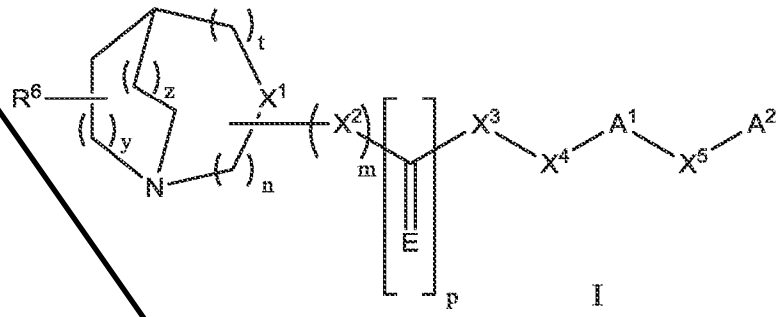
Claims

1. A compound represented by the following structural formula,



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or a pharmaceutically acceptable salt or prodrug thereof, wherein:

n is 1, 2 or 3;

m is 0 or 1;

p is 0 or 1;

t is 0, 1 or 2;

y is 1 or 2;

z is 0, 1 or 2;

E is S, O, NH, NOH, NNO_2, NCN, NR, NOR or NSO_2R;

$X^1$is CR^1 when m is 1 or N when m is 0;

X^2 is O, -NH, $-CH_2-$, SO_2, NH-SO_2;$CH(C_1-C_6)$ alkyl or $-NR^2$;

X^3 is O, -NH, $-CH_2-$, CO, - $CH(C_1-C_6)$ alkyl, SO_2NH, -CO-NH- or $-NR^3$;

X^4 is CR^4R^5, CH_2 CR^4R^5 or CH_2 –(C_1-C_6) alkyl-CR^4R^5;

X^5 is a direct bond, O, S, SO_2, CR^4R^5; (C_1-C_6)alkyl, (C_1-C_6)alkyloxy, (C_1-C_6)alkenyl, (C_1-C_6)alkenyloxy;

R is (C_6-C_{12})aryl, (C_2-C_9)heteroaryl, (C_1-C_6)alkyl, (C_2-C_9)heteroaryl(C_1-C_6)alkyl;

R^1 is H, CN, (C_1-C_6)alkylcarbonyl, or (C_1-C_6)alkyl;

R^2 and R^3 are each independently -H, (C_1-C_6)alkyl optionally substituted by one or more substituents selected from the group consisting of halogen, (C_1-C_6)alkyl, (C_6-C_{12})aryl, (C_2-C_9)heteroaryl, (C_1-C_6)alkyl(C_6-C_{12})aryl, halo(C_6-C_{12})aryl, and halo(C_2-C_9)heteroaryl, or optionally when X^2 is $-NR^2$ and X^3 is $-NR^3$, R^2 and R^3 may be taken together with the

nitrogen atoms to which they are attached form a non-aromatic heterocyclic ring optionally substituted by with one or more substituents selected from halogen, (C_1-C_6)alkyl, (C_6-C_{12})aryl, (C_2-C_9)heteroaryl, (C_1-C_6)alkyl(C_6-C_{12})aryl, halo(C_6-C_{12})aryl, and halo(C_2-C_9)heteroaryl;

R^4 and R^5 are independently selected from H, (C_1-C_6)alkyl, or taken together with the carbon to which they are attached to form a spiro (C_3-C_{10})cycloalkyl ring or spiro (C_3-C_{10})cycloalkoxy ring;

R^6 is -H, halogen, -CN, (C_6-C_{12})aryl, (C_6-C_{12})aryloxy, (C_1-C_6)alkyloxy; (C_1-C_6)alkyl optionally substituted by one to four halo or (C_1-C_6)alkyl;

A^1 is (C_2-C_6)alkynyl; (C_3-C_{10})cycloalkyl, (C_6-C_{12})aryl, (C_2-C_9)heteroaryl, (C_2-C_9)heterocycloalkyl or benzo(C_2-C_9)heterocycloalkyl optionally substituted with one or more substituents selected from the group consisting of halo, (C_1-C_6)alkyl optionally substituted by one to three halo; (C_1-C_6)alkenyl, amino, (C_1-C_6)alkylamino, (C_1-C_6)dialkylamino, (C_1-C_6)alkoxy, nitro, CN, -OH, (C_1-C_6)alkyloxy optionally substituted by one to three halo; (C_1-C_6)alkoxycarbonyl, and (C_1-C_6) alkylcarbonyl;

A^2 is H, (C_3-C_{10})cycloalkyl, (C_6-C_{12})aryl, (C_2-C_9)heteroaryl, (C_2-C_9)heterocycloalkyl or benzo(C_2-C_9)heterocycloalkyl optionally substituted with one or more substituents selected from the group consisting of halo, (C_1-C_6)alkyl optionally substituted by one to three halo; (C_1-C_6)alkylenyl, amino, (C_1-C_6) alkylamino, (C_1-C_6)dialkylamino, (C_1-C_6)alkoxy, O(C3-C6 cycloalkyl), (C_3-C_6) cycloalkoxy, nitro, CN, OH, (C_1-C_6)alkyloxy optionally substituted by one to three halo; (C_3-C_6) cycloalkyl, (C_1-C_6) alkoxycarbonyl, (C_1-C_6) alkylcarbonyl, (C_1-C_6) haloalkyl;

with the proviso that the sum of n + t + y + z is not greater than 6;

with the proviso that when p is 0; X^2 is NH-SO_2 and X^3 is NH;

with the proviso that when n is 1; t is 0; y is 1; z is 1; X^2 is NH; E is O; X^3 is NH; A^2 is H and X^5 is a direct bond; A^1 is not unsubstituted phenyl, halophenyl or isopropenyl phenyl;

with the proviso that when n is 1; t is 0; y is 1; z is 1; X^2 is O; E is O; X^3 is NH; A^1 is (C_6-C_{12})aryl and X^5 is a direct bond; A^2 is H and R^4 is H then R^5 is not cyclohexyl; and

with the proviso that when n is 1; t is 0; y is 1; z is 1; X^2 is NH; E is O; X^3 is CH_2; R^4 and R^5 are both hydrogen; A^2 is H and X^5 is a direct bond; then A^1 is not unsubstituted phenyl.

2. A compound according to claim 1, wherein n is 1; t is 0; y is 1 and z is 1.

3 A compound according to claim 1, wherein n is 1; t is 1; y is 1 and z is 1.

4. A compound according to claim 1, wherein n is 2; t is 0; y is 1 and z is 1.

5. A compound according to claim 1, wherein n is 2; t is 1; y is 1 and z is 1.

6. A compound according to claim 1, wherein n is 3; t is 0; y is 1 and z is 1.

7. A compound according to claim 1, wherein n is 1; t is 2; y is 1 and z is 1.

8. A compound according to claim 1, wherein n is 1; t is 0; y is 1 and z is 0.

9. A compound according to claim 1, wherein n is 1; t is 1; y is 1 and z is 0.

10. A compound according to claim 1, wherein n is 2; t is 0; y is 1 and z is 0.

11. A compound according to claim 1, wherein n is 2; t is 1; y is 1 and z is 0.

12. A compound according to claim 1, wherein n is 3; t is 0; y is 1 and z is 0.

13. A compound according to claim 1, wherein n is 1; t is 2; y is 1 and z is 0.

14. A compound according to claim 1, wherein n is 1; t is 1; y is 2 and z is 0.

15. A compound according to claim 1, wherein n is 2; t is 0; y is 2 and z is 0.

16. A compound according to claim 1, wherein m is 1 and X^1 is CR^1.

17. A compound according to claim 1, wherein m is 0 and X^1 is N.

18. A compound according to claim 1, wherein m is 1; E is O; X^2 is O and X^3 is NH.

19. A compound according to claim 1, wherein m is 1; E is O; X^2 is NH and X^3 is NH.

20. A compound according to claim 1, wherein m is 1; E is O; X^2 is CH^2 and X^5 is NH.

21. A compound according to claim 1, wherein m is 1; E is O; X^2 is NH and X^3 is CH^2.

22. A compound according to claim 1, wherein m is 1; E is S; X^2 is NH and X^3 is NH.

23. A compound according to claim 1, wherein m is 0; E is O; X^1 is NH and X^3 is NH.

24. A compound according to claim 1, wherein m is 1; E is O; X^2 is NH and X^3 is CO-NH.

25. A compound according to claim 1, wherein m is 1; p is 0; X^2 is NH-SO_2 and X^3 is NH.

26. A compound according to claim 1, wherein R^4 and R^5 are each (C_1-C_6)alkyl or taken together with the carbon to which they are attached to form a spiro (C_3-C_{10})cycloalkyl ring or a spiro (C_3-C_{10})cycloalkoxy ring.

27. A compound according to claim 26, wherein R^4 and R^5 are each methyl.

28. A compound according to claim 26, wherein R^4 and R^5 are taken together with the carbon to which they are attached to form a spiro (C_3-C_{10})cycloalkyl ring.

29. A compound according to claim 28, wherein R^4 and R^5 are taken together with the carbon to which they are attached to form a spiro cyclopropyl ring.

30. A compound according to claim 26, wherein R^4 and R^5 are taken together with the carbon to which they are attached to form a spiro $(C_3$-$C_{10})$cycloalkoxy ring.

31. A compound according to claim 1, wherein A^1 is $(C_2$-$C_6)$alkynyl or $(C_6$-$C_{12})$aryl.

32. A compound according to claim 1, wherein A^1 is $(C_2$-$C_9)$heteroaryl.

33. A compound according to claim 32, wherein A^1 is thiophene, thiazole, isothiazole, furane, oxazole, isoxazole, pyrrole, imidazole, pyrazole, triazole, pyridine, pymiridine, pyridazine, indole, benzotiazole, benzoisoxazole, benzopyrazole, benzoimidazole, benzofuran, benzooxazole or benzoisoxazole.

34. A compound according to claim 1, wherein A^1 is $(C_2$-$C_9)$heterocycloalkyl.

35. A compound according to claim 34, wherein A^1 is pyrrolidinyl, tetrahydrofuranyl, dihydrofuranyl, tetrahydropyranyl, pyranyl, thiopyranyl, aziridinyl, azetidinyl, oxiranyl, methylenedioxyl, chromenyl, barbituryl, isoxazolidinyl, 1,3-oxazolidin-3-yl, isothiazolidinyl, 1,3-thiazolidin-3-yl, 1,2-pyrazolidin-2-yl, 1,3-pyrazolidin-1-yl, piperidinyl, thiomorpholinyl, 1,2-tetrahydrothiazin-2-yl, 1,3-tetrahydrothiazin-3-yl, tetrahydrothiadiazinyl, morpholinyl, 1,2-tetrahydrodiazin-2-yl, 1,3-tetrahydrodiazin-1-yl, tetrahydroazepinyl, piperazinyl, piperizin-2-onyl, piperizin-3-onyl, chromanyl, 2-

pyrrolinyl, 3-pyrrolinyl, imidazolidinyl, 2-imidazolidinyl, 1,4-dioxanyl, 8-azabicyclo[3.2.1]octanyl, 3-azabicyclo[3.2.1]octanyl, 3,8-diazabicyclo[3.2.1]octanyl, 2,5-diazabicyclo[2.2.1]heptanyl, 2,5-diazabicyclo[2.2.2]octanyl, octahydro-2H-pyrido[1,2-a]pyrazinyl, 3-azabicyclo[4.1.0]heptanyl, 3-azabicyclo[3.1.0]hexanyl 2-azaspiro[4.4]nonanyl, 7-oxa-1-aza-spiro[4.4]nonanyl, 7-azabicyclo[2.2.2]heptanyl or octahydro-1H-indolyl.

36. A compound according to claim 1, wherein A^1 is benzo(C_2-C_9)heterocycloalkyl.

37. A compound according to claim 36, wherein A^1 is 2,3-dihydrobenzo[b][1,4] dioxine or 2,2-difluorobenzo[d][1,3]dioxole.

38. A compound according to claim 1, wherein R^6 is H.

39. A compound according to claim 1, X^5 is a direct bond.

40. A compound according to claim 1, X^5 is a CR^4R^5.

41. A compound according to claim 40, wherein R^4 and R^5 are each methyl.

42. A compound according to claim 40, wherein R^4 and R^5 are taken together with the carbon to which they are attached to form a spiro (C_3-C_{10})cycloalkyl ring.

43. A compound according to claim 42, wherein R^4 and R^5 are taken together with the carbon to which they are attached to form a spiro cyclopropyl ring.

44. A compound according to claim 40, wherein R^4 and R^5 are taken together with the carbon to which they are attached to form a spiro $(C_3$-$C_{10})$cycloalkoxy ring.

45. A compound according to claim 1, wherein A^2 is $(C_6$-$C_{12})$aryl.

46. A compound according to claim 1, wherein A^2 is $(C_2$-$C_9)$heteroaryl.

47. A compound according to claim 46, wherein A^2 is pyridine.

48. A compound according to claim 1, wherein A^2 is $(C_2$-$C_9)$heterocycloalkyl.

49. A compound according to claim 48, wherein A^2 is pyrrolidinyl, tetrahydrofuranyl, dihydrofuranyl, tetrahydropyranyl, pyranyl, thiopyranyl, aziridinyl, azetidinyl, oxiranyl, methylenedioxyl, chromenyl, barbituryl, isoxazolidinyl, 1,3-oxazolidin-3-yl, isothiazolidinyl, 1,3-thiazolidin-3-yl, 1,2-pyrazolidin-2-yl, 1,3-pyrazolidin-1-yl, piperidinyl, thiomorpholinyl, 1,2-tetrahydrothiazin-2-yl, 1,3-tetrahydrothiazin-3-yl, tetrahydrothiadiazinyl, morpholinyl, 1,2-tetrahydrodiazin-2-yl, 1,3-tetrahydrodiazin-1-yl, tetrahydroazepinyl, piperazinyl, piperizin-2-onyl, piperizin-3-onyl, chromanyl, 2-pyrrolinyl, 3-pyrrolinyl, imidazolidinyl, 2-imidazolidinyl, 1,4-dioxanyl, 8-azabicyclo[3.2.1]octanyl, 3-azabicyclo[3.2.1]octanyl, 3,8-diazabicyclo[3.2.1]octanyl, 2,5-diazabicyclo[2.2.1]heptanyl, 2,5-diazabicyclo[2.2.2]octanyl, octahydro-2H-pyrido[1,2-a]pyrazinyl, 3-azabicyclo[4.1.0]heptanyl, 3-azabicyclo[3.1.0]hexanyl 2-azaspiro[4.4]nonanyl, 7-oxa-1-aza-spiro[4.4]nonanyl, 7-azabicyclo[2.2.2]heptanyl or octahydro-1H-indolyl.

50. A compound according to claim 1, wherein A^2 is benzo$(C_2$-$C_9)$heterocycloalkyl.

51. A compound according to claim 50, wherein A^2 is 2,3-dihydrobenzo[b][1,4] dioxine or 2,2-difluorobenzo[d][1,3]dioxole.

52. A compound according to claim 1, where R^1 is hydrogen or methyl.

53. A compound according to claim 1, wherein n is 1; 2 or 3; t is 0, 1 or 2; y is 0 or 1; z is 0, 1 or 2; X^1 is CR^1; m is 1; p is 1; E is O; X^2 is O; X^3 is NH; R^1 is H; R^4 and R^5 are taken together with the carbon to which they are attached to form a spiro (C_3-C_{10})cycloalkyl ring or spiro (C_3-C_{10})cycloalkoxy ring; R^6 is a hydrogen or methyl; A^1 is (C_6-C_{12})aryl; X^5 is a direct bond, O or CR^4R^5 and A^2 is (C_6-C_{12})aryl.

54. A compound according to claim 1, wherein n is 1; 2 or 3; t is 0, 1 or 2; y is 0 or 1; z is 0, 1 or 2; X^1 is CR^1; m is 1; p is 1; E is O; X^2 is O; X^3 is NH; R^1 is H; R^4 and R^5 are each independently methyl; R^6 is a hydrogen or methyl; A^1 is (C_6-C_{12})aryl; X^5 is a direct bond, O or CR^4R^5 and A^2 is (C_6-C_{12})aryl.

55. A compound according to claim 1, wherein n is 1; 2 or 3; t is 0, 1 or 2; y is 0 or 1; z is 0, 1 or 2; X^1 is CR^1; m is 1; p is 1; E is O; X^2 is O; X^3 is NH; R^1 is H; R^4 and R^5 are taken together with the carbon to which they are attached to form a spiro (C_3-C_{10})cycloalkyl ring or spiro (C_3-C_{10})cycloalkoxy ring; R^6 is a hydrogen or methyl; A^1 is (C_6-C_{12})aryl; X^5 is a direct bond, O or CR^4R^5 and A^2 is (C_2-C_9)heteroaryl.

56. A compound according to claim 1, wherein n is 1; 2 or 3; t is 0, 1 or 2; y is 0 or 1; z is 0, 1 or 2; X^1 is CR^1; m is 1; p is 1; E is O; X^2 is O; X^3 is NH; R^1 is H; R^4 and R^5 are each independently methyl; R^6 is a hydrogen or methyl; A^1 is (C_6-C_{12})aryl; X^5 is a direct bond, O or CR^4R^5 and A^2 is (C_2-C_9)heteroaryl.

