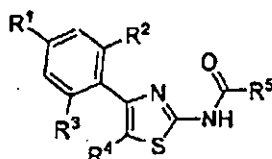


AMENDED CLAIMS
received by the International Bureau on 14 May 2013 (14.05.13)

What is claimed is:

1. A compound having a structure according to Formula I



Formula I

or a pharmaceutically acceptable salt thereof, wherein:

R^1 is alkenyl, alkynyl, aryl, nitro, cyano, cycloalkyl, heterocycloalkyl, cycloalkenyl, heterocycloalkenyl, OR_a , SR_a , NR_aR_b , $-S(O)_2R_a$, $-S(O)_2NR_aR_b$, $-C(O)R_a$, $-C(O)NR_aR_b$, $-NR_aC(O)R_b$, $-NR_aS(O)_2R_b$, $-N=CR_aR_b$, or $-NR_aC(O)NHR_b$;

R_a and R_b are independently alkenyl, alkynyl, aryloxy, alkoxy, hydroxy, heteroaryl, heterocycloalkyl, cycloalkenyl, or heterocycloalkenyl, or R_a and R_b , together with a nitrogen atom to which they are bonded, are heteroaryl, heterocycloalkyl, or heterocycloalkenyl;

R^2 , R^3 , and R^4 are independently hydrogen, C_1 - C_6 alkyl, halogen, or OR_a ; and

R^5 is alkyl, phenylalkyl, heteroarylalkyl, phenylalkenyl, heteroarylalkenyl, phenyl, heteroaryl, heterocycloalkyl, or heterocycloalkenyl;

wherein each of R^1 , R^2 , R^3 , R^4 , R^5 , R_a , and R_b is independently optionally substituted; and with the proviso that

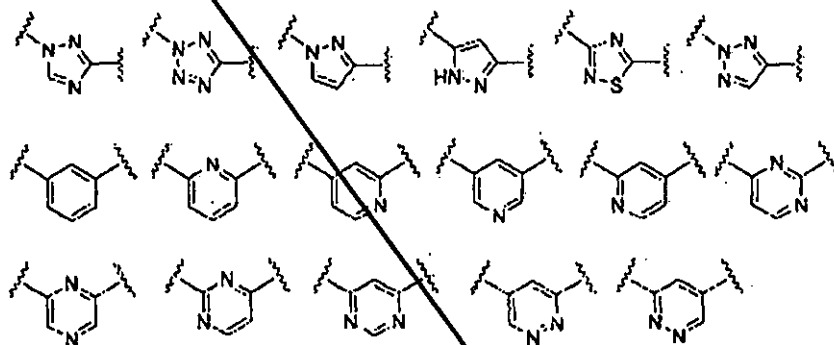
(I) where R^1 and R^2 are methyl and where R^3 is hydrogen, R^5 is not thiazolyl, N-methylimidazolyl, pyrazinyl, pyridinyl, morpholinyl, phenyl, or dimethoxyphenyl;

(II) where R^1 , R^2 , and R^3 are methyl, R^5 is not thiazolyl, N-methylimidazolyl, pyrazinyl, pyridinyl, morpholinyl, phenyl, methoxyphenyl, dihydroxyphenyl, hydroxymethoxyphenyl, trifluoromethylphenyl, or dimethoxyphenyl;

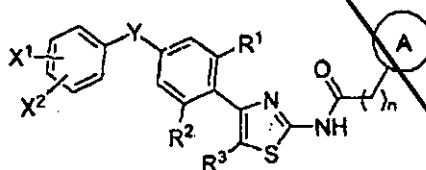
(III) where R^1 and R^2 are methyl and where R^3 is hydroxyl or methoxy, R^5 is not phenyl.

2. The compound of claim 1 wherein R^1 is alkoxy, SR_a , OR_a , or $-S(O)_2R_a$, wherein R_a is alkyl or optionally substituted aryl, R^2 , R^3 , and R^4 are independently hydrogen or C_1 - C_6 alkyl, and wherein R^5 is optionally substituted heteroaryl.

