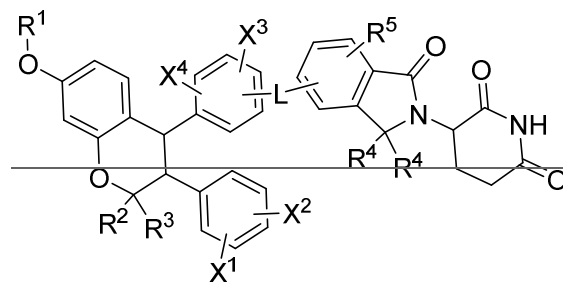


WHAT IS CLAIMED IS:

1. A compound of Formula (I), a stereoisomer or a mixture of stereoisomers, a pharmaceutically acceptable salt, or hydrate thereof:



Formula (I)

wherein:

R¹ is selected from H, or C₁-C₆ alkyl, each of which is substituted with 0, 1, 2, or 3 R⁶;

R² and R³ are each independently selected from H, C₁-C₃ alkyl, or C₁-C₃ haloalkyl, each of which is substituted with 0, 1, 2, or 3 R⁶;

each R⁴ is independently selected from H, hydroxyl, C₁-C₃ alkyl, C₁-C₃ alkoxy, or C₁-C₃ haloalkyl, each of which is substituted with 0, 1, 2, or 3 R⁶, or two R⁴ groups are taken together to form an oxo;

R⁵ is selected from halogen, hydroxy, C₁-C₃ alkyl, C₁-C₃ alkoxy, C₁-C₃ haloalkyl, N(R⁷)₂, and CN, each of which is substituted with 0, 1, 2, or 3 R⁶;

X¹ and X² are each independently selected from H, halogen, cyano, C₁-C₆ alkyl, C₁-C₆ alkoxy, or C₁-C₆ haloalkyl each of which is substituted with 0, 1, 2, or 3 R⁶;

X³ and X⁴ are each independently selected from H or halo;

L is a linker of 1 to 22 carbon atoms in length, wherein one or more carbon atoms are each optionally and independently replaced by a group selected from C(O), O, NR⁷, S, C₂-alkenyl, C₂-alkynyl, cycloalkyl, aryl, heterocycle, and heteroaryl, each of which is substituted with 0, 1, 2, or 3 R⁶;

each R⁶ is independently selected from C₁-C₆ alkyl, halo, cyano, and hydroxy;

each R⁷ is independently selected from hydrogen, C₁-C₆ alkyl, and acyl, each of which is substituted with 0, 1, 2, or 3 R⁶, or two R⁷ groups are taken together to form a 3- to 6-membered heterocycle or heteroaryl.

2. The compound according to claim 1, or a pharmaceutically acceptable salt thereof, wherein R¹ is selected from H, or C₁-C₆ alkyl, each of which is substituted with 0, 1, 2, or 3 R⁶.

3. The compound according to claim 2, or a pharmaceutically acceptable salt thereof, wherein R¹ is selected from H or methyl, each of which is substituted with 0, 1, 2, or 3 R⁶.

4. The compound according to claim 3, or a pharmaceutically acceptable salt thereof, wherein R¹ is selected from H or methyl.

5. The compound according to any one of claims 1 to 4, or a pharmaceutically acceptable salt thereof, wherein R¹ is H.

6. The compound according to any one of claims 1 to 4, or a pharmaceutically acceptable salt thereof, wherein R^1 is methyl.

7. The compound according to any one of claims 1 to 6, or a pharmaceutically acceptable salt thereof, wherein R^2 and R^3 are each independently selected from H, C_1-C_3 -alkyl, or C_1-C_3 -haloalkyl, each of which is substituted with 0, 1, 2, or 3 R^6 .

8. The compound according to any one of claims 1 to 7, or a pharmaceutically acceptable salt thereof, wherein R^2 and R^3 are each independently selected from H and methyl, each of which is substituted with 0, 1, 2, or 3 R^6 .

9. The compound according to any one of claims 1 to 8, or a pharmaceutically acceptable salt thereof, wherein R^2 and R^3 are each independently selected from H and methyl.

10. The compound according to any one of claims 1 to 9, or a pharmaceutically acceptable salt thereof, wherein R^2 and R^3 are each H.

11. The compound according to any one of claims 1 to 9, or a pharmaceutically acceptable salt thereof, wherein R^2 and R^3 are each methyl.

12. The compound according to any one of claims 1 to 9, or a pharmaceutically acceptable salt thereof, wherein R^2 and R^3 are H and methyl, respectively.

13. The compound according to any one claims 1 to 12, or a pharmaceutically acceptable salt thereof, wherein each R^4 is independently selected from H, hydroxyl, C_1-C_3 -alkyl, C_1-C_3 -alkoxy, or C_1-C_3 -haloalkyl, each of which is substituted with 0, 1, 2, or 3 R^6 , or two R^4 -groups are taken together to form an oxo.

14. The compound according to any one claims 1 to 13, or a pharmaceutically acceptable salt thereof, wherein each R^4 is independently selected from H, hydroxyl, C_1-C_3 -alkyl, C_1-C_3 -alkoxy, or C_1-C_3 -haloalkyl, or two R^4 -groups are taken together to form an oxo.

15. The compound according to any one claims 1 to 14, or a pharmaceutically acceptable salt thereof, wherein R^4 is H.

16. The compound according to any one claims 1 to 14, or a pharmaceutically acceptable salt thereof, wherein two R^4 -groups are taken together to form an oxo.

17. The compound according to any one claims 1 to 16, or a pharmaceutically acceptable salt thereof, wherein R^5 is selected from halogen, hydroxy, C_1-C_3 -alkyl, C_1-C_3 -alkoxy, C_1-C_3 -haloalkyl, $N(R^7)_2$, and CN , each of which is substituted with 0, 1, 2, or 3 R^6 .

18. The compound according to any one claims 1 to 17, or a pharmaceutically acceptable salt thereof, wherein R^5 is selected from halogen, hydroxy, C_1-C_3 -alkyl, C_1-C_3 -alkoxy, C_1-C_3 -haloalkyl, $N(R^7)_2$, and CN .

19. The compound according to any one claims 1 to 18, or a pharmaceutically acceptable salt thereof, wherein R^5 is selected from halogen.

20. The compound according to any one claims 1 to 19, or a pharmaceutically acceptable salt thereof, wherein R^5 is F.

21. The compound according to any one of claims 1 to 20, or a pharmaceutically acceptable salt thereof, wherein X^1 and X^2 are each independently selected from H, halogen, cyano, C_1 - C_6 alkyl, C_1 - C_6 alkoxy, or C_1 - C_6 haloalkyl, each of which is substituted with 0, 1, 2, or 3 R^6 .

22. The compound according to any one of claims 1 to 21, or a pharmaceutically acceptable salt thereof, wherein X^1 and X^2 are each independently selected from H, halogen, cyano, C_1 - C_6 alkyl, C_1 - C_6 alkoxy, or C_1 - C_6 haloalkyl.

23. The compound according to any one of claims 1 to 22, or a pharmaceutically acceptable salt thereof, wherein X^1 and X^2 are each independently selected from H, F, CN, methyl, methoxy, trifluoromethyl.

24. The compound according to any one of claims 1 to 23, or a pharmaceutically acceptable salt thereof, wherein X^1 and X^2 are each H.

25. The compound according to any one of claims 1 to 23, or a pharmaceutically acceptable salt thereof, wherein X^1 and X^2 are each F.

26. The compound according to any one of claims 1 to 23, or a pharmaceutically acceptable salt thereof, wherein X^1 and X^2 are H and methyl, respectively.

27. The compound according to any one of claims 1 to 23, or a pharmaceutically acceptable salt thereof, wherein X^1 and X^2 are H and F, respectively.

28. The compound according to any one of claims 1 to 23, or a pharmaceutically acceptable salt thereof, wherein X^1 and X^2 are H and methoxy, respectively.

29. The compound according to any one of claims 1 to 23, or a pharmaceutically acceptable salt thereof, wherein X^1 and X^2 are F and methyl, respectively.

30. The compound according to any one of claims 1 to 23, or a pharmaceutically acceptable salt thereof, wherein X^1 and X^2 are F and methoxy, respectively.

31. The compound according to any one of claims 1 to 23, or a pharmaceutically acceptable salt thereof, wherein X^1 and X^2 are F and trifluoromethyl, respectively.

32. The compound according to any one of claims 1 to 31, or a pharmaceutically acceptable salt thereof, wherein X^3 and X^4 are each independently selected from H or halo.

33. The compound according to any one of claims 1 to 32, or a pharmaceutically acceptable salt thereof, wherein X^3 and X^4 are each independently selected from H or F.

34. The compound according to any one of claims 1 to 33, or a pharmaceutically acceptable salt thereof, wherein X^3 and X^4 are each H.

35. The compound according to any one of claims 1 to 33, or a pharmaceutically acceptable salt thereof, wherein X^3 and X^4 are each F.

36. The compound according to any one of claims 1 to 33, or a pharmaceutically acceptable salt thereof, wherein X^3 and X^4 are H and F, respectively.

37. The compound according to any one of claims 1 to 36, or pharmaceutically acceptable salt thereof, wherein L is a linker of 1 to 22 carbon atoms in length, wherein one or more carbon atoms are each optionally and independently replaced by a group selected from C(O), O, NR^7 , S, C_2 -alkenyl, C_2 -

alkynyl, cycloalkyl, aryl, heterocycle, and heteroaryl, each of which is independently substituted with 0, 1, 2, or 3 R⁶.

38. The compound according to any one of claims 1 to 37, or pharmaceutically acceptable salt thereof, wherein L is a linker of 1 to 20 carbon atoms in length, wherein one or more carbon atoms are each optionally and independently replaced by a group selected from C(O), O, NR⁷, S, C₂-alkenyl, C₂-alkynyl, cycloalkyl, aryl, heterocycle, and heteroaryl, each of which is independently substituted with 0, 1, 2, or 3 R⁶.

39. The compound according to any one of claims 1 to 38, or pharmaceutically acceptable salt thereof, wherein L is a linker of 1 to 18 carbon atoms in length, wherein one or more carbon atoms are each optionally and independently replaced by a group selected from C(O), O, NR⁷, S, C₂-alkenyl, C₂-alkynyl, cycloalkyl, aryl, heterocycle, and heteroaryl, each of which is independently substituted with 0, 1, 2, or 3 R⁶.

40. The compound according to any one of claims 1 to 39, or pharmaceutically acceptable salt thereof, wherein L is a linker of 1 to 16 carbon atoms in length, wherein one or more carbon atoms are each optionally and independently replaced by a group selected from C(O), O, NR⁷, S, C₂-alkenyl, C₂-alkynyl, cycloalkyl, aryl, heterocycle, and heteroaryl, each of which is independently substituted with 0, 1, 2, or 3 R⁶.

41. The compound according to any one of claims 1 to 40, or pharmaceutically acceptable salt thereof, wherein L is a linker of 1 to 14 carbon atoms in length, wherein one or more carbon atoms are each optionally and independently replaced by a group selected from C(O), O, NR⁷, S, C₂-alkenyl, C₂-alkynyl, cycloalkyl, aryl, heterocycle, and heteroaryl, each of which is independently substituted with 0, 1, 2, or 3 R⁶.

42. The compound according to any one of claims 1 to 41, or pharmaceutically acceptable salt thereof, wherein L is a linker of 1 to 12 carbon atoms in length, wherein one or more carbon atoms are each optionally and independently replaced by a group selected from C(O), O, NR⁷, S, C₂-alkenyl, C₂-alkynyl, cycloalkyl, aryl, heterocycle, and heteroaryl, each of which is independently substituted with 0, 1, 2, or 3 R⁶.

43. The compound according to any one of claims 1 to 42, or pharmaceutically acceptable salt thereof, wherein L is a linker of 1 to 10 carbon atoms in length, wherein one or more carbon atoms are each optionally and independently replaced by a group selected from C(O), O, NR⁷, S, C₂-alkenyl, C₂-alkynyl, cycloalkyl, aryl, heterocycle, and heteroaryl, each of which is independently substituted with 0, 1, 2, or 3 R⁶.

44. The compound according to any one of claims 1 to 43, or pharmaceutically acceptable salt thereof, wherein L is a linker of 1 to 8 carbon atoms in length, wherein one or more carbon atoms are each optionally and independently replaced by a group selected from O, NR⁷, S, C₂-alkenyl, C₂-alkynyl, cycloalkyl, aryl, heterocycle, and heteroaryl, each of which is independently substituted with 0, 1, 2, or 3 R⁶.

