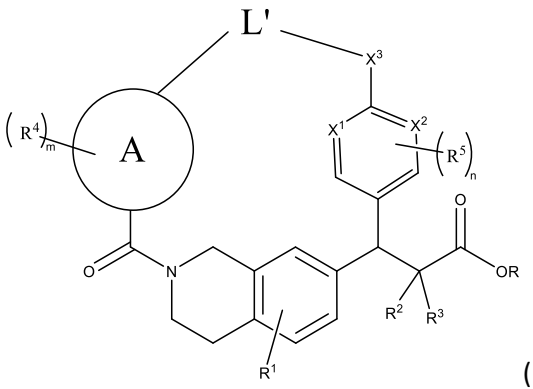
Claims

1. A compound of Formula (IA):



(IA)

or a pharmaceutically acceptable salt thereof, wherein:

R is H or C_{1-6}alkyl optionally substituted with one substituent selected from -OH, C_{1-6} alkyloxy, or C_{6-12} aryl;

R^1 is H or C_{1-6} alkyl;

R^2 is H or C_{1-6} alkyl;

R^3 is H or C_{1-6} alkyl;

n is 0, 1, or 2;

one of X^1 and X^2 is CH and the other is N, or X^1 and X^2 are each N;

X^3 is CH_2 or O

each R^5 is independently halo, C_{1-6} alkyl, or C_{1-6} alkyloxy;

Ring A is C_{6-12} arylene or C_{3-12} heteroarylene containing 1-2 heteroatoms independently selected from N and O;

m is 1, 2, 3, or 4;

each R^4 is independently H, halo, C_{1-6} alkyl, or C_{1-6} alkoxy, wherein the C_{1-6} alkyl and C_{1-6} alkoxy groups are optionally substituted with 1-3 groups independently selected from halo, C_{1-6} alkyloxy, amido, and N,N-dimethylamido groups; and

L' is C_{4-6} alkylene, C_{4-6} alkenylene, C_{4-6} heteroalkylene, or C_{4-6} heteroalkenylene, each of which is optionally substituted with 1 or 2 groups independently selected from halo and C_{1-6} alkyl, and wherein the heteroalkylene and heteroalkenylene comprise 1 or 2 oxygen atoms.

2. The compound of claim 1, or a pharmaceutically acceptable salt thereof, wherein each R^5 is independently C_{1-4} alkyl or C_{1-4} alkyloxy, preferably methyl or methoxy.

3. The compound of claim 1 or 2, or a pharmaceutically acceptable salt thereof, wherein L' is C_{4-6} alkylene, C_{4-6} alkenylene, C_{4-6} heteroalkylene, or C_{4-6} heteroalkenylene, wherein the heteroalkylene and heteroalkenylene comprise 1 or 2 oxygen atoms, wherein the C_{4-6} alkenylene or C_{4-6} heteroalkenylene preferably comprise one unsaturated bond.

4. The compound of any one of claims 1 to 3, or a pharmaceutically acceptable salt thereof, wherein:

(i) X^3 is CH_2 and L' is C_{4-6} alkenylene or C_{4-6} heteroalkenylene containing one unsaturated bond;

(ii) X^3 is O and L' is C_{4-6} alkenylene or C_{4-6} heteroalkenylene containing one unsaturated bond;

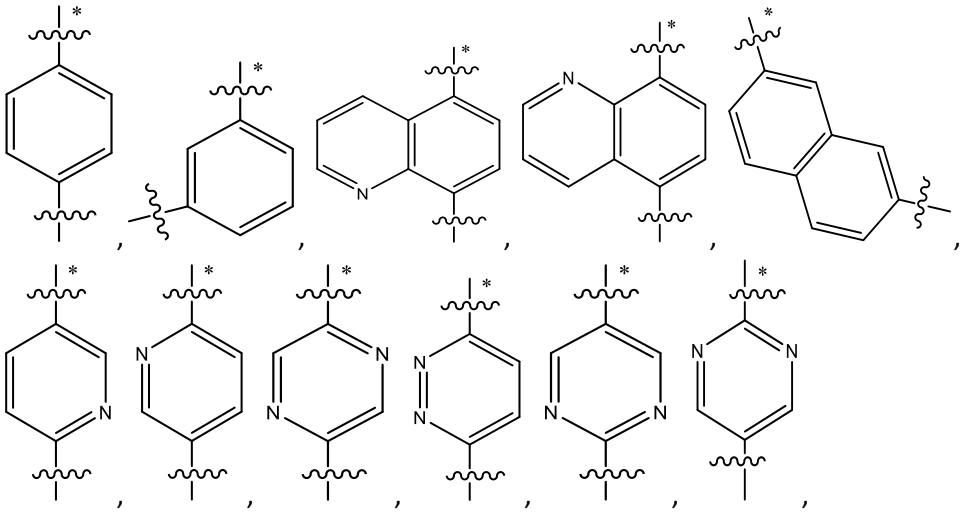
(iii) X^3 is CH_2 and L' is C_{4-6} alkylene or C_{4-6} heteroalkylene, wherein C_{4-6} heteroalkylene comprises 1 or 2 oxygen atoms;

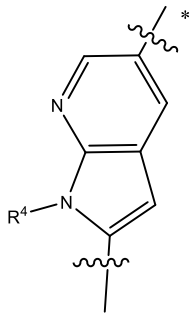
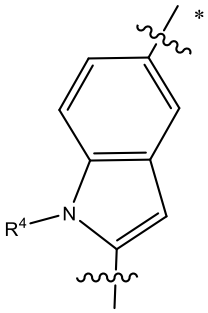
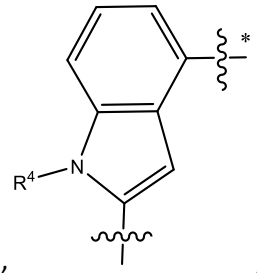
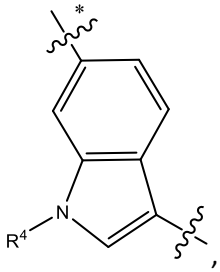
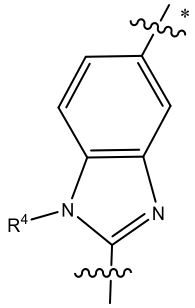
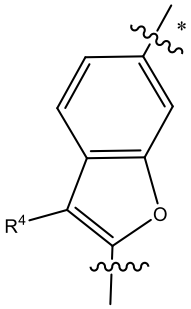
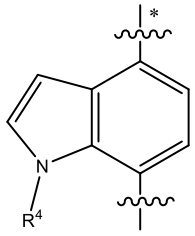
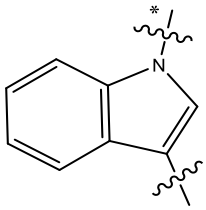
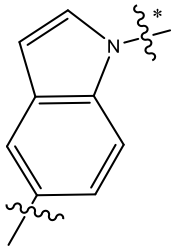
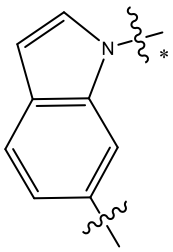
(iv) X^3 is O and L' is C_{4-6} alkylene or C_{4-6} heteroalkylene, wherein the C_{4-6} heteroalkylene comprises 1 oxygen atom;

(v) X^3 is O and L' is C_{4-6} alkylene; or

(vi) X^3 is CH_2 and L' is C_{4-6} alkylene.

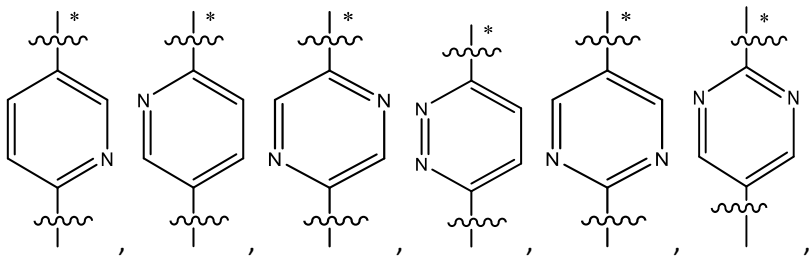
5. The compound of any one of claims 1 to 4, or a pharmaceutically acceptable salt thereof, wherein Ring A is

