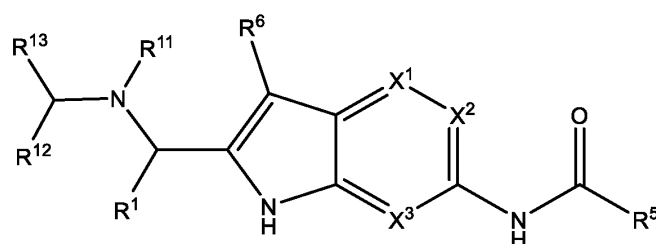


CLAIMS

1. A compound of formula Ia



Ia

wherein:

X^1 , X^2 , and X^3 are independently chosen from N and CR^4 , with the provisos that

- (1) no more than two of X^1 , X^2 , and X^3 are N; and
- (2) when X^1 and/or X^2 are CR^4 , then X^3 is not N;

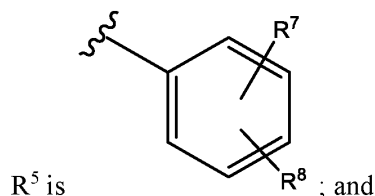
R^1 is chosen from: H, (C₁₋₆)alkyl, aryl(C₁₋₆)alkyl, (C₃₋₁₂)cycloalkyl(C₁₋₆)alkyl, heterocyclyl, heterocyclyl(C₁₋₆)alkyl, (C₁₋₆)alkylamino(C₁₋₆)alkyl, heterocyclylamino(C₁₋₆)alkyl, heterocyclyl(C₁₋₆)alkylamino(C₁₋₆)alkyl, (C₃₋₁₂)cycloalkylamino(C₁₋₆)alkyl, (C₃₋₁₂)cycloalkyl(C₁₋₆)alkylamino(C₁₋₆)alkyl, arylamino(C₁₋₆)alkyl, and aryl(C₁₋₆)alkylamino(C₁₋₆)alkyl;

R^4 is chosen from H, CH₃, and Cl;

R^5 is chosen from 5- or 6- member carbocycle or heterocycle; bicyclic 5:6 carbocycle or heterocycle and bicyclic 6:6 carbocycle or heterocycle, not attached at a nitrogen of said heterocycle, wherein said carbocycle or heterocycle may be optionally substituted with one or more groups chosen from (C₁₋₈)hydrocarbyl, (C₁₋₁₀)oxaalkyl, halogen, (C₁₋₆)haloalkyl, -SO₂(C₁₋₆)alkyl, -SO₂NH(C₀₋₃H₁₋₇), -CONH(C₀₋₃H₁₋₇), -SO₂NH(C₁₋₆)oxaalkyl, -CN, CH₂CN, CH₂NH₂, -NH₂, NR¹⁴ where R^{14} is independently chosen from hydrogen, (C₁₋₆)fluoroalkyl, and (C₁₋₃)oxaalkyl, -CH₂OH, benzyloxy, -C(=NH)-NH₂, -A-Het and additionally, when R^5 is a 5- or 6- member heterocycle, bicyclic 5:6 heterocycle, quinoline, isoquinolin, quinazolin, or benzo[*b*][1,4]oxazine, =O; wherein A is chosen from direct bond, -(C₁₋₆)alkyl-, -(C₁₋₁₀)oxaalkyl-, -CO(C₁₋₆)alkyl-, -SO₂(C₁₋₆)alkyl-, -SO₂NH(C₁₋₆)alkyl-, and -CONH(C₁₋₆)alkyl-; and Het is heterocyclyl optionally substituted with (C₁₋₆)hydrocarbyl, (C₁₋₁₀)oxaalkyl, (C₁₋₁₀)oxaalkyl(C=O)-, hydroxy, =O, or halogen and

with the provisos that

- (1) when all of X^1 , X^2 , and X^3 are carbon and R^5 is optionally substituted phenyl, then



- (2) R^5 is not a 1,3-disubstituted pyrazole or 5-oxaalkylindazole

R^6 is selected from: H, Me, F, and Cl;