3. The compound of claim 2 wherein R^1 is alkoxy, SR_a , OR_a , or $-S(O)_2R_a$, wherein R_a is alkyl or optionally substituted aryl, R^2 and R^3 are C_1 - C_6 alkyl, and wherein R^5 is optionally substituted pyridinyl.
4. The compound of claim 3 wherein R^1 is OR_a , wherein R_a is optionally substituted aryl, R^2 and R^3 are C_1 - C_6 alkyl, and wherein R^5 is optionally substituted pyridinyl.
5. The compound of claim 1 wherein the thizole ring is substituted by a compound selected from the group of



6. The compound of claim 1 having a structure according to Formula II



Formula II

wherein X^1 and X^2 are independently H, alkyl, alkenyl, alkynyl, halogen, nitro, cyano, cycloalkyl, heterocycloalkyl, cycloalkenyl, heterocycloalkenyl, OR_a , NR_aR_b , $-S(O)_2R_a$, $-S(O)_2NR_aR_b$, $-C(O)R_a$, $-C(O)NR_aR_b$, $-NR_aC(O)R_b$, $-NR_aS(O)_2R_b$, $-N=CR_aR_b$, $-NR_aC(O)NHR_b$, or $\Lambda^1(CH_2)_m\Lambda^2(CH_2)_p\Lambda^3(CH_2)_q\Lambda^4R_c$;

where Λ^1 , Λ^2 , Λ^3 , and Λ^4 are independently selected from null, CH_2 , CHR^a , CR_aR_b , O, NH, NR^a , S, SO, and SO_2 ;

where R^c is independently hydrogen, alkyl, alkenyl, alkynyl, alkoxy, aryl, halogen, nitro, cyano, cycloalkyl, heterocycloalkyl, cycloalkenyl, heterocycloalkenyl, OR_a , SR_a , NR_aR_b , $-S(O)_2R_a$, $-S(O)_2NR_aR_b$, $-C(O)R_a$, $-C(O)NR_aR_b$, $-NR_aC(O)R_b$, $-NR_aS(O)_2R_b$, $N=CR_aR_b$, or $-NR_aC(O)NHR_b$;

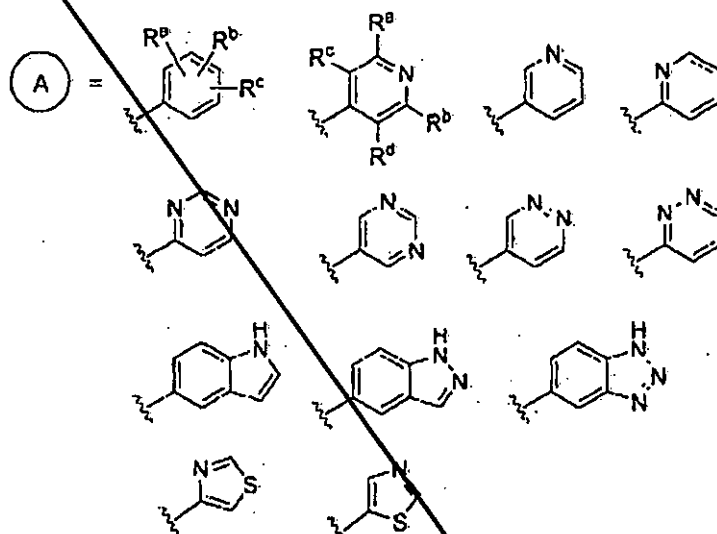
where m, p, and q are independently 0, 1, 2, 3, or 4;

Y is CH_2 , CHR_a , CR_aR_b , O, NH, NR_a , S, SO, or SO_2 ;

R^1 , R^2 , and R^3 are independently H, alkyl, alkoxy, or halogen;

n is 0, 1, or 2;

wherein each of X^1 and X^2 is independently optionally substituted;

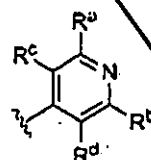


; and

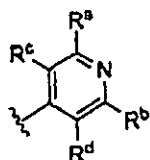
wherein R_c and R_d is independently R_a .

7. The compound of claim 6 wherein Y is O, S, or SO_2 .

8. The compound of claim 6 wherein



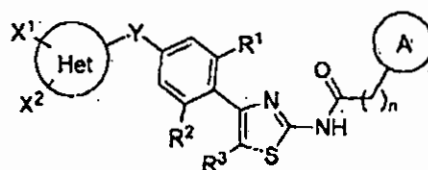
9. The compound of claim 6 wherein Y is O, S, or SO_2 , wherein



, and wherein R^1 , R^2 , and R^3 are independently H or alkyl.

