CLAIMS

1. A fusion polypeptide comprising an FGFR3 polypeptide and a BAIAP2L1 polypeptide or TACC3 polypeptide:
wherein the FGFR3 polypeptide is the whole or a part of a wild-type polypeptide consisting of the amino acid sequence of SEQ ID NO: 6 or 7, or the whole or a part of a mutant polypeptide with one or more amino acid substitutions, deletions, or insertions in the wild-type polypeptide;
the BAIAP2L1 polypeptide is the whole or a part of a wild-type polypeptide consisting of the amino acid sequence of SEQ ID NO: 8, or the whole or a part of a mutant polypeptide with one or more amino acid substitutions, deletions, or insertions in the wild-type polypeptide; and
the TACC3 polypeptide is the whole or a part of a wild-type polypeptide consisting of the amino acid sequence of SEQ ID NO: 9, or the whole or a part of a mutant polypeptide with one or more amino acid substitutions, deletions, or insertions in the wild type polypeptide.

2. The fusion polypeptide of claim 1, wherein the FGFR3 polypeptide is a wild-type polypeptide consisting of the amino acid sequence of SEQ ID NO: 6 or 7.

3. The fusion polypeptide of claim 1 or 2, wherein the fusion polypeptide comprises an FGFR3 polypeptide and a BAIAP2L1 polypeptide.

4. The fusion polypeptide of claim 3, wherein the fusion polypeptide consists of the amino acid sequence of SEQ ID NO: 32 or 38.

5. The fusion polypeptide of claim 1 or 2, wherein the fusion polypeptide comprises an FGFR3 polypeptide and a TACC3 polypeptide.

6. The fusion polypeptide of claim 5, wherein the fusion polypeptide consists of the amino acid sequence of SEQ ID NO: 28, 30, 34, or 36.

7. The fusion polypeptide of any one of claims 1 to 5, wherein the fusion polypeptide is derived from bladder cancer or lung cancer.

8. A polynucleotide encoding the fusion polypeptide of any one of claims 1 to 7.

9. The polynucleotide of claim 8, which comprises the nucleotide sequence of SEQ ID NO: 14, 15, or 16.

10. The polynucleotide of claim 9, which comprises the nucleotide sequence of SEQ ID NO: 27, 29, 31, 33, 35, or 37.

11. A vector comprising the polynucleotide of any one of claims 8 to 10.

12. A recombinant cell comprising the vector of claim 11.

13. An antibody or antigen-binding fragment thereof which specifically binds to the fusion polypeptide of any one of claims 1 to 7.

14. A pair of oligonucleotide primers consisting of sense and antisense primers each hybridizing to a polynucleotide encoding the fusion polypeptide of any one of claims 1 to 7 for detecting or amplifying the polynucleotide.

15. An oligonucleotide that binds to an mRNA polynucleotide encoding the fusion polypeptide of any one of claims 1 to 7 and has an activity to inhibit translation of the mRNA polynucleotide into protein.

16. The oligonucleotide of claim 15, which is an siRNA that cleaves the mRNA polypeptide.

17. A pharmaceutical composition comprising the antibody or antigen-binding fragment thereof of claim 13.

18. A pharmaceutical composition comprising the oligonucleotide of claim 15 or 16.

19. A method for detecting a fusion polypeptide that comprises an FGFR3 polypeptide and a BAIAP2L1 polypeptide or TACC3 polypeptide, which comprises the step of detecting the fusion polypeptide in a sample isolated from a subject by using an antibody or antigen-binding fragment thereof that binds to the fusion polypeptide of any one of claims 1 to 7.

20. A method for detecting a polynucleotide encoding a fusion polypeptide that comprises an FGFR3 polypeptide and a BAIAP2L1 polypeptide or TACC3 polypeptide, which comprises the step of detecting a polynucleotide encoding the fusion polypeptide in a sample isolated from a subject by using a pair of oligonucleotide primers consisting of sense and antisense primers each hybridizing to a polynucleotide encoding the fusion polypeptide of any one of claims 1 to 7 for

detecting or amplifying the polynucleotide.

21. A kit for detecting a polynucleotide encoding a fusion polypeptide that comprises an FGFR3 polypeptide and a BAIAP2L1 polypeptide or TACC3 polypeptide, which comprises a pair of oligonucleotide primers consisting of sense and antisense primers each hybridizing to a polynucleotide encoding the fusion polypeptide of any one of claims 1 to 7 for detecting or amplifying the polynucleotide.

22. A kit for detecting a fusion polypeptide that comprises an FGFR3 polypeptide and a BAIAP2L1 polypeptide or TACC3 polypeptide, which comprises an antibody or antigen-binding fragment thereof that binds to the fusion polypeptide of any one of claims 1 to 7.

23. A method for testing cancer susceptibility of a subject, whether a subject is affected with cancer, or whether cancer has progressed in a subject by determining the presence or absence of the fusion polypeptide of any one of claims 1 to 7 in a sample isolated from the subject, wherein the method is based on the criterion that a subject is more likely to develop cancer, is affected with cancer, or has progressed cancer when the fusion polypeptide is detected.

24. A method for testing cancer susceptibility of a subject, whether a subject is affected with cancer, or whether cancer has progressed in a subject by determining the presence or absence of a polynucleotide encoding the fusion polypeptide of any one of claims 1 to 7 in a sample isolated from the subject, wherein the method is based on the criterion that a subject is more likely to develop cancer, is affected with cancer, or has progressed cancer when the polynucleotide encoding the fusion polypeptide is detected.

25. The method of claim 23 or 24, wherein the cancer is bladder cancer, brain tumor, head and neck squamous cell carcinoma, lung cancer, lung adenocarcinoma, lung squamous cell carcinoma, skin melanoma, esophageal cancer, gastric cancer, or liver cancer.

26. A method for selecting a patient to which an anticancer agent comprising a compound having FGFR inhibitory activity or a pharmaceutically acceptable salt thereof is applicable, which comprises the steps of:

(a) determining the presence or absence of the fusion polypeptide of any one of claims 1 to 7 in a sample isolated from a subject; and

(b) selecting a patient confirmed to have the fusion polypeptide as a patient to which the anticancer agent is applicable.

27. A method for selecting a patient to which an anticancer agent comprising a compound having FGFR inhibitory activity or a pharmaceutically acceptable salt thereof is applicable, which comprises the steps of:

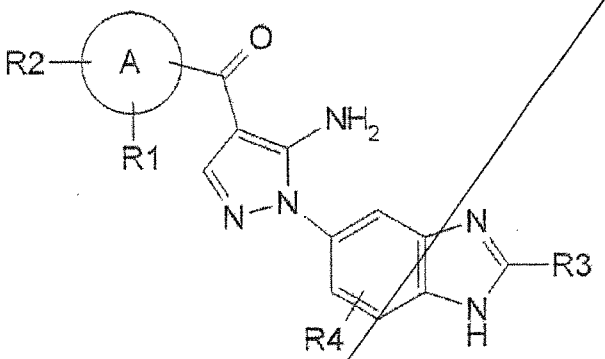
(a) determining the presence or absence of a polynucleotide encoding the fusion polypeptide of any one of claims 1 to 7 in a sample isolated from a subject; and

(b) selecting a patient confirmed to have a polynucleotide encoding the fusion polypeptide as a patient to which the anticancer agent is applicable.

28. The method of claim 26 or 27, wherein the cancer is bladder cancer, brain tumor, head and neck squamous cell carcinoma, lung cancer, lung adenocarcinoma, lung squamous cell carcinoma, skin melanoma, esophageal cancer, gastric cancer, or liver cancer.

29. The method of any one of claims 26 to 28, wherein the compound having FGFR inhibitory activity or a pharmaceutically acceptable salt thereof is any one of the compounds or a pharmaceutically acceptable salt thereof represented by:

[Compound 1]



(I)

wherein R_1, R_2, R_3, and R_4 each independently represents the group listed below:

R_1 represents hydrogen, hydroxy, halogen, cyano, nitro, C_{1-4} haloalkyl, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-7} cycloalkyl, C_{6-10} aryl C_{1-4} alkyl, $-OR_5$, $-NR_6R_7$, $-(CR_8R_9)_nZ_1$, $-C(O)NR_{12}R_{13}$, $-SR_{14}$, $-SOR_{15}$, $-SO_2R_{16}$, $-NR_{17}SO_2R_{18}$, COOH, C_{6-10} aryl which is optionally substituted by one or more groups independently selected from group P, 5- to 10-membered heteroaryl or 3- to 10-membered heterocyclyl which is optionally substituted by one or more groups independently selected from group Q, $-COR_{19}$, $-COOR_{20}$, $-OC(O)R_{21}$, $-NR_{22}C(O)R_{23}$, $-NR_{24}C(S)R_{25}$, $-C(S)NR_{26}R_{27}$, $-SO_2NR_{28}R_{29}$, $-OSO_2R_{30}$, $-SO_3R_{31}$, or $-Si(R_{32})_3$;

R_2 represents hydrogen, hydroxy, halogen, cyano, nitro, C_{1-4} haloalkyl, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-7} cycloalkyl, C_{6-10} aryl C_{1-4} alkyl, $-OR_5$, $-NR_6R_7$, $-(CR_8R_9)_nZ_1$, $-C(O)NR_{12}R_{13}$, -

SR_{14}, $-SOR_{15}$, $-SO_2R_{16}$, $-NR_{17}SO_2R_{18}$, COOH, C_{6-10} aryl which is optionally substituted by one or more groups independently selected from group P, 5- to 10-membered heteroaryl or 3- to 10-membered heterocyclyl which is optionally substituted by one or more groups independently selected from group Q, $-COR_{19}$, $-COOR_{20}$, $-OC(O)R_{21}$, $-NR_{22}C(O)R_{23}$, $-NR_{24}C(S)R_{25}$, $-C(S)NR_{26}R_{27}$, $-SO_2NR_{28}R_{29}$, $-OSO_2R_{30}$, $-SO_3R_{31}$, or $-Si(R_{32})_3$; or

R_1 and R_2, together with an atom linked thereto, form 3- to 10-membered heterocyclyl or 5- to 10-membered heteroaryl, wherein the heterocyclyl or heteroaryl is optionally substituted by halogen;

R_3 represents hydrogen, C_{1-5} alkyl, C_{6-10} aryl C_{1-6} alkyl, or C_{1-4} haloalkyl;

R_4 represents hydrogen, halogen, C_{1-3} alkyl, C_{1-4} haloalkyl, hydroxy, cyano, nitro, C_{1-4} alkoxy, $-(CH_2)_nZ_1$, $-NR_6R_7$, $-OR_5$, $-C(O)NR_{12}R_{13}$, $-SR_{14}$, $-SOR_{15}$, $-SO_2R_{16}$, $NR_{17}SO_2R_{18}$, COOH, $-COR_{19}$, $-COOR_{20}$, $-OC(O)R_{21}$, $-NR_{22}C(O)R_{23}$, $-NR_{24}C(S)R_{25}$, $-C(S)NR_{26}R_{27}$, $-SO_2NR_{28}R_{29}$, $-OSO_2R_{30}$, $-SO_3R_{31}$, or $-Si(R_{32})_3$;

A represents a 5- to 10-membered heteroaryl ring or C_{6-10} aryl ring;

R_5 represents C_{1-5} alkyl, C_{3-7} cycloalkyl, C_{3-7} cycloalkyl C_{1-3} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-4} haloalkyl, C_{1-3} alkoxy C_{1-4} alkyl, C_{1-3} alkoxy C_{1-4} alkoxy C_{1-4} alkyl, C_{1-4} aminoalkyl, C_{1-4} alkylamino C_{1-4} alkyl, di(C_{1-4} alkyl)amino C_{1-4} alkyl, C_{6-10} aryl, C_{6-10} aryl C_{1-3} alkyl, or 3- to 10-membered heterocyclyl C_{1-3} alkyl, 3- to 10-membered heterocyclyl, 5- to 10-membered heteroaryl, 5- to 10-membered heteroaryl C_{1-3} alkyl, C_{1-6} monohydroxy alkyl, C_{1-6} dihydroxy alkyl, or C_{1-6} trihydroxy alkyl which is optionally substituted by one or more groups independently selected from group Q;

R_6 and R_7, which can be the same or different, each represents hydrogen, C_{1-4} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-4} haloalkyl, C_{1-3} alkoxy C_{1-4} alkyl, C_{6-10} aryl C_{1-3} alkyl, 3- to 10-membered heterocyclyl C_{1-3} alkyl, 5- to 10-membered heteroaryl C_{1-3} alkyl, C_{1-6} monohydroxy alkyl, C_{1-6} dihydroxy alkyl, C_{1-6} trihydroxy alkyl, 3- to 10-membered heterocyclyl, C_{1-4} aminoalkyl, C_{1-4} alkylamino C_{1-4} alkyl, di(C_{1-4} alkyl)amino C_{1-4} alkyl, or cyano(C_{1-3} alkyl); or alternatively R_6 and R_7, together with a nitrogen atom linked thereto, form 3- to 10-membered heterocyclyl or 5- to 10-membered heteroaryl;

n represents 1 to 3;

R_8 and R_9, which can be the same or different, each represents hydrogen, C_{1-4} alkyl, or halogen; or alternatively R_8 and R_9, together with a carbon atom linked thereto, form a cycloaliphatic ring;

Z_1 represents hydrogen, $NR_{10}R_{11}$, -OH, or 3- to 10-membered heterocyclyl or 5- to 10-membered heteroaryl which is optionally substituted by one or more groups independently selected from group Q;

R_{10} and R_{11}, which can be the same or different, each represents C_{1-4} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-4} haloalkyl, C_{1-3} alkoxy C_{1-4} alkyl, cyano(C_{1-3} alkyl), or C_{1-3} alkylsulfonyl C_{1-4} alkyl;

or alternatively R_{10} and R_{11}, together with a nitrogen atom linked thereto, form 3- to 10-membered heterocyclyl or 5- to 10-membered heteroaryl;

R_{12} and R_{13}, which can be the same or different, each represents hydrogen, C_{1-4} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-4} haloalkyl, C_{1-3} alkoxy C_{1-4} alkyl, C_{6-10} aryl, 5- to 10-membered heteroaryl, 3- to 10-membered heterocyclyl, C_{6-10} aryl C_{1-4} alkyl, 3- to 10-membered heterocyclyl C_{1-3} alkyl, 5- to 10-membered heteroaryl C_{1-3} alkyl, cyano(C_{1-3} alkyl), C_{1-3} alkylsulfonyl C_{1-4} alkyl, 3- to 10-membered cycloaliphatic ring, 5- to 10-membered heteroaryl, or 3- to 10-membered heterocyclyl; or alternatively R_{12} and R_{13}, together with a nitrogen atom linked thereto, form 3- to 10-membered heterocyclyl or 5- to 10-membered heteroaryl which is optionally substituted by one or more groups independently selected from group Q;

R_{14} represents C_{1-4} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-4} haloalkyl, C_{6-10} aryl which is optionally substituted by one or more groups independently selected from group P, or 5- to 10-membered heteroaryl or 3- to 10-membered heterocyclyl which is optionally substituted by one or more groups independently selected from group Q;

R_{15} represents C_{1-4} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-4} haloalkyl, C_{6-10} aryl which is optionally substituted by one or more groups independently selected from group P, or 5- to 10-membered heteroaryl or 3- to 10-membered heterocyclyl which is optionally substituted by one or more groups independently selected from group Q;

R_{16} represents C_{1-4} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-4} haloalkyl, C_{6-10} aryl which is optionally substituted by one or more groups independently selected from group P, or 5- to 10-membered heteroaryl or 3- to 10-membered heterocyclyl which is optionally substituted by one or more groups independently selected from group Q;

R_{17} represents hydrogen or C_{1-4} alkyl;

R_{18} represents C_{1-4} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-4} haloalkyl, C_{6-10} aryl which is optionally substituted by one or more groups independently selected from group P, or 5- to 10-membered heteroaryl or 3- to 10-membered heterocyclyl which is optionally substituted by one or more groups independently selected from group Q;

R_{19} represents hydrogen, C_{1-4} alkyl, C_{3-7} cycloalkyl, C_{1-4} haloalkyl, C_{6-10} aryl, or 5- to 10-membered heteroaryl or 3- to 10-membered heterocyclyl which is optionally substituted by one or more groups independently selected from group Q;

R_{20} represents C_{1-4} alkyl, C_{3-7} cycloalkyl, C_{1-4} haloalkyl, C_{6-10} aryl, 5- to 10-membered heteroaryl, or 3- to 10-membered heterocyclyl;

R_{21} represents C_{1-4} alkyl, C_{3-7} cycloalkyl, C_{1-4} haloalkyl, C_{6-10} aryl, 5- to 10-membered heteroaryl, or 3- to 10-membered heterocyclyl;

R_{22} represents hydrogen, C_{1-4} alkyl, or C_{1-4} haloalkyl;

R_{23} represents hydrogen, C_{1-4} alkyl, C_{3-7} cycloalkyl, C_{1-4} haloalkyl, C_{6-10} aryl, 5- to 10-membered

heteroaryl, or 3- to 10-membered heterocyclyl;

R_{24} represents hydrogen, C_{1-4} alkyl, or C_{1-4} haloalkyl;

R_{25} represents C_{1-4} alkyl, C_{3-7} cycloalkyl, C_{1-4} haloalkyl, C_{6-10} aryl, 5- to 10-membered heteroaryl, or 3- to 10-membered heterocyclyl;

R_{26} and R_{27}, which can be the same or different, each represents hydrogen, C_{1-4} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-4} haloalkyl, C_{1-3} alkoxyl C_{1-4} alkyl, C_{6-10} aryl, 5- to 10-membered heteroaryl, 3- to 10-membered heterocyclyl, C_{6-10} aryl C_{1-4} alkyl, 3- to 10-membered heterocyclyl C_{1-3} alkyl, 5- to 10-membered heteroaryl C_{1-3} alkyl, cyano(C_{1-3} alkyl), C_{1-3} alkylsulfonyl C_{1-4} alkyl, or 3- to 10-membered cycloaliphatic ring; or alternatively R_{26} and R_{27}, together with a nitrogen atom linked thereto, form 3- to 10-membered heterocyclyl or 5- to 10-membered heteroaryl;

R_{28} and R_{29}, which can be the same or different, each represents hydrogen, C_{1-4} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-4} haloalkyl, C_{1-3} alkoxyl C_{1-4} alkyl, C_{6-10} aryl, 5- to 10-membered heteroaryl, 3- to 10-membered heterocyclyl, C_{6-10} aryl C_{1-4} alkyl, 3- to 10-membered heterocyclyl C_{1-3} alkyl, 5- to 10-membered heteroaryl C_{1-3} alkyl, cyano(C_{1-3} alkyl), C_{1-3} alkylsulfonyl C_{1-4} alkyl, or 3- to 10-membered cycloaliphatic ring; or alternatively R_{28} and R_{29}, together with a nitrogen atom linked thereto, form 3- to 10-membered heterocyclyl or 5- to 10-membered heteroaryl;

R_{30} represents C_{1-4} alkyl, C_{3-7} cycloalkyl, C_{1-4} haloalkyl, C_{6-10} aryl, 5- to 10-membered heteroaryl, or 3- to 10-membered heterocyclyl;

R_{31} represents C_{1-4} alkyl, C_{3-7} cycloalkyl, C_{1-4} haloalkyl, C_{6-10} aryl, 5- to 10-membered heteroaryl, or 3- to 10-membered heterocyclyl;

R_{32} represents C_{1-4} alkyl or C_{6-10} aryl;

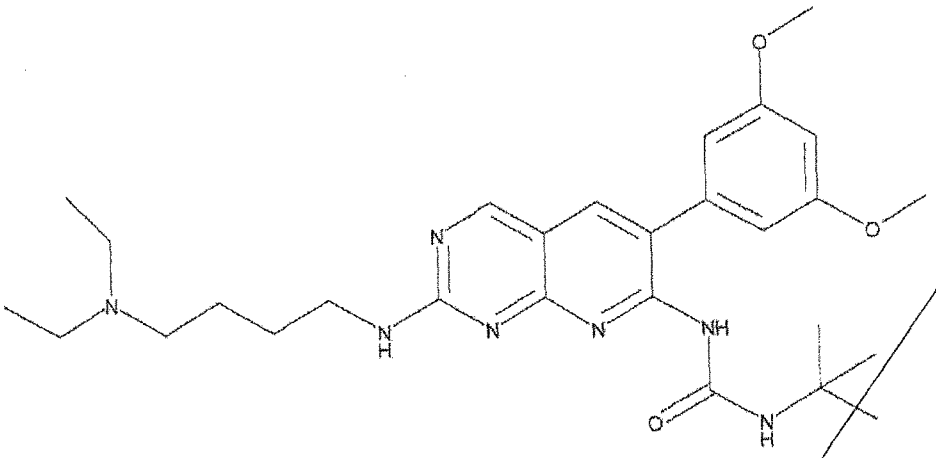
<group P>

halogen, C_{1-4} alkyl, C_{1-4} haloalkyl, -OH, C_{1-3} alkoxy, C_{1-3} haloalkoxy, 3- to 10-membered heterocyclylamino, $-SO_2R_{16}$, -CN, $-NO_2$, and 3- to 10-membered heterocyclyl;

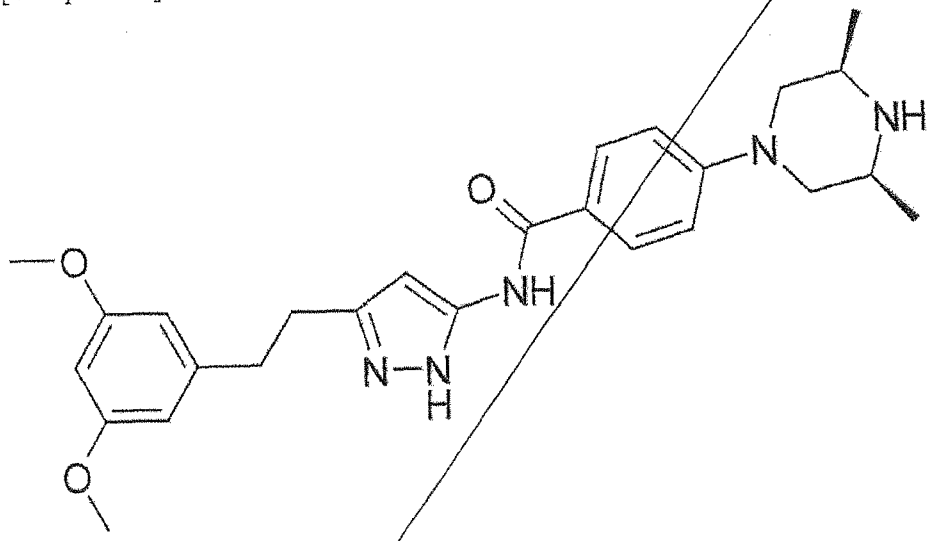
<group Q>

halogen, C_{1-4} alkyl, C_{1-4} haloalkyl, -OH, C_{1-3} alkoxy, C_{1-6} monohydroxy alkyl, C_{1-6} dihydroxy alkyl, C_{1-6} trihydroxy alkyl, 3- to 10-membered heterocyclyl amine, $-SO_2R_{16}$, -CN, $-NO_2$, C_{3-7} cycloalkyl, $-COR_{19}$, and 3- to 10-membered heterocyclyl which is optionally substituted by C_{1-4} alkyl.

