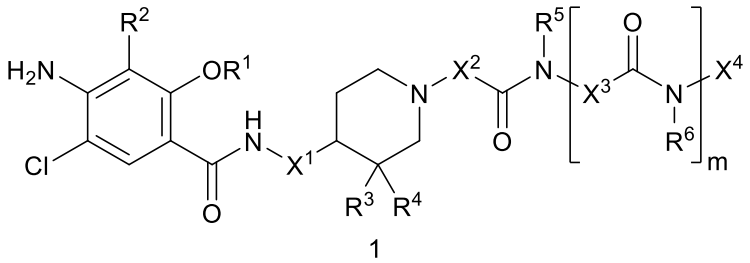
WHAT IS CLAIMED IS:

1. A compound of Formula 1,



1

or a pharmaceutically acceptable salt thereof in which:

m is an integer selected from 0 and 1;

R^1 is methyl and R^2 is hydrogen, or R^1 and R^2 together form an ethane-1,2-diyl which bridges the oxygen and carbon atoms to which R^1 and R^2 are respectively attached;

R^3 and R^4 are each independently selected from hydrogen, halo, C_{1-4} alkyl and C_{1-3} alkoxy;

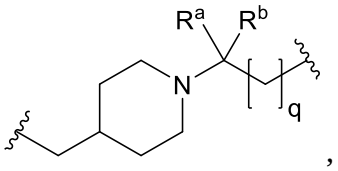
R^5 and R^6 are each independently selected from hydrogen and C_{1-4} alkyl which is unsubstituted or substituted with an optional substituent selected from hydroxy, phosphono, sulfo and amino, wherein the amino optional substituent is unsubstituted or substituted with 1 or 2 optional substituents independently selected from C_{1-3} alkyl;

X^1 is selected from a bond and methane-1,1-diyl;

X^2 is selected from

(a) pentane-1,5-diyl which is unsubstituted or substituted with 1 to 5 optional substituents independently selected from halo and C_{1-3} alkyl, wherein one of the carbon atoms of the pentane-1,5-diyl substituent may be optionally replaced with one oxygen atom, provided the oxygen atom is directly bonded to two carbon atoms within the pentane-1,5-diyl substituent; and

(b) a moiety represented by the formula



,

wherein

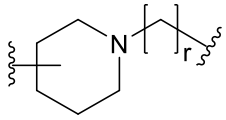
R^a and R^b are each hydrogen or together represent oxo; and

q is an integer selected from 1, 2, 3, 4, 5, 6, 7, 8, 9 and 10;

X^3 is selected from

(a) C_{1-11} alkanediyl, wherein 0 to 3 carbon atoms of the alkanediyl substituent may be optionally replaced, one-to-one, with oxygen atoms, provided each replacement oxygen atom is directly bonded to two carbon atoms within the alkanediyl substituent and any two replacement oxygen atoms are separated by at least one carbon atom; and

(b) a moiety represented by the formula,



,

wherein r is an integer selected from 1, 2, 3, 4, 5, 6 and 7; and

X^4 is selected from

(a) C_{3-6} alkyl which is substituted with 3 to 6 hydroxy substituents;

(b) C_{1-3} alkyl which is substituted with phosphono or sulfo substituents; and

(c) cyclohexyl which is substituted with 3 to 6 substituents independently selected from hydroxy and hydroxymethyl;

wherein the bracketed moieties in Formula 1 and in the formulas for X^2 and X^3 are present m, q or r times, respectively, and each ~~~ represents a point of attachment in the formulas for X^2 and X^3.

2. The compound or pharmaceutically acceptable salt thereof according to claim 1, wherein R^1 is methyl and R^2 is hydrogen.

3. The compound or pharmaceutically acceptable salt thereof according to claim 1, wherein R^1 and R^2 together form an ethane-1,2-diyl which bridges the oxygen and carbon atoms to which R^1 and R^2 are respectively attached.

4. The compound or pharmaceutically acceptable salt thereof according to any one of claims 1 to 3, wherein X^1 is a bond.

5. The compound or pharmaceutically acceptable salt thereof according to any one of claims 1 to 3, wherein X^1 is methane-1,1-diyl.

