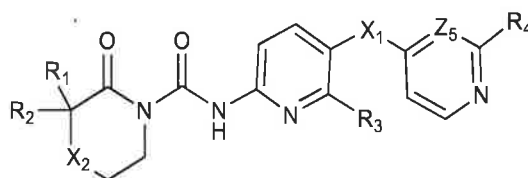


We claim

1. A compound of formula (IIa), a stereoisomer or pharmaceutically acceptable salt thereof:



(IIa)

wherein, X<sub>1</sub> is -O- or -CH<sub>2</sub>-;

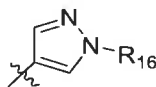
X<sub>2</sub> is bond, -O- or -CH<sub>2</sub>-;

Z<sub>5</sub> is CH;

10 R<sub>1</sub> and R<sub>2</sub> are each independently selected from the group consisting of hydrogen, deuterium, hydroxy, methyl, ethyl, propyl, cyclopropyl, cyclopropylmethyl, methoxy, ethoxy, phenylmethoxy, methoxyethyl, hydroxymethyl, cyanomethyl, trifluoromethyl, trideuteriomethyl, difluoromethyl, dideuteriomethyl and aminomethyl, or, R<sub>1</sub> and R<sub>2</sub>, together with the carbon atom directly attached thereto, form C<sub>3-6</sub> cycloalkyl;

15 R<sub>3</sub> is selected from the group consisting of hydrogen, deuterium, methyl, ethyl, cyclopropyl, cyclopropylmethyl, trifluoromethyl, trideuteriomethyl, difluoromethyl and dideuteriomethyl;

R<sub>4</sub> is



20 wherein, R<sub>16</sub> is selected from the group consisting of hydrogen, deuterium, C<sub>1-4</sub> alkyl, C<sub>1-4</sub> haloalkyl, C<sub>3-8</sub> cycloalkyl, 3-8 membered heterocyclyl, C<sub>5-8</sub> aryl, 5-8 membered heteroaryl, -C<sub>0-4</sub>-S(O)<sub>r</sub>R<sub>11</sub>, -C<sub>0-4</sub>-C(O)OR<sub>12</sub> and -C<sub>0-4</sub>-C(O)R<sub>13</sub>, above groups are optionally further substituted by one or more substituents selected from the group consisting of deuterium, halogen, cyano, nitro, azido, C<sub>1-4</sub> alkyl, C<sub>2-4</sub> alkenyl, C<sub>2-4</sub> alkynyl, C<sub>1-4</sub> haloalkyl, C<sub>3-8</sub> cycloalkyl, 3-8 membered heterocyclyl, C<sub>5-8</sub> aryl, 5-8 membered heteroaryl, -C<sub>0-4</sub>-S(O)<sub>r</sub>R<sub>11</sub>, -C<sub>0-4</sub>-O-R<sub>12</sub>, -C<sub>0-4</sub>-C(O)OR<sub>12</sub>, -C<sub>0-4</sub>-C(O)R<sub>13</sub>, -C<sub>0-4</sub>-O-C(O)R<sub>13</sub>, -C<sub>0-4</sub>-NR<sub>14</sub>R<sub>15</sub>, -C<sub>0-4</sub>-C(O)NR<sub>14</sub>R<sub>15</sub> and -C<sub>0-4</sub>-N(R<sub>14</sub>)-C(O)R<sub>13</sub>, wherein the cycloalkyl, heterocyclyl, aryl, and heteroaryl are optionally further substituted by one or more substituents selected from the group consisting of deuterium, halogen, cyano, nitro, azido, C<sub>1-4</sub> alkyl, C<sub>2-4</sub> alkenyl, C<sub>2-4</sub> alkynyl, C<sub>1-4</sub> haloalkyl, C<sub>3-8</sub> cycloalkyl, 3-8 membered heterocyclyl, C<sub>5-8</sub> aryl, 5-8 membered heteroaryl, -C<sub>0-4</sub>-S(O)<sub>r</sub>R<sub>11</sub>, -C<sub>0-4</sub>-O-R<sub>12</sub>, -C<sub>0-4</sub>-C(O)OR<sub>12</sub>, -C<sub>0-4</sub>-C(O)R<sub>13</sub>, -C<sub>0-4</sub>-O-C(O)R<sub>13</sub>, -C<sub>0-4</sub>-NR<sub>14</sub>R<sub>15</sub>, -C<sub>0-4</sub>-C(O)NR<sub>14</sub>R<sub>15</sub> and -C<sub>0-4</sub>-N(R<sub>14</sub>)-C(O)R<sub>13</sub>;

