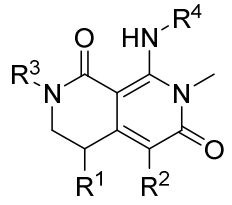
CLAIMS

We claim:

1. A compound of Formula I:



I

or a pharmaceutically acceptable salt thereof, wherein:

R^1 is H, Br, C1-C6 alkyl or phenyl;

R^2 is H, halogen or CH_3-;

R^3 is H, hydroxyC1-C6 alkyl-, hydroxyC1-C6 alkoxy-, C1-C6 alkoxy, fluoroC1-C6 alkoxy, C3-C6 cycloalkyl, or (C3-C6 cycloalkyl)C1-C6 alkoxy-; and

R^4 is phenyl substituted with 1, 2 or 3 substituents independently selected from halogen, C1-C6 alkyl, C1-C6 alkylthio, fluoroC1-C6 alkylthio, fluoroC1-C6 alkyl, C1-C6 alkoxy, fluoroC1-C6 alkoxy, C3-C6 cycloalkyl, and C1-C6 alkyl-C(=O)-.

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

3. A compound according to claim 1 or 2 or a pharmaceutically acceptable salt thereof, wherein R^2 is H.

4. A compound according to claim 1 or 2 or a pharmaceutically acceptable salt thereof, wherein R^2 is CH_3-.

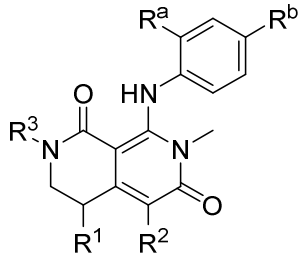
5. A compound according to any one of claims 1 to 4 or a pharmaceutically acceptable salt thereof, wherein R^3 is hydroxyC1-C6 alkyl-.

6. A compound according to any one of claims 1 to 5 or a pharmaceutically acceptable salt thereof, wherein R^4 is phenyl substituted with 1 or 2 substituents independently selected from

halogen, C1-C6 alkyl, C1-C6 alkylthio, fluoroC1-C6 alkylthio, fluoroC1-C6 alkyl, C1-C6 alkoxy, fluoroC1-C6 alkoxy, C3-C6 cycloalkyl, and C1-C6 alkyl-C(=O)-.

7. A compound according to any one of claims 1 to 5 or a pharmaceutically acceptable salt thereof, wherein R^4 is phenyl substituted with 1 or 2 substituents independently selected from halogen and C1-C6 alkylthio.

8. A compound of Formula II:



II

or a pharmaceutically acceptable salt thereof, wherein

R^1 is H, Br, C1-C6 alkyl or phenyl;

R^2 is H, halogen or CH_3-;

R^3 is H, hydroxyC1-C6 alkyl-, hydroxyC1-C6 alkoxy-, C1-C6 alkoxy, fluoroC1-C6 alkoxy, C3-C6 cycloalkyl, or (C3-C6 cycloalkyl)C1-C6 alkoxy-; and

R^a and R^b are independently selected from halogen, C1-C6 alkyl, C1-C6 alkylthio, fluoroC1-C6 alkylthio, fluoroC1-C6 alkyl, C1-C6 alkoxy, fluoroC1-C6 alkoxy, C3-C6 cycloalkyl, and C1-C6 alkyl-C(=O)-.

9. A compound according to claim 8 or a pharmaceutically acceptable salt thereof, wherein R^a is halogen.

10. A compound according to claim 8 or 9 or a pharmaceutically acceptable salt thereof, wherein R^b is halogen, C1-C6 alkyl, C1-C6 alkylthio, or fluoroC1-C6 alkoxy.

