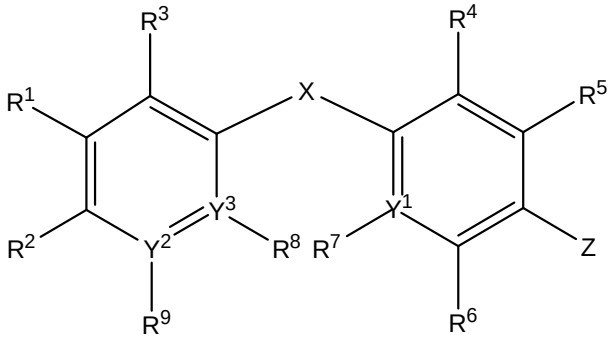
Claims

1. A compound of formula (I)



Formula (I)

pharmaceutically-acceptable salts, hydrates, solvates, or stereoisomers thereof,

wherein X is selected from CH_2, CO, CHOH, CHO(C_1-C_3) alkyl, NH, and O;

wherein Y^1 is N and R^7 is absent, Y^2 is selected from N and C and Y^3 is C;

wherein Z is $NR^{10}R^{11}$, wherein R^{10} and R^{11} are each independently selected from H and C_1-C_6 alkyl;

wherein R^1 is selected from H, halogen, C_1-C_6 alkyl, C_3-C_{12} cycloalkyl, C_3-C_{12} heterocyclyl, C_1-C_6 alkoxy, C_1-C_6 heteroalkyl, C_0-C_3 alkylOC_0-C_3 alkyl aryl wherein the aryl is optionally substituted by NH_2, OC_1-C_6 alkyl, C_1-C_6 alkyl, C_1-C_6 heteroalkyl, halogen, CN, C_3-C_{12} cycloalkyl, C_3-C_{12} heterocyclyl; C_0-C_3 alkylOC_0-C_3 alkyl heteroaryl wherein the heteroaryl is optionally substituted by NH_2, OC_1-C_6 alkyl, C_1-C_6 alkyl, C_1-C_6 heteroalkyl, halogen, CN, C_3-C_{12} cycloalkyl, C_3-C_{12} heterocyclyl; and C_1-C_6 alkyl substituted by aryl or heteroaryl wherein the aryl and the heteroaryl are optionally substituted by NH_2, OC_1-C_6 alkyl, C_1-C_6 alkyl, C_1-C_6 heteroalkyl, halogen, CN, C_3-C_{12} cycloalkyl, C_3-C_{12} heterocyclyl;

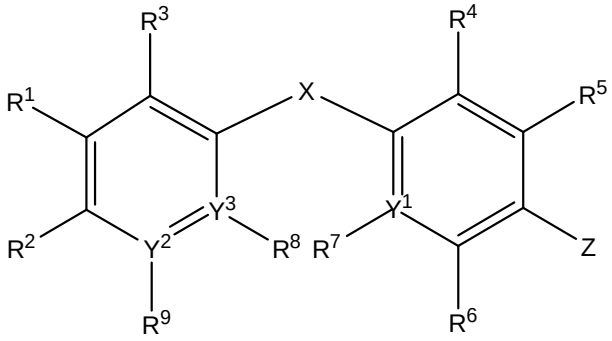
wherein R^2 is selected from aryl and heteroaryl wherein the aryl and the heteroaryl are optionally substituted by NH_2, OC_1-C_6 alkyl, C_1-C_6 alkyl, C_1-C_6 heteroalkyl, halogen, CN, C_3-C_{12} cycloalkyl, C_3-C_{12} heterocyclyl, $C(O)R^{12}$, C_1-C_6 alkyl $C(O)R^{12}$;

wherein R^3 is selected from H, halogen, C_1-C_6 alkyl and C_3-C_{12} cycloalkyl;

wherein R^4 is selected from H and halogen and R^5 and R^6 are each independently selected from H and C_1-C_6 alkyl;

wherein R^8 is selected from H, halogen, C_1-C_6 alkyl and C_3-C_{12} cycloalkyl;
wherein R^9 is absent when Y^2 is N or is selected from H, halogen, C_1-C_6 alkyl and C_3-C_{12} cycloalkyl when Y^2 is C; and
wherein R^{12} is selected from NH_2, NHC_1-C_6 alkyl, C_1-C_6 alkyl, and C_1-C_6 heteroalkyl,
with the proviso that the compound of formula (I) is not 6-([1,1'-biphenyl]-4-yloxy)-pyridine-3-amine, 6-([1,1'-biphenyl]-4-yloxy)-2-methylpyridin-3-amine, 6-([1,1'-biphenyl]-4-yloxy)-4-methylpyridin-3-amine, 6-[4-(6-methoxy-3-pyridinyl)phenoxy]-3-pyridinamine, 6-[(5'-fluoro-2'-methoxy-([1,1'-biphenyl]-4-yl)oxy]-3-pyridinamine, 5-methyl-6-(4-phenylphenoxy)pyridin-3-amine, 6-([1,1'-biphenyl]-4-yloxy)-5-chloro-3-pyridinamine, 6-([1,1'-biphenyl]-4-yloxy)-5-bromo-3-pyridinamine, 6-[(3-chloro([1,1'-biphenyl]-4-yl)oxy]-3-pyridinamine, 6-[4-(5-methyl-1H-indol-3-yl)phenoxy]-3-pyridinamine, or 6-[4-(1H-pyrazol-4-yl)phenoxy]-3-pyridinamine.

