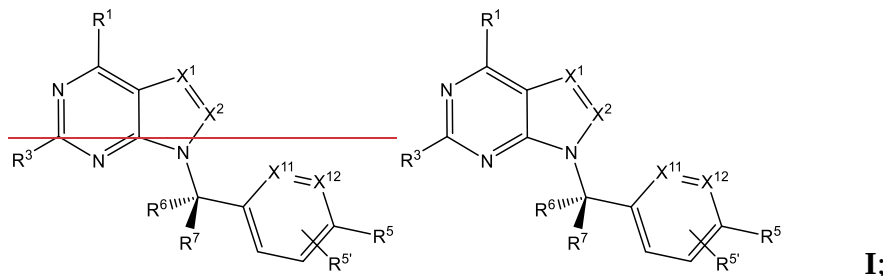


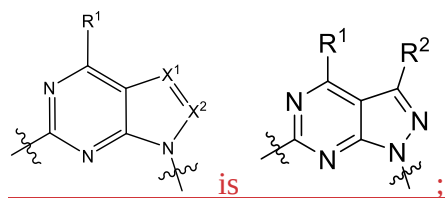
WHAT IS CLAIMED IS:

CLAIMS

1. A compound having Formula I:



or a pharmaceutically acceptable salt or solvate thereof, wherein:



~~each of X¹ and X² is independently selected from N and CR²;~~

each of R¹ and R² is independently selected from hydrogen, halo, cyano, optionally substituted alkyl, optionally substituted alkenyl, and optionally substituted alkynyl;

R³ is an optionally substituted phenyl, optionally substituted pyridyl, optionally substituted pyrimidinyl, optionally substituted pyrazinyl, optionally substituted pyridazinyl, or optionally substituted pyrazolyl;

each of X¹¹ and X¹² is independently selected from N and CH;

R^{5'} is selected from hydrogen, optionally substituted (C₁-C₆) alkyl, optionally substituted (C₂-C₆) alkenyl, optionally substituted (C₂-C₆) alkynyl, optionally substituted (C₁-C₆) alkoxy, (C₁-C₆) haloalkyl, (C₁-C₆) haloalkoxy, (C₁-C₆) hydroxyalkyl, cyano, halo, sulfonamido, -C(=O)R²³, -C(=O)OR²⁴, -NR^{32a}R^{32b}, -NR^{31a}C(=O)R²⁵, -NR^{31a}C(=O)NR^{31a}R^{31b}, -C(=O)NR^{31a}R^{31b}, -S(O)₂R²⁷, -NR^{31a}SO₂R²⁷, optionally substituted (C₆-C₁₄) aryl, optionally substituted (C₆-C₁₄) ar-(C₁-C₂)

alkyl, optionally substituted heteroaryl, optionally substituted heteroar-(C₁-C₂) alkyl, optionally substituted (C₃-C₈) cycloalkyl, optionally substituted ((C₃-C₈) cycloalkyl)-(C₁-C₂) alkyl, optionally substituted heterocyclo, optionally substituted heterocyclo-(C₁-C₂) alkyl, optionally substituted

—O—(C₆-C₁₄) aryl, optionally substituted —O—(C₆-C₁₄) ar-(C₁-C₂) alkyl, optionally substituted —O—heteroaryl, optionally substituted —O—heteroar-(C₁-C₂) alkyl, optionally substituted —O—(C₃-C₈) cycloalkyl, optionally substituted —O—((C₃-C₈) cycloalkyl)-(C₁-C₂) alkyl, optionally substituted —O—heterocyclo, optionally substituted —O—heterocyclo-(C₁-C₂) alkyl;

R⁵ is selected from optionally substituted (C₁-C₆) alkyl, optionally substituted (C₂-C₆) alkenyl, optionally substituted (C₂-C₆) alkynyl, optionally substituted (C₁-C₆) alkoxy, (C₁-C₆) haloalkyl, (C₁-C₆) haloalkoxy, (C₁-C₆) hydroxyalkyl, cyano, halo, sulfonamido, -C(=O)R²³, -C(=O)OR²⁴, -NR^{32a}R^{32b}, -NR^{31a}C(=O)R²⁵, -NR^{31a}C(=O)NR^{31a}R^{31b}, -C(=O)NR^{31a}R^{31b}, -S(O)₂R²⁷, -NR^{31a}SO₂R²⁷, optionally substituted (C₆-C₁₄) aryl, optionally substituted (C₆-C₁₄) ar-(C₁-C₂) alkyl, optionally substituted heteroaryl, optionally substituted heteroar-(C₁-C₂) alkyl, optionally substituted (C₃-C₈) cycloalkyl, optionally substituted ((C₃-C₈) cycloalkyl)-(C₁-C₂) alkyl, optionally substituted heterocyclo, optionally substituted heterocyclo-(C₁-C₂) alkyl, optionally substituted

—O—(C₆-C₁₄) aryl, optionally substituted —O—(C₆-C₁₄) ar-(C₁-C₂) alkyl, optionally substituted —O—heteroaryl, optionally substituted —O—heteroar-(C₁-C₂) alkyl, optionally substituted —O—(C₃-C₈) cycloalkyl, optionally substituted —O—((C₃-C₈) cycloalkyl)-(C₁-C₂) alkyl, optionally substituted —O—heterocyclo, optionally substituted —O—heterocyclo-(C₁-C₂) alkyl; or

one of R⁵ and one of R^{5'} on adjacent atoms are taken together with the atoms to which they are attached to form an optionally substituted (C₆-C₁₄) aryl ring; or one of R⁵ and one of R^{5'} on adjacent atoms are taken together with the atoms to which they are attached to form an optionally substituted heteroaryl ring; or one of R⁵ and one of R^{5'} on adjacent atoms are taken together with the atoms to which they are attached to form an optionally substituted (C₃-C₈) cycloalkyl ring; or one of R⁵ and one of R^{5'} on adjacent atoms are taken together with the atoms to which they are attached to form an optionally substituted heterocycloalkyl ring; or one of R⁵ and one of R^{5'} on adjacent atoms on the same atom to which they are attached are taken together to form an

optionally substituted spirocycloalkyl ring; or one of R⁵ and one of R^{5'} on adjacent atoms on the same atom to which they are attached are taken together to form an optionally substituted spiroheterocycloalkyl ring;

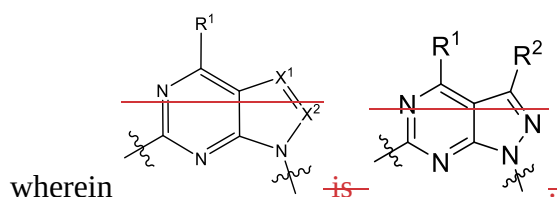
each of R⁶ and R⁷ is independently selected from hydrogen, halo, cyano, optionally substituted alkyl, optionally substituted alkenyl, and optionally substituted alkynyl;

R²³ is selected from the group consisting of hydrogen, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, amino, alkylamino, dialkylamino, cycloalkylamino, hydroxyalkyl, (amino)alkyl, (alkylamino)alkyl, (dialkylamino)alkyl, (cycloalkylamino)alkyl, (cycloalkyl)alkyl, aralkyl, (heterocyclo)alkyl, (heteroaryl)alkyl, (amino)(hydroxy)alkyl, (aralkylamino)alkyl, optionally substituted heterocyclo, optionally substituted heteroaryl, optionally substituted aryl, and optionally substituted cycloalkyl;

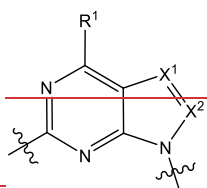
R^{31a} and R^{31b} are each independently selected from the group consisting of hydrogen, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, hydroxyalkyl, (amino)alkyl, (alkylamino)alkyl, (dialkylamino)alkyl, alkoxyalkyl, cycloalkyl, (cycloalkyl)alkyl, (heterocyclo)alkyl, aralkyl, and (heteroaryl)alkyl; and

each of R²⁴, R²⁵, R²⁷, R^{32a}, and R^{32b} is independently selected from the group consisting of hydrogen, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, amino, alkylamino, dialkylamino, cycloalkylamino, hydroxyalkyl, (amino)alkyl, (alkylamino)alkyl, (dialkylamino)alkyl, (cycloalkylamino)alkyl, (cycloalkyl)alkyl, aralkyl, (heterocyclo)alkyl, (heteroaryl)alkyl, (amino)(hydroxy)alkyl, (aralkylamino)alkyl, alkoxyalkyl, optionally substituted heterocyclo, optionally substituted heteroaryl, optionally substituted aryl, and optionally substituted cycloalkyl.

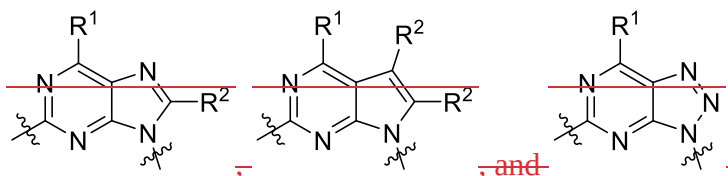
2. The compound of claim 1, or a pharmaceutically acceptable salt or solvate thereof,



3. ~~The compound of claim 1, or a pharmaceutically acceptable salt or solvate thereof,~~



~~wherein~~ ~~is independently selected from:~~



4. ~~The compound of claim 1, or a pharmaceutically acceptable salt or solvate thereof,~~
~~wherein the optional substituents on R³ are independently selected from hydrogen, halo, nitro,~~
~~cyano, hydroxy, amino, alkylamino, dialkylamino, haloalkyl, hydroxyalkyl, alkoxy, haloalkoxy,~~
~~aryloxy, heteroaryloxy, aralkyl aralkyloxy, alkylthio, carboxamido, sulfonamido, alkylcarbonyl,~~
~~arylcabonyl, alkylsulfonyl, arylsulfonyl, carboxy, carboxyalkyl, alkyl, optionally substituted~~
~~cycloalkyl, alkenyl, alkynyl, optionally substituted aryl, optionally substituted heteroaryl,~~
~~optionally substituted heterocyclo, alkoxyalkyl, (amino)alkyl, hydroxyalkylamino,~~
~~(alkylamino)alkyl, (dialkylamino)alkyl, (cyano)alkyl, (carboxamido)alkyl, mercaptoalkyl,~~
~~(heterocyclo)alkyl, (cycloalkylamino)alkyl, (C₁-₄ haloalkoxy)alkyl, and (heteroaryl)alkyl; or~~

~~wherein two of the optional substituents on R³ are taken together with the carbon or nitrogen~~
~~atoms to which they are attached to form an optionally substituted cycloalkyl, optionally~~
~~substituted heterocyclo, optionally substituted aryl, or optionally substituted heteroaryl group.~~

5. ~~The compound of claim 1 or 4, or a pharmaceutically acceptable salt or solvate thereof,~~
~~wherein R³ is an optionally substituted phenyl, wherein the phenyl is an~~ optionally substituted ~~at~~
~~the 2-position, pyrid-3-yl, an~~ optionally substituted ~~at the 6-position, pyrid-4-yl, an~~ optionally
~~disubstituted at the 2- and 6-position~~ substituted pyrimidin-5-yl, or ~~an~~ optionally ~~disubstituted at~~
~~the 2- and 3-position~~ substituted pyrazol-5-yl.

6. ~~The compound of claim 1 or 4, or a pharmaceutically acceptable salt or solvate thereof,~~
~~wherein R³ is an optionally substituted pyrid-3-yl or optionally substituted pyrid-4-yl,~~

wherein the pyrid-3-yl is optionally substituted at the 2-position, optionally substituted at the 4-position, or optionally disubstituted at the 2- and 4-positions; and

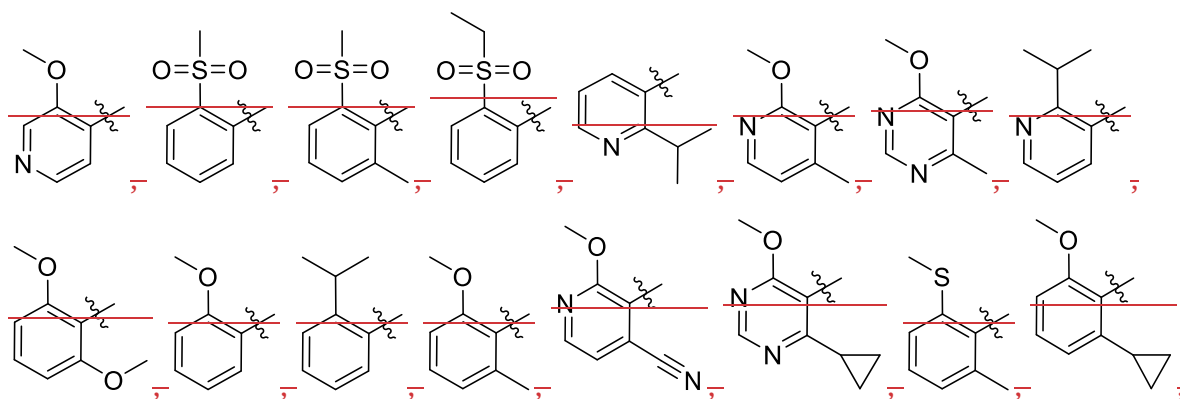
wherein the pyrid-4-yl is optionally substituted at the 3-position, optionally substituted at the 5-position, or optionally disubstituted at the 3- and 5-positions.

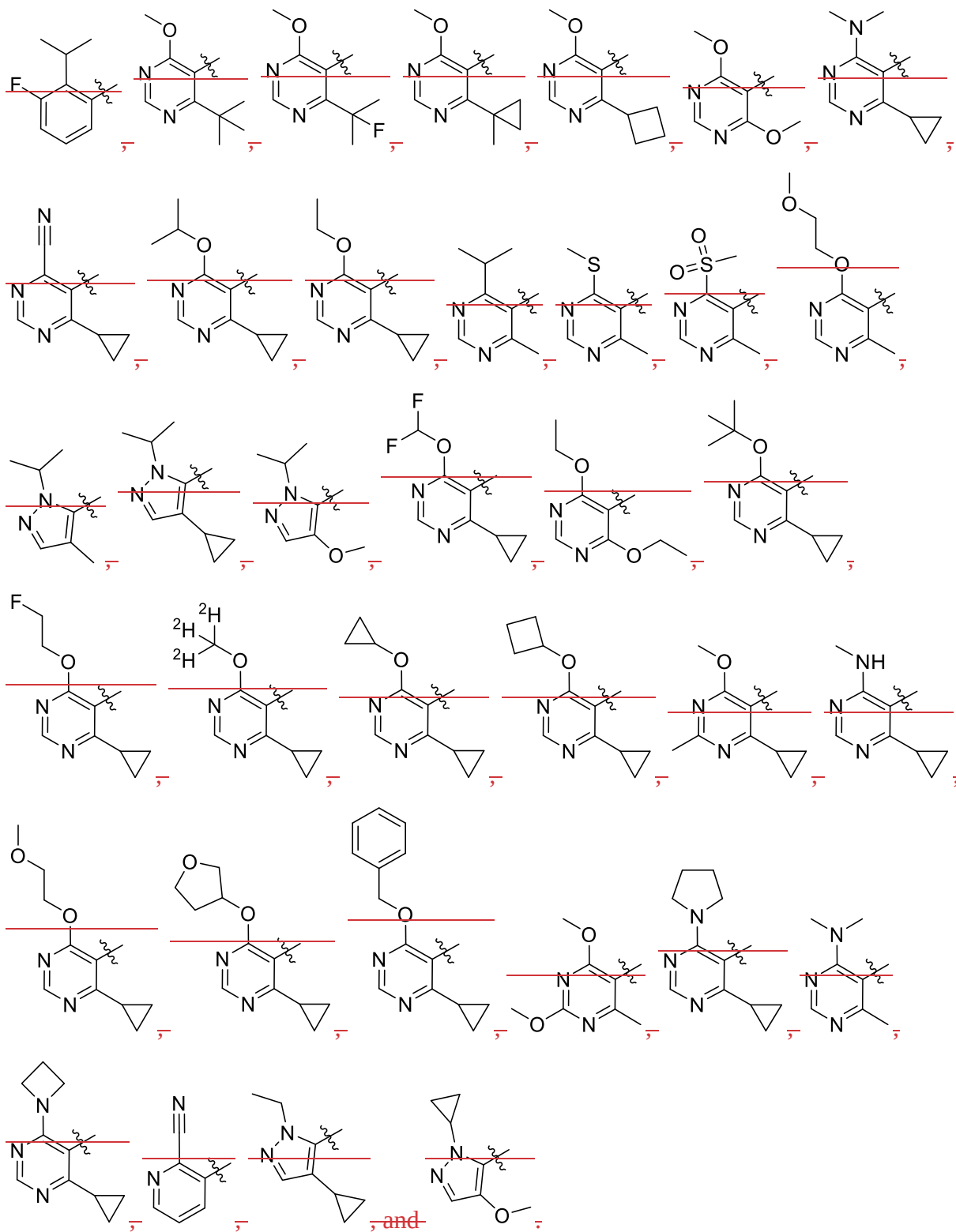
7. ~~The compound of claim 1 or 4, or a pharmaceutically acceptable salt or solvate thereof, wherein R³ is an optionally substituted pyrimidin-5-yl, wherein the pyrimidin-5-yl is optionally substituted at the 4-position, optionally substituted at the 6-position, optionally disubstituted at the 4- and 6-positions, or optionally trisubstituted at the 2-, 4-, and 6-positions.~~