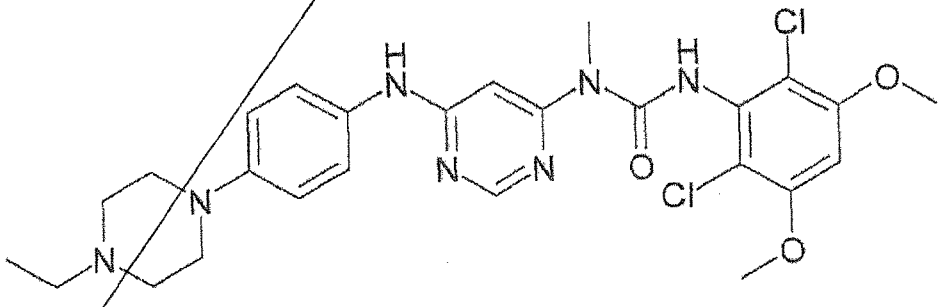
[Compound 2]



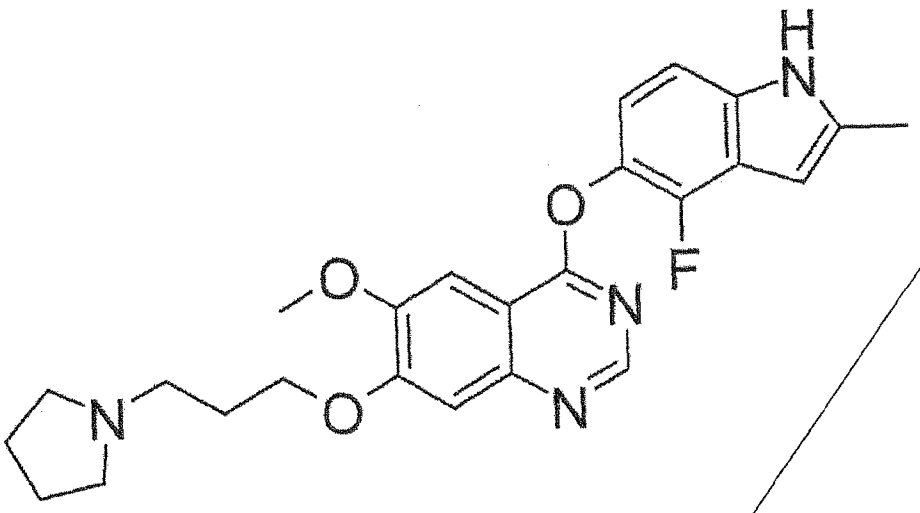
[Compound 3]



[Compound 4]

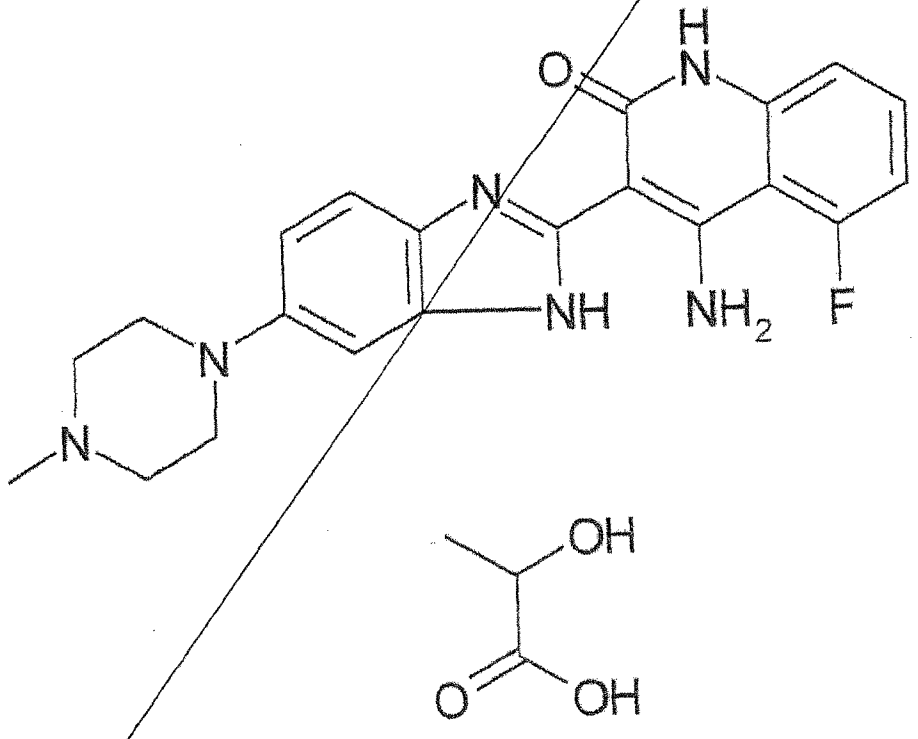


[Compound 5]



, or

[Compound 6]



30. The method of claim 29, wherein the compound having FGFR inhibitory activity or a

pharmaceutically acceptable salt thereof is a compound of formula (I), wherein A is indole, and R_3 and R_4 are both hydrogen, or a pharmaceutically acceptable salt thereof.

31. A pharmaceutical composition for cancer treatment, which comprises a compound having FGFR inhibitory activity or a pharmaceutically acceptable salt thereof and is used in such a manner that the compound or a pharmaceutically acceptable salt thereof is administered to a patient who expresses the fusion polypeptide of any one of claims 1 to 7 or has a polynucleotide that encodes the fusion polypeptide.

32. The pharmaceutical composition of claim 31 for cancer treatment, wherein the patient is selected by the method of any one of claims 26 to 30.

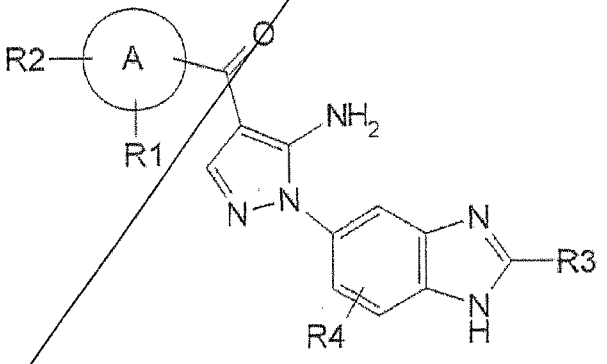
33. The pharmaceutical composition of claim 31 or 32 for cancer treatment, wherein the cancer is bladder cancer, brain tumor, head and neck squamous cell carcinoma, lung cancer, lung adenocarcinoma, lung squamous cell carcinoma, skin melanoma, esophageal cancer, gastric cancer, or liver cancer.

34. The pharmaceutical composition of claim 31 or 32 for cancer treatment, wherein the cancer is bladder cancer.

35. The pharmaceutical composition of claim 34 for cancer treatment, wherein the bladder cancer is classified as stage 3 or later according to TNM classification.

36. The pharmaceutical composition of any one of claims 31 to 35 for cancer treatment, wherein the compound having FGFR inhibitory activity or a pharmaceutically acceptable salt thereof is any one of the compounds or a pharmaceutically acceptable salt thereof represented by:

[Compound 1]



(I)

wherein R_1, R_2, R_3, and R_4 each independently represents the group listed below:

R_1 represents hydrogen, hydroxy, halogen, cyano, nitro, C_{1-4} haloalkyl, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-7} cycloalkyl, C_{6-10} aryl C_{1-4} alkyl, $-OR_5$, $-NR_6R_7$, $-(CR_8R_9)_nZ_1$, $-C(O)NR_{12}R_{13}$, $-SR_{14}$, $-SOR_{15}$, $-SO_2R_{16}$, $-NR_{17}SO_2R_{18}$, COOH, C_{6-10} aryl which is optionally substituted by one or more groups independently selected from group P, 5- to 10-membered heteroaryl or 3- to 10-membered heterocyclyl which is optionally substituted by one or more groups independently selected from group Q, $-COR_{19}$, $-COOR_{20}$, $-OC(O)R_{21}$, $-NR_{22}C(O)R_{23}$, $-NR_{24}C(S)R_{25}$, $-C(S)NR_{26}R_{27}$, $-SO_2NR_{28}R_{29}$, $-OSO_2R_{30}$, $-SO_3R_{31}$, or $-Si(R_{32})_3$;

R_2 represents hydrogen, hydroxy, halogen, cyano, nitro, C_{1-4} haloalkyl, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-7} cycloalkyl, C_{6-10} aryl C_{1-4} alkyl, $-OR_5$, $-NR_6R_7$, $-(CR_8R_9)_nZ_1$, $-C(O)NR_{12}R_{13}$, $-SR_{14}$, $-SOR_{15}$, $-SO_2R_{16}$, $-NR_{17}SO_2R_{18}$, COOH, C_{6-10} aryl which is optionally substituted by one or more groups independently selected from group P, 5- to 10-membered heteroaryl or 3- to 10-membered heterocyclyl which is optionally substituted by one or more groups independently selected from group Q, $-COR_{19}$, $-COOR_{20}$, $-OC(O)R_{21}$, $-NR_{22}C(O)R_{23}$, $-NR_{24}C(S)R_{25}$, $-C(S)NR_{26}R_{27}$, $-SO_2NR_{28}R_{29}$, $-OSO_2R_{30}$, $-SO_3R_{31}$, or $-Si(R_{32})_3$; or

R_1 and R_2, together with an atom linked thereto, form 3- to 10-membered heterocyclyl or 5- to 10-membered heteroaryl, wherein the heterocyclyl or heteroaryl is optionally substituted by halogen;

R_3 represents hydrogen, C_{1-5} alkyl, C_{6-10} aryl C_{1-6} alkyl, or C_{1-4} haloalkyl;

R_4 represents hydrogen, halogen, C_{1-3} alkyl, C_{1-4} haloalkyl, hydroxy, cyano, nitro, C_{1-4} alkoxy, $-(CH_2)_nZ_1$, $-NR_6R_7$, $-OR_5$, $-C(O)NR_{12}R_{13}$, $-SR_{14}$, $-SOR_{15}$, $-SO_2R_{16}$, $NR_{17}SO_2R_{18}$, COOH, $-COR_{19}$, $-COOR_{20}$, $-OC(O)R_{21}$, $-NR_{22}C(O)R_{23}$, $-NR_{24}C(S)R_{25}$, $-C(S)NR_{26}R_{27}$, $-SO_2NR_{28}R_{29}$, $-OSO_2R_{30}$, $-SO_3R_{31}$, or $-Si(R_{32})_3$;

A represents a 5- to 10-membered heteroaryl ring or C_{6-10} aryl ring;

R_5 represents C_{1-5} alkyl, C_{3-7} cycloalkyl, C_{3-7} cycloalkyl C_{1-3} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-4} haloalkyl, C_{1-3} alkoxy C_{1-4} alkyl, C_{1-3} alkoxy C_{1-4} alkoxy C_{1-4} alkyl, C_{1-4} aminoalkyl, C_{1-4} alkylamino C_{1-4} alkyl, di(C_{1-4} alkyl)amino C_{1-4} alkyl, C_{6-10} aryl, C_{6-10} aryl C_{1-3} alkyl, or 3- to 10-membered heterocyclyl C_{1-3} alkyl, 3- to 10-membered heterocyclyl, 5- to 10-membered heteroaryl, 5- to 10-membered heteroaryl C_{1-3} alkyl, C_{1-6} monohydroxy alkyl, C_{1-6} dihydroxy alkyl, or C_{1-6} trihydroxy alkyl which is optionally substituted by one or more groups independently selected from group Q;

R_6 and R_7, which can be the same or different, each represents hydrogen, C_{1-4} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-4} haloalkyl, C_{1-3} alkoxy C_{1-4} alkyl, C_{6-10} aryl C_{1-3} alkyl, 3- to 10-membered heterocyclyl C_{1-3} alkyl, 5- to 10-membered heteroaryl C_{1-3} alkyl, C_{1-6} monohydroxy alkyl, C_{1-6} dihydroxy alkyl, C_{1-6} trihydroxy alkyl, 3- to 10-membered heterocyclyl, C_{1-4} aminoalkyl, C_{1-4} alkylamino C_{1-4} alkyl, di(C_{1-4} alkyl)amino C_{1-4} alkyl, or cyano(C_{1-3} alkyl); or alternatively R_6 and

R_7, together with a nitrogen atom linked thereto, form 3- to 10-membered heterocyclyl or 5- to 10-membered heteroaryl;

n represents 1 to 3;

R_8 and R_9, which can be the same or different, each represents hydrogen, C_{1-4} alkyl, or halogen; or alternatively R_8 and R_9, together with a carbon atom linked thereto, form a cycloaliphatic ring;

Z_1 represents hydrogen, $NR_{10}R_{11}$, -OH, or 3- to 10-membered heterocyclyl or 5- to 10-membered heteroaryl which is optionally substituted by one or more groups independently selected from group Q;

R_{10} and R_{11}, which can be the same or different, each represents C_{1-4} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-4} haloalkyl, C_{1-3} alkoxy C_{1-4} alkyl, cyano(C_{1-3} alkyl), or C_{1-3} alkylsulfonyl C_{1-4} alkyl; or alternatively R_{10} and R_{11}, together with a nitrogen atom linked thereto, form 3- to 10-membered heterocyclyl or 5- to 10-membered heteroaryl;

R_{12} and R_{13}, which can be the same or different, each represents hydrogen, C_{1-4} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-4} haloalkyl, C_{1-3} alkoxy C_{1-4} alkyl, C_{6-10} aryl, 5- to 10-membered heteroaryl, 3- to 10-membered heterocyclyl, C_{6-10} aryl C_{1-4} alkyl, 3- to 10-membered heterocyclyl C_{1-3} alkyl, 5- to 10-membered heteroaryl C_{1-3} alkyl, cyano(C_{1-3} alkyl), C_{1-3} alkylsulfonyl C_{1-4} alkyl, 3- to 10-membered cycloaliphatic ring, 5- to 10-membered heteroaryl, or 3- to 10-membered heterocyclyl; or alternatively R_{12} and R_{13}, together with a nitrogen atom linked thereto, form 3- to 10-membered heterocyclyl or 5- to 10-membered heteroaryl which is optionally substituted by one or more groups independently selected from group Q;

R_{14} represents C_{1-4} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-4} haloalkyl, C_{6-10} aryl which is optionally substituted by one or more groups independently selected from group P, or 5- to 10-membered heteroaryl or 3- to 10-membered heterocyclyl which is optionally substituted by one or more groups independently selected from group Q;

R_{15} represents C_{1-4} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-4} haloalkyl, C_{6-10} aryl which is optionally substituted by one or more groups independently selected from group P, or 5- to 10-membered heteroaryl or 3- to 10-membered heterocyclyl which is optionally substituted by one or more groups independently selected from group Q;

R_{16} represents C_{1-4} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-4} haloalkyl, C_{6-10} aryl which is optionally substituted by one or more groups independently selected from group P, or 5- to 10-membered heteroaryl or 3- to 10-membered heterocyclyl which is optionally substituted by one or more groups independently selected from group Q;

R_{17} represents hydrogen or C_{1-4} alkyl;

R_{18} represents C_{1-4} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-4} haloalkyl, C_{6-10} aryl which is optionally substituted by one or more groups independently selected from group P, or 5- to 10-membered heteroaryl or 3- to 10-membered heterocyclyl which is optionally substituted by one or more

groups independently selected from group Q;

R_{19} represents hydrogen, C_{1-4} alkyl, C_{3-7} cycloalkyl, C_{1-4} haloalkyl, C_{6-10} aryl, or 5- to 10-membered heteroaryl or 3- to 10-membered heterocyclyl which is optionally substituted by one or more groups independently selected from group Q;

R_{20} represents C_{1-4} alkyl, C_{3-7} cycloalkyl, C_{1-4} haloalkyl, C_{6-10} aryl, 5- to 10-membered heteroaryl, or 3- to 10-membered heterocyclyl;

R_{21} represents C_{1-4} alkyl, C_{3-7} cycloalkyl, C_{1-4} haloalkyl, C_{6-10} aryl, 5- to 10-membered heteroaryl, or 3- to 10-membered heterocyclyl;

R_{22} represents hydrogen, C_{1-4} alkyl, or C_{1-4} haloalkyl;

R_{23} represents hydrogen, C_{1-4} alkyl, C_{3-7} cycloalkyl, C_{1-4} haloalkyl, C_{6-10} aryl, 5- to 10-membered heteroaryl, or 3- to 10-membered heterocyclyl;

R_{24} represents hydrogen, C_{1-4} alkyl, or C_{1-4} haloalkyl;

R_{25} represents C_{1-4} alkyl, C_{3-7} cycloalkyl, C_{1-4} haloalkyl, C_{6-10} aryl, 5- to 10-membered heteroaryl, or 3- to 10-membered heterocyclyl;

R_{26} and R_{27}, which can be the same or different, each represents hydrogen, C_{1-4} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-4} haloalkyl, C_{1-3} alkoxyl C_{1-4} alkyl, C_{6-10} aryl, 5- to 10-membered heteroaryl, 3- to 10-membered heterocyclyl, C_{6-10} aryl C_{1-4} alkyl, 3- to 10-membered heterocyclyl C_{1-3} alkyl, 5- to 10-membered heteroaryl C_{1-3} alkyl, cyano(C_{1-3} alkyl), C_{1-3} alkylsulfonyl C_{1-4} alkyl, or 3- to 10-membered cycloaliphatic ring; or alternatively R_{26} and R_{27}, together with a nitrogen atom linked thereto, form 3- to 10-membered heterocyclyl or 5- to 10-membered heteroaryl;

R_{28} and R_{29}, which can be the same or different, each represents hydrogen, C_{1-4} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-4} haloalkyl, C_{1-3} alkoxyl C_{1-4} alkyl, C_{6-10} aryl, 5- to 10-membered heteroaryl, 3- to 10-membered heterocyclyl, C_{6-10} aryl C_{1-4} alkyl, 3- to 10-membered heterocyclyl C_{1-3} alkyl, 5- to 10-membered heteroaryl C_{1-3} alkyl, cyano(C_{1-3} alkyl), C_{1-3} alkylsulfonyl C_{1-4} alkyl, or 3- to 10-membered cycloaliphatic ring; or alternatively R_{28} and R_{29}, together with a nitrogen atom linked thereto, form 3- to 10-membered heterocyclyl or 5- to 10-membered heteroaryl;

R_{30} represents C_{1-4} alkyl, C_{3-7} cycloalkyl, C_{1-4} haloalkyl, C_{6-10} aryl, 5- to 10-membered heteroaryl, or 3- to 10-membered heterocyclyl;

R_{31} represents C_{1-4} alkyl, C_{3-7} cycloalkyl, C_{1-4} haloalkyl, C_{6-10} aryl, 5- to 10-membered heteroaryl, or 3- to 10-membered heterocyclyl;

R_{32} represents C_{1-4} alkyl or C_{6-10} aryl;

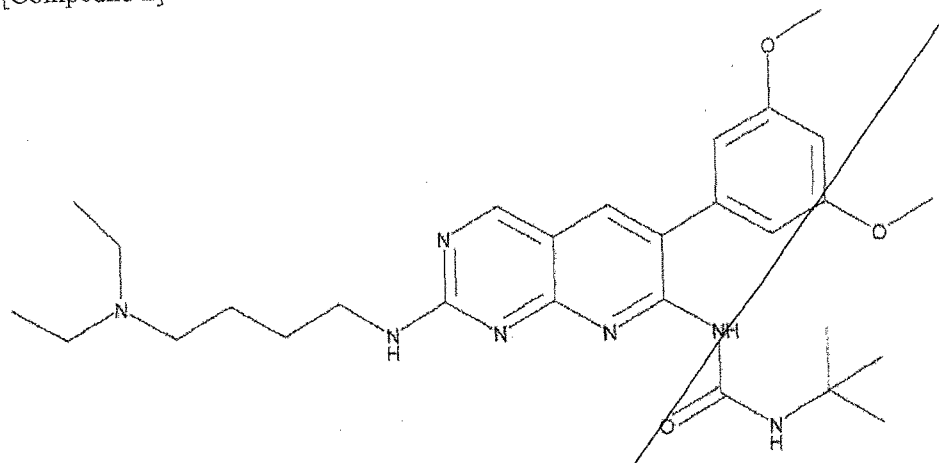
<group P>

halogen, C_{1-4} alkyl, C_{1-4} haloalkyl, -OH, C_{1-3} alkoxy, C_{1-3} haloalkoxy, 3- to 10-membered heterocyclylamino, $-SO_2R_{16}$, -CN, $-NO_2$, and 3- to 10-membered heterocyclyl;

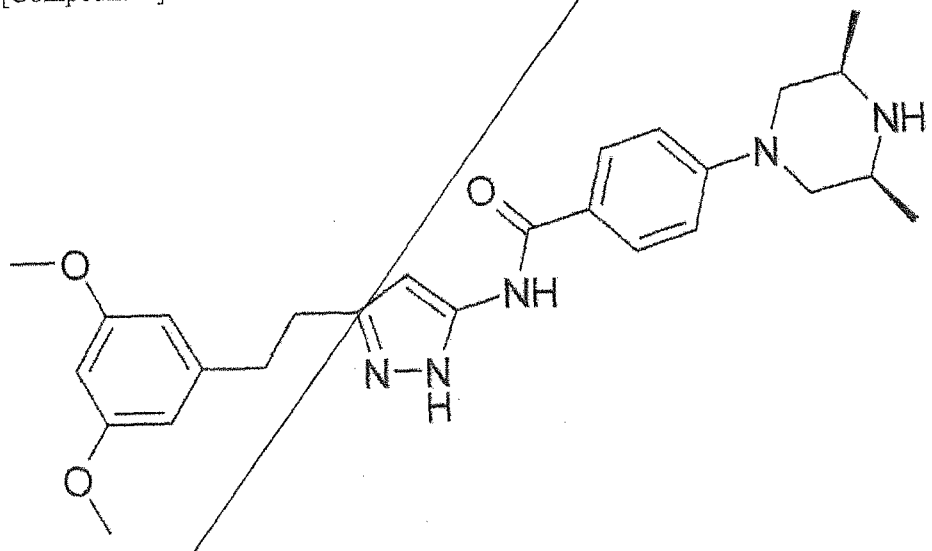
<group Q>

halogen, C_{1-4} alkyl, C_{1-4} haloalkyl, -OH, C_{1-3} alkoxy, C_{1-6} monohydroxy alkyl, C_{1-6} dihydroxy alkyl, C_{1-6} trihydroxy alkyl, 3- to 10-membered heterocyclyl amine, $-SO_2R_{16}$, -CN, $-NO_2$, C_{3-7} cycloalkyl, $-COR_{19}$, and 3- to 10-membered heterocyclyl which is optionally substituted by C_{1-4} alkyl.

