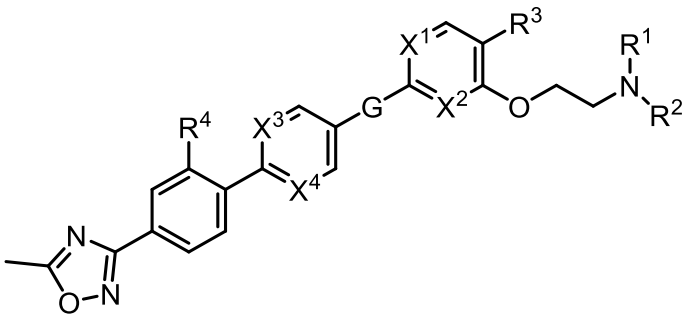
CLAIMS

~~1.~~ 1. A compound of formula (I):



(I)

wherein:

- G represents a group selected from:
  a) -C(O)NH-,
  b) --NHC(O)-,
- X^1, X^2, X^3 and X^4 represent a N atom or C-R^5 group,
- R^1 and R^2 are independently selected from the group consisting of:
  a) hydrogen atom,
  b) linear or branched C_1-C_6 alkyl optionally substituted by 1, 2 or 3 substituents selected from -N(R^6)R^7, -OR^6, halogen atom and C_3-C_6 cycloalkyl,
  c) C_3-C_6 cycloalkyl,
- or R^1 and R^2 form together with the nitrogen atom to which they are attached a four to six-membered heterocyclic group, comprising additionally a second heteroatom selected from N and O;
- R^3 represents a group selected from:
  a) cyano group, and
  b) halogen atom,
- R^4 represents a group selected from:
  a) halogen atom,
  b) C_3-C_4 cycloalkyl group,
  c) C_1-C_3 alkoxy group,
  d) C_1-C_3 haloalkyl group,
  e) cyano group,
- R^5 represents a group selected from:
  a) hydrogen atom,
  b) C_1-C_3 alkyl,
  c) halogen atom,

- R^6 and R^7 represent independently a group selected from:
  a) C_1-C_3 alkyl,
  b) hydrogen atom,

with the proviso that at least one of the X^1, X^2, X^3 and X^4 represents a N atom,

and pharmaceutically acceptable salts thereof.

~~2~~ 2. ~~A compound according to claim 1 wherein R^1 and R^2 are methyl groups.~~

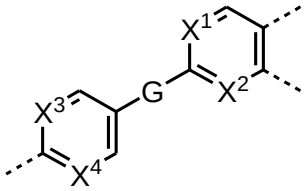
~~3.~~ 3. A compound according to any one claims 1 to 2 wherein G represents -C(O)NH wherein the carbonyl group is linked to the cycle comprising X^3 and X^4 and the amine group is linked to the cycle comprising X^1 and X^2.

~~4.~~ 4. A compound according to any one claims 1 to 3 wherein R^3 is cyano group.

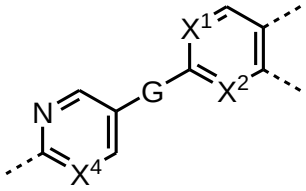
~~5.~~ 5. A compound according to any one claims 1 to 4 wherein R^4 is selected from halogen atom and C_3-C_4 cycloalkyl group.

~~6.~~ 6. A compound according to claim 5 wherein R^4 is selected from chlorine atom, fluorine atom and cyclopropyl group.

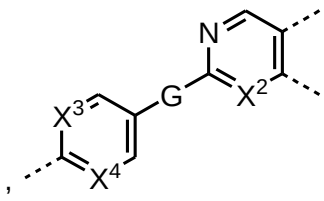
~~7.~~ 7. A compound according to any one claims 1 to 5 wherein the core:



is selected from:

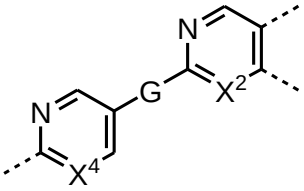


wherein X^3 is N and X^1, X^2, X^4 and G are as defined in anyone of claims 1 and 3



