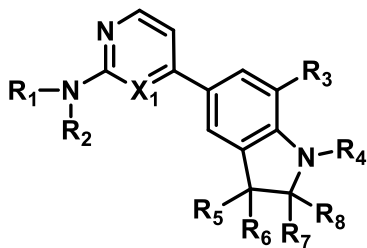


Claims

1. A compound of Formula (Ie), or a stereoisomer, racemate, geometric isomer, tautomer, hydrate, solvate, or pharmaceutically acceptable salt thereof,



Ie

wherein,

X₁ is selected from the group consisting of CH, CD, and N;

R₁ is selected from the group consisting of H and D;

R₂ is selected from the group consisting of C₁₋₆alkyl optionally substituted with one or more hydroxyl, C₃₋₈cycloalkyl optionally substituted with one or more hydroxyl, 3-8 membered heterocyclyl, and 5-7 membered heteroaryl optionally substituted with one or more substituents selected from -CD₃, C₁₋₆alkyl and hydroxylC₁₋₆alkyl;

R₃ is selected from the group consisting of halo and C₁₋₆alkyl;

R₄ is -CO(CR₁₀R₁₁)_mR₁₂; wherein m is 0, 1, 2 or 3, and wherein

R₁₀ and R₁₁ are each independently selected from the group consisting of H, D, and C₁₋₄alkyl optionally substituted with hydroxyl; and

R₁₂ is each independently selected from optionally substituted phenyl and optionally substituted pyridinyl, wherein the optional substituent is one or more substituents independently selected from the group consisting of D, halo, C₁₋₄alkyl, cyano, and C₃₋₈heterocyclyl-(CH₂)₀₋₄; and

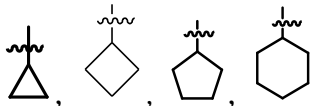
R₅, R₆, R₇ and R₈ are each independently selected from the group consisting of -H, and C₁₋₆alkyl optionally substituted with hydroxyl or -OC₁₋₆alkyl,

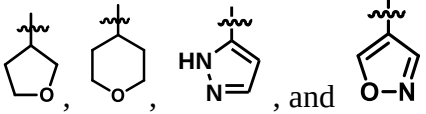
provided that the compound is not

2-(2-chloropyridin-3-yl)-1-(7-fluoro-2-(hydroxymethyl)-5-(2-(isopropylamino)pyrimidin-4-yl)indolin-1-yl)ethan-1-one.

2. The compound according to claim 1, wherein

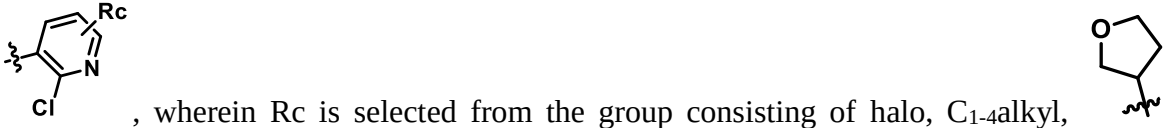
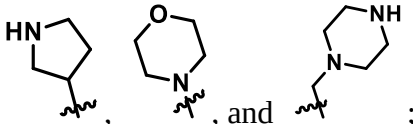
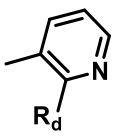
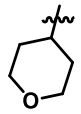
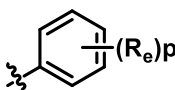
R₂ is selected from the group consisting of C₁₋₄alkyl optionally substituted with one or

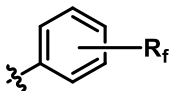
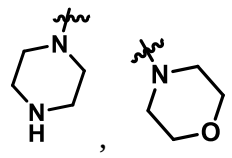
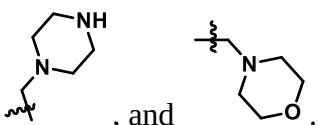
more hydroxyl; , which are optionally substituted with one or more

hydroxyl; , which are optionally substituted with one or more substituents independently selected from the group consisting of C₁₋₄alkyl, -CD₃ and hydroxylC₁₋₄alkyl.

3. The compound according to claim 1, wherein R₃ is selected from the group consisting of fluoro, chloro, bromo, iodo, -CH₃, -CH₂CH₃, -CH(CH₃)₂, and -CH₂CH₂CH₃.

