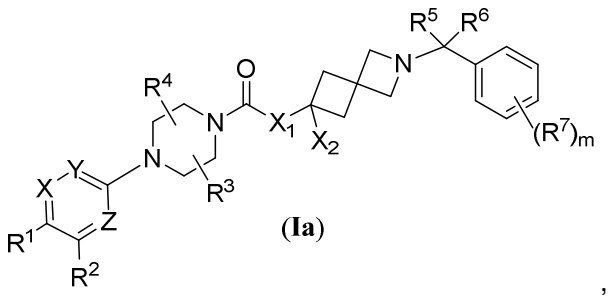
CLAIMS

1. A compound of Formula (**Ia**):



(**Ia**)

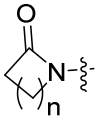
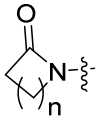
,

or a pharmaceutically acceptable salt thereof:

wherein:

each of X, Y, Z is independently CR^8 or N, wherein R^8 is hydrogen, C_1-C_4 alkyl, halogen, C_1-C_4 alkoxy, or cyano;

R^1 is R^9-$S(=O)_2$-;

R^2 is hydrogen, halogen, amino, $R^{10}NH$-$S(=O)_2$-, R^9-$S(=O)_2$-, R^9-S(=O)-, R^9-S-, R^9-S(=O)(=NR^{10})-, R^9-O-,  (n = 1, 2, or 3), cyano or C_1-C_4 alkyl, wherein R^9 is selected from C_1-C_4 alkyl, C_3-C_7-cycloalkyl, and 3-7 membered heterocyclyl, wherein R^9 or  is optionally substituted with C_1-C_4 alkyl, C_1-C_4 alkoxy, -OH, -NHR^{10}, halogen, or cyano, and wherein R^{10} is hydrogen, C_1-C_4 alkyl, or C_3-C_7 cycloalkyl; or R^1, R^2 and the carbon atoms they are attached to form a 3-7 membered ring with one or more heteroatoms selected from N, O, and S;

X_1 is O or NH;

X_2 is hydrogen or C_1-C_4 alkyl;

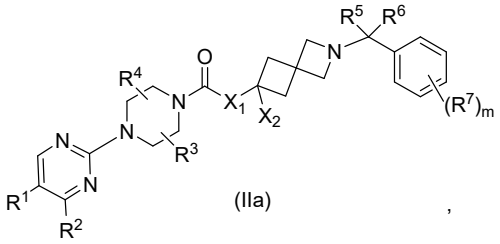
R^3 and R^4 are each independently selected from hydrogen and C_1-C_4 alkyl, and R^3 and R^4 are bonded to different ethylene groups of the piperazine ring;

each of R^5 and R^6 is independently hydrogen or C_1-C_4 alkyl, or R^5, R^6 and the carbon atom they are attached to form a C_3-C_7 cycloalkyl or a 3-7 membered heterocyclyl, each optionally substituted with C_1-C_4 alkyl, C_1-C_4 alkoxy, -OH, -NHR^{10}, halogen, and cyano;

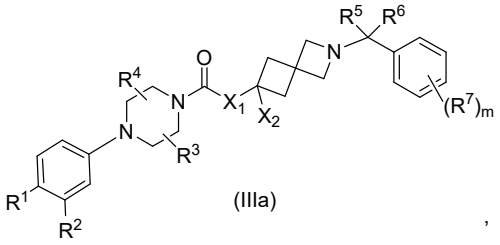
R^7 is hydrogen, halogen, or C_1-C_4 alkyl, wherein the C_1-C_4 alkyl is optionally substituted with halogen, amino, -OH, C_1-C_4 alkoxy, or cyano; and

m is 0, 1, or 2.

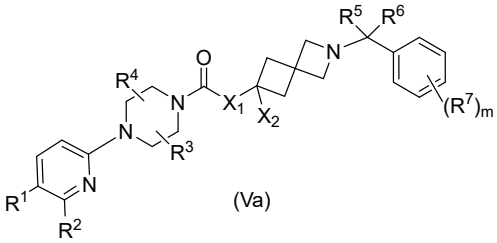
2. The compound according to claim 1, or a pharmaceutically acceptable salt thereof, selected from:



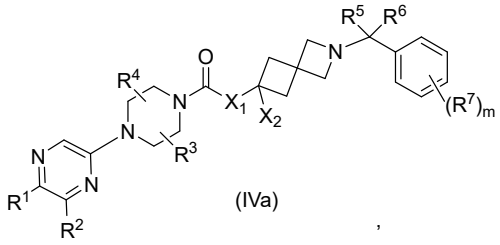
(IIa) ,



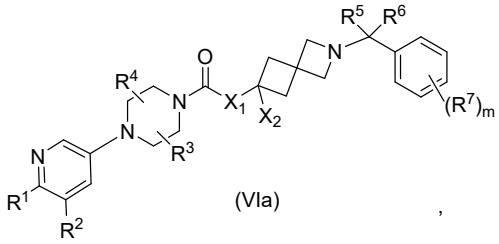
(IIIa) ,



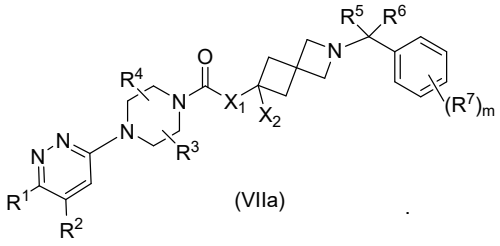
(Va)



(IVa) ,

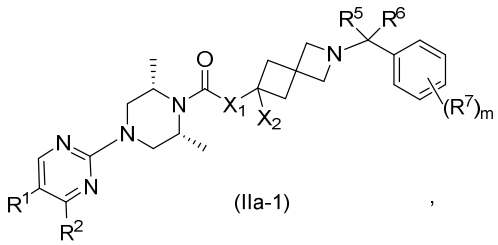


(VIa) , and

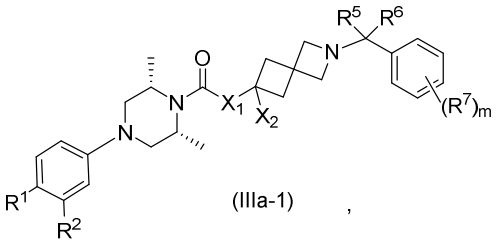


(VIIa) .

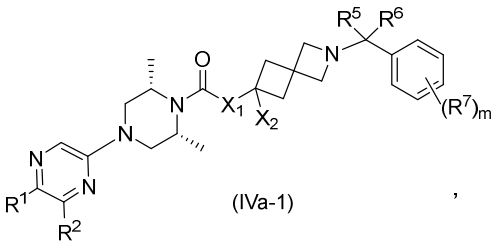
3. The compound according to claim 1, or a pharmaceutically acceptable salt thereof, selected from:



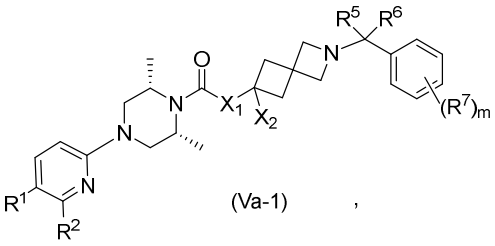
(IIa-1) ,



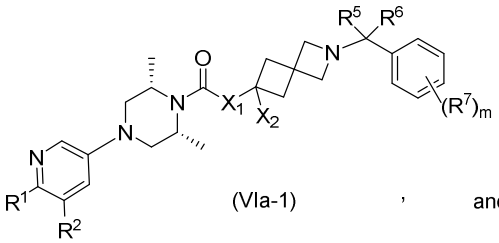
(IIIa-1) ,



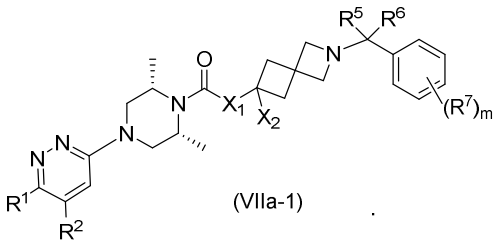
(IVa-1) ,



(Va-1) ,

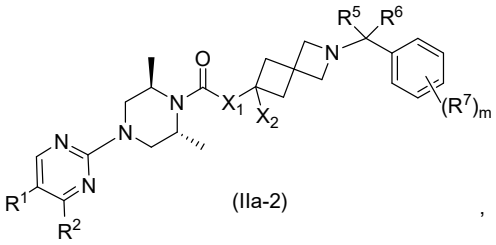


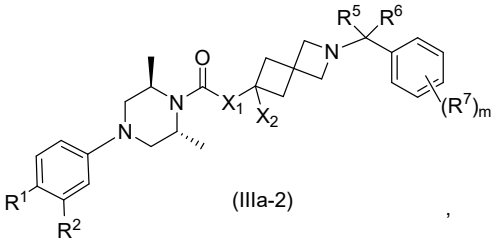
(VIa-1) , and

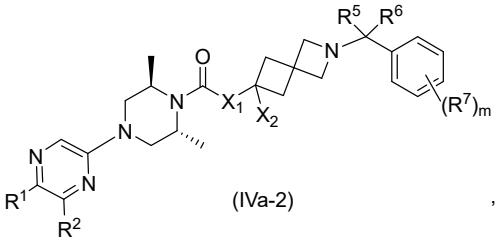


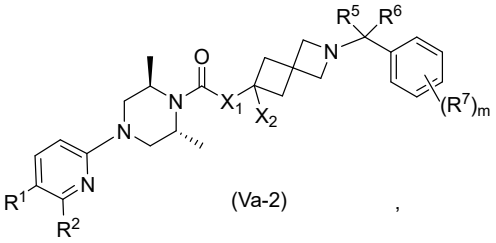
(VIIa-1) .

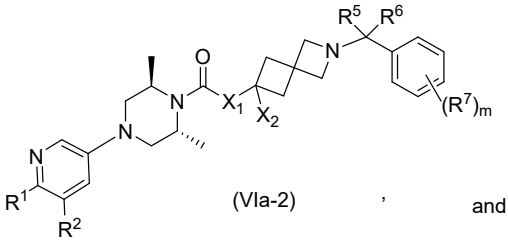
4. The compound according to claim 1, or a pharmaceutically acceptable salt thereof, selected from:

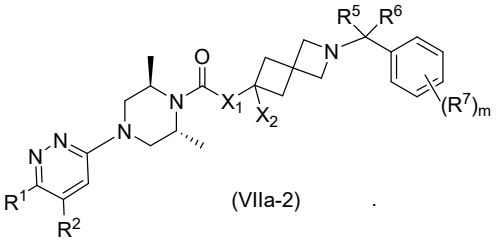

(IIa-2) ,


(IIIa-2) ,

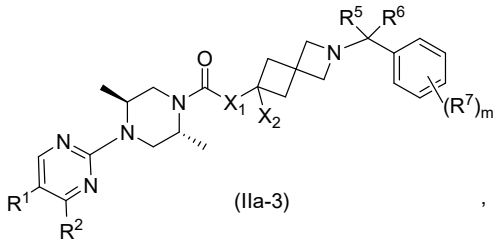

(IVa-2) ,

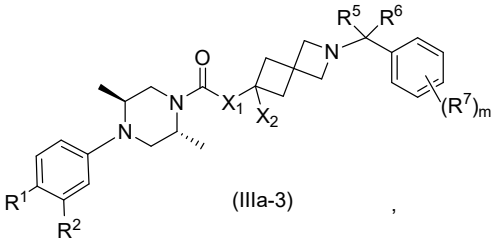

(Va-2) ,

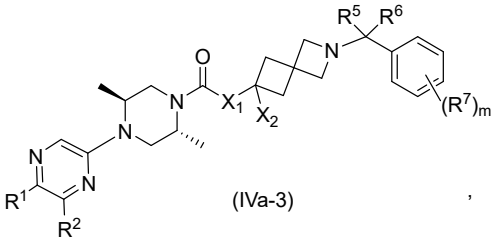

(VIa-2) , and

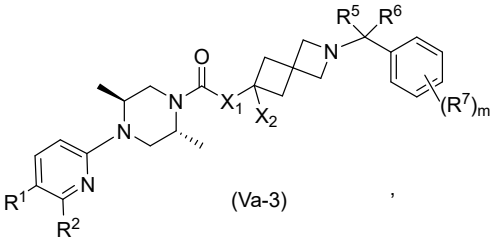

(VIIa-2) .

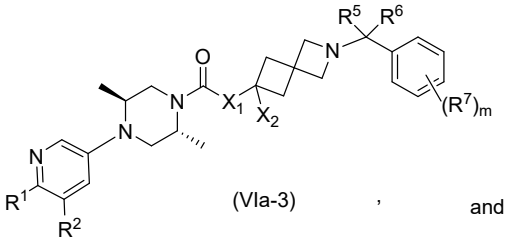
5. The compound according to claim 1, or a pharmaceutically acceptable salt thereof, selected from:

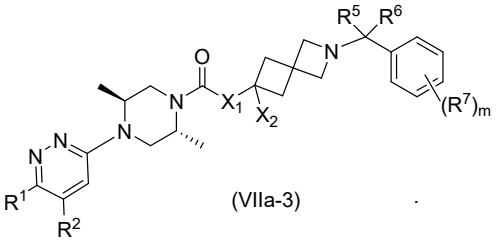

(IIa-3) ,


(IIIa-3) ,

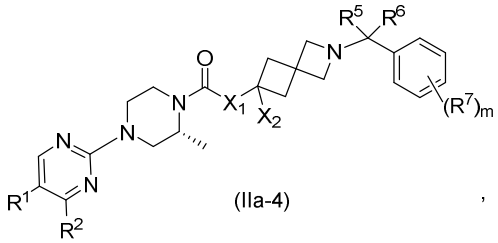

(IVa-3) ,

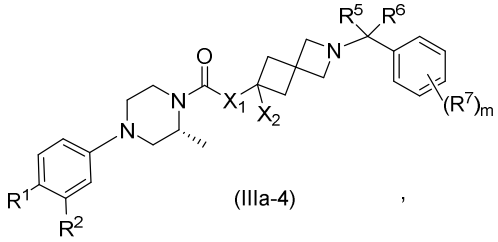

(Va-3) ,

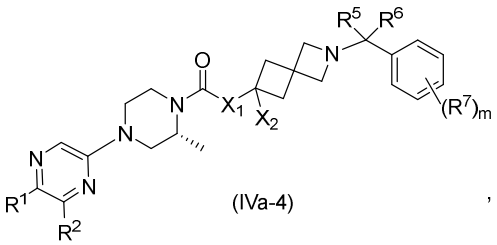

(VIa-3) , and

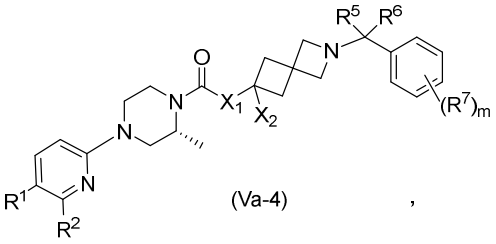

(VIIa-3) .

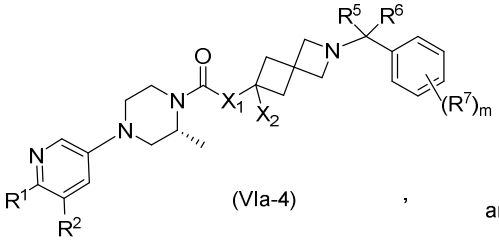
6. The compound according to claim 1, or a pharmaceutically acceptable salt thereof, selected from:

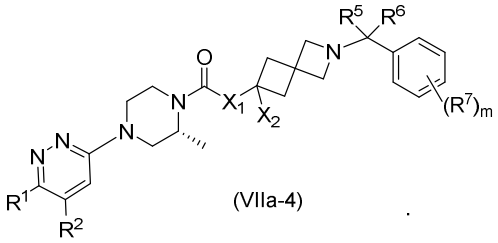

(IIa-4) ,


(IIIa-4) ,


(IVa-4) ,


(Va-4) ,


(VIa-4) , and


(VIIa-4) .

7. The compound according to any one of claims 1-6, wherein:
R^2 is hydrogen.

8. The compound according to any one of claims 1-6, wherein:
R^2 is halogen.

9. The compound according to any one of claims 1-6, wherein:
R^2 is C_1-C_4 alkyl.

10. The compound according to any one of claims 1-9, wherein:
X_1 is NH.

11. The compound according to any one of claims 1-9, wherein:
X_1 is O.

12. The compound according to any one of claims 1-11, wherein:
X_2 is hydrogen.

13. The compound according to any one of claims 1-11, wherein:
X_2 is C_1-C_4 alkyl.

14. The compound according to any one of claims 1-9, wherein:
X_1 is O; and
X_2 is hydrogen.

15. The compound according to any one of claims 1-14, wherein:
each of R^5 and R^6 is hydrogen.

16. The compound according to any one of claims 1-14, wherein:
each of R^5 and R^6 is C_1-C_4 alkyl.

17. The compound according to any one of claims 1-14, wherein:
R^5 is hydrogen; and
R^6 is C_1-C_4 alkyl.

18. The compound according to any one of claims 1-17, wherein:
m is 0.

19. The compound according to any one of claims 1-17, wherein:
m is 1.

20. The compound according to any one of claims 1-17, wherein:
m is 2.

21. The compound according to any one of claims 1-20, wherein:
R^{10} is hydrogen.

22. The compound according to any one of claims 1-20, wherein:
R^{10} is C_1-C_4 alkyl.

23. The compound according to any one of claims 1-22, wherein:
R^9 is C_1-C_4 alkyl.

24. The compound according to any one of claims 1-22, wherein:
R^9 is C_3-C_7 cycloalkyl.

25. The compound according to any one of claims 1-22, wherein:
R^9 is 3-7 membered heterocyclyl.

26. The compound according to any one of claims 23-25, wherein:
said C_1-C_4 alkyl, C_3-C_7 cycloalkyl, or 3-7 membered heterocyclyl is optionally substituted with halogen, cyano, or -OH.

