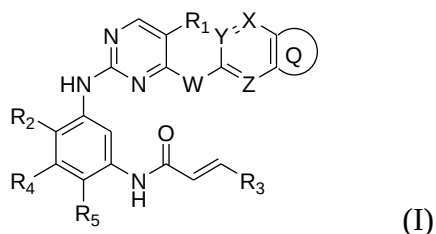


Claims

1. A compound of formula I, or a pharmaceutically acceptable salt or stereoisomer thereof:



wherein R₁ is one selected from the group consisting of halogen, cyano, substituted or unsubstituted C₁-C₆ alkyl, substituted or unsubstituted C₃-C₆ cycloalkyl, substituted or unsubstituted C₁-C₆ alkoxy, and substituted or unsubstituted C₃-C₆ cycloalkoxy;

R₂ is one selected from the group consisting of H, halogen, cyano, substituted or unsubstituted C₁-C₆ alkyl, substituted or unsubstituted C₃-C₆ cycloalkyl, substituted or unsubstituted C₁-C₆ alkoxy, and substituted or unsubstituted C₃-C₆ cycloalkoxy

R₃ is H or -(CH₂)_mNR₈R₉; R₄ and R₅ are independently H, substituted or unsubstituted C₁-C₆ alkyl, substituted or unsubstituted C₁-C₆ alkoxy, halogen, -(CH₂)_mNR₈R₉, and -(CH₂)_mCR₆R₈R₉; wherein each m is independently 0, 1, 2 or 3; R₆ is H or C₁-C₃ alkyl; each R₈ and each R₉ are independently selected from H, substituted or unsubstituted C₁-C₆ alkyl, or R₈, R₉ and attached N or C together form an unsubstituted or substituted 3-8 membered monocyclic or fused ring containing 1, 2 or 3 heteroatoms selected from O, N, S;

W is NH, N(C₁-C₃ alkyl), O or S;

X, Y, Z are each independently N or -CR₁₀, wherein R₁₀ is H, halogen, substituted or unsubstituted C₁-C₃ alkyl, or substituted or unsubstituted C₁-C₃ alkoxy;



is a substituted or unsubstituted 5 to 7 membered aromatic ring containing 0, 1, 2 or 3 heteroatoms selected from O, N or S;

Wherein each substituted independently means substituted by substituents selected from the group consisting of: halogen, hydroxy, amino, C₁-C₃ alkyl, C₁-C₃ alkoxy, -NH(C₁-C₃ alkyl), -N(C₁-C₃ alkyl)(C₁-C₃ alkyl), and -C(=O)(C₁-C₃ alkyl).

2. The compound of claim 1, wherein,

R₁ is one selected from the group consisting of halogen, cyano, C₁-C₆ alkyl, C₁-C₆ alkoxy, C₃-C₆ cycloalkyl, C₃-C₆ cycloalkoxy, C₁-C₆ haloalkyl or C₁-C₆ haloalkoxy;

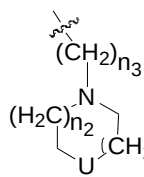
R₂ is one selected from the group consisting of H, halogen, cyano, C₁-C₆ alkyl, C₁-C₆ alkoxy, C₃-C₆ cycloalkyl, C₃-C₆ cycloalkoxy, C₁-C₆ haloalkyl or C₁-C₆ haloalkoxy.

3. The compound of claim 1, wherein,



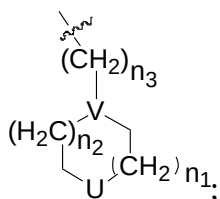
is phenyl, furanyl, thienyl, pyrrolyl, pyrazolyl, thiazolyl, isothiazolyl, oxazolyl, isoxazolyl, pyrazinyl, pyridazinyl, pyridyl, imidazolyl or pyrimidinyl.

