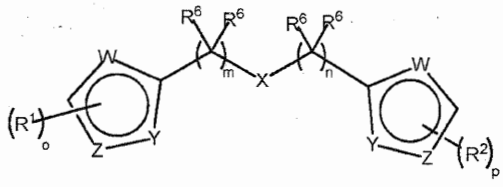
CLAIMS

What is claimed is:

1. A compound of formula (I) or a pharmaceutically acceptable salt thereof:



Formula (I),

wherein

X is a bond, -S-, -S(O)-, -SO_2-, -CH=CH-, -NH-, or –C(O)-;

each W, Y and Z is independently –S-, -CH=, -CH=CH-, -CH=CR^1-, -CR^1=CR^1-, -O-, -N=, or –NH-, provided that (1) for each ring at least one of W, Y and Z is not –CH= and (2) when one of W is –S- and the Y in the same ring is N, then the Z in the same ring is not –CH=;

each R^1 and R^2 is independently C_{1-6} alkylene-R^4, -N(R^3)-R^4, –N(R^3)-C(O)-R^4, -C(O)-N(R^3)-R^4, -N(R^3)-C(O)-O-R^4, -N(R^3)-C(O)-N(R^3)-R^4, -O-C(O)-N(R^3)-R^4, -N(R^3)-C(O)-C_{1-6} alkylene-C(O)-R^4, -N(R^3)-C(O)-C_{1-6} alkylene-N(R^3)-C(O)-R^4 or -N(R^{3a})-C(O)-CH_2-N(R^3)-C(O)-R^4;

each R^3 is independently hydrogen, C_{1-6} alkyl or aryl;

each R^4 is independently C_{1-6} alkyl, C_{1-6} alkenyl, aryl, heteroaryl, aralkyl, heteroaralkyl, heterocyclylalkyl, heterocyclyl, cycloalkyl or cycloalkylalkyl, each of which is substituted with 0-3 occurrences of R^5, or two adjacent R^5 moieties, taken together with the atoms to which they are attached form a heterocyclyl, heteroaryl, cycloalkyl or aryl;

each R^5 is independently oxo (=O), C_{1-6} alkyl, C_{1-6} haloalkyl, C_{1-6} alkoxy, cyano, halo, -OH, -SH, -OCF_3, -SO_2-C_{1-6} alkyl, -NO_2, -N(R^7)-C(O)-C_{1-6} alkyl, -N(R^6)$_2$, -O-C(O)-C_{1-6} alkyl, C_{3-7} cycloalkyl, (C_{3-7} cycloalkyl)alkyl, aryl, aryloxy, -C(O)-aryl, heteroaryl, aralkyl, heteroaralkyl, heterocyclylalkyl or heterocyclyl, wherein each aryl, heteroaryl or heterocyclyl is further substituted with 0-3 occurrences of R^7;

each R^6 is independently hydrogen, fluoro, OH or C_{1-6} alkyl;

each R^7 is independently hydrogen, C_{1-6} alkyl, -OH, -SH, cyano, halo, $-CF_3$, $-OCF_3$, $-SO_2-C_{1-6}$ alkyl, $-NO_2$, $-N(R^7)-C(O)-C_{1-6}$ alkyl, $-N(R^6)_2$ or C_{1-6} alkoxy;

m is 1, 2 or 3;

n is 1, 2 or 3; provided that when X is bond, the sum of m and n is from 3 to 6 and when X is -S-, -S(O)-, $-SO_2-$, -CH=CH-, or –C(O)-, the sum of m and n is from 2 to 4;

o is 1, 2 or 3; and

p is 1, 2 or 3;

with the proviso that: (1) when X is –S-, m and n are both 2, each R^6 is H, then (i) R^1 and R^2 are not both –NHC(O)-R^4, wherein R^4 is C_{1-6} alkyl, a monocyclic ring, monocyclic aralkyl, monocyclic heterocyclylalkyl, monocyclic heteroaralkyl and each member of R^4 is substituted with 0-3 occurrences of R^5; and (ii) R^1 and R^2 are not both –NHC(O)O-methyl, -NHC(O)O-ethyl, -NHC(O)-6-pyrimidine-2,4(1*H*,3*H*)-dionyl, -N(ethyl)C(O)-benzyl, or -NHC(O)NH-phenyl wherein said phenyl of the -NHC(O)NH-phenyl moiety is optionally substituted with 1 or 2 groups selected from methyl, nitro, and halo;

(2) when X is –S-, m and n are both 1, each R^6 is H, then (i) R^1 and R^2 are not both –NH-phenyl or –NH-4-methoxy-phenyl or –NHC(O)-benzyl;

(3) when X is a bond, the sum of m and n is 3, each R^6 is H, then R^1 and R^2 are not both–NHC(O)-R^4, wherein R^4 is monocyclic aryl or monocyclic aralkyl or methyl, and each member of R^4 is optionally substituted with 0-3 occurrences of R^5;

(4) when X is a bond, m and n are both 2, each R^6 is H, then R^1 and R^2 are not both -NHC(O)-furanyl, -NHC(O)-phenyl, -NHC(O)-o-methoxy-phenyl, -NHC(O)-C_{1-6} alkyl, -NH-benzyl, -NHC(O)-NH-phenyl, -NHC(O)-NH-benzyl, or -NH-phenyl wherein said phenyl of the -NH-phenyl moiety is substituted with 0-3 occurrences of R^5;

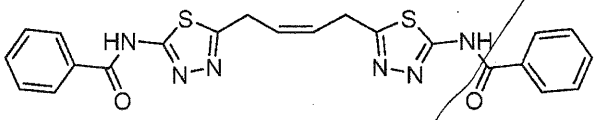
(5) when X is a bond, the sum of m and n is 5, each R^6 is H, then R^1 and R^2 are not both -NHC(O)-C_{1-6} alkyl, -NHC(O)-cyclohexyl, or -NH-phenyl wherein said phenyl of the -NH-phenyl moiety is optionally substituted with methyl; and

(6) when X is a bond, m and n are both 3, each R^6 is H, then R^1 and R^2 are not both NH-phenyl;

(7) when X is a bond, m and n are both 2, and one of W, Y or Z is -CH=CH- or -CH=CR^1 -, then R^1 and R^2 are not both –NHC(O)C(R*)$_2$-phenyl wherein the phenyl is unsubstituted or substituted with 0-3 occurrences of R^5 and R* is H, -OH, -C_{1-2} alkyl-OH, -C_{1-2} alkyl-OCH_3, or -CH_3;

(8) when X is a bond, m and n are both 2, one of W, Y or Z is -CH=CH- or -CH=CR^1 -, and one of R^1 and R^2 is -NHC(O)CH_2-R^, wherein R^ is hydrogen, –NH_2, heteroaryl, or a fused ring, wherein the heteroaryl is unsubstituted or substituted with 0-3 occurrences of R^5; –NHC(O)NH-benzyl; or –$NHCO_2$-benzyl; then the other of R^1 and R^2 is not –NHC(O)C(R*)$_2$-phenyl, wherein the phenyl is unsubstituted or substituted with 0-3 occurrences of R^5, and R* is H, -OH, -C_{1-2} alkyl-OH, -C_{1-2} alkyl-OCH_3, or methyl;

(9) the compound of formula (I) is not:



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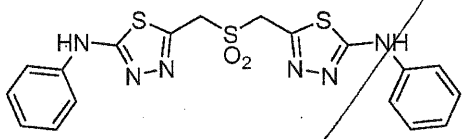

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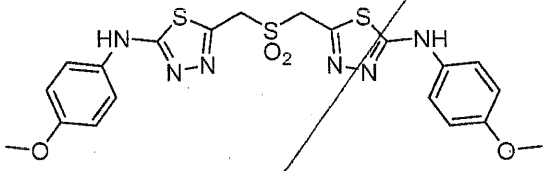

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2. The compound of claim 1, wherein X is –S-, –S(O)-, –SO_2-, a bond, -C(O)- or –CH=CH-.

3. The compound of claim 1, wherein X is–S(O)-, –SO_2-, -C(O)- or –CH=CH-.

4. The compound of claim 1, wherein each R^1 and R^2 is independently -$N(R^3)$-R^4, -C(O)-$N(R^3)$-R^4, -$N(R^3)$-C(O)-O-R^4 or -$N(R^3)$-C(O)-$N(R^3)$-R^4.

5. The compound of claim 4, wherein X is –S- and m and n are both 2.

6. The compound of claim 1, wherein at least one of W, Y and Z is -CH=CH-, -CH=CR^1- or -CR^1=CR^1-.

7. The compound of claim 1, wherein each W is –S-, each Y is –N= and each Z is –N=.

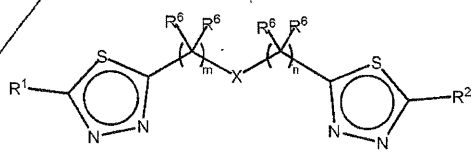
8. The compound of claim 1, wherein each W is –CH=, each Z is –O- and each Y is –N=.