11. A compound according to claim 1, selected from:

8-((4-bromo-2-fluorophenyl)amino)-2-cyclopropyl-7-methyl-3,4-dihydro-2,7-naphthyridine-1,6(2H,7H)-dione;

8-((4-bromo-2-fluorophenyl)amino)-2-(cyclopropylmethoxy)-7-methyl-3,4-dihydro-

2,7-naphthyridine-1,6(2H,7H)-dione;

8-((4-bromo-2-fluorophenyl)amino)-2-ethoxy-7-methyl-3,4-dihydro-2,7-naphthyridine-1,6(2H,7H)-dione;

2-cyclopropyl-8-((2-fluoro-4-(methylthio)phenyl)amino)-7-methyl-3,4-dihydro-2,7-naphthyridine-1,6(2H,7H)-dione;

2-cyclopropyl-8-((2-fluoro-4-iodophenyl)amino)-7-methyl-3,4-dihydro-2,7-naphthyridine-1,6(2H,7H)-dione;

8-((2-fluoro-4-(methylthio)phenyl)amino)-2-(2-hydroxyethoxy)-7-methyl-3,4-dihydro-2,7-naphthyridine-1,6(2H,7H)-dione;

8-((4-bromo-2-fluorophenyl)amino)-2-(2-hydroxyethoxy)-7-methyl-3,4-dihydro-2,7-naphthyridine-1,6(2H,7H)-dione;

8-((2-fluoro-4-iodophenyl)amino)-2-(2-hydroxyethoxy)-7-methyl-3,4-dihydro-2,7-naphthyridine-1,6(2H,7H)-dione;

8-((2-chloro-4-iodophenyl)amino)-2-(2-hydroxyethoxy)-7-methyl-3,4-dihydro-2,7-naphthyridine-1,6(2H,7H)-dione;

8-((4-bromo-2-chlorophenyl)amino)-2-(2-hydroxyethoxy)-7-methyl-3,4-dihydro-2,7-naphthyridine-1,6(2H,7H)-dione;

8-((4-bromo-2,3-difluorophenyl)amino)-2-(2-hydroxyethoxy)-7-methyl-3,4-dihydro-2,7-naphthyridine-1,6(2H,7H)-dione;

8-((4-bromo-3-chloro-2-fluorophenyl)amino)-2-(2-hydroxyethoxy)-7-methyl-3,4-dihydro-2,7-naphthyridine-1,6(2H,7H)-dione;

8-((2-fluoro-4-(trifluoromethyl)phenyl)amino)-2-(2-hydroxyethoxy)-7-methyl-3,4-dihydro-2,7-naphthyridine-1,6(2H,7H)-dione;

8-((4-ethyl-2-fluorophenyl)amino)-2-(2-hydroxyethoxy)-7-methyl-3,4-dihydro-2,7-naphthyridine-1,6(2H,7H)-dione;

8-((4-cyclopropyl-2-fluorophenyl)amino)-2-(2-hydroxyethoxy)-7-methyl-3,4-dihydro-2,7-naphthyridine-1,6(2H,7H)-dione;

8-((2-fluoro-4-methoxyphenyl)amino)-2-(2-hydroxyethoxy)-7-methyl-3,4-dihydro-2,7-naphthyridine-1,6(2H,7H)-dione;

8-((2-fluoro-4-((trifluoromethyl)thio)phenyl)amino)-2-(2-hydroxyethoxy)-7-methyl-3,4-dihydro-2,7-naphthyridine-1,6(2H,7H)-dione;

8-((2-fluoro-4-isopropylphenyl)amino)-2-(2-hydroxyethoxy)-7-methyl-3,4-dihydro-2,7-naphthyridine-1,6(2H,7H)-dione;

8-((2-chloro-4-cyclopropylphenyl)amino)-2-(2-hydroxyethoxy)-7-methyl-3,4-

dihydro-2,7-naphthyridine-1,6(2H,7H)-dione;

8-((4-acetyl-2-fluorophenyl)amino)-2-(2-hydroxyethoxy)-7-methyl-3,4-dihydro-2,7-naphthyridine-1,6(2H,7H)-dione;

8-((2-chloro-4-(methylthio)phenyl)amino)-2-(2-hydroxyethoxy)-7-methyl-3,4-dihydro-2,7-naphthyridine-1,6(2H,7H)-dione;

8-((4-(difluoromethoxy)-2-fluorophenyl)amino)-2-(2-hydroxyethoxy)-7-methyl-3,4-dihydro-2,7-naphthyridine-1,6(2H,7H)-dione;

