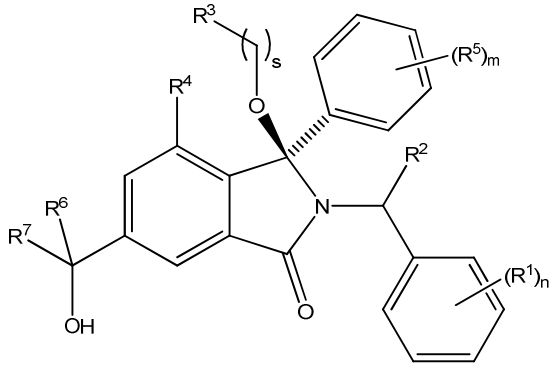
CLAIMS

1. A compound of formula (Ir):



(Ir)

or a tautomer or a solvate or a pharmaceutically acceptable salt thereof, wherein:

R^1 is independently selected from hydroxy, halogen, nitro, nitrile, C_{1-4}alkyl, haloC_{1-4}alkyl, hydroxyC_{1-4}alkyl, C_{2-6}alkenyl, C_{1-4}alkoxy, haloC_{1-4}alkoxy, C_{2-4}alkynyl, $-O_{0,1}-(CR^xR^y)_v-CO_2H$, $-(CR^xR^y)_v-CO_2C_{1-4}$alkyl, $-(CR^xR^y)_v-CON(C_{1-4}alkyl)_2$, $-P(=O)(R^x)_2$, $-S(O)_d-R^x$, $-S(O)_d$-heterocyclic group with 3 to 6 ring members and $-S(O)_d-N(R^8)_2$;

R^2 is selected from hydrogen, C_{1-4} alkyl, C_{2-6}alkenyl, hydroxyC_{1-4}alkyl, $-(CR^xR^y)_u-CO_2H$, $-(CR^xR^y)_u-CO_2C_{1-4}$alkyl, and $-(CR^xR^y)_u-CONR^xR^y$;

s is selected from 0 and 1;

R^3 is hydrogen or $-(A)_t-(CR^xR^y)_q-X$;

t is selected from 0 and 1;

q is selected from 0, 1 and 2;

wherein when R^3 is $-(A)_t-(CR^xR^y)_q-X$ then (i) at least one of s, t and q is other than 0 and (ii) when t is 0 then s is 1 and q is other than 0;

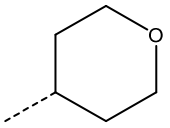
A is a C_{3-6}cycloalkyl group or a heterocyclic group with 3 to 6 ring members, wherein the heterocyclic group comprises one or more heteroatoms selected from N, O, S and oxidised forms thereof;

X is selected from hydrogen, halogen, -CN, $-OR^9$, $-(CH_2)_v-CO_2H$, $-(CH_2)_v-CO_2C_{1-4}$alkyl, $-S(O)_d-R^x$, $-C(=O)-C_{1-4}$alkyl, $-S(O)_d-N(H)_e(C_{1-4}alkyl)_{2-e}$, $-NR^xR^y$, $-NHSO_2R^x$, $-NR^xCOR^y$, and -

$C(=O)NR^xR^y$;

R^4 and R^5 are independently selected from halogen, nitrile, C_{1-4}alkyl, haloC_{1-4}alkyl, C_{1-4}alkoxy and haloC_{1-4}alkoxy;

R^6 is selected from hydrogen and C_{1-6}alkyl;

R^7 is  optionally substituted by one R^z group;

R^8 and R^9 are independently selected from hydrogen, C_{1-6}alkyl, haloC_{1-6}alkyl, hydroxyC_{1-6}alkyl, $-(CH_2)_k$-O-C_{1-6}alkyl, $-(CH_2)_k$-O-(hydroxyC_{1-6}alkyl), hydroxyC_{1-6}alkoxy, $-(CH_2)_k$-CO_2C_{1-6}alkyl, $-(CH_2)_k$-CO_2H, -C_{1-6} alkyl-$N(H)_e(C_{1-4}alkyl)_{2-e}$, $-(CH_2)_j$-C_{3-8}cycloalkyl and $-(CH_2)_j$-C_{3-8}cycloalkenyl;