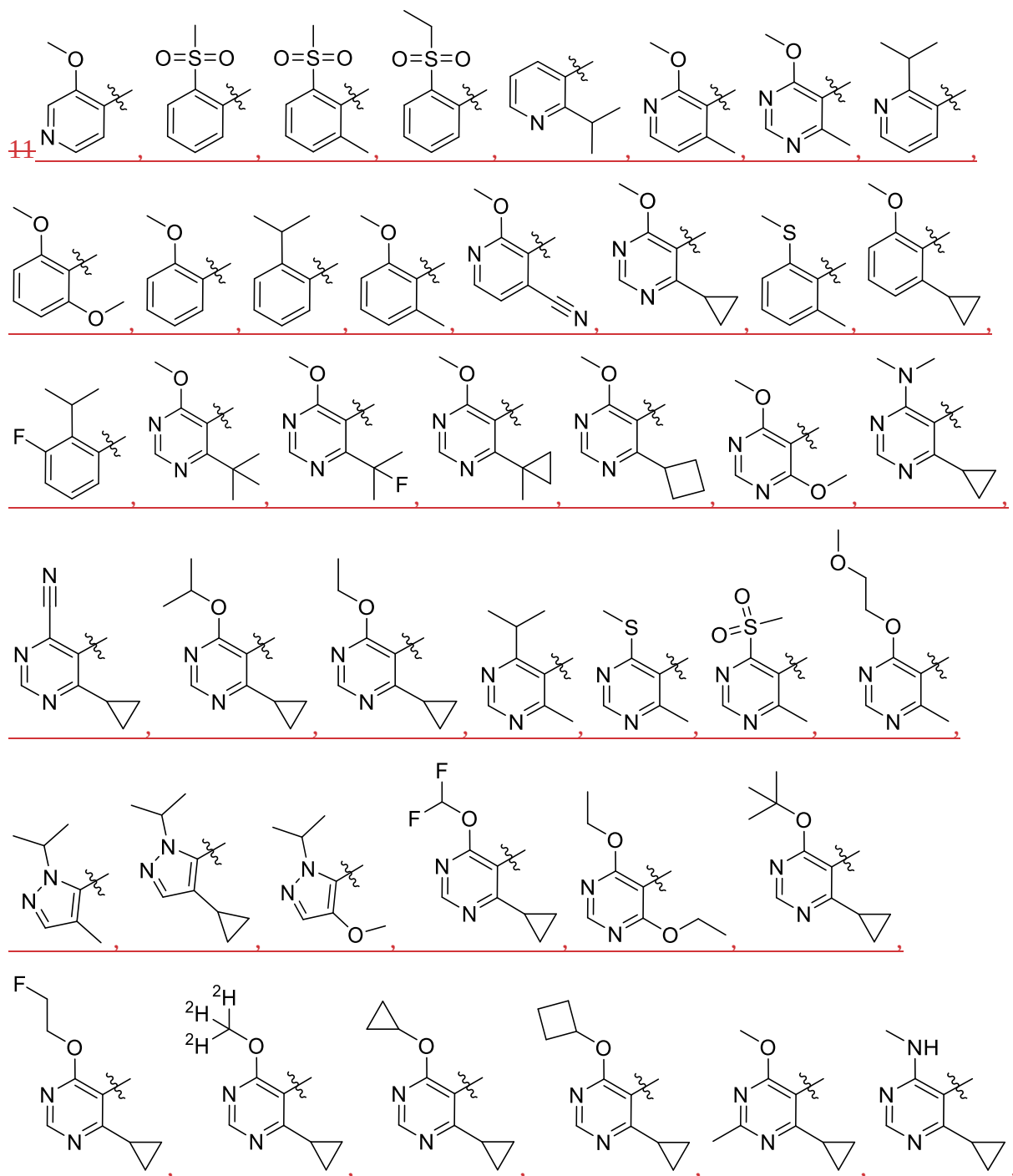
8. ~~The compound of claim 1 or 4, or a pharmaceutically acceptable salt or solvate thereof, wherein R³ is an optionally substituted pyrazol-5-yl, wherein the pyrazol-5-yl is optionally substituted at the 1-position, optionally substituted at the 4-position, or optionally disubstituted at the 1- and 4-positions.~~

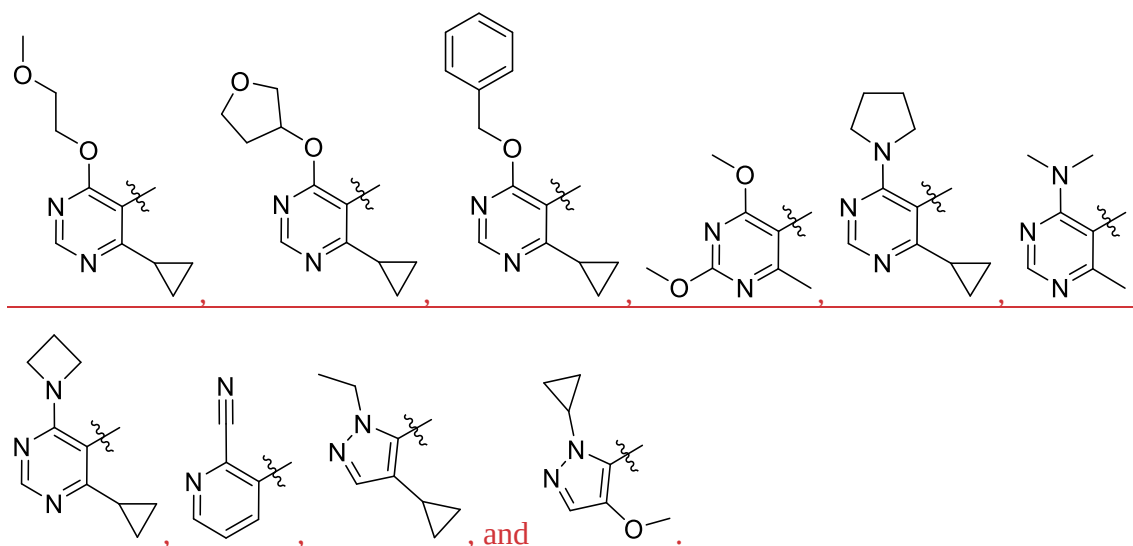
9. ~~The compound of any one of claims 5, 6, 7, or 83.~~ The compound of claim 2, wherein R³ is substituted and the substituents are independently selected from methoxy, deuteromethoxy, ethoxy, isopropoxy, t-butoxy, difluoromethoxy, 2-fluoroethoxy, 2-methoxyethoxy, cyclopropoxy, cyclobutoxy, (tetrahydrofuran-3-yl)oxy, benzyloxy, methyl, ethyl, isopropyl, 2-fluoroisopropyl, t-butyl, cyclopropyl, cyclobutyl, methylcyclopropyl, pyrrolidin-1-yl, azetidin-1-yl, methylamino, dimethylamino, cyano, halo, methylthio, methylsulfonyl, and ethylsulfonyl.

104. The compound of claim 1 ~~or 4~~, or a pharmaceutically acceptable salt or solvate thereof, wherein R³ is selected from the group consisting of:









5. The compound of claim 1, or a pharmaceutically acceptable salt or solvate thereof, wherein ~~at least one of X¹¹ and X¹²~~R⁵ is N.

12. — ~~The compound of claim 1, or a pharmaceutically acceptable salt or solvate thereof, wherein the optional substituents on R⁵ are independently selected from hydrogen, halo, nitro, cyano, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, alkoxy, hydroxy, carboxy, carboxyalkyl, amino, alkylamino, dialkylamino, cycloalkylamino, heterocycloalkylamino, aralkylamino, heteroaralkylamino, alkylthio, haloalkyl, haloalkoxy, hydroxyalkyl, hydroxyalkylamino, alkoxyalkyl, (alkoxyalkyl)amino, (amino)alkyl, (alkylamino)alkyl, (dialkylamino)alkyl, (cycloalkylamino)alkyl, (carboxamido)alkyl, mercaptoalkyl, (cyano)alkyl, (cycloalkyl)alkyl, aralkyl, aralkyloxy, alkylcarbonyl, arylcarbonyl, (heterocyclo)alkyl, (heteroaryl)alkyl, (amino)(hydroxy)alkyl, (aralkylamino)alkyl, (C₁₋₄ haloalkoxy)alkyl, optionally substituted heterocyclo, optionally substituted heteroaryl, optionally substituted aryl, optionally substituted cycloalkyl, carboxamido, sulfonyl, sulfonamido, sulfamido, alkylsulfonyl, alkylsulfonamido, alkylsulfamido, arylsulfonyl, aryloxy, heteroaryloxy, —C(=O)R²³, —C(=O)OR²⁴, —C(=O)NR^{31a}R^{31b}, —NR^{31a}C(=O)R²⁵, —NR^{31a}C(=O)OR²⁶, —NR^{31a}C(=O)NR^{31a}R^{31b}, —NR^{31a}SO₂R²⁷, —OC(=O)R²⁸, —OC(=O)OR²⁹, —OC(=O)NR^{31a}R^{31b}, —OSO₂R³⁰, and —NR^{32a}R^{32b}; or~~

~~wherein two of the optional substituents on R⁵ are taken together with the carbon atoms to which they are attached to form an optionally substituted cycloalkyl, optionally substituted heterocyclo, optionally substituted aryl, or optionally substituted heteroaryl group;~~

and

~~each of R^{24} , R^{25} , R^{26} , R^{27} , R^{28} , R^{29} , R^{30} , R^{32a} , and R^{32b} is selected from the group consisting of hydrogen, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, amino, alkylamino, dialkylamino, cycloalkylamino, hydroxyalkyl, (amino)alkyl, (alkylamino)alkyl, (dialkylamino)alkyl, (cycloalkylamino)alkyl, (cycloalkyl)alkyl, aralkyl, (heterocyclo)alkyl, (heteroaryl)alkyl, (amino)(hydroxy)alkyl, (aralkylamino)alkyl, alkoxyalkyl, optionally substituted heterocyclo, optionally substituted heteroaryl, optionally substituted aryl, and optionally substituted cycloalkyl.~~

~~13. — The compound of claim 1 or 12, or a pharmaceutically acceptable salt or solvate thereof, wherein R^5 is selected from optionally substituted (C_1-C_6) alkyl, optionally substituted (C_2-C_6) alkenyl, optionally substituted (C_2-C_6) alkynyl, optionally substituted (C_1-C_6) alkoxy, (C_1-C_6) haloalkyl, (C_1-C_6) haloalkoxy, (C_1-C_6) hydroxyalkyl, cyano, halo, sulfonamido, $C(-O)R^{23}$, $C(-O)OR^{24}$, $NR^{32a}R^{32b}$, $NR^{31a}C(-O)R^{25}$, $NR^{31a}C(-O)NR^{31a}R^{31b}$, $C(-O)NR^{31a}R^{31b}$, $S(O)_2R^{27}$, $NR^{31a}SO_2R^{27}$, optionally substituted $-O-((C_6-C_{14})$ aryl, optionally substituted $-O-((C_6-C_{14})$ ar-(C_1-C_2) alkyl, optionally substituted $-O-$ heteroaryl, optionally substituted $-O-$ heteroar-(C_1-C_2) alkyl, optionally substituted $-O-((C_3-C_8)$ cycloalkyl, optionally substituted $-O-(((C_3-C_8)$ cycloalkyl)-(C_1-C_2) alkyl, optionally substituted $-O-$ heterocyclo, optionally substituted $-O-$ heterocyclo-(C_1-C_2) alkyl.~~

~~14. — The compound of claim 1 or 12, or a pharmaceutically acceptable salt or solvate thereof, wherein R^5 is selected from optionally substituted (C_6-C_{14}) aryl, optionally substituted (C_6-C_{14}) ar-(C_1-C_2) alkyl, optionally substituted heteroaryl, optionally substituted heteroar-(C_1-C_2) alkyl, optionally substituted (C_3-C_8) cycloalkyl, optionally substituted $((C_3-C_8)$ cycloalkyl)-(C_1-C_2) alkyl, optionally substituted heterocyclo, optionally substituted heterocyclo-(C_1-C_2) alkyl.~~

~~15. — The compound of claim 1, 12, or 146.~~ The compound of claim 1, or a pharmaceutically acceptable salt or solvate thereof, wherein R^5 is an optionally substituted pyrrolyl, optionally substituted imidazolyl, optionally substituted pyrazolyl, optionally substituted triazolyl, or optionally substituted tetrazolyl.

~~16.—The compound of any one of claims 1, 12, 14, or 15, or a pharmaceutically acceptable salt or solvate thereof, wherein R⁵ is an optionally substituted imidazolyl.~~

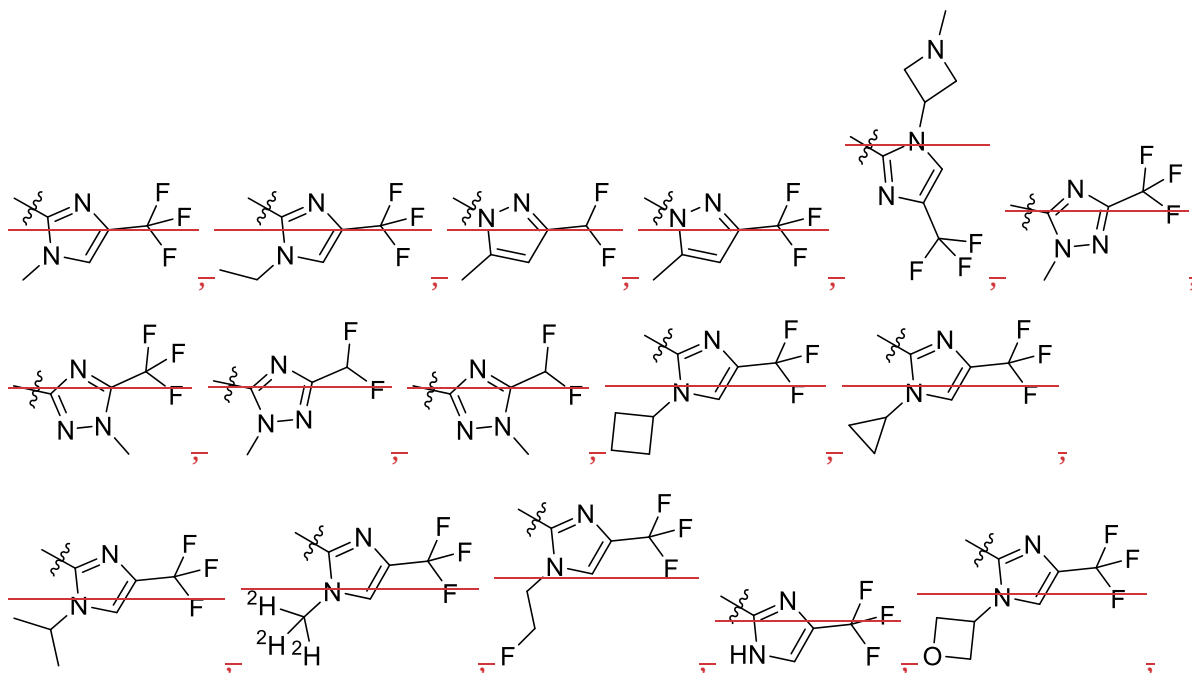
~~17. — The compound of any one of claims 1, 12, 14, or 15, or a pharmaceutically acceptable salt or solvate thereof, wherein R⁵ is an optionally substituted pyrazolyl.~~

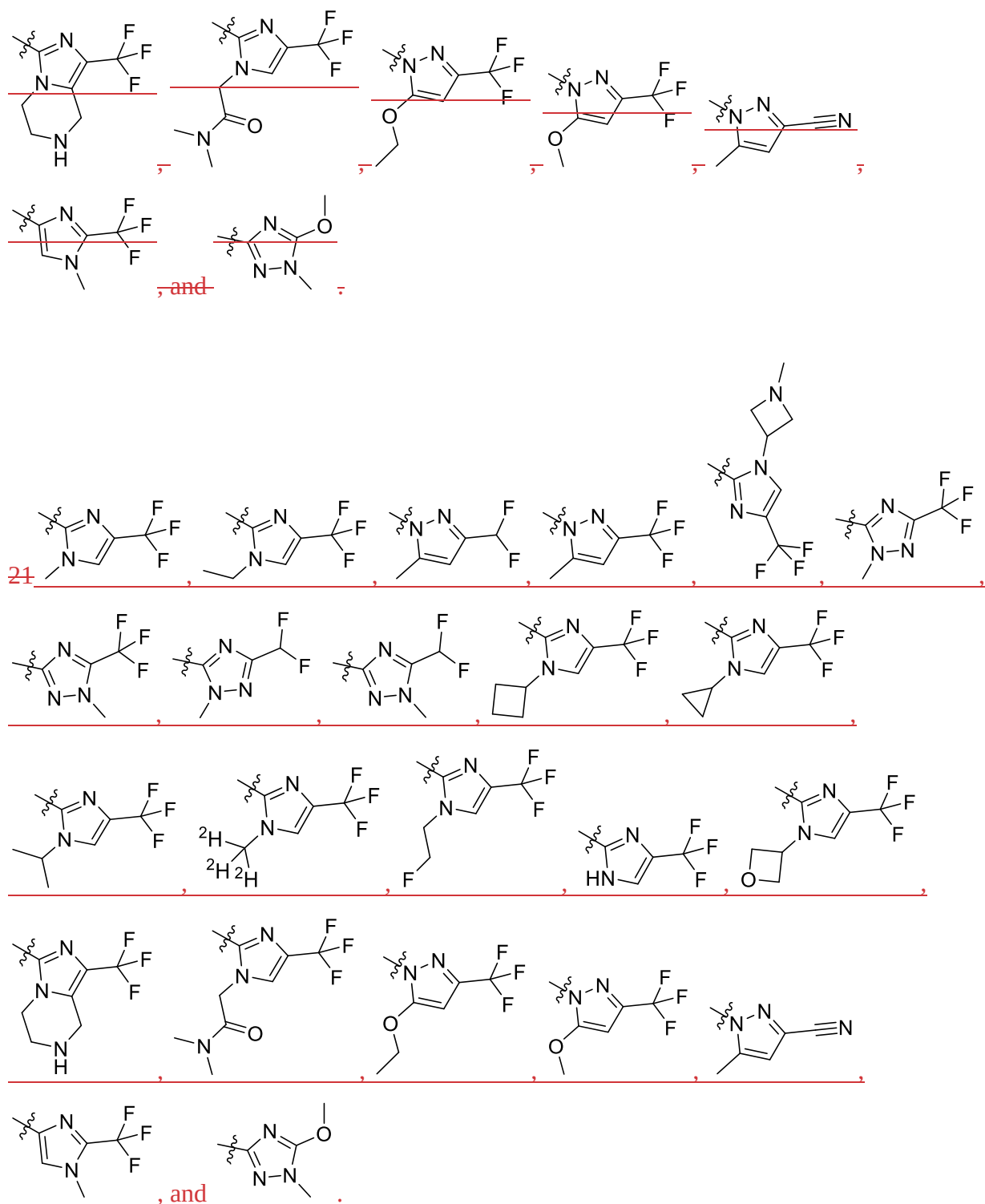
7. The compound of claim 6

~~19. The compound of any one of claims 1, 12, 14, or 15, or a pharmaceutically acceptable salt or solvate thereof, wherein R⁵ is an optionally substituted triazolyl.~~

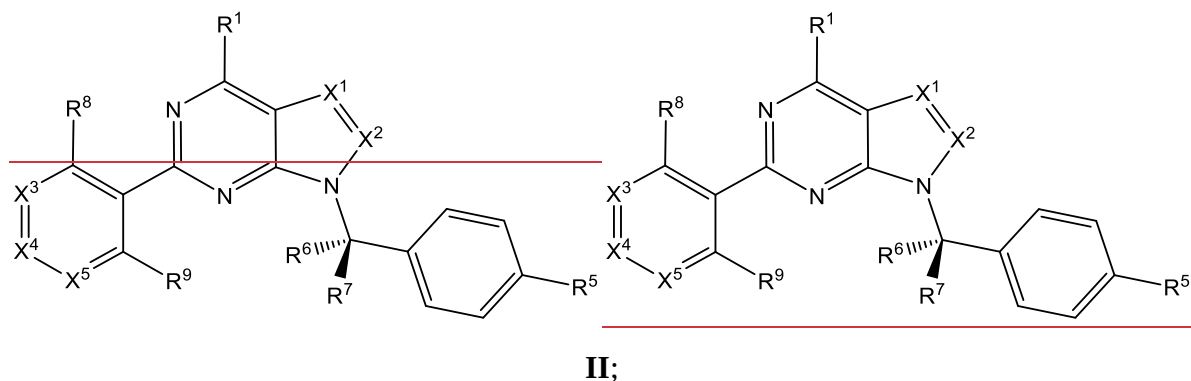
~~19. The compound of any one of claims 15, 16, or 17, wherein R⁵ is substituted and the substituents are independently selected from halo, methyl, ethyl, isopropyl, cyclopropyl, cyclobutyl, methoxy, ethoxy, triazolyl, cyano, optionally substituted alkyl, amino, alkylamino, dialkylamino, difluoromethyl, trifluoromethyl, methylsulfonyl, oxetan-3-yl, and methylazetidiny.~~

