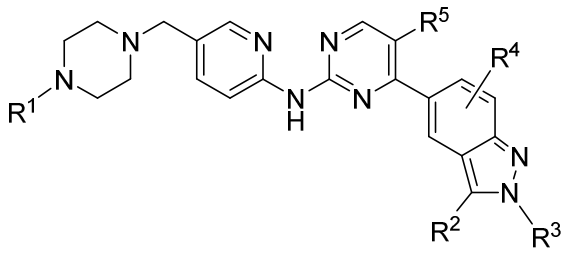
CLAIMS

What is claimed is:

1. A compound of formula (I)



(I)

or a pharmaceutically acceptable salt, solvate, or prodrug thereof, wherein:

R^1 is hydrogen, C_1-C_8 alkyl, or C_3-C_7 cycloalkyl;

R^2 and R^3 are each independently hydrogen, C_1-C_8 alkyl, C_3-C_7 cycloalkyl, or C_3-C_7 cycloalkylmethyl;

R^4 is hydrogen, halogen, C_1-C_8 alkyl, or C_3-C_7 cycloalkyl; and

R^5 is hydrogen or halogen.

2. The compound of claim 0, or a pharmaceutically acceptable salt, solvate, or prodrug thereof, wherein R^1 is C_1-C_6 alkyl.

3. The compound of claim 0, or a pharmaceutically acceptable salt, solvate, or prodrug thereof, wherein R^1 is methyl, ethyl, propyl, or isopropyl.

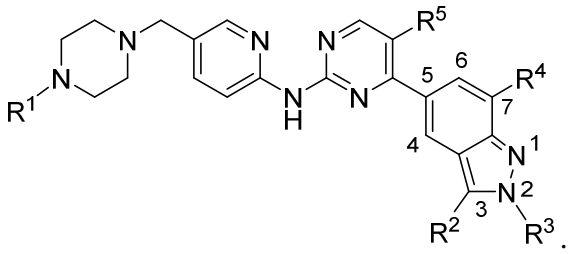
4. The compound of claim 2, or a pharmaceutically acceptable salt, solvate, or prodrug thereof, wherein R^2 is C_1-C_6 alkyl, C_3-C_6 cycloalkyl, or C_3-C_6 cycloalkylmethyl.

5. The compound of claim 3, or a pharmaceutically acceptable salt, solvate, or prodrug thereof, wherein R^2 is methyl, ethyl, propyl, isopropyl, cyclopropyl, cyclopentyl, cyclopropylmethyl, or cyclopentylmethyl.

6. The compound of claim 4, or a pharmaceutically acceptable salt, solvate, or prodrug thereof, wherein R^3 is C_1-C_6 alkyl or C_3-C_6 cycloalkyl.

7. The compound of claim 5, or a pharmaceutically acceptable salt, solvate, or prodrug thereof, wherein R^3 is methyl, ethyl, propyl, isopropyl, or cyclopropyl.

8. The compound of claim 0, or a pharmaceutically acceptable salt, solvate, or prodrug thereof, wherein R^4 is located at the 7-position of the indazole ring, characterized by formula Ia:



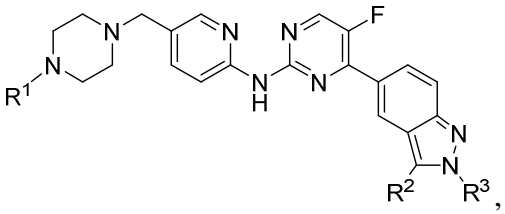
(Ia)

9. The compound of claim 8, or a pharmaceutically acceptable salt, solvate, or prodrug thereof, wherein R^4 is hydrogen or halogen.

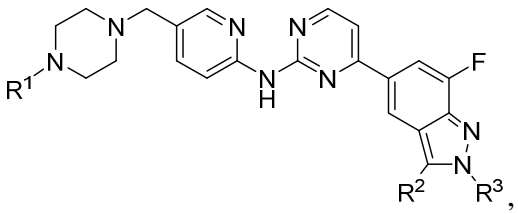
10. The compound of claim 0, or a pharmaceutically acceptable salt, solvate, or prodrug thereof, wherein R^5 is hydrogen or fluoro.

11. The compound of claim 8, or a pharmaceutically acceptable salt, solvate, or prodrug thereof, wherein R^1 is methyl or ethyl; R^2 is isopropyl, cyclopropyl, cyclopropylmethyl, or cyclopentyl; R^3 is methyl or ethyl; R^4 is hydrogen or fluoro; and R^5 is hydrogen or fluoro.

