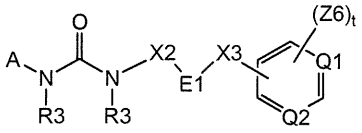
Claims

1. The use of a compound of formula Ia:



Ia

wherein Q1 and Q2 are each individually and independently selected from the group consisting of N and C-Z6, provided that both Q1 and Q2 are not simultaneously C-Z6;

wherein E1 is selected from the group consisting of cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, pyrrolidinyl piperidinyl, phenyl, thienyl, oxazolyl, thiazolyl, isoxazolyl, isothiazolyl, pyrrolyl, pyrazolyl, oxadiazolyl, thiadiazolyl, furyl, imidazolyl, pyridyl, pyrimidinyl and naphthyl, and wherein the E1 ring is substituted with one or more R16 moieties and wherein the E1 ring is substituted with one or more R18 moieties;

wherein A is selected from the group consisting of phenyl, C3-C8carbocyclyl, pyrrolyl, furyl, thienyl, oxazolyl, thiazolyl, isoxazolyl, isothiazolyl, imidazolyl, pyrazolyl, oxadiazolyl, thiadiazolyl, triazolyl, tetrazolyl, pyrazinyl, pyridazinyl, triazinyl, pyridinyl, pyrimidinyl, and G4;

G1 is a heteroaryl taken from the group consisting of pyrrolyl, furyl, thienyl, oxazolyl, thiazolyl, isoxazolyl, isothiazolyl, imidazolyl, pyrazolyl, oxadiazolyl, thiadiazolyl, triazolyl, tetrazolyl, pyrazinyl, pyridazinyl, triazinyl, pyridinyl, and pyrimidinyl;

G2 is a fused bicyclic heteroaryl taken from the group consisting of indolyl, indolinyl, isoindolyl, isoindolinyl, indazolyl, benzofuranyl, benzothienyl, benzothiazolyl, benzothiazolonyl, benzoxazolyl, benzoxazolonyl, benzisoxazolyl, benzisothiazolyl, benzimidazolyl, benzimidazolonyl, benztriazolyl, imidazopyridinyl, pyrazolopyridinyl, imidazolonopyridinyl, thiazolopyridinyl, thiazolonopyridinyl, oxazolopyridinyl, oxazolonopyridinyl, isoxazolopyridinyl, isothiazolopyridinyl, triazolopyridinyl, imidazopyrimidinyl, pyrazolopyrimidinyl, imidazolonopyrimidinyl, thiazolopyridiminyl, thiazolonopyrimidinyl, oxazolopyridiminyl, oxazolonopyrimidinyl, isoxazolopyrimidinyl, isothiazolopyrimidinyl,

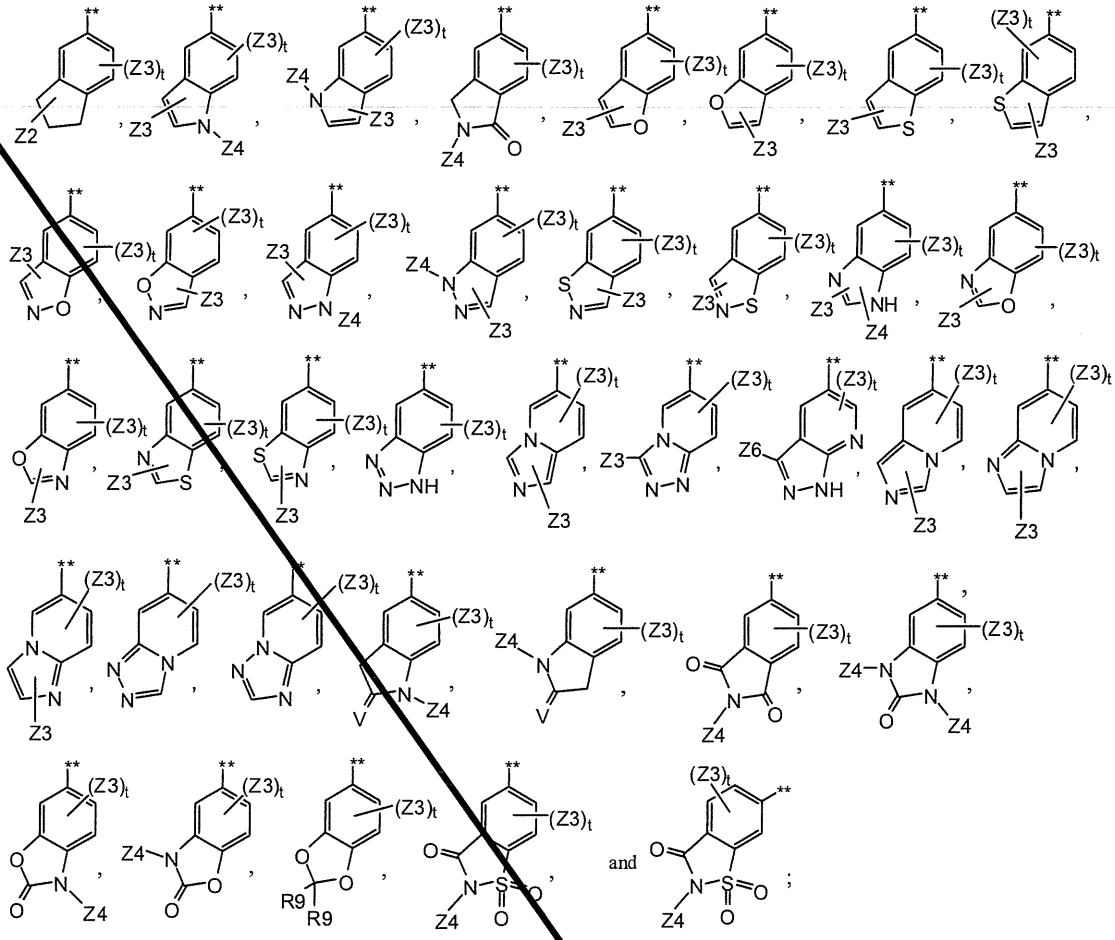
triazolopyrimidinyl, dihydropurinonyl, pyrrolopyrimidinyl, purinyl, pyrazolopyrimidinyl, phthalimidyl, phthalimidinyl, pyrazinylpyridinyl, pyridinopyrimidinyl, pyrimidinopyrimidinyl, cinnolinyl, quinoxalinyl, quinazolinyl, quinolinyl, isoquinolinyl, phthalazinyl, benzodioxyl, benzisothiazoline-1,1,3-trionyl, dihydroquinolinyl, tetrahydroquinolinyl, dihydroisoquinolyl, tetrahydroisoquinolinyl, benzoazepinyl, benzodiazepinyl, benzoxapinyl, and benzoxazepinyl;

G3 is a non-fused bicyclic heteroaryl taken from the group consisting of pyridylpyridiminyl pyrimidinylpyrimidinyl, oxazolylpyrimidinyl, thiazolylpyrimidinyl, imidazolylpyrimidinyl, isoxazolylpyrimidinyl, isothiazolylpyrimidinyl, pyrazolylpyrimidinyl, triazolylpyrimidinyl, oxadiazoylpyrimidinyl, thiadiazoylpyrimidinyl, morpholinylpyrimidinyl, dioxothiomorpholinylpyrimidinyl, and thiomorpholinylpyrimidinyl;

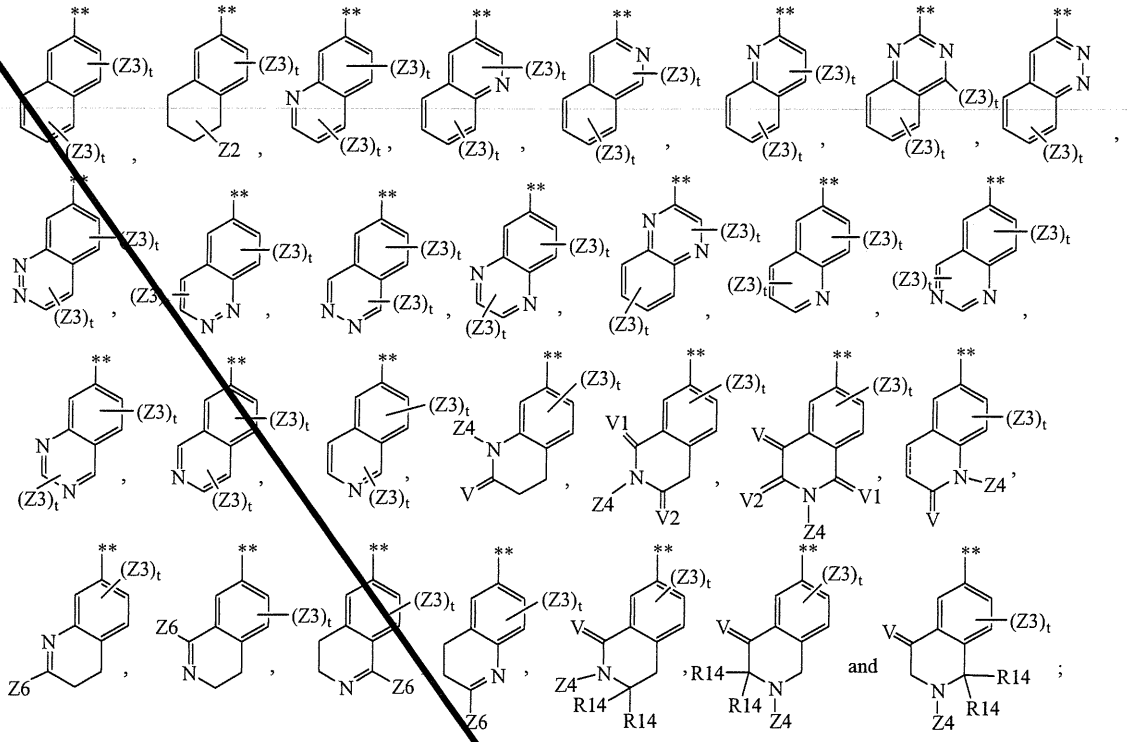
G4 is a heterocyclyl taken from the group consisting of oxetanyl, azetadinyl, tetrahydrofuranyl, pyrrolidinyl, oxazolinyl, oxazolidinyl, imidazolonyl, pyranyl, thiopyranyl, tetrahydropyranyl, dioxalinyl, piperidinyl, morpholinyl, thiomorpholinyl, thiomorpholinyl S-oxide, thiomorpholinyl S-dioxide, piperazinyl, azepinyl, oxepinyl, diazepinyl, tropanyl, and homotropanyl;

