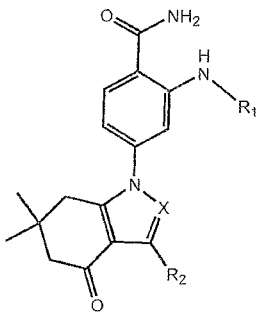
What is claimed is:

1. A method for treating a mammalian subject affected by prostate cancer comprising administering to the mammalian subject i) an oligonucleotide which reduces clusterin expression and ii) a Heat Shock Protein 90 (Hsp90) inhibitor having the structure:



or a pharmaceutically acceptable salt thereof, wherein

R_1 is H, C_1-C_{14} alkyl, C_1-C_{10} haloalkyl, C_3-C_7 cycloalkyl, heterocycloalkyl, C_1-C_6 acyl, aryl, or heteroaryl, wherein each alkyl, cycloalkyl, heterocycloalkyl, aryl, and heteroaryl group is optionally substituted with from 1-4 groups that are independently C_1-C_6 alkyl, C_1-C_6 alkoxy, halogen, hydroxy, amino, mono- or di-(C_1-C_6)alkylamino, nitro, halo(C_1-C_6)alkyl, halo(C_1-C_6)alkoxy, or carboxamide, wherein

when R_1 is a C_1-C_{14} alkyl group, up to five of the carbon atoms in the alkyl group are optionally replaced independently by R_4, carbonyl, ethenyl, ethynyl or a moiety selected from N, O, S, SO_2, or SO, with the proviso that two O atoms, two S atoms, or an O and S atom are not immediately adjacent each other, wherein

R_4 is

(i) heteroaryl,

(ii) aryl,

(iii) saturated or unsaturated C_3-C_{10} cycloalkyl, or

(iv) saturated or unsaturated C_2-C_{10} heterocycloalkyl,

wherein

each aryl, heteroaryl, saturated or unsaturated cycloalkyl, or saturated or unsaturated heterocycloalkyl, independently, is optionally substituted with at least one group, which independently is hydroxy, halo, amino, cyano, carboxy, carboxamido, nitro, oxo, -S-(C_1-C_6) alkyl, -SO_2(C_1-C_6) alkyl, -SO_2-aryl, -SO-(C_1-C_6)alkyl, -SO-aryl, -SO_2NH_2, -SO_2NH-(C_1-C_6)alkyl, -SO_2NH-aryl, (C_1-C_6)alkoxy, or mono- or di-(C_1-C_{10})alkylamino; and R_4 is optionally fused to a C_6-C_{10} aryl group, C_5-C_8 saturated cyclic group, or a C_4-C_{10} heterocycloalkyl group; and

R_1 is optionally substituted at any available position with C_1-C_{10} alkyl, C_1-C_{10} haloalkyl, C_2-C_{10} alkenyl, C_2-C_{10} alkynyl, hydroxy, carboxy, carboxamido, oxo, halo, amino, cyano, nitro, -SH, -S-(C_1-C_6)alkyl, -SO_2-(C_1-C_6)alkyl, -SO_2NH_2, -SO_2NH(C_1-C_6)alkyl, -SO_2NH-aryl, -SO_2-aryl, -SO-(C_1C_6)alkyl, -SO_2-aryl, C_1-C_6 alkoxy, C_2-C_{10} alkenyloxy, C_2-C_{10} alkynyloxy, mono- or di-(C_1-C_{10})alkylamino, -C_1-C_{10} alkyl-Z, -OC_1-C_{10} alkyl-Z, or R_5, wherein

Z is OR_6 or -$N(R_6)_2$, wherein

each R_6 is independently -H or C_1-C_6 alkyl, or $N(R_6)_2$ represents pyrrolidinyl, piperidinyl, piperazinyl, azepanyl, 1,3- or 1,4-diazepanyl, or morpholinyl, each of which is optionally substituted with hydroxy,

amino, aminoalkyl, C_1-C_6 alkyl, mono- or di(C_1-C_6)alkylamino, C_1-C_6 alkoxy, or halogen, and

