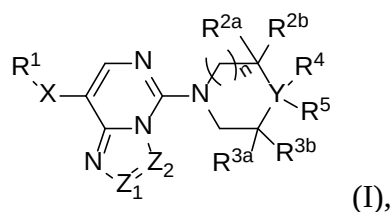


Claims

1. A pyrimidine-fused compound represented by formula (I), a pharmaceutically acceptable salt thereof, or a solvate thereof,



or an isotope-labeled compound of the pyrimidine-fused compound represented by formula (I), the pharmaceutically acceptable salt, or the solvate, wherein the isotope is selected from ^2H , ^3H , ^{11}C , ^{13}C , ^{14}C , ^{15}N , ^{18}F , ^{31}P , ^{32}P , ^{35}S , ^{36}Cl , and ^{125}I ;

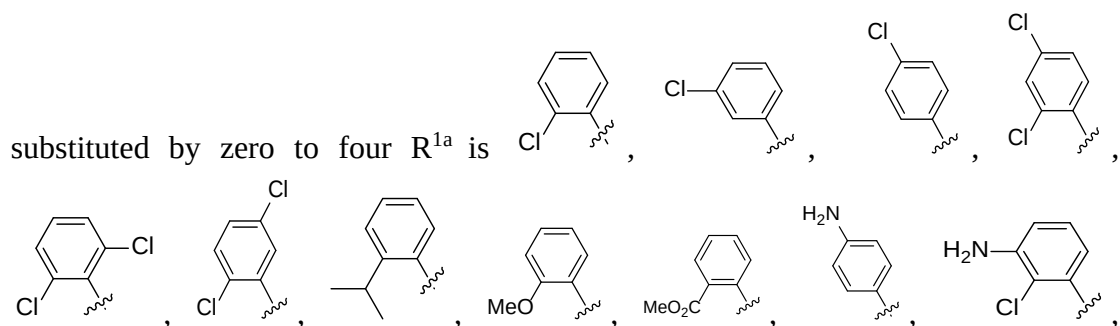
wherein, Z_1 and Z_2 are both CH; or one of Z_1 and Z_2 is N, and the other is CH;

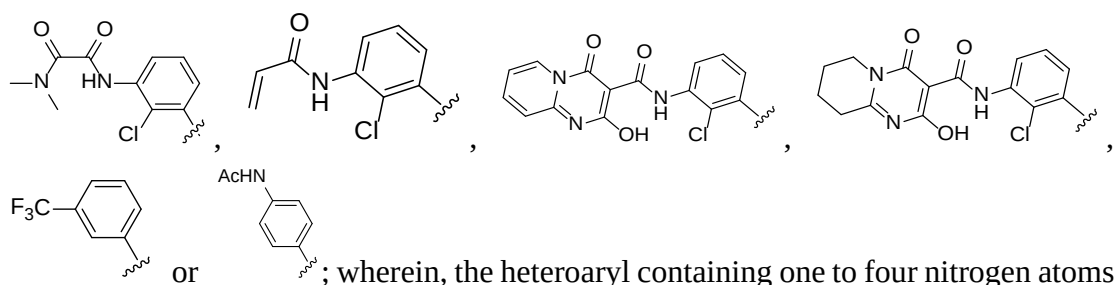
X is independently S or absent;

Y is independently C or N;

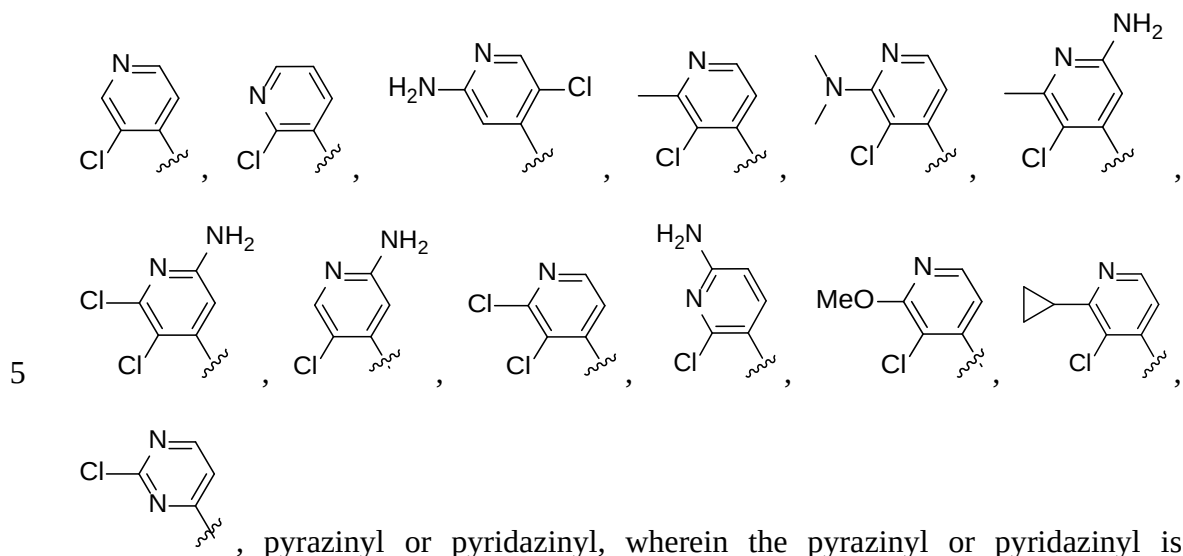
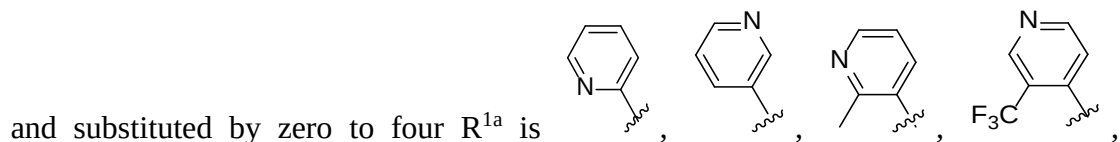
n is independently 0, 1 or 2;

R^1 is independently phenyl substituted by zero to four R^{1a} , heteroaryl containing one to four nitrogen atoms and substituted by zero to four R^{1a} , naphthyl substituted by zero to four R^{1a} , benzoheterocyclyl substituted by zero to four R^{1a} , fused heteroaryl containing one to four nitrogen atoms and substituted by zero to four R^{1a} , heteroaryl containing one to four heteroatoms selected from N, NR^{1b} , O and $\text{S}(\text{O})_m$ and substituted by zero to four R^{1a} , C_{1-8} alkyl unsubstituted or substituted by R^{1c} , or C_{1-8} haloalkyl unsubstituted or substituted by R^{1c} ; wherein m is 0, 1 or 2; wherein, the phenyl



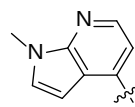


wherein, the heteroaryl containing one to four nitrogen atoms



substituted by zero to four R^{1a} ; wherein the fused heteroaryl containing one to four

nitrogen atoms and substituted by zero to four R^{1a} is



and, wherein the heteroaryl containing one to four heteroatoms selected from N, NR^{1b} , O and $S(O)_m$ is

imidazolyl, thiazolyl, oxazolyl, thiadiazolyl or benzothiazolyl;

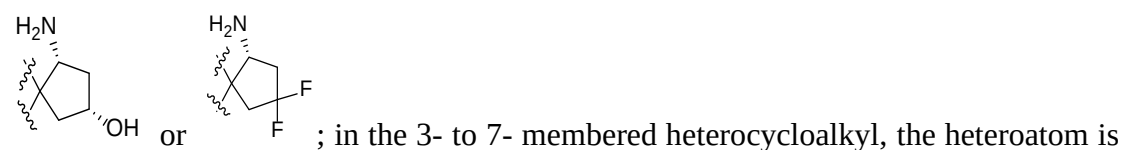
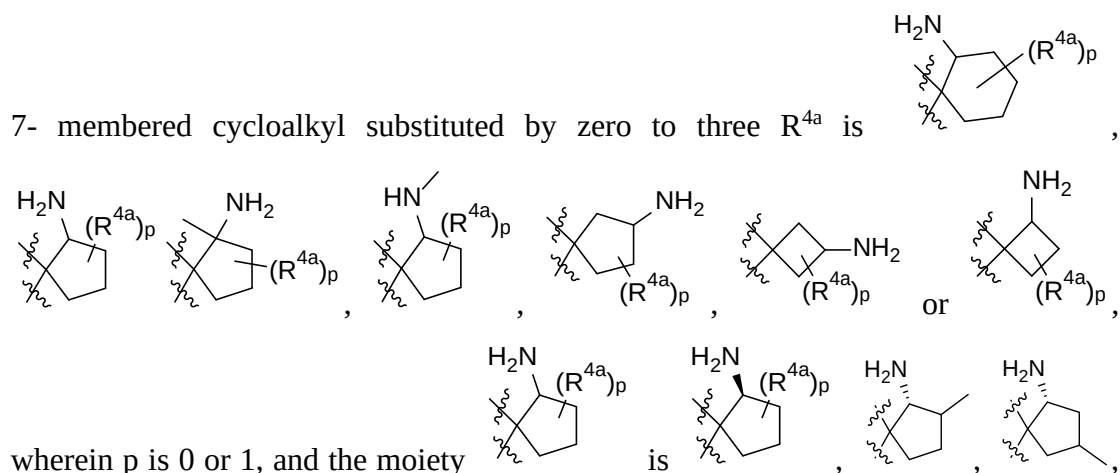
R^{2a} , R^{2b} , R^{3a} and R^{3b} are independently hydrogen, or C_{1-4} alkyl unsubstituted or substituted by R^{1a1} ;

when Y is N, then R^4 is independently hydrogen, or C_{1-4} alkyl unsubstituted or substituted by R^{1a1} ; and R_5 is absent;

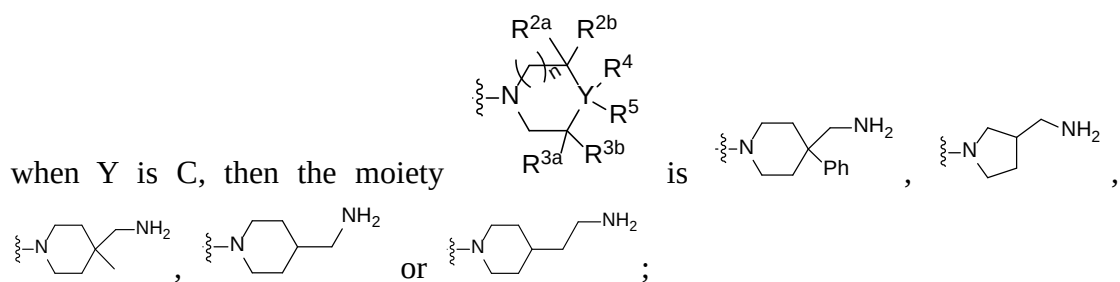
when Y is C, then R^4 and R^5 are independently hydrogen, aryl, C_{1-4} alkyl, C_{1-4} alkoxy, amino, amino substituted by C_{1-4} alkyl or amino substituted by $-O-C_{1-4}$ alkyl,

or R⁴ and R⁵ together with Y form 3- to 7- membered saturated or partially unsaturated spiro ring substituted by zero to three R^{4a}, wherein the ring contains one to three heteroatoms or groups independently selected from N, C(=O) and/or O; or, R⁴ and R⁵ together with Y form 3- to 7- membered cycloalkyl substituted by zero to three R^{4a}, or

5 3- to 7- membered heterocycloalkyl substituted by zero to three R^{4a}; wherein the 3- to



10 selected from one or more of N, O and S, and the number of the heteroatom is 1–3; or,



or, any two adjacent groups of R^{2a}, R^{2b}, R^{3a}, R^{3b}, R⁴ and R⁵, together with the carbon atom and Y to which they are attached, form 3- to 7- membered cycloalkyl

15 substituted by zero to three R^{4a}, or 3- to 7- membered heterocycloalkyl substituted by zero to three R^{4a}; in the 3- to 7- membered heterocycloalkyl, the heteroatom is selected from one or more of N, O and S, and the number of the heteroatom is 1–3;

R^{1a} is independently halogen, C_{1-4} alkoxy unsubstituted or substituted by R^{1a1} , C_{1-4} alkyl unsubstituted or substituted by R^{1a1} , trifluoromethyl, $-C(=O)OR^{1a2}$, $-NR^{1a2}R^{1a3}$, $-NHC(=O)R^{1a4}$, or C_{3-8} cycloalkyl unsubstituted or substituted by R^{1a1} ;

R^{1b} is independently hydrogen, or C_{1-4} alkyl unsubstituted or substituted by R^{1a1} ;

5 R^{1c} is independently hydrogen, $-C(=O)OR^{1a2}$, or C_{1-4} alkyl unsubstituted or substituted by R^{1a1} ;

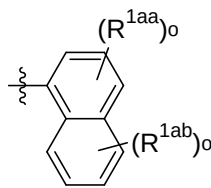
R^{4a} is independently hydrogen, halogen, C_{1-4} alkoxy unsubstituted or substituted by R^{1a1} , C_{1-4} alkyl unsubstituted or substituted by R^{1a1} , hydroxyl, amino or C_{1-4} alkylamino;

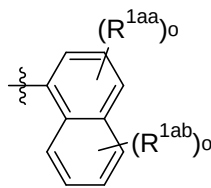
10 R^{1a1} is independently halogen or C_{1-4} alkyl;

R^{1a2} and R^{1a3} are independently hydrogen or C_{1-4} alkyl;

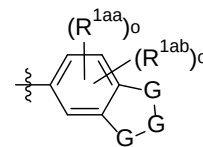
R^{1a4} is independently C_{1-4} alkyl, alkenyl, $-C(=O)NH_2$ substituted by one or two R^{1a1} , amide, C_{3-12} monocyclic or polycyclic heterocyclyl, or substituted C_{3-12} monocyclic or polycyclic heterocyclyl; the substituent in the substituted C_{3-12} monocyclic or polycyclic heterocyclyl is independently one or more substituents selected from R^{1a1} , $-OH$ and $=O$; when there are multiple substituents, then the substituents are the same or different.

