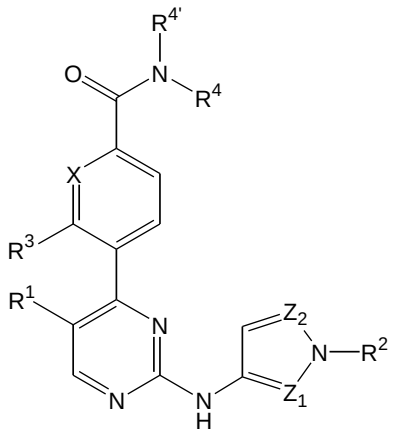
Amended CLAIMS

(Clean)

1. A compound having the structural formula (I):



(I)

wherein

X is N or CR^x, wherein R^x is R', halogen, CN or OR';

each of Z_1 and Z_2 is independently selected from N and CR', *provided* that one of Z_1 and Z_2 is N and the other is CR';

R^1 is Cl;

R^2 is a C_3-C_6 cyclic alkyl;

R^3 is R', halogen or CN;

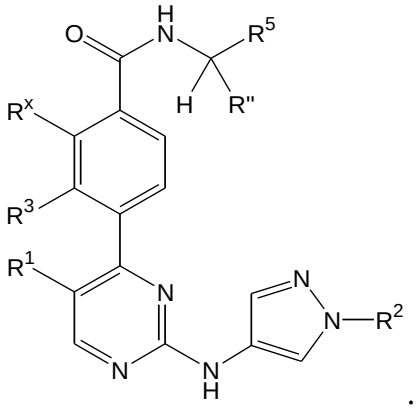
$R^{4'}$ is H;

R^4 is -CHR"-R^5, wherein R" is H or a C_1-C_6 alkyl and R^5 is a CN or CF_3; and

each R' is independently hydrogen or a C_1-C_{12} unsubstituted or substituted alkyl group,

or a pharmaceutically acceptable salt thereof.

2. The compound of claim 1, wherein X is CR^x, Z_1 is CH and Z_2 is N, having the structural formula (II):



(II)

3. The compound of claim 1 or 2, wherein R^x is hydrogen, halogen, C_1-C_6 unsubstituted or substituted alkyl or alkoxy.

4. The compound of claim 3, wherein R^x is H.

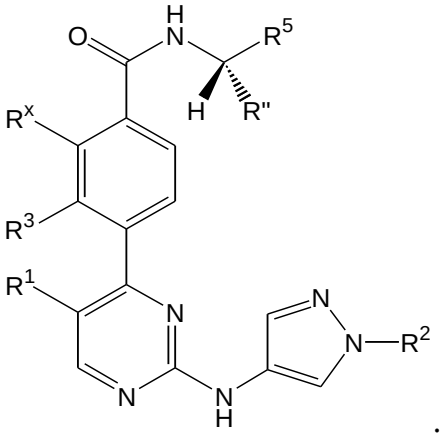
5. The compound of claim 1, wherein X is N.

6. The compound of any one of claims 1-5, wherein R^3 is H.

7. The compound of any one of claims 1-5, wherein R^3 is F, CH_3 or Cl.

8. The compound of any one of claims 1-5, wherein R^3 is F.

9. The compound of claim 1, wherein X is CR^x, Z_1 is CH and Z_2 is N, having the structural formula (III):

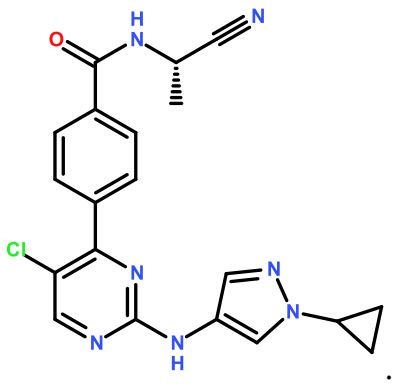


(III)

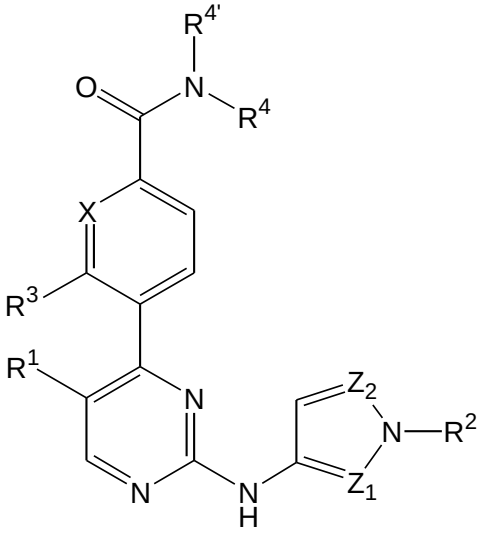
10. The compound of claim 9, wherein R^x is H, $R^{''}$ is CH_3, R^3 is H and R^5 is CN.

11. The compound of any one of claims 1-10, wherein R^2 is cyclopropyl.

12. The compound of claim 1, having the structural formula:



13. A compound having the structural formula (I):



(I)

wherein

X is N or CR^x, wherein R^x is R', halogen, CN or OR';

each of Z_1 and Z_2 is independently selected from N and CR', *provided* that one of Z_1 and Z_2 is N and the other is CR';

R^1 is CH_3;

R^2 is a C_1-C_3 alkyl group substituted with CN;

R^3 is R', halogen or CN;

$R^{4'}$ is H;

R^4 is -CHR"-R^5, wherein R" is H or a C_1-C_6 alkyl and R^5 is a CN or CF_3; and

each R' is independently hydrogen or a C_1-C_{12} unsubstituted or substituted alkyl group,

or a pharmaceutically acceptable salt thereof.

14. The compound of claim 13, wherein R^2 is CH_2CN.

15. The compound of claim 13 or 14, wherein R" is H.

16. The compound of claim 13, wherein R^5 is CN.

17. The compound of any one of claims 13-16, wherein X is CR^x.

18. The compound of claim 17, wherein R^x is H.

19. The compound of any one of claims 13-16, wherein X is N.

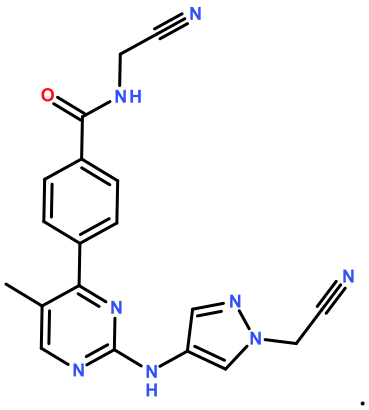
20. The compound of any one of claims 13-19, wherein R^3 is H.

21. The compound of claim 20, wherein Z_1 is CH and Z_2 is N.

22. The compound of claim 13, wherein R^2 is CH_2CN, R^3 is H, X is CH, Z_1 is CH and Z_2 is N.

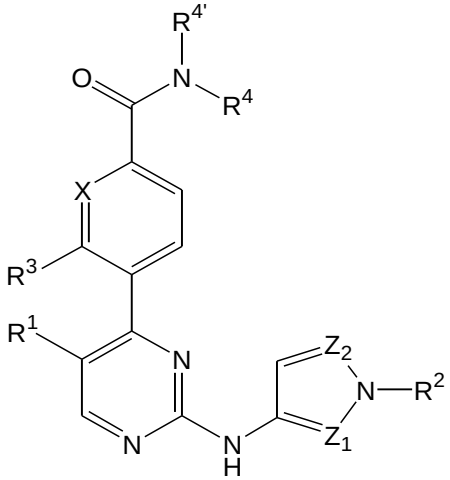
23. The compound of claim 22, wherein R^4 is $-CH_2CN$.

24. The compound of claim 13, having the structural formula:



.

