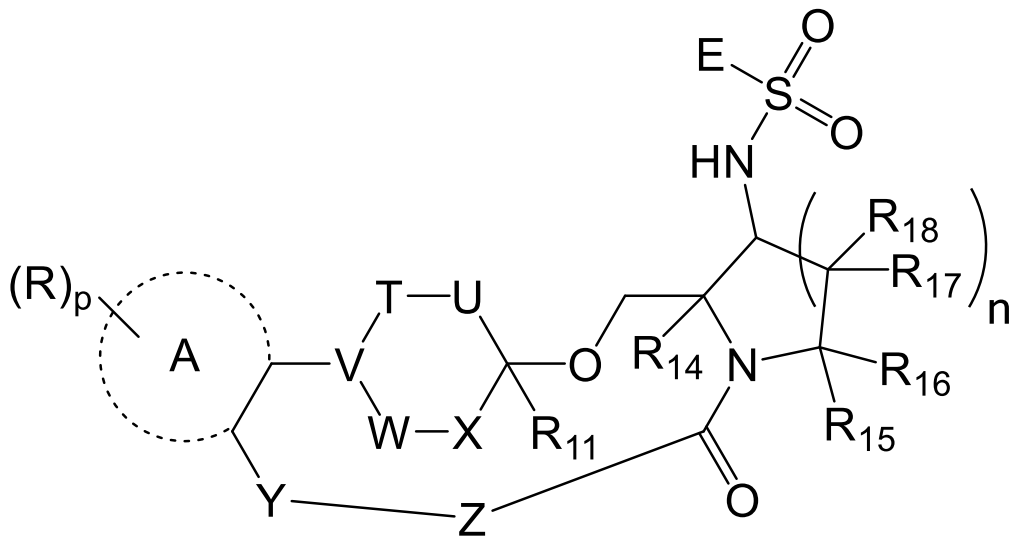
What is claimed is:

1. A compound of Formula I-A or a pharmaceutically acceptable salt thereof:



(I-A)

wherein:

ring A is selected from the group consisting of phenyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, and triazinyl;

n is 1, 2, or 3;

E is selected from the group consisting of C_1-C_3 alkylene-NR_aR_b, C_1-C_3 alkyl, C_2-C_4 alkenyl, C_2-C_4 alkynyl, C_3-C_8 cycloalkyl, C_1-C_3 alkylene-(C_3-C_8 cycloalkyl), 4- to 10-membered heterocyclyl, C_1-C_3 alkylene-(4- to 10-membered heterocyclyl), C_6-C_{10} aryl, C_1-C_3 alkylene-(C_6-C_{10} aryl), 5- to 10-membered heteroaryl, and C_1-C_3 alkylene-(5- to 10-membered heteroaryl), wherein the C_1-C_3 alkylene-NR_aR_b, C_1-C_3alkyl, C_2-C_4 alkenyl, C_2-C_4 alkynyl, C_3-C_8 cycloalkyl, C_1-C_3 alkylene-(C_3-C_8 cycloalkyl), 4- to 10-membered heterocyclyl, C_1-C_3 alkylene-(4- to 10-membered heterocyclyl), C_6-C_{10} aryl, C_1-C_3 alkylene-(C_6-C_{10} aryl), 5- to 10-membered heteroaryl, or C_1-C_3 alkylene-(5- to 10-membered heteroaryl) is unsubstituted or substituted with one or more halogen, hydroxyl, C_1-C_3 alkyl, or C_1-C_3 alkoxyl;

T is CR_1R_2 or O;

W is CR_4R_5 or O;

U is CR_6R_7;

X is CR_8R_9;

V is CR_3 or N;

Y is O;

Z is $(CR_{12}R_{13})_m$;

each R is, independently, selected from the group consisting of halogen, deuterium, hydroxyl, cyano, unsubstituted C_1-C_3 alkyl, and C_1-C_3 alkyl substituted with one or more halogen or deuterium;

p is 0, 1, 2, 3, or 4;

R_a and R_b are each, independently, H or unsubstituted C_1-C_3 alkyl;

m is 1;

and further wherein:

R_1, R_2, R_4, and R_5 are each, independently, selected from the group consisting of H, hydroxyl, halogen, and deuterium;

or, alternatively, R_2 and R_5 together with the carbon atoms to which they are attached, form a single bond;

R_3 is selected from the group consisting of H, deuterium, halogen, hydroxyl, and cyano;

R_6, R_7, R_8, R_9, and R_{11} are each, independently, selected from the group consisting of H, hydroxyl, halogen, and deuterium;

each R_{12} and R_{13} is, independently, selected from the group consisting of H, halogen, deuterium, unsubstituted C_1-C_3 alkyl, and C_1-C_3 alkyl substituted with hydroxyl or one or more halogen; and

R_{14}, R_{15}, and R_{16} are each, independently, selected from the group consisting of H, unsubstituted C_1-C_3 alkyl or C_1-C_3 alkyl substituted with one or more halogen; and

each R_{17} and R_{18} is, independently, selected from the group consisting of H, unsubstituted C_1-C_3 alkyl or C_1-C_3 alkyl substituted with one or more halogen;

with the proviso that one or more of (a)-(f) is present:

(a) at least one R is selected from the group consisting of hydroxyl, cyano, unsubstituted C_1-C_3 alkyl, and C_1-C_3 alkyl substituted with one or more halogen or deuterium;

(b) E is NR_aR_b, C_1-C_3 alkylene-NR_aR_b, C_2-C_3 alkyl, C_2-C_4 alkenyl, C_2-C_4 alkynyl, C_3-C_8 cycloalkyl, C_1-C_3 alkylene-(C_3-C_8 cycloalkyl), 4- to 10-membered heterocyclyl, C_1-C_3

alkylene-(4- to 10-membered heterocyclyl), C_6-C_{10} aryl, C_1-C_3 alkylene-(C_6-C_{10} aryl), 5- to 10-membered heteroaryl, or C_1-C_3 alkylene-(5- to 10-membered heteroaryl), wherein the C_1-C_3 alkylene-NR_aR_b, C_2-C_3 alkyl, C_2-C_4 alkenyl, C_2-C_4 alkynyl, C_3-C_8 cycloalkyl, C_1-C_3 alkylene-(C_3-C_8 cycloalkyl), 4- to 10-membered heterocyclyl, C_1-C_3 alkylene-(4- to 10-membered heterocyclyl), C_6-C_{10} aryl, C_1-C_3 alkylene-(C_6-C_{10} aryl), 5- to 10-membered heteroaryl, or C_1-C_3 alkylene-(5- to 10-membered heteroaryl) is unsubstituted or substituted with one or more halogen, hydroxyl, C_1-C_3 alkyl, or C_1-C_3 alkoxyl;

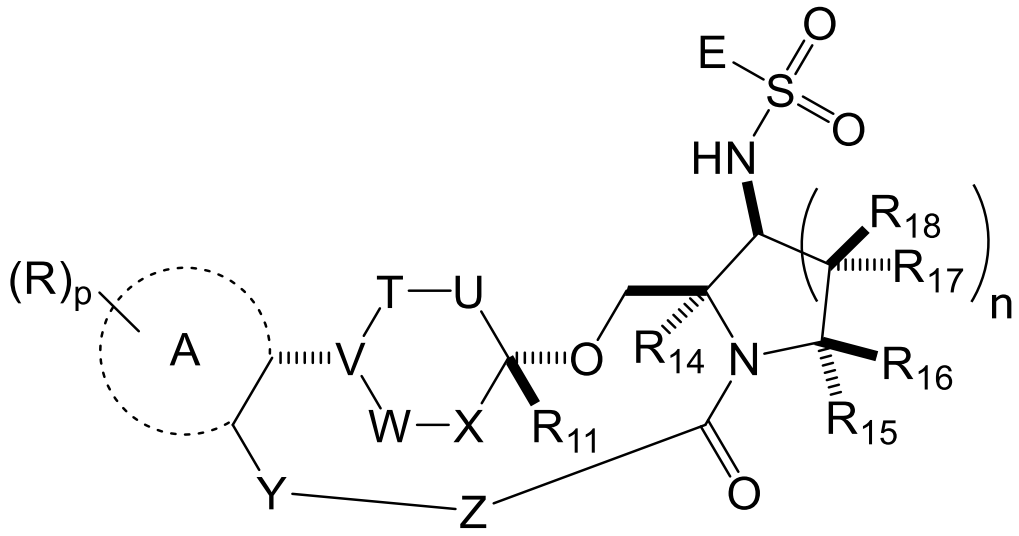
(c) E is C_1 alkyl substituted with one or more halogen, hydroxyl, C_1-C_3 alkyl, or C_1-C_3 alkoxyl;

(d) at least one of R_{14}, R_{15}, R_{16}, R_{17}, and R_{18} is unsubstituted C_1-C_3 alkyl or C_1-C_3 alkyl substituted with one or more halogen;

(e) at least one of R_1, R_2, R_4, R_5, R_6, R_7, R_8, R_9, and R_{11} is hydroxyl; or

(f) at least one of R_{12} and R_{13} is C_1-C_3 alkyl substituted with hydroxyl.

2. The compound of claim 1, wherein the compound of Formula I-A or a pharmaceutically acceptable salt thereof is a compound of Formula I:



(I) or a pharmaceutically acceptable salt thereof

3. The compound of claim 1 or 2, wherein n is 1 or 2.

4. The compound of claim 2, wherein n is 1.

5. The compound of claim 2, wherein n is 2.

6. The compound of any one of claims 1-5, wherein ring A is phenyl or pyridinyl.

7. The compound of claim 6, wherein ring A is phenyl.

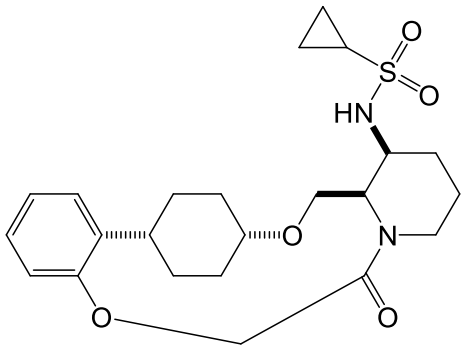
8. The compound of claim 6, wherein ring A is pyridinyl.

