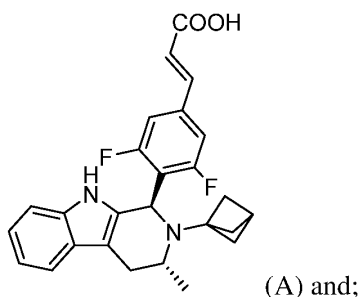


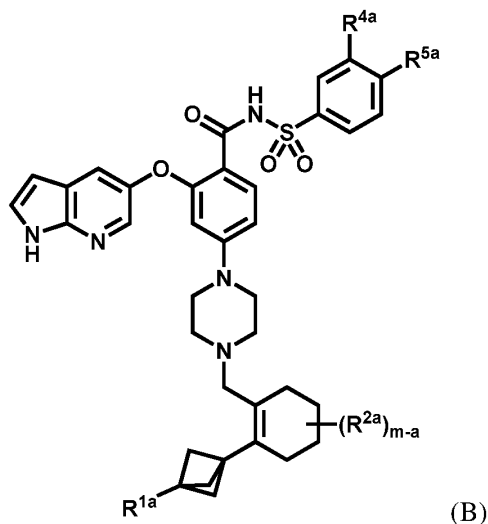
WHAT IS CLAIMED IS:

1. Use of a combination of compounds for treating a disease or condition, wherein the combination includes an effective amount of Compound (A), or a pharmaceutically acceptable salt thereof, and an effective amount of one or more of Compound (B), or a pharmaceutically acceptable salt thereof, wherein:

the Compound (A) has the structure:



the one or more of Compound (B) has the structure:



wherein:

R^{1a} is selected from the group consisting of hydrogen, halogen, a substituted or unsubstituted C_1 - C_6 alkyl, a substituted or unsubstituted C_1 - C_6 haloalkyl, a substituted or unsubstituted C_3 - C_6 cycloalkyl, a substituted or unsubstituted C_1 - C_6 alkoxy, an unsubstituted mono- C_1 - C_6 alkylamine and an unsubstituted di- C_1 - C_6 alkylamine;

each R^{2a} is independently selected from the group consisting of halogen, a substituted or unsubstituted C_1 - C_6 alkyl, a substituted or unsubstituted C_1 - C_6 haloalkyl and a substituted or unsubstituted C_3 - C_6 cycloalkyl; or

when m-a is 2 or 3, each R^{2a} is independently selected from the group consisting of halogen, a substituted or unsubstituted C_1 - C_6 alkyl, a substituted or unsubstituted C_1 - C_6 haloalkyl and a substituted or unsubstituted C_3 - C_6 cycloalkyl, or two R^{2a} groups taken together with the atom(s) to which they are attached form a substituted or unsubstituted C_3 - C_6 cycloalkyl or a substituted or unsubstituted 3 to 6 membered heterocyclyl;

R^{4a} is selected from the group consisting of NO_2 , $S(O)R^{6a}$, SO_2R^{6a} , halogen, cyano and an unsubstituted C_1 - C_6 haloalkyl;

R^{5a} is $-X^{1a}-(Alk^{1a})_{n-a}-R^{7a}$;

Alk^{1a} is selected from an unsubstituted C_1 - C_4 alkylene and a C_1 - C_4 alkylene substituted with 1, 2 or 3 substituents independently selected from fluoro, chloro, an unsubstituted C_1 - C_3 alkyl and an unsubstituted C_1 - C_3 haloalkyl;

R^{6a} is selected from the group consisting of a substituted or unsubstituted C_1 - C_6 alkyl, a substituted or unsubstituted C_1 - C_6 haloalkyl and a substituted or unsubstituted C_3 - C_6 cycloalkyl;

R^{7a} is selected from a substituted or unsubstituted C_1 - C_6 alkoxy, a substituted or unsubstituted C_3 - C_{10} cycloalkyl, a substituted or unsubstituted 3 to 10 membered heterocyclyl, hydroxy, amino, a substituted or unsubstituted mono-substituted amine group, a substituted or unsubstituted di-substituted amine group, a substituted or unsubstituted N-carbamyl, a substituted or unsubstituted C-amido and a substituted or unsubstituted N-amido;

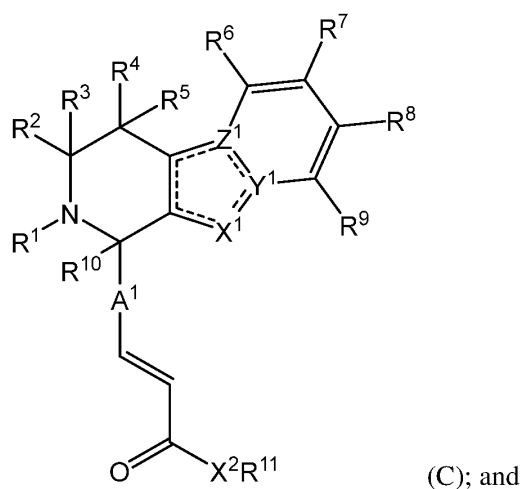
m-a is 0, 1, 2 or 3;

n-a is selected from the group consisting of 0 and 1; and

X^{1a} is selected from the group consisting of $-O-$, $-S-$ and $-NH-$.

2. Use of a combination of compounds for treating a disease or condition, wherein the combination includes an effective amount of Compound (C) and an effective amount of one or more of Compound (B), or a pharmaceutically acceptable salt thereof, wherein:

the Compound (C) has the structure:



wherein:

X^1 , Y^1 and Z^1 are each independently C or N;

with the first proviso that at least one of X^1 , Y^1 and Z^1 is N;

with the second proviso that each of X^1 , Y^1 and Z^1 is uncharged;

with third proviso that two of the dotted lines indicate double bonds;

with the fourth proviso that the valencies of X^1 , Y^1 and Z^1 can be each independently satisfied by attachment to a substituent selected from H and R^{12} ;

X^2 is O;

A^1 is selected from the group consisting of an optionally substituted cycloalkyl, an optionally substituted aryl, an optionally substituted heteroaryl and an optionally substituted heterocyclyl;

R^1 is selected from the group consisting of an optionally substituted C_{1-6} alkyl, an optionally substituted cycloalkyl, an optionally substituted cycloalkenyl, an optionally substituted aryl, an optionally substituted heteroaryl, an optionally substituted heterocyclyl, an optionally substituted cycloalkyl(C_{1-6} alkyl), an optionally substituted cycloalkenyl(C_{1-6} alkyl), an optionally substituted aryl(C_{1-6} alkyl), an optionally substituted heteroaryl(C_{1-6} alkyl) and an optionally substituted heterocyclyl(C_{1-6} alkyl);

R^2 and R^3 are each independently selected from the group consisting of hydrogen, halogen, an optionally substituted C_{1-6} alkyl and an optionally substituted C_{1-6} haloalkyl; or R^2

and R³ together with the carbon to which R² and R³ are attached form an optionally substituted cycloalkyl, an optionally substituted cycloalkenyl or an optionally substituted heterocyclyl;

R⁴ and R⁵ are each independently selected from the group consisting of hydrogen, halogen, an optionally substituted C₁₋₆ alkyl and an optionally substituted C₁₋₆ haloalkyl; or R⁴ and R⁵ together with the carbon to which R⁴ and R⁵ are attached form an optionally substituted cycloalkyl, an optionally substituted cycloalkenyl or an optionally substituted heterocyclyl;

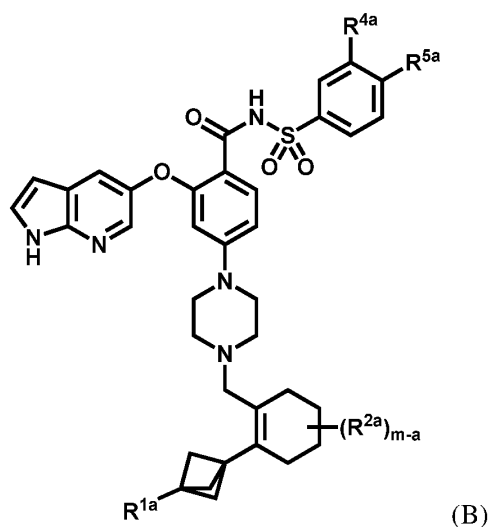
R⁶, R⁷, R⁸ and R⁹ are each independently selected from the group consisting of hydrogen, halogen, hydroxy, an optionally substituted alkyl, an optionally substituted alkoxy, an optionally substituted haloalkyl, an optionally substituted mono-substituted amine, and an optionally substituted di-substituted amine;