25. A compound having the structural formula (I):



(I)

wherein

X is N or CR^x, wherein R^x is R', halogen, CN or OR';

each of Z_1 and Z_2 is independently selected from N and CR', *provided* that one of Z_1 and Z_2 is N and the other is CR';

R^1 is CH_3;

R^2 is a six-membered cyclic aliphatic group comprising an N or O, wherein the cyclic aliphatic group is substituted with one or more C_1-C_3 alkyl groups;

R^3 is R', halogen or CN;

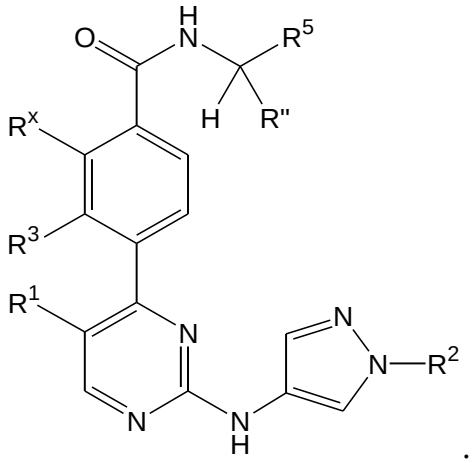
$R^{4'}$ is H;

R^4 is -CHR"-R^5, wherein R" is H or a C_1-C_6 alkyl and R^5 is a CN or CF_3; and

each R' is independently hydrogen or a C_1-C_3 unsubstituted or substituted alkyl group,

or a pharmaceutically acceptable salt thereof.

26. The compound of claim 25, wherein X is CR^x, Z_1 is CH, and Z_2 is N, having the structural formula (II):



(II)

27. The compound of claim 25, wherein X is CH.

28. The compound of claim 25, wherein X is N.

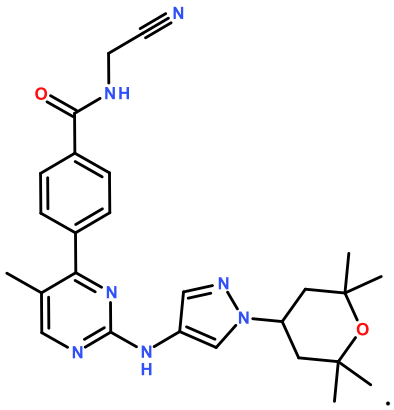
29. The compound of claim 25, wherein R^2 is a six-membered cyclic aliphatic group comprising an O substituted with two or more C_1-C_3 alkyl groups.

30. The compound of any one of claims 25-29, wherein R^3 is H, F, CH_3 or Cl.

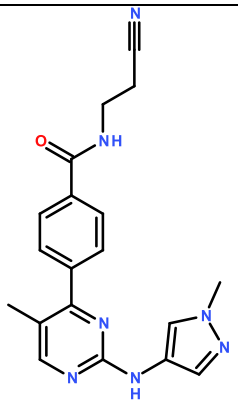
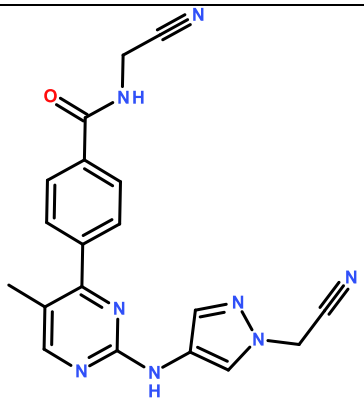
31. The compound of claim 30, wherein R^3 is H.

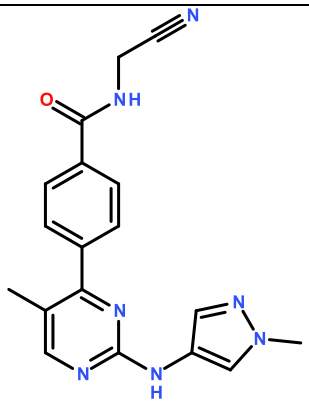
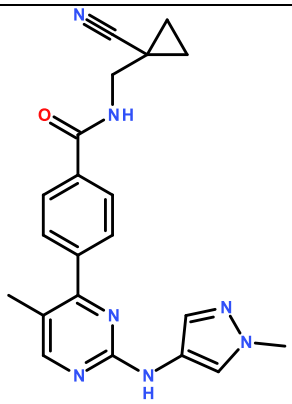
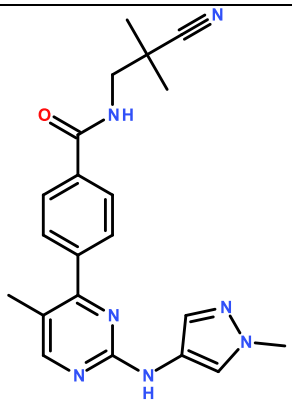
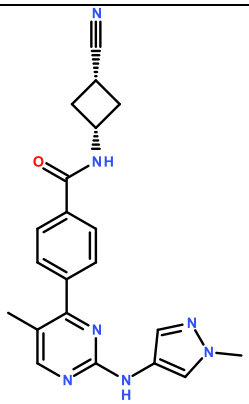
32. The compound of claim 31, wherein $R^{"}$ is H and R^5 is CN.

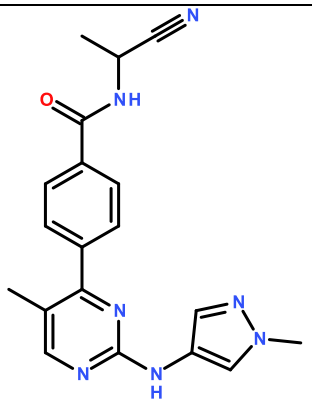
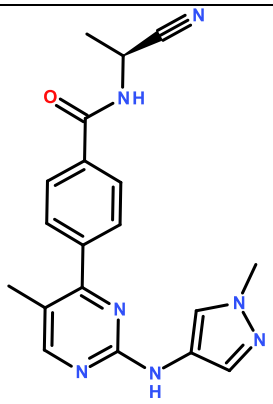
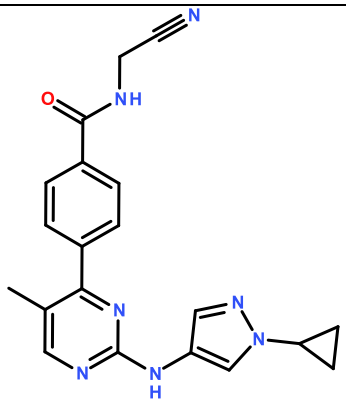
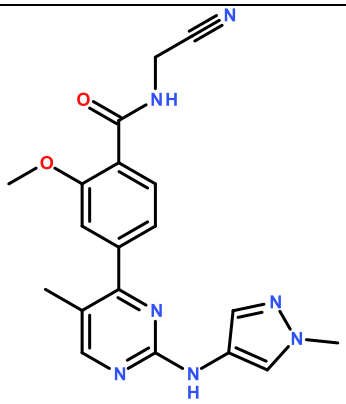
33. The compound of claim 25, having the structural formula:

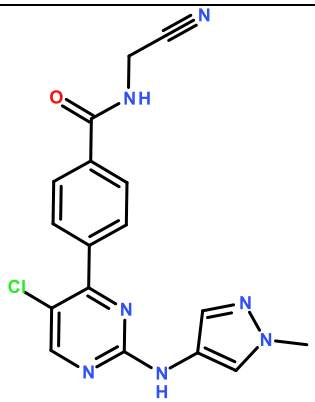
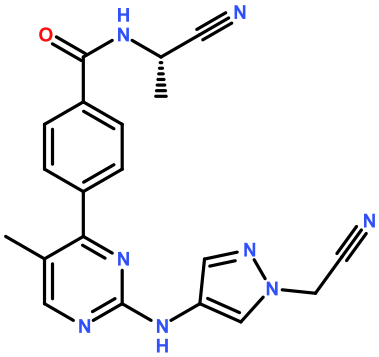
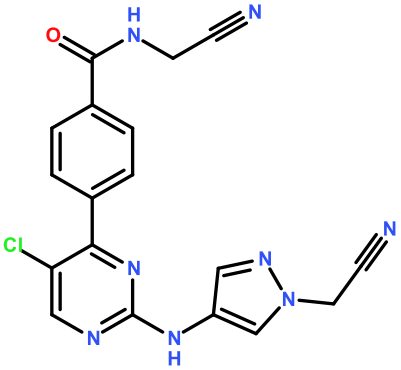
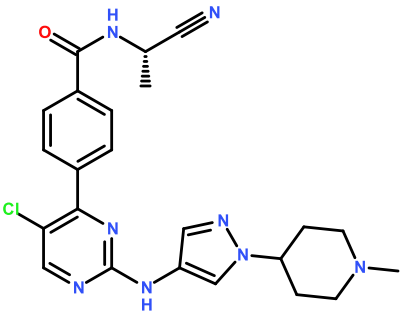


