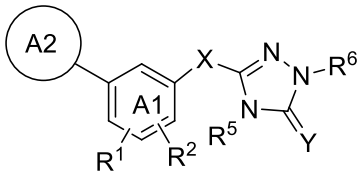
CLAIMS

WHAT IS CLAIMED IS:

1. A compound of Formula I

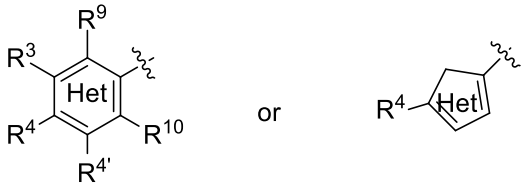


Formula I

or a pharmaceutical acceptable salt thereof wherein:

A1 is phenyl or a 6-membered heteroaromatic ring having 1, 2 or 3 N in the heteroaromatic ring;

A2 is selected from A2a or A2b



A2a A2b

wherein A2a is phenyl or a 6 membered heteroaromatic ring having 1, 2 or 3 N in the heteroaromatic ring, and

A2b is a 5 membered heteroaromatic ring having 1, 2 or 3 heteroatoms independently selected from O, S and N;

X is selected from the group consisting of -$(CH_2)_{m2}$-, ~~-$(CH_2)_m$-O-$(CH_2)_n$-,~~ -$(CH_2)_{m3}$-, ~~NH~~-$(CH_2)_{n4}$-, and -$(CH_2)_m$-O-$(CH_2)_n$-, ~~-$(CH_2)_m$-S(=O)$_o$-$(CH_2)_n$-,~~ optionally mono- or di-substituted with halogen, wherein m and n are independently 0, 1, 2, 3 or 4, ~~and each o is independently 0, 1 or 2~~ with the proviso that m+n is 2, 3, or 4;

Y is O ~~or S~~;

R^1 and R^2 are each independently selected from the group consisting of:

(a) hydrogen,
(b) halogen,
(c) CN,
(d) CF_3,
(e) -C_{1-6}alkyl,
(f) -C_{1-6}alkyl-C(=O)OH,
(g) -O-(R^7),
(h) -S(=O)$_o$$R^7$,
(i) -N(R^7)(R^8),
(j) -N(R^7)-C(=O)-(R^8),
(k) -N(R^7)-C(=O)-O-(R^8),
(l) -N(R^7)S(=O)$_2$(R^8),
(m) -C_{3-6}cycloalkyl,

(n) -C(=O)(R^7),
(o) aryl,
(p) heteroaryl,
(q) -OC(=O)N(R^7)(R^8),
(r) -S(=O)$_2$N(R^7)(R^8),
(s) -C(=O)N(R^7)(R^8), and
(t) -C(R^7)(R^8)OH,

wherein the alkyl portion of choices (e) and (f), and the cycloalkyl portion of choice (m) are optionally substituted with halogen, and

wherein the aryl of choice (o) and the heteroaryl of choice (p) are optionally mono- or di-substituted with substituents selected from halogen, nitro, C_{1-6}alkyl, C_{1-6}alkoxy, halo C_{1-6}alkyl, C_{3-6}cycloalkyl, C_{3-6}cycloalkoxy, -NH(C_{1-6}alkyl), -NH(C_{3-6}cycloalkyl), -N(C_{1-6}alkyl)$_2$, -N(C_{3-6} cycloalkyl)$_2$, -S(=O)$_o$$C_{1-6}$alkyl, -S(=O)$_o$$C_{3-6}$cycloalkyl, and CN;

R^3 is selected from the group consisting of:

(a) hydrogen,
(b) halogen,
(c) CN,
(d) CF_3,
(e) -C_{1-6}alkyl,
(f) -C_{1-6}alkyl-C(=O)OH,
(g) -O-(R^7),
(h) -S(=O)$_o$$R^7$,
(i) -N(R^7)(R^8),
(j) -N(R^7)-C(=O)-(R^8),
(k) -N(R^7)-C(=O)-O-(R^8),
(l) -N(R^7)S(=O)$_2$(R^8),
(m) -C_{3-6}cycloalkyl,
(n) -C(=O)(R^7),
(o) aryl,
(p) heteroaryl,
(q) -OC(=O)N(R^7)(R^8),
(r) -S(=O)$_2$N(R^7)(R^8),
(s) -C(=O)N(R^7)(R^8),
(t) -C(R^7)(R^8)OH,
(u) -NHC(=O)-N(R^7)(R^8),
(v) -C_{3-6}cycloalkyl-COOH,
(w) heterocycle, and
(x) -C_{1-6}alkylC(=O)-N(R^7)(R^8),

wherein the alkyl portion of choices (e), (f) and (x), and the cycloalkyl portion of choices (m) and (v) are optionally substituted with halogen or hydroxyl, and

wherein the aryl of choice (o), the heteroaryl of choice (p), and the heterocycle of choice (w) are optionally mono- or di-substituted with substituents selected from halogen, nitro, C_{1-6} alkyl, C_{1-6}alkoxy, halo C_{1-6}alkyl, C_{3-6}cycloalkyl, C_{3-6}cycloalkoxy, -NH(C_{1-6}alkyl), -NH(C_{3-6} cycloalkyl), -N(C_{1-6}alkyl)$_2$, -N(C_{3-6}cycloalkyl)$_2$, -S(=O)$_o$$C_{1-6}$alkyl, -S(=O)$_o$$C_{3-6}$cycloalkyl, hydroxyl and CN;

R^4 and $R^{4'}$ are each independently selected from the group consisting of:

(a) hydrogen,
(b) -N(R^7)(R^8),
(c) -N(R^7)S(=O)$_2$$R^8$,
(d) -N(R^7)-C(=O)R^8,
(e) -N(R^7)C(=O)OR_8,
(f) -S(=O)$_o$$R^7$,
(g) -S(=O)$_2$N(R^7)(R^8),
(h) -C(=O)R^7,
(i) -C(=O)N(R^7)(R^8),
(j) -OC(=O)N(R^7)(R^8),
(k) -O-R^7,
(l) -C(R^7)(R^8)OH,
(m) -C_{1-4}alkyl-C(=O)NHS(=O)$_2$$R^7$,
(n) -C_{1-4}alkyl-S(=O)$_2$NHC(=O)R^7,
(o) -C_{1-4}alkyl-C(=O)-N(R^7)(R^8),
(p) -C_{1-4}alkyl-N(R^7)C(=O)(R^8),
(q) -C_{1-4}alkyl-N(R^7)S(=O)$_2$(R^8),
(r) -C_{1-4}alkyl-S(=O)$_2$N(R^7)(R^8),
(s) -C_{1-4}alkyl-N(R^7)C(=O)O(R^8)
(t) -C_{1-4}alkyl-O-C(=O)N(R^7)(R^8)
(u) -C_{1-4}alkyl-C(=O)(R^7),
(v) -C_{1-4}alkyl-C(R^7)(R^8)OH,
(w) -C_{1-4}alkyl-O(R^7),
(x) -C_{1-6}alkyl-C(=O)OH,
(y) -C_{2-6}alkenyl-C(=O)OH,
(z) -C_{3-6}cycloalkyl-C(=O)OH,
(aa) -C_{3-6}cycloalkyl-C(=O)NHS(=O)$_2$$R^7$,
(bb) -C_{3-6}cycloalkyl-S(=O)$_2$NHC(=O)R^7,
(cc) -C_{3-6}cycloalkyl-C(=O)-N(R^7)(R^8),
(dd) -C_{3-6}cycloalkyl-N(R^7)C(=O)(R^8),
(ee) -C_{3-6}cycloalkyl-N(R^7)S(=O)$_2$(R^8),