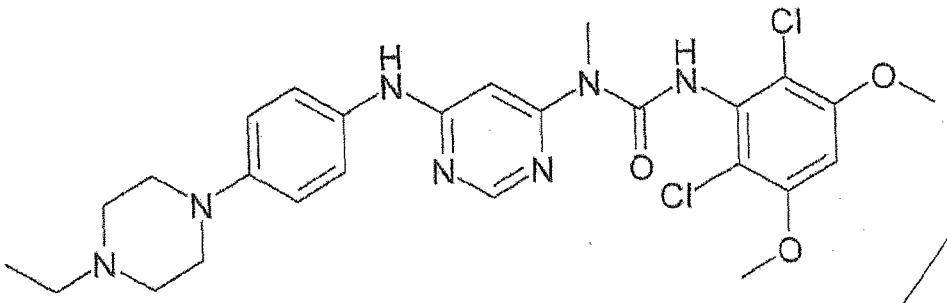
[Compound 2]



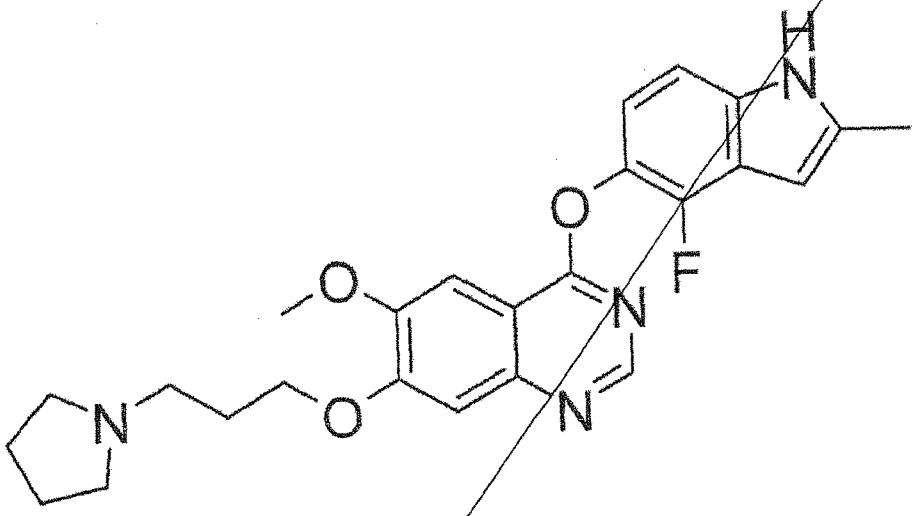
[Compound 3]



[Compound 4]

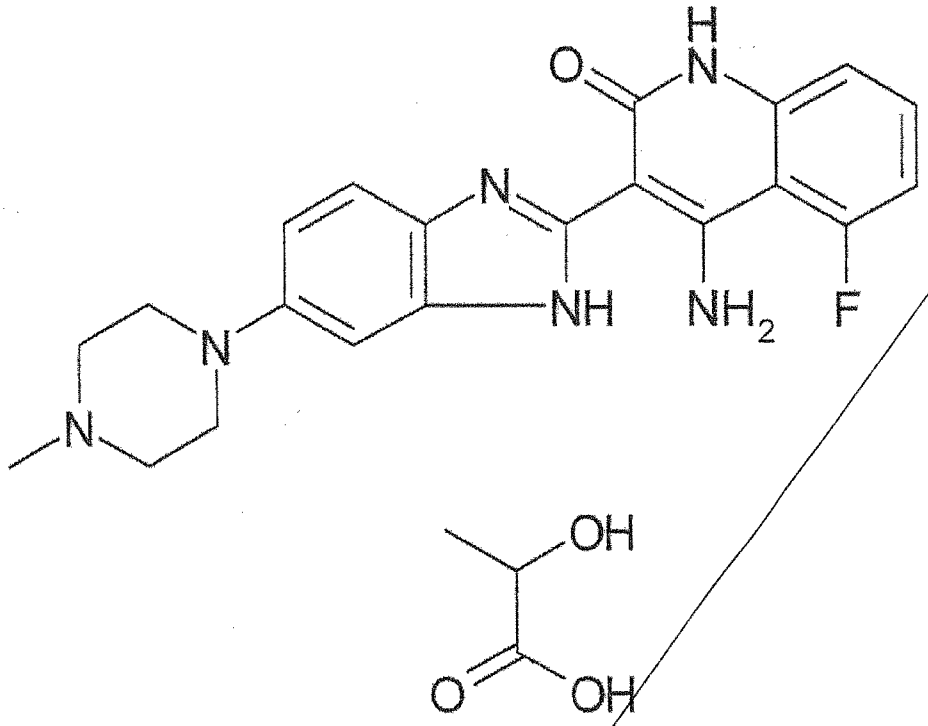


[Compound 5]



, or

[Compound 6]



37. The pharmaceutical composition of claim 36 for cancer treatment, wherein the compound having FGFR inhibitory activity or a pharmaceutically acceptable salt thereof is a compound of formula (I), wherein A is indole, and R_3 and R_4 are both hydrogen, or a pharmaceutically acceptable salt thereof.

38. A method for treating or preventing cancer, comprising the step of administering an effective amount of a compound having FGFR inhibitory activity or a pharmaceutically acceptable salt thereof to a cancer patient expressing the fusion polypeptide of any one of claims 1 to 7 or carrying a polynucleotide encoding the fusion polypeptide.

39. The method of claim 38, wherein the patient is selected by the method of any one of claims 26 to 30.

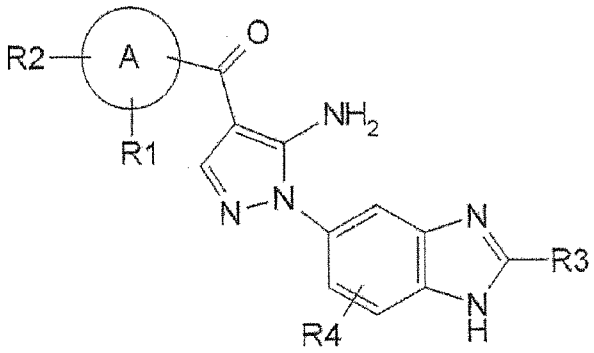
40. The method of claim 38 or 39, wherein the cancer is bladder cancer, brain tumor, head and neck squamous cell carcinoma, lung cancer, lung adenocarcinoma, lung squamous cell carcinoma, skin melanoma, esophageal cancer, gastric cancer, or liver cancer.

41. The method of claim 38 or 39, wherein the cancer is bladder cancer.

42. The method of claim 41, wherein the bladder cancer is classified as stage 3 or later according to TNM classification.

43. The method of any one of claims 38 to 42, wherein the compound having FGFR inhibitory activity or a pharmaceutically acceptable salt thereof is any one of the compounds or a pharmaceutically acceptable salt thereof represented by:

[Compound 1]



(I)

wherein R_1, R_2, R_3, and R_4 each independently represents the group listed below:

R_1 represents hydrogen, hydroxy, halogen, cyano, nitro, C_{1-4} haloalkyl, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-7} cycloalkyl, C_{6-10} aryl C_{1-4} alkyl, $-OR_5$, $-NR_6R_7$, $-(CR_8R_9)_nZ_1$, $-C(O)NR_{12}R_{13}$, $-SR_{14}$, $-SOR_{15}$, $-SO_2R_{16}$, $-NR_{17}SO_2R_{18}$, COOH, C_{6-10} aryl which is optionally substituted by one or more groups independently selected from group P, 5- to 10-membered heteroaryl or 3- to 10-membered heterocyclyl which is optionally substituted by one or more groups independently selected from group Q, $-COR_{19}$, $-COOR_{20}$, $-OC(O)R_{21}$, $-NR_{22}C(O)R_{23}$, $-NR_{24}C(S)R_{25}$, $-C(S)NR_{26}R_{27}$, $-SO_2NR_{28}R_{29}$, $-OSO_2R_{30}$, $-SO_3R_{31}$, or $-Si(R_{32})_3$;

R_2 represents hydrogen, hydroxy, halogen, cyano, nitro, C_{1-4} haloalkyl, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-7} cycloalkyl, C_{6-10} aryl C_{1-4} alkyl, $-OR_5$, $-NR_6R_7$, $-(CR_8R_9)_nZ_1$, $-C(O)NR_{12}R_{13}$, $-SR_{14}$, $-SOR_{15}$, $-SO_2R_{16}$, $-NR_{17}SO_2R_{18}$, COOH, C_{6-10} aryl which is optionally substituted by one or more groups independently selected from group P, 5- to 10-membered heteroaryl or 3- to 10-membered heterocyclyl which is optionally substituted by one or more groups independently selected from group Q, $-COR_{19}$, $-COOR_{20}$, $-OC(O)R_{21}$, $-NR_{22}C(O)R_{23}$, $-NR_{24}C(S)R_{25}$, $-C(S)NR_{26}R_{27}$, $-SO_2NR_{28}R_{29}$, $-OSO_2R_{30}$, $-SO_3R_{31}$, or $-Si(R_{32})_3$; or

R_1 and R_2, together with an atom linked thereto, form 3- to 10-membered heterocyclyl or 5- to 10-membered heteroaryl, wherein the heterocyclyl or heteroaryl is optionally substituted by halogen;

R_3 represents hydrogen, C_{1-5} alkyl, C_{6-10} aryl C_{1-6} alkyl, or C_{1-4} haloalkyl;

R_4 represents hydrogen, halogen, C_{1-3} alkyl, C_{1-4} haloalkyl, hydroxy, cyano, nitro, C_{1-4} alkoxy, $-(CH_2)_nZ_1$, $-NR_6R_7$, $-OR_5$, $-C(O)NR_{12}R_{13}$, $-SR_{14}$, $-SOR_{15}$, $-SO_2R_{16}$, $NR_{17}SO_2R_{18}$, COOH, $-COR_{19}$, $-COOR_{20}$, $-OC(O)R_{21}$, $-NR_{22}C(O)R_{23}$, $-NR_{24}C(S)R_{25}$, $-C(S)NR_{26}R_{27}$, $-SO_2NR_{28}R_{29}$, $-OSO_2R_{30}$, $-SO_3R_{31}$, or $-Si(R_{32})_3$;

A represents a 5- to 10-membered heteroaryl ring or C_{6-10} aryl ring;

R_5 represents C_{1-5} alkyl, C_{3-7} cycloalkyl, C_{3-7} cycloalkyl C_{1-3} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-4} haloalkyl, C_{1-3} alkoxy C_{1-4} alkyl, C_{1-3} alkoxy C_{1-4} alkoxy C_{1-4} alkyl, C_{1-4} aminoalkyl, C_{1-4} alkylamino C_{1-4} alkyl, di(C_{1-4} alkyl)amino C_{1-4} alkyl, C_{6-10} aryl, C_{6-10} aryl C_{1-3} alkyl, or 3- to 10-membered heterocyclyl C_{1-3} alkyl, 3- to 10-membered heterocyclyl, 5- to 10-membered heteroaryl, 5- to 10-membered heteroaryl C_{1-3} alkyl, C_{1-6} monohydroxy alkyl, C_{1-6} dihydroxy alkyl, or C_{1-6} trihydroxy alkyl which is optionally substituted by one or more groups independently selected from group Q;

R_6 and R_7, which can be the same or different, each represents hydrogen, C_{1-4} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-4} haloalkyl, C_{1-3} alkoxy C_{1-4} alkyl, C_{6-10} aryl C_{1-3} alkyl, 3- to 10-membered heterocyclyl C_{1-3} alkyl, 5- to 10-membered heteroaryl C_{1-3} alkyl, C_{1-6} monohydroxy alkyl, C_{1-6} dihydroxy alkyl, C_{1-6} trihydroxy alkyl, 3- to 10-membered heterocyclyl, C_{1-4} aminoalkyl, C_{1-4} alkylamino C_{1-4} alkyl, di(C_{1-4} alkyl)amino C_{1-4} alkyl, or cyano(C_{1-3} alkyl); or alternatively R_6 and R_7, together with a nitrogen atom linked thereto, form 3- to 10-membered heterocyclyl or 5- to 10-membered heteroaryl;

n represents 1 to 3;

R_8 and R_9, which can be the same or different, each represents hydrogen, C_{1-4} alkyl, or halogen; or alternatively R_8 and R_9, together with a carbon atom linked thereto, form a cycloaliphatic ring;

Z_1 represents hydrogen, $NR_{10}R_{11}$, -OH, or 3- to 10-membered heterocyclyl or 5- to 10-membered heteroaryl which is optionally substituted by one or more groups independently selected from group Q;

R_{10} and R_{11}, which can be the same or different, each represents C_{1-4} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-4} haloalkyl, C_{1-3} alkoxy C_{1-4} alkyl, cyano(C_{1-3} alkyl), or C_{1-3} alkylsulfonyl C_{1-4} alkyl; or alternatively R_{10} and R_{11}, together with a nitrogen atom linked thereto, form 3- to 10-membered heterocyclyl or 5- to 10-membered heteroaryl;

R_{12} and R_{13}, which can be the same or different, each represents hydrogen, C_{1-4} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-4} haloalkyl, C_{1-3} alkoxy C_{1-4} alkyl, C_{6-10} aryl, 5- to 10-membered heteroaryl, 3- to 10-membered heterocyclyl, C_{6-10} aryl C_{1-4} alkyl, 3- to 10-membered heterocyclyl C_{1-3} alkyl, 5- to 10-membered heteroaryl C_{1-3} alkyl, cyano(C_{1-3} alkyl), C_{1-3} alkylsulfonyl C_{1-4} alkyl, 3- to 10-membered cycloaliphatic ring, 5- to 10-membered heteroaryl, or 3- to 10-membered heterocyclyl; or alternatively R_{12} and R_{13}, together with a nitrogen atom

linked thereto, form 3- to 10-membered heterocyclyl or 5- to 10-membered heteroaryl which is optionally substituted by one or more groups independently selected from group Q;

R_{14} represents C_{1-4} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-4} haloalkyl, C_{6-10} aryl which is optionally substituted by one or more groups independently selected from group P, or 5- to 10-membered heteroaryl or 3- to 10-membered heterocyclyl which is optionally substituted by one or more groups independently selected from group Q;

R_{15} represents C_{1-4} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-4} haloalkyl, C_{6-10} aryl which is optionally substituted by one or more groups independently selected from group P, or 5- to 10-membered heteroaryl or 3- to 10-membered heterocyclyl which is optionally substituted by one or more groups independently selected from group Q;

R_{16} represents C_{1-4} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-4} haloalkyl, C_{6-10} aryl which is optionally substituted by one or more groups independently selected from group P, or 5- to 10-membered heteroaryl or 3- to 10-membered heterocyclyl which is optionally substituted by one or more groups independently selected from group Q;

R_{17} represents hydrogen or C_{1-4} alkyl;

R_{18} represents C_{1-4} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-4} haloalkyl, C_{6-10} aryl which is optionally substituted by one or more groups independently selected from group P, or 5- to 10-membered heteroaryl or 3- to 10-membered heterocyclyl which is optionally substituted by one or more groups independently selected from group Q;

R_{19} represents hydrogen, C_{1-4} alkyl, C_{3-7} cycloalkyl, C_{1-4} haloalkyl, C_{6-10} aryl, or 5- to 10-membered heteroaryl or 3- to 10-membered heterocyclyl which is optionally substituted by one or more groups independently selected from group Q;

R_{20} represents C_{1-4} alkyl, C_{3-7} cycloalkyl, C_{1-4} haloalkyl, C_{6-10} aryl, 5- to 10-membered heteroaryl, or 3- to 10-membered heterocyclyl;

R_{21} represents C_{1-4} alkyl, C_{3-7} cycloalkyl, C_{1-4} haloalkyl, C_{6-10} aryl, 5- to 10-membered heteroaryl, or 3- to 10-membered heterocyclyl;

R_{22} represents hydrogen, C_{1-4} alkyl, or C_{1-4} haloalkyl;

R_{23} represents hydrogen, C_{1-4} alkyl, C_{3-7} cycloalkyl, C_{1-4} haloalkyl, C_{6-10} aryl, 5- to 10-membered heteroaryl, or 3- to 10-membered heterocyclyl;

R_{24} represents hydrogen, C_{1-4} alkyl, or C_{1-4} haloalkyl;

R_{25} represents C_{1-4} alkyl, C_{3-7} cycloalkyl, C_{1-4} haloalkyl, C_{6-10} aryl, 5- to 10-membered heteroaryl, or 3- to 10-membered heterocyclyl;

R_{26} and R_{27}, which can be the same or different, each represents hydrogen, C_{1-4} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-4} haloalkyl, C_{1-3} alkoxyl C_{1-4} alkyl, C_{6-10} aryl, 5- to 10-membered heteroaryl, 3- to 10-membered heterocyclyl, C_{6-10} aryl C_{1-4} alkyl, 3- to 10-membered heterocyclyl C_{1-3} alkyl, 5- to 10-membered heteroaryl C_{1-3} alkyl, cyano(C_{1-3} alkyl), C_{1-3}

alkylsulfonyl C_{1-4} alkyl, or 3- to 10-membered cycloaliphatic ring; or alternatively R_{26} and R_{27}, together with a nitrogen atom linked thereto, form 3- to 10-membered heterocyclyl or 5- to 10-membered heteroaryl;

R_{28} and R_{29}, which can be the same or different, each represents hydrogen, C_{1-4} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-4} haloalkyl, C_{1-3} alkoxyl C_{1-4} alkyl, C_{6-10} aryl, 5- to 10-membered heteroaryl, 3- to 10-membered heterocyclyl, C_{6-10} aryl C_{1-4} alkyl, 3- to 10-membered heterocyclyl C_{1-3} alkyl, 5- to 10-membered heteroaryl C_{1-3} alkyl, cyano(C_{1-3} alkyl), C_{1-3} alkylsulfonyl C_{1-4} alkyl, or 3- to 10-membered cycloaliphatic ring; or alternatively R_{28} and R_{29}, together with a nitrogen atom linked thereto, form 3- to 10-membered heterocyclyl or 5- to 10-membered heteroaryl;

R_{30} represents C_{1-4} alkyl, C_{3-7} cycloalkyl, C_{1-4} haloalkyl, C_{6-10} aryl, 5- to 10-membered heteroaryl, or 3- to 10-membered heterocyclyl;

R_{31} represents C_{1-4} alkyl, C_{3-7} cycloalkyl, C_{1-4} haloalkyl, C_{6-10} aryl, 5- to 10-membered heteroaryl, or 3- to 10-membered heterocyclyl;

R_{32} represents C_{1-4} alkyl or C_{6-10} aryl;

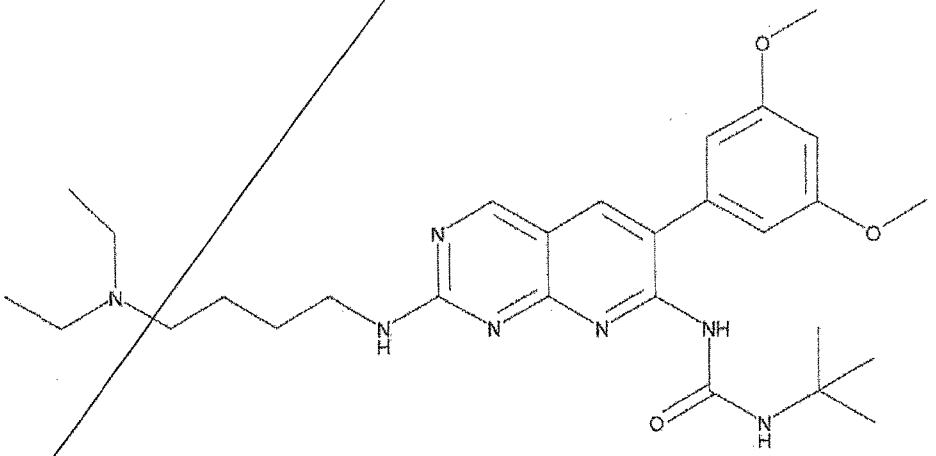
<group P>

halogen, C_{1-4} alkyl, C_{1-4} haloalkyl, -OH, C_{1-3} alkoxy, C_{1-3} haloalkoxy, 3- to 10-membered heterocyclylamino, $-SO_2R_{16}$, -CN, $-NO_2$, and 3- to 10-membered heterocyclyl;

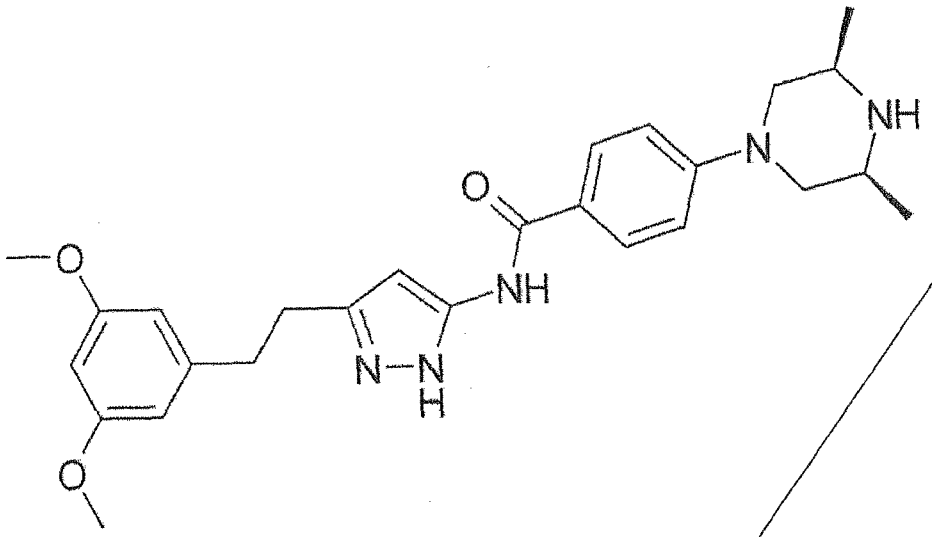
<group Q>

halogen, C_{1-4} alkyl, C_{1-4} haloalkyl, -OH, C_{1-3} alkoxy, C_{1-6} monohydroxy alkyl, C_{1-6} dihydroxy alkyl, C_{1-6} trihydroxy alkyl, 3- to 10-membered heterocyclyl amine, $-SO_2R_{16}$, -CN, $-NO_2$, C_{3-7} cycloalkyl, $-COR_{19}$, and 3- to 10-membered heterocyclyl which is optionally substituted by C_{1-4} alkyl.

