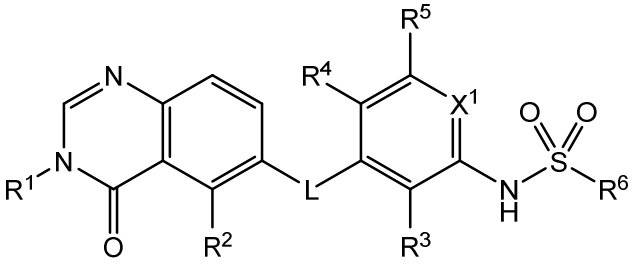
What is claimed is:

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;

$R^3$ 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 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-((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,

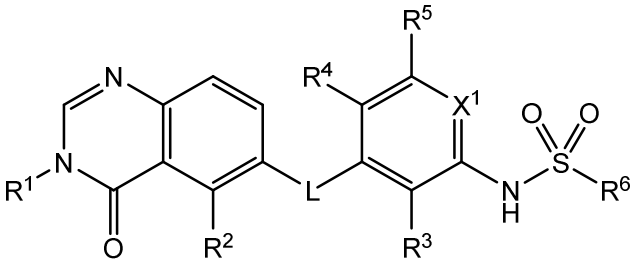
N-(2-chloro-3-((3,5-dimethyl-4-oxo-3,4-dihydroquinazolin-6-yl)amino)-4-fluorophenyl)-

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.

9. 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 $R^aR^bN$-;

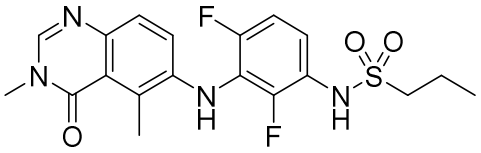
$Cyc^1$ is a 3-6 membered saturated carbocyclic ring;

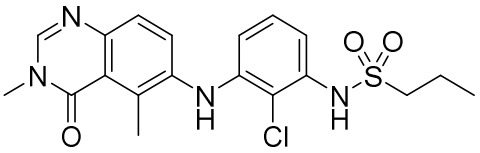
$Ar^2$ is phenyl optionally substituted with 1-5 substituents independently selected from halogen and C1-C3 alkyl; and

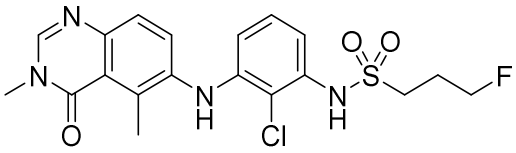
$R^a$ and $R^b$ are independently C1-C6 alkyl, or

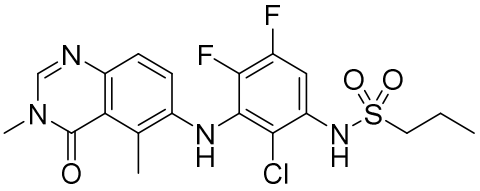
$R^a$ and $R^b$ together with the nitrogen atom to which they are attached form a 5-6 membered saturated monocyclic heterocyclic ring optionally substituted with fluoro.

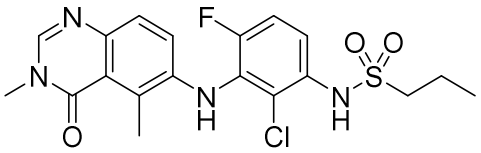
10. The compound according to claim 9, selected from:

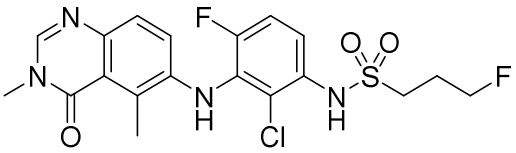


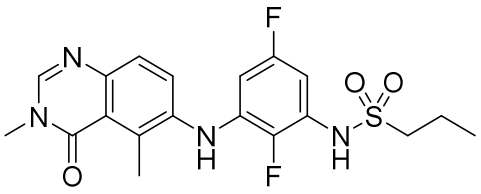


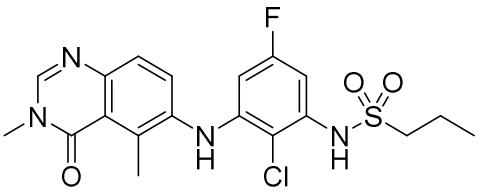


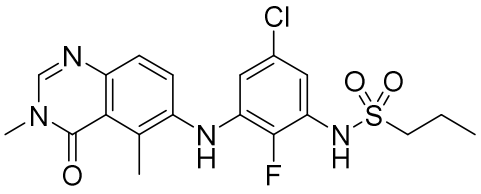


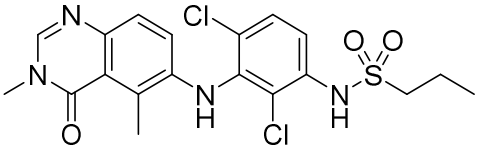


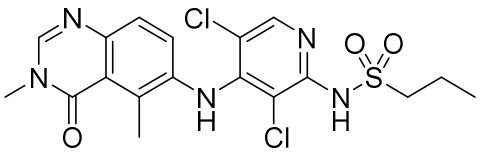


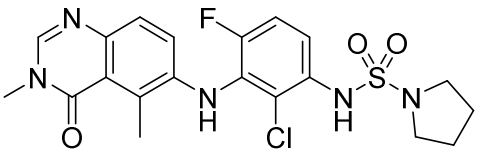


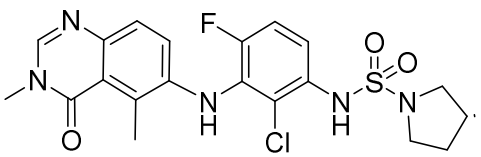


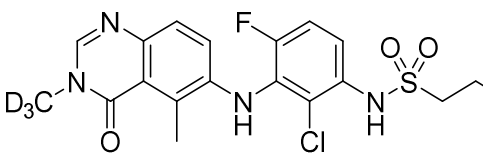


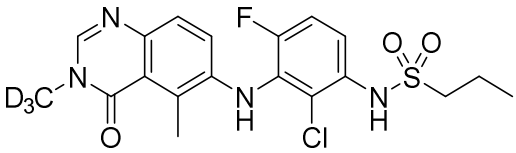


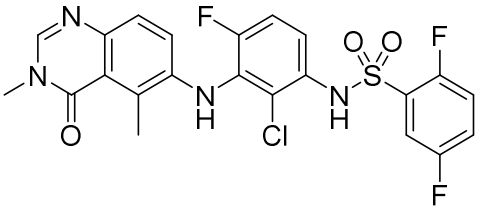


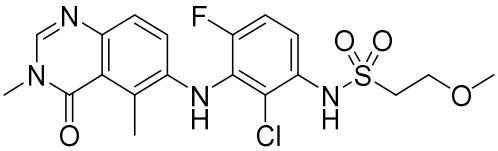


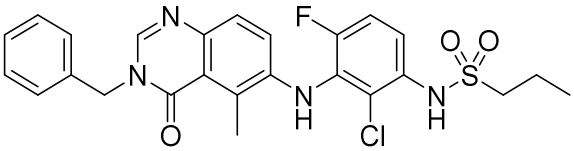


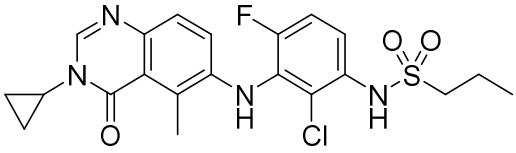


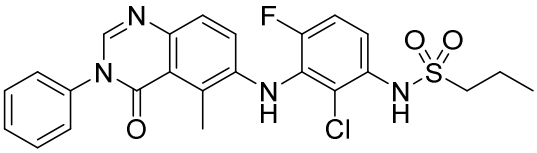


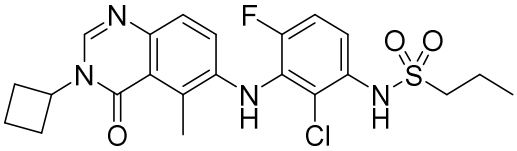


