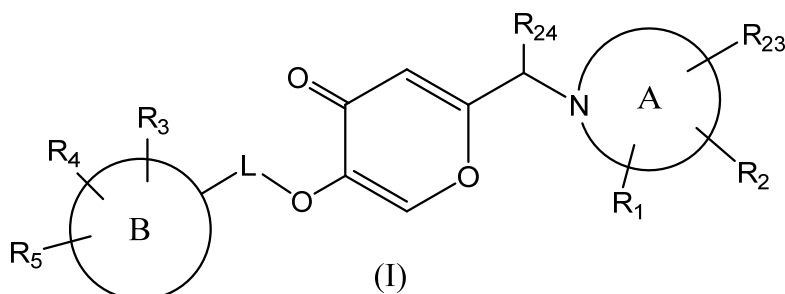


Claims

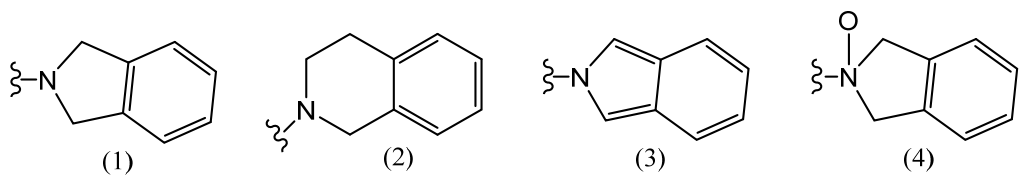
1. A compound of formula (I)



5 wherein

ring B is a 4-10 membered monocyclic or bicyclic ring containing 0-4 hetero-atoms independently selected from N, O or S

ring A is any of the following groups



10 L is absent, -CH₂-, -CH₂-CH₂- or -CH₂-CH₂-CH₂-, or in case ring A is (1), L can also be -C(O)-CH₂-;

R₁ is hydrogen, C₁₋₇ alkyl, C₁₋₇ alkoxy, halogen, cyano, nitro, halo C₁₋₇ alkyl, halo C₁₋₇ alkoxy or C₁₋₇ alkylthio;

15 R₂ is hydrogen, C₁₋₇ alkyl, halogen, hydroxy, halo C₁₋₇ alkyl, nitro, halo C₁₋₇ alkoxy or thiol;

or R₁ and R₂ together with the carbon atoms to which they are attached form a fused 1,3 dioxole ring;

R₃ is hydrogen, halogen, nitro, cyano, oxo, C₁₋₇ alkyl, C₂₋₇ alkenyl, C₃₋₇ cycloalkyl, hydroxy C₃₋₇ cycloalkyl, C₁₋₇ alkoxy, hydroxy C₁₋₇ alkyl, halo C₁₋₇ alkyl, cyano
20 C₁₋₇ alkyl, C₁₋₇ alkoxy C₁₋₇ alkyl, C₁₋₇ alkylthio, aminocarbonyl C₂₋₇ alkenyl, halo C₁₋₇ alkylthio, C₁₋₇ alkoxycarbonyl C₁₋₇ alkyl, C₁₋₇ alkoxycarbonyl C₂₋₇ alkenyl,
=NSO₂R₂₀, -S(O)-C₁₋₇ alkyl, -S(O)(NR₁₄)(R₂₂), -S(NR₁₅)(C₁₋₇ alkyl), -C(S)NR₁₈R₁₉, -
D-C(O)-NR₆R₇,

-C(O)R₈, -D-NR₉R₁₀, -SO₂R₁₁, optionally substituted 3-10 membered carbocyclyl,
25 optionally substituted 3-10 membered carbocyclyl C₁₋₇ alkyl, optionally substituted

4-10 membered heterocyclyl or optionally substituted 4-10 membered heterocyclyl
C₁₋₇ alkyl;

R₄ is hydrogen, halogen, hydroxy, C₁₋₇ alkyl, halo C₁₋₇ alkyl or oxo;

R₅ is hydrogen, halogen or C₁₋₇ alkyl;

5 R₆ is hydrogen, C₁₋₇ alkyl, C₂₋₇ alkenyl, C₃₋₇ cycloalkyl, hydroxy C₁₋₇ alkyl,
cyano C₁₋₇ alkyl, -C₁₋₇ alkyl-O-C(O)C₁₋₇ alkyl or optionally substituted 4-10
membered heterocyclyl;

R₈ is hydrogen, C₁₋₇ alkyl, C₂₋₇ alkenyl, C₃₋₇ cycloalkyl, C₁₋₇ alkoxy, halo C₁₋₇
alkyl, C₁₋₇ alkoxy C₁₋₇ alkyl, C₁₋₇ alkylcarbonyl, C₁₋₇ alkoxycarbonyl, -C₁₋₇ alkyl-O-
10 C(O)-C₁₋₇ alkyl, -C₁₋₇ alkyl-SO₂(C₁₋₇ alkyl), -N=S(O)(C₁₋₇ alkyl)(C₁₋₇ alkyl) or
optionally substituted 4-10 membered heterocyclyl;

R₉ is hydrogen, C₁₋₇ alkyl, C₃₋₇ cycloalkyl, C₁₋₇ alkylcarbonyl, -SO₂(C₁₋₇ alkyl)
or -SO₂(C₃₋₇ cycloalkyl);

R₁₁ is C₁₋₇ alkyl, C₂₋₇ alkenyl, C₃₋₇ cycloalkyl, halo C₁₋₇ alkyl, cyano C₁₋₇ alkyl,
15 C₁₋₇ alkoxy C₁₋₇ alkyl, -NR₁₂R₁₃, optionally substituted 3-10 membered carbocyclyl
or optionally substituted 4-10 membered heterocyclyl;

R₁₂ is hydrogen, C₁₋₇ alkyl, hydroxy C₁₋₇ alkyl, cyano C₁₋₇ alkyl, C₁₋₇ alkoxy,
C₁₋₇ alkoxy C₁₋₇ alkyl or C₁₋₇ alkylcarbonyl;

R₇, R₁₀, R₁₃, R₁₈, and R₁₉ are, independently, hydrogen, C₁₋₇ alkyl or C₃₋₇
20 cycloalkyl;

R₁₄ is hydrogen, C₁₋₇ alkyl, C₁₋₇ alkylcarbonyl or -SO₂R₂₁;

R₁₅ is hydrogen, C₁₋₇ alkyl, C₃₋₇ cycloalkyl, C₁₋₇ alkylcarbonyl, -SO₂R₁₇;

R₁₇ is C₁₋₇ alkyl or an optionally substituted 3-10 membered carbocyclyl;

R₂₀ and R₂₁ are, independently, C₁₋₇ alkyl, C₃₋₇ cycloalkyl or optionally
25 substituted 3-10 membered carbocyclyl;

R₂₂ is C₁₋₇ alkyl or C₃₋₇ cycloalkyl;

R₂₃ is hydrogen or oxo;

R₂₄ is hydrogen or C₁₋₇ alkyl;

D is absent, C₁₋₇ alkyl or C₂₋₇ alkenyl;

30 wherein the optional substitution in each occurrence is selected from 1-3
substituents independently selected from C₁₋₇ alkyl, halogen, hydroxy, C₁₋₇ alkoxy,
C₁₋₇ alkoxy C₁₋₇ alkyl, C₁₋₇ alkoxycarbonyl or oxo; and

wherein the heterocyclyl group in each occurrence has 1-4 heteroatoms independently selected from N, O and S;

or a pharmaceutically acceptable salt thereof;

with the proviso that the compound is not

- 5 2-[(3,4-Dihydro-2(1*H*)-isoquinolinyl)methyl]-5-[(2,5-dimethylphenyl) methoxy]-4*H*-pyran-4-one;
- 5-[(2,4-Dichlorophenyl)methoxy]-2-[(3,4-dihydro-2(1*H*)-isoquinolinyl) methyl]-4*H*-pyran-4-one;
- 5-[(3-Chlorophenyl)methoxy]-2-[(3,4-dihydro-2(1*H*)-isoquinolinyl)methyl]-
10 4*H*-pyran-4-one;
- 2-[(3,4-Dihydro-2(1*H*)-isoquinolinyl)methyl]-5-[(4-methylphenyl)methoxy]-
4*H*-pyran-4-one;
- 5-[(3,4-Dichlorophenyl)methoxy]-2-[(3,4-dihydro-2(1*H*)-isoquinolinyl) methyl]-4*H*-pyran-4-one;
- 15 2-[(3,4-Dihydro-2(1*H*)-isoquinolinyl)methyl]-5-[(3-fluorophenyl)methoxy]-
4*H*-pyran-4-one;
- 2-[(3,4-Dihydro-2(1*H*)-isoquinolinyl)methyl]-5-(1-naphthalenylmethoxy)-
4*H*-pyran-4-one;
- 2-[(3,4-Dihydro-2(1*H*)-isoquinolinyl)methyl]-5-[[3-(trifluoromethyl)phenyl]
20 methoxy]-4*H*-pyran-4-one;
- 5-[(2-Chlorophenyl)methoxy]-2-[(3,4-dihydro-2(1*H*)-isoquinolinyl)methyl]-
4*H*-pyran-4-one;
- 5-[(2-Chloro-6-fluorophenyl)methoxy]-2-[(3,4-dihydro-2(1*H*)-isoquinolinyl) methyl]-4*H*-pyran-4-one;
- 25 5-[(4-Chlorophenyl)methoxy]-2-[(3,4-dihydro-2(1*H*)-isoquinolinyl)methyl]-
4*H*-pyran-4-one;
- 5-[(4-Bromophenyl)methoxy]-2-[(3,4-dihydro-2(1*H*)-isoquinolinyl)methyl]-
4*H*-pyran-4-one;
- 2-[(3,4-Dihydro-2(1*H*)-isoquinolinyl)methyl]-5-[(2-fluorophenyl)methoxy]-
30 4*H*-pyran-4-one;
- 2-[(3,4-Dihydro-2(1*H*)-isoquinolinyl)methyl]-5-[(2-methylphenyl)methoxy]-
4*H*-pyran-4-one;

