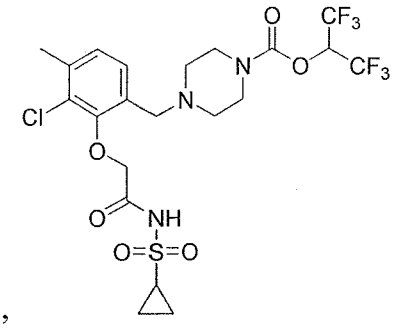
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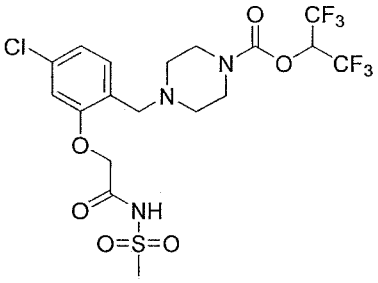
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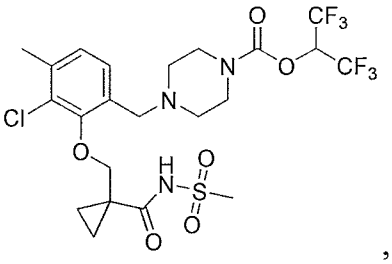
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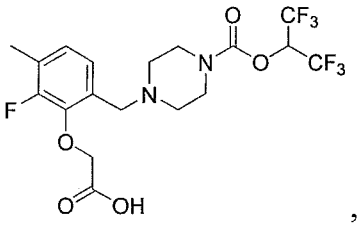
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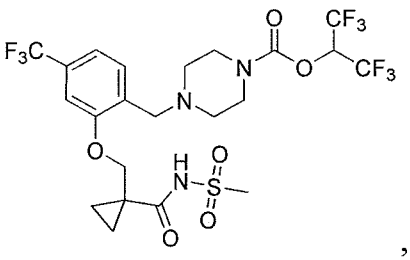
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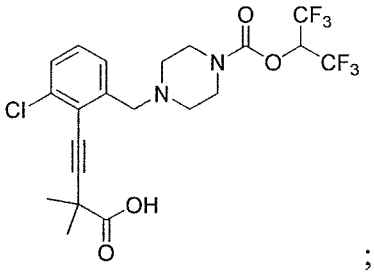

;

or a pharmaceutically acceptable salt or solvate thereof.

[0008] In another embodiment is a pharmaceutical composition comprising a compound of Formula (I) described herein, or a pharmaceutically acceptable salt or solvate thereof, and at least one pharmaceutically acceptable excipient.

[0008a] In another aspect is a compound as described herein, or a pharmaceutically acceptable salt or solvate thereof for use in therapy.

[0009] In another embodiment is a method of treating pain in a patient in need thereof comprising administering to the patient a therapeutically effective amount of a compound of Formula (I) described herein, or a pharmaceutically acceptable salt or solvate thereof. In some embodiments, the pain is neuropathic pain. In some embodiments, the pain is inflammatory pain.

[0009a] In another aspect is a use of a compound as described herein, or a pharmaceutically acceptable salt or solvate thereof in the manufacture of a medicament for treating pain in a patient.

[0010] In another embodiment is a method of treating a disease or disorder in a patient in need thereof comprising administering to the patient a therapeutically effective amount of a compound of Formula (I) described herein, or a pharmaceutically acceptable salt or solvate thereof, wherein the disease or disorder is selected from the group consisting of epilepsy/seizure disorder, multiple sclerosis, neuromyelitis optica (NMO), Tourette syndrome, Alzheimer's disease, and abdominal pain associated with irritable bowel syndrome. In some embodiments, the disease or disorder is epilepsy/seizure disorder. In some embodiments, the disease or disorder is multiple sclerosis. In some embodiments, the disease or disorder is neuromyelitis optica (NMO). In some embodiments, the disease or disorder is Tourette syndrome. In some embodiments, the disease or disorder is Alzheimer's disease. In some embodiments, the disease or disorder is abdominal pain associated with irritable bowel syndrome.

[0010a] In another aspect is a use of a compound as described herein, or a pharmaceutically acceptable salt or solvate thereof in the manufacture of a medicament for treating a disease or disorder in a patient, wherein the disease or disorder is selected from the group consisting of epilepsy/seizure disorder, multiple sclerosis, neuromyelitis optica (NMO), Tourette syndrome, Alzheimer's disease, and abdominal pain associated with irritable bowel syndrome.

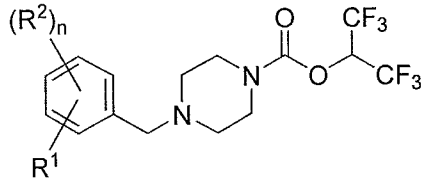
[0011] In another embodiment is a method of treating attention deficit and hyperactivity disorder (ADHD) in a patient in need thereof comprising administering to the patient a therapeutically effective amount of a compound of Formula (I) described herein, or a pharmaceutically acceptable salt or solvate thereof.

[0011a] In another aspect is a use of a compound as described herein, or a pharmaceutically acceptable salt or solvate thereof in the manufacture of a medicament for treating attention deficit and hyperactivity disorder (ADHD) in a patient.

