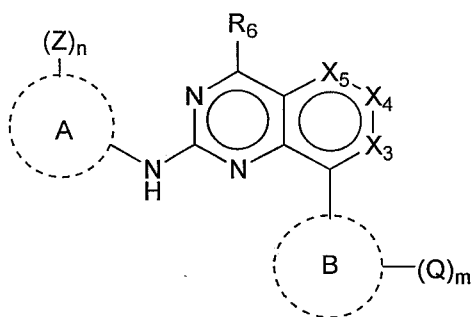


SUMMARY OF THE INVENTION

[004a] In one aspect, the present disclosure provides a compound of Formula I:



Formula I

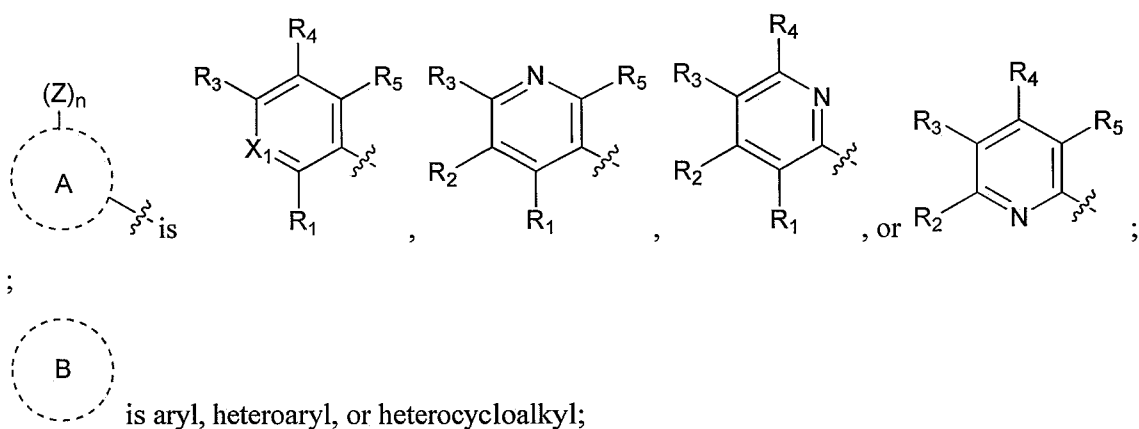
or a pharmaceutically acceptable salt thereof, wherein

X₃ is C-R₁₂, or N;

X₄ is C-R₁₃, or N;

X₅ is C-R₁₄, or N;

m is 0, 1, 2, 3, 4, or 5;



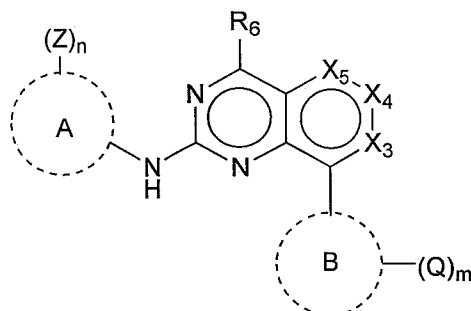
X₁ is C-R₂, or N;

R₁, R₂, R₄, R₅, R₆, R₁₂, R₁₃, and R₁₄ are independently hydrogen, cyano, halo, hydroxy, azido, nitro, carboxy, sulfinyl, sulfanyl, sulfonyl, optionally substituted alkoxy, optionally substituted cycloalkyloxy, optionally substituted aryloxy, optionally substituted heteroaryloxy, optionally substituted heterocycloalkyloxy, optionally substituted alkyl, optionally substituted cycloalkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted aryl, optionally substituted heteroaryl, optionally substituted heterocycloalkyl, optionally substituted amino, optionally substituted acyl, optionally substituted alkoxycarbonyl, optionally substituted aminocarbonyl, optionally substituted aminosulfonyl, or optionally substituted carbamimidoyl;

R₃ is optionally substituted pyrrolidinyl, optionally substituted piperidinyl, optionally substituted piperazinyl, optionally substituted azetidiny, optionally substituted diazepanyl, optionally substituted diazocanyl, optionally substituted imidazolidinyl, optionally substituted pyrazolidinyl, optionally substituted dihydrofuranyl, optionally substituted tetrahydrofuranyl, optionally substituted piperidinyl N-oxide, optionally substituted oxo-thiomorpholinyl or optionally substituted dioxo-thiomorpholinyl; and

each Q is independently hydrogen, cyano, halo, hydroxy, azido, nitro, carboxy, oxo, sulfinyl, sulfanyl, sulfonyl, optionally substituted alkoxy, optionally substituted cycloalkyloxy, optionally substituted aryloxy, optionally substituted heteroaryloxy, optionally substituted heterocycloalkyloxy, optionally substituted alkyl, optionally substituted cycloalkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted aryl, optionally substituted heteroaryl, optionally substituted heterocycloalkyl, optionally substituted amino, optionally substituted acyl, optionally substituted alkoxycarbonyl, optionally substituted aminocarbonyl, optionally substituted aminosulfonyl, or optionally substituted carbamimidoyl.

[005] In one aspect, the present disclosure provides a compound of Formula I



Formula I

or a pharmaceutically acceptable salt thereof, wherein

X₃ is C-R₁₂, or N;

X₄ is C-R₁₃, or N;

X₅ is C-R₁₄, or N;

n is 0, 1, 2, 3, 4, or 5;

m is 0, 1, 2, 3, 4, or 5;



is aryl or heteroaryl;

[016] In some embodiments, R_a is C_1 - C_6 alkyl, optionally substituted with C_1 - C_4 alkyl, aryl, heteroaryl, aryl- C_1 - C_4 alkyl-, heteroaryl- C_1 - C_4 alkyl-, C_1 - C_4 haloalkyl, - OC_1 - C_4 alkyl, - OC_1 - C_4 alkylphenyl, - C_1 - C_4 alkyl-OH, - OC_1 - C_4 haloalkyl, halo, -OH, - NH_2 , - C_1 - C_4 alkyl- NH_2 , - $N(C_1$ - C_4 alkyl)(C_1 - C_4 alkyl), - $NH(C_1$ - C_4 alkyl), - $N(C_1$ - C_4 alkyl)(C_1 - C_4 alkylphenyl), - $NH(C_1$ - C_4 alkylphenyl), cyano, nitro, oxo (as a substituent for cycloalkyl or heterocycloalkyl), - CO_2H , - $C(O)OC_1$ - C_4 alkyl, - $CON(C_1$ - C_4 alkyl)(C_1 - C_4 alkyl), - $CONH(C_1$ - C_4 alkyl), - $CONH_2$, - $NHC(O)(C_1$ - C_4 alkyl), - $NHC(O)(phenyl)$, - $N(C_1$ - C_4 alkyl) $C(O)(C_1$ - C_4 alkyl), - $N(C_1$ - C_4 alkyl) $C(O)(phenyl)$, - $C(O)C_1$ - C_4 alkyl, - $C(O)C_1$ - C_4 alkylphenyl, - $C(O)C_1$ - C_4 haloalkyl, - $OC(O)C_1$ - C_4 alkyl, - $SO_2(C_1$ - C_4 alkyl), - $SO_2(phenyl)$, - $SO_2(C_1$ - C_4 haloalkyl), - SO_2NH_2 , - $SO_2NH(C_1$ - C_4 alkyl), - $SO_2NH(phenyl)$, - $NHSO_2(C_1$ - C_4 alkyl), - $NHSO_2(phenyl)$, or - $NHSO_2(C_1$ - C_4 haloalkyl).

[017] In some embodiments, R_a is C_1 - C_6 alkyl, optionally substituted with -OH, halo, C_1 - C_4 alkyl, or - OC_1 - C_4 alkyl. In some embodiments, R_a is - CH_3 , - CH_2CH_2OH , - CH_2CH_2F , - CH_2CH_2OMe , - $CH_2C(CH_3)_2OH$, or - $CH_2CH(CH_3)OH$.