2. Use of the compound of formula (I)



Formula (I)

pharmaceutically-acceptable salts, hydrates, solvates, or stereoisomers thereof,
wherein X is selected from CH_2, CO, CHOH, CHO(C_1-C_3) alkyl, NH, and O;
wherein Y^1 is N and R^7 is absent, Y^2 is selected from N and C and Y^3 is C;
wherein Z is $NR^{10}R^{11}$, wherein R^{10} and R^{11} are each independently selected from H and C_1-C_6 alkyl;
wherein R^1 is selected from H, halogen, C_1-C_6 alkyl, C_3-C_{12} cycloalkyl, C_3-C_{12} heterocyclyl, C_1-C_6 alkoxy, C_1-C_6 heteroalkyl, C_0-C_3 alkylOC_0-C_3 alkyl aryl wherein the aryl is optionally substituted by NH_2, OC_1-C_6 alkyl, C_1-C_6 alkyl, C_1-C_6 heteroalkyl, halogen, CN, C_3-C_{12} cycloalkyl, C_3-C_{12} heterocyclyl; C_0-C_3 alkylOC_0-C_3 alkyl heteroaryl wherein the heteroaryl is optionally substituted by NH_2, OC_1-C_6 alkyl, C_1-C_6

alkyl, C_1-C_6 heteroalkyl, halogen, CN, C_3-C_{12} cycloalkyl, C_3-C_{12} heterocyclyl; and C_1-C_6 alkyl substituted by aryl or heteroaryl wherein the aryl and the heteroaryl are optionally substituted by NH_2, OC_1-C_6 alkyl, C_1-C_6 alkyl, C_1-C_6 heteroalkyl, halogen, CN, C_3-C_{12} cycloalkyl, C_3-C_{12} heterocyclyl;

wherein R^2 is selected from aryl and heteroaryl wherein the aryl and the heteroaryl are optionally substituted by NH_2, OC_1-C_6 alkyl, C_1-C_6 alkyl, C_1-C_6 heteroalkyl, halogen, CN, C_3-C_{12} cycloalkyl, C_3-C_{12} heterocyclyl, $C(O)R^{12}$, C_1-C_6 alkyl $C(O)R^{12}$;

wherein R^3 is selected from H, halogen, C_1-C_6 alkyl and C_3-C_{12} cycloalkyl;

wherein R^4 is selected from H and halogen and R^5 and R^6 are each independently selected from H and C_1-C_6 alkyl;

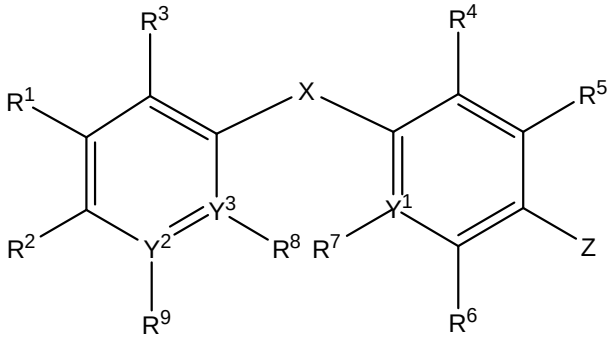
wherein R^8 is selected from H, halogen, C_1-C_6 alkyl and C_3-C_{12} cycloalkyl;

wherein R^9 is absent when Y^2 is N or is selected from H, halogen, C_1-C_6 alkyl and C_3-C_{12} cycloalkyl when Y^2 is C; and

wherein R^{12} is selected from NH_2, NHC_1-C_6 alkyl, C_1-C_6 alkyl, and C_1-C_6 heteroalkyl,

in the manufacture of a medicament for the treatment and/or prevention of cancers in a subject.

3. A pharmaceutical composition comprising a compound of formula (I)



Formula (I)

pharmaceutically-acceptable salts, hydrates, solvates, or stereoisomers thereof,

wherein X is selected from CH_2, CO, CHOH, $CHO(C_1$-$C_3)$ alkyl, NH, and O;

wherein Y^1 is N and R^7 is absent, Y^2 is selected from N and C and Y^3 is C;

wherein Z is $NR^{10}R^{11}$, wherein R^{10} and R^{11} are each independently selected from H and C_1-C_6 alkyl;

wherein R^1 is selected from H, halogen, C_1-C_6 alkyl, C_3-C_{12} cycloalkyl, C_3-C_{12} heterocyclyl, C_1-C_6 alkoxy, C_1-C_6 heteroalkyl, C_0-C_3 alkylOC_0-C_3 alkyl aryl wherein the aryl is optionally substituted by NH_2, OC_1-C_6 alkyl, C_1-C_6 alkyl, C_1-C_6 heteroalkyl, halogen, CN, C_3-C_{12} cycloalkyl, C_3-C_{12} heterocyclyl; C_0-C_3 alkylOC_0-C_3 alkyl heteroaryl wherein the heteroaryl is optionally substituted by NH_2, OC_1-C_6 alkyl, C_1-C_6 alkyl, C_1-C_6 heteroalkyl, halogen, CN, C_3-C_{12} cycloalkyl, C_3-C_{12} heterocyclyl; and C_1-C_6 alkyl substituted by aryl or heteroaryl wherein the aryl and the heteroaryl are optionally substituted by NH_2, OC_1-C_6 alkyl, C_1-C_6 alkyl, C_1-C_6 heteroalkyl, halogen, CN, C_3-C_{12} cycloalkyl, C_3-C_{12} heterocyclyl;