57. A compound according to claim 1, wherein n is 1; 2 or 3; t is 0, 1 or 2; y is 0 or 1; z is 0, 1 or 2; X^1 is CR^1; m is 1; p is 1; E is O; X^2 is O; X^3 is NH; R^1 is H; R^4 and R^5 are taken together with the carbon to which they are attached to form a spiro (C_3-C_{10})cycloalkyl ring or spiro (C_3-C_{10})cycloalkoxy ring; R^6 is a hydrogen or methyl; A^1 is (C_2-C_9)heteroaryl; X^5 is a direct bond, O or CR^4R^5 and A^2 is (C_6-C_{12})aryl.

58. A compound according to claim 1, wherein n is 1; 2 or 3; t is 0, 1 or 2; y is 0 or 1; z is 0, 1 or 2; X^1 is CR^1; m is 1; p is 1; E is O; X^2 is O; X^3 is NH; R^1 is H; R^4 and R^5 are each independently methyl; R^6 is a hydrogen or methyl; A^1 is (C_2-C_9)heteroaryl; X^5 is a direct bond, O or CR^4R^5 and A^2 is (C_6-C_{12})aryl.

59. A compound according to claim 1, wherein n is 1; 2 or 3; t is 0, 1 or 2; y is 0 or 1; z is 0, 1 or 2; X^1 is CR^1; m is 1; E is O; X^2 is NH; X^3 is NH; R^4 and R^5 are taken together with the carbon to which they are attached to form a spiro (C_3-C_{10})cycloalkyl ring or spiro (C_3-C_{10})cycloalkoxy ring; R^6 is a hydrogen or methyl; A^1 is (C_6-C_{12})aryl; X^5 is a direct bond, O or CR^4R^5 and A^2 is (C_6-C_{12})aryl.

60. A compound according to claim 1, wherein n is 1; 2 or 3; t is 0, 1 or 2; y is 0 or 1; z is 0, 1 or 2; X^1 is CR^1; m is 1; E is O; X^2 is NH; X^3 is NH; R^4 and R^5 are each independently methyl; R^6 is a hydrogen or methyl; A^1 is (C_6-C_{12})aryl; X^5 is a direct bond, O or CR^4R^5 and A^2 is (C_6-C_{12})aryl.

61. A compound according to claim 1, wherein n is 1; 2 or 3; t is 0, 1 or 2; y is 0 or 1; z is 0, 1 or 2; X^1 is CR^1; m is 1; E is O; X^2 is NH; X^3 is NH; R^4 and R^5 are taken together with the carbon to which they are attached to form a spiro $(C_3$-$C_{10})$cycloalkyl ring or spiro $(C_3$-$C_{10})$cycloalkoxy ring; R^6 is a hydrogen or methyl; A^1 is $(C_6$-$C_{12})$aryl; X^5 is a direct bond, O or CR^4R^5 and A^2 is $(C_2$-$C_9)$heteroaryl.

62. A compound according to claim 1, wherein n is 1; 2 or 3; t is 0, 1 or 2; y is 0 or 1; z is 0, 1 or 2; X^1 is CR^1; m is 1; E is O; X^2 is NH; X^3 is NH; R^4 and R^5 are each independently methyl; R^6 is a hydrogen or methyl; A^1 is $(C_6$-$C_{12})$aryl; X^5 is a direct bond, O or CR^4R^5 and A^2 is $(C_2$-$C_9)$heteroaryl.

63. A compound according to claim 1, wherein n is 1; 2 or 3; t is 0, 1 or 2; y is 0 or 1; z is 0, 1 or 2; X^1 is CR^1; m is 1; E is O; X^2 is NH; X^3 is NH; R^4 and R^5 are taken together with the carbon to which they are attached to form a spiro $(C_3$-$C_{10})$cycloalkyl ring or spiro $(C_3$-$C_{10})$cycloalkoxy ring; R^6 is a hydrogen or methyl; A^1 is $(C_2$-$C_9)$heteroaryl; X^5 is a direct bond, O or CR^4R^5 and A^2 is $(C_6$-$C_{12})$aryl.

64. A compound according to claim 1, wherein n is 1; 2 or 3; t is 0, 1 or 2; y is 0 or 1; z is 0, 1 or 2; X^1 is CR^1; m is 1; E is O; X^2 is NH; X^3 is NH; R^4 and R^5 are each independently methyl; R^6 is a hydrogen or methyl; A^1 is $(C_2$-$C_9)$heteroaryl; X^5 is a direct bond, O or CR^4R^5 and A^2 is $(C_6$-$C_{12})$aryl.

65. A compound according to claim 1, wherein n is 1; 2 or 3; t is 0, 1 or 2; y is 0 or 1; z is 0, 1 or 2; X^1 is CR^1; m is 1; E is O; X^2 is NH; X^3 is CH_2; R^4 and R^5 are taken together with the carbon to which they are attached to form a spiro (C_3-C_{10})cycloalkyl ring or spiro (C_3-C_{10})cycloalkoxy ring; R^6 is a hydrogen or methyl; A^1 is (C_6-C_{12})aryl; X^5 is a direct bond, O or CR^4R^5 and A^2 is (C_6-C_{12})aryl.

66. A compound according to claim 1, wherein n is 1; 2 or 3; t is 0, 1 or 2; y is 0 or 1; z is 0, 1 or 2; X^1 is CR^1; m is 1; E is O; X^2 is NH; X^3 is CH_2; R^4 and R^5 are each independently methyl; R^6 is a hydrogen or methyl; A^1 is (C_6-C_{12})aryl; X^5 is a direct bond, O or CR^4R^5 and A^2 is (C_6-C_{12})aryl.

67. A compound according to claim 1, wherein n is 1; 2 or 3; t is 0, 1 or 2; y is 0 or 1; z is 0, 1 or 2; X^1 is CR^1; m is 1; E is O; X^2 is NH; X^3 is CH_2; R^4 and R^5 are taken together with the carbon to which they are attached to form a spiro (C_3-C_{10})cycloalkyl ring or spiro (C_3-C_{10})cycloalkoxy ring; R^6 is a hydrogen or methyl; A^1 is (C_6-C_{12})aryl; X^5 is a direct bond, O or CR^4R^5 and A^2 is (C_2-C_9)heteroaryl.

68. A compound according to claim 1, wherein n is 1; 2 or 3; t is 0, 1 or 2; y is 0 or 1; z is 0, 1 or 2; X^1 is CR^1; m is 1; E is O; X^2 is NH; X^3 is CH_2; R^4 and R^5 are each independently methyl; R^6 is a hydrogen or methyl; A^1 is (C_6-C_{12})aryl; X^5 is a direct bond, O or CR^4R^5 and A^2 is (C_2-C_9)heteroaryl.

69. A compound according to claim 1, wherein n is 1; 2 or 3; t is 0, 1 or 2; y is 0 or 1; z is 0, 1 or 2; X^1 is CR^1; m is 1; E is O; X^2 is NH; X^3 is CH_2; R^4 and R^5 are taken together with the carbon to which they are attached to form a spiro (C_3-C_{10})cycloalkyl ring or spiro (C_3-C_{10})cycloalkoxy ring; R^6 is a hydrogen or methyl; A^1 is (C_2-C_9)heteroaryl; X^5 is a direct bond, O or CR^4R^5 and A^2 is (C_6-C_{12})aryl.

70. A compound according to claim 1, wherein n is 1; 2 or 3; t is 0, 1 or 2; y is 0 or 1; z is 0, 1 or 2; X^1 is CR^1; m is 1; E is O; X^2 is NH; X^3 is CH_2; R^4 and R^5 are each independently methyl; R^6 is a hydrogen or methyl; A^1 is (C_2-C_9)heteroaryl; X^5 is a direct bond, O or CR^4R^5 and A^2 is (C_6-C_{12})aryl.

71. A compound according to claim 1, wherein n is 1; 2 or 3; t is 0, 1 or 2; y is 0 or 1; z is 0, 1 or 2; X^1 is CR^1; m is 1; E is O; X^2 is CH_2; X^3 is NH; R^4 and R^5 are taken together with the carbon to which they are attached to form a spiro (C_3-C_{10})cycloalkyl ring or spiro (C_3-C_{10})cycloalkoxy ring; R^6 is a hydrogen or methyl; A^1 is (C_6-C_{12})aryl; X^5 is a direct bond, O or CR^4R^5 and A^2 is (C_6-C_{12})aryl.

72. A compound according to claim 1, wherein n is 1; 2 or 3; t is 0, 1 or 2; y is 0 or 1; z is 0, 1 or 2; X^1 is CR^1; m is 1; E is O; X^2 is CH_2; X^3 is NH; R^4 and R^5 are each independently methyl; R^6 is a hydrogen or methyl; A^1 is (C_6-C_{12})aryl; X^5 is a direct bond, O or CR^4R^5 and A^2 is (C_6-C_{12})aryl.

73. A compound according to claim 1, wherein n is 1; 2 or 3; t is 0, 1 or 2; y is 0 or 1; z is 0, 1 or 2; X^1 is CR^1; m is 1; E is O; X^2 is CH_2; X^3 is NH; R^4 and R^5 are taken together with the carbon to which they are attached to form a spiro (C_3-C_{10})cycloalkyl ring or spiro (C_3-C_{10})cycloalkoxy ring; R^6 is a hydrogen or methyl; A^1 is (C_6-C_{12})aryl; X^5 is a direct bond, O or CR^4R^5 and A^2 is (C_2-C_9)heteroaryl.

74. A compound according to claim 1, wherein n is 1; 2 or 3; t is 0, 1 or 2; y is 0 or 1; z is 0, 1 or 2; X^1 is CR^1; m is 1; E is O; X^2 is CH_2; X^3 is NH; R^4 and R^5 are each independently methyl; R^6 is a hydrogen or methyl; A^1 is (C_6-C_{12})aryl; X^5 is a direct bond, O or CR^4R^5 and A^2 is (C_2-C_9)heteroaryl.

75. A compound according to claim 1, wherein n is 1; 2 or 3; t is 0, 1 or 2; y is 0 or 1; z is 0, 1 or 2; X^1 is CR^1; m is 1; E is O; X^2 is CH_2; X^3 is NH; R^4 and R^5 are taken together with the carbon to which they are attached to form a spiro (C_3-C_{10})cycloalkyl ring or spiro (C_3-C_{10})cycloalkoxy ring; R^6 is a hydrogen or methyl; A^1 is (C_2-C_9)heteroaryl; X^5 is a direct bond, O or CR^4R^5 and A^2 is (C_6-C_{12})aryl.

76. A compound according to claim 1, wherein n is 1; 2 or 3; t is 0, 1 or 2; y is 0 or 1; z is 0, 1 or 2; X^1 is CR^1; m is 1; E is O; X^2 is CH_2; X^3 is NH; R^4 and R^5 are each independently methyl; R^6 is a hydrogen or methyl; A^1 is (C_2-C_9)heteroaryl; X^5 is a direct bond, O or CR^4R^5 and A^2 is (C_6-C_{12})aryl.

77. A compound according to claim 1, wherein n is 1; 2 or 3; t is 0, 1 or 2; y is 0 or 1; z is 0, 1 or 2; X^1 is CR^1; m is 1; E is S; X^2 is NH; X^3 is NH; R^4 and R^5 are taken together with the carbon to which they are attached to form a spiro (C_3-C_{10})cycloalkyl ring or spiro (C_3-C_{10})cycloalkoxy ring; R^6 is a hydrogen or methyl; A^1 is (C_6-C_{12})aryl; X^5 is a direct bond, O or CR^4R^5 and A^2 is (C_6-C_{12})aryl.

78. A compound according to claim 1, wherein n is 1; 2 or 3; t is 0, 1 or 2; y is 0 or 1; z is 0, 1 or 2; X^1 is CR^1; m is 1; E is S; X^2 is NH; X^3 is NH; R^4 and R^5 are each independently methyl; R^6 is a hydrogen or methyl; A^1 is (C_6-C_{12})aryl; X^5 is a direct bond, O or CR^4R^5 and A^2 is (C_6-C_{12})aryl.

79. A compound according to claim 1, wherein n is 1; 2 or 3; t is 0, 1 or 2; y is 0 or 1; z is 0, 1 or 2; X^1 is CR^1; m is 1; E is S; X^2 is NH; X^3 is NH; R^4 and R^5 are taken together with the carbon to which they are attached to form a spiro (C_3-C_{10})cycloalkyl ring or spiro (C_3-C_{10})cycloalkoxy ring; R^6 is a hydrogen or methyl; A^1 is (C_6-C_{12})aryl; X^5 is a direct bond, O or CR^4R^5 and A^2 is (C_2-C_9)heteroaryl.

80. A compound according to claim 1, wherein n is 1; 2 or 3; t is 0, 1 or 2; y is 0 or 1; z is 0, 1 or 2; X^1 is CR^1; m is 1; E is S; X^2 is NH; X^3 is NH; R^4 and R^5 are each independently methyl; R^6 is a hydrogen or methyl; A^1 is (C_6-C_{12})aryl; X^5 is a direct bond, O or CR^4R^5 and A^2 is (C_2-C_9)heteroaryl.

81. A compound according to claim 1, wherein n is 1; 2 or 3; t is 0, 1 or 2; y is 0 or 1; z is 0, 1 or 2; X^1 is CR^1; m is 1; E is S; X^2 is NH; X^3 is NH; R^4 and R^5 are taken together with the carbon to which they are attached to form a spiro (C_3-C_{10})cycloalkyl ring or spiro (C_3-C_{10})cycloalkoxy ring; R^6 is a hydrogen or methyl; A^1 is (C_2-C_9)heteroaryl; X^5 is a direct bond, O or CR^4R^5 and A^2 is (C_6-C_{12})aryl.

82. A compound according to claim 1, wherein n is 1; 2 or 3; t is 0, 1 or 2; y is 0 or 1; z is 0, 1 or 2; X^1 is CR^1; m is 1; E is S; X^2 is NH; X^3 is NH; R^4 and R^5 are each independently methyl; R^6 is a hydrogen or methyl; A^1 is (C_2-C_9)heteroaryl; X^5 is a direct bond, O or CR^4R^5 and A^2 is (C_6-C_{12})aryl.

83. A compound according to claim 1, wherein n is 1; 2 or 3; t is 0, 1 or 2; y is 0 or 1; z is 0, 1 or 2; X^1 is CR^1; m is 1; E is SO_2; X^2 is NH; X^3 is NH; R^4 and R^5 are taken together with the carbon to which they are attached to form a spiro (C_3-C_{10})cycloalkyl ring or spiro (C_3-C_{10})cycloalkoxy ring; R^6 is a hydrogen or methyl; A^1 is (C_6-C_{12})aryl; X^5 is a direct bond, O or CR^4R^5 and A^2 is (C_6-C_{12})aryl.

84. A compound according to claim 1, wherein n is 1; 2 or 3; t is 0, 1 or 2; y is 0 or 1; z is 0, 1 or 2; X^1 is CR^1; m is 1; E is SO_2; X^2 is NH; X^3 is NH; R^4 and R^5 are each independently methyl; R^6 is a hydrogen or methyl; A^1 is (C_6-C_{12})aryl; X^5 is a direct bond, O or CR^4R^5 and A^2 is (C_6-C_{12})aryl.

85. A compound according to claim 1, wherein n is 1; 2 or 3; t is 0, 1 or 2; y is 0 or 1; z is 0, 1 or 2; X^1 is CR^1; m is 1; E is SO_2; X^2 is NH; X^3 is NH; R^4 and R^5 are taken

together with the carbon to which they are attached to form a spiro (C_3-C_{10})cycloalkyl ring or spiro (C_3-C_{10})cycloalkoxy ring; R^6 is a hydrogen or methyl; A^1 is (C_6-C_{12})aryl; X^5 is a direct bond, O or CR^4R^5 and A^2 is (C_2-C_9)heteroaryl.

86. A compound according to claim 1, wherein n is 1; 2 or 3; t is 0, 1 or 2; y is 0 or 1; z is 0, 1 or 2; X^1 is CR^1; m is 1; E is SO_2; X^2 is NH; X^3 is NH; R^4 and R^5 are each independently methyl; R^6 is a hydrogen or methyl; A^1 is (C_6-C_{12})aryl; X^5 is a direct bond, O or CR^4R^5 and A^2 is (C_2-C_9)heteroaryl.

87. A compound according to claim 1, wherein n is 1; 2 or 3; t is 0, 1 or 2; y is 0 or 1; z is 0, 1 or 2; X^1 is CR^1; m is 1; E is SO_2; X^2 is NH; X^3 is NH; R^4 and R^5 are taken together with the carbon to which they are attached to form a spiro (C_3-C_{10})cycloalkyl ring or spiro (C_3-C_{10})cycloalkoxy ring; R^6 is a hydrogen or methyl; A^1 is (C_2-C_9)heteroaryl; X^5 is a direct bond, O or CR^4R^5 and A^2 is (C_6-C_{12})aryl.

