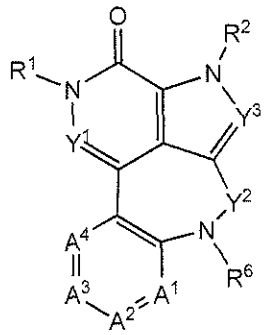
Accordingly, there is an ongoing medical need to develop new drugs to treat these indications.

SUMMARY

In one aspect the present ~~invention~~ disclosure relates to compounds of formula (I) or a salt thereof,



(I)

wherein

Y^1 is N or CH;

R^1 is CD_3, C_1-C_3 alkyl, or C_1-C_3 haloalkyl;

R^2 is H or C_1-C_3 alkyl;

Y^3 is N or CR^3;

R^3 is H, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, halogen, C_1-C_6 haloalkyl, -CN, $-C(O)R^{3a}$, $-C(O)OR^{3a}$, $-C(O)NR^{3b}R^{3c}$, $-S(O)R^{3d}$, $-S(O)_2R^{3a}$, $-S(O)_2NR^{3b}R^{3c}$, or G^1; wherein the C_1-C_6 alkyl, C_2-C_6 alkenyl, and C_2-C_6 alkynyl are each independently unsubstituted or substituted with 1 or 2 substituents independently selected from the group consisting of G^1, -CN, $-C(O)R^{3a}$, $-C(O)OR^{3a}$, $-C(O)NR^{3b}R^{3c}$, $-C(O)N(R^{3b})NR^{3b}R^{3c}$, $-S(O)R^{3d}$, $-S(O)_2R^{3a}$, $-S(O)_2NR^{3b}R^{3c}$, $-OR^{3a}$, $-OC(O)R^{3d}$, $-NR^{3b}R^{3c}$, $N(R^{3b})C(O)R^{3d}$, $N(R^{3b})SO_2R^{3d}$, $N(R^{3b})C(O)OR^{3d}$, $N(R^{3b})C(O)NR^{3b}R^{3c}$, $N(R^{3b})SO_2NR^{3b}R^{3c}$, and $N(R^{3b})C(NR^{3b}R^{3c})=NR^{3b}R^{3c}$;

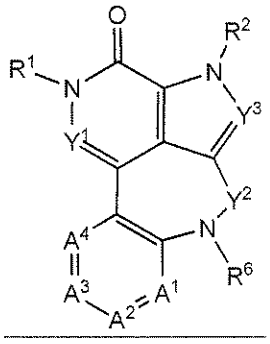
Y^2 is C(O), $S(O)_2$, or CR^4R^5;

R^4 is H, deuterium, C_1-C_6 alkyl, halogen, or C_1-C_6 haloalkyl;

R^5 is H, deuterium, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, halogen, C_1-C_6 haloalkyl, $-C(O)R^{5a}$, $-C(O)OR^{5a}$, $-C(O)NR^{5b}R^{5c}$, $-S(O)R^{5d}$, $-S(O)_2R^{5a}$, $-S(O)_2NR^{5b}R^{5c}$, or G^1; wherein the C_1-C_6 alkyl, C_2-C_6 alkenyl, and C_2-C_6 alkynyl are each independently unsubstituted or substituted with 1 or 2 substituents independently selected from the group consisting of G^1, -CN, $-C(O)R^{5a}$, $-C(O)OR^{5a}$, $-C(O)NR^{5b}R^{5c}$, $-C(O)N(R^{5b})NR^{5b}R^{5c}$, $-S(O)R^{5d}$, $-S(O)_2R^{5a}$, $-S(O)_2NR^{5b}R^{5c}$, $-OR^{5a}$, $-OC(O)R^{5d}$,

R^{z2}, at each occurrence, is independently C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, or C_1-C_6 haloalkyl.

In another aspect, the present disclosure provides a compound of formula (I) or a pharmaceutically acceptable salt thereof.



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Y^3 is N or CR^3;

R^3 is H, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, halogen, C_1-C_6 haloalkyl, $-C(O)R^{3a}$, $-C(O)OR^{3a}$, $-C(O)NR^{3b}R^{3c}$, $-S(O)R^{3d}$, $-S(O)_2R^{3a}$, $-S(O)_2NR^{3b}R^{3c}$, or G^1; wherein the C_1-C_6 alkyl, C_2-C_6 alkenyl, and C_2-C_6 alkynyl are each independently unsubstituted or substituted with 1 or 2 substituents independently selected from the group consisting of G^1, $-C(O)R^{3a}$, $-C(O)OR^{3a}$, $-C(O)NR^{3b}R^{3c}$, $-C(O)N(R^{3b})NR^{3b}R^{3c}$, $-S(O)R^{3d}$, $-S(O)_2R^{3a}$, $-S(O)_2NR^{3b}R^{3c}$, $-OR^{3a}$, $-OC(O)R^{3d}$, $-NR^{3b}R^{3c}$, $N(R^{3b})C(O)R^{3d}$, $N(R^{3b})SO_2R^{3d}$, $N(R^{3b})C(O)OR^{3d}$, $N(R^{3b})C(O)NR^{3b}R^{3c}$, $N(R^{3b})SO_2NR^{3b}R^{3c}$, and $N(R^{3b})C(NR^{3b}R^{3c})=NR^{3b}R^{3c}$;

Y^2 is C(O), $S(O)_2$, or CR^4R^5;

R^4 is H, deuterium, C_1-C_6 alkyl, halogen, or C_1-C_6 haloalkyl;

R^5 is H, deuterium, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, halogen, C_1-C_6 haloalkyl, $-C(O)R^{5a}$, $-C(O)OR^{5a}$, $-C(O)NR^{5b}R^{5c}$, $-S(O)R^{5d}$, $-S(O)_2R^{5a}$, $-S(O)_2NR^{5b}R^{5c}$, or G^1; wherein the C_1-C_6 alkyl, C_2-C_6 alkenyl, and C_2-C_6 alkynyl are each independently unsubstituted or substituted with 1 or 2 substituents independently selected from the group consisting of G^1, $-C(O)R^{5a}$, $-C(O)OR^{5a}$, $-C(O)NR^{5b}R^{5c}$, $-C(O)N(R^{5b})NR^{5b}R^{5c}$, $-S(O)R^{5d}$, $-S(O)_2R^{5a}$, $-S(O)_2NR^{5b}R^{5c}$, $-OR^{5a}$, $-OC(O)R^{5d}$, $-NR^{5b}R^{5c}$, $N(R^{5b})C(O)R^{5d}$, $N(R^{5b})SO_2R^{5d}$, $N(R^{5b})C(O)OR^{5d}$, $N(R^{5b})C(O)NR^{5b}R^{5c}$, $N(R^{5b})SO_2NR^{5b}R^{5c}$, and $N(R^{5b})C(NR^{5b}R^{5c})=NR^{5b}R^{5c}$;

R^{3a}, R^{3b}, R^{3c}, R^{5a}, R^{5b}, and R^{5c}, at each occurrence, are each independently H, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_1-C_6 haloalkyl, G^1, or -(C_1-C_6 alkylenyl)-G^1;

R^{3d} and R^{5d}, at each occurrence, are each independently C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_1-C_6 haloalkyl, G^1, or -(C_1-C_6 alkylenyl)-G^1;

G^1, at each occurrence, is independently aryl, heteroaryl, heterocycle, cycloalkyl, or cycloalkenyl; and each G^1 is optionally substituted with 1, 2, 3, 4, or 5 R^{1g} groups;

