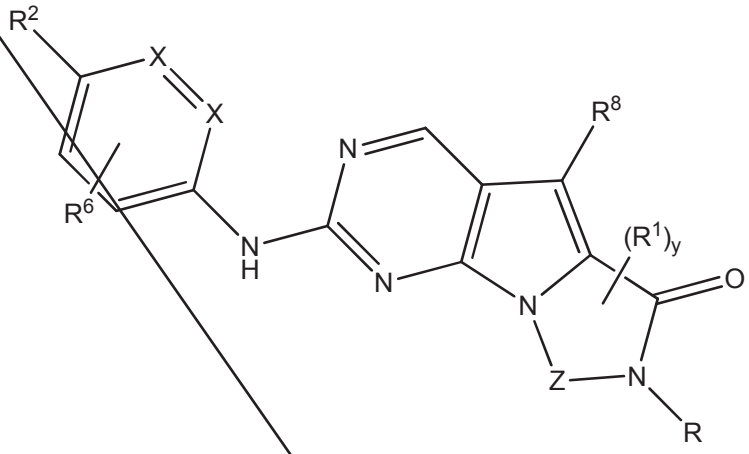
CLAIMS

1. A compound of formula:



or a pharmaceutically acceptable salt thereof, wherein:

Z is —$(CH_2)_x$— wherein x is 1, 2, 3 or 4 or —O—$(CH_2)_z$— wherein z is 2, 3 or 4;

each X is independently CH or N;

each of R and R^8 are independently H, C_1-C_3 alkyl or haloalkyl;

each R^1 is independently aryl, alkyl, cycloalkyl or haloalkyl, wherein each of said alkyl, cycloalkyl and haloalkyl groups optionally includes O or N heteroatoms in place of a carbon in the chain and two R^1's on adjacent ring atoms or on the same ring atom together with the ring atom(s) to which they are attached optionally form a 3-8-membered cycle;

y is 0, 1, 2, 3 or 4;

R^2 is -$(alkylene)_m$-heterocyclo, -$(alkylene)_m$-heteroaryl, -$(alkylene)_m$-NR^3R^4, -$(alkylene)_m$-C(O)—NR^3R^4; -$(alkylene)_m$-C(O)—O-alkyl; -$(alkylene)_m$-O—R^5, -$(alkylene)_m$-$S(O)_n$—R^5, or -$(alkylene)_m$-$S(O)_n$—NR^3R^4 any of which may be optionally independently substituted with one or more R^x groups as allowed by valance, and wherein two R^x groups bound to the same or adjacent atom may optionally combine to form a ring and wherein m is 0 or 1 and n is 0, 1 or 2;

R^3 and R^4 at each occurrence are independently:

(i) hydrogen or

(ii) alkyl, cycloalkyl, heterocyclo, aryl, heteroaryl, cycloalkylalkyl, heterocycloalkyl, arylalkyl, or heteroarylalkyl any of which may be optionally independently substituted with one or more R^x groups as allowed by valance, and wherein two R^x groups bound to the same or adjacent atom may optionally combine to form a ring; or R^3 and R^4 together with the nitrogen atom to which they are attached may combine to form a heterocyclo ring optionally independently substituted with one or more R^x groups as allowed by valance, and wherein two R^x groups bound to the same or adjacent atom may optionally combine to form a ring;

R^5 and R^5* at each occurrence is:

(i) hydrogen or

(ii) alkyl, alkenyl, alkynyl, cycloalkyl, heterocyclo, aryl, heteroaryl, cycloalkylalkyl, heterocycloalkyl, arylalkyl, or heteroarylalkyl any of which may be optionally independently substituted with one or more R^x groups as allowed by valance;