45. The compound according to any one of claims 1 to 44, or pharmaceutically acceptable salt thereof, wherein L is a linker of 1 to 8 carbon atoms in length, wherein one or more carbon atoms are each optionally and independently replaced by a group selected from C(O), O, NR⁷, S, C₂-alkenyl, C₂-alkynyl, cycloalkyl, aryl, heterocycle, and heteroaryl, each of which is independently substituted with 0, 1, 2, or 3 R⁶.

46. The compound according to any one of claims 1 to 45, or pharmaceutically acceptable salt thereof, wherein L is a linker of 1 to 6 carbon atoms in length, wherein one or more carbon atoms are each optionally and independently replaced by a group selected from C(O), O, NR⁷, S, C₂-alkenyl, C₂-alkynyl, cycloalkyl, aryl, heterocycle, and heteroaryl, each of which is independently substituted with 0, 1, 2, or 3 R⁶.

47. The compound according to any one of claims 1 to 46, or pharmaceutically acceptable salt thereof, wherein L is a linker of 1 to 4 carbon atoms in length, wherein one or more carbon atoms are each optionally and independently replaced by a group selected from C(O), O, NR⁷, S, C₂-alkenyl, C₂-alkynyl, cycloalkyl, aryl, heterocycle, and heteroaryl, each of which is independently substituted with 0, 1, 2, or 3 R⁶.

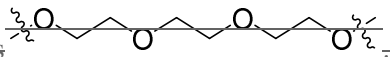
48. The compound according to any one of claims 1 to 47, or a pharmaceutically acceptable salt thereof, wherein L is a linker wherein two carbon atoms are each independently replaced by a heterocycle, each of which is independently substituted with 0, 1, 2, or 3 R⁶.

49. The compound according to any one of claims 1 to 47, or a pharmaceutically acceptable salt thereof, wherein L is a linker wherein one carbon atom is replaced by a heterocycle and one carbon atom is replaced by a cycloalkyl, each of which is independently substituted with 0, 1, 2, or 3 R⁶.

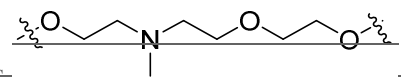
50. The compound according to any one of claims 1 to 47, or a pharmaceutically acceptable salt thereof, wherein L is a linker wherein more than one carbon atoms are each independently replaced by a group selected from C(O), O, NR⁴, S, C₂-alkenyl, C₂-alkynyl, cycloalkyl, aryl, heterocycle, and heteroaryl, each of which is substituted with 0, 1, 2, or 3 R⁶.

51. The compound according to any one of claims 1 to 47, or a pharmaceutically acceptable salt thereof, wherein L is a linker wherein more than one carbon atoms are each independently replaced by a group selected from C(O), O, and NR⁴, each of which is substituted with 0, 1, 2, or 3 R⁶.

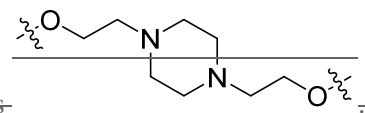
52. The compound according to any one of claims 1 to 36, or a pharmaceutically acceptable salt thereof, wherein L is



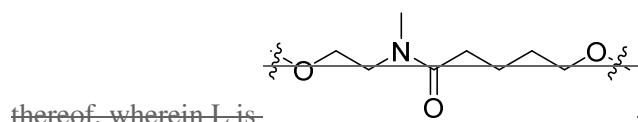
53. The compound according to any one of claims 1 to 36, or a pharmaceutically acceptable salt thereof, wherein L is



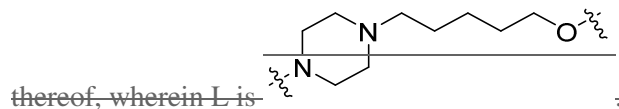
54. The compound according to any one of claims 1 to 36, or a pharmaceutically acceptable salt thereof, wherein L is



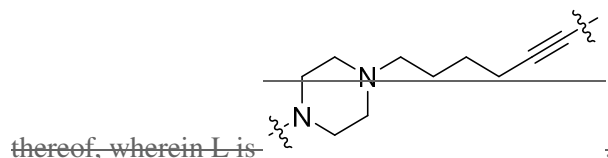
55. The compound according to any one of claims 1 to 36, or a pharmaceutically acceptable salt



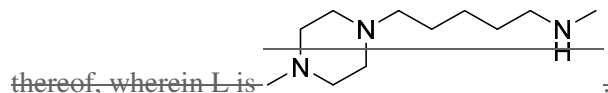
56. The compound according to any one of claims 1 to 36, or a pharmaceutically acceptable salt



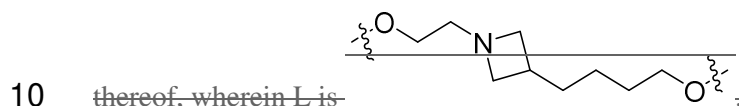
5 57. The compound according to any one of claims 1 to 36, or a pharmaceutically acceptable salt



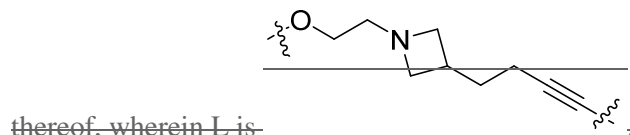
58. The compound according to any one of claims 1 to 36, or a pharmaceutically acceptable salt



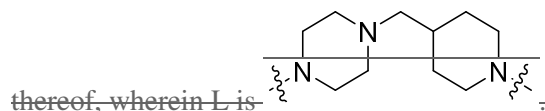
59. The compound according to any one of claims 1 to 36, or a pharmaceutically acceptable salt



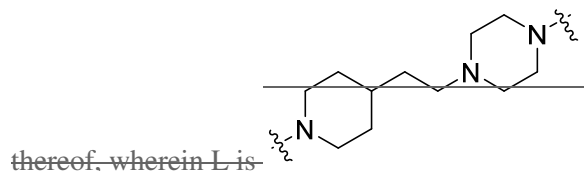
60. The compound according to any one of claims 1 to 36, or a pharmaceutically acceptable salt



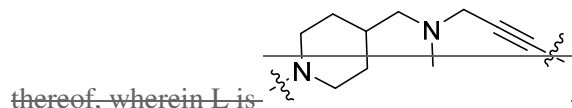
61. The compound according to any one of claims 1 to 36, or a pharmaceutically acceptable salt



15 62. The compound according to any one of claims 1 to 36, or a pharmaceutically acceptable salt



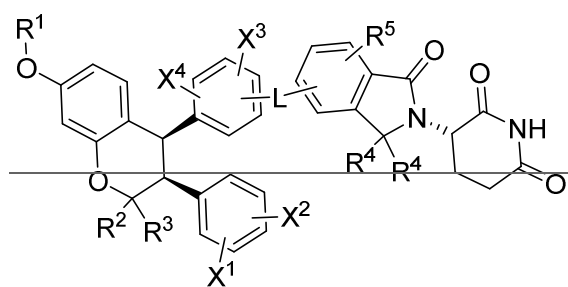
63. The compound according to any one of claims 1 to 36, or a pharmaceutically acceptable salt



20 64. The compound according to any one of claims 1 to 63, or a pharmaceutically acceptable salt thereof, wherein the compound is stereoisomer.

65. The compound according to claim 64, wherein the compound is *cis*-isomer.

66. The compound according to claim 64, wherein the compound has a Formula (I)*:



Formula (I)*

67. The compound according to claim 1, or a pharmaceutically acceptable salt thereof, selected from:

- 5 ~~*cis*-3-(5-(2-(2-(2-(4-(7-hydroxy-3-phenylchroman-4-yl)phenoxy)ethoxy)ethoxy)ethoxy)-1-oxoisindolin-2-yl)piperidine-2,6-dione;~~
- ~~*cis*-3-(5-(2-(2-((2-(4-(7-hydroxy-3-phenylchroman-4-yl)phenoxy)ethyl)(methylamino)ethoxy)ethoxy)-1-oxoisindolin-2-yl)piperidine-2,6-dione;~~
- ~~*cis*-3-(5-(2-(4-(2-(4-(7-hydroxy-3-phenylchroman-4-yl)phenoxy)ethyl)piperazin-1-yl)ethoxy)-1-~~
- 10 ~~oxoisindolin-2-yl)piperidine-2,6-dione;~~
- ~~*cis*-5-((2-(2,6-dioxopiperidin-3-yl)-1-oxoisindolin-5-yl)oxy)-N-(2-(4-(7-hydroxy-3-phenylchroman-4-yl)phenoxy)ethyl)-N-methylpentanamide;~~
- ~~*cis*-3-(5-((5-(4-(4-(7-hydroxy-3-phenylchroman-4-yl)phenyl)piperazin-1-yl)pentyl)oxy)-1-oxoisindolin-2-yl)piperidine-2,6-dione;~~
- 15 ~~*cis*-3-(5-(6-(4-(4-(7-hydroxy-3-phenylchroman-4-yl)phenyl)piperazin-1-yl)hex-1-yn-1-yl)-1-oxoisindolin-2-yl)piperidine-2,6-dione;~~
- ~~*cis*-3-(4-(6-(4-(4-(7-hydroxy-3-phenylchroman-4-yl)phenyl)piperazin-1-yl)hex-1-yn-1-yl)-1-oxoisindolin-2-yl)piperidine-2,6-dione;~~
- ~~*cis*-2-(2,6-dioxopiperidin-3-yl)-5-((5-(4-(4-(7-hydroxy-3-phenylchroman-4-yl)phenyl)piperazin-1-~~
- 20 ~~yl)pentyl)amino)isoindoline-1,3-dione;~~
- ~~*cis*-3-(5-(3-(1-(2-(4-(7-hydroxy-3-phenylchroman-4-yl)phenoxy)ethyl)azetidin-3-yl)propoxy)-1-oxoisindolin-2-yl)piperidine-2,6-dione;~~
- ~~*cis*-3-(5-(4-(1-(2-(4-(7-hydroxy-3-phenylchroman-4-yl)phenoxy)ethyl)azetidin-3-yl)but-1-yn-1-yl)-1-oxoisindolin-2-yl)piperidine-2,6-dione;~~
- 25 ~~*cis*-3-(4-(4-(1-(2-(4-(7-hydroxy-3-phenylchroman-4-yl)phenoxy)ethyl)azetidin-3-yl)but-1-yn-1-yl)-1-oxoisindolin-2-yl)piperidine-2,6-dione;~~
- ~~*cis*-2-(2,6-dioxopiperidin-3-yl)-5-(4-(5-(4-(7-hydroxy-3-phenylchroman-4-yl)phenoxy)pentyl)piperazin-1-yl)isoindoline-1,3-dione;~~
- ~~*cis*-3-(5-(4-(5-(4-(7-hydroxy-3-phenylchroman-4-yl)phenoxy)pentyl)piperazin-1-yl)-1-oxoisindolin-2-~~
- 30 ~~yl)piperidine-2,6-dione;~~
- ~~*cis*-3-(5-(4-(5-(2-fluoro-4-(3-(4-fluoro-3-(trifluoromethyl)phenyl)-7-hydroxychroman-4-yl)phenoxy)pentyl)piperazin-1-yl)-1-oxoisindolin-2-yl)piperidine-2,6-dione;~~