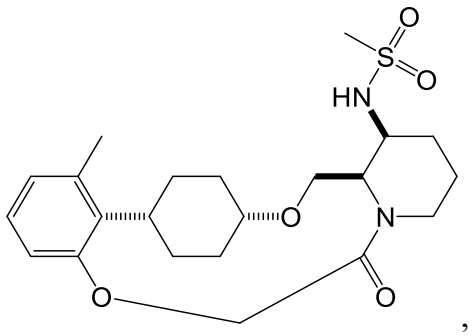
9. The compound of any one of the preceding claims, wherein T is CR_1R_2.

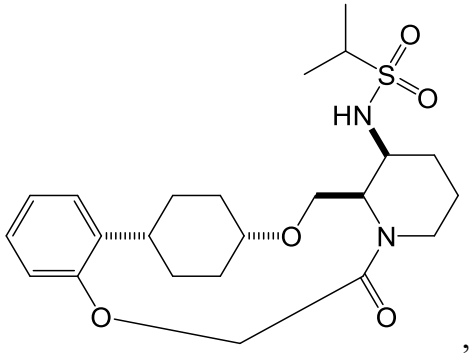
10. The compound of any one of the preceding claims, wherein W is CR_4R_5.

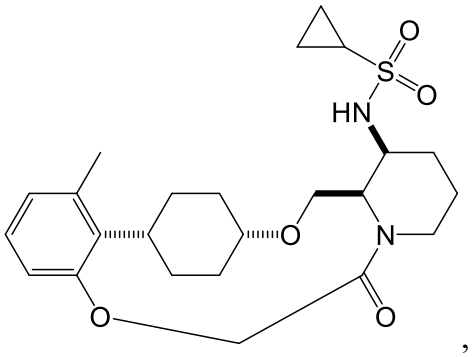
11. The compound of any one of the preceding claims, wherein V is CR_3.

12. The compound of claim 2, wherein the compound or a pharmaceutically acceptable salt thereof is selected from the group consisting of:

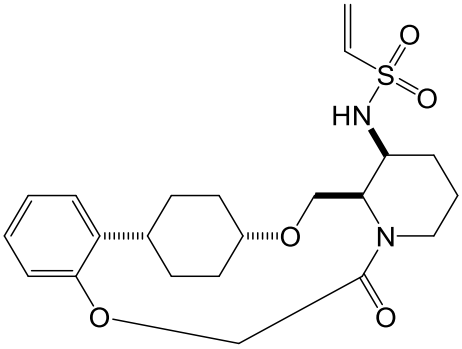
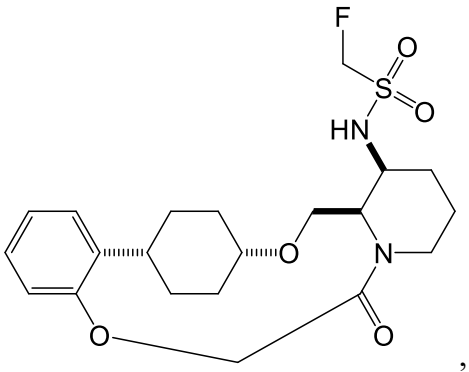
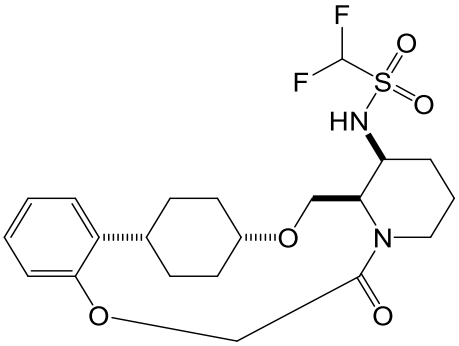
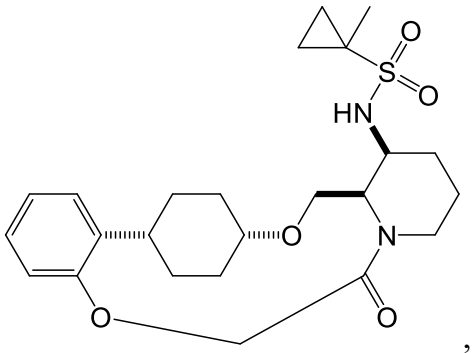
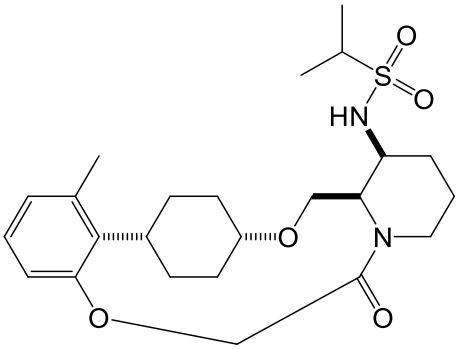
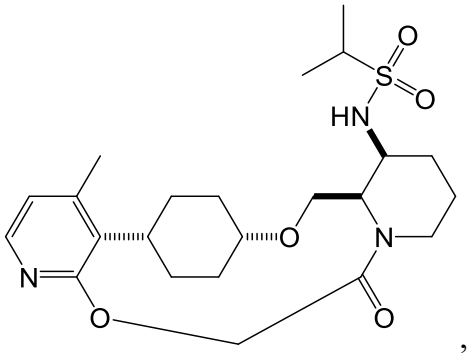
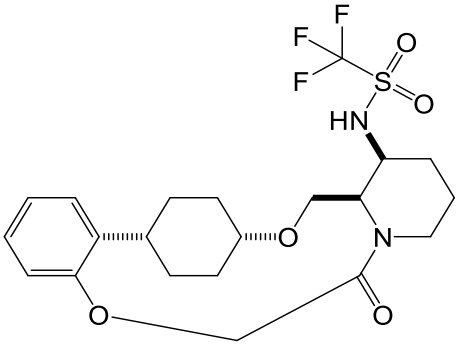
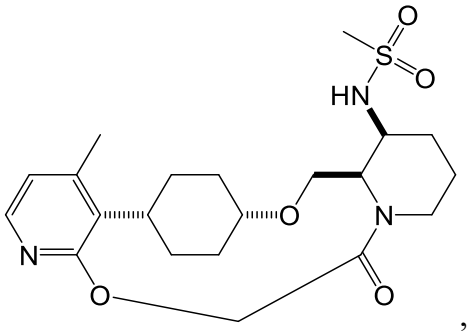