R_o is -H, -C_1-C_{10} alkyl, -C_2-C_{10} alkenyl, -C_2-C_{10} alkynyl, aryl, heteroaryl, or -C_1-C_6 acyl; and

R_5 is

(1) heteroaryl,

(2) aryl,

(3) saturated or unsaturated C_5-C_{10} cycloalkyl, or

(4) saturated or unsaturated C_5-C_{10} heterocycloalkyl,

and

the R_5 groups are optionally substituted at least one group which is independently hydroxy, oxo, halo, amino, cyano, nitro, -SH, -S-(C_1-C_6)alkyl, -SO_2-(C_1-C_6)alkyl, -SO_2-aryl, -SO-(C_1-C_6) alkyl, -SO-aryl, -SO_2NH_2, -SO_2NH-(C_1-C_6) alkyl, -SO_2NH-aryl, (C_1-C_6)alkoxy, or mono- or di-(C_1-C_{10})alkylamino;

R_2 is H, Cl, halogen, CF_3, CHF_2, CH_3, C_1-C_{10} alkyl, or halo(C_1-C_6)alkyl; and

X is N or CR_3, wherein

R_3 is H, halogen, or CH_3,

or a prodrug thereof, each in an amount that when in combination with the other is effective to treat the mammalian subject.

2. A method for treating a mammalian subject affected by prostate cancer comprising administering to the mammalian subject i) an oligonucleotide which reduces clusterin expression and ii) a Hsp90 inhibitor, which inhibitor is other than Hsp90i-1, each

in an amount that when in combination with the other is effective to treat the mammalian subject.

3. A method for treating a mammalian subject affected by prostate cancer comprising administering to the mammalian subject i) an oligonucleotide which reduces clusterin expression and ii) a Hsp90 inhibitor which binds to Hsp90α and Hsp90β with a K_a of less than 50 nmol/L, or a prodrug thereof, each in an amount that when in combination with the other is effective to treat the mammalian subject.

4. The method of any one of claims 1 to 3, wherein the cancer is androgen-independent prostate cancer.

5. The method of any of claims 1 to 4, wherein the amount of the oligonucleotide and the amount of the Hsp90 inhibitor when taken together is more effective to treat the subject than when each agent is administered alone.

6. The method of any one of claims 1-5, wherein the amount of the oligonucleotide in combination with the amount of the Hsp90 inhibitor is less than is clinically effective when administered alone.

7. The method of any one of claims 1-5, wherein the amount of the Hsp90 inhibitor in combination with the amount of the oligonucleotide is less than is clinically effective when administered alone.

8. The method of any one of claims 1-7, wherein the amount of the oligonucleotide and the amount of the Hsp90 inhibitor when taken together is effective to reduce a clinical symptom of prostate cancer in the subject.

9. The method of any one of claims 1-8, wherein the mammalian subject is human.

10. The method of any one of claims 1-7, wherein the oligonucleotide is an antisense oligonucleotide.

11. The method of claim 10, wherein the antisense oligonucleotide spans either the translation initiation site or the termination site of clusterin-encoding mRNA.

12. The method of claim 10, wherein the antisense oligonucleotide comprises nucleotides in the sequence set forth in SEQ ID NO: to 11.

13. The method of claim 11, wherein the antisense oligonucleotide comprises nucleotides in the sequence set forth in SEQ ID NO: 3.

14. The method of claim 13, wherein the antisense oligonucleotide is modified to enhance *in vivo* stability relative to an unmodified oligonucleotide of the same sequence.

15. The method of claim 14, wherein the oligonucleotide is custirsen.

16. The method of claim 15, wherein the amount of custirsen is less than 640mg.

17. The method of claim 16, wherein the amount of custirsen is less than 480mg.

18. The method of any one of claims 15-17, wherein the amount of custirsen is administered intravenously once in a seven day period.