12. The compound of claim 6, or a pharmaceutically acceptable salt, solvate, or prodrug thereof, selected from the group consisting of:

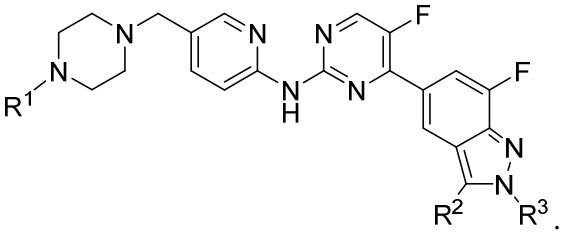


(Ic)



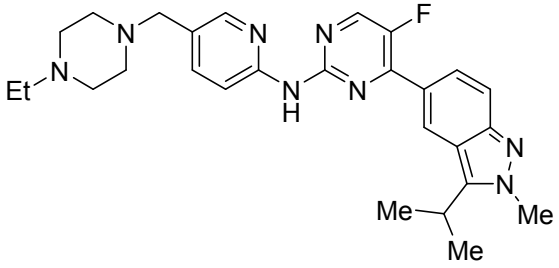
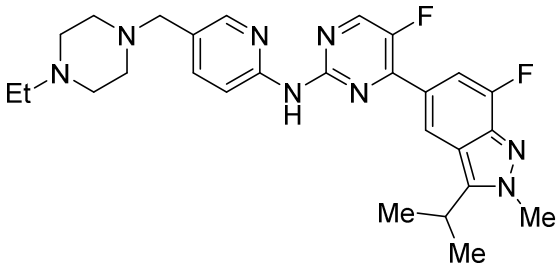
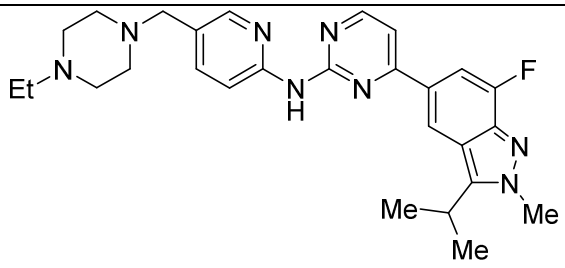
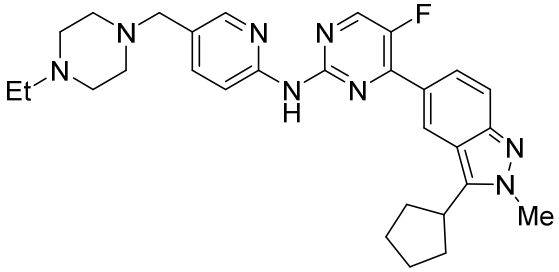
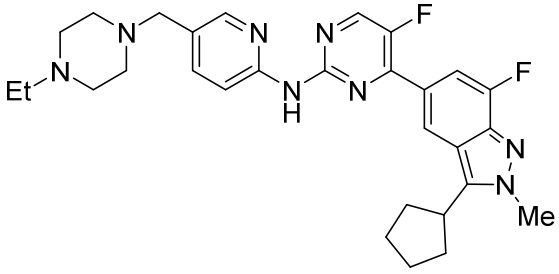
(Id)

