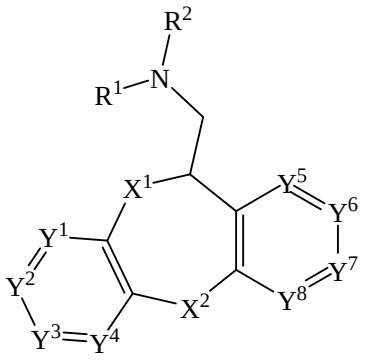
CLAIMS

1. A compound of Formula I



Formula I

, or a pharmaceutically acceptable salt thereof, wherein:

one of X^1 and X^2 is O, and the other is independently $C(R^3)_2$ or O;

each R^3 is independently H, $(C_1\text{-}C_4)$alkyl, $(C_2\text{-}C_4)$alkenyl, or $(C_2\text{-}C_4)$alkynyl;

Y^1, Y^2, Y^3, Y^4, Y^5, Y^6, Y^7, and Y^8 are each independently $C(R^4)$ or N, and no more than one of Y^1, Y^2, Y^3, Y^4, Y^5, Y^6, Y^7, and Y^8 is N;

each R^4 is independently H, halogen, -CN, $(C_1\text{-}C_4)$alkyl, $(C_2\text{-}C_4)$alkenyl, $(C_2\text{-}C_4)$alkynyl, $(C_1\text{-}C_4)$haloalkyl, $(C_1\text{-}C_4)$alkoxy, or $(C_1\text{-}C_4)$haloalkoxy; and

R^1 and R^2 are each independently H, $(C_1\text{-}C_4)$alkyl, or $(C_2\text{-}C_4)$alkenyl.

2. The compound of claim 1, wherein X^1 is $C(R^3)_2$ and X^2 is O.

3. The compound of claim 1, wherein X^1 and X^2 are each O.

4. The compound of claim 1, wherein X^1 is O and X^2 is $C(R^3)_2$.

5. The compound of any one of claims 1-4, wherein each R^3 is independently H or $(C_1\text{-}C_4)$alkyl.

6. The compound of claim 5, wherein each R^3 is independently H or methyl.

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

8. The compound of any one of claims 1-7, wherein Y^1, Y^2, Y^3, Y^4, Y^5, Y^6, Y^7, and Y^8 are each $C(R^4)$.

9. The compound of any one of claims 1-7, wherein Y^1 is N.

10. The compound of any one of claims 1-7, wherein Y^2 is N.

11. The compound of any one of claims 1-7, wherein Y^3 is N.

12. The compound of any one of claims 1-7, wherein Y^4 is N.

13. The compound of any one of claims 1-7, wherein Y^5 is N.

14. The compound of any one of claims 1-7, wherein Y^6 is N.

15. The compound of any one of claims 1-7, wherein Y^7 is N.

16. The compound of any one of claims 1-7, wherein Y^8 is N.

17. The compound of any one of claims 1-16, wherein each R^4 is independently H, halogen, -CN, $(C_1$-$C_4)$alkyl or $(C_1$-$C_4)$alkoxy.

18. The compound of claim 17, wherein each R^4 is independently H or halogen.

19. The compound of claim 18, wherein each R^4 is independently H or F.

20. The compound of claim 19, wherein each R^4 is H.

21. The compound of any one of claims 1-16, wherein one R^4 is halogen and the rest are H.

22. The compound of claim 21, wherein one R^4 is F and the rest are H.

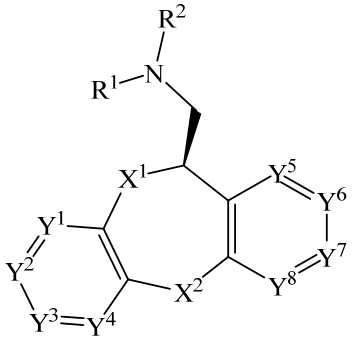
23. The compound of any one of claims 1-22, wherein R^1 and R^2 are each independently H or $(C_1$-$C_4)$alkyl.

24. The compound of claim 23, wherein R^1 and R^2 are each independently H or methyl.

25. The compound of any one of claims 1-23, wherein R^1 is H and R^2 is $(C_1$-$C_4)$alkyl.

26. The compound of claim 25, wherein R^1 is H and R^2 is methyl.

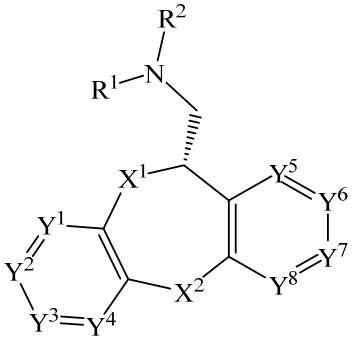
27. The compound of any one of claims 1-26, having Formula I(A)



Formula I(A) ,

or a pharmaceutically acceptable salt thereof.

28. The compound of any one of claims 1-26, having Formula I(B)



Formula I(B) ,

or a pharmaceutically acceptable salt thereof.

