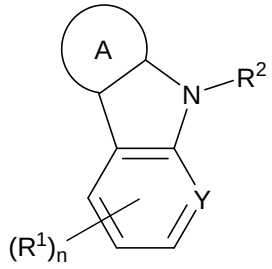
CLAIMS

1. A compound having a structure represented by Formula I or a pharmaceutically acceptable salt thereof:



I

wherein

each R^1 is independently alkyl, alkoxy, alkenyl, alkynyl, aralkyl, heteroaralkyl, aryl, heteroaryl, halo, haloalkyl, hydroxyl, carboxyl, acyl, ester, thioester, phosphoryl, amino, amido, cyano, nitro, azido, cycloalkyl, heterocyclyl, alkylsulfoxidyl, alkylsulfonyl, or sulfonamido;

A is an aryl, heteroaryl, or heterocyclyl;

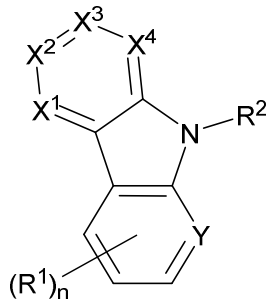
Y is CH, CR^1, or N;

R^2 is aralkyl, heteroaralkyl, heterocyclylalkyl, or cycloalkylalkyl; and

n is 0, 1, 2, 3, or 4.

2. The compound of claim 1, wherein A is a heteroaryl (*e.g.*, pyridinyl, pyrimidinyl, or pyridazinyl, preferably pyridinyl) or a heterocyclyl (*e.g.*, piperidinyl, piperidonyl, tetrahydropyridazinonyl).

3. The compound of claim 1, wherein the compound has a structure represented by Formula Ia or a pharmaceutically acceptable salt thereof:



Ia

wherein,

X^1 is CR^3 or N;

X^2 is CR^4 or N;

X^3 is CR^5 or N;

X^4 is CR^6 or N; and

R^3, R^4, R^5, and R^6 are each independently selected from H, alkyl, alkoxy, alkenyl, alkynyl, aralkyl, heteroaralkyl, aryl, heteroaryl, halo, haloalkyl, hydroxyl, carboxyl, acyl, ester, thioester, phosphoryl, amino, amido, cyano, nitro, azido, cycloalkyl, heterocyclyl, alkylsulfoxidyl, alkylsulfonyl, and sulfonamido.

4. The compound of claim 3, wherein X^1 is N.

5. The compound of claim 3, wherein X^1 is CR^3.

6. The compound of claim 5, wherein R^3 is H.

7. The compound of any one of claims 3-6, wherein X^2 is N.

8. The compound of any one of claims 3-6, wherein X^2 is CR^4.

9. The compound of claim 8, wherein R^4 is H.

10. The compound of any one of claims 3-9, wherein X^3 is N.

11. The compound of any one of claims 3-9, wherein X^3 is CR^5.

12. The compound of claim 11, wherein R^5 is H.

13. The compound of any one of claims 3-12, wherein X^4 is N.

14. The compound of any one of claims 3-12, wherein X^4 is CR^6.

15. The compound of claim 14, wherein R^6 is H.

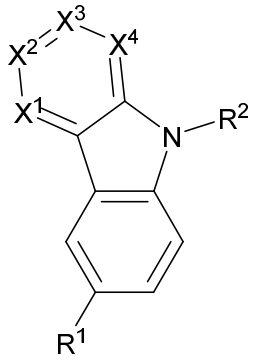
16. The compound of any one of claims 1-11, wherein n is 1.

17. The compound of any one of claims 1-11, wherein n is 2.

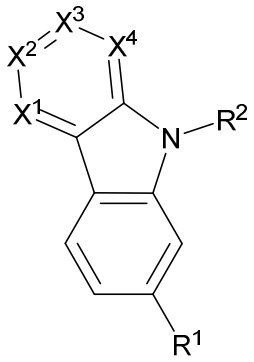
18. The compound of any one of claims 1-15, wherein Y is CH.