10. The compound of claim 9 wherein X^1 and X^2 are independently H, alkyl, and alkoxy, and wherein n is 0 or 1.

11. The compound of claim 6 wherein n is 0.
12. The compound of claim 1 having a structure according to Formula III.



Formula III

wherein X^1 and X^2 are independently H, alkyl, alkenyl, alkynyl, halogen, nitro, cyano, cycloalkyl, heterocycloalkyl, cycloalkenyl, heterocycloalkenyl, OR_a , NR_aR_b , $S(O)_2R_a$, $-S(O)_2NR_aR_b$, $-C(O)R_a$, $-C(O)NR_aR_b$, $-NR_aC(O)R_b$, $-NR_aS(O)_2R_b$, $-N=CR_aR_b$, $-NR_aC(O)NHR_b$, or $-A^1(CH_2)_m A^2(CH_2)_p A^3(CH_2)_q A^4R_c$;

where A^1 , A^2 , A^3 , and A^4 are independently selected from null, CH_2 , CHR_a , CR_aR_b , O, NH, NR_a , S, SO, and SO_2 ;

where R_c is independently hydrogen, alkyl, alkenyl, alkynyl, alkoxy, aryl, halogen, nitro, cyano, cycloalkyl, heterocycloalkyl, cycloalkenyl, heterocycloalkenyl, OR_a , SR_a , NR_aR_b , $-S(O)_2R_a$, $-S(O)_2NR_aR_b$, $-C(O)R_a$, $-C(O)NR_aR_b$, $-NR_aC(O)R_b$, $-NR_aS(O)_2R_b$, $-N=CR_aR_b$, or $-NR_aC(O)NHR_b$;

where m , p , and q are independently 0, 1, 2, 3, or 4;

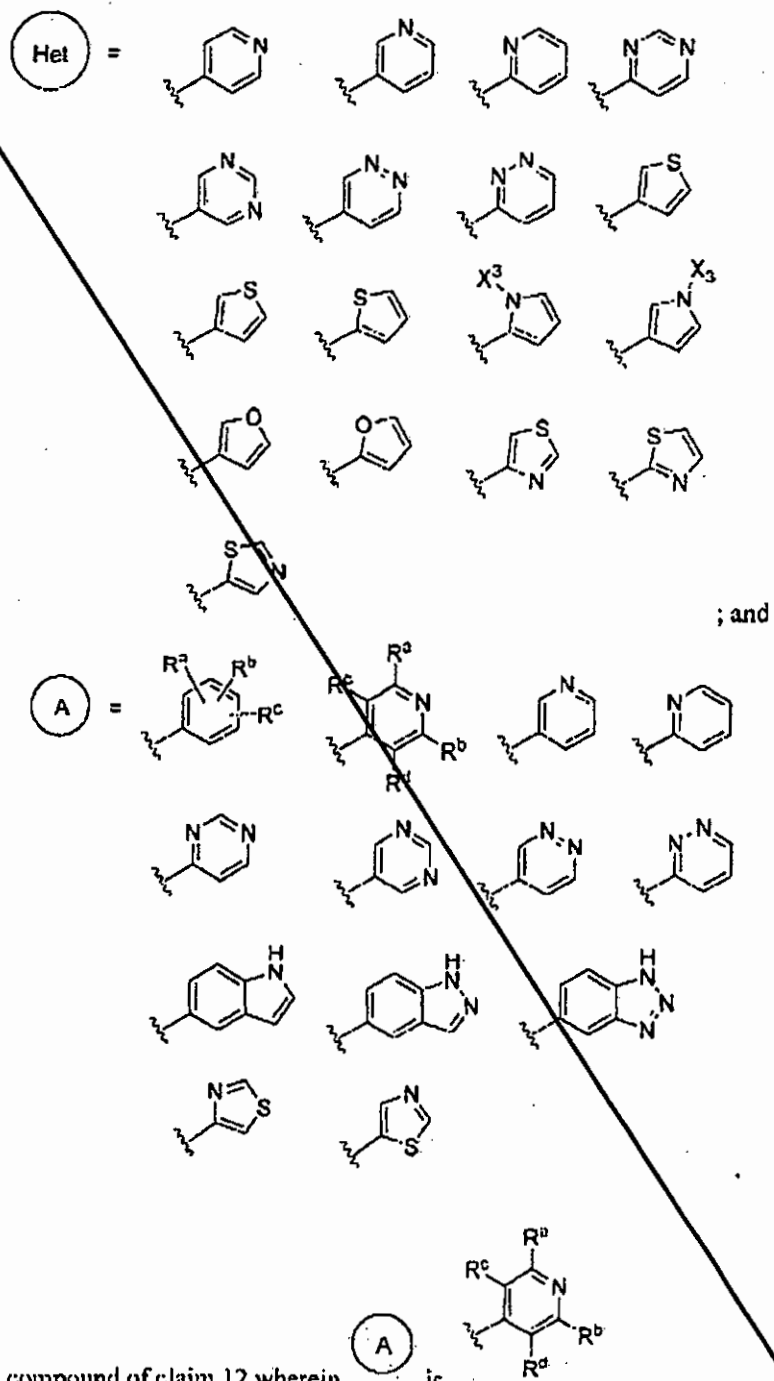
Y is CH_2 , CHR_a , CR_aR_b , O, NH, NR_a , S, SO, or SO_2 ;