29. The compound of claim 1, 27, or 28, wherein:

X^1 is $C(R^3)_2$ or O, and X^2 is O;

each R^3 is independently H or methyl;

Y^1, Y^2, Y^3, Y^4, Y^5, Y^6, Y^7, and Y^8 are each independently $C(R^4)$ or N, and no more than one of Y^1, Y^2, Y^3, Y^4, Y^5, Y^6, Y^7, and Y^8 are N;

one R^4 is H, halogen, -CN, $(C_1\text{-}C_4)$alkyl or $(C_1\text{-}C_4)$alkoxy, and the rest are H;

R^1 is H; and

R^2 is $(C_1\text{-}C_4)$alkyl.

30. The compound of claim 29, wherein X^1 is $C(R^3)_2$ and X^2 is O.

31. The compound of claim 29 or 30, wherein each R^3 is H.

32. The compound of claim 29, wherein X^1 and X^2 are each O.

33. The compound of any one of claims 29-32, wherein Y^1, Y^2, Y^3, Y^4, Y^5, Y^6, Y^7, and Y^8 are each $C(R^4)$.

34. The compound of any one of claims 29-32, wherein one of Y^1, Y^2, Y^3, Y^4, Y^5, Y^6, Y^7, and Y^8 is N, and the rest are each $C(R^4)$.

35. The compound of claim 34, wherein one of Y^1, Y^3 and Y^5 is N.

36. The compound of claim 35, wherein Y^1 is N.

37. The compound of claim 34, wherein one of Y^5, Y^6, Y^7 and Y^8 is N.

38. The compound of claim 35 or 37, wherein Y^5 is N.

39. The compound of any one of claims 29-38, wherein each R^4 is H.

40. The compound of any one of claims 29-38, wherein one R^4 is halogen, -CN or (C_1-C_4)alkyl, and the rest are H.

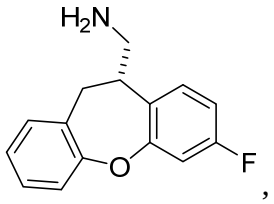
41. The compound of claim 40, wherein one R^4 is fluoro, chloro, bromo, methyl, ethyl or cyano, and the rest are H.

42. The compound of any one of claims 29-38, wherein one R^4 is halogen, and the rest are H.

43. The compound of claim 41 or 42, wherein one R^4 is fluoro, and the rest are H.

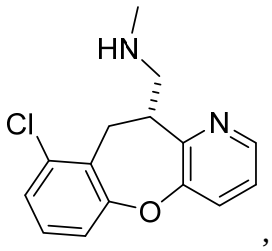
44. The compound of any one of claims 29-43, wherein R^2 is methyl.

45. The compound of claim 1, having the following formula:



or a pharmaceutically acceptable salt thereof.

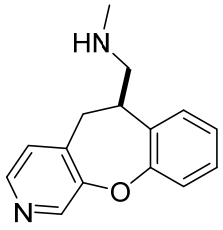
46. The compound of claim 1, having the following formula:



,

or a pharmaceutically acceptable salt thereof.

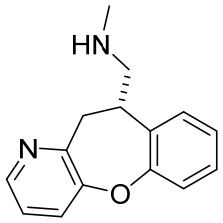
47. The compound of claim 1, having the following formula:



,

or a pharmaceutically acceptable salt thereof.

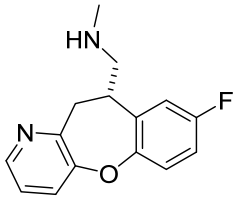
48. The compound of claim 1, having the following formula:



,

or a pharmaceutically acceptable salt thereof.

49. The compound of claim 1, having the following formula:



,

or a pharmaceutically acceptable salt thereof.

50. A pharmaceutical composition comprising a compound of any one of claims 1-49, or a pharmaceutically acceptable salt thereof, and one or more pharmaceutically acceptable excipients.

51. A pharmaceutical combination, comprising a compound of any one of claims 1-49, or a pharmaceutically acceptable salt thereof, and one or more additional therapeutic agents.

52. Use of a compound according to any one of claims 1-49, or a pharmaceutically acceptable salt thereof, or pharmaceutical composition of claim 50 in the manufacture of a medicament for treating a neurological or psychiatric disease or disorder in a subject in need thereof.

53. Use of a compound according to any one of claims 1-49, or a pharmaceutically acceptable salt thereof, a pharmaceutical composition of claim 50 or a pharmaceutical combination of claim 51 in the manufacture of a medicament to agonize TAAR1 in the subject.

54. Use of a compound according to any one of claims 1-49, or a pharmaceutically acceptable salt thereof, a pharmaceutical composition of claim 50 or a pharmaceutical combination of claim 51 in the manufacture of a medicament to antagonize 5-HT2A, 5-HT7, or 5-HT2A and 5-HT7, respectively, in the subject.