R^6 is H, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, halogen, C_1-C_6 haloalkyl, $-C(O)R^{6a}$, $-C(O)OR^{6a}$, $-C(O)NR^{6b}R^{6c}$, $-S(O)_2R^{6a}$, $-S(O)_2NR^{6b}R^{6c}$, or G^2; wherein the C_1-C_6 alkyl, C_2-C_6 alkenyl, and C_2-C_6 alkynyl are each independently unsubstituted or substituted with 1 or 2 substituents independently selected from the group consisting of G^2, $-C(O)R^{6a}$, $-C(O)OR^{6a}$, $-C(O)NR^{6b}R^{6c}$, $-C(O)N(R^{6b})NR^{6b}R^{6c}$, $-S(O)R^{6d}$, $-S(O)_2R^{6a}$, $-S(O)_2NR^{6b}R^{6c}$, $-OR^{6a}$, $-OC(O)R^{6d}$, $-NR^{6b}R^{6c}$, $N(R^{6b})C(O)R^{6d}$, $N(R^{6b})SO_2R^{6d}$, $N(R^{6b})C(O)OR^{6d}$, $N(R^{6b})C(O)NR^{6b}R^{6c}$, $N(R^{6b})SO_2NR^{6b}R^{6c}$, and $N(R^{6b})C(NR^{6b}R^{6c})=NR^{6b}R^{6c}$;

R^{6a}, R^{6b}, and R^{6c}, at each occurrence, are each independently H, alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, haloalkyl, G^2, -(C_1-C_6 alkylenyl)-G^2, –(C_1-C_6 alkylenyl)-OR^a, -(C_1-C_6 alkylenyl)-$S(O)_2R^a$, -(C_1-C_6 alkylenyl)-$S(O)_2NR^cR^d$, -(C_1-C_6 alkylenyl)-$C(O)R^a$, –(C_1-C_6 alkylenyl)-$C(O)OR^a$, -(C_1-C_6 alkylenyl)-$C(O)NR^cR^d$, -(C_1-C_6 alkylenyl)-NR^cR^d, -(C_1-C_6 alkylenyl)-$N(R^e)C(O)R^b$, -(C_1-C_6 alkylenyl)-$N(R^e)S(O)_2R^b$, –(C_1-C_6 alkylenyl)-$N(R^e)C(O)O(R^b)$, –(C_1-C_6 alkylenyl)-$N(R^e)C(O)NR^cR^d$, or -(C_1-C_6 alkylenyl)-$N(R^e)S(O)_2NR^cR^d$;

R^{6d}, at each occurrence, is independently alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, haloalkyl, G^2, -(C_1-C_6 alkylenyl)-G^2, –(C_1-C_6 alkylenyl)-OR^a, -(C_1-C_6 alkylenyl)-$S(O)_2R^a$, -(C_1-C_6 alkylenyl)-$S(O)_2NR^cR^d$, -(C_1-C_6 alkylenyl)-$C(O)R^a$, –(C_1-C_6 alkylenyl)-$C(O)OR^a$, -(C_1-C_6 alkylenyl)-$C(O)NR^cR^d$, -(C_1-C_6 alkylenyl)-NR^cR^d, -(C_1-C_6 alkylenyl)-$N(R^e)C(O)R^b$, -(C_1-C_6 alkylenyl)-$N(R^e)S(O)_2R^b$, –(C_1-C_6 alkylenyl)-$N(R^e)C(O)O(R^b)$, –(C_1-C_6 alkylenyl)-$N(R^e)C(O)NR^cR^d$, or -(C_1-C_6 alkylenyl)-$N(R^e)S(O)_2NR^cR^d$;

G^2, at each occurrence, is independently aryl, heteroaryl, heterocycle, cycloalkyl, or cycloalkenyl; and each G^2 is optionally substituted with 1, 2, 3, 4, or 5 R^{2g} groups;

A^1 is $C(R^7)$ or N; A^2 is $C(R^8)$ or N; A^3 is $C(R^9)$ or N; and A^4 is $C(R^{10})$ or N; wherein zero, one, or two of A^1, A^2, A^3, and A^4 are N;

R^7, R^8, and R^9, are each independently H, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, halogen, C_1-C_6 haloalkyl, -CN, NO_2, $-OR^{y1}$, $-OC(O)R^{y2}$, $-OC(O)NR^{y3}R^{y4}$, $-SR^{y1}$, $-S(O)_2R^{y1}$,

-$S(O)_2NR^{y3}R^{y4}$, -$C(O)R^{y1}$, -$C(O)OR^{y1}$, -$C(O)NR^{y3}R^{y4}$, -$NR^{y3}R^{y4}$, -$N(R^{y3})C(O)R^{y2}$, -$N(R^{y3})S(O)_2R^{y2}$, -$N(R^{y3})C(O)O(R^{y2})$, -$N(R^{y3})C(O)NR^{y3}R^{y4}$, -$N(R^{y3})S(O)_2NR^{y3}R^{y4}$, G^3, -(C_1-C_6 alkylenyl)-CN, -(C_1-C_6 alkylenyl)-OR^{y1}, -(C_1-C_6 alkylenyl)-$OC(O)R^{y2}$, -(C_1-C_6 alkylenyl)-$OC(O)NR^{y3}R^{y4}$, -(C_1-C_6 alkylenyl)-$S(O)_2R^{y1}$, -(C_1-C_6 alkylenyl)-$S(O)_2NR^{y3}R^{y4}$, -(C_1-C_6 alkylenyl)-$C(O)R^{y1}$, -(C_1-C_6 alkylenyl)-$C(O)OR^{y1}$, -(C_1-C_6 alkylenyl)-$C(O)NR^{y3}R^{y4}$, -(C_1-C_6 alkylenyl)-$NR^{y3}R^{y4}$, -(C_1-C_6 alkylenyl)-$N(R^{y3})C(O)R^{y2}$, -(C_1-C_6 alkylenyl)-$N(R^{y3})S(O)_2R^{y2}$, -(C_1-C_6 alkylenyl)-$N(R^{y3})C(O)O(R^{y2})$, -(C_1-C_6 alkylenyl)-$N(R^{y3})C(O)NR^{y3}R^{y4}$, -($C_1$-$C_6$ alkylenyl)-$N(R^{y3})S(O)_2NR^{y3}R^{y4}$, -($C_1$-$C_6$ alkylenyl)-CN, or -(C_1-C_6 alkylenyl)-G^3;

R^{y1}, R^{y3}, and R^{y4}, at each occurrence, are each independently H, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_1-C_6 haloalkyl, G^3, -(C_1-C_6 alkylenyl)-G^3, -(C_1-C_6 alkylenyl)-OR^a, -(C_1-C_6 alkylenyl)-$S(O)_2R^a$, -(C_1-C_6 alkylenyl)-$S(O)_2NR^cR^d$, -(C_1-C_6 alkylenyl)-$C(O)R^a$, -(C_1-C_6 alkylenyl)-$C(O)OR^a$, -(C_1-C_6 alkylenyl)-$C(O)NR^cR^d$, -(C_1-C_6 alkylenyl)-NR^cR^d, -(C_1-C_6 alkylenyl)-$N(R^e)C(O)R^b$, -(C_1-C_6 alkylenyl)-$N(R^e)S(O)_2R^b$, -(C_1-C_6 alkylenyl)-$N(R^e)C(O)O(R^b)$, -(C_1-C_6 alkylenyl)-$N(R^e)C(O)NR^cR^d$, or -(C_1-C_6 alkylenyl)-$N(R^e)S(O)_2NR^cR^d$;

