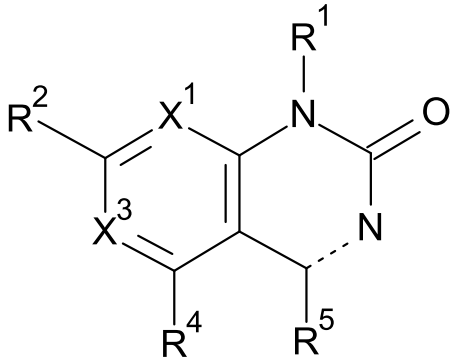
Amidopyrimidone derivatives

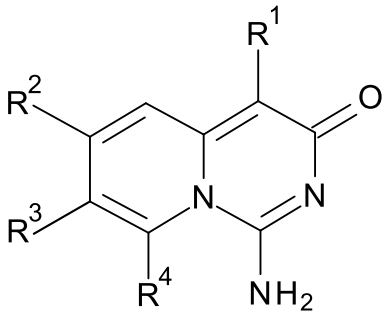
The present ~~invention~~disclosure provides compounds which are inhibitors of the Human methionine adenosyltransferase 2A (Mat2A), for use in the treatment, prevention and/or delay of progression of Cancer.

~~The~~ In one aspect, the present ~~invention~~disclosure relates to a compound~~s~~ of formula I or II:



(I)

or



(II)

wherein

X^1 is either N or CH;

X^3 is either N or CR^3;

the dotted line represents a single bond when R^5 is oxo or a double bond when R^5 is $-NH_2$,

R^1 is (C_1-C_6)alkyl optionally substituted with one or more, particularly one to three, more particularly one or two substituents R^{1a}, (C_1-C_6)alkoxy optionally substituted with one or more, particularly one to three, more particularly one or two substituents R^{1b}, halo(C_1-C_6)alkyl optionally substituted with one or more, particularly one to three, more particularly one or two substituents R^{1a}, halo(C_1-C_6)alkoxy optionally substituted with one or more, particularly one to

R^3 is hydrogen, halogen, cyano, amino, (C_1-C_6)alkyl, (C_1-C_6)alkoxy, halo(C_1-C_6)alkyl, halo(C_1-C_6)alkoxy, (C_3-C_6)cycloalkyl optionally substituted with one or more, particularly one to three, more particularly one or two substituents R^{3a}, (C_3-C_6)cycloalkyl-(C_1-C_6)alkyl optionally substituted with one or more, particularly one to three, more particularly one or two substituents R^{3b}, (C_3-C_6)cycloalkyl-(C_1-C_6)alkoxy optionally substituted with one or more, particularly one to three, more particularly one or two substituents R^{3c}, heterocycloalkyl optionally substituted with one or more, particularly one to three, more particularly one or two substituents R^{3d} or phenyl optionally substituted with one or more, particularly one to three, more particularly one or two substituents R^{3e};

R^{3a}, R^{3b}, R^{3c}, R^{3d} and R^{3e} are each independently selected from halogen, (C_1-C_6)alkyl, (C_1-C_6)alkoxy, halo(C_1-C_6)alkyl and halo(C_1-C_6)alkoxy;

R^4 is hydrogen, cyano, hydroxy, halogen, amino, (C_1-C_6)alkyl, (C_1-C_6)alkoxy, halo(C_1-C_6)alkyl, halo(C_1-C_6)alkoxy, (C_1-C_6)alkoxy-(C_1-C_6)alkyl, (C_3-C_6)cycloalkyl, (C_3-C_6)cycloalkyl-(C_1-C_6)alkyl, (C_3-C_6)cycloalkyl optionally substituted with one or more, particularly one to three, more particularly one or two substituents R^{4a}, (C_3-C_6)cycloalkyl-(C_1-C_6)alkyl optionally substituted with one or more, particularly one to three, more particularly one or two substituents R^{4b}, (C_3-C_6)cycloalkyl-(C_1-C_6)alkoxy optionally substituted with one or more, particularly one to three, more particularly one or two substituents R^{4c}, heterocycloalkyl optionally substituted with one or more, particularly one to three, more particularly one or two substituents R^{4d}, $-CO_2R^{4a}$ or $-CONR^{4b}R^{4c}$;

R^{4a}, R^{4b}, R^{4c} and R^{4d} are each independently selected from hydrogen and (C_1-C_6)alkyl;

R^5 is $–NH_2$ or oxo;

and pharmaceutically acceptable salts thereof.

In particular, the present ~~invention~~disclosure relates to compounds of formula I or II:

C_6)alkyl, (C_3-C_6)cycloalkyl optionally substituted with one or more, particularly one to three, more particularly one or two substituents R^{4a}, (C_3-C_6)cycloalkyl-(C_1-C_6)alkyl optionally substituted with one or more, particularly one to three, more particularly one or two substituents R^{4b}, (C_3-C_6)cycloalkyl-(C_1-C_6)alkoxy optionally substituted with one or more, particularly one to three, more particularly one or two substituents R^{4c}, heterocycloalkyl optionally substituted with one or more, particularly one to three, more particularly one or two substituents R^{4d}, $-CO_2R^{4a}$ or $-CONR^{4b}R^{4c}$;

R^{4a}, R^{4b}, R^{4c} and R^{4d} are each independently selected from hydrogen and (C_1-C_6)alkyl;

R^5 is $–NH_2$ or oxo;

and pharmaceutically acceptable salts thereof.

In another aspect, the present disclosure relates to a compound as described herein for use as therapeutically active substance.

In another aspect, the present disclosure relates to pharmaceutical compositions comprising compounds of formula I or II as described herein or their pharmaceutically acceptable salts and one or more pharmaceutically acceptable excipients.

In another aspect, the present disclosure relates to compounds of formula I or II as described herein or their pharmaceutically acceptable salts above for use as therapeutically active substances.

In another aspect, the present disclosure relates to compounds of formula I or II as described herein or their pharmaceutically acceptable salts for the use in the treatment, prevention and/or delay of progression of Lung Aenocarcinoma, Melanoma, Pancreatic Adenocarcinoma, Head and Neck Squamous Cell Carcinoma, Lung Squamous Cell Carcinoma, Esophageal Carcinoma, Glioblastmoa Multiforme, and Mesothelioma.

In another aspect, the present disclosure relates to use of compounds of formula I as described herein or their pharmaceutically acceptable salts in the preparation of a medicament for the treatment or prevention of Lung Aenocarcinoma, Melanoma, Pancreatic Adenocarcinoma, Head and Neck Squamous Cell Carcinoma, Lung Squamous Cell Carcinoma, Esophageal Carcinoma, Glioblastmoa Multiforme, and Mesothelioma.

Unless otherwise defined, all technical and scientific terms used herein have the same meaning as commonly understood by one of ordinary skill in the art to which this invention belongs. Although methods and materials similar or equivalent to those described herein can be used in the practice or testing of the invention, suitable methods and materials are described below.

All publications, patent applications, patents, and other references mentioned herein are incorporated by reference in their entirety.