9. The compound of claim 1, wherein o is 1 and p is 1.

10. The compound of claim 1, wherein R^1 and R^2 are each –$N(R^3)$-C(O)-O-R^4, wherein R^3 is hydrogen.

11. The compound of claim 10, wherein R^1 and R^2 are the same.

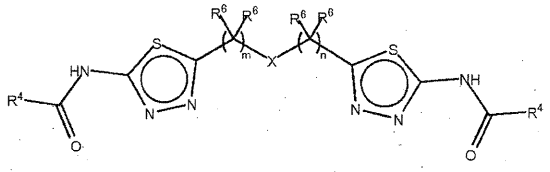
12. The compound of claim 1, wherein the compound is a compound of Formula (II):



(II).

13. The compound of claim 12, wherein R^1 and R^2 are the same.

14. The compound of claim 1, wherein the compound is a compound of Formula (III):



(III).

15. The compound of claim 1, wherein the compound of Formula (I) is selected from Compounds 1-132 of Table 1.

16. A pharmaceutical composition comprising a compound of Formula (I) or a pharmaceutically acceptable salt thereof.

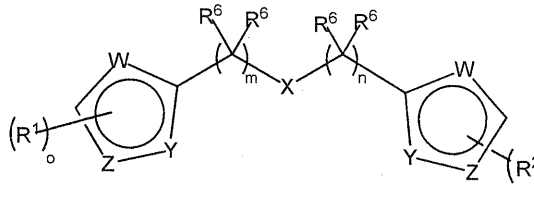
17. A method of treating cancer, the method comprising administering a compound of claim 1 or a composition of claim 16 to a subject in need thereof.

18. The method of claim 17, wherein the cancer is selected from a cancer characterized by i) a low level of E-cadherin expression compared to a reference standard, ii) a high level of vimentin expression compared to a reference standard, or iii) a low or decreased level of pyruvate carboxylase expression.

19. The method of claim 17, wherein the cancer is lung cancer, non-small cell lung cancer, breast cancer, hepatocellular carcninoma, osteosarcoma, lipomas, chondrosarcoma or mesothelioma.

What is claimed is:

1. A compound of formula (I) or a pharmaceutically acceptable salt thereof:



Formula (I),

wherein

X is a bond, -S-, -S(O)-, $-SO_2$-, -CH=CH-, -NH-, or –C(O)-;

each W, Y and Z is independently –S-, -CH=, -CH=CH-, -CH=CR^1-, -CR^1=CR^1-, -O-, -N=, or –NH-, provided that (1) for each ring at least one of W, Y and Z is not –CH= and (2) when one of W is –S- and the Y in the same ring is N, then the Z in the same ring is not –CH=;

each R^1 and R^2 is independently C_{1-6} alkylene-R^4, -N(R^3)-R^4, –N(R^3)-C(O)-R^4, -C(O)-N(R^3)-R^4, -N(R^3)-C(O)-O-R^4, -N(R^3)-C(O)-N(R^3)-R^4, -O-C(O)-N(R^3)-R^4, -N(R^3)-C(O)-C_{1-6} alkylene-C(O)-R^4, -N(R^3)-C(O)-C_{1-6} alkylene-N(R^3)-C(O)-R^4 or -N(R^{3a})-C(O)-CH_2-N(R^3)-C(O)-R^4;

each R^3 is independently hydrogen, C_{1-6} alkyl or aryl;

each R^4 is independently C_{1-6} alkyl, C_{1-6} alkenyl, aryl, heteroaryl, aralkyl, heteroaralkyl, heterocyclylalkyl, heterocyclyl, cycloalkyl or cycloalkylalkyl, each of which is substituted with 0-3 occurrences of R^5, or two adjacent R^5 moieties, taken together with the atoms to which they are attached form a heterocyclyl, heteroaryl, cycloalkyl or aryl;

each R^5 is independently oxo (=O), C_{1-6} alkyl, C_{1-6} haloalkyl, C_{1-6} alkoxy, cyano, halo, -OH, -SH, $-OCF_3$, $-SO_2$-C_{1-6} alkyl, $-NO_2$, -N(R^7)-C(O)-C_{1-6} alkyl, -N(R^6)$_2$, -O-C(O)-C_{1-6} alkyl, C_{3-7} cycloalkyl, (C_{3-7} cycloalkyl)alkyl, aryl, aryloxy, -C(O)-aryl, heteroaryl, aralkyl, heteroaralkyl, heterocyclylalkyl or heterocyclyl, wherein each aryl, heteroaryl or heterocyclyl is further substituted with 0-3 occurrences of R^7;

each R^6 is independently hydrogen, fluoro, OH or C_{1-6} alkyl;

each R^7 is independently hydrogen, C_{1-6} alkyl, -OH, -SH, cyano, halo, $-CF_3$, $-OCF_3$, $-SO_2-C_{1-6}$ alkyl, $-NO_2$, $-N(R^7)-C(O)-C_{1-6}$ alkyl, $-N(R^6)_2$ or C_{1-6} alkoxy;

m is 1, 2 or 3;

n is 1, 2 or 3; provided that when X is bond, the sum of m and n is from 3 to 6 and when X is -S-, -S(O)-, $-SO_2-$, -CH=CH-, or –C(O)-, the sum of m and n is from 2 to 4;

o is 1, 2 or 3; and

p is 1, 2 or 3;

with the proviso that: (1) when X is -S-, m and n are both 2 and each R^6 is H, then (i) R^1 and R^2 are not both $-NHC(O)-R^4$, wherein R^4 is C_{1-6} alkyl, a monocyclic ring, monocyclic aralkyl, monocyclic heterocyclylalkyl or monocyclic heteroaralkyl and each member of R^4 is substituted with 0-3 occurrences of R^5; and (ii) R^1 and R^2 are not both –NHC(O)O-methyl, -NHC(O)O-ethyl, -NHC(O)-6-pyrimidine-2,4(1*H*,3*H*)-dionyl, -N(ethyl)C(O)-benzyl, or -NHC(O)NH-phenyl wherein said phenyl of the -NHC(O)NH-phenyl moiety is optionally substituted with 1 or 2 groups selected from the group consisting of methyl, nitro, and halo;

(2) when X is -S-, m and n are both 1 and each R^6 is H, then (i) R^1 and R^2 are not both –NH-phenyl, –NH-4-methoxy-phenyl or –NHC(O)-benzyl;

(3) when X is a bond, the sum of m and n is 3 and each R^6 is H, then R^1 and R^2 are not both–$NHC(O)-R^4$, wherein R^4 is monocyclic aryl, monocyclic aralkyl or methyl, and each member of R^4 is optionally substituted with 0-3 occurrences of R^5;

(4) when X is a bond, m and n are both 2 and each R^6 is H, then R^1 and R^2 are not both -NHC(O)-furanyl, -NHC(O)-phenyl, -NHC(O)-o-methoxy-phenyl, $-NHC(O)-C_{1-6}$ alkyl, -NH-benzyl, -NHC(O)-NH-phenyl, -NHC(O)-NH-benzyl, or -NH-phenyl wherein said phenyl of the -NH-phenyl moiety is substituted with 0-3 occurrences of R^5;

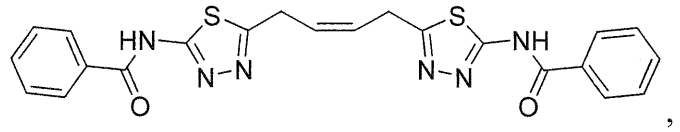
(5) when X is a bond, the sum of m and n is 5 and each R^6 is H, then R^1 and R^2 are not both $-NHC(O)-C_{1-6}$ alkyl, -NHC(O)-cyclohexyl, or -NH-phenyl wherein said phenyl of the -NH-phenyl moiety is optionally substituted with methyl; and

(6) when X is a bond, m and n are both 3 and each R^6 is H, then R^1 and R^2 are not both NH-phenyl;

(7) when X is a bond, m and n are both 2 and one of W, Y or Z is -CH=CH- or -CH=CR^1 -, then R^1 and R^2 are not both –NHC(O)C(R*)$_2$-phenyl wherein the phenyl is substituted with 0-3 occurrences of R^5 and R* is H, -OH, -C$_{1-2}$ alkyl-OH, -C$_{1-2}$ alkyl-OCH$_3$, or -CH$_3$;

(8) when X is a bond, m and n are both 2, one of W, Y or Z is -CH=CH- or -CH=CR^1 -, and one of R^1 and R^2 is -NHC(O)CH$_2$-R^, wherein R^ is hydrogen, –NH$_2$, heteroaryl, or a fused ring, wherein the heteroaryl is substituted with 0-3 occurrences of R^5, –NHC(O)NH-benzyl or –NHCO$_2$-benzyl, then the other of R^1 and R^2 is not –NHC(O)C(R*)$_2$-phenyl, wherein the phenyl is substituted with 0-3 occurrences of R^5, and R* is H, -OH, -C$_{1-2}$ alkyl-OH, -C$_{1-2}$ alkyl-OCH$_3$, or methyl;

(9) the compound of formula (I) is not:



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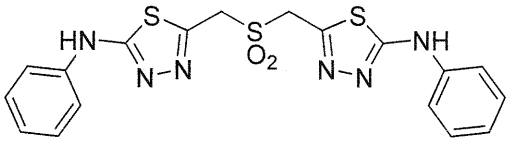
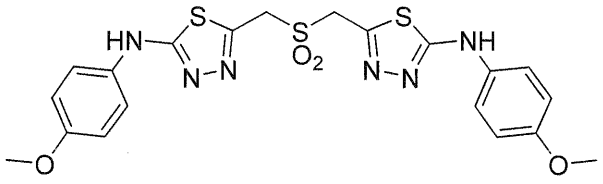


or



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2. The compound of claim 1, wherein X is –S-, –S(O)-, –SO$_2$-, a bond, -C(O)- or –CH=CH-.