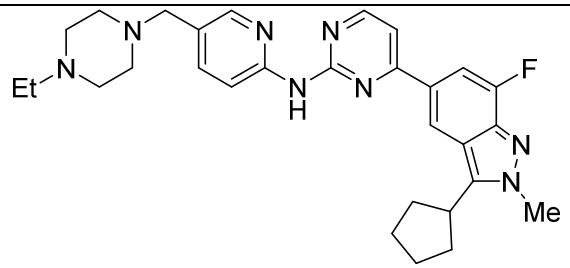
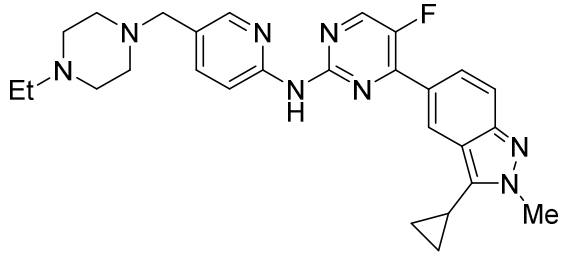
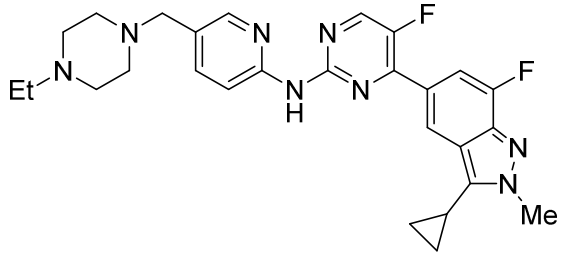
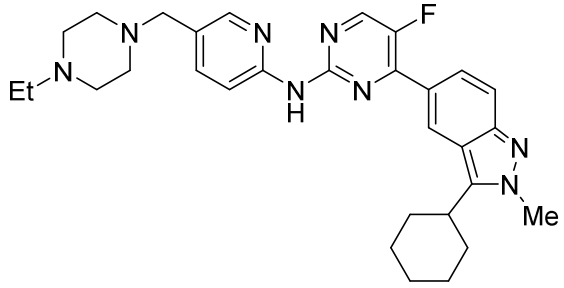
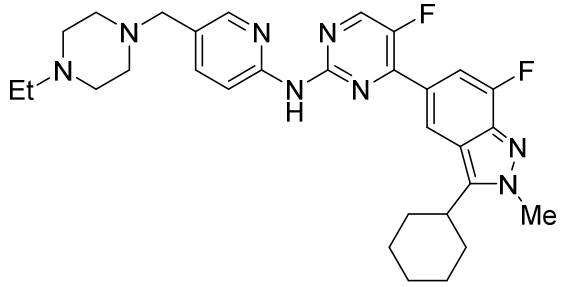
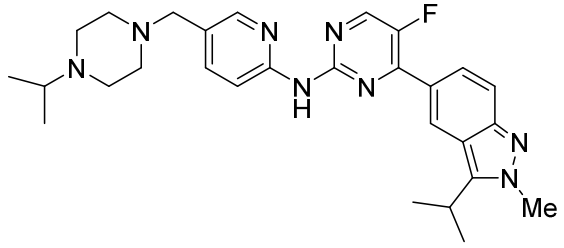
and

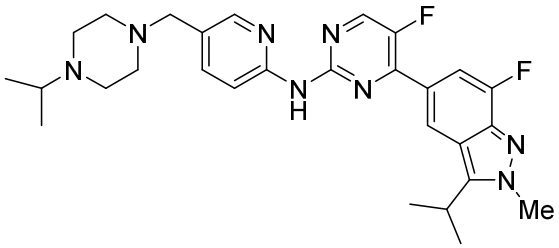
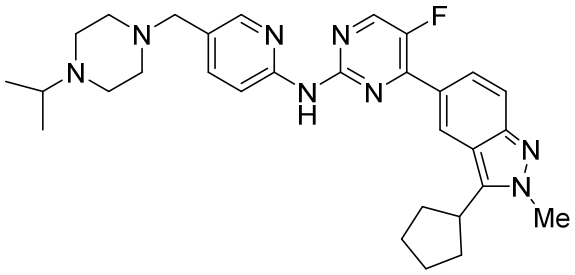
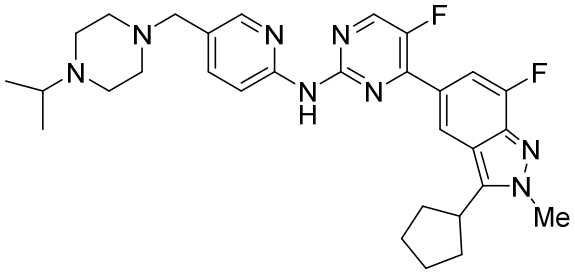
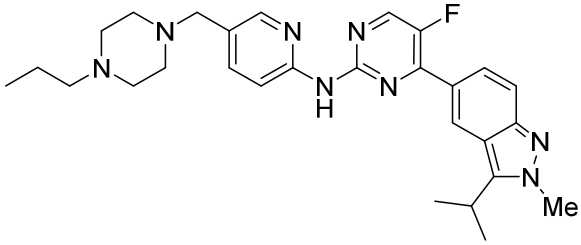
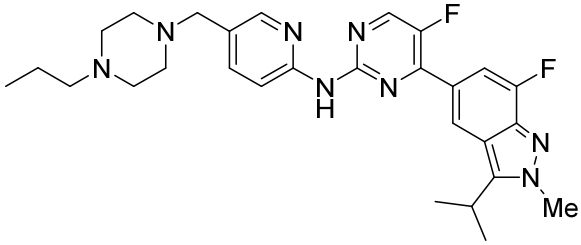
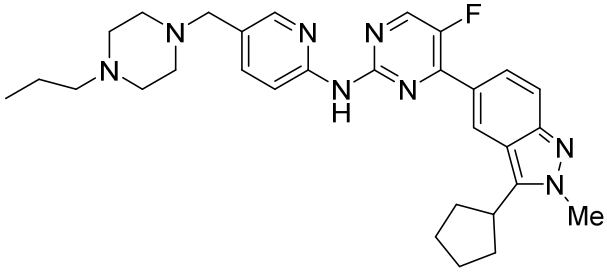