The nomenclature used in this application is based on IUPAC systematic nomenclature, unless indicated otherwise.

Any open valency appearing on a carbon, oxygen, sulfur or nitrogen atom in the structures herein indicates the presence of a hydrogen, unless indicated otherwise.

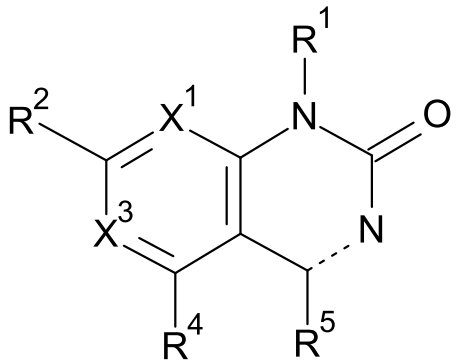
When indicating the number of substituents, the term “one or more” refers to the range from one substituent to the highest possible number of substitution, i.e. replacement of one hydrogen up to replacement of all hydrogens by substituents, in particular wherein “one or more” refers to one, two or three, most particularly “one or more” refers to one or two.

The term “substituent” denotes an atom or a group of atoms replacing a hydrogen atom on the parent molecule.

The term “substituted” denotes that a specified group bears one or more substituents. Where any group can carry multiple substituents and a variety of possible substituents is

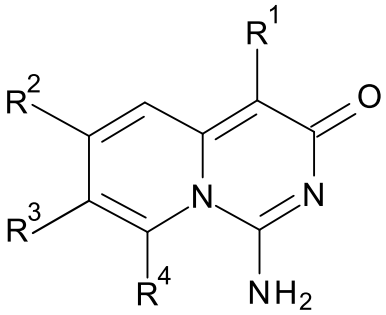
Claims

1. A compound of formula I or II:



(I)

or



(II)

wherein

X^1 is either N or CH;

X^3 is either N or CR^3;

the dotted line represents a single bond when R^5 is oxo or a double bond when R^5 is $-NH_2$,

R^1 is (C_1-C_6)alkyl optionally substituted with one or more, particularly one to three, more particularly one or two substituents R^{1a}, (C_1-C_6)alkoxy optionally substituted with one or more, particularly one to three, more particularly one or two substituents R^{1b}, halo(C_1-C_6)alkyl optionally substituted with one or more, particularly one to three, more particularly one or two substituents R^{1a}, halo(C_1-C_6)alkoxy optionally substituted with one or more, particularly one to three, more particularly one or two substituents R^{1b}, (C_3-C_8)cycloalkyl optionally substituted with one or more, particularly one to three, more particularly one or two substituents R^{1c}, heteroaryl optionally substituted with one or more, particularly one to three, more particularly one or two substituents R^{1d}, heterocycloalkyl optionally substituted with one or more, particularly one to three, more particularly one or two substituents R^{1e} or phenyl optionally substituted with one or more, particularly one to three, more particularly one or two substituents R^{1f} ;

R^{1a} and R^{1b} are each independently selected from (C_3-C_6)cycloalkyl, hydroxyl, heteroaryl, heterocycloalkyl and phenyl, wherein heteroaryl, heterocycloalkyl or phenyl

are optionally substituted with one or more, particularly one to three, more particularly one or two substituents R^{1g};

R^{1c}, R^{1d}, R^{1e} and R^{1f} are each independently selected from halogen, oxo, cyano, hydroxyl, $(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$alkoxy, $(C_3$-$C_6)$cycloalkyl, $(C_3$-$C_6)$cycloalkyl-$(C_1$-$C_6)$alkyl, halo$(C_1$-$C_6)$alkyl, halo$(C_1$-$C_6)$alkoxy, hydroxy$(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$alkoxy-$(C_1$-$C_6)$alkyl, heteroaryl, heterocycloalkyl and phenyl;

R^{1g} are each independently selected from halogen, cyano, hydroxyl, $(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$alkoxy, $(C_3$-$C_6)$cycloalkyl, $(C_3$-$C_6)$cycloalkyl-$(C_1$-$C_6)$alkyl, halo$(C_1$-$C_6)$alkyl, halo$(C_1$-$C_6)$alkoxy, hydroxy$(C_1$-$C_6)$alkyl and$(C_1$-$C_6)$alkoxy-$(C_1$-$C_6)$alkyl;

R^2 is hydrogen, halogen, amino, $(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$alkoxy, halo$(C_1$-$C_6)$alkyl, halo$(C_1$-$C_6)$alkoxy, $(C_3$-$C_6)$cycloalkyl optionally substituted with one or more, particularly one to three, more particularly one or two substituents R^{2a}, $(C_3$-$C_6)$cycloalkyl-$(C_1$-$C_6)$alkyl optionally substituted with one or more, particularly one to three, more particularly one or two substituents R^{2b}, $(C_3$-$C_6)$cycloalkyl-$(C_1$-$C_6)$alkoxy optionally substituted with one or more, particularly one to three, more particularly one or two substituents R^{2c}, heterocycloalkyl optionally substituted with one or more, particularly one to three, more particularly one or two substituents R^{2d} $NR^{2f}R^{2g}$ or phenyl optionally substituted with one or more, particularly one to three, more particularly one or two substituents R^{2e};

R^{2a}, R^{2b}, R^{2c}, R^{2d} and R^{2e} are each independently selected from halogen, $(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$alkoxy, halo$(C_1$-$C_6)$alkyl and halo$(C_1$-$C_6)$alkoxy;

R^{2f} and R^{2g} are each independently selected from hydrogen or $(C_1$-$C_6)$alkyl;

R^3 is hydrogen, halogen, cyano, amino, $(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$alkoxy, halo$(C_1$-$C_6)$alkyl, halo$(C_1$-$C_6)$alkoxy, $(C_3$-$C_6)$cycloalkyl optionally substituted with one or more, particularly one to three, more particularly one or two substituents R^{3a}, $(C_3$-$C_6)$cycloalkyl-$(C_1$-$C_6)$alkyl optionally substituted with one or more, particularly one to three, more particularly one or two substituents R^{3b}, $(C_3$-$C_6)$cycloalkyl-$(C_1$-$C_6)$alkoxy optionally substituted with one or more, particularly one to three, more particularly one or two substituents R^{3c}, heterocycloalkyl optionally substituted with one or more, particularly one to three, more particularly one or two substituents R^{3d} or phenyl optionally substituted with one or more, particularly one to three, more particularly one or two substituents R^{3e};

R^{3a}, R^{3b}, R^{3c}, R^{3d} and R^{3e} are each independently selected from halogen, (C_1-C_6)alkyl, (C_1-C_6)alkoxy, halo(C_1-C_6)alkyl and halo(C_1-C_6)alkoxy;