3. The compound of claim 1, wherein X is–S(O)-, –SO$_2$-, -C(O)- or –CH=CH-.

4. The compound of claim 1, wherein each R^1 and R^2 is independently -N(R^3)-R^4, -C(O)-N(R^3)-R^4, -N(R^3)-C(O)-O-R^4 or -N(R^3)-C(O)-N(R^3)-R^4.

5. The compound of claim 4, wherein X is –S- and m and n are both 2.

6. The compound of claim 1, wherein at least one of W, Y and Z is -CH=CH-, -CH=CR^1- or -CR^1=CR^1-.

7. The compound of claim 1, wherein each W is –S-, each Y is –N= and each Z is –N=.

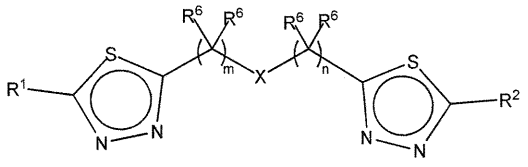
8. The compound of claim 1, wherein each W is –CH=, each Z is –O- and each Y is –N=.

9. The compound of claim 1, wherein o is 1 and p is 1.

10. The compound of claim 1, wherein R^1 and R^2 are each –N(R^3)-C(O)-O-R^4, wherein R^3 is hydrogen.

11. The compound of claim 10, wherein R^1 and R^2 are the same.

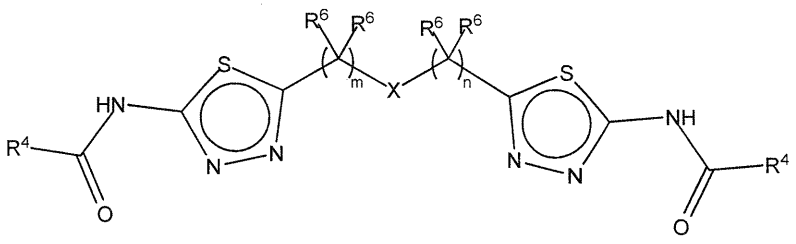
12. The compound of claim 1, wherein the compound is a compound of Formula (II):



(II).

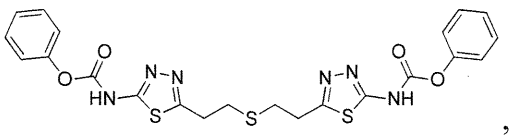
13. The compound of claim 12, wherein R^1 and R^2 are the same.

14. The compound of claim 1, wherein the compound is a compound of Formula (III):



(III).

15. The compound of claim 1, selected from the group consisting of: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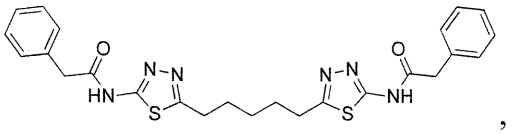
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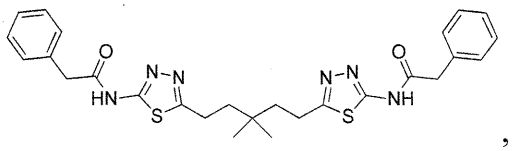
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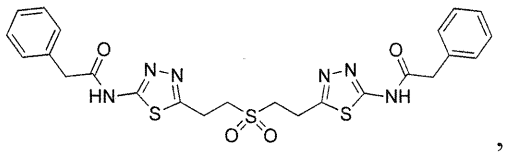
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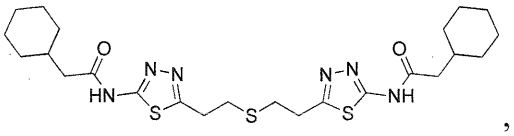
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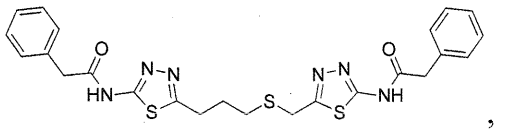
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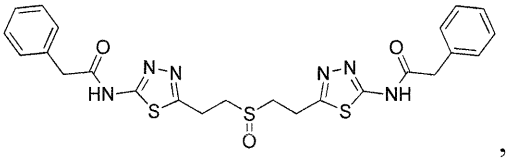
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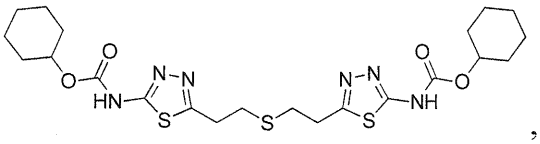
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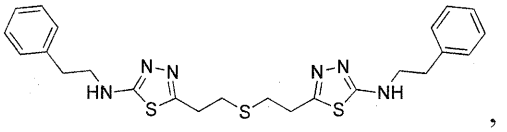
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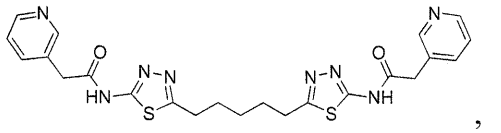
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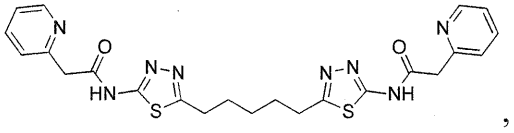
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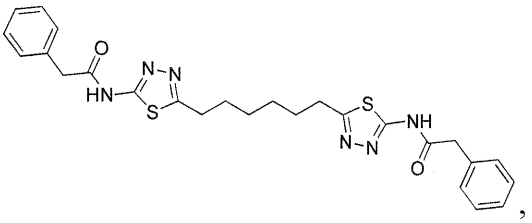
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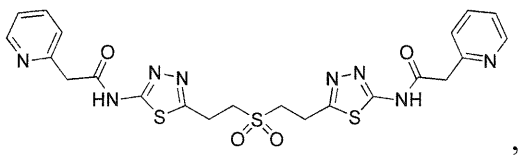
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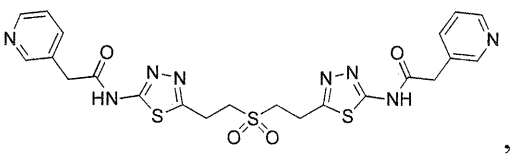
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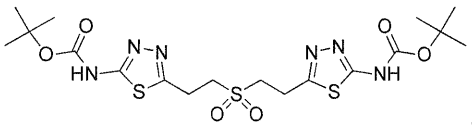

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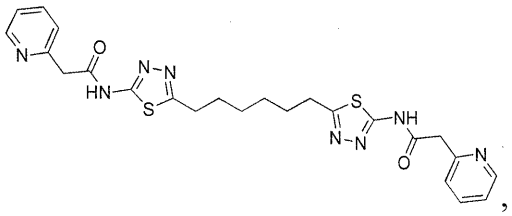

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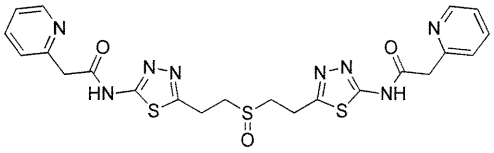

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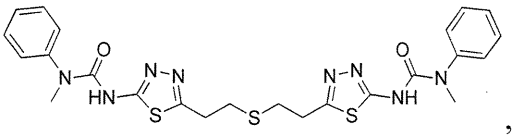

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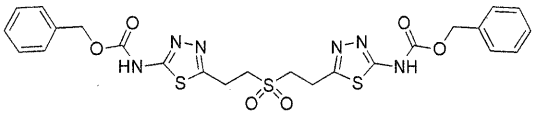

