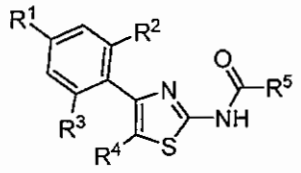
CLAIMS

What is claimed is:

1. A compound having a structure according to Formula I



Formula I

R^1 is 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 $-NR_aC(O)NHR_b$;

R_a and R_b are independently hydrogen, alkyl, alkenyl, alkynyl, aryl, aryloxy, alkoxy, hydroxy, heteroaryl, cycloalkyl, 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, phenyalkenyl, 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;

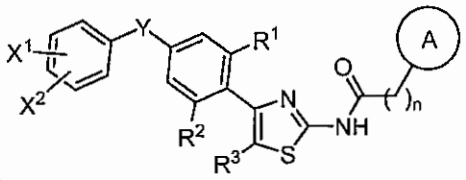
(III) where R^1 and R^2 are methyl and where R^3 is hydroxyl or methoxy, R^5 is not phenyl.

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 having a structure according to Formula II



Formula II

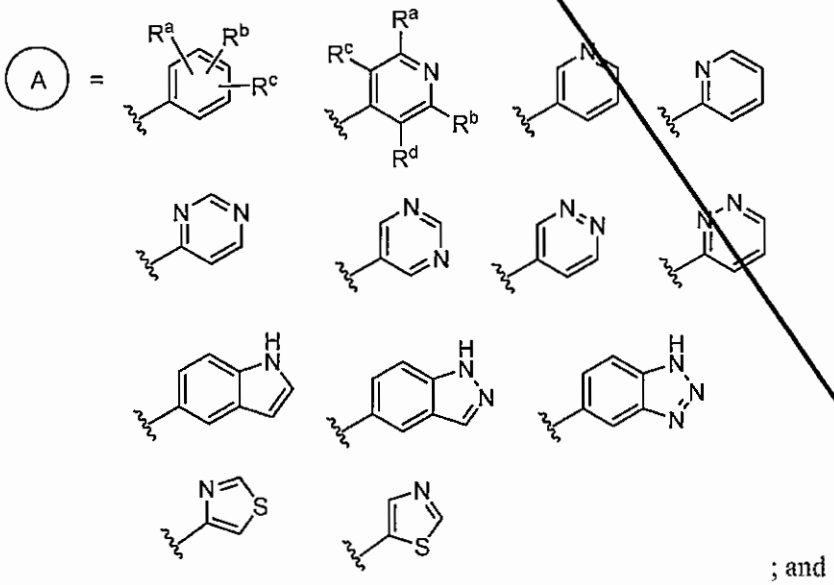
wherein X^1 and X^2 are independently H, alkyl, alkenyl, alkynyl, halogen, nitro, cyano, cycloalkyl, heterocycloalkyl, cycloalkenyl, heterocycloalkenyl, OR_a, NR_aR_b, $-S(O)_2R_a$, $-S(O)_2NR_aR_b$, $-C(O)R_a$, $-C(O)NR_aR_b$, $-NR_aC(O)R_b$, $-NR_aS(O)_2R_b$, $-N=CR_aR_b$, or $-NR_aC(O)NHR_b$;

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;

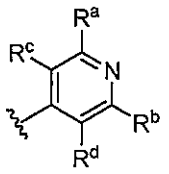
wherein each of X^1 and X^2 is independently optionally substituted;

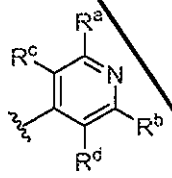


; and

wherein R_c and R_d is independently R_a.

6. The compound of claim 5 wherein Y is O, S, or SO_2.

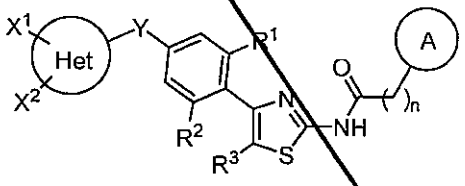
7. The compound of claim 5 wherein  is .