(ff) -C_{3-6}cycloalkyl-$S(=O)_2N(R^7)(R^8)$,
(gg) -C_{3-6}cycloalkyl-$N(R^7)C(=O)O(R^8)$,
(hh) -C_{3-6}cycloalkyl-O-$C(=O)N(R^7)(R^8)$,
(ii) -C_{3-6}cycloalkyl-$C(=O)(R^7)$,
(jj) -C_{3-6}cycloalkyl-$C(R^7)(R^8)OH$,
(kk) -C_{3-6}cycloalkyl-$O(R^7)$,
(ll) -C(=O)OH,
(mm) aryl,
(nn) heteroaryl,
(oo) -$C(=O)N(R^7)S(=O)_2(R^8)$,
(pp) -$S(=O)_2N(R^7)C(=O)(R^8)$,
(qq) -$NHS(=O)_2N(R^7)(R^8)$,
(rr) -$NHC(=O)N(R^7)(R^8)$,
(ss) -$CH(OH)$–$C(=O)$–$N(R^7)(R^8)$,
(tt) -$C(=O)$–$C(=O)$–$N(R^7)(R^8)$,
(uu) -C_{3-6}cycloalkyl,
(vv) -CF_3,
(ww) -C_{1-6}alkyl $N(R^7)(R^8)$,
(xx) -heterocycle,
(yy) -C_{1-6}alkyl,
(zz) halogen, and
(aaa) -O-C_{1-6}alkyl-$N(R^7)(R^8)$,

wherein the alkyl portion of choices (m), (n), (o), (p), (q), (r), (s), (t), (u), (v), (w), (x), (ww), (yy) and (aaa), the alkenyl portion of choice (y), and the cycloalkyl portion of choices (z), (aa), (bb), (cc), (dd), (ee), (ff), (gg), (hh), (ii), (jj), (kk) and (uu), are optionally mono- or di-substituted with halogen, CN, aryl, C_{1-6}alkyl, halo C_{1-6}alkyl, C_{3-6}cycloalkyl, C_{1-6}alkoxy, or C_{3-6} cycloalkoxy, and

wherein the aryl of choice (mm), the heteroaryl of choice (nn), and the heterocycle of choice (xx) are optionally mono- or di-substituted with substituents selected from halogen, nitro, C_{1-6}alkyl, C_{1-6}alkoxy, halo C_{1-6}alkyl, C_{3-6}cycloalkyl, C_{3-6}cycloalkoxy, -$NH(C_{1-6}$alkyl), -$NH(C_{3-6}$ cycloalkyl), -$N(C_{1-6}$alkyl$)_2$, -$N(C_{3-6}$cycloalkyl$)_2$, -$S(=O)_oC_{1-6}$alkyl, -$S(=O)_oC_{3-6}$cycloalkyl, hydroxyl and CN, or

wherein R^3 and R^4 or R^4 and $R^{4'}$ are joined together to form a 5- or 6-membered heterocyclic ring, said ring having one heteroatom selected from O and N, wherein said ring is optionally substituted with -C(=O)OH, or -C_{1-6}alkyl-C(=O)OH, with the proviso that at least one of R^3, R^4 and $R^{4'}$ is other than hydrogen;

R^5 is selected from the group consisting of:

(a) hydrogen,
(b) -C_{1-6}alkyl,
(c) -C_{1-4}alkyl(R^7),
(d) aryl,

(e) heteroaryl,
(f) -C_{3-6}cycloalkyl,
(g) -C_{3-6}cycloalkyl(R^7),
(h) -C_{3-6}cycloalkyl-O(R^7),
(i) -C_{1-4}alkyl-C_{3-6}cycloalkyl,
(j) C_{1-6}alkoxy, and
(k) C_{3-6}cycloalkoxy,

wherein the alkyl portion of choices (b), (c), (i) and (j), the cycloalkyl portion of choices (f), (g), (h), (i) and (k) are optionally substituted with halogen or C_{1-4}alkyl, and

wherein the aryl of choice (d) and the heteroaryl of choice (e), are optionally mono- or di-substituted with substituents selected from halogen, nitro, C_{1-6}alkyl, CF_3, C_{1-6}alkoxy, halo C_{1-6} alkyl, aryl, heteroaryl, C_{3-6}cycloalkyl, C_{3-6}cycloalkoxy, and CN;

R^6 is selected from the group consisting of:

(a) hydrogen,
(b) -C_{1-6}alkyl,
(c) -C_{1-6}alkylaryl,
(d) -C_{1-6}alkylheteroaryl,
(e) -S(=O)$_o$$C_{1-6}$alkyl($R^7$),
(f) -C(=O)C_{1-6}alkyl(R^7),
(g) -C_{3-6}cycloalkyl,
(h) aryl,
(i) hetereoaryl,
(j) -C(=O)C_{3-6}cycloalkyl(R^7),
(k) -S(=O)$_o$$C_{3-6}$cycloalkyl($R^7$), and
(l) -C_{1-6}alkyl(R^7),

wherein the alkyl portion of choices (b), (c), (d), (e), (f), and (l) and the cycloalkyl portion of choices (g), (j), and (k), are optionally substituted with halogen or C_{1-4}alkyl, and

wherein the aryl portion of choices (c) and (h), and the heteroaryl portion of choices (d) and (i), are optionally mono- or di-substituted with substituents selected from halogen, nitro, -CF_3, C_{1-6}alkyl, C_{1-6}alkoxy, halo C_{1-6}alkyl, C_{3-6}cycloalkyl, C_{3-6}cycloalkoxy, aryl, heteroaryl, heterocycle optionally substituted with halogen, -NH(C_{1-6}alkyl), -NH(C_{3-6}cycloalkyl), -N(C_{1-6} alkyl)$_2$, -N(C_{3-6}cycloalkyl)$_2$, -S(=O)$_o$$C_{1-6}$alkyl, S(=O)$_o$$C_{3-6}$cycloalkyl, and CN;

R^7 and R^8 are each independently selected from the following:

(a) hydrogen,
(b) -C_{1-6}alkyl,
(c) -C_{3-6}cycloalkyl,
(d) -aryl,
(e) -heteroaryl,

(f) -C_{1-6}alkylaryl,
(g) -C_{1-6}alkylheteroaryl,
(h) -C(=O)C_{1-6}alkyl,
(i) -$S(=O)_o$-aryl,
(j) -C_{1-6}alkyl-C_{3-6}cycloalkyl, and
(k) CF_3,

wherein the alkyl of choices (b), (f), (g), (h), and (j), and the cycloalkyl of choices (c) and (j), are each optionally mono-, di- or tri-substituted with halogen, and

wherein the aryl portion of choices (d), (f) and (i), and the heteroaryl portion of choices (e) and (g), are each optionally mono- or di-substituted with substituents selected from halogen, -C(=O)OH, -CF_3, -NHC(=O)CH_3, nitro, C_{1-6}alkyl, C_{1-6}alkoxy, halo C_{1-6}alkyl, C_{3-6}cycloalkyl, C_{3-6} cycloalkoxy, -NH(C_{1-3}alkyl), -NH(C_{3-6}cycloalkyl), -N(C_{1-3}alkyl)$_2$, -N(C_{3-6}cycloalkyl)$_2$, -$S(=O)_oC_{1-4}$alkyl, $S(=O)_oC_{3-6}$cycloalkyl, aryl, heteroaryl, hydroxyl, and CN;

R^9 and R^{10} are each independently selected from the following

(a) hydrogen,
(b) -C_{1-6}alkyl,
(c) -C_{3-6}cycloalkyl,
(d) halogen,
(e) -OC_{3-6}cycloalkyl,
(f) CF_3, and
(g) C_{1-6}alkoxy,

wherein the alkyl portion of choice (b) and the cycloalkyl portion of choices (c) and (e), are each optionally mono-, di- or tri- substituted with halogen; and

wherein each o is independently 0, 1, or 2.

~~2. A compound according Claim 1, or a pharmaceutically acceptable salt thereof, wherein: X is selected from the group consisting of -$(CH_2)_m$-, and -$(CH_2)_m$-O-$(CH_2)_n$-, optionally mono- or di-substituted with halo, where m + n is 2, 3 or 4.~~

~~3~~2. A compound according Claim ~~2~~1, or a pharmaceutically acceptable salt thereof, wherein:

X is selected from -$CH_2CH_2CH_2$-, or -$CF_2CH_2CH_2$-.

~~4. A compound according Claim 1, or a pharmaceutically acceptable salt thereof, wherein: A1 is a substituted phenyl or substituted pyridine.~~

~~5~~3. A compound according Claim 1, or a pharmaceutically acceptable salt thereof, wherein:

A2 is A2a and A2a is a substituted phenyl, substituted pyrimidine, substituted pyrazine, or substituted pyridine.

