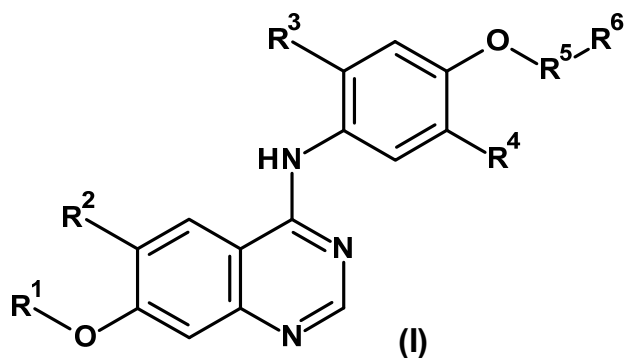


Claims

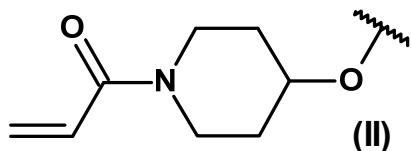
1. A compound represented by Formula (I) or a pharmaceutically acceptable salt thereof:



wherein

R¹ represents a C₁-C₃ alkyl group optionally substituted with 1 to 3 halogen atoms,

R² represents Formula (II) below:



or -NH-CO-CH=CH-CH₂-X;

X represents an amino group optionally having 1 or 2 substituents independently selected from Group A below, a pyrrolidinyl group optionally having 1 or 2 substituents independently selected from Group A below, an azetidiny group optionally having 1 or 2 substituents independently selected from Group A below, or a morpholyl group;

R³ represents a halogen atom;

R⁴ represents a hydrogen atom or a halogen atom;

R⁵ represents a benzene ring, a thiazole ring, or a pyrazole ring optionally having 1 or 2 substituents independently selected from the group consisting of a halogen atom and a C₁-C₃ alkyl group;

R⁶ represents an oxadiazolyl group optionally having 1 or 2 substituents independently selected from Group B below, a triazolyl group optionally having 1 or 2 substituents independently selected from Group B below, a pyridyl group optionally having 1 or 2 substituents independently selected from Group B below, a pyrimidyl group optionally having 1 or 2 substituents independently selected from Group B below, a thiadiazolyl group optionally having 1 or 2 substituents independently selected from Group B below, -CO-N(Y)(Z), or -CH₂-CO-N(Y)(Z);

Y and Z each independently represents a hydrogen atom, a C₁-C₆ alkyl group optionally substituted with 1 to 3 halogen atoms, or a C₃-C₆ cycloalkyl group substituted with a C₁-C₃ alkyl group optionally substituted with 1 to 3 halogen atoms, or

Y, Z and the nitrogen atom to which they are bonded may be taken together to form a 4- to 6-membered nitrogen-containing saturated heterocyclic ring,

Group A: a halogen atom, a C₁-C₃ alkyl group, a C₁-C₃ alkoxy group, and a tetrahydrofuryl group, and

Group B: a halogen atom, a C₁-C₃ alkyl group, a C₃-C₆ cycloalkyl group, and a C₁-C₃ alkoxy group.

2. The compound or a pharmaceutically acceptable salt thereof according to claim 1, wherein R¹ is a methyl group.

3. The compound or a pharmaceutically acceptable salt thereof according to claim 1 or 2, wherein R² is a group represented by Formula (II).

4. The compound or a pharmaceutically acceptable salt thereof according to any one of claims 1 to 3, wherein R³ is a chlorine atom or a fluorine atom, and R⁴ is a hydrogen atom.

5. The compound or a pharmaceutically acceptable salt thereof according to any one of claims 1 to 4, wherein R⁵ is a benzene ring or a pyrazole ring.

6. The compound or a pharmaceutically acceptable salt thereof according to any one of claims 1 to 5, wherein

R⁶ is an oxadiazolyl group optionally substituted with a methyl group, a pyridyl group optionally substituted with 1 or 2 substituents independently selected from the group consisting of a fluorine atom and a methyl group, or -CO-NH-Y; and

Y is a tert-butyl group optionally substituted with 1 to 3 fluorine atoms.