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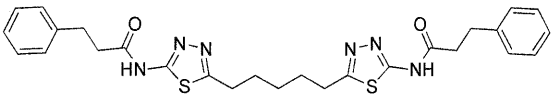

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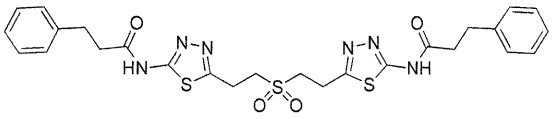

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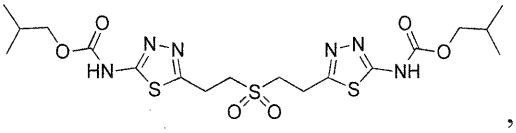

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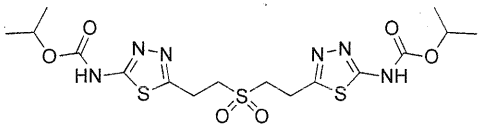

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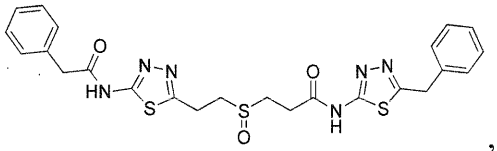

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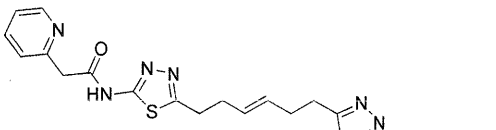

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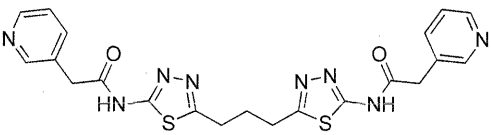

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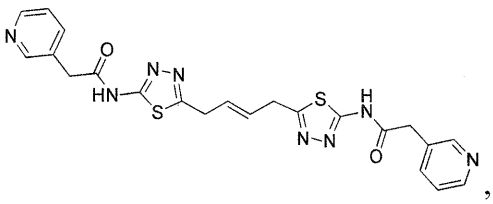

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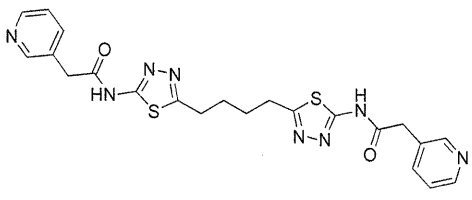

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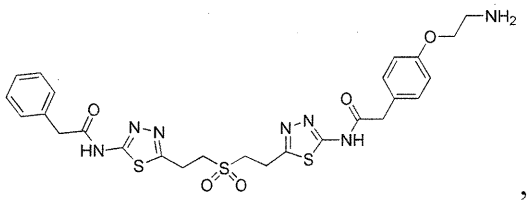

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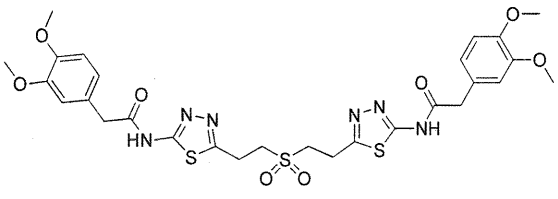

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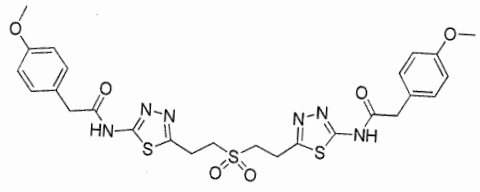
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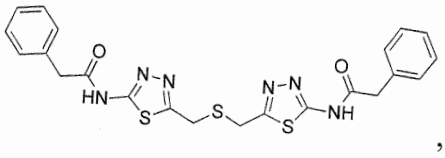
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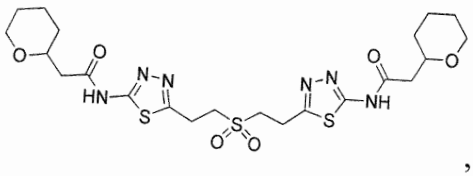
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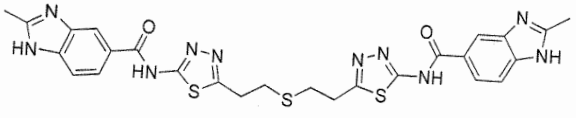
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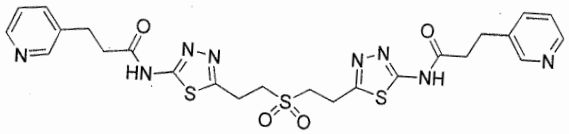
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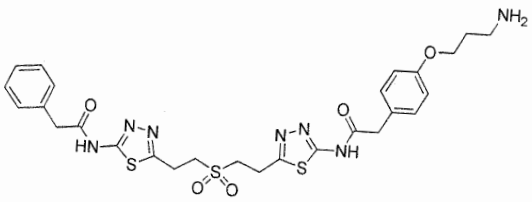
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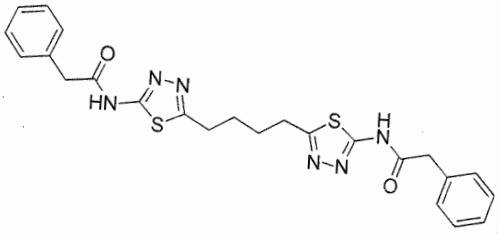
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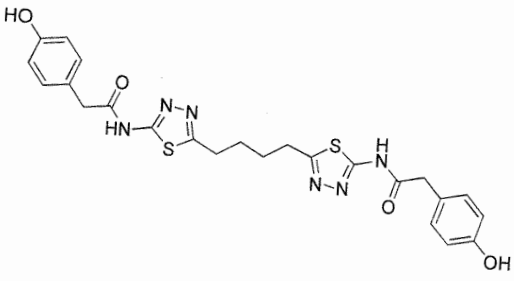
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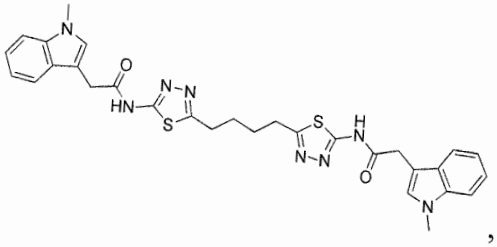
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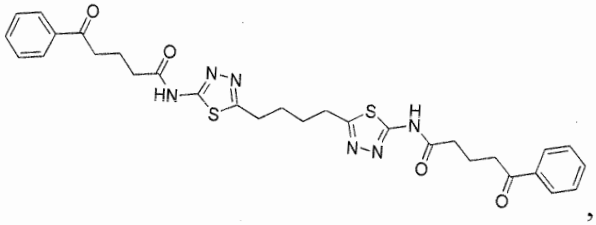
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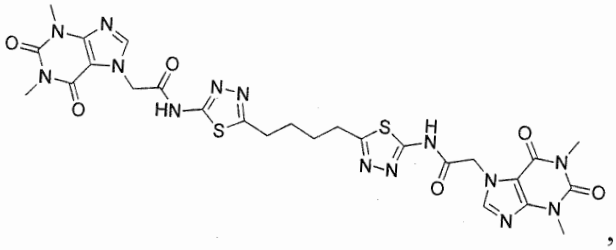
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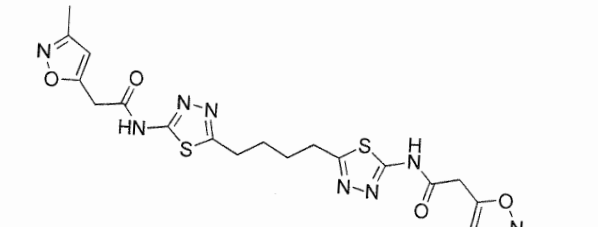
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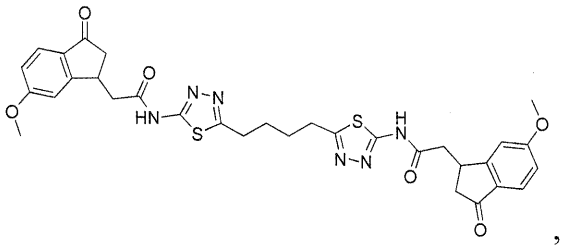