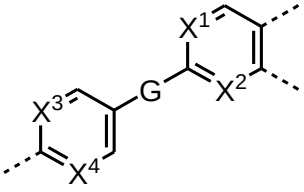
,

wherein X^1 is N and X^2, X^3, X^4 and G are as defined in anyone of claims 1 and 3; and

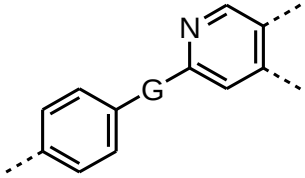


wherein X^1 and X^3 are N and X^2, X^4 and G are as defined in anyone of claims 1 and 3.

~~8.~~ 8. A compound according to claim 7 wherein the core:

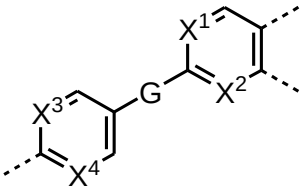


is:

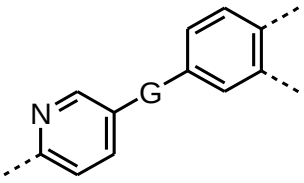


wherein G is as defined in anyone of claims 1 and 3.

~~9.~~ 9. A compound according to claim 7 wherein the core:

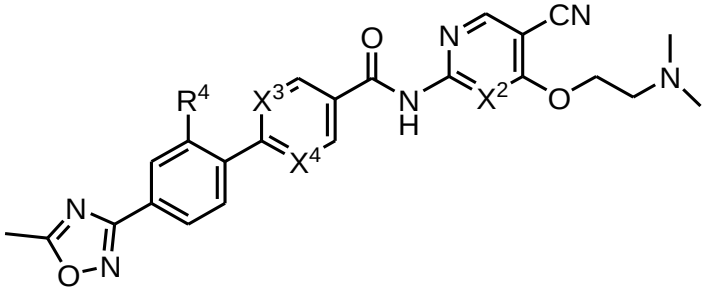


is:

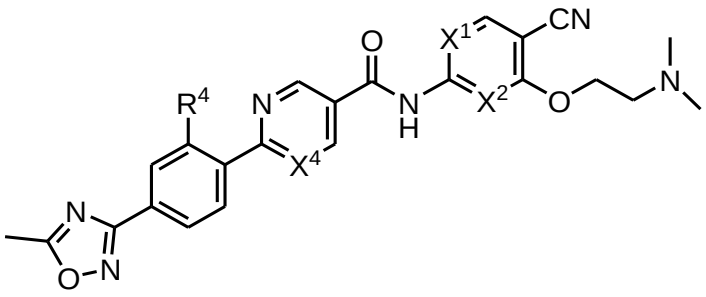


wherein G is as defined in anyone of claims 1 and 3.

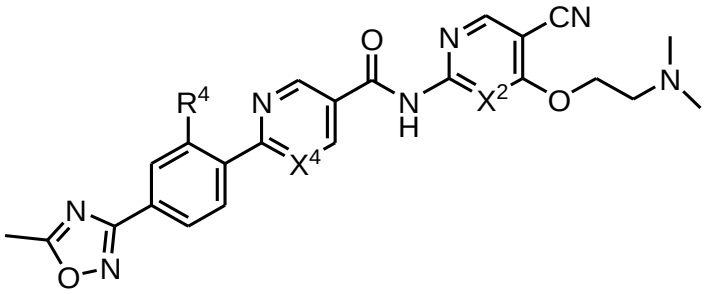
~~10.~~ 10. A compound according to claim 1 having one of the following formula (Ia), (Ib) and (Ic)



(Ia),



(Ib) and



(Ic)

wherein R^4 represents a group selected from halogen atom and cyclopropyl group.