2-[(3,4-Dihydro-2(1*H*)-isoquinolinyl)methyl]-5-(phenylmethoxy)-4*H*-pyran-4-one;

2-[(3,4-Dihydro-2(1*H*)-isoquinolinyl)methyl]-5-[[4-(trifluoromethyl)phenyl]methoxy]-4*H*-pyran-4-one;

5 Methyl 4-(((6-((3,4-dihydroisoquinolin-2(1*H*)-yl)methyl)-4-oxo-4*H*-pyran-3-yl)oxy)methyl)benzoate;

2-[(3,4-Dihydro-2(1*H*)-isoquinolinyl)methyl]-5-[(4-fluorophenyl)methoxy]-4*H*-pyran-4-one;

10 2-[(3,4-Dihydro-2(1*H*)-isoquinolinyl)methyl]-5-[(3,5-dimethoxyphenyl)methoxy]-4*H*-pyran-4-one;

2-[(3,4-Dihydro-2(1*H*)-isoquinolinyl)methyl]-5-[(3-nitrophenyl)methoxy]-4*H*-pyran-4-one;

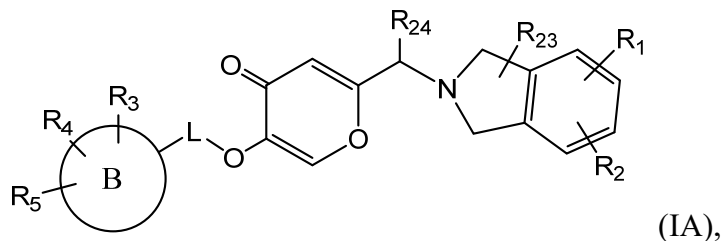
Methyl 5-(((6-((3,4-dihydroisoquinolin-2(1*H*)-yl)methyl)-4-oxo-4*H*-pyran-3-yl)oxy)methyl)furan-2-carboxylate;

15 2-[(3,4-Dihydro-2(1*H*)-isoquinolinyl)methyl]-5-(2-phenylethoxy)-4*H*-pyran-4-one;

2-[(3,4-Dihydro-2(1*H*)-isoquinolinyl)methyl]-5-[(3-methylphenyl)methoxy]-4*H*-pyran-4-one; or

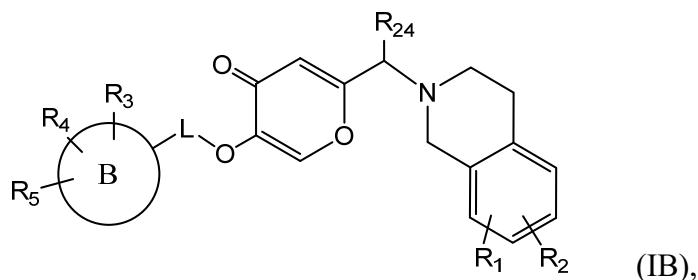
20 2-[(3,4-Dihydro-2(1*H*)-isoquinolinyl)methyl]-5-[(4-nitrophenyl)methoxy]-4*H*-pyran-4-one.

2. A compound according to claim 1, wherein the compound is represented by formula (IA):



25 wherein R₁, R₂, R₃, R₄, R₅, R₂₃, R₂₄, L and B are as defined in claim 1, or a pharmaceutically acceptable salt thereof.

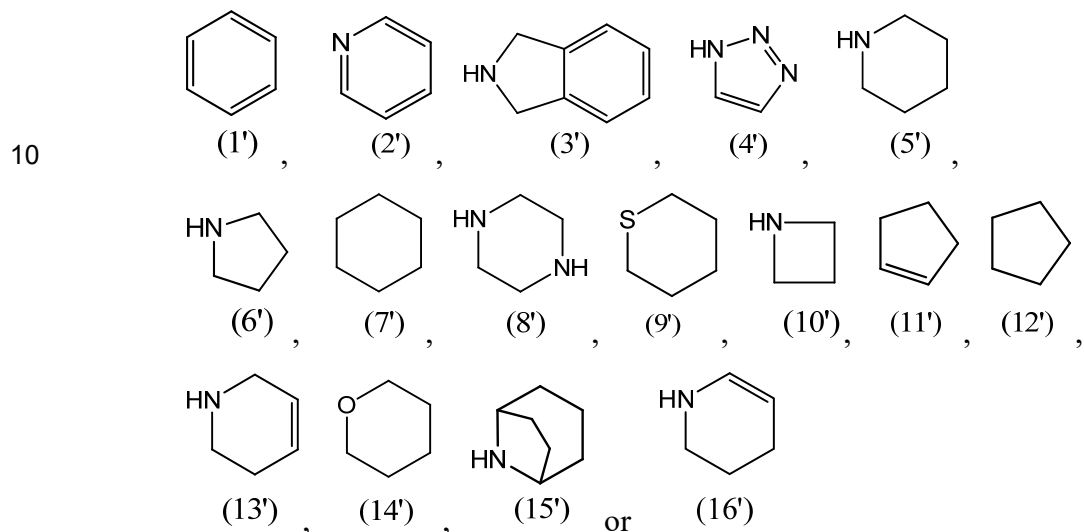
3. A compound according to claim 1, wherein the compound is represented by formula (IB):



wherein R_1 , R_2 , R_3 , R_4 , R_5 , R_{24} , L and B are as defined in claim 1, or a pharmaceutically acceptable salt thereof.

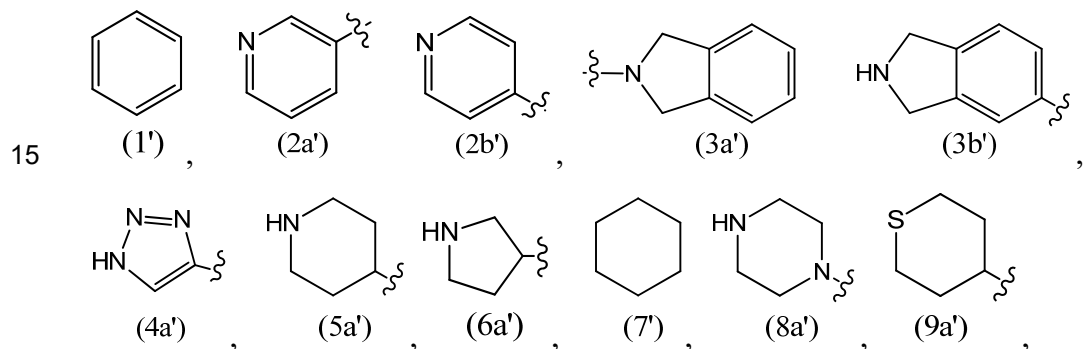
5 4. A compound according to any of claims 1 to 3, wherein L is $-\text{CH}_2-$ or $-\text{CH}_2\text{-CH}_2-$.

