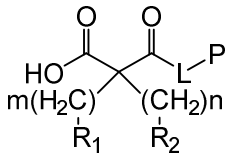
CLAIMS

1. A compound of formula (I) or a pharmaceutically acceptable salt thereof:



(I),

wherein:

R_1 and R_2 are independently selected from CH_3, OH, CO_2H, $CH=CH_2$ and $C\equiv CH$;

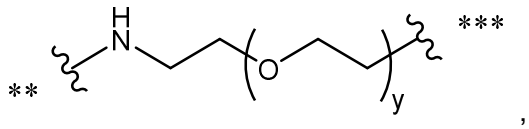
n and m are each an integer independently selected from 5 to 30;

L is an optional linker;

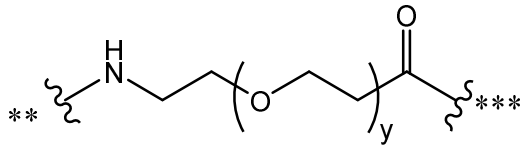
P is GLP-1 or a GLP-1 analogue.

2. A compound of formula (I) or a pharmaceutically acceptable salt thereof according to claim 1, wherein P is bound to L via an NH group.

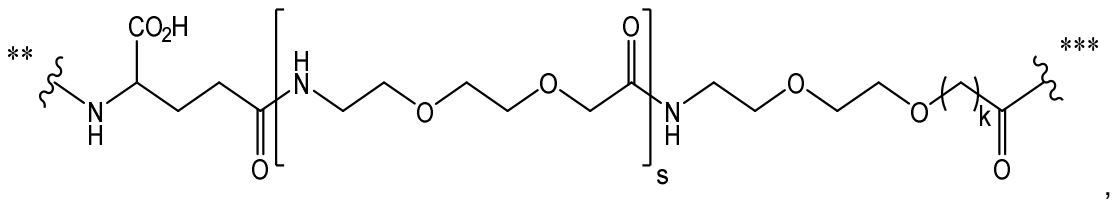
3. A compound of formula (I) or a pharmaceutically acceptable salt thereof according to claim 1 or 2, wherein L is selected from:



,



, and



,

wherein:

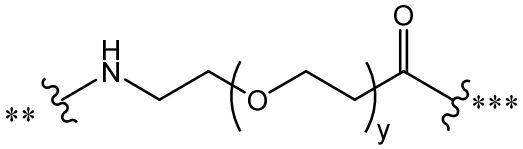
y is an integer selected from 1 to 36,

s is 0, 1 or 2 and k is 1, 2 or 3, and

the wavy line marked ** indicate the attachment to the CO-group of formula (I), and

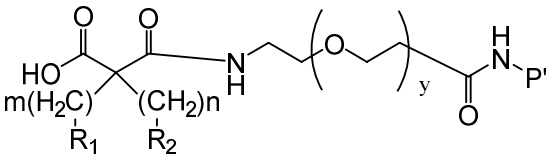
the wavy line marked *** indicate the attachment to group P.

4. A compound of formula (I) or a pharmaceutically acceptable salt thereof according to claim 3, wherein L is:



wherein y is an integer selected from 1 to 36.

5. A compound of formula (I) according to claim 1 or 4, which is a compound of formula (II) or a pharmaceutically acceptable salt thereof,



(II)

wherein:

NH-P' represents a group P which is attached via a NH-moiety to the CO-group of linker L;

R_1 and R_2 are independently selected from CH_3, OH and CO_2H;

n and m are each an integer independently selected from 5 to 30;

and

y is an integer selected from 1 to 36.

6. A compound of formula (II) according to claim 5, wherein:

R_1 is CO_2H and R_2 is CH_3; n is 10 and m is 10;

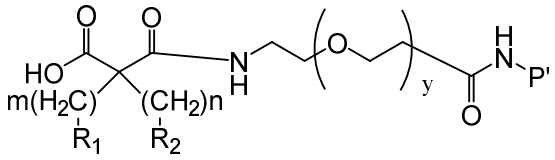
R_1 is CO_2H and R_2 is CO_2H; n is 10 and m is 10;

R_1 is CO_2H and R_2 is CO_2H; n is 10 and m is 11;

R_1 is CO_2H and R_2 is CO_2H; n is 10 and m is 13; or

R_1 is CO_2H and R_2 is CO_2H; n is 10 and m is 14.