R^{y2}, at each occurrence, is independently C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_1-C_6 haloalkyl, G^3, -(C_1-C_6 alkylenyl)-G^3, -(C_1-C_6 alkylenyl)-OR^a, -(C_1-C_6 alkylenyl)-$S(O)_2R^a$, -(C_1-C_6 alkylenyl)-$S(O)_2NR^cR^d$, -(C_1-C_6 alkylenyl)-$C(O)R^a$, -(C_1-C_6 alkylenyl)-$C(O)OR^a$, -(C_1-C_6 alkylenyl)-$C(O)NR^cR^d$, -(C_1-C_6 alkylenyl)-NR^cR^d, -(C_1-C_6 alkylenyl)-$N(R^e)C(O)R^b$, -(C_1-C_6 alkylenyl)-$N(R^e)S(O)_2R^b$, -(C_1-C_6 alkylenyl)-$N(R^e)C(O)O(R^b)$, -(C_1-C_6 alkylenyl)-$N(R^e)C(O)NR^cR^d$, or -(C_1-C_6 alkylenyl)-$N(R^e)S(O)_2NR^cR^d$;

G^3, at each occurrence, is independently aryl, heteroaryl, cycloalkyl, cycloalkenyl, or heterocycle; and each G^3 group is optionally substituted with 1, 2, 3, 4, or 5 R^{4g} groups;

R^{10} is H, C_1-C_3 alkyl, halogen, C_1-C_3 haloalkyl, or -CN;

R^{1g}, R^{2g}, and R^{4g}, at each occurrence, is independently selected from the group consisting of oxo, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, halogen, C_1-C_6 haloalkyl, -CN, NO_2, G^{2a}, -OR^a, -$OC(O)R^b$, -$OC(O)NR^cR^d$, -SR^a, -$S(O)_2R^a$, -$S(O)_2NR^cR^d$, -$C(O)R^a$, -$C(O)OR^a$, -$C(O)NR^cR^d$, -NR^cR^d, -$N(R^e)C(O)R^b$, -$N(R^e)S(O)_2R^b$, -$N(R^e)C(O)O(R^b)$, -$N(R^e)C(O)NR^cR^d$, -$N(R^e)S(O)_2NR^cR^d$, -(C_1-C_6 alkylenyl)-CN, -(C_1-C_6 alkylenyl)-G^{2a}, -(C_1-C_6 alkylenyl)-OR^a, -(C_1-C_6 alkylenyl)-$OC(O)R^b$, -(C_1-C_6 alkylenyl)-$OC(O)NR^cR^d$, -(C_1-C_6 alkylenyl)-$S(O)_2R^a$, -(C_1-C_6 alkylenyl)-$S(O)_2NR^cR^d$,

-(C_1-C_6 alkylenyl)-C(O)R^a, –(C_1-C_6 alkylenyl)-C(O)OR^a, -(C_1-C_6 alkylenyl)-C(O)NR^cR^d, -(C_1-C_6 alkylenyl)-NR^cR^d, -(C_1-C_6 alkylenyl)-N(R^e)C(O)R^b, -(C_1-C_6 alkylenyl)-N(R^e)S(O)$_2R^b$, –(C_1-C_6 alkylenyl)-N(R^e)C(O)O(R^b), –(C_1-C_6 alkylenyl)-N(R^e)C(O)NR^cR^d, –(C_1-C_6 alkylenyl)-N(R^e)S(O)$_2$NR^cR^d, or -(C_1-C_6 alkylenyl)-CN;

R^a, R^c, R^d, and R^e, at each occurrence, are each independently H, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_1-C_6 haloalkyl, G^{2a}, or –(C_1-C_6 alkylenyl)-G^{2a};

R^b, at each occurrence, is independently C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_1-C_6 haloalkyl, G^{2a}, or –(C_1-C_6 alkylenyl)-G^{2a};

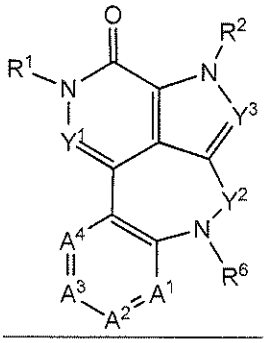
G^{2a}, at each occurrence, are each independently aryl, heteroaryl, heterocycle, cycloalkyl, or cycloalkenyl; and each G^{2a} group is optionally substituted with 1, 2, 3, 4, or 5 R^{3g} groups;

R^{3g}, at each occurrence, is independently oxo, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, halogen, C_1-C_6 haloalkyl, -CN, NO_2, -OR^{z1}, -OC(O)R^{z2}, -OC(O)N$R^{z3}R^{z4}$, -SR^{z1}, -S(O)$_2R^{z1}$, -S(O)$_2$N$R^{z3}R^{z4}$, -C(O)R^{z1}, -C(O)OR^{z1}, -C(O)N$R^{z3}R^{z4}$, -N$R^{z3}R^{z4}$, -N(R^{z3})C(O)R^{z2}, -N(R^{z3})S(O)$_2R^{z2}$, -N(R^{z3})C(O)O(R^{z2}), -N(R^{z3})C(O)N$R^{z3}R^{z4}$, -N(R^{z3})S(O)$_2$N$R^{z3}R^{z4}$, –(C_1-C_6 alkylenyl)-OR^{z1}, -(C_1-C_6 alkylenyl)-OC(O)R^{z2}, –(C_1-C_6 alkylenyl)-OC(O)N$R^{z3}R^{z4}$, -(C_1-C_6 alkylenyl)-S(O)$_2R^{z1}$, -(C_1-C_6 alkylenyl)-S(O)$_2$N$R^{z3}R^{z4}$, -(C_1-C_6 alkylenyl)-C(O)R^{z1}, –(C_1-C_6 alkylenyl)-C(O)OR^{z1}, -(C_1-C_6 alkylenyl)-C(O)N$R^{z3}R^{z4}$, -(C_1-C_6 alkylenyl)-N$R^{z3}R^{z4}$, -(C_1-C_6 alkylenyl)-N(R^{z3})C(O)R^{z2}, -(C_1-C_6 alkylenyl)-N(R^{z3})S(O)$_2R^{z2}$, –(C_1-C_6 alkylenyl)-N(R^{z3})C(O)O(R^{z2}), –(C_1-C_6 alkylenyl)-N(R^{z3})C(O)N$R^{z3}R^{z4}$, –(C_1-C_6 alkylenyl)-N(R^{z3})S(O)$_2$N$R^{z3}R^{z4}$, or –(C_1-C_6 alkylenyl)-CN;

R^{z1}, R^{z3}, and R^{z4}, at each occurrence, are each independently H, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, or C_1-C_6 haloalkyl; and

R^{z2}, at each occurrence, is independently C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, or C_1-C_6 haloalkyl.

