Pyrazolopyrimidine Compound, Preparation Method for Same and Applications Thereof

[0001] The present application claims the priority of Chinese patent application 201910579671.0 filed on June 28, 2019. The contents of the Chinese patent application are incorporated herein by reference in their entireties.

Technical Field

[0002] The present disclosure relates to a pyrazolopyrimidine compound, a preparation method therefor and an application thereof.

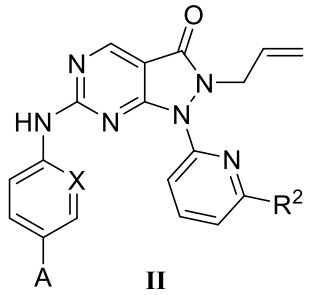
Background

[0003] Cell cycle is closely related to DNA damage repair process. Cell cycle refers to the whole process of cell division, which is divided into two stages: interphase and mitotic phase (M). Cell cycle checkpoint is a key point to regulate the cell cycle, its main function is to ensure that every event in the cycle can be completed on time and orderly, and to adjust the cell state to adapt to the external environment. The main checkpoints of cells are as follows: 1) G1/S checkpoint, which is called R (restriction) point in mammals and controls cells from static G1 phase to DNA synthesis phase; 2) S-phase checkpoint: whether DNA replication is completed; 3) G2/M checkpoint: it is the control point that regulates the cell to enter the division stage; 4) middle-late checkpoint: also called spindle assembly checkpoint, if the centromere is not connected to the spindle correctly, it will cause the interruption of cell cycle. If there is abnormality in some processes of cell division cycle, such as DNA damage, the checkpoint will sense in time and start repair. P53 protein is an important protein that regulates G1 checkpoint, when DNA is damaged, P53 protein prevents cells from entering S phase and activates DNA repair mechanism, which is very important for maintaining the integrity of cell genome. However, since P53 mutation often exists in tumor cells, which makes G1 checkpoint defective, therefore, the regulation of cell division cycle in P53 mutated cells depends on G2/M checkpoint. WEE1 kinase is a cell cycle regulatory protein, which can regulate the phosphorylation state of cyclin-dependent kinase 1 (CDK1), thus regulating the activity of CDK1 and cyclin B complex, realizing the regulation of cell cycle, and playing an important role in regulating DNA damage checkpoints. WEE1 is a key gene in G2/M phase block, plays an important monitoring role, and is overexpressed in some cancers, inhibition or downregulation of WEE1 kinase may trigger mitotic catastrophe, so WEE1 kinase inhibitors have a key role in anticancer therapy and have become a hot spot for the development of anticancer drugs.

[0004] International patent applications WO2019037678, WO2019028008, WO2018133829, WO2010098367, WO2010067886, WO2008115742, WO2008115738, WO2007126122, WO2007126128 WO2004007499 and others have disclosed part of small molecule WEE1 kinase inhibitors, but there are no small molecule WEE1 kinase inhibitors on the market, and there is still a need in the art to develop new WEE1 kinase inhibitors with good anticancer activity and high safety.

Summary

[0004a] In a first aspect, the present disclosure refers to a pyrazolopyrimidine compound represented by formula **II**, a pharmaceutically acceptable salt thereof, a solvate thereof, a solvate of the pharmaceutically acceptable salt thereof, a metabolite thereof or a prodrug thereof:



II

wherein, A is C_3-C_{20} cycloalkyl substituted by one or two R^1;

X is CH or N;

R^1 is independently halogen, $-OR^{1-1}$, $-SR^{1-2}$, -CN, $-NR^{1-3}R^{1-4}$, $-C(=O)R^{1-5}$, $-C(=NR^{1-6})R^{1-7}$, =N-O-R^{1-9} or "C_2-C_7 alkenyl, C_2-C_8 alkynyl, C_3-C_{14} cycloalkyl, C_3-C_{14} heterocycloalkyl, C_6-C_{10} aryl or C_1-C_7 heteroaryl" optionally substituted by one, two or three R^{1-8};

R^{1-1} is independently "C_1-C_7 alkyl, C_2-C_7 alkenyl, C_2-C_7 alkynyl, C_3-C_{14} cycloalkyl, C_3-C_{14} heterocycloalkyl, C_6-C_{10} aryl, or C_1-C_7 heteroaryl" optionally substituted by one, two or three R^{1-1-1};

R^{1-1-1} is independently halogen, hydroxyl, amino, mercapto, cyano, C_1-C_7 alkyl, C_1-C_7 alkoxy, C_1-C_7 alkylthio, C_2-C_7 alkenyl, C_2-C_7 alkynyl, C_3-C_{14} cycloalkyl, C_3-C_{14} heterocycloalkyl, C_6-C_{10} aryl, C_1-C_7 heteroaryl or "amino substituted by one or two $R^{1-1-1-1}$"; $R^{1-1-1-1}$ is independently C_1-C_7 alkyl or C_3-C_{14} cycloalkyl;

R^{1-2} is independently hydrogen or "C_1-C_7 alkyl, C_2-C_7 alkenyl, C_2-C_7 alkynyl, C_3-C_{14} cycloalkyl, C_3-C_{14} heterocycloalkyl, C_6-C_{10} aryl, or C_1-C_7 heteroaryl" optionally substituted by one, two or three R^{1-2-1};

R^{1-2-1} is independently hydrogen, halogen, hydroxyl, amino, mercapto, cyano, C_1-C_7 alkyl, C_1-C_7 alkoxy, C_1-C_7 alkylthio, C_2-C_7 alkenyl, C_2-C_7 alkynyl, C_3-C_{14} cycloalkyl, C_3-C_{14} heterocycloalkyl, C_6-C_{10} aryl, C_1-C_7 heteroaryl or "amino substituted by one or two $R^{1-2-1-1}$"; $R^{1-2-1-1}$ is independently C_1-C_7 alkyl or C_3-C_{14} cycloalkyl;

R^{1-3} and R^{1-4} are independently hydrogen, $-S(=O)_2R^{1-3-1}$, $-C(=O)R^{1-3-2}$, $-C(=NR^{1-3-3})NR^{1-3-5}R^{1-3-6}$, $-S(=O)_2NR^{1-3-7}R^{1-3-8}$, $-C(=O)NR^{1-3-9}R^{1-3-10}$ or "C_1-C_7 alkyl, C_2-C_7 alkenyl, C_2-C_7 alkynyl, C_3-C_{14} cycloalkyl, C_3-C_{14} heterocycloalkyl, C_6-C_{10} aryl or C_1-C_7 heteroaryl" optionally substituted by one, two or three R^{1-3-11};

or, R^{1-3} and R^{1-4} together with the nitrogen atom they are attached to form a C_3-C_{14} heterocycloalkyl optionally substituted by one, two or three R^{1-3-12}; one or more methylenes in the C_3-C_{14} heterocycloalkyl are optionally and independently substituted by oxygen atom, sulfur atom, sulfinyl, sulfonyl, carbonyl, vinylidene or $-N(R^{1-3-13})$-; R^{1-3-13} is independently C_1-C_7 alkyl or C_3-C_{14} cycloalkyl;

R^{1-3-1} and R^{1-3-2} are independently "C_1-C_7 alkyl, C_2-C_7 alkenyl, C_2-C_7 alkynyl, C_3-C_{14} cycloalkyl, C_3-C_{14} heterocycloalkyl or C_6-C_{10} aryl" optionally substituted by one or two $R^{1-3-1-1}$; $R^{1-3-1-1}$ is independently C_1-C_7 alkyl or C_3-C_{14} cycloalkyl;

R^{1-3-3} is independently hydrogen, -CN, C_1-C_7 alkyl, C_2-C_7 alkenyl, C_2-C_7 alkynyl or C_3-C_{14} cycloalkyl;

R^{1-3-5}, R^{1-3-6}, R^{1-3-7}, R^{1-3-8}, R^{1-3-9} and R^{1-3-10} are independently hydrogen, C_1-C_7 alkyl, C_2-C_7 alkenyl, C_2-

C_7 alkynyl or C_3-C_{14} cycloalkyl;

or, R^{1-3-5} and R^{1-3-6} together with the nitrogen atom they are attached to form a C_3-C_{14} heterocycloalkyl optionally substituted by one, two or three $R^{1-3-5-1}$; one or more methylenes in the C_3-C_{14} heterocycloalkyl are optionally and independently substituted by oxygen atom, sulfur atom, sulfinyl, sulfonyl, carbonyl, vinylidene or -N($R^{1-3-5-2}$)-; $R^{1-3-5-1}$ is independently C_1-C_7 alkyl or C_3-C_{14} cycloalkyl; $R^{1-3-5-2}$ is independently C_1-C_7 alkyl or C_3-C_{14} cycloalkyl;

or, R^{1-3-7} and R^{1-3-8} together with the nitrogen atom they are attached to form a C_3-C_{14} heterocycloalkyl optionally substituted by one, two or three $R^{1-3-7-1}$; one or more methylenes in the C_3-C_{14} heterocycloalkyl are optionally and independently substituted by oxygen atom, sulfur atom, sulfinyl, sulfonyl, carbonyl, vinylidene or -N($R^{1-3-7-2}$)-; $R^{1-3-7-1}$ is independently C_1-C_7 alkyl or C_3-C_{14} cycloalkyl; $R^{1-3-7-2}$ is independently C_1-C_7 alkyl or C_3-C_{14} cycloalkyl;

or, R^{1-3-9} and R^{1-3-10} together with the nitrogen atom they are attached to form a C_3-C_{14} heterocycloalkyl optionally substituted by one, two or three $R^{1-3-9-1}$; one or more methylenes in the C_3-C_{14} heterocycloalkyl are optionally and independently substituted by oxygen atom, sulfur atom, sulfinyl, sulfonyl, carbonyl, vinylidene or -N($R^{1-3-9-2}$)-; $R^{1-3-9-1}$ is independently C_1-C_7 alkyl or C_3-C_{14} cycloalkyl; $R^{1-3-9-2}$ is independently C_1-C_7 alkyl or C_3-C_{14} cycloalkyl;

R^{1-3-11} is independently halogen, hydroxyl, amino, mercapto, cyano, C_1-C_7 alkyl, C_1-C_7 alkoxy, C_1-C_7 alkylthio, C_2-C_7 alkenyl, C_2-C_7 alkynyl, C_3-C_{14} cycloalkyl, C_3-C_{14} heterocycloalkyl, C_6-C_{10} aryl, C_1-C_7 heteroaryl or “amino substituted by one or two $R^{1-3-11-1}$”; $R^{1-3-11-1}$ is independently C_1-C_7 alkyl or C_3-C_{14} cycloalkyl;

R^{1-3-12} is independently halogen, hydroxyl, amino, mercapto, cyano, C_1-C_7 alkyl, C_1-C_7 alkoxy, C_1-C_7 alkylthio, C_2-C_7 alkenyl, C_2-C_7 alkynyl, C_3-C_{14} cycloalkyl, C_3-C_{14} heterocycloalkyl, C_6-C_{10} aryl, C_1-C_7 heteroaryl or “amino substituted by one or two $R^{1-3-12-1}$”; $R^{1-3-12-1}$ is independently C_1-C_7 alkyl or C_3-C_{14} cycloalkyl;

R^{1-5} is independently hydrogen, -$NR^{1-5-1}R^{1-5-2}$, -OR^{1-5-3} or “C_1-C_7 alkyl, C_2-C_7 alkenyl, C_2-C_7 alkynyl, C_3-C_{14} cycloalkyl, C_3-C_{14} heterocycloalkyl, C_6-C_{10} aryl, or C_1-C_7 heteroaryl” optionally substituted by one, two or three R^{1-5-4};

R^{1-5-1} and R^{1-5-2} are independently hydrogen, C_1-C_7 alkyl, C_2-C_7 alkenyl, C_2-C_7 alkynyl or C_3-C_{14} cycloalkyl;

or, R^{1-5-1} and R^{1-5-2} together with the nitrogen atom they are attached to form a C_3-C_{14} heterocycloalkyl optionally substituted by one, two or three $R^{1-5-1-1}$; one or more methylenes in the C_3-C_{14} heterocycloalkyl are optionally and independently substituted by oxygen atom, sulfur atom, sulfinyl, sulfonyl, carbonyl, vinylidene or -N($R^{1-5-1-2}$)-; $R^{1-5-1-1}$ is independently C_1-C_7 alkyl or C_3-C_{14} cycloalkyl; $R^{1-5-1-2}$ is independently C_1-C_7 alkyl or C_3-C_{14} cycloalkyl;

R^{1-5-3} is independently hydrogen, C_1-C_7 alkyl, C_2-C_7 alkenyl, C_2-C_7 alkynyl, C_3-C_{14} cycloalkyl, C_3-C_{14} heterocycloalkyl, C_6-C_{10} aryl or C_1-C_7 heteroaryl;

R^{1-5-4} is independently halogen, hydroxyl, amino, mercapto, cyano, C_1-C_7 alkyl, C_1-C_7 alkoxy, C_1-C_7 alkylthio, C_2-C_7 alkenyl, C_2-C_7 alkynyl, C_3-C_{14} cycloalkyl, C_3-C_{14} heterocycloalkyl, C_6-C_{10} aryl, C_1-C_7

heteroaryl or "amino substituted by one or two $R^{1-5-4-1}$"; $R^{1-5-4-1}$ is independently C_1-C_7 alkyl or C_3-C_{14} cycloalkyl;

R^{1-6} is independently hydrogen, -CN, -OH or "C_1-C_7 alkyl, C_2-C_7 alkenyl, C_2-C_7 alkynyl, C_3-C_{14} cycloalkyl, C_3-C_{14} heterocycloalkyl, C_6-C_{10} aryl, or C_1-C_7 heteroaryl" optionally substituted by one, two or three R^{1-6-1};

R^{1-6-1} is independently halogen, hydroxyl, amino, mercapto, cyano, C_1-C_7 alkyl, C_1-C_7 alkoxy, C_1-C_7 alkylthio, C_2-C_7 alkenyl, C_2-C_7 alkynyl, C_3-C_{14} cycloalkyl, C_3-C_{14} heterocycloalkyl, C_6-C_{10} aryl, C_1-C_7 heteroaryl or "amino substituted by one or two $R^{1-6-1-1}$"; $R^{1-6-1-1}$ is independently C_1-C_7 alkyl or C_3-C_{14} cycloalkyl;

R^{1-7} is independently hydrogen, -OR^{1-7-1}, -$NR^{1-7-2}R^{1-7-3}$ or "C_1-C_7 alkyl, C_2-C_7 alkenyl, C_2-C_7 alkynyl, C_3-C_{14} cycloalkyl, C_3-C_{14} heterocycloalkyl, C_6-C_{10} aryl or C_1-C_7 heteroaryl" optionally substituted by one, two or three R^{1-7-4};

R^{1-7-1} is independently hydrogen, C_1-C_7 alkyl, C_2-C_7 alkenyl, C_2-C_7 alkynyl, C_3-C_{14} cycloalkyl, C_3-C_{14} heterocycloalkyl, C_6-C_{10} aryl or C_1-C_7 heteroaryl;

R^{1-7-2} and R^{1-7-3} are independently C_1-C_7 alkyl, C_2-C_7 alkenyl, C_2-C_7 alkynyl or C_3-C_{14} cycloalkyl;

or, R^{1-7-2} and R^{1-7-3} together with the nitrogen atom they are attached to form a C_3-C_{14} heterocycloalkyl optionally substituted by one, two or three $R^{1-7-2-1}$; one or more methylenes in the C_3-C_{14} heterocycloalkyl are optionally and independently substituted by oxygen atom, sulfur atom, sulfinyl, sulfonyl, carbonyl, vinylidene or -$N(R^{1-7-2-2})$-; $R^{1-7-2-1}$ is independently C_1-C_7 alkyl or C_3-C_{14} cycloalkyl; $R^{1-7-2-2}$ is independently C_1-C_7 alkyl or C_3-C_{14} cycloalkyl;

R^{1-7-4} is independently halogen, hydroxyl, amino, mercapto, cyano, C_1-C_7 alkyl, C_1-C_7 alkoxy, C_1-C_7 alkylthio, C_2-C_7 alkenyl, C_2-C_7 alkynyl, C_3-C_{14} cycloalkyl, C_3-C_{14} heterocycloalkyl, C_6-C_{10} aryl, C_1-C_7 heteroaryl or "amino substituted by one or two $R^{1-7-4-1}$"; $R^{1-7-4-1}$ is independently C_1-C_7 alkyl or C_3-C_{14} cycloalkyl;

R^{1-8} is independently oxo, halogen, -OH, amino, mercapto, cyano, C_1-C_7 alkyl, C_1-C_7 alkoxy, C_1-C_7 alkylthio, C_2-C_7 alkenyl, C_2-C_7 alkynyl, C_3-C_{14} cycloalkyl, C_3-C_{14} heterocycloalkyl, C_6-C_{10} aryl, C_1-C_7 heteroaryl or "amino substituted by one or two R^{1-8-1}"; R^{1-8-1} is independently C_1-C_7 alkyl or C_3-C_{14} cycloalkyl;

R^{1-9} is independently hydrogen or C_1-C_7 alkyl;

R^2 is -OR^{2-1}, cyano, carboxyl; or "C_2-C_7 alkyl, C_3-C_{14} cycloalkyl or C_3-C_{14} heterocycloalkyl" optionally substituted by one, two or three R^{2-2};

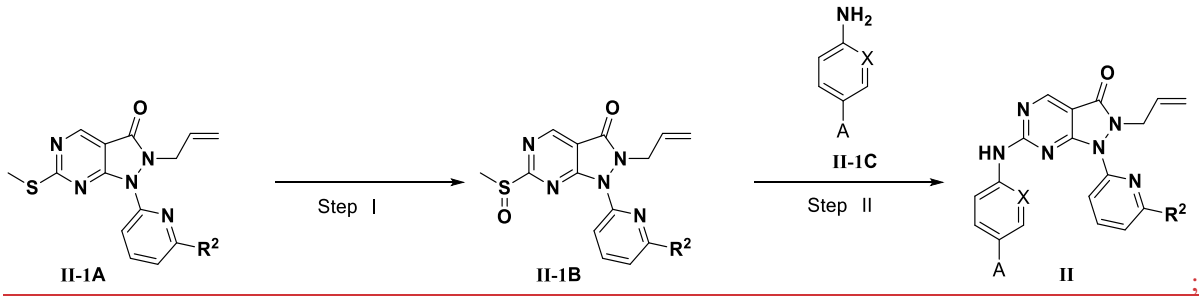
R^{2-1} is C_1-C_7 alkyl, C_2-C_7 alkenyl, C_2-C_7 alkynyl, C_3-C_{14} cycloalkyl, C_3-C_{14} heterocycloalkyl, C_6-C_{10} aryl or C_1-C_7 heteroaryl;

R^{2-2} is independently halogen, hydroxyl, amino, C_1-C_7 alkyl, C_1-C_7 alkoxy, C_3-C_{14} cycloalkyl or C_3-C_{14} heterocycloalkyl;

in any one of the above cases, the heteroatoms in the C_3-C_{14} heterocycloalkyl, C_1-C_7 heteroaryl are independently selected from one or more of boron, silicon, oxygen, sulfur, selenium, nitrogen and phosphorus; the number of heteroatoms is independently 1, 2, 3 or 4.

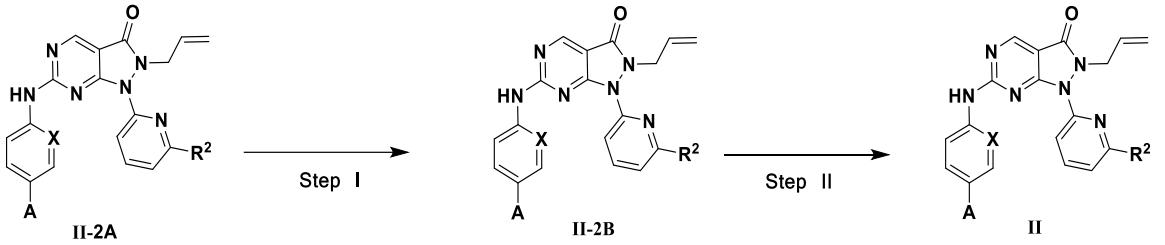
[0004b] In another aspect, the present disclosure refers to a preparation method of the pyrazolopyrimidine compound represented by formula **II** disclosed herein, the method is any of the following methods:

method 1, comprising the following steps: step I, oxidizing compound **II-1A** by an oxidant in an organic solvent to obtain compound **II-1B**; step II, reacting compound **II-1B** with compound **II-1C** in an organic solvent and under alkaline conditions to obtain compound **II**;



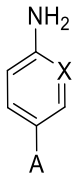
;

method 2, comprising the following steps: step I, hydrolyzing compound **II-2A** (R^1 is -(C=O)-O-C_2H_5) to obtain compound **II-2B** (R^1 is -(C=O)-OH); step II, a condensation reaction is carried out between compound **II-2B** and an amino compound in an organic solvent to obtain compound **II** (R^1 is -(C=O)-$NR^{1-5-1}R^{1-5-2}$);



.

[0004c] In yet another aspect, the present disclosure refers to a compound represented by formula **II-1C**:



II-1C

wherein, X is CH or N, A is as disclosed herein.

[0004d] In a further aspect, the present disclosure refers to a ase of the substance **X** in the preparation of kinase inhibitors or medicaments for treating and/or preventing diseases or cancers related to WEE1 kinase; wherein

the substance X is the pyrazolopyrimidine compound represented by formula **II** disclosed herein, the pharmaceutically acceptable salt thereof, the solvate thereof, the solvate of the pharmaceutically acceptable salt thereof, the metabolite thereof or the prodrug thereof.

