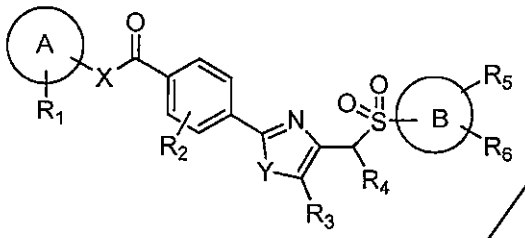
WHAT IS CLAIMED IS:

1. A compound of Formula I:



Formula I

or a pharmaceutically acceptable salt, hydrate, solvate, prodrug, enantiomer or stereoisomer thereof,

wherein:

A is a nitrogen-containing heteroaryl ring chosen from pyridinyl, pyrazinyl, and imidazolyl, each of which is optionally substituted;

X is CH_2CH_2NR, CH_2NR, or NR wherein each R is independently chosen from hydrogen, alkyl, alkenyl, alkynyl, cycloalkyl, aryl, heterocycloalkyl, and heteroaryl, each of which, except for hydrogen, is optionally substituted;

R_1, R_2, R_3, R_4. R_5 and R_6 are each independently chosen from hydrogen, alkyl, alkenyl, alkynyl, cycloalkyl, aryl, heterocycloalkyl, and heteroaryl, each of which, except for hydrogen, is optionally substituted;

Y is chosen from O, S, NR; wherein each R is independently chosen from hydrogen, alkyl, alkenyl, alkynyl, cycloalkyl, aryl, heterocycloalkyl, and heteroaryl, each of which, except for hydrogen, is optionally substituted;

B is an optionally substituted aryl ring;

provided that if A is 3-pyridinyl, X is CH_2NH, R_1, R_2, and R_4 are each hydrogen, R_3 is methyl, and Y is O, then B is not phenyl or 4-methylphenyl.

2. The compound of claim 1, wherein A is chosen from 2-pyrazinyl, 2-pyridinyl, 3-pyridinyl, 4-pyridinyl, 2-imidazolyl, and 5-imidazolyl, each of which is optionally substituted.

3. The compound of claim 1, wherein A is chosen from 2-pyrazinyl, 2-pyridinyl, 3-pyridinyl, 4-pyridinyl, (1-methyl)-2-imidazolyl, and (1-methyl)-5-imidazolyl.

4. The compound of claim 1, wherein A is chosen from 2-pyridinyl, 3-pyridinyl, and 4-pyridinyl.

5. The compound of claim 1, wherein A is 3-pyridinyl.

6. The compound of claim 1, wherein R1 is chosen from hydrogen and optionally substituted alkyl.

7. The compound of claim 1, wherein R1 is chosen from hydrogen and lower alkyl.

8. The compound of claim 1, wherein R1 is hydrogen or methyl.

9. The compound of claim 1, R1 is hydrogen.

10. The compound of claim 1, wherein R2, R3 and R4 are each independently chosen from hydrogen and optionally substituted alkyl.

11. The compound of claim 1, wherein R_2 is hydrogen.

12. The compound of claim 1, wherein R_3 is chosen from hydrogen and lower alkyl.

13. The compound of claim 1, wherein R_3 is hydrogen or methyl.

14. The compound of claim 1, wherein R_4 is chosen from hydrogen and lower alkyl.

15. The compound of claim 1, wherein R_4 is hydrogen.

16. The compound of claim 1, wherein X is chosen from CH_2CH_2NR, CH_2NR, or NR.

17. The compound of claim 1, wherein R is chosen from hydrogen and lower alkyl.

18. The compound of claim 1, wherein R is hydrogen.

19. The compound of claim 1, wherein Y is chosen from O, S, or NR.

20. The compound of claim 1, wherein R is chosen from hydrogen and lower alkyl.

21. The compound of claim 1, wherein R is hydrogen.

22. The compound of claim 1, wherein R is O.

23. The compound of claim 1, wherein R is S.

24. The compound of claim 1, wherein B is phenyl optionally substituted with one or more groups chosen from halo, alkyl, alkenyl, alkynyl, cycloalkyl, aryl, heteroaryl, heterocycloalkyl, hydroxyl, alkoxy, aryloxy, acyl, carboxy, alkoxycarbonyl, NO_2, optionally substituted amino, and CN, wherein each of said alkyl, alkenyl, alkynyl, alkoxy, cycloalkyl, aryl, heteroaryl, heterocycloalkyl, alkoxy, and aryloxy groups may be optionally independently substituted with one or more groups chosen from halo, alkyl, hydroxyl, alkoxy, carboxy, alkoxycarbonyl, heterocycloalkyl, and optionally substituted amino.

25. The compound of claim 1, wherein B is phenyl optionally substituted with one or more groups chosen from optionally substituted amino, halo, and lower alkyl optionally substituted with optionally substituted amino, heterocycloalkyl, alkoxy, or hydroxyl.

26. The compound of claim 1, wherein B is phenyl optionally substituted with one or more groups chosen from halo, optionally substituted amino and lower alkyl optionally substituted with optionally substituted amino or heterocycloalkyl.

27. The compound of claim 1, wherein B is chosen from phenyl, 3-methylphenyl, 3-methoxyphenyl, 4-chlorophenyl, 4-tert-butylphenyl, 4-bromophenyl, 4-fluorophenyl, 4-methoxyphenyl, 4-(4-methylpiperazinyl)phenyl, 4-morpholinylphenyl, 3,5-dimethylphenyl, 2,4-dimethylphenyl, 3,4-dimethoxyphenyl.