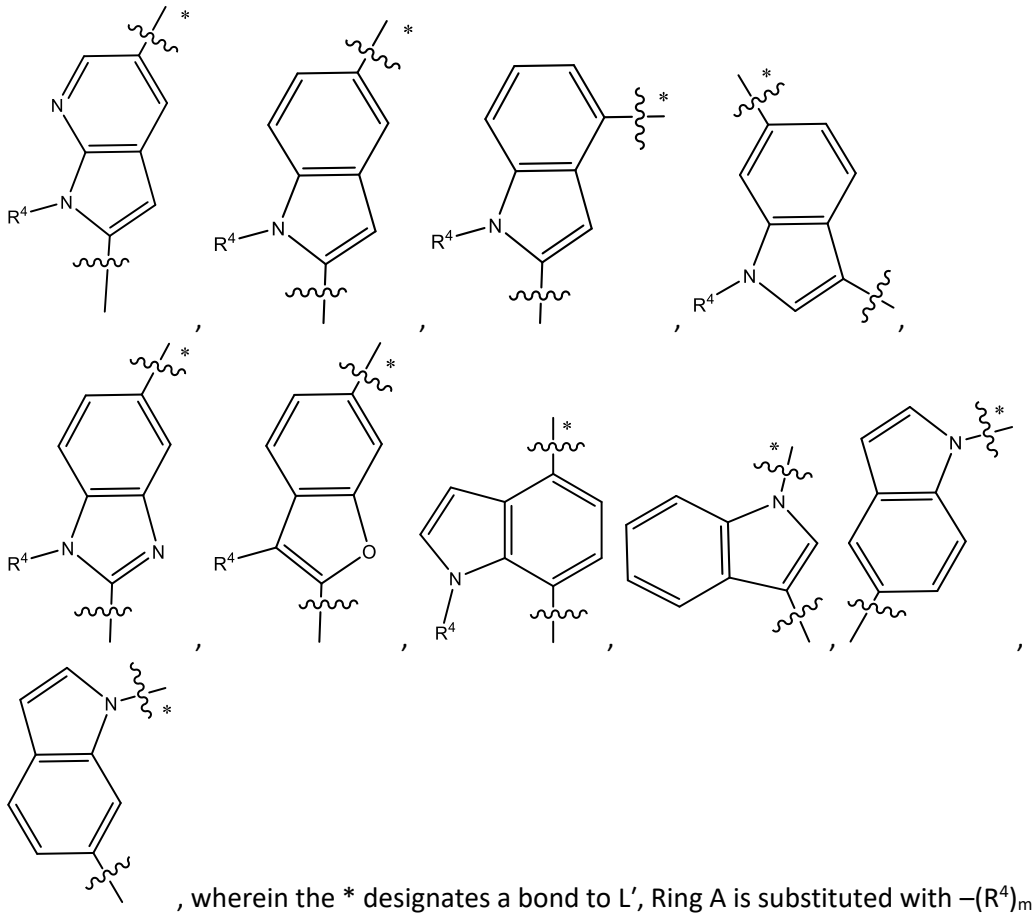


, wherein the * designates a bond to L', Ring A is substituted with $-(R^4)_m$ where m is 1, 2, 3, or 4; and each R^4 is independently H, halo, C_{1-6} alkyl, or C_{1-6} alkoxy, wherein the C_{1-6} alkyl and C_{1-6} alkoxy groups are optionally substituted with 1-3 groups independently selected from halo, C_{1-6} alkyloxy, amido, and N,N-dimethylamido groups.

6. The compound of any one of claims 1 to 4, or a pharmaceutically acceptable salt thereof, wherein Ring A is




, wherein the * designates a bond to L', Ring A is substituted with $-(R^4)_m$ where m is 1 or 2; and each R^4 is independently H, halo, C_{1-4} alkyl, or C_{1-4} alkoxy, wherein the C_{1-4} alkyl and C_{1-4} alkoxy groups are optionally substituted with 1-3 groups independently selected from halo, C_{1-4} alkyloxy, amido, and N,N-dimethylamido groups.

7. The compound of any one of claims 1 to 6, or a pharmaceutically acceptable salt thereof, wherein each R^4 is independently selected from H, halo, C_{1-4} alkyl, and C_{1-4} alkoxy, wherein the C_{1-4} alkyl and C_{1-4} alkoxy groups are optionally substituted with 1-3 groups independently selected from halo, C_{1-4} alkyloxy, amido, and N,N-dimethylamido, preferably selected from F, Cl, methoxy, amido, and N,N-dimethylamido.

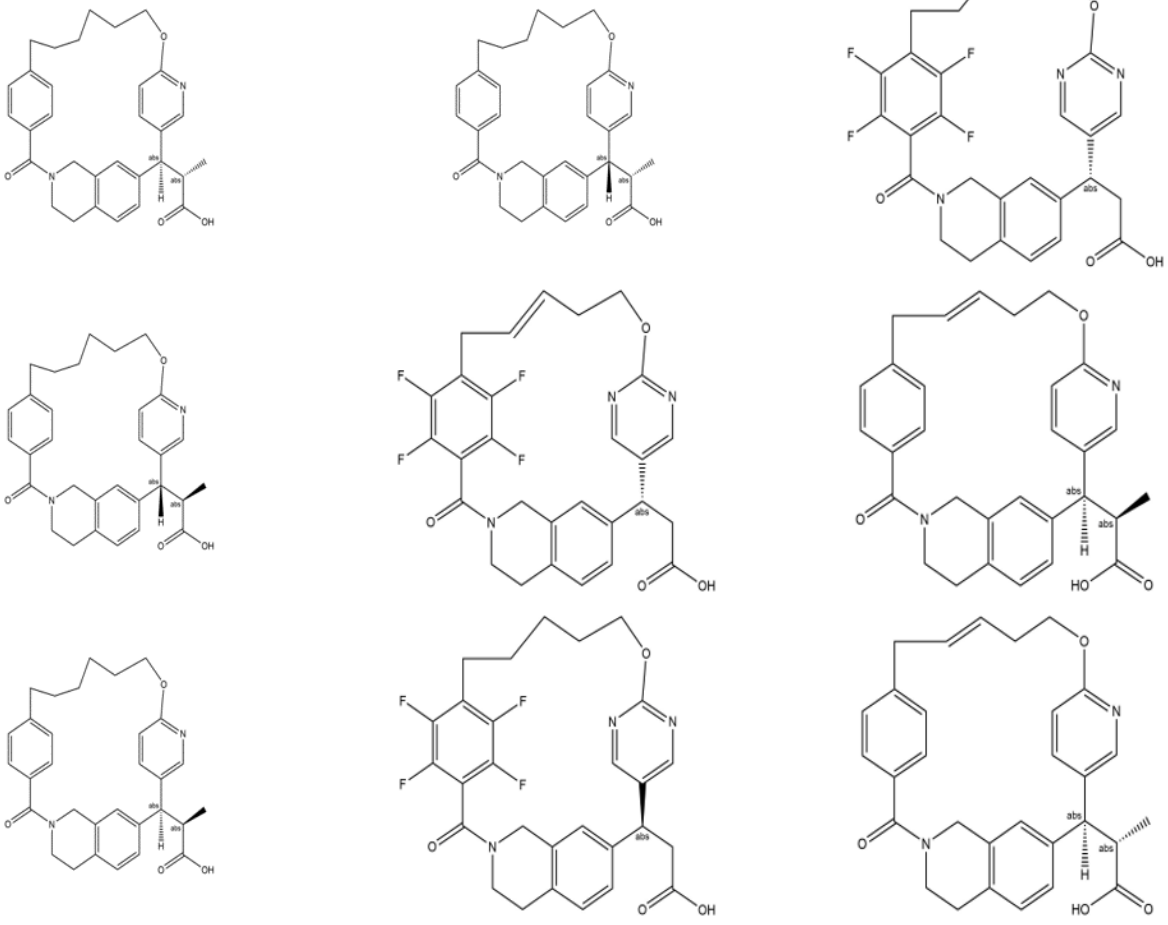
8. The compound of any one of claims 1 to 7, or a pharmaceutically acceptable salt thereof, wherein each R^4 is independently selected from H, methyl, isobutyl, F, Cl, trifluoromethyl, methoxy, difluoromethoxy, trifluoromethoxy, N,N-dimethylamido, 3,3,3-trifluoropropyl, 2,2-difluoroethyl, 3-fluoropropyl, and methoxyethyl.