6. The compound or pharmaceutically acceptable salt thereof according to any one of claims 1 to 5, wherein R^3 and R^4 are each independently selected from hydrogen and methoxy.

7. The compound or pharmaceutically acceptable salt thereof according to any one of claims 1 to 5, wherein R^3 and R^4 are each hydrogen.

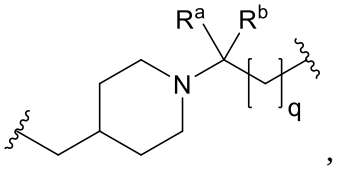
8. The compound or pharmaceutically acceptable salt thereof according to any one of claims 1 to 7, wherein X_2 is pentane-1,5-diyl which is unsubstituted or substituted with 1 to 5 optional substituents independently selected from halo and C_{1-3} alkyl, wherein one of the carbon atoms of the pentane-1,5-diyl substituent may be optionally replaced with one oxygen atom, provided the oxygen atom is directly bonded to two carbon atoms within the pentane-1,5-diyl substituent.

9. The compound or pharmaceutically acceptable salt thereof according to any one of claims 1 to 7, wherein X_2 is pentane-1,5-diyl which is unsubstituted or substituted with 1 to 5 optional substituents selected from methyl, wherein one of the carbon atoms of the pentane-1,5-diyl substituent may be optionally replaced with one oxygen atom, provided the oxygen atom is directly bonded to two carbon atoms within the pentane-1,5-diyl substituent.

10. The compound or pharmaceutically acceptable salt thereof according to any one of claims 1 to 7, wherein X_2 is pentane-1,5-diyl which is unsubstituted, and wherein one of the carbon atoms of the pentane-1,5-diyl substituent may be optionally replaced with one oxygen atom, provided the oxygen atom is directly bonded to two carbon atoms within the pentane-1,5-diyl substituent.

11. The compound or pharmaceutically acceptable salt thereof according to any one of claims 8 to 10, wherein X_2 is pentane-1,5-diyl in which none of the carbon atoms of the pentane-1,5-diyl substituent is optionally replaced with an oxygen atom.

12. The compound or pharmaceutically acceptable salt thereof according to any one of claims 1 to 11, wherein X^2 is a moiety represented by the formula



,

wherein

R^a and R^b are each hydrogen or together represent oxo; and

q is an integer selected from 1, 2, 3, 4, 5, 6, 7, 8, 9 and 10.

13. The compound or pharmaceutically acceptable salt thereof according to claim 12, wherein R^a and R^b are each hydrogen.

14. The compound or pharmaceutically acceptable salt thereof according to claim 12, wherein R^a and R^b together represent oxo.

15. The compound or pharmaceutically acceptable salt thereof according to any one of claims 12 to 14, wherein q is an integer selected from 3, 4, 5, 6, 7, 8, 9 and 10.

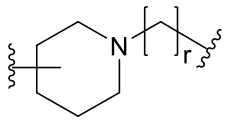
16. The compound or pharmaceutically acceptable salt thereof according to any one of claims 1 to 14, wherein R^5 is selected from hydrogen and methyl.

17. The compound or pharmaceutically acceptable salt thereof according to any one of claims 1 to 14, wherein R^5 is hydrogen.

18. The compound or pharmaceutically acceptable salt thereof according to any one of claims 1 to 17, wherein X^3 is $C_{1\text{-}11}$ alkanediyl, wherein 0 to 3 carbon atoms of the alkanediyl substituent may be optionally replaced, one-to-one, with oxygen atoms, provided each replacement oxygen atom is directly bonded to two carbon atoms within the alkanediyl substituent and any two replacement oxygen atoms are separated by at least one carbon atom.

19. The compound or pharmaceutically acceptable salt thereof according to any one of claims 1 to 17, wherein X^3 is $C_{1\text{-}7}$ alkanediyl in which none of the carbon atoms of the alkanediyl substituent is replaced with oxygen atoms.

20. The compound or pharmaceutically acceptable salt thereof according to any one of claims 1 to 17, wherein X^3 is a moiety represented by the formula,



,

wherein r is an integer selected from 1, 2, 3, 4, 5, 6 and 7.

