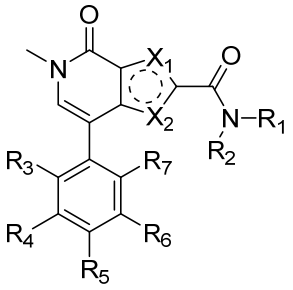
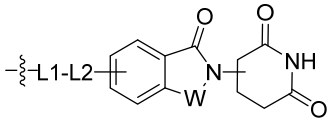
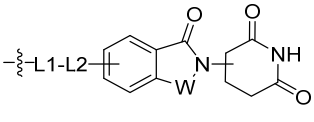
Claims

1. An acylaminopyrrolo-pyridone compound represented by general formula I, or the pharmaceutically acceptable salt thereof, or the enantiomer, the diastereomer, the tautomer, the solvate or the polymorph thereof, wherein



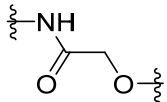
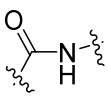
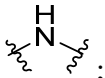
I

X1 is CH; X2 is NH;

R1 is C1-C8 alkyl, 3-8 membered cycloalkyl, C1-C8 alkyl substituted by 3-8 membered cycloalkyl or ; the C1-C8 alkyl, 3-8 membered cycloalkyl, C1-C8 alkyl substituted by 3-8 membered cycloalkyl and  are optionally substituted by one or more substituents, the substituents are independently selected from: halogen, cyano, C1-C6 alkyl, C1-C6 alkyl-O- and C1-C6 alkyl-(SO_2)-; when there are multiple substituents, they are the same or different;

L1 is -(C1-C8 alkyl)-, -(C2-C6 alkynyl)-, or -(C1-C6 alkyl)-$(CH_2OCH_2)_{m1}$-(C1-C6 alkyl)-;

m1 is 1, 2, 3 or 4;

L2 is a connecting bond, -O-, ,  or ;

W is -CH_2- or -C(O)-;

R2 is hydrogen;

R3 and R5 are each independently hydrogen;

R4 is - L-R10;

L is independently a connecting bond, -O-, -(SO_2)- or -(SO_2)-NH-;

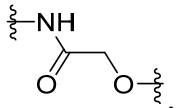
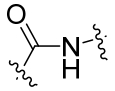
R10 is independently C1-C6 alkyl or C1-C6 alkyl substituted by one or more substituents; the substituents in the C1-C6 alkyl substituted by one or more substituents are independently

halogen, hydroxy, cyano or C1 -C6 alkyl; when there are multiple substituents, they are the same or different;

R6 together with R7 and the carbon atoms they are attached to form: a 6-membered heterocycloalkyl or a 6-membered heterocycloalkyl substituted by one or more substituents, the heteroatoms in the 6-membered heterocycloalkyl are selected from one or more of N, O, S, -S(=O)- and -$S(=O)_2$-, and the number of the heteroatom is 1, 2 or 3; the substituent is independently C1-C6 alkyl or = O; when the substituents are multiple, they are the same or different.

2. The acylaminopyrrolo-pyridone compound represented by general formula I as defined in claim 1, or the pharmaceutically acceptable salt thereof, or the enantiomer, the diastereomer, the tautomer, the solvate or the polymorph thereof, wherein

m1 is 3;

or, L2 is a connecting bond, ,  or ;

or, L is a connecting bond, -O- or -(SO_2)-;

or, when R1 is 3-8 membered cycloalkyl, C1-C8 alkyl substituted by 3-8-membered cycloalkyl, the 3-8-membered cycloalkyl and the C1-C8 alkyl substituted by 3-8-membered cycloalkyl are independently substituted by one or more substituents, the substituents are selected from halogen and C1-C6 alkyl.