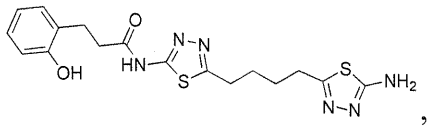

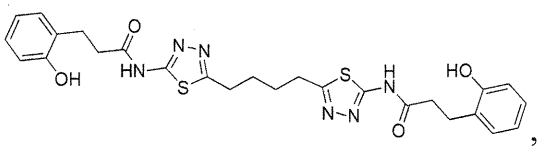

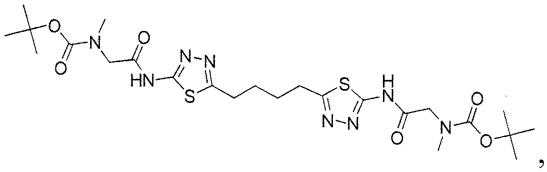

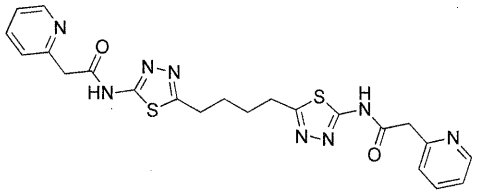

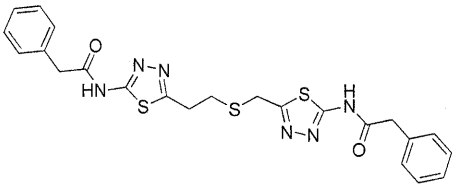

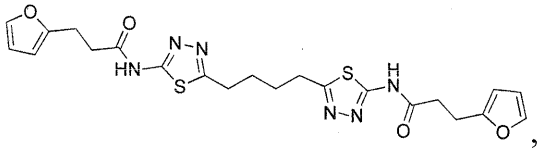

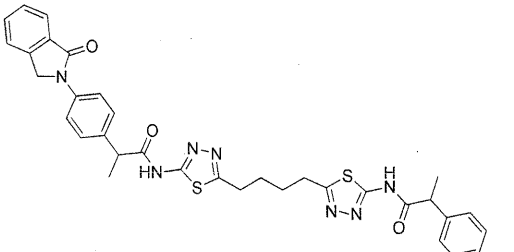

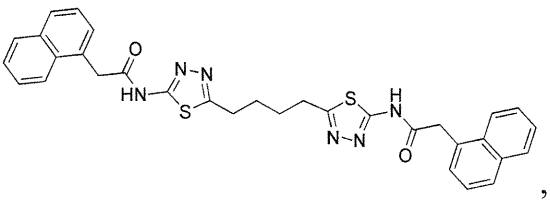

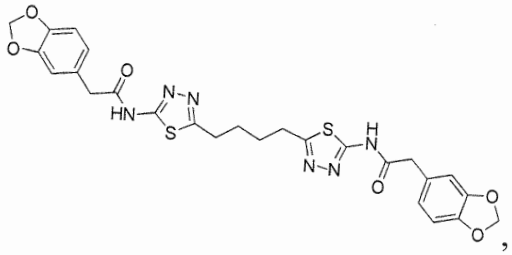

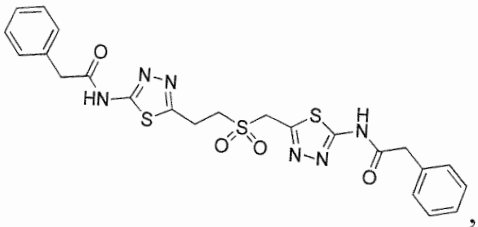

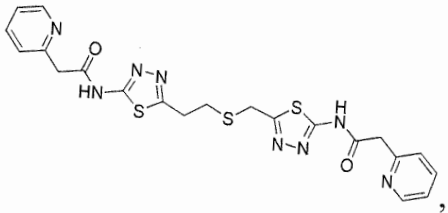

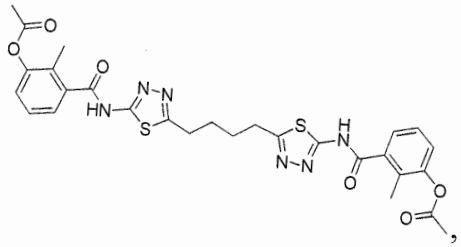

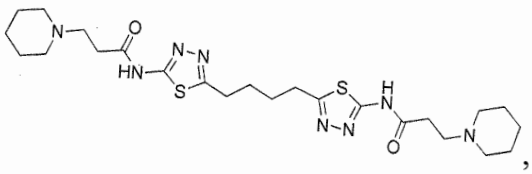

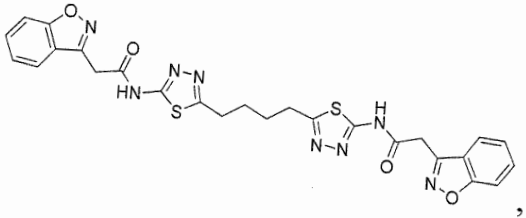

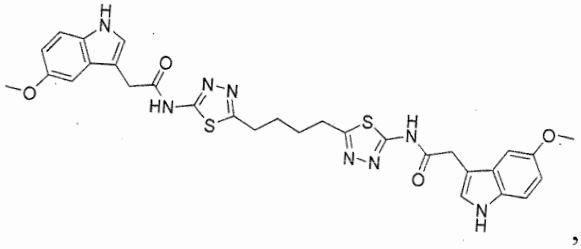

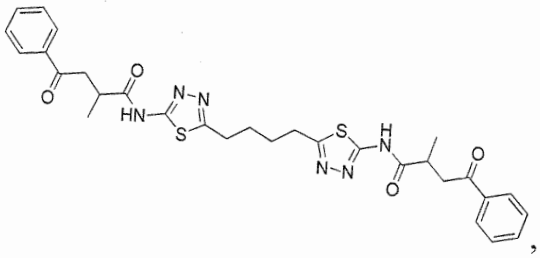

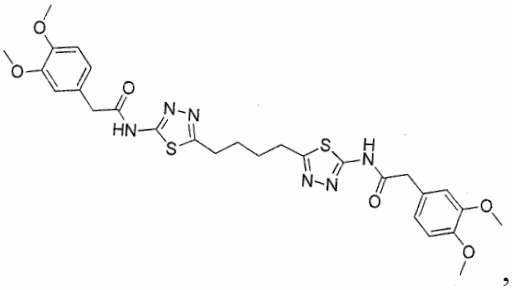

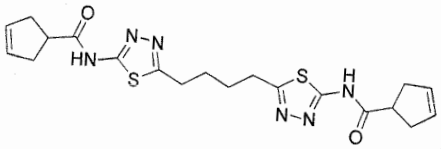

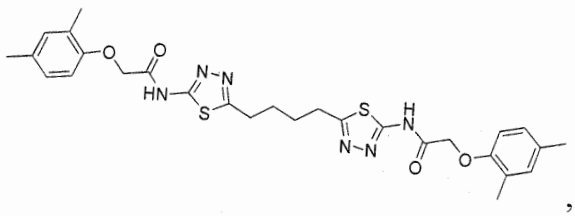

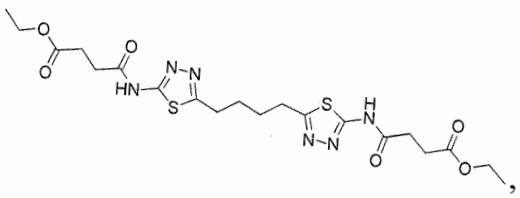

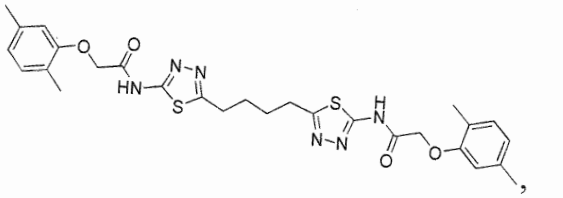

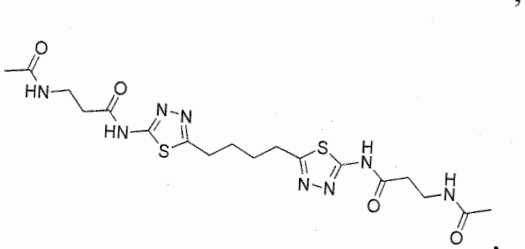





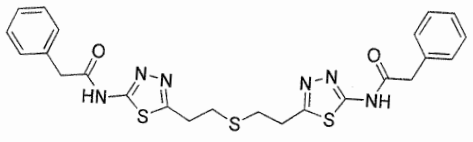

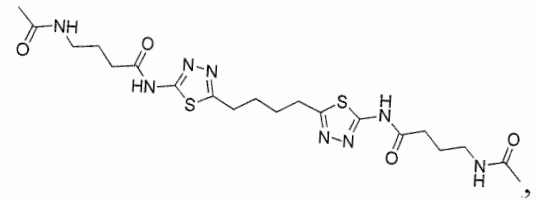

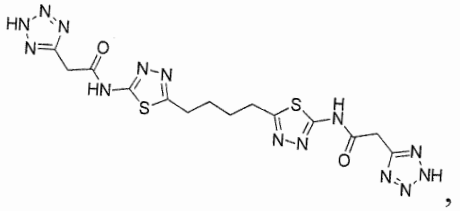

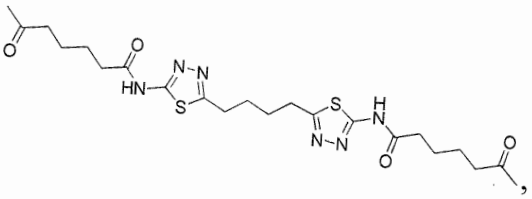

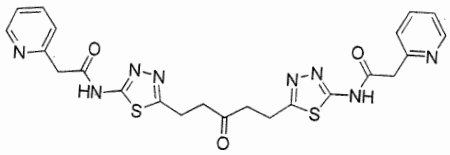

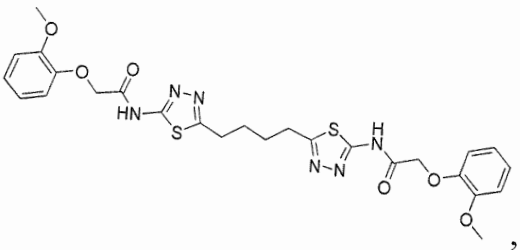

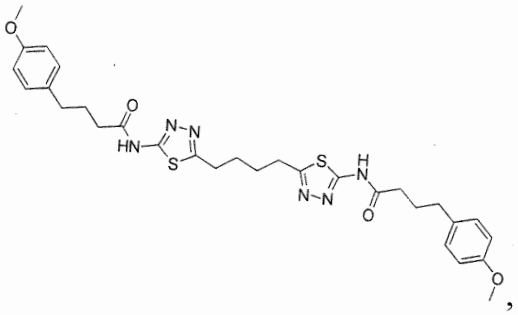

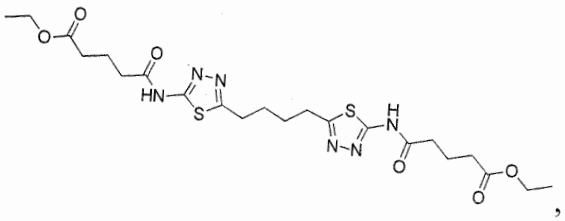