CLAIMS

We Claim:

1. A compound having the structure of Formula (I):



Formula (I);

wherein:

R^1 is $-R^{14}$, $-OR^3$, $-SR^4$, $-S(O)_2R^4$, $-N(R^4)(R^5)$, $-NH(R^{4'})$, or $-C\equiv C-(CR^6R^7)-R^8$;

each R^2 is independently selected from C_{1-6}alkyl, halogen, -CN, C_{1-6}haloalkyl, $-C_{1-6}$alkyl(heterocycloalkyl), $-OR^{17}$, and $-C(O)NR^{18}R^{19}$;

R^3 is $-(CR^6R^7)_m-R^8$, $-(CR^6R^7)_p-Y-(CR^6R^7)_q-R^8$, or $-(CR^6R^7)_t-C_{3-6}$cycloalkyl$-R^8$;

R^4 is $-(CR^6R^7)_m-R^{8'}$, $-(CR^6R^7)_v-C(O)OH$, or $-(CR^6R^7)_p-Y-(CR^6R^7)_q-R^8$;

$R^{4'}$ is $-(CR^6R^7)_m-R^{8'}$, $-(CR^6R^7)_p-Y-(CR^6R^7)_q-R^8$, $-C_{4-6}$alkyl-C(O)OH, $-C_{3-6}$cycloalkyl-C(O)OH, or $-C_{1-6}$alkyl$-C_{3-6}$cycloalkyl-C(O)OH;

Y is -O- or $-N(R^{22})-$;

R^5 is C_{1-6}alkyl or $-CH_2$-phenyl optionally substituted with one, two, or three groups independently selected from halogen, C_{1-6}alkyl, C_{1-6}haloalkyl, and C_{1-6}alkoxy;

each R^6 and R^7 is each independently selected from H, F, and C_{1-6}alkyl; or R^6 and R^7, together with the carbon to which they are attached, form a C_{3-6}cycloalkyl ring;

R^8 is $-C(O)OR^9$, $-C(O)R^{10}$, or $-C(O)O-(CR^{12}R^{13})-OC(O)R^{11}$;

$R^{8'}$ is $-C(O)OR^{9'}$, $-C(O)R^{10'}$, or $-C(O)O-(CR^{12}R^{13})-OC(O)R^{11}$;

R^9 is H or C_{1-6}alkyl;

$R^{9'}$ is C_{1-6}alkyl;

R^{10} is C_{1-6}alkyl or $-NHSO_2R^{21}$;

$R^{10'}$ is C_{2-6}alkyl or $-NHSO_2R^{21}$;

R^{11} is C_{1-6}alkyl or C_{1-6}alkoxy;

R^{12} and R^{13} is each independently H or C_{1-6}alkyl;

R^{14} is $-(CR^{15}R^{16})_m-R^8$ or $-(CR^6R^7)_p-Y-(CR^6R^7)_q-R^8$;

each R^{15} and R^{16} is each independently selected from H, F, and C_{1-6}alkyl;

each R^{17} is independently selected from H, C_{1-6}alkyl, C_{1-6}haloalkyl, and C_{3-6}cycloalkyl;

each R^{18} and R^{19} is each independently selected from H, C_{1-6}alkyl, C_{3-6}cycloalkyl, aryl, and heteroaryl; or R^{18} and R^{19}, together with the nitrogen to which they are attached, form a heterocycloalkyl ring optionally substituted with one, two, or three R^{20};

each R^{20} is independently selected from halogen, C_{1-6}alkyl, C_{1-6}haloalkyl, oxo, -CN, and C_{3-6}cycloalkyl;

R^{21} is C_{1-6}alkyl or C_{3-6}cycloalkyl;

R^{22} is H, C_{1-6}alkyl, or $-SO_2R^{23}$;

R^{23} is C_{1-6}alkyl;

m is 1, 2, 3 or 4;

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

p is 2, 3, or 4;

q is 1, 2, or 3;

t is 0, 1, or 2; and

v is 3 or 4;

or a pharmaceutically acceptable salt or solvate thereof.

2. The compound of claim 1, or a pharmaceutically acceptable salt or solvate thereof, wherein R^1 is $-OR^3$.
3. The compound of claim 1 or 2, or a pharmaceutically acceptable salt or solvate thereof, wherein R^3 is $-(CR^6R^7)_m-R^8$.
4. The compound of any one of claims 1-3, or a pharmaceutically acceptable salt or solvate thereof, wherein m is 1, 2, or 3.
5. The compound of any one of claims 1-4, or a pharmaceutically acceptable salt or solvate thereof, wherein m is 1.
6. The compound of any one of claims 1-4, or a pharmaceutically acceptable salt or solvate thereof, wherein m is 2.
7. The compound of any one of claims 1-4, or a pharmaceutically acceptable salt or solvate thereof, wherein m is 3.
8. The compound of claim 1 or 2, or a pharmaceutically acceptable salt or solvate thereof, wherein R^3 is $-(CR^6R^7)_p-Y-(CR^6R^7)_q-R^8$.
9. The compound of claim 8, or a pharmaceutically acceptable salt or solvate thereof, wherein Y is -O-.
10. The compound of claim 8, or a pharmaceutically acceptable salt or solvate thereof, wherein Y is $-N(R^{22})-$.

