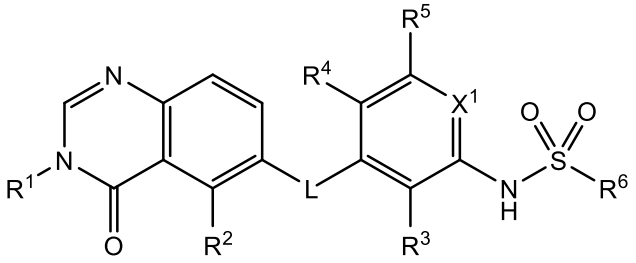
What is claimed is:

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,

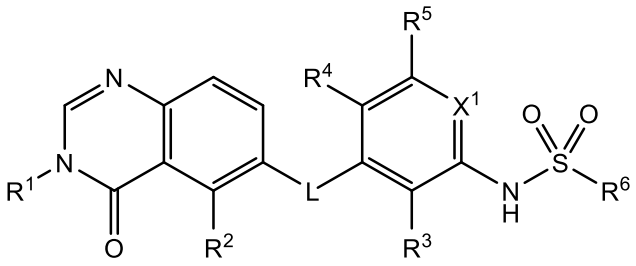
N-(2-chloro-3-((3,5-dimethyl-4-oxo-3,4-dihydroquinazolin-6-yl)amino)-4-fluorophenyl)-3-fluoropropane-1-sulfonamide Form C mono-anisole,

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-;

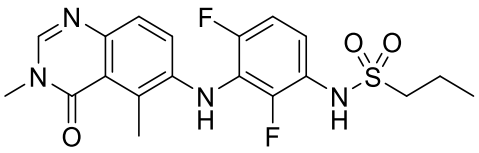
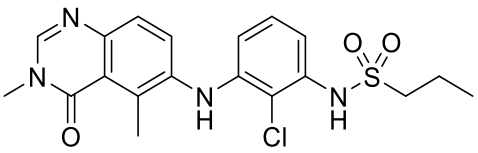
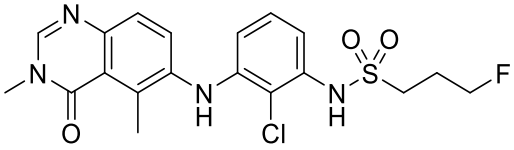
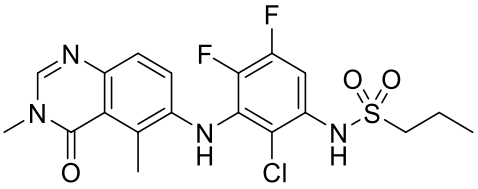
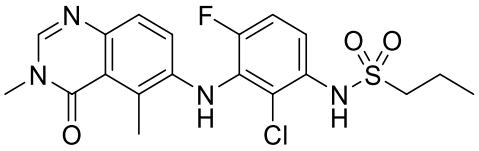
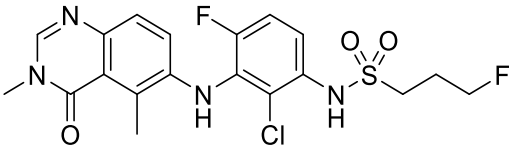
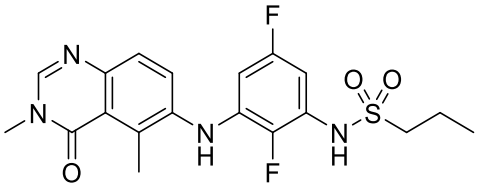
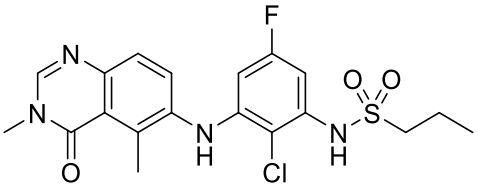
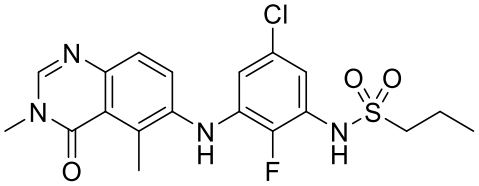
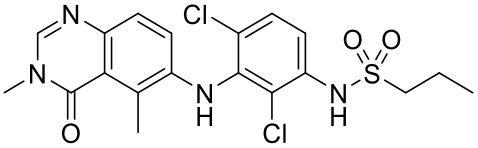
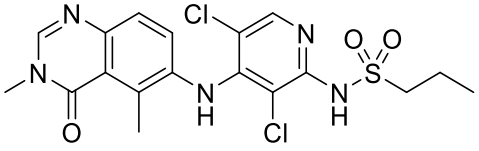
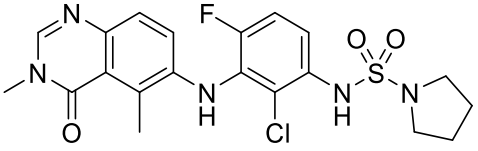
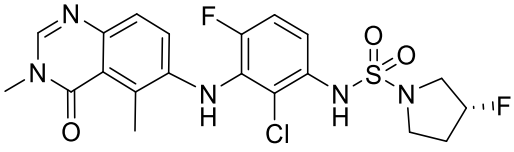
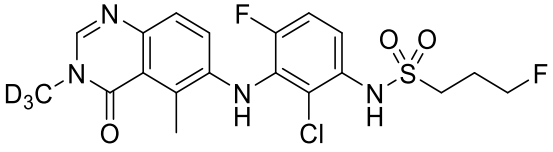
Cyc^1 is a 3-6 membered saturated carbocyclic ring;

