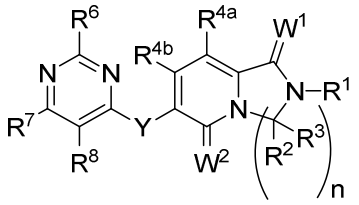
CLAIMS:

1. Use of (i) a compound according to Formula (I):



(I)

or a stereoisomer, tautomer or pharmaceutically acceptable salt thereof or (ii) use of a pharmaceutical composition comprising at least one compound according to Formula (I) or a stereoisomer, tautomer or pharmaceutically acceptable salt thereof; in combination with a pharmaceutically acceptable carrier, diluent or excipient in the manufacture of a medicament for the treatment of a Mnk dependent condition in a mammal in need thereof; wherein:

W^1 and W^2 are independently O, S or N-OR', where R' is C_1-C_4 alkyl;

Y is $–N(R^5)–$, -O-, -S-, -C(O)-, or $–CH_2–$;

R^1 is hydrogen, C_1-C_4 alkyl, CN, C_3-C_6 cycloalkyl or 6 membered heteroaryl wherein an C_1-C_4 alkyl, C_3-C_6 cycloalkyl or 6 membered heteroaryl is optionally substituted with 1, 2 or 3 J groups;

n is 1, 2 or 3;

R^2 and R^3 are each independently hydrogen, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_6-C_9 aryl, C_1-C_6 alkylene(C_6-C_9 aryl), 5-10 membered heteroaryl, or C_3-C_{10} cycloalkyl, wherein any C_1-C_6 alkyl, C_6-C_9 aryl, C_1-C_6 alkylene(C_6-C_9 aryl), 5-10 membered heteroaryl, or C_3-C_{10} cycloalkyl, is optionally substituted with 1, 2 or 3 J groups;

or R^2 and R^3 taken together with the carbon atom to which they are attached form a C_3-C_{10} cycloalkyl or 3-9 membered heterocyclyl, wherein any C_3-C_{10} cycloalkyl or 3-9 membered heterocyclyl is optionally substituted with 1, 2 or 3 J groups;

R^{4a} and R^{4b} are each independently hydrogen, halogen, thiol, cyano, C_1-C_6 alkyl, C_1-C_6 alkoxy, thio(C_1-C_6)alkyl, C_2-C_6 alkenyl, C_3-C_6 cycloalkyl, C_6-C_9 aryl, or 3-9 membered heterocyclyl;

R^5 is hydrogen or C_1-C_4 alkyl;

or R^5 and R^8 taken together with the atoms to which they are attached form a fused 3-9 membered heterocyclyl optionally substituted with 1, 2 or 3 J groups;

R^6, R^7 and R^8 are each independently hydrogen, hydroxy, halogen, cyano, amino, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, –O-C_1-C_6 alkyl, C_3-C_6 cycloalkyl, C_2-C_6 alkenylene(C_3-C_6 cycloalkyl), –N(H)(C_1-C_4 alkyl), –N(C_1-C_4 alkyl)$_2$, –N(H)CO(C_1-C_6 cycloalkyl), –N(C_1-C_6 alkyl)CO(C_1-C_6 cycloalkyl), or 6 membered heteroaryl, and wherein any amino, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, –O-C_1-C_6 alkyl, C_3-C_6 cycloalkyl, C_2-C_6 alkenylene(C_3-C_6 cycloalkyl), –N(H)(C_1-C_4 alkyl), –N(C_1-C_4 alkyl)$_2$, -N(H)CO(C_1-C_6 cycloalkyl), –N(C_1-C_6 alkyl)CO(C_1-C_6 cycloalkyl), or 6 membered heteroaryl is optionally substituted with 1, 2 or 3 J groups;

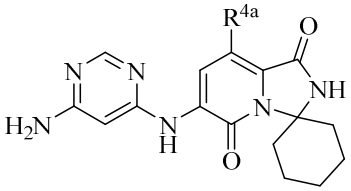
or R^7 and R^8 taken together with the atoms to which they are attached form a fused 3-9 membered heterocyclyl or 5-10 membered heteroaryl optionally substituted with 1, 2 or 3 J groups; and

J is hydroxy, cyano, halogen, acetyl, C_1-C_6 alkyl, –O-C_1-C_6 alkyl, halo(C_1-C_6)alkyl, C_3-C_6 cycloalkyl, or 3-6 membered heterocyclyl; or any two J groups bound to the same carbon or hetero atom may be taken together to form oxo.