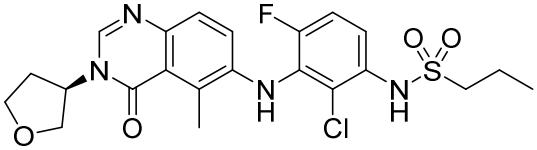


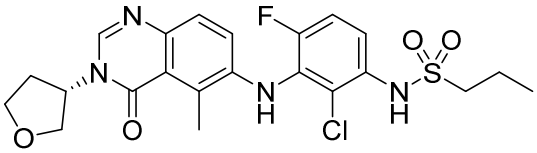


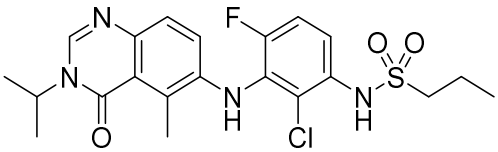


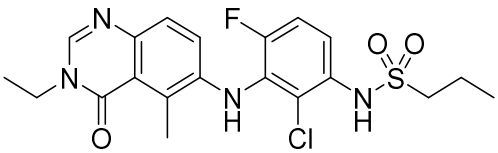


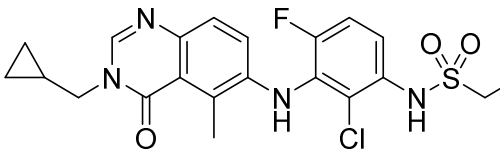


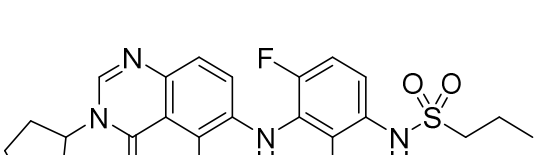


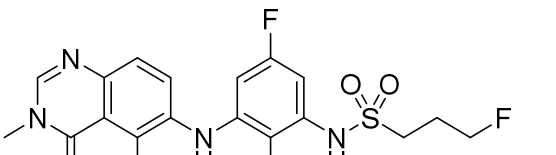


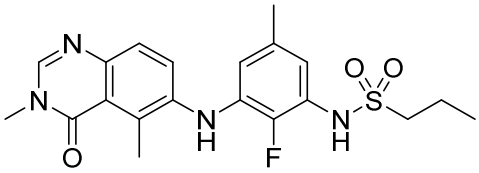


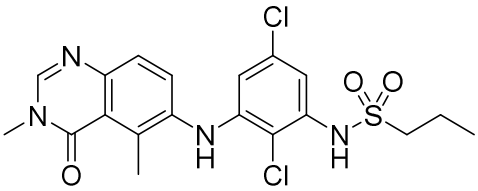


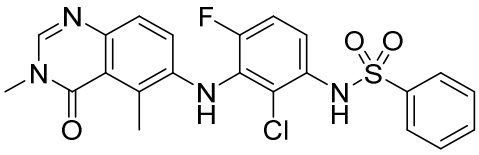


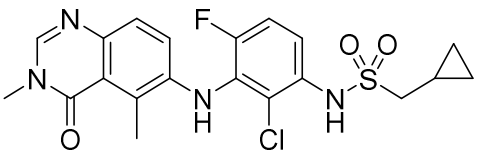


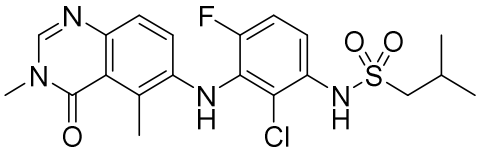


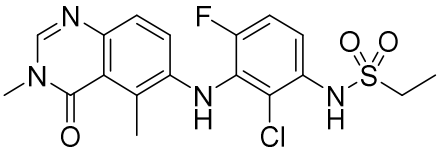


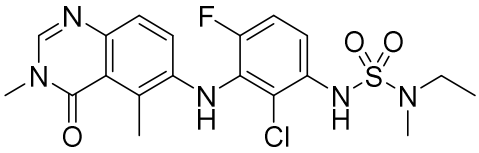


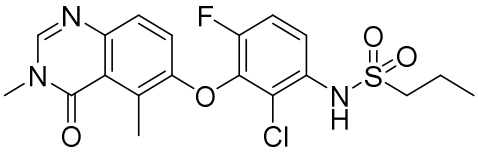


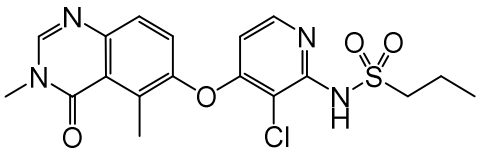


