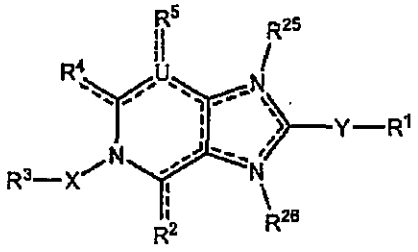
We Claim:

1. A compound of formula (A)



(A)

wherein:

the dotted lines represent optional double bonds, provided that no two double bonds are adjacent to one another, and that the dotted lines represent at least 3, optionally 4 double bonds;

U is N;

R^1 is selected from hydrogen, aryl, heterocycle, C_1-C_{10} alkoxy, C_1-C_{10} thioalkyl, C_1-C_{10} alkyl-amino, C_1-C_{10} dialkyl-amino, C_{3-10} cycloalkyl, C_{4-10} cycloalkenyl, and C_{4-10} cycloalkynyl, wherein each are optionally substituted with 1 or more R^6;

Y is selected from a single bond, O, S(O)m (where m is an integer from 0 to 2), NR^{11}, C_{1-10} alkylene, C_{2-10} alkenylene, and C_{2-10} alkynylene, or C_{1-10} alkylene, C_{2-20} alkenylene or C_{2-10} alkynylene, wherein 1 to 3 methylene groups optionally are independently replaced by 1 to 3 heteroatoms selected from O, S or NR^{11};

R^2 and R^4 are independently selected from hydrogen, C_{1-18} alkyl, C_{2-18} alkenyl, C_{2-18} alkynyl, C_{1-18} alkoxy, C_{1-18} alkylthio, halogen, -OH, -CN, -NO_2, -NR^7R^8, haloalkyloxy, haloalkyl, -C(=O)R^9, -C(=S)R^9, SH, aryl, aryloxy, arylthio, arylalkyl, C_{1-18} hydroxyalkyl, C_{3-10} cycloalkyl, C_{3-10} cycloalkyloxy, C_{3-10} cycloalkylthio, C_{3-10} cycloalkenyl, C_{7-10} cycloalkynyl, and heterocycle, provided that when one of R^{25} or R^{26} is present, then either R^2 or R^4 is selected from =O, =S, or =NR^{27};

X is selected from C_1-C_{10} alkylene, C_{2-10} alkenylene or C_{2-10} alkynylene, where each may include one or more heteroatoms selected from O, S, or NR^{11}, provided any such heteroatom is not adjacent to the N in the ring;

R^3 is selected from aryl, aryloxy, arylthio, cycloalkyl, cycloalkenyl, cycloalkynyl, aryl-N(R^{10})-, or heterocycle, where each said substituent is optionally substituted with at least one R^{17}, provided that for cycloalkenyl the double bond is not adjacent to a nitrogen;

R^5 independently is absent or is selected from hydrogen, C_{1-18} alkyl, C_{2-18} alkenyl, C_{2-18} alkynyl, C_{1-18} alkoxy, C_{1-18} alkylthio, halogen, -OH, -CN, -NO_2, -NR^7R^8, haloalkyloxy, haloalkyl, -C(=O)R^9, -C(=O)OR^9, -C(=S)R^9, SH, aryl, aryloxy, arylthio, arylalkyl, C_{1-18} hydroxyalkyl, C_{3-10} cycloalkyl, C_{3-10} cycloalkyloxy, C_{3-10} cycloalkylthio, C_{3-10} cycloalkenyl, C_{7-10} cycloalkynyl, and heterocycle;

R^6 is selected from hydrogen, C_{1-18} alkyl, C_{2-18} alkenyl, C_{2-18} alkynyl, C_{1-18} alkoxy, C_{1-18} alkylthio, C_{1-18} alkylsulfoxide, C_{1-18} alkylsulfone, C_{1-18} halo-alkyl, C_{2-18} halo-alkenyl, C_{2-18} halo-alkynyl, C_{1-18} halo-alkoxy, C_{1-18} halo-alkylthio, C_{3-10} cycloalkyl, C_{3-10} cycloalkenyl, C_{7-10} cycloalkynyl, halogen, OH, CN, cyanoalkyl, -CO_2R^{18}, NO_2, -NR^7R^8, C_{1-18} haloalkyl, C(=O)R^{18}, C(=S)R^{18}, SH, aryl, aryloxy, arylthio, arylsulfoxide, arylsulfone, arylsulfonamide, aryl(C_{1-18})alkyl, aryl(C_{1-18})alkyloxy, aryl(C_{1-18})alkylthio, heterocycle, and C_{1-18} hydroxyalkyl, where each may be optionally substituted with at least 1 R^{19};

R^7 and R^8 are independently selected from hydrogen, C_{1-18} alkyl, C_{1-18} alkenyl, aryl, C_{3-10} cycloalkyl, C_{4-10} cycloalkenyl, heterocycle, -C(=O)R^{12}; -C(=S) R^{12}, an amino acid residue linked through a carboxyl group thereof, and the group formed when R^7 and R^8 are taken together with the nitrogen to form a heterocycle;

R^9 and R^{18} are independently selected from hydrogen, OH, C_{1-18} alkyl, C_{2-18} alkenyl, C_{3-10} cycloalkyl, C_{4-10} cycloalkenyl, C_{1-18} alkoxy, -$NR^{15}R^{16}$, aryl, an amino acid residue linked through an amino group of the amino acid, $CH_2OCH(=O)R^{9a}$, and $CH_2OC(=O)OR^{9a}$ where R^{9a} is C_1-C_{12} alkyl, C_6-C_{20} aryl, C_6-C_{20} alkylaryl or C_6-C_{20} aralkyl;

R^{10} and R^{11} are independently selected from the group consisting of hydrogen, C_{1-18} alkyl, C_{2-18} alkenyl, C_{3-10} cycloalkyl, C_{4-10} cycloalkenyl, aryl, -C(=O)R^{12}, heterocycle, and an amino acid residue;

R^{12} is selected from the group consisting of hydrogen, C_{1-18} alkyl, C_{2-18} alkenyl, aryl, C_{3-10} cycloalkyl, C_{4-10} cycloalkenyl, and an amino acid residue;

R^{15} and R^{16} are independently selected from hydrogen, C_{1-18} alkyl, C_{2-18} alkenyl, C_{2-18} alkynyl, aryl, arylalkyl (unsubstituted, or substituted with C(O)OR^{18}), C_{3-10} cycloalkyl, C_{4-10} cycloalkenyl, and an amino acid residue;

R^{17} is independently selected from the group consisting of (a) hydrogen, C_{1-18} alkyl, C_{2-18} alkenyl, C_{2-18} alkynyl, C_{1-18} alkoxy, C_{1-18} alkylthio, C_{1-18} alkylsulfoxide, C_{1-18} alkylsulfone, C_{1-18} halogenated alkyl, C_{2-18} halogenated alkenyl, C_{2-18} halogenated alkynyl, C_{1-18} halogenated alkoxy, C_{1-18} halogenated alkylthio, C_{3-10} cycloalkyl, C_{3-10} cycloalkenyl, C_{7-10} cycloalkynyl, halogen, OH, CN, CO_2H, CO_2R^{18}, NO_2, NR^7R^8, haloalkyl, C(=O)R^{18}, C(=S)R^{18}, SH; aryl, heterocycle, aryloxy, arylthio, arylsulfoxide, arylsulfone, arylsulfonamide, arylalkyl, arylalkyloxy, arylalkylthio, heterocycle and C_{1-18} hydroxyalkyl, where each of said aryl, aryloxy, arylthio, arylsulfoxide, arylsulfone, arylsulfonamide, arylalkyl, arylalkyloxy, arylalkylthio, heterocycle, or C_{1-18} hydroxyalkyl is optionally substituted with 1 or more R^{19}, and (b) M-Q- wherein M is a ring optionally substituted with 1 or more R^{19}, and Q is a bond or a linking group connecting M to R^5 having 1 to 10 atoms selected from C and optionally 1 or more O, N or S atoms and optionally substituted with 1 or more R^{19};

R^{19} is selected from

(a) H;

(b) NO_2, SH, $NR^{20}R^{21}$, OH, halogen and CN;

(c) Sulfone, sulfonamide and sulfoxide;