R^x and R^y are independently selected from hydrogen, halogen, nitro, nitrile, C_{1-6}alkyl, haloC_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, hydroxy, hydroxyC_{1-6}alkyl, C_{1-6}alkoxy, $-(CH_2)_k$-O-C_{1-6}alkyl, hydroxyC_{1-6}alkoxy, -$COOC_{1-6}$alkyl, $-N(H)_e(C_{1-4}alkyl)_{2-e}$, $-C_{1-6}$alkyl-$N(H)_e(C_{1-4}alkyl)_{2-e}$, $-(CH_2)_k$-$C(=O)N(H)_e(C_{1-4}alkyl)_{2-e}$, C_{3-8}cycloalkyl and C_{3-8}cycloalkenyl;

or the R^x and R^y groups, together with the carbon or nitrogen atom to which they are attached, can join to form a C_{3-6}cycloalkyl or saturated heterocyclyl group with 3 to 6 ring members which may be optionally fused to an aromatic heterocyclyl group of 3 to 5 ring members;

or when on a carbon atom the R^x and R^y groups can join together to form a $=CH_2$ group;

R^z is selected from halogen, nitro, nitrile, C_{1-6}alkyl, haloC_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, =O, hydroxy, hydroxyC_{1-6}alkyl, C_{1-6}alkoxy, $-(CH_2)_k$-O-C_{1-6}alkyl, hydroxyC_{1-6}alkoxy, $-C(=O)C_{1-6}$alkyl, $-C(=O)C_{1-6}$alkyl-OH, $-C(=O)C_{1-6}$alkyl-$N(H)_e(C_{1-4}alkyl)_{2-e}$, $-C(=O)N(H)_e(C_{1-4}alkyl)_{2-e}$, $-(CH_2)_r$-CO_2C_{1-6}alkyl, $-(CH_2)_r$-CO_2H, $-N(H)_e(C_{1-4}alkyl)_{2-e}$, $-C_{1-6}$alkyl-$N(H)_e(C_{1-4}alkyl)_{2-e}$, heterocyclyl group with 3 to 6 ring members, heterocyclyl group with 3 to 6 ring members substituted by $-C(=O)C_{1-4}$alkyl, heterocyclyl group with 3 to 6 ring members substituted by $-C(=O)OC_{1-4}$alkyl, heterocyclyl group with 3 to 6 ring members substituted by $-C(=O)N(H)_e(C_{1-4}alkyl)_{2-e}$, -C(=O)heterocyclyl group with 3 to 6 ring members, C_{3-8}cycloalkyl and C_{3-8}cycloalkenyl;

j, d, e, n, r and p are independently selected from 0, 1 and 2;

k and m are independently selected from 1 and 2;

u is selected from 0, 1, 2 and 3; and

v is selected from 0 and 1.

2. A compound according to claim 1, or a tautomer or a solvate or a pharmaceutically acceptable salt thereof, wherein R^1 is:

(i) halogen, hydroxy, nitrile, C_{1-4}alkyl, C_{2-4}alkynyl, or C_{1-4}alkoxy; or

(ii) hydroxy, halogen, nitrile, C_{1-4}alkyl, haloC_{1-4}alkyl, hydroxyC_{1-4}alkyl, C_{2-6}alkenyl, C_{1-4}alkoxy, haloC_{1-4}alkoxy, C_{2-4}alkynyl, $-(CH_2)_v-CO_2H$, $-(CR^xR^y)_v-CO_2C_{1-4}$alkyl, $-(CH_2)_v-CON(C_{1-4}alkyl)_2$, $-P(=O)(R^x)_2$, $-S(O)_d-C_{1-6}$alkyl, $-S(O)_d$-heterocyclic group with 3 to 6 ring members or $-S(O)_d-N(R^8)_2$.