3. The acylaminopyrrolo-pyridone compound represented by general formula I as defined in claim 1, or the pharmaceutically acceptable salt thereof, or the enantiomer, the diastereomer, the tautomer, the solvate or the polymorph thereof, wherein the acylaminopyrrolo-pyridone compound represented by formula (I) is as shown in the scheme 1 or scheme 2;

scheme 1: X1 is CH; X2 is NH;

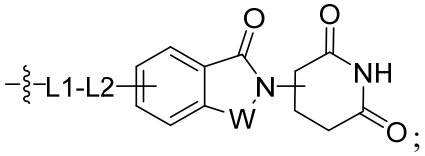
R1 is C1-C8 alkyl and 3-8 membered cycloalkyl; the C1-C8 alkyl and 3-8 membered cycloalkyl are optionally substituted by one or more substituents;

R2, R3 and R5 are each independently hydrogen;

R4 is - L-R10;

R6 together with R7 and the carbon atoms they are attached to form: a 6 membered heterocycloalkyl or a 6 membered heterocycloalkyl substituted by one or more substituents, the substituents are independently selected from C1-C6 alkyl or =O;

scheme 2: X1 is CH; X2 is NH;

R1 is independently C1-C8 alkyl or 

;

R2, R3 and R5 are each independently hydrogen;

R4 is - L-R10;

R6 together with R7 and the carbon atoms they are attached to form: a 6 membered heterocycloalkyl or a 6 membered heterocycloalkyl substituted by one or more substituents, the substituents are independently selected from C1-C6 alkyl or =O.

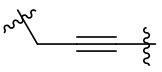
4. The acylaminopyrrolo-pyridone compound represented by general formula I as defined in any one of claims 1-3, or the pharmaceutically acceptable salt thereof, or the enantiomer, the diastereomer, the tautomer, the solvate or the polymorph thereof, wherein

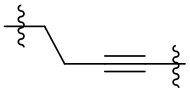
when R1 is C1-C8 alkyl or C1-C8 alkyl substituted by 3-8-membered cycloalkyl, the C1-C8 alkyl in the C1-C8 alkyl and C1-C8 alkyl substituted by 3-8-membered cycloalkyl is independently methyl, ethyl, *n*-propyl, isopropyl, *n*-butyl, isobutyl, *sec*-butyl or *tert*-butyl; for example, methyl, ethyl or isopropyl;

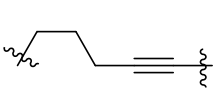
or, when R1 is 3-8 membered cycloalkyl or C1-C8 alkyl substituted by 3-8 membered cycloalkyl, the 3-8 membered cycloalkyl in the 3-8 membered cycloalkyl or the C1-C8 alkyl substituted by 3-8 membered cycloalkyl is independently cyclopropyl, cyclobutyl, cyclopentyl and cyclohexyl; for example, cyclopropyl or cyclobutyl;

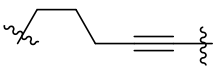
or, when the substituent in R1 is C1-C6 alkyl, C1-C6 alkyl-O- or C1-C6 alkyl-(SO_2)-, the C1-C6 alkyl in the C1-C6 alkyl, the C1-C6 alkyl -O- and the C1-C6 alkyl-(SO_2)- is independently methyl, ethyl, *n*-propyl, isopropyl, *n*-butyl, isobutyl, *sec*-butyl or *tert*-butyl; for example, methyl or ethyl;

or, when L1 is -(C1-C8 alkyl)-, the C1-C8 alkyl is methyl, ethyl, *n*-propyl, isopropyl, *n*-butyl, isobutyl, *sec*-butyl, *tert*-butyl, *n*-pentyl or *n*-hexyl; for another example, *n*-butyl, *n*-pentyl or *n*-hexyl;

or, when L1 is -(C2-C6 alkynyl)-, the C2-C6 alkynyl is ethynyl, 

, 

or 

, for another example 

, wherein, the

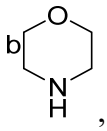
terminal a means that it is connected to L2;

