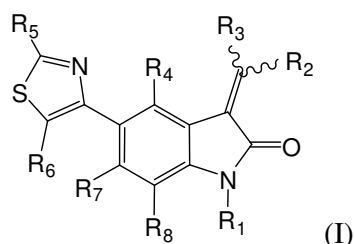


CLAIMS

1. Use of (a) a therapeutically effective amount of a pharmaceutical composition, and (b) a pharmaceutically acceptable excipient, carrier, or diluent in the manufacture of a medicament for the treatment of a condition selected from the group consisting of obesity, overweight and the metabolic syndrome in a mammal including a human, wherein the medicament is to be administered to a mammalian subject in need thereof, the pharmaceutical composition comprises a compound of Formula I:



or an enantiomer, diastereomer, tautomer, or pharmaceutically acceptable salt, solvate, ester or pro-drug thereof that is effective in the treatment or prevention of a condition selected from the group consisting of obesity, overweight and the metabolic syndrome in a mammal including a human, and wherein the symbols have the following meanings and are, for each occurrence, independently selected:

R_1 is hydrogen, alkyl or substituted alkyl, alkenyl or substituted alkenyl, alkynyl or substituted alkynyl, cycloalkyl or substituted cycloalkyl, cycloalkenyl or substituted cycloalkenyl, heterocycle or substituted heterocycle, aryl or substituted aryl, OR_a , SR_a , $S(=O)_2R_e$, $S(=O)_2OR_e$, $C(=O)OR_d$, $C(=O)R_a$, or $C(=O)NR_bR_c$;

R_2 is heterocycle or substituted heterocycle, aryl or substituted aryl;

R_3 is hydrogen, alkyl or substituted alkyl, cycloalkyl or substituted cycloalkyl, heterocycle or substituted heterocycle, aryl or substituted aryl;

R_4 , R_7 , and R_8 are each independently hydrogen, halogen, cyano, nitro, CF_3 , OCF_3 , alkyl or substituted alkyl, alkenyl or substituted alkenyl, alkynyl or substituted alkynyl, cycloalkyl or substituted cycloalkyl, cycloalkenyl or substituted cycloalkenyl, heterocycle or substituted heterocycle, aryl or substituted aryl, OR_a , SR_a ,

$S(=O)R_e$, $S(=O)_2R_e$, $P(=O)_2R_e$, $S(=O)_2OR_e$, $P(=O)_2OR_e$, NR_bR_c , $NR_bS(=O)_2R_e$, $NR_bP(=O)_2R_e$, $S(=O)_2NR_bR_c$, $P(=O)_2NR_bR_c$, $C(=O)OR_e$, $C(=O)R_a$, $C(=O)NR_bR_c$, $OC(=O)R_a$, $OC(=O)NR_bR_c$, $NR_bC(=O)OR_e$, $NR_dC(=O)NR_bR_c$, $NR_dS(=O)_2NR_bR_c$, $NR_dP(=O)_2NR_bR_c$, $NR_bC(=O)R_a$, or $NR_bP(=O)_2R_e$;

R_5 is alkyl or substituted alkyl, heterocycle or substituted heterocycle, aryl or substituted aryl, amino or substituted amino;

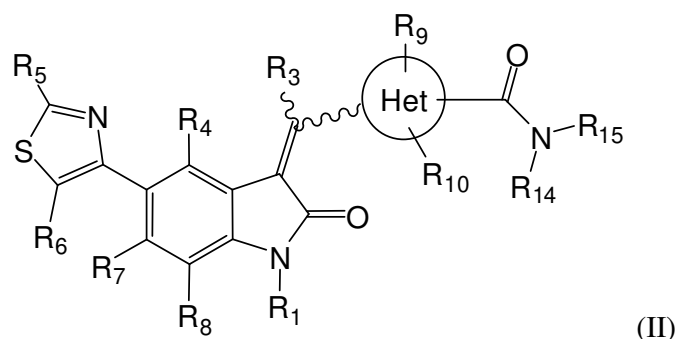
R_6 is hydrogen, halogen, cyano, nitro, CF_3 , OCF_3 , alkyl or substituted alkyl, heterocycle or substituted heterocycle, aryl or substituted aryl, or OR_a ;

R_a is hydrogen, alkyl or substituted alkyl, alkenyl or substituted alkenyl, alkynyl or substituted alkynyl, cycloalkyl or substituted cycloalkyl, cycloalkenyl or substituted cycloalkenyl, heterocycle or substituted heterocycle, or aryl or substituted aryl;

R_b , R_c and R_d are independently hydrogen, alkyl or substituted alkyl, cycloalkyl or substituted cycloalkyl, heterocycle or substituted heterocycle, or aryl or substituted aryl, or said R_b and R_c together with the N to which they are bonded optionally form a heterocycle or substituted heterocycle;

R_e is alkyl or substituted alkyl, alkenyl or substituted alkenyl, alkynyl or substituted alkynyl, cycloalkyl or substituted cycloalkyl, cycloalkenyl or substituted cycloalkenyl, heterocycle or substituted heterocycle, or aryl or substituted aryl.

2. The use of claim 1, wherein the compound of Formula I is a compound of Formula II:



or an enantiomer, diastereomer, tautomer, or pharmaceutically acceptable salt, solvate, ester or pro-drug thereof that is effective in the treatment or prevention of a condition selected from the group consisting of obesity, overweight and the metabolic syndrome in a mammal including a human, and

wherein the symbols have the following meanings and are, for each occurrence,
independently selected:

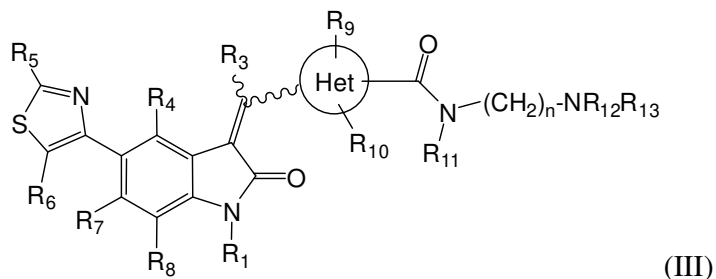
Het is a 5- or 6-membered aromatic ring containing at least one heteroatom selected from N, O and S;

R₃ and R₁₀ are each independently hydrogen, alkyl or substituted alkyl, cycloalkyl or substituted cycloalkyl, heterocycle or substituted heterocycle, aryl or substituted aryl;

R₆ and R₉ are each independently hydrogen, halogen, cyano, nitro, CF₃, OCF₃, alkyl or substituted alkyl, heterocycle or substituted heterocycle, aryl or substituted aryl, or OR_a;

R₁₄ and R₁₅ are independently hydrogen, alkyl or substituted alkyl, cycloalkyl or substituted cycloalkyl, heterocycle or substituted heterocycle, or aryl or substituted aryl, or said R₁₄ and R₁₅ together with the N to which they are bonded optionally form a heterocycle or substituted heterocycle

3. The use of claim 1, wherein the compound of Formula I is a compound of Formula III:



or an enantiomer, diastereomer, tautomer, or pharmaceutically acceptable salt, solvate, ester or pro-drug thereof that is effective in the treatment or prevention of a condition selected from the group consisting of obesity, overweight and the metabolic syndrome thereof in a mammal including a human, and
wherein the symbols have the following meanings and are, for each occurrence,
independently selected:

Het is a 5- or 6-membered aromatic ring containing at least one heteroatom selected from N, O and S;

R₃ and R₁₀ are each independently hydrogen, alkyl or substituted alkyl, cycloalkyl or substituted cycloalkyl, heterocycle or substituted heterocycle, aryl or substituted aryl;

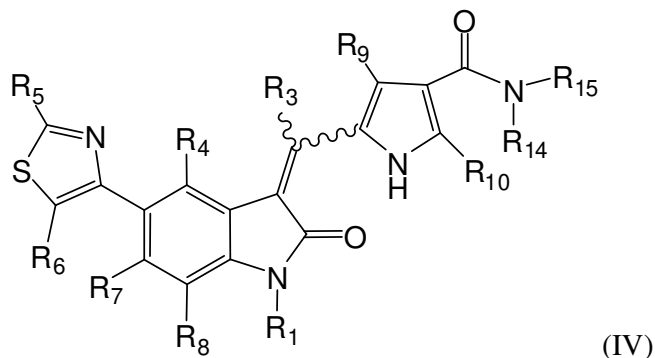
R₆ and R₉ are each independently hydrogen, halogen, cyano, nitro, CF₃, OCF₃, alkyl or substituted alkyl, heterocycle or substituted heterocycle, aryl or substituted aryl, or OR_a;