11. The compound of claim 10, or a pharmaceutically acceptable salt or solvate thereof, wherein R^{22} is $-SO_2R^{23}$.
12. The compound of any one of claims 8-11, or a pharmaceutically acceptable salt or solvate thereof, wherein q is 1.
13. The compound of any one of claims 8-12, or a pharmaceutically acceptable salt or solvate thereof, wherein p is 2.
14. The compound of claim 1, or a pharmaceutically acceptable salt or solvate thereof, wherein R^1 is $-C\equiv C-(CR^6R^7)-R^8$.
15. The compound of claim 1 or 2, or a pharmaceutically acceptable salt or solvate thereof, wherein R^3 is $-(CR^6R^7)_t-C_{3-6}$cycloalkyl-R^8.
16. The compound of claim 15, or a pharmaceutically acceptable salt or solvate thereof, wherein t is 1.
17. The compound of claim 15, or a pharmaceutically acceptable salt or solvate thereof, wherein t is 0.
18. The compound of any one of claims 1-16, or a pharmaceutically acceptable salt or solvate thereof, wherein each R^6 and R^7 is each independently selected from H and C_{1-6}alkyl.
19. The compound of any one of claims 1-16, or a pharmaceutically acceptable salt or solvate thereof, wherein each R^6 and R^7 is H.
20. The compound of any one of claims 1-16, or a pharmaceutically acceptable salt or solvate thereof, wherein R^6 and R^7, together with the carbon to which they are attached, form a C_{3-6}cycloalkyl ring.
21. The compound of any one of claims 1-20, or a pharmaceutically acceptable salt or solvate thereof, wherein R^8 is $-C(O)OR^9$.
22. The compound of claim 21, or a pharmaceutically acceptable salt or solvate thereof, wherein R^9 is H.
23. The compound of claim 21, or a pharmaceutically acceptable salt or solvate thereof, wherein R^9 is C_{1-6}alkyl.
24. The compound of any one of claims 1-20, or a pharmaceutically acceptable salt or solvate thereof, wherein R^8 is $-C(O)R^{10}$.
25. The compound of claim 24, or a pharmaceutically acceptable salt or solvate thereof, wherein R^{10} is $-NHSO_2R^{21}$.
26. The compound of any one of claims 1-20, or a pharmaceutically acceptable salt or solvate thereof, wherein R^8 is $-C(O)O-(CR^{12}R^{13})-OC(O)R^{11}$.

27. The compound of claim 26, or a pharmaceutically acceptable salt or solvate thereof, wherein R^{11} is C_{1-6}alkyl.
28. The compound of claim 26, or a pharmaceutically acceptable salt or solvate thereof, wherein R^{11} is C_{1-6}alkoxy.
29. The compound of claim 1, or a pharmaceutically acceptable salt or solvate thereof, wherein R^1 is $-N(R^4)(R^5)$.
30. The compound of claim 29, or a pharmaceutically acceptable salt or solvate thereof, wherein R^5 is $-CH_3$.
31. The compound of claim 29, or a pharmaceutically acceptable salt or solvate thereof, wherein R^5 is $-CH_2$-phenyl optionally substituted with one, two, or three groups independently selected from halogen, C_{1-6}alkyl, C_{1-6}haloalkyl, and C_{1-6}alkoxy.
32. The compound of claim 1, or a pharmaceutically acceptable salt or solvate thereof, wherein R^1 is $-SR^4$.
33. The compound of claim 1, or a pharmaceutically acceptable salt or solvate thereof, wherein R^1 is $-S(O)_2R^4$.
34. The compound of any one of claims 29-33, or a pharmaceutically acceptable salt or solvate thereof, wherein R^4 is $-(CR^6R^7)_v$-C(O)OH.
35. The compound of claim 34, or a pharmaceutically acceptable salt or solvate thereof, wherein v is 3.
36. The compound of claim 34, or a pharmaceutically acceptable salt or solvate thereof, wherein v is 4.
37. The compound of any one of claims 29-33, or a pharmaceutically acceptable salt or solvate thereof, wherein R^4 is $-(CR^6R^7)_m$-$R^{8'}$.
38. The compound of claim 37, or a pharmaceutically acceptable salt or solvate thereof, wherein m is 1, 2, or 3.
39. The compound of claim 37, or a pharmaceutically acceptable salt or solvate thereof, wherein m is 1.
40. The compound of claim 37, or a pharmaceutically acceptable salt or solvate thereof, wherein m is 2.
41. The compound of claim 37, or a pharmaceutically acceptable salt or solvate thereof, wherein m is 3.
42. The compound of any one of claims 37-41, or a pharmaceutically acceptable salt or solvate thereof, wherein $R^{8'}$ is $-C(O)OR^{9'}$.

43. The compound of any one of claims 37-41, or a pharmaceutically acceptable salt or solvate thereof, wherein $R^{8'}$ is $-C(O)R^{10'}$.
44. The compound of claim 43, or a pharmaceutically acceptable salt or solvate thereof, wherein $R^{10'}$ is $-NHSO_2R^{21}$.
45. The compound of any one of claims 37-41, or a pharmaceutically acceptable salt or solvate thereof, wherein $R^{8'}$ is $-C(O)O-(CR^{12}R^{13})-OC(O)R^{11}$.
46. The compound of claim 45, or a pharmaceutically acceptable salt or solvate thereof, wherein R^{11} is C_{1-6}alkyl.
47. The compound of claim 45, or a pharmaceutically acceptable salt or solvate thereof, wherein R^{11} is C_{1-6}alkoxy.
48. The compound of any one of claims 29-33, or a pharmaceutically acceptable salt or solvate thereof, wherein R^4 is $-(CR^6R^7)_p-Y-(CR^6R^7)_q-R^8$.
49. The compound of claim 48, or a pharmaceutically acceptable salt or solvate thereof, wherein Y is -O-.
50. The compound of claim 48, or a pharmaceutically acceptable salt or solvate thereof, wherein Y is $-N(R^{22})-$.
51. The compound of claim 50, or a pharmaceutically acceptable salt or solvate thereof, wherein R^{22} is $-SO_2R^{23}$.
52. The compound of any one of claims 48-51, or a pharmaceutically acceptable salt or solvate thereof, wherein q is 1.
53. The compound of any one of claims 48-52, or a pharmaceutically acceptable salt or solvate thereof, wherein p is 2.
54. The compound of any one of claims 48-53, or a pharmaceutically acceptable salt or solvate thereof, wherein R^8 is $-C(O)OR^9$.
55. The compound of claim 54, or a pharmaceutically acceptable salt or solvate thereof, wherein R^9 is H.
56. The compound of claim 54, or a pharmaceutically acceptable salt or solvate thereof, wherein R^9 is C_{1-6}alkyl.
57. The compound of any one of claims 48-53, or a pharmaceutically acceptable salt or solvate thereof, wherein R^8 is $-C(O)R^{10}$.
58. The compound of claim 57, or a pharmaceutically acceptable salt or solvate thereof, wherein R^{10} is $-NHSO_2R^{21}$.
59. The compound of any one of claims 48-53, or a pharmaceutically acceptable salt or solvate thereof, wherein R^8 is $-C(O)O-(CR^{12}R^{13})-OC(O)R^{11}$.

60. The compound of claim 59, or a pharmaceutically acceptable salt or solvate thereof, wherein R^{11} is C_{1-6}alkyl.
61. The compound of claim 59, or a pharmaceutically acceptable salt or solvate thereof, wherein R^{11} is C_{1-6}alkoxy.
62. The compound of claim 1, or a pharmaceutically acceptable salt or solvate thereof, wherein R^1 is $-NH(R^{4'})$.
63. The compound of claim 62, or a pharmaceutically acceptable salt or solvate thereof, wherein $R^{4'}$ is $-(CR^6R^7)_m-R^{8'}$.
64. The compound of claim 63, or a pharmaceutically acceptable salt or solvate thereof, wherein m is 1, 2, or 3.
65. The compound of claim 63, or a pharmaceutically acceptable salt or solvate thereof, wherein m is 1.
66. The compound of claim 63, or a pharmaceutically acceptable salt or solvate thereof, wherein m is 2.
67. The compound of claim 63, or a pharmaceutically acceptable salt or solvate thereof, wherein m is 3.
68. The compound of any one of claims 63-67, or a pharmaceutically acceptable salt or solvate thereof, wherein $R^{8'}$ is $-C(O)OR^{9'}$.
69. The compound of any one of claims 63-67, or a pharmaceutically acceptable salt or solvate thereof, wherein $R^{8'}$ is $-C(O)R^{10'}$.
70. The compound of claim 69, or a pharmaceutically acceptable salt or solvate thereof, wherein $R^{10'}$ is $-NHSO_2R^{21}$.
71. The compound of any one of claims 63-67, or a pharmaceutically acceptable salt or solvate thereof, wherein $R^{8'}$ is $-C(O)O-(CR^{12}R^{13})-OC(O)R^{11}$.
72. The compound of claim 71, or a pharmaceutically acceptable salt or solvate thereof, wherein R^{11} is C_{1-6}alkyl.
73. The compound of claim 71, or a pharmaceutically acceptable salt or solvate thereof, wherein R^{11} is C_{1-6}alkoxy.
74. The compound of claim 62, or a pharmaceutically acceptable salt or solvate thereof, wherein $R^{4'}$ is $-(CR^6R^7)_p-Y-(CR^6R^7)_q-R^8$.
75. The compound of claim 74, or a pharmaceutically acceptable salt or solvate thereof, wherein Y is -O-.
76. The compound of claim 74, or a pharmaceutically acceptable salt or solvate thereof, wherein Y is $-N(R^{22})-$.

77. The compound of claim 76, or a pharmaceutically acceptable salt or solvate thereof, wherein R^{22} is $-SO_2R^{23}$.
78. The compound of any one of claims 74-77, or a pharmaceutically acceptable salt or solvate thereof, wherein q is 1.
79. The compound of any one of claims 74-78, or a pharmaceutically acceptable salt or solvate thereof, wherein p is 2.
80. The compound of any one of claims 74-79, or a pharmaceutically acceptable salt or solvate thereof, wherein R^8 is $-C(O)OR^9$.
81. The compound of claim 80, or a pharmaceutically acceptable salt or solvate thereof, wherein R^9 is H.
82. The compound of claim 80, or a pharmaceutically acceptable salt or solvate thereof, wherein R^9 is C_{1-6}alkyl.
83. The compound of any one of claims 74-79, or a pharmaceutically acceptable salt or solvate thereof, wherein R^8 is $-C(O)R^{10}$.
84. The compound of claim 83, or a pharmaceutically acceptable salt or solvate thereof, wherein R^{10} is $-NHSO_2R^{21}$.
85. The compound of any one of claims 74-79, or a pharmaceutically acceptable salt or solvate thereof, wherein R^8 is $-C(O)O-(CR^{12}R^{13})-OC(O)R^{11}$.
86. The compound of claim 85, or a pharmaceutically acceptable salt or solvate thereof, wherein R^{11} is C_{1-6}alkyl.
87. The compound of claim 85, or a pharmaceutically acceptable salt or solvate thereof, wherein R^{11} is C_{1-6}alkoxy.
88. The compound of any one of claims 34-87, or a pharmaceutically acceptable salt or solvate thereof, wherein each R^6 and R^7 is each independently selected from H and C_{1-6}alkyl.
89. The compound of any one of claims 34-87, or a pharmaceutically acceptable salt or solvate thereof, wherein each R^6 and R^7 is H.
90. The compound of any one of claims 34-87, or a pharmaceutically acceptable salt or solvate thereof, wherein R^6 and R^7, together with the carbon to which they are attached, form a C_{3-6}cycloalkyl ring.
91. The compound of claim 62, or a pharmaceutically acceptable salt or solvate thereof, wherein $R^{4'}$ is $-C_{4-6}$alkyl-C(O)OH.
92. The compound of claim 62, or a pharmaceutically acceptable salt or solvate thereof, wherein $R^{4'}$ is $-C_{3-6}$cycloalkyl-C(O)OH.

93. The compound of claim 62, or a pharmaceutically acceptable salt or solvate thereof, wherein $R^{4'}$ is -C_{1-6}alkyl-C_{3-6}cycloalkyl-C(O)OH.

94. The compound of claim 1, or a pharmaceutically acceptable salt or solvate thereof, wherein R^1 is -R^{14}.

95. The compound of claim 94, or a pharmaceutically acceptable salt or solvate thereof, wherein R^{14} is -$(CR^{15}R^{16})_m$-R^8.

96. The compound of claim 95, or a pharmaceutically acceptable salt or solvate thereof, wherein m is 1.

97. The compound of claim 95, or a pharmaceutically acceptable salt or solvate thereof, wherein m is 2.

98. The compound of claim 95, or a pharmaceutically acceptable salt or solvate thereof, wherein m is 3.

99. The compound of claim 95, or a pharmaceutically acceptable salt or solvate thereof, wherein m is 4.

100. The compound of any one of claims 95-99, or a pharmaceutically acceptable salt or solvate thereof, wherein R^8 is -C(O)OR^9.

101. The compound of claim 100, or a pharmaceutically acceptable salt or solvate thereof, wherein R^9 is H.

102. The compound of claim 100, or a pharmaceutically acceptable salt or solvate thereof, wherein R^9 is C_{1-6}alkyl.

103. The compound of any one of claims 1-102, or a pharmaceutically acceptable salt or solvate thereof, wherein each R^2 is independently selected from C_{1-6}alkyl, halogen, -CN, and C_{1-6}haloalkyl.

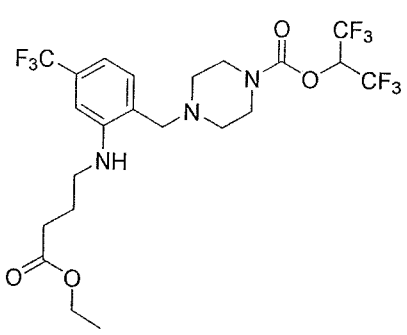
104. The compound of any one of claims 1-103, or a pharmaceutically acceptable salt or solvate thereof, wherein each R^2 is independently selected from C_{1-6}alkyl, halogen, and C_{1-6}haloalkyl.

105. The compound of any one of claims 1-104, or a pharmaceutically acceptable salt or solvate thereof, wherein n is 1.

106. The compound of claim 105, or a pharmaceutically acceptable salt or solvate thereof, wherein R^2 is -Cl.

107. The compound of claim 105, or a pharmaceutically acceptable salt or solvate thereof, wherein R^2 is -CF_3.

108. A compound having the structure selected from: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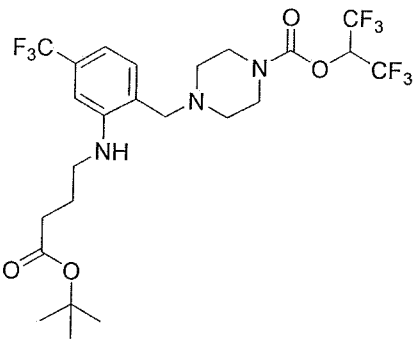
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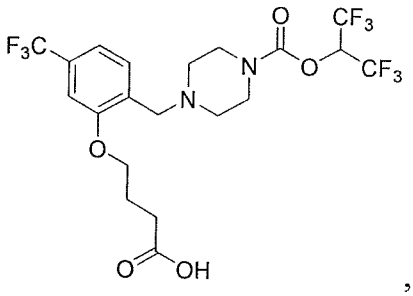
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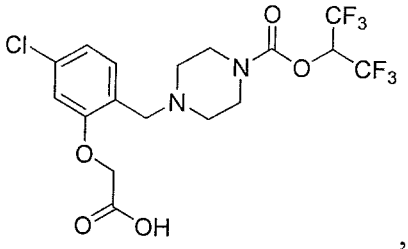
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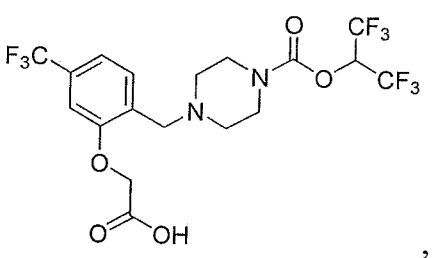
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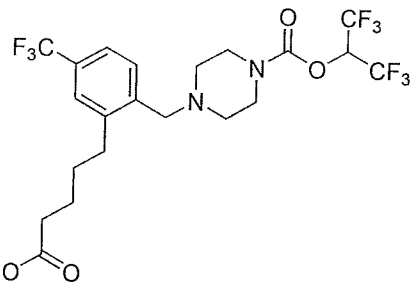
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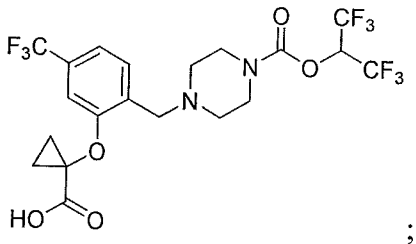
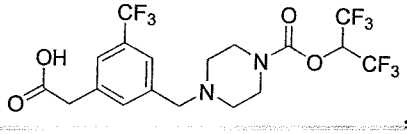

and ;

or a pharmaceutically acceptable salt or solvate thereof.

109. A compound having the structure selected from: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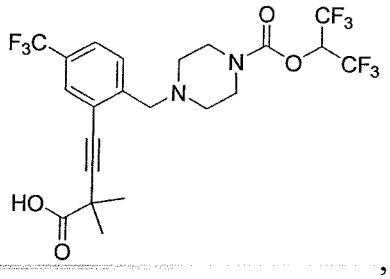
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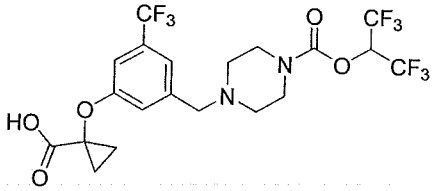
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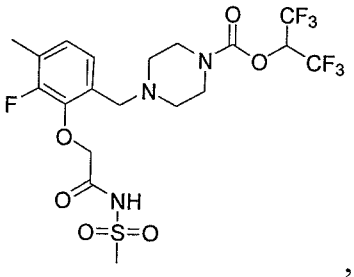
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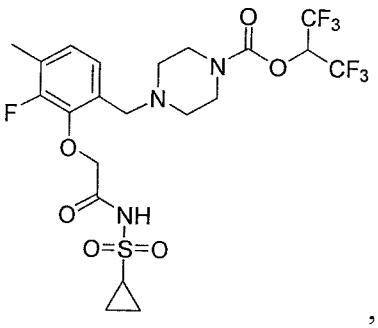
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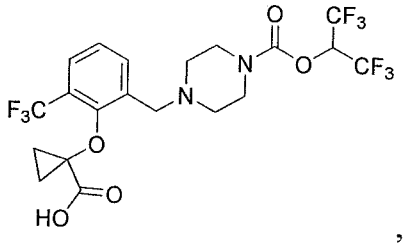
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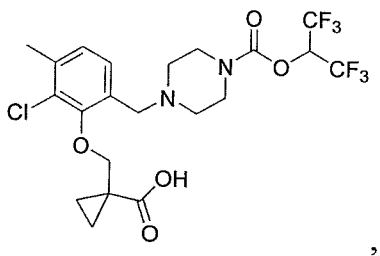
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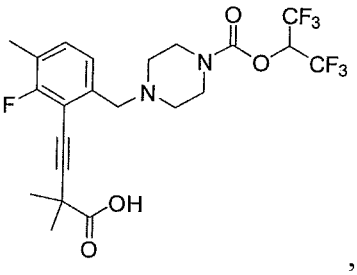
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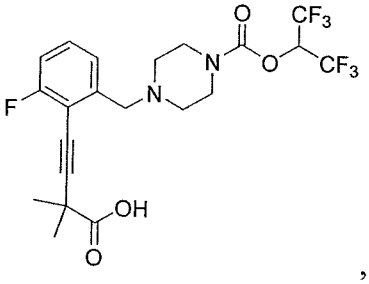
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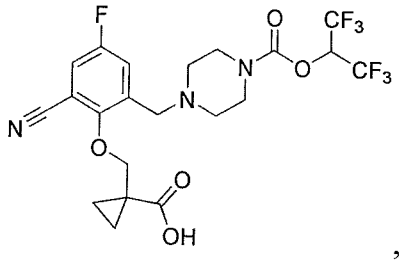
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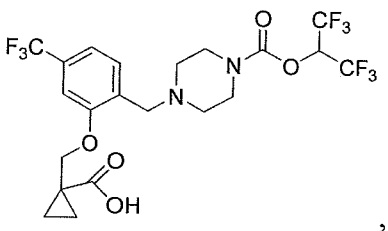
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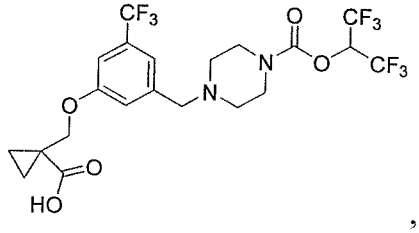
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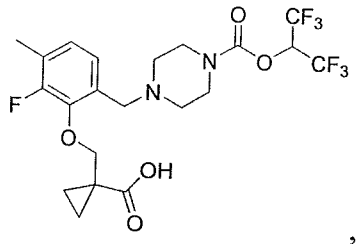
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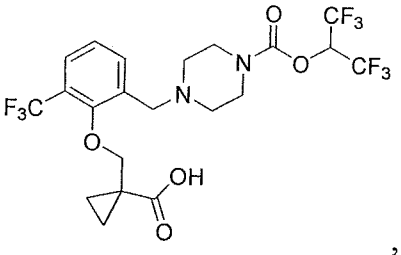
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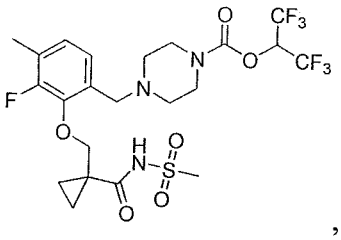
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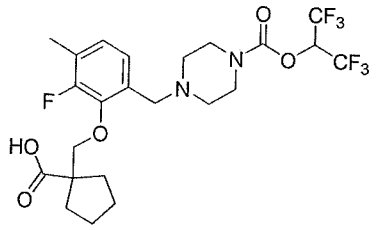
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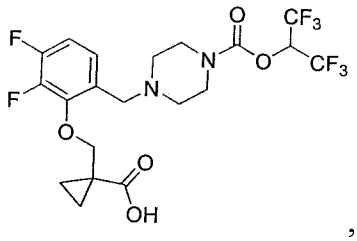
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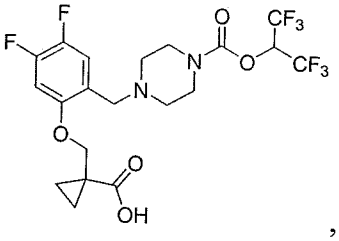
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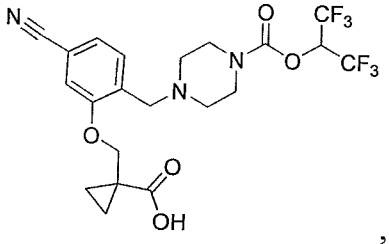
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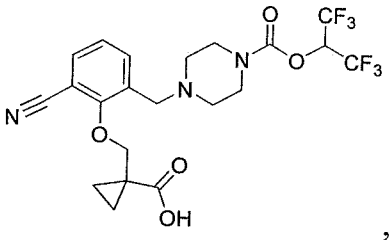
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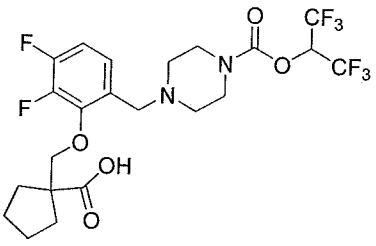
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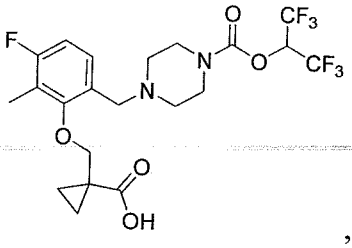
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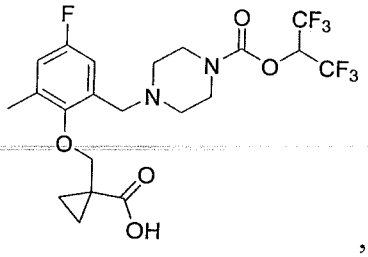
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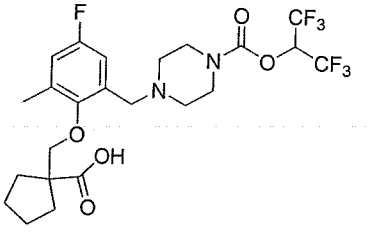
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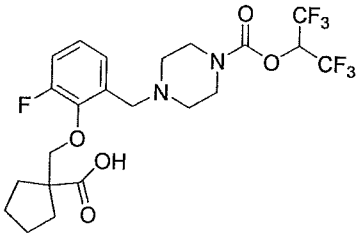
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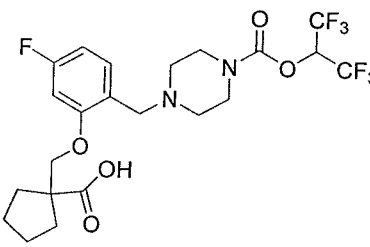
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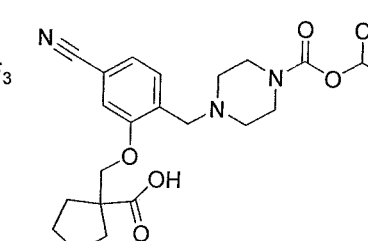
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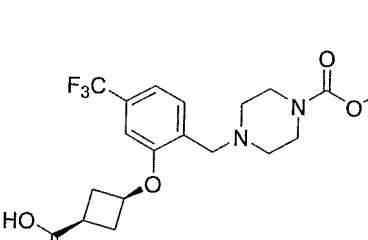
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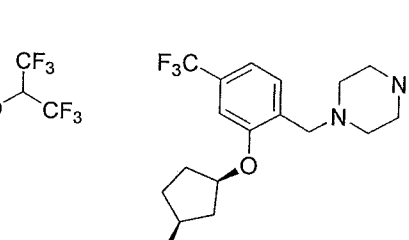
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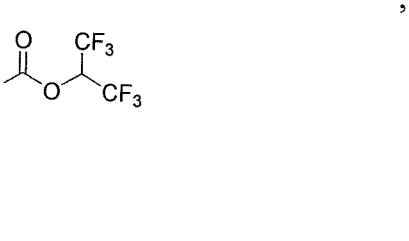
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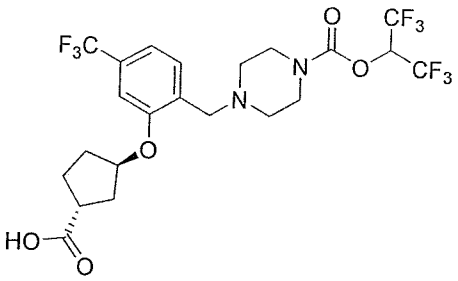
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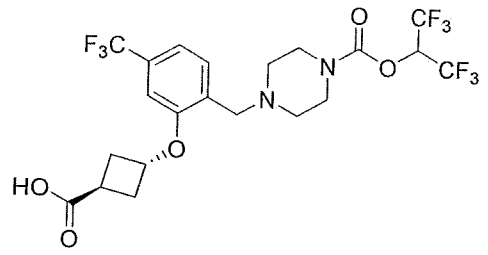
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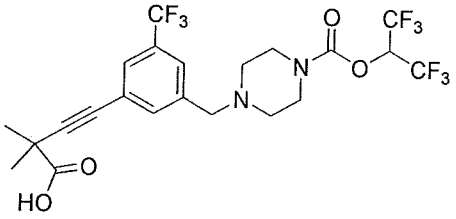
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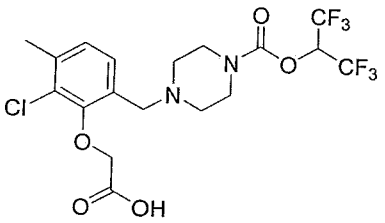
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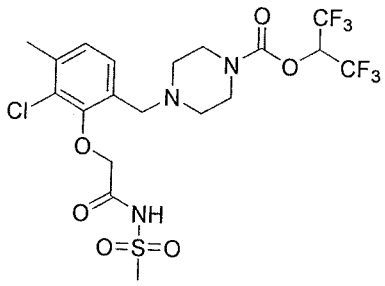
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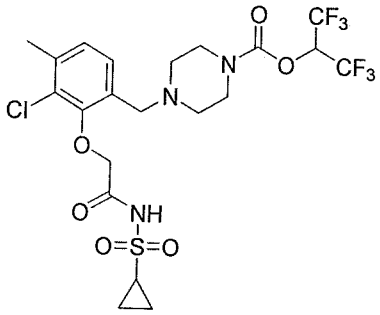
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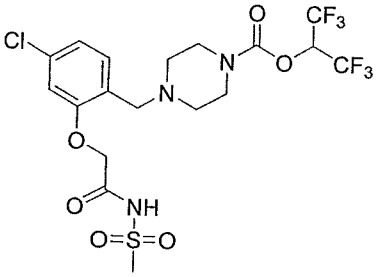
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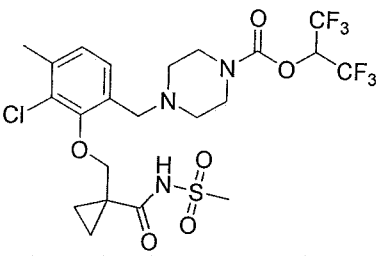
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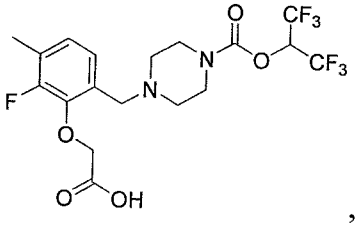
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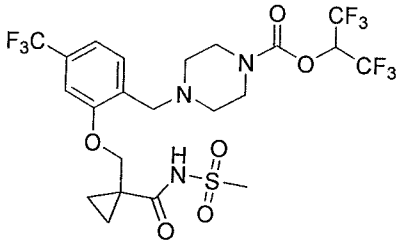
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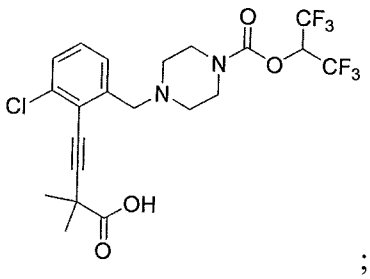
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or a pharmaceutically acceptable salt or solvate thereof.

110. A pharmaceutical composition comprising a compound of any one of claims 1-109, or a pharmaceutically acceptable salt or solvate thereof, and at least one pharmaceutically acceptable excipient.

111. The compound of any one of claims 1-109, or a pharmaceutically acceptable salt or solvate thereof for use in therapy.

112. Use of a compound of any one of claims 1-109, or a pharmaceutically acceptable salt or solvate thereof in the manufacture of a medicament for treating pain in a patient.

113. The use of claim 112, wherein the pain is neuropathic pain.

114. The use of claim 112, wherein the pain is inflammatory pain.

115. Use of a compound of any one of claims 1-109, or a pharmaceutically acceptable salt or solvate thereof in the manufacture of a medicament for treating a disease or disorder in a patient,

wherein the disease or disorder is selected from the group consisting of epilepsy/seizure disorder, multiple sclerosis, neuromyelitis optica (NMO), Tourette syndrome, Alzheimer's disease, and abdominal pain associated with irritable bowel syndrome.

116. The use of claim 115, wherein the disease or disorder is multiple sclerosis.

117. The use of claim 115, wherein the disease or disorder is Tourette syndrome.

118. The use of claim 115, wherein the disease or disorder is Alzheimer's disease.

119. Theuse of claim 115, wherein the disease or disorder is abdominal pain associated with irritable bowel syndrome.

120. Use of a compound of any one of claims 1-109, or a pharmaceutically acceptable salt or solvate thereof in the manufacture of a medicament for treating attention deficit and hyperactivity disorder (ADHD) in a patient.