R^x at each occurrence is independently, halo, cyano, nitro, oxo, alkyl, haloalkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, heterocyclo, aryl, heteroaryl, arylalkyl, heteroarylalkyl, cycloalkylalkyl, heterocycloalkyl, -(alkylene)$_m$-OR^5, -(alkylene)$_m$-O-alkylene-OR^5, -(alkylene)$_m$-S(O)$_n$—R^5, -(alkylene)$_m$-NR^3R^4, -(alkylene)$_m$-CN, -(alkylene)$_m$-C(O)—R^5, -(alkylene)$_m$-C(S)—R^5, -(alkylene)$_m$-C(O)—OR^5, -(alkylene)$_m$-O—C(O)—R^5, -(alkylene)$_m$-C(S)—OR^5, -(alkylene)$_m$-C(O)-(alkylene)$_m$-NR^3R^4, -(alkylene)$_m$-C(S)—NR^3R^4, -(alkylene)$_m$-N(R^3)—C(O)—NR^3R^4, -(alkylene)$_m$-N(R^3)—C(S)—NR^3R^4, -(alkylene)$_m$-N(R^3)—C(O)—R^5, -(alkylene)$_m$-N(R^3)—C(S)—R^5, -(alkylene)$_m$-O—C(O)—NR^3R^4, -(alkylene)$_m$-O—C(S)—NR^3R^4, -(alkylene)$_m$-SO_2—NR^3R^4, -(alkylene)$_m$-N(R^3)—SO_2—R^5, -(alkylene)$_m$-N(R^3)—SO_2—NR^3R^4, -(alkylene)$_m$-N(R^3)—C(O)—OR^5)-(alkylene)$_m$-N(R^3)—C(S)—OR^5, or -(alkylene)$_m$-N(R^3)—SO_2—R^5; wherein:

said alkyl, haloalkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, heterocyclo, aryl, heteroaryl, arylalkyl, heteroarylalkyl, cycloalkylalkyl, and heterocycloalkyl groups may be further independently substituted with one or more -(alkylene)$_m$-CN, -(alkylene)$_m$-OR^5*, -(alkylene)$_m$-S(O)$_n$—R^5*, -(alkylene)$_m$-NR^3*R^4*, -(alkylene)$_m$-C(O)—R^5*, -(alkylene)$_m$-C(=S)R^5*, -(alkylene)$_m$-C(=O)OR^5*, -(alkylene)$_m$-OC(=O)R^5*, -(alkylene)$_m$-C(S)—

OR^5*, -(alkylene)$_m$-C(O)—NR^3*R^4*, -(alkylene)$_m$-C(S)—NR^3*R^4*, -(alkylene)$_m$-N(R^3*)—C(O)—NR^3*R^4*, -(alkylene)$_m$-N(R^3*)—C(S)—NR^3*R^4*, (alkylene)$_m$-N(R^3*)—C(O)—R^5*, -(alkylene)$_m$-N(R^3*)—C(S)—R^5*, -(alkylene)$_m$-O—C(O)—NR^3*R^4*, -(alkylene)$_m$-O—C(S)—NR^3*R^4*, -(alkylene)$_m$-SO_2—NR^3*R^4*, -(alkylene)$_m$-N(R^3*)—SO_2—R^5*, -(alkylene)$_m$-N(R^3*)—SO_2—NR^3*R^4*, -(alkylene)$_m$-N(R^3*)—C(O)—OR^5*, -(alkylene)$_m$-N(R^3*)—C(S)—OR^5*, or -(alkylene)$_m$-N(R^3*)—SO_2—R^5*,

n is 0, 1 or 2, and

m is 0 or 1; and

R^3* and R^4* at each occurrence are independently:

(i) hydrogen or

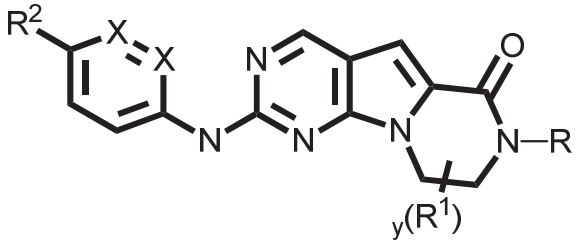
(ii) alkyl, alkenyl, alkynyl cycloalkyl, heterocyclo, aryl, heteroaryl, cycloalkylalkyl, heterocycloalkyl, arylalkyl, or heteroarylalkyl any of which may be optionally independently substituted with one or more R^x groups as allowed by valance; or R^3* and R^4* together with the nitrogen atom to which they are attached may combine to form a heterocyclo ring optionally independently substituted with one or more Rx groups as allowed by valance, and

R^6 is a lower alkyl or absent.

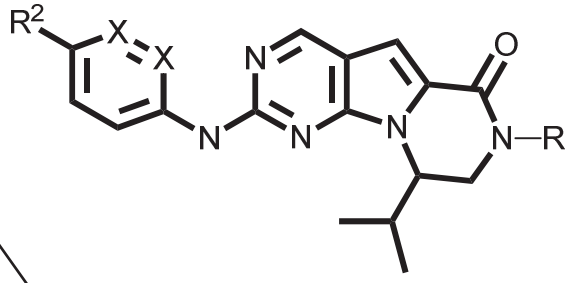
2. The compound of claim 1, wherein R^8 is hydrogen or C_1-C_3 alkyl.