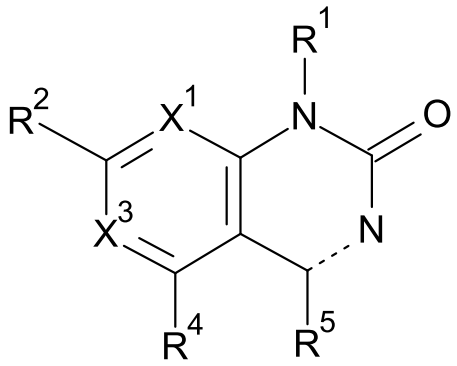
R^4 is hydrogen, cyano, hydroxy, halogen, amino, (C_1-C_6)alkyl, (C_1-C_6)alkoxy, halo(C_1-C_6)alkyl, halo(C_1-C_6)alkoxy, (C_1-C_6)alkoxy-(C_1-C_6)alkyl, (C_3-C_6)cycloalkyl, (C_3-C_6)cycloalkyl-(C_1-C_6)alkyl, (C_3-C_6)cycloalkyl optionally substituted with one or more, particularly one to three, more particularly one or two substituents R^{4a}, (C_3-C_6)cycloalkyl-(C_1-C_6)alkyl optionally substituted with one or more, particularly one to three, more particularly one or two substituents R^{4b}, (C_3-C_6)cycloalkyl-(C_1-C_6)alkoxy optionally substituted with one or more, particularly one to three, more particularly one or two substituents R^{4c}, heterocycloalkyl optionally substituted with one or more, particularly one to three, more particularly one or two substituents R^{4d}, $-CO_2R^{4a}$ or $-CONR^{4b}R^{4c}$;

R^{4a}, R^{4b}, R^{4c} and R^{4d}, R^{4e} are each independently selected from hydrogen and (C_1-C_6)alkyl,;

R^5 is $–NH_2$ or oxo;

and pharmaceutically acceptable salts thereof.

2. A compound according to claim 1, wherein the compound is of formula I:



(I)

~~or~~

wherein

X^1 is either N or CH;

X^3 is either N or CR^3;

the dotted line represents a single bond when R^5 is oxo or a double bond when R^5 is $-NH_2$,

R^1 is $(C_1$-$C_6)$alkyl optionally substituted with one or more, particularly one to three, more particularly one or two substituents R^{1a}, $(C_1$-$C_6)$alkoxy optionally substituted with one or more, particularly one to three, more particularly one or two substituents R^{1b}, $(C_3$-$C_8)$cycloalkyl optionally substituted with one or more, particularly one to three, more particularly one or two substituents R^{1c}, heteroaryl optionally substituted with one or more, particularly one to three, more particularly one or two substituents R^{1d}, heterocycloalkyl optionally substituted with one or more, particularly one to three, more particularly one or two substituents R^{1e} or phenyl optionally substituted with one or more, particularly one to three, more particularly one or two substituents R^{1f};

R^{1a} and R^{1b} are each independently selected from $(C_3$-$C_6)$cycloalkyl, hydroxyl, heteroaryl, heterocycloalkyl and phenyl, wherein heteroaryl, heterocycloalkyl or phenyl are optionally substituted with one or more, particularly one to three, more particularly one or two substituents R^{1g};

R^{1c}, R^{1d}, R^{1e} and R^{1f} are each independently selected from halogen, oxo, cyano, hydroxy, $(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$alkoxy, $(C_3$-$C_6)$cycloalkyl, $(C_3$-$C_6)$cycloalkyl-$(C_1$-$C_6)$alkyl, halo$(C_1$-$C_6)$alkyl, halo$(C_1$-$C_6)$alkoxy, hydroxy$(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$alkoxy-$(C_1$-$C_6)$alkyl, heteroaryl, heterocycloalkyl and phenyl;

R^{1g} are each independently selected from halogen, cyano, hydroxyl, $(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$alkoxy, $(C_3$-$C_6)$cycloalkyl, $(C_3$-$C_6)$cycloalkyl-$(C_1$-$C_6)$alkyl, halo$(C_1$-$C_6)$alkyl, halo$(C_1$-$C_6)$alkoxy, hydroxy$(C_1$-$C_6)$alkyl and $(C_1$-$C_6)$alkoxy-$(C_1$-$C_6)$alkyl;

R^2 is hydrogen, halogen, amino, $(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$alkoxy, halo$(C_1$-$C_6)$alkyl, halo$(C_1$-$C_6)$alkoxy, $(C_3$-$C_6)$cycloalkyl optionally substituted with one or more, particularly one to three, more particularly one or two substituents R^{2a}, $(C_3$-$C_6)$cycloalkyl-$(C_1$-$C_6)$alkyl optionally substituted with one or more, particularly one to three, more particularly one or two substituents R^{2b}, $(C_3$-$C_6)$cycloalkyl-$(C_1$-$C_6)$alkoxy optionally substituted with one or more, particularly one to three, more particularly one or two substituents R^{2c}, heterocycloalkyl optionally substituted with one or more, particularly one to three, more particularly one or two substituents R^{2d} or phenyl optionally substituted with one or more, particularly one to three, more particularly one or two substituents R^{2e};

R^{2a}, R^{2b}, R^{2c}, R^{2d} and R^{2e} are each independently selected from halogen, $(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$alkoxy, halo$(C_1$-$C_6)$alkyl and halo$(C_1$-$C_6)$alkoxy;

R^3 is hydrogen, halogen, cyano, amino, (C_1-C_6)alkyl, (C_1-C_6)alkoxy, halo(C_1-C_6)alkyl, halo(C_1-C_6)alkoxy, (C_3-C_6)cycloalkyl optionally substituted with one or more, particularly one to three, more particularly one or two substituents R^{3a}, (C_3-C_6)cycloalkyl-(C_1-C_6)alkyl optionally substituted with one or more, particularly one to three, more particularly one or two substituents R^{3b}, (C_3-C_6)cycloalkyl-(C_1-C_6)alkoxy optionally substituted with one or more, particularly one to three, more particularly one or two substituents R^{3c}, heterocycloalkyl optionally substituted with one or more, particularly one to three, more particularly one or two substituents R^{3d} or phenyl optionally substituted with one or more, particularly one to three, more particularly one or two substituents R^{3e};

R^{3a}, R^{3b}, R^{3c}, R^{3d} and R^{3e} are each independently selected from halogen, (C_1-C_6)alkyl, (C_1-C_6)alkoxy, halo(C_1-C_6)alkyl and halo(C_1-C_6)alkoxy;

