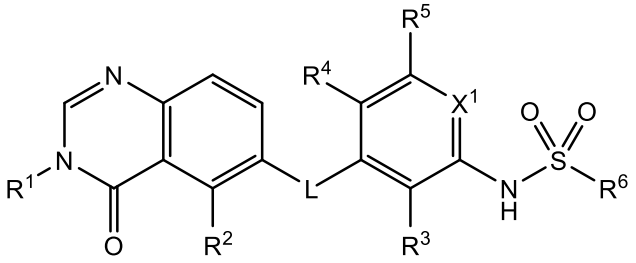
What is claimed is:

1. A compound of Formula I



I

and pharmaceutically acceptable salts, solvates and polymorphs thereof, wherein:

L is O, NH or S;

X^1 is CH or N;

R^1 is C1-C6 alkyl, C1-C6 deuteroalkyl, C1-C6 fluoroalkyl, C3-C6 cycloalkyl, (C3-C6 cycloalkyl)CH_2-, (C1-C6 alkoxy)C1-C6 alkyl-, Ar^1, Ar^1CH_2-, $hetAr^1$ or $hetCyc^1$;

Ar^1 is phenyl which is optionally substituted with 1-5 substituents independently selected from halogen and C1-C3 alkyl;

$hetAr^1$ is a 5-6 membered heteroaryl ring having 1-2 ring nitrogen atoms and optionally substituted with 1-3 substituents independently selected from halogen and C1-C3 alkyl;

$hetCyc^1$ is a 4-6 membered saturated monocyclic heterocyclic ring having one ring oxygen atom;

R^2 is methyl, -CD_3 or HC≡C-;

R^3 is F, Cl, CN or methyl;

R^4 is H, F or Cl;

R^5 is H, F, Cl, methyl;

R^6 is C1-C6 alkyl, C1-C6 fluoroalkyl, (Cyc^1)C1-C6 alkyl-, (C1-C3 alkoxy)C1-C6 alkyl-, $hetAr^2$, Ar^2 or R^aR^bN-;

Cyc^1 is a 3-6 membered saturated carbocyclic ring;

$hetAr^2$ is a 5-6 membered heteroaryl having 1-2 ring heteroatoms independently selected from N, O and S and optionally substituted with 1-3 substituents independently selected from halogen and C1-C3 alkyl;

Ar^2 is phenyl optionally substituted with 1-5 substituents independently selected from halogen and C1-C6 alkyl; and

R^a and R^b are independently C1-C3 alkyl, or

R^a and R^b together with the nitrogen atom to which they are attached form a 5-6 membered saturated monocyclic heterocyclic ring optionally substituted with fluoro.

2. The compound according to claim 1 or a pharmaceutically acceptable salt, solvate or polymorph thereof, wherein X^1 is CH.

3. The compound according to any one of claims 1-2 a pharmaceutically acceptable salt, solvate or polymorph thereof, wherein R^6 is C1-C6 alkyl, C1-C6 fluoroalkyl, (Cyc^1)C1-C6 alkyl-, (C1-C3 alkoxy)C1-C6 alkyl-, $hetAr^2$ or Ar^2.

4. The compound according to any one of claims 1-3 or a pharmaceutically acceptable salt, solvate or polymorph thereof, wherein R^1 is C1-C6 alkyl.

5. The compound according to any one of claims 1-3 or a pharmaceutically acceptable salt, solvate or polymorph thereof, wherein R^1 is C1-C6 fluoroalkyl.

6. The compound according to any one of claims 1-5 or a pharmaceutically acceptable salt, solvate or polymorph thereof, wherein L is NH.

7. The compound according to any one of claims 1-5 or a pharmaceutically acceptable salt, solvate or polymorph thereof, wherein L is O.

8. The compound according to any one of claims 1-7 or a pharmaceutically acceptable salt, solvate or polymorph thereof, wherein R^2 is methyl.

9. The compound according to claim 1, selected from:

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

(R)-*N*-(2-chloro-3-((3,5-dimethyl-4-oxo-3,4-dihydroquinazolin-6-yl)amino)-4-fluorophenyl)-3-fluoropyrrolidine-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-4-fluoro-3-((5-methyl-3-(methyl-d3)-4-oxo-3,4-dihydroquinazolin-6-yl)amino)phenyl)propane-1-sulfonamide,

N-(2-chloro-3-((3,5-dimethyl-4-oxo-3,4-dihydroquinazolin-6-yl)amino)-4-fluorophenyl)-2,5-difluorobenzenesulfonamide,

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

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

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

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

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

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

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

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

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

(S)-N-(2-chloro-4-fluoro-3-((5-methyl-4-oxo-3-(tetrahydrofuran-3-yl)-3,4-dihydroquinazolin-6-yl)amino)phenyl)propane-1-sulfonamide,

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

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

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

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

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

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

1-cyclopropyl-*N*-(4-((3,5-dimethyl-4-oxo-3,4-dihydroquinazolin-6-yl)amino)-3,5-difluoropyridin-2-yl)methanesulfonamide,

N-(4-((3,5-dimethyl-4-oxo-3,4-dihydroquinazolin-6-yl)amino)-3,5-difluoropyridin-2-yl)ethanesulfonamide,

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

N-(3-chloro-4-((3,5-dimethyl-4-oxo-3,4-dihydroquinazolin-6-yl)amino)-5-fluoropyridin-2-yl)ethanesulfonamide,

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

N-(3-chloro-4-((3,5-dimethyl-4-oxo-3,4-dihydroquinazolin-6-yl)amino)-5-fluoropyridin-2-yl)-1-cyclopropylmethanesulfonamide,

N-(2,5-dichloro-3-((3,5-dimethyl-4-oxo-3,4-dihydroquinazoli-6-yl)amino)phenyl)propane-1-sulfonamide,