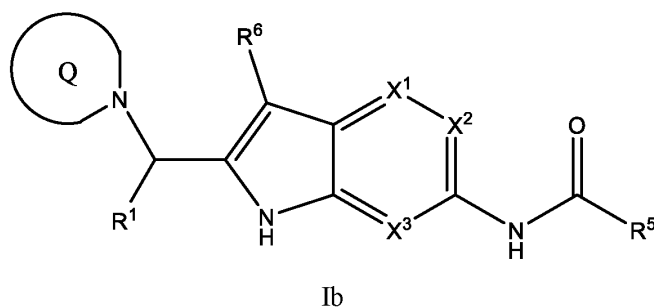
R^7 is hydrogen or halogen; and

R^8 is chosen from (C_{1-10}) oxaalkyl, heterocyclyl, and heterocyclyl (C_{1-10}) oxaalkyl

R^{11} , R^{12} and R^{13} are chosen from the following three groups:

- (a) R^{11} is H or CH_3 ;
 R^{12} is chosen from H, (C_1-C_6) hydrocarbyl, hydroxy (C_1-C_6) hydrocarbyl, and 5- or 6-membered monocyclic heterocyclyl, wherein said heterocycle may be optionally substituted with (C_1-C_6) hydrocarbyl, hydroxyl, or hydroxy (C_1-C_6) hydrocarbyl; and
 R^{13} is hydrogen or methyl; or
- (b) R^{11} and R^{12} taken together form an optionally substituted nitrogenous heterocycle attached via nitrogen, said nitrogenous heterocycle chosen from (a) a monocyclic aliphatic nitrogenous heterocycle, (b) a 5:5 or 5:6 bicyclic aliphatic nitrogenous heterocycle, (c) a spirobicyclic aliphatic nitrogenous heterocycle, and (d) an 8-azabicyclo[3.2.1]octane, wherein said optional substituents are independently chosen from (C_{1-10}) hydrocarbyl, halo (C_{1-10}) hydrocarbyl, halo (C_{1-10}) hydrocarbyloxy, $-(C_{1-10})$ oxaalkyl, $COOH$, $-SO_2(C_{1-6})$ alkyl, $=O$, $=S$, $=NH$, and additionally, when R^{11} and R^{12} taken together for a spirobicyclic aliphatic nitrogenous heterocycle, halogen; and
 R^{13} is chosen from H, (C_{1-10}) hydrocarbyl, halo (C_{1-10}) hydrocarbyl, halo (C_{1-10}) hydrocarbyloxy, $-(C_{1-10})$ oxaalkyl, $-SO_2(C_{1-6})$ alkyl, $=O$, $=S$, and $=NH$; or
- (c) R^{11} is H; and
 R^{12} and R^{13} taken together form a 3- to 7- membered aliphatic carbocycle, wherein said carbocycle may be optionally substituted with (C_1-C_6) hydrocarbyl, hydroxyl, or hydroxy (C_1-C_6) hydrocarbyl.

2. A compound according to claim 1 of formula Ib



wherein R^{11} and R^{12} taken together form an optionally substituted nitrogenous heterocycle, Q, chosen from (a) a monocyclic aliphatic nitrogenous heterocycle, (b) a 5:5 or 5:6 bicyclic aliphatic nitrogenous heterocycle, (c) a spirobicyclic aliphatic nitrogenous heterocycle, and (d) an 8-azabicyclo[3.2.1]octane, wherein said optional substituents are independently chosen from (C_{1-10}) hydrocarbyl, halo (C_{1-10}) hydrocarbyl, halo (C_{1-10}) hydrocarbyloxy, $-(C_{1-10})$ oxaalkyl, COOH, $-SO_2(C_{1-6})$ alkyl, =O, =S, =NH, and additionally, when R^{11} and R^{12} taken together for a spirobicyclic aliphatic nitrogenous heterocycle, halogen;

R^1 is chosen from: H, (C_{1-6}) alkyl, aryl (C_{1-6}) alkyl, (C_{3-12}) cycloalkyl (C_{1-6}) alkyl, heterocyclyl, heterocyclyl (C_{1-6}) alkyl, (C_{1-6}) alkylamino (C_{1-6}) alkyl, heterocyclylamino (C_{1-6}) alkyl, heterocyclyl (C_{1-6}) alkylamino (C_{1-6}) alkyl, (C_{3-12}) cycloalkylamino (C_{1-6}) alkyl, (C_{3-12}) cycloalkyl (C_{1-6}) alkylamino (C_{1-6}) alkyl, arylamino (C_{1-6}) alkyl, and aryl (C_{1-6}) alkylamino (C_{1-6}) alkyl.