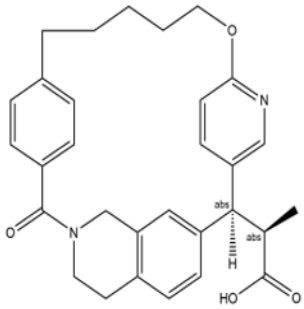
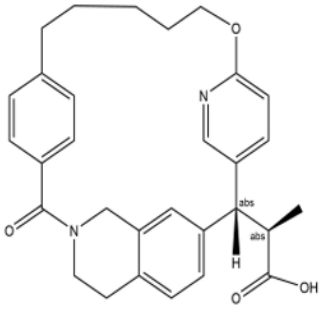
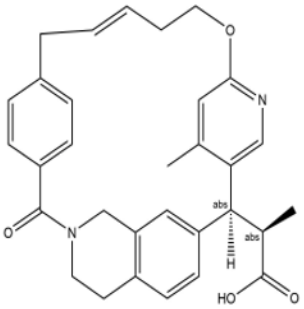
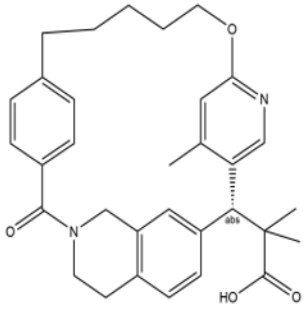
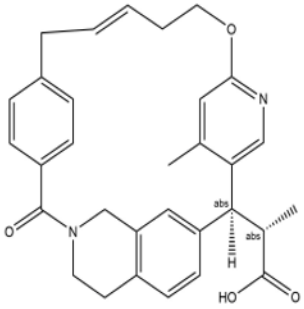
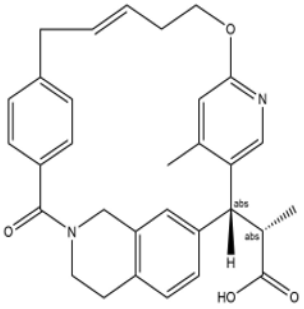
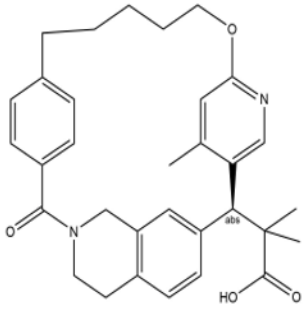
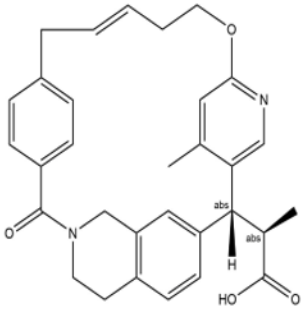
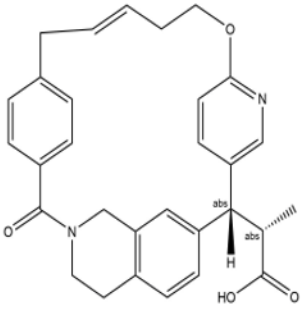
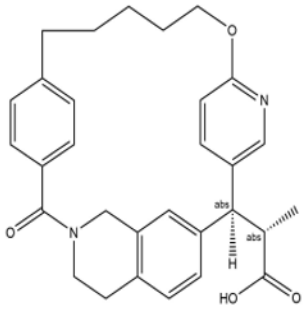
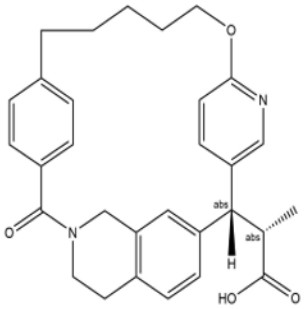
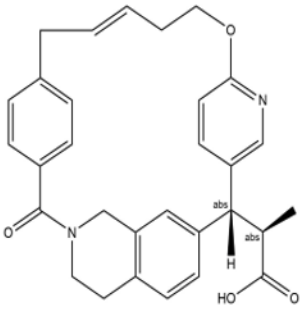
9. The compound of any one of claims 1 to 8, or a pharmaceutically acceptable salt thereof, wherein R is H, methyl, ethyl, 2-hydroxy-ethyl, or benzyl.

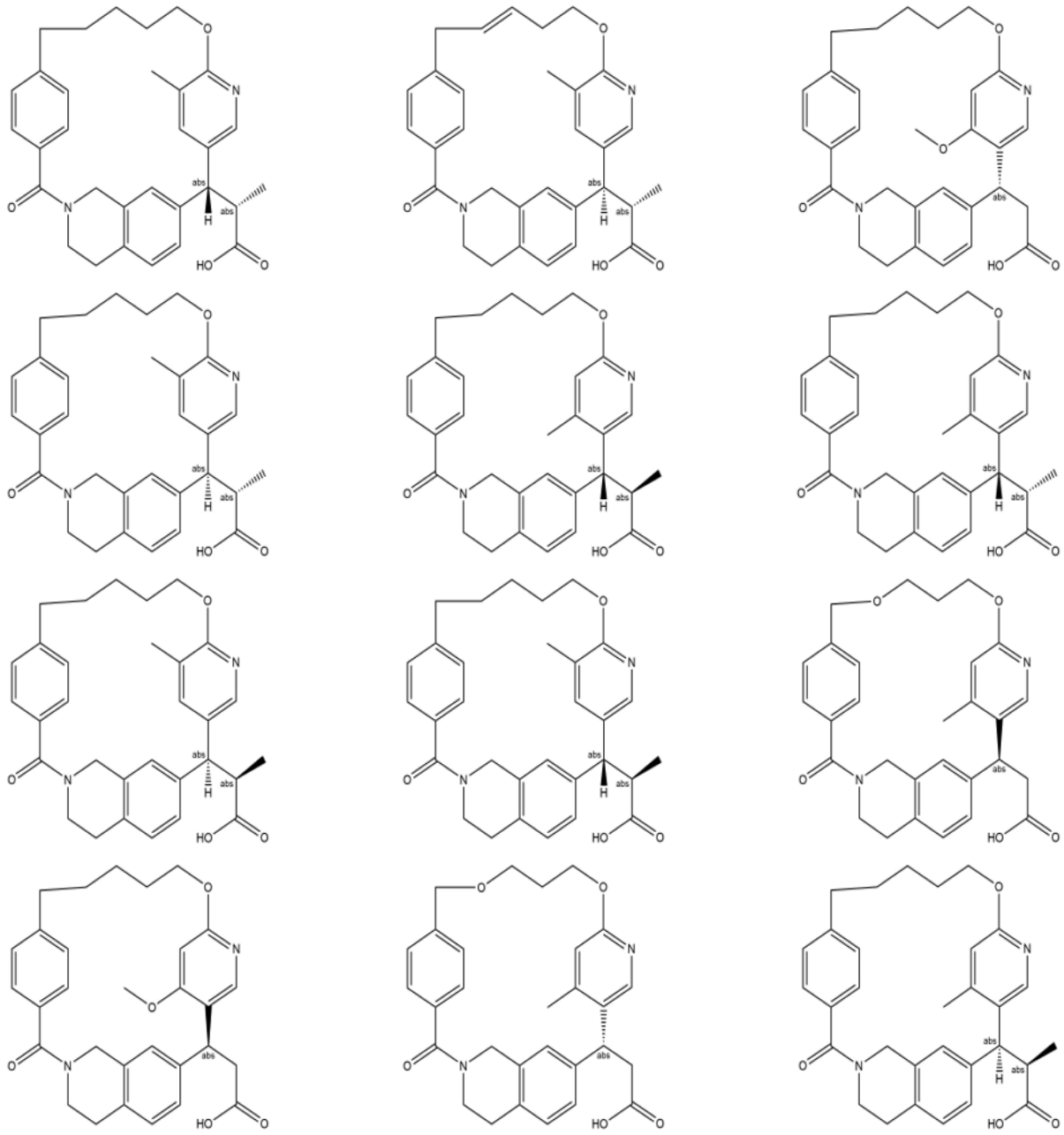
10. The compound of any one of claims 1 to 9, or a pharmaceutically acceptable salt thereof, wherein R^1 is H or C_{1-4} alkyl, preferably methyl
wherein R^2 is H or C_{1-4} alkyl, preferably methyl; and/or
wherein R^3 is H or C_{1-4} alkyl, preferably methyl.