R₁₁ is hydrogen or C₁₋₄ alkyl;

R₁₂ and R₁₃ are independently hydrogen, alkyl or substituted alkyl, cycloalkyl or substituted cycloalkyl, heterocycle or substituted heterocycle, or aryl or substituted aryl, or said R₁₂ and R₁₃ together with the N to which they are bonded optionally form a heterocycle or substituted heterocycle;

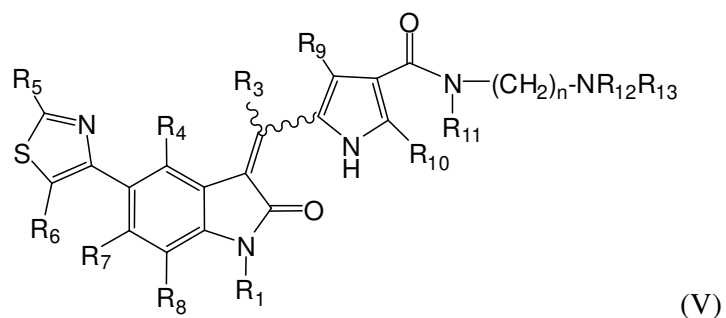
n is an integer selected from 2, 3, 4, 5 and 6.

4. The use of claim 2, wherein the compound of Formula II is a compound of Formula IV:



or an enantiomer, diastereomer, tautomer, or pharmaceutically acceptable salt, solvate, ester or pro-drug thereof that is effective in the treatment or prevention of a condition selected from the group consisting of obesity, overweight and the metabolic syndrome thereof in a mammal including a human.

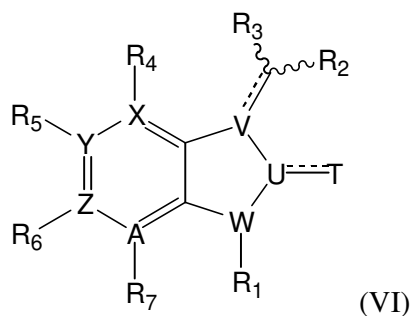
5. The use of claim 3, wherein the compound of Formula III is a compound of Formula V:



or an enantiomer, diastereomer, tautomer, or pharmaceutically acceptable salt, solvate, ester or pro-drug thereof that is effective in the treatment or prevention of a condition selected from the group consisting of obesity, overweight and the metabolic syndrome thereof in a mammal including a human.

6. Use of (a) a therapeutically effective amount of a pharmaceutical composition, and (b) a pharmaceutically acceptable excipient, carrier, or diluent in the manufacture of a medicament for the treatment of a condition selected from the group consisting of obesity, overweight and the metabolic syndrome in a mammal including a human, wherein the medicament is to be administered to a mammalian subject in need thereof,

the pharmaceutical composition comprises a compound of Formula VI:



or an enantiomer, diastereomer, tautomer, or pharmaceutically acceptable salt, solvate, ester or pro-drug thereof that is effective in the treatment or prevention of a condition selected from the group consisting of obesity, overweight and the metabolic syndrome in a mammal including a human, and wherein the symbols have the following meanings and are, for each occurrence, independently selected:

- R_1 is hydrogen, alkyl or substituted alkyl, alkenyl or substituted alkenyl, alkynyl or substituted alkynyl, cycloalkyl or substituted cycloalkyl, cycloalkenyl or substituted cycloalkenyl, heterocycle or substituted heterocycle, aryl or substituted aryl, OR_a , SR_a , $S(=O)_2R_e$, $S(=O)_2OR_e$, $C(=O)OR_d$, $C(=O)R_a$, or $C(=O)NR_bR_c$;
- R_2 is monocyclic or bicyclic heterocycle or substituted heterocycle, aryl or substituted aryl;
- R_3 is hydrogen, alkyl or substituted alkyl, cycloalkyl or substituted cycloalkyl, heterocycle or substituted heterocycle, aryl or substituted aryl, halogen, $-OR_a$, $-C(O)R_a$, $-C(O)OR_a$, $-NR_aR_b$, or $S(O)_2NR_aR_b$;
- R_4 , R_5 , R_6 , and R_7 are each independently hydrogen, halogen, cyano, nitro, trihalomethyl, OCF_3 , alkyl or substituted alkyl, alkenyl or substituted alkenyl, alkynyl or substituted alkynyl, cycloalkyl or substituted cycloalkyl, cycloalkenyl or substituted cycloalkenyl, heterocycle or substituted heterocycle, aryl or substituted aryl, OR_a , SR_a , $S(=O)R_e$, $S(=O)_2R_e$, $P(=O)_2R_e$, $S(=O)_2OR_e$, $P(=O)_2OR_e$, NR_bR_c , $NR_bS(=O)_2R_e$, $NR_bP(=O)_2R_e$, $S(=O)_2NR_bR_c$, $P(=O)_2NR_bR_c$, $C(=O)OR_e$, $C(=O)R_a$, $C(=O)NR_bR_c$, $OC(=O)R_a$, $OC(=O)NR_bR_c$, $NR_bC(=O)OR_e$, $NR_dC(=O)NR_bR_c$, $NR_dS(=O)_2NR_bR_c$, $NR_dP(=O)_2NR_bR_c$, $NR_bC(=O)R_a$, or $NR_bP(=O)_2R_e$;
- T is O, S or R_a ;
- U, V, and W are each independently a carbon, N, O, or S;
- X, Y, Z, and A are each independently a carbon or N, with the proviso that the ring in which X, Y, Z, and A exist is aromatic;

with the provision that

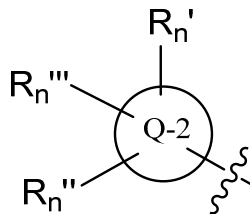
one of R_4 , R_5 , R_6 , and R_7 is substituted heterocycle or substituted aryl,

and

R_4 , R_5 , R_6 , or R_7 is absent if X, Y, Z, or A, respectively, is a heteroatom;

wherein

substituted heterocycle and substituted aryl in R_4 , R_5 , R_6 , and R_7 is the following group:



wherein

Q-2 is heterocycle, C(=O)NR_bR_c or aryl;

R_n', R_n'' and R_n''' are each independently hydrogen, halogen, cyano, nitro, trihalomethyl, OCF₃, alkyl or substituted alkyl, OR_a, SR_a, C(=O)R_a, C(=O)OR_a, NH₂, S(O)₂NH₂, NR_bR_c, heterocycle or substituted heterocycle, or aryl or substituted aryl;

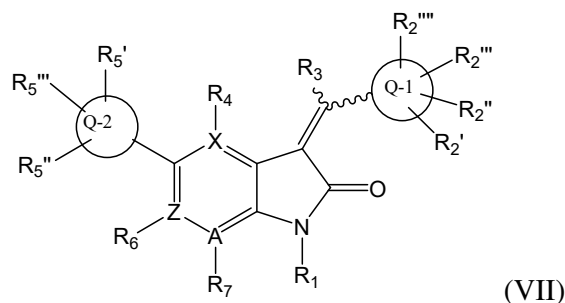
R_a is hydrogen, alkyl or substituted alkyl, alkenyl or substituted alkenyl, alkynyl or substituted alkynyl, cycloalkyl or substituted cycloalkyl, cycloalkenyl or substituted cycloalkenyl, heterocycle or substituted heterocycle, or aryl or substituted aryl;