~~6. A compound according Claim 5, or a pharmaceutically acceptable salt thereof, wherein: A2a is a substituted phenyl, substituted pyrimidine, substituted pyrazine, or substituted pyridine.~~

~~7. A compound according Claim 1, or a pharmaceutically acceptable salt thereof, wherein: Y is O.~~

~~8~~4. A compound according Claim 1, or a pharmaceutically acceptable salt thereof, wherein:

R^1 and R^2 are each independently selected from the group consisting of:

(a) hydrogen,
(b) halogen,
(c) CN,
(d) CF_3,
(e) -$C_{1\text{-}6}$alkyl,
(f) -O-(R^7),
(g) -$C_{3\text{-}6}$cycloalkyl, and
(h) -N(R^7)(R^8),

wherein the alkyl portion of choice (e) and the cycloalkyl portion of choice (g) are optionally substituted with halogen.

~~9. A compound according Claim 8, or a pharmaceutically acceptable salt thereof, wherein:~~

~~R^1 and R^2 are each independently selected from:~~

~~(a) hydrogen,~~
~~(b) halogen,~~
~~(c) CF_3,~~
~~(d) -$C_{1\text{-}6}$alkyl, and~~
~~(e) -O-(R^7),~~

~~wherein the alkyl portion of choice (d) is optionally substituted with halogen.~~

~~10~~5. A compound according Claim ~~9~~1, or a pharmaceutically acceptable salt thereof, wherein:

R^1 and R^2 are each hydrogen.

~~11~~6. A compound according Claim 1, or a pharmaceutically acceptable salt thereof, wherein:

R_3 is selected from the group consisting of:

(a) hydrogen,
~~(b) halogen,~~
~~(c) CF_3,~~
~~(d) -$C_{1\text{-}6}$alkyl,~~
(~~e~~b) -O-(R^7),

~~(f) -S(=O)$_o$R^7;~~
~~(g) C$_{3-6}$cycloalkyl,~~
~~(h) aryl,~~
~~(i) heteroaryl,~~
~~(j) -S(=O)$_2$N(R^7)(R^8),~~
~~(k) -C(R^7)(R^8)OH,~~
~~(l) heterocycle, and~~
(~~m~~c) -N(R^7)S(=O)$_2$(R^8), and
(d) -C$_{1-6}$alkyl

wherein the alkyl portion of choice (d) ~~and the cycloalkyl portion of choice (g) are~~is optionally substituted with halogen or hydroxyl~~, and~~

~~wherein the aryl of choice (h), the heteroaryl of choice (i), and the heterocycle of choice (l) are optionally mono- or di-substituted with substituents selected from halogen, nitro, C$_{1-6}$ alkyl, C$_{1-6}$alkoxy, halo C$_{1-6}$alkyl, C$_{3-6}$cycloalkyl, C$_{3-6}$cycloalkoxy, -NH(C$_{1-6}$alkyl), -NH(C$_{3-6}$ cycloalkyl), -N(C$_{1-6}$alkyl)$_2$, -N(C$_{3-6}$cycloalkyl)$_2$, -S(=O)$_o$C$_{1-6}$alkyl, -S(=O)$_o$C$_{3-6}$cycloalkyl, hydroxyl and CN~~.

~~12. A compound according Claim 11, or a pharmaceutically acceptable salt thereof, wherein:~~

~~R^3 is selected from the group consisting of:~~
~~(a) hydrogen,~~
~~(b) -O-(R^7),~~
~~(c) -N(R^7)S(=O)$_2$(R^8), and~~
~~(d) C$_{1-6}$alkyl,~~

~~wherein the alkyl portion of choice (d) is optionally substituted with halogen or hydroxyl.~~

~~13~~7. A compound according Claim 1, or a pharmaceutically acceptable salt thereof, wherein:

R^4 and R$^{4'}$ are each independently selected from the group consisting of:
(a) hydrogen,
(b) -N(R^7)S(=O)$_2$R^8,
(c) -N(R^7)-C(=O)R^8,
(d) -S(=O)$_o$R^7,
(e) -S(=O)$_2$N(R^7)(R^8),
(f) -C(=O)N(R^7)(R^8),
(g) -O-(R^7),
(h) -C(R^7)(R^8)OH,
(i) -C$_{1-4}$alkyl-C(=O)NHS(=O)$_2$R^7,
(j) -C$_{1-4}$alkyl-S(=O)$_2$NHC(=O)R^7,
(k) -C$_{1-4}$alkyl-C(=O)-N(R^7)(R^8),
(l) -C$_{1-4}$alkyl-N(R^7)C(=O)(R^8),
(m) -C$_{1-4}$alkyl-N(R^7)S(=O)$_2$(R^8),

(n) -C_{1-4}alkyl-$S(=O)_2N(R^7)(R^8)$,
(o) -C_{1-4}alkyl-$C(R^7)(R^8)OH$,
(p) -C_{1-4}alkyl-$O(R^7)$,
(q) -C_{1-6}alkyl-C(=O)OH,
(r) -C_{2-6}alkenyl-C(=O)OH,
(s) -C_{3-6}cycloalkyl-C(=O)OH,
(t) -C_{3-6}cycloalkyl-$C(=O)NHS(=O)_2R^7$,
(u) -C_{3-6}cycloalkyl-$S(=O)_2NHC(=O)R^7$,
(v) -C_{3-6}cycloalkyl-$C(=O)$-$N(R^7)(R^8)$,
(w) -C_{3-6}cycloalkyl-$N(R^7)S(=O)_2(R^8)$,
(x) -C_{3-6}cycloalkyl-$S(=O)_2N(R^7)(R^8)$,
(y) -C_{3-6}cycloalkyl-$N(R^7)C(=O)O(R^8)$,
(z) -C_{3-6}cycloalkyl-$C(R^7)(R^8)OH$,
(aa) -C_{3-6}cycloalkyl-$O(R^7)$,
(bb) -C(=O)OH,
(cc) aryl,
(dd) heteroaryl,
(ee) -$C(=O)N(R^7)S(=O)_2(R^8)$,
(ff) -$S(=O)_2N(R^7)C(=O)(R^8)$,
(gg) -$NHS(=O)_2N(R^7)(R^8)$,
(hh) -$NHC(=O)N(R^7)(R^8)$,
(ii) C_{3-6}cycloalkyl,
(jj) CF_3,
(kk) heterocycle,
(ll) -C_{1-6}alkyl, and
(mm) halogen,

wherein the alkyl portion of choices (i), (j), (k), (l), (m), (n), (o), (p), (q), and (ll), the alkenyl portion of choice (r), and the cycloalkyl portion of choices (s), (t), (u), (v), (w), (x), (y), (z), and (aa) are optionally mono- or di-substituted with halogen, CN, aryl, C_{1-6}alkyl, halo C_{1-6} alkyl, C_{3-6}cycloalkyl, C_{1-6}alkoxy, or C_{3-6}cycloalkoxy and,

wherein the aryl of choice (cc), the heteroaryl of choice (dd), and the heterocycle of choice (kk) are optionally mono- or di-substituted with substituents selected from halogen, hydroxyl, nitro, C_{1-6}alkyl, C_{1-6}alkoxy, halo C_{1-6}alkyl, C_{3-6}cycloalkyl, C_{3-6}cycloalkoxy, -$NH(C_{1-6}$ alkyl), -$NH(C_{3-6}$cycloalkyl), -$N(C_{1-6}$alkyl$)_2$, -$N(C_{3-6}$cycloalkyl$)_2$, -$S(=O)_oC_{1-6}$alkyl, -$S(=O)_oC_{3-6}$ cycloalkyl, and CN.