(d) C_{1-18} alkyl, C_{2-18} alkenyl and C_{2-18} alkynyl;

(e) C_{1-18} alkyl, C_{2-18} alkenyl and C_{2-18} alkynyl wherein 1 or more methylene are replaced by 1 or more O, S, NR^{20}, C(O)$NR^{20}R^{21}$, OC(O)R^{12}, C(O)OR^{12} or N(R^{20})C(O);

(f) Substituents c), d) or e) substituted further by C_{3-10} cycloalkyl, C_{4-10} cycloalkenyl, C_{4-10} cycloalkynyl, aryl or heterocycle;

(g) C_{3-10} cycloalkyl, C_{4-10} cycloalkenyl, C_{4-10} cycloalkynyl, aryl and heterocycle, or said groups substituted with C_{1-6} alkyl, $C(O)OR^{12}$ =O, halogen, CN, $C(O)NR^{20}R^{21}$, $C(O)R^{18}$ or $OC(O)R^{18}$;

(h) $C(O)R^{18}$, $C(O)OR^{18}$, $OC(O)R^{18}$, $C(S)R^{18}$ and $C(O)N(R^{12})_2$;

(i) Substituents d) or e) substituted with =O, CN, halogen, $C(O)R^{18}$, $C(O)NR^{20}R^{21}$, $OC(O)R^{18}$, heterocycle, and heterocycle substituted with C_1-C_6 alkyl, $C(O)OR^{12}$, =O, CN, halogen, $OC(O)R^{18}$ or $C(O)NR^{20}R^{21}$;

(j) Substituents c) substituted further with C_{1-18} alkyl; and

(k) Substituents f) or g) substituted further with C_{1-18} alkyl, =O, $NR^{20}R^{21}$, CN, C_{1-18} alkoxy, heterocycle, C_{1-18} haloalkyl, heterocyclealkyl or halogen;

R^{20} and R^{21} are independently selected from hydrogen, C_{1-18} alkyl, C_{2-18} alkenyl, C_{2-18} alkynyl, aryl, heterocycle, C_{3-10} cycloalkyl, C_{4-10} cycloalkenyl, $-C(=O)R^{12}$, and $-C(=S)R^{12}$;

R^{25} and R^{26} are independently not present or are selected from hydrogen, C_{1-18} alkyl, C_{3-10} cycloalkyl, aryl and heterocycle, where each is optionally independently substituted with 1 to 4 of C_{1-6} alkyl, C_{1-6} alkoxy, halo, CH_2OH, benzyloxy, and OH;

R^{27} is selected from hydrogen, C_{1-18} alkyl, C_{3-10} cycloalkyl, (C_{3-10} cycloalkyl)-C_{1-6} alkyl, aryl, and arylC_{1-18} alkyl; and

salts, tautomers, polymorphs, isomers and solvates thereof.

2. The compound of claim 1 wherein R^1 is haloaryl, X is methylene, R^3 is heterocycle substituted with 1 or 2 R^{17}.

3. The compound of claim 1 wherein R^1 is an aryl or aromatic heterocycle substituted with 1 or 2 R^6.

4. The compound of claim 1 wherein R^3 is heterocycle.

5. The compound of claim 1 wherein YR^1 is haloaryl.

6. The compound of claim 5 wherein haloaryl is ortho-fluorophenyl.

7. The compound of claim 1 wherein R^3 is isoxazolyl substituted with 1 R^{17}.

8. The compound of claim 2 wherein R^{17} is aryl or an aromatic heterocycle which is substituted with 1, 2 or 3 R^{19}.

9. The compound of claim 1 wherein YR^1 is none of hydrogen, C_{3-10} cycloalkyl, or C_{1-6} alkyl.

10. The compound of claim 9 wherein YR^1 is not hydrogen or C_{1-6} alkyl.

11. The compound of claim 1 wherein R^{19} is trihalomethyl, trihalomethoxy, alkoxy or halogen.

12. The compound of claim 1 wherein R^1 is aryl or aromatic heterocyle substituted with 1, 2 or 3 R^6 wherein R^6 is halogen, C_{1-16} alkoxy; or C_{1-16} haloalkyl.

13. The compound of claim 12 wherein R^1 is phenyl substituted with 1, 2 or 3 halogens.

14. The compound of claim 13 wherein halogen is fluoro.

15. The compound of claim 1 wherein Y is a single bond, O, C_{1-6} alkylene, C_{2-6} alkenylene, C_{2-6} alkynylene or one of said groups containing 1 to 3 heteroatoms selected from O, S or NR^{11}.

16. The compound of claim 15 wherein Y is $-O(CH_2)_{1-5}-$, $-(CH_2)_{1-4}-O-(CH_2)_{1-4}-$, $-S-(CH_2)_{1-5}-$, $-(CH_2)_{1-4}-S-(CH_2)_{1-4}-$, $-NR^{11}-(CH_2)_{1-5}-$, $-(CH_2)_{1-4}-NR^{11}-(CH_2)_{1-4}-$ or C_{3-10} cycloalkylidene.

17. The compound of claim 15 wherein Y is $-OCH_2-$, $-CH_2O-$, C_{1-2} alkylene, C_{2-3} alkenylene, C_{2-3} alkynylene, O or a bond.

18. The compound of claim 15 wherein Y is a bond.

19. The compound of claim 1 wherein YR^1 is a single ring aromatic carbocycle or a heterocycle containing 1 or 2 N, S or O atoms in the ring.

20. The compound of claim 19 wherein the carbocycle or heterocycle contains 4 to 6 ring atoms.

21. The compound of claim 1 wherein YR^1 is halo- or halomethyl-substituted phenyl.

22. The compound of claim 1 wherein aryl or heteroaryl are substituted ortho or meta with halo- or halomethyl.

23. The compound of claim 1 wherein X is selected from the group consisting of alkylene, alkynylene or alkenylene and said hydrocarbons having an intrachain N, O or S heteroatom.

24. The compound of claim 1 wherein X is alkylene.

25. The compound of claim 23 wherein X is selected from the group consisting of $-CH_2-$, $-CH(CH_3)-$, $-CH_2-CH_2-$, $-CH_2-CH_2-CH_2-$, $-CH_2-CH_2-CH_2-CH_2-$, $-(CH_2)_{2-4}-O-(CH_2)_{2-4}-$, $-(CH_2)_{2-4}-S-(CH_2)_{2-4}-$, $-(CH_2)_{2-4}-NR^{10}-(CH_2)_{2-4}-$, C_{3-10} cycloalkylidene, C_{2-6} alkenylene and C_{2-6} alkynylene.

26. The compound of claim 1 wherein X is methylene.

27. The compound of claim 1 wherein R^3 is aryl or a heterocycle substituted with 0 to 3 R^{17}.

28. The compound of claim 27 wherein the heterocycle is an aromatic heterocycle.

29. The compound of claim 28 wherein the heterocycle contains 1, 2 or 3 N, S or O atoms in the ring, is linked to X through a ring carbon atom and contains 4 to 6 total ring atoms.

30. The compound of claim 29 wherein R^3 is isoxazolyl substituted with 1 to 3 R^{17}.

31. The compound of claim 1 wherein R^{17} is aryl or a heterocycle further substituted with 1 to 3 R^{19}.

32. The compound of claim 1 wherein M is aryl or aromatic heterocycle.

33. The compound of claim 1 wherein Q contains 0 to 20 atoms selected from C, O, S, N and H.

34. The compound of claim 1 wherein M is a cyclic group selected from R^{17}.

35. The compound of claim 1 wherein R^{17} is selected from the group consisting of C_{3-10} cycloalkyl, C_{3-10} cycloalkenyl, C_{7-10} cycloalkynyl, halogen, aryl, aryloxy, arylthio, arylsulfoxide, arylsulfone, arylsulfonamide, arylalkyl; arylalkyloxy; arylalkylthio; heterocycle; C_{1-18} hydroxyalkyl, each of said C_{3-10} cycloalkyl, C_{3-10} cycloalkenyl, C_{7-10} cycloalkynyl, halogen, aryl, aryloxy, arylthio, arylsulfoxide, arylsulfone, arylsulfonamide, arylalkyl; arylalkyloxy; arylalkylthio; heterocycle; and C_{1-18} hydroxyalkyl is unsubstituted or is substituted 1 or more R^{19}.