3. The compound of claim 1 having the formula selected from the structures shown in FIG. 4.

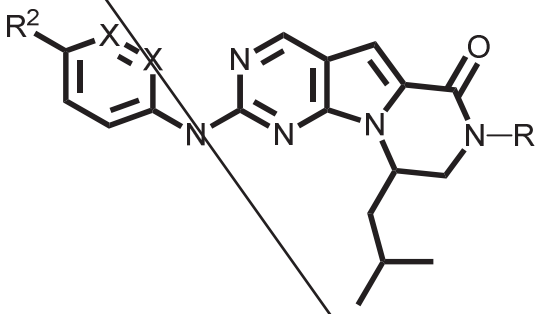
4. The compound of claim 1 having formula:



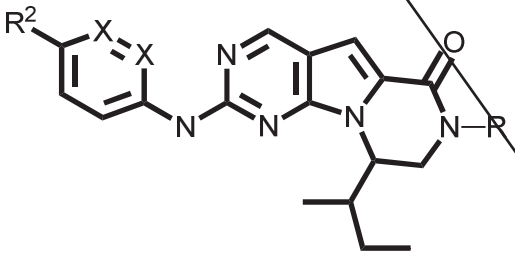
5. The compound of claim 1 having formula:



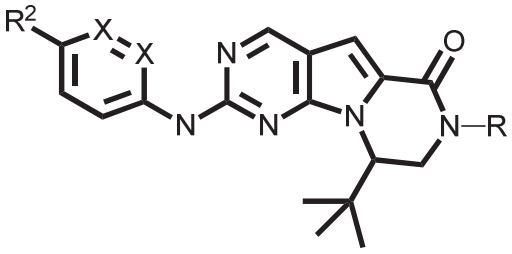
6. The compound of claim 1 having formula:



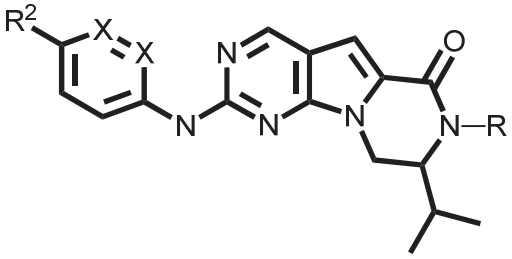
7. The compound of claim 1 having formula:



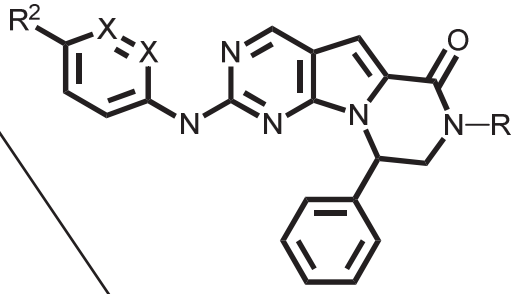
8. The compound of claim 1 having formula:



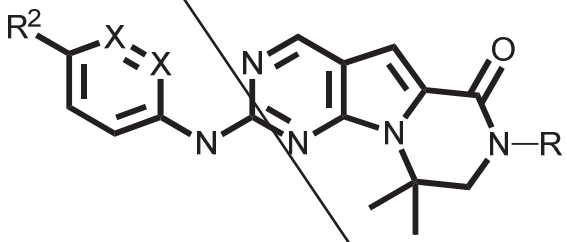
9. The compound of claim 1 having formula:



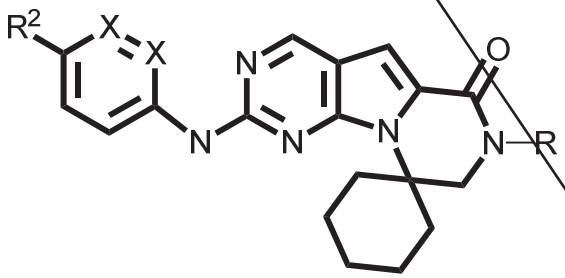
10. The compound of claim 1 having formula:



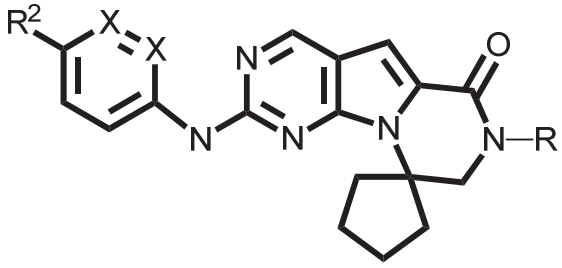
11. The compound of claim 1 having formula:



12. The compound of claim 1 having formula:



13. The compound of claim 1 having formula:



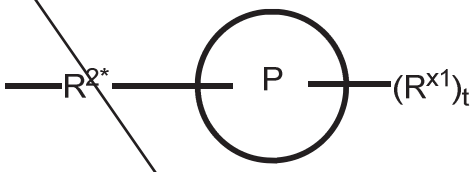
14. The compound of claim 1, wherein both of X are N.