[018] In another aspect, the present disclosure provides a pharmaceutical composition comprising a pharmaceutically acceptable carrier and a compound or pharmaceutically acceptable salt of any one of compounds described herein. The pharmaceutical composition may be formulated in a form which is a tablet, capsule, powder, liquid, suspension, suppository, or aerosol. The pharmaceutical composition may be packaged with instructions for using the composition to treat a subject suffering from cancer.

[018a] In another aspect, the present disclosure provides a use of the compound or pharmaceutically acceptable salt as described herein in the manufacture of a medicament for treating a cancer in a subject.

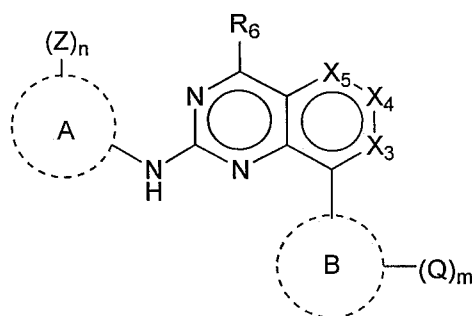
[018b] In another aspect, the present disclosure provides a use of the compound or pharmaceutically acceptable salt as described herein in the manufacture of a medicament for treating a cancer in a subject in need thereof, wherein the subject has an EGFR mutation or double mutation.

[019] In another aspect, the present disclosure provides a method of treating cancer in a subject which comprises administering to a subject in need thereof a therapeutically effective amount of a compound or pharmaceutically acceptable salt of any one of the compounds described herein. The cancer may be colon carcinoma, pancreatic cancer, breast cancer, ovarian cancer, prostate cancer, thyroid cancer, fibrosarcoma, myxosarcoma, liposarcoma, chondrosarcoma, osteogenic sarcoma, chondroma, angiosarcoma, endotheliosarcoma, lymphangiosarcoma, lymphangioendotheliosarcoma, synovioma, mesothelioma, Ewing's tumor, leiomyosarcoma, rhabdomyosarcoma, squamous cell carcinoma, basal cell carcinoma,

adenocarcinoma, sweat gland carcinoma, sebaceous gland carcinoma, papillary carcinoma, papillary adenocarcinomas, cystadenocarcinoma, medullary carcinoma, bronchogenic carcinoma, renal cell carcinoma, hepatoma, bile duct carcinoma, choriocarcinoma, seminoma, embryonal carcinoma, Wilms' tumor, cervical cancer, testicular tumor, lung carcinoma, small cell lung carcinoma, non-small cell lung cancer, bladder carcinoma, epithelial carcinoma, glioma, astrocytoma, medulloblastoma, craniopharyngioma,

What is claimed is:

1. A compound of Formula I:



Formula I

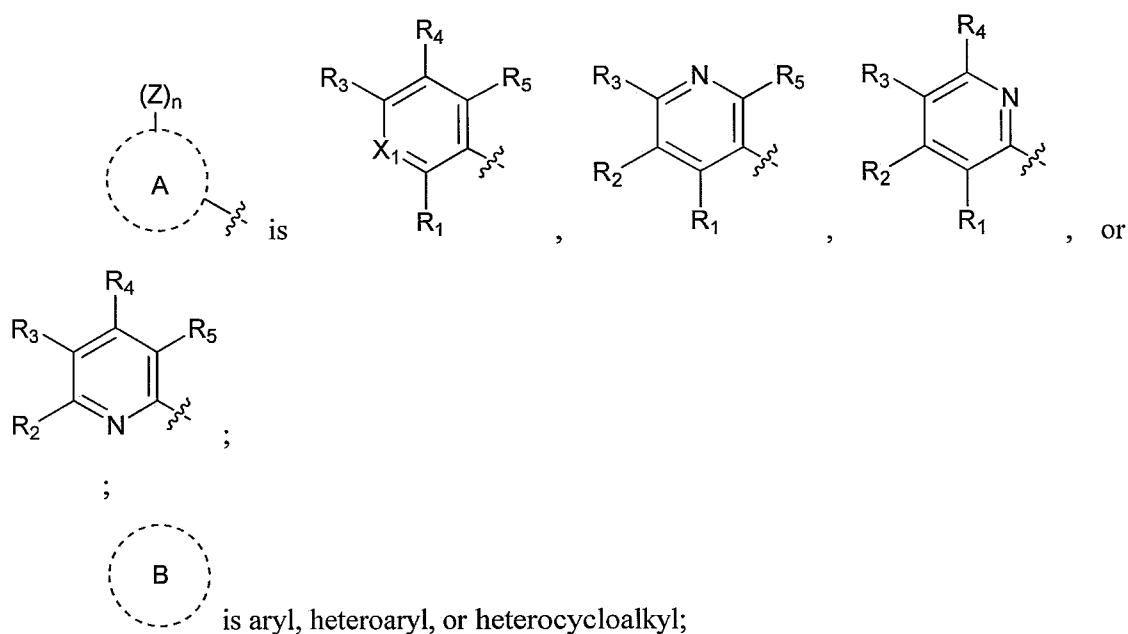
or a pharmaceutically acceptable salt thereof, wherein

X₃ is C-R₁₂, or N;

X₄ is C-R₁₃, or N;

X₅ is C-R₁₄, or N;

m is 0, 1, 2, 3, 4, or 5;



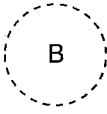
X₁ is C-R₂, or N;

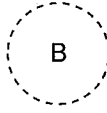
R₁, R₂, R₄, R₅, R₆, R₁₂, R₁₃, and R₁₄ are independently hydrogen, cyano, halo, hydroxy, azido, nitro, carboxy, sulfinyl, sulfanyl, sulfonyl, optionally substituted alkoxy, optionally substituted cycloalkyloxy, optionally substituted aryloxy, optionally substituted heteroaryloxy, optionally substituted heterocycloalkyloxy, optionally substituted alkyl, optionally substituted cycloalkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted aryl, optionally substituted heteroaryl, optionally substituted heterocycloalkyl, optionally substituted amino, optionally substituted acyl, optionally substituted

alkoxycarbonyl, optionally substituted aminocarbonyl, optionally substituted aminosulfonyl, or optionally substituted carbamimidoyl;

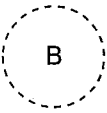
R₃ is optionally substituted pyrrolidinyl, optionally substituted piperidinyl, optionally substituted piperazinyl, optionally substituted azetidiny, optionally substituted diazepanyl, optionally substituted diazocanyl, optionally substituted imidazolidinyl, optionally substituted pyrazolidinyl, optionally substituted dihydrofuranyl, optionally substituted tetrahydrofuranyl, optionally substituted piperidinyl N-oxide, optionally substituted oxo-thiomorpholinyl or optionally substituted dioxo-thiomorpholinyl; and

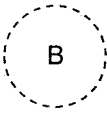
each Q is independently hydrogen, cyano, halo, hydroxy, azido, nitro, carboxy, oxo, sulfinyl, sulfanyl, sulfonyl, optionally substituted alkoxy, optionally substituted cycloalkyloxy, optionally substituted aryloxy, optionally substituted heteroaryloxy, optionally substituted heterocycloalkyloxy, optionally substituted alkyl, optionally substituted cycloalkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted aryl, optionally substituted heteroaryl, optionally substituted heterocycloalkyl, optionally substituted amino, optionally substituted acyl, optionally substituted alkoxycarbonyl, optionally substituted aminocarbonyl, optionally substituted aminosulfonyl, or optionally substituted carbamimidoyl.

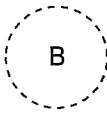
2. The compound or pharmaceutically acceptable salt of claim 1, wherein  is selected from the group consisting of: piperazinyl, morpholinyl, piperidinyl, thiomorpholinyl, pyrrolidinyl, tetrahydrofuranyl, diazepanyl, azetidiny, oxetanyl, oxiranyl, aziridinyl, pyrrolyl, furanyl, thienyl, imidazolyl, pyrazolyl, oxazolyl, isoxazolyl, thiazolyl, isothiazolyl, 1,2,3-triazolyl, 1,2,4-triazolyl, furazanyl, 1,2,3-oxadiazolyl, 1,2,4-oxadiazole, 1,2,5-oxadiazole, 1,3,4-oxadiazole, thiadiazolyl, dithiazolyl, tetrazolyl, pyridinyl, pyranyl, thiopyranyl, diazinyl, pyrazinyl, pyrimidinyl, pyridazinyl, oxazinyl, thiazinyl, dioxinyl, dithiinyl, 1,2,3-triazinyl, 1,2,4-triazinyl, 1,3,5-triazinyl, tetrazinyl, and phenyl.