3. A compound according to claims 1 or 2, or a tautomer or a solvate or a pharmaceutically acceptable salt thereof, wherein R^2 is:

(i) hydrogen, C_{1-4} alkyl, C_{2-6}alkenyl, or hydroxyC_{1-4}alkyl; or

(ii) hydrogen or $-(CR^xR^y)_u-CO_2H$.

4. A compound according to any one of claims 1 to 3, or a tautomer or a solvate or a pharmaceutically acceptable salt thereof, wherein:

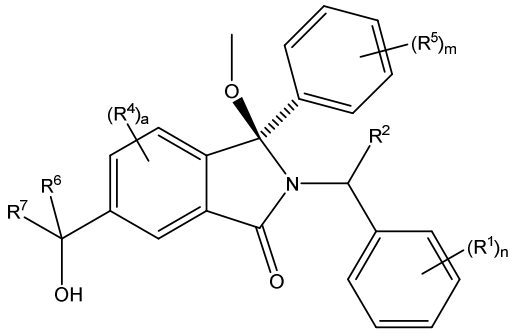
(i) R^3 is $-(A)_t-(CR^xR^y)_q-X$ and A is either a C_{3-6}cycloalkyl group or a heterocyclic group with 3 to 5 ring members; or

(ii) R^3 is $-(A)_t-(CR^xR^y)_q-X$ and A is a heterocyclic group with 3 to 5 ring members.

5. A compound according to any one of claims 1 to 4, or a tautomer or a solvate or a pharmaceutically acceptable salt thereof, wherein s is 1.

6. A compound according to any one of claims 1 to 5, or a tautomer or a solvate or a pharmaceutically acceptable salt thereof, wherein X is hydrogen, halogen, -CN, $-OR^9$, or $-C(=O)NR^xR^y$.

7. A compound according to any one of claims 1 to 3, wherein the compound is a compound of the formula



wherein a is 1 and R^4 is at the 4-position of the isoindolinone ring,

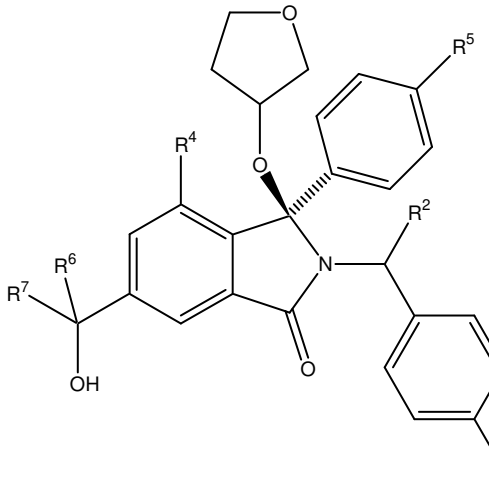
or a tautomer or a solvate or a pharmaceutically acceptable salt thereof.

8. A compound according to any one of claims 1 to 7, or a tautomer or a solvate or a pharmaceutically acceptable salt thereof, wherein R^4 is F.

9. A compound according to any one of claims 1 to 8, or a tautomer or a solvate or a pharmaceutically acceptable salt thereof, wherein R^5 is chloro and m is 1 and the substituent R^5 is at the *para*-position of the phenyl group.

10. A compound according to any one of claims 1 to 9, or a tautomer or a solvate or a pharmaceutically acceptable salt thereof, wherein R^6 is methyl or ethyl.

11. A compound according to any one of claims 1 to 4, wherein the compound is a compound of formula (bb) or a tautomer or a solvate or a pharmaceutically acceptable salt thereof:



(bb).