19. The compound of any one of claims 1-15, wherein Y is N.

20. The compound of any one of claims 1-16 and 18, wherein the compound has a structure represented by Formula Ib, Formula Ic, or a pharmaceutically acceptable salt thereof:

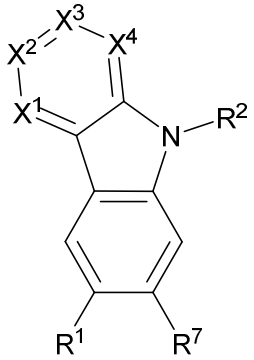


Ib, or

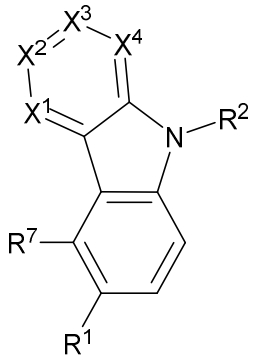


Ic.

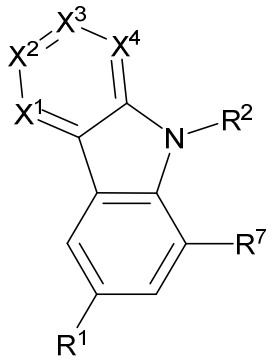
21. The compound of any one of claims 1-15, 17, and 18, wherein the compound has a structure represented by Formula Id, Formula (Ie), Formula (If), or a pharmaceutically acceptable salt thereof:



Id,



Ie, or



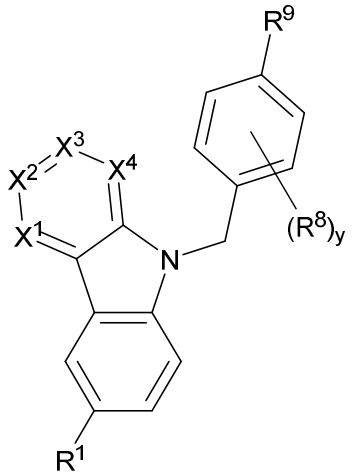
If,

wherein,

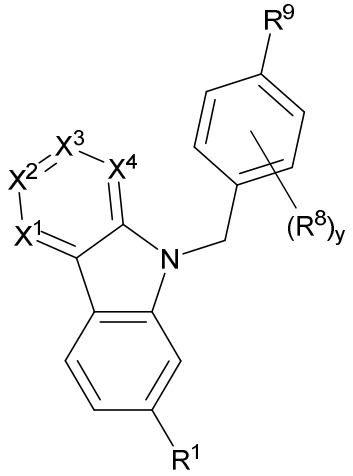
R^7 is alkyl, alkoxy, alkenyl, alkynyl, aralkyl, heteroaralkyl, aryl, heteroaryl, halo, haloalkyl, hydroxyl, carboxyl, acyl, ester, thioester, phosphoryl, amino, amido, cyano, nitro, azido, cycloalkyl, heterocyclyl, alkylsulfoxidyl, alkylsulfonyl, or sulfonamido.

22. The compound of any one of claims 1-21, wherein R^2 is aralkyl (*e.g.*, phenylalkyl, such as phenylmethylenyl or phenylethylenyl, preferably phenylmethylenyl), or R^2 is heterocyclylalkyl (*e.g.*, piperidinylmethylenyl).

23. The compound of any one of claims 1-16 and 18, wherein the compound has a structure represented by Formula IIa, Formula IIb, Formula IIc, Formula IId, Formula IIe, or a pharmaceutically acceptable salt thereof:



IIa,



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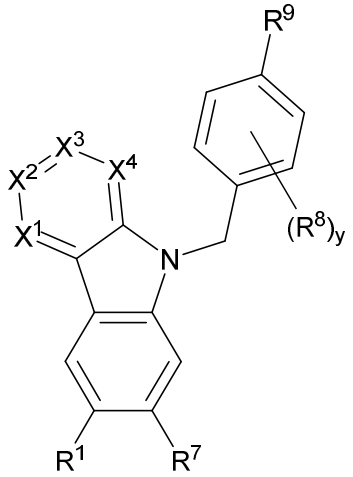
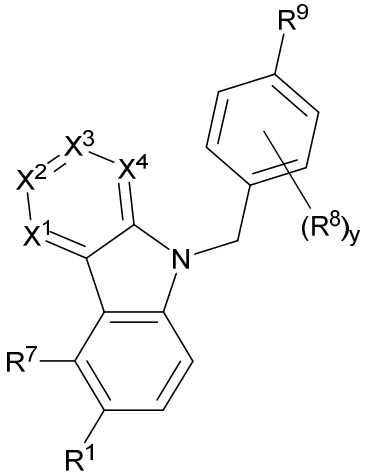
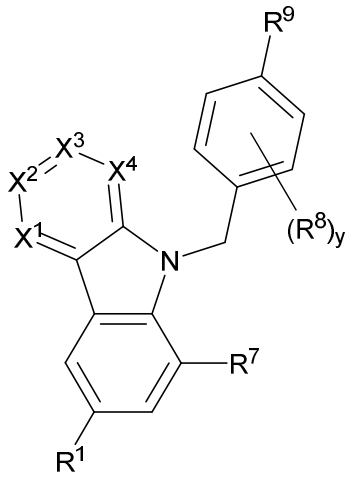