15. The compound of claim 1, wherein R^2 is selected from the structures of FIG. 1.

16. The compound of claim 1, wherein R^2 is -(alkylene)$_m$-heterocyclo, -(alkylene)$_m$-NR^3R^4, -(alkylene)$_m$-C(O)—NR^3R^4, -(alkylene)$_m$-C(O)—O-alkyl or -(alkylene)$_m$-OR^5 any of

which may be optionally independently substituted with one or more R^x groups as allowed by valance, and wherein two R^x groups bound to the same or adjacent atom may optionally combine to form a ring.

17. The compound of claim 1, wherein R^2 is



wherein:

R^2* is a bond, alkylene, -(alkylene)$_m$-O-(alkylene)$_m$-, -(alkylene)$_m$-C(O)-(alkylene)$_m$-, -(alkylene)$_m$-S(O)$_2$-(alkylene)$_m$- or -(alkylene)$_m$-NH-(alkylene)$_m$- wherein each m is independently 0 or 1;

P is a 4- to 8-membered mono- or bicyclic saturated heterocyclyl group;

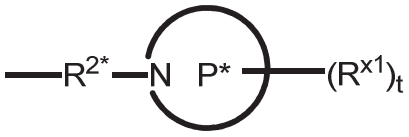
each R^{x1} is independently -(alkylene)$_m$-(C(O))$_m$-(alkylene)$_m$-(N(R^N))$_m$-(alkyl)$_m$ wherein each m is independently 0 or 1 provided at least one m is 1, —(C(O))—O-alkyl, -(alkylene)$_m$-cycloalkyl wherein m is 0 or 1, —N(R^N)-cycloalkyl, —C(O)-cycloalkyl, -(alkylene)$_m$-heterocyclyl wherein m is 0 or 1, or —N(R^N)-heterocyclyl, —C(O)-heterocyclyl, —S(O)$_2$-(alkylene)$_m$ wherein:

R^N is H, C_1 to C_4 alkyl or C_1 to C_6 heteroalkyl, and

wherein two R^{x1} can, together with the atoms to which they attach on P, which may be the same atom, form a ring; and

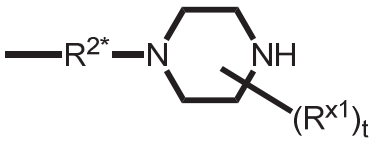
t is 0, 1 or 2.

18. The compound of claim 17, wherein R^2 is

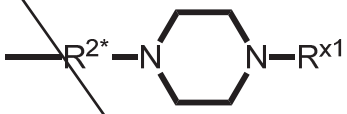


wherein P* is a 4- to 8-membered mono- or bicyclic saturated heterocyclyl group and R^2*, R^{x1} and t are as previously defined.

19. The compound of claim 17, wherein R^2 is



20. The compound of claim 18, wherein R^2 is



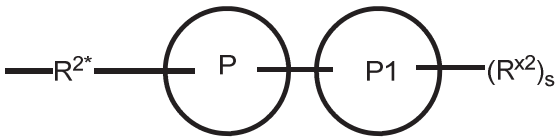
21. The compound of claim 17, wherein each R^{x1} is only optionally substituted by C_1-C_4 alkyl, halogen or hydroxy.

22. The compound of claim 18, wherein each R^{x1} is only optionally substituted by C_1-C_4 alkyl, halogen or hydroxy.

23. The compound of claim 19, wherein each R^{x1} is only optionally substituted by C_1-C_4 alkyl, halogen or hydroxy.

24. The compound of claim 20, wherein each R^{x1} is only optionally substituted by C_1-C_4 alkyl, halogen or hydroxy.

25. The compound of claim 1, wherein R^2 is



wherein:

R^{2*} is a bond, alkylene, -(alkylene)$_m$-O-(alkylene)$_m$-, -(alkylene)$_m$-C(O)-(alkylene)$_m$-, -(alkylene)$_m$-S(O)-2-(alkylene)$_m$ or -(alkylene)$_m$-NH-(alkylene)$_m$-, wherein each m is independently 0 or 1;

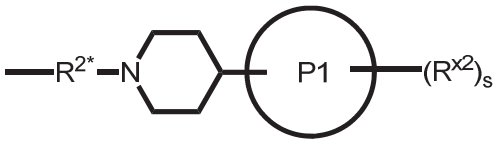
P is a 4- to 8-membered mono- or bicyclic saturated heterocyclyl group;

P1 is a 4- to 6-membered monocyclic saturated heterocyclyl group;

each R^{x2} is independently hydrogen or alkyl; and

s is 0, 1 or 2.

