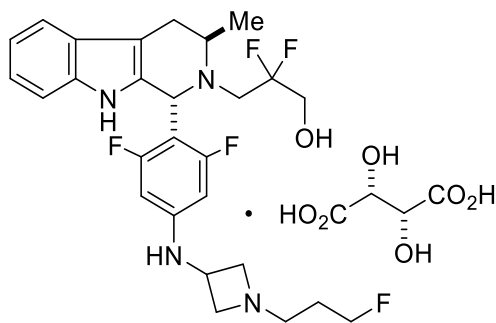


[0011] Provided herein is a compound, Compound B, having the name 3-((1R,3R)-1-(2,6-difluoro-4-((1-(3-fluoropropyl)azetidin-3-yl)amino)phenyl)-3-methyl-1,3,4,9-tetrahydro-2H-pyrido[3,4-b]indol-2-yl)-2,2-difluoropropan-1-ol tartrate, as described herein.

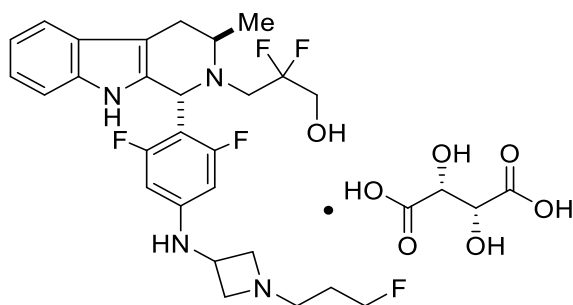
[0011a] In one aspect, provided herein is a compound having the structure:



B.

[0012] Provided herein is a crystal form of Compound B having an X-ray powder diffraction pattern comprising peaks at 19.32, 20.26, 21.63, 23.28, or 24.81 $\pm 0.1^\circ 2\theta$ ($\pm 0.1^\circ 2\theta$).

[0012a] In another aspect, provided herein is a crystal form comprising Compound B

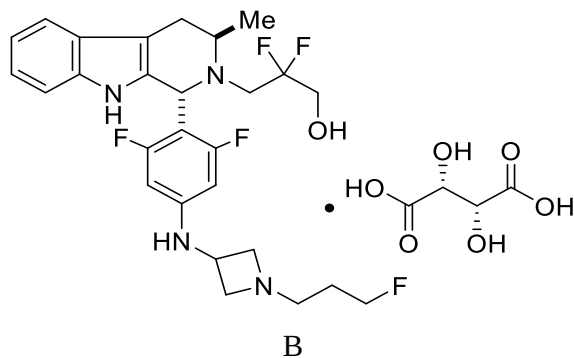


B

having an X-ray powder diffraction pattern comprising peaks at 19.32, 20.26, 21.63, 23.28, or 24.81 $\pm 0.1^\circ 2\theta$ ($\pm 0.1^\circ 2\theta$).

[0013] Provided herein is a crystal form of Compound B having an X-ray powder diffraction pattern comprising peaks at 11.49, 12.54, 19.16, 19.42, or $24.67 \pm 0.1^\circ 2\theta$ ($\pm 0.1^\circ 2\theta$).

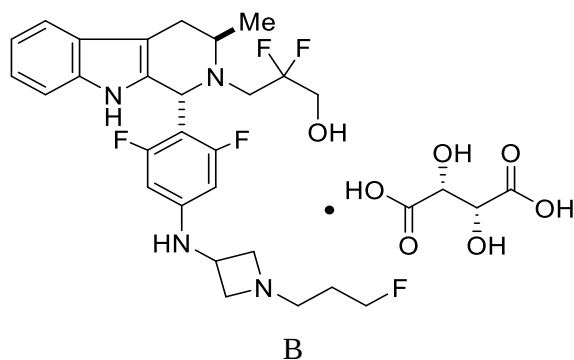
[0013a] In another aspect, provided herein is a crystal form comprising Compound B



having an X-ray powder diffraction pattern comprising peaks at 11.49, 12.54, 19.16, 19.42, or $24.67 \pm 0.1^\circ 2\theta$ ($\pm 0.1^\circ 2\theta$).