8. The compound of claim 5 wherein Y is O, S, or SO_2 , wherein  is , and wherein R^1, R^2, and R^3 are independently H or alkyl.

9. The compound of claim 8 wherein X^1 and X^2 are independently H, alkyl, and alkoxy, and wherein n is 0 or 1.

10. The compound of claim 5 wherein n is 0.

11. The compound of claim 1 having a structure according to Formula III



Formula III

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

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

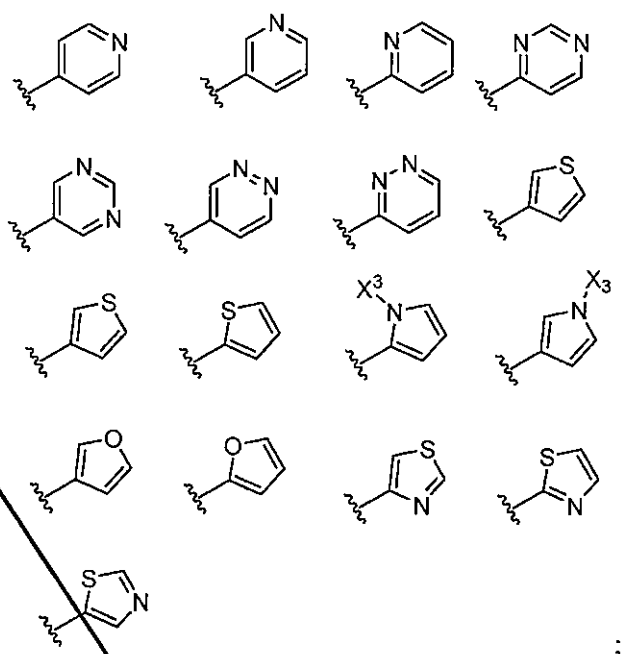
R^1, R^2, and R^3 are independently H, alkyl, alkoxy, or halogen;

n is 0, 1, or 2;

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

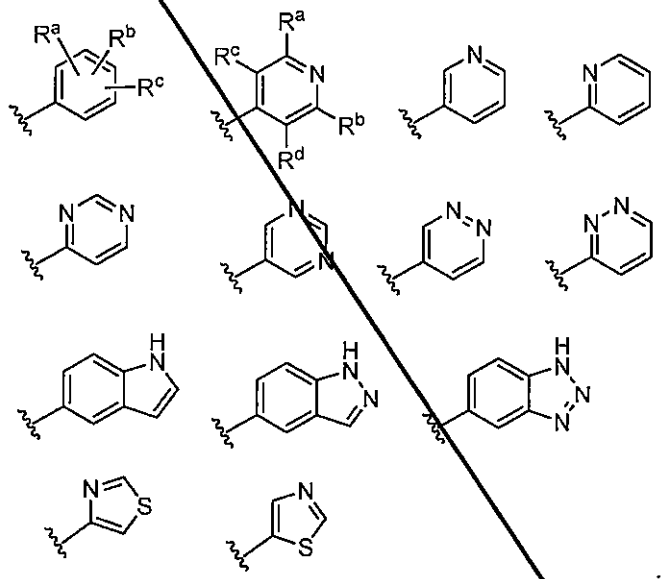
wherein R_c and R_d is independently R_a;