IIc,



IId, or



IIe,

wherein,

each R^8 is independently alkyl, alkoxy, alkenyl, alkynyl, aralkyl, heteroaralkyl, aryl, heteroaryl, halo, haloalkyl, hydroxyl, carboxyl, acyl, ester, thioester, phosphoryl, amino, amido, cyano, nitro, azido, cycloalkyl, heterocyclyl, alkylsulfoxidyl, alkylsulfonyl, or sulfonamido;

R^9 is alkyl, alkoxy, alkenyl, alkynyl, aralkyl, heteroaralkyl, aryl, heteroaryl, halo, haloalkyl, hydroxyl, carboxyl, acyl, ester, thioester, phosphoryl, phosphoramidityl, phosphoramidatyl, amino, amido, cyano, nitro, azido, cycloalkyl, heterocyclyl, alkylsulfoxidyl, alkylsulfonyl, sulfonamido, iminosulfanonyl, or sulfamidyl; and

y is 1, 2, 3, or 4.

24. The compound of any one of claims 1-23, wherein R^1 is alkyl (*e.g.*, methyl), alkoxy (*e.g.*, methoxy, trifluoromethoxy, or ethoxy, preferably methoxy), or halo (*e.g.*, fluoro or chloro).

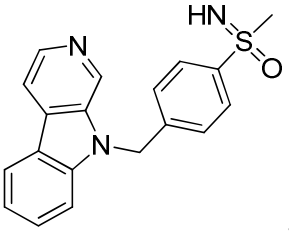
25. The compound of any one of claims 21-24, wherein R^7 is alkyl (*e.g.*, methyl), alkoxy (*e.g.*, methoxy), or halo (*e.g.*, fluoro or chloro).

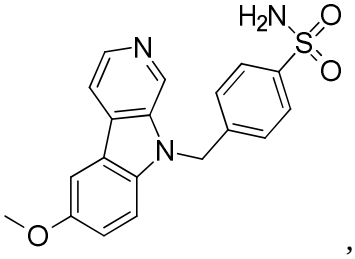
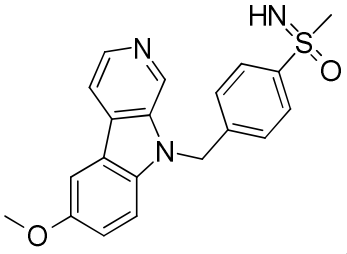
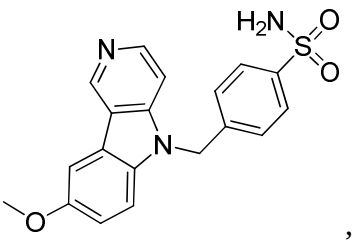
26. The compound of any one of claims 23-25, wherein y is 0 or 1.

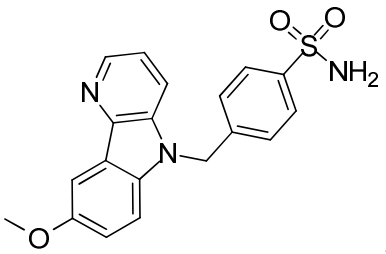
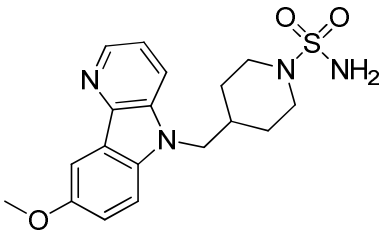
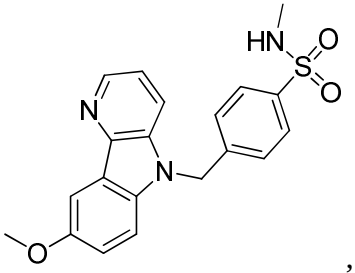
27. The compound of any one of claims 23-26, wherein R^8 is halo (*e.g.*, fluoro or chloro) or alkyl (*e.g.*, methyl or trifluoromethyl).