4. The compound of claim 1, wherein the compound of formula I have one or more of the following characteristics:



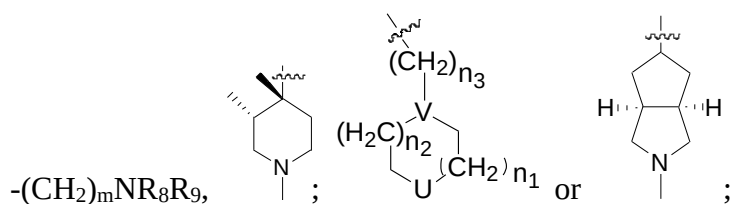
(1) R₃ is H, -(CH₂)_sN(C₁-C₃ alkyl)(C₁-C₃ alkyl), or

(2) R₄ is H, C₁-C₃ alkyl, C₁-C₃ haloalkyl, C₁-C₃ alkoxy, C₁-C₃ haloalkoxy, halogen,



-(CH₂)_mNR₈R₉, or

(3) R_5 is H, C₁-C₃ alkyl, C₁-C₃ haloalkyl, C₁-C₃ alkoxy, C₁-C₃ haloalkoxy, halogen,



Wherein each m is independently 0, 1, 2 or 3;

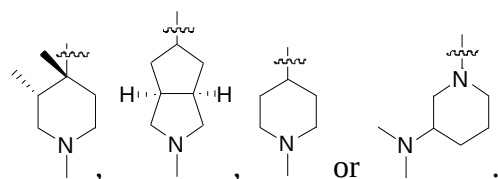
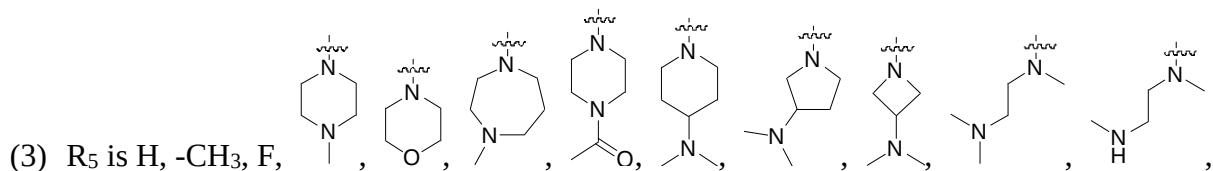
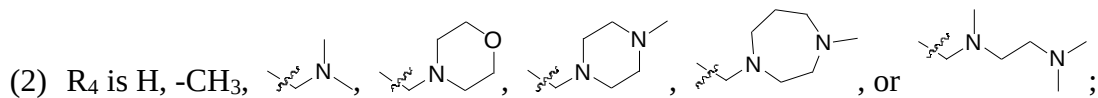
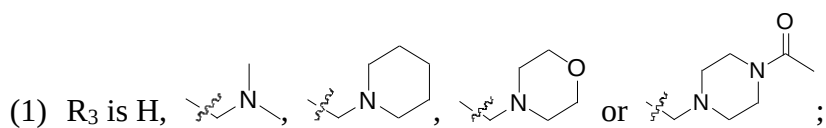
Each R_8 and each R_9 are independently selected from H, substituted or unsubstituted C₁-C₃ alkyl, the term substituted means substituted by substituents selected from the group consisting of: halogen, -NH(C₁-C₃ alkyl), -N(C₁-C₃ alkyl)(C₁-C₃ alkyl), and -C(=O)(C₁-C₃ alkyl);

Each n_1 , each n_2 , and each n_3 are independently 0, 1, 2 or 3;

Each V is independently CH, C(C₁-C₃ alkyl) or N;

Each U is independently none, O, S, CR₁₁R₁₂ or NR₁₃, wherein R_{11} , R_{12} , R_{13} are independently H, C₁-C₃ alkyl, C₃-C₆ cycloalkyl, -NH(C₁-C₃ alkyl), -N(C₁-C₃ alkyl)(C₁-C₃ alkyl) or -C(=O)(C₁-C₃ alkyl).

5. The compound of claim 4, wherein the compound of formula I have one or more of the following characteristics:



6. The compound of claim 1, wherein the compound of formula I is:

(E)-N-((3-((5-chloro-4-((naphthalen-2-yl)amino))pyrimidine-2-yl)amino)-4-methoxyphenyl)-4-(dimethylamino)-2-butenamide;

(E)-N-((3-((5-chloro-4-((quinoline-6-yl)amino))pyrimidine-2-yl)amino)-4-methoxyphenyl)-4-(dimethylamino)-2-butenamide;

(E)-N-((3-((5-chloro-4-((quinoline-3-yl)amino))pyrimidine-2-yl)amino)-4-methoxyphenyl)-4-(dimethylamino)-2-butenamide;