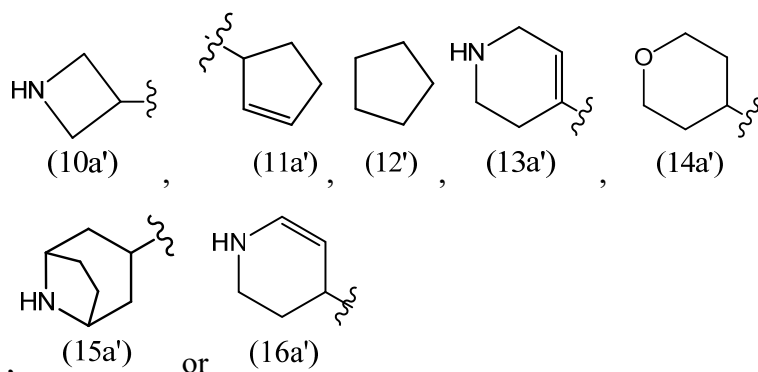
5. A compound according to any of the preceding claims, wherein ring B is any one of the following groups



R_3 , R_4 and R_5 being attached to the above B -rings, optionally wherein ring B is:

a) any one of the following groups





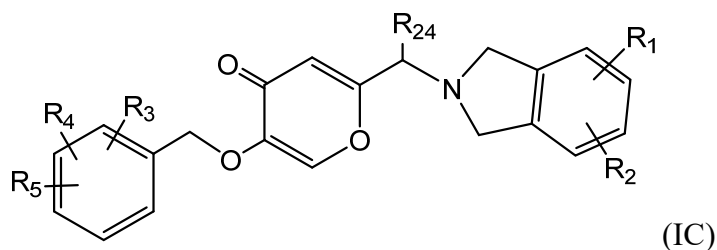
R₃, R₄ and R₅ being attached to the above B-rings and the wavy line denoting the site of attachment to L;

- 5 b) (1'), (5'), (7'), (9'), (13') or (14'); or
 c) (1'), (5a'), (7'), (9a'), (13a') or (14a').

6. A compound according to any of the preceding claims, wherein

- 10 a) R₃ is hydrogen, C₁₋₇ alkyl, C₂₋₇ alkenyl, hydroxy C₁₋₇ alkyl, cyano, C₁₋₇ alkylthio, C₁₋₇ alkoxy carbonyl C₂₋₇ alkenyl, -D-C(O)-NR₆R₇, -C(O)R₈, -SO₂R₁₁, -D-NR₉R₁₀, -S(O)(NR₁₄)(R₂₂), -S(NR₁₅)(C₁₋₇ alkyl), -C(S)NR₁₈R₁₉, an optionally substituted 3-10 membered carbocyclyl, an optionally substituted 4-10 membered heterocyclyl, or an optionally substituted 4-10 membered heterocyclyl C₁₋₇ alkyl; wherein the optional substitution in each occurrence is selected from 1-3 substituents
- 15 independently selected from C₁₋₇ alkyl, halogen, hydroxy, C₁₋₇ alkoxy, C₁₋₇ alkoxy C₁₋₇ alkyl, C₁₋₇ alkoxy carbonyl or oxo, and wherein the heterocyclyl group in each occurrence has 1-3 heteroatoms independently selected from N, O and S and/or
- b) R₄ and R₅ are hydrogen.

- 20 7. A compound according to claim 1 or 2, wherein the compound is represented by formula (IC):



wherein R₁, R₂, R₃, R₄, R₅ and R₂₄ are as defined in claim 1, or a pharmaceutically acceptable salt thereof, optionally wherein

- i) R₁ is hydrogen, C₁₋₇ alkoxy, halogen, nitro, halo C₁₋₇ alkyl, halo C₁₋₇ alkoxy or C₁₋₇ alkylthio;
 R₂ is hydrogen or halogen;
 R₃ is C₂₋₇ alkenyl, hydroxy C₁₋₇ alkyl, cyano, C₁₋₇ alkoxycarbonyl C₂₋₇ alkenyl,
 5 -D-C(O)-NR₆R₇, -C(O)R₈, -SO₂R₁₁, -D-NR₉R₁₀, -S(O)(NR₁₄)(R₂₂), -S(NR₁₅)(C₁₋₇ alkyl), a 3-6 membered carbocyclyl which is optionally substituted with 1-2 hydroxyl substituents, or a 4-6 membered heterocyclyl which is optionally substituted with 1-2 substituents selected from halogen or hydroxyl;
 R₄ is hydrogen, hydroxy or halogen;
 10 R₅ is hydrogen or halogen;
 R₆ is C₁₋₇ alkyl, hydroxy C₁₋₇ alkyl or -C₁₋₇ alkyl-O-C(O)C₁₋₇ alkyl;
 R₇ is hydrogen or C₁₋₇ alkyl;
 R₈ is C₁₋₇ alkyl, halo C₁₋₇ alkyl, -N=S(O)(C₁₋₇ alkyl)(C₁₋₇ alkyl) or a 4-6 membered heterocyclyl which is optionally substituted with 1-2 halogen substituents;
 15 R₉ is C₁₋₇ alkylcarbonyl or -SO₂(C₁₋₇ alkyl);
 R₁₀ is hydrogen or C₁₋₇ alkyl;
 R₁₁ is C₁₋₇ alkyl, C₃₋₇ cycloalkyl, halo C₁₋₇ alkyl, C₁₋₇ alkoxy C₁₋₇ alkyl, -NR₁₂R₁₃ or a 4-6 membered heterocyclyl;
 R₁₂ is C₁₋₇ alkyl, hydroxy C₁₋₇ alkyl, cyano C₁₋₇ alkyl, C₁₋₇ alkoxy C₁₋₇ alkyl or
 20 C₁₋₇ alkylcarbonyl;
 R₁₃ is hydrogen or C₁₋₇ alkyl;
 R₁₄ is hydrogen, C₁₋₇ alkyl or C₁₋₇ alkylcarbonyl;
 R₁₅ is hydrogen or -SO₂R₁₇;
 R₁₇ is a 3-6 membered carbocyclyl which is optionally substituted by 1-2
 25 C₁₋₇ alkyl substituents;
 R₂₂ is C₁₋₇ alkyl or C₃₋₇ cycloalkyl;
 R₂₄ is hydrogen or C₁₋₇ alkyl;
 D is absent, C₁₋₇ alkyl or C₂₋₇ alkenyl;
 wherein the heterocyclyl group in each occurrence has 1-3 heteroatoms
 30 independently selected from N, O and S; or
 ii) R₁ is hydrogen, C₁₋₇ alkoxy, halogen, nitro, halo C₁₋₇ alkyl or halo C₁₋₇ alkoxy;
 R₂ and R₁₀ are hydrogen;

- R₃ is C₂₋₇ alkenyl, hydroxy C₁₋₇ alkyl, cyano, C₁₋₇ alkoxy carbonyl C₂₋₇ alkenyl, -D-C(O)-NR₆R₇, -C(O)R₈, -SO₂R₁₁, -D-NR₉R₁₀, -S(O)(NR₁₄)(R₂₂), -S(NR₁₅)(C₁₋₇ alkyl), oxazolyl, cyclobutyl optionally substituted with a hydroxy substituent, or oxetanyl optionally substituted with a hydroxy substituent;
- 5 R₄ and R₅ are hydrogen or halogen;
 R₆ is C₁₋₇ alkyl or hydroxy C₁₋₇ alkyl;
 R₇, R₁₃, R₁₄ and R₂₄ are hydrogen or C₁₋₇ alkyl;
 R₈ is C₁₋₇ alkyl, pyrrolidinyl, oxetanyl, or azetidinyll optionally substituted with 1-2 halogen substituents, -N=S(O)(C₁₋₇ alkyl)(C₁₋₇ alkyl);
- 10 R₉ is -SO₂(C₁₋₇ alkyl);
 R₁₁ is C₁₋₇ alkyl, C₃₋₇ cycloalkyl, halo C₁₋₇ alkyl, C₁₋₇ alkoxy C₁₋₇ alkyl, -NR₁₂R₁₃, pyrrolidinyl, piperidinyl, azetidinyll or morpholinyl;
 R₁₂ is C₁₋₇ alkyl, hydroxy C₁₋₇ alkyl, cyano C₁₋₇ alkyl, C₁₋₇ alkoxy C₁₋₇ alkyl or C₁₋₇ alkyl carbonyl;
- 15 R₁₅ is hydrogen or -SO₂R₁₇;
 R₁₇ is phenyl optionally substituted by a C₁₋₇ alkyl substituent;
 R₂₂ is C₁₋₇ alkyl or C₃₋₇ cycloalkyl;
 D is absent, C₁₋₇ alkyl or C₂₋₇ alkenyl; or
 iii) R₁ is hydrogen, C₁₋₇ alkoxy, halogen, halo C₁₋₇ alkyl or halo C₁₋₇ alkoxy;
- 20 R₂ and R₁₀ are hydrogen;
 R₃ is hydroxy C₁₋₇ alkyl, cyano, C₁₋₇ alkoxy carbonyl C₂₋₇ alkenyl, -D-C(O)-NR₆R₇, -C(O)R₈, -SO₂R₁₁, -D-NR₉R₁₀, -S(O)(NR₁₄)(R₂₂), -S(NR₁₅)(C₁₋₇ alkyl), oxazolyl, cyclobutyl optionally substituted with a hydroxy substituent, or oxetanyl optionally substituted with a hydroxy substituent;
- 25 R₄ and R₅ are hydrogen or halogen;
 R₆ is C₁₋₇ alkyl;
 R₇, R₁₃, R₁₄ and R₂₄ are hydrogen or C₁₋₇ alkyl;
 R₈ is pyrrolidinyl, azetidinyll or -N=S(O)(C₁₋₇ alkyl)(C₁₋₇ alkyl);
- 30 R₉ is -SO₂(C₁₋₇ alkyl);
 R₁₁ is C₁₋₇ alkyl, halo C₁₋₇ alkyl, -NR₁₂R₁₃ or pyrrolidinyl;
 R₁₂ is C₁₋₇ alkyl, hydroxy C₁₋₇ alkyl, cyano C₁₋₇ alkyl, C₁₋₇ alkoxy C₁₋₇ alkyl or C₁₋₇ alkyl carbonyl;