36. The compound of claim 1 wherein R^{17} is selected from the group consisting of aryl and heterocycle, and where said aryl or heterocycle is optionally substituted with 1 or more R^{19}.

37. The compound of claim 1 wherein R^9 and R^{18} are H, OH or alkyl.

38. The compound of claim 1 wherein R^5 is H.

39. The compound of claim 1 wherein R^6 is halogen.

40. The compound of claim 1 wherein R^7, R^8, R^{10}, R^{11}, R^{15}, R^{16}, R^{20}, and R^{21} are independently H or C_{1-16} alkyl.

41. The compound of claim 1 wherein R^{12} is OH or alkyl.

42. The compound of claim 1 wherein R^{19} is selected from the group consisting of H; C_{1-16} alkyl; C_{2-16} alkenyl; C_{2-16} alkynyl; C_{1-16} alkoxy; alkenyloxy; alkynyloxy; C_{1-16} alkylthio; C_{3-10} cycloalkyl; C_{4-10} cycloalkenyl; C_{4-10} cycloalkynyl; halogen; OH; CN; cyanoalkyl; NO_2; $NR^{20}R^{21}$; haloalkyl; haloalkyloxy; $C(=O)R^{18}$; $C(=O)OR^{18}$; OalkenylC(=O)OR^{18}; -OalkylC(=O)$NR^{20}R^{21}$; aryl; heterocycle; -OalkylOC(=O)R^{18}; $C(=O)N(C_{1-6}$ alkyl), N(H)S(O)(O)(C_{1-6} alkyl); arylalkyloxy; aryloxy; arylalkyloxy; and arylalkyl.

43. The compound of claim 42 wherein R^{19} is independently selected from the group consisting of halogen, $N(R^{20}R^{21})$, alkoxy, halo-substituted alkyl and halo-substituted alkoxy.

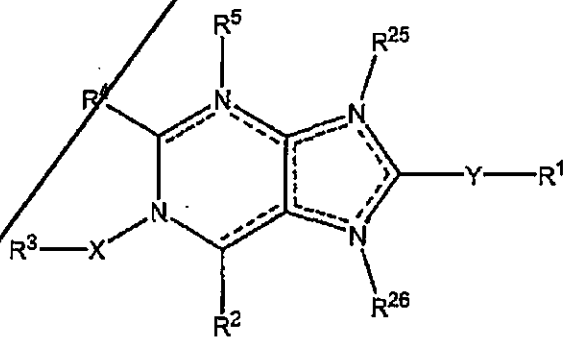
44. The compound of claim 1 wherein R^{25} and R^{26} are not present.

45. The compound of claim 1 which is not substituted at R^{25} but is substituted at R^{26}, and either R^2 or R^4 is selected from (=O), (=S), and (=NR^7).

46. The compound of claim 1 wherein haloalkyl or haloalkyloxy is $-CF_3$ or $-OCF_3$.

47. The compound of claim 1 wherein R^{19} is any individual, combination or subcombination of substituents (a) – (k).

48. A compound having the general formula (A),



(A)

wherein:

the dotted lines represent optional double bonds, provided that no two double bonds are adjacent to one another, and that the dotted lines represent at least 3, optionally 4 double bonds;

R^1 is selected from hydrogen, aryl, heterocycle (other than piperazinyl, piperidinyl, or either substituted with 1 or more R^6), C_1-C_{10} alkoxy, C_1-C_{10} thioalkyl,

C_1-C_{10} alkyl-amino, C_1-C_{10} dialkyl-amino, C_{3-10} cycloalkyl, C_{4-10} cycloalkenyl, and C_{4-10} cycloalkynyl, wherein each are optionally substituted with 1 or more R^6;

Y is selected from a single bond, O, S(O)m (where m is an integer from 0 to 2), NR^{11}, C_{1-10} alkylene, C_{2-10} alkenylene, C_{2-10} alkynylene, or C_{1-10} alkylene, C_{2-20} alkenylene or C_{2-10} alkynylene wherein 1 to 3 methylene groups optionally are independently replaced by 1 to 3 heteroatoms selected from O, S or NR^{11}; provided, however, that YR^1 is not H;

R^2 and R^4 are independently selected from hydrogen, C_{1-18} alkyl, C_{2-18} alkenyl, C_{2-18} alkynyl, C_{1-18} alkoxy, C_{1-18} alkylthio, halogen, -OH, -CN, $-NO_2$, $-NR^7R^8$, haloalkyloxy, haloalkyl, $-C(=O)R^9$, $-C(=S)R^9$, SH, aryl, aryloxy, arylthio, arylalkyl, C_{1-18} hydroxyalkyl, C_{3-10} cycloalkyl, C_{3-10} cycloalkyloxy, C_{3-10} cycloalkylthio, C_{3-10} cycloalkenyl, C_{7-10} cycloalkynyl, or heterocycle, provided that when one of R^{25} or R^{26} is present, then either R^2 or R^4 is selected from (=O), (=S), and $=NR^{27}$; and further provided that not both of R^2 and R^4 is OH, SH, thio or oxo;

X is selected from C_1-C_{10} alkylene, C_{2-10} alkenylene or C_{2-10} alkynylene, where each may include one or more heteroatoms selected from O, S, or NR^{11}, provided any such heteroatom is not adjacent to the N in the ring;

R^3 is selected from aryl, aryloxy, arylthio, cycloalkyl, cycloalkenyl, cycloalkynyl, aryl-$N(R^{10})$-, or heterocycle, where each said substituent may be optionally substituted with at least one R^{17}, provided that for cycloalkenyl the double bond is not adjacent to a nitrogen;

R^5 independently is absent or is selected from hydrogen, C_{1-18} alkyl, C_{2-18} alkenyl, C_{2-18} alkynyl, C_{1-18} alkoxy, C_{1-18} alkylthio, halogen, -OH, -CN, $-NO_2$, $-NR^7R^8$, haloalkyloxy, haloalkyl, $-C(=O)R^9$, $-C(=O)OR^9$, $-C(=S)R^9$, SH, aryl, aryloxy, arylthio, arylalkyl, C_{1-18} hydroxyalkyl, C_{3-10} cycloalkyl, C_{3-10} cycloalkyloxy, C_{3-10} cycloalkylthio, C_{3-10} cycloalkenyl, C_{7-10} cycloalkynyl, or heterocycle;

R^6 is selected from hydrogen, C_{1-18} alkyl, C_{2-18} alkenyl, C_{2-18} alkynyl, C_{1-18} alkoxy, C_{1-18} alkylthio, C_{1-18} alkylsulfoxide, C_{1-18} alkylsulfone, C_{1-18} halo-alkyl, C_{2-18} halo-alkenyl, C_{2-18} halo-alkynyl, C_{1-18} halo-alkoxy, C_{1-18} halo-alkylthio, C_{3-10} cycloalkyl, C_{3-10} cycloalkenyl, C_{7-10} cycloalkynyl, halogen, OH, CN, cyanoalkyl,

$-CO_2R^{18}$, NO_2, $-NR^7R^8$, C_{1-16} haloalkyl, $C(=O)R^{18}$, $C(=S)R^{18}$, SH, aryl, aryloxy, arylthio, arylsulfoxide, arylsulfone, arylsulfonamide, aryl(C_{1-16})alkyl, aryl(C_{1-16})alkyloxy, aryl(C_{1-16})alkylthio, heterocycle, C_{1-16} hydroxyalkyl, where each may be optionally substituted with at least 1 R^{19};

R^7 and R^8 are independently selected from hydrogen, C_{1-16} alkyl, C_{1-16} alkenyl, aryl, C_{3-10} cycloalkyl, C_{4-10} cycloalkenyl, heterocycle, $-C(=O)R^{12}$; $-C(=S)R^{12}$, an amino acid residue linked through a carboxyl group thereof, or where R^7 and R^8 together with the nitrogen form a heterocycle;