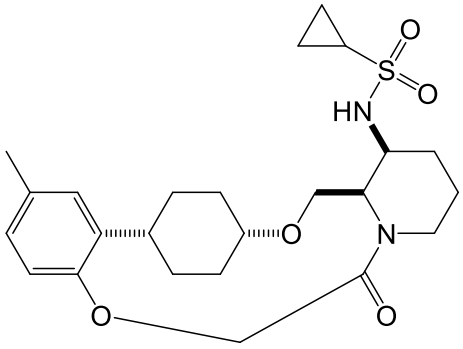
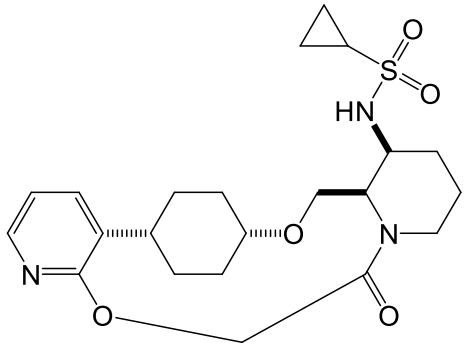
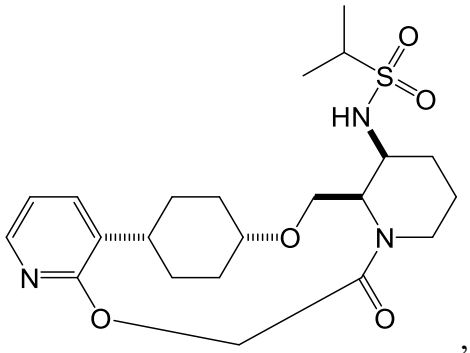
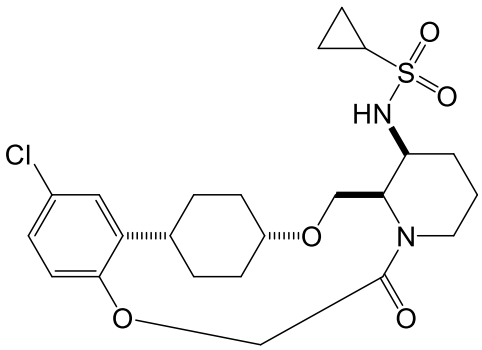
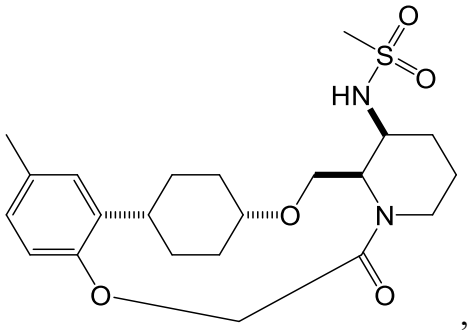
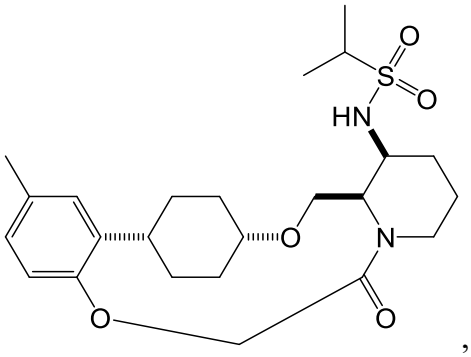
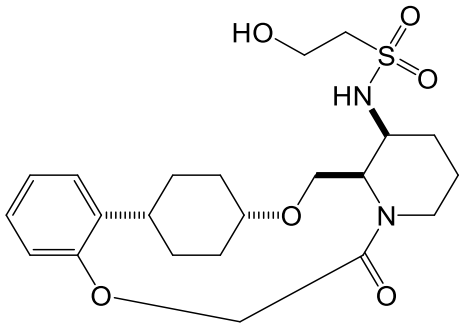
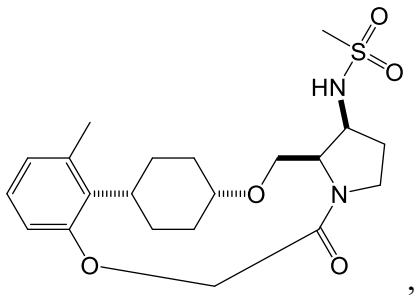
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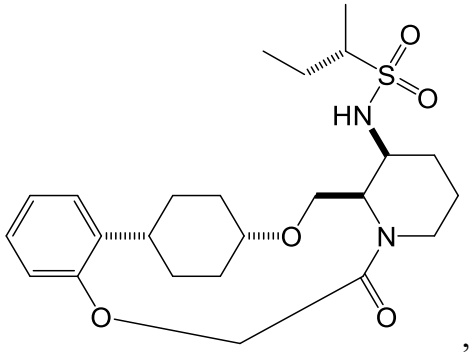
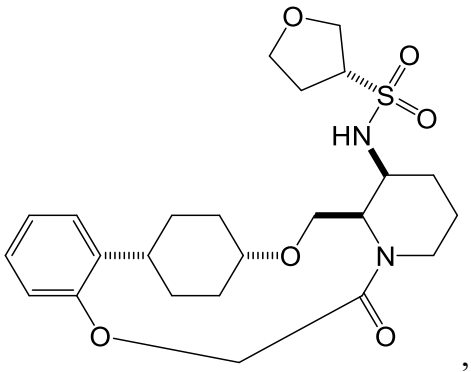
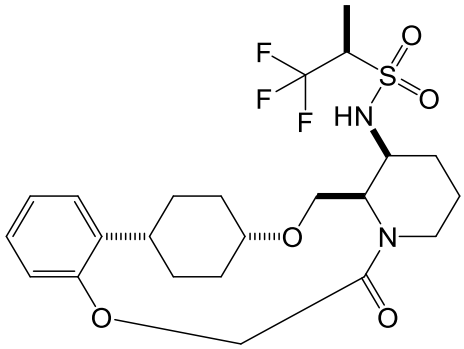
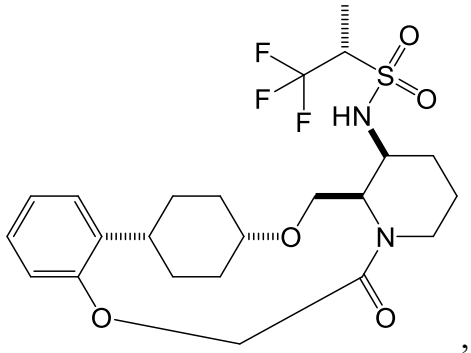
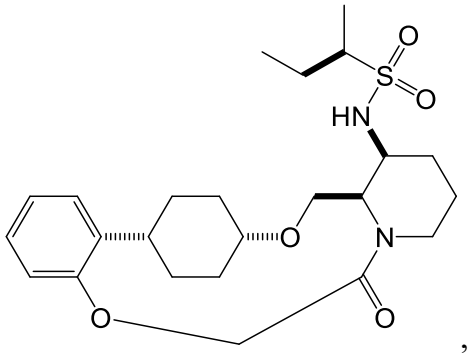
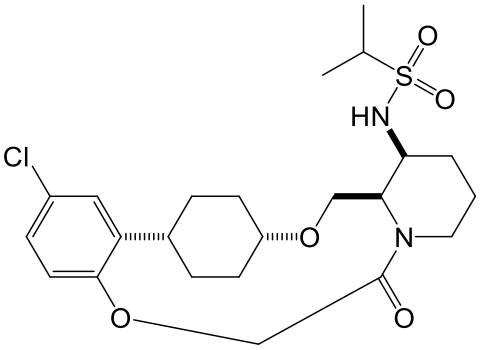
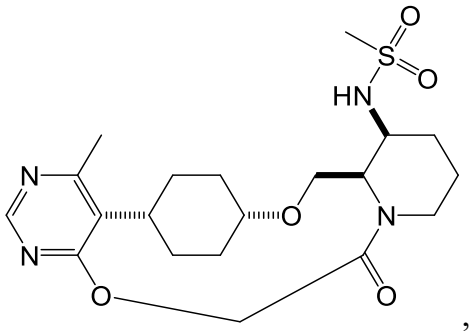
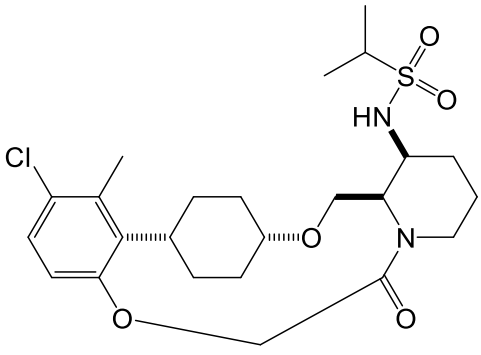
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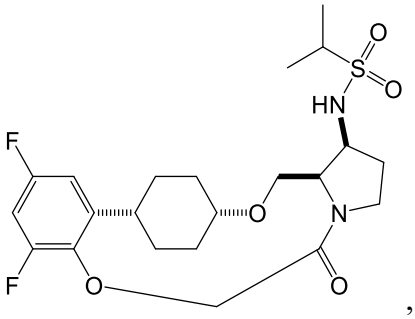
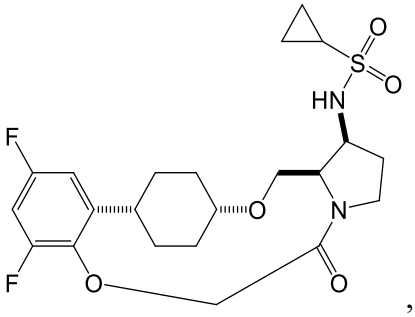
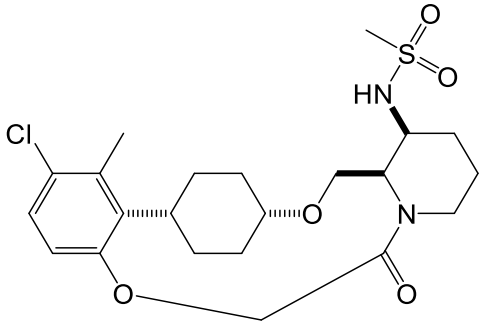
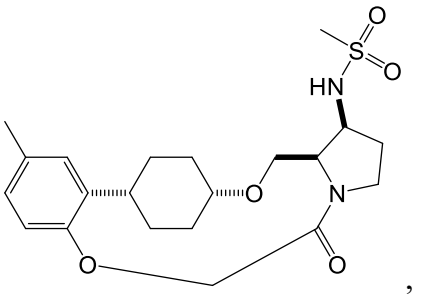
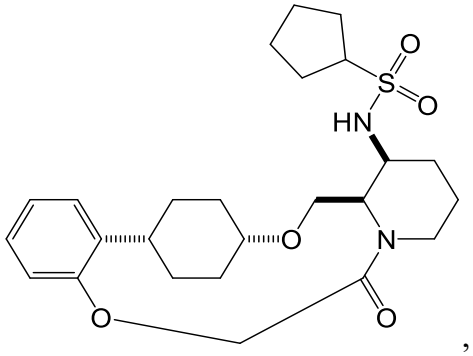
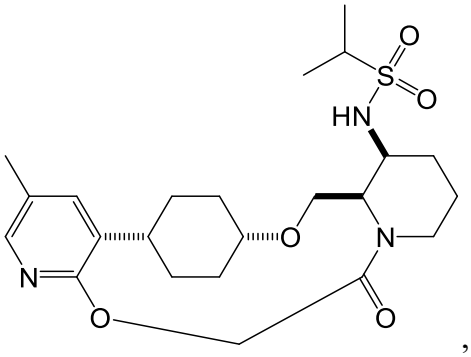
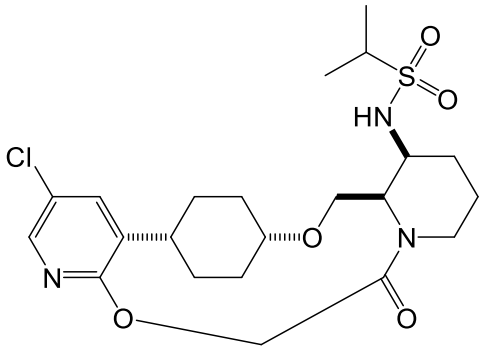
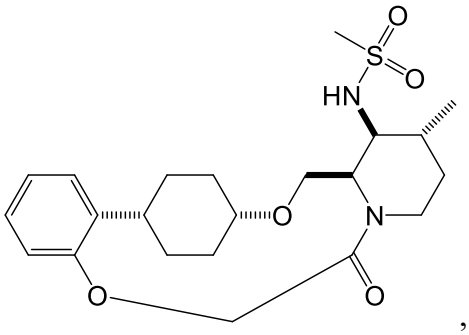
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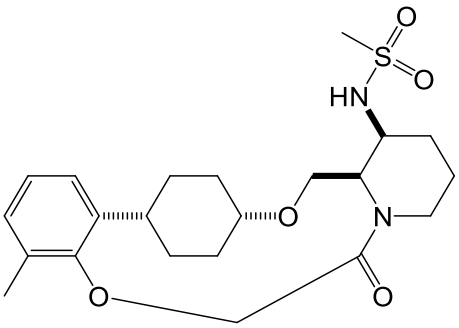
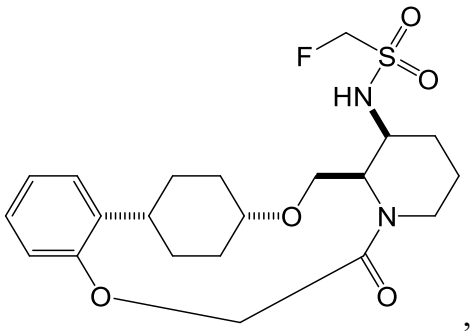
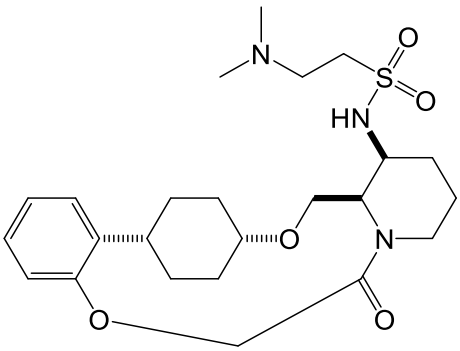
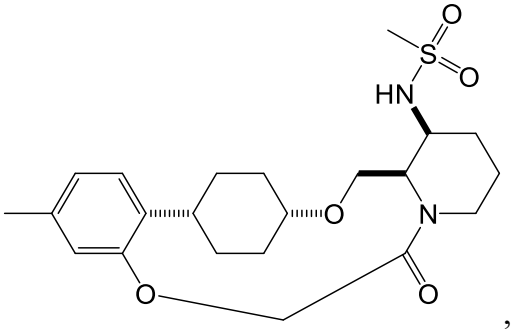
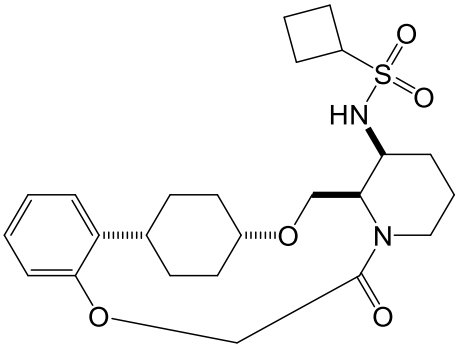
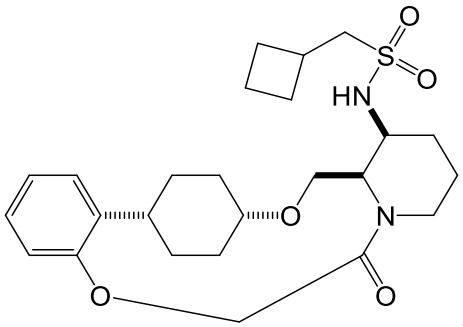
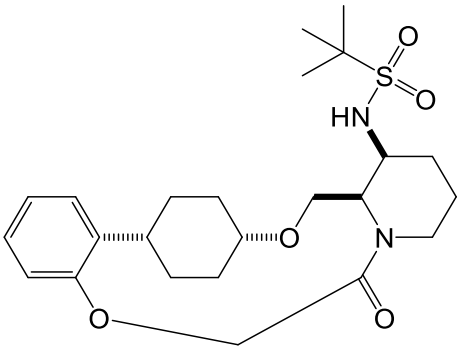
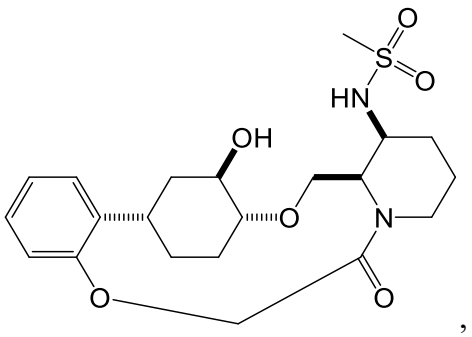
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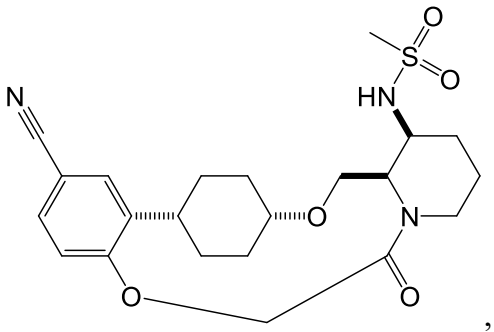
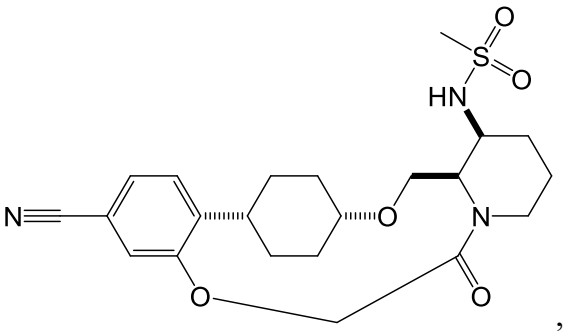
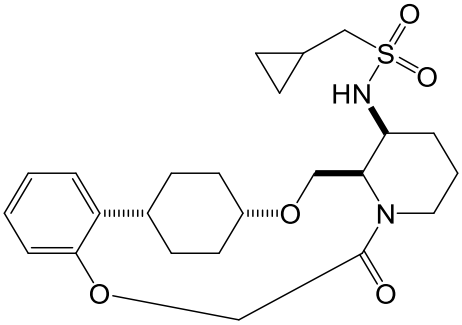
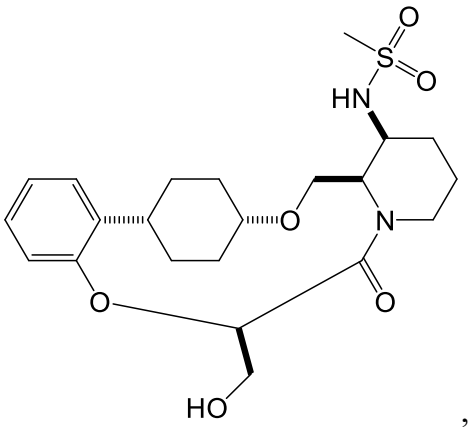
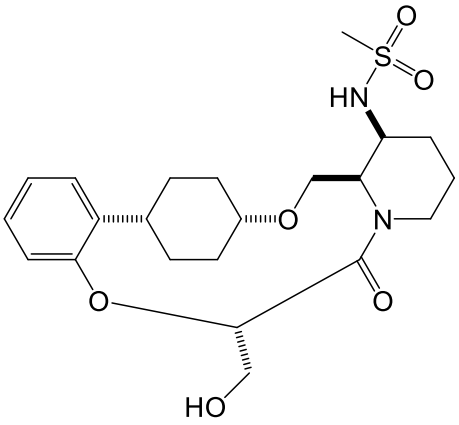
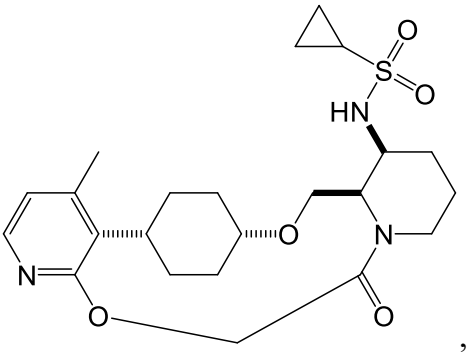
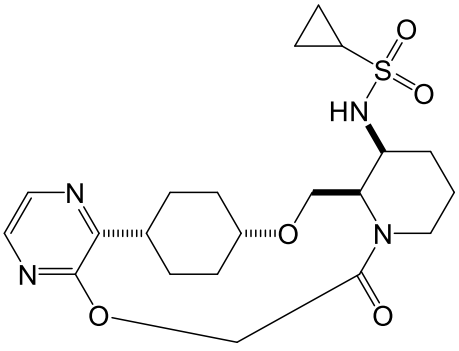
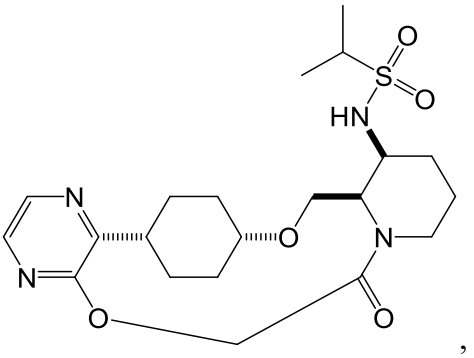