11. A compound according to claim 1, which is selected from the group consisting of:

N-(4-bromo-3-(2-(dimethylamino)ethoxy)phenyl)-6-(2-cyclopropyl-4-(5-methyl-1,2,4-oxadiazol-3-yl)phenyl)nicotinamide

N-(4-bromo-3-(2-(dimethylamino)ethoxy)phenyl)-6-(2-fluoro-4-(5-methyl-1,2,4-oxadiazol-3-yl)phenyl)nicotinamide

N-(4-bromo-3-(2-(dimethylamino)ethoxy)phenyl)-6-(2-chloro-4-(5-methyl-1,2,4-oxadiazol-3-yl)phenyl)nicotinamide

N-(4-bromo-3-(2-(dimethylamino)ethoxy)phenyl)-6-(4-(5-methyl-1,2,4-oxadiazol-3-yl)-2-(trifluoromethyl)phenyl)nicotinamide

N-(4-bromo-3-(2-(dimethylamino)ethoxy)phenyl)-6-(2-methoxy-4-(5-methyl-1,2,4-oxadiazol-3-yl)phenyl)nicotinamide

N-(4-bromo-3-(2-(dimethylamino)ethoxy)phenyl)-6-(2-cyano-4-(5-methyl-1,2,4-oxadiazol-3-yl)phenyl)nicotinamide

N-(4-cyano-3-(2-(dimethylamino)ethoxy)phenyl)-6-(2-cyclopropyl-4-(5-methyl-1,2,4-oxadiazol-3-yl)phenyl)nicotinamide

N-(4-cyano-3-(2-(dimethylamino)ethoxy)phenyl)-6-(2-fluoro-4-(5-methyl-1,2,4-oxadiazol-3-yl)phenyl)nicotinamide

6-(2-chloro-4-(5-methyl-1,2,4-oxadiazol-3-yl)phenyl)-N-(4-cyano-3-(2-(dimethylamino)ethoxy)phenyl)nicotinamide

N-(4-cyano-3-(2-(dimethylamino)ethoxy)phenyl)-6-(4-(5-methyl-1,2,4-oxadiazol-3-yl)-2-(trifluoromethyl)phenyl)nicotinamide

N-(4-cyano-3-(2-(dimethylamino)ethoxy)phenyl)-6-(2-methoxy-4-(5-methyl-1,2,4-oxadiazol-3-yl)phenyl)nicotinamide

N-(4-cyano-3-(2-(dimethylamino)ethoxy)phenyl)-6-(2-cyano-4-(5-methyl-1,2,4-oxadiazol-3-yl)phenyl)nicotinamide

N-(4-bromo-3-(2-(dimethylamino)ethoxy)phenyl)-2-(2-cyclopropyl-4-(5-methyl-1,2,4-oxadiazol-3-yl)phenyl)pyrimidine-5-carboxamide

N-(4-cyano-3-(2-(dimethylamino)ethoxy)phenyl)-2-(2-cyclopropyl-4-(5-methyl-1,2,4-oxadiazol-3-yl)phenyl)pyrimidine-5-carboxamide

N-(5-bromo-4-(2-(dimethylamino)ethoxy)pyridin-2-yl)-2'-cyclopropyl-4'-(5-methyl-1,2,4-oxadiazol-3-yl)-[1,1'-biphenyl]-4-carboxamide

N-(5-bromo-4-(2-(dimethylamino)ethoxy)pyridin-2-yl)-2'-fluoro-4'-(5-methyl-1,2,4-oxadiazol-3-yl)-[1,1'-biphenyl]-4-carboxamide

N-(5-bromo-4-(2-(dimethylamino)ethoxy)pyridin-2-yl)-2'-chloro-4'-(5-methyl-1,2,4-oxadiazol-3-yl)-[1,1'-biphenyl]-4-carboxamide

N-(5-bromo-4-(2-(dimethylamino)ethoxy)pyridin-2-yl)-4'-(5-methyl-1,2,4-oxadiazol-3-yl)-2'-(trifluoromethyl)-[1,1'-biphenyl]-4-carboxamide

N-(5-bromo-4-(2-(dimethylamino)ethoxy)pyridin-2-yl)-2'-methoxy-4'-(5-methyl-1,2,4-oxadiazol-3-yl)-[1,1'-biphenyl]-4-carboxamide

