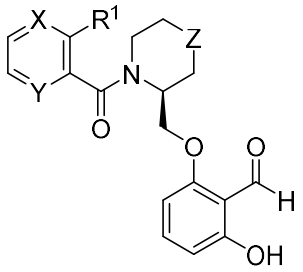
CLAIMS:

1. A compound of formula I:



I,

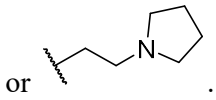
or a pharmaceutically acceptable salt thereof, wherein:

X is CH or N;

Y is CH or N;

Z is absent, CH_2, O, or S; and

R^1 is mono-hydroxy-(C_{1-4} alkyl), di-hydroxy-(C_{1-4} alkyl), $-CH_2CH_2OCH_3$, $-CH_2CH_2CN$,



or .

2. The compound of claim 1, wherein X is CH.

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

4. The compound of any one of claims 1-3, wherein Y is CH.

5. The compound of any one of claims 1-3, wherein Y is N.

6. The compound of any one of claims 1-5, wherein Z is absent, CH_2, or O.

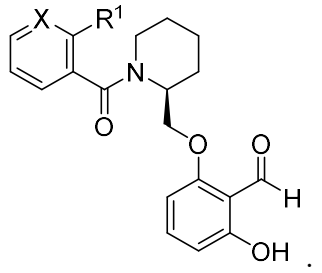
7. The compound of any one of claims 1-5, wherein Z is absent.

8. The compound of any one of claims 1-5, wherein Z is CH_2.

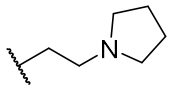
9. The compound of any one of claims 1-5, wherein Z is O.

10. The compound of any one of claims 1-5, wherein Z is S.

11. The compound of claim 1, of formula Ia:



.