2. The pyrimidine-fused compound, the pharmaceutically acceptable salt thereof,
20 or the solvate thereof, or the isotope-labeled compound as defined in claim 1, wherein,

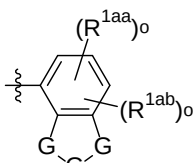


the naphthyl substituted by zero to four R^{1a} is , wherein o is independently 0, 1, 2, 3 or 4, and the total number of R^{1aa} and R^{1ab} is 0–4, the definitions

of R^{1aa} and R^{1ab} are the same as R^{1a};

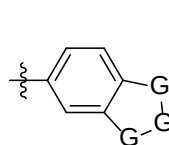


and/or, the benzoheterocyclyl substituted by zero to four R^{1a} is

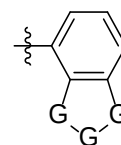


or , wherein G is independently a heteroatom or group selected from C, C(=O), N, S and O; o is 0, 1, 2, 3 or 4, and the total number of R^{1aa} and R^{1ab} is 0–4, the

- 5 definitions of R^{1aa} and R^{1ab} are the same as R^{1a};
benzoheterocyclyl;



or



is the

and/or, in the C_{1–8} alkyl unsubstituted or substituted by R^{1c} and C_{1–8} haloalkyl unsubstituted or substituted by R^{1c}, the C_{1–8} alkyl in the C_{1–8} alkyl and C_{1–8} haloalkyl is
10 independently methyl, ethyl, *n*-propyl, isopropyl, *n*-butyl, *tert*-butyl, *sec*-butyl, isobutyl, *n*-pentyl, 1-ethylpropyl, 1-methylbutyl, 2-methyl-1-butyl, 3-methyl-1-butyl, neopentyl, 3-methyl-2-butyl, *tert*-amyl, *n*-hexyl or isohexyl;

and/or, in the C_{1–8} haloalkyl unsubstituted or substituted by R^{1c}, the halogen in the C_{1–8} haloalkyl is fluorine, chlorine, bromine or iodine;

- 15 and/or, in the C_{1–8} haloalkyl unsubstituted or substituted by R^{1c}, the number of the halogen in the C_{1–8} haloalkyl is 1, 2, 3, 4, 5 or 6;

and/or, in the C_{1–4} alkyl unsubstituted or substituted by R^{1a1}, the C_{1–4} alkyl is methyl, ethyl, *n*-propyl, isopropyl, *n*-butyl, isobutyl, *sec*-butyl or *tert*-butyl;

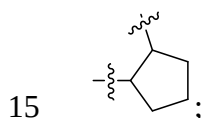
and/or, when R^4 and/or R^5 are aryl, then the aryl is C_6 – C_{10} aryl;

and/or, when R^4 and/or R^5 are C_{1-4} alkyl, amino substituted by C_{1-4} alkyl, or amino substituted by $-O-C_{1-4}$ alkyl, then the C_{1-4} alkyl is methyl, ethyl, *n*-propyl, isopropyl, *n*-butyl, isobutyl, *sec*-butyl or *tert*-butyl;

5 and/or, when R^4 and/or R^5 are C_{1-4} alkoxy, then the C_{1-4} alkoxy is methyloxy, ethyloxy, *n*-propyloxy, isopropyloxy, *n*-butyloxy, isobutyloxy, *sec*-butyloxy or *tert*-butyloxy;

and/or, when R^4 and R^5 together with Y form 3- to 7- membered heterocycloalkyl substituted by zero to three R^{4a} , then the 3- to 7- membered heterocycloalkyl is 5- to 6-
10 membered heterocycloalkyl; in the 5- to 6- membered heterocycloalkyl, the heteroatom is selected from one or more of N, O and S, and the number of the heteroatom is 1–2;

and/or, when any two adjacent groups of R^{2a} , R^{2b} , R^{3a} , R^{3b} , R^4 and R^5 , together with the carbon atom and Y to which they are attached, form 3- to 7- membered cycloalkyl substituted by zero to three R^{4a} , then the 3- to 7- membered cycloalkyl is



and/or, when one or more of R^{1a} , R^{1a1} , and R^{4a} is independently halogen, then the halogen is fluorine, chlorine, bromine or iodine;

and/or, in the C_{1-4} alkoxy unsubstituted or substituted by R^{1a1} , the C_{1-4} alkoxy is methyloxy, ethyloxy, *n*-propyloxy, isopropyloxy, *n*-butyloxy, isobutyloxy, *sec*-butyloxy
20 or *tert*-butyloxy;

and/or, in the C_{3-8} cycloalkyl unsubstituted or substituted by R^{1a1} , the C_{3-8} cycloalkyl is cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, cycloheptyl or cyclooctyl;

and/or, when one or more of R^{1a1} , R^{1a2} , R^{1a3} and R^{1a4} is independently C_{1-4} alkyl, then the C_{1-4} alkyl is methyl, ethyl, *n*-propyl, isopropyl, *n*-butyl, isobutyl, *sec*-butyl or *tert*-butyl;

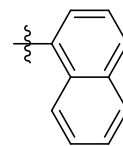
and/or, when R^{4a} is C_{1-4} alkylamino, then the C_{1-4} alkyl is methyl, ethyl, *n*-propyl, isopropyl, *n*-butyl, isobutyl, *sec*-butyl or *tert*-butyl;

and/or, the alkenyl is C_2-C_{10} alkenyl;

and/or, the amide is $-C(=O)NH_2$ or $-NHC(=O)H$;

and/or, in the C_{3-12} monocyclic or polycyclic heterocyclyl, or the C_{3-12} monocyclic or polycyclic heterocyclyl contained in the substituted C_{3-12} monocyclic or polycyclic heterocyclyl, the heteroatom is selected from one or more of N, O and S, and the number of the heteroatom is 1–4.

3. The pyrimidine-fused compound, the pharmaceutically acceptable salt thereof, or the solvate thereof, or the isotope-labeled compound as defined in claim 1 or 2,

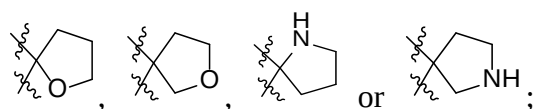


wherein, in the naphthyl substituted by zero to four R^{1a} , the naphthyl is ; and/or, in the benzoheterocyclyl substituted by zero to four R^{1a} , the benzoheterocyclyl is 2,3-dihydrobenzofuranyl or indolinyl;

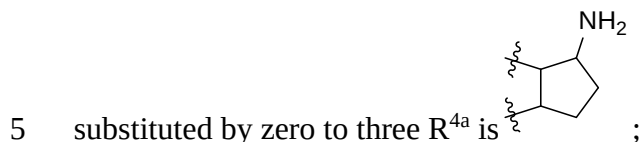
and/or, when R^4 and/or R^5 are aryl, then the aryl is phenyl or naphthyl;

and/or, the amino substituted by C_{1-4} alkyl in the definition of R^4 and R^5 , or the C_{1-4} alkylamino in the definition of R^{4a} , is $NH(CH_3)$;

and/or, when R^4 and R^5 together with Y form 3- to 7- membered heterocycloalkyl substituted by zero to three R^{4a} , then the 3- to 7- membered heterocycloalkyl is



and/or, in the 3- to 7- membered cycloalkyl substituted by zero to three R^{4a} formed by any two adjacent groups of R^{2a} , R^{2b} , R^{3a} , R^{3b} , R^4 and R^5 together with the carbon atom and Y to which they are attached, the 3- to 7- membered cycloalkyl



and/or, the alkenyl is ethenyl, 1-propenyl, allyl, but-1-enyl, but-2-enyl, pent-1-enyl or pent-1,4-dienyl;

and/or, the $-C(=O)OR^{1a2}$ is $-C(=O)OCH_3$;

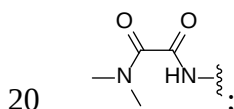
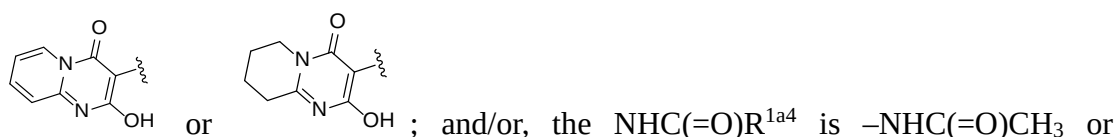
and/or, the $NR^{1a2}R^{1a3}$ is $-NH_2$ or $N(CH_3)$;

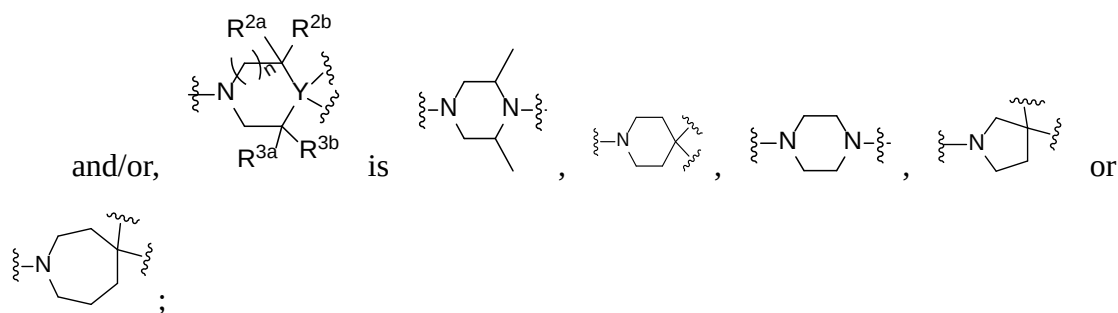
10 and/or, the $-C(=O)NH_2$ substituted by two R^{1a1} is $-C(=O)N(CH_3)_2$;

and/or, the C_{3-12} monocyclic or polycyclic heterocyclyl, or the C_{3-12} monocyclic or polycyclic heterocyclyl contained in the substituted C_{3-12} monocyclic or polycyclic heterocyclyl, is monocyclic or bicyclic heterocyclyl, the heteroatom is selected from one or more of N, O and S, and the number of the heteroatom is 1–2.

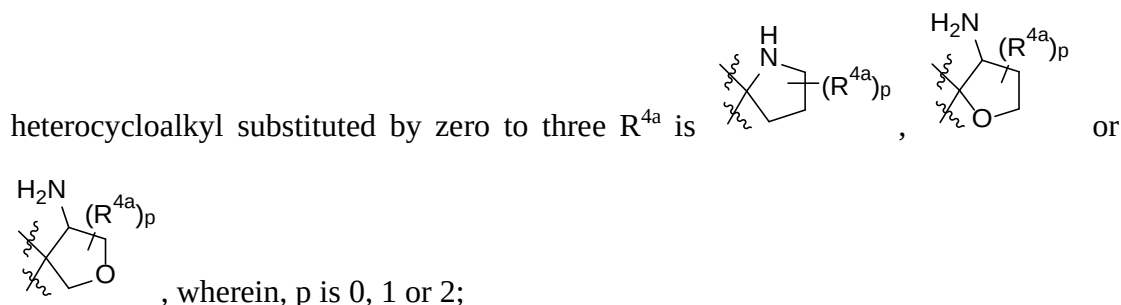
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4. The pyrimidine-fused compound, the pharmaceutically acceptable salt thereof, or the solvate thereof, or the isotope-labeled compound as defined in any one of claims 1 to 3, wherein, the substituted C_{3-12} monocyclic or polycyclic heterocyclyl is

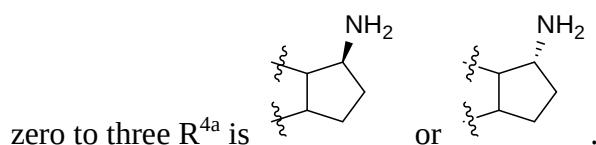




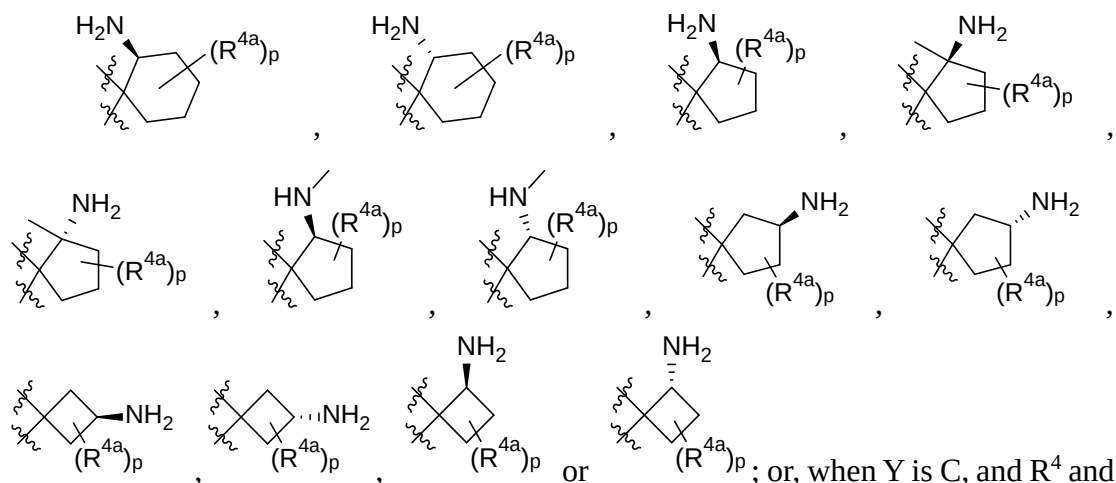
and/or, when Y is C, and R⁴ and R⁵ together with Y form 3- to 7- membered
 5 heterocycloalkyl substituted by zero to three R^{4a}, then the 3- to 7- membered



and/or, in the 3- to 7- membered cycloalkyl substituted by zero to three R^{4a} formed
 by any two adjacent groups of R^{2a}, R^{2b}, R^{3a}, R^{3b}, R⁴ and R⁵ together with the carbon
 10 atom and Y to which they are attached, the 3- to 7- membered cycloalkyl substituted by

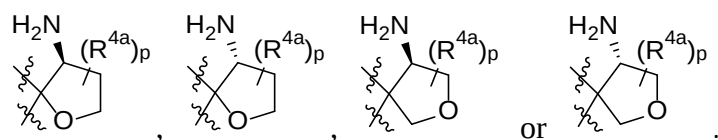


5. The pyrimidine-fused compound, the pharmaceutically acceptable salt thereof,
 or the solvate thereof, or the isotope-labeled compound as defined in any one of claims
 15 1 to 4, wherein, when Y is C, and R⁴ and R⁵ together with Y form 3- to 7- membered
 cycloalkyl substituted by zero to three R^{4a}, then the 3- to 7- membered cycloalkyl
 substituted by zero to three R^{4a} is