[0004e] In another aspect, the present disclosure refers to a pharmaceutical composition comprising the substance **X** and a pharmaceutical excipient;

the substance X is the pyrazolopyrimidine compound represented by formula **II** disclosed herein, the pharmaceutically acceptable salt thereof, the solvate thereof, the solvate of the pharmaceutically acceptable

salt thereof, the metabolite thereof or the prodrug thereof.

[0004f] In yet another aspect, the present disclosure refers to a combination comprising the substance **X** and an anticancer drug,

the substance X is the pyrazolopyrimidine compound represented by formula **II** disclosed herein, the pharmaceutically acceptable salt thereof, the solvate thereof, the solvate of the pharmaceutically acceptable salt thereof, the metabolite thereof or the prodrug thereof.

[0004g] In a further aspect, the present disclosure refers to a use of the combination disclosed herein in the preparation of a medicament for preventing and/or treating cancer.

[0004h] In another aspect, the present disclosure refers to a use of the substance **X** in the preparation of a medicament for preventing and/or treating cancer, wherein the medicament is to be administered in combination with an anticancer drug; and

the substance X is the pyrazolopyrimidine compound represented by formula **II** disclosed herein, the pharmaceutically acceptable salt thereof, the solvate thereof, the solvate of the pharmaceutically acceptable salt thereof, the metabolite thereof or the prodrug thereof.

[0004i] In yet another aspect, the present disclosure refers to a use of an anticancer drug in the preparation of a medicament for preventing and/or treating cancer, wherein the medicament is to be administered in combination with the substance **X**; and

the substance X is the pyrazolopyrimidine compound represented by formula **II** disclosed herein, the pharmaceutically acceptable salt thereof, the solvate thereof, the solvate of the pharmaceutically acceptable salt thereof, the metabolite thereof or the prodrug thereof.

[0004j] In a further aspect, the present disclosure refers to a pharmaceutical composition comprising the combination disclosed herein and a pharmaceutical excipient.

[0004k] In another aspect, the present disclosure refers to a combination drug kit comprising a pharmaceutical composition A and a pharmaceutical composition B;

the pharmaceutical composition A comprises the substance **X**, and pharmaceutical excipients;

the pharmaceutical composition B comprises the anticancer drugs and pharmaceutical excipients;

the substance **X** is the pyrazolopyrimidine compound represented by formula **II** disclosed herein, the pharmaceutically acceptable salt thereof, the solvate thereof, the solvate of the pharmaceutically acceptable salt thereof, the metabolite thereof or the prodrug thereof.

[0004l] In yet another aspect, the present disclosure refers to the substance X for use in treating and/or preventing diseases or cancers related to WEE1 kinase; wherein

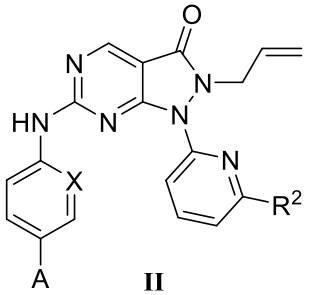
the substance X is the pyrazolopyrimidine compound represented by formula **II** disclosed herein, the pharmaceutically acceptable salt thereof, the solvate thereof, the solvate of the pharmaceutically acceptable salt thereof, the metabolite thereof or the prodrug thereof.

[0004m] In a further aspect, the present disclosure refers to the combination according to claim 19 for use in treating and/or preventing cancer.

Content of the present invention

What is claimed is:

1. A pyrazolopyrimidine compound represented by formula **II**, a pharmaceutically acceptable salt thereof, a solvate thereof, a solvate of the pharmaceutically acceptable salt thereof, a metabolite thereof or a prodrug thereof:



II

wherein, A is C_3-C_{20} cycloalkyl substituted by one or two R^1;

X is CH or N;

R^1 is independently halogen, -OR^{1-1}, -SR^{1-2}, -CN, -$NR^{1-3}R^{1-4}$, -$C(=O)R^{1-5}$, -$C(=NR^{1-6})R^{1-7}$, =N-O-R^{1-9} or "C_2-C_7 alkenyl, C_2-C_8 alkynyl, C_3-C_{14} cycloalkyl, C_3-C_{14} heterocycloalkyl, C_6-C_{10} aryl or C_1-C_7 heteroaryl" optionally substituted by one, two or three R^{1-8};

R^{1-1} is independently "C_1-C_7 alkyl, C_2-C_7 alkenyl, C_2-C_7 alkynyl, C_3-C_{14} cycloalkyl, C_3-C_{14} heterocycloalkyl, C_6-C_{10} aryl, or C_1-C_7 heteroaryl" optionally substituted by one, two or three R^{1-1-1};

R^{1-1-1} is independently halogen, hydroxyl, amino, mercapto, cyano, C_1-C_7 alkyl, C_1-C_7 alkoxy, C_1-C_7 alkylthio, C_2-C_7 alkenyl, C_2-C_7 alkynyl, C_3-C_{14} cycloalkyl, C_3-C_{14} heterocycloalkyl, C_6-C_{10} aryl, C_1-C_7 heteroaryl or "amino substituted by one or two $R^{1-1-1-1}$"; $R^{1-1-1-1}$ is independently C_1-C_7 alkyl or C_3-C_{14} cycloalkyl;

R^{1-2} is independently hydrogen or "C_1-C_7 alkyl, C_2-C_7 alkenyl, C_2-C_7 alkynyl, C_3-C_{14} cycloalkyl, C_3-C_{14} heterocycloalkyl, C_6-C_{10} aryl, or C_1-C_7 heteroaryl" optionally substituted by one, two or three R^{1-2-1};

R^{1-2-1} is independently hydrogen, halogen, hydroxyl, amino, mercapto, cyano, C_1-C_7 alkyl, C_1-C_7 alkoxy, C_1-C_7 alkylthio, C_2-C_7 alkenyl, C_2-C_7 alkynyl, C_3-C_{14} cycloalkyl, C_3-C_{14} heterocycloalkyl, C_6-C_{10} aryl, C_1-C_7 heteroaryl or "amino substituted by one or two $R^{1-2-1-1}$"; $R^{1-2-1-1}$ is independently C_1-C_7 alkyl or C_3-C_{14} cycloalkyl;

R^{1-3} and R^{1-4} are independently hydrogen, -$S(=O)_2R^{1-3-1}$, -$C(=O)R^{1-3-2}$, -$C(=NR^{1-3-3})NR^{1-3-5}R^{1-3-6}$, -$S(=O)_2NR^{1-3-7}R^{1-3-8}$, -$C(=O)NR^{1-3-9}R^{1-3-10}$ or "C_1-C_7 alkyl, C_2-C_7 alkenyl, C_2-C_7 alkynyl, C_3-C_{14} cycloalkyl, C_3-C_{14} heterocycloalkyl, C_6-C_{10} aryl or C_1-C_7 heteroaryl" optionally substituted by one, two or three R^{1-3-11};

or, R^{1-3} and R^{1-4} together with the nitrogen atom they are attached to form a C_3-C_{14} heterocycloalkyl optionally substituted by one, two or three R^{1-3-12}; one or more methylenes in the C_3-C_{14} heterocycloalkyl are optionally and independently substituted by oxygen atom, sulfur atom, sulfinyl, sulfonyl, carbonyl, vinylidene or -$N(R^{1-3-13})$-; R^{1-3-13} is independently C_1-C_7 alkyl or C_3-C_{14} cycloalkyl;

R^{1-3-1} and R^{1-3-2} are independently "C_1-C_7 alkyl, C_2-C_7 alkenyl, C_2-C_7 alkynyl, C_3-C_{14} cycloalkyl, C_3-C_{14} heterocycloalkyl or C_6-C_{10} aryl" optionally substituted by one or two $R^{1-3-1-1}$; $R^{1-3-1-1}$ is independently C_1-C_7 alkyl or C_3-C_{14} cycloalkyl;

R^{1-3-3} is independently hydrogen, -CN, C_1-C_7 alkyl, C_2-C_7 alkenyl, C_2-C_7 alkynyl or C_3-C_{14} cycloalkyl;

R^{1-3-5}, R^{1-3-6}, R^{1-3-7}, R^{1-3-8}, R^{1-3-9} and R^{1-3-10} are independently hydrogen, C_1-C_7 alkyl, C_2-C_7 alkenyl, C_2-C_7 alkynyl or C_3-C_{14} cycloalkyl;

or, R^{1-3-5} and R^{1-3-6} together with the nitrogen atom they are attached to form a C_3-C_{14} heterocycloalkyl optionally substituted by one, two or three $R^{1-3-5-1}$; one or more methylenes in the C_3-C_{14} heterocycloalkyl are optionally and independently substituted by oxygen atom, sulfur atom, sulfinyl, sulfonyl, carbonyl, vinylidene or -N($R^{1-3-5-2}$)-; $R^{1-3-5-1}$ is independently C_1-C_7 alkyl or C_3-C_{14} cycloalkyl; $R^{1-3-5-2}$ is independently C_1-C_7 alkyl or C_3-C_{14} cycloalkyl;

or, R^{1-3-7} and R^{1-3-8} together with the nitrogen atom they are attached to form a C_3-C_{14} heterocycloalkyl optionally substituted by one, two or three $R^{1-3-7-1}$; one or more methylenes in the C_3-C_{14} heterocycloalkyl are optionally and independently substituted by oxygen atom, sulfur atom, sulfinyl, sulfonyl, carbonyl, vinylidene or -N($R^{1-3-7-2}$)-; $R^{1-3-7-1}$ is independently C_1-C_7 alkyl or C_3-C_{14} cycloalkyl; $R^{1-3-7-2}$ is independently C_1-C_7 alkyl or C_3-C_{14} cycloalkyl;

or, R^{1-3-9} and R^{1-3-10} together with the nitrogen atom they are attached to form a C_3-C_{14} heterocycloalkyl optionally substituted by one, two or three $R^{1-3-9-1}$; one or more methylenes in the C_3-C_{14} heterocycloalkyl are optionally and independently substituted by oxygen atom, sulfur atom, sulfinyl, sulfonyl, carbonyl, vinylidene or -N($R^{1-3-9-2}$)-; $R^{1-3-9-1}$ is independently C_1-C_7 alkyl or C_3-C_{14} cycloalkyl; $R^{1-3-9-2}$ is independently C_1-C_7 alkyl or C_3-C_{14} cycloalkyl;

R^{1-3-11} is independently halogen, hydroxyl, amino, mercapto, cyano, C_1-C_7 alkyl, C_1-C_7 alkoxy, C_1-C_7 alkylthio, C_2-C_7 alkenyl, C_2-C_7 alkynyl, C_3-C_{14} cycloalkyl, C_3-C_{14} heterocycloalkyl, C_6-C_{10} aryl, C_1-C_7 heteroaryl or "amino substituted by one or two $R^{1-3-11-1}$"; $R^{1-3-11-1}$ is independently C_1-C_7 alkyl or C_3-C_{14} cycloalkyl;

R^{1-3-12} is independently halogen, hydroxyl, amino, mercapto, cyano, C_1-C_7 alkyl, C_1-C_7 alkoxy, C_1-C_7 alkylthio, C_2-C_7 alkenyl, C_2-C_7 alkynyl, C_3-C_{14} cycloalkyl, C_3-C_{14} heterocycloalkyl, C_6-C_{10} aryl, C_1-C_7 heteroaryl or "amino substituted by one or two $R^{1-3-12-1}$"; $R^{1-3-12-1}$ is independently C_1-C_7 alkyl or C_3-C_{14} cycloalkyl;

R^{1-5} is independently hydrogen, -$NR^{1-5-1}R^{1-5-2}$, -OR^{1-5-3} or "C_1-C_7 alkyl, C_2-C_7 alkenyl, C_2-C_7 alkynyl, C_3-C_{14} cycloalkyl, C_3-C_{14} heterocycloalkyl, C_6-C_{10} aryl, or C_1-C_7 heteroaryl" optionally substituted by one, two or three R^{1-5-4};

R^{1-5-1} and R^{1-5-2} are independently hydrogen, C_1-C_7 alkyl, C_2-C_7 alkenyl, C_2-C_7 alkynyl or C_3-C_{14} cycloalkyl;

or, R^{1-5-1} and R^{1-5-2} together with the nitrogen atom they are attached to form a C_3-C_{14} heterocycloalkyl optionally substituted by one, two or three $R^{1-5-1-1}$; one or more methylenes in the C_3-C_{14} heterocycloalkyl are optionally and independently substituted by oxygen atom, sulfur atom, sulfinyl, sulfonyl, carbonyl, vinylidene or -N($R^{1-5-1-2}$)-; $R^{1-5-1-1}$ is independently C_1-C_7 alkyl or C_3-C_{14} cycloalkyl; $R^{1-5-1-2}$ is independently C_1-C_7 alkyl or C_3-C_{14} cycloalkyl;

R^{1-5-3} is independently hydrogen, C_1-C_7 alkyl, C_2-C_7 alkenyl, C_2-C_7 alkynyl, C_3-C_{14} cycloalkyl, C_3-C_{14} heterocycloalkyl, C_6-C_{10} aryl or C_1-C_7 heteroaryl;

R^{1-5-4} is independently halogen, hydroxyl, amino, mercapto, cyano, C_1-C_7 alkyl, C_1-C_7 alkoxy, C_1-C_7

alkylthio, C_2-C_7 alkenyl, C_2-C_7 alkynyl, C_3-C_{14} cycloalkyl, C_3-C_{14} heterocycloalkyl, C_6-C_{10} aryl, C_1-C_7 heteroaryl or "amino substituted by one or two $R^{1-5-4-1}$"; $R^{1-5-4-1}$ is independently C_1-C_7 alkyl or C_3-C_{14} cycloalkyl;

R^{1-6} is independently hydrogen, -CN, -OH or "C_1-C_7 alkyl, C_2-C_7 alkenyl, C_2-C_7 alkynyl, C_3-C_{14} cycloalkyl, C_3-C_{14} heterocycloalkyl, C_6-C_{10} aryl, or C_1-C_7 heteroaryl" optionally substituted by one, two or three R^{1-6-1};

R^{1-6-1} is independently halogen, hydroxyl, amino, mercapto, cyano, C_1-C_7 alkyl, C_1-C_7 alkoxy, C_1-C_7 alkylthio, C_2-C_7 alkenyl, C_2-C_7 alkynyl, C_3-C_{14} cycloalkyl, C_3-C_{14} heterocycloalkyl, C_6-C_{10} aryl, C_1-C_7 heteroaryl or "amino substituted by one or two $R^{1-6-1-1}$"; $R^{1-6-1-1}$ is independently C_1-C_7 alkyl or C_3-C_{14} cycloalkyl;

R^{1-7} is independently hydrogen, -OR^{1-7-1}, -$NR^{1-7-2}R^{1-7-3}$ or "C_1-C_7 alkyl, C_2-C_7 alkenyl, C_2-C_7 alkynyl, C_3-C_{14} cycloalkyl, C_3-C_{14} heterocycloalkyl, C_6-C_{10} aryl or C_1-C_7 heteroaryl" optionally substituted by one, two or three R^{1-7-4};

R^{1-7-1} is independently hydrogen, C_1-C_7 alkyl, C_2-C_7 alkenyl, C_2-C_7 alkynyl, C_3-C_{14} cycloalkyl, C_3-C_{14} heterocycloalkyl, C_6-C_{10} aryl or C_1-C_7 heteroaryl;

R^{1-7-2} and R^{1-7-3} are independently C_1-C_7 alkyl, C_2-C_7 alkenyl, C_2-C_7 alkynyl or C_3-C_{14} cycloalkyl;

or, R^{1-7-2} and R^{1-7-3} together with the nitrogen atom they are attached to form a C_3-C_{14} heterocycloalkyl optionally substituted by one, two or three $R^{1-7-2-1}$; one or more methylenes in the C_3-C_{14} heterocycloalkyl are optionally and independently substituted by oxygen atom, sulfur atom, sulfinyl, sulfonyl, carbonyl, vinylidene or -$N(R^{1-7-2-2})$-; $R^{1-7-2-1}$ is independently C_1-C_7 alkyl or C_3-C_{14} cycloalkyl; $R^{1-7-2-2}$ is independently C_1-C_7 alkyl or C_3-C_{14} cycloalkyl;

R^{1-7-4} is independently halogen, hydroxyl, amino, mercapto, cyano, C_1-C_7 alkyl, C_1-C_7 alkoxy, C_1-C_7 alkylthio, C_2-C_7 alkenyl, C_2-C_7 alkynyl, C_3-C_{14} cycloalkyl, C_3-C_{14} heterocycloalkyl, C_6-C_{10} aryl, C_1-C_7 heteroaryl or "amino substituted by one or two $R^{1-7-4-1}$"; $R^{1-7-4-1}$ is independently C_1-C_7 alkyl or C_3-C_{14} cycloalkyl;

R^{1-8} is independently oxo, halogen, -OH, amino, mercapto, cyano, C_1-C_7 alkyl, C_1-C_7 alkoxy, C_1-C_7 alkylthio, C_2-C_7 alkenyl, C_2-C_7 alkynyl, C_3-C_{14} cycloalkyl, C_3-C_{14} heterocycloalkyl, C_6-C_{10} aryl, C_1-C_7 heteroaryl or "amino substituted by one or two R^{1-8-1}"; R^{1-8-1} is independently C_1-C_7 alkyl or C_3-C_{14} cycloalkyl;

R^{1-9} is independently hydrogen or C_1-C_7 alkyl;

R^2 is -OR^{2-1}, cyano, carboxyl; or "C_2-C_7 alkyl, C_3-C_{14} cycloalkyl or C_3-C_{14} heterocycloalkyl" optionally substituted by one, two or three R^{2-2};

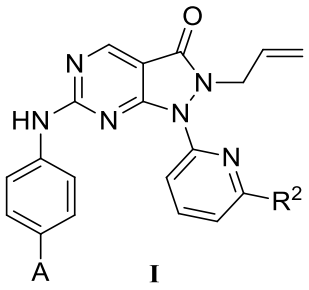
R^{2-1} is C_1-C_7 alkyl, C_2-C_7 alkenyl, C_2-C_7 alkynyl, C_3-C_{14} cycloalkyl, C_3-C_{14} heterocycloalkyl, C_6-C_{10} aryl or C_1-C_7 heteroaryl;

R^{2-2} is independently halogen, hydroxyl, amino, C_1-C_7 alkyl, C_1-C_7 alkoxy, C_3-C_{14} cycloalkyl or C_3-C_{14} heterocycloalkyl;

in any one of the above cases, the heteroatoms in the C_3-C_{14} heterocycloalkyl, C_1-C_7 heteroaryl are independently selected from one or more of boron, silicon, oxygen, sulfur, selenium, nitrogen and

phosphorus; the number of heteroatoms is independently 1, 2, 3 or 4.