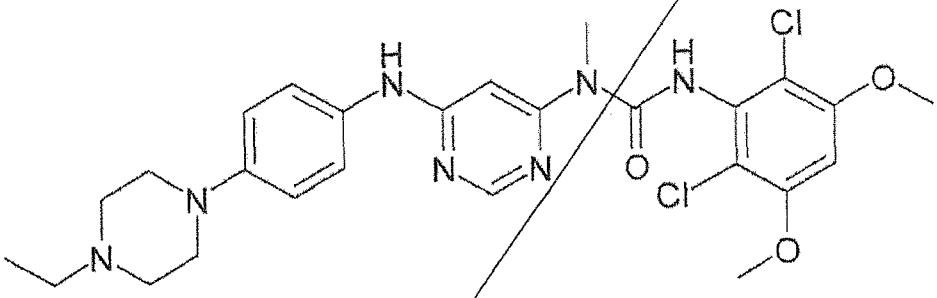
[Compound 2]



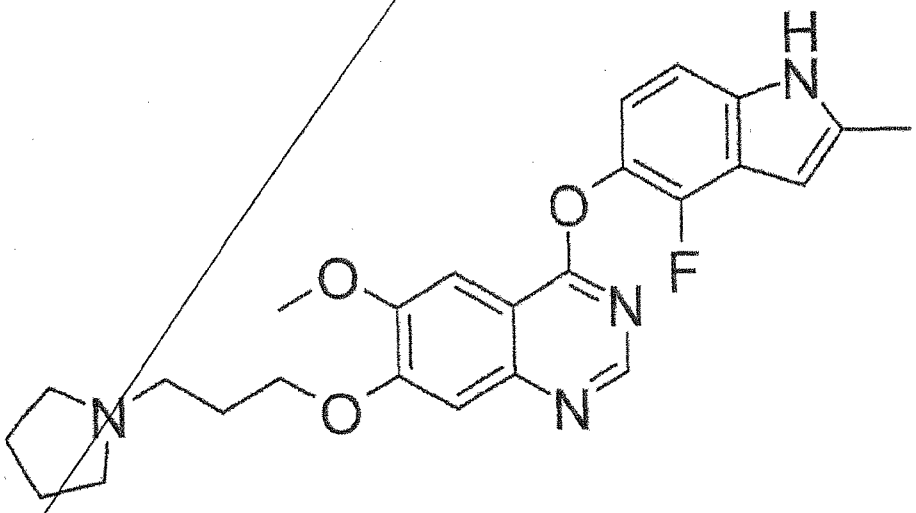
[Compound 3]



[Compound 4]



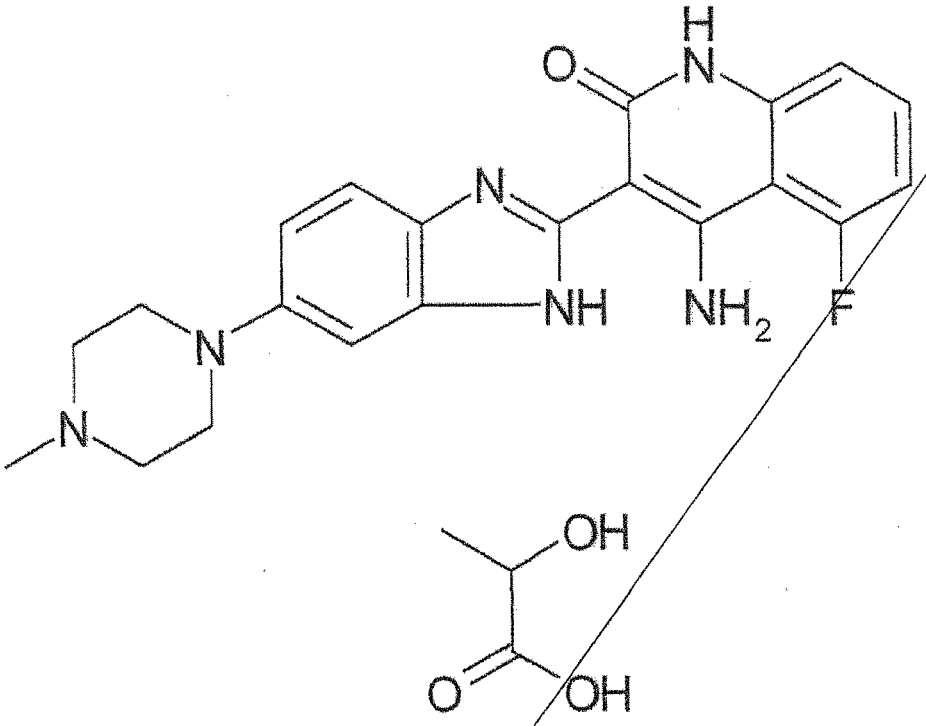
[Compound 5]



5

, or

[Compound 6]



44. The method of claim 43, wherein the compound having FGFR inhibitory activity or a pharmaceutically acceptable salt thereof is a compound of formula (I), wherein A is indole, and R_3 and R_4 are both hydrogen, or a pharmaceutically acceptable salt thereof.

45. Use of a compound having FGFR inhibitory activity or a pharmaceutically acceptable salt thereof in the manufacture of a pharmaceutical composition for cancer treatment to be administered to a patient expressing the fusion polypeptide of any one of claims 1 to 7 or carrying a polynucleotide encoding the fusion polypeptide.

46. The use of claim 45, wherein the patient is selected by the method of any one of claims 26 to 30.

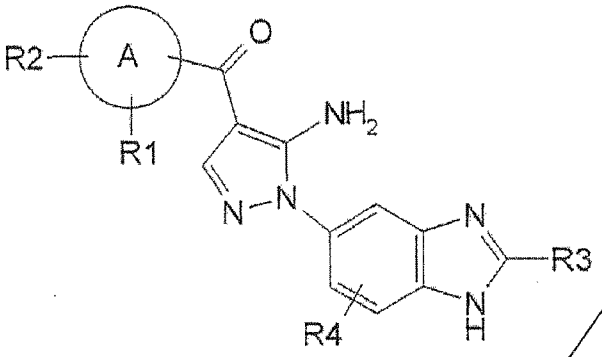
47. The use of claim 45 or 46, wherein the cancer is bladder cancer, brain tumor, head and neck squamous cell carcinoma, lung cancer, lung adenocarcinoma, lung squamous cell carcinoma, skin melanoma, esophageal cancer, gastric cancer, or liver cancer.

48. The use of claim 45 or 46, wherein the cancer is bladder cancer.

49. The use of claim 48, wherein the bladder cancer is classified as stage 3 or later according to TNM classification.

50. The use of any one of claims 45 to 49, wherein the compound having FGFR inhibitory activity or a pharmaceutically acceptable salt thereof is any one of the compounds or a pharmaceutically acceptable salt thereof represented by:

[Compound 1]



(I)

wherein R_1, R_2, R_3, and R_4 each independently represents the group listed below:

R_1 represents hydrogen, hydroxy, halogen, cyano, nitro, C_{1-4} haloalkyl, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-7} cycloalkyl, C_{6-10} aryl C_{1-4} alkyl, $-OR_5$, $-NR_6R_7$, $-(CR_8R_9)_nZ_1$, $-C(O)NR_{12}R_{13}$, $-SR_{14}$, $-SOR_{15}$, $-SO_2R_{16}$, $-NR_{17}SO_2R_{18}$, COOH, C_{6-10} aryl which is optionally substituted by one or more groups independently selected from group P, 5- to 10-membered heteroaryl or 3- to 10-membered heterocyclyl which is optionally substituted by one or more groups independently selected from group Q, $-COR_{19}$, $-COOR_{20}$, $-OC(O)R_{21}$, $-NR_{22}C(O)R_{23}$, $-NR_{24}C(S)R_{25}$, $-C(S)NR_{26}R_{27}$, $-SO_2NR_{28}R_{29}$, $-OSO_2R_{30}$, $-SO_3R_{31}$, or $-Si(R_{32})_3$;

R_2 represents hydrogen, hydroxy, halogen, cyano, nitro, C_{1-4} haloalkyl, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-7} cycloalkyl, C_{6-10} aryl C_{1-4} alkyl, $-OR_5$, $-NR_6R_7$, $-(CR_8R_9)_nZ_1$, $-C(O)NR_{12}R_{13}$, $-SR_{14}$, $-SOR_{15}$, $-SO_2R_{16}$, $-NR_{17}SO_2R_{18}$, COOH, C_{6-10} aryl which is optionally substituted by one or more groups independently selected from group P, 5- to 10-membered heteroaryl or 3- to 10-membered heterocyclyl which is optionally substituted by one or more groups independently selected from group Q, $-COR_{19}$, $-COOR_{20}$, $-OC(O)R_{21}$, $-NR_{22}C(O)R_{23}$, $-NR_{24}C(S)R_{25}$, $-C(S)NR_{26}R_{27}$, $-SO_2NR_{28}R_{29}$, $-OSO_2R_{30}$, $-SO_3R_{31}$, or $-Si(R_{32})_3$; or

R_1 and R_2, together with an atom linked thereto, form 3- to 10-membered heterocyclyl or 5- to 10-membered heteroaryl, wherein the heterocyclyl or heteroaryl is optionally substituted by

halogen;

R_3 represents hydrogen, C_{1-5} alkyl, C_{6-10} aryl C_{1-6} alkyl, or C_{1-4} haloalkyl;

R_4 represents hydrogen, halogen, C_{1-3} alkyl, C_{1-4} haloalkyl, hydroxy, cyano, nitro, C_{1-4} alkoxy, -$(CH_2)_nZ_1$, -NR_6R_7, -OR_5, -$C(O)NR_{12}R_{13}$, -SR_{14}, -SOR_{15}, -SO_2R_{16}, $NR_{17}SO_2R_{18}$, COOH, -COR_{19}, -$COOR_{20}$, -$OC(O)R_{21}$, -$NR_{22}C(O)R_{23}$, -$NR_{24}C(S)R_{25}$, -$C(S)NR_{26}R_{27}$, -$SO_2NR_{28}R_{29}$, -OSO_2R_{30}, -SO_3R_{31}, or -$Si(R_{32})_3$;

A represents a 5- to 10-membered heteroaryl ring or C_{6-10} aryl ring;

R_5 represents C_{1-5} alkyl, C_{3-7} cycloalkyl, C_{3-7} cycloalkyl C_{1-3} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-4} haloalkyl, C_{1-3} alkoxy C_{1-4} alkyl, C_{1-3} alkoxy C_{1-4} alkoxy C_{1-4} alkyl, C_{1-4} aminoalkyl, C_{1-4} alkylamino C_{1-4} alkyl, di(C_{1-4} alkyl)amino C_{1-4} alkyl, C_{6-10} aryl, C_{6-10} aryl C_{1-3} alkyl, or 3- to 10-membered heterocyclyl C_{1-3} alkyl, 3- to 10-membered heterocyclyl, 5- to 10-membered heteroaryl, 5- to 10-membered heteroaryl C_{1-3} alkyl, C_{1-6} monohydroxy alkyl, C_{1-6} dihydroxy alkyl, or C_{1-6} trihydroxy alkyl which is optionally substituted by one or more groups independently selected from group Q;

R_6 and R_7, which can be the same or different, each represents hydrogen, C_{1-4} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-4} haloalkyl, C_{1-3} alkoxy C_{1-4} alkyl, C_{6-10} aryl C_{1-3} alkyl, 3- to 10-membered heterocyclyl C_{1-3} alkyl, 5- to 10-membered heteroaryl C_{1-3} alkyl, C_{1-6} monohydroxy alkyl, C_{1-6} dihydroxy alkyl, C_{1-6} trihydroxy alkyl, 3- to 10-membered heterocyclyl, C_{1-4} aminoalkyl, C_{1-4} alkylamino C_{1-4} alkyl, di(C_{1-4} alkyl)amino C_{1-4} alkyl, or cyano(C_{1-3} alkyl); or alternatively R_6 and R_7, together with a nitrogen atom linked thereto, form 3- to 10-membered heterocyclyl or 5- to 10-membered heteroaryl;

n represents 1 to 3;

R_8 and R_9, which can be the same or different, each represents hydrogen, C_{1-4} alkyl, or halogen; or alternatively R_8 and R_9, together with a carbon atom linked thereto, form a cycloaliphatic ring;

Z_1 represents hydrogen, $NR_{10}R_{11}$, -OH, or 3- to 10-membered heterocyclyl or 5- to 10-membered heteroaryl which is optionally substituted by one or more groups independently selected from group Q;

R_{10} and R_{11}, which can be the same or different, each represents C_{1-4} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-4} haloalkyl, C_{1-3} alkoxy C_{1-4} alkyl, cyano(C_{1-3} alkyl), or C_{1-3} alkylsulfonyl C_{1-4} alkyl; or alternatively R_{10} and R_{11}, together with a nitrogen atom linked thereto, form 3- to 10-membered heterocyclyl or 5- to 10-membered heteroaryl;

R_{12} and R_{13}, which can be the same or different, each represents hydrogen, C_{1-4} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-4} haloalkyl, C_{1-3} alkoxy C_{1-4} alkyl, C_{6-10} aryl, 5- to 10-membered heteroaryl, 3- to 10-membered heterocyclyl, C_{6-10} aryl C_{1-4} alkyl, 3- to 10-membered heterocyclyl C_{1-3} alkyl, 5- to 10-membered heteroaryl C_{1-3} alkyl, cyano(C_{1-3} alkyl), C_{1-3} alkylsulfonyl C_{1-4} alkyl, 3- to 10-membered cycloaliphatic ring, 5- to 10-membered heteroaryl,

or 3- to 10-membered heterocyclyl; or alternatively R_{12} and R_{13}, together with a nitrogen atom linked thereto, form 3- to 10-membered heterocyclyl or 5- to 10-membered heteroaryl which is optionally substituted by one or more groups independently selected from group Q;

R_{14} represents C_{1-4} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-4} haloalkyl, C_{6-10} aryl which is optionally substituted by one or more groups independently selected from group P, or 5- to 10-membered heteroaryl or 3- to 10-membered heterocyclyl which is optionally substituted by one or more groups independently selected from group Q;

R_{15} represents C_{1-4} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-4} haloalkyl, C_{6-10} aryl which is optionally substituted by one or more groups independently selected from group P, or 5- to 10-membered heteroaryl or 3- to 10-membered heterocyclyl which is optionally substituted by one or more groups independently selected from group Q;

R_{16} represents C_{1-4} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-4} haloalkyl, C_{6-10} aryl which is optionally substituted by one or more groups independently selected from group P, or 5- to 10-membered heteroaryl or 3- to 10-membered heterocyclyl which is optionally substituted by one or more groups independently selected from group Q;

R_{17} represents hydrogen or C_{1-4} alkyl;

R_{18} represents C_{1-4} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-4} haloalkyl, C_{6-10} aryl which is optionally substituted by one or more groups independently selected from group P, or 5- to 10-membered heteroaryl or 3- to 10-membered heterocyclyl which is optionally substituted by one or more groups independently selected from group Q;

R_{19} represents hydrogen, C_{1-4} alkyl, C_{3-7} cycloalkyl, C_{1-4} haloalkyl, C_{6-10} aryl, or 5- to 10-membered heteroaryl or 3- to 10-membered heterocyclyl which is optionally substituted by one or more groups independently selected from group Q;

R_{20} represents C_{1-4} alkyl, C_{3-7} cycloalkyl, C_{1-4} haloalkyl, C_{6-10} aryl, 5- to 10-membered heteroaryl, or 3- to 10-membered heterocyclyl;

R_{21} represents C_{1-4} alkyl, C_{3-7} cycloalkyl, C_{1-4} haloalkyl, C_{6-10} aryl, 5- to 10-membered heteroaryl, or 3- to 10-membered heterocyclyl;

R_{22} represents hydrogen, C_{1-4} alkyl, or C_{1-4} haloalkyl;

R_{23} represents hydrogen, C_{1-4} alkyl, C_{3-7} cycloalkyl, C_{1-4} haloalkyl, C_{6-10} aryl, 5- to 10-membered heteroaryl, or 3- to 10-membered heterocyclyl;

R_{24} represents hydrogen, C_{1-4} alkyl, or C_{1-4} haloalkyl;

R_{25} represents C_{1-4} alkyl, C_{3-7} cycloalkyl, C_{1-4} haloalkyl, C_{6-10} aryl, 5- to 10-membered heteroaryl, or 3- to 10-membered heterocyclyl;

R_{26} and R_{27}, which can be the same or different, each represents hydrogen, C_{1-4} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-4} haloalkyl, C_{1-3} alkoxyl C_{1-4} alkyl, C_{6-10} aryl, 5- to 10-membered heteroaryl, 3- to 10-membered heterocyclyl, C_{6-10} aryl C_{1-4} alkyl, 3- to 10-membered

heterocyclyl C_{1-3} alkyl, 5- to 10-membered heteroaryl C_{1-3} alkyl, cyano(C_{1-3} alkyl), C_{1-3} alkylsulfonyl C_{1-4} alkyl, or 3- to 10-membered cycloaliphatic ring; or alternatively R_{26} and R_{27}, together with a nitrogen atom linked thereto, form 3- to 10-membered heterocyclyl or 5- to 10-membered heteroaryl;

R_{28} and R_{29}, which can be the same or different, each represents hydrogen, C_{1-4} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-4} haloalkyl, C_{1-3} alkoxyl C_{1-4} alkyl, C_{6-10} aryl, 5- to 10-membered heteroaryl, 3- to 10-membered heterocyclyl, C_{6-10} aryl C_{1-4} alkyl, 3- to 10-membered heterocyclyl C_{1-3} alkyl, 5- to 10-membered heteroaryl C_{1-3} alkyl, cyano(C_{1-3} alkyl), C_{1-3} alkylsulfonyl C_{1-4} alkyl, or 3- to 10-membered cycloaliphatic ring; or alternatively R_{28} and R_{29}, together with a nitrogen atom linked thereto, form 3- to 10-membered heterocyclyl or 5- to 10-membered heteroaryl;

R_{30} represents C_{1-4} alkyl, C_{3-7} cycloalkyl, C_{1-4} haloalkyl, C_{6-10} aryl, 5- to 10-membered heteroaryl, or 3- to 10-membered heterocyclyl;

R_{31} represents C_{1-4} alkyl, C_{3-7} cycloalkyl, C_{1-4} haloalkyl, C_{6-10} aryl, 5- to 10-membered heteroaryl, or 3- to 10-membered heterocyclyl;

R_{32} represents C_{1-4} alkyl or C_{6-10} aryl;

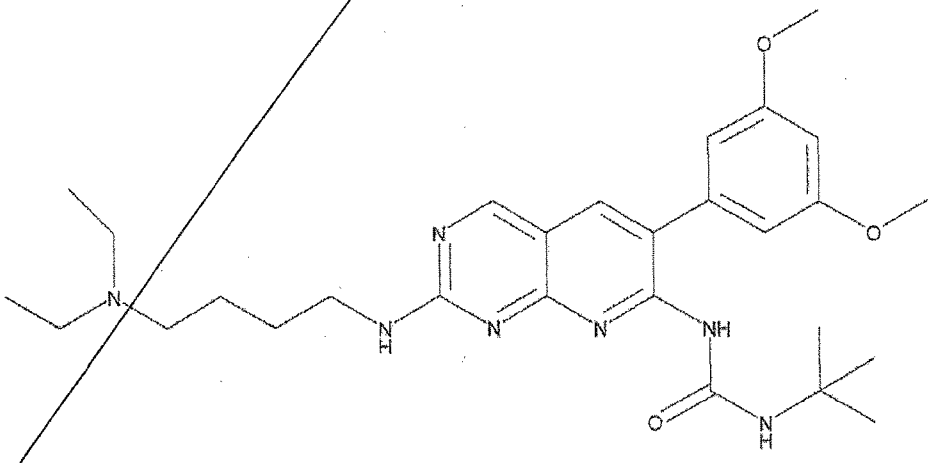
<group P>

halogen, C_{1-4} alkyl, C_{1-4} haloalkyl, -OH, C_{1-3} alkoxy, C_{1-3} haloalkoxy, 3- to 10-membered heterocyclylamino, $-SO_2R_{16}$, -CN, $-NO_2$, and 3- to 10-membered heterocyclyl;

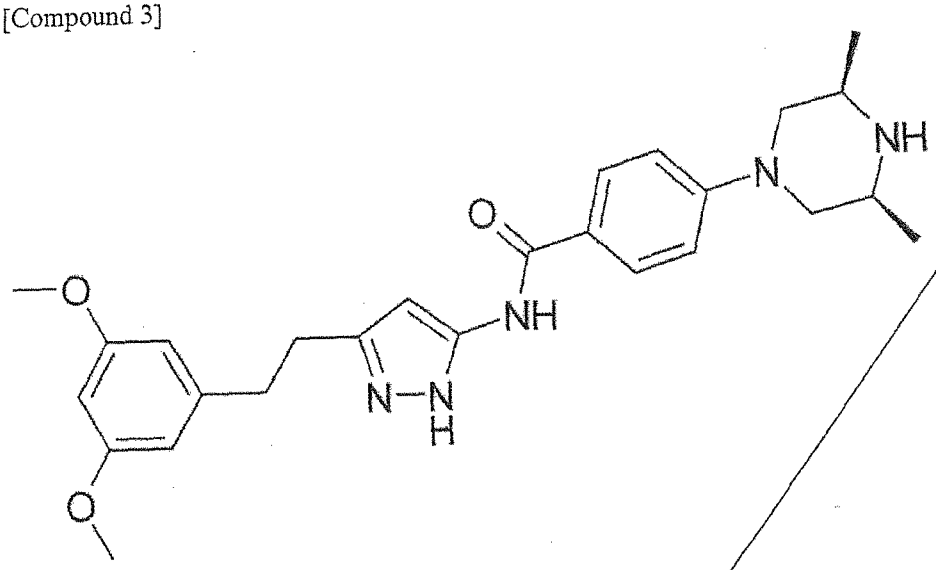
<group Q>

halogen, C_{1-4} alkyl, C_{1-4} haloalkyl, -OH, C_{1-3} alkoxy, C_{1-6} monohydroxy alkyl, C_{1-6} dihydroxy alkyl, C_{1-6} trihydroxy alkyl, 3- to 10-membered heterocyclyl amine, $-SO_2R_{16}$, -CN, $-NO_2$, C_{3-7} cycloalkyl, $-COR_{19}$, and 3- to 10-membered heterocyclyl which is optionally substituted by C_{1-4} alkyl.

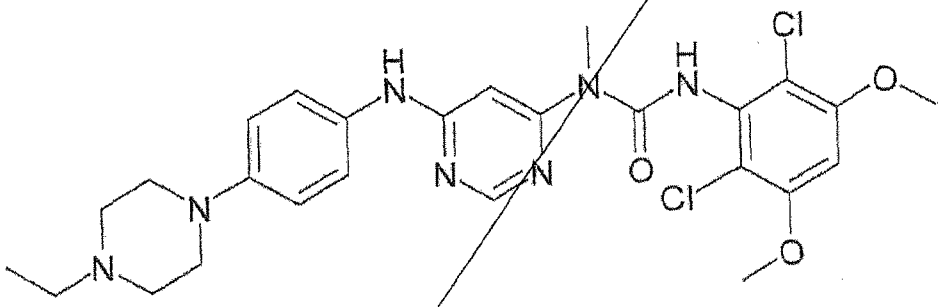
[Compound 2]



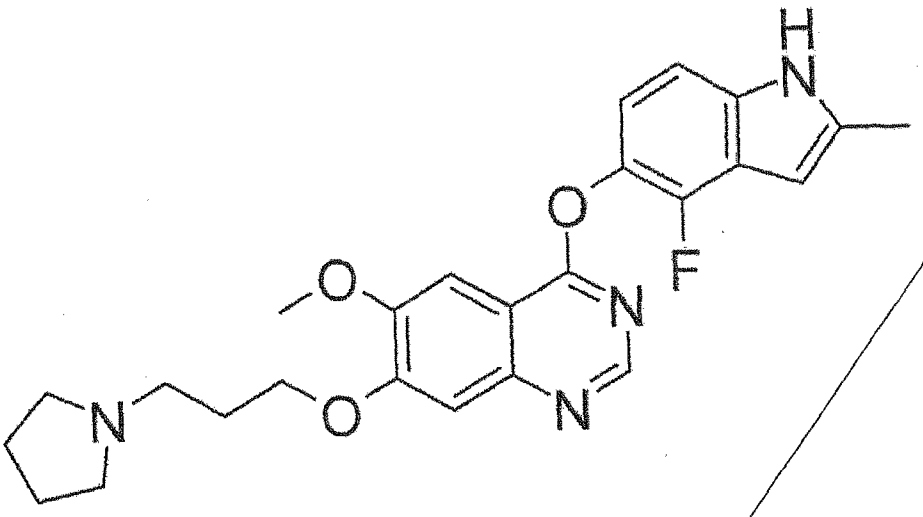
[Compound 3]



[Compound 4]

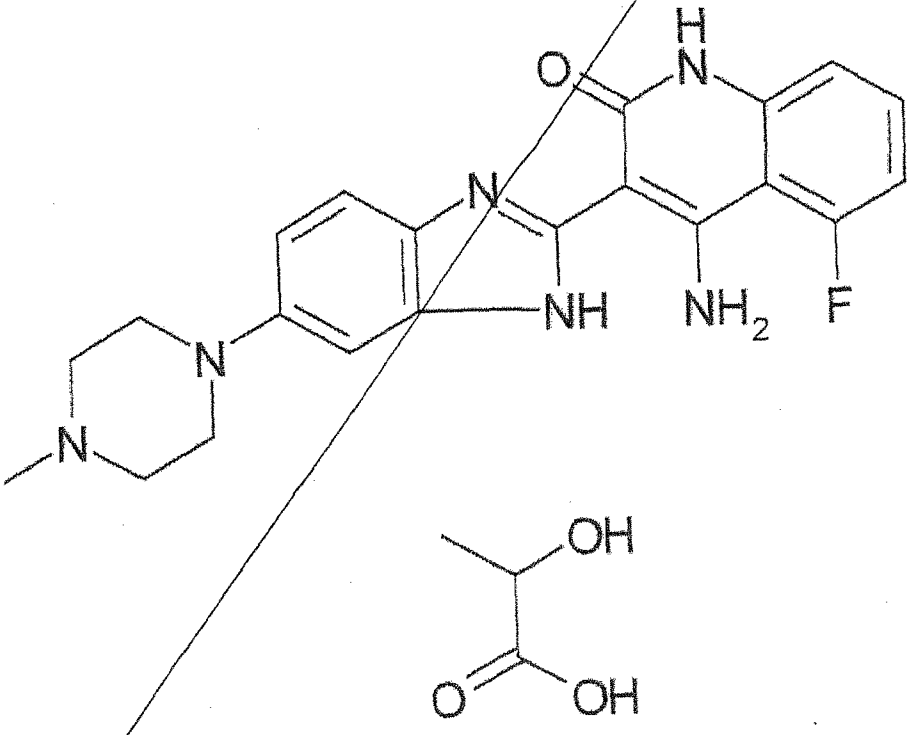


[Compound 5]



, or

[Compound 6]



51. The use of claim 50, wherein the compound having FGFR inhibitory activity or a pharmaceutically acceptable salt thereof is a compound of formula (I), wherein A is indole, and

R_3 and R_4 are both hydrogen, or a pharmaceutically acceptable salt thereof.