26. The compound of claim 25, wherein R^2 is



27. The compound of claim 1, wherein R^x is not further substituted.

28. The compound of claim 17, wherein R^2* is alkylene, -(alkylene)$_m$-O-(alkylene)$_m$- , -(alkylene)$_m$-C(O)-(alkylene)$_m$-, -(alkylene)$_m$-S(O)$_2$-(alkylene)$_m$- and or -(alkylene)$_m$-NH-(alkylene)$_m$- wherein each m is independently 0 or 1, and wherein any alkylene is not further substituted.

29. The compound of claim 18, wherein R^2* is alkylene, -(alkylene)$_m$-O-(alkylene)$_m$- , -(alkylene)$_m$-C(O)-(alkylene)$_m$-, -(alkylene)$_m$-S(O)$_2$-(alkylene)$_m$- and or -(alkylene)$_m$-NH-(alkylene)$_m$- wherein each m is independently 0 or 1, and wherein any alkyleneis not further substituted.

30. The compound of claim 19, wherein R^2* is alkylene, -(alkylene)$_m$-O-(alkylene)$_m$-, -(alkylene)$_m$-C(O)-(alkylene)$_m$-, -(alkylene)$_m$-S(O)$_2$-(alkylene)$_m$- and or -(alkylene)$_m$-NH-(alkylene)$_m$- wherein each m is independently 0 or 1, and wherein any alkylene is not further substituted.

31. The compound of claim 20, wherein R^2* is alkylene, -(alkylene)$_m$-O-(alkylene)$_m$-, -(alkylene)$_m$-C(O)-(alkylene)$_m$-, -(alkylene)$_m$-S(O)$_2$-(alkylene)$_m$- and or -(alkylene)$_m$-NH-(alkylene)$_m$- wherein each m is independently 0 or 1, and wherein any alkylene is not further substituted.

32. The compound of claim 21, wherein R^2* is alkylene, -(alkylene)$_m$-O-(alkylene)$_m$-, -(alkylene)$_m$-C(O)-(alkylene)$_m$-, -(alkylene)$_m$-S(O)$_2$-(alkylene)$_m$- and or -(alkylene)$_m$-NH-(alkylene)$_m$- wherein each m is independently 0 or 1, and wherein any alkylene is not further substituted.

33. The compound of claim 22 wherein R^2* is alkylene, -(alkylene)$_m$-O-(alkylene)$_m$-, -(alkylene)$_m$-C(O)-(alkylene)$_m$-, -(alkylene)$_m$-S(O)$_2$-(alkylene)$_m$- and or -(alkylene)$_m$-NH-(alkylene)$_m$- wherein each m is independently 0 or 1, and wherein any alkylene is not further substituted.

34. The compound of claim 23 wherein R^2* is alkylene, -(alkylene)$_m$-O-(alkylene)$_m$-, -(alkylene)$_m$-C(O)-(alkylene)$_m$-, -(alkylene)$_m$-S(O)$_2$-(alkylene)$_m$- and or -(alkylene)$_m$-NH-

$(alkylene)_m$- wherein each m is independently 0 or 1, and wherein any alkylene is not further substituted.

35. The compound of claim 24, wherein R^2* is alkylene, -$(alkylene)_m$-O-$(alkylene)_m$-, -$(alkylene)_m$-C(O)-$(alkylene)_m$-, -$(alkylene)_m$-$S(O)_2$-$(alkylene)_m$- and or -$(alkylene)_m$-NH-$(alkylene)_m$- wherein each m is independently 0 or 1, and wherein any alkylene is not further substituted.

36. The compound of claim 25, wherein R^2* is alkylene, -$(alkylene)_m$-O-$(alkylene)_m$-, -$(alkylene)_m$-C(O)-$(alkylene)_m$-, -$(alkylene)_m$-$S(O)_2$-$(alkylene)_m$- and or -$(alkylene)_m$-NH-$(alkylene)_m$- wherein each m is independently 0 or 1, and wherein any alkylene is not further substituted.