2. The pyrazolopyrimidine compound represented by formula **II** according to claim 1, the pharmaceutically acceptable salt thereof, the solvate thereof, the solvate of the pharmaceutically acceptable salt thereof, the metabolite thereof or the prodrug thereof, wherein, the compound is a pyrazolopyrimidine compound represented by formula **I**:



I

wherein, A is C_3-C_{20} cycloalkyl substituted by one or two R^1;

R^1 is independently halogen, -OR^{1-1}, -SR^{1-2}, -CN, -$NR^{1-3}R^{1-4}$, -$C(=O)R^{1-5}$, -$C(=NR^{1-6})R^{1-7}$ or "C_2-C_7 alkenyl, C_2-C_8 alkynyl, C_3-C_{14} cycloalkyl, C_3-C_{14} heterocycloalkyl, C_6-C_{10} aryl or C_1-C_7 heteroaryl" optionally substituted by one, two or three R^{1-8};

R^{1-1} is independently "C_1-C_7 alkyl, C_2-C_7 alkenyl, C_2-C_7 alkynyl, C_3-C_{14} cycloalkyl, C_3-C_{14} heterocycloalkyl, C_6-C_{10} aryl, or C_1-C_7 heteroaryl" optionally substituted by one, two or three R^{1-1-1};

R^{1-1-1} is independently halogen, hydroxyl, amino, mercapto, cyano, C_1-C_7 alkyl, C_1-C_7 alkoxy, C_1-C_7 alkylthio, C_2-C_7 alkenyl, C_2-C_7 alkynyl, C_3-C_{14} cycloalkyl, C_3-C_{14} heterocycloalkyl, C_6-C_{10} aryl, C_1-C_7 heteroaryl or "amino substituted by one or two $R^{1-1-1-1}$"; $R^{1-1-1-1}$ is independently C_1-C_7 alkyl or C_3-C_{14} cycloalkyl;

R^{1-2} is independently hydrogen, or "C_1-C_7 alkyl, C_2-C_7 alkenyl, C_2-C_7 alkynyl, C_3-C_{14} cycloalkyl, C_3-C_{14} heterocycloalkyl, C_6-C_{10} aryl, or C_1-C_7 heteroaryl" optionally substituted by one, two or three R^{1-2-1};

R^{1-2-1} is independently hydrogen, halogen, hydroxyl, amino, mercapto, cyano, C_1-C_7 alkyl, C_1-C_7 alkoxy, C_1-C_7 alkylthio, C_2-C_7 alkenyl, C_2-C_7 alkynyl, C_3-C_{14} cycloalkyl, C_3-C_{14} heterocycloalkyl, C_6-C_{10} aryl, C_1-C_7 heteroaryl or "amino substituted by one or two $R^{1-2-1-1}$"; $R^{1-2-1-1}$ is independently C_1-C_7 alkyl or C_3-C_{14} cycloalkyl;

R^{1-3} and R^{1-4} are independently hydrogen, -$S(=O)_2R^{1-3-1}$, -$C(=O)R^{1-3-2}$, -$C(=NR^{1-3-3})NR^{1-3-5}R^{1-3-6}$, -$S(=O)_2NR^{1-3-7}R^{1-3-8}$, -$C(=O)NR^{1-3-9}R^{1-3-10}$ or "C_1-C_7 alkyl, C_2-C_7 alkenyl, C_2-C_7 alkynyl, C_3-C_{14} cycloalkyl, C_3-C_{14} heterocycloalkyl, C_6-C_{10} aryl or C_1-C_7 heteroaryl" optionally substituted by one, two or three R^{1-3-11};

or, R^{1-3} and R^{1-4} together with the nitrogen atom they are attached to form a C_3-C_{14} heterocycloalkyl optionally substituted by one, two or three R^{1-3-12}; one or more methylenes in the C_3-C_{14} heterocycloalkyl are optionally and independently substituted by oxygen atom, sulfur atom, sulfinyl, sulfonyl, carbonyl, vinylidene or -$N(R^{1-3-13})$-; R^{1-3-13} is independently C_1-C_7 alkyl or C_3-C_{14} cycloalkyl;

R^{1-3-1} and R^{1-3-2} are independently "C_1-C_7 alkyl, C_2-C_7 alkenyl, C_2-C_7 alkynyl, C_3-C_{14} cycloalkyl, C_3-C_{14} heterocycloalkyl or C_6-C_{10} aryl" optionally substituted by one or two $R^{1-3-1-1}$; $R^{1-3-1-1}$ is independently C_1-C_7 alkyl or C_3-C_{14} cycloalkyl;

R^{1-3-3} is independently hydrogen, -CN, C_1-C_7 alkyl, C_2-C_7 alkenyl, C_2-C_7 alkynyl or C_3-C_{14} cycloalkyl;

R^{1-3-5}, R^{1-3-6}, R^{1-3-7}, R^{1-3-8}, R^{1-3-9} and R^{1-3-10} are independently C_1-C_7 alkyl, C_2-C_7 alkenyl, C_2-C_7 alkynyl or C_3-C_{14} cycloalkyl;

or, R^{1-3-5} and R^{1-3-6} together with the nitrogen atom they are attached to form a C_3-C_{14} heterocycloalkyl optionally substituted by one, two or three $R^{1-3-5-1}$; one or more methylenes in the C_3-C_{14} heterocycloalkyl are optionally and independently substituted by oxygen atom, sulfur atom, sulfinyl, sulfonyl, carbonyl, vinylidene or -N($R^{1-3-5-2}$)-; $R^{1-3-5-1}$ is independently C_1-C_7 alkyl or C_3-C_{14} cycloalkyl; $R^{1-3-5-2}$ is independently C_1-C_7 alkyl or C_3-C_{14} cycloalkyl;

or, R^{1-3-7} and R^{1-3-8} together with the nitrogen atom they are attached to form a C_3-C_{14} heterocycloalkyl optionally substituted by one, two or three $R^{1-3-7-1}$; one or more methylenes in the C_3-C_{14} heterocycloalkyl are optionally and independently substituted by oxygen atom, sulfur atom, sulfinyl, sulfonyl, carbonyl, vinylidene or -N($R^{1-3-7-2}$)-; $R^{1-3-7-1}$ is independently C_1-C_7 alkyl or C_3-C_{14} cycloalkyl; $R^{1-3-7-2}$ is independently C_1-C_7 alkyl or C_3-C_{14} cycloalkyl;

or, R^{1-3-9} and R^{1-3-10} together with the nitrogen atom they are attached to form a C_3-C_{14} heterocycloalkyl optionally substituted by one, two or three $R^{1-3-9-1}$; one or more methylenes in the C_3-C_{14} heterocycloalkyl are optionally and independently substituted by oxygen atom, sulfur atom, sulfinyl, sulfonyl, carbonyl, vinylidene or -N($R^{1-3-9-2}$)-; $R^{1-3-9-1}$ is independently C_1-C_7 alkyl or C_3-C_{14} cycloalkyl; $R^{1-3-9-2}$ is independently C_1-C_7 alkyl or C_3-C_{14} cycloalkyl;

R^{1-3-11} is independently halogen, hydroxyl, amino, mercapto, cyano, C_1-C_7 alkyl, C_1-C_7 alkoxy, C_1-C_7 alkylthio, C_2-C_7 alkenyl, C_2-C_7 alkynyl, C_3-C_{14} cycloalkyl, C_3-C_{14} heterocycloalkyl, C_6-C_{10} aryl, C_1-C_7 heteroaryl or "amino substituted by one or two $R^{1-3-11-1}$"; $R^{1-3-11-1}$ is independently C_1-C_7 alkyl or C_3-C_{14} cycloalkyl;

R^{1-3-12} is independently halogen, hydroxyl, amino, mercapto, cyano, C_1-C_7 alkyl, C_1-C_7 alkoxy, C_1-C_7 alkylthio, C_2-C_7 alkenyl, C_2-C_7 alkynyl, C_3-C_{14} cycloalkyl, C_3-C_{14} heterocycloalkyl, C_6-C_{10} aryl, C_1-C_7 heteroaryl or "amino substituted by one or two $R^{1-3-12-1}$"; $R^{1-3-12-1}$ is independently C_1-C_7 alkyl or C_3-C_{14} cycloalkyl;

R^{1-5} is independently hydrogen, -$NR^{1-5-1}R^{1-5-2}$, -OR^{1-5-3} or "C_1-C_7 alkyl, C_2-C_7 alkenyl, C_2-C_7 alkynyl, C_3-C_{14} cycloalkyl, C_3-C_{14} heterocycloalkyl, C_6-C_{10} aryl, or C_1-C_7 heteroaryl" optionally substituted by one, two or three R^{1-5-4};

R^{1-5-1} and R^{1-5-2} are independently hydrogen, C_1-C_7 alkyl, C_2-C_7 alkenyl, C_2-C_7 alkynyl or C_3-C_{14} cycloalkyl;

or, R^{1-5-1} and R^{1-5-2} together with the nitrogen atom they are attached to form a C_3-C_{14} heterocycloalkyl optionally substituted by one, two or three $R^{1-5-1-1}$; one or more methylenes in the C_3-C_{14} heterocycloalkyl are optionally and independently substituted by oxygen atom, sulfur atom, sulfinyl, sulfonyl, carbonyl, vinylidene or -N($R^{1-5-1-2}$)-; $R^{1-5-1-1}$ is independently C_1-C_7 alkyl or C_3-C_{14} cycloalkyl; $R^{1-5-1-2}$ is independently C_1-C_7 alkyl or C_3-C_{14} cycloalkyl;

R^{1-5-3} is independently hydrogen, C_1-C_7 alkyl, C_2-C_7 alkenyl, C_2-C_7 alkynyl, C_3-C_{14} cycloalkyl, C_3-C_{14} heterocycloalkyl, C_6-C_{10} aryl or C_1-C_7 heteroaryl;

R^{1-5-4} is independently halogen, hydroxyl, amino, mercapto, cyano, C_1-C_7 alkyl, C_1-C_7 alkoxy, C_1-C_7

alkylthio, C_2-C_7 alkenyl, C_2-C_7 alkynyl, C_3-C_{14} cycloalkyl, C_3-C_{14} heterocycloalkyl, C_6-C_{10} aryl, C_1-C_7 heteroaryl or "amino substituted by one or two $R^{1-5-4-1}$"; $R^{1-5-4-1}$ is independently C_1-C_7 alkyl or C_3-C_{14} cycloalkyl;

R^{1-6} is independently hydrogen, -CN, -OH or "C_1-C_7 alkyl, C_2-C_7 alkenyl, C_2-C_7 alkynyl, C_3-C_{14} cycloalkyl, C_3-C_{14} heterocycloalkyl, C_6-C_{10} aryl, or C_1-C_7 heteroaryl" optionally substituted by one, two or three R^{1-6-1};

R^{1-6-1} is independently halogen, hydroxyl, amino, mercapto, cyano, C_1-C_7 alkyl, C_1-C_7 alkoxy, C_1-C_7 alkylthio, C_2-C_7 alkenyl, C_2-C_7 alkynyl, C_3-C_{14} cycloalkyl, C_3-C_{14} heterocycloalkyl, C_6-C_{10} aryl, C_1-C_7 heteroaryl or "amino substituted by one or two $R^{1-6-1-1}$"; $R^{1-6-1-1}$ is independently C_1-C_7 alkyl or C_3-C_{14} cycloalkyl;

R^{1-7} is independently hydrogen, $-OR^{1-7-1}$, $-NR^{1-7-2}R^{1-7-3}$ or "C_1-C_7 alkyl, C_2-C_7 alkenyl, C_2-C_7 alkynyl, C_3-C_{14} cycloalkyl, C_3-C_{14} heterocycloalkyl, C_6-C_{10} aryl or C_1-C_7 heteroaryl" optionally substituted by one, two or three R^{1-7-4};

R^{1-7-1} is independently hydrogen, C_1-C_7 alkyl, C_2-C_7 alkenyl, C_2-C_7 alkynyl, C_3-C_{14} cycloalkyl, C_3-C_{14} heterocycloalkyl, C_6-C_{10} aryl or C_1-C_7 heteroaryl;

R^{1-7-2} and R^{1-7-3} are independently C_1-C_7 alkyl, C_2-C_7 alkenyl, C_2-C_7 alkynyl or C_3-C_{14} cycloalkyl;

or, R^{1-7-2} and R^{1-7-3} together with the nitrogen atom they are attached to form a C_3-C_{14} heterocycloalkyl optionally substituted by one, two or three $R^{1-7-2-1}$; one or more methylenes in the C_3-C_{14} heterocycloalkyl are optionally and independently substituted by oxygen atom, sulfur atom, sulfinyl, sulfonyl, carbonyl, vinylidene or $-N(R^{1-7-2-2})-$; $R^{1-7-2-1}$ is independently C_1-C_7 alkyl or C_3-C_{14} cycloalkyl; $R^{1-7-2-2}$ is independently C_1-C_7 alkyl or C_3-C_{14} cycloalkyl;

R^{1-7-4} is independently halogen, hydroxyl, amino, mercapto, cyano, C_1-C_7 alkyl, C_1-C_7 alkoxy, C_1-C_7 alkylthio, C_2-C_7 alkenyl, C_2-C_7 alkynyl, C_3-C_{14} cycloalkyl, C_3-C_{14} heterocycloalkyl, C_6-C_{10} aryl, C_1-C_7 heteroaryl or "amino substituted by one or two $R^{1-7-4-1}$"; $R^{1-7-4-1}$ is independently C_1-C_7 alkyl or C_3-C_{14} cycloalkyl;

R^{1-8} is independently halogen, -OH, amino, mercapto, cyano, C_1-C_7 alkyl, C_1-C_7 alkoxy, C_1-C_7 alkylthio, C_2-C_7 alkenyl, C_2-C_7 alkynyl, C_3-C_{14} cycloalkyl, C_3-C_{14} heterocycloalkyl, C_6-C_{10} aryl, C_1-C_7 heteroaryl or "amino substituted by one or two R^{1-8-1}"; R^{1-8-1} is independently C_1-C_7 alkyl or C_3-C_{14} cycloalkyl;

R^2 is $-OR^{2-1}$, cyano, carboxyl; or "C_2-C_7 alkyl, C_3-C_{14} cycloalkyl or C_3-C_{14} heterocycloalkyl" optionally substituted by one, two or three R^{2-2};

R^{2-1} is C_1-C_7 alkyl, C_2-C_7 alkenyl, C_2-C_7 alkynyl, C_3-C_{14} cycloalkyl, C_3-C_{14} heterocycloalkyl, C_6-C_{10} aryl or C_1-C_7 heteroaryl;

R^{2-2} is independently halogen, hydroxyl, amino, C_1-C_7 alkyl, C_1-C_7 alkoxy, C_3-C_{14} cycloalkyl or C_3-C_{14} heterocycloalkyl;

in any one of the above cases, the heteroatoms in the C_3-C_{14} heterocycloalkyl, C_1-C_7 heteroaryl are independently selected from one or more of boron, silicon, oxygen, sulfur, selenium, nitrogen and phosphorus; the number of heteroatoms is independently 1, 2, 3 or 4.

3. The pyrazolopyrimidine compound represented by formula **II** according to claim 1 or 2, the

pharmaceutically acceptable salt thereof, the solvate thereof, the solvate of the pharmaceutically acceptable salt thereof, the metabolite thereof or the prodrug thereof, wherein, when A is C_3-C_{20} cycloalkyl substituted by one or two R^1, the C_3-C_{20} cycloalkyl is C_3-C_{20} monocyclic cycloalkyl, C_3-C_{20} spiro cycloalkyl, C_3-C_{20} fused cycloalkyl or C_3-C_{20} bridged cycloalkyl;

and/or, when A is C_3-C_{20} cycloalkyl substituted by one or two R^1, the C_3-C_{20} cycloalkyl is C_3-C_{20} saturated cycloalkyl;

and/or, when R^1 is independently C_3-C_{14} heterocycloalkyl, the C_3-C_{14} heterocycloalkyl is C_3-C_{14} monocyclic heterocycloalkyl, C_3-C_{14} spiro heterocycloalkyl, C_3-C_{14} fused heterocycloalkyl or C_3-C_{14} bridged heterocycloalkyl;

and/or, when R^1 is independently C_3-C_{14} heterocycloalkyl, the heteroatom of the C_3-C_{14} heterocycloalkyl is not substituted;

and/or, when R^1 is independently C_3-C_{14} heterocycloalkyl, the methylene in the C_3-C_{14} heterocycloalkyl is not substituted;

and/or, when R^1 is independently C_3-C_{14} heterocycloalkyl substituted by one R^{1-8}, the C_3-C_{14} heterocycloalkyl is C_3-C_{14} monocyclic heterocycloalkyl, C_3-C_{14} spiro heterocycloalkyl, C_3-C_{14} fused heterocycloalkyl or C_3-C_{14} bridged heterocycloalkyl;

and/or, when R^1 is independently C_3-C_{14} heterocycloalkyl substituted by one R^{1-8}, the heteroatom of the C_3-C_{14} heterocycloalkyl is not substituted except R^{1-8};

and/or, when R^1 is independently C_3-C_{14} heterocycloalkyl substituted by one R^{1-8}, the methylene in the C_3-C_{14} heterocycloalkyl is not substituted;

and/or, when R^{1-3} and R^{1-4} are independently C_1-C_7 alkyl, the C_1-C_7 alkyl is C_1-C_3 alkyl;

and/or, when R^{1-3-1} is independently C_1-C_7 alkyl, the C_1-C_7 alkyl is C_1-C_3 alkyl;

and/or, when R^{1-3-2} is independently C_3-C_{14} cycloalkyl, the C_3-C_{14} cycloalkyl is C_3-C_{14} monocyclic cycloalkyl, C_3-C_{14} spiro cycloalkyl, C_3-C_{14} fused cycloalkyl or C_3-C_{14} bridged cycloalkyl;

and/or, when R^{1-3-2} is C_3-C_{14} cycloalkyl, the C_3-C_{14} cycloalkyl is C_3-C_{14} saturated cycloalkyl;

and/or, when R^{1-5} is independently C_3-C_{14} heterocycloalkyl, the C_3-C_{14} heterocycloalkyl is C_3-C_{14} monocyclic heterocycloalkyl, C_3-C_{14} spiro heterocycloalkyl, C_3-C_{14} fused heterocycloalkyl or C_3-C_{14} bridged heterocycloalkyl;

and/or, when R^{1-5} is independently C_3-C_{14} heterocycloalkyl, the heteroatom of the C_3-C_{14} heterocycloalkyl is not substituted;

and/or, when R^{1-5} is independently C_3-C_{14} heterocycloalkyl, the methylene in the C_3-C_{14} heterocycloalkyl is not substituted;

and/or, when R^{1-5-1} and R^{1-5-2} are independently C_1-C_7 alkyl, the C_1-C_7 alkyl is C_1-C_3 alkyl;

and/or, when R^{1-5-1} and R^{1-5-2} are independently C_3-C_{14} cycloalkyl, the C_3-C_{14} cycloalkyl is C_3-C_{14} monocyclic cycloalkyl, C_3-C_{14} spiro cycloalkyl, C_3-C_{14} fused cycloalkyl or C_3-C_{14} bridged cycloalkyl;

and/or, when R^{1-5-1} and R^{1-5-2} are independently C_3-C_{14} cycloalkyl, the C_3-C_{14} cycloalkyl is C_3-C_{14} saturated cycloalkyl;

and/or, when R^{1-5-3} is independently C_1-C_7 alkyl, the C_1-C_7 alkyl is C_1-C_3 alkyl;

and/or, when R^{1-9} is independently C_1-C_7 alkyl, the C_1-C_7 alkyl is C_1-C_3 alkyl;

and/or, when R^2 is C_2-C_7 alkyl optionally substituted by one, two or three R^{2-2}, the C_2-C_7 alkyl is C_2-C_4 alkyl;

and/or, when R^2 is C_3-C_{14} heterocycloalkyl optionally substituted by one, two or three R^{2-2}, the C_3-C_{14} heterocycloalkyl is C_3-C_{14} monocyclic heterocycloalkyl, C_3-C_{14} spiro heterocycloalkyl, C_3-C_{14} fused heterocycloalkyl or C_3-C_{14} bridged heterocycloalkyl;

and/or, when R^2 is C_3-C_{14} heterocycloalkyl optionally substituted by one, two or three R^{2-2}, the heteroatom of the C_3-C_{14} heterocycloalkyl is not substituted except R^{2-2};

and/or, when R^2 is C_3-C_{14} heterocycloalkyl optionally substituted by one, two or three R^{2-2}, the methylene in the C_3-C_{14} heterocycloalkyl is not substituted;

and/or, the ratio of each isomer in the pyrazolopyrimidine compound represented by formula **II** is equal;

and/or, the atoms in the pyrazolopyrimidine compound represented by formula **II**, the pharmaceutically acceptable salt thereof, the solvate thereof, the solvate of the pharmaceutically acceptable salt thereof, the metabolite thereof or the prodrug thereof all exist in their natural abundance.

4. The pyrazolopyrimidine compound represented by formula **II** according to claim 3, the pharmaceutically acceptable salt thereof, the solvate thereof, the solvate of the pharmaceutically acceptable salt thereof, the metabolite thereof or the prodrug thereof, wherein, when A is C_3-C_{20} cycloalkyl substituted by one or two R^1, the C_3-C_{20} cycloalkyl is C_3-C_{20} monocyclic cycloalkyl, C_3-C_{20} monocyclic cycloalkyl is C_3-C_6 monocyclic cycloalkyl;

and/or, when A is C_3-C_{20} cycloalkyl substituted by one or two R^1, the C_3-C_{20} cycloalkyl is C_3-C_{20} bridged cycloalkyl; the C_3-C_{20} bridged cycloalkyl is C_5-C_8 bridged cycloalkyl;

and/or, when R^1 is independently C_3-C_{14} heterocycloalkyl, the C_3-C_{14} heterocycloalkyl is C_3-C_{14} monocyclic heterocycloalkyl; the C_3-C_{14} monocyclic heterocycloalkyl is "C_3-C_9 monocyclic heterocycloalkyl having one or two heteroatoms selected from one or two of N, O and S";

and/or, when R^1 is independently C_3-C_{14} heterocycloalkyl substituted by one R^{1-8}, the C_3-C_{14} heterocycloalkyl is C_3-C_{14} monocyclic heterocycloalkyl; the C_3-C_{14} monocyclic heterocycloalkyl is the "C_3-C_9 monocyclic heterocycloalkyl having one or two heteroatoms selected from one or two of N, O and S";

and/or, when R^{1-3} and R^{1-4} are independently C_1-C_7 alkyl, the C_1-C_7 alkyl is methyl, ethyl, *n*-propyl or isopropyl;

and/or, when R^{1-3-1} is independently C_1-C_7 alkyl, the C_1-C_7 alkyl is methyl, ethyl, *n*-propyl or isopropyl;

and/or, when R^{1-3-2} is independently C_3-C_{14} cycloalkyl, the C_3-C_{14} cycloalkyl is C_3-C_{14} monocyclic cycloalkyl; the C_3-C_{14} monocyclic cycloalkyl is C_3-C_6 monocyclic cycloalkyl;

and/or, when R^{1-5} is independently C_3-C_{14} heterocycloalkyl, the C_3-C_{14} heterocycloalkyl is C_3-C_{14} monocyclic heterocycloalkyl; the C_3-C_{14} monocyclic heterocycloalkyl is "C_3-C_9 monocyclic heterocycloalkyl having one or two heteroatoms selected from one or two of N, O and S";

and/or, when R^{1-5-1} and R^{1-5-2} are independently C_1-C_7 alkyl, the C_1-C_7 alkyl is methyl, ethyl, *n*-propyl or isopropyl;

and/or, when R^{1-5-1} and R^{1-5-2} are independently C_3-C_{14} cycloalkyl, the C_3-C_{14} cycloalkyl is C_3-C_{14}

monocyclic cycloalkyl; the C_3-C_{14} monocyclic cycloalkyl is C_3-C_6 monocyclic cycloalkyl;

and/or, when R^{1-5-3} is independently C_1-C_7 alkyl, the C_1-C_7 alkyl is methyl, ethyl, *n*-propyl or isopropyl;

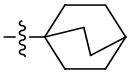
and/or, when R^2 is C_2-C_7 alkyl optionally substituted by one, two or three R^{2-2}, the C_2-C_7 alkyl is ethyl, *n*-propyl, isopropyl, *n*-butyl, isobutyl, *sec*-butyl or *tert*-butyl;

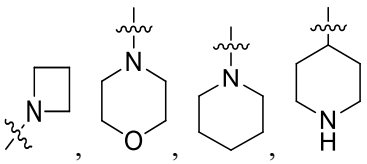
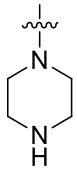
and/or, when R^2 is independently C_3-C_{14} heterocycloalkyl substituted by one, two or three R^{2-2}, the C_3-C_{14} heterocycloalkyl is C_3-C_{14} monocyclic heterocycloalkyl; the C_3-C_{14} monocyclic heterocycloalkyl is " C_3-C_9 monocyclic heterocycloalkyl having one or two heteroatoms selected from one or two of N, O and S";

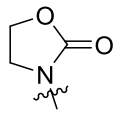
and/or, the ratio of each isomer in the pyrazolopyrimidine compound represented by formula **I** is equal;

and/or, the atoms in the pyrazolopyrimidine compound represented by formula **I**, the pharmaceutically acceptable salt thereof, the solvate thereof, the solvate of the pharmaceutically acceptable salt thereof, the metabolite thereof or the prodrug thereof all exist in their natural abundance.