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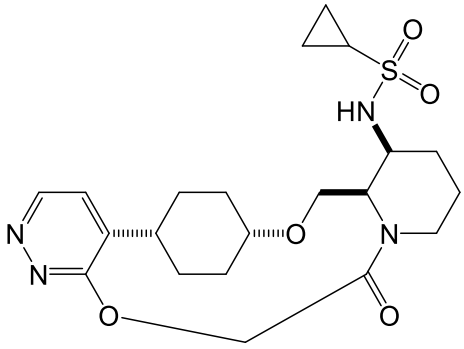
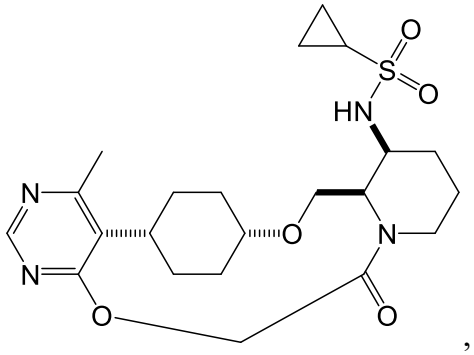
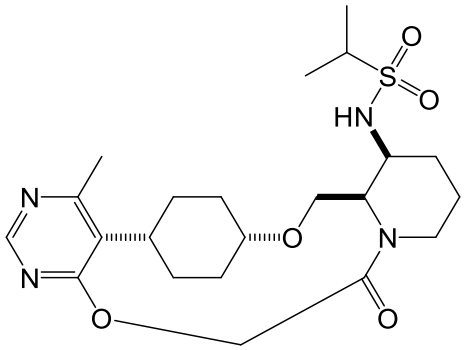
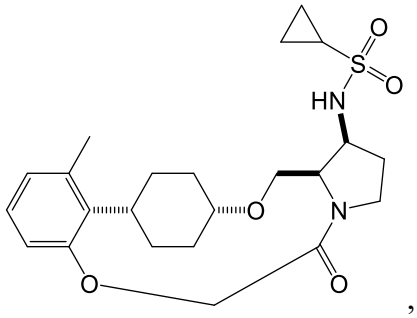
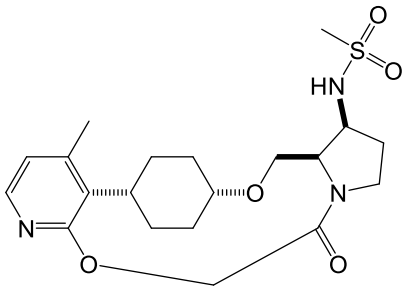
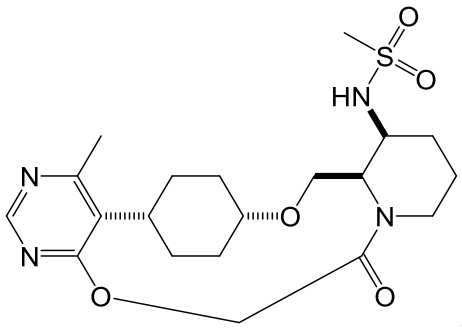
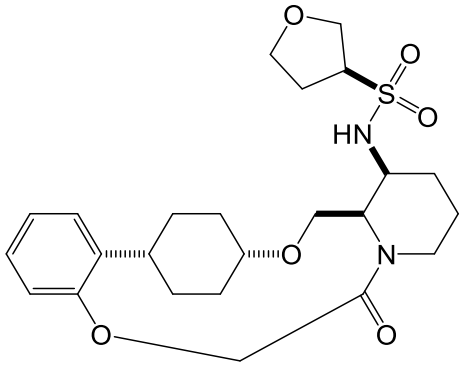
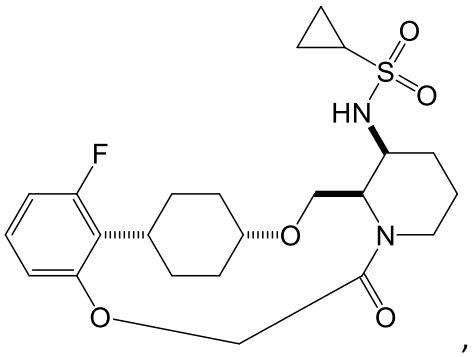