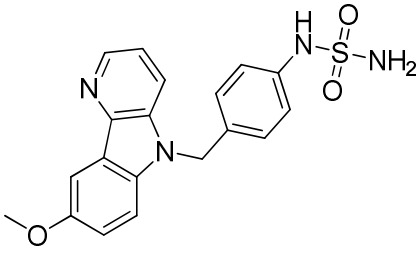
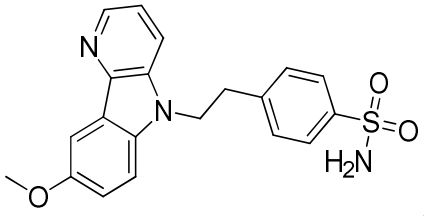
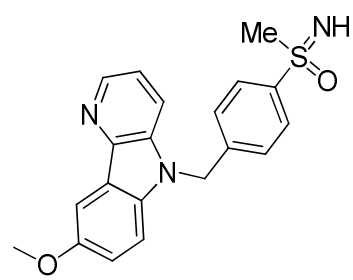
28. The compound of any one of claims 23-26, wherein R^8 is alkoxy (*e.g.*, methoxy).

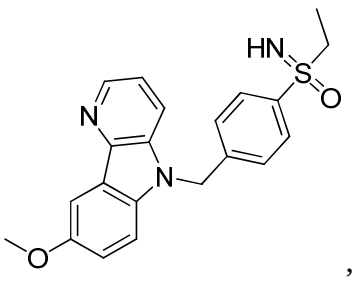
29. The compound of any one of claims 23-28, wherein R^9 is sulfonamido (*e.g.*, methylsulfonamido), iminosulfanonyl (*e.g.*, (methyl)iminosulfanonyl, (ethyl)iminosulfanonyl, (benzyl)iminosulfanonyl, or (cyclopropyl)iminosulfanonyl), sulfamidyl (*e.g.*, (methyl)sulfamidyl), phosphoryl, alkyl (*e.g.*, phosphorylmethyl or phosphoryldifluoromethyl), phosphoramidityl, or phosphoramidatyl.