12. The compound of any one of claim 1-11, wherein R^1 is -CH_2OH, -CH_2CH_2OH, -CH_2CH_2CN, or 

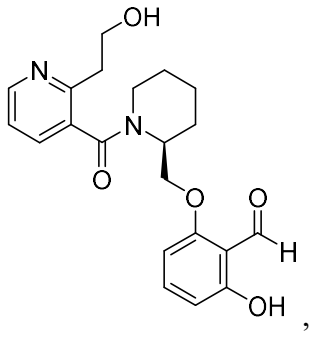
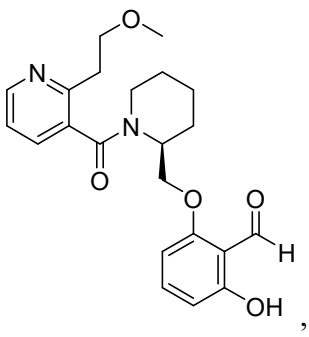
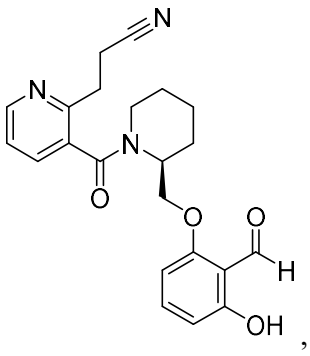
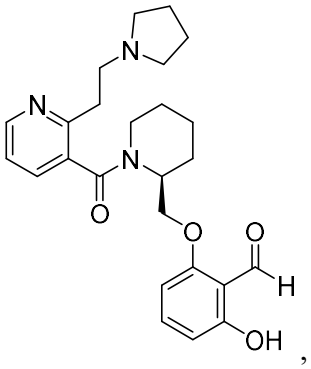
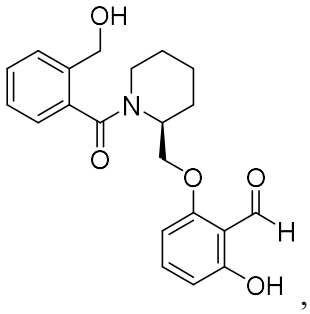
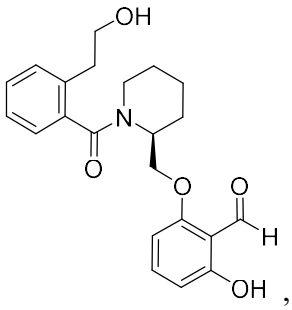
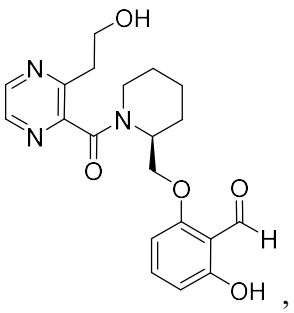
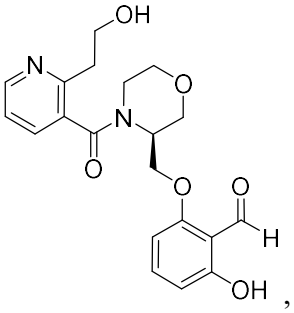
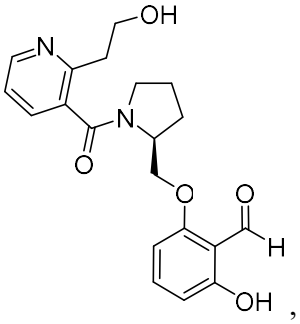
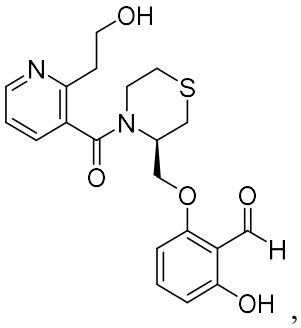
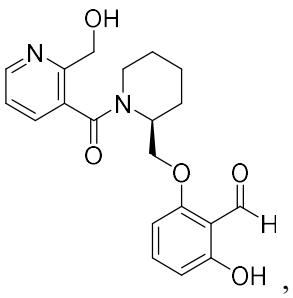
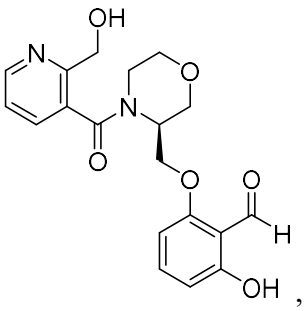
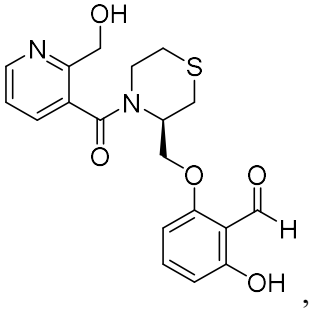
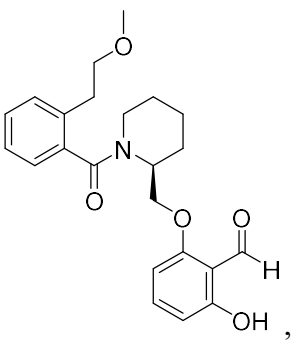
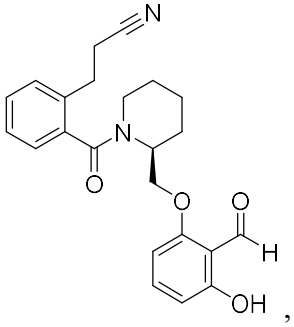
.