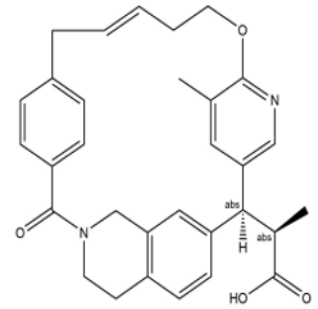
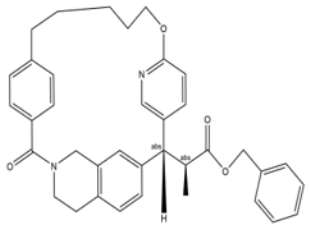
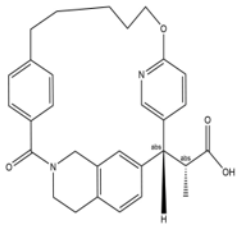
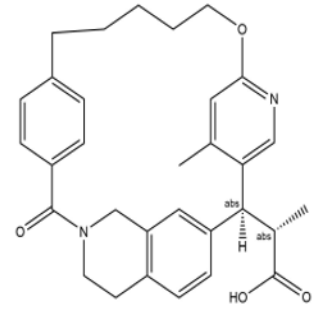
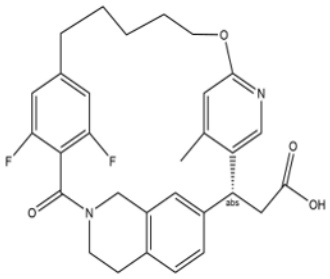
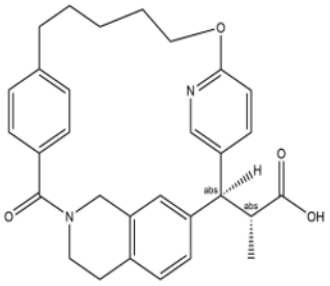
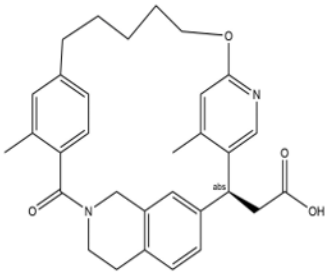
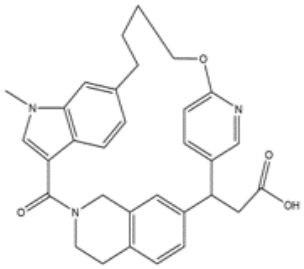
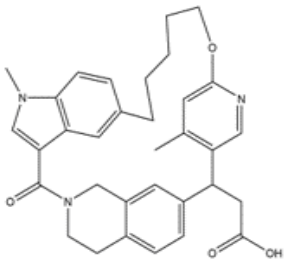
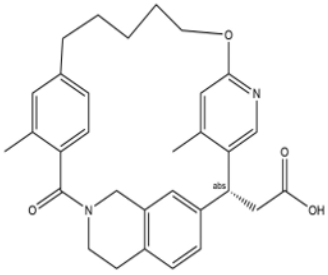
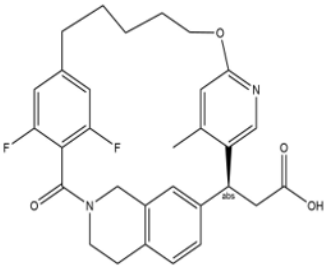
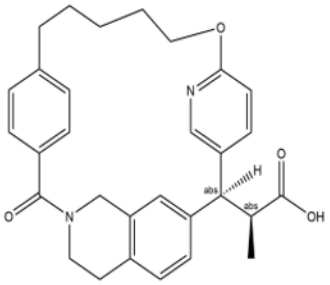
11. The compound of any one of claims 1 to 10, or a pharmaceutically acceptable salt thereof, wherein R^2 is H or C_{1-4} alkyl, preferably methyl.

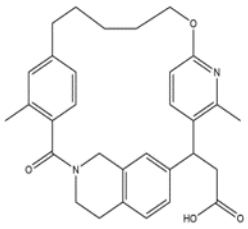
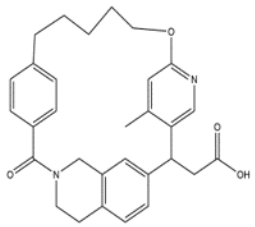
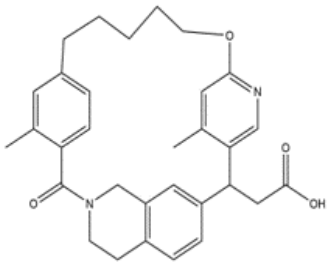
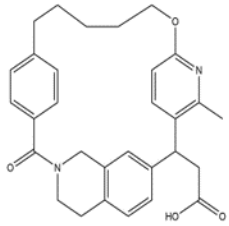
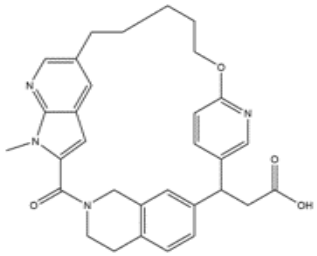
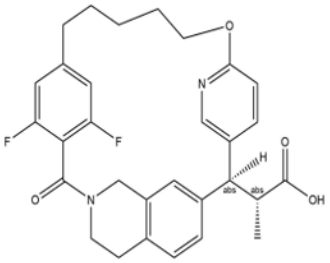
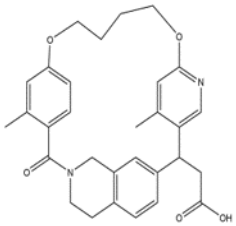
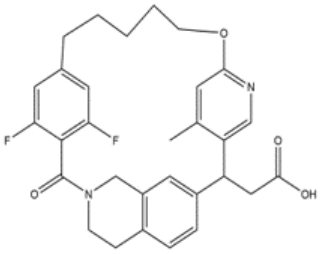
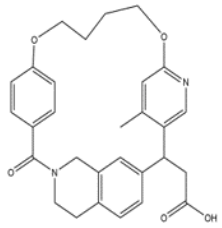
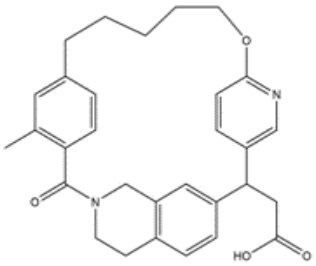
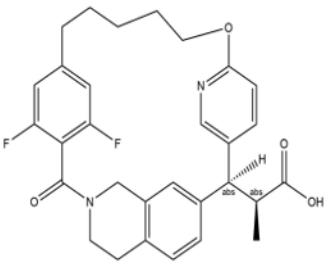
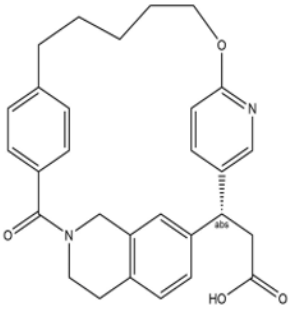
12. A compound selected from the following compounds, or a pharmaceutically acceptable salt thereof:

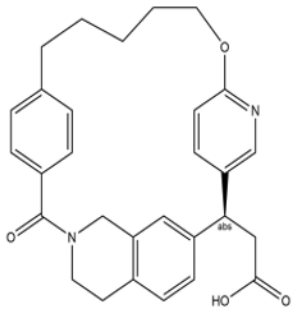


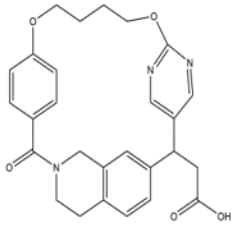













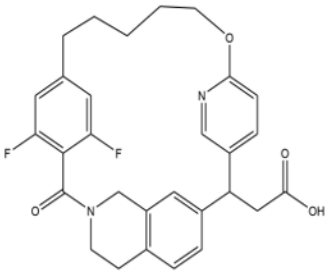


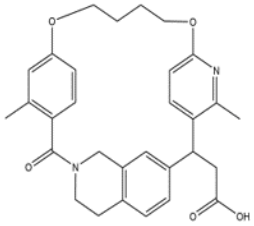













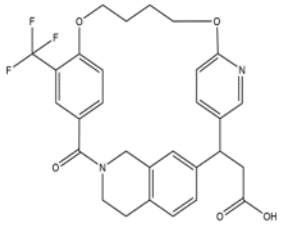













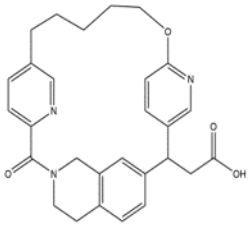


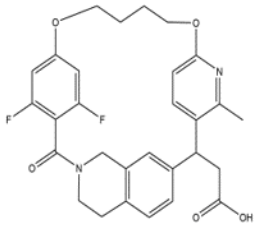


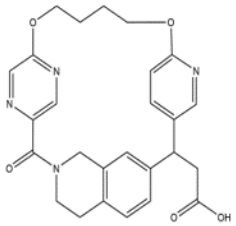


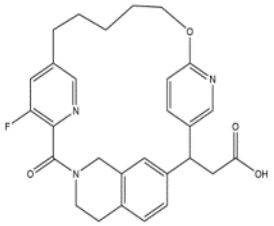


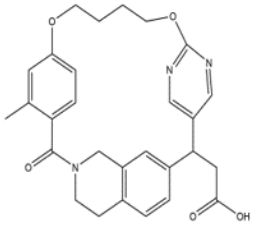


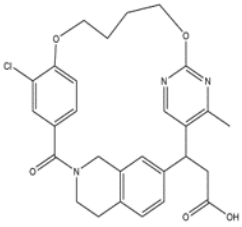


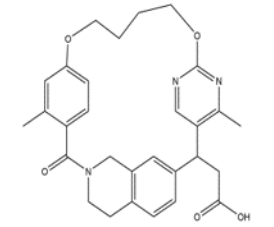


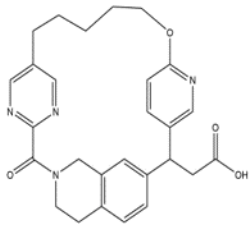


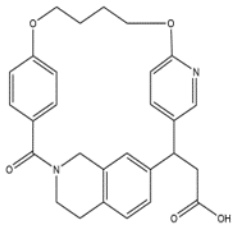


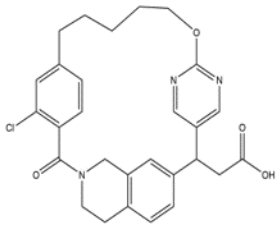


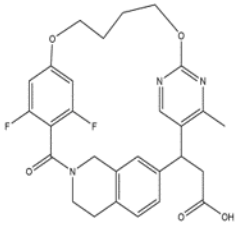


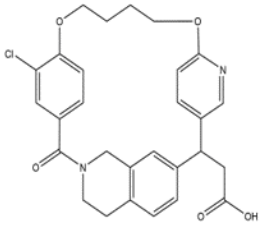


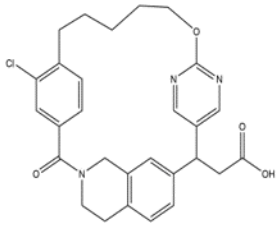


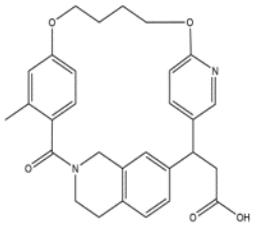


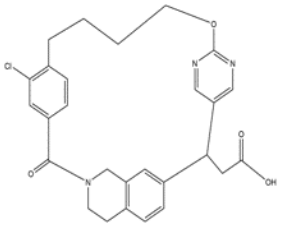


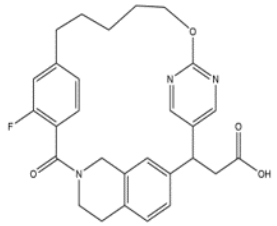


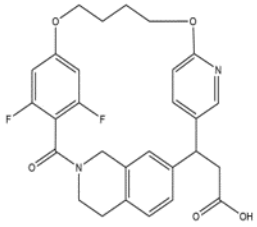


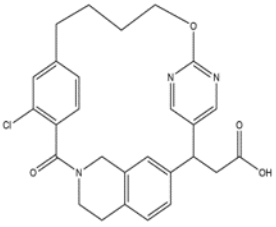


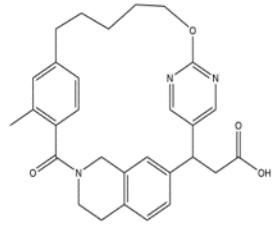


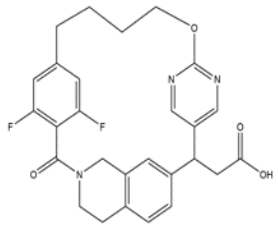
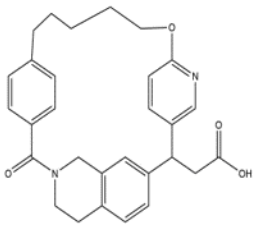
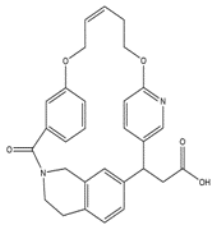
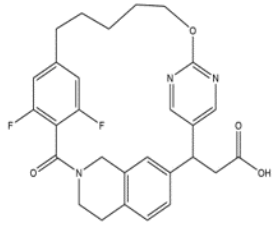
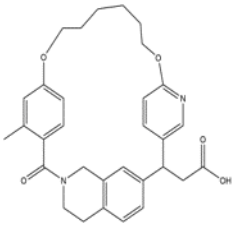
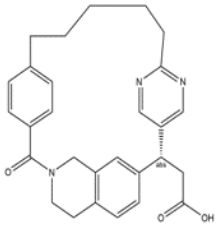
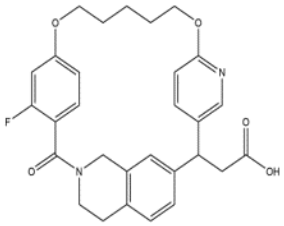
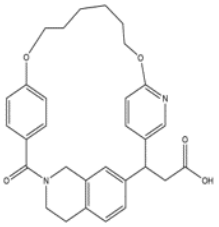
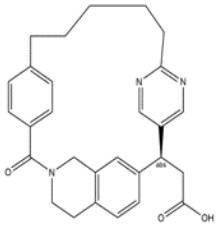
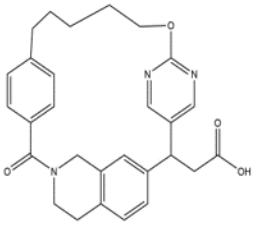
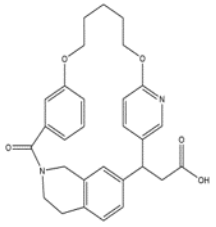
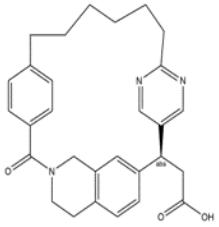


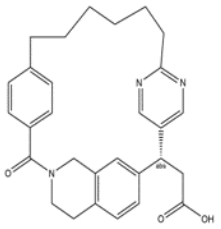
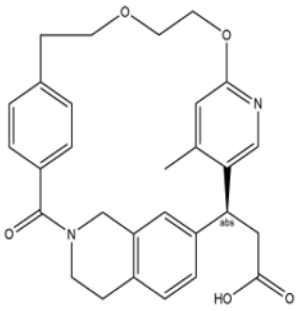
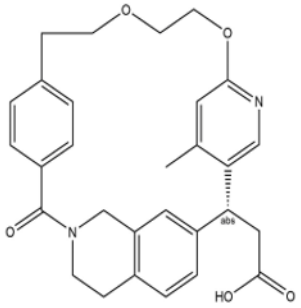
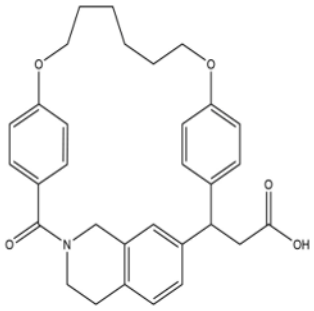
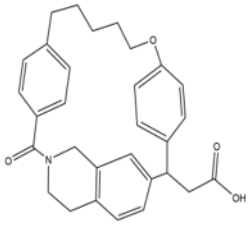
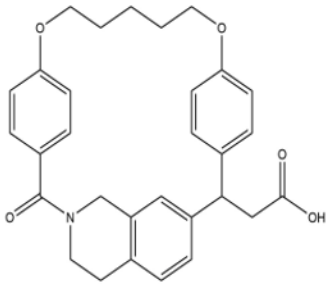




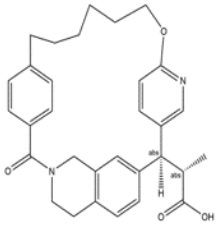
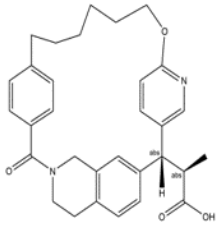
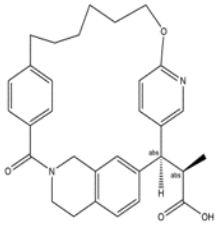