30. The compound of claim 1, wherein the compound is selected from  ,

 ,  ,  ,

 ,  ,  ,

 ,  ,  ,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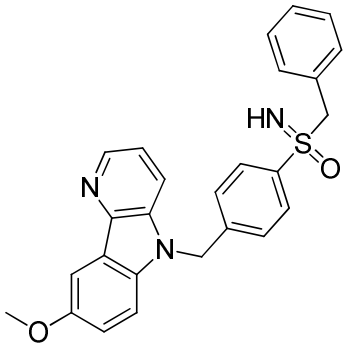
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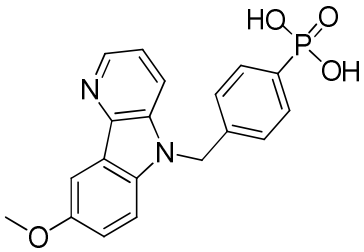
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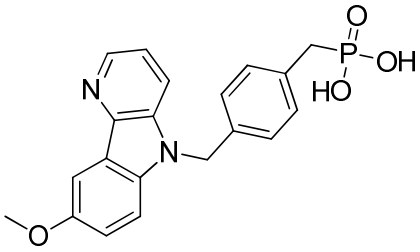
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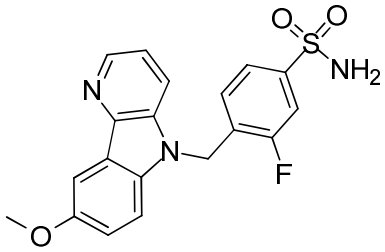
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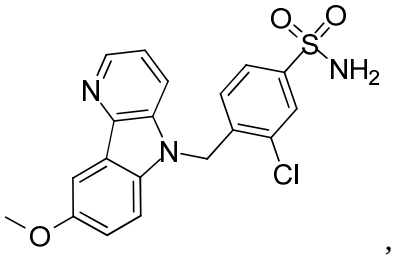
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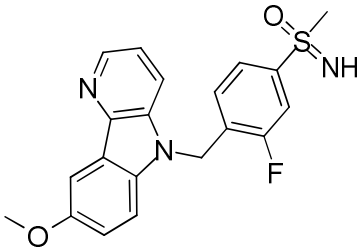
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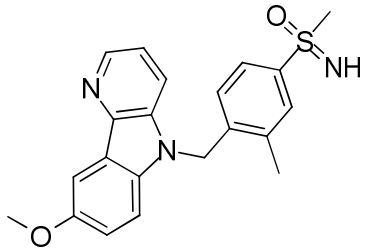
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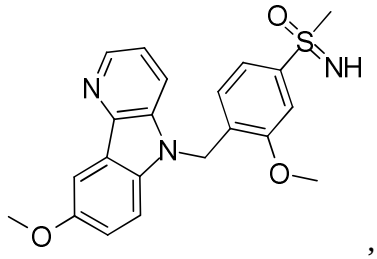
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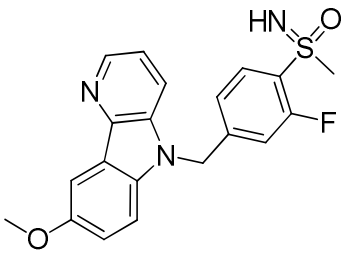
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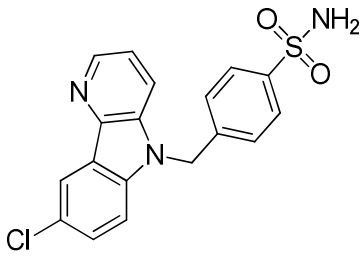
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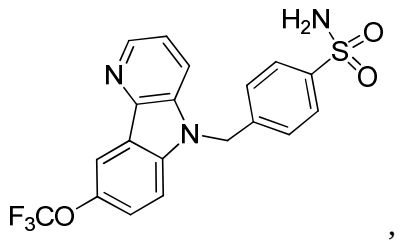
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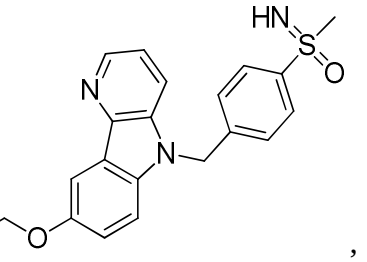
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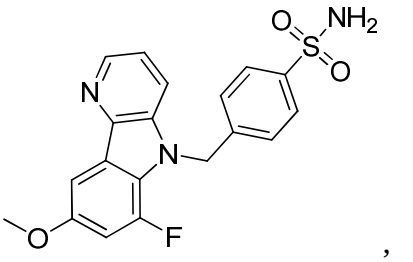
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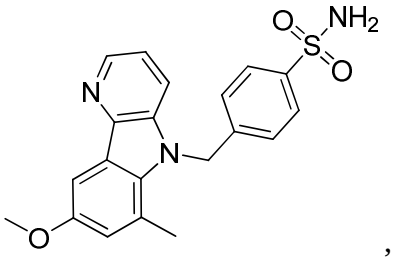
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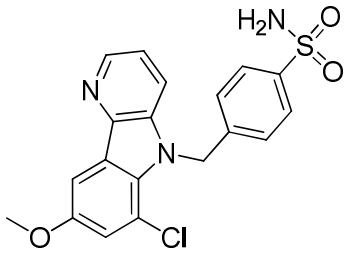
