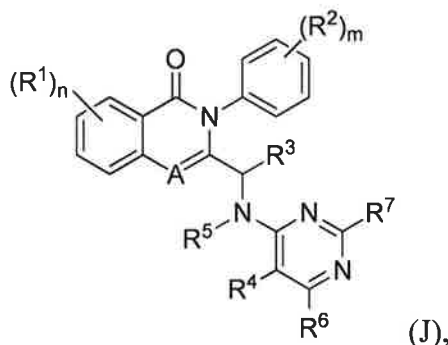


CLAIMS

What is claimed is:

1. A compound having the structure of formula (J):



wherein:

A is N;

n is 0, 1, 2, 3, or 4;

m is 1, 2, 3, or 4;

each R^1 is independently selected from optionally substituted alkyl, optionally substituted haloalkyl, optionally substituted aryl, optionally substituted heteroaryl, halo, cyano, $\text{NHC(=O)alkylene-N(R}^{1x})_2$, NO_2 , OR^{1x} , $\text{N(R}^{1x})_2$, OC(=O)R^{1x} , C(=O)R^{1x} , C(=O)OR^{1x} , aryl-OR^{1y} , optionally substituted cycloalkyl, optionally substituted heterocycloalkyl, $\text{NR}^{1x}\text{C(=O)alkylene-C(=O)OR}^{1x}$, $\text{aryl-O-alkylene-N(R}^{1x})_2$, $\text{aryl-O-C(=O)R}^{1x}$, $\text{alkylene-C(=O)OR}^{1x}$, $\text{alkylene-C(=O)N(R}^{1x})_2$, $\text{alkylene-C(=O)-Het}$, $\text{O-alkylene-C(=O)OR}^{1x}$, $\text{alkylene-O-alkylene-C(=O)OR}^{1x}$, $\text{C(=O)NR}^{1x}\text{SO}_2\text{R}^{1x}$, $\text{alkylene-N(R}^{1x})_2$, $\text{alkenylene-N(R}^{1x})_2$, $\text{C(=O)NR}^{1x}\text{-alkylene-OR}^{1x}$, $\text{C(=O)NR}^{1x}\text{alkylene-Het}$, $\text{O-alkylene-N(R}^{1x})_2$, $\text{O-alkylene-CH(OR}^{1y})\text{CH}_2\text{N(R}^{1x})_2$, O-alkylene-Het , $\text{O-alkylene-C(=O)-Het}$, $\text{S-alkylene-OR}^{1x}$, $\text{O-alkylene-OR}^{1x}$, $\text{O-C}_{1-6}\text{alkylene-CH(OR}^{1y})\text{C}_{1-6}\text{alkylene-OR}^{1x}$, $\text{O-alkylene-NR}^{1x}\text{C(=O)OR}^{1x}$, $\text{NR}^{1x}\text{-alkylene-N(R}^{1x})_2$, $\text{NR}^{1x}\text{C(=O)R}^{1x}$, $\text{NR}^{1x}\text{C(=O)N(R}^{1x})_2$, $\text{N(SO}_2\text{-alkyl)}_2$, $\text{NR}^{1x}(\text{SO}_2\text{-alkyl})$, SO_2R^{1z} , $\text{SO}_2\text{N(R}^{1x})_2$, alkylene-aryl , alkylene-Het , alkylene-OR^{1y} , $\text{C(=O)N(R}^{1x})_2$, $\text{NHC(=O)alkylene-aryl}$, aryl-OC(=O)R^{1y} , $\text{NHC(=O)alkylene-heterocycloalkyl}$, $\text{NHC(=O)alkylene-Het}$, $\text{O-alkylene-O-alkylene-C(=O)OR}^{1y}$, C(=O)alkylene-Het , and NHC(=O)halo-alkyl ,

wherein Het is optionally substituted heteroaryl or optionally substituted heterocycloalkyl, wherein R^{1x} is independently hydrogen, optionally substituted alkyl, optionally substituted haloalkyl, optionally substituted cycloalkyl, optionally substituted heterocycloalkyl, or optionally substituted aryl, wherein R^{1y} is independently hydrogen, optionally substituted alkyl, optionally substituted haloalkyl, optionally substituted aryl, or optionally substituted heteroaryl, and wherein R^{1z} is independently optionally substituted alkyl, optionally substituted haloalkyl, optionally substituted cycloalkyl, optionally substituted heterocycloalkyl, or optionally substituted aryl;

each R^2 is independently selected from halo, cyano, optionally substituted alkyl, haloalkyl, $SO_2N(R^{2x})_2$, and optionally substituted alkoxy,

wherein R^{2x} is hydrogen, optionally substituted alkyl, or optionally substituted haloalkyl;