4. The compound according to claim 1, wherein R₁₂ is selected from the group consisting of

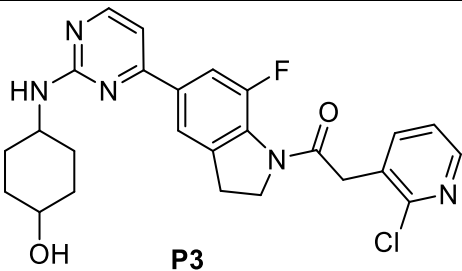
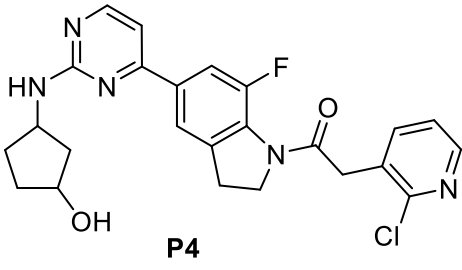
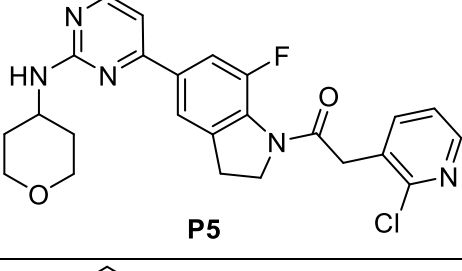
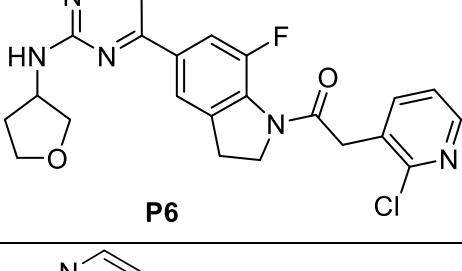
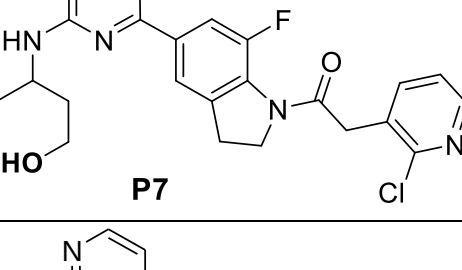
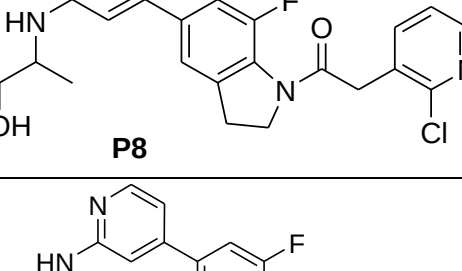
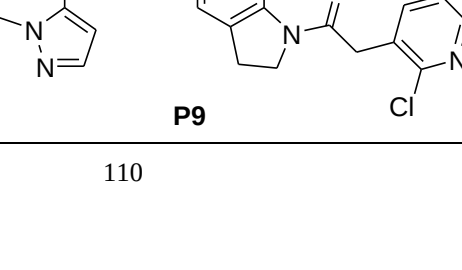
, wherein R_c is selected from the group consisting of halo, C₁₋₄alkyl, ; , wherein R_d is selected from the group consisting of H, C₁₋₄alkyl, and ; , wherein R_e is selected from the group consisting of halo, and p is 1 or 2; and

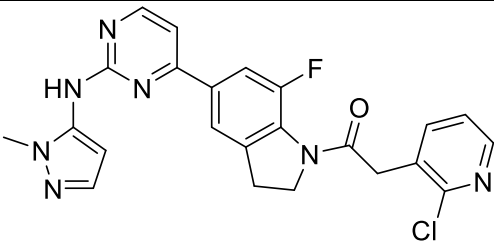
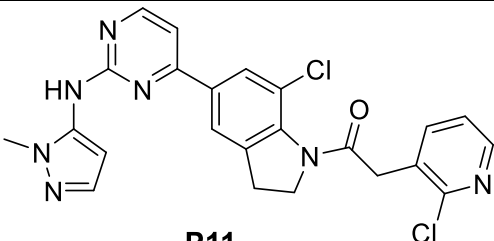
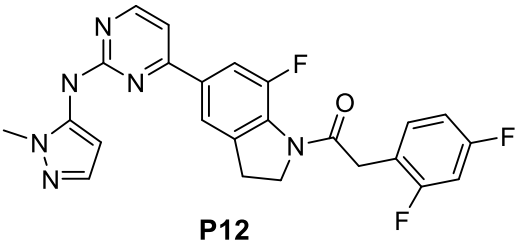
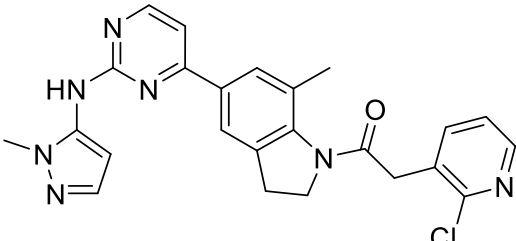
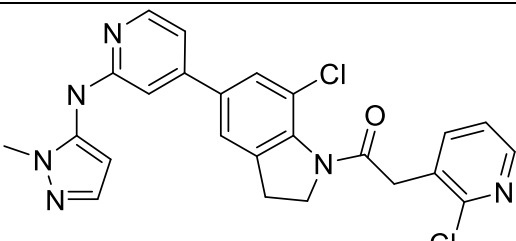
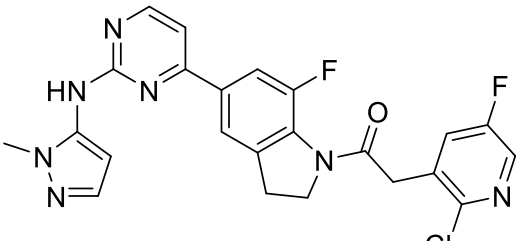
, wherein R_f is selected from the group consisting of , , and