2. The use according to claim 1 wherein the Mnk dependent condition is solid tumor, colon cancer, rectal cancer, colorectal cancer, bladder cancer, gastric cancer, esophageal cancer, head and neck cancer, myelodysplastic syndrome, brain cancer, CNS cancer, malignant glioma, glioblastoma, hepatocellular cancers, hepatocellular carcinoma, thyroid cancer, lung cancer, non-small cell lung cancer, a hematological cancer, leukemia, B-cell lymphoma, T-cell lymphoma, hairy cell lymphoma, diffuse large B cell lymphoma, Hodgkins lymphoma, non-Hodgkins lymphoma, Burkitt lymphoma, pancreatic cancer, melanoma, myeloma, multiple myeloma, pancreatic carcinoma, renal cell carcinoma, renal cancer, cervical cancer, urothelial cancer, prostate cancer, castration-resistant prostate cancer, ovarian cancer, breast cancer, or triple-negative breast cancer.

3. The use according to claim 1 wherein the Mnk dependent condition is B-cell lymphoma, T-cell lymphoma, hairy cell lymphoma, non-Hodgkins lymphoma, diffuse large B cell lymphoma, Burkitts lymphoma, leukemia, breast cancer, bladder cancer, ovarian cancer, melanoma, non-small cell lung cancer, head and neck cancer, colorectal cancer or prostate cancer.

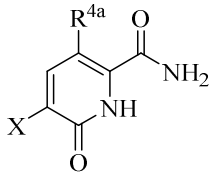
4. A process for preparing a compound according to **5a**



(**5a**)

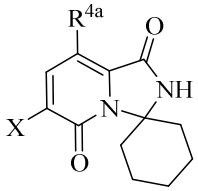
comprising:

(a) contacting a compound of **1a**



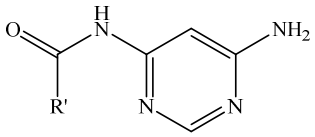
(**1a**)

with a cyclohexanone to obtain a compound of **2a**



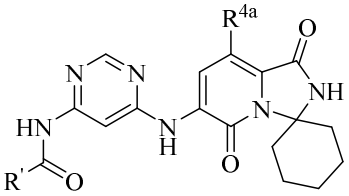
(**2a**);

(b) coupling a compound of **2a** with a compound of **3a**



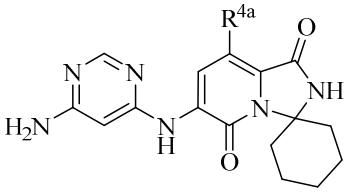
(**3a**)

in the presence of a metal catalyst, an inorganic base, and a phosphine ligand in a non-polar aprotic solvent to obtain compound (**4a**)



(**4a**); and

(c) reacting a compound of **4a** in an aqueous base and organic solvent to obtain a compound of **5a**



(**5a**),

wherein:

X is halogen, -OTf, $-B(OH)_2$ or $-B(OR')_2$,

R^{4a} is -H, halogen, -OH, -SH, hydroxyalkylene, -CN, alkyl, alkoxy, acyl, thioalkyl, alkenyl, alkynyl, cycloalkyl, aryl or heterocyclyl; and

R′ is alkyl, cycloalkyl, aryl, heterocyclyl or heteroaryl.

5. The process according to claim 4, further comprising reacting a compound of **5a** with an acid to afford a pharmaceutically acceptable salt.

6. The process according to claim 5, wherein the acid is HCl, sulfuric or methanesulfonic acid.

7. The process according to claim 4, step a, wherein compound **1a** is contacted with cyclohexanone in a non-polar organic solvent and an acid to obtain compound **2a**.

8. The process according to claim 7, wherein the acid is sulfuric or hydrochloric acid in an amount ranging from about 0.1 to 0.9 molar equivalents with respect to compound **1a.**

9. The process according to claim 7, wherein the non-polar organic solvent is 1,4-dioxane.

10. The process according to claim 7, wherein the reaction temperature is between 90 °C and 105 °C.

11. The process according to claim 4, step b, wherein the metal catalyst is a palladium catalyst, the inorganic base is Cs_2CO_3, and the phosphine ligand is xantphos.