R^9 and R^{10} are independently selected from hydrogen, OH, C_{1-16} alkyl, C_{2-16} alkenyl, C_{3-10} cycloalkyl, C_{4-10} cycloalkenyl, C_{1-16} alkoxy, $-NR^{15}R^{16}$, aryl, an amino acid residue linked through an amino group of the amino acid, $CH_2OCH(=O)R^{9a}$, or $CH_2OC(=O)OR^{9a}$ where R^{9a} is C_1-C_{12} alkyl, C_6-C_{20} aryl, C_6-C_{20} alkylaryl or C_6-C_{20} aralkyl;

R^{10} and R^{11} are independently selected from the group consisting of hydrogen, C_{1-16} alkyl, C_{2-16} alkenyl, C_{3-10} cycloalkyl, C_{4-10} cycloalkenyl, aryl, $-C(=O)R^{12}$, heterocycle, or an amino acid residue;

R^{12} is selected from the group consisting of hydrogen, C_{1-16} alkyl, C_{2-16} alkenyl, aryl, C_{3-10} cycloalkyl, C_{4-10} cycloalkenyl, or an amino acid residue;

R^{15} and R^{16} are independently selected from hydrogen, C_{1-16} alkyl, C_{2-16} alkenyl, C_{2-16} alkynyl, aryl, C_{3-10} cycloalkyl, C_{4-10} cycloalkenyl, or an amino acid residue;

R^{17} is independently M-Q- wherein M is a ring optionally substituted with 1 or more R^{19}, and Q is a bond or a linking group connecting M to R^3 having 1 to 10 atoms selected from C and optionally 1 or more O, N or S atoms and optionally substituted with 1 or more R^{19};

R^{19} is selected from

(a) H;

(b) NO_2, SH, $NR^{20}R^{21}$, OH, halogen and CN;

(c) Sulfone, sulfonamide and sulfoxide;

(d) C_{1-16} alkyl, C_{2-16} alkenyl and C_{2-16} alkynyl;

(e) C_{1-18} alkyl, C_{2-18} alkenyl and C_{2-18} alkynyl wherein 1 or more methylene are replaced by 1 or more O, S, NR^{20}, $C(O)NR^{20}R^{21}$, $OC(O)R^{12}$, $C(O)OR^{12}$ or $N(R^{20})C(O)$;

(f) Substituents c), d) or e) substituted further by C_{3-10} cycloalkyl, C_{4-10} cycloalkenyl, C_{4-10} cycloalkynyl, aryl or heterocycle;

(g) C_{3-10} cycloalkyl, C_{4-10} cycloalkenyl, C_{4-10} cycloalkynyl, aryl and heterocycle, or said groups substituted with C_{1-6} alkyl, $C(O)OR^{12}$ =O, halogen, CN, $C(O)NR^{20}R^{21}$, $C(O)R^{18}$ or $OC(O)R^{18}$;

(h) $C(O)R^{18}$, $C(O)OR^{18}$, $OC(O)R^{18}$, $C(S)R^{18}$ and $C(O)N(R^{12})_2$;

(i) Substituents d) or e) substituted with =O, CN, halogen, $C(O)R^{18}$, $C(O)NR^{20}R^{21}$, $OC(O)R^{18}$, heterocycle and heterocycle substituted with C_1-C_6 alkyl, $C(O)OR^{12}$, =O, CN, halogen, $OC(O)R^{18}$ or $C(O)NR^{20}R^{21}$;

(j) Substituents c) substituted further with C_{1-18} alkyl; and

(k) Substituents f) or g) substituted further with C_{1-18} alkyl, =O, $NR^{20}R^{21}$, CN, C_{1-18} alkoxy, heterocycle, C_{1-18} haloalkyl, heterocyclealkyl or halogen;

R^{23} and R^{21} are independently selected from hydrogen, C_{1-18} alkyl, C_{2-18} alkenyl, C_{2-18} alkynyl, aryl, heterocycle, C_{3-10} cycloalkyl, C_{4-10} cycloalkenyl, $-C(=O)R^{12}$, or $-C(=S)R^{12}$;

R^{25} and R^{26} are independently not present or are selected from hydrogen, C_{1-18} alkyl, C_{3-10} cycloalkyl, aryl and heterocycle, where each is optionally independently substituted with 1 to 4 of C_{1-6} alkyl, C_{1-6} alkoxy, halo, CH_2OH, benzyloxy, and OH; and

R^{27} is selected from hydrogen, C_{1-18} alkyl, C_{3-10} cycloalkyl, (C_{3-10} cycloalkyl)-C_{1-6} alkyl, aryl, and aryl C_{1-18} alkyl, and

salts, tautomers, polymorphs, isomers and solvates thereof.

49. The compound of claim 48 wherein Y is a single bond, and R^1 is aryl or aromatic heterocycle which is unsubstituted or substituted with one or more R^6.

50. The compound of claim 48 wherein X is C_1-C_{10} alkylene, $C_{2\text{-}10}$ alkenylene or $C_{2\text{-}10}$ alkynylene.

51. The compound of claim 48 wherein R^3 is heterocyle.

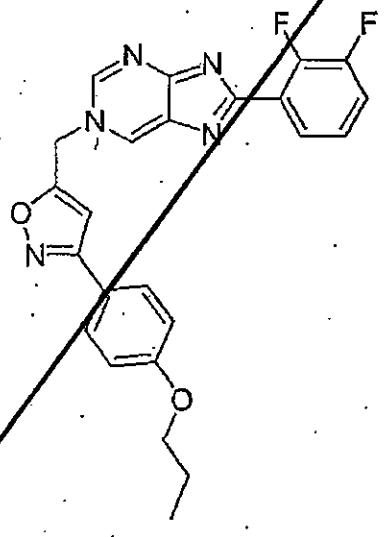
52. The compound of claim 48 wherein R^3 is heterocycle substituted with R^{17} where Q is a bond and M is aryl substituted with 1 or 2 R^{19}.

53. The compound of claim 48 wherein Y is a single bond, and R^1 is phenyl.

54. The compound of claim 48 wherein R^3 is isoxazole substituted with R^{17} where Q is a bond and M is aryl substituted with 1 or 2 R^{19}.

55. The compound of claim 48 wherein R^3 is isoxazole substituted with R^{17} where Q is a bond and M is phenyl substituted with 1 or 2 R^{19}.

56. A compound having the structure

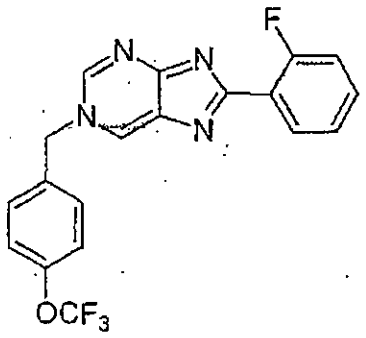


and its salts, tautomers, polymorphs and solvates.

57. 8-(2-Fluorophenyl)-1-[(4-trifluoromethyl)phenylmethyl]-1*H*-purine and its salts, tautomers, polymorphs and solvates.

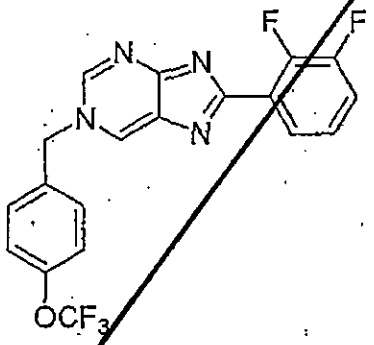
58. 1-((3-(4-chlorophenyl)isoxazol-5-yl)methyl)-8-(2,3-difluorophenyl)-1H-purine and its salts, tautomers, polymorphs and solvates.

59. The compound



and its salts, tautomers, polymorphs and solvates.

60. A compound of the structure



and its salts, tautomers, polymorphs and solvates.

61. A composition comprising a pharmaceutically acceptable excipient and a compound of claims 1, 48, and 64-70.

62. A method comprising administering to a subject in need of treatment or prophylaxis of a viral infection an antivirally effective amount of a composition of claim 61.

63. The method of claim 62, wherein the viral infection is an HCV infection.

64. The method of claim 63 further comprising administering at least one additional antiviral therapy to the subject.

65. The method of claim 64 wherein the additional therapy is is selected from the group consisting of an interferon alpha and ribavirin.

