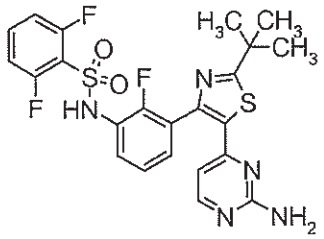
CLAIMS

We claim:

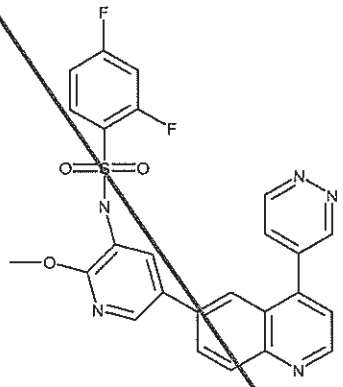
1. A combination comprising:

(i) a first compound of Structure (I):



or a pharmaceutically acceptable salt or solvate thereof; and

(ii) a second compound which is a compound of Structure (II)



or a pharmaceutically acceptable salt thereof.

2. A combination according to claim 1 where the compound of Structure (I) is in the form of a methanesulfonate salt and the compound of Structure (II) is in the form of a free base.

3. A combination kit comprising a combination according to claim 1 or claim 2 together with a pharmaceutically acceptable carrier or carriers.

4. A combination according to any one of claims 1 to 3 where the amount of the compound of Structure (I) is an amount selected from 10mg to 300mg, and that amount is administered from 1 to 4 times per day, and the amount of the compound of Structure (II) is an amount selected from 0.5 mg to 20 mg, and that amount is administered once per day.

5. A combination kit comprising a combination according to any one of claims 1-4 together with a pharmaceutically acceptable carrier or carriers.

6. A method of treating cancer in a human in need thereof which comprises the in vivo administration of a therapeutically effective amount of a combination of *N*-{3-[5-(2-amino-4-pyrimidinyl)-2-(1,1-dimethylethyl)-1,3-thiazol-4-yl]-2-fluorophenyl}-2,6-difluorobenzenesulfonamide or a pharmaceutically acceptable salt thereof and 2,4-difluoro-*N*-{2-(methyloxy)-5-[4-(4-pyridazinyl)-6-quinolinyl]-3-pyridinyl}benzenesulfonamide, to such human,

wherein the combination is administered within a specified period, and

wherein the combination is administered for a duration of time.

7. A method of claim 6, which comprises the in vivo administration of a therapeutically effective amount of a combination of *N*-{3-[5-(2-amino-4-pyrimidinyl)-2-(1,1-dimethylethyl)-1,3-thiazol-4-yl]-2-fluorophenyl}-2,6-difluorobenzenesulfonamide methanesulfonate salt and 2,4-difluoro-*N*-{2-(methyloxy)-5-[4-(4-pyridazinyl)-6-quinolinyl]-3-pyridinyl}benzenesulfonamide, to such human,

wherein the combination is administered within a specified period, and

wherein the combination is administered for a duration of time.

8. A method according to claim 6 wherein the amount of *N*-{3-[5-(2-amino-4-pyrimidinyl)-2-(1,1-dimethylethyl)-1,3-thiazol-4-yl]-2-fluorophenyl}-2,6-difluorobenzenesulfonamide or a pharmaceutically acceptable salt thereof is selected from about 10mg to about 300mg, and that amount is administered from 1 to 3 times per day, and the amount of 2,4-difluoro-*N*-{2-(methyloxy)-5-[4-(4-pyridazinyl)-6-quinolinyl]-3-pyridinyl}benzenesulfonamide is selected from about 0.5 mg to about 10 mg.

9. A method according to claim 6 wherein the amount of *N*-{3-[5-(2-amino-4-pyrimidinyl)-2-(1,1-dimethylethyl)-1,3-thiazol-4-yl]-2-fluorophenyl}-2,6-difluorobenzenesulfonamide or a pharmaceutically acceptable salt thereof, is selected from about 70mg to about 260mg, and that amount is administered twice per day, and the amount of 2,4-difluoro-*N*-{2-(methyloxy)-5-[4-(4-pyridazinyl)-6-quinolinyl]-3-pyridinyl}benzenesulfonamide is selected from about 0.5 mg to about 6 mg

10. A method according to claim 8 wherein *N*-{3-[5-(2-amino-4-pyrimidinyl)-2-(1,1-dimethylethyl)-1,3-thiazol-4-yl]-2-fluorophenyl}-2,6-difluorobenzenesulfonamide or a pharmaceutically acceptable salt thereof, and 2,4-difluoro-*N*-{2-(methyloxy)-5-[4-(4-pyridazinyl)-6-quinolinyl]-3-pyridinyl}benzenesulfonamide are administered within 12 hours of each other each day for a period of at least 7 consecutive days, optionally followed by one of more repeating cycles.

