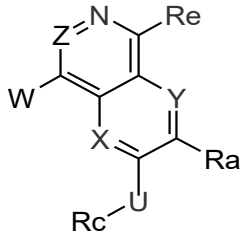
Claims

1. A compound as shown in the following formula II, or pharmaceutically acceptable salts or deuterated products thereof:



II

wherein, X and Y are N, and Z is CR; wherein the R is selected from the grup consisting of H, halogn, and substituted or unsubstituted C_1-C_6 alkyl;

Ra is selected from the group consisting of H, substituted or unsubstituted C_1-C_6 alkyl, substituted or unsubstituted C2-C6 alkenyl, and substitute or unsubstitute C_2-C_6 alkynyl;

U is chemical bond, or -NH-;

Rc is selected from the group consisting of substituted or unsubstituted C_1-C_6 alkyl, substituted or unsubstituted C_3-C_8 carbocyclic ring, substituted or unsubstituted 3-8 membered heterocyclic ring containing 1-3 heteroatoms selected from oxygen, sulfur and nitrogen, substituted or unsubstituted C_6-C_{10} aryl, substituted or unsubstituted 5-12 membered heteroaromatic ring containing 1-3 heteroatoms selected from oxygen, sulfur, and nitrogen;

Re is selected from the group consisting of -NHR; wherein the R is selected from the grup consisting of H, substituted or unsubstituted C_1-C_6 alkyl, substituted or unsubstituted phenyl;

W is selected from the group consisting of substituted or unsubstituted C_6-C_{10} aryl, and substituted or unsubstituted 5-12 membered heteroaromatic ring containing 1-3 heteroatoms selected from the group consisting of oxygen, sulfur, and nitrogen;

the W group is substituted by at least one group having the structure of -M-A, wherein M is selected from the group consisting of chemical bond, or -CHR-, carbonyl, S, O, -NH-, -NHC(O)-, -$NHS(O)_2$-, -NHC(O)NH-, -NHC(S)NH-, -COO-, and -$O-S(O)_2$-;

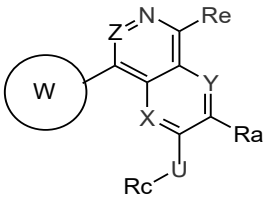
A is selected from the group consisting of H, halogen, cyano, amino, nitro, hydroxyl, sulfhydryl, aldehyde, carboxyl, sulfonyl, substituted or unsubstituted C_1-C_6 alkyl, substituted or unsubstituted C_1-C_6 alkoxy, substituted or unsubstituted C_6-C_{10} aryl, substituted or unsubstituted 4-12 membered heterocyclic ring containing 1-3 heteroatoms selected from oxygen, sulfur and nitrogen, substituted or unsubstituted 5-12 membered heteroaromatic ring containing 1-3 heteroatoms selected from oxygen, sulfur and nitrogen, substituted or unsubstituted -C_1-C_6 alkyl-phenyl, substituted or

unsubstituted C_3-C_{12} cycloalkyl, substituted or unsubstituted C_2-C_{10} acyl, substituted or unsubstituted C_2-C_{10} ester group, substituted or unsubstituted C_6-C_{10} aryloxy, substituted or unsubstituted C_1-C_6 amide, substituted or unsubstituted C_1-C_4 alkyl-$S(O)_2$-, and substituted or unsubstituted C_1-C_4 alkyl-SO-;