19. The method of any one of claims 1-18, wherein the amount of the Hsp90 inhibitor is less than 50mg/kg.

20. The method of any one of claims 1-19, wherein the amount of the Hsp90 inhibitor is 25mg/kg or less.

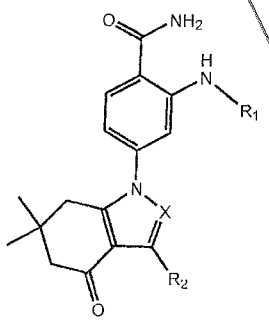
21. The method of any one of claims 1-20, wherein the Hsp90 inhibitor is Hsp90i-2.

22. The method of any one of claims 1-20, wherein a prodrug of the Hsp90 inhibitor is administered to the mammalian subject which prodrug is Hsp90i-2-PRO.

23. The method of any one of claims 1-20, wherein a prodrug of the Hsp90 inhibitor is administered to the mammalian subject which prodrug is Hsp90i-2-PRO2.

24. The method of any one of claims 1-23, wherein the combination of the oligonucleotide and the Hsp90 inhibitor is effective to inhibit the proliferation of prostate cancer cells.

25. A pharmaceutical composition comprising an amount of an oligonucleotide which reduces clusterin expression, and a Hsp90 inhibitor having the structure:



or a pharmaceutically acceptable salt thereof, wherein

R_1 is H, C_1-C_{14} alkyl, C_1-C_{10} haloalkyl, C_3-C_7 cycloalkyl, heterocycloalkyl, C_1-C_6 acyl, aryl, or heteroaryl, wherein each alkyl, cycloalkyl, heterocycloalkyl, aryl, and heteroaryl group is optionally substituted with from 1-4 groups that are independently C_1-C_6 alkyl, C_1-C_6 alkoxy, halogen, hydroxy, amino, mono- or di-(C_1-C_6)alkylamino, nitro, halo(C_1-C_6)alkyl, halo(C_1-C_6)alkoxy, or carboxamide, wherein

when R_1 is a C_1-C_{14} alkyl group, up to five of the carbon atoms in the alkyl group are optionally replaced independently by R_4, carbonyl, ethenyl, ethynyl or a moiety selected from N, O, S, SO_2, or SO, with the proviso that two O atoms, two S atoms, or an O and S atom are not immediately adjacent each other, wherein

R_4 is

(i) heteroaryl,

(ii) aryl,

(iii) saturated or unsaturated C_3-C_{10} cycloalkyl, or

(iv) saturated or unsaturated C_2-C_{10} heterocycloalkyl,

wherein

each aryl, heteroaryl, saturated or unsaturated cycloalkyl, or saturated or unsaturated heterocycloalkyl, independently, is optionally substituted with at least one group, which independently is hydroxy, halo, amino, cyano, carboxy, carboxamido, nitro, oxo, -S-(C_1-C_6) alkyl, -SO_2(C_1-C_6) alkyl, -SO_2-aryl, -SO-(C_1-C_6)alkyl, -SO-aryl, -SO_2NH_2, -SO_2NH-(C_1-C_6)alkyl, -SO_2NH-aryl, (C_1-C_6)alkoxy, or mono- or di-(C_1-C_{10})alkylamino; and R_4 is optionally fused

to a C_6-C_{10} aryl group, C_5-C_9 saturated cyclic group, or a C_4-C_{10} heterocycloalkyl group; and

R_1 is optionally substituted at any available position with C_1-C_{10} alkyl, C_1-C_{10} haloalkyl, C_2-C_{10} alkenyl, C_2-C_{10} alkynyl, hydroxy, carboxy, carboxamido, oxo, halo, amino, cyano, nitro, -SH, -S-(C_1-C_6)alkyl, -SO_2-(C_1-C_6)alkyl, -SO_2NH_2, -SO_2NH(C_1-C_6)alkyl, -SO_2NH-aryl, -SO_2-aryl, -SO-(C_1C_6)alkyl, -SO_2-aryl, C_1-C_6 alkoxy, C_2-C_{10} alkenyloxy, C_2-C_{10} alkynyloxy, mono- or di-(C_1-C_{10})alkylamino, -C_1-C_{10} alkyl-Z, -OC_1-C_{10} alkyl-Z, or R_5, wherein