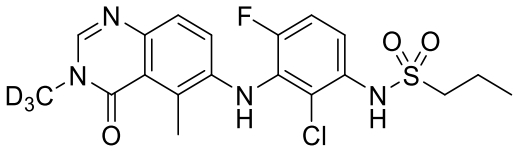
Ar^2 is phenyl optionally substituted with 1-5 substituents independently selected from halogen and C1-C3 alkyl; and

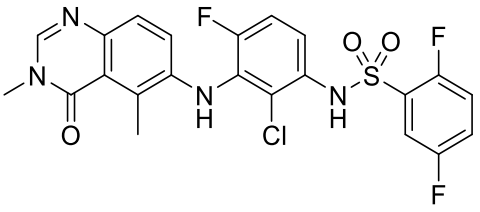
R^a and R^b are independently C1-C6 alkyl, or

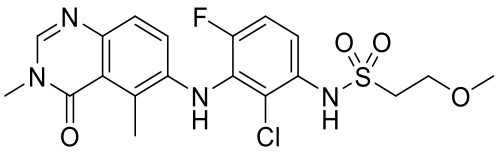
R^a and R^b together with the nitrogen atom to which they are attached form a 5-6 membered saturated monocyclic heterocyclic ring optionally substituted with fluoro.

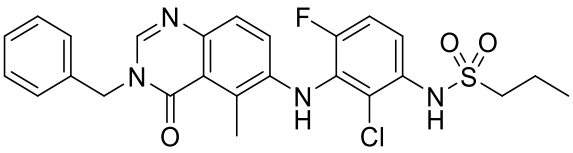
11. The compound according to claim 10, selected from:

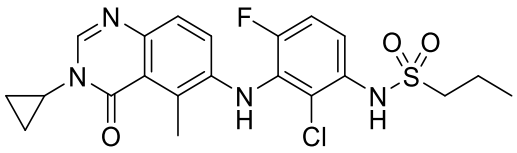















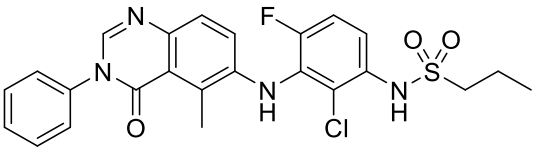


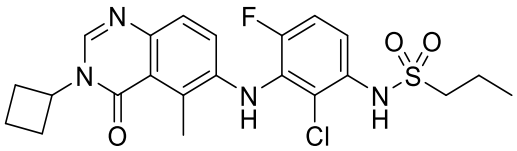


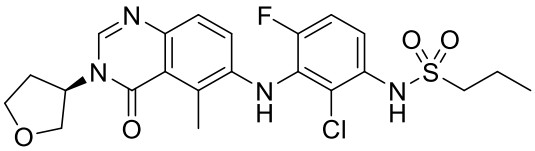


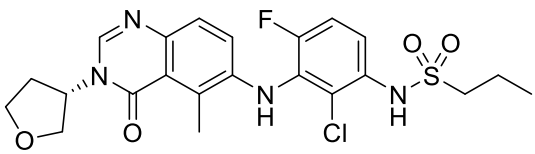


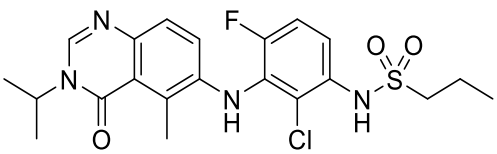


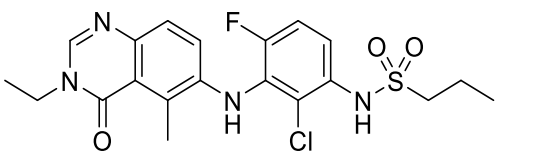


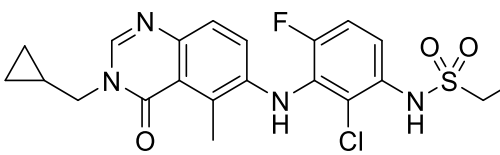


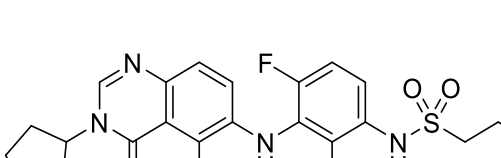


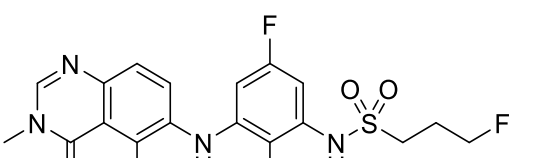


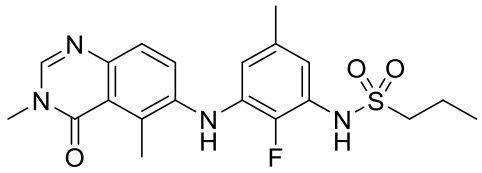


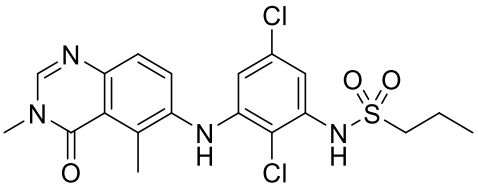


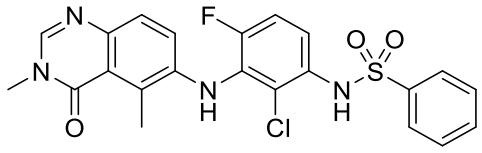


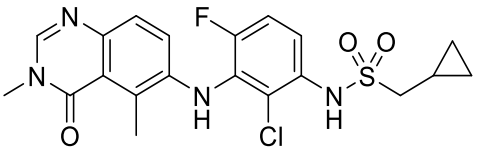


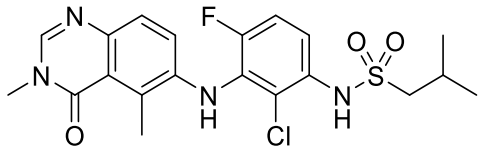


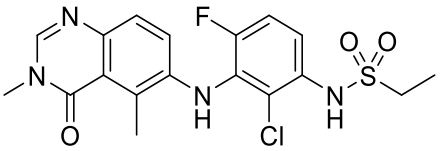


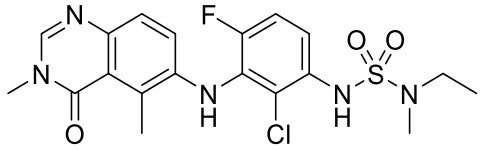