R^3 is optionally substituted cycloalkyl, optionally substituted aryl, optionally substituted heteroaryl, or optionally substituted heterocycloalkyl;

R^5 is hydrogen or alkyl, or R^5 and R^3 together with the atoms to which they are attached form an optionally substituted four-, five- or six-membered heterocyclic ring;

R^4 is cyano, $C(=O)NR^{4x}R^{4y}$, SO_2 -alkyl, halo, haloalkyl, or $C(=O)R^{4x}$,

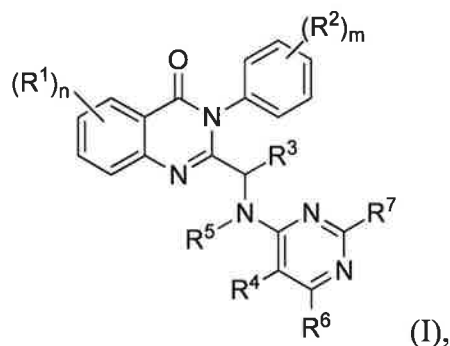
wherein each R^{4x} and R^{4y} is independently hydrogen, optionally substituted alkyl, or optionally substituted haloalkyl;

R^6 is NH_2 , halo, or optionally substituted haloalkyl; and

R^7 is NH_2 , halo, optionally substituted alkyl, or optionally substituted haloalkyl;

wherein the optional substituents are selected from the group consisting of alkyl, alkenyl, alkynyl, alkoxy, acyl, amino, amido, amidino, aryl, azido, carbamoyl, carboxyl, carboxyl ester, cyano, guanidino, halo, haloalkyl, heteralkyl, heteraryl, heterocycloalkyl, hydroxy, hydrazino, imino, oxo, nitro, alkylsulfinyl, sulfonic acid, alkylsulfonyl, thiocyanate, thiol and thione, or a pharmaceutically acceptable salt, enantiomer, atropisomer, or a mixture thereof.

2. The compound of claim 1, or a pharmaceutically acceptable salt thereof, wherein the compound is a compound of formula (I):



wherein:

n is 1 or 2;

m is 1 or 2;

each R^1 is independently C_{1-6} alkyl, C_{1-6} haloalkyl, C_{3-8} cycloalkyl, C_{2-8} heterocycloalkyl, C_{3-8} heteroaryl, C_{6-10} aryl, halo, cyano, C_{6-10} aryl- OR^{1y} , C_{1-6} alkylene- C_{6-10} aryl, C_{1-6} alkylene-Het, C_{1-6} alkylene- C_{3-8} cycloalkyl, C_{1-6} alkylene- OR^{1y} , C_{1-6} alkylene- $N(R^{1x})_2$, C_{2-6} alkenylene- OR^{1y} , C_{2-6} alkenylene- $N(R^{1x})_2$, C_{1-6} alkylene- $C(=O)OR^{1x}$, C_{1-6} alkylene- $C(=O)N(R^{1x})_2$, C_{1-6} alkylene- $C(=O)$ -Het, O - C_{1-6} alkylene- $C(=O)OR^{1x}$, C_{1-6} alkylene- O - C_{1-6} alkylene- $C(=O)OR^{1x}$, C_{1-6} alkenylene- $N(R^{1x})_2$, OR^{1x} , O - C_{1-6} alkylene- $N(R^{1x})_2$, O - C_{1-6} alkylene- $CH(OR^{1y})CH_2N(R^{1x})_2$, O - C_{1-6} alkylene-Het, O - C_{1-6} alkylene- $C(=O)OR^{1x}$, O - C_{1-6} alkylene- $C(=O)$ -Het, O - C_{1-6} alkylene- OR^{1x} , O - C_{1-6} alkylene- $CH(OR^{1y})C_{1-6}$ alkylene- OR^{1x} , O - C_{2-6} alkenylene- OR^{1y} , O - C_{2-6} alkenylene- $N(R^{1x})_2$, O - C_{1-6} alkylene- $NR^{1x}C(=O)OR^{1x}$, O - C_{1-6} alkylene- O - C_{1-6} alkylene- $C(=O)OR^{1y}$, SO_2R^{1z} , S - C_{1-6} alkylene- OR^{1x} , or $SO_2N(R^{1x})_2$,

wherein Het is C_{3-8} heteroaryl or C_{2-8} heterocycloalkyl, wherein R^{1x} is independently hydrogen, C_{1-6} alkyl, C_{1-6} haloalkyl, C_{3-8} cycloalkyl, C_{6-10} aryl, C_{2-8} heterocycloalkyl, or C_{3-8} heteroaryl, wherein R^{1y} is independently hydrogen, C_{1-6} alkyl, C_{1-6} haloalkyl, C_{6-10} aryl, or C_{3-8} heteroaryl, wherein R^{1z} is independently C_{1-6} alkyl, C_{1-6} haloalkyl, C_{3-8} cycloalkyl, C_{6-10} aryl, C_{2-8} heterocycloalkyl, or C_{3-8} heteroaryl, and wherein each of Het, R^{1x} , R^{1y} and R^{1z} is optionally substituted with one, two, three, or four members independently selected from halo, oxo, C_{1-6} alkyl, and C_{6-10} aryl;

each R^2 is independently halo, cyano, C_{1-6} alkyl, C_{1-6} haloalkyl, or $SO_2N(R^{2x})_2$, wherein R^{2x} is hydrogen, C_{1-6} alkyl, or C_{1-6} haloalkyl;