Z is OR_o or -$N(R_6)_2$, wherein

each R_6 is independently -H or C_1-C_6 alkyl, or $N(R_6)_2$ represents pyrrolidinyl, piperidinyl, piperazinyl, azepanyl, 1,3- or 1,4-diazepanyl, or morpholinyl, each of which is optionally substituted with hydroxy, amino, aminoalkyl, C_1-C_6 alkyl, mono- or di(C_1-C_6)alkylamino, C_1-C_6 alkoxy, or halogen, and

R_o is -H, -C_1-C_{10} alkyl, -C_2-C_{10} alkenyl, -C_2-C_{10} alkynyl, aryl, heteroaryl, or -C_1-C_6 acyl; and

R_5 is

(1) heteroaryl,

(2) aryl,

(3) saturated or unsaturated C_5-C_{10} cycloalkyl, or

(4) saturated or unsaturated C_5-C_{10} heterocycloalkyl,

and

the R_5 groups are optionally substituted at least one group which is independently hydroxy, oxo, halo, amino, cyano, nitro, -SH,

-S-(C_1-C_6)alkyl, -SO_2-(C_1-C_6)alkyl, -SO_2-aryl, -SO-(C_1-C_6) alkyl, -SO-aryl, -SO_2NH_2, -SO_2NH-(C_1-C_6) alkyl, -SO_2NH-aryl, (C_1-C_6)alkoxy, or mono- or di-(C_1-C_{10})alkylamino;

R_2 is H, Cl, halogen, CF_3, CHF_2, CH_3, C_1-C_{10} alkyl, or halo(C_1-C_6)alkyl; and

X is N or CR_3, wherein

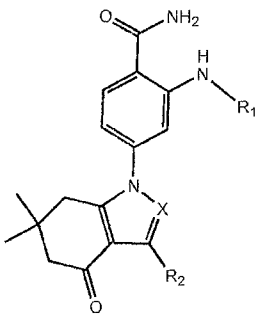
R_3 is H, halogen, or CH_3,

or a prodrug thereof, for use in treating a mammalian subject affected by prostate cancer.

26. A pharmaceutical composition comprising an amount of an oligonucleotide which reduces clusterin expression, and a Hsp90 inhibitor, which inhibitor is other than Hsp90i-1, for use in treating a mammalian subject affected by prostate cancer.

27. A pharmaceutical composition comprising an amount of an oligonucleotide which reduces clusterin expression, and a Hsp90 inhibitor which binds to Hsp90α and Hsp90β with a K_a of less than 50 nmol/L, or a prodrug thereof, for use in treating a mammalian subject affected by prostate cancer.

28. An oligonucleotide which reduces clusterin expression for use in combination with a Hsp90 inhibitor having the structure:



or a pharmaceutically acceptable salt thereof, wherein

R_1 is H, C_1-C_{14} alkyl, C_1-C_{10} haloalkyl, C_3-C_7 cycloalkyl, heterocycloalkyl, C_1-C_6 acyl, aryl, or heteroaryl, wherein each alkyl, cycloalkyl, heterocycloalkyl, aryl, and heteroaryl group is optionally substituted with from 1-4 groups that are independently C_1-C_6 alkyl, C_1-C_6 alkoxy, halogen, hydroxy, amino, mono- or di-(C_1-C_6)alkylamino, nitro, halo(C_1-C_6)alkyl, halo(C_1-C_6)alkoxy, or carboxamide, wherein

when R_1 is a C_1-C_{14} alkyl group, up to five of the carbon atoms in the alkyl group are optionally replaced independently by R_4, carbonyl, ethenyl, ethynyl or a moiety selected from N, O, S, SO_2, or SO, with the proviso that two O atoms, two S atoms, or an O and S atom are not immediately adjacent each other, wherein

