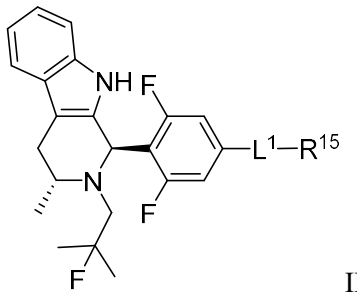
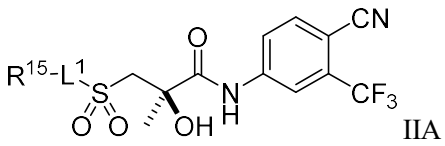
What is Claimed is:

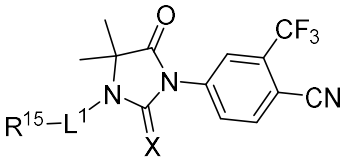
1 . A compound of Formula IID, IIA, IIB, IIC, IIK, or IIL, or a stereoisomer, mixture of stereoisomers, hydrate, solvate, isotopically enriched analog or pharmaceutically acceptable salt thereof:



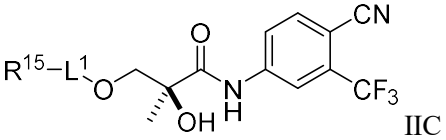
IID



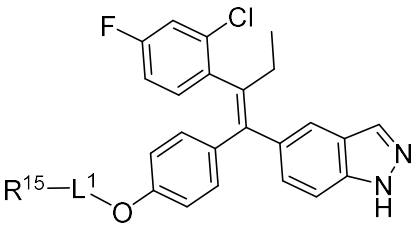
IIA



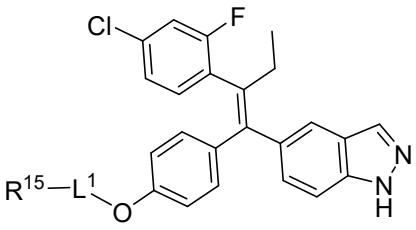
IIB



IIC



IIK



IIL

wherein:

X is O or S;

L^1 is a covalent bond, optionally substituted alkylene or optionally substituted heteroalkylene; and

R^{15} is a nuclear payload;

provided that when the compound is of Formula IIA or IIC, the nuclear payload is not a curcumin derivative.

2. The compound of claim 1, wherein L^1 is a covalent bond or optionally substituted alkylene.

3. The compound of claim 1, wherein L^1 is a covalent bond or optionally substituted heteroalkylene.

4. The compound of claim 1, wherein L^1 is optionally substituted alkylene or optionally substituted heteroalkylene.

5. The compound of claim 1, wherein L^1 is alkylene or heteroalkylene.

6. The compound of claim 1, wherein L^1 is a covalent bond.

7. The compound of any preceding claim, wherein X is S.

8. The compound of any preceding claim, wherein X is O.

9. The compound of any preceding claim, wherein the nuclear payload binds to a protein involved in the DNA damage repair process.

10. The compound of any preceding claim, wherein the nuclear payload binds poly(ADP-ribose) polymerase (PARP), DNA-dependent protein kinase (DNA-PK), histone deacetylase (HDAC), enhancer of zeste homolog 2 (EZH2), histone acetyl transferase (HAT), methyltransferase, a bromodomain, myelin transcription factor 1 (MYT1), p53, melanocyte-stimulating hormone (MSH), mutL homolog (MLH), ERCC1, apurinic/apyrimidinic endonuclease 1 (APE1), topoisomerase I (Topo I), topoisomerase II (Topo II), Wee1, checkpoint kinase1 (Chk1), checkpoint kinase2 (Chk2), ataxia telangiectasia (ATR), or ataxia-telangiectasia mutated (ATM).

11. The compound of any preceding claim, wherein the nuclear payload comprises olaparib (AZD-2281), rucaparib (AG014699, PF-01367338), niraparib, talazoparib (BMN-673), veliparib (ABT-888), CEP 9722, E7016, BGB-290, 3-aminobenzamide, methoxyamine, CC-115, MSC2490484A, AZD6738, VX-970, AZD0156, GDC-0575, MK-8776, LY2606368, AZD1775, belotecan, CRLX101, irinotecan, LMP 400, LMP 776, NKTR-102, topotecan, doxorubicin, epirubicin, etoposide, idarubicin, mitoxantrone, teniposide, vorinostat, romidepsin (Istodax), chidamide, panobinostat (Farydak), belinostat (PXD101), panobinostat (LBH589), valproic acid (as Mg valproate), mocetinostat (MGCD0103), abexinostat (PCI-24781), entinostat (MS-275), SB939, resminostat (4SC-201), givinostat (ITF2357), quisinostat (JNJ-26481585), HBI-8000, kevetrin, CUDC-101, AR-42, CHR-2845, CHR-3996, 4SC-202, CG200745, ACY-1215, ME-344, sulforaphane, tazemetostat, MAK638, CPI-1205), DS-3201b, anacardic acid, MG149, C646, S-adenosyl methionine, JQ1, I-BET 151 (GSK1210151A), I-BET 762 (GSK525762), OTX-015, TEN-010, CPI-203, CPI-0610, olinone, LY294002, or an analog thereof.