R₁₅ is -SO₂R₁₇;

R₁₇ is phenyl optionally substituted by a C₁₋₇ alkyl substituent;

R₂₂ is C₁₋₇ alkyl or C₃₋₇ cycloalkyl;

D is absent, C₁₋₇ alkyl or C₂₋₇ alkenyl; or

5 iv) R₁ is hydrogen, halogen, halo C₁₋₇ alkyl or halo C₁₋₇ alkoxy;

R₂, R₄, R₅ and R₁₀ are hydrogen;

R₃ is hydroxy C₁₋₇ alkyl, -D-C(O)-NR₆R₇, -C(O)R₈, -SO₂R₁₁, -D-NR₉R₁₀,
-S(O)(NR₁₄)(R₂₂) or oxetanyl optionally substituted with a hydroxy substituent;

R₆ and R₇ is C₁₋₇ alkyl;

10 R₈ is pyrrolidinyl, or -N=S(O)(C₁₋₇ alkyl)(C₁₋₇ alkyl);

R₉ is -SO₂(C₁₋₇ alkyl);

R₁₁ is C₁₋₇ alkyl, -NR₁₂R₁₃ or pyrrolidinyl;

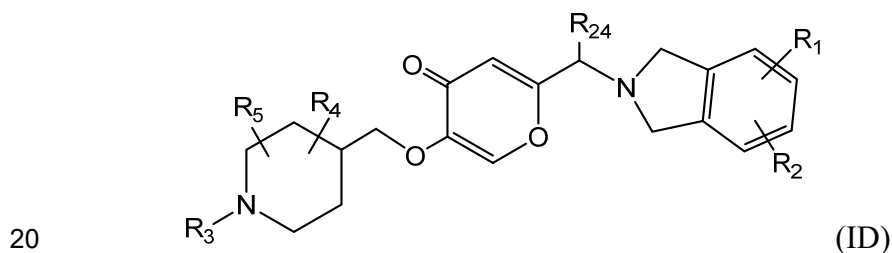
R₁₂ is C₁₋₇ alkyl, hydroxy C₁₋₇ alkyl, or C₁₋₇ alkoxy C₁₋₇ alkyl;

R₁₃ and R₁₄ is hydrogen or C₁₋₇ alkyl;

15 R₂₂ is C₁₋₇ alkyl or C₃₋₇ cycloalkyl;

D is C₁₋₇ alkyl or C₂₋₇ alkenyl.

8. A compound according to claim 1 or 2, wherein the compound is represented by formula (ID):



wherein R₁, R₂, R₃, R₄, R₅ and R₂₄ are as defined in claim 1, or a pharmaceutically acceptable salt thereof, optionally wherein

25 i) R₁ is hydrogen, C₁₋₇ alkyl, cyano, halogen, nitro, halo C₁₋₇ alkyl, halo C₁₋₇ alkoxy or C₁₋₇ alkylthio;

R₂ is hydrogen or halogen;

R₃ is -D-C(O)-NR₆R₇, -C(O)R₈, -SO₂R₁₁, or -C(S)NR₁₈R₁₉;

R₄ is hydrogen, C₁₋₇ alkyl, hydroxy or halogen;

R₅ is hydrogen;

R₆ is C₁₋₇ alkyl or C₃₋₇ cycloalkyl;

R₇ and R₂₄ are hydrogen or C₁₋₇ alkyl;

R₈ is hydrogen, C₁₋₇ alkyl, C₂₋₇ alkenyl, C₃₋₇ cycloalkyl, halo C₁₋₇ alkyl, C₁₋₇ alkylcarbonyl, C₁₋₇ alkoxy carbonyl, C₁₋₇ alkoxy C₁₋₇ alkyl, -C₁₋₇ alkyl-O-C(O)-C₁₋₇ alkyl, -C₁₋₇ alkyl-SO₂(C₁₋₇ alkyl) or a 4-10 membered heterocyclyl;

- 5 R₁₁ is C₁₋₇ alkyl, C₃₋₇ cycloalkyl, halo C₁₋₇ alkyl, cyano C₁₋₇ alkyl, C₁₋₇ alkoxy C₁₋₇ alkyl, -NR₁₂R₁₃, a 3-6 membered carbocyclyl which is optionally substituted with 1-2 halogen substituents, or a 4-6 membered heterocyclyl which is optionally substituted with 1-2 substituents selected from halogen or C₁₋₇ alkyl;

R₁₂ and R₁₃ are C₁₋₇ alkyl;

- 10 R₁₈, and R₁₉ are, independently, hydrogen or C₁₋₇ alkyl;

D is absent;

wherein the heterocyclyl group in each occurrence has 1-3 heteroatoms independently selected from N, O and S; or

ii) R₁ is hydrogen, C₁₋₇ alkyl, halogen, halo C₁₋₇ alkyl or halo C₁₋₇ alkoxy;

- 15 R₂ and R₅ are hydrogen;

R₃ is -D-C(O)-NR₆R₇, -C(O)R₈, -SO₂R₁₁, or -C(S)NR₁₈R₁₉, or oxetanyl optionally substituted by a hydroxy substituent;

R₄ is hydrogen, C₁₋₇ alkyl or halogen;

R₆ is C₁₋₇ alkyl;

- 20 R₇ is hydrogen or C₁₋₇ alkyl;

R₈ is C₁₋₇ alkyl, C₂₋₇ alkenyl, C₃₋₇ cycloalkyl, halo C₁₋₇ alkyl, C₁₋₇ alkylcarbonyl, C₁₋₇ alkoxy carbonyl, C₁₋₇ alkoxy C₁₋₇ alkyl, -C₁₋₇ alkyl-O-C(O)-C₁₋₇ alkyl, -C₁₋₇ alkyl-SO₂(C₁₋₇ alkyl), azetidiny, morpholinyl, furanyl or pyrrolidinyl;

- 25 R₁₁ is C₁₋₇ alkyl, C₃₋₇ cycloalkyl, halo C₁₋₇ alkyl, cyano C₁₋₇ alkyl, C₁₋₇ alkoxy C₁₋₇ alkyl, -NR₁₂R₁₃, pyrrolidinyl, phenyl optionally substituted with a halogen substituent, oxetanyl, or pyrazolyl optionally substituted with a C₁₋₇ alkyl substituent;

R₁₂ and R₁₃ are C₁₋₇ alkyl;

R₁₈, and R₁₉ are, independently, hydrogen or C₁₋₇ alkyl;

R₂₄ is hydrogen or C₁₋₇ alkyl;

- 30 D is absent; or

iii) R₁ is hydrogen, C₁₋₇ alkyl, halogen, halo C₁₋₇ alkyl or halo C₁₋₇ alkoxy;

R₂, R₅ and R₇ are hydrogen;

R₃ is -D-C(O)-NR₆R₇, -C(O)R₈ or -SO₂R₁₁;

R₄ is hydrogen or C₁₋₇ alkyl;

R₆ is C₁₋₇ alkyl;

R₈ is C₁₋₇ alkyl, C₃₋₇ cycloalkyl, halo C₁₋₇ alkyl, C₁₋₇ alkylcarbonyl,
-C₁₋₇ alkyl-O-C(O)-C₁₋₇ alkyl, -C₁₋₇ alkyl-SO₂(C₁₋₇ alkyl), morpholinyl or
5 pyrrolidinyl;

R₁₁ is C₁₋₇ alkyl, C₃₋₇ cycloalkyl, cyano C₁₋₇ alkyl, C₁₋₇ alkoxy C₁₋₇ alkyl,
-NR₁₂R₁₃, oxetanyl, or pyrazolyl optionally substituted with a C₁₋₇ alkyl substituent;

R₁₂ and R₁₃ are C₁₋₇ alkyl;

R₂₄ is hydrogen or C₁₋₇ alkyl;

10 D is absent; or

iv) R₁ is hydrogen, halogen, halo C₁₋₇ alkyl or halo C₁₋₇ alkoxy;

R₂, R₄, R₅ and R₇ are hydrogen;

R₃ is -D-C(O)-NR₆R₇, -C(O)R₈ or -SO₂R₁₁;

R₆, R₁₂ and R₁₃ are C₁₋₇ alkyl;

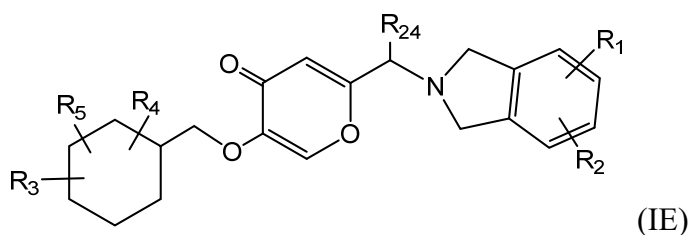
15 R₈ is C₁₋₇ alkyl or halo C₁₋₇ alkyl;

R₁₁ is C₁₋₇ alkyl, C₃₋₇ cycloalkyl, C₁₋₇ alkoxy C₁₋₇ alkyl, -NR₁₂R₁₃ or oxetanyl;

R₂₄ is hydrogen;

D is absent.