52. A compound having FGFR inhibitory activity or a pharmaceutically acceptable salt thereof for therapeutic or prophylactic use in a cancer patient expressing the fusion polypeptide of any one of claims 1 to 7 or carrying a polynucleotide encoding the fusion polypeptide.

53. The compound or a pharmaceutically acceptable salt thereof of claim 52, wherein the patient is selected by the method of any one of claims 26 to 30.

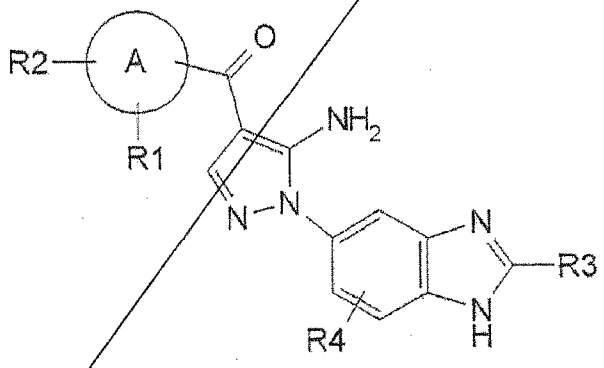
54. The compound or a pharmaceutically acceptable salt thereof of claim 52 or 53, wherein the cancer is bladder cancer, brain tumor, head and neck squamous cell carcinoma, lung cancer, lung adenocarcinoma, lung squamous cell carcinoma, skin melanoma, esophageal cancer, gastric cancer, or liver cancer.

55. The compound or a pharmaceutically acceptable salt thereof of claim 52 or 53, wherein the cancer is bladder cancer.

56. The compound or a pharmaceutically acceptable salt thereof of claim 55, wherein the bladder cancer is classified as stage 3 or later according to TNM classification.

57. The compound or a pharmaceutically acceptable salt thereof of any one of claims 52 to 56, wherein the compound having FGFR inhibitory activity or a pharmaceutically acceptable salt thereof is any one of the compounds or a pharmaceutically acceptable salt thereof represented by:

[Compound 1]



(I)

wherein R_1, R_2, R_3, and R_4 each independently represents the group listed below:
R_1 represents hydrogen, hydroxy, halogen, cyano, nitro, C_{1-4} haloalkyl, C_{1-6} alkyl, C_{2-6} alkenyl,

C_{2-6} alkynyl, C_{3-7} cycloalkyl, C_{6-10} aryl C_{1-4} alkyl, $-OR_5$, $-NR_6R_7$, $-(CR_8R_9)_nZ_1$, $-C(O)NR_{12}R_{13}$, $-SR_{14}$, $-SOR_{15}$, $-SO_2R_{16}$, $-NR_{17}SO_2R_{18}$, COOH, C_{6-10} aryl which is optionally substituted by one or more groups independently selected from group P, 5- to 10-membered heteroaryl or 3- to 10-membered heterocyclyl which is optionally substituted by one or more groups independently selected from group Q, $-COR_{19}$, $-COOR_{20}$, $-OC(O)R_{21}$, $-NR_{22}C(O)R_{23}$, $-NR_{24}C(S)R_{25}$, $-C(S)NR_{26}R_{27}$, $-SO_2NR_{28}R_{29}$, $-OSO_2R_{30}$, $-SO_3R_{31}$, or $-Si(R_{32})_3$;

R_2 represents hydrogen, hydroxy, halogen, cyano, nitro, C_{1-4} haloalkyl, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-7} cycloalkyl, C_{6-10} aryl C_{1-4} alkyl, $-OR_5$, $-NR_6R_7$, $-(CR_8R_9)_nZ_1$, $-C(O)NR_{12}R_{13}$, $-SR_{14}$, $-SOR_{15}$, $-SO_2R_{16}$, $-NR_{17}SO_2R_{18}$, COOH, C_{6-10} aryl which is optionally substituted by one or more groups independently selected from group P, 5- to 10-membered heteroaryl or 3- to 10-membered heterocyclyl which is optionally substituted by one or more groups independently selected from group Q, $-COR_{19}$, $-COOR_{20}$, $-OC(O)R_{21}$, $-NR_{22}C(O)R_{23}$, $-NR_{24}C(S)R_{25}$, $-C(S)NR_{26}R_{27}$, $-SO_2NR_{28}R_{29}$, $-OSO_2R_{30}$, $-SO_3R_{31}$, or $-Si(R_{32})_3$; or

R_1 and R_2, together with an atom linked thereto, form 3- to 10-membered heterocyclyl or 5- to 10-membered heteroaryl, wherein the heterocyclyl or heteroaryl is optionally substituted by halogen;

R_3 represents hydrogen, C_{1-5} alkyl, C_{6-10} aryl C_{1-6} alkyl, or C_{1-4} haloalkyl;

R_4 represents hydrogen, halogen, C_{1-3} alkyl, C_{1-4} haloalkyl, hydroxy, cyano, nitro, C_{1-4} alkoxy, $-(CH_2)_nZ_1$, $-NR_6R_7$, $-OR_5$, $-C(O)NR_{12}R_{13}$, $-SR_{14}$, $-SOR_{15}$, $-SO_2R_{16}$, $NR_{17}SO_2R_{18}$, COOH, $-COR_{19}$, $-COOR_{20}$, $-OC(O)R_{21}$, $-NR_{22}C(O)R_{23}$, $-NR_{24}C(S)R_{25}$, $-C(S)NR_{26}R_{27}$, $-SO_2NR_{28}R_{29}$, $-OSO_2R_{30}$, $-SO_3R_{31}$, or $-Si(R_{32})_3$;

A represents a 5- to 10-membered heteroaryl ring or C_{6-10} aryl ring;

R_5 represents C_{1-5} alkyl, C_{3-7} cycloalkyl, C_{3-7} cycloalkyl C_{1-3} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-4} haloalkyl, C_{1-3} alkoxy C_{1-4} alkyl, C_{1-3} alkoxy C_{1-4} alkoxy C_{1-4} alkyl, C_{1-4} aminoalkyl, C_{1-4} alkylamino C_{1-4} alkyl, di(C_{1-4} alkyl)amino C_{1-4} alkyl, C_{6-10} aryl, C_{6-10} aryl C_{1-3} alkyl, or 3- to 10-membered heterocyclyl C_{1-3} alkyl, 3- to 10-membered heterocyclyl, 5- to 10-membered heteroaryl, 5- to 10-membered heteroaryl C_{1-3} alkyl, C_{1-6} monohydroxy alkyl, C_{1-6} dihydroxy alkyl, or C_{1-6} trihydroxy alkyl which is optionally substituted by one or more groups independently selected from group Q;

R_6 and R_7, which can be the same or different, each represents hydrogen, C_{1-4} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-4} haloalkyl, C_{1-3} alkoxy C_{1-4} alkyl, C_{6-10} aryl C_{1-3} alkyl, 3- to 10-membered heterocyclyl C_{1-3} alkyl, 5- to 10-membered heteroaryl C_{1-3} alkyl, C_{1-6} monohydroxy alkyl, C_{1-6} dihydroxy alkyl, C_{1-6} trihydroxy alkyl, 3- to 10-membered heterocyclyl, C_{1-4} aminoalkyl, C_{1-4} alkylamino C_{1-4} alkyl, di(C_{1-4} alkyl)amino C_{1-4} alkyl, or cyano(C_{1-3} alkyl); or alternatively R_6 and R_7, together with a nitrogen atom linked thereto, form 3- to 10-membered heterocyclyl or 5- to 10-membered heteroaryl;

n represents 1 to 3;

R_8 and R_9, which can be the same or different, each represents hydrogen, C_{1-4} alkyl, or halogen; or alternatively R_8 and R_9, together with a carbon atom linked thereto, form a cycloaliphatic ring;

Z_1 represents hydrogen, $NR_{10}R_{11}$, -OH, or 3- to 10-membered heterocyclyl or 5- to 10-membered heteroaryl which is optionally substituted by one or more groups independently selected from group Q;

R_{10} and R_{11}, which can be the same or different, each represents C_{1-4} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-4} haloalkyl, C_{1-3} alkoxy C_{1-4} alkyl, cyano(C_{1-3} alkyl), or C_{1-3} alkylsulfonyl C_{1-4} alkyl; or alternatively R_{10} and R_{11}, together with a nitrogen atom linked thereto, form 3- to 10-membered heterocyclyl or 5- to 10-membered heteroaryl;

R_{12} and R_{13}, which can be the same or different, each represents hydrogen, C_{1-4} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-4} haloalkyl, C_{1-3} alkoxy C_{1-4} alkyl, C_{6-10} aryl, 5- to 10-membered heteroaryl, 3- to 10-membered heterocyclyl, C_{6-10} aryl C_{1-4} alkyl, 3- to 10-membered heterocyclyl C_{1-3} alkyl, 5- to 10-membered heteroaryl C_{1-3} alkyl, cyano(C_{1-3} alkyl), C_{1-3} alkylsulfonyl C_{1-4} alkyl, 3- to 10-membered cycloaliphatic ring, 5- to 10-membered heteroaryl, or 3- to 10-membered heterocyclyl; or alternatively R_{12} and R_{13}, together with a nitrogen atom linked thereto, form 3- to 10-membered heterocyclyl or 5- to 10-membered heteroaryl which is optionally substituted by one or more groups independently selected from group Q;

R_{14} represents C_{1-4} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-4} haloalkyl, C_{6-10} aryl which is optionally substituted by one or more groups independently selected from group P, or 5- to 10-membered heteroaryl or 3- to 10-membered heterocyclyl which is optionally substituted by one or more groups independently selected from group Q;

R_{15} represents C_{1-4} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-4} haloalkyl, C_{6-10} aryl which is optionally substituted by one or more groups independently selected from group P, or 5- to 10-membered heteroaryl or 3- to 10-membered heterocyclyl which is optionally substituted by one or more groups independently selected from group Q;

R_{16} represents C_{1-4} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-4} haloalkyl, C_{6-10} aryl which is optionally substituted by one or more groups independently selected from group P, or 5- to 10-membered heteroaryl or 3- to 10-membered heterocyclyl which is optionally substituted by one or more groups independently selected from group Q;

R_{17} represents hydrogen or C_{1-4} alkyl;

R_{18} represents C_{1-4} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-4} haloalkyl, C_{6-10} aryl which is optionally substituted by one or more groups independently selected from group P, or 5- to 10-membered heteroaryl or 3- to 10-membered heterocyclyl which is optionally substituted by one or more groups independently selected from group Q;

R_{19} represents hydrogen, C_{1-4} alkyl, C_{3-7} cycloalkyl, C_{1-4} haloalkyl, C_{6-10} aryl, or 5- to 10-

membered heteroaryl or 3- to 10-membered heterocyclyl which is optionally substituted by one or more groups independently selected from group Q;

R_{20} represents C_{1-4} alkyl, C_{3-7} cycloalkyl, C_{1-4} haloalkyl, C_{6-10} aryl, 5- to 10-membered heteroaryl, or 3- to 10-membered heterocyclyl;

R_{21} represents C_{1-4} alkyl, C_{3-7} cycloalkyl, C_{1-4} haloalkyl, C_{6-10} aryl, 5- to 10-membered heteroaryl, or 3- to 10-membered heterocyclyl;

R_{22} represents hydrogen, C_{1-4} alkyl, or C_{1-4} haloalkyl;

R_{23} represents hydrogen, C_{1-4} alkyl, C_{3-7} cycloalkyl, C_{1-4} haloalkyl, C_{6-10} aryl, 5- to 10-membered heteroaryl, or 3- to 10-membered heterocyclyl;

R_{24} represents hydrogen, C_{1-4} alkyl, or C_{1-4} haloalkyl;

R_{25} represents C_{1-4} alkyl, C_{3-7} cycloalkyl, C_{1-4} haloalkyl, C_{6-10} aryl, 5- to 10-membered heteroaryl, or 3- to 10-membered heterocyclyl;

R_{26} and R_{27}, which can be the same or different, each represents hydrogen, C_{1-4} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-4} haloalkyl, C_{1-3} alkoxyl C_{1-4} alkyl, C_{6-10} aryl, 5- to 10-membered heteroaryl, 3- to 10-membered heterocyclyl, C_{6-10} aryl C_{1-4} alkyl, 3- to 10-membered heterocyclyl C_{1-3} alkyl, 5- to 10-membered heteroaryl C_{1-3} alkyl, cyano(C_{1-3} alkyl), C_{1-3} alkylsulfonyl C_{1-4} alkyl, or 3- to 10-membered cycloaliphatic ring; or alternatively R_{26} and R_{27}, together with a nitrogen atom linked thereto, form 3- to 10-membered heterocyclyl or 5- to 10-membered heteroaryl;

R_{28} and R_{29}, which can be the same or different, each represents hydrogen, C_{1-4} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-4} haloalkyl, C_{1-3} alkoxyl C_{1-4} alkyl, C_{6-10} aryl, 5- to 10-membered heteroaryl, 3- to 10-membered heterocyclyl, C_{6-10} aryl C_{1-4} alkyl, 3- to 10-membered heterocyclyl C_{1-3} alkyl, 5- to 10-membered heteroaryl C_{1-3} alkyl, cyano(C_{1-3} alkyl), C_{1-3} alkylsulfonyl C_{1-4} alkyl, or 3- to 10-membered cycloaliphatic ring; or alternatively R_{28} and R_{29}, together with a nitrogen atom linked thereto, form 3- to 10-membered heterocyclyl or 5- to 10-membered heteroaryl;

R_{30} represents C_{1-4} alkyl, C_{3-7} cycloalkyl, C_{1-4} haloalkyl, C_{6-10} aryl, 5- to 10-membered heteroaryl, or 3- to 10-membered heterocyclyl;

R_{31} represents C_{1-4} alkyl, C_{3-7} cycloalkyl, C_{1-4} haloalkyl, C_{6-10} aryl, 5- to 10-membered heteroaryl, or 3- to 10-membered heterocyclyl;

R_{32} represents C_{1-4} alkyl or C_{6-10} aryl;

<group P>

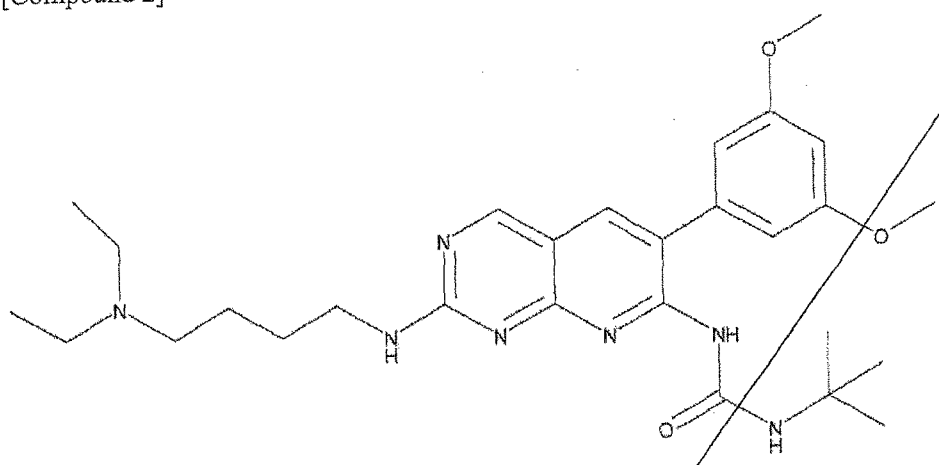
halogen, C_{1-4} alkyl, C_{1-4} haloalkyl, -OH, C_{1-3} alkoxy, C_{1-3} haloalkoxy, 3- to 10-membered heterocyclylamino, $-SO_2R_{16}$, -CN, $-NO_2$, and 3- to 10-membered heterocyclyl;

<group Q>

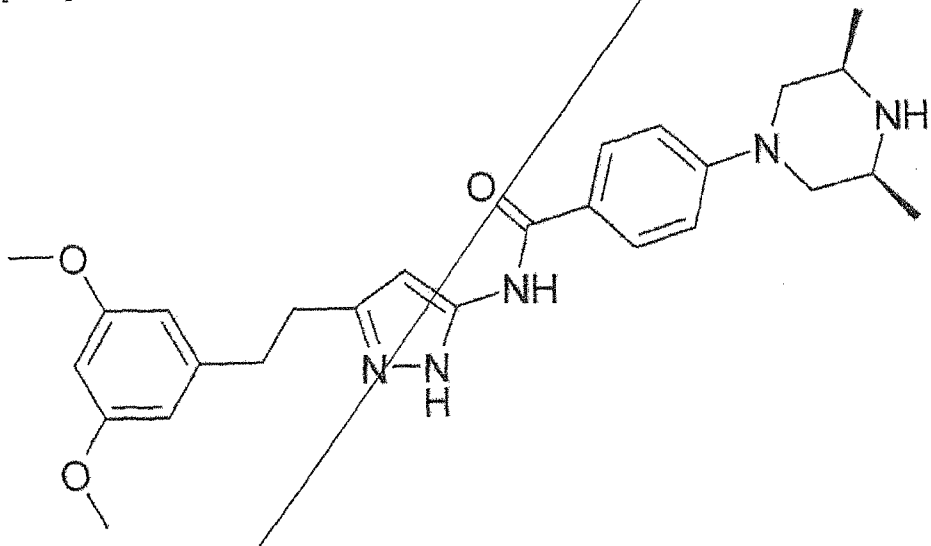
halogen, C_{1-4} alkyl, C_{1-4} haloalkyl, -OH, C_{1-3} alkoxy, C_{1-6} monohydroxy alkyl, C_{1-6} dihydroxy

alkyl, C_{1-6} trihydroxy alkyl, 3- to 10-membered heterocyclyl amine, $-SO_2R_{16}$, -CN, $-NO_2$, C_{3-7} cycloalkyl, $-COR_{19}$, and 3- to 10-membered heterocyclyl which is optionally substituted by C_{1-4} alkyl.

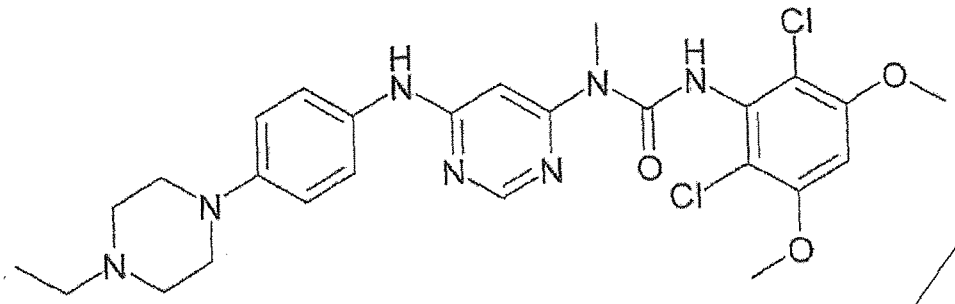
[Compound 2]



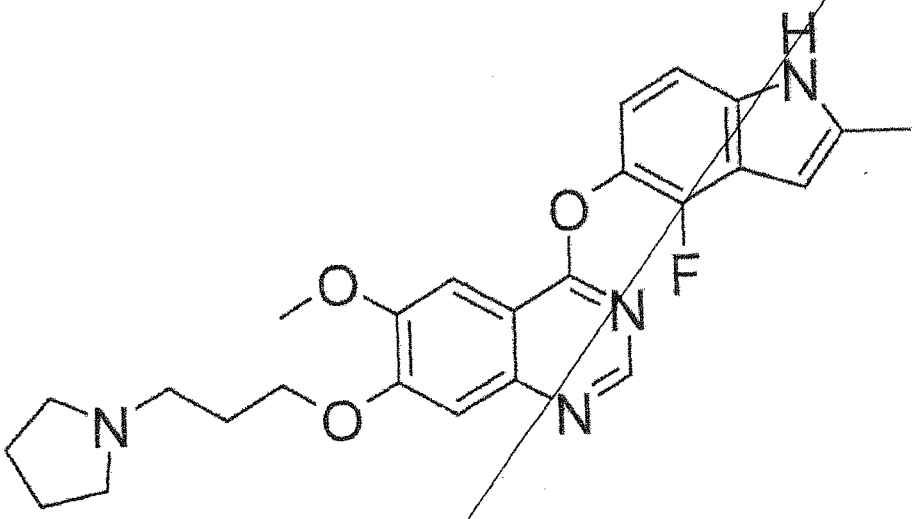
[Compound 3]



[Compound 4]

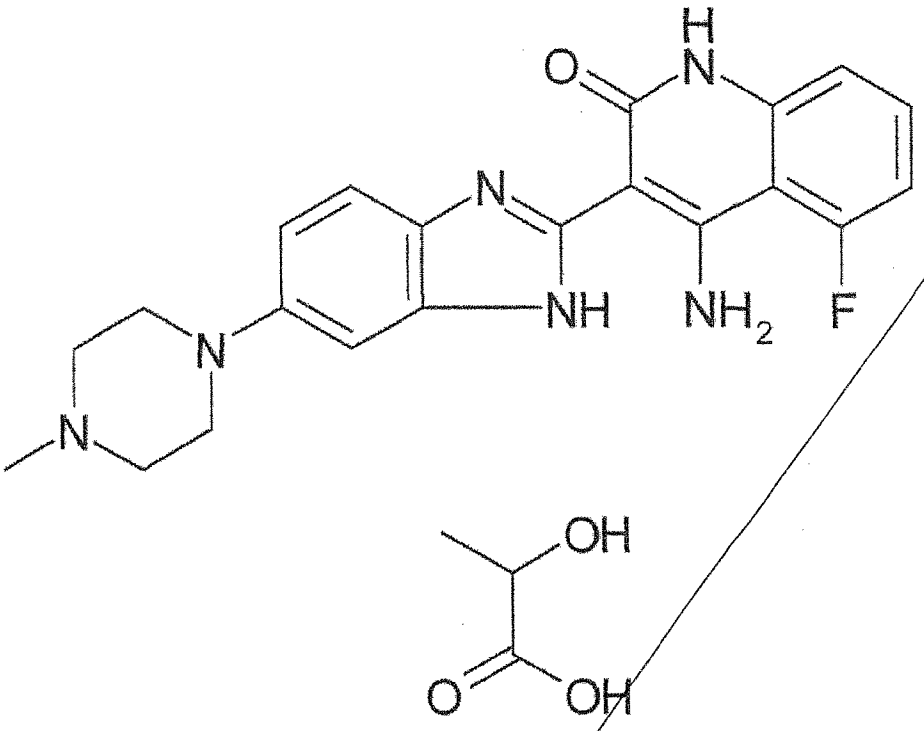


[Compound 5]



, or

[Compound 6]



58. The compound or a pharmaceutically acceptable salt thereof of claim 57, wherein the compound having FGFR inhibitory activity or a pharmaceutically acceptable salt thereof is a compound of formula (I), wherein A is indole, and R_3 and R_4 are both hydrogen, or a pharmaceutically acceptable salt thereof.