5. The pyrazolopyrimidine compound represented by formula **II** according to claim 4, the pharmaceutically acceptable salt thereof, the solvate thereof, the solvate of the pharmaceutically acceptable salt thereof, the metabolite thereof or the prodrug thereof, wherein, when A is C_3-C_{20} cycloalkyl substituted by one or two R^1, the C_3-C_{20} cycloalkyl is C_3-C_{20} monocyclic cycloalkyl, the C_3-C_{20} monocyclic cycloalkyl is cyclopropyl, cyclobutyl, cyclopentyl or cyclohexyl;

and/or, when A is C_3-C_{20} cycloalkyl substituted by one or two R^1, the C_3-C_{20} cycloalkyl is C_3-C_{20} bridged cycloalkyl; the C_3-C_{20} bridged cycloalkyl is  or ;

and/or, when R^1 is independently C_3-C_{14} heterocycloalkyl, the C_3-C_{14} heterocycloalkyl is C_3-C_{14} monocyclic heterocycloalkyl; the C_3-C_{14} monocyclic heterocycloalkyl is , , , or ;

and/, when R^1 is independently C_3-C_{14} heterocycloalkyl substituted by one R^{1-8}, the C_3-C_{14} heterocycloalkyl substituted by one R^{1-8} is ;

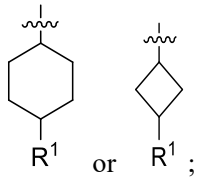
and/or, when R^{1-3-2} is C_3-C_{14} cycloalkyl, the C_3-C_{14} cycloalkyl is C_3-C_{14} monocyclic cycloalkyl; the C_3-C_{14} monocyclic cycloalkyl is cyclopropyl, cyclobutyl, cyclopentyl or cyclohexyl;

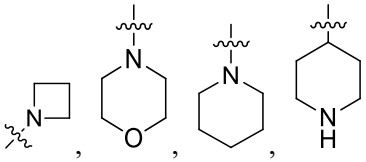
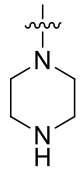
and/or, when R^{1-5} is independently C_3-C_{14} heterocycloalkyl, the C_3-C_{14} heterocycloalkyl is C_3-C_{14} monocyclic heterocycloalkyl; the C_3-C_{14} monocyclic heterocycloalkyl is ;

and/or, when R^{1-5-1} and R^{1-5-2} are independently C_3-C_{14} cycloalkyl, the C_3-C_{14} cycloalkyl is C_3-C_{14}

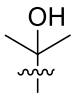
monocyclic cycloalkyl; the C_3-C_{14} monocyclic cycloalkyl is cyclopropyl, cyclobutyl, cyclopentyl or cyclohexyl;

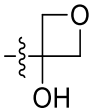
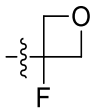
and/or, when R^2 is C_3-C_{14} heterocycloalkyl optionally substituted by one, two or three R^{2-2}, the C_3-C_{14} heterocycloalkyl is C_3-C_{14} monocyclic heterocycloalkyl; the C_3-C_{14} monocyclic heterocycloalkyl is oxetan-3-yl.

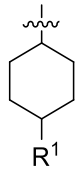
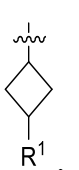
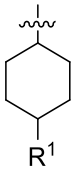
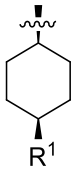
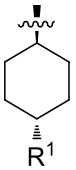
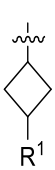
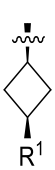
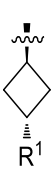
6. The pyrazolopyrimidine compound represented by formula **II** according to claim 1 or 2, the pharmaceutically acceptable salt thereof, the solvate thereof, the solvate of the pharmaceutically acceptable salt thereof, the metabolite thereof or the prodrug thereof, wherein, when A is C_3-C_{20} cycloalkyl substituted by one R^1, the A is  ;

and/or, when R^1 is independently C_3-C_{14} heterocycloalkyl, the C_3-C_{14} heterocycloalkyl is C_3-C_{14} monocyclic heterocycloalkyl; the C_3-C_{14} monocyclic heterocycloalkyl is  or  ;

and/or, when R^{1-5} is independently C_3-C_{14} heterocycloalkyl, the C_3-C_{14} heterocycloalkyl is C_3-C_{14} monocyclic heterocycloalkyl; the C_3-C_{14} monocyclic heterocycloalkyl is  ;

and/or, when R^2 is C_2-C_7 alkyl substituted by one R^{2-2}, R^{2-2} is hydroxyl; the C_2-C_7 alkyl substituted by one R^{2-2} is  ;

and/or, when R^2 is C_3-C_{14} heterocycloalkyl substituted by one R^{2-2}, R^{2-2} is halogen or hydroxyl; the C_3-C_{14} heterocycloalkyl substituted by one R^{2-2} is  or  .

7. The pyrazolopyrimidine compound represented by formula **II** according to claim 6, the pharmaceutically acceptable salt thereof, the solvate thereof, the solvate of the pharmaceutically acceptable salt thereof, the metabolite thereof or the prodrug thereof, wherein, when A is C_3-C_{20} cycloalkyl substituted by one R^1; the A is  or  ,  is  and/or  ,  is  and/or  .

8. The pyrazolopyrimidine compound represented by formula **II** according to claim 1 or 2, the pharmaceutically acceptable salt thereof, the solvate thereof, the solvate of the pharmaceutically acceptable salt thereof, the metabolite thereof or the prodrug thereof, wherein, A is C_3-C_{20} cycloalkyl substituted by one R^1;

and/or, X is N;

and/or, R^1 is independently cyano, halogen, $-NR^{1-3}R^{1-4}$, $-C(=O)R^{1-5}$, $-C(=NR^{1-6})R^{1-7}$, $=N-O-R^{1-9}$, C_1-C_7 heteroaryl or "C_3-C_{14} heterocycloalkyl" optionally substituted by one R^{1-8};

and/or, R^{1-3} and R^{1-4} are independently hydrogen, $-S(=O)_2R^{1-3-1}$, $-C(=O)R^{1-3-2}$, $-C(=NR^{1-3-3})NR^{1-3-5}R^{1-3-6}$, or C_1-C_7 alkyl; R^{1-3-1} and R^{1-3-2} are independently C_1-C_7 alkyl or C_3-C_{14} cycloalkyl; R^{1-3-3} is hydrogen; R^{1-3-5} and R^{1-3-6} are hydrogen;

and/or, R^{1-5} is independently $-NR^{1-5-1}R^{1-5-2}$, $-OR^{1-5-3}$ or C_3-C_{14} heterocycloalkyl; R^{1-5-1} and R^{1-5-2} are independently hydrogen, C_1-C_7 alkyl or C_3-C_{14} cycloalkyl; R^{1-5-3} is independently hydrogen or C_1-C_7 alkyl;

and/or, R^{1-8} is independently oxo;

and/or, R^2 is "C_2-C_7 alkyl, C_3-C_{14} cycloalkyl or C_3-C_{14} heterocycloalkyl" optionally substituted by one, two or three R^{2-2}; R^{2-2} is independently halogen or hydroxyl.

9. The pyrazolopyrimidine compound represented by formula **II** according to claim 1 or 2, the pharmaceutically acceptable salt thereof, the solvate thereof, the solvate of the pharmaceutically acceptable salt thereof, the metabolite thereof or the prodrug thereof, wherein, A is C_3-C_{20} cycloalkyl substituted by one R^1;

and/or, R^1 is independently cyano, halogen, $-NR^{1-3}R^{1-4}$, $-C(=O)R^{1-5}$, $-C(=NR^{1-6})R^{1-7}$, C_1-C_7 heteroaryl or C_3-C_{14} heterocycloalkyl;

and/or, R^{1-3} and R^{1-4} are independently hydrogen, $-S(=O)_2R^{1-3-1}$ or C_1-C_7 alkyl; R^{1-3-1} is independently C_1-C_7 alkyl;

and/or, R^{1-5} is independently $-NR^{1-5-1}R^{1-5-2}$, $-OR^{1-5-3}$ or C_3-C_{14} heterocycloalkyl; R^{1-5-1} and R^{1-5-2} are independently hydrogen, C_1-C_7 alkyl or C_3-C_{14} cycloalkyl; R^{1-5-3} is independently hydrogen or C_1-C_7 alkyl;

and/or, R^2 is "C_2-C_7 alkyl, C_3-C_{14} cycloalkyl or C_3-C_{14} heterocycloalkyl" optionally substituted by one, two or three R^{2-2}; R^{2-2} is independently halogen or hydroxyl.

10. The pyrazolopyrimidine compound represented by formula **II** according to claim 9, the pharmaceutically acceptable salt thereof, the solvate thereof, the solvate of the pharmaceutically acceptable salt thereof, the metabolite thereof or the prodrug thereof, wherein, R^1 is independently $-NR^{1-3}R^{1-4}$, $-C(=O)R^{1-5}$ or C_3-C_{14} heterocycloalkyl;

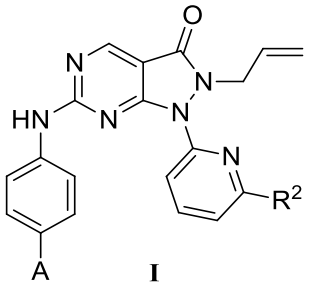
and/or, R^{1-5} is independently $-NR^{1-5-1}R^{1-5-2}$, $-OR^{1-5-3}$ or C_3-C_{14} heterocycloalkyl; R^{1-5-1} and R^{1-5-2} are independently hydrogen, C_1-C_7 alkyl or C_3-C_{14} cycloalkyl; R^{1-5-3} is hydrogen;

and/or, R^2 is "C_2-C_7 alkyl or C_3-C_{14} heterocycloalkyl substituted by one R^{2-2}"; R^{2-2} is halogen or hydroxyl.

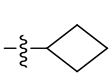
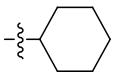
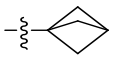
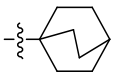
11. The pyrazolopyrimidine compound represented by formula **II** according to claim 1 or 2, the pharmaceutically acceptable salt thereof, the solvate thereof, the solvate of the pharmaceutically acceptable salt thereof, the metabolite thereof or the prodrug thereof, wherein, the pyrazolopyrimidine compound

represented by formula **II** is any of the following schemes:

scheme (1):



I

A is , ,  or  substituted by one or two R^1;

R^1 is independently halogen, -CN, $-NR^{1-3}R^{1-4}$, $-C(=O)R^{1-5}$, $-C(=NR^{1-6})R^{1-7}$ or "C_3-C_{14} cycloalkyl, C_3-C_{14} heterocycloalkyl, C_6-C_{10} aryl, or C_1-C_7 heteroaryl" optionally substituted by one, two or three R^{1-8};

R^{1-3} and R^{1-4} are independently hydrogen, $-S(=O)_2R^{1-3-1}$, $-C(=O)R^{1-3-2}$, $-C(=NR^{1-3-3})NR^{1-3-5}R^{1-3-6}$, $-S(=O)_2NR^{1-3-7}R^{1-3-8}$, $-C(=O)NR^{1-3-9}R^{1-3-10}$ or "C_1-C_7 alkyl, C_3-C_{14} cycloalkyl, C_3-C_{14} heterocycloalkyl, C_6-C_{10} aryl or C_1-C_7 heteroaryl" optionally substituted by one, two or three R^{1-3-11};

R^{1-3-1} and R^{1-3-2} are independently "C_1-C_7 alkyl, C_3-C_{14} cycloalkyl, C_3-C_{14} heterocycloalkyl or C_6-C_{10} aryl" optionally substituted by one or two $R^{1-3-1-1}$; $R^{1-3-1-1}$ is independently C_1-C_7 alkyl;

R^{1-3-3} is independently hydrogen;

R^{1-3-5}, R^{1-3-6}, R^{1-3-7}, R^{1-3-8}, R^{1-3-9} and R^{1-3-10} are independently C_1-C_7 alkyl or C_3-C_{14} cycloalkyl;

R^{1-3-11} is independently halogen, hydroxyl, amino, mercapto, cyano, C_1-C_7 alkyl, C_1-C_7 alkoxy, C_1-C_7 alkylthio, C_3-C_{14} cycloalkyl, C_3-C_{14} heterocycloalkyl, C_6-C_{10} aryl, C_1-C_7 heteroaryl or "amino substituted by one or two $R^{1-3-11-1}$"; $R^{1-3-11-1}$ is independently C_1-C_7 alkyl or C_3-C_{14} cycloalkyl;

R^{1-5} is independently hydrogen, $-NR^{1-5-1}R^{1-5-2}$, $-OR^{1-5-3}$ or "C_1-C_7 alkyl, C_3-C_{14} cycloalkyl, C_3-C_{14} heterocycloalkyl, C_6-C_{10} aryl or C_1-C_7 heteroaryl" optionally substituted by one, two or three R^{1-5-4};

R^{1-5-1} and R^{1-5-2} are independently hydrogen, C_1-C_7 alkyl or C_3-C_{14} cycloalkyl;

R^{1-5-3} is independently hydrogen, C_1-C_7 alkyl, C_3-C_{14} cycloalkyl, C_3-C_{14} heterocycloalkyl, C_6-C_{10} aryl or C_1-C_7 heteroaryl;

R^{1-5-4} is independently halogen, hydroxyl, amino, mercapto, cyano, C_1-C_7 alkyl, C_1-C_7 alkoxy, C_1-C_7 alkylthio, C_3-C_{14} cycloalkyl, C_3-C_{14} heterocycloalkyl, C_6-C_{10} aryl, C_1-C_7 heteroaryl or "amino substituted by one or two $R^{1-5-4-1}$"; $R^{1-5-4-1}$ is independently C_1-C_7 alkyl or C_3-C_{14} cycloalkyl;

R^{1-6} is independently hydrogen, -CN, -OH;

R^{1-7} is independently hydrogen, $-NR^{1-7-2}R^{1-7-3}$;

R^{1-7-2} and R^{1-7-3} are independently C_1-C_7 alkyl or C_3-C_{14} cycloalkyl;

or, R^{1-7-2} and R^{1-7-3} together with the nitrogen atom they are attached to form a C_3-C_{14} heterocycloalkyl optionally substituted by one, two or three $R^{1-7-2-1}$; one or more methylenes in the C_3-C_{14} heterocycloalkyl are optionally and independently substituted by oxygen atom, sulfur atom; $R^{1-7-2-1}$ is independently C_1-C_7 alkyl or C_3-C_{14} cycloalkyl;

R^{1-8} is independently halogen, -OH, amino, mercapto, cyano, C_1-C_7 alkyl, C_1-C_7 alkoxy, C_1-C_7 alkylthio,

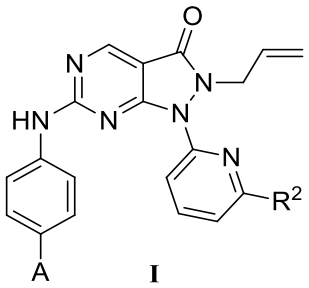
C_3-C_{14} cycloalkyl, C_3-C_{14} heterocycloalkyl, C_6-C_{10} aryl, C_1-C_7 heteroaryl or "amino substituted by one or two R^{1-8-1}"; R^{1-8-1} is independently C_1-C_7 alkyl or C_3-C_{14} cycloalkyl;

R^2 is "C_2-C_7 alkyl, C_3-C_{14} cycloalkyl or C_3-C_{14} heterocycloalkyl" optionally substituted by one, two or three R^{2-2};

R^{2-2} is independently halogen or hydroxyl;

in any one of the above cases, the heteroatoms in the C_3-C_{14} heterocycloalkyl, C_1-C_7 heteroaryl are independently selected from one or more of boron, silicon, oxygen, sulfur, selenium, nitrogen and phosphorus; the number of heteroatoms is independently 1, 2, 3 or 4;

scheme (2):



I

A is C_3-C_{20} cycloalkyl substituted by one or two R^1;

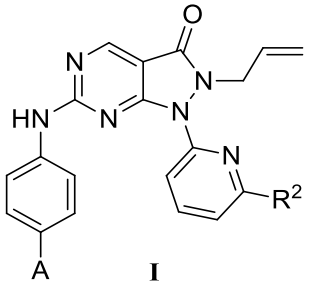
R^1 is independently cyano, halogen, $-NR^{1-3}R^{1-4}$, $-C(=O)R^{1-5}$, $-C(=NR^{1-6})R^{1-7}$, C_1-C_7 heteroaryl or C_3-C_{14} heterocycloalkyl;

R^{1-3} and R^{1-4} are independently hydrogen, $-S(=O)_2R^{1-3-1}$ or C_1-C_7 alkyl; R^{1-3-1} is independently C_1-C_7 alkyl;

R^{1-5} is independently $-NR^{1-5-1}R^{1-5-2}$, $-OR^{1-5-3}$ or C_3-C_{14} heterocycloalkyl; R^{1-5-1} and R^{1-5-2} are independently hydrogen, C_1-C_7 alkyl or C_3-C_{14} cycloalkyl; R^{1-5-3} is independently hydrogen or C_1-C_7 alkyl;

R^2 is "C_2-C_7 alkyl or C_3-C_{14} heterocycloalkyl substituted by one R^{2-2}"; R^{2-2} is halogen or hydroxyl;

scheme (3):



I

A is C_3-C_{20} cycloalkyl substituted by one R^1;

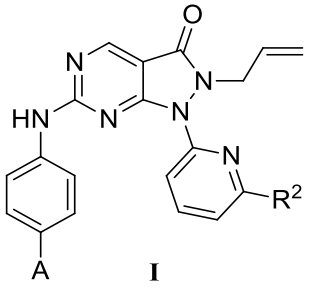
R^1 is $-NR^{1-3}R^{1-4}$, $-C(=O)R^{1-5}$ or C_3-C_{14} heterocycloalkyl;

R^{1-3} and R^{1-4} are independently hydrogen, $-S(=O)_2R^{1-3-1}$ or C_1-C_7 alkyl; R^{1-3-1} is independently C_1-C_7 alkyl;

R^{1-5} is $-NR^{1-5-1}R^{1-5-2}$, $-OR^{1-5-3}$ or C_3-C_{14} heterocycloalkyl; R^{1-5-1} and R^{1-5-2} are independently hydrogen, C_1-C_7 alkyl or C_3-C_{14} cycloalkyl; R^{1-5-3} is hydrogen or C_1-C_7 alkyl;

R^2 is "C_2-C_7 alkyl or C_3-C_{14} heterocycloalkyl substituted by one R^{2-2}"; R^{2-2} is hydroxyl;

scheme (4):



I

A is C_3-C_{20} cycloalkyl substituted by one R^1;

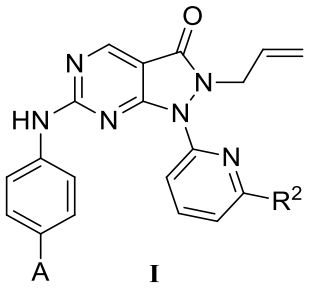
R^1 is -$NR^{1-3}R^{1-4}$, -$C(=O)R^{1-5}$ or C_3-C_{14} heterocycloalkyl;

R^{1-3} and R^{1-4} are independently hydrogen, -$S(=O)_2R^{1-3-1}$ or C_1-C_7 alkyl; R^{1-3-1} is independently C_1-C_7 alkyl;

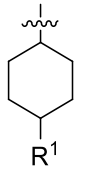
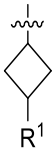
R^{1-5} is -$NR^{1-5-1}R^{1-5-2}$, -OR^{1-5-3} or C_3-C_{14} heterocycloalkyl; R^{1-5-1} and R^{1-5-2} are independently hydrogen, C_1-C_7 alkyl or C_3-C_{14} cycloalkyl; R^{1-5-3} is hydrogen;

R^2 is "C_2-C_7 alkyl or C_3-C_{14} heterocycloalkyl substituted by one R^{2-2}"; R^{2-2} is hydroxyl;

scheme (5):



I

A is  or ;

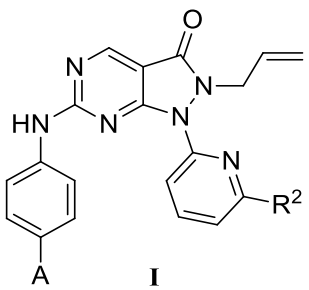
R^1 is -$NR^{1-3}R^{1-4}$, -$C(=O)R^{1-5}$ or C_3-C_{14} heterocycloalkyl;

R^{1-3} and R^{1-4} are independently hydrogen, -$S(=O)_2R^{1-3-1}$ or C_1-C_7 alkyl; R^{1-3-1} is independently C_1-C_7 alkyl;

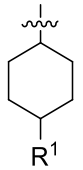
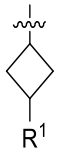
R^{1-5} is -$NR^{1-5-1}R^{1-5-2}$, -OR^{1-5-3} or C_3-C_{14} heterocycloalkyl; R^{1-5-1} and R^{1-5-2} are independently hydrogen, C_1-C_7 alkyl or C_3-C_{14} cycloalkyl; R^{1-5-3} is hydrogen or C_1-C_7 alkyl;