3. The compound or pharmaceutically acceptable salt of claim 2, wherein  is selected from the group consisting of: phenyl, pyridinyl, pyrimidinyl, pyrazinyl, thiazolyl, oxazolyl, imidazolyl, pyrazolyl, isoxazolyl, and thienyl.

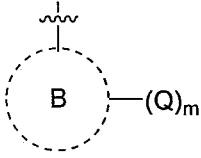
4. The compound or pharmaceutically acceptable salt of claim 3, wherein  is phenyl or pyridinyl.

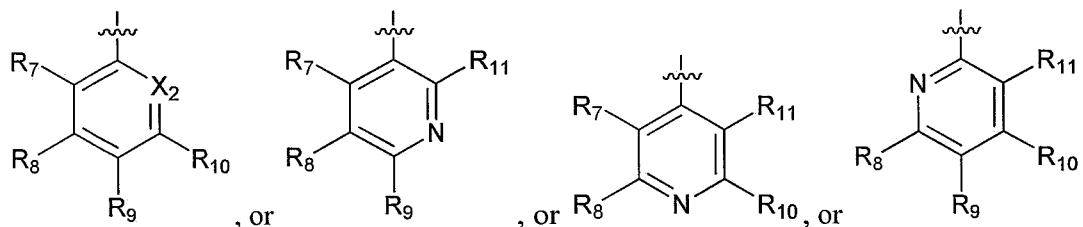
5. The compound or pharmaceutically acceptable salt of claim 2, wherein  is selected from the group consisting of: piperazinyl, morpholinyl, piperidinyl, thiomorpholinyl, pyrrolidinyl, tetrahydrofuranyl, diazepanyl, azetidiny, oxetanyl, oxiranyl, and aziridinyl.

6. The compound or pharmaceutically acceptable salt of claim 5, wherein  is selected from the group consisting of: piperazinyl, morpholinyl, piperidinyl, pyrrolidinyl, tetrahydrofuranyl, and diazepanyl.

7. The compound or pharmaceutically acceptable salt of claim 6, wherein  is selected from the group consisting of: piperazinyl, morpholinyl, piperidinyl, and pyrrolidinyl.

8. The compound or pharmaceutically acceptable salt of any one of claims 1 to 7, wherein m is 1, 2, or 3.

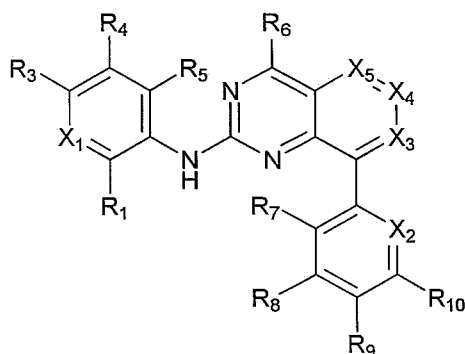
9. The compound or pharmaceutically acceptable salt of claim 1, wherein  is



X₂ is C-R₁₁, or N; and

R₁₁, R₇, R₈, R₉, and R₁₀ are independently, hydrogen, cyano, halo, hydroxy, azido, nitro, carboxy, sulfinyl, sulfanyl, sulfonyl, optionally substituted alkoxy, optionally substituted cycloalkoxy, optionally substituted aryloxy, optionally substituted heteroaryloxy, optionally substituted heterocycloalkoxy, optionally substituted alkyl, optionally substituted cycloalkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted aryl, optionally substituted heteroaryl, optionally substituted heterocycloalkyl, optionally substituted amino, optionally substituted acyl, optionally substituted alkoxycarbonyl, optionally substituted aminocarbonyl, optionally substituted aminosulfonyl, or optionally substituted carbamimidoyl.

10. The compound of claim 1, having the structure of Formula Ia



Formula Ia

or a pharmaceutically acceptable salt thereof, wherein

X₂ is C-R₁₁, or N;

R₇ and R₁₁ are independently hydrogen, cyano, halo, hydroxy, azido, nitro, carboxy, sulfinyl, sulfanyl, sulfonyl, optionally substituted alkoxy, optionally substituted cycloalkyloxy, optionally substituted aryloxy, optionally substituted heteroaryloxy, optionally substituted heterocycloalkyloxy, optionally substituted alkyl, optionally substituted cycloalkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted aryl, optionally substituted heteroaryl, optionally substituted heterocycloalkyl, optionally substituted amino, optionally substituted acyl, optionally substituted alkoxycarbonyl, optionally substituted aminocarbonyl, optionally substituted aminosulfonyl, or optionally substituted carbamimidoyl; and

R₈, R₉, and R₁₀ are independently hydrogen, cyano, halo, hydroxy, azido, nitro, carboxy, sulfinyl, sulfanyl, sulfonyl, optionally substituted alkoxy, optionally substituted cycloalkyloxy, optionally substituted aryloxy, optionally substituted heteroaryloxy, optionally substituted heterocycloalkyloxy, optionally substituted alkyl, optionally substituted cycloalkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted aryl, optionally substituted heteroaryl, optionally substituted heterocycloalkyl, optionally substituted amino, optionally substituted acyl, optionally substituted alkoxycarbonyl, optionally substituted aminocarbonyl, optionally substituted aminosulfonyl, or optionally substituted carbamimidoyl;.

11. The compound or pharmaceutically acceptable salt of claim 10, wherein R₁ is hydrogen, cyano, halo, hydroxy, -CONH₂, optionally substituted alkoxy, or optionally substituted cycloalkyloxy.
12. The compound or pharmaceutically acceptable salt of claim 11, wherein R₁ is hydrogen, cyano, fluoro, chloro, hydroxy, hydroxymethyl, -CONH₂, or methoxy.

13. The compound or pharmaceutically acceptable salt of claim 10, wherein R₂, and R₄ are independently hydrogen, cyano, halo, hydroxy, carboxy, optionally substituted alkoxy, optionally substituted C₁-C₆ alkyl, optionally substituted heterocycloalkyl, optionally substituted aryl, optionally substituted heteroaryl, optionally substituted amino, optionally substituted acyl, optionally substituted alkoxycarbonyl, or optionally substituted aminocarbonyl.
14. The compound or pharmaceutically acceptable salt of claim 13, wherein R₂ and R₄ are hydrogen.
15. The compound or pharmaceutically acceptable salt of claim 14, wherein R₂ and R₄ are hydrogen, and R₃ is optionally substituted piperazinyl, optionally substituted pyrrolidinyl, optionally substituted piperidinyl, optionally substituted azetidiny.
16. The compound or pharmaceutically acceptable salt of claim 13, wherein R₂ is hydrogen, and R₄ is optionally substituted heteroaryl, optionally substituted heterocycloalkyl, or optionally substituted amino.
17. The compound or pharmaceutically acceptable salt of claim 16, wherein R₂ is hydrogen, and R₄ is optionally substituted morpholinyl, optionally substituted piperazinyl, optionally substituted pyrrolidinyl, optionally substituted piperidinyl, optionally substituted azetidiny, or substituted amino.
18. The compound or pharmaceutically acceptable salt of any one of claims 10 to 17, wherein R₅ is hydrogen, halo, cyano, optionally substituted alkoxy, or optionally substituted alkyl.
19. The compound or pharmaceutically acceptable salt of claim 18, wherein R₅ is hydrogen.
20. The compound or pharmaceutically acceptable salt of any one of claims 1 to 19, wherein R₆ is hydrogen or optionally substituted amino.
21. The compound or pharmaceutically acceptable salt of claim 20, wherein R₆ is hydrogen or amino.
22. The compound or pharmaceutically acceptable salt of any one of claims 10 to 21, wherein R₇ and R₁₁ are independently hydrogen, cyano, optionally substituted lower alkyl, halo, or methoxy.
23. The compound or pharmaceutically acceptable salt of claim 22, wherein R₇ and R₁₁ are independently hydrogen, cyano, fluoro, chloro, methyl, hydroxymethyl, -CH₂F, or methoxy.