R^3 is C_{3-8} cycloalkyl or C_{6-10} aryl;

R^5 is hydrogen or C_{1-6} alkyl, or R^5 and R^3 together with the atoms to which they are attached form a four-, five- or six-membered heterocyclic ring, wherein the heterocyclic ring is optionally substituted with one, two, or three members independently selected from halo, C_{1-6} alkyl, C_{1-6} haloalkyl, and $NR^{5x}C(O)R^{5y}$ where R^{5x} is hydrogen or C_{1-6} alkyl, and R^{5y} is C_{1-6} alkylene- NH_2 , C_{1-6} alkylene- C_{3-8} cycloalkyl, or C_{1-6} haloalkyl;

R^4 is cyano, $C(=O)NR^{4x}R^{4y}$, SO_2-C_{1-6} alkyl, halo, C_{1-6} haloalkyl, or $C(=O)R^{4x}$, wherein each R^{4x} and R^{4y} is independently hydrogen, C_{1-6} alkyl, or C_{1-6} haloalkyl;

R^6 is NH_2 , halo, or C_{1-6} haloalkyl; and

R^7 is NH_2 , halo, C_{1-6} alkyl, or C_{1-6} haloalkyl.

3. The compound of claim 1 or 2, or a pharmaceutically acceptable salt thereof, wherein each R^1 is independently methyl, chloro, fluoro, cyano, tetrahydropyridinyl, $-CH_2-C(=O)OH$, $-C_2H_4-C(=O)OH$, $-C_3H_6-C(=O)OH$, $-CH_2-C(=O)NH_2$, $-CH_2-C(=O)N(CH_3)_2$, $-C_2H_4-C(=O)NH_2$, $-C_2H_4-C(=O)N(CH_3)_2$, $-C_3H_6-C(=O)NH_2$, $-C_3H_6-C(=O)N(CH_3)_2$, $-CH_2-C(=O)-Het$, $C_2H_4-C(=O)-Het$, $-C_3H_6-C(=O)-Het$, $O-CH_2-C(=O)OC_3H_7$, $O-C_2H_4-C(=O)OC_3H_7$, $O-C_3H_6-C(=O)OC_3H_7$, $-CH_2-Het$, $-C_2H_4-Het$, $-C_3H_6-Het$, $-CH_2-cyclopropyl$, $-C_2H_4-cyclopropyl$, $-C_3H_6-cyclopropyl$, $-CH_2-cyclobutyl$, $-C_2H_4-cyclobutyl$, $-C_3H_6-cyclobutyl$, $-CH_2-cyclopentyl$, $-C_2H_4-cyclopentyl$, $-C_3H_6-cyclopentyl$, $-CH_2-cyclohexyl$, $-C_2H_4-cyclohexyl$, $-C_3H_6-cyclohexyl$, $O-CH_2-NH_2$, $O-C_2H_4-NH_2$, $O-C_3H_6-NH_2$, $O-CH_2-N(CH_3)_2$, $O-C_2H_4-N(CH_3)_2$, $O-C_3H_6-N(CH_3)_2$, $O-CH_2-Het$, $O-C_2H_4-Het$, $O-C_3H_6-Het$, $O-CH_2-C(=O)OH$, $O-C_2H_4-C(=O)OH$, $O-C_3H_6-C(=O)OH$, $O-CH_2-C(=O)OCH_3$, $O-C_2H_4-C(=O)OCH_3$, $O-C_3H_6-C(=O)OCH_3$, $O-CH_2-C(=O)-Het$, $O-CH_2C(CH_3)(CH_2OH)_2$, $S-C_2H_4OH$, $S-C_3H_6OH$, SO_2 -phenyl, SO_2 -methylphenyl, $-SO_2$ -ethylphenyl, $-SO_2$ -cyclopropyl, $-SO_2$ -cyclobutyl, $-SO_2$ -cyclopentyl, $-SO_2C_2H_4-Het$, $-SO_2CH_3$, $-SO_2C_2H_5$, $-SO_2C_3H_7$, $-SO_2C_2H_4OH$, or $-SO_2C_3H_6OH$; wherein Het is independently selected from piperidinyl, morpholinyl, piperazinyl, azepanyl, imidazolyl, oxetanyl, azetidiny, pyrrolidinyl, tetrahydropyridinyl, 2-oxa-7-azaspiro[3.5]nonanyl, 2-oxa-6-azaspiro[3.4]octanyl, and 6-oxa-1-azaspiro[3.3]heptanyl, wherein each of the piperidinyl, morpholinyl, piperazinyl, azepanyl, imidazolyl, oxetanyl, azetidiny, pyrrolidinyl, tetrahydropyridinyl, 2-oxa-7-azaspiro[3.5]nonanyl, 2-oxa-6-azaspiro[3.4]octanyl, 6-oxa-1-azaspiro[3.3]heptanyl, cyclopropyl, cyclobutyl, cyclopentyl, and cyclohexyl moieties is optionally substituted with one, two, three, or four members independently selected from fluoro, chloro, methyl, ethyl, propyl, oxo, or phenyl.