28. The compound of claim 1 selected from the group consisting of:

4-(5-Methyl-4-{[(4-methylphenyl)sulfonyl]methyl}-1,3-oxazol-2-yl)-*N*-(3-pyridinyl)benzamide;

4-(5-Methyl-4-{[(4-methylphenyl)sulfonyl]methyl}-1,3-oxazol-2-yl)-*N*-(4-pyridinyl)benzamide;

N-Methyl-4-(5-methyl-4-{[(4-methylphenyl)sulfonyl]methyl}-1,3-oxazol-2-yl)-*N*-(3-pyridinyl)benzamide;

4-(5-Methyl-4-{[(4-methylphenyl)sulfonyl]methyl}-1,3-oxazol-2-yl)-*N*-(2-pyridinylmethyl)benzamide;

4-(5-Methyl-4-{[(4-methylphenyl)sulfonyl]methyl}-1,3-oxazol-2-yl)-*N*-(3-pyridinylmethyl)benzamide;

4-(5-Methyl-4-{[(4-methylphenyl)sulfonyl]methyl}-1,3-oxazol-2-yl)-*N*-(4-pyridinylmethyl)benzamide;

N-Methyl-4-(5-methyl-4-{[(4-methylphenyl)sulfonyl]methyl}-1,3-oxazol-2-yl)-*N*-(3-pyridinylmethyl)benzamide;

4-(5-Methyl-4-{[(4-methylphenyl)sulfonyl]methyl}-1,3-oxazol-2-yl)-*N*-[2-(3-pyridinyl)ethyl]benzamide;

4-(5-Methyl-4-{[(4-methylphenyl)sulfonyl]methyl}-1,3-oxazol-2-yl)-*N*-(2-pyrazinylmethyl)benzamide;

N-[(1-Methyl-1*H*-imidazol-2-yl)methyl]-4-(5-methyl-4-{[(4-methylphenyl)sulfonyl]methyl}-1,3-oxazol-2-yl)benzamide;

N-[(1-Methyl-1*H*-imidazol-5-yl)methyl]-4-(5-methyl-4-{[(4-methylphenyl)sulfonyl]methyl}-1,3-oxazol-2-yl)benzamide;

4-{5-Methyl-4-[(phenylsulfonyl)methyl]-1,3-oxazol-2-yl}-*N*-(3-pyridinylmethyl)benzamide;

4-(4-{[(4-Chlorophenyl)sulfonyl]methyl}-5-methyl-1,3-oxazol-2-yl)-*N*-(3-pyridinylmethyl)benzamide;

4-(4-{[(4-*tert*-Butylphenyl)sulfonyl]methyl}-5-methyl-1,3-oxazol-2-yl)-*N*-(3-pyridinylmethyl)benzamide;

4-(4-{[(3,5-Dimethylphenyl)sulfonyl]methyl}-5-methyl-1,3-oxazol-2-yl)-*N*-(3-pyridinylmethyl)benzamide;

4-(4-{[(4-Bromophenyl)sulfonyl]methyl}-5-methyl-1,3-oxazol-2-yl)-*N*-(3-pyridinylmethyl)benzamide;

4-(5-Methyl-4-{[(3-methylphenyl)sulfonyl]methyl}-1,3-oxazol-2-yl)-*N*-(3-pyridinylmethyl)benzamide;

4-(4-{[(4-Methoxyphenyl)sulfonyl]methyl}-5-methyl-1,3-oxazol-2-yl)-*N*-(3-pyridinylmethyl)benzamide;

4-(5-Methyl-4-{[(3-methoxyphenyl)sulfonyl]methyl}-1,3-oxazol-2-yl)-*N*-(3-pyridinylmethyl)benzamide;

4-(4-{[(3,4-Dimethoxyphenyl)sulfonyl]methyl}-5-methyl-1,3-oxazol-2-yl)-*N*-(3-pyridinylmethyl)benzamide;

4-(5-Methyl-4-{[(2,4-dimethylphenyl)sulfonyl]methyl}-1,3-oxazol-2-yl)-*N*-(3-pyridinylmethyl)benzamide;

4-(4-{[(4-Fluorophenyl)sulfonyl]methyl}-5-methyl-1,3-oxazol-2-yl)-*N*-(3-pyridinylmethyl)benzamide;

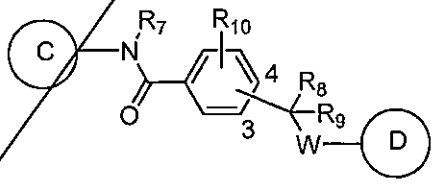
4-[5-Methyl-4-({[4-(4-methyl-1-piperazinyl)phenyl]sulfonyl}methyl)-1,3-oxazol-2-yl]-*N*-(3-pyridinylmethyl)benzamide;

4-[5-Methyl-4-({[4-(4-morpholinyl)phenyl]sulfonyl}methyl)-1,3-oxazol-2-yl]-*N*-(3-pyridinylmethyl)benzamide;

4-(4-{[(4-Methylphenyl)sulfonyl]methyl}-1,3-thiazol-2-yl)-*N*-(3-pyridinylmethyl)benzamide;

or a pharmaceutically acceptable salt thereof.