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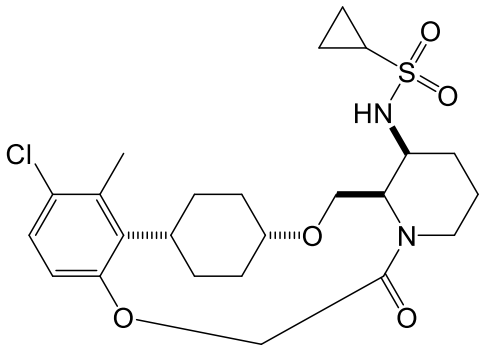
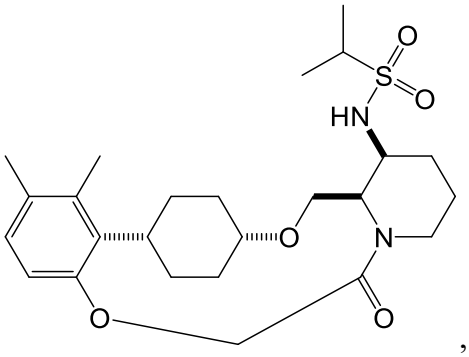
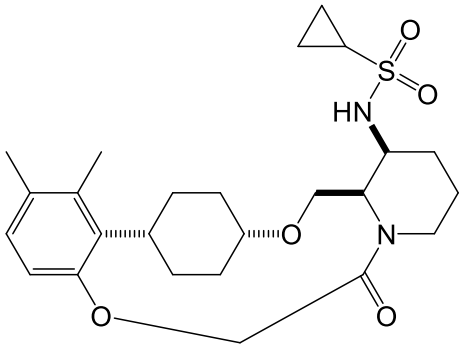
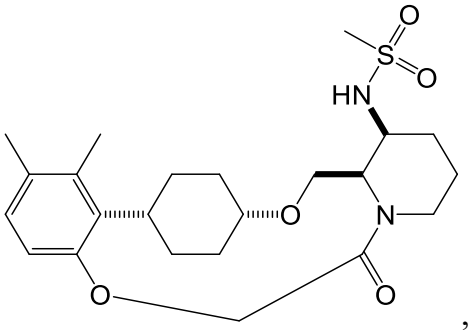
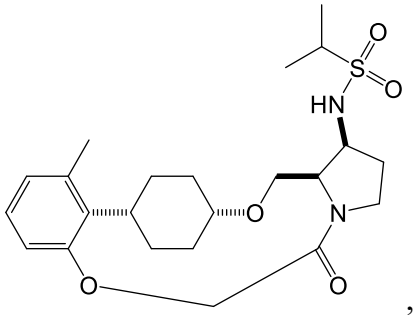
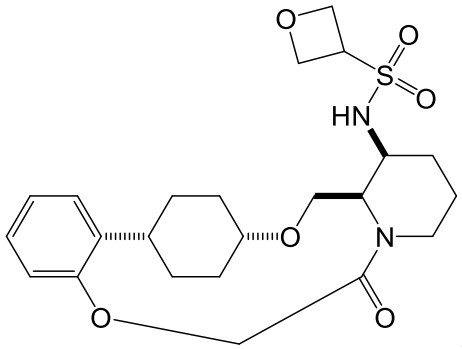
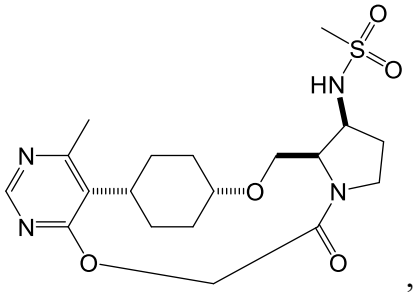
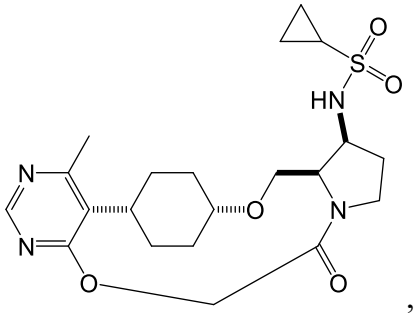

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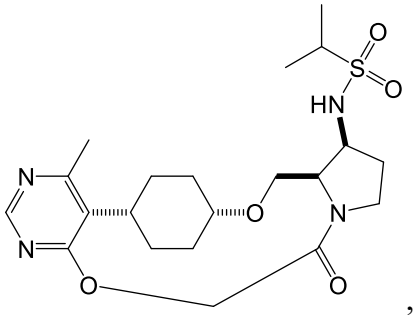
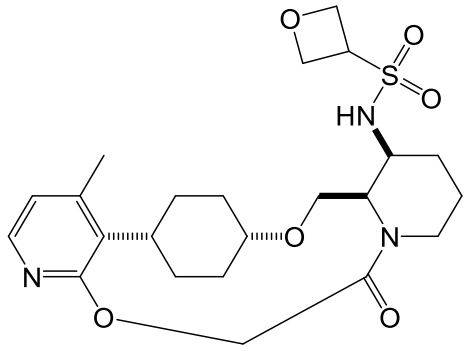
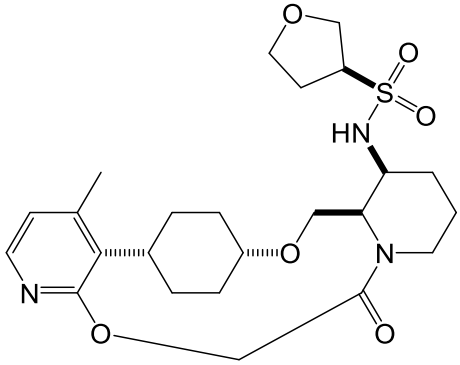
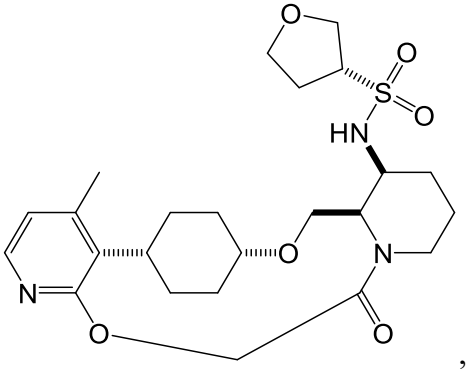
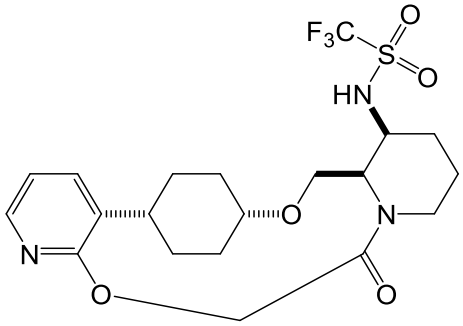
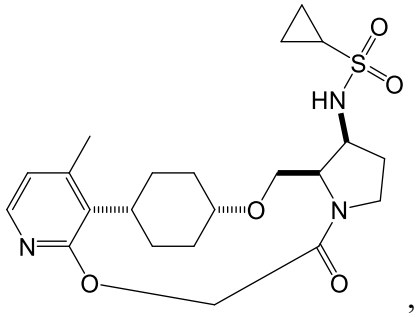
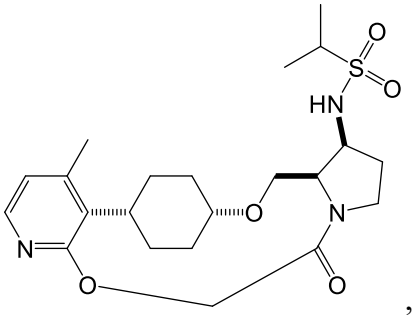
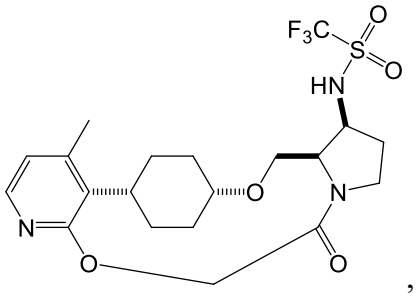