20 9. A compound according to claim 1 or 2, wherein the compound is
represented by formula (IE):



wherein R₁, R₂, R₃, R₄, R₅ and R₂₄ are as defined in claim 1, or a
pharmaceutically acceptable salt thereof, optionally wherein

25 i) R₁, R₂, R₄, R₅ and R₂₄ are hydrogen;

R₃ is hydrogen, -D-C(O)-NR₆R₇, -C(O)R₈, -SO₂R₁₁, -D-NR₉R₁₀,
-S(O)(NR₁₄)(R₂₂), a 4-6 membered heterocyclyl which is optionally substituted with
1-2 oxo substituents, or a 4-6 membered heterocyclyl C₁₋₇ alkyl optionally substituted
with 1-2 oxo substituents;

- R₆, R₁₁ and R₂₂ are C₁₋₇ alkyl;
 R₇ is hydrogen or C₁₋₇ alkyl;
 R₈ is C₁₋₇ alkyl, C₁₋₇ alkoxy, or a 4-6 membered heterocyclyl;
 R₉ is -SO₂(C₁₋₇ alkyl);
 5 R₁₀ is hydrogen, C₁₋₇ alkyl or C₃₋₇ cycloalkyl;
 R₁₄ is hydrogen or -SO₂R₂₁;
 R₂₁ is 3-6 membered carbocyclyl optionally substituted with 1-2 C₁₋₇ alkyl;
 D is absent or C₁₋₇ alkyl;
 wherein the heterocyclyl group in each occurrence has 1-3 heteroatoms
 10 independently selected from N, O and S; or
 ii) R₁, R₂, R₄, R₅ and R₂₄ are hydrogen;
 R₃ is -D-C(O)-NR₆R₇, -C(O)R₈, -SO₂R₁₁, -D-NR₉R₁₀, -S(O)(NR₁₄)(R₂₂),
 1,1-dioxidoisothiazolidinyl or 1,1-dioxidoisothiazolidinyl C₁₋₇ alkyl;
 R₆, R₁₁ and R₂₂ are C₁₋₇ alkyl;
 15 R₇ is C₁₋₇ alkyl;
 R₈ is C₁₋₇ alkyl or azetidiny;
 R₉ is -SO₂(C₁₋₇ alkyl);
 R₁₀ is hydrogen, C₁₋₇ alkyl or C₃₋₇ cycloalkyl;
 R₁₄ is -SO₂R₂₁;
 20 R₂₁ is phenyl optionally substituted with a C₁₋₇ alkyl substituent;
 D is absent or C₁₋₇ alkyl.
10. A compound according to any of claims 7-9, wherein
 R₁ is hydrogen, C₁₋₇ alkyl, C₁₋₇ alkoxy, halogen, cyano, nitro, halo C₁₋₇ alkyl,
 25 halo C₁₋₇ alkoxy or C₁₋₇ alkylthio;
 R₂ is hydrogen or halogen;
 R₃ is hydrogen, C₁₋₇ alkyl, C₂₋₇ alkenyl, hydroxy C₁₋₇ alkyl, cyano, C₁₋₇
 alkylthio,
 C₁₋₇ alkoxycarbonyl C₂₋₇ alkenyl, -D-C(O)-NR₆R₇, -C(O)R₈, -SO₂R₁₁, -D-NR₉R₁₀,
 30 -S(O)(NR₁₄)(R₂₂), -S(NR₁₅)(C₁₋₇ alkyl), -C(S)NR₁₈R₁₉, 4-6 membered carbocyclyl
 which is optionally substituted with 1-2 hydroxyl substituents, 4-6 membered
 heterocyclyl which is optionally substituted with 1-2 substituents selected from

- halogen, hydroxyl, C₁₋₇ alkoxycarbonyl or oxo, or 4-6 membered heterocyclyl C₁₋₇ alkyl optionally substituted with 1-2 oxo substituents;
- R₄ is hydrogen, C₁₋₇ alkyl, hydroxy or halogen;
- R₅ is hydrogen or halogen;
- 5 R₆ is C₁₋₇ alkyl, C₃₋₇ cycloalkyl, hydroxy C₁₋₇ alkyl, -C₁₋₇ alkyl-O-C(O)C₁₋₇ alkyl;
- R₇ is hydrogen or C₁₋₇ alkyl;
- R₈ is hydrogen, C₁₋₇ alkyl, C₂₋₇ alkenyl, C₃₋₇ cycloalkyl, C₁₋₇ alkoxy, halo C₁₋₇ alkyl, C₁₋₇ alkoxy C₁₋₇ alkyl, C₁₋₇ alkylcarbonyl, C₁₋₇ alkoxycarbonyl,
- 10 -C₁₋₇ alkyl-O-C(O)-C₁₋₇ alkyl, -C₁₋₇ alkyl-SO₂(C₁₋₇ alkyl), -N=S(O)(C₁₋₇ alkyl)(C₁₋₇ alkyl) or a 4-6 membered heterocyclyl which is optionally substituted with 1-2 halogen substituents;
- R₉ is C₁₋₇ alkylcarbonyl, -SO₂(C₁₋₇ alkyl) or -SO₂(C₃₋₇ cycloalkyl);
- R₁₀ is hydrogen, C₁₋₇ alkyl or C₃₋₇ cycloalkyl;
- 15 R₁₁ is C₁₋₇ alkyl, C₃₋₇ cycloalkyl, halo C₁₋₇ alkyl, cyano C₁₋₇ alkyl, C₁₋₇ alkoxy C₁₋₇ alkyl, -NR₁₂R₁₃, 3-6 membered carbocyclyl which is optionally substituted with 1-2 substituents selected from halogen or C₁₋₇ alkyl, or 4-6 membered heterocyclyl which is optionally substituted with 1-2 substituents selected from halogen or C₁₋₇ alkyl;
- 20 R₁₂ is C₁₋₇ alkyl, hydroxy C₁₋₇ alkyl, cyano C₁₋₇ alkyl, C₁₋₇ alkoxy C₁₋₇ alkyl or C₁₋₇ alkylcarbonyl;
- R₁₃ is hydrogen or C₁₋₇ alkyl;
- R₁₄ is hydrogen, C₁₋₇ alkyl, C₁₋₇ alkylcarbonyl or -SO₂R₂₁;
- R₁₅ is hydrogen, C₁₋₇ alkyl, -SO₂R₁₇;
- 25 R₁₇ is C₁₋₇ alkyl or 3-6 membered carbocyclyl which is optionally substituted by 1-2 C₁₋₇ alkyl substituent;
- R₁₈, and R₁₉ are, independently, hydrogen or C₁₋₇ alkyl;
- R₂₁ is 3-6 membered carbocyclyl optionally substituted with 1-2 C₁₋₇ alkyl;
- R₂₂ is C₁₋₇ alkyl or C₃₋₇ cycloalkyl;
- 30 R₂₄ is hydrogen or C₁₋₇ alkyl;
- wherein the heterocyclyl group in each occurrence has 1-3 heteroatoms independently selected from N, O and S;
- or a pharmaceutically acceptable salt thereof.