7. A compound selected from the group consisting of:

N-tert-butyl-3-{3-fluoro-4-[(7-methoxy-6-{[1-(prop-2-enoyl)piperidin-4-yl]oxy}quinazolin-4-yl)amino]phenoxy}-1H-pyrazole-1-carboxamide,

3-{3-fluoro-4-[(7-methoxy-6-{[1-(prop-2-enoyl)piperidin-4-yl]oxy}quinazolin-4-yl)amino]phenoxy}-N-(1-fluoro-2-methylpropan-2-yl)-1H-pyrazole-1-carboxamide,

1-{4-[(4-{2-chloro-4-[3-(5-methyl-1,3,4-oxadiazol-2-yl)phenoxy]anilino)-7-methoxyquinazolin-6-yl]oxy]piperidin-1-yl}prop-2-en-1-one,

1-{4-[(4-{2-fluoro-4-[3-(5-methyl-1,3,4-oxadiazol-2-yl)phenoxy]anilino)-7-methoxyquinazolin-6-yl]oxy]piperidin-1-yl}prop-2-en-1-one,

1-(4-{[4-(2-fluoro-4-{[1-(5-fluoro-6-methylpyridin-3-yl)-1H-pyrazol-3-yl]oxy}anilino)-7-methoxyquinazolin-6-yl]oxy}piperidin-1-yl)prop-2-en-1-one; and

1-(4-{[4-(2-fluoro-4-{[1-(6-methylpyridin-3-yl)-1H-pyrazol-3-yl]oxy}anilino)-7-methoxyquinazolin-6-yl]oxy}piperidin-1-yl)prop-2-en-1-one,

or a pharmaceutically acceptable salt thereof.

8. N-tert-Butyl-3-{3-fluoro-4-[(7-methoxy-6-{[1-(prop-2-enoyl)piperidin-4-yl]oxy}quinazolin-4-yl)amino]phenoxy}-1H-pyrazole-1-carboxamide, or a pharmaceutically acceptable salt thereof.

9. N-tert-Butyl-3-{3-fluoro-4-[(7-methoxy-6-{[1-(prop-2-enoyl)piperidin-4-yl]oxy}quinazolin-4-yl)amino]phenoxy}-1H-pyrazole-1-carboxamide methanesulfonate.

10. 3-{3-Fluoro-4-[(7-methoxy-6-{[1-(prop-2-enoyl)piperidin-4-yl]oxy}quinazolin-4-yl)amino]phenoxy}-N-(1-fluoro-2-methylpropan-2-yl)-1H-pyrazole-1-carboxamide, or a pharmaceutically acceptable salt thereof.

11. 3-{3-Fluoro-4-[(7-methoxy-6-{[1-(prop-2-enoyl)piperidin-4-yl]oxy}quinazolin-4-yl)amino]phenoxy}-N-(1-fluoro-2-methylpropan-2-yl)-1H-pyrazole-1-carboxamide 1,5-naphthalenedisulfonate.

12. 1-{4-[(4-{2-Chloro-4-[3-(5-methyl-1,3,4-oxadiazol-2-yl)phenoxy]anilino}-7-methoxyquinazolin-6-yl)oxy]piperidin-1-yl}prop-2-en-1-one, or a pharmaceutically acceptable salt thereof.

13. 1-{4-[(4-{2-Chloro-4-[3-(5-methyl-1,3,4-oxadiazol-2-yl)phenoxy]anilino}-7-methoxyquinazolin-6-yl)oxy]piperidin-1-yl}prop-2-en-1-one methanesulfonate.

14. 1-{4-[(4-{2-Fluoro-4-[3-(5-methyl-1,3,4-oxadiazol-2-yl)phenoxy]anilino}-7-methoxyquinazolin-6-

yl)oxy]piperidin-1-yl}prop-2-en-1-one, or a pharmaceutically acceptable salt thereof.