R¹⁰ is hydrogen, halogen, an optionally substituted alkyl, or an optionally substituted cycloalkyl;

R¹¹ is hydrogen; and

R¹² is hydrogen, halogen, an optionally substituted C₁₋₃ alkyl, an optionally substituted C₁₋₃ haloalkyl or an optionally substituted C₁₋₃ alkoxy; and

the one or more of Compound (B) has the structure



wherein:

R^{1a} is selected from the group consisting of hydrogen, halogen, a substituted or unsubstituted C_{1-C6} alkyl, a substituted or unsubstituted C_{1-C6} haloalkyl, a substituted or

unsubstituted C₃-C₆ cycloalkyl, a substituted or unsubstituted C₁-C₆ alkoxy, an unsubstituted mono-C₁-C₆ alkylamine and an unsubstituted di-C₁-C₆ alkylamine;

each R^{2a} is independently selected from the group consisting of halogen, a substituted or unsubstituted C₁-C₆ alkyl, a substituted or unsubstituted C₁-C₆ haloalkyl and a substituted or unsubstituted C₃-C₆ cycloalkyl; or

when m-a is 2 or 3, each R^{2a} is independently selected from the group consisting of halogen, a substituted or unsubstituted C₁-C₆ alkyl, a substituted or unsubstituted C₁-C₆ haloalkyl and a substituted or unsubstituted C₃-C₆ cycloalkyl, or two R^{2a} groups taken together with the atom(s) to which they are attached form a substituted or unsubstituted C₃-C₆ cycloalkyl or a substituted or unsubstituted 3 to 6 membered heterocyclyl;

R^{4a} is selected from the group consisting of NO₂, S(O)R^{6a}, SO₂R^{6a}, halogen, cyano and an unsubstituted C₁-C₆ haloalkyl;

R^{5a} is -X^{1a}-(Alk^{1a})_{n-a}-R^{7a};

Alk^{1a} is selected from an unsubstituted C₁-C₄ alkylene and a C₁-C₄ alkylene substituted with 1, 2 or 3 substituents independently selected from fluoro, chloro, an unsubstituted C₁-C₃ alkyl and an unsubstituted C₁-C₃ haloalkyl;

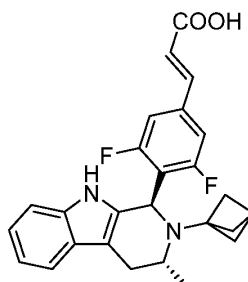
R^{6a} is selected from the group consisting of a substituted or unsubstituted C₁-C₆ alkyl, a substituted or unsubstituted C₁-C₆ haloalkyl and a substituted or unsubstituted C₃-C₆ cycloalkyl;

R^{7a} is selected from a substituted or unsubstituted C₁-C₆ alkoxy, a substituted or unsubstituted C₃-C₁₀ cycloalkyl, a substituted or unsubstituted 3 to 10 membered heterocyclyl, hydroxy, amino, a substituted or unsubstituted mono-substituted amine group, a substituted or unsubstituted di-substituted amine group, a substituted or unsubstituted N-carbamyl, a substituted or unsubstituted C-amido and a substituted or unsubstituted N-amido;

m-a is 0, 1, 2 or 3;

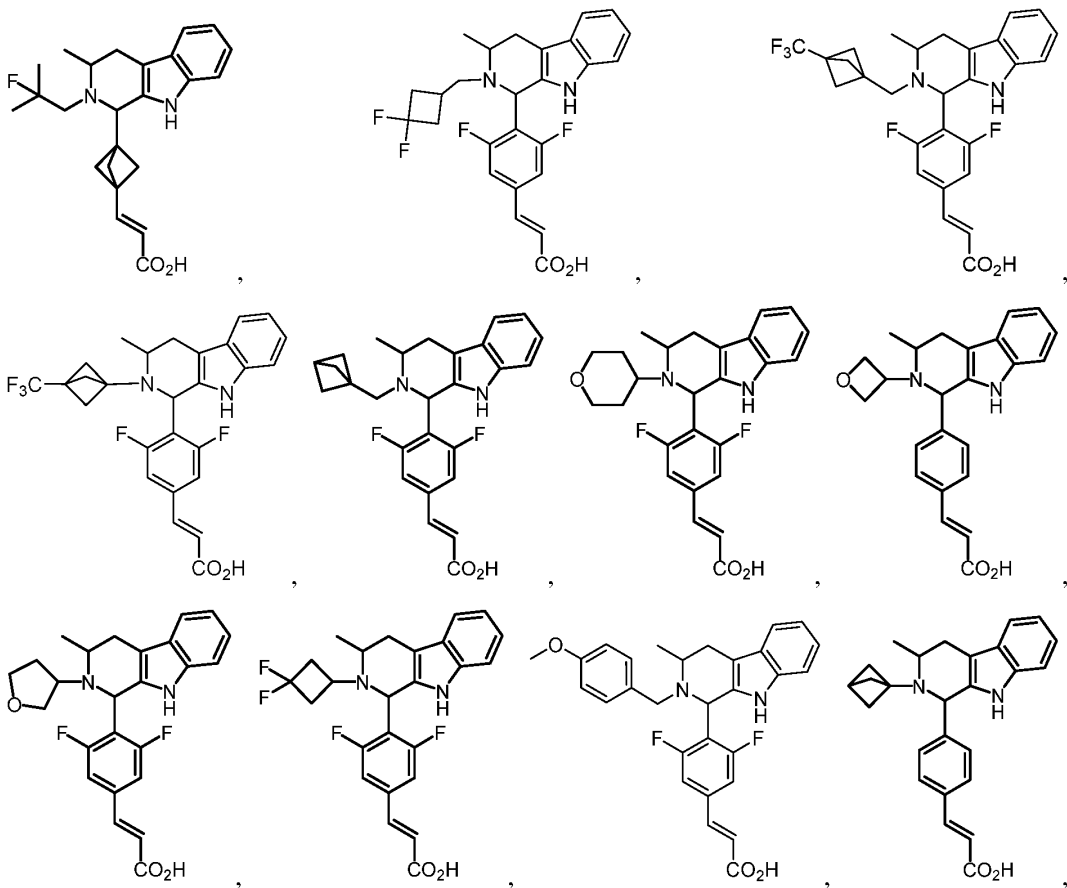
n-a is selected from the group consisting of 0 and 1;

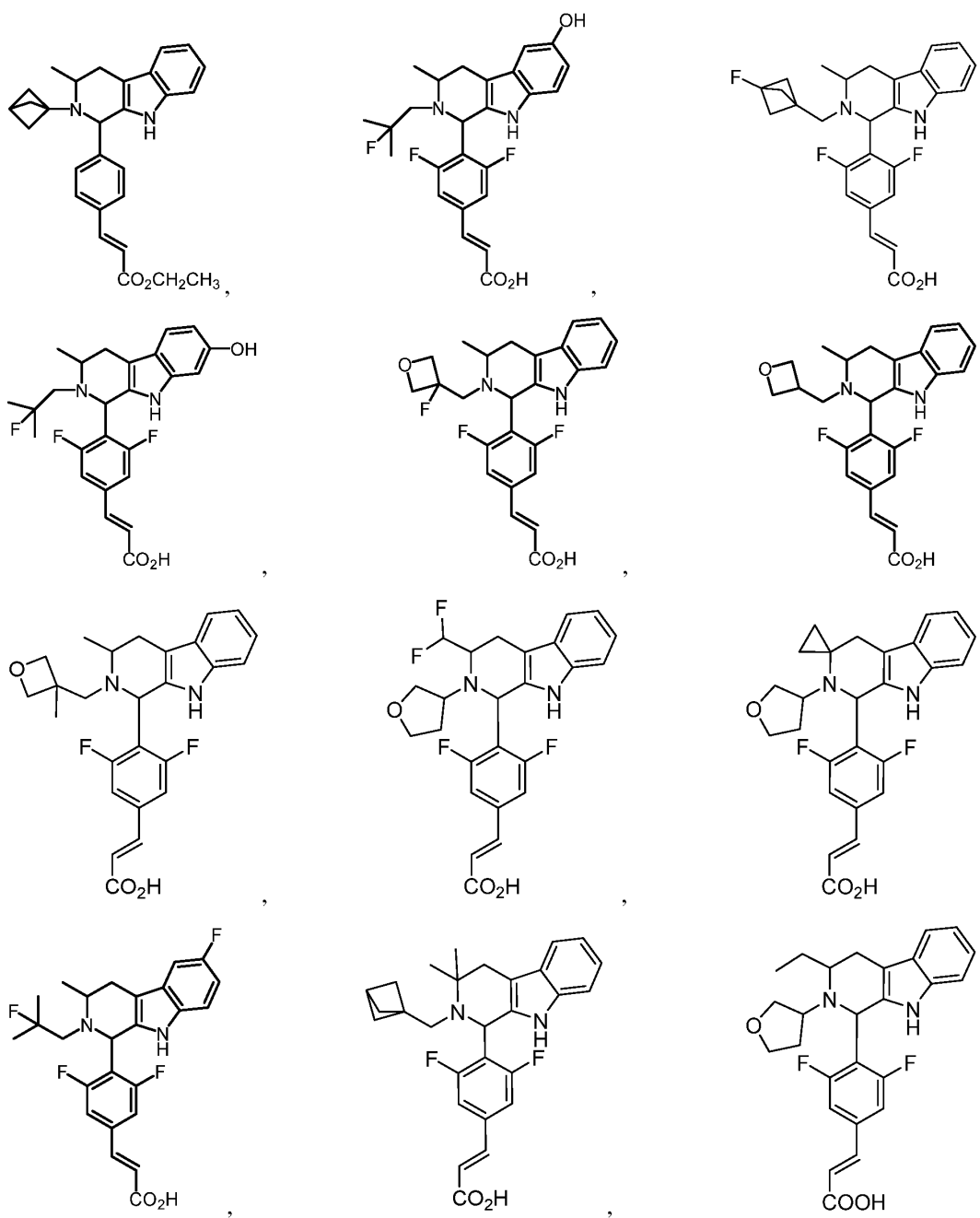
X^{1a} is selected from the group consisting of -O-, -S- and -NH-; and