4. The compound of any one of claims 1 to 3, or a pharmaceutically acceptable salt thereof, wherein each R^2 is independently fluoro, chloro, bromo, iodo, cyano, methyl, ethyl, propyl, fluoromethyl, difluoromethyl, trifluoromethyl, fluoroethyl, difluoroethyl, trifluoroethyl, or SO_2NH_2 .
5. The compound of any one of claims 1 to 4, or a pharmaceutically acceptable salt thereof, wherein R^3 is cyclopropyl, cyclobutyl, or phenyl.
6. The compound of any one of claims 1 to 5, or a pharmaceutically acceptable salt thereof, wherein R^3 is cyclobutyl or phenyl.
7. The compound of any one of claims 1 to 5, or a pharmaceutically acceptable salt thereof, wherein R^3 is cyclopropyl.
8. The compound of any one of claims 1 to 7, or a pharmaceutically acceptable salt thereof, wherein R^4 is cyano, chloro, bromo, iodo, or $C(=O)CH_3$.
9. The compound of any one of claims 1 to 8, or a pharmaceutically acceptable salt thereof, wherein R^5 is hydrogen, methyl, ethyl, or propyl.
10. The compound of any one of claims 1 to 9, or a pharmaceutically acceptable salt thereof, wherein R^6 is NH_2 , chloro, or fluoro.
11. The compound of any one of claims 1 to 10, or a pharmaceutically acceptable salt thereof, wherein R^7 is NH_2 , fluoro, chloro, methyl, ethyl, or propyl.
12. The compound of any one of claims 1 to 11, or a pharmaceutically acceptable salt thereof, wherein R^5 and R^3 together with the atoms to which they are attached form a heterocyclic ring, wherein the heterocyclic ring is azetidiny, morpholinyl, or pyrrolidinyl, wherein each of the azetidiny, morpholinyl, and pyrrolidinyl moieties is optionally substituted with 1, 2 or 3 groups which are independently C_{1-4} alkyl, methoxy, ethoxy, halo, $N(CH_3)C(=O)CH_2NH_2$, $N(CH_3)C(=O)CHF_2$, $N(CH_3)C(=O)CH_2CF_3$,

N(CH₃)C(=O)cyclopropyl, NHC(=O)CH₂NH₂, NHC(=O)CHF₂, NHC(=O)CH₂CF₃, NHC(=O)CH₂cyclopropyl or NHC(=O)cyclopropyl.

13. The compound of claim 12, or a pharmaceutically acceptable salt thereof, wherein each R¹ is independently chloro, fluoro, cyano, methyl, SO₂-phenyl, -SO₂CH₃, or -C₃H₆-C(=O)OH.

14. The compound of any one of claims 1 to 13, or a pharmaceutically acceptable salt thereof, wherein the compound is an (*S*)-enantiomer.

15. The compound of any one of claims 1 to 13, or a pharmaceutically acceptable salt thereof, wherein the compound is an (*R*)-enantiomer.

16. A compound selected from the group consisting of:

(S)-2-(cyclopropyl((2,6-diamino-5-cyanopyrimidin-4-yl)amino)methyl)-3-(3-(difluoromethyl)-5-fluorophenyl)-4-oxo-3,4-dihydroquinazoline-5-carbonitrile;

(S)-2,4-diamino-6-((cyclopropyl(3-(3-fluorophenyl)-5-(methylsulfonyl)-4-oxo-3,4-dihydroquinazolin-2-yl)methyl)amino)pyrimidine-5-carbonitrile;

(S)-2,4-diamino-6-((cyclopropyl(3-(2-fluorophenyl)-5-(methylsulfonyl)-4-oxo-3,4-dihydroquinazolin-2-yl)methyl)amino)pyrimidine-5-carbonitrile;