12. The compound of claim 11, wherein the analog maintains a biological activity which is comparable to that observed in the original, unmodified nuclear payload.

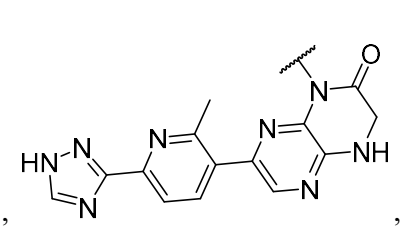
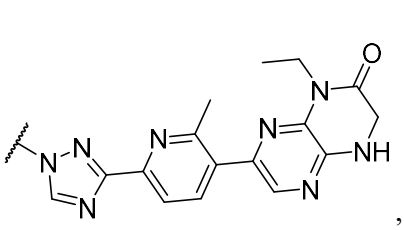
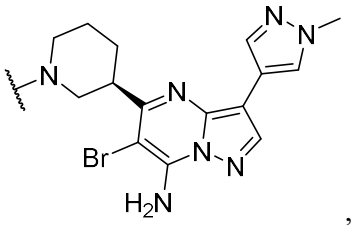
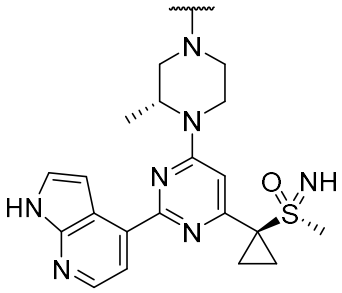
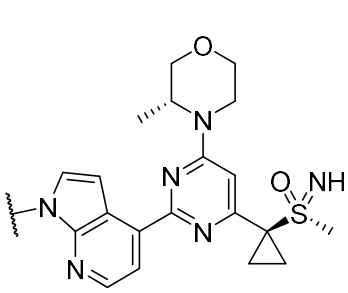
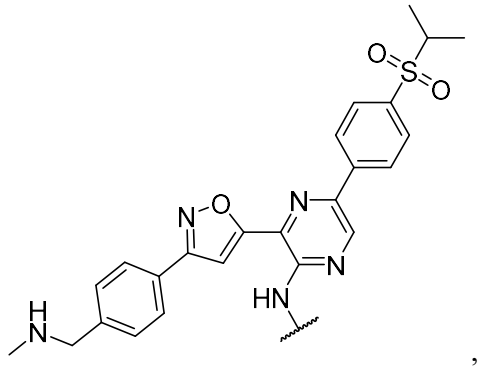
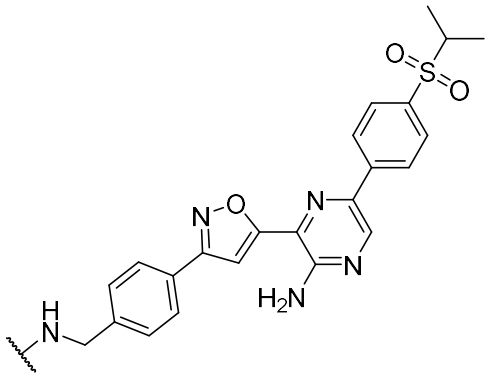
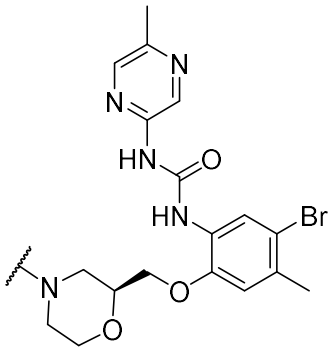
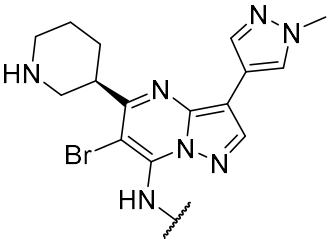
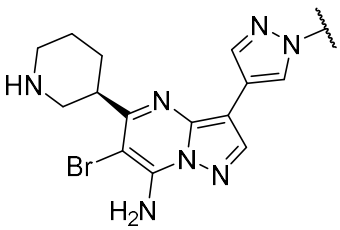
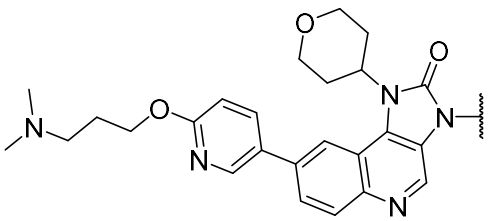
13. The compound of any preceding claim, wherein the nuclear payload binds to a catalytic domain of poly(ADP-ribose) polymerase (PARP).