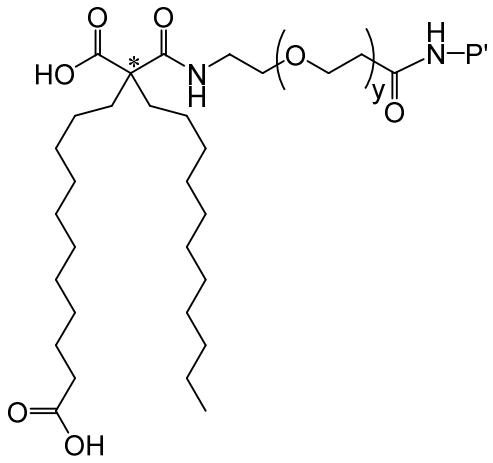
7. A compound of formula (II) according to claim 5 or 6, which is a compound of formula (III) or pharmaceutically acceptable salt thereof,



(III),

wherein R_1 is CO_2H and R_2 is CH_3.

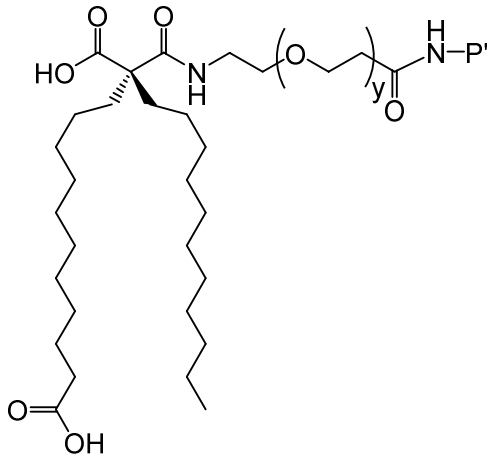
8. A compound of formula (III) according to claim 7, which is a compound of formula (IV) or a pharmaceutically acceptable salt thereof,



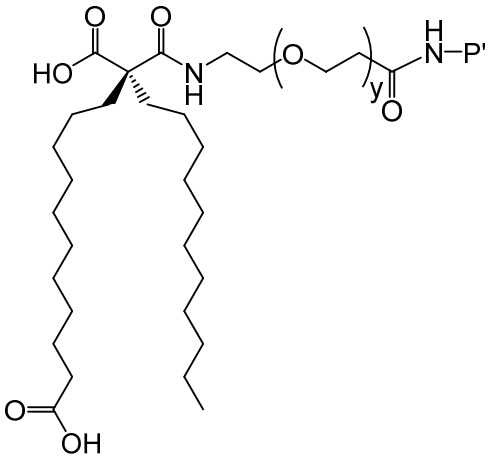
(IV)

wherein the compound is present as a racemate, or as a stereochemically enriched mixture, or is stereochemically pure in respect of the carbon atom marked *.

9. A compound of formula (IV) according to claim 8, which is a compound of formula (IVa) or a compound of formula (IVb) or a pharmaceutically acceptable salt thereof,



(IVa)



(IVb)

wherein y is an integer selected from 1 to 36.

10. A compound of formula (IVa) or a compound of formula (IVb) according to claim 9, wherein y is an integer selected from 2 to 24.

11. A compound of formula (IVa) or a compound of formula (IVb) according to claim 10, wherein y is 24.

12. A compound according to any one of the claims 1 to 11, or a pharmaceutically acceptable salt thereof, wherein P is selected from

GLP-1 (7-37): His-Ala-Glu-Gly-Thr-Phe-Thr-Ser-Asp-Val-Ser-Ser-Tyr-Leu-Glu-Gly-Gln-Ala-Ala-Lys-Glu-Phe-Ile-Ala-Trp-Leu-Val-Lys-Gly-Arg-Gly (**SEQ ID NO:1**), and

a GLP-1 analogue comprising a non-natural amino acid residue in position 7, or in position 8, or in position 7 and 8, relative to the sequence GLP-1 (7-37).