29. A compound of Formula **II**:

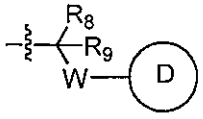


II

or a pharmaceutically acceptable salt, hydrate, solvate, prodrug, enantiomer, or stereoisomer thereof;

wherein:

C is a nitrogen-containing heteroaryl ring chosen from pyridinyl, pyrimidinyl, pyrazinyl, quinolinyl, pyrazolyl, imidazolyl, and thiazolyl, each of which is optionally substituted;



is attached to the phenyl ring at either the 3 or 4 position;

R_7, R_8, and R_9 are each independently chosen from hydrogen, optionally substituted alkyl, and optionally substituted alkenyl;

R_{10} is chosen from hydrogen, hydroxy, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkoxy, optionally substituted cycloalkyl, optionally substituted aryl, optionally substituted heterocycloalkyl, optionally substituted heteroaryl, halo, carboxy, nitro, sulfonyl, sulfinyl, and optionally substituted amino;

W is chosen from $-NRSO_2-$, $-SO_2NR-$, and $-NRCO-$, wherein each R is independently chosen from hydrogen, alkyl, alkenyl, alkynyl, cycloalkyl, aryl, heterocycloalkyl, and heteroaryl, each of which, except for hydrogen, is optionally substituted; and

D is heteroaryl.

30. The compound according to claim 29, wherein C is chosen from 2-thiazolyl, 3-pyrazolyl, 3-quinolinyl, 5-quinolinyl, 2-pyrazinyl, 2-pyrimidinyl, 2-pyridinyl, 3-pyridinyl, and 4-pyridinyl, each of which is optionally substituted.

31. The compound according to claim 30, wherein C is chosen from 2-pyridinyl, 3-pyridinyl, and 4-pyridinyl.

32. The compound according to claim 31, wherein C is 3-pyridinyl.

33. The compound according to claim 29, wherein W is $-NRSO_2-$.

34. The compound according to claim 33, wherein R is chosen from hydrogen and lower alkyl.

35. The compound according to claim 34, wherein R is hydrogen.

36. The compound according to claim 29, wherein D is selected from pyridyl, pyrazinyl, pyrimidinyl, pyrazolinyl, thiazolyl, imidazolinyl, isoxazolinyl, oxazolinyl, thiazolinyl, thiadiazolinyl, tetrazolyl, thienyl, benzothiophenyl, furanyl, benzofuranyl, benzoimidazolinyl, indolinyl, pyridizinyl, triazolyl, quinolinyl, and pyrazolyl..

37. The compound according to claim 36, wherein D is selected from pyridyl, thiazolyl, imidazolinyl, thienyl, furanyl, triazolyl, and pyrazolyl.

38. The compound according to claim 29, wherein the compound is selected from

N-(3-Pyridinyl)-4-{[(3-pyridylsulfonyl)amino]methyl}benzamide **II-1;**

4-({[(6-Chloro-3-pyridinyl)sulfonyl]amino}methyl)-*N*-(3-pyridinyl)benzamide **II-2**;

4-({[(6-Phenoxy-3-pyridinyl)sulfonyl]amino}methyl)-*N*-(3-pyridinyl)benzamide **II-3**;

N-(3-Pyridinyl)-4-{[(2-thienylsulfonyl)amino]methyl}benzamide **II-4**;

N-(3-Pyridinyl)-4-{[(3-thienylsulfonyl)amino]methyl}benzamide **II-5**;

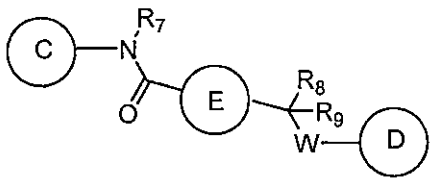
4-({[(1,2-Dimethyl-1*H*-imidazol-5-yl)sulfonyl]amino}methyl)-*N*-(3-pyridinyl)benzamide **II-6**;

N-(3-pyridinyl)-4-{[(4*H*-1,2,4-triazol-3-ylsulfonyl)amino]methyl}benzamide **II-7**; and

N-(3-Pyridinyl)-4-{[(2-furanylsulfonyl)amino]methyl}benzamide **II-8**.

or a pharmaceutically acceptable salt thereof.

39. A compound of Formula **III**:



III

or a pharmaceutically acceptable salt, hydrate, solvate, prodrug, enantiomer, or stereoisomer thereof;

wherein:

C is a nitrogen-containing heteroaryl ring chosen from pyridinyl, pyrimidinyl, pyrazinyl, quinolinyl, pyrazolyl, imidazolyl, and thiazolyl, each of which is optionally substituted;

R_7, R_8, and R_9 are each independently chosen from hydrogen, optionally substituted alkyl, and optionally substituted alkenyl;

W is chosen from $-N(R)SO_2R_X-$, $-SO_2N(R)R_X-$, and $-N(R)COR_X-$, wherein each R is independently chosen from hydrogen, alkyl, alkenyl, alkynyl, cycloalkyl, aryl, heterocycloalkyl, and heteroaryl, each of which, except for hydrogen, is optionally substituted; and R_X is an bivalent C_0-C_6alkylene, bivalent C_3-C_6cycloalkyl, or phenyl, each of which is optionally substituted;

E is selected from C_5-C_6cycloalkyl, C_5-C_6heterocycle, phenyl, wherein E is optionally substituted hydrogen, hydroxy, optionally substituted alkyl, optionally substituted alkenyl, optionally substituted alkoxy, optionally substituted cycloalkyl, optionally substituted aryl, optionally substituted heterocycloalkyl, optionally substituted heteroaryl, halo, carboxy, nitro, sulfonyl, sulfinyl, and optionally substituted amino; and

D is an optionally substituted heterocycle.

