X_6 is selected from the group consisting of F, αMeF, Iva, L, αMeL, and αMeF(2F);

X_{13} is selected from the group consisting of αMeL, A, L, and Aib;

X_{16} is selected from the group consisting of K, E, and Orn;

X_{17} is selected from the group consisting of I and K(2-[2-(2-amino-ethoxy)-ethoxy]-acetyl)$_2$-(γ-Glu)-CO-$(CH_2)_q$-CO_2H;

X_{18} is selected from the group consisting of H, A, and R;

X_{20} is selected from the group consisting of Aib and Q;

X_{21} is selected from the group consisting of D and E;

X_{22} is selected from the group consisting of F and αMeF;

X_{24} is selected from the group consisting of E, N, Q, and D-Glu;

X_{25} is selected from the group consisting of Y, 4-Pal, W, and αMeY;

X_{26} is selected from the group consisting of L, and K(2-[2-(2-amino-ethoxy)-ethoxy]-acetyl)$_2$-(γ-Glu)-CO-$(CH_2)_q$-CO_2H;

X_{28} is selected from the group consisting of E and A;

X_{29} is selected from the group consisting of G, A, Q, and T; q is selected from the group consisting of 16 and 18; and

Z_2 is absent or a modification of the C-terminal group, wherein the modification is amidation;

wherein one and only one selected from X_{17} and X_{26} is K(2-[2-(2-amino-ethoxy)-ethoxy]-acetyl)$_2$-(γ-Glu)-CO-$(CH_2)_q$-CO_2H; or a pharmaceutically acceptable salt thereof.

2. A compound, or a pharmaceutically acceptable salt thereof, as claimed by Claim 1 wherein X_1 is Y and Z_1 is absent.

3. A compound, or a pharmaceutically acceptable salt thereof, as claimed by Claim 1 or Claim 2 wherein X_2 is Aib.

4. A compound, or a pharmaceutically acceptable salt thereof, as claimed by any one of Claims 1 to 3 wherein:

X_6 is selected from the group consisting of F and αMeF(2F).

5. A compound, or a pharmaceutically acceptable salt thereof, as claimed by any one of Claims 1 to 4 wherein:

X_{13} is selected from the group consisting of L and αMeL.

6. A compound, or a pharmaceutically acceptable salt thereof, as claimed by any one of Claims 1 to 5 wherein X_{16} is K or Orn.

7. A compound, or a pharmaceutically acceptable salt thereof, as claimed by claim 6 wherein X_{16} is K.

8. A compound, or a pharmaceutically acceptable salt thereof, as claimed by any one of Claims 1 to 7 wherein X_{18} is H.

9. A compound, or a pharmaceutically acceptable salt thereof, as claimed by any one of Claims 1 to 8 wherein X_{20} is Aib; and X_{22} is F.

10. A compound, or a pharmaceutically acceptable salt thereof, as claimed by any one of claims 1 to 9 wherein X_{21} is D.

11. A compound, or pharmaceutically acceptable salt thereof, as claimed by any one of Claims 1 to 10 wherein X_{25} is 4-Pal or Y.

12. A compound, or a pharmaceutically acceptable salt thereof, as claimed by any one of Claims 1 to 10 wherein:

X_{17} is K(2-[2-(2-amino-ethoxy)-ethoxy]-acetyl)$_2$-(γ-Glu)-CO-$(CH_2)_q$-CO_2H; and X_{26} is L.

13. A compound, or a pharmaceutically acceptable salt thereof, as claimed by any one of Claims 1 to 10 wherein X_{17} is I; and X_{26} is K(2-[2-(2-amino-ethoxy)-ethoxy]- acetyl)$_2$-(γ-Glu)-CO-$(CH_2)_q$-CO_2H.