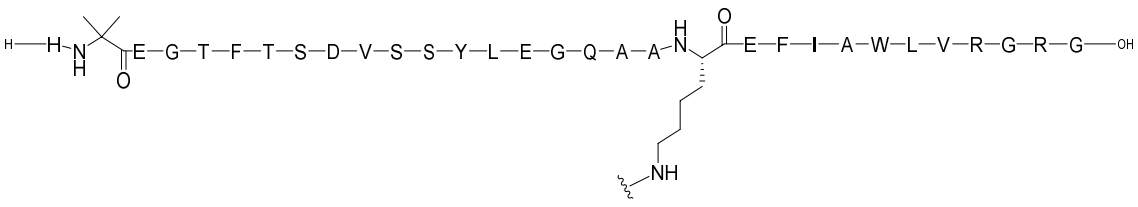
13. A compound of formula (I) according to any one of claims 1 to 11, or a pharmaceutically acceptable salt thereof, wherein P is selected from:

[Aib8, Arg34]GLP-1 (7-37): His-Aib-Glu-Gly-Thr-Phe-Thr-Ser-Asp-Val-Ser-Ser-Tyr-Leu-Glu-Gly-Gln-Ala-Ala-Lys-Glu-Phe-Ile-Ala-Trp-Leu-Val-Arg-Gly-Arg-Gly (**SEQ ID NO:3**); and

[Arg34]GLP-1 (7-37): His-Ala-Glu-Gly-Thr-Phe-Thr-Ser-Asp-Val-Ser-Ser-Tyr-Leu-Glu-Gly-Gln-Ala-Ala-Lys-Glu-Phe-Ile-Ala-Trp-Leu-Val-Arg-Gly-Arg-Gly (**SEQ ID NO:4**).

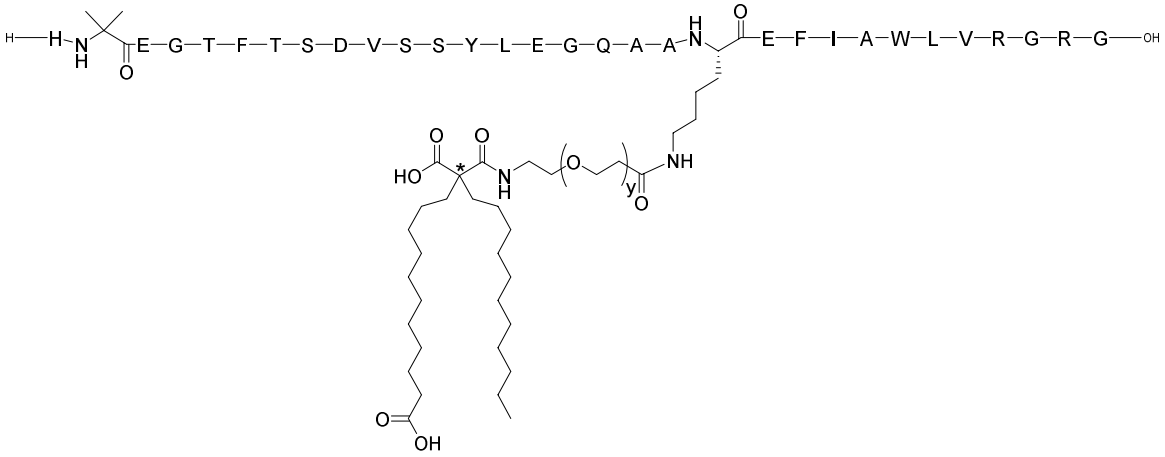
14. A compound of formula (I) according to any one of claims 1 to 11, or a pharmaceutically acceptable salt thereof, wherein the P is [Aib8, Arg34]GLP-1 (7-37)

as shown below:



and wherein the wavy line on the amino-acid member Lys indicates the point of attachment to L.