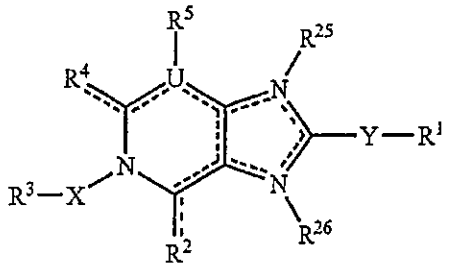
66. A method of screening antiviral compounds which comprises providing a compound of claims 1 or 48 and determining the anti-viral activity of said compound.

67. The method of claim 66 wherein said anti-viral activity is determined by the activity of said compound against one or more viruses belonging to the family of the Flaviviridae and/or of the Picornaviridae.

We claim:

1. A compound of formula (A)

(A)



wherein:

the dotted lines represent optional double bonds, provided that no two double bonds are adjacent to one another, and that the dotted lines represent at least 3, optionally 4 double bonds;

U is N;

R^1 is selected from hydrogen, aryl, heterocycle, C_1-C_{10} alkoxy, C_1-C_{10} alkyl-amino, C_1-C_{10} dialkyl-amino, C_{3-10} cycloalkyl, C_{4-10} cycloalkenyl, and C_{4-10} cycloalkynyl, wherein each are optionally substituted with 1 or more R^6;

Y is selected from a single bond, O, S(O)m (where m is an integer from 0 to 2), NR^{11}, C_{1-10} alkylene, C_{2-10} alkenylene, and C_{2-10} alkynylene, or C_{1-10} alkylene, C_{2-20} alkenylene or C_{2-10} alkynylene, wherein 1 to 3 methylene groups optionally are independently replaced by 1 to 3 heteroatoms selected from O, S or NR^{11}, provided that when Y is a single bond, R^1 is not hydrogen;

R^2 and R^4 are independently selected from hydrogen, C_{1-18} alkyl, C_{2-18} alkenyl, C_{2-18} alkynyl, C_{1-18} alkoxy, C_{1-18} alkylthio, halogen, —OH, —CN, —NO_2, —NR^7R^8, haloalkyloxy, haloalkyl, —C(=O)R^9, —C(=S)R^9, SH, aryl, aryloxy, arylthio, arylalkyl, C_{1-18} hydroxyalkyl, C_{3-10} cycloalkyl, C_{3-10} cycloalkyloxy, C_{3-10} cycloalkylthio, C_{3-10} cycloalkenyl, C_{7-10} cycloalkynyl, and heterocycle, provided that when one of R^{25} or R^{26} is present, then either R^4 is selected from =O, =S, or =NR^{27} or R^2 is selected from =S or =NR^{27};

X is selected from C_1-C_{10} alkylene, C_{2-10} alkenylene or C_{2-10} alkynylene;

R^3 is selected from aryl, aryloxy, arylthio, cycloalkyl, cycloalkenyl, cycloalkynyl, aryl-N(R^{10})—, or heterocycle, where each said substituent is optionally substi-

tuted with at least one R^{17}, provided that for cycloalkenyl the double bond is not adjacent to a nitrogen;

R^5 independently is absent or is selected from hydrogen, C_{1-18} alkyl, C_{2-18} alkenyl, C_{2-18} alkynyl, C_{1-18} alkoxy, C_{1-18} alkylthio, halogen, —OH, —CN, —NO_2, —NR^7R^8, haloalkyloxy, haloalkyl, —$C(=O)R^9$, —$C(=O)OR^9$, —$C(=S)R^9$, SH, aryl, aryloxy, arylthio, arylalkyl, C_{1-18} hydroxyalkyl, C_{3-10} cycloalkyl, C_{3-10} cycloalkyloxy, C_{3-10} cycloalkylthio, C_{3-10} cycloalkenyl, C_{7-10} cycloalkynyl, and heterocycle;

R^6 is selected from hydrogen, C_{1-18} alkyl, C_{2-18} alkenyl, C_{2-18} alkynyl, C_{1-18} alkoxy, C_{1-18} alkylthio, C_{1-18} alkylsulfoxide, C_{1-18} alkylsulfone, C_{1-18} halo-alkyl, C_{2-18} halo-alkenyl, C_{2-18} halo-alkynyl, C_{1-18} halo-alkoxy, C_{1-18} halo-alkylthio, C_{3-10} cycloalkyl, C_{3-10} cycloalkenyl, C_{7-10} cycloalkynyl, halogen, OH, CN, cyanoalkyl, —CO_2R^{18}, NO_2, —NR^7R^8, C_{1-18} haloalkyl, $C(=O)R^{18}$, $C(=S)R^{18}$, SH, aryl, aryloxy, arylthio, arylsulfoxide, arylsulfone, arylsulfonamide, aryl(C_{1-18})alkyl, aryl(C_{1-18})alkyloxy, aryl(C_{1-18})alkylthio, heterocycle, and C_{1-18} hydroxyalkyl, where each may be optionally substituted with at least 1 R^{19};

R^7 and R^8 are independently selected from hydrogen, C_{1-18} alkyl, C_{1-18} alkenyl, aryl, C_{3-10} cycloalkyl, C_{4-10} cycloalkenyl, heterocycle, —$C(=O)R^{12}$; —$C(=S)R^{12}$, an amino acid residue linked through a carboxyl group thereof, and the group formed when R^7 and R^8 are taken together with the nitrogen to form a heterocycle;

R^9 and R^{18} are independently selected from hydrogen, OH, C_{1-18} alkyl, C_{2-18} alkenyl, C_{3-10} cycloalkyl, C_{4-10} cycloalkenyl, C_{1-18} alkoxy, —$NR^{15}R^{16}$, aryl, an amino acid residue linked through an amino group of the amino acid, $CH_2OCH(=O)R^{9a}$, and $CH_2OC(=O)OR^{9a}$ where R^{9a} is C_1-C_{12} alkyl, C_6-C_{20} aryl, C_6C_7-C_{20} alkylaryl or C_7-C_{20} aralkyl;

R^{10} and R^{11} are independently selected from the group consisting of hydrogen, C_{1-18}alkyl, C_{2-18} alkenyl, C_{3-10} cycloalkyl, C_{4-10} cycloalkenyl, aryl, —$C(=O)R^{12}$, heterocycle, and an amino acid residue linked through an amino group or carboxyl group of the amino acid;

R^{12} is selected from the group consisting of hydrogen, C_{1-18} alkyl, C_{2-18} alkenyl, aryl, C_{3-10} cycloalkyl, C_{4-10}

cycloalkenyl, and an amino acid residue linked through an amino group or carboxyl group of the amino acid;

R^{15} and R^{16} are independently selected from hydrogen, C_{1-48} alkyl, C_{2-18} alkenyl, C_{2-18} alkynyl, aryl, arylalkyl (unsubstituted, or substituted with $C(O)OR^{18}$), C_{3-10} cycloalkyl, C_{4-10} cycloalkenyl, and an amino acid residue linked through an amino group or carboxyl group of the amino acid;

R^{17} is independently selected from the group consisting of (a) hydrogen, C_{1-18} alkyl, C_{2-18} alkenyl, C_{2-18} alkynyl, C_{1-18} alkoxy, C_{1-48} alkylthio, C_{1-18} alkylsulfoxide, C_{1-18} alkylsulfone, C_{1-18} halogenated alkyl, C_{2-18} halogenated alkenyl, C_{2-48} halogenated alkynyl, C_{1-48} halogenated alkoxy, C_{1-18} halogenated alkylthio, C_{3-10} cycloalkyl, C_{3-10} cycloalkenyl, C_{7-10} cycloalkynyl, halogen, OH, CN, CO_2H, CO_2R^{18}, NO_2, NR^7R^8, haloalkyl, $C(=O)R^{18}$, $C(=S)R^{18}$, SH, aryl, heterocycle, aryloxy, arylthio, arylsulfoxide, arylsulfone, arylsulfonamide, arylalkyl, arylalkyloxy, arylalkylthio, heterocycle and C_{1-18} hydroxyalkyl, where each of said aryl, aryloxy, arylthio, arylsulfoxide, arylsulfone, arylsulfonamide, arylalkyl, arylalkyloxy, arylalkylthio, heterocycle, or C_{1-18} hydroxyalkyl is optionally substituted with 1 or more R^{19}, and (b) M-Q- wherein M is a ring optionally substituted with 1 or more R^{19}, and Q is a bond or a linking group connecting M to R^3 having 1 to 10 atoms selected from C and optionally 1 or more O, N or S atoms and optionally substituted with 1 or more R^{19};