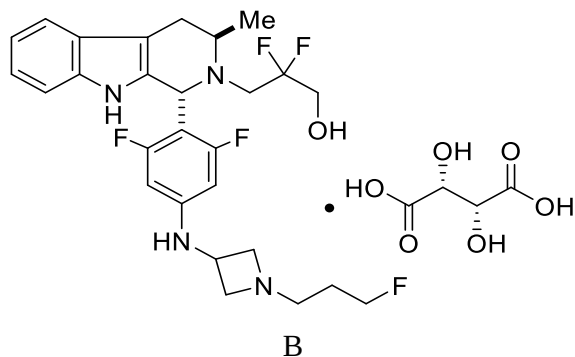
[0014] Provided herein is a crystal form of Compound B having an X-ray powder diffraction pattern substantially as shown in FIG. 10 or FIG. 14.

[0014a] In another aspect, provided herein is a crystal form comprising Compound B



having an X-ray powder diffraction pattern substantially as shown in FIG. 10.

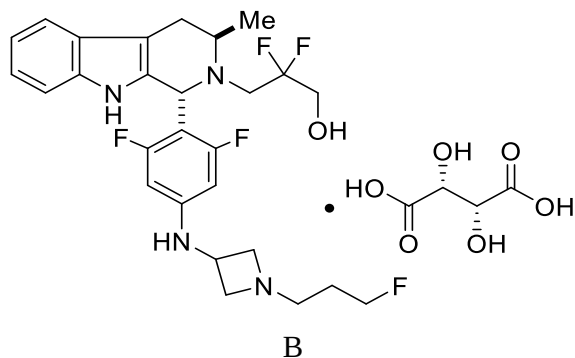
[0014b] In another aspect, provided herein is a crystal form comprising Compound B



having an X-ray powder diffraction pattern substantially as shown in FIG. 14.

[0015] Provided herein is a crystal form of Compound B having an X-ray powder diffraction pattern comprising peaks at 11.31, 15.70, 16.54, 19.10, or $22.76 \pm 0.1^\circ 2\theta$.

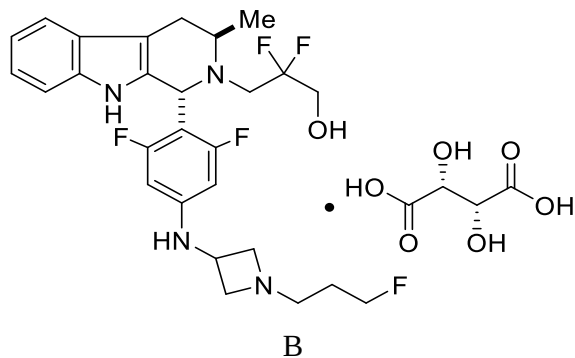
[0015a] In another aspect, provided herein is a crystal form comprising Compound B



having an X-ray powder diffraction pattern comprising peaks at 11.31, 15.70, 16.54, 19.10, or $22.76 \pm 0.1^\circ 2\theta$.

[0016] Provided herein is a crystal form of Compound B having an X-ray powder diffraction pattern comprising peaks at 12.52, 15.90, 19.66, 20.65, or $24.99 \pm 0.1^\circ 2\theta$.

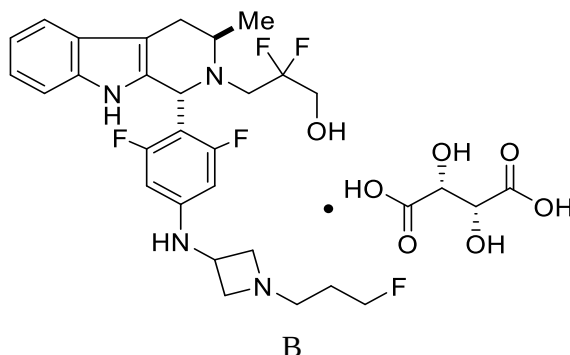
[0016a] In another aspect, provided herein is a crystal form comprising Compound B



having an X-ray powder diffraction pattern comprising peaks at 12.52, 15.90, 19.66, 20.65, or 24.99 $\pm 0.1^\circ 2\theta$.

[0017] Provided herein is a crystal form of Compound B having an X-ray powder diffraction pattern comprising peaks at 11.46, 12.51, 19.29, 19.42, or 20.23 $\pm 0.1^\circ 2\theta$.