R^1 , R^2 , and R^3 are independently H, alkyl, alkoxy, or halogen;

n is 0, 1, or 2;

wherein each of X^1 and X^2 is independently optionally substituted;

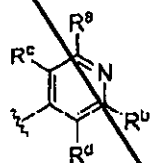
wherein R_c and R_d is independently R_a ;



14. The compound of claim 12 wherein Y is O, S, or SO₂, wherein

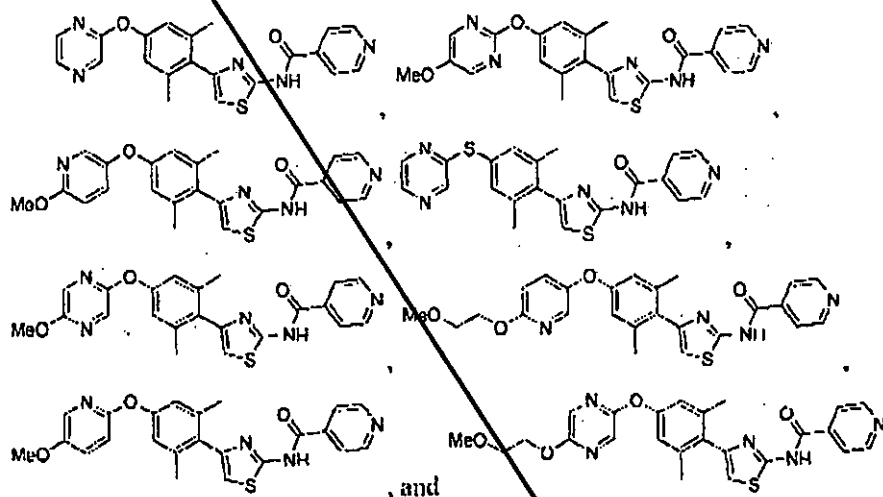
(A)

is

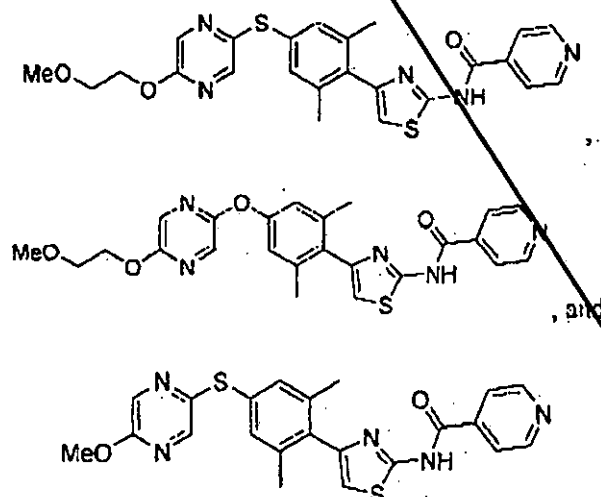


, and wherein R¹, R², and R³ are independently H or alkyl.