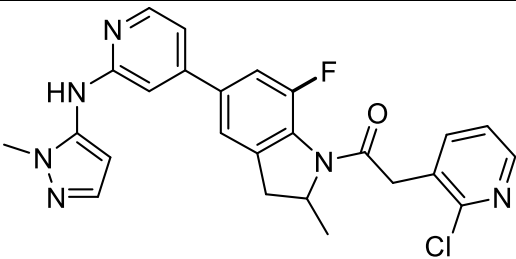
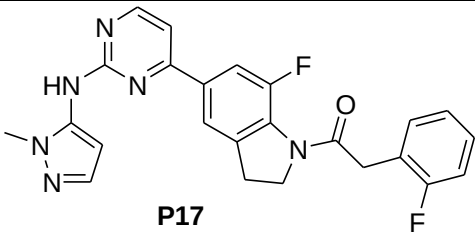
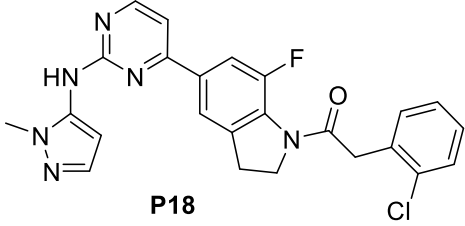
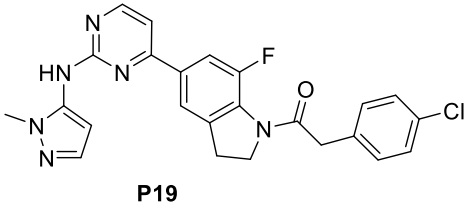
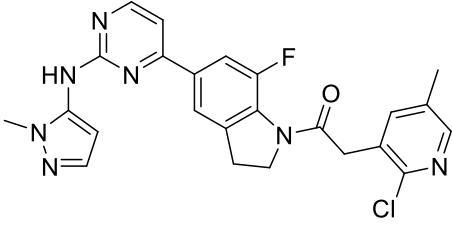
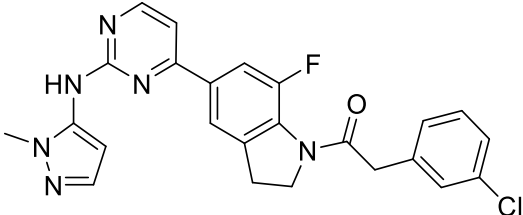
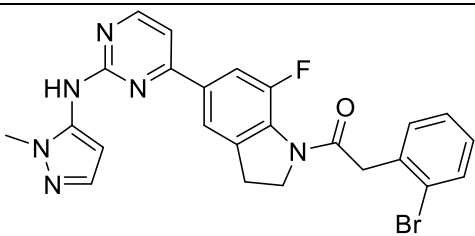
5. The compound according to claim 1, wherein R₄ is selected from the group consisting of -CO(CR₁₀R₁₁)_mR₁₂, wherein m is 0, 1, 2 or 3, and wherein