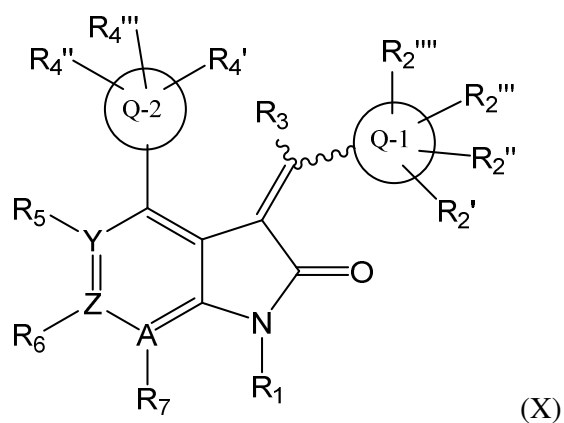
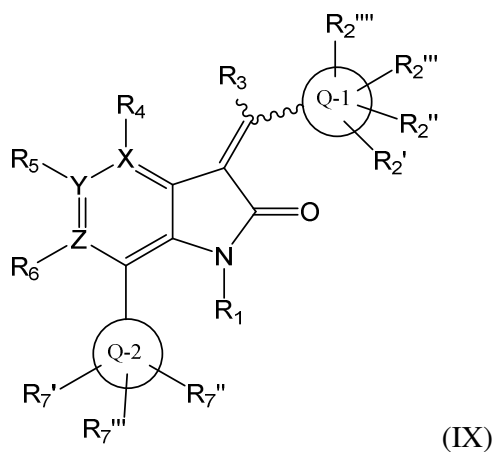
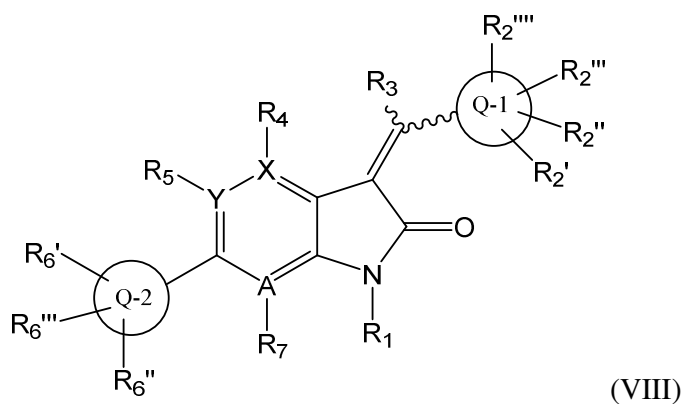
R_b, R_c and R_d are independently hydrogen, alkyl or substituted alkyl, cycloalkyl or substituted cycloalkyl, heterocycle or substituted heterocycle, or aryl or substituted aryl, or said R_b and R_c together with the N to which they are bonded optionally form a heterocycle or substituted heterocycle; and

R_e is hydrogen, alkyl or substituted alkyl, alkenyl or substituted alkenyl, alkynyl or substituted alkynyl, cycloalkyl or substituted cycloalkyl, cycloalkenyl or substituted cycloalkenyl, heterocycle or substituted heterocycle, or aryl or substituted aryl; and

(b) a pharmaceutically acceptable excipient, carrier, or diluent.

7. The use of claim 6, wherein the compound of Formula VI is a compound selected from the group consisting of Formula VII, Formula VIII, Formula IX and Formula X:





or an enantiomer, diastereomer, tautomer, or pharmaceutically acceptable salt, solvate, ester or pro-drug thereof that is effective in the treatment or prevention of a condition selected from the group consisting of obesity, overweight and the metabolic syndrome in a mammal including a human, and wherein the symbols have the following meanings and are, for each occurrence, independently selected:

X, Y, Z, and A are each independently a carbon or N, with the proviso that the ring in which X, Z, and A exist is aromatic;

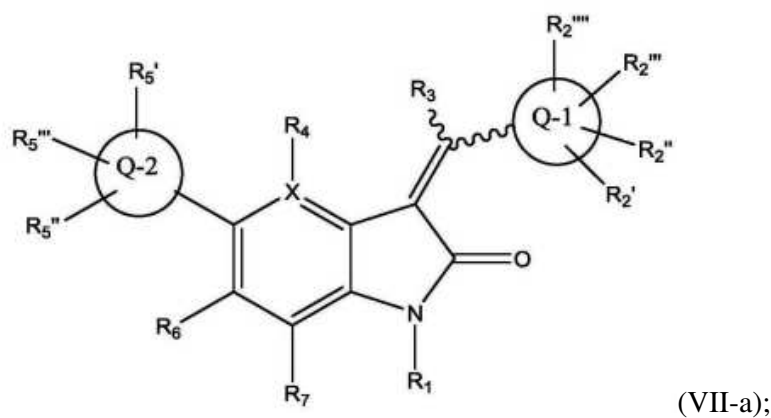
Q-1 and Q-2 are independently heterocycle, C(=O)NR_bR_c or aryl;

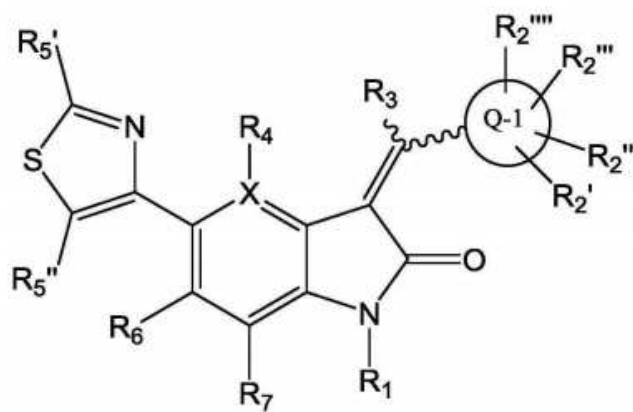
R₂, R₂^{''}, R₂^{'''} and R₂^{''''} are each independently absent, hydrogen, halogen, cyano, nitro, trihalomethyl, OCF₃, alkyl or substituted alkyl, cycloalkyl or substituted cycloalkyl, heterocycle or substituted heterocycle, aryl or substituted aryl, or OR_a, NR_bR_c, NR_bS(=O)₂R_e, NR_bP(=O)₂R_e, S(=O)₂NR_bR_c, P(=O)₂NR_bR_c, C(=O)OR_e, C(=O)R_a, C(=O)NR_bR_c, OC(=O)R_a, OC(=O)NR_bR_c, NR_bC(=O)OR_e, NR_dC(=O)NR_bR_c, NR_dS(=O)₂NR_bR_c, NR_dP(=O)₂NR_bR_c, NR_bC(=O)R_a, or NR_bP(=O)₂R_e,

R₅['], R₅^{''} and R₅^{'''}

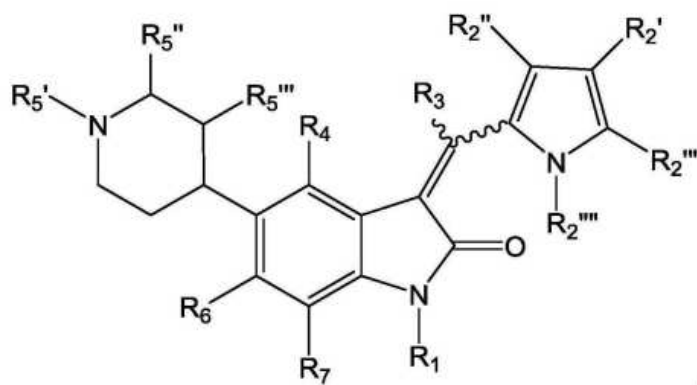
in Formula VII, R₆['], R₆^{''} and R₆^{'''} in Formula VIII, R₇['], R₇^{''} and R₇^{'''} in Formula IX and R₄['], R₄^{''} and R₄^{'''} in Formula X correspond to R_n['], R_n^{''} and R_n^{'''}, respectively.

8. The use of claim 7, wherein the compound of formula (VII) is selected from the group consisting of formula (VII-a), (VII-c), (VII-m), (VII-n), and (VII-o);

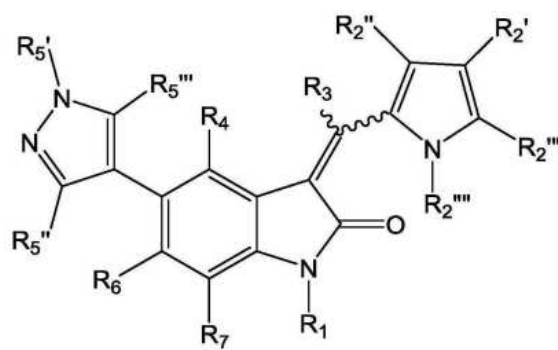




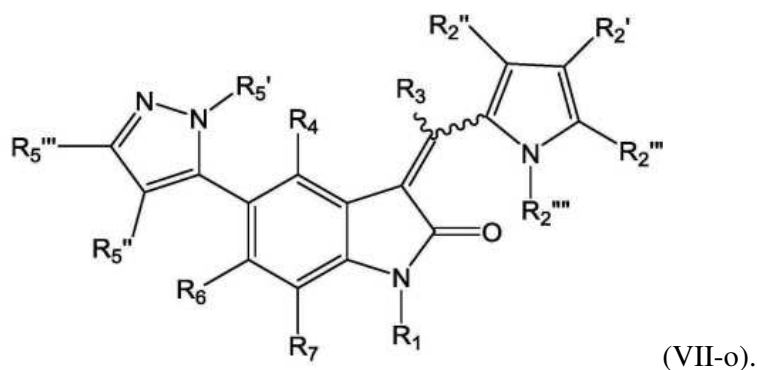
(VII-c);