11. A method according to claim 6 wherein *N*-{3-[5-(2-amino-4-pyrimidinyl)-2-(1,1-dimethylethyl)-1,3-thiazol-4-yl]-2-fluorophenyl}-2,6-difluorobenzenesulfonamide methanesulfonate salt and the amount of 2,4-difluoro-*N*-{2-(methyloxy)-5-[4-(4-pyridazinyl)-6-quinolinyl]-3-pyridinyl}benzenesulfonamide are administered within 12 hours of each other each day for a period of at least 14 consecutive days, optionally followed by one of more repeating cycles.

12. A method of treating cancer in a human in need thereof which comprises one or more dosing cycles, wherein each said cycle comprises (1) administering to the human from about 10 to 300 mg of *N*-{3-[5-(2-amino-4-pyrimidinyl)-2-(1,1-dimethylethyl)-1,3-thiazol-4-yl]-2-fluorophenyl}-2,6-difluorobenzenesulfonamide, or a pharmaceutically acceptable salt or solvate thereof, 1-4 times a day for 1-30 days; and (2) periodically administering to the human from about 0.05 mg to 10 mg of 2,4-difluoro-*N*-{2-(methyloxy)-5-[4-(4-pyridazinyl)-6-quinolinyl]-3-pyridinyl}benzenesulfonamide, or a pharmaceutically acceptable salt or solvate.

13. A method of treating cancer in a human in need thereof which comprises one or more dosing cycles, wherein each said cycle comprises (1) administering to the human from about 70 to 260 mg of *N*-{3-[5-(2-amino-4-pyrimidinyl)-2-(1,1-dimethylethyl)-1,3-thiazol-4-yl]-2-fluorophenyl}-2,6-difluorobenzenesulfonamide, or a pharmaceutically acceptable salt or solvate thereof, 1-4 times for 1-30 days; and (2) periodically administering to the human from about 0.5 mg to 5 mg of 2,4-difluoro-*N*-{2-(methyloxy)-5-[4-(4-pyridazinyl)-6-quinolinyl]-3-pyridinyl}benzenesulfonamide, or a pharmaceutically acceptable salt or solvate thereof for 1-30 days.

14. A method of treating cancer in a human in need thereof which comprises one or more dosing cycles, wherein each said cycle comprises (1) administering to the human from about 0.05 to 10 mg of 2,4-difluoro-*N*-{2-(methyloxy)-5-[4-(4-pyridazinyl)-6-quinolinyl]-3-pyridinyl}benzenesulfonamide, or a pharmaceutically acceptable salt or solvate thereof, once or twice a day for 1-30 days; and (2) periodically administering to the human from about 10 to 300 mg of *N*-{3-[5-(2-amino-4-pyrimidinyl)-2-(1,1-dimethylethyl)-1,3-thiazol-4-yl]-2-fluorophenyl}-2,6-difluorobenzenesulfonamide, or a pharmaceutically acceptable salt or solvate thereof for 1-30 days.

15. A method of treating cancer in a human in need thereof which comprises one or more dosing cycles, wherein each said cycle comprises (1) administering to the human from about 0.5 to 5 mg of 2,4-difluoro-*N*-{2-(methyloxy)-5-[4-(4-pyridazinyl)-6-quinolinyl]-3-pyridinyl}benzenesulfonamide, or a pharmaceutically acceptable salt or solvate thereof, once or twice a day for 1-30 days; and (2) periodically administering to the human from about 70 to 260 mg of *N*-{3-[5-(2-amino-4-pyrimidinyl)-2-(1,1-dimethylethyl)-1,3-thiazol-4-yl]-2-fluorophenyl}-2,6-difluorobenzenesulfonamide, or a pharmaceutically acceptable salt or solvate thereof for 1-30 days.

16. A method of claim 12 or 13, wherein 2,4-difluoro-*N*-{2-(methyloxy)-5-[4-(4-pyridazinyl)-6-quinolinyl]-3-pyridinyl}benzenesulfonamide is administered, once every 2-4 days.

17. A method of claim 12 or 13, wherein 2,4-difluoro-*N*-{2-(methyloxy)-5-[4-(4-pyridazinyl)-6-quinolinyl]-3-pyridinyl}benzenesulfonamide is administered, once every 5-7 days.

18. A method of claim 12 or 13, wherein 2,4-difluoro-*N*-{2-(methyloxy)-5-[4-(4-pyridazinyl)-6-quinolinyl]-3-pyridinyl}benzenesulfonamide is administered, once every 8-15 days.