or, when L1 is -(C1-C6 alkyl)-$(CH_2OCH_2)_{m1}$-(C1-C6 alkyl)-, the C1-C6 alkyl is independently methyl, ethyl , *n*-propyl, isopropyl, *n*-butyl, isobutyl, *sec*-butyl or *tert*-butyl; for example, methyl, ethyl or *n*-propyl;

or, m1 is 2 or 3;

or, when R10 is independently C1-C6 alkyl or C1-C6 alkyl substituted by one or more substituents, the C1-C6 alkyl is independently methyl, ethyl, *n*-propyl, isopropyl, *n*-butyl, isobutyl, *sec*-butyl or *tert*-butyl; for example, methyl or ethyl;

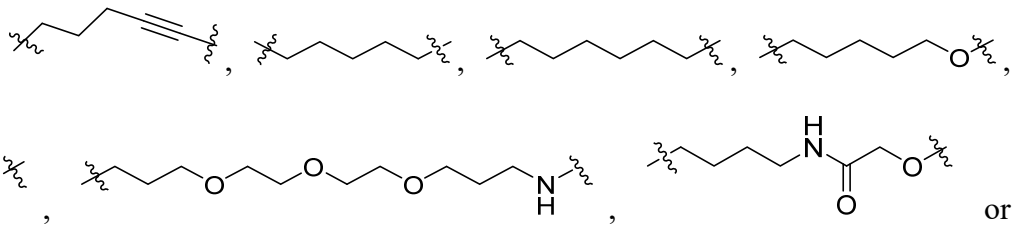
or, when the substituent in R10 is C1-C6 alkyl, the substituent is independently methyl, ethyl, *n*-propyl, isopropyl, *n*-butyl, isobutyl, *sec*-butyl or *tert*-butyl; for example, methyl or ethyl;

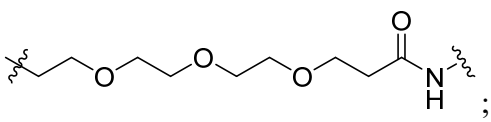
or, when R6 together with R7 and the carbon atoms they are attached to form a 6 membered heterocycloalkyl or a 6 membered heterocycloalkyl substituted by one or more substituents; the 6 membered heterocycloalkyl in the 6 membered heterocycloalkyl or the 6 membered heterocycloalkyl substituted by one or more substituents is 

, wherein, the terminal b means that it is connected to the benzene ring by a fused ring;

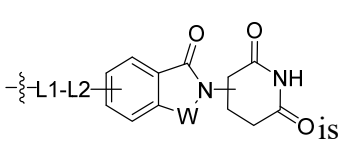
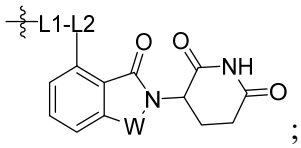
or, when R6 together with R7 and the carbon atoms they are attached to form: a 6 membered heterocycloalkyl or a 6 membered heterocycloalkyl substituted by one or more substituents, and the substituents are independently C1-C6 alkyl, the C1-C6 alkyl is independently methyl, ethyl, *n*-propyl, isopropyl, *n*-butyl, isobutyl, *sec*-butyl or *tert*-butyl; for example, methyl or ethyl.

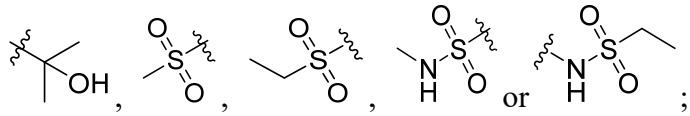
5. The acylaminopyrrolo-pyridone compound represented by general formula I as defined in claim 1, or the pharmaceutically acceptable salt thereof, or the enantiomer, the diastereomer, the tautomer, the solvate or the polymorph thereof, wherein

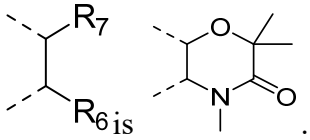
-L1-L2- is 

or 

;

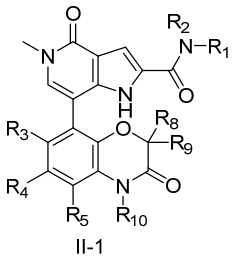
or,  is ;

or, R4 is ;

or, R6 together with R7 and the carbon atoms they are attached to form: a 6 membered heterocycloalkyl or a 6 membered heterocycloalkyl substituted by one or more substituents,  is .