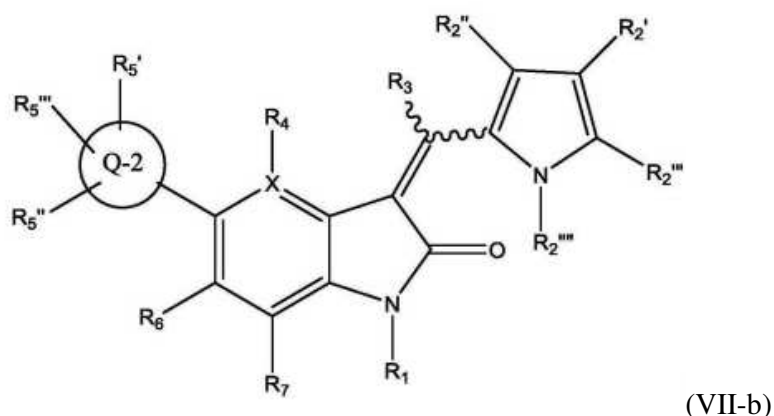
(VII-m);



(VII-n);



9. The use of claim 7, wherein the compound of formula (VII) is formula (VII-b);

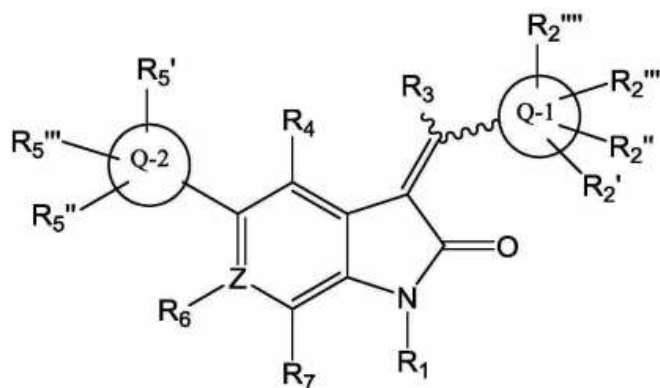


wherein

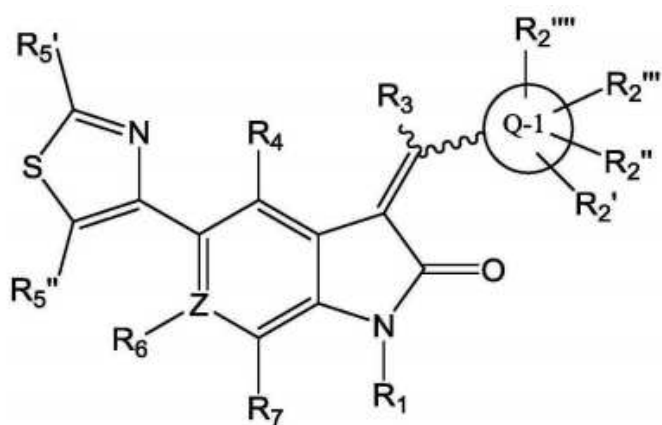
R_2 , R_2'' , R_2''' are each independently absent, hydrogen, halogen, cyano, nitro, trihalomethyl, OCF_3 , alkyl or substituted alkyl, cycloalkyl or substituted cycloalkyl, heterocycle or substituted heterocycle, aryl or substituted aryl, or OR_a , NR_bR_c , $\text{NR}_b\text{S}(=\text{O})_2\text{R}_e$, $\text{NR}_b\text{P}(=\text{O})_2\text{R}_e$, $\text{S}(=\text{O})_2\text{NR}_b\text{R}_c$, $\text{P}(=\text{O})_2\text{NR}_b\text{R}_c$, $\text{C}(=\text{O})\text{OR}_e$, $\text{C}(=\text{O})\text{R}_a$, $\text{C}(=\text{O})\text{NR}_b\text{R}_c$, $\text{OC}(=\text{O})\text{R}_a$, $\text{OC}(=\text{O})\text{NR}_b\text{R}_c$, $\text{NR}_b\text{C}(=\text{O})\text{OR}_e$, $\text{NR}_d\text{C}(=\text{O})\text{NR}_b\text{R}_c$, $\text{NR}_d\text{S}(=\text{O})_2\text{NR}_b\text{R}_c$, $\text{NR}_d\text{P}(=\text{O})_2\text{NR}_b\text{R}_c$, $\text{NR}_b\text{C}(=\text{O})\text{R}_a$, or $\text{NR}_b\text{P}(=\text{O})_2\text{R}_e$, and

R_2''' is hydrogen, alkyl or substituted alkyl, alkenyl or substituted alkenyl, alkynyl or substituted alkynyl, cycloalkyl or substituted cycloalkyl, cycloalkenyl or substituted cycloalkenyl, heterocycle or substituted heterocycle, aryl or substituted aryl, OR_a , SR_a , $\text{S}(=\text{O})_2\text{R}_e$, $\text{S}(=\text{O})_2\text{OR}_e$, $\text{C}(=\text{O})\text{OR}_d$, $\text{C}(=\text{O})\text{R}_a$, $\text{C}(=\text{O})\text{NR}_b\text{R}_c$.

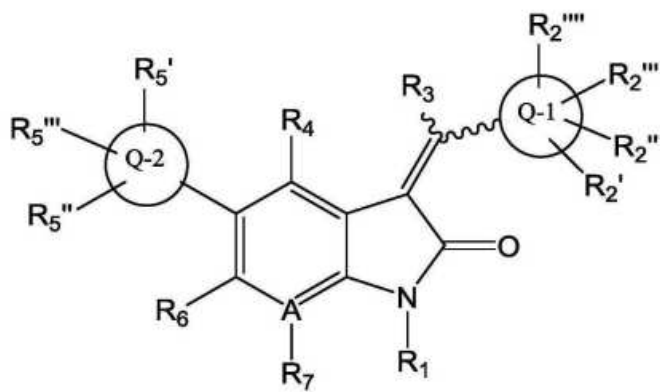
10. The use of claim 7, wherein the compound of formula (VII) is selected from the group consisting of formula (VII-e), (VII-g), (VII-i), and (VII-k);



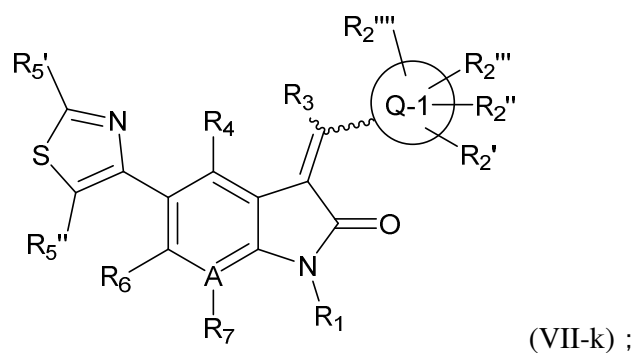
(VII-e) ;



(VII-g) ;



(VII-i) ;

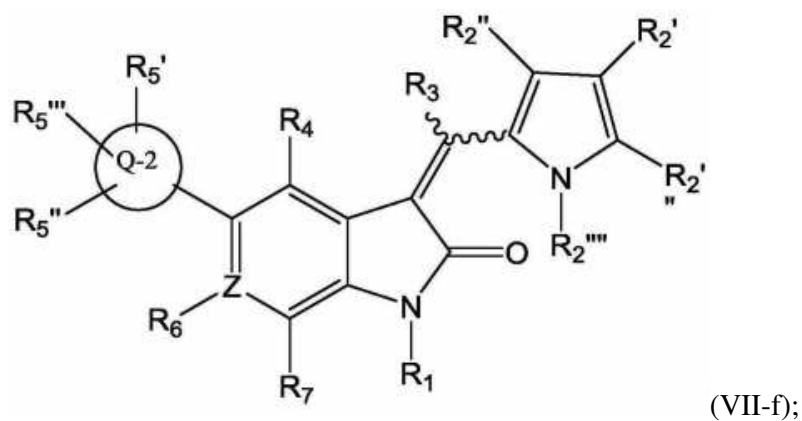
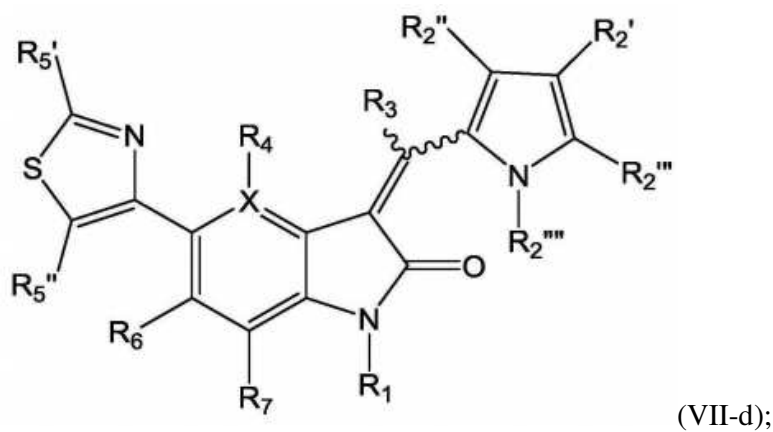