in the group A, substitution means substitutedn by one or more groups selected from group B, wherein the group B comprises H, halogen, =O, cyano, amino, nitro, hydroxyl, sulfhydryl, aldehyde, carboxyl, sulfonyl, substituted or unsubstituted C_1-C_6 alkyl, substituted or unsubstituted C_1-C_6 alkoxy, substituted or unsubstituted C_6-C_{10} aryl, substituted or unsubstituted 3-12 membered heterocyclic ring containing 1-3 heteroatoms selected from oxygen, sulfur and nitrogen, substituted or unsubstituted 5-12 membered heteroaromatic ring containing 1-3 heteroatoms selected from oxygen, sulfur and nitrogen, substituted or unsubstituted -C_1-C_6 alkyl-phenyl, substituted or unsubstituted C_3-C_{12} cycloalkyl, substituted or unsubstituted C_2-C_{10} acyl, substituted or unsubstituted C_2-C_{10} ester group, substituted or unsubstituted C_6-C_{10} aryloxy, substituted or unsubstituted C_1-C_6 amide, substituted or unsubstituted C_1-C_4 alkyl-$S(O)_2$-, substituted or unsubstituted C_1-C_4 alkyl-SO-, and in the group B, the substitution means substituted by one or more R groups; wherein the R is selected from the group consisting of H, halogen, cyano, amino, nitro, hydroxyl, sulfhydryl, aldehyde, carboxyl, sulfonyl, substituted or unsubstituted C_1-C_6 alkyl, substituted or unsubstituted C_1-C_6 alkoxy, substituted or unsubstituted C_6-C_{10} aryl, substituted or unsubstituted 5-7 membered heterocyclic ring containing 1-3 heteroatoms selected from oxygen, sulfur and nitrogen, substituted or unsubstituted -C_1-C_6 alkyl-phenyl, substituted or unsubstituted C_3-C_{12} cycloalkyl, substituted or unsubstituted C_2-C_{10} acyl, substituted or unsubstituted C_2-C_{10} ester group, substituted or unsubstituted C_6-C_{10} aryloxy, substituted or unsubstituted C_1-C_6 amide, a substituted or unsubstituted C_1-C_4 alkyl-$S(O)_2$-, and a substituted or unsubstituted C_1-C_4 alkyl-SO-;

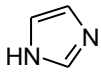
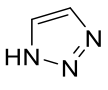
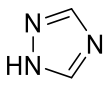
unless otherwise specified, in the above formulae, the substitution means that the hydrogen atom on the corresponding group is replaced by one or more substituents selected from the group consisting of deuterium, tritium, halogen, hydroxyl, carboxyl, sulfhydryl, benzyl, C_1-C_{12} alkoxycarbonyl, C_1-C_6 aldehyde, amino, C_1-C_6 amide, nitro, cyano, unsubstituted or halogenated C_1-C_6 alkyl, unsubstituted or halogenated C_3-C_8 cycloalkyl, C_2-C_{10} alkenyl, C_1-C_6 alkoxy, C_1-C_6 alkyl-amino, C_6-C_{10} aryl, five or six membered heteroaryl, five or six membered nonaromatic heterocyclyl, -O-(C_6-C_{10} aryl), -O-(five and six membered heteroaryl), C_1-C_{12} alkylaminocarbonyl, unsubstituted or halogenated C_2-C_{10} acyl, sulfonyl, phosphoryl, unsubstituted or halogenated C_1-C_4 alkyl-$S(O)_2$-, and unsubstituted or halogenated C_1-C_4 alkyl-SO-.

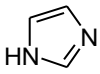
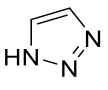
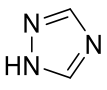
2. The compound of claim 1, or pharmaceutically acceptable salts or deuterated forms thereof, wherein the compound has the structure as shown in formula IIa:



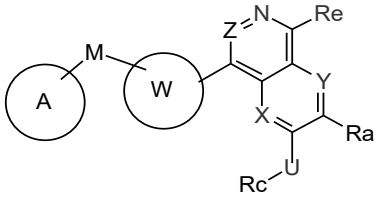
IIa

wherein, the W ring is selected from the group consisting of a substituted or unsubstituted phenyl, and substituted or unsubstituted 5-6 membered heteroaromatic ring containing 1-3 heteroatoms selected from oxygen, sulfur and nitrogen; wherein in the W group, said substitution means substituted by one or more groups selected from group A.