12. The process according to claim 11, wherein the palladium catalyst is $Pd_2(dba)_3$ or $Pd(OAc)_2$.

13. The process according to claim 11, wherein the non-polar aprotic solvent is 1,4-dioxane.

14. The process according to claim 11, wherein the reaction temperature is between 90 °C and 105 °C.

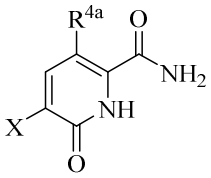
15. The process according to claim 4, step c, wherein the aqueous base is KOH and the organic solvent is a mixture of ethanol, tetrahydrofuran and water.

16. The process according to claim 4, wherein R^{4a} is alkyl.

17. The process according to claim 4, wherein X is bromine.

18. The process according to claim 4, wherein R′ is cycloalkyl.

19. Compound **1a** or a stereoisomer or tautomer thereof:



1a

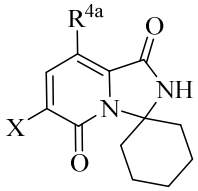
wherein,

X is halogen, -OTf, $-B(OH)_2$ or $-B(OR')_2$, and

R^{4a} is -H, halogen, -OH, -SH, hydroxyalkylene, -CN, alkyl, alkoxy, acyl, thioalkyl, alkenyl, alkynyl, cycloalkyl, aryl or heterocyclyl.

20. The compound according to claim 19, wherein R^{4a} is alkyl and X is Br.

21. Compound **2a** or a stereoisomer or tautomer thereof:



2a

wherein:

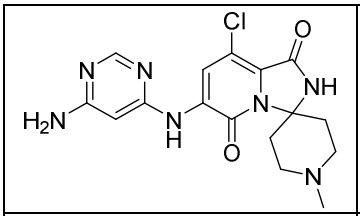
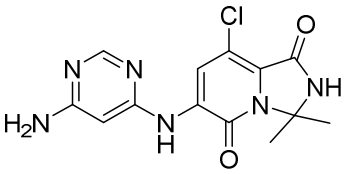
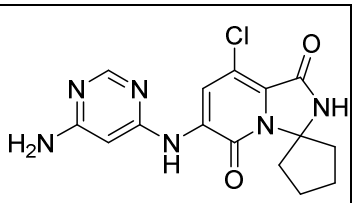
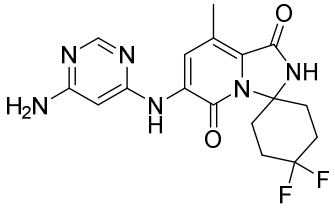
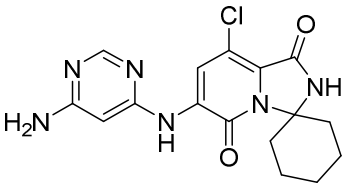
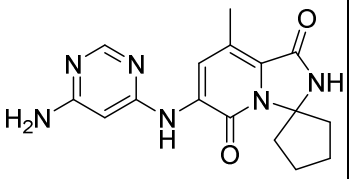
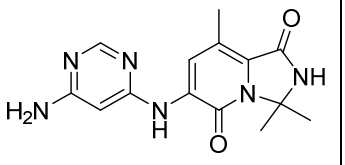
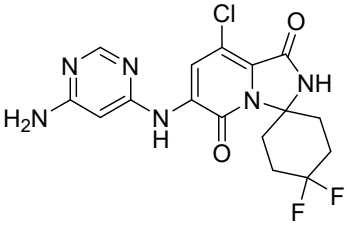
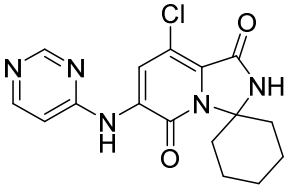
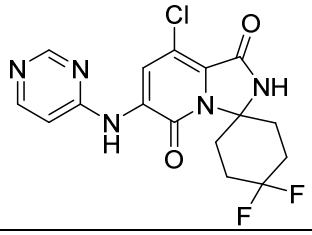
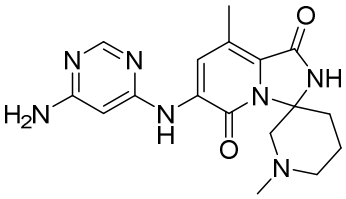
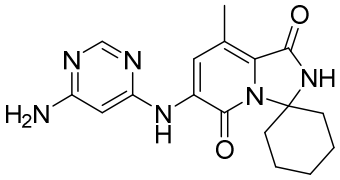
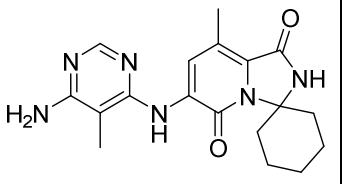
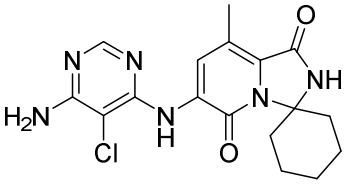
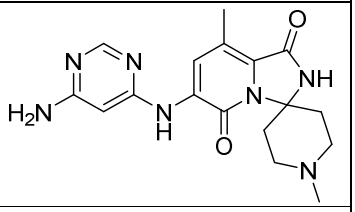
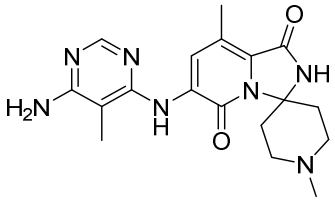
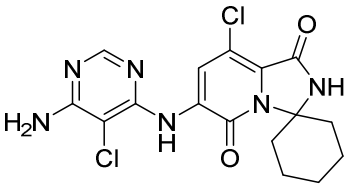
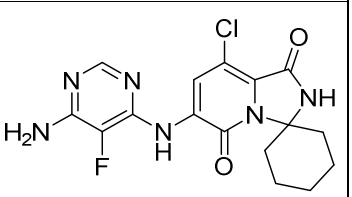
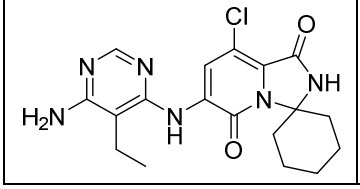
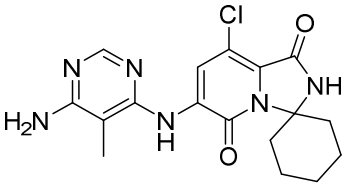
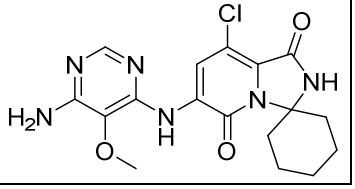
X is halogen, -OTf, $-B(OH)_2$ or $-B(OR')_2$, and