27. A pharmaceutical product selected from a pharmaceutical composition, a formulation, a unit dosage form, and a kit; each comprising a compound according to any one of claims 1-26, or a pharmaceutically acceptable salt thereof.

28. A pharmaceutical composition comprising a compound according to any one of claims 1-26, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier.

29. A method for preparing a pharmaceutical composition comprising the step of admixing a compound according to any one of claims 1-26, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier.

30. An *in vitro* method for antagonizing a muscarinic receptor 4 (M_4) of a cell, comprising contacting the cell with the compound according to any one of claims 1-26, or a pharmaceutically acceptable salt thereof.

31. Use of a compound, or a pharmaceutically acceptable salt thereof, according to any one of claims 1-26, or a pharmaceutical product according to claim 27, or a pharmaceutical composition according to claim 28, in the manufacture of a medicament for treating or preventing a neurological disease, disorder, or symptom in an individual.

32. Use of a compound, or a pharmaceutically acceptable salt thereof, according to any one of claims 1-26, or a pharmaceutical product according to claim 27, or a pharmaceutical composition according to claim 28, in the manufacture of a medicament for treating or preventing a muscarinic receptor 4 (M_4) mediated disease, disorder, or symptom in an individual.

33. The use according to claim 31 or 32, wherein the disease, disorder, or symptom is selected from: Tourette's syndrome (TS), Alzheimer's Disease (AD), schizophrenia, Lewy Body Dementia (LBD), cognitive deficits associated with schizophrenia, Parkinson's Disease, parkinsonism, tremor, dyskinesias, excessive daytime sleepiness, dystonia, chorea, levodopa induced dyskinesia, attention deficit hyperactivity disorder (ADHD), cerebral palsy, progressive supranuclear palsy (PSP), Multiple System Atrophy (MSA), Huntington's disease (HD), and chorea associate with Huntington's disease.

34. A compound according to any one of claims 1-26, or a pharmaceutically acceptable salt thereof, or a pharmaceutical product according to claim 27, or a pharmaceutical composition according to claim 28, for use in treatment or prophylaxis of a human or animal body by therapy.

35. A compound according to any one of claims 1 to 26, or a pharmaceutically acceptable salt thereof, or a pharmaceutical product according to claim 27, or a pharmaceutical composition according to claim 28, for use in treating or preventing a neurological disease, disorder, or symptom in an individual.

36. A compound according to any one of claims 1 to 26, or a pharmaceutically acceptable salt thereof, or a pharmaceutical product according to claim 27, or a pharmaceutical composition according to claim 28, for use in treating or preventing a muscarinic receptor 4 (M_4) mediated disease, disorder, or symptom in an individual.

37. The compound, pharmaceutically acceptable salt thereof, pharmaceutical product, or pharmaceutical composition for use according to claim 35 or 36, wherein the disease, disorder, or symptom is selected from: Tourette's syndrome (TS), Alzheimer's Disease (AD), schizophrenia, Lewy Body Dementia (LBD), cognitive deficits associated with schizophrenia, Parkinson's Disease, parkinsonism, tremor, dyskinesias, excessive daytime sleepiness, dystonia, chorea, levodopa induced dyskinesia, attention deficit hyperactivity disorder (ADHD), cerebral palsy, progressive supranuclear palsy (PSP), Multiple System Atrophy (MSA), Huntington's disease (HD), and chorea associate with Huntington's disease.

38. The use, or compound, pharmaceutical product, or pharmaceutical composition for use according to any one of claims 31-37, wherein the disease, disorder, or symptom is parkinsonism.

39. The use, or compound, pharmaceutical product, or pharmaceutical composition for use according to any one of claims 31-37, wherein the disease, disorder, or symptom is tremor.

40. The use, or compound, pharmaceutical product, or pharmaceutical composition for use according to any one of claims 31-37, wherein the disease, disorder, or symptom is dystonia.

41. Use of a compound according to any one of claims 1-26, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for antagonizing a muscarinic receptor 4 (M_4) of a cell *in vivo*.