88. A compound according to claim 1, wherein n is 1; 2 or 3; t is 0, 1 or 2; y is 0 or 1; z is 0, 1 or 2; X^1 is CR^1; m is 1; E is SO_2; X^2 is NH; X^3 is NH; R^4 and R^5 are each independently methyl; R^6 is a hydrogen or methyl; A^1 is (C_2-C_9)heteroaryl; X^5 is a direct bond, O or CR^4R^5 and A^2 is (C_6-C_{12})aryl.

89. A compound according to claim 1, wherein n is 1; 2 or 3; t is 0, 1 or 2; y is 0 or 1; z is 0, 1 or 2; X^1 is N; m is 0; E is O; X^3 is NH; R^4 and R^5 are taken together with the carbon to which they are attached to form a spiro (C_3-C_{10})cycloalkyl ring or spiro (C_3-

C_{10})cycloalkoxy ring; R^6 is a hydrogen or methyl; A^1 is (C_6-C_{12})aryl; X^5 is a direct bond, O or CR^4R^5 and A^2 is (C_6-C_{12})aryl.

90. A compound according to claim 1, wherein n is 1; 2 or 3; t is 0, 1 or 2; y is 0 or 1; z is 0, 1 or 2; X^1 is N; m is 0; E is O; X^3 is NH; R^4 and R^5 are each independently methyl; R^6 is a hydrogen or methyl; A^1 is (C_6-C_{12})aryl; X^5 is a direct bond, O or CR^4R^5 and A^2 is (C_6-C_{12})aryl.

91. A compound according to claim 1, wherein n is 1; 2 or 3; t is 0, 1 or 2; y is 0 or 1; z is 0, 1 or 2; X^1 is N; m is 0; E is O; X^3 is NH; R^4 and R^5 are taken together with the carbon to which they are attached to form a spiro (C_3-C_{10})cycloalkyl ring or spiro (C_3-C_{10})cycloalkoxy ring; R^6 is a hydrogen or methyl; A^1 is (C_6-C_{12})aryl; X^5 is a direct bond, O or CR^4R^5 and A^2 is (C_2-C_9)heteroaryl.

92. A compound according to claim 1, wherein n is 1; 2 or 3; t is 0, 1 or 2; y is 0 or 1; z is 0, 1 or 2; X^1 is N; m is 0; E is O; X^3 is NH; R^4 and R^5 are each independently methyl; R^6 is a hydrogen or methyl; A^1 is (C_6-C_{12})aryl; X^5 is a direct bond, O or CR^4R^5 and A^2 is (C_2-C_9)heteroaryl.

93. A compound according to claim 1, wherein n is 1; 2 or 3; t is 0, 1 or 2; y is 0 or 1; z is 0, 1 or 2; X^1 is N; m is 0; E is O; X^3 is NH; R^4 and R^5 are taken together with the carbon to which they are attached to form a spiro (C_3-C_{10})cycloalkyl ring or spiro (C_3-

C_{10})cycloalkoxy ring; R^6 is a hydrogen or methyl; A^1 is (C_2-C_9)heteroaryl; X^5 is a direct bond, O or CR^4R^5 and A^2 is (C_6-C_{12})aryl.

94. A compound according to claim 1, wherein n is 1; 2 or 3; t is 0, 1 or 2; y is 0 or 1; z is 0, 1 or 2; X^1 is N; m is 0; E is O; X^3 is NH; R^4 and R^5 are each independently methyl; R^6 is a hydrogen or methyl; A^1 is (C_2-C_9)heteroaryl; X^5 is a direct bond, O or CR^4R^5 and A^2 is (C_6-C_{12})aryl.

95. A compound according to claim 1, wherein n is 1; 2 or 3; t is 0, 1 or 2; y is 0 or 1; z is 0, 1 or 2; X^1 is CR^1; m is 1; E is O; X^2 is NH; X^3 is CO-NH; R^4 and R^5 are taken together with the carbon to which they are attached to form a spiro (C_3-C_{10})cycloalkyl ring or spiro (C_3-C_{10})cycloalkoxy ring; R^6 is a hydrogen or methyl; A^1 is (C_6-C_{12})aryl; X^5 is a direct bond, O or CR^4R^5 and A^2 is (C_6-C_{12})aryl.

96. A compound according to claim 1, wherein n is 1; 2 or 3; t is 0, 1 or 2; y is 0 or 1; z is 0, 1 or 2; X^1 is CR^1; m is 1; E is O; X^2 is NH; X^3 is CO-NH; R^4 and R^5 are each independently methyl; R^6 is a hydrogen or methyl; A^1 is (C_6-C_{12})aryl; X^5 is a direct bond, O or CR^4R^5 and A^2 is (C_6-C_{12})aryl.

97. A compound according to claim 1, wherein n is 1; 2 or 3; t is 0, 1 or 2; y is 0 or 1; z is 0, 1 or 2; X^1 is CR^1; m is 1; E is O; X^2 is NH; X^3 is CO-NH; R^4 and R^5 are taken together with the carbon to which they are attached to form a spiro (C_3-C_{10})cycloalkyl

ring or spiro (C_3-C_{10})cycloalkoxy ring; R^6 is a hydrogen or methyl; A^1 is (C_6-C_{12})aryl; X^5 is a direct bond, O or CR^4R^5 and A^2 is (C_2-C_9)heteroaryl.

98. A compound according to claim 1, wherein n is 1; 2 or 3; t is 0, 1 or 2; y is 0 or 1; z is 0, 1 or 2; X^1 is CR^1; m is 1; E is O; X^2 is NH; X^3 is CO-NH; R^4 and R^5 are each independently methyl; R^6 is a hydrogen or methyl; A^1 is (C_6-C_{12})aryl; X^5 is a direct bond, O or CR^4R^5 and A^2 is (C_2-C_9)heteroaryl.

99. A compound according to claim 1, wherein n is 1; 2 or 3; t is 0, 1 or 2; y is 0 or 1; z is 0, 1 or 2; X^1 is CR^1; m is 1; E is O; X^2 is NH; X^3 is CO-NH; R^4 and R^5 are taken together with the carbon to which they are attached to form a spiro (C_3-C_{10})cycloalkyl ring or spiro (C_3-C_{10})cycloalkoxy ring; R^6 is a hydrogen or methyl; A^1 is (C_2-C_9)heteroaryl; X^5 is a direct bond, O or CR^4R^5 and A^2 is (C_6-C_{12})aryl.

100. A compound according to claim 1, wherein n is 1; 2 or 3; t is 0, 1 or 2; y is 0 or 1; z is 0, 1 or 2; X^1 is CR^1; m is 1; E is O; X^2 is NH; X^3 is CO-NH; R^4 and R^5 are each independently methyl; R^6 is a hydrogen or methyl; A^1 is (C_2-C_9)heteroaryl; X^5 is a direct bond, O or CR^4R^5 and A^2 is (C_6-C_{12})aryl.

101. A compound according to claim 1, wherein n is 1; 2 or 3; t is 0, 1 or 2; y is 0 or 1; z is 0, 1 or 2; X^1 is CR^1; m is 1; p is 1; E is O; X^2 is O; X^3 is NH; R^1 is H; R^4 and R^5 are taken together with the carbon to which they are attached to form a spiro (C_3-C_{10})cycloalkyl ring or spiro (C_3-C_{10})cycloalkoxy ring; R^6 is a hydrogen or methyl; A^1 is (C_6-C_{12})aryl; X^5 is a direct bond, O or CR^4R^5 and A^2 is (C_2-C_9)heterocycloalkyl.

102. A compound according to claim 1, wherein n is 1; 2 or 3; t is 0, 1 or 2; y is 0 or 1; z is 0, 1 or 2; X^1 is CR^1; m is 1; p is 1; E is O; X^2 is O; X^3 is NH; R^1 is H; R^4 and R^5 are each independently methyl; R^6 is a hydrogen or methyl; A^1 is $(C_6$-$C_{12})$aryl; X^5 is a direct bond, O or CR^4R^5 and A^2 is $(C_2$-$C_9)$heterocycloalkyl.

103. A compound according to claim 1, wherein n is 1; 2 or 3; t is 0, 1 or 2; y is 0 or 1; z is 0, 1 or 2; X^1 is CR^1; m is 1; p is 1; E is O; X^2 is O; X^3 is NH; R^1 is H; R^4 and R^5 are taken together with the carbon to which they are attached to form a spiro $(C_3$-$C_{10})$cycloalkyl ring or spiro $(C_3$-$C_{10})$cycloalkoxy ring; R^6 is a hydrogen or methyl; A^1 is $(C_2$-$C_9)$heterocycloalkyl; X^5 is a direct bond, O or CR^4R^5 and A^2 is $(C_6$-$C_{12})$aryl.

104. A compound according to claim 1, wherein n is 1; 2 or 3; t is 0, 1 or 2; y is 0 or 1; z is 0, 1 or 2; X^1 is CR^1; m is 1; p is 1; E is O; X^2 is O; X^3 is NH; R^1 is H; R^4 and R^5 are each independently methyl; R^6 is a hydrogen or methyl; A^1 is $(C_2$-$C_9)$heterocycloalkyl; X^5 is a direct bond, O or CR^4R^5 and A^2 is $(C_6$-$C_{12})$aryl.

105. A compound according to claim 1, wherein n is 1; 2 or 3; t is 0, 1 or 2; y is 0 or 1; z is 0, 1 or 2; X^1 is CR^1; m is 1; E is O; X^2 is NH; X^3 is NH; R^4 and R^5 are taken together with the carbon to which they are attached to form a spiro $(C_3$-$C_{10})$cycloalkyl ring or spiro $(C_3$-$C_{10})$cycloalkoxy ring; R^6 is a hydrogen or methyl; A^1 is $(C_6$-$C_{12})$aryl; X^5 is a direct bond, O or CR^4R^5 and A^2 is $(C_2$-$C_9)$heterocycloalkyl.

106. A compound according to claim 1, wherein n is 1; 2 or 3; t is 0, 1 or 2; y is 0 or 1; z is 0, 1 or 2; X^1 is CR^1; m is 1; E is O; X^2 is NH; X^3 is NH; R^4 and R^5 are each independently methyl; R^6 is a hydrogen or methyl; A^1 is $(C_6$-$C_{12})$aryl; X^5 is a direct bond, O or CR^4R^5 and A^2 is $(C_2$-$C_9)$heterocycloalkyl.

107. A compound according to claim 1, wherein n is 1; 2 or 3; t is 0, 1 or 2; y is 0 or 1; z is 0, 1 or 2; X^1 is CR^1; m is 1; E is O; X^2 is NH; X^3 is NH; R^4 and R^5 are taken together with the carbon to which they are attached to form a spiro $(C_3$-$C_{10})$cycloalkyl ring or spiro $(C_3$-$C_{10})$cycloalkoxy ring; R^6 is a hydrogen or methyl; A^1 is $(C_2$-$C_9)$heterocycloalkyl; X^5 is a direct bond, O or CR^4R^5 and A^2 is $(C_6$-$C_{12})$aryl.

108. A compound according to claim 1, wherein n is 1; 2 or 3; t is 0, 1 or 2; y is 0 or 1; z is 0, 1 or 2; X^1 is CR^1; m is 1; E is O; X^2 is NH; X^3 is NH; R^4 and R^5 are each independently methyl; R^6 is a hydrogen or methyl; A^1 is $(C_2$-$C_9)$heterocycloalkyl; X^5 is a direct bond, O or CR^4R^5 and A^2 is $(C_6$-$C_{12})$aryl.

109. A compound according to claim 1, wherein n is 1; 2 or 3; t is 0, 1 or 2; y is 0 or 1; z is 0, 1 or 2; X^1 is CR^1; m is 1; E is O; X^2 is NH; X^3 is CH_2; R^4 and R^5 are taken together with the carbon to which they are attached to form a spiro $(C_3$-$C_{10})$cycloalkyl ring or spiro $(C_3$-$C_{10})$cycloalkoxy ring; R^6 is a hydrogen or methyl; A^1 is $(C_6$-$C_{12})$aryl; X^5 is a direct bond, O or CR^4R^5 and A^2 is $(C_2$-$C_9)$heterocycloalkyl.

110. A compound according to claim 1, wherein n is 1; 2 or 3; t is 0, 1 or 2; y is 0 or 1; z is 0, 1 or 2; X^1 is CR^1; m is 1; E is O; X^2 is NH; X^3 is CH_2; R^4 and R^5 are each independently methyl; R^6 is a hydrogen or methyl; A^1 is $(C_6$-$C_{12})$aryl; X^5 is a direct bond, O or CR^4R^5 and A^2 is $(C_2$-$C_9)$heterocycloalkyl.

111. A compound according to claim 1, wherein n is 1; 2 or 3; t is 0, 1 or 2; y is 0 or 1; z is 0, 1 or 2; X^1 is CR^1; m is 1; E is O; X^2 is NH; X^3 is CH_2; R^4 and R^5 are taken together with the carbon to which they are attached to form a spiro $(C_3$-$C_{10})$cycloalkyl ring or spiro $(C_3$-$C_{10})$cycloalkoxy ring; R^6 is a hydrogen or methyl; A^1 is $(C_2$-$C_9)$heterocycloalkyl; X^5 is a direct bond, O or CR^4R^5 and A^2 is $(C_6$-$C_{12})$aryl.

112. A compound according to claim 1, wherein n is 1; 2 or 3; t is 0, 1 or 2; y is 0 or 1; z is 0, 1 or 2; X^1 is CR^1; m is 1; E is O; X^2 is NH; X^3 is CH_2; R^4 and R^5 are each independently methyl; R^6 is a hydrogen or methyl; A^1 is $(C_2$-$C_9)$heterocycloalkyl; X^5 is a direct bond, O or CR^4R^5 and A^2 is $(C_6$-$C_{12})$aryl.

113. A compound according to claim 1, wherein n is 1; 2 or 3; t is 0, 1 or 2; y is 0 or 1; z is 0, 1 or 2; X^1 is CR^1; m is 1; E is O; X^2 is CH_2; X^3 is NH; R^4 and R^5 are taken together with the carbon to which they are attached to form a spiro $(C_3$-$C_{10})$cycloalkyl ring or spiro $(C_3$-$C_{10})$cycloalkoxy ring; R^6 is a hydrogen or methyl; A^1 is $(C_6$-$C_{12})$aryl; X^5 is a direct bond, O or CR^4R^5 and A^2 is $(C_2$-$C_9)$heterocycloalkyl.

114. A compound according to claim 1, wherein n is 1; 2 or 3; t is 0, 1 or 2; y is 0 or 1; z is 0, 1 or 2; X^1 is CR^1; m is 1; E is O; X^2 is CH_2; X^3 is NH; R^4 and R^5 are each independently methyl; R^6 is a hydrogen or methyl; A^1 is $(C_6$-$C_{12})$aryl; X^5 is a direct bond, O or CR^4R^5 and A^2 is $(C_2$-$C_9)$heterocycloalkyl.

115. A compound according to claim 1, wherein n is 1; 2 or 3; t is 0, 1 or 2; y is 0 or 1; z is 0, 1 or 2; X^1 is CR^1; m is 1; E is O; X^2 is CH_2; X^3 is NH; R^4 and R^5 are taken together with the carbon to which they are attached to form a spiro $(C_3$-$C_{10})$cycloalkyl ring or spiro $(C_3$-$C_{10})$cycloalkoxy ring; R^6 is a hydrogen or methyl; A^1 is $(C_2$-$C_9)$heterocycloalkyl; X^5 is a direct bond, O or CR^4R^5 and A^2 is $(C_6$-$C_{12})$aryl.

116. A compound according to claim 1, wherein n is 1; 2 or 3; t is 0, 1 or 2; y is 0 or 1; z is 0, 1 or 2; X^1 is CR^1; m is 1; E is O; X^2 is CH_2; X^3 is NH; R^4 and R^5 are each independently methyl; R^6 is a hydrogen or methyl; A^1 is $(C_2$-$C_9)$heterocycloalkyl; X^5 is a direct bond, O or CR^4R^5 and A^2 is $(C_6$-$C_{12})$aryl.

117. A compound according to claim 1, wherein n is 1; 2 or 3; t is 0, 1 or 2; y is 0 or 1; z is 0, 1 or 2; X^1 is CR^1; m is 1; E is S; X^2 is NH; X^3 is NH; R^4 and R^5 are taken together with the carbon to which they are attached to form a spiro $(C_3$-$C_{10})$cycloalkyl ring or spiro $(C_3$-$C_{10})$cycloalkoxy ring; R^6 is a hydrogen or methyl; A^1 is $(C_6$-$C_{12})$aryl; X^5 is a direct bond, O or CR^4R^5 and A^2 is $(C_2$-$C_9)$heterocycloalkyl.

118. A compound according to claim 1, wherein n is 1; 2 or 3; t is 0, 1 or 2; y is 0 or 1; z is 0, 1 or 2; X^1 is CR^1; m is 1; E is S; X^2 is NH; X^3 is NH; R^4 and R^5 are each independently methyl; R^6 is a hydrogen or methyl; A^1 is $(C_6$-$C_{12})$aryl; X^5 is a direct bond, O or CR^4R^5 and A^2 is $(C_2$-$C_9)$heterocycloalkyl.