24. The compound or pharmaceutically acceptable salt of any one of claims 10 to 23, wherein R₈, R₉, and R₁₀ are independently hydrogen, cyano, halo, hydroxy, carboxy, optionally substituted alkoxy, optionally substituted cycloalkyloxy, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted amino, optionally substituted acyl, optionally substituted alkoxycarbonyl, or optionally substituted aminocarbonyl.
25. The compound or pharmaceutically acceptable salt of claim 24, wherein at least one of R₈, R₉, and R₁₀ is halo or optionally substituted amino.
26. The compound or pharmaceutically acceptable salt of claim 24, wherein at least one of R₈, R₉, and R₁₀ is optionally substituted alkoxy.
27. The compound or pharmaceutically acceptable salt of claim 26, wherein at least one of R₈, R₉, and R₁₀ is alkoxy substituted with optionally substituted amino or optionally substituted heterocycloalkyl.
28. The compound or pharmaceutically acceptable salt of any one of claims 1 to 27, wherein R₁₂ is hydrogen, halo, cyano, -CONH₂, -NHCOCH₃, or optionally substituted lower alkyl.
29. The compound or pharmaceutically acceptable salt of claim 28, wherein R₁₂ is hydrogen, fluoro, chloro, cyano, methyl, ethyl, propyl, -CF₃, -CH₂F, -CHF₂, -CH₂CF₃, -CH₂CH₂F, -CH₂CHF₂, -CH₂OH, -CONH₂, -CH₂CONH₂, or -NHCOCH₃.
30. The compound or pharmaceutically acceptable salt of any one of claims 1 to 29, wherein R₁₃ and R₁₄ are independently hydrogen, cyano, optionally substituted lower alkyl, halo, or methoxy.
31. The compound or pharmaceutically acceptable salt of claim 22, wherein R₁₃ and R₁₄ are independently hydrogen, cyano, fluoro, chloro, methyl, hydroxymethyl, -CH₂F, or methoxy.
32. The compound or pharmaceutically acceptable salt of any one of claims 1 to 31, wherein X₃ is C-R₁₂, X₄ is C-R₁₃, and X₅ is C-R₁₄.
33. The compound or pharmaceutically acceptable salt of any one of claims 1 to 31, wherein X₃ is N, X₄ is C-R₁₃, and X₅ is C-R₁₄.
34. The compound or pharmaceutically acceptable salt of any one of claims 1 to 31, wherein X₃ is C-R₁₂, X₄ is N, and X₅ is C-R₁₄.
35. The compound or pharmaceutically acceptable salt of any one of claims 1 to 31, wherein X₃ is C-R₁₂, X₄ is C-R₁₃, and X₅ is N.

36. The compound or pharmaceutically acceptable salt of claim 10, wherein X_1 is C-R₂, X_2 is C-R₁₁, X_3 is C-R₁₂, X_4 is C-R₁₃, and X_5 is C-R₁₄.
37. The compound or pharmaceutically acceptable salt of claim 10, wherein X_1 is N, X_2 is C-R₁₁, X_3 is C-R₁₂, X_4 is C-R₁₃, and X_5 is C-R₁₄.
38. The compound or pharmaceutically acceptable salt of claim 10, wherein X_1 is C-R₂, X_2 is N, X_3 is C-R₁₂, X_4 is C-R₁₃, and X_5 is C-R₁₄.
39. The compound or pharmaceutically acceptable salt of claim 10, wherein X_1 is C-R₂, X_2 is C-R₁₁, X_3 is N, X_4 is C-R₁₃, and X_5 is C-R₁₄.
40. The compound or pharmaceutically acceptable salt of claim 10, wherein X_1 is C-R₂, X_2 is C-R₁₁, X_3 is C-R₁₂, X_4 is N, and X_5 is C-R₁₄.
41. The compound or pharmaceutically acceptable salt of claim 10, wherein X_1 is C-R₂, X_2 is C-R₁₁, X_3 is C-R₁₂, X_4 is C-R₁₃, and X_5 is N.
42. The compound or pharmaceutically acceptable salt of claim 10, wherein X_1 is N, X_2 is N, X_3 is C-R₁₂, X_4 is C-R₁₃, and X_5 is C-R₁₄.
43. The compound or pharmaceutically acceptable salt of claim 10, wherein X_1 is N, X_2 is C-R₁₁, X_3 is N, X_4 is C-R₁₃, and X_5 is C-R₁₄.
44. The compound or pharmaceutically acceptable salt of claim 10, wherein X_1 is C-R₂, X_2 is N, X_3 is N, X_4 is C-R₁₃, and X_5 is C-R₁₄.
45. The compound or pharmaceutically acceptable salt of claim 10, wherein X_1 is N, X_2 is N, X_3 is N, X_4 is C-R₁₃, and X_5 is C-R₁₄.
46. The compound or pharmaceutically acceptable salt of claim 10, wherein R_1 is hydrogen or halo.
47. The compound or pharmaceutically acceptable salt of claim 10, wherein X_1 is C-R₂ and R_2 is hydrogen or halo.
48. The compound or pharmaceutically acceptable salt of claim 10, wherein X_1 is C-R₂, and R_1 and R_2 are fluoro.
49. The compound or pharmaceutically acceptable salt of any of claims 46-48, wherein R_3 is optionally substituted piperazinyl, optionally substituted pyrrolidinyl, optionally substituted piperidinyl, optionally substituted azetidiny, or substituted amino.

50. The compound or pharmaceutically acceptable salt of claim 49, wherein R₃ is optionally substituted pyrrolidinyl.
51. The compound or pharmaceutically acceptable salt of claim 49, wherein R₃ is optionally substituted piperazinyl.
52. The compound or pharmaceutically acceptable salt of claim 49, wherein R₃ is optionally substituted piperidinyl.

53. The compound or pharmaceutically acceptable salt of claim 49, wherein:

R₃ is piperazinyl, piperidinyl, or pyrrolidinyl, optionally substituted with -R^a, -OR^b, optionally substituted amino (including -NR^cCOR^b, -NR^cCO₂R^a, -NR^cCONR^bR^c, -NR^bC(NR^c)NR^bR^c, -NR^bC(NCN)NR^bR^c, and -NR^cSO₂R^a), halo, cyano, azido, nitro, oxo (as a substituent for cycloalkyl or heterocycloalkyl), optionally substituted acyl, optionally substituted alkoxycarbonyl, aminocarbonyl, -OCOR^b, -OCO₂R^a, -OCONR^bR^c, -OP(^o)(OR^b)OR^c, sulfanyl, sulfinyl or sulfonyl,

where R^a is optionally substituted C₁-C₆ alkyl, optionally substituted cycloalkyl, optionally substituted heterocycloalkyl, optionally substituted alkenyl, optionally substituted alkynyl, optionally substituted aryl, or optionally substituted heteroaryl;

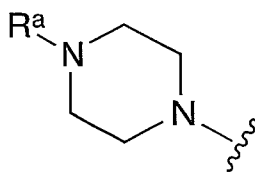
R^b is hydrogen, optionally substituted C₁-C₆ alkyl, optionally substituted cycloalkyl, optionally substituted heterocycloalkyl, optionally substituted aryl, or optionally substituted heteroaryl; and