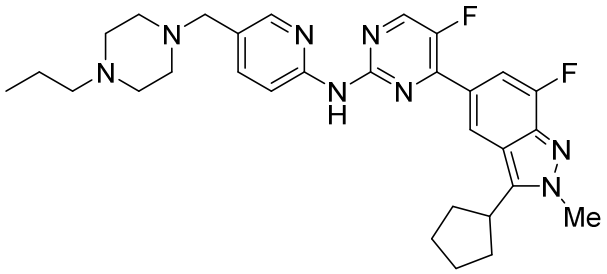
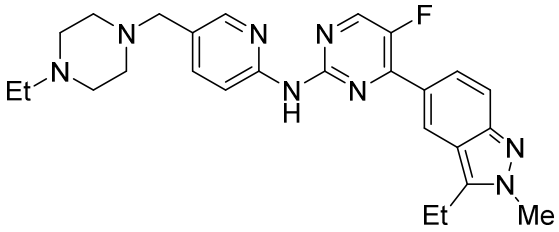
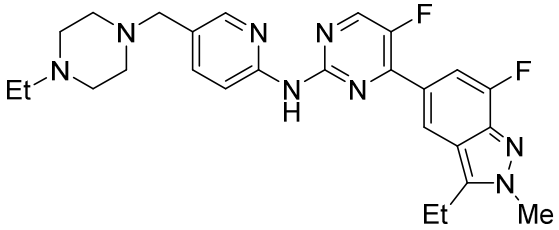
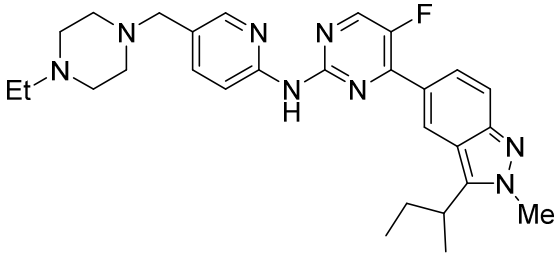
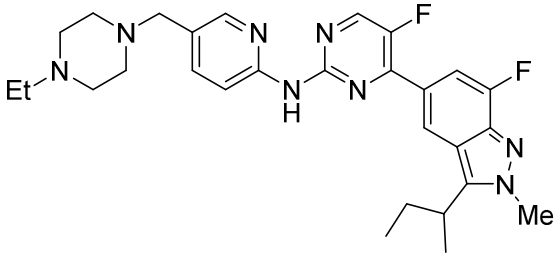
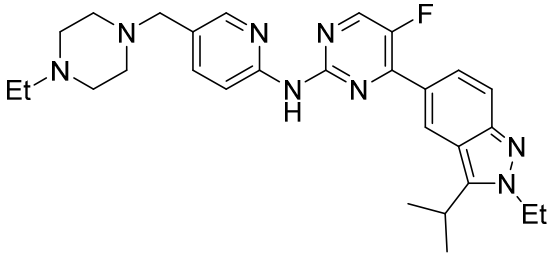
(Ie)