8-((2-chloro-4-ethylphenyl)amino)-2-(2-hydroxyethoxy)-7-methyl-3,4-dihydro-2,7-naphthyridine-1,6(2H,7H)-dione;

8-((2-fluoro-4-(trifluoromethoxy)phenyl)amino)-2-(2-hydroxyethoxy)-7-methyl-3,4-dihydro-2,7-naphthyridine-1,6(2H,7H)-dione;

8-((4-((difluoromethyl)thio)-2-fluorophenyl)amino)-2-(2-hydroxyethoxy)-7-methyl-3,4-dihydro-2,7-naphthyridine-1,6(2H,7H)-dione;

8-((4-bromo-2-fluorophenyl)amino)-2-isopropoxy-7-methyl-3,4-dihydro-2,7-naphthyridine-1,6(2H,7H)-dione;

8-((2-fluoro-4-iodophenyl)amino)-2-isopropoxy-7-methyl-3,4-dihydro-2,7-naphthyridine-1,6(2H,7H)-dione;

2-ethoxy-8-((2-fluoro-4-iodophenyl)amino)-7-methyl-3,4-dihydro-2,7-naphthyridine-1,6(2H,7H)-dione;

8-((2-fluoro-4-iodophenyl)amino)-2-methoxy-7-methyl-3,4-dihydro-2,7-naphthyridine-1,6(2H,7H)-dione;

2-(tert-butoxy)-8-((2-fluoro-4-iodophenyl)amino)-7-methyl-3,4-dihydro-2,7-naphthyridine-1,6(2H,7H)-dione;

(S)-8-((2-fluoro-4-iodophenyl)amino)-2-(2-hydroxypropoxy)-7-methyl-3,4-dihydro-2,7-naphthyridine-1,6(2H,7H)-dione;

(R)-8-((2-fluoro-4-iodophenyl)amino)-2-(2-hydroxypropoxy)-7-methyl-3,4-dihydro-2,7-naphthyridine-1,6(2H,7H)-dione;

(S)-8-((4-bromo-2-fluorophenyl)amino)-2-(2-hydroxypropoxy)-7-methyl-3,4-dihydro-2,7-naphthyridine-1,6(2H,7H)-dione;

(R)-8-((4-bromo-2-fluorophenyl)amino)-2-(2-hydroxypropoxy)-7-methyl-3,4-dihydro-2,7-naphthyridine-1,6(2H,7H)-dione;

(R)-8-((4-bromo-2-fluorophenyl)amino)-2-(2-hydroxypropoxy)-5,7-dimethyl-3,4-dihydro-2,7-naphthyridine-1,6(2H,7H)-dione;

8-((4-bromo-2-fluorophenyl)amino)-2-(2-hydroxyethoxy)-5,7-dimethyl-3,4-

dihydro-2,7-naphthyridine-1,6(2H,7H)-dione;

8-((4-bromo-2-fluorophenyl)amino)-5-chloro-2-(2-hydroxyethoxy)-7-methyl-3,4-dihydro-2,7-naphthyridine-1,6(2H,7H)-dione;

5-chloro-8-((2-fluoro-4-iodophenyl)amino)-2-(2-hydroxyethoxy)-7-methyl-3,4-dihydro-2,7-naphthyridine-1,6(2H,7H)-dione;

8-((4-bromo-2-fluorophenyl)amino)-5-fluoro-2-(2-hydroxyethoxy)-7-methyl-3,4-dihydro-2,7-naphthyridine-1,6(2H,7H)-dione;

8-((2-fluoro-4-iodophenyl)amino)-2-(2-hydroxyethoxy)-5,7-dimethyl-3,4-dihydro-2,7-naphthyridine-1,6(2H,7H)-dione;

8-((2-fluorophenyl)amino)-2-(2-hydroxyethoxy)-5-iodo-7-methyl-3,4-dihydro-2,7-naphthyridine-1,6(2H,7H)-dione;

5-bromo-8-((4-bromo-2-fluorophenyl)amino)-2-(2-hydroxyethoxy)-7-methyl-3,4-dihydro-2,7-naphthyridine-1,6(2H,7H)-dione;