R^c is hydrogen or optionally substituted C₁-C₄ alkyl; or

R^b and R^c, and the nitrogen to which they are attached, form an optionally substituted heterocycloalkyl group; and

where each optionally substituted group is unsubstituted or independently substituted with one or more, such as one, two, or three, substituents independently chosen from C₁-C₄ alkyl, aryl, heteroaryl, aryl-C₁-C₄ alkyl-, heteroaryl-C₁-C₄ alkyl-, C₁-C₄ haloalkyl, -OC₁-C₄ alkyl, -OC₁-C₄ alkylphenyl, -C₁-C₄ alkyl-OH, -OC₁-C₄ haloalkyl, halo, -OH, -NH₂, -C₁-C₄ alkyl-NH₂, -N(C₁-C₄ alkyl)(C₁-C₄ alkyl), -NH(C₁-C₄ alkyl), -N(C₁-C₄ alkyl)(C₁-C₄ alkylphenyl), -NH(C₁-C₄ alkylphenyl), cyano, nitro, oxo (as a substituent for cycloalkyl or heterocycloalkyl), -CO₂H, -C(O)OC₁-C₄ alkyl, -CON(C₁-C₄ alkyl)(C₁-C₄ alkyl), -CONH(C₁-C₄ alkyl), -CONH₂, -NHC(O)(C₁-C₄ alkyl), -NHC(O)(phenyl), -N(C₁-C₄ alkyl)C(O)(C₁-C₄ alkyl), -N(C₁-C₄ alkyl)C(O)(phenyl), -C(O)C₁-C₄ alkyl, -C(O)C₁-C₄ alkylphenyl, -C(O)C₁-C₄ haloalkyl, -OC(O)C₁-C₄ alkyl, -SO₂(C₁-C₄ alkyl), -SO₂(phenyl), -SO₂(C₁-C₄ haloalkyl), -SO₂NH₂, -SO₂NH(C₁-C₄ alkyl), -SO₂NH(phenyl), -NHSO₂(C₁-C₄ alkyl), -NHSO₂(phenyl), and -NHSO₂(C₁-C₄ haloalkyl).

54. The compound or pharmaceutically acceptable salt of claim 53, wherein R₃ is



55. The compound or pharmaceutically acceptable salt of claim 71, wherein R^a is C₁-C₆ alkyl, optionally substituted with C₁-C₄ alkyl, aryl, heteroaryl, aryl-C₁-C₄ alkyl-, heteroaryl-C₁-C₄ alkyl-, C₁-C₄ haloalkyl, -OC₁-C₄ alkyl, -OC₁-C₄ alkylphenyl, -C₁-C₄ alkyl-OH, -OC₁-C₄ haloalkyl, halo, -OH, -NH₂, -C₁-C₄ alkyl-NH₂, -N(C₁-C₄ alkyl)(C₁-C₄ alkyl), -NH(C₁-C₄ alkyl), -N(C₁-C₄ alkyl)(C₁-C₄ alkylphenyl), -NH(C₁-C₄ alkylphenyl), cyano, nitro, -CO₂H, -C(O)OC₁-C₄ alkyl, -CON(C₁-C₄ alkyl)(C₁-C₄ alkyl), -CONH(C₁-C₄ alkyl), -CONH₂, -NHC(O)(C₁-C₄ alkyl), -NHC(O)(phenyl), -N(C₁-C₄ alkyl)C(O)(C₁-C₄ alkyl), -N(C₁-C₄ alkyl)C(O)(phenyl), -C(O)C₁-C₄ alkyl, -C(O)C₁-C₄ alkylphenyl, -C(O)C₁-C₄ haloalkyl, -OC(O)C₁-C₄ alkyl, -SO₂(C₁-C₄ alkyl), -SO₂(phenyl), -SO₂(C₁-C₄ haloalkyl), -SO₂NH₂, -SO₂NH(C₁-C₄ alkyl), -SO₂NH(phenyl), -NHSO₂(C₁-C₄ alkyl), -NHSO₂(phenyl), or -NHSO₂(C₁-C₄ haloalkyl).
56. The compound or pharmaceutically acceptable salt of claim 55, wherein R^a is C₁-C₆ alkyl, optionally substituted with -OH, halo, C₁-C₄ alkyl, or -OC₁-C₄ alkyl.
57. The compound or pharmaceutically acceptable salt of claim 56, wherein R^a is -CH₃, -CH₂CH₂OH, -CH₂CH₂F, -CH₂CH₂OMe, -CH₂C(CH₃)₂OH, or -CH₂CH(CH₃)OH.
58. A compound or pharmaceutically acceptable salt thereof, wherein the compound is chosen from the group consisting of:
- N-(3-(2-((4-(piperazin-1-yl)phenyl)amino)pyrido[3,2-d]pyrimidin-8-yl)phenyl)acetamide
- N-(3-(2-((4-(piperazin-1-yl)phenyl)amino)pyrido[4,3-d]pyrimidin-8-yl)phenyl)acetamide
- N-(3-(2-((4-(piperazin-1-yl)phenyl)amino)pyrido[3,4-d]pyrimidin-8-yl)phenyl)acetamide
- 8-phenyl-N-(4-(piperazin-1-yl)phenyl)pyrido[3,4-d]pyrimidin-2-amine
- 8-(2-fluorophenyl)-N-(4-(piperazin-1-yl)phenyl)pyrido[3,4-d]pyrimidin-2-amine
- 8-(2-chlorophenyl)-N-(4-(piperazin-1-yl)phenyl)pyrido[3,4-d]pyrimidin-2-amine
- 8-(2,6-difluorophenyl)-N-(4-(piperazin-1-yl)phenyl)pyrido[3,4-d]pyrimidin-2-amine
- 8-(5-chloro-2-fluorophenyl)-N-(4-(piperazin-1-yl)phenyl)pyrido[3,4-d]pyrimidin-2-amine
- 8-(3-chlorophenyl)-N-(4-(piperazin-1-yl)phenyl)pyrido[3,4-d]pyrimidin-2-amine
- 8-(3-fluorophenyl)-N-(4-(piperazin-1-yl)phenyl)pyrido[3,4-d]pyrimidin-2-amine
- N-(4-fluoro-3-(2-((4-(piperazin-1-yl)phenyl)amino)pyrido[3,4-d]pyrimidin-8-yl)phenyl)acetamide

8-(2-fluoro-5-(2-morpholinoethoxy)phenyl)-N-(4-(piperazin-1-yl)phenyl)pyrido[3,4-d]pyrimidin-2-amine
 8-(5-(2-(dimethylamino)ethoxy)-2-fluorophenyl)-N-(4-(piperazin-1-yl)phenyl)pyrido[3,4-d]pyrimidin-2-amine
 8-(3-(2-morpholinoethoxy)phenyl)-N-(4-(piperazin-1-yl)phenyl)pyrido[3,4-d]pyrimidin-2-amine
 8-(3-(2-(dimethylamino)ethoxy)phenyl)-N-(4-(piperazin-1-yl)phenyl)pyrido[3,4-d]pyrimidin-2-amine
 8-(4-(2-morpholinoethoxy)phenyl)-N-(4-(piperazin-1-yl)phenyl)pyrido[3,4-d]pyrimidin-2-amine
 8-(4-(2-(dimethylamino)ethoxy)phenyl)-N-(4-(piperazin-1-yl)phenyl)pyrido[3,4-d]pyrimidin-2-amine
 8-(2-fluoro-4-(2-morpholinoethoxy)phenyl)-N-(4-(piperazin-1-yl)phenyl)pyrido[3,4-d]pyrimidin-2-amine
 8-(4-(2-(dimethylamino)ethoxy)-2-fluorophenyl)-N-(4-(piperazin-1-yl)phenyl)pyrido[3,4-d]pyrimidin-2-amine
 N1-(1-(2-fluoroethyl)azetidin-3-yl)-N4-(8-(2-fluorophenyl)pyrido[3,4-d]pyrimidin-2-yl)benzene-1,4-diamine
 N1-(1-(2-fluoroethyl)azetidin-3-yl)-N4-(8-(3-(2-morpholinoethoxy)phenyl)pyrido[3,4-d]pyrimidin-2-yl)benzene-1,4-diamine
 N1-(8-(2-fluoro-5-(2-morpholinoethoxy)phenyl)pyrido[3,4-d]pyrimidin-2-yl)-N4-(1-(2-fluoroethyl)azetidin-3-yl)benzene-1,4-diamine
 N1-(8-(5-chloro-2-fluorophenyl)pyrido[3,4-d]pyrimidin-2-yl)-N4-(1-(2-fluoroethyl)azetidin-3-yl)benzene-1,4-diamine
 8-(3-aminophenyl)-N-(4-(piperazin-1-yl)phenyl)quinazolin-2-amine
 8-(3-aminophenyl)-N-(4-(4-methylpiperazin-1-yl)phenyl)quinazolin-2-amine