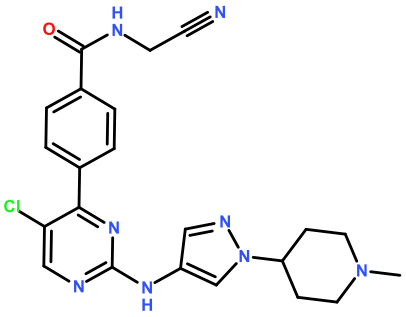
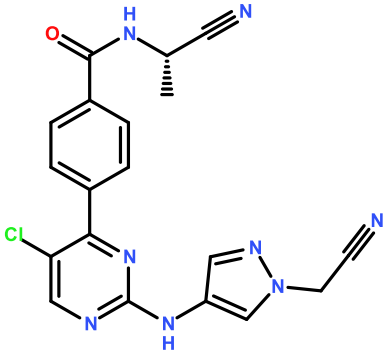
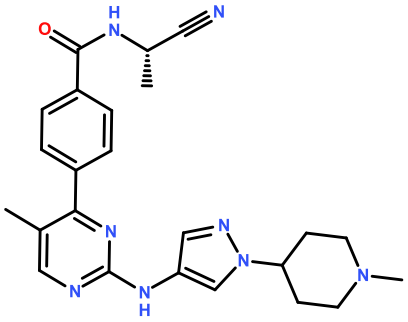
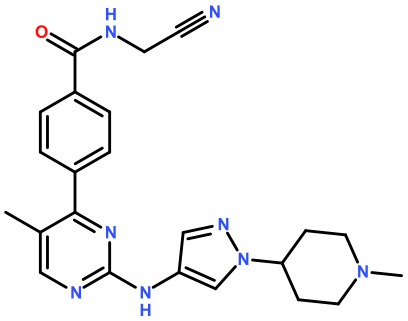
34. The compound of any of claims 1, 13 and 25, selected from the group consisting of:

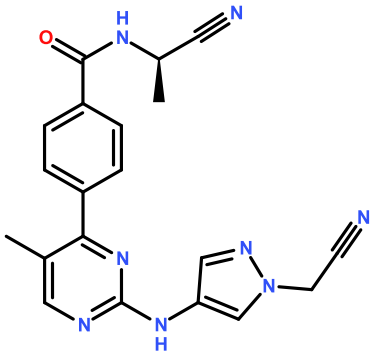
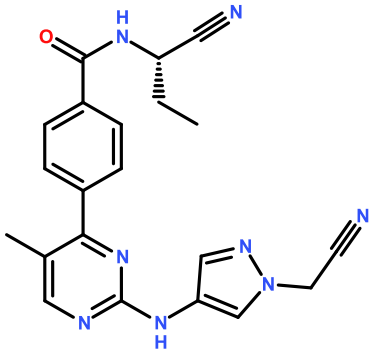
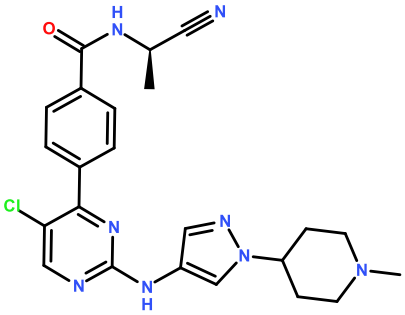
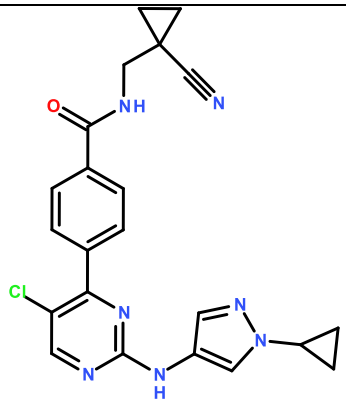
Example	Structure	IUPAC Name
2		N-(2-cyanoethyl)-4-(5-methyl-2-((1-methyl-1H-pyrazol-4-yl)amino)pyrimidin-4-yl)benzamide
4		N-(cyanomethyl)-4-(2-((1-(cyanomethyl)-1H-pyrazol-4-yl)amino)-5-methylpyrimidin-4-yl)benzamide

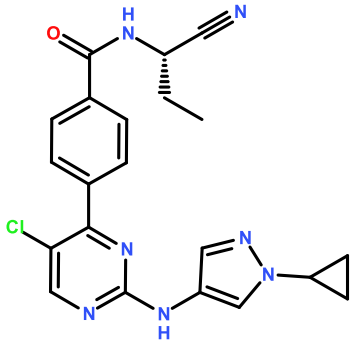
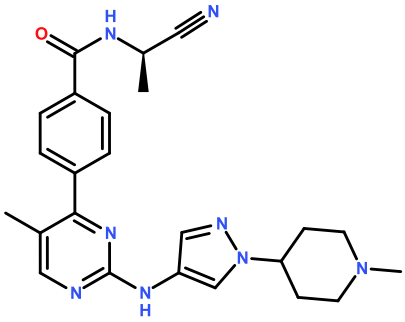
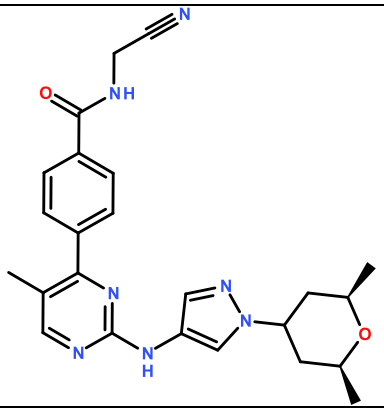
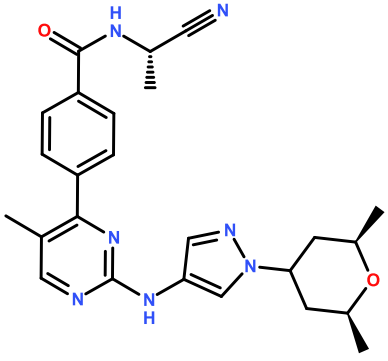
11		N-(cyanomethyl)-4-(5-methyl-2-((1-methyl-1H-pyrazol-4-yl)amino)pyrimidin-4-yl)benzamide
12		N-((1-cyanocyclopropyl)methyl)-4-(5-methyl-2-((1-methyl-1H-pyrazol-4-yl)amino)pyrimidin-4-yl)benzamide
13		N-(2-cyano-2-methylpropyl)-4-(5-methyl-2-((1-methyl-1H-pyrazol-4-yl)amino)pyrimidin-4-yl)benzamide
16		N-((1s,3s)-3-cyanocyclobutyl)-4-(5-methyl-2-((1-methyl-1H-pyrazol-4-yl)amino)pyrimidin-4-yl)benzamide

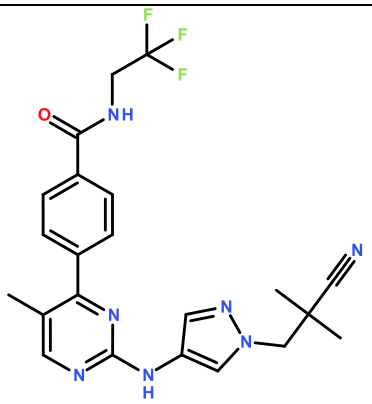
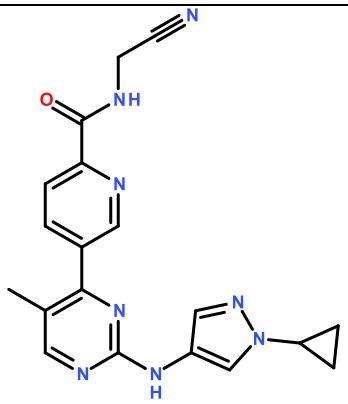
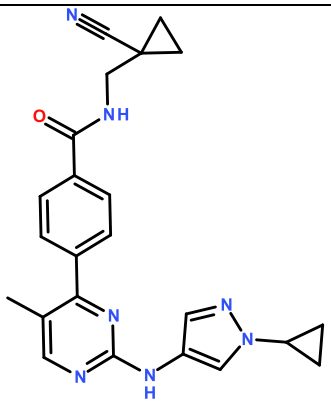
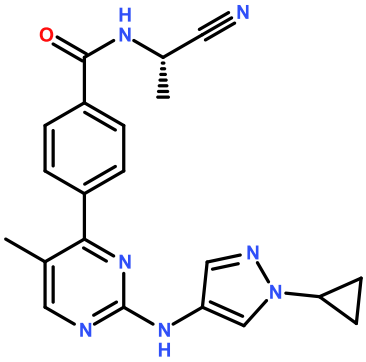
17		N-(1-cyanoethyl)-4-(5-methyl-2-((1-methyl-1H-pyrazol-4-yl)amino)pyrimidin-4-yl)benzamide
18		(S)-N-(1-cyanoethyl)-4-(5-methyl-2-((1-methyl-1H-pyrazol-4-yl)amino)pyrimidin-4-yl)benzamide
25		N-(cyanomethyl)-4-(2-((1-cyclopropyl-1H-pyrazol-4-yl)amino)-5-methylpyrimidin-4-yl)benzamide
33		N-(cyanomethyl)-2-methoxy-4-(5-methyl-2-((1-methyl-1H-pyrazol-4-yl)amino)pyrimidin-4-yl)benzamide