R^{19} is selected from

(a) H;

(b) NO_2, SH, $NR^{20}R^{21}$, OH, halogen and CN;

(c) C_{1-18} alkyl, C_{2-18} alkenyl and C_{2-18} alkynyl;

(d) C_{1-18} alkyl, C_{2-18} alkenyl and C_{2-18} alkynyl wherein 1 or more methylene are replaced by 1 or more O, S, NR^{20}, or $N(R^{20})C(O)$;

(e) Substituents c), or d) substituted further by C_{3-10} cycloalkyl, C_{4-10} cycloalkenyl, C_{4-10} cycloalkynyl, aryl or heterocycle;

(f) C_{3-10} cycloalkyl, C_{4-10} cycloalkenyl, C_{4-10} cycloalkynyl, aryl and heterocycle, or said groups substituted with C_{1-6} alkyl, $C(O)OR^{12}$=O, halogen, CN, $C(O)NR^{20}R^{21}$, $C(O)R^{18}$ or $OC(O)R^{18}$;

(g) $C(O)R^{18}$, $C(O)OR^{18}$, $OC(O)R^{18}$, $C(S)R^{18}$ and $C(O)N(R^{12})_2$;

(h) Substituents c) or d) substituted with =O, CN, halogen, $C(O)R^{18}$, $C(O)NR^{20}R^{21}$, $OC(O)R^{18}$, heterocycle, and heterocycle substituted with C_1-C_6 alkyl, $C(O)OR^{12}$, =O, CN, halogen, $OC(O)R^{18}$ or $C(O)NR^{20}R^{21}$; and

(i) Substituents e) or f) substituted further with C_{1-18} alkyl, =O, $NR^{20}R^{21}$, CN, C_{1-18} alkoxy, heterocycle, C_{1-18} haloalkyl, heterocyclealkyl or halogen;

R^{20} and R^{21} are independently selected from hydrogen, C_{1-18} alkyl, C_{2-18} alkenyl, C_{2-18} alkynyl, aryl, heterocycle, C_{3-10} cycloalkyl, C_{4-10} cycloalkenyl, —C(=O)R^{12}, and —C(=S)R^{12};

R^{25} is not present or is selected from hydrogen, C_{3-10} cycloalkyl, aryl and heterocycle, where each is optionally independently substituted with 1 to 4 of C_{1-6} alkyl, C_{1-8} alkoxy, halo, CH_2OH, and benzyloxy;

R^{26} is not present or is selected from hydrogen, C_{1-18} alkyl, C_{3-10} cycloalkyl, aryl and heterocycle, where each is optionally independently substituted with 1 to 4 of C_{1-6} alkyl, C_{1-6} alkoxy, halo, CH_2OH, and benzyloxy;

R^{27} is selected from hydrogen, C_{1-18} alkyl, C_{3-10} cycloalkyl, (C_{3-10} cycloalkyl)-C_{1-6} alkyl, aryl, and arylC_{1-18} alkyl; and

salts, tautomers, polymorphs, and stereoisomers thereof.

2. The compound of claim 1 wherein R^1 is haloaryl, X is methylene, R^3 is heterocycle substituted with 1 or 2 R^{17}.

3. The compound of claim 1 wherein R^1 is an aryl or aromatic heterocycle substituted with 1 or 2 R^6.

4. The compound of claim 1 wherein R^3 is heterocycle.

5. The compound of claim 1 wherein YR^1 is haloaryl.

6. The compound of claim 5 wherein haloaryl is ortho-fluorophenyl.

7. The compound of claim 1 wherein R^3 is isoxazolyl substituted with 1 R^{17}.

8. The compound of claim 2 wherein R^{17} is aryl or an aromatic heterocycle, wherein each of said aryl and aromatic heterocycle is substituted with 1, 2 or 3 R^{19}.

9. The compound of claim 1 wherein YR^1 is none of hydrogen, C_{3-10} cycloalkyl, or C_{1-6} alkyl.

10. The compound of claim 1 wherein YR^1 is not hydrogen or C_{1-6} alkyl.

11. The compound of claim 1 wherein R^{19} is trihalomethyl, trihalomethoxy, alkoxy or halogen.

12. The compound of claim 1 wherein R^1 is aryl or aromatic heterocyle substituted with 1, 2 or 3 R^6 wherein R^6 is halogen, C_{1-18} alkoxy; or C_{1-18} haloalkyl.

13. The compound of claim 12 wherein R^1 is phenyl substituted with 1, 2 or 3 halogens.

14. The compound of claim 13 wherein halogen is fluoro.

15. The compound of claim 1 wherein Y is a single bond, O, C_{1-6} alkylene, C_{2-6} alkenylene, C_{2-6} alkynylene or one of said groups containing 1 to 3 heteroatoms selected from O, S or NR^{11}.

16. The compound of claim 15 wherein Y is $—O(CH_2)_{1-5}—$, $—(CH_2)_{1-4}—O—(CH_2)_{1-4}—$, $—S—(CH_2)_{1-5}—$, $—(CH_2)_{1-4}—S—(CH_2)_{1-4}—$, $—NR^{11}—(CH_2)_{1-5}—$, $—(CH_2)_{1-4}—NR^{11}—(CH_2)_{1-4}$ or C_{3-10} cycloalkylidene.

17. The compound of claim 15 wherein Y is —OCH_2—, —CH_2O—, C_{1-2} alkylene, C_{2-3} alkenylene, C_{2-3} alkynylene, O or a bond.

18. The compound of claim 15 wherein Y is a bond.

19. The compound of claim 1 wherein YR^1 is a single ring aromatic carbocycle or a heterocycle containing 1 or 2 N, S or O atoms in the ring.

20. The compound of claim 19 wherein the carbocycle or heterocycle contains 4 to 6 ring atoms.

21. The compound of claim 1 wherein YR^1 is halo- or halomethyl-substituted phenyl.

22. The compound of claim 1 wherein aryl or heteroaryl are substituted ortho or meta with halo- or halomethyl.

23. The compound of claim 1 wherein X is alkylene.

24. The compound of claim 1 wherein X is selected from the group consisting of —CH_2—, —$CH(CH_3)$—, —CH_2—CH_2—, —CH_2—CH_2—CH_2—, —CH_2—CH_2—CH_2—CH_2, C_{3-10} cycloalkylidene, C_{2-6} alkenylene and C_{2-6} alkynylene.

25. The compound of claim 1 wherein X is methylene.

26. The compound of claim 1 wherein R^3 is aryl or a heterocycle substituted with 0 to 3 R^{17}.

27. The compound of claim 26 wherein the heterocycle is an aromatic heterocycle.

28. The compound of claim 27 wherein the heterocycle contains 1, 2 or 3 N, S or O atoms in the ring, is linked to X through a ring carbon atom and contains 4 to 6 total ring atoms.

29. The compound of claim 28 wherein R^3 is isoxazolyl substituted with 1 to 3 R^{17}.

30. The compound of claim 1 wherein R^{17} is aryl or a heterocycle further substituted with 1 to 3 R^{19}.

31. The compound of claim 1 wherein M is aryl or aromatic heterocycle.

32. The compound of claim **1** wherein Q contains 0 to 20 atoms selected from C, O, S, N and H.

33. The compound of claim **1** wherein M is selected from the group consisting of C_{3-10} cycloalkyl, C_{3-10} cycloalkenyl, C_{7-10} cycloalkynyl, aryl and heterocycle.

34. The compound of claim **1** wherein R^{17} is selected from the group consisting of C_{3-10} cycloalkyl, C_{3-10} cycloalkenyl, C_{7-10} cycloalkynyl, halogen, aryl, aryloxy, arylthio, arylsulfoxide, arylsulfone, arylsulfonamide, arylalkyl; arylalkyloxy; arylalkylthio; heterocycle; C_{1-18} hydroxyalkyl, each of said C_{3-10} cycloalkyl, C_{3-10} cycloalkenyl, C_{7-10} cycloalkynyl, halogen, aryl, aryloxy, arylthio, arylsulfoxide, arylsulfone, arylsulfonamide, arylalkyl; arylalkyloxy; arylalkylthio; heterocycle; and C_{1-18} hydroxyalkyl is unsubstituted or is substituted 1 or more R^{19}.