208. The compound of ~~any one of claims 1, 12, 14, or 15~~claim 1, or a pharmaceutically acceptable salt or solvate thereof, wherein R⁵ is selected from the group consisting of:





9. The compound of claim 1, or a pharmaceutically acceptable salt or solvate thereof, having a Formula II:



wherein:

X¹ is CR²;

X² is N;

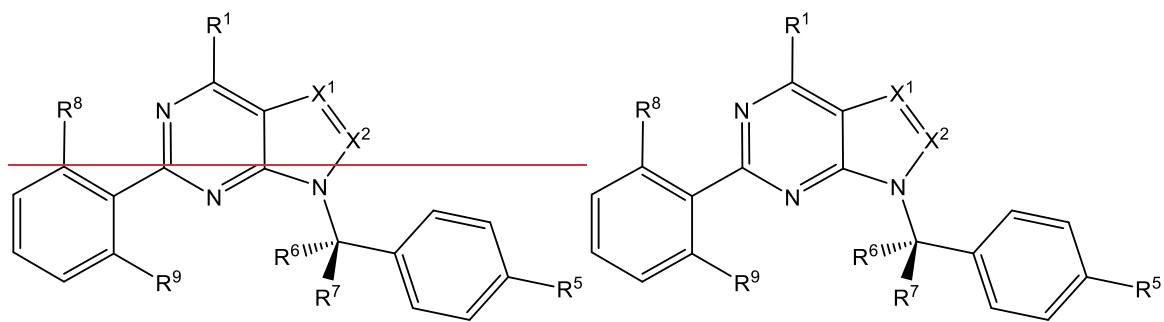
X³ is selected from N and CR¹⁰;

X⁴ is selected from N and CR¹¹;

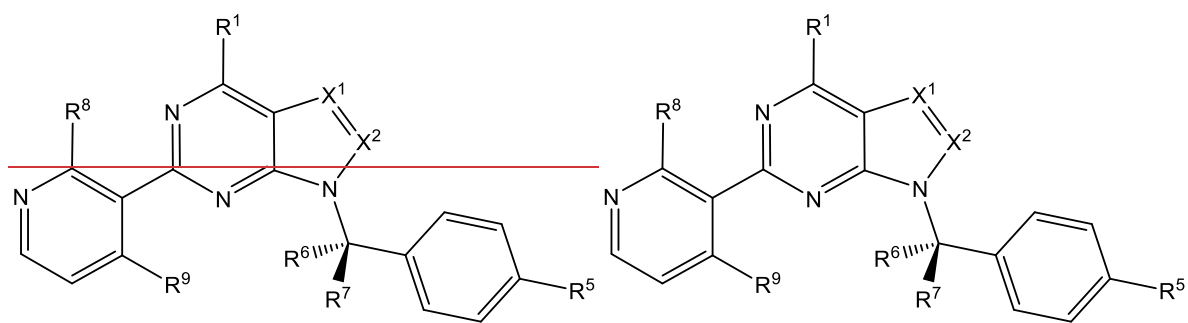
X⁵ is selected from N and CR¹²; and

each of R⁸, R⁹, R¹⁰, R¹¹, and R¹² is independently selected from the group consisting of hydrogen, halo, nitro, cyano, hydroxy, amino, alkylamino, dialkylamino, haloalkyl, hydroxyalkyl, alkoxy, haloalkoxy, aryloxy, heteroaryloxy, aralkyl aralkyloxy, alkylthio, carboxamido, sulfonamido, alkylcarbonyl, arylcarbonyl, alkylsulfonyl, arylsulfonyl, carboxy, carboxyalkyl, alkyl, optionally substituted cycloalkyl, alkenyl, alkynyl, optionally substituted aryl, optionally substituted heteroaryl, optionally substituted heterocyclo, alkoxyalkyl, (amino)alkyl, hydroxyalkylamino, (alkylamino)alkyl, (dialkylamino)alkyl, (cyano)alkyl, (carboxamido)alkyl, mercaptoalkyl, (heterocyclo)alkyl, (cycloalkylamino)alkyl, (C₁₋₄ haloalkoxy)alkyl, or (heteroaryl)alkyl.

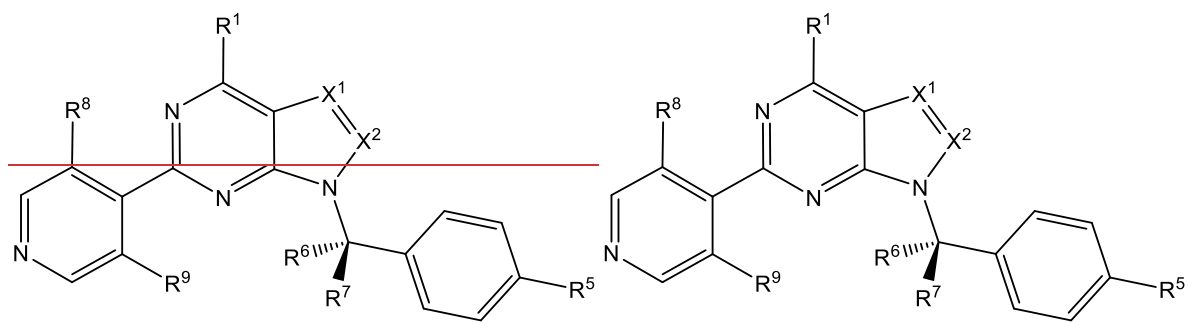
2210. The compound of claim 219, or a pharmaceutically acceptable salt or solvate thereof, having Formula **III**, Formula **IV**, Formula **V**, Formula **VI**, or Formula **VIa**:



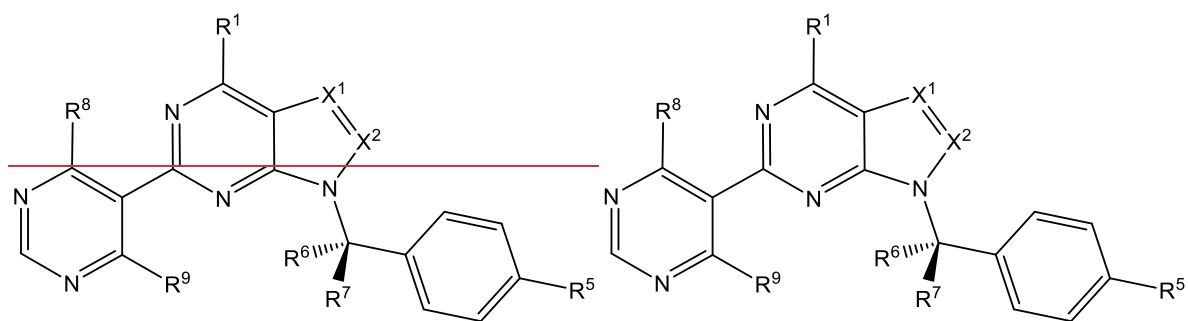
III;



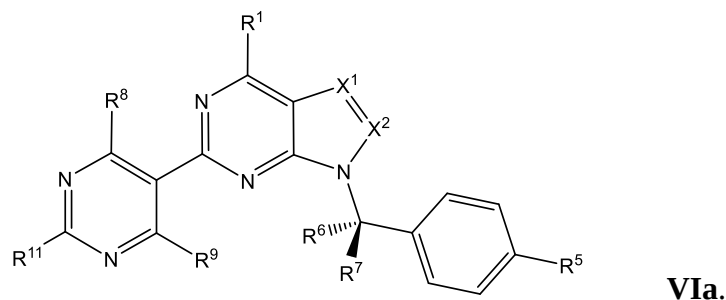
IV;



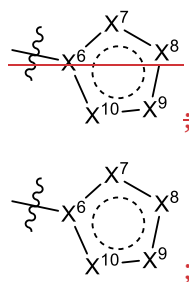
V;



VI;



2311. The compound of claim ~~21~~ or 229, or a pharmaceutically acceptable salt or solvate thereof, wherein R⁵ is:



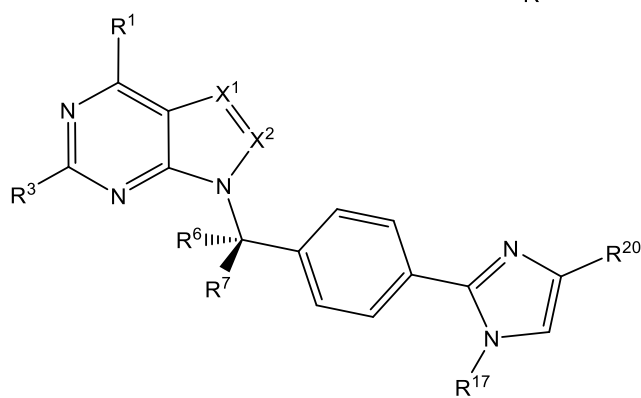
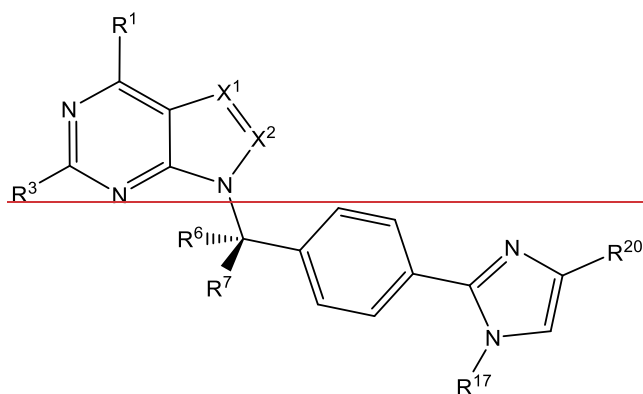
wherein:

X⁶ is selected from NR¹³ and CR¹⁸;
X⁷ is selected from NR¹⁴ and CR¹⁹;
X⁸ is selected from NR¹⁵ and CR²⁰;
X⁹ is selected from NR¹⁶ and CR²¹;
X¹⁰ is selected from NR¹⁷ and CR²²;

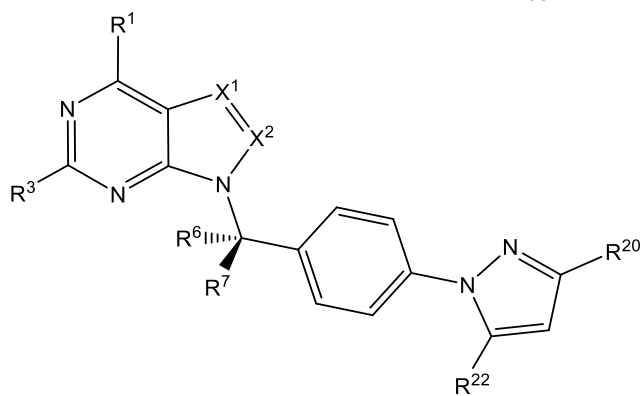
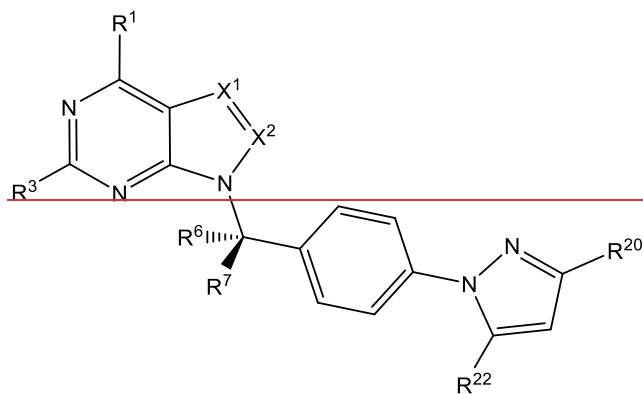
each of R¹³, R¹⁴, R¹⁵, R¹⁶, and R¹⁷ is absent, or independently selected from hydrogen, halo, methyl, ethyl, isopropyl, cyclopropyl, methoxy, triazolyl, cyano, optionally substituted alkyl, amino, alkylamino, dialkylamino, difluoromethyl, trifluoromethyl, methylsulfonyl, and methylazetidiny; and

each of R¹⁸, R¹⁹, R²⁰, R²¹, and R²² is independently selected from hydrogen, halo, methyl, ethyl, isopropyl, cyclopropyl, methoxy, triazolyl, cyano, optionally substituted alkyl, amino, alkylamino, dialkylamino, difluoromethyl, trifluoromethyl, methylsulfonyl, and methylazetidiny.

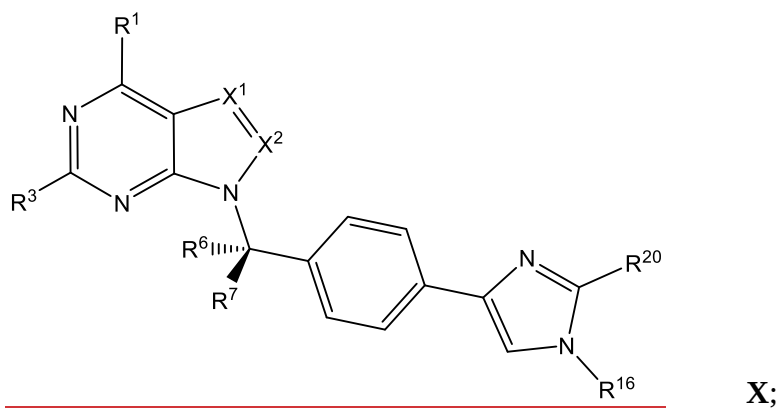
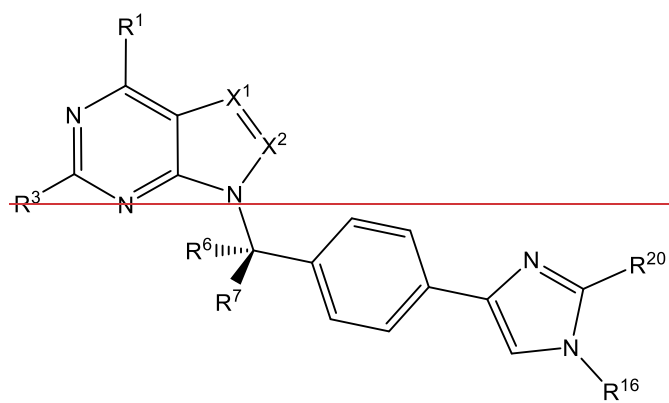
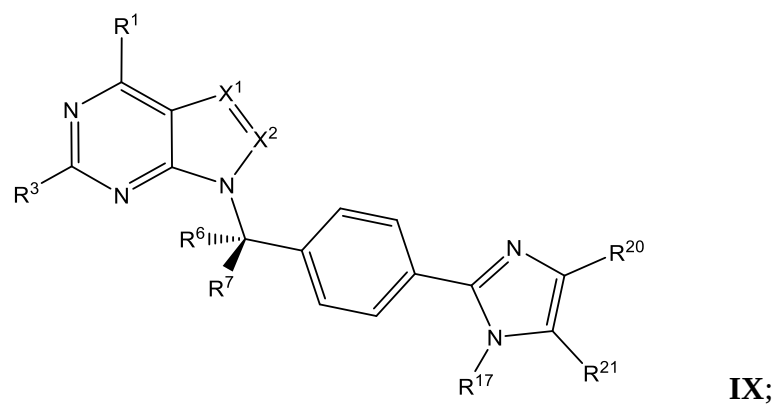
2412. The compound of claim **2311**, or a pharmaceutically acceptable salt or solvate thereof, having Formula **VII**, Formula **VIII**, Formula **IX**, Formula **X**, Formula **XI**, or Formula **XII**:

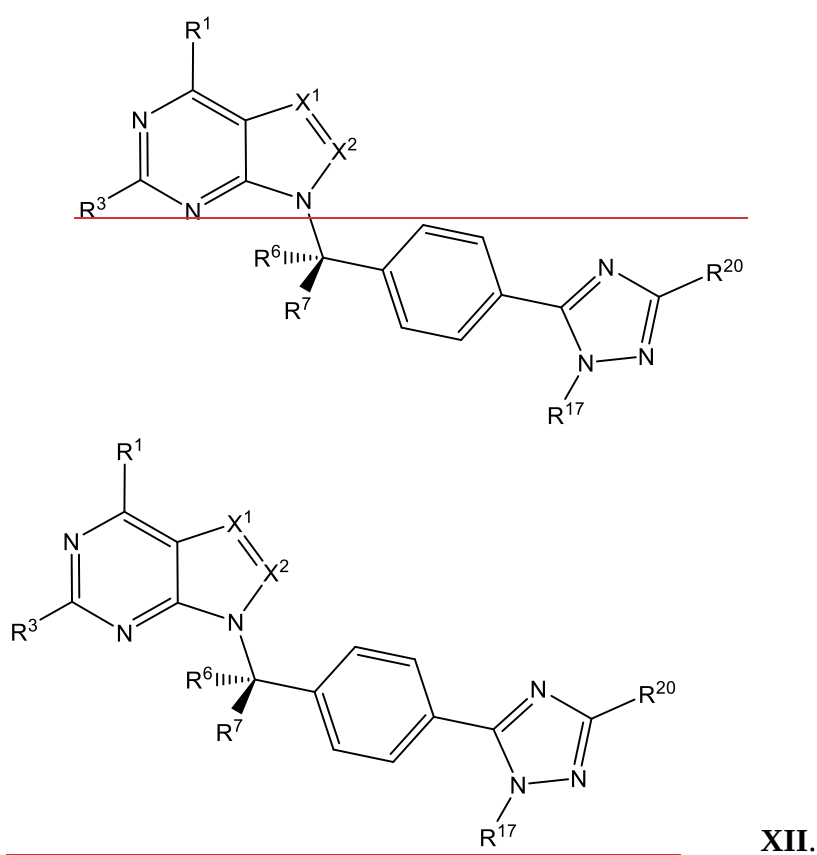
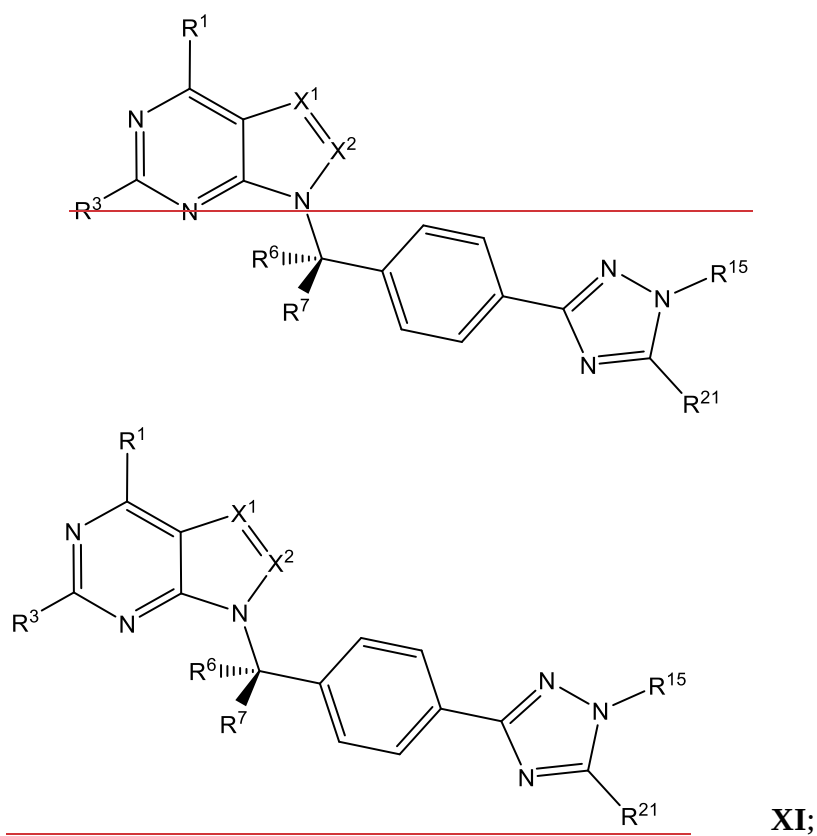