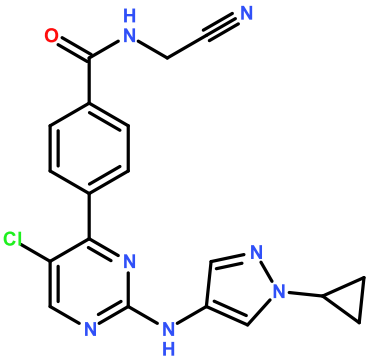
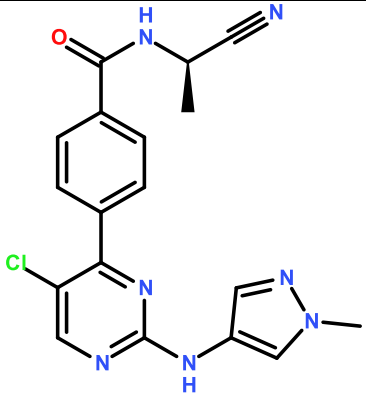
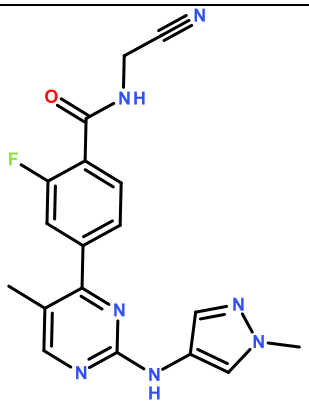
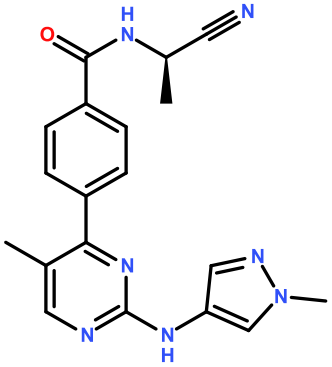
34		4-(5-chloro-2-((1-methyl-1H-pyrazol-4-yl)amino)pyrimidin-4-yl)-N-(cyanomethyl)benzamide
40		(S)-N-(1-cyanoethyl)-4-(2-((1-(cyanomethyl)-1H-pyrazol-4-yl)amino)-5-methylpyrimidin-4-yl)benzamide
41		4-(5-chloro-2-((1-(cyanomethyl)-1H-pyrazol-4-yl)amino)pyrimidin-4-yl)-N-(cyanomethyl)benzamide
43		(S)-4-(5-chloro-2-((1-(1-methylpiperidin-4-yl)-1H-pyrazol-4-yl)amino)pyrimidin-4-yl)-N-(1-cyanoethyl)benzamide

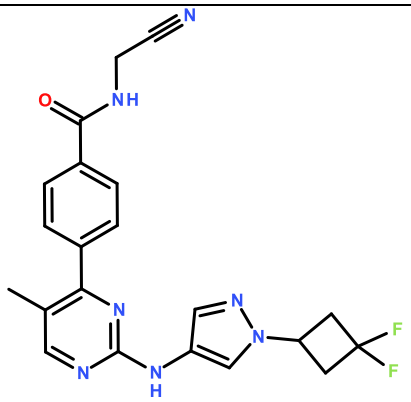
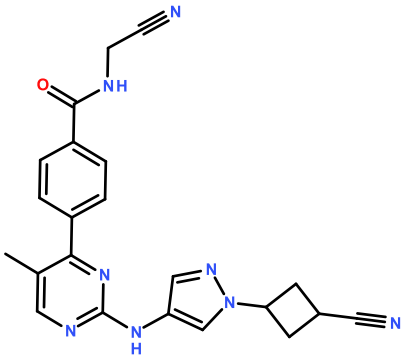
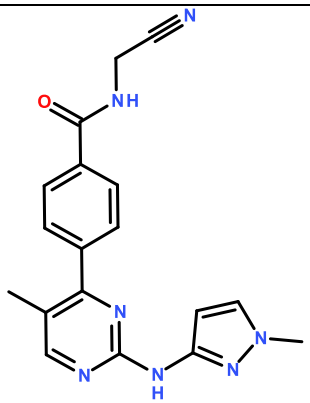
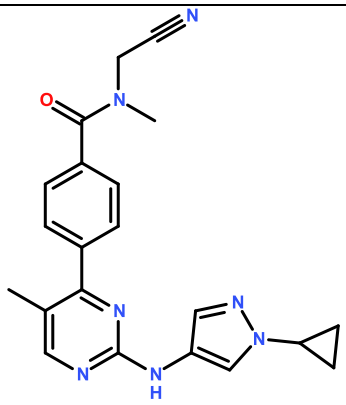
44		4-(5-chloro-2-((1-(1-methylpiperidin-4-yl)-1H-pyrazol-4-yl)amino)pyrimidin-4-yl)-N-(cyanomethyl)benzamide
46		(S)-4-(5-chloro-2-((1-(cyanomethyl)-1H-pyrazol-4-yl)amino)pyrimidin-4-yl)-N-(1-cyanoethyl)benzamide
48		(S)-N-(1-cyanoethyl)-4-(5-methyl-2-((1-(1-methylpiperidin-4-yl)-1H-pyrazol-4-yl)amino)pyrimidin-4-yl)benzamide
49		N-(cyanomethyl)-4-(5-methyl-2-((1-(1-methylpiperidin-4-yl)-1H-pyrazol-4-yl)amino)pyrimidin-4-yl)benzamide

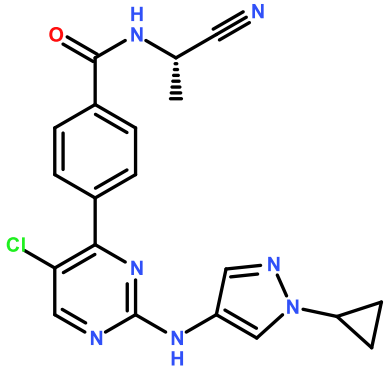
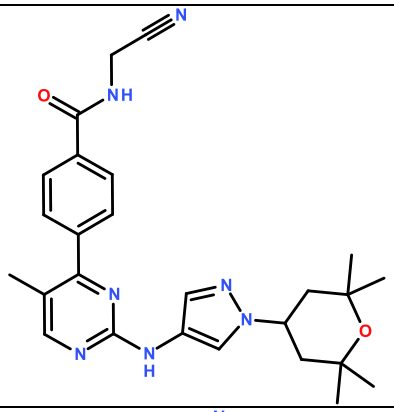
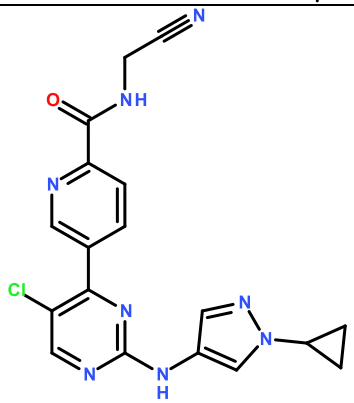
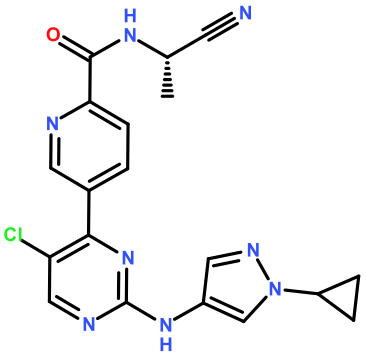
54		(R)-N-(1-cyanoethyl)-4-(2-((1-(cyanomethyl)-1H-pyrazol-4-yl)amino)-5-methylpyrimidin-4-yl)benzamide
55		(S)-4-(2-((1-(cyanomethyl)-1H-pyrazol-4-yl)amino)-5-methylpyrimidin-4-yl)-N-(1-cyanopropyl)benzamide
58		(R)-4-(5-chloro-2-((1-(1-methylpiperidin-4-yl)-1H-pyrazol-4-yl)amino)pyrimidin-4-yl)-N-(1-cyanoethyl)benzamide
60		4-(5-chloro-2-((1-cyclopropyl-1H-pyrazol-4-yl)amino)pyrimidin-4-yl)-N-((1-cyanocyclopropyl)methyl)benzamide