21. The compound or pharmaceutically acceptable salt thereof according to claim 20, wherein r is an integer selected from 3, 4, 5, 6 and 7.

22. The compound or pharmaceutically acceptable salt thereof according to any one of claims 1 to 21, wherein R^6 is selected from hydrogen, methyl, hydroxyethyl, phosphonoethyl, sulfoethyl and dimethylaminopropyl.

23. The compound or pharmaceutically acceptable salt thereof according to any one of claims 1 to 22, wherein X^4 is C_{3-6} alkyl which is substituted with 3 to 6 hydroxy substituents.

24. The compound or pharmaceutically acceptable salt thereof according to any one of claims 1 to 22, wherein X^4 is (2*S*,3*R*,4*R*,5*R*)-2,3,4,5,6-pentahydroxyhexyl or a stereoisomer thereof.

25. The compound or pharmaceutically acceptable salt thereof according to any one of claims 1 to 22, wherein X^4 is C_{1-3} alkyl which is substituted with phosphono or sulfo substituents.

26. The compound or pharmaceutically acceptable salt thereof according to any one of claims 1 to 22, wherein X^4 is cyclohexyl which is substituted with 3 to 6 substituents independently selected from hydroxy and hydroxymethyl.

27. The compound or pharmaceutically acceptable salt thereof according to any one of claims 1 to 22, wherein X^4 is (2*S*,3*R*,4*S*,5*S*)-2,3,4,5-tetrahydroxy-5-(hydroxymethyl)cyclohexyl or a stereoisomer thereof.

28. The compound according to claim 1, which is selected from the following compounds:

4-amino-5-chloro-2-methoxy-*N*-((3*S*,4*R*)-3-methoxy-1-(6-oxo-6-(((2*S*,3*R*,4*R*,5*R*)-2,3,4,5,6-pentahydroxyhexyl)amino)hexyl)piperidin-4-yl)benzamide;

4-amino-5-chloro-2-methoxy-*N*-((3*S*,4*R*)-3-methoxy-1-(6-oxo-6-((8-oxo-8-(((2*S*,3*R*,4*R*,5*R*)-2,3,4,5,6-pentahydroxyhexyl)amino)octyl)amino)hexyl)piperidin-4-yl)benzamide;

4-amino-5-chloro-2-methoxy-*N*-((3*S*,4*R*)-3-methoxy-1-(6-oxo-6-((6-oxo-6-(((2*S*,3*R*,4*R*,5*R*)-2,3,4,5,6-pentahydroxyhexyl)amino)hexyl)amino)hexyl)piperidin-4-yl)benzamide;

4-amino-5-chloro-2-methoxy-*N*-((3*S*,4*R*)-3-methoxy-1-(6-oxo-6-((4-oxo-4-(((2*S*,3*R*,4*R*,5*R*)-2,3,4,5,6-pentahydroxyhexyl)amino)butyl)amino)hexyl)piperidin-4-yl)benzamide;

4-amino-5-chloro-2-methoxy-*N*-((3*S*,4*R*)-3-methoxy-1-(6-oxo-6-((2-oxo-2-(((2*S*,3*R*,4*R*,5*R*)-2,3,4,5,6-pentahydroxyhexyl)amino)ethyl)amino)hexyl)piperidin-4-yl)benzamide;

4-amino-5-chloro-2-methoxy-*N*-((3*S*,4*R*)-3-methoxy-1-((22*S*,23*R*,24*R*,25*R*)-22,23,24,25,26-pentahydroxy-6,19-dioxo-10,13,16-trioxa-7,20-diazahexacosyl)piperidin-4-yl)benzamide;

4-amino-5-chloro-2-methoxy-*N*-((3*S*,4*R*)-3-methoxy-1-((19*S*,20*R*,21*R*,22*R*)-19,20,21,22,23-pentahydroxy-6,16-dioxo-10,13-dioxa-7,17-diazatricosyl)piperidin-4-yl)benzamide;