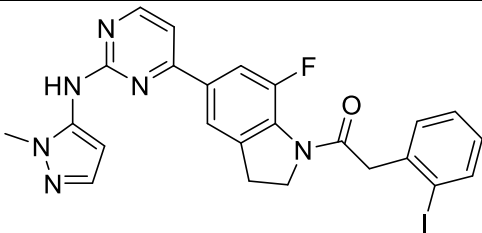
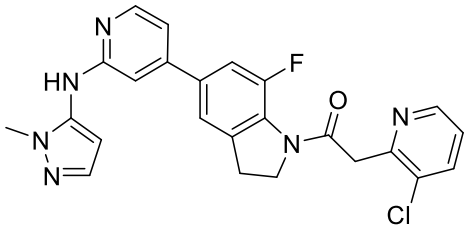
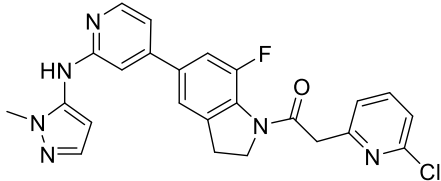
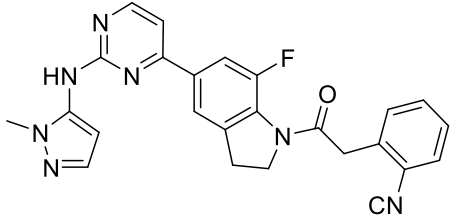
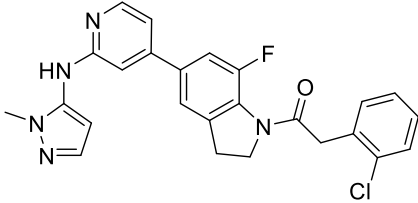
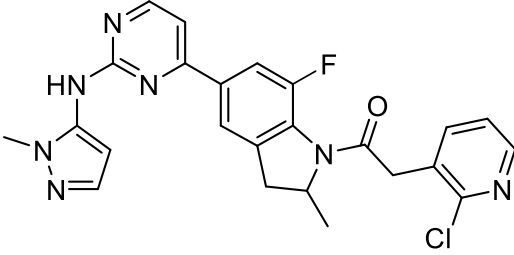
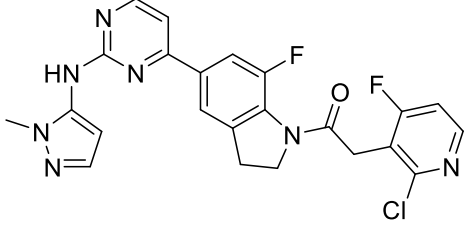
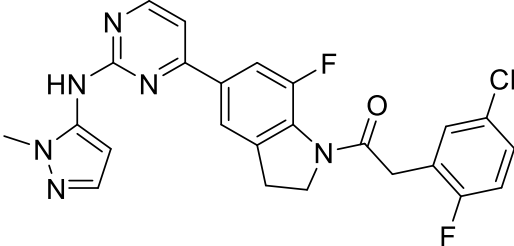
R₁₀ and R₁₁ are each independently H; and

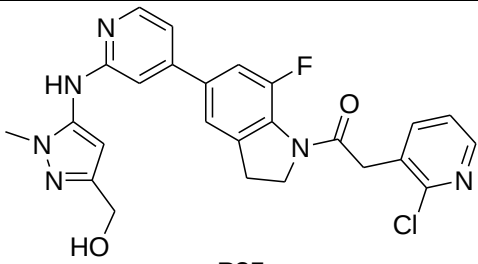
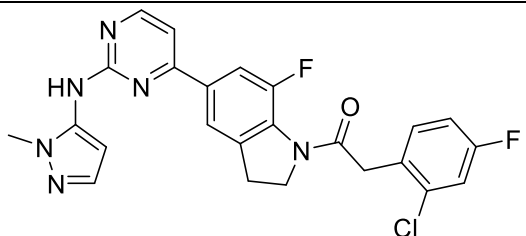
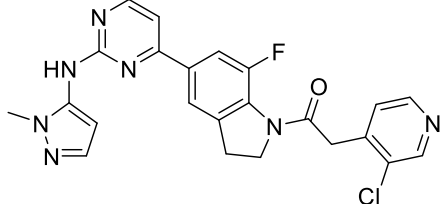
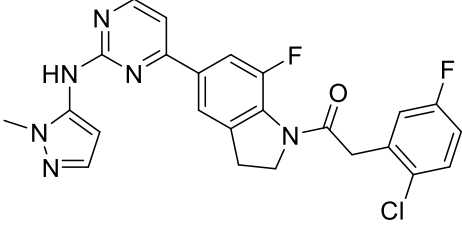
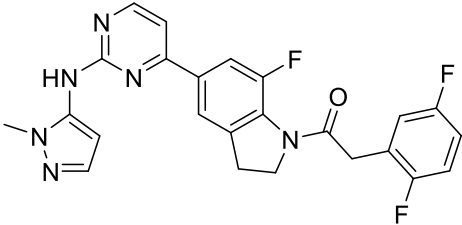
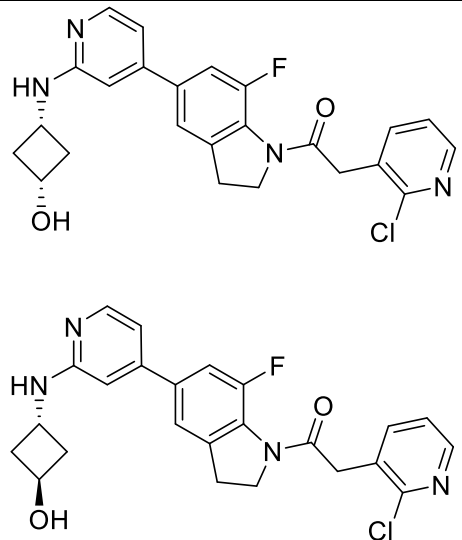
R₁₂ is selected from the group consisting of