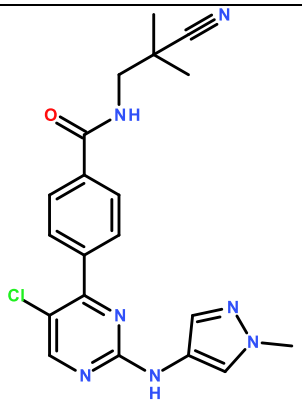
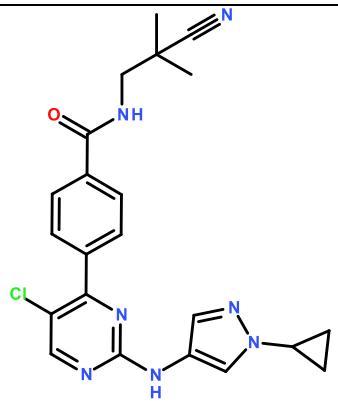
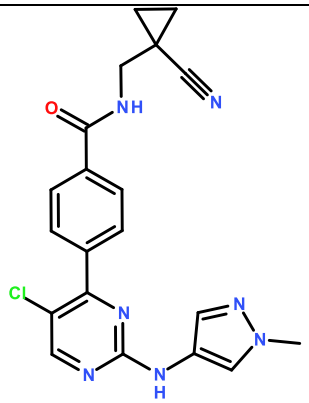
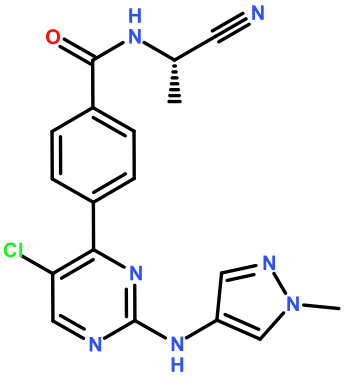
61		(S)-4-(5-chloro-2-((1-cyclopropyl-1H-pyrazol-4-yl)amino)pyrimidin-4-yl)-N-(1-cyanopropyl)benzamide
62		(R)N-(1-cyanoethyl)-4-(5-methyl-2-((1-(1-methylpiperidin-4-yl)-1H-pyrazol-4-yl)amino)pyrimidin-4-yl)benzamide
68		N-(cyanomethyl)-4-(2-(1-cis-2,6-dimethyltetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)amino)-5-methylpyrimidin-4-yl)benzamide
73		N-((S)-1-cyanoethyl)-4-(2-((1-(cis-2,6-dimethyltetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)amino)-5-methylpyrimidin-4-yl)benzamide

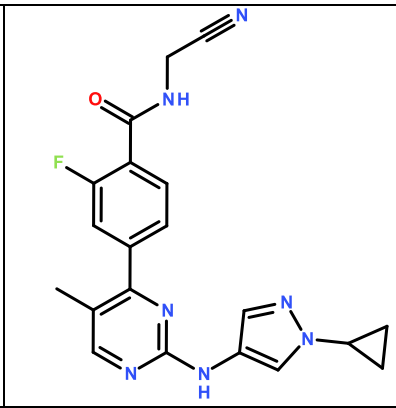
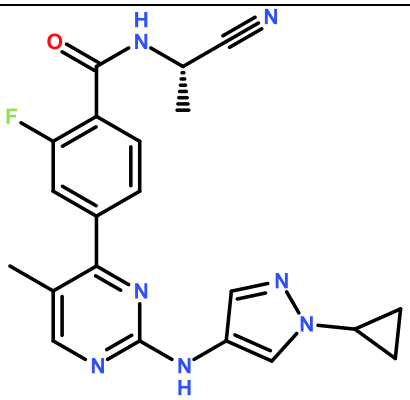
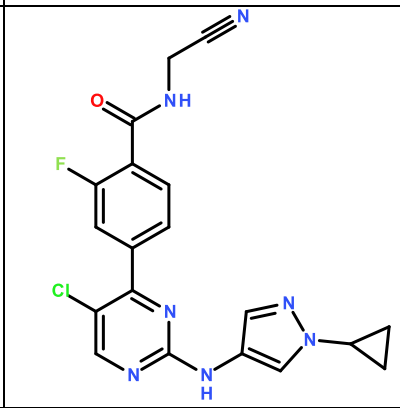
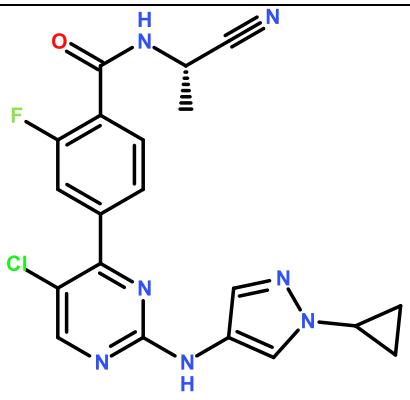
81		4-(2-((1-(2-cyano-2-methylpropyl)-1H-pyrazol-4-yl)amino)-5-methylpyrimidin-4-yl)-N-(2,2,2-trifluoroethyl)benzamide
83		N-(cyanomethyl)-5-(2-((1-cyclopropyl-1H-pyrazol-4-yl)amino)-5-methylpyrimidin-4-yl)picolinamide
93		N-((1-cyanocyclopropyl)methyl)-4-(2-((1-cyclopropyl-1H-pyrazol-4-yl)amino)-5-methylpyrimidin-4-yl)benzamide
94		(S)-N-(1-cyanoethyl)-4-(2-((1-cyclopropyl-1H-pyrazol-4-yl)amino)-5-methylpyrimidin-4-yl)benzamide

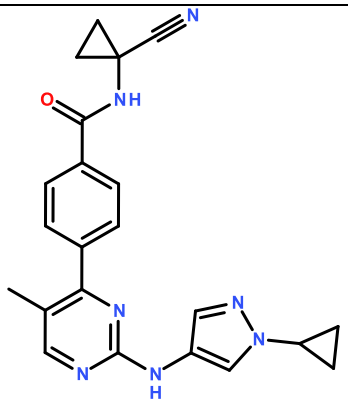
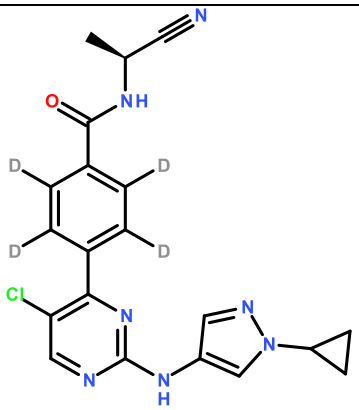
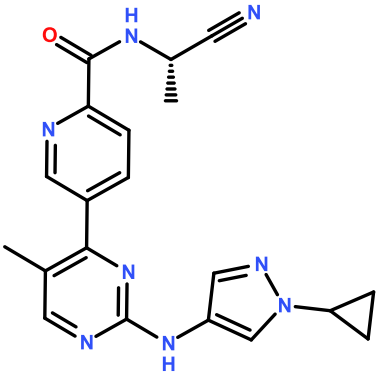
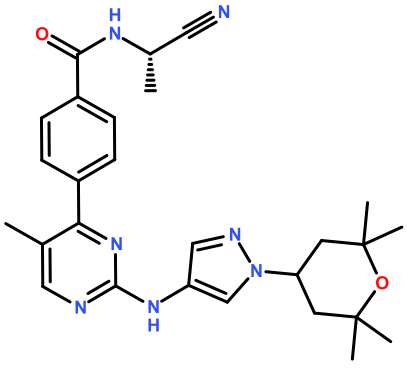
95		4-(5-chloro-2-((1-cyclopropyl-1H-pyrazol-4-yl)amino)pyrimidin-4-yl)-N-(cyanomethyl)benzamide
97		(R)-4-(5-chloro-2-((1-methyl-1H-pyrazol-4-yl)amino)pyrimidin-4-yl)-N-(1-cyanoethyl)benzamide
100		N-(cyanomethyl)-2-fluoro-4-(5-methyl-2-((1-methyl-1H-pyrazol-4-yl)amino)pyrimidin-4-yl)benzamide
101		(R)-N-(1-cyanoethyl)-4-(5-methyl-2-((1-methyl-1H-pyrazol-4-yl)amino)pyrimidin-4-yl)benzamide