35. The compound of claim **1** wherein R^{17} is selected from the group consisting of aryl and heterocycle, and where said aryl or heterocycle is optionally substituted with 1 or more R^{19}.

36. The compound of claim **1** wherein R^9 and R^{18} are H, OH or alkyl.

37. The compound of claim **1** wherein R^5 is H.

38. The compound of claim **1** wherein R^6 is halogen.

39. The compound of claim **1** wherein R^7, R^8, R^{10}, R^{11}, R^{15}, R^{16}, R^{20}, and R^{21} are independently H or C_{1-18} alkyl.

40. The compound of claim **1** wherein R^{12} is OH or alkyl.

41. The compound of claim **1** wherein R^{19} is selected from the group consisting of H; C_{1-18} alkyl; C_{2-18} alkenyl; C_{2-18} alkynyl; C_{1-18} alkoxy; alkenyloxy; alkynyloxy; C_{1-18} alkylthio; C_{3-10} cycloalkyl; C_{4-10} cycloalkenyl; C_{4-10} cycloalkynyl; halogen; OH; CN; cyanoalkyl; NO_2; $NR^{20}R^{21}$; haloalkyl; haloalkyloxy; $C(=O)R^{18}$; $C(=O)OR^{18}$; $Oalkenyl C(=O)OR^{18}$; $—Oalkyl C(=O)NR^{20}R^{21}$; aryl; heterocycle; $—Oalkyl OC(=O)R^{18}$; $C(=O)N(C_{1-6}alkyl)$, N(H)S(O)(O)(C_{1-6} alkyl); arylalkyloxy; aryloxy; arylalkyloxy; and arylalkyl.

42. The compound of claim **41** wherein R^{19} is independently selected from the group consisting of halogen, $N(R^{20}R^{21})$, alkoxy, halo-substituted alkyl and halo-substituted alkoxy.

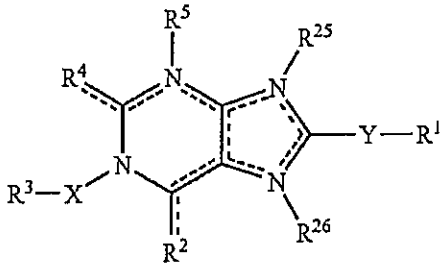
43. The compound of claim **1** wherein R^{25} and R^{26} are not present.

44. The compound of claim **1** which is not substituted at R^{25} but is substituted at R^{26}, and either R^2 or R^4 is selected from (=O), (=S), and (=NR^{27}).

45. The compound of claim **1** wherein haloalkyl or haloalkyloxy is —CF_3 or —OCF_3.

46. A compound having the general formula (A),

(A)



wherein:

the dotted lines represent optional double bonds, provided that no two double bonds are adjacent to one another, and that the dotted lines represent at least 3, optionally 4 double bonds;

R^1 is selected from hydrogen, aryl, heterocycle (other than piperazinyl, piperidinyl, or either substituted with 1 or more R^6), C_1-C_{10} alkoxy, C_1-C_{10} alkyl-amino, C_1-C_{10} dialkyl-amino, C_{3-10} cycloalkyl, C_{4-10} cycloalkenyl, and C_{4-10} cycloalkynyl, wherein each are optionally substituted with 1 or more R^6;

Y is selected from a single bond, $S(O)_m$ (where m is an integer from 0 to 2), NR^{11}, C_{1-10} alkylene, C_{2-10} alkenylene, C_{2-10} alkynylene, or C_{1-10} alkylene, C_{2-20} alkenylene or C_{2-10} alkynylene wherein 1 to 3 methylene groups optionally are independently replaced by 1 to 3 heteroatoms selected from O, S or NR^{11}; provided, however, that YR^1 is not H;

R^2 and R^4 are independently selected from hydrogen, C_{1-18} alkyl, C_{2-18} alkenyl, C_{2-18} alkynyl, C_{1-18} alkoxy, C_{1-18} alkylthio, halogen, —OH, —CN, —NO_2, —NR^7R^8,

haloalkyloxy, haloalkyl, —C(=O)R^9, —C(=S)R^9, SH, aryl, aryloxy, arylthio, arylalkyl, C_{1-18} hydroxyalkyl, C_{3-10} cycloalkyl, C_{3-10} cycloalkyloxy, C_{3-10} cycloalkylthio, C_{3-10} cycloalkenyl, C_{7-10} cycloalkynyl, or heterocycle, provided that when one of R^{25} or R^{26} is present, then either R^4 is selected from (=O), (=S), and =NR^{27} or R^2 is selected from =S or =NR^{27}; and further provided that not both of R^2 and R^4 is OH, SH, thio or oxo;

X is selected from C_1-C_{10} alkylene, C_{2-10} alkenylene or C_{2-10} alkynylene;

R^3 is selected from aryl, aryloxy, arylthio, cycloalkyl, cycloalkenyl, cycloalkynyl, aryl-N(R^{10})—, or heterocycle, where each said substituent may be optionally substituted with at least one R^{17}, provided that for cycloalkenyl the double bond is not adjacent to a nitrogen;

R^5 independently is absent or is selected from hydrogen, C_{1-18} alkyl, C_{2-18} alkenyl, C_{2-18} alkynyl, C_{1-18} alkoxy, C_{1-18} alkylthio, halogen, —OH, —CN, —NO_2, —NR^7R^8, haloalkyloxy, haloalkyl, —C(=O)R^9, —C(=O)OR^9, —C(=S)R^9, SH, aryl, aryloxy, arylthio, arylalkyl, C_{1-18} hydroxyalkyl, C_{3-10} cycloalkyl, C_{3-10} cycloalkyloxy, C_{3-10} cycloalkylthio, C_{3-10} cycloalkenyl, C_{7-10} cycloalkynyl, or heterocycle;

R^6 is selected from hydrogen, C_{1-18} alkyl, C_{2-18} alkenyl, C_{2-18} alkynyl, C_{1-18} alkoxy, C_{1-18} alkylthio, C_{1-18} alkylsulfoxide, C_{1-18} alkylsulfone, C_{1-18} halo-alkyl, C_{2-18} halo-alkenyl, C_{2-18} halo-alkynyl, C_{1-18} halo-alkoxy, C_{1-18} halo-alkylthio, C_{3-10} cycloalkyl, C_{3-10} cycloalkenyl, C_{7-10} cycloalkynyl, halogen, OH, CN, cyanoalkyl, —CO_2R^{18}, NO_2, —NR^7R^8, C_{1-18} haloalkyl, C(=O)R^{18}, C(=S)R^{18}, SH, aryl, aryloxy, arylthio, arylsulfoxide, arylsulfone, arylsulfonamide, aryl(C_{1-18})alkyl, aryl(C_{1-18})alkyloxy, aryl(C_{1-18})alkylthio, heterocycle, C_{1-18} hydroxyalkyl, where each may be optionally substituted with at least 1 R^{19};

R^7 and R^8 are independently selected from hydrogen, C_{1-18} alkyl, C_{1-18} alkenyl, aryl, C_{3-10} cycloalkyl, O_{4-10} cycloalkenyl, heterocycle, —C(=O)R^{12}; —C(=S)R^{12}, an amino acid residue linked through a carboxyl group thereof, or where R^7 and R^8 together with the nitrogen form a heterocycle;

R^9 and R^{18} are independently selected from hydrogen, OH, C_{1-18} alkyl, C_{2-18} alkenyl, C_{3-10} cycloalkyl, C_{4-10} cycloalkenyl, C_{1-18} alkoxy, —$NR^{15}R^{16}$aryl, an amino acid residue linked through an amino group of the amino acid, $CH_2OCH(=O)R^{9a}$, or $CH_2OC(=O)OR^{9a}$ where R^{9a} is C_1-C_{12} alkyl, C_6-C_{20} aryl, C_7-C_{20} alkylaryl or C_7-C_{20} aralkyl;