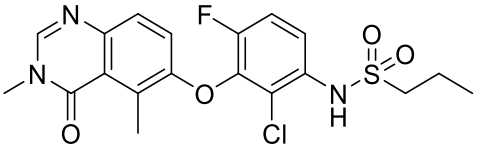


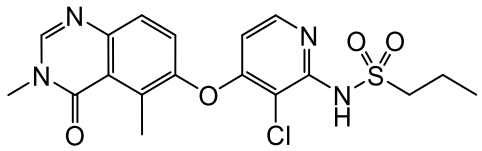


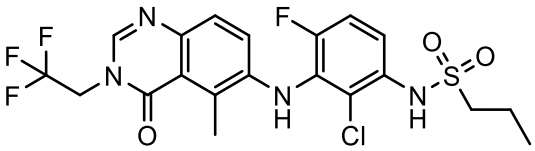


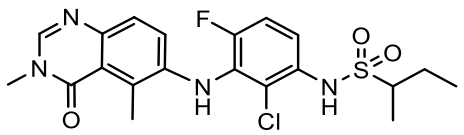


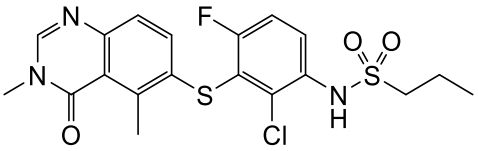


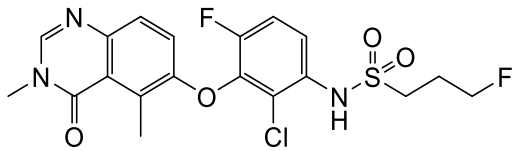


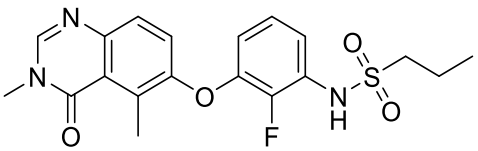


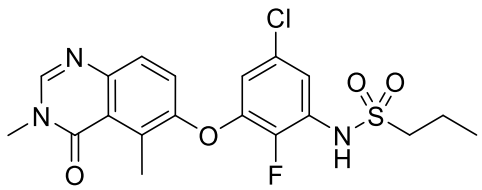


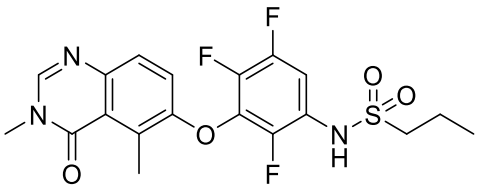
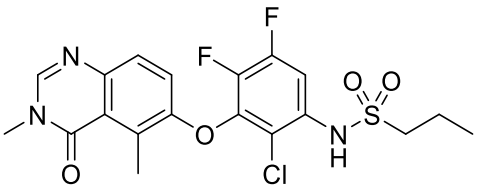
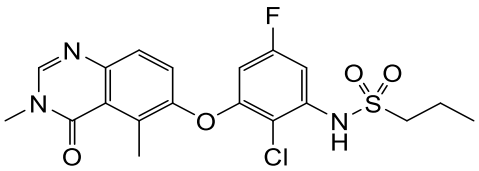
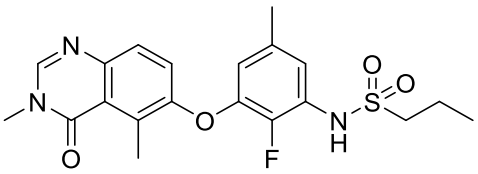
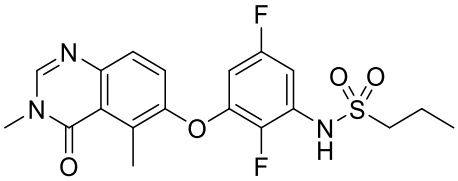
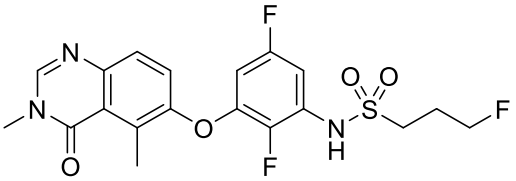
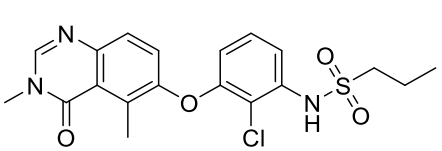
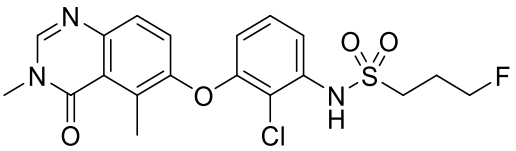
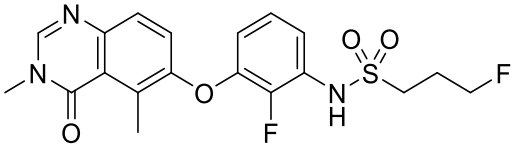