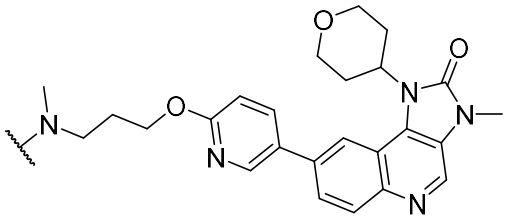
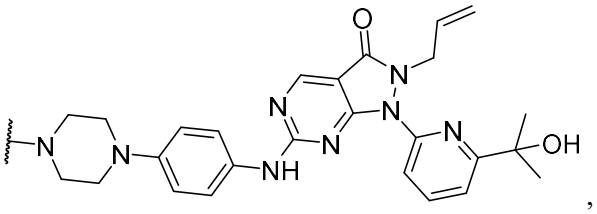
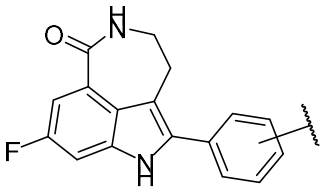
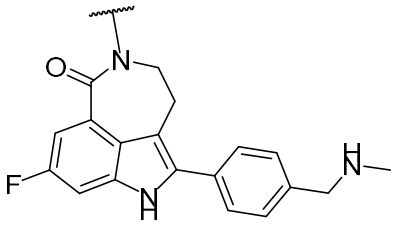
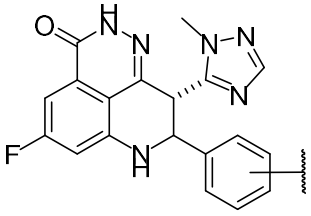
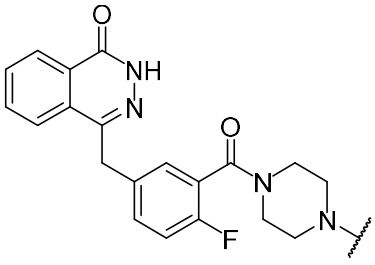
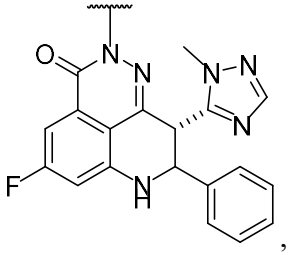
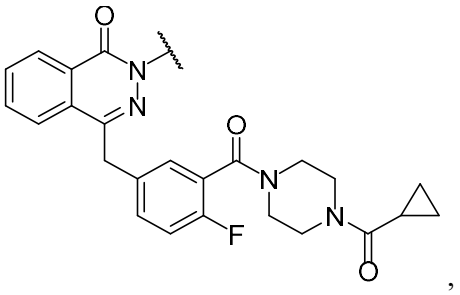
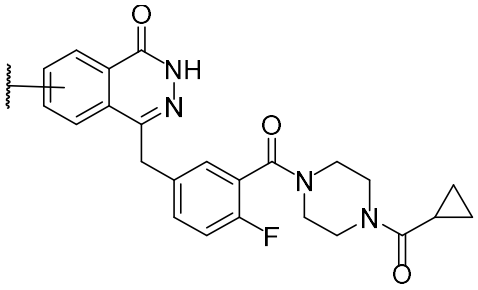
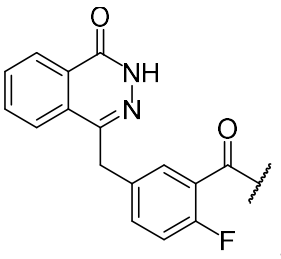
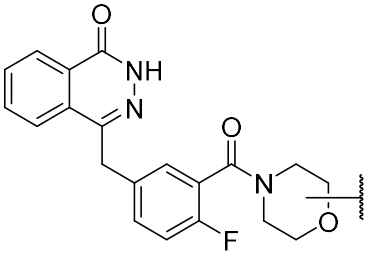
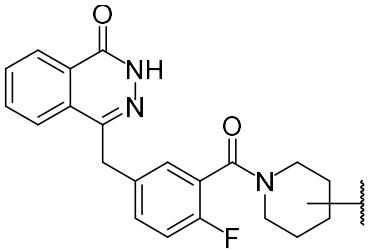
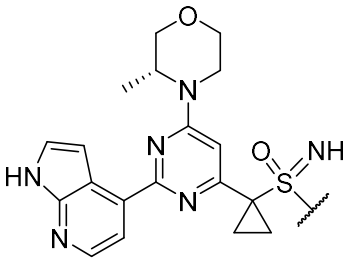
14. The compound of any preceding claim, wherein the catalytic domain comprises a conserved HYE motif.

15. The compound of any preceding claim, wherein the nuclear payload binds to a poly(ADP-ribose) polymerase (PARP) with an IC_{50} of less than about 500 nM.

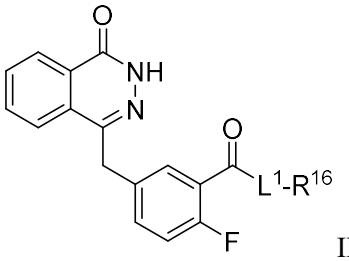
16. The compound of any one of claims 13-15, wherein the PARP comprises PARP-1 and/or PARP-2, or a variant thereof.

17. The compound of any preceding claim, wherein R^{15} is:

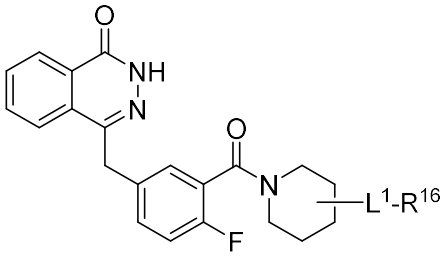

,

,

,

,

,

,

,

,

,

,

,


,

,

,

,

,

,

,

,

,

,

,

, or

where the wavy line indicates the point of attachment.