(S)-2,4-diamino-6-((cyclopropyl(3-(2-fluorophenyl)-5-(methylsulfonyl)-4-oxo-3,4-dihydroquinazolin-2-yl)methyl)amino)pyrimidine-5-carbonitrile;

(S)-2,4-diamino-6-((cyclopropyl(3-(2,6-difluorophenyl)-5-(methylsulfonyl)-4-oxo-3,4-dihydroquinazolin-2-yl)methyl)amino)pyrimidine-5-carbonitrile;

(S)-2-(cyclopropyl((2,6-diamino-5-cyanopyrimidin-4-yl)amino)methyl)-6-fluoro-3-(3-fluorophenyl)-4-oxo-3,4-dihydroquinazoline-8-carbonitrile;

(S)-2,4-diamino-6-(((3-(3-cyano-5-fluorophenyl)-5-methyl-4-oxo-3,4-dihydroquinazolin-2-yl)(cyclopropyl)methyl)amino)pyrimidine-5-carbonitrile;

(S)-2,4-diamino-6-((cyclopropyl(3-(3,5-difluorophenyl)-5-methyl-4-oxo-3,4-dihydroquinazolin-2-yl)methyl)amino)pyrimidine-5-carbonitrile;

(S)-2,4-diamino-6-(((5-chloro-3-(3,5-difluorophenyl)-4-oxo-3,4-dihydroquinazolin-2-yl)(cyclopropyl)methyl)amino)pyrimidine-5-carbonitrile;

(S)-2,4-diamino-6-((cyclopropyl(3-(3,5-difluorophenyl)-5-fluoro-4-oxo-3,4-dihydroquinazolin-2-yl)methyl)amino)pyrimidine-5-carbonitrile;

(S)-2,4-diamino-6-((cyclopropyl(5-fluoro-3-(3-fluorophenyl)-4-oxo-3,4-dihydroquinazolin-2-yl)methyl)amino)pyrimidine-5-carbonitrile;

(S)-2,4-diamino-6-((cyclopropyl(6-fluoro-3-(3-fluorophenyl)-4-oxo-3,4-dihydroquinazolin-2-yl)methyl)amino)pyrimidine-5-carbonitrile;

2,4-diamino-6-((2S)-2-(5-chloro-3-(3,5-difluorophenyl)-4-oxo-3,4-dihydroquinazolin-2-yl)-4-methoxypyrrolidin-1-yl)pyrimidine-5-carbonitrile;

(S)-2,4-diamino-6-(2-(5-chloro-3-(3,5-difluorophenyl)-4-oxo-3,4-dihydroquinazolin-2-yl)azetidin-1-yl)pyrimidine-5-carbonitrile;

(S)-2,4-diamino-6-(2-(3-(3-fluorophenyl)-5-(methylsulfonyl)-4-oxo-3,4-dihydroquinazolin-2-yl)pyrrolidin-1-yl)pyrimidine-5-carbonitrile;

(S)-2,4-diamino-6-(2-(3-(2-fluorophenyl)-5-(methylsulfonyl)-4-oxo-3,4-dihydroquinazolin-2-yl)pyrrolidin-1-yl)pyrimidine-5-carbonitrile;

(S)-2,4-diamino-6-(2-(3-(2,6-difluorophenyl)-5-(methylsulfonyl)-4-oxo-3,4-dihydroquinazolin-2-yl)pyrrolidin-1-yl)pyrimidine-5-carbonitrile;

(S)-2,4-diamino-6-(2-(3-(3-fluorophenyl)-5-(methylsulfonyl)-4-oxo-3,4-dihydroquinazolin-2-yl)pyrrolidin-1-yl)pyrimidine-5-carbonitrile;

(S)-2,4-diamino-6-(2-(5-chloro-3-(3,5-difluorophenyl)-4-oxo-3,4-dihydroquinazolin-2-yl)pyrrolidin-1-yl)pyrimidine-5-carbonitrile;

(S)-2,4-diamino-6-(2-(5-chloro-3-(3,5-difluorophenyl)-8-methyl-4-oxo-3,4-dihydroquinazolin-2-yl)pyrrolidin-1-yl)pyrimidine-5-carbonitrile;

(S)-2,4-diamino-6-(2-(8-chloro-3-(3,5-difluorophenyl)-4-oxo-3,4-dihydroquinazolin-2-yl)pyrrolidin-1-yl)pyrimidine-5-carbonitrile;

(S)-2,4-diamino-6-(2-(3-(3,5-difluorophenyl)-8-methyl-4-oxo-3,4-dihydroquinazolin-2-yl)pyrrolidin-1-yl)pyrimidine-5-carbonitrile;