40. The compound according to claim 39, wherein C is chosen from 2-thiazolyl, 3-pyrazolyl, 3-quinolinyl, 5-quinolinyl, 2-pyrazinyl, 2-pyrimidinyl, 2-pyridinyl, 3-pyridinyl, and 4-pyridinyl, each of which is optionally substituted.

41. The compound according to claim 40, wherein C is chosen from 2-pyridinyl, 3-pyridinyl, and 4-pyridinyl.

42. The compound according to claim 41, wherein C is 3-pyridinyl.

43. The compound according to claim 39, wherein W is $-N(R)SO_2Rx-$.

44. The compound according to claim 43, wherein R is chosen from hydrogen and lower alkyl.

45. The compound according to claim 44, wherein R is hydrogen.

46. The compound according to claim 43, wherein Rx is is an optionally substituted bivalent C_0-C_6alkylene.

47. The compound according to claim 46, wherein Rx is C4 alkyl.

48. The compound according to claim 43, wherein Rx is a bivalent C_3-C_6cycloalkyl.

49. The compound according to claim 48, wherein Rx is C_6cycloalkyl.

50. The compound according to claim 43, wherein Rx is phenyl.

51. The compound according to claim 39, wherein D is C_5-C_6cycloalkyl.

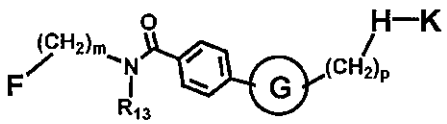
52. The compound according to claim 39, wherein D is phenyl.

53. The compound according to claim 39, wherein D is selected from the group consisting of 2-pyrrolinyl, 2,4-imidazolidinyl, 2,3-pyrazolidinyl, 2-piperidyl, 3-piperidyl, 4-piperdyl, and 2,5-piperzinyl, 2-morpholinyl and 3-morpholinyl.

54. The compound according to claim 53, wherein D is selected from the group consisting of 2,5-piperzinyl.

55. The compound according to claim 39, wherein the compound is 4-((4-(4-methylpiperazin-1-yl)cyclohexanesulfonamido)methyl)-N-(pyridin-3-yl)benzamide **III-1**.

56. A compound of **Formula IV** are provided:



Formula IV

or a pharmaceutically acceptable salt, hydrate, solvate, prodrug, enantiomer, or stereoisomer thereof;

wherein:

F is a heteroaryl selected from pyridine, pyrazine, pyridazine, pyrimidine, 1,2,4-triazine or 1,3,5-triazine, optionally substituted with halogen, hydroxyl group, -CF3 group, C1-C6 alkoxy group, C1-C6 straight chain alkyl, C3-C6 branched chain alkyl or C3-C6 cycloalkyl group, wherein the number of substituents does not exceed the number of available C-H bonds of the heteroaryl; with multiple substitutions, each substituent on the heteroaryl is chosen independent of the other substituents;

G is a 5 membered heteroaryl selected from thiophene, imidazole, pyrazole, thiazole, oxazole, isoxazole, isothiazole, triazole, oxadiazole, and thiadiazole;

m is an integer ranging from 0 to 3;

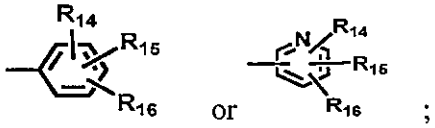
p is an integer ranging from 1 to 5;

H is –S(O)n–(CH2)q–, –O–(CH2)q–, or –C(O)–(CH2)q–;

n is an integer ranging from 0 to 2;

q is an integer ranging from 0 to 5;

K is selected from

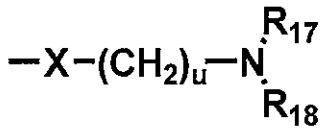


;

R13 is H, C1-C6 straight chain alkyl, C3-C6 branched chain alkyl or C3-C6 cycloalkyl;

R14, R15 and R16 are each independently H, C1-C6 straight chain alkyl, C3-C6 branched chain alkyl, C1-C6 hydroxyalkyl, C1-C6 alkoxy, alkoxyalkyl in which the alkoxy and alkyl portions each independently contain from 1 to 6 carbon atoms,

alkoxyalkoxy in which the alkoxy portions each independently contain from 1 to 6 carbon atoms, halogen, -OH, -NH2, -CF3, C1-C6 monoalkylamino, C1-C6 dialkylamino, optionally substituted nitrogen containing heterocycles selected from pyrrolidine, piperidine, piperazine, morpholine, thiomorpholine, azepane, 1,4-diazepane, 1,4-oxazepane and 1,4-thiazepane; or



wherein X can be a bond, O, S or NR19;

R17, R18 and R19 are each independently H, C1-C6 straight chain alkyl, C3-C6 branched chain alkyl, C1-C6 hydroxyalkyl, alkoxyalkyl in which the alkoxy and alkyl portions each independently contain from 1 to 6 carbon atoms, -CF3; or R17 and R18 can be taken together to form a 4 to 7 membered optionally substituted ring containing 0-4 heteroatoms selected from N, O or S;

r is an integer ranging from 0 to 3;

t is an integer ranging from 1 to 2; and

u is an integer ranging from 1 to 6.

57. The compound according to claim 56, wherein F is chosen from 2-thiazolyl, 3-pyrazolyl, 2-pyrazinyl, 2-pyrimidinyl, 2-pyridinyl, 3-pyridinyl, and 4-pyridinyl, each of which is optionally substituted.