- ~~*cis*-3-(5-(4-(5-(2-fluoro-4-(3-(4-fluorophenyl)-7-hydroxychroman-4-yl)phenoxy)pentyl)piperazin-1-yl)-1-oxoisoindolin-2-yl)piperidine-2,6-dione;~~
- ~~*cis*-3-(5-(4-(5-(2-fluoro-4-(3-(4-fluoro-3-methylphenyl)-7-hydroxychroman-4-yl)phenoxy)pentyl)piperazin-1-yl)-1-oxoisoindolin-2-yl)piperidine-2,6-dione;~~
- 5 ~~*cis*-3-(5-(4-(5-(2-fluoro-4-(7-hydroxy-3-(*m*-tolyl)chroman-4-yl)phenoxy)pentyl)piperazin-1-yl)-1-oxoisoindolin-2-yl)piperidine-2,6-dione;~~
- ~~*cis*-3-(5-(4-(5-(2-fluoro-4-(3-(4-fluoro-2-methylphenyl)-7-hydroxychroman-4-yl)phenoxy)pentyl)piperazin-1-yl)-1-oxoisoindolin-2-yl)piperidine-2,6-dione;~~
- 10 ~~*cis*-3-(5-(4-(5-(4-(3-(3,4-difluorophenyl)-7-hydroxychroman-4-yl)-2-fluorophenoxy)pentyl)piperazin-1-yl)-1-oxoisoindolin-2-yl)piperidine-2,6-dione;~~
- ~~*cis*-3-(5-(4-(5-(4-(3-(4-fluoro-3-(trifluoromethyl)phenyl)-7-hydroxychroman-4-yl)phenoxy)pentyl)piperazin-1-yl)-1-oxoisoindolin-2-yl)piperidine-2,6-dione;~~
- ~~*cis*-3-(5-(4-(5-(4-(3-(4-fluoro-3-methoxyphenyl)-7-hydroxychroman-4-yl)phenoxy)pentyl)piperazin-1-yl)-1-oxoisoindolin-2-yl)piperidine-2,6-dione;~~
- 15 ~~*cis*-3-(5-(4-(5-(4-(3-(4-fluoro-2-(trifluoromethyl)phenyl)-7-hydroxychroman-4-yl)phenoxy)pentyl)piperazin-1-yl)-1-oxoisoindolin-2-yl)piperidine-2,6-dione;~~
- ~~*cis*-3-(5-(4-(5-(4-(3-(4-fluoro-3-methylphenyl)-7-hydroxychroman-4-yl)phenoxy)pentyl)piperazin-1-yl)-1-oxoisoindolin-2-yl)piperidine-2,6-dione;~~
- 20 ~~*cis*-3-(5-(4-(5-(4-(7-hydroxy-3-(*o*-tolyl)chroman-4-yl)phenoxy)pentyl)piperazin-1-yl)-1-oxoisoindolin-2-yl)piperidine-2,6-dione;~~
- ~~*cis*-3-(5-(4-(4-(4-(7-hydroxy-3-phenylchroman-4-yl)phenoxy)butyl)piperazin-1-yl)-1-oxoisoindolin-2-yl)piperidine-2,6-dione;~~
- ~~*cis*-3-(5-(4-(5-(4-(7-hydroxy-2,2-dimethyl-3-phenylchroman-4-yl)phenoxy)pentyl)piperazin-1-yl)-1-oxoisoindolin-2-yl)piperidine-2,6-dione;~~
- 25 ~~*cis*-3-(5-(4-(5-(4-(7-methoxy-3-phenylchroman-4-yl)phenoxy)pentyl)piperazin-1-yl)-1-oxoisoindolin-2-yl)piperidine-2,6-dione;~~
- ~~3-(5-(4-(5-(4-((2*R*,3*S*,4*R*)-7-hydroxy-2-methyl-3-phenylchroman-4-yl)phenoxy)pentyl)piperazin-1-yl)-1-oxoisoindolin-2-yl)piperidine-2,6-dione;~~
- ~~3-(5-(4-(5-(4-((2*S*,3*S*,4*R*)-7-hydroxy-2-methyl-3-phenylchroman-4-yl)phenoxy)pentyl)piperazin-1-yl)-1-oxoisoindolin-2-yl)piperidine-2,6-dione;~~
- 30 ~~3-(5-(4-(5-(4-((2*R*,3*R*,4*S*)-7-hydroxy-2-methyl-3-phenylchroman-4-yl)phenoxy)pentyl)piperazin-1-yl)-1-oxoisoindolin-2-yl)piperidine-2,6-dione;~~
- ~~3-(5-(4-(5-(4-((2*S*,3*R*,4*S*)-7-hydroxy-2-methyl-3-phenylchroman-4-yl)phenoxy)pentyl)piperazin-1-yl)-1-oxoisoindolin-2-yl)piperidine-2,6-dione;~~
- 35 ~~*cis*-(*S*)-3-(5-(4-((1-(4-(7-hydroxy-3-phenylchroman-4-yl)phenyl)piperidin-4-yl)methyl)piperazin-1-yl)-1-oxoisoindolin-2-yl)piperidine-2,6-dione;~~
- ~~(*S*)-3-(5-(4-((1-(4-((3*S*,4*R*)-7-hydroxy-3-phenylchroman-4-yl)phenyl)piperidin-4-yl)methyl)piperazin-1-yl)-1-oxoisoindolin-2-yl)piperidine-2,6-dione;~~

- (S)-3-(5-(4-((1-(4-((3R,4S)-7-hydroxy-3-phenylchroman-4-yl)phenyl)piperidin-4-yl)methyl)piperazin-1-yl)-1-oxoisindolin-2-yl)piperidine-2,6-dione;
cis-3-(5-(4-((1-(4-(7-hydroxy-3-phenylchroman-4-yl)phenyl)piperidin-4-yl)methyl)piperazin-1-yl)-1-oxoisindolin-2-yl)piperidine-2,6-dione;
- 5 *cis*-2-(2,6-dioxopiperidin-3-yl)-5-(4-((1-(4-(7-hydroxy-3-phenylchroman-4-yl)phenyl)piperidin-4-yl)methyl)piperazin-1-yl)isoindoline-1,3-dione;
cis-2-(2,6-dioxopiperidin-3-yl)-5-(4-(2-(1-(4-(7-hydroxy-3-phenylchroman-4-yl)phenyl)piperidin-4-yl)ethyl)piperazin-1-yl)isoindoline-1,3-dione;
cis-2-(2,6-dioxopiperidin-3-yl)-5-fluoro-6-(4-((1-(4-(7-hydroxy-3-phenylchroman-4-yl)phenyl)piperidin-
- 10 4-yl)methyl)piperazin-1-yl)isoindoline-1,3-dione;
cis-(S)-3-(6-fluoro-5-(4-((1-(4-(7-hydroxy-3-phenylchroman-4-yl)phenyl)piperidin-4-yl)methyl)piperazin-1-yl)-1-oxoisindolin-2-yl)piperidine-2,6-dione;
cis-(S)-3-(6-fluoro-5-(4-((1-(2-fluoro-4-(7-hydroxy-3-phenylchroman-4-yl)phenyl)piperidin-4-yl)methyl)piperazin-1-yl)-1-oxoisindolin-2-yl)piperidine-2,6-dione;
- 15 (S)-3-(6-fluoro-5-(4-((1-(2-fluoro-4-((3S,4R)-7-hydroxy-3-phenylchroman-4-yl)phenyl)piperidin-4-yl)methyl)piperazin-1-yl)-1-oxoisindolin-2-yl)piperidine-2,6-dione;
(S)-3-(6-fluoro-5-(4-((1-(4-((3S,4R)-7-hydroxy-3-phenylchroman-4-yl)phenyl)piperidin-4-yl)methyl)piperazin-1-yl)-1-oxoisindolin-2-yl)piperidine-2,6-dione;
(S)-3-(6-fluoro-5-(4-((1-(4-((3R,4S)-7-hydroxy-3-phenylchroman-4-yl)phenyl)piperidin-4-
- 20 yl)methyl)piperazin-1-yl)-1-oxoisindolin-2-yl)piperidine-2,6-dione;
cis-(S)-3-(5-(4-(2-(1-(4-(7-hydroxy-3-phenylchroman-4-yl)phenyl)piperidin-4-yl)ethyl)piperazin-1-yl)-1-oxoisindolin-2-yl)piperidine-2,6-dione;
(S)-3-(5-(4-((1-(2-fluoro-4-((3R,4S)-7-hydroxy-3-phenylchroman-4-yl)phenyl)piperidin-4-yl)methyl)piperazin-1-yl)-1-oxoisindolin-2-yl)piperidine-2,6-dione;
- 25 (S)-3-(5-(4-((1-(2-fluoro-4-((3S,4R)-7-hydroxy-2,2-dimethyl-3-phenylchroman-4-yl)phenyl)piperidin-4-yl)methyl)piperazin-1-yl)-1-oxoisindolin-2-yl)piperidine-2,6-dione;
(S)-3-(5-(4-((1-(2-fluoro-4-((2R,3S,4R)-7-hydroxy-2-methyl-3-phenylchroman-4-yl)phenyl)piperidin-4-yl)methyl)piperazin-1-yl)-1-oxoisindolin-2-yl)piperidine-2,6-dione;
(S)-3-(5-(4-((1-(2-fluoro-4-((2S,3S,4R)-7-hydroxy-2-methyl-3-phenylchroman-4-yl)phenyl)piperidin-4-
- 30 yl)methyl)piperazin-1-yl)-1-oxoisindolin-2-yl)piperidine-2,6-dione;
(S)-3-(5-(4-((1-(2-fluoro-4-((3S,4R)-7-methoxy-3-phenylchroman-4-yl)phenyl)piperidin-4-yl)methyl)piperazin-1-yl)-1-oxoisindolin-2-yl)piperidine-2,6-dione;
cis-(S)-3-(5-(4-((1-(2-fluoro-4-(3-(4-fluorophenyl)-7-hydroxychroman-4-yl)phenyl)piperidin-4-yl)methyl)piperazin-1-yl)-1-oxoisindolin-2-yl)piperidine-2,6-dione;
- 35 *cis*-(S)-3-(5-(4-((1-(4-(3-(4-fluorophenyl)-7-hydroxychroman-4-yl)phenyl)piperidin-4-yl)methyl)piperazin-1-yl)-1-oxoisindolin-2-yl)piperidine-2,6-dione;
cis-(S)-3-(5-(4-((1-(2-fluoro-4-(7-hydroxy-3-(*m*-tolyl)chroman-4-yl)phenyl)piperidin-4-yl)methyl)piperazin-1-yl)-1-oxoisindolin-2-yl)piperidine-2,6-dione;

~~*cis* (S) 3-(5-(4-((1-(4-(7-hydroxy-3-(*m*-tolyl)chroman-4-yl)phenyl)piperidin-4-yl)methyl)piperazin-1-yl)-1-oxoisoindolin-2-yl)piperidine-2,6-dione;~~

~~*cis* (S) 3-(5-(4-((1-(2-fluoro-4-(7-hydroxy-3-(3-methoxyphenyl)chroman-4-yl)phenyl)piperidin-4-yl)methyl)piperazin-1-yl)-1-oxoisoindolin-2-yl)piperidine-2,6-dione;~~

5 ~~(S) 3-(5-(4-((1-(2-fluoro-4-((3*S*,4*R*)-7-hydroxy-3-(3-methoxyphenyl)chroman-4-yl)phenyl)piperidin-4-yl)methyl)piperazin-1-yl)-1-oxoisoindolin-2-yl)piperidine-2,6-dione;~~

~~*cis* (S) 3-(5-(4-((1-(4-(7-hydroxy-3-(3-methoxyphenyl)chroman-4-yl)phenyl)piperidin-4-yl)methyl)piperazin-1-yl)-1-oxoisoindolin-2-yl)piperidine-2,6-dione;~~

10 ~~*cis* 3-(5-(4-((1-(4-(7-hydroxy-3-(3-methoxyphenyl)chroman-4-yl)phenyl)piperidin-4-yl)methyl)piperazin-1-yl)-1-oxoisoindolin-2-yl)piperidine-2,6-dione;~~

~~*cis* (S) 3-(5-(4-((1-(2-fluoro-4-(7-hydroxy-3-(3-methoxyphenyl)-2,2-dimethylchroman-4-yl)phenyl)piperidin-4-yl)methyl)piperazin-1-yl)-1-oxoisoindolin-2-yl)piperidine-2,6-dione;~~

~~*cis* (S) 3-(5-(4-((1-(4-(7-hydroxy-3-(3-methoxyphenyl)-2,2-dimethylchroman-4-yl)phenyl)piperidin-4-yl)methyl)piperazin-1-yl)-1-oxoisoindolin-2-yl)piperidine-2,6-dione;~~

15 ~~*cis* (S) 3-(5-(4-((1-(2-fluoro-4-(3-(4-fluoro-3-methylphenyl)-7-hydroxychroman-4-yl)phenyl)piperidin-4-yl)methyl)piperazin-1-yl)-1-oxoisoindolin-2-yl)piperidine-2,6-dione;~~

~~*cis* (S) 3-(5-(4-((1-(2-fluoro-4-(3-(4-fluoro-3-methoxyphenyl)-7-hydroxychroman-4-yl)phenyl)piperidin-4-yl)methyl)piperazin-1-yl)-1-oxoisoindolin-2-yl)piperidine-2,6-dione;~~

20 ~~*cis* (S) 3-(5-(4-((1-(4-(3-(4-fluoro-3-methylphenyl)-7-hydroxychroman-4-yl)phenyl)piperidin-4-yl)methyl)piperazin-1-yl)-1-oxoisoindolin-2-yl)piperidine-2,6-dione;~~

~~*cis* (S) 3-(5-(4-((1-(4-(3-(4-fluoro-3-methoxyphenyl)-7-hydroxychroman-4-yl)phenyl)piperidin-4-yl)methyl)piperazin-1-yl)-1-oxoisoindolin-2-yl)piperidine-2,6-dione;~~

~~*cis* (S) 3-(5-(4-((1-(2-fluoro-4-(3-(4-fluoro-2-methylphenyl)-7-hydroxychroman-4-yl)phenyl)piperidin-4-yl)methyl)piperazin-1-yl)-1-oxoisoindolin-2-yl)piperidine-2,6-dione;~~