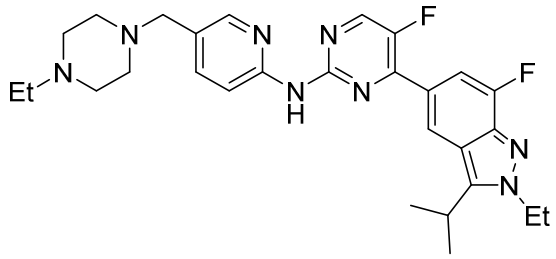
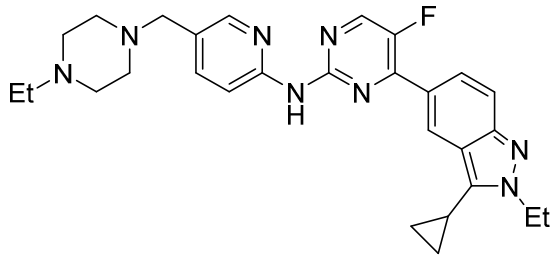
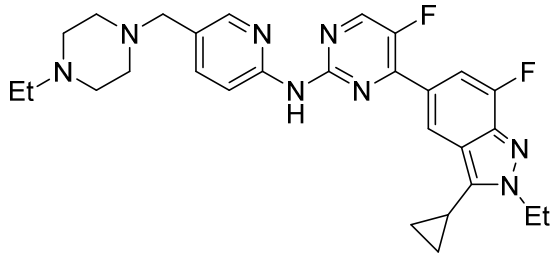
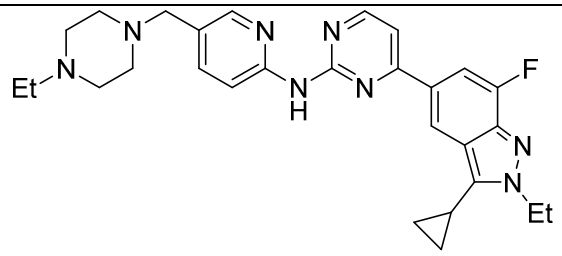
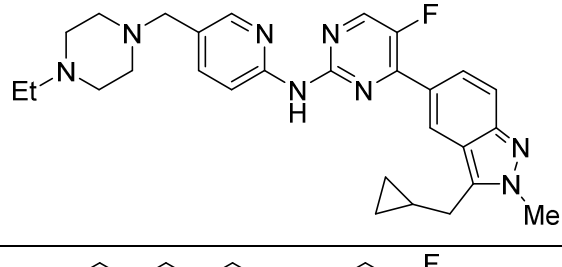
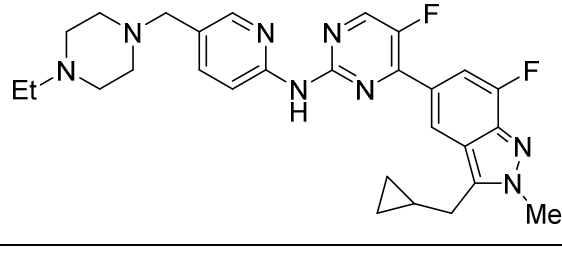
13. The compound of claim 0, or a pharmaceutically acceptable salt, solvate, or prodrug thereof, selected from the list in the table below:

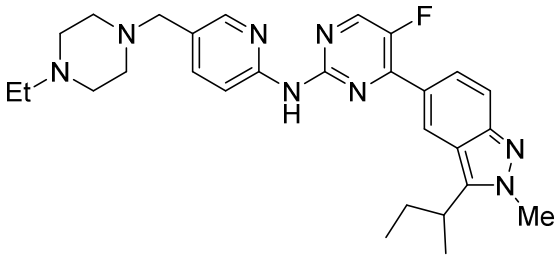
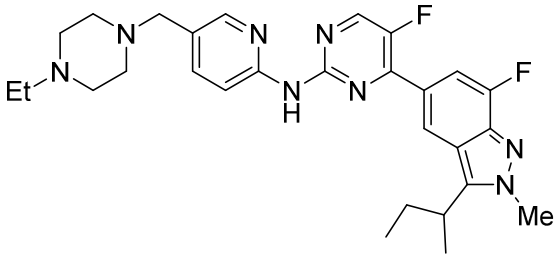
Compound No.	**Structure**	**Name**
1		*N*-(5-((4-ethylpiperazin-1-yl)methyl)pyridin-2-yl)-5-fluoro-4-(3-isopropyl-2-methyl-2H-indazol-5-yl)pyrimidin-2-amine
2		*N*-(5-((4-ethylpiperazin-1-yl)methyl)pyridin-2-yl)-5-fluoro-4-(7-fluoro-3-isopropyl-2-methyl-2H-indazol-5-yl)pyrimidin-2-amine
3		*N*-(5-((4-ethylpiperazin-1-yl)methyl)pyridin-2-yl)-4-(7-fluoro-3-isopropyl-2-methyl-2H-indazol-5-yl)pyrimidin-2-amine
4		4-(3-cyclopentyl-2-methyl-2H-indazol-5-yl)-*N*-(5-((4-ethylpiperazin-1-yl)methyl)pyridin-2-yl)-5-fluoropyrimidin-2-amine
5		4-(3-cyclopentyl-7-fluoro-2-methyl-2H-indazol-5-yl)-*N*-(5-((4-ethylpiperazin-1-yl)methyl)pyridin-2-yl)-5-fluoropyrimidin-2-amine