VII;



VIII;





25. — The 13. A compound ~~of claim 1~~ selected from the group consisting of:

6-(3-methoxypyridin-4-yl)-1-(4-(1-methyl-4-(trifluoromethyl)-1H-imidazol-2-yl)benzyl)-1H-pyrazolo[3,4-d]pyrimidine;

1-(4-(1-methyl-4-(trifluoromethyl)-1H-imidazol-2-yl)benzyl)-6-(2-(methylsulfonyl)phenyl)-1H-pyrazolo[3,4-d]pyrimidine;

1-(4-(1-methyl-4-(trifluoromethyl)-1H-imidazol-2-yl)benzyl)-6-(2-methyl-6-(methylsulfonyl)phenyl)-1H-pyrazolo[3,4-d]pyrimidine;

6-(2-(ethylsulfonyl)phenyl)-1-(4-(1-methyl-4-(trifluoromethyl)-1H-imidazol-2-yl)benzyl)-1H-pyrazolo[3,4-d]pyrimidine;

1-(4-(3-(difluoromethyl)-5-methyl-1H-pyrazol-1-yl)benzyl)-6-(2-isopropylpyridin-3-yl)-1H-pyrazolo[3,4-d]pyrimidine;

6-(2-methoxy-4-methylpyridin-3-yl)-1-(4-(1-methyl-4-(trifluoromethyl)-1H-imidazol-2-yl)benzyl)-1H-pyrazolo[3,4-d]pyrimidine;

6-(4-methoxy-6-methylpyrimidin-5-yl)-1-(4-(1-methyl-4-(trifluoromethyl)-1H-imidazol-2-yl)benzyl)-1H-pyrazolo[3,4-d]pyrimidine;

6-(2-isopropylpyridin-3-yl)-1-(4-(5-methyl-3-(trifluoromethyl)-1H-pyrazol-1-yl)benzyl)-1H-pyrazolo[3,4-d]pyrimidine;

6-(2,6-dimethoxyphenyl)-1-(4-(1-methyl-4-(trifluoromethyl)-1H-imidazol-2-yl)benzyl)-1H-pyrazolo[3,4-d]pyrimidine;

6-(2-methoxyphenyl)-1-(4-(1-methyl-4-(trifluoromethyl)-1H-imidazol-2-yl)benzyl)-1H-pyrazolo[3,4-d]pyrimidine;

6-(2-isopropylphenyl)-1-(4-(5-methyl-3-(trifluoromethyl)-1H-pyrazol-1-yl)benzyl)-1H-pyrazolo[3,4-d]pyrimidine;

6-(2-methoxy-6-methylphenyl)-1-(4-(1-methyl-4-(trifluoromethyl)-1H-imidazol-2-yl)benzyl)-1H-pyrazolo[3,4-d]pyrimidine;

2-methoxy-3-(1-(4-(1-methyl-4-(trifluoromethyl)-1H-imidazol-2-yl)benzyl)-1H-pyrazolo[3,4-d]pyrimidin-6-yl)isonicotinonitrile;

2-(2-isopropylphenyl)-9-(4-(1-methyl-4-(trifluoromethyl)-1H-imidazol-2-yl)benzyl)-9H-purine;

6-(4-cyclopropyl-6-methoxypyrimidin-5-yl)-1-(4-(1-methyl-4-(trifluoromethyl)-1H-imidazol-2-yl)benzyl)-1H-pyrazolo[3,4-d]pyrimidine;

6-(2-isopropylpyridin-3-yl)-1-(4-(1-methyl-4-(trifluoromethyl)-1H-imidazol-2-yl)benzyl)-1H-pyrazolo[3,4-d]pyrimidine;

1-(4-(1-methyl-4-(trifluoromethyl)-1H-imidazol-2-yl)benzyl)-6-(2-methyl-6-(methylthio)phenyl)-1H-pyrazolo[3,4-d]pyrimidine;

6-(4-cyclopropyl-6-methoxypyrimidin-5-yl)-1-(4-(5-methyl-3-(trifluoromethyl)-1H-pyrazol-1-yl)benzyl)-1H-pyrazolo[3,4-d]pyrimidine;

6-(2-cyclopropyl-6-methoxyphenyl)-1-(4-(1-methyl-4-(trifluoromethyl)-1H-imidazol-2-yl)benzyl)-1H-pyrazolo[3,4-d]pyrimidine;

6-(2-isopropylphenyl)-1-(4-(1-(1-methylazetidin-3-yl)-4-(trifluoromethyl)-1H-imidazol-2-yl)benzyl)-1H-pyrazolo[3,4-d]pyrimidine;

6-(2-isopropylphenyl)-1-(1-(4-(1-methyl-4-(trifluoromethyl)-1H-imidazol-2-yl)phenyl)ethyl)-1H-pyrazolo[3,4-d]pyrimidine;

6-(2-isopropylphenyl)-4-methyl-1-(4-(1-methyl-4-(trifluoromethyl)-1H-imidazol-2-yl)benzyl)-1H-pyrazolo[3,4-d]pyrimidine;

6-(3-fluoro-2-isopropylphenyl)-1-(4-(1-methyl-4-(trifluoromethyl)-1H-imidazol-2-yl)benzyl)-1H-pyrazolo[3,4-d]pyrimidine;

6-(2-isopropylphenyl)-3-methyl-1-(4-(1-methyl-4-(trifluoromethyl)-1H-imidazol-2-yl)benzyl)-1H-pyrazolo[3,4-d]pyrimidine;

6-(2-isopropylphenyl)-1-(4-(1-methyl-4-(trifluoromethyl)-1H-imidazol-2-yl)benzyl)-1H-pyrazolo[3,4-d]pyrimidine;

6-(4-(tert-butyl)-6-methoxypyrimidin-5-yl)-1-(4-(1-methyl-4-(trifluoromethyl)-1H-imidazol-2-yl)benzyl)-1H-pyrazolo[3,4-d]pyrimidine;

6-(4-(2-fluoropropan-2-yl)-6-methoxypyrimidin-5-yl)-1-(4-(1-methyl-4-(trifluoromethyl)-1H-imidazol-2-yl)benzyl)-1H-pyrazolo[3,4-d]pyrimidine;

6-(4-methoxy-6-(1-methylcyclopropyl)pyrimidin-5-yl)-1-(4-(1-methyl-4-(trifluoromethyl)-1H-imidazol-2-yl)benzyl)-1H-pyrazolo[3,4-d]pyrimidine;

6-(4-cyclobutyl-6-methoxypyrimidin-5-yl)-1-(4-(1-methyl-4-(trifluoromethyl)-1H-imidazol-2-yl)benzyl)-1H-pyrazolo[3,4-d]pyrimidine;

(S)-6-(4-cyclopropyl-6-methoxypyrimidin-5-yl)-1-(1-(4-(1-methyl-4-(trifluoromethyl)-1H-imidazol-2-yl)phenyl)ethyl)-1H-pyrazolo[3,4-d]pyrimidine;

(R)-6-(4-cyclopropyl-6-methoxypyrimidin-5-yl)-1-(1-(4-(1-methyl-4-(trifluoromethyl)-1H-imidazol-2-yl)phenyl)ethyl)-1H-pyrazolo[3,4-d]pyrimidine;

6-(4-cyclopropyl-6-ethoxypyrimidin-5-yl)-1-(4-(1-methyl-4-(trifluoromethyl)-1H-imidazol-2-yl)benzyl)-1H-pyrazolo[3,4-d]pyrimidine;

6-(4-cyclopropyl-6-isopropoxypyrimidin-5-yl)-1-(4-(1-methyl-4-(trifluoromethyl)-1H-imidazol-2-yl)benzyl)-1H-pyrazolo[3,4-d]pyrimidine;

6-cyclopropyl-5-(1-(4-(1-methyl-4-(trifluoromethyl)-1H-imidazol-2-yl)benzyl)-1H-pyrazolo[3,4-d]pyrimidin-6-yl)pyrimidine-4-carbonitrile;

6-cyclopropyl-N,N-dimethyl-5-(1-(4-(1-methyl-4-(trifluoromethyl)-1H-imidazol-2-yl)benzyl)-1H-pyrazolo[3,4-d]pyrimidin-6-yl)pyrimidin-4-amine;

6-(4,6-dimethoxypyrimidin-5-yl)-1-(4-(1-methyl-4-(trifluoromethyl)-1H-imidazol-2-yl)benzyl)-1H-pyrazolo[3,4-d]pyrimidine;

6-(4-cyclopropyl-6-methoxypyrimidin-5-yl)-1-(4-(1-ethyl-4-(trifluoromethyl)-1H-imidazol-2-yl)benzyl)-1H-pyrazolo[3,4-d]pyrimidine;

6-(4-isopropyl-6-methylpyrimidin-5-yl)-1-(4-(5-methyl-3-(trifluoromethyl)-1H-pyrazol-1-yl)benzyl)-1H-pyrazolo[3,4-d]pyrimidine;

1-(4-(5-methyl-3-(trifluoromethyl)-1H-pyrazol-1-yl)benzyl)-6-(4-methyl-6-(methylthio)pyrimidin-5-yl)-1H-pyrazolo[3,4-d]pyrimidine;

2-(4-cyclopropyl-6-methoxypyrimidin-5-yl)-8-methyl-9-(4-(5-methyl-3-(trifluoromethyl)-1H-pyrazol-1-yl)benzyl)-9H-purine;

1-(4-(5-methyl-3-(trifluoromethyl)-1H-pyrazol-1-yl)benzyl)-6-(4-methyl-6-(methylsulfonyl)pyrimidin-5-yl)-1H-pyrazolo[3,4-d]pyrimidine;

6-(4-(2-methoxyethoxy)-6-methylpyrimidin-5-yl)-1-(4-(5-methyl-3-(trifluoromethyl)-1H-pyrazol-1-yl)benzyl)-1H-pyrazolo[3,4-d]pyrimidine;

6-(1-isopropyl-4-methyl-1H-pyrazol-5-yl)-1-(4-(5-methyl-3-(trifluoromethyl)-1H-pyrazol-1-yl)benzyl)-1H-pyrazolo[3,4-d]pyrimidine;

6-(1-isopropyl-4-methoxy-1H-pyrazol-5-yl)-1-(4-(5-methyl-3-(trifluoromethyl)-1H-pyrazol-1-yl)benzyl)-1H-pyrazolo[3,4-d]pyrimidine;

6-(4-cyclopropyl-1-isopropyl-1H-pyrazol-5-yl)-1-(4-(5-methyl-3-(trifluoromethyl)-1H-pyrazol-1-yl)benzyl)-1H-pyrazolo[3,4-d]pyrimidine;

2-(4-cyclopropyl-6-methoxypyrimidin-5-yl)-7-(4-(1-methyl-4-(trifluoromethyl)-1H-imidazol-2-yl)benzyl)-7H-pyrrolo[2,3-d]pyrimidine; ~~and~~

5-(4-cyclopropyl-6-methoxypyrimidin-5-yl)-3-(4-(1-methyl-4-(trifluoromethyl)-1H-imidazol-2-yl)benzyl)-3H-[1,2,3]triazolo[4,5-d]pyrimidine;

~~— or a pharmaceutically acceptable salt or solvate thereof.~~

~~26. — The compound of claim 1 selected from the group consisting of:~~

—6-(4,6-diethoxypyrimidin-5-yl)-1-(4-(1-ethyl-4-(trifluoromethyl)-1H-imidazol-2-yl)benzyl)-1H-pyrazolo[3,4-d]pyrimidine;

—6-(4-cyclopropyl-6-methoxypyrimidin-5-yl)-1-(4-(1-(trifluoromethyl)-5,6,7,8-tetrahydroimidazo[1,5-a]pyrazin-3-yl)benzyl)-1H-pyrazolo[3,4-d]pyrimidine;

—6-(4-cyclopropyl-6-methoxypyrimidin-5-yl)-1-(4-(1-methyl-5-(trifluoromethyl)-1H-1,2,4-triazol-3-yl)benzyl)-1H-pyrazolo[3,4-d]pyrimidine;

—6-(1-cyclopropyl-4-methoxy-1H-pyrazol-5-yl)-1-(4-(1-ethyl-4-(trifluoromethyl)-1H-imidazol-2-yl)benzyl)-1H-pyrazolo[3,4-d]pyrimidine;

—6-(4-cyclopropyl-6-methoxypyrimidin-5-yl)-1-((6-(5-methoxy-3-(trifluoromethyl)-1H-pyrazol-1-yl)pyridin-3-yl)methyl)-1H-pyrazolo[3,4-d]pyrimidine;

—(R)-6-(4-cyclobutyl-6-methoxypyrimidin-5-yl)-1-(1-(4-(1-ethyl-4-(trifluoromethyl)-1H-imidazol-2-yl)phenyl)ethyl)-1H-pyrazolo[3,4-d]pyrimidine;

—(S)-6-(4-cyclobutyl-6-methoxypyrimidin-5-yl)-1-(1-(4-(1-ethyl-4-(trifluoromethyl)-1H-imidazol-2-yl)phenyl)ethyl)-1H-pyrazolo[3,4-d]pyrimidine;

—(R)-6-(4-cyclopropyl-6-methoxypyrimidin-5-yl)-1-(1-(4-(1-ethyl-4-(trifluoromethyl)-1H-imidazol-2-yl)phenyl)ethyl)-1H-pyrazolo[3,4-d]pyrimidine;

—(S)-6-(4-cyclopropyl-6-methoxypyrimidin-5-yl)-1-(1-(4-(1-ethyl-4-(trifluoromethyl)-1H-imidazol-2-yl)phenyl)ethyl)-1H-pyrazolo[3,4-d]pyrimidine;

—6-(4-cyclopropyl-6-methoxypyrimidin-5-yl)-1-(4-(1-methyl-2-(trifluoromethyl)-1H-imidazol-4-yl)benzyl)-1H-pyrazolo[3,4-d]pyrimidine;

—6-(4-(2-fluoropropan-2-yl)-6-methoxypyrimidin-5-yl)-1-(4-(1-methyl-4-(trifluoromethyl)-1H-imidazol-2-yl)benzyl)-1H-pyrazolo[3,4-d]pyrimidine;

—6-(4-cyclopropyl-6-methoxypyrimidin-5-yl)-1-(4-(5-ethoxy-3-(trifluoromethyl)-1H-pyrazol-1-yl)benzyl)-1H-pyrazolo[3,4-d]pyrimidine;

—6-(4-cyclopropyl-6-methoxypyrimidin-5-yl)-1-((6-(1-ethyl-4-(trifluoromethyl)-1H-imidazol-2-yl)pyridin-3-yl)methyl)-1H-pyrazolo[3,4-d]pyrimidine;

—1-(4-((6-(4-cyclopropyl-6-methoxypyrimidin-5-yl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)methyl)phenyl)-5-methyl-1H-pyrazole-3-carbonitrile;

—6-(4-cyclopropyl-1-ethyl-1H-pyrazol-5-yl)-1-(4-(1-ethyl-4-(trifluoromethyl)-1H-imidazol-2-yl)benzyl)-1H-pyrazolo[3,4-d]pyrimidine;

—6-(4-cyclopropyl-6-(methoxy-d₃)pyrimidin-5-yl)-1-(4-(1-ethyl-4-(trifluoromethyl)-1H-imidazol-2-yl)benzyl)-1H-pyrazolo[3,4-d]pyrimidine;

—6-cyclopropyl-5-(1-(4-(1-methyl-4-(trifluoromethyl)-1H-imidazol-2-yl)benzyl)-1H-pyrazolo[3,4-d]pyrimidin-6-yl)pyrimidine-4-carbonitrile;

—6-(4-cyclopropoxy-6-cyclopropylpyrimidin-5-yl)-1-(4-(1-ethyl-4-(trifluoromethyl)-1H-imidazol-2-yl)benzyl)-1H-pyrazolo[3,4-d]pyrimidine;

—6-(4-cyclobutoxy-6-cyclopropylpyrimidin-5-yl)-1-(4-(1-ethyl-4-(trifluoromethyl)-1H-imidazol-2-yl)benzyl)-1H-pyrazolo[3,4-d]pyrimidine;

—6-(4-cyclopropyl-6-(difluoromethoxy)pyrimidin-5-yl)-1-(4-(1-ethyl-4-(trifluoromethyl)-1H-imidazol-2-yl)benzyl)-1H-pyrazolo[3,4-d]pyrimidine;

—6-(4-cyclopropyl-6-methoxy-2-methylpyrimidin-5-yl)-1-(4-(1-methyl-4-(trifluoromethyl)-1H-imidazol-2-yl)benzyl)-1H-pyrazolo[3,4-d]pyrimidine;

—6-(4-cyclopropyl-6-methoxypyrimidin-5-yl)-1-(4-(1-(oxetan-3-yl)-4-(trifluoromethyl)-1H-imidazol-2-yl)benzyl)-1H-pyrazolo[3,4-d]pyrimidine;

—6-(4-(tert-butyl)-6-methoxypyrimidin-5-yl)-1-(4-(1-methyl-4-(trifluoromethyl)-1H-imidazol-2-yl)benzyl)-1H-pyrazolo[3,4-d]pyrimidine;

—6-(4-(tert-butoxy)-6-cyclopropylpyrimidin-5-yl)-1-(4-(1-ethyl-4-(trifluoromethyl)-1H-imidazol-2-yl)benzyl)-1H-pyrazolo[3,4-d]pyrimidine;

—6-(4-cyclopropyl-6-(2-fluoroethoxy)pyrimidin-5-yl)-1-(4-(1-ethyl-4-(trifluoromethyl)-1H-imidazol-2-yl)benzyl)-1H-pyrazolo[3,4-d]pyrimidine;