14. A compound, or a pharmaceutically acceptable salt thereof, as claimed by any one of claims 1 to 12 wherein q is 16.

~~15. A compound, or a pharmaceutically acceptable salt thereof, as claimed by any one of claims 1 to 12 wherein q is 18.~~

~~16. A compound, or pharmaceutically acceptable salt thereof, as claimed by Claim 1 wherein:~~

~~X_1 is Y and Z_1 is absent;~~

~~X_2 is selected from the group consisting of Aib and D-Ala; X_6 is F;~~

~~X_{13} is selected from the group consisting of αMeL and L;~~

~~X_{16} is selected from the group consisting of K and Orn;~~

~~X_{18} is selected from the group consisting of H and A; X_{20} is Aib;~~

~~X_{22} is F;~~

~~X_{24} is selected from the group consisting of E, N, and D-Glu; X_{25} is selected from the group consisting of Y, 4-Pal, and W;~~

~~X_{28} is selected from the group consisting of E and A;~~

~~X_{29} is selected from the group consisting of G, A, and Q; q is selected from the group consisting of 16 and 18.~~

~~17. A compound, or pharmaceutically acceptable salt thereof, as claimed by Claim 16 wherein:~~

~~X_2 is Aib;~~

~~X_{13} is αMeL;~~

~~X_{18} is H;~~

~~X_{24} is selected from the group consisting of E and D-Glu;~~

~~X_{25} is selected from the group consisting of Y and 4-Pal;~~

~~X_{28} is E;~~

~~X_{29} is selected from the group consisting of G and A.~~

~~18. A compound or pharmaceutically acceptable salt thereof, as claimed by Claim 17 wherein: X_{17} is K(2-[2-(2-amino-ethoxy)-ethoxy]-acetyl)$_2$-(γ-Glu)-CO-(CH_2)q-CO_2H; and X_{26} is L.~~

~~19. A compound or pharmaceutically acceptable salt thereof, as claimed by Claim 17 wherein: X_{17} is I; and X_{26} is K(2-[2-(2-amino-ethoxy)-ethoxy]-acetyl)$_2$-(γ-Glu)-CO-(CH_2)q-CO2H.~~

~~20.~~1. A compound, or pharmaceutically acceptable salt thereof, ~~as claimed by~~

~~Claim 1 wherein the compound is selected from the group consisting of SEQ ID NO:5, SEQ ID NO:6,~~ wherein the compound is SEQ ID NO:7~~, SEQ ID NO:8, SEQ ID NO:9,~~ or SEQ ID NO:10~~, and SEQ ID NO:11~~.

~~21.~~2. ~~A~~ The compound, or a pharmaceutically acceptable salt thereof, as claimed by Claim ~~20~~ 1 wherein the compound is SEQ ID NO: 7.

~~22. A compound, or pharmaceutically acceptable salt thereof, as claimed by Claim 20 wherein the compound is SEQ ID NO:8.~~

~~23.~~3. ~~A~~ The compound, or a pharmaceutically acceptable salt thereof, as claimed by Claim ~~20~~ 1 wherein the compound is SEQ ID NO:10.

~~24. A method for treating a condition selected from the group consisting of diabetes mellitus, obesity, and metabolic syndrome, comprising administering to a patient in need thereof, an effective amount of a compound, or a pharmaceutically acceptable salt thereof, as claimed by any one of Claims 1 to 22.~~

~~25. A method as claimed by Claim 24 wherein the condition is obesity.~~

~~26. A method as claimed by Claim 24 wherein the condition is type 2 diabetes mellitus.~~

~~27. A method for treating diabetes in a patient receiving insulin therapy comprising administering an effective amount of a compound or pharmaceutically acceptable salt thereof, as claimed by any one of Claims 1 to 22 to a patient in need thereof.~~

~~28.~~4. A pharmaceutical composition comprising the compound, or a pharmaceutically acceptable salt thereof, as claimed by any one of claims 1-3~~Claims 1 to 22~~ and at least one pharmaceutically acceptable carrier, diluent, or excipient.

~~29.~~5. Use of the~~A~~ compound, or a pharmaceutically acceptable salt thereof, as claimed by any one of claims 1-3, in the manufacture of a medicament for~~Claims 1 to 22 for use in~~ treating a condition selected from the group consisting of diabetes mellitus, obesity, and metabolic syndrome.

6. Use of the compound, or a pharmaceutically acceptable salt thereof, as claimed by any one of claims 1-3 in the manufacture of a medicament for treating diabetes in a patient receiving insulin therapy.

7. The use as claimed by Claim 5 wherein the condition is obesity.

8. The use as claimed by Claim 5 wherein the condition is type 2 diabetes mellitus.

9. A compound as claimed in any one of claims 1-3, or a pharmaceutically acceptable salt thereof, for use in therapy.

~~30. A compound, or a pharmaceutically acceptable salt thereof, as claimed by Claim 29 wherein the condition is type 2 diabetes mellitus.~~