119. A compound according to claim 1, wherein n is 1; 2 or 3; t is 0, 1 or 2; y is 0 or 1; z is 0, 1 or 2; X^1 is CR^1; m is 1; E is S; X^2 is NH; X^3 is NH; R^4 and R^5 are taken together with the carbon to which they are attached to form a spiro $(C_3$-$C_{10})$cycloalkyl ring or spiro $(C_3$-$C_{10})$cycloalkoxy ring; R^6 is a hydrogen or methyl; A^1 is $(C_2$-$C_9)$heterocycloalkyl; X^5 is a direct bond, O or CR^4R^5 and A^2 is $(C_6$-$C_{12})$aryl.

120. A compound according to claim 1, wherein n is 1; 2 or 3; t is 0, 1 or 2; y is 0 or 1; z is 0, 1 or 2; X^1 is CR^1; m is 1; E is S; X^2 is NH; X^3 is NH; R^4 and R^5 are each independently methyl; R^6 is a hydrogen or methyl; A^1 is $(C_2$-$C_9)$heterocycloalkyl; X^5 is a direct bond, O or CR^4R^5 and A^2 is $(C_6$-$C_{12})$aryl.

121. A compound according to claim 1, wherein n is 1; 2 or 3; t is 0, 1 or 2; y is 0 or 1; z is 0, 1 or 2; X^1 is CR^1; m is 1; E is SO_2; X^2 is NH; X^3 is NH; R^4 and R^5 are taken together with the carbon to which they are attached to form a spiro $(C_3$-$C_{10})$cycloalkyl ring or spiro $(C_3$-$C_{10})$cycloalkoxy ring; R^6 is a hydrogen or methyl; A^1 is $(C_6$-$C_{12})$aryl; X^5 is a direct bond, O or CR^4R^5 and A^2 is $(C_2$-$C_9)$heterocycloalkyl.

122. A compound according to claim 1, wherein n is 1; 2 or 3; t is 0, 1 or 2; y is 0 or 1; z is 0, 1 or 2; X^1 is CR^1; m is 1; E is SO_2; X^2 is NH; X^3 is NH; R^4 and R^5 are each independently methyl; R^6 is a hydrogen or methyl; A^1 is $(C_6$-$C_{12})$aryl; X^5 is a direct bond, O or CR^4R^5 and A^2 is $(C_2$-$C_9)$heterocycloalkyl.

123. A compound according to claim 1, wherein n is 1; 2 or 3; t is 0, 1 or 2; y is 0 or 1; z is 0, 1 or 2; X^1 is CR^1; m is 1; E is SO_2; X^2 is NH; X^3 is NH; R^4 and R^5 are taken together with the carbon to which they are attached to form a spiro $(C_3$-$C_{10})$cycloalkyl ring or spiro $(C_3$-$C_{10})$cycloalkoxy ring; R^6 is a hydrogen or methyl; A^1 is $(C_2$-$C_9)$heterocycloalkyl; X^5 is a direct bond, O or CR^4R^5 and A^2 is $(C_6$-$C_{12})$aryl.

124. A compound according to claim 1, wherein n is 1; 2 or 3; t is 0, 1 or 2; y is 0 or 1; z is 0, 1 or 2; X^1 is CR^1; m is 1; E is SO_2; X^2 is NH; X^3 is NH; R^4 and R^5 are each independently methyl; R^6 is a hydrogen or methyl; A^1 is $(C_2$-$C_9)$heterocycloalkyl; X^5 is a direct bond, O or CR^4R^5 and A^2 is $(C_6$-$C_{12})$aryl.

125. A compound according to claim 1, wherein n is 1; 2 or 3; t is 0, 1 or 2; y is 0 or 1; z is 0, 1 or 2; X^1 is N; m is 0; E is O; X^3 is NH; R^4 and R^5 are taken together with the carbon to which they are attached to form a spiro $(C_3$-$C_{10})$cycloalkyl ring or spiro $(C_3$-$C_{10})$cycloalkoxy ring; R^6 is a hydrogen or methyl; A^1 is $(C_6$-$C_{12})$aryl; X^5 is a direct bond, O or CR^4R^5 and A^2 is $(C_2$-$C_9)$heterocycloalkyl.

126. A compound according to claim 1, wherein n is 1; 2 or 3; t is 0, 1 or 2; y is 0 or 1; z is 0, 1 or 2; X^1 is N; m is 0; E is O; X^3 is NH; R^4 and R^5 are each independently methyl; R^6 is a hydrogen or methyl; A^1 is $(C_6$-$C_{12})$aryl; X^5 is a direct bond, O or CR^4R^5 and A^2 is $(C_2$-$C_9)$heterocycloalkyl.

127. A compound according to claim 1, wherein n is 1; 2 or 3; t is 0, 1 or 2; y is 0 or 1; z is 0, 1 or 2; X^1 is N; m is 0; E is O; X^3 is NH; R^4 and R^5 are taken together with the carbon to which they are attached to form a spiro $(C_3$-$C_{10})$cycloalkyl ring or spiro $(C_3$-$C_{10})$cycloalkoxy ring; R^6 is a hydrogen or methyl; A^1 is $(C_2$-$C_9)$heterocycloalkyl; X^5 is a direct bond, O or CR^4R^5 and A^2 is $(C_6$-$C_{12})$aryl.

128. A compound according to claim 1, wherein n is 1; 2 or 3; t is 0, 1 or 2; y is 0 or 1; z is 0, 1 or 2; X^1 is N; m is 0; E is O; X^3 is NH; R^4 and R^5 are each independently methyl; R^6 is a hydrogen or methyl; A^1 is $(C_2$-$C_9)$heterocycloalkyl; X^5 is a direct bond, O or CR^4R^5 and A^2 is $(C_6$-$C_{12})$aryl.

129. A compound according to claim 1, wherein n is 1; 2 or 3; t is 0, 1 or 2; y is 0 or 1; z is 0, 1 or 2; X^1 is CR^1; m is 1; E is O; X^2 is NH; X^3 is CO-NH; R^4 and R^5 are taken together with the carbon to which they are attached to form a spiro $(C_3$-$C_{10})$cycloalkyl ring or spiro $(C_3$-$C_{10})$cycloalkoxy ring; R^6 is a hydrogen or methyl; A^1 is $(C_6$-$C_{12})$aryl; X^5 is a direct bond, O or CR^4R^5 and A^2 is $(C_2$-$C_9)$heterocycloalkyl.

130. A compound according to claim 1, wherein n is 1; 2 or 3; t is 0, 1 or 2; y is 0 or 1; z is 0, 1 or 2; X^1 is CR^1; m is 1; E is O; X^2 is NH; X^3 is CO-NH; R^4 and R^5 are each independently methyl; R^6 is a hydrogen or methyl; A^1 is $(C_6$-$C_{12})$aryl; X^5 is a direct bond, O or CR^4R^5 and A^2 is $(C_2$-$C_9)$heterocycloalkyl.

131. A compound according to claim 1, wherein n is 1; 2 or 3; t is 0, 1 or 2; y is 0 or 1; z is 0, 1 or 2; X^1 is CR^1; m is 1; E is O; X^2 is NH; X^3 is CO-NH; R^4 and R^5 are taken together with the carbon to which they are attached to form a spiro $(C_3$-$C_{10})$cycloalkyl ring or spiro $(C_3$-$C_{10})$cycloalkoxy ring; R^6 is a hydrogen or methyl; A^1 is $(C_2$-$C_9)$heterocycloalkyl; X^5 is a direct bond, O or CR^4R^5 and A^2 is $(C_6$-$C_{12})$aryl.

132. A compound according to claim 1, wherein n is 1; 2 or 3; t is 0, 1 or 2; y is 0 or 1; z is 0, 1 or 2; X^1 is CR^1; m is 1; E is O; X^2 is NH; X^3 is CO-NH; R^4 and R^5 are each independently methyl; R^6 is a hydrogen or methyl; A^1 is $(C_2$-$C_9)$heterocycloalkyl; X^5 is a direct bond, O or CR^4R^5 and A^2 is $(C_6$-$C_{12})$aryl.

133. A compound according to claim 1, wherein n is 1; 2 or 3; t is 0, 1 or 2; y is 0 or 1; z is 0, 1 or 2; X^1 is CR^1; m is 1; p is 1; E is O; X^2 is O; X^3 is NH; R^1 is H; R^4 and R^5 are taken together with the carbon to which they are attached to form a spiro $(C_3$-$C_{10})$cycloalkyl ring or spiro $(C_3$-$C_{10})$cycloalkoxy ring; R^6 is a hydrogen or methyl; A^1 is $(C_2$-$C_9)$heteroaryl; X^5 is a direct bond, O or CR^4R^5 and A^2 is $(C_2$-$C_9)$heterocycloalkyl.

134. A compound according to claim 1, wherein n is 1; 2 or 3; t is 0, 1 or 2; y is 0 or 1; z is 0, 1 or 2; X^1 is CR^1; m is 1; p is 1; E is O; X^2 is O; X^3 is NH; R^1 is H; R^4 and R^5 are

each independently methyl; R^6 is a hydrogen or methyl; A^1 is $(C_2$-$C_9)$heteroaryl; X^5 is a direct bond, O or CR^4R^5 and A^2 is $(C_2$-$C_9)$heterocycloalkyl.

135. A compound according to claim 1, wherein n is 1; 2 or 3; t is 0, 1 or 2; y is 0 or 1; z is 0, 1 or 2; X^1 is CR^1; m is 1; p is 1; E is O; X^2 is O; X^3 is NH; R^1 is H; R^4 and R^5 are taken together with the carbon to which they are attached to form a spiro $(C_3$-$C_{10})$cycloalkyl ring or spiro $(C_3$-$C_{10})$cycloalkoxy ring; R^6 is a hydrogen or methyl; A^1 is $(C_2$-$C_9)$heterocycloalkyl; X^5 is a direct bond, O or CR^4R^5 and A^2 is $(C_2$-$C_9)$heteroaryl.

136. A compound according to claim 1, wherein n is 1; 2 or 3; t is 0, 1 or 2; y is 0 or 1; z is 0, 1 or 2; X^1 is CR^1; m is 1; p is 1; E is O; X^2 is O; X^3 is NH; R^1 is H; R^4 and R^5 are each independently methyl; R^6 is a hydrogen or methyl; A^1 is $(C_2$-$C_9)$heterocycloalkyl; X^5 is a direct bond, O or CR^4R^5 and A^2 is $(C_2$-$C_9)$heteroaryl.

137. A compound according to claim 1, wherein n is 1; 2 or 3; t is 0, 1 or 2; y is 0 or 1; z is 0, 1 or 2; X^1 is CR^1; m is 1; E is O; X^2 is NH; X^3 is NH; R^4 and R^5 are taken together with the carbon to which they are attached to form a spiro $(C_3$-$C_{10})$cycloalkyl ring or spiro $(C_3$-$C_{10})$cycloalkoxy ring; R^6 is a hydrogen or methyl; A^1 is $(C_2$-$C_9)$heteroaryl; X^5 is a direct bond, O or CR^4R^5 and A^2 is $(C_2$-$C_9)$heterocycloalkyl.

138. A compound according to claim 1, wherein n is 1; 2 or 3; t is 0, 1 or 2; y is 0 or 1; z is 0, 1 or 2; X^1 is CR^1; m is 1; E is O; X^2 is NH; X^3 is NH; R^4 and R^5 are each

independently methyl; R^6 is a hydrogen or methyl; A^1 is $(C_2$-$C_9)$heteroaryl; X^5 is a direct bond, O or CR^4R^5 and A^2 is $(C_2$-$C_9)$heterocycloalkyl.

139. A compound according to claim 1, wherein n is 1; 2 or 3; t is 0, 1 or 2; y is 0 or 1; z is 0, 1 or 2; X^1 is CR^1; m is 1; E is O; X^2 is NH; X^3 is NH; R^4 and R^5 are taken together with the carbon to which they are attached to form a spiro $(C_3$-$C_{10})$cycloalkyl ring or spiro $(C_3$-$C_{10})$cycloalkoxy ring; R^6 is a hydrogen or methyl; A^1 is $(C_2$-$C_9)$heterocycloalkyl; X^5 is a direct bond, O or CR^4R^5 and A^2 is $(C_2$-$C_9)$heteroaryl.

140. A compound according to claim 1, wherein n is 1; 2 or 3; t is 0, 1 or 2; y is 0 or 1; z is 0, 1 or 2; X^1 is CR^1; m is 1; E is O; X^2 is NH; X^3 is NH; R^4 and R^5 are each independently methyl; R^6 is a hydrogen or methyl; A^1 is $(C_2$-$C_9)$heterocycloalkyl; X^5 is a direct bond, O or CR^4R^5 and A^2 is $(C_2$-$C_9)$heteroaryl.

141. A compound according to claim 1, wherein n is 1; 2 or 3; t is 0, 1 or 2; y is 0 or 1; z is 0, 1 or 2; X^1 is CR^1; m is 1; E is O; X^2 is NH; X^3 is CH_2; R^4 and R^5 are taken together with the carbon to which they are attached to form a spiro $(C_3$-$C_{10})$cycloalkyl ring or spiro $(C_3$-$C_{10})$cycloalkoxy ring; R^6 is a hydrogen or methyl; A^1 is $(C_2$-$C_9)$heteroaryl; X^5 is a direct bond, O or CR^4R^5 and A^2 is $(C_2$-$C_9)$heterocycloalkyl.

142. A compound according to claim 1, wherein n is 1; 2 or 3; t is 0, 1 or 2; y is 0 or 1; z is 0, 1 or 2; X^1 is CR^1; m is 1; E is O; X^2 is NH; X^3 is CH_2; R^4 and R^5 are each

independently methyl; R^6 is a hydrogen or methyl; A^1 is $(C_2$-$C_9)$heteroaryl; X^5 is a direct bond, O or CR^4R^5 and A^2 is $(C_2$-$C_9)$heterocycloalkyl.

143. A compound according to claim 1, wherein n is 1; 2 or 3; t is 0, 1 or 2; y is 0 or 1; z is 0, 1 or 2; X^1 is CR^1; m is 1; E is O; X^2 is NH; X^3 is CH_2; R^4 and R^5 are taken together with the carbon to which they are attached to form a spiro $(C_3$-$C_{10})$cycloalkyl ring or spiro $(C_3$-$C_{10})$cycloalkoxy ring; R^6 is a hydrogen or methyl; A^1 is $(C_2$-$C_9)$heterocycloalkyl; X^5 is a direct bond, O or CR^4R^5 and A^2 is $(C_2$-$C_9)$heteroaryl.

144. A compound according to claim 1, wherein n is 1; 2 or 3; t is 0, 1 or 2; y is 0 or 1; z is 0, 1 or 2; X^1 is CR^1; m is 1; E is O; X^2 is NH; X^3 is CH_2; R^4 and R^5 are each independently methyl; R^6 is a hydrogen or methyl; A^1 is $(C_2$-$C_9)$heterocycloalkyl; X^5 is a direct bond, O or CR^4R^5 and A^2 is $(C_2$-$C_9)$heteroaryl.

145. A compound according to claim 1, wherein n is 1; 2 or 3; t is 0, 1 or 2; y is 0 or 1; z is 0, 1 or 2; X^1 is CR^1; m is 1; E is O; X^2 is CH_2; X^3 is NH; R^4 and R^5 are taken together with the carbon to which they are attached to form a spiro $(C_3$-$C_{10})$cycloalkyl ring or spiro $(C_3$-$C_{10})$cycloalkoxy ring; R^6 is a hydrogen or methyl; A^1 is $(C_2$-$C_9)$heteroaryl; X^5 is a direct bond, O or CR^4R^5 and A^2 is $(C_2$-$C_9)$heterocycloalkyl.

146. A compound according to claim 1, wherein n is 1; 2 or 3; t is 0, 1 or 2; y is 0 or 1; z is 0, 1 or 2; X^1 is CR^1; m is 1; E is O; X^2 is CH_2; X^3 is NH; R^4 and R^5 are each

independently methyl; R^6 is a hydrogen or methyl; A^1 is $(C_2$-$C_9)$heteroaryl; X^5 is a direct bond, O or CR^4R^5 and A^2 is $(C_2$-$C_9)$heterocycloalkyl.

147. A compound according to claim 1, wherein n is 1; 2 or 3; t is 0, 1 or 2; y is 0 or 1; z is 0, 1 or 2; X^1 is CR^1; m is 1; E is O; X^2 is CH_2; X^3 is NH; R^4 and R^5 are taken together with the carbon to which they are attached to form a spiro $(C_3$-$C_{10})$cycloalkyl ring or spiro $(C_3$-$C_{10})$cycloalkoxy ring; R^6 is a hydrogen or methyl; A^1 is $(C_2$-$C_9)$heterocycloalkyl; X^5 is a direct bond, O or CR^4R^5 and A^2 is $(C_2$-$C_9)$heteroaryl.

148. A compound according to claim 1, wherein n is 1; 2 or 3; t is 0, 1 or 2; y is 0 or 1; z is 0, 1 or 2; X^1 is CR^1; m is 1; E is O; X^2 is CH_2; X^3 is NH; R^4 and R^5 are each independently methyl; R^6 is a hydrogen or methyl; A^1 is $(C_2$-$C_9)$heterocycloalkyl; X^5 is a direct bond, O or CR^4R^5 and A^2 is $(C_2$-$C_9)$heteroaryl.

