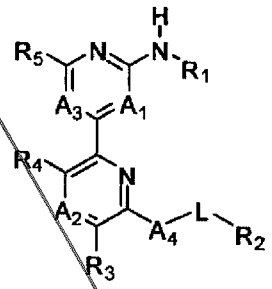
CLAIMS

1. A compound of formula (I):



or a pharmaceutically acceptable salt thereof, wherein:

A_1 is N or CR_6;

A_2 is N, N(O) or CR_7;

A_3 is N or CR_8;

A_4 is selected from a bond, SO_2, NR_9, or O;

L is selected from a bond, optionally substituted C_{1-4}alkyl, C_{3-6} cycloalkyl, C_{3-6} heterocycloalkyl, or C_{2-4} alkenyl;

R_1 is X-R_{16};

X is a bond, or C_{1-4} alkyl and;

R_{16} is selected from the group consisting of C_{1-6} alkyl, C_{3-6}branched alkyl, C_{3-8}cycloalkyl, heterocycloalkyl, C_{3-8}-partially unsaturated cycloalkyl, aryl, and heteroaryl;

wherein R_{16} is substituted with one to three groups independently selected from halogen, hydrogen, C_{1-6}alkyl, C_{1-6}haloalkyl, C_{3-6}branched alkyl, C_{3-6}branched haloalkyl, OH, C_{1-6}alkoxy, R_{22}-OR_{12}, $S(O)_{0-2}R_{12}$, R_{22}-$S(O)_{0-2}R_{12}$, $S(O)_2NR_{13}R_{14}$, R_{22}-$S(O)_2NR_{13}R_{14}$, $C(O)OR_{12}$, R_{22}-$C(O)OR_{12}$, $C(O)R_{19}$, R_{22}-$C(O)R_{19}$, O-C_{1-3} alkyl, OC_{1-3} haloalkyl, $OC(O)R_{19}$, R_{22}-$OC(O)R_{19}$, $C(O)NR_{13}R_{14}$, R_{22}-$C(O)NR_{13}R_{14}$, $NR_{15}S(O)_2R_{12}$, R_{22}-$NR_{15}S(O)_2R_{12}$, $NR_{17}R_{18}$, R_{22}-$NR_{17}R_{18}$, $NR_{15}C(O)R_{19}$, R_{22}-$NR_{15}C(O)R_{19}$, $NR_{15}C(O)OCH_2Ph$, R_{22}-$NR_{15}C(O)OCH_2Ph$, $NR_{15}C(O)OR_{12}$, R_{22}-$NR_{15}C(O)OR_{12}$, $NR_{15}C(O)NR_{13}R_{14}$, and R_{22}-$NR_{15}C(O)NR_{13}R_{14}$;

R_{17} and R_{18} are each, independently, selected from the group consisting of hydrogen, hydroxyl, C_{1-6}alkyl, C_{1-6}haloalkyl, C_{3-6}branched alkyl, C_{3-6} cycloalkyl, R_{22}-OR_{12}, R_{22}-$S(O)_{0-2}R_{12}$,

R_{22}-$S(O)_2NR_{13}R_{14}$, R_{22}-$C(O)OR_{12}$, R_{22}-$C(O)R_{19}$, R_{22}-$OC(O)R_{19}$, R_{22}-$C(O)NR_{13}R_{14}$, R_{22}-$NR_{15}S(O)_2R_{12}$, R_{22}-$NR_{23}R_{24}$, R_{22}-$NR_{15}C(O)R_{19}$, R_{22}-$NR_{15}C(O)OCH_2Ph$, R_{22}-$NR_{15}C(O)OR_{12}$, R_{22}-$NR_{15}C(O)NR_{13}R_{14}$, cycloalkyl, heterocycloalkyl and heteroaryl; alternatively, R_{17} and R_{18} along with the nitrogen atom to which they are attached to can be taken together to form a four to six membered heterocyclic ring wherein the carbon atoms of said ring are optionally substituted with R_{20}, and the nitrogen atoms of said ring are optionally substituted with R_{21};

R_{19} is selected from optionally substituted alkyl, optionally substituted cycloalkyl, optionally substituted heterocycloalkyl, optionally substituted aryl, and optionally substituted heteroaryl;

R_{20} is selected from the group consisting of C_{1-6} alkyl or C_{1-6} haloalkyl;

R_{21} is selected from the group consisting of C_{1-6}alkyl, C_{1-6}haloalkyl, $C(O)R_{12}$, $C(O)OR_{12}$, $S(O)_2R_{12}$;

R_{22} is selected from the group consisting of C_{1-6} alkyl, C_{1-6}haloalkyl, C_{3-6} branched alkyl, C_{3-6}branched haloalkyl;

R_{23} and R_{24} are each, independently, selected from the group consisting of hydrogen, C_{1-6} alkyl, C_{1-6}haloalkyl, C_{3-6} branched alkyl, C_{3-6} branched haloalkyl;

R_2 is selected from the group consisting of optionally substituted C_{1-6} alkyl, optionally substituted C_{3-6} branched alkyl, optionally substituted C_{3-8} cycloalkyl, optionally substituted heterocycloalkyl, optionally substituted aryl, and optionally substituted heteroaryl;

R_4, R_5, and R_6 are each, independently, selected from the group consisting of hydrogen, hydroxyl, cyano, halogen, C_{1-4} alkyl, C_{1-4}haloalkyl, C_{2-4} alkenyl, C_{2-4} alkynyl, amino, $NR_{10}R_{11}$, and alkoxy;

R_3, R_7 and R_8 are each, independently, selected from the group consisting of hydrogen, hydroxyl, cyano, halogen, alkyl, haloalkyl, alkenyl, alkynyl, alkoxy, $NR_{10}R_{11}$, $C(O)R_{12}$, $C(O)OR_{12}$, $C(O)NR_{13}R_{14}$, $S(O)_{0-2}R_{12}$, $S(O)_{0-2}NR_{13}R_{14}$, and optionally substituted C_{3-4} cycloalkyl;

R_9 is selected from the group consisting of hydrogen, C_{1-4} alkyl, alkoxy, $C(O)R_{12}$, $C(O)OR_{15}$, $C(O)NR_{13}R_{14}$, $S(O)_{0-2}R_{12}$, $S(O)_{0-2}NR_{13}R_{14}$, optionally substituted C_{3-4} cycloalkyl, and optionally substituted heterocycloalkyl;

R_{10} and R_{11} are each, independently, selected from the group consisting of hydrogen, hydroxyl, alkyl, alkoxy, $C(O)R_{12}$, $C(O)OR_{12}$, $C(O)NR_{13}R_{14}$, $S(O)_{0-2}R_{12}$, and $S(O)_{0-2}NR_{13}R_{14}$;

alternatively, R_{10} and R_{11} along with the nitrogen atom to which they are attached to can be taken together to form an optionally substituted four to six membered heteroaromatic, or a non-aromatic heterocyclic ring;

R_{12} and R_{15} are each, individually, selected from the group consisting of hydrogen, alkyl, branched alkyl, haloalkyl, branched haloalkyl, $(CH_2)_{0-3}$-cycloalkyl, $(CH_2)_{0-3}$- heterocycloalkyl, $(CH_2)_{0-3}$- aryl, and heteroaryl;

R_{13} and R_{14} are each, independently, selected from the group consisting of hydrogen, hydroxyl, alkyl, branched alkyl, haloalkyl, branched haloalkyl, alkoxy, cycloalkyl or heterocycloalkyl; and alternatively, R_{13} and R_{14} along with the nitrogen atom to which they are attached to can be taken together to form an optionally substituted four to six membered heteroaromatic, or non-aromatic heterocyclic ring.

2. A compound of Claim 1, wherein:
A_1 is N;
A_2 is N; and
A_3 is CR_8.

3. A compound of Claim 1, wherein A_1 is CR_6, A_2 is CR_7, and A_3 is CR_8.

4. A compound of Claim 1, wherein A_1 is CR_6, A_2 is N, and A_3 is CR_8.

5. A compound of Claims1, wherein:
A_1 is N;
A_2 is CR_7; and
A_3 is CR_8.

6. A compound of Claims 1, 2, 3, 4, or 5, wherein:
R_8 is selected from halogen, hydrogen, CN, CF_3, O-C_{1-3}-alkyl, and C_{1-3}-alkyl.

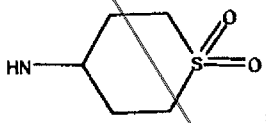
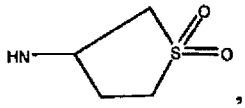
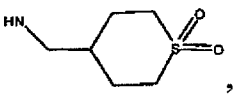
7. A compound of Claims 1, 5, or 6, wherein:
R_8 is selected from Cl, F, and methyl.