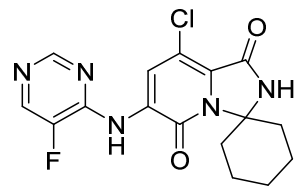
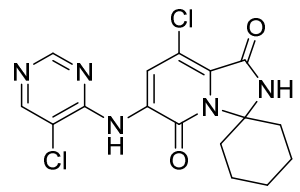
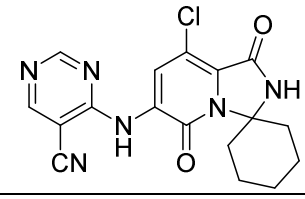
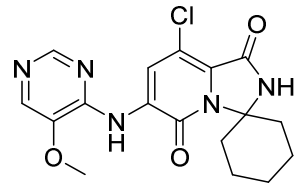
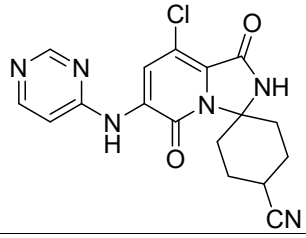
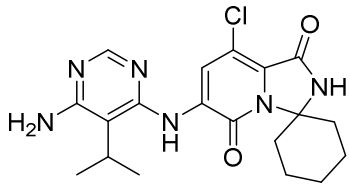
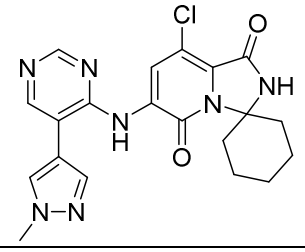
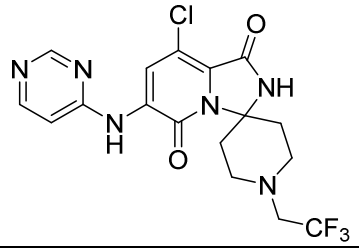
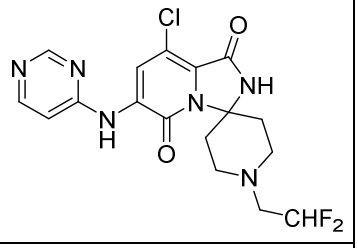
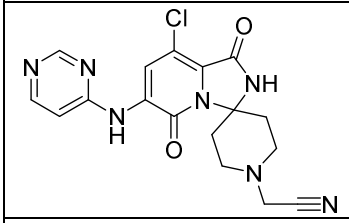
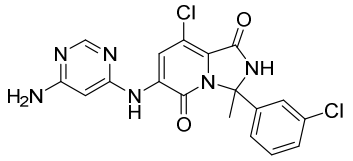
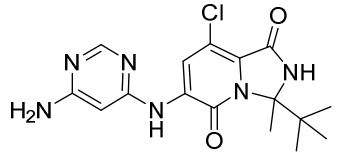
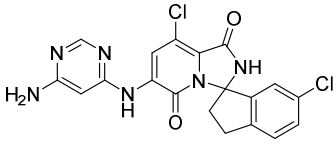
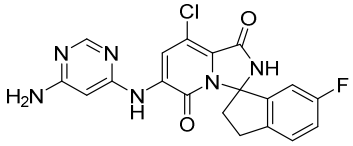
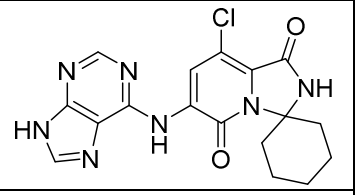
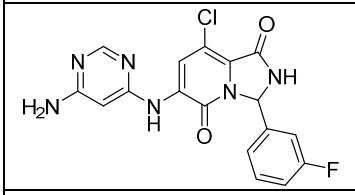
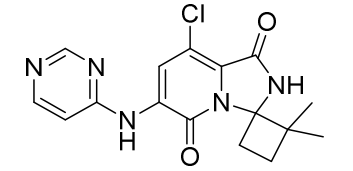
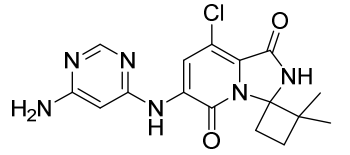
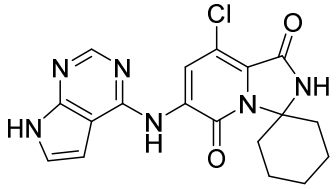
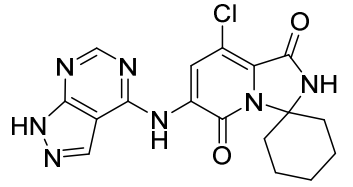
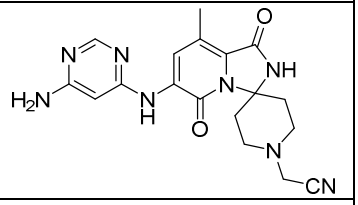
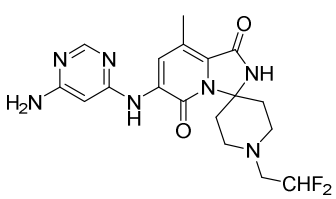
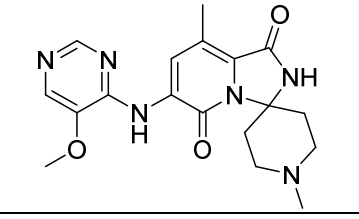
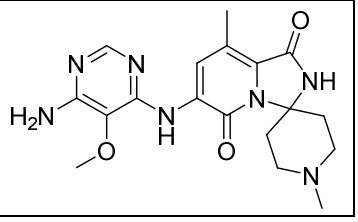
R^{4a} is -H, halogen, -OH, -SH, hydroxyalkylene, -CN, alkyl, alkoxy, acyl, thioalkyl, alkenyl, alkynyl, cycloalkyl, aryl or heterocyclyl.