wherein R^2 is selected from aryl and heteroaryl wherein the aryl and the heteroaryl are optionally substituted by NH_2, OC_1-C_6 alkyl, C_1-C_6 alkyl, C_1-C_6 heteroalkyl, halogen, CN, C_3-C_{12} cycloalkyl, C_3-C_{12} heterocyclyl, $C(O)R^{12}$, C_1-C_6 alkyl $C(O)R^{12}$;

wherein R^3 is selected from H, halogen, C_1-C_6 alkyl and C_3-C_{12} cycloalkyl;

wherein R^4 is selected from H and halogen and R^5 and R^6 are each independently selected from H and C_1-C_6 alkyl;

wherein R^8 is selected from H, halogen, C_1-C_6 alkyl and C_3-C_{12} cycloalkyl;

wherein R^9 is absent when Y^2 is N or is selected from H, halogen, C_1-C_6 alkyl and C_3-C_{12} cycloalkyl when Y^2 is C; and

wherein R^{12} is selected from NH_2, NHC_1-C_6 alkyl, C_1-C_6 alkyl, and C_1-C_6 heteroalkyl

, and a pharmaceutically acceptable carrier.

4. The compound of formula (I) according to claim 1, the use of the compound of formula (I) according to claim 2, and the pharmaceutical composition comprising a compound of formula (I) according to claim 3,

wherein X is selected from CH_2, CO, CHOH, $CHO(C_1$-$C_3)$ alkyl, NH, and O;

wherein Y^1 is N and R^7 is absent, Y^2 is selected from N and C and Y^3 is C;

wherein Z is $NR^{10}R^{11}$, wherein R^{10} and R^{11} are each independently selected from H and C_1-C_6 alkyl;

wherein R^1 is selected from H, C_1-C_6 alkyl, C_0-C_3 alkylOC_0-C_3 alkyl aryl wherein the aryl is optionally substituted by NH_2; C_0-C_3 alkylOC_0-C_3 alkyl heteroaryl wherein the heteroaryl is optionally substituted by NH_2;

wherein R^2 is selected from aryl and heteroaryl wherein the aryl and the heteroaryl are optionally substituted by OC_1-C_6 alkyl, C_1-C_6 alkyl, C_1-C_6 heteroalkyl, halogen, C_1-C_6 alkyl $C(O)R^{12}$;

wherein R^3 is H;

wherein R^4 is selected from H and halogen;

wherein R^5 and R^6 are each independently selected from H and C_1-C_6 alkyl;

wherein R^8 is H;

wherein R^9 is absent when Y^2 is N or is H when Y^2 is C; and

wherein R^{12} is NH_2.

5. The compound of formula (I) according to claim 1, the use of the compound of formula (I) according to claim 2, and the pharmaceutical composition comprising a compound of formula (I) according to claim 3,

wherein X is selected from CH_2, NH and O;

wherein Y^1 is N and R^7 is absent, Y^2 is selected from N and C and Y^3 is C;

wherein Z is $NR^{10}R^{11}$, wherein R^{10} and R^{11} are each independently selected from H and C_1-C_6 alkyl;

wherein R^1 is selected from H, halogen, C_1-C_6 alkyl, C_3-C_{12} cycloalkyl, C_3-C_{12} heterocyclyl, C_1-C_6 alkoxy, C_1-C_6 heteroalkyl, C_0-C_3 alkylOC_0-C_3 alkyl aryl wherein the aryl is optionally substituted by NH_2, OC_1-C_6 alkyl, C_1-C_6 alkyl, C_1-C_6 heteroalkyl, halogen, CN, C_3-C_{12} cycloalkyl, C_3-C_{12} heterocyclyl; C_0-C_3 alkylOC_0-C_3 alkyl heteroaryl wherein the heteroaryl is optionally substituted by NH_2, OC_1-C_6 alkyl, C_1-C_6 alkyl, C_1-C_6 heteroalkyl, halogen, CN, C_3-C_{12} cycloalkyl, C_3-C_{12} heterocyclyl; and C_1-C_6 alkyl substituted by aryl or heteroaryl wherein the aryl and the heteroaryl are optionally substituted by NH_2, OC_1-C_6 alkyl, C_1-C_6 alkyl, C_1-C_6 heteroalkyl, halogen, CN, C_3-C_{12} cycloalkyl, C_3-C_{12} heterocyclyl;

wherein R^2 is selected from aryl and heteroaryl wherein the aryl and the heteroaryl are optionally substituted by NH_2, OC_1-C_6 alkyl, C_1-C_6 alkyl, C_1-C_6 heteroalkyl, halogen, CN, C_3-C_{12} cycloalkyl, C_3-C_{12} heterocyclyl, $C(O)R^{12}$, C_1-C_6 alkyl $C(O)R^{12}$;

wherein R^3 is selected from H, halogen, C_1-C_6 alkyl and C_3-C_{12} cycloalkyl;

wherein R^4 is selected from H and halogen and R^5 and R^6 are each independently selected from H and C_1-C_6 alkyl;

wherein R^8 is selected from H, halogen, C_1-C_6 alkyl and C_3-C_{12} cycloalkyl;

wherein R^9 is absent when Y^2 is N or is selected from H, halogen, C_1-C_6 alkyl and C_3-C_{12} cycloalkyl when Y^2 is C; and

wherein R^{12} is selected from NH_2, NHC_1-C_6 alkyl, C_1-C_6 alkyl, and C_1-C_6 heteroalkyl.

6. The compound of formula (I) according to claim 1, the use of the compound of formula (I) according to claim 2, and the pharmaceutical composition comprising a compound of formula (I) according to claim 3,
wherein X is selected from CH_2, CO, CHOH, CHO(C_1-C_3) alkyl, NH, and O;
wherein Y^1 is N and R^7 is absent, Y^2 is selected from N and C and Y^3 is C;
wherein Z is $NR^{10}R^{11}$, wherein R^{10} and R^{11} are each independently selected from H and C_1-C_6 alkyl;
wherein R^1 is selected from H, halogen, C_1-C_6 alkyl, C_3-C_{12} cycloalkyl, C_3-C_{12} heterocyclyl, C_1-C_6 alkoxy and C_1-C_6 heteroalkyl;
wherein R^2 is selected from aryl and heteroaryl wherein the aryl and the heteroaryl are optionally substituted by NH_2, OC_1-C_6 alkyl, C_1-C_6 alkyl, C_1-C_6 heteroalkyl, halogen, CN, C_3-C_{12} cycloalkyl, C_3-C_{12} heterocyclyl, $C(O)R^{12}$, C_1-C_6 alkyl $C(O)R^{12}$;
wherein R^3 is selected from H, halogen, C_1-C_6 alkyl and C_3-C_{12} cycloalkyl;
wherein R^4 is selected from H and halogen and R^5 and R^6 are each independently selected from H and C_1-C_6 alkyl;
wherein R^8 is selected from H, halogen, C_1-C_6 alkyl and C_3-C_{12} cycloalkyl;
wherein R^9 is absent when Y^2 is N or is selected from H, halogen, C_1-C_6 alkyl and C_3-C_{12} cycloalkyl when Y^2 is C; and
wherein R^{12} is selected from NH_2, NHC_1-C_6 alkyl, C_1-C_6 alkyl, and C_1-C_6 heteroalkyl.

7. The compound of formula (I) according to claim 1, the use of the compound of formula (I) according to claim 2, and the pharmaceutical composition comprising a compound of formula (I) according to claim 3,
wherein X is selected from CH_2, NH and O;
wherein Y^1 is N and R^7 is absent, Y^2 is selected from N and C and Y^3 is C;
wherein Z is $NR^{10}R^{11}$, wherein R^{10} and R^{11} are each independently selected from H and C_1-C_6 alkyl;
wherein R^1 is selected from H, halogen, C_1-C_6 alkyl, C_3-C_{12} cycloalkyl, C_3-C_{12} heterocyclyl, C_1-C_6 alkoxy and C_1-C_6 heteroalkyl;
wherein R^2 is selected from aryl and heteroaryl wherein the aryl and the heteroaryl are optionally substituted by NH_2, OC_1-C_6 alkyl, C_1-C_6 alkyl, C_1-C_6 heteroalkyl, halogen, CN, C_3-C_{12} cycloalkyl, C_3-C_{12} heterocyclyl, $C(O)R^{12}$, C_1-C_6 alkyl $C(O)R^{12}$;
wherein R^3 is selected from H, halogen, C_1-C_6 alkyl and C_3-C_{12} cycloalkyl;

wherein R^4 is selected from H and halogen and R^5 and R^6 are each independently selected from H and C_1-C_6 alkyl;

wherein R^8 is selected from H, halogen, C_1-C_6 alkyl and C_3-C_{12} cycloalkyl;

wherein R^9 is absent when Y^2 is N or is selected from H, halogen, C_1-C_6 alkyl and C_3-C_{12} cycloalkyl when Y^2 is C; and

wherein R^{12} is selected from NH_2, NHC_1-C_6 alkyl, C_1-C_6 alkyl, and C_1-C_6 heteroalkyl.

8. The compound of formula (I) according to claim 1, the use of the compound of formula (I) according to claim 2, and the pharmaceutical composition comprising a compound of formula (I) according to claim 3,

wherein X is selected from CH_2, CO, CHOH, CHO(C_1-C_3) alkyl, NH, and O;

wherein Y^1 is N and R^7 is absent, Y^2 is selected from N and C and Y^3 is C;

wherein Z is $NR^{10}R^{11}$, wherein R^{10} and R^{11} are each independently selected from H and C_1-C_6 alkyl;

wherein R^1 is selected from H and C_1-C_6 alkyl;

wherein R^2 is selected from aryl and heteroaryl wherein the aryl and the heteroaryl are optionally substituted by OC_1-C_6 alkyl, C_1-C_6 alkyl, C_1-C_6 heteroalkyl, halogen, C_1-C_6 alkyl $C(O)R^{12}$;

wherein R^3 is H;

wherein R^4 is selected from H and halogen;

wherein R^5 and R^6 are each independently selected from H and C_1-C_6 alkyl;

wherein R^8 is H;

wherein R^9 is absent when Y^2 is N or is H when Y^2 is C; and

wherein R^{12} is NH_2.

9. The compound of formula (I) according to claim 1, the use of the compound of formula (I) according to claim 2, and the pharmaceutical composition comprising a compound of formula (I) according to claim 3,

wherein X is selected from CH_2, CO, CHOH, CHO(C_1-C_3) alkyl, NH, and O;

wherein Y^1 is N and R^7 is absent, Y^2 is selected from N and C and Y^3 is C;

wherein Z is $NR^{10}R^{11}$, wherein R^{10} and R^{11} are each independently selected from H and C_1-C_6 alkyl;

wherein R^1 is selected from C_0-C_3 alkylOC_0-C_3 alkyl aryl wherein the aryl is optionally substituted by NH_2, OC_1-C_6 alkyl, C_1-C_6 alkyl, C_1-C_6 heteroalkyl, halogen, CN, C_3-C_{12}

cycloalkyl, C_3-C_{12} heterocyclyl; and C_0-C_3 alkylOC_0-C_3 alkyl heteroaryl wherein the heteroaryl is optionally substituted by NH_2, OC_1-C_6 alkyl, C_1-C_6 alkyl, C_1-C_6 heteroalkyl, halogen, CN, C_3-C_{12} cycloalkyl, C_3-C_{12} heterocyclyl;

wherein R^2 is selected from aryl and heteroaryl wherein the aryl and the heteroaryl are optionally substituted by NH_2, halogen, C_1-C_6 alkyl, CN;

wherein R^3 is selected from H, halogen and C_1-C_4 alkyl;

wherein R^4 is selected from H and halogen and R^5 and R^6 are each independently selected from H and C_1-C_6 alkyl;

wherein R^8 is selected from H, halogen and C_1-C_4 alkyl; and

wherein R^9 is absent when Y^2 is N or is selected from H, halogen and C_1-C_4 alkyl when Y^2 is C.

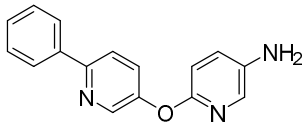
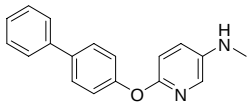
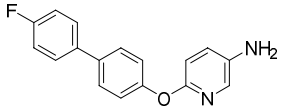
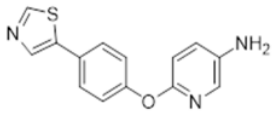
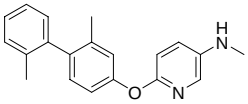
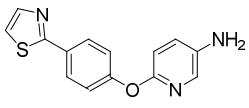
10. The compound of formula (I) according to claim 1 or 5, the use of the compound of formula (I) according to claim 2 or 5, and the pharmaceutical composition comprising a compound of formula (I) according to according to claim 3 or 5, wherein R^1 is selected from H, halogen, C_1-C_6 alkyl, C_1-C_6 heteroalkyl, C_0-C_3 alkylOC_0-C_3 alkyl aryl wherein the aryl is optionally substituted by NH_2, C_1-C_6 alkyl, C_1-C_6 heteroalkyl, halogen, CN, preferably is optionally substituted by NH_2; and C_0-C_3 alkylOC_0-C_3 alkyl heteroaryl wherein the heteroaryl is optionally substituted by NH_2, OC_1-C_6 alkyl, C_1-C_6 alkyl, C_1-C_6 heteroalkyl, halogen, CN, C_3-C_{12} cycloalkyl, C_3-C_{12} heterocyclyl, preferably is optionally substituted by NH_2.

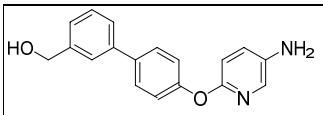
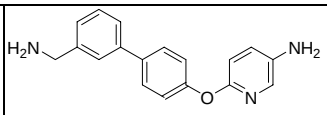
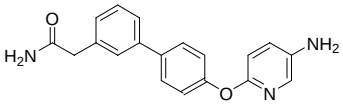
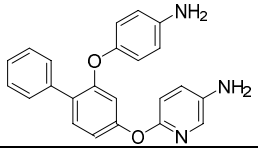
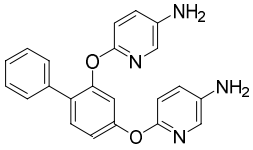
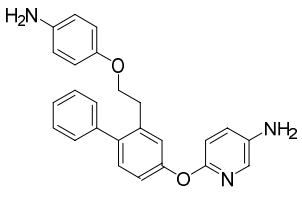
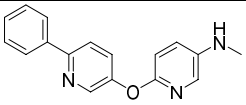
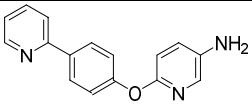
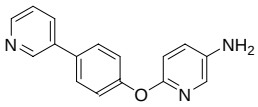
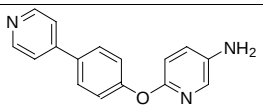
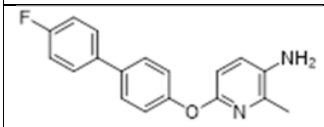
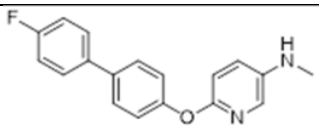
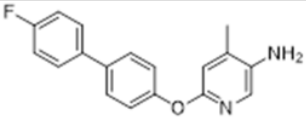
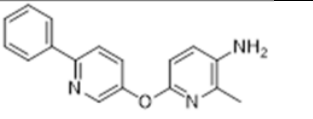
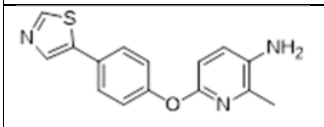
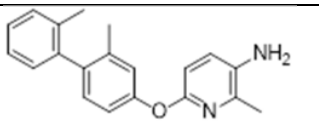
11. The compound of formula (I) according to any one of claims 1 and 4-10, the use of thecompound of formula (I) according to any one of claims 2 and 4-10, and the pharmaceutical composition comprising a compound of formula (I) according to any one of claims 3 and 4-10, wherein R^2 is selected from aryl and heteroaryl, wherein the aryl is a phenyl group which is optionally substituted, wherein the optional substitution of the phenyl group is in meta or para position, preferably in para position.

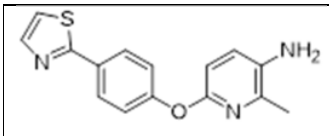
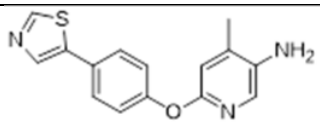
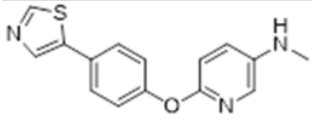
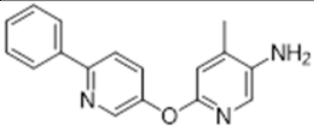
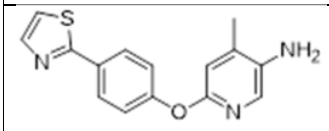
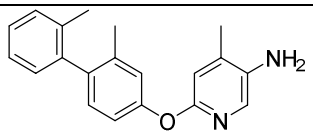
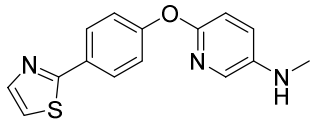
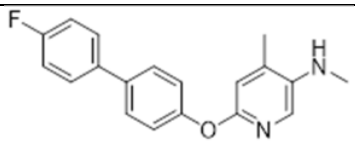
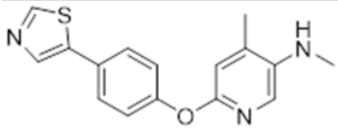
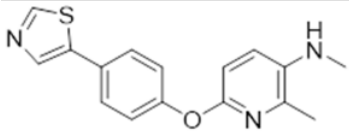
12. The compound of formula (I) according to any one of claims 1 and 4-10, the use of the compound of formula (I) according to any one of claims 2 and 4-10, and/or the pharmaceutical composition comprising a compound of formula (I) according to any one of claims 3 and 4-10, wherein R^2 is selected from aryl and heteroaryl wherein the

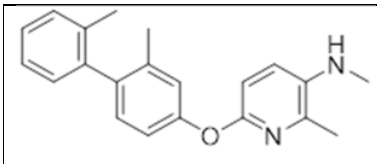
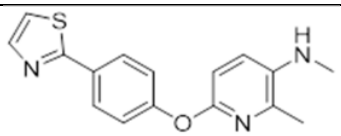
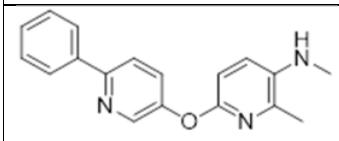
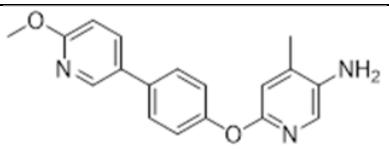
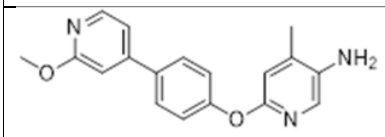
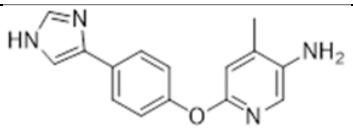
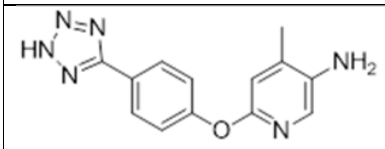
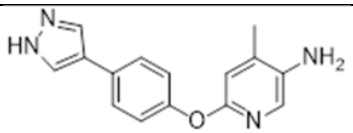
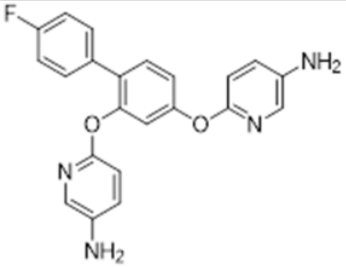
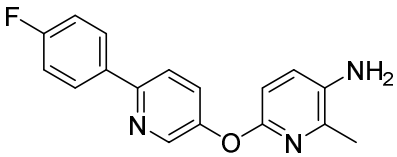
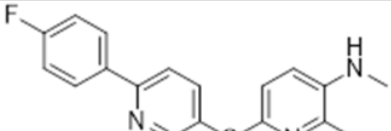
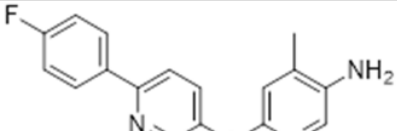
heteroaryl is an optionally substituted aromatic 5-, or 6- membered monocyclic group.

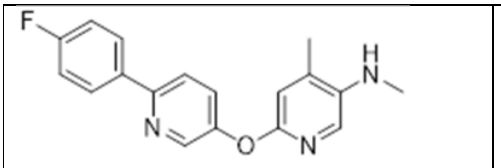
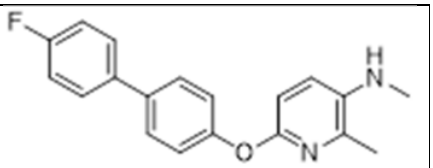
13. The compound of formula (I) according to claim 1, the use of the compound of formula (I) according to claim 2, and/or the pharmaceutical composition comprising a compound of formula (I) according to claim 3, selected from the group consisting of

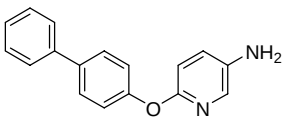
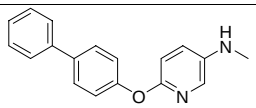
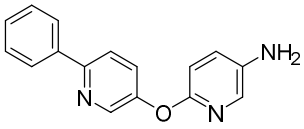
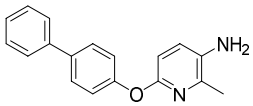
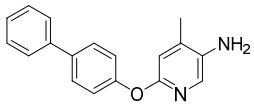
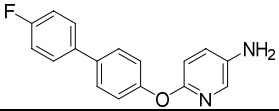
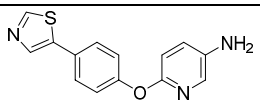
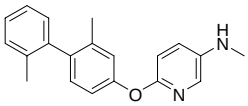
	
	
	
	
	
	
	
	

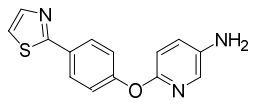
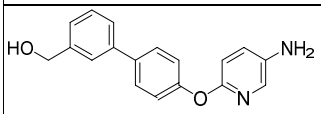
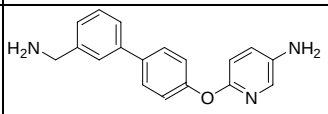
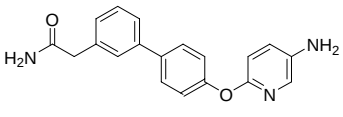
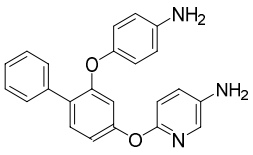
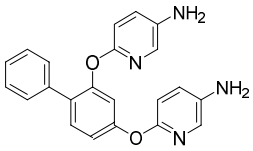
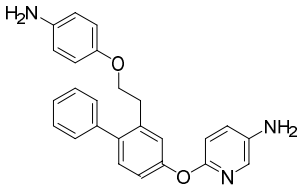
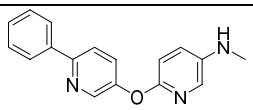
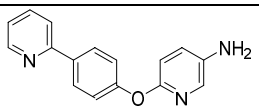
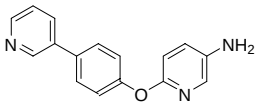
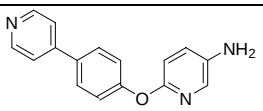
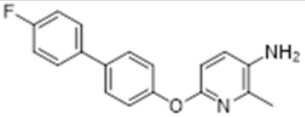
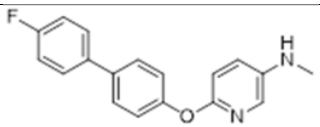
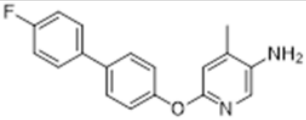
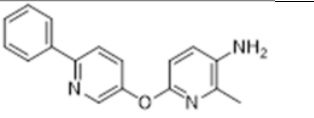
	
	
	
	
	
	

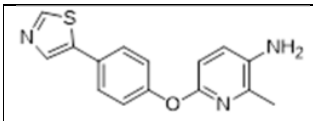
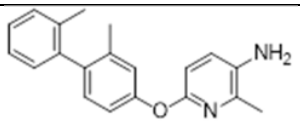
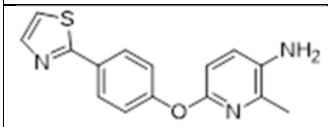
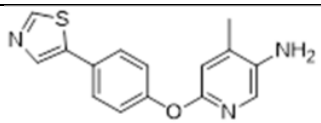
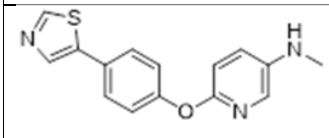
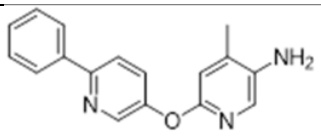
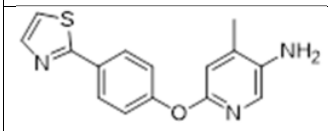
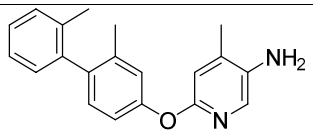
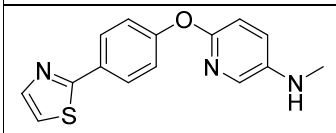
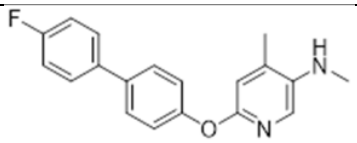
	
	
	
	
	
	

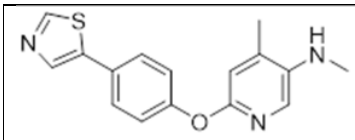
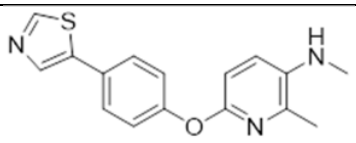
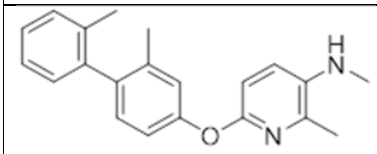
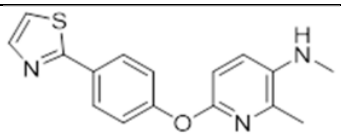
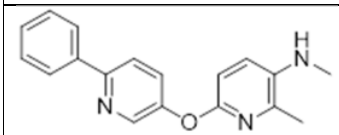
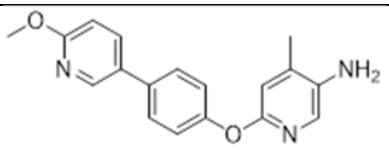
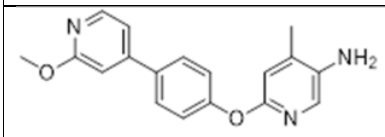
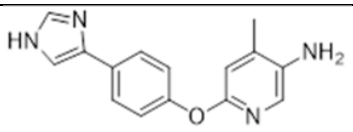
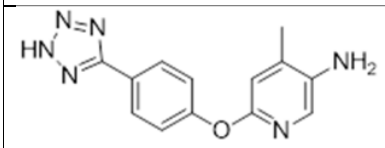
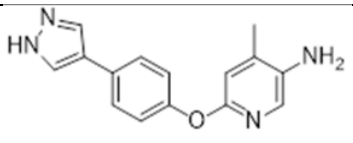
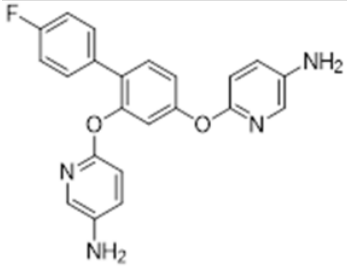
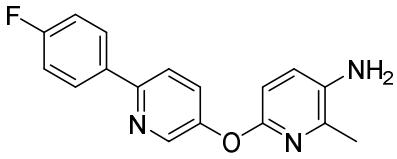
	

14. The use of the compound of formula (I) according to claim 2, selected from the group consisting of

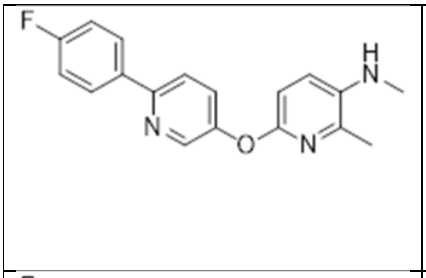
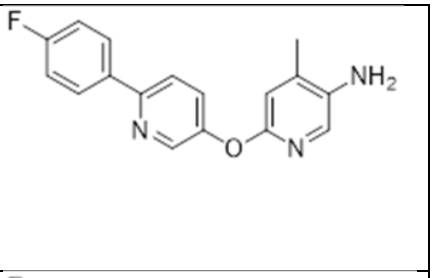
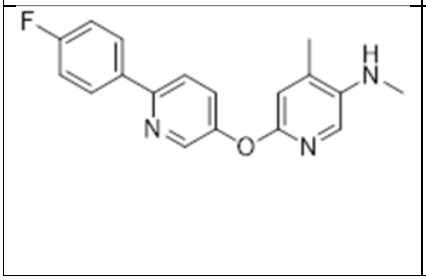
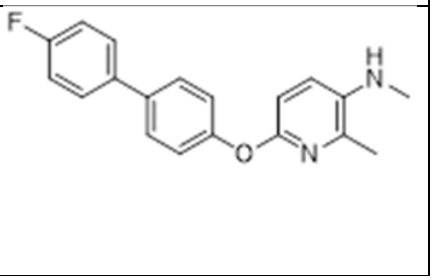
	
	
	
	
	
	

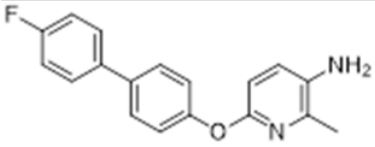
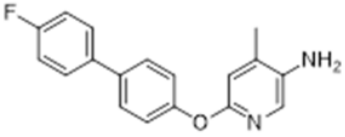
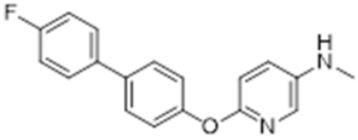
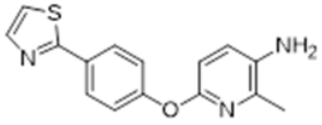
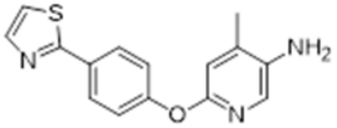
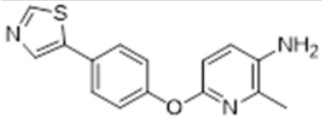
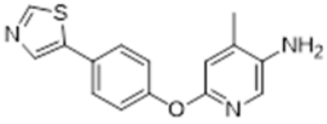
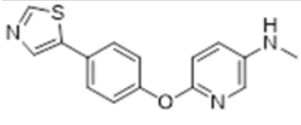
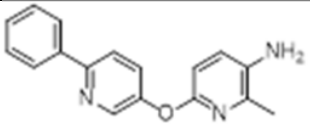
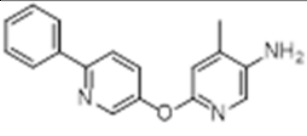
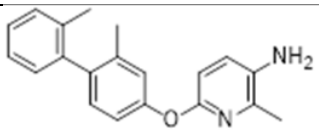
	
	
	
	
	
	

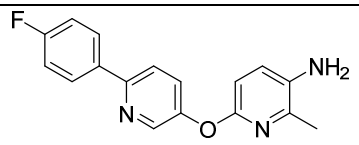
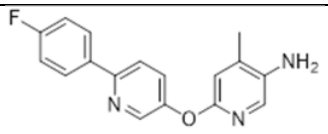
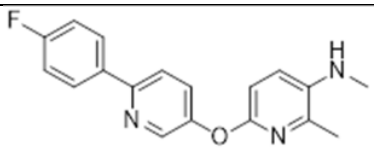
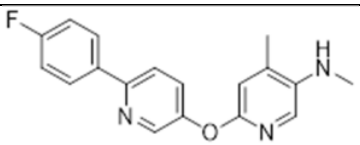
	
	
	
	
	
	

S
N
H
N
O
N
NH2
F

15. The compound of formula (I) according to claim 1, the use of the compound of formula (I) according to claim 2, and/or the pharmaceutical composition comprising a compound of formula (I) according to claim 3, selected from the group consisting of

16. The use of the compound of formula (I) according to any one of claims 2 and 4-15, wherein the cancer is a Notch dependent cancer.