18. A compound of Formula IIIA or IIIB, or a stereoisomer, mixture of stereoisomers, hydrate, solvate, isotopically enriched analog or pharmaceutically acceptable salt thereof:



IIIA



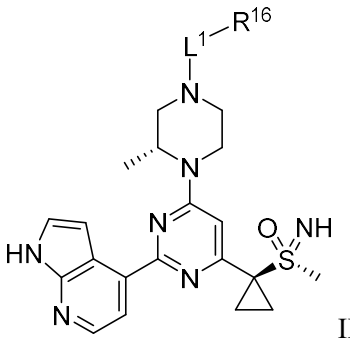
IIIB

wherein:

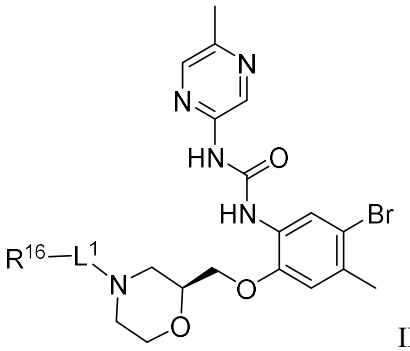
L^1 is a covalent bond, optionally substituted alkylene or optionally substituted heteroalkylene; and

R^{16} is a nuclear receptor-targeting epitope.

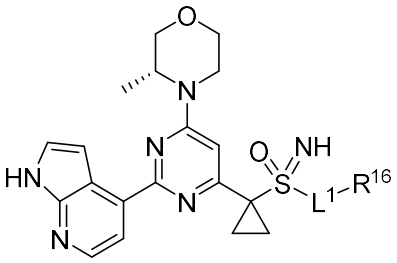
19. A compound of Formula IIIC, IIID, or IIIJ, or a stereoisomer, mixture of stereoisomers, hydrate, solvate, isotopically enriched analog or pharmaceutically acceptable salt thereof:



IIIC



IIID



IIIJ

wherein:

L^1 is a covalent bond or a linking moiety; and

R^{16} is a nuclear receptor-targeting epitope.

20. The compound of claim 19, wherein L^1 is of the formula:

$$-Y^1-(CH_2)_n-Y^2-(CH_2)_p-Y^3-$$

wherein each of Y^1, Y^2, and Y^3 are independently a bond, $-CR^{11}R^{12}-$, $-NR^{11}-$, -O-, $-S(O)_{0-2}-$, $-NR^{11}C(O)-$, $-C(O)NR^{11}-$, $-NR^{11}S(O)_2-$, $-S(O)_2NR^{11}-$, $-CR^{12}=N-NR^{11}-$, $-NR^{11}-N=CR^{12}-$, or -C(O)-;

each R^{11} is independently hydrogen, C_{1-4} alkyl, C_{1-4} haloalkyl, aryl, heteroaryl, cycloalkyl or heterocyclyl;

each R^{12} is independently hydrogen, C_{1-4} alkyl, C_{1-4} haloalkyl, aryl, heteroaryl, cycloalkyl or heterocyclyl; and

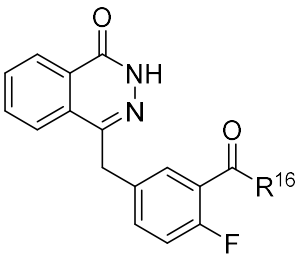
n and p are each independently 0, 1, 2, 3, 4, 5, 6, 7, or 8.

21. The compound of claim 19 or 20, wherein L^1 comprises a non-biocleavable moiety.

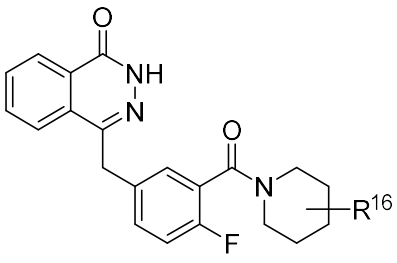
22. The compound of claim 19 or 20, wherein L^1 comprises an acid-labile moiety.

23. The compound of claim 19 or 20, wherein L^1 comprises a hydrazone moiety.

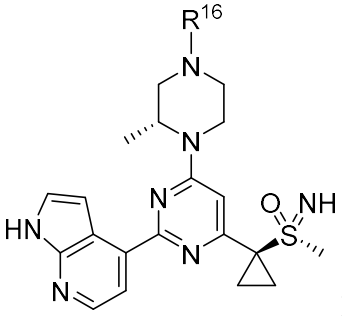
24. A compound of Formula IIIE, IIIF, IIIG, IIIH, or IIII, or a stereoisomer, mixture of stereoisomers, hydrate, solvate, isotopically enriched analog or pharmaceutically acceptable salt thereof:



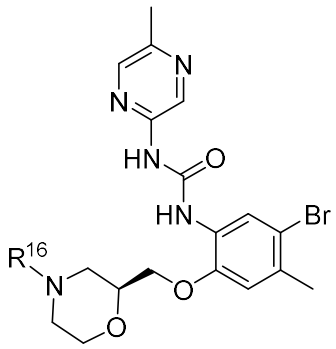
IIIE



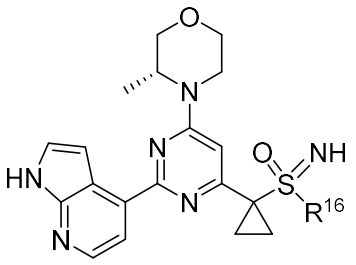
IIIF



IIIG



IIIH



IIII

wherein R^{16} is a nuclear receptor-targeting epitope.