3. A compound according to claim 1 wherein

R^{11} is H; and

R^{12} and R^{13} taken together form a 3- to 7- membered aliphatic carbocycle, wherein said carbocycle may be optionally substituted with (C_1-C_6) hydrocarbyl, hydroxyl, or hydroxy (C_1-C_6) hydrocarbyl.

4. A compound according to claim 1 wherein

R^{11} is H or CH_3 ;

R¹² is chosen from H, (C₁-C₆)hydrocarbyl, hydroxy(C₁-C₆)hydrocarbyl, and 5- or 6-membered monocyclic heterocyclyl, wherein said heterocycle may be optionally substituted with (C₁-C₆)hydrocarbyl, hydroxyl, or hydroxy(C₁-C₆)hydrocarbyl; and
R¹³ is hydrogen or methyl.

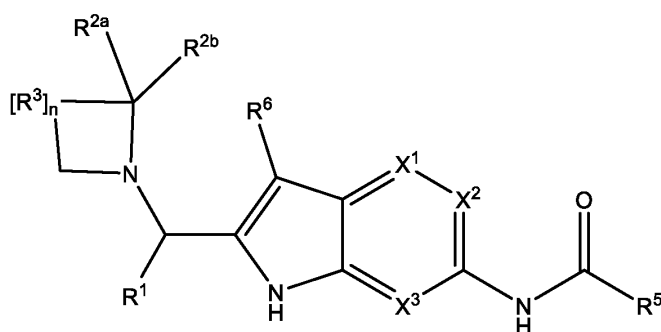
5. A compound of claim 1 wherein R⁵ is chosen from bicyclic 5:6 carbocycle or heterocycle and bicyclic 6:6 carbocycle or heterocycle, not attached at a nitrogen of said heterocycle, wherein said carbocycle or heterocycle may be optionally substituted with a group chosen from (C₁-6)alkyl, (C₁-6)alkoxy, halogen, (C₁-6)haloalkyl, CH₂CN, CH₂NH₂, -NH₂, NR¹⁴ where R¹⁴ is independently chosen from hydrogen, (C₁-6)fluoroalkyl, and (C₁-3)oxaalkyl, -CH₂OH, and -A-Het, and additionally, when R⁵ is a 5- or 6- member heterocycle, bicyclic 5:6 heterocycle, quinoline, isoquinolin, quinazolin, or benzo[b][1,4]oxazine, =O; wherein A is chosen from direct bond, -(C₁-6)alkyl-, -(C₁-10)oxaalkyl-, -CO(C₁-6)alkyl-, -SO₂(C₁-6)alkyl-, -SO₂NH(C₁-6)alkyl-, and -CONH(C₁-6)alkyl-; and Het is heterocyclyl optionally substituted with (C₁-6)hydrocarbyl, (C₁-10)oxaalkyl, (C₁-10)oxaalkyl(C=O)-, hydroxy, =O, or halogen.

6. A compound of claim 1 wherein R⁵ is chosen from bicyclic 5:6 carbocycle or heterocycle and bicyclic 6:6 carbocycle or heterocycle wherein said carbocycle or heterocycle may be optionally substituted with a group chosen from (C₁-6)alkyl, (C₁-6)alkoxy, halogen, and (C₁-6)haloalkyl.

7. A compound according to claim 2 wherein Q is a monocyclic aliphatic nitrogenous heterocycle optionally substituted with one or more groups chosen from (C₁-10)hydrocarbyl, halo(C₁-10)hydrocarbyl, halo(C₁-10)hydrocarbyloxy, -(C₁-10)oxaalkyl, COOH, -SO₂(C₁-6)alkyl, =O, =S, and =NH.

8. A compound according to claim 2 wherein Q is a 5:5 or 5:6 bicyclic aliphatic nitrogenous heterocycle optionally substituted with one or more groups chosen from (C₁-10)hydrocarbyl, halo(C₁-10)hydrocarbyl, halo(C₁-10)hydrocarbyloxy, -(C₁-10)oxaalkyl, COOH, -SO₂(C₁-6)alkyl, =O, =S, and =NH.