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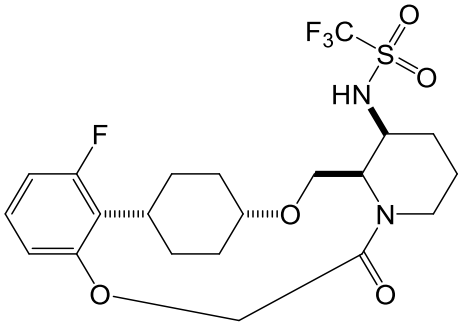
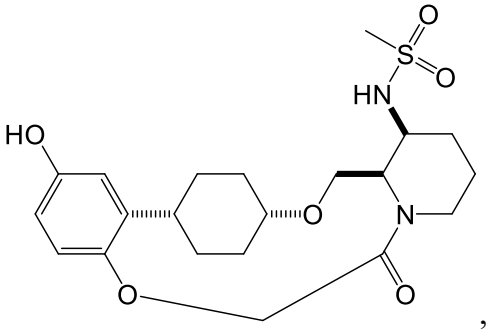
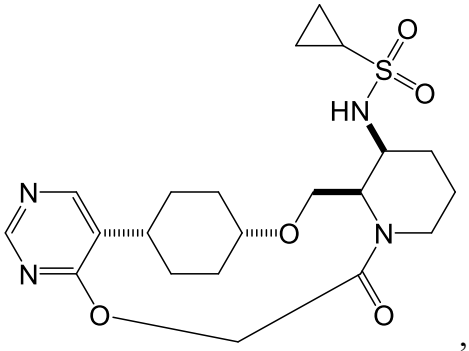
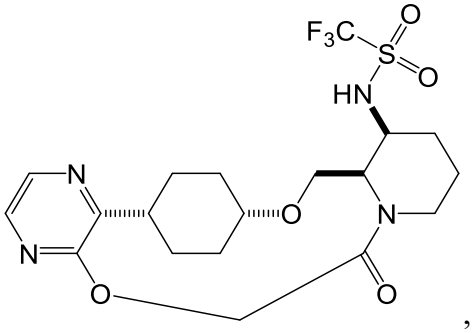
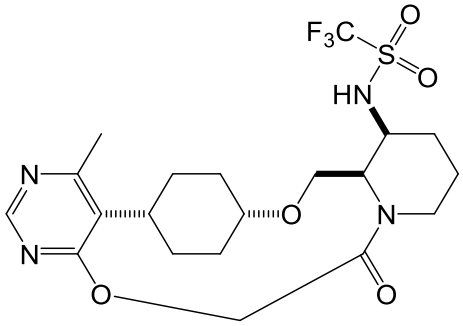
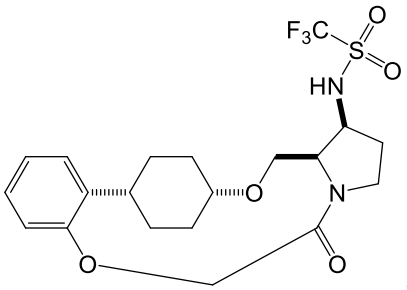
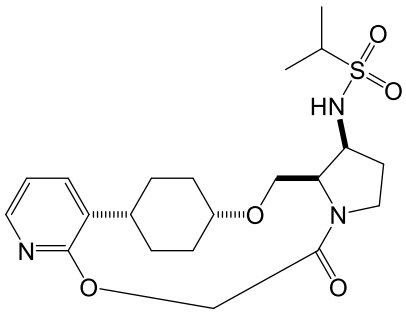
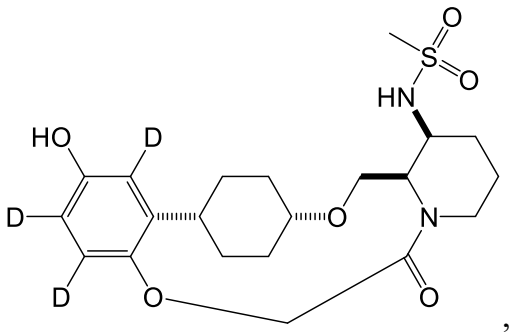

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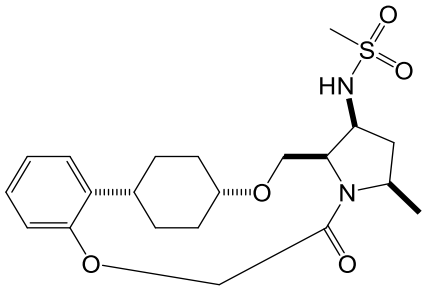
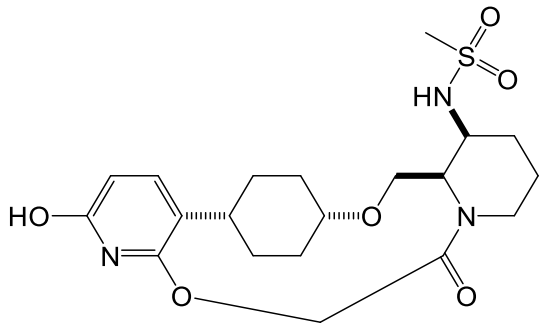
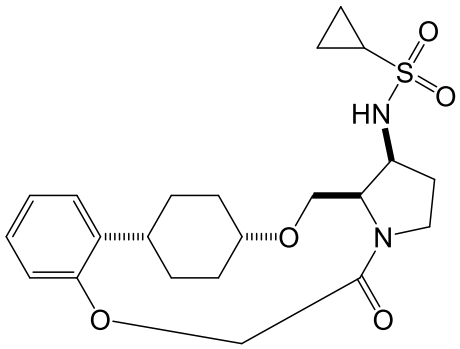
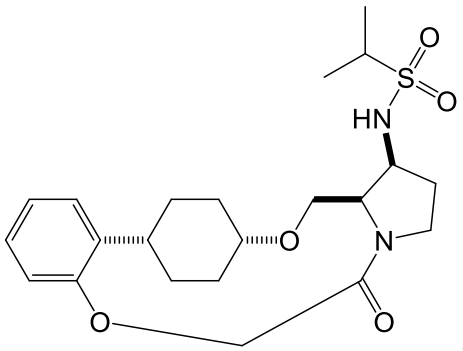
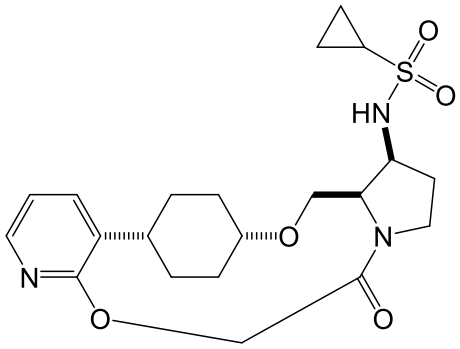
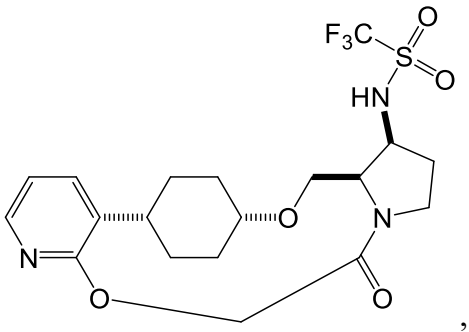
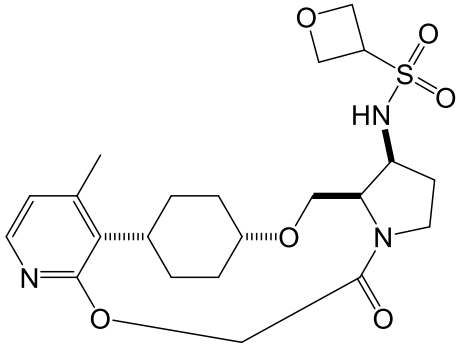
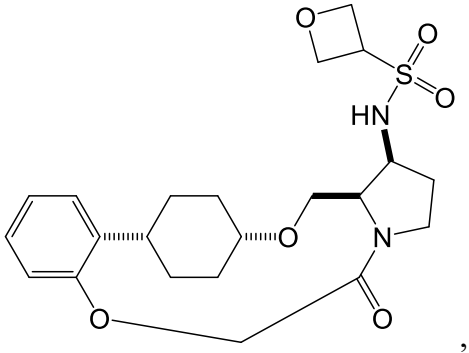

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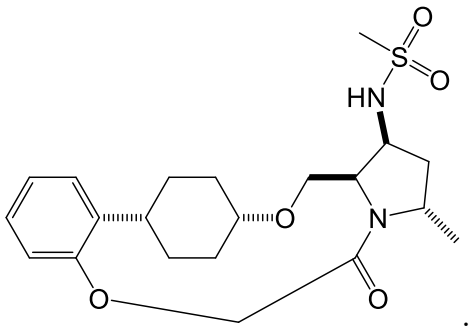

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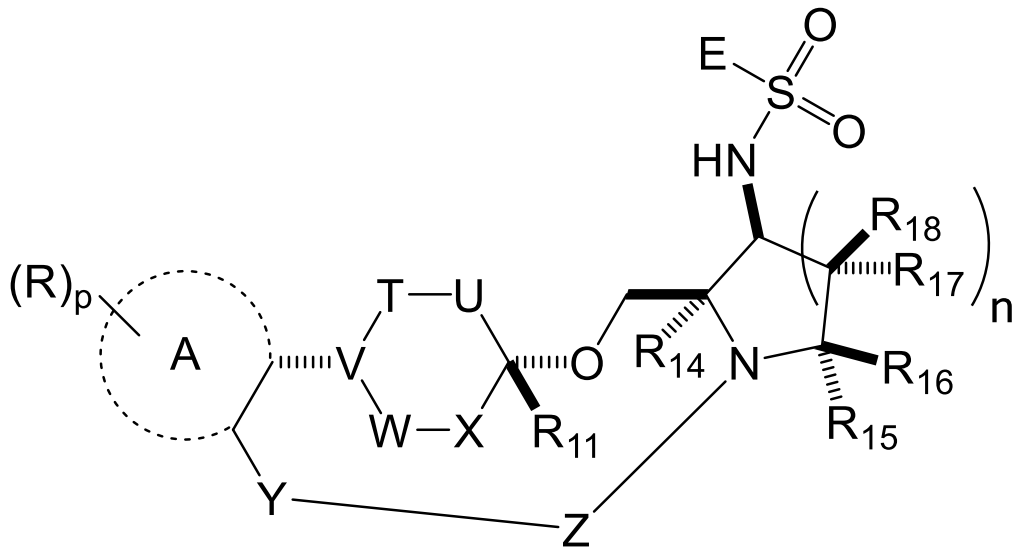

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13. A compound of Formula II-A or a pharmaceutically acceptable salt thereof:



(II-A)

wherein:

ring A is selected from the group consisting of phenyl, pyridinyl, pyridazinyl, pyrimidinyl, pyrazinyl, and triazinyl;

n is 1, 2, or 3;