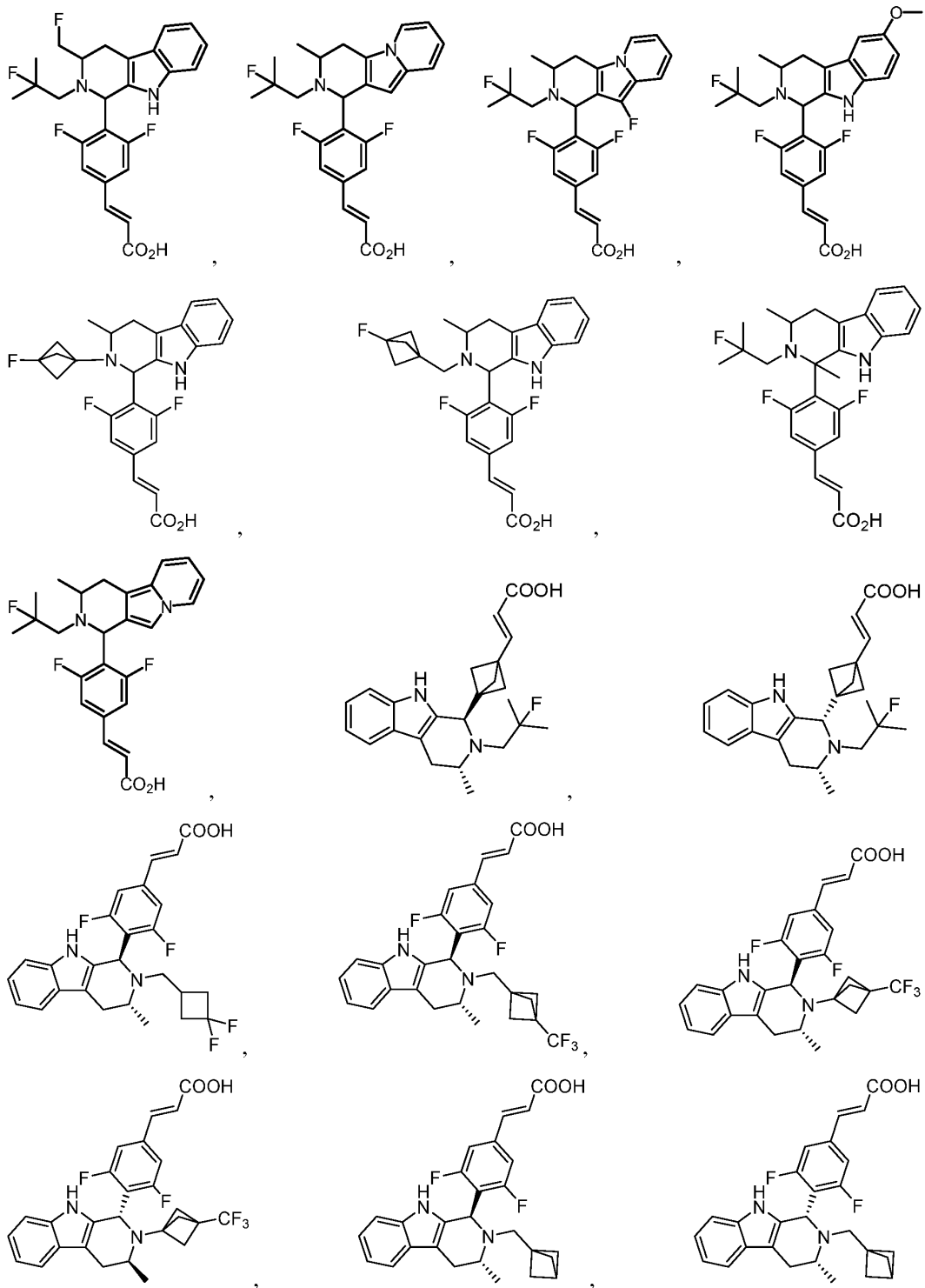
provided that the Compound (C) cannot be , or a pharmaceutically acceptable salt thereof.

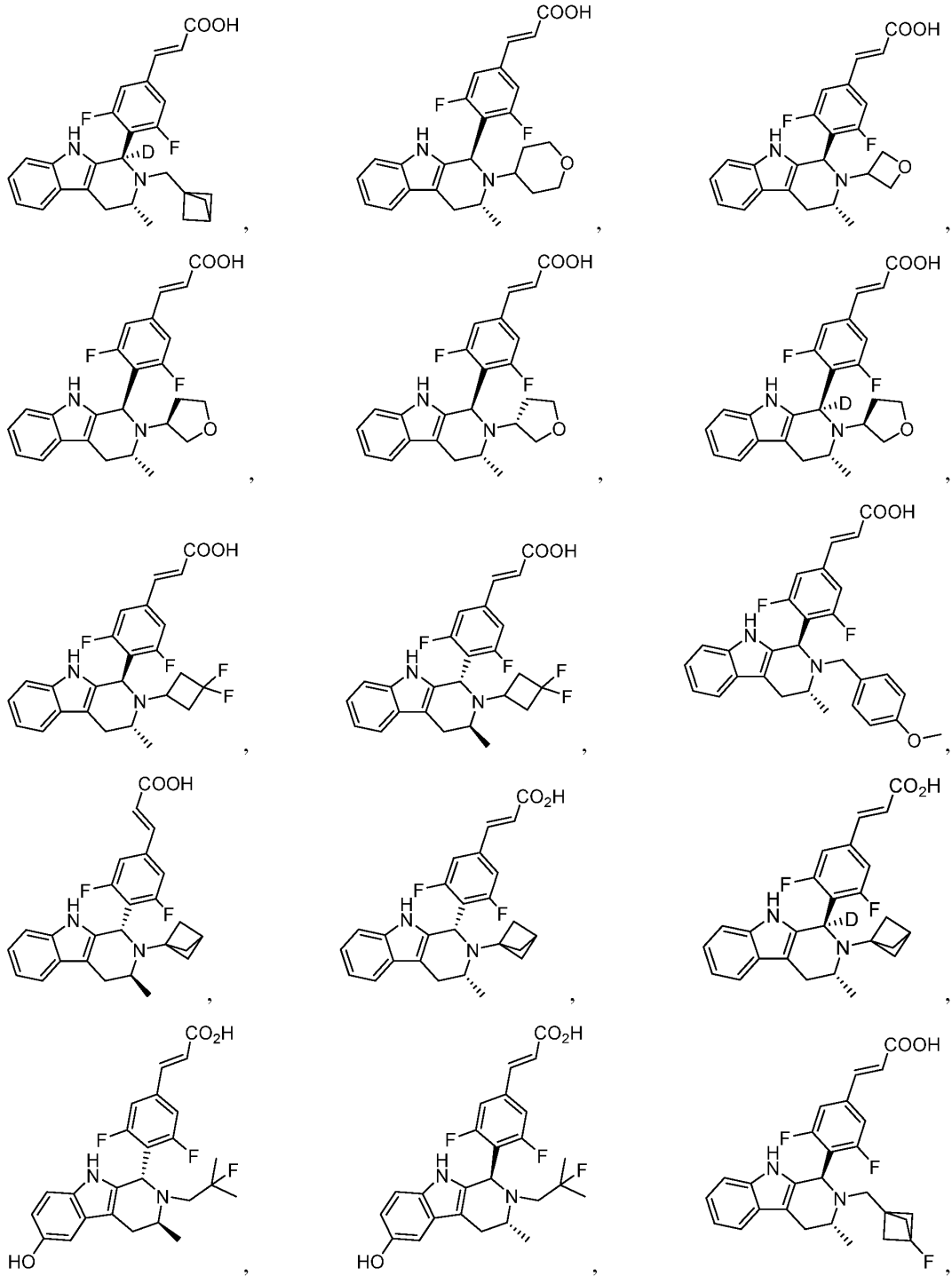
3. The use of Claim 1 or 2, wherein the Compound (C) is selected from the group consisting of:

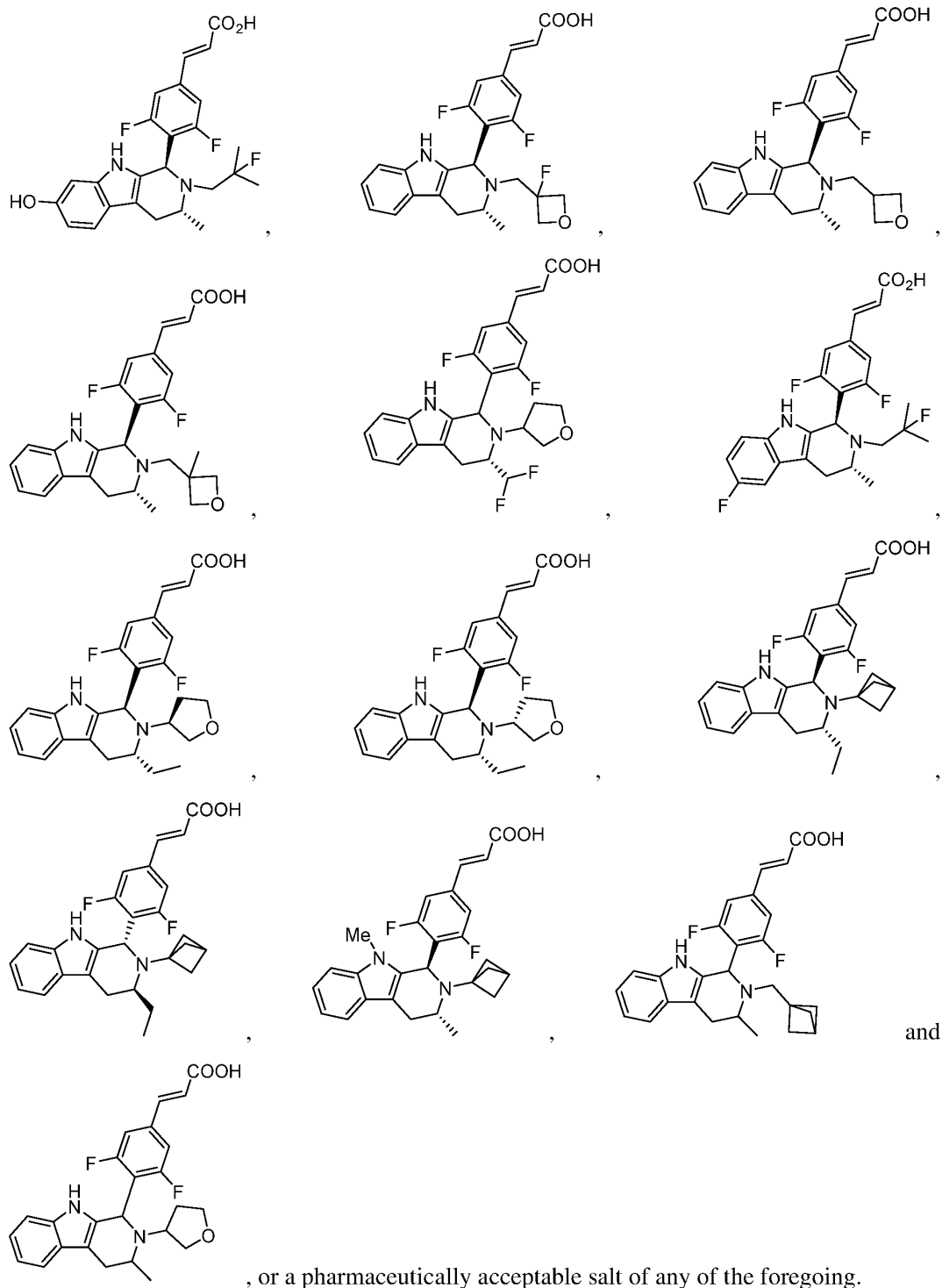




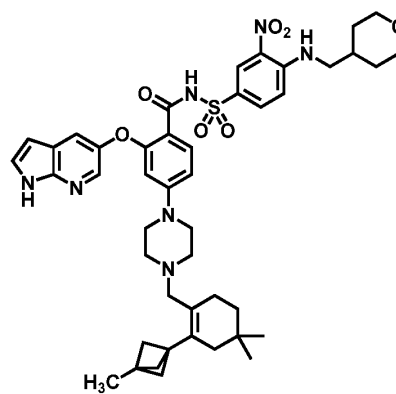
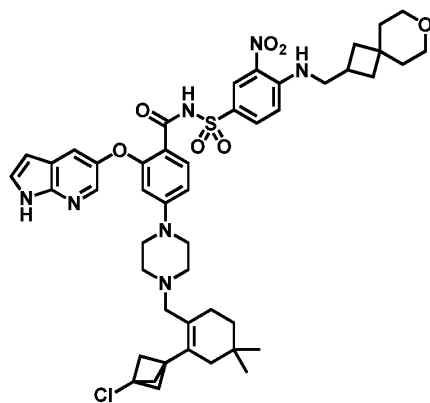
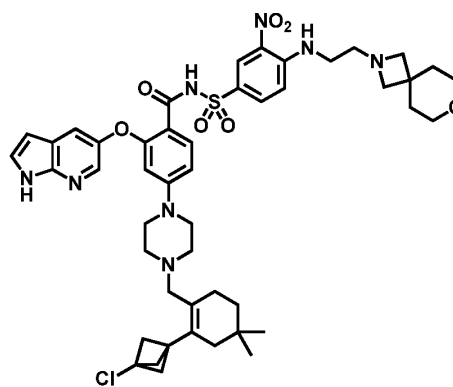
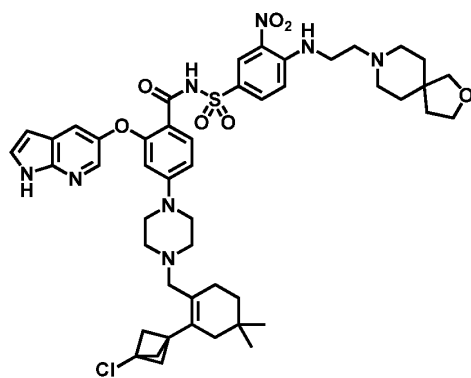
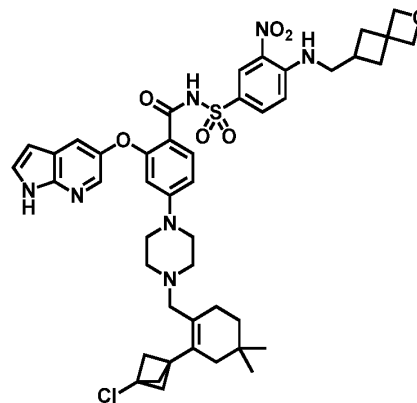
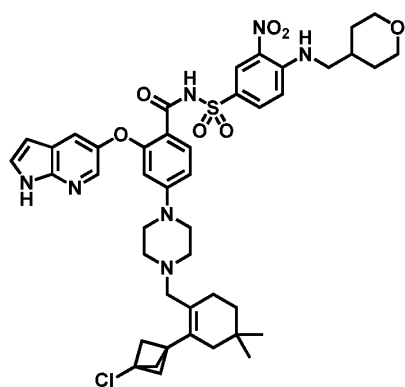