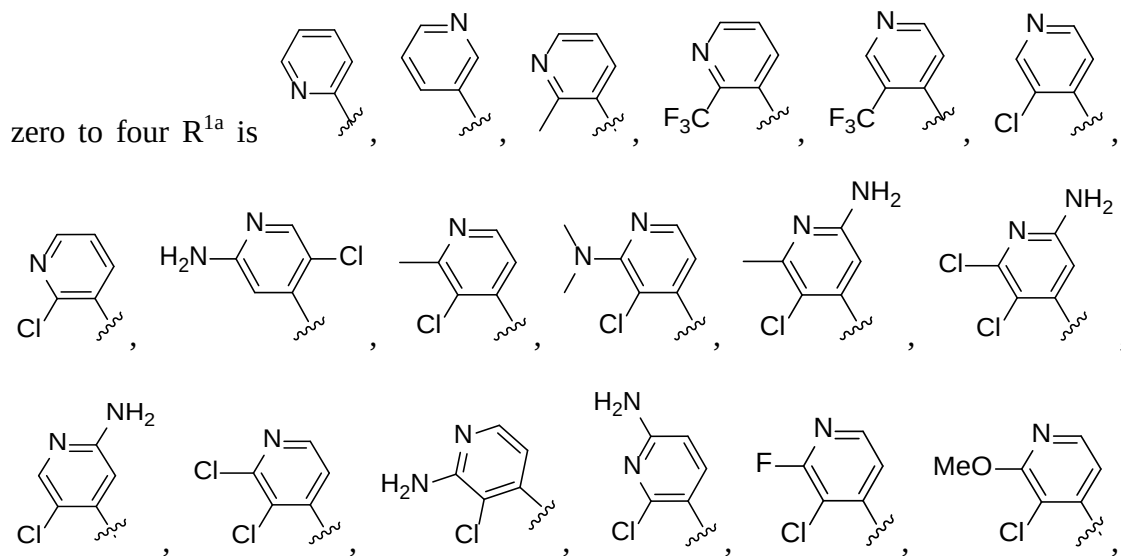
or, when Y is C, and R^4 and R^5 together with Y form 3- to 7- membered heterocycloalkyl substituted by zero to three

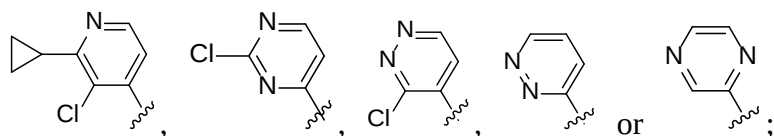
5 R^{4a} , then the 3- to 7- membered heterocycloalkyl substituted by zero to three R^{4a} is



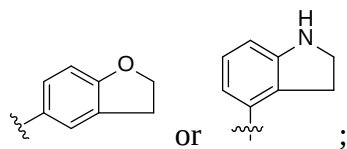
6. The pyrimidine-fused compound, the pharmaceutically acceptable salt thereof, or the solvate thereof, or the isotope-labeled compound as defined in any one of claims

10 1 to 4, wherein, the heteroaryl containing one to four nitrogen atoms and substituted by



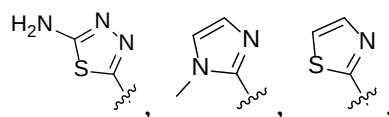
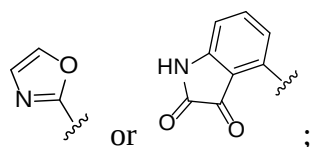


and/or, the benzoheterocyclyl unsubstituted or substituted by zero to four R^{1a} is

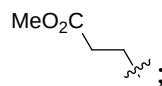


and/or, the heteroaryl containing one to four heteroatoms selected from N, NR^{1b} ,

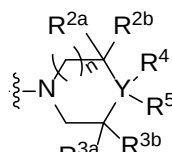
5 O and $S(O)_m$ and substituted by zero to four R^{1a} is



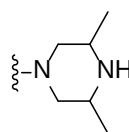
and/or, the C_{1-8} alkyl substituted by R^{1c} is



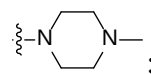
and/or, when Y is N, then



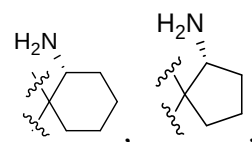
is



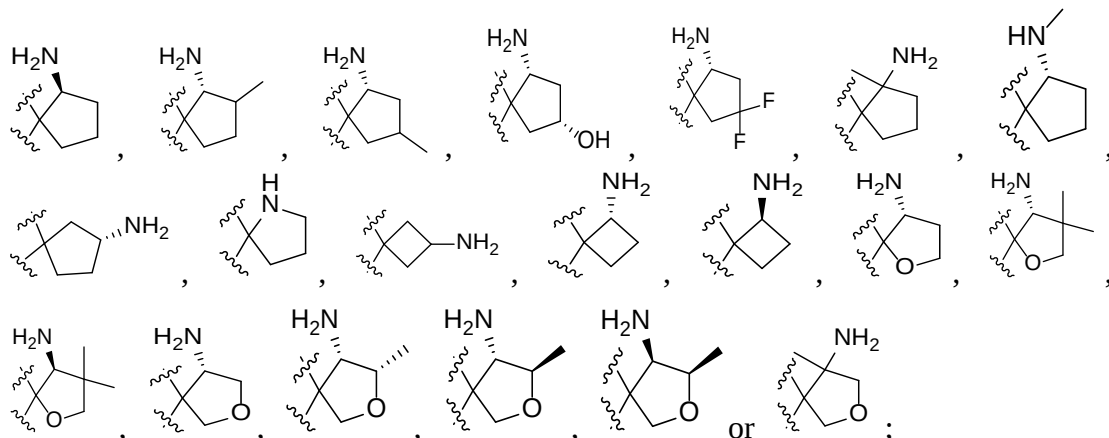
or



and/or, when Y is C, and R^4 and R^5 together with Y form



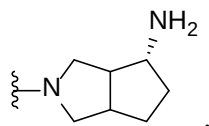
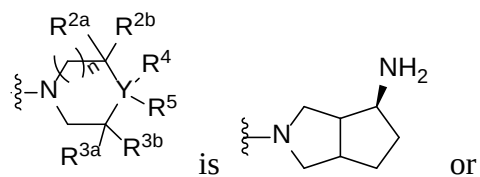
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and/or, when any two adjacent groups of R^{2a} , R^{2b} , R^{3a} , R^{3b} , R^4 and R^5 , together

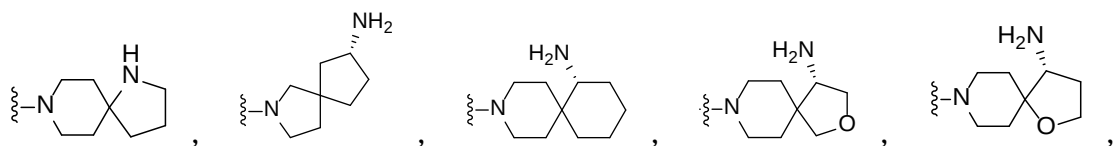
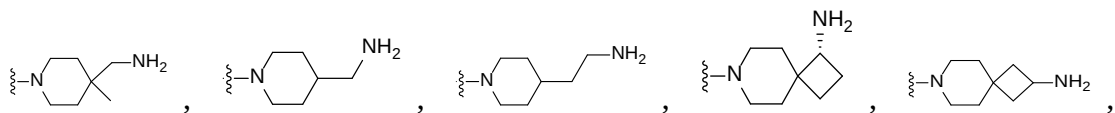
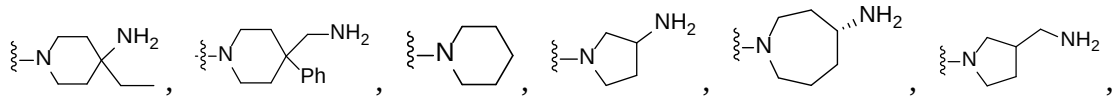
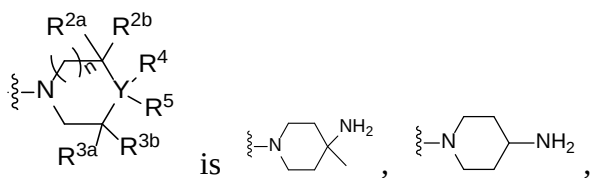
with the carbon atom and Y to which they are attached, form 3- to 7- membered

cycloalkyl substituted by zero to three R^{4a}, then

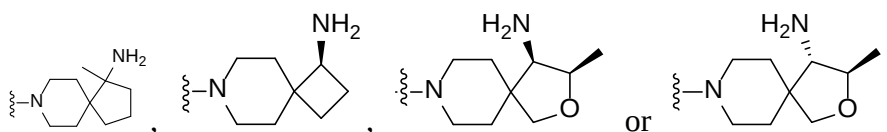
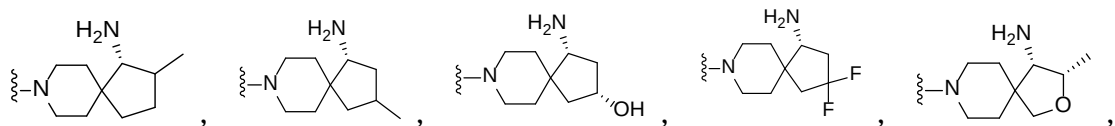
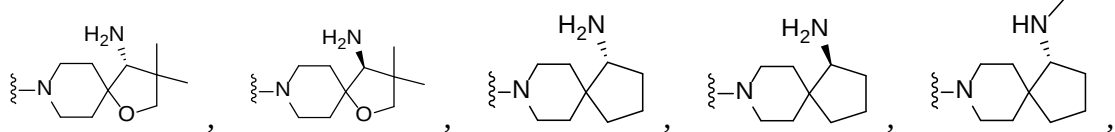


7. The pyrimidine-fused compound, the pharmaceutically acceptable salt thereof,
5 or the solvate thereof, or the isotope-labeled compound as defined in any one of claims

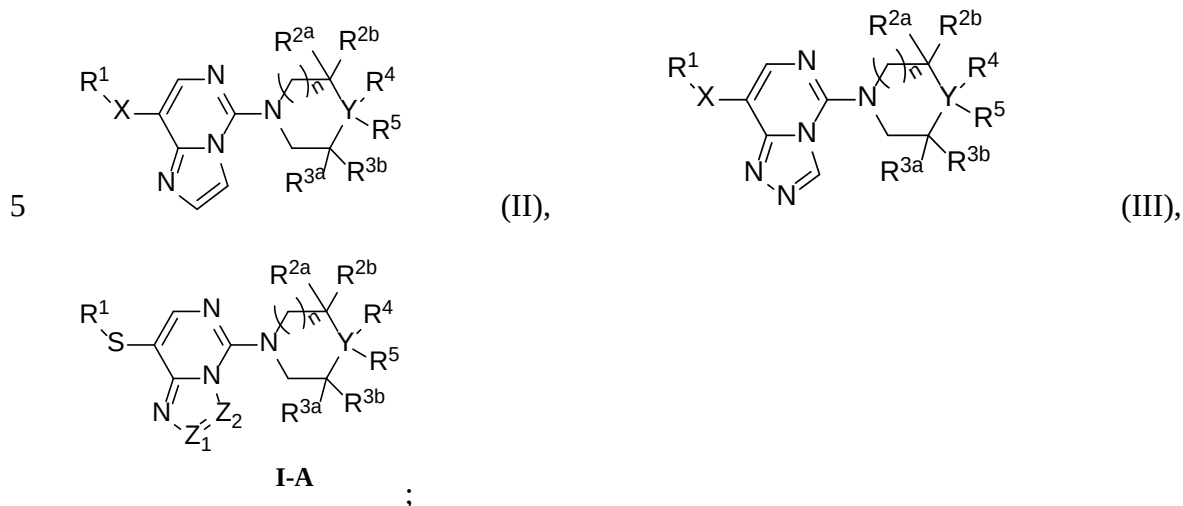
1 to 3, wherein, when Y is C, then



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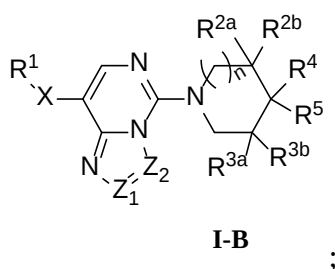


8. The pyrimidine-fused compound, the pharmaceutically acceptable salt thereof, or the solvate thereof, or the isotope-labeled compound as defined in claim 1, wherein, the pyrimidine-fused compound is represent by formula (II), formula (III), or formula (I-A),



wherein Z₁, Z₂, X, Y, n, R¹, R^{2a}, R^{2b}, R^{3a}, R^{3b}, R⁴ and R⁵ are as defined in any one of claims 1-7.

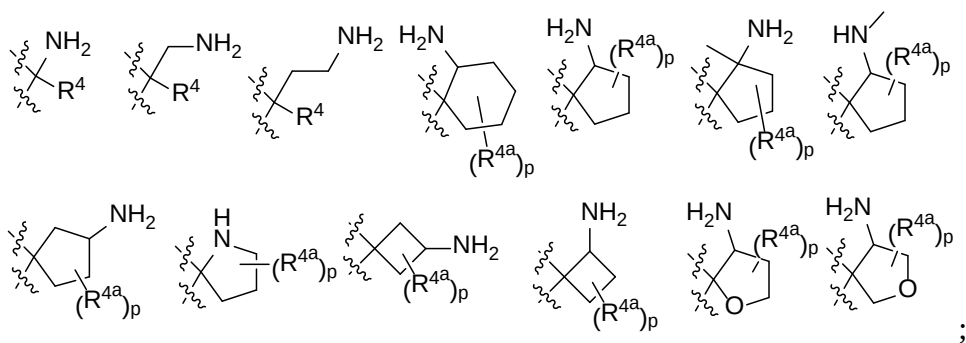
10 9. A pyrimidine-fused compound represented by formula I-B, a pharmaceutically acceptable salt thereof, or a solvate thereof,

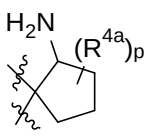
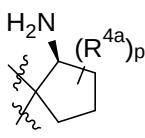
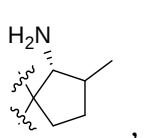
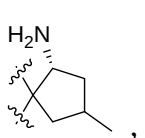


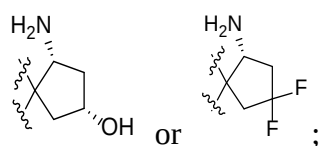
or an isotope-labeled compound of the pyrimidine-fused compound, the pharmaceutically acceptable salt, or the solvate, wherein the isotope is selected from

15 ²H, ³H, ¹¹C, ¹³C, ¹⁴C, ¹⁵N, ¹⁸F, ³¹P, ³²P, ³⁵S, ³⁶Cl, and ¹²⁵I;

in formula (I-B), R⁴ and R⁵ together with the carbon atom to which they are attached form



wherein the moiety  is , , ,

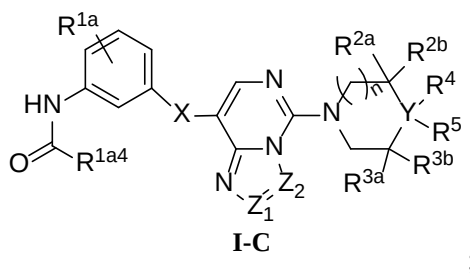


p is 0 or 1;

- 5 R^4 is independently hydrogen, aryl, C_{1-4} alkyl, C_{1-4} alkoxy, amino, amino substituted by C_{1-4} alkyl or amino substituted by $-O-C_{1-4}$ alkyl;

Z_1 , Z_2 , X, n, R^1 , R^{2a} , R^{2b} , R^{3a} , R^{3b} , and R^{4a} are as defined in any one of claims 1-7.