[0017a] In another aspect, provided herein is a crystal form comprising Compound B



having an X-ray powder diffraction pattern comprising peaks at 11.46, 12.51, 19.29, 19.42, or 20.23 $\pm 0.1^\circ 2\theta$.

[0018] Provided herein is an amorphous solid comprising Compound A.

[0019] Further provided herein are pharmaceutical compositions comprising Compound B or a crystal salt thereof. Such compounds and pharmaceutical compositions can be used in methods of treating cancer as set forth herein.

[0019a] In another aspect, provided herein is a pharmaceutical composition comprising the solid form as described herein and at least one pharmaceutically acceptable excipient.

[0019b] In another aspect, provided herein is a compound as described herein or the pharmaceutical composition as described herein for use in therapy.

[0019c] In another aspect, provided herein is a use of a compound as described herein or the pharmaceutical composition as described herein in the manufacture of a medicament for treating lung cancer, ovarian cancer, endometrial cancer, prostate cancer, uterine cancer, or breast cancer in a patient having said cancer.

[0019d] In another aspect, provided herein is a use of a compound as described herein or the pharmaceutical composition as described herein in the manufacture of a medicament for treating breast cancer in a breast cancer patient.

[0020] Provided herein is a process for preparing a compound of formula (IV) or a salt thereof as set forth herein. The process comprises (1) reacting a reaction mixture comprising a compound of formula (I) as described herein, an organic solvent and thionyl chloride to form a compound of formula (IIa) as described herein and (2) reacting a reaction mixture comprising the compound of formula (IIa), a catalyst, an oxidant and a solvent to form a compound of formula (II) as described herein. The process further comprises reacting a reaction mixture comprising the compound of formula (II) and a compound of formula (III) as described herein in an organic solvent to form a compound of formula (IV) or a salt thereof as described herein.

[0021] Provided herein is a process for preparing a compound of formula (VIII) or a pharmaceutically acceptable salt thereof as described herein. The process comprises

reacting a reaction mixture comprising a compound of formula (IV) as described herein, a compound of formula (V) as described herein or a compound of formula (X) as described herein, and an organic solvent to form a compound of formula (VI) as described herein. The process further comprises reacting a reaction mixture comprising the compound of formula (VI), an organic solvent, and a compound of formula (VII) as described herein or a salt thereof to form a compound of formula (VIII) or a salt thereof.

[0022] Provided herein is a process for preparing a compound of formula (VIII) or a pharmaceutically acceptable salt thereof as described herein. The process comprises reacting a reaction mixture comprising a compound of formula (IX) as described herein or a compound of formula (X) as described herein, a compound of formula (IV) as described herein and an organic solvent to form the compound of formula (VIII) or a salt thereof as described herein.

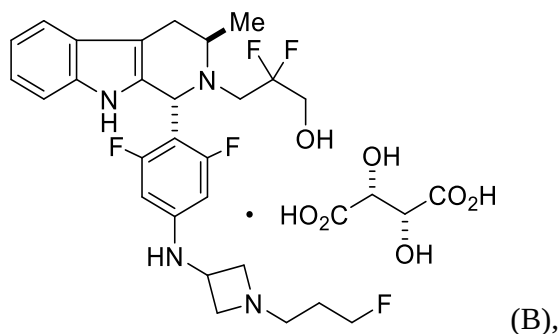
[0023] Provided herein is a process for preparing a compound of formula (IX) or a salt thereof as described herein. The process comprises reacting a reaction mixture comprising a compound of formula (X) as described herein, a compound of formula (VII), or a salt thereof, as described herein an organic solvent and a catalyst to form a compound of formula (XI) or a salt thereof as described herein.

[0024] Provided herein is a process for preparing a compound of formula (III) or a salt thereof as described herein. The process comprises reacting a reaction mixture comprising a compound of formula (XII) as described herein, a compound B and an organic solvent to form the compound of formula (XIII) as described herein.