59. A method for identifying a compound having FGFR inhibitory activity, which comprises the steps of:

(a) culturing a cell that expresses the fusion polypeptide of any one of claims 1 to 7 in the presence or absence of a test compound and determining the level of cell proliferation;

(b) comparing the proliferation level of the cultured cell between in the presence and absence of the test compound; and

(c) judging that the test compound has FGFR inhibitory activity when the proliferation level of the cell cultured in the presence of the test compound is lower than that of the cell cultured in the absence of the test compound.

60. A method for identifying a compound having FGFR inhibitory activity, which comprises the steps of:

(a) administering a test compound to a non-human mammal transplanted with a cell that expresses the fusion polypeptide of any one of claims 1 to 7 and determining the proliferation level of the cell;

(b) comparing the cell proliferation level determined in step (a) with that determined using a non-human mammal transplanted with the cell but not administered with the test compound; and

(c) judging that the test compound has FGFR inhibitory activity when the cell proliferation level determined in step (a) is lower than that determined using a non-human mammal transplanted with the cell but not administered with the test compound.

61. The method of claim 59 or 60, wherein the cell is a cancer cell.

62. The method of claim 61, wherein the cancer cell is a bladder cancer cell, brain tumor cell, head and neck squamous cell carcinoma cell, lung cancer cell, lung adenocarcinoma cell, lung squamous cell carcinoma cell skin melanoma cell, esophageal cancer cell, gastric cancer cell, or liver cancer cell.

CLAIMS

1.Use of a compound having FGFR inhibitory activity or a pharmaceutically acceptable salt thereof in the manufacture of a pharmaceutical composition for cancer treatment to be administered to a patient expressing a fusion polypeptide comprising an FGFR3 polypeptide and a BAIAP2L1 polypeptide or carrying a polynucleotide encoding the fusion polypeptide,

wherein the FGFR3 polypeptide is the whole or a part of a wild-type polypeptide consisting of the amino acid sequence of SEQ ID NO: 6 or 7, or the whole or a part of a mutant polypeptide with one or more amino acid substitutions, deletions, or insertions in the wild-type polypeptide; and

wherein the BAIAP2L1 polypeptide is the whole or a part of a wild-type polypeptide consisting of the amino acid sequence of SEQ ID NO: 8, or the whole or a part of a mutant polypeptide with one or more amino acid substitutions, deletions, or insertions in the wild-type polypeptide.

2.The use of claim 1, wherein the fusion polypeptide has an activity to induce autophosphorylation of an FGFR3 polypeptide, transformation of normal cells, or tumorigenesis.

3.The use claim 1 or 2, wherein the BAIAP2L1 polypeptide:

i) is the whole or a part of a wild-type polypeptide consisting of the amino acid sequence of SEQ ID NO: 8, or the whole or a part of a mutant polypeptide with one or more amino acid substitutions, deletions, or insertions in the wild-type polypeptide; and

ii) comprises a dimerization-promoting region.

4.The use of any one of claims 1 to 3, wherein the compound or a pharmaceutically acceptable salt thereof is capable of inhibiting a growth of a cancer cell expressing the fusion polypeptide or having a nucleotide encoding the fusion polypeptide.

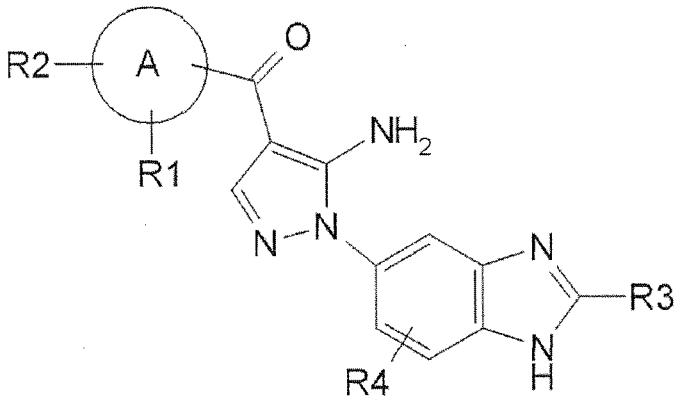
5.The use of any one of claims 1 to 4, wherein the cancer is bladder cancer, brain tumor, head and neck squamous cell carcinoma, lung cancer, lung adenocarcinoma, lung squamous cell carcinoma, skin melanoma, esophageal cancer, gastric cancer, or liver cancer.

6.The use of any one of claims 1 to 5, wherein the cancer is bladder cancer.

7.The use of claim 6, wherein the bladder cancer is classified as stage 3 or later according to TNM classification.

8.The use of any one of claims 1 to 7, wherein the compound having FGFR inhibitory activity or a pharmaceutically acceptable salt thereof is any one of the compounds or a pharmaceutically acceptable salt thereof represented by:

[Compound 1]



(I)

wherein R_1, R_2, R_3, and R_4 each independently represents the group listed below:

R_1 represents hydrogen, hydroxy, halogen, cyano, nitro, C_{1-4} haloalkyl, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-7} cycloalkyl, C_{6-10} aryl C_{1-4} alkyl, $-OR_5$, $-NR_6R_7$, $-(CR_8R_9)_nZ_1$, $-C(O)NR_{12}R_{13}$, $-SR_{14}$, $-SOR_{15}$, $-SO_2R_{16}$, $-NR_{17}SO_2R_{18}$, COOH, C_{6-10} aryl which is optionally substituted by one or more groups independently selected from group P, 5- to 10-membered heteroaryl or 3- to 10-membered heterocyclyl which is optionally substituted by one or more groups independently selected from group Q, $-COR_{19}$, $-COOR_{20}$, $-OC(O)R_{21}$, $-NR_{22}C(O)R_{23}$, $-NR_{24}C(S)R_{25}$, $-C(S)NR_{26}R_{27}$, $-SO_2NR_{28}R_{29}$, $-OSO_2R_{30}$, $-SO_3R_{31}$, or $-Si(R_{32})_3$;

R_2 represents hydrogen, hydroxy, halogen, cyano, nitro, C_{1-4} haloalkyl, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-7} cycloalkyl, C_{6-10} aryl C_{1-4} alkyl, $-OR_5$, $-NR_6R_7$, $-(CR_8R_9)_nZ_1$, $-C(O)NR_{12}R_{13}$, $-SR_{14}$, $-SOR_{15}$, $-SO_2R_{16}$, $-NR_{17}SO_2R_{18}$, COOH, C_{6-10} aryl which is optionally substituted by one or more groups independently selected from group P, 5- to 10-membered heteroaryl or 3- to 10-membered heterocyclyl which is optionally substituted by one or more groups independently selected from group Q, $-COR_{19}$, $-COOR_{20}$, $-OC(O)R_{21}$, $-NR_{22}C(O)R_{23}$, $-NR_{24}C(S)R_{25}$, $-C(S)NR_{26}R_{27}$, $-SO_2NR_{28}R_{29}$, $-OSO_2R_{30}$, $-SO_3R_{31}$, or $-Si(R_{32})_3$; or

R_1 and R_2, together with an atom linked thereto, form 3- to 10-membered heterocyclyl or 5- to 10-membered heteroaryl, wherein the heterocyclyl or heteroaryl is optionally substituted by halogen;

R_3 represents hydrogen, C_{1-5} alkyl, C_{6-10} aryl C_{1-6} alkyl, or C_{1-4} haloalkyl;

R_4 represents hydrogen, halogen, C_{1-3} alkyl, C_{1-4} haloalkyl, hydroxy, cyano, nitro, C_{1-4} alkoxy, $-(CH_2)_nZ_1$, $-NR_6R_7$, $-OR_5$, $-C(O)NR_{12}R_{13}$, $-SR_{14}$, $-SOR_{15}$, $-SO_2R_{16}$, $NR_{17}SO_2R_{18}$, COOH, $-COR_{19}$, $-COOR_{20}$, $-OC(O)R_{21}$, $-NR_{22}C(O)R_{23}$, $-NR_{24}C(S)R_{25}$, $-C(S)NR_{26}R_{27}$, $-SO_2NR_{28}R_{29}$, $-OSO_2R_{30}$, $-SO_3R_{31}$, or $-Si(R_{32})_3$;

A represents a 5- to 10-membered heteroaryl ring or C_{6-10} aryl ring;

R_5 represents C_{1-5} alkyl, C_{3-7} cycloalkyl, C_{3-7} cycloalkyl C_{1-3} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-4}

haloalkyl, C_{1-3} alkoxy C_{1-4} alkyl, C_{1-3} alkoxy C_{1-4} alkoxy C_{1-4} alkyl, C_{1-4} aminoalkyl, C_{1-4} alkylamino C_{1-4} alkyl, di(C_{1-4} alkyl)amino C_{1-4} alkyl, C_{6-10} aryl, C_{6-10} aryl C_{1-3} alkyl, or 3- to 10-membered heterocyclyl C_{1-3} alkyl, 3- to 10-membered heterocyclyl, 5- to 10-membered heteroaryl, 5- to 10-membered heteroaryl C_{1-3} alkyl, C_{1-6} monohydroxy alkyl, C_{1-6} dihydroxy alkyl, or C_{1-6} trihydroxy alkyl which is optionally substituted by one or more groups independently selected from group Q;

R_6 and R_7, which can be the same or different, each represents hydrogen, C_{1-4} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-4} haloalkyl, C_{1-3} alkoxy C_{1-4} alkyl, C_{6-10} aryl C_{1-3} alkyl, 3- to 10-membered heterocyclyl C_{1-3} alkyl, 5- to 10-membered heteroaryl C_{1-3} alkyl, C_{1-6} monohydroxy alkyl, C_{1-6} dihydroxy alkyl, C_{1-6} trihydroxy alkyl, 3- to 10-membered heterocyclyl, C_{1-4} aminoalkyl, C_{1-4} alkylamino C_{1-4} alkyl, di(C_{1-4} alkyl)amino C_{1-4} alkyl, or cyano(C_{1-3} alkyl); or alternatively R_6 and R_7, together with a nitrogen atom linked thereto, form 3- to 10-membered heterocyclyl or 5- to 10-membered heteroaryl;

n represents 1 to 3;

R_8 and R_9, which can be the same or different, each represents hydrogen, C_{1-4} alkyl, or halogen; or alternatively R_8 and R_9, together with a carbon atom linked thereto, form a cycloaliphatic ring;

Z_1 represents hydrogen, $NR_{10}R_{11}$, -OH, or 3- to 10-membered heterocyclyl or 5- to 10-membered heteroaryl which is optionally substituted by one or more groups independently selected from group Q;

R_{10} and R_{11}, which can be the same or different, each represents C_{1-4} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-4} haloalkyl, C_{1-3} alkoxy C_{1-4} alkyl, cyano(C_{1-3} alkyl), or C_{1-3} alkylsulfonyl C_{1-4} alkyl; or alternatively R_{10} and R_{11}, together with a nitrogen atom linked thereto, form 3- to 10-membered heterocyclyl or 5- to 10-membered heteroaryl;

R_{12} and R_{13}, which can be the same or different, each represents hydrogen, C_{1-4} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-4} haloalkyl, C_{1-3} alkoxy C_{1-4} alkyl, C_{6-10} aryl, 5- to 10-membered heteroaryl, 3- to 10-membered heterocyclyl, C_{6-10} aryl C_{1-4} alkyl, 3- to 10-membered heterocyclyl C_{1-3} alkyl, 5- to 10-membered heteroaryl C_{1-3} alkyl, cyano(C_{1-3} alkyl), C_{1-3} alkylsulfonyl C_{1-4} alkyl, 3- to 10-membered cycloaliphatic ring, 5- to 10-membered heteroaryl, or 3- to 10-membered heterocyclyl; or alternatively R_{12} and R_{13}, together with a nitrogen atom linked thereto, form 3- to 10-membered heterocyclyl or 5- to 10-membered heteroaryl which is optionally substituted by one or more groups independently selected from group Q;

R_{14} represents C_{1-4} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-4} haloalkyl, C_{6-10} aryl which is optionally substituted by one or more groups independently selected from group P, or 5- to 10-membered heteroaryl or 3- to 10-membered heterocyclyl which is optionally substituted by one or more groups independently selected from group Q;

R_{15} represents C_{1-4} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-4} haloalkyl, C_{6-10} aryl which is optionally substituted by one or more groups independently selected from group P, or 5- to

10-membered heteroaryl or 3- to 10-membered heterocyclyl which is optionally substituted by one or more groups independently selected from group Q;

R_{16} represents C_{1-4} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-4} haloalkyl, C_{6-10} aryl which is optionally substituted by one or more groups independently selected from group P, or 5- to 10-membered heteroaryl or 3- to 10-membered heterocyclyl which is optionally substituted by one or more groups independently selected from group Q;

R_{17} represents hydrogen or C_{1-4} alkyl;

R_{18} represents C_{1-4} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-4} haloalkyl, C_{6-10} aryl which is optionally substituted by one or more groups independently selected from group P, or 5- to 10-membered heteroaryl or 3- to 10-membered heterocyclyl which is optionally substituted by one or more groups independently selected from group Q;

R_{19} represents hydrogen, C_{1-4} alkyl, C_{3-7} cycloalkyl, C_{1-4} haloalkyl, C_{6-10} aryl, or 5- to 10-membered heteroaryl or 3- to 10-membered heterocyclyl which is optionally substituted by one or more groups independently selected from group Q;

R_{20} represents C_{1-4} alkyl, C_{3-7} cycloalkyl, C_{1-4} haloalkyl, C_{6-10} aryl, 5- to 10-membered heteroaryl, or 3- to 10-membered heterocyclyl;

R_{21} represents C_{1-4} alkyl, C_{3-7} cycloalkyl, C_{1-4} haloalkyl, C_{6-10} aryl, 5- to 10-membered heteroaryl, or 3- to 10-membered heterocyclyl;

R_{22} represents hydrogen, C_{1-4} alkyl, or C_{1-4} haloalkyl;

R_{23} represents hydrogen, C_{1-4} alkyl, C_{3-7} cycloalkyl, C_{1-4} haloalkyl, C_{6-10} aryl, 5- to 10-membered heteroaryl, or 3- to 10-membered heterocyclyl;

R_{24} represents hydrogen, C_{1-4} alkyl, or C_{1-4} haloalkyl;

R_{25} represents C_{1-4} alkyl, C_{3-7} cycloalkyl, C_{1-4} haloalkyl, C_{6-10} aryl, 5- to 10-membered heteroaryl, or 3- to 10-membered heterocyclyl;

R_{26} and R_{27}, which can be the same or different, each represents hydrogen, C_{1-4} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-4} haloalkyl, C_{1-3} alkoxyl C_{1-4} alkyl, C_{6-10} aryl, 5- to 10-membered heteroaryl, 3- to 10-membered heterocyclyl, C_{6-10} aryl C_{1-4} alkyl, 3- to 10-membered heterocyclyl C_{1-3} alkyl, 5- to 10-membered heteroaryl C_{1-3} alkyl, cyano(C_{1-3} alkyl), C_{1-3} alkylsulfonyl C_{1-4} alkyl, or 3- to 10-membered cycloaliphatic ring; or alternatively R_{26} and R_{27}, together with a nitrogen atom linked thereto, form 3- to 10-membered heterocyclyl or 5- to 10-membered heteroaryl;

R_{28} and R_{29}, which can be the same or different, each represents hydrogen, C_{1-4} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-4} haloalkyl, C_{1-3} alkoxyl C_{1-4} alkyl, C_{6-10} aryl, 5- to 10-membered heteroaryl, 3- to 10-membered heterocyclyl, C_{6-10} aryl C_{1-4} alkyl, 3- to 10-membered heterocyclyl C_{1-3} alkyl, 5- to 10-membered heteroaryl C_{1-3} alkyl, cyano(C_{1-3} alkyl), C_{1-3} alkylsulfonyl C_{1-4} alkyl, or 3- to 10-membered cycloaliphatic ring; or alternatively R_{28} and R_{29}, together with a nitrogen atom linked thereto, form 3- to 10-membered heterocyclyl or 5- to 10-membered heteroaryl;

R_{30} represents C_{1-4} alkyl, C_{3-7} cycloalkyl, C_{1-4} haloalkyl, C_{6-10} aryl, 5- to 10-membered heteroaryl, or 3- to 10-membered heterocyclyl;

R_{31} represents C_{1-4} alkyl, C_{3-7} cycloalkyl, C_{1-4} haloalkyl, C_{6-10} aryl, 5- to 10-membered heteroaryl, or 3- to 10-membered heterocyclyl;

R_{32} represents C_{1-4} alkyl or C_{6-10} aryl;

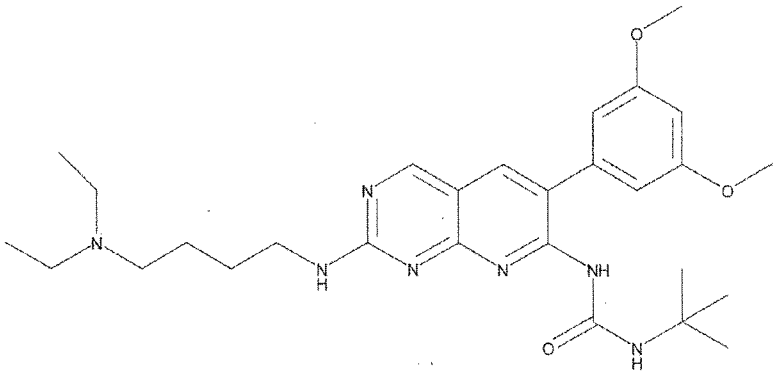
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halogen, C_{1-4} alkyl, C_{1-4} haloalkyl, -OH, C_{1-3} alkoxy, C_{1-3} haloalkoxy, 3- to 10-membered heterocyclylamino, $-SO_2R_{16}$, -CN, $-NO_2$, and 3- to 10-membered heterocyclyl;

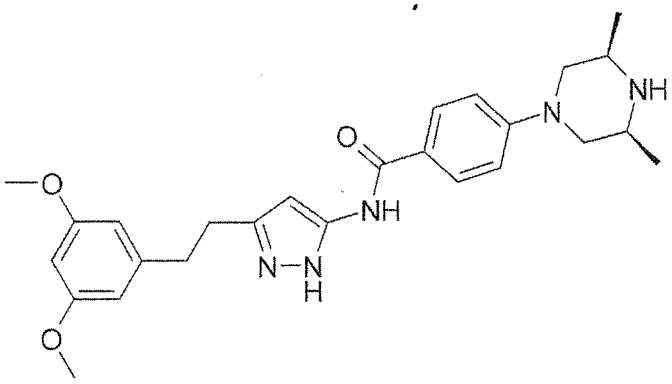
<group Q>

halogen, C_{1-4} alkyl, C_{1-4} haloalkyl, -OH, C_{1-3} alkoxy, C_{1-6} monohydroxy alkyl, C_{1-6} dihydroxy alkyl, C_{1-6} trihydroxy alkyl, 3- to 10-membered heterocyclyl amine, $-SO_2R_{16}$, -CN, $-NO_2$, C_{3-7} cycloalkyl, $-COR_{19}$, and 3- to 10-membered heterocyclyl which is optionally substituted by C_{1-4} alkyl.

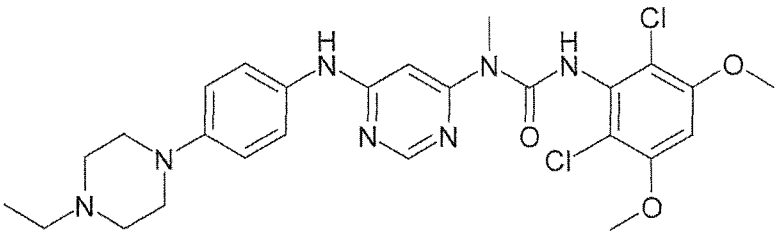
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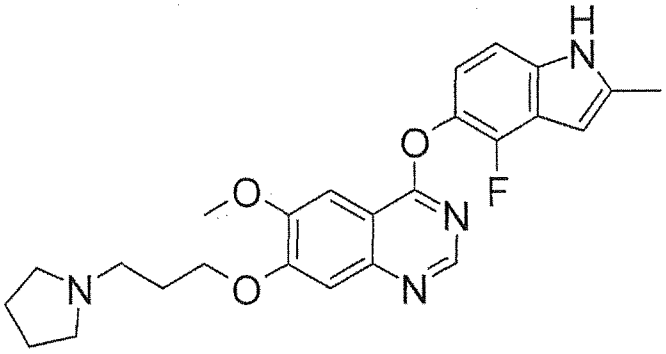
[Compound 3]



[Compound 4]

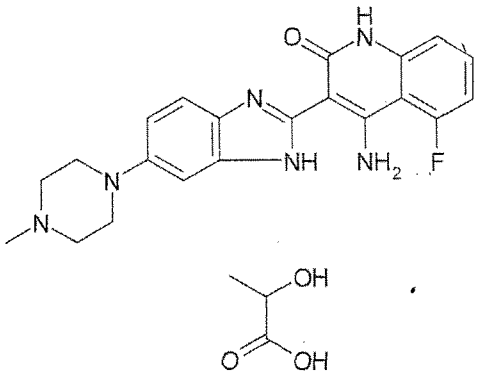


[Compound 5]



, or

[Compound 6]



9.The use of claim 8, wherein the compound having FGFR inhibitory activity or a pharmaceutically acceptable salt thereof is a compound of formula (I), wherein A is indole, and R_3 and R_4 are both hydrogen, or a pharmaceutically acceptable salt thereof.

10. The use of any one of claims 1 to 9, wherein the fusion polypeptide consists of the amino acid sequence of SEQ ID NO: 32 or 38.