~~14~~8. A compound according to Claim ~~13~~1, or a pharmaceutically acceptable salt thereof, wherein:

R^4 and $R^{4'}$ are each independently selected from the group consisting of:

(a)~~hydrogen,~~ -$C(R^7)(R^8)OH$,

(b) -$N(R^7)S(=O)_2R^8$,
~~(c) -$N(R^7)$-C(=O)R^8,~~
(~~d~~c) -O-(R^7),
~~(e) -$C(R^7)(R^8)$OH,~~
~~(f) -C_{1-4}alkyl-$S(=O)_2NHC(=O)R^7$,~~
~~(g) -C_{1-4}alkyl-$N(R^7)S(=O)_2(R^8)$,~~
~~(h) -C_{1-4}alkyl-$S(=O)_2N(R^7)(R^8)$,~~
~~(i) -C_{1-4}alkyl-$O(R^7)$,~~
(~~j~~d) -C_{1-6}alkyl-C(=O)OH,
~~(k) -C_{3-6}cycloalkyl-C(=O)OH,~~
~~(l) -C_{3-6}cycloalkyl-$N(R^7)S(=O)_2(R^8)$,~~
~~(m) -C_{3-6}cycloalkyl-$S(=O)_2N(R^7)(R^8)$,~~
~~(n) -C_{3-6}cycloalkyl-$O(R^7)$,~~
(~~o~~e) -C(=O)OH,
~~(o) -C(=O)OH,~~
~~(p) -$C(=O)N(R^7)S(=O)_2(R^8)$,~~
~~(q) -$S(=O)_2N(R^7)C(=O)(R^8)$,~~
(~~r~~f) -$NHS(=O)_2N(R^7)(R^8)$,
(~~s~~g) -C_{3-6}cycloalkyl,
(~~t~~h) CF_3,
(~~u~~i) heterocycle,
(~~v~~j) -C_{1-6}alkyl, and
(~~w~~k) halogen,

wherein the alkyl portion of choices ~~(f), (g), (h), (i), (j), and (v)~~(d) and (j), and the cycloalkyl portion of choice~~s~~ (~~k~~g), ~~(l), (m), (n), and (s),~~ are optionally mono- or di-substituted with halogen, CN, aryl, C_{1-6}alkyl, halo C_{1-6}alkyl, C_{3-6}cycloalkyl, C_{1-6}alkoxy, or C_{3-6}cycloalkoxy, and

wherein the heterocycle of choice (~~u~~i) is optionally mono- or di-substituted with substituents selected from halogen, hydroxyl, nitro, C_{1-6}alkyl, C_{1-6}alkoxy, halo C_{1-6}alkyl, C_{3-6} cycloalkyl, C_{3-6}cycloalkoxy, -$NH(C_{1-6}$alkyl), -$NH(C_{3-6}$cycloalkyl), -$N(C_{1-6}$alkyl)$_2$, -$N(C_{3-6}$ cycloalkyl)$_2$, -$S(=O)_oC_{1-6}$alkyl, -$S(=O)_oC_{3-6}$cycloalkyl and CN.

~~15. A compound according to Claim 14, or a pharmaceutically acceptable salt thereof wherein:~~

~~R^4 and $R^{4'}$ are each independently selected from the group consisting of:~~

~~(a) -$C(R^7)(R^8)$OH,~~
~~(b) -$N(R^7)S(=O)_2R^8$,~~
~~(c) -O-(R^7),~~
~~(d) -C_{1-6}alkyl-C(=O)OH,~~
~~(e) -C(=O)OH,~~
~~(f) -$NHS(=O)_2N(R^7)(R^8)$,~~
~~(g) -C_{3-6}cycloalkyl,~~

~~(h) CF_3,~~
~~(i) heterocycle,~~
~~(j) -C_{1-6}alkyl, and~~
~~(k) halogen,~~
~~wherein the alkyl portion of choices (d) and (j), and the cycloalkyl portion of choice (g) are optionally mono- or di-substituted with halogen, CN, aryl, C_{1-6}alkyl, halo C_{1-6}alkyl, C_{3-6} cycloalkyl, C_{1-6}alkoxy, or C_{3-6}cycloalkoxy, and~~
~~wherein the heterocycle of choice (i) is optionally mono- or di-substituted with substituents selected from halogen, hydroxyl, nitro, C_{1-6}alkyl, C_{1-6}alkoxy, halo C_{1-6}alkyl, C_{3-6} cycloalkyl, C_{3-6}cycloalkoxy, -NH(C_{1-6}alkyl), -NH(C_{3-6}cycloalkyl), -N(C_{1-6}alkyl)$_2$, -N(C_{3-6} cycloalkyl)$_2$, -S(=O)$_0$$C_{1-6}$alkyl, -S(=O)$_0$$C_{3-6}$cycloalkyl, and CN.~~

~~16~~9. A compound according Claim 1, or a pharmaceutically acceptable salt thereof, wherein:

R^5 is selected from the group consisting of:

(a) hydrogen,
(b) -C_{1-6}alkyl, and
(c) -C_{1-4}alkyl(R^7),
~~(d) aryl,~~
~~(e) heteroaryl,~~
~~(f) -C_{3-6}cycloalkyl, and~~
~~(g) -C_{1-4}alkyl-C_{3-6}cycloalkyl,~~

wherein the alkyl portion of choices (b)~~,~~ and (c) ~~, and (g), the cycloalkyl portion of choices (f) and (g),~~ ~~are~~ is optionally substituted with halogen or C_{1-4}alkyl~~, and~~

~~wherein the aryl of choice (d) and the heteroaryl of choice (e), is optionally mono- or di-substituted with substituents selected from halogen, nitro, C_{1-6}alkyl, CF_3, C_{1-6}alkoxy, halo C_{1-6} alkyl, aryl, heteroaryl, C_{3-6}cycloalkyl, C_{3-6}cycloalkoxy, and CN~~.

~~17. A compound according Claim 16, or a pharmaceutically acceptable salt thereof, wherein:~~

~~R^5 is selected from the group consisting of:~~
~~(a) hydrogen,~~
~~(b) -C_{1-6}alkyl, and~~
~~(c) -C_{1-4}alkyl(R^7),~~

~~wherein the alkyl portion of choices (b) and (c) is optionally substituted with halogen or C_{1-4}alkyl.~~

~~18~~10. A compound according Claim 1, or a pharmaceutically acceptable salt thereof, wherein:

R^6 is selected from the group consisting of:

(a) -C_{1-6}alkylaryl,
(b) -C_{1-6}alkylheteroaryl, and
~~(c) -C_{3-6}cycloalkyl,~~

~~(d) aryl,~~

~~(e) hetereoaryl, and~~

(~~f~~c) -C_{1-6}alkyl(R^7),

wherein the alkyl portion of choices (a), (b) and (~~f~~c), ~~and the cycloalkyl portion of choice (c)~~ ~~are~~ is optionally substituted with halogen or C_{1-4}alkyl, and

wherein the aryl portion of choice~~s~~ (a) ~~and (d)~~, and the heteroaryl portion of choice~~s~~ (b) ~~and (e)~~, are optionally mono- or di-substituted with substituents selected from halogen, nitro, CF_3, C_{1-6}alkyl, C_{1-6}alkoxy, halo C_{1-6}alkyl, C_{3-6}cycloalkyl, C_{3-6}cycloalkoxy, aryl, heteroaryl, heterocycle optionally substituted with halogen, -NH(C_{1-6}alkyl), -NH(C_{3-6}cycloalkyl), -N(C_{1-6} alkyl)$_2$, -N(C_{3-6}cycloalkyl)$_2$, -S(=O)$_o$$C_{1-6}$alkyl, -S(=O)$_o$$C_{3-6}$cycloalkyl, and CN.

~~19. A compound according to Claim 18, or a pharmaceutically acceptable salt thereof, wherein:~~

~~R^6 is selected from the group consisting of:~~

~~(a) -C_{1-6}alkylaryl,~~

~~(b) -C_{1-6}alkylheteroaryl, and~~

~~(c) -C_{1-6}alkyl(R^7),~~

~~wherein the alkyl portion of choices (a), (b), and (c) is optionally substituted with halogen or C_{1-4}alkyl, and~~

~~wherein the aryl portion of choice (a), and the heteroaryl portion of choice (b), are optionally mono- or di-substituted with substituents selected from halogen, nitro, CF_3, C_{1-6}alkyl, C_{1-6}alkoxy, halo C_{1-6}alkyl, C_{3-6}cycloalkyl, C_{3-6}cycloalkoxy, aryl, heteroaryl, heterocycle optionally substituted with halogen, -NH(C_{1-6}alkyl), -NH(C_{3-6}cycloalkyl), -N(C_{1-6}alkyl)$_2$, -N(C_{3-6} cycloalkyl)$_2$, -S(=O)$_o$$C_{1-6}$alkyl, -S(=O)$_o$$C_{3-6}$cycloalkyl, and CN.~~

~~20. A compound according Claim 1, or a pharmaceutically acceptable salt thereof, wherein:~~