In another aspect, the present disclosure provides a compound of formula (I) or a pharmaceutically acceptable salt thereof,



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Y^3 is N or CR^3;

R^3 is H, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, halogen, C_1-C_6 haloalkyl, -CN, $-C(O)R^{3a}$, $-C(O)OR^{3a}$, $-C(O)NR^{3b}R^{3c}$, $-S(O)R^{3d}$, $-S(O)_2R^{3a}$, $-S(O)_2NR^{3b}R^{3c}$, or G^1; wherein the C_1-C_6 alkyl, C_2-C_6 alkenyl, and C_2-C_6 alkynyl are each independently unsubstituted or substituted with 1 or 2 substituents independently selected from the group consisting of G^1, -CN, $-C(O)R^{3a}$, $-C(O)OR^{3a}$, $-C(O)NR^{3b}R^{3c}$, $-C(O)N(R^{3b})NR^{3b}R^{3c}$, $-S(O)R^{3d}$, $-S(O)_2R^{3a}$, $-S(O)_2NR^{3b}R^{3c}$, $-OR^{3a}$, $-OC(O)R^{3d}$, $-NR^{3b}R^{3c}$, $N(R^{3b})C(O)R^{3d}$, $N(R^{3b})SO_2R^{3d}$, $N(R^{3b})C(O)OR^{3d}$, $N(R^{3b})C(O)NR^{3b}R^{3c}$, $N(R^{3b})SO_2NR^{3b}R^{3c}$, and $N(R^{3b})C(NR^{3b}R^{3c})=NR^{3b}R^{3c}$;

Y^2 is C(O), $S(O)_2$, or CR^4R^5;

R^4 is H, deuterium, C_1-C_6 alkyl, halogen, or C_1-C_6 haloalkyl;

R^5 is H, deuterium, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, halogen, C_1-C_6 haloalkyl, $-C(O)R^{5a}$, $-C(O)OR^{5a}$, $-C(O)NR^{5b}R^{5c}$, $-S(O)R^{5d}$, $-S(O)_2R^{5a}$, $-S(O)_2NR^{5b}R^{5c}$, or G^1; wherein the C_1-C_6 alkyl, C_2-C_6 alkenyl, and C_2-C_6 alkynyl are each independently unsubstituted or substituted with 1 or 2 substituents independently selected from the group consisting of G^1, $-C(O)R^{5a}$, $-C(O)OR^{5a}$, $-C(O)NR^{5b}R^{5c}$, $-C(O)N(R^{5b})NR^{5b}R^{5c}$, $-S(O)R^{5d}$, $-S(O)_2R^{5a}$, $-S(O)_2NR^{5b}R^{5c}$, $-OR^{5a}$, $-OC(O)R^{5d}$, $-NR^{5b}R^{5c}$, $N(R^{5b})C(O)R^{5d}$, $N(R^{5b})SO_2R^{5d}$, $N(R^{5b})C(O)OR^{5d}$, $N(R^{5b})C(O)NR^{5b}R^{5c}$, $N(R^{5b})SO_2NR^{5b}R^{5c}$, and $N(R^{5b})C(NR^{5b}R^{5c})=NR^{5b}R^{5c}$;

R^{3a}, R^{3b}, R^{3c}, R^{5a}, and R^{5b}, at each occurrence, are each independently H, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_1-C_6 haloalkyl, G^1, or -(C_1-C_6 alkylenyl)-G^1;

R^{5c}, at each occurrence, is independently H, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_1-C_6 haloalkyl, G^1, -(C_1-C_6 alkylenyl)-G^1, -(C_1-C_6 alkylenyl)-CN, -(C_1-C_6 alkylenyl)-OR^a, or -(C_1-C_6 alkylenyl)-C(O)OR^a;

R^{3d}, at each occurrence, is independently C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_1-C_6 haloalkyl, G^1, or -(C_1-C_6 alkylenyl)-G^1;

R^{5d}, at each occurrence, is independently C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_1-C_6 haloalkyl, G^1, -(C_1-C_6 alkylenyl)-G^1, -(C_1-C_6 alkylenyl)-NR^cR^d, or –(C_1-C_6 alkylenyl)-N(R^e)C(O)O(R^b);

G^1, at each occurrence, is independently aryl, heteroaryl, heterocycle, cycloalkyl, or cycloalkenyl; and each G^1 is optionally substituted with 1, 2, 3, 4, or 5 R^{1g} groups;

R^6 is H, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, halogen, C_1-C_6 haloalkyl, -C(O)R^{6a}, -C(O)OR^{6a}, -C(O)$NR^{6b}R^{6c}$, -$S(O)_2R^{6a}$, -$S(O)_2NR^{6b}R^{6c}$, or G^2; wherein the C_1-C_6 alkyl, C_2-C_6 alkenyl, and C_2-C_6 alkynyl are each independently unsubstituted or substituted with 1 or 2 substituents independently selected from the group consisting of G^2, -C(O)R^{6a}, -C(O)OR^{6a}, -C(O)$NR^{6b}R^{6c}$, -C(O)N(R^{6b})$NR^{6b}R^{6c}$, -S(O)R^{6d}, -$S(O)_2R^{6a}$, -$S(O)_2NR^{6b}R^{6c}$, -OR^{6a}, -OC(O)R^{6d}, –$NR^{6b}R^{6c}$, N(R^{6b})C(O)R^{6d}, N(R^{6b})SO_2R^{6d}, N(R^{6b})C(O)OR^{6d}, N(R^{6b})C(O)$NR^{6b}R^{6c}$, N(R^{6b})$SO_2NR^{6b}R^{6c}$, and N(R^{6b})C($NR^{6b}R^{6c}$)=$NR^{6b}R^{6c}$;

R^{6a}, R^{6b}, and R^{6c}, at each occurrence, are each independently H, alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, haloalkyl, G^2, -(C_1-C_6 alkylenyl)-G^2, –(C_1-C_6 alkylenyl)-OR^a, -(C_1-C_6 alkylenyl)-$S(O)_2R^a$, -(C_1-C_6 alkylenyl)-$S(O)_2NR^cR^d$, -(C_1-C_6 alkylenyl)-C(O)R^a, –(C_1-C_6 alkylenyl)-C(O)OR^a, -(C_1-C_6 alkylenyl)-C(O)NR^cR^d, -(C_1-C_6 alkylenyl)-NR^cR^d, -(C_1-C_6 alkylenyl)-N(R^e)C(O)R^b, -(C_1-C_6 alkylenyl)-N(R^e)$S(O)_2R^b$, –(C_1-C_6 alkylenyl)-N(R^e)C(O)O(R^b), –(C_1-C_6 alkylenyl)-N(R^e)C(O)NR^cR^d, or -(C_1-C_6 alkylenyl)-N(R^e)$S(O)_2NR^cR^d$;

R^{6d}, at each occurrence, is independently alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, haloalkyl, G^2, -(C_1-C_6 alkylenyl)-G^2, –(C_1-C_6 alkylenyl)-OR^a, -(C_1-C_6 alkylenyl)-$S(O)_2R^a$, -(C_1-C_6 alkylenyl)-$S(O)_2NR^cR^d$, -(C_1-C_6 alkylenyl)-C(O)R^a, –(C_1-C_6 alkylenyl)-C(O)OR^a, -(C_1-C_6 alkylenyl)-C(O)NR^cR^d, -(C_1-C_6 alkylenyl)-NR^cR^d, -(C_1-C_6 alkylenyl)-N(R^e)C(O)R^b, -(C_1-C_6 alkylenyl)-N(R^e)$S(O)_2R^b$, –(C_1-C_6 alkylenyl)-N(R^e)C(O)O(R^b), –(C_1-C_6 alkylenyl)-N(R^e)C(O)NR^cR^d, or -(C_1-C_6 alkylenyl)-N(R^e)$S(O)_2NR^cR^d$;