Het =

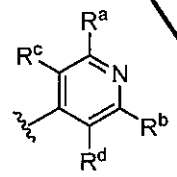


; and

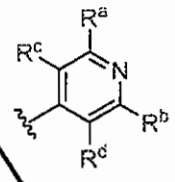
A =



12. The compound of claim 11 wherein A is

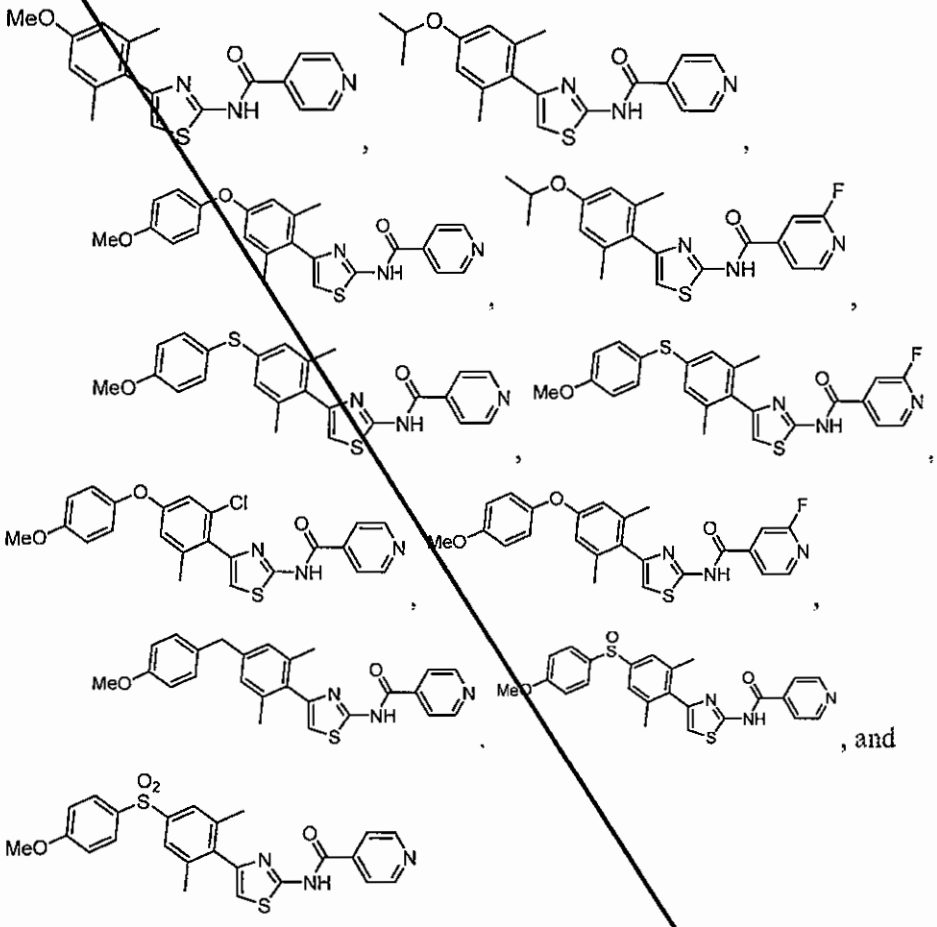


13. The compound of claim 11 wherein Y is O, S, or SO_2, wherein (A) is



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

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



15. A pharmaceutical composition comprising a pharmaceutically acceptable carrier and a compound according to claim 1 in a concentration effective to disrupt Hec1/Nek2 binding in a patient when the composition is administered to the patient.

16. The pharmaceutical composition of claim 15, further comprising a drug that interferes with microtubule formation or degradation.

17. The pharmaceutical composition of claim 15 wherein the compound is a compound according to claim 14.

18. Use of a compound according to claim 1 in the manufacture of a medicament for the disruption of Nek2/Hec1 interaction, wherein the compound is present in the medicament in an amount effective to disrupt Nek2/Hec1 binding.

19. The use of claim 18 wherein the disruption is performed *in vivo* in a mammal, and wherein the compound is administered to the mammal orally, topically, or parenterally.

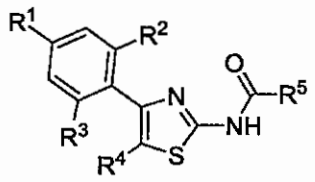
20. The use of claim 18 wherein the medicament is co-administered with an agent that interferes with microtubule formation or degradation.