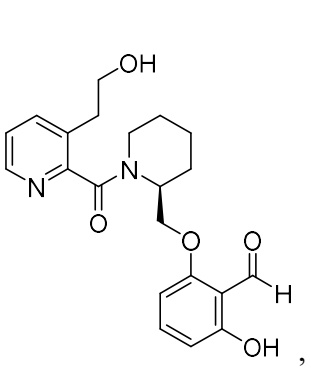
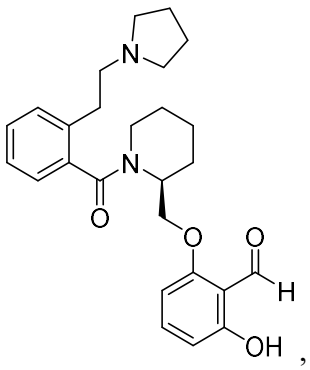
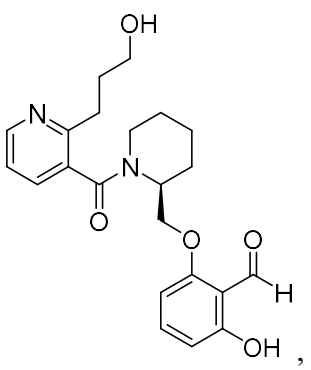
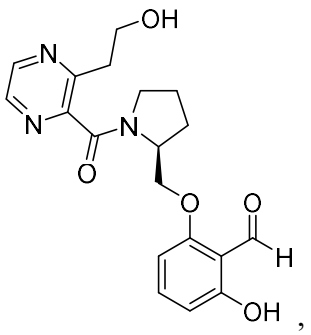
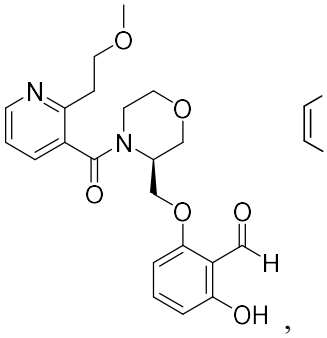
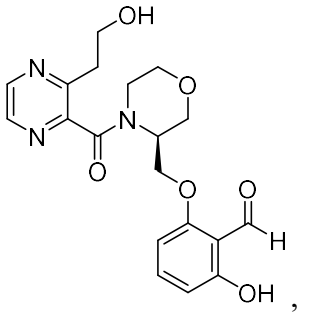
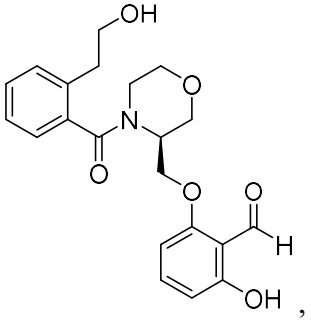
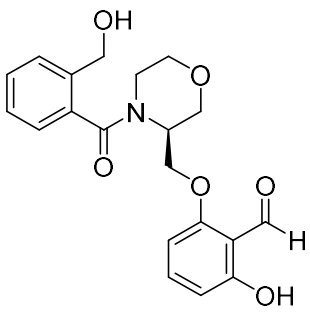
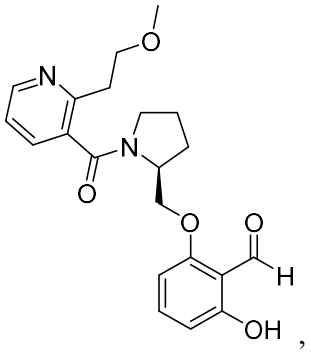
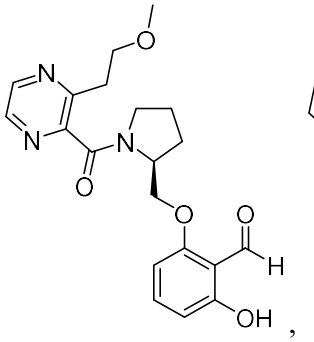
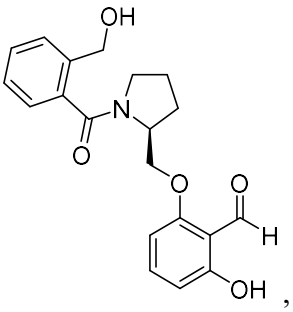
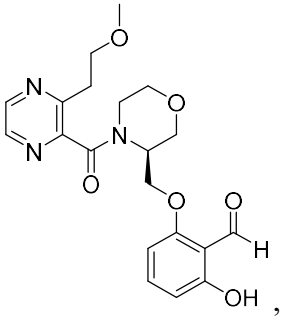
13. The compound of any one of claims 1-11, wherein R^1 is −CH_2OH or −CH_2CH_2OH.