11. A compound according to claim 1, which is
- Methyl (E)-3-(4-(((6-(isoindolin-2-ylmethyl)-4-oxo-4H-pyran-3-yl)oxy)-methyl)phenyl)acrylate (Compound 2);
- 5 2-(Isoindolin-2-ylmethyl)-5-(((4-(pyrrolidin-1-ylsulfonyl)benzyl)oxy)-4H-pyran-4-one (Compound 5);
- 4-(((6-(Isoindolin-2-ylmethyl)-4-oxo-4H-pyran-3-yl)oxy)methyl)-N-methylbenzenesulfonamide (Compound 8);
- 4-(((6-(Isoindolin-2-ylmethyl)-4-oxo-4H-pyran-3-yl)oxy)methyl)-N,N-dimethylbenzenesulfonamide (Compound 10);
- 10 4-(((6-(Isoindolin-2-ylmethyl)-4-oxo-4H-pyran-3-yl)oxy)methyl)-N-(2-methoxyethyl)benzenesulfonamide (Compound 11);
- N-(2-Hydroxyethyl)-4-(((6-(isoindolin-2-ylmethyl)-4-oxo-4H-pyran-3-yl)oxy)methyl)-N-methylbenzenesulfonamide (Compound 12);
- 15 N-(2-Hydroxyethyl)-4-(((6-(isoindolin-2-ylmethyl)-4-oxo-4H-pyran-3-yl)oxy)methyl)benzenesulfonamide (Compound 15);
- N-Ethyl-N-(2-hydroxyethyl)-4-(((6-(isoindolin-2-ylmethyl)-4-oxo-4H-pyran-3-yl)oxy)methyl)benzenesulfonamide (Compound 21);
- 5-((4-((Difluoromethyl)sulfonyl)benzyl)oxy)-2-(isoindolin-2-ylmethyl)-4H-pyran-4-one (Compound 22);
- 20 N-(2-Cyanoethyl)-4-(((6-(isoindolin-2-ylmethyl)-4-oxo-4H-pyran-3-yl)oxy)methyl)-N-methylbenzenesulfonamide (Compound 23);
- 2-(Isoindolin-2-ylmethyl)-5-((1-(oxetan-3-ylsulfonyl)piperidin-4-yl)methoxy)-4H-pyran-4-one (Compound 36);
- 25 5-((4-(Methylsulfonyl)benzyl)oxy)-2-((5-(trifluoromethoxy)isoindolin-2-yl)methyl)-4H-pyran-4-one (Compound 37);
- 2-((3,4-dihydroisoquinolin-2(1H)-yl)methyl)-5-((4-(2-hydroxypropan-2-yl)benzyl)oxy)-4H-pyran-4-one (Compound 44);
- 2-Isoindolin-2-ylmethyl)-5-((4-(prop-1-en-2-yl)benzyl)oxy)-4H-pyran-4-one (Compound 47);
- 30 5-((4-(2-Hydroxypropan-2-yl)benzyl)oxy)-2-(isoindolin-2-ylmethyl)-4H-pyran-4-one (Compound 49);

- 5-(Cyclohexylmethoxy)-2-(isoindolin-2-ylmethyl)-4H-pyran-4-one
(Compound 65);
- 5-((1-(Oxetan-3-ylsulfonyl)piperidin-4-yl)methoxy)-2-((5-(trifluoromethyl)-isoindolin-2-yl)methyl)-4H-pyran-4-one (Compound 69a);
- 5 N-((4-(((6-(Isoindolin-2-ylmethyl)-4-oxo-4H-pyran-3-yl)oxy)methyl)phenyl)-sulfonyl)-N-methylacetamide (Compound 70);
- 5-((4-(Cyclobutanesulfonimidoyl)benzyl)oxy)-2-(isoindolin-2-ylmethyl)-4H-pyran-4-one (Compound 71);
- 5-((4-(Cyclopropylsulfonyl)benzyl)oxy)-2-(isoindolin-2-ylmethyl)-4H-pyran-4-one (Compound 72);
- 10 5-((4-(Isobutylsulfonyl)benzyl)oxy)-2-(isoindolin-2-ylmethyl)-4H-pyran-4-one (Compound 73);
- 5-((4-(S-methylsulfonimidoyl)benzyl)oxy)-2-((5-(trifluoromethyl)isoindolin-2-yl)methyl)-4H-pyran-4-one (Compound 74);
- 15 4-({[6-(1,3-Dihydro-2*H*-isoindol-2-ylmethyl)-4-oxo-4*H*-pyran-3-yl]oxy}-methyl)-*N*-[dimethyl(oxido)- λ^6 -sulfanylidene]benzamide (Compound 83);
- N*-[Dimethyl(oxido)- λ^6 -sulfanylidene]-4-([6-[(5-fluoro-1,3-dihydro-2*H*-isoindol-2-yl)methyl]-4-oxo-4*H*-pyran-3-yl]oxy)methyl]benzamide (Compound 84);
- 5-((4-(S-Methylsulfonimidoyl)benzyl)oxy)-2-((5-(trifluoromethyl)isoindolin-2-yl)methyl)-4H-pyran-4-one (Compound 89);
- 20 5-((4-(S-Methylsulfonimidoyl)benzyl)oxy)-2-((5-(trifluoromethoxy)isoindolin-2-yl)methyl)-4H-pyran-4-one (Compound 90);
- 2-(1-(Isoindolin-2-yl)ethyl)-5-((4-(S-methylsulfonimidoyl)benzyl)oxy)-4H-pyran-4-one (Compound 91);
- 25 5-((4-(*N,S*-Dimethylsulfonimidoyl)benzyl)oxy)-2-(isoindolin-2-ylmethyl)-4H-pyran-4-one (Compound 92);
- N*-{[4-([6-(1,3-dihydro-2*H*-isoindol-2-ylmethyl)-4-oxo-4*H*-pyran-3-yl]oxy)-methyl]phenyl}(methyl)- λ^4 -sulfanylidene}-4-methylbenzenesulfonamide (Compound 93);
- 30 5-((4-(Azetidine-1-carbonyl)-2-fluorobenzyl)oxy)-2-(isoindolin-2-ylmethyl)-4H-pyran-4-one (Compound 95);
- 2-(Isoindolin-2-ylmethyl)-5-((4-(propan-2-ylsulfonimidoyl)benzyl)oxy)-4H-pyran-4-one (Compound 103);

- 5-((5-Fluoro-1-(methylsulfonyl)-1,2,3,6-tetrahydropyridin-4-yl)methoxy)-2-(isoindolin-2-ylmethyl)-4H-pyran-4-one (Compound 104);
- 2-(Isoindolin-2-ylmethyl)-5-((4-(oxazol-2-yl)benzyl)oxy)-4H-pyran-4-one (Compound 109);
- 5-((4-(1-Hydroxycyclobutyl)benzyl)oxy)-2-(isoindolin-2-ylmethyl)-4H-pyran-4-one (Compound 111);
- N*-(4-(((6-(Isoindolin-2-ylmethyl)-4-oxo-4H-pyran-3-yl)oxy)methyl)benzyl)-methanesulfonamide (Compound 113);
- 5-((4-(3-Hydroxyoxetan-3-yl)benzyl)oxy)-2-(isoindolin-2-ylmethyl)-4H-pyran-4-one (Compound 114);
- 2-((5-Fluoroisoindolin-2-yl)methyl)-5-((4-(3-hydroxyoxetan-3-yl)benzyl)oxy)-4H-pyran-4-one (Compound 115);
- 5-((4-(3-Hydroxyoxetan-3-yl)benzyl)oxy)-2-((5-(trifluoromethyl)isoindolin-2-yl)methyl)-4H-pyran-4-one (Compound 116);
- 2-(Isoindolin-2-ylmethyl)-5-((4-(pyrrolidine-1-carbonyl)benzyl)oxy)-4H-pyran-4-one (Compound 122);
- 5-((4-(Azetidine-1-carbonyl)benzyl)oxy)-2-(isoindolin-2-ylmethyl)-4H-pyran-4-one (Compound 129);
- 2-((5-Bromoisindolin-2-yl)methyl)-5-((4-(pyrrolidine-1-carbonyl)benzyl)oxy)-4H-pyran-4-one (Compound 130);
- N*-(tert-Butyl)-4-(((6-(isoindolin-2-ylmethyl)-4-oxo-4H-pyran-3-yl)oxy)methyl)benzamide (Compound 131);
- 4-(((6-Isoindolin-2-ylmethyl)-4-oxo-4H-pyran-3-yl)oxy)methyl)-*N,N*-diisopropylbenzamide (Compound 134);
- 4-(((6-((5-Chloroisindolin-2-yl)methyl)-4-oxo-4H-pyran-3-yl)oxy)methyl)-*N,N*-dimethylbenzamide (Compound 137);
- 4-(((6-((5-Methoxyisindolin-2-yl)methyl)-4-oxo-4H-pyran-3-yl)oxy)methyl)-*N,N*-dimethylbenzamide (Compound 138);
- N,N*-Dimethyl-4-(((4-oxo-6-((5-(trifluoromethyl)isoindolin-2-yl)methyl)-4H-pyran-3-yl)oxy)methyl)benzamide (Compound 139);
- (*E*)-3-(4-(((6-(Isoindolin-2-ylmethyl)-4-oxo-4H-pyran-3-yl)oxy)methyl)-phenyl)-*N,N*-dimethylacrylamide (Compound 146);