6		4-(3-cyclopentyl-7-fluoro-2-methyl-2H-indazol-5-yl)-*N*-(5-((4-ethylpiperazin-1-yl)methyl)pyridin-2-yl)pyrimidin-2-amine
7		4-(3-cyclopropyl-2-methyl-2H-indazol-5-yl)-*N*-(5-((4-ethylpiperazin-1-yl)methyl)pyridin-2-yl)-5-fluoropyrimidin-2-amine
8		4-(3-cyclopropyl-7-fluoro-2-methyl-2H-indazol-5-yl)-*N*-(5-((4-ethylpiperazin-1-yl)methyl)pyridin-2-yl)-5-fluoropyrimidin-2-amine
9		4-(3-cyclohexyl-2-methyl-2H-indazol-5-yl)-*N*-(5-((4-ethylpiperazin-1-yl)methyl)pyridin-2-yl)-5-fluoropyrimidin-2-amine
10		4-(3-cyclohexyl-7-fluoro-2-methyl-2H-indazol-5-yl)-*N*-(5-((4-ethylpiperazin-1-yl)methyl)pyridin-2-yl)-5-fluoropyrimidin-2-amine
11		5-fluoro-4-(3-isopropyl-2-methyl-2H-indazol-5-yl)-*N*-(5-((4-isopropylpiperazin-1-yl)methyl)pyridin-2-yl)pyrimidin-2-amine

12		5-fluoro-4-(7-fluoro-3-isopropyl-2-methyl-2H-indazol-5-yl)-*N*-(5-((4-isopropylpiperazin-1-yl)methyl)pyridin-2-yl)pyrimidin-2-amine
13		4-(3-cyclopentyl-2-methyl-2H-indazol-5-yl)-5-fluoro-*N*-(5-((4-isopropylpiperazin-1-yl)methyl)pyridin-2-yl)pyrimidin-2-amine
14		4-(3-cyclopentyl-7-fluoro-2-methyl-2H-indazol-5-yl)-5-fluoro-*N*-(5-((4-isopropylpiperazin-1-yl)methyl)pyridin-2-yl)pyrimidin-2-amine
15		5-fluoro-4-(3-isopropyl-2-methyl-2H-indazol-5-yl)-*N*-(5-((4-propylpiperazin-1-yl)methyl)pyridin-2-yl)pyrimidin-2-amine
16		5-fluoro-4-(7-fluoro-3-isopropyl-2-methyl-2H-indazol-5-yl)-*N*-(5-((4-propylpiperazin-1-yl)methyl)pyridin-2-yl)pyrimidin-2-amine
17		4-(3-cyclopentyl-2-methyl-2H-indazol-5-yl)-5-fluoro-*N*-(5-((4-propylpiperazin-1-yl)methyl)pyridin-2-yl)pyrimidin-2-amine

18		4-(3-cyclopentyl-7-fluoro-2-methyl-2H-indazol-5-yl)-5-fluoro-*N*-(5-((4-propylpiperazin-1-yl)methyl)pyridin-2-yl)pyrimidin-2-amine
19		4-(3-ethyl-2-methyl-2H-indazol-5-yl)-*N*-(5-((4-ethylpiperazin-1-yl)methyl)pyridin-2-yl)-5-fluoropyrimidin-2-amine
20		4-(3-ethyl-7-fluoro-2-methyl-2H-indazol-5-yl)-*N*-(5-((4-ethylpiperazin-1-yl)methyl)pyridin-2-yl)-5-fluoropyrimidin-2-amine
21		4-(3-(sec-butyl)-2-methyl-2H-indazol-5-yl)-*N*-(5-((4-ethylpiperazin-1-yl)methyl)pyridin-2-yl)-5-fluoropyrimidin-2-amine
22		4-(3-(sec-butyl)-7-fluoro-2-methyl-2H-indazol-5-yl)-*N*-(5-((4-ethylpiperazin-1-yl)methyl)pyridin-2-yl)-5-fluoropyrimidin-2-amine
23		4-(2-ethyl-3-isopropyl-2H-indazol-5-yl)-*N*-(5-((4-ethylpiperazin-1-yl)methyl)pyridin-2-yl)-5-fluoropyrimidin-2-amine