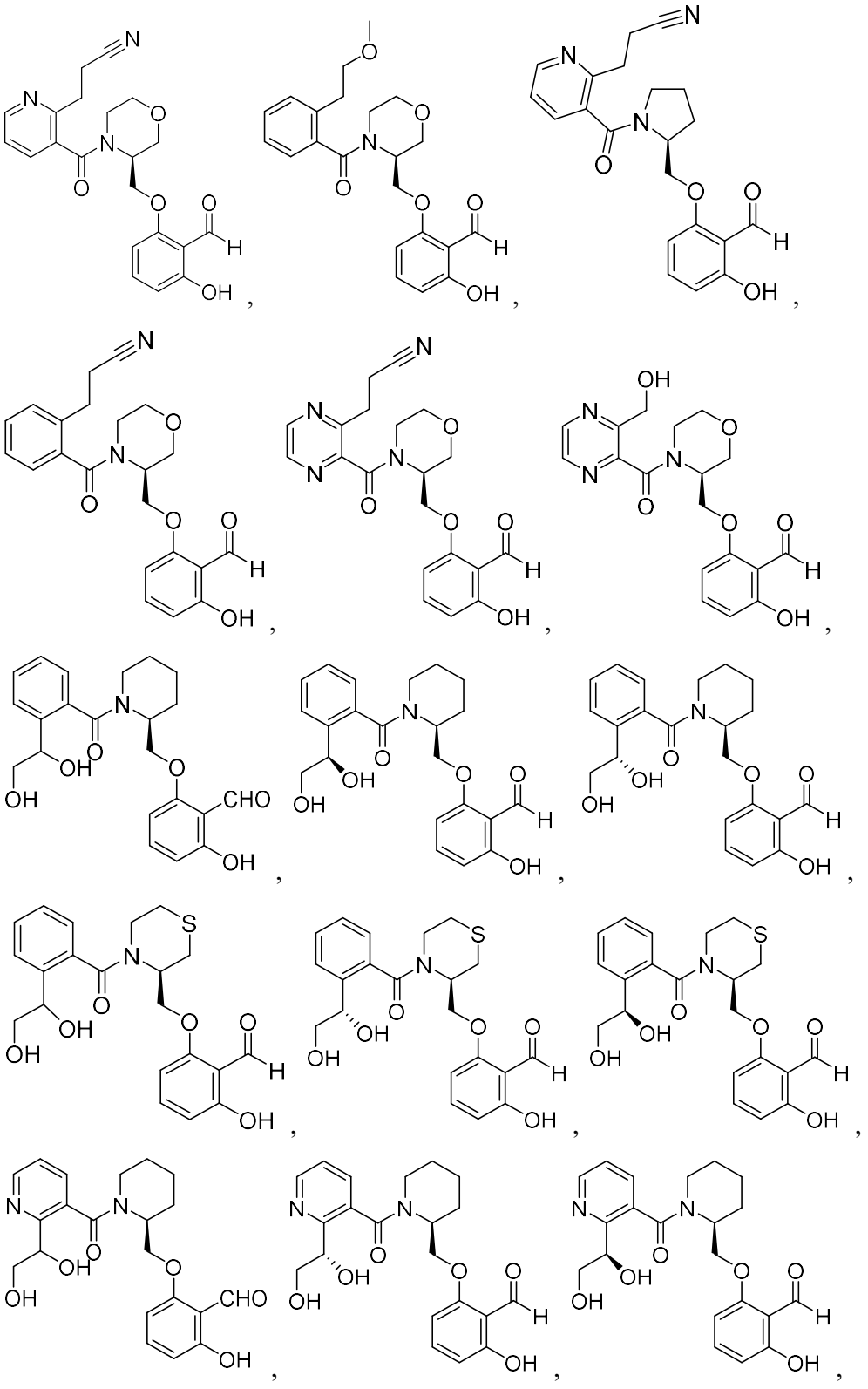
14. The compound of any one of claims 1-11, wherein R^1 is mono-hydroxy-(C_{1-4} alkyl) or di-hydroxy-(C_{1-4} alkyl).