15. The compound of claim 1 having a structure selected from the group consisting of



16. The compound of claim 1 having a structure selected from the group consisting of

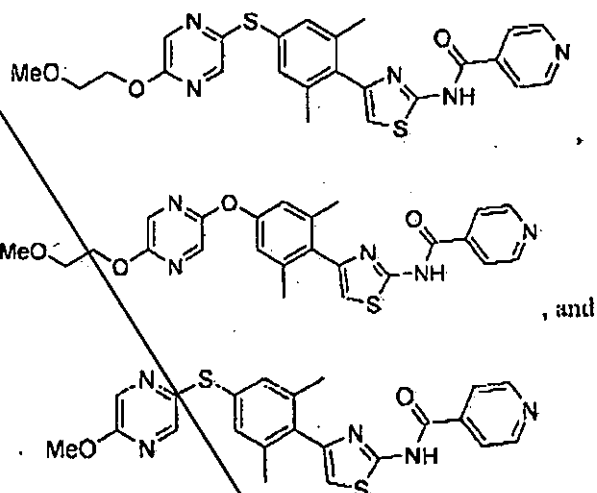


17. The compound of any one of claim 1, claim 15, or claim 16, in combination with an ion to thereby form a pharmaceutically acceptable salt.

18. A metabolite of the compound of any one of claim 1, claim 15, or claim 16.
19. The metabolite of claim 18, wherein R^1 is SR_n , and wherein the S in SR_n is a sulfone or a sulfoxide.
20. A pharmaceutical composition comprising a pharmaceutically acceptable carrier and a compound, optionally present as a pharmaceutically acceptable salt, according to claim 1 in a concentration effective to disrupt Hec1/Nck2 binding in a mammal when the composition is administered to the mammal.
21. The pharmaceutical composition of claim 20, further comprising a drug that interferes with microtubule formation or degradation.
22. The pharmaceutical composition of claim 20 wherein the compound is a compound according to claim 16.
23. The pharmaceutical composition of claim 20 formulated as an orally administerable drug or an injectable drug.
24. A method of disrupting Hec1/Nck2 interaction, comprising contacting a Hec1/Nck2 complex with a compound according to claim 1 in an amount effective to disrupt Nck2/Hec1 binding.
25. The method of claim 24 wherein the step of contacting the Hec1/Nck2 complex is performed *in vivo* in a mammal, and wherein the compound is administered orally, topically, or parenterally.
26. The method of claim 24 further comprising a step of co-administering an agent that interferes with microtubule formation or degradation.
27. A method of treating a mammal having a neoplastic disease, comprising:
administering to a mammal in need thereof a compound according to claim 1 in an amount effective to disrupt Hec1/Nck2 binding or to disrupt a Nck2/Hec1 complex.
28. The method of claim 27 wherein the step of administering comprises injection or oral administration of the compound.

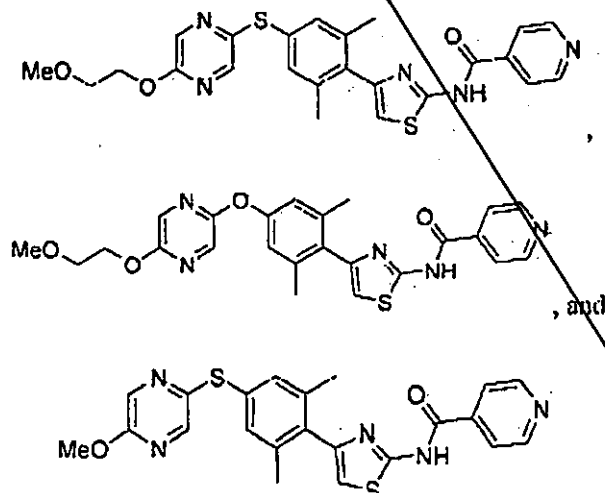
29. The method of claim 27 further comprising administering a second antineoplastic compound to the patient.