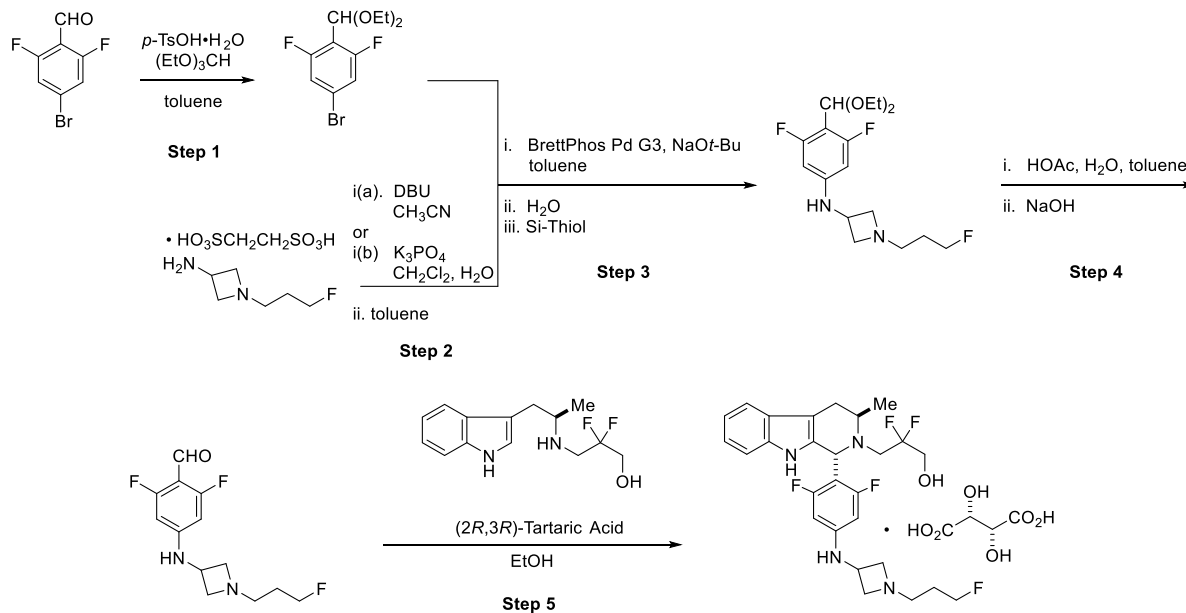
[0025] Provided herein is a compound of formula (XVI) as described herein.

[0026] Still further provided herein is a process for preparing a compound having formula (XX) is provided, where the process comprises contacting a compound of formula (XXI) as described herein with a protein transaminase to form a compound of formula (3). The compound of formula (3) is contacted with a compound of formula (II) as described herein to form compound formula (XX).

[0026a] In another aspect, provided herein is a process for the preparation of Compound B,



wherein the process comprises the steps of:



[0026b] In another aspect, provided herein is a process for the preparation of Compound B,



Step 1

i. AcOH, PhMe
ii. Charcoal
iii. Heptane

Step 2

i. $\text{HO}_3\text{SCH}_2\text{CH}_2\text{SO}_3\text{H}$
H₂N-aziridine-CH₂CH₂F
ii. Pd-175, DBU, MeCN
iii. MTBE
iv. SiliaMetS Thiol
v. EtOH

Step 3

(2*R*,3*R*)-Tartaric Acid
EtOH

Step 4

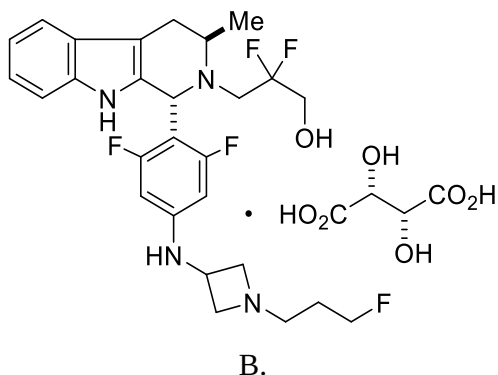
i. MTBE
ii. NaOH
iii. EtOH
iv. (2*R*,3*R*)-Tartaric Acid