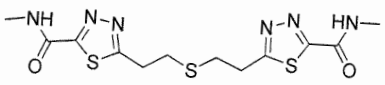

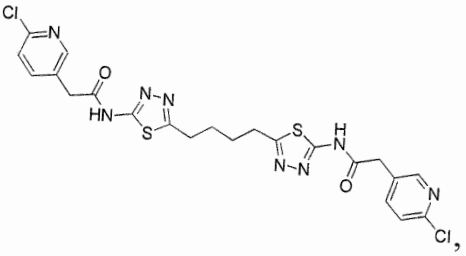

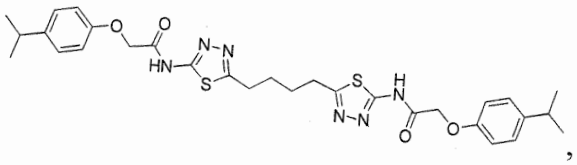

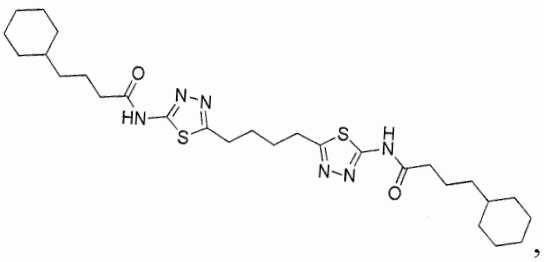

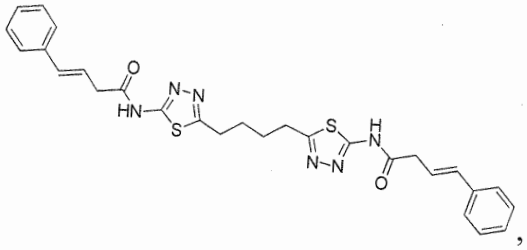

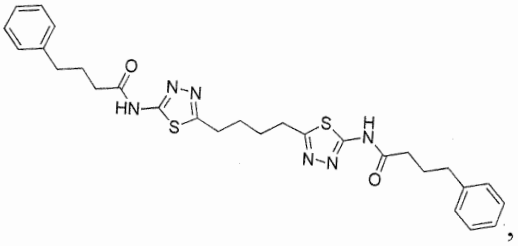

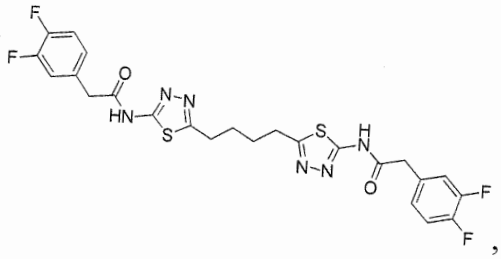

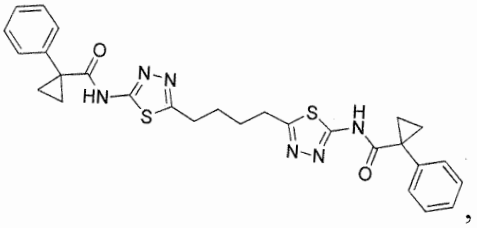

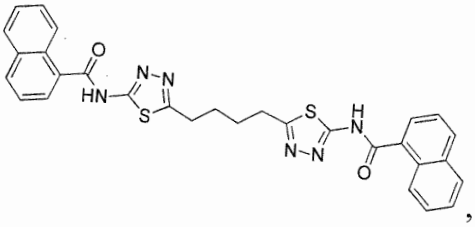

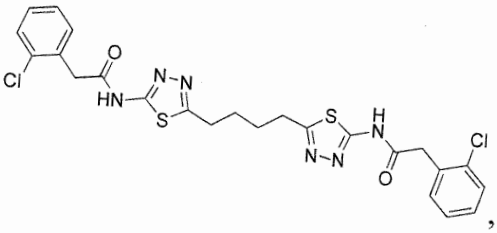

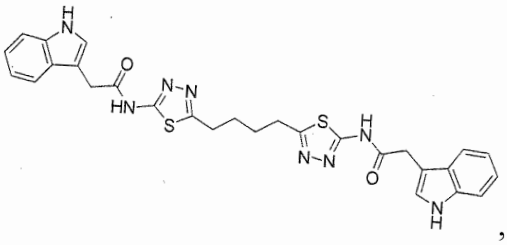

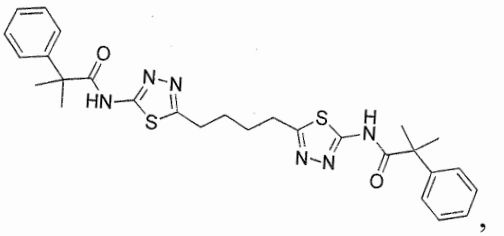

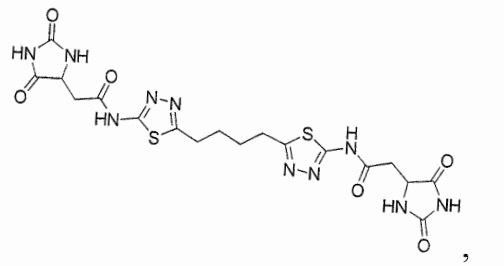

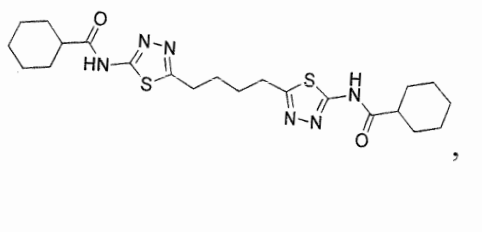

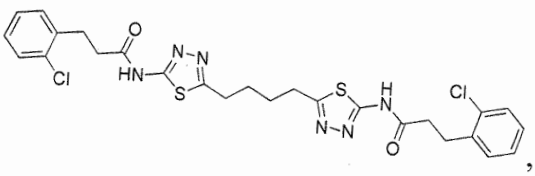

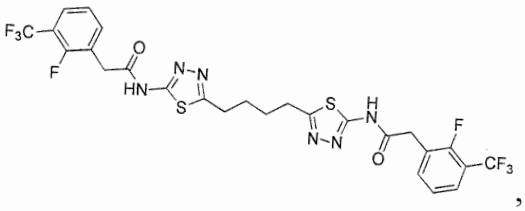

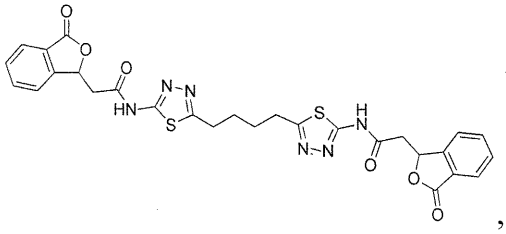

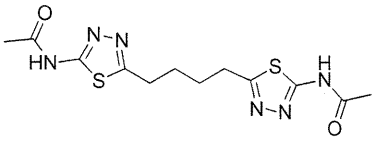

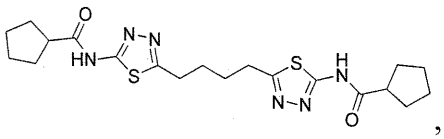

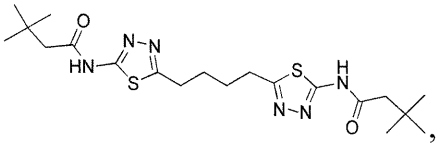

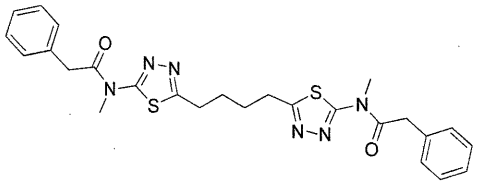

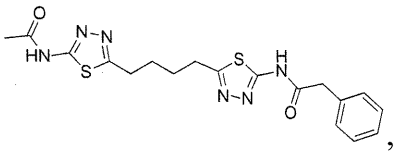

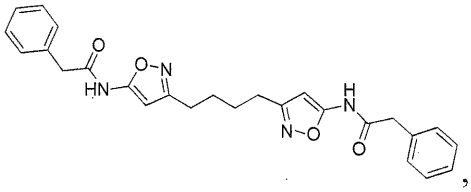

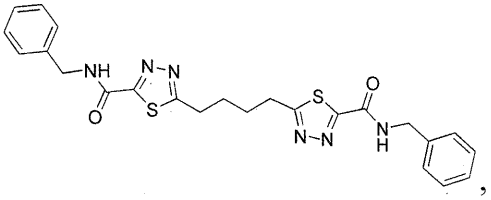

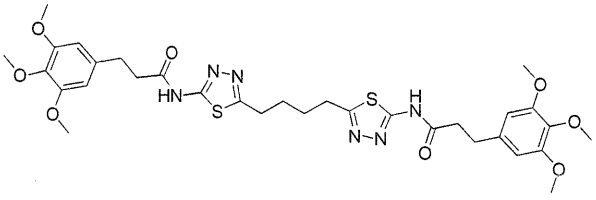

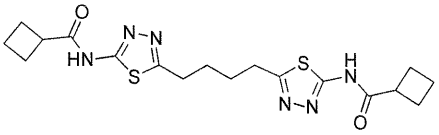

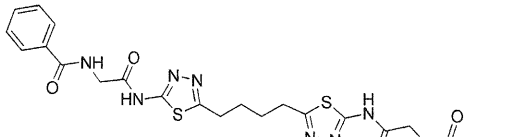

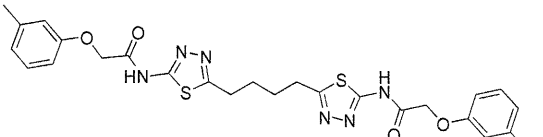

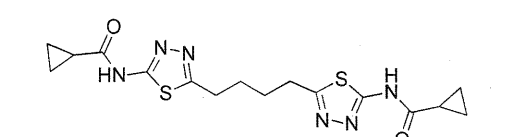

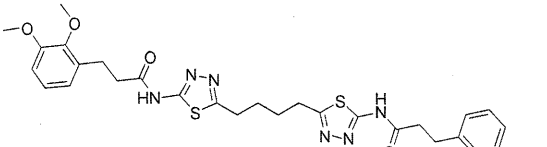