~~R^7 and R^8 are each independently selected from the following:~~

~~(a) hydrogen,~~

~~(b) -C_{1-6}alkyl,~~

~~(c) C_{3-6}cycloalkyl,~~

~~(d) aryl,~~

~~(e) heteroaryl, and~~

~~(f) CF_3,~~

~~wherein the alkyl of choice (b) and the cycloalkyl of choice (c) are optionally mono-, di- or tri-substituted with halogen, and~~

~~wherein the aryl of choice (d) and the heteroaryl of choice (e) are optionally mono- or di-substituted with substituents selected from halogen, -C(=O)OH, CF_3, -NHC(=O) CH_3, nitro, C_{1-6}alkyl, C_{1-6}alkoxy, halo C_{1-6}alkyl, C_{3-6}cycloalkyl, C_{3-6}cycloalkoxy, -NH(C_{1-3}alkyl), -NH(C_{3-6} cycloalkyl), -N(C_{1-3}alkyl)$_2$, -N(C_{3-6}cycloalkyl)$_2$, -S(=O)$_o$$C_{1-4}$alkyl, -S(=O)$_o$$C_{3-6}$cycloalkyl, aryl, heteroaryl, hydroxyl, and CN.~~

~~21~~11. A compound according Claim 1, or a pharmaceutically acceptable salt thereof, wherein:

R^9 and R^{10} are each independently

(a) hydrogen,

(b) -C_{1-6}alkyl,

(c) halogen,

(d) CF_3, and

(e) C_{1-6}alkoxy,

wherein the alkyl of choice (b) is optionally mono-, di- or tri-substituted with halogen.

~~22. A compound according to Claim 1, or a pharmaceutically acceptable salt thereof, wherein: X is selected from the group consisting of -$(CH_2)_m$-, and -$(CH_2)_m$-O-$(CH_2)_n$-, optionally mono or di-substituted with halogen, where m + n is 2, 3 or 4;~~

~~Y is O;~~

~~A1 is a substituted phenyl or substituted pyridine;~~

~~A2 is A2a;~~

~~R^1 and R^2 are each independently selected from the group consisting of:~~

~~(a) hydrogen,~~

~~(b) halogen,~~

~~(c) CN,~~

~~(d) CF_3,~~

~~(e) -C_{1-6}alkyl,~~

~~(f) -O-(R^7),~~

~~(g) C_{3-6}cycloalkyl, and~~

~~(h) -N(R^7)(R^8),~~

~~wherein the alkyl portion of choice (e) and the cycloalkyl portion of choice (g) are optionally substituted with halogen;~~

~~R^3 is selected from the group consisting of:~~

~~(a) hydrogen,~~

~~(b) halogen,~~

~~(c) CF_3,~~

~~(d) -C_{1-6}alkyl,~~

~~(e) -O-(R^7),~~

~~(f) -S(=O)$_e$$R^7$,~~

~~(g) C_{3-6}cycloalkyl,~~

~~(h) aryl,~~

~~(i) heteroaryl,~~

~~(j) -S(=O)$_2$N(R^7)(R^8),~~

~~(k) -C(R^7)(R^8)OH,~~

(l) heterocycle, and

(m) $-N(R^7)S(=O)_2(R^8)$,

wherein the alkyl portion of choice (d) and the cycloalkyl portion of choice (g) are optionally substituted with halogen or hydroxyl, and

wherein the aryl of choice (h), the heteroaryl of choice (i), and the heterocycle of choice (l) are optionally mono- or di-substituted with substituents selected from halogen, nitro, C_{1-6}alkyl, C_{1-6}alkoxy, halo C_{1-6}alkyl, C_{3-6}cycloalkyl, C_{3-6}cycloalkoxy, $-NH(C_{1-6}$alkyl), $-NH(C_{3-6}$cycloalkyl), $-N(C_{1-6}$alkyl)$_2$, $-N(C_{3-6}$cycloalkyl)$_2$, $-S(=O)_oC_{1-6}$alkyl, $-S(=O)_oC_{3-6}$cycloalkyl, hydroxyl and CN;

R^4 and $R^{4'}$ are each independently selected from the group consisting of:

(a) hydrogen,

(b) $-N(R^7)S(=O)_2R^8$,

(c) $-N(R^7)-C(=O)R^8$,

(d) $-S(=O)_oR^7$,

(e) $-S(=O)_2N(R^7)(R^8)$,

(f) $-C(=O)N(R^7)(R^8)$,

(g) $-O-(R^7)$,

(h) $-C(R^7)(R^8)OH$,

(i) $-C_{1-4}$alkyl-$C(=O)NHS(=O)_2R^7$,

(j) $-C_{1-4}$alkyl-$S(=O)_2NHC(=O)R^7$,

(k) $-C_{1-4}$alkyl-$C(=O)-N(R^7)(R^8)$,

(l) $-C_{1-4}$alkyl-$N(R^7)C(=O)(R^8)$,

(m) $-C_{1-4}$alkyl-$N(R^7)S(=O)_2(R^8)$,

(n) $-C_{1-4}$alkyl-$S(=O)_2N(R^7)(R^8)$,

(o) $-C_{1-4}$alkyl-$C(R^7)(R^8)OH$,

(p) $-C_{1-4}$alkyl-$O(R^7)$,

(q) $-C_{1-6}$alkyl-$C(=O)OH$,

(r) $-C_{2-6}$alkenyl-$C(=O)OH$,

(s) $-C_{3-6}$cycloalkyl-$C(=O)OH$,

(t) $-C_{3-6}$cycloalkyl-$C(=O)NHS(=O)_2R^7$,

(u) $-C_{3-6}$cycloalkyl-$S(=O)_2NHC(=O)R^7$,

(v) $-C_{3-6}$cycloalkyl-$C(=O)-N(R^7)(R^8)$,

(w) $-C_{3-6}$cycloalkyl-$N(R^7)S(=O)_2(R^8)$,

(x) $-C_{3-6}$cycloalkyl-$S(=O)_2N(R^7)(R^8)$,

(y) $-C_{3-6}$cycloalkyl-$N(R^7)C(=O)O(R^8)$,

(z) $-C_{3-6}$cycloalkyl-$C(R^7)(R^8)OH$,

(aa) $-C_{3-6}$cycloalkyl-$O(R^7)$,

(bb) $-C(=O)OH$,

(cc) aryl,

(dd) heteroaryl,
(ee) -C(=O)N(R^7)S(=O)$_2$(R^8),
(ff) -S(=O)$_2$N(R^7)C(=O)(R^8),
(gg) -NHS(=O)$_2$N(R^7)(R^8),
(hh) -NHC(=O)N(R^7)(R^8),
(ii) C_{3-6}cycloalkyl,
(jj) CF_3,
(kk) heterocycle,
(ll) -C_{1-6}alkyl, and
(mm) halogen,

wherein the alkyl portion of choices (i), (j), (k), (l), (m), (n), (o), (p), (q), and (ll), the alkenyl portion of choice (r), and the cycloalkyl portion of choices (s), (t), (u), (v), (w), (x), (y), (z), and (aa) are optionally mono- or di-substituted with halogen, CN, aryl, C_{1-6}alkyl, halo C_{1-6} alkyl, C_{3-6}cycloalkyl, C_{1-6}alkoxy, or C_{3-6}cycloalkoxy and,

wherein the aryl of choice (cc), the heteroaryl of choice (dd), and the heterocycle of choice (kk) are optionally mono- or di-substituted with substituents selected from halogen, hydroxyl, nitro, C_{1-6}alkyl, C_{1-6}alkoxy, halo C_{1-6}alkyl, C_{3-6}cycloalkyl, C_{3-6}cycloalkoxy, -NH(C_{1-6} alkyl), -NH(C_{3-6}cycloalkyl), -N(C_{1-6}alkyl)$_2$, -N(C_{3-6}cycloalkyl)$_2$, -S(=O)$_6$$C_{1-6}$alkyl, -S(=O)$_6$$C_{3-6}$ cycloalkyl, and CN;

R^5 is selected from the group consisting of:
(a) hydrogen,
(b) -C_{1-6}alkyl,
(c) -C_{1-4}alkyl(R^7),
(d) aryl,
(e) heteroaryl,
(f) C_{3-6}cycloalkyl, and
(g) -C_{1-4}alkyl-C_{3-6}cycloalkyl,

wherein the alkyl portion of choices (b), (c) and (g), the cycloalkyl portion of choices (f) and (g), are optionally substituted with halogen or C_{1-4}alkyl, and

wherein the aryl of choice (d) and the heteroaryl of choice (e), are optionally mono- or di-substituted with substituents selected from halogen, nitro, C_{1-6}alkyl, CF_3, C_{1-6}alkoxy, halo C_{1-6} alkyl, aryl, heteroaryl, C_{3-6}cycloalkyl, C_{3-6}cycloalkoxy, and CN;