E is selected from the group consisting of C_1-C_3 alkylene-NR_aR_b, C_1-C_3 alkyl, C_2-C_4 alkenyl, C_2-C_4 alkynyl, C_3-C_8 cycloalkyl, C_1-C_3 alkylene-(C_3-C_8 cycloalkyl), 4- to 10-membered heterocyclyl, C_1-C_3 alkylene-(4- to 10-membered heterocyclyl), C_6-C_{10} aryl, C_1-C_3 alkylene-(C_6-C_{10} aryl), 5- to 10-membered heteroaryl, and C_1-C_3 alkylene-(5- to 10-membered heteroaryl), wherein the C_1-C_3 alkylene-NR_aR_b, C_1-C_3alkyl, C_2-C_4 alkenyl, C_2-C_4 alkynyl, C_3-C_8 cycloalkyl, C_1-C_3 alkylene-(C_3-C_8 cycloalkyl), 4- to 10-membered heterocyclyl, C_1-C_3 alkylene-(4- to 10-membered heterocyclyl), C_6-C_{10} aryl, C_1-C_3 alkylene-(C_6-C_{10} aryl), 5- to 10-membered heteroaryl,

or C_1-C_3 alkylene-(5- to 10-membered heteroaryl) is unsubstituted or substituted with one or more halogen, hydroxyl, C_1-C_3 alkyl, or C_1-C_3 alkoxyl;

T is CR_1R_2 or O;

W is CR_4R_5 or O;

U is CR_6R_7;

X is CR_8R_9;

V is CR_3 or N;

Y is O;

Z is $(CR_{12}R_{13})_m$;

each R is, independently, selected from the group consisting of halogen, deuterium, hydroxyl, cyano, unsubstituted C_1-C_3 alkyl, and C_1-C_3 alkyl substituted with one or more halogen or deuterium;

p is 0, 1, 2, 3, or 4;

R_a and R_b are each, independently, H or unsubstituted C_1-C_3 alkyl;

m is 1, 2, 3, or 4;

and further wherein:

R_1, R_2, R_4, and R_5 are each, independently, selected from the group consisting of H, hydroxyl, halogen, and deuterium;

or, alternatively, R_2 and R_5 together with the carbon atoms to which they are attached, form a single bond;

R_3 is selected from the group consisting of H, deuterium, halogen, hydroxyl, and cyano;

R_6, R_7, R_8, R_9, and R_{11} are each, independently, selected from the group consisting of H, hydroxyl, halogen, and deuterium;

each R_{12} and R_{13} is, independently, selected from the group consisting of H, halogen, deuterium, unsubstituted C_1-C_3 alkyl, and C_1-C_3 alkyl substituted with hydroxyl or one or more halogen; and

R_{14}, R_{15}, and R_{16} are each, independently, selected from the group consisting of H, unsubstituted C_1-C_3 alkyl or C_1-C_3 alkyl substituted with one or more halogen; and

each R_{17} and R_{18} is, independently, selected from the group consisting of H, unsubstituted C_1-C_3 alkyl or C_1-C_3 alkyl substituted with one or more halogen;

with the proviso that one or more of (a)-(f) is present:

(a) at least one R is selected from the group consisting of hydroxyl, cyano, unsubstituted C_1-C_3 alkyl, and C_1-C_3 alkyl substituted with one or more halogen or deuterium;

(b) E is NR_aR_b, C_1-C_3 alkylene-NR_aR_b, C_2-C_3 alkyl, C_2-C_4 alkenyl, C_2-C_4 alkynyl, C_3-C_8 cycloalkyl, C_1-C_3 alkylene-(C_3-C_8 cycloalkyl), 4- to 10-membered heterocyclyl, C_1-C_3 alkylene-(4- to 10-membered heterocyclyl), C_6-C_{10} aryl, C_1-C_3 alkylene-(C_6-C_{10} aryl), 5- to 10-membered heteroaryl, or C_1-C_3 alkylene-(5- to 10-membered heteroaryl), wherein the C_1-C_3 alkylene-NR_aR_b, C_2-C_3 alkyl, C_2-C_4 alkenyl, C_2-C_4 alkynyl, C_3-C_8 cycloalkyl, C_1-C_3 alkylene-(C_3-C_8 cycloalkyl), 4- to 10-membered heterocyclyl, C_1-C_3 alkylene-(4- to 10-membered heterocyclyl), C_6-C_{10} aryl, C_1-C_3 alkylene-(C_6-C_{10} aryl), 5- to 10-membered heteroaryl, or C_1-C_3 alkylene-(5- to 10-membered heteroaryl) is unsubstituted or substituted with one or more halogen, hydroxyl, C_1-C_3 alkyl, or C_1-C_3 alkoxyl;

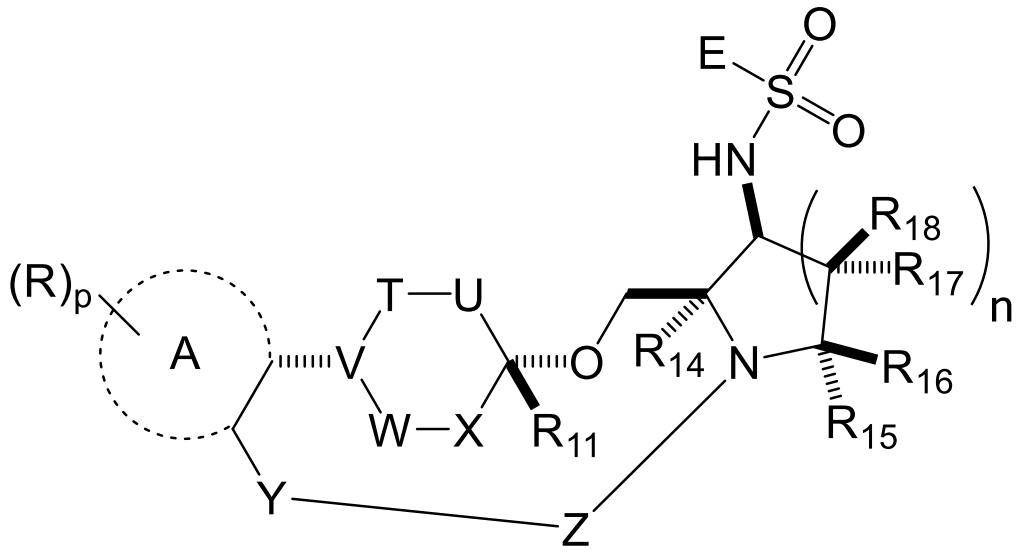
(c) E is C_1 alkyl substituted with one or more halogen, hydroxyl, C_1-C_3 alkyl, or C_1-C_3 alkoxyl;

(d) at least one of R_{14}, R_{15}, R_{16}, R_{17}, and R_{18} is unsubstituted C_1-C_3 alkyl or C_1-C_3 alkyl substituted with one or more halogen;

(e) at least one of R_1, R_2, R_4, R_5, R_6, R_7, R_8, R_9, and R_{11} is hydroxyl; or

(f) at least one of R_{12} and R_{13} is C_1-C_3 alkyl substituted with hydroxyl.

14. The compound of claim 13, wherein the compound of Formula II-A or a pharmaceutically acceptable salt thereof is a compound of Formula II:



(II) or a pharmaceutically acceptable salt thereof.

15. The compound of claim 13 or 14, wherein n is 1 or 2.

16. The compound of claim 15, wherein n is 1.

17. The compound of claim 15, wherein n is 2.

18. The compound of any one of claims 13-17, wherein ring A is phenyl or pyridinyl.

19. The compound of claim 18, wherein ring A is phenyl.

20. The compound of claim 18, wherein ring A is pyridinyl.

21. The compound of any one of claims 13-20, wherein T is CR_1R_2.

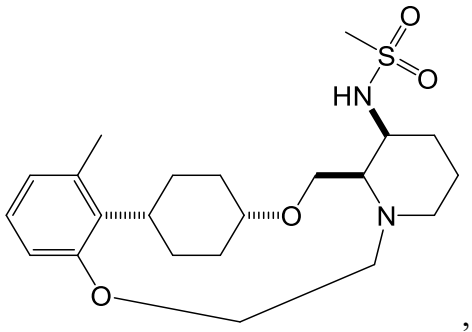
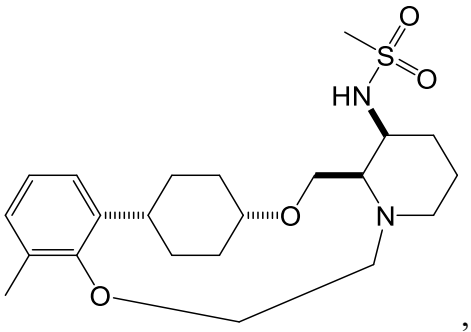
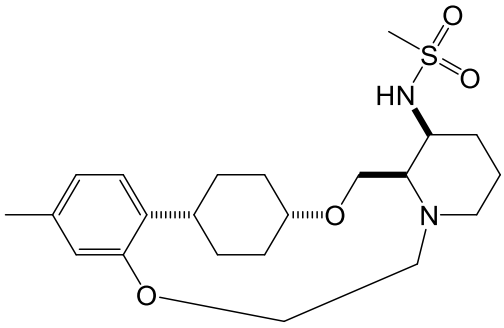
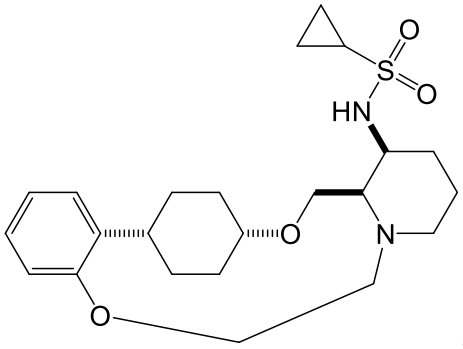
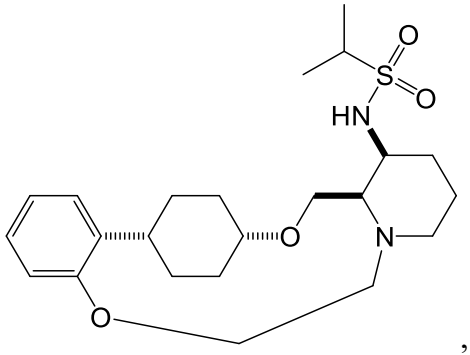
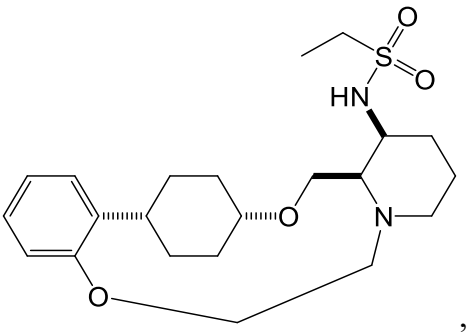
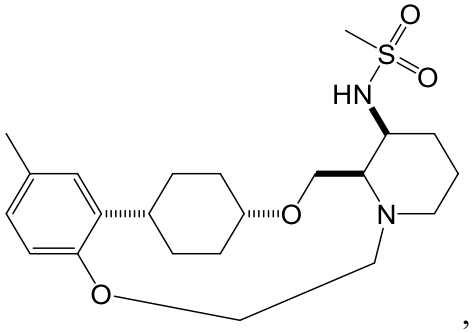
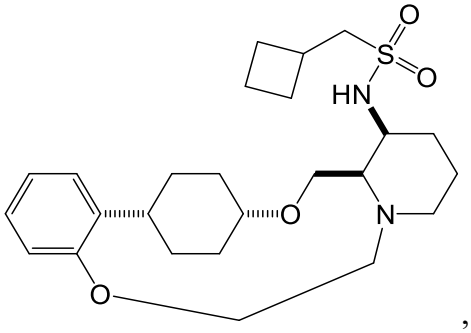
22. The compound of any one of claims 13-21, wherein W is CR_4R_5.