58. The compound according to claim 57, wherein F is chosen from 2-pyridinyl, 3-pyridinyl, and 4-pyridinyl.

59. The compound according to claim 58, wherein F is 3-pyridinyl.

60. The compound of claim 56, wherein G is oxazole.

61. The compound according to claim 56, wherein H is $-SO_2-$.

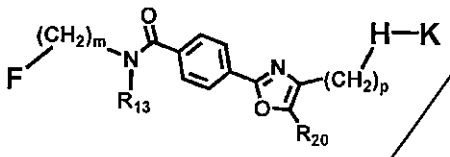
62. The compound according to claim 61, wherein R1 is chosen from hydrogen and lower alkyl.

63. The compound according to claim 62, wherein R1 is hydrogen.

64. The compound according to claim 56, wherein K is phenyl.

65. The compound according to claim 64, wherein K is pyridyl.

66. A compound of **Formula Va**:



Formula Va

or a pharmaceutically acceptable salt, hydrate, solvate, prodrug, enantiomer, or stereoisomer thereof;

wherein:

F is a heteroaryl selected from pyridine, pyrazine, pyridazine, pyrimidine, 1,2,4-triazine or 1,3,5-triazine, optionally substituted with halogen, hydroxyl group, -CF3 group, C1-C6 alkoxy group, C1-C6 straight chain alkyl, C3-C6 branched chain alkyl or C3-C6 cycloalkyl group, wherein the number of substituents does not exceed the number of available C-H bonds of the heteroaryl; with multiple substitutions, each substituent on the heteroaryl is chosen independent of the other substituents;

m is an integer ranging from 0 to 3;

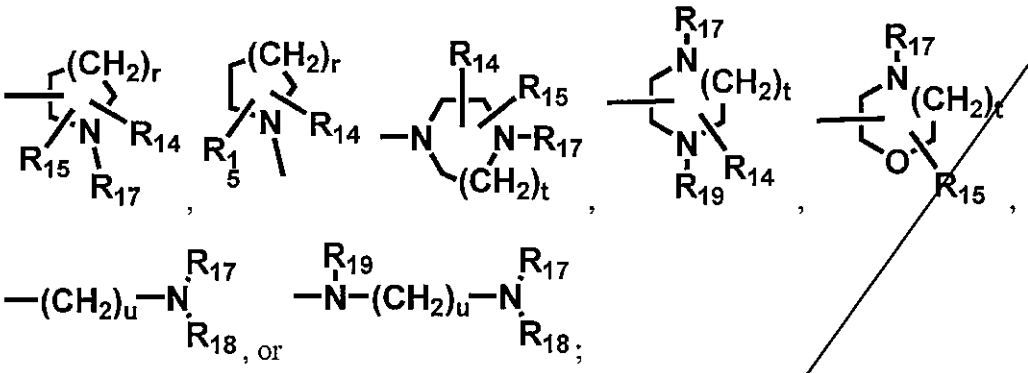
p is an integer ranging from 1 to 5;

H is selected from –S(O)n–(CH2)q–, –O–(CH2)q–, or –C(O)–(CH2)q–;

n is an integer ranging from 0 to 2;

q is an integer ranging from 0 to 5;

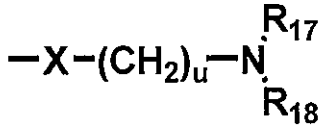
K is selected from C3-C7 cycloalkyl optionally substituted with two or more of R14, R15, and R16, C1-C6 straight or branched optionally substituted alkyl,



R13 is selected from H, C1-C6 straight chain alkyl, C3-C6 branched chain alkyl or C3-C6 cycloalkyl;

R20 is selected from H, -CF3, C1-C6 straight chain alkyl, C3-C6 branched chain alkyl or C3-C6 cycloalkyl;

R14, R15 and R16 can independently be H, C1-C6 straight chain alkyl, C3-C6 branched chain alkyl, C1-C6 hydroxyalkyl, C1-C6 alkoxy, alkoxyalkyl in which the alkoxy and alkyl portions each independently contain from 1 to 6 carbon atoms, alkoxyalkoxy in which the alkoxy portions each independently contain from 1 to 6 carbon atoms, halogen, -OH, -NH2, -CF3, C1-C6 monoalkylamino, C1-C6 dialkylamino, optionally substituted nitrogen containing heterocycles such as pyrrolidine, piperidine, piperazine, morpholine, thiomorpholine, azepane, 1,4-diazepane, 1,4-oxazepane and 1,4-thiazepane; or



wherein X can be a bond, O, S or NR19;

R17, R18 and R19 are independently selected from H, C1-C6 straight chain alkyl, C3-C6 branched chain alkyl, C3-C6 cycloalkyl, C1-C6 hydroxyalkyl, alkoxyalkyl in which the alkoxy and alkyl portions each independently contain from 1 to 6 carbon

atoms, -CF3, or –C(O)O-, or R17 and R18 can be taken together to form a 4 to 7 membered optionally substituted monocycloalkyl ring or 8-14 bicycloalkyl ring, each optionally containing between 1-3 heteroatoms selected from N, O or S, or ;

r is an integer ranging from 0 to 3;

t is an integer ranging from 1 to 2; and

u is an integer ranging from 1 to 6.

67. The compound according to claim 66, wherein F is chosen from 2-thiazolyl, 3-pyrazolyl, 2-pyrazinyl, 2-pyrimidinyl, 2-pyridinyl, 3-pyridinyl, and 4-pyridinyl, each of which is optionally substituted.