G^2, at each occurrence, is independently aryl, heteroaryl, heterocycle, cycloalkyl, or cycloalkenyl; and each G^2 is optionally substituted with 1, 2, 3, 4, or 5 R^{2g} groups;

A^1 is $C(R^7)$ or N; A^2 is $C(R^8)$ or N; A^3 is $C(R^9)$ or N; and A^4 is $C(R^{10})$ or N; wherein zero, one, or two of A^1, A^2, A^3, and A^4 are N;

R^7, R^8, and R^9, are each independently H, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, halogen, C_1-C_6 haloalkyl, -CN, NO_2, $-OR^{y1}$, $-OC(O)R^{y2}$, $-OC(O)NR^{y3}R^{y4}$, $-SR^{y1}$, $-S(O)_2R^{y1}$, $-S(O)_2NR^{y3}R^{y4}$, $-C(O)R^{y1}$, $-C(O)OR^{y1}$, $-C(O)NR^{y3}R^{y4}$, $-NR^{y3}R^{y4}$, $-N(R^{y3})C(O)R^{y2}$, $-N(R^{y3})S(O)_2R^{y2}$, $-N(R^{y3})C(O)O(R^{y2})$, $-N(R^{y3})C(O)NR^{y3}R^{y4}$, $-N(R^{y3})S(O)_2NR^{y3}R^{y4}$, G^3, -(C_1-C_6 alkylenyl)-CN, -(C_1-C_6 alkylenyl)-OR^{y1}, -(C_1-C_6 alkylenyl)-$OC(O)R^{y2}$, -(C_1-C_6 alkylenyl)-$OC(O)NR^{y3}R^{y4}$, -(C_1-C_6 alkylenyl)-$S(O)_2R^{y1}$, -(C_1-C_6 alkylenyl)-$S(O)_2NR^{y3}R^{y4}$, -(C_1-C_6 alkylenyl)-$C(O)R^{y1}$, -(C_1-C_6 alkylenyl)-$C(O)OR^{y1}$, -(C_1-C_6 alkylenyl)-$C(O)NR^{y3}R^{y4}$, -(C_1-C_6 alkylenyl)-$NR^{y3}R^{y4}$, -(C_1-C_6 alkylenyl)-$N(R^{y3})C(O)R^{y2}$, -(C_1-C_6 alkylenyl)-$N(R^{y3})S(O)_2R^{y2}$, -(C_1-C_6 alkylenyl)-$N(R^{y3})C(O)O(R^{y2})$, -(C_1-C_6 alkylenyl)-$N(R^{y3})C(O)NR^{y3}R^{y4}$, -($C_1$-$C_6$ alkylenyl)-$N(R^{y3})S(O)_2NR^{y3}R^{y4}$, -($C_1$-$C_6$ alkylenyl)-CN, or -(C_1-C_6 alkylenyl)-G^3;

R^{y1}, R^{y3}, and R^{y4}, at each occurrence, are each independently H, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_1-C_6 haloalkyl, G^3, -(C_1-C_6 alkylenyl)-G^3, -(C_1-C_6 alkylenyl)-OR^a, -(C_1-C_6 alkylenyl)-$S(O)_2R^a$, -(C_1-C_6 alkylenyl)-$S(O)_2NR^cR^d$, -(C_1-C_6 alkylenyl)-$C(O)R^a$, -(C_1-C_6 alkylenyl)-$C(O)OR^a$, -(C_1-C_6 alkylenyl)-$C(O)NR^cR^d$, -(C_1-C_6 alkylenyl)-NR^cR^d, -(C_1-C_6 alkylenyl)-$N(R^e)C(O)R^b$, -(C_1-C_6 alkylenyl)-$N(R^e)S(O)_2R^b$, -(C_1-C_6 alkylenyl)-$N(R^e)C(O)O(R^b)$, -(C_1-C_6 alkylenyl)-$N(R^e)C(O)NR^cR^d$, or -(C_1-C_6 alkylenyl)-$N(R^e)S(O)_2NR^cR^d$;

R^{y2}, at each occurrence, is independently C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_1-C_6 haloalkyl, G^3, -(C_1-C_6 alkylenyl)-G^3, -(C_1-C_6 alkylenyl)-OR^a, -(C_1-C_6 alkylenyl)-$S(O)_2R^a$, -(C_1-C_6 alkylenyl)-$S(O)_2NR^cR^d$, -(C_1-C_6 alkylenyl)-$C(O)R^a$, -(C_1-C_6 alkylenyl)-$C(O)OR^a$, -(C_1-C_6 alkylenyl)-$C(O)NR^cR^d$, -(C_1-C_6 alkylenyl)-NR^cR^d, -(C_1-C_6 alkylenyl)-$N(R^e)C(O)R^b$, -(C_1-C_6 alkylenyl)-$N(R^e)S(O)_2R^b$, -(C_1-C_6 alkylenyl)-$N(R^e)C(O)O(R^b)$, -(C_1-C_6 alkylenyl)-$N(R^e)C(O)NR^cR^d$, or -(C_1-C_6 alkylenyl)-$N(R^e)S(O)_2NR^cR^d$;

G^3, at each occurrence, is independently aryl, heteroaryl, cycloalkyl, cycloalkenyl, or heterocycle; and each G^3 group is optionally substituted with 1, 2, 3, 4, or 5 R^{4g} groups;

R^{10} is H, C_1-C_3 alkyl, halogen, C_1-C_3 haloalkyl, or -CN;

R^{1g}, R^{2g}, and R^{4g}, at each occurrence, is independently selected from the group consisting of oxo, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, halogen, C_1-C_6 haloalkyl, -CN, NO_2, G^{2a}, $-OR^a$, $-OC(O)R^b$, $-OC(O)NR^cR^d$, $-SR^a$, $-S(O)_2R^a$, $-S(O)_2NR^cR^d$, $-C(O)R^a$,

-C(O)OR^a, -C(O)NR^{c}R^d, -NR^{c}R^d, -N(R^e)C(O)R^b, -N(R^e)S(O)$_2$R^b, -N(R^e)C(O)O(R^b), -N(R^e)C(O)NR^{c}R^d, -N(R^e)S(O)$_2$NR^{c}R^d, –(C$_1$-C$_6$ alkylenyl)-CN, –(C$_1$-C$_6$ alkylenyl)-G^{2a}, –(C$_1$-C$_6$ alkylenyl)-OR^a, -(C$_1$-C$_6$ alkylenyl)-OC(O)R^b, -(C$_1$-C$_6$ alkylenyl)-OC(O)NR^{c}R^d, -(C$_1$-C$_6$ alkylenyl)-S(O)$_2$R^a, -(C$_1$-C$_6$ alkylenyl)-S(O)$_2$NR^{c}R^d, -(C$_1$-C$_6$ alkylenyl)-C(O)R^a, –(C$_1$-C$_6$ alkylenyl)-C(O)OR^a, -(C$_1$-C$_6$ alkylenyl)-C(O)NR^{c}R^d, -(C$_1$-C$_6$ alkylenyl)-NR^{c}R^d, -(C$_1$-C$_6$ alkylenyl)-N(R^e)C(O)R^b, -(C$_1$-C$_6$ alkylenyl)-N(R^e)S(O)$_2$R^b, –(C$_1$-C$_6$ alkylenyl)-N(R^e)C(O)O(R^b), –(C$_1$-C$_6$ alkylenyl)-N(R^e)C(O)NR^{c}R^d, –(C$_1$-C$_6$ alkylenyl)-N(R^e)S(O)$_2$NR^{c}R^d, or -(C$_1$-C$_6$ alkylenyl)-CN;