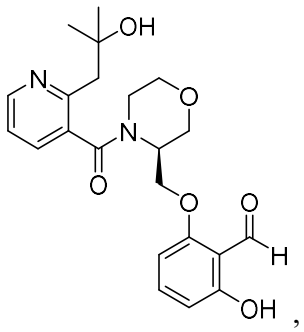
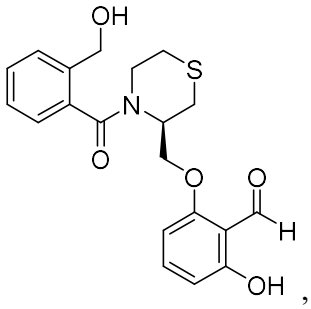
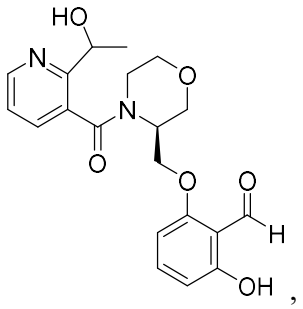
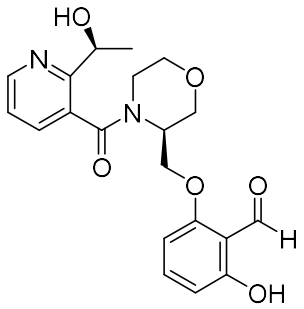
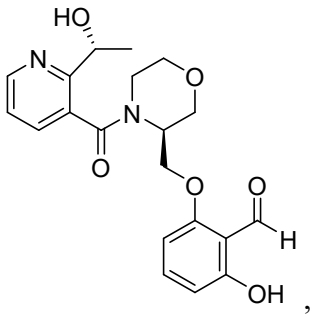
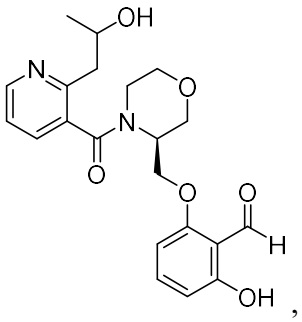
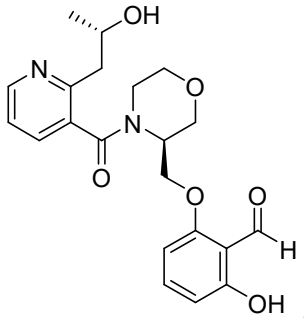
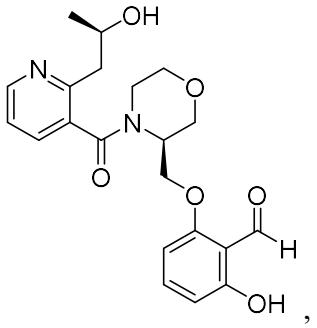
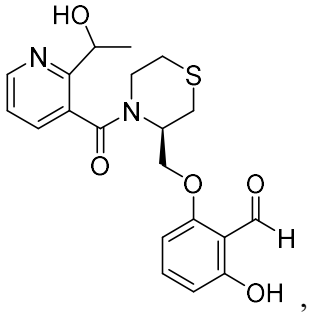
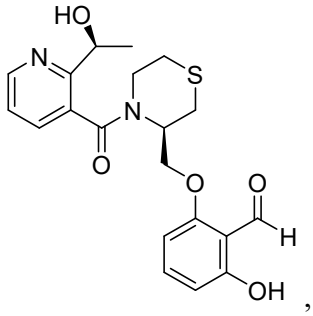
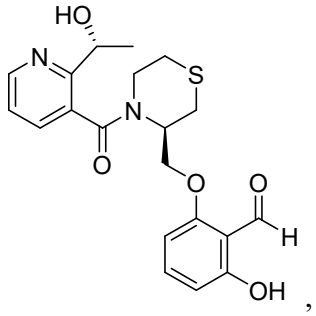
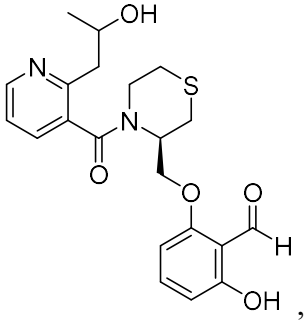
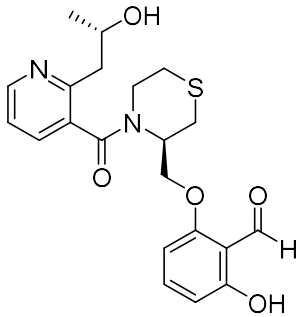
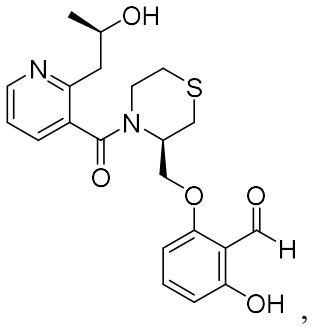
15. The compound of any one of claims 1-11, wherein R^1 is hydroxymethyl, 1-hydroxyethyl, 2-hydroxyethyl, 1,2-dihydroxyethyl, 2-hydroxypropyl, 3-hydroxypropyl, or 2-hydroxy-2-methylpropyl.