15. 1-(4-{[4-(2-Fluoro-4-{[1-(5-fluoro-6-methylpyridin-3-yl)-1H-pyrazol-3-yl]oxy}anilino)-7-methoxyquinazolin-6-yl]oxy}piperidin-1-yl)prop-2-en-1-one, or a pharmaceutically acceptable salt thereof.

16. 1-(4-{[4-(2-Fluoro-4-{[1-(5-fluoro-6-methylpyridin-3-yl)-1H-pyrazol-3-yl]oxy}anilino)-7-methoxyquinazolin-6-yl]oxy}piperidin-1-yl)prop-2-en-1-one benzenesulfonate.

17. 1-(4-{[4-(2-Fluoro-4-{[1-(5-fluoro-6-methylpyridin-3-yl)-1H-pyrazol-3-yl]oxy}anilino)-7-methoxyquinazolin-6-yl]oxy}piperidin-1-yl)prop-2-en-1-one tartrate.

18. 1-(4-{[4-(2-Fluoro-4-{[1-(5-fluoro-6-methylpyridin-3-yl)-1H-pyrazol-3-yl]oxy}anilino)-7-methoxyquinazolin-6-yl]oxy}piperidin-1-yl)prop-2-en-1-one citrate.

19. 1-(4-{[4-(2-Fluoro-4-{[1-(6-methylpyridin-3-yl)-1H-pyrazol-3-yl]oxy}anilino)-7-methoxyquinazolin-6-yl]oxy}piperidin-1-yl)prop-2-en-1-one, or a pharmaceutically acceptable salt thereof.

20. 1-(4-{[4-(2-Fluoro-4-{[1-(6-methylpyridin-3-yl)-1H-pyrazol-3-yl]oxy}anilino)-7-methoxyquinazolin-6-yl]oxy}piperidin-1-yl)prop-2-en-1-one hydrochloride.

21. 1-(4-{[4-((2-Fluoro-4-{[1-(6-methylpyridin-3-yl)-1H-pyrazol-3-yl]oxy}anilino)-7-methoxyquinazolin-6-yl]oxy}piperidin-1-yl)prop-2-en-1-one 1,5-naphthalenedisulfonate.

22. 1-(4-{[4-(2-Fluoro-4-{[1-(6-methylpyridin-3-yl)-1H-pyrazol-3-yl]oxy}anilino)-7-methoxyquinazolin-6-yl]oxy}piperidin-1-yl)prop-2-en-1-one citrate.

23. A crystal of 3-{3-fluoro-4-[(7-methoxy-6-{[1-(prop-2-enoyl)piperidin-4-yl]oxy}quinazolin-4-yl)amino]phenoxy}-N-(1-fluoro-2-methylpropan-2-yl)-1H-pyrazole-1-carboxamide, having at least five peaks at diffraction angles (2θ) selected from 5.78 ± 0.2 , 15.48 ± 0.2 , 16.38 ± 0.2 , 17.24 ± 0.2 , 19.28 ± 0.2 , 19.90 ± 0.2 , 20.42 ± 0.2 , 20.82 ± 0.2 , 22.04 ± 0.2 , and 24.50 ± 0.2 in powder X-ray diffraction with $\text{CuK}\alpha$ radiation.

24. A crystal of 3-{3-fluoro-4-[(7-methoxy-6-{[1-(prop-2-enoyl)piperidin-4-yl]oxy}quinazolin-4-yl)amino]phenoxy}-N-(1-fluoro-2-methylpropan-2-yl)-1H-pyrazole-1-carboxamide 1,5-naphthalenedisulfonate, having at least five peaks at diffraction angles (2θ) selected

from 5.74 ± 0.2 , 10.32 ± 0.2 , 11.58 ± 0.2 , 14.62 ± 0.2 , 14.94 ± 0.2 , 18.72 ± 0.2 , 19.60 ± 0.2 , 20.84 ± 0.2 , 22.96 ± 0.2 and 26.42 ± 0.2 in powder X-ray diffraction with $\text{CuK}\alpha$ radiation.

