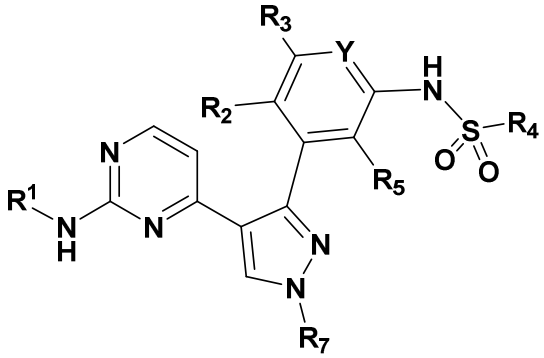
CLAIMS

1. A compound of Formula I for use in a method of treating cancer, wherein the compound of Formula I is



I

in which:

Y is selected from N and CR_6;

R_1 is $–CH_2CHMeNH(CO)OMe$;

R_2, R_3, R_5 and R_6 are independently selected from hydrogen, halo, cyano, C_{1-4}alkyl, halo-substituted-C_{1-4}alkyl, C_{1-4}alkoxy and halo-substituted-C_{1-4}alkoxy; with the proviso that when R_5 is fluoro, R_3 and R_6 are not both hydrogen;

R_4 is selected from $–R_9$ and $–NR_{10}R_{11}$; wherein R_9 is selected from C_{1-6}alkyl, C_{3-8}cycloalkyl, C_{3-8}heterocycloalkyl, aryl and heteroaryl; wherein

said alkyl, cycloalkyl, heterocycloalkyl, aryl or heteroaryl of R_9 is optionally substituted with 1 to 3 radicals independently selected from halo, cyano, C_{1-4}alkyl, halo-substituted-C_{1-4}alkyl, C_{1-4}alkoxy and halo-substituted-C_{1-4}alkoxy; and R_{10} and R_{11} are independently selected from hydrogen and R_9;

R_7 is selected from C_{1-4}alkyl, C_{3-5}cycloalkyl and C_{3-5}heterocycloalkyl; wherein said alkyl, cycloalkyl or heterocycloalkyl of R_7 is optionally substituted with 1 to 3 radicals independently selected from halo, cyano, hydroxyl, C_{1-4}alkyl, halo-substituted-C_{1-4}alkyl, C_{1-4}alkoxy and halo-substituted-C_{1-4}alkoxy;

or R_7 is hydrogen;

and the N-oxide derivatives, the tautomers, and the pharmaceutically acceptable salts and solvates (e.g. hydrates) of such compounds.

2. The compound for use in a method of treatment according to claim 1, wherein R_7 is selected from C_{1-4}alkyl, C_{3-5}cycloalkyl and C_{3-5}heterocycloalkyl; wherein said alkyl, cycloalkyl or heterocycloalkyl of R_7 is optionally substituted with 1 to 3 radicals independently selected from halo, cyano, hydroxyl, C_{1-4}alkyl, halo-substituted-C_{1-4}alkyl, C_{1-4}alkoxy and halo-substituted-C_{1-4}alkoxy.

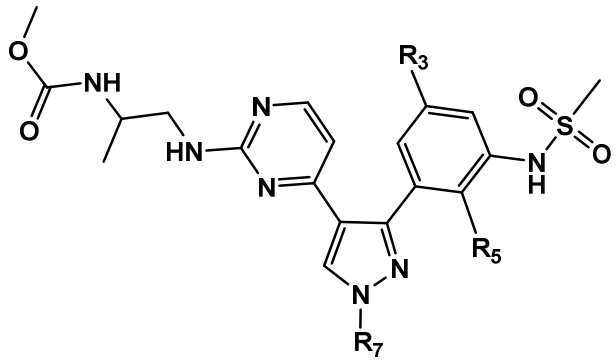
3. The compound for use in a method of treatment according to any preceding claim in which R_4 is $–R_9$; wherein R_9 is selected from C_{1-3}alkyl and C_{3-8}cycloalkyl; wherein said alkyl or cycloalkyl of R_9 is optionally substituted with 1 to 3 radicals independently selected from halo and halo-substituted-C_{1-4}alkyl.