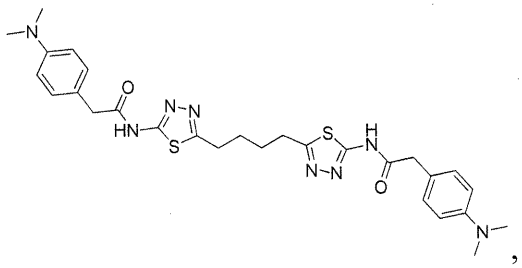

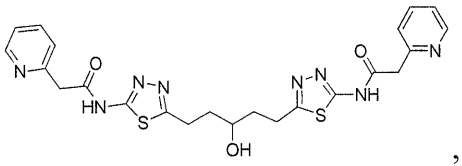

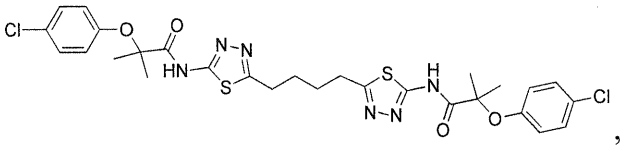

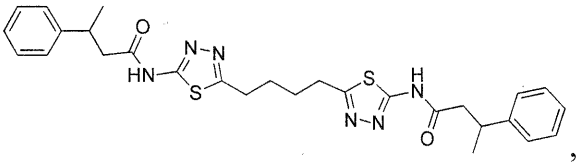

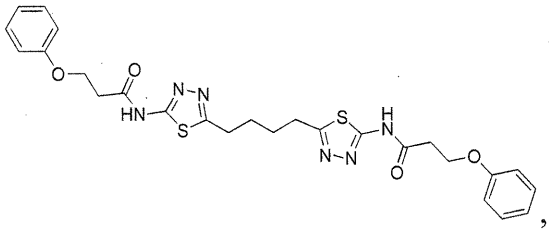

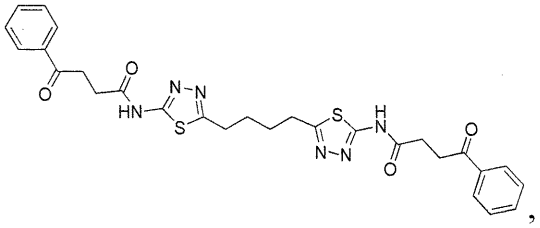

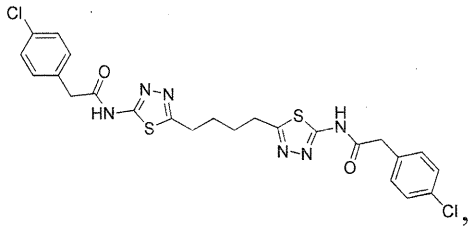

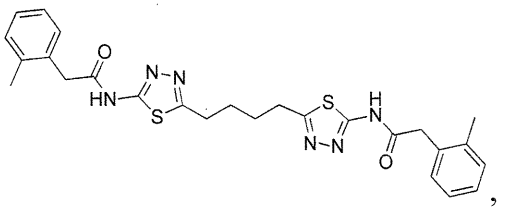

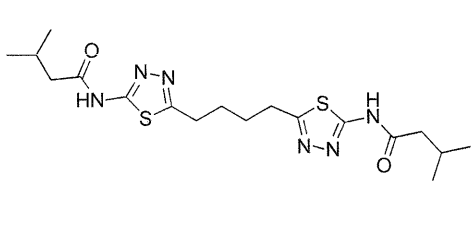

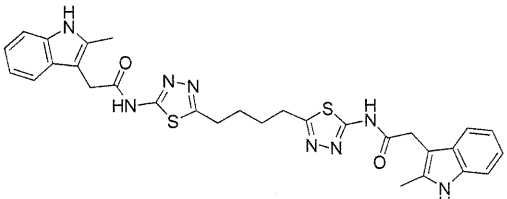

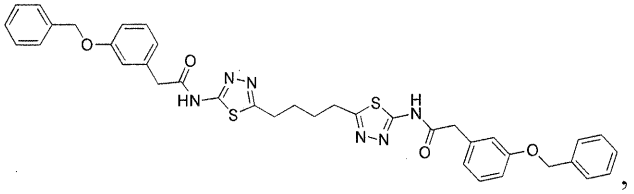

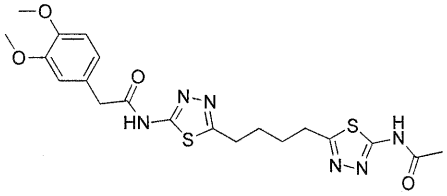

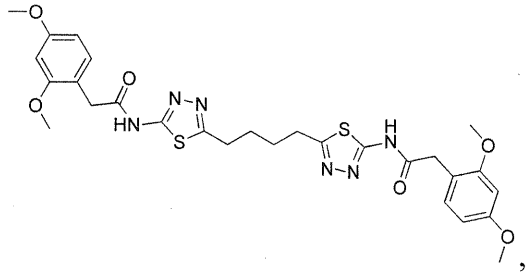

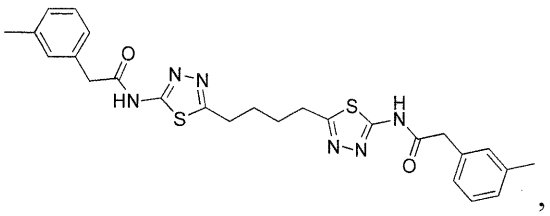

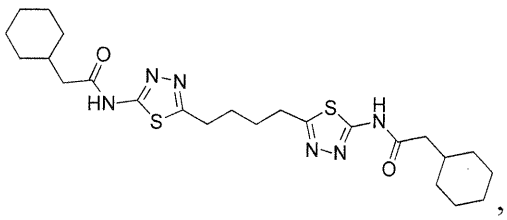

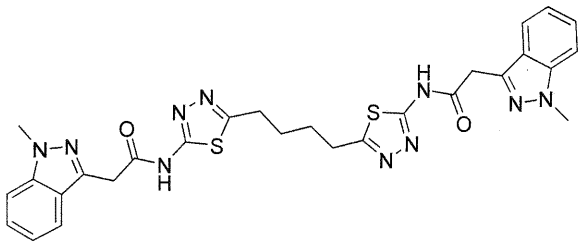

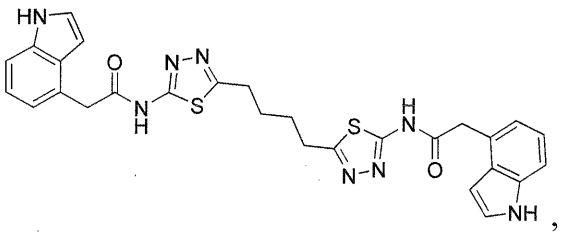

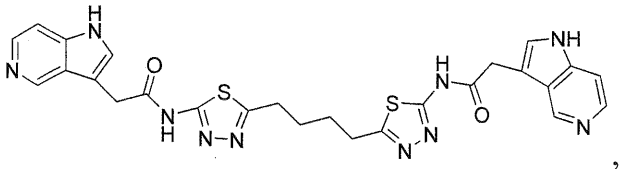

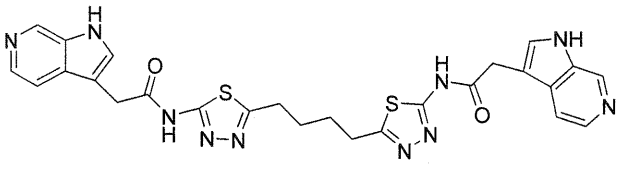

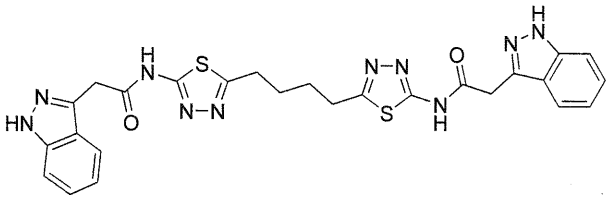

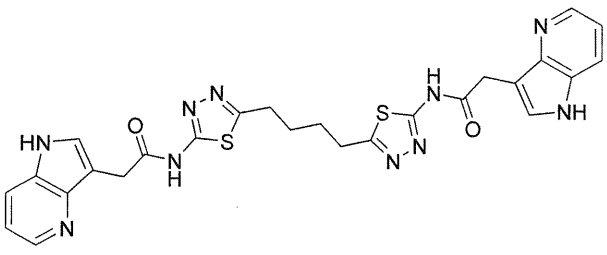

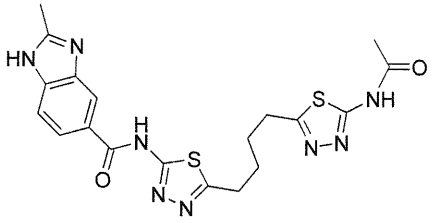

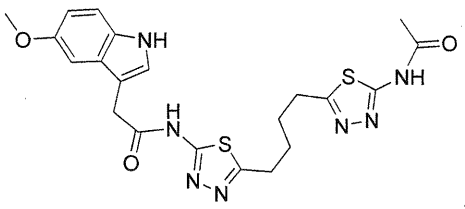

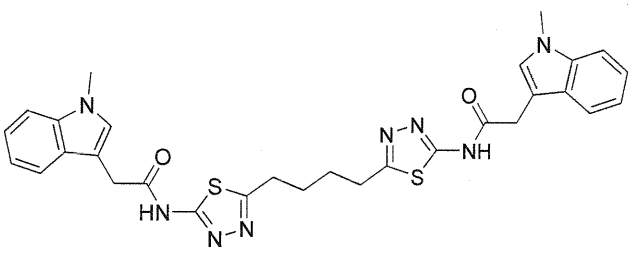

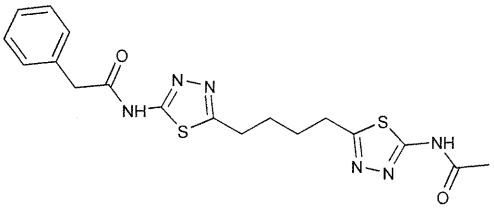

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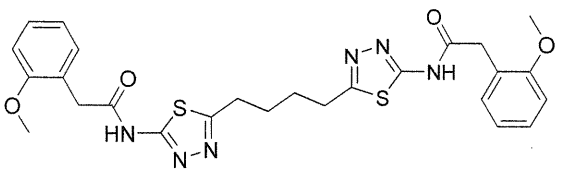
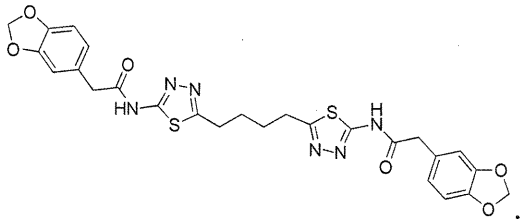
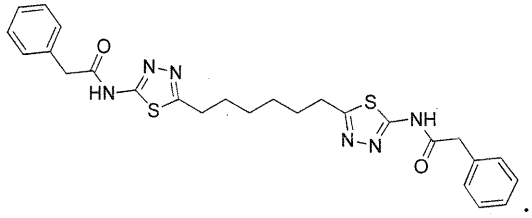


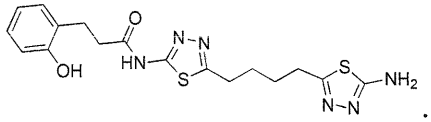