25. A crystal of 1-{4-[(4-{2-chloro-4-[3-(5-methyl-1,3,4-oxadiazol-2-yl)phenoxy]anilino)-7-methoxyquinazolin-6-yl)oxy]piperidin-1-yl}prop-2-en-1-one, having at least five peaks at diffraction angles (2θ) selected from 4.26 ± 0.2 , 8.66 ± 0.2 , 13.64 ± 0.2 , 14.34 ± 0.2 , 14.98 ± 0.2 , 17.60 ± 0.2 , 19.08 ± 0.2 , 22.10 ± 0.2 , 23.02 ± 0.2 and 25.88 ± 0.2 in powder X-ray diffraction with $\text{CuK}\alpha$ radiation.

26. A crystal of 1-{4-[(4-{2-chloro-4-[3-(5-methyl-1,3,4-oxadiazol-2-yl)phenoxy]anilino)-7-methoxyquinazolin-6-yl)oxy]piperidin-1-yl}prop-2-en-1-one methanesulfonate, having at least five peaks at diffraction angles (2θ) selected from 3.56 ± 0.2 , 7.24 ± 0.2 , 15.02 ± 0.2 , 16.84 ± 0.2 , 17.68 ± 0.2 , 20.26 ± 0.2 , 21.88 ± 0.2 , 22.92 ± 0.2 , 25.76 ± 0.2 and 27.08 ± 0.2 in powder X-ray diffraction with $\text{CuK}\alpha$ radiation.

27. A crystal of 1-(4-{[4-(2-fluoro-4-{[1-(5-fluoro-6-methylpyridin-3-yl)-1H-pyrazol-3-yl]oxy}anilino)-7-methoxyquinazolin-6-yl]oxy}piperidin-1-yl)prop-2-en-1-one, having at least five peaks at diffraction angles

(2 θ) selected from 8.08 $\pm$ 0.2, 10.32 $\pm$ 0.2, 12.90 $\pm$ 0.2, 13.48 $\pm$ 0.2, 13.82 $\pm$ 0.2, 15.44 $\pm$ 0.2, 19.76 $\pm$ 0.2, 23.60 $\pm$ 0.2, 24.24 $\pm$ 0.2 and 25.90 $\pm$ 0.2 in powder X-ray diffraction with CuK α radiation.

28. A crystal of 1-(4-{[4-(2-fluoro-4-{[1-(5-fluoro-6-methylpyridin-3-yl)-1H-pyrazol-3-yl]oxy}anilino)-7-methoxyquinazolin-6-yl]oxy}piperidin-1-yl)prop-2-en-1-one benzenesulfonate, having at least five peaks at diffraction angles (2 θ) selected from 6.22 $\pm$ 0.2, 12.16 $\pm$ 0.2, 13.60 $\pm$ 0.2, 16.26 $\pm$ 0.2, 18.50 $\pm$ 0.2, 19.58 $\pm$ 0.2, 20.58 $\pm$ 0.2, 21.06 $\pm$ 0.2, 23.30 $\pm$ 0.2, and 25.76 $\pm$ 0.2 in powder X-ray diffraction with CuK α radiation.

29. A crystal of 1-(4-{[4-(2-fluoro-4-{[1-(5-fluoro-6-methylpyridin-3-yl)-1H-pyrazol-3-yl]oxy}anilino)-7-methoxyquinazolin-6-yl]oxy}piperidin-1-yl)prop-2-en-1-one tartrate, having at least five peaks at diffraction angles (2 θ) selected from 3.58 $\pm$ 0.2, 14.50 $\pm$ 0.2, 16.50 $\pm$ 0.2, 24.28 $\pm$ 0.2, 24.70 $\pm$ 0.2, 24.98 $\pm$ 0.2, 25.76 $\pm$ 0.2, 26.12 $\pm$ 0.2, 26.60 $\pm$ 0.2 and 27.40 $\pm$ 0.2 in powder X-ray diffraction with CuK α radiation.