4. The compound for use in a method of treatment according to claim 3 in which:

R_2 is selected from hydrogen and fluoro;
R_3 is selected from chloro, fluoro and methyl;
R_5 is selected from hydrogen, chloro and fluoro;
Y is selected from N and CR_6; and
R_6 is selected from hydrogen and fluoro.

5. The compound for use in a method of treatment according to claim 1, wherein the compound is selected from:
methyl N-[(2S)-1-({4-[3-(3-ethanesulfonamido-2,4-difluorophenyl)-1-(propan-2-yl)-1H-pyrazol-4-yl]pyrimidin-2-yl}amino)propan-2-yl]carbamate;
methyl N-[(2S)-2-({4-[3-(5-chloro-2-fluoro-3-methanesulfonamidophenyl)-1-(propan-2-yl)-1H-pyrazol-4-yl]pyrimidin-2-yl}amino)propyl]carbamate;
methyl N-[(2S)-1-({4-[3-(5-chloro-2-fluoro-3-methanesulfonamidophenyl)-1-(oxan-2-yl)-1H-pyrazol-4-yl]pyrimidin-2-yl}amino)propan-2-yl]carbamate; and
methyl N-[(2S)-1-({4-[3-(5-chloro-2-fluoro-3-methanesulfonamidophenyl)-1H-pyrazol-4-yl]pyrimidin-2-yl}amino)propan-2-yl]carbamate.

6. The compound for use in a method of treatment according to claim 1, wherein the compound is a compound of Formula Ib:



Ib

in which:

R_3 is selected from chloro, fluoro and methyl;

R_5 is selected from fluoro and chloro; and

R_7 is selected from ethyl and isopropyl.

7. A pharmaceutical composition comprising the compound of any one of claims 1-6, admixed with at least one pharmaceutically acceptable excipient for use in a method of treating cancer.

8. The compound for use in a method of treatment of any one of claims 1-6 or the pharmaceutical composition for use in a method of treatment according to claim 7, wherein the cancer to be treated is selected from the group consisting of lung carcinoma, pancreatic carcinoma, bladder carcinoma, colon carcinoma, myeloid disorders, prostate cancer, thyroid cancer, melanoma, adenomas and carcinomas of the ovary, eye, liver, biliary tract, and nervous system.

9. The compound for use in a method of treatment of any one of claims 1-6 or the pharmaceutical composition for use in a method of treatment according to claim 7, the method further comprising administering to the subject an additional therapeutic agent, optionally wherein the additional therapeutic agent is administered to the subject concurrently with the compound.

10. The compound for use in a method of treatment of any one of claims 1-6 or the pharmaceutical composition for use in a method of treatment according to claim 7, the method further comprising administering to the subject an additional therapeutic agent,

optionally wherein the additional therapeutic agent is administered to the subject sequentially with the compound.

11. The compound for use in a method of treatment or the pharmaceutical composition for use in a method of treatment of claim 10, wherein the compound of Formula I is methyl N-[(2S)-1-({4-[3-(5-chloro-2-fluoro-3-methanesulfonamidophenyl)-1-(propan-2-yl)-1H-pyrazol-4-yl]pyrimidin-2-yl}amino)propan-2-yl]carbamate.

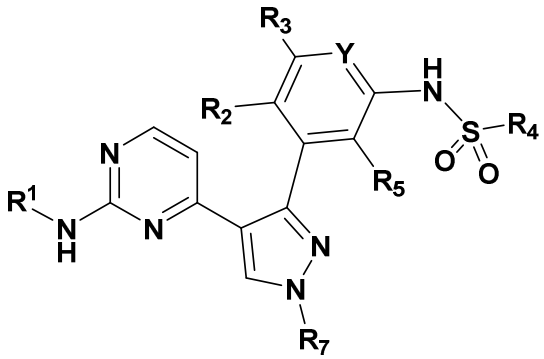
12. The compound for use in a method of treatment or the pharmaceutical composition for use in a method of treatment of any one of claims 9-11, wherein:
(a) the additional therapeutic agent comprises an anticancer drug, a pain medication, an antiemetic, an antidepressant or an anti-inflammatory agent; or
(b) the additional therapeutic agent is a different Raf kinase inhibitor or an inhibitor of MEK, mTOR, HSP90, AKT, PI3K, CDK9, PAK, Protein Kinase C, a MAP kinase, a MAPK Kinase, or ERK; or
(c) a MEK inhibitor selected from: AS703026; MSC1936369B; GSK1120212; AZD6244; PD-0325901; ARRY-438162; RDEA119; GDC0941; GDC0973; TAK-733; RO5126766; and XL-518.