11. A method for selecting a patient to which an anticancer agent comprising a compound having FGFR inhibitory activity or a pharmaceutically acceptable salt thereof is applicable, which comprises the steps of:

(a) determining the presence or absence of a fusion polypeptide comprising an FGFR3 polypeptide and a BAIAP2L1 polypeptide in a sample isolated from a subject,

wherein the FGFR3 polypeptide is the whole or a part of a wild-type polypeptide consisting of the amino acid sequence of SEQ ID NO: 6 or 7, or the whole or a part of a mutant polypeptide with one or more amino acid substitutions, deletions, or insertions in the wild-type polypeptide; and

wherein the BAIAP2L1 polypeptide is the whole or a part of a wild-type polypeptide consisting of the amino acid sequence of SEQ ID NO: 8, or the whole or a part of a mutant polypeptide with one or more amino acid substitutions, deletions, or insertions in the wild-type polypeptide; and

(b) selecting a patient confirmed to have the fusion polypeptide as a patient to which the anticancer agent is applicable.

12. The method of claim 11, wherein the fusion polypeptide has an activity to induce autophosphorylation of an FGFR3 polypeptide, transformation of normal cells, or tumorigenesis.

13. The method of claim 11 or 12, wherein the BAIAP2L1 polypeptide:

i) is the whole or a part of a wild-type polypeptide consisting of the amino acid sequence of SEQ ID NO: 8, or the whole or a part of a mutant polypeptide with one or more amino acid substitutions, deletions, or insertions in the wild-type polypeptide; and

ii) comprises a dimerization-promoting region.

14. An *ex vivo* method for selecting a patient to which an anticancer agent comprising a compound having FGFR inhibitory activity or a pharmaceutically acceptable salt thereof is applicable, which comprises the steps of:

(a) determining the presence or absence of a polynucleotide encoding a fusion polypeptide comprising an FGFR3 polypeptide and a BAIAP2L1 polypeptide in a sample isolated from a subject,

wherein the FGFR3 polypeptide is the whole or a part of a wild-type polypeptide consisting of the amino acid sequence of SEQ ID NO: 6 or 7, or the whole or a part of a mutant polypeptide with one or more amino acid substitutions, deletions, or insertions in the wild-type polypeptide; and

wherein the BAIAP2L1 polypeptide is the whole or a part of a wild-type polypeptide consisting of the amino acid sequence of SEQ ID NO: 8, or the whole or a part of a mutant polypeptide with one or more amino acid substitutions, deletions, or insertions in the wild-type polypeptide; and

(b) selecting a patient confirmed to have a polynucleotide encoding the fusion polypeptide

as a patient to which the anticancer agent is applicable.

15. The method of claim 14, wherein the fusion polypeptide has an activity to induce autophosphorylation of an FGFR3 polypeptide, transformation of normal cells, or tumorigenesis.

16. The method of claim 14 or 15, wherein the BAIAP2L1 polypeptide:

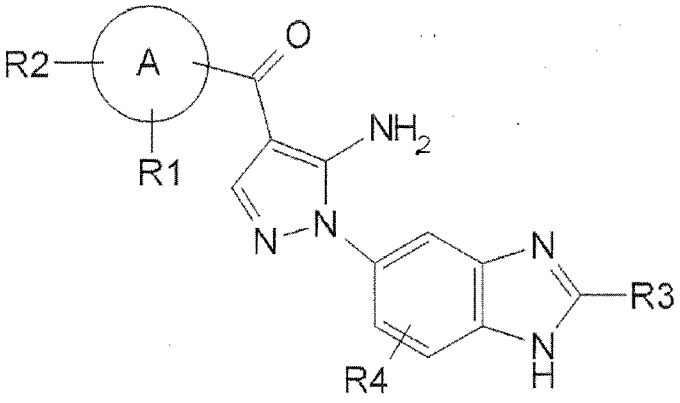
i) is the whole or a part of a wild-type polypeptide consisting of the amino acid sequence of SEQ ID NO: 8, or the whole or a part of a mutant polypeptide with one or more amino acid substitutions, deletions, or insertions in the wild-type polypeptide; and

ii) comprises a dimerization-promoting region.

17. The method of any one of claims 11 to 16, wherein the cancer is bladder cancer, brain tumor, head and neck squamous cell carcinoma, lung cancer, lung adenocarcinoma, lung squamous cell carcinoma, skin melanoma, esophageal cancer, gastric cancer, or liver cancer.

18. The method of any one of claims 11 to 17, wherein the compound having FGFR inhibitory activity or a pharmaceutically acceptable salt thereof is any one of the compounds or a pharmaceutically acceptable salt thereof represented by:

[Compound 1]



(I)

wherein R_1, R_2, R_3, and R_4 each independently represents the group listed below:

R_1 represents hydrogen, hydroxy, halogen, cyano, nitro, C_{1-4} haloalkyl, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-7} cycloalkyl, C_{6-10} aryl C_{1-4} alkyl, $-OR_5$, $-NR_6R_7$, $-(CR_8R_9)_nZ_1$, $-C(O)NR_{12}R_{13}$, $-SR_{14}$, $-SOR_{15}$, $-SO_2R_{16}$, $-NR_{17}SO_2R_{18}$, COOH, C_{6-10} aryl which is optionally substituted by one or more groups independently selected from group P, 5- to 10-membered heteroaryl or 3- to 10-membered heterocyclyl which is optionally substituted by one or more groups independently selected from group Q, $-COR_{19}$, $-COOR_{20}$, $-OC(O)R_{21}$, $-NR_{22}C(O)R_{23}$, $-NR_{24}C(S)R_{25}$, $-C(S)NR_{26}R_{27}$, $-SO_2NR_{28}R_{29}$, $-OSO_2R_{30}$, $-SO_3R_{31}$, or $-Si(R_{32})_3$;

R_2 represents hydrogen, hydroxy, halogen, cyano, nitro, C_{1-4} haloalkyl, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{3-7} cycloalkyl, C_{6-10} aryl C_{1-4} alkyl, $-OR_5$, $-NR_6R_7$, $-(CR_8R_9)_nZ_1$, $-C(O)NR_{12}R_{13}$, $-SR_{14}$, $-SOR_{15}$, $-SO_2R_{16}$, $-NR_{17}SO_2R_{18}$, COOH, C_{6-10} aryl which is optionally substituted by one or more groups independently selected from group P, 5- to 10-membered heteroaryl or 3- to 10-membered heterocyclyl which is optionally substituted by one or more groups independently selected from group Q, $-COR_{19}$, $-COOR_{20}$, $-OC(O)R_{21}$, $-NR_{22}C(O)R_{23}$, $-NR_{24}C(S)R_{25}$, $-C(S)NR_{26}R_{27}$, $-SO_2NR_{28}R_{29}$, $-OSO_2R_{30}$, $-SO_3R_{31}$, or $-Si(R_{32})_3$; or

R_1 and R_2, together with an atom linked thereto, form 3- to 10-membered heterocyclyl or 5- to 10-membered heteroaryl, wherein the heterocyclyl or heteroaryl is optionally substituted by halogen;

R_3 represents hydrogen, C_{1-5} alkyl, C_{6-10} aryl C_{1-6} alkyl, or C_{1-4} haloalkyl;

R_4 represents hydrogen, halogen, C_{1-3} alkyl, C_{1-4} haloalkyl, hydroxy, cyano, nitro, C_{1-4} alkoxy, $-(CH_2)_nZ_1$, $-NR_6R_7$, $-OR_5$, $-C(O)NR_{12}R_{13}$, $-SR_{14}$, $-SOR_{15}$, $-SO_2R_{16}$, $NR_{17}SO_2R_{18}$, COOH, $-COR_{19}$, $-COOR_{20}$, $-OC(O)R_{21}$, $-NR_{22}C(O)R_{23}$, $-NR_{24}C(S)R_{25}$, $-C(S)NR_{26}R_{27}$, $-SO_2NR_{28}R_{29}$, $-OSO_2R_{30}$, $-SO_3R_{31}$, or $-Si(R_{32})_3$;

A represents a 5- to 10-membered heteroaryl ring or C_{6-10} aryl ring;

R_5 represents C_{1-5} alkyl, C_{3-7} cycloalkyl, C_{3-7} cycloalkyl C_{1-3} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-4} haloalkyl, C_{1-3} alkoxy C_{1-4} alkyl, C_{1-3} alkoxy C_{1-4} alkoxy C_{1-4} alkyl, C_{1-4} aminoalkyl, C_{1-4} alkylamino C_{1-4} alkyl, di(C_{1-4} alkyl)amino C_{1-4} alkyl, C_{6-10} aryl, C_{6-10} aryl C_{1-3} alkyl, or 3- to 10-membered heterocyclyl C_{1-3} alkyl, 3- to 10-membered heterocyclyl, 5- to 10-membered heteroaryl, 5- to 10-membered heteroaryl C_{1-3} alkyl, C_{1-6} monohydroxy alkyl, C_{1-6} dihydroxy alkyl, or C_{1-6} trihydroxy alkyl which is optionally substituted by one or more groups independently selected from group Q;

R_6 and R_7, which can be the same or different, each represents hydrogen, C_{1-4} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-4} haloalkyl, C_{1-3} alkoxy C_{1-4} alkyl, C_{6-10} aryl C_{1-3} alkyl, 3- to 10-membered heterocyclyl C_{1-3} alkyl, 5- to 10-membered heteroaryl C_{1-3} alkyl, C_{1-6} monohydroxy alkyl, C_{1-6} dihydroxy alkyl, C_{1-6} trihydroxy alkyl, 3- to 10-membered heterocyclyl, C_{1-4} aminoalkyl, C_{1-4} alkylamino C_{1-4} alkyl, di(C_{1-4} alkyl)amino C_{1-4} alkyl, or cyano(C_{1-3} alkyl); or alternatively R_6 and R_7, together with a nitrogen atom linked thereto, form 3- to 10-membered heterocyclyl or 5- to 10-membered heteroaryl;

n represents 1 to 3;

R_8 and R_9, which can be the same or different, each represents hydrogen, C_{1-4} alkyl, or halogen; or alternatively R_8 and R_9, together with a carbon atom linked thereto, form a cycloaliphatic ring;

Z_1 represents hydrogen, $NR_{10}R_{11}$, -OH, or 3- to 10-membered heterocyclyl or 5- to 10-membered heteroaryl which is optionally substituted by one or more groups independently selected from group Q;

R_{10} and R_{11}, which can be the same or different, each represents C_{1-4} alkyl, C_{2-6} alkenyl,

C_{2-6} alkynyl, C_{1-4} haloalkyl, C_{1-3} alkoxy C_{1-4} alkyl, cyano(C_{1-3} alkyl), or C_{1-3} alkylsulfonyl C_{1-4} alkyl; or alternatively R_{10} and R_{11}, together with a nitrogen atom linked thereto, form 3- to 10-membered heterocyclyl or 5- to 10-membered heteroaryl;

R_{12} and R_{13}, which can be the same or different, each represents hydrogen, C_{1-4} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-4} haloalkyl, C_{1-3} alkoxy C_{1-4} alkyl, C_{6-10} aryl, 5- to 10-membered heteroaryl, 3- to 10-membered heterocyclyl, C_{6-10} aryl C_{1-4} alkyl, 3- to 10-membered heterocyclyl C_{1-3} alkyl, 5- to 10-membered heteroaryl C_{1-3} alkyl, cyano(C_{1-3} alkyl), C_{1-3} alkylsulfonyl C_{1-4} alkyl, 3- to 10-membered cycloaliphatic ring, 5- to 10-membered heteroaryl, or 3- to 10-membered heterocyclyl; or alternatively R_{12} and R_{13}, together with a nitrogen atom linked thereto, form 3- to 10-membered heterocyclyl or 5- to 10-membered heteroaryl which is optionally substituted by one or more groups independently selected from group Q;

R_{14} represents C_{1-4} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-4} haloalkyl, C_{6-10} aryl which is optionally substituted by one or more groups independently selected from group P, or 5- to 10-membered heteroaryl or 3- to 10-membered heterocyclyl which is optionally substituted by one or more groups independently selected from group Q;

R_{15} represents C_{1-4} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-4} haloalkyl, C_{6-10} aryl which is optionally substituted by one or more groups independently selected from group P, or 5- to 10-membered heteroaryl or 3- to 10-membered heterocyclyl which is optionally substituted by one or more groups independently selected from group Q;

R_{16} represents C_{1-4} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-4} haloalkyl, C_{6-10} aryl which is optionally substituted by one or more groups independently selected from group P, or 5- to 10-membered heteroaryl or 3- to 10-membered heterocyclyl which is optionally substituted by one or more groups independently selected from group Q;

R_{17} represents hydrogen or C_{1-4} alkyl;

R_{18} represents C_{1-4} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-4} haloalkyl, C_{6-10} aryl which is optionally substituted by one or more groups independently selected from group P, or 5- to 10-membered heteroaryl or 3- to 10-membered heterocyclyl which is optionally substituted by one or more groups independently selected from group Q;

R_{19} represents hydrogen, C_{1-4} alkyl, C_{3-7} cycloalkyl, C_{1-4} haloalkyl, C_{6-10} aryl, or 5- to 10-membered heteroaryl or 3- to 10-membered heterocyclyl which is optionally substituted by one or more groups independently selected from group Q;

R_{20} represents C_{1-4} alkyl, C_{3-7} cycloalkyl, C_{1-4} haloalkyl, C_{6-10} aryl, 5- to 10-membered heteroaryl, or 3- to 10-membered heterocyclyl;

R_{21} represents C_{1-4} alkyl, C_{3-7} cycloalkyl, C_{1-4} haloalkyl, C_{6-10} aryl, 5- to 10-membered heteroaryl, or 3- to 10-membered heterocyclyl;

R_{22} represents hydrogen, C_{1-4} alkyl, or C_{1-4} haloalkyl;

R_{23} represents hydrogen, C_{1-4} alkyl, C_{3-7} cycloalkyl, C_{1-4} haloalkyl, C_{6-10} aryl, 5- to 10-membered heteroaryl, or 3- to 10-membered heterocyclyl;

R_{24} represents hydrogen, C_{1-4} alkyl, or C_{1-4} haloalkyl;

R_{25} represents C_{1-4} alkyl, C_{3-7} cycloalkyl, C_{1-4} haloalkyl, C_{6-10} aryl, 5- to 10-membered heteroaryl, or 3- to 10-membered heterocyclyl;

R_{26} and R_{27}, which can be the same or different, each represents hydrogen, C_{1-4} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-4} haloalkyl, C_{1-3} alkoxyl C_{1-4} alkyl, C_{6-10} aryl, 5- to 10-membered heteroaryl, 3- to 10-membered heterocyclyl, C_{6-10} aryl C_{1-4} alkyl, 3- to 10-membered heterocyclyl C_{1-3} alkyl, 5- to 10-membered heteroaryl C_{1-3} alkyl, cyano(C_{1-3} alkyl), C_{1-3} alkylsulfonyl C_{1-4} alkyl, or 3- to 10-membered cycloaliphatic ring; or alternatively R_{26} and R_{27}, together with a nitrogen atom linked thereto, form 3- to 10-membered heterocyclyl or 5- to 10-membered heteroaryl;

R_{28} and R_{29}, which can be the same or different, each represents hydrogen, C_{1-4} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, C_{1-4} haloalkyl, C_{1-3} alkoxyl C_{1-4} alkyl, C_{6-10} aryl, 5- to 10-membered heteroaryl, 3- to 10-membered heterocyclyl, C_{6-10} aryl C_{1-4} alkyl, 3- to 10-membered heterocyclyl C_{1-3} alkyl, 5- to 10-membered heteroaryl C_{1-3} alkyl, cyano(C_{1-3} alkyl), C_{1-3} alkylsulfonyl C_{1-4} alkyl, or 3- to 10-membered cycloaliphatic ring; or alternatively R_{28} and R_{29}, together with a nitrogen atom linked thereto, form 3- to 10-membered heterocyclyl or 5- to 10-membered heteroaryl;

R_{30} represents C_{1-4} alkyl, C_{3-7} cycloalkyl, C_{1-4} haloalkyl, C_{6-10} aryl, 5- to 10-membered heteroaryl, or 3- to 10-membered heterocyclyl;

R_{31} represents C_{1-4} alkyl, C_{3-7} cycloalkyl, C_{1-4} haloalkyl, C_{6-10} aryl, 5- to 10-membered heteroaryl, or 3- to 10-membered heterocyclyl;

R_{32} represents C_{1-4} alkyl or C_{6-10} aryl;

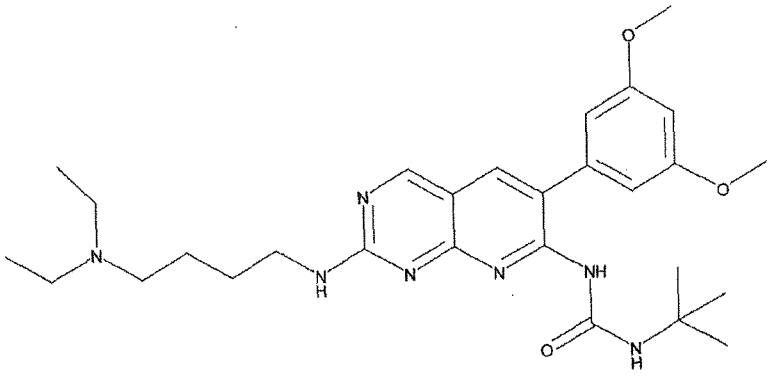
<group P>

halogen, C_{1-4} alkyl, C_{1-4} haloalkyl, -OH, C_{1-3} alkoxy, C_{1-3} haloalkoxy, 3- to 10-membered heterocyclylamino, $-SO_2R_{16}$, -CN, $-NO_2$, and 3- to 10-membered heterocyclyl;

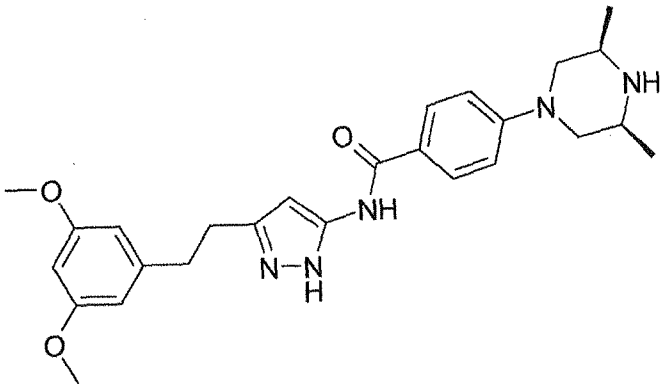
<group Q>

halogen, C_{1-4} alkyl, C_{1-4} haloalkyl, -OH, C_{1-3} alkoxy, C_{1-6} monohydroxy alkyl, C_{1-6} dihydroxy alkyl, C_{1-6} trihydroxy alkyl, 3- to 10-membered heterocyclyl amine, $-SO_2R_{16}$, -CN, $-NO_2$, C_{3-7} cycloalkyl, $-COR_{19}$, and 3- to 10-membered heterocyclyl which is optionally substituted by C_{1-4} alkyl.

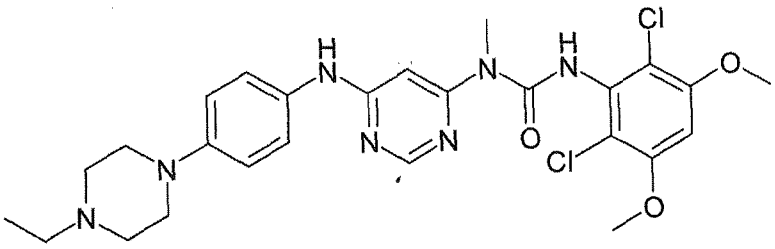
[Compound 2]



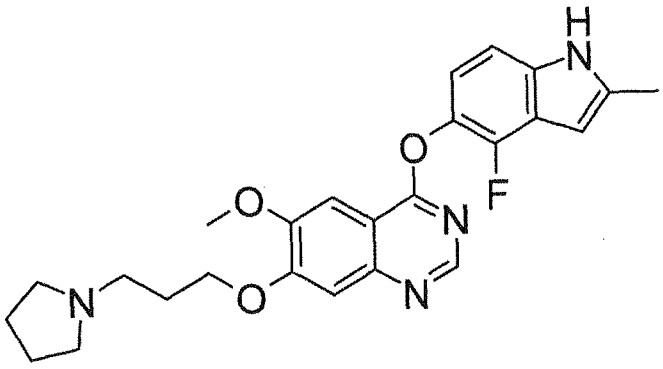
[Compound 3]



[Compound 4]

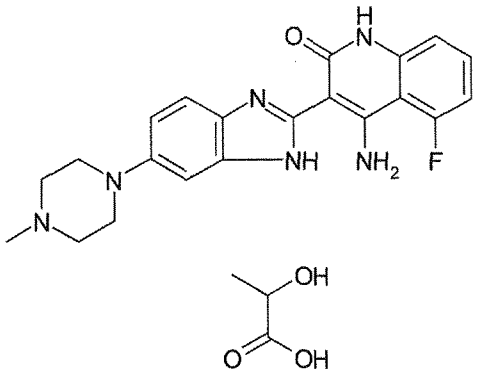


[Compound 5]



, or

[Compound 6]



19. The method of claim 18, wherein the compound having FGFR inhibitory activity or a pharmaceutically acceptable salt thereof is a compound of formula (I), wherein A is indole, and R_3 and R_4 are both hydrogen, or a pharmaceutically acceptable salt thereof.

20. The method of any one of claims 11 to 19, wherein the fusion polypeptide consists of the amino acid sequence of SEQ ID NO: 32 or 38.

21. An *ex vivo* method for testing cancer susceptibility of a subject, whether a subject is affected with cancer, or whether cancer has progressed in a subject by determining the presence or absence of a fusion polypeptide comprising an FGFR3 polypeptide and a BAIAP2L1 polypeptide in a sample isolated from the subject,

wherein the FGFR3 polypeptide is the whole or a part of a wild-type polypeptide consisting of the amino acid sequence of SEQ ID NO: 6 or 7, or the whole or a part of a mutant polypeptide with one or more amino acid substitutions, deletions, or insertions in the wild-type polypeptide;

wherein the BAIAP2L1 polypeptide is the whole or a part of a wild-type polypeptide consisting of the amino acid sequence of SEQ ID NO: 8, or the whole or a part of a mutant polypeptide with one or more amino acid substitutions, deletions, or insertions in the wild-type polypeptide;

wherein the method is based on the criterion that a subject is more likely to develop cancer, is affected with cancer, or has progressed cancer when the fusion polypeptide is detected.

22. The method of claim 21, wherein the fusion polypeptide has an activity to induce autophosphorylation of an FGFR3 polypeptide, transformation of normal cells, or tumorigenesis.

23. The method of claim 21 or 22, wherein the BAIAP2L1 polypeptide:

i) is the whole or a part of a wild-type polypeptide consisting of the amino acid sequence of SEQ ID NO: 8, or the whole or a part of a mutant polypeptide with one or more amino acid substitutions, deletions, or insertions in the wild-type polypeptide; and

ii) comprises a dimerization-promoting region.

24. An *ex vivo* method for testing cancer susceptibility of a subject, whether a subject is affected with cancer, or whether cancer has progressed in a subject by determining the presence or absence of a polynucleotide encoding a fusion polypeptide comprising an FGFR3 polypeptide and a BAIAP2L1 polypeptide in a sample isolated from the subject,

wherein the FGFR3 polypeptide is the whole or a part of a wild-type polypeptide consisting of the amino acid sequence of SEQ ID NO: 6 or 7, or the whole or a part of a mutant polypeptide with one or more amino acid substitutions, deletions, or insertions in the wild-type polypeptide;

wherein the BAIAP2L1 polypeptide is the whole or a part of a wild-type polypeptide consisting of the amino acid sequence of SEQ ID NO: 8, or the whole or a part of a mutant polypeptide with one or more amino acid substitutions, deletions, or insertions in the wild-type polypeptide; and

wherein the method is based on the criterion that a subject is more likely to develop cancer, is affected with cancer, or has progressed cancer when the polynucleotide encoding the fusion polypeptide is detected.