R^a, R^c, R^d, and R^e, at each occurrence, are each independently H, C$_1$-C$_6$ alkyl, C$_2$-C$_6$ alkenyl, C$_2$-C$_6$ alkynyl, C$_1$-C$_6$ haloalkyl, G^{2a}, or –(C$_1$-C$_6$ alkylenyl)-G^{2a};

R^b, at each occurrence, is independently C$_1$-C$_6$ alkyl, C$_2$-C$_6$ alkenyl, C$_2$-C$_6$ alkynyl, C$_1$-C$_6$ haloalkyl, G^{2a}, or –(C$_1$-C$_6$ alkylenyl)-G^{2a};

G^{2a}, at each occurrence, are each independently aryl, heteroaryl, heterocycle, cycloalkyl, or cycloalkenyl; and each G^{2a} group is optionally substituted with 1, 2, 3, 4, or 5 R^{3g} groups;

R^{3g}, at each occurrence, is independently oxo, C$_1$-C$_6$ alkyl, C$_2$-C$_6$ alkenyl, C$_2$-C$_6$ alkynyl, halogen, C$_1$-C$_6$ haloalkyl, -CN, NO$_2$, -OR^{z1}, -OC(O)R^{z2}, -OC(O)NR^{z3}R^{z4}, -SR^{z1}, -S(O)$_2$R^{z1}, -S(O)$_2$NR^{z3}R^{z4}, -C(O)R^{z1}, -C(O)OR^{z1}, -C(O)NR^{z3}R^{z4}, -NR^{z3}R^{z4}, -N(R^{z3})C(O)R^{z2}, -N(R^{z3})S(O)$_2$R^{z2}, -N(R^{z3})C(O)O(R^{z2}), -N(R^{z3})C(O)NR^{z3}R^{z4}, -N(R^{z3})S(O)$_2$NR^{z3}R^{z4}, –(C$_1$-C$_6$ alkylenyl)-OR^{z1}, -(C$_1$-C$_6$ alkylenyl)-OC(O)R^{z2}, –(C$_1$-C$_6$ alkylenyl)-OC(O)NR^{z3}R^{z4}, -(C$_1$-C$_6$ alkylenyl)-S(O)$_2$R^{z1}, -(C$_1$-C$_6$ alkylenyl)-S(O)$_2$NR^{z3}R^{z4}, -(C$_1$-C$_6$ alkylenyl)-C(O)R^{z1}, –(C$_1$-C$_6$ alkylenyl)-C(O)OR^{z1}, -(C$_1$-C$_6$ alkylenyl)-C(O)NR^{z3}R^{z4}, -(C$_1$-C$_6$ alkylenyl)-NR^{z3}R^{z4}, -(C$_1$-C$_6$ alkylenyl)-N(R^{z3})C(O)R^{z2}, -(C$_1$-C$_6$ alkylenyl)-N(R^{z3})S(O)$_2$R^{z2}, –(C$_1$-C$_6$ alkylenyl)-N(R^{z3})C(O)O(R^{z2}), –(C$_1$-C$_6$ alkylenyl)-N(R^{z3})C(O)NR^{z3}R^{z4}, –(C$_1$-C$_6$ alkylenyl)-N(R^{z3})S(O)$_2$NR^{z3}R^{z4}, or –(C$_1$-C$_6$ alkylenyl)-CN;

R^{z1}, R^{z3}, and R^{z4}, at each occurrence, are each independently H, C$_1$-C$_6$ alkyl, C$_2$-C$_6$ alkenyl, C$_2$-C$_6$ alkynyl, or C$_1$-C$_6$ haloalkyl; and

R^{z2}, at each occurrence, is independently C$_1$-C$_6$ alkyl, C$_2$-C$_6$ alkenyl, C$_2$-C$_6$ alkynyl, or C$_1$-C$_6$ haloalkyl.

In another aspect, the present ~~invention~~ disclosure provides for methods for treating or preventing disorders that are ameliorated by inhibition of BET. Such methods comprise of

administering to the subject a therapeutically effective amount of a compound of formula (I), alone, or in combination with a pharmaceutically acceptable carrier.

Some of the methods are directed to treating or preventing an inflammatory disease or cancer or AIDS.

In another aspect, the present ~~invention~~ disclosure relates to methods of treating cancer in a subject comprising administering a therapeutically effective amount of a compound of formula (I) or a pharmaceutically acceptable salt thereof, to a subject in need thereof. In certain embodiments, the cancer is selected from the group consisting of: acoustic neuroma, acute leukemia, acute lymphocytic leukemia, acute myelocytic leukemia (monocytic, myeloblastic, adenocarcinoma, angiosarcoma, astrocytoma, myelomonocytic and promyelocytic), acute t-cell leukemia, basal cell carcinoma, bile duct carcinoma, bladder cancer, brain cancer, breast cancer, bronchogenic carcinoma, cervical cancer, chondrosarcoma, chordoma, choriocarcinoma, chronic leukemia, chronic lymphocytic leukemia, chronic myelocytic (granulocytic) leukemia, chronic myelogenous leukemia, colon cancer, colorectal cancer, craniopharyngioma, cystadenocarcinoma, diffuse large B-cell lymphoma, dysproliferative changes (dysplasias and metaplasias), embryonal carcinoma, endometrial cancer, endotheliosarcoma, ependymoma, epithelial carcinoma, erythroleukemia, esophageal cancer, estrogen-receptor positive breast cancer, essential thrombocythemia, Ewing's tumor, fibrosarcoma, follicular lymphoma, germ cell testicular cancer, glioma, glioblastoma, gliosarcoma, heavy chain disease, hemangioblastoma, hepatoma, hepatocellular cancer, hormone insensitive prostate cancer, leiomyosarcoma, leukemia, liposarcoma, lung cancer, lymphagioendotheliosarcoma, lymphangiosarcoma, lymphoblastic leukemia, lymphoma (Hodgkin's and non-Hodgkin's), malignancies and hyperproliferative disorders of the bladder, breast, colon, lung, ovaries, pancreas, prostate, skin and uterus, lymphoid malignancies of T-cell or B-cell origin, leukemia, lymphoma, medullary carcinoma, medulloblastoma, melanoma, meningioma, mesothelioma, multiple myeloma, myelogenous leukemia, myeloma, myxosarcoma, neuroblastoma, NUT midline carcinoma (NMC), non-small cell lung cancer, oligodendroglioma, oral cancer, osteogenic sarcoma, ovarian cancer, pancreatic cancer, papillary adenocarcinomas, papillary carcinoma, pinealoma, polycythemia vera, prostate cancer, rectal cancer, renal cell carcinoma, retinoblastoma,

rhabdomyosarcoma, sarcoma, sebaceous gland carcinoma, seminoma, skin cancer, small cell lung carcinoma, solid tumors (carcinomas and sarcomas), small cell lung cancer, stomach cancer, squamous cell carcinoma, synovioma, sweat gland carcinoma, thyroid cancer, Waldenström's macroglobulinemia, testicular tumors, uterine cancer and Wilms' tumor. In certain embodiments, the methods further comprise administering a therapeutically effective amount of at least one additional therapeutic agent. In certain embodiments, the additional therapeutic agent is selected from the group consisting of cytarabine, bortezomib, and 5-azacitidine.