The A ring is substituted at any substitutable position with one A1 moiety, wherein A1 is selected from the group consisting of A2, A3 and A4;

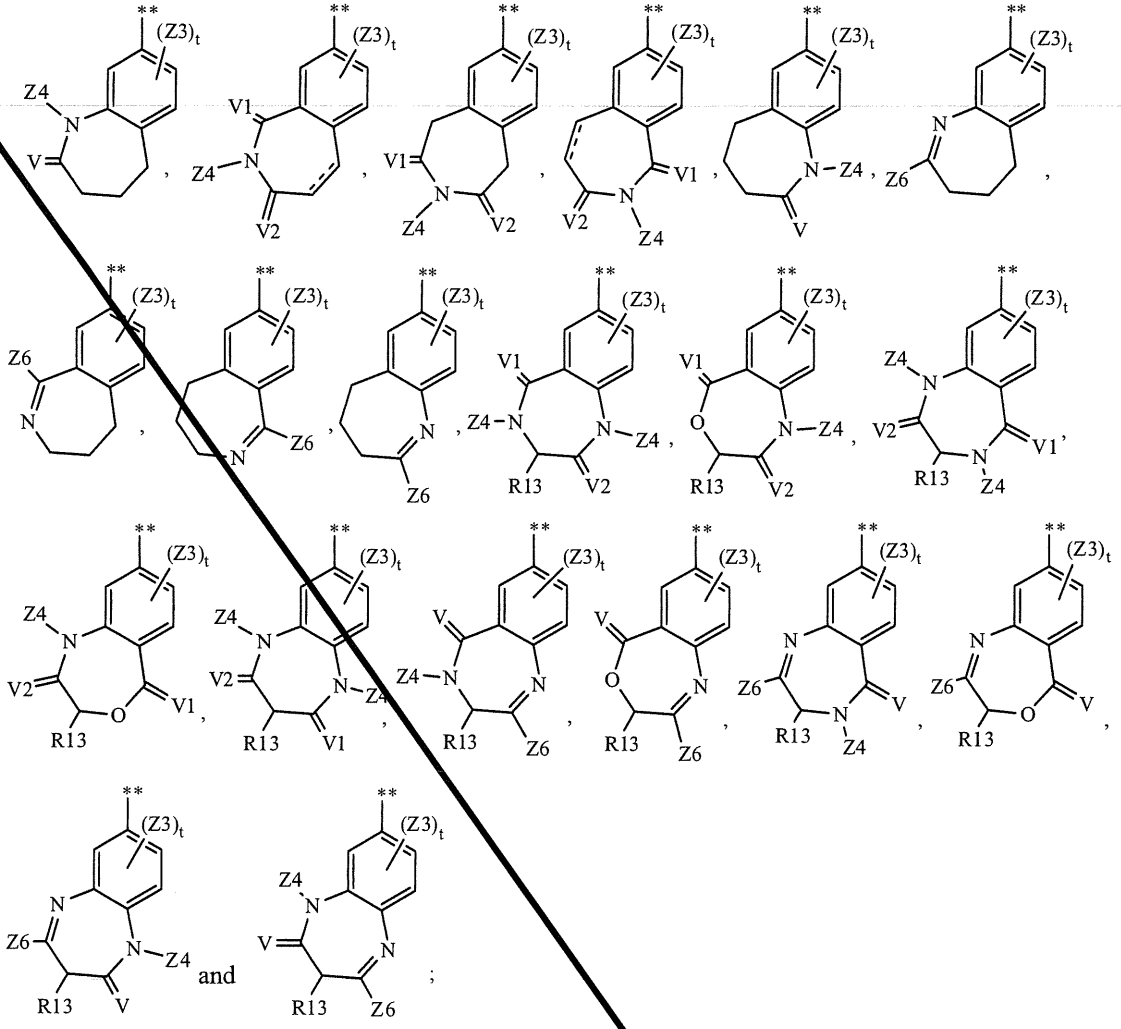
A2 is selected from the group consisting of:



A3 is selected from the group consisting of:



A4 is selected from the group consisting of:



and wherein the symbol (**) is the point of attachment to the A ring of formula Ia;

and wherein ---- indicates either a saturated or unsaturated bond;

the A ring is optionally substituted with one or more R2 moieties;

X2 is selected from the group consisting of C1-C6 alkyl, C2-C6 branched alkyl, and a direct bond wherein E1 is directly linked to the NR3 group of formula Ia;

X3 is selected from the group consisting of -C(O)-, -O-, -O-$(CH_2)_n$-, -S-$(CH_2)_n$-, -NR3-$(CH_2)_n$-, -O$(CH_2)_q$O-, -O$(CH_2)_q$N(R3)-, -N(R3)$(CH_2)_q$N(R3)-, -$(CH_2)_n$N(R4)C(O)-, -$(CH_2)_n$N(R4)C(O)$(CH_2)_n$-, -$(CH_2)_n$C(O)N(R4)-, -$(CH_2)_p$-, -C2-C5alkenyl, -C2-C5alkynyl, and -

C3-C6cycloalkyl and wherein the carbon atoms of $-(CH_2)_n-$, $-(CH_2)_q-$, $-(CH_2)_p-$, C2-C5alkenyl, and C2-C5alkynyl moieties of X3 may be further substituted by one or more C1-C6alkyl;

V, V1 and V2 are each independently and respectively selected from the group consisting of O and H_2;

each Z2 is independently and individually selected from the group consisting of hydrogen, aryl, C1-C6alkyl, C3-C8carbocyclyl, hydroxyl, hydroxyC1-C6alkyl-, cyano, $(R3)_2N-$, $(R4)_2N-$, $(R4)_2NC1$-C6alkyl-, $(R4)_2NC2$-C6alkylN(R4)$(CH_2)_n-$, $(R4)_2NC2$-C6alkylO$(CH_2)_n-$, $(R3)_2NC(O)-$, $(R4)_2NC(O)-$, $(R4)_2NC(O)C1$-C6alkyl-, carboxyl, carboxyC1-C6alkyl, C1-C6alkoxycarbonyl-, C1-C6alkoxycarbonylC1-C6alkyl-, $(R3)_2NSO_2-$, $(R4)_2NSO_2-$, $-SO_2R5$, $-SO_2R8$, $-(CH_2)_nN(R4)C(O)R8$, -C(O)R8, =O, =NOH, =N(OR6), $-(CH_2)_nG1$, $-(CH_2)_nG4$, $-(CH_2)_nO(CH_2)_nG1$, $-(CH_2)_nO(CH_2)_nG4$, $-(CH_2)_nN(R3)(CH_2)_n$-aryl, $-(CH_2)_nN(R3)(CH_2)_nG1$, $-(CH_2)_nN(R3)(CH_2)_nG4$, $-(CH_2)_nNHC(O)NHS(O)_2R8$, $-(CH_2)_nNHS(O)_2NHC(O)R8$, $-C(O)NHS(O)_2R8$, $-(CH_2)NHC(O)(CH_2)_nR5$, $-(CH_2)_nNHS(O)_2R5$, $-(CH_2)_nC(O)NH(CH_2)_qR5$, $-(CH_2)_nC(O)R5$, $-(CH_2)_nOC(O)R5$, and $-(CH_2)_nR5$;

in the event that Z2 contains an alkyl or alkylene moiety, such moieties may be further substituted with one or more C1-C6alkyls;

each Z3 is independently and individually selected from the group consisting of H, C1-C6alkyl, branched C3-C7alkyl, C3-C8carbocyclyl, halogen, fluoroC1-C6alkyl wherein the alkyl moiety can be partially or fully fluorinated, cyano, hydroxyl, methoxy, oxo, $(R3)_2NC(O)-$, $(R4)_2NC(O)-$, $-N(R4)C(O)R8$, $(R3)_2NSO_2-$, $(R4)_2NSO_2-$, $-N(R4)SO_2R5$, $-N(R4)SO_2R8$, $-(CH_2)N(R3)_2$, $-(CH_2)_nN(R4)_2$, $-O(CH_2)_qN(R4)_2$, $-O(CH_2)_qO$-C1-C6alkyl, $-N(R3)(CH_2)_qO$-C1-C6alkyl, $-N(R3)(CH_2)_qN(R4)_2$, $-O(CH_2)_qR5$, $-N(R3)(CH_2)_qR5$, -C(O)R5, -C(O)R8, -R5, and nitro;

in the event that Z3 contains an alkyl or alkylene moiety, such moieties may be further substituted with one or more C1-C6alkyls;

each Z4 is independently and individually selected from the group consisting of H, C1-C6alkyl, hydroxyC2-C6alkyl, C1-C6alkoxyC2-C6alkyl, $(R4)_2N$-C2-C6alkyl, $(R4)_2N$-C2-C6alkylN(R4)-C2-C6alkyl, $(R4)_2N$-C2-C6alkyl-O-C2-C6alkyl, $(R4)_2NC(O)$-C1-C6alkyl, carboxyC1-C6alkyl-, C1-C6alkoxycarbonylC1-C6alkyl-, -C2-C6alkylN(R4)C(O)R8, R8-C(=NR3)-, $-SO_2R8$, -C(O)R8, $-(CH_2)_nG1$, $-(CH_2)_nG4$, $-(CH_2)_qO(CH_2)_nG1$, $-(CH_2)_qO(CH_2)_nG4$, $-(CH_2)_qN(R3)(CH_2)_nG1$, $-(CH_2)_qN(R3)(CH_2)_nG4$, $-(CH_2)_qNHC(O)(CH_2)_nR5$, $-(CH_2)_qC(O)NH(CH_2)_qR5$, $-(CH_2)_qC(O)R5$, $-(CH_2)_qOC(O)R5$, $-(CH_2)_qR5$, $-(CH_2)_qNR4(CH_2)_qR5$, and $-(CH_2)_qO(CH_2)_qR5$;

in the event that Z4 contains an alkyl or alkylene moiety, such moieties may be further substituted with one or more C1-C6alkyls;