4-bromo-8-((2-fluorophenyl)amino)-2-(2-hydroxyethoxy)-5,7-dimethyl-3,4-dihydro-2,7-naphthyridine-1,6(2H,7H)-dione;

8-((4-ethyl-2-fluorophenyl)amino)-2-(2-hydroxyethoxy)-5,7-dimethyl-3,4-dihydro-2,7-naphthyridine-1,6(2H,7H)-dione;

8-((4-cyclopropyl-2-fluorophenyl)amino)-2-(2-hydroxyethoxy)-5,7-dimethyl-3,4-dihydro-2,7-naphthyridine-1,6(2H,7H)-dione;

8-((4-bromo-2-fluorophenyl)amino)-7-methyl-3,4-dihydro-2,7-naphthyridine-1,6(2H,7H)-dione ;

8-((4-bromo-2-fluorophenyl)amino)-5,7-dimethyl-3,4-dihydro-2,7-naphthyridine-1,6(2H,7H)-dione;

8-((2-fluoro-4-iodophenyl)amino)-5,7-dimethyl-3,4-dihydro-2,7-naphthyridine-1,6(2H,7H)-dione;

8-((4-iodo-2-fluorophenyl)amino)-7-methyl-3,4-dihydro-2,7-naphthyridine-1,6(2H,7H)-dione;

8-((2-fluoro-4-(methylthio)phenyl)amino)-7-methyl-3,4-dihydro-2,7-naphthyridine-1,6(2H,7H)-dione;

8-((4-ethyl-2-fluorophenyl)amino)-7-methyl-3,4-dihydro-2,7-naphthyridine-1,6(2H,7H)-dione;

8-((4-cyclopropyl-2-fluorophenyl)amino)-7-methyl-3,4-dihydro-2,7-naphthyridine-1,6(2H,7H)-dione;

8-((4-(difluoromethoxy)-2-fluorophenyl)amino)-7-methyl-3,4-dihydro-2,7-naphthyridine-1,6(2H,7H)-dione;

8-((2-fluoro-4-propylphenyl)amino)-7-methyl-3,4-dihydro-2,7-naphthyridine-1,6(2H,7H)-dione;

8-((2-fluoro-4-(methylthio)phenyl)amino)-5,7-dimethyl-3,4-dihydro-2,7-naphthyridine-1,6(2H,7H)-dione;

8-((4-ethyl-2-fluorophenyl)amino)-5,7-dimethyl-3,4-dihydro-2,7-naphthyridine-1,6(2H,7H)-dione;

8-((4-cyclopropyl-2-fluorophenyl)amino)-5,7-dimethyl-3,4-dihydro-2,7-naphthyridine-1,6(2H,7H)-dione;

8-((4-(difluoromethoxy)-2-fluorophenyl)amino)-5,7-dimethyl-3,4-dihydro-2,7-naphthyridine-1,6(2H,7H)-dione;

8-((4-bromo-2-chlorophenyl)amino)-7-methyl-3,4-dihydro-2,7-naphthyridine-1,6(2H,7H)-dione;

8-((4-bromo-2-fluorophenyl)amino)-2-(2-hydroxyethyl)-7-methyl-3,4-dihydro-2,7-naphthyridine-1,6(2H,7H)-dione;

8-((2-fluoro-4-(methylthio)phenyl)amino)-2-(2-hydroxyethoxy)-5,7-dimethyl-3,4-dihydro-2,7-naphthyridine-1,6(2H,7H)-dione;

8-((4-(difluoromethoxy)-2-fluorophenyl)amino)-2-(2-hydroxyethoxy)-5,7-dimethyl-3,4-dihydro-2,7-naphthyridine-1,6(2H,7H)-dione;

2-(2,2-difluoroethoxy)-8-((2-fluoro-4-(methylthio)phenyl)amino)-7-methyl-3,4-dihydro-2,7-naphthyridine-1,6(2H,7H)-dione;

8-((4-bromo-2-fluorophenyl)amino)-7-methyl-4-phenyl-3,4-dihydro-2,7-naphthyridine-1,6(2H,7H)-dione;