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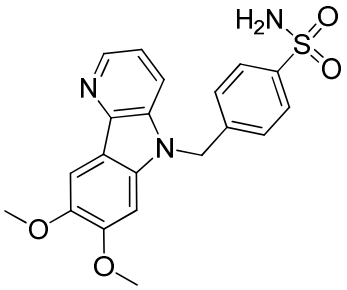
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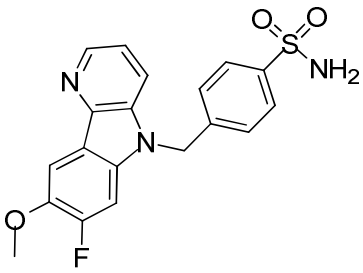
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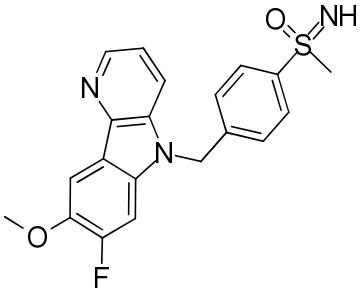
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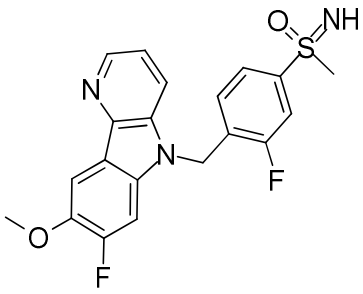
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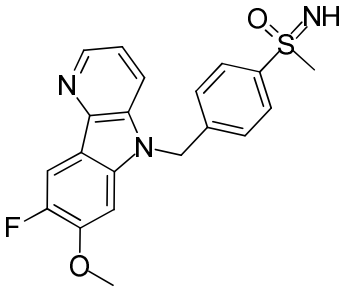
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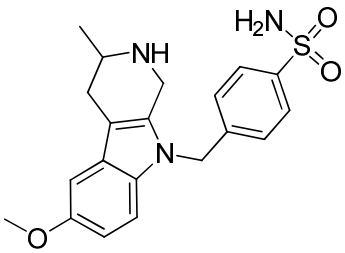
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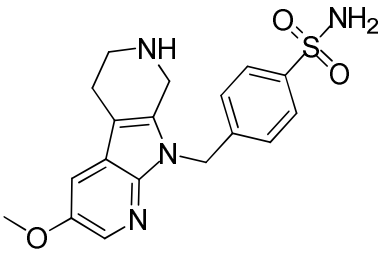
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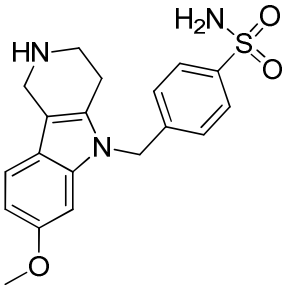
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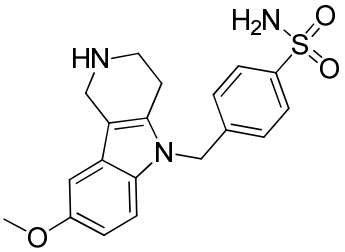
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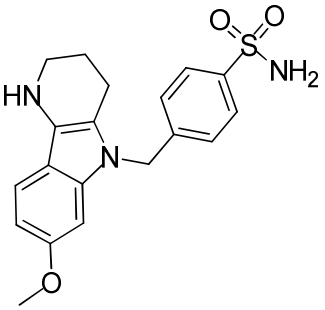
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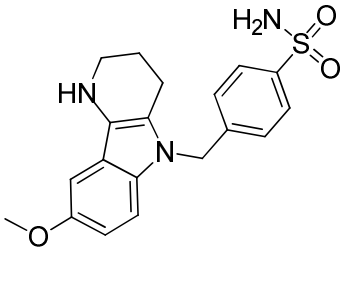
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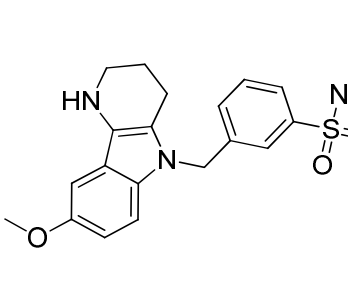
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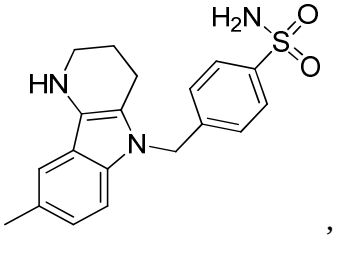
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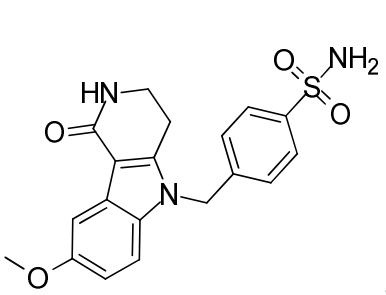
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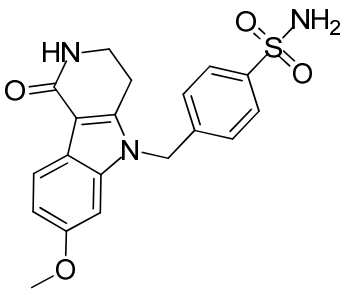
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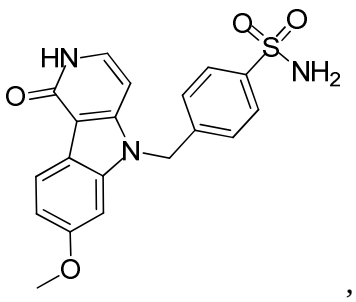