25. The compound of any one of claims 18-24, wherein the nuclear receptor-targeting epitope is a nuclear steroid receptor-targeting epitope.

26. The compound of any one of claims 18-24, wherein the nuclear receptor-targeting epitope is selected from an estrogen receptor-targeting epitope, glucocorticoid receptor-targeting epitope, progesterone receptor-targeting epitope or androgen receptor-targeting epitope.

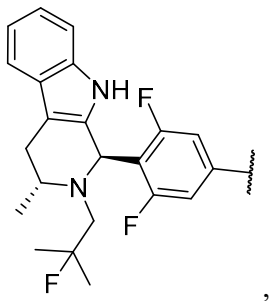
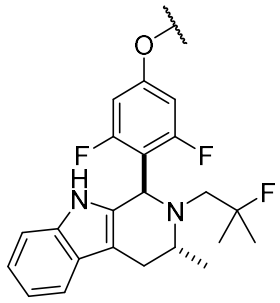
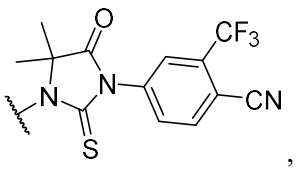
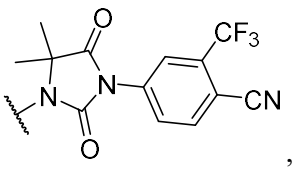
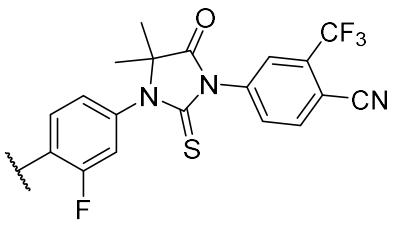
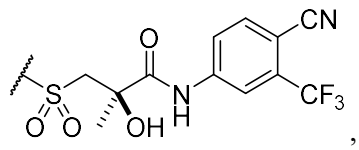
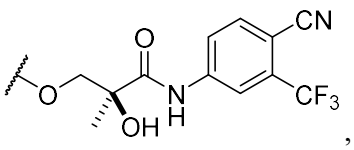
27. The compound of any one of claims 18-24, wherein the nuclear receptor-targeting epitope is derived from an androgen receptor agonist, an androgen receptor antagonist, a selective androgen-receptor modulator (SARM), an estrogen receptor agonist, an estrogen receptor antagonist, a selective estrogen receptor modulator (SERM), a glucocorticoid receptor antagonist, a glucocorticoid receptor agonist, a selective glucocorticoid receptor modulator (SGRM), a progesterone receptor antagonist, a progesterone receptor agonist, a selective progesterone receptor modulator (SPRM), or combination thereof.

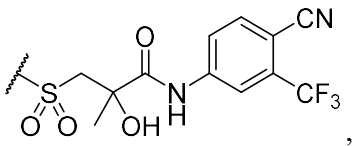
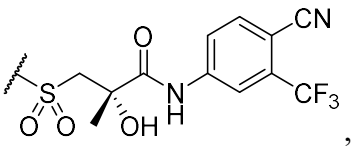
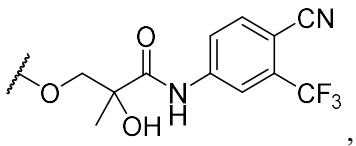
28. The compound of any one of claims 18-24, wherein the nuclear receptor-targeting epitope is derived from estrogen, estetrol, estriol, estrone, progesterone, enobosarm, bicalutamide, apalutamide, testosterone, dihydrotestosterone, estradiol, flutamide, nilutamide, enzalutamide, tamoxifen, toremifene, raloxifene, bazedoxifene, ospemifene, megestrol acetate, estramustine, abiraterone, LGD-2941, BMS-564929, ostarine, or an analog thereof.

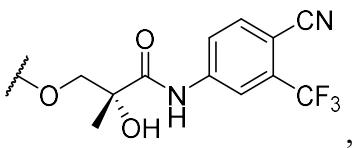
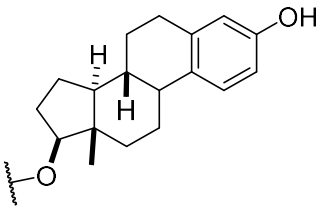
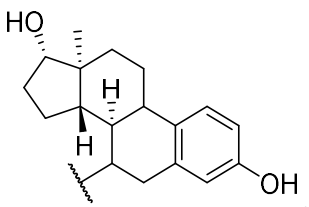
29. The compound of any one of claims 18-24, wherein the nuclear receptor-targeting epitope is capable of binding to a ligand-binding domain of a nuclear steroid receptor.