(E)-N-((3-((5-chloro-4-((indole-5-yl)amino))pyrimidine-2-yl)amino)-4-methoxyphenyl)-4-(dimethylamino)-2-butenamide;

(E)-N-((3-((5-chloro-4-(N-methyl-(naphthalen-2-yl)amino))pyrimidine-2-yl)amino)-4-methoxyphenyl)-4-(dimethylamino)-2-butenamide;

(E)-N-((3-((5-chloro-4-((naphthalen-2-yl)oxy))pyrimidine-2-yl)amino)-4-methoxyphenyl)-4-(dimethylamino)-2-butenamide;

(E)-N-((3-((5-chloro-4-((naphthalen-2-yl)thio))pyrimidine-2-yl)amino)-4-methoxyphenyl)-4-(dimethylamino)-2-butenamide;

(E)-N-((3-((5-bromo-4-((naphthalen-2-yl)amino))pyrimidine-2-yl)amino)-4-methoxyphenyl)-4-(dimethylamino)-2-butenamide;

(E)-N-((3-((5-fluoro-4-((naphthalen-2-yl)amino))pyrimidine-2-yl)amino)-4-methoxyphenyl)-4-(dimethylamino)-2-butenamide;

(E)-N-((3-((5-methyl-4-((naphthalen-2-yl)amino))pyrimidine-2-yl)amino)-4-methoxyphenyl)-4-(dimethylamino)-2-butenamide;

(E)-N-((3-((5-methoxy-4-((naphthalen-2-yl)amino))pyrimidine-2-yl)amino)-4-methoxyphenyl)-4-(dimethylamino)-2-butenamide;

(E)-N-((3-((5-cyano-4-((naphthalen-2-yl)amino))pyrimidine-2-yl)amino)-4-methoxyphenyl)-4-(dimethylamino)-2-butenamide;

(E)-N-((3-((5-trifluoromethyl-4-((naphthalen-2-yl)amino))pyrimidine-2-yl)amino)-4-methoxyphenyl)-4-(dimethylamino)-2-butenamide;

(E)-N-((3-((5-isopropyl-4-((naphthalen-2-yl)amino))pyrimidine-2-yl)amino)-4-methoxyphenyl)-4-(dimethylamino)-2-butenamide;

(E)-N-((3-((5-chloro-4-((naphthalen-2-yl)amino))pyrimidine-2-yl)amino)phenyl)-4-(dimethylamino)-2-butenamide;

(E)-N-((3-((5-chloro-4-((naphthalen-2-yl)amino))pyrimidine-2-yl)amino)-4-methylphenyl)-4-(dimethylamino)-2-butenamide;

(E)-N-((3-((5-chloro-4-((naphthalen-2-yl)amino))pyrimidine-2-yl)amino)-4-fluorophenyl)-4-(dimethylamino)-2-butenamide;

(E)-N-((3-((5-chloro-4-((naphthalen-2-yl)amino))pyrimidine-2-yl)amino)-4-ethoxyphenyl)-4-(dimethylamino)-2-butenamide;

(E)-N-((3-((5-chloro-4-((naphthalen-2-yl)amino))pyrimidine-2-yl)amino)-4-isopropoxyphenyl)-4-(dimethylamino)-2-butenamide;

(E)-N-((3-((5-chloro-4-((naphthalen-2-yl)amino))pyrimidine-2-yl)amino)-5-methylphenyl)-4-(dimethylamino)-2-butenamide;

(E)-N-((5-((5-chloro-4-((naphthalen-2-yl)amino))pyrimidine-2-yl)amino)-2-methylphenyl)-4-(dimethylamino)-2-butenamide;

(E)-N-((5-((5-chloro-4-((naphthalen-2-yl)amino))pyrimidine-2-yl)amino)-2-fluoro-4-methoxyphenyl)-4-(dimethylamino)-2-butenamide;

(E)-N-((3-((5-bromo-4-((naphthalen-2-yl)amino))pyrimidine-2-yl)amino)phenyl)-4-(dimethylamino)-2-butenamide;

(E)-N-((3-((5-bromo-4-((naphthalen-2-yl)amino))pyrimidine-2-yl)amino)-4-methylphenyl)-4-(dimethylamino)-2-butenamide;