8. A compound of Claims 1, 2, 3, 4 or 5, wherein:
R_8 is Cl.

9. A compound of Claims 1, or 8, wherein:
R_1 is X-R_{16};
X is a bond, or C_{1-2} alkyl;
R_{16} is selected from the group consisting of C_{1-2}-alkyl, C_{4-6}cycloalkyl, heterocycloalkyl, phenyl, and heteroaryl;
wherein R_{16} is substituted with one to three groups independently selected from halogen, hydrogen, C_{1-3}alkyl, C_{3-6}branched alkyl, OH, C_{1-2}alkoxy, R_{22}-OR_{12}, $S(O)_{1-2}R_{12}$, $C(O)OR_{12}$, R_{22}-$C(O)OR_{12}$, $C(O)R_{19}$, R_{22}-$OC(O)R_{19}$, $C(O)NR_{13}R_{14}$, $NR_{15}S(O)_2R_{12}$, $NR_{17}R_{18}$, R_{22}-$NR_{17}R_{18}$, $NR_{15}C(O)R_{19}$, R_{22}-$NR_{15}C(O)R_{19}$, and $NR_{15}C(O)OCH_2Ph$.

10. A compound of Claims 1 or 9, wherein:
R_{16} is selected from the group consisting of C_{1-2}-alkyl, cyclopentyl, cyclohexyl, piperidine, piperazine, morpholine, pyridine, pyrrolidine, cyclohexenyl, and tetrahydro-2H-pyran;
wherein R_{16} is substituted with one to three groups selected from amino, hydroxyl, $NHCH_2$-phenyl, CH_2-amino, COO-*t*-butyl, H, methoxy, NH-SO_2-ethyl, CH_2-$NHSO_2$-ethyl, SO_2-ethyl, *t*-butyl, methyl, CH_2-COOH, CO-$NHCH_3$, $CON(CH_3)_2$, $NHC(CH_3)$-CH_2-SO_2-CH_3, NH-COO-CH_2-phenyl, hydroxy-methyl, CH_2-NH-CH_3, CH_2-NH-ethyl, NH-CH_2-CH_2-methoxy, CH_2-NH-CO-CH_3, NH-CH_2-CH_2OH, NH-CO-CH_2-$N(CH_3)_2$. NH-CO-methylpyrrolidine, NH-CH_2-$C(CH_3)$-dioxolane, NH-CO-pyridyl, NH-ethyl, pyrrolidine, CH_2-NH-CO-pyridyl, NH-tetrahydropyran, $COCH_2$-$N(CH_3)_2$, NH-CH_2-$C(CH_3)$-dimethyldioxolane, tetrahydropyran, CO-methylpyrrolidine, CH_2-methylpiperidine, NH-CO-CH_3, NH-SO_2-CH_3, NH-$CH(CH_2$-$OCH_3)_2$, NH-CH_2-tetrahydrofuran, NH-CH_2-oxetane, NH-tetrahydropyran, NH-CH_2-dioxane, $N(CH_3)$-CH_2CH_2-OCH_3, CH(OH)-CH_2-amino, NH-CH_2CH_2-OCF_3, $NHCH_2$-OCH_3, NH-CH_2-$CH(CF_3)$-OCH_3, NH-$CH(CH_3)$-CH_2-OH, F, NH-oxetane, CH_2-CH_2-OCH_3, CH_2-OCH_3, CH_2-tetrahydropyran, CH_2-methylpiperizine, NH_2-CH_2-CH(OH)-CF_3, piperidine, CH_2-

pyrrolidine, NH-CH(CH$_3$)CH$_2$OCH$_3$, NH-tetrahydrofuran, (CH$_2$)$_3$-NH$_2$, hydroxyethyl, propyl, CH$_2$-pyridyl, CH$_2$-piperidine, morpholine, NH-chloropyrimidine, NH-CH$_2$CH$_2$-SO$_2$-methyl, (CH$_3$)$_3$-N(CH$_3$)$_2$, piperizine,


,

,

,

and CH$_2$-morpholine.

11. A compound of Claims 1, 6, 8, 9, or 10 wherein:

R_3 is selected from H, methyl, cyano, chloro, $CONH_2$, amino, cyclopropyl, ethyl, and fluoro;

R_4 is selected from halogen, methyl, hydrogen, and halo-methyl;

R_6 is H;

R_7 is selected from H, COOH, Cl, F, $CONH_2$, CN, and CF_3;

R_8 is Cl;

R_{17} and R_{18} are each, independently, selected from the group consisting of hydrogen, C_{1-3}alkyl, C_{1-4}haloalkyl, C_{3-6}branched alkyl, R_{22}-OR_{12}, R_{22}-$S(O)_2R_{12}$, R_{22}-$NR_{15}S(O)_2R_{12}$, heterocycloalkyl or heteroaryl; alternatively, R_{17} and R_{18} along with the nitrogen atom to which they are attached to can be taken together to form a four to six membered heterocyclic ring wherein said ring carbon atoms are optionally substituted with R_{20}, and the ring nitrogen atoms are optionally substituted with R_{21};

R_{19} is selected from C_{1-3}-alkyl, optionally substituted heterocycloalkyl, optionally substituted aryl or optionally substituted heteroaryl;

R_{20} represents the group C_{1-3}alkyl; and

R_{22} is selection from the group consisting of C_{1-4}alkyl, and C_{3-6} branched alkyl.

12. A compound of Claims 1, 8, 9, 10, or 11, wherein:

A_4 is selected from NR_9, O, and a bond;

L is selected from a bond, C_{1-4}-alkyl, and cyclopropyl;

R_2 is selected from the group consisting of C_{3-7} cycloalkyl, a five to seven membered heterocycloalkyl, phenyl, and pyridyl, wherein each said R_2 group is substituted with one, two, or three substituents independently selected from hydrogen, cyano, $CO\text{-}NH_2$, halogen, methoxy, dihalo-methoxy, trihalo-methoxy, trihalo alkyl, C_{1-3}-alkyl, and hydroxy; and

R_9 represents methyl, hydrogen, or ethyl.

13. A compound of Claim 1, wherein:

A_1 is CR_6;

A_2 is CR_7;

A_3 is CR_8;

A_4 is selected from NR_9, O, and a bond;

L is a bond, C_{1-2} alkyl, or C_{3-4}-cycloalkyl;

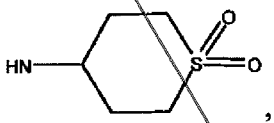
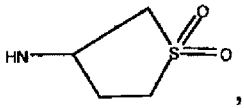
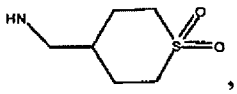
R_1 is $X\text{-}R_{16}$;

X is a bond, or C_{1-2} alkyl;

R_{16} is selected from the group consisting of C_{1-2}-alkyl, cyclopentyl, cyclohexyl, piperidine, piperazine, morpholine, pyridine, pyrrolidine, cyclohexenyl, and tetrahydro-2H-pyran;

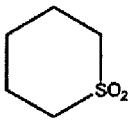
wherein R_{16} is substituted with one to three groups independently selected from amino, hydroxyl, $NHCH_2$-phenyl, CH_2-amino, COO-t-butyl, H, methoxy, $NH\text{-}SO_2$-ethyl, $CH_2\text{-}NHSO_2$-ethyl, SO_2-ethyl, t-butyl, methyl, $CH_2\text{-}COOH$, $CO\text{-}NHCH_3$, $CON(CH_3)_2$, $NHCH_2\text{-}CH_2\text{-}SO_2\text{-}CH_3$, $NH\text{-}COO\text{-}CH_2$-phenyl, hydroxy-methyl, $CH_2\text{-}NH\text{-}CH_3$, $CH_2\text{-}NH$-ethyl, $NH\text{-}CH_2\text{-}CH_2$-methoxy, $CH_2\text{-}NH\text{-}CO\text{-}CH_3$, $NH\text{-}CH_2\text{-}CH_2OH$, $NH\text{-}CO\text{-}CH_2\text{-}N(CH_3)_2$. NH-CO-methylpyrrolidine, NH-CO-pyridyl, NH-ethyl, pyrrolidine, $CH_2\text{-}NH\text{-}CO$-pyridyl, $COCH_2\text{-}N(CH_3)_2$, tetrahydropyran, CO-methylpyrrolidine, CH_2-methylpiperidine, $NH\text{-}CO\text{-}CH_3$, $NH\text{-}SO_2\text{-}CH_3$, $NH\text{-}CH_2$-tetrahydrofuran, $NH\text{-}CH_2$-dioxane, $N(CH_3)\text{-}CH_2CH_2\text{-}OCH_3$, $CH(OH)\text{-}CH_2$-amino, $NH\text{-}CH_2CH_2\text{-}OCF_3$, $NH(CH_3)\text{-}CH_2\text{-}OCH_3$, $NH\text{-}CH_2\text{-}CH(CF_3)\text{-}OCH_3$, F, NH-oxetane, $CH_2\text{-}CH_2\text{-}OCH_3$, $CH_2\text{-}OCH_3$, CH_2-tetrahydropyran, CH_2-methylpiperizine, $NH_2\text{-}CH_2\text{-}CH(OH)\text{-}CF_3$, piperidine, CH_2-pyrrolidine, $NH\text{-}CH(CH_3)CH_2OCH_3$, NH-tetrahydrofuran, $(CH_2)_3\text{-}NH_2$, hydroxyethyl, propyl, CH_2-pyridyl, CH_2-piperidine, morpholine, NH-chloropyrimidine, $NH\text{-}CH_2CH_2\text{-}SO_2$-methyl, $(CH_3)_3\text{-}N(CH_3)_2$, piperizine, CH_2-morpholine, $NH\text{-}CH_2\text{-}C(CH_3)$-dioxolane, NH-

tetrahydropyran, NH-CH_2-C(CH_3)-dimethyldioxolane, NH-CH(CH_2-OCH_3)$_2$, NH-CH_2-oxetane, NH-tetrahydropyran, N(CH_3)-CH_2CH_2-OCH_3, NH-CH(CH_3)-CH_2-OH,

and NH-CH(CH_3)-CH_2-OH;