R^6 is selected from the group consisting of:
(a) -C_{1-6}alkylaryl,
(b) -C_{1-6}alkylheteroaryl,
(c) -C_{3-6}cycloalkyl,
(d) aryl,
(e) hetereoaryl, and
(f) -C_{1-6}alkyl(R^7),

~~wherein the alkyl portion of choices (a), (b) and (f), and the cycloalkyl portion of choice (c) are optionally substituted with halogen or C_{1-4}alkyl, and~~

~~wherein the aryl portion of choices (a) and (d), and the heteroaryl portion of choices (b) and (e), are optionally mono- or di-substituted with substituents selected from halogen, nitro, CF_3, C_{1-6}alkyl, C_{1-6}alkoxy, halo C_{1-6}alkyl, C_{3-6}cycloalkyl, C_{3-6}cycloalkoxy, aryl, heteroaryl, heterocycle optionally substituted with halogen, -NH(C_{1-6}alkyl), -NH(C_{3-6}cycloalkyl), -N(C_{1-6}alkyl)$_2$, -N(C_{3-6}cycloalkyl)$_2$, -S(=O)$_o$$C_{1-6}$alkyl, -S(=O)$_o$$C_{3-6}$cycloalkyl, and CN;~~

~~R^7 and R^8 are each independently selected from the following:~~

- ~~(a) hydrogen,~~
- ~~(b) -C_{1-6}alkyl,~~
- ~~(c) C_{3-6}cycloalkyl,~~
- ~~(d) aryl,~~
- ~~(e) heteroaryl, and~~
- ~~(f) CF_3,~~

~~wherein the alkyl of choice (b) and the cycloalkyl of choice (c) are optionally mono-, di- or tri-substituted with halo, and~~

~~wherein the aryl of choice (d) and the heteroaryl of choice (e) are optionally mono- or di-substituted with substituents selected from halogen, -C(=O)OH, CF_3, -NHC(=O)-CH_3, nitro, C_{1-6}alkyl, C_{1-6}alkoxy, haloC_{1-6}alkyl, C_{3-6}cycloalkyl, C_{3-6}cycloalkoxy, -NH(C_{1-3}alkyl), -NH(C_{3-6}cycloalkyl), -N(C_{1-3}alkyl)$_2$, -N(C_{3-6}cycloalkyl)$_2$, -S(=O)$_o$$C_{1-4}$alkyl, -S(=O)$_o$$C_{3-6}$cycloalkyl, aryl, heteroaryl, hydroxyl, and CN;~~

~~and~~

~~R^9 and R^{10} are each independently~~

- ~~(a) hydrogen,~~
- ~~(b) -C_{1-6}alkyl,~~
- ~~(c) halogen,~~
- ~~(d) CF_3, and~~
- ~~(e) C_{1-6}alkoxy,~~

~~wherein the alkyl of choice (b) is optionally mono-, di- or tri-substituted with halogen.~~

~~23~~12. A compound according to Claim ~~21~~11, or a pharmaceutically acceptable salt thereof, wherein:

A2 is A2a, and A2a is a substituted phenyl, substituted pyrimidine, substituted pyrazine, or substituted pyridine;

R^1 and R^2 are each independently selected from:

(a) hydrogen,
(b) halogen,
(c) CF_3,
(d) C_{1-6}alkyl, and
(e) -O-(R^7),

wherein the alkyl portion of choice (d) is optionally substituted with halogen;

R^3 is selected from the group consisting of:

(a) hydrogen,

(b) -O-(R^7),

(c) -N(R^7)S(=O)$_2$(R^8), and

(d) -C_{1-6}alkyl,

wherein the alkyl portion of choice (d) is optionally substituted with halogen or hydroxyl;

R^4 and $R^{4'}$ are each independently selected from the group consisting of:

~~(a) hydrogen,~~

~~(b) -N(R^7)S(=O)$_2$$R^8$,~~

~~(c) -N(R^7)-C(=O)R^8,~~

~~(d) -O-(R^7),~~

~~(e) -C(R^7)(R^8)OH,~~

~~(f) -C_{1-4}alkyl-S(=O)$_2$NHC(=O)R^7,~~

~~(g) -C_{1-4}alkyl-N(R^7)S(=O)$_2$(R^8),~~

~~(h) -C_{1-4}alkyl-S(=O)$_2$N(R^7)(R^8),~~

~~(i) -C_{1-4}alkyl-O(R^7),~~

~~(j) -C_{1-6}alkyl-C(=O)OH,~~

~~(k) -C_{3-6}cycloalkyl-C(=O)OH,~~

~~(l) -C_{3-6}cycloalkyl-N(R^7)S(=O)$_2$(R^8),~~

~~(m) -C_{3-6}cycloalkyl-S(=O)$_2$N(R^7)(R^8),~~

~~(n) -C_{3-6}cycloalkyl-O(R^7),~~

~~(o) -C(=O)OH,~~

~~(p) -C(=O)N(R^7)S(=O)$_2$(R^8),~~

~~(q) -S(=O)$_2$N(R^7)C(=O)(R^8),~~

~~(r) -NHS(=O)$_2$N(R^7)(R^8),~~

~~(s) -C_{3-6}cycloalkyl,~~

~~(t) CF_3,~~

~~(u) heterocycle,~~

~~(v) -C_{1-6}alkyl, and~~

~~(w) halogen,~~

~~wherein the alkyl portion of choices (f), (g), (h), (i), (j), and (v), and the cycloalkyl portion of choices (k), (l), (m), (n), and (s), are optionally mono- or di-substituted with halogen, CN, aryl, C_{1-6}alkyl, halo C_{1-6}alkyl, C_{3-6}cycloalkyl, C_{1-6}alkoxy, or C_{3-6}cycloalkoxy, and~~

~~wherein the heterocycle of choice (u) is optionally mono- or di-substituted with substituents selected from halogen, hydroxyl, nitro, C_{1-6}alkyl, C_{1-6}alkoxy, halo C_{1-6}alkyl, C_{3-6} cycloalkyl, C_{3-6}cycloalkoxy, -NH(C_{1-6}alkyl), -NH(C_{3-6}cycloalkyl), -N(C_{1-6}alkyl)$_2$, -N(C_{3-6} cycloalkyl)$_2$, S(=O)$_o$$C_{1-6}$alkyl, -S(=O)$_o$$C_{3-6}$cycloalkyl and CN;~~

(a) -C(R^7)(R^8)OH,

(b) -N(R^7)S(=O)$_2$$R^8$,

(c) -O-(R^7),

(d) -C_{1-6}alkyl-C(=O)OH,

(e) -C(=O)OH,

(f) -NHS(=O)$_2$N(R^7)(R^8),

(g) C_{3-6}cycloalkyl,

(h) CF_3,

(i) heterocycle,
(j) -C_{1-6}alkyl, and
(k) halogen,

wherein the alkyl portion of choices (d) and (j), and the cycloalkyl portion of choice (g) are optionally mono- or di-substituted with halo, CN, aryl, C_{1-6}alkyl, halo C_{1-6}alkyl, C_{3-6} cycloalkyl, C_{1-6}alkoxy, or C_{3-6}cycloalkoxy, and

wherein the heterocycle of choice (i) is optionally mono- or di-substituted with substituents selected from halogen, hydroxyl, nitro, C_{1-6}alkyl, C_{1-6}alkoxy, halo C_{1-6}alkyl, C_{3-6} cycloalkyl, C_{3-6}cycloalkoxy, -NH(C_{1-6}alkyl), -NH(C_{3-6}cycloalkyl), -N(C_{1-6}alkyl)$_2$, -N(C_{3-6} cycloalkyl)$_2$, -S(=O)$_o$$C_{1-6}$alkyl, -S(=O)$_o$$C_{3-6}$cycloalkyl, and CN;

R^5 is selected from the group consisting of:

(a) hydrogen,
(b) -C_{1-6}alkyl, and
(c) -C_{1-4}alkyl(R^7),

wherein the alkyl portion of choices (b) and (c) is optionally substituted with halogen or C_{1-4}alkyl;

R^6 is selected from the group consisting of:

(a) -C_{1-6}alkylaryl,
(b) -C_{1-6}alkylheteroaryl, and
(c) -C_{1-6}alkyl(R^7),

wherein the alkyl portion of choices (a), (b), and (c) is optionally substituted with halogen or C_{1-4}alkyl, and

wherein the aryl portion of choice (a), and the heteroaryl portion of choice (b), are optionally mono- or di-substituted with substituents selected from halogen, nitro, CF_3, C_{1-6}alkyl, C_{1-6}alkoxy, halo C_{1-6}alkyl, C_{3-6}cycloalkyl, C_{3-6}cycloalkoxy, aryl, heteroaryl, heterocycle optionally substituted with halogen, -NH(C_{1-6}alkyl), -NH(C_{3-6}cycloalkyl), -N(C_{1-6}alkyl)$_2$, -N(C_{3-6} cycloalkyl)$_2$, -S(=O)$_o$$C_{1-6}$alkyl, -S(=O)$_o$$C_{3-6}$cycloalkyl, and CN.