21. A Nek2/Hec1 complex with a compound according to claim 1 for use in the disruption of Nek2/Hec1 interaction.

CLAIMS

What is claimed is:

1. A compound having a structure according to Formula I



Formula I

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;

R^4 is independently hydrogen, C_1–C_6 alkyl, halogen, or OR_a; and

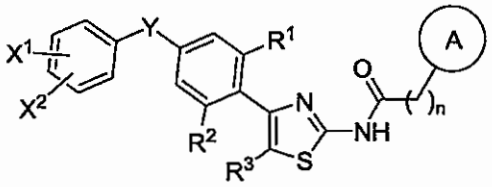
R^5 is optionally substituted pyridinyl;

wherein each of R^1, R^2, R^3, R^4, R^5, and R_a is independently optionally substituted.

2. The compound of claim 1 wherein R^4 is independently hydrogen or C_1–C_6 alkyl.

3. The compound of claim 1 wherein R^1 is OR_a and R_a is optionally substituted aryl.

4. 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, $-S(O)_2R_a$, $-S(O)_2NR_aR_b$, $-C(O)R_a$, $-C(O)NR_aR_b$, $-NR_aC(O)R_b$, $-NR_aS(O)_2R_b$, $-N=CR_aR_b$, or $-NR_aC(O)NHR_b$;

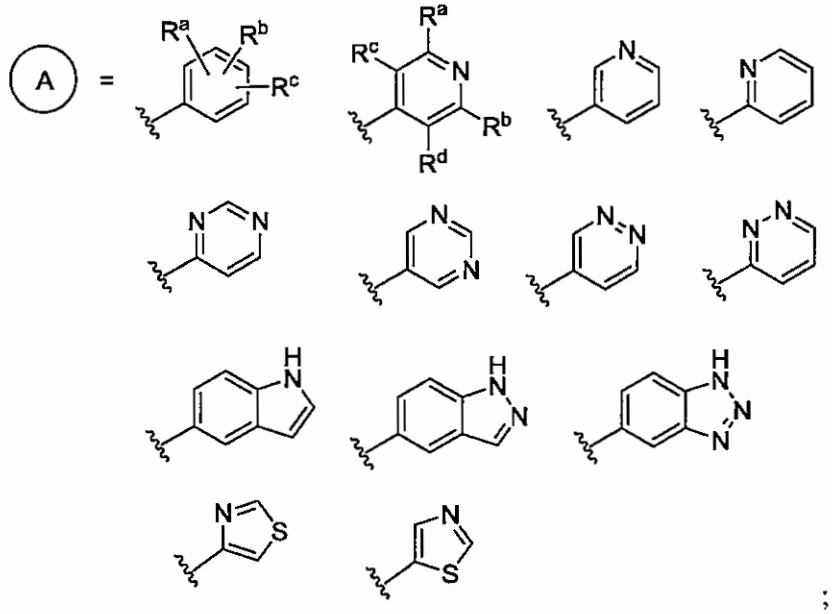
R_b is independently hydrogen, alkyl, alkenyl, alkynyl, aryl, aryloxy, alkoxy, hydroxy, heteroaryl, cycloalkyl, heterocycloalkyl, cycloalkenyl, or heterocycloalkenyl;

Y is O, S, or SO_2;

R^1, R^2, and R^3 are independently H, alkyl, alkoxy, or halogen, wherein at least one of R^1 and R^2 is alkyl or halogen;

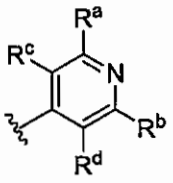
n is 0, 1, or 2;

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

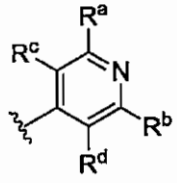


; and

wherein R_c and R_d is independently R_a.

5. The compound of claim 4 wherein  is .

7. The compound of claim 4 wherein Y is O, S, or SO_2, wherein  is

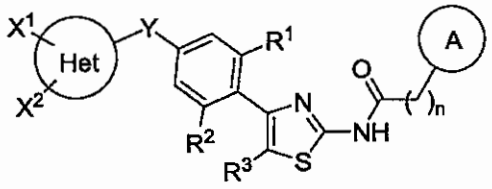


, and wherein R^1, R^2, and R^3 are independently H or alkyl.