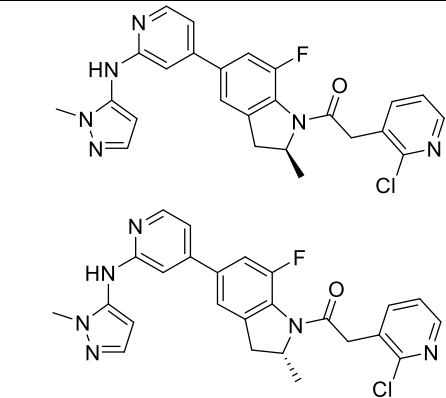
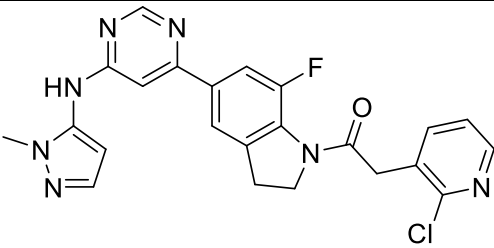
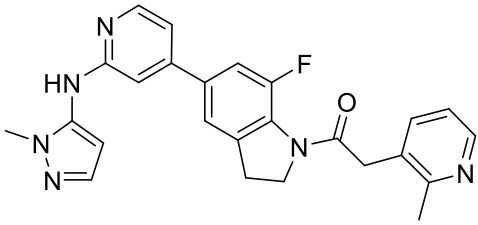
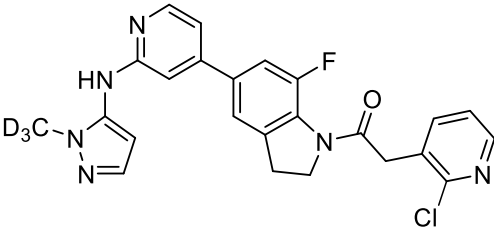
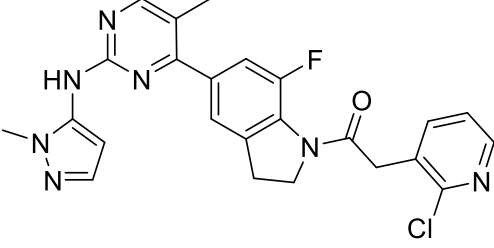
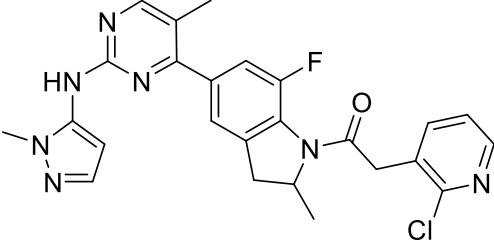
P3	 P3
P4	 P4
P5	 P5
P6	 P6
P7	 P7
P8	 P8
P9	 P9