N-(5-bromo-4-(2-(dimethylamino)ethoxy)pyridin-2-yl)-2'-cyano-4'-(5-methyl-1,2,4-oxadiazol-3-yl)-[1,1'-biphenyl]-4-carboxamide

N-(5-cyano-4-(2-(dimethylamino)ethoxy)pyridin-2-yl)-2'-cyclopropyl-4'-(5-methyl-1,2,4-oxadiazol-3-yl)-[1,1'-biphenyl]-4-carboxamide

N-(5-cyano-4-(2-(dimethylamino)ethoxy)pyridin-2-yl)-2'-fluoro-4'-(5-methyl-1,2,4-oxadiazol-3-yl)-[1,1'-biphenyl]-4-carboxamide

2'-chloro-N-(5-cyano-4-(2-(dimethylamino)ethoxy)pyridin-2-yl)-4'-(5-methyl-1,2,4-oxadiazol-3-yl)-[1,1'-biphenyl]-4-carboxamide

N-(5-cyano-4-(2-(dimethylamino)ethoxy)pyridin-2-yl)-4'-(5-methyl-1,2,4-oxadiazol-3-yl)-2'-(trifluoromethyl)-[1,1'-biphenyl]-4-carboxamide

N-(5-cyano-4-(2-(dimethylamino)ethoxy)pyridin-2-yl)-2'-methoxy-4'-(5-methyl-1,2,4-oxadiazol-3-yl)-[1,1'-biphenyl]-4-carboxamide

2'-cyano-N-(5-cyano-4-(2-(dimethylamino)ethoxy)pyridin-2-yl)-4'-(5-methyl-1,2,4-oxadiazol-3-yl)-[1,1'-biphenyl]-4-carboxamide

N-(5-bromo-6-(2-(dimethylamino)ethoxy)pyridin-2-yl)-2'-cyclopropyl-4'-(5-methyl-1,2,4-oxadiazol-3-yl)-[1,1'-biphenyl]-4-carboxamide

N-(5-bromo-6-(2-(dimethylamino)ethoxy)pyridin-2-yl)-2'-fluoro-4'-(5-methyl-1,2,4-oxadiazol-3-yl)-[1,1'-biphenyl]-4-carboxamide

N-(5-bromo-6-(2-(dimethylamino)ethoxy)pyridin-2-yl)-2'-chloro-4'-(5-methyl-1,2,4-oxadiazol-3-yl)-[1,1'-biphenyl]-4-carboxamide

N-(5-cyano-6-(2-(dimethylamino)ethoxy)pyridin-2-yl)-2'-cyclopropyl-4'-(5-methyl-1,2,4-oxadiazol-3-yl)-[1,1'-biphenyl]-4-carboxamide

N-(5-cyano-6-(2-(dimethylamino)ethoxy)pyridin-2-yl)-2'-fluoro-4'-(5-methyl-1,2,4-oxadiazol-3-yl)-[1,1'-biphenyl]-4-carboxamide

2'-chloro-N-(5-cyano-6-(2-(dimethylamino)ethoxy)pyridin-2-yl)-4'-(5-methyl-1,2,4-oxadiazol-3-yl)-[1,1'-biphenyl]-4-carboxamide

N-(5-bromo-4-(2-(dimethylamino)ethoxy)pyrimidin-2-yl)-2'-cyclopropyl-4'-(5-methyl-1,2,4-oxadiazol-3-yl)-[1,1'-biphenyl]-4-carboxamide

N-(5-bromo-4-(2-(dimethylamino)ethoxy)pyrimidin-2-yl)-2'-fluoro-4'-(5-methyl-1,2,4-oxadiazol-3-yl)-[1,1'-biphenyl]-4-carboxamide

N-(5-bromo-4-(2-(dimethylamino)ethoxy)pyrimidin-2-yl)-2'-chloro-4'-(5-methyl-1,2,4-oxadiazol-3-yl)-[1,1'-biphenyl]-4-carboxamide