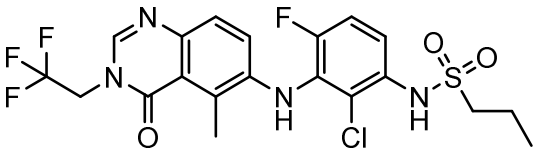


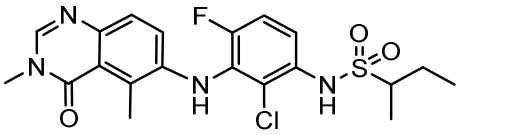


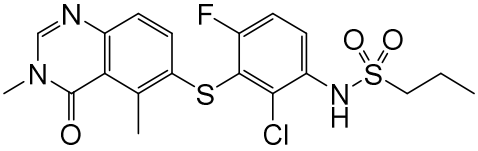


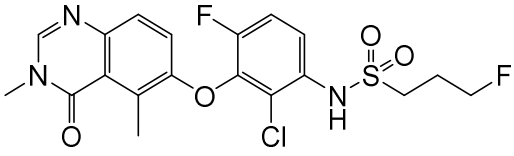


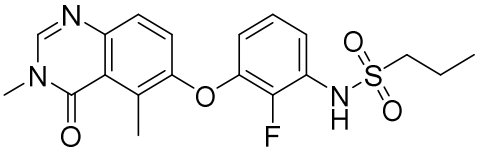


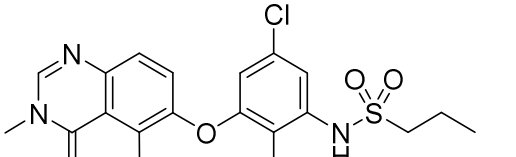


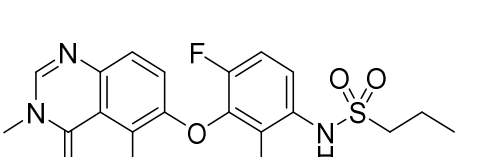


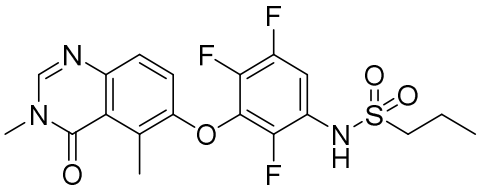
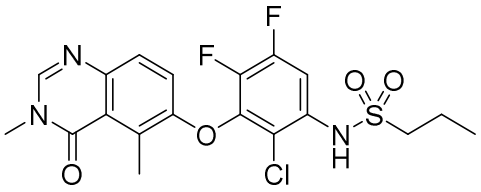
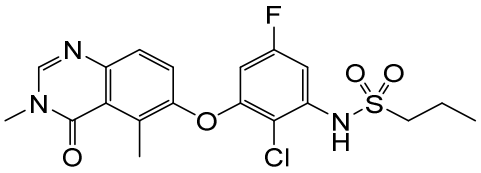
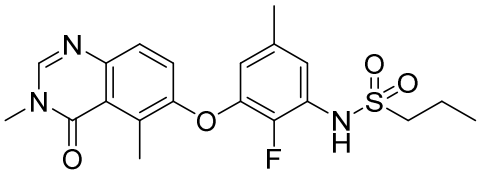
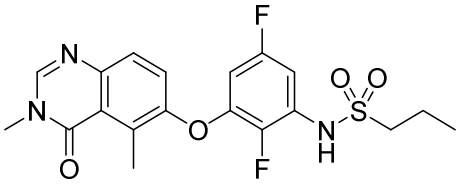
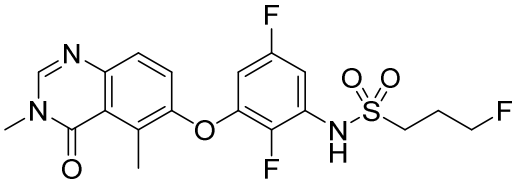
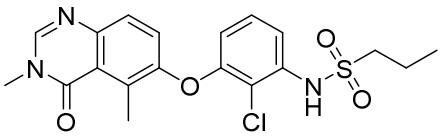
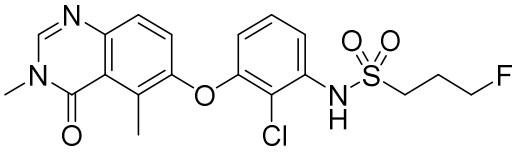
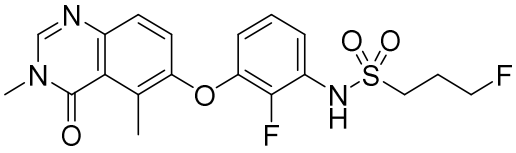