R^2 is "C_2-C_7 alkyl or C_3-C_{14} heterocycloalkyl substituted by one R^{2-2}"; R^{2-2} is hydroxyl;

scheme (6):



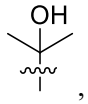
I

A is  or ;

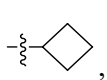
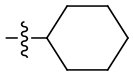
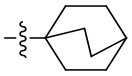
R^1 is $-NR^{1-3}R^{1-4}$, $-C(=O)R^{1-5}$ or C_3-C_{14} heterocycloalkyl;

R^{1-3} and R^{1-4} are independently hydrogen, $-S(=O)_2R^{1-3-1}$ or C_1-C_7 alkyl; R^{1-3-1} is independently C_1-C_7 alkyl;

R^{1-5} is $-NR^{1-5-1}R^{1-5-2}$, $-OR^{1-5-3}$ or C_3-C_{14} heterocycloalkyl; R^{1-5-1} and R^{1-5-2} are independently hydrogen, C_1-C_7 alkyl or C_3-C_{14} cycloalkyl; R^{1-5-3} is hydrogen or C_1-C_7 alkyl;

R^2 is ,  or ;

scheme (7):

A is , ,  or  substituted by one or two R^1;

X is CH or N;

R^1 is independently halogen, -CN, $-NR^{1-3}R^{1-4}$, $-C(=O)R^{1-5}$, $-C(=NR^{1-6})R^{1-7}$, $=N-O-R^{1-9}$ or "C_3-C_{14} cycloalkyl, C_3-C_{14} heterocycloalkyl, C_6-C_{10} aryl, or C_1-C_7 heteroaryl" optionally substituted by one, two or three R^{1-8};

R^{1-3} and R^{1-4} are independently hydrogen, $-S(=O)_2R^{1-3-1}$, $-C(=O)R^{1-3-2}$, $-C(=NR^{1-3-3})NR^{1-3-5}R^{1-3-6}$, $-S(=O)_2NR^{1-3-7}R^{1-3-8}$, $-C(=O)NR^{1-3-9}R^{1-3-10}$ or "C_1-C_7 alkyl, C_3-C_{14} cycloalkyl, C_3-C_{14} heterocycloalkyl, C_6-C_{10} aryl or C_1-C_7 heteroaryl" optionally substituted by one, two or three R^{1-3-11};

R^{1-3-1} and R^{1-3-2} are independently "C_1-C_7 alkyl, C_3-C_{14} cycloalkyl, C_3-C_{14} heterocycloalkyl or C_6-C_{10} aryl optionally substituted" by one or two $R^{1-3-1-1}$; $R^{1-3-1-1}$ is independently C_1-C_7 alkyl;

R^{1-3-3} is independently hydrogen;

R^{1-3-5}, R^{1-3-6}, R^{1-3-7}, R^{1-3-8}, R^{1-3-9} and R^{1-3-10} are independently hydrogen, C_1-C_7 alkyl or C_3-C_{14} cycloalkyl;

R^{1-3-11} is independently halogen, hydroxyl, amino, mercapto, cyano, C_1-C_7 alkyl, C_1-C_7 alkoxy, C_1-C_7 alkylthio, C_3-C_{14} cycloalkyl, C_3-C_{14} heterocycloalkyl, C_6-C_{10} aryl, C_1-C_7 heteroaryl or "amino substituted by one or two $R^{1-3-11-1}$"; $R^{1-3-11-1}$ is independently C_1-C_7 alkyl or C_3-C_{14} cycloalkyl;

R^{1-5} is independently hydrogen, $-NR^{1-5-1}R^{1-5-2}$, $-OR^{1-5-3}$ or "C_1-C_7 alkyl, C_3-C_{14} cycloalkyl, C_3-C_{14} heterocycloalkyl, C_6-C_{10} aryl or C_1-C_7 heteroaryl" optionally substituted by one, two or three R^{1-5-4};

R^{1-5-1} and R^{1-5-2} are independently hydrogen, C_1-C_7 alkyl or C_3-C_{14} cycloalkyl;

R^{1-5-3} is independently hydrogen, C_1-C_7 alkyl, C_3-C_{14} cycloalkyl, C_3-C_{14} heterocycloalkyl, C_6-C_{10} aryl or C_1-C_7 heteroaryl;

R^{1-5-4} is independently halogen, hydroxyl, amino, mercapto, cyano, C_1-C_7 alkyl, C_1-C_7 alkoxy, C_1-C_7 alkylthio, C_3-C_{14} cycloalkyl, C_3-C_{14} heterocycloalkyl, C_6-C_{10} aryl, C_1-C_7 heteroaryl or "amino substituted by one or two $R^{1-5-4-1}$"; $R^{1-5-4-1}$ is independently C_1-C_7 alkyl or C_3-C_{14} cycloalkyl;

R^{1-6} is independently hydrogen, -CN, -OH;

R^{1-7} is independently hydrogen, $-NR^{1-7-2}R^{1-7-3}$;

R^{1-7-2} and R^{1-7-3} are independently C_1-C_7 alkyl or C_3-C_{14} cycloalkyl;

or, R^{1-7-2} and R^{1-7-3} together with the nitrogen atom they are attached to form a C_3-C_{14} heterocycloalkyl optionally substituted by one, two or three $R^{1-7-2-1}$; one or more methylenes in the C_3-C_{14} heterocycloalkyl are optionally and independently substituted by oxygen atom, sulfur atom; $R^{1-7-2-1}$ is independently C_1-C_7 alkyl or C_3-C_{14} cycloalkyl;

R^{1-8} is independently oxo, halogen, -OH, amino, mercapto, cyano, C_1-C_7 alkyl, C_1-C_7 alkoxy, C_1-C_7 alkylthio, C_3-C_{14} cycloalkyl, C_3-C_{14} heterocycloalkyl, C_6-C_{10} aryl, C_1-C_7 heteroaryl or "amino substituted by one or two R^{1-8-1}"; R^{1-8-1} is independently C_1-C_7 alkyl or C_3-C_{14} cycloalkyl;

R^{1-9} is independently hydrogen or C_1-C_7 alkyl;

R^2 is "C_2-C_7 alkyl, C_3-C_{14} cycloalkyl or C_3-C_{14} heterocycloalkyl" optionally substituted by one, two or three R^{2-2};

R^{2-2} is independently halogen or hydroxyl;

in any one of the above cases, the heteroatoms in the C_3-C_{14} heterocycloalkyl, C_1-C_7 heteroaryl are independently selected from one or more of boron, silicon, oxygen, sulfur, selenium, nitrogen and phosphorus; the number of heteroatoms is independently 1, 2, 3 or 4;

scheme (8):

A is C_3-C_{20} cycloalkyl substituted by one or two R^1;

X is CH or N;

R^1 is independently cyano, halogen, $-NR^{1-3}R^{1-4}$, $-C(=O)R^{1-5}$, $-C(=NR^{1-6})R^{1-7}$, $=N-O-R^{1-9}$, C_1-C_7 heteroaryl or "C_3-C_{14} heterocycloalkyl" optionally substituted by one R^{1-8};

R^{1-3} and R^{1-4} are independently hydrogen, $-S(=O)_2R^{1-3-1}$, $-C(=O)R^{1-3-2}$, $-C(=NR^{1-3-3})NR^{1-3-5}R^{1-3-6}$, or C_1-C_7 alkyl;

R^{1-3-1} and R^{1-3-2} are independently C_1-C_7 alkyl, or C_3-C_{14} cycloalkyl;

R^{1-3-3} is hydrogen;

R^{1-3-5} and R^{1-3-6} are hydrogen;

R^{1-5} is independently $-NR^{1-5-1}R^{1-5-2}$, $-OR^{1-5-3}$ or C_3-C_{14} heterocycloalkyl; R^{1-5-1} and R^{1-5-2} are independently hydrogen, C_1-C_7 alkyl or C_3-C_{14} cycloalkyl; R^{1-5-3} is independently hydrogen or C_1-C_7 alkyl;

R^{1-8} is independently oxo;

R^{1-9} is independently hydrogen or C_1-C_7 alkyl;

R^2 is "C_2-C_7 alkyl or C_3-C_{14} heterocycloalkyl substituted by one R^{2-2}"; R^{2-2} is halogen or hydroxyl;

scheme (9):

A is C_3-C_{20} cycloalkyl substituted by one R^1;

X is CH or N;

R^1 is -CN, $-NR^{1-3}R^{1-4}$, $-C(=O)R^{1-5}$, $=N-O-R^{1-9}$ or "C_3-C_{14} heterocycloalkyl" optionally substituted by one R^{1-8};

R^{1-3} and R^{1-4} are independently hydrogen, $-S(=O)_2R^{1-3-1}$, $-C(=O)R^{1-3-2}$, $-C(=NR^{1-3-3})NR^{1-3-5}R^{1-3-6}$, or C_1-C_7 alkyl;

R^{1-3-1} and R^{1-3-2} are independently C_1-C_7 alkyl, or C_3-C_{14} cycloalkyl;

R^{1-3-3} is hydrogen;

R^{1-3-5} and R^{1-3-6} are hydrogen;

R^{1-5} is $-NR^{1-5-1}R^{1-5-2}$, $-OR^{1-5-3}$ or C_3-C_{14} heterocycloalkyl;

R^{1-5-1} and R^{1-5-2} are independently hydrogen, C_1-C_7 alkyl or C_3-C_{14} cycloalkyl;

R^{1-5-3} is independently hydrogen or C_1-C_7 alkyl;

R^{1-8} is independently oxo;

R^{1-9} is independently hydrogen or C_1-C_7 alkyl;

R^2 is "C_2-C_7 alkyl or C_3-C_{14} heterocycloalkyl substituted by one R^{2-2}"; R^{2-2} is hydroxyl;

scheme (10):

A is C_3-C_{20} cycloalkyl substituted by one R^1;

X is CH or N;

R^1 is -CN, $-NR^{1-3}R^{1-4}$, $-C(=O)R^{1-5}$, $=N-O-R^{1-9}$, or "C_3-C_{14} heterocycloalkyl" optionally substituted by one R^{1-8};

R^{1-3} and R^{1-4} are independently hydrogen, $-S(=O)_2R^{1-3-1}$, $-C(=O)R^{1-3-2}$, $-C(=NR^{1-3-3})NR^{1-3-5}R^{1-3-6}$, or C_1-C_7 alkyl;

R^{1-3-1} and R^{1-3-2} are independently C_1-C_7 alkyl, or C_3-C_{14} cycloalkyl;

R^{1-3-3} is hydrogen;

R^{1-3-5} and R^{1-3-6} are hydrogen;

R^{1-5} is $-NR^{1-5-1}R^{1-5-2}$, $-OR^{1-5-3}$ or C_3-C_{14} heterocycloalkyl;

R^{1-5-1} and R^{1-5-2} are independently hydrogen, C_1-C_7 alkyl or C_3-C_{14} cycloalkyl;

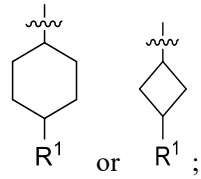
R^{1-5-3} is hydrogen;

R^{1-8} is independently oxo;

R^{1-9} is independently hydrogen or C_1-C_7 alkyl;

R^2 is "C_2-C_7 alkyl or C_3-C_{14} heterocycloalkyl substituted by one R^{2-2}"; R^{2-2} is hydroxyl;

scheme (11):

A is  ;

X is CH or N;

R^1 is -CN, $-NR^{1-3}R^{1-4}$, $-C(=O)R^{1-5}$, $=N-O-R^{1-9}$, or "C_3-C_{14} heterocycloalkyl" optionally substituted by one R^{1-8};

R^{1-3} and R^{1-4} are independently hydrogen, $-S(=O)_2R^{1-3-1}$, $-C(=O)R^{1-3-2}$, $-C(=NR^{1-3-3})NR^{1-3-5}R^{1-3-6}$, or C_1-C_7 alkyl;

R^{1-3-1} and R^{1-3-2} are independently C_1-C_7 alkyl, or C_3-C_{14} cycloalkyl;

R^{1-3-3} is hydrogen;

R^{1-3-5} and R^{1-3-6} are hydrogen;

R^{1-5} is $-NR^{1-5-1}R^{1-5-2}$, $-OR^{1-5-3}$ or C_3-C_{14} heterocycloalkyl; R^{1-5-1} and R^{1-5-2} are independently hydrogen,

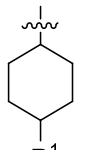
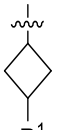
C_1-C_7 alkyl or C_3-C_{14} cycloalkyl; R^{1-5-3} is hydrogen or C_1-C_7 alkyl;

R^{1-8} is independently oxo;

R^{1-9} is independently hydrogen or C_1-C_7 alkyl;

R^2 is "C_2-C_7 alkyl or C_3-C_{14} heterocycloalkyl substituted by one R^{2-2}"; R^{2-2} is hydroxyl;

scheme (12):

A is  or ;

X is CH or N;

R^1 is independently -CN, $-NR^{1-3}R^{1-4}$, $-C(=O)R^{1-5}$, $=N-O-R^{1-9}$, or "C_3-C_{14} heterocycloalkyl" optionally substituted by one R^{1-8};

R^{1-3} and R^{1-4} are independently hydrogen, $-S(=O)_2R^{1-3-1}$, $-C(=O)R^{1-3-2}$, $-C(=NR^{1-3-3})NR^{1-3-5}R^{1-3-6}$, or C_1-C_7 alkyl;

R^{1-3-1} and R^{1-3-2} are independently C_1-C_7 alkyl, or C_3-C_{14} cycloalkyl;

R^{1-3-3} is hydrogen;

R^{1-3-5} and R^{1-3-6} are hydrogen;

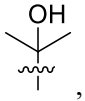
R^{1-5} is independently $-NR^{1-5-1}R^{1-5-2}$, $-OR^{1-5-3}$, or C_3-C_{14} heterocycloalkyl;

R^{1-5-1} and R^{1-5-2} are independently hydrogen, C_1-C_7 alkyl, or C_3-C_{14} cycloalkyl;

R^{1-5-3} is independently hydrogen or C_1-C_7 alkyl;

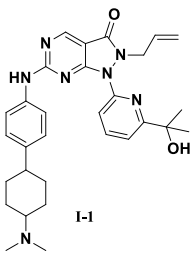
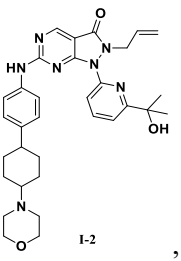
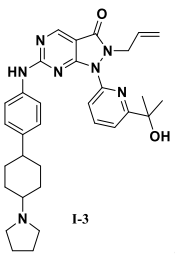
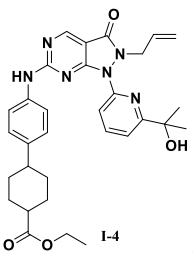
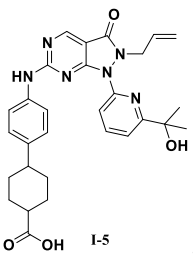
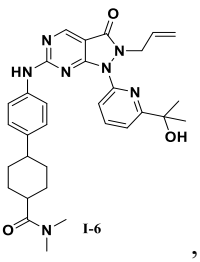
R^{1-8} is independently oxo;

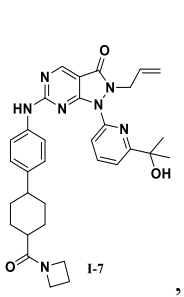
R^{1-9} is independently hydrogen or C_1-C_7 alkyl;

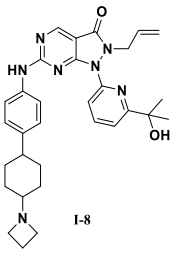
R^2 is ,  or .

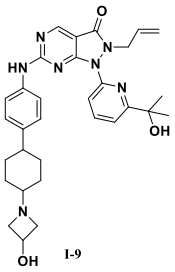
12. The pyrazolopyrimidine compound represented by formula **II** according to claim 1 or 2, the pharmaceutically acceptable salt thereof, the solvate thereof, the solvate of the pharmaceutically acceptable salt thereof, the metabolite thereof or the prodrug thereof, wherein, the pyrazolopyrimidine compound represented by formula **II** is any of the compounds described in any of the following schemes:

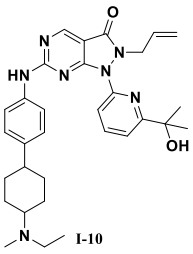
scheme A:

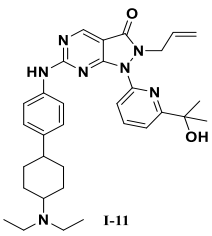

I-1,

I-2,

I-3,

I-4,

I-5,

I-6,

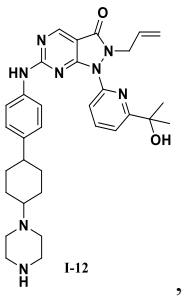

I-7

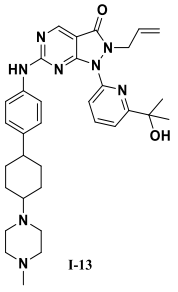

I-8

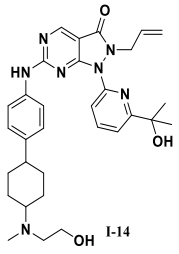

I-9

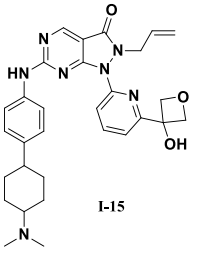

I-10

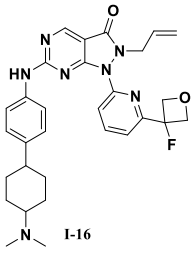

I-11

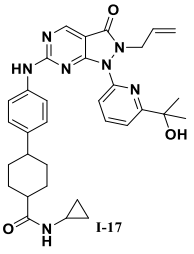

I-12

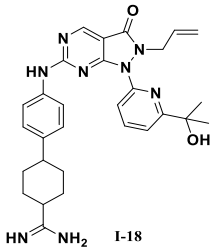

I-13

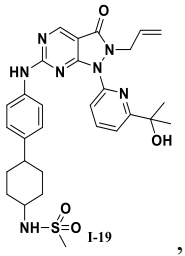

I-14

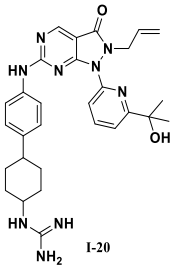

I-15

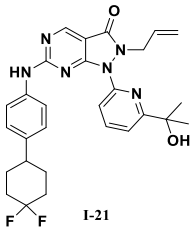

I-16

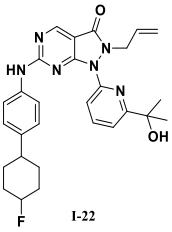

I-17

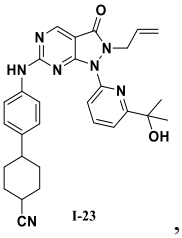

I-18

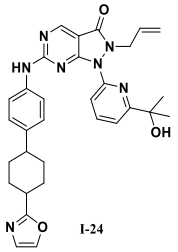

I-19

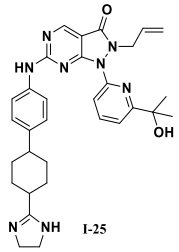

I-20

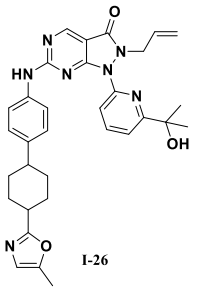

I-21

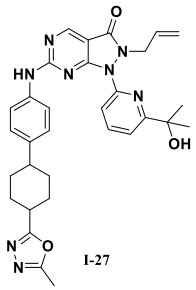

I-22

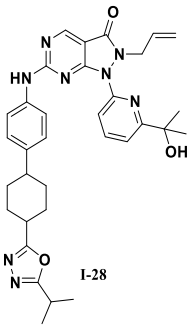

I-23

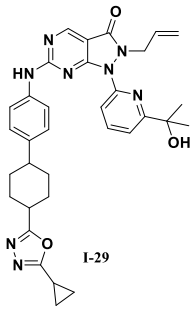

I-24

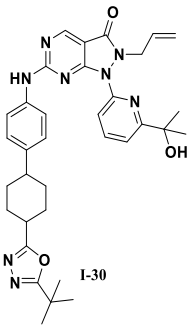

I-25

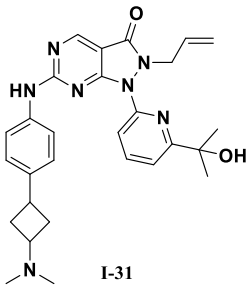

I-26

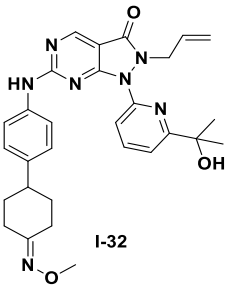

I-27

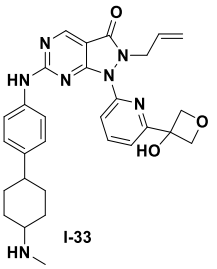

I-28

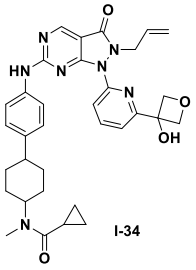
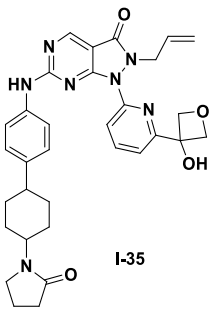
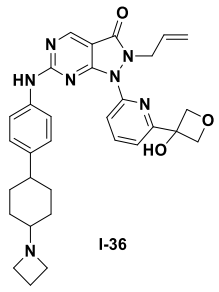
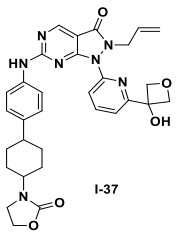
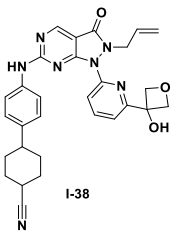
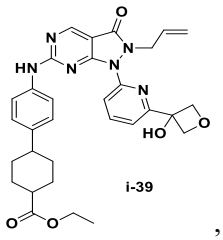
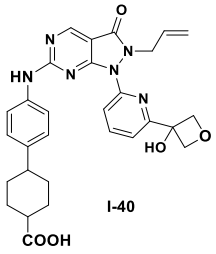
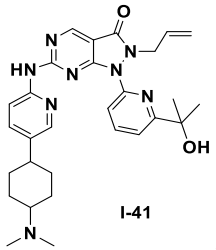