—6-(4-cyclopropyl-6-methoxypyrimidin-5-yl)-1-(4-(1-(methyl-d3)-4-(trifluoromethyl)-1H-imidazol-2-yl)benzyl)-1H-pyrazolo[3,4-d]pyrimidine;

—1-(4-(1-cyclobutyl-4-(trifluoromethyl)-1H-imidazol-2-yl)benzyl)-6-(4-cyclopropyl-6-methoxypyrimidin-5-yl)-1H-pyrazolo[3,4-d]pyrimidine;

—6-(4,6-dimethoxypyrimidin-5-yl)-1-(4-(1-ethyl-4-(trifluoromethyl)-1H-imidazol-2-yl)benzyl)-1H-pyrazolo[3,4-d]pyrimidine;

—6-(4-cyclopropyl-6-methoxypyrimidin-5-yl)-1-(4-(1-isopropyl-4-(trifluoromethyl)-1H-imidazol-2-yl)benzyl)-1H-pyrazolo[3,4-d]pyrimidine;

—1-(4-(1-cyclopropyl-4-(trifluoromethyl)-1H-imidazol-2-yl)benzyl)-6-(4-cyclopropyl-6-methoxypyrimidin-5-yl)-1H-pyrazolo[3,4-d]pyrimidine;

—6-(4-cyclopropyl-6-methoxypyrimidin-5-yl)-1-(4-(1-(2-fluoroethyl)-4-(trifluoromethyl)-1H-imidazol-2-yl)benzyl)-1H-pyrazolo[3,4-d]pyrimidine;

—6-(4-cyclopropyl-6-methoxypyrimidin-5-yl)-1-(4-(4-(trifluoromethyl)-1H-imidazol-2-yl)benzyl)-1H-pyrazolo[3,4-d]pyrimidine;

—6-(4-cyclopropyl-6-methoxypyrimidin-5-yl)-1-(3-fluoro-4-(1-methyl-4-(trifluoromethyl)-1H-imidazol-2-yl)benzyl)-1H-pyrazolo[3,4-d]pyrimidine;

—6-(4-cyclopropyl-6-methoxypyrimidin-5-yl)-1-(2-fluoro-4-(1-methyl-4-(trifluoromethyl)-1H-imidazol-2-yl)benzyl)-1H-pyrazolo[3,4-d]pyrimidine;

—6-(2,4-dimethoxy-6-methylpyrimidin-5-yl)-1-(4-(1-methyl-4-(trifluoromethyl)-1H-imidazol-2-yl)benzyl)-1H-pyrazolo[3,4-d]pyrimidine;

—6-(4-cyclopropyl-6-methoxypyrimidin-5-yl)-1-(4-(5-methoxy-3-(trifluoromethyl)-1H-pyrazol-1-yl)benzyl)-1H-pyrazolo[3,4-d]pyrimidine;

—6-(4-cyclopropyl-6-(2-methoxyethoxy)pyrimidin-5-yl)-1-(4-(1-methyl-4-(trifluoromethyl)-1H-imidazol-2-yl)benzyl)-1H-pyrazolo[3,4-d]pyrimidine;

—6-(4-cyclopropyl-6-(2-methoxyethoxy)pyrimidin-5-yl)-1-(4-(5-methyl-3-(trifluoromethyl)-1H-pyrazol-1-yl)benzyl)-1H-pyrazolo[3,4-d]pyrimidine;

—6-(4-methoxy-6-(1-methylcyclopropyl)pyrimidin-5-yl)-1-(4-(1-methyl-4-(trifluoromethyl)-1H-imidazol-2-yl)benzyl)-1H-pyrazolo[3,4-d]pyrimidine;

—6-(1-isopropyl-4-methyl-1H-pyrazol-5-yl)-1-(4-(5-methyl-3-(trifluoromethyl)-1H-pyrazol-1-yl)benzyl)-1H-pyrazolo[3,4-d]pyrimidine;

—(S)-6-(4-cyclopropyl-6-methoxypyrimidin-5-yl)-1-(1-(4-(1-methyl-4-(trifluoromethyl)-1H-imidazol-2-yl)phenyl)ethyl)-1H-pyrazolo[3,4-d]pyrimidine;

—(R)-6-(4-cyclopropyl-6-methoxypyrimidin-5-yl)-1-(1-(4-(1-methyl-4-(trifluoromethyl)-1H-imidazol-2-yl)phenyl)ethyl)-1H-pyrazolo[3,4-d]pyrimidine;

—6-(4-cyclobutyl-6-methoxypyrimidin-5-yl)-1-(4-(1-methyl-4-(trifluoromethyl)-1H-imidazol-2-yl)benzyl)-1H-pyrazolo[3,4-d]pyrimidine;

—6-(4-cyclopropyl-6-isopropoxypyrimidin-5-yl)-1-(4-(1-methyl-4-(trifluoromethyl)-1H-imidazol-2-yl)benzyl)-1H-pyrazolo[3,4-d]pyrimidine;

—6-(4-isopropyl-6-methylpyrimidin-5-yl)-1-(4-(5-methyl-3-(trifluoromethyl)-1H-pyrazol-1-yl)benzyl)-1H-pyrazolo[3,4-d]pyrimidine;

—6-(4-cyclopropyl-6-ethoxypyrimidin-5-yl)-1-(4-(1-methyl-4-(trifluoromethyl)-1H-imidazol-2-yl)benzyl)-1H-pyrazolo[3,4-d]pyrimidine;

—N,N,6-trimethyl-5-(1-(4-(5-methyl-3-(trifluoromethyl)-1H-pyrazol-1-yl)benzyl)-1H-pyrazolo[3,4-d]pyrimidin-6-yl)pyrimidin-4-amine;

—1-(4-(5-methyl-3-(trifluoromethyl)-1H-pyrazol-1-yl)benzyl)-6-(4-methyl-6-(methylthio)pyrimidin-5-yl)-1H-pyrazolo[3,4-d]pyrimidine;

—6-(4-cyclopropyl-6-methoxypyrimidin-5-yl)-1-(4-(1-ethyl-4-(trifluoromethyl)-1H-imidazol-2-yl)benzyl)-1H-pyrazolo[3,4-d]pyrimidine;

—6-(4,6-dimethoxypyrimidin-5-yl)-1-(4-(1-methyl-4-(trifluoromethyl)-1H-imidazol-2-yl)benzyl)-1H-pyrazolo[3,4-d]pyrimidine;

—6-(4-(2-methoxyethoxy)-6-methylpyrimidin-5-yl)-1-(4-(5-methyl-3-(trifluoromethyl)-1H-pyrazol-1-yl)benzyl)-1H-pyrazolo[3,4-d]pyrimidine;

—6-(4-cyclopropyl-6-methoxypyrimidin-5-yl)-1-(4-(1-(1-methylazetidin-3-yl)-4-(trifluoromethyl)-1H-imidazol-2-yl)benzyl)-1H-pyrazolo[3,4-d]pyrimidine;

—6-(4-methoxy-6-methylpyrimidin-5-yl)-1-(4-(5-methyl-3-(trifluoromethyl)-1H-pyrazol-1-yl)benzyl)-1H-pyrazolo[3,4-d]pyrimidine;

—3-(1-(4-(5-methyl-3-(trifluoromethyl)-1H-pyrazol-1-yl)benzyl)-1H-pyrazolo[3,4-d]pyrimidin-6-yl)picolinonitrile;

—6-(4-cyclopropyl-6-methoxypyrimidin-5-yl)-1-(4-(3-(difluoromethyl)-5-methyl-1H-pyrazol-1-yl)benzyl)-1H-pyrazolo[3,4-d]pyrimidine;

—6-cyclopropyl-N-methyl-5-(1-(4-(1-methyl-4-(trifluoromethyl)-1H-imidazol-2-yl)benzyl)-1H-pyrazolo[3,4-d]pyrimidin-6-yl)pyrimidin-4-amine;

—1-(4-(5-methoxy-3-(trifluoromethyl)-1H-pyrazol-1-yl)benzyl)-6-(4-methoxy-6-methylpyrimidin-5-yl)-1H-pyrazolo[3,4-d]pyrimidine;

—6-(4-cyclopropyl-6-((tetrahydrofuran-3-yl)oxy)pyrimidin-5-yl)-1-(4-(1-methyl-4-(trifluoromethyl)-1H-imidazol-2-yl)benzyl)-1H-pyrazolo[3,4-d]pyrimidine;

—6-(4-(benzyloxy)-6-cyclopropylpyrimidin-5-yl)-1-(4-(1-ethyl-4-(trifluoromethyl)-1H-imidazol-2-yl)benzyl)-1H-pyrazolo[3,4-d]pyrimidine;

—6-(4-cyclopropyl-6-methoxypyrimidin-5-yl)-1-(4-(3-(difluoromethyl)-1-methyl-1H-1,2,4-triazol-5-yl)benzyl)-1H-pyrazolo[3,4-d]pyrimidine;

—6-(4-(benzyloxy)-6-cyclopropylpyrimidin-5-yl)-1-(4-(1-methyl-4-(trifluoromethyl)-1H-imidazol-2-yl)benzyl)-1H-pyrazolo[3,4-d]pyrimidine;

—6-(4-cyclopropyl-6-methoxypyrimidin-5-yl)-1-(4-(5-methoxy-1-methyl-1H-1,2,4-triazol-3-yl)benzyl)-1H-pyrazolo[3,4-d]pyrimidine;

—2-(2-(4-((6-(4-cyclopropyl-6-methoxypyrimidin-5-yl)-1H-pyrazolo[3,4-d]pyrimidin-1-yl)methyl)phenyl)-4-(trifluoromethyl)-1H-imidazol-1-yl)-N,N-dimethylacetamide;

—6-cyclopropyl-N,N-dimethyl-5-(1-(4-(1-methyl-4-(trifluoromethyl)-1H-imidazol-2-yl)benzyl)-1H-pyrazolo[3,4-d]pyrimidin-6-yl)pyrimidin-4-amine;

~~—6-(4-cyclopropyl-6-methoxypyrimidin-5-yl)-1-(4-(5-(difluoromethyl)-1-methyl-1H-1,2,4-triazol-3-yl)benzyl)-1H-pyrazolo[3,4-d]pyrimidine;~~

~~—6-(4-cyclopropyl-6-(pyrrolidin-1-yl)pyrimidin-5-yl)-1-(4-(1-methyl-4-(trifluoromethyl)-1H-imidazol-2-yl)benzyl)-1H-pyrazolo[3,4-d]pyrimidine;~~

~~—6-(4-(azetidin-1-yl)-6-cyclopropylpyrimidin-5-yl)-1-(4-(1-methyl-4-(trifluoromethyl)-1H-imidazol-2-yl)benzyl)-1H-pyrazolo[3,4-d]pyrimidine; and~~

~~—5-(4-cyclopropyl-6-methoxypyrimidin-5-yl)-3-(4-(1-methyl-4-(trifluoromethyl)-1H-imidazol-2-yl)benzyl)-3H-[1,2,3]triazolo[4,5-d]pyrimidine;~~

or a pharmaceutically acceptable salt or solvate thereof.

~~27. The compound of any one of claims 1-25, wherein the compound inhibits a USP1 protein.~~

~~28. The compound of any one of claims 1-25, wherein the compound inhibits a USP1 protein with an IC₅₀ value of less than about 1 μ M in a Ub-Rho deubiquitinating assay.~~

~~29. The compound of claim 28, wherein the Ub-Rho deubiquitinating assay is the assay disclosed in Example 21814.~~

~~30. A method of treating cancer in a patient comprising administering to the patient a therapeutically effective amount of the compound of any one of claims 1-29.~~

31. A pharmaceutical composition comprising the compound of ~~any one of claims 1-29~~claim 1, or a pharmaceutically acceptable salt or solvate thereof, and a pharmaceutically acceptable carrier.

~~3215. The pharmaceutical composition~~compound of claim 31 ~~for use in treatment of cancer~~wherein R⁵ is an optionally substituted imidazolyl.

~~33.~~

16. The compound of ~~any one of claims 1-29~~claim 2, wherein R³ is an optionally substituted pyrimidin-5-yl.

17. The compound of claim 13, wherein the compound is 6-(4-cyclopropyl-6-methoxypyrimidin-5-yl)-1-(4-(1-isopropyl-4-(trifluoromethyl)-1H-imidazol-2-yl)benzyl)-1H-pyrazolo[3,4-d]pyrimidine or a pharmaceutically acceptable salt or solvate thereof, ~~for use in treatment of cancer.~~

18. The compound of claim 13, wherein the compound is 6-(4-cyclopropyl-6-methoxypyrimidin-5-yl)-1-(4-(1-methyl-4-(trifluoromethyl)-1H-imidazol-2-yl)benzyl)-1H-pyrazolo[3,4-d]pyrimidine

~~34. Use of the compound of any one of claims 1-29, or a pharmaceutically acceptable salt or solvate thereof, for the manufacture of a medicament for treatment of cancer.~~

19. The compound of claim 13, wherein the compound is 6-(4-cyclopropyl-6-methoxypyrimidin-5-yl)-1-(4-(5-methyl-3-(trifluoromethyl)-1H-pyrazol-1-yl)benzyl)-1H-pyrazolo[3,4-d]pyrimidine

~~35. A kit comprising the compound of any one of claims 1-29, or a pharmaceutically acceptable salt or solvate thereof, or the.~~

20. A pharmaceutical composition of any one of claims 26-27 and instructions for administering comprising the compound of claim 17, or a pharmaceutically acceptable salt or solvate thereof, or the and a pharmaceutically acceptable carrier.

21. A pharmaceutical composition to a patient having cancer.

~~36. A method of treating cancer in a patient comprising administering to the patient the compound of any one of claims 1-29 claim 18, or a pharmaceutically acceptable salt or solvate thereof or the, and a pharmaceutically acceptable carrier.~~

22. A pharmaceutical composition of any one of claims 31-32.

~~37. The method of any one of claims 30 and 36, the pharmaceutical composition of claim 32, the compound of claim 33, the use of claim 34, or the kit of claim 35, wherein the cancer is selected from the group consisting of a hematological cancer, a lymphatic cancer, a DNA damage repair pathway deficient cancer, a homologous recombination deficient cancer, a cancer~~

comprising ~~cancer cells with a mutation in a gene encoding p53, and a cancer comprising cancer cells with a loss of function mutation in a gene encoding p53.~~

~~38. The method of any one of claims 30 and 36, the pharmaceutical composition of claim 32, the compound of claim 33, the use of claim 34, or the kit of claim 35, wherein the cancer is selected from the group consisting of lung cancer, non-small cell lung cancer (NSCLC), colon cancer, bladder cancer, osteosarcoma, ovarian cancer, skin cancer, and breast cancer.~~

~~39. The method of any one of claims 30 and 36, the pharmaceutical composition of claim 32, the compound of claim 33, the use of claim 34, or the kit of claim 35, wherein the cancer is ovarian cancer or breast cancer.~~

~~40. The method of any one of claims 30 and 36, the pharmaceutical composition of claim 32, the compound of claim 33, the use of claim 34, or the kit of claim 35, wherein the cancer is ovarian cancer.~~

~~41. The method of any one of claims 30 and 36, the pharmaceutical composition of claim 32, the compound of claim 33, the use of claim 34, or the kit of claim 35, wherein the cancer is a breast cancer.~~

~~42. The method of any one of claims 30 and 36, the pharmaceutical composition of claim 32, the compound of claim 33, the use19, or a pharmaceutically acceptable salt or solvate thereof, and a pharmaceutically acceptable carrier.~~

~~23. The compound of claim 34, or the kit of claim 3512, wherein the cancer is a triple negative breast cancer.~~
~~each of R¹, R⁶, and R⁷~~

~~43. The method of any one of claims 30 and 36-42, the pharmaceutical composition of claim 32, the compound of claim 33, the use of claim 34, or the kit of claim 35, wherein the cancer comprises cancer cells with elevated levels of RAD18.~~

~~44. are hydrogen.~~

~~24. The method, pharmaceutical composition, compound, use, or kit of claim 43, wherein the elevated levels of RAD18 are elevated RAD18 protein levels.~~

~~45. The method, pharmaceutical composition, compound, use, or kit of claim 43, wherein the elevated levels of RAD18 are elevated RAD18 mRNA levels.~~

~~46. The method of any one of claims 43-45, wherein the elevated levels of RAD18 have been detected prior to the administration.~~

~~47. The method of claim 46, further comprising detecting RAD18 levels in a cancer sample obtained from the subject.~~

~~48. The method of any one of claims 30 and 36, the pharmaceutical composition of claim 32, the compound of claim 33, the use of claim 34, or the kit of claim 35, wherein the cancer is a DNA damage repair pathway deficient cancer.~~

~~49. The method, pharmaceutical composition, compound, use, or kit of claim 48, wherein the cancer is a homologous recombination deficient cancer.~~

~~50. The method of any one of claims 30 and 36, the pharmaceutical composition of claim 32, the compound of claim 33, the use of claim 34, or the kit of claim 35, wherein the cancer comprises cancer cells with a mutation in a gene encoding p53, optionally wherein the mutation in the gene encoding p53 is a loss of function mutation.~~

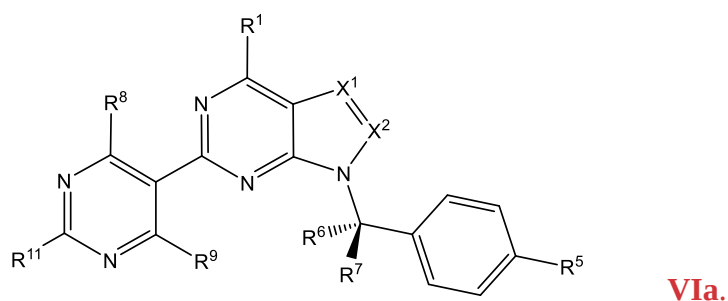
~~51. The method of any one of claims 30, 36, and 38-47, the pharmaceutical composition of claim 32, the compound of claim 33, the use of claim 34, or the kit of claim 35, wherein the cancer is a BRCA1 mutant cancer.~~

~~52. The method of any one of claims 30, 36, and 38-47, the pharmaceutical composition of claim 32, the compound of claim 33, the use of claim 34, or the kit of claim 35, wherein the cancer is a BRCA2 mutant cancer.~~

~~53. The method of any one of claims 30, 36, and 38-47, the pharmaceutical composition of claim 32, the compound of claim 33, the use of claim 34, or the kit of claim 35, wherein the cancer is a BRCA1 mutant cancer and a BRCA2 mutant cancer.~~

~~54. The method of any one of claims 30, 36, and 38-47, the pharmaceutical composition of claim 32, the compound of claim 33, the use of claim 34, or the kit of claim 35, wherein the cancer is a PARP inhibitor resistant or refractory cancer or a PARP inhibitor resistant or refractory BRCA1 or BRCA2 mutant cancer.~~

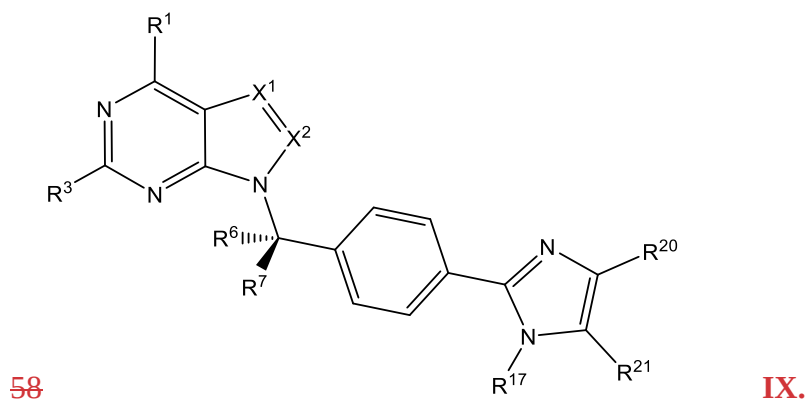
~~55. A method of treating a USP1 protein mediated disorder comprising administering to a patient in need thereof a compound of any one of claims 1-29~~10, or a pharmaceutically acceptable salt or solvate thereof, ~~or the pharmaceutical composition of claim 31 in an effective amount to treat the USP1 protein mediated disorder.~~having Formula VIa:



25. The compound of claim 24, wherein R⁸ is optionally substituted cycloalkyl, R⁹ is alkoxy, and R¹¹ is hydrogen.

~~26. 56. The method of any one of claims 30 and 36-53, the compound of any one of claims 28-29 and 33, the use of claim 34, the kit of claim 35, or the pharmaceutical composition of any one of claims 31-32, wherein the USP1 protein comprises the amino acid sequence of SEQ ID NO:1.~~

~~57. A method of inhibiting a USP1 protein comprising contacting a USP1 protein with the compound of any one of claims 1-29~~The compound of claim 12, or a pharmaceutically acceptable salt or solvate thereof, ~~or the pharmaceutical composition of claim 31.~~having Formula IX:



27. The ~~method~~compound of claim ~~5726~~, wherein ~~the contacting occurs in vitro~~ R^{17} is optionally substituted alkyl, R^{20} is optionally substituted alkyl, and R^{21} is hydrogen.