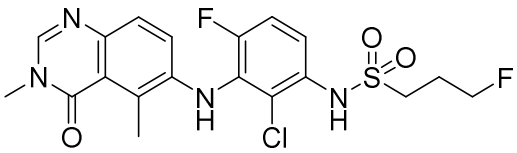




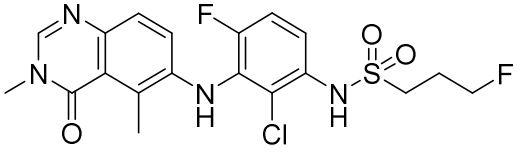


and pharmaceutically acceptable salts and solvates thereof,

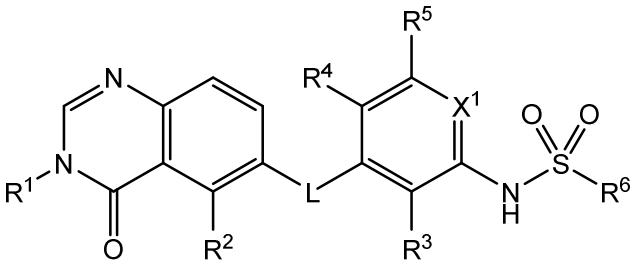


Form B anhydrous; and



Form A anhydrous.

11. 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;

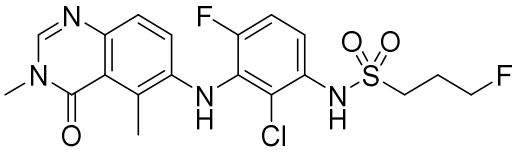
$R^3$ is F or Cl;

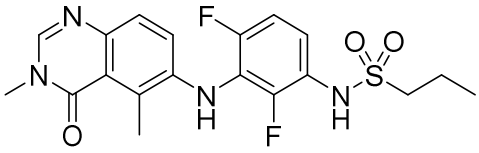
$R^4$ is H or F;

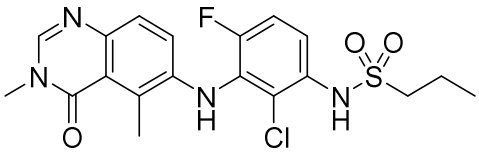
$R^5$ is H or F; and

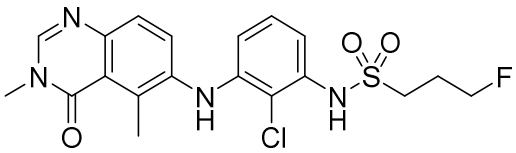
$R^6$ C1-C6 alkyl or C1-C6 fluoroalkyl.