68. The compound according to claim 67, wherein F is chosen from 2-pyridinyl, 3-pyridinyl, and 4-pyridinyl.

69. The compound according to claim 68, wherein F is 3-pyridinyl.

70. The compound of claim 66, wherein G is oxazole.

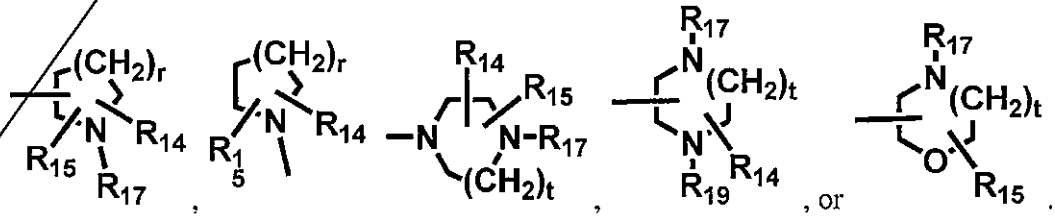
71. The compound according to claim 66, wherein H is - SO_2-.

72. The compound according to claim 66, wherein R1 is chosen from hydrogen and lower alkyl.

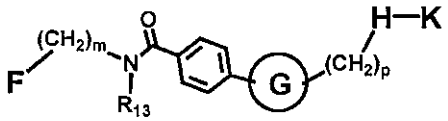
73. The compound according to claim 72, wherein R1 is hydrogen.

74. The compound according to claim 66, wherein K is C3-C7 cycloalkyl optionally substituted with two or more of R14, R15, and R16.

75. The compound according to claim 66, wherein K is



76. A compound of **Formula VI**:

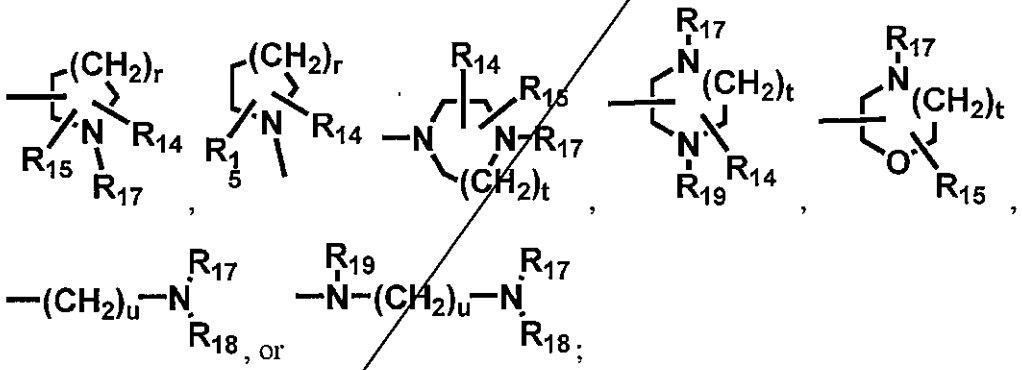


Formula VI

or a pharmaceutically acceptable salt, hydrate, solvate, prodrug, enantiomer, or stereoisomer thereof;

wherein:

F is selected from the group consisting of C3-C7 cycloalkyl optionally substituted with two or more of R14, R15, and R16, or C1-C6 straight or branched optionally substituted alkyl,



G is a 5 membered heteroaryl selected from thiophene, imidazole, pyrazole, thiazole, oxazole, isoxazole, isothiazole, triazole, oxadiazole, and thiadiazole;

m is an integer ranging from 0 to 3;

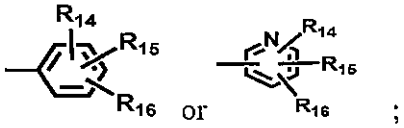
p is an integer ranging from 1 to 5;

H is –S(O)n–(CH2)q–, –O–(CH2)q–, or –C(O)–(CH2)q–;

n is an integer ranging from 0 to 2;

q is an integer ranging from 0 to 5;

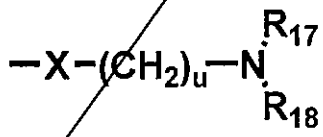
K is selected from



;

R13 is H, C1-C6 straight chain alkyl, C3-C6 branched chain alkyl or C3-C6 cycloalkyl;

R14, R15 and R16 can independently be H, C1-C6 straight chain alkyl, C3-C6 branched chain alkyl, C1-C6 hydroxyalkyl, C1-C6 alkoxy, alkoxyalkyl in which the alkoxy and alkyl portions each independently contain from 1 to 6 carbon atoms, alkoxyalkoxy in which the alkoxy portions each independently contain from 1 to 6 carbon atoms, halogen, -OH, -NH2, -CF3, C1-C6 monoalkylamino, C1-C6 dialkylamino, optionally substituted nitrogen containing heterocycles such as pyrrolidine, piperidine, piperazine, morpholine, thiomorpholine, azepane, 1,4-diazepane, 1,4-oxazepane and 1,4-thiazepane; or



wherein X can be a bond, O, S or NR19;

R17, R18 and R19 are each independently be H, C1-C6 straight chain alkyl, C3-C6 branched chain alkyl, C1-C6 hydroxyalkyl, alkoxyalkyl in which the alkoxy and alkyl portions each independently contain from 1 to 6 carbon atoms, -CF3; or R17 and R18 can be taken together to form a 4 to 7 membered optionally substituted ring that can contain additional heteroatoms such as N, O or S;

r is an integer ranging from 0 to 3;

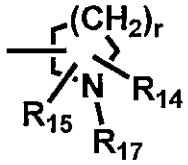
t is an integer ranging from 1 to 2; and

u is an integer ranging from 1 to 6.