R_4 is

(i) heteroaryl,

(ii) aryl,

(iii) saturated or unsaturated C_3-C_{10} cycloalkyl, or

(iv) saturated or unsaturated C_2-C_{10} heterocycloalkyl,

wherein

each aryl, heteroaryl, saturated or unsaturated cycloalkyl, or saturated or unsaturated heterocycloalkyl, independently, is optionally substituted with at least one group, which independently is hydroxy, halo, amino, cyano, carboxy, carboxamido, nitro, oxo, -S-(C_1-C_6) alkyl, -SO_2(C_1-C_6) alkyl, -SO_2-aryl, -SO-(C_1-C_6)alkyl, -SO-aryl, -SO_2NH_2, -SO_2NH-(C_1-C_6)alkyl, -SO_2NH-aryl, (C_1-C_6)alkoxy, or mono- or di-(C_1-

C_{10})alkylamino; and R_4 is optionally fused to a C_6-C_{10} aryl group, C_5-C_8 saturated cyclic group, or a C_4-C_{10} heterocycloalkyl group; and

R_1 is optionally substituted at any available position with C_1-C_{10} alkyl, C_1-C_{10} haloalkyl, C_2-C_{10} alkenyl, C_2-C_{10} alkynyl, hydroxy, carboxy, carboxamido, oxo, halo, amino, cyano, nitro, -SH, -S-(C_1-C_6)alkyl, -SO_2-(C_1-C_6)alkyl, -SO_2NH_2, -SO_2NH(C_1-C_6)alkyl, -SO_2NH-aryl, -SO_2-aryl, -SO-(C_1C_6)alkyl, -SO_2-aryl, C_1-C_6 alkoxy, C_2-C_{10} alkenyloxy, C_2-C_{10} alkynyloxy, mono- or di-(C_1-C_{10})alkylamino, -C_1-C_{10} alkyl-Z, -OC_1-C_{10} alkyl-Z, or R_5, wherein

Z is OR_o or -$N(R_6)_2$, wherein

each R_6 is independently -H or C_1-C_6 alkyl, or $N(R_6)_2$ represents pyrrolidinyl, piperidinyl, piperazinyl, azepanyl, 1,3- or 1,4-diazepanyl, or morpholinyl, each of which is optionally substituted with hydroxy, amino, aminoalkyl, C_1-C_6 alkyl, mono- or di(C_1-C_6)alkylamino, C_1-C_6 alkoxy, or halogen, and

R_o is -H, -C_1-C_{10} alkyl, -C_2-C_{10} alkenyl, -C_2-C_{10} alkynyl, aryl, heteroaryl, or -C_1-C_6 acyl; and

R_5 is

(1) heteroaryl,

(2) aryl,

(3) saturated or unsaturated C_5-C_{10} cycloalkyl, or

(4) saturated or unsaturated C_5-C_{10} heterocycloalkyl,

and

the R_5 groups are optionally substituted at least one group which is independently

hydroxy, oxo, halo, amino, cyano, nitro, -SH, -S-(C_1-C_6)alkyl, -SO_2-(C_1-C_6)alkyl, -SO_2-aryl, -SO-(C_1-C_6) alkyl, -SO-aryl, -SO_2NH_2, -SO_2NH-(C_1-C_6) alkyl, -SO_2NH-aryl, (C_1-C_6)alkoxy, or mono- or di-(C_1-C_{10})alkylamino;

R_2 is H, Cl, halogen, CF_3, CHF_2, CH_3, C_1-C_{10} alkyl, or halo(C_1-C_6)alkyl; and

X is N or CR_3, wherein

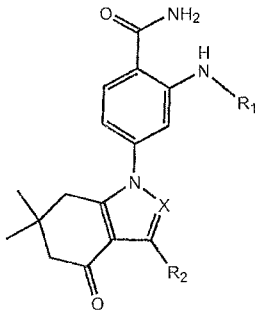
R_3 is H, halogen, or CH_3,

or a prodrug thereof, in treating a mammalian subject affected by prostate cancer.