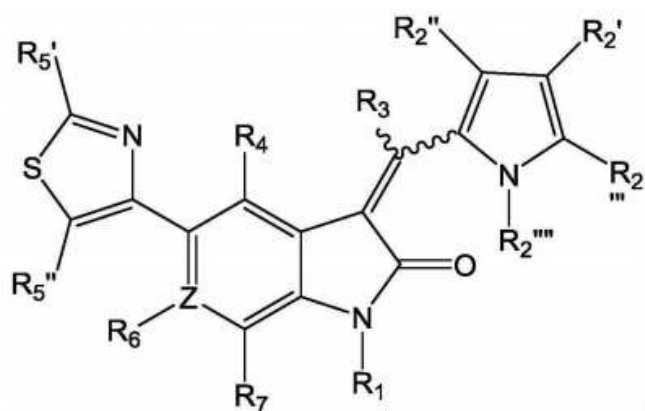
wherein

Z is C or N,

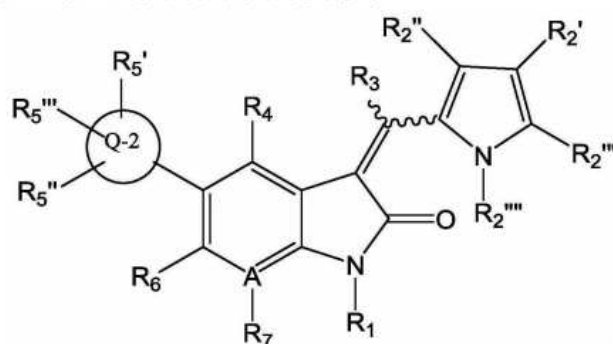
A is C or N.

11. The use of claim 7, wherein the compound of formula (VII) is selected from the group consisting of formula (VII-d), (VII-f), (VII-h), (VII-j), and (VII-l);

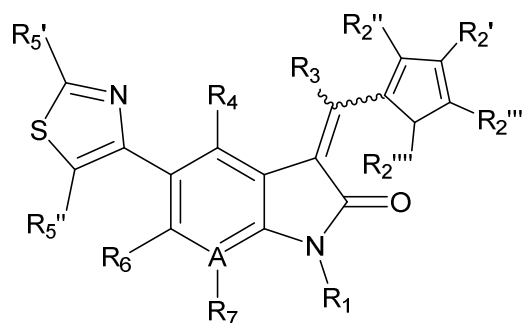




(VII-h);



(VII-j);



(VII-l);

wherein

R_2' , R_2'' , R_2''' are each independently absent, hydrogen, halogen, cyano, nitro, trihalomethyl, OCF_3 , alkyl or substituted alkyl, cycloalkyl or substituted cycloalkyl, heterocycle or substituted heterocycle, aryl or substituted aryl, or OR_a , NR_bR_c , $NR_bS(=O)_2R_e$, $NR_bP(=O)_2R_e$, $S(=O)_2NR_bR_c$, $P(=O)_2NR_bR_c$, $C(=O)OR_e$, $C(=O)R_a$, $C(=O)NR_bR_c$, $OC(=O)R_a$, $OC(=O)NR_bR_c$, $NR_bC(=O)OR_e$, $NR_dC(=O)NR_bR_c$, $NR_dS(=O)_2NR_bR_c$, $NR_dP(=O)_2NR_bR_c$, $NR_bC(=O)R_a$, or $NR_bP(=O)_2R_e$, and

R_2''' is hydrogen, alkyl or substituted alkyl, alkenyl or substituted alkenyl, alkynyl or substituted

alkynyl, cycloalkyl or substituted cycloalkyl, cycloalkenyl or substituted cycloalkenyl, heterocycle or substituted heterocycle, aryl or substituted aryl, OR_a , SR_a , $S(=O)_2R_e$, $S(=O)_2OR_e$, $C(=O)OR_d$, $C(=O)R_a$, $C(=O)NR_bR_c$,

X is C or N,

Z is C or N,

A is C or N.

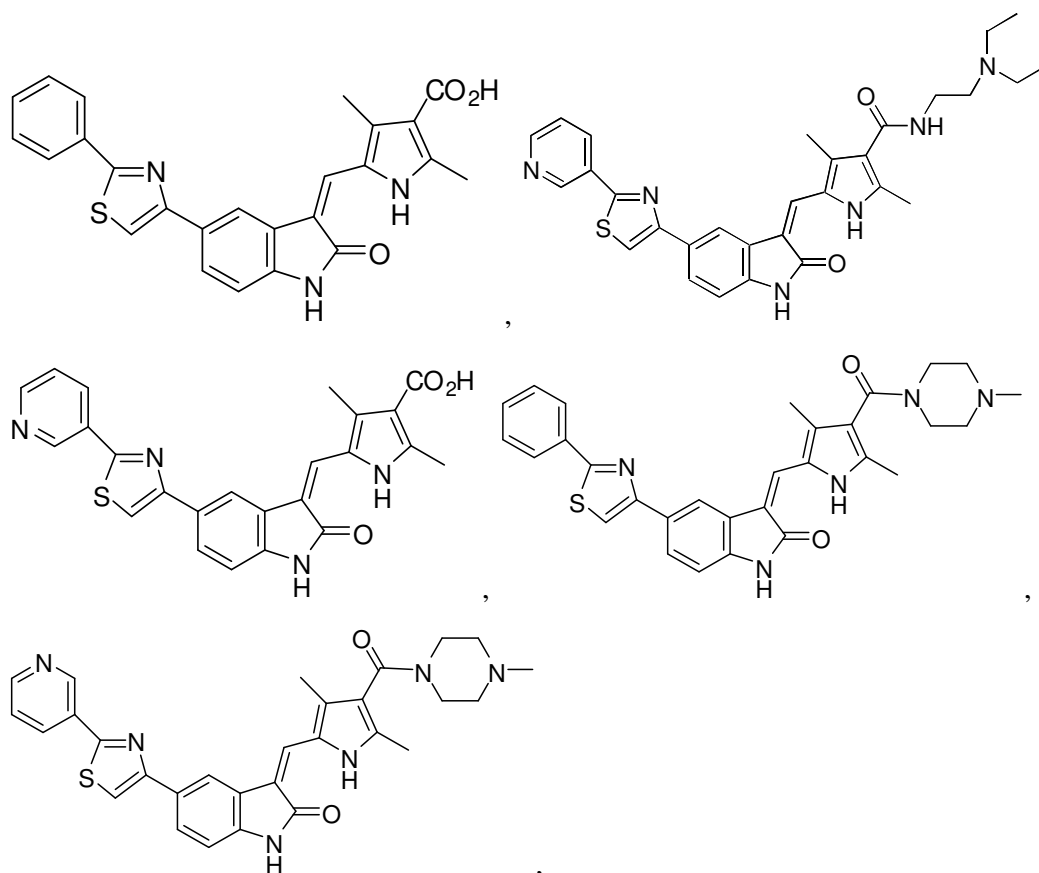
12. The use of claim 7, wherein Q-1 is selected from the group consisting of phenyl, pyrrole, furan, thiophene, pyridine, pyrimidine, pyrazine, pyridazine, imidazole, indole, pyrrolopyridinone, pyridone, pyrrolidine, piridinone, piperidine, and pyrroloazepinone; wherein one of R_2' , R_2'' , R_2''' , and R_2'''' is $C(=O)NR_bR_c$, and wherein R_b is hydrogen, and R_c is alkyl substituted with $NR_{bn}R_{cn}$; wherein R_{bn} and R_{cn} are alkyl, or said R_{bn} and R_{cn} together with the N to which they are bonded optionally form a substituted heterocycle; wherein said heterocycle is piperidine, or morpholine; or R_b and R_c together with the N to which they are bonded optionally form a substituted heterocycle; wherein said heterocycle is piperidine, or morpholine; and two of R_2' , R_2'' , R_2''' , and R_2'''' are independently alkyl, and the other is hydrogen.