 N-(3-(2-((4-(piperazin-1-yl)phenyl)amino)quinazolin-8-yl)phenyl)acetamide
 N-(3-(2-((4-(4-methylpiperazin-1-yl)phenyl)amino)quinazolin-8-yl)phenyl)acetamide
 8-phenyl-N-(4-(piperazin-1-yl)phenyl)quinazolin-2-amine
 8-(2-fluorophenyl)-N-(4-(piperazin-1-yl)phenyl)quinazolin-2-amine
 8-(2-chlorophenyl)-N-(4-(piperazin-1-yl)phenyl)quinazolin-2-amine
 8-(2,6-difluorophenyl)-N-(4-(piperazin-1-yl)phenyl)quinazolin-2-amine
 8-(5-chloro-2-fluorophenyl)-N-(4-(piperazin-1-yl)phenyl)quinazolin-2-amine
 8-(3-chlorophenyl)-N-(4-(piperazin-1-yl)phenyl)quinazolin-2-amine
 8-(3-fluorophenyl)-N-(4-(piperazin-1-yl)phenyl)quinazolin-2-amine
 N-(4-fluoro-3-(2-((4-(piperazin-1-yl)phenyl)amino)quinazolin-8-yl)phenyl)acetamide

8-(2-fluoro-5-(2-morpholinoethoxy)phenyl)-N-(4-(piperazin-1-yl)phenyl)quinazolin-2-amine
 8-(5-(2-(dimethylamino)ethoxy)-2-fluorophenyl)-N-(4-(piperazin-1-yl)phenyl)quinazolin-2-amine
 8-(3-(2-morpholinoethoxy)phenyl)-N-(4-(piperazin-1-yl)phenyl)quinazolin-2-amine
 8-(3-(2-(dimethylamino)ethoxy)phenyl)-N-(4-(piperazin-1-yl)phenyl)quinazolin-2-amine
 8-(4-(2-morpholinoethoxy)phenyl)-N-(4-(piperazin-1-yl)phenyl)quinazolin-2-amine
 8-(4-(2-(dimethylamino)ethoxy)phenyl)-N-(4-(piperazin-1-yl)phenyl)quinazolin-2-amine
 8-(2-fluoro-4-(2-morpholinoethoxy)phenyl)-N-(4-(piperazin-1-yl)phenyl)quinazolin-2-amine
 8-(4-(2-(dimethylamino)ethoxy)-2-fluorophenyl)-N-(4-(piperazin-1-yl)phenyl)quinazolin-2-amine
 N-(3-(2-((6-(piperazin-1-yl)pyridin-3-yl)amino)pyrido[3,2-d]pyrimidin-8-yl)phenyl)acetamide
 N-(3-(2-((6-(piperazin-1-yl)pyridin-3-yl)amino)pyrido[4,3-d]pyrimidin-8-yl)phenyl)acetamide
 N-(3-(2-((6-(piperazin-1-yl)pyridin-3-yl)amino)pyrido[3,4-d]pyrimidin-8-yl)phenyl)acetamide
 8-phenyl-N-(6-(piperazin-1-yl)pyridin-3-yl)pyrido[3,4-d]pyrimidin-2-amine
 8-(2-fluorophenyl)-N-(6-(piperazin-1-yl)pyridin-3-yl)pyrido[3,4-d]pyrimidin-2-amine
 8-(2-chlorophenyl)-N-(6-(piperazin-1-yl)pyridin-3-yl)pyrido[3,4-d]pyrimidin-2-amine
 8-(2,6-difluorophenyl)-N-(6-(piperazin-1-yl)pyridin-3-yl)pyrido[3,4-d]pyrimidin-2-amine
 8-(5-chloro-2-fluorophenyl)-N-(6-(piperazin-1-yl)pyridin-3-yl)pyrido[3,4-d]pyrimidin-2-amine
 8-(3-chlorophenyl)-N-(6-(piperazin-1-yl)pyridin-3-yl)pyrido[3,4-d]pyrimidin-2-amine
 8-(3-fluorophenyl)-N-(6-(piperazin-1-yl)pyridin-3-yl)pyrido[3,4-d]pyrimidin-2-amine
 N-(4-fluoro-3-(2-((6-(piperazin-1-yl)pyridin-3-yl)amino)pyrido[3,4-d]pyrimidin-8-yl)phenyl)acetamide
 8-(2-fluoro-5-(2-morpholinoethoxy)phenyl)-N-(6-(piperazin-1-yl)pyridin-3-yl)pyrido[3,4-d]pyrimidin-2-amine
 8-(5-(2-(dimethylamino)ethoxy)-2-fluorophenyl)-N-(6-(piperazin-1-yl)pyridin-3-yl)pyrido[3,4-d]pyrimidin-2-amine
 8-(3-(2-morpholinoethoxy)phenyl)-N-(6-(piperazin-1-yl)pyridin-3-yl)pyrido[3,4-d]pyrimidin-2-amine
 8-(3-(2-(dimethylamino)ethoxy)phenyl)-N-(6-(piperazin-1-yl)pyridin-3-yl)pyrido[3,4-d]pyrimidin-2-amine
 8-(4-(2-morpholinoethoxy)phenyl)-N-(6-(piperazin-1-yl)pyridin-3-yl)pyrido[3,4-d]pyrimidin-2-amine

8-(4-(2-(dimethylamino)ethoxy)phenyl)-N-(6-(piperazin-1-yl)pyridin-3-yl)pyrido[3,4-d]pyrimidin-2-amine
 8-(2-fluoro-4-(2-morpholinoethoxy)phenyl)-N-(6-(piperazin-1-yl)pyridin-3-yl)pyrido[3,4-d]pyrimidin-2-amine
 8-(4-(2-(dimethylamino)ethoxy)-2-fluorophenyl)-N-(6-(piperazin-1-yl)pyridin-3-yl)pyrido[3,4-d]pyrimidin-2-amine
 8-(3-aminophenyl)-N-(6-(piperazin-1-yl)pyridin-3-yl)quinazolin-2-amine
 8-(3-aminophenyl)-N-(6-(4-methylpiperazin-1-yl)pyridin-3-yl)quinazolin-2-amine
 N-(3-(2-((6-(piperazin-1-yl)pyridin-3-yl)amino)quinazolin-8-yl)phenyl)acetamide
 N-(3-(2-((6-(4-methylpiperazin-1-yl)pyridin-3-yl)amino)quinazolin-8-yl)phenyl)acetamide
 8-phenyl-N-(6-(piperazin-1-yl)pyridin-3-yl)quinazolin-2-amine
 8-(2-fluorophenyl)-N-(6-(piperazin-1-yl)pyridin-3-yl)quinazolin-2-amine
 8-(2-chlorophenyl)-N-(6-(piperazin-1-yl)pyridin-3-yl)quinazolin-2-amine
 8-(2,6-difluorophenyl)-N-(6-(piperazin-1-yl)pyridin-3-yl)quinazolin-2-amine
 8-(5-chloro-2-fluorophenyl)-N-(6-(piperazin-1-yl)pyridin-3-yl)quinazolin-2-amine
 8-(3-chlorophenyl)-N-(6-(piperazin-1-yl)pyridin-3-yl)quinazolin-2-amine
 8-(3-fluorophenyl)-N-(6-(piperazin-1-yl)pyridin-3-yl)quinazolin-2-amine
 N-(4-fluoro-3-(2-((6-(piperazin-1-yl)pyridin-3-yl)amino)quinazolin-8-yl)phenyl)acetamide
 8-(2-fluoro-5-(2-morpholinoethoxy)phenyl)-N-(6-(piperazin-1-yl)pyridin-3-yl)quinazolin-2-amine
 8-(5-(2-(dimethylamino)ethoxy)-2-fluorophenyl)-N-(6-(piperazin-1-yl)pyridin-3-yl)quinazolin-2-amine
 8-(3-(2-morpholinoethoxy)phenyl)-N-(6-(piperazin-1-yl)pyridin-3-yl)quinazolin-2-amine
 8-(3-(2-(dimethylamino)ethoxy)phenyl)-N-(6-(piperazin-1-yl)pyridin-3-yl)quinazolin-2-amine
 8-(4-(2-morpholinoethoxy)phenyl)-N-(6-(piperazin-1-yl)pyridin-3-yl)quinazolin-2-amine
 8-(4-(2-(dimethylamino)ethoxy)phenyl)-N-(6-(piperazin-1-yl)pyridin-3-yl)quinazolin-2-amine
 8-(2-fluoro-4-(2-morpholinoethoxy)phenyl)-N-(6-(piperazin-1-yl)pyridin-3-yl)quinazolin-2-amine
 8-(4-(2-(dimethylamino)ethoxy)-2-fluorophenyl)-N-(6-(piperazin-1-yl)pyridin-3-yl)quinazolin-2-amine
 8-(4-aminopyridin-2-yl)-N-(4-(piperazin-1-yl)phenyl)quinazolin-2-amine
 8-(4-aminopyridin-2-yl)-N-(4-(4-methylpiperazin-1-yl)phenyl)quinazolin-2-amine
 N-(2-(2-((4-(4-methylpiperazin-1-yl)phenyl)amino)quinazolin-8-yl)pyridin-4-yl)acetamide
 N-(4-(piperazin-1-yl)phenyl)-8-(pyridin-2-yl)quinazolin-2-amine
 N-(2-(2-((4-(piperazin-1-yl)phenyl)amino)quinazolin-8-yl)pyridin-4-yl)acetamide