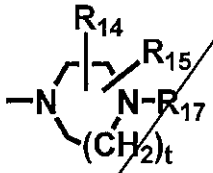
77. The compound of claim 76, wherein F is C3-C7 cycloalkyl optionally substituted with two or more of R14, R15, and R16.

78. The compound of claim 76, wherein F is C1-C6 straight or branched optionally substituted alkyl.

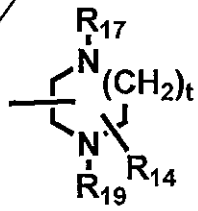
79. The compound of claim 76, wherein F is



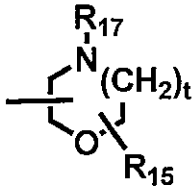
80. The compound of claim 76, wherein F is



81. The compound of claim 76, wherein F is



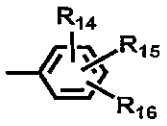
82. The compound of claim 76, wherein F is



83. The compound of claim 76 wherein G is oxazole.

84. The compound of claim 76, wherein H is $-S(O)_2$.

85. The compound of claim 76, wherein K is



86. A pharmaceutical composition comprising a compound of Formula I, II, III, IV, V, or VI.

87. A method for treating a disease mediated by HIF-1α and/or HIF-2α, the method comprising administering to a subject a compound of Formula I, II, III, IV, V, or VI.

88. The method of claim 87, wherein said disease is cancer or Von Hippel Lindau syndrome.

89. A method of targeting cells which express HIF-1α and/or HIF-2α the method comprising administering to a subject a compound of Formula I, II, III, IV, V, or VI.

90. A method for treating a disease mediated by defective pVHL protein, the method comprising administering to a subject a compound of Formula I, II, III, IV, V, or VI.

91. A method for treating a disease mediated by defective pVHL protein, the method comprising administering to a subject a compound of Formula I, II, III, IV, V, or VI, wherein said compound or pharmaceutically acceptable salt is specifically cytotoxic to cells that have elevated HIF levels due to their increased rate and dependence on glucose uptake and glycolysis.

92. The method of claim 91, wherein the at least one compound, or a pharmaceutically acceptable salt thereof, selectively disrupts glucose uptake and utilization in the subject.

93. The method of claim 91 or 92, wherein the at least one compound, or a pharmaceutically acceptable salt thereof, inhibits HIF-mediated induction of *PDK1*.

94. A method of targeting cells which have defective pVHL protein, the method comprising administering to a subject a compound of Formula I, II, III, IV, V, or VI.

95. The method of claim 94, wherein the at least one compound, or a pharmaceutically acceptable salt thereof, selectively disrupts glucose uptake and utilization in the cells.

96. The method of claim 94 or 95, wherein the at least one compound, or a pharmaceutically acceptable salt thereof, inhibits HIF-mediated induction of *PDK1*.

97. A method for selectively killing cells which have defective pVHL protein, the method comprising administering to a subject a compound of Formula I, II, III, IV, V, or VI, wherein said at least one compound, or a pharmaceutically acceptable salt thereof, is capable of targeting cells having defective pVHL protein and killing said selected cells.

98. The method of claim 97, wherein the at least one compound, or a pharmaceutically acceptable salt thereof, selectively disrupts glucose uptake and utilization in the cells.

99. The method of claim 97, wherein the at least one compound, or a pharmaceutically acceptable salt thereof, inhibits HIF-mediated induction of *PDK1*.

100. A method for treating a disease mediated by HIF-1α and/or HIF-2α, the method comprising administering to a subject a compound of Formula I, II, III, IV, V, or VI, wherein said at least one compound, or a pharmaceutically acceptable salt thereof is specifically cytotoxic to cells that have elevated HIF levels due to their increased rate and dependence on glucose uptake and glycolysis.

101. The method of claim 100, wherein the at least one compound, or a pharmaceutically acceptable salt thereof, selectively disrupts glucose uptake and utilization in the subject.

102. The method of claim 100, wherein the at least one compound, or a pharmaceutically acceptable salt thereof, inhibits HIF-mediated induction of *PDK1*.

103. A method for treating a disease mediated by cells comprising genetic or epigenetic alterations that make them highly dependent on aerobic glycolysis for energy production, the method comprising administering to a subject a compound of Formula I, II, III, IV, V, or VI, wherein said at least one compound, or a pharmaceutically acceptable salt thereof,

is specifically cytotoxic to cells comprising genetic or epigenetic alterations that make them highly dependent on aerobic glycolysis for energy production.

104. A method for selectively killing cells comprising genetic or epigenetic alterations that make them highly dependent on aerobic glycolysis for energy production, the method comprising administering to a subject a compound of Formula I, II, III, IV, V, or VI, wherein said at least one compound, or a pharmaceutically acceptable salt thereof, is specifically cytotoxic to cells comprising genetic or epigenetic alterations that make them highly dependent on aerobic glycolysis for energy production.

105. The method of claim 104, wherein the at least one compound, or a pharmaceutically acceptable salt thereof, selectively disrupts glucose uptake and utilization in cells comprising genetic or epigenetic alterations that make them highly dependent on aerobic glycolysis for energy production.

106. A method for treating a disease mediated by GLUT1, the method comprising administering to a subject a compound of Formula I, II, III, IV, V, or VI.

107. The method of claim 106, wherein the at least one compound, or a pharmaceutically acceptable salt thereof, selectively disrupts glucose uptake and utilization in the subject.

108. The method of claim 106, wherein the at least one compound, or a pharmaceutically acceptable salt thereof, inhibits glucose transport by GLUT1.