BRIEF DESCRIPTION OF THE FIGURES

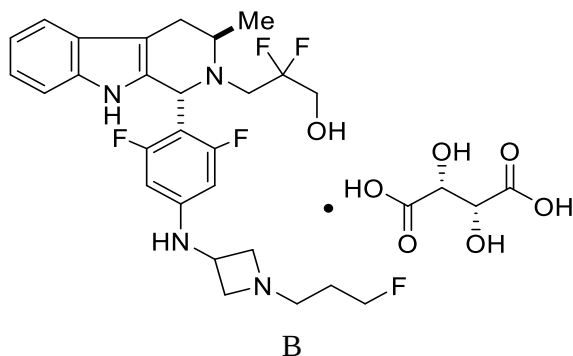
-4b-

What is claimed is:

1. A compound having the structure:



2. A crystal form comprising Compound B



having an X-ray powder diffraction pattern comprising peaks at 19.32, 20.26, 21.63, 23.28, or $24.81 \pm 0.1^\circ 2\theta$ ($\pm 0.1^\circ 2\theta$).

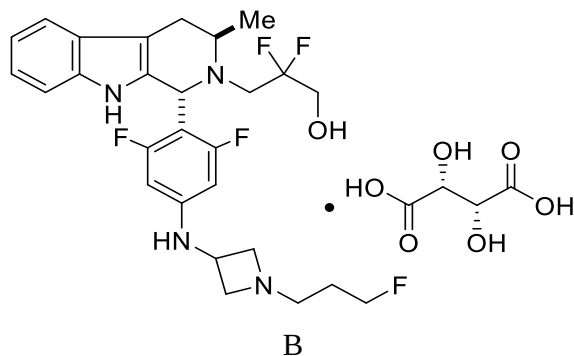
3. The crystal form of claim 2, wherein the crystal form of Compound B has an X-ray powder diffraction pattern one, two, three, four, five, six, seven, eight, nine, ten, eleven, twelve, thirteen, fourteen, fifteen, sixteen, seventeen, eighteen, nineteen, or twenty, characteristic X-ray powder diffraction peaks as set forth in Table 16.

4. The crystal form of claim 2, wherein the crystal form of Compound B has an X-ray powder diffraction pattern substantially as shown in FIG. 1.

5. The crystal form of any one of claims 2-4, wherein the crystal form of Compound B has a TGA thermograph corresponding substantially to the representative TGA thermogram as depicted in FIG. 2A.

6. The crystal form of any one of claims 2-5, wherein the crystal form of Compound B has a DSC thermogram substantially as depicted in FIG. 2B.

7. A crystal form comprising Compound B



having an X-ray powder diffraction pattern comprising peaks at 11.49, 12.54, 19.16, 19.42, or $24.67 \pm 0.1^\circ 2\theta$ ($\pm 0.1^\circ 2\theta$).

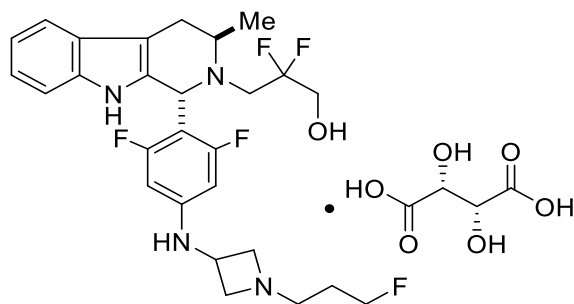
8. The crystal form of claim 7, wherein the crystal form of Compound B has an X-ray powder diffraction pattern one, two, three, four, five, six, seven, eight, nine, ten, eleven, twelve, thirteen, fourteen, fifteen, sixteen, seventeen, eighteen, nineteen, or twenty, characteristic X-ray powder diffraction peaks as set forth in Table 11.

9. The crystal form of claim 7, wherein the crystal form of Compound A has an X-ray powder diffraction pattern substantially as shown in FIG. 4.

10. The crystal form of any one of claims 7-9, wherein the crystal form of Compound A has a TGA thermograph corresponding substantially to the representative TGA thermogram as depicted in FIG. 5.

11. The crystal form of any one of claims 7-10, wherein the crystal form of Compound A has a DSC thermogram substantially as depicted in FIG. 5.