N-(2-chloro-3-((3,5-dimethyl-4-oxo-3,4-dihydroquinazolin-6-yl)amino)-4-fluorophenyl)benzenesulfonamide,

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

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

N-(2-chloro-3-((3,5-dimethyl-4-oxo-3,4-dihydroquinazolin-6-yl)amino)-4-fluorophenyl)ethanesulfonamide,

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

N-(2-chloro-3-((3,5-dimethyl-4-oxo-3,4-dihydroquinazolin-6-yl)amino)-4-fluorophenyl)-*N*-ethyl-*N*-methylamino-1-sulfonamide,

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

N-(3-((3,5-dimethyl-4-oxo-3,4-dihydroquinazolin-6-yl)oxy)-2,4-difluorophenyl)-3-fluoropropane-1-sulfonamide,

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

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

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

N-(2-chloro-3-((5-ethynyl-3-methyl-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)butane-2-sulfonamide,

N-(4-((3,5-dimethyl-4-oxo-3,4-dihydroquinazolin-6-yl)oxy)-3,5-difluoropyridin-2-yl)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,

N-(4-((3,5-dimethyl-4-oxo-3,4-dihydroquinazolin-6-yl)oxy)-3,5-difluoropyridin-2-yl)-3-fluoropropane-1-sulfonamide,

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

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

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

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

N-(2-cyano-3-((3,5-dimethyl-4-oxo-3,4-dihydroquinazolin-6-yl)oxy)-4-fluorophenyl)propane-1-sulfonamide,

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

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

N-(3-((3,5-dimethyl-4-oxo-3,4-dihydroquinazolin-6-yl)oxy)-2,4,5-trifluorophenyl)propane-1-sulfonamide,

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

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

N-(3-((3,5-dimethyl-4-oxo-3,4-dihydroquinazolin-6-yl)oxy)-2-fluoro-5-methylphenyl)propane-1-sulfonamide,

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

N-(3-((3,5-dimethyl-4-oxo-3,4-dihydroquinazolin-6-yl)oxy)-2,5-difluorophenyl)-3-fluoropropane-1-sulfonamide,

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

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

N-(3-((3,5-dimethyl-4-oxo-3,4-dihydroquinazolin-6-yl)oxy)-2-fluorophenyl)-3-fluoropropane-1-sulfonamide, and

pharmaceutically acceptable salts and solvates thereof, and

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

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

3-fluoropropane-1-sulfonamide Form B anhydrous,

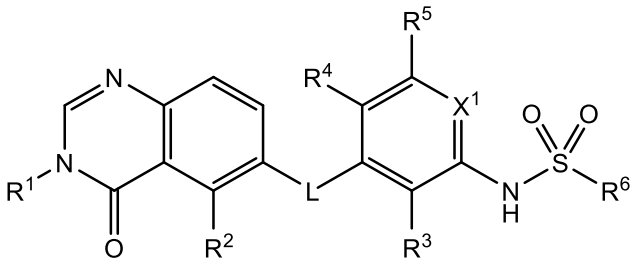
N-(2-chloro-3-((3,5-dimethyl-4-oxo-3,4-dihydroquinazolin-6-yl)amino)-4-fluorophenyl)-3-fluoropropane-1-sulfonamide Form C mono-anisole,

N-(2-chloro-3-((3,5-dimethyl-4-oxo-3,4-dihydroquinazolin-6-yl)amino)-4-fluorophenyl)-3-fluoropropane-1-sulfonamide Form D hemi-dichloromethane solvate,

N-(2-chloro-3-((3,5-dimethyl-4-oxo-3,4-dihydroquinazolin-6-yl)amino)-4-fluorophenyl)-3-fluoropropane-1-sulfonamide Form E mono-toluene solvate, and

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

10. A compound of Formula II



II

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

L is NH, O or S;

X^1 is CH or N;

R^1 is C1-C6 alkyl, C1-C6 deuteroalkyl, C1-C6 fluoroalkyl, C3-C6 cycloalkyl, (C3-C6 cycloalkyl)CH_2-, Ar^1, Ar^1CH_2- or $hetCyc^1$;

Ar^1 is phenyl which is optionally substituted with 1-5 substituents independently selected from halogen and C1-C3 alkyl;

$hetCyc^1$ is a 4-6 membered saturated monocyclic heterocyclic ring having one ring oxygen atom;

R^2 is methyl;

R^3 is F or Cl;

R^4 is H, F or Cl;

R^5 is H, F, Cl or methyl;

R^6 is C1-C6 alkyl, C1-C6 fluoroalkyl, (Cyc^1)C1-C6 alkyl-, (C1-C3 alkoxy)C1-C6 alkyl-, Ar^2 or R^aR^bN-;