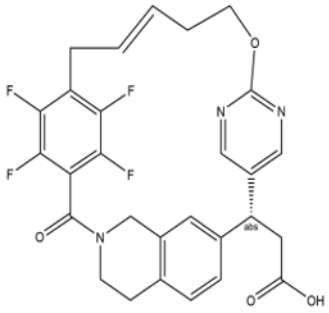
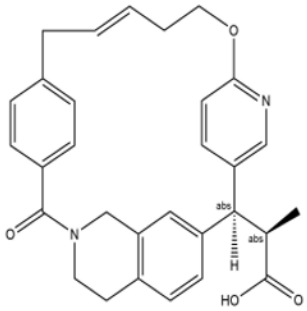
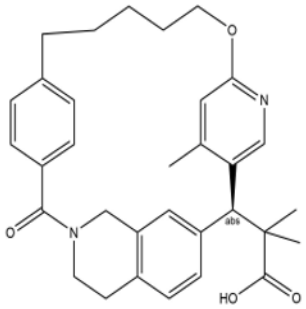
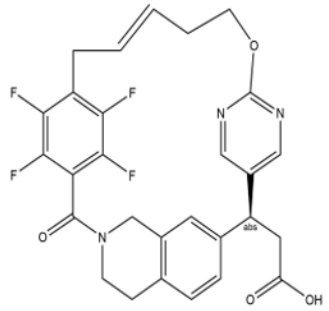
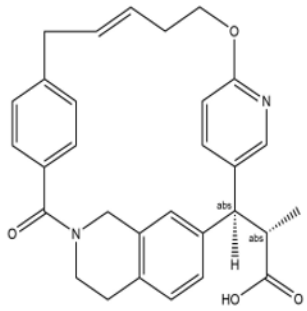
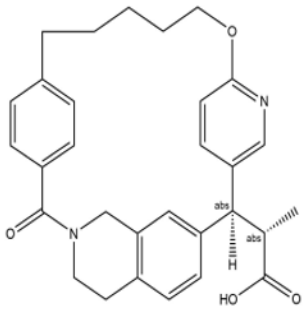
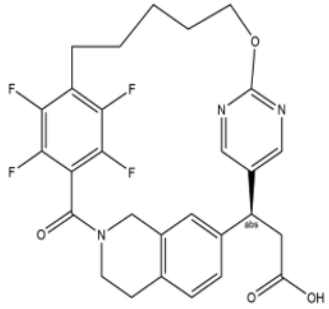
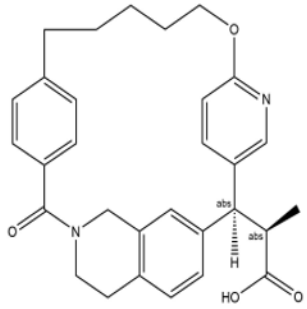
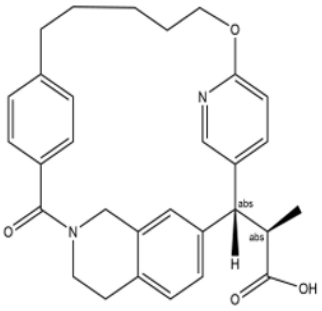
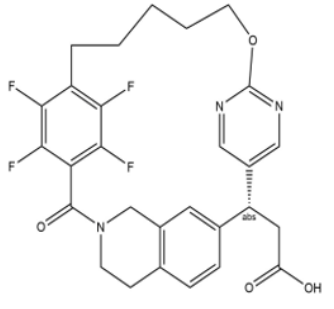
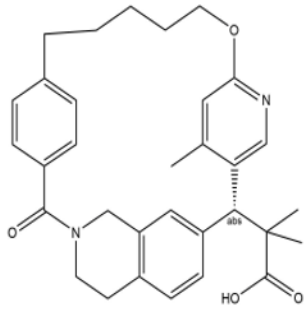
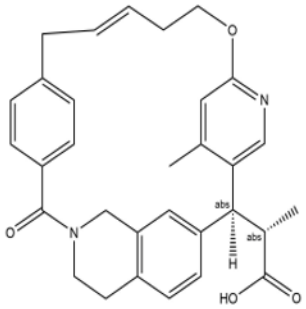


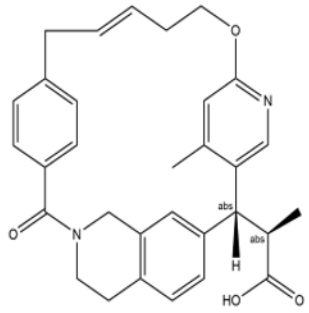
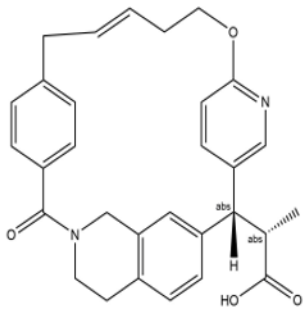
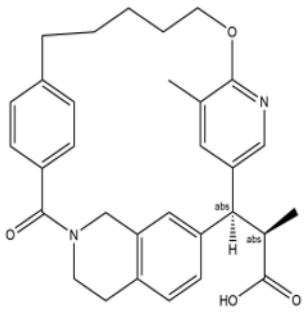
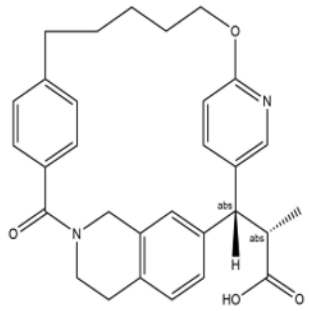
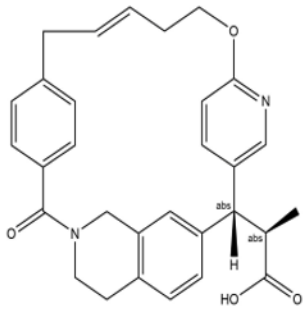
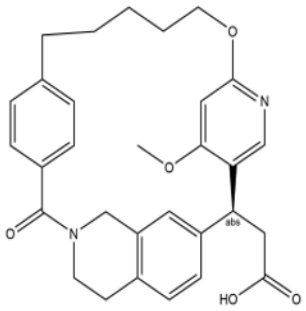
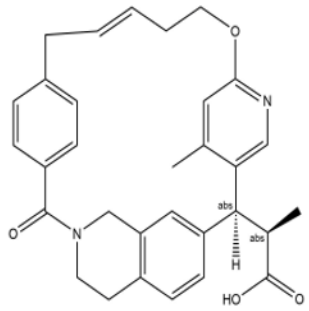
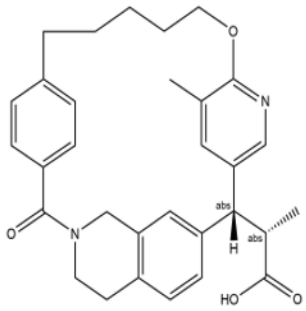
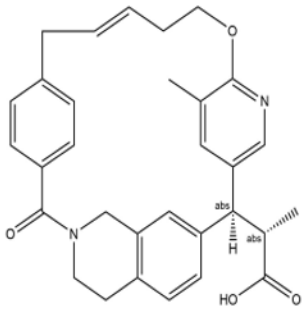
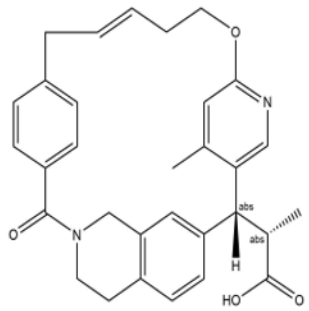
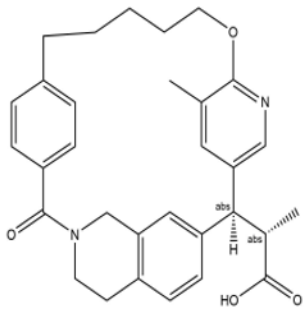
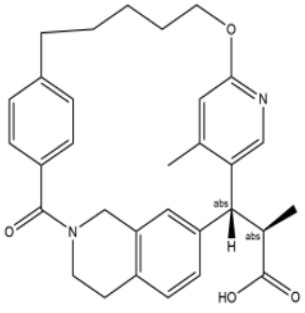