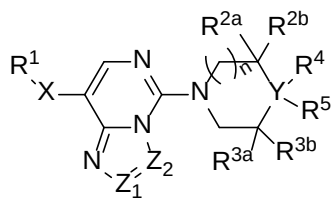
10. A pyrimidine-fused compound represented by formula I-C, a pharmaceutically acceptable salt thereof, or a solvate thereof,



or an isotope-labeled compound of the pyrimidine-fused compound, the pharmaceutically acceptable salt, or the solvate, wherein the isotope is selected from ^2H , ^3H , ^{11}C , ^{13}C , ^{14}C , ^{15}N , ^{18}F , ^{31}P , ^{32}P , ^{35}S , ^{36}Cl , and ^{125}I ;

- 15 Z_1 , Z_2 , X, n, Y, R^{1a} , R^{1a4} , R^{2a} , R^{2b} , R^{3a} , R^{3b} , R^4 and R^5 are as defined in any one of claims 1-7.

11. A pyrimidine-fused compound represented by formula (I), a pharmaceutically



acceptable salt thereof, or a solvate thereof, (I),

or an isotope-labeled compound of the pyrimidine-fused compound, the pharmaceutically acceptable salt, or the solvate, wherein the isotope is selected from ^2H , ^3H , ^{11}C , ^{13}C , ^{14}C , ^{15}N , ^{18}F , ^{31}P , ^{32}P , ^{35}S , ^{36}Cl , and ^{125}I ;

5 wherein, in the pyrimidine-fused compound represented by formula (I), Z_1 and Z_2 are both C, or one of them is N;

X is independently S or absent;

Y is independently C or N;

n is independently 0, 1 or 2;

10 R^1 is independently phenyl substituted by zero to four R^{1a} , heteroaryl containing one to four nitrogen atoms and substituted by zero to four R^{1a} , naphthyl substituted by zero to four R^{1a} , heteronaphthyl containing one to four nitrogen atoms and substituted by zero to four R^{1a} , benzoheterocyclyl substituted by zero to four R^{1a} , fused heteroaryl containing one to four nitrogen atoms and substituted by zero to four R^{1a} , heteroaryl
15 containing one to four heteroatoms selected from N, NR^{1b} , O and $\text{S}(\text{O})_m$, and substituted by zero to four R^{1a} , C_{1-8} alkyl unsubstituted or substituted by R^{1c} , or C_{1-8} haloalkyl unsubstituted or substituted by R^{1c} ; wherein m is 0, 1 or 2; R^{1a} is independently halogen, C_{1-4} alkoxy unsubstituted or substituted by R^{1a1} , C_{1-4} alkyl unsubstituted or substituted by R^{1a1} , trifluoromethyl, $\text{C}(=\text{O})\text{OR}^{1a2}$, $\text{NR}^{1a2}\text{R}^{1a3}$, $\text{NHC}(=\text{O})\text{R}^{1a4}$, or C_{3-8} cycloalkyl
20 unsubstituted or substituted by R^{1a1} ; R^{1a1} is independently halogen or C_{1-4} alkyl; R^{1a2} is hydrogen or C_{1-4} alkyl; R^{1a3} is C_{1-4} alkyl; R^{1a4} is independently C_{1-4} alkyl, alkenyl, amide, or C_{3-12} monocyclic or polycyclic heterocyclyl;

R^{1b} is independently hydrogen, or C_{1-4} alkyl unsubstituted or substituted by R^{1a1} ;

R^{1c} is independently hydrogen, $-C(=O)OR^{1a2}$, or C_{1-4} alkyl unsubstituted or substituted by R^{1a1} ;

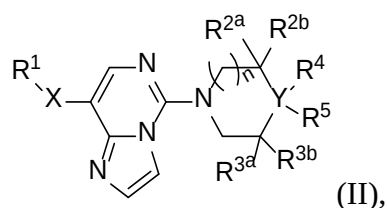
R^{2a} , R^{2b} , R^{3a} and R^{3b} are independently hydrogen, or C_{1-4} alkyl unsubstituted or substituted by R^{1a1} ;

when Y is N, then R^4 is independently hydrogen, or C_{1-4} alkyl unsubstituted or substituted by R^{1a1} ; and R_5 is absent;

when Y is C, then R^4 and R^5 are independently hydrogen, aryl, ethyl, C_{1-4} alkoxy, amino, amino substituted by C_{1-4} alkyl or amino substituted by $-O-C_{1-4}$ alkyl, or R^4 and R^5 together with Y form 3- to 7- membered saturated or partially unsaturated spiro ring substituted by zero to three R^{4a} , wherein the ring optionally contains one to three heteroatoms or groups independently selected from N, $C(=O)$ and/or O;

R^{4a} is independently hydrogen, halogen, C_{1-4} alkoxy unsubstituted or substituted by R^{1a1} , C_{1-4} alkyl unsubstituted or substituted by R^{1a1} , hydroxyl, amino or C_{1-4} alkylamino.

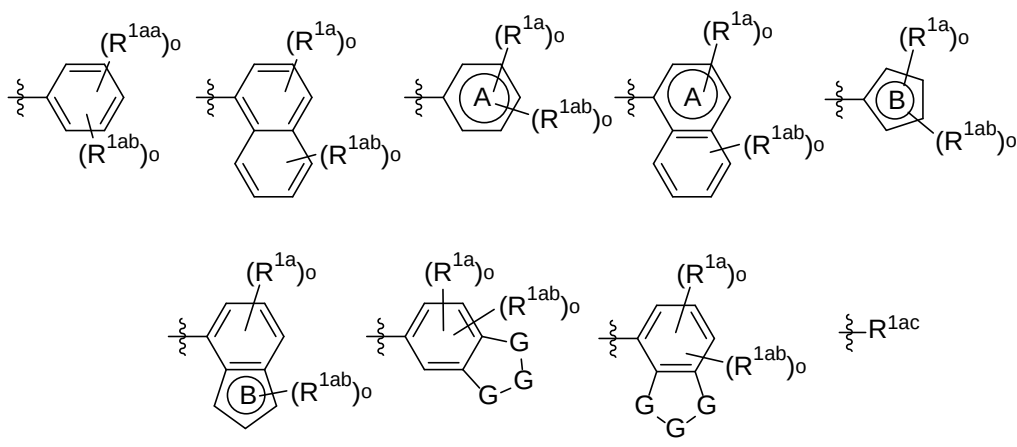
12. The pyrimidine-fused compound, the pharmaceutically acceptable salt thereof, or the solvate thereof, or the isotope-labeled compound as defined in claim 11, wherein, the pyrimidine-fused compound is represent by formula (II),



13. The pyrimidine-fused compound, the pharmaceutically acceptable salt thereof,

or the solvate thereof, or the isotope-labeled compound as defined in claim 11 or 12,

wherein, R^1 is selected from



wherein, o is 0, 1, 2, 3 or 4; ring A is heteroaryl containing one to four nitrogen

atoms; ring B is heteroaryl containing one to four heteroatoms selected from N, S and

O; G is independently a heteroatom or group selected from C, C(=O), N, S and O; the

definitions of R^{1aa} and R^{1ab} are independently the same as R^{1a} as defined in claim 11;

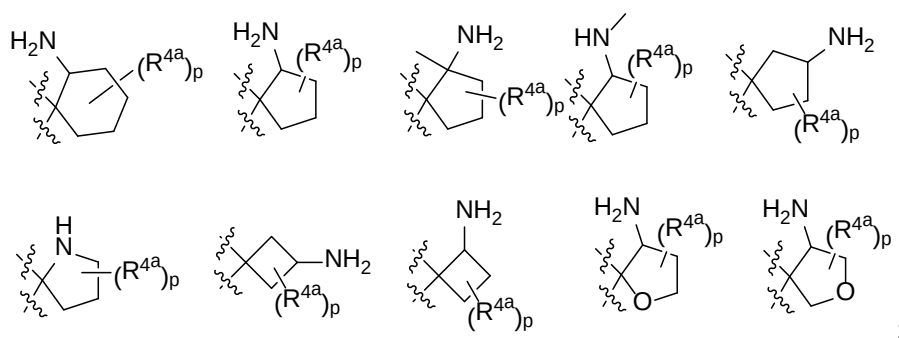
R^{1ac} is independently C_{1-8} alkyl unsubstituted or substituted by R^{1c} , or C_{1-8} haloalkyl unsubstituted or substituted by R^{1c} ;

and/or, R^{2a} , R^{2b} , R^{3a} and R^{3b} are independently hydrogen or methyl;

and/or, when Y is N, then R^4 is independently hydrogen or methyl; and R_5 is absent;

and/or, when Y is C, then R^4 and R^5 are independently hydrogen, ethyl, phenyl, amino, methylamino or ethylamino;

and/or, when Y is C, then R^4 and R^5 together with Y form

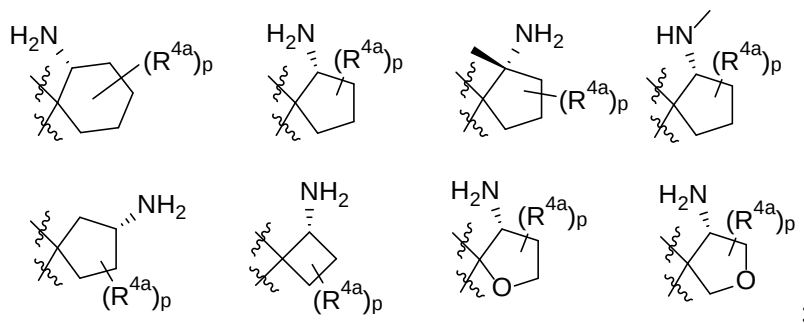


15

wherein, p is 0 or 1; R^{4a} is as defined in claim 11.

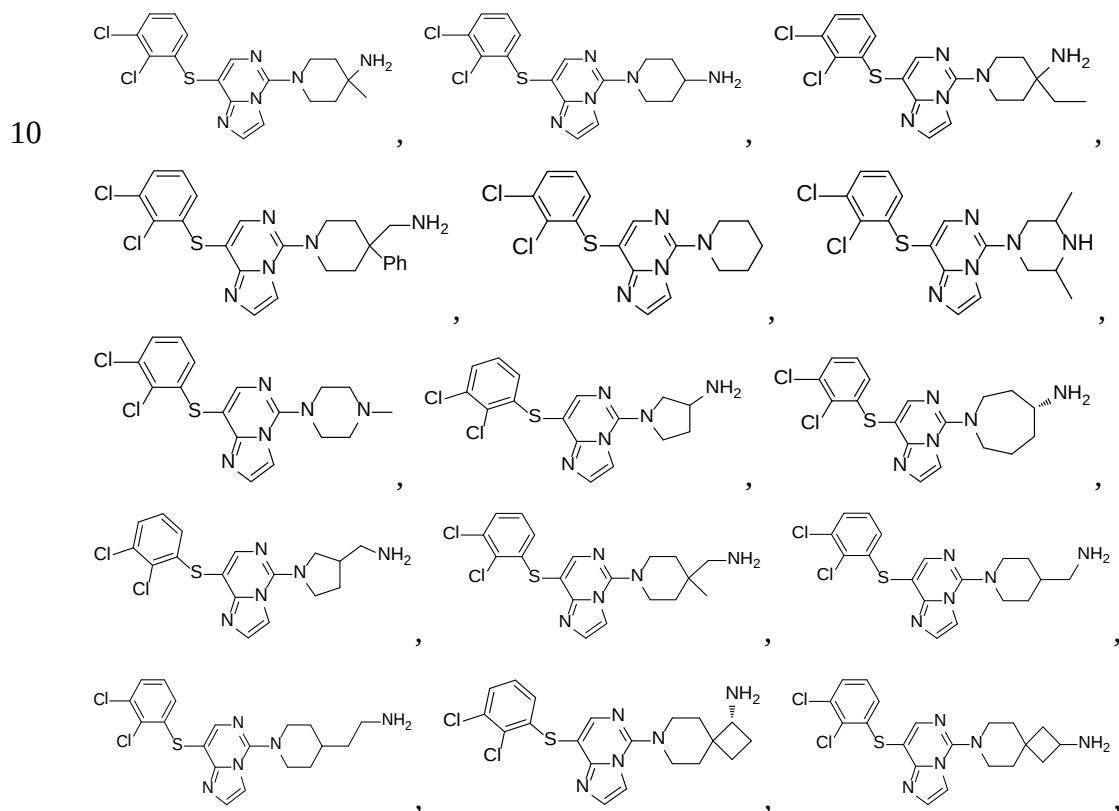
14. The pyrimidine-fused compound, the pharmaceutically acceptable salt thereof, or the solvate thereof, or the isotope-labeled compound as defined in any one of claims

5 11-13, wherein, when Y is C, then R⁴ and R⁵ together with Y form

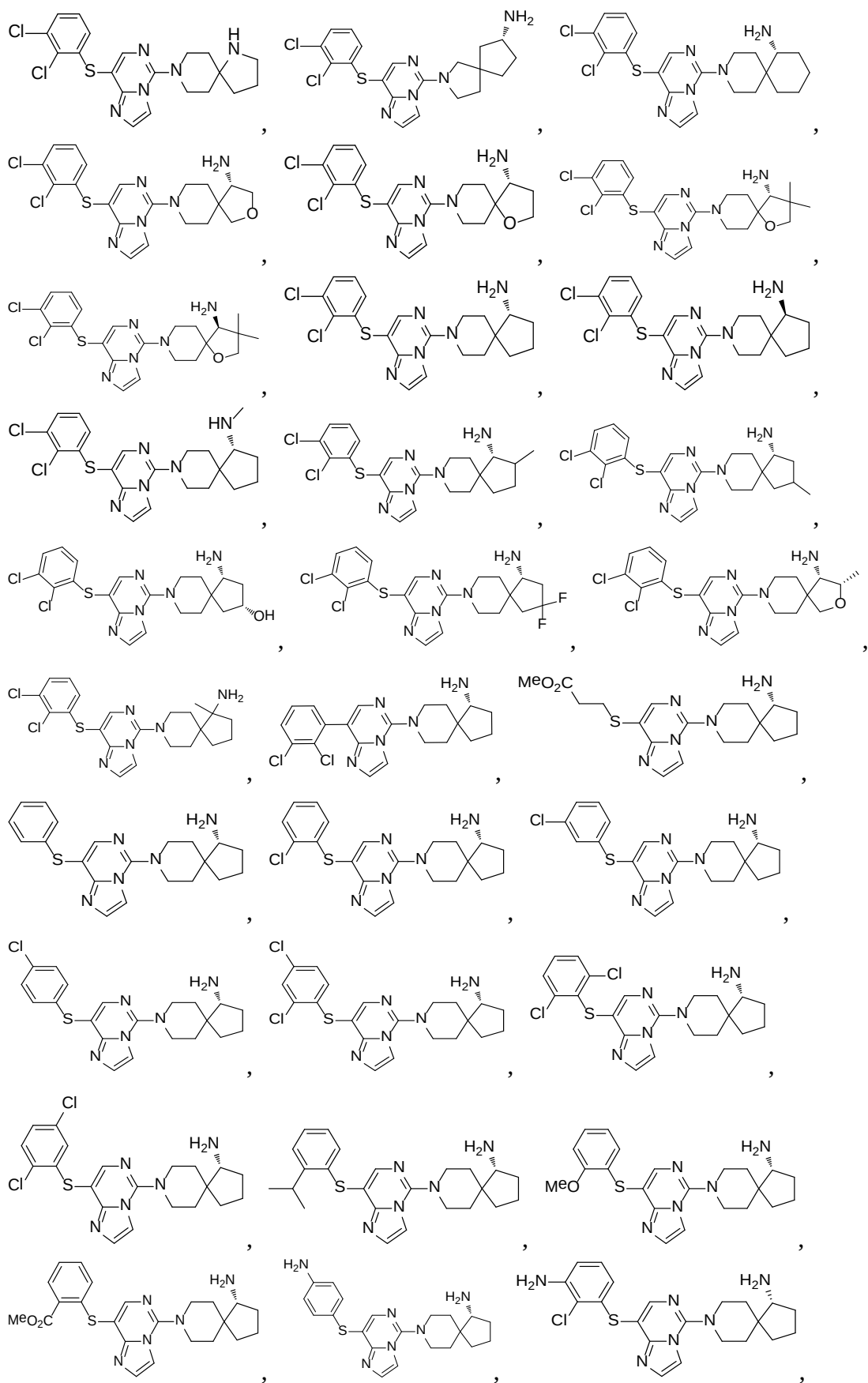


wherein, p is 0 or 1; R^{4a} is as defined in any one claims 11-13.