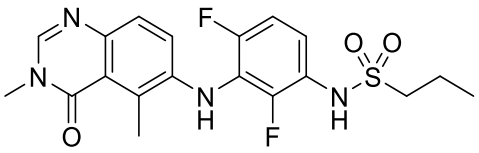
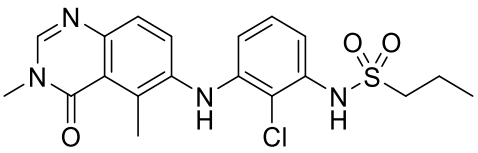
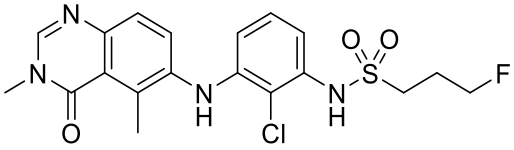
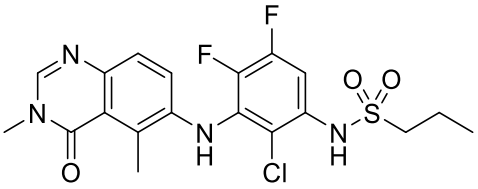
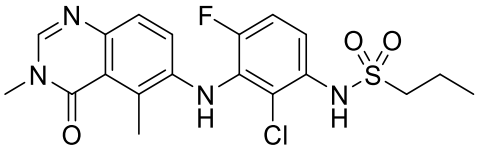
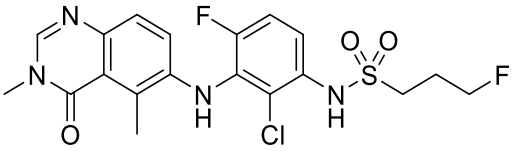
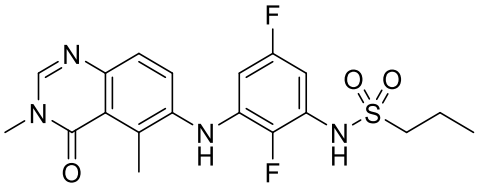
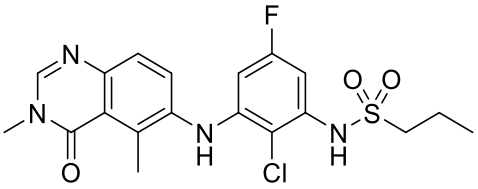
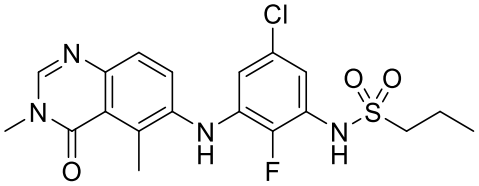
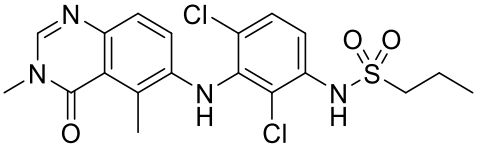
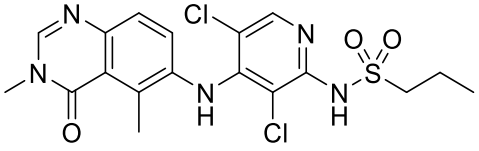
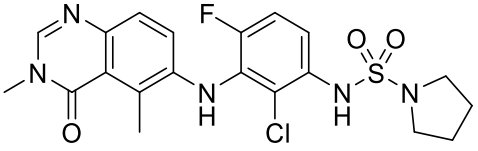
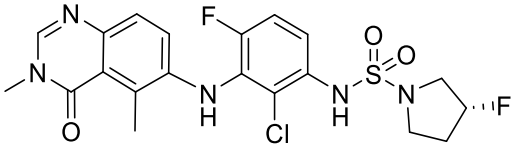
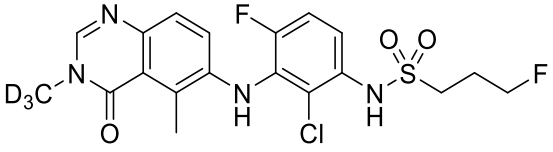
Cyc^1 is a 3-6 membered saturated carbocyclic ring;

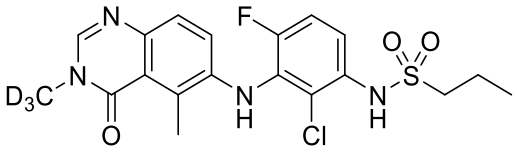
Ar^2 is phenyl optionally substituted with 1-5 substituents independently selected from halogen and C1-C3 alkyl; and

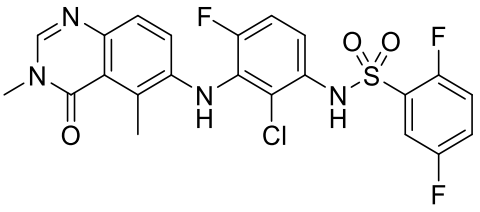
R^a and R^b are independently C1-C6 alkyl, or

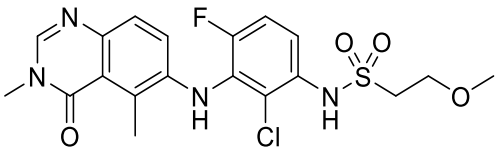
R^a and R^b together with the nitrogen atom to which they are attached form a 5-6 membered saturated monocyclic heterocyclic ring optionally substituted with fluoro.

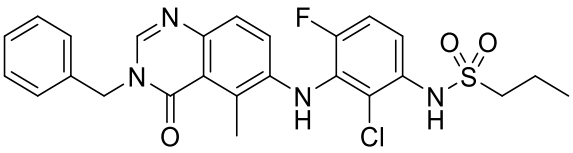
11. The compound according to claim 10, selected from:

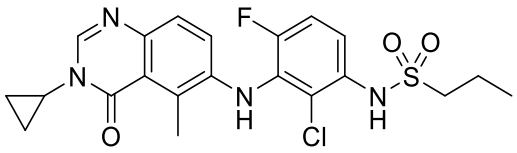















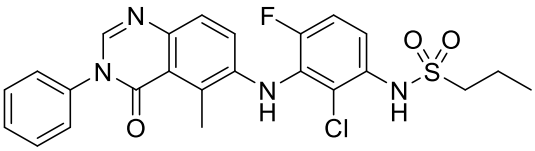


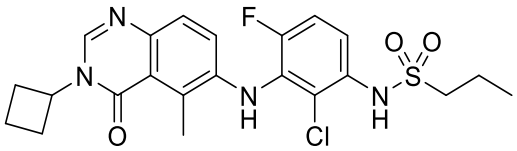


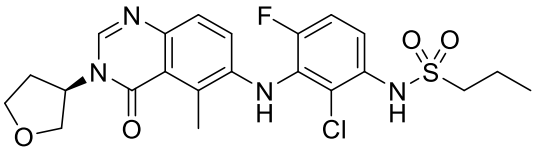


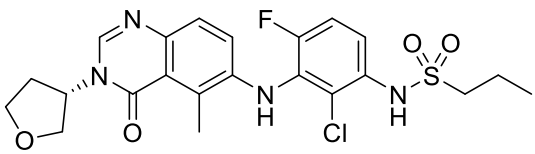


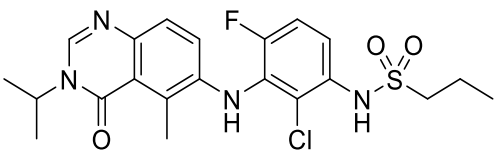


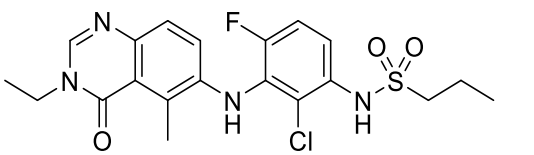


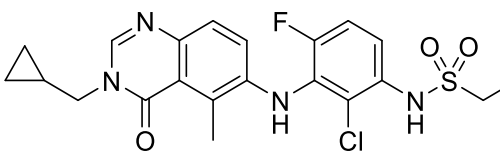


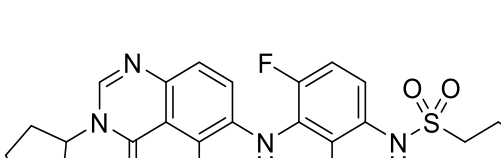


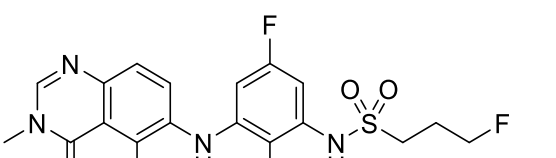


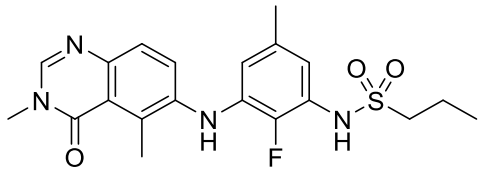


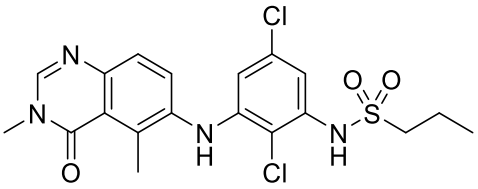


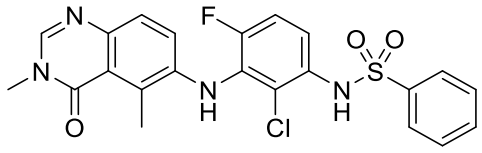


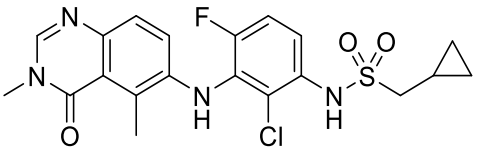


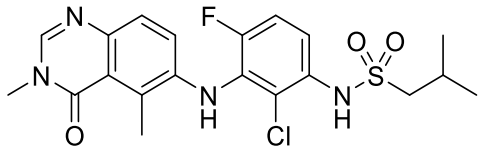


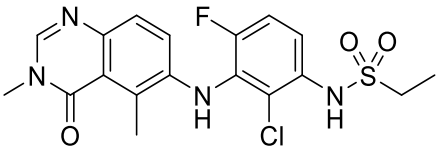


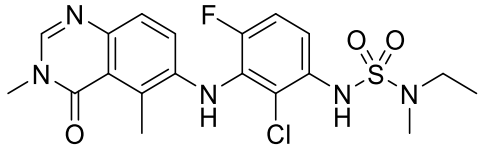


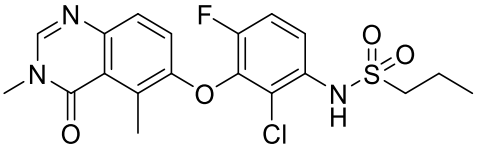


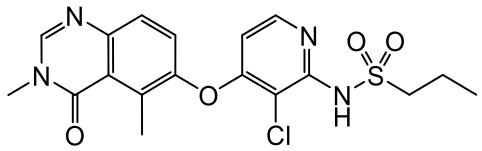


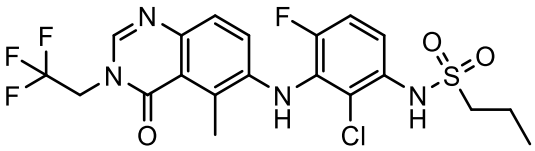


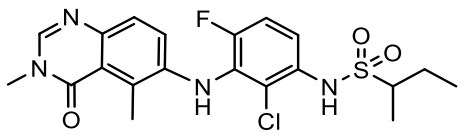


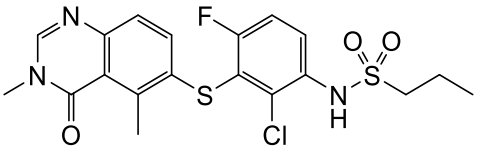


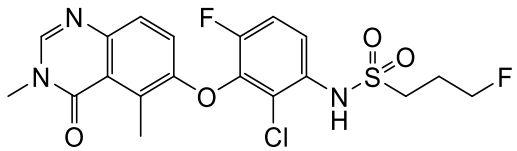


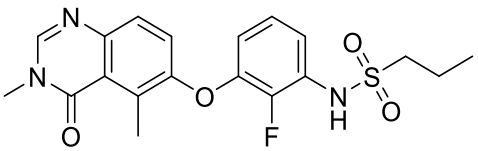


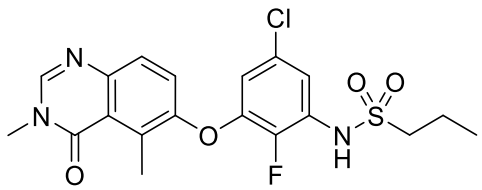