each Z6 is independently and individually selected from the group consisting of H, C1-C6alkyl, branched C3-C7alkyl, hydroxyl, hydroxyC1-C6alkyl, hydroxyC2-C6 branched alkyl, C1-C6alkoxy, C1-C6alkoxyC1-C6alkyl-, C1-C6alkoxyC2-C6 branched alkyl-, C2-C6 branched alkoxy-, C1-C6alkylthio-, $(R3)_2N$-, -N(R3)C(O)R8, $(R4)_2N$-, -R5, -N(R4)C(O)R8, $-N(R3)SO_2R6$, $-C(O)N(R3)_2$, $-C(O)N(R4)_2$, -C(O)R5, $-SO_2N(R4)_2$, $-SO_2N(R5)_2$, halogen, fluoroC1-C6alkyl wherein the alkyl is fully or partially fluorinated, cyano, fluoroC1-C6alkoxy wherein the alkyl is fully or partially fluorinated, $-O(CH_2)_qN(R4)_2$, $-N(R3)(CH_2)_qN(R4)_2$, $-O(CH_2)_qO$-C1-C6Alkyl, $-O(CH_2)_qN(R4)_2$, $-N(R3)(CH_2)_qO$-C1-C6Alkyl, $-N(R3)(CH_2)_qN(R4)_2$, $-O(CH_2)_qR5$, and $-N(R3)(CH_2)_qR5$, $-(NR3)_rR17$, $-(O)_rR17$, $-(S)_rR17$, $-(CH_2)_nR17$, -R17, $-(CH_2)_nG1$, $-(CH_2)_nG4$, $-(CH_2)_nO(CH_2)_nG1$, $-(CH_2)_nO(CH_2)_nG4$, $-(CH_2)_nN(R3)(CH_2)_nG1$, and $-(CH_2)_nN(R3)(CH_2)_nG4$;

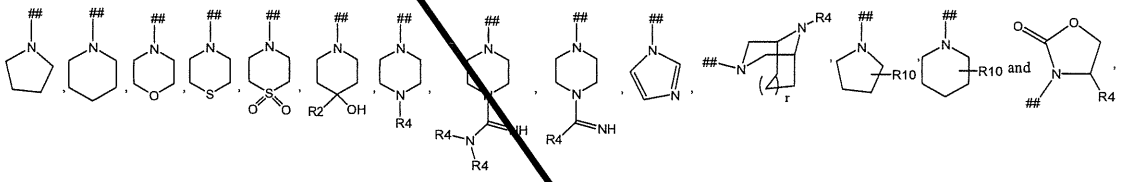
each R2 is selected from the group consisting of Z3-substituted aryl, Z3-substituted G1-, Z3-substituted G4-, C1-C6 alkyl, branched C3-C8alkyl, R19 substituted C3-C8carbocyclyl, hydroxylC1-C6alkyl-, hydroxyl branched C3-C6alkyl-, hydroxyl substituted C3-C8carbocyclyl-, cyanoC1-C6alkyl-, cyano substituted branched C3-C6alkyl, cyano substituted C3-C8carbocyclyl, $(R4)_2NC(O)$C1-C6alkyl-, $(R4)_2NC(O)$ substituted branched C3-C6alkyl-, $(R4)_2NC(O)$ substituted C3-C8carbocyclyl-, fluoroC1-C6alkyl wherein the alkyl is fully or partially

fluorinated, halogen, cyano, C1-C6alkoxy, and fluoroC1-C6alkoxy wherein the alkyl group is fully or partially fluorinated;

wherein each R3 is independently and individually selected from the group consisting of H, C1-C6alkyl, branched C3-C7alkyl, C3-C8carbocyclyl, and Z3-substituted phenyl;

each R4 is independently and individually selected from the group consisting of H, C1-C6alkyl, hydroxyC1-C6alkyl-, dihydroxyC1-C6alkyl-, C1-C6alkoxyC1-C6alkyl-, branched C3-C7alkyl-, branched hydroxyC1-C6alkyl-, branched C1-C6alkoxyC1-C6alkyl-, branched dihydroxyC2-C6alkyl-, $-(CH_2)_pN(R7)_2$, $-(CH_2)_pR5$, $-(CH_2)_pC(O)N(R7)_2$, $-(CH_2)_nC(O)R5$, $-(CH_2)_nC(O)OR3$, C3-C8carbocyclyl, hydroxyl substituted C3-C8carbocyclyl-, alkoxy substituted C3-C8carbocyclyl-, dihydroxyl substituted C3-C8carbocyclyl-, and $-(CH_2)_nR17$;

each R5 is independently and individually selected from the group consisting of



and wherein the symbol (##) is the point of attachment of the R5 moiety;

each R6 is independently and individually selected from the group consisting of C1-C6alkyl, branched C3-C7alkyl, C3-C8carbocyclyl, phenyl, G1, and G4;

each R7 is independently and individually selected from the group consisting of H, C1-C6alkyl, hydroxyC2-C6alkyl-, dihydroxyC2-C6alkyl-, C2-C6alkoxyC2-C6alkyl-, branched C3-C7alkyl-, branched hydroxyC2-C6 alkyl-, branched C2-C6alkoxyC2-C6alkyl-, branched dihydroxyC2-C6alkyl-, $-(CH_2)_qR5$, $-(CH_2)_nC(O)R5$, $-(CH_2)_nC(O)OR3$, C3-C8carbocyclyl, hydroxyl substituted C3-C8carbocyclyl-, alkoxy substituted C3-C8carbocyclyl-, dihydroxy substituted C3-C8carbocyclyl, and $-(CH_2)_nR17$;

each R8 is independently and individually selected from the group consisting of C1-C6alkyl, branched C3-C7alkyl, fluoroC1-C6alkyl wherein the alkyl moiety is partially or fully

fluorinated, C3-C8carbocyclyl, Z3-substituted phenyl-, Z3-substituted phenylC1-C6alkyl-, Z3-substituted G1, Z3-substituted G1-C1-C6alkyl-, Z2-substituted G4, Z2-substituted G4-C1-C6alkyl-, OH, C1-C6alkoxy, $N(R3)_2$, $N(R4)_2$, and R5;

each R9 is independently and individually selected from the group consisting of H, F, C1-C6alkyl, branched C3-C7alkyl, C3-C7carbocyclyl, phenyl, phenyl-C1-C6alkyl-, $-(CH_2)_nG1$, and $-(CH_2)_nG4$;

each R10 is independently and individually selected from the group consisting of CO_2H, CO_2C1-C6alkyl, $-C(O)N(R4)_2$, OH, C1-C6alkoxy, and $-N(R4)_2$;

each R13 is independently and individually selected from the group consisting of H, C1-C6alkyl, branched C3-C7alkyl, C3-C8carbocyclyl, hydroxyC2-C7alkyl, C1-C6alkoxyC2-C7alkyl, $(R4)_2NC(O)$-, $(R4)_2NC(O)$-C1-C6alkyl, carboxyC1-C6alkyl, C1-C6alkoxycarbonyl-, C1-C6alkoxycarbonylC1-C6alkyl-, $(R4)_2N$-C2-C6alkyl-, $(R4)_2N$-C2-C6alkylN(R4)$(CH_2)_q$-, R5-C2-C6alkylN(R4)$(CH_2)_q$-, $(R4)_2N$-C2-C6alkylO$(CH_2)_q$-, R5-C2-C6alkyl-O$(CH_2)_q$, $-(CH_2)_qN(R4)C(O)R8$, aryl, arylC1-C6alkyl-, aryloxyC2-C6alkyl-, arylaminoC2-C6alkyl-, C1-C6alkoxycarbonylC1-C6alkyl-, -C2-C6alkylN(R4)C(O)R8, R8-C(=NR3)-, $-SO_2R8$, -C(O)R8, $-(CH_2)_nG1$, $-(CH_2)_nG4$, $-(CH_2)_nO(CH_2)_nG1$, $-(CH_2)_nO(CH_2)_nG4$, $-(CH_2)_nN(R3)(CH_2)_nG1$, and $-(CH_2)_nN(R3)(CH_2)_nG4$;

each R14 is independently and respectively selected from the group consisting of H, C1-C6alkyl, branched C3-C6alkyl, and C3-C8carbocyclyl;

R16 is independently and individually selected from the group consisting of C1-C6alkyl, branched C3-C7alkyl, C3-C8carbocyclyl, halogen, fluoroC1-C6alkyl wherein the alkyl moiety can be partially or fully fluorinated, cyano, hydroxyl, C1-C6alkoxy, fluoro C1-C6alkoxy wherein the alkyl moiety can be partially or fully fluorinated, $-N(R3)_2$, $-N(R4)_2$, C2-C3alkynyl, and nitro;

each R17 is taken from the group comprising phenyl, naphthyl, pyrrolyl, furyl, thienyl, oxazolyl, thiazolyl, isoxazolyl, isothiazolyl, imidazolyl, pyrazolyl, oxadiazolyl, thiadiazolyl, triazolyl,

tetrazolyl, pyrazinyl, pyridazinyl, triazinyl, oxetanyl, azetadinyl, tetrahydrofuranyl, oxazolinyl, oxazolidinyl, pyranyl, thiopyranyl, tetrahydropyranyl, dioxalinyl, azepinyl, oxepinyl, diazepinyl, pyrrolidinyl, and piperidinyl;

wherein R17 can be further substituted with one or more Z2, Z3 or Z4 moieties;

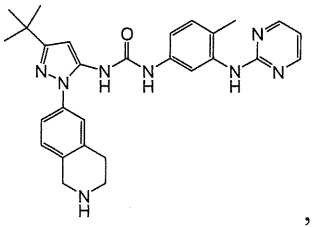
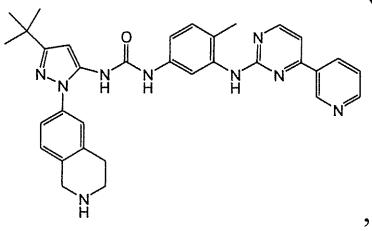
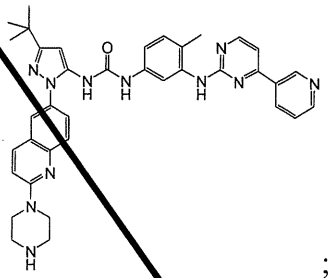
R18 is independently and individually selected from the group consisting of hydrogen, C1-C6alkyl, branched C3-C7alkyl, C3-C8carbocyclyl, halogen, fluoroC1-C6alkyl wherein the alkyl moiety can be partially or fully fluorinated, cyano, hydroxyl, C1-C6alkoxy, fluoroC1-C6alkoxy wherein the alkyl moiety can be partially or fully fluorinated, $-N(R3)_2$, $-N(R4)_2$, C2-C3alkynyl, and nitro;