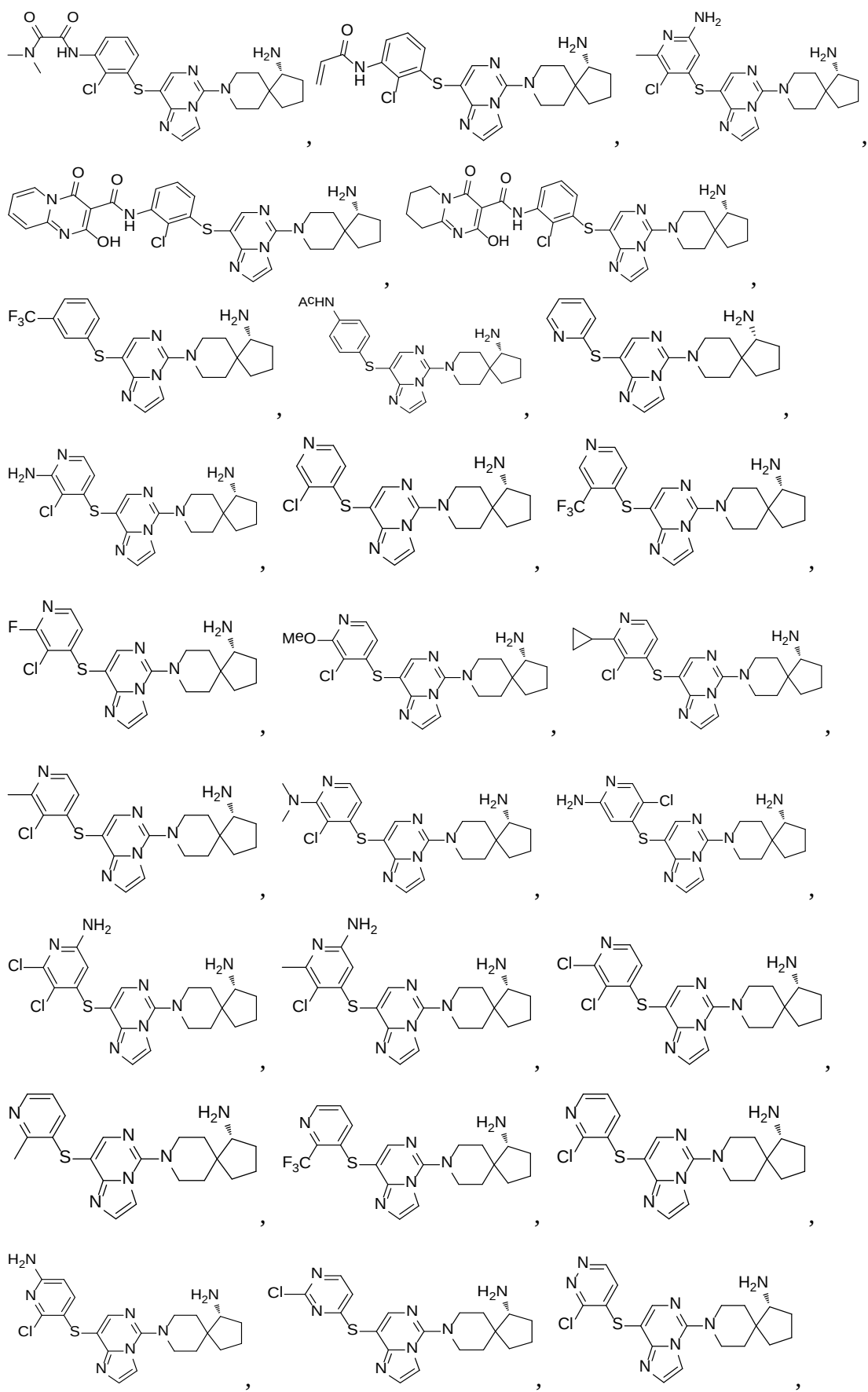
15. A pyrimidine-fused compound selected from



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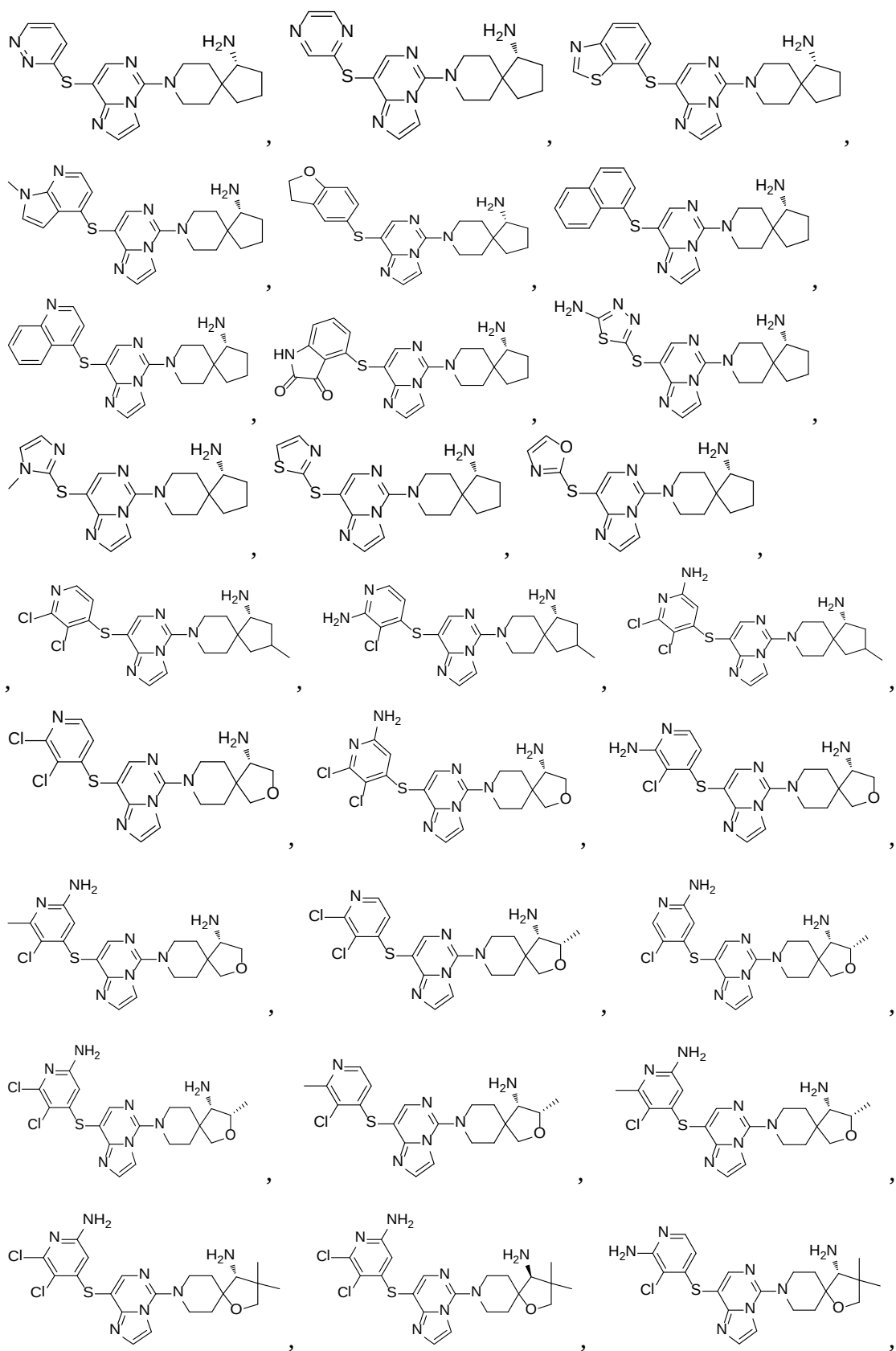


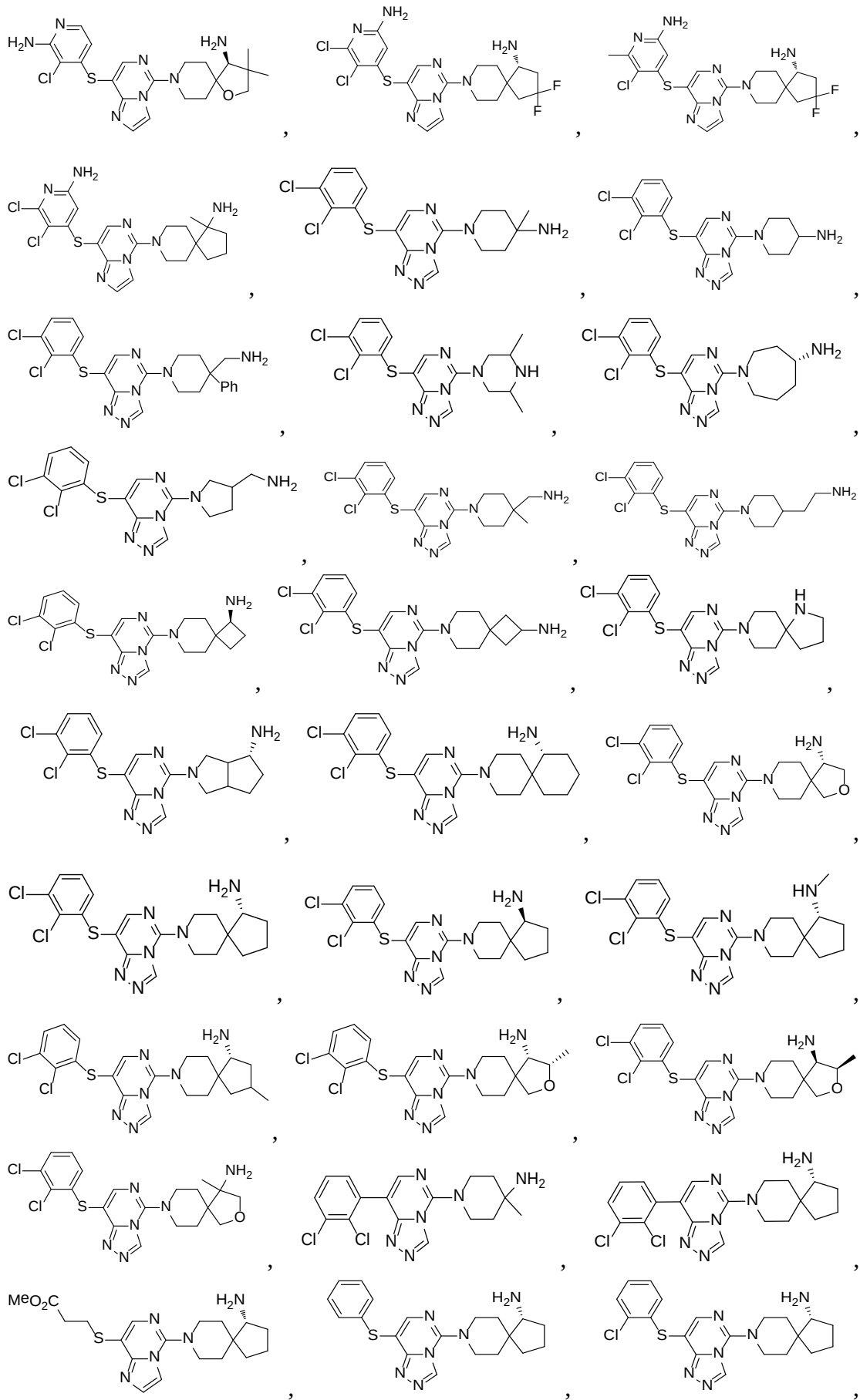
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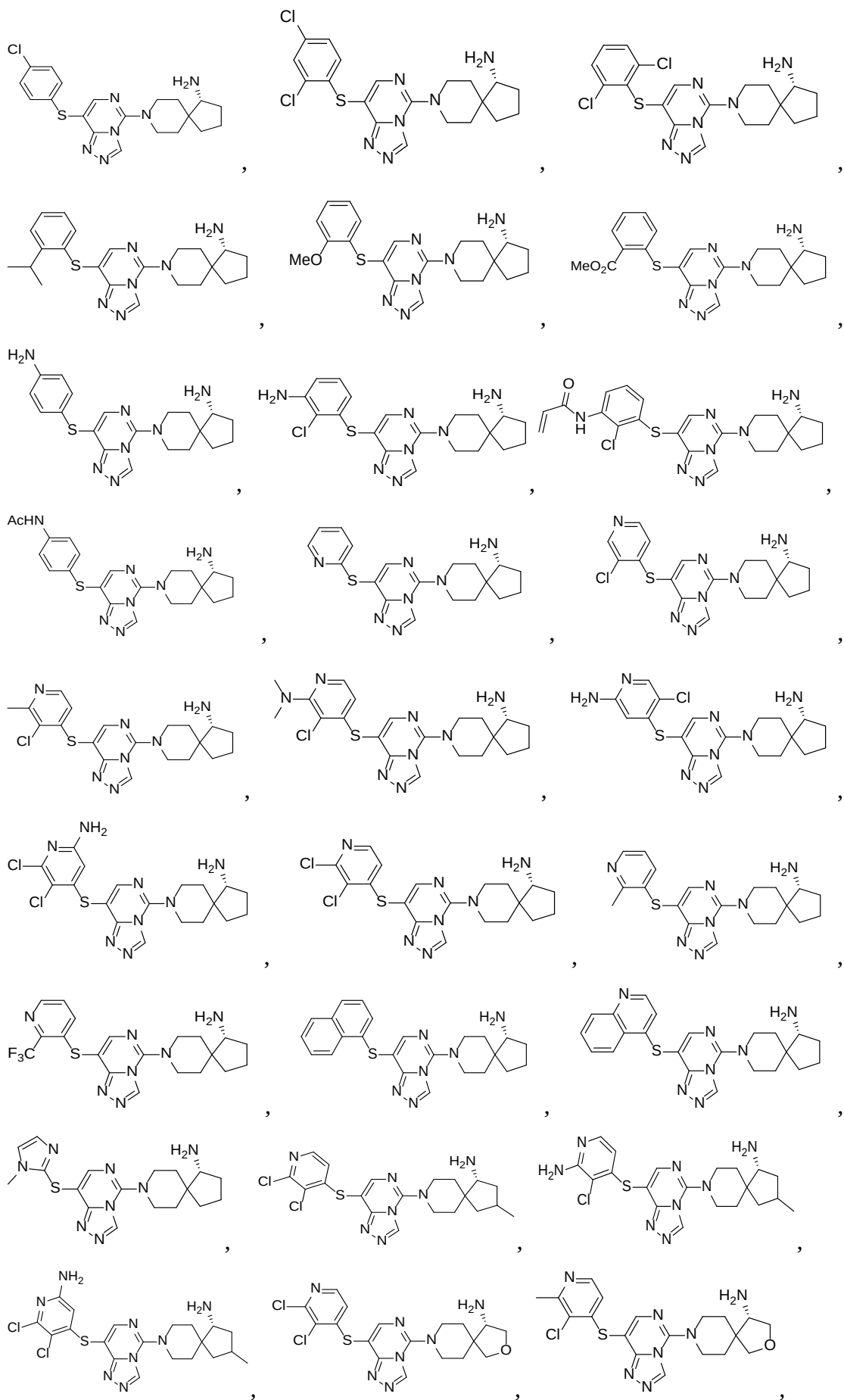