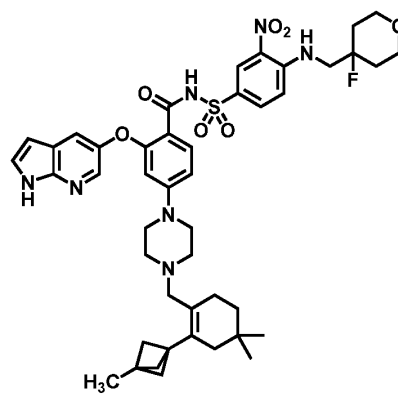
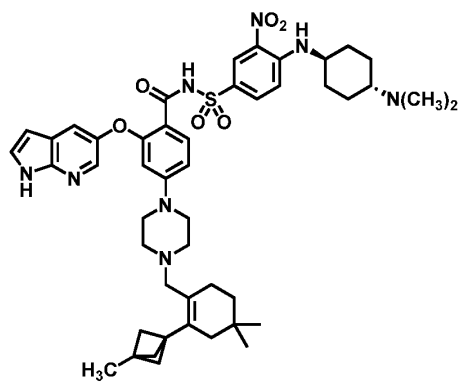
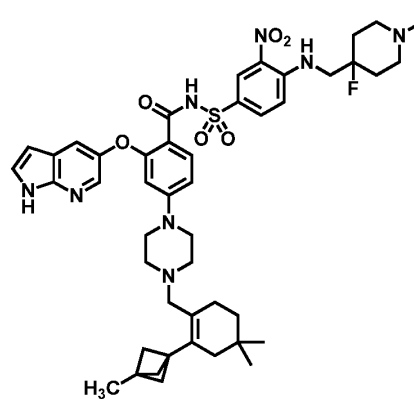
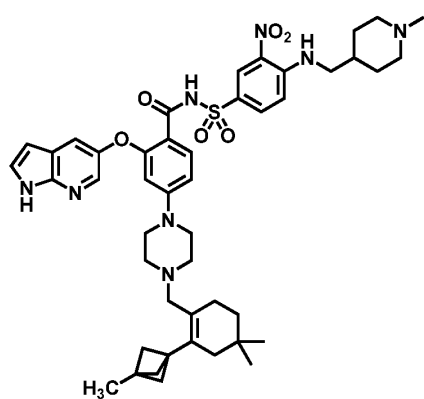
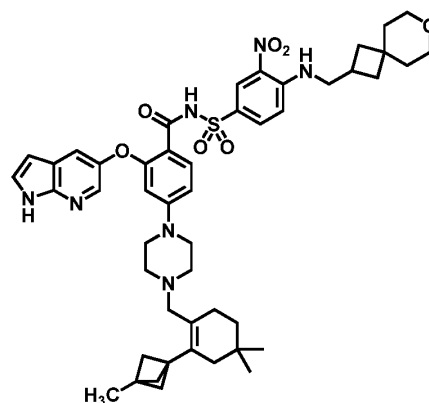
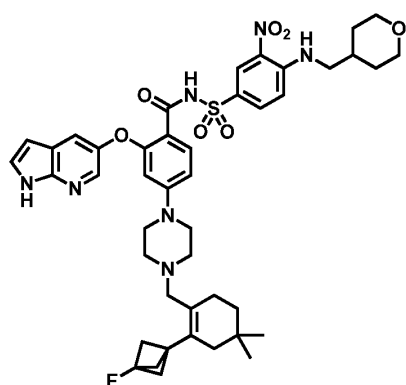


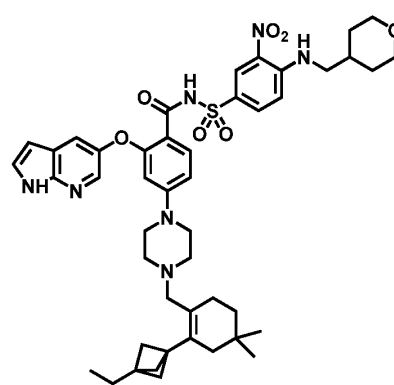
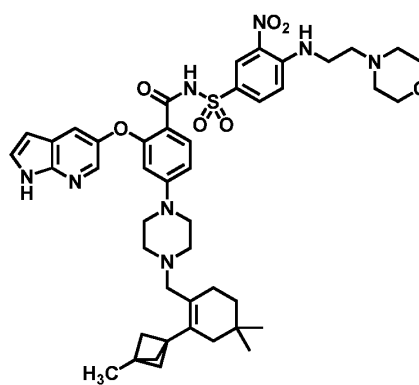
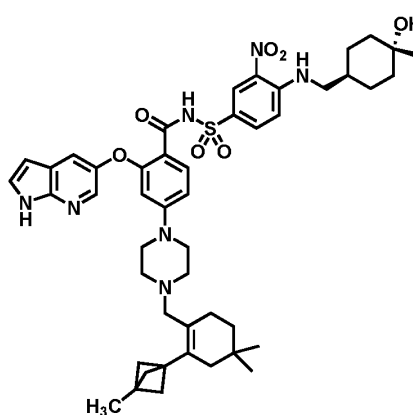
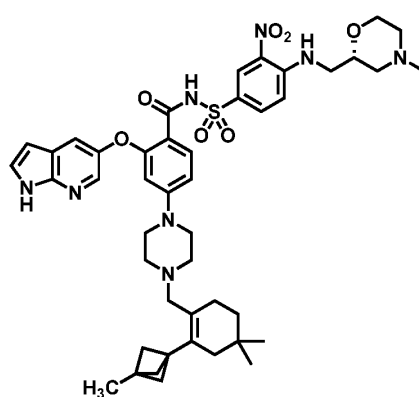
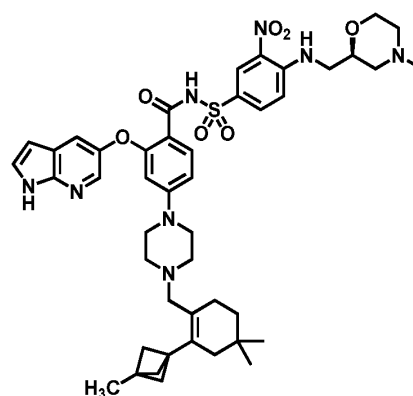
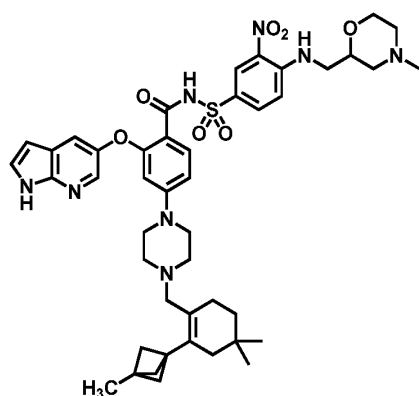


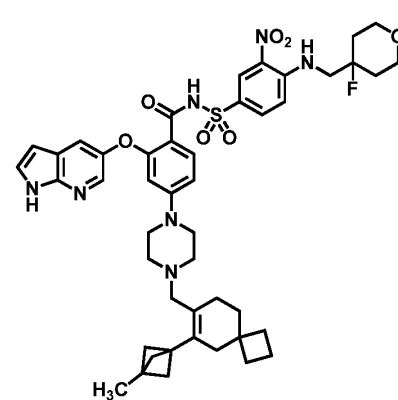
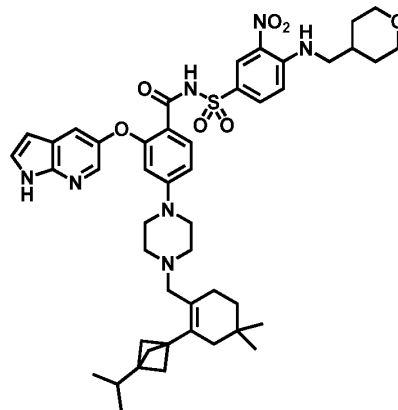
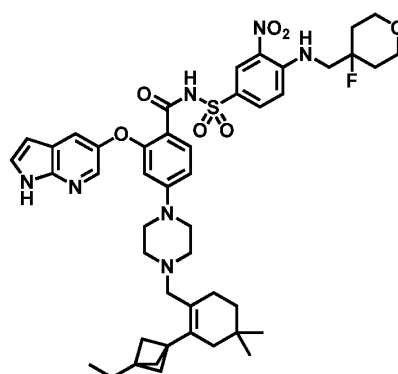