24		4-(2-ethyl-7-fluoro-3-isopropyl-2H-indazol-5-yl)-*N*-(5-((4-ethylpiperazin-1-yl)methyl)pyridin-2-yl)-5-fluoropyrimidin-2-amine
25		4-(3-cyclopropyl-2-ethyl-2H-indazol-5-yl)-*N*-(5-((4-ethylpiperazin-1-yl)methyl)pyridin-2-yl)-5-fluoropyrimidin-2-amine
26		4-(3-cyclopropyl-2-ethyl-7-fluoro-2H-indazol-5-yl)-*N*-(5-((4-ethylpiperazin-1-yl)methyl)pyridin-2-yl)-5-fluoropyrimidin-2-amine
27		4-(3-(cyclopropylmethyl)-2-methyl-2H-indazol-5-yl)-*N*-(5-((4-ethylpiperazin-1-yl)methyl)pyridin-2-yl)-5-fluoropyrimidin-2-amine
28		4-(3-(cyclopropylmethyl)-7-fluoro-2-methyl-2H-indazol-5-yl)-*N*-(5-((4-ethylpiperazin-1-yl)methyl)pyridin-2-yl)-5-fluoropyrimidin-2-amine
29		4-(3-cyclopropyl-2-ethyl-7-fluoro-2H-indazol-5-yl)-*N*-(5-((4-ethylpiperazin-1-yl)methyl)pyridin-2-yl)pyrimidin-2-amine

30		4-(3-(sec-butyl)-2-methyl-2H-indazol-5-yl)-*N*-(5-((4-ethylpiperazin-1-yl)methyl)pyridin-2-yl)-5-fluoropyrimidin-2-amine
31		4-(3-(sec-butyl)-7-fluoro-2-methyl-2H-indazol-5-yl)-*N*-(5-((4-ethylpiperazin-1-yl)methyl)pyridin-2-yl)-5-fluoropyrimidin-2-amine

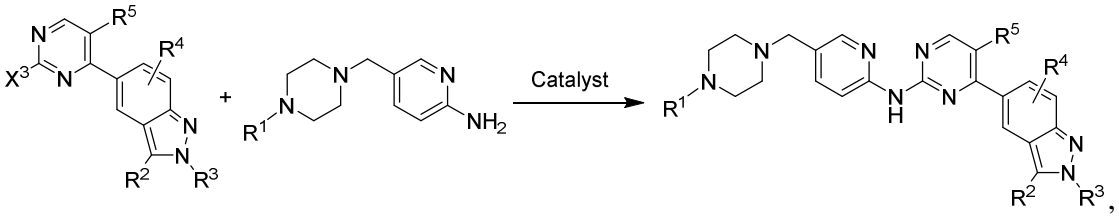
14. A pharmaceutical composition comprising a compound of claim 0, or a pharmaceutically acceptable salt, solvate, or prodrug thereof, and one or more pharmaceutically acceptable adjuvants, diluents, and/or carriers.

15. An in vitro method of inhibiting cell proliferation comprising treating proliferative cells with an effective amount of a compound according to claim 0, or a salt, solvate, or prodrug thereof.

16. An in vitro method of inhibiting a cyclin-dependent kinase (CDK) comprising treating said kinase with an effective amount of a compound of claim 0, or a salt, solvate, prodrug, or composition thereof.

17. The in vitro method of claim 16, wherein said cyclin-dependent kinase is CDK4, CDK6, or a combination thereof.

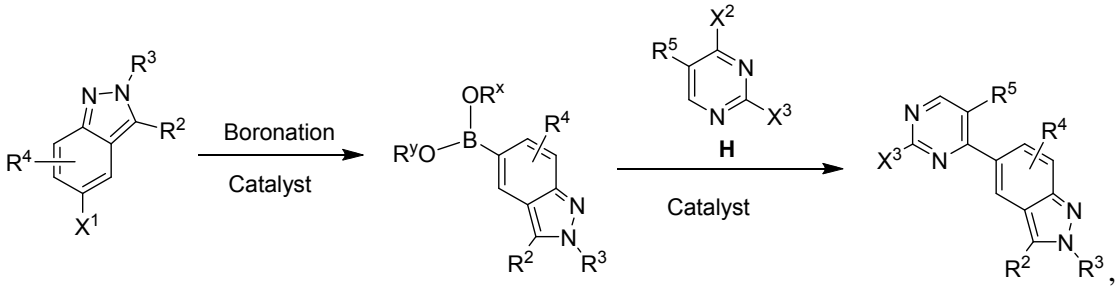
18. A method of preparing a compound of formula (I), comprising a step of coupling intermediate **E** with intermediate **G**:



E **G** (**I**)

wherein R^1 through R^5 are defined as in claim 0, and X^3 is Cl, Br, or I.