4-amino-5-chloro-2-methoxy-*N*-((3*S*,4*R*)-3-methoxy-1-(6-oxo-6-((1-(8-oxo-8-(((2*S*,3*R*,4*R*,5*R*)-2,3,4,5,6-pentahydroxyhexyl)amino)octyl)piperidin-4-yl)amino)hexyl)piperidin-4-yl)benzamide;

4-amino-5-chloro-2-methoxy-*N*-((3*S*,4*R*)-3-methoxy-1-(6-oxo-6-((1-(6-oxo-6-(((2*S*,3*R*,4*R*,5*R*)-2,3,4,5,6-pentahydroxyhexyl)amino)hexyl)piperidin-4-yl)amino)hexyl)piperidin-4-yl)benzamide;

4-amino-5-chloro-2-methoxy-*N*-((3*S*,4*R*)-3-methoxy-1-(6-(methyl(1-(8-oxo-8-(((2*S*,3*R*,4*R*,5*R*)-2,3,4,5,6-pentahydroxyhexyl)amino)octyl)piperidin-4-yl)amino)-6-oxohexyl)piperidin-4-yl)benzamide;

4-amino-5-chloro-2-methoxy-*N*-((3*S*,4*R*)-3-methoxy-1-(6-(methyl(1-(6-oxo-6-(((2*S*,3*R*,4*R*,5*R*)-2,3,4,5,6-pentahydroxyhexyl)amino)hexyl)piperidin-4-yl)amino)-6-oxohexyl)piperidin-4-yl)benzamide;

4-amino-5-chloro-2-methoxy-*N*-((3*S*,4*R*)-3-methoxy-1-(6-oxo-6-(((*R*)-1-(8-oxo-8-(((2*S*,3*R*,4*R*,5*R*)-2,3,4,5,6-pentahydroxyhexyl)amino)octyl)piperidin-3-yl)amino)hexyl)piperidin-4-yl)benzamide;

4-amino-5-chloro-2-methoxy-*N*-((3*S*,4*R*)-3-methoxy-1-(6-oxo-6-(((*R*)-1-(6-oxo-6-(((2*S*,3*R*,4*R*,5*R*)-2,3,4,5,6-pentahydroxyhexyl)amino)hexyl)piperidin-3-yl)amino)hexyl)piperidin-4-yl)benzamide;

4-amino-5-chloro-2-methoxy-*N*-((3*S*,4*R*)-3-methoxy-1-(6-(methyl((*R*)-1-(8-oxo-8-(((2*S*,3*R*,4*R*,5*R*)-2,3,4,5,6-pentahydroxyhexyl)amino)octyl)piperidin-3-yl)amino)-6-oxohexyl)piperidin-4-yl)benzamide;

4-amino-5-chloro-2-methoxy-*N*-((3*S*,4*R*)-3-methoxy-1-(6-(methyl((*R*)-1-(6-oxo-6-(((2*S*,3*R*,4*R*,5*R*)-2,3,4,5,6-pentahydroxyhexyl)amino)hexyl)piperidin-3-yl)amino)-6-oxohexyl)piperidin-4-yl)benzamide;

4-amino-5-chloro-2-methoxy-*N*-((3*S*,4*R*)-3-methoxy-1-(6-(methyl(8-oxo-8-(((2*S*,3*R*,4*R*,5*R*)-2,3,4,5,6-pentahydroxyhexyl)amino)octyl)amino)-6-oxohexyl)piperidin-4-yl)benzamide;

4-amino-5-chloro-2-methoxy-*N*-((3*S*,4*R*)-3-methoxy-1-(2-(3-oxo-3-((8-oxo-8-(((2*S*,3*R*,4*R*,5*R*)-2,3,4,5,6-pentahydroxyhexyl)amino)octyl)amino)propoxy)ethyl)piperidin-4-yl)benzamide;

4-amino-5-chloro-2-methoxy-*N*-((3*S*,4*R*)-3-methoxy-1-(7-oxo-7-((8-oxo-8-(((2*S*,3*R*,4*R*,5*R*)-2,3,4,5,6-pentahydroxyhexyl)amino)octyl)amino)heptan-2-yl)piperidin-4-yl)benzamide;