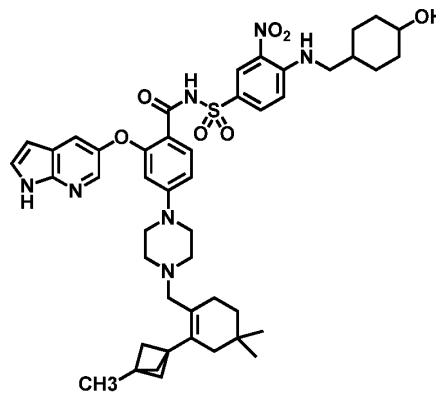
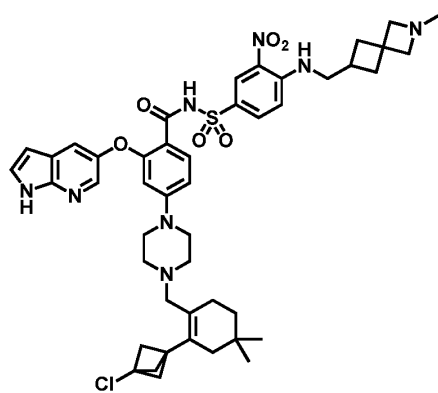
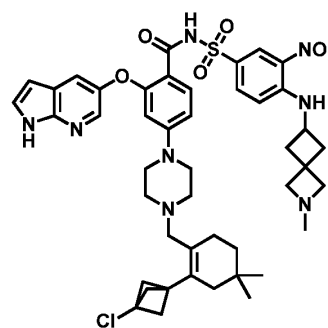
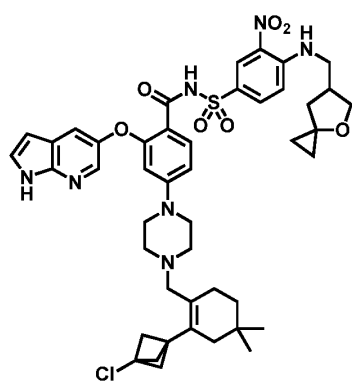
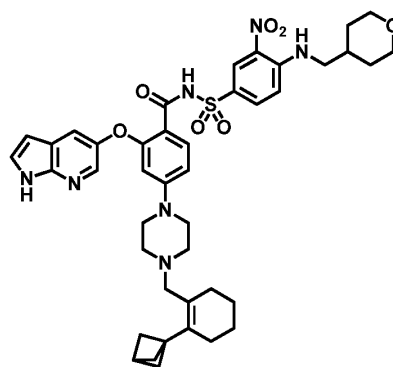
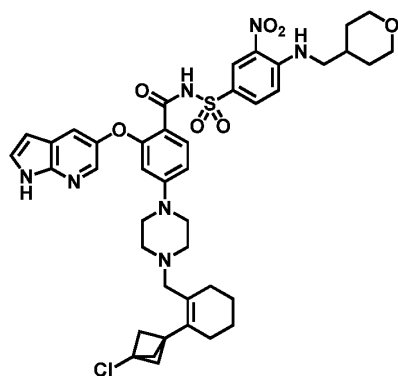
4. The use of any one of Claims 1-3, wherein the Compound (B) is selected from the group consisting of:

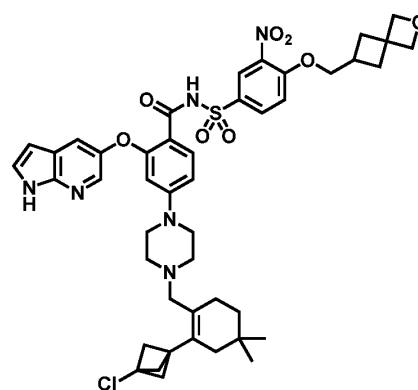
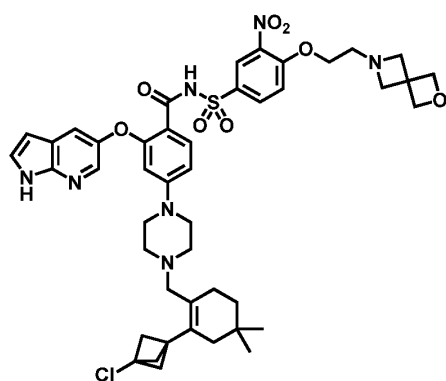
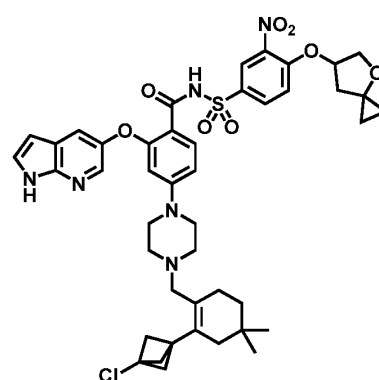
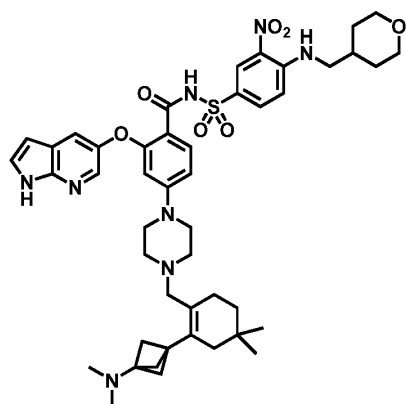
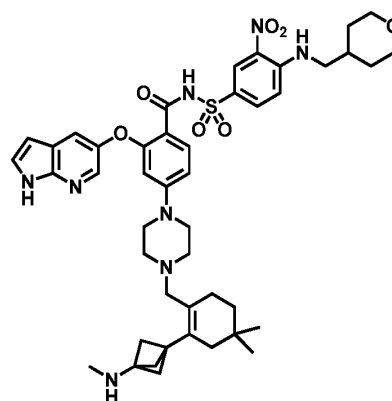
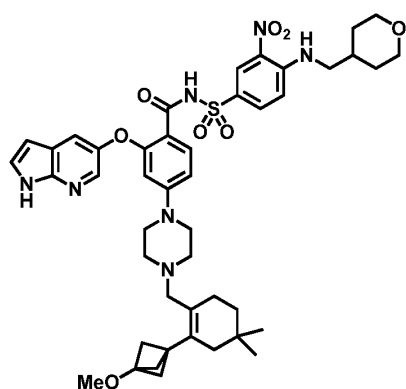


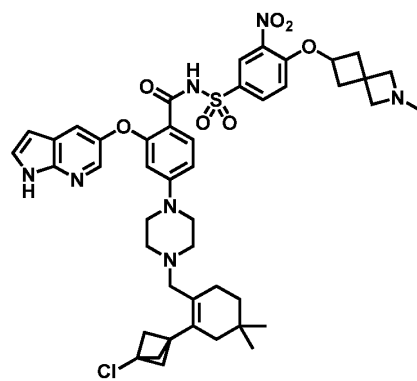
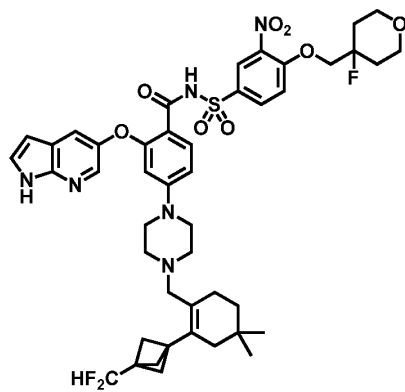
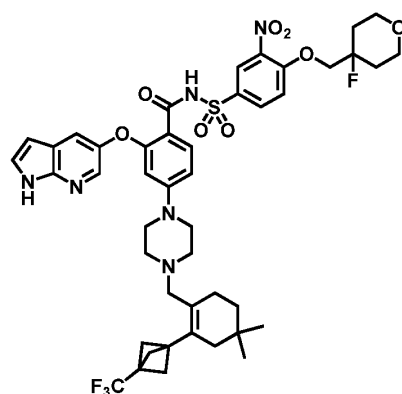
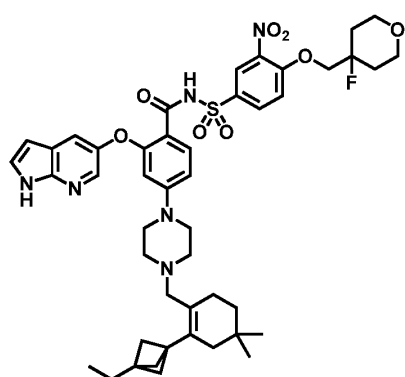
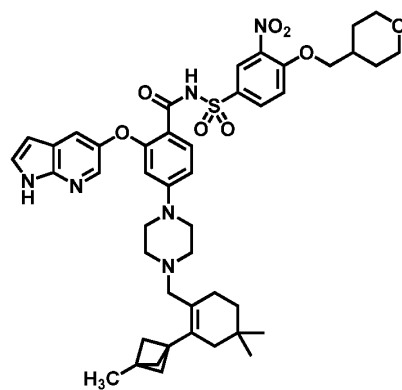
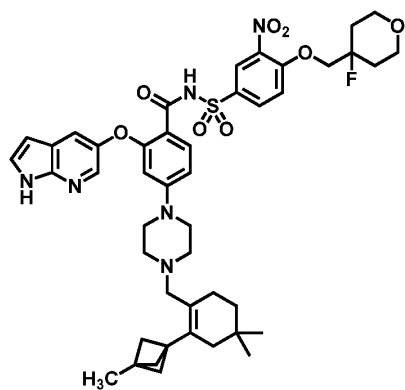