149. A compound according to claim 1, wherein n is 1; 2 or 3; t is 0, 1 or 2; y is 0 or 1; z is 0, 1 or 2; X^1 is CR^1; m is 1; E is S; X^2 is NH; X^3 is NH; R^4 and R^5 are taken together with the carbon to which they are attached to form a spiro $(C_3$-$C_{10})$cycloalkyl ring or spiro $(C_3$-$C_{10})$cycloalkoxy ring; R^6 is a hydrogen or methyl; A^1 is $(C_2$-$C_9)$heteroaryl; X^5 is a direct bond, O or CR^4R^5 and A^2 is $(C_2$-$C_9)$heterocycloalkyl.

150. A compound according to claim 1, wherein n is 1; 2 or 3; t is 0, 1 or 2; y is 0 or 1; z is 0, 1 or 2; X^1 is CR^1; m is 1; E is S; X^2 is NH; X^3 is NH; R^4 and R^5 are each

independently methyl; R^6 is a hydrogen or methyl; A^1 is $(C_2$-$C_9)$heteroaryl; X^5 is a direct bond, O or CR^4R^5 and A^2 is $(C_2$-$C_9)$heterocycloalkyl.

151. A compound according to claim 1, wherein n is 1; 2 or 3; t is 0, 1 or 2; y is 0 or 1; z is 0, 1 or 2; X^1 is CR^1; m is 1; E is S; X^2 is NH; X^3 is NH; R^4 and R^5 are taken together with the carbon to which they are attached to form a spiro $(C_3$-$C_{10})$cycloalkyl ring or spiro $(C_3$-$C_{10})$cycloalkoxy ring; R^6 is a hydrogen or methyl; A^1 is $(C_2$-$C_9)$heterocycloalkyl; X^5 is a direct bond, O or CR^4R^5 and A^2 is $(C_2$-$C_9)$heteroaryl.

152. A compound according to claim 1, wherein n is 1; 2 or 3; t is 0, 1 or 2; y is 0 or 1; z is 0, 1 or 2; X^1 is CR^1; m is 1; E is S; X^2 is NH; X^3 is NH; R^4 and R^5 are each independently methyl; R^6 is a hydrogen or methyl; A^1 is $(C_2$-$C_9)$heterocycloalkyl; X^5 is a direct bond, O or CR^4R^5 and A^2 is $(C_2$-$C_9)$heteroaryl.

153. A compound according to claim 1, wherein n is 1; 2 or 3; t is 0, 1 or 2; y is 0 or 1; z is 0, 1 or 2; X^1 is CR^1; m is 1; E is SO_2; X^2 is NH; X^3 is NH; R^4 and R^5 are taken together with the carbon to which they are attached to form a spiro $(C_3$-$C_{10})$cycloalkyl ring or spiro $(C_3$-$C_{10})$cycloalkoxy ring; R^6 is a hydrogen or methyl; A^1 is $(C_2$-$C_9)$heteroaryl; X^5 is a direct bond, O or CR^4R^5 and A^2 is $(C_2$-$C_9)$heterocycloalkyl.

154. A compound according to claim 1, wherein n is 1; 2 or 3; t is 0, 1 or 2; y is 0 or 1; z is 0, 1 or 2; X^1 is CR^1; m is 1; E is SO_2; X^2 is NH; X^3 is NH; R^4 and R^5 are each

independently methyl; R^6 is a hydrogen or methyl; A^1 is (C_2-C_9)heteroaryl; X^5 is a direct bond, O or CR^4R^5 and A^2 is (C_2-C_9)heterocycloalkyl.

155. A compound according to claim 1, wherein n is 1; 2 or 3; t is 0, 1 or 2; y is 0 or 1; z is 0, 1 or 2; X^1 is CR^1; m is 1; E is SO_2; X^2 is NH; X^3 is NH; R^4 and R^5 are taken together with the carbon to which they are attached to form a spiro (C_3-C_{10})cycloalkyl ring or spiro (C_3-C_{10})cycloalkoxy ring; R^6 is a hydrogen or methyl; A^1 is (C_2-C_9)heterocycloalkyl; X^5 is a direct bond, O or CR^4R^5 and A^2 is (C_2-C_9)heteroaryl.

156. A compound according to claim 1, wherein n is 1; 2 or 3; t is 0, 1 or 2; y is 0 or 1; z is 0, 1 or 2; X^1 is CR^1; m is 1; E is SO_2; X^2 is NH; X^3 is NH; R^4 and R^5 are each independently methyl; R^6 is a hydrogen or methyl; A^1 is (C_2-C_9)heterocycloalkyl; X^5 is a direct bond, O or CR^4R^5 and A^2 is (C_2-C_9)heteroaryl.

157. A compound according to claim 1, wherein n is 1; 2 or 3; t is 0, 1 or 2; y is 0 or 1; z is 0, 1 or 2; X^1 is N; m is 0; E is O; X^3 is NH; R^4 and R^5 are taken together with the carbon to which they are attached to form a spiro (C_3-C_{10})cycloalkyl ring or spiro (C_3-C_{10})cycloalkoxy ring; R^6 is a hydrogen or methyl; A^1 is (C_2-C_9)heteroaryl; X^5 is a direct bond, O or CR^4R^5 and A^2 is (C_2-C_9)heterocycloalkyl.

158. A compound according to claim 1, wherein n is 1; 2 or 3; t is 0, 1 or 2; y is 0 or 1; z is 0, 1 or 2; X^1 is N; m is 0; E is O; X^3 is NH; R^4 and R^5 are each independently methyl;

R^6 is a hydrogen or methyl; A^1 is $(C_2$-$C_9)$heteroaryl; X^5 is a direct bond, O or CR^4R^5 and A^2 is $(C_2$-$C_9)$heterocycloalkyl.

159. A compound according to claim 1, wherein n is 1; 2 or 3; t is 0, 1 or 2; y is 0 or 1; z is 0, 1 or 2; X^1 is N; m is 0; E is O; X^3 is NH; R^4 and R^5 are taken together with the carbon to which they are attached to form a spiro $(C_3$-$C_{10})$cycloalkyl ring or spiro $(C_3$-$C_{10})$cycloalkoxy ring; R^6 is a hydrogen or methyl; A^1 is $(C_2$-$C_9)$heterocycloalkyl; X^5 is a direct bond, O or CR^4R^5 and A^2 is $(C_2$-$C_9)$heteroaryl.

160. A compound according to claim 1, wherein n is 1; 2 or 3; t is 0, 1 or 2; y is 0 or 1; z is 0, 1 or 2; X^1 is N; m is 0; E is O; X^3 is NH; R^4 and R^5 are each independently methyl; R^6 is a hydrogen or methyl; A^1 is $(C_2$-$C_9)$heterocycloalkyl; X^5 is a direct bond, O or CR^4R^5 and A^2 is $(C_2$-$C_9)$heteroaryl.

161. A compound according to claim 1, wherein n is 1; 2 or 3; t is 0, 1 or 2; y is 0 or 1; z is 0, 1 or 2; X^1 is CR^1; m is 1; E is O; X^2 is NH; X^3 is CO-NH; R^4 and R^5 are taken together with the carbon to which they are attached to form a spiro $(C_3$-$C_{10})$cycloalkyl ring or spiro $(C_3$-$C_{10})$cycloalkoxy ring; R^6 is a hydrogen or methyl; A^1 is $(C_2$-$C_9)$heteroaryl; X^5 is a direct bond, O or CR^4R^5 and A^2 is $(C_2$-$C_9)$heterocycloalkyl.

162. A compound according to claim 1, wherein n is 1; 2 or 3; t is 0, 1 or 2; y is 0 or 1; z is 0, 1 or 2; X^1 is CR^1; m is 1; E is O; X^2 is NH; X^3 is CO-NH; R^4 and R^5 are each

independently methyl; R^6 is a hydrogen or methyl; A^1 is $(C_2$-$C_9)$heteroaryl; X^5 is a direct bond, O or CR^4R^5 and A^2 is $(C_2$-$C_9)$heterocycloalkyl.

163. A compound according to claim 1, wherein n is 1; 2 or 3; t is 0, 1 or 2; y is 0 or 1; z is 0, 1 or 2; X^1 is CR^1; m is 1; E is O; X^2 is NH; X^3 is CO-NH; R^4 and R^5 are taken together with the carbon to which they are attached to form a spiro $(C_3$-$C_{10})$cycloalkyl ring or spiro $(C_3$-$C_{10})$cycloalkoxy ring; R^6 is a hydrogen or methyl; A^1 is $(C_2$-$C_9)$heterocycloalkyl; X^5 is a direct bond, O or CR^4R^5 and A^2 is $(C_2$-$C_9)$heteroaryl.

164. A compound according to claim 1, wherein n is 1; 2 or 3; t is 0, 1 or 2; y is 0 or 1; z is 0, 1 or 2; X^1 is CR^1; m is 1; E is O; X^2 is NH; X^3 is CO-NH; R^4 and R^5 are each independently methyl; R^6 is a hydrogen or methyl; A^1 is $(C_2$-$C_9)$heterocycloalkyl; X^5 is a direct bond, O or CR^4R^5 and A^2 is $(C_2$-$C_9)$heteroaryl.

165. A compound according to claim 1, wherein n is 1; 2 or 3; t is 0, 1 or 2; y is 0 or 1; z is 0, 1 or 2; X^1 is CR^1; m is 1; p is 1; E is O; X^2 is O; X^3 is NH; R^1 is H; R^4 and R^5 are taken together with the carbon to which they are attached to form a spiro $(C_3$-$C_{10})$cycloalkyl ring or spiro $(C_3$-$C_{10})$cycloalkoxy ring; R^6 is a hydrogen or methyl; A^1 is $(C_2$-$C_9)$heteroaryl; X^5 is a direct bond, O or CR^4R^5 and A^2 is $(C_2$-$C_9)$heteroaryl.

166. A compound according to claim 1, wherein n is 1; 2 or 3; t is 0, 1 or 2; y is 0 or 1; z is 0, 1 or 2; X^1 is CR^1; m is 1; p is 1; E is O; X^2 is O; X^3 is NH; R^1 is H; R^4 and R^5 are each independently methyl; R^6 is a hydrogen or methyl; A^1 is $(C_2$-$C_9)$heteroaryl; X^5 is a direct bond, O or CR^4R^5 and A^2 is $(C_2$-$C_9)$heteroaryl.

167. A compound according to claim 1, wherein n is 1; 2 or 3; t is 0, 1 or 2; y is 0 or 1; z is 0, 1 or 2; X^1 is CR^1; m is 1; E is O; X^2 is NH; X^3 is NH; R^4 and R^5 are taken together with the carbon to which they are attached to form a spiro (C_3-C_{10})cycloalkyl ring or spiro (C_3-C_{10})cycloalkoxy ring; R^6 is a hydrogen or methyl; A^1 is (C_2-C_9)heteroaryl; X^5 is a direct bond, O or CR^4R^5 and A^2 is (C_2-C_9)heteroaryl.

168. A compound according to claim 1, wherein n is 1; 2 or 3; t is 0, 1 or 2; y is 0 or 1; z is 0, 1 or 2; X^1 is CR^1; m is 1; E is O; X^2 is NH; X^3 is NH; R^4 and R^5 are each independently methyl; R^6 is a hydrogen or methyl; A^1 is (C_2-C_9)heteroaryl; X^5 is a direct bond, O or CR^4R^5 and A^2 is (C_2-C_9)heteroaryl.

169. A compound according to claim 1, wherein n is 1; 2 or 3; t is 0, 1 or 2; y is 0 or 1; z is 0, 1 or 2; X^1 is CR^1; m is 1; E is O; X^2 is NH; X^3 is CH_2; R^4 and R^5 are taken together with the carbon to which they are attached to form a spiro (C_3-C_{10})cycloalkyl ring or spiro (C_3-C_{10})cycloalkoxy ring; R^6 is a hydrogen or methyl; A^1 is (C_2-C_9)heteroaryl; X^5 is a direct bond, O or CR^4R^5 and A^2 is (C_2-C_9)heteroaryl.

170. A compound according to claim 1, wherein n is 1; 2 or 3; t is 0, 1 or 2; y is 0 or 1; z is 0, 1 or 2; X^1 is CR^1; m is 1; E is O; X^2 is NH; X^3 is CH_2; R^4 and R^5 are each independently methyl; R^6 is a hydrogen or methyl; A^1 is (C_2-C_9)heteroaryl; X^5 is a direct bond, O or CR^4R^5 and A^2 is (C_2-C_9)heteroaryl.

171. A compound according to claim 1, wherein n is 1; 2 or 3; t is 0, 1 or 2; y is 0 or 1; z is 0, 1 or 2; X^1 is CR^1; m is 1; E is O; X^2 is CH_2; X^3 is NH; R^4 and R^5 are taken together with the carbon to which they are attached to form a spiro (C_3-C_{10})cycloalkyl ring or spiro (C_3-C_{10})cycloalkoxy ring; R^6 is a hydrogen or methyl; A^1 is (C_2-C_9)heteroaryl; X^5 is a direct bond, O or CR^4R^5 and A^2 is (C_2-C_9)heteroaryl.

172. A compound according to claim 1, wherein n is 1; 2 or 3; t is 0, 1 or 2; y is 0 or 1; z is 0, 1 or 2; X^1 is CR^1; m is 1; E is O; X^2 is CH_2; X^3 is NH; R^4 and R^5 are each independently methyl; R^6 is a hydrogen or methyl; A^1 is (C_2-C_9)heteroaryl; X^5 is a direct bond, O or CR^4R^5 and A^2 is (C_2-C_9)heteroaryl.

173. A compound according to claim 1, wherein n is 1; 2 or 3; t is 0, 1 or 2; y is 0 or 1; z is 0, 1 or 2; X^1 is CR^1; m is 1; E is S; X^2 is NH; X^3 is NH; R^4 and R^5 are taken together with the carbon to which they are attached to form a spiro (C_3-C_{10})cycloalkyl ring or spiro (C_3-C_{10})cycloalkoxy ring; R^6 is a hydrogen or methyl; A^1 is (C_2-C_9)heteroaryl; X^5 is a direct bond, O or CR^4R^5 and A^2 is (C_2-C_9)heteroaryl.

174. A compound according to claim 1, wherein n is 1; 2 or 3; t is 0, 1 or 2; y is 0 or 1; z is 0, 1 or 2; X^1 is CR^1; m is 1; E is S; X^2 is NH; X^3 is NH; R^4 and R^5 are each independently methyl; R^6 is a hydrogen or methyl; A^1 is (C_2-C_9)heteroaryl; X^5 is a direct bond, O or CR^4R^5 and A^2 is (C_2-C_9)heteroaryl.

175. A compound according to claim 1, wherein n is 1; 2 or 3; t is 0, 1 or 2; y is 0 or 1; z is 0, 1 or 2; X^1 is CR^1; m is 1; E is SO_2; X^2 is NH; X^3 is NH; R^4 and R^5 are taken together with the carbon to which they are attached to form a spiro (C_3-C_{10})cycloalkyl ring or spiro (C_3-C_{10})cycloalkoxy ring; R^6 is a hydrogen or methyl; A^1 is (C_2-C_9)heteroaryl; X^5 is a direct bond, O or CR^4R^5 and A^2 is (C_2-C_9)heteroaryl.

176. A compound according to claim 1, wherein n is 1; 2 or 3; t is 0, 1 or 2; y is 0 or 1; z is 0, 1 or 2; X^1 is CR^1; m is 1; E is SO_2; X^2 is NH; X^3 is NH; R^4 and R^5 are each independently methyl; R^6 is a hydrogen or methyl; A^1 is (C_2-C_9)heteroaryl; X^5 is a direct bond, O or CR^4R^5 and A^2 is (C_2-C_9)heteroaryl.

177. A compound according to claim 1, wherein n is 1; 2 or 3; t is 0, 1 or 2; y is 0 or 1; z is 0, 1 or 2; X^1 is N; m is 0; E is O; X^3 is NH; R^4 and R^5 are taken together with the carbon to which they are attached to form a spiro (C_3-C_{10})cycloalkyl ring or spiro (C_3-C_{10})cycloalkoxy ring; R^6 is a hydrogen or methyl; A^1 is (C_2-C_9)heteroaryl; X^5 is a direct bond, O or CR^4R^5 and A^2 is (C_2-C_9)heteroaryl.

178. A compound according to claim 1, wherein n is 1; 2 or 3; t is 0, 1 or 2; y is 0 or 1; z is 0, 1 or 2; X^1 is N; m is 0; E is O; X^3 is NH; R^4 and R^5 are each independently methyl; R^6 is a hydrogen or methyl; A^1 is (C_2-C_9)heteroaryl; X^5 is a direct bond, O or CR^4R^5 and A^2 is (C_2-C_9)heteroaryl.