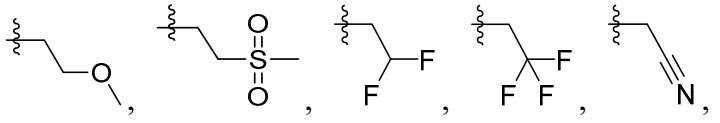
6. The acylaminopyrrolo-pyridone compound represented by general formula I as defined in claim 1, or the pharmaceutically acceptable salt thereof, or the enantiomer, the diastereomer, the tautomer, the solvate or the polymorph thereof, wherein

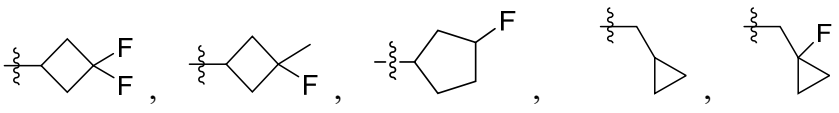
the acylaminopyrrolo-pyridone compound represented by formula I is as shown in formula II-1:

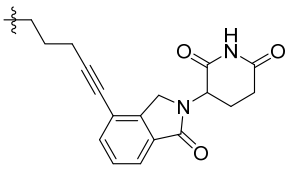
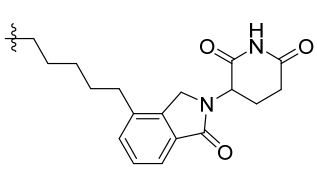
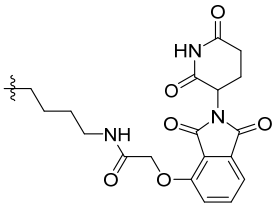
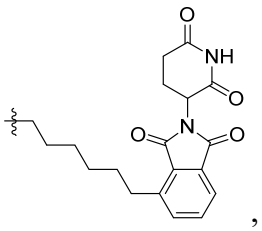
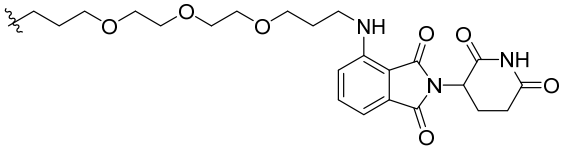
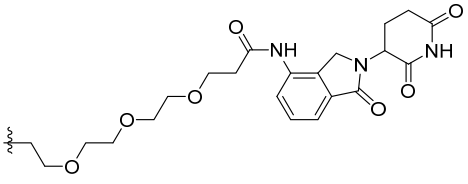
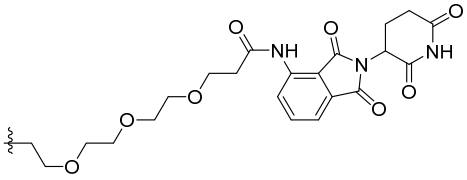

II-1 ;

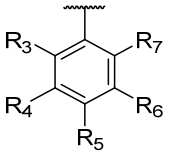
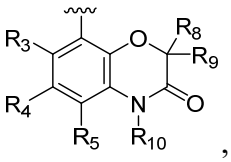
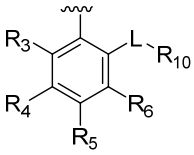
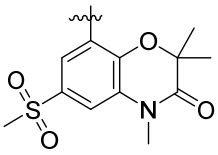
wherein R1, R2, R3, R4, R5 and R10 are as defined in claim 1; R8 and R9 are independently C1-C6 alkyl.