R19 is H or C1-C6 alkyl;

wherein two R3 or R4 moieties are independently and individually taken from the group consisting of C1-C6alkyl and branched C3-C6alkyl, hydroxyalkyl, and alkoxyalkyl and are attached to the same nitrogen atom, said moieties may cyclize to form a C3-C7 heterocyclyl ring;

and n is 0-6; p is 1-4; q is 2-6; r is 0 or 1; t is 1-3, v is 1 or 2;

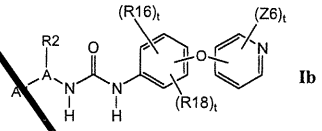
with the proviso that compounds of formula Ia cannot be


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in the manufacture of a medicament for the treatment a disease caused by c-Abl kinase, oncogenic forms thereof, aberrant fusion proteins thereof and polymorphs thereof, chronic myelogenous leukemia, acute lymphocytic leukemia, other myeloproliferative disorders, gastrointestinal stromal tumors, hypereosinophilic syndrome, glioblastomas, ovarian cancer, pancreatic cancer, prostate cancer, lung cancers, breast cancers, kidney cancers, cervical

carcinomas, metastasis of primary solid tumor secondary sites, ocular diseases characterized by hyperproliferation leading to blindness including retinopathies, diabetic retinopathy and age-related macular degeneration, rheumatoid arthritis, melanomas, colon cancer, thyroid cancer, a disease caused by a mutation in the RAS-RAF-MEK-ERK-MAP kinase pathway, human inflammation, rheumatoid spondylitis, ostero-arthritis, asthma, gouty arthritis, sepsis, septic shock, endotoxic shock, Gram-negative sepsis, toxic shock syndrome, adult respiratory distress syndrome, stroke, reperfusion injury, neural trauma, neural ischemia, psoriasis, restenosis, chronic obstructive pulmonary disease, bone resorptive diseases, graft-versus-host reaction, Chron's disease, ulcerative colitis, inflammatory bowel disease, pyresis, and combinations thereof.

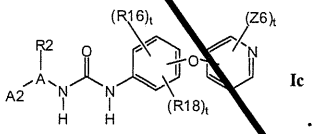
2. The use of claim 1, wherein the compound has the formula Ib



Ib

wherein A is pyrazolyl.

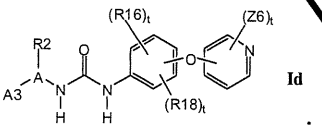
3. The use of claim 2, wherein the compound has the formula Ic



Ic

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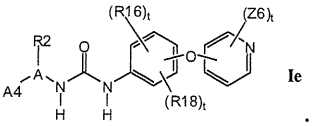
4. The use of claim 2, wherein the compound has the formula Id:



Id

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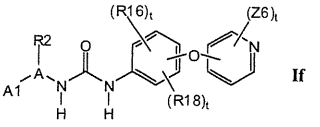
5. The use of claim 2, wherein the compound has the formula Ie:



Ie

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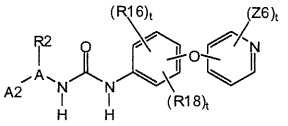
6. The use of claim 2, wherein the compound has the formula If:



If

wherein A is isoxazolyl.

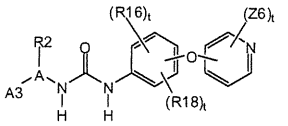
7. The use of claim 6, wherein the compound has the formula Ig:



Ig

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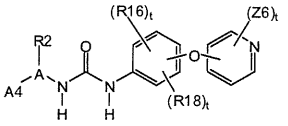
8. The use of claim 6, wherein the compound has the formula Ih:



Ih

.

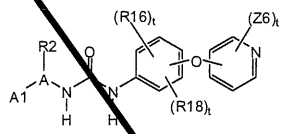
9. The use of claim 6, wherein the compound has the formula Ii:



Ii

.

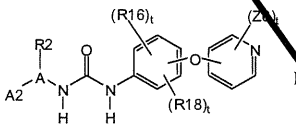
10. The use of claim 1, wherein the compound has the formula Ij:



Ij

wherein A is thienyl.

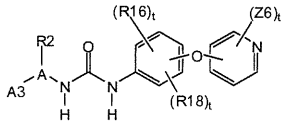
11. The use of claim 10, wherein the compound has the formula Ik:



Ik

.

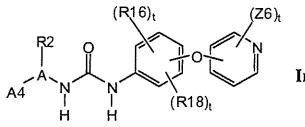
12. The use of claim 10, wherein the compound has the formula Il:



Il

.

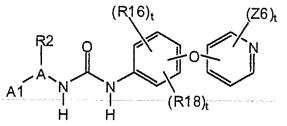
13. The use of claim 10, wherein the compound has the formula Im:



Im

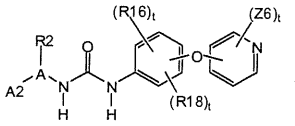
.

14. The use of claim 1, wherein the compound has the formula In:

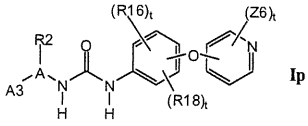

In

wherein A is furyl.

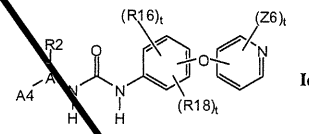
15. The use of claim 14, wherein the compound has the formula Io:


Io

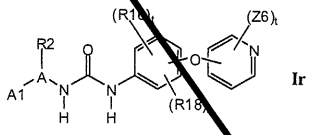
16. The use of claim 14, wherein the compound has the formula Ip:


Ip

17. The use of claim 14, wherein the compound has the formula Iq:

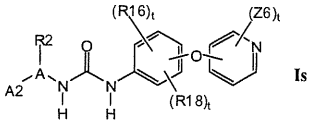

Iq

18. The use of claim 1, wherein the compound has the formula Ir:

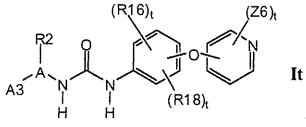

Ir

wherein A is pyrrolyl.

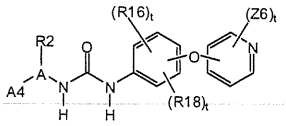
19. The use of claim 18, wherein the compound has the formula Is:


Is

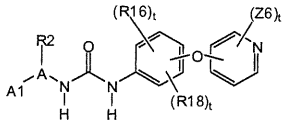
20. The use of claim 18, wherein the compound has the the formula It:


It

21. The use of claim 18, wherein the compound has the formula Iu:

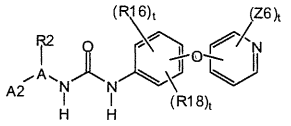

Iu

22. The use of claim 1, wherein the compound has the formula Iv:

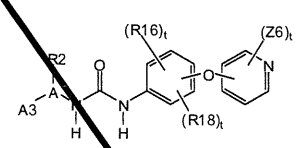

Iv

wherein A is imidazolyl.

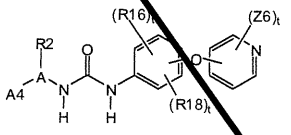
23. The use of claim 22, wherein the compound has the formula Iw:


Iw

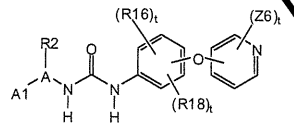
24. The use of claim 22, wherein the compound has the formula Ix:


Ix

25. The use of claim 22, wherein the compound has the formula Iy:

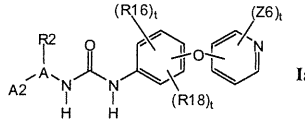

Iy

26. The use of claim 1, wherein the compound has the formula Iz:

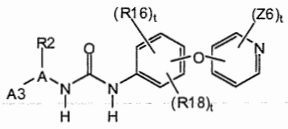

Iz

wherein A is thiazolyl.

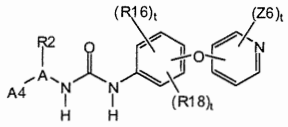
27. The use of claim 26, wherein the compound has the formula Iaa:


Iaa

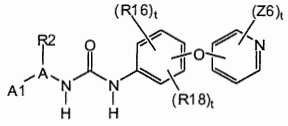
28. The use of claim 26, wherein the compound has the formula Ibb:


Ibb

29. The use of claim 26, wherein the compound has the formula Icc:

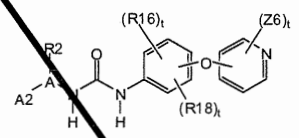

Icc

30. The use of claim 1, wherein the compound has the formula Idd:

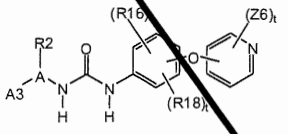

Idd

wherein A is oxazolyl.

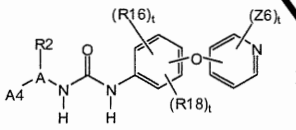
31. The use of claim 30, wherein the compound has the formula Iee:


Iee

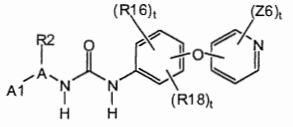
32. The use of claim 30, wherein the compound has the formula Iff:


Iff

33. The use of claim 30, wherein the compound has the formula Igg:

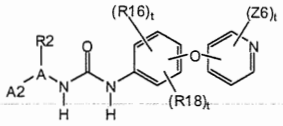

Igg

34. The use of claim 1, wherein the compound has the formula Ihh:

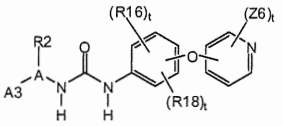

Ihh

wherein A is isothiazolyl.