12. A compound according to claim 1, or a tautomer, pharmaceutically acceptable salt or solvate thereof, wherein the compound is selected from:

(3R)-2-[(4-chloro-2-methanesulfonylphenyl)methyl]-3-(4-chlorophenyl)-4-fluoro-6-[1-hydroxy-1-(oxan-4-yl)ethyl]-3-{[1-(hydroxymethyl)cyclopropyl]methoxy}-2,3-dihydro-1H-isoindol-1-one;

(3R)-2-[(4-chloro-2-methanesulfonylphenyl)methyl]-3-(4-chlorophenyl)-4-fluoro-6-[hydroxy(oxan-4-yl)methyl]-3-{[1-(hydroxymethyl)cyclopropyl]methoxy}-2,3-dihydro-1H-isoindol-1-one;

1-({[(1R)-2-[(4-chloro-2-methanesulfonylphenyl)methyl]-1-(4-chlorophenyl)-7-fluoro-5-[1-hydroxy-1-(oxan-4-yl)ethyl]-3-oxo-2,3-dihydro-1H-isoindol-1-yl]oxy}methyl)cyclopropane-1-carboxamide;

(3S)-3-(4-chlorophenyl)-3-[(1R)-1-(4-chlorophenyl)-7-fluoro-5-[1-hydroxy-1-(oxan-4-yl)ethyl]-1-methoxy-3-oxo-2,3-dihydro-1H-isoindol-2-yl]propanoic acid;

(3S)-3-(4-chlorophenyl)-3-[(1R)-1-(4-chlorophenyl)-7-fluoro-5-[1-(4-fluorooxan-4-yl)-1-hydroxyethyl]-1-methoxy-3-oxo-2,3-dihydro-1H-isoindol-2-yl]propanoic acid;

(3S)-3-(4-chlorophenyl)-3-[(1R)-1-(4-chlorophenyl)-7-fluoro-5-[1-(4-fluorooxan-4-yl)-1-hydroxypropyl]-1-methoxy-3-oxo-2,3-dihydro-1H-isoindol-2-yl]propanoic acid;

(3S)-3-(4-chlorophenyl)-3-[(1R)-1-(4-chlorophenyl)-7-fluoro-5-[(1S)-1-hydroxy-1-(oxan-4-yl)propyl]-1-methoxy-3-oxo-2,3-dihydro-1H-isoindol-2-yl]propanoic acid;

(3S)-3-(4-chlorophenyl)-3-[(1R)-1-(4-chlorophenyl)-7-fluoro-5-[(1R)-1-hydroxy-1-(oxan-