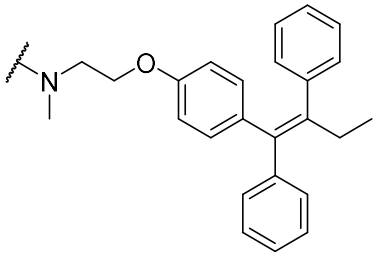
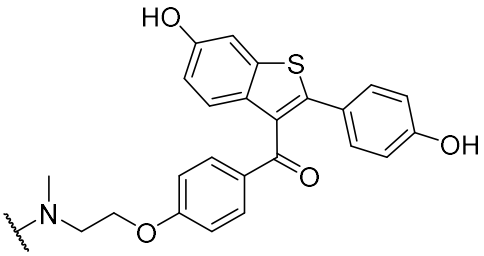
30. The compound of any one of claims 18-29, wherein the nuclear receptor-targeting epitope binds to a nuclear steroid receptor with an IC_{50} of less than about 500 nM or an EC_{50} of less than about 1 μM.

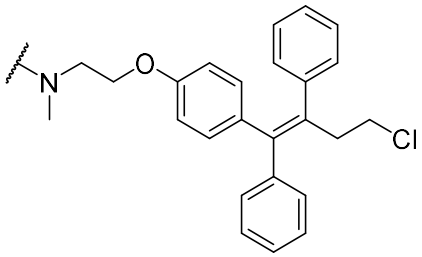
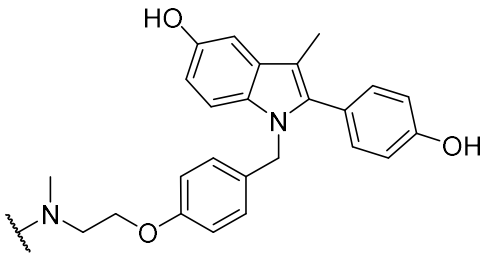
31. The compound of any one of claims 18-24, wherein R^{16} is:

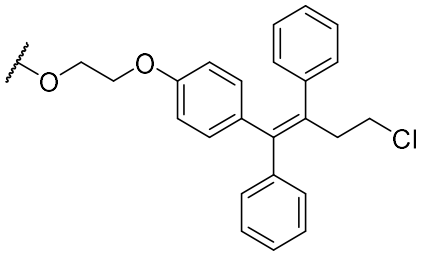
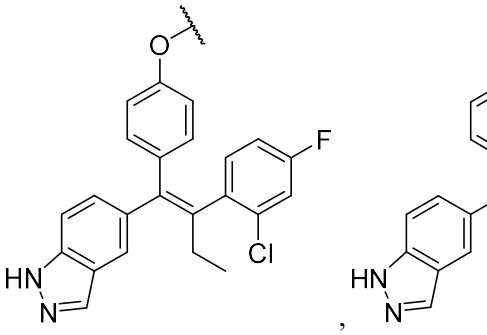
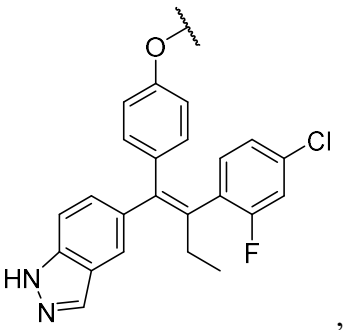

,

,

,

,

,

,

,

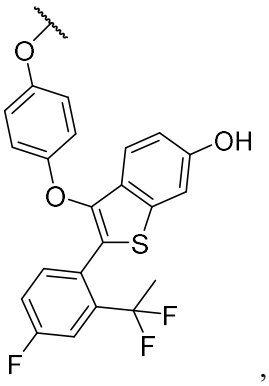
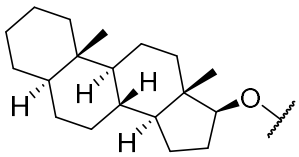
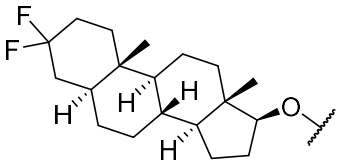
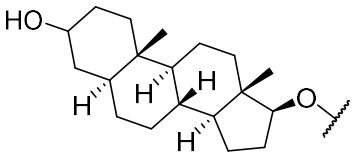
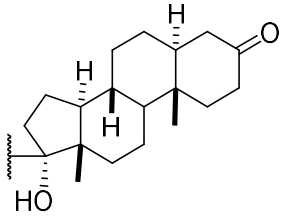
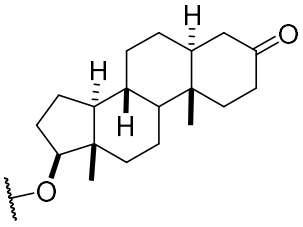
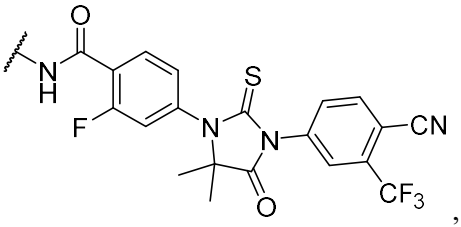
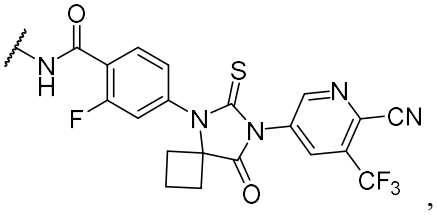
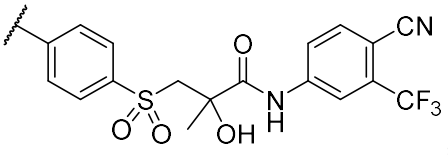
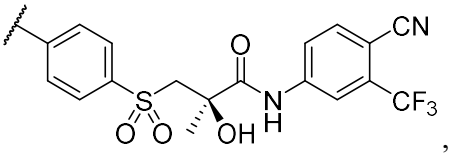
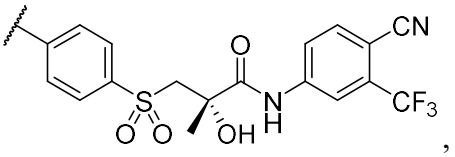
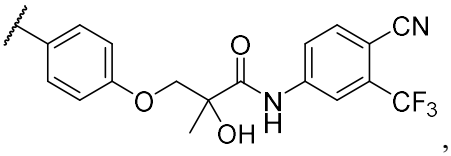
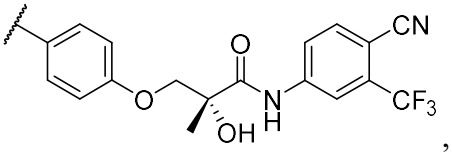
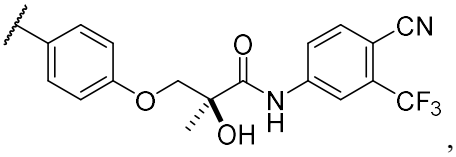
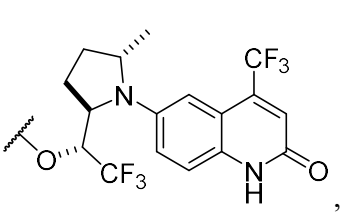
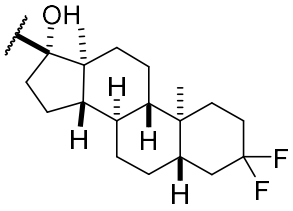
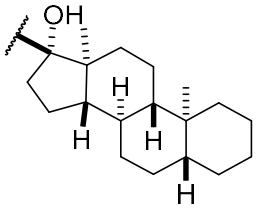
 ,  ,  ,