8. The compound of claim 7 wherein X^1 and X^2 are independently H, alkyl, and alkoxy, and wherein n is 0 or 1.

9. The compound of claim 4 wherein n is 0.

10. 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, $-S(O)_2R_a$, $-S(O)_2NR_aR_b$, $-C(O)R_a$, $-C(O)NR_aR_b$, $-NR_aC(O)R_b$, $-NR_aS(O)_2R_b$, $-N=CR_aR_b$, or $-NR_aC(O)NHR_b$;

R_b is independently hydrogen, alkyl, alkenyl, alkynyl, aryl, aryloxy, alkoxy, hydroxy, heteroaryl, cycloalkyl, heterocycloalkyl, cycloalkenyl, or heterocycloalkenyl;

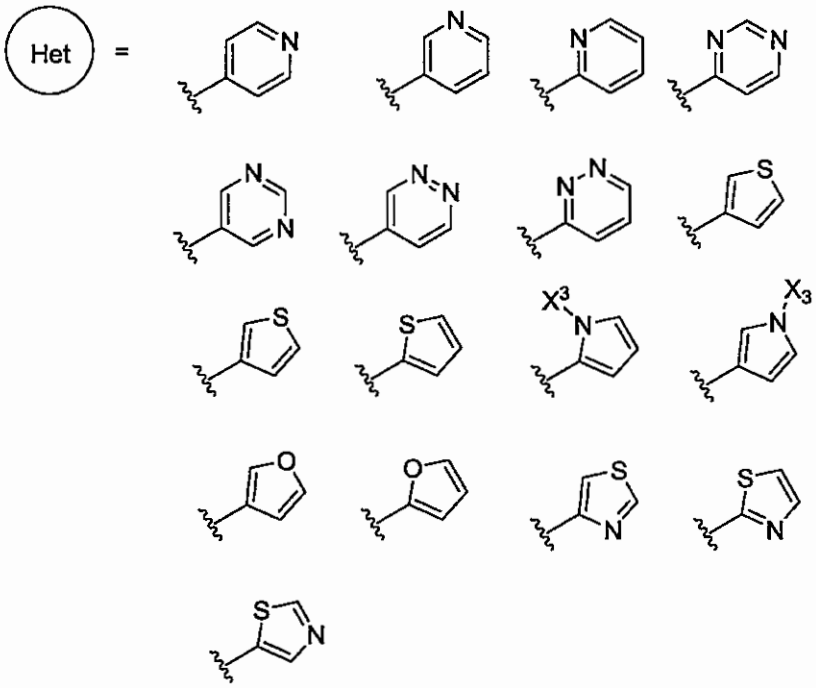
Y is CH_2, CHR_a, CR_aR_b, O, NH, NR_a, S, SO, or SO_2;

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

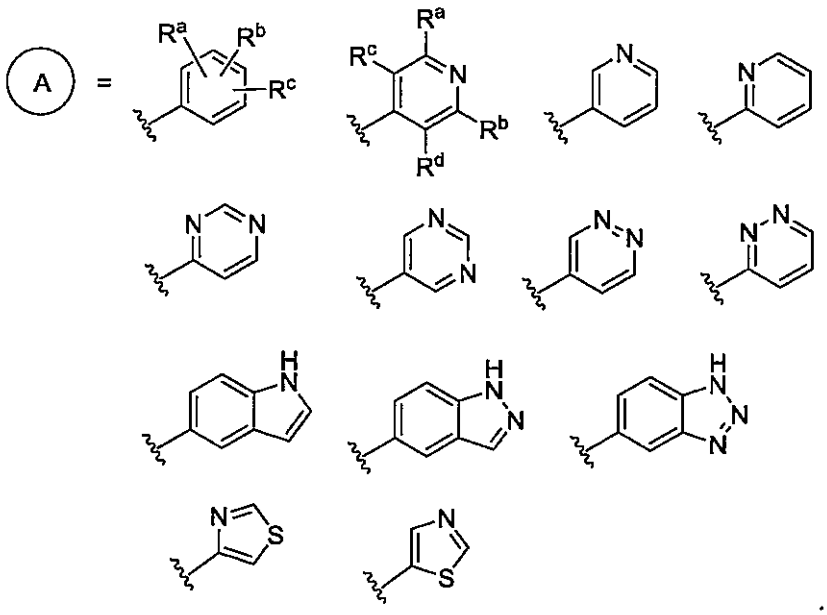
n is 0, 1, or 2;