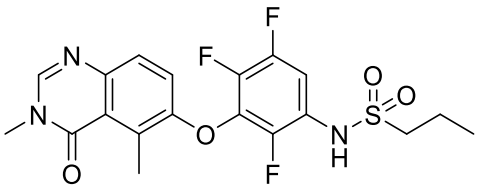
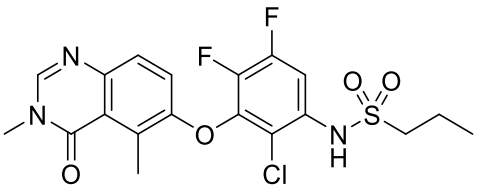
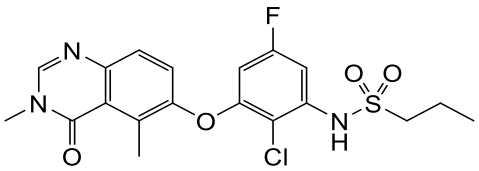
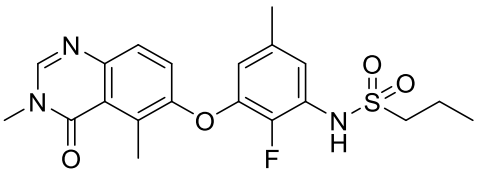
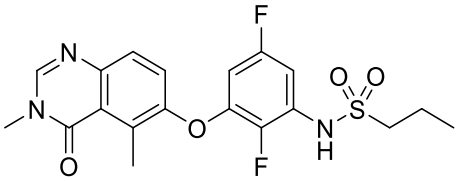
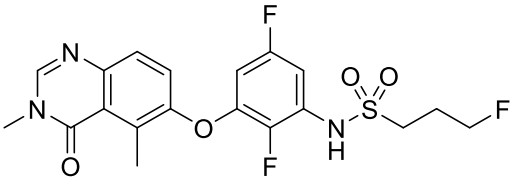
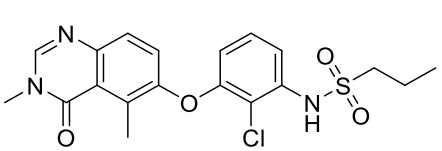
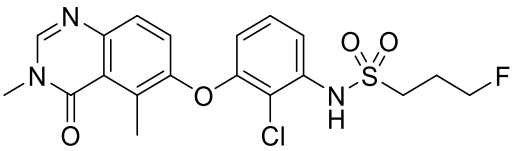
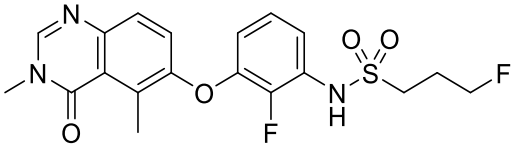




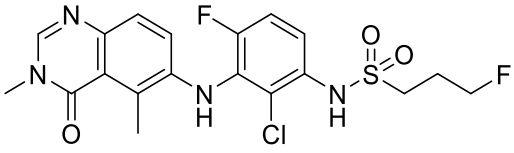




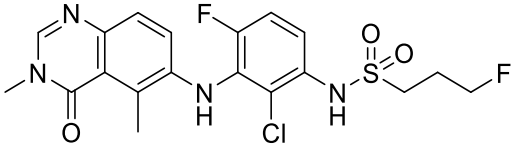


and pharmaceutically acceptable salts and solvates thereof,

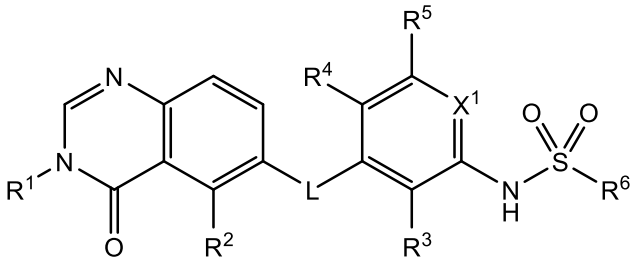


Form B anhydrous; and



Form A anhydrous.

12. A compound of Formula III



III

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

L is NH or O;

X^1 is CH or N;

R^1 is C1-C6 alkyl or C1-C6 deuteroalkyl;

R^2 is methyl;

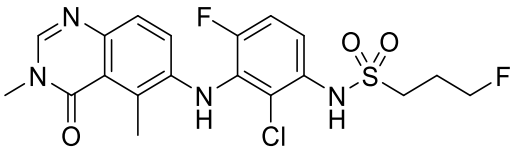
R^3 is F or Cl;

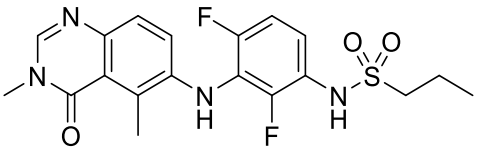
R^4 is H or F;

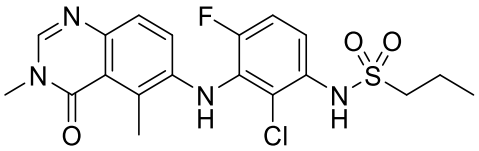
R^5 is H or F; and

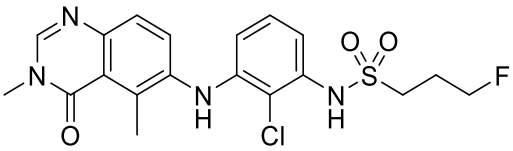
R^6 C1-C6 alkyl or C1-C6 fluoroalkyl.