37. The compound of claim 26 wherein R^2* is alkylene, -$(alkylene)_m$-O-$(alkylene)_m$-, -$(alkylene)_m$-C(O)-$(alkylene)_m$-, -$(alkylene)_m$-S(O)2-$(alkylene)_m$- and or -$(alkylene)_m$-NH-$(alkylene)_m$- wherein each m is independently 0 or 1, and wherein any alkylene is not further substituted.

38. The compound of claim 1, wherein R is hydrogen or C_1-C_3 alkyl.

39. The compound of claim 16, wherein the alkylene in R^2 is methylene.

40. The compound of claim 17, wherein the alkylene in R^2 is methylene.

41. The compound of claim 25, wherein the alkylene in R^2 is methylene.

42. The compound of claim 1, wherein R^2 is -$(alkylene)_m$-heterocyclo or -$(alkylene)_m$-heteroaryl,

R is hydrogen, and,

X is independently CH or N.

43. The compound of claim 42, wherein R^2 is -$(alkylene)_m$-heterocyclo.

44. The compound of claim 42, wherein m is 0.

45. The compound of claim 43, wherein m is 0.

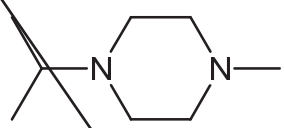
46. The compound of claim 42, wherein m is 1.

47. The compound of claim 43, wherein m is 1.

48. The compound of claim 42, wherein the heterocyclo is not substituted.

49. The compound of claim 43, wherein the heterocyclo is not substituted.

50. The compound of claim 42, wherein R^2 is



51. A pharmaceutical composition comprising the compound of claim 1, or a pharmaceutically acceptable salt thereof.

52. The compound of claim 1 having the formula selected from the structures shown in FIG. 5.

53. The compound of claim 1 having the formula selected from the structures shown in FIG. 6.

54. The compound of claim 1 having the formula selected from the structures shown in FIG. 7.

55. The compound of claim 1 having the formula selected from the structures shown in FIG. 8, wherein the selected structure falls within claim 1.

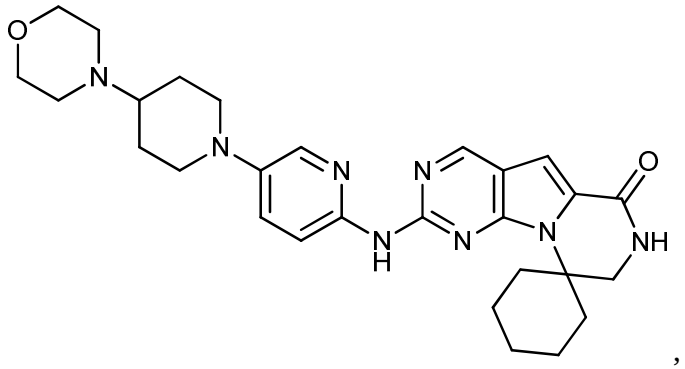
56. The compound of claim 1, wherein R^2 is selected from the structures of FIG. 2.

57. The compound of claim 1, wherein R^2 is selected from the structures of FIG. 3.

58. The compound of claim 1, wherein R^6 is absent.

What is claimed is:

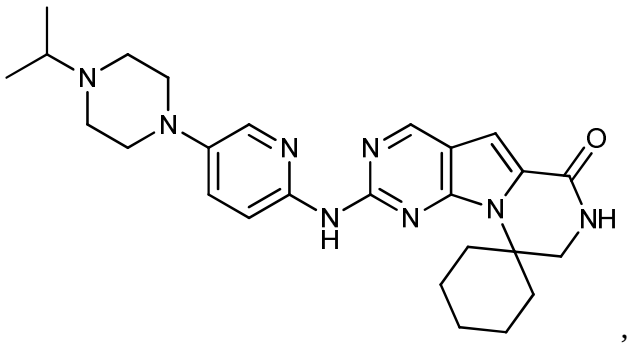
1. A compound of the formula:



, or a pharmaceutically acceptable salt thereof.

2. A pharmaceutical composition comprising an effective amount of the compound of claim 1 in a pharmaceutically acceptable carrier.

3. A compound of the formula:



, or a pharmaceutically acceptable salt thereof.

4. A pharmaceutical composition comprising an effective amount of the compound of claim 3 in a pharmaceutically acceptable carrier.