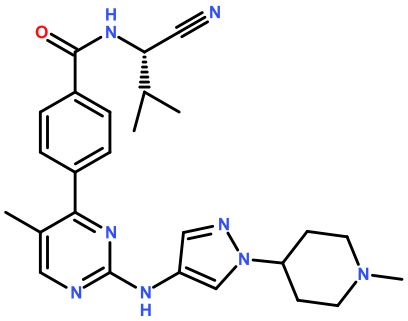
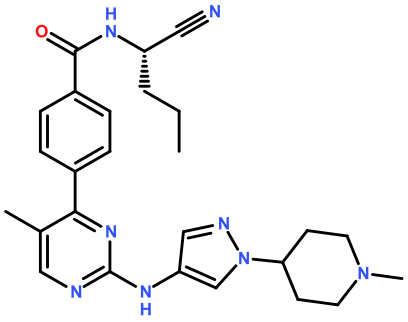
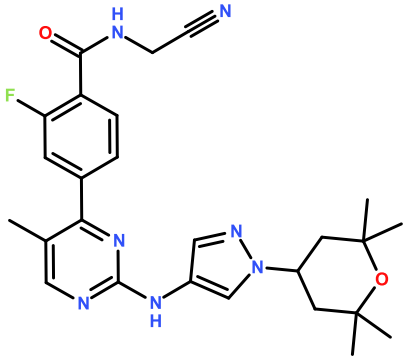
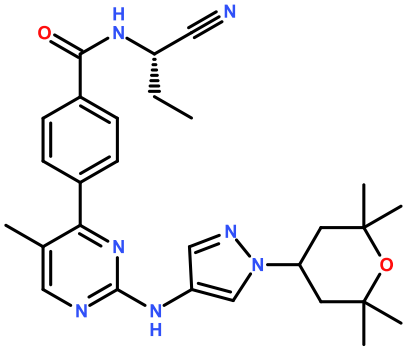
104		N-(cyanomethyl)-4-(2-((1-(3,3-difluorocyclobutyl)-1H-pyrazol-4-yl)amino)-5-methylpyrimidin-4-yl)benzamide
106		4-(2-((1-(3-cyanocyclobutyl)-1H-pyrazol-4-yl)amino)-5-methylpyrimidin-4-yl)-N-(cyanomethyl)benzamide
107		N-(cyanomethyl)-4-(5-methyl-2-((1-methyl-1H-pyrazol-3-yl)amino)pyrimidin-4-yl)benzamide
108		N-(cyanomethyl)-4-(2-((1-cyclopropyl-1H-pyrazol-4-yl)amino)-5-methylpyrimidin-4-yl)-N-methylbenzamide

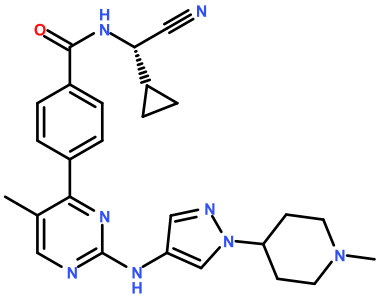
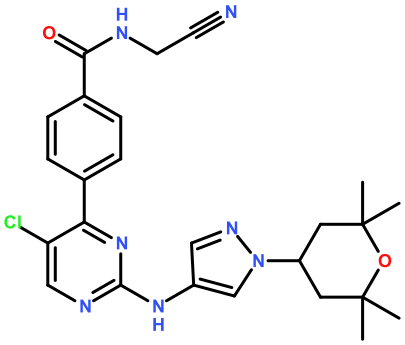
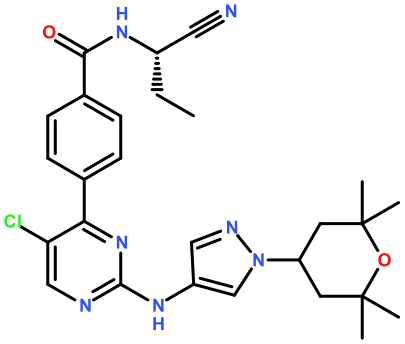
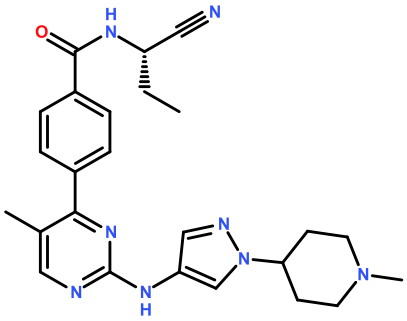
111		(S)-4-(5-chloro-2-((1-cyclopropyl-1H-pyrazol-4-yl)amino)pyrimidin-4-yl)-N-(1-cyanoethyl)benzamide
113		N-(cyanomethyl)-4-(5-methyl-2-((1-(2,2,6,6-tetramethyltetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)amino)pyrimidin-4-yl)benzamide
120		5-(5-chloro-2-((1-cyclopropyl-1H-pyrazol-4-yl)amino)pyrimidin-4-yl)-N-(cyanomethyl)picolinamide
121		(S)-5-(5-chloro-2-((1-cyclopropyl-1H-pyrazol-4-yl)amino)pyrimidin-4-yl)-N-(1-cyanoethyl)picolinamide

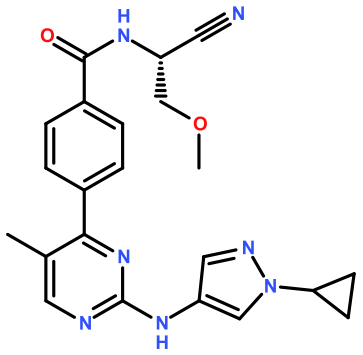
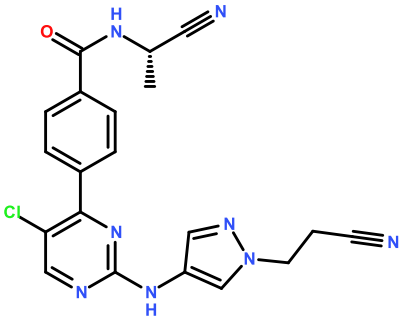
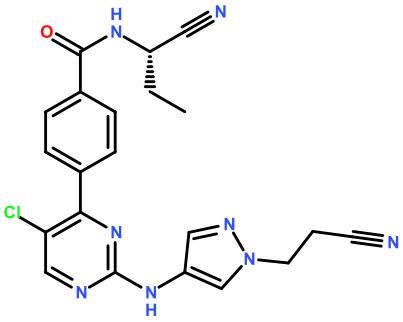
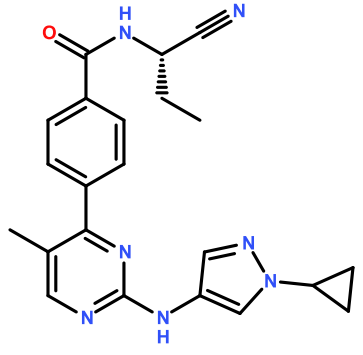
122		4-(5-chloro-2-((1-methyl-1H-pyrazol-4-yl)amino)pyrimidin-4-yl)-N-(2-cyano-2-methylpropyl)benzamide
123		4-(5-chloro-2-((1-cyclopropyl-1H-pyrazol-4-yl)amino)pyrimidin-4-yl)-N-(2-cyano-2-methylpropyl)benzamide
124		4-(5-chloro-2-((1-methyl-1H-pyrazol-4-yl)amino)pyrimidin-4-yl)-N-((1-cyanocyclopropyl)methyl)benzamide
125		(S)-4-(5-chloro-2-((1-methyl-1H-pyrazol-4-yl)amino)pyrimidin-4-yl)-N-(1-cyanoethyl)benzamide