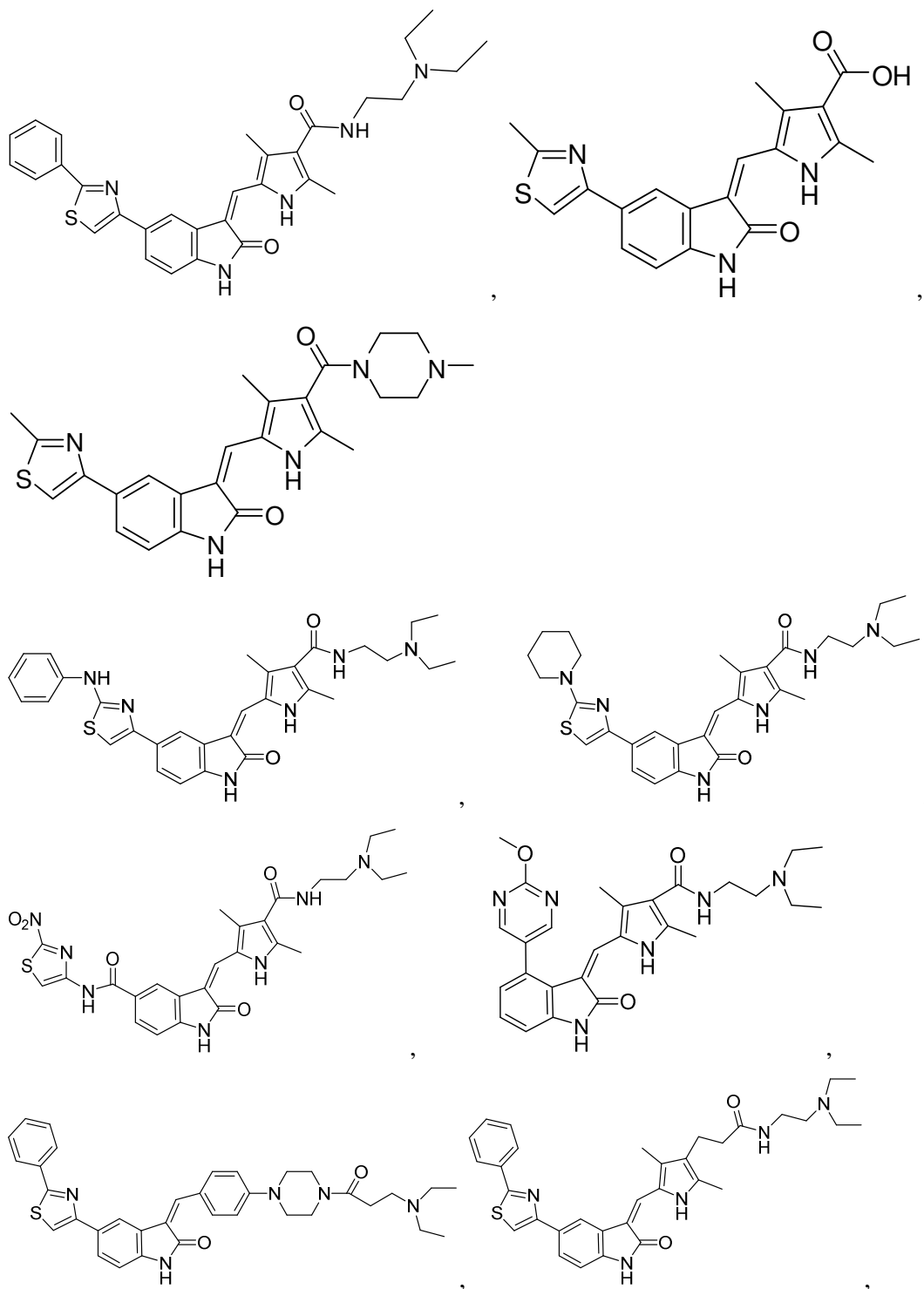
13. The use of claim 7, wherein Q-2 is selected from the group consisting of pyrimidine, pyrrole, furan, thiophene, imidazole, pyrazole, oxazole, isoxazole, thiazole, isothiazole, triazole, thiadiazole, oxadiazole, pyrrolidine, piperidine, azepane, tetrahydrofuran, oxane, oxepane, indole, indolinone, indazole, benzothiazole, quinoline, quinazoline, quinoxaline, imidazopyridine, imidazopyridazine, pyrazolopyridine, pyrazolopyrimidine, phthalazinone, and phenyl; R_n' is pyrrolidinyl, piperidinyl, azepanyl, tetrahydrofuranyl, oxanyl, oxepanyl, pyranlyl, phenyl, thiophenyl, pyrazinyl, pyrimidinyl, pyridazinyl, or pyridyl; said piperidinyl, pyranlyl, phenyl, thiophenyl, pyrazinyl, pyrimidinyl, pyridazinyl, and pyridyl are optionally substituted with halogen, cyano, nitro, alkyl or substituted alkyl, OR_a , NR_bR_c , $C(=O)OR_e$, $C(=O)R_a$, or

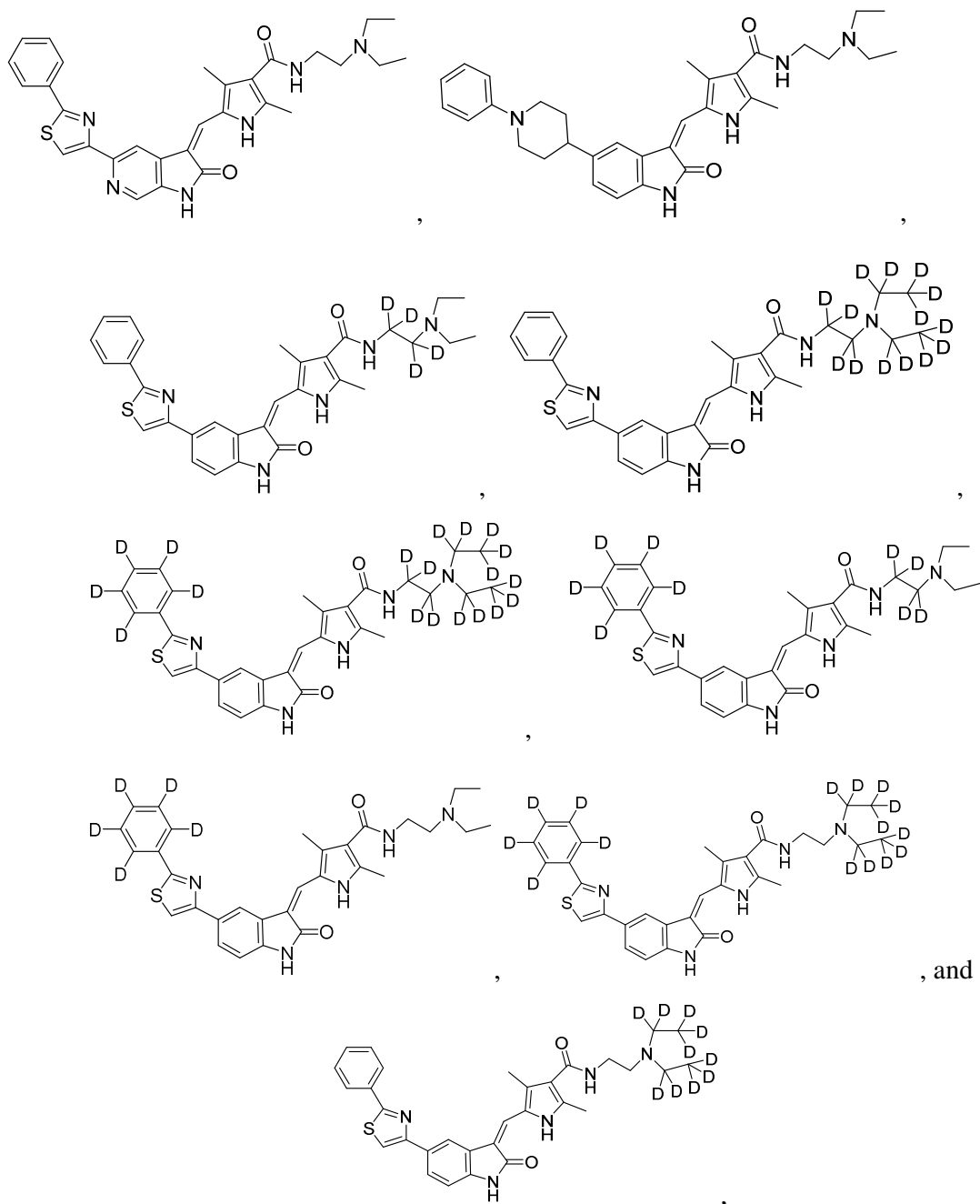
$C(=O)NR_bR_c$; wherein R_a is hydrogen, or alkyl or substituted alkyl, R_b and R_c are independently hydrogen, or alkyl or substituted alkyl, and R_e is alkyl or substituted alkyl; said substituted alkyl is optionally substituted with one or more substituent(s) selected from the group consisting of hydroxy, amino, nitro, cyano, halogen, alkoxy, alkylcarbonyl, alkoxycarbonyl, aminocarbonyl, aryl, cycloalkyl, and heterocycle; and wherein