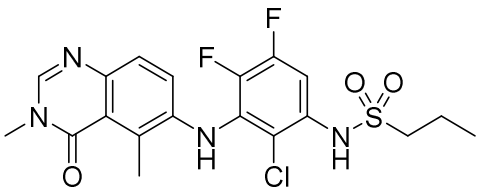
12. The compound according to claim 11, selected from:

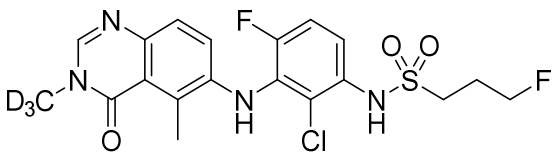


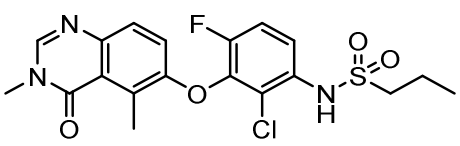


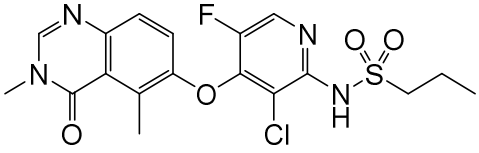


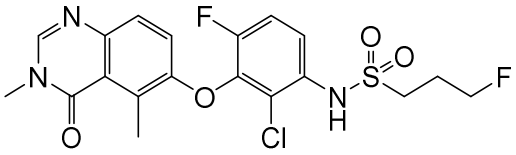




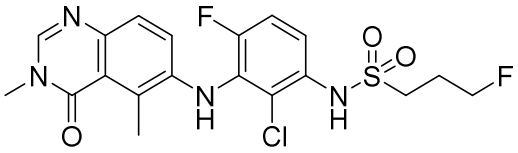




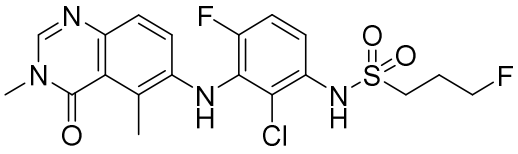




and pharmaceutically acceptable salts and solvates thereof,

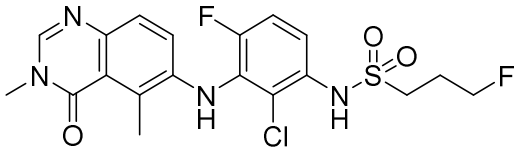


Form B anhydrous, and



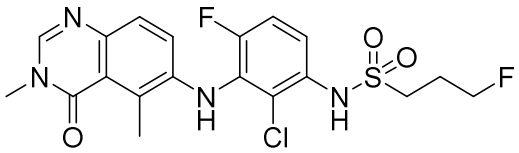
Form A anhydrous.

13. A compound , which is



or a pharmaceutically acceptable salt or solvate thereof.

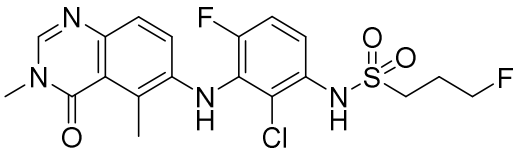
14. A compound , which is



Form B anhydrous.

15. The compound according to claim 14, 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).

16. A compound which is A compound which is



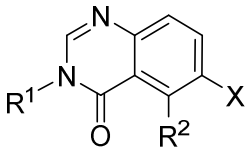
Form A anhydrous.

17. The compound of claim 16, 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).

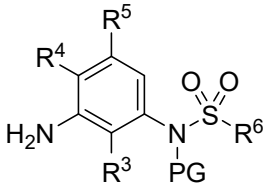
18. A pharmaceutical composition, comprising a compound according to any one of claims 1 to 17 in admixture with a pharmaceutically acceptable diluent or carrier.