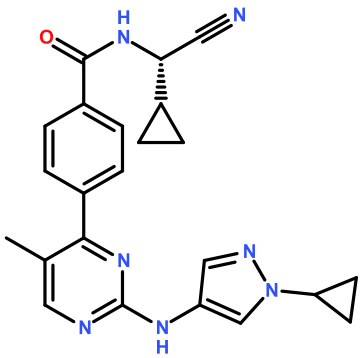
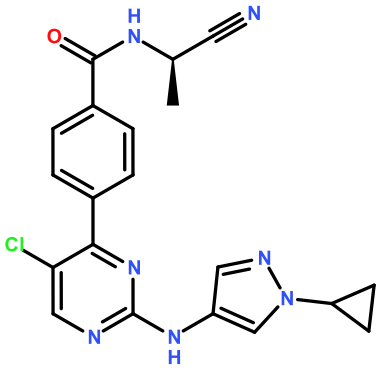
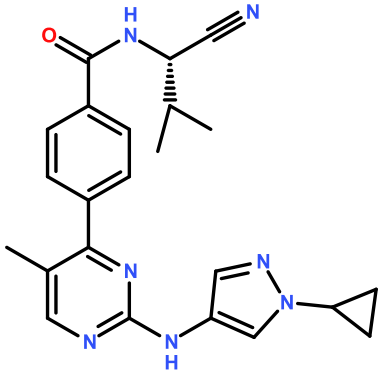
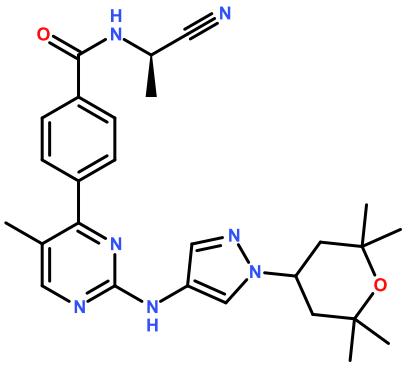
128		N-(cyanomethyl)-4-(2-((1-cyclopropyl-1H-pyrazol-4-yl)amino)-5-methylpyrimidin-4-yl)-2-fluorobenzamide
129		(S)-N-(1-cyanoethyl)-4-(2-((1-cyclopropyl-1H-pyrazol-4-yl)amino)-5-methylpyrimidin-4-yl)-2-fluorobenzamide
135		4-(5-chloro-2-((1-cyclopropyl-1H-pyrazol-4-yl)amino)pyrimidin-4-yl)-N-(cyanomethyl)-2-fluorobenzamide
137		(S)-4-(5-chloro-2-((1-cyclopropyl-1H-pyrazol-4-yl)amino)pyrimidin-4-yl)-N-(1-cyanoethyl)-2-fluorobenzamide

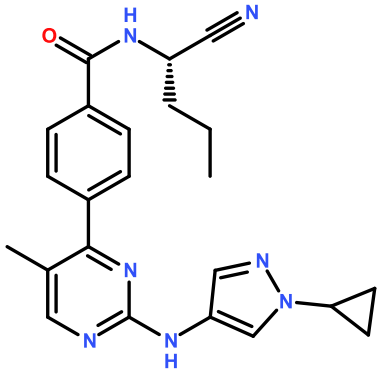
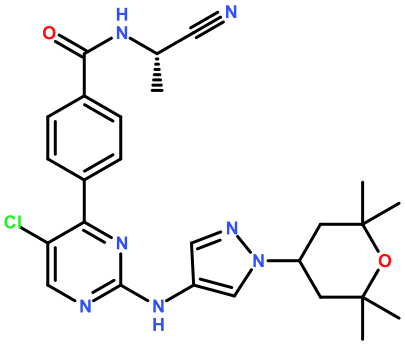
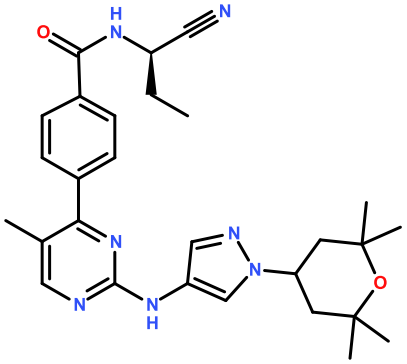
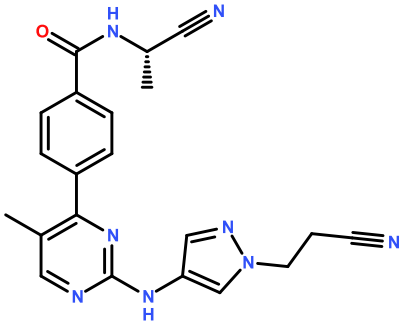
160		N-(1-cyanocyclopropyl)-4-(2-((1-cyclopropyl-1H-pyrazol-4-yl)amino)-5-methylpyrimidin-4-yl)benzamide
162		(S)-4-(5-chloro-2-((1-cyclopropyl-1H-pyrazol-4-yl)amino)pyrimidin-4-yl)-N-(1-cyanoethyl)benzamide-2,3,5,6-d_4
164		(S)-N-(1-cyanoethyl)-5-(2-((1-cyclopropyl-1H-pyrazol-4-yl)amino)-5-methylpyrimidin-4-yl)picolinamide
173		(S)-N-(1-cyanoethyl)-4-(5-methyl-2-((1-(2,2,6,6-tetramethyltetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)amino)pyrimidin-4-yl)benzamide

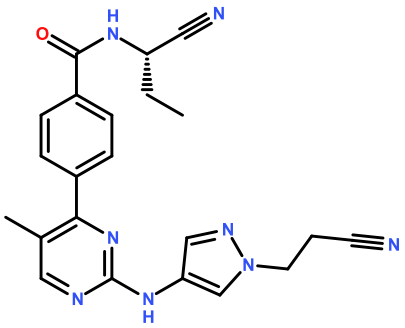
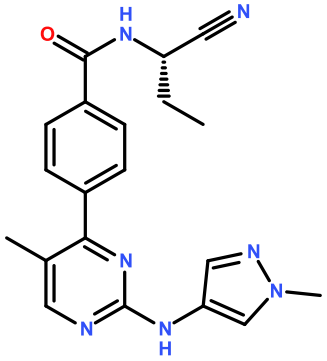
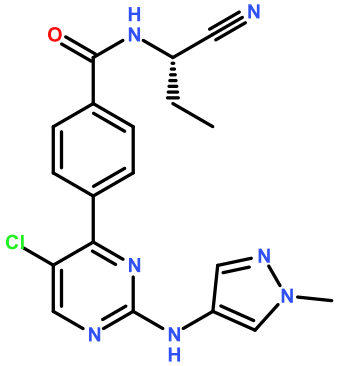
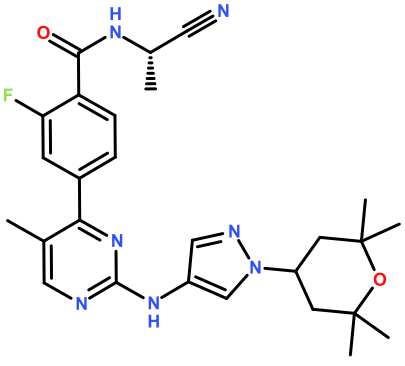
174		(S)-N-(1-cyano-2-methylpropyl)-4-(5-methyl-2-((1-(1-methylpiperidin-4-yl)-1H-pyrazol-4-yl)amino)pyrimidin-4-yl)benzamide
176		(S)-N-(1-cyanobutyl)-4-(5-methyl-2-((1-(1-methylpiperidin-4-yl)-1H-pyrazol-4-yl)amino)pyrimidin-4-yl)benzamide
178		N-(cyanomethyl)-2-fluoro-4-(5-methyl-2-((1-(2,2,6,6-tetramethyltetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)amino)pyrimidin-4-yl)benzamide
179		(S)-N-(1-cyanopropyl)-4-(5-methyl-2-((1-(2,2,6,6-tetramethyltetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)amino)pyrimidin-4-yl)benzamide