13. The compound for use in a method of treatment or the pharmaceutical composition for use in a method of treatment according to any one of claims 9 to 12, wherein the cancer is melanoma or colorectal cancer.

14. The compound for use in a method of treatment or the pharmaceutical composition for use in a method of treatment according to claim 13, wherein the melanoma is metastatic melanoma or the colorectal cancer is colon carcinoma.

15. The compound for use in a method of treatment according to any one of claims 1-6 and 8-14 or the pharmaceutical composition for use in a method of treatment according to any one of claims 7-14, wherein the compound is for treating a condition mediated by Raf kinase, optionally wherein the Raf kinase is a mutant b-Raf kinase such as b-Raf (V600E).

16. The use of a compound of Formula I in the manufacture of a medicament for the treatment of cancer, wherein the compound of Formula I is



I

in which:

Y is selected from N and CR_6;

R_1 is $–CH_2CHMeNH(CO)OMe$;

R_2, R_3, R_5 and R_6 are independently selected from hydrogen, halo, cyano, C_{1-4}alkyl, halo-substituted-C_{1-4}alkyl, C_{1-4}alkoxy and halo-substituted-C_{1-4}alkoxy; with the proviso that when R_5 is fluoro, R_3 and R_6 are not both hydrogen;

R_4 is selected from $–R_9$ and $–NR_{10}R_{11}$; wherein R_9 is selected from C_{1-6}alkyl, C_{3-8}cycloalkyl, C_{3-8}heterocycloalkyl, aryl and heteroaryl; wherein

said alkyl, cycloalkyl, heterocycloalkyl, aryl or heteroaryl of R_9 is optionally substituted with 1 to 3 radicals independently selected from halo, cyano, C_{1-4}alkyl, halo-substituted-C_{1-4}alkyl, C_{1-4}alkoxy and halo-substituted-C_{1-4}alkoxy; and R_{10} and R_{11} are independently selected from hydrogen and R_9;

R_7 is selected from C_{1-4}alkyl, C_{3-5}cycloalkyl and C_{3-5}heterocycloalkyl; wherein said alkyl, cycloalkyl or heterocycloalkyl of R_7 is optionally substituted with 1 to 3 radicals independently selected from halo, cyano, hydroxyl, C_{1-4}alkyl, halo-substituted-C_{1-4}alkyl, C_{1-4}alkoxy and halo-substituted-C_{1-4}alkoxy;

or R_7 is hydrogen;

and the N-oxide derivatives, the tautomers, and the pharmaceutically acceptable salts and solvates (e.g. hydrates) of such compounds.

17. The use of claim 16 wherein R_7 is selected from C_{1-4}alkyl, C_{3-5}cycloalkyl and C_{3-5}heterocycloalkyl; wherein said alkyl, cycloalkyl or heterocycloalkyl of R_7 is optionally

substituted with 1 to 3 radicals independently selected from halo, cyano, hydroxyl, C_{1-4}alkyl, halo-substituted-C_{1-4}alkyl, C_{1-4}alkoxy and halo-substituted-C_{1-4}alkoxy.

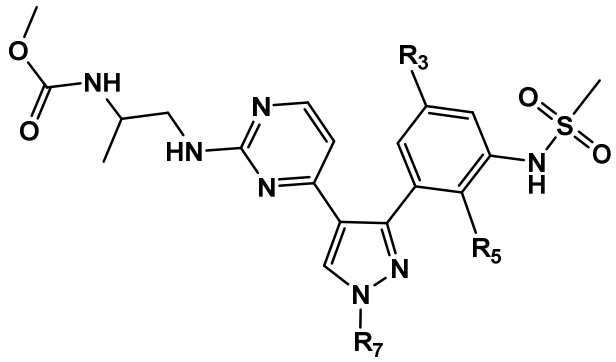
18. The use of any one of claims 16-17 in which R_4 is $-R_9$; wherein R_9 is selected from C_{1-3}alkyl and C_{3-8}cycloalkyl; wherein said alkyl or cycloalkyl of R_9 is optionally substituted with 1 to 3 radicals independently selected from halo and halo-substituted-C_{1-4}alkyl.