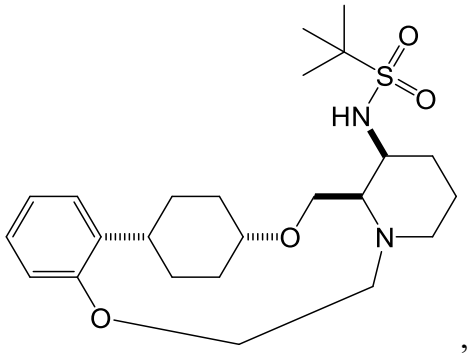
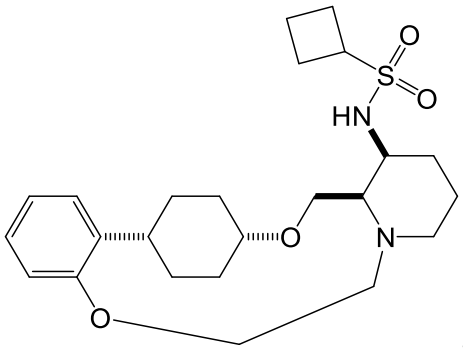
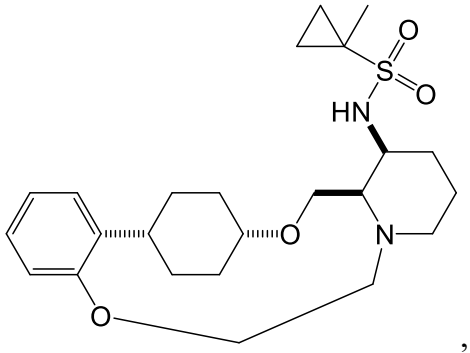
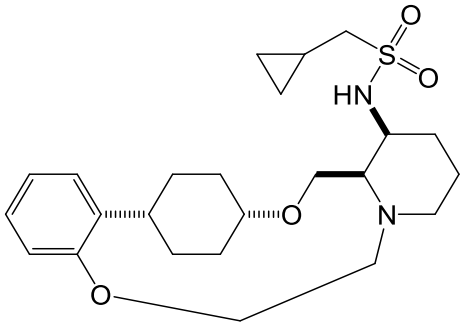
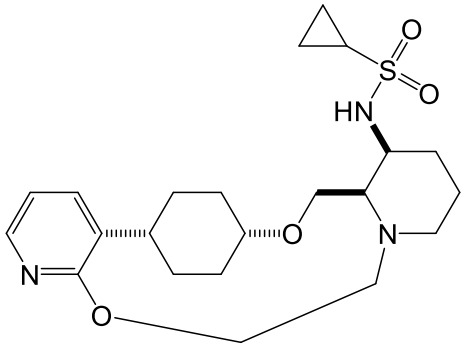
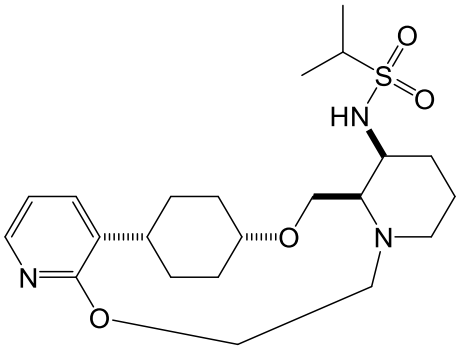
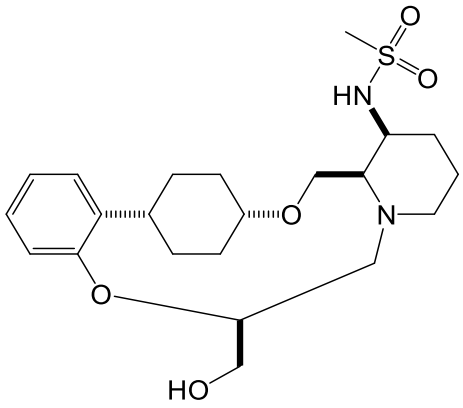
23. The compound of any one of claims 13-22, wherein V is CR_3.

24. The compound of any one of claims 13-23, wherein m is 2 or 3.

25. The compound of any one of claims 24, wherein m is 2.

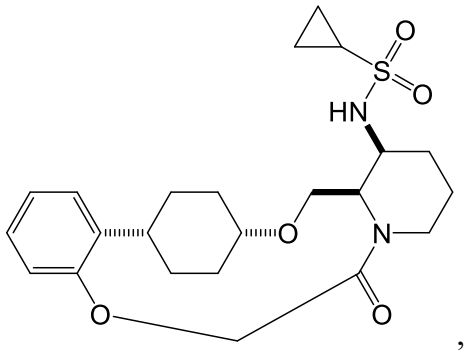
26. The compound of claim 14, wherein the compound or a pharmaceutically acceptable salt thereof is selected from the group consisting of:


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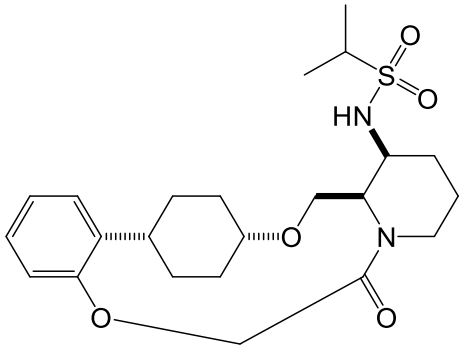
27. The compound according to claim 12, wherein the compound is:



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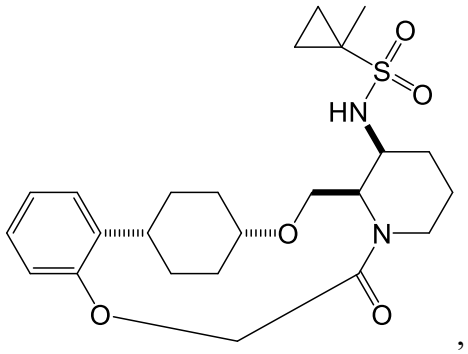
or a pharmaceutically acceptable salt thereof.

28. The compound of claim 12, wherein the compound is:



or a pharmaceutically acceptable salt thereof.

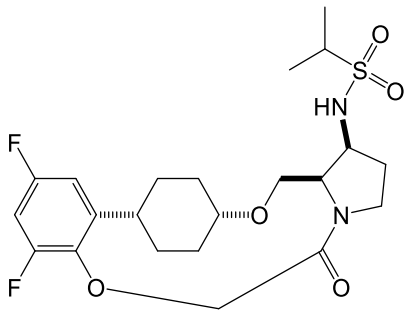
29. The compound according to claim 12, wherein the compound is:



,

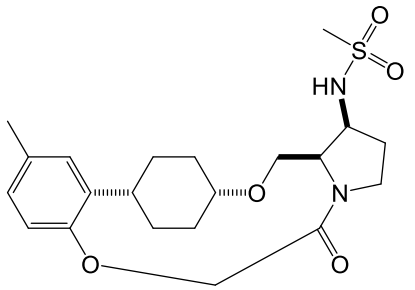
or a pharmaceutically acceptable salt thereof.

30. The compound of claim 12, wherein the compound is:



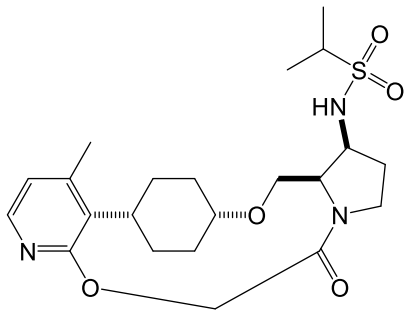
or a pharmaceutically acceptable salt thereof.

31. The compound of claim 12, wherein the compound is:



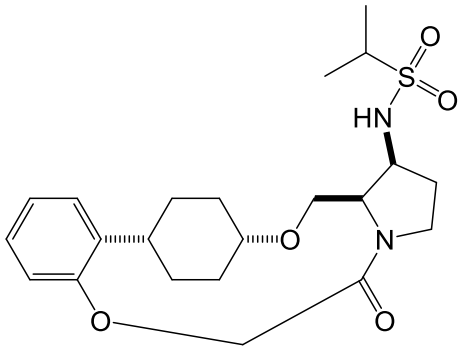
or a pharmaceutically acceptable salt thereof.

32. The compound of claim 12, wherein the compound is:



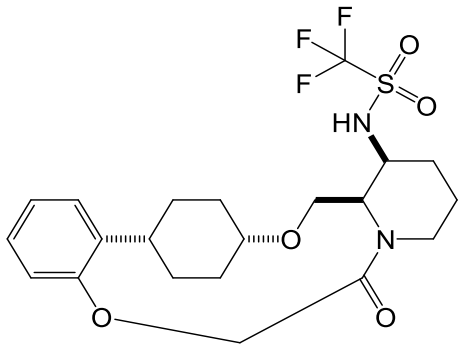
or a pharmaceutically acceptable salt thereof.

33. The compound of claim 12, wherein the compound is:



or a pharmaceutically acceptable salt thereof.

34. The compound of claim 12, wherein the compound is:



or a pharmaceutically acceptable salt thereof.

35. A pharmaceutical composition comprising a compound of any one of claims 1-34 or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier.

36. Use of a compound of any one of claims 1-34 or a pharmaceutically acceptable salt thereof, or a composition according to claim 35 for the manufacture of a medicament for narcolepsy and/or cataplexy.