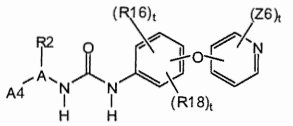
35. The use of claim 34, wherein the compound has the formula Iii:


Iii

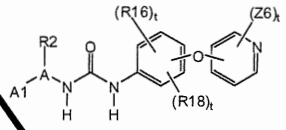
36. The use of claim 34, wherein the compound has the formula Ijj:


Ijj

37. The use of claim 34, wherein the compound has the formula Ikk:

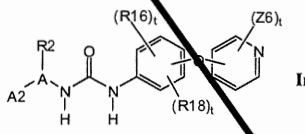

Ikk

38. The use of claim 1, wherein the compound has the formula Ill:

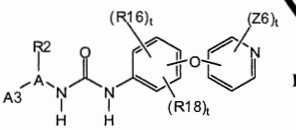

Ill

wherein A is phenyl.

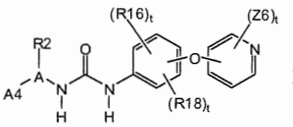
39. The use of claim 38, wherein the compound has the formula Imm:


Imm

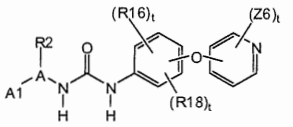
40. The use of claim 38, wherein the compound has the formula Inn:


Inn

41. The use of claim 38, wherein the compound has the formula Ioo:

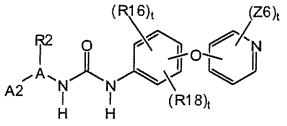

Ioo

42. The use of claim 1, wherein the compound has the formula Ipp:


Ipp

wherein A is pyrimidinyl.

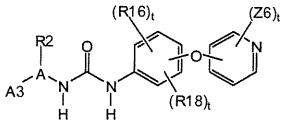
43. The use of claim 42, wherein the compound has the formula Iqq:



Iqq

.

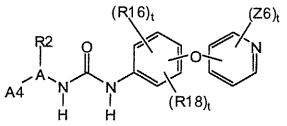
44. The use of claim 42, wherein the compound has the formula Irr:



Irr

.

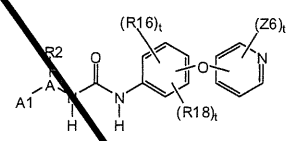
45. The use of claim 42, wherein the compound has the formula Iss:



Iss

.

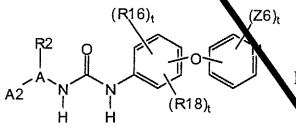
46. The use of claim 1, wherein the compound has the formula Itt:



Itt

wherein A is pyridinyl.

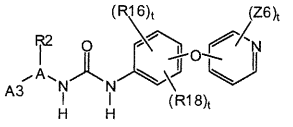
47. The use of claim 46, wherein the compound has the formula Iuu:



Iuu

.

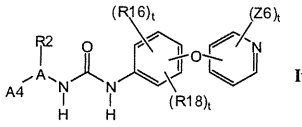
48. The use of claim 46, wherein the compound has the formula Ivv:



Ivv

.

49. The use of claim 46, wherein the compound has the formula Iww:



Iww

.

50. The use of claim 1, wherein the disease is selected from the group consisting of cancer, hyperproliferative diseases, secondary cancer growth arising from metastasis, diseases characterized by hyper-vascularization, inflammation, osteoarthritis, respiratory diseases, stroke, systemic shock, immunological diseases, cardiovascular disease and diseases characterized by angiogenesis.

51. The use of claim 1, wherein the compound is selected from the group consisting of 1-(3-tert-butyl-1-(1,2,3,4-tetrahydroisoquinolin-6-yl)-1H-pyrazol-5-yl)-3-(3-fluoro-4-(2-(methylcarbamoyl)pyridin-4-yloxy)phenyl)urea, l-(3-tert-butyl-l-(1,2,3,4-tetrahydroisoquinolin-6-yl)-1H-pyrazol-5-yl)-3-(2-fluoro-4-(2-(methylcarbamoyl)pyridin-4-yloxy)phenyl)urea, 1-(3-tert-butyl-1-(quinolin-6-yl)-1H-pyrazo1-5-yl)-3-(3-fluoro-4-(2-(methylcarbamoyl)pyridin-4-yloxy)phenyl)urea, 1-(3-tert-butyl-l-(quinolin-6-yl)-1H-pyrazol-5-yl)-3-(2-fluoro-5-(pyridin-3-yloxy)phenyl)urea, 1-(3-tert-butyl-1-(1H-indazol-5-yl)-1H-pyrazol-5-yl)-3-(2-fluoro-4-(2-(methylcarbamoyl)pyridin-4-yloxy)phenyl)urea, 1-(3-tert-butyl-l-(quinolin-6-yl)-1H-pyrazol-5-yl)-3-(2-fluoro-4-(2-(methylcarbamoyl)pyridin-4-yloxy)phenyl)urea, 1-(3-tertbutyl-1-(quinolin-6-yl)-1H-pyrazol-5-yl)-3-(3-methyl-4-(2-(methylcarbamoyl)pyridin-4-yloxy)phenyl)urea, l-(3-tert-butyl-1-(1,2,3,4-tetrahydroisoquinolin-6-yl)-1H-pyrazol-5-yl)-3-(3-fluoro-4-(2-(methylcarbamoyl)pyridin-4-yloxy)phenyl)urea, 1-(3-tert-butyl-1-(quinolin-6-y1)-1H-pyrazol-5-y1)-3-(4-(2-carbamoylpyridin-4-yloxy)-2-fluorophenyl)urea, 1-(3-tert-butyl-1-(quinolin-6-yl)-1H-pyrazol-5-yl)-3-(2-fluoro-4-(2-(methylamino)pyridin-4-yloxy)phenyl)urea, 1-(2-fluoro-4-(2-(methylcarbamoyl)pyridin-4-yloxy)phenyl)-3-(3-isopropyl-1-(quinolin-6-yl)-1H-pyrazol-5-yl)urea, 1-(3-ethyl-1-(quinolin-6-yl)-1H-pyrazol-5-y1)-3-(2-fluoro-4-(2-(methylcarbamoyl)pyridin-4-yloxy)phenyl)urea, 1-(3-cyclopentyl-l-(quinolin-6-yl)-1H-pyrazol-5-yl)-3-(2-fluoro-4-(2-(methylcarbamoyl)pyridin-4-yloxy)phenyl)urea, 1-(3-tert-butyl-1-(quinolin-6-y1)-1H-pyrazol-5-yl)-3-(2-fluoro-5-(6-(hydroxymethyl)pyridin-3-yloxy)phenyl)urea, 1-(4-(2-carbamoylpyridin-4-yloxy)-2-fluorophenyl)-3-(3-isopropyl-l-(quinolin-6-yl)-1H-pyrazol-5-y1)urea, 1-(3-isopropyl-l-(quinolin-6-yl)-1H-pyrazol-5-yl)-3-(3-methyl-4-(2-(methylcarbamoyl)pyridin-4-yloxy)phenyl)urea, 1-(4-(2-carbamoylpyridin-4-yloxy)-2-fluorophenyl)-3-(3-ethyl-1-(quinolin-6-yl)-1H-pyrazol-5-yl)urea, 1-(3-tert-butyl-l-(quinolin-6-yl)-1H -pyrazol-5-yl)-3-(2-fluoro-5-(6-(methylcarbamoyl)pyridin-3-yloxy)phenyl)urea, 1-(1-(1 H-indazol-5-yl)-3-isopropyl-lH-pyrazol-5-yl)-3-(4-(2-carbamoylpyridin-4-yloxy)-2-

fluorophenyl)urea, 1-(4-(2-carbamimidoylpyridin-4-yloxy)-2-fluorophenyl)-3-(3-isopropyl-1-(quinolin-6-yl)-1H-pyrazol-5-yl)urea, 1-(4-(2-carbamoylpyridin-4-yloxy)-3-methylphenyl)-3-(3-isopropyl-1-(quinolin-6-yl)-1H-pyrazol-5-yl)urea, 1-(2-fluoro-4-(2-(1-methyl-1H-pyrazol-4-yl)pyridin-4-yloxy)phenyl)-3-(3-isopropyl-1-(quinolin-6-yl)-1H-pyrazol-5-yl)urea, 1-(3-ethyl-1-(quinolin-6-yl)-1H-pyrazol-5-yl)-3-(2-fluoro-4-(2-(1-methyl-lH-pyrazol-4-yl)pyridin-4-yloxy)phenyl)urea, 1-(4-(2-(1H-pyrazol-4-yl)pyridin-4-yloxy)-3-methylphenyl)-3-(3-isopropyl-l-(quinolin-6-yl)-1H-pyrazol-5-yl)urea, 1-(3-tert-butyl-1-(l,2,3,4-tetrahydroisoquinolin-6-yl)-1H-pyrazol-5-yl)-3-(2-fluoro-4-(2-(1-methyl-lH-pyrazol-4-yl)pyridin-4-yloxy)phenyl)urea, 1-(4-(2-(1H-pyrazol-4-yl)pyridin-4-yloxy)-2-fluorophenyl)-3-(3-tert-butyl-l-(1,2,3,4-tetrahydroisoquinolin-6-yl)-1H-pyrazol-5-yl)urea, 1-(4-(2-(1H-pyrazol-4-yl)pyridin-4-yloxy)-2-fluorophenyl)-3-(3-tert-butyl-l-(1-oxo-l,2,3,4-tetrahydroisoquinolin-7-yl)-1H-pyrazol-5-yl)urea, 1-(4-(2-(1H-pyrazol-4-yl)pyridin-4-yloxy)-2-fluorophenyl)-3-(3-tertbutyl-l-(1,2,3,4-tetrahydroisoquinolin-7-yl)-IH-pyrazol-5-yl)urea, 1-(3-fluoro-4-(2-(isopropylamino)pyridin-4-yloxy)phenyl)-3-(3-isopropyl-1-(quinolin-6-yl)-1H -pyrazol-5-yl)urea, 1-(3-isopropyl-l-(quinolin-6-yl)-1H-pyrazol-5-yl)-3-(4-(2-(isopropylamino)pyridin-4-yloxy)-3-ethylphenyl)urea, 1-(3-ethyl-l-(quinolin-6-yl)-1H-pyrazol-5-yl)-3-(2-fluoro-3-methyl-4-(2-(1-methyl-lH-pyrazol-4-yl)pyridin-4-yloxy)phenyl)urea, and 1-(2,3-difluoro-4-(2-(1-methyl-lH-pyrazol-4-yl)pyridin-4-yloxy)phenyl)-3-(3-ethyl-l-(quinolin-6-yl)-1H-pyrazol-5-yl)urea.