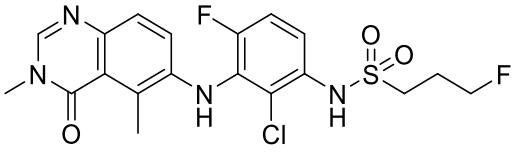




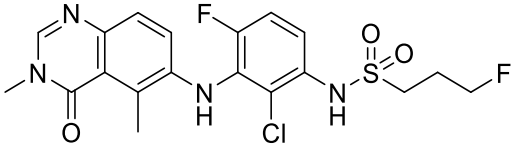


and pharmaceutically acceptable salts and solvates thereof,

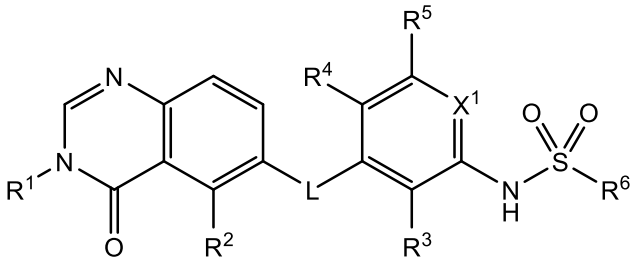


Form B anhydrous; and



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;

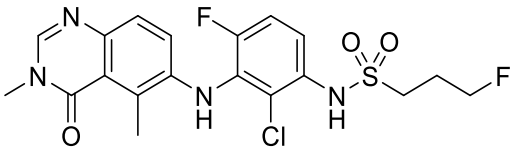
R^3 is F or Cl;

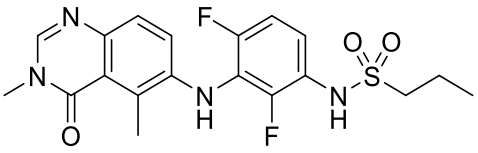
R^4 is H or F;

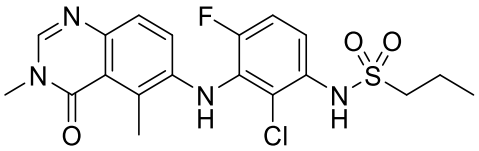
R^5 is H or F; and

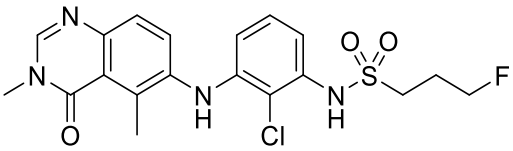
R^6 C1-C6 alkyl or C1-C6 fluoroalkyl.