5928. The ~~method~~compound of claim ~~5727~~, wherein ~~the contacting occurs in vivo~~ R^{17} is isopropyl, R^{20} is trifluoroalkyl, and R^{21} is hydrogen.

~~60.~~ A method of treating cancer in a patient comprising administering to the subject a USP1 inhibitor, wherein the cancer comprises cancer cells with a mutation in a gene encoding p53.

~~6129.~~ The ~~method~~compound of claim 1, wherein each of R^1 , R^5 , R^6 , and R^7 are hydrogen.

30.60 The compound of claim 1, wherein ~~the mutation in a gene encoding p53 has been detected prior to the administration.~~ each of X^{11} and X^{12} are CH

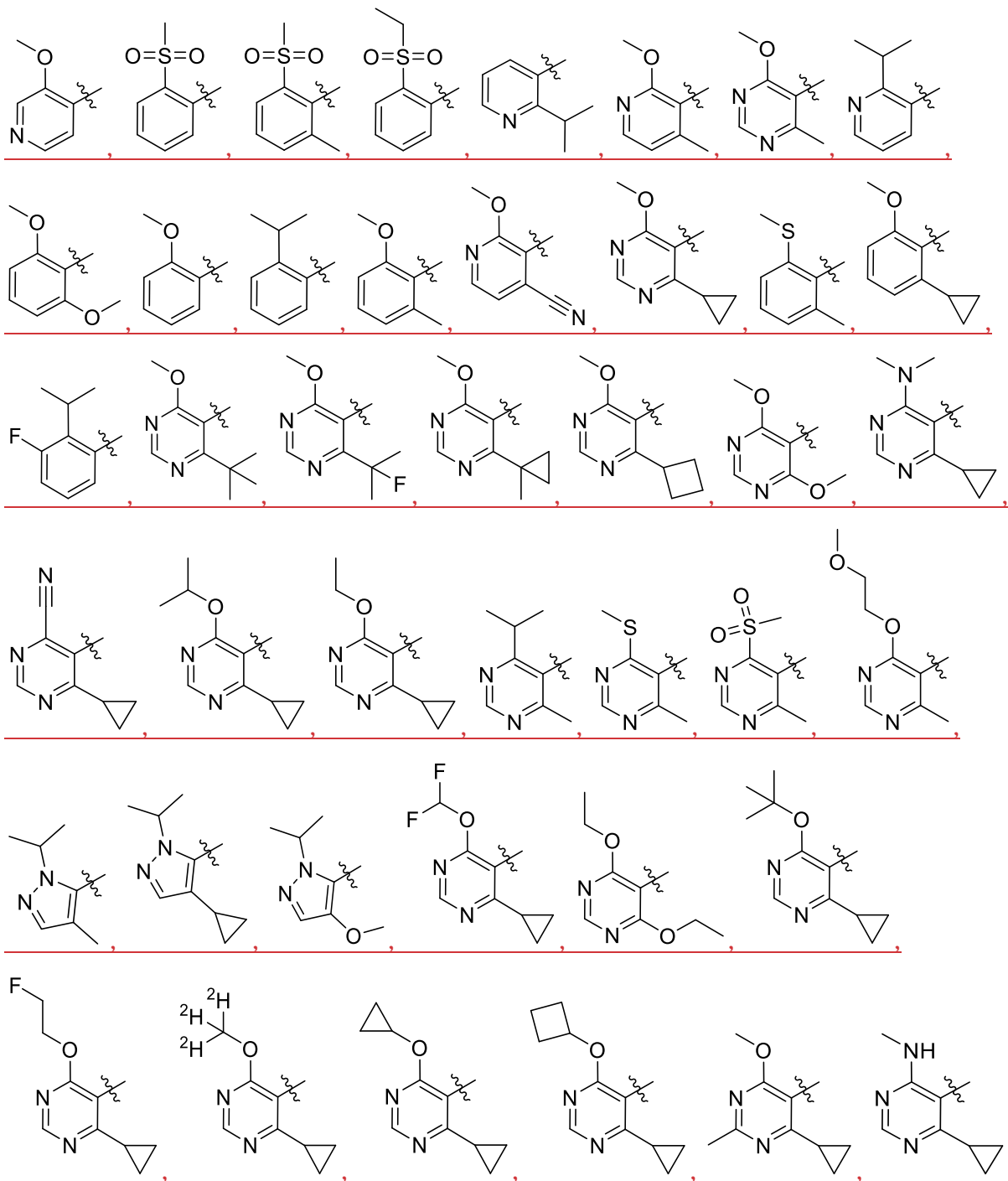
31. The compound of claim 29, wherein each of X^{11} and X^{12} are CH

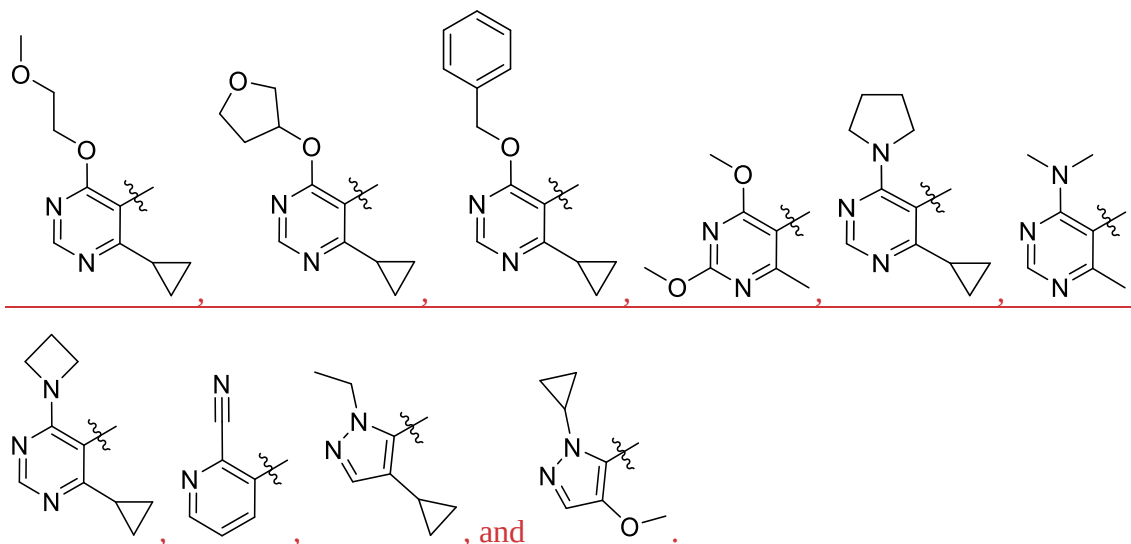
32. The compound of claim 31, wherein R^3 is optionally substituted pyrimidin-5-yl.

33. ~~62.~~ The ~~method of 60 or 61, further comprising detecting the mutation in the gene encoding p53 in a cancer sample obtained from the patient.~~

~~63.~~ A method of selecting a patient with cancer for treatment with a USP1 inhibitor, comprising detecting whether the cancer comprises cancer cells with a mutation in a gene

encoding p53 compound of claim 31, wherein if the cancer comprises cancer cells with a mutation in a gene encoding p53, the patient R^3 is selected for treatment with a USP1 inhibitor, from the group consisting of:



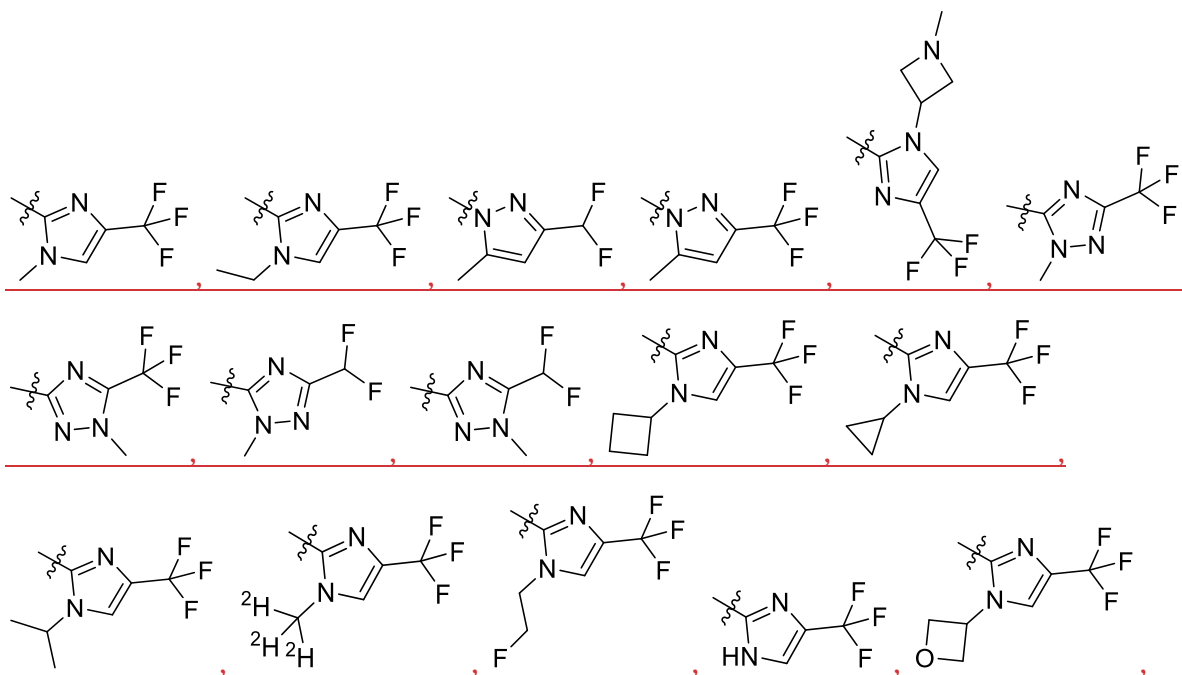


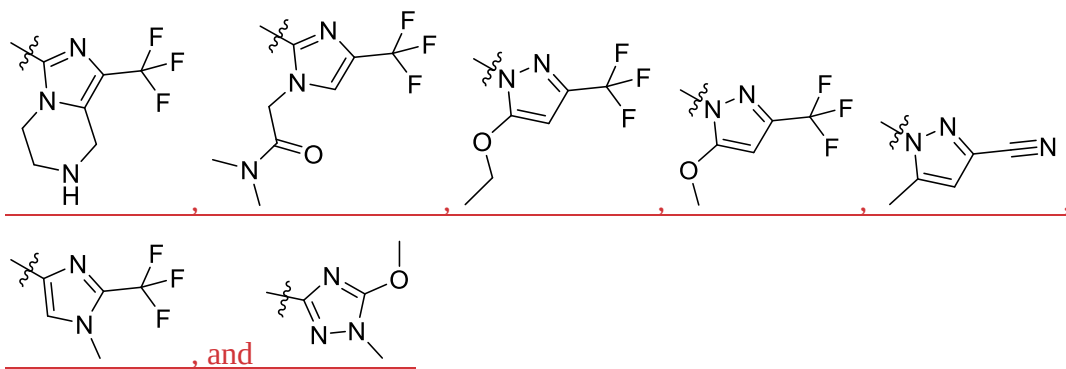
34. The compound of claim 31, wherein R^5 is optionally substituted imidazolyl.

35. The compound of claim 32, wherein R^5 is optionally substituted imidazolyl.

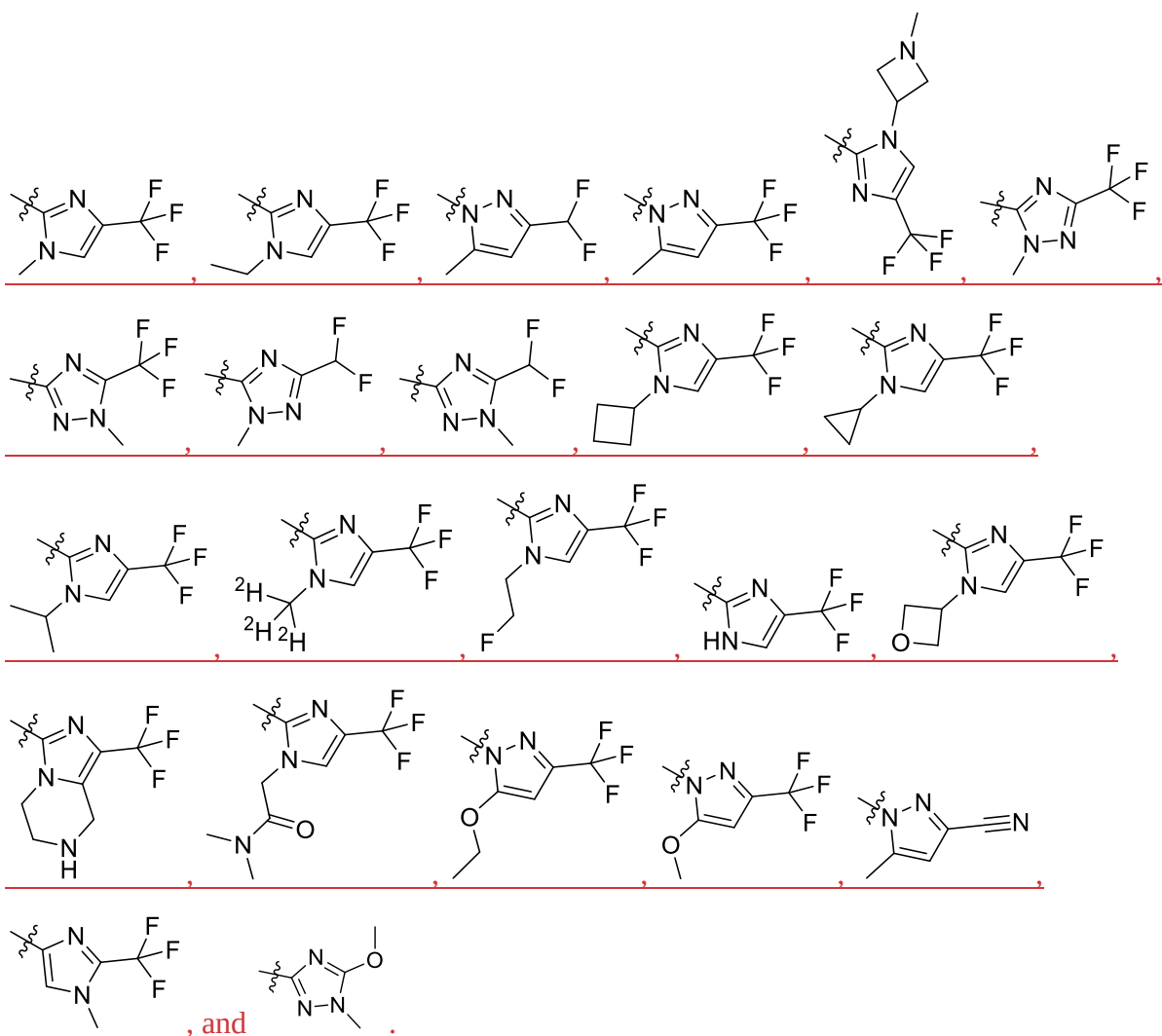
36. The compound of claim 33, wherein R^5 is optionally substituted imidazolyl.