19. The use of claim 18 in which:

R_2 is selected from hydrogen and fluoro;
R_3 is selected from chloro, fluoro and methyl;
R_5 is selected from hydrogen, chloro and fluoro;
Y is selected from N and CR_6; and
R_6 is selected from hydrogen and fluoro.

20. The use of claim 16, wherein the compound is selected from:
methyl N-[(2S)-1-({4-[3-(3-ethanesulfonamido-2,4-difluorophenyl)-1-(propan-2-yl)-1H-pyrazol-4-yl]pyrimidin-2-yl}amino)propan-2-yl]carbamate;
methyl N-[(2S)-2-({4-[3-(5-chloro-2-fluoro-3-methanesulfonamidophenyl)-1-(propan-2-yl)-1H-pyrazol-4-yl]pyrimidin-2-yl}amino)propyl]carbamate;
methyl N-[(2S)-1-({4-[3-(5-chloro-2-fluoro-3-methanesulfonamidophenyl)-1-(oxan-2-yl)-1H-pyrazol-4-yl]pyrimidin-2-yl}amino)propan-2-yl]carbamate; and
methyl N-[(2S)-1-({4-[3-(5-chloro-2-fluoro-3-methanesulfonamidophenyl)-1H-pyrazol-4-yl]pyrimidin-2-yl}amino)propan-2-yl]carbamate.

21. The use of claim 16, wherein the compound is a compound of Formula Ib:



Ib

in which:

R_3 is selected from chloro, fluoro and methyl;

R_5 is selected from fluoro and chloro; and

R_7 is selected from ethyl and isopropyl.

22. The use of any one of claims 16-21, wherein the cancer to be treated is selected from the group consisting of lung carcinoma, pancreatic carcinoma, bladder carcinoma, colon carcinoma, myeloid disorders, prostate cancer, thyroid cancer, melanoma, adenomas and carcinomas of the ovary, eye, liver, biliary tract, and nervous system.

23. The use of any one of claims 16-21, the treatment further comprising administering to the subject an additional therapeutic agent, optionally wherein the additional therapeutic agent is administered to the subject concurrently with the compound.

24. The use of any one of claims 16-21, the treatment further comprising administering to the subject an additional therapeutic agent, optionally wherein the additional therapeutic agent is administered to the subject sequentially with the compound.

25. The use of claim 24, wherein the compound of Formula I is methyl N-[(2S)-1-({4-[3-(5-chloro-2-fluoro-3-methanesulfonamidophenyl)-1-(propan-2-yl)-1H-pyrazol-4-yl]pyrimidin-2-yl}amino)propan-2-yl]carbamate.

26. The use according to any one of claims 23-25, wherein:
(a) the additional therapeutic agent comprises an anticancer drug, a pain medication, an antiemetic, an antidepressant or an anti-inflammatory agent; or

(b) the additional therapeutic agent is a different Raf kinase inhibitor or an inhibitor of MEK, mTOR, HSP90, AKT, PI3K, CDK9, PAK, Protein Kinase C, a MAP kinase, a MAPK Kinase, or ERK; or
(c) a MEK inhibitor selected from: AS703026; MSC1936369B; GSK1120212; AZD6244; PD-0325901; ARRY-438162; RDEA119; GDC0941; GDC0973; TAK-733; RO5126766; and XL-518.

27. The use according to any one of claims 23 to 26, wherein the cancer is melanoma or colorectal cancer.

28. The use according to claim 27, wherein the melanoma is metastatic melanoma or the colorectal cancer is colon carcinoma.

29. The use according to any one of claims 16-28, wherein the compound is for treating a condition mediated by Raf kinase, optionally wherein the Raf kinase is a mutant b-Raf kinase such as b-Raf (V600E).