25 ~~*cis* (S) 3-(5-(4-((1-(4-(3-(4-fluoro-2-methylphenyl)-7-hydroxychroman-4-yl)phenyl)piperidin-4-yl)methyl)piperazin-1-yl)-1-oxoisoindolin-2-yl)piperidine-2,6-dione;~~

~~*cis* (S) 3-(5-(4-((1-(4-((2*R*)-7-hydroxy-3-(3-methoxyphenyl)-2-methylchroman-4-yl)phenyl)piperidin-4-yl)methyl)piperazin-1-yl)-1-oxoisoindolin-2-yl)piperidine-2,6-dione;~~

30 ~~*cis* (S) 3-(5-(4-((1-(4-((2*S*)-7-hydroxy-3-(3-methoxyphenyl)-2-methylchroman-4-yl)phenyl)piperidin-4-yl)methyl)piperazin-1-yl)-1-oxoisoindolin-2-yl)piperidine-2,6-dione;~~

~~*cis* 3-(5-(3-(((1-(4-(7-hydroxy-3-(3-methoxyphenyl)chroman-4-yl)phenyl)piperidin-4-yl)methyl)(methyl)amino)prop-1-yn-1-yl)-1-oxoisoindolin-2-yl)piperidine-2,6-dione;~~

~~*cis* 3-(5-(3-(((1-(2-fluoro-4-(7-hydroxy-3-(3-methoxyphenyl)chroman-4-yl)phenyl)piperidin-4-yl)methyl)(methyl)amino)prop-1-yn-1-yl)-1-oxoisoindolin-2-yl)piperidine-2,6-dione;~~

35 ~~*cis* 3-(5-(3-(((1-(2-fluoro-4-(7-hydroxy-3-(*m*-tolyl)chroman-4-yl)phenyl)piperidin-4-yl)methyl)(methyl)amino)prop-1-yn-1-yl)-1-oxoisoindolin-2-yl)piperidine-2,6-dione;~~

~~*cis* 3-(5-(3-(((1-(4-(7-hydroxy-3-(*m*-tolyl)chroman-4-yl)phenyl)piperidin-4-yl)methyl)(methyl)amino)prop-1-yn-1-yl)-1-oxoisoindolin-2-yl)piperidine-2,6-dione;~~

- cis* (S) 3-(6-fluoro-5-(4-((1-(2-fluoro-4-(7-hydroxy-3-(3-methoxyphenyl)chroman-4-yl)phenyl)piperidin-4-yl)methyl)piperazin-1-yl)-1-oxoisindolin-2-yl)piperidine-2,6-dione;
- cis* 2-(2,6-dioxopiperidin-3-yl)-5-fluoro-6-(4-((1-(2-fluoro-4-(7-hydroxy-3-(3-methoxyphenyl)chroman-4-yl)phenyl)piperidin-4-yl)methyl)piperazin-1-yl)isoindoline-1,3-dione;
- 5 *cis* (S) 3-(6-fluoro-5-(4-((1-(4-(7-hydroxy-3-(3-methoxyphenyl)chroman-4-yl)phenyl)piperidin-4-yl)methyl)piperazin-1-yl)-1-oxoisindolin-2-yl)piperidine-2,6-dione;
- cis* 2-(2,6-dioxopiperidin-3-yl)-5-fluoro-6-(4-((1-(4-(7-hydroxy-3-(3-methoxyphenyl)chroman-4-yl)phenyl)piperidin-4-yl)methyl)piperazin-1-yl)isoindoline-1,3-dione;
- 10 *cis* (S) 3-(6-fluoro-5-(4-((1-(2-fluoro-4-(3-(4-fluoro-3-methylphenyl)-7-hydroxychroman-4-yl)phenyl)piperidin-4-yl)methyl)piperazin-1-yl)-1-oxoisindolin-2-yl)piperidine-2,6-dione;
- cis* (S) 3-(6-fluoro-5-(4-((1-(4-(3-(4-fluoro-3-methylphenyl)-7-hydroxychroman-4-yl)phenyl)piperidin-4-yl)methyl)piperazin-1-yl)-1-oxoisindolin-2-yl)piperidine-2,6-dione;
- cis* (S) 3-(6-fluoro-5-(4-((1-(2-fluoro-4-(7-hydroxy-3-(*m*-tolyl)chroman-4-yl)phenyl)piperidin-4-yl)methyl)piperazin-1-yl)-1-oxoisindolin-2-yl)piperidine-2,6-dione;
- 15 *cis* (S) 3-(6-fluoro-5-(4-((1-(4-(7-hydroxy-3-(*m*-tolyl)chroman-4-yl)phenyl)piperidin-4-yl)methyl)piperazin-1-yl)-1-oxoisindolin-2-yl)piperidine-2,6-dione;
- cis* (S) 3-(6-fluoro-5-(4-((1-(2-fluoro-4-(3-(4-fluoro-3-methoxyphenyl)-7-hydroxychroman-4-yl)phenyl)piperidin-4-yl)methyl)piperazin-1-yl)-1-oxoisindolin-2-yl)piperidine-2,6-dione;
- cis* (S) 3-(5-(4-((1-(2,6-difluoro-4-(7-hydroxy-3-(*m*-tolyl)chroman-4-yl)phenyl)piperidin-4-yl)methyl)piperazin-1-yl)-1-oxoisindolin-2-yl)piperidine-2,6-dione;
- 20 *cis* (S) 3-(5-(4-((1-(2-fluoro-4-(7-methoxy-3-phenylchroman-4-yl)phenyl)piperidin-4-yl)methyl)piperazin-1-yl)-1-oxoisindolin-2-yl)piperidine-2,6-dione;
- cis* 2-(2,6-dioxopiperidin-3-yl)-5-(4-((1-(2-fluoro-4-(7-methoxy-3-phenylchroman-4-yl)phenyl)piperidin-4-yl)methyl)piperazin-1-yl)isoindoline-1,3-dione;
- 25 *cis* (S) 3-(5-(4-((1-(4-(3-(3,4-difluorophenyl)-7-hydroxychroman-4-yl)-2-fluorophenyl)piperidin-4-yl)methyl)piperazin-1-yl)-1-oxoisindolin-2-yl)piperidine-2,6-dione;
- cis* (S) 3-(5-(4-((1-(2-fluoro-4-(7-hydroxy-3-phenylchroman-4-yl)phenyl)piperidin-4-yl)methyl)piperazin-1-yl)-1-oxoisindolin-2-yl)piperidine-2,6-dione;
- (S) 3-(5-(4-((1-(2-fluoro-4-((3*S*,4*R*)-7-hydroxy-3-phenylchroman-4-yl)phenyl)piperidin-4-yl)methyl)piperazin-1-yl)-1-oxoisindolin-2-yl)piperidine-2,6-dione;
- 30 *cis* 2-(2,6-dioxopiperidin-3-yl)-5-(4-((1-(2-fluoro-4-(7-hydroxy-3-phenylchroman-4-yl)phenyl)piperidin-4-yl)methyl)piperazin-1-yl)isoindoline-1,3-dione;
- cis* (S) 3-(5-(4-((1-(2,6-difluoro-4-(7-hydroxy-3-(3-methoxyphenyl)chroman-4-yl)phenyl)piperidin-4-yl)methyl)piperazin-1-yl)-1-oxoisindolin-2-yl)piperidine-2,6-dione;
- 35 *cis* (S) 3-(5-(4-((1-(4-(7-hydroxy-3-(4-methoxyphenyl)chroman-4-yl)phenyl)piperidin-4-yl)methyl)piperazin-1-yl)-1-oxoisindolin-2-yl)piperidine-2,6-dione; and
- cis* (S) 3-(6-fluoro-5-(4-((1-(4-(7-hydroxy-3-(4-methoxyphenyl)chroman-4-yl)phenyl)piperidin-4-yl)methyl)piperazin-1-yl)-1-oxoisindolin-2-yl)piperidine-2,6-dione.

68. The compound according to claim 1, or a pharmaceutically acceptable salt thereof, selected from:

~~cis (S) 3 (5 (4 ((1 (4 (7 hydroxy 3 phenylchroman 4 yl)phenyl)piperidin 4 yl)methyl)piperazin 1 yl) 1-oxoisindolin 2 yl)piperidine 2,6 dione;~~

~~(S) 3 (5 (4 ((1 (4 ((3S,4R) 7 hydroxy 3 phenylchroman 4 yl)phenyl)piperidin 4 yl)methyl)piperazin 1 yl) 1-oxoisindolin 2 yl)piperidine 2,6 dione;~~

~~(S) 3 (5 (4 ((1 (4 ((3R,4S) 7 hydroxy 3 phenylchroman 4 yl)phenyl)piperidin 4 yl)methyl)piperazin 1 yl) 1-oxoisindolin 2 yl)piperidine 2,6 dione;~~

~~cis 2 (2,6-dioxopiperidin 3 yl) 5 (4 ((1 (4 (7 hydroxy 3 phenylchroman 4 yl)phenyl)piperidin 4 yl)methyl)piperazin 1 yl)isoindoline 1,3 dione;~~

~~(S) 3 (6 fluoro 5 (4 ((1 (2 fluoro 4 ((3S,4R) 7 hydroxy 3 phenylchroman 4 yl)phenyl)piperidin 4 yl)methyl)piperazin 1 yl) 1-oxoisindolin 2 yl)piperidine 2,6 dione;~~

~~(S) 3 (6 fluoro 5 (4 ((1 (4 ((3S,4R) 7 hydroxy 3 phenylchroman 4 yl)phenyl)piperidin 4 yl)methyl)piperazin 1 yl) 1-oxoisindolin 2 yl)piperidine 2,6 dione;~~

~~(S) 3 (5 (4 ((1 (2 fluoro 4 ((3R,4S) 7 hydroxy 3 phenylchroman 4 yl)phenyl)piperidin 4 yl)methyl)piperazin 1 yl) 1-oxoisindolin 2 yl)piperidine 2,6 dione;~~

~~cis (S) 3 (5 (4 ((1 (2 fluoro 4 (7 hydroxy 3 (m-tolyl)chroman 4 yl)phenyl)piperidin 4 yl)methyl)piperazin 1 yl) 1-oxoisindolin 2 yl)piperidine 2,6 dione;~~

~~cis (S) 3 (5 (4 ((1 (2 fluoro 4 (3 (4 fluoro 3 methylphenyl) 7 hydroxychroman 4 yl)phenyl)piperidin 4 yl)methyl)piperazin 1 yl) 1-oxoisindolin 2 yl)piperidine 2,6 dione;~~

~~cis (S) 3 (5 (4 ((1 (4 (3 (3,4 difluorophenyl) 7 hydroxychroman 4 yl) 2-fluorophenyl)piperidin 4 yl)methyl)piperazin 1 yl) 1-oxoisindolin 2 yl)piperidine 2,6 dione;~~

~~cis (S) 3 (5 (4 ((1 (2 fluoro 4 (7 hydroxy 3 phenylchroman 4 yl)phenyl)piperidin 4 yl)methyl)piperazin 1 yl) 1-oxoisindolin 2 yl)piperidine 2,6 dione;~~

~~(S) 3 (5 (4 ((1 (2 fluoro 4 ((3S,4R) 7 hydroxy 3 phenylchroman 4 yl)phenyl)piperidin 4 yl)methyl)piperazin 1 yl) 1-oxoisindolin 2 yl)piperidine 2,6 dione; and~~

~~cis 2 (2,6-dioxopiperidin 3 yl) 5 (4 ((1 (2 fluoro 4 (7 hydroxy 3 phenylchroman 4 yl)phenyl)piperidin 4 yl)methyl)piperazin 1 yl)isoindoline 1,3 dione.~~

69. The compound according to claim 1, or a pharmaceutically acceptable salt thereof, selected from:

~~(S) 3 (5 (4 ((1 (4 ((3S,4R) 7 hydroxy 3 phenylchroman 4 yl)phenyl)piperidin 4 yl)methyl)piperazin 1 yl) 1-oxoisindolin 2 yl)piperidine 2,6 dione;~~

~~cis 2 (2,6-dioxopiperidin 3 yl) 5 (4 ((1 (4 (7 hydroxy 3 phenylchroman 4 yl)phenyl)piperidin 4 yl)methyl)piperazin 1 yl)isoindoline 1,3 dione;~~

~~(S) 3 (6 fluoro 5 (4 ((1 (2 fluoro 4 ((3S,4R) 7 hydroxy 3 phenylchroman 4 yl)phenyl)piperidin 4 yl)methyl)piperazin 1 yl) 1-oxoisindolin 2 yl)piperidine 2,6 dione;~~

(S)-3-(6-fluoro-5-(4-((1-(4-((3S,4R)-7-hydroxy-3-phenylchroman-4-yl)phenyl)piperidin-4-yl)methyl)piperazin-1-yl)-1-oxoisindolin-2-yl)piperidine-2,6-dione;
cis-(S)-3-(5-(4-((1-(2-fluoro-4-(7-hydroxy-3-(*m*-tolyl)chroman-4-yl)phenyl)piperidin-4-yl)methyl)piperazin-1-yl)-1-oxoisindolin-2-yl)piperidine-2,6-dione;
5 *cis*-(S)-3-(5-(4-((1-(2-fluoro-4-(3-(4-fluoro-3-methylphenyl)-7-hydroxychroman-4-yl)phenyl)piperidin-4-yl)methyl)piperazin-1-yl)-1-oxoisindolin-2-yl)piperidine-2,6-dione;
cis-(S)-3-(5-(4-((1-(4-(3-(3,4-difluorophenyl)-7-hydroxychroman-4-yl)-2-fluorophenyl)piperidin-4-yl)methyl)piperazin-1-yl)-1-oxoisindolin-2-yl)piperidine-2,6-dione;
(S)-3-(5-(4-((1-(2-fluoro-4-((3S,4R)-7-hydroxy-3-phenylchroman-4-yl)phenyl)piperidin-4-yl)methyl)piperazin-1-yl)-1-oxoisindolin-2-yl)piperidine-2,6-dione; and
10 *cis*-2-(2,6-dioxopiperidin-3-yl)-5-(4-((1-(2-fluoro-4-(7-hydroxy-3-phenylchroman-4-yl)phenyl)piperidin-4-yl)methyl)piperazin-1-yl)isoindoline-1,3-dione.