16. The compound of claim 1, which is



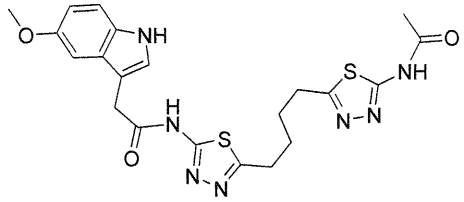
17. The compound of claim 1, which is



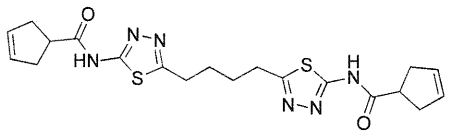
18. The compound of claim 1, which is



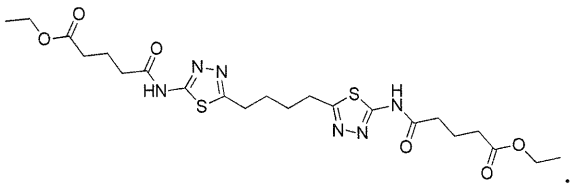
19. The compound of claim 1, which is



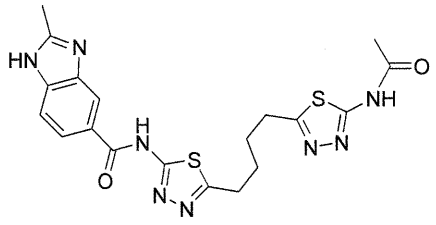
20. The compound of claim 1, which is



21. The compound of claim 1, which is



22. The compound of claim 1, which is



23. A pharmaceutical composition comprising a compound of Formula (I) according to any one of claims 1 to 22 and a pharmaceutically acceptable carrier.

24. A use of a compound of Formula (I) according to any one of claims 1 to 22 in the manufacture of a medicament for the treatment of cancer in a subject in need thereof.

25. The use of claim 24, wherein the cancer is characterized by i) a low level of E-cadherin expression compared to a reference standard, ii) a high level of vimentin expression compared to a reference standard, or iii) a low or decreased level of pyruvate carboxylase expression.

26. The use of claim 24, wherein the cancer is lung cancer, non-small cell lung cancer, breast cancer, hepatocellular carcninoma, osteosarcoma, lipomas, chondrosarcoma or mesothelioma.