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


,

,

,

,

,

,

,

,

,

,

,

,

,

,

,

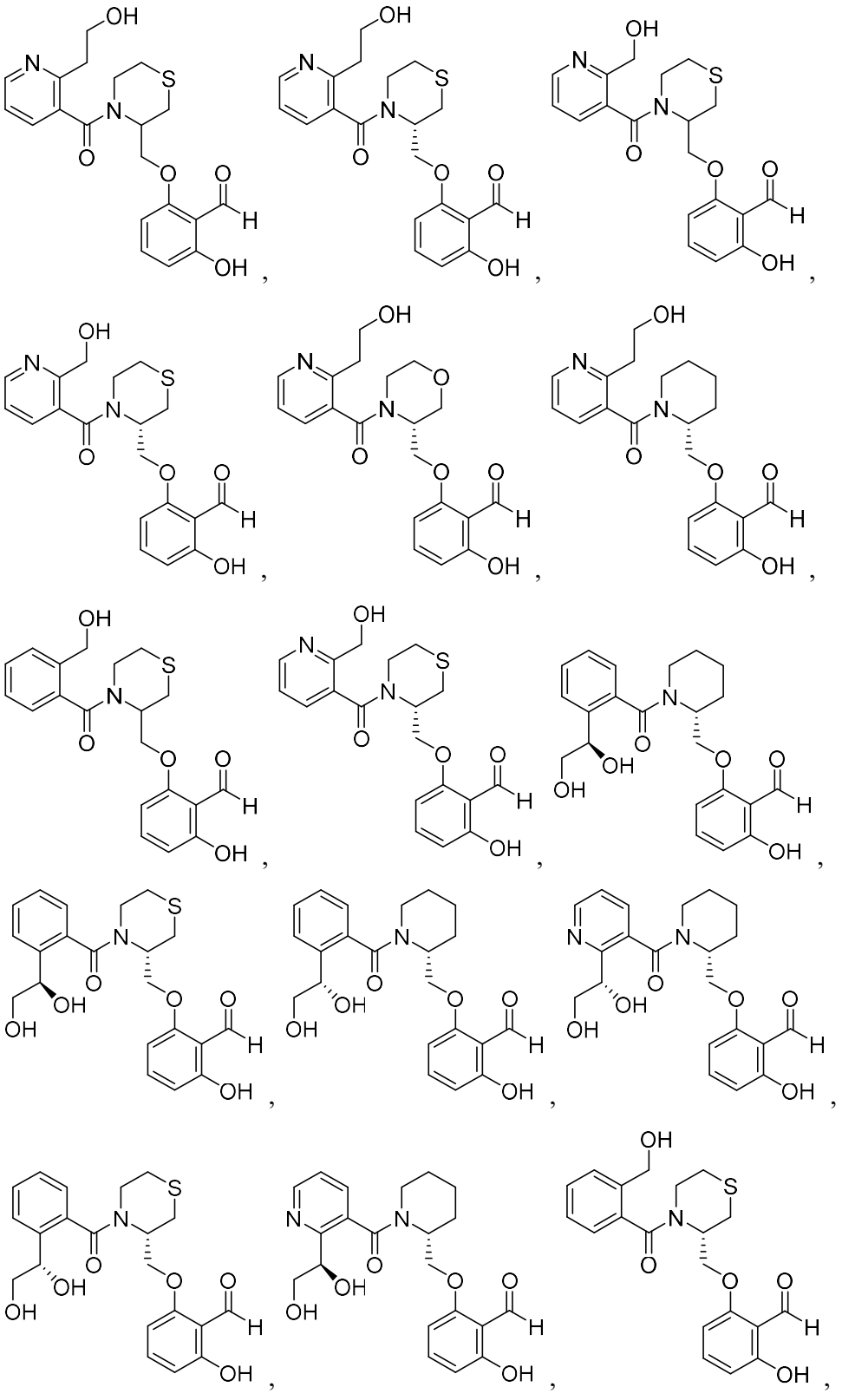

,

,

,

,

,

,

,

,

,

,

,

,

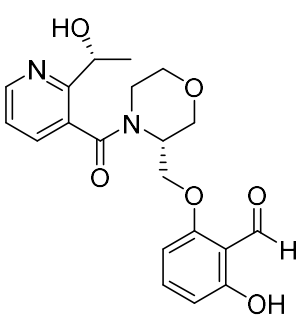
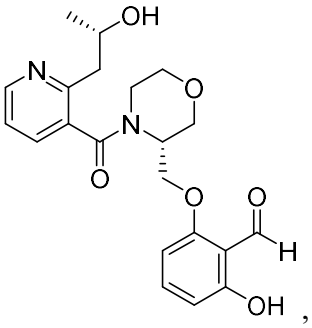