37. The compound of claim 31, wherein R^5 is selected from the group consisting of:

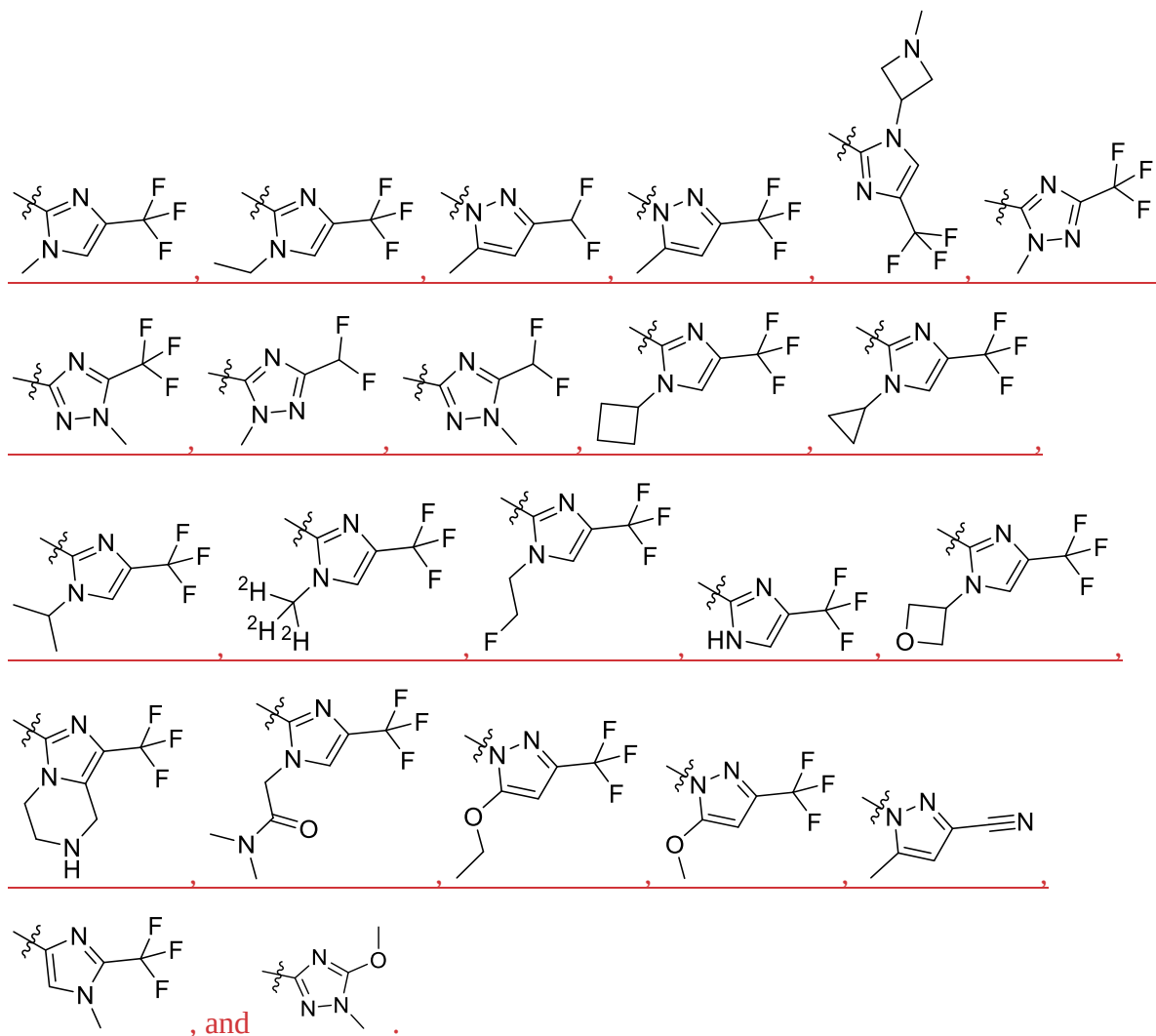




38. The compound of claim 34, wherein R⁵ is selected from the group consisting of:



39. The compound of claim 35, wherein R⁵ is selected from the group consisting of:



40.

~~64. A USP1 inhibitor for use in the treatment of cancer in a patient, wherein the cancer comprises cancer cells with a mutation in a gene encoding p53.~~

~~65. The USP1 inhibitor for use of claim 64, wherein the patient is identified to be responsive to the treatment with the USP1 inhibitor by detecting cancer cells with a mutation in a gene encoding p53 in a cancer sample obtained from the patient, wherein cancer cells with a mutation in a gene encoding p53 in the cancer sample identify the patient to be responsive to the treatment with an USP1 inhibitor.~~

~~66. — A USP1 inhibitor for use in the treatment of cancer in a subject identified to be responsive to the treatment with the USP1 inhibitor by cancer cells with a mutation in a gene encoding p53 in a cancer sample obtained from the subject, wherein cancer cells with a mutation in a gene encoding p53 in the cancer sample identify the patient to be responsive to the treatment with an USP1 inhibitor.~~

~~67. — The USP1 inhibitor for use of any of claims 64-66, wherein the USP1 inhibitor is not administered to a subject in case a mutation in a gene encoding p53 is not detected in a cancer sample obtained from the subject.~~

~~68. — An *in vitro* method for identifying a subject with cancer to be responsive to the treatment with an USP1 inhibitor, comprising detecting a mutation in a gene encoding p53 in a cancer sample obtained from the subject, wherein a mutation in a gene encoding p53 in the cancer sample is indicative for the patient to be responsive to the treatment with an USP1 inhibitor.~~

~~69. — An *in vitro* use of at least one agent capable of specifically detecting a mutation in a gene encoding p53, for identifying a subject with cancer to be responsive to the treatment with an USP1 inhibitor.~~

~~70. — The method, the USP1 inhibitor, or the use of any one of claims 60-69, where the mutation in the gene encoding p53 is a loss of function mutation.~~

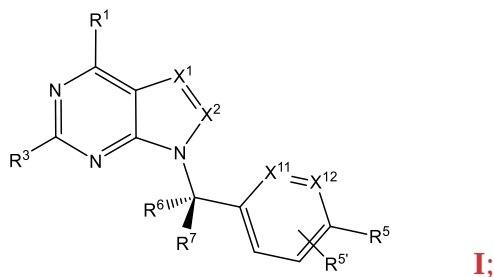
~~71. — The method, the USP1 inhibitor, or the use of any one of claims 60-70, wherein the cancer is a BRCA1 mutant cancer.~~

~~72. — The method, the USP1 inhibitor, or the use of any one of claims 60-71, wherein the cancer is a BRCA2 mutant cancer.~~

~~73. — The method, the USP1 inhibitor, or the use of any one of claims 60-72, wherein the cancer is a breast cancer.~~

~~74. — The method, the USP1 inhibitor, or the use of any one of claims 60-72, wherein the cancer is an ovarian cancer.~~

75. ~~The method, the USP1 inhibitor, or the use of any one of claims 60-74, wherein the USP1 inhibitor is the compound of any one of claims 1-29, A compound having Formula I:~~

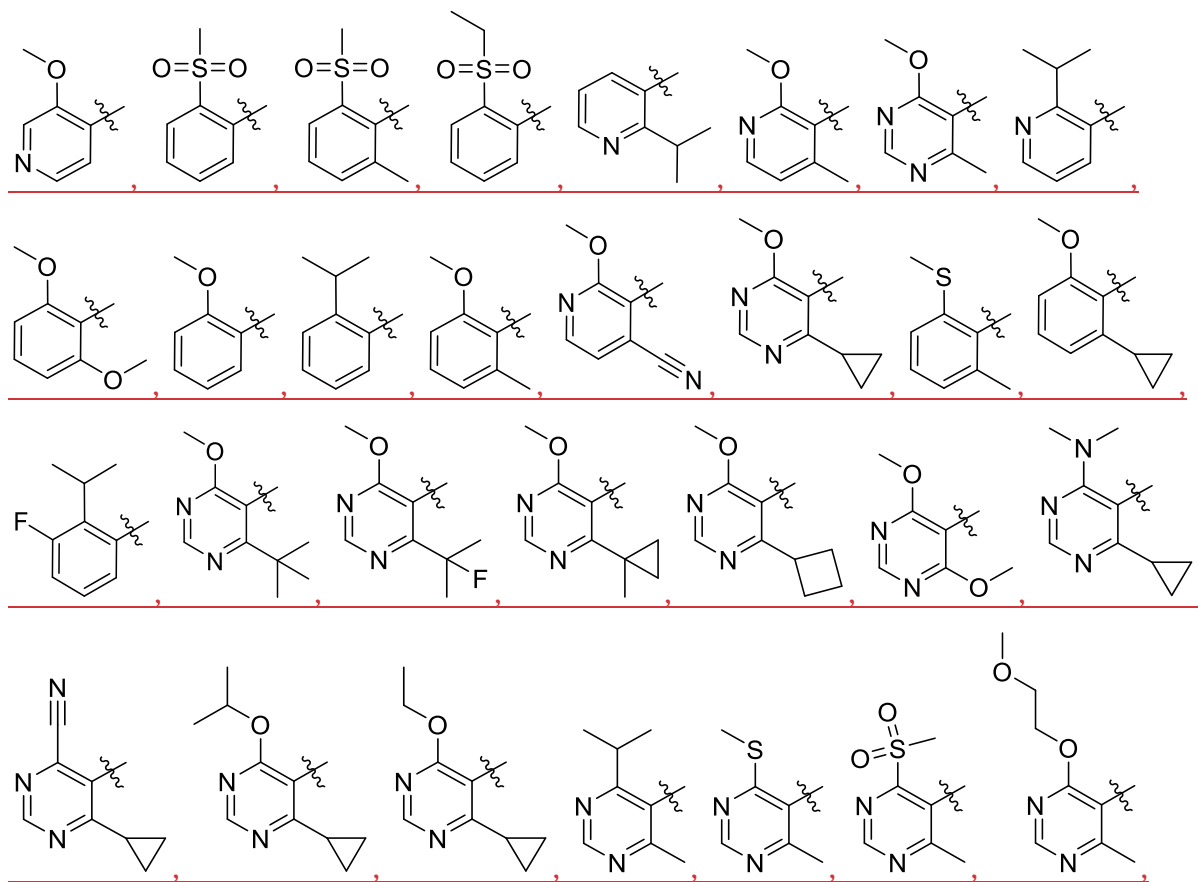


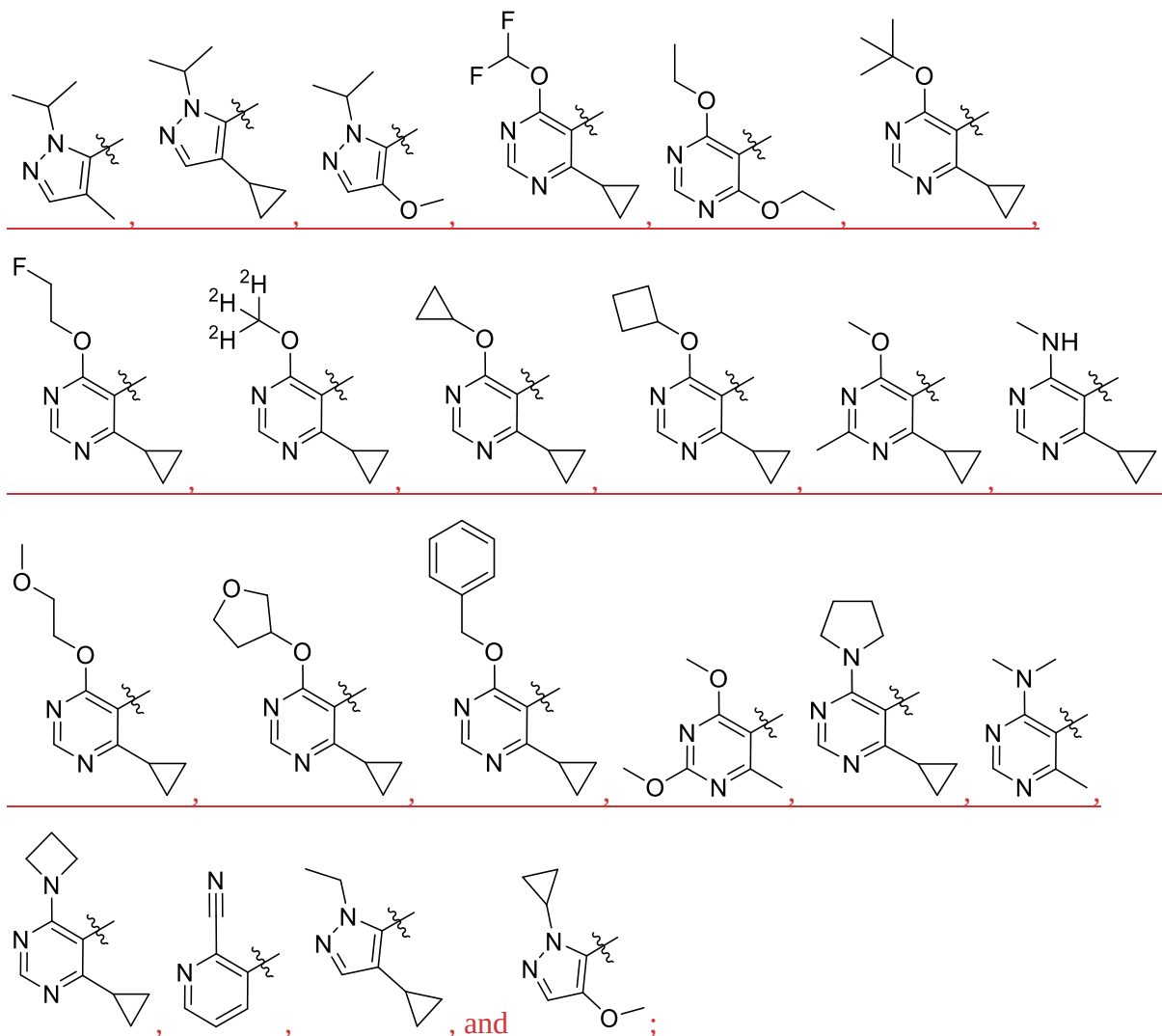
or a pharmaceutically acceptable salt or solvate thereof:

each of X¹ and X² is independently selected from N and CR²;

each of R¹ and R² is independently selected from hydrogen, halo, cyano, optionally substituted alkyl, optionally substituted alkenyl, and optionally substituted alkynyl;

R³ is selected from the group consisting of:





each of X^{11} and X^{12} is independently selected from N and CH;

$R^{5'}$ is selected from hydrogen, optionally substituted (C_1 - C_6) alkyl, optionally substituted (C_2 - C_6) alkenyl, optionally substituted (C_2 - C_6) alkynyl, optionally substituted (C_1 - C_6) alkoxy, (C_1 - C_6) haloalkyl, (C_1 - C_6) haloalkoxy, (C_1 - C_6) hydroxyalkyl, cyano, halo, sulfonamido, $-C(=O)R^{23}$, $-C(=O)OR^{24}$, $-NR^{32a}R^{32b}$, $-NR^{31a}C(=O)R^{25}$, $-NR^{31a}C(=O)NR^{31a}R^{31b}$, $-C(=O)NR^{31a}R^{31b}$, $-S(O)_2R^{27}$, $-NR^{31a}SO_2R^{27}$, optionally substituted (C_6 - C_{14}) aryl, optionally substituted (C_6 - C_{14}) ar-(C_1 - C_2) alkyl, optionally substituted heteroaryl, optionally substituted heteroar-(C_1 - C_2) alkyl, optionally substituted (C_3 - C_8) cycloalkyl, optionally substituted ((C_3 - C_8) cycloalkyl)-(C_1 - C_2) alkyl, optionally substituted heterocyclo, optionally substituted heterocyclo-(C_1 - C_2) alkyl, optionally substituted

$-O-(C_6-C_{14})$ aryl, optionally substituted $-O-(C_6-C_{14})$ ar-(C_1 - C_2) alkyl, optionally substituted

—O—heteroaryl, optionally substituted —O—heteroar-(C₁-C₂) alkyl, optionally substituted —O—(C₃-C₈) cycloalkyl, optionally substituted —O—((C₃-C₈) cycloalkyl)-(C₁-C₂) alkyl, optionally substituted —O—heterocyclo, optionally substituted —O—heterocyclo-(C₁-C₂) alkyl;

R⁵ is selected from optionally substituted (C₁-C₆) alkyl, optionally substituted (C₂-C₆) alkenyl, optionally substituted (C₂-C₆) alkynyl, optionally substituted (C₁-C₆) alkoxy, (C₁-C₆) haloalkyl, (C₁-C₆) haloalkoxy, (C₁-C₆) hydroxyalkyl, cyano, halo, sulfonamido, -C(=O)R²³, -C(=O)OR²⁴, -NR^{32a}R^{32b}, -NR^{31a}C(=O)R²⁵, -NR^{31a}C(=O)NR^{31a}R^{31b}, -C(=O)NR^{31a}R^{31b}, -S(O)₂R²⁷, -NR^{31a}SO₂R²⁷, optionally substituted (C₆-C₁₄) aryl, optionally substituted (C₆-C₁₄) ar-(C₁-C₂) alkyl, optionally substituted heteroaryl, optionally substituted heteroar-(C₁-C₂) alkyl, optionally substituted (C₃-C₈) cycloalkyl, optionally substituted ((C₃-C₈) cycloalkyl)-(C₁-C₂) alkyl, optionally substituted heterocyclo, optionally substituted heterocyclo-(C₁-C₂) alkyl, optionally substituted —O—(C₆-C₁₄) aryl, optionally substituted —O—(C₆-C₁₄) ar-(C₁-C₂) alkyl, optionally substituted —O—heteroaryl, optionally substituted —O—heteroar-(C₁-C₂) alkyl, optionally substituted —O—(C₃-C₈) cycloalkyl, optionally substituted —O—((C₃-C₈) cycloalkyl)-(C₁-C₂) alkyl, optionally substituted —O—heterocyclo, optionally substituted —O—heterocyclo-(C₁-C₂) alkyl; or

one of R⁵ and one of R^{5'} on adjacent atoms are taken together with the atoms to which they are attached to form an optionally substituted (C₆-C₁₄) aryl ring; or one of R⁵ and one of R^{5'} on adjacent atoms are taken together with the atoms to which they are attached to form an optionally substituted heteroaryl ring; or one of R⁵ and one of R^{5'} on adjacent atoms are taken together with the atoms to which they are attached to form an optionally substituted (C₃-C₈) cycloalkyl ring; or one of R⁵ and one of R^{5'} on adjacent atoms are taken together with the atoms to which they are attached to form an optionally substituted heterocycloalkyl ring; or one of R⁵ and one of R^{5'} on adjacent atoms on the same atom to which they are attached are taken together to form an optionally substituted spirocycloalkyl ring; or one of R⁵ and one of R^{5'} on adjacent atoms on the same atom to which they are attached are taken together to form an optionally substituted spiroheterocycloalkyl ring;

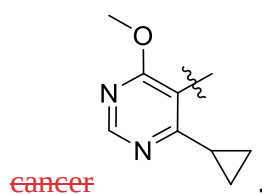
each of R⁶ and R⁷ is independently selected from hydrogen, halo, cyano, optionally substituted alkyl, optionally substituted alkenyl, and optionally substituted alkynyl;

R²³ is selected from the group consisting of hydrogen, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, amino, alkylamino, dialkylamino, cycloalkylamino, hydroxyalkyl, (amino)alkyl, (alkylamino)alkyl, (dialkylamino)alkyl, (cycloalkylamino)alkyl, (cycloalkyl)alkyl, aralkyl, (heterocyclo)alkyl, (heteroaryl)alkyl, (amino)(hydroxy)alkyl, (aralkylamino)alkyl, optionally substituted heterocyclo, optionally substituted heteroaryl, optionally substituted aryl, and optionally substituted cycloalkyl;

R^{31a} and R^{31b} are each independently selected from the group consisting of hydrogen, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, hydroxyalkyl, (amino)alkyl, (alkylamino)alkyl, (dialkylamino)alkyl, alkoxyalkyl, cycloalkyl, (cycloalkyl)alkyl, (heterocyclo)alkyl, aralkyl, and (heteroaryl)alkyl; and

each of R²⁴, R²⁵, R²⁷, R^{32a}, and R^{32b} is independently selected from the group consisting of hydrogen, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, amino, alkylamino, dialkylamino, cycloalkylamino, hydroxyalkyl, (amino)alkyl, (alkylamino)alkyl, (dialkylamino)alkyl, (cycloalkylamino)alkyl, (cycloalkyl)alkyl, aralkyl, (heterocyclo)alkyl, (heteroaryl)alkyl, (amino)(hydroxy)alkyl, (aralkylamino)alkyl, alkoxyalkyl, optionally substituted heterocyclo, optionally substituted heteroaryl, optionally substituted aryl, and optionally substituted cycloalkyl.