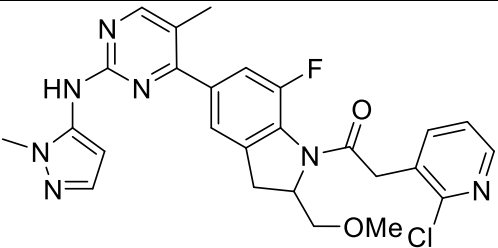
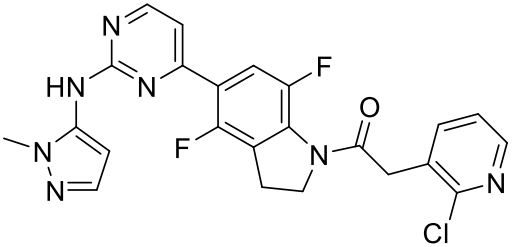
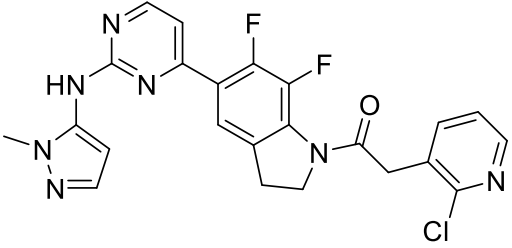
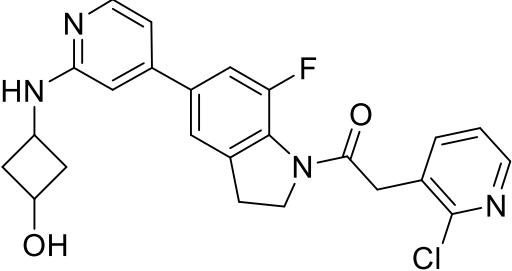
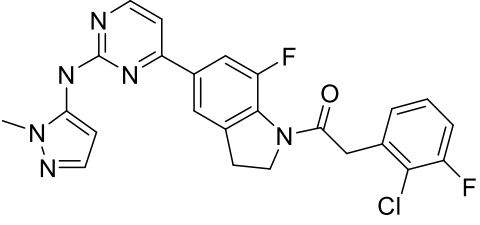
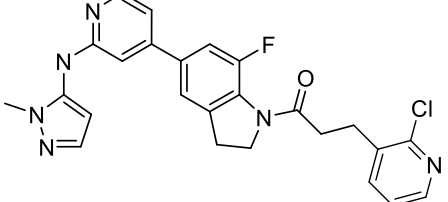
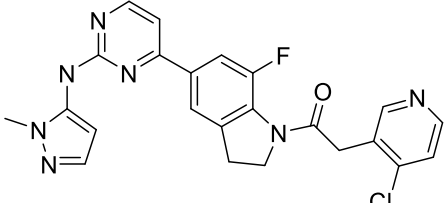
P10	 P10
P11	 P11
P12	 P12
P13	 P13
P14	 P14
P15	

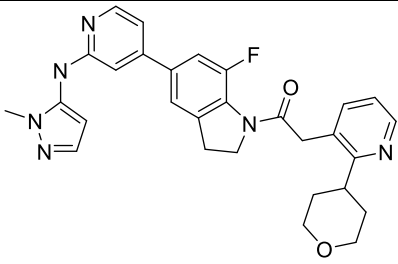
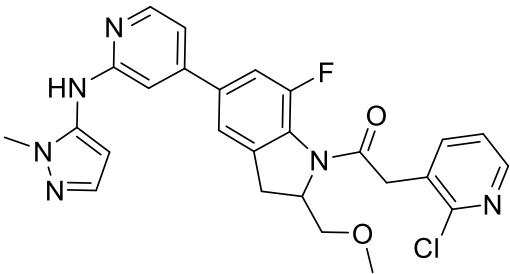
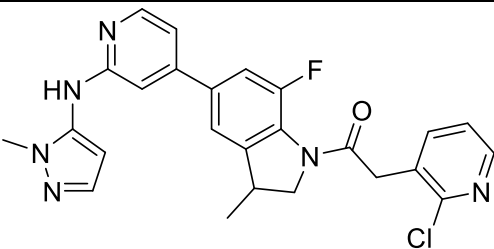
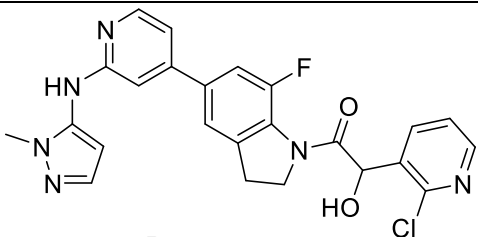
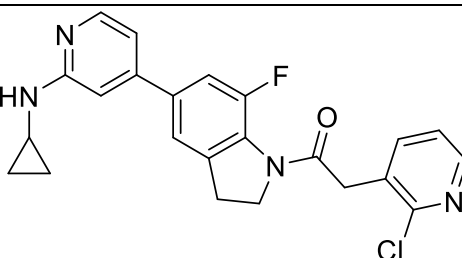
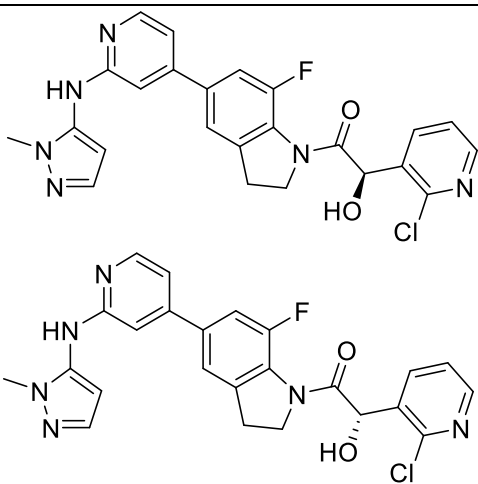
P16	
P17	 P17
P18	 P18
P19	 P19
P20	
P23	
P24	