~~24. A compound according to Claim 23, or a pharmaceutically acceptable salt thereof, wherein:~~

~~R^4 and $R^{4'}$ are each independently selected from the group consisting of:~~

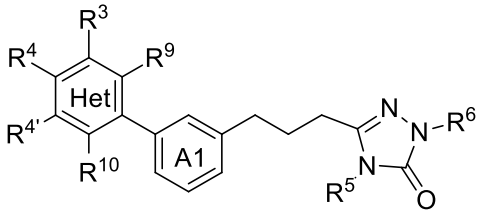
~~(a) -C(R^7)(R^8)OH,~~
~~(b) -N(R^7)S(=O)$_2$$R^8$,~~
~~(c) -O-(R^7),~~
~~(d) -C_{1-6}alkyl-C(=O)OH,~~
~~(e) -C(=O)OH,~~
~~(f) -NHS(=O)$_2$N(R^7)(R^8),~~
~~(g) C_{3-6}cycloalkyl,~~
~~(h) CF_3,~~
~~(i) heterocycle,~~
~~(j) -C_{1-6}alkyl, and~~
~~(k) halogen,~~

~~wherein the alkyl portion of choices (d) and (j), and the cycloalkyl portion of choice (g) are optionally mono- or di-substituted with halo, CN, aryl, C_{1-6}alkyl, halo C_{1-6}alkyl, C_{3-6} cycloalkyl, C_{1-6}alkoxy, or C_{3-6}cycloalkoxy, and~~

~~wherein the heterocycle of choice (i) is optionally mono- or di-substituted with substituents selected from halogen, hydroxyl, nitro, C_{1-6}alkyl, C_{1-6}alkoxy, halo C_{1-6}alkyl, C_{3-6}~~

~~cycloalkyl, C_{3-6}cycloalkoxy, $-NH(C_{1-6}alkyl)$, $-NH(C_{3-6}cycloalkyl)$, $-N(C_{1-6}alkyl)_2$, $-N(C_{3-6}cycloalkyl)_2$, $-S(=O)_eC_{1-6}alkyl$, $-S(=O)_eC_{3-6}cycloalkyl$, and CN.~~

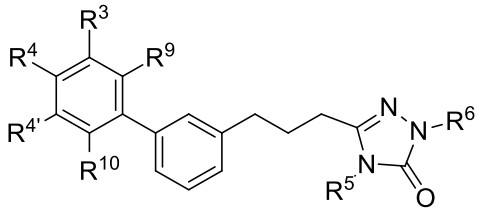
~~25~~13. A compound according to Claim ~~24~~ 12 of Formula 1a



1a

or a pharmaceutically acceptable salt thereof.

~~26~~14. A compound according to Claim ~~25~~ 13 of Formula 1b



1b

or a pharmaceutically acceptable salt thereof.

~~27~~15. A compound according to Claim 1 selected from the group consisting of:

2-(3'-(3-(1-(4-(*tert*-butyl)benzyl)-4-ethyl-5-oxo-4,5-dihydro-1*H*-1,2,4-triazol-3-yl)propyl)-[1,1'-biphenyl]-3-yl)acetic acid,

2-(3'-(3-(1-(4-(*tert*-butyl)benzyl)-4-ethyl-5-oxo-4,5-dihydro-1*H*-1,2,4-triazol-3-yl)propyl)-[1,1'-biphenyl]-4-yl)acetic acid,

3'-(3-(1-(4-(*tert*-butyl)benzyl)-4-ethyl-5-oxo-4,5-dihydro-1*H*-1,2,4-triazol-3-yl)propyl)-[1,1'-biphenyl]-3-carboxylic acid,

3'-(3-(1-(4-(*tert*-butyl)benzyl)-4-ethyl-5-oxo-4,5-dihydro-1*H*-1,2,4-triazol-3-yl)propyl)-[1,1'-biphenyl]-4-carboxylic acid,

1-(3'-(3-(1-(4-(*tert*-butyl)benzyl)-4-ethyl-5-oxo-4,5-dihydro-1*H*-1,2,4-triazol-3-yl)propyl)-4-ethoxy-[1,1'-biphenyl]-3-yl)cyclopropanecarboxylic acid,

2-(3'-(3-(1-(4-(*tert*-butyl)benzyl)-4-ethyl-5-oxo-4,5-dihydro-1*H*-1,2,4-triazol-3-yl)propyl)-4-ethoxy-[1,1'-biphenyl]-3-yl)acetic acid,

1-(3'-(3-(1-(4-(*tert*-butyl)benzyl)-4-ethyl-5-oxo-4,5-dihydro-1*H*-1,2,4-triazol-3-yl)propyl)-[1,1'-biphenyl]-3-yl)cyclopropanecarboxylic acid,

1-(3'-(3-(1-(4-(*tert*-butyl)benzyl)-4-ethyl-5-oxo-4,5-dihydro-1*H*-1,2,4-triazol-3-yl)propyl)-[1,1'-biphenyl]-4-yl)cyclopropanecarboxylic acid,

3'-(3-(1-(4-(*tert*-butyl)benzyl)-4-ethyl-5-oxo-4,5-dihydro-1*H*-1,2,4-triazol-3-yl)propyl)-4-methoxy-[1,1'-biphenyl]-3-carboxylic acid,

3'-(3-(1-(4-(*tert*-butyl)benzyl)-4-ethyl-5-oxo-4,5-dihydro-1*H*-1,2,4-triazol-3-yl)propyl)-4-ethoxy-[1,1'-biphenyl]-3-carboxylic acid,

2-(3'-(3-(1-(4-(*tert*-butyl)benzyl)-4-ethyl-5-oxo-4,5-dihydro-1*H*-1,2,4-triazol-3-yl)propyl)-4-propoxy-[1,1'-biphenyl]-3-yl)acetic acid,

N-(6-(3-(3-(1-(4-(*tert*-butyl)benzyl)-4-ethyl-5-oxo-4,5-dihydro-1*H*-1,2,4-triazol-3-yl)propyl)phenyl)pyridin-3-yl)benzenesulfonamide,

2-(3'-(3-(1-(4-(*tert*-butyl)benzyl)-4-ethyl-5-oxo-4,5-dihydro-1*H*-1,2,4-triazol-3-yl)propyl)-4-methoxy-[1,1'-biphenyl]-3-yl)acetic acid,

1-(3'-(3-(1-(4-(*tert*-butyl)benzyl)-4-ethyl-5-oxo-4,5-dihydro-1*H*-1,2,4-triazol-3-yl)propyl)-4-methyl-[1,1'-biphenyl]-3-yl)cyclopropanecarboxylic acid,

2-(4-(benzyloxy)-3'-(3-(1-(4-(*tert*-butyl)benzyl)-4-ethyl-5-oxo-4,5-dihydro-1*H*-1,2,4-triazol-3-yl)propyl)-[1,1'-biphenyl]-3-yl)acetic acid,

2-(3'-(3-(1-(4-(*tert*-butyl)benzyl)-4-ethyl-5-oxo-4,5-dihydro-1*H*-1,2,4-triazol-3-yl)propyl)-4-(cyclopropylmethoxy)-[1,1'-biphenyl]-3-yl)acetic acid,