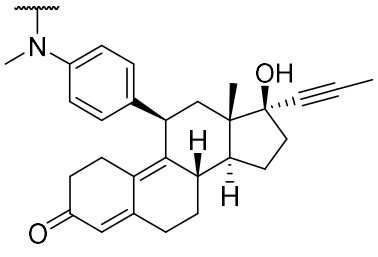
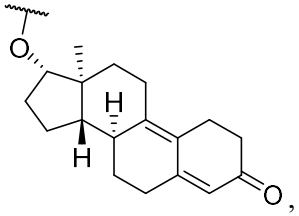
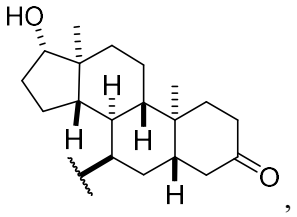
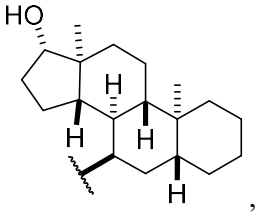
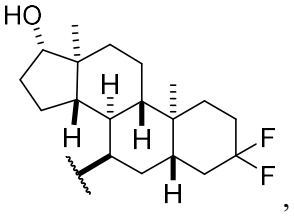
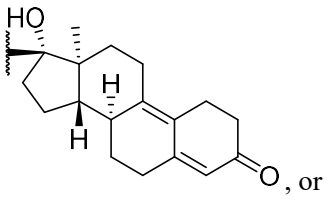
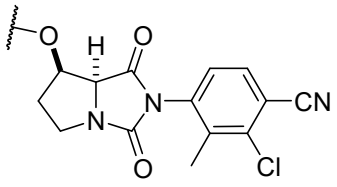
 ,  ,  ,

 ,  ,

 ,  ,

 ,  ,  ,


,

,

,

,

,

,

,

,

,

,

,

,

,

,

,

,

,

where the wavy line indicates the point of attachment.

32. A compound as provided in Table 1A or Table 1B, or a stereoisomer, mixture of stereoisomers, hydrate, solvate, isotopically enriched analog or pharmaceutically acceptable salt thereof.

33. A pharmaceutical composition comprising a compound as in any preceding claim, or a stereoisomer, mixture of stereoisomers, hydrate, solvate, isotopically enriched analog or pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable excipient.

34. Use of the pharmaceutical composition of claim 33 in the preparation of a medicament for the treatment or prevention of a condition which can be ameliorated by inhibition of PARP.

35. Use of the pharmaceutical composition of claim 33 in the preparation of a medicament for treating or preventing cancer.