52. The use of claim 51, which is 1-(4-(2-carbamoylpyridin-4-yloxy)-2-fluorophenyl)-3-(3-isopropyl-1-(quinolin-6-yl)-1H-pyrazol-5-yl)urea and pharmaceutically acceptable salts, and tautomers thereof.

53. The use of claim 51, which is 1-(3-tert-butyl-l-(quinolin-6-yl)-1H-pyrazol-5-yl)-3-(3-methyl-4-(2-(methylcarbamoyl)pyridin-4-yloxy)phenyl)urea and pharmaceutically acceptable salts, and tautomers thereof.

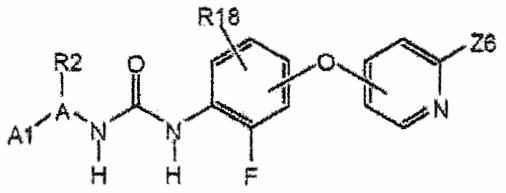
54. The use of claim 51, which is 1-(3-tert-butyl-1-(quinolin-6-yl)-1H-pyrazol-5-yl)-3-(2-fluoro-4-(2-(methylcarbamoyl)pyridin-4-yloxy)phenyl)urea and pharmaceutically acceptable salts, and tautomers thereof.

55. The use of claim 51, which is 1-(3-tert-butyl-l-(quinolin-6-yl)-1H-pyrazol-5-yl)-3-(4-(2-carbamoylpyridin-4-yloxy)-2-fluorophenyl)urea and pharmaceutically acceptable salts, and tautomers thereof.

56. The compound of claim 51, which is 1-(2-fluoro-4-(2-(methylcarbamoyl)pyridin-4-yloxy)phenyl)-3-(3-isopropyl-l-(quinolin-6-yl)-1H-pyrazol-5-yl)urea and pharmaceutically acceptable salts and tautomers thereof.

Claims

1. A compound of formula I-1h:

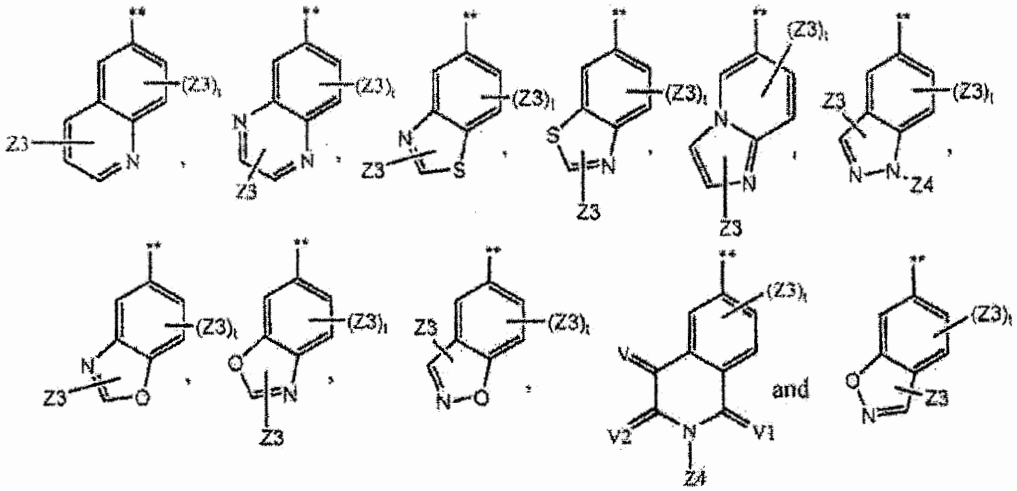


I-1h

wherein:

A is pyrazolyl, wherein the A ring is optionally substituted with one or more R2 moieties;

A1 is selected from the group consisting of



wherein the symbol (**) is the point of attachment to the A ring of formula I-1h;

G1 is a heteroaryl taken from the group consisting of pyrrolyl, furyl, thienyl, oxazolyl, thiazolyl, isoxazolyl, isothiazolyl, imidazolyl, pyrazolyl, oxadiazolyl, thiadiazolyl, triazolyl, tetrazolyl, pyrazinyl, pyridazinyl, triazinyl, pyridinyl, and pyrimidinyl;

G4 is a heterocyclyl taken from the group consisting of oxetanyl, azetadinyl, tetrahydrofuranyl, pyrrolidinyl, oxazolinyl, oxazolidinyl, imidazolonyl, pyranyl, thiopyranyl, tetrahydropyranyl,

dioxalinyl, piperidinyl, morpholinyl, thiomorpholinyl, thiomorpholinyl S-oxide, thiomorpholinyl S-dioxide, piperazinyl, azepinyl, oxepinyl, diazepinyl, tropanyl, and homotropanyl;

V, V1, and V2 are each independently and respectively selected from the group consisting of O and H_2;

each Z2 is independently and individually selected from the group consisting of hydrogen, aryl, C1-C6alkyl, C3-C8carbocyclyl, hydroxyl, hydroxyC1-C6alkyl-, cyano, $(R3)_2N$-, $(R4)_2N$-, $(R4)_2NC1$-C6alkyl-, $(R4)_2NC2$-C6alkyl$N(R4)$-$(CH_2)_n$-, $(R4)_2NC2$-C6alkyl$O(CH_2)_n$-, $(R3)_2NC(O)$-, $(R4)_2NC(O)$-, $(R4)_2NC(O)C1$-C6alkyl-, carboxyl, carboxyC1-C6alkyl-, C1-C6alkoxycarbonyl-, C1-C6alkoxycarbonylC1-C6alkyl-, $(R3)_2NSO_2$-, $(R4)_2NSO_2$-, $-SO_2R5$, $-SO_2R8$, $-(CH_2)_nN(R4)C(O)R8$, $-C(O)R8$, =O, =NOH, =N(OR6), $-(CH_2)_nG1$, $-(CH_2)_nG4$, $-(CH_2)_nO(CH_2)_nG1$, $-(CH_2)_nO(CH_2)_nG4$, $-(CH_2)_nNR3(CH_2)_n$-aryl, $-(CH_2)_nNR3(CH_2)_nG1$, $-(CH_2)_nNR3(CH_2)_nG4$, $-(CH_2)_nNHC(O)NHS(O)_2R8$, $-(CH_2)_nNHS(O)_2NHC(O)R8$, $-C(O)NHS(O)_2R8$, $-(CH_2)_nNHC(O)(CH_2)_nR5$, $-(CH_2)_nNHS(O)_2R5$, $-(CH_2)_nC(O)NH(CH_2)_qR5$, $-(CH_2)_nC(O)R5$, $-(CH_2)_nOC(O)R5$, and $-(CH_2)_nR5$;

in the event that Z2 contains an alkyl or alkylene moiety, such moieties may be further substituted with one or more C1-C6alkyls;

each Z3 is independently and individually selected from the group consisting of H, C1-C6alkyl, branched C3-C7alkyl, C3-C8carbocyclyl, halogen, fluoroC1-C6alkyl wherein the alkyl moiety can be partially or fully fluorinated, cyano, hydroxyl, methoxy, oxo, $(R3)_2NC(O)$-, $(R4)_2NC(O)$-, $-N(R4)C(O)R8$, $(R3)_2NSO_2$-, $(R4)_2NSO_2$-, $-N(R4)SO_2R5$, $-N(R4)SO_2R8$, $-(CH_2)_nN(R3)_2$, $-(CH_2)_nN(R4)_2$, $-O(CH_2)_qN(R4)_2$, $-O(CH_2)_qO$-C1-C6alkyl, $-N(R3)(CH_2)_qO$-C1-C6alkyl, $-N(R3)(CH_2)_qN(R4)_2$, $-O(CH_2)_qR5$, $-NR3(CH_2)_qR5$, $-C(O)R5$, $-C(O)R8$, -R5, and nitro;

in the event that Z3 contains an alkyl or alkylene moiety, such moieties may be further substituted with one or more C1-C6alkyls;

each Z4 is independently and individually selected from the group consisting of H, C1-C6alkyl, hydroxyC2-C6alkyl, C1-C6alkoxyC2-C6alkyl-, $(R4)_2N$-C2-C6alkyl-, $(R4)_2N$-C2-C6alkylN(R4)-C2-C6alkyl-, $(R4)_2N$-C2-C6alkyl-O-C2-C6alkyl- $(R4)_2NC(O)$-C1-C6alkyl-, carboxyC1-C6alkyl-, C1-C6alkoxycarbonylC1-C6alkyl-, -C2-C6alkylN(R4)C(O)R8, R8-C(=NR3)-, -SO_2R8, -COR8, -$(CH_2)_n$G1, -$(CH_2)_n$G4, -$(CH_2)_q$-O$(CH_2)_n$G1, -$(CH_2)_q$O$(CH_2)_n$G4, -$(CH_2)_q$NR3$(CH_2)_n$G1, -$(CH_2)_q$NR3$(CH_2)_n$G4, -$(CH_2)_q$NHC(O)$(CH_2)_n$R5, -$(CH_2)_q$C(O)NH$(CH_2)_q$R5, -$(CH_2)_q$C(O)R5, -$(CH_2)_q$OC(O)R5, -$(CH_2)_q$R5, -$(CH_2)_q$NR4$(CH_2)_q$R5, and -$(CH_2)_q$O$(CH_2)_q$R5;

in the event that Z4 contains an alkyl or alkylene moiety, such moieties may be further substituted with one or more C1-C6alkyls;