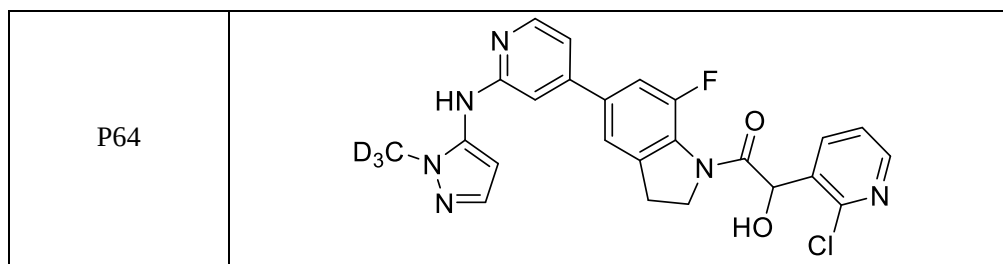
P25	
P28	
P29	
P30	
P31	
P32	
P33	
P34	

P35	 P35
P36	
P37	
P38	
P39	
P40 and P41	

P42 and P43	
P44	
P45	
P46	
P47	
P48	

P49	
P50	
P51	
P53	 (racemate)
P54	
P55	
P56	

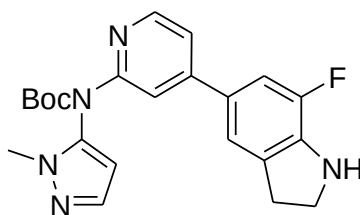
P57	
P58	
P59	
P60	 P ₆₀
P61	
P62 and P63	



9. A pharmaceutical composition, comprising the compound according to claim 1 or a pharmaceutically acceptable salt thereof, and optionally a pharmaceutically acceptable carrier.

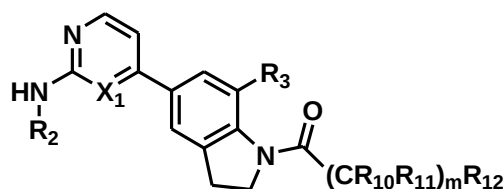
10. A non-therapeutic method of inhibiting ERK kinase activity, comprising contacting an effective amount of the compound according to claim 1 or a pharmaceutically acceptable salt thereof, with an ERK kinase, thereby inhibiting the ERK kinase.

11. The compound t-butyl (4-(7-fluoroindolin-5-yl)pyridin-2-yl)(1-methyl-1H-pyrazol-5-yl)carbamate represented by the formula:



or a stereoisomer, racemate, geometric isomer, tautomer, hydrate, solvate, or pharmaceutically acceptable salt thereof.

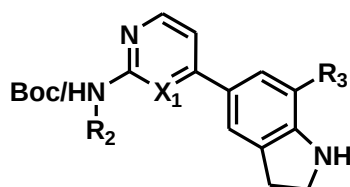
12. A method for preparing the compound of formula (Ie) according to claim 1, wherein said compound of formula (Ie) is the compound of formula C3:



C3

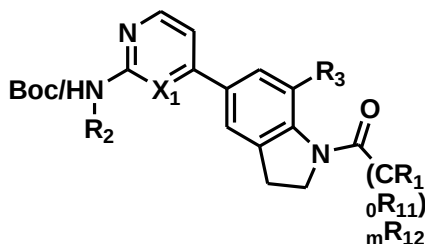
wherein X_1 , R_2 , R_3 , R_{10} , R_{11} , R_{12} and m are as defined in claim 1, comprising the steps of:

(a) subjecting the compound of formula C1



C1

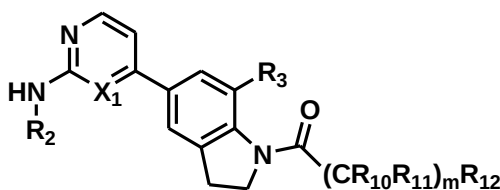
and the compound $\text{HO}-\text{C}(=\text{O})-(\text{CR}_{10}\text{R}_{11})_m\text{R}_{12}$ to amide coupling reaction, to give the compound of formula C2,



C2

; and

(b) When the compound of C2 is Boc-protected, deprotecting it, to give the compound of formula C3,



C3

13. The method according to claim 12, wherein the amide coupling reaction is carried out in the presence of a condensing agent and a base in an inert solvent.