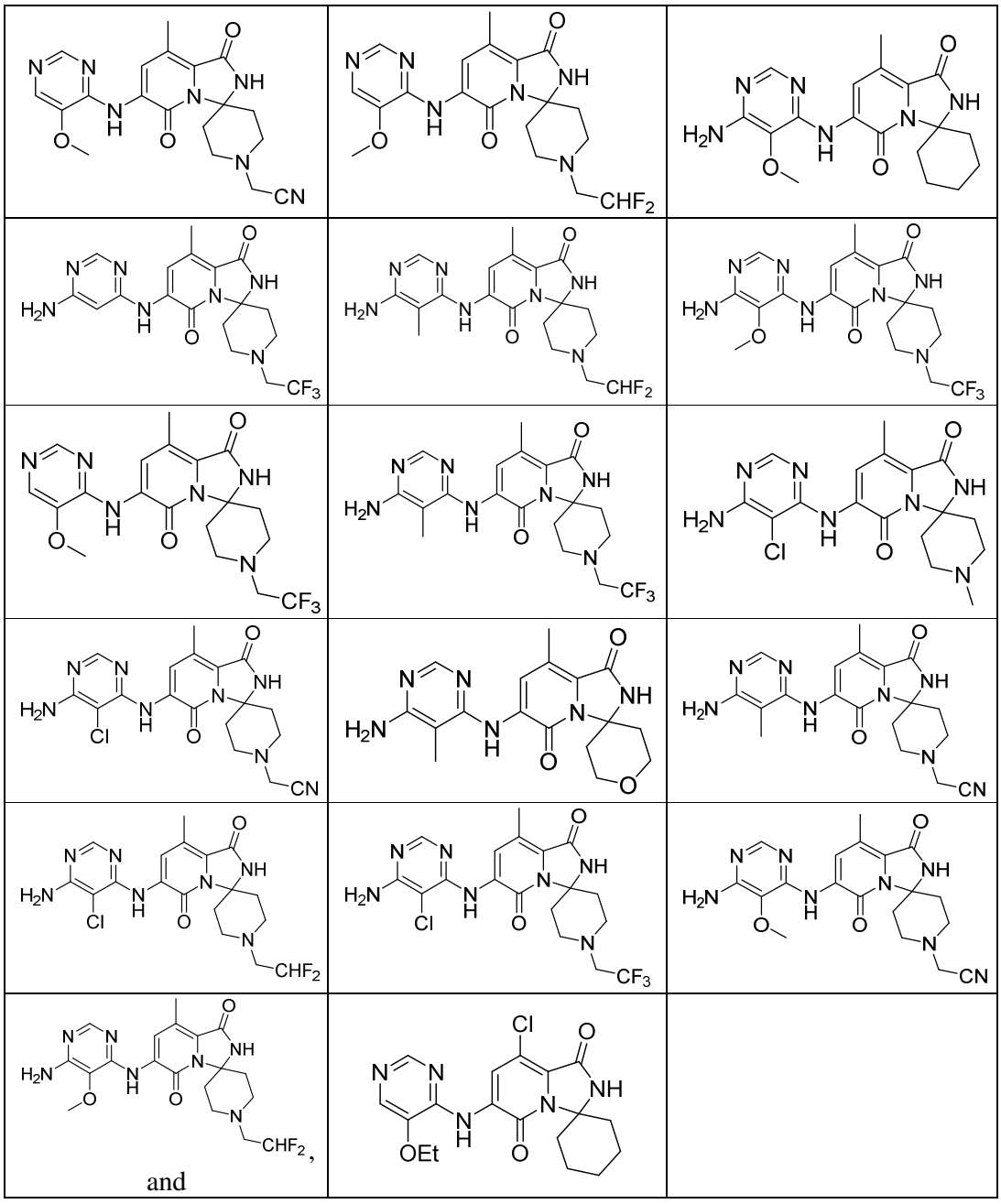
22. The compound according to claim 21, wherein R^{4a} is alkyl and X is Br.