R_2 is selected from the group consisting of cyclohexyl, 1,3-dioxane, pyridinyl, phenyl, tetrahydropyranyl, cycloheptyl, 1,4-dioxane, morpholinyl, alkyl substituted dioxane,



tetrahydrofuranyl, dioxepane , piperidinyl, and ,

wherein each said R_2 group is substituted with one, two, or three substituents independently selected from Cl, Br, F, methoxy, hydroxy-methyl, hydrogen, carboxamide, cyano, dihalo-methoxy, trihalo-methoxy, trifluoro-methyl, hydroxyl, and methyl; and

R_4, is chloro, hydrogen, trifluoro-methyl, fluoro, or bromo;

R_5, and R_6 are each independently hydrogen;

R_3 is selected from hydrogen, fluoro, cyano, CO-NH_2, chloro, amino, methyl, and cyclopropyl;

R_7 is selected from H, trifluoro-methyl, COOH, CO-NH_2, and cyano;

R_8 represents Cl; and

R_9 is selected from the group consisting of H, ethyl, and methyl.

14. A compound of Claims 1, or 12 selected from:

N2'-(trans-4-aminocyclohexyl)-5'-chloro-3,5-difluoro-N6-((tetrahydro-2H-pyran-4-yl)methyl)-2,4'-bipyridine-2',6-diamine;

N2'-(trans-4-aminocyclohexyl)-5'-fluoro-N6-(3-fluorobenzyl)-2,4'-bipyridine-2',6-diamine;

3,5'-dichloro-N2'-(trans-4-(((R)-2,2-dimethyl-1,3-dioxolan-4-yl)methyl)aminocyclohexyl)-N6-((tetrahydro-2H-pyran-4-yl)methyl)-2,4'-bipyridine-2',6-diamine;

5'-chloro-N6-((tetrahydro-2H-pyran-4-yl)dideuteromethyl)-N2'-(*trans*-4-(((S)-tetrahydrofuran-2-yl)methyl)aminocyclohexyl)-2,4'-bipyridine-2',6-diamine;

5'-chloro-5-fluoro-N2'-(trans-4-(2-(methylsulfonyl)ethylamino)cyclohexyl)-N6-((tetrahydro-2H-pyran-4-yl)methyl)-2,4'-bipyridine-2',6-diamine;

5'-chloro-5-fluoro-N2'-(trans-4-(oxetan-2-yl-methylamino)cyclohexyl)-N6-((tetrahydro-2H-pyran-4-yl)methyl)-2,4'-bipyridine-2',6-diamine;

3,5'-dichloro-N2'-(trans-4-((R)-1-methoxypropan-2-yl-amino)cyclohexyl)-N6-(((S)-tetrahydro-2H-pyran-3-yl)methyl)-2,4'-bipyridine-2',6-diamine;

3,5'-dichloro-N2'-(trans-4-((R)-1-methoxypropan-2-yl-amino)cyclohexyl)-N6-(((R)-tetrahydro-2H-pyran-3-yl)methyl)-2,4'-bipyridine-2',6-diamine;

4-((5'-chloro-2'-(trans-4-((R)-1-methoxypropan-2-yl-amino)cyclohexylamino)-2,4'-bipyridin-6-yl-amino)methyl)tetrahydro-2H-pyran-4-carbonitrile;

N2'-(trans-4-aminocyclohexyl)-5'-chloro-5-fluoro-N6-(3-fluorobenzyl)-2,4'-bipyridine-2',6-diamine;

2'-(trans-4-aminocyclohexylamino)-5'-chloro-6-(3-fluorobenzylamino)-2,4'-bipyridine-5-carbonitrile;

N2'-(trans-4-aminocyclohexyl)-3-chloro-5'-fluoro-N6-((tetrahydro-2H-pyran-4-yl)methyl)-2,4'-bipyridine-2',6-diamine;

5'-chloro-N6-(3-fluorobenzyl)-N2'-((1R,3S)-3-((methylamino)methyl)cyclopentyl)-2,4'-bipyridine-2',6-diamine;

3,5'-dichloro-N2'-(trans-4-((R)-1-methoxypropan-2-yl-amino)cyclohexyl)-N6-((tetrahydro-2H-pyran-4-yl)methyl)-2,4'-bipyridine-2',6-diamine;

5'-chloro-3-fluoro-N2'-(trans-4-((R)-1-methoxypropan-2-yl-amino)cyclohexyl)-N6-((tetrahydro-2H-pyran-4-yl)methyl)-2,4'-bipyridine-2',6-diamine;

5'-chloro-5-fluoro-N2'-(trans-4-((R)-1-methoxypropan-2-yl-amino)cyclohexyl)-N6-((tetrahydro-2H-pyran-4-yl)methyl)-2,4'-bipyridine-2',6-diamine;

5'-chloro-N6-((2,2-dimethyltetrahydro-2H-pyran-4-yl)methyl)-N2'-(trans-4-((R)-1-methoxypropan-2-yl-amino)cyclohexyl)-2,4'-bipyridine-2',6-diamine;

5'-chloro-N6-(((S)-2,2-dimethyltetrahydro-2H-pyran-4-yl)methyl)-N2'-(trans-4-((R)-1-methoxypropan-2-yl-amino)cyclohexyl)-2,4'-bipyridine-2',6-diamine;

5'-chloro-5-fluoro-N6-((tetrahydro-2H-pyran-4-yl)methyl)-N2'-(trans-4-((1,1-dioxotetrahydro-2H-thiopyran-4-yl)methyl)aminocyclohexyl)-2,4'-bipyridine-2',6-diamine;

5'-chloro-5-fluoro-N2'-(trans-4-(2-methoxyethylamino)cyclohexyl)-N6-((tetrahydro-2H-pyran-4-yl)methyl)-2,4'-bipyridine-2',6-diamine;

N2'-(trans-4-aminocyclohexyl)-5'-chloro-N6-(3-fluorobenzyl)-2,4'-bipyridine-2',6-diamine;

N2'-(trans-4-aminocyclohexyl)-5'-chloro-N6-(3,5-difluorobenzyl)-2,4'-bipyridine-2',6-diamine;

N2'-(trans-4-aminocyclohexyl)-5'-chloro-N6-((5-fluoropyridin-3-yl)methyl)-2,4'-bipyridine-2',6-diamine;

trans-4-(5'-chloro-6-(3,5-difluorobenzylamino)-2,4'-bipyridin-2'-yl-amino)cyclohexanol;

(R)-5'-chloro-N6-(3-fluorobenzyl)-N2'-(2-(piperidin-3-yl)ethyl)-2,4'-bipyridine-2',6-diamine;

N2'-(trans-4-aminocyclohexyl)-3,5'-dichloro-N6-((tetrahydro-2H-pyran-4-yl)methyl)-2,4'-bipyridine-2',6-diamine;

N2'-(trans-4-aminocyclohexyl)-3,5'-dichloro-N6-((tetrahydro-2H-pyran-4-yl)methyl)-2,4'-bipyridine-2',6-diamine;

3,5'-dichloro-N2'-(trans-4-(2-methoxyethylamino)cyclohexyl)-N6-((tetrahydro-2H-pyran-4-yl)methyl)-2,4'-bipyridine-2',6-diamine;

2-(trans-4-(3,5'-dichloro-6-((tetrahydro-2H-pyran-4-yl)methyl)amino-2,4'-bipyridin-2'-yl-amino)cyclohexylamino)ethanol;

trans-N1-(5-chloro-4-(6-(((R)-tetrahydro-2H-pyran-3-yl)methyl)aminopyrazin-2-yl)pyridin-2-yl)cyclohexane-1,4-diamine;

3,5'-dichloro-N6-((tetrahydro-2H-pyran-4-yl)methyl)-N2'-(trans-4-(((R)-tetrahydrofuran-2-yl)methyl)aminocyclohexyl)-2,4'-bipyridine-2',6-diamine;

3,5'-dichloro-N6-((tetrahydro-2H-pyran-4-yl)methyl)-N2'-(trans-4-(((S)-tetrahydrofuran-2-yl)methyl)aminocyclohexyl)-2,4'-bipyridine-2',6-diamine;

3,5'-dichloro-N2'-(trans-4-((2-methoxyethyl)(methyl)amino)cyclohexyl)-N6-((tetrahydro-2H-pyran-4-yl)methyl)-2,4'-bipyridine-2',6-diamine;

5'-chloro-N6-((tetrahydro-2H-pyran-4-yl)methyl)-N2'-(trans-4-(((R)-tetrahydrofuran-2-yl)methyl)aminocyclohexyl)-2,4'-bipyridine-2',6-diamine;

5'-chloro-N6-((tetrahydro-2H-pyran-4-yl)methyl)-N2'-(trans-4-(((S)-tetrahydrofuran-2-yl)methyl)aminocyclohexyl)-2,4'-bipyridine-2',6-diamine;