R_n and $R_{n'}$ are independently hydrogen, or alkyl or substituted alkyl; said substituted alkyl is optionally substituted with one or more substituent(s) selected from the group consisting of hydroxy, amino, nitro, cyano, halogen, alkoxy, alkylcarbonyl, alkoxycarbonyl, aminocarbonyl, aryl, cycloalkyl, and heterocycle.

14. The use of claim 6, wherein the compound of Formula VI is a compound selected from the group consisting of:

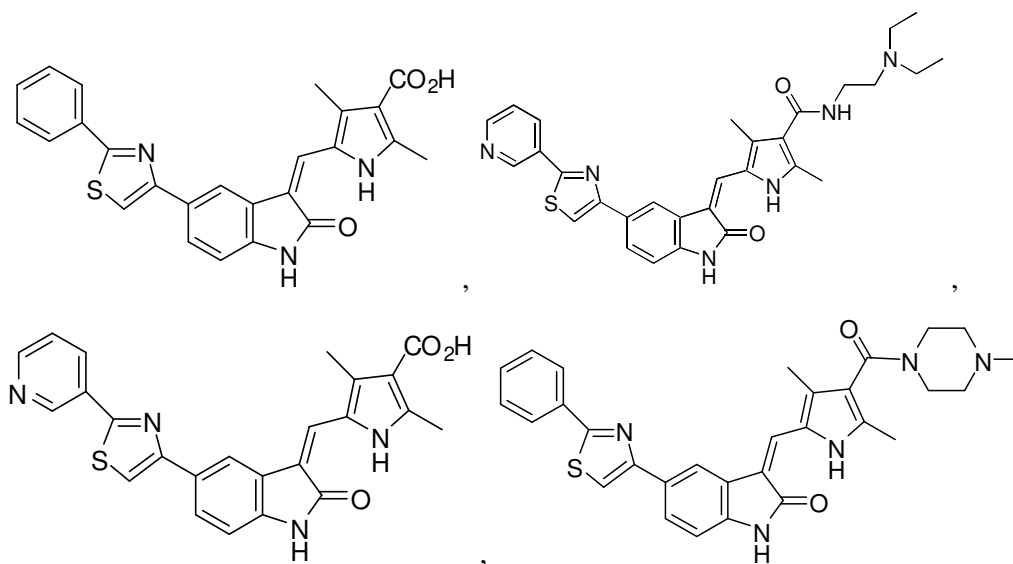


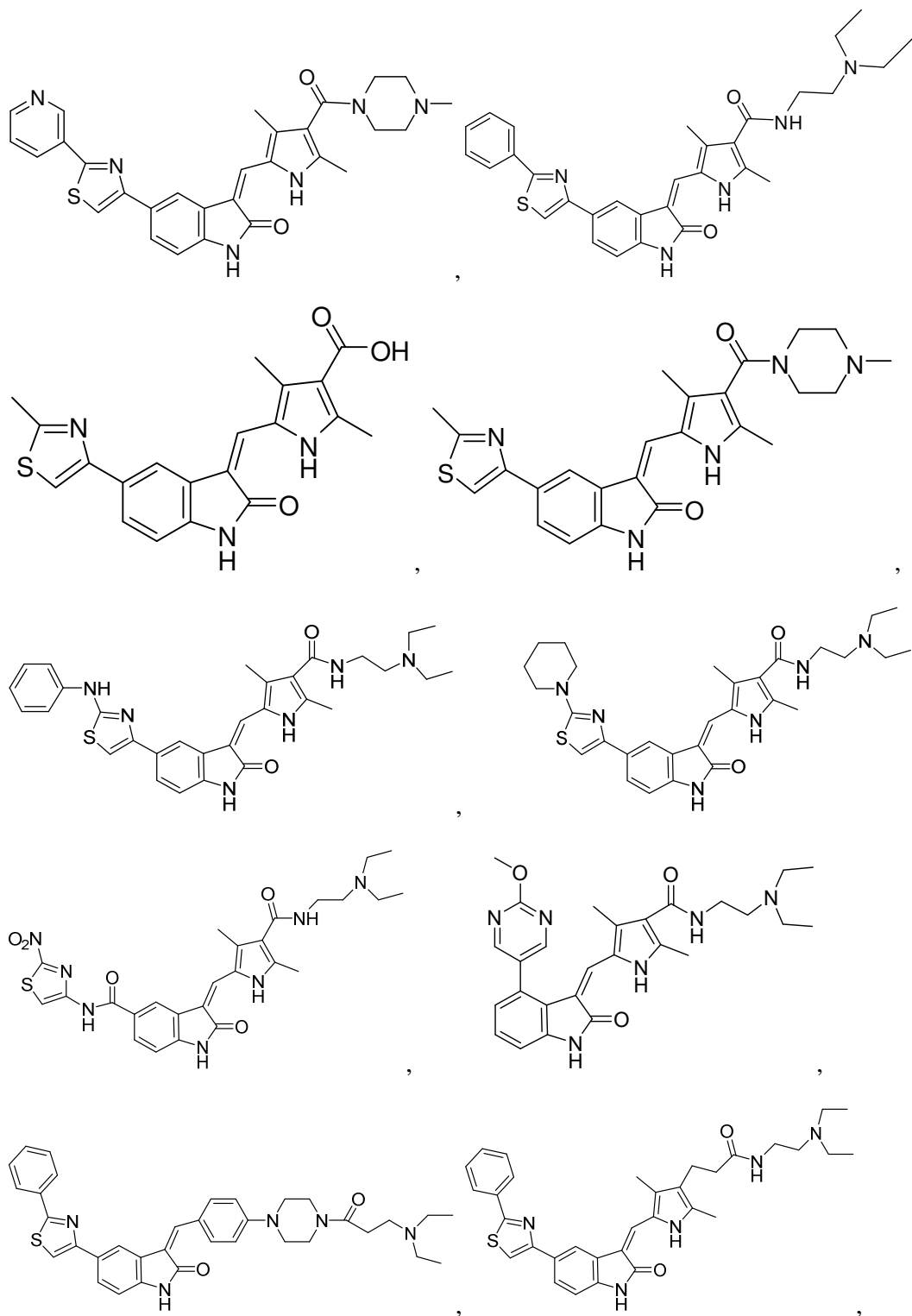


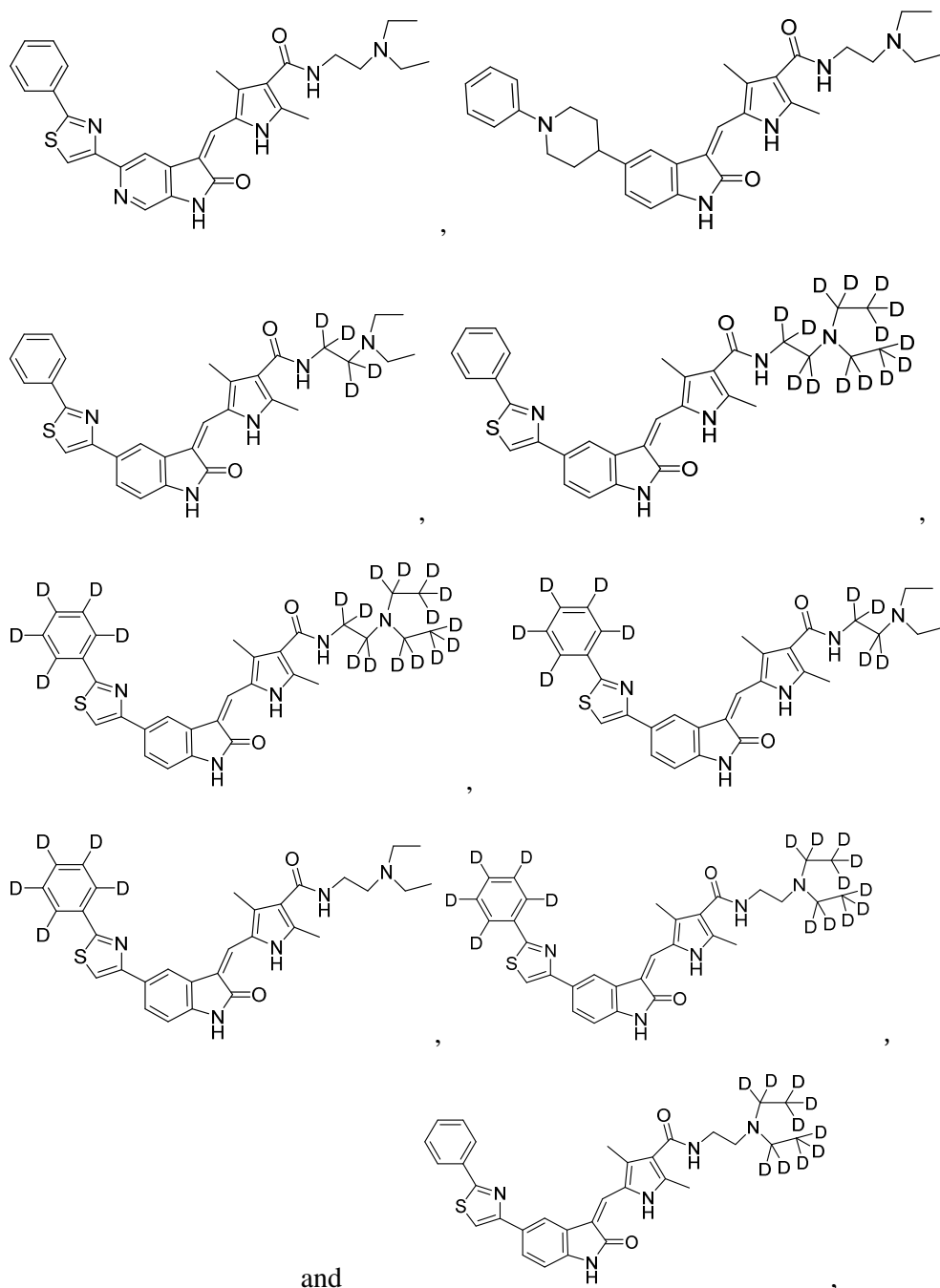


or an enantiomer, diastereomer, tautomer, or pharmaceutically acceptable salt, solvate, ester or pro-drug thereof.

15. The use of any of Claims 1-14, further comprising administering an additional agent selected from the group consisting of: an insulin sensitizing medication, a diabetes medication, a therapeutic for the metabolic syndromes, and a weight-loss medication.
16. Use of (a) a therapeutically effective amount of a pharmaceutical composition ,and (b) a pharmaceutically acceptable excipient, carrier, or diluent in the manufacture of a medicament for the treatment of reducing or ameliorating morbidity or