4-yl)propyl]-1-methoxy-3-oxo-2,3-dihydro-1H-isoindol-2-yl]propanoic acid;
(4S)-4-(4-chlorophenyl)-4-[(1R)-1-(4-chlorophenyl)-7-fluoro-5-[(1S)-1-hydroxy-1-(oxan-4-yl)propyl]-1-methoxy-3-oxo-2,3-dihydro-1H-isoindol-2-yl]butanoic acid;
(4S)-4-(4-chlorophenyl)-4-[(1R)-1-(4-chlorophenyl)-7-fluoro-5-[(1R)-1-hydroxy-1-(oxan-4-yl)propyl]-1-methoxy-3-oxo-2,3-dihydro-1H-isoindol-2-yl]butanoic acid;
(4S)-4-(4-Chlorophenyl)-4-[(1R)-1-(4-chlorophenyl)-7-fluoro-5-[(1R)-1-(4-fluorooxan-4-yl)-1-hydroxypropyl]-1-methoxy-3-oxo-2,3-dihydro-1H-isoindol-2-yl]butanoic acid;
(3S)-3-(4-chlorophenyl)-3-[(1R)-1-(4-chlorophenyl)-7-fluoro-5-[(1R)-1-(4-fluorooxan-4-yl)-1-hydroxypropyl]-1-trideuteromethoxy-3-oxo-2,3-dihydro-1H-isoindol-2-yl]propanoic acid;
(3S)-3-(4-chlorophenyl)-3-[(1R)-1-(4-chlorophenyl)-1-ethoxy-7-fluoro-5-[(1R)-1-(4-fluorooxan-4-yl)-1-hydroxypropyl]-3-oxo-2,3-dihydro-1H-isoindol-2-yl]propanoic acid;
(4S)-4-[(1R)-1-(4-chlorophenyl)-7-fluoro-5-[(1R)-1-(4-fluorooxan-4-yl)-1-hydroxypropyl]-1-methoxy-3-oxo-2,3-dihydro-1H-isoindol-2-yl]-4-(4-methoxyphenyl)butanoic acid;
2-(5-chloro-2-{[1-(4-chlorophenyl)-7-fluoro-5-[(1R)-1-(4-fluorooxan-4-yl)-1-hydroxypropyl]-1-methoxy-3-oxo-2,3-dihydro-1H-isoindol-2-yl]methyl}phenoxy)acetic acid;
5-chloro-2-{[(1R)-1-(4-chlorophenyl)-7-fluoro-5-[(1S)-1-hydroxy-1-(oxan-4-yl)propyl]-1-methoxy-3-oxo-2,3-dihydro-1H-isoindol-2-yl]methyl}benzoic acid;
5-chloro-2-{[(1R)-1-(4-chlorophenyl)-7-fluoro-5-[(1R)-1-hydroxy-1-(oxan-4-yl)propyl]-1-methoxy-3-oxo-2,3-dihydro-1H-isoindol-2-yl]methyl}benzoic acid;
5-chloro-2-{[(1R)-1-(4-chlorophenyl)-1-ethoxy-7-fluoro-5-[(1S)-1-hydroxy-1-(oxan-4-yl)propyl]-3-oxo-2,3-dihydro-1H-isoindol-2-yl]methyl}benzoic acid;
2-{[(1R)-1-(4-chlorophenyl)-7-fluoro-5-[(1R)-1-(4-fluorooxan-4-yl)-1-hydroxypropyl]-1-methoxy-3-oxo-2,3-dihydro-1H-isoindol-2-yl]methyl}-5-methylbenzoic acid;
2-{[(1R)-1-(4-chlorophenyl)-7-fluoro-5-[(1R)-1-(4-fluorooxan-4-yl)-1-hydroxypropyl]-1-methoxy-3-oxo-2,3-dihydro-1H-isoindol-2-yl]methyl}-5-methoxybenzoic acid;
2-(5-chloro-2-{[(1R)-1-(4-chlorophenyl)-7-fluoro-5-[(1S)-1-hydroxy-1-(oxan-4-yl)propyl]-1-methoxy-3-oxo-2,3-dihydro-1H-isoindol-2-yl]methyl}phenyl)-2-methylpropanoic acid;
2-(5-chloro-2-{[(1R)-1-(4-chlorophenyl)-7-fluoro-5-[(1S)-1-hydroxy-1-(oxan-4-yl)propyl]-1-methoxy-3-oxo-2,3-dihydro-1H-isoindol-2-yl]methyl}phenyl)acetic acid;

2-(5-chloro-2-{[(1R)-1-(4-chlorophenyl)-7-fluoro-5-[(1R)-1-hydroxy-1-(oxan-4-yl)propyl]-1-methoxy-3-oxo-2,3-dihydro-1H-isoindol-2-yl]methyl}phenyl)acetic acid; and
(2S,3S)-3-(4-chlorophenyl)-3-[(1R)-1-(4-chlorophenyl)-7-fluoro-5-[(1S)-1-hydroxy-1-(oxan-4-yl)propyl]-1-methoxy-3-oxo-2,3-dihydro-1H-isoindol-2-yl]-2-methylpropanoic acid.