R^{10} and R^{11} are independently selected from the group consisting of hydrogen, C_{1-18} alkyl, C_{2-18} alkenyl, C_{3-10} cycloalkyl, C_{4-10} cycloalkenyl, aryl, —C(=O)R^{12}, heterocycle, or an amino acid residue linked through an amino group or carboxyl group of the amino acid;

R^{12} is selected from the group consisting of hydrogen, C_{1-18} alkyl, C_{2-18} alkenyl, aryl, C_{3-10} cycloalkyl, C_{4-10} cycloalkenyl, or an amino acid residue linked through an amino group or carboxyl group of the amino acid;

R^{15} and R^{16} are independently selected from hydrogen, C_{1-18} alkyl, C_{2-18} alkenyl, C_{2-18} alkynyl, aryl, C_{3-10} cycloalkyl, C_{4-10} cycloalkenyl, or an amino acid residue linked through an amino group or carboxyl group of the amino acid;

R^{17} is independently M-Q- wherein M is a ring optionally substituted with 1 or more R^{19}, and Q is a bond or a linking group connecting M to R^3 having 1 to 10 atoms selected from C and optionally 1 or more O, N or S atoms and optionally substituted with 1 or more R^{19};

R^{19} is selected from

(a) H;

(b) NO_2, SH, $NR^{20}R^{21}$, OH, halogen and CN;

(c) C_{1-18} alkyl, C_{2-18} alkenyl and C_{2-18} alkynyl;

(d) C_{1-18} alkyl, C_{2-18} alkenyl and C_{2-18} alkynyl wherein 1 or more methylene are replaced by 1 or more O, S, NR^{20}, or $N(R^{20})C(O)$;

(e) Substituents c), or d) substituted further by C_{3-10} cycloalkyl, C_{4-10} cycloalkenyl, C_{4-10} cycloalkynyl, aryl or heterocycle;

(f) C_{3-10} cycloalkyl, C_{4-10} cycloalkenyl, C_{4-10} cycloalkynyl, aryl and heterocycle, or said groups substituted with C_{1-6} alkyl, $C(O)OR^{12}$=O, halogen, CN, $C(O)NR^{20}R^{21}$, $C(O)R^{18}$ or $OC(O)R^{18}$;

(g) $C(O)R^{18}$, $C(O)OR^{18}$, $OC(O)R^{18}$, $C(S)R^{18}$ and $C(O)N(R^{12})_2$;

(h) Substituents c) or d) substituted with =O, CN, halogen, $C(O)R^{18}$, $C(O)NR^{20}R^{21}$, $OC(O)R^{18}$, heterocycle and heterocycle substituted with C_1-C_6 alkyl, $C(O)OR^{12}$, =O, CN, halogen, $OC(O)R^{18}$ or $C(O)NR^{20}R^{21}$; and

(i) Substituents e) or f) substituted further with C_{1-18} alkyl, =O, $NR^{20}R^{21}$, CN, C_{1-18} alkoxy, heterocycle, C_{1-18} haloalkyl, heterocyclealkyl or halogen;

R^{20} and R^{21} are independently selected from hydrogen, C_{1-18} alkyl, C_{2-18} alkenyl, C_{2-18} alkynyl, aryl, heterocycle, C_{3-10} cycloalkyl, C_{4-10} cycloalkenyl, —C(=O)R^{12}, or —C(=S)R^{12};

R^{25} and R^{26} are independently not present or are selected from hydrogen, C_{1-18} alkyl, C_{3-10} cycloalkyl, aryl and heterocycle, where each is optionally independently substituted with 1 to 4 of C_{1-6} alkyl, C_{1-6} alkoxy, halo, CH_2OH, and benzyloxy; and

R^{27} is selected from hydrogen, C_{1-18} alkyl, C_{3-10} cycloalkyl, (C_{3-10} cycloalkyl)-C_{1-6} alkyl, aryl, and aryl C_{1-18} alkyl, and

salts, tautomers, polymorphs, and stereoisomers thereof.

47. The compound of claim **46** wherein Y is a single bond, and R^1 is aryl or aromatic heterocycle which is unsubstituted or substituted with one or more R^6.

48. The compound of claim 46 wherein X is C_1-C_{10} alkylene, C_{2-10} alkenylene or C_{2-10} alkynylene.

49. The compound of claim 46 wherein R^3 is heterocyle.

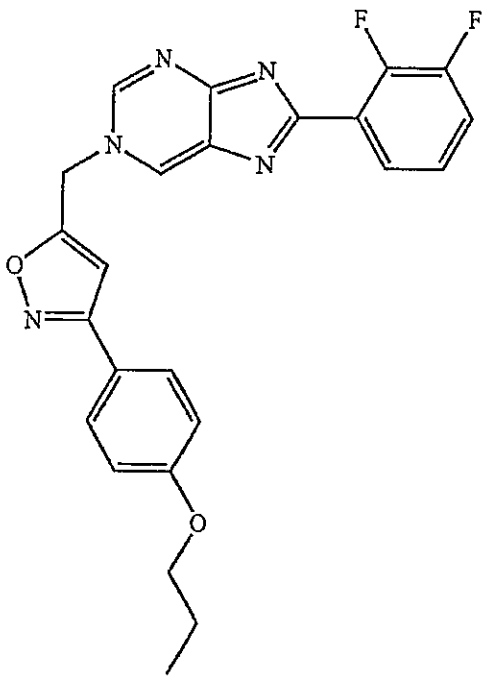
50. The compound of claim 46 wherein R^3 is heterocycle substituted with R^{17} where Q is a bond and M is aryl substituted with 1 or 2 R^{19}.

51. The compound of claim 46 wherein Y is a single bond, and R^1 is phenyl.

52. The compound of claim 46 wherein R^3 is isoxazole substituted with R^{17} where Q is a bond and M is aryl substituted with 1 or 2 R^{19}.

53. The compound of claim 46 wherein R^3 is isoxazole substituted with R^{17} where Q is a bond and M is phenyl substituted with 1 or 2 R^{19}.

54. A compound having the structure

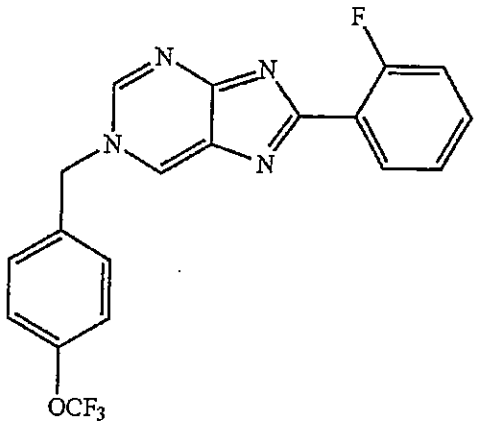


and its salts, tautomers, and polymorphs.

55. 8-(2-Fluorophenyl)-1-[(4-trifluoromethyl)phenylmethyl]-1H-purine and its salts, tautomers, and polymorphs.

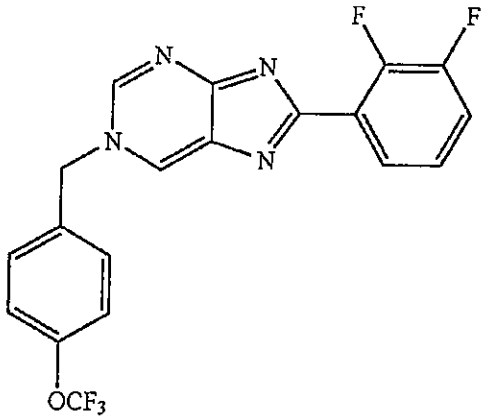
56. 1-((3-(4-chlorophenyl)isoxazol-5-yl)methyl)-8-(2,3-difluorophenyl)-1H-purine and its salts, tautomers, and polymorphs.

57. The compound



and its salts, tautomers, and polymorphs.

58. A compound of the structure



and its salts, tautomers, and polymorphs.

59. 1-((3-(4-chlorophenyl)isoxazol-5-yl)methyl)-8-(2,3-difluorophenyl)-1H-purine and its salts, tautomers, and polymorphs.

60. A composition comprising a pharmaceutically acceptable excipient and a compound of claim **1**, **46**, and or **54-59**.