9. A compound according to claim 2 wherein Q is a spirobicyclic aliphatic nitrogenous heterocycle.
10. A compound according to claim 1 wherein R⁵ is phenyl substituted with one or more groups chosen from (C₁₋₈)hydrocarbyl, (C₁₋₁₀)oxaalkyl, halogen, (C₁₋₆)haloalkyl, -SO₂(C₁₋₆)alkyl, -SO₂NH(C₀₋₃H₁₋₇), -CONH(C₀₋₃H₁₋₇), -SO₂NH(C₁₋₆)oxaalkyl, -CN, -NH₂, -CH₂OH, benzyloxy, and -A-Het, wherein A is chosen from direct bond, -(C₁₋₆)alkyl-, -(C₁₋₁₀)oxaalkyl-, -CO(C₁₋₆)alkyl-, -SO₂(C₁₋₆)alkyl-, -SO₂NH(C₁₋₆)alkyl-, and -CONH(C₁₋₆)alkyl-; and Het is heterocyclyl optionally substituted with (C₁₋₆)hydrocarbyl, (C₁₋₁₀)oxaalkyl, (C₁₋₁₀)oxaalkyl(C=O)-, hydroxy, =O, or halogen.
11. A compound according to claim 4 wherein R¹¹ is H; R¹² is chosen from optionally substituted pyrazole, triazole, oxadiazole, and pyridine, where the optional substituents may be hydroxy or methyl; and R¹³ is hydrogen.
12. A compound according to claim 7 wherein Q is a monocyclic aliphatic nitrogenous heterocycle optionally substituted with one or more groups chosen from methyl and =O.
13. A compound according to claim 9 wherein Q is chosen from the group consisting of azaspirohexanes, heptanes and octanes and oxazaspirohexanes, heptanes and octanes.
14. A compound according to claim 1 of formula I



I

wherein:

X^1 , X^2 , and X^3 are independently chosen from N and CR^4 , with the proviso that no more than two of X^1 , X^2 , and X^3 are N;

n is 1, 2 or 3;

R^1 is chosen from: H, (C_{1-6}) alkyl, aryl (C_{1-6}) alkyl, (C_{3-12}) cycloalkyl (C_{1-6}) alkyl, heterocyclyl, heterocyclyl (C_{1-6}) alkyl, (C_{1-6}) alkylamino (C_{1-6}) alkyl, heterocyclylamino (C_{1-6}) alkyl, heterocyclyl (C_{1-6}) alkylamino (C_{1-6}) alkyl, (C_{3-12}) cycloalkylamino (C_{1-6}) alkyl, (C_{3-12}) cycloalkyl (C_{1-6}) alkylamino (C_{1-6}) alkyl, arylamino (C_{1-6}) alkyl, and aryl (C_{1-6}) alkylamino (C_{1-6}) alkyl;

R^{2a} and R^{2b} are independently chosen from H and (C_{1-6}) alkyl, or taken together, R^{2a} and R^{2b} form a spiro 4, 5, or 6 member carbocycle or heterocycle;

R^3 is chosen independently in each occurrence from $CHCOOH$, NR^{10} , O, and $CR^{10a}R^{10b}$;

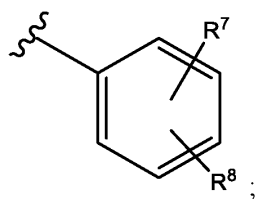
R^{10} , R^{10a} and R^{10b} are independently chosen from H and (C_{1-6}) alkyl, or taken together, R^{10a} and R^{10b} form a spiro 4, 5, or 6 member carbocycle or heterocycle; or

taken together, R^{2a} and R^{10a} form a fused 4, 5, or 6-member carbocycle or heterocycle;

R^4 is chosen from H, CH_3 , F and Cl;

R^5 is chosen from 5- or 6- member carbocycle or heterocycle; bicyclic 5-6 carbocycle or heterocycle and bicyclic 6-6 carbocycle or heterocycle, wherein said carbocycle or heterocycle may be optionally substituted with one or more groups chosen from (C_{1-6}) hydrocarbyl, (C_{1-6}) alkoxy, halogen, (C_{1-6}) haloalkyl, $-SO_2(C_{1-6})$ alkyl, $-SO_2NH(C_{0-3}H_{1-7})$, $-CONH(C_{0-3}H_{1-7})$, $-CN$, $-NH_2$, $-CH_2OH$, benzyloxy, and heterocyclyl optionally substituted with (C_{1-6}) hydrocarbyl, (C_{1-6}) alkoxy, hydroxy, $=O$, or halogen