3. The compound of claim 2, or pharmaceutically acceptable salts or deuterated forms thereof, wherein the W ring is a substituted or unsubstituted ring structure selected from the group consisting of phenyl, , , , , , , , , , , , , , , and .

4. The compound of claim 2, or pharmaceutically acceptable salts or deuterated forms thereof, wherein the W ring is a substituted or unsubstituted ring structure selected from the group consisting of phenyl, , , , , , , , and .

5. The compound of claim 2, or pharmaceutically acceptable salts or deuterated products thereof, wherein the compound has the structure as shown in formula III:



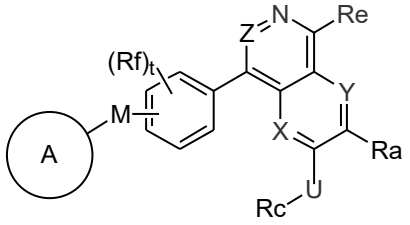
III

wherein, the A ring is selected from the group consisting of substituted or unsubstituted 4-12 membered heterocyclic ring containing 1-3 heteroatoms selected from oxygen, sulfur and nitrogen, substituted or unsubstituted 5-12 membered heteroaromatic ring containing 1-3 heteroatoms selected from oxygen, sulfur and nitrogen, substituted or unsubstituted C_6-C_{10} aryl, substituted or unsubstituted -C_1-C_6

alkyl-phenyl, and substituted or unsubstituted C_3-C_{12} cycloalkyl;

M is selected from the group consisting of a chemical bond, or -O-, -CHR-, carbonyl, S, -NH-, -NHC(O)-, -$NHS(O)_2$-, -NHC(O)NH-, -NHC(S)NH-, -COO-, and -$O\text{-}S(O)_2$-.

6. The compound of claim 5, or pharmaceutically acceptable salts or deuterated products thereof, wherein the compound has the structure as shown in the following formula:



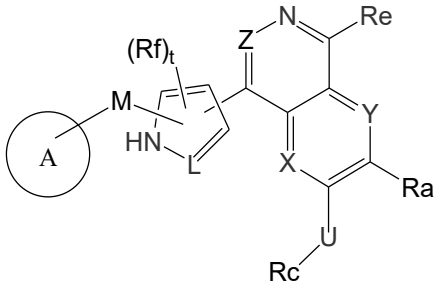
wherein,

Rf is selected from the group consisting of H, halogen, cyano, amino, nitro, hydroxyl, sulfhydryl, aldehyde, carboxyl, sulfonyl, C_1-C_4 alkyl-$S(O)_2$-, substituted or unsubstituted C_1-C_6 alkyl, and substituted or unsubstituted C_1-C_6 alkoxy;

t is 0, 1, 2, 3 or 4;

the A ring is selected from the group consisting of substituted or unsubstituted 5-12 membered saturated ring, substituted or unsubstituted 5-12 membered heteroaromatic ring containing 1-3 heteroatoms selected from oxygen, sulfur and nitrogen, and substituted or unsubstituted C_6-C_{10} aryl; and the A ring have at least one heteroatom selected from N or O.

7. The compound of claim 5, or pharmaceutically acceptable salts or deuterated products thereof, wherein the compound has the structure as shown in the following formula:



wherein,

Rf is selected from the group consisting of H, halogen, cyano, amino, nitro, hydroxyl, sulfhydryl, aldehyde, carboxyl, sulfonyl, C_1-C_4 alkyl-$S(O)_2$-, a substituted or unsubstituted C_1-C_6 alkyl, and a substituted or unsubstituted C_1-C_6 alkoxy;

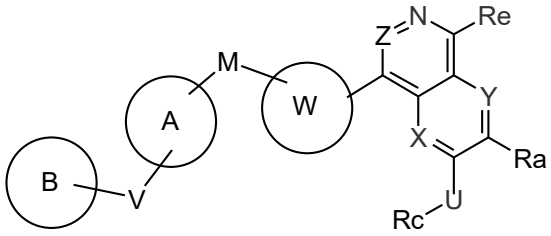
t is 0, 1, 2, 3 or 4;