(S)-2,4-diamino-6-(2-(3-(3,5-difluorophenyl)-5-fluoro-4-oxo-3,4-dihydroquinazolin-2-yl)pyrrolidin-1-yl)pyrimidine-5-carbonitrile;

(S)-2,4-diamino-6-(2-(5-chloro-3-(3-cyano-5-fluorophenyl)-4-oxo-3,4-dihydroquinazolin-2-yl)pyrrolidin-1-yl)pyrimidine-5-carbonitrile;

(S)-2-(1-(2,6-diamino-5-cyanopyrimidin-4-yl)pyrrolidin-2-yl)-3-(3-(difluoromethyl)phenyl)-4-oxo-3,4-dihydroquinazoline-8-carbonitrile

(S)-3-(5,8-dichloro-2-(1-(2,6-diamino-5-cyanopyrimidin-4-yl)pyrrolidin-2-yl)-4-oxoquinazolin-3(4*H*)-yl)benzenesulfonamide;

(S)-3-(5,8-dichloro-2-(1-(2,6-diamino-5-cyanopyrimidin-4-yl)pyrrolidin-2-yl)-4-oxoquinazolin-3(4*H*)-yl)benzenesulfonamide;

2,4-diamino-6-((2*S*,4*R*)-2-(5-chloro-3-(3,5-difluorophenyl)-4-oxo-3,4-dihydroquinazolin-2-yl)-4-fluoropyrrolidin-1-yl)pyrimidine-5-carbonitrile;

N-((3*R*,5*S*)-5-(5-chloro-3-(3,5-difluorophenyl)-4-oxo-3,4-dihydroquinazolin-2-yl)-1-(2,6-diamino-5-cyanopyrimidin-4-yl)pyrrolidin-3-yl)-2,2-difluoroacetamide;

N-((3*R*,5*S*)-5-(5-chloro-3-(3-(difluoromethyl)-5-fluorophenyl)-4-oxo-3,4-dihydroquinazolin-2-yl)-1-(2,6-diamino-5-cyanopyrimidin-4-yl)pyrrolidin-3-yl)-2,2-difluoroacetamide;

N-((3*R*,5*S*)-1-(2,6-diamino-5-cyanopyrimidin-4-yl)-5-(3-(3,5-difluorophenyl)-5-fluoro-4-oxo-3,4-dihydroquinazolin-2-yl)pyrrolidin-3-yl)-2,2-difluoroacetamide;

N-((3*R*,5*S*)-5-(5-chloro-3-(3,5-difluorophenyl)-4-oxo-3,4-dihydroquinazolin-2-yl)-1-(2,6-diamino-5-cyanopyrimidin-4-yl)pyrrolidin-3-yl)-2,2-difluoro-N-methylacetamide; and

2-amino-N-((3*R*,5*S*)-5-(5-chloro-3-(3,5-difluorophenyl)-4-oxo-3,4-dihydroquinazolin-2-yl)-1-(2,6-diamino-5-cyanopyrimidin-4-yl)pyrrolidin-3-yl)acetamide, or a pharmaceutically acceptable salt thereof.

17. A compound selected from the group consisting of:

2,4-diamino-6-((2*S*)-2-(5-chloro-3-(3,5-difluorophenyl)-4-oxo-3,4-dihydroquinazolin-2-yl)-4-methoxypyrrolidin-1-yl)pyrimidine-5-carbonitrile;

(S)-2,4-diamino-6-(2-(5-chloro-3-(3,5-difluorophenyl)-4-oxo-3,4-dihydroquinazolin-2-yl)azetidin-1-yl)pyrimidine-5-carbonitrile;

(S)-2,4-diamino-6-(2-(3-(3-fluorophenyl)-5-(methylsulfonyl)-4-oxo-3,4-dihydroquinazolin-2-yl)pyrrolidin-1-yl)pyrimidine-5-carbonitrile;

(S)-2,4-diamino-6-(2-(3-(2-fluorophenyl)-5-(methylsulfonyl)-4-oxo-3,4-dihydroquinazolin-2-yl)pyrrolidin-1-yl)pyrimidine-5-carbonitrile;

(S)-2,4-diamino-6-(2-(3-(2,6-difluorophenyl)-5-(methylsulfonyl)-4-oxo-3,4-dihydroquinazolin-2-yl)pyrrolidin-1-yl)pyrimidine-5-carbonitrile;

(S)-2,4-diamino-6-(2-(3-(3-fluorophenyl)-5-(methylsulfonyl)-4-oxo-3,4-dihydroquinazolin-2-yl)pyrrolidin-1-yl)pyrimidine-5-carbonitrile;

(S)-2,4-diamino-6-(2-(5-chloro-3-(3,5-difluorophenyl)-4-oxo-3,4-dihydroquinazolin-2-yl)pyrrolidin-1-yl)pyrimidine-5-carbonitrile;