with the proviso that when all of X^1 , X^2 , and X^3 are carbon and R^5 is optionally substituted



phenyl, then R^5 is

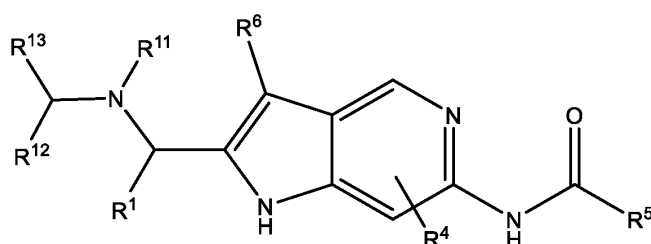
R^6 is selected from: H, Me, F, and Cl;

R^7 is hydrogen or halogen; and

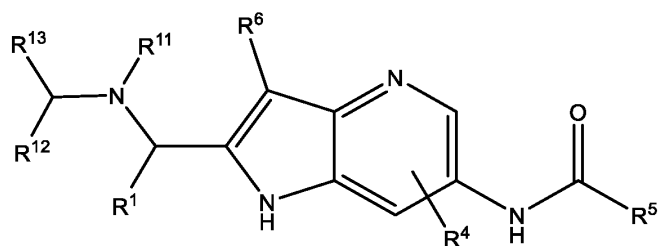
R^8 is heterocyclyl.

15. A compound according to any one of claims 1 to 14 wherein one of X^1 , X^2 or X^3 is N and the other two instances of X are C.

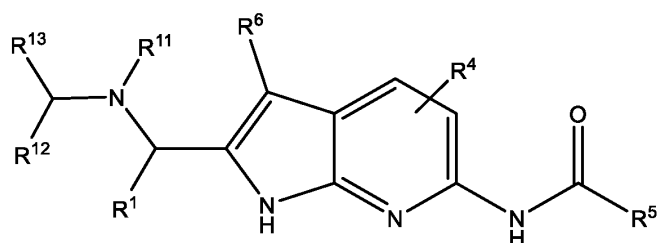
16. A pyrrolo[3,2-c]pyridine according to claim 6 of formula



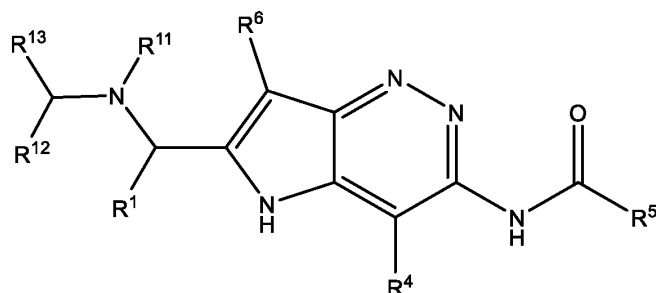
17. A pyrrolo[3,2-b]pyridine according to claim 15 of formula



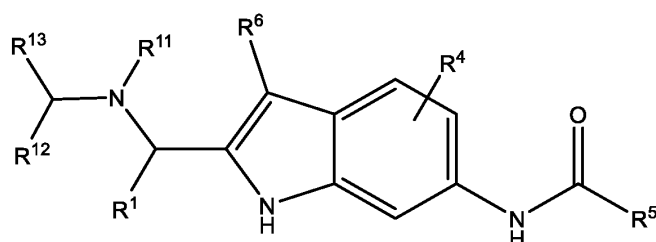
18. A pyrrolo[2,3-b]pyridine according to claim 15 of formula



19. A pyrrolo[3,2-c]pyridazine according to claim 1 of formula

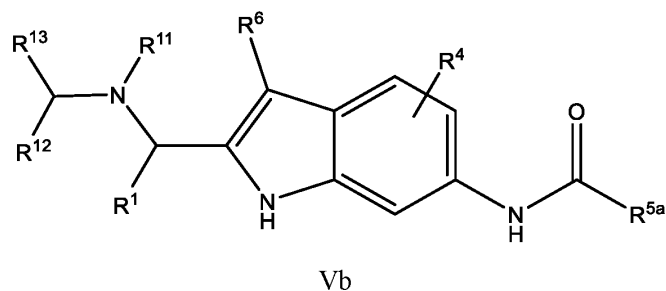


20. An indole according to claim 1 of formula



21. A compound according to any of claims 1-20 wherein R⁵ is a carbocycle or heterocycle chosen from phenyl, indazole, pyridine, imidazolopyridine, pyrazolopyrimidine, imidazolopyrazine, triazolopyridine, and benzoxazine, or reduced forms thereof, wherein said carbocycle or heterocycle may be optionally substituted.