L is N or CH;

the A ring is selected from the group consisting of a substituted or unsubstituted 4-12 membered heterocyclic ring containing 1-3 heteroatoms selected from oxygen,

sulfur and nitrogen, a substituted or unsubstituted C_3-C_{12} cycloalkyl, a substituted or unsubstituted 5-12 membered heteroaromatic ring containing 1-3 heteroatoms selected from oxygen, sulfur and nitrogen, and a substituted or unsubstituted C_6-C_{10} aryl.

8. The compound, or pharmaceutically acceptable salts or deuterated products thereof of claim 5, the compound has the structure as shown in the following formula IV:



IV

wherein, the A ring is selected from the group consisting of substituted or unsubstituted 4-12 membered heterocyclic ring containing 1-3 heteroatoms selected from oxygen, sulfur and nitrogen, substituted or unsubstituted 5-12 membered heteroaromatic ring containing 1-3 heteroatoms selected from oxygen, sulfur and nitrogen, a substituted or unsubstituted C_6-C_{10} aryl, substituted or unsubstituted -C_1-C_6 alkyl-phenyl, and substituted or unsubstituted C_3-C_{12} cycloalkyl;

M is selected from the group consisting of a chemical bond, or -O-, -CHR-, carbonyl, S, -NH-, -NHC(O)-, -NHS$(O)_2$-, -NHC(O)NH-, -NHC(S)NH-, -COO-, and -O-S$(O)_2$-;

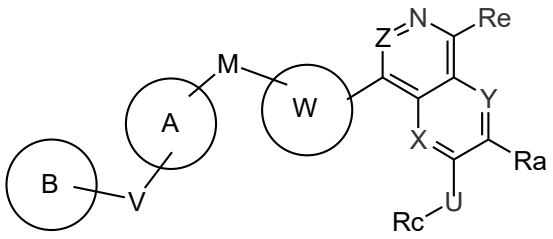
B ring is selected from the group consisting of substituted or unsubstituted 4-12 membered heterocyclic ring containing 1-3 heteroatoms selected from oxygen, sulfur and nitrogen, substituted or unsubstituted 5-12 membered heteroaromatic ring containing 1-3 heteroatoms selected from oxygen, sulfur and nitrogen, substituted or unsubstituted C_6-C_{10} aryl, and substituted or unsubstituted C_3-C_{12} carbocyclic ring;

V is chemical bond.

9. The compound of claim 5, or pharmaceutically acceptable salts or deuterated products thereof, wherein the A ring has at least one substituent G, and the group G is selected from the group consisting of amino, =O, substituted or unsubstituted 4-7 membered heterocyclic ring containing 1-3 heteroatoms selected from oxygen and nitrogen, substituted or unsubstituted C_2-C_{10} acyl, substituted or unsubstituted C_2-C_{10} ester, and substituted or unsubstituted C_1-C_6 amide.

10. The compound claim 1, or pharmaceutically acceptable salts or deuterated products thereof of, wherein the compound is selected from the compounds described in Table 1 of the specification.