30 each R<sub>11</sub> is independently selected from the group consisting of hydrogen, deuterium, hydroxy, C<sub>1-8</sub> alkyl, C<sub>1-8</sub> alkoxy, C<sub>2-8</sub> alkenyl, C<sub>3-10</sub> cycloalkyl, C<sub>3-10</sub> cycloalkyloxy, 3-10 membered heterocyclyl, 3-10 membered heterocyclyloxy, C<sub>5-10</sub> aryl, C<sub>5-10</sub> aryloxy, 5-10 membered heteroaryl, 5-10 membered heteroaryloxy and -NR<sub>14</sub>R<sub>15</sub>, above groups are optionally further substituted by one or more substituents selected from the group consisting

of deuterium, halogen, hydroxy, carbonyl, C<sub>1-8</sub> alkyl, C<sub>1-8</sub> alkoxy, C<sub>3-10</sub> cycloalkyl, C<sub>3-10</sub> cycloalkyloxy, 3-10 membered heterocyclyl, 3-10 membered heterocyclyloxy, C<sub>5-10</sub> aryl, C<sub>5-10</sub> aryloxy, 5-10 membered heteroaryl, 5-10 membered heteroaryloxy and -NR<sub>14</sub>R<sub>15</sub>;

each R<sub>12</sub> is independently selected from the group consisting of hydrogen, deuterium, C<sub>1-8</sub> alkyl, C<sub>2-8</sub> alkenyl, C<sub>3-10</sub> cycloalkyl, 3-10 membered heterocyclyl, C<sub>5-10</sub> aryl and 5-10 membered heteroaryl, above groups are optionally further substituted by one or more substituents selected from the group consisting of deuterium, halogen, hydroxy, carbonyl, cyano, C<sub>1-8</sub> alkyl, C<sub>1-8</sub> alkoxy, C<sub>3-10</sub> cycloalkyl, C<sub>3-10</sub> cycloalkyloxy, 3-10 membered heterocyclyl, 3-10 membered heterocyclyloxy, C<sub>5-10</sub> aryl, C<sub>5-10</sub> aryloxy, 5-10 membered heteroaryl, 5-10 membered heteroaryloxy and -NR<sub>14</sub>R<sub>15</sub>;

each R<sub>13</sub> is independently selected from the group consisting of hydrogen, deuterium, hydroxy, C<sub>1-8</sub> alkyl, C<sub>1-8</sub> alkoxy, C<sub>2-8</sub> alkenyl, C<sub>2-8</sub> alkynyl, C<sub>3-10</sub> cycloalkyl, C<sub>3-10</sub> cycloalkyloxy, 3-10 membered heterocyclyl, 3-10 membered heterocyclyloxy, C<sub>5-10</sub> aryl, C<sub>5-10</sub> aryloxy, 5-10 membered heteroaryl, 5-10 membered heteroaryloxy and -NR<sub>14</sub>R<sub>15</sub>, above groups are optionally further substituted by one or more substituents selected from the group consisting of deuterium, halogen, hydroxy, cyano, C<sub>1-8</sub> alkyl, C<sub>1-8</sub> alkoxy, C<sub>3-10</sub> cycloalkyl, C<sub>3-10</sub> cycloalkyloxy, 3-10 membered heterocyclyl, 3-10 membered heterocyclyloxy, C<sub>5-10</sub> aryl, C<sub>5-10</sub> aryloxy, 5-10 membered heteroaryl, 5-10 membered heteroaryloxy and -NR<sub>14</sub>R<sub>15</sub>;

each of R<sub>14</sub> and R<sub>15</sub> is independently selected from the group consisting of hydrogen, deuterium, hydroxy, C<sub>1-8</sub> alkyl, C<sub>2-8</sub> alkenyl, C<sub>2-8</sub> alkynyl, C<sub>3-10</sub> cycloalkyl, 3-10 membered heterocyclyl, C<sub>5-10</sub> aryl, 5-10 membered heteroaryl, sulfonyl, methanesulfonyl, isopropylsulfonyl, cyclopropylsulfonyl, p-toluenesulfonyl, amino, monoalkylamino, dialkylamino and C<sub>1-8</sub> alkanoyl, above groups are optionally further substituted by one or more substituents selected from the group consisting of deuterium, halogen, hydroxy, C<sub>1-8</sub> alkyl, C<sub>1-8</sub> alkoxy, C<sub>3-10</sub> cycloalkyl, C<sub>3-10</sub> cycloalkyloxy, 3-10 membered heterocyclyl, 3-10 membered heterocyclyloxy, C<sub>5-10</sub> aryl, C<sub>5-10</sub> aryloxy, 5-10 membered heteroaryl, 5-10 membered heteroaryloxy, amino, monoalkylamino, dialkylamino and C<sub>1-8</sub> alkanoyl;