29. An oligonucleotide which reduces clusterin expression for use in combination with a Hsp90 inhibitor, which inhibitor is other than Hsp90i-1, in treating a mammalian subject affected by prostate cancer.

30. An oligonucleotide which reduces clusterin expression for use in combination with a Hsp90 inhibitor which binds to Hsp90α and Hsp90β with a K_a of less than 50 nmol/L, or a prodrug thereof, in treating a mammalian subject affected by prostate cancer.

31. A composition for treating a mammalian subject affected by prostate cancer comprising i) an oligonucleotide which reduces clusterin expression and ii) a Hsp90 inhibitor having the structure:



or a pharmaceutically acceptable salt thereof, wherein

R_1 is H, C_1-C_{14} alkyl, C_1-C_{10} haloalkyl, C_3-C_7 cycloalkyl, heterocycloalkyl, C_1-C_6 acyl, aryl, or heteroaryl, wherein each alkyl, cycloalkyl, heterocycloalkyl, aryl, and heteroaryl group is optionally substituted with from 1-4 groups that are independently C_1-C_6 alkyl, C_1-C_6 alkoxy, halogen, hydroxy, amino, mono- or di-(C_1-C_6)alkylamino, nitro, halo(C_1-C_6)alkyl, halo(C_1-C_6)alkoxy, or carboxamide, wherein

when R_1 is a C_1-C_{14} alkyl group, up to five of the carbon atoms in the alkyl group are optionally replaced independently by R_4, carbonyl, ethenyl, ethynyl or a moiety selected from N, O, S, SO_2, or SO, with the proviso that two O atoms, two S atoms, or an O and S atom are not immediately adjacent each other, wherein

R_4 is

(i) heteroaryl,

(ii) aryl,

(iii) saturated or unsaturated C_3-C_{10} cycloalkyl, or

(iv) saturated or unsaturated C_2-C_{10} heterocycloalkyl,

wherein

each aryl, heteroaryl, saturated or unsaturated cycloalkyl, or saturated or unsaturated heterocycloalkyl,

independently, is optionally substituted with at least one group, which independently is hydroxy, halo, amino, cyano, carboxy, carboxamido, nitro, oxo, -S-(C_1-C_6) alkyl, -SO_2(C_1-C_6) alkyl, -SO_2-aryl, -SO-(C_1-C_6)alkyl, -SO-aryl, -SO_2NH_2, -SO_2NH-(C_1-C_6)alkyl, -SO_2NH-aryl, (C_1-C_6)alkoxy, or mono- or di-(C_1-C_{10})alkylamino; and R_4 is optionally fused to a C_6-C_{10} aryl group, C_5-C_8 saturated cyclic group, or a C_4-C_{10} heterocycloalkyl group; and

R_1 is optionally substituted at any available position with C_1-C_{10} alkyl, C_1-C_{10} haloalkyl, C_2-C_{10} alkenyl, C_2-C_{10} alkynyl, hydroxy, carboxy, carboxamido, oxo, halo, amino, cyano, nitro, -SH, -S-(C_1-C_6)alkyl, -SO_2-(C_1-C_6)alkyl, -SO_2NH_2, -SO_2NH(C_1-C_6)alkyl, -SO_2NH-aryl, -SO_2-aryl, -SO-(C_1C_6)alkyl, -SO_2-aryl, C_1-C_6 alkoxy, C_2-C_{10} alkenyloxy, C_2-C_{10} alkynyloxy, mono- or di-(C_1-C_{10})alkylamino, -C_1-C_{10} alkyl-Z, -OC_1-C_{10} alkyl-Z, or R_5, wherein

Z is OR_o or -$N(R_6)_2$, wherein

each R_6 is independently -H or C_1-C_6 alkyl, or $N(R_6)_2$ represents pyrrolidinyl, piperidinyl, piperazinyl, azepanyl, 1,3- or 1,4-diazepanyl, or morpholinyl, each of which is optionally substituted with hydroxy, amino, aminoalkyl, C_1-C_6 alkyl, mono- or di(C_1-C_6)alkylamino, C_1-C_6 alkoxy, or halogen, and