- 5-((4-(3,3-Difluoroazetidine-1-carbonyl)benzyl)oxy)-2-((5-methoxyisoindolin-2-yl)methyl)-4H-pyran-4-one (Compound 162);
- 3,5-Difluoro-4-(((6-(isoindolin-2-ylmethyl)-4-oxo-4H-pyran-3-yl)oxy)-methyl)-N,N-dimethylbenzamide (Compound 172);
- 5 N-((4-(((6-(Isoindolin-2-ylmethyl)-4-oxo-4H-pyran-3-yl)oxy)methyl)cyclohexyl)methyl)methanesulfonamide (Compound 173);
- 5-((4-((1,1-Dioxidoisothiazolidin-2-yl)methyl)cyclohexyl)methoxy)-2-(isoindolin-2-ylmethyl)-4H-pyran-4-one (Compound 176);
- 5-((1-(Methylsulfonyl)piperidin-4-yl)methoxy)-2-((5-(trifluoromethyl)isoindolin-2-yl)methyl)-4H-pyran-4-one (Compound 184);
- 10 2-(Isoindolin-2-ylmethyl)-5-((1-(methylsulfonyl)piperidin-4-yl)methoxy)-4H-pyran-4-one (Compound 185);
- 2-((5-Fluoroisoindolin-2-yl)methyl)-5-((1-(methylsulfonyl)piperidin-4-yl)methoxy)-4H-pyran-4-one (Compound 186);
- 15 5-((1-(Cyclopropylsulfonyl)piperidin-4-yl)methoxy)-2-(isoindolin-2-ylmethyl)-4H-pyran-4-one (Compound 187);
- 5-((1-(Ethylsulfonyl)piperidin-4-yl)methoxy)-2-(isoindolin-2-ylmethyl)-4H-pyran-4-one (Compound 188);
- 5-((1-(Ethylsulfonyl)piperidin-4-yl)methoxy)-2-((5-fluoroisoindolin-2-yl)methyl)-4H-pyran-4-one (Compound 189);
- 20 5-((1-(Cyclopropylsulfonyl)piperidin-4-yl)methoxy)-2-((5-fluoroisoindolin-2-yl)methyl)-4H-pyran-4-one (Compound 190);
- 5-((1-(Ethylsulfonyl)-4-methylpiperidin-4-yl)methoxy)-2-(isoindolin-2-ylmethyl)-4H-pyran-4-one (Compound 192);
- 25 2-(1-Isoindolin-2-yl)ethyl)-5-((1-(methylsulfonyl)piperidin-4-yl)methoxy)-4H-pyran-4-one (Compound 195);
- 2-(Isoindolin-2-ylmethyl)-5-((tetrahydro-2H-thiopyran-4-yl)methoxy)-4H-pyran-4-one (Compound 196);
- 5-((1-(Methylsulfonyl)piperidin-4-yl)methoxy)-2-((5-(trifluoromethoxy)-isoindolin-2-yl)methyl)-4H-pyran-4-one (Compound 205);
- 30 2-((5-Methylisoindolin-2-yl)methyl)-5-((1-(methylsulfonyl)piperidin-4-yl)methoxy)-4H-pyran-4-one (Compound 211);

- 2-(Isoindolin-2-ylmethyl)-5-(3-(1-(methylsulfonyl)piperidin-4-yl)propoxy)-4H-pyran-4-one (Compound 213);
- 2-(Isoindolin-2-ylmethyl)-5-((1-(pyrrolidine-1-carbonyl)piperidin-4-yl)-methoxy)-4H-pyran-4-one (Compound 215);
- 5 5-(((1*r*,4*r*)-4-(1,1-Dioxidoisothiazolidin-2-yl)cyclohexyl)methoxy)-2-(isoindolin-2-ylmethyl)-4H-pyran-4-one (Compound 216);
- 4-(((6-(Isoindolin-2-ylmethyl)-4-oxo-4H-pyran-3-yl)oxy)methyl)-*N,N*-dimethylcyclohexane-1-carboxamide (Compound 217);
- N*-Cyclopropyl-*N*-(4-(((6-(isoindolin-2-ylmethyl)-4-oxo-4H-pyran-3-yl)oxy)-methyl)cyclohexyl)methanesulfonamide (Compound 219);
- 10 5-((1-Butyrylpiperidin-4-yl)methoxy)-2-(isoindolin-2-ylmethyl)-4H-pyran-4-one (Compound 221);
- 5-((1-(2,2-Difluoropropanoyl)piperidin-4-yl)methoxy)-2-(isoindolin-2-ylmethyl)-4H-pyran-4-one (Compound 222);
- 15 2-((5-Fluoroisoindolin-2-yl)methyl)-5-((1-propionylpiperidin-4-yl)methoxy)-4H-pyran-4-one (Compound 224);
- 4-(((6-(Isoindolin-2-ylmethyl)-4-oxo-4*H*-pyran-3-yl)oxy)methyl)-*N,N*-dimethylpiperidine-1-sulfonamide (Compound 225);
- 5-((1-(Cyclopropanecarbonyl)piperidin-4-yl)methoxy)-2-(isoindolin-2-ylmethyl)-4*H*-pyran-4-one (Compound 226);
- 20 4-(((6-(Isoindolin-2-ylmethyl)-4-oxo-4*H*-pyran-3-yl)oxy)methyl)-*N*-isopropylpiperidine-1-carboxamide (Compound 229);
- 4-(((6-((5-Fluoroisoindolin-2-yl)methyl)-4-oxo-4*H*-pyran-3-yl)oxy)methyl)-*N,N*-dimethylpiperidine-1-sulfonamide (Compound 230);
- 25 2-(Isoindolin-2-ylmethyl)-5-((1-(morpholine-4-carbonyl)piperidin-4-yl)-methoxy)-4*H*-pyran-4-one (Compound 232);
- 5-((4-(Azetidine-1-carbonyl)cyclohexyl)methoxy)-2-(isoindolin-2-ylmethyl)-4H-pyran-4-one (Compound 234);
- 2-(Isoindolin-2-ylmethyl)-5-((1-(2-(methylsulfonyl)acetyl)piperidin-4-yl)-methoxy)-4H-pyran-4-one (Compound 238);
- 30 5-(((1*r*,4*r*)-4-Acetylcyclohexyl)methoxy)-2-(isoindolin-2-ylmethyl)-4H-pyran-4-one (Compound 244);

5-((1-Propionylpiperidin-4-yl)methoxy)-2-((5-(trifluoromethyl)isoindolin-2-yl)methyl)-4H-pyran-4-one (Compound 244a);

2-((5-((1-(methylsulfonyl)piperidin-4-yl)methoxy)-4-oxo-4H-pyran-2-yl)methyl)isoindoline-5-carbonitrile (Compound 245a);

5 1-(4-(((6-(Isoindolin-2-ylmethyl)-4-oxo-4H-pyran-3-yl)oxy)methyl)piperidin-1-yl)-4-methylpentane-1,2-dione (Compound 249);

2-(Isoindolin-2-ylmethyl)-5-((1-pivaloylpiperidin-4-yl)methoxy)-4H-pyran-4-one (Compound 251);

10 2-((4-(((6-(Isoindolin-2-ylmethyl)-4-oxo-4H-pyran-3-yl)oxy)methyl)piperidin-1-yl)sulfonyl)acetonitrile (Compound 254);

2-(Isoindolin-2-ylmethyl)-5-((1-((1-methyl-1H-pyrazol-5-yl)sulfonyl)piperidin-4-yl)methoxy)-4H-pyran-4-one (Compound 255);

2-(4-(((6-(Isoindolin-2-ylmethyl)-4-oxo-4H-pyran-3-yl)oxy)methyl)piperidin-1-yl)-2-oxoethyl acetate (Compound 257);

15 2-(Isoindolin-2-ylmethyl)-5-((1-propionylpiperidin-4-yl)methoxy)-4H-pyran-4-one (Compound 261);

2-(Isoindolin-2-ylmethyl)-5-((1-((2-methoxyethyl)sulfonyl)piperidin-4-yl)methoxy)-4H-pyran-4-one (Compound 262);

20 5-((1-(Isobutylsulfonyl)piperidin-4-yl)methoxy)-2-(isoindolin-2-ylmethyl)-4H-pyran-4-one (Compound 271);

5-((1-Isobutyrylpiperidin-4-yl)methoxy)-2-(isoindolin-2-ylmethyl)-4H-pyran-4-one (Compound 272);

4-((6-((5-Bromoisindolin-2-yl)methyl)-4-oxo-4H-pyran-3-yloxy)methyl)-benzonitrile (Compound 278);

25 5-((4-(S-Methylsulfonimidoyl)benzyl)oxy)-2-((5-(trifluoromethyl)isoindolin-2-yl)methyl)-4H-pyran-4-one (Compound 285);

5-((4-(R-Methylsulfonimidoyl)benzyl)oxy)-2-((5-(trifluoromethyl)isoindolin-2-yl)methyl)-4H-pyran-4-one (Compound 286);

and tautomers and pharmaceutically acceptable salts thereof.