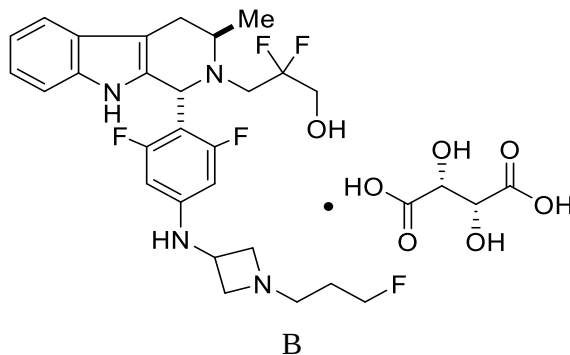
12. A crystal form comprising Compound B



B

having an X-ray powder diffraction pattern substantially as shown in FIG. 10.

13. A crystal form comprising Compound B



B

having an X-ray powder diffraction pattern comprising peaks at 11.31, 15.70, 16.54, 19.10, or $22.76 \pm 0.1^\circ 2\theta$.

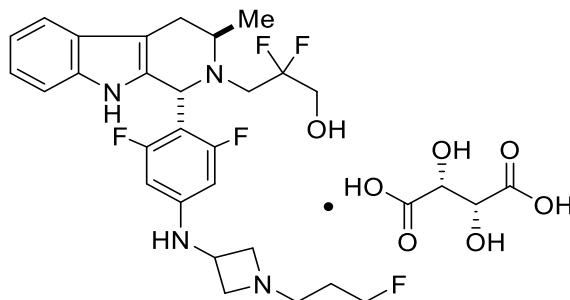
14. The crystal form of claim 13, wherein the crystal form of Compound B has an X-ray powder diffraction pattern one, two, three, four, five, six, seven, eight, nine, ten, eleven, twelve, thirteen, fourteen, fifteen, sixteen, seventeen, eighteen, nineteen, or twenty, characteristic X-ray powder diffraction peaks as set forth in Table 13.

15. The crystal form of claim 13, wherein the crystal form of Compound B has an X-ray powder diffraction pattern substantially as shown in FIG. 12.

16. The crystal form of any one of claims 13-15, wherein the crystal form of Compound B has a TGA thermograph corresponding substantially to the representative TGA thermogram as depicted in FIG. 13.

17. The crystal form of any one of claims 13-16, wherein the crystal form of Compound B has a DSC thermogram substantially as depicted in FIG. 13.

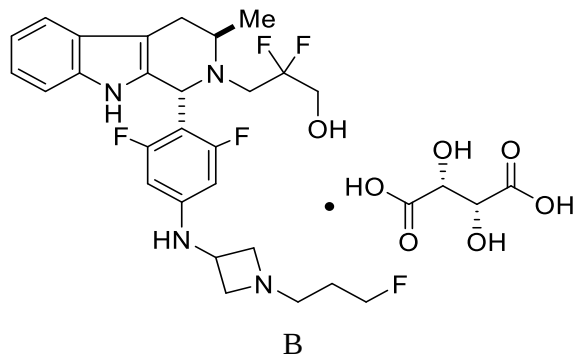
18. A crystal form comprising Compound B



B

having an X-ray powder diffraction pattern substantially as shown in FIG. 14.

19. A crystal form comprising Compound B



B

having an X-ray powder diffraction pattern comprising peaks at 12.52, 15.90, 19.66, 20.65, or $24.99 \pm 0.1^\circ 2\theta$.

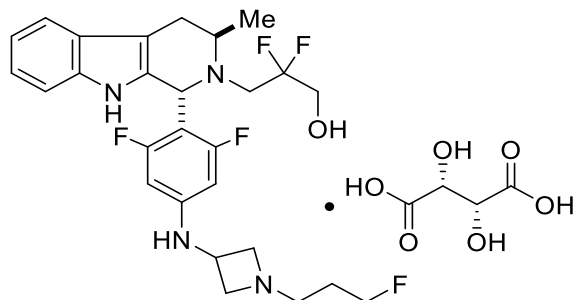
20. The crystal form of claim 19, wherein the crystal form of Compound B has an X-ray powder diffraction pattern one, two, three, four, five, six, seven, eight, nine, ten, eleven, twelve, thirteen, fourteen, fifteen, sixteen, seventeen, eighteen, nineteen, or twenty, characteristic X-ray powder diffraction peaks as set forth in Table 14.