N2'-(trans-4-aminocyclohexyl)-5'-chloro-3-fluoro-N6-((tetrahydro-2H-pyran-4-yl)methyl)-2,4'-bipyridine-2',6-diamine;

5'-chloro-3-fluoro-N2'-(trans-4-(2-methoxyethylamino)cyclohexyl)-N6-((tetrahydro-2H-pyran-4-yl)methyl)-2,4'-bipyridine-2',6-diamine;

N2'-(trans-4-aminocyclohexyl)-3-bromo-5'-chloro-N6-((tetrahydro-2H-pyran-4-yl)methyl)-2,4'-bipyridine-2',6-diamine;

3-bromo-5'-chloro-N2'-(trans-4-(2-methoxyethylamino)cyclohexyl)-N6-((tetrahydro-2H-pyran-4-yl)methyl)-2,4'-bipyridine-2',6-diamine;

trans-4-(3,5'-dichloro-6-((2,2-dimethyltetrahydro-2H-pyran-4-yl)methyl)amino-2,4'-bipyridin-2'-yl-amino)cyclohexanol;

(2S)-3-(trans-4-(3,5'-dichloro-6-((2,2-dimethyltetrahydro-2H-pyran-4-yl)methyl)amino-2,4'-bipyridin-2'-yl-amino)cyclohexylamino)-1,1,1-trifluoropropan-2-ol;

(2R)-3-(trans-4-(3,5'-dichloro-6-((2,2-dimethyltetrahydro-2H-pyran-4-yl)methyl)amino-2,4'-bipyridin-2'-yl-amino)cyclohexylamino)-1,1,1-trifluoropropan-2-ol;

3,5'-dichloro-N6-((tetrahydro-2H-pyran-4-yl)methyl)-N2'-(trans-4-(2-(trifluoromethoxy)ethylamino)cyclohexyl)-2,4'-bipyridine-2',6-diamine;

N2'-(trans-4-aminocyclohexyl)-5'-chloro-N6-(((R)-2,2-dimethyltetrahydro-2H-pyran-4-yl)methyl)-2,4'-bipyridine-2',6-diamine;

N2'-(trans-4-aminocyclohexyl)-5'-chloro-N6-(((S)-2,2-dimethyltetrahydro-2H-pyran-4-yl)methyl)-2,4'-bipyridine-2',6-diamine;

N2'-(trans-4-aminocyclohexyl)-3,5,5'-trichloro-N6-((tetrahydro-2H-pyran-4-yl)methyl)-2,4'-bipyridine-2',6-diamine;

N2'-(trans-4-aminocyclohexyl)-5'-chloro-5-fluoro-N6-((tetrahydro-2H-pyran-4-yl)methyl)-2,4'-bipyridine-2',6-diamine;

N2'-(trans-4-aminocyclohexyl)-5'-chloro-N6-((4-methyltetrahydro-2H-pyran-4-yl)methyl)-2,4'-bipyridine-2',6-diamine;

N2'-(trans-4-aminocyclohexyl)-5'-chloro-5-fluoro-N6-((4-methyltetrahydro-2H-pyran-4-yl)methyl)-2,4'-bipyridine-2',6-diamine;

N2'-(trans-4-aminocyclohexyl)-5'-chloro-N6-((4-fluorotetrahydro-2H-pyran-4-yl)methyl)-2,4'-bipyridine-2',6-diamine;

trans-4-(5'-chloro-6-(3-fluorobenzylamino)-2,4'-bipyridin-2'-yl-amino)cyclohexanol;

5'-chloro-N2'-(trans-4-(dimethylamino)cyclohexyl)-N6-(3-fluorobenzyl)-2,4'-bipyridine-2',6-diamine;

5'-chloro-N6-(3-fluorobenzyl)-N2'-(trans-4-(2-methoxyethylamino)cyclohexyl)-2,4'-bipyridine-2',6-diamine;

2-(trans-4-(5'-chloro-6-(3-fluorobenzylamino)-2,4'-bipyridin-2'-yl-amino)cyclohexylamino)ethanol;

5'-chloro-N6-(3,5-difluorobenzyl)-N2'-(trans-4-(2-methoxyethylamino)cyclohexyl)-2,4'-bipyridine-2',6-diamine;

5'-chloro-N6-(3-fluorobenzyl)-N2'-(trans-4-((2-methoxyethyl)(methyl)amino)cyclohexyl)-2,4'-bipyridine-2',6-diamine;

N2'-(trans-4-aminocyclohexyl)-5'-chloro-N6-(((2R,6S)-2,6-dimethyltetrahydro-2H-pyran-4-yl)methyl)-2,4'-bipyridine-2',6-diamine;

((5'-chloro-5-fluoro-2'-(trans-4-(2-methoxyethylamino)cyclohexylamino)-2,4'-bipyridin-6-yl-amino)methyl)tetrahydro-2H-pyran-4-carbonitrile;

((2'-(trans-4-aminocyclohexylamino)-5'-chloro-5-fluoro-2,4'-bipyridin-6-yl-amino)methyl)tetrahydro-2H-pyran-4-carbonitrile;

((5'-chloro-5-fluoro-2'-(trans-4-(propylamino)cyclohexylamino)-2,4'-bipyridin-6-yl-amino)methyl)tetrahydro-2H-pyran-4-carbonitrile;

((5'-chloro-2'-(trans-4-(dipropylamino)cyclohexylamino)-5-fluoro-2,4'-bipyridin-6-yl-amino)methyl)tetrahydro-2H-pyran-4-carbonitrile;

((5'-chloro-5-fluoro-2'-(trans-4-((R)-1-methoxypropan-2-yl-amino)cyclohexylamino)-2,4'-bipyridin-6-yl-amino)methyl)tetrahydro-2H-pyran-4-carbonitrile;

((5'-chloro-2'-(trans-4-((2-methyl-1,3-dioxolan-2-yl)methyl)aminocyclohexylamino)-2,4'-bipyridin-6-yl-amino)methyl)tetrahydro-2H-pyran-4-carbonitrile;

(4-((5'-chloro-2'-(trans-4-((R)-1-methoxypropan-2-yl-amino)cyclohexylamino)-2,4'-bipyridin-6-yl-amino)methyl)tetrahydro-2H-pyran-4-yl)methanol; and

5'-chloro-5-fluoro-N6-((4-methyltetrahydro-2H-pyran-4-yl)methyl)-N2'-(trans-4-(1,1-dioxotetrahydrothiophen-3-yl-amino)cyclohexyl)-2,4'-bipyridine-2',6-diamine.

15. A compound of Claims 1 or 4, selected from:

trans-N1-(4-(3-chloro-6-((tetrahydro-2H-pyran-4-yl)methyl)aminopyrazin-2-yl)pyridin-2-yl)cyclohexane-1,4-diamine;

trans-N1-(5-chloro-4-(3-chloro-6-((tetrahydro-2H-pyran-4-yl)methyl)aminopyrazin-2-yl)pyridin-2-yl)cyclohexane-1,4-diamine;

trans-4-(5-chloro-4-(5-chloro-6-((tetrahydro-2H-pyran-4-yl)methyl)aminopyrazin-2-yl)pyridin-2-yl-amino)cyclohexanol;

trans-N1-(5-chloro-4-(5-chloro-6-((tetrahydro-2H-pyran-4-yl)methyl)aminopyrazin-2-yl)pyridin-2-yl)cyclohexane-1,4-diamine;

trans-4-(5-chloro-4-(6-(((S)-tetrahydro-2H-pyran-3-yl)methyl)aminopyrazin-2-yl)pyridin-2-yl-amino)cyclohexanol;

trans-4-(5-chloro-4-(6-(((R)-tetrahydro-2H-pyran-3-yl)methyl)aminopyrazin-2-yl)pyridin-2-yl-amino)cyclohexanol;

trans-N1-(5-chloro-4-(6-(((S)-tetrahydro-2H-pyran-3-yl)methyl)aminopyrazin-2-yl)pyridin-2-yl)cyclohexane-1,4-diamine;

trans-N1-(5-chloro-4-(6-(((R)-tetrahydro-2H-pyran-3-yl)methyl)aminopyrazin-2-yl)pyridin-2-yl)cyclohexane-1,4-diamine;

trans-N1-(5-chloro-4-(6-(methyl((tetrahydro-2H-pyran-4-yl)methyl)amino)pyrazin-2-yl)pyridin-2-yl)cyclohexane-1,4-diamine;

trans-N1-(5-chloro-4-(6-((tetrahydro-2H-pyran-4-yl)methyl)aminopyrazin-2-yl)pyridin-2-yl)-N4-(2-methoxyethyl)cyclohexane-1,4-diamine;

trans-4-(5-chloro-4-(6-((tetrahydro-2H-pyran-3-yl)methyl)aminopyrazin-2-yl)pyridin-2-yl-amino)cyclohexanol;

trans-4-(5-chloro-4-(6-((tetrahydro-2H-pyran-4-yl)methyl)aminopyrazin-2-yl)pyridin-2-yl-amino)cyclohexanol; and

trans-N1-(5-chloro-4-(6-(3-fluorobenzylamino)pyrazin-2-yl)pyridin-2-yl)cyclohexane-1,4-diamine.

