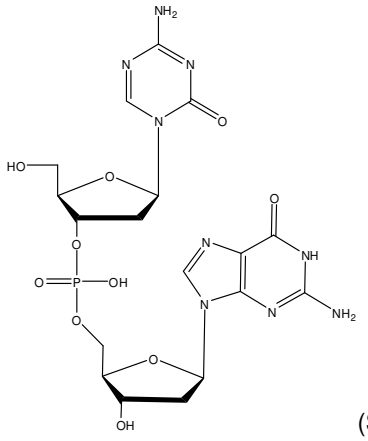
CLAIMS

1. A combination comprising (i) a compound which 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, *N*-oxide, pharmaceutically acceptable salt or solvate thereof; and

   (ii) a compound which is SGI-110



(SGI-110)

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

2. A combination comprising a combination as defined in claim 1 and one or more (e.g. 1 or 2) other therapeutic agents (e.g. anticancer agents).

3. A combination according to claim 1 or 2 wherein the compound which 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 the tautomer, *N*-oxide, pharmaceutically acceptable salt or solvate thereof and SGI-110 are physically associated.

4. The combination of claim 3 wherein the compound which 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 the tautomer, *N*-oxide, pharmaceutically acceptable salt or solvate thereof and SGI-110 are: (a) in admixture; (b) chemically/physicochemically linked; (c) chemically/physicochemically co-packaged; or (d) unmixed but co-packaged or co-presented.

5. A pharmaceutical composition comprising a combination as defined in any one of claims 1 to 4.

6. A combination according to any one of claims 1 to 4 or a pharmaceutical composition according to claim 5 for use in therapy.

7. A combination according to any one of claims 1 to 4 or a pharmaceutical composition according to claim 5 for use in the prophylaxis or treatment of a disease state or condition as described herein.

8. A use of a combination according to any one of claims 1 to 4 or a pharmaceutical composition according to claim 5 for the manufacture of a medicament for use in the prophylaxis or treatment of a disease state or condition as described herein.

9. A combination or a pharmaceutical composition for use according to claim 7 or a use according to claim 8, wherein the disease state or condition is mediated by MDM2-p53.

10. A combination or a pharmaceutical composition for use according to claim 7, or a use according to claim 8 wherein the disease state or condition is cancer.

11. A combination for use, a pharmaceutical composition for use, or a use according to claim 10, wherein the disease state or condition is a cancer which is acute myeloid leukaemia.

12. A combination of (i) (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, *N*-oxide, pharmaceutically acceptable salt or solvate thereof; and (ii) and SGI-110 , or a tautomer, *N*-oxide, pharmaceutically acceptable salt or solvate thereof, for use in the prophylaxis or treatment of a disease state or condition which is cancer.

13. A combination for use according to claim 12, wherein the cancer is acute myeloid leukaemia.

14. A combination for use according to claim 12 or 13, wherein the combination is physically associated.

15. A compound which 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, *N*-oxide, pharmaceutically acceptable salt or solvate thereof, for use in the prophylaxis or treatment of a disease state or condition as described herein, wherein the compound is used in combination with SGI-110, or a tautomer, *N*-oxide, pharmaceutically acceptable salt or solvate thereof.

16. The compound for use according to claim 15, wherein the compound and SGI-110 are physically associated.

17. The compound for use according to claim 15 or 16, wherein the disease state or condition is cancer (e.g. acute myeloid leukaemia).

18. SGI-110, or a tautomer, *N*-oxide, pharmaceutically acceptable salt or solvate thereof, for use in the prophylaxis or treatment of a disease state or condition as described herein, wherein SGI-110 is used in combination with a compound which 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, *N*-oxide, pharmaceutically acceptable salt or solvate thereof.

19. SGI-110 for use for use according to claim 18, wherein SGI-110 and the compound are physically associated.

20. SGI-110 for use according to claim 18 or 19, wherein the disease state or condition is cancer (e.g. acute myeloid leukaemia).

21. A compound which 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, *N*-oxide, pharmaceutically acceptable salt or solvate thereof, for use in combination therapy with SGI-110, and optionally with one or more other therapeutic agent to prevent, treat or manage cancer in a patient in need thereof.

22. The use of (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, *N*-oxide, pharmaceutically acceptable salt or solvate thereof, for treatment of a patient suffering from a cancer where the patient is being treated with SGI-110, or a tautomer, *N*-oxide, pharmaceutically acceptable salt or solvate thereof.

23. The use of SGI-110, or a tautomer, *N*-oxide, pharmaceutically acceptable salt or solvate thereof, for treatment of a patient suffering from a cancer where the patient is being treated with (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, *N*-oxide, pharmaceutically acceptable salt or solvate thereof.

24. The use of (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, *N*-oxide, pharmaceutically acceptable salt or solvate thereof, for the manufacture of a medicament for use in enhancing or potentiating the response rate in a patient suffering from a cancer where the patient is being treated with SGI-110, or a tautomer, *N*-oxide, pharmaceutically acceptable salt or solvate thereof.

25. (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, *N*-oxide, pharmaceutically acceptable salt or solvate thereof, for use in

    a. treating a disease or condition comprising or arising from abnormal cell growth in a mammal, or

b. in alleviating or reducing the incidence of a disease or condition comprising or arising from abnormal cell growth in a mammal,

wherein the mammal is undergoing treatment with SGI-110, or a tautomer, *N*-oxide, pharmaceutically acceptable salt or solvate thereof.

26. The use of a combination according to any one of claims 1 to 25 in the manufacture of a pharmaceutical composition for inhibiting the growth of tumour cells.

27. A product containing as a first active ingredient (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, *N*-oxide, pharmaceutically acceptable salt or solvate thereof, and as a further active ingredient SGI-110, or a tautomer, *N*-oxide, pharmaceutically acceptable salt or solvate thereof, as a combined preparation for simultaneous, separate or sequential use in the treatment of patients suffering from cancer.