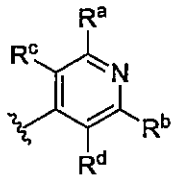
wherein each of X^1 and X^2 is independently optionally substituted;

wherein R_c and R_d is independently R_a;

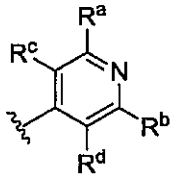


; and



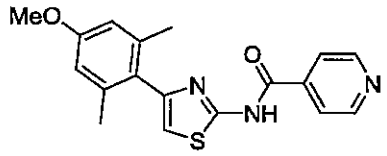
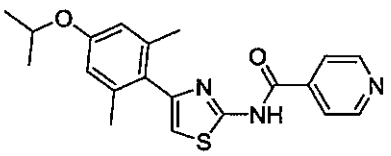
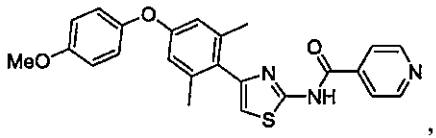
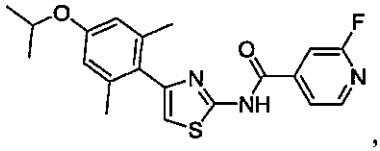
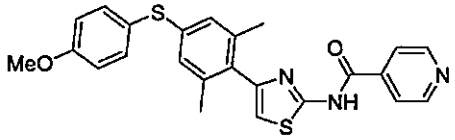
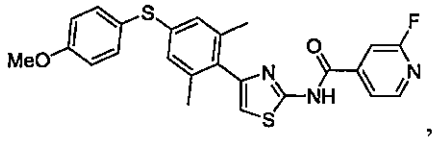
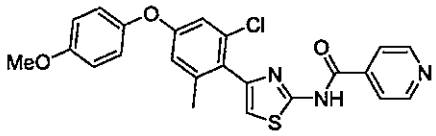
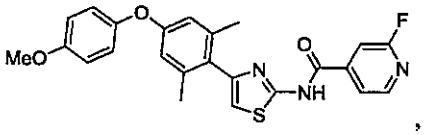
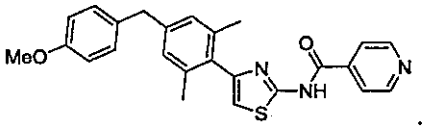
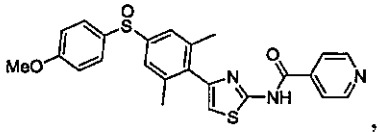
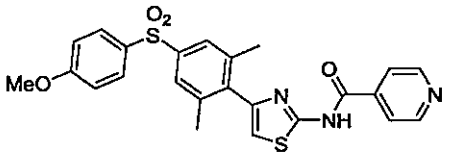
11. The compound of claim 10 wherein (A) is .

12. The compound of claim 10 wherein Y is O, S, or SO_2, wherein (A) is



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

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


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14. A pharmaceutical composition comprising a pharmaceutically acceptable carrier and a compound according to claim 1 in a concentration effective to disrupt Hec1/Nek2 binding in a patient when the composition is administered to the patient.

15. The pharmaceutical composition of claim 14, further comprising a drug that interferes with microtubule formation or degradation.

16. The pharmaceutical composition of claim 14 wherein the compound is a compound according to claim 13.