30. A method of improving a pharmacokinetic parameter for a compound having a structure selected from the group consisting of



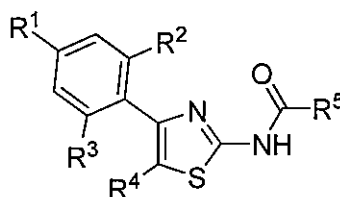
comprising a step of forming a tosylate salt of the compound.

31. A pharmaceutical composition comprising a carrier and a tosylate salt of a compound having a structure selected from the group consisting of



CLAIMS

1. A compound having a structure according to Formula I



Formula I

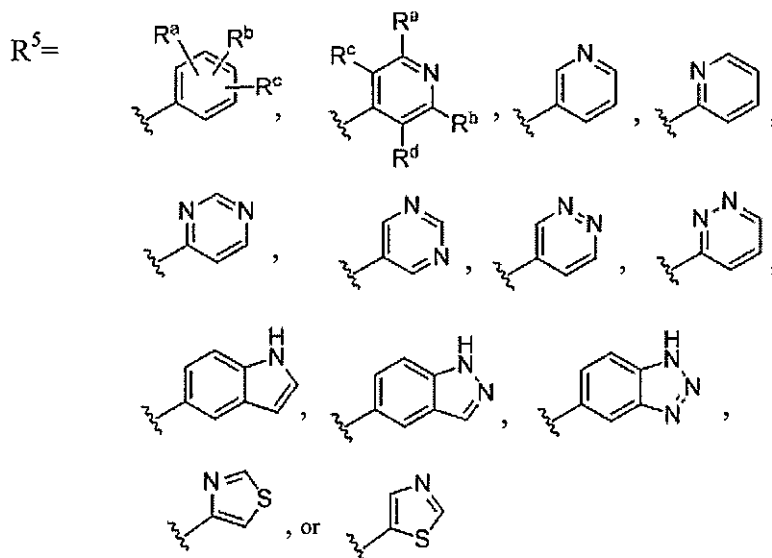
or a pharmaceutically acceptable salt thereof, wherein:

R^1 is OR_a or SR_a ;

R_a of OR_a or SR_a is pyrazine, wherein R_a of OR_a or SR_a is optionally substituted with alkoxy or methoxyalkoxy;

R^2 and R^3 are independently hydrogen, C_1 - C_6 alkyl, or halogen;

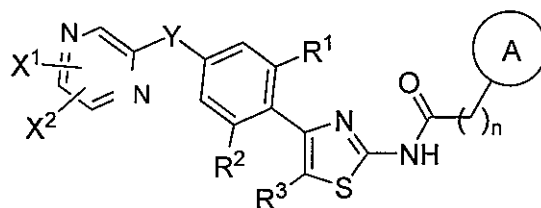
R^4 is hydrogen or halogen;



; and

wherein R^a , R^b , R^c , and R^d in R^5 are independently hydrogen, halogen, C_1 - C_6 alkyl, or amino.

2. The compound of claim 1 having a structure according to Formula II



Formula II

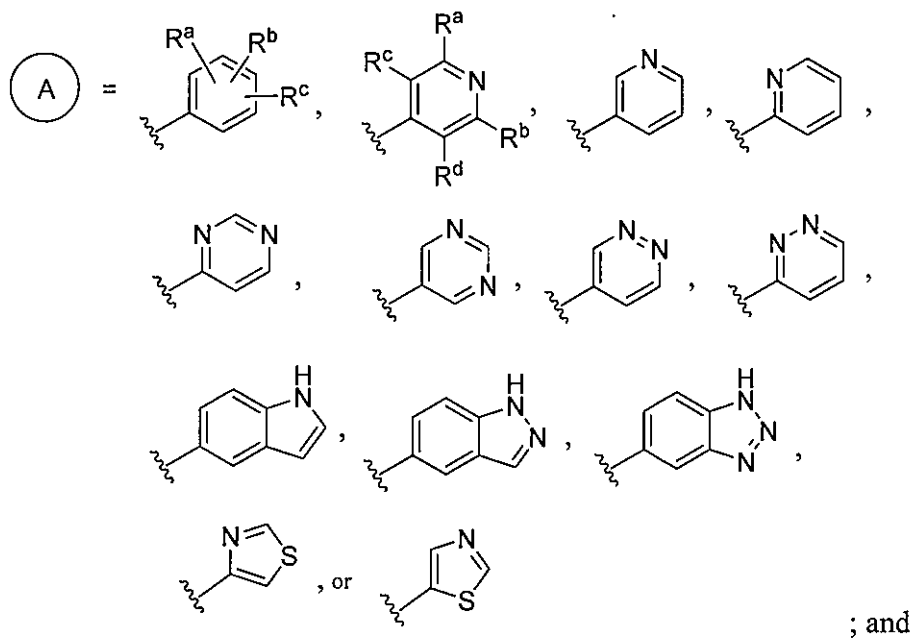
wherein X^1 is alkoxy or methoxyalkoxy and X^2 is hydrogen;