8-((2-fluoro-4-(methylthio)phenyl)amino)-7-methyl-4-phenyl-3,4-dihydro-2,7-naphthyridine-1,6(2H,7H)-dione;

8-((4-bromo-2-fluorophenyl)amino)-4,7-dimethyl-3,4-dihydro-2,7-naphthyridine-1,6(2H,7H)-dione;

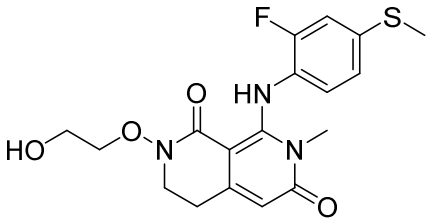
8-((2-fluoro-4-(methylthio)phenyl)amino)-4,7-dimethyl-3,4-dihydro-2,7-naphthyridine-1,6(2H,7H)-dione;

8-((4-bromo-2-fluorophenyl)amino)-2-(2-hydroxyethoxy)-4,7-dimethyl-3,4-dihydro-2,7-naphthyridine-1,6(2H,7H)-dione;

8-((2-fluoro-4-(methylthio)phenyl)amino)-2-(2-hydroxyethoxy)-4,7-dimethyl-3,4-dihydro-2,7-naphthyridine-1,6(2H,7H)-dione;

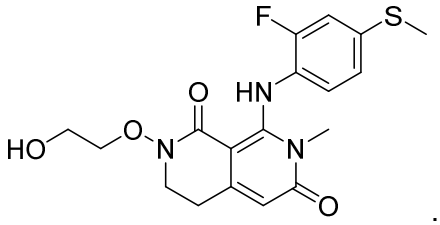
or a pharmaceutically acceptable salt thereof.

12. A compound which is 8-((2-fluoro-4-(methylthio)phenyl)amino)-2-(2-hydroxyethoxy)-7-methyl-3,4-dihydro-2,7-naphthyridine-1,6(2H,7H)-dione having the structure:



or a pharmaceutically acceptable salt thereof.

13. A compound which is 8-((2-fluoro-4-(methylthio)phenyl)amino)-2-(2-hydroxyethoxy)-7-methyl-3,4-dihydro-2,7-naphthyridine-1,6(2H,7H)-dione having the structure:



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14. Crystalline anhydrous 8-((2-fluoro-4-(methylthio)phenyl)amino)-2-(2-hydroxyethoxy)-7-methyl-3,4-dihydro-2,7-naphthyridine-1,6(2H,7H)-dione (Form 1), having a PXRD pattern measured using copper wavelength radiation comprising characterizing peaks at 5.0, 8.7, 9.3, 10.8, 14.5, 15.3, 18.8 and 20.5 degrees 2-theta ± 0.2 degrees 2-theta.

15. Crystalline anhydrous 8-((2-fluoro-4-(methylthio)phenyl)amino)-2-(2-hydroxyethoxy)-7-methyl-3,4-dihydro-2,7-naphthyridine-1,6(2H,7H)-dione (Form 2), having a PXRD pattern measured using copper wavelength radiation comprising characterizing peaks at 7.1, 9.4, 12.4, 12.8, 14.3, 15.6, 16.4, 17.4, 18.5, 18.9, 19.5, 19.9, 21.1, 21.4, 23.2, 23.7, 24.8, 25.6, 27.6, 30.3, 33.2, 33.5, and 37.5 degrees 2-theta ± 0.2 degrees 2-theta.

16. Crystalline monohydrate 8-((2-fluoro-4-(methylthio)phenyl)amino)-2-(2-hydroxyethoxy)-7-methyl-3,4-dihydro-2,7-naphthyridine-1,6(2H,7H)-dione (Form 3), having a PXRD pattern measured using copper wavelength radiation comprising characterizing peaks at 13.7, 18.0 and

18.3 degrees 2-theta ± 0.2 degrees 2-theta.