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12. A compound according to claim 11, which is

N-Ethyl-N-(2-hydroxyethyl)-4-(((6-(isoindolin-2-ylmethyl)-4-oxo-4H-pyran-3-yl)oxy)methyl)benzenesulfonamide (Compound 21);

- 5-((4-(2-Hydroxypropan-2-yl)benzyl)oxy)-2-(isoindolin-2-ylmethyl)-4H-pyran-4-one (Compound 49);
- 4-({[6-(1,3-Dihydro-2*H*-isoindol-2-ylmethyl)-4-oxo-4*H*-pyran-3-yl]oxy}-methyl)-*N*-[dimethyl(oxido)- λ^6 -sulfanylidene]benzamide (Compound 83);
- 5 5-((4-(*S*-Methylsulfonimidoyl)benzyl)oxy)-2-((5-(trifluoromethoxy)isoindolin-2-yl)methyl)-4H-pyran-4-one (Compound 90);
- 2-(1-(Isoindolin-2-yl)ethyl)-5-((4-(*S*-methylsulfonimidoyl)benzyl)oxy)-4H-pyran-4-one (Compound 91);
- 2-(Isoindolin-2-ylmethyl)-5-((4-(pyrrolidine-1-carbonyl)benzyl)oxy)-4H-pyran-4-one (Compound 122);
- 10 5-((4-((1,1-Dioxidoisothiazolidin-2-yl)methyl)cyclohexyl)methoxy)-2-(isoindolin-2-ylmethyl)-4H-pyran-4-one (Compound 176);
- 5-((1-(Methylsulfonyl)piperidin-4-yl)methoxy)-2-((5-(trifluoromethyl)isoindolin-2-yl)methyl)-4*H*-pyran-4-one (Compound 184);
- 15 2-(Isoindolin-2-ylmethyl)-5-((1-(methylsulfonyl)piperidin-4-yl)methoxy)-4H-pyran-4-one (Compound 185);
- 5-((1-(Cyclopropylsulfonyl)piperidin-4-yl)methoxy)-2-(isoindolin-2-ylmethyl)-4H-pyran-4-one (Compound 187);
- 5-((1-(Ethylsulfonyl)piperidin-4-yl)methoxy)-2-(isoindolin-2-ylmethyl)-4H-pyran-4-one (Compound 188);
- 20 5-((1-(Ethylsulfonyl)piperidin-4-yl)methoxy)-2-((5-fluoroisoindolin-2-yl)methyl)-4H-pyran-4-one (Compound 189);
- 2-(1-Isoindolin-2-yl)ethyl)-5-((1-(methylsulfonyl)piperidin-4-yl)methoxy)-4H-pyran-4-one (Compound 195);
- 25 2-(Isoindolin-2-ylmethyl)-5-(3-(1-(methylsulfonyl)piperidin-4-yl)propoxy)-4H-pyran-4-one (Compound 213);
- 5-(((1*r*,4*r*)-4-(1,1-Dioxidoisothiazolidin-2-yl)cyclohexyl)methoxy)-2-(isoindolin-2-ylmethyl)-4H-pyran-4-one (Compound 216);
- 4-(((6-(Isoindolin-2-ylmethyl)-4-oxo-4*H*-pyran-3-yl)oxy)methyl)-*N,N*-dimethylcyclohexane-1-carboxamide (Compound 217);
- 30 4-(((6-(Isoindolin-2-ylmethyl)-4-oxo-4*H*-pyran-3-yl)oxy)methyl)-*N,N*-dimethylpiperidine-1-sulfonamide (Compound 225);

5-(((1r,4r)-4-Acetylcyclohexyl)methoxy)-2-(isoindolin-2-ylmethyl)-4H-pyran-4-one (Compound 244);

5-((1-Propionylpiperidin-4-yl)methoxy)-2-((5-(trifluoromethyl)isoindolin-2-yl)methyl)-4H-pyran-4-one (Compound 244a);

5 2-(Isoindolin-2-ylmethyl)-5-((1-propionylpiperidin-4-yl)methoxy)-4H-pyran-4-one (Compound 261);

4-((6-((5-Bromoisindolin-2-yl)methyl)-4-oxo-4H-pyran-3-yloxy)methyl)-benzonitrile (Compound 278);

and tautomers and pharmaceutically acceptable salts thereof.

10

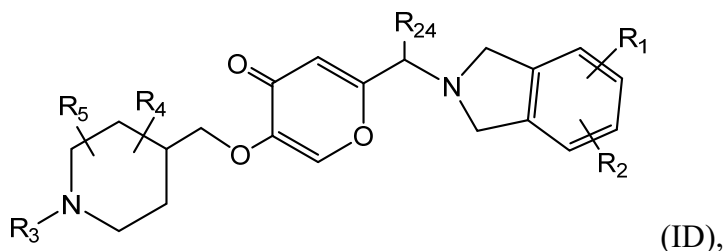
13. A pharmaceutical composition comprising a compound according to any one of claims 1-12 together with a pharmaceutically acceptable carrier.

15 14. Pharmaceutical combination comprising a compound according to any one of claims 1-12 and at least one additional active ingredient selected from the list consisting of

- glucocorticoids;
- mineralocorticoids;
- non-steroidal androgen receptor antagonists;
- 20 - steroidogenesis inhibitors;
- chemotherapeutic agents;
- antiestrogens;
- epigenetic modulators;
- mTOR inhibitors (e.g. everolimus);
- 25 - AKT inhibitors (e.g. AZ5363);
- radiopharmaceuticals (e.g. alpharadin);
- GnRH/LHRH analogues (such as leuprorelin);
- PI3K inhibitors; and
- CDK4/6 inhibitors;

30 for simultaneous, separate or sequential administration.

15. A compound of formula (ID):



or a tautomer or pharmaceutically acceptable salt thereof,

wherein R₁ is hydrogen, halogen, C₁₋₇ alkyl, halo C₁₋₇ alkyl, or halo C₁₋₇ alkoxy;

5 R₃ is -D-C(O)-NR₆R₇, -C(O)R₈ or -SO₂R₁₁;

R₂, R₄, R₅, and R₇ are hydrogen;

R₁₁ is C₁₋₇ alkyl, C₃₋₇ cycloalkyl, C₁₋₇ alkoxy C₁₋₇ alkyl, -NR₁₂R₁₃ or oxetanyl;

R₆, R₁₂ and R₁₃ are C₁₋₇ alkyl;

R₈ is C₁₋₇ alkyl or halo C₁₋₇ alkyl;

10 R₂₄ is hydrogen; and

D is absent.

16. Compound 5-((1-(methylsulfonyl)piperidin-4-yl)methoxy)-2-((5-(trifluoromethyl)isoindolin-2-yl)methyl)-4H-pyran-4-one or a tautomer or
15 pharmaceutically acceptable salt thereof.

17. Compound 2-(isoindolin-2-ylmethyl)-5-((1-(methylsulfonyl)piperidin-4-yl)methoxy)-4H-pyran-4-one or a tautomer or pharmaceutically acceptable salt thereof.

20

18. Use of the compound according to any one of claims 15 to 17 in the manufacture of a medicament for treating a steroid receptor dependent condition or disease.

25 19. Use of the compound according to any one of claims 15 to 17 in the manufacture of a medicament for treating an androgen receptor dependent condition or disease.

20. The use according to claim 18, wherein the steroid receptor dependent disease is cancer.

21. The use according to claim 20, wherein the cancer is prostate cancer.

5

22. The use according to claim 21, wherein the prostate cancer is castration-resistant prostate cancer (CRPC).

23. The use according to any of claims 18-22, wherein the medicament is further comprises a glucocorticoid and/or a mineralocorticoid and, optionally, one or more anti-cancer agents.

10

24. The use according to claim 23, wherein the one or more anti-cancer agents is selected from the group consisting of:

15

- a non-steroidal androgen receptor antagonist;
- a steroidogenesis inhibitor;
- a chemotherapeutic agent;
- an antiestrogen;
- an epigenetic modulator;
- an mTOR inhibitor;
- an AKT inhibitor;
- a radiopharmaceutical;
- a GnRH/LHRH analogue;
- a PI3K inhibitor; and
- a CDK4/6 inhibitor.

20

25

25. A pharmaceutical composition comprising the compound according to any one of claims 15 to 17 together with a pharmaceutically acceptable carrier.

30

26. A pharmaceutical combination comprising a compound according to any one of claims 15 to 17 and at least one additional active ingredient selected from the group consisting of

- a glucocorticoid;

- a mineralocorticoid;
 - a non-steroidal androgen receptor antagonist;
 - a steroidogenesis inhibitor;
 - a chemotherapeutic agent;
 - 5 - an antiestrogen;
 - an epigenetic modulator;
 - an mTOR inhibitor;
 - an AKT inhibitor;
 - a radiopharmaceutical;
 - 10 - a GnRH/LHRH analogue;
 - aPI3K inhibitor; and
 - a CDK4/6 inhibitor,
- for simultaneous, separate, or sequential administration.