I-29


I-30

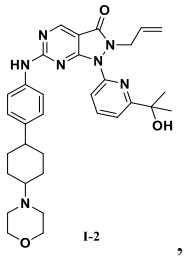

I-31

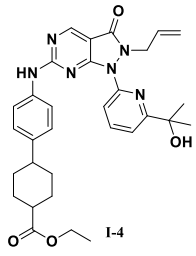

I-32

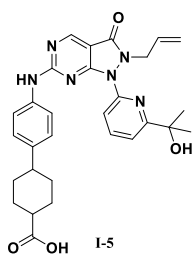

I-33


I-34 ,

I-35 ,

I-36 ,

I-37 ,

I-38 ,

i-39 ,

I-40 and

I-41 ;

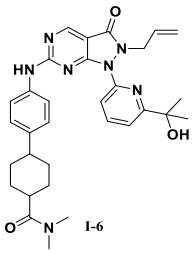
scheme B:


I-2 , its ^{1}H NMR (400 MHz, MeOD) is δ 8.85 (s, 1H), 8.00 (t, J = 7.9 Hz, 1H), 7.80 (d, J = 8.1 Hz, 1H), 7.68 (d, J = 7.7 Hz, 1H), 7.62 (d, J = 8.6 Hz, 2H), 7.28 (d, J = 8.6 Hz, 2H), 5.78 - 5.68 (m, 1H), 5.06 (d, J = 10.3 Hz, 1H), 4.95 (s, 1H), 4.82 (s, 2H), 3.82 - 3.76 (m, 1H), 2.81 (s, 1H), 2.71 (s, 3H), 2.49 (s, 1H), 2.08 (d, J = 10.9 Hz, 3H), 1.94 (d, J = 15.0 Hz, 3H), 1.72 (s, 4H), 1.59 (d, J = 7.0 Hz, 6H);


I-4 , its ^{1}H NMR (400 MHz, $CDCl_3$) is δ 8.87 (d, *J* = 2.1 Hz, 1H), 7.91 (td, *J* = 7.9, 1.5 Hz, 1H), 7.78 (d, *J* = 8.0 Hz, 1H), 7.54 (t, *J* = 7.9 Hz, 2H), 7.39 (d, *J* = 7.7 Hz, 1H), 7.21 (d, *J* = 8.5 Hz, 2H), 5.72 (ddt, *J* = 16.4, 10.2, 6.2 Hz, 1H), 5.07 (dd, *J* = 10.2, 1.1 Hz, 1H), 4.96 (dd, *J* = 17.1, 1.2 Hz, 1H), 4.77 (d, *J* = 6.2 Hz, 2H), 4.25 - 4.10 (m, 2H), 3.95 (s, 1H), 2.73 (s, 1H), 2.56 (dt, *J* = 15.5, 10.8 Hz, 1H), 2.28 (d, *J* = 7.9 Hz, 1H), 2.14 (d, *J* = 10.6 Hz, 1H), 2.05 - 1.97 (m, 1H), 1.78 (dd, *J* = 19.0, 8.5 Hz, 1H), 1.67 (dt, *J* = 10.1, 6.1 Hz, 3H), 1.61 (s, 6H), 1.59 - 1.44 (m, 1H), 1.34 - 1.26 (m, 3H);

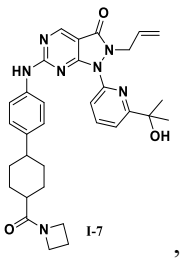

I-5 , its ^{1}H NMR (400 MHz, MeOD) is δ 8.84 (d, *J*= 1.4 Hz, 1H), 8.00 (td, *J* = 7.9, 4.0

Hz, 1H), 7.83 - 7.76 (m, 1H), 7.67 (dd, *J* = 7.7, 0.7 Hz, 1H), 7.60 (dd, *J* = 8.4, 5.7 Hz, 2H), 7.19 (dd, *J* = 13.2, 8.6 Hz, 2H), 5.73 (ddd, *J* = 17.0, 6.1, 4.1 Hz, 1H), 5.08 - 5.03 (m, 1H), 4.95 (d, *J* = 1.3 Hz, 1H), 4.86 - 4.79 (m, 2H), 2.72 (s, 1H), 2.58 (s, 1H), 2.27 (d, *J* = 6.7 Hz, 1H), 2.13 (d, *J* = 10.0 Hz, 1H), 1.96 (d, *J* = 10.2 Hz, 1H), 1.80 - 1.66 (m, 4H), 1.64 - 1.52 (m, 7H);



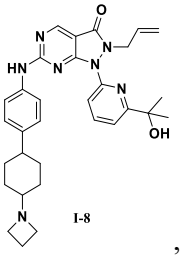
I-6

, its ^{1}H NMR (400 MHz, $CDCl_3$) is δ 8.86 (d, *J* = 4.2 Hz, 1H), 7.97 - 7.88 (m, 1H), 7.79 (d, *J* = 8.0 Hz, 1H), 7.53 (dd, *J* = 12.3, 8.5 Hz, 2H), 7.39 (d, *J* = 7.6 Hz, 1H), 7.28 - 7.15 (m, 2H), 5.80 - 5.65 (m, 1H), 5.06 (d, *J* = 10.0 Hz, 1H), 4.95 (d, *J* = 17.1 Hz, 1H), 4.77 (d, *J* = 6.0 Hz, 2H), 3.10 (d, *J* = 12.1 Hz, 3H), 2.98 (s, 3H), 2.67 - 2.57 (m, 1H), 2.14 (dd, *J* = 20.9, 10.3 Hz, 1H), 2.06 - 1.97 (m, 2H), 1.92 (d, *J* = 14.0 Hz, 1H), 1.78 - 1.66 (m, 4H), 1.61 (s, 6H), 1.49 (dd, *J* = 22.8, 12.2 Hz, 1H);



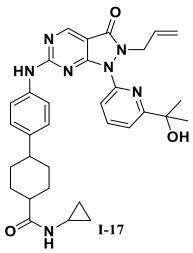
I-7

, its ^{1}H NMR (400 MHz, $CDCl_3$) is δ 8.85 (d, *J* = 4.7 Hz, 1H), 7.91 (dt, *J* = 10.7, 7.9 Hz, 1H), 7.78 (d, *J* = 7.8 Hz, 1H), 7.53 (dd, *J* = 12.0, 8.5 Hz, 2H), 7.39 (dd, *J* = 7.6, 2.4 Hz, 1H), 7.22 (dd, *J* = 19.5, 8.5 Hz, 2H), 5.71 (ddt, *J* = 16.4, 10.2, 6.2 Hz, 1H), 5.06 (d, *J* = 10.2 Hz, 1H), 4.95 (d, *J* = 17.1 Hz, 1H), 4.77 (d, *J* = 6.1 Hz, 2H), 4.21 (dd, *J* = 16.4, 8.6 Hz, 2H), 4.10 - 4.02 (m, 2H), 2.63 - 2.52 (m, 2H), 2.35 - 2.20 (m, 2H), 2.15 - 2.07 (m, 1H), 2.00 (dd, *J* = 13.4, 3.0 Hz, 2H), 1.92 - 1.83 (m, 1H), 1.79 - 1.63 (m, 4H), 1.60 (s, 6H), 1.48 (ddd, *J* = 24.7, 12.5, 2.5 Hz, 1H);

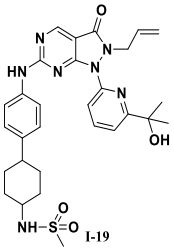


I-8

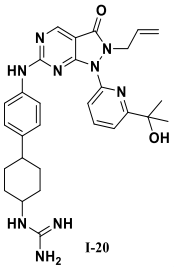
, its ^{1}H NMR (400 MHz, $CDCl_3$) is δ 8.86 (s, 1H), 7.93 - 7.85 (m, 1H), 7.78 (d, *J* = 7.8 Hz, 1H), 7.52 (d, *J* = 8.5 Hz, 2H), 7.39 (dd, *J* = 7.6, 0.7 Hz, 1H), 7.19 (d, *J* = 8.5 Hz, 2H), 5.71 (ddt, *J* = 16.4, 10.2, 6.2 Hz, 1H), 5.05 (dd, *J* = 10.2, 1.1 Hz, 1H), 4.94 (dd, *J* = 17.1, 1.3 Hz, 1H), 4.77 (d, *J* = 6.2 Hz, 2H), 4.11 (d, *J* = 8.9 Hz, 1H), 3.24 (t, *J* = 7.0 Hz, 4H), 2.52 - 2.43 (m, 1H), 2.14 - 2.00 (m, 3H), 1.92 (d, *J* = 11.2 Hz, 4H), 1.60 (s, 6H), 1.45 (dt, *J* = 14.9, 7.5 Hz, 2H), 1.23 - 1.08 (m, 2H);



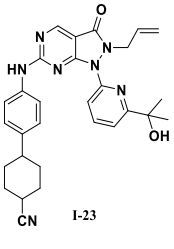
I-17 , its ^{1}H NMR (400 MHz, $CDCl_3$) is δ 8.84 (d, J = 3.7 Hz, 1H), 7.94 (dd, J = 14.8, 6.9 Hz, 1H), 7.76 (d, J = 7.9 Hz, 1H), 7.58 - 7.50 (m, 2H), 7.42 (dd, J = 7.5, 4.1 Hz, 1H), 7.22 (dd, J = 15.8, 8.5 Hz, 2H), 5.71 (dd, J = 11.5, 5.4 Hz, 2H), 5.07 (d, J = 10.2 Hz, 1H), 4.95 (d, J = 17.1 Hz, 1H), 4.77 (d, J = 6.1 Hz, 2H), 2.82 - 2.72 (m, 1H), 2.60 (s, 1H), 2.12 - 2.01 (m, 3H), 1.92 (d, J = 12.5 Hz, 1H), 1.81 - 1.67 (m, 3H), 1.62 (s, 6H), 1.54 - 1.43 (m, 1H), 0.93 - 0.78 (m, 3H), 0.52 (s, 2H);



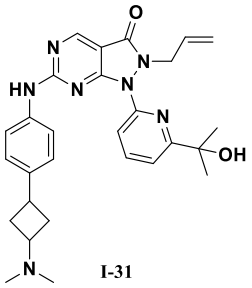
I-19 , its ^{1}H NMR (400 MHz, $CDCl_3$) is δ 8.88 (s, 1H), 7.91 (t, J = 7.9 Hz, 1H), 7.77 (d, J = 7.9 Hz, 1H), 7.56 (d, J = 8.5 Hz, 2H), 7.40 (d, J = 7.4 Hz, 1H), 7.19 (d, J = 8.5 Hz, 2H), 5.78 - 5.66 (m, 1H), 5.07 (dd, J = 10.2, 1.0 Hz, 1H), 4.96 (dd, J = 17.1, 1.2 Hz, 1H), 4.77 (d, J = 6.2 Hz, 2H), 4.42 (d, J = 7.6 Hz, 1H), 3.49 - 3.35 (m, 1H), 3.04 (s, 3H), 2.57 - 2.46 (m, 1H), 2.29 - 2.17 (m, 2H), 2.05 - 1.96 (m, 8H), 1.56-1.65 (m , 2H), 1.41-1.50 (m, 2H);



I-20 , its ^{1}H NMR (400 MHz, MeOD) is δ 8.84 (s, 1H), 8.02 (m, 1H), 7.80 (m, 1H), 7.72-7.58 (m, 3H), 7.25 (m, 2H), 5.73 (ddt, J = 16.5, 10.3, 6.1 Hz, 1H), 5.05 (dd, J = 10.2, 1.0 Hz, 1H), 4.95 (d, 1H), 4.83 (d, J = 6.1 Hz, 2H), 3.54-3.42 (m, 1H), 2.59 (m, 1H), 2.14 (m, 1H), 1.98 (m, 2H), 1.83 (m, 1H), 1.68 (m, 2H), 1.60 (s, 6H), 1.50 (m, 2H);

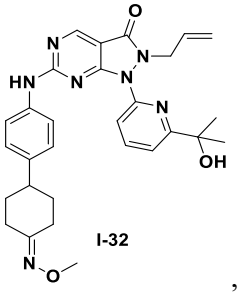


I-23 , its ^{1}H NMR (400 MHz, DMSO) is δ 10.28 (s, 1H), 8.88 (d, J = 1.8 Hz, 1H), 8.09 - 7.97 (m, 1H), 7.75 (d, J = 8.4 Hz, 1H), 7.66 (dd, J = 20.6, 8.5 Hz, 3H), 7.19 (dd, J = 11.1, 8.7 Hz, 2H), 5.74 - 5.61 (m, 1H), 5.00 (d, J = 10.2 Hz, 1H), 4.82 (d, J = 17.1 Hz, 1H), 4.69 (d, J = 5.5 Hz, 2H), 3.23 (s, 1H), 2.74 (t, J = 12.1 Hz, 1H), 2.53 (s,1H), 2.12 (d, J = 10.1 Hz, 1H), 1.98 (d, J = 13.2 Hz, 1H), 1.82 (d, J = 13.2 Hz, 2H), 1.77-1.57 (m, 3H), 1.49 (d, J = 18.2 Hz, 6H);



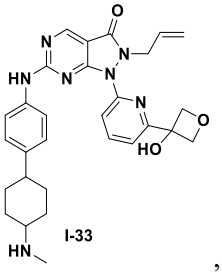
I-31

, its ^{1}H NMR (400 MHz, DMSO) is δ 10.27 (s, 1H), 8.89 (s, 1H), 8.12 (s, 1H), 7.74 (dd, J = 22.6, 8.3 Hz, 3H),7.64 (d, J = 7.3 Hz, 1H), 7.37 (d, J = 8.5 Hz, 2H), 5.76-5.61 (m, 1H), 5.34 (s, 1H), 5.01 (dd, J = 10.3, 1.2Hz, 1H), 4.84 (d, J = 17.1 Hz, 1H), 4.70 (d, J = 5.7 Hz, 2H), 3.62 (s, 1H), 3.12 (s, 1H), 2.71-2.58 (m,8H), 2.38 (d, J = 9.2 Hz, 2H), 1.47 (s, 6H), 1.32-1.24 (m, 1H);



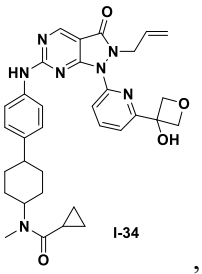
I-32

, its ^{1}H NMR (400 MHz, DMSO) is δ 10.26 (s, 1H), 8.88 (s, 1H), 8.07 (t, J = 7.8 Hz, 1H), 7.76 (d, J = 8.0 Hz, 1H), 7.65 (dd, J = 14.5, 7.9 Hz, 2H), 7.22 (d, J = 8.5 Hz, 2H), 5.74 - 5.60 (m, 1H), 5.35 (s, 1H), 5.00 (d, J = 10.3 Hz,1H), 4.83 (d, J = 17.1 Hz, 1H), 4.69 (d, J = 5.6 Hz, 2H), 3.74 (s, 3H), 3.24 - 3.15 (m, 1H), 2.77 (t, J = 12.0 Hz, 1H), 2.37 (d, J = 14.0 Hz, 1H), 2.25 (td, J = 13.4, 4.6 Hz, 1H), 1.99 - 1.84 (m, 3H), 1.67 - 1.50 (m, 2H), 1.49 (d, J = 14.0 Hz, 6H);



I-33

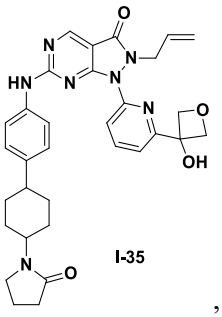
, its ^{1}H NMR (400 MHz, MeOD) is δ 8.86 (s, 0H), 8.11-8.01 (m, 1H), 7.94 (d, J = 7.9 Hz, 2H), 7.67 (d, J = 7.6 Hz, 2H), 7.62 (d, J = 8.6 Hz,2H), 7.28 (d, J = 8.5 Hz, 2H), 5.83-5.74(m, 1H), 5.09 (dd, J = 7.9, 4.4 Hz, 3H), 4.98 (dd, J = 17.1, 1.3 Hz, 2H), 4.85 (d, J = 6.7 Hz, 2H), 2.87 (s, 1H), 2.64 (s, 1H), 2.47 (s, 3H), 1.97 - 1.67 (m,8H);



I-34

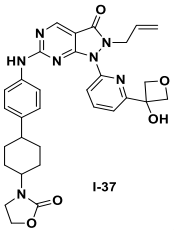
, its ^{1}H NMR (400 MHz, MeOD) is δ 8.87 (d, J = 6.6 Hz, 1H), 8.06 (t, J = 7.9 Hz, 1H), 7.95 (d, J = 7.9 Hz, 1H), 7.68 (dd, J = 7.8, 5.4 Hz, 2H), 7.61 (d, J = 8.6 Hz, 1H), 7.41 (d, J = 8.4 Hz, 1H), 7.24 (t, J = 8.7 Hz, 1H), 5.84 - 5.72 (m, 1H), 5.09 (d, J = 6.2 Hz,2H), 5.07 (d, J = 1.3 Hz, 1H), 5.02 - 4.94 (m, 2H), 4.90 (s, 2H), 4.84 (d, J = 6.7 Hz, 2H), 3.15 (d, J = 2.6 Hz, 1H), 3.08 (s,1H), 2.95 (s, 1H), 2.71 (s, 1H), 2.43 (s, 1H), 1.93-2.03 (m, 3H), 1.76 (s, 2H), 1.51 (s, 1H), 1.31 (d, J = 4.3 Hz, 3H), 0.89 (dd, J = 20.1,

9.0 Hz, 4H);



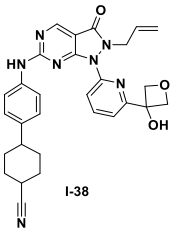
I-35

, its ^{1}H NMR (400 MHz, $CDCl_3$) is δ 8.87-8.79 (m, 1H), 8.14-8.07 (m, 1H), 8.04-7.96 (m, 1H), 7.89-7.80 (m, 1H), 7.61-7.50 (m, 2H), 7.38-7.32 (m, 1H), 7.25 - 7.19 (m, 1H), 7.01 (t, J = 3.4 Hz, 1H), 5.72 (ddd, J = 16.6, 11.1, 8.6 Hz, 1H), 5.17 - 5.09 (m, 2H), 5.04 - 4.98 (m, 1H), 4.98 - 4.92 (m, 1H), 4.87 - 4.77 (m, 2H), 4.73 - 4.64 (m, 2H), 4.20 - 4.06 (m, 1H), 3.47 - 3.38 (m, 1H), 3.38 - 3.29 (m, 1H), 3.05-2.98 (m, 1H), 2.49-2.35 (m, 2H), 2.27-2.17 (m, 1H), 2.07-1.86 (m,4H), 1.75-1.60 (m, 3H);



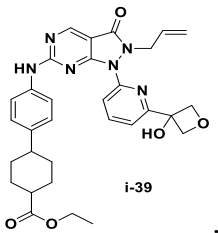
I-37

, its ^{1}H NMR (400 MHz, $CDCl_3$) is δ 8.77 (s,1H), 8.16-8.07 (m, 1H), 8.03 (d, J = 7.6 Hz, 1H), 7.83-7.75 (m, 1H), 7.56 (dd, J = 12.6, 6.1 Hz, 2H), 7.33 (d, J = 8.5 Hz, 1H), 7.21 (d, J = 8.5 Hz, 1H), 5.72 (dd, J = 17.0, 10.3 Hz, 1H), 5.13 (dd, J = 9.1, 6.1 Hz, 2H), 4.96 (d, J = 17.0 Hz, 2H), 4.81 (d, J = 7.2 Hz, 2H), 4.69 (d, J = 6.2 Hz, 2H), 4.41 - 4.28 (m, 2H), 3.86 (s, 1H), 3.77 (t, J = 6.6 Hz, 1H), 3.63-3.50 (m, 2H), 2.98 (m, 1H), 2.15 (m, 1H), 1.97 (dd, J = 18.9, 9.6 Hz, 2H), 1.78 (d, J = 5.0 Hz, 2H), 1.65 (d, J = 8.7 Hz, 2H);