16. A compound according to any one of Claims 1 to 5, 14, or 15, or pharmaceutically acceptable salt or solvate thereof, for use in therapy.

17. A compound according to Claims 1, 13, 14, 15, or a pharmaceutically acceptable salt or solvate thereof for use in therapy.

18. A compound according to any one of Claims 1 to 5, 14 or 15, or pharmaceutically acceptable salt or solvate thereof, for use in a method of treating a disease or condition mediated by CDK9.

19. A compound according to any one of Claims 1, 13, 14, or 15 or pharmaceutically acceptable salt or solvate thereof, for use in a method of treating a disease or condition mediated by CDK9.

20. A method of treatment of a disease or condition mediated by CDK9 comprising administration to a subject in need thereof a therapeutically effective amount of a compound according to any one of Claims 1 to 5, 14 or 15, or a pharmaceutically acceptable salt thereof.

21. A method of treatment of a disease or condition mediated by CDK9 comprising administration to a subject in need thereof a therapeutically effective amount of a compound according to any one of Claims 1, 13, 14, or 15 or a pharmaceutically acceptable salt thereof.

22. A compound as claimed in Claim 19, the use of claim 20 or the method of claim 21, wherein the disease or condition mediated by CDK9 is selected from cancer, cardiac hypotrophy, HIV and inflammatory diseases.

23. A method of Claim 21 wherein the disease or condition mediated by CDK9 is selected from cancer, cardiac hypotrophy, HIV, and inflammatory diseases.

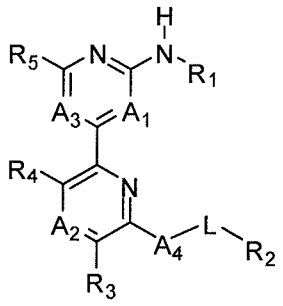
24. A method of Claim 23 wherein the cancer is selected from the group consisting of bladder, head and neck, breast, stomach, ovary, colon, lung, brain, larynx, lymphatic system, hematopoetic system, genitourinary tract, gastrointestinal, ovarian, prostate, gastric, bone, small-cell lung, glioma, colorectal. and pancreatic cancer.

25. A pharmaceutical composition comprising a compound according to any one of claims 1 to 5, 14 or 15, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier, diluent or excipient.

CLAIMS

THE CLAIMS DEFINING THE INVENTION ARE AS FOLLOWS:

1. A compound of formula (I):



or a pharmaceutically acceptable salt thereof, wherein:

A_1 is N or CR_6;

A_2 is N, N(O) or CR_7;

A_3 is N or CR_8;

A_4 is NR_9, or O;

L is selected from a bond, optionally substituted C_{1-4}alkyl, C_{3-6} cycloalkyl, C_{3-6} heterocycloalkyl, or C_{2-4} alkenyl;

R_1 is X-R_{16};

X is a bond, or C_{1-2} alkyl;

R_{16} is selected from the group consisting of C_{1-2}-alkyl, C_{4-6}cycloalkyl, heterocycloalkyl, and heteroaryl;

wherein R_{16} is substituted with one to three groups independently selected from halogen, hydrogen, C_{1-3}alkyl, C_{3-6}branched alkyl, OH, C_{1-2}alkoxy, R_{22}-OR_{12}, $S(O)_{1-2}R_{12}$, $C(O)OR_{12}$, R_{22}-$C(O)OR_{12}$, $C(O)R_{19}$, R_{22}-$OC(O)R_{19}$, $C(O)NR_{13}R_{14}$, $NR_{15}S(O)_2R_{12}$, $NR_{17}R_{18}$, R_{22}-$NR_{17}R_{18}$, $NR_{15}C(O)R_{19}$, R_{22}-$NR_{15}C(O)R_{19}$, and $NR_{15}C(O)OCH_2Ph$;

R_{17} and R_{18} are each, independently, selected from the group consisting of hydrogen, hydroxyl, C_{1-6}alkyl, C_{1-6}haloalkyl, C_{3-6}branched alkyl, C_{3-6} cycloalkyl, R_{22}-OR_{12}, R_{22}-$S(O)_{0-2}R_{12}$, R_{22}-$S(O)_2NR_{13}R_{14}$, R_{22}-$C(O)OR_{12}$, R_{22}-$C(O)R_{19}$, R_{22}-

$OC(O)R_{19}$, R_{22}-$C(O)NR_{13}R_{14}$, R_{22}-$NR_{15}S(O)_2R_{12}$, R_{22}-$NR_{23}R_{24}$, R_{22}-$NR_{15}C(O)R_{19}$, R_{22}-$NR_{15}C(O)OCH_2Ph$, R_{22}-$NR_{15}C(O)OR_{12}$, R_{22}-$NR_{15}C(O)NR_{13}R_{14}$, cycloalkyl, heterocycloalkyl and heteroaryl; alternatively, R_{17} and R_{18} along with the nitrogen atom to which they are attached to can be taken together to form a four to six membered heterocyclic ring wherein the carbon atoms of said ring are optionally substituted with R_{20}, and the nitrogen atoms of said ring are optionally substituted with R_{21};

R_{19} is selected from optionally substituted alkyl, optionally substituted cycloalkyl, optionally substituted heterocycloalkyl, optionally substituted aryl, and optionally substituted heteroaryl;

R_{20} is selected from the group consisting of C_{1-6} alkyl or C_{1-6} haloalkyl;

R_{21} is selected from the group consisting of C_{1-6}alkyl, C_{1-6}haloalkyl, $C(O)R_{12}$, $C(O)OR_{12}$, $S(O)_2R_{12}$;

R_{22} is selected from the group consisting of C_{1-6} alkyl, C_{1-6}haloalkyl, C_{3-6} branched alkyl, C_{3-6}branched haloalkyl;

R_{23} and R_{24} are each, independently, selected from the group consisting of hydrogen, C_{1-6} alkyl, C_{1-6}haloalkyl, C_{3-6} branched alkyl, C_{3-6} branched haloalkyl;

R_2 is selected from the group consisting of optionally substituted C_{1-6} alkyl, optionally substituted C_{3-6} branched alkyl, optionally substituted C_{3-8} cycloalkyl, optionally substituted heterocycloalkyl, and optionally substituted heteroaryl;

R_4, R_5, and R_6 are each, independently, selected from the group consisting of hydrogen, hydroxyl, cyano, halogen, C_{1-4} alkyl, C_{1-4}haloalkyl, C_{2-4} alkenyl, C_{2-4} alkynyl, amino, $NR_{10}R_{11}$, and alkoxy;

R_3 and R_7 are each, independently, selected from the group consisting of hydrogen, hydroxyl, cyano, halogen, alkyl, haloalkyl, alkenyl, alkynyl, alkoxy, $NR_{10}R_{11}$, $C(O)R_{12}$, $C(O)OR_{12}$, $C(O)NR_{13}R_{14}$, $S(O)_{0-2}R_{12}$, $S(O)_{0-2}NR_{13}R_{14}$, and optionally substituted C_{3-4} cycloalkyl;

R_8 is Cl, F or methyl;

R_9 is selected from the group consisting of hydrogen, C_{1-4} alkyl, alkoxy, $C(O)R_{12}$, $C(O)OR_{15}$, $C(O)NR_{13}R_{14}$, $S(O)_{0-2}R_{12}$, $S(O)_{0-2}NR_{13}R_{14}$, optionally substituted C_{3-4} cycloalkyl, and optionally substituted heterocycloalkyl;

R_{10} and R_{11} are each, independently, selected from the group consisting of hydrogen, hydroxyl, alkyl, alkoxy, $C(O)R_{12}$, $C(O)OR_{12}$, $C(O)NR_{13}R_{14}$, $S(O)_{0-2}R_{12}$, and $S(O)_{0-2}NR_{13}R_{14}$; alternatively, R_{10} and R_{11} along with the nitrogen atom to which they are attached to can be taken together to form an optionally substituted four to six membered heteroaromatic, or a non-aromatic heterocyclic ring;
R_{12} and R_{15} are each, individually, selected from the group consisting of hydrogen, alkyl, branched alkyl, haloalkyl, branched haloalkyl, $(CH_2)_{0-3}$-cycloalkyl, $(CH_2)_{0-3}$-heterocycloalkyl, $(CH_2)_{0-3}$- aryl, and heteroaryl;
R_{13} and R_{14} are each, independently, selected from the group consisting of hydrogen, hydroxyl, alkyl, branched alkyl, haloalkyl, branched haloalkyl, alkoxy, cycloalkyl or heterocycloalkyl; and alternatively, R_{13} and R_{14} along with the nitrogen atom to which they are attached to can be taken together to form an optionally substituted four to six membered heteroaromatic, or non-aromatic heterocyclic ring.

2. A compound of claim 1, wherein:
A_1 is N;
A_2 is N; and
A_3 is CR_8.

3. A compound of claim 1, wherein A_1 is CR_6, A_2 is CR_7, and A_3 is CR_8.

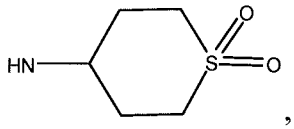
4. A compound of claim 1, wherein A_1 is CR_6, A_2 is N, and A_3 is CR_8.