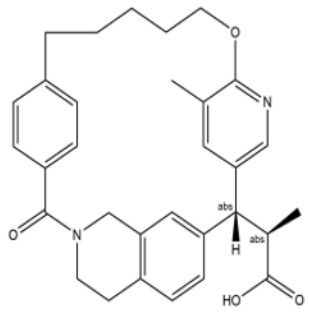
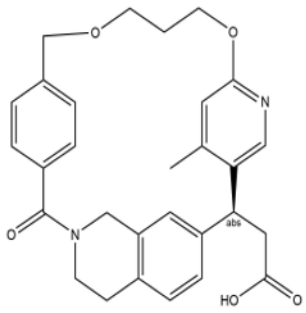
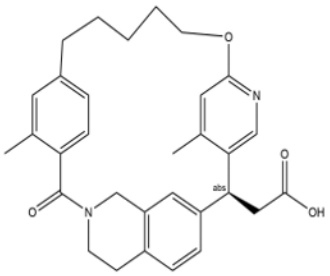
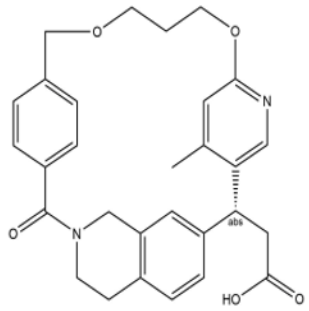
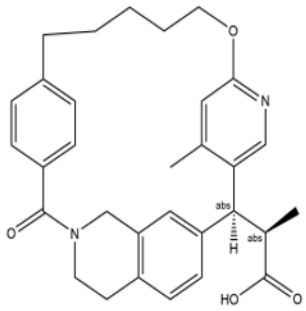
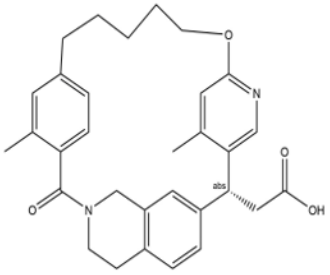
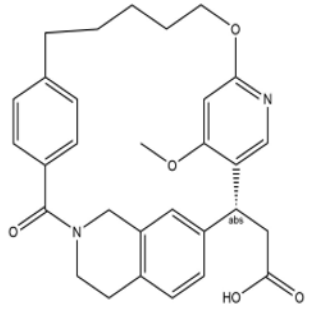
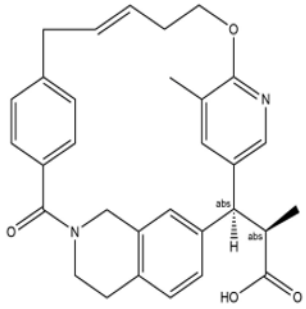
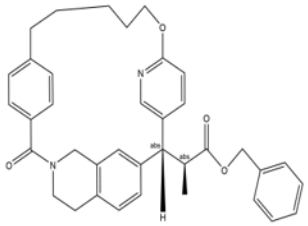
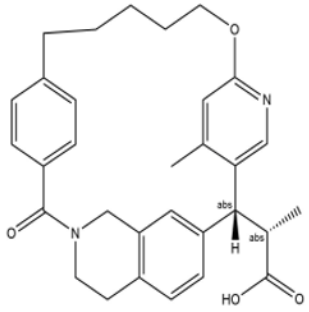
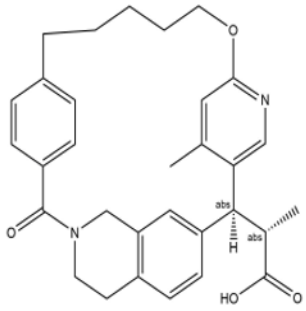
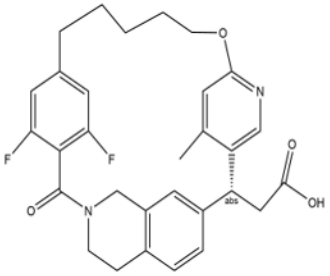







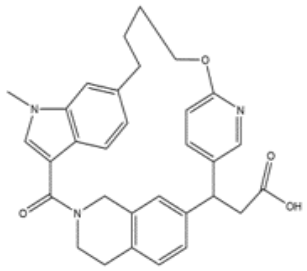
13. A compound selected from the following compounds, or a pharmaceutically acceptable salt thereof:

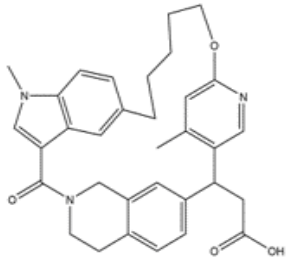




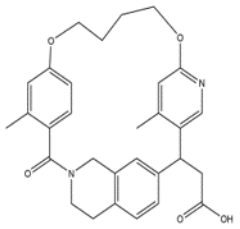













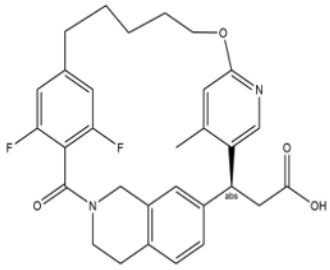













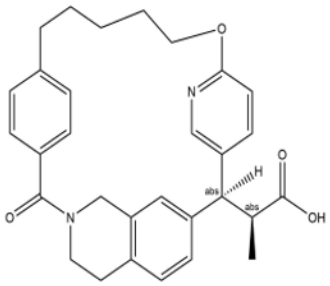













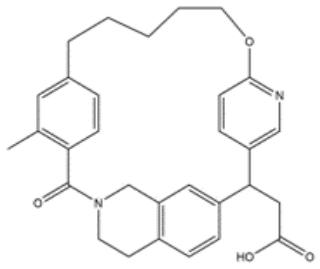


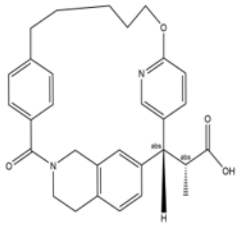


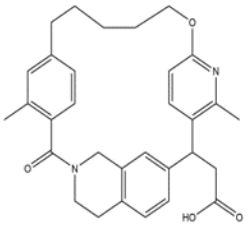


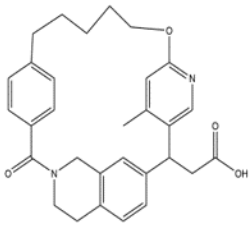


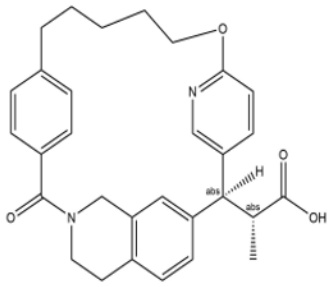


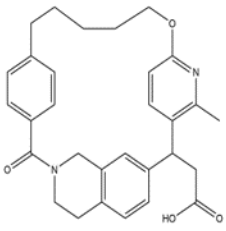


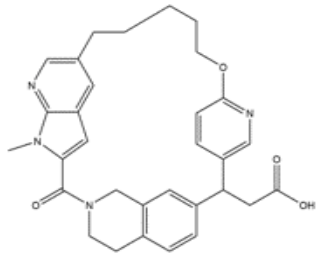


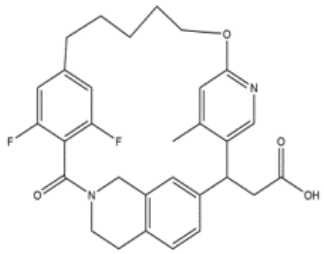
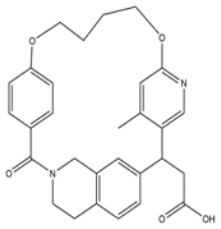
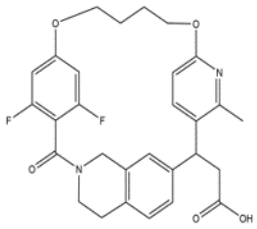
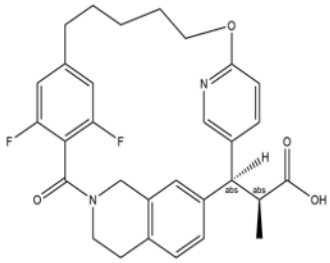
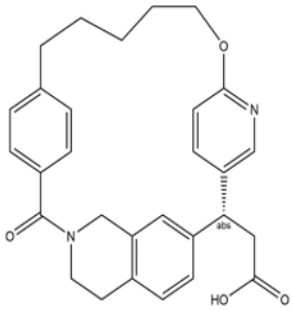
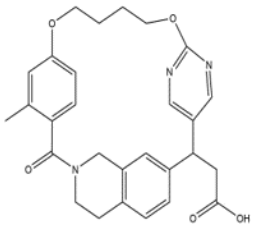
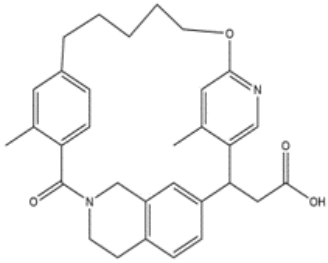
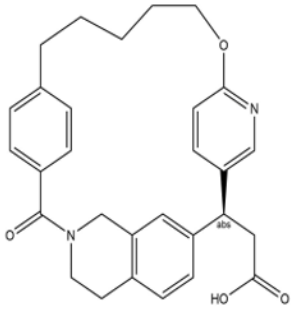
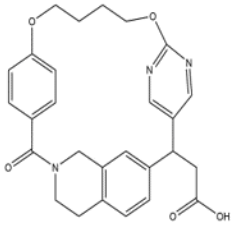
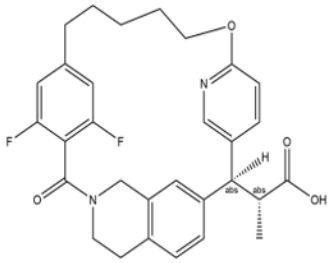
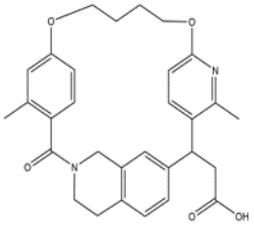
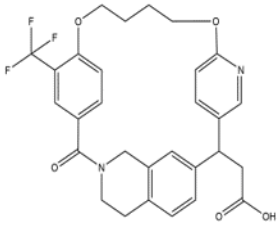