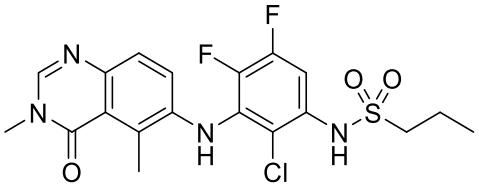
13. The compound according to claim 12, selected from:

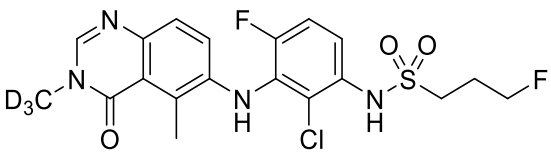


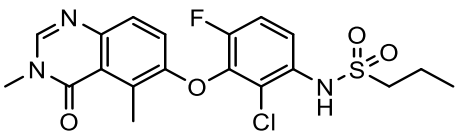


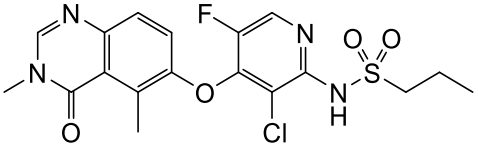


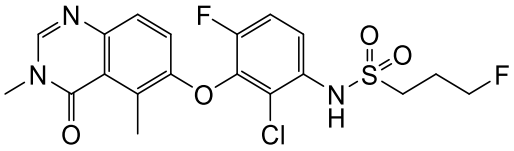




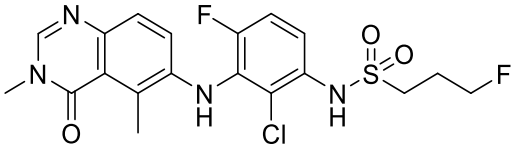




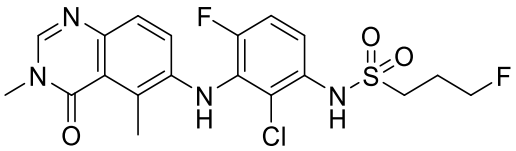




and pharmaceutically acceptable salts and solvates thereof,

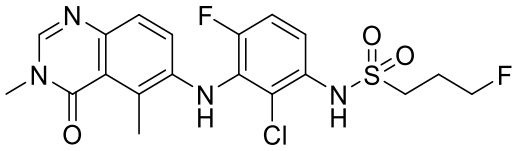


Form B anhydrous, and



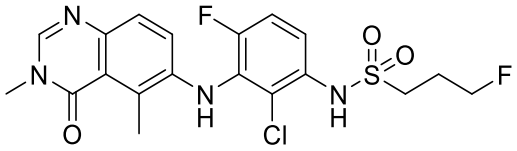
Form A anhydrous.

14. A compound , which is



or a pharmaceutically acceptable salt or solvate thereof.

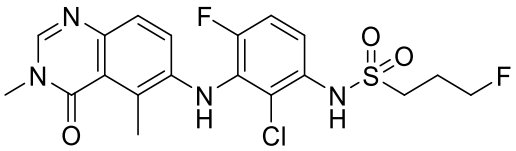
15. A compound , which is



Form B anhydrous.

16. The compound according to claim 15, characterized by having an XRPD pattern comprising peaks at 2θ values of 17.23, 22.93, 25.54, 26.22 and 27.69 (± 0.2 º2θ).

17. A compound which is A compound which is



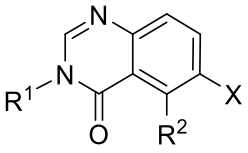
Form A anhydrous.

18. The compound of claim 17, characterized by having an XRPD pattern comprising peaks at 2θ values of 10.4, 10.8, 12.3, 14.2, 14.5, 16.3, 20.5, and 23.6 (± 0.2 º2θ).

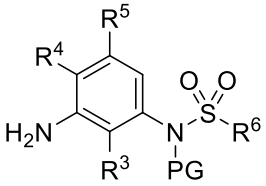
19. A pharmaceutical composition, comprising a compound according to any one of claims 1-18 in admixture with a pharmaceutically acceptable diluent or carrier.

20. A process for preparing a compound according to claim 1 or a pharmaceutically acceptable salt or solvate thereof, comprising:

(a) for a compound of claim 1 wherein X^1 is CH, L is NH, and R^1, R^2, R^3, R^4, R^5 and R^6 are as defined for claim 1, coupling a compound having the formula:

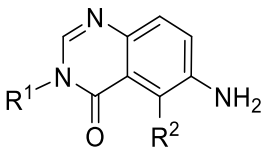


wherein R^1 and R^2 are as defined in claim 1 and X is a halogen, with a compound having the formula:



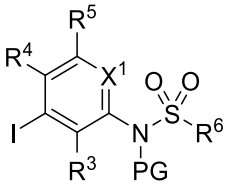
wherein R^3, R^4, R^5 and R^6 are as in claim 1 and PG is an amine protecting group, in the presence of a catalyst and a ligand, followed by removal of the amine protecting group; or

(b) for a compound of claim 1 wherein L is NH, and X^1, R^1, R^2, R^3, R^4, R^5 and R^6 are as defined for claim 1, coupling a compound having the formula (23):



(23)

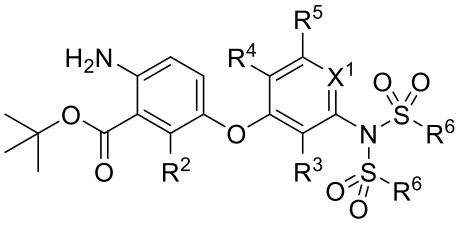
wherein R^1 and R^2 are as defined in claim 1, with a compound having the formula (18)