41. 76.—~~The method, pharmaceutical composition, compound, use, or the kit of claim 5440, wherein the BRCA1 or BRCA2 mutant cancer~~R³ ~~is a BRCA1 or BRCA2 deficient~~



42.

~~77.~~—~~A method of treating cancer in a patient comprising administering to the subject a USP1 inhibitor, wherein the cancer comprises cancer cells with a mutation in a gene encoding BRCA1.~~

~~78.~~—~~The method of claim 77, wherein the mutation in a gene encoding BRCA1 has been detected prior to the administration.~~

~~79.—The method of claim 77 or 78, further comprising detecting the mutation in the gene encoding BRCA1 in a cancer sample obtained from the patient.~~

~~80.—A method of selecting a patient with cancer for treatment with a USP1 inhibitor, comprising detecting whether the cancer comprises cancer cells with a mutation in a gene encoding BRCA1, wherein if the cancer comprises cancer cells with a mutation in a gene encoding BRCA1, the patient is selected for treatment with a USP1 inhibitor.~~

~~81.—A USP1 inhibitor for use in the treatment of cancer in a patient, wherein the cancer comprises cancer cells with a mutation in a gene encoding BRCA1.~~

~~82.—The USP1 inhibitor for use of claim 81, wherein the patient is identified to be responsive to the treatment with the USP1 inhibitor by detecting cancer cells with a mutation in a gene encoding BRCA1 in a cancer sample obtained from the patient, wherein cancer cells with a mutation in a gene encoding BRCA1 in the cancer sample identify the patient to be responsive to the treatment with an USP1 inhibitor.~~

~~83.—A USP1 inhibitor for use in the treatment of cancer in a subject identified to be responsive to the treatment with the USP1 inhibitor by cancer cells with a mutation in a gene encoding BRCA1 in a cancer sample obtained from the subject, wherein cancer cells with a mutation in a gene encoding BRCA1 in the cancer sample identify the patient to be responsive to the treatment with an USP1 inhibitor.~~

~~84.—A method of treating cancer in a patient comprising administering to the subject a USP1 inhibitor, wherein the cancer comprises cancer cells with a mutation in a gene encoding BRCA2.~~

~~85.—The method of claim 84, wherein the mutation in a gene encoding BRCA2 has been detected prior to the administration.~~

~~86.—The method of claim 84 or 85, further comprising detecting the mutation in the gene encoding BRCA2 in a cancer sample obtained from the patient.~~

~~87.— A method of selecting a patient with cancer for treatment with a USP1 inhibitor, comprising detecting whether the cancer comprises cancer cells with a mutation in a gene encoding BRCA2, wherein if the cancer comprises cancer cells with a mutation in a gene encoding BRCA2, the patient is selected for treatment with a USP1 inhibitor.~~

~~88.— A USP1 inhibitor for use in the treatment of cancer in a patient, wherein the cancer comprises cancer cells with a mutation in a gene encoding BRCA2.~~

~~89.— The USP1 inhibitor for use of claim 88, wherein the patient is identified to be responsive to the treatment with the USP1 inhibitor by detecting cancer cells with a mutation in a gene encoding BRCA2 in a cancer sample obtained from the patient, wherein cancer cells with a mutation in a gene encoding BRCA2 in the cancer sample identify the patient to be responsive to the treatment with an USP1 inhibitor.~~

~~90.— A USP1 inhibitor for use in the treatment of cancer in a subject identified to be responsive to the treatment with the USP1 inhibitor by cancer cells with a mutation in a gene encoding BRCA2 in a cancer sample obtained from the subject, wherein cancer cells with a mutation in a gene encoding BRCA2 in the cancer sample identify the patient to be responsive to the treatment with an USP1 inhibitor.~~

~~91.— A method of treating cancer in a patient comprising administering to the subject a USP1 inhibitor, wherein the cancer comprises cancer cells with a mutation in a gene encoding ATM.~~

~~92.— The method of claim 91, wherein the mutation in a gene encoding ATM has been detected prior to the administration.~~

~~93.— The method of claim 91 or 92, further comprising detecting the mutation in the gene encoding ATM in a cancer sample obtained from the patient.~~

~~94.— A method of selecting a patient with cancer for treatment with a USP1 inhibitor, comprising detecting whether the cancer comprises cancer cells with a mutation in a gene encoding ATM, wherein if the cancer comprises cancer cells with a mutation in a gene encoding ATM, the patient is selected for treatment with a USP1 inhibitor.~~

95. — ~~A USP1 inhibitor for use in the treatment of cancer in a patient, wherein the cancer comprises cancer cells with a mutation in a gene encoding ATM.~~

96. — ~~The USP1 inhibitor for use of claim 95, wherein the patient is identified to be responsive to the treatment with the USP1 inhibitor by detecting cancer cells with a mutation in a gene encoding ATM in a cancer sample obtained from the patient, wherein cancer cells with a mutation in a gene encoding ATM in the cancer sample identify the patient to be responsive to the treatment with an USP1 inhibitor.~~

97. — ~~A USP1 inhibitor for use in the treatment of cancer in a subject identified to be responsive to the treatment with the USP1 inhibitor by cancer cells with a mutation in a gene encoding ATM in a cancer sample obtained from the subject, wherein cancer cells with a mutation in a gene encoding ATM in the cancer sample identify the patient to be responsive to the treatment with an USP1 inhibitor.~~

98. — ~~A method of treating cancer in a patient comprising administering to the subject a USP1 inhibitor, wherein the cancer comprises cancer cells with a mutation in one or more genes encoding at least two of p53, BRCA1, BRCA2, and ATM.~~

99. — ~~The method of claim 98, wherein the mutation in one or more genes encoding at least two of p53, BRCA1, BRCA2, and ATM has been detected prior to the administration.~~

100. — ~~The method of claim 98 or 99, further comprising detecting the mutation in one or more genes encoding at least two of p53, BRCA1, BRCA2, and ATM in a cancer sample obtained from the patient.~~

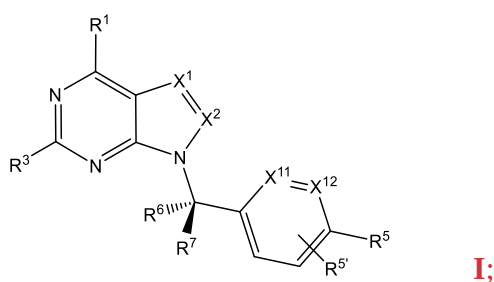
101. — ~~A method of selecting a patient with cancer for treatment with a USP1 inhibitor, comprising detecting whether the cancer comprises cancer cells with a mutation in one or more genes encoding at least two of p53, BRCA1, BRCA2, and ATM, wherein if the cancer comprises cancer cells with a mutation in one or more genes encoding at least two of p53, BRCA1, BRCA2, and ATM, the patient is selected for treatment with a USP1 inhibitor.~~

~~102. A USP1 inhibitor for use in the treatment of cancer in a patient, wherein the cancer comprises cancer cells with a mutation in one or more genes encoding at least two of p53, BRCA1, BRCA2, and ATM.~~

~~103. The USP1 inhibitor for use of claim 102, wherein the patient is identified to be responsive to the treatment with the USP1 inhibitor by detecting cancer cells with a mutation in one or more genes encoding at least two of p53, BRCA1, BRCA2, and ATM in a cancer sample obtained from the patient, wherein cancer cells with a mutation in one or more genes encoding at least two of p53, BRCA1, BRCA2, and ATM in the cancer sample identify the patient to be responsive to the treatment with an USP1 inhibitor.~~

~~104. A USP1 inhibitor for use in the treatment of cancer in a subject identified to be responsive to the treatment with the USP1 inhibitor by cancer cells with a mutation in one or more genes encoding at least two of p53, BRCA1, BRCA2, and ATM in a cancer sample obtained from the subject, wherein cancer cells with a mutation in one or more genes encoding at least two of p53, BRCA1, BRCA2, and ATM in the cancer sample identify the patient to be responsive to the treatment with an USP1 inhibitor.~~

~~105. The method or the USP1 inhibitor of any one of claims 77-104, wherein the USP1 inhibitor is the compound of any one of claims 1-29, A compound having Formula I:~~



or a pharmaceutically acceptable salt or solvate thereof, wherein:

each of X¹ and X² is independently selected from N and CR²;

each of R¹ and R² is independently selected from hydrogen, halo, cyano, optionally substituted alkyl, optionally substituted alkenyl, and optionally substituted alkynyl;

R³ is an optionally substituted phenyl, optionally substituted pyridyl, optionally substituted pyrimidinyl, optionally substituted pyrazinyl, optionally substituted pyridazinyl, or optionally substituted pyrazolyl;

each of X¹¹ and X¹² is independently selected from N and CH;

R^{5'} is selected from hydrogen, optionally substituted (C₁-C₆) alkyl, optionally substituted (C₂-C₆) alkenyl, optionally substituted (C₂-C₆) alkynyl, optionally substituted (C₁-C₆) alkoxy, (C₁-C₆) haloalkyl, (C₁-C₆) haloalkoxy, (C₁-C₆) hydroxyalkyl, cyano, halo, sulfonamido, -C(=O)R²³, -C(=O)OR²⁴, -NR^{32a}R^{32b}, -NR^{31a}C(=O)R²⁵, -NR^{31a}C(=O)NR^{31a}R^{31b}, -C(=O)NR^{31a}R^{31b}, -S(O)₂R²⁷,

-NR^{31a}SO₂R²⁷, optionally substituted (C₆-C₁₄) aryl, optionally substituted (C₆-C₁₄) ar-(C₁-C₂) alkyl, optionally substituted heteroaryl, optionally substituted heteroar-(C₁-C₂) alkyl, optionally substituted (C₃-C₈) cycloalkyl, optionally substituted ((C₃-C₈) cycloalkyl)-(C₁-C₂) alkyl, optionally substituted heterocyclo, optionally substituted heterocyclo-(C₁-C₂) alkyl, optionally substituted

—O—(C₆-C₁₄) aryl, optionally substituted —O—(C₆-C₁₄) ar-(C₁-C₂) alkyl, optionally substituted —O—heteroaryl, optionally substituted —O—heteroar-(C₁-C₂) alkyl, optionally substituted —O—(C₃-C₈) cycloalkyl, optionally substituted —O—((C₃-C₈) cycloalkyl)-(C₁-C₂) alkyl, optionally substituted —O—heterocyclo, optionally substituted —O—heterocyclo-(C₁-C₂) alkyl;

R⁵ is selected from optionally substituted (C₆-C₁₄) aryl, optionally substituted (C₆-C₁₄) ar-(C₁-C₂) alkyl, optionally substituted heteroaryl, optionally substituted heteroar-(C₁-C₂) alkyl, optionally substituted (C₃-C₈) cycloalkyl, optionally substituted ((C₃-C₈) cycloalkyl)-(C₁-C₂) alkyl, optionally substituted heterocyclo, optionally substituted heterocyclo-(C₁-C₂) alkyl;

each of R⁶ and R⁷ is independently selected from hydrogen, halo, cyano, optionally substituted alkyl, optionally substituted alkenyl, and optionally substituted alkynyl;

R²³ is selected from the group consisting of hydrogen, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, amino, alkylamino, dialkylamino, cycloalkylamino, hydroxyalkyl, (amino)alkyl, (alkylamino)alkyl, (dialkylamino)alkyl, (cycloalkylamino)alkyl, (cycloalkyl)alkyl, aralkyl, (heterocyclo)alkyl, (heteroaryl)alkyl,

(amino)(hydroxy)alkyl, (aralkylamino)alkyl, optionally substituted heterocyclo, optionally substituted heteroaryl, optionally substituted aryl, and optionally substituted cycloalkyl;

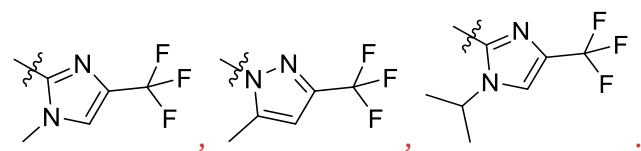
R^{31a} and R^{31b} are each independently selected from the group consisting of hydrogen, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, hydroxyalkyl, (amino)alkyl, (alkylamino)alkyl, (dialkylamino)alkyl, alkoxyalkyl, cycloalkyl, (cycloalkyl)alkyl, (heterocyclo)alkyl, aralkyl, and (heteroaryl)alkyl; and

each of R²⁴, R²⁵, R²⁷, R^{32a}, and R^{32b} is independently selected from the group consisting of hydrogen, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, amino, alkylamino, dialkylamino, cycloalkylamino, hydroxyalkyl, (amino)alkyl, (alkylamino)alkyl, (dialkylamino)alkyl, (cycloalkylamino)alkyl, (cycloalkyl)alkyl, aralkyl, (heterocyclo)alkyl, (heteroaryl)alkyl, (amino)(hydroxy)alkyl, (aralkylamino)alkyl, alkoxyalkyl, optionally substituted heterocyclo, optionally substituted heteroaryl, optionally substituted aryl, and optionally substituted cycloalkyl.

43. ~~106.~~—A method of treating a triple negative breast cancer in a subject comprising administering to the subject a USP1 inhibitor.

~~107.—A USP1 inhibitor for use in the treatment of triple negative breast cancer in a subject.~~

~~108.—The method or USP1 inhibitor compound of claim 106 or 107~~42, wherein ~~the cancer is a BRCA2 mutant cancer.~~R⁵ is selected from the group consisting of:



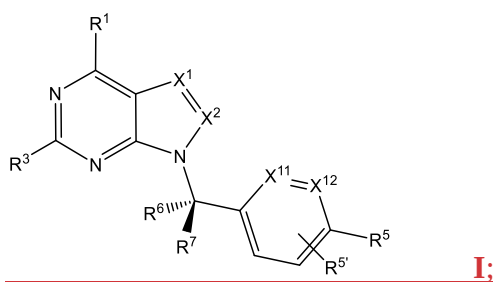
44.

~~109.—The method or USP1 inhibitor compound of claim 106 or 107~~43, wherein ~~the cancer is a~~

BRCA1 mutant cancer.R⁵ is

The image shows a chemical structure of an imidazole derivative, which is the same as the third structure in the previous block: an imidazole ring with a trifluoromethyl group (-CF₃) at the 2-position and a wavy bond at the 1-position, with an isopropyl group at the 4-position.

~~110. The method 45.~~ A compound having Formula I:



~~or USP1 inhibitor of claim 106a pharmaceutically acceptable salt or 107solvate thereof, wherein the cancer is a BRCA1 mutant cancer;~~

~~each of X¹ and a BRCA2 mutant cancer.~~ X² is independently selected from N and CR²;

~~111. The method or USP1 inhibitor of any one of claims 106-110, wherein the cancer comprises cancer cells with a mutation in a gene encoding p53, optionally wherein the mutation in the gene encoding p53 is a loss of function mutation.~~

~~each of R¹ and R² is independently selected from hydrogen, halo, cyano, optionally substituted alkyl, optionally substituted alkenyl, and optionally substituted alkynyl;~~

~~R³ is an optionally substituted phenyl, optionally substituted pyridyl, optionally substituted pyrimidinyl, optionally substituted pyrazinyl, optionally substituted pyridazinyl, or optionally substituted pyrazolyl;~~

~~each of X¹¹ and X¹² is independently selected from N and CH;~~

~~R^{5'} is selected from hydrogen, optionally substituted (C₁-C₆) alkyl, optionally substituted (C₂-C₆) alkenyl, optionally substituted (C₂-C₆) alkynyl, optionally substituted (C₁-C₆) alkoxy, (C₁-C₆) haloalkyl, (C₁-C₆) haloalkoxy, (C₁-C₆) hydroxyalkyl, cyano, halo, sulfonamido, -C(=O)R²³, -C(=O)OR²⁴, -NR^{32a}R^{32b}, -NR^{31a}C(=O)R²⁵, -NR^{31a}C(=O)NR^{31a}R^{31b}, -C(=O)NR^{31a}R^{31b}, -S(O)₂R²⁷, -NR^{31a}SO₂R²⁷, optionally substituted (C₆-C₁₄) aryl, optionally substituted (C₆-C₁₄) ar-(C₁-C₂) alkyl, optionally substituted heteroaryl, optionally substituted heteroar-(C₁-C₂) alkyl, optionally~~

substituted (C₃-C₈) cycloalkyl, optionally substituted ((C₃-C₈) cycloalkyl)-(C₁-C₂) alkyl, optionally substituted heterocyclo, optionally substituted heterocyclo-(C₁-C₂) alkyl, optionally substituted

—O—(C₆-C₁₄) aryl, optionally substituted —O—(C₆-C₁₄) ar-(C₁-C₂) alkyl, optionally substituted —O—heteroaryl, optionally substituted —O—heteroar-(C₁-C₂) alkyl, optionally substituted —O—(C₃-C₈) cycloalkyl, optionally substituted —O—((C₃-C₈) cycloalkyl)-(C₁-C₂) alkyl, optionally substituted —O—heterocyclo, optionally substituted —O—heterocyclo-(C₁-C₂) alkyl;

R⁵ is an optionally substituted pyrrolyl, optionally substituted imidazolyl, optionally substituted pyrazolyl, optionally substituted triazolyl, or optionally substituted tetrazolyl;

each of R⁶ and R⁷ is independently selected from hydrogen, halo, cyano, optionally substituted alkyl, optionally substituted alkenyl, and optionally substituted alkynyl;

R²³ is selected from the group consisting of hydrogen, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, amino, alkylamino, dialkylamino, cycloalkylamino, hydroxyalkyl, (amino)alkyl, (alkylamino)alkyl, (dialkylamino)alkyl, (cycloalkylamino)alkyl, (cycloalkyl)alkyl, aralkyl, (heterocyclo)alkyl, (heteroaryl)alkyl, (amino)(hydroxy)alkyl, (aralkylamino)alkyl, optionally substituted heterocyclo, optionally substituted heteroaryl, optionally substituted aryl, and optionally substituted cycloalkyl;

R^{31a} and R^{31b} are each independently selected from the group consisting of hydrogen, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, hydroxyalkyl, (amino)alkyl, (alkylamino)alkyl, (dialkylamino)alkyl, alkoxyalkyl, cycloalkyl, (cycloalkyl)alkyl, (heterocyclo)alkyl, aralkyl, and (heteroaryl)alkyl; and

each of R²⁴, R²⁵, R²⁷, R^{32a}, and R^{32b} is independently selected from the group consisting of hydrogen, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkynyl, amino, alkylamino, dialkylamino, cycloalkylamino, hydroxyalkyl, (amino)alkyl, (alkylamino)alkyl, (dialkylamino)alkyl, (cycloalkylamino)alkyl, (cycloalkyl)alkyl, aralkyl, (heterocyclo)alkyl, (heteroaryl)alkyl, (amino)(hydroxy)alkyl, (aralkylamino)alkyl, alkoxyalkyl, optionally substituted heterocyclo, optionally substituted heteroaryl, optionally substituted aryl, and optionally substituted cycloalkyl.