70. The compound according to claim 1, or a pharmaceutically acceptable salt thereof, selected from:

(S)-3-(5-(4-((1-(4-((3S,4R)-7-hydroxy-3-phenylchroman-4-yl)phenyl)piperidin-4-yl)methyl)piperazin-1-yl)-1-oxoisindolin-2-yl)piperidine-2,6-dione;
cis-2-(2,6-dioxopiperidin-3-yl)-5-(4-((1-(4-(7-hydroxy-3-phenylchroman-4-yl)phenyl)piperidin-4-yl)methyl)piperazin-1-yl)isoindoline-1,3-dione;
20 (S)-3-(6-fluoro-5-(4-((1-(2-fluoro-4-((3S,4R)-7-hydroxy-3-phenylchroman-4-yl)phenyl)piperidin-4-yl)methyl)piperazin-1-yl)-1-oxoisindolin-2-yl)piperidine-2,6-dione;
(S)-3-(6-fluoro-5-(4-((1-(4-((3S,4R)-7-hydroxy-3-phenylchroman-4-yl)phenyl)piperidin-4-yl)methyl)piperazin-1-yl)-1-oxoisindolin-2-yl)piperidine-2,6-dione;
cis-(S)-3-(5-(4-((1-(4-(3-(3,4-difluorophenyl)-7-hydroxychroman-4-yl)-2-fluorophenyl)piperidin-4-yl)methyl)piperazin-1-yl)-1-oxoisindolin-2-yl)piperidine-2,6-dione;
25 (S)-3-(5-(4-((1-(2-fluoro-4-((3S,4R)-7-hydroxy-3-phenylchroman-4-yl)phenyl)piperidin-4-yl)methyl)piperazin-1-yl)-1-oxoisindolin-2-yl)piperidine-2,6-dione; and
cis-2-(2,6-dioxopiperidin-3-yl)-5-(4-((1-(2-fluoro-4-(7-hydroxy-3-phenylchroman-4-yl)phenyl)piperidin-4-yl)methyl)piperazin-1-yl)isoindoline-1,3-dione.

71. A pharmaceutical composition comprising the compound according to any one of claims 1 to 70 and at least one additional component selected from pharmaceutically acceptable carriers, pharmaceutically acceptable vehicles, and pharmaceutically acceptable excipients.

72. The pharmaceutical composition according to claim 71, wherein the compound is present in a therapeutically effective amount.

73. A method of treating cancer in a subject in need thereof, comprising administering to said subject an effective amount of the compound according to any one of claims 1 to 70 or of the pharmaceutical composition according to claim 66 or 67, wherein the cancer is selected from breast cancer, lung cancer, ovarian cancer, endometrial cancer, prostate cancer, and esophageal cancer.

74. The method according to claim 73, wherein the cancer is breast cancer.

75. The method according to claim 74, wherein the cancer is ovarian cancer.

76. The method according to any one of claims 73 to 75, wherein the cancer is positive for ER α .

77. The method according to any one of claims 74 to 76, wherein the subject has been previously

5 treated with an anti-cancer agent.

78. The method according to claim 77, wherein the anti-cancer agent is tamoxifen.

79. The method according to claim 77, wherein the anti-cancer agent is fulvestrant.

80. A use of the compound according to any one of claims 1 to 70 in a method of therapeutic
treatment, wherein said therapeutic treatment is selected from treatment of breast cancer, lung cancer,
10 ovarian cancer, endometrial cancer, prostate cancer, esophageal cancer, infertility, ovulatory dysfunction,
postmenopausal osteoporosis, estrogen-related gynecomastia, dyspareunia due to menopause,
retroperitoneal fibrosis, and idiopathic sclerosing mesenteritis.

81. A use of the compound according to any one of claims 1 to 70 in the preparation of a
medicament.

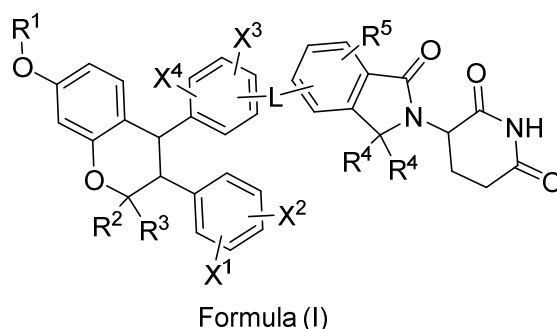
82. The use according to claim 81, wherein the medicament is for the treatment of breast cancer,
lung cancer, ovarian cancer, endometrial cancer, prostate cancer, esophageal cancer, infertility, ovulatory
dysfunction, postmenopausal osteoporosis, estrogen-related gynecomastia, dyspareunia due to
menopause, retroperitoneal fibrosis, and idiopathic sclerosing mesenteritis.

83. A method of inhibiting cell growth, comprising contacting a cell with the compound
20 according to any one of claims 1 to 70 or the pharmaceutical composition according to claim 71 or 72.

84. The method according to claim 83, wherein the cell is a cancer cell.

85. The method according to claim 83 or 84, wherein the cell expresses ER α .

1. A compound of Formula (I), a stereoisomer or a mixture of stereoisomers, a pharmaceutically
25 acceptable salt, or hydrate thereof:



wherein:

R¹ is selected from H, C₁-C₆ acyl or C₁-C₆ alkyl, each of which is substituted with 0, 1, 2, or 3 R⁶;

R² and R³ are each independently selected from H, C₁-C₃ alkyl, or C₁-C₃ haloalkyl, each of which
30 is substituted with 0, 1, 2, or 3 R⁶;

each R⁴ is independently selected from H, hydroxyl, C₁-C₃ alkyl, C₁-C₃ alkoxy, or C₁-C₃ haloalkyl, each of which is substituted with 0, 1, 2, or 3 R⁶, or two R⁴ groups are taken together to form an oxo;

R⁵ is selected from halogen, hydroxy, C₁-C₃ alkyl, C₁-C₃ alkoxy, C₁-C₃ haloalkyl, -N(R⁷)₂, and -CN, each of which is substituted with 0, 1, 2, or 3 R⁶;

X¹ and X² are each independently selected from H, halogen, cyano, C₁-C₆ alkyl, C₁-C₆ alkoxy, or C₁-C₆ haloalkyl each of which is substituted with 0, 1, 2, or 3 R⁶;

X³ and X⁴ are each independently selected from H or halo;

L is a linker of 1 to 22 carbon atoms in length, wherein one or more carbon atoms are each optionally and independently replaced by a group selected from C(O), O, NR⁷, S, C₂-alkenyl, C₂-alkynyl, cycloalkyl, aryl, heterocycle, and heteroaryl, each of which is substituted with 0, 1, 2, or 3 R⁶;

each R⁶ is independently selected from C₁-C₆ alkyl, halo, cyano, and hydroxy,

each R⁷ is independently selected from hydrogen, C₁-C₆ alkyl, and acyl, each of which is substituted with 0, 1, 2, or 3 R⁶, or two R⁷ groups are taken together to form a 3- to 6-membered heterocycle or heteroaryl.

2. The compound according to claim 1, or a pharmaceutically acceptable salt thereof, wherein R¹ is selected from H or methyl.

3. The compound according to claim 1, or a pharmaceutically acceptable salt thereof, wherein R² and R³ are each independently selected from H and methyl.

4. The compound according to claim 1, or a pharmaceutically acceptable salt thereof, wherein R⁴ is H.

5. The compound according to claim 1, or a pharmaceutically acceptable salt thereof, wherein two R⁴ groups are taken together to form an oxo.

6. The compound according to claim 1, or a pharmaceutically acceptable salt thereof, wherein R⁵ is selected from halogen.

7. The compound according to claim 1, or a pharmaceutically acceptable salt thereof, wherein X¹ and X² are each independently selected from H, F, CN, methyl, methoxy, trifluoromethyl.

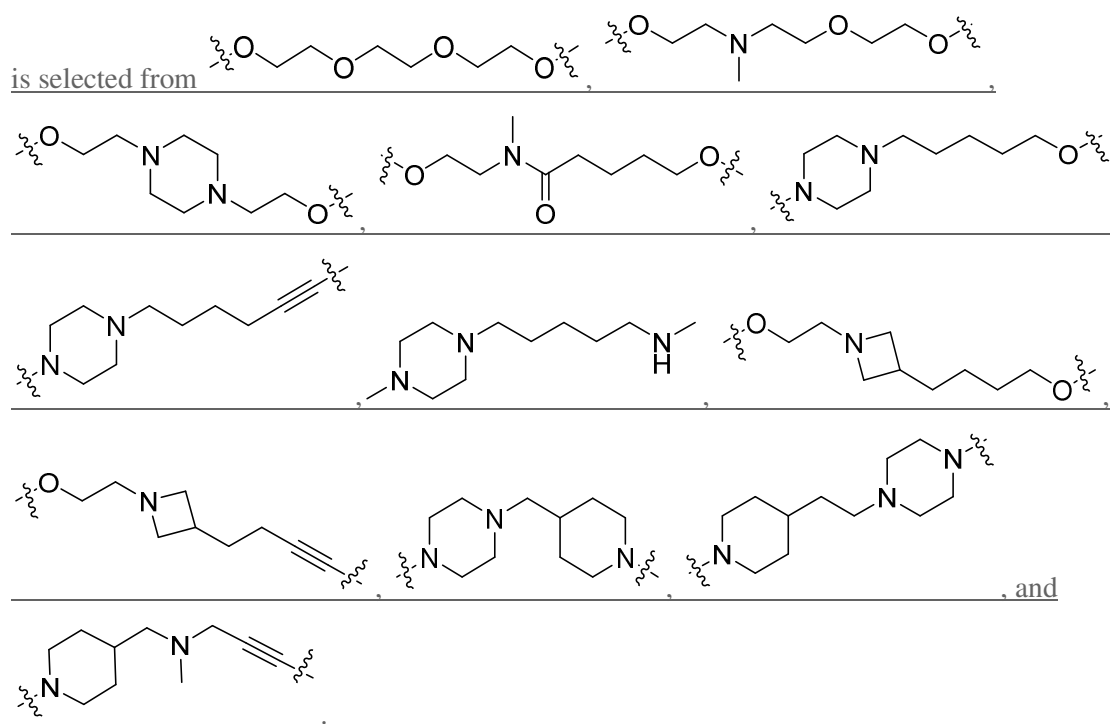
8. The compound according to claim 7, or a pharmaceutically acceptable salt thereof, wherein X³ and X⁴ are each independently selected from H or halo.

9. The compound according to claim 7, or a pharmaceutically acceptable salt thereof, wherein X^3 and X^4 are each independently selected from H or F.

10. The compound according to claim 1, or pharmaceutically acceptable salt thereof, wherein L is a linker of 1 to 22 carbon atoms in length, wherein one or more carbon atoms are each optionally and independently replaced by a group selected from C(O), O, NR^7 , S, C₂-alkenyl, C₂-alkynyl, cycloalkyl, aryl, heterocycle, and heteroaryl, each of which is independently substituted with 0, 1, 2, or 3 R^6 .

11. The compound according to claim 1, or a pharmaceutically acceptable salt thereof, wherein L is a linker wherein one carbon atom is replaced by a heterocycle and one carbon atom is replaced by a cycloalkyl, each of which is independently substituted with 0, 1, 2, or 3 R^6 .