(S)-2,4-diamino-6-(2-(5-chloro-3-(3,5-difluorophenyl)-8-methyl-4-oxo-3,4-dihydroquinazolin-2-yl)pyrrolidin-1-yl)pyrimidine-5-carbonitrile;

(S)-2,4-diamino-6-(2-(8-chloro-3-(3,5-difluorophenyl)-4-oxo-3,4-dihydroquinazolin-2-yl)pyrrolidin-1-yl)pyrimidine-5-carbonitrile;

(S)-2,4-diamino-6-(2-(3-(3,5-difluorophenyl)-8-methyl-4-oxo-3,4-dihydroquinazolin-2-yl)pyrrolidin-1-yl)pyrimidine-5-carbonitrile;

(S)-2,4-diamino-6-(2-(3-(3,5-difluorophenyl)-5-fluoro-4-oxo-3,4-dihydroquinazolin-2-yl)pyrrolidin-1-yl)pyrimidine-5-carbonitrile;

(S)-2,4-diamino-6-(2-(5-chloro-3-(3-cyano-5-fluorophenyl)-4-oxo-3,4-dihydroquinazolin-2-yl)pyrrolidin-1-yl)pyrimidine-5-carbonitrile;

(S)-2-(1-(2,6-diamino-5-cyanopyrimidin-4-yl)pyrrolidin-2-yl)-3-(3-(difluoromethyl)phenyl)-4-oxo-3,4-dihydroquinazoline-8-carbonitrile;

(S)-3-(5,8-dichloro-2-(1-(2,6-diamino-5-cyanopyrimidin-4-yl)pyrrolidin-2-yl)-4-oxoquinazolin-3(4*H*)-yl)benzenesulfonamide;

(S)-3-(5,8-dichloro-2-(1-(2,6-diamino-5-cyanopyrimidin-4-yl)pyrrolidin-2-yl)-4-oxoquinazolin-3(4*H*)-yl)benzenesulfonamide;

2,4-diamino-6-((2*S*,4*R*)-2-(5-chloro-3-(3,5-difluorophenyl)-4-oxo-3,4-dihydroquinazolin-2-yl)-4-fluoropyrrolidin-1-yl)pyrimidine-5-carbonitrile;

N-((3*R*,5*S*)-5-(5-chloro-3-(3,5-difluorophenyl)-4-oxo-3,4-dihydroquinazolin-2-yl)-1-(2,6-diamino-5-cyanopyrimidin-4-yl)pyrrolidin-3-yl)-2,2-difluoroacetamide;

N-((3*R*,5*S*)-5-(5-chloro-3-(3-(difluoromethyl)-5-fluorophenyl)-4-oxo-3,4-dihydroquinazolin-2-yl)-1-(2,6-diamino-5-cyanopyrimidin-4-yl)pyrrolidin-3-yl)-2,2-difluoroacetamide;

N-((3*R*,5*S*)-1-(2,6-diamino-5-cyanopyrimidin-4-yl)-5-(3-(3,5-difluorophenyl)-5-fluoro-4-oxo-3,4-dihydroquinazolin-2-yl)pyrrolidin-3-yl)-2,2-difluoroacetamide;

N-((3*R*,5*S*)-5-(5-chloro-3-(3,5-difluorophenyl)-4-oxo-3,4-dihydroquinazolin-2-yl)-1-(2,6-diamino-5-cyanopyrimidin-4-yl)pyrrolidin-3-yl)-2,2-difluoro-N-methylacetamide; and

2-amino-N-((3*R*,5*S*)-5-(5-chloro-3-(3,5-difluorophenyl)-4-oxo-3,4-dihydroquinazolin-2-yl)-1-(2,6-diamino-5-cyanopyrimidin-4-yl)pyrrolidin-3-yl)acetamide, or a pharmaceutically acceptable salt thereof.

18. A compound selected from the group consisting of:

(S)-2-(cyclopropyl((2,6-diamino-5-cyanopyrimidin-4-yl)amino)methyl)-3-(3-(difluoromethyl)-5-fluorophenyl)-4-oxo-3,4-dihydroquinazoline-5-carbonitrile;

(S)-2,4-diamino-6-((cyclopropyl(3-(3-fluorophenyl)-5-(methylsulfonyl)-4-oxo-3,4-dihydroquinazolin-2-yl)methyl)amino)pyrimidine-5-carbonitrile;

(S)-2,4-diamino-6-((cyclopropyl(3-(2-fluorophenyl)-5-(methylsulfonyl)-4-oxo-3,4-dihydroquinazolin-2-yl)methyl)amino)pyrimidine-5-carbonitrile;

