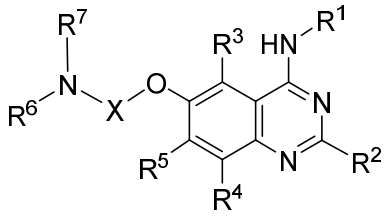
CLAIMS

We Claim:

1. A compound of Formula (I), or a pharmaceutically acceptable salt or solvate thereof:



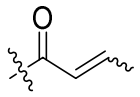
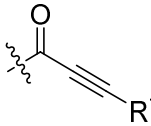
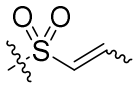
Formula (I);

wherein:

X is C_{3-8}cycloalkylene optionally substituted with one, two, three, or four R^8;

R^1 is selected from C_{3-8}cycloalkyl, C_{2-9}heterocycloalkyl, C_{6-10}aryl, and C_{1-9}heteroaryl, wherein C_{3-8}cycloalkyl, C_{2-9}heterocycloalkyl, C_{6-10}aryl, and C_{1-9}heteroaryl, are optionally substituted with one, two, three, or four R^9;

R^2, R^3, R^4, and R^5 are each independently selected from hydrogen, halogen, -CN, C_{1-6}alkyl, C_{1-6}haloalkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-6}cycloalkyl, C_{2-9}heterocycloalkyl, C_{6-10}aryl, C_{1-9}heteroaryl, $-OR^{10}$, $-SR^{10}$, $-N(R^{10})(R^{11})$, $-C(O)OR^{10}$, $-OC(O)N(R^{10})(R^{11})$, $-N(R^{12})C(O)N(R^{10})(R^{11})$, $-N(R^{12})C(O)OR^{13}$, $-N(R^{12})S(O)_2R^{13}$, $-C(O)R^{13}$, $-C(O)N(R^{10})(R^{11})$, $-N(R^{12})C(O)R^{13}$, $-S(O)_2R^{13}$, $-S(O)_2N(R^{10})(R^{11})$-, wherein C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-6}cycloalkyl, C_{2-9}heterocycloalkyl, C_{6-10}aryl, and C_{1-9}heteroaryl are optionally substituted with one, two, or three groups selected from halogen, C_{1-6}alkyl, C_{1-6}haloalkyl, $-OR^{10}$, and $-N(R^{10})(R^{11})$;

R^6 is selected from , , and ;

R^7 is selected from hydrogen, C_{1-6}alkyl, and C_{1-6}haloalkyl;

each R^8 is independently selected from halogen, oxo, C_{1-6}alkyl, C_{1-6}haloalkyl, C_{3-6}cycloalkyl, C_{2-9}heterocycloalkyl, $-OR^{10}$, $-SR^{10}$, $-N(R^{10})(R^{11})$, $-C(O)OR^{10}$, $-C(O)R^{13}$, $-C(O)N(R^{10})(R^{11})$, $-S(O)_2R^{13}$, $-S(O)_2N(R^{10})(R^{11})$-, wherein C_{1-6}alkyl, C_{3-6}cycloalkyl, and C_{2-9}heterocycloalkyl are optionally substituted with one, two, or three groups selected from halogen, C_{1-6}alkyl, C_{1-6}haloalkyl, $-OR^{10}$, and $-N(R^{10})(R^{11})$;

each R^9 is independently selected from halogen, oxo, -CN, C_{1-6}alkyl, C_{1-6}haloalkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-6}cycloalkyl, C_{2-9}heterocycloalkyl, C_{6-10}aryl, C_{1-9}heteroaryl, $-OR^{10}$, $-SR^{10}$, $-N(R^{10})(R^{11})$, $-C(O)OR^{10}$, $-OC(O)N(R^{10})(R^{11})$, $-N(R^{12})C(O)N(R^{10})(R^{11})$, $-N(R^{12})C(O)OR^{13}$, $-N(R^{12})S(O)_2R^{13}$, $-C(O)R^{13}$, $-C(O)N(R^{10})(R^{11})$, $-N(R^{12})C(O)R^{13}$, $-S(O)_2R^{13}$, $-S(O)_2N(R^{10})(R^{11})$-, wherein C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-}