25. The method of claim 24, wherein the fusion polypeptide has an activity to induce autophosphorylation of an FGFR3 polypeptide, transformation of normal cells, or tumorigenesis.

26. The method of claim 24 or 25, wherein the BAIAP2L1 polypeptide:

i) is the whole or a part of a wild-type polypeptide consisting of the amino acid sequence of SEQ ID NO: 8, or the whole or a part of a mutant polypeptide with one or more amino acid substitutions, deletions, or insertions in the wild-type polypeptide; and

ii) comprises a dimerization-promoting region.

27. The method of any one of claims 21 to 26, wherein the cancer is bladder cancer, brain tumor, head and neck squamous cell carcinoma, lung cancer, lung adenocarcinoma, lung squamous cell carcinoma, skin melanoma, esophageal cancer, gastric cancer, or liver cancer.

28. The method of any one of claims 21 to 27, wherein the fusion polypeptide consists of the amino acid sequence of SEQ ID NO: 32 or 38.

29. A fusion polypeptide comprising an FGFR3 polypeptide and a BAIAP2L1 polypeptide:

wherein the FGFR3 polypeptide is the whole or a part of a wild-type polypeptide consisting of the amino acid sequence of SEQ ID NO: 6 or 7, or the whole or a part of a mutant polypeptide with one or more amino acid substitutions, deletions, or insertions in the wild-type polypeptide; and

the BAIAP2L1 polypeptide is the whole or a part of a wild-type polypeptide consisting of the amino acid sequence of SEQ ID NO: 8, or the whole or a part of a mutant polypeptide with one or more amino acid substitutions, deletions, or insertions in the wild-type polypeptide.

30. The fusion polypeptide of claim 29, wherein the fusion polypeptide has an activity to induce autophosphorylation of an FGFR3 polypeptide, transformation of normal cells, or tumorigenesis.

31. The fusion polypeptide of claim 29 or 30, wherein the BAIAP2L1 polypeptide:

i) is the whole or a part of a wild-type polypeptide consisting of the amino acid sequence of SEQ ID NO: 8, or the whole or a part of a mutant polypeptide with one or more amino acid substitutions, deletions, or insertions in the wild-type polypeptide; and

ii) comprises a dimerization-promoting region.

32. The fusion polypeptide of claim 31, wherein the fusion polypeptide consists of the amino acid sequence of SEQ ID NO: 32 or 38.

33. The fusion polypeptide of any one of claims 29 to 32, wherein the fusion polypeptide is derived from bladder cancer or lung cancer.

34. A polynucleotide encoding the fusion polypeptide of any one of claims 29 to 33.

35. The polynucleotide of claim 34, which comprises the nucleotide sequence of SEQ ID NO: 16.

36. The polynucleotide of claim 35, which comprises the nucleotide sequence of SEQ ID NO:31 or 37.

37. A vector comprising the polynucleotide of any one of claims 34 to 36.

38. A recombinant cell comprising the vector of claim 37.

39. An antibody or antigen-binding fragment thereof which specifically binds to the fusion polypeptide of any one of claims 29 to 33.

40. A pair of oligonucleotide primers consisting of sense and antisense primers each hybridizing to a polynucleotide encoding the fusion polypeptide of any one of claims 29 to 33 for detecting or amplifying the polynucleotide.

41. An oligonucleotide that binds to an mRNA polynucleotide encoding the fusion polypeptide of any one of claims 29 to 33 and has an activity to inhibit translation of the mRNA polynucleotide into protein.

42. The oligonucleotide of claim 41, which is an siRNA that cleaves the mRNA polynucleotide.

43. A pharmaceutical composition comprising the antibody or antigen-binding fragment thereof of claim 39.

44. A pharmaceutical composition comprising the oligonucleotide of claim 41 or 42.

45. An *in vitro* method for detecting a fusion polypeptide that comprises an FGFR3 polypeptide and a BAIAP2L1 polypeptide, which comprises the step of detecting the fusion polypeptide in a sample isolated from a subject by using an antibody or antigen-binding fragment thereof that binds to the fusion polypeptide of any one of claims 29 to 33.

46. An *in vitro* method for detecting a polynucleotide encoding a fusion polypeptide that comprises an FGFR3 polypeptide and a BAIAP2L1 polypeptide, which comprises the step of detecting a polynucleotide encoding the fusion polypeptide in a sample isolated from a subject by using a pair of oligonucleotide primers consisting of sense and antisense primers each hybridizing to a polynucleotide encoding the fusion polypeptide of any one of claims 29 to 33 for detecting or amplifying the polynucleotide.

47. A kit for detecting a polynucleotide encoding a fusion polypeptide that

comprises an FGFR3 polypeptide and a BAIAP2L1 polypeptide, which comprises a pair of oligonucleotide primers consisting of sense and antisense primers each hybridizing to a polynucleotide encoding the fusion polypeptide of any one of claims 29 to 33 for detecting or amplifying the polynucleotide.

48. A kit for detecting a fusion polypeptide that comprises an FGFR3 polypeptide and a BAIAP2L1 polypeptide, which comprises an antibody or antigen-binding fragment thereof that binds to the fusion polypeptide of any one of claims 29 to 33.

(Non-patent Document 2); gene mutation is observed in bladder cancer (Non-patent Document 3); and overexpression is observed in ovarian cancer, non-small cell lung carcinoma, and hepatocellular carcinoma.

The findings described above suggest a connection between FGFR and cancer. Thus, attempts have been made to develop compounds with FGFR inhibitory activity as anticancer agents (Non-patent Documents 4 and 5).

While it has been reported very recently that genetic translocation that suggests the presence of a fusion polypeptide of FGFR3 and transforming acidic coiled-coil protein 3 (TACC3) or a fusion polypeptide of FGFR1 and TACC1 was found in very few cases of brain tumor glioblastoma multiforme (GBM) (three of 97 samples, 3.1%) (Non-patent Document 6), the connection between fusion polypeptides of FGFR with other proteins and other types of cancer remains unclear.

Prior Art Documents

[Non-patent Documents]

[Non-patent Document 1] Cytokine & Growth Factor Reviews, 2005, 16: 139-149
[Non-patent Document 2] Blood, 2003, 101: 4569-4575
[Non-patent Document 3] Nature Genetics, 1999 Sep., 23(1): 18-20
[Non-patent Document 4] Cancer Research, 2012, 72: 2045-2056
[Non-patent Document 5] J. Med. Chem., 2011, 54: 7066-7083
[Non-patent Document 6] Science, Vol. 337, Issue 6099, 7 September 2012: 1231-1235

Summary of the Invention

[Problems to be Solved by the Invention]

In view of the above circumstances, the present invention aims to identify and provide cancer cell-specific molecules that can be used as a biomarker to enable personalized medicine for FGFR inhibitor-based cancer therapy, and cancer cell-specific molecules that are useful in development of molecularly targeted drugs targeting FGFR, as well as to provide various materials and methods to be used in personalized medicine and development of molecularly targeted drugs that utilize such molecules as a biomarker or molecular target.

Thus, in a first aspect, the present invention refers to the use of a compound having FGFR inhibitory activity or a pharmaceutically acceptable salt thereof in the manufacture of a pharmaceutical composition for cancer treatment to be administered to a patient expressing a fusion polypeptide comprising an FGFR3 polypeptide and a BAIAP2L1 polypeptide or carrying a polynucleotide encoding the fusion polypeptide, wherein the FGFR3 polypeptide is the whole or a part of a wild-type polypeptide consisting of the amino acid sequence of SEQ ID NO: 6 or 7, or the whole or a part of a mutant polypeptide with one or more amino acid substitutions, deletions, or insertions in the wild-type polypeptide; and wherein the BAIAP2L1 polypeptide is the whole or a part of a wild-type polypeptide consisting of the amino acid sequence of SEQ ID NO: 8, or the whole or a part of a mutant polypeptide with one or more amino acid substitutions, deletions, or insertions in the wild-type polypeptide.

In a second aspect, the present invention refers to a method for selecting a patient to which an anticancer agent comprising a compound having FGFR inhibitory activity or a pharmaceutically acceptable salt thereof is applicable, which comprises the steps of: (a determining the presence or absence of a fusion polypeptide comprising an FGFR3 polypeptide and a BAIAP2L1 polypeptide in a sample isolated from a subject, wherein the FGFR3 polypeptide is the whole or a part of a wild-type polypeptide consisting of the amino acid sequence of SEQ ID NO: 6 or 7, or the whole or a part of a mutant polypeptide with one

or more amino acid substitutions, deletions, or insertions in the wild-type polypeptide; and wherein the BAIAP2L1 polypeptide is the whole or a part of a wild-type polypeptide consisting of the amino acid sequence of SEQ ID NO: 8, or the whole or a part of a mutant polypeptide with one or more amino acid substitutions, deletions, or insertions in the wild-type polypeptide; and (b) selecting a patient confirmed to have the fusion polypeptide as a patient to which the anticancer agent is applicable.

In a third aspect, the present invention refers to an *ex vivo* method for selecting a patient to which an anticancer agent comprising a compound having FGFR inhibitory activity or a pharmaceutically acceptable salt thereof is applicable, which comprises the steps of: (a) determining the presence or absence of a polynucleotide encoding a fusion polypeptide comprising an FGFR3 polypeptide and a BAIAP2L1 polypeptide in a sample isolated from a subject, wherein the FGFR3 polypeptide is the whole or a part of a wild-type polypeptide consisting of the amino acid sequence of SEQ ID NO: 6 or 7, or the whole or a part of a mutant polypeptide with one or more amino acid substitutions, deletions, or insertions in the wild-type polypeptide; and wherein the BAIAP2L1 polypeptide is the whole or a part of a wild-type polypeptide consisting of the amino acid sequence of SEQ ID NO: 8, or the whole or a part of a mutant polypeptide with one or more amino acid substitutions, deletions, or insertions in the wild-type polypeptide; and (b) selecting a patient confirmed to have a polynucleotide encoding the fusion polypeptide as a patient to which the anticancer agent is applicable.

In a fourth aspect, the present invention refers to an *ex vivo* method for testing cancer susceptibility of a subject, whether a subject is affected with cancer, or whether cancer has progressed in a subject by determining the presence or absence of a fusion polypeptide comprising an FGFR3 polypeptide and a BAIAP2L1 polypeptide in a sample isolated from the subject, wherein the FGFR3 polypeptide is the whole or a part of a wild-type polypeptide consisting of the amino acid sequence of SEQ ID NO: 6 or 7, or the whole or a part of a mutant polypeptide with one or more amino acid substitutions, deletions, or insertions in the wild-type polypeptide; wherein the BAIAP2L1 polypeptide is the whole or a part of a wild-type polypeptide consisting of the amino acid sequence of SEQ ID NO: 8, or the whole or a part of a mutant polypeptide with one or more amino acid substitutions, deletions, or insertions in the wild-type polypeptide; wherein the method is based on the criterion that a subject is more likely to develop cancer, is affected with cancer, or has progressed cancer when the fusion polypeptide is detected.

In a fifth aspect, the present invention refers to an *ex vivo* method for testing cancer susceptibility of a subject, whether a subject is affected with cancer, or whether cancer has progressed in a subject by determining the presence or absence of a polynucleotide encoding a fusion polypeptide comprising an FGFR3 polypeptide and a BAIAP2L1 polypeptide in a sample isolated from the subject, wherein the FGFR3 polypeptide is the whole or a part of a wild-type polypeptide consisting of the amino acid sequence of SEQ ID NO: 6 or 7, or the whole or a part of a mutant polypeptide with one or more amino acid substitutions, deletions, or insertions in the wild-type polypeptide; wherein the BAIAP2L1 polypeptide is the whole or a part of a wild-type polypeptide consisting of the amino acid sequence of SEQ ID NO: 8, or the whole or a part of a mutant polypeptide with one or more amino acid substitutions, deletions, or insertions in the wild-type polypeptide; and wherein the method is based on the criterion that a subject is more likely to develop cancer, is affected with cancer, or has progressed cancer when the polynucleotide encoding the fusion polypeptide is detected.

In a sixth aspect, the present invention refers to a fusion polypeptide comprising an FGFR3 polypeptide and a BAIAP2L1 polypeptide: wherein the FGFR3 polypeptide is the whole or a part of a wild-type polypeptide consisting of the amino acid sequence of SEQ ID NO: 6 or 7, or the whole or a part of a mutant polypeptide with one or more amino acid substitutions, deletions, or insertions in the wild-type polypeptide; and the BAIAP2L1 polypeptide is the whole or a part of a wild-type

polypeptide consisting of the amino acid sequence of SEQ ID NO: 8, or the whole or a part of a mutant polypeptide with one or more amino acid substitutions, deletions, or insertions in the wild-type polypeptide.

In a seventh aspect, the present invention refers to a polynucleotide encoding the fusion polypeptide of the present invention.

In an eighth aspect, the present invention refers to a vector comprising the polynucleotide of the present invention.

In a ninth aspect, the present invention refers to a recombinant cell comprising the vector of the present invention.

In a tenth aspect, the present invention refers to an antibody or antigen-binding fragment thereof which specifically binds to the fusion polypeptide of the present invention.

In an eleventh aspect, the present invention refers to a pair of oligonucleotide primers consisting of sense and antisense primers each hybridizing to a polynucleotide encoding the fusion polypeptide of the present invention for detecting or amplifying the polynucleotide.

In a twelve aspect, the present invention refers to an oligonucleotide that binds to an mRNA polynucleotide encoding the fusion polypeptide of the present invention and has an activity to inhibit translation of the mRNA polynucleotide into protein.

In a thirteen aspect, the present invention refers to a pharmaceutical composition comprising the antibody or antigen-binding fragment thereof of the present invention.

In a fourteen aspect, the present invention refers to a pharmaceutical composition comprising the oligonucleotide of the present invention.

In a fifteen aspect, the present invention refers to an *in vitro* method for detecting a fusion polypeptide that comprises an FGFR3 polypeptide and a BAIAP2L1 polypeptide, which comprises the step of detecting the fusion polypeptide in a sample isolated from a subject by using an antibody or antigen-binding fragment thereof that binds to the fusion polypeptide of the present invention.

In a sixteen aspect, the present invention refers to an *in vitro* method for detecting a polynucleotide encoding a fusion polypeptide that comprises an FGFR3 polypeptide and a BAIAP2L1 polypeptide, which comprises the step of detecting a polynucleotide encoding the fusion polypeptide in a sample isolated from a subject by using a pair of oligonucleotide primers consisting of sense and antisense primers each hybridizing to a polynucleotide encoding the fusion polypeptide of the present invention for detecting or amplifying the polynucleotide.

In a seventeen aspect, the present invention refers to a kit for detecting a polynucleotide encoding a fusion polypeptide that comprises an FGFR3 polypeptide and a BAIAP2L1 polypeptide, which comprises a pair of oligonucleotide primers consisting of sense and antisense primers each hybridizing to a polynucleotide encoding the fusion polypeptide of the present invention for detecting or amplifying the polynucleotide.

In an eighteen aspect, the present invention refers to a kit for detecting a fusion polypeptide that comprises an FGFR3 polypeptide and a BAIAP2L1 polypeptide, which comprises an antibody or antigen-binding fragment thereof that binds to the fusion polypeptide of the present invention.

[Means for Solving the Problems]

As mentioned above, a connection between FGFR and cancer has been suggested; however, connections between fusion proteins of FGFR with other proteins and various types of cancer remain unrevealed.

To achieve the above-described objective, the present inventors conducted dedicated

derived from ~~bladder~~ lung cancer samples collected from lung cancer patients (40 patients) and cDNA synthesized from SW780 RNA.

View A shows a result of the test using a pair of oligonucleotide primers (SEQ ID NOs: 3 and 4). The leftmost lanes on the top and bottom gels show the results for molecular-weight markers.

View B shows a result of the test using a pair of oligonucleotide primers (SEQ ID NOs: 17 and 18).

The leftmost lanes on the top and bottom gels show the results for molecular-weight markers.

Fig. 5 is a photograph showing results of detecting a polynucleotide encoding a FGFR3-BAIAP2L1 polypeptide in various types of bladder cancer cell lines tested by FISH analysis.

View A1 shows a test result of the RT112/84 cell line using a split-signal probe.

View A2 shows a test result of the SW780 cell line using a split-signal probe.

View B1 shows a test result of the RT112/84 cell line using a fusion-signal probe.

View B2 shows a test result of the SW780 cell line using a fusion-signal probe.

Fig. 6 shows results of testing the presence or absence of FGFR3 dependency in the proliferation of various bladder cancer cell lines using siRNA against FGFR3 or BAIAP2L1.

View A shows a result of the test using the BFTC-905 cell line.

View B shows a result of the test using the UM-UC-14 cell line.

View C shows a result of the test using the RT4 cell line.

View D shows a result of the test using the SW780 cell line.

Fig. 7 shows results of testing the effect of FGFR inhibitors in inducing apoptosis in various cancer cells expressing the FGFR3-BAIAP2L1 fusion polypeptide.

Fig. 8 shows results of examining the ability of the FGFR3-BAIAP2L1 fusion polypeptide to transform normal cells by testing the cells in monolayer culture.

The upper figure shows a result of wild-type FGFR3-expressing cells in monolayer culture.

The lower figure shows a result of FGFR3-BAIAP2L1 fusion polypeptide-expressing cells in monolayer culture.

Fig. 9 shows results of examining the transforming ability and tumorigenic ability of the FGFR3-BAIAP2L1 fusion polypeptide in normal cells by testing the cells in spheroid culture.

The upper row photographs show results of culturing the untreated parent cells.

The middle row photographs show results of culturing the wild-type FGFR3-expressing cells.

The lower row photographs show results of culturing the FGFR3-BAIAP2L1 fusion polypeptide-expressing cells.

Fig. 10 presents photographs showing results of examining the ability of the FGFR3-BAIAP2L1 fusion polypeptide to transform normal cells and the contribution of BAIAP2L1 to the transforming ability, by performing tests using the autophosphorylation ability of FGFR3 as an indicator.

in that whether a patient expresses the fusion polypeptide or carries a polynucleotide encoding the fusion polypeptide is tested using a fusion polypeptide of the present invention as a biomarker before an above-described anticancer agent comprising an FGFR inhibitor is administered to the patient, and the anticancer agent containing an FGFR inhibitor is administered to the patient only if the patient expresses the fusion polypeptide or carries a polynucleotide encoding the fusion polypeptide. This enables one to avoid side effects in therapies using the agent and control the therapeutic condition to produce the best therapeutic effect, thus enabling personalized medicine.

In the present invention, specifically in the case of bladder cancer, the fusion genes of the present invention are found to be significantly expressed when bladder cancer progresses to stage 3 or later in stage classification.

Stage classification of bladder cancer is, specifically, classification by TNM classification. TNM classification is composed of a T factor (initial of tumor) showing the extent of tumor, an N factor (initial of lymph node) showing the presence or absence of lymph node metastasis of tumor, and an M factor (initial of metastasis) showing the presence or absence of distal metastasis other than lymph node metastasis. Among them, cancers in which the tumor has infiltrated into the subepithelial connective tissue are classified as stage 1, those in which the tumor has infiltrated into muscularis propria are classified as stage 2, those in which the tumor has infiltrated into the fatty tissue surrounding the bladder to those in which the tumor has infiltrated into any one of prostate interstitium, uterus, or vagina are classified as stage 3, and those in which the tumor has infiltrated into either the pelvic wall or the ~~subwall~~abdomen wall, or those that show lymph node metastasis or distal metastasis are classified as stage 4.

Whether a patient expresses a fusion polypeptide of the present invention or carries a polynucleotide encoding the fusion polypeptide can be tested by using methods of the present invention described above.

The present invention also relates to methods for identifying compounds having FGFR inhibitory activity.

Specifically, methods for identifying compounds having FGFR inhibitory activity in the present invention include methods comprising the steps of:

(a) culturing cells that express an above-described fusion polypeptide of the present invention in the presence or absence of a test compound and determining the level of cell proliferation;

(b) comparing the proliferation level of cultured cell between in the presence and absence of the test compound; and

(c) judging that the test compound has FGFR inhibitory activity when the proliferation level of the cell cultured in the presence of the test compound is lower than that of the cell cultured in the absence of the test compound.

seconds at 60°C, and one minute at 68°C) with Tks Gflex™ DNA Polymerase (Takara bio) using as primers, oligonucleotides having the nucleotide sequences of SEQ ID NOs: 1 and 5, and as a substrate, cDNA (Origene) derived from bladder cancer samples collected from bladder cancer patients (20 patients) or cDNA synthesized from RT4 (ATCC) RNA. Each of the amplified samples was electrophoresed together with size marker DNAs (Invitrogen).

As shown in Fig. 2, the result showed that a cDNA fragment of polynucleotide v2 encoding the FGFR3-TACC3 fusion polypeptide was detected in a single case.

The above finding shows that the method described above allows detection of polynucleotide v2 encoding the FGFR3-TACC3 fusion polypeptide in samples derived from clinical specimens of bladder cancer, and thus enables selection of patients who are positive for polynucleotide v2 encoding the FGFR3-TACC3 fusion polypeptide.

(3) Detection of a polynucleotide encoding the FGFR3-BAIAP2L1 fusion polypeptide

In order to detect cDNA for an FGFR3-BAIAP2L1 polynucleotide in clinical samples, PCR was carried out (42 cycles of 10 seconds at 98°C, 15 seconds at 60°C, and one minute at 68°C) with Tks Gflex™ DNA Polymerase (Takara bio) using, as primers, oligonucleotides having the nucleotide sequences of SEQ ID NOs: 3 and 4, and, as a substrate, cDNA (Origene) derived from bladder cancer samples collected from bladder cancer patients (20 patients) or cDNA synthesized from SW780 (ATCC) RNA. Each of the amplified samples was electrophoresed together with size marker DNAs (Invitrogen).

As shown in Fig. 3, the result showed that a cDNA fragment of the FGFR3-BAIAP2L1 fusion polynucleotide was detected in a total of two cases.

The above finding shows that the method described above allows detection of a polynucleotide encoding the FGFR3-BAIAP2L1 fusion polypeptide in samples derived from clinical specimens of bladder cancer, and thus enables selection of patients who are positive for a polynucleotide encoding the FGFR3-BAIAP2L1 fusion polypeptide.

[Example 5]

Detection of polynucleotides encoding the FGFR3-BAIAP2L1 fusion polypeptide and FGFR3-~~BAIAP2L1~~ TACC3 fusion polypeptide in clinical specimens of various types of cancers

(1) Detection of a polynucleotide encoding the FGFR3-BAIAP2L1 fusion polypeptide in clinical specimens of lung cancer (non-bladder cancer) (Test 1)

In order to detect cDNA for an FGFR3-BAIAP2L1 polynucleotide from clinical specimens of non-bladder cancer, PCR was carried out (42 cycles of 98°C for 10 seconds, 60°C for 15 seconds, and 68°C for one minute) with Tks Gflex(tm) DNA Polymerase (TAKARA BIO INC.) using a pair of oligonucleotide primers having the nucleotide sequences of SEQ ID NO: 3