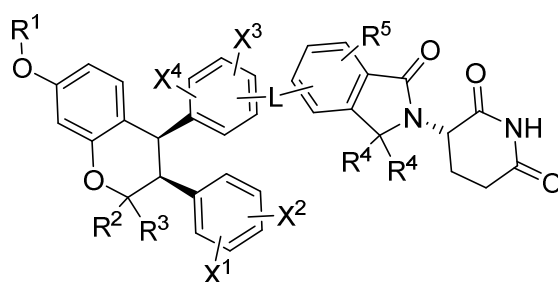
12. The compound according to claim 1, or a pharmaceutically acceptable salt thereof, wherein L



13. The compound according to claim 1, or a pharmaceutically acceptable salt thereof, wherein the compound is stereoisomer.

14. The compound according to claim 13, wherein the compound is *cis*- isomer.

15. The compound according to claim 13, wherein the compound has a Formula (I)*:



Formula (I)*

16. A compound, or a pharmaceutically acceptable salt thereof, selected from:

cis-3-(5-(2-(2-(2-(4-(7-hydroxy-3-phenylchroman-4-yl)phenoxy)ethoxy)ethoxy)ethoxy)-1-oxoisindolin-

5 2-yl)piperidine-2,6-dione;

cis-3-(5-(2-(2-((2-(4-(7-hydroxy-3-phenylchroman-4-yl)phenoxy)ethyl)(methyl)amino)ethoxy)ethoxy)-1-
oxoisindolin-2-yl)piperidine-2,6-dione;

cis-3-(5-(2-(4-(2-(4-(7-hydroxy-3-phenylchroman-4-yl)phenoxy)ethyl)piperazin-1-yl)ethoxy)-1-
oxoisindolin-2-yl)piperidine-2,6-dione;

10 cis-5-((2-(2,6-dioxopiperidin-3-yl)-1-oxoisindolin-5-yl)oxy)-N-(2-(4-(7-hydroxy-3-phenylchroman-4-
yl)phenoxy)ethyl)-N-methylpentanamide;

cis-3-(5-((5-(4-(4-(7-hydroxy-3-phenylchroman-4-yl)phenyl)piperazin-1-yl)pentyl)oxy)-1-oxoisindolin-
2-yl)piperidine-2,6-dione;

cis-3-(5-(6-(4-(4-(7-hydroxy-3-phenylchroman-4-yl)phenyl)piperazin-1-yl)hex-1-yn-1-yl)-1-
15 oxoisindolin-2-yl)piperidine-2,6-dione;

cis-3-(4-(6-(4-(4-(7-hydroxy-3-phenylchroman-4-yl)phenyl)piperazin-1-yl)hex-1-yn-1-yl)-1-
oxoisindolin-2-yl)piperidine-2,6-dione;

cis-2-(2,6-dioxopiperidin-3-yl)-5-((5-(4-(4-(7-hydroxy-3-phenylchroman-4-yl)phenyl)piperazin-1-
yl)pentyl)amino)isoindoline-1,3-dione;

20 cis-3-(5-(3-(1-(2-(4-(7-hydroxy-3-phenylchroman-4-yl)phenoxy)ethyl)azetidin-3-yl)propoxy)-1-
oxoisindolin-2-yl)piperidine-2,6-dione;

cis-3-(5-(4-(1-(2-(4-(7-hydroxy-3-phenylchroman-4-yl)phenoxy)ethyl)azetidin-3-yl)but-1-yn-1-yl)-1-
oxoisindolin-2-yl)piperidine-2,6-dione;

cis-3-(4-(4-(1-(2-(4-(7-hydroxy-3-phenylchroman-4-yl)phenoxy)ethyl)azetidin-3-yl)but-1-yn-1-yl)-1-
25 oxoisindolin-2-yl)piperidine-2,6-dione;

cis-2-(2,6-dioxopiperidin-3-yl)-5-(4-(5-(4-(7-hydroxy-3-phenylchroman-4-yl)phenoxy)pentyl)piperazin-
1-yl)isoindoline-1,3-dione;

cis-3-(5-(4-(5-(4-(7-hydroxy-3-phenylchroman-4-yl)phenoxy)pentyl)piperazin-1-yl)-1-oxoisindolin-2-
yl)piperidine-2,6-dione;

30 cis-3-(5-(4-(5-(2-fluoro-4-(3-(4-fluoro-3-(trifluoromethyl)phenyl)-7-hydroxychroman-4-
yl)phenoxy)pentyl)piperazin-1-yl)-1-oxoisindolin-2-yl)piperidine-2,6-dione;

- cis-3-(5-(4-(5-(2-fluoro-4-(3-(4-fluorophenyl)-7-hydroxychroman-4-yl)phenoxy)pentyl)piperazin-1-yl)-1-oxoisindolin-2-yl)piperidine-2,6-dione;
- cis-3-(5-(4-(5-(2-fluoro-4-(3-(4-fluoro-3-methylphenyl)-7-hydroxychroman-4-yl)phenoxy)pentyl)piperazin-1-yl)-1-oxoisindolin-2-yl)piperidine-2,6-dione;
- 5 cis-3-(5-(4-(5-(2-fluoro-4-(7-hydroxy-3-(m-tolyl)chroman-4-yl)phenoxy)pentyl)piperazin-1-yl)-1-oxoisindolin-2-yl)piperidine-2,6-dione;
- cis-3-(5-(4-(5-(2-fluoro-4-(3-(4-fluoro-2-methylphenyl)-7-hydroxychroman-4-yl)phenoxy)pentyl)piperazin-1-yl)-1-oxoisindolin-2-yl)piperidine-2,6-dione;
- 10 cis-3-(5-(4-(5-(4-(3-(3,4-difluorophenyl)-7-hydroxychroman-4-yl)-2-fluorophenoxy)pentyl)piperazin-1-yl)-1-oxoisindolin-2-yl)piperidine-2,6-dione;
- cis-3-(5-(4-(5-(4-(3-(4-fluoro-3-(trifluoromethyl)phenyl)-7-hydroxychroman-4-yl)phenoxy)pentyl)piperazin-1-yl)-1-oxoisindolin-2-yl)piperidine-2,6-dione;
- cis-3-(5-(4-(5-(4-(3-(4-fluoro-3-methoxyphenyl)-7-hydroxychroman-4-yl)phenoxy)pentyl)piperazin-1-yl)-1-oxoisindolin-2-yl)piperidine-2,6-dione;
- 15 cis-3-(5-(4-(5-(4-(3-(4-fluoro-2-(trifluoromethyl)phenyl)-7-hydroxychroman-4-yl)phenoxy)pentyl)piperazin-1-yl)-1-oxoisindolin-2-yl)piperidine-2,6-dione;
- cis-3-(5-(4-(5-(4-(3-(4-fluoro-3-methylphenyl)-7-hydroxychroman-4-yl)phenoxy)pentyl)piperazin-1-yl)-1-oxoisindolin-2-yl)piperidine-2,6-dione;
- 20 cis-3-(5-(4-(5-(4-(7-hydroxy-3-(o-tolyl)chroman-4-yl)phenoxy)pentyl)piperazin-1-yl)-1-oxoisindolin-2-yl)piperidine-2,6-dione;
- cis-3-(5-(4-(4-(4-(7-hydroxy-3-phenylchroman-4-yl)phenoxy)butyl)piperazin-1-yl)-1-oxoisindolin-2-yl)piperidine-2,6-dione;
- cis-3-(5-(4-(5-(4-(7-hydroxy-2,2-dimethyl-3-phenylchroman-4-yl)phenoxy)pentyl)piperazin-1-yl)-1-oxoisindolin-2-yl)piperidine-2,6-dione;
- 25 cis-3-(5-(4-(5-(4-(7-methoxy-3-phenylchroman-4-yl)phenoxy)pentyl)piperazin-1-yl)-1-oxoisindolin-2-yl)piperidine-2,6-dione;
- 3-(5-(4-(5-(4-((2R,3S,4R)-7-hydroxy-2-methyl-3-phenylchroman-4-yl)phenoxy)pentyl)piperazin-1-yl)-1-oxoisindolin-2-yl)piperidine-2,6-dione;
- 3-(5-(4-(5-(4-((2S,3S,4R)-7-hydroxy-2-methyl-3-phenylchroman-4-yl)phenoxy)pentyl)piperazin-1-yl)-1-oxoisindolin-2-yl)piperidine-2,6-dione;
- 30 3-(5-(4-(5-(4-((2R,3R,4S)-7-hydroxy-2-methyl-3-phenylchroman-4-yl)phenoxy)pentyl)piperazin-1-yl)-1-oxoisindolin-2-yl)piperidine-2,6-dione;
- 3-(5-(4-(5-(4-((2S,3R,4S)-7-hydroxy-2-methyl-3-phenylchroman-4-yl)phenoxy)pentyl)piperazin-1-yl)-1-oxoisindolin-2-yl)piperidine-2,6-dione;
- 35 cis-(S)-3-(5-(4-((1-(4-(7-hydroxy-3-phenylchroman-4-yl)phenyl)piperidin-4-yl)methyl)piperazin-1-yl)-1-oxoisindolin-2-yl)piperidine-2,6-dione;
- (S)-3-(5-(4-((1-(4-((3S,4R)-7-hydroxy-3-phenylchroman-4-yl)phenyl)piperidin-4-yl)methyl)piperazin-1-yl)-1-oxoisindolin-2-yl)piperidine-2,6-dione;

- (S)-3-(5-(4-((1-(4-((3R,4S)-7-hydroxy-3-phenylchroman-4-yl)phenyl)piperidin-4-yl)methyl)piperazin-1-yl)-1-oxoisindolin-2-yl)piperidine-2,6-dione;
cis-3-(5-(4-((1-(4-(7-hydroxy-3-phenylchroman-4-yl)phenyl)piperidin-4-yl)methyl)piperazin-1-yl)-1-oxoisindolin-2-yl)piperidine-2,6-dione;
- 5 cis-2-(2,6-dioxopiperidin-3-yl)-5-(4-((1-(4-(7-hydroxy-3-phenylchroman-4-yl)phenyl)piperidin-4-yl)methyl)piperazin-1-yl)isoindoline-1,3-dione;
cis-2-(2,6-dioxopiperidin-3-yl)-5-(4-(2-(1-(4-(7-hydroxy-3-phenylchroman-4-yl)phenyl)piperidin-4-yl)ethyl)piperazin-1-yl)isoindoline-1,3-dione;
cis-2-(2,6-dioxopiperidin-3-yl)-5-fluoro-6-(4-((1-(4-(7-hydroxy-3-phenylchroman-4-yl)phenyl)piperidin-
- 10 4-yl)methyl)piperazin-1-yl)isoindoline-1,3-dione;
cis-(S)-3-(6-fluoro-5-(4-((1-(4-(7-hydroxy-3-phenylchroman-4-yl)phenyl)piperidin-4-yl)methyl)piperazin-1-yl)-1-oxoisindolin-2-yl)piperidine-2,6-dione;
cis-(S)-3-(6-fluoro-5-(4-((1-(2-fluoro-4-(7-hydroxy-3-phenylchroman-4-yl)phenyl)piperidin-4-yl)methyl)piperazin-1-yl)-1-oxoisindolin-2-yl)piperidine-2,6-dione;
- 15 (S)-3-(6-fluoro-5-(4-((1-(2-fluoro-4-((3S,4R)-7-hydroxy-3-phenylchroman-4-yl)phenyl)piperidin-4-yl)methyl)piperazin-1-yl)-1-oxoisindolin-2-yl)piperidine-2,6-dione;
(S)-3-(6-fluoro-5-(4-((1-(4-((3S,4R)-7-hydroxy-3-phenylchroman-4-yl)phenyl)piperidin-4-yl)methyl)piperazin-1-yl)-1-oxoisindolin-2-yl)piperidine-2,6-dione;
(S)-3-(6-fluoro-5-(4-((1-(4-((3R,4S)-7-hydroxy-3-phenylchroman-4-yl)phenyl)piperidin-4-yl)methyl)piperazin-1-yl)-1-oxoisindolin-2-yl)piperidine-2,6-dione;
- 20 cis-(S)-3-(5-(4-(2-(1-(4-(7-hydroxy-3-phenylchroman-4-yl)phenyl)piperidin-4-yl)ethyl)piperazin-1-yl)-1-oxoisindolin-2-yl)piperidine-2,6-dione;
(S)-3-(5-(4-((1-(2-fluoro-4-((3R,4S)-7-hydroxy-3-phenylchroman-4-yl)phenyl)piperidin-4-yl)methyl)piperazin-1-yl)-1-oxoisindolin-2-yl)piperidine-2,6-dione;
- 25 (S)-3-(5-(4-((1-(2-fluoro-4-((3S,4R)-7-hydroxy-2,2-dimethyl-3-phenylchroman-4-yl)phenyl)piperidin-4-yl)methyl)piperazin-1-yl)-1-oxoisindolin-2-yl)piperidine-2,6-dione;
(S)-3-(5-(4-((1-(2-fluoro-4-((2R,3S,4R)-7-hydroxy-2-methyl-3-phenylchroman-4-yl)phenyl)piperidin-4-yl)methyl)piperazin-1-yl)-1-oxoisindolin-2-yl)piperidine-2,6-dione;
(S)-3-(5-(4-((1-(2-fluoro-4-((2S,3S,4R)-7-hydroxy-2-methyl-3-phenylchroman-4-yl)phenyl)piperidin-4-yl)methyl)piperazin-1-yl)-1-oxoisindolin-2-yl)piperidine-2,6-dione;
- 30 (S)-3-(5-(4-((1-(2-fluoro-4-((3S,4R)-7-methoxy-3-phenylchroman-4-yl)phenyl)piperidin-4-yl)methyl)piperazin-1-yl)-1-oxoisindolin-2-yl)piperidine-2,6-dione;
cis-(S)-3-(5-(4-((1-(2-fluoro-4-(3-(4-fluorophenyl)-7-hydroxychroman-4-yl)phenyl)piperidin-4-yl)methyl)piperazin-1-yl)-1-oxoisindolin-2-yl)piperidine-2,6-dione;
- 35 cis-(S)-3-(5-(4-((1-(4-(3-(4-fluorophenyl)-7-hydroxychroman-4-yl)phenyl)piperidin-4-yl)methyl)piperazin-1-yl)-1-oxoisindolin-2-yl)piperidine-2,6-dione;
cis-(S)-3-(5-(4-((1-(2-fluoro-4-(7-hydroxy-3-(m-tolyl)chroman-4-yl)phenyl)piperidin-4-yl)methyl)piperazin-1-yl)-1-oxoisindolin-2-yl)piperidine-2,6-dione;