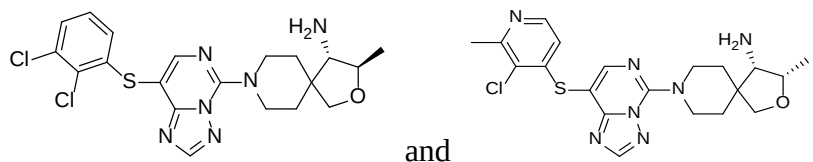
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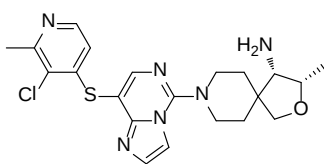


or a pharmaceutically acceptable salt thereof, or a solvate thereof,

or an isotope-labeled compound of the pyrimidine-fused compound, the pharmaceutically acceptable salt, or the solvate, wherein the isotope is selected from

5 ^2H , ^3H , ^{11}C , ^{13}C , ^{14}C , ^{15}N , ^{18}F , ^{35}S , and ^{36}Cl .

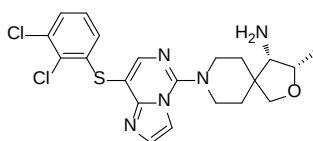
16. A pyrimidine-fused compound having a structure of:



or a pharmaceutically acceptable salt thereof.

10

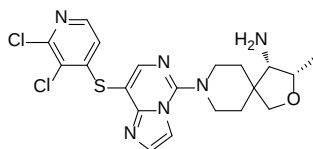
17. A pyrimidine-fused compound having a structure of:



or a pharmaceutically acceptable salt thereof.

15

18. A pyrimidine-fused compound having a structure of:



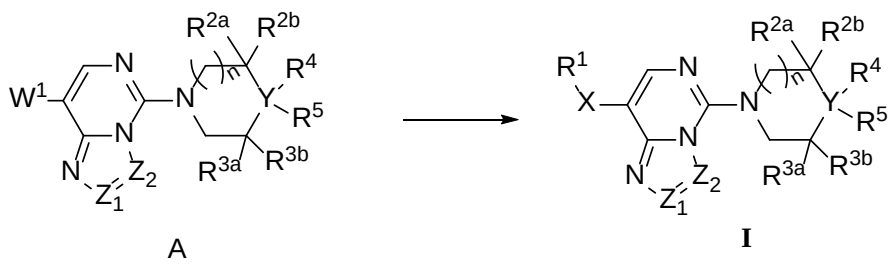
or a pharmaceutically acceptable salt thereof.

20

19. A preparation method of a pyrimidine-fused compound, wherein the preparation method comprises any one of the following schemes:

scheme 1 in the case the pyrimidine-fused compound is a pyrimidine-fused

compound represented by formula (I), comprising a step of conducting a coupling reaction of a halogenated intermediate compound represented by formula **A** with a compound **F** to obtain the pyrimidine-fused compound represented by formula (I), and the reaction equation is as shown below:



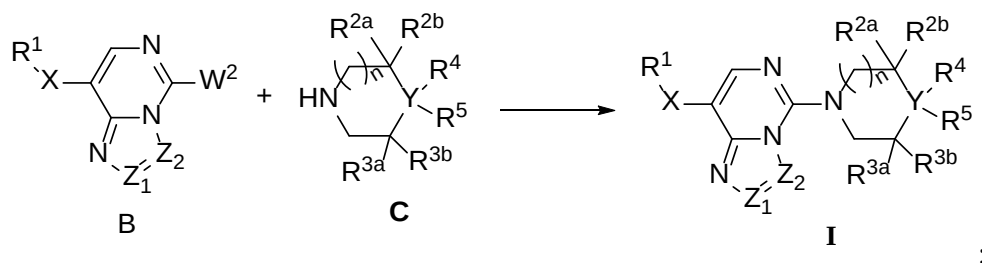
wherein, , X, Y, Z₁, Z₂, n, R¹, R^{2a}, R^{2b}, R^{3a}, R^{3b}, R⁴ and R⁵ are as defined in any one of claims 1-8 and 11-14; and

when X is absent, then the compound **F** is boronic acid, thiol or sodium thiolate of R¹; when X is S, then the compound **F** is thiol or sodium thiolate;

10 W¹ is halogen;

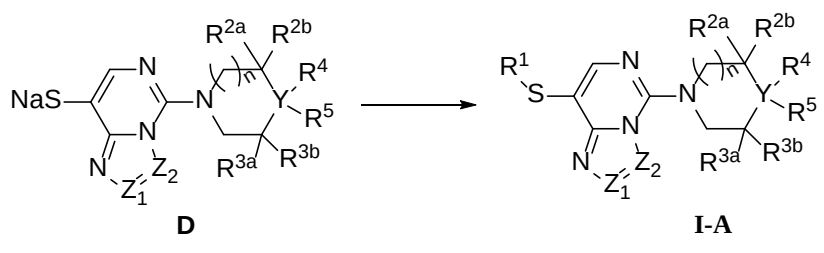
scheme 2 in the case the pyrimidine-fused compound is a pyrimidine-fused compound represented by formula (I), comprising a step of conducting a substitution reaction of an

intermediate represented by formula **B** with an amine represented by formula **C** to obtain the pyrimidine-fused compound represented by formula (**I**), and the reaction equation is as shown below:



5 wherein, W^2 is halogen; X , Y , Z_1 , Z_2 , n , R^1 , R^{2a} , R^{2b} , R^{3a} , R^{3b} , R^4 and R^5 are as defined in any one of claims 1-8 and 11-14;

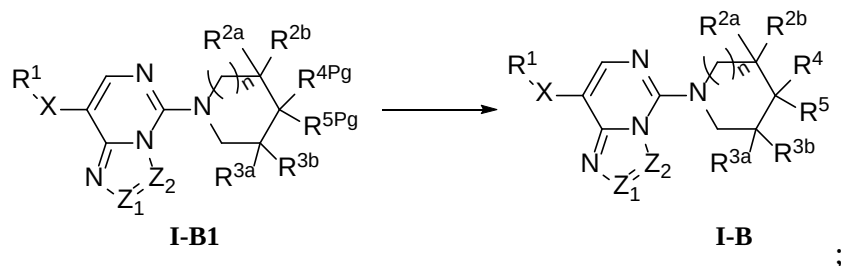
scheme 5 in the case the pyrimidine-fused compound is a pyrimidine-fused compound represented by formula (**I-A**), comprising a step of conducting a coupling reaction of sodium thiolate intermediate compound represented by formula **D** with a
10 halogenated compound R^1 - W^1 to obtain the pyrimidine-fused compound represented by formula (**I-A**), and the reaction equation is as shown below:



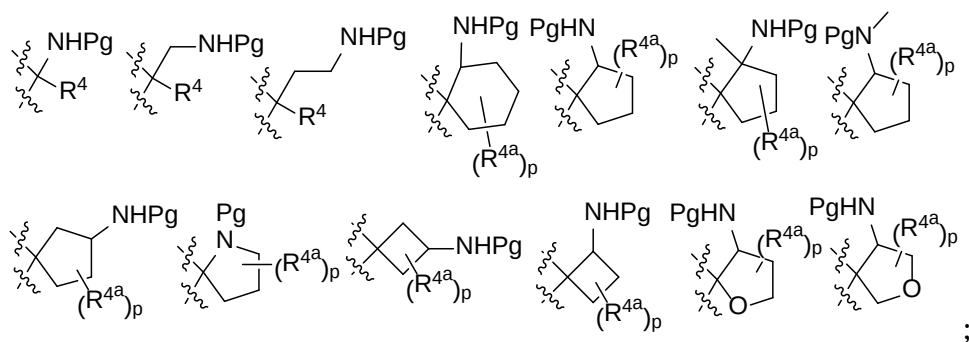
wherein W^1 is halogen; Y , Z_1 , Z_2 , n , R^1 , R^{2a} , R^{2b} , R^{3a} , R^{3b} , R^4 and R^5 are as defined in any one of claims 1-8 and 11-14.

15

20. A preparation method of a pyrimidine-fused compound represented by formula (**I-B**) as defined in claim 9, comprising a step of removing the amino protecting group Pg from an intermediate represented by formula **I-B1** under acidic or basic condition to obtain the pyrimidine-fused compound represented by formula (**I-B**), and
20 the reaction equation is as shown below:



wherein, R^{4Pg} and R^{5Pg} together with the carbon atom to which they are attached, form

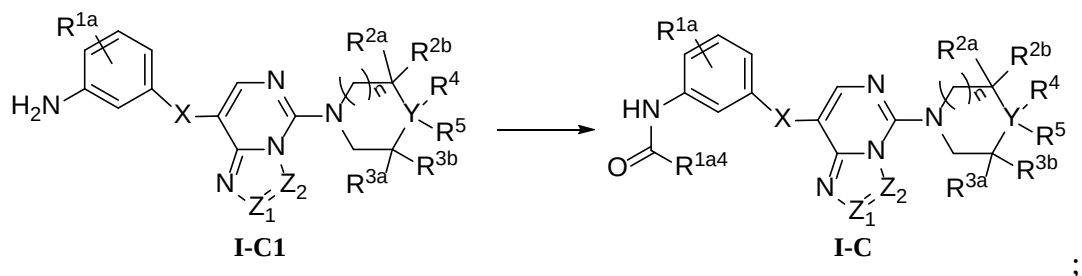


5 Pg is a protecting group selected from Boc, Ac and $S(=O)^tBu$;

p is 0, or 1;

X, Z_1 , Z_2 , n, R^1 , R^{2a} , R^{2b} , R^{3a} , R^{3b} , R^4 , R^{4a} and R^5 are as defined in claim 9.

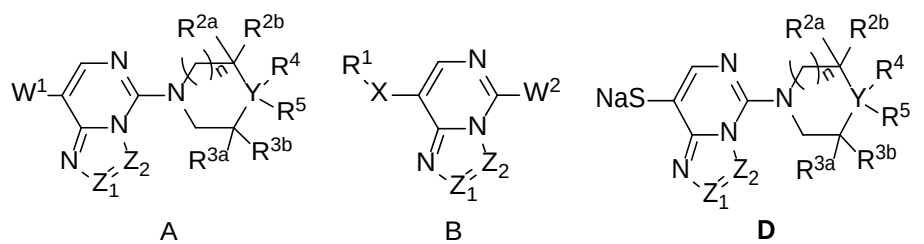
21. A preparation method of a pyrimidine-fused compound represented by formula 10 (**I-C**) as defined in claim 10, comprising a step of conducting an amidation reaction of an intermediate represented by formula **I-C1** to obtain the pyrimidine-fused compound represented by formula (**I-C**), and the reaction equation is as shown below:



wherein X, Y, Z_1 , Z_2 , n, R^{1a} , R^{1a4} , R^{2a} , R^{2b} , R^{3a} , R^{3b} , R^4 and R^5 are as defined in claim

15 10.