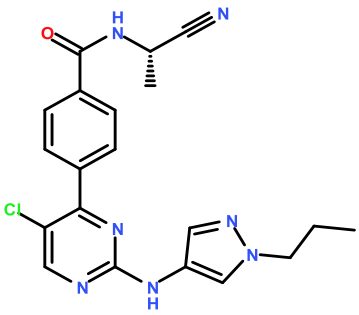
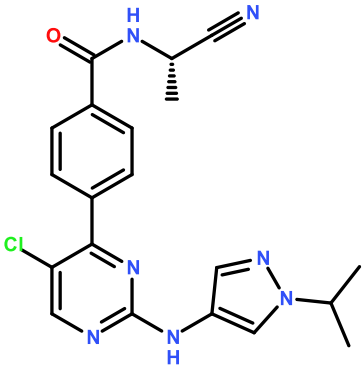
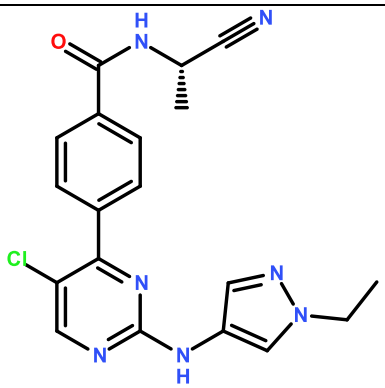
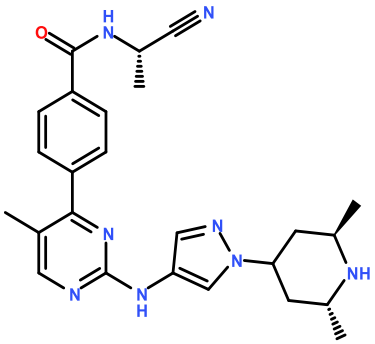
180		(S)-N-(cyano(cyclopropyl)methyl)-4-(5-methyl-2-((1-(1-methylpiperidin-4-yl)-1H-pyrazol-4-yl)amino)pyrimidin-4-yl)benzamide
181		4-(5-chloro-2-((1-(2,2,6,6-tetramethyltetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)amino)pyrimidin-4-yl)-N-(cyanomethyl)benzamide
182		(S)-4-(5-chloro-2-((1-(2,2,6,6-tetramethyltetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)amino)pyrimidin-4-yl)-N-(1-cyanopropyl)benzamide
184		(S)-N-(1-cyanopropyl)-4-(5-methyl-2-((1-(1-methylpiperidin-4-yl)-1H-pyrazol-4-yl)amino)pyrimidin-4-yl)benzamide

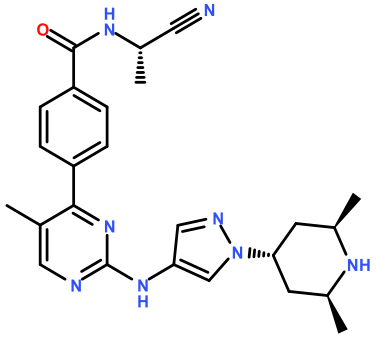
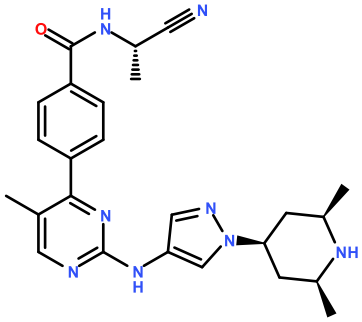
187		(R)-N-(1-cyano-2-methoxyethyl)-4-(2-((1-cyclopropyl-1H-pyrazol-4-yl)amino)-5-methylpyrimidin-4-yl)benzamide
189		(S)-4-(5-chloro-2-((1-(2-cyanoethyl)-1H-pyrazol-4-yl)amino)pyrimidin-4-yl)-N-(1-cyanoethyl)benzamide
190		(S)-4-(5-chloro-2-((1-(2-cyanoethyl)-1H-pyrazol-4-yl)amino)pyrimidin-4-yl)-N-(1-cyanopropyl)benzamide
193		(S)-N-(1-cyanopropyl)-4-(2-((1-cyclopropyl-1H-pyrazol-4-yl)amino)-5-methylpyrimidin-4-yl)benzamide

194		(S)-N-(cyano(cyclopropyl)methyl)-4-(2-((1-cyclopropyl-1H-pyrazol-4-yl)amino)-5-methylpyrimidin-4-yl)benzamide
196		(R)-4-(5-chloro-2-((1-cyclopropyl-1H-pyrazol-4-yl)amino)pyrimidin-4-yl)-N-(1-cyanoethyl)benzamide
197		(S)-N-(1-cyano-2-methylpropyl)-4-(2-((1-cyclopropyl-1H-pyrazol-4-yl)amino)-5-methylpyrimidin-4-yl)benzamide
198		(R)-N-(1-cyanoethyl)-4-(5-methyl-2-((1-(2,2,6,6-tetramethyltetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)amino)pyrimidin-4-yl)benzamide

202		(S)-N-(1-cyanobutyl)-4-(2-((1-cyclopropyl-1H-pyrazol-4-yl)amino)-5-methylpyrimidin-4-yl)benzamide
206		(S)-4-(5-chloro-2-((1-(2,2,6,6-tetramethyltetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)amino)pyrimidin-4-yl)-N-(1-cyanoethyl)benzamide
208		(R)-N-(1-cyanopropyl)-4-(5-methyl-2-((1-(2,2,6,6-tetramethyltetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)amino)pyrimidin-4-yl)benzamide
216		(S)-N-(1-cyanoethyl)-4-(2-((1-(2-cyanoethyl)-1H-pyrazol-4-yl)amino)-5-methylpyrimidin-4-yl)benzamide

217		(S)-4-(2-((1-(2-cyanoethyl)-1H-pyrazol-4-yl)amino)-5-methylpyrimidin-4-yl)-N-(1-cyanopropyl)benzamide
219		(S)-N-(1-cyanopropyl)-4-(5-methyl-2-((1-methyl-1H-pyrazol-4-yl)amino)pyrimidin-4-yl)benzamide
220		(S)-4-(5-chloro-2-((1-methyl-1H-pyrazol-4-yl)amino)pyrimidin-4-yl)-N-(1-cyanopropyl)benzamide
224		(S)-N-(1-cyanoethyl)-2-fluoro-4-(5-methyl-2-((1-(2,2,6,6-tetramethyltetrahydro-2H-pyran-4-yl)-1H-pyrazol-4-yl)amino)pyrimidin-4-yl)benzamide

227		(S)-4-(5-chloro-2-((1-propyl-1H-pyrazol-4-yl)amino)pyrimidin-4-yl)-N-(1-cyanoethyl)benzamide
228		(S)-4-(5-chloro-2-((1-isopropyl-1H-pyrazol-4-yl)amino)pyrimidin-4-yl)-N-(1-cyanoethyl)benzamide
229		(S)-4-(5-chloro-2-((1-ethyl-1H-pyrazol-4-yl)amino)pyrimidin-4-yl)-N-(1-cyanoethyl)benzamide
230		N-((S)-1-cyanoethyl)-4-(2-((1-(trans-2,6-dimethylpiperidin-4-yl)-1H-pyrazol-4-yl)amino)-5-methylpyrimidin-4-yl)benzamide

231		N-((S)-1-cyanoethyl)-4-(2-((1-((2S,4s,6R)-2,6-dimethylpiperidin-4-yl)-1H-pyrazol-4-yl)amino)-5-methylpyrimidin-4-yl)benzamide
232		N-((S)-1-cyanoethyl)-4-(2-((1-((2S,4r,6R)-2,6-dimethylpiperidin-4-yl)-1H-pyrazol-4-yl)amino)-5-methylpyrimidin-4-yl)benzamide.

35. A pharmaceutical composition comprising a compound according to any of claims 1-34, effective to treat or reduce one or more diseases or disorders, in a mammal, including a human, and a pharmaceutically acceptable excipient, carrier, or diluent.

36. The pharmaceutical composition of claim 35, being suitable for oral administration, topical administration or GI-restricted administration.

37. The pharmaceutical composition of claim 35 or 36, being useful to treat or reduce one or more of inflammatory diseases, immune-mediated diseases and cancers, or a related disease or disorder.

38. A unit dosage form comprising a pharmaceutical composition according to any of claims 35-37.