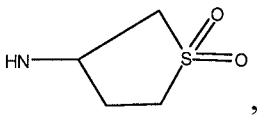
5. A compound of claim 1, wherein:
A_1 is N;
A_2 is CR_7; and
A_3 is CR_8.

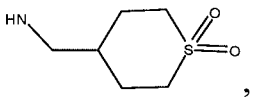
6. A compound of any one of claims 1 to 5, wherein:
R_8 is Cl.

7. A compound of claim 1, wherein:

R_{16} is selected from the group consisting of C_{1-2}-alkyl, cyclopentyl, cyclohexyl, piperidine, piperazine, morpholine, pyridine, pyrrolidine, and tetrahydro-2H-pyran; wherein R_{16} is substituted with one to three groups selected from amino, hydroxyl, $NHCH_2$-phenyl, CH_2-amino, COO-*t*-butyl, H, methoxy, NH-SO_2-ethyl, CH_2-$NHSO_2$-ethyl, SO_2-ethyl, *t*-butyl, methyl, CH_2-COOH, CO-$NHCH_3$, $CON(CH_3)_2$, $NHC(CH_3)$-CH_2-SO_2-CH_3, NH-COO-CH_2-phenyl, hydroxy-methyl, CH_2-NH-CH_3, CH_2-NH-ethyl, NH-CH_2-CH_2-methoxy, CH_2-NH-CO-CH_3, NH-CH_2-CH_2OH, NH-CO-CH_2-$N(CH_3)_2$. NH-CO-methylpyrrolidine, NH-CH_2-$C(CH_3)$-dioxolane, NH-CO-pyridyl, NH-ethyl, pyrrolidine, CH_2-NH-CO-pyridyl, NH-tetrahydropyran, $COCH_2$-$N(CH_3)_2$, NH-CH_2-$C(CH_3)$-dimethyldioxolane, tetrahydropyran, CO-methylpyrrolidine, CH_2-methylpiperidine, NH-CO-CH_3, NH-SO_2-CH_3, NH-$CH(CH_2$-$OCH_3)_2$, NH-CH_2-tetrahydrofuran, NH-CH_2-oxetane, NH-tetrahydropyran, NH-CH_2-dioxane, $N(CH_3)$-CH_2CH_2-OCH_3, CH(OH)-CH_2-amino, NH-CH_2CH_2-OCF_3, $NHCH_2$-OCH_3, NH-CH_2-$CH(CF_3)$-OCH_3, NH-$CH(CH_3)$-CH_2-OH, F, NH-oxetane, CH_2-CH_2-OCH_3, CH_2-OCH_3, CH_2-tetrahydropyran, CH_2-methylpiperizine, NH_2-CH_2-CH(OH)-CF_3, piperidine, CH_2-pyrrolidine, NH-$CH(CH_3)CH_2OCH_3$, NH-tetrahydrofuran, $(CH_2)_3$-NH_2, hydroxyethyl, propyl, CH_2-pyridyl, CH_2-piperidine, morpholine, NH-chloropyrimidine, NH-CH_2CH_2-SO_2-methyl, $(CH_3)_3$-$N(CH_3)_2$, piperazine,



,


,


,

and CH_2-morpholine.

8. A compound of any one of claims 1 to 7 wherein:

R_3 is selected from H, methyl, cyano, chloro, $CONH_2$, amino, cyclopropyl, ethyl, and fluoro;

R_4 is selected from halogen, methyl, hydrogen, and halo-methyl;

R_6 is H;

R_7 is selected from H, COOH, Cl, F, $CONH_2$, CN, and CF_3;

R_8 is Cl;

R_{17} and R_{18} are each, independently, selected from the group consisting of hydrogen, C_{1-3}alkyl, C_{1-4}haloalkyl, C_{3-6}branched alkyl, R_{22}-OR_{12}, R_{22}-$S(O)_2R_{12}$, R_{22}-$NR_{15}S(O)_2R_{12}$, heterocycloalkyl or heteroaryl; alternatively, R_{17} and R_{18} along with the nitrogen atom to which they are attached to can be taken together to form a four to six membered heterocyclic ring wherein said ring carbon atoms are optionally substituted with R_{20}, and the ring nitrogen atoms are optionally substituted with R_{21};

R_{19} is selected from C_{1-3}-alkyl, optionally substituted heterocycloalkyl, optionally substituted aryl or optionally substituted heteroaryl;

R_{20} represents the group C_{1-3}alkyl; and

R_{22} is selection from the group consisting of C_{1-4}alkyl, and C_{3-6} branched alkyl.

9. A compound of any one of claims 1 to 8 wherein:

L is selected from a bond, C_{1-4}-alkyl, and cyclopropyl;

R_2 is selected from the group consisting of C_{3-7} cycloalkyl, a five to seven membered heterocycloalkyl, and pyridyl, wherein each said R_2 group is substituted with one, two, or three substituents independently selected from hydrogen, cyano, CO-NH_2, halogen, methoxy, dihalo-methoxy, trihalo-methoxy, trihalo alkyl, C_{1-3}-alkyl, and hydroxy; and

R_9 represents methyl, hydrogen, or ethyl.

10. A compound of claim 1, wherein:

A_1 is CR_6;

A_2 is CR_7;

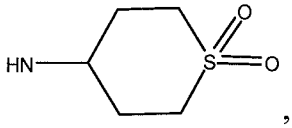
A_3 is CR_8;

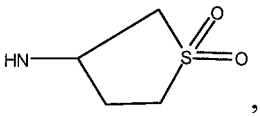
L is a bond, C_{1-2} alkyl, or C_{3-4}-cycloalkyl;

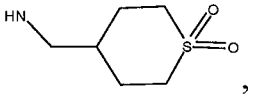
R_1 is X-R_{16};

X is a bond, or C_{1-2} alkyl;

R_{16} is selected from the group consisting of C_{1-2}-alkyl, cyclopentyl, cyclohexyl, piperidine, piperazine, morpholine, pyridine, pyrrolidine, and tetrahydro-2H-pyran; wherein R_{16} is substituted with one to three groups independently selected from amino, hydroxyl, $NHCH_2$-phenyl, CH_2-amino, COO-t-butyl, H, methoxy, NH-SO_2-ethyl, CH_2-$NHSO_2$-ethyl, SO_2-ethyl, t-butyl, methyl, CH_2-COOH, CO-$NHCH_3$, $CON(CH_3)_2$, $NHCH_2$-CH_2-SO_2-CH_3, NH-COO-CH_2-phenyl, hydroxy-methyl, CH_2-NH-CH_3, CH_2-NH-ethyl, NH-CH_2-CH_2-methoxy, CH_2-NH-CO-CH_3, NH-CH_2-CH_2OH, NH-CO-CH_2-$N(CH_3)_2$. NH-CO-methylpyrrolidine, NH-CO-pyridyl, NH-ethyl, pyrrolidine, CH_2-NH-CO-pyridyl, $COCH_2$-$N(CH_3)_2$, tetrahydropyran, CO-methylpyrrolidine, CH_2-methylpiperidine, NH-CO-CH_3, NH-SO_2-CH_3, NH-CH_2-tetrahydrofuran, NH-CH_2-dioxane, N(CH_3)-CH_2CH_2-OCH_3, CH(OH)-CH_2-amino, NH-CH_2CH_2-OCF_3, NH(CH_3)-CH_2-OCH_3, NH-CH_2-CH(CF_3)-OCH_3, F, NH-oxetane, CH_2-CH_2-OCH_3, CH_2-OCH_3, CH_2-tetrahydropyran, CH_2-methylpiperizine, NH_2-CH_2-CH(OH)-CF_3, piperidine, CH_2-pyrrolidine, NH-$CH(CH_3)CH_2OCH_3$, NH-tetrahydrofuran, $(CH_2)_3$-NH_2, hydroxyethyl, propyl, CH_2-pyridyl, CH_2-piperidine, morpholine, NH-chloropyrimidine, NH-CH_2CH_2-SO_2-methyl, $(CH_3)_3$-$N(CH_3)_2$, piperazine, CH_2-morpholine, NH-CH_2-C(CH_3)-dioxolane, NH-tetrahydropyran, NH-CH_2-C(CH_3)-dimethyldioxolane, NH-$CH(CH_2$-$OCH_3)_2$, NH-CH_2-oxetane, NH-tetrahydropyran, N(CH_3)-CH_2CH_2-OCH_3, NH-CH(CH_3)-CH_2-OH,

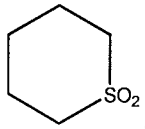


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and NH-CH(CH_3)-CH_2-OH;

R_2 is selected from the group consisting of cyclohexyl, 1,3-dioxane, pyridinyl, tetrahydropyranyl, cycloheptyl, 1,4-dioxane, morpholinyl, alkyl substituted dioxane, tetrahydrofuranyl, dioxepane , piperidinyl, and 

,

wherein each said R_2 group is substituted with one, two, or three substituents independently selected from Cl, Br, F, methoxy, hydroxy-methyl, hydrogen,

carboxamide, cyano, dihalo-methoxy, trihalo-methoxy, trifluoro-methyl, hydroxyl, and methyl; and

R_4, is chloro, hydrogen, trifluoro-methyl, fluoro, or bromo;

R_5, and R_6 are each independently hydrogen;

R_3 is selected from hydrogen, fluoro, cyano, CO-NH_2, chloro, amino, methyl, and cyclopropyl;

R_7 is selected from H, trifluoro-methyl, COOH, CO-NH_2, and cyano;

R_8 represents Cl; and

R_9 is selected from the group consisting of H, ethyl, and methyl.