In another aspect, the present ~~invention~~ disclosure relates to methods of treating a disease or condition in a subject comprising administering a therapeutically effective amount of a compound of formula (I) or a pharmaceutically acceptable salt thereof, to a subject in need thereof, wherein said disease or condition is selected from the group consisting of: Addison's disease, acute gout, ankylosing spondylitis, asthma, atherosclerosis, Behcet's disease, bullous skin diseases, cardiac myopathy, cardiac hypertrophy, chronic obstructive pulmonary disease (COPD), Crohn's disease, dermatitis, eczema, giant cell arteritis, glomerulonephritis, heart failure, hepatitis, hypophysitis, inflammatory bowel disease, Kawasaki disease, lupus nephritis, multiple sclerosis, myocarditis, myositis, nephritis, organ transplant rejection, osteoarthritis, pancreatitis, pericarditis, Polyarteritis nodosa, pneumonitis, primary biliary cirrhosis, psoriasis, psoriatic arthritis, rheumatoid arthritis, scleritis, sclerosing cholangitis, sepsis, systemic lupus erythematosus, Takayasu's Arteritis, toxic shock, thyroiditis, type I diabetes, ulcerative colitis, uveitis, vitiligo, vasculitis, and Wegener's granulomatosis. In certain embodiments, the methods further comprise administering a therapeutically effective amount of at least one additional therapeutic agent.

In another aspect, the present ~~invention~~ disclosure relates to methods of treating a chronic kidney disease or condition in a subject comprising administering a therapeutically effective amount of a compound of formula (I) or a pharmaceutically acceptable salt thereof, to a subject in need thereof, wherein said disease or condition is selected from the group consisting of: diabetic nephropathy, hypertensive nephropathy, HIV-associated nephropathy, glomerulonephritis, lupus nephritis, IgA nephropathy, focal segmental glomerulosclerosis, membranous glomerulonephritis, minimal change disease, polycystic kidney disease and tubular interstitial nephritis. In certain embodiments, the methods further comprise administering a therapeutically effective amount of at least one additional therapeutic agent.

In another aspect, the present ~~invention~~ disclosure relates to methods of treating an acute kidney injury or disease or condition in a subject comprising administering a therapeutically

effective amount of a compound of formula (I) or a pharmaceutically acceptable salt thereof, to a subject in need thereof, wherein said acute kidney injury or disease or condition is selected from the group consisting of: ischemia-reperfusion induced kidney disease, cardiac and major surgery induced kidney disease, percutaneous coronary intervention induced kidney disease, radio-contrast agent induced kidney disease, sepsis induced kidney disease, pneumonia induced kidney disease, and drug toxicity induced kidney disease. In certain embodiments, the methods further comprise administering a therapeutically effective amount of at least one additional therapeutic agent.

In another aspect, the present ~~invention~~ disclosure relates to methods of treating AIDS in a subject comprising administering a therapeutically effective amount of a compound of formula (I) or a pharmaceutically acceptable salt thereof, to a subject in need thereof. In certain embodiments, the methods further comprise administering a therapeutically effective amount of at least one additional therapeutic agent.

In another aspect, the present ~~invention~~ disclosure relates to methods of treating obesity, dyslipidemia, hypercholesterolemia, Alzheimer's disease, metabolic syndrome, hepatic steatosis, type II diabetes, insulin resistance, diabetic retinopathy or diabetic neuropathy in a subject comprising administering a therapeutically effective amount of a compound of formula (I) or a pharmaceutically acceptable salt thereof, to a subject in need thereof. In certain embodiments, the methods further comprise administering a therapeutically effective amount of at least one additional therapeutic agent.

In another aspect, the present ~~invention~~ disclosure provides for contraception in a male subject comprising administering a therapeutically effective amount of a compound of formula (I), or a pharmaceutically acceptable salt thereof, to a subject in need thereof. In certain embodiments, the methods further comprise administering a therapeutically effective amount of at least one additional therapeutic agent.

A further aspect of the ~~invention~~ disclosure provides the use of a compound of formula (I), alone or in combination with a second active pharmaceutical agent, in the manufacture of a medicament for treating or preventing conditions and disorders disclosed herein, with or without a pharmaceutically acceptable carrier.

Pharmaceutical compositions comprising a compound of formula (I), or a pharmaceutically acceptable salt, alone or in combination with a second active pharmaceutical agent, are also provided. In certain embodiments, pharmaceutical compositions comprise a therapeutically effective amount of a compound of formula (I), or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier.

In another aspect, the present disclosure relates to a pharmaceutical composition comprising a therapeutically effective amount of a compound of formula (I) as disclosed herein, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier.

In another aspect, the present disclosure relates to the use of a therapeutically effective amount of a compound of formula (I) as disclosed herein or a pharmaceutically acceptable salt thereof in the manufacture of a medicament for treating cancer in a subject.

In another aspect, the present disclosure relates to the use of a therapeutically effective amount of a compound of formula (I) as disclosed herein or a pharmaceutically acceptable salt thereof in the manufacture of a medicament for treating a disease or condition in a subject, wherein said disease or condition is selected from the group consisting of Addison's disease, acute gout, ankylosing spondylitis, asthma, atherosclerosis, Behcet's disease, bullous skin diseases, cardiac myopathy, cardiac hypertrophy, chronic obstructive pulmonary disease (COPD), Crohn's disease, dermatitis, eczema, giant cell arteritis, glomerulonephritis, heart failure, hepatitis, hypophysitis, inflammatory bowel disease, Kawasaki disease, lupus nephritis, multiple sclerosis, myocarditis, myositis, nephritis, organ transplant rejection, osteoarthritis, pancreatitis, pericarditis, Polyarteritis nodosa, pneumonitis, primary biliary cirrhosis, psoriasis, psoriatic arthritis, rheumatoid arthritis, scleritis, sclerosing cholangitis, sepsis systemic lupus erythematosus, Takayasu's Arteritis, toxic shock, thyroiditis, type I diabetes, ulcerative colitis, uveitis, vitiligo, vasculitis, and Wegener's granulomatosis.

In another aspect, the present disclosure relates to the use of a therapeutically effective amount of a compound of formula (I) as disclosed herein or a pharmaceutically acceptable salt thereof in the manufacture of a medicament for treating a chronic kidney disease or condition in a subject, wherein said disease or condition is selected from the group consisting of: diabetic nephropathy, hypertensive nephropathy, HIV-associated nephropathy, glomerulonephritis, lupus nephritis, IgA nephropathy, focal segmental glomerulosclerosis, membranous glomerulonephritis, minimal change disease, polycystic kidney disease, and tubular interstitial nephritis.

In another aspect, the present disclosure relates to the use of a therapeutically effective amount of a compound of formula (I) as disclosed herein or a pharmaceutically acceptable salt thereof in the manufacture of a medicament for treating an acute kidney disease or condition in a subject, wherein said acute kidney disease or condition is selected from the group consisting of:

ischemia-reperfusion induced kidney disease, cardiac and major surgery induced kidney disease, percutaneous coronary intervention induced kidney disease, radio-contrast agent induced kidney disease, sepsis induced kidney disease, pneumonia induced kidney disease, and drug toxicity induced kidney disease.

In another aspect, the present disclosure relates to the use of a therapeutically effective amount of a compound of formula (I) as disclosed herein or a pharmaceutically acceptable salt thereof in the manufacture of a medicament for treating an acquired immunodeficiency syndrome (AIDS) in a subject.