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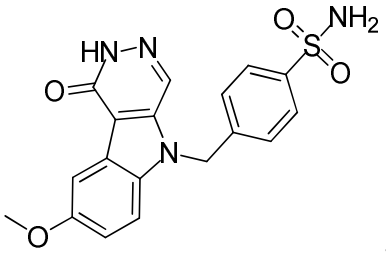
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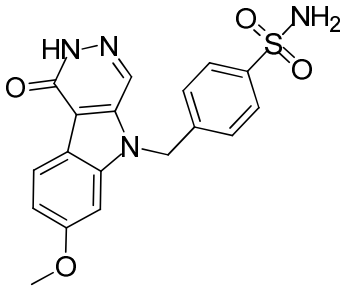
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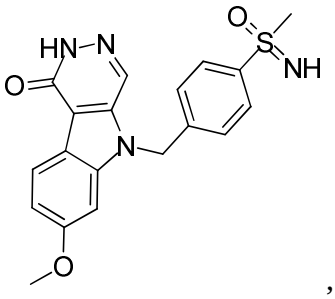
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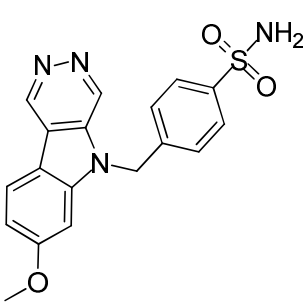
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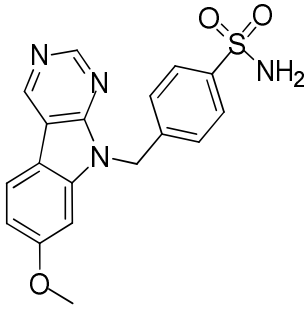
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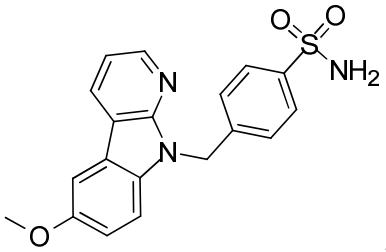
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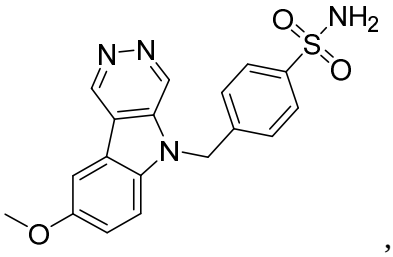
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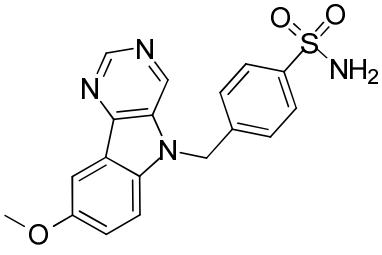
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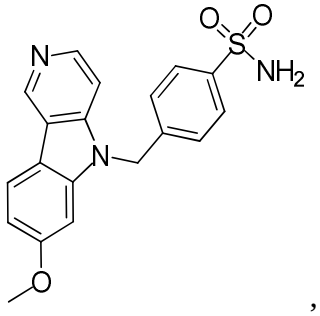
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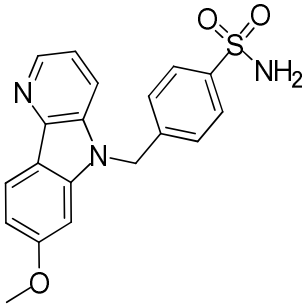
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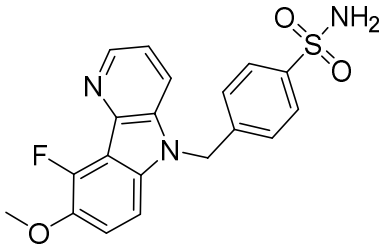
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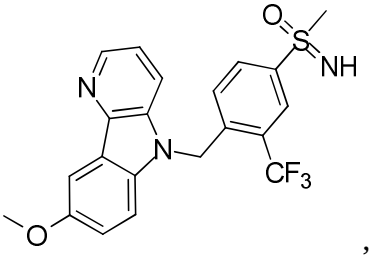
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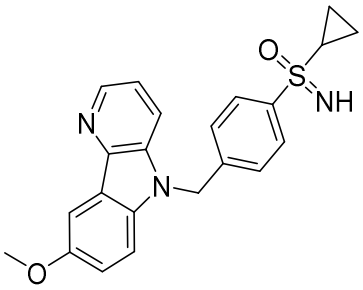
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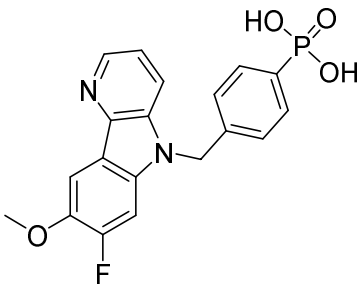
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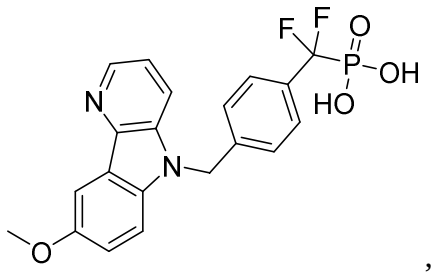
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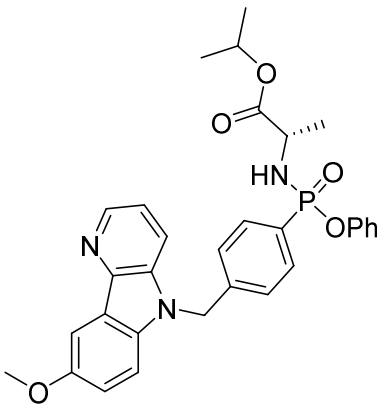