19. 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:

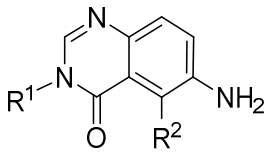


wherein $R^1$ and $R^2$ are as defined in claim 1 and X is a halogen, with a compound having the formula:



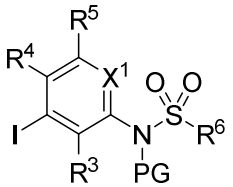
wherein $R^3$, $R^4$, $R^5$ and $R^6$ are as in claim 1 and PG is an amine protecting group, in the presence of a catalyst and a ligand, followed by removal of the amine protecting group; or

(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)

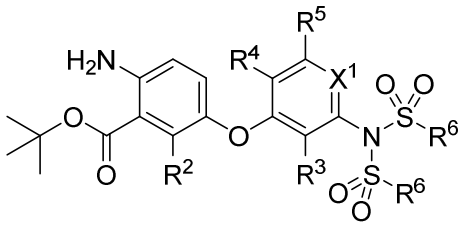
wherein $R^1$ and $R^2$ are as defined in claim 1, with a compound having the formula (18)



(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

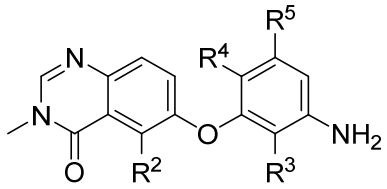
(c) for a compound of claim 1 wherein L is O and $X^1$, $R^1$, $R^2$, $R^3$, $R^4$, $R^5$ and $R^6$ are as defined for claim 1, cyclizing a compound having the formula (33):



(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

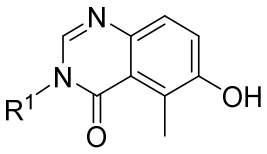
(d) for a compound of claim 1 wherein $R^1$ is methyl, L is O, $X^1$ is CH, $R^3$, $R^4$, $R^5$ and $R^6$ are as defined in claim 1, coupling a compound having the formula (36)



(36)

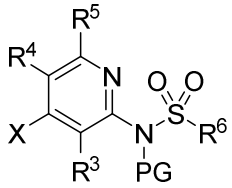
with a reagent having the formula $R^6SO_2Cl$ in the presence of an amine base, followed by hydrolysis; or

(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)

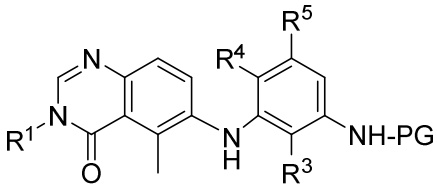
wherein $R^1$ is as defined in claim 1, with a compound having the formula (39)



(39)

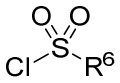
wherein X is a halogen, PG is an amine protecting group, and $R^3$, $R^4$, $R^5$ and $R^6$ are as defined in claim 1, in the presence of an alkaline carbonate base, followed by removal of the amine protecting group; or

(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)

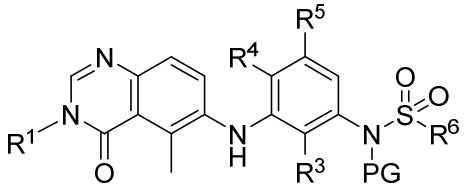


(51)

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

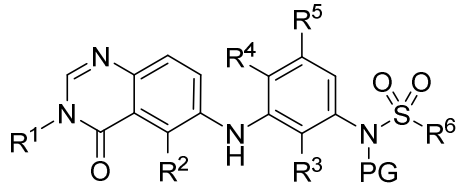
optionally forming a pharmaceutically acceptable salt or solvate thereof.

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

21. A compound according to any one of claims 1 to 17 for use in the treatment of a BRAF-associated metastatic cancer in a subject, wherein the subject was previously treated with an anticancer therapy.

22. A compound according to any one of claims 9 to 17 for use in the treatment of a BRAF-associated glioma in a subject, wherein the subject was previously treated with another anticancer therapy.

23. 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;

$R^3$ 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;

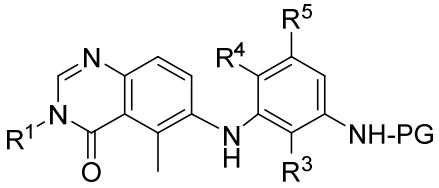
$Ar^2$ is phenyl optionally substituted with 1-5 substituents independently selected from halogen and C1-C6 alkyl;

$R^a$ 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.

24. 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.