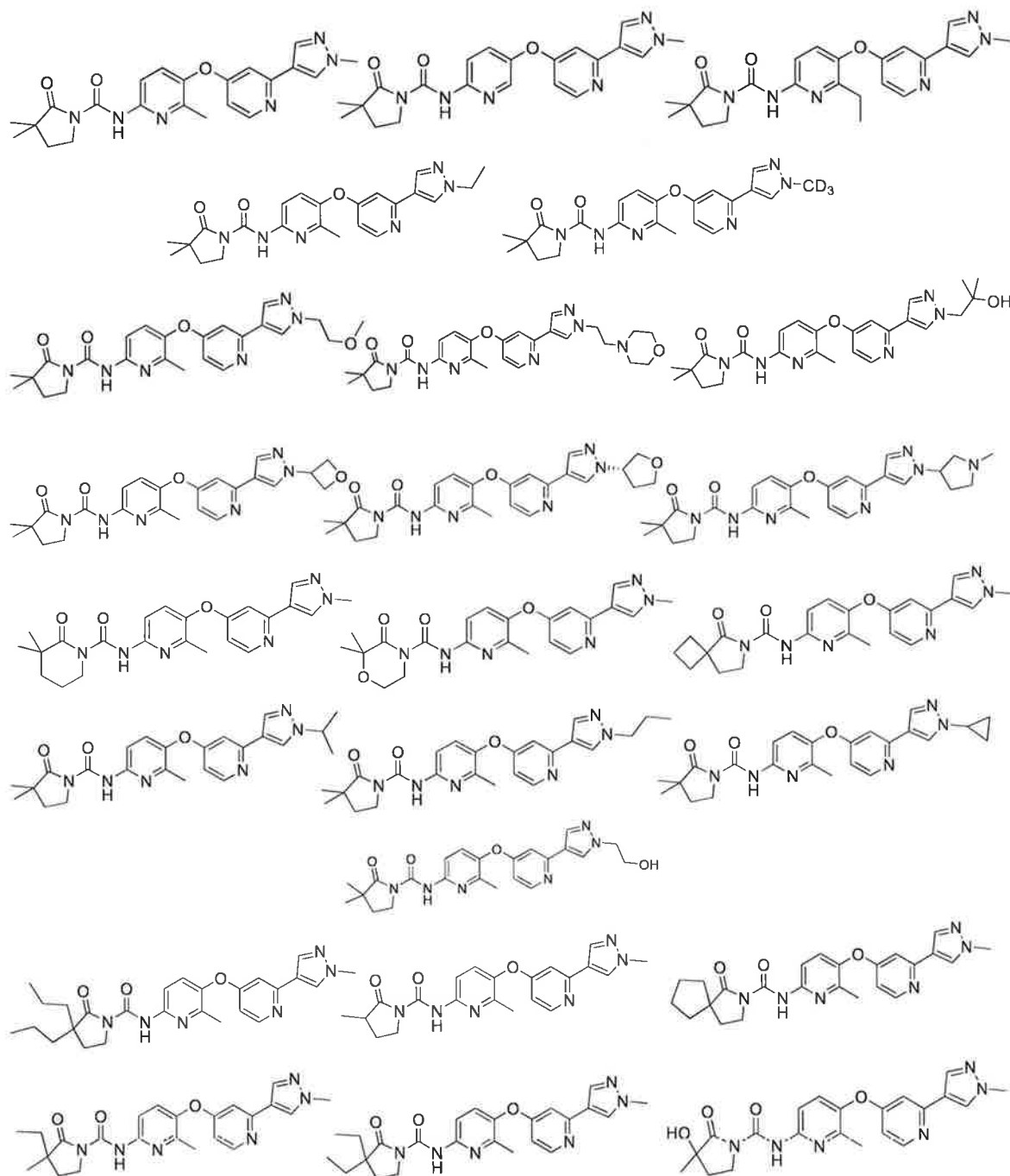
or R<sub>14</sub> and R<sub>15</sub>, together with nitrogen atom directly attached thereto, form 5-10 membered heterocyclyl, above groups are optionally further substituted by one or more substituents selected from the group consisting of deuterium, halogen, hydroxy, C<sub>1-8</sub> alkyl, C<sub>1-8</sub> alkoxy, C<sub>3-10</sub> cycloalkyl, C<sub>3-10</sub> cycloalkyloxy, 3-10 membered heterocyclyl, 3-10 membered heterocyclyloxy, C<sub>5-10</sub> aryl, C<sub>5-10</sub> aryloxy, 5-10 membered heteroaryl, 5-10 membered heteroaryloxy, amino, monoalkylamino, dialkylamino and C<sub>1-8</sub> alkanoyl;