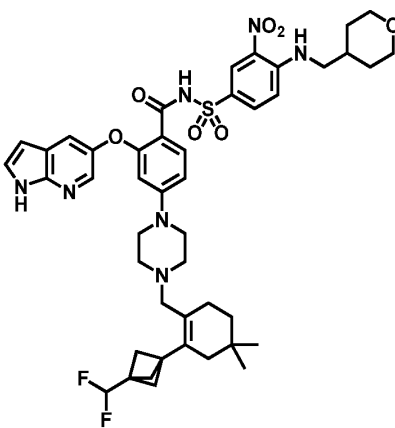
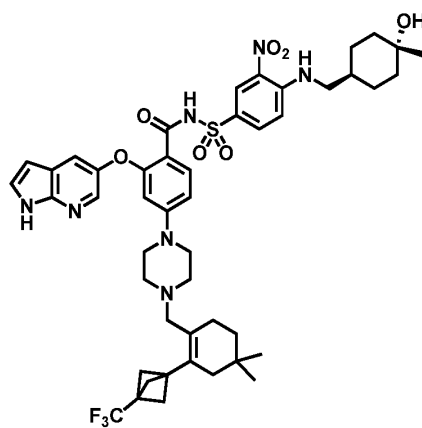
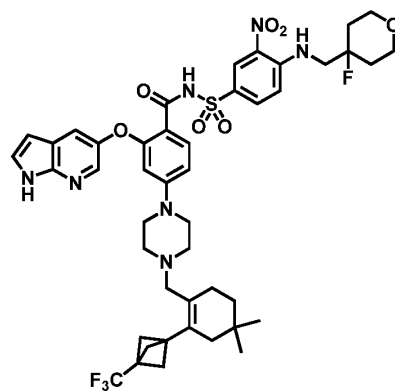
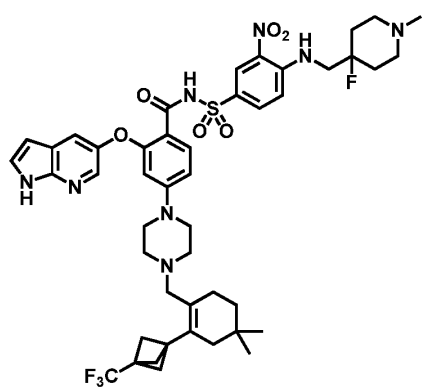
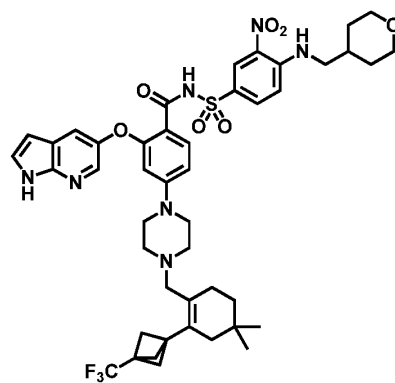
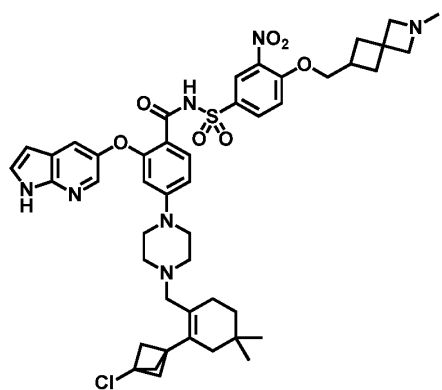


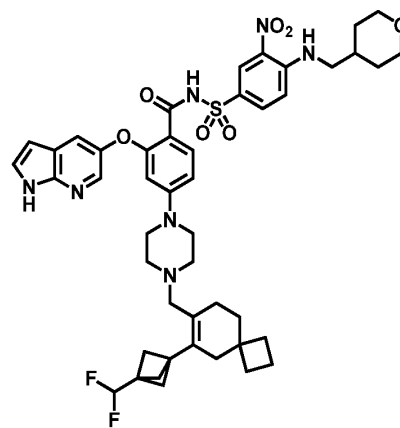
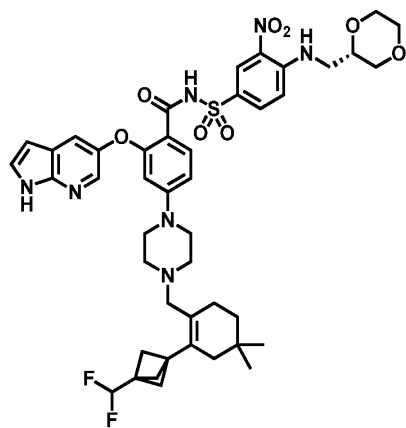
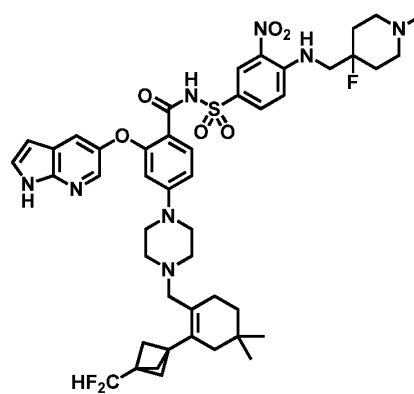
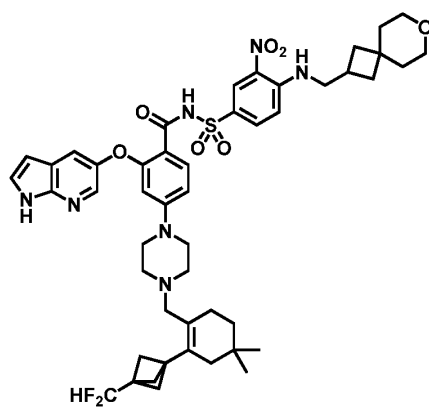
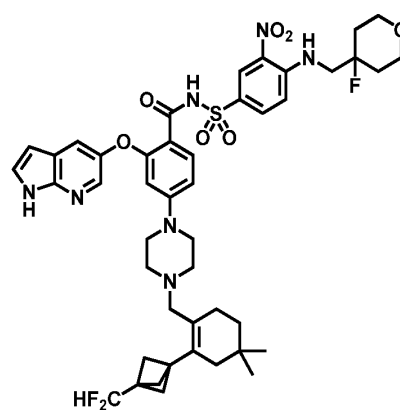
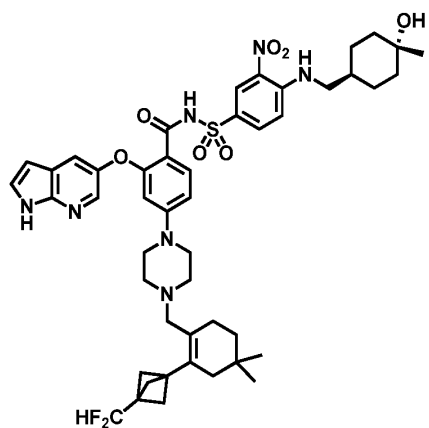


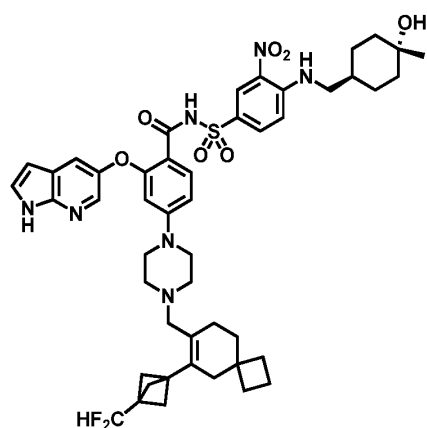




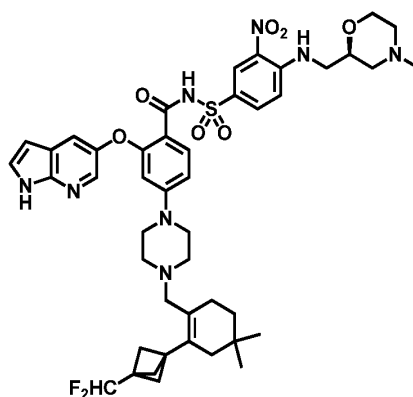








, and



, or a

pharmaceutically acceptable salt of any of the foregoing.