(E)-N-((3-((5-bromo-4-((naphthalen-2-yl)amino))pyrimidine-2-yl)amino)-4-fluorophenyl)-4-(dimethylamino)-2-butenamide;

(E)-N-((3-((5-bromo-4-((naphthalen-2-yl)amino))pyrimidine-2-yl)amino)-4-ethoxyphenyl)-4-(dimethylamino)-2-butenamide;

(E)-N-((3-((5-bromo-4-((naphthalen-2-yl)amino))pyrimidine-2-yl)amino)-4-isopropoxyphenyl)-4-(dimethylamino)-2-butenamide;

(E)-N-((3-((5-bromo-4-((naphthalen-2-yl)amino))pyrimidine-2-yl)amino)-5-methylphenyl)-4-(dimethylamino)-2-butenamide;

(E)-N-((5-((5-bromo-4-((naphthalen-2-yl)amino))pyrimidine-2-yl)amino)-2-methylphenyl)-4-(dimethylamino)-2-butenamide;

(E)-N-((5-((5-bromo-4-((naphthalen-2-yl)amino))pyrimidine-2-yl)amino)-2-fluoro-4-methoxyphenyl)-4-(dimethylamino)-2-butenamide;

N-((3-((5-chloro-4-((naphthalen-2-yl)amino))pyrimidine-2-yl)amino)-4-methoxyphenyl)acrylamide;

(E)-N-((3-((5-chloro-4-((naphthalen-2-yl)amino))pyrimidine-2-yl)amino)-4-methoxyphenyl)-4-(piperidine-1-yl)-2-butenamide;

(E)-N-((3-((5-chloro-4-((naphthalen-2-yl)amino))pyrimidine-2-yl)amino)-4-methoxyphenyl)-4-(morpholine-1-yl)-2-butenamide;

(E)-N-((3-((5-chloro-4-((naphthalen-2-yl)amino))pyrimidine-2-yl)amino)-4-methoxyphenyl)-4-(4-acetylpiperazine-1-yl)-2-butenamide;

N-((3-((5-chloro-4-((naphthalen-2-yl)amino))pyrimidine-2-yl)amino)-5- morpholine methylphenyl)acrylamide;

N-((3-((5-chloro-4-((naphthalen-2-yl)amino))pyrimidine-2-yl)amino)-5-(dimethylaminomethyl)phenyl)acrylamide;

N-((3-((5-chloro-4-((naphthalen-2-yl)amino))pyrimidine-2-yl)amino)-5-((N-methyl-N-dimethyl aminoethyl)methylamine)phenyl)acrylamide;

N-((3-((5-chloro-4-((naphthalen-2-yl)amino))pyrimidine-2-yl)amino)-5-((4-methylpiperazine-1-yl)methyl)phenyl)acrylamide;

N-((3-((5-chloro-4-((naphthalen-2-yl)amino))pyrimidine-2-yl)amino)-5-((4-methylhomopiperazine-1-yl)methyl)phenyl)acrylamide;

N-((5-((5-chloro-4-((naphthalen-2-yl)amino))pyrimidine-2-yl)amino)-2-((N-methyl-N-dimethyl aminoethyl)amino)-4-methoxyphenyl)acrylamide;

N-((5-((5-chloro-4-((naphthalen-2-yl)amino))pyrimidine-2-yl)amino)-2-(4-acetylpiperazine)-4-methoxyphenyl)acrylamide;

N-((5-((5-chloro-4-((naphthalen-2-yl)amino))pyrimidine-2-yl)amino)-2-(4-methylpiperazine)-4-methoxyphenyl)acrylamide;

N-((5-((5-chloro-4-((naphthalen-2-yl)amino))pyrimidine-2-yl)amino)-2-morpholinyl-4-methoxyphenyl)acrylamide;

N-((5-((5-chloro-4-((naphthalen-2-yl)amino))pyrimidine-2-yl)amino)-2-(4-methylhomopiperazinyl)-4-methoxyphenyl)acrylamide;