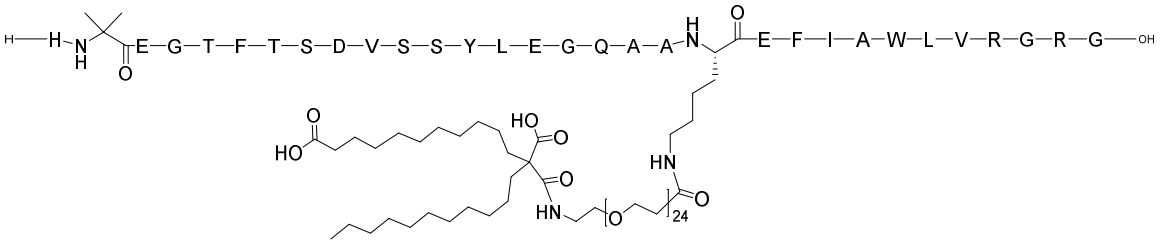
15. A compound of formula (I) according to any one of claims 1 to 11 and 14, or a pharmaceutically acceptable salt thereof, which is



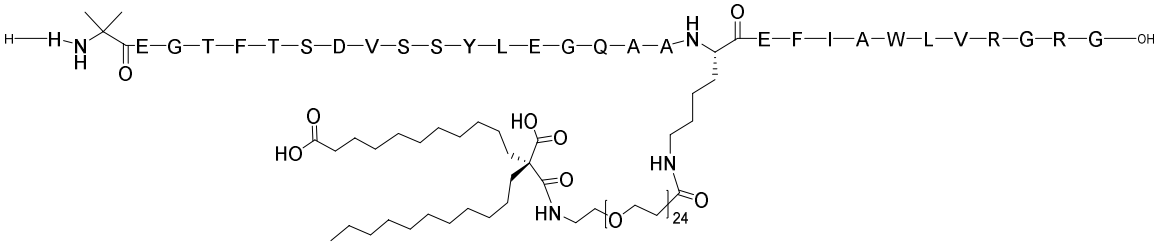
wherein y is an integer selected from 1 to 36, and

wherein the compound is present as a a diastereomeric mixture, a stereochemically enriched mixture or is stereochemically pure in respect of the carbon atom marked *.

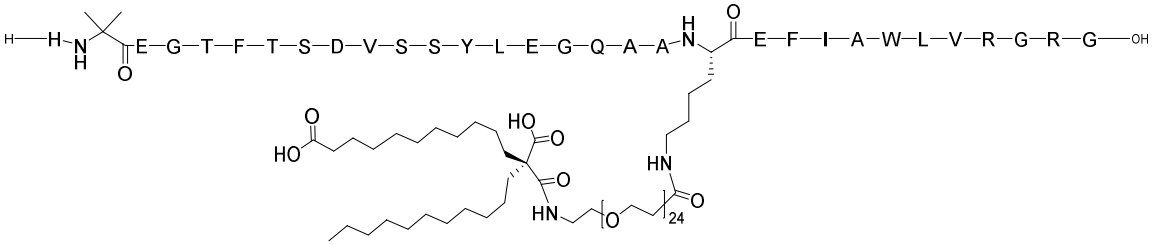
16. A compound of formula (I) according to any one of claims 1 to 11 and 15, or a pharmaceutically acceptable salt thereof, which is selected from:



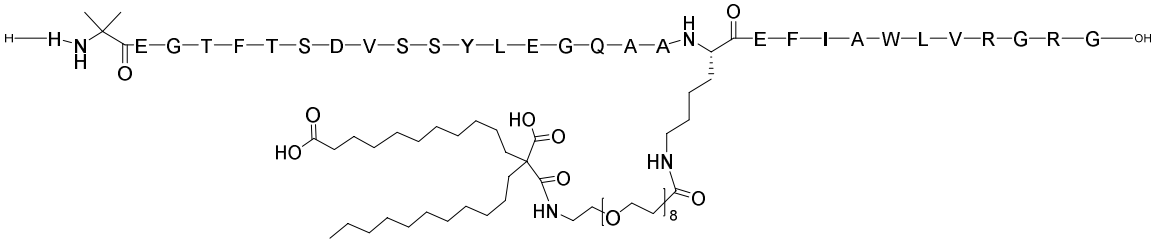
(Compound 1),



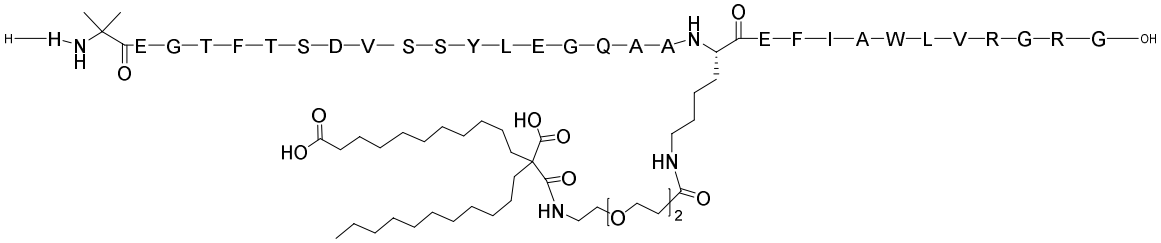
(Compound 2),



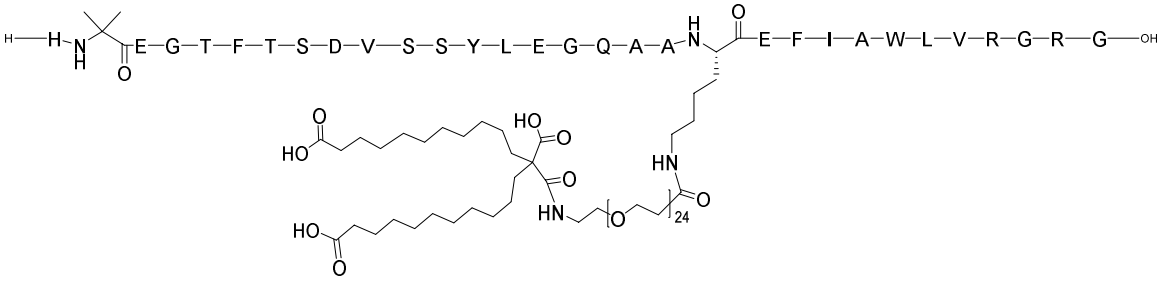
(Compound 3),



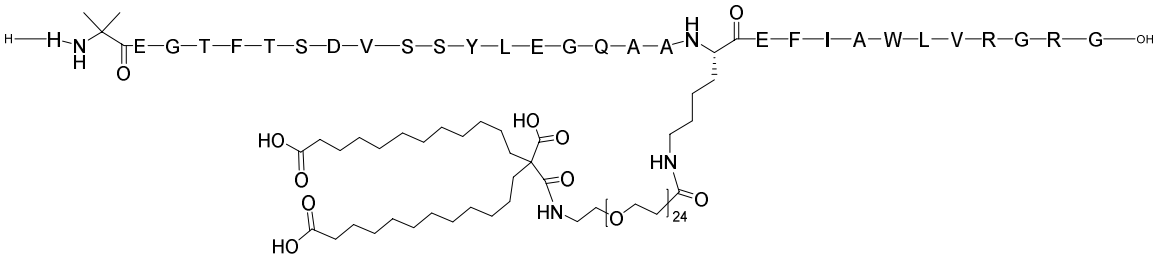
(Compound 4),