I-38

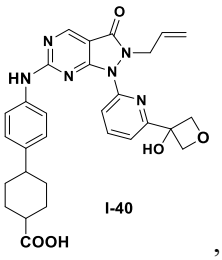
, its ^{1}H NMR (400 MHz, $CDCl_3$) is δ 8.69 (s, 1H), 8.18 (d, J = 8.0 Hz, 1H), 8.10 (dd, J = 17.9, 7.6 Hz, 1H), 7.81- 7.72 (m, 1H), 7.63-7.49 (m, 2H), 7.25 (d, J = 8.4 Hz, 1H), 7.19 (d, J = 8.3 Hz, 1H), 5.70 (d, J = 6.8 Hz, 1H), 5.15 (d, J = 10.1 Hz, 1H), 5.14 - 5.07 (m, 1H), 4.95 (d, J = 16.6 Hz, 1H), 4.83 (t, J = 6.7 Hz, 2H), 4.71 (s, 2H), 2.54 (dd, J = 24.9, 12.6 Hz, 2H), 2.30 (d, J = 11.2 Hz, 1H), 2.18 (d, J = 13.5 Hz, 1H), 2.02 (d, J = 12.9 Hz, 1H), 1.96-1.80 (m, 2H), 1.78 (d, J = 16.1 Hz, 1H), 1.49 (dd, J = 26.4, 11.2 Hz, 2H);



i-39

, its ^{1}H NMR (400 MHz, Methanol-d_4) is δ 8.85 (d, J = 1.1 Hz, 1H), 8.05 (td, J = 7.9, 4.8 Hz, 1H), 7.96 - 7.86 (m, 1H), 7.67 (d, J = 7.6 Hz, 1H), 7.59 (ddd, J = 9.2, 4.6, 2.3 Hz, 2H), 7.25 - 7.19

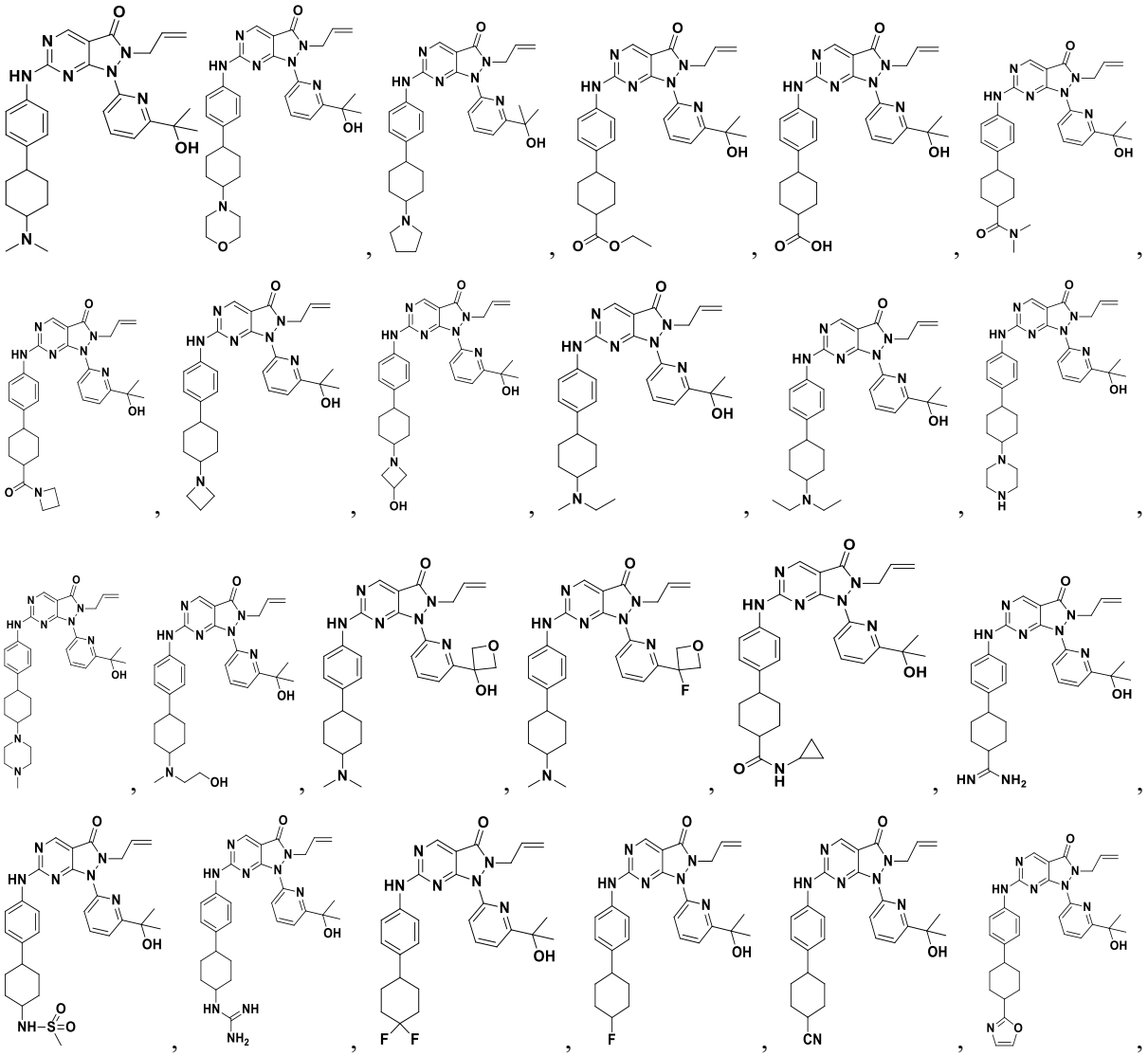
(m, 1H), 7.19 - 7.11 (m, 1H), 5.78 (ddt, *J* = 16.5, 10.1, 6.1 Hz, 1H), 5.12 - 5.07 (m, 2H), 5.06 (t, *J* = 1.3 Hz, 1H), 4.98 (dd, *J* = 17.0, 1.4 Hz, 1H), 4.90 (d, *J* = 1.4 Hz, 2H), 4.25 - 4.19 (m, 1H), 4.14 (dd, *J* = 14.1, 7.1 Hz, 1H), 2.34 - 2.12 (m, 2H), 2.07 (dd, *J* = 17.0, 4.1 Hz, 1H), 1.99 - 1.82 (m, 1H), 1.74 - 1.65 (m, 2H), 1.65 - 1.53 (m, 2H), 1.31 (d, *J* = 4.2 Hz, 3H), 1.29 - 1.25 (m, 2H);

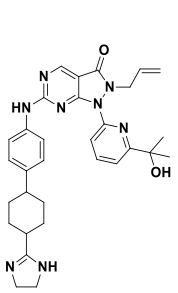
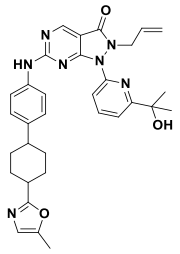
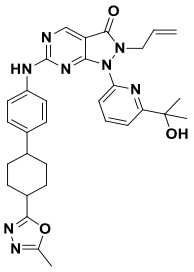
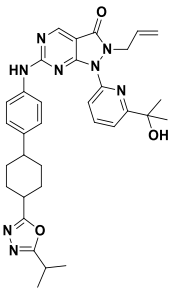
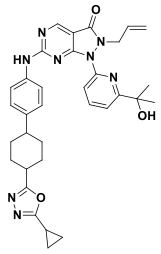
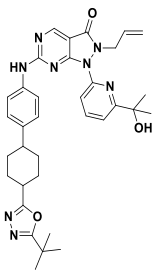
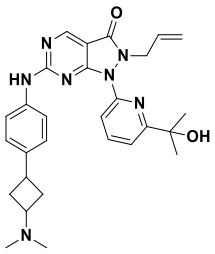
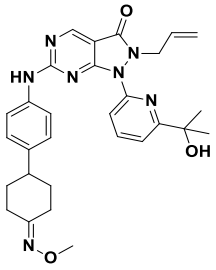
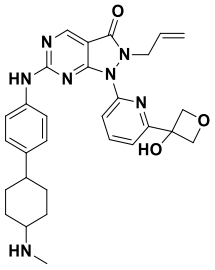
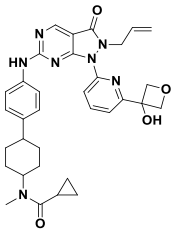
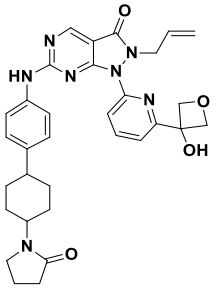
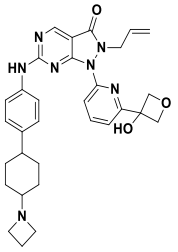
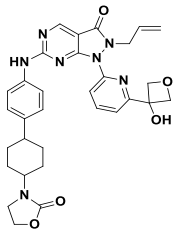
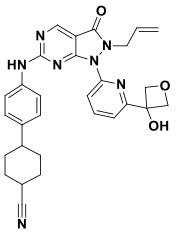
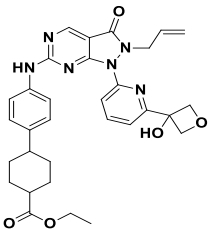
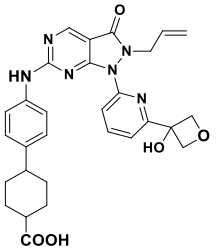
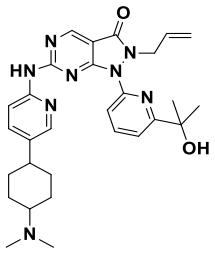


I-40

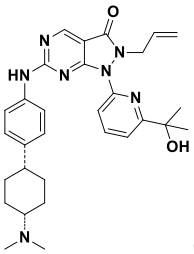
, its ^{1}H NMR (400 MHz, Methanol-d$_4$) is δ 8.84 (s, 1H), 8.05 (t, J = 7.9 Hz, 1H), 7.92 (d, J = 8.1 Hz, 1H), 7.66 (dd, J = 7.6, 0.9 Hz, 1H), 7.63 - 7.53 (m, 2H), 7.22 - 7.14 (m, 2H), 5.84 - 5.74 (m, 1H), 5.10 - 5.07 (m, 2H), 5.06 (q, J = 1.3 Hz, 1H), 4.98 (dq, J = 17.0, 1.4 Hz, 1H), 4.89 (dt, J = 6.1, 1.4 Hz, 2H), 2.71 (d, J = 6.9 Hz, 1H), 2.59 (s, 1H), 2.24 (dd, J = 16.4, 7.8 Hz, 2H), 2.04 (d, J = 8.5 Hz, 1H), 1.73 (td, J = 10.9, 6.8 Hz, 6H);

scheme C:

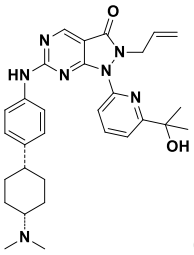


, , , , , , , , , , , , , , , , and ;

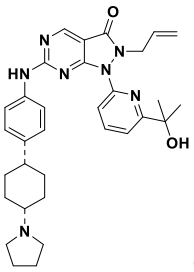
scheme D:



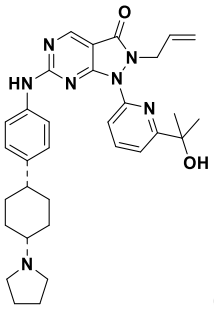
(I-1-1), its ^{1}H NMR (400 MHz, MeOD) is δ 8.85 (s, 1H), 8.46 (s, 2H), 7.99 (t, J = 7.9 Hz, 1H), 7.79 (d, J = 8.0 Hz,1H), 7.65 (dd, J = 16.6, 8.1 Hz, 3H), 7.22 (d, J = 8.6 Hz, 2H), 5.73 (ddt, J = 16.3, 10.2, 6.1 Hz, 1H), 5.05(dd, J = 10.3, 1.1 Hz, 1H), 4.93 (dd, J = 17.1, 1.3 Hz, 1H), 4.82 (d, J = 6.1 Hz, 2H), 2.90 (s, 6H), 2.60 (d,J = 8.4 Hz, 1H), 2.21 (s, 2H), 2.10 (d, J = 10.6 Hz, 2H), 1.70 (d, J = 11.4 Hz, 4H), 1.59 (s, 6H);



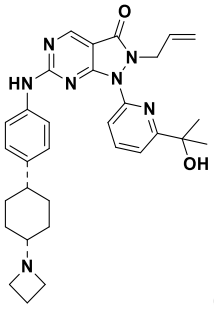
(I-1-2), its ^{1}H NMR (400 MHz, $CDCl_3$) is δ 8.86 (s, 1H), 8.54 (s, 1H), 7.95 (t, J = 7.9 Hz, 1H), 7.75 (d, J = 8.0 Hz, 1H), 7.59 (d, J = 8.5 Hz, 2H), 7.43 (d, *J* = 7.6 Hz, 1H), 7.32 (d, *J* = 8.5 Hz, 2H), 5.72 (ddt, *J* = 16.5, 10.3, 6.2 Hz, 1H), 5.06 (d, *J* = 10.2 Hz, 1H), 4.95 (dd, *J* = 17.1, 1.0 Hz, 1H), 4.75 (d, *J* = 6.1 Hz, 2H), 3.05 (m, 1H), 2.93 (m, 1H), 2.68 (s, 6H), 2.32 (m, 2H), 1.84 (m, 6H), 1.60 (s, 6H);



(I-3-1), its ^{1}H NMR (400 MHz, $CDCl_3$) is δ 8.87 (s, 1H), 7.90 (t, J = 7.9 Hz, 1H), 7.78 (d, J = 8.0 Hz, 1H), 7.53 (d, J = 8.5 Hz, 2H), 7.39 (dd, J = 7.6, 0.5 Hz, 1H), 7.20 (d, J = 8.5 Hz, 2H), 5.72 (ddt, J = 16.4, 10.2, 6.2 Hz, 1H), 5.06 (dd, J = 10.2, 1.0 Hz, 1H), 4.95 (dd, J = 17.1, 1.2 Hz, 1H), 4.76 (d, J = 6.2 Hz, 2H), 4.04 (s, 1H), 2.66 (m, 4H), 2.58 - 2.47 (m, 1H), 2.16 (m, 4H), 1.96 (m, 2H), 1.87 - 1.78 (m, 4H), 1.60 (s, 6H), 1.58 - 1.39 (m, 4H);

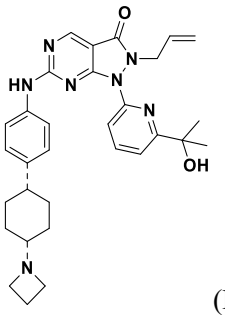


(I-3-2), its ^{1}H NMR (400 MHz, $CDCl_3$) is δ 8.87 (s, 1H), 7.92 (t, J = 7.9 Hz, 1H), 7.80 (d, J = 8.0 Hz, 1H), 7.52 (d, J = 8.5 Hz, 2H), 7.38 (d, J = 7.6 Hz, 1H), 7.29 (t, J = 4.2 Hz, 2H), 5.79 - 5.66 (m, 1H), 5.06 (dd, J = 10.2, 1.0 Hz, 1H), 4.96 (dd, J = 17.1, 1.2 Hz, 1H), 4.77 (d, J = 6.2 Hz, 2H), 4.02 (s, 1H), 2.70 - 2.50 (m, 5H), 2.26 (s, 1H), 1.98 (m, 4H), 1.82 (s, 4H), 1.69 - 1.56 (m, 10H);

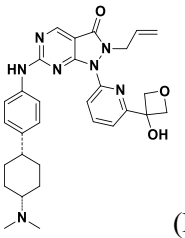


(I-8-1), its ^{1}H NMR (400 MHz, $CDCl_3$) is δ 8.86 (s, 1H), 7.93 - 7.85 (m, 1H), 7.78 (d, J = 7.8 Hz, 1H), 7.52 (d, J = 8.5 Hz, 2H), 7.39 (dd, J = 7.6, 0.7 Hz, 1H), 7.19 (d, J = 8.5 Hz, 2H), 5.71 (ddt, J = 16.4, 10.2, 6.2 Hz, 1H), 5.05 (dd, J = 10.2, 1.1 Hz, 1H), 4.94 (dd, J = 17.1, 1.3 Hz, 1H), 4.77 (d, J = 6.2 Hz, 2H), 4.11 (d, J = 8.9 Hz, 1H), 3.24 (t, J = 7.0 Hz, 4H), 2.52 - 2.43 (m, 1H), 2.14 - 2.00 (m, 3H),

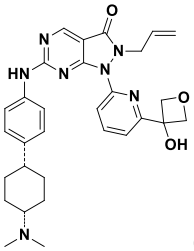
1.92 (d, J = 11.2 Hz, 4H), 1.60 (s, 6H), 1.45 (dt, J = 14.9, 7.5 Hz, 2H), 1.23 - 1.08 (m, 2H);



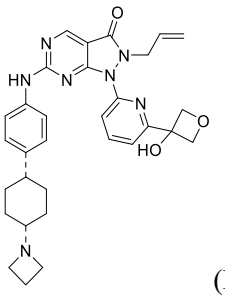
(I-8-2), its ^{1}H NMR (400 MHz, $CDCl_3$) is δ8.87 (s, 1H), 7.92 (d, J = 7.8 Hz, 1H), 7.80 (d, J = 8.0 Hz, 1H), 7.52 (d, J =8.4 Hz, 2H), 7.39 (d, J = 7.6 Hz, 1H), 7.29 - 7.25 (m, 2H), 5.82-5.63 (m, 1H), 5.12-4.91 (m, 2H), 4.78(d, J = 6.2 Hz, 2H), 4.01 (s, 1H), 3.17 (s, 4H), 2.53 (s, 1H), 2.33 (s, 1H), 2.06 (d, J = 4.4 Hz, 2H), 1.89 (d,J = 11.6 Hz, 2H), 1.75 (d, J = 14.1 Hz, 2H), 1.59 (d, J = 17.2 Hz, 8H), 1.46 (t, J = 13.1 Hz, 2H);



(I-15-1), its ^{1}H NMR (400 MHz, MeOD) is δ 8.84 (s, 1H), 8.04 (t, *J* = 7.9 Hz, 1H), 7.92 (d, *J* = 8.1 Hz, 1H), 7.67 (d, *J* = 7.6 Hz, 1H), 7.60 (d, *J* = 8.6 Hz, 2H), 7.21 (d, *J* = 8.6 Hz, 2H), 5.78 (ddt, *J* = 16.3, 10.3, 6.1 Hz, 1H), 5.12 - 5.05 (m, 3H), 4.98 (dd, *J* = 17.1, 1.3 Hz, 1H), 4.89 (d, *J* = 6.1 Hz, 2H), 4.84 (s, 2H), 3.68 (s, 2H), 2.97 - 2.86 (m, 1H), 2.66 (s, 6H), 2.60 - 2.50 (m, 1H), 2.15 (d, *J* = 8.6 Hz, 2H), 2.04 (d, *J* = 9.0 Hz, 2H), 1.66 - 1.54 (m, 4H);

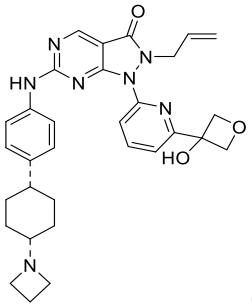


(I-15-2), its ^{1}H NMR (400 MHz, MeOD) is δ 8.83 (s, 1H), 8.04 (t, J = 7.9 Hz, 1H), 7.92 (d, J = 8.0 Hz, 1H), 7.67 - 7.62 (m, 1H), 7.59 (d, J = 8.6 Hz, 2H), 7.29 (d, J = 8.5 Hz, 2H), 5.76 (ddt, J = 16.3, 10.2, 6.1 Hz, 1 H), 5.10 - 5.02 (m, 3H), 4.96 (dd, J = 17.1, 1.3 Hz, 1H),4.87 (d, J = 6.8 Hz, 2H), 4.82 (d, J = 6.8 Hz, 2H), 2.73 (d, J = 4.2 Hz, 1H), 2.29 (d, J = 21.9 Hz, 7H), 2.04 - 1.90 (m, 4H), 1.66 (dd, J = 15.6, 6.1 Hz, 4H);

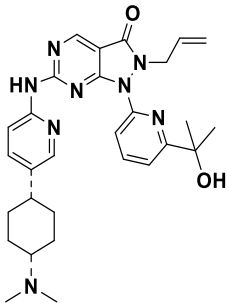


(I-36-1), its ^{1}H NMR (400 MHz, $CDCl_3$) is δ 8.88 (d, J = 2.6 Hz, 1H), 8.09 (dd, J = 15.0, 7.8 Hz, 1H), 7.99-7.83 (m, 2H), 7.54 (t, J = 9.5 Hz, 2H), 7.39 (d, J = 8.7 Hz, 1H), 7.21 (d, J = 8.5 Hz,

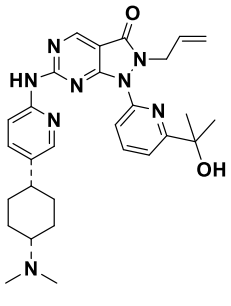
1H), 5.74 (dq, J = 10.5, 5.9 Hz, 1H), 5.12 (t, J = 8.8 Hz, 3H), 4.99 (d, J = 17.1 Hz, 1H), 4.80 (d, J = 6.3 Hz, 2H), 4.67 (d, J = 6.0 Hz, 2H), 3.39-3.24 (m, 4H), 2.60-2.34 (m, 3H), 2.14 (dt, J = 14.0, 6.8 Hz, 3H), 1.96 (d, J = 10.8 Hz, 4H), 1.55-1.37 (m, 2H), 1.27-1.12 (m, 2H);



(I-36-2), its ^{1}H NMR (400 MHz, MeOD) is δ 8.86 (s, 1H), 8.02 (dt, J = 24.0, 7.9 Hz, 3H), 7.64 (dd, J = 27.1, 8.1 Hz, 3H), 7.27 (t, J = 8.6 Hz, 2H), 7.01-6.91 (m, 3H), 6.72-6.64 (m, 3H), 5.79 (ddd, J = 16.3, 11.2, 6.1 Hz, 1H), 5.10-5.05 (m, 2H), 4.85 (d, J = 6.8 Hz, 2H), 2.57 (d, J = 10.7 Hz, 1H), 2.48-2.28 (m, 3H), 2.23-2.06 (m, 3H), 1.98-1.71 (m, 6H), 1.58 (dd, J = 23.2, 12.9 Hz, 3H), 1.44 (ddd, J = 16.1, 13.2, 3.5 Hz, 2H), 1.19-1.00 (m, 2H);