109. A method of treating diseases mediated by HIF-1α and/or HIF-2α, comprising administering to a patient in need thereof, a compound of Formula I, II, III, IV, V, or VI or a pharmaceutically acceptable salt, hydrate, solvate, prodrug, enantiomer or stereoisomer thereof.

110. A method of treating a disease mediated by cells comprising genetic or epigenetic alterations that make them highly dependant on aerobic glycolysis for energy production, comprising administering to a subject in need thereof, at least one compound of Formula I, II, III, IV, V, or VI, or a pharmaceutically acceptable salt, hydrate, solvate, prodrug, enantiomer or stereoisomer thereof.

111. A method of identifying a compound as a candidate cancer therapy, comprising expositing a first population of cells that have elevated expression of GLUT1 but not GLUT2 to a test compound and assaying cytotoxicity of the test compound, exposing a second population of cells that have elevated expression of GLUT2 but not GLUT1 to the test compound and assaying cytotoxicity of the test compound, as a candidate cancer therapy if the test compound induces significantly higher cytotoxicity in the first population of cells than in the second population of cells.

WHAT IS CLAIMED IS:

1. A compound selected from the group consisting of

4-(5-methyl-4-((piperazin-1-ylsulfonyl)methyl)oxazol-2-yl)-N-(pyridin-3-ylmethyl)benzamide,

4-(5-methyl-4-((4-methylpiperazin-1-ylsulfonyl)methyl)oxazol-2-yl)-N-(pyridin-3-ylmethyl)benzamide,

4-(4-((4-isobutylpiperazin-1-ylsulfonyl)methyl)-5-methyloxazol-2-yl)-N-(pyridin-3-ylmethyl)benzamide,

4-(4-((4-tert-butylpiperazin-1-ylsulfonyl)methyl)-5-methyloxazol-2-yl)-N-(pyridin-3-ylmethyl)benzamide;

4-(4-((4-cyclopropylpiperazin-1-ylsulfonyl)methyl)-5-methyloxazol-2-yl)-N-(pyridin-3-ylmethyl)benzamide,

4-(5-methyl-4-((4-(2,2,2-trifluoroethyl)piperazin-1-ylsulfonyl)methyl)oxazol-2-yl)-N-(pyridin-3-ylmethyl)benzamide;

4-(5-methyl-4-(morpholinosulfonylmethyl)oxazol-2-yl)-N-(pyridin-3-ylmethyl)benzamide,

4-(4-((4-isopropylpiperazin-1-ylsulfonyl)methyl)-5-methyloxazol-2-yl)-N-(pyridin-3-ylmethyl)benzamide,

4-(5-methyl-4-(((4-neopentylpiperazin-1-yl)sulfonyl)methyl)oxazol-2-yl)-*N*-(pyridin-3-ylmethyl)benzamide,

4-(4-(((4-ethylpiperazin-1-yl)sulfonyl)methyl)-5-methyloxazol-2-yl)-*N*-(pyridin-3-ylmethyl)benzamide,

4-(4-(((4-cyclobutylpiperazin-1-yl)sulfonyl)methyl)-5-methyloxazol-2-yl)-*N*-(pyridin-3-ylmethyl)benzamide,

4-(5-methyl-4-((thiomorpholinosulfonyl)methyl)oxazol-2-yl)-*N*-(pyridin-3-ylmethyl)benzamide,

or a pharmaceutically acceptable salt thereof.

2. The compound of claim 1 wherein the compound is

4-(5-methyl-4-((piperazin-1-ylsulfonyl)methyl)oxazol-2-yl)-N-(pyridin-3-ylmethyl)benzamide.

3. The compound of claim 1 wherein the compound is

4-(5-methyl-4-((4-methylpiperazin-1-ylsulfonyl)methyl)oxazol-2-yl)-N-(pyridin-3-ylmethyl)benzamide.

4. The compound of claim 1 wherein the compound is

4-(4-((4-isobutylpiperazin-1-ylsulfonyl)methyl)-5-methyloxazol-2-yl)-N-(pyridin-3-ylmethyl)benzamide.

5. The compound of claim 1 wherein the compound is

4-(5-methyl-4-(morpholinosulfonylmethyl)oxazol-2-yl)-N-(pyridin-3-ylmethyl)benzamide.

6. A pharmaceutical composition comprising a compound of any one of claims 1-5 and a pharmaceutically acceptable carrier.

7. Use of a compound of any one of claims 1-5 in the manufacture of a medicament for treating a disease.

8. The use of claim 7, where in the disease is mediated by HIF-1α and/or HIF-2α.

9. The use of claim 8, wherein the disease mediated by HIF-1α and/or HIF-2α is selected from the group consisting of cancer and Von Hippel Lindau syndrome.

10. The use of claim 9, wherein the disease mediated by HIF-1α and/or HIF-2α is Von Hippel Lindau syndrome.

11. The use of claim 9, wherein the disease mediated by HIF-1α and/or HIF-2α is cancer.

12. A compound or composition according to one of claims 1-6 for use in a medicament for treating a disease mediated by HIF-1α and/or HIF-2α.

13. The compound or composition of claim 12 wherein the disease mediated by HIF-1α and/or HIF-2α is selected from cancer and Von Hippel Lindau syndrome.

14. The compound or composition of claim 13, wherein the disease mediated by HIF-1α and/or HIF-2α is cancer.

15. The compound or composition of claim 13 wherein the disease mediated by HIF-1α and/or HIF-2α is Von Hippel Lindau syndrome.