7. The acylaminopyrrolo-pyridone compound represented by general formula I as defined in claim 1, or the pharmaceutically acceptable salt thereof, or the enantiomer, the diastereomer, the tautomer, the solvate or the polymorph thereof, wherein

R1 is ethyl, isopropyl, ,

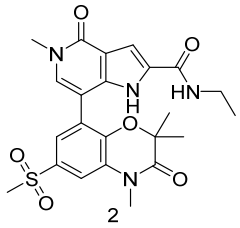
cyclopropyl, cyclopentyl, ,

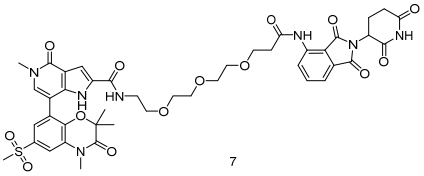

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or

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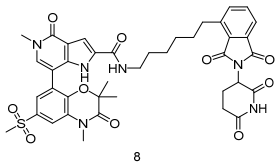
or, when  is ,  is .

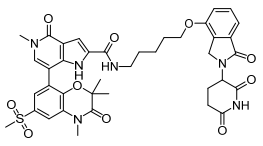
8. The acylaminopyrrolo-pyridone compound represented by general formula I as defined in claim 1, or the pharmaceutically acceptable salt thereof, or the enantiomer, the diastereomer, the tautomer, the solvate or the polymorph thereof, wherein

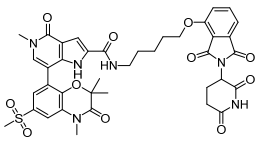
the acylaminopyrrolo-pyridone compound represented by formula I is selected from any one of the structures as follows:


2


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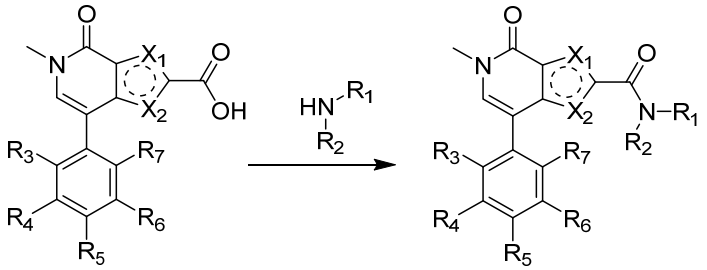

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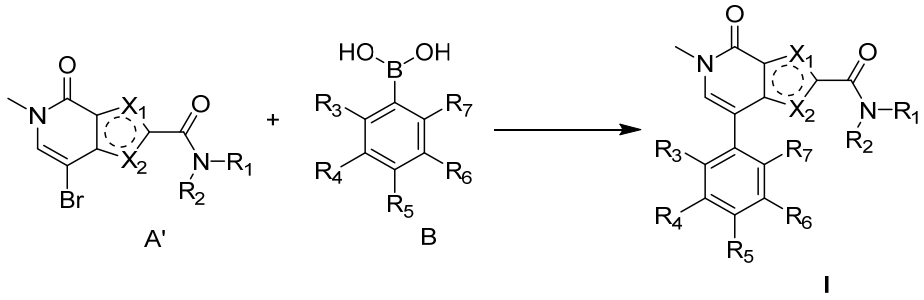
9. A preparation method of the acylaminopyrrolo-pyridone compound represented by formula I as defined in any one of claims 1-8, wherein the preparation method comprises scheme 1 or scheme 2;

scheme 1 comprises the following steps: in a solvent, in the presence of alkali and condensation reagent, a condensation reaction shown as follows between a compound represented by formula D and R1R2NH is carried out to obtain the acylaminopyrrolo-pyridone compound represented by formula I;



D I

scheme 2 comprises the following steps: in a solvent, in the presence of alkali and transition metal catalyst, a metal-catalyzed coupling reaction shown as follows between a compound represented by formula A' and a compound represented by formula B is carried out to obtain the acylaminopyrrolo-pyridone compound represented by formula I;



A' B I

wherein, X1, X2, R1, R2, R3, R4, R5, R6 and R7 are as defined in any one of claims 1-8.