5. The use of any one of Claims 1-4, wherein the disease or condition is selected from the group consisting of a breast cancer, a cervical cancer, an ovarian cancer, an uterine cancer, a vaginal cancer, a vulvar cancer, a bladder cancer, a brain cancer, a bone marrow cancer, a colorectal cancer, an esophageal cancer, a hepatocellular cancer, a lymphoblastic leukemia, a follicular lymphoma, a lymphoid malignancy of T-cell or B-cell origin, a melanoma, a myelogenous leukemia, a Hodgkin's lymphoma, a Non-Hodgkin's lymphoma, a head and neck cancer (including oral cancer), a non-small cell lung cancer, a chronic lymphocytic leukemia, a myeloma, a prostate cancer, a small cell lung cancer, a spleen cancer, a polycythemia vera, a thyroid cancer, an endometrial cancer, a stomach cancer, a gallbladder cancer, a bile duct cancer, a testicular cancer, a neuroblastoma, an osteosarcoma, an Ewings's tumor and a Wilm's tumor.

6. The use of any one of Claims 1-4, wherein the disease or condition is selected from the group consisting of a breast cancer, a cervical cancer, an ovarian cancer, an uterine cancer, a vaginal cancer, and a vulvar cancer.

7. The use of Claim 6, wherein the disease or condition is a breast cancer.

8. The use of any one of Claims 5-7, wherein the breast cancer that does not include any point mutations ER mutations.

9. The use of any one of Claims 5-7, wherein the disease or condition is breast cancer that has at least one point mutation within the Estrogen Receptor 1 (ESR1) that encodes Estrogen receptor alpha (ER α), wherein the mutation is selected from the group consisting of: K303R, D538G, Y537S, E380Q, Y537C, Y537N, A283V, A546D, A546T, A58T, A593D, A65V, C530L, D411H, E279V, E471D, E471V, E523Q, E542G, F461V, F97L, G145D, G160D,

G274R, G344D, G420D, G442R, G557R, H524L, K252N, K481N, K531E, L370F, L453F, L466Q, L497R, L536H, L536P, L536Q, L536R, L540Q, L549P, M388L, M396V, M421V, M437I, M522I, N156T, N532K, N69K, P147Q, P222S, P535H, R233G, R477Q, R503W, R555H, S282C, S329Y, S338G, S432L, S463P, S47T, S576L, V392I, V418E, V478L, V533M, V534E, Y537D and Y537H.

10. The use of any one of Claims 5-9, wherein the breast cancer is ER positive breast cancer.

11. The use of any one of Claims 5-9, wherein the breast cancer is ER positive/HER2-negative breast cancer.

12. The use of any one of Claims 5-11, wherein the breast cancer is local breast cancer.

13. The use of any one of Claims 5-11, wherein the breast cancer is metastatic breast cancer.

14. The use of any one of Claims 5-13, wherein the breast cancer is recurrent breast cancer.

15. The use of any one of Claims 5-14, wherein the breast cancer has been previously treated with an endocrine therapy.

16. The use of Claim 15, wherein the treatment was with a selective ER modulator (SERM).

17. The use of Claim 16, wherein the selective ER modulator is selected from the group consisting of tamoxifen, raloxifene, ospemifene, bazedoxifene, toremifene and lasofoxifene, or a pharmaceutically acceptable salt of any of the foregoing.

18. The use of Claim 15, wherein the treatment was with a selective ER degrader (SERD).

19. The use of Claim 18, wherein the selective ER degrader is selected from the group consisting of fulvestrant, (E)-3-[3,5-Difluoro-4-[(1R,3R)-2-(2-fluoro-2-methylpropyl)-3-methyl-1,3,4,9-tetrahydropyrido[3,4-b]indol-1-yl]phenyl]prop-2-enoic acid (AZD9496), (R)-6-(2-(ethyl(4-(2-(ethylamino)ethyl)benzyl)amino)-4-methoxyphenyl)-5,6,7,8-tetrahydronaphthalen-2-ol (elacestrant, RAD1901), (E)-3-(4-((E)-2-(2-chloro-4-fluorophenyl)-1-(1H-indazol-5-yl)but-1-en-1-yl)phenyl)acrylic acid (Brilanestrant, ARN-810, GDC-0810), (E)-3-(4-((2-(2-(1,1-difluoroethyl)-4-fluorophenyl)-6-hydroxybenzo[b]thiophen-3-yl)oxy)phenyl)acrylic acid

(LSZ102), (E)-N,N-dimethyl-4-((2-((5-((Z)-4,4,4-trifluoro-1-(3-fluoro-1H-indazol-5-yl)-2-phenylbut-1-en-1-yl)pyridin-2-yl)oxy)ethyl)amino)but-2-enamide (H3B-6545), (E)-3-(4-((2-(4-fluoro-2,6-dimethylbenzoyl)-6-hydroxybenzo[b]thiophen-3-yl)oxy)phenyl)acrylic acid (rintodestrant, G1T48), D-0502, SHR9549, ARV-471, 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 (giredestrant, GDC-9545), (S)-8-(2,4-dichlorophenyl)-9-(4-((1-(3-fluoropropyl)pyrrolidin-3-yl)oxy)phenyl)-6,7-dihydro-5H-benzo[7]annulene-3-carboxylic acid (SAR439859), N-[1-(3-fluoropropyl)azetidin-3-yl]-6-[(6S,8R)-8-methyl-7-(2,2,2-trifluoroethyl)-6,7,8,9-tetrahydro-3H-pyrazolo[4,3-f]isoquinolin-6-yl]pyridin-3-amine (AZD9833), OP-1250 and LY3484356, or a pharmaceutically acceptable salt of any of the foregoing.

20. The use of Claim 15, wherein the treatment was with an aromatase inhibitor.
21. The use of Claim 20, wherein the aromatase inhibitor is a steroidal aromatase inhibitor.
22. The use of Claim 21, wherein the steroidal aromatase inhibitor is selected from the group consisting of exemestane and testolactone, or a pharmaceutically acceptable salt of any of the foregoing.
23. The use of Claim 20, wherein the aromatase inhibitor is a non-steroidal aromatase inhibitor.
24. The use of Claim 23, wherein the non-steroidal aromatase inhibitor is selected from the group consisting of anastazole and letrozole, or a pharmaceutically acceptable salt of any of the foregoing.
25. The use of any one of Claims 5-13, wherein the breast cancer has not been previously treated.
26. The use of any one of Claim 5-25, wherein the breast cancer is present in a woman.
27. The use of Claim 26, wherein the subject is a premenopausal woman.
28. The use of Claim 26, wherein the subject is a perimenopausal woman.
29. The use of Claim 26, wherein the subject is a menopausal woman.
30. The use of Claim 26, wherein the breast cancer is present in a postmenopausal woman.
31. The use of any one of Claim 5-25, wherein the breast cancer is present a man.

32. The use of any one of Claim 5-31, wherein the breast cancer is present in a subject that has a serum estradiol level in the range of >15 pg/mL to 350 pg/mL.

33. The use of any one of Claim 5-31, wherein the breast cancer is present in a subject that has a serum estradiol level ≤ 15 pg/mL.

34. The use of any one of Claim 5-31, wherein the breast cancer is present in a subject that has a serum estradiol level ≤ 10 pg/mL.