17. Amorphous 8-((2-fluoro-4-(methylthio)phenyl)amino)-2-(2-hydroxyethoxy)-7-methyl-3,4-dihydro-2,7-naphthyridine-1,6(2H,7H)-dione, Form 4.

18. A pharmaceutical composition, comprising a compound according to any one of claims 1 to 17 or a pharmaceutically acceptable salt thereof, and at least one pharmaceutically acceptable excipient.

19. A compound according to any one of claims 1 to 17, or a pharmaceutically acceptable salt thereof, for use as a medicament.

20. A compound according to one of claims 1 to 17, or a pharmaceutically acceptable salt thereof, for use in the treatment of a MEK-associated tumor.

21. Use of a compound according to any one of claims 1 to 17 or a pharmaceutically acceptable salt thereof, for the manufacture of a medicament for the treatment of a MEK-associated tumor in a subject in need thereof.

22. The use according to claim 21, wherein the MEK-associated tumor has a BRAF V600 mutation selected from V600E, V600K, V600D, V600R and V600S.

23. The use according to claim 21 or 22, wherein the MEK-associated tumor has a BRAF V600E mutation.

24. The use according to any one of claims 21 to 23, wherein the MEK-associated tumor is a CNS tumor.

25. The use according to claim 24, wherein the CNS tumor is an intracranial tumor.

26. The use according to claim 25, wherein the intracranial tumor is a brain cancer.

27. The use according to claim 26, wherein the brain cancer is a metastatic brain cancer.

28. The use according to claim 27, wherein the metastatic brain cancer is selected from metastatic melanoma, metastatic colorectal cancer, metastatic non-small cell lung cancer, metastatic thyroid cancer, and metastatic ovarian cancer.

29. The use according to claim 24, wherein the CNS tumor is intracranial LMD or extracranial LMD.

30. The use according to claim 29, wherein the LMD is selected from metastatic melanoma, metastatic colorectal cancer, and metastatic non-small cell lung cancer.

31. The use according to claim 25, wherein the intracranial tumor is a primary tumor.

32. The use according to claim 31, wherein the primary brain tumor is a malignant tumor.

33. The use according to claim 32, wherein the primary brain tumor is a Grade 2 glioma, a Grade 3 glioma or a Grade 4 glioma.

34. The use according to claim 31, wherein the primary brain tumor is a benign tumor.

35. The use according to claim 21, wherein the MEK-associated tumor has a BRAF fusion.

36. The use according to claim 35, wherein the MEK-associated tumor has a BRAF fusion selected from *KIAA11549-BRAF, MKRN1-BRAF, TRIM24-BRAF, AGAP3-BRAF, ZC3HAV1-BRAF, AKAP9-BRAF, CCDC6-BRAF, AGK-BRAF, EPS15-BRAF, NUP214-BRAF, ARMC10-BRAF, BTF3L4-BRAF, GHR-BRAF, ZC3HAV1-BRAF, ZNF767-BRAF, CCDC91-BRAF, DYNC112-BRAF, ZKSCAN1-BRAF, GTF2I-BRAF, MZT1-BRAF, RAD18-BRAF, CUX1-BRAF, SLC12A7-BRAF, MYRIP-BRAF, SND1-BRAF, NUB1-BRAF, KLHL7-BRAF, TANK-BRAF, RBMS3-BRAF, STRN3-BRAF, STK35-BRAF, ETFA-BRAF, SVOPL-BRAF,* and *JHDM1D-BRAF*.

37. The use according to claim 36, wherein the MEK-associated tumor is breast carcinoma, colorectal carcinoma, esophageal carcinoma, glioma, head and neck carcinoma, lung carcinoma, melanoma, pancreatic carcinoma, prostatic carcinoma, sarcoma, thyroid carcinoma,

unknown primary carcinoma, pleura mesothelioma, rectum adenocarcinoma, uterus endometrial carcinoma, or ovary serous carcinoma.

38. The use according to claim 21, wherein the MEK-associated tumor is a BRAF wild-type tumor.

39. The use according to any one of claims 21 to 38, wherein said compound is to be used in combination with one or more additional anticancer therapies.

40. The use according to claim 39, wherein the additional anticancer therapy is selected from one or more anticancer agents.

41. The use according to claim 40, where in the anticancer agent is a BRAF inhibitor.

42. The use according to claim 41, wherein the BRAF inhibitor is encorafenib or a pharmaceutically acceptable salt thereof.

43. The use according to claim 41, wherein the BRAF inhibitor is selected from:

N-(3-((3,5-dimethyl-4-oxo-3,4-dihydroquinazolin-6-yl)amino)-2,4-difluorophenyl)propane-1-sulfonamide;

N-(2-chloro-3-((3,5-dimethyl-4-oxo-3,4-dihydroquinazolin-6-yl)amino)phenyl)-3-fluoropropane-1-sulfonamide;

N-(2-chloro-3-((3,5-dimethyl-4-oxo-3,4-dihydroquinazolin-6-yl)amino)-4,5-difluorophenyl)propane-1-sulfonamide;

N-(2-chloro-3-((3,5-dimethyl-4-oxo-3,4-dihydroquinazolin-6-yl)amino)-4-fluorophenyl)propane-1-sulfonamide;

N-(2-chloro-3-((3,5-dimethyl-4-oxo-3,4-dihydroquinazolin-6-yl)amino)-4-fluorophenyl)-3-fluoropropane-1-sulfonamide;

N-(2-chloro-4-fluoro-3-((5-methyl-3-(methyl-d3)-4-oxo-3,4-dihydroquinazolin-6-yl)amino)-phenyl)-3-fluoropropane-1-sulfonamide;

N-{2-chloro-3-[(3,5-dimethyl-4-oxo-3,4-dihydroquinazolin-6-yl)oxy]-4-fluorophenyl}propane-1-sulfonamide;

N-(3-chloro-4-((3,5-dimethyl-4-oxo-3,4-dihydroquinazolin-6-yl)oxy)-5-fluoropyridin-2-yl)propane-1-sulfonamide; and

N-{2-chloro-3-[(3,5-dimethyl-4-oxo-3,4-dihydroquinazolin-6-yl)oxy]-4-fluorophenyl}-3-fluoropropane-1-sulfonamide;

or a pharmaceutically acceptable salt thereof.

44. The use according to claim 43, wherein the BRAF inhibitor is *N*-(2-chloro-3-((3,5-dimethyl-4-oxo-3,4-dihydroquinazolin-6-yl)amino)-4-fluorophenyl)-3-fluoropropane-1-sulfonamide or a pharmaceutically acceptable salt thereof.

45. The use according to claim 41, wherein the BRAF inhibitor is selected from:

N-(2-chloro-4-fluoro-3-((5-fluoro-3-methyl-4-oxo-3,4-dihydroquinazolin-6-yl)amino)phenyl)-2-azabicyclo[2.1.1]hexane-2-sulfonamide,

(R)-N-(2-chloro-4-fluoro-3-((5-fluoro-3-methyl-4-oxo-3,4-dihydroquinazolin-6-yl)amino)phenyl)-3-fluoropyrrolidine-1-sulfonamide, and

N-(2-chloro-3-((5-chloro-3-methyl-4-oxo-3,4-dihydroquinazolin-6-yl)amino)-4-fluorophenyl)-3-fluoroazetidine-1-sulfonamide,

or a pharmaceutically acceptable salt thereof.

46. The use according to claim 45, wherein the BRAF inhibitor is N-(2-chloro-3-((5-chloro-3-methyl-4-oxo-3,4-dihydroquinazolin-6-yl)amino)-4-fluorophenyl)-3-fluoroazetidine-1-sulfonamide, or a pharmaceutically acceptable salt thereof.

47. The use according to claim 40, wherein the anticancer agent is a SHP2 inhibitor.

48. The use according to claim 47, wherein the SHP2 inhibitor is (S)-1'-(6-((2-amino-3-chloropyridin-4-yl)thio)-1,2,4-triazin-3-yl)-1,3-dihydrospiro[indene-2,4'-piperidin]-1-amine or a pharmaceutically acceptable salt thereof.

49. The use according to any one of claims 21 to 48, wherein the subject is a human.