30. A crystal of 1-(4-{[4-(2-fluoro-4-{[1-(5-fluoro-6-methylpyridin-3-yl)-1H-pyrazol-3-yl]oxy}anilino)-7-methoxyquinazolin-6-yl]oxy}piperidin-1-yl)prop-2-en-1-one citrate, having at least five peaks at diffraction angles

(2 θ) selected from 7.36 $\pm$ 0.2, 8.74 $\pm$ 0.2, 13.62 $\pm$ 0.2, 15.32 $\pm$ 0.2, 16.32 $\pm$ 0.2, 17.56 $\pm$ 0.2, 19.02 $\pm$ 0.2, 19.44 $\pm$ 0.2, 21.28 $\pm$ 0.2, and 25.02 $\pm$ 0.2 in powder X-ray diffraction with CuK α radiation.

31. A crystal of 1-(4-{[4-(2-fluoro-4-{[1-(6-methylpyridin-3-yl)-1H-pyrazol-3-yl]oxy}anilino)-7-methoxyquinazolin-6-yl]oxy}piperidin-1-yl)prop-2-en-1-one, having at least five peaks at diffraction angles (2 θ) selected from 8.14 $\pm$ 0.2, 10.56 $\pm$ 0.2, 13.10 $\pm$ 0.2, 15.16 $\pm$ 0.2, 15.50 $\pm$ 0.2, 15.92 $\pm$ 0.2, 19.30 $\pm$ 0.2, 20.18 $\pm$ 0.2, 23.92 $\pm$ 0.2, and 25.54 $\pm$ 0.2 in powder X-ray diffraction with CuK α radiation.

32. A crystal of 1-(4-{[4-(2-fluoro-4-{[1-(6-methylpyridin-3-yl)-1H-pyrazol-3-yl]oxy}anilino)-7-methoxyquinazolin-6-yl]oxy}piperidin-1-yl)prop-2-en-1-one hydrochloride, having at least five peaks at diffraction angles (2 θ) selected from 5.28 $\pm$ 0.2, 5.98 $\pm$ 0.2, 7.70 $\pm$ 0.2, 8.28 $\pm$ 0.2, 10.64 $\pm$ 0.2, 12.60 $\pm$ 0.2, 13.48 $\pm$ 0.2, 16.68 $\pm$ 0.2, 17.66 $\pm$ 0.2 and 20.80 $\pm$ 0.2 in powder X-ray diffraction with CuK α radiation.

33. A crystal of 1-(4-{[4-(2-fluoro-4-{[1-(6-methylpyridin-3-yl)-1H-pyrazol-3-yl]oxy}anilino)-7-methoxyquinazolin-6-yl]oxy}piperidin-1-yl)prop-2-en-1-one 1,5-naphthalenedisulfonate, having at least five peaks at

diffraction angles (2θ) selected from 8.50 ± 0.2 , 13.98 ± 0.2 , 15.56 ± 0.2 , 16.94 ± 0.2 , 18.28 ± 0.2 , 19.52 ± 0.2 , 20.04 ± 0.2 , 25.16 ± 0.2 , 25.44 ± 0.2 and 26.10 ± 0.2 in powder X-ray diffraction with $\text{CuK}\alpha$ radiation.

34. A crystal of 1-(4-{[4-(2-fluoro-4-{[1-(6-methylpyridin-3-yl)-1H-pyrazol-3-yl]oxy}anilino)-7-methoxyquinazolin-6-yl]oxy}piperidin-1-yl)prop-2-en-1-one citrate, having at least five peaks at diffraction angles (2θ) selected from 5.34 ± 0.2 , 7.32 ± 0.2 , 7.86 ± 0.2 , 8.68 ± 0.2 , 13.56 ± 0.2 , 16.26 ± 0.2 , 17.50 ± 0.2 , 19.36 ± 0.2 , 21.22 ± 0.2 and 24.90 ± 0.2 in powder X-ray diffraction with $\text{CuK}\alpha$ radiation.