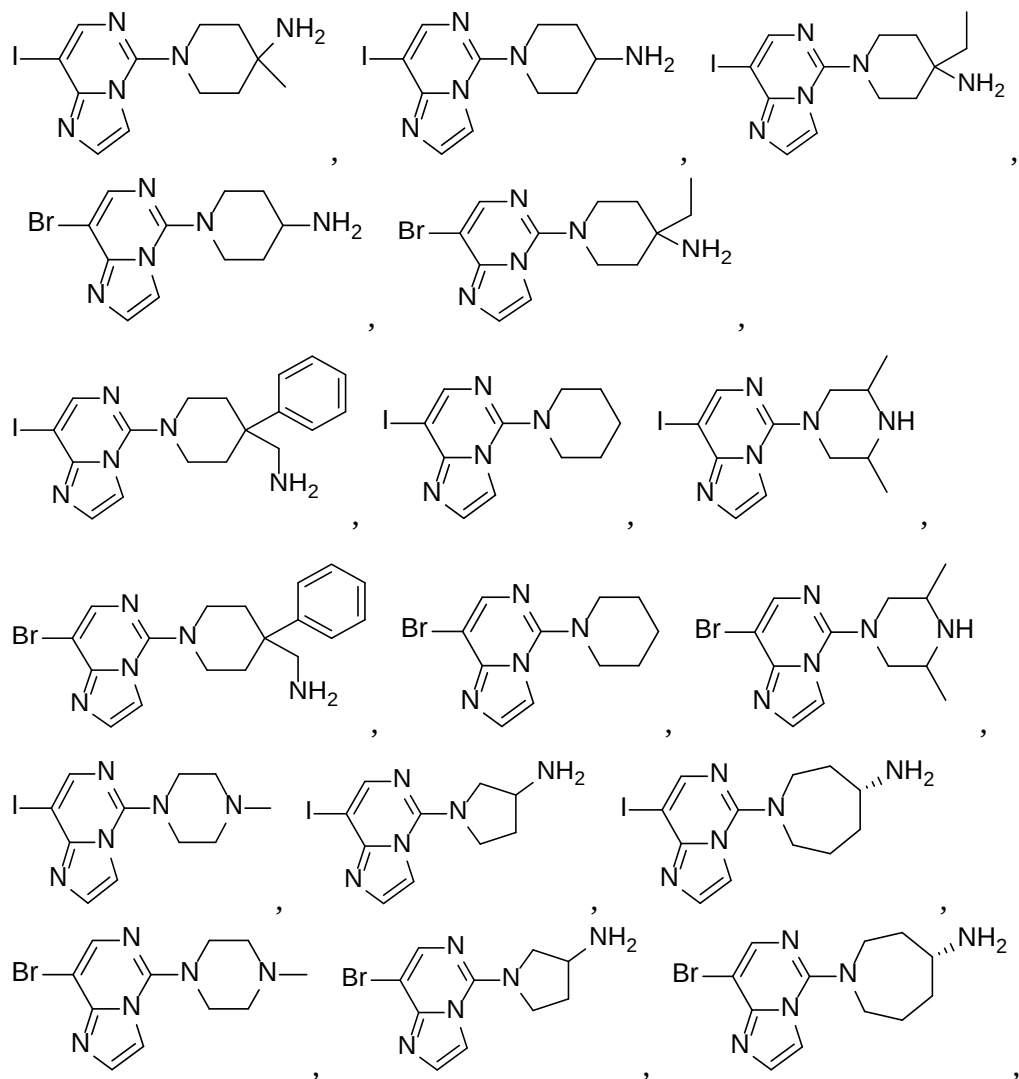
22. A compound represented by formula **A**, or **D**,



wherein, W^1 is I; W^2 is halogen; Z_1 , Z_2 , X, Y, n, R^1 , R^{2a} , R^{2b} , R^{3a} , R^{3b} , R^4 and R^5 are as defined in any one of claims 1 to 8 and 11 - 14.

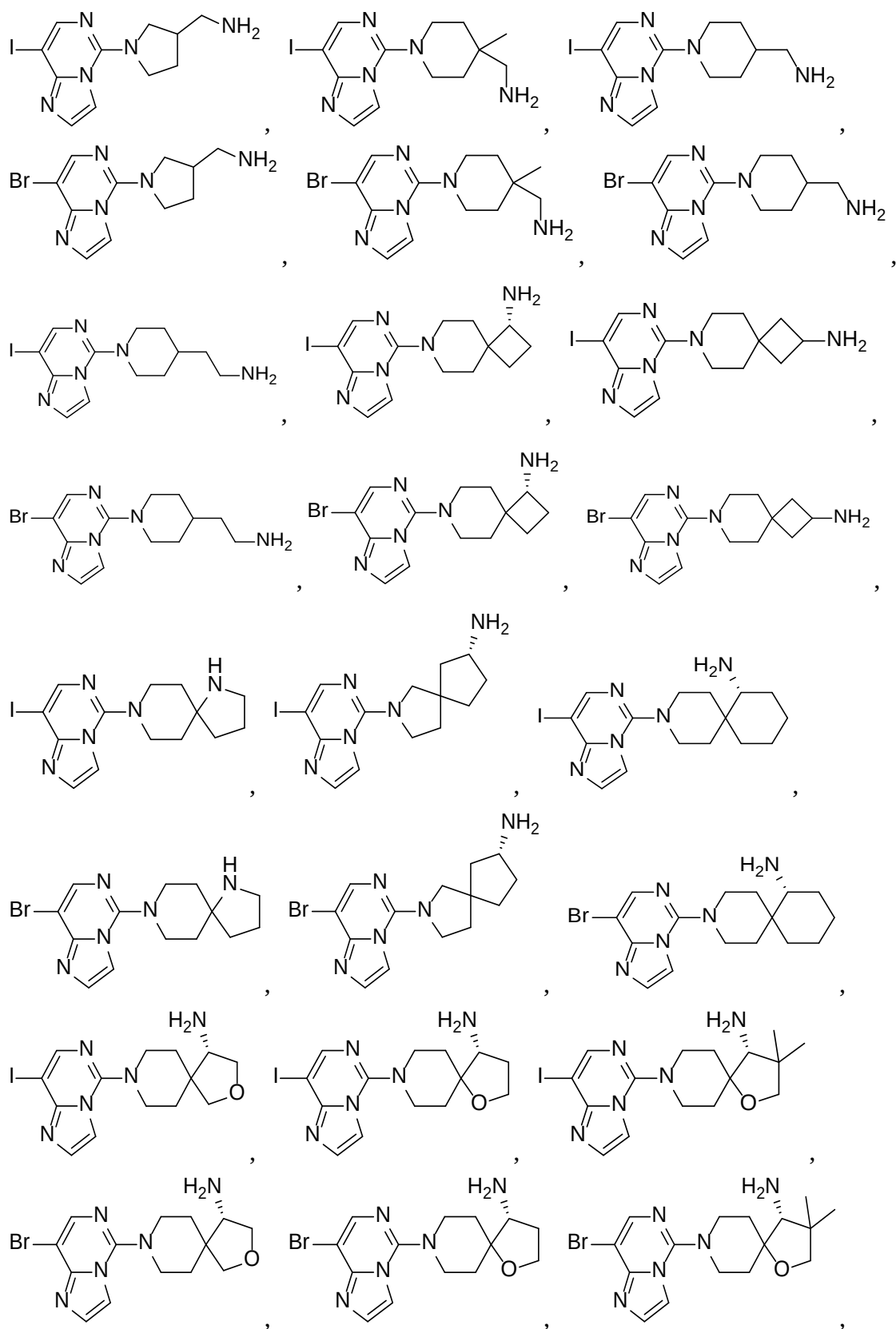
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23. A compound selected from