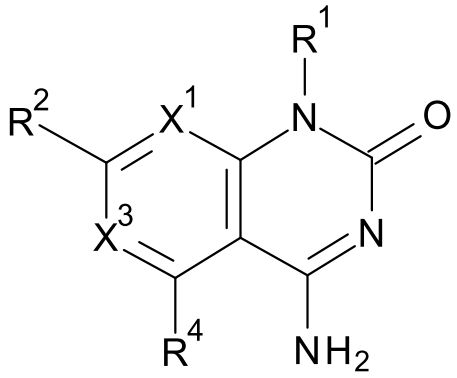
R^4 is hydrogen, cyano, hydroxy, halogen, amino, (C_1-C_6)alkyl, (C_1-C_6)alkoxy, halo(C_1-C_6)alkyl, halo(C_1-C_6)alkoxy, (C_1-C_6)alkoxy-(C_1-C_6)alkyl, (C_3-C_6)cycloalkyl, (C_3-C_6)cycloalkyl-(C_1-C_6)alkyl, (C_3-C_6)cycloalkyl optionally substituted with one or more, particularly one to three, more particularly one or two substituents R^{4a}, (C_3-C_6)cycloalkyl-(C_1-C_6)alkyl optionally substituted with one or more, particularly one to three, more particularly one or two substituents R^{4b}, (C_3-C_6)cycloalkyl-(C_1-C_6)alkoxy optionally substituted with one or more, particularly one to three, more particularly one or two substituents R^{4c}, heterocycloalkyl optionally substituted with one or more, particularly one to three, more particularly one or two substituents R^{4d}, phenyl optionally substituted with one or more R^{4e}, -CO_2R^{4a}, -$CONR^{4b}R^{4c}$, -SO_2R^{4d}, -SOR^{4e}, –SR^{4f} or $SO(NR^{4h})R^{4g}$

R^{4a}, R^{4b}, R^{4c}, R^{4d}, R^{4e}. R^{4f}, R^{4g} and R^{4h} are each independently selected from hydrogen and (C_1-C_6)alkyl;

R^5 is $–NH_2$ or oxo;

and pharmaceutically acceptable salts thereof.

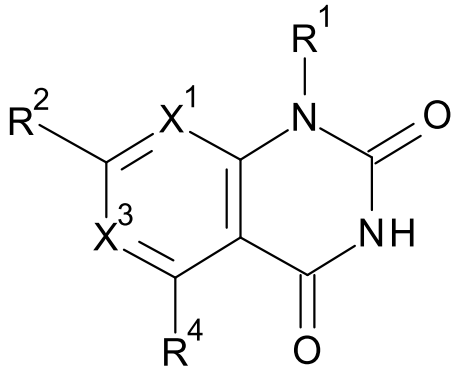
3. The compound according to claim 1 or 2, wherein the compound is of formula I':



(I')

wherein X^1, X^3, R^1, R^2 and R^4 are as defined according to claim 1 or 2.

4. The compound according to claim 1 or 2, wherein the compound is of formula I":



(I")

wherein X^1, X^3, R^1, R^2 and R^4 are as defined according to claim 1 or 2.

5. The compound according to any one of claims 1 to 4, wherein X^3 is CR^3.

6. The compound according to any one of claims 1 to 5, wherein X^1 is N.

7. The compound according to any one of claims 1 to 6, wherein R^1 is $(C_1\text{-}C_6)$alkyl optionally substituted with one R^{1a}, $(C_3\text{-}C_6)$cycloalkyl optionally substituted with one R^{1c}, heteroaryl optionally substituted with one or two R^{1d}, heterocycloalkyl optionally substituted with one R^{1e} or phenyl optionally substituted with one or two R^{1f}.

8. The compound according to any one of claims 1 to 7, wherein R^1 is $(C_1\text{-}C_3)$alkyl optionally substituted with one R^{1a}, $(C_3\text{-}C_6)$cycloalkyl optionally substituted with one R^{1c}, pyrazolyl optionally substituted with one R^{1d}, indazolyl optionally substituted with one R^{1d}, indolyl optionally substituted with one R^{1d}, benzo[d]oxazolyl optionally

substituted with one R^{1d}, benzo[d]thiazolyl optionally substituted with one R^{1d}, benzo[d]imidazolyl optionally substituted with one R^{1d}, dioxepanyl optionally substituted with one R^{1d}, oxazolyl optionally substituted with one R^{1d}, thiazolyl optionally substituted with one R^{1d}, pyridinyl optionally substituted with one or two R^{1d}, pyrimidinyl optionally substituted with one R^{1d}, dihydropyrrolo[1,2-c]imidazolyl optionally substituted with one R^{1e}, oxepanyl optionally substituted with one R^{1e}, dihydro-indolyl optionally substituted with one R^{1e}, 1,4-dioxepanyl optionally substituted with one R^{1e}, tetrahydrofuranyl optionally substituted with one R^{1e}, tetrahydropyranyl optionally substituted with one R^{1e}, piperidinyl optionally substituted with one R^{1e}, oxaspiro[2.5]octanyl optionally substituted with one R^{1e}, dihydrobenzofuranyl optionally substituted with one R^{1e} or phenyl optionally substituted with one or two R^{1f}.

9. The compound according to any one of claims 1 to 8,wherein R^1 is $(C_1\text{-}C_3)$alkyl optionally substituted by R^{1a}, cyclopentyl optionally substituted with one R^{1c}, indazol-4-yl, pyrazolyl optionally substituted with one R^{1d}, oxazolyl optionally substituted with one R^{1d}, thiazolyl optionally substituted with one R^{1d}, pyridinyl optionally substituted with one or two R^{1d}, pyrimidinyl optionally substituted with one R^{1d}, oxepanyl, tetrahydrofuranyl, tetrahydropyranyl, piperidinyl optionally substituted with one R^{1e}, oxaspiro[2.5]octanyl, 2,3-dihydrobenzofuranyl or phenyl optionally substituted with one or two R^{1f}.

10. The compound according to any one of claims 1 to 7, wherein R^1 is $(C_1\text{-}C_3)$alkyl optionally substituted by R^{1a}, cyclopentyl optionally substituted with one R^{1c}, pyrazolyl optionally substituted with one R^{1d}, oxazolyl optionally substituted with one R^{1d}, thiazolyl optionally substituted with one R^{1d}, pyridinyl optionally substituted with one or two R^{1d}, pyrimidinyl optionally substituted with one R^{1d}, tetrahydrofuranyl, tetrahydropyranyl, piperidinyl optionally substituted with one R^{1e}, oxaspiro[2.5]octanyl, 2,3-dihydrobenzofuranyl or phenyl optionally substituted with one or two R^{1f}.

11. The compound according to any one of claims 1 to 7, wherein R^1 is heteroaryl optionally substituted with one or two R^{1d}, heterocycloalkyl optionally substituted with one R^{1e} or phenyl optionally substituted with one or two R^{1f}.

12. The compound according to any one of claims 1 to 11, wherein R^1 is pyridinyl optionally substituted with one or two R^{1d}, oxaspiro[2.5]octanyl, 2,3-dihydrobenzofuranyl, tetrahydropyrany optionally optionally substituted with one R^{1e} or phenyl optionally substituted with one or two R^{1f}.

13. The compound according to any one of claims 1 to 11, wherein R^1 is oxaspiro[2.5]octanyl or tetrahydropyranyl optionally substituted with one $(C_1\text{-}C_3)$alkyl.

14. The compound according to any one of claims 1 to 11, wherein R^1 is tetrahydropyranyl optionally substituted with one (C_1-C_3)alkyl in *alpha*.

15. The compound according to any one of claims 1 to 7, wherein R^1 is heteroaryl substituted with one or two R^{1d} wherein at least of one R^{1d} is substituted in *ortho*, heterocycloalkyl substituted with one R^{1e} substituted in *alpha* or phenyl substituted with one or two R^{1f} wherein at least of one R^{1f} is substituted in *ortho.*

16. The compound according to any one of claims 1 to 7, wherein R^1 is pyridinyl substituted with one or two R^{1d} wherein at least of one R^{1d} is substituted in *ortho*, tetrahydrofuranyl substituted with one R^{1e} substituted in *alpha*, tetrahydropyranyl substituted with one R^{1e} substituted in *alpha*, oxaspiro[2.5]octanyl or 2,3-dihydrobenzofuranyl substituted with one R^{1e}.

17. The compound according to any one of claims 1 to 7, wherein R^1 is tetrahydrofuranyl substituted with one R^{1e} substituted in *alpha*, tetrahydropyranyl substituted with one R^{1e} substituted in *alpha*, oxaspiro[2.5]octanyl or 2,3-dihydrobenzofuranyl substituted with one R^{1e}.

18. The compound according to any one of claims 1 to 7, wherein R^1 is tetrahydropyranyl substituted with one R^{1e} substituted in *alpha.*

19. The compound according to any one of claims 1 to 10, wherein R^{1a} and R^{1b} are each independently selected from heteroaryl, heterocycloalkyl and phenyl.

20. The compound according to any one of claims 1 to 10, wherein R^{1a} is selected from tetrahydrofuranyl, pyridinyl, oxetanyl or oxazolyl.

21. The compound according to any one of claims 1 to 18, wherein R^{1c}, R^{1d}, R^{1e} and R^{1f} are each independently selected from halogen, oxo, cyano, hydroxy, (C_1-C_6)alkyl, (C_1-C_6)alkoxy, halo(C_1-C_6)alkyl and halo(C_1-C_6)alkoxy.

22. The compound according to any one of claims 1 to 18, wherein R^{1c}, R^{1d}, R^{1e} and R^{1f} are each independently selected from chloro, fluoro, oxo, cyano, hydroxy, (C_1-C_3)alkyl, (C_1-C_3)alkoxy and halo(C_1-C_3)alkyl

23. The compound according to any one of claims 1 to 18, wherein R^{1c}, R^{1d}, R^{1e} and R^{1f} are each independently selected from cyano, cloro and (C_1-C_3)alkyl

24. The compound according to any one of claims 1 to 18, wherein wherein R^{1d} are each independently selected from cyano, chloro and methyl.

25. The compound according to any one of claims 1 to 12, wherein R^1 is 2,3-dihydrobenzofuranyl, 2-hydroxycyclopentyl, 3-hydroxycyclopentyl, 1-(tetrahydrofuran-2-yl)ethyl, 1-tetrahydrofuran-3-yl-ethyl, 1-pyridin-2-yl-ethyl, oxepan-3-yl, 1,4-dioxepan-6-yl, dihydro-1H-indol-4-yl, 1-(oxetan-3-yl)ethyl, 1-(oxazol-5-yl)ethyl, indazol-4-yl,

oxaspiro[2.5]octanyl, 4-methyloxazol-5-yl, 2-methoxy-phenyl, 3-methyl-phenyl, 2-methyl-phenyl, 3-fluoro-2-methoxyphenyl, 2-methylbenzonitrile, 2-methoxybenzonitrile, 2-ethoxybenzonitrile, 2-chlorophenyl, 3-chlorophenyl, 4-fluoro-2-methylphenyl, 3-fluoro-2-methylphenyl, 3-fluorophenyl, 2-fluorophenyl, 2,6-difluorophenyl, 2,3-dimethylphenyl, phenyl, 2,3-difluorophenyl, 2-fluoro-3-methylphenyl, 3-methoxyphenyl, 3,5-difluorophenyl, 3,4-difluorophenyl, 2-trifluoromethyl-phenyl, 3-(fluoromethyl)-2-methylphenyl, 3-ethylphenyl, 3-chloro-2-fluorophenyl, 2-chloro-5-fluorophenyl, 2-chloro-4-fluorophenyl, 2,3-dichlorophenyl, benzo[d]oxazol-4-yl, benzo[d]imidazolyl, benzo[d]thiazol-7-yl, 2-oxopiperidin-4-yl, 2-methylpyrazol-3-yl, 1-ethyl-1H-pyrazol-5-yl, 2-methylpyridin-3-yl, picolinonitrile, 2-methoxypyridin-3-yl, 2-(trifluoromethyl)pyridin-3-yl, 4-methylpyridin-3-yl, 4-fluoro-2-methoxypyridin-3-yl, indolyl, 2-chloropyridin-3-yl, 6-methoxypyridin-2-yl, 4-methylpyrimidin-5-yl, trifluoromethoxypyridin-2-yl, dihydrobenzofuranyl, tetrahydrofuranyl, 4-methyltetrahydrofuran-3-yl, methyl-tetrahydro-2H-pyran-3-yl, 6,7-dihydro-5H-pyrrolo[1,2-c]imidazol-7-yl, tetrahydro-2H-pyran-3-yl, tetrahydro-2H-pyran-4-yl or 4-methylthiazol-5-yl,

26. The compound according to any one of claims 1 to 12, wherein R^1 is 2,3-dihydrobenzofuranyl, 2-hydroxycyclopentyl, 3-hydroxycyclopentyl, 1-(tetrahydrofuran-2-yl)ethyl, 1-tetrahydrofuran-3-yl-ethyl, 1-pyridin-2-yl-ethyl, 1-(oxetan-3-yl)ethyl, 1-(oxazol-5-yl)ethyl, oxaspiro[2.5]octanyl, 4-methyloxazol-5-yl, 2-methoxy-phenyl, 3-methyl-phenyl, 2-methyl-phenyl, 3-fluoro-2-methoxyphenyl, 2-methylbenzonitrile, 2-methoxybenzonitrile, 2-ethoxybenzonitrile, 2-chlorophenyl, 4-fluoro-2-methylphenyl, 3-fluorophenyl, 2-fluorophenyl, 2,6-difluorophenyl, phenyl, 2,3-difluorophenyl, 3-methoxyphenyl, 3,5-difluorophenyl, 3-ethylphenyl, 2-oxopiperidin-4-yl, 2-methylpyrazol-3-yl, 1-ethyl-1H-pyrazol-5-yl, 2-methylpyridin-3-yl, picolinonitrile, 2-methoxypyridin-3-yl, 2-(trifluoromethyl)pyridin-3-yl, 4-methylpyridin-3-yl, 4-fluoro-2-methoxypyridin-3-yl, 2-chloropyridin-3-yl, 6-methoxypyridin-2-yl, 4-methylpyrimidin-5-yl, tetrahydrofuranyl, 4-methyltetrahydrofuran-3-yl, tetrahydro-2H-pyran-3-yl, tetrahydro-2H-pyran-4-yl or 4-methylthiazol-5-yl.