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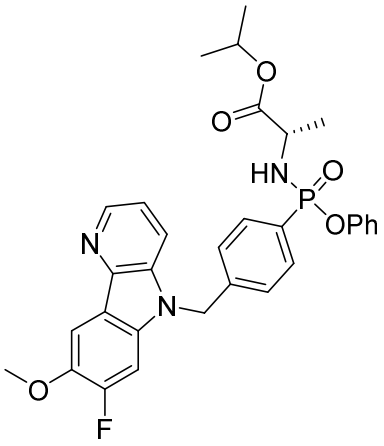
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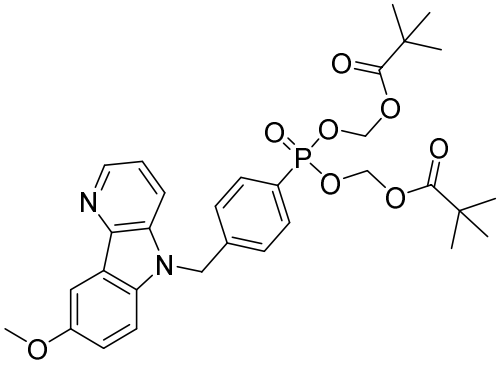
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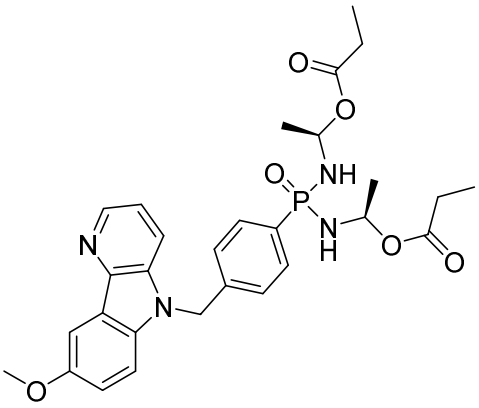
; or a pharmaceutically acceptable salt thereof.

31. A pharmaceutical composition comprising the compound of any one of claims 1-30 and a pharmaceutically acceptable excipient.

32. Use of a compound of any one of claims 1-30, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for treating cancer.

33. The use of claim 32, wherein the cancer is gastric cancer, lung cancer, liver cancer, colorectal cancer, small intestine cancer, pancreatic cancer, brain cancer, bone cancer,

melanoma, breast cancer, sclerosing adenosis, uterine cancer, cervical cancer, head and neck cancer, esophageal cancer, thyroid cancer, parathyroid cancer, kidney cancer, sarcoma, prostate cancer, urethral cancer, bladder cancer, hematologic malignancy (*e.g.*, leukemia, multiple myeloma, and myelodysplastic syndrome), lymphoma (*e.g.*, Hodgkin's lymphoma or non-Hodgkin's lymphoma), or fibroadenoma.

34. Use of a compound of any one of claims 1-30, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for treating a disease or disorder characterized by ENPP-1 over-expression.

35. A compound of any one of claims 1-30, or a pharmaceutically acceptable salt thereof, for use in therapy.