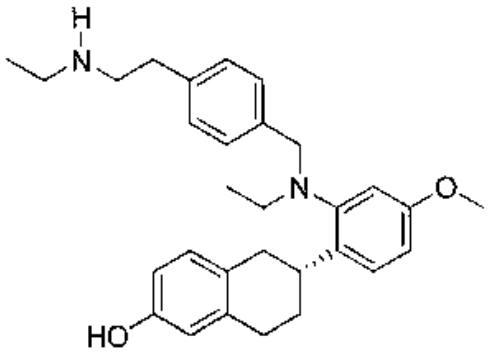
What is claimed is:

1. Use of a combination of everolimus and RAD1901 having the structure:



or a salt or solvate thereof, in the manufacture of a medicament for inhibiting tumor growth or producing tumor regression in a subject having a mutant estrogen receptor alpha-positive cancer.

2. The use of claim 1, wherein the cancer is selected from the group consisting of breast cancer, uterine cancer, ovarian cancer, and pituitary cancer.

3. The use of claim 1, wherein the cancer is a metastatic cancer.

4. The use of claim 1, wherein said cancer is positive for the mutant estrogen receptor alpha comprising one or more mutations selected from the group consisting of $Y537X_1$, $L536X_2$, P535H, V534E, S463P, V392I, E380Q, D538G and combinations thereof, wherein:

X_1 is S, N, or C; and X_2 is R or Q.

5. The use of claim 4, wherein the mutation is Y537S.

6. The use of claim 1, wherein the ratio of the concentration of RAD1901 or a salt or solvate thereof in the tumor to the concentration of RAD1901 or a salt or solvate thereof in plasma (T/P) following administration is at least about 15.

7. The use of claim 1, wherein the subject is a postmenopausal woman who had relapsed or progressed after previous treatment with SERMs and/or AIs.

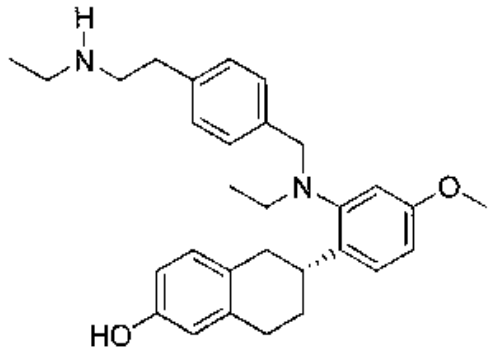
8. The use of claim 1, wherein the salt thereof is RAD1901 dihydrochloride.

9. The use of claim 1, wherein the tumor is resistant to a drug selected from the group consisting of anti-estrogens, aromatase inhibitors, and combinations thereof.

10. The use of claim 1, wherein the therapeutically effective amount is 150 mg to 2,000 mg.

11. A pharmaceutical composition comprising everolimus and RAD1901 or a salt or solvate thereof.

12. Use of a combination of an m-TOR inhibitor and RAD1901 having the structure:



or a salt or solvate thereof, in the manufacture of a medicament for the treatment of breast cancer in a subject having a mutant and drug-resistant estrogen receptor alpha-positive cancer, wherein said subject expresses at least one mutant estrogen receptor alpha selected from the group consisting of D538G, Y537S, Y537N, Y537C, E380Q, S463P, L536R, L536Q, P535H, V392I and V534E.

13. The use of claim 12 wherein said drug resistant breast cancer is resistant to one or more antiestrogen and/or or aromatase inhibitor therapies.

14. The use of claim 13 wherein said one or more antiestrogens are selected from the group consisting of tamoxifen, toremifene and fulvestrant and said one or more aromatase inhibitors are selected from the group consisting of aromasin, letrozole and anastrozole.

~~15. The use according to claim 12 wherein said subject expresses at least one mutant estrogen receptor alpha selected from the group consisting of D538G, Y537S, Y537N, Y537C, E380Q, S463P, L536R, L536Q, P535H, V392I and V534E.~~

15.~~16.~~ The use according to claim 12 wherein said RAD1901 is to be administered in a total daily dosage of from between 100 mg and 1,500 mg.

16.~~17.~~ The use according to claim 12 wherein said subject is first identified for treatment through measuring for increased expression of one or more genes selected from ABL1, AKT1,

AKT2, ALK, APC, AR, ARID1A, ASXL1, ATM, AURKA, BAP, BAP1, BCL2L11, BCR, BRAF, BRCA1, BRCA2, CCND1, CCND2, CCND3, CCNE1, CDH1, CDK4, CDK6, CDK8, CDKN1A, CDKN1B, CDKN2A, CDKN2B, CEBPA, CTNNB1, DDR2, DNMT3A, E2F3, EGFR, EML4, EPHB2, ERBB2, ERBB3, ESR1, EWSR1, FBXW7, FGF4, FGFR1, FGFR2, FGFR3, FLT3, FRS2, HIF1A, HRAS, IDH1, IDH2, IGF1R, JAK2, KDM6A, KDR, KIF5B, KIT, KRAS, LRP1B, MAP2K1, MAP2K4, MCL1, MDM2, MDM4, MET, MGMT, MLL, MPL, MSH6, MTOR, MYC, NF1, NF2, NKX2-1, NOTCH1, NPM, NRAS, PDGFRA, PIK3CA, PIK3R1, PML, PTEN, PTPRD, RARA, RB1, RET, RICTOR, ROS1, RPTOR, RUNX1, SMAD4, SMARCA4, SOX2, STK11, TET2, TP53, TSC1, TSC2, and VHL.

17.~~18.~~ The use according to claim 12 wherein said m-TOR inhibitor is selected from the group consisting of sirolimus, temsirolimus, everolimus, and ridafarolimus.

18.~~19.~~ The use according to claim 12 wherein said m-TOR inhibitor is to be dosed at from between 1mg and 500 mg daily.

19.~~20.~~ The use according to claim 17~~18~~ wherein said m-TOR inhibitor is everolimus.

20.~~21.~~ The use according to claim 19~~20~~ wherein said everolimus is to be dosed at a daily dose of 10 mg.

21.~~22.~~ The use according to claim 12 wherein said m-TOR inhibitor is to be dosed once per day.