(18)

wherein X^1, R^3, R^4, R^5 and R^6 are as defined in claim 1 and PG is an amine protecting group, in the presence of a catalyst and a ligand, followed by removal of the amine protecting group; or

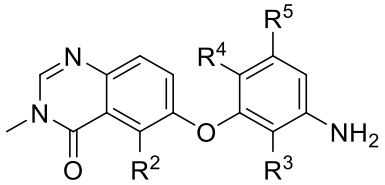
(c) for a compound of claim 1 wherein L is O and X^1, R^1, R^2, R^3, R^4, R^5 and R^6 are as defined for claim 1, cyclizing a compound having the formula (33):



(33)

wherein R^2, R^3, R^4, R^5 and R^6 are as defined in claim 1, with N-methylformamide in the presence of an acid; or

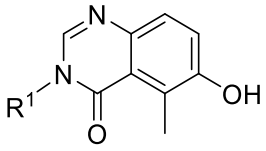
(d) for a compound of claim 1 wherein R^1 is methyl, L is O, X^1 is CH, R^3, R^4, R^5 and R^6 are as defined in claim 1, coupling a compound having the formula (36)



(36)

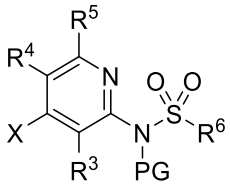
with a reagent having the formula R^6SO_2Cl in the presence of an amine base, followed by hydrolysis; or

(e) for a compound of claim 1 wherein L is O, R^2 is methyl, X^1 is N, and R^1, R^3, R^4, R^5 and R^6 are as defined for claim 1, coupling a compound having the formula (38)



(38)

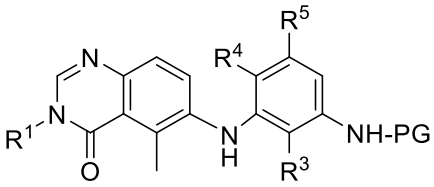
wherein R^1 is as defined in claim 1, with a compound having the formula (39)



(39)

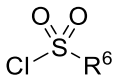
wherein X is a halogen, PG is an amine protecting group, and R^3, R^4, R^5 and R^6 are as defined in claim 1, in the presence of an alkaline carbonate base, followed by removal of the amine protecting group; or

(f) for a compound of claim 1 wherein X^1 is CH, R^1 is methyl, and R^2, R^3, R^4, R^5 and R^6 are as defined for claim 1, reacting a compound having the formula (51)

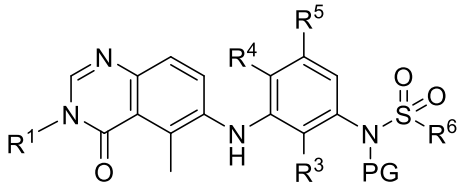


(51)

wherein X^1 is CH, R^1 is methyl, and R^2, R^3, R^4, R^5 and R^6 are as defined for claim 1, with a compound having the formula:



wherein R^6 is as defined for claim 1, in the presence of a base, to provide a compound having the formula (52)



(52)

followed by removal of the protecting group; and

optionally forming a pharmaceutically acceptable salt or solvate thereof.

21. ~~A method of treating a BRAF-associated tumor in a subject in need thereof, comprising administering a therapeutically effective amount of~~ A ~~a~~ compound according to any one of claims 1-18 or a pharmaceutically acceptable salt, solvate or polymorph thereof for use in the treatment of a BRAF-associated tumor.

~~22. The method according to claim 21, wherein said BRAF-associated tumor has a BRAF V600 mutation selected from a V600E and a V600K mutation.~~

~~23. The method according to any one of claims 21-22, wherein said BRAF-associated tumor is a CNS tumor, wherein said method comprises administering a therapeutically effective amount of a compound according to any one of claims 10-18 or a pharmaceutically acceptable salt, solvate or polymorph thereof.~~

~~24. The method according to claim 23, wherein said CNS tumor is a metastatic CNS cancer.~~

~~25. The method according to claim 24, wherein said metastatic CNS cancer is selected from metastatic melanoma, metastatic colorectal cancer, metastatic non-small cell lung cancer, metastatic thyroid cancer, and metastatic ovarian cancer.~~

~~26. The method according to claim 23, wherein said CNS tumor is intracranial LMD or extracranial LMD.~~

~~27. The method according to any one of claims 21-26, wherein the method further comprises administering a second anticancer therapy.~~

~~28. The method of claim 27, wherein the second anticancer therapy is an anticancer agent is selected from one or more of MEK inhibitors, BRAF inhibitors, EGFR inhibitors, inhibitors of HER2 and/or HER3, SHP2 inhibitors, Axl inhibitors, PI3K inhibitors, SOS1 inhibitors, signal transduction pathway inhibitors, checkpoint inhibitors, modulators of~~

~~the apoptosis pathway, cytotoxic chemotherapeutics, angiogenesis-targeted therapies, and immune-targeted agents.~~

~~29. The method of claim 28, wherein the anticancer agent is a MEK inhibitor.~~

~~30. The method of claim 29, wherein the MEK inhibitor is binimetinib.~~

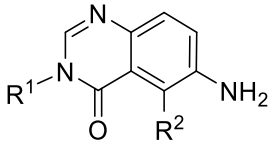
~~31. The method according to claim 23, wherein said CNS tumor is a primary brain tumor.~~

~~32~~22. ~~A method of treating a subject having a BRAF-associated metastatic cancer, wherein the subject was previously treated with an anticancer therapy, the method comprising administering to the subject a therapeutically effective amount of~~ A ~~a~~ compound according to any one of claims 1-18 for use in the treatment of a BRAF-associated metastatic cancer in a subject, wherein the subject was previously treated with an anticancer therapy.~~.~~