11. A compound of claim 1 selected from:

N2'-(trans-4-aminocyclohexyl)-5'-chloro-3,5-difluoro-N6-((tetrahydro-2H-pyran-4-yl)methyl)-2,4'-bipyridine-2',6-diamine;

3,5'-dichloro-N2'-(trans-4-(((R)-2,2-dimethyl-1,3-dioxolan-4-yl)methyl)aminocyclohexyl)-N6-((tetrahydro-2H-pyran-4-yl)methyl)-2,4'-bipyridine-2',6-diamine;

5'-chloro-N6-((tetrahydro-2H-pyran-4-yl)dideuteromethyl)-N2'-(*trans*-4-(((S)-tetrahydrofuran-2-yl)methyl)aminocyclohexyl)-2,4'-bipyridine-2',6-diamine;

5'-chloro-5-fluoro-N2'-(trans-4-(2-(methylsulfonyl)ethylamino)cyclohexyl)-N6-((tetrahydro-2H-pyran-4-yl)methyl)-2,4'-bipyridine-2',6-diamine;

3,5'-dichloro-N2'-(trans-4-((R)-1-methoxypropan-2-yl-amino)cyclohexyl)-N6-(((S)-tetrahydro-2H-pyran-3-yl)methyl)-2,4'-bipyridine-2',6-diamine;

3,5'-dichloro-N2'-(trans-4-((R)-1-methoxypropan-2-yl-amino)cyclohexyl)-N6-(((R)-tetrahydro-2H-pyran-3-yl)methyl)-2,4'-bipyridine-2',6-diamine;

4-((5'-chloro-2'-(trans-4-((R)-1-methoxypropan-2-yl-amino)cyclohexylamino)-2,4'-bipyridin-6-yl-amino)methyl)tetrahydro-2H-pyran-4-carbonitrile;

N2'-(trans-4-aminocyclohexyl)-3-chloro-5'-fluoro-N6-((tetrahydro-2H-pyran-4-yl)methyl)-2,4'-bipyridine-2',6-diamine;

3,5'-dichloro-N2'-(trans-4-((R)-1-methoxypropan-2-yl-amino)cyclohexyl)-N6-((tetrahydro-2H-pyran-4-yl)methyl)-2,4'-bipyridine-2',6-diamine;

5'-chloro-3-fluoro-N2'-(trans-4-((R)-1-methoxypropan-2-yl-amino)cyclohexyl)-N6-((tetrahydro-2H-pyran-4-yl)methyl)-2,4'-bipyridine-2',6-diamine;
5'-chloro-5-fluoro-N2'-(trans-4-((R)-1-methoxypropan-2-yl-amino)cyclohexyl)-N6-((tetrahydro-2H-pyran-4-yl)methyl)-2,4'-bipyridine-2',6-diamine;
5'-chloro-N6-((2,2-dimethyltetrahydro-2H-pyran-4-yl)methyl)-N2'-(trans-4-((R)-1-methoxypropan-2-yl-amino)cyclohexyl)-2,4'-bipyridine-2',6-diamine;
5'-chloro-N6-(((S)-2,2-dimethyltetrahydro-2H-pyran-4-yl)methyl)-N2'-(trans-4-((R)-1-methoxypropan-2-yl-amino)cyclohexyl)-2,4'-bipyridine-2',6-diamine;
5'-chloro-5-fluoro-N6-((tetrahydro-2H-pyran-4-yl)methyl)-N2'-(trans-4-((1,1-dioxotetrahydro-2H-thiopyran-4-yl)methyl)aminocyclohexyl)-2,4'-bipyridine-2',6-diamine;
5'-chloro-5-fluoro-N2'-(trans-4-(2-methoxyethylamino)cyclohexyl)-N6-((tetrahydro-2H-pyran-4-yl)methyl)-2,4'-bipyridine-2',6-diamine;
N2'-(trans-4-aminocyclohexyl)-5'-chloro-N6-((5-fluoropyridin-3-yl)methyl)-2,4'-bipyridine-2',6-diamine;
N2'-(trans-4-aminocyclohexyl)-3,5'-dichloro-N6-((tetrahydro-2H-pyran-4-yl)methyl)-2,4'-bipyridine-2',6-diamine;
N2'-(trans-4-aminocyclohexyl)-3,5'-dichloro-N6-((tetrahydro-2H-pyran-4-yl)methyl)-2,4'-bipyridine-2',6-diamine;
3,5'-dichloro-N2'-(trans-4-(2-methoxyethylamino)cyclohexyl)-N6-((tetrahydro-2H-pyran-4-yl)methyl)-2,4'-bipyridine-2',6-diamine;
2-(trans-4-(3,5'-dichloro-6-((tetrahydro-2H-pyran-4-yl)methyl)amino-2,4'-bipyridin-2'-yl-amino)cyclohexylamino)ethanol;
trans-N1-(5-chloro-4-(6-(((R)-tetrahydro-2H-pyran-3-yl)methyl)aminopyrazin-2-yl)pyridin-2-yl)cyclohexane-1,4-diamine;
3,5'-dichloro-N6-((tetrahydro-2H-pyran-4-yl)methyl)-N2'-(trans-4-(((R)-tetrahydrofuran-2-yl)methyl)aminocyclohexyl)-2,4'-bipyridine-2',6-diamine;
3,5'-dichloro-N6-((tetrahydro-2H-pyran-4-yl)methyl)-N2'-(trans-4-(((S)-tetrahydrofuran-2-yl)methyl)aminocyclohexyl)-2,4'-bipyridine-2',6-diamine;
3,5'-dichloro-N2'-(trans-4-((2-methoxyethyl)(methyl)amino)cyclohexyl)-N6-((tetrahydro-2H-pyran-4-yl)methyl)-2,4'-bipyridine-2',6-diamine;

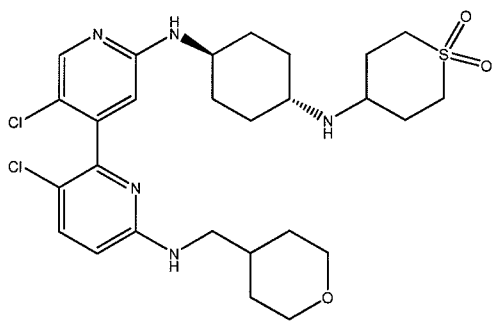
5'-chloro-N6-((tetrahydro-2H-pyran-4-yl)methyl)-N2'-(trans-4-(((R)-tetrahydrofuran-2-yl)methyl)aminocyclohexyl)-2,4'-bipyridine-2',6-diamine;
5'-chloro-N6-((tetrahydro-2H-pyran-4-yl)methyl)-N2'-(trans-4-(((S)-tetrahydrofuran-2-yl)methyl)aminocyclohexyl)-2,4'-bipyridine-2',6-diamine;
N2'-(trans-4-aminocyclohexyl)-5'-chloro-3-fluoro-N6-((tetrahydro-2H-pyran-4-yl)methyl)-2,4'-bipyridine-2',6-diamine;
5'-chloro-3-fluoro-N2'-(trans-4-(2-methoxyethylamino)cyclohexyl)-N6-((tetrahydro-2H-pyran-4-yl)methyl)-2,4'-bipyridine-2',6-diamine;
N2'-(trans-4-aminocyclohexyl)-3-bromo-5'-chloro-N6-((tetrahydro-2H-pyran-4-yl)methyl)-2,4'-bipyridine-2',6-diamine;
3-bromo-5'-chloro-N2'-(trans-4-(2-methoxyethylamino)cyclohexyl)-N6-((tetrahydro-2H-pyran-4-yl)methyl)-2,4'-bipyridine-2',6-diamine;
trans-4-(3,5'-dichloro-6-((2,2-dimethyltetrahydro-2H-pyran-4-yl)methyl)amino-2,4'-bipyridin-2'-yl-amino)cyclohexanol;
(2S)-3-(trans-4-(3,5'-dichloro-6-((2,2-dimethyltetrahydro-2H-pyran-4-yl)methyl)amino-2,4'-bipyridin-2'-yl-amino)cyclohexylamino)-1,1,1-trifluoropropan-2-ol;
(2R)-3-(trans-4-(3,5'-dichloro-6-((2,2-dimethyltetrahydro-2H-pyran-4-yl)methyl)amino-2,4'-bipyridin-2'-yl-amino)cyclohexylamino)-1,1,1-trifluoropropan-2-ol;
3,5'-dichloro-N6-((tetrahydro-2H-pyran-4-yl)methyl)-N2'-(trans-4-(2-(trifluoromethoxy)ethylamino)cyclohexyl)-2,4'-bipyridine-2',6-diamine;
N2'-(trans-4-aminocyclohexyl)-5'-chloro-N6-(((R)-2,2-dimethyltetrahydro-2H-pyran-4-yl)methyl)-2,4'-bipyridine-2',6-diamine;
N2'-(trans-4-aminocyclohexyl)-5'-chloro-N6-(((S)-2,2-dimethyltetrahydro-2H-pyran-4-yl)methyl)-2,4'-bipyridine-2',6-diamine;
N2'-(trans-4-aminocyclohexyl)-3,5,5'-trichloro-N6-((tetrahydro-2H-pyran-4-yl)methyl)-2,4'-bipyridine-2',6-diamine;
N2'-(trans-4-aminocyclohexyl)-5'-chloro-5-fluoro-N6-((tetrahydro-2H-pyran-4-yl)methyl)-2,4'-bipyridine-2',6-diamine;