R_o is -H, -C_1-C_{10} alkyl, -C_2-C_{10} alkenyl, -C_2-C_{10} alkynyl, aryl, heteroaryl, or -C_1-C_6 acyl; and

R_5 is

(1) heteroaryl,

(2) aryl,

(3) saturated or unsaturated C_5-C_{10} cycloalkyl, or

(4) saturated or unsaturated C_5-C_{10} heterocycloalkyl,

and

the R_5 groups are optionally substituted at least one group which is independently hydroxy, oxo, halo, amino, cyano, nitro, -SH, -S-(C_1-C_6)alkyl, -SO_2-(C_1-C_6)alkyl, -SO_2-aryl, -SO-(C_1-C_6) alkyl, -SO-aryl, -SO_2NH_2, -SO_2NH-(C_1-C_6) alkyl, -SO_2NH-aryl, (C_1-C_6)alkoxy, or mono- or di-(C_1-C_{10})alkylamino;

R_2 is H, Cl, halogen, CF_3, CHF_2, CH_3, C_1-C_{10} alkyl, or halo(C_1-C_6)alkyl; and

X is N or CR_3, wherein

R_3 is H, halogen, or CH_3,

or a prodrug thereof, each in an amount that when in combination with the other is effective to treat the mammalian subject.

32. A composition for treating a mammalian subject affected by prostate cancer comprising i) an oligonucleotide which reduces clusterin expression and ii) a Hsp90 inhibitor, which inhibitor is other than Hsp90i-1, each in an amount that when in combination with the other is effective to treat the mammalian subject.

33. A composition for treating a mammalian subject affected by prostate cancer comprising i) an oligonucleotide which reduces clusterin expression and ii) a Hsp90 inhibitor which binds to Hsp90α and Hsp90β with a K_a of less than 50 nmol/L, or a prodrug thereof, each in an amount that when in combination with the other is effective to treat the mammalian subject.

What is claimed is:

1. Use of
i) an antisense or RNAi oligonucleotide that is complementary to the sequence of clusterin of a mammalian subject, and that reduces clusterin expression; and
ii) a Heat Shock Protein 90 (Hsp90) inhibitor comprising 4-(6,6-Dimethyl-4-oxo-3-trifluoromethyl-4,5,6,7-tetrahydro-indazol-1-yl)-2-(4-hydroxy-cyclohexylamino)-benzamide, or a pharmaceutically acceptable salt thereof, or a prodrug that is metabolized to release 4-(6,6-Dimethyl-4-oxo-3-trifluoromethyl-4,5,6,7-tetrahydro-indazol-1-yl)-2-(4-hydroxy-cyclohexylamino)-benzamide
in the manufacture of a medicament for treating prostate cancer in the mammalian subject.

2. The use of claim 1, wherein the cancer is androgen-independent prostate cancer.

3. The use of claim 1 or 2, wherein the mammalian subject is human.

4. The use of any one of claims 1-4, wherein the oligonucleotide is an antisense oligonucleotide.

5. The use of claim 5, wherein the antisense oligonucleotide comprises one of Seq ID NOs: 1-11.

6. The use of claim 5, wherein the antisense oligonucleotide comprises SEQ ID NO: 3.

7. The use of claim 6, wherein the antisense oligonucleotide is modified to enhance *in vivo* stability relative to an unmodified oligonucleotide of the same sequence.

8. The use of claim 7, wherein the oligonucleotide is custirsen.

9. The use of any one of claims 1-4, wherein the oligonucleotide is an RNAi oligonucleotide.

10. The use of claim 9, wherein the RNAi oligonucleotide comprises one of SEQ ID NOs: 19-42.

11. The use of any one of claims 1-10, wherein the combination comprises Hsp90i-2-PRO.

12. The use of any one of claims 1-11, wherein the combination of the oligonucleotide and the Hsp90 inhibitor is effective to inhibit the proliferation of prostate cancer cells.