35. A crystal of N-tert-butyl-3-{3-fluoro-4-[(7-methoxy-6-{[1-(prop-2-enoyl)piperidin-4-yl]oxy}quinazolin-4-yl)amino]phenoxy}-1H-pyrazole-1-carboxamide methanesulfonate, having at least five peaks at diffraction angles (2θ) selected from 6.72 ± 0.2 , 8.38 ± 0.2 , 11.10 ± 0.2 , 13.62 ± 0.2 , 16.28 ± 0.2 , 17.92 ± 0.2 , 19.02 ± 0.2 , 21.66 ± 0.2 , 22.40 ± 0.2 and 25.64 ± 0.2 in powder X-ray diffraction with $\text{CuK}\alpha$ radiation.

36. A pharmaceutical composition, comprising as an active ingredient a compound or a pharmaceutically acceptable salt thereof according to any one of claims 1

to 22, or a crystal according to any one of claims 23 to 35.

37. An inhibitor of an EGFR tyrosine kinase having an exon 20 insertion mutation and/or a HER2 tyrosine kinase having an exon 20 insertion mutation, comprising as an active ingredient a compound or a pharmaceutically acceptable salt thereof according to any one of claims 1 to 22, or a crystal according to any one of claims 23 to 35.

38. An antitumor agent, comprising as an active ingredient a compound or a pharmaceutically acceptable salt thereof according to any one of claims 1 to 22, or a crystal according to any one of claims 23 to 35.

39. The antitumor agent according to claim 38, wherein the tumor is lung cancer, breast cancer, bladder cancer, or ovarian cancer.

40. The antitumor agent according to claim 38 or 39, wherein the tumor is a tumor having an exon 20 insertion mutation of an EGFR tyrosine kinase and/or an exon 20 insertion mutation of a HER2 tyrosine kinase.

~~41. A method for treating a tumor, comprising administering a compound or a pharmaceutically acceptable~~

~~salt thereof according to any one of claims 1 to 22, or a crystal according to any one of claims 23 to 35.~~

~~42. The method according to claim 41, wherein the tumor is lung cancer, breast cancer, bladder cancer, or ovarian cancer.~~

~~43. The method according to claim 41 or 42, wherein the tumor is a tumor having an exon 20 insertion mutation of an EGFR tyrosine kinase and/or an exon 20 insertion mutation of a HER2 tyrosine kinase.~~

~~44~~41. A compound or a pharmaceutically acceptable salt thereof according to any one of claims 1 to 22, or a crystal according to any one of claims 23 to 35, for the treatment of a tumor.

~~45~~42. The compound or a pharmaceutically acceptable salt thereof, or the crystal according to claim ~~44~~41, wherein the tumor is lung cancer, breast cancer, bladder cancer, or ovarian cancer.

~~46~~43. The compound or a pharmaceutically acceptable salt thereof, or the crystal according to claim ~~44~~41 or

~~45~~42, wherein the tumor is a tumor having an exon 20 insertion mutation of an EGFR tyrosine kinase and/or an exon 20 insertion mutation of a HER2 tyrosine kinase.

~~47~~44. Use of a compound or a pharmaceutically acceptable salt thereof according to any one of claims 1 to 22, or a crystal according to any one of claims 23 to 35, in the manufacture of a pharmaceutical composition for use in treating a tumor.

~~48~~45. Use according to claim ~~47~~ 44, wherein the tumor is lung cancer, breast cancer, bladder cancer, or ovarian cancer.

~~49~~46. Use according to claim ~~47~~ 44 or ~~48~~ 45, wherein the tumor is a tumor having an exon 20 insertion mutation of an EGFR tyrosine kinase and/or an exon 20 insertion mutation of a HER2 tyrosine kinase.