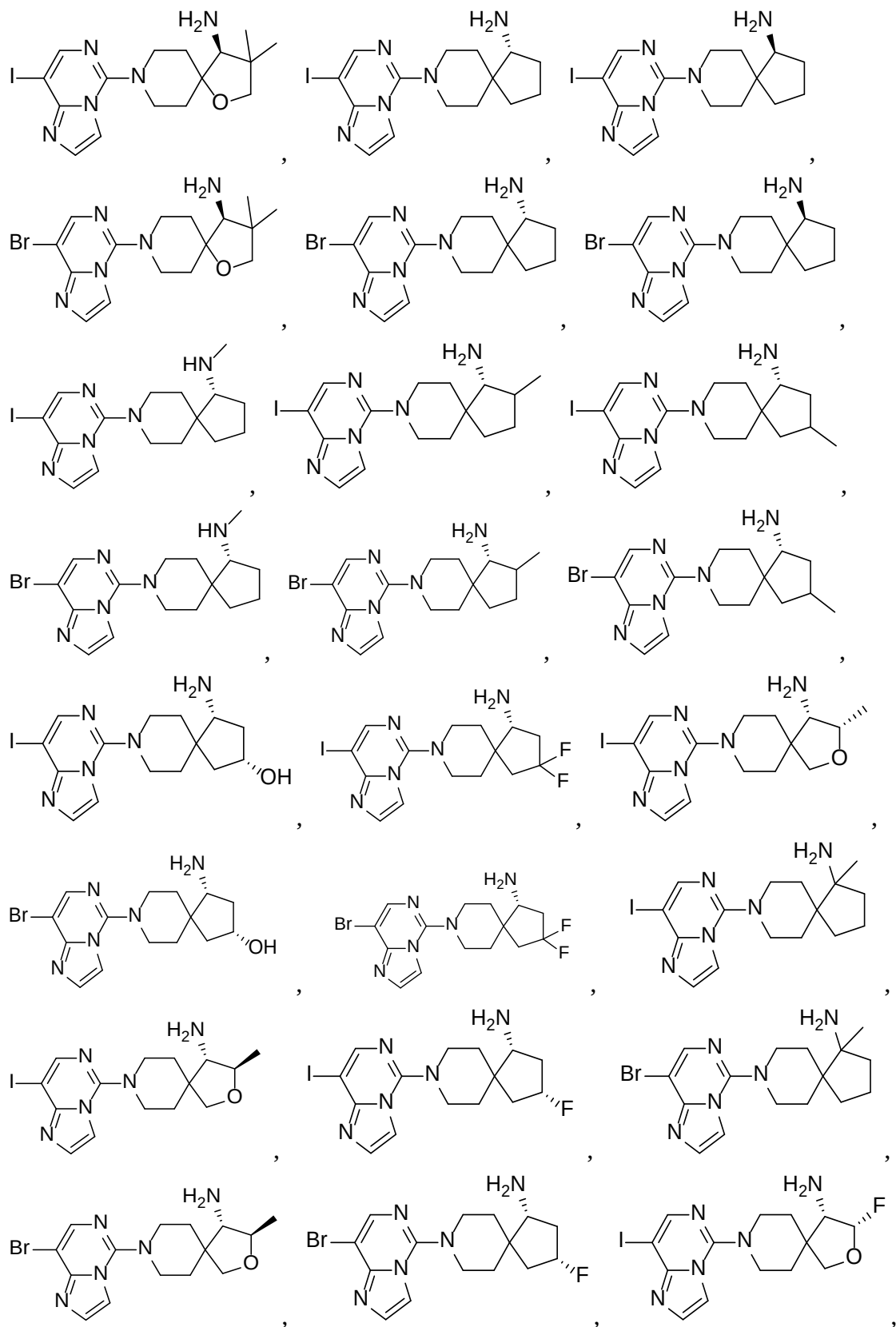


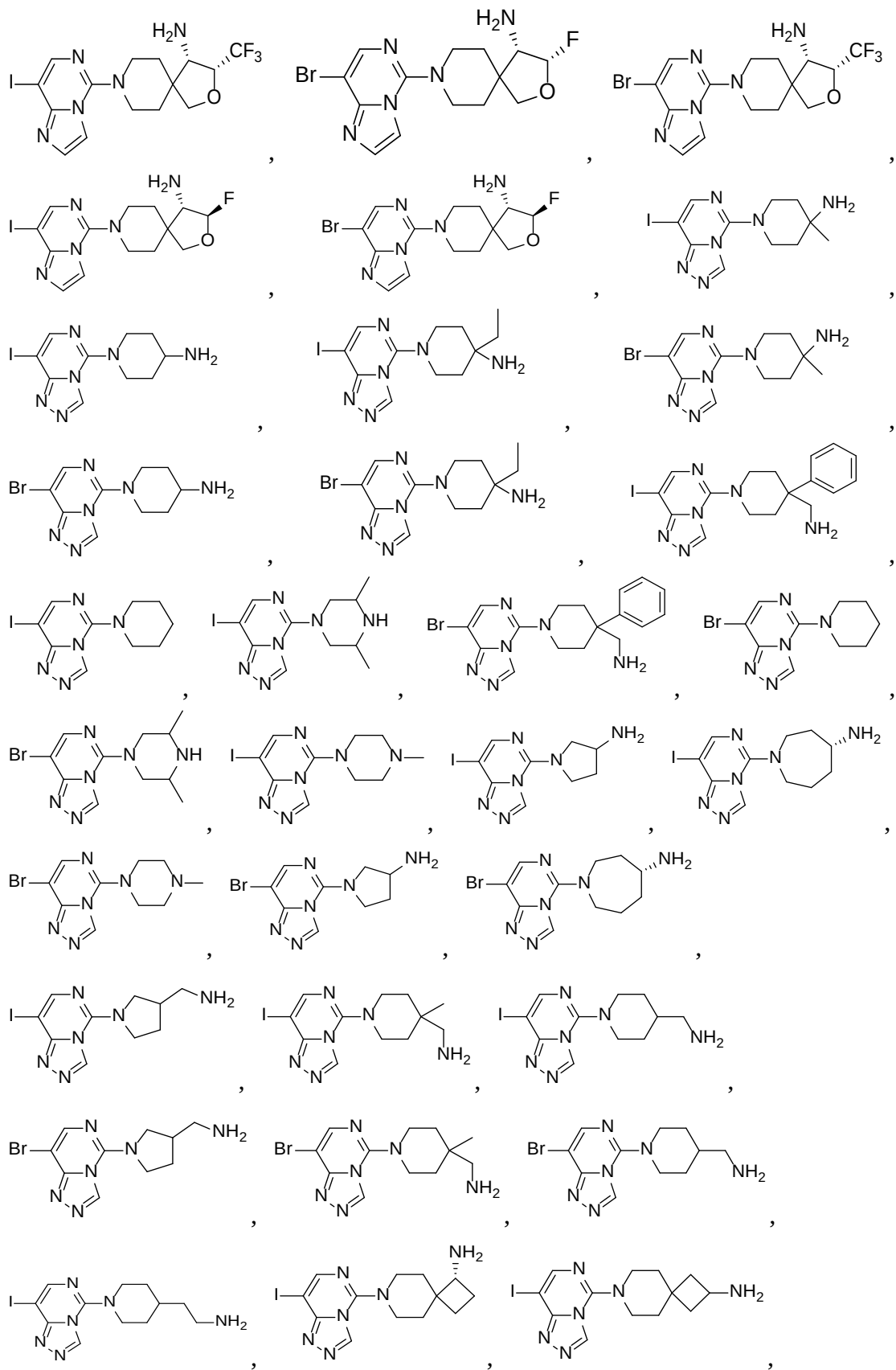
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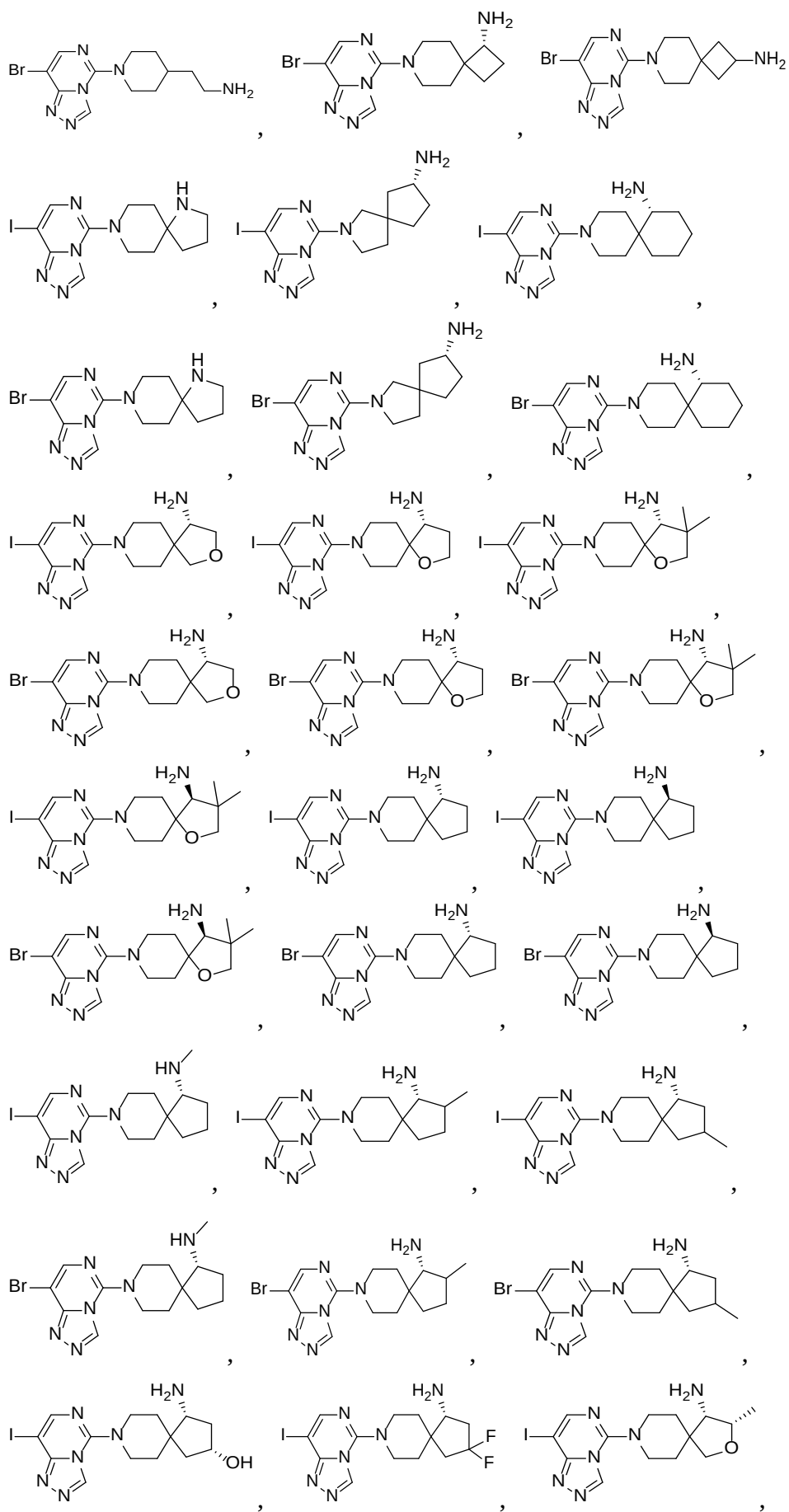
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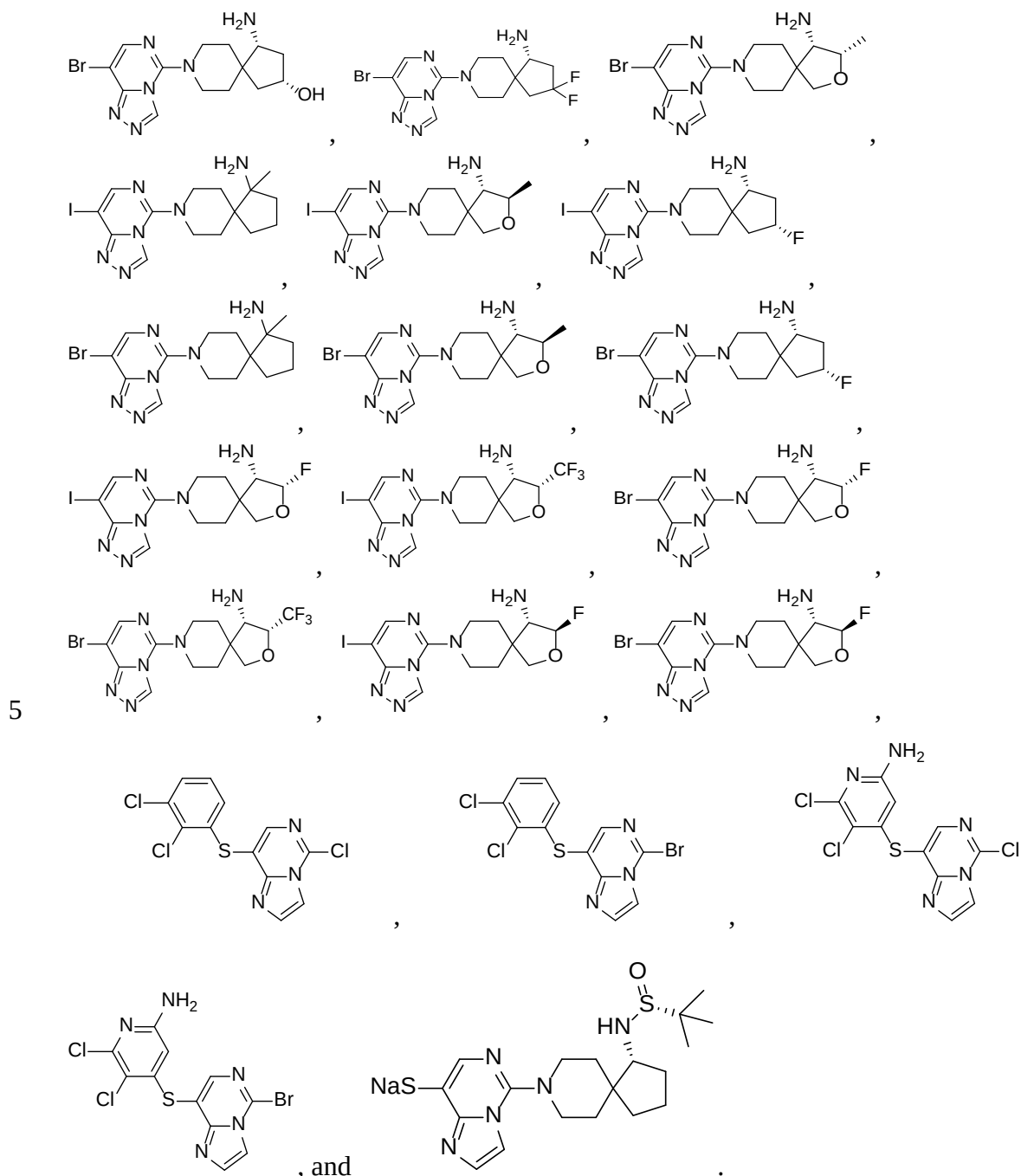






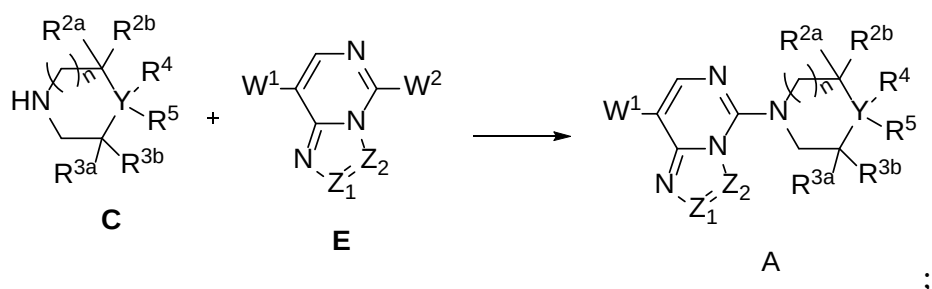
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10 24. A preparation method of a compound represented by formula **A**, **B** or **D**, wherein the preparation method of the compound represented by formula **A** comprises a step of conducting a substitution reaction of a halogenated intermediate **E** with an intermediate amine **C** under basic condition to obtain the compound **A**, and the reaction

equation is as shown below:

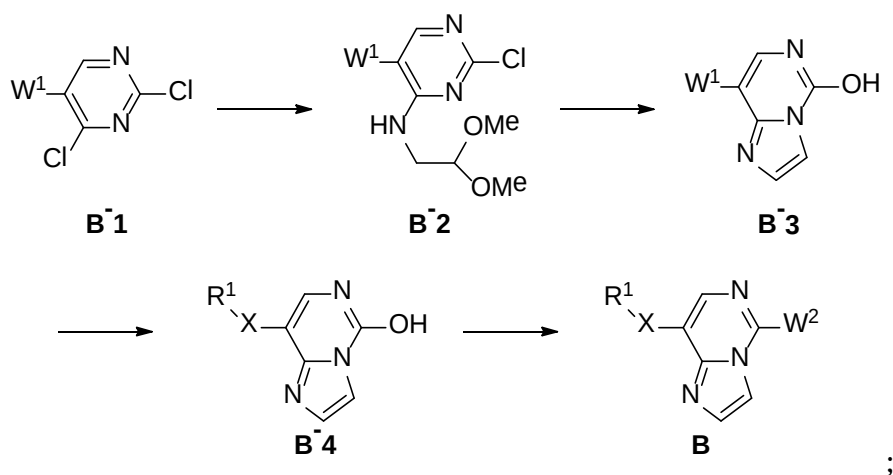


wherein, W^1 , W^2 , Z_1 , Z_2 , Y , n , R^{2a} , R^{2b} , R^{3a} , R^{3b} , R^4 and R^5 are as defined in claim 22;

5 the preparation method of the compound represented by formula **B** comprises the following steps:

conducting a substitution reaction of a dichloropyrimidine compound **B-1** with an amine to obtain intermediate **B-2**; conducting a condensation cyclization reaction of the intermediate **B-2** under strong acid condition to obtain a halogenated intermediate **B-3**;

10 coupling the halogenated intermediate **B-3** under catalytic coupling condition to obtain an intermediate **B-4**, and then converting into the intermediate **B**, and the reaction equation is as shown below:

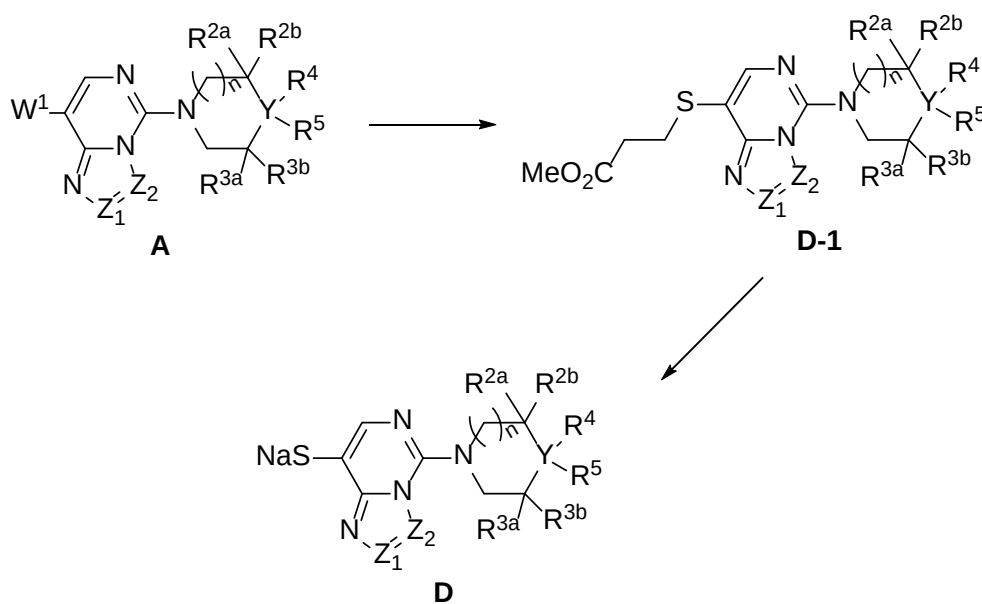


wherein, W^1 is halogen, W^2 , X and R^1 are as defined in claim 22;

15 the preparation method the compound represented by formula **D** comprises the following steps:

coupling an intermediate compound **A** with methyl mercaptopropionate under catalytic coupling condition to obtain an intermediate **D-1**, and then obtaining the corresponding sodium thiolate compound **D** under basic condition, and the reaction

equation is as shown below:



wherein, W^1 , Y, Z_1 , Z_2 , n, R^{2a} , R^{2b} , R^{3a} , R^{3b} , R^4 and R^5 are as defined in claim 22.

25. A pharmaceutical composition or a pharmaceutical preparation, or a combination product, wherein the pharmaceutical composition comprises (i) the compound, the pharmaceutically acceptable salt thereof, or the solvate thereof, or the isotope-labeled compound as defined in any one of claims 1-15, or the compound or the pharmaceutically acceptable salt thereof as defined in any one of claims 16-18, and (ii) a pharmaceutically acceptable excipient;

wherein the pharmaceutical preparation comprises the compound, the pharmaceutically acceptable salt thereof, or the solvate thereof, or the isotope-labeled compound as defined in any one of claims 1-15, or the compound or the pharmaceutically acceptable salt thereof as defined in any one of claims 16-18;

wherein the combination product comprises:

(i) the compound, the pharmaceutically acceptable salt thereof, or the solvate thereof, or the isotope-labeled compound as defined in any one of claims 1-15, or the compound or the pharmaceutically acceptable salt thereof as defined in any one of claims 16-18; and

(ii) another medicament, wherein the another medicament is selected from anticancer medicaments, tumor immune medicaments, antiallergic medicaments, antiemetic medicaments, analgesics, and cell protection medicaments.

5 26. A use of the compound, the pharmaceutically acceptable salt thereof, or the solvate thereof, or the isotope-labeled compound as defined in any one of claims 1-15, or the compound or the pharmaceutically acceptable salt thereof as defined in any one of claims 16-18, or the pharmaceutical composition or the pharmaceutical preparation, or the combination product as defined in claim 25 in the manufacture of a medicament
10 for the prevention and/or treatment of a disease or condition associated with abnormal activity of SHP2.

 27. The use as defined in claim 26, wherein the disease or condition is selected from Noonan syndrome, Leopard syndrome, juvenile myelomonocytic leukemia,
15 neuroblastoma, melanoma, acute myeloid leukemia, breast cancer, esophageal cancer, lung cancer, colon cancer, head cancer, neuroblastoma, head and neck squamous cell carcinoma, gastric cancer, anaplastic large cell lymphoma and glioblastoma.

 28. The pharmaceutical preparation as defined in claim 25, wherein the method of
20 administration of the pharmaceutical preparation is adapted for oral administration, sublingual administration, subcutaneous injection, intravenous injection, intramuscular injection, intrasternal injection, nasal administration, local topical administration or rectal administration;

 and/or, the pharmaceutical preparation is adapted to be administered once or

multiple times a day.