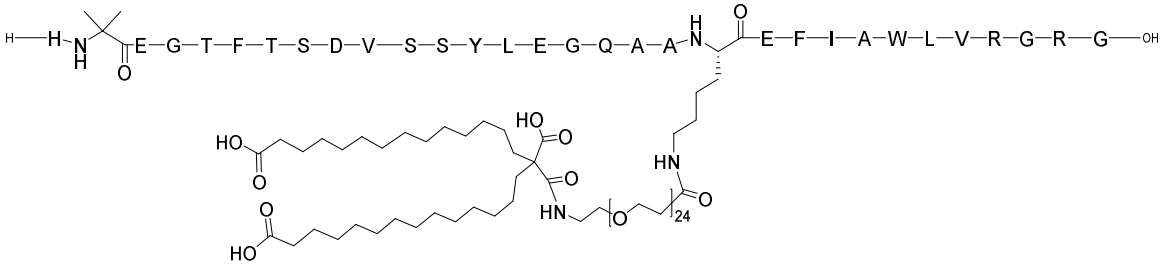
(Compound 5),



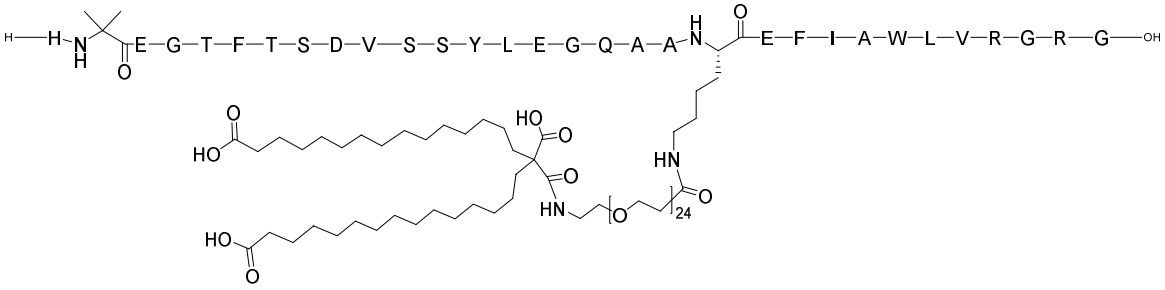
(Compound 6),



(Compound 7),

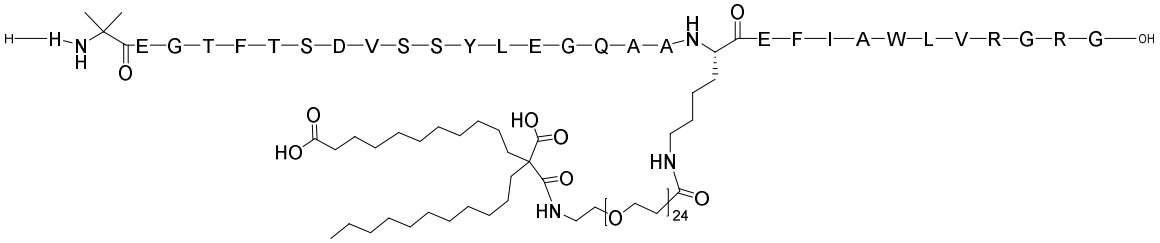


(Compound 8), and

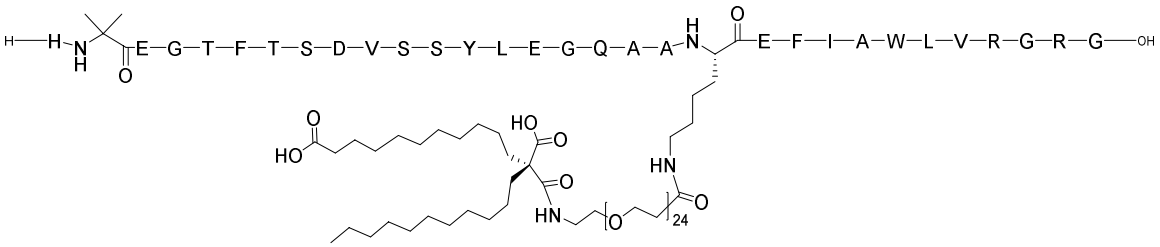


(Compound 9).