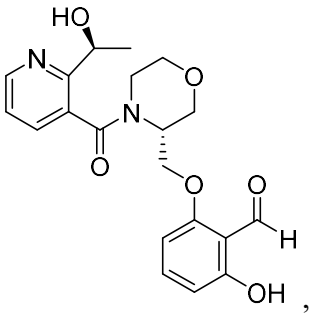
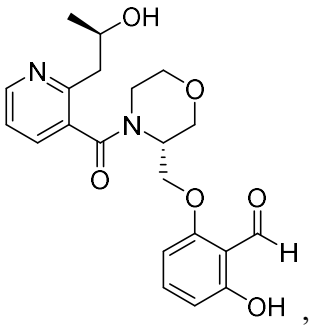
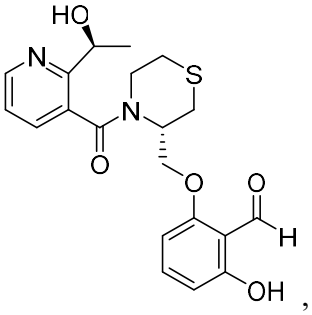
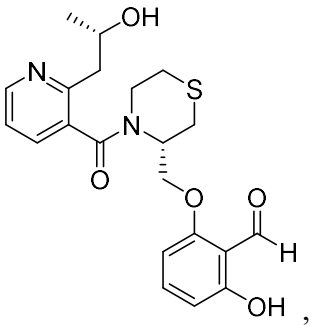
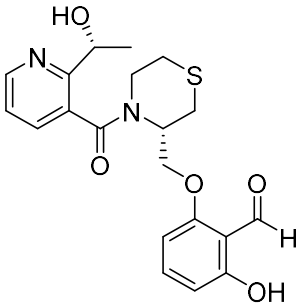
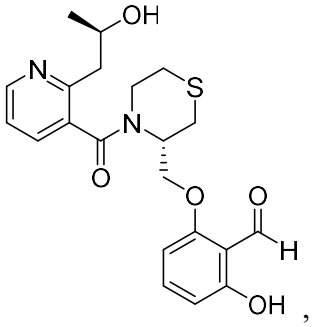