$_{6}$cycloalkyl, C_{2-9}heterocycloalkyl, C_{6-10}aryl, and C_{1-9}heteroaryl are optionally substituted with one, two, or three groups selected from halogen, C_{1-6}alkyl, C_{1-6}haloalkyl, $-OR^{10}$, $-N(R^{10})(R^{11})$, and $-C(O)OR^{10}$; or two R^9 substituents are combined to form a cycloalkyl or heterocycloalkyl ring;

each R^{10} is independently selected from hydrogen, C_{1-6}alkyl, C_{1-6} haloalkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-6}cycloalkyl, C_{2-9}heterocycloalkyl, C_{6-10}aryl, and C_{1-9}heteroaryl, wherein C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-6}cycloalkyl, C_{2-9}heterocycloalkyl, C_{6-10}aryl, and C_{1-9}heteroaryl are optionally substituted with one, two, or three groups selected from halogen, C_{1-6}alkyl, C_{1-6}haloalkyl, C_{1-6}alkoxy, C_{3-6}cycloalkyl, C_{2-9}heterocycloalkyl, C_{6-10}aryl, and C_{1-9}heteroaryl;

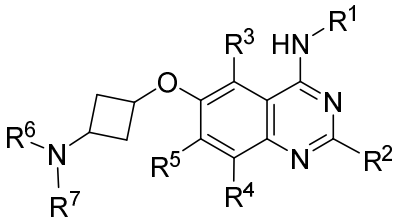
each R^{11} is independently selected from hydrogen, C_{1-6}alkyl, and C_{1-6}haloalkyl;

each R^{12} is independently selected from hydrogen, C_{1-6}alkyl, and C_{1-6}haloalkyl;

each R^{13} is independently selected C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-6}cycloalkyl, C_{2-9}heterocycloalkyl, C_{6-10}aryl, and C_{1-9}heteroaryl, wherein C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-6}cycloalkyl, C_{2-9}heterocycloalkyl, C_{6-10}aryl, and C_{1-9}heteroaryl are optionally substituted with one, two, or three groups selected from halogen, C_{1-6}alkyl, C_{1-6}haloalkyl, C_{1-6}alkoxy, C_{3-6}cycloalkyl, C_{2-9}heterocycloalkyl, C_{6-10}aryl, and C_{1-9}heteroaryl; and

R^{14} is selected from hydrogen and C_{1-6}alkyl optionally substituted with $-N(R^{10})(R^{11})$.

2. The compound of claim 1, or a pharmaceutically acceptable salt or solvate thereof, having the structure of Formula (Ia):



Formula (Ia).

3. The compound of claim 1 or claim 2, or a pharmaceutically acceptable salt or solvate thereof, wherein R^7 is hydrogen.

4. The compound of any one of claims 1-3, or a pharmaceutically acceptable salt or solvate thereof, wherein R^1 is phenyl optionally substituted with one, two, three, or four R^9.

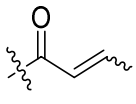
5. The compound of any one of claims 1-4, or a pharmaceutically acceptable salt or solvate thereof, wherein each R^9 is independently selected from halogen, C_{1-6}alkyl, and C_{1-6}haloalkyl; or two R^9 substituents are combined to form a cycloalkyl or heterocycloalkyl ring.

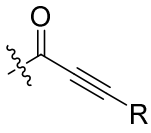
6. The compound of any one of claims 1-5, or a pharmaceutically acceptable salt or solvate thereof, wherein each R^9 is independently selected from halogen.

7. The compound of any one of claims 1-3, or a pharmaceutically acceptable salt or solvate thereof, wherein R^1 is unsubstituted C_{6-10}aryl.