Y is O or S;

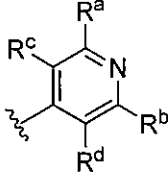
R^1 and R^2 are independently CH_3 ; and

R^3 is hydrogen;

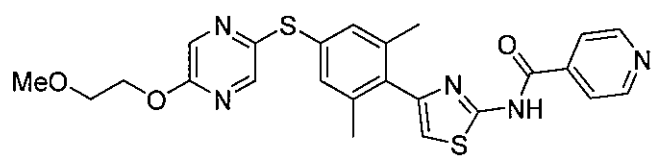
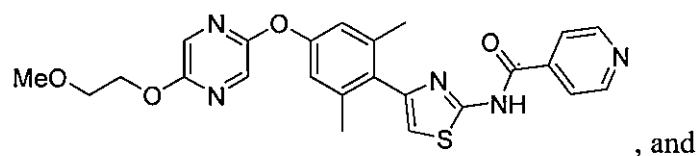
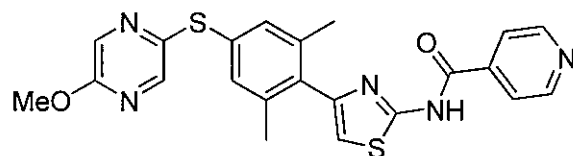
n is 0;



wherein R^a , R^b , R^c , and R^d in (A) are independently hydrogen, halogen, C_1 - C_6 -alkyl, or amino.

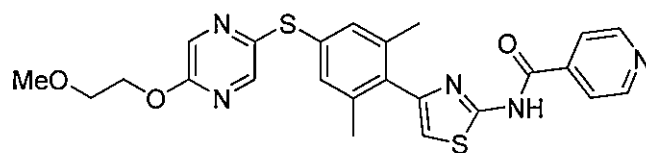
3. The compound of claim 2 wherein  is .

4. The compound of claim 1 having a structure selected from the group consisting of

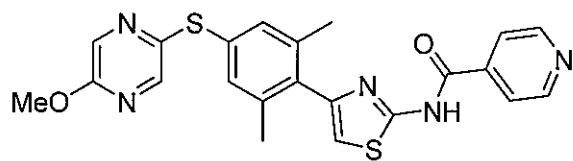


5. The compound of any one of claim 1, claim 2, or claim 4, in combination with an ion to thereby form a pharmaceutically acceptable salt.
6. A metabolite of the compound of any one of claim 1, claim 2, or claim 4.

7. The metabolite of claim 6, wherein R^1 is SR_a , and wherein the S in SR_a is a sulfone or a sulphoxide.
8. A pharmaceutical composition comprising a pharmaceutically acceptable carrier and a compound, optionally present as a pharmaceutically acceptable salt, according to claim 1 in a concentration effective to disrupt Hec1/Nek2 binding in a mammal when the composition is administered to the mammal.
9. The pharmaceutical composition of claim 8, further comprising a drug that interferes with microtubule formation or degradation.
10. The pharmaceutical composition of claim 8 wherein the compound is a compound according to claim 4.
11. The pharmaceutical composition of claim 8 formulated as an orally administerable drug or an injectable drug.
12. A method of improving a pharmacokinetic parameter for a compound having a structure selected from the group consisting of



, and



comprising a step of forming a tosylate salt of the compound;
 wherein the pharmacokinetic parameter comprises an area under the curve (AUC); and
 wherein the improvement is increasing AUC in oral administration of the compound.

13. A pharmaceutical composition comprising a carrier and a tosylate salt of a compound having a structure selected from the group consisting of