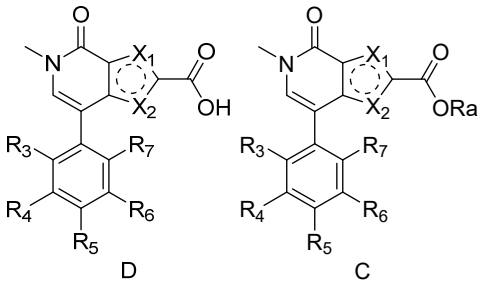
10. A pharmaceutical composition, comprising the acylaminopyrrolo-pyridone compound represented by general formula I as defined in any one of claims 1-8, or the pharmaceutically acceptable salt thereof, or the enantiomer, the diastereomer, the tautomer, the solvate or the polymorph thereof, and a pharmaceutically acceptable carrier.

11. A use of the acylaminopyrrolo-pyridone compound represented by general formula I as defined in any one of claims 1-8, or the pharmaceutically acceptable salt thereof, or the enantiomer, the diastereomer, the tautomer, the solvate or the polymorph thereof, or the pharmaceutical composition as defined in claim 10 in the preparation of BRD or c-Myc inhibitors, or a medicament for the treatment or prevention of tumors, immune diseases or inflammatory

diseases;

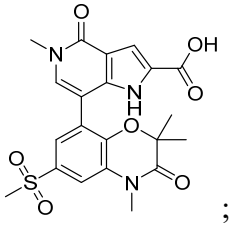
the tumor is selected from non-small cell lung cancer, small cell lung cancer, lung adenocarcinoma, lung squamous carcinoma, breast cancer, prostate cancer, liver cancer, skin cancer, gastric cancer, intestinal cancer, cholangiocarcinoma, brain cancer, leukemia, lymph cancer, fibroma, sarcoma, basal cell carcinoma, glioma, kidney cancer, melanoma, bone cancer, thyroid cancer, nasopharyngeal cancer and pancreatic cancer; the immune diseases and inflammatory diseases are independently selected from the rejection of transplanted organs, gout, rhinitis, alopecia, Alzheimer's disease, appendicitis, atherosclerosis, asthma, arthritis, allergic dermatitis, Behcet's disease, bullous dermatosis cholecystitis, chronic idiopathic thrombocytopenic purpura, chronic obstructive pulmonary disease, liver cirrhosis, degenerative joint disease, dermatitis, dermatomyositis, eczema, enteritis, encephalitis, gastritis, nephritis, Hashimoto's thyroiditis, hepatitis, hypophysitis, inflammatory bowel disease, irritable bowel syndrome, Kawasaki disease, cerebrospinal meningitis, multiple sclerosis, myocarditis, myasthenia gravis, mycosis fungoides, myositis, nephritis, osteomyelitis, pancreatitis, Parkinson's disease, pericarditis, pernicious anemia, pneumonia, primary biliary sclerosing cholangitis, polyarteritis nodosa, psoriasis, fibrosis, lupus erythematosus, tissue graft rejection, thyroiditis, type I diabetes, urethritis, uveitis, vasculitis, vitiligo and Waldenstrom's macroglobulinemia.

12. A compound represented by formula D, formula C,



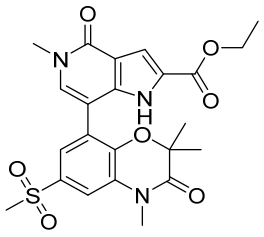
wherein, X1, X2, R1, R3, R4, R5, R6 and R7 are as defined in any one of claims 1-8; Ra is C1-6 alkyl.

13. The compound represented by formula D, formula C as defined in claim 12, wherein, the compound represented by formula D is selected from any of the following structures:



;

or, the compound represented by formula C is selected from any of the following structures:



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