,

,

,

,

,

,

,

,

,

,

,

,

, and

,

or a pharmaceutically acceptable salt of each thereof.

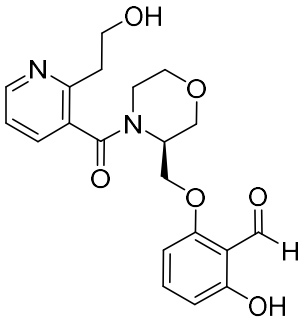
17. A compound selected from:




,

,

,

,

,

,

, and

,

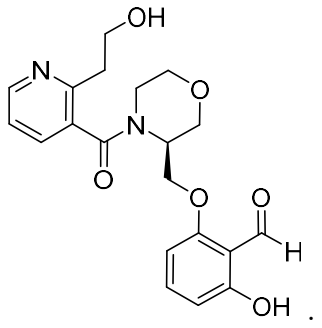
or a pharmaceutically acceptable salt of each thereof.

18. A compound of formula:



or a pharmaceutically acceptable salt thereof.

19. A compound of formula:



20. A pharmaceutical composition comprising a compound according to any one of claims 1-18, or a pharmaceutically acceptable salt of each thereof, and a pharmaceutically acceptable excipient.

21. A pharmaceutical composition comprising a compound according to claim 19, and a pharmaceutically acceptable excipient.

22. Use of a compound according to any one of claims 1-18, or a pharmaceutically acceptable salt of each thereof, or a pharmaceutical composition of claim 20, in the manufacture of a medicament for the increase of oxygen affinity of hemoglobin S in a subject in need thereof.

23. Use of a compound according to claim 19, or a pharmaceutically acceptable salt of each thereof, or a pharmaceutical composition of claim 21, in the manufacture of a medicament for the increase of oxygen affinity of hemoglobin S in a subject in need thereof.

24. Use of a compound according to any one of claims 1-18, or a pharmaceutically acceptable salt of each thereof, or a pharmaceutical composition of claim 20, in the manufacture of a medicament for the treatment of a disorder mediated by hemoglobin in a subject in need thereof.

25. Use of a compound according to claim 19, or a pharmaceutically acceptable salt of each thereof, or a pharmaceutical composition of claim 21, in the manufacture of a medicament for the treatment of a disorder mediated by hemoglobin in a subject in need thereof.

26. The use of claim 24 or 25, wherein the hemoglobin is sickle hemoglobin.

27. Use of a compound according to any one of claims 1-18, or a pharmaceutically acceptable salt of each thereof, or a pharmaceutical composition of claim 20, in the manufacture of a medicament for the treatment of sickle cell disease in a subject in need thereof.

28. Use of a compound according to claim 19, or a pharmaceutically acceptable salt of each thereof, or a pharmaceutical composition of claim 21, in the manufacture of a medicament for the treatment of sickle cell disease in a subject in need thereof.