mortality known to be associated with obesity, overweight and the metabolic syndrome in a mammal including a human, wherein the medicament is to be administered to a mammalian subject in need thereof,
the pharmaceutical composition selected from the group consisting of:





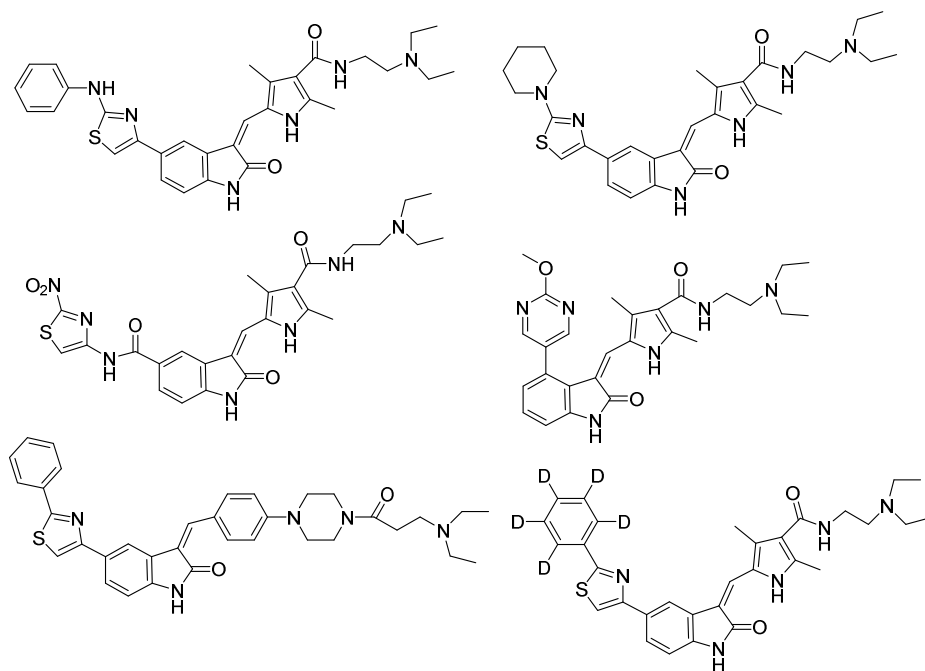


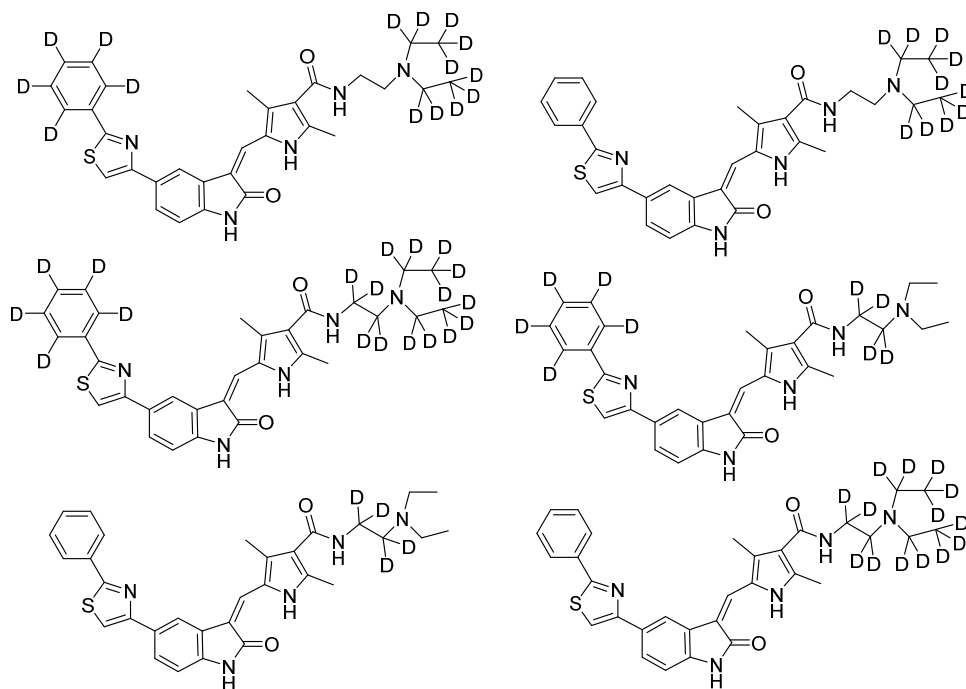
and an enantiomer, diastereomer, tautomer, or pharmaceutically acceptable salt, solvate, ester or pro-drug thereof; and

wherein morbidity or mortality known to be associated with obesity, overweight and the metabolic syndrome is selected from the group consisting of: excessive weight, excessive fat, a BMI ≥ 25 kg/m², insulin resistance, frequent urination, increased

thirst, increased hunger, elevated blood pressure, elevated fasting plasma glucose, high serum triglycerides, low high-density lipoprotein (HDL) levels, and elevated waist circumference.

17. The method of Claim 16, wherein the morbidity or mortality is a BMI ≥ 30 kg/m².
18. A compound selected from the group consisting of:





and a pharmaceutically acceptable salt thereof.

19. The compound of Claim 18 wherein at least one of the hydrogens is a deuterium.