179. A compound according to claim 1, wherein n is 1; 2 or 3; t is 0, 1 or 2; y is 0 or 1; z is 0, 1 or 2; X^1 is CR^1; m is 1; E is O; X^2 is NH; X^3 is CO-NH; R^4 and R^5 are taken together with the carbon to which they are attached to form a spiro (C_3-C_{10})cycloalkyl ring or spiro (C_3-C_{10})cycloalkoxy ring; R^6 is a hydrogen or methyl; A^1 is (C_2-C_9)heteroaryl; X^5 is a direct bond, O or CR^4R^5 and A^2 is (C_2-C_9)heteroaryl.

180. A compound according to claim 1, wherein n is 1; 2 or 3; t is 0, 1 or 2; y is 0 or 1; z is 0, 1 or 2; X^1 is CR^1; m is 1; E is O; X^2 is NH; X^3 is CO-NH; R^4 and R^5 are each independently methyl; R^6 is a hydrogen or methyl; A^1 is (C_2-C_9)heteroaryl; X^5 is a direct bond, O or CR^4R^5 and A^2 is (C_2-C_9)heteroaryl.

181. A compound according to claim 1, wherein n is 1; 2 or 3; t is 0, 1 or 2; y is 0 or 1; z is 0, 1 or 2; X^1 is CR^1; m is 1; p is 1; E is O; X^2 is O; X^3 is NH; R^1 is H; R^4 and R^5 are taken together with the carbon to which they are attached to form a spiro (C_3-C_{10})cycloalkyl ring or spiro (C_3-C_{10})cycloalkoxy ring; R^6 is a hydrogen or methyl; A^1 is (C_6-C_{12})aryl; X^5 is a direct bond, O or CR^4R^5 and A^2 is (C_3-C_{10})cycloalkyl.

182. A compound according to claim 1, wherein n is 1; 2 or 3; t is 0, 1 or 2; y is 0 or 1; z is 0, 1 or 2; X^1 is CR^1; m is 1; p is 1; E is O; X^2 is O; X^3 is NH; R^1 is H; R^4 and R^5 are each independently methyl; R^6 is a hydrogen or methyl; A^1 is (C_6-C_{12})aryl; X^5 is a direct bond, O or CR^4R^5 and A^2 is (C_3-C_{10})cycloalkyl.

183. A compound according to claim 1, wherein n is 1; 2 or 3; t is 0, 1 or 2; y is 0 or 1; z is 0, 1 or 2; X^1 is CR^1; m is 1; p is 1; E is O; X^2 is O; X^3 is NH; R^1 is H; R^4 and R^5 are

taken together with the carbon to which they are attached to form a spiro (C_3-C_{10})cycloalkyl ring or spiro (C_3-C_{10})cycloalkoxy ring; R^6 is a hydrogen or methyl; A^1 is (C_3-C_{10})cycloalkyl; X^5 is a direct bond, O or CR^4R^5 and A^2 is (C_6-C_{12})aryl.

184. A compound according to claim 1, wherein n is 1; 2 or 3; t is 0, 1 or 2; y is 0 or 1; z is 0, 1 or 2; X^1 is CR^1; m is 1; p is 1; E is O; X^2 is O; X^3 is NH; R^1 is H; R^4 and R^5 are each independently methyl; R^6 is a hydrogen or methyl; A^1 is (C_3-C_{10})cycloalkyl; X^5 is a direct bond, O or CR^4R^5 and A^2 is (C_6-C_{12})aryl.

185. A compound according to claim 1, wherein n is 1; 2 or 3; t is 0, 1 or 2; y is 0 or 1; z is 0, 1 or 2; X^1 is CR^1; m is 1; E is O; X^2 is NH; X^3 is NH; R^4 and R^5 are taken together with the carbon to which they are attached to form a spiro (C_3-C_{10})cycloalkyl ring or spiro (C_3-C_{10})cycloalkoxy ring; R^6 is a hydrogen or methyl; A^1 is (C_6-C_{12})aryl; X^5 is a direct bond, O or CR^4R^5 and A^2 is (C_3-C_{10})cycloalkyl.

186. A compound according to claim 1, wherein n is 1; 2 or 3; t is 0, 1 or 2; y is 0 or 1; z is 0, 1 or 2; X^1 is CR^1; m is 1; E is O; X^2 is NH; X^3 is NH; R^4 and R^5 are each independently methyl; R^6 is a hydrogen or methyl; A^1 is (C_6-C_{12})aryl; X^5 is a direct bond, O or CR^4R^5 and A^2 is (C_3-C_{10})cycloalkyl.

187. A compound according to claim 1, wherein n is 1; 2 or 3; t is 0, 1 or 2; y is 0 or 1; z is 0, 1 or 2; X^1 is CR^1; m is 1; E is O; X^2 is NH; X^3 is NH; R^4 and R^5 are taken together with the carbon to which they are attached to form a spiro (C_3-C_{10})cycloalkyl ring or spiro

(C_3-C_{10})cycloalkoxy ring; R^6 is a hydrogen or methyl; A^1 is (C_3-C_{10})cycloalkyl; X^5 is a direct bond, O or CR^4R^5 and A^2 is (C_6-C_{12})aryl.

188. A compound according to claim 1, wherein n is 1; 2 or 3; t is 0, 1 or 2; y is 0 or 1; z is 0, 1 or 2; X^1 is CR^1; m is 1; E is O; X^2 is NH; X^3 is NH; R^4 and R^5 are each independently methyl; R^6 is a hydrogen or methyl; A^1 is (C_3-C_{10})cycloalkyl; X^5 is a direct bond, O or CR^4R^5 and A^2 is (C_6-C_{12})aryl.

189. A compound according to claim 1, wherein n is 1; 2 or 3; t is 0, 1 or 2; y is 0 or 1; z is 0, 1 or 2; X^1 is CR^1; m is 1; E is O; X^2 is NH; X^3 is CH_2; R^4 and R^5 are taken together with the carbon to which they are attached to form a spiro (C_3-C_{10})cycloalkyl ring or spiro (C_3-C_{10})cycloalkoxy ring; R^6 is a hydrogen or methyl; A^1 is (C_6-C_{12})aryl; X^5 is a direct bond, O or CR^4R^5 and A^2 is (C_3-C_{10})cycloalkyl.

190. A compound according to claim 1, wherein n is 1; 2 or 3; t is 0, 1 or 2; y is 0 or 1; z is 0, 1 or 2; X^1 is CR^1; m is 1; E is O; X^2 is NH; X^3 is CH_2; R^4 and R^5 are each independently methyl; R^6 is a hydrogen or methyl; A^1 is (C_6-C_{12})aryl; X^5 is a direct bond, O or CR^4R^5 and A^2 is (C_3-C_{10})cycloalkyl.

191. A compound according to claim 1, wherein n is 1; 2 or 3; t is 0, 1 or 2; y is 0 or 1; z is 0, 1 or 2; X^1 is CR^1; m is 1; E is O; X^2 is NH; X^3 is CH_2; R^4 and R^5 are taken together with the carbon to which they are attached to form a spiro (C_3-C_{10})cycloalkyl ring or spiro

$(C_3$-$C_{10})$cycloalkoxy ring; R^6 is a hydrogen or methyl; A^1 is $(C_3$-$C_{10})$cycloalkyl; X^5 is a direct bond, O or CR^4R^5 and A^2 is $(C_6$-$C_{12})$aryl.

192. A compound according to claim 1, wherein n is 1; 2 or 3; t is 0, 1 or 2; y is 0 or 1; z is 0, 1 or 2; X^1 is CR^1; m is 1; E is O; X^2 is NH; X^3 is CH_2; R^4 and R^5 are each independently methyl; R^6 is a hydrogen or methyl; A^1 is $(C_3$-$C_{10})$cycloalkyl; X^5 is a direct bond, O or CR^4R^5 and A^2 is $(C_6$-$C_{12})$aryl.

193. A compound according to claim 1, wherein n is 1; 2 or 3; t is 0, 1 or 2; y is 0 or 1; z is 0, 1 or 2; X^1 is CR^1; m is 1; E is O; X^2 is CH_2; X^3 is NH; R^4 and R^5 are taken together with the carbon to which they are attached to form a spiro $(C_3$-$C_{10})$cycloalkyl ring or spiro $(C_3$-$C_{10})$cycloalkoxy ring; R^6 is a hydrogen or methyl; A^1 is $(C_6$-$C_{12})$aryl; X^5 is a direct bond, O or CR^4R^5 and A^2 is $(C_3$-$C_{10})$cycloalkyl.

194. A compound according to claim 1, wherein n is 1; 2 or 3; t is 0, 1 or 2; y is 0 or 1; z is 0, 1 or 2; X^1 is CR^1; m is 1; E is O; X^2 is CH_2; X^3 is NH; R^4 and R^5 are each independently methyl; R^6 is a hydrogen or methyl; A^1 is $(C_6$-$C_{12})$aryl; X^5 is a direct bond, O or CR^4R^5 and A^2 is $(C_3$-$C_{10})$cycloalkyl.

195. A compound according to claim 1, wherein n is 1; 2 or 3; t is 0, 1 or 2; y is 0 or 1; z is 0, 1 or 2; X^1 is CR^1; m is 1; E is O; X^2 is CH_2; X^3 is NH; R^4 and R^5 are taken together with the carbon to which they are attached to form a spiro $(C_3$-$C_{10})$cycloalkyl ring or spiro

$(C_3$-$C_{10})$cycloalkoxy ring; R^6 is a hydrogen or methyl; A^1 is $(C_3$-$C_{10})$cycloalkyl; X^5 is a direct bond, O or CR^4R^5 and A^2 is $(C_6$-$C_{12})$aryl.

196. A compound according to claim 1, wherein n is 1; 2 or 3; t is 0, 1 or 2; y is 0 or 1; z is 0, 1 or 2; X^1 is CR^1; m is 1; E is O; X^2 is CH_2; X^3 is NH; R^4 and R^5 are each independently methyl; R^6 is a hydrogen or methyl; A^1 is $(C_3$-$C_{10})$cycloalkyl; X^5 is a direct bond, O or CR^4R^5 and A^2 is $(C_6$-$C_{12})$aryl.

197. A compound according to claim 1, wherein n is 1; 2 or 3; t is 0, 1 or 2; y is 0 or 1; z is 0, 1 or 2; X^1 is CR^1; m is 1; E is S; X^2 is NH; X^3 is NH; R^4 and R^5 are taken together with the carbon to which they are attached to form a spiro $(C_3$-$C_{10})$cycloalkyl ring or spiro $(C_3$-$C_{10})$cycloalkoxy ring; R^6 is a hydrogen or methyl; A^1 is $(C_6$-$C_{12})$aryl; X^5 is a direct bond, O or CR^4R^5 and A^2 is $(C_3$-$C_{10})$cycloalkyl.

198. A compound according to claim 1, wherein n is 1; 2 or 3; t is 0, 1 or 2; y is 0 or 1; z is 0, 1 or 2; X^1 is CR^1; m is 1; E is S; X^2 is NH; X^3 is NH; R^4 and R^5 are each independently methyl; R^6 is a hydrogen or methyl; A^1 is $(C_6$-$C_{12})$aryl; X^5 is a direct bond, O or CR^4R^5 and A^2 is $(C_3$-$C_{10})$cycloalkyl.

199. A compound according to claim 1, wherein n is 1; 2 or 3; t is 0, 1 or 2; y is 0 or 1; z is 0, 1 or 2; X^1 is CR^1; m is 1; E is S; X^2 is NH; X^3 is NH; R^4 and R^5 are taken together with the carbon to which they are attached to form a spiro $(C_3$-$C_{10})$cycloalkyl ring or spiro

(C_3-C_{10})cycloalkoxy ring; R^6 is a hydrogen or methyl; A^1 is (C_3-C_{10})cycloalkyl; X^5 is a direct bond, O or CR^4R^5 and A^2 is (C_6-C_{12})aryl.

200. A compound according to claim 1, wherein n is 1; 2 or 3; t is 0, 1 or 2; y is 0 or 1; z is 0, 1 or 2; X^1 is CR^1; m is 1; E is S; X^2 is NH; X^3 is NH; R^4 and R^5 are each independently methyl; R^6 is a hydrogen or methyl; A^1 is (C_3-C_{10})cycloalkyl; X^5 is a direct bond, O or CR^4R^5 and A^2 is (C_6-C_{12})aryl.

201. A compound according to claim 1, wherein n is 1; 2 or 3; t is 0, 1 or 2; y is 0 or 1; z is 0, 1 or 2; X^1 is CR^1; m is 1; E is SO_2; X^2 is NH; X^3 is NH; R^4 and R^5 are taken together with the carbon to which they are attached to form a spiro (C_3-C_{10})cycloalkyl ring or spiro (C_3-C_{10})cycloalkoxy ring; R^6 is a hydrogen or methyl; A^1 is (C_6-C_{12})aryl; X^5 is a direct bond, O or CR^4R^5 and A^2 is (C_3-C_{10})cycloalkyl.

202. A compound according to claim 1, wherein n is 1; 2 or 3; t is 0, 1 or 2; y is 0 or 1; z is 0, 1 or 2; X^1 is CR^1; m is 1; E is SO_2; X^2 is NH; X^3 is NH; R^4 and R^5 are each independently methyl; R^6 is a hydrogen or methyl; A^1 is (C_6-C_{12})aryl; X^5 is a direct bond, O or CR^4R^5 and A^2 is (C_3-C_{10})cycloalkyl.

203. A compound according to claim 1, wherein n is 1; 2 or 3; t is 0, 1 or 2; y is 0 or 1; z is 0, 1 or 2; X^1 is CR^1; m is 1; E is SO_2; X^2 is NH; X^3 is NH; R^4 and R^5 are taken together with the carbon to which they are attached to form a spiro (C_3-C_{10})cycloalkyl

ring or spiro (C_3-C_{10})cycloalkoxy ring; R^6 is a hydrogen or methyl; A^1 is (C_3-C_{10})cycloalkyl; X^5 is a direct bond, O or CR^4R^5 and A^2 is (C_6-C_{12})aryl.

204. A compound according to claim 1, wherein n is 1; 2 or 3; t is 0, 1 or 2; y is 0 or 1; z is 0, 1 or 2; X^1 is CR^1; m is 1; E is SO_2; X^2 is NH; X^3 is NH; R^4 and R^5 are each independently methyl; R^6 is a hydrogen or methyl; A^1 is (C_3-C_{10})cycloalkyl; X^5 is a direct bond, O or CR^4R^5 and A^2 is (C_6-C_{12})aryl.

205. A compound according to claim 1, wherein n is 1; 2 or 3; t is 0, 1 or 2; y is 0 or 1; z is 0, 1 or 2; X^1 is N; m is 0; E is C; X^3 is NH; R^4 and R^5 are taken together with the carbon to which they are attached to form a spiro (C_3-C_{10})cycloalkyl ring or spiro (C_3-C_{10})cycloalkoxy ring; R^6 is a hydrogen or methyl; A^1 is (C_6-C_{12})aryl; X^5 is a direct bond, O or CR^4R^5 and A^2 is (C_3-C_{10})cycloalkyl.

206. A compound according to claim 1, wherein n is 1; 2 or 3; t is 0, 1 or 2; y is 0 or 1; z is 0, 1 or 2; X^1 is N; m is 0; E is O; X^3 is NH; R^4 and R^5 are each independently methyl; R^6 is a hydrogen or methyl; A^1 is (C_6-C_{12})aryl; X^5 is a direct bond, O or CR^4R^5 and A^2 is (C_3-C_{10})cycloalkyl.

207. A compound according to claim 1, wherein n is 1; 2 or 3; t is 0, 1 or 2; y is 0 or 1; z is 0, 1 or 2; X^1 is N; m is 0; E is O; X^3 is NH; R^4 and R^5 are taken together with the carbon to which they are attached to form a spiro (C_3-C_{10})cycloalkyl ring or spiro (C_3-

C_{10})cycloalkoxy ring; R^6 is a hydrogen or methyl; A^1 is (C_3-C_{10})cycloalkyl; X^5 is a direct bond, O or CR^4R^5 and A^2 is (C_6-C_{12})aryl.

208. A compound according to claim 1, wherein n is 1; 2 or 3; t is 0, 1 or 2; y is 0 or 1; z is 0, 1 or 2; X^1 is N; m is 0; E is O; X^3 is NH; R^4 and R^5 are each independently methyl; R^6 is a hydrogen or methyl; A^1 is (C_3-C_{10})cycloalkyl; X^5 is a direct bond, O or CR^4R^5 and A^2 is (C_6-C_{12})aryl.

209. A compound according to claim 1, wherein n is 1; 2 or 3; t is 0, 1 or 2; y is 0 or 1; z is 0, 1 or 2; X^1 is CR^1; m is 1; E is O; X^2 is NH; X^3 is CO-NH; R^4 and R^5 are taken together with the carbon to which they are attached to form a spiro (C_3-C_{10})cycloalkyl ring or spiro (C_3-C_{10})cycloalkoxy ring; R^6 is a hydrogen or methyl; A^1 is (C_6-C_{12})aryl; X^5 is a direct bond, O or CR^4R^5 and A^2 is (C_3-C_{10})cycloalkyl.