(S)-2,4-diamino-6-((cyclopropyl(3-(2-fluorophenyl)-5-(methylsulfonyl)-4-oxo-3,4-dihydroquinazolin-2-yl)methyl)amino)pyrimidine-5-carbonitrile;

(S)-2,4-diamino-6-((cyclopropyl(3-(2,6-difluorophenyl)-5-(methylsulfonyl)-4-oxo-3,4-dihydroquinazolin-2-yl)methyl)amino)pyrimidine-5-carbonitrile;

(S)-2-(cyclopropyl((2,6-diamino-5-cyanopyrimidin-4-yl)amino)methyl)-6-fluoro-3-(3-fluorophenyl)-4-oxo-3,4-dihydroquinazoline-8-carbonitrile;

(S)-2,4-diamino-6-(((3-(3-cyano-5-fluorophenyl)-5-methyl-4-oxo-3,4-dihydroquinazolin-2-yl)(cyclopropyl)methyl)amino)pyrimidine-5-carbonitrile;

(S)-2,4-diamino-6-((cyclopropyl(3-(3,5-difluorophenyl)-5-methyl-4-oxo-3,4-dihydroquinazolin-2-yl)methyl)amino)pyrimidine-5-carbonitrile;

(S)-2,4-diamino-6-(((5-chloro-3-(3,5-difluorophenyl)-4-oxo-3,4-dihydroquinazolin-2-yl)(cyclopropyl)methyl)amino)pyrimidine-5-carbonitrile;

(S)-2,4-diamino-6-((cyclopropyl(3-(3,5-difluorophenyl)-5-fluoro-4-oxo-3,4-dihydroquinazolin-2-yl)methyl)amino)pyrimidine-5-carbonitrile;

(S)-2,4-diamino-6-((cyclopropyl(5-fluoro-3-(3-fluorophenyl)-4-oxo-3,4-dihydroquinazolin-2-yl)methyl)amino)pyrimidine-5-carbonitrile; and

(S)-2,4-diamino-6-((cyclopropyl(6-fluoro-3-(3-fluorophenyl)-4-oxo-3,4-dihydroquinazolin-2-yl)methyl)amino)pyrimidine-5-carbonitrile,

or a pharmaceutically acceptable salt thereof.

19. The compound of any one of claims 1 to 18, or a pharmaceutically acceptable salt thereof, wherein the compound is an atropisomer.

20. A pharmaceutical composition comprising the compound of any one of claims 1 to 19 or a pharmaceutically acceptable salt thereof, and at least one pharmaceutically acceptable vehicle.

21. Use of the compound of any one of claims 1-19 or a pharmaceutically acceptable salt thereof for the manufacture of a medicament for inhibiting the activity of a phosphatidylinositol 3-kinase polypeptide or treating a disease that is mediated by phosphatidylinositol 3-kinase, wherein the disease is selected from the group consisting of acute lymphocytic leukemia (ALL), acute myeloid leukemia (AML), chronic lymphocytic leukemia (CLL), small lymphocytic lymphoma (SLL), myelodysplastic syndrome (MDS), myeloproliferative disease (MPD), chronic myeloid leukemia (CML), juvenile myelomonocytic leukemia (JMML), multiple myeloma (MM), Hodgkin lymphoma, indolent non-Hodgkin's lymphoma (iNHL), refractory iNHL, non-Hodgkin's lymphoma (NHL), mantle cell lymphoma (MCL), follicular lymphoma, Waldstrom's macroglobulinemia (WM), minimal residual disease (MRD), T-cell lymphoma, B-cell lymphoma, diffuse large B-cell lymphoma (DLBCL), T-cell acute lymphoblastic leukemia (T-ALL), B-cell acute lymphoblastic leukemia (B-ALL), lymphoplasmacytic lymphoma, marginal zone lymphoma, Burkitt lymphoma, pancreatic cancer, bladder cancer, colorectal cancer, breast cancer, prostate cancer, renal cancer, hepatocellular cancer, lung cancer, ovarian cancer, cervical cancer, gastric cancer, esophageal cancer, head and neck cancer, melanoma, neuroendocrine cancers, CNS cancers, brain tumors, bone cancer, soft tissue sarcoma, systemic lupus erythematosus (SLE), myasthenia gravis, rheumatoid arthritis (RA), psoriasis, acute disseminated encephalomyelitis, idiopathic thrombocytopenic purpura, multiple sclerosis (MS), Sjogren's syndrome, psoriasis, autoimmune hemolytic anemia, asthma, and chronic obstructive pulmonary disease (COPD).

22. The use of claim 21, wherein the medicament inhibits excessive or destructive immune reactions or growth or a proliferation of cancer cells.

23. A kit comprising the compound of any one of claims 1-19, or a pharmaceutically acceptable salt thereof, and a label and/or instructions for use.