11. A compound of the formula IV, or the pharmaceutically acceptable salts or deuterated products thereof,



IV

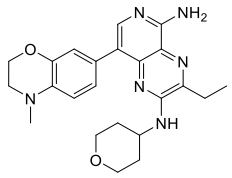
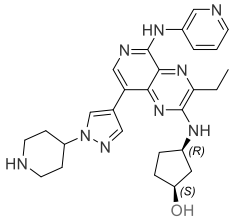
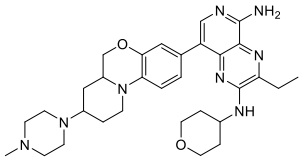
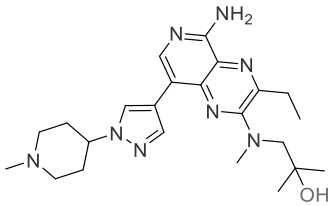
wherein, the A ring is selected from the group consisting of substituted or unsubstituted 4-12 membered heterocyclic ring containing 1-3 heteroatoms selected from oxygen, sulfur and nitrogen, substituted or unsubstituted 5-12 membered heteroaromatic ring containing 1-3 heteroatoms selected from oxygen, sulfur and nitrogen, a substituted or unsubstituted C_6-C_{10} aryl, substituted or unsubstituted -C_1-C_6 alkyl-phenyl, and substituted or unsubstituted C_3-C_{12} cycloalkyl;

M is selected from the group consisting of a chemical bond, or -O-, -CHR-, carbonyl, S, -NH-, -NHC(O)-, -NHS$(O)_2$-, -NHC(O)NH-, -NHC(S)NH-, -COO-, and -O-S$(O)_2$-;

B ring is selected from the group consisting of substituted or unsubstituted 4-12 membered heterocyclic ring containing 1-3 heteroatoms selected from oxygen, sulfur and nitrogen, substituted or unsubstituted 5-12 membered heteroaromatic ring containing 1-3 heteroatoms selected from oxygen, sulfur and nitrogen, substituted or unsubstituted C_6-C_{10} aryl, and substituted or unsubstituted C_3-C_{12} carbocyclic ring;

V is selected from the group consisting of -O-, -CHR-, carbonyl, S, -NH-, -NHC(O)-, -NHS$(O)_2$-, -NHC(O)NH-, -NHC(S)NH-, -COO-, and -O-S$(O)_2$-.

12. A compound selected from the group consisting of:

61		262	
62		264	

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13. A pharmaceutical composition comprising a therapeutically effective amount of one or more of the compounds of any one of claims 1-12, or pharmaceutically acceptable salts, racemates, R-isomers and S-isomers, stereoisomers or tautomers thereof and one or more pharmaceutically acceptable carriers, excipients, adjuvants, excipients and diluents.

14. A use of the compound of any one of claims 1-12, racemates, R-isomers, S-isomers or pharmaceutically acceptable salts thereof in the manufacture of a medicament for the treatment or prevention of diseases associated with abnormal gene levels or abnormal expression of kinases selected from the group consisting of FLT3, ALK, RET, ROS, AXL, and EGFR.

15. The use of claim 14, wherein the disease is selected from the group consisting of acute myeloid leukemia, neurofibroma type I, multiple myeloma, glioblastoma, non-small cell lung cancer, liver cancer, hepatocellular carcinoma, cervical cancer, lymphoma, bone metastases, hormone refractory prostate cancer, hormone dependent prostate cancer, thyroid adenoma, medullary thyroid carcinoma, mesothelioma, glioblastoma, sphincter metastases, Merkel cell carcinoma, urogenital tract tumor, Merkel cell carcinoma, bladder cancer, papillary thyroid cancer, breast cancer, soft tissue sarcoma, glioma, neuroendocrine tumor, renal cell carcinoma, advanced solid tumor, undifferentiated astrocytic cell carcinoma, gastrointestinal stromal tumor, Hipper-Lindau syndrome, small cell lung cancer, pancreatic cancer, pancreatic endocrine carcinoma, central nervous system tumor, metastatic renal cancer, endometrioid carcinoma, endometrioid adenocarcinoma, lung cancer, colorectal cancer, ovarian cancer, rhabdomyosarcoma, melanoma, retinoblastoma, tumors of the central and peripheral nervous system, acute leukemia, chronic leukemia, cholangiocarcinoma, bronchiocarcinoma, esophageal cancer, testicular cancer, skin cancer, oral cancer, neuroblastoma, and anaplastic large cell lymphoma.