4-amino-5-chloro-2-methoxy-*N*-((3*S*,4*R*)-3-methoxy-1-(2-methyl-6-oxo-6-((8-oxo-8-(((2*S*,3*R*,4*R*,5*R*)-2,3,4,5,6-pentahydroxyhexyl)amino)octyl)amino)hexyl)piperidin-4-yl)benzamide;

4-amino-5-chloro-2-methoxy-*N*-((3*S*,4*R*)-3-methoxy-1-(3-methyl-6-oxo-6-((8-oxo-8-(((2*S*,3*R*,4*R*,5*R*)-2,3,4,5,6-pentahydroxyhexyl)amino)octyl)amino)hexyl)piperidin-4-yl)benzamide;

4-amino-5-chloro-2-methoxy-*N*-((3*S*,4*R*)-3-methoxy-1-(4-methyl-6-oxo-6-((8-oxo-8-(((2*S*,3*R*,4*R*,5*R*)-2,3,4,5,6-pentahydroxyhexyl)amino)octyl)amino)hexyl)piperidin-4-yl)benzamide;

4-amino-5-chloro-*N*-((3S,4R)-1-(6-((8-((2-hydroxyethyl)((2*S*,3*R*,4*R*,5*R*)-2,3,4,5,6-pentahydroxyhexyl)amino)-8-oxooctyl)amino)-6-oxohexyl)-3-methoxypiperidin-4-yl)-2-methoxybenzamide;

2-(8-(6-((3*S*,4*R*)-4-(4-amino-5-chloro-2-methoxybenzamido)-3-methoxypiperidin-1-yl)hexanamido)octanamido)ethane-1-sulfonic acid;

4-amino-5-chloro-2-methoxy-*N*-((3*S*,4*R*)-3-methoxy-1-(6-oxo-6-((8-oxo-8-(((1*S*,2*S*,3*R*,4*S*,5*S*)-2,3,4,5-tetrahydroxy-5-(hydroxymethyl)cyclohexyl)amino)octyl)amino)hexyl)piperidin-4-yl)benzamide;

(2-(8-(6-((3*S*,4*R*)-4-(4-amino-5-chloro-2-methoxybenzamido)-3-methoxypiperidin-1-yl)hexanamido)octanamido)ethyl)phosphonic acid;

(2-(8-(6-((3*S*,4*R*)-4-(4-amino-5-chloro-2-methoxybenzamido)-3-methoxypiperidin-1-yl)hexanamido)-N-((2*S*,3*R*,4*R*,5*R*)-2,3,4,5,6-pentahydroxyhexyl)octanamido)ethyl)phosphonic acid;

2-(8-(6-((3*S*,4*R*)-4-(4-amino-5-chloro-2-methoxybenzamido)-3-methoxypiperidin-1-yl)hexanamido)-N-(3-(dimethylamino)propyl)octanamido)ethane-1-sulfonic acid;

4-amino-5-chloro-*N*-(1-(6-oxo-6-(((*R*)-1-(8-oxo-8-(((2*S*,3*R*,4*R*,5*R*)-2,3,4,5,6-pentahydroxyhexyl)amino)octyl)piperidin-3-yl)amino)hexyl)piperidin-4-yl)-2,3-dihydrobenzofuran-7-carboxamide;

4-amino-5-chloro-*N*-(1-(6-oxo-6-(((*R*)-1-(6-oxo-6-(((2*S*,3*R*,4R,5R)-2,3,4,5,6-pentahydroxyhexyl)amino)hexyl)piperidin-3-yl)amino)hexyl)piperidin-4-yl)-2,3-dihydrobenzofuran-7-carboxamide;

4-amino-5-chloro-*N*-(1-(6-oxo-6-((1-(8-oxo-8-(((2*S*,3*R*,4*R*,5*R*)-2,3,4,5,6-pentahydroxyhexyl)amino)octyl)piperidin-4-yl)amino)hexyl)piperidin-4-yl)-2,3-dihydrobenzofuran-7-carboxamide;

4-amino-5-chloro-*N*-(1-(6-oxo-6-((1-(6-oxo-6-(((2*S*,3*R*,4*R*,5*R*)-2,3,4,5,6-pentahydroxyhexyl)amino)hexyl)piperidin-4-yl)amino)hexyl)piperidin-4-yl)-2,3-dihydrobenzofuran-7-carboxamide;

4-amino-5-chloro-*N*-(1-(6-oxo-6-((8-oxo-8-(((2*S*,3*R*,4*R*,5*R*)-2,3,4,5,6-pentahydroxyhexyl)amino)octyl)amino)hexyl)piperidin-4-yl)-2,3-dihydrobenzofuran-7-carboxamide;

4-amino-5-chloro-*N*-(1-(6-oxo-6-((6-oxo-6-(((2*S*,3*R*,4*R*,5*R*)-2,3,4,5,6-pentahydroxyhexyl)amino)hexyl)amino)hexyl)piperidin-4-yl)-2,3-dihydrobenzofuran-7-carboxamide;

4-amino-5-chloro-*N*-(1-(6-oxo-6-((4-oxo-4-(((2*S*,3*R*,4*R*,5*R*)-2,3,4,5,6-pentahydroxyhexyl)amino)butyl)amino)hexyl)piperidin-4-yl)-2,3-dihydrobenzofuran-7-carboxamide;

4-amino-5-chloro-*N*-((1-((1-(9-oxo-9-(((2*S*,3*R*,4*R*,5*R*)-2,3,4,5,6-pentahydroxyhexyl)amino)nonyl)piperidin-4-yl)methyl)piperidin-4-yl)methyl)-2,3-dihydrobenzofuran-7-carboxamide;

4-amino-5-chloro-*N*-((1-((1-(11-oxo-11-(((2*S*,3*R*,4*R*,5*R*)-2,3,4,5,6-pentahydroxyhexyl)amino)undecyl)piperidin-4-yl)methyl)piperidin-4-yl)methyl)-2,3-dihydrobenzofuran-7-carboxamide;

4-amino-5-chloro-*N*-((1-((1-(7-oxo-7-(((2*S*,3*R*,4*R*,5*R*)-2,3,4,5,6-pentahydroxyhexyl)amino)heptyl)piperidin-4-yl)methyl)piperidin-4-yl)methyl)-2,3-dihydrobenzofuran-7-carboxamide;

4-amino-5-chloro-*N*-((1-((1-(12-oxo-12-(((2*S*,3*R*,4*R*,5*R*)-2,3,4,5,6-pentahydroxyhexyl)amino)dodecanoyl)piperidin-4-yl)methyl)piperidin-4-yl)methyl)-2,3-dihydrobenzofuran-7-carboxamide;

4-amino-5-chloro-*N*-((1-((1-(10-oxo-10-(((2*S*,3*R*,4*R*,5*R*)-2,3,4,5,6-pentahydroxyhexyl)amino)decanoyl)piperidin-4-yl)methyl)piperidin-4-yl)methyl)-2,3-dihydrobenzofuran-7-carboxamide;

4-amino-5-chloro-*N*-((1-((1-(8-oxo-8-(((2*S*,3*R*,4*R*,5*R*)-2,3,4,5,6-pentahydroxyhexyl)amino)octanoyl)piperidin-4-yl)methyl)piperidin-4-yl)methyl)-2,3-dihydrobenzofuran-7-carboxamide;

4-amino-5-chloro-*N*-((3*S*,4*R*)-3-methoxy-1-((1-(9-oxo-9-(((2*S*,3*R*,4*R*,5*R*)-2,3,4,5,6-pentahydroxyhexyl)amino)nonanoyl)piperidin-4-yl)methyl)piperidin-4-yl)-2,3-dihydrobenzofuran-7-carboxamide;

4-amino-5-chloro-*N*-((3*S*,4*R*)-3-methoxy-1-((1-(7-oxo-7-(((2*S*,3*R*,4*R*,5*R*)-2,3,4,5,6-pentahydroxyhexyl)amino)heptanoyl)piperidin-4-yl)methyl)piperidin-4-yl)-2,3-dihydrobenzofuran-7-carboxamide;