21. The crystal form of claim 19, wherein the crystal form of Compound B has an X-ray powder diffraction pattern substantially as shown in FIG. 16.

22. The crystal form of any one of claims 19-21, wherein the crystal form of Compound B has a TGA thermograph corresponding substantially to the representative TGA thermogram as depicted in FIG. 17.

23. The crystal form of any one of claims 19-22, wherein the crystal form of Compound B has a DSC thermogram substantially as depicted in FIG. 18.

24. A crystal form comprising Compound B



B

having an X-ray powder diffraction pattern comprising peaks at 11.46, 12.51, 19.29, 19.42, or $20.23 \pm 0.1^\circ 2\theta$.

25. The crystal form of claim 24, wherein the crystal form of Compound B has an X-ray powder diffraction pattern one, two, three, four, five, six, seven, eight, nine, ten, eleven, twelve, thirteen, fourteen, fifteen, sixteen, seventeen, eighteen, nineteen, or twenty, characteristic X-ray powder diffraction peaks as set forth in Table 15.

26. The crystal form of any one of claims 24-25, wherein the crystal form of Compound B has an X-ray powder diffraction pattern substantially as shown in FIG. 19.

27. The crystal form of any one of claims 24-26, wherein the crystal form of Compound A has a TGA thermograph corresponding substantially to the representative TGA thermogram as depicted in FIG. 20.

28. A pharmaceutical composition comprising the solid form of any one of claims 1 to 27 and at least one pharmaceutically acceptable excipient.

29. A compound of any one of claims 1 to 27 or the pharmaceutical composition of claim 28 for use in therapy.

30. Use of a compound of any one of claims 1 to 27 or the pharmaceutical composition of claim 28 in the manufacture of a medicament for treating lung cancer, ovarian cancer, endometrial cancer, prostate cancer, uterine cancer, or breast cancer in a patient having said cancer.

31. Use of a compound of any one of claims 1 to 27 or the pharmaceutical composition of claim 28 in the manufacture of a medicament for treating breast cancer in a breast cancer patient.

32. The use of claim 31, wherein said breast cancer is hormone receptor positive breast cancer, HER2-positive breast cancer or triple negative breast cancer.

33. The use of claim 31, wherein the breast cancer is metastatic breast cancer.

34. The use of any one of claims 31-33, wherein the compound or pharmaceutical composition is to be administered as a component of adjuvant therapy.

35. The use of any one of claims 31-33, wherein the compound or pharmaceutical composition is to be administered as a component of neoadjuvant therapy.

36. The use of any one of claims 31-35, wherein the breast cancer is stage 0, I, II, III, or IV.
37. The use of claim 32, wherein the hormone receptor positive breast cancer is HER2 negative.
38. The use of any one of claims 31-37, wherein the patient has had previous treatment with one or more anti-cancer agents or radiation therapy.
39. The use of any one of claims 31-38, wherein the patient has had surgery prior to treatment with a compound of any one of claims 1 to 27.
40. The use of any one of claims 31-39, wherein the compound of any one of claims 1 to 27 is to be administered in combination with one or more of radiation therapy, hormone therapy, or an anti-cancer agent.
41. The use of claim 40, wherein anti-cancer agent comprises one or more of doxorubicin, pegylated liposomal doxorubicin, epirubicin, paclitaxel, albumin-bound paclitaxel, docetaxel, 5-fluorouracil, cyclophosphamide, cisplatin, carboplatin, vinorelbine, capecitabine, gemcitabine, ixabepilone, eribulin, olaparib, methotrexate, anastrozole, exemestane, toremifene, letrozole, tamoxifen, 4-hydroxy tamoxifen, raloxifene, droloxifene, trioxifene, keoxifene, ftutamide, nilutamide, bicalutamide, lapatinib, vinblastine, goserelin, leuprolide, pegfilgrastim, filgrastim, venetoclax.
42. The use of claim 40, wherein the anti-cancer agent comprises one or more of an AKT inhibitor, a CDK4/6 inhibitor, a PARP inhibitor, an aromatase inhibitor.
43. The use of claim 40, wherein the anti-cancer agent is abemaciclib, ribociclib, or palbociclib.
44. The use of claim 40, wherein the anti-cancer agent is ipatasertib.
45. The use of claim 40, wherein the anti-cancer agent is everolimus or fulvestrant.
46. The use of claim 40, wherein the anti-cancer agent is ado-trastuzumab emtansine, trastuzumab, pertuzumab, atezolizumab.
47. The use of claim 40, wherein the anti-cancer agent is alemtuzumab, bevacizumab, cetuximab, panitumumab, rituximab, tositumomab, or a combination thereof.
48. A process for the preparation of Compound B,