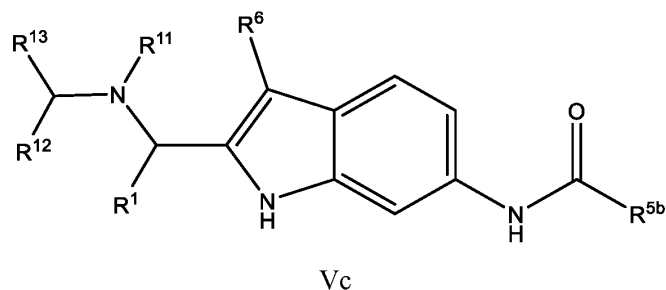
22. An indole according to claim 11 of formula Vb:



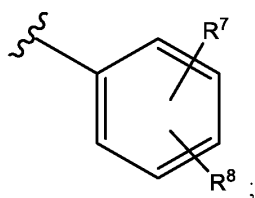
wherein:

R^{5a} is chosen from 5- or 6- member heterocycle or aliphatic carbocycle; bicyclic 5:6 carbocycle or heterocycle and bicyclic 6:6 carbocycle or heterocycle wherein said carbocycle, heterocycle or aliphatic carbocycle may be optionally substituted with a group chosen from (C₁₋₆)alkyl, (C₁₋₆)alkoxy, halogen, and (C₁₋₆)haloalkyl.

23. An indole according to claim 16 of formula Vc



wherein:



R^{5b} is

R^7 is hydrogen or halogen; and

R^8 is heterocyclyl.

24. An indole according to claim 23 wherein R^8 is chosen from pyrazine, pyrimidine, pyridazine, and pyridine.
25. A compound according to any of claims 1-20 or 22-24 wherein R^1 is hydrogen.
26. A compound according to any of claims 1-20 or 22-24 wherein n is 2.
27. A compound according to claim 26 wherein one of R^{2a} , R^{2b} , R^{10a} , and R^{10b} is chosen from methyl and carboxy and the remaining instances are hydrogen.
28. A compound according to claim 26 wherein R^3 is CHCOOH and R^{2a} , R^{2b} , R^{10a} , and R^{10b} are hydrogen.

29. A compound according to claim 27 wherein, when R^{2a} is methyl, R³ is CR^{10a}R^{10b}, and R^{2b}, R^{10a}, and R^{10b} are hydrogen, the carbon to which R^{2a} and R^{2b} is attached is of the (S) absolute configuration.
30. A compound according to any of claims 1-20 or 22-24 wherein R⁴ is hydrogen.
31. A compound according to any of claims 1-20 or 22-24 wherein R⁶ is hydrogen or methyl.
32. A compound according to any of claims 1-20 or 22-24 wherein R⁵ is chosen from optionally substituted pyridine, indazole, pyrazine, pyrazole, thiazole, and pyrimidine, substituted with an optionally substituted heterocycle, -CN or -SO₂NHCH₃.
33. A compound according to any of claims 15-18 wherein R⁵ is phenyl substituted with one or more groups chosen from (C₁₋₆)hydrocarbyl, (C₁₋₆)alkoxy, halogen, (C₁₋₆)haloalkyl, -SO₂(C₁₋₆)alkyl, -SO₂NH(C₀₋₃H₁₋₇), -CN, -NH₂, -CH₂OH, benzyloxy, and heterocyclyl optionally substituted with (C₁₋₆)hydrocarbyl, (C₁₋₆)alkoxy, hydroxy, =O, or halogen.
34. A compound according to claim 33 wherein R⁵ is phenyl substituted with fluoro and an optionally substituted heterocycle.
35. A compound according to claim 21 wherein R⁵ is indazole substituted with methyl.
36. A method of suppressing oncogene expression in a cell comprising exposing said cell to a compound according to any of claims 1-20, or 22-24.
37. An *in vitro* method according to claim 36.
38. An *in vivo* method according to claim 36.
39. A method for treating a patient with leukemia comprising administering an effective dose of a compound according to any of claims 1-20, or 22-24.

40. A method according to claim 39 additionally comprising administering a BET inhibitor.