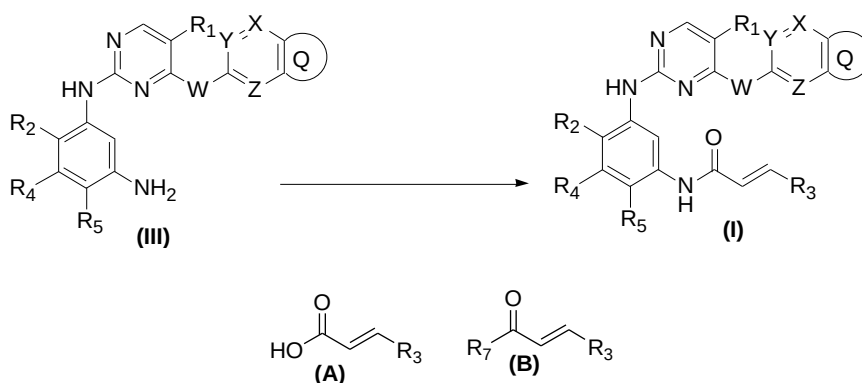
N-((5-((5-chloro-4-((naphthalen-2-yl)amino))pyrimidine-2-yl)amino)-2-(4-dimethylaminopiperidine)-4-methoxyphenyl)acrylamide;

N-((5-((5-chloro-4-((naphthalen-2-yl)amino))pyrimidine-2-yl)amino)-2-(3-dimethylaminopyrrolidine-1-yl)-4-methoxyphenyl)acrylamide;

N-((5-((5-chloro-4-((naphthalen-2-yl)amino))pyrimidine-2-yl)amino)-2-(3-dimethylaminoazetidine-1-yl)-4-methoxyphenyl)acrylamide; or

N-((5-((5-chloro-4-((naphthalen-2-yl)amino))pyrimidine-2-yl)amino)-4-methoxy-2-(methyl(2-methylamino)ethyl)amino)phenyl)acrylamide.

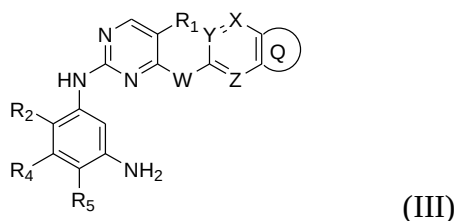
7. A preparation method of the compound of any of claims 1 to 6, wherein a compound of formula III or a salt thereof is used to react with a compound of formula A or a salt thereof, or with a compound of formula B or a salt thereof so as to obtain a compound of formula I,



Wherein R₁, R₂, R₃, R₄, R₅, W, X, Y and Z and  are defined as in claims 1 to 6;

R₇ is halogen, -OCOR₁₄ or OR₁₄, R₁₄ is C₁-C₆ alkyl, C₁-C₆ haloalkyl, C₆-C₁₀ aryl or C₆-C₁₀ aryl C₁-C₆ alkyl.

8. The method of claim 7, wherein the R_{14} is selected from the group consisting of, C_1 - C_3 alkyl, C_1 - C_3 haloalkyl, phenyl or phenyl C_1 - C_3 alkyl.
9. A pharmaceutical composition comprising a compound of formula I of claim 1, or a pharmaceutically acceptable salt or stereoisomer thereof; and pharmaceutically acceptable carriers.
10. A use of a compound of formula I of claim 1, or a pharmaceutically acceptable salt or stereoisomer thereof, or or a pharmaceutical composition of claim 9, wherein used in the preparation of medicine for treatment of tumor.
11. A use of a compound of formula I of claim 1, or a pharmaceutically acceptable salt or stereoisomer thereof, or a pharmaceutical composition of claim 9, wherein used in the preparation of EGFR protease inhibitor medicine, or in the preparation of IGF1R protease inhibitor medicine.
12. The use of claim 10, wherein the tumor is selected from: non-small cell lung cancer, small cell lung cancer, lung adenocarcinoma, lung squamous cell carcinoma, pancreatic cancer, breast cancer, prostate cancer, liver cancer, skin cancer, epithelial cell carcinoma, gastrointestinal stromal tumor, leukemia, histiocytic lymphoma, nasopharyngeal carcinoma, head and neck cancer, colon cancer, rectal cancer, glioma.
13. A compound of formula III or a salt thereof:



wherein R_1 , R_2 , R_4 , R_5 , , W , X , Y and Z are defined as claims 1 to 5, with the proviso that the compound of formula III does not include the following structure:

