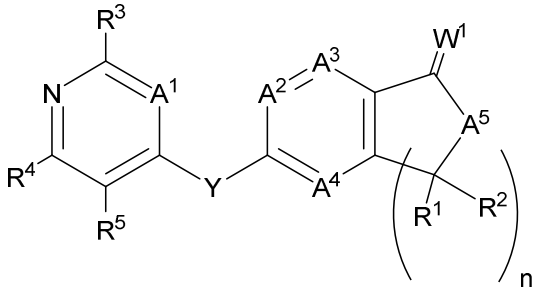
CLAIMS

1. A compound according to Formula (I):



I

or a stereoisomer, a tautomer or a pharmaceutically acceptable salt thereof wherein:

A^1 is –N–; A^2 is –N– or $–CR^{6a}$;

A^3 is –N– or $–CR^7$;

A^4 is –N– or $–CR^{6b}$;

A^5 is $–NR^8$ or $–CR^{8a}R^{8b}$;

W^1 is O, S, NH, $NO(R^9)$ or $CR^{9a}R^{9b}$;

Y is –O–, –S–, –C(O)–, $–NR^{10}$, –S=O, $–S(O)_2–$, $–CH_2–$ or –CH(OH);

n is 1, 2 or 3;

R^1 and R^2 independently are –H, $–NHR^{10}$, NHR^{10}-alkylene, $(C_1\text{-}C_8)$alkyl, $(C_2\text{-}C_8)$alkenyl, $(C_2\text{-}C_8)$alkynyl, cycloalkyl, heterocyclyl, heteroaryl, aryl, arylalkylene, cycloalkylalkylene, heterocyclylalkylene, or heteroarylalkylene, such that at least one of R^1 or R^2 is not –H; or

R^1 and R^2 together with the carbon atom to which they are attached form a cycloalkyl or heterocyclyl ring;

R^3 , R^4 , R^5 and R^{6b} independently are –H, –OH, –CN, $–SR^{10}$, halogen, $–S(O)_2(C_1\text{-}C_8)$ alkyl, $–C(O)NHR^{10}$, $–C(O)NR^{10}R^{10}$, $–NHR^{10}$, $–NR^{10}R^{10}$, NHR^{10}-alkylene, $NR^{10}R^{10}$-alkylene, $(C_1\text{-}C_8)$alkyl, $(C_2\text{-}C_8)$alkenyl, $(C_2\text{-}C_8)$alkynyl, $(C_1\text{-}C_8)$haloalkyl, $–O(C_1\text{-}C_8)$alkyl, $–O(C_1\text{-}C_8)$haloalkyl, $–O(C_1\text{-}C_8)$alkyleneNHR^{10}, $–O(C_1\text{-}C_8)$alkyleneNR^{10}R^{10}, cycloalkyl, heterocyclyl, heteroaryl, aryl, arylalkylene, cycloalkylalkylene, heterocyclylalkylene, heteroarylalkylene, alkylaminyl, alkylcarbonylaminyl, cycloalkylcarbonylaminyl, cycloalkylaminyl, or heterocyclylaminyl; or

R^4 and R^5 together with the respective carbon atoms to which they are attached form a fused aryl, cycloalkyl, heterocyclyl or heteroaryl ring;

R^{6a} is –H, –OH, halogen, –CN, acetyl, –(C_1-C_8)alkyl, –S(C_1-C_8)alkyl, –(C_2-C_8)alkenyl, –(C_2-C_8)alkynyl, –O(C_1-C_8)alkyl, –(C_1-C_8)haloalkyl, –NHR^{10}, –$NR^{10}R^{10}$, NHR^{10}-alkylene, $NR^{10}R^{10}$-alkylene or –O(C_1-C_8)haloalkyl;

R^7 is –H, –OH, –SH, –CN, –$S(O)_2R^{10}$, halogen, –S(C_1-C_8)alkyl, –NHR^{10}, –$NR^{10}R^{10}$, (C_1-C_8)alkyl, (C_2-C_8)alkenyl, (C_2-C_8)alkynyl, (C_1-C_8)haloalkyl, -O(C_1-C_8)haloalkyl, -O(C_1-C_8)alkyl, –O(C_1-C_8)alkyleneNHR^{10}, –O(C_1-C_8)alkyleneNR^{10}R^{10}, –(C_1-C_8)alkyleneNHR^{10}, –(C_1-C_8)alkyleneNR^{10}R^{10}, –S(C_1-C_8)alkyl, cycloalkyl, heterocyclyl, heteroaryl or aryl;

R^8 is –H, –OH, acetyl, –(C_1-C_8)alkyl, –C(O)alkyl, –C(O)cycloalkyl, –C(O)O-(C_1-C_8)alkyl, cycloalkyl, aryl, heteroaryl or heterocyclyl;

R^{8a} and R^{8b} independently are –H, –OH, acetyl, –(C_1-C_8)alkyl, –O(C_1-C_8)alkyl, –C(O)alkyl, –C(O)cycloalkyl, –C(O)O-(C_1-C_8)alkyl, cycloalkyl, aryl, heteroaryl or heterocyclyl;

R^9, R^{9a} and R^{9b} are independently –H, (C_1-C_8)alkyl, (C_2-C_8)alkenyl, (C_2-C_8)alkynyl, cycloalkyl, heterocyclyl, heteroaryl, aryl, arylalkylene, cycloalkylalkylene, heterocyclylalkylene, or heteroarylalkylene; or

R^{9a} and R^{9b} together with the carbon atom to which they are attached form a cycloalkyl or heterocyclyl ring;

R^{10} is –H, –OH, –C(O)O(C_1-C_8)alkyl, –C(O)(C_1-C_8)alkyl, –C(O)-NH_2, –C(O)-NH(C_1-C_8)alkyl, NH_2-C(O)-alkylene, –S(C_1-C_8)alkyl, acetyl, –(C_1-C_8)alkyl, (C_2-C_8)alkenyl, (C_2-C_8)alkynyl, –O(C_1-C_8)alkyl, (C_1-C_8) haloalkyl, alkylcarbonylaminyl, alkylaminyl, –C(O)alkyl, –C(O)cycloalkyl, –C(O)O-(C_1-C_8)alkyl, aryl, heteroaryl, heterocyclyl or cycloalkyl;

wherein any alkyl, cycloalkyl, heterocyclyl, heteroaryl, aryl, arylalkylene, cycloalkylalkylene, heterocyclylalkylene, heteroarylalkylene, alkylaminyl, alkylcarbonylaminyl, cycloalkylcarbonylaminyl, cycloalkylaminyl, or heterocyclylaminyl is optionally substituted with 1, 2, or 3 groups selected from –OH, –CN, –SH , –S(O)NH_2, –$S(O)NH_2$, halogen, –NH_2, –NH(C_1-C_4)alkyl, –N[(C_1-C_4)alkyl]$_2$, –C(O)NH_2, –COOH, –COOMe, acetyl, –(C_1-C_8)alkyl, –O(C_1-C_8)alkyl (C_2-C_8)alkenyl, (C_2-C_8)alkynyl, haloalkyl, thioalkyl, cyanomethylene, alkylaminyl, NH_2-C(O)-alkylene , NH_2-C(O)-alkylene, –NH(Me)-C(O)-alkylene, –CH_2-C(O)-lower alkyl, –C(O)-lower alkyl, alkylcarbonylaminyl, cycloalkyl, cycloalkylalkylene, cycloalkylalkenylene, cycloalkylcarbonylaminyl, cycloalkylaminyl, –CH_2-C(O)-cycloalkyl, –C(O)-cycloalkyl, –CH_2-C(O)-aryl, –CH_2-aryl, –C(O)-aryl, –CH_2-C(O)-heterocycloalkyl, –C(O)-heterocycloalkyl, heterocyclylaminyl or heterocyclyl.

2. The compound according to claim 1 wherein W^1 is O, A^5 is $–NR^8$ and R^8 is –H.

3. The compound according to claim 1 wherein Y is $–NR^{10}$ and subscript "n" is 1.

4. The compound according to claim 3 wherein R^{10} is –H or $–(C_1\text{-}C_8)$alkyl.

5. The compound according to claim 1 wherein at least one of R^1 or R^2 is methyl, ethyl, *i*-propyl, $\text{-}NH_2$, aminomethylene, CH_3-OC(O)NH-methylene or thiophene.

6. The compound according to claim 1 wherein R^1 and R^2 together with the carbon atom to which they are attached form a cycloalkyl ring selected from the group consisting of cyclobutyl, cyclopentyl, cyclohexyl, 2,2-dimethylcyclobutyl, 4-aminocyclohexyl, 4-methylcyclohexyl, 4-ethylcyclohexyl, 2,2-difluoroethyl-4-cyclohexyl, 4,4-difluorocyclohexy, 4-cyanocyclohexyl, 4-trifluoromethylcyclohexyl, 4-hydroxycyclohexyl, 3-hydroxycyclopently, 3-aminocyclopentyl and 3-methylcyclopentyl.

7. The compound according to claim 1 wherein A^2 is –CH, A^4 is $–CR^{6b}$ and $–CR^{6b}$ is –C(OH), –C(CN), –C(F), –C(Cl), –C(OMe), –C(Me), –C(Et), $–C(CF_3)$, –C(aminoalkylene), –C(SMe) or –C[C(O)Me].

8. The compound according to claim 1 wherein A^2 is –CH, A^3 is $–CR^7$ and $–CR^7$- is –C(OH), –C(CN), –C(F), –C(Cl), –C(OMe), –C(Me), –C(Et), $–C(CHF_2)$ or $–C(CF_3)$.

9. The compound according to claim 1 wherein R^3, R^4 and R^5 independently are –H.

10. The compound according to claim 1 wherein R^3 is –H and R^4 and R^5 independently are chlorine, fluorine, methyl, ethyl, difluoromethyl, trifluoromethyl, methoxy, -CN, $–NHR^{10}$ or $–O(C_1\text{-}C_8)$alkylNHR^{10}.

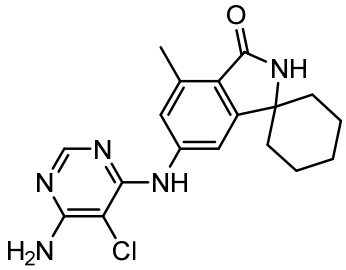
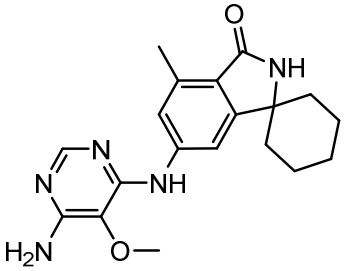
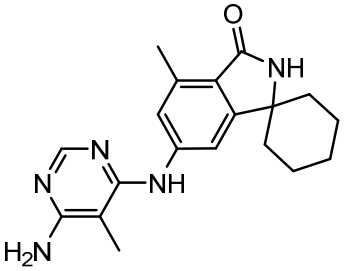
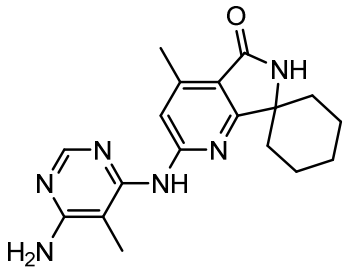
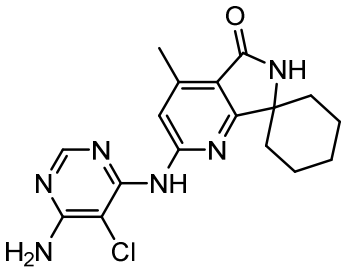
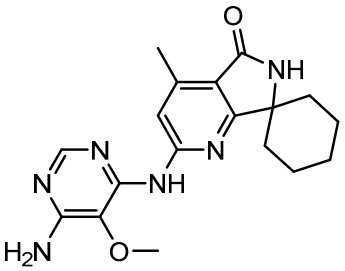
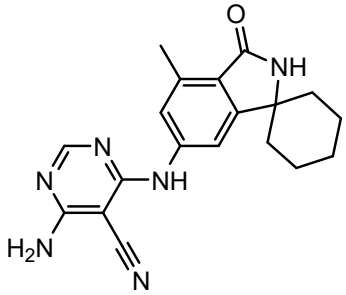
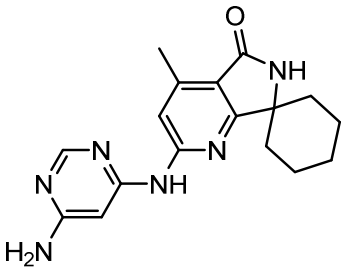
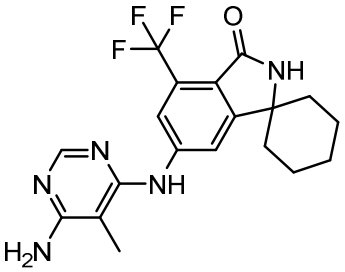
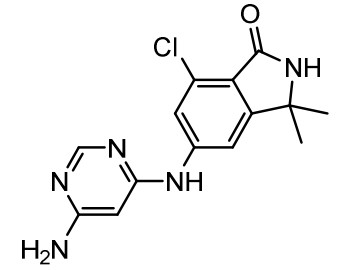
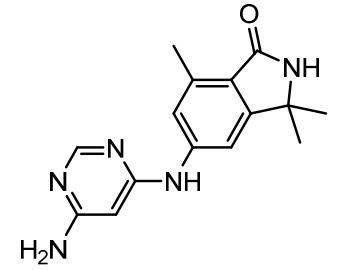
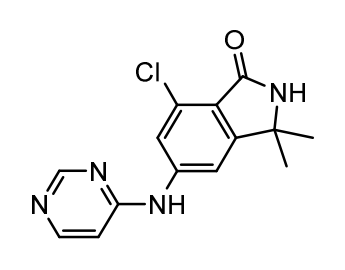
11. The compound according to claim 9 wherein R^{10} is –H, –C(O)alkyl or –C(O)cycloalkyl.

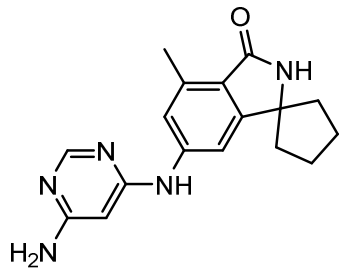
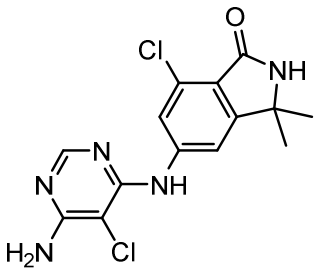
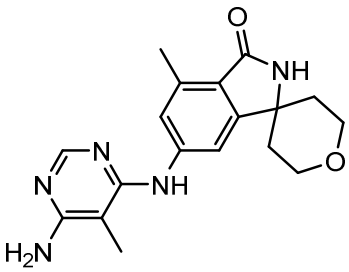
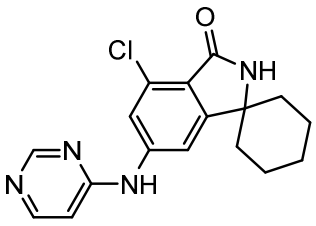
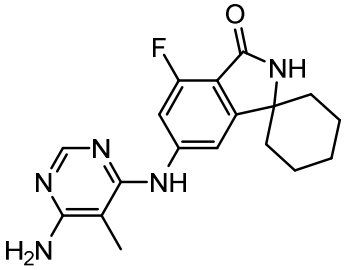
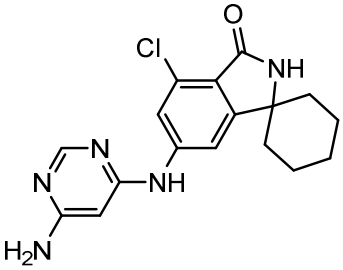
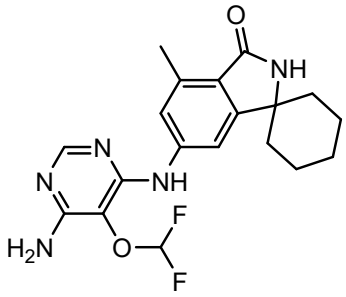
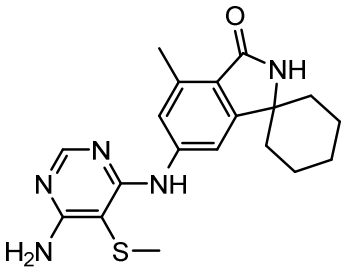
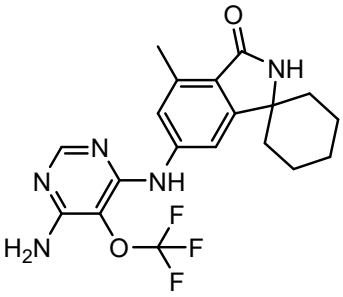
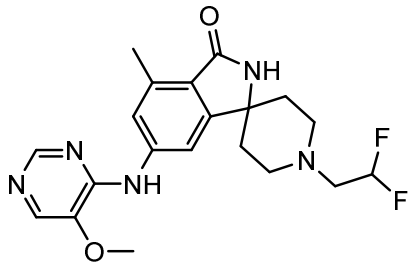
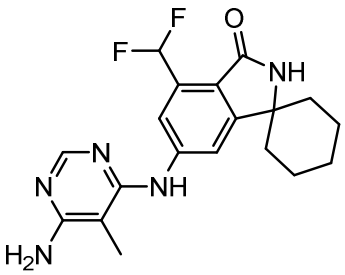
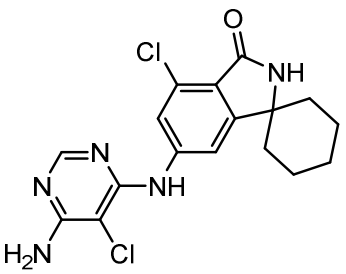
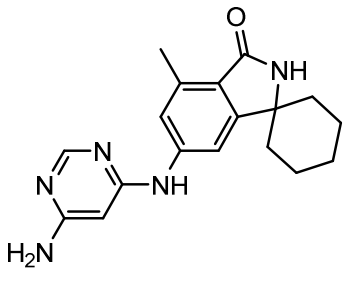
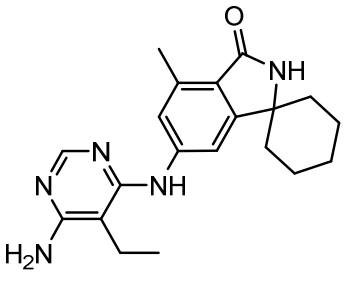
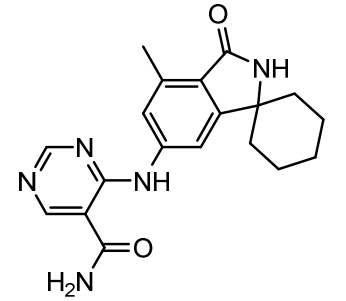
12. The compound according to claim 1 wherein R^3 is –H and R^4 and R^5 together with the respective carbon atoms to which they are attached form a fused cycloalkyl, heterocyclyl, or heteroaryl ring.

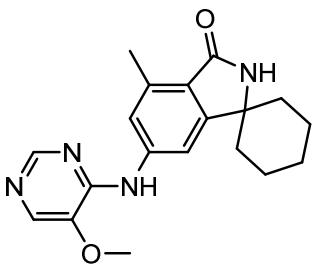
13. The compound according to claim 11 wherein the heterocyclyl ring is morpholine, pyrrolidine or pyrrolidin-2-one.

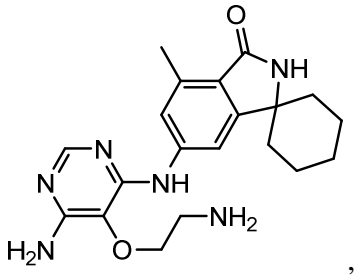
14. The compound according to claim 11 wherein the heteroaryl ring is imidazole, thiazole, thiophene, pyrazole, N-methylpyrazole or pyridine.

15. The compound according to claim 1 selected from





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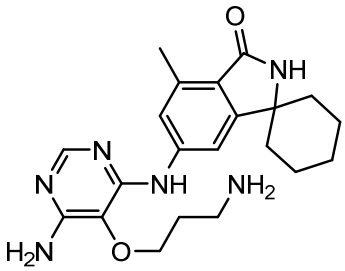

or a stereoisomer, a tautomer, or a pharmaceutically acceptable salt thereof.

16. A pharmaceutical composition comprising (i) a therapeutically effective amount of at least one compound according to claim 1 or a stereoisomer, a tautomer or a pharmaceutically acceptable salt thereof; (ii) in combination with a pharmaceutically acceptable carrier, diluent or excipient.

17. A compound according to claim 1 or a stereoisomer, tautomer or pharmaceutically acceptable salt thereof for use in attenuating or inhibiting the activity of Mnk in at least one cell overexpressing Mnk.

18. The compound of claim 17 or a stereoisomer, tautomer or pharmaceutically acceptable salt thereof, wherein the at least one cell is a colorectal cancer cell, a gastric cancer cell, a bladder cancer cell, an esophageal cancer cell, a head and neck cancer cell, a malignant glioma cell, a glioblastoma cell, a hepatocellular cancer cell, a thyroid cancer cell, a lung cancer cell, a leukemia cell, a B-cell lymphoma cell, a T-cell lymphoma cell, a hairy cell lymphoma cell, a non-small cell cancer cell, a small-cell lung cancer cell, a Hodgkin's lymphoma cell, a non-Hodgkin's lymphoma cell, a Burkitt's lymphoma cell, a pancreatic cancer cell, a pancreatic carcinoma cell, a melanoma cell, a multiple myeloma cell, a myelodysplastic syndrome, a brain cancer cell, a CNS cancer cell, a renal cell carcinoma cell, a prostate cancer cell, a castration-resistant prostate cancer cell, a cervical cancer cell, an urothelial cancer cell, an ovarian cancer cell, a breast cancer cell, or a triple-negative breast cancer cell.

19. The compound of claim 17 or a stereoisomer, tautomer or pharmaceutically acceptable salt thereof, wherein the at least one cell is a cancer cell.