N-(5-cyano-4-(2-(dimethylamino)ethoxy)pyrimidin-2-yl)-2'-cyclopropyl-4'-(5-methyl-1,2,4-oxadiazol-3-yl)-[1,1'-biphenyl]-4-carboxamide

N-(5-cyano-4-(2-(dimethylamino)ethoxy)pyrimidin-2-yl)-2'-fluoro-4'-(5-methyl-1,2,4-oxadiazol-3-yl)-[1,1'-biphenyl]-4-carboxamide

2'-chloro-N-(5-cyano-4-(2-(dimethylamino)ethoxy)pyrimidin-2-yl)-4'-(5-methyl-1,2,4-oxadiazol-3-yl)-[1,1'-biphenyl]-4-carboxamide

N-(5-bromo-4-(2-(dimethylamino)ethoxy)pyridin-2-yl)-6-(2-cyclopropyl-4-(5-methyl-1,2,4-oxadiazol-3-yl)phenyl)nicotinamide

N-(5-bromo-4-(2-(dimethylamino)ethoxy)pyridin-2-yl)-6-(2-fluoro-4-(5-methyl-1,2,4-oxadiazol-3-yl)phenyl)nicotinamide

N-(5-bromo-4-(2-(dimethylamino)ethoxy)pyridin-2-yl)-6-(2-chloro-4-(5-methyl-1,2,4-oxadiazol-3-yl)phenyl)nicotinamide

N-(5-bromo-4-(2-(dimethylamino)ethoxy)pyridin-2-yl)-6-(4-(5-methyl-1,2,4-oxadiazol-3-yl)-2-(trifluoromethyl)phenyl)nicotinamide

N-(5-bromo-4-(2-(dimethylamino)ethoxy)pyridin-2-yl)-6-(2-methoxy-4-(5-methyl-1,2,4-oxadiazol-3-yl)phenyl)nicotinamide

N-(5-bromo-4-(2-(dimethylamino)ethoxy)pyridin-2-yl)-6-(2-cyano-4-(5-methyl-1,2,4-oxadiazol-3-yl)phenyl)nicotinamide

N-(5-cyano-4-(2-(dimethylamino)ethoxy)pyridin-2-yl)-6-(2-cyclopropyl-4-(5-methyl-1,2,4-oxadiazol-3-yl)phenyl)nicotinamide

N-(5-cyano-4-(2-(dimethylamino)ethoxy)pyridin-2-yl)-6-(2-fluoro-4-(5-methyl-1,2,4-oxadiazol-3-yl)phenyl)nicotinamide

6-(2-chloro-4-(5-methyl-1,2,4-oxadiazol-3-yl)phenyl)-N-(5-cyano-4-(2(dimethylamino)ethoxy)pyridin-2-yl)nicotinamide

N-(5-cyano-4-(2-(dimethylamino)ethoxy)pyridin-2-yl)-6-(4-(5-methyl-1,2,4-oxadiazol-3-yl)-2-(trifluoromethyl)phenyl)nicotinamide

N-(5-cyano-4-(2-(dimethylamino)ethoxy)pyridin-2-yl)-6-(2-methoxy-4-(5-methyl-1,2,4-oxadiazol-3-yl)phenyl)nicotinamide

N-(5-cyano-4-(2-(dimethylamino)ethoxy)pyridin-2-yl)-6-(2-cyano-4-(5-methyl-1,2,4-oxadiazol-3-yl)phenyl)nicotinamide

N-(5-bromo-6-(2-(dimethylamino)ethoxy)pyridin-2-yl)-6-(2-cyclopropyl-4-(5-methyl-1,2,4-oxadiazol-3-yl)phenyl)nicotinamide

N-(5-bromo-6-(2-(dimethylamino)ethoxy)pyridin-2-yl)-6-(2-fluoro-4-(5-methyl-1,2,4-oxadiazol-3-yl)phenyl)nicotinamide

N-(5-bromo-6-(2-(dimethylamino)ethoxy)pyridin-2-yl)-6-(2-chloro-4-(5-methyl-1,2,4-oxadiazol-3-yl)phenyl)nicotinamide