8. The compound of any one of claims 1-7, or a pharmaceutically acceptable salt or solvate thereof, wherein R^5 is $-OR^{10}$ and R^{10} is C_{1-6}alkyl.

9. The compound of any one of claims 1-8, or a pharmaceutically acceptable salt or solvate thereof, wherein R^4 is hydrogen, R^3 is hydrogen, and R^2 is hydrogen.

10. The compound of any one of claims 1-9, or a pharmaceutically acceptable salt or solvate thereof, wherein R^6 is .

11. The compound of any one of claims 1-9, or a pharmaceutically acceptable salt or solvate thereof, wherein R^6 is .

12. The compound of any one of claims 1-11, or a pharmaceutically acceptable salt or solvate thereof, wherein R^{14} is hydrogen.

13. A compound of claim 1, or a pharmaceutically acceptable salt or solvate thereof, selected from:

40) N-((1s,3s)-3-((4-((3,4-dichloro-2-fluorophenyl)amino)-7-methoxyquinazolin-6-yl)oxy)cyclobutyl)-2-fluoroacrylamide

42) (E)-N-(3-((4-((3,4-dichloro-2-fluorophenyl)amino)-7-methoxyquinazolin-6-yl)oxy)cyclobutyl)-4-(dimethylamino)but-2-enamide

43) N-(3-((4-((3,4-dichloro-2-fluorophenyl)amino)-7-methoxyquinazolin-6-yl)oxy)cyclobutyl)but-2-ynamide

44) N-((1r,3r)-3-((4-((2,3-dihydro-1H-inden-4-yl)amino)-7-methoxyquinazolin-6-yl)oxy)cyclobutyl)propiolamide

45) N-((1s,3s)-3-((4-((2,3-dihydro-1H-inden-4-yl)amino)-7-methoxyquinazolin-6-yl)oxy)cyclobutyl)propiolamide

46) N-(3-((7-methoxy-4-(naphthalen-1-ylamino)quinazolin-6-yl)oxy)cyclobutyl)propiolamide

47) N-((1s,3s)-3-((7-methoxy-4-(naphthalen-1-ylamino)quinazolin-6-yl)oxy)cyclobutyl)propiolamide

48) N-((1r,3r)-3-((7-methoxy-4-(naphthalen-2-ylamino)quinazolin-6-yl)oxy)cyclobutyl)propiolamide

49) N-(3-((4-((3,4-dichloro-2-fluorophenyl)amino)-7-methoxyquinazolin-6-yl)oxy)cyclobutyl)propiolamide

66) N-((1s,3s)-3-((4-((3,4-dichloro-2-fluorophenyl)amino)-7-methoxyquinazolin-6-yl)oxy)cyclobutyl)acrylamide

67) N-(3-((7-methoxy-4-((7-methyl-2,3-dihydro-1H-inden-4-yl)amino)quinazolin-6-yl)oxy)cyclobutyl)acrylamide

72) N-(3-((4-((3,4-dichloro-2-fluorophenyl)amino)-7-methoxyquinazolin-6-yl)oxy)cyclobutyl)-N-methylacrylamide

73) N-(3-((4-((3,4-dichlorophenyl)amino)-7-methoxyquinazolin-6-yl)oxy)cyclobutyl)acrylamide

74) N-(3-((4-((3-chloro-2-fluorophenyl)amino)-7-methoxyquinazolin-6-yl)oxy)cyclobutyl)acrylamide

75) N-(3-((4-((2,4-dichloro-3-fluorophenyl)amino)-7-methoxyquinazolin-6-yl)oxy)cyclobutyl)acrylamide

76) N-(3-((4-((2,3-dichloro-4-fluorophenyl)amino)-7-methoxyquinazolin-6-yl)oxy)cyclobutyl)acrylamide

77) N-(3-((4-((2-fluorophenyl)amino)-7-methoxyquinazolin-6-yl)oxy)cyclobutyl)acrylamide