N2'-(trans-4-aminocyclohexyl)-5'-chloro-N6-((4-methyltetrahydro-2H-pyran-4-yl)methyl)-2,4'-bipyridine-2',6-diamine;
N2'-(trans-4-aminocyclohexyl)-5'-chloro-5-fluoro-N6-((4-methyltetrahydro-2H-pyran-4-yl)methyl)-2,4'-bipyridine-2',6-diamine;
N2'-(trans-4-aminocyclohexyl)-5'-chloro-N6-((4-fluorotetrahydro-2H-pyran-4-yl)methyl)-2,4'-bipyridine-2',6-diamine;
N2'-(trans-4-aminocyclohexyl)-5'-chloro-N6-(((2R,6S)-2,6-dimethyltetrahydro-2H-pyran-4-yl)methyl)-2,4'-bipyridine-2',6-diamine;
((5'-chloro-5-fluoro-2'-(trans-4-(2-methoxyethylamino)cyclohexylamino)-2,4'-bipyridin-6-yl-amino)methyl)tetrahydro-2H-pyran-4-carbonitrile;
((2'-(trans-4-aminocyclohexylamino)-5'-chloro-5-fluoro-2,4'-bipyridin-6-yl-amino)methyl)tetrahydro-2H-pyran-4-carbonitrile;
((5'-chloro-5-fluoro-2'-(trans-4-(propylamino)cyclohexylamino)-2,4'-bipyridin-6-yl-amino)methyl)tetrahydro-2H-pyran-4-carbonitrile;
((5'-chloro-2'-(trans-4-(dipropylamino)cyclohexylamino)-5-fluoro-2,4'-bipyridin-6-yl-amino)methyl)tetrahydro-2H-pyran-4-carbonitrile;
((5'-chloro-5-fluoro-2'-(trans-4-((R)-1-methoxypropan-2-yl-amino)cyclohexylamino)-2,4'-bipyridin-6-yl-amino)methyl)tetrahydro-2H-pyran-4-carbonitrile;
((5'-chloro-2'-(trans-4-((2-methyl-1,3-dioxolan-2-yl)methyl)aminocyclohexylamino)-2,4'-bipyridin-6-yl-amino)methyl)tetrahydro-2H-pyran-4-carbonitrile;
(4-((5'-chloro-2'-(trans-4-((R)-1-methoxypropan-2-yl-amino)cyclohexylamino)-2,4'-bipyridin-6-yl-amino)methyl)tetrahydro-2H-pyran-4-yl)methanol; and
5'-chloro-5-fluoro-N6-((4-methyltetrahydro-2H-pyran-4-yl)methyl)-N2'-(trans-4-(1,1-dioxotetrahydrothiophen-3-yl-amino)cyclohexyl)-2,4'-bipyridine-2',6-diamine.

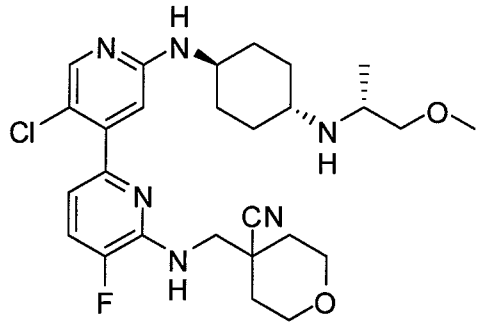
12. A compound of claims 1 or 4, selected from:
trans-N1-(4-(3-chloro-6-((tetrahydro-2H-pyran-4-yl)methyl)aminopyrazin-2-yl)pyridin-2-yl)cyclohexane-1,4-diamine;

trans-N1-(5-chloro-4-(3-chloro-6-((tetrahydro-2H-pyran-4-yl)methyl)aminopyrazin-2-yl)pyridin-2-yl)cyclohexane-1,4-diamine;
trans-4-(5-chloro-4-(5-chloro-6-((tetrahydro-2H-pyran-4-yl)methyl)aminopyrazin-2-yl)pyridin-2-yl-amino)cyclohexanol;
trans-N1-(5-chloro-4-(5-chloro-6-((tetrahydro-2H-pyran-4-yl)methyl)aminopyrazin-2-yl)pyridin-2-yl)cyclohexane-1,4-diamine;
trans-4-(5-chloro-4-(6-(((S)-tetrahydro-2H-pyran-3-yl)methyl)aminopyrazin-2-yl)pyridin-2-yl-amino)cyclohexanol;
trans-4-(5-chloro-4-(6-(((R)-tetrahydro-2H-pyran-3-yl)methyl)aminopyrazin-2-yl)pyridin-2-yl-amino)cyclohexanol;
trans-N1-(5-chloro-4-(6-(((S)-tetrahydro-2H-pyran-3-yl)methyl)aminopyrazin-2-yl)pyridin-2-yl)cyclohexane-1,4-diamine;
trans-N1-(5-chloro-4-(6-(((R)-tetrahydro-2H-pyran-3-yl)methyl)aminopyrazin-2-yl)pyridin-2-yl)cyclohexane-1,4-diamine;
trans-N1-(5-chloro-4-(6-(methyl((tetrahydro-2H-pyran-4-yl)methyl)amino)pyrazin-2-yl)pyridin-2-yl)cyclohexane-1,4-diamine;
trans-N1-(5-chloro-4-(6-((tetrahydro-2H-pyran-4-yl)methyl)aminopyrazin-2-yl)pyridin-2-yl)-N4-(2-methoxyethyl)cyclohexane-1,4-diamine;
trans-4-(5-chloro-4-(6-((tetrahydro-2H-pyran-3-yl)methyl)aminopyrazin-2-yl)pyridin-2-yl-amino)cyclohexanol; and
trans-4-(5-chloro-4-(6-((tetrahydro-2H-pyran-4-yl)methyl)aminopyrazin-2-yl)pyridin-2-yl-amino)cyclohexanol.

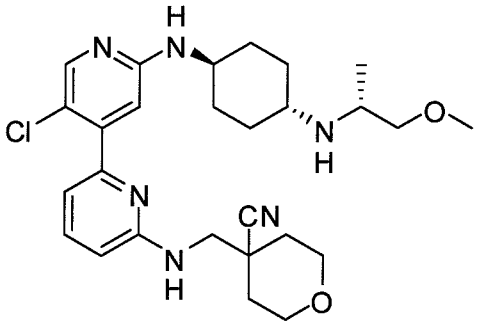
13. A compound of claim 1, which is of the formula:



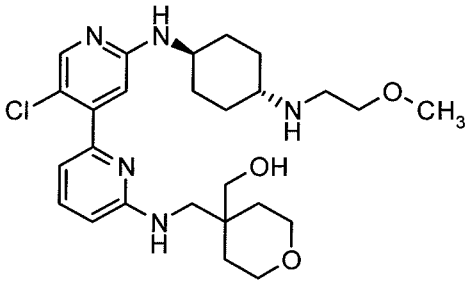
14. A compound of claim 1, which is of the formula:



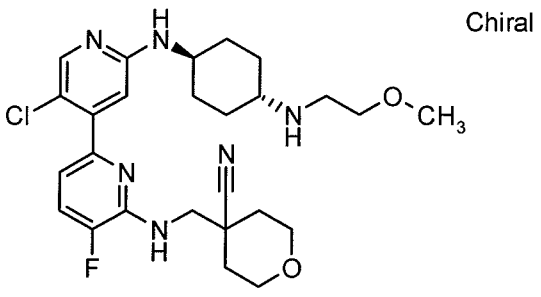
15. A compound of claim 1, which is of the formula:



16. A compound of claim 1, which is of the formula:



17. A compound of claim 1, which is of the formula:



18. A compound according to any one of claims 1 to 17, or a pharmaceutically acceptable salt or solvate thereof for use in therapy.

19. A pharmaceutical composition comprising a compound according to any one of claims 1 to 17, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier, diluent or excipient.

20. Use of a compound according to any one of claims 1 to 17 or a pharmaceutically acceptable salt thereof in the manufacture of a medicament for treating a disease or condition mediated by CDK9.

21. Use of claim 20 wherein the disease or condition mediated by CDK9 is selected from cancer, cardiac hypotrophy, HIV, and inflammatory diseases.

22. Use of claim 21 wherein the cancer is selected from the group consisting of bladder, head and neck, breast, stomach, ovary, colon, lung, brain, larynx, lymphatic system, hematopoetic system, genitourinary tract, gastrointestinal, ovarian, prostate, gastric, bone, small-cell lung, glioma, colorectal, and pancreatic cancer.