2-(3'-(3-(1-(4-(*tert*-butyl)benzyl)-4-ethyl-5-oxo-4,5-dihydro-1*H*-1,2,4-triazol-3-yl)propyl)-4-fluoro-[1,1'-biphenyl]-3-yl)acetic acid,

2-(3'-(3-(1-(4-(*tert*-butyl)benzyl)-4-ethyl-5-oxo-4,5-dihydro-1*H*-1,2,4-triazol-3-yl)propyl)-6-ethoxy-[1,1'-biphenyl]-3-yl)acetic acid,

3'-(3-(1-(4-(*tert*-butyl)benzyl)-4-ethyl-5-oxo-4,5-dihydro-1*H*-1,2,4-triazol-3-yl)propyl)-4-propoxy-[1,1'-biphenyl]-3-carboxylic acid,

N-((3'-(3-(1-(4-(*tert*-butyl)benzyl)-4-ethyl-5-oxo-4,5-dihydro-1*H*-1,2,4-triazol-3-yl)propyl)-[1,1'-biphenyl]-3-yl)methyl)benzenesulfonamide,

3-(3'-(3-(1-(4-(*tert*-butyl)benzyl)-4-ethyl-5-oxo-4,5-dihydro-1*H*-1,2,4-triazol-3-yl)propyl)-4-methoxy-[1,1'-biphenyl]-3-yl)propanoic acid,

2-(3'-(3-(1-(4-(*tert*-butyl)benzyl)-4-ethyl-5-oxo-4,5-dihydro-1*H*-1,2,4-triazol-3-yl)-1,1-difluoropropyl)-4-ethoxy-[1,1'-biphenyl]-3-yl)acetic acid,

N-(6-(3-(3-(1-(4-(*tert*-butyl)benzyl)-4-ethyl-5-oxo-4,5-dihydro-1*H*-1,2,4-triazol-3-yl)-1,1-difluoropropyl)phenyl)pyridin-3-yl)benzenesulfonamide,

2-(5-(6-(3-(1-(4-(*tert*-butyl)benzyl)-4-ethyl-5-oxo-4,5-dihydro-1*H*-1,2,4-triazol-3-yl)propyl)pyridin-2-yl)-2-methoxyphenyl)acetic acid,

3-(3-(3'-(1*H*-tetrazol-5-yl)-[1,1'-biphenyl]-3-yl)propyl)-1-(4-(*tert*-butyl)benzyl)-4-ethyl-1*H*-1,2,4-triazol-5(4*H*)-one,

2-(5-(4-(3-(1-(4-(*tert*-butyl)benzyl)-4-ethyl-5-oxo-4,5-dihydro-1*H*-1,2,4-triazol-3-yl)propyl)pyrimidin-2-yl)-2-ethoxyphenyl)acetic acid,

2-(5-(6-(3-(1-(4-(*tert*-butyl)benzyl)-4-ethyl-5-oxo-4,5-dihydro-1*H*-1,2,4-triazol-3-yl)propyl)pyrimidin-4-yl)-2-ethoxyphenyl)acetic acid,

(3'-(3-(1-(4-(tert-Butyl)benzyl)-4-ethyl-5-oxo-4,5-dihydro-1H-1,2,4-triazol-3-yl)propyl)-3-methoxy-[1,1'-biphenyl]-4-yl)acetic acid,

(3'-(3-(1-(4-(tert-Butyl)benzyl)-4-ethyl-5-oxo-4,5-dihydro-1H-1,2,4-triazol-3-yl)propyl)-3-ethoxy-[1,1'-biphenyl]-4-yl)acetic acid,

(3'-(3-(1-(4-(tert-Butyl)benzyl)-4-ethyl-5-oxo-4,5-dihydro-1H-1,2,4-triazol-3-yl)propyl)-3-propoxy-[1,1'-biphenyl]-4-yl)acetic acid,

2-(3'-(3-(1-(4-(*tert*-butyl)benzyl)-4-ethyl-5-oxo-4,5-dihydro-1*H*-1,2,4-triazol-3-yl)propyl)-3-hydroxy-[1,1'-biphenyl]-4-yl)acetic acid,

2-(3'-(3-(1-(4-(*tert*-butyl)benzyl)-4-ethyl-5-oxo-4,5-dihydro-1*H*-1,2,4-triazol-3-yl)propyl)-4-isopropoxy-[1,1'-biphenyl]-3-yl)acetic acid, and

2-(3'-(3-(1-(4-(*tert*-butyl)benzyl)-4-ethyl-5-oxo-4,5-dihydro-1*H*-1,2,4-triazol-3-yl)propyl)-4-(2-(dimethylamino)ethoxy)-[1,1'-biphenyl]-3-yl)acetic acid,

or a pharmaceutically acceptable salt thereof.

~~28~~16. A compound according to Claim 1 selected from the group consisting of:

3'-(3-(1-(4-(tert-butyl)benzyl)-4-ethyl-5-oxo-4,5-dihydro-1H-1,2,4-triazol-3-yl)propyl)-[1,1'-biphenyl]-4-carboxylic acid;

2-(3'-(3-(1-(4-(tert-butyl)benzyl)-4-ethyl-5-oxo-4,5-dihydro-1H-1,2,4-triazol-3-yl)propyl)-4-ethoxy-[1,1'-biphenyl]-3-yl)acetic acid;

1-(3'-(3-(1-(4-(tert-butyl)benzyl)-4-ethyl-5-oxo-4,5-dihydro-1H-1,2,4-triazol-3-yl)propyl)-[1,1'-biphenyl]-3-yl)cyclopropanecarboxylic acid;

2-(3'-(3-(1-(4-(tert-butyl)benzyl)-4-ethyl-5-oxo-4,5-dihydro-1H-1,2,4-triazol-3-yl)propyl)-4-propoxy-[1,1'-biphenyl]-3-yl)acetic acid;

2-(3'-(3-(1-(4-(tert-butyl)benzyl)-4-ethyl-5-oxo-4,5-dihydro-1H-1,2,4-triazol-3-yl)propyl)-4-fluoro-[1,1'-biphenyl]-3-yl)acetic acid;

2-(3'-(3-(1-(4-(tert-butyl)benzyl)-4-ethyl-5-oxo-4,5-dihydro-1H-1,2,4-triazol-3-yl)-1,1-difluoropropyl)-4-ethoxy-[1,1'-biphenyl]-3-yl)acetic acid;

(3'-(3-(1-(4-(tert-Butyl)benzyl)-4-ethyl-5-oxo-4,5-dihydro-1H-1,2,4-triazol-3-yl)propyl)-3-ethoxy-[1,1'-biphenyl]-4-yl)acetic acid;

(3'-(3-(1-(4-(tert-Butyl)benzyl)-4-ethyl-5-oxo-4,5-dihydro-1H-1,2,4-triazol-3-yl)propyl)-3-propoxy-[1,1'-biphenyl]-4-yl)acetic acid,

or a pharmaceutically acceptable salt thereof.

~~A pharmaceutical composition comprising a compound according to Claim 1, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier.~~

~~29~~17. A pharmaceutical composition comprising a compound according to Claim 1, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier. ~~A method of treating a cancer in a mammal which is negatively impacted by diminution in its metabolism of fatty acid, through the adminstration of a therapeutically effective amount of a compound of Claim 1, or a pharmaceutically acceptable salt thereof, to the mammal in need thereof.~~

~~30~~18. A compound according to Claim 1 for use in treating a cancer in a mammal which is negatively impacted by diminution in its metabolism of fatty acid, through the adminstration of a therapeutically effective amount of a compound of Claim 1, or a pharmaceutically acceptable salt thereof, to the mammal in need thereof, ~~A method of treating a cancer in a mammal according to Claim 29,~~ wherein ~~the~~said cancer is selected from prostate, breast, ovarian, liver, kidney, colon, pancreatic, human chronic lymphocytic leukemia, and melanoma.

~~31. A method of treating cancer in a mammal involving the administration of a therapeutically effective amount of a compound according to Claim 1, or a pharmaceutically acceptable salt thereof, to the mammal in need thereof.~~

~~32. A method of preventing the onset of and/or recurrence of acute and chronic myeloid leukemia or other cancers in a mammal through the administration of a therapeutically effective amount of a compound according to Claim 1, or a pharmaceutically acceptable salt thereof, to the mammal in need thereof.~~