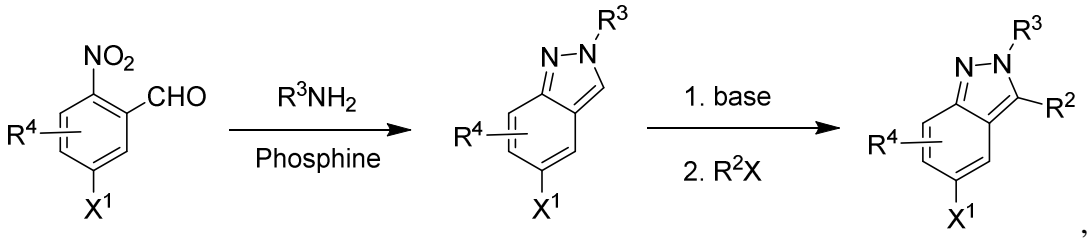
19. The method of claim 18, further comprising the steps of converting intermediate **C** to intermediate **D** and coupling the intermediate **D** with a pyrimidine compound **H** to form the intermediate **E**:



C **D** **E**

wherein R^x and R^y are independent alkyl, aryl, cycloalkyl, or alternatively together form an alkylene group, each optionally substituted by one or more substituents independently selected from C_1-C_4 alkyl, halogen and phenyl; and wherein X^1, X^2, and X^3 are each independently Cl, Br, or I, on condition that the intermediate **D** couples with the compound **H** selectively at the X^2 site over the X^3 site.

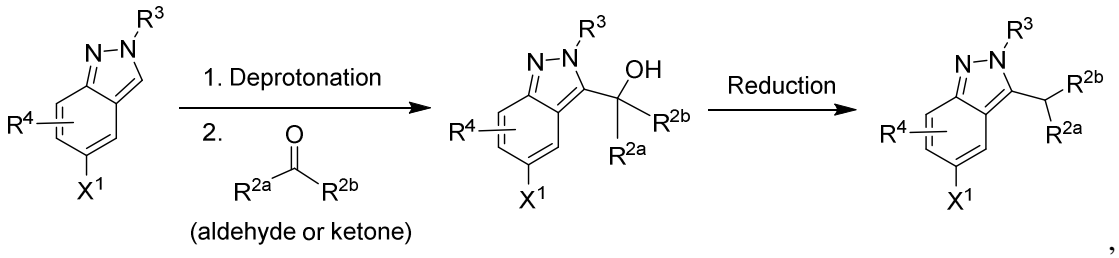
20. The method of claim 18, further comprising the steps of converting starting material **S1** to intermediate **A** and converting the intermediate **A** to the intermediate **C**:



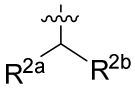
S1 **A** **C**

wherein X is Cl, Br, I, or $MeSO_3$-; and R^2 and R^3 are defined as in claim 18.

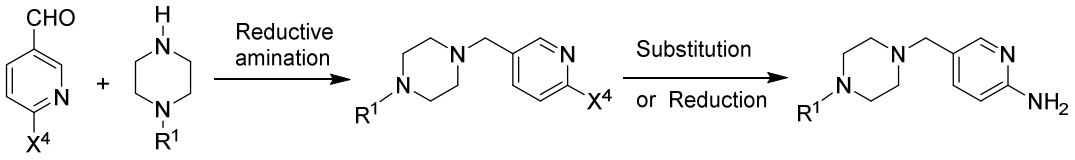
21. The method of claim 20, wherein said converting the intermediate **A** to the intermediate **C**, alternatively, comprises converting the intermediate **A** to an alcohol intermediate **B** followed by reduction of the alcohol intermediate **B** to form the intermediate **C**.



A **B** **C**

wherein R^{2a} and R^{2b} are each independently hydrogen, alkyl, cycloalkyl, or together form an alkylene group so that the group  formed in the intermediate C is R^2 as defined in claim 20.

22. The method of claim 18, further comprising a step of forming the intermediate **G** through coupling the pyridine aldehyde compound **S2** and the piperazine compound **S3** to form an intermediate F, followed by converting the intermediate F to the intermediate G:



S2 **S3** **F** **G**

wherein X^4 is selected from the group consisting of Cl, Br, I, and $-NO_2$; and

wherein said converting the intermediate F to the intermediate G comprises replacing $-X^4$ with $-NH_2$ when X^4 is Cl, Br, or I; or reducing the nitro group ($-NO_2$) to amino group ($-NH_2$) when X^4 is NO_2.