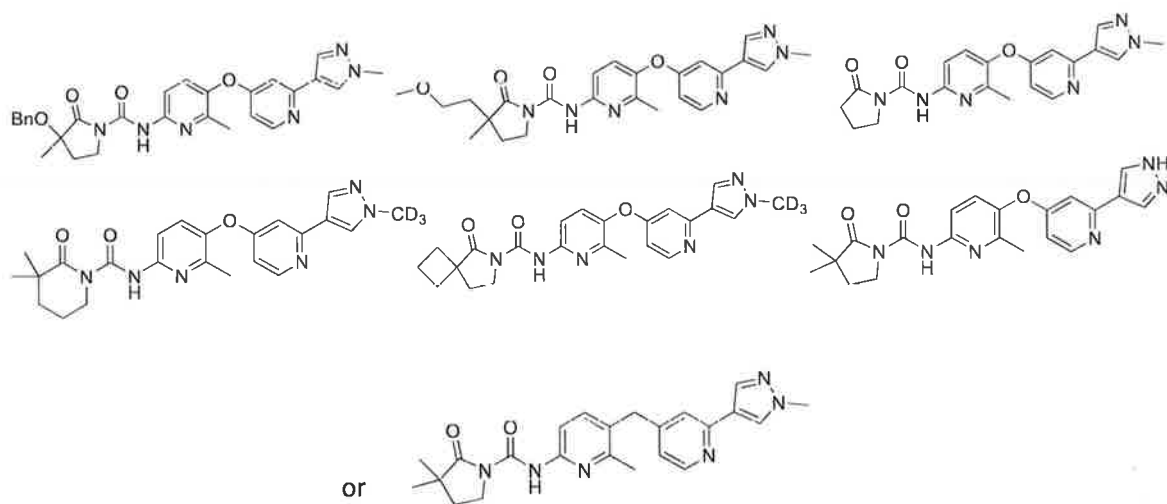
and r is 0, 1 or 2.

2. The compound of formula (IIa), the stereoisomer or pharmaceutically acceptable salt thereof according to claim 1, wherein R<sub>16</sub> is selected from the group consisting of hydrogen, deuterium, C<sub>1-4</sub> alkyl, C<sub>3-6</sub> cycloalkyl, 3-6 membered heterocyclyl, phenyl and 5-6 membered heteroaryl, above groups are optionally further substituted by one or more substituents selected from the group consisting of deuterium, halogen, cyano, nitro, azido, C<sub>1-4</sub> alkyl, C<sub>2-4</sub> alkenyl, C<sub>2-4</sub> alkynyl, C<sub>1-4</sub> haloalkyl, C<sub>3-8</sub> cycloalkyl, 3-8 membered heterocyclyl, C<sub>5-8</sub> aryl, 5-8 membered heteroaryl, -C<sub>0-4</sub>-S(O)<sub>r</sub>R<sub>11</sub>, -C<sub>0-4</sub>-O-R<sub>12</sub>, -C<sub>0-4</sub>-C(O)OR<sub>12</sub>, -C<sub>0-4</sub>-C(O)R<sub>13</sub>, -C<sub>0-4</sub>-O-C(O)R<sub>13</sub>, -C<sub>0-4</sub>-NR<sub>14</sub>R<sub>15</sub>, -C<sub>0-4</sub>-C(O)NR<sub>14</sub>R<sub>15</sub> and -C<sub>0-4</sub>-N(R<sub>14</sub>)-C(O)R<sub>13</sub>;

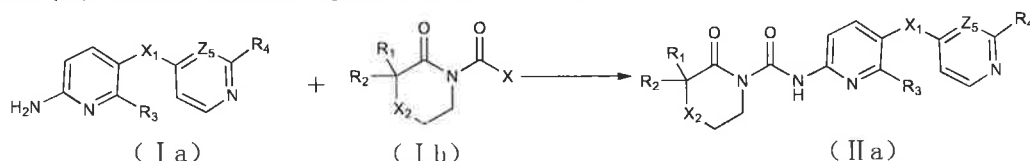
wherein, R<sub>11</sub>, R<sub>12</sub>, R<sub>13</sub>, R<sub>14</sub>, R<sub>15</sub>, and r are defined as in claim 1.