78) N-(3-((4-((4-chloro-2-fluorophenyl)amino)-7-methoxyquinazolin-6-yl)oxy)cyclobutyl)acrylamide

79) N-((1r,3r)-3-((4-((3,4-dichloro-2-fluorophenyl)amino)-7-methoxyquinazolin-6-yl)oxy)cyclobutyl)acrylamide

80) N-(3-((7-methoxy-4-(naphthalen-2-ylamino)quinazolin-6-yl)oxy)cyclobutyl)acrylamide

81) N-(3-((7-methoxy-4-(naphthalen-1-ylamino)quinazolin-6-yl)oxy)cyclobutyl)acrylamide

82) N-((1s,3s)-3-((4-((3,4-dichlorophenyl)amino)-7-methoxyquinazolin-6-yl)oxy)cyclobutyl)acrylamide

83) N-((1s,3s)-3-((7-methoxy-4-(naphthalen-1-ylamino)quinazolin-6-yl)oxy)cyclobutyl)acrylamide

85) N-(3-((4-((3-chloro-4-fluorophenyl)amino)-7-methoxyquinazolin-6-yl)oxy)cyclobutyl)acrylamide

86) N-(3-((4-((3-chloro-4-cyanophenyl)amino)-7-methoxyquinazolin-6-yl)oxy)cyclobutyl)acrylamide

87) N-(3-((4-((3-cyano-4-fluorophenyl)amino)-7-methoxyquinazolin-6-yl)oxy)cyclobutyl)acrylamide

88) N-(3-((4-((2,3-dihydro-1H-inden-4-yl)amino)-7-methoxyquinazolin-6-yl)oxy)cyclobutyl)acrylamide

89) N-(3-((7-methoxy-4-((5,6,7,8-tetrahydronaphthalen-1-yl)amino)quinazolin-6-yl)oxy)cyclobutyl)acrylamide

90) N-((1s,4s)-4-((4-((3,4-dichloro-2-fluorophenyl)amino)-7-methoxyquinazolin-6-yl)oxy)cyclohexyl)acrylamide

91) N-((1r,4r)-4-((4-((3,4-dichloro-2-fluorophenyl)amino)-7-methoxyquinazolin-6-yl)oxy)cyclohexyl)acrylamide

99) N-((1R,3s)-3-((4-((3,4-dichloro-2-fluorophenyl)amino)-7-(((S)-tetrahydrofuran-3-yl)oxy)quinazolin-6-yl)oxy)cyclobutyl)acrylamide

102) N-((1s,3s)-3-((4-((3,4-dichloro-2-fluorophenyl)amino)-7-(methoxy-d3)quinazolin-6-yl)oxy)cyclobutyl)acrylamide

103) N-((1s,3s)-3-((4-((3,4-dichloro-2-fluorophenyl)amino)-7-(methylamino)quinazolin-6-yl)oxy)cyclobutyl)acrylamide

104) N-((1s,3s)-3-((4-((3,4-dichloro-2-fluorophenyl)amino)-7-(oxetan-3-yloxy)quinazolin-6-yl)oxy)cyclobutyl)acrylamide

105) N-((1s,3s)-3-((4-((3,4-dichloro-2-fluorophenyl)amino)-7-ethoxyquinazolin-6-yl)oxy)cyclobutyl)acrylamide

and 191) N-(3-((4-((3,4-dichloro-2-fluorophenyl)amino)-7-methoxyquinazolin-6-yl)oxy)cyclobutyl)ethenesulfonamide

14. A pharmaceutical composition comprising a compound of any one of claims 1-13, or a pharmaceutically acceptable salt or solvate thereof, and at least one pharmaceutically acceptable excipient.

15. Use of a compound of any one of claims 1-13, or a pharmaceutically acceptable salt or solvate thereof, in the manufacture of a medicament for treating cancer in an individual.