N-(5-cyano-6-(2-(dimethylamino)ethoxy)pyridin-2-yl)-6-(2-cyclopropyl-4-(5-methyl-1,2,4-oxadiazol-3-yl)phenyl)nicotinamide

N-(5-cyano-6-(2-(dimethylamino)ethoxy)pyridin-2-yl)-6-(2-fluoro-4-(5-methyl-1,2,4-oxadiazol-3-yl)phenyl)nicotinamide

6-(2-chloro-4-(5-methyl-1,2,4-oxadiazol-3-yl)phenyl)-N-(5-cyano-6-(2-(dimethylamino)ethoxy)pyridin-2-yl)nicotinamide

N-(5-bromo-4-(2-(dimethylamino)ethoxy)pyrimidin-2-yl)-6-(2-cyclopropyl-4-(5-methyl-1,2,4-oxadiazol-3-yl)phenyl)nicotinamide

N-(5-bromo-4-(2-(dimethylamino)ethoxy)pyrimidin-2-yl)-6-(2-fluoro-4-(5-methyl-1,2,4-oxadiazol-3-yl)phenyl)nicotinamide

N-(5-bromo-4-(2-(dimethylamino)ethoxy)pyrimidin-2-yl)-6-(2-chloro-4-(5-methyl-1,2,4-oxadiazol-3-yl)phenyl)nicotinamide

N-(5-cyano-4-(2-(dimethylamino)ethoxy)pyrimidin-2-yl)-6-(2-cyclopropyl-4-(5-methyl-1,2,4-oxadiazol-3-yl)phenyl)nicotinamide

N-(5-cyano-4-(2-(dimethylamino)ethoxy)pyrimidin-2-yl)-6-(2-fluoro-4-(5-methyl-1,2,4-oxadiazol-3-yl)phenyl)nicotinamide

6-(2-chloro-4-(5-methyl-1,2,4-oxadiazol-3-yl)phenyl)-N-(5-cyano-4-(2-(dimethylamino)ethoxy)pyrimidin-2-yl)nicotinamide

N-(5-bromo-4-(2-(dimethylamino)ethoxy)pyridin-2-yl)-2-(2-cyclopropyl-4-(5-methyl-1,2,4-oxadiazol-3-yl)phenyl)pyrimidine-5-carboxamide

N-(5-cyano-4-(2-(dimethylamino)ethoxy)pyridin-2-yl)-2-(2-cyclopropyl-4-(5-methyl-1,2,4-oxadiazol-3-yl)phenyl)pyrimidine-5-carboxamide

4-bromo-3-(2-(dimethylamino)ethoxy)-N-(6-(2-fluoro-4-(5-methyl-1,2,4-oxadiazol-3-yl)phenyl)pyridin-3-yl)benzamide

4-bromo-N-(6-(2-cyclopropyl-4-(5-methyl-1,2,4-oxadiazol-3-yl)phenyl)pyridin-3-yl)-3-(2-(dimethylamino)ethoxy)benzamide

4-bromo-N-(6-(2-chloro-4-(5-methyl-1,2,4-oxadiazol-3-yl)phenyl)pyridin-3-yl)-3-(2-(dimethylamino)ethoxy)benzamide

4-bromo-3-(2-(dimethylamino)ethoxy)-N-(6-(4-(5-methyl-1,2,4-oxadiazol-3-yl)-2-(trifluoromethyl)phenyl)pyridin-3-yl)benzamide

4-bromo-3-(2-(dimethylamino)ethoxy)-N-(6-(2-methoxy-4-(5-methyl-1,2,4-oxadiazol-3-yl)phenyl)pyridin-3-yl)benzamide

4-bromo-N-(6-(2-cyano-4-(5-methyl-1,2,4-oxadiazol-3-yl)phenyl)pyridin-3-yl)-3-(2-(dimethylamino)ethoxy)benzamide

4-cyano-N-(6-(2-cyclopropyl-4-(5-methyl-1,2,4-oxadiazol-3-yl)phenyl)pyridin-3-yl)-3-(2-(dimethylamino)ethoxy)benzamide