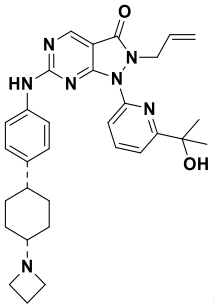
(I-41-1), its ^{1}H NMR (400 MHz, Chloroform-d) is δ 9.00 (s, 1H), 8.30 (d, J = 8.6 Hz, 1H), 8.22 (d, J = 2.4 Hz, 1H), 7.96 (t, J = 7.9 Hz, 1H), 7.73 (dd, J = 8.1, 0.8 Hz, 1H), 7.55 (dd, J = 8.7, 2.4 Hz, 1H), 7.44 (dd, J = 7.7, 0.8 Hz, 1H), 5.77 - 5.66 (m, 1H), 5.12 - 5.05 (m, 1H), 4.97 (dq, J = 17.0, 1.4 Hz, 1H), 4.76 (dt, J = 6.3, 1.3 Hz, 2H), 2.70 (s, 1H), 2.56 (s, 6H), 2.23 (q, J = 9.5 Hz, 4H), 2.11 - 2.01 (m, 4H), 1.58 (t, J = 10.3 Hz, 6H);



(I-41-2), its ^{1}H NMR (400 MHz, Chloroform-d) is δ8.99 (s, 1H), 8.54 (s, 1H), 8.32 (d, J = 8.7 Hz, 1H), 8.26 (d, J = 2.4 Hz, 1H), 8.10 (t, J = 7.7 Hz, 1H), 7.92 (s, 1H), 7.78 (dd, J = 8.1, 0.8 Hz, 1H), 7.47 - 7.41 (m, 1H), 5.79 - 5.71 (m, 1H), 5.08 (dq, J = 10.1, 1.2 Hz, 1H), 4.97 (dq, J = 17.0, 1.3 Hz, 1H), 4.77 (dt, J = 6.2, 1.4 Hz, 2H), 3.99 (s, 1H), 2.75 (d, J = 11.0 Hz, 1H), 2.52 (s, 6H), 2.32 - 2.18 (m, 1H), 2.09 (d, J = 14.4 Hz, 4H), 1.31 (d, J = 22.8 Hz, 4H) ;

wherein, ⟋ means that the *cis-trans* conformation is uncertain;

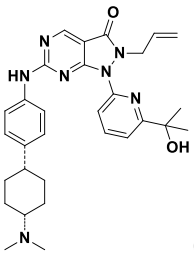
scheme E:



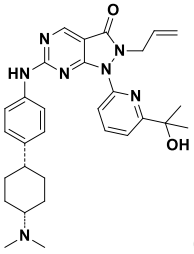
(I-8-1), its ^{1}H NMR (400 MHz, $CDCl_3$) has a peak of 1.23-1.08;

wherein, ⋰ means that the *cis-trans* conformation is uncertain;

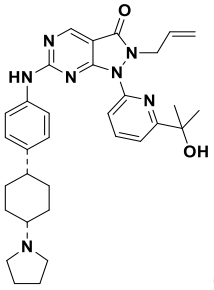
scheme F:



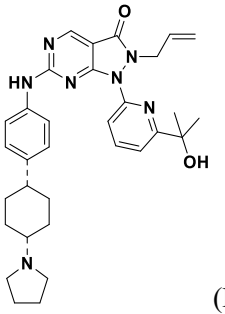
(I-1-1) with a retention time of 10.55 min under the following conditions: Agilent 1260 high performance liquid chromatograph; mobile phase A: water (0.1% formic acid), mobile phase B: acetonitrile; column time: 15 min; column type: Waters' Xselect, 5 μm, 4.6×250mm; gradient elution, 5% mobile phase B→50% mobile phase B;



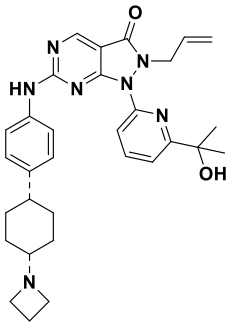
(I-1-2) with a retention time of 10.78 min under the following conditions: Agilent 1260 high performance liquid chromatograph; mobile phase A: water (0.1% formic acid), mobile phase B: acetonitrile; column time: 15 min; column type: Waters' Xselect, 5 μm, 4.6×250 mm; gradient elution, 5 % mobile phase B→50 % mobile phase B;



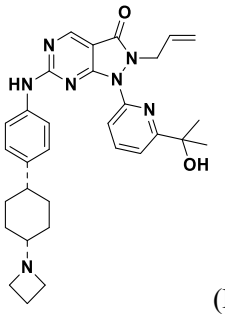
(I-3-1) with a retention time of 11.01 min under the following conditions: Agilent 1260 high performance liquid chromatograph; mobile phase A: water (0.1 % formic acid), mobile phase B: acetonitrile; column time: 15 min; column type: Waters' Xselect, 5 μm, 4.6×250 mm; gradient elution, 5 % mobile phase B→50 % mobile phase B;



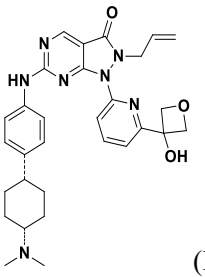
(I-3-2) with a retention time of 11.20 min under the following conditions: Agilent 1260 high performance liquid chromatograph; mobile phase A: water (0.1 % formic acid), mobile phase B: acetonitrile; column time: 15 min; column type: Waters' Xselect, 5 μm, 4.6×250 mm; gradient elution, 5 % mobile phase B→50 % mobile phase B;



(I-8-1) with a retention time of 10.78 min under the following conditions: Agilent 1260 high performance liquid chromatograph; mobile phase A: water (0.1 % formic acid), mobile phase B: acetonitrile; column time: 15 min; column type: Waters' Xselect, 5 μm, 4.6×250 mm; gradient elution, 5 % mobile phase B→50 % mobile phase B;

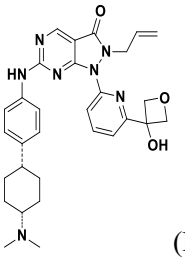


(I-8-2) with a retention time of 11.00 min under the following conditions: Agilent 1260 high performance liquid chromatograph; mobile phase A: water (0.1 % formic acid), mobile phase B: acetonitrile; column time: 15 min; column type: Waters' Xselect, 5 μm, 4.6×250 mm; gradient elution, 5 % mobile phase B→50 % mobile phase B;

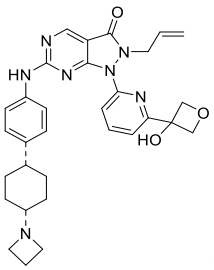


(I-15-1) with a retention time of 7.02 min under the following conditions: Agilent 1260 high performance liquid chromatograph; mobile phase A: water (0.1 % formic acid), mobile phase B: acetonitrile; column time: 15 min; column type: Waters' Xselect, 5 μm, 4.6×250 mm; gradient elution, 5 %

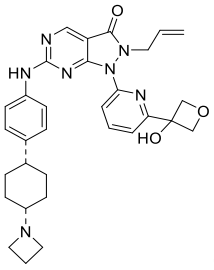
mobile phase B→95 % mobile phase B;



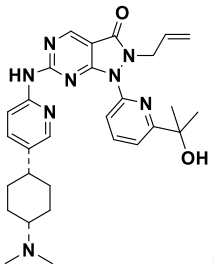
(I-15-2) with a retention time of 7.16 min under the following conditions: Agilent 1260 high performance liquid chromatograph; mobile phase A: water (0.1 % formic acid), mobile phase B: acetonitrile; column time: 15 min; column type: Waters' Xselect, 5 μm, 4.6×250 mm; gradient elution, 5 % mobile phase B→95 % mobile phase B;



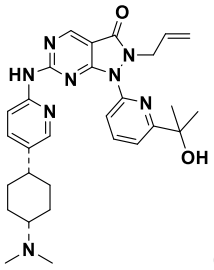
(I-36-1) with a retention time of 7.14 min under the following conditions: Agilent 1260 high performance liquid chromatograph; mobile phase A: water (0.1 % formic acid), mobile phase B: acetonitrile; column time: 15 min; column type: Waters' Xselect, 5 μm, 4.6×250 mm; gradient elution, 5 % mobile phase B→95 % mobile phase B;



(I-36-2) with a retention time of 7.15 min under the following conditions: Agilent 1260 high performance liquid chromatograph; mobile phase A: water (0.1 % formic acid), mobile phase B: acetonitrile; column time: 15 min; column type: Waters' Xselect, 5 μm, 4.6×250 mm; gradient elution, 5 % mobile phase B→95 % mobile phase B;



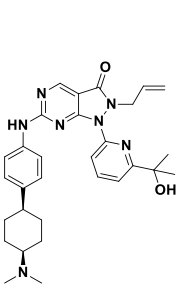
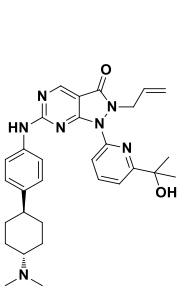
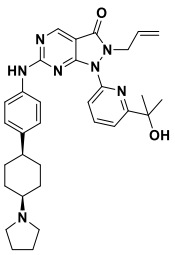
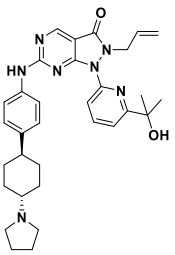
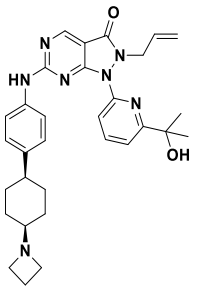
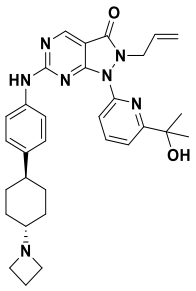
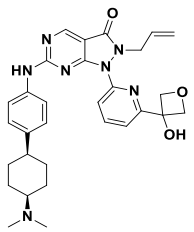
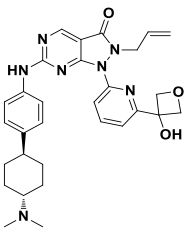
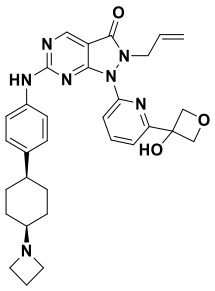
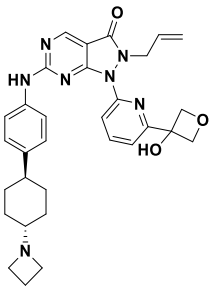
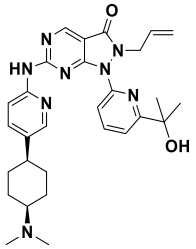
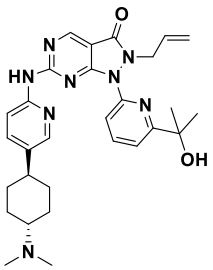
(I-41-1) with a retention time of 6.17 min under the following conditions: Agilent 1260 high performance liquid chromatograph; mobile phase A: water (0.1 % formic acid), mobile phase B: acetonitrile; column time: 15min; column type: Waters' Xselect, 5 μm, 4.6×250 mm; gradient elution, 5 % mobile phase B→95 % mobile phase B;



(I-41-2) with a retention time of 6.28 min under the following conditions: Agilent 1260 high performance liquid chromatograph; mobile phase A: water (0.1 % formic acid), mobile phase B: acetonitrile; column time: 15 min; column type: Waters' Xselect, 5 μm, 4.6×250 mm; gradient elution, 5 % mobile phase B→95 % mobile phase B;

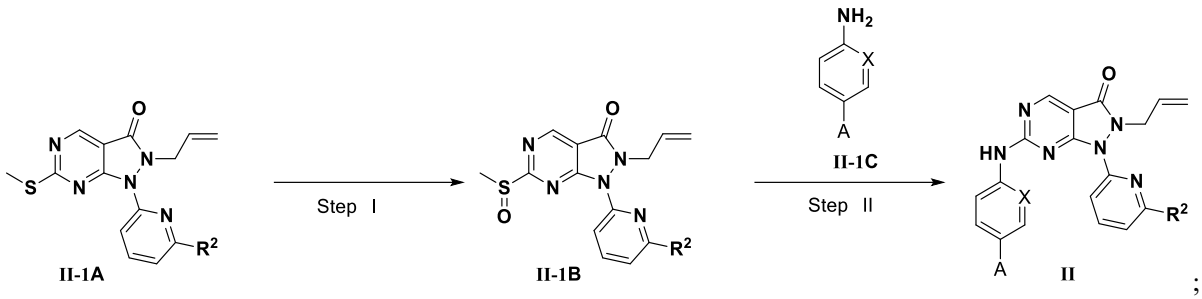
wherein, ⋰ means that the *cis-trans* conformation is uncertain;

scheme G:


,

,

,

,

,

,

,

,

,

,

and

.

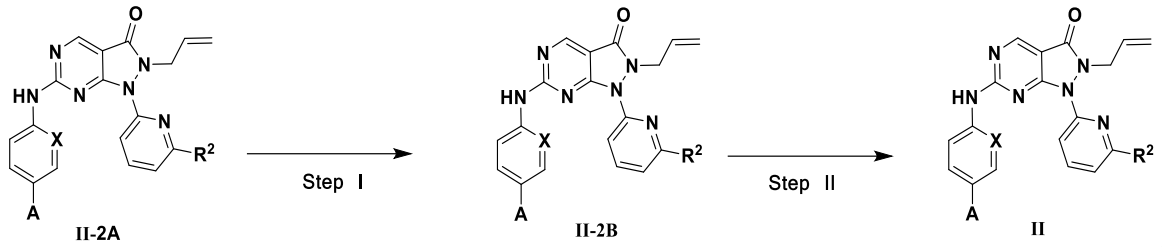
13. A preparation method of the pyrazolopyrimidine compound represented by formula **II** according to at least one of claims 1-12, the method is any of the following methods:

method 1, comprising the following steps: step I, oxidizing compound **II-1A** by an oxidant in an organic solvent to obtain compound **II-1B**; step II, reacting compound **II-1B** with compound **II-1C** in an organic solvent and under alkaline conditions to obtain compound **II**;



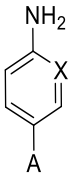
;

method 2, comprising the following steps: step I, hydrolyzing compound **II-2A** (R^1 is -(C=O)-O-C_2H_5) to obtain compound **II-2B** (R^1 is -(C=O)-OH); step II, a condensation reaction is carried out between compound **II-2B** and an amino compound in an organic solvent to obtain compound **II** (R^1 is -(C=O)-$NR^{1-5-1}R^{1-5-2}$);



.

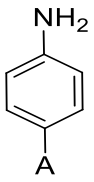
14. A compound represented by formula **II-1C**:



II-1C

wherein, X is CH or N, A is as defined in at least one of claims 1-12.

15. The compound represented by formula **II-1C** according to claim 14, wherein, the compound is a compound represented by formula **1C**:

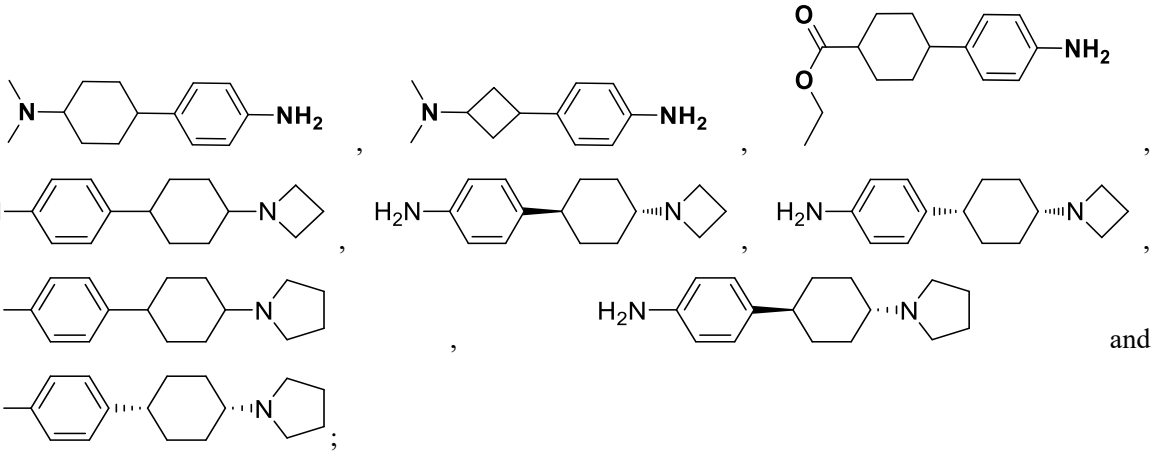


1C ;

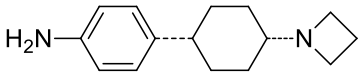
wherein, A is C_3-C_{20} cycloalkyl substituted by one R^1, R^1 is -$NR^{1-3}R^{1-4}$ or -C(=O)R^{1-5}, and R^{1-3}, R^{1-4} and R^{1-5} are as defined in at least one of claims 1-12.

16. The compound represented by formula **II-1C** according to claim 14, wherein, the compound is any one of the compounds described in any of the following schemes:

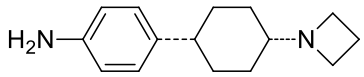
scheme a:



scheme b:



, its ^{1}H NMR (400 MHz, $CDCl_3$) is δ 7.08 - 6.96 (m, 2H), 6.70 - 6.60 (m, 2H), 3.57 (s, 2H), 3.22 (t, J = 7.0 Hz, 4H), 2.38 (tt, J = 12.1, 3.2 Hz, 1H), 2.15 - 1.95 (m, 5H), 1.95 - 1.81 (m, 4H), 1.51 - 1.30 (m, 2H), 1.21 - 1.04 (m, 2H);

or, , its ^{1}H NMR (400 MHz, MeOD) is δ 7.10 - 6.97 (m, 2H), 6.74 - 6.63 (m, 2H), 4.22 - 4.08 (t, J = 8.0 Hz, 4H), 3.47 - 3.38 (m, 1H), 2.61 - 2.52 (m, 1H), 2.52 - 2.28 (m, 2H), 1.92 - 1.62 (m, 8H).

17. ~~An application~~Use of the substance **X** in the preparation of kinase inhibitors or medicaments~~; the medicament can be used~~ for treating and/or preventing diseases or cancers related to WEE1 kinase; wherein

the substance X is the pyrazolopyrimidine compound represented by formula **II** according to at least one of claims 1-12, the pharmaceutically acceptable salt thereof, the solvate thereof, the solvate of the pharmaceutically acceptable salt thereof, the metabolite thereof or the prodrug thereof.

18. A pharmaceutical composition comprising the substance **X** and a pharmaceutical excipient;

the substance X is the pyrazolopyrimidine compound represented by formula **II** according to at least one of claims 1-12, the pharmaceutically acceptable salt thereof, the solvate thereof, the solvate of the pharmaceutically acceptable salt thereof, the metabolite thereof or the prodrug thereof.

19. A combination comprising the substance **X** and an anticancer drug,

the substance X is the pyrazolopyrimidine compound represented by formula **II** according to at least one of claims 1-12, the pharmaceutically acceptable salt thereof, the solvate thereof, the solvate of the pharmaceutically acceptable salt thereof, the metabolite thereof or the prodrug thereof.

20. ~~An application~~Use of the combination according to claim 19 in the preparation of a medicament for preventing and/or treating cancer.

21. ~~An application~~Use of the substance **X** in the preparation of a medicament for preventing and/or treating cancer, wherein the medicament is to be administered in combination with an anticancer drug ~~used for preventing and/or treating cancer~~; and

the substance X is the pyrazolopyrimidine compound represented by formula **II** according to at least one of claims 1-12, the pharmaceutically acceptable salt thereof, the solvate thereof, the solvate of the

pharmaceutically acceptable salt thereof, the metabolite thereof or the prodrug thereof.

22. ~~An application~~Use of an anticancer drug in the preparation of a medicament for preventing and/or treating cancer, wherein the medicament is to be administered in combination with the substance **X** ~~used for preventing and/or treating cancer~~; and

the substance X is the pyrazolopyrimidine compound represented by formula **II** according to at least one of claims 1-12, the pharmaceutically acceptable salt thereof, the solvate thereof, the solvate of the pharmaceutically acceptable salt thereof, the metabolite thereof or the prodrug thereof.

23. A pharmaceutical composition comprising the combination according to claim 19 and a pharmaceutical excipient.

24. A combination drug kit comprising a pharmaceutical composition A and a pharmaceutical composition B;

the pharmaceutical composition A comprises the substance **X**, and pharmaceutical excipients;

the pharmaceutical composition B comprises the anticancer drugs and pharmaceutical excipients;

the substance **X** is the pyrazolopyrimidine compound represented by formula **II** according to at least one of claims 1-12, the pharmaceutically acceptable salt thereof, the solvate thereof, the solvate of the pharmaceutically acceptable salt thereof, the metabolite thereof or the prodrug thereof.

25. The substance X for use in ~~A method for~~ treating and/or preventing diseases or cancers related to WEE1 kinase ~~comprising administering a therapeutically effective amount of the substance **X** to a patient~~; wherein

the substance X is the pyrazolopyrimidine compound represented by formula **II** according to at least one of claims 1-12, the pharmaceutically acceptable salt thereof, the solvate thereof, the solvate of the pharmaceutically acceptable salt thereof, the metabolite thereof or the prodrug thereof.

26. The combination according to claim 19 for use in ~~A method for~~ treating and/or preventing cancer ~~comprising administering a therapeutically effective amount of the combination according to claim 19 to a patient~~.