14. The method according to claim 12, wherein the deprotection is carried out in the presence of an acid in an inert solvent.

15. The method according to claim 13, wherein the inert solvent is selected from the group consisting of ethyl acetate, tetrahydrofuran, methyltetrahydrofuran, acetonitrile, dimethyl sulfoxide, N,N-dimethylformamide, dichloromethane, 1,2-dichloroethane, N-methyl-2-pyrrolidone, or a combination thereof.

16. The method according to claim 13, wherein the condensing agent is one or more selected from the group consisting of 1-hydroxylbenzotriazole (HOBT), 1-hydroxyl-7-azobenzotriazole (HOAT), benzotriazol-1-yl-oxytripyrrolidino-phosphonium hexafluorophosphate (PyBOP), benzotriazol-1-yloxytris(dimethylamino)phosphonium hexafluorophosphate (BOP), 1,1-carbonyldiimidazole (CDI), 1-propylphosphonic anhydride (T3P), 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride (EDC·HCl),

N,N-dicyclohexylcarbodiimide (DCC), acetic anhydride, acetyl chloride, oxalyl chloride, O-(7-azabenzotriazol-1-yl)-N,N,N',N'-tetramethyluronium hexafluorophosphate (HATU), and O-(benzotriazol-1-yl)-N,N,N',N'-tetramethyluronium hexafluorophosphate (HBTU).

17. The method according to claim 13, wherein the base is one or more selected from the group consisting of triethylamine, DIPEA, pyridine, 2,4-dimethylpyridine, NaOH, KOH, LiOH, Na₂CO₃, K₂CO₃, NaHCO₃, Cs₂CO₃, Na₃PO₄, or K₃PO₄.

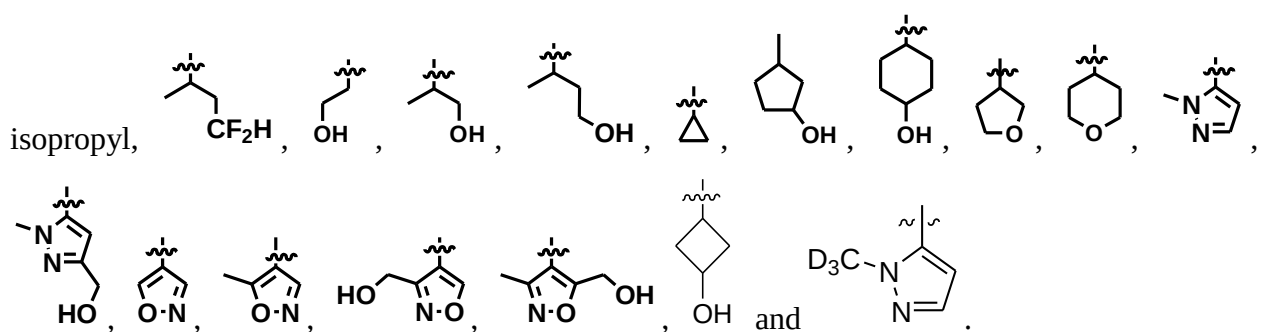
18. The method according to claim 12, wherein the amide coupling reaction is carried out at a temperature from room temperature to reflux for 0.5 -24 h.

19. The method according to claim 14, wherein the acid is one or more selected from the group consisting of hydrochloric acid, sulfuric acid, trifluoroacetic acid, acetic acid, formic acid, and phosphoric acid.

20. The method according to claim 12, wherein the deprotection is carried out at a temperature from -10°C to 80°C for 0.5 – 24 h.

21. The method according to claim 14, wherein the inert solvent is selected from the group consisting of ethyl acetate, tetrahydrofuran, methyltetrahydrofuran, acetonitrile, dimethyl sulfoxide, N,N-dimethylformamide, dichloromethane, 1,2-dichloroethane, N-methyl-2-pyrrolidone, or a combination thereof.

22. The compound according to claim 1, wherein R₂ is selected from the group consisting of



23. The compound according to claim 1, wherein R₃ is selected from the group consisting of fluoro, chloro and -CH₃.

24. The compound according to claim 1, wherein R₃ is selected from the group consisting of fluoro.

25. The compound according to claim 1, wherein R₅, R₆, R₇ and R₈ are each independently selected from the group consisting of -H, -CH₃, and -CH₂OH.