13. A compound according to claim 1, or a tautomer, pharmaceutically acceptable salt or solvate thereof, wherein the compound is selected from:

(2S,3S)-3-(4-chlorophenyl)-3-[(1R)-1-(4-chlorophenyl)-7-fluoro-5-[(1S)-1-hydroxy-1-(oxan-4-yl)propyl]-1-methoxy-3-oxo-2,3-dihydro-1H-isoindol-2-yl]-2-methylpropanoic acid;
(3S)-3-(4-chlorophenyl)-3-[(1R)-1-(4-chlorophenyl)-7-fluoro-5-[1-hydroxy-1-(oxan-4-yl)ethyl]-1-methoxy-3-oxo-2,3-dihydro-1H-isoindol-2-yl]propanoic acid; and
2-(5-chloro-2-{[(1R)-1-(4-chlorophenyl)-7-fluoro-5-[(1S)-1-hydroxy-1-(oxan-4-yl)propyl]-1-methoxy-3-oxo-2,3-dihydro-1H-isoindol-2-yl]methyl}phenyl)-2-methylpropanoic acid.

14. A combination comprising a compound of formula (Ir) as defined in any one of claims 1 to 13, or a tautomer or a solvate or a pharmaceutically acceptable salt thereof, with one or more other therapeutic agents.

15. A pharmaceutical composition comprising a compound of formula (Ir) as defined in any one of claims 1 to 13, or a tautomer or a solvate or a pharmaceutically acceptable salt thereof.

16. A pharmaceutical composition comprising a compound of formula (Ir) as defined in any one of claims 1 to 13, or a tautomer or a solvate or a pharmaceutically acceptable salt thereof, one or more other therapeutic agents, and a pharmaceutically acceptable carrier.

17. A compound according to any one of claims 1 to 11, or a tautomer or a solvate or a pharmaceutically acceptable salt thereof, wherein n is 1 and R^1 is chloro or nitrile.

18. A compound according to claim 17, or a tautomer or a solvate or a pharmaceutically acceptable salt thereof, wherein R^1 is chloro.

19. A compound according to any one of claims 1 to 11, or a tautomer or a solvate or a pharmaceutically acceptable salt thereof, wherein R^2 is -COOH, $-CH_2COOH$, $-CH_2CH_2-CO_2H$, $-(CH(CH_3))-CO_2H$ or $-(C(CH_3)_2)-CO_2H$.

20. A compound according to any one of claims 1 to 6, or a tautomer or a solvate or a pharmaceutically acceptable salt thereof, wherein R^3 is $-(A)_t-(CR^xR^y)_q-X$ and A is a cyclopropyl group.

21. A compound according to any one of claims 1 to 6 or 11, or a tautomer or a solvate or a pharmaceutically acceptable salt thereof, wherein R^3 is $-(A)_t-(CR^xR^y)_q-X$ and A is a heterocyclic group with 5 ring members.

22. A compound according to claim 1, wherein the compound is (2S,3S)-3-(4-chlorophenyl)-3-[(1R)-1-(4-chlorophenyl)-7-fluoro-5-[(1S)-1-hydroxy-1-(oxan-4-yl)propyl]-1-methoxy-3-oxo-2,3-dihydro-1H-isoindol-2-yl]-2-methylpropanoic acid or a tautomer, pharmaceutically acceptable salt or solvate thereof.

23. A compound according to claim 1, wherein the compound is (3S)-3-(4-chlorophenyl)-3-[(1R)-1-(4-chlorophenyl)-7-fluoro-5-[1-hydroxy-1-(oxan-4-yl)ethyl]-1-methoxy-3-oxo-2,3-dihydro-1H-isoindol-2-yl]propanoic acid or a tautomer, pharmaceutically acceptable salt or

solvate thereof.

24. A compound according to claim 1, wherein the compound is 2-(5-chloro-2-{[(1R)-1-(4-chlorophenyl)-7-fluoro-5-[(1S)-1-hydroxy-1-(oxan-4-yl)propyl]-1-methoxy-3-oxo-2,3-dihydro-1H-isoindol-2-yl]methyl}phenyl)-2-methylpropanoic acid or a tautomer, pharmaceutically acceptable salt or solvate thereof.