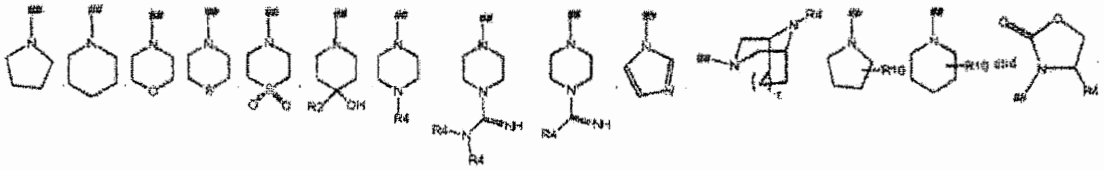
each Z6 is independently and individually selected from the group consisting of -C(O)N$(R3)_2$, -C(O)N$(R4)_2$, -$(CH_2)_n$G1, -N(R4)C(O)R8, $(R4)_2N$-, -N(R3)COR8, $(R3)_2N$-, H, C1-C6alkyl, branched C3-C7alkyl, hydroxyl, hydroxyC1-C6alkyl, hydroxyC2-C6 branched alkyl-, C1-C6alkoxy, C1-C6alkoxyC1-C6alkyl-, C1-C6alkoxyC2-C6 branched alkyl-, branched C2-C6alkoxy-, C1-C6alkylthio, -R5, -N(R3)SO_2R6, -C(O)R5, -SO_2NHR4, halogen, fluoroC1-C6alkyl wherein the alkyl is fully or partially fluorinated, cyano, fluoroC1-C6alkoxy wherein the alkyl is fully or partially fluorinated, -O$(CH_2)_q$N$(R4)_2$, -N(R3)$(CH_2)_q$N$(R4)_2$, -O$(CH_2)_q$O-C1-C6alkyl, -O$(CH_2)_q$N$(R4)_2$, -N(R3)$(CH_2)_q$O-C1-C6alkyl, -N(R3)$(CH_2)_q$N$(R4)_2$, -O$(CH_2)_q$R5, -N(R3)$(CH_2)_q$R5, -$(NR3)_r$R17, -$(O)_r$R17, -$(S)_r$R17, -$(CH_2)_n$R17, -$(CH_2)_n$G4, -$(CH_2)_q$O$(CH_2)_n$G1, -$(CH_2)_q$O$(CH_2)_n$G4, -$(CH_2)_q$N(R3)$(CH_2)_n$G1, and -$(CH_2)_q$NR3$(CH_2)_n$G4;

each R2 is selected from the group consisting of branched C3-C8alkyl, C1-C6alkyl, fluoroC1-C6alkyl wherein the alkyl is fully or partially fluorinated, R19 substituted C3-C8carbocyclyl, Z3-substituted aryl, Z3-substituted G1, Z3-substituted G4, hydroxylC1-C6alky, hydroxyl branched C3-C6alkyl-, hydroxyl substituted C3-C8carbocyclyl-, cyanoC1-C6alkyl-, cyano substituted branched C3-C6alkyl-, cyano substituted C3-C8carbocyclyl-, $(R4)_2NC(O)$C1-C6alkyl-, $(R4)_2NC(O)$ substituted branched C3-C6alkyl-, $(R4)_2NC(O)$ substituted C3-C8carbocyclyl-, halogen, cyano, C1-C6alkoxy, and fluoroC1-C6alkoxy wherein the alkyl group is fully or partially fluorinated;

each R3 is independently and individually selected from the group consisting of H, C1-C6alkyl, branched C3-C7alkyl, C3-C7cycloalkyl, and Z3-substituted phenyl-;

each R4 is independently and individually selected from the group consisting of H, C1-C6alkyl, hydroxyC1-C6alkyl-, dihydroxyC1-C6alkyl-, C1-C6alkoxyC1-C6alkyl-, branched C3-C7alkyl-, branched hydroxyC1-C6alkyl-, branched C1-C6alkoxyC1-C6alkyl-, branched dihydroxyC2-C6alkyl-, $-(CH_2)_pN(R7)_2$, $-(CH_2)_pR5$, $-(CH_2)_pC(O)N(R7)_2$, $-(CH_2)_nC(O)R5$, $-(CH_2)_nC(O)OR3$, C3-C8carbocyclyl, hydroxyl substituted C3-C8carbocyclyl-, alkoxy substituted C3-C8carbocyclyl-, dihydroxyl substituted C3-C8carbocyclyl-, and $-(CH_2)_nR17$;

each R5 is independently and individually selected from the group consisting of



and wherein the symbol (##) is the point of attachment of the R5 moiety;

each R6 is independently and individually selected from the group consisting of C1-C6alkyl, branched C3-C7alkyl, C3-C8carbocyclyl, phenyl, G1, and G4;

each R7 is independently and individually selected from the group consisting of H, C1-C6alkyl, hydroxyC2-C6alkyl-, dihydroxyC2-C6alkyl-, C2-C6alkoxyC2-C6alkyl-, branched C3-C7alkyl-, branched hydroxyC2-C6 alkyl-, branched C2-C6alkoxyC2-C6alkyl-, branched dihydroxyC2-C6alkyl-, $-(CH_2)_qR5$, $-(CH_2)_nC(O)R5$, $-(CH_2)_nC(O)OR3$, C3-C8carbocyclyl, hydroxyl substituted C3-C8carbocyclyl-, alkoxy substituted C3-C8carbocyclyl-, dihydroxy substituted C3-C8carbocyclyl, and $-(CH_2)_nR17$;

each R8 is independently and individually selected from the group consisting of C1-C6alkyl, branched C3-C7alkyl, fluoroC1-C6alkyl wherein the alkyl moiety is partially or fully fluorinated, C3-C8carbocyclyl, Z3-substituted phenyl-, Z3-substituted phenylC1-C6alkyl-, Z3-

substituted G1-, Z3-substituted G1-C1-C6alkyl-, Z2-substituted G4-, Z2-substituted G4-C1-C6alkyl-, OH, C1-C6alkoxy, $N(R3)_2$, $N(R4)_2$, and R5;

each R10 is independently and individually selected from the group consisting of CO_2H, CO_2C1-C6alkyl, $-C(O)N(R4)_2$, OH, C1-C6alkoxy, and $-N(R4)_2$;

each R17 is taken from the group comprising phenyl, naphthyl, pyrrolyl, furyl, thienyl, oxazolyl, thiazolyl, isoxazolyl, isothiazolyl, imidazolyl, pyrazolyl, oxadiazolyl, thiadiazolyl, triazolyl, tetrazolyl, pyrazinyl, pyridazinyl, triazinyl, oxetanyl, azetadinyl, tetrahydrofuranyl, oxazolinyl, oxazolidinyl, pyranyl, thiopyranyl, tetrahydropyranyl, dioxalinyl, azepinyl, oxepinyl, diazepinyl, pyrrolidinyl, and piperidinyl;

wherein R17 can be further substituted with one or more Z2, Z3 or Z4 moieties;

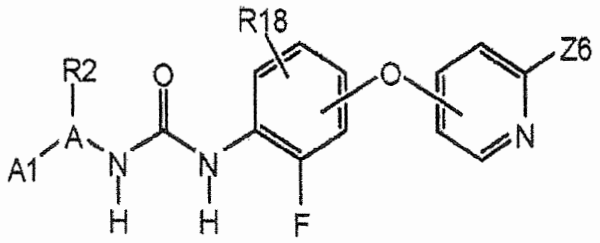
R18 is independently and individually selected from the group consisting of hydrogen, halogen, C1-C6alkyl, fluoroC1-C6alkyl wherein the alkyl moiety can be partially or fully fluorinated, branched C3-C7alkyl, C3-C8carbocyclyl, cyano, hydroxyl, C1-C6alkoxy, fluoroC1-C6alkoxy wherein the alkyl moiety can be partially or fully fluorinated, $-N(R3)_2$, $-N(R4)_2$, C2-C3alkynyl, and nitro;

R19 is H or C1-C6alkyl;

wherein two R3 or R4 moieties are independently and individually taken from the group consisting of C1-C6alkyl and branched C3-C6alkyl, hydroxyalkyl, and alkoxyalkyl and are attached to the same nitrogen atom, said moieties may cyclize to form a C3-C7 heterocyclyl ring;

and n is 0-6; p is 1-4; q is 2-6; t is 1-3.

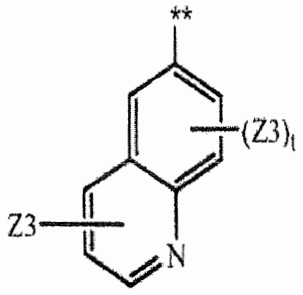
2. The compound of claim 1, wherein the compound of Formula I-1h is a compound of formula I-1i:



I-1i

wherein Z6 is -C(O)NHR4, -NHR4 or R19 substituted pyrazole.

3. The compound of claim 1, wherein Al is



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

1-(3-tert-butyl-1-(1,2,3,4-tetrahydroisoquinolin-6-yl)-1H-pyrazol-5-yl)-3-(2-fluoro-4-(2-(methylcarbamoyl)pyridin-4-yloxy)phenyl)urea,

1-(3-tert-butyl-1-(quinolin-6-yl)-1H-pyrazo1-5-yl)-3-(2-fluoro-5-(pyridin-3-yloxy)phenyl)urea,

1-(3-tert-butyl-1-(1H-indazol-5-yl)-1H-pyrazol-5-yl)-3-(2-fluoro-4-(2-methylcarbamoyl)pyridin-4-yloxy)phenyl)urea,

1-(3-tert-butyl-1-(quinolin-6-yl)-1H-pyrazol-5-yl)-3-(2-fluoro-4-(2-(methylcarbamoyl)pyridin-4-yloxy)phenyl)urea,

1-(3-tert-butyl-1-(quinolin-6-yl)-1H-pyrazol-5-yl)-3-(4-(2-carbamoylpyridin-4-yloxy)-2-fluorophenyl)urea,

1-(3-tert-butyl-1-(quinolin-6-yl)-1H-pyrazol-5-yl)-3-(2-fluoro-4-(2-(methylamino)pyridin-4-yloxy)phenyl)urea,

1-(2-fluoro-4-(2-(methylcarbamoyl)pyridin-4-yloxy)phenyl)-3-(3-isopropyl-1-(quinolin-6-yl)-1H-pyrazol-5-yl)urea,

1-(3-ethyl-1-(quinolin-6-yl)-1H-pyrazol-5-yl)-3-(2-fluoro-4-(2-(methylcarbamoyl)pyridin-4-yloxy) phenyl)urea,

1-(3-cyclopentyl-1-(quinolin-6-yl)-1H-pyrazol-5-yl)-3-(2-fluoro-4-(2-(methylcarbamoyl)pyridin-4-yloxy)phenyl)urea,

1-(3-tert-butyl-1-(quinolin-6-yl)-1H-pyrazol-5-yl)-3-(2-fluoro-5-(6-(hydroxymethyl)pyridin-3-yloxy) phenyl)urea,