8-(4-(2-morpholinoethoxy)pyridin-2-yl)-N-(4-(piperazin-1-yl)phenyl)quinazolin-2-amine
 8-(4-(2-(dimethylamino)ethoxy)pyridin-2-yl)-N-(4-(piperazin-1-yl)phenyl)quinazolin-2-amine
 8-(5-(2-morpholinoethoxy)pyridin-2-yl)-N-(4-(piperazin-1-yl)phenyl)quinazolin-2-amine
 8-(5-(2-(dimethylamino)ethoxy)pyridin-2-yl)-N-(4-(piperazin-1-yl)phenyl)quinazolin-2-amine
 N-(2-(2-((6-(piperazin-1-yl)pyridin-3-yl)amino)pyrido[3,2-d]pyrimidin-8-yl)pyridin-4-yl)acetamide
 N-(2-(2-((6-(piperazin-1-yl)pyridin-3-yl)amino)pyrido[4,3-d]pyrimidin-8-yl)pyridin-4-yl)acetamide
 N-(6-(piperazin-1-yl)pyridin-3-yl)-8-(pyridin-2-yl)pyrido[3,4-d]pyrimidin-2-amine
 N-(2-(2-((6-(piperazin-1-yl)pyridin-3-yl)amino)pyrido[3,4-d]pyrimidin-8-yl)pyridin-4-yl)acetamide
 8-(4-(2-morpholinoethoxy)pyridin-2-yl)-N-(6-(piperazin-1-yl)pyridin-3-yl)pyrido[3,4-d]pyrimidin-2-amine
 8-(4-(2-(dimethylamino)ethoxy)pyridin-2-yl)-N-(6-(piperazin-1-yl)pyridin-3-yl)pyrido[3,4-d]pyrimidin-2-amine
 8-(5-(2-morpholinoethoxy)pyridin-2-yl)-N-(6-(piperazin-1-yl)pyridin-3-yl)pyrido[3,4-d]pyrimidin-2-amine
 8-(5-(2-(dimethylamino)ethoxy)pyridin-2-yl)-N-(6-(piperazin-1-yl)pyridin-3-yl)pyrido[3,4-d]pyrimidin-2-amine
 8-(4-aminopyridin-2-yl)-N-(6-(piperazin-1-yl)pyridin-3-yl)quinazolin-2-amine
 8-(4-aminopyridin-2-yl)-N-(6-(4-methylpiperazin-1-yl)pyridin-3-yl)quinazolin-2-amine
 N-(2-(2-((6-(piperazin-1-yl)pyridin-3-yl)amino)quinazolin-8-yl)pyridin-4-yl)acetamide
 N-(2-(2-((6-(4-methylpiperazin-1-yl)pyridin-3-yl)amino)quinazolin-8-yl)pyridin-4-yl)acetamide
 N-(6-(piperazin-1-yl)pyridin-3-yl)-8-(pyridin-2-yl)quinazolin-2-amine
 8-(4-(2-morpholinoethoxy)pyridin-2-yl)-N-(6-(piperazin-1-yl)pyridin-3-yl)quinazolin-2-amine
 8-(4-(2-(dimethylamino)ethoxy)pyridin-2-yl)-N-(6-(piperazin-1-yl)pyridin-3-yl)quinazolin-2-amine
 8-(5-(2-morpholinoethoxy)pyridin-2-yl)-N-(6-(piperazin-1-yl)pyridin-3-yl)quinazolin-2-amine
 8-(5-(2-(dimethylamino)ethoxy)pyridin-2-yl)-N-(6-(piperazin-1-yl)pyridin-3-yl)quinazolin-2-amine
 8-(4-(2-morpholinoethoxy)pyridin-2-yl)-N2-(6-(piperazin-1-yl)pyridin-3-yl)quinazoline-2,4-diamine

N2-(6-(piperazin-1-yl)pyridin-3-yl)-8-(pyridin-2-yl)quinazoline-2,4-diamine
 8-(5-chloro-2-fluorophenyl)-N2-(6-(piperazin-1-yl)pyridin-3-yl)pyrido[3,4-d]pyrimidine-2,4-diamine
 8-(2,6-difluorophenyl)-N2-(6-(piperazin-1-yl)pyridin-3-yl)pyrido[3,4-d]pyrimidine-2,4-diamine
 8-(2-fluorophenyl)-N2-(6-(piperazin-1-yl)pyridin-3-yl)pyrido[3,4-d]pyrimidine-2,4-diamine
 N2-(6-(piperazin-1-yl)pyridin-3-yl)-8-(pyridin-2-yl)pyrido[3,4-d]pyrimidine-2,4-diamine
 8-(2-fluoro-4-(2-morpholinoethoxy)phenyl)-N2-(6-(piperazin-1-yl)pyridin-3-yl)pyrido[3,4-d]pyrimidine-2,4-diamine
 N2-(4-(piperazin-1-yl)phenyl)-8-(pyridin-2-yl)pyrido[3,4-d]pyrimidine-2,4-diamine
 N2-(4-(piperazin-1-yl)phenyl)-8-(pyridin-2-yl)quinazoline-2,4-diamine
 8-(3-fluorophenyl)-N2-(6-(piperazin-1-yl)pyridin-3-yl)quinazoline-2,4-diamine
 8
 8-(5-chloro-2-fluorophenyl)-N2-(6-(piperazin-1-yl)pyridin-3-yl)quinazoline-2,4-diamine
 8-(2,6-difluorophenyl)-N2-(6-(piperazin-1-yl)pyridin-3-yl)quinazoline-2,4-diamine
 8-(2-fluoro-5-(2-morpholinoethoxy)phenyl)-N2-(6-(piperazin-1-yl)pyridin-3-yl)quinazoline-2,4-diamine
 8-(5-(2-(dimethylamino)ethoxy)-2-fluorophenyl)-N2-(6-(piperazin-1-yl)pyridin-3-yl)quinazoline-2,4-diamine
 8-(2-fluorophenyl)-N2-(6-(piperazin-1-yl)pyridin-3-yl)quinazoline-2,4-diamine
 8-(2-fluoro-4-(2-morpholinoethoxy)phenyl)-N2-(6-(piperazin-1-yl)pyridin-3-yl)quinazoline-2,4-diamine
 8-(5-chloro-2-fluorophenyl)-N2-(4-(piperazin-1-yl)phenyl)pyrido[3,4-d]pyrimidine-2,4-diamine
 8-(2,6-difluorophenyl)-N2-(4-(piperazin-1-yl)phenyl)pyrido[3,4-d]pyrimidine-2,4-diamine
 8-(2-fluoro-5-(2-morpholinoethoxy)phenyl)-N2-(4-(piperazin-1-yl)phenyl)pyrido[3,4-d]pyrimidine-2,4-diamine
 8-(5-(2-(dimethylamino)ethoxy)-2-fluorophenyl)-N2-(4-(piperazin-1-yl)phenyl)pyrido[3,4-d]pyrimidine-2,4-diamine
 8-(2-fluorophenyl)-N2-(4-(piperazin-1-yl)phenyl)pyrido[3,4-d]pyrimidine-2,4-diamine
 8-(2-fluoro-4-(2-morpholinoethoxy)phenyl)-N2-(4-(piperazin-1-yl)phenyl)pyrido[3,4-d]pyrimidine-2,4-diamine
 8-(2-fluorophenyl)-N2-(4-(piperazin-1-yl)phenyl)quinazoline-2,4-diamine
 8-(5-chloro-2-fluorophenyl)-N2-(4-(piperazin-1-yl)phenyl)quinazoline-2,4-diamine
 8-(2,6-difluorophenyl)-N2-(4-(piperazin-1-yl)phenyl)quinazoline-2,4-diamine
 8-(2-fluoro-5-(2-morpholinoethoxy)phenyl)-N2-(4-(piperazin-1-yl)phenyl)quinazoline-2,4-diamine