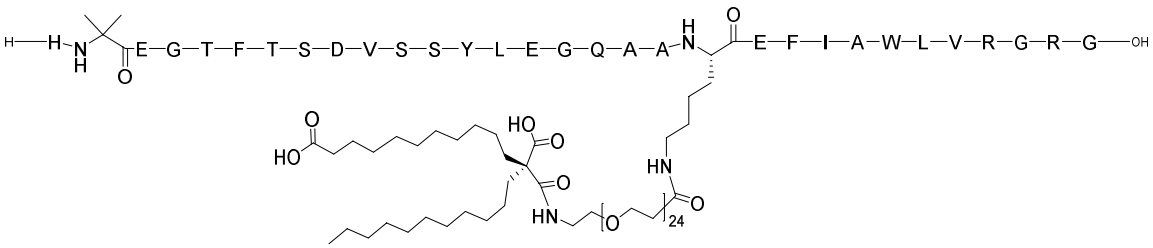
17. A compound of formula (I) according to claim 16, or a pharmaceutically acceptable salt thereof, which is:



18. A compound of formula (I) according to claim 16, or a pharmaceutically acceptable salt thereof, which is:



19. A compound of formula (I) according to claim 16, or a pharmaceutically acceptable salt thereof, which is:



20. A pharmaceutical composition comprising a compound according to any one of claims 1 to 19 or a pharmaceutically acceptable salt thereof and one or more pharmaceutically acceptable carriers.

21. A combination comprising a therapeutically effective amount of a compound according to any one of claims 1 to 19 or a pharmaceutically acceptable salt thereof, and one or more therapeutically active agents.

22. A combination according to claim 21, wherein the compound is selected from Compound 1, 2 and 3.

23. A compound according to any one of claims 1 to 19 or a pharmaceutically acceptable salt thereof, for use as a medicament.

24. Use of a~~A~~ compound according to any one of claims 1 to 19 or a pharmaceutically acceptable salt thereof, ~~for use~~ in the manufacture of a medicament for the treatment of a disease or disorder selected from obesity, type 2 diabetes mellitus, insulin resistance, hyperinsulinemia, glucose intolerance, hyperglycemia, one or more diabetic complications selected from chronic kidney disease and diabetic nephropathy, dyslipidemia, metabolic syndrome, progressive liver disease selected from NAFLD and NASH, cardiovascular disease and peripheral neuropathy associated with diabetes.

25. ~~A compound for~~The use according to claim 24, wherein the cardiovascular disease is selected from hypertension, atherosclerosis, peripheral arterial disease, stroke, cardiomyopathy, atrial fibrillation, heart failure selected from heart failure with reduced ejection fraction (HFrEF), heart failure with mid-range ejection fraction (HFmrEF) and heart failure with preserved ejection fraction (HFpEF), coronary heart disease and arrhythmias selected from atrial arrhythmias and ventricular arrhythmias.

26. ~~A compound for~~The use according to ~~any one of~~ claims ~~23~~ 24 ~~to~~ or claim 25, wherein the compound is selected from Compound 1, 2, and 3.

~~27. A method for treating a patient in need of a therapy being susceptible to an agonist of the Glucagon-like Peptide-1 Receptor (GLP1R), comprising administering to the patient a therapeutically effective amount of a compound of any one of claims 1 to 19 or a pharmaceutically acceptable salt thereof.~~

~~28. A method of treating a disease or disorder selected from obesity, type 2 diabetes mellitus, insulin resistance, hyperinsulinemia, glucose intolerance, hyperglycemia, one or more diabetic complications selected from chronic kidney disease and diabetic nephropathy, dyslipidemia, metabolic syndrome, progressive liver disease selected from NAFLD and NASH, cardiovascular disease and peripheral neuropathy associated with diabetes, in a patient in need thereof, comprising administering to the patient a therapeutically effective amount of a compound of any one of claims 1 to 19 or a pharmaceutically acceptable salt thereof.~~

~~29. The method of claim 28, wherein the cardiovascular disease is selected from hypertension, atherosclerosis, peripheral arterial disease, stroke, cardiomyopathy, atrial fibrillation, heart failure selected from heart failure with reduced ejection fraction (HFrEF), heart failure with mid-range ejection fraction (HFmrEF) and heart failure with preserved ejection fraction (HFpEF), coronary heart disease and arrhythmias selected from atrial arrhythmias and ventricular arrhythmias.~~

~~30. The method according to claim 28 or 29, wherein the compound is selected from Compound 1, 2, and 3.~~