1-(4-(2-carbamoylpyridin-4-yloxy)-2-fluorophenyl)-3-(3 -isopropyl-1-(quinolin-6-yl)-1H-pyrazol-5-yl)urea,

1-(4-(2-carbamoylpyridin-4-yloxy)-2-fluorophenyl)-3-(3-ethyl-1-(quinolin-6-yl)-1H-pyrazol-5-yl) urea,

1-(3-tert-butyl-1-(quinolin-6-yl)-1H -pyrazol-5-yl)-3-(2-fluoro-5-(6-(methylcarbamoyl)pyridin-3yloxy) phenyl)urea,

1-(1-(1H-indazol-5-yl)-3-isopropyl-1H-pyrazol-5-yl)-3-(4-(2-carbamoylpyridin-4-yloxy)-2-fluorophenyl)urea,

1-(4-(2-carbamimidoylpyridin-4-yloxy)-2-fluorophenyl)-3-(3-isopropyl-1-(quinolin-6-yl)-1H-pyrazol-5-yl)urea,

1-(2-fluoro-4-(2-(1-methyl-1H-pyrazol-4-yl)pyridin-4-yloxy)phenyl)-3-(3-isopropyl-1-(quinolin-6-yl)-1H-pyrazol-5-yl)urea,

1-(3-ethyl-1-(quinolin-6-yl)-1H-pyrazol-5-yl)-3-(2-fluoro-4-(2-(1-methyl-1H-pyrazol-4yl) pyridin-4-yloxy)phenyl)urea,

1-(3-tert-butyl-1-(1,2,3,4-tetrahydroisoquinolin-6-yl)-1H-pyrazol-5-yl)-3-(2-fluoro-4-(2-(1-methyl-1H-pyrazol-4-yl)pyridin-4-yloxy)phenyl)urea,

1-(4-(2-(1H-pyrazol-4-yl)pyridin-4-yloxy)-2-fluorophenyl)-3-(3-tert-butyl-l-(1,2,3,4-tetrahydroisoquinolin-6-yl)-1H-pyrazol-5-yl)urea,

1-(4-(2-(1H-pyrazol-4-yl)pyridin-4-yloxy)-2-fluorophenyl)-3-(3-tert-butyl-l-(1-oxo-l,2,3,4-tetrahydroisoquinolin-7-yl)-1H-pyrazol-5-yl)urea,

1-(4-(2-(1H-pyrazol-4-yl)pyridin-4-yloxy)-2-fluorophenyl)-3-(3-tertbutyl-1-(1,2,3,4-tetrahydroisoquinolin-7-yl)-1H-pyrazol-5-yl)urea,

1-(3-ethyl-1-(quinolin-6-yl)-1H-pyrazol-5-yl)-3-(2-fluoro-3-methyl-4-(2-(1-methyl-1H-pyrazol-4-yl) pyridin-4-yloxy)phenyl)urea, and
1-(2,3-difluoro-4-(2-(1-methyl-1H-pyrazol-4-yl)pyridin-4-yloxy)phenyl)-3-(3-ethyl-1-(quinolin-6-yl)-1H-pyrazol-5-yl)urea.

5. The compound of claim 4, which is 1-(4-(2-carbamoylpyridin-4-yloxy)-2-fluorophenyl)-3-(3-isopropyl-1-(quinolin-6-yl)-1H-pyrazol-5-yl)urea, and pharmaceutically acceptable salts thereof.

6. The compound of claim 4, which is 1-(3-tert-butyl-1-(quinolin-6-yl)-1H-pyrazol-5-yl)-3-(2-fluoro-4-(2-(methylcarbamoyl)pyridin-4-yloxy)phenyl)urea, and pharmaceutically acceptable salts thereof.

7. The compound of claim 4, which is 1-(3-tert-butyl-1-(quinolin-6-yl)-1H-pyrazol-5-yl)-3-(4-(2-carbamoylpyridin-4-yloxy)-2-fluorophenyl)urea, and pharmaceutically acceptable salts thereof.

8. The compound of claim 4, which is 1-(2-fluoro-4-(2-(methylcarbamoyl)pyridin-4-yloxy)phenyl)-3-(3-isopropyl-1-(quinolin-6-yl)-1H-pyrazol-5-yl)urea, and pharmaceutically acceptable salts thereof.

9. A pharmaceutical composition comprising a compound of any one of claims 1-3 or a salt thereof, together with a pharmaceutically acceptable carrier, said carrier including an additive selected from the group including adjuvants, excipients, diluents, and stablilizers.

10. A pharmaceutical composition comprising a compound of claim 4 or claim 20, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier.

11. A pharmaceutical composition comprising the compound of claim 5, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier.

12. A pharmaceutical composition comprising the compound of claim 21, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier.

13. A pharmaceutical composition comprising the compound of claim 6, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier.

14. A pharmaceutical composition comprising the compound of claim 7, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier.

15. A pharmaceutical composition comprising the compound of claim 8, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier.

16. A compound of any one of claims 1-3 for use in modulating a kinase activity of a wildtype kinase species, oncogenic forms thereof, aberrant fusion proteins thereof and polymorphs of any of the foregoing.

17. A compound of any one of claims l-3 for use in the treatment of a condition selected from the group consisting of cancer, hyperproliferative diseases, secondary cancer growth arising from metastasis, diseases characterized by hyper-vascularization, inflammation, osteoarthritis, respiratory diseases, stroke, systemic shock, immunological diseases, cardiovascular disease and diseases characterized by angiogenesis, a disease caused by c-Abl kinase, oncogenic forms thereof, aberrant fusion proteins thereof and polymorphs thereof, chronic myelogenous leukemia, acute lymphocytic leukemia, other myeloproliferative disorders, gastrointestinal stromal tumors, hypereosinophilic syndrome, glioblastomas, ovarian cancer, pancreatic cancer, prostate cancer, lung cancers, breast cancers, kidney cancers, cervical carcinomas, metastasis of primary solid tumor secondary sites, ocular diseases characterized by hyperproliferation leading to blindness including various retinopathies i.e. diabetic retinopathy and age-related macular degeneration, rheumatoid arthritis, melanomas, colon cancer, thyroid cancer, a disease caused by a mutation in the RAS-RAF-MEK-ERK-MAP kinase pathway, human inflammation, rheumatoid spondylitis, ostero-arthritis, asthma, gouty arthritis, sepsis, septic shock, endotoxic shock, Gram-negative sepsis, toxic shock syndrome, adult respiratory distress syndrome, stroke, reperfusion injury, neural trauma, neural ischemia, psoriasis, restenosis, chronic obstructive pulmonary disease, bone resorptive diseases, graft-versus-host reaction, Chron's disease, ulcerative colitis, inflammatory bowel disease, pyresis, and combinations thereof.

18. The use of a compound of any one of claims 1-3 in the manufacture of a medicament for treating cancer, hyperproliferative diseases, secondary cancer growth arising from metastasis, diseases characterized by hyper-vascularization, inflammation, osteoarthritis, respiratory diseases, stroke, systemic shock, immunological diseases, cardiovascular disease and diseases characterized by angiogenesis, a disease caused by c-Abl kinase, oncogenic forms thereof, aberrant fusion proteins thereof and polymorphs thereof, chronic myelogenous leukemia, acute lymphocytic leukemia, other myeloproliferative disorders, gastrointestinal stromal tumors, hypereosinophilic syndrome, glioblastomas, ovarian cancer, pancreatic cancer, prostate cancer, lung cancers, breast cancers, kidney cancers, cervical carcinomas, metastasis of primary solid tumor secondary sites, ocular diseases characterized by hyperproliferation leading to blindness including various retinopathies i.e. diabetic retinopathy and age-related macular degeneration, rheumatoid arthritis, melanomas, colon cancer, thyroid cancer, a disease caused by a mutation in the RAS-RAF-MEK-ERK-MAP kinase pathway, human inflammation, rheumatoid spondylitis, ostero-arthritis, asthma, gouty arthritis, sepsis, septic shock, endotoxic shock, Gram-negative sepsis, toxic shock syndrome, adult respiratory distress syndrome, stroke, reperfusion injury, neural trauma, neural ischemia, psoriasis, restenosis, chronic obstructive pulmonary disease, bone resorptive diseases, graft-versus-host reaction, Chron's disease, ulcerative colitis, inflammatory bowel disease, pyresis, or combinations thereof.

19. A compound selected from the group consisting of:

1-(3-tert-butyl-1-(1,2,3,4-tetrahydroisoquinolin-6-yl)-1H-pyrazol-5-yl)-3-(3-fluoro-4-(2-(methylcarbamoyl)pyridin-4-yloxy)phenyl)urea,

1-(3-tert-butyl-1-(quinolin-6-yl)-1H-pyrazol-5-yl)-3-(3-fluoro-4-(2-(methylcarbamoyl)pyridin-4-yloxy)phenyl)urea,

1-(3-tertbutyl-1-(quinolin-6-yl)-1H-pyrazol-5-yl)-3-(3-methyl-4-(2-(methylcarbamoyl)pyridin-4-yloxy)phenyl)urea,

1-(3-isopropyl-1-(quinolin-6-yl)-1H-pyrazol-5-yl)-3-(3-methyl-4-(2-(methylcarbamoyl)pyridin-4-yloxy)phenyl)urea,

1-(4-(2-carbamoylpyridin-4-yloxy)-3-methylphenyl)-3-(3-isopropyl-1-(quinolin-6-yl)-1H-pyrazol-5-yl)urea,

1-(4-(2-(1H-pyrazol-4-yl)pyridin-4-yloxy)-3-methylphenyl)-3-(3-isopropyl-1-(quinolin-6-yl)-1H-pyrazol-5-yl)urea,

1-(3-fluoro-4-(2-(isopropylamino)pyridin-4-yloxy)phenyl)-3-(3-isopropyl-1-(quinolin-6-yl)-1H pyrazol-5-yl)urea,

1-(3-isopropyl-1-(quinolin-6-yl)-1H-pyrazol-5-yl)-3-(4-(2-(isopropylamino)pyridin-4-yloxy)-3-methylphenyl)urea.

20. The compound of claim **19**, which is 1-(3-tert-butyl-1-(quinolin-6-yl)-1H-pyrazol-5-yl)-3-(3-methyl-4-(2-(methylcarbamoyl)pyridin-4-yloxy)phenyl)urea, and pharmaceutically acceptable salts thereof.