27. The compound according to any one of claims 1 to 12, wherein R^1 is 2,3-dihydrobenzofuranyl, oxaspiro[2.5]octanyl, oxepan-3-yl, 3-methyl-phenyl, 2-methyl-phenyl, 2-methylbenzonitrile, 2-chlorophenyl, phenyl, 2-methylpyridin-3-yl, 4-methylpyridin-3-yl, 4 2-chloropyridin-3-yl, methyl-tetrahydro-2H-pyran-3-yl or 4-methylpyrimidin-5-yl .

28. The compound according to any one of claims 1 to 12, wherein R^1 is is 2,3-dihydrobenzofuranyl, oxaspiro[2.5]octanyl, 3-methyl-phenyl, 2-methyl-phenyl, 2-methylbenzonitrile, 2-chlorophenyl, phenyl, 2-methylpyridin-3-yl, 4-methylpyridin-3-yl, 4 2-chloropyridin-3-yl or 4-methylpyrimidin-5-yl .

29. The compound according to any one of claims 1 to 28, wherein R^2 is hydrogen, halogen, amino , $(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$alkoxy, halo$(C_1$-$C_6)$alkyl, halo$(C_1$-$C_6)$alkoxy, $(C_3$-$C_6)$cycloalkyl optionally substituted with one or more, particularly one to three, more particularly one or two substituents R^{2a}, $(C_3$-$C_6)$cycloalkyl-$(C_1$-$C_6)$alkyl optionally substituted with one or more, particularly one to three, more particularly one or two substituents R^{2b}, $(C_3$-$C_6)$cycloalkyl-$(C_1$-$C_6)$alkoxy optionally substituted with one or more, particularly one to three, more particularly one or two substituents R^{2c}, heterocycloalkyl optionally substituted with one or more, particularly one to three, more particularly one or two substituents R^{2d} or phenyl optionally substituted with one or more, particularly one to three, more particularly one or two substituents R^{2e}; and R^{2a}, R^{2b} , R^{2c}, R^{2d} and R^{2e} are each independently selected from halogen, $(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$alkoxy, halo$(C_1$-$C_6)$alkyl and halo$(C_1$-$C_6)$alkoxy.

30. The compound according to any one of claims 1 to 29, wherein R^2 is halogen, $(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$alkoxy, halo$(C_1$-$C_6)$alkyl, halo$(C_1$-$C_6)$alkoxy, $(C_3$-$C_6)$cycloalkyl optionally substituted with one R^{2a}, $(C_3$-$C_6)$cycloalkyl-$(C_1$-$C_6)$alkoxy or heterocycloalkyl optionally substituted with one or two R^{2d} or phenyl.

31. The compound according to any one of claims 1 to 30, wherein R^2 is halogen, $(C_1$-$C_3)$alkyl, $(C_1$-$C_3)$alkoxy, halo$(C_1$-$C_3)$alkyl, halo$(C_1$-$C_3)$alkoxy, cyclopropyl optionally substituted with one R^{2a}, cyclobutyl optionally substituted with one R^{2a}, cyclopentyl optionally substituted with one R^{2a} (, $(C_3$-$C_6)$cycloalkyl-$(C_1$-$C_3)$alkoxy, 4,5-dihydrofuran-3-yl, 7-azabicyclo[2.2.1]heptan-7-yl, 3-azabicyclo[2.2.1]heptan-3-yl, tetrahydrofuranyl, tetrahydropyranyl or azetidinyl optionally substituted with one or two R^{2d} or phenyl.

32. The compound according to any one of claims 1 to 31, wherein R^2 is halogen, $(C_1$-$C_3)$alkyl, $(C_1$-$C_3)$alkoxy, halo$(C_1$-$C_3)$alkyl, halo$(C_1$-$C_3)$alkoxy, cyclopropyl optionally substituted by halogen or $(C_1$-$C_3)$alkyl, cyclobutyl, cyclopentyl, cyclopropyloxy, 4,5-dihydrofuran-3-yl, 7-azabicyclo[2.2.1]heptan-7-yl, 3-azabicyclo[2.2.1]heptan-3-yl, tetrahydrofuranyl, tetrahydropyranyl or azetidinyl optionally substituted by one or two $(C_1$-$C_3)$alkyl.

33. The compound according to any one of claims 1 to 32, wherein R^2 is (halo$(C_1$-$C_3)$alkyl, halo$(C_1$-$C_3)$alkoxy or cyclopropyl optionally substituted by halogen or $(C_1$-$C_3)$alkyl,.

34. The compound according to any one of claims 1 to 33, wherein R^2 is trifluoromethyl, difluoromethoxy, trifluoromethoxy or cyclopropyl.
35. The compound according to any one of claims 1 to 33, wherein R^{2a}, R^{2b}, R^{2c}, R^{2d} and R^{2e} are each independently selected from halogen and (C_1-C_6)alkyl.
36. The compound according to any one of claims 1 to 35, wherein R^{2a}, R^{2b}, R^{2c}, R^{2d} and R^{2e} are each independently selected from halogen and (C_1-C_3)alkyl.
37. The compound according to any one of claims 1 to 36, wherein R^{2a}, R^{2b}, R^{2c}, R^{2d} and R^{2e} are each independently selected from chloro, fluoro and methyl.
38. The compound according to any one of claims 1 to 33, wherein R^{2f} and R^{2g} are each independently selected from hydrogen or (C_1-C_3)alkyl, particularly wherein one of R^{2f} and R^{2g} is hydrogen while the other is (C_1-C_3)alkyl.
39. The compound according to any one of claims 1 to 37, wherein R^3 is hydrogen, halogen or cyano.
40. The compound according to any one of claims 1 to 39, wherein R^3 is hydrogen, chloro, fluoro or cyano.
41. The compound according to any one of claims 1 to 40, wherein R^3 is hydrogen.
42. The compound according to any one of claims 1 to 37, wherein R^{3a}, R^{3b}, R^{3c}, R^{3d} and R^{3e} are each independently selected from halogen and (C_1-C_3)alkyl.
43. The compound according to any one of claims 1 to 41, R^4 is hydrogen, cyano, halogen, (C_1-C_6)alkyl, (C_1-C_6)alkoxy or -$CONR^{4b}R^{4c}$.
44. The compound according to any one of claims 1 to 43, wherein R^4 is hydrogen, cyano, chloro, fluoro or (C_1-C_3)alkyl.
45. The compound according to any one of claims 1 to 44, wherein R^4 is hydrogen.
46. The compound according to any one of claims 1 to 43, wherein R^{4b} or R^{4c} are hydrogen.
47. The compound according to any one of claims 1 to 46, wherein, wherein R^5 is $–NH_2$.
48. The compound according to any one of claims 1 to 47, selected from the group consisting of:

4-amino-7-cyclopropyl-1-(o-tolyl)pyrido[2,3-d]pyrimidin-2(1H)-one

4-amino-7-cyclopropyl-1-(2-methoxyphenyl)pyrido[2,3-d]pyrimidin-2(1H)-one

4-amino-7-(tert-butyl)-1-(o-tolyl)pyrido[2,3-d]pyrimidin-2(1H)-one

4-amino-1-(2-methoxyphenyl)-7-phenylpyrido[2,3-d]pyrimidin-2(1H)-one

4-amino-7-(3,3-difluoroazetidin-1-yl)-1-(o-tolyl)pyrido[2,3-d]pyrimidin-2(1H)-one

4-amino-7-cyclopropyl-1-(tetrahydrofuran-3-yl)pyrido[2,3-d]pyrimidin-2(1H)-one

4-amino-7-cyclopropyl-1-(2-methylpyridin-3-yl)pyrido[2,3-d]pyrimidin-2(1H)-one

4-amino-7-cyclopropyl-1-(2-oxopiperidin-4-yl)pyrido[2,3-d]pyrimidin-2(1H)-one

4-amino-7-cyclopropyl-1-((cis)-2-methyltetrahydrofuran-3-yl)pyrido[2,3-d]pyrimidin-2(1H)-one

4-amino-7-cyclopropyl-1-(o-tolyl)pyrido[4,3-d]pyrimidin-2(1H)-one

4-amino-7-cyclopropyl-1-(2-methylpyridin-3-yl)quinazolin-2-one

4-amino-7-cyclopropyl-1-(2-methylphenyl)quinazolin-2-one

7-cyclopropyl-1-(2-methylphenyl)quinazoline-2,4-dione

4-amino-7-cyclopropyl-1-(o-tolyl)pyrimido[4,5-d]pyrimidin-2(1H)-one

7-cyclopropyl-1-(2-methylpyridin-3-yl)quinazoline-2,4-dione

4-amino-7-cyclopropyl-1-(2-methoxypyridin-3-yl)pyrido[2,3-d]pyrimidin-2(1H)-one

4-amino-7-cyclopropyl-6-fluoro-1-(2-methylpyridin-3-yl)pyrido[2,3-d]pyrimidin-2(1H)-one

7-cyclopropyl-1-(2-methylphenyl)pyrido[2,3-d]pyrimidine-2,4-dione

3-(4-amino-7-cyclopropyl-2-oxopyrido[2,3-d]pyrimidin-1(2H)-yl)picolinonitrile

4-amino-7-cyclopropyl-1-(oxan-3-yl)pyrido[2,3-d]pyrimidin-2-one

4-amino-7-cyclopropyl-1-[1-(oxolan-3-yl)ethyl]pyrido[2,3-d]pyrimidin-2-one

4-amino-7-cyclopropyl-1-(3-fluoro-2-methoxyphenyl)pyrido[2,3-d]pyrimidin-2(1H)-one

3-(4-amino-7-cyclopropyl-2-oxopyrido[2,3-d]pyrimidin-1(2H)-yl)-2-methylbenzonitrile

4-amino-1-(2-methylpyridin-3-yl)-7-propan-2-ylpyrido[2,3-d]pyrimidin-2-one

4-amino-7-cyclopropyl-1-(2,3-dihydrobenzofuran-4-yl)pyrido[2,3-d]pyrimidin-2(1H)-one

4-amino-6-chloro-7-cyclopropyl-1-(2-methylpyridin-3-yl)pyrido[2,3-d]pyrimidin-2(1H)-one

3-(4-amino-7-cyclopropyl-2-oxopyrido[2,3-d]pyrimidin-1(2H)-yl)-2-methoxybenzonitrile

3-(4-amino-7-cyclopropyl-2-oxopyrido[2,3-d]pyrimidin-1(2H)-yl)-2-ethoxybenzonitrile

4-amino-7-cyclopropyl-1-(1-(tetrahydrofuran-2-yl)ethyl)pyrido[2,3-d]pyrimidin-2(1H)-one

4-amino-1-(2-methylpyridin-3-yl)-7-(oxetan-3-yl)quinazolin-2(1H)-one

7-cyclopropyl-1-(2-methylpyridin-3-yl)pyrido[2,3-d]pyrimidine-2,4-dione

4-amino-7-((1RS,2RS)-2-methylcyclopropyl)-1-(2-methylpyridin-3-yl)pyrido[2,3-d]pyrimidin-2(1H)-one

4-amino-7-cyclopentyl-1-(2-methyl-3-pyridyl)pyrido[2,3-d]pyrimidin-2-one

4-amino-7-cyclopropyl-1-((1SR,2RS)-2-hydroxycyclopentyl)pyrido[2,3-d]pyrimidin-2(1H)-one

4-amino-2-cyclopentyl-7-(o-tolyl)pyrazolo[3,4-d]pyrimidin-6-one; formic acid

4-amino-7-cyclopentyl-1-(4-methylpyrimidin-5-yl)pyrido[2,3-d]pyrimidin-2-one

4-amino-7-cyclopropyl-1-(3-fluoro-2-methylphenyl)pyrido[2,3-d]pyrimidin-2(1H)-one