~~33. The method according to claim 32, wherein said anticancer therapy is an anticancer agent selected from MEK inhibitors, BRAF inhibitors, EGFR inhibitors, inhibitors of HER2 and/or HER3, Axl inhibitors, PI3K inhibitors, SOS1 inhibitors, signal transduction pathway inhibitors, checkpoint inhibitors, modulators of the apoptosis pathway, cytotoxic chemotherapeutics, angiogenesis-targeted therapies, and immune-targeted agents.~~

~~34~~23. ~~A method of treating a BRAF-associated glioma, wherein the subject was previously treated with another anticancer therapy, the method comprising administering a therapeutically effective amount of~~ A~~a~~ compound according to any one of claims 10-18 for use in the treatment of a BRAF-associated glioma in a subject, wherein the subject was previously treated with another anticancer therapy.

~~35~~24. A compound having the formula (23)



(23)

wherein:

R^1 is C1-C6 alkyl, C1-C6 deuteroalkyl, C1-C6 fluoroalkyl, C3-C6 cycloalkyl, (C3-C6 cycloalkyl)CH_2-, (C1-C6 alkoxy)C1-C6 alkyl-, Ar^1, Ar^1CH_2-, $hetAr^1$ or $hetCyc^1$;

Ar^1 is phenyl which is optionally substituted with 1-5 substituents independently selected from halogen and C1-C3 alkyl;

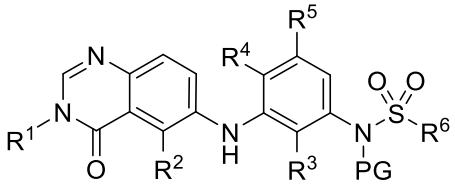
$hetAr^1$ is a 5-6 membered heteroaryl ring having 1-2 ring nitrogen atoms and optionally substituted with 1-3 substituents independently selected from halogen and C1-C3 alkyl;

$hetCyc^1$ is a 4-6 membered saturated monocyclic heterocyclic ring having one ring oxygen atom;

and

R^2 is methyl, $-CD_3$ or HC≡C-.

~~36~~25. A compound having the formula (24)



(24)

wherein:

R^1 is C1-C6 alkyl, C1-C6 deuteroalkyl, C1-C6 fluoroalkyl, C3-C6 cycloalkyl, (C3-C6 cycloalkyl)CH_2-, (C1-C6 alkoxy)C1-C6 alkyl-, Ar^1, Ar^1CH_2-, $hetAr^1$ or $hetCyc^1$;

Ar^1 is phenyl which is optionally substituted with 1-5 substituents independently selected from halogen and C1-C3 alkyl;

$hetAr^1$ is a 5-6 membered heteroaryl ring having 1-2 ring nitrogen atoms and optionally substituted with 1-3 substituents independently selected from halogen and C1-C3 alkyl;

$hetCyc^1$ is a 4-6 membered saturated monocyclic heterocyclic ring having one ring oxygen atom;

R^2 is methyl, -CD_3 or HC≡C-;

R^3 is F, Cl, CN or methyl;

R^4 is H, F or Cl;

R^5 is H, F, Cl, methyl;

R^6 is C1-C6 alkyl, C1-C6 fluoroalkyl, (Cyc^1)C1-C6 alkyl-, (C1-C3 alkoxy)C1-C6 alkyl-, $hetAr^2$, Ar^2 or R^aR^bN-;

Cyc^1 is a 3-6 membered saturated carbocyclic ring;

$hetAr^2$ is a 5-6 membered heteroaryl having 1-2 ring heteroatoms independently selected from N, O and S and optionally substituted with 1-3 substituents independently selected from halogen and C1-C3 alkyl;

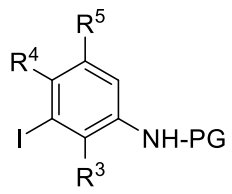
Ar^2 is phenyl optionally substituted with 1-5 substituents independently selected from halogen and C1-C6 alkyl;

R^a and R^b are independently C1-C3 alkyl, or

R^a and R^b together with the nitrogen atom to which they are attached form a 5-6 membered saturated monocyclic heterocyclic ring optionally substituted with fluoro; and

PG is an amine protecting group.

~~37~~26. A compound having the formula (45)



(45)

wherein:

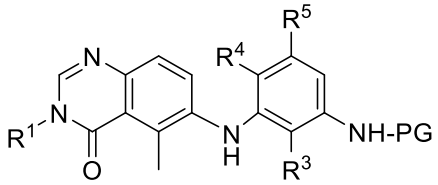
R^3 is F, Cl, CN or methyl;

R^4 is H, F or Cl;

R^5 is H, F, Cl, methyl; and

PG is an amine protecting group.

~~38~~27. A compound having the formula (51)



(51)

wherein:

R^1 is C1-C6 alkyl, C1-C6 deuteroalkyl, C1-C6 fluoroalkyl, C3-C6 cycloalkyl, (C3-C6 cycloalkyl)CH_2-, (C1-C6 alkoxy)C1-C6 alkyl-, Ar^1, Ar^1CH_2-, $hetAr^1$ or $hetCyc^1$;

Ar^1 is phenyl which is optionally substituted with 1-5 substituents independently selected from halogen and C1-C3 alkyl;

$hetAr^1$ is a 5-6 membered heteroaryl ring having 1-2 ring nitrogen atoms and optionally substituted with 1-3 substituents independently selected from halogen and C1-C3 alkyl;

$hetCyc^1$ is a 4-6 membered saturated monocyclic heterocyclic ring having one ring oxygen atom;

R^3 is F, Cl, CN or methyl;

R^4 is H, F or Cl;

R^5 is H, F, Cl, methyl; and

PG is an amine protecting group.