210. A compound according to claim 1, wherein n is 1; 2 or 3; t is 0, 1 or 2; y is 0 or 1; z is 0, 1 or 2; X^1 is CR^1; m is 1; E is O; X^2 is NH; X^3 is CO-NH; R^4 and R^5 are each independently methyl; R^6 is a hydrogen or methyl; A^1 is (C_6-C_{12})aryl; X^5 is a direct bond, O or CR^4R^5 and A^2 is (C_3-C_{10})cycloalkyl.

211. A compound according to claim 1, wherein n is 1; 2 or 3; t is 0, 1 or 2; y is 0 or 1; z is 0, 1 or 2; X^1 is CR^1; m is 1; E is O; X^2 is NH; X^3 is CO-NH; R^4 and R^5 are taken together with the carbon to which they are attached to form a spiro (C_3-C_{10})cycloalkyl

ring or spiro (C_3-C_{10})cycloalkoxy ring; R^6 is a hydrogen or methyl; A^1 is (C_3-C_{10})cycloalkyl; X^5 is a direct bond, O or CR^4R^5 and A^2 is (C_6-C_{12})aryl.

212. A compound according to claim 1, wherein n is 1; 2 or 3; t is 0, 1 or 2; y is 0 or 1; z is 0, 1 or 2; X^1 is CR^1; m is 1; E is O; X^2 is NH; X^3 is CO-NH; R^4 and R^5 are each independently methyl; R^6 is a hydrogen or methyl; A^1 is (C_3-C_{10})cycloalkyl; X^5 is a direct bond, O or CR^4R^5 and A^2 is (C_6-C_{12})aryl.

213. A compound according to claim 1, wherein n is 1; 2 or 3; t is 0, 1 or 2; y is 0 or 1; z is 0, 1 or 2; X^1 is CR^1; m is 1; p is 1; E is O; X^2 is O; X^3 is NH; R^1 is H; R^4 and R^5 are taken together with the carbon to which they are attached to form a spiro (C_3-C_{10})cycloalkyl ring or spiro (C_3-C_{10})cycloalkoxy ring; R^6 is a hydrogen or methyl; A^1 is (C_2-C_9)heteroaryl; X^5 is a direct bond, O or CR^4R^5 and A^2 is (C_3-C_{10})cycloalkyl.

214. A compound according to claim 1, wherein n is 1; 2 or 3; t is 0, 1 or 2; y is 0 or 1; z is 0, 1 or 2; X^1 is CR^1; m is 1; p is 1; E is O; X^2 is O; X^3 is NH; R^1 is H; R^4 and R^5 are each independently methyl; R^6 is a hydrogen or methyl; A^1 is (C_2-C_9)heteroaryl; X^5 is a direct bond, O or CR^4R^5 and A^2 is (C_3-C_{10})cycloalkyl.

215. A compound according to claim 1, wherein n is 1; 2 or 3; t is 0, 1 or 2; y is 0 or 1; z is 0, 1 or 2; X^1 is CR^1; m is 1; p is 1; E is O; X^2 is O; X^3 is NH; R^1 is H; R^4 and R^5 are taken together with the carbon to which they are attached to form a spiro (C_3-C_{10})cycloalkyl ring or spiro (C_3-C_{10})cycloalkoxy ring; R^6 is a hydrogen or methyl; A^1 is (C_3-C_{10})cycloalkyl; X^5 is a direct bond, O or CR^4R^5 and A^2 is (C_2-C_9)heteroaryl.

216. A compound according to claim 1, wherein n is 1; 2 or 3; t is 0, 1 or 2; y is 0 or 1; z is 0, 1 or 2; X^1 is CR^1; m is 1; p is 1; E is O; X^2 is O; X^3 is NH; R^1 is H; R^4 and R^5 are each independently methyl; R^6 is a hydrogen or methyl; A^1 is $(C_3$-$C_{10})$cycloalkyl; X^5 is a direct bond, O or CR^4R^5 and A^2 is $(C_2$-$C_9)$heteroaryl.

217. A compound according to claim 1, wherein n is 1; 2 or 3; t is 0, 1 or 2; y is 0 or 1; z is 0, 1 or 2; X^1 is CR^1; m is 1; E is O; X^2 is NH; X^3 is NH; R^4 and R^5 are taken together with the carbon to which they are attached to form a spiro $(C_3$-$C_{10})$cycloalkyl ring or spiro $(C_3$-$C_{10})$cycloalkoxy ring; R^6 is a hydrogen or methyl; A^1 is $(C_2$-$C_9)$heteroaryl; X^5 is a direct bond, O or CR^4R^5 and A^2 is $(C_3$-$C_{10})$cycloalkyl.

218. A compound according to claim 1, wherein n is 1; 2 or 3; t is 0, 1 or 2; y is 0 or 1; z is 0, 1 or 2; X^1 is CR^1; m is 1; E is O; X^2 is NH; X^3 is NH; R^4 and R^5 are each independently methyl; R^6 is a hydrogen or methyl; A^1 is $(C_2$-$C_9)$heteroaryl; X^5 is a direct bond, O or CR^4R^5 and A^2 is $(C_3$-$C_{10})$cycloalkyl.

219. A compound according to claim 1, wherein n is 1; 2 or 3; t is 0, 1 or 2; y is 0 or 1; z is 0, 1 or 2; X^1 is CR^1; m is 1; E is O; X^2 is NH; X^3 is NH; R^4 and R^5 are taken together with the carbon to which they are attached to form a spiro $(C_3$-$C_{10})$cycloalkyl ring or spiro $(C_3$-$C_{10})$cycloalkoxy ring; R^6 is a hydrogen or methyl; A^1 is $(C_3$-$C_{10})$cycloalkyl; X^5 is a direct bond, O or CR^4R^5 and A^2 is $(C_2$-$C_9)$heteroaryl.

220. A compound according to claim 1, wherein n is 1; 2 or 3; t is 0, 1 or 2; y is 0 or 1; z is 0, 1 or 2; X^1 is CR^1; m is 1; E is O; X^2 is NH; X^3 is NH; R^4 and R^5 are each independently methyl; R^6 is a hydrogen or methyl; A^1 is $(C_3$-$C_{10})$cycloalkyl; X^5 is a direct bond, O or CR^4R^5 and A^2 is $(C_2$-$C_9)$heteroaryl.

221. A compound according to claim 1, wherein n is 1; 2 or 3; t is 0, 1 or 2; y is 0 or 1; z is 0, 1 or 2; X^1 is CR^1; m is 1; E is O; X^2 is NH; X^3 is CH_2; R^4 and R^5 are taken together with the carbon to which they are attached to form a spiro $(C_3$-$C_{10})$cycloalkyl ring or spiro $(C_3$-$C_{10})$cycloalkoxy ring; R^6 is a hydrogen or methyl; A^1 is $(C_2$-$C_9)$heteroaryl; X^5 is a direct bond, O or CR^4R^5 and A^2 is $(C_3$-$C_{10})$cycloalkyl.

222. A compound according to claim 1, wherein n is 1; 2 or 3; t is 0, 1 or 2; y is 0 or 1; z is 0, 1 or 2; X^1 is CR^1; m is 1; E is O; X^2 is NH; X^3 is CH_2; R^4 and R^5 are each independently methyl; R^6 is a hydrogen or methyl; A^1 is $(C_2$-$C_9)$heteroaryl; X^5 is a direct bond, O or CR^4R^5 and A^2 is $(C_3$-$C_{10})$cycloalkyl.

223. A compound according to claim 1, wherein n is 1; 2 or 3; t is 0, 1 or 2; y is 0 or 1; z is 0, 1 or 2; X^1 is CR^1; m is 1; E is O; X^2 is NH; X^3 is CH_2; R^4 and R^5 are taken together with the carbon to which they are attached to form a spiro $(C_3$-$C_{10})$cycloalkyl ring or spiro $(C_3$-$C_{10})$cycloalkoxy ring; R^6 is a hydrogen or methyl; A^1 is $(C_3$-$C_{10})$cycloalkyl; X^5 is a direct bond, O or CR^4R^5 and A^2 is $(C_2$-$C_9)$heteroaryl.

224. A compound according to claim 1, wherein n is 1; 2 or 3; t is 0, 1 or 2; y is 0 or 1; z is 0, 1 or 2; X^1 is CR^1; m is 1; E is O; X^2 is NH; X^3 is CH_2; R^4 and R^5 are each independently methyl; R^6 is a hydrogen or methyl; A^1 is $(C_3$-$C_{10})$cycloalkyl; X^5 is a direct bond, O or CR^4R^5 and A^2 is $(C_2$-$C_9)$heteroaryl.

225. A compound according to claim 1, wherein n is 1; 2 or 3; t is 0, 1 or 2; y is 0 or 1; z is 0, 1 or 2; X^1 is CR^1; m is 1; E is O; X^2 is CH_2; X^3 is NH; R^4 and R^5 are taken together with the carbon to which they are attached to form a spiro $(C_3$-$C_{10})$cycloalkyl ring or spiro $(C_3$-$C_{10})$cycloalkoxy ring; R^6 is a hydrogen or methyl; A^1 is $(C_2$-$C_9)$heteroaryl; X^5 is a direct bond, O or CR^4R^5 and A^2 is $(C_3$-$C_{10})$cycloalkyl.

226. A compound according to claim 1, wherein n is 1; 2 or 3; t is 0, 1 or 2; y is 0 or 1; z is 0, 1 or 2; X^1 is CR^1; m is 1; E is O; X^2 is CH_2; X^3 is NH; R^4 and R^5 are each independently methyl; R^6 is a hydrogen or methyl; A^1 is $(C_2$-$C_9)$heteroaryl; X^5 is a direct bond, O or CR^4R^5 and A^2 is $(C_3$-$C_{10})$cycloalkyl.

227. A compound according to claim 1, wherein n is 1; 2 or 3; t is 0, 1 or 2; y is 0 or 1; z is 0, 1 or 2; X^1 is CR^1; m is 1; E is O; X^2 is CH_2; X^3 is NH; R^4 and R^5 are taken together with the carbon to which they are attached to form a spiro $(C_3$-$C_{10})$cycloalkyl ring or spiro $(C_3$-$C_{10})$cycloalkoxy ring; R^6 is a hydrogen or methyl; A^1 is $(C_3$-$C_{10})$cycloalkyl; X^5 is a direct bond, O or CR^4R^5 and A^2 is $(C_2$-$C_9)$heteroaryl.

228. A compound according to claim 1, wherein n is 1; 2 or 3; t is 0, 1 or 2; y is 0 or 1; z is 0, 1 or 2; X^1 is CR^1; m is 1; E is O; X^2 is CH_2; X^3 is NH; R^4 and R^5 are each independently methyl; R^6 is a hydrogen or methyl; A^1 is $(C_3$-$C_{10})$cycloalkyl; X^5 is a direct bond, O or CR^4R^5 and A^2 is $(C_2$-$C_9)$heteroaryl.

229. A compound according to claim 1, wherein n is 1; 2 or 3; t is 0, 1 or 2; y is 0 or 1; z is 0, 1 or 2; X^1 is CR^1; m is 1; E is S; X^2 is NH; X^3 is NH; R^4 and R^5 are taken together with the carbon to which they are attached to form a spiro $(C_3$-$C_{10})$cycloalkyl ring or spiro $(C_3$-$C_{10})$cycloalkoxy ring; R^6 is a hydrogen or methyl; A^1 is $(C_2$-$C_9)$heteroaryl; X^5 is a direct bond, O or CR^4R^5 and A^2 is $(C_3$-$C_{10})$cycloalkyl.

230. A compound according to claim 1, wherein n is 1; 2 or 3; t is 0, 1 or 2; y is 0 or 1; z is 0, 1 or 2; X^1 is CR^1; m is 1; E is S; X^2 is NH; X^3 is NH; R^4 and R^5 are each independently methyl; R^6 is a hydrogen or methyl; A^1 is $(C_2$-$C_9)$heteroaryl; X^5 is a direct bond, O or CR^4R^5 and A^2 is $(C_3$-$C_{10})$cycloalkyl.

231. A compound according to claim 1, wherein n is 1; 2 or 3; t is 0, 1 or 2; y is 0 or 1; z is 0, 1 or 2; X^1 is CR^1; m is 1; E is S; X^2 is NH; X^3 is NH; R^4 and R^5 are taken together with the carbon to which they are attached to form a spiro $(C_3$-$C_{10})$cycloalkyl ring or spiro $(C_3$-$C_{10})$cycloalkoxy ring; R^6 is a hydrogen or methyl; A^1 is $(C_3$-$C_{10})$cycloalkyl; X^5 is a direct bond, O or CR^4R^5 and A^2 is $(C_2$-$C_9)$heteroaryl.

232. A compound according to claim 1, wherein n is 1; 2 or 3; t is 0, 1 or 2; y is 0 or 1; z is 0, 1 or 2; X^1 is CR^1; m is 1; E is S; X^2 is NH; X^3 is NH; R^4 and R^5 are each independently methyl; R^6 is a hydrogen or methyl; A^1 is $(C_3$-$C_{10})$cycloalkyl; X^5 is a direct bond, O or CR^4R^5 and A^2 is $(C_2$-$C_9)$heteroaryl.

233. A compound according to claim 1, wherein n is 1; 2 or 3; t is 0, 1 or 2; y is 0 or 1; z is 0, 1 or 2; X^1 is CR^1; m is 1; E is SO_2; X^2 is NH; X^3 is NH; R^4 and R^5 are taken together with the carbon to which they are attached to form a spiro $(C_3$-$C_{10})$cycloalkyl ring or spiro $(C_3$-$C_{10})$cycloalkoxy ring; R^6 is a hydrogen or methyl; A^1 is $(C_2$-$C_9)$heteroaryl; X^5 is a direct bond, O or CR^4R^5 and A^2 is $(C_3$-$C_{10})$cycloalkyl.

234. A compound according to claim 1, wherein n is 1; 2 or 3; t is 0, 1 or 2; y is 0 or 1; z is 0, 1 or 2; X^1 is CR^1; m is 1; E is SO_2; X^2 is NH; X^3 is NH; R^4 and R^5 are each independently methyl; R^6 is a hydrogen or methyl; A^1 is $(C_2$-$C_9)$heteroaryl; X^5 is a direct bond, O or CR^4R^5 and A^2 is $(C_3$-$C_{10})$cycloalkyl.

235. A compound according to claim 1, wherein n is 1; 2 or 3; t is 0, 1 or 2; y is 0 or 1; z is 0, 1 or 2; X^1 is CR^1; m is 1; E is SO_2; X^2 is NH; X^3 is NH; R^4 and R^5 are taken together with the carbon to which they are attached to form a spiro $(C_3$-$C_{10})$cycloalkyl ring or spiro $(C_3$-$C_{10})$cycloalkoxy ring; R^6 is a hydrogen or methyl; A^1 is $(C_3$-$C_{10})$cycloalkyl; X^5 is a direct bond, O or CR^4R^5 and A^2 is $(C_2$-$C_9)$heteroaryl.

236. A compound according to claim 1, wherein n is 1; 2 or 3; t is 0, 1 or 2; y is 0 or 1; z is 0, 1 or 2; X^1 is CR^1; m is 1; E is SO_2; X^2 is NH; X^3 is NH; R^4 and R^5 are each independently methyl; R^6 is a hydrogen or methyl; A^1 is $(C_3$-$C_{10})$cycloalkyl; X^5 is a direct bond, O or CR^4R^5 and A^2 is $(C_2$-$C_9)$heteroaryl.

237. A compound according to claim 1, wherein n is 1; 2 or 3; t is 0, 1 or 2; y is 0 or 1; z is 0, 1 or 2; X^1 is N; m is 0; E is O; X^3 is NH; R^4 and R^5 are taken together with the carbon to which they are attached to form a spiro $(C_3$-$C_{10})$cycloalkyl ring or spiro $(C_3$-$C_{10})$cycloalkoxy ring; R^6 is a hydrogen or methyl; A^1 is $(C_2$-$C_9)$heteroaryl; X^5 is a direct bond, O or CR^4R^5 and A^2 is $(C_3$-$C_{10})$cycloalkyl.

238. A compound according to claim 1, wherein n is 1; 2 or 3; t is 0, 1 or 2; y is 0 or 1; z is 0, 1 or 2; X^1 is N; m is 0; E is O; X^3 is NH; R^4 and R^5 are each independently methyl; R^6 is a hydrogen or methyl; A^1 is $(C_2$-$C_9)$heteroaryl; X^5 is a direct bond, O or CR^4R^5 and A^2 is $(C_3$-$C_{10})$cycloalkyl.

239. A compound according to claim 1, wherein n is 1; 2 or 3; t is 0, 1 or 2; y is 0 or 1; z is 0, 1 or 2; X^1 is N; m is 0; E is O; X^3 is NH; R^4 and R^5 are taken together with the carbon to which they are attached to form a spiro $(C_3$-$C_{10})$cycloalkyl ring or spiro $(C_3$-$C_{10})$cycloalkoxy ring; R^6 is a hydrogen or methyl; A^1 is $(C_3$-$C_{10})$cycloalkyl; X^5 is a direct bond, O or CR^4R^5 and A^2 is $(C_2$-$C_9)$heteroaryl.