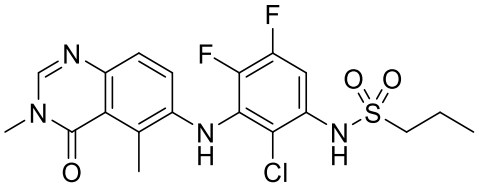
13. The compound according to claim 12, selected from:

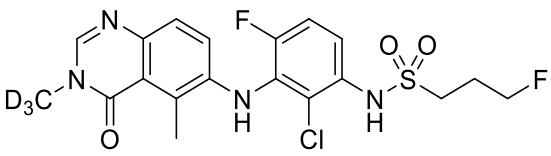


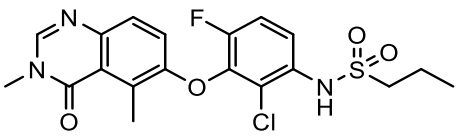


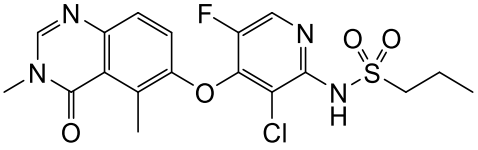


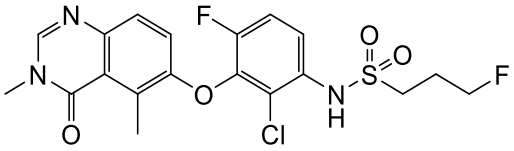




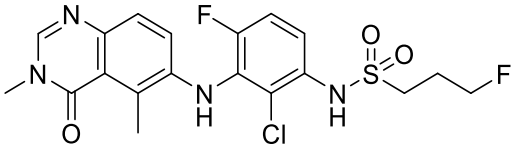




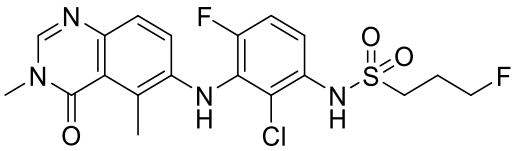




and pharmaceutically acceptable salts and solvates thereof,

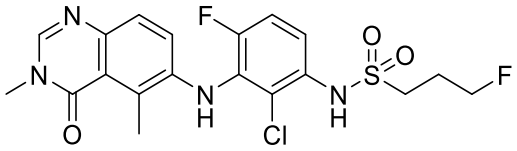


Form B anhydrous, and



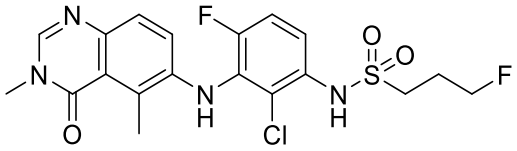
Form A anhydrous.

14. A compound , which is



or a pharmaceutically acceptable salt or solvate thereof.

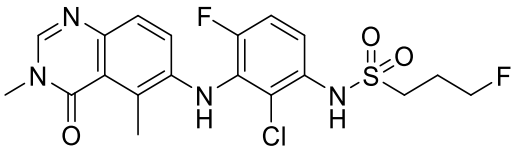
15. A compound , which is



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



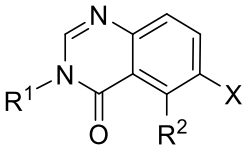
Form A anhydrous.

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).

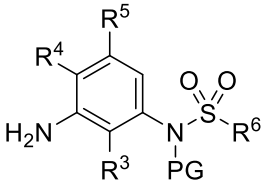
19. A pharmaceutical composition, comprising a compound according to any one of claims 1-18 in admixture with a pharmaceutically acceptable diluent or carrier.

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:

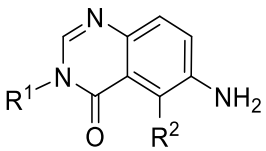


wherein R^1 and R^2 are as defined in claim 1 and X is a halogen, with a compound having the formula:



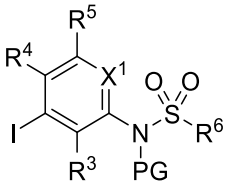
wherein R^3, R^4, R^5 and R^6 are as in claim 1 and PG is an amine protecting group, in the presence of a catalyst and a ligand, followed by removal of the amine protecting group; or

(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)