8-(2-fluoro-4-(2-morpholinoethoxy)phenyl)-N2-(4-(piperazin-1-yl)phenyl)quinazoline-2,4-diamine

tert-butyl 4-(4-((8-(2-fluorophenyl)quinazolin-2-yl)amino)phenyl)piperazine-1-carboxylate

tert-butyl 4-(4-((8-(2-chlorophenyl)quinazolin-2-yl)amino)phenyl)piperazine-1-carboxylate

tert-butyl 4-(4-((8-(3-fluorophenyl)quinazolin-2-yl)amino)phenyl)piperazine-1-carboxylate

tert-butyl 4-(4-((8-(5-chloro-2-fluorophenyl)quinazolin-2-yl)amino)phenyl)piperazine-1-carboxylate

tert-butyl 4-(4-((8-(3-chlorophenyl)quinazolin-2-yl)amino)phenyl)piperazine-1-carboxylate

tert-butyl 4-(4-((8-phenylquinazolin-2-yl)amino)phenyl)piperazine-1-carboxylate

tert-butyl 4-(4-((8-(2-fluoro-5-(2-morpholinoethoxy)phenyl)quinazolin-2-yl)amino)phenyl)piperazine-1-carboxylate

N-(3-(2-((4-(4-methylpiperazin-1-yl)phenyl)amino)quinazolin-8-yl)phenyl)propionamide, and

N-(3-(7-methyl-2-((4-(4-methylpiperazin-1-yl)phenyl)amino)quinazolin-8-yl)phenyl)propionamide.

59. The compound or pharmaceutically acceptable salt of any one of claims 1-58, wherein the pharmaceutically acceptable salt is a chloride, carbonate, gluconate, benzoate, acetate, lactate, citrate, propionate, hydrogenphosphate, fumarate, succinate, or TRIS (hydroxymethyl-aminomethane), maleate, malonate, tartrate, oxalate, pamoate, or stearate salt.
60. The compound or pharmaceutically acceptable salt of claim 59, wherein the pharmaceutically acceptable salt is a chloride, fumarate, malonate, maleate, acetate, lactate, citrate, succinate, or tartrate salt.
61. The compound or pharmaceutically acceptable salt of claim 60, wherein the pharmaceutically acceptable salt is a chloride, fumarate, malonate, maleate, or tartrate salt.
62. A pharmaceutical composition comprising a pharmaceutically acceptable carrier and the compound or pharmaceutically acceptable salt of any one of claims 1 to 61.
63. The pharmaceutical composition of claim 62, wherein the pharmaceutical composition is formulated in a form chosen from the group consisting of tablets, capsules, powders, liquids, suspensions, suppositories, and aerosols.
64. A packaged pharmaceutical composition comprising the pharmaceutical composition of claim 62 or 63 and instructions for using the pharmaceutical composition to treat a subject suffering from a cancer.
65. Use of the compound or pharmaceutically acceptable salt of any one of claims 1 to 61 in the manufacture of a medicament for treating a cancer in a subject.

66. The use of claim 65, wherein the cancer is colon carcinoma, pancreatic cancer, breast cancer, ovarian cancer, prostate cancer, thyroid cancer, fibrosarcoma, myxosarcoma, liposarcoma, chondrosarcoma, osteogenic sarcoma, chondroma, angiosarcoma, endotheliosarcoma, lymphangiosarcoma, lymphangioendotheliosarcoma, synovioma, mesothelioma, Ewing's tumor, leiomyosarcoma, rhabdomyosarcoma, squamous cell carcinoma, basal cell carcinoma, adenocarcinoma, sweat gland carcinoma, thyroid cancer, sebaceous gland carcinoma, papillary carcinoma, papillary adenocarcinomas, cystadenocarcinoma, medullary carcinoma, bronchogenic carcinoma, renal cell carcinoma, hepatoma, bile duct carcinoma, choriocarcinoma, seminoma, embryonal carcinoma, Wilms' tumor, cervical cancer, testicular tumor, lung carcinoma, small cell lung carcinoma, non-small cell lung cancer, bladder carcinoma, epithelial carcinoma, glioma, astrocytoma, medulloblastoma, craniopharyngioma, ependymoma, pinealoma, hemangioblastoma, acoustic neuroma, oligodendroglioma, meningioma, melanoma, neuroblastoma, retinoblastoma, leukemia, acute lymphocytic leukemia, acute myelocytic leukemia, chronic leukemia, polycythemia vera, lymphoma, multiple myeloma, Waldenstrom's macroglobulinemia, or heavy chain disease.
67. The use of claim 66, wherein the cancer is non-small cell lung cancer, breast cancer, colon cancer, thyroid cancer, or ovarian cancer.
68. Use of the compound or pharmaceutically acceptable salt of any one of claims 1 to 61, in the manufacture of a medicament for treating a cancer in a subject in need thereof, wherein the subject has an EGFR mutation or double mutation.
69. The use of claim 68, wherein the EGFR mutation is in codon 790.
70. The use of claim 68 wherein the EGFR mutation is del E746-A750, del E747-E749/A750P, del E747-S752/P753S, del E747-T751/Sins/A750P, del S752-I759, G719S, G719C, L861Q, L858R, T790M, or L858R/T790M.
71. The use of claim 68, wherein the cancer is colon carcinoma, pancreatic cancer, breast cancer, ovarian cancer, prostate cancer, thyroid cancer, fibrosarcoma, myxosarcoma, liposarcoma, chondrosarcoma, osteogenic sarcoma, chondroma, angiosarcoma, endotheliosarcoma, lymphangiosarcoma, lymphangioendotheliosarcoma, synovioma, mesothelioma, Ewing's tumor, leiomyosarcoma, rhabdomyosarcoma, squamous cell carcinoma, basal cell carcinoma, adenocarcinoma, sweat gland carcinoma, sebaceous gland carcinoma, papillary carcinoma, papillary adenocarcinomas, cystadenocarcinoma, medullary carcinoma, bronchogenic carcinoma, renal cell carcinoma, hepatoma, bile duct carcinoma, choriocarcinoma, seminoma, embryonal carcinoma, Wilms' tumor, cervical cancer, testicular tumor, lung carcinoma, small cell lung carcinoma, non-small cell lung cancer, bladder carcinoma, epithelial carcinoma,

glioma, astrocytoma, medulloblastoma, craniopharyngioma, ependymoma, pinealoma, hemangioblastoma, acoustic neuroma, oligodendroglioma, meningioma, melanoma, neuroblastoma, retinoblastoma, leukemia, acute lymphocytic leukemia, acute myelocytic leukemia, chronic leukemia, polycythemia vera, lymphoma, multiple myeloma, Waldenstrom's macroglobulinemia, or heavy chain disease.

72. The use of claim 71, wherein the cancer is non-small cell lung cancer, colon cancer, thyroid cancer, or ovarian cancer.
73. The use of any one of claims 65-72, wherein the medicament is to be administered with an additional anti-cancer and/or cytotoxic agent.