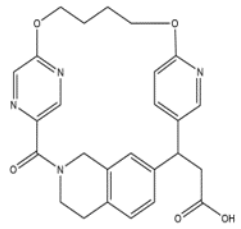


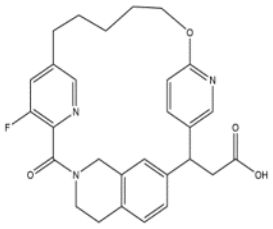


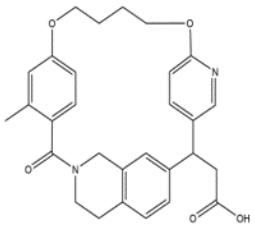


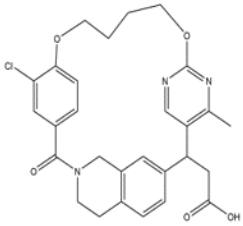


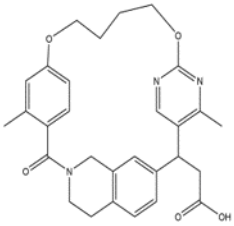













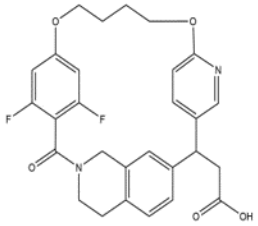


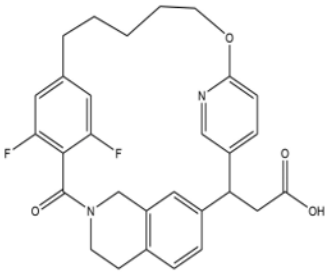


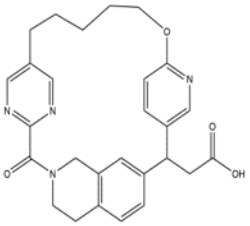


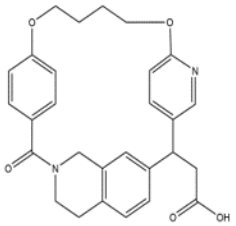


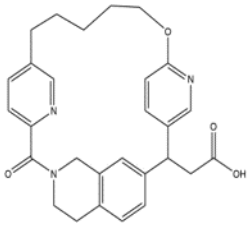


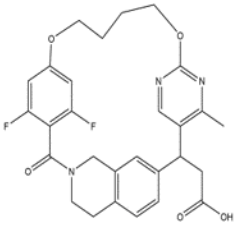


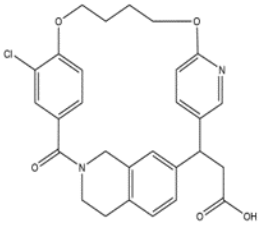


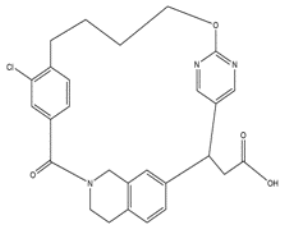
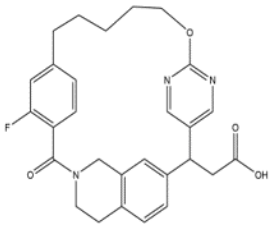
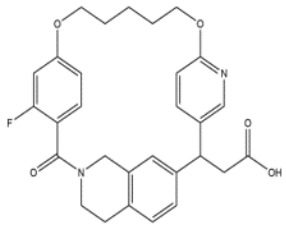
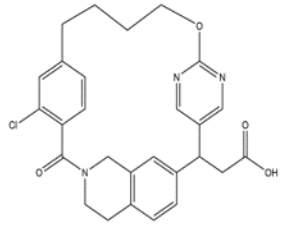
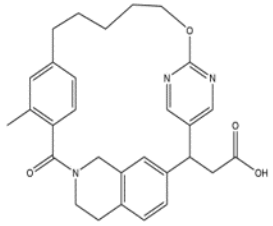
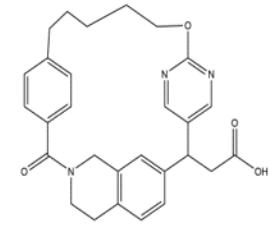
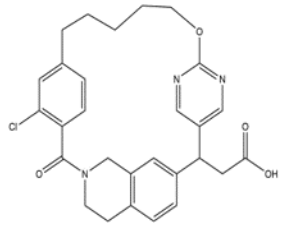
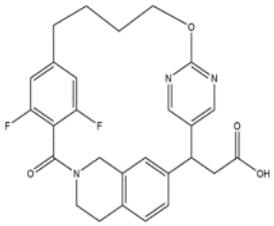
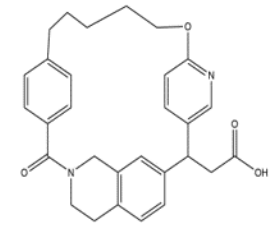
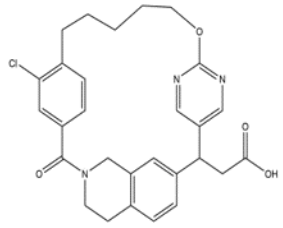
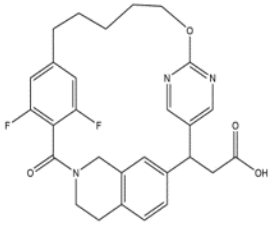
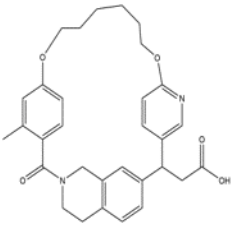


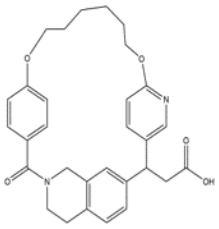
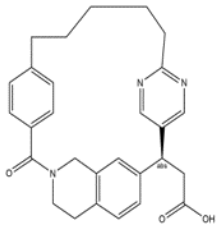
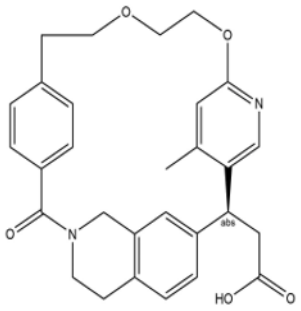
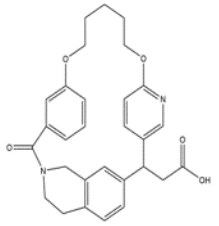
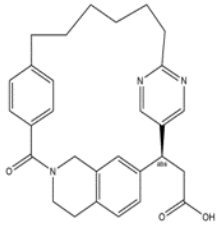
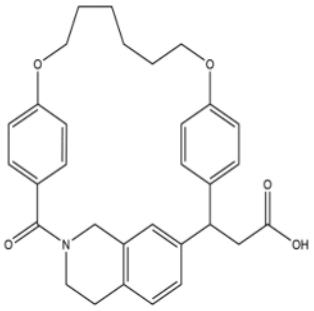
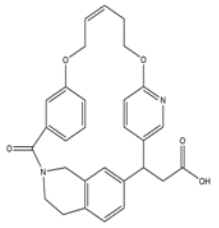
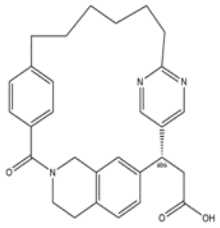
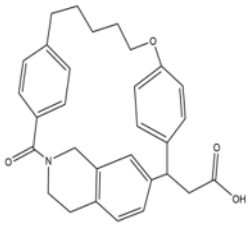
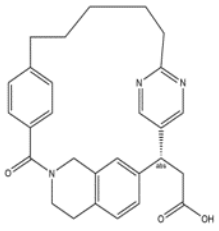
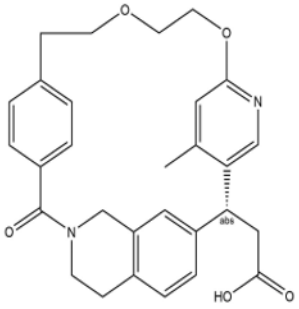
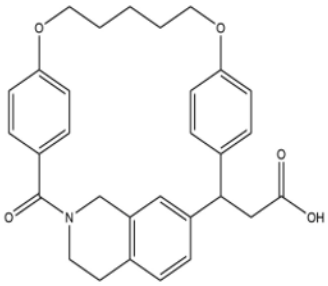








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14. A pharmaceutical composition comprising the compound of any one of claims 1 to 13, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable excipient.

15. The compound of any one of claims 1-13, or a pharmaceutically acceptable salt thereof, or the pharmaceutical composition of claim 14, for use in the treatment of sickle cell disease in a subject in need thereof.

16. Use of the compound of any one of claims 1-13, or a pharmaceutically acceptable salt thereof, or the pharmaceutical composition of claim 14 in the manufacture of a medicament for the treatment of sickle cell disease in a subject in need thereof.