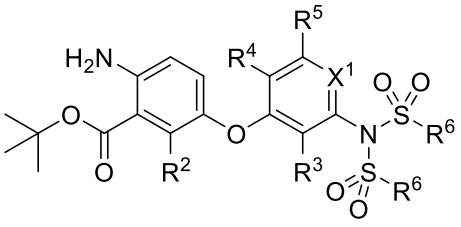
wherein R^1 and R^2 are as defined in claim 1, with a compound having the formula (18)



(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

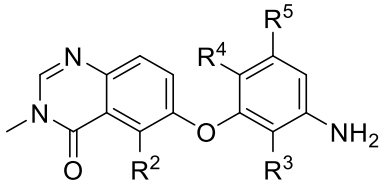
(c) for a compound of claim 1 wherein L is O and X^1, R^1, R^2, R^3, R^4, R^5 and R^6 are as defined for claim 1, cyclizing a compound having the formula (33):



(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

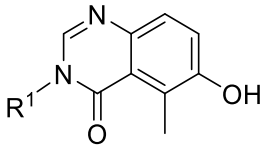
(d) for a compound of claim 1 wherein R^1 is methyl, L is O, X^1 is CH, R^3, R^4, R^5 and R^6 are as defined in claim 1, coupling a compound having the formula (36)



(36)

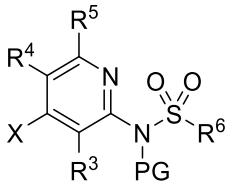
with a reagent having the formula R^6SO_2Cl in the presence of an amine base, followed by hydrolysis; or

(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)

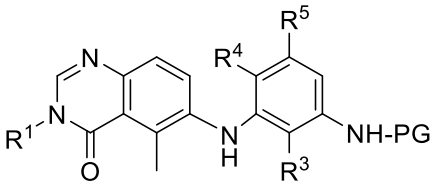
wherein R^1 is as defined in claim 1, with a compound having the formula (39)



(39)

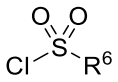
wherein X is a halogen, PG is an amine protecting group, and R^3, R^4, R^5 and R^6 are as defined in claim 1, in the presence of an alkaline carbonate base, followed by removal of the amine protecting group; or

(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)

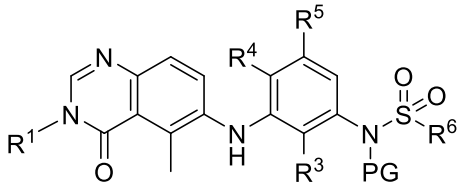


(51)

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)

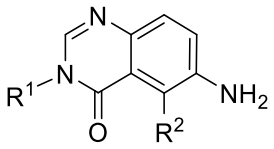
followed by removal of the protecting group; and

optionally forming a pharmaceutically acceptable salt or solvate thereof.

21. A 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. 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.

23. 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. 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;

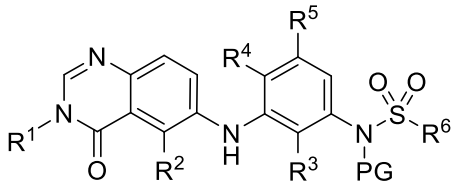
$hetAr^1$ is a 5-6 membered heteroaryl ring having 1-2 ring nitrogen atoms and optionally substituted with 1-3 substituents independently selected from halogen and C1-C3 alkyl;

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

and

R^2 is methyl, $-CD_3$ or HC≡C-.

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;

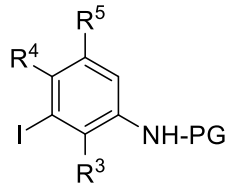
Ar^2 is phenyl optionally substituted with 1-5 substituents independently selected from halogen and C1-C6 alkyl;

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.

26. A compound having the formula (45)



(45)

wherein:

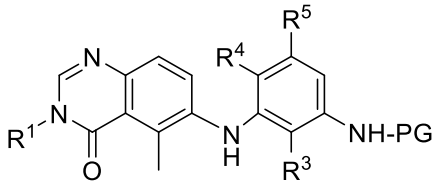
R^3 is F, Cl, CN or methyl;

R^4 is H, F or Cl;

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

PG is an amine protecting group.

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.