3. The compound of formula (IIa), the stereoisomer or pharmaceutically acceptable salt thereof according to any one of claims 1 to 2, wherein the compound is selected from the following compounds:





- 5 4. A process for preparing the compound of formula (IIa), the stereoisomer or pharmaceutically acceptable salt thereof according to any one of claims 1 to 3, comprising the following steps: the compound of formula (IIa) is synthesized through a condensation reaction of the compound of formula (Ia) or an acidic salt thereof and the compound of formula (Ib), and the reaction equation is as follows:



10

wherein, X is chlorine or bromine; X<sub>1</sub>, X<sub>2</sub>, Z<sub>5</sub>, R<sub>1</sub>, R<sub>2</sub>, R<sub>3</sub>, and R<sub>4</sub> are defined as in claim 1.

- 15 5. A pharmaceutical composition, comprising the compound of formula (IIa), the stereoisomer or pharmaceutically acceptable salt thereof of any one of claims 1 to 3, and a pharmaceutically acceptable carrier.

- 20 6. Use of the compound of formula (IIa), the stereoisomer or pharmaceutically acceptable salt thereof of any one of claims 1 to 3, or the pharmaceutical composition of claim 5 in the preparation of medicament for treating cancer, tumor, autoimmune disease, metabolic disease or metastatic disease.

- 25 7. Use of the compound of formula (IIa), the stereoisomer or pharmaceutically acceptable salt thereof of any one of claims 1 to 3, or the pharmaceutical composition of claim 5 in the preparation of medicament for treating ovarian cancer, pancreatic cancer, prostate cancer, lung cancer, breast cancer, renal carcinoma, liver cancer, cervical cancer, osseous metastasis cancer, papillary thyroid cancer, non-small cell lung cancer, colon cancer, gastrointestinal stromal tumor, solid tumor, melanoma, mesothelioma, glioblastoma, osteosarcoma, multiple myeloma, hyperproliferative disease, metabolic disease, 30 neurodegenerative disease, primary tumor site metastasis, myeloproliferative disease, leukemia, rheumatic arthritis, rheumatoid arthritis, osteoarthritis, multiple sclerosis,

autoimmune nephritis, lupus, Crohn's disease, asthma, chronic obstructive pulmonary disease, osteoporosis, hypereosinophilic syndrome, mastocytosis or mast cell leukemia.

8. Use of the compound of formula (IIa), the stereoisomer or pharmaceutically acceptable salt thereof of any one of claims 1 to 3, or the pharmaceutical composition of claim 5 in the preparation of medicament for treating ovarian cancer, pancreatic cancer, prostate cancer, breast cancer, cervical cancer, glioblastoma, multiple myeloma, metabolic disease, neurodegenerative disease, primary tumor site metastasis or osseous metastasis cancer.

9. The compound of formula (IIa), the stereoisomer or pharmaceutically acceptable salt thereof of any one of claims 1 to 3, or the pharmaceutical composition of claim 5 for use as a medicament for treating ovarian cancer, pancreatic cancer, prostate cancer, lung cancer, breast cancer, renal carcinoma, liver cancer, cervical cancer, osseous metastasis cancer, papillary thyroid cancer, non-small cell lung cancer, colon cancer, gastrointestinal stromal tumor, solid tumor, melanoma, mesothelioma, glioblastoma, osteosarcoma, multiple myeloma, hyperproliferative disease, metabolic disease, neurodegenerative disease, primary tumor site metastasis, myeloproliferative disease, leukemia, rheumatic arthritis, rheumatoid arthritis, osteoarthritis, multiple sclerosis, autoimmune nephritis, lupus, Crohn's disease, asthma, chronic obstructive pulmonary disease, osteoporosis, hypereosinophilic syndrome, mastocytosis or mast cell leukemia.

10. The compound of formula (IIa), the stereoisomer or pharmaceutically acceptable salt thereof of any one of claims 1 to 3, or the pharmaceutical composition of claim 5 for use as a medicament for treating ovarian cancer, pancreatic cancer, prostate cancer, breast cancer, cervical cancer, glioblastoma, multiple myeloma, metabolic disease, neurodegenerative disease, primary tumor site metastasis or osseous metastasis cancer.