19. A method of claim 14 or 15, wherein *N*-{3-[5-(2-amino-4-pyrimidinyl)-2-(1,1-dimethylethyl)-1,3-thiazol-4-yl]-2-fluorophenyl}-2,6-difluorobenzenesulfonamide methanesulfonate is administered, once every 2-4 days.

20. A method of claim 14 or 15, wherein *N*-{3-[5-(2-amino-4-pyrimidinyl)-2-(1,1-dimethylethyl)-1,3-thiazol-4-yl]-2-fluorophenyl}-2,6-difluorobenzenesulfonamide methanesulfonate is administered once every 5-7 days.

21. A method of claim 14 or 15, wherein *N*-{3-[5-(2-amino-4-pyrimidinyl)-2-(1,1-dimethylethyl)-1,3-thiazol-4-yl]-2-fluorophenyl}-2,6-difluorobenzenesulfonamide methanesulfonate is administered once every 8-15 days.

22. A method of treating cancer in a human in need thereof which comprises one or more repeating dosing cycles, wherein each said cycle comprises administering to the human from about 10 to 300 mg of *N*-{3-[5-(2-amino-4-pyrimidinyl)-2-(1,1-dimethylethyl)-1,3-thiazol-4-yl]-2-fluorophenyl}-2,6-difluorobenzenesulfonamide, or a pharmaceutically acceptable salt or solvate thereof, 1-4 times a day for 5-14 days, followed by administering to the human from about 0.05 mg to 10 mg of 2,4-difluoro-*N*-{2-(methyloxy)-5-[4-(4-pyridazinyl)-6-quinolinyl]-3-pyridinyl}benzenesulfonamide, or a pharmaceutically acceptable salt or solvate for 5-14 days.

23. A method of treating cancer in a human in need thereof which comprises one or more repeating dosing cycles, wherein each said cycle comprises administering to the human from about 70 to 260 mg of *N*-{3-[5-(2-amino-4-pyrimidinyl)-2-(1,1-dimethylethyl)-1,3-thiazol-4-yl]-2-fluorophenyl}-2,6-difluorobenzenesulfonamide, or a pharmaceutically

acceptable salt or solvate thereof, 1-2 times a day for 5-14 days, followed by administering to the human from about 0.5 mg to 5 mg of 2,4-difluoro-*N*-{2-(methyloxy)-5-[4-(4-pyridazinyl)-6-quinolinyl]-3-pyridinyl}benzenesulfonamide, or a pharmaceutically acceptable salt or solvate for 5-14 days.

24. A method according any one of claims 12-23, wherein said cancer is melanoma or colon.

25. A method of claim 24, wherein said cancer is a BRAF mutant.

26. A combination according to any of claims 1 – 4 wherein said second compound is in the form of free base.

27. A combination according to any proceeding claim for use in therapy.

28. A combination according to any of claims 1 – 4 for use in treating cancer.

29. A pharmaceutical composition comprising a combination according to any of claims 1 –4 together with a pharmaceutically acceptable carrier.

30. Use of a combination according to any of claims 1 – 4 in the manufacture of a medicament for the treatment of cancer.

31. A method of claim 8 or 9, wherein said cancer is melanoma, lung, pancreatic, breast or colon.

32. A method of claim 17, wherein said cancer is melanoma or colon.

33. A method of claim 32, wherein said cancer is a BRaf mutant.

34. A method according to any one of claims 12-15, wherein said cancer is melanoma which has progressed after being treated with a BRaf inhibitor.

35. A method according to any one of claims 12-15, wherein said cancer is melanoma which is resistant to a BRaf inhibitor.

36. A method according to any one of claims 12-15, wherein said cancer is colon cancer which has progressed after being treated with a BRaf inhibitor.

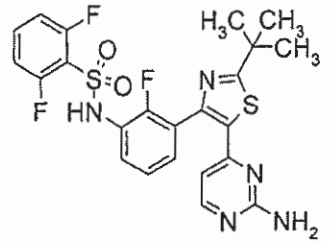
37. A method according to any one of claims 12-15, wherein said cancer is colon cancer which is resistant to a BRaf inhibitor.

CLAIMS

We claim:

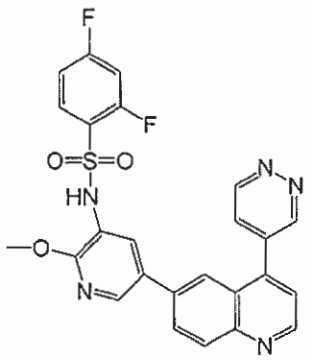
1 . Use of a combination comprising:

(i) a first compound of Structure (I):



or a pharmaceutically acceptable salt or solvate thereof; and

(ii) a second compound of Structure (II):



or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for the treatment of cancer.