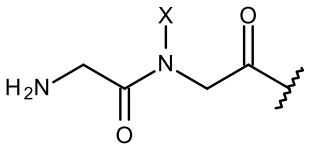
CLAIMS

1. A compound comprising Formula I:

A – Z (Formula I)

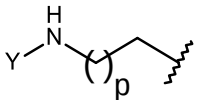
wherein Z comprises a GLP-1 polypeptide;

wherein A is of Formula II:



(Formula II);

wherein X is of Formula III:



wherein p = 1-5 (Formula III);

wherein Y comprises a lipophilic moiety with a distal carboxylic acid;

or a pharmaceutical acceptable salt, ester or amide thereof.

2. The compound according to any preceding claim, wherein the N-terminal amino group of the GLP-1 polypeptide is linked to A via an amide bond.

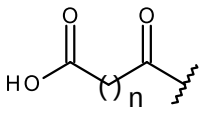
3. The compound according to any preceding claim, wherein the N-terminal residue of the GLP-1 polypeptide is His.

4. The compound according to any preceding claim, wherein the GLP-1 polypeptide is a GLP-1 analogue which has maximum of 2 amino acid changes as compared to GLP-1(7-37) (SEQ ID NO: 1).

5. The compound according to any preceding claim, wherein Z is semaglutide.

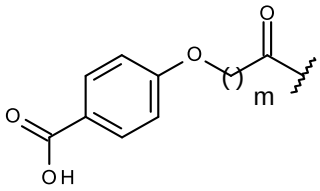
6. The compound according to any preceding claim, wherein the lipophilic moiety with a distal carboxylic acid is a moiety selected from a group consisting of Chem. 12 and Chem. 13:

Chem. 12:



wherein n = 12, 14, 16 or 18,

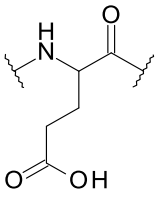
Chem. 13:



wherein m = 9 or 10,

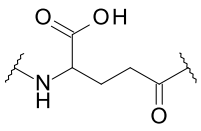
7. The compound according to any preceding claim, wherein Y comprises a moiety selected from a group consisting of Chem. 6 and Chem. 7:

Chem. 6:



,

Chem. 7:

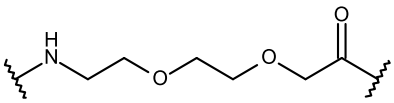


8. The compound according to any preceding claim, wherein Y is of Formula IV:

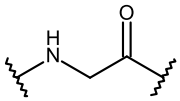
A_5-A_4-A_3-A_2-A_1- (Formula IV)

wherein A_1, A_2 and A_3 are each individually selected from a group consisting of Chem. 6, Chem. 7, Chem. 8, Chem. 9, Chem. 10, and Chem. 11, or is absent:

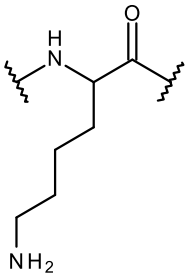
Chem. 8:



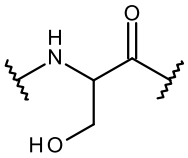
Chem. 9:



Chem. 10:



Chem. 11:



;

wherein A_4 is selected from a group consisting of Chem. 6 and Chem. 7;

wherein A_5 is selected from the group consisting of Chem. 12 and Chem. 13.

9. The compound according to claim 8, wherein the residues A_5, A_4, A_3, A_2, A_1 are interconnected via amide bonds.

10. The compound according to any preceding claim, wherein the compound is a prodrug and Z is a parent drug, and wherein the prodrug to drug conversion half-life, determined in vitro at 37°C and pH 7.4, is at least 3.0 days.

11. The compound according to any preceding claim, wherein the compound is a prodrug and Z is a parent drug, and wherein the observed terminal half-life of the parent drug, determined upon administration of the prodrug in mini-pigs, is >80 hours.

12. The compound according to any preceding claim selected from a group consisting of Chem. 14, Chem. 15, Chem. 16, Chem. 17, Chem. 18, Chem. 19, Chem. 20, Chem. 21, Chem. 22, Chem. 23, Chem. 24, Chem. 25, Chem. 26, Chem. 27, Chem. 28, Chem. 29, Chem. 30, Chem. 31, Chem. 32, Chem. 33, and Chem. 34;

or a pharmaceutical acceptable salt, ester or amide thereof.

13. Use of the compound according to any one of claims 1-12 in the manufacture of a medicament for the treatment of (i) diabetes, (ii) obesity, (iii) non-alcoholic fatty liver disease (NAFLD) and non-alcoholic steatohepatitis (NASH), (iv) cardiovascular disease, (v) neurodegenerative disorders, (vi) chronic kidney disease (CKD), (vii) diabetic kidney disease (DKD), (viii) peripheral arterial disease (PAD), and/or (ix) heart failure (HF).

14. Use of the compound according to claim 13 in the manufacture of a medicament for the treatment of obesity.

15. A compound selected from a group consisting of Chem. 14, Chem. 15, Chem. 16, Chem. 17, Chem. 18, Chem. 19, Chem. 20, Chem. 21, Chem. 22, Chem. 23, Chem. 24, Chem. 25, Chem. 26, Chem. 27, Chem. 28, Chem. 29, Chem. 30, Chem. 31, Chem. 32, Chem. 33, and Chem. 34;

or a pharmaceutical acceptable salt, ester or amide thereof.