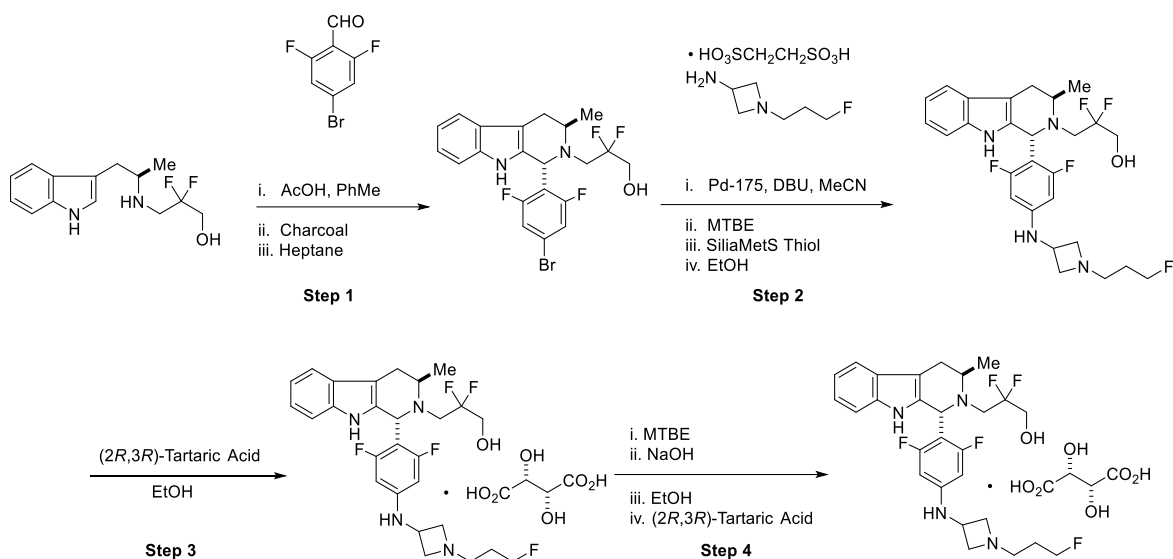
wherein the process comprises the steps of:



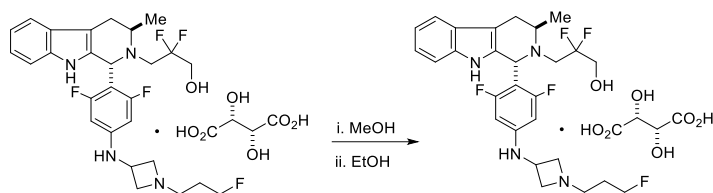
49. A process for the preparation of Compound B,



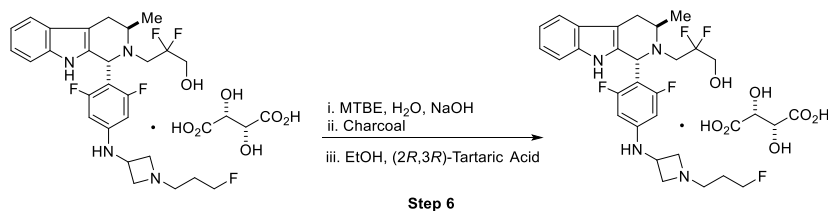
wherein the process comprises the steps of:



50. The process of claim 48 or 49, wherein the process further comprises recrystallization of Compound B in methanol and ethanol;



51. The process of claim 48 or 49, wherein the process further comprises recrystallization of Compound B in MTBE, water, NaOH and ethanol;



52. The process of any one of claims 48-51, wherein the indolyl intermediates are synthesized according to the steps:

