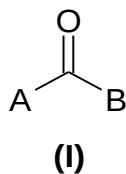


DETAILED DESCRIPTION OF THE INVENTION

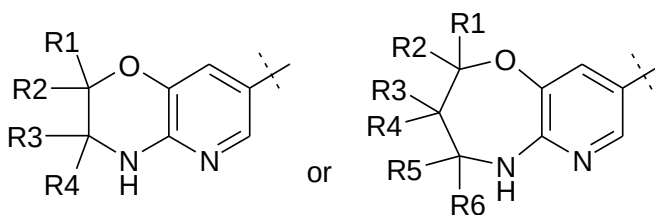
It has surprisingly been found that the problem mentioned above is solved by compounds of
5 formula I of the present invention.

Summary

There is provided a compound of the formula (I)

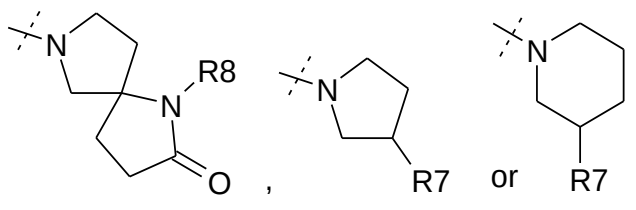


wherein A is:

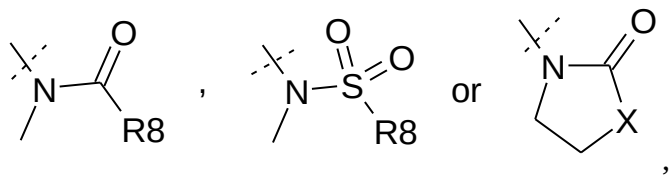


wherein each R1, R2, R3, R4, R5, and R6 is independently H, C₁₋₄-alkyl, or C₁₋₄-alkyl
15 substituted with a hydroxyl or halogen group, phenyl, 5-6 membered heteroaryl, or R1
and R2, R3 and R4 or R5 and R6 together form a 3-4 membered carbocycle, and

wherein B is:



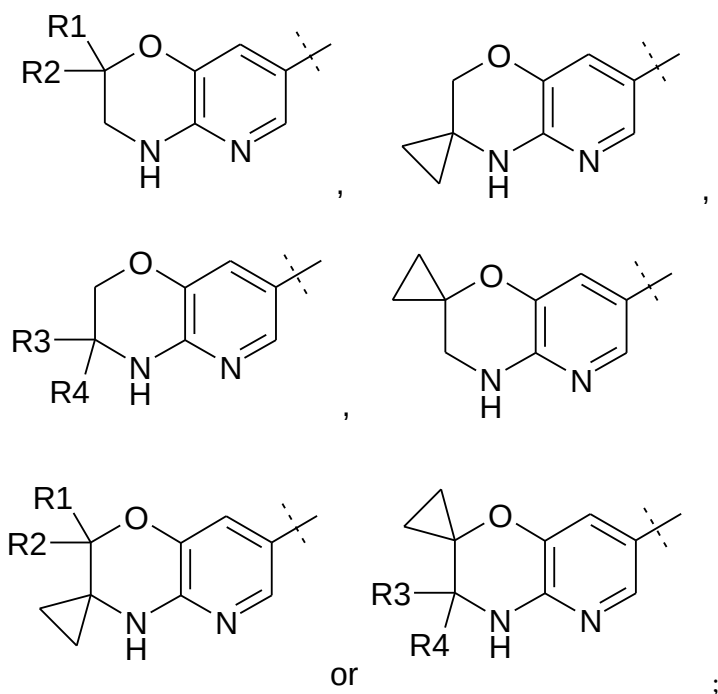
wherein R7 is H, C₁₋₃-alkyl, halogen, C₁₋₃-alkoxy, 5-6 membered heteroaryl, or



wherein R8 is C₁₋₆-alkyl, C₃₋₆-cycloalkyl, or heterocycle and X is CH₂ or O; or a pharmaceutically acceptable salt or hydrate thereof.

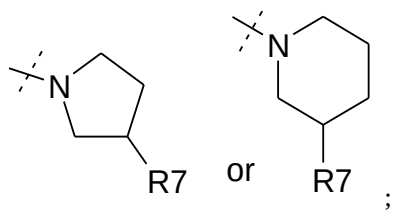
In an example, there is provided a compound of the formula (I)

5 wherein A is:



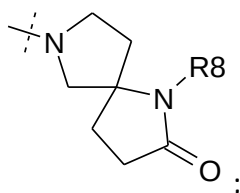
10 or a pharmaceutically acceptable salt or hydrate thereof.

In another example, there is provided a compound of the formula (I) wherein B is:



or a pharmaceutically acceptable salt or hydrate thereof.

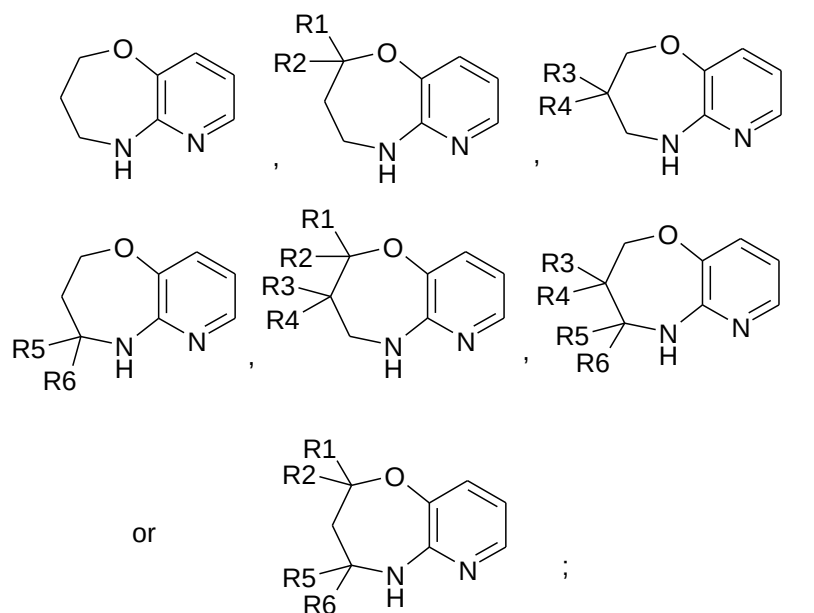
5 In another example, there is provided a compound of the formula (I) wherein B is:



or a pharmaceutically acceptable salt or hydrate thereof.

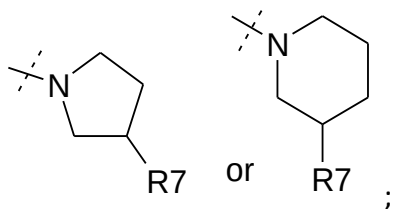
10

In another example, there is provided a compound of the formula (I) wherein A is:



or a pharmaceutically acceptable salt or hydrate thereof.

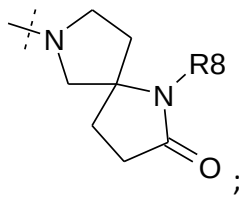
5 In another example, there is provided a compound of the formula (I) wherein B is:



or a pharmaceutically acceptable salt or hydrate thereof.

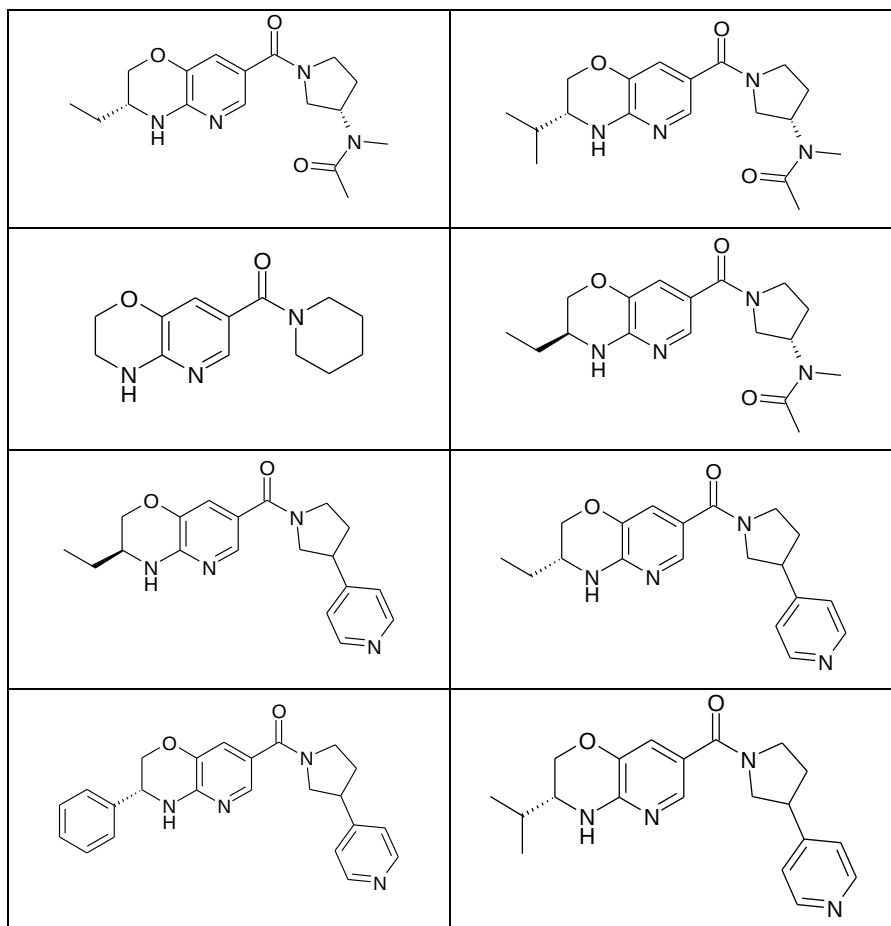
10

In another example, there is provided a compound of the formula (I) wherein B is:



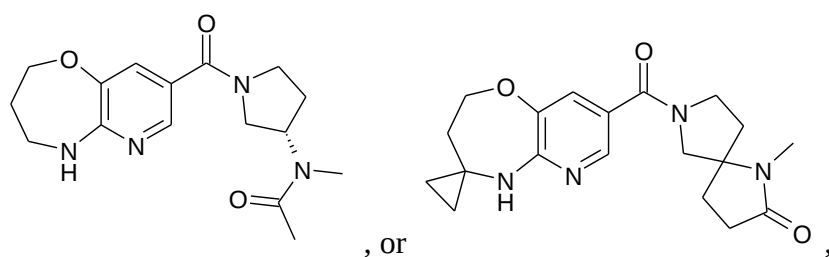
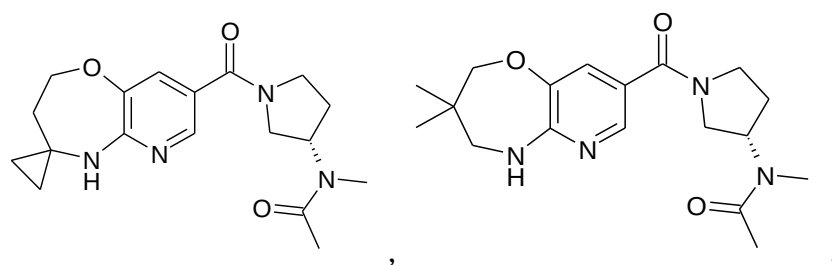
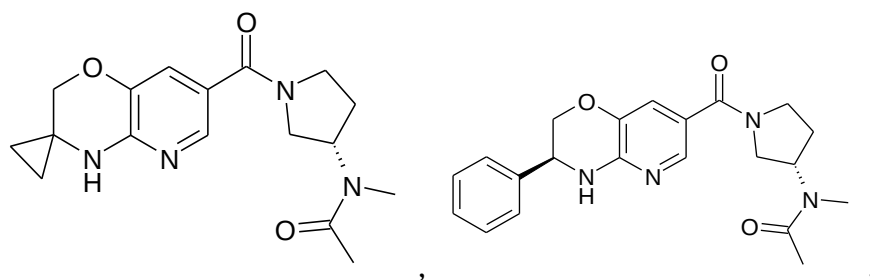
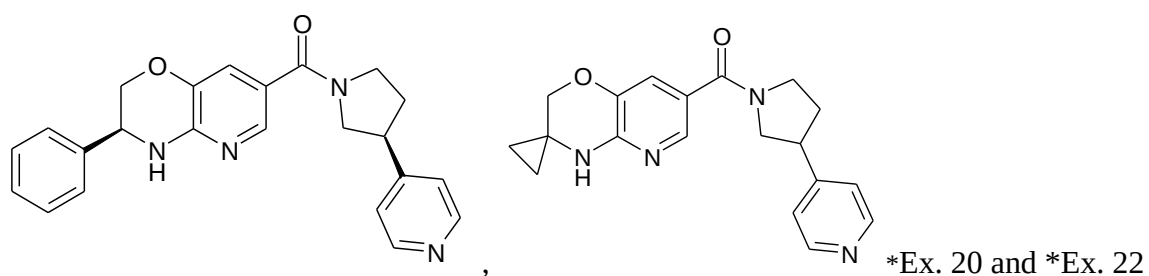
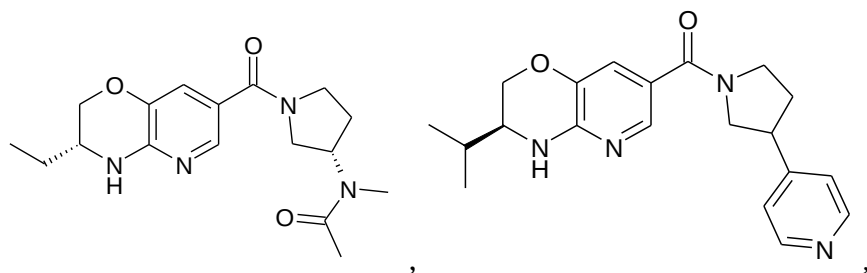
or a pharmaceutically acceptable salt or hydrate thereof.

5 There is provided a compound chosen from:



In an example, the compound is:

5



10 or the pharmaceutically acceptable salt or hydrate thereof.

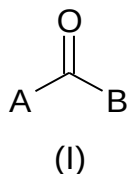
There is provided a pharmaceutical composition comprising a therapeutically effective amount of a compound according to the disclosure or any of its related examples or a pharmaceutically acceptable salt thereof.

- 5 There is provided a method of treating a disease chosen from Crohn's disease, ulcerative colitis, atopic dermatitis, psoriasis, chronic kidney disease, chronic obstructive pulmonary disease, idiopathic pulmonary fibrosis, rheumatoid arthritis, scleroderma, asthma, allergic rhinitis, allergic eczema, juvenile rheumatoid arthritis, juvenile idiopathic arthritis, graft versus host disease, psoriatic arthritis, colorectal cancer and pancreatic cancer related new onset diabetes
- 10 comprising administering to a patient a therapeutically effective amount of a compound according to the first embodiment or any of its related embodiments or a pharmaceutically acceptable salt thereof.

There is provided a process for preparation of a compound according to the first embodiment or any of its related embodiments by the methods shown herein below.

15

In one aspect, the present disclosure therefore relates to a compound of formula (I),



20 wherein

A is a group of formula A.1 or A.2:

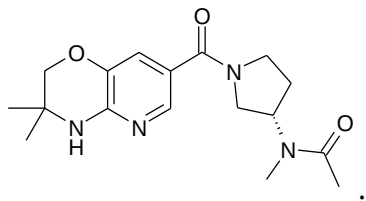
R^8 is selected from the group consisting of C_{1-6} -alkyl, C_{3-6} -cycloalkyl and 3-14 membered heterocyclyl and

X is CH_2 or O;

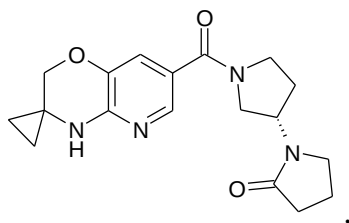
or a pharmaceutically acceptable salt thereof.

5

In another aspect, the present disclosure relates to a compound of formula:

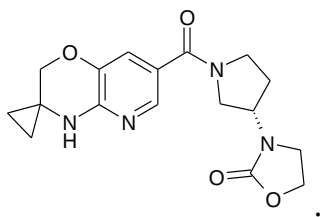


In another aspect, the present disclosure relates to a compound of formula:

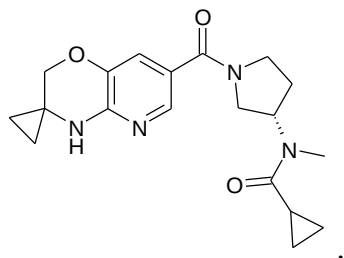


10

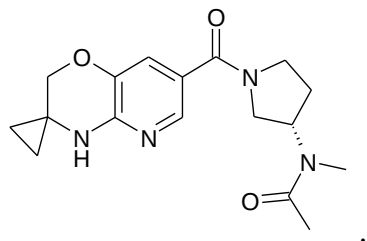
In another aspect, the present disclosure relates to a compound of formula:



In another aspect, the present disclosure relates to a compound of formula:

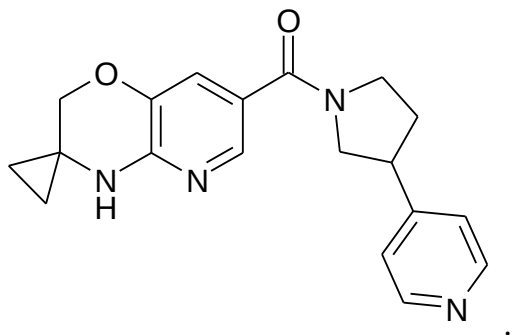


In another aspect, the present disclosure relates to a compound of formula:

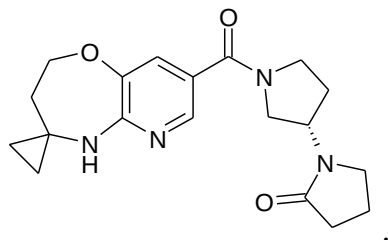


5

In another aspect, the present disclosure relates to a compound of formula:



10 In another aspect, the present disclosure relates to a compound of formula:

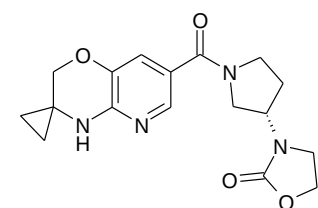


O=C1CCN1C(=O)c2cc3c(nc2)OCC4(CCC4)N3CN(C)C(=O)[C@H]1CCN(C1)C(=O)c2ccnc3c2OCCN3C4CC4CC(=O)N[C@H]1CCN1C(=O)c2cc3nc4c(c2)OCC(C)(C)CN4CC(=O)N[C@H]1CCCN1C(=O)c2cc3c(nc2)OCC(C)(C)N3

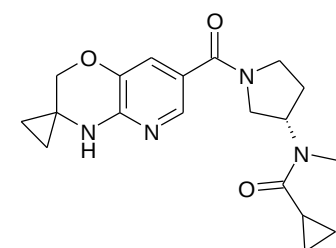
14b

O=C1CC[C@H](C1)C(=O)c2cnc3c2OCC4C5C(C3)NCC5

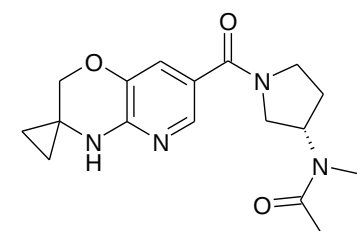
In another aspect, the present disclosure relates to a compound of formula:



In another aspect, the present disclosure relates to a compound of formula:

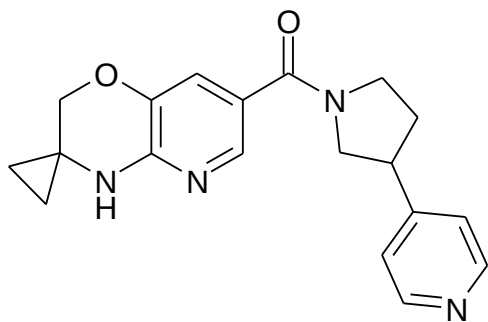


In another aspect, the present disclosure relates to a compound of formula:



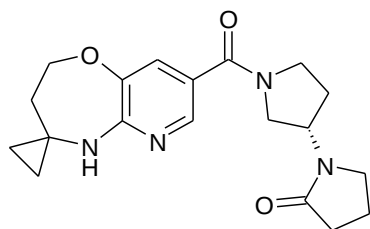
or a pharmaceutically acceptable salt thereof.

In another aspect, the present disclosure relates to a compound of formula:



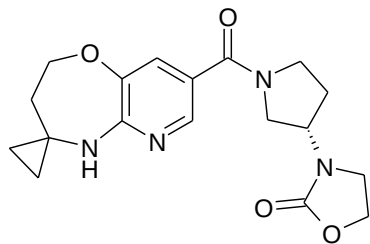
or a pharmaceutically acceptable salt thereof.

5 In another aspect, the present disclosure relates to a compound of formula:



or a pharmaceutically acceptable salt thereof.

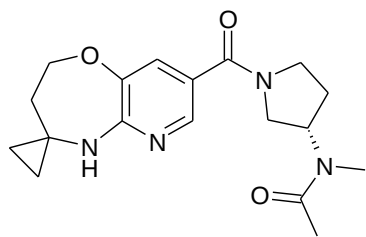
In another aspect, the present disclosure relates to a compound of formula:



10

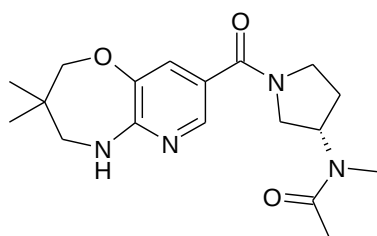
or a pharmaceutically acceptable salt thereof.

In another aspect, the present disclosure relates to a compound of formula:



or a pharmaceutically acceptable salt thereof.

5 In another aspect, the present disclosure relates to a compound of formula:



or a pharmaceutically acceptable salt thereof.

10 In another aspect, the present disclosure relates to a pharmaceutical composition comprising a therapeutically effective amount of at least one compound of formula I according to the disclosure or a pharmaceutically acceptable salt thereof and one or more pharmaceutically acceptable excipients.

15 In another aspect, the present disclosure relates to a compound according to the disclosure, or a pharmaceutically acceptable salt thereof for use as a medicament.

In another aspect, the present disclosure relates to the use of the compound according to the disclosure in the manufacture of a medicament for treating a patient suffering from Crohn's disease, ulcerative colitis, atopic dermatitis, systemic sclerosis, Non-Alcoholic Steatohepatitis

(NASH), psoriasis, chronic kidney disease, chronic obstructive pulmonary disease, idiopathic pulmonary fibrosis, rheumatoid arthritis, scleroderma, asthma, allergic rhinitis, allergic eczema, juvenile rheumatoid arthritis, juvenile idiopathic arthritis, graft versus host disease, psoriatic arthritis, colorectal cancer or pancreatic cancer related new onset diabetes.

5

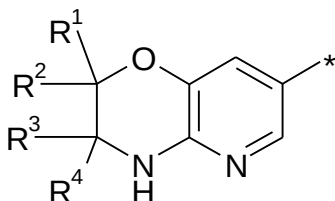
In another aspect, the present disclosure relates to the use of the compound according to the disclosure in the manufacture of a medicament for treating a patient suffering from Crohn's disease.

10 In another aspect, the present disclosure relates to the use of the compound according to the disclosure in the manufacture of a medicament for treating a patient suffering from atopic dermatitis.

15 In another aspect, the present disclosure relates to the use of the compound according to the disclosure in the manufacture of a medicament for treating a patient suffering from ulcerative colitis.

Preferred Embodiments

In another embodiment of the present invention A denotes a group of formula A.1.

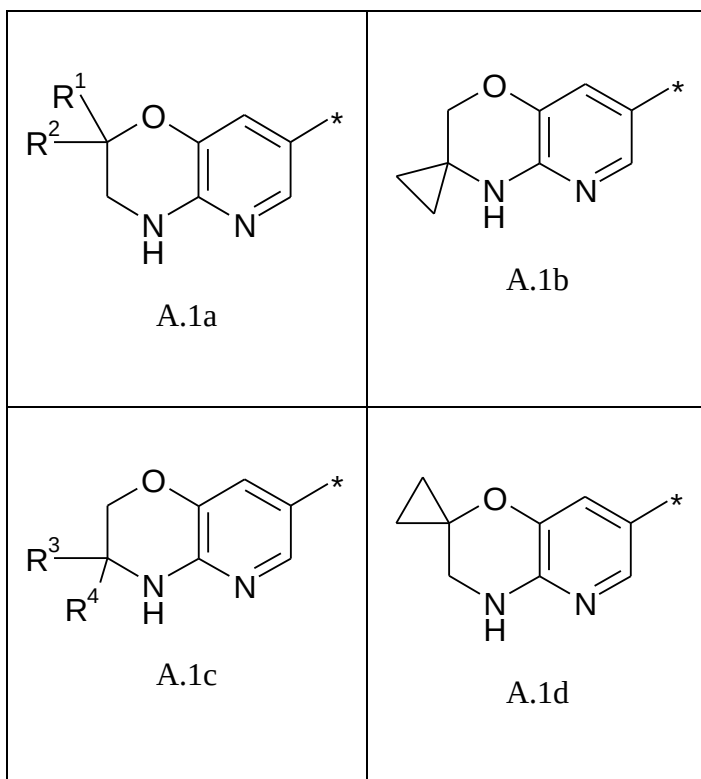


A.1

20

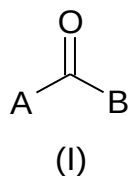
In another embodiment of the present invention

A is selected from the group consisting of formulas A.1a to A.1f



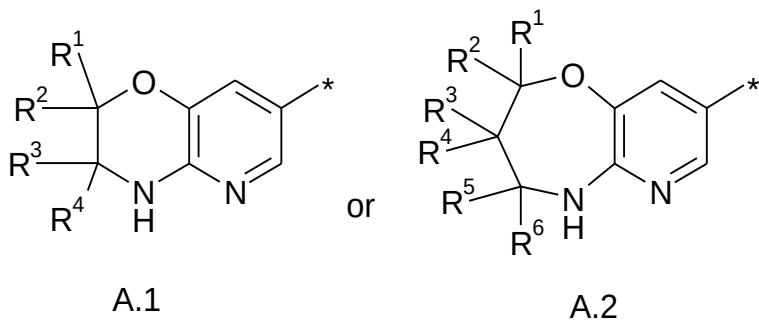
WE CLAIM:

1. A compound of the formula (I),



wherein

A is a group of formula A.1 or A.2:

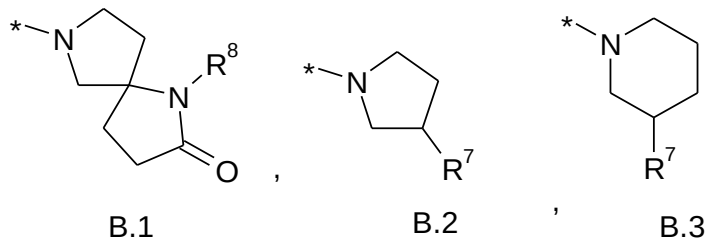


wherein each R^1 , R^2 , R^3 , R^4 , R^5 and R^6 is independently selected from the group consisting of H, C_{1-4} -alkyl, C_{1-4} -alkyl substituted with a hydroxyl or halogen group, phenyl and a 5-6 membered heteroaryl, or

R^1 and R^2 , R^3 and R^4 , or R^5 and R^6 together form a 3-4 membered carbocycle, and

wherein

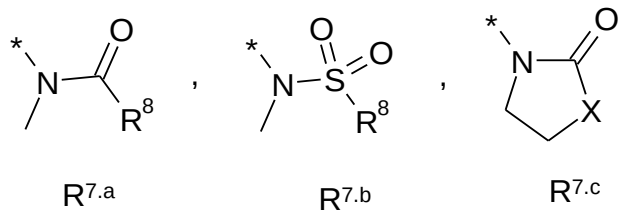
B is selected from the group consisting of formulas B.1, B.2 and B.3:



wherein

R^7 is H, C₁₋₃-alkyl, halogen, C₁₋₃-alkoxy, 5-6 membered heteroaryl, or

R^7 is selected from the group consisting of $R^{7.a}$, $R^{7.b}$ and $R^{7.c}$



wherein

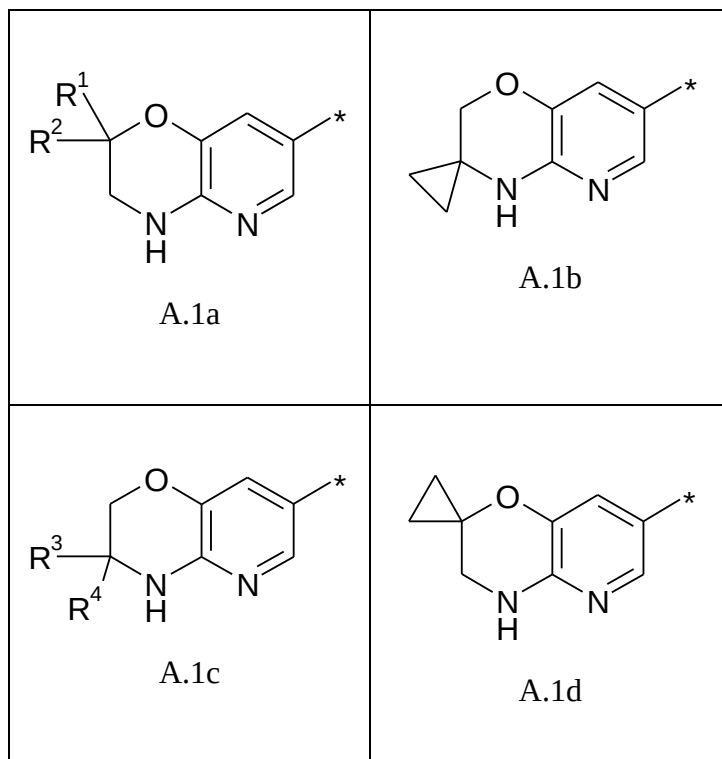
R^8 is selected from the group consisting of C₁₋₆-alkyl, C₃₋₆-cycloalkyl, and 3-14 membered heterocyclyl and

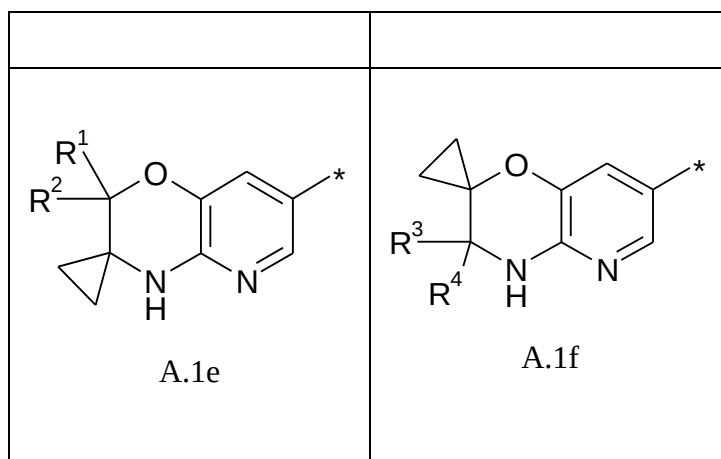
X is CH₂ or O;

or a pharmaceutically acceptable salt thereof.

2. The compound according to claim 1, wherein

A is selected from the group consisting of formulas A.1a to A.1f

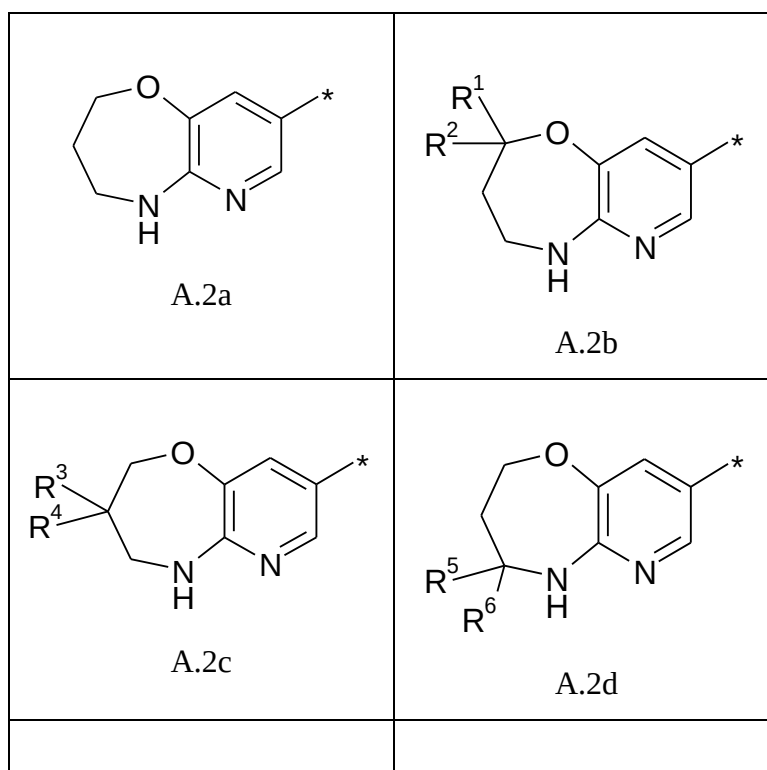


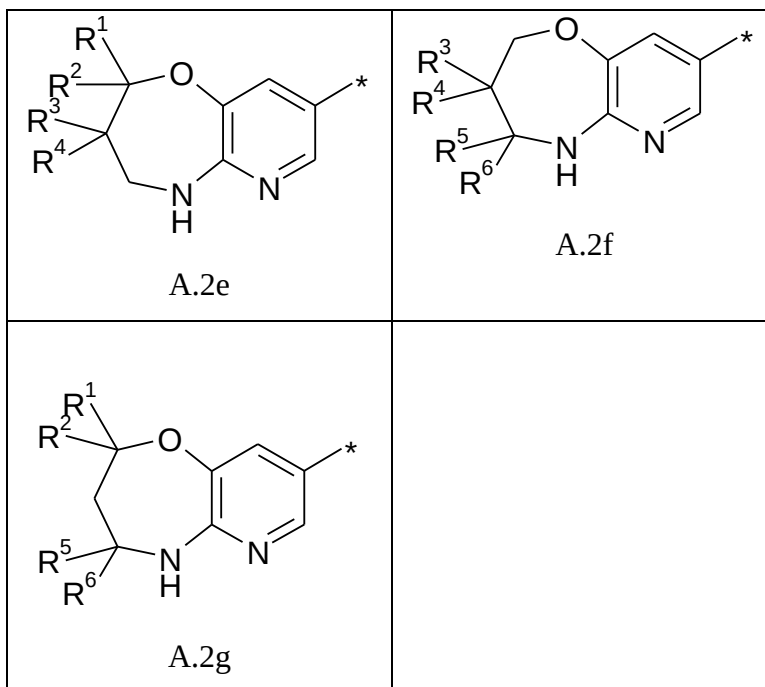


or a pharmaceutically acceptable salt thereof.

3. The compound according to claim 1, wherein

A is selected from the group consisting of formulas A.2a to A.2g

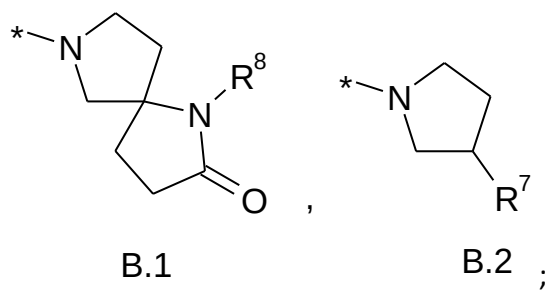




or a pharmaceutically acceptable salt thereof.

4. The compound according to claim 1, wherein

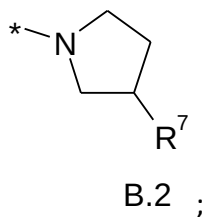
B denotes B.1 or B.2



or a pharmaceutically acceptable salt thereof.

5. The compound according to claim 1, wherein

B denotes B.2

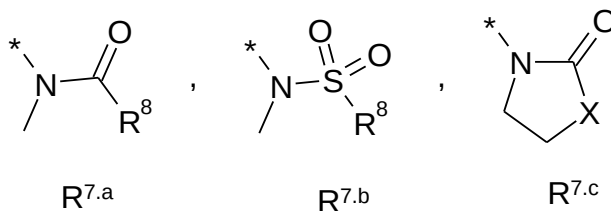


or a pharmaceutically acceptable salt thereof.

6. The compound according to claim 1, wherein each R^1 and R^2 is independently selected from the group consisting of H, CH_3 and $-CH_2OH$; or a pharmaceutically acceptable salt thereof.
7. The compound according to claim 1, wherein R^1 and R^2 together form a 3-4 membered carbocycle; or a pharmaceutically acceptable salt thereof.
8. The compound according claim 1, wherein each R^3 and R^4 is independently selected from the group consisting of H, C_{1-3} -alkyl and phenyl; or a pharmaceutically acceptable salt thereof.
9. The compound according to claim 1, wherein R^3 and R^4 together form a 3-4 membered carbocycle; or a pharmaceutically acceptable salt thereof
10. The compound according to claim 1, wherein R^5 and R^6 denote H or

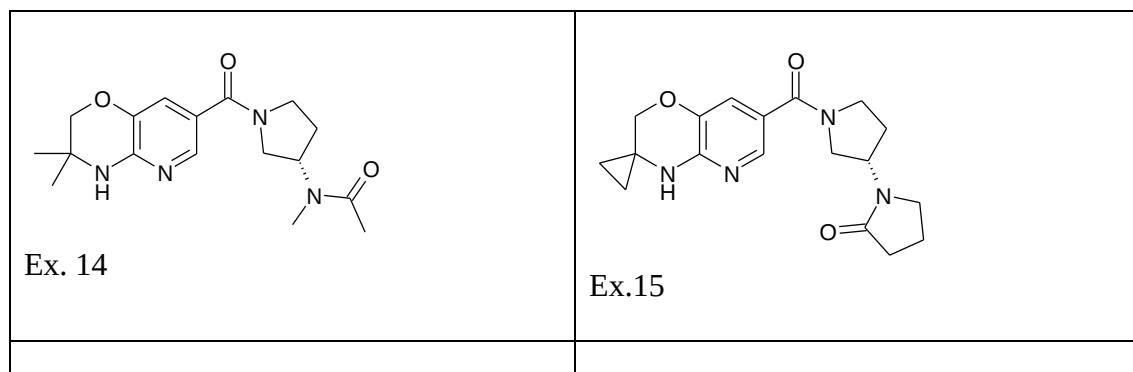
R⁵ and R⁶ together form a 3-4 membered carbocycle;
or a pharmaceutically acceptable salt thereof.

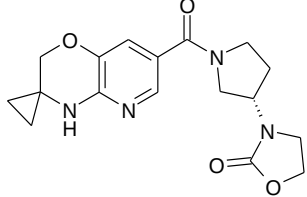
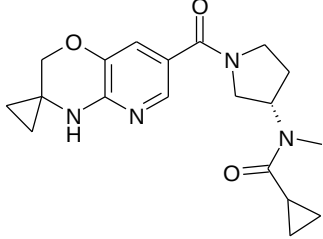
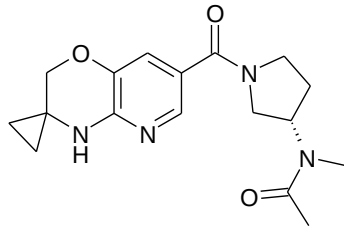
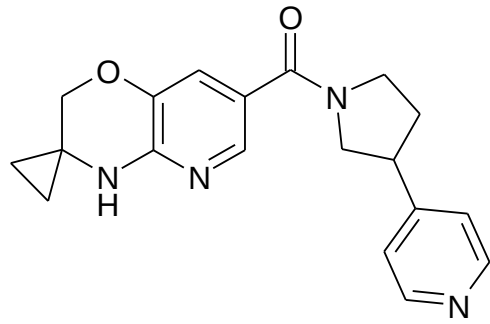
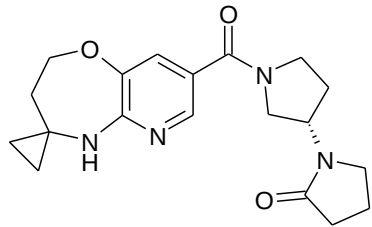
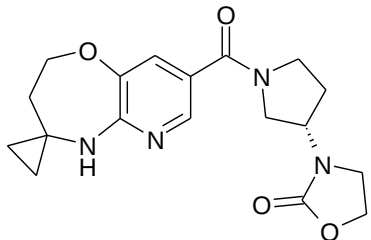
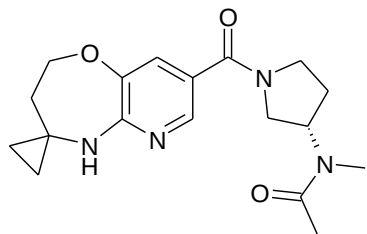
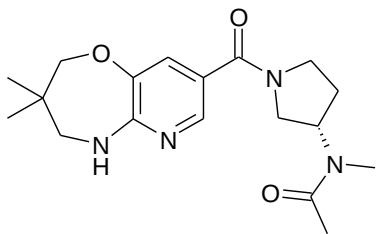
11. The compound according to claim 1, wherein
R⁷ is 5-6 membered heteroaryl or
R⁷ is selected from the group consisting of formulas R^{7.a}, R^{7.b} and R^{7.c};



or a pharmaceutically acceptable salt thereof.

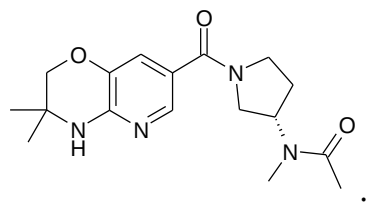
12. The compound according to claim 1, wherein
R⁸ is selected from the group consisting of C₁₋₃-alkyl, C₃₋₆-cycloalkyl and 3-6
membered heterocyclyl;
or a pharmaceutically acceptable salt thereof.
13. The compound according to claim 1, wherein
X is CH₂ or O;
or a pharmaceutically acceptable salt thereof.
14. The compound of formula I, according to claim 1 selected from the group consisting of
examples 14, 15, 16,17, 21, 22, 25, 26, 37 and 42.



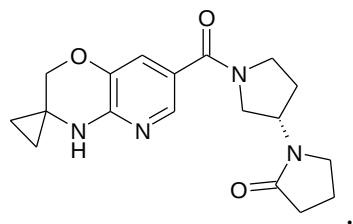
 Ex. 16	 Ex.17
 Ex.21	 Ex.22
 Ex.25	 Ex.26
 Ex.37	 Ex.42

or a pharmaceutically acceptable salt thereof.

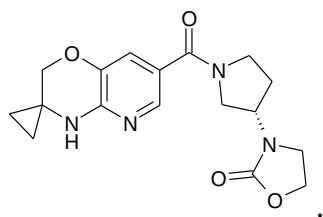
15. A compound of formula:



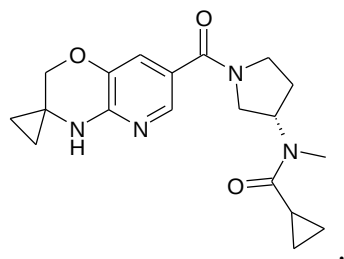
16. A compound of formula:



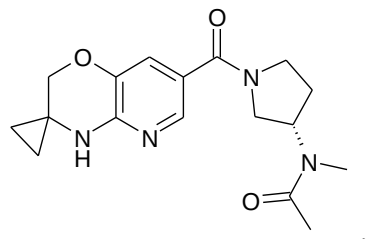
17. A compound of formula:



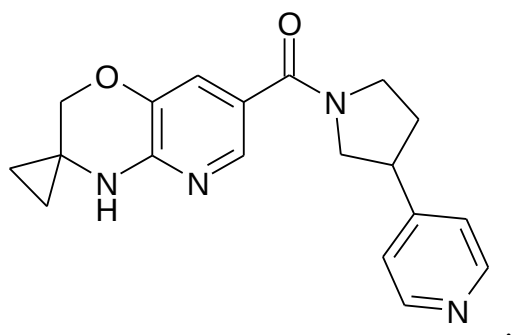
18. A compound of formula:



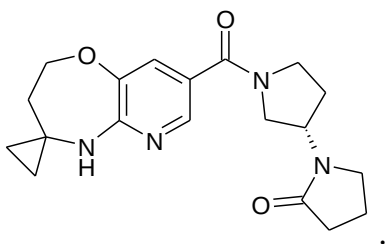
19. A compound of formula:



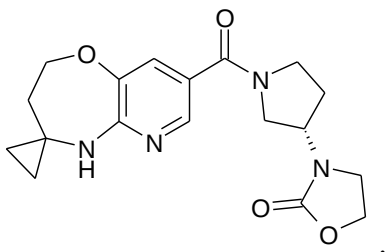
20. A compound of formula:



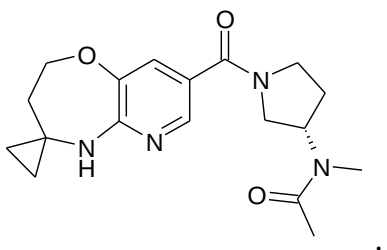
21. A compound of formula:



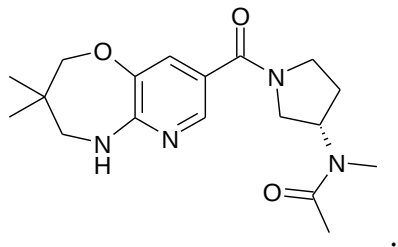
22. A compound of formula:



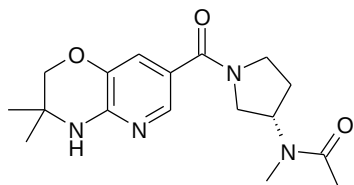
23. A compound of formula:



24. A compound of formula:

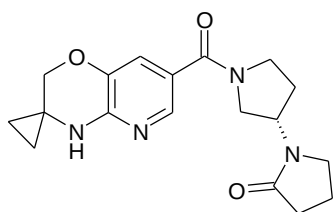


25. A compound of formula:



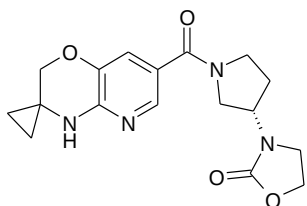
or a pharmaceutically acceptable salt thereof.

26. A compound of formula:



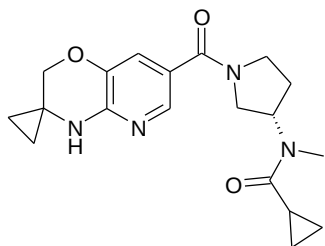
or a pharmaceutically acceptable salt thereof.

27. A compound of formula:



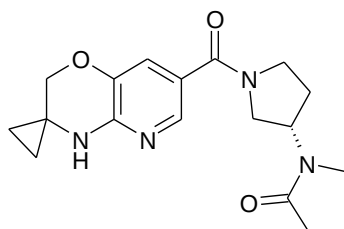
or a pharmaceutically acceptable salt thereof.

28. A compound of formula:



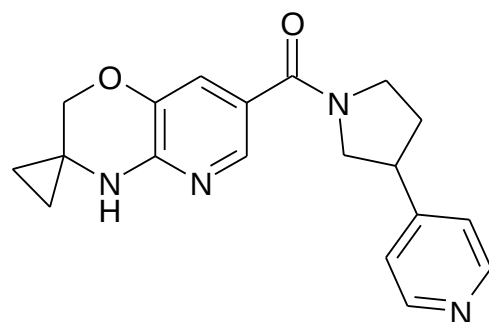
or a pharmaceutically acceptable salt thereof.

29. A compound of formula:



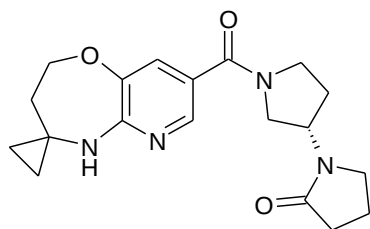
or a pharmaceutically acceptable salt thereof.

30. A compound of formula:



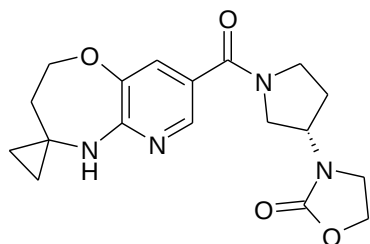
or a pharmaceutically acceptable salt thereof.

31. A compound of formula:



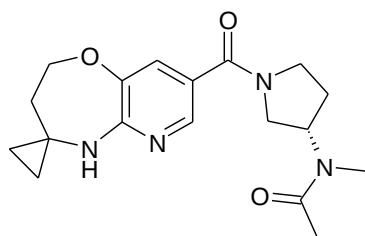
or a pharmaceutically acceptable salt thereof.

32. A compound of formula:



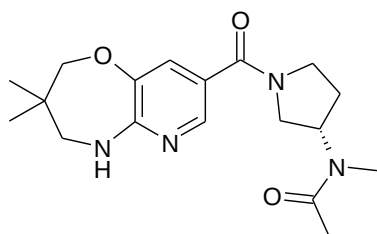
or a pharmaceutically acceptable salt thereof.

33. A compound of formula:



or a pharmaceutically acceptable salt thereof.

34. A compound of formula:



or a pharmaceutically acceptable salt thereof.

35. A pharmaceutical composition comprising a therapeutically effective amount of at least one compound of formula I according to claim 1 or a pharmaceutically acceptable salt thereof and one or more pharmaceutically acceptable excipients.
36. A compound according to one or more of claims 1 to 34, or a pharmaceutically acceptable salt thereof for use as a medicament.

37. Use of the compound according to one or more of claims 1 to 34 in the manufacture of a medicament for treating a patient suffering from Crohn's disease, ulcerative colitis, atopic dermatitis, systemic sclerosis, Non-Alcoholic Steatohepatitis (NASH), psoriasis, chronic kidney disease, chronic obstructive pulmonary disease, idiopathic pulmonary fibrosis, rheumatoid arthritis, scleroderma, asthma, allergic rhinitis, allergic eczema, juvenile rheumatoid arthritis, juvenile idiopathic arthritis, graft versus host disease, psoriatic arthritis, colorectal cancer or pancreatic cancer related new onset diabetes.
38. Use of the compound according to one or more of claims 1 to 34 in the manufacture of a medicament for treating a patient suffering from Crohn's disease.
39. Use of the compound according to one or more of claims 1 to 34 in the manufacture of a medicament for treating a patient suffering from atopic dermatitis.
40. Use of the compound according to one or more of claims 1 to 34 in the manufacture of a medicament for treating a patient suffering from ulcerative colitis.