23. The compound according to claim 22, wherein R^{4a} is methyl.

24. Use of a compound selected from the group consisting of:

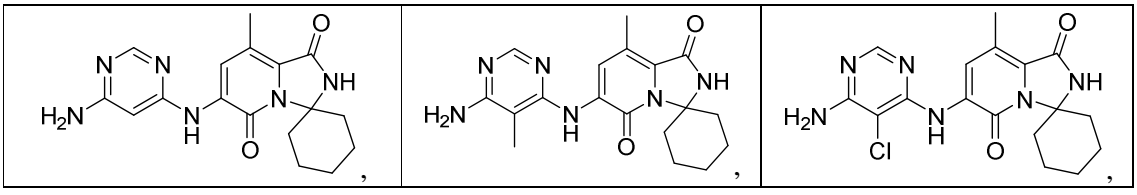
		
		
		
		
		
		
		
		

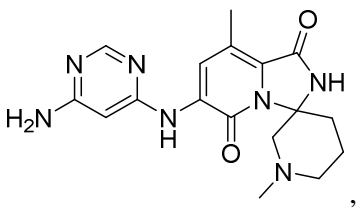
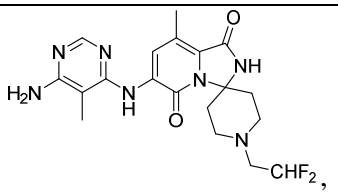
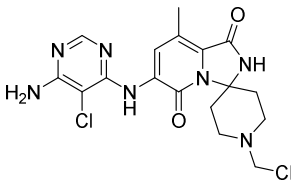


and

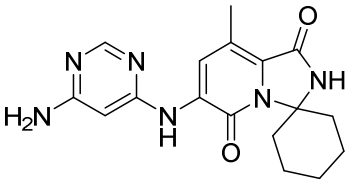
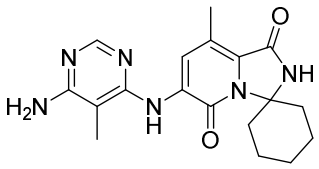
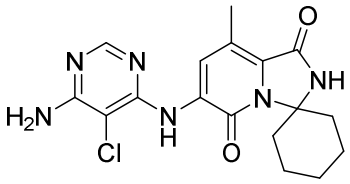
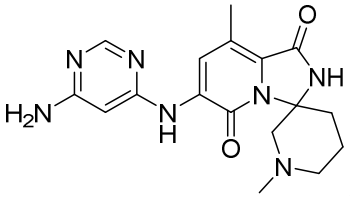
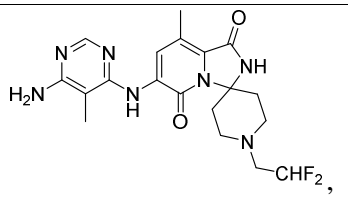
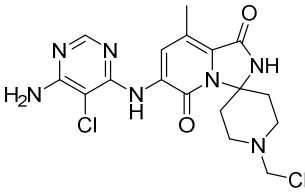
or a stereoisomer, tautomer or pharmaceutically acceptable salt in the manufacture of a medicament for the treatment of a Mnk dependent condition in a mammal in need thereof.

25. The use according to claim 24 wherein the compound or a stereoisomer, tautomer or pharmaceutically acceptable salt thereof is selected from

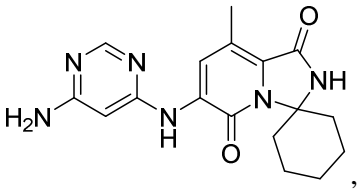


 ,	 , and	 .

26. The use of a pharmaceutical composition according to claim 1, wherein the compound is selected from

 ,	 ,	 ,
 ,	 , and	 .

27. Use of a compound

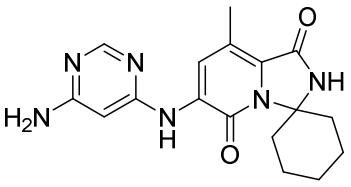
 ,

or a stereoisomer, tautomer or pharmaceutically acceptable salt thereof in the manufacture of a medicament for the treatment of a Mnk dependent condition in a mammal in need thereof.

28. The use of a pharmaceutically acceptable salt according to claim 27 wherein the pharmaceutically acceptable salt is selected from the group consisting of mesylate, sulfate and hydrochloride.

29. The use of a pharmaceutically acceptable salt according to claim 28 wherein the pharmaceutically acceptable salt is hydrochloride.

30. Use of a compound



in the manufacture of a medicament for the treatment of a Mnk dependent condition in a mammal in need thereof.