- cis*-(S)-3-(5-(4-((1-(4-(7-hydroxy-3-(*m*-tolyl)chroman-4-yl)phenyl)piperidin-4-yl)methyl)piperazin-1-yl)-1-oxoisindolin-2-yl)piperidine-2,6-dione;
- cis*-(S)-3-(5-(4-((1-(2-fluoro-4-(7-hydroxy-3-(3-methoxyphenyl)chroman-4-yl)phenyl)piperidin-4-yl)methyl)piperazin-1-yl)-1-oxoisindolin-2-yl)piperidine-2,6-dione;
- 5 *(S)*-3-(5-(4-((1-(2-fluoro-4-((3*S*,4*R*)-7-hydroxy-3-(3-methoxyphenyl)chroman-4-yl)phenyl)piperidin-4-yl)methyl)piperazin-1-yl)-1-oxoisindolin-2-yl)piperidine-2,6-dione;
- cis*-(S)-3-(5-(4-((1-(4-(7-hydroxy-3-(3-methoxyphenyl)chroman-4-yl)phenyl)piperidin-4-yl)methyl)piperazin-1-yl)-1-oxoisindolin-2-yl)piperidine-2,6-dione;
- cis*-3-(5-(4-((1-(4-(7-hydroxy-3-(3-methoxyphenyl)chroman-4-yl)phenyl)piperidin-4-yl)methyl)piperazin-1-yl)-1-oxoisindolin-2-yl)piperidine-2,6-dione;
- 10 *cis*-(S)-3-(5-(4-((1-(2-fluoro-4-(7-hydroxy-3-(3-methoxyphenyl)-2,2-dimethylchroman-4-yl)phenyl)piperidin-4-yl)methyl)piperazin-1-yl)-1-oxoisindolin-2-yl)piperidine-2,6-dione;
- cis*-(S)-3-(5-(4-((1-(4-(7-hydroxy-3-(3-methoxyphenyl)-2,2-dimethylchroman-4-yl)phenyl)piperidin-4-yl)methyl)piperazin-1-yl)-1-oxoisindolin-2-yl)piperidine-2,6-dione;
- 15 *cis*-(S)-3-(5-(4-((1-(2-fluoro-4-(3-(4-fluoro-3-methylphenyl)-7-hydroxychroman-4-yl)phenyl)piperidin-4-yl)methyl)piperazin-1-yl)-1-oxoisindolin-2-yl)piperidine-2,6-dione;
- cis*-(S)-3-(5-(4-((1-(2-fluoro-4-(3-(4-fluoro-3-methoxyphenyl)-7-hydroxychroman-4-yl)phenyl)piperidin-4-yl)methyl)piperazin-1-yl)-1-oxoisindolin-2-yl)piperidine-2,6-dione;
- cis*-(S)-3-(5-(4-((1-(4-(3-(4-fluoro-3-methylphenyl)-7-hydroxychroman-4-yl)phenyl)piperidin-4-yl)methyl)piperazin-1-yl)-1-oxoisindolin-2-yl)piperidine-2,6-dione;
- 20 *cis*-(S)-3-(5-(4-((1-(4-(3-(4-fluoro-3-methoxyphenyl)-7-hydroxychroman-4-yl)phenyl)piperidin-4-yl)methyl)piperazin-1-yl)-1-oxoisindolin-2-yl)piperidine-2,6-dione;
- cis*-(S)-3-(5-(4-((1-(2-fluoro-4-(3-(4-fluoro-2-methylphenyl)-7-hydroxychroman-4-yl)phenyl)piperidin-4-yl)methyl)piperazin-1-yl)-1-oxoisindolin-2-yl)piperidine-2,6-dione;
- 25 *cis*-(S)-3-(5-(4-((1-(4-(3-(4-fluoro-2-methylphenyl)-7-hydroxychroman-4-yl)phenyl)piperidin-4-yl)methyl)piperazin-1-yl)-1-oxoisindolin-2-yl)piperidine-2,6-dione;
- cis*-(S)-3-(5-(4-((1-(4-((2*R*)-7-hydroxy-3-(3-methoxyphenyl)-2-methylchroman-4-yl)phenyl)piperidin-4-yl)methyl)piperazin-1-yl)-1-oxoisindolin-2-yl)piperidine-2,6-dione;
- cis*-(S)-3-(5-(4-((1-(4-((2*S*)-7-hydroxy-3-(3-methoxyphenyl)-2-methylchroman-4-yl)phenyl)piperidin-4-yl)methyl)piperazin-1-yl)-1-oxoisindolin-2-yl)piperidine-2,6-dione;
- 30 *cis*-3-(5-(3-(((1-(4-(7-hydroxy-3-(3-methoxyphenyl)chroman-4-yl)phenyl)piperidin-4-yl)methyl)(methyl)amino)prop-1-yn-1-yl)-1-oxoisindolin-2-yl)piperidine-2,6-dione;
- cis*-3-(5-(3-(((1-(2-fluoro-4-(7-hydroxy-3-(3-methoxyphenyl)chroman-4-yl)phenyl)piperidin-4-yl)methyl)(methyl)amino)prop-1-yn-1-yl)-1-oxoisindolin-2-yl)piperidine-2,6-dione;
- 35 *cis*-3-(5-(3-(((1-(2-fluoro-4-(7-hydroxy-3-(*m*-tolyl)chroman-4-yl)phenyl)piperidin-4-yl)methyl)(methyl)amino)prop-1-yn-1-yl)-1-oxoisindolin-2-yl)piperidine-2,6-dione;
- cis*-3-(5-(3-(((1-(4-(7-hydroxy-3-(*m*-tolyl)chroman-4-yl)phenyl)piperidin-4-yl)methyl)(methyl)amino)prop-1-yn-1-yl)-1-oxoisindolin-2-yl)piperidine-2,6-dione;

- cis*-(S)-3-(6-fluoro-5-(4-((1-(2-fluoro-4-(7-hydroxy-3-(3-methoxyphenyl)chroman-4-yl)phenyl)piperidin-4-yl)methyl)piperazin-1-yl)-1-oxoisindolin-2-yl)piperidine-2,6-dione;
- cis*-2-(2,6-dioxopiperidin-3-yl)-5-fluoro-6-(4-((1-(2-fluoro-4-(7-hydroxy-3-(3-methoxyphenyl)chroman-4-yl)phenyl)piperidin-4-yl)methyl)piperazin-1-yl)isoindoline-1,3-dione;
- 5 *cis*-(S)-3-(6-fluoro-5-(4-((1-(4-(7-hydroxy-3-(3-methoxyphenyl)chroman-4-yl)phenyl)piperidin-4-yl)methyl)piperazin-1-yl)-1-oxoisindolin-2-yl)piperidine-2,6-dione;
- cis*-2-(2,6-dioxopiperidin-3-yl)-5-fluoro-6-(4-((1-(4-(7-hydroxy-3-(3-methoxyphenyl)chroman-4-yl)phenyl)piperidin-4-yl)methyl)piperazin-1-yl)isoindoline-1,3-dione;
- 10 *cis*-(S)-3-(6-fluoro-5-(4-((1-(2-fluoro-4-(3-(4-fluoro-3-methylphenyl)-7-hydroxychroman-4-yl)phenyl)piperidin-4-yl)methyl)piperazin-1-yl)-1-oxoisindolin-2-yl)piperidine-2,6-dione;
- cis*-(S)-3-(6-fluoro-5-(4-((1-(4-(3-(4-fluoro-3-methylphenyl)-7-hydroxychroman-4-yl)phenyl)piperidin-4-yl)methyl)piperazin-1-yl)-1-oxoisindolin-2-yl)piperidine-2,6-dione;
- cis*-(S)-3-(6-fluoro-5-(4-((1-(2-fluoro-4-(7-hydroxy-3-(*m*-tolyl)chroman-4-yl)phenyl)piperidin-4-yl)methyl)piperazin-1-yl)-1-oxoisindolin-2-yl)piperidine-2,6-dione;
- 15 *cis*-(S)-3-(6-fluoro-5-(4-((1-(4-(7-hydroxy-3-(*m*-tolyl)chroman-4-yl)phenyl)piperidin-4-yl)methyl)piperazin-1-yl)-1-oxoisindolin-2-yl)piperidine-2,6-dione;
- cis*-(S)-3-(6-fluoro-5-(4-((1-(2-fluoro-4-(3-(4-fluoro-3-methoxyphenyl)-7-hydroxychroman-4-yl)phenyl)piperidin-4-yl)methyl)piperazin-1-yl)-1-oxoisindolin-2-yl)piperidine-2,6-dione;
- cis*-(S)-3-(5-(4-((1-(2,6-difluoro-4-(7-hydroxy-3-(*m*-tolyl)chroman-4-yl)phenyl)piperidin-4-yl)methyl)piperazin-1-yl)-1-oxoisindolin-2-yl)piperidine-2,6-dione;
- 20 *cis*-(S)-3-(5-(4-((1-(2-fluoro-4-(7-methoxy-3-phenylchroman-4-yl)phenyl)piperidin-4-yl)methyl)piperazin-1-yl)-1-oxoisindolin-2-yl)piperidine-2,6-dione;
- cis*-2-(2,6-dioxopiperidin-3-yl)-5-(4-((1-(2-fluoro-4-(7-methoxy-3-phenylchroman-4-yl)phenyl)piperidin-4-yl)methyl)piperazin-1-yl)isoindoline-1,3-dione;
- 25 *cis*-(S)-3-(5-(4-((1-(4-(3-(3,4-difluorophenyl)-7-hydroxychroman-4-yl)-2-fluorophenyl)piperidin-4-yl)methyl)piperazin-1-yl)-1-oxoisindolin-2-yl)piperidine-2,6-dione;
- cis*-(S)-3-(5-(4-((1-(2-fluoro-4-(7-hydroxy-3-phenylchroman-4-yl)phenyl)piperidin-4-yl)methyl)piperazin-1-yl)-1-oxoisindolin-2-yl)piperidine-2,6-dione;
- (S)-3-(5-(4-((1-(2-fluoro-4-((3*S*,4*R*)-7-hydroxy-3-phenylchroman-4-yl)phenyl)piperidin-4-yl)methyl)piperazin-1-yl)-1-oxoisindolin-2-yl)piperidine-2,6-dione;
- 30 *cis*-2-(2,6-dioxopiperidin-3-yl)-5-(4-((1-(2-fluoro-4-(7-hydroxy-3-phenylchroman-4-yl)phenyl)piperidin-4-yl)methyl)piperazin-1-yl)isoindoline-1,3-dione;
- cis*-(S)-3-(5-(4-((1-(2,6-difluoro-4-(7-hydroxy-3-(3-methoxyphenyl)chroman-4-yl)phenyl)piperidin-4-yl)methyl)piperazin-1-yl)-1-oxoisindolin-2-yl)piperidine-2,6-dione;
- 35 *cis*-(S)-3-(5-(4-((1-(4-(7-hydroxy-3-(4-methoxyphenyl)chroman-4-yl)phenyl)piperidin-4-yl)methyl)piperazin-1-yl)-1-oxoisindolin-2-yl)piperidine-2,6-dione; and
- cis*-(S)-3-(6-fluoro-5-(4-((1-(4-(7-hydroxy-3-(4-methoxyphenyl)chroman-4-yl)phenyl)piperidin-4-yl)methyl)piperazin-1-yl)-1-oxoisindolin-2-yl)piperidine-2,6-dione.