4-amino-5-chloro-*N*-((3*S*,4*R*)-3-methoxy-1-((1-(5-oxo-5-(((2*S*,3*R*,4*R*,5*R*)-2,3,4,5,6-pentahydroxyhexyl)amino)pentanoyl)piperidin-4-yl)methyl)piperidin-4-yl)-2,3-dihydrobenzofuran-7-carboxamide;

4-amino-5-chloro-*N*-((3*S*,4*R*)-3-methoxy-1-(6-oxo-6-((8-oxo-8-(((2*S*,3*R*,4*R*,5*R*)-2,3,4,5,6-pentahydroxyhexyl)amino)octyl)amino)hexyl)piperidin-4-yl)-2,3-dihydrobenzofuran-7-carboxamide;

4-amino-5-chloro-*N*-((3*S*,4*R*)-3-methoxy-1-(6-oxo-6-((6-oxo-6-(((2*S*,3*R*,4*R*,5*R*)-2,3,4,5,6-pentahydroxyhexyl)amino)hexyl)amino)hexyl)piperidin-4-yl)-2,3-dihydrobenzofuran-7-carboxamide;

4-amino-5-chloro-*N*-((3*S*,4*R*)-3-methoxy-1-(6-oxo-6-((4-oxo-4-(((2*S*,3*R*,4*R*,5*R*)-2,3,4,5,6-pentahydroxyhexyl)amino)butyl)amino)hexyl)piperidin-4-yl)-2,3-dihydrobenzofuran-7-carboxamide; and

a pharmaceutically acceptable salt of any one of the aforementioned compounds.

29. A pharmaceutical composition comprising:

a compound or pharmaceutically acceptable salt thereof as defined in any one of claims 1 to 28; and

a pharmaceutically acceptable excipient.

30. A compound or pharmaceutically acceptable salt as defined in any one of claims 1 to 28 for use as a medicament.

31. A compound or pharmaceutically acceptable salt as defined in any one of claims 1 to 28 for use in treating a disease, disorder or condition selected from chronic idiopathic constipation, slow transit constipation, opioid-induced constipation, irritable bowel syndrome, Crohn's Disease, ulcerative colitis, enteral feeding intolerance, postoperative ileus, postoperative gastrointestinal dysfunction, diabetic gastroparesis, idiopathic gastroparesis, functional abdominal pain, chronic intestinal pseudo-obstruction, Hirschsprung Disease, Celiac Disease and short bowel syndrome.

32. ~~A method~~ A compound or pharmaceutically acceptable salt as defined in any one of claims 1 to 28 for use in activating 5-HT_4R in a subject~~, the method comprising administering to the subject a compound or pharmaceutically acceptable salt as defined in any one of claims 1 to 28~~.

33. ~~A method of treating a disease, disorder or condition in a subject, the method comprising administering to the subject~~ Use of a compound or pharmaceutically acceptable salt as defined in any one of claims 1 to 28, in the manufacture of a medicament for treating a disease, disorder or condition in a subject, wherein the disease, disorder or condition is associated with 5-HT_4R.

34. ~~A method of treating a disease, disorder or condition in a subject, the method comprising administering to the subject~~ Use of a compound or pharmaceutically acceptable salt as defined in any one of claims 1 to 28, in the manufacture of a medicament for treating a disease, disorder or condition in a subject, wherein the disease, disorder or condition is selected from gastrointestinal motility disorders.

35. ~~A method of treating a disease, disorder or condition in a subject, the method comprising administering to the subject~~ Use of a compound or pharmaceutically acceptable salt as defined in any one of claims 1 to 28, in the manufacture of a medicament for treating a disease, disorder or condition in a subject, wherein the disease, disorder or condition is selected from chronic idiopathic constipation, slow transit constipation, opioid-induced constipation, irritable bowel syndrome, Crohn's Disease, ulcerative colitis, enteral feeding intolerance, postoperative ileus, postoperative gastrointestinal dysfunction, diabetic

gastroparesis, idiopathic gastroparesis, functional abdominal pain, chronic intestinal pseudo-obstruction, Hirschsprung Disease, Celiac Disease and short bowel syndrome.

36. A combination comprising a compound or pharmaceutically acceptable salt as defined in any one of claims 1 to 28, and at least one additional pharmacologically active agent.