240. A compound according to claim 1, wherein n is 1; 2 or 3; t is 0, 1 or 2; y is 0 or 1; z is 0, 1 or 2; X^1 is N; m is 0; E is O; X^3 is NH; R^4 and R^5 are each independently methyl; R^6 is a hydrogen or methyl; A^1 is $(C_3$-$C_{10})$cycloalkyl; X^5 is a direct bond, O or CR^4R^5 and A^2 is $(C_2$-$C_9)$heteroaryl.

241. A compound according to claim 1, wherein n is 1; 2 or 3; t is 0, 1 or 2; y is 0 or 1; z is 0, 1 or 2; X^1 is CR^1; m is 1; E is O; X^2 is NH; X^3 is CO-NH; R^4 and R^5 are taken together with the carbon to which they are attached to form a spiro $(C_3$-$C_{10})$cycloalkyl ring or spiro $(C_3$-$C_{10})$cycloalkoxy ring; R^6 is a hydrogen or methyl; A^1 is $(C_2$-$C_9)$heteroaryl; X^5 is a direct bond, O or CR^4R^5 and A^2 is $(C_3$-$C_{10})$cycloalkyl.

242. A compound according to claim 1, wherein n is 1; 2 or 3; t is 0, 1 or 2; y is 0 or 1; z is 0, 1 or 2; X^1 is CR^1; m is 1; E is O; X^2 is NH; X^3 is CO-NH; R^4 and R^5 are each independently methyl; R^6 is a hydrogen or methyl; A^1 is $(C_2$-$C_9)$heteroaryl; X^5 is a direct bond, O or CR^4R^5 and A^2 is $(C_3$-$C_{10})$cycloalkyl.

243. A compound according to claim 1, wherein n is 1; 2 or 3; t is 0, 1 or 2; y is 0 or 1; z is 0, 1 or 2; X^1 is CR^1; m is 1; E is O; X^2 is NH; X^3 is CO-NH; R^4 and R^5 are taken together with the carbon to which they are attached to form a spiro $(C_3$-$C_{10})$cycloalkyl ring or spiro $(C_3$-$C_{10})$cycloalkoxy ring; R^6 is a hydrogen or methyl; A^1 is $(C_3$-$C_{10})$cycloalkyl; X^5 is a direct bond, O or CR^4R^5 and A^2 is $(C_2$-$C_9)$heteroaryl.

244. A compound according to claim 1, wherein n is 1; 2 or 3; t is 0, 1 or 2; y is 0 or 1; z is 0, 1 or 2; X^1 is CR^1; m is 1; E is O; X^2 is NH; X^3 is CO-NH; R^4 and R^5 are each independently methyl; R^6 is a hydrogen or methyl; A^1 is $(C_3$-$C_{10})$cycloalkyl; X^5 is a direct bond, O or CR^4R^5 and A^2 is $(C_2$-$C_9)$heteroaryl.

245. A compound according to claim 1, wherein A^1 is $(C_3$-$C_{10})$cycloalkyl.

246. A compound according to claim 1, wherein A^2 is $(C_3$-$C_{10})$cycloalkyl.

247. A compound according to claim 1, or a pharmaceutically acceptable salt or prodrug thereof, selected from the group consisting of:

1-azabicyclo[2.2.2]oct-3-yl [2-(2,4'-difluorobiphenyl-4-yl)propan-2-yl]carbamate;

1-azabicyclo[2.2.2]oct-3-yl {2-[4-(1,3-benzothiazol-6-yl)phenyl]propan-2-yl}carbamate;

1-azabicyclo[3.2.2]non-4-yl {1-[5-(4-fluorophenyl)pyridin-2-yl]cyclopropyl}carbamate;

1-azabicyclo[2.2.2]oct-3-yl {1-[3-(4-fluorophenoxy)phenyl]cyclopropyl}carbamate;

1-azabicyclo[2.2.2]oct-3-yl {1-[4-(1,3-benzothiazol-5-yl)phenyl]cyclopropyl}carbamate;

1-azabicyclo[2.2.2]oct-3-yl [1-(4'-fluoro-3'-methoxybiphenyl-4-yl)cyclopropyl]carbamate;

1-azabicyclo[2.2.2]oct-3-yl [3-(4'-fluorobiphenyl-4-yl)oxetan-3-yl]carbamate;

1-azabicyclo[2.2.2]oct-3-yl {1-[6-(4-fluorophenoxy)pyridin-2-yl]cyclopropyl}carbamate;

1-azabicyclo[2.2.2]oct-3-yl [3-(4'-fluorobiphenyl-4-yl)pentan-3-yl]carbamate;

1-azabicyclo[2.2.2]oct-3-yl {2-[2-(4-fluorophenyl)-2H-indazol-6-yl]propan-2-yl}carbamate;

1-azabicyclo[2.2.2]oct-3-yl {2-[2-(1H-pyrrol-1-yl)pyridin-4-yl]propan-2-yl}carbamate;

1-(3-ethyl-1-azabicyclo[2.2.2]oct-3-yl)-3-[1-(4'-fluorobiphenyl-4-yl)cyclopropyl]urea;

N-(1-azabicyclo[2.2.2]oct-3-yl)-N'-[1-(4'-fluorobiphenyl-4yl)cyclopropyl]ethanediamide;

1-azabicyclo[2.2.2]oct-3-yl (1-{4[(4,4difluorocyclohexyl)oxy]phenyl}cyclopropyl) carbamate;

1-(4-methyl-1-azabicyclo[3.2.2]non-4-yl)-3-[1-(5-phenylpyridin-2-yl)cyclopropyl]urea;

1-[1-(4'-fluorobiphenyl-4-yl)cyclopropyl]-1-methyl-3-(3-methyl-1-azabicyclo[2.2.2]oct-3-yl)urea;

1-[1-(4'-fluorobiphenyl-4-yl)cyclopropyl]-1-methyl-3-(3-methyl-1-azabicyclo[2.2.2]oct-3-yl)urea;

1-{2-[4'-(2-methoxyethoxy)biphenyl-4-yl]propan-2-yl}-3-(3-methyl-1-azabicyclo[2.2.2]oct-3-yl)urea;

2-(1-azabicyclo[3.2.2]non-4-yl)-N-[1-(5-phenylpyridin-2-yl)cyclopropyl]acetamide;

3-(4'-fluorobiphenyl-4-yl)-3-methyl-N-(4-methyl-1-azabicyclo[3.2.2]non-4-yl)butanamide;

N-[2-(biphenyl-4-yl)propan-2-yl]-N'-(3-methyl-1-azabicyclo[2.2.2]oct-3-yl)sulfuric diamide;

N-[2-(4'-fluorobiphenyl-4-yl)propan-2-yl]-N'-(3-methyl-1-azabicyclo[2.2.2]oct-3-yl)sulfuric diamide;

1-(3-butyl-1-azabicyclo[2.2.2]oct-3-yl)-3-{2-[1-(4-fluorophenyl)-1H-pyrazol-4-yl]propan-2-yl}urea;

1-azabicyclo[2.2.2]oct-3-yl [4-(4-fluorophenyl)-2-methylbut-3-yn-2-yl]carbamate;

1-(3-butyl-1-azabicyclo[2.2.2]oct-3-yl)-3-[4-(4-fluorophenyl)-2-methylbut-3-yn-2-yl]urea;

N-[1-(4'-fluorobiphenyl-4-yl)cyclopropyl]-1,4-diazabicyclo[3.2.2]nonane-4-carboxamide;

1-(2-(4'-fluoro-[1,1'-biphenyl]-4-yl)propan-2-yl)-3-(3-methyl-1-azabicyclo[3.2.2]nonan-3-yl)urea;

1-(2-(4'-fluoro-[1,1'-biphenyl]-4-yl)propan-2-yl)-3-(4-methyl-1-azabicyclo[4.2.2]decan-4-yl)urea;

1-(2-(4'-fluoro-[1,1'-biphenyl]-4-yl)propan-2-yl)-3-(3-methyl-1-azabicyclo[4.2.2]decan-3-yl)urea; and

1-(2-(4'-fluoro-[1,1'-biphenyl]-4-yl)propan-2-yl)-3-(5-methyl-1-azabicyclo[4.2.2]decan-5-yl)urea.

248. A pharmaceutical composition for treating a disease or disorder mediated by glucosylceramide synthase (GCS) or a disease or disorder in which GCS is implicated in a subject in need of such treatment comprising administering to the subject an effective amount of a compound according to claim 1.

249. A method for treating a disease or disorder mediated by glucosylceramide synthase (GCS) or a disease or disorder in which GCS is implicated in a subject in need of such treatment comprising administering to the subject an effective amount of a compound according to claim 1.

250. The method of claim 249, wherein the disease or disorder is cancer.

251. The method of claim 249, wherein the disease or disorder is a metabolic disorder.

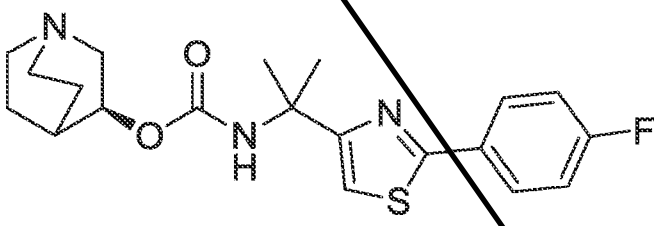
252. The method of claim 249, wherein the disease or disorder is a neuropathic disease.

253. The method of claim 252, wherein the neuropathic disease is Alzheimers disease.

254. The method of claim 252, wherein the neuropathic disease is Parkinsons disease.

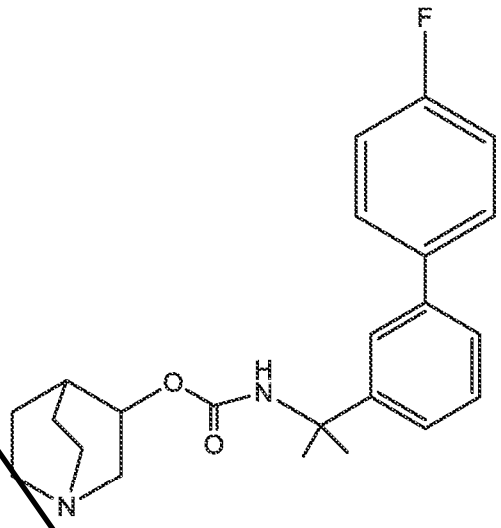
255. The method for inducing decreased glucosylceramide synthase catalytic activity in a cell, in vitro, comprising contacting the cell with an effect amount of a compound according to claim 1.

256. A compound according to claim 1, represented by the following structural formula,



or a pharmaceutically acceptable salt or prodrug thereof.

257. A compound according to claim 1, represented by the following structural formula,



or a pharmaceutically acceptable salt or prodrug thereof.

258. A method of treating a subject diagnosed as having a lysosomal storage disease, comprising administering to the subject an effective amount of the compound according to claim 1.

259. The method of claim 258, wherein the lysosomal storage disease results from a defect in the glycosphingolipid pathway.

260. The method of claim 259, wherein the lysosomal storage disease is selected from the group consisting of Gaucher, Fabry, G_{M1}-gangliosidosis, G_{M2} Activator deficiency, Tay-Sachs and Sandhoff.

261. The method of claim 260, wherein the lysosomal storage disease is Fabry.

262. The method of claim 258, further comprising the step of administering to the subject a therapeutically effective amount of a lysosomal enzyme.

263. The method of claim 262, wherein the lysosomal enzyme is selected from the group consisting of glucocerebrosidase, alpha-galactosidase A, Hexosaminidase A, Hexosaminidase B and G_{M1}-ganglioside-β-galactosidase.

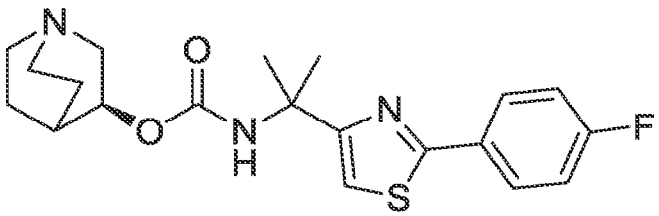
264. The method of claim 262, wherein the lysosomal enzyme is alpha-galactosidase A.

265. The method of claim 262, wherein prior to treatment the subject has elevated levels of a lysosomal substrate.

266. The method of claim 265, wherein the subject undergoing treatment has lower combined amounts of the lysosomal substrate in the urine and plasma than a subject treated with either the lysosomal enzyme or compound alone.

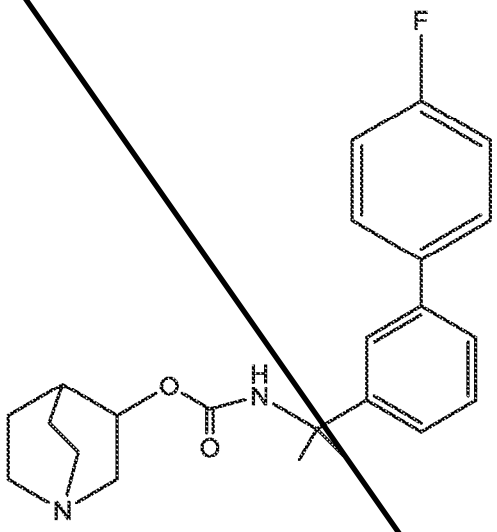
267. The method of claim 266, wherein the substrate is selected from the group consisting of globotriaosylceramide and lyso-globotriaosylceramide, and combinations thereof.

268. The method of claim 258, wherein the compound is represented by the following structural formula,



or a pharmaceutically acceptable salt or prodrug thereof.

269. The method of claim 258, wherein the compound is represented by the following structural formula,



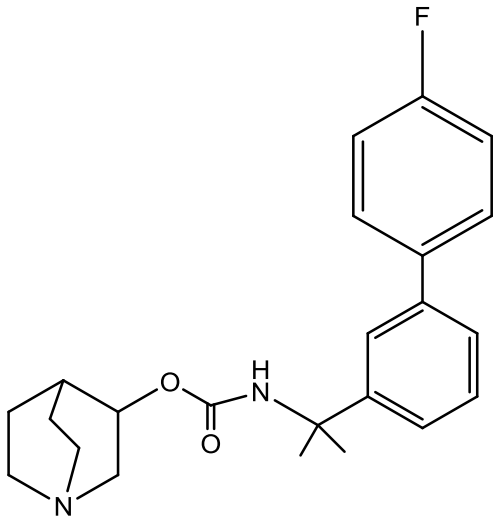
or a pharmaceutically acceptable salt or prodrug thereof.

270. A method of reducing glucosylceramide synthase (GCS) activity in a subject diagnosed as having a lysosomal storage disease, comprising administering to the patient an effective amount of the compound according to claim 1, either alone or as a combination therapy with an enzyme replacement therapy.

271. A method of reducing accumulation of a GCS-derived material in a subject diagnosed as having a lysosomal storage disease, comprising administering to the patient an effective amount of the compound according to claim 1, either alone or as a combination therapy with an enzyme replacement therapy.

Claims

1. A compound represented by the following structural formula,



or a pharmaceutically acceptable salt thereof.

2. The compound according to claim 1, wherein said compound is used in the treatment of a lysosomal storage disease.

3. The compound according to claim 2, wherein the lysosomal storage disease results from a defect in the glycosphingolipid pathway.

4. The compound according to claim 3, wherein the lysosomal storage disease is selected from the group consisting of Gaucher, Fabry, G_{M1}-gangliosidosis, G_{M2} Activator deficiency, Tay-Sachs and Sandhoff.

5. The compound according to claim 4, wherein the lysosomal storage disease is Fabry.

6. The compound according to claim 4, wherein the lysosomal storage disease is Gaucher type 2 or type 3.

7. The compound according to any one of claims 2 to 6, wherein said compound is used in combination with a therapeutically effective amount of a lysosomal enzyme.

8. The compound according to claim 7, wherein the lysosomal enzyme is selected from the group consisting of glucocerebrosidase, alpha-galactosidase A, Hexosaminidase A, Hexosaminidase B and G_{M1}-ganglioside-β-galactosidase.

9. The compound according to claim 8, wherein the lysosomal enzyme is alpha-galactosidase A.

10. The compound according to claim 8, wherein the lysosomal enzyme is glucocerebrosidase.

11. The compound according to claim 7, wherein prior to treatment the subject undergoing treatment has elevated levels of a lysosomal substrate.

12. The compound according to claim 11, wherein the subject has lower combined amounts of the lysosomal substrate in the urine and plasma than a subject treated with either the lysosomal enzyme or compound alone.

13. The compound according to claim 12, wherein the substrate is selected from the group consisting of globotriaosylceramide and lyso-globotriaosylceramide, and combinations thereof.

14. The compound according to claim 1, wherein said compound is used in the treatment of a disease or disorder mediated by glucosylceramide synthase (GCS) or a disease or disorder in which GCS is implicated.

15. The compound according to claim 14, wherein said disease or disorder is cancer, a metabolic disorder, a neuropathic disease, or a disease in which excessive glycolipid synthesis occurs selected from atherosclerosis, polycystic kidney disease, and renal hypertrophy.

16. The compound according to claim 14, wherein the neuropathic disease is Alzheimers disease or Parkinsons disease.