17. A pharmaceutical composition comprising a therapeutically effective amount of the compound according to claim 1 or claim 16 and at least one additional component selected from pharmaceutically acceptable carriers, pharmaceutically acceptable vehicles, and pharmaceutically acceptable excipients.

18. Use of the compound according to claim 1 or of the pharmaceutical composition according to claim 17, in the manufacture of a medicament for the treatment of cancer in a subject wherein the cancer is selected from breast cancer, lung cancer, ovarian cancer, endometrial cancer, prostate cancer, and esophageal cancer.

19. The use according to claim 18, wherein the cancer is positive for ER α .

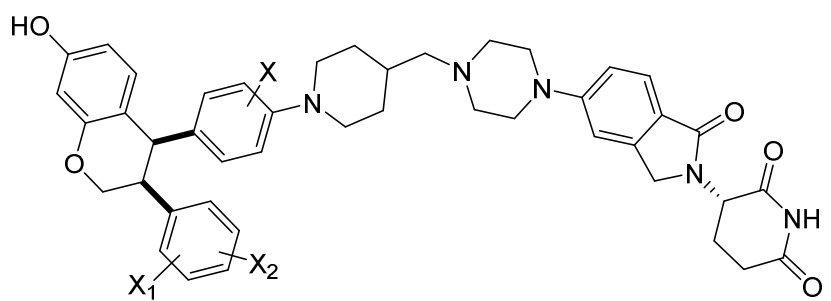
20. The use according to claim 18, wherein the subject has been previously treated with an anti-cancer agent.

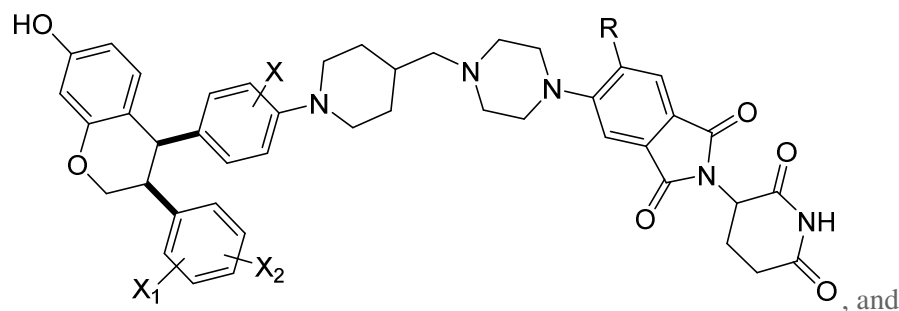
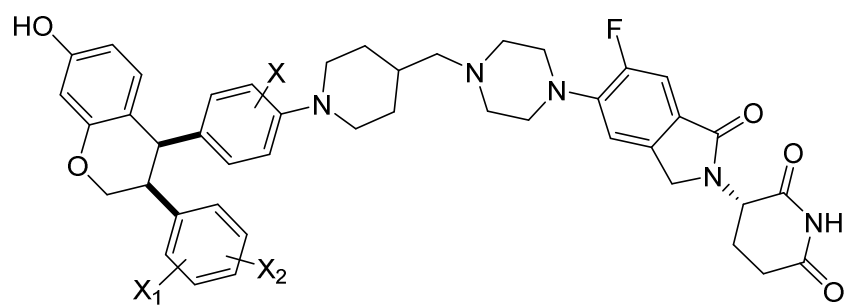
21. The use according to claim 20, wherein the anti-cancer agent is selected from tamoxifen or fulvestrant.

22. Use of the compound according to claim 1 or claim 16, in the manufacture of a medicament for the treatment of a disease or condition in a subject wherein the disease or condition is selected from breast cancer, lung cancer, ovarian cancer, endometrial cancer, prostate cancer, esophageal cancer, infertility, ovulatory dysfunction, postmenopausal osteoporosis, estrogen-related gynecomastia, dyspareunia due to menopause, retroperitoneal fibrosis, and idiopathic sclerosing mesenteritis.

23. The compound according to claim 1 or claim 16, for use in therapy.

24. A process for the preparation of a compound chosen from the following chemical structures:





stereoisomers, and pharmaceutically acceptable salts thereof,

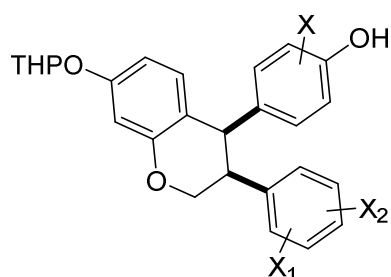
wherein:

5 X is chosen from H and F,

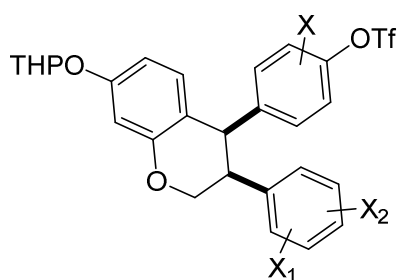
X₁ and X₂ are independently chosen from H, F, OCH₃, CH₃, and CF₃,

R is chosen from H and F,

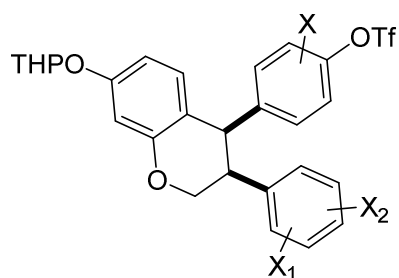
comprising the steps of:



a) reacting _____ with Tf₂O and an organic base in an organic solvent to

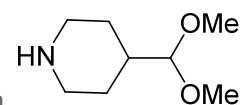


10 obtain intermediate _____;

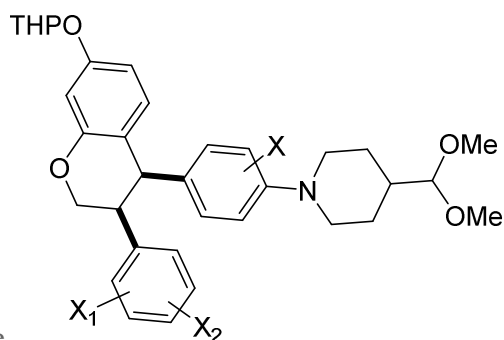


b) mixing the intermediate

from step a) with

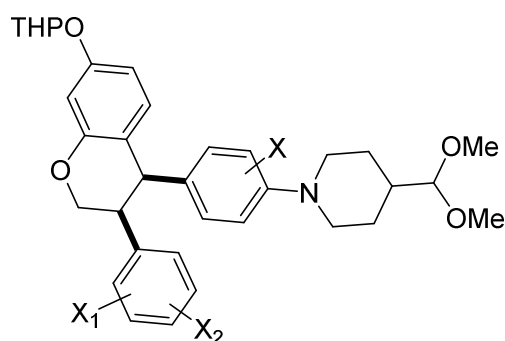


presence of a palladium catalyst, 2,2'-bis(diphenylphosphino)-1,1'-binaphthyl (BINAP) and a base in an



organic solvent to obtain intermediate

;

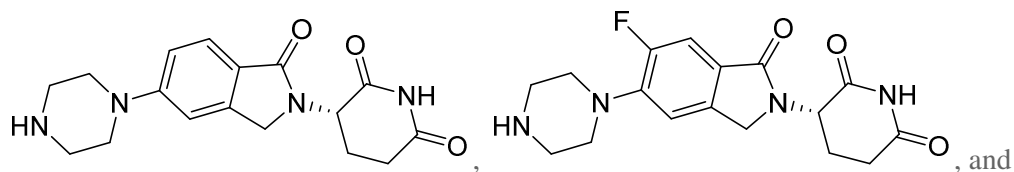


c) deprotecting the intermediate

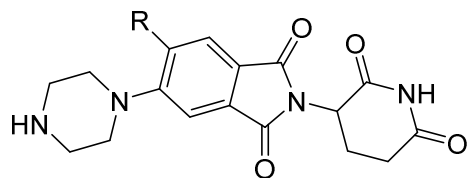
from step b) with an acid to

5 obtain an aldehyde product; and

d) reductive amination of the aldehyde product with an intermediate chosen from,



, and



in the presence of a reducing agent.

10 25. The process according to claim 24, wherein the organic base used in step a) is N,N-diisopropylethylamine (DIEA).

26. The process according to claim 24, wherein the palladium catalyst used in step b) is $\text{Pd}(\text{OAc})_2$.

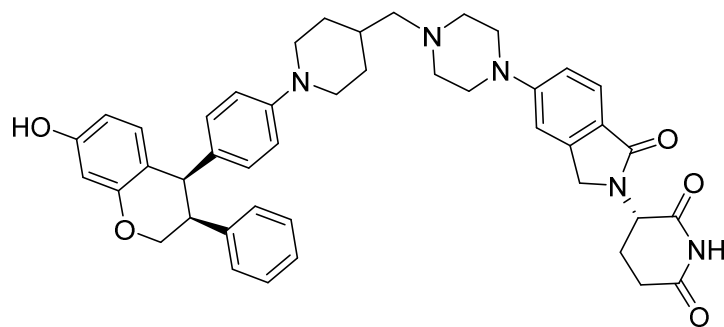
15

27. The process according to claim 24, wherein the acid used in step c) is a sulfuric acid.

28. The process according to claim 24, wherein the reducing agent used in step d) is $\text{NaBH}(\text{AcO})_3$.

5

29. The process according to claim 24, wherein the compound is

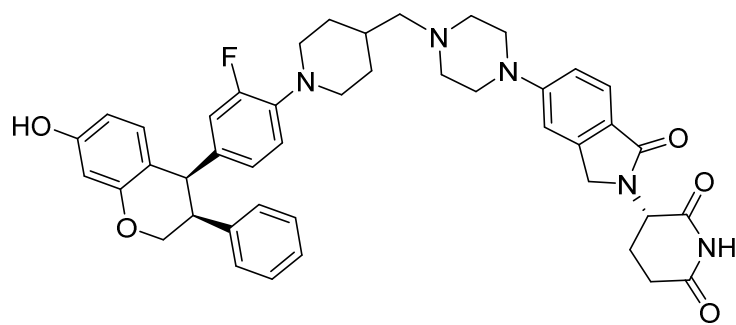


, or a pharmaceutically acceptable salt

thereof.

10

30. The process according to claim 24, wherein the compound is

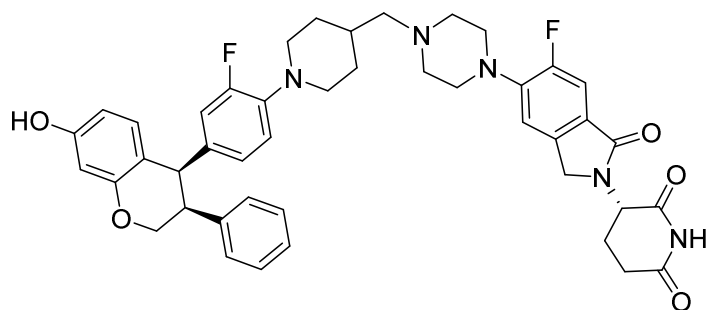


, or a pharmaceutically acceptable salt

thereof.

15

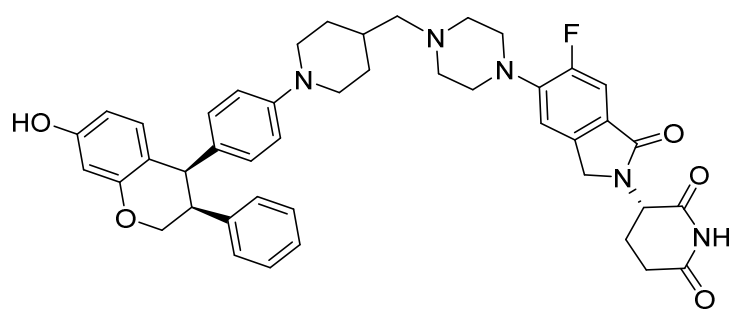
31. The process according to claim 24, wherein the compound is



, or a pharmaceutically acceptable salt

thereof.

32. The process according to claim 24, wherein the compound is



or a pharmaceutically acceptable salt thereof.