36. The use of claim 35, wherein the medicament is an oral medicament.

37. The use of claim 35, wherein the medicament is for administration with an additional chemotherapeutic agent.

38. The use of claim 37, wherein the additional chemotherapeutic agent is cisplatin or etoposide, irinotecan, camptostar, topotecan, paclitaxel, docetaxel, epothilones, taxotere, tamoxifen, 5-fluorouracil, methoxtrexate, temozolomide, cyclophosphamide, SCH 66336, R115777, L778123, BMS 214662, gefitinib, erlotinib hydrochloride, antibodies to EGFR, matinib, intron, cytarabine, adriamycin, cytoxan, gemcitabine, uracil mustard, chlormethine, ifosfamide, melphalan, chlorambucil, pipobroman,

triethylenemelamine, triethylenethiophosphoramine, busulfan, carmustine, lomustine, streptozocin, dacarbazine, floxuridine, cytarabine, 6-mercaptopurine, 6-thioguanine, fludarabine phosphate, pentostatine, vinblastine, vincristine, vindesine, bleomycin, doxorubicin, dactinomycin, daunorubicin, epirubicin, idarubicin, mithramycin, deoxycoformycin, mitomycin-C, L-asparaginase, teniposide, 17α-ethinylestradiol, diethylstilbestrol, testosterone, prednisone, fluoxymesterone, drostanolone propionate, testolactone, megestrolacetate, methylprednisolone, methyltestosterone, prednisolone, triamcinolone, chlorotrianisene, hydroxyprogesterone, aminoglutethimide, estramustine, medroxyprogesterone acetate, leuprolide, flutamide, toremifene, goserelin, carboplatin, hydroxyurea, amsacrine, procarbazine, mitotane, mitoxantrone, levamisole, navelbene, anastrazole, letrazole, capecitabine, droloxifenehexamethylmelamine, avastin, herceptin, bexxar, velcade, zevalin, trisenox, xeloda, vinorelbine, porfimer, cetuximab, liposomal, Thiotepa, Altretamine, melphalan, Trastuzumab, lertozole, fulvestrant, exemestane, ifosfomide, rituximab, C225, Campath, carboplatin, procarbazine, mechlorethamine, cyclophosphamide, camptothecin, ifosfamide, melphalan, chlorambucil, busulfan, nitrosurea, dactinomycin, daunorubicin, doxorubicin, bleomycin, plicomycin, mitomycin, etoposide (VP 16), raloxifene, estrogen receptor binding agents, paclitaxel, gemcitabine, navelbine, farnesyl-protein transferase inhibitors, transplatinum, 5-fluorouracil, vincristine, vinblastine and methotrexate, or an analog or derivative thereof.

39. The use of any one of claims 34-38, further comprising radiotherapy.

40. The use of any one of claims 34-38, wherein the cancer is a BRCA positive cancer.

41. The use of any one of claims 34-38, wherein the cancer is a solid tumor.

42. The use of any one of claims 34-38, wherein the cancer is a cancer affecting B cells.

43. The use of any one of claims 34-38, wherein the cancer is a blood cancer, lung cancer, breast cancer, fallopian tube cancer, brain cancer, head and neck cancer, esophageal cancer, ovarian cancer, pancreatic cancer, peritoneal cancer, prostate cancer or skin cancer.

44. The ues of claim 43, wherein the cancer is liver cancer, melanoma, Hodgkin's disease, non-Hodgkin's lymphomas, acute lymphocytic leukemia, chronic lymphocytic leukemia, multiple myeloma, neuroblastoma, breast carcinoma, ovarian carcinoma, lung carcinoma, Wilms' tumor, cervical carcinoma, testicular carcinoma, soft-tissue sarcoma, chronic lymphocytic leukemia, primary macroglobulinemia, bladder carcinoma, chronic granulocytic leukemia, primary brain carcinoma, malignant melanoma, small-cell lung carcinoma, stomach carcinoma, colon carcinoma, malignant pancreatic insulinoma, malignant carcinoid carcinoma, malignant melanoma, choriocarcinoma, mycosis fungoides, head neck carcinoma, osteogenic sarcoma, pancreatic carcinoma, acute granulocytic leukemia, hairy cell leukemia,

rhabdomyosarcoma, Kaposi's sarcoma, genitourinary carcinoma, thyroid carcinoma, esophageal carcinoma, malignant hypercalcemia, cervical hyperplasia, renal cell carcinoma, endometrial carcinoma, polycythemia vera, essential thrombocytosis, adrenal cortex carcinoma, skin cancer, or prostatic carcinoma.

45. The use of claim 44, wherein the cancer is bladder cancer, breast cancer, fallopian tube cancer, ovarian cancer, prostate cancer, peritoneal cancer, testicular cancer, endometrial cancer, or uterine cancer.

46. Use of the pharmaceutical composition of claim 33 in the preparation of a medicament for treating or preventing an androgen receptor overexpressing cancer.

47. The use of claim 46, wherein the cancer is prostate, breast, triple negative breast cancer, bladder, or liver cancer.

48. The use of claim 46, wherein the androgen receptor-targeting epitope comprises an androgen receptor agonist, a selective androgen-receptor modulator (SARM), an androgen receptor antagonist, a selective estrogen receptor modulator (SERM), an estrogen receptor antagonist, a progestin, or an estrogen.

49. Use of the pharmaceutical composition of claim 33 in the preparation of a medicament for treating or preventing an estrogen and/or progesterone receptor overexpressing cancer.

50. The use of claim 49, wherein the cancer is breast, uterine, or ovarian cancer.

51. A method of treating or preventing a glucocorticoid receptor overexpressing cancer, comprising administering an effective amount of the pharmaceutical composition claim 33 to an individual in need thereof.

52. The method of claim 51, wherein the cancer is prostate, breast, uterine, or ovarian cancer.