In another aspect, the present disclosure relates to the use of a therapeutically effective amount of a compound of formula (I) as disclosed herein or a pharmaceutically acceptable salt thereof in the manufacture of a medicament for treating a disease or condition in a subject, wherein said disease or condition is selected from the group consisting of: obesity, dyslipidemia, hypercholesterolemia, Alzheimer's disease, metabolic syndrome, hepatic steatosis, type II diabetes, insulin resistance, diabetic retinopathy, and diabetic neuropathy.

In another aspect, the present disclosure relates to the use of a therapeutically effective amount of a compound of formula (I) as disclosed herein or a pharmaceutically acceptable acceptable salt thereof in the manufacture of a medicament for contraception in a male subject.

40. ~~A method for treating cancer in a subject comprising administering~~ Use of a therapeutically effective amount of a compound of formula (I) according to claim 1 or a pharmaceutically acceptable salt thereof~~, to a subject in need thereof~~ in the manufacture of a medicament for treating cancer in a subject.

41. The ~~method~~ use of claim 40 wherein the cancer is selected from the group consisting of: acoustic neuroma, acute leukemia, acute lymphocytic leukemia, acute myelocytic leukemia (monocytic, myeloblastic, adenocarcinoma, angiosarcoma, astrocytoma, myelomonocytic and promyelocytic), acute t-cell leukemia, basal cell carcinoma, bile duct carcinoma, bladder cancer, brain cancer, breast cancer, bronchogenic carcinoma, cervical cancer, chondrosarcoma, chordoma, choriocarcinoma, chronic leukemia, chronic lymphocytic leukemia, chronic myelocytic (granulocytic) leukemia, chronic myelogenous leukemia, colon cancer, colorectal cancer, craniopharyngioma, cystadenocarcinoma, diffuse large B-cell lymphoma, dysproliferative changes (dysplasias and metaplasias), embryonal carcinoma, endometrial cancer, endotheliosarcoma, ependymoma, epithelial carcinoma, erythroleukemia, esophageal cancer, estrogen-receptor positive breast cancer, essential thrombocythemia, Ewing's tumor, fibrosarcoma, follicular lymphoma, germ cell testicular cancer, glioma, glioblastoma, gliosarcoma, heavy chain disease, hemangioblastoma, hepatoma, hepatocellular cancer, hormone insensitive prostate cancer, leiomyosarcoma, leukemia, liposarcoma, lung cancer, lymphagioendotheliosarcoma, lymphangiosarcoma, lymphoblastic leukemia, lymphoma (Hodgkin's and non-Hodgkin's), malignancies and hyperproliferative disorders of the bladder, breast, colon, lung, ovaries, pancreas, prostate, skin, and uterus, lymphoid malignancies of T-cell or B-cell origin, leukemia, lymphoma, medullary carcinoma, medulloblastoma, melanoma, meningioma, mesothelioma, multiple myeloma, myelogenous leukemia, myeloma, myxosarcoma, neuroblastoma, NUT midline carcinoma (NMC), non-small cell lung cancer, oligodendroglioma, oral cancer, osteogenic sarcoma, ovarian cancer, pancreatic cancer, papillary adenocarcinomas, papillary carcinoma, pinealoma, polycythemia vera, prostate cancer, rectal cancer, renal cell carcinoma, retinoblastoma, rhabdomyosarcoma, sarcoma, sebaceous gland carcinoma, seminoma, skin cancer, small cell lung carcinoma, solid tumors (carcinomas and sarcomas), small cell lung cancer, stomach cancer, squamous cell carcinoma,

synovioma, sweat gland carcinoma, thyroid cancer, Waldenström's macroglobulinemia, testicular tumors, uterine cancer and Wilms' tumor.

42. ~~A method for treating a disease or condition in a subject comprising administering~~ Use of a therapeutically effective amount of a compound of formula (I) according to claim 1 or a pharmaceutically acceptable salt thereof~~, to a subject in need thereof~~ in the manufacture of a medicament for treating a disease or condition in a subject, wherein said disease or condition is selected from the group consisting of Addison's disease, acute gout, ankylosing spondylitis, asthma, atherosclerosis, Behcet's disease, bullous skin diseases, cardiac myopathy, cardiac hypertrophy, chronic obstructive pulmonary disease (COPD), Crohn's disease, dermatitis, eczema, giant cell arteritis, glomerulonephritis, heart failure, hepatitis, hypophysitis, inflammatory bowel disease, Kawasaki disease, lupus nephritis, multiple sclerosis, myocarditis, myositis, nephritis, organ transplant rejection, osteoarthritis, pancreatitis, pericarditis, Polyarteritis nodosa, pneumonitis, primary biliary cirrhosis, psoriasis, psoriatic arthritis, rheumatoid arthritis, scleritis, sclerosing cholangitis, sepsis systemic lupus erythematosus, Takayasu's Arteritis, toxic shock, thyroiditis, type I diabetes, ulcerative colitis, uveitis, vitiligo, vasculitis, and Wegener's granulomatosis.

43. ~~A method for treating a chronic kidney disease or condition in a subject comprising administering~~ Use of a therapeutically effective amount of a compound of formula (I) according to claim 1 or a pharmaceutically acceptable salt thereof~~, to a subject in need thereof~~ in the manufacture of a medicament for treating a chronic kidney disease or condition in a subject, wherein said disease or condition is selected from the group consisting of: diabetic nephropathy, hypertensive nephropathy, HIV-associated nephropathy, glomerulonephritis, lupus nephritis, IgA nephropathy, focal segmental glomerulosclerosis, membranous glomerulonephritis, minimal change disease, polycystic kidney disease, and tubular interstitial nephritis.

44. ~~A method for treating an acute kidney disease or condition in a subject comprising administering~~ Use of a therapeutically effective amount of a compound of formula (I) according to claim 1 or a pharmaceutically acceptable salt thereof~~, to a subject in need thereof~~ in the manufacture of a medicament for treating an acute kidney disease or condition in a subject, wherein said acute kidney disease or condition is selected from the group consisting of:

ischemia-reperfusion induced kidney disease, cardiac and major surgery induced kidney disease, percutaneous coronary intervention induced kidney disease, radio-contrast agent induced kidney disease, sepsis induced kidney disease, pneumonia induced kidney disease, and drug toxicity induced kidney disease.

45. ~~A method for treating an acquired immunodeficiency syndrome (AIDS) in a subject comprising administering~~ Use of a therapeutically effective amount of a compound of formula (I) according to claim 1 or a pharmaceutically acceptable salt thereof~~, to a subject in need thereof~~ in the manufacture of a medicament for treating an acquired immunodeficiency syndrome (AIDS) in a subject.

46. ~~A method for treating a disease or condition in a subject comprising administering~~ Use of a therapeutically effective amount of a compound of formula (I) according to claim 1 or a pharmaceutically acceptable salt thereof~~, to a subject in need thereof~~ in the manufacture of a medicament for treating a disease or condition in a subject, wherein said disease or condition is selected from the group consisting of: obesity, dyslipidemia, hypercholesterolemia, Alzheimer's disease, metabolic syndrome, hepatic steatosis, type II diabetes, insulin resistance, diabetic retinopathy, and diabetic neuropathy.

47. ~~A method of contraception in a male subject comprising administering~~ Use of a therapeutically effective amount of a compound of formula (I) according to claim 1 or a pharmaceutically acceptable acceptable salt thereof~~, to a subject in need thereof~~ in the manufacture of a medicament for contraception in a male subject.