4-cyano-3-(2-(dimethylamino)ethoxy)-N-(6-(2-fluoro-4-(5-methyl-1,2,4-oxadiazol-3-yl)phenyl)pyridin-3-yl)benzamide

N-(6-(2-chloro-4-(5-methyl-1,2,4-oxadiazol-3-yl)phenyl)pyridin-3-yl)-4-cyano-3-(2-(dimethylamino)ethoxy)benzamide

4-cyano-3-(2-(dimethylamino)ethoxy)-N-(6-(4-(5-methyl-1,2,4-oxadiazol-3-yl)-2-(trifluoromethyl)phenyl)pyridin-3-yl)benzamide

4-cyano-3-(2-(dimethylamino)ethoxy)-N-(6-(2-methoxy-4-(5-methyl-1,2,4-oxadiazol-3-yl)phenyl)pyridin-3-yl)benzamide

4-cyano-N-(6-(2-cyano-4-(5-methyl-1,2,4-oxadiazol-3-yl)phenyl)pyridin-3-yl)-3-(2-(dimethylamino)ethoxy)benzamide.

~~12.~~ 12. A pharmaceutical composition comprising a compound as defined in anyone of claims 1 to 11 and a pharmaceutically acceptable diluent or carrier.

~~13.~~ 13. A combination product comprising a compound as defined in anyone of claims 1 to 11 and a therapeutic agent is selected from chemotherapy drugs selected from Vincristine, Daunorubicin, Cytarabine, 6-mercaptopurine, Methotrexate, Cyclophosphamide, Prednisone, Dexamethasone, Nelarabine, and one or more immunotherapeutic agent selected from the group consisting of antibodies anti-PD1, antibodies anti-PDL1 and antibodies anti-CTLA4, such as ipilimumab, tremelimumab, nivolumab, pembrolizumab, CT-011, AMP-224, MPDL3280A, MEDI4736 and MDX-1105.

~~14. Compound as defined in anyone of claims 1 to 11, pharmaceutical composition according to claim 12 or combination product according to claim 13 for use as a medicament.~~

~~15. Compound as defined in anyone of claims 1 to 11, pharmaceutical composition according to claim 12 or combination product according to claim 13 for use in the treatment of a disease or pathological condition susceptible of improvement by antagonism of 5-HT_{1B} receptor selected from cancer, respiratory diseases and hepatic disorders.~~

~~16. Compound, pharmaceutical composition or combination product for use according to claim 15, wherein the disease or pathological condition susceptible of improvement by antagonism of 5-HT_{1B} receptor is selected from blood cancer and solid tumours.~~

~~17. Compound, pharmaceutical composition or combination product for use according to claim 16, wherein the blood cancer is acute myeloid leukemia.~~

14.~~18.~~ Use of a compound as defined in anyone of claims 1 to 11, of a pharmaceutical composition according to claim 12 or of a combination product according to claim 13 for the manufacture of a medicament for the treatment of a disease or pathological condition susceptible of improvement by antagonism of 5-HT_{1B} receptor selected from cancer, respiratory diseases and hepatic disorders.

15.~~19.~~ Use according to claim 14~~18~~, wherein the disease or pathological condition susceptible of improvement by antagonism of 5-HT_{1B} receptor is selected from blood cancer and solid tumours.

16.~~20.~~ Use according to claim 15~~19~~, wherein the blood cancer is acute myeloid leukemia.

~~21. A method for the treatment of a disease or pathological condition susceptible of improvement by antagonism of 5-HT_{1B} receptor selected from cancer, respiratory diseases and hepatic disorders by administering to a subject in need thereof a~~

~~therapeutically effective amount of a compound as defined in anyone of claims 1 to 11, a pharmaceutical composition according to claim 12 or a combination product according to claim 13.~~

~~22- A method according to claim 21, wherein the disease or pathological condition susceptible of improvement by antagonism of 5-HT_{1B} receptor is selected from blood cancer and solid tumours.~~

~~23- A method according to claim 22, wherein the blood cancer is acute myeloid leukemia.~~