4-amino-7-cyclopropyl-1-[(3R)-oxan-3-yl]pyrido[2,3-d]pyrimidin-2-one

4-amino-7-cyclopropyl-1-[(3S)-oxan-3-yl]pyrido[2,3-d]pyrimidin-2-one

4-amino-7-cyclopropyl-1-(4-methyltetrahydrofuran-3-yl)pyrido[2,3-d]pyrimidin-2(1H)-one
4-amino-7-cyclopropyl-2-oxo-1-(o-tolyl)-1,2-dihydropyrido[2,3-d]pyrimidine-5-carboxamide
4-amino-1-(2-methoxy-3-pyridyl)-7-tetrahydropyran-2-yl-pyrido[2,3-d]pyrimidin-2-one
4-amino-7-[(1S,4R)-3-azabicyclo[2.2.1]heptan-3-yl]-1-(2-methylpyrazol-3-yl)pyrido[2,3-d]pyrimidin-2-one; formic acid
4-amino-1-(2-methylpyridin-3-yl)-7-(trifluoromethyl)quinazolin-2-one
4-amino-7-cyclopropyl-1-[rac-(2R,3S)-2-methyloxolan-3-yl]pyrido[2,3-d]pyrimidin-2-one
4-amino-7-cyclobutyl-1-(2-methyl-3-pyridyl)pyrido[2,3-d]pyrimidin-2-one; formic acid
4-amino-7-cyclopropyloxy-1-(2-methylpyridin-3-yl)quinazolin-2-one
4-amino-1-(2-methylpyridin-3-yl)-7-(trifluoromethyl)pyrido[2,3-d]pyrimidin-2(1H)-one
4-amino-7-(7-azabicyclo[2.2.1]heptan-7-yl)-1-(4-methylthiazol-5-yl)pyrido[2,3-d]pyrimidin-2-one; formic acid
4-amino-7-cyclopropyl-1-(3-hydroxycyclopentyl)pyrido[2,3-d]pyrimidin-2(1H)-one
4-amino-7-(difluoromethoxy)-1-(2-methylpyridin-3-yl)quinazolin-2(1H)-one
4-amino-7-(difluoromethyl)-1-(2-methylpyridin-3-yl)quinazolin-2(1H)-one
4-amino-7-[(1R,2S)-2-fluorocyclopropyl]-1-(2-methyl-3-pyridyl)pyrido[2,3-d]pyrimidin-2-one
4-amino-7-cyclopropyl-1-(2-methylpyridin-3-yl)-2-oxo-1,2-dihydropyrido[2,3-d]pyrimidine-6-carbonitrile
3-(4-amino-7-isopropyl-2-oxopyrido[2,3-d]pyrimidin-1(2H)-yl)-2-methoxybenzonitrile
4-amino-7-cyclopropyl-2-oxo-1-(o-tolyl)-1,2-dihydropyrido[2,3-d]pyrimidine-5-carbonitrile
4-amino-7-methoxy-1-(2-methylpyridin-3-yl)quinazolin-2(1H)-one
4-amino-1-(2-methylpyridin-3-yl)-7-(trifluoromethoxy)quinazolin-2(1H)-one
4-amino-7-(4,5-dihydrofuran-3-yl)-1-(2-methylpyridin-3-yl)pyrido[2,3-d]pyrimidin-2(1H)-one
4-amino-1-(2-methylpyridin-3-yl)-7-(tetrahydrofuran-3-yl)pyrido[2,3-d]pyrimidin-2(1H)-one
4-amino-7-cyclopropyl-1-(2-methylpyridin-3-yl)pyrido[2,3-d]pyrimidin-2-one
4-amino-7-cyclopropyl-1-(2-methylpyridin-3-yl)pyrido[2,3-d]pyrimidin-2-one
4-amino-7-cyclopropyl-1-(4-methylthiazol-5-yl)pyrido[2,3-d]pyrimidin-2-one
4-amino-7-cyclopropyl-1-(4-methylpyrimidin-5-yl)pyrido[2,3-d]pyrimidin-2(1H)-one
4-amino-7-cyclopropyl-1-(2-(trifluoromethyl)pyridin-3-yl)pyrido[2,3-d]pyrimidin-2(1H)-one
4-amino-7-cyclopropyl-1-(2-methylpyrazol-3-yl)pyrido[2,3-d]pyrimidin-2-one
4-amino-7-cyclopropyl-1-(2,3-dihydrobenzofuran-4-yl)quinazolin-2(1H)-one
(R)-4-amino-1-(tetrahydro-2H-pyran-3-yl)-7-(trifluoromethyl)quinazolin-2(1H)-one
4-amino-7-cyclopropyl-1-(4-methylpyridin-3-yl)pyrido[2,3-d]pyrimidin-2(1H)-one
4-amino-7-ethyl-1-(2-methylpyridin-3-yl)quinazolin-2(1H)-one

4-amino-7-[(1S,2R)-2-fluorocyclopropyl]-1-[(3R)-tetrahydropyran-3-yl]pyrido[2,3-d]pyrimidin-2-one

4-amino-7-cyclopropyl-1-(4-methyloxazol-5-yl)pyrido[2,3-d]pyrimidin-2-one

3-(4-amino-6-chloro-7-isopropyl-2-oxopyrido[2,3-d]pyrimidin-1(2H)-yl)-2-methoxybenzonitrile

4-amino-7-cyclopropyl-1-((R)-1-((S)-tetrahydrofuran-3-yl)ethyl)pyrido[2,3-d]pyrimidin-2(1H)-one

4-amino-7-cyclopropyl-1-((R)-1-((R)-tetrahydrofuran-3-yl)ethyl)pyrido[2,3-d]pyrimidin-2(1H)-one

4-amino-7-(2-fluoropropan-2-yl)-1-(2-methylpyridin-3-yl)quinazolin-2-one

4-amino-5-methoxy-1-(2-methylpyridin-3-yl)-7-(trifluoromethyl)quinazolin-2(1H)-one

4-amino-7-cyclopropyl-1-(4-fluoro-2-methoxypyridin-3-yl)pyrido[2,3-d]pyrimidin-2(1H)-one

4-amino-5-fluoro-1-(2-methylpyridin-3-yl)-7-(trifluoromethyl)quinazolin-2(1H)-one

4-amino-7-cyclopropyl-1-(1-ethyl-1H-pyrazol-5-yl)pyrido[2,3-d]pyrimidin-2(1H)-one

4-amino-7-chloro-1-(o-tolyl)pyrido[2,3-d]pyrimidin-2(1H)-one

4-amino-7-cyclopropyl-1-(2,3-dihydrobenzofuran-7-yl)pyrido[2,3-d]pyrimidin-2(1H)-one

1-amino-4-(2-methoxyphenyl)-6-(trifluoromethyl)-3H-pyrido[1,2-c]pyrimidin-3-one

4-amino-1-(2-chlorophenyl)-7-cyclopropylpyrido[2,3-d]pyrimidin-2-one

4-amino-7-cyclopropyl-1-[(1R)-1-[(3S)-oxolan-3-yl]ethyl]pyrido[2,3-d]pyrimidin-2-one

4-amino-7-cyclopropyl-1-[(1R)-1-[(3R)-oxolan-3-yl]ethyl]pyrido[2,3-d]pyrimidin-2-one

3-(4-amino-6-chloro-7-cyclopropyl-2-oxopyrido[2,3-d]pyrimidin-1(2H)-yl)-2-methoxybenzonitrile

4-amino-7-cyclopropyl-1-(4-oxaspiro[2.5]octan-8-yl)pyrido[2,3-d]pyrimidin-2(1H)-one

4-amino-6-chloro-7-cyclopropyl-1-(2-methoxypyridin-3-yl)pyrido[2,3-d]pyrimidin-2(1H)-one

4-amino-7-cyclopropyl-1-(4-fluoro-2-methylphenyl)pyrido[2,3-d]pyrimidin-2-one

4-amino-7-cyclopropyl-1-(3-ethylphenyl)pyrido[2,3-d]pyrimidin-2(1H)-one

4-amino-7-cyclopropyl-1-(m-tolyl)pyrido[2,3-d]pyrimidin-2(1H)-one

4-amino-7-cyclopropyl-1-(3,5-difluorophenyl)pyrido[2,3-d]pyrimidin-2(1H)-one

4-amino-7-cyclopropyl-1-(6-methoxypyridin-2-yl)pyrido[2,3-d]pyrimidin-2(1H)-one

4-amino-7-cyclopropyl-1-(3-methoxyphenyl)pyrido[2,3-d]pyrimidin-2(1H)-one

4-amino-7-cyclopropyl-1-(2,3-difluorophenyl)pyrido[2,3-d]pyrimidin-2(1H)-one

4-amino-7-cyclopropyl-1-phenylpyrido[2,3-d]pyrimidin-2(1H)-one

4-amino-7-cyclopropyl-1-(1-(oxazol-5-yl)ethyl)pyrido[2,3-d]pyrimidin-2(1H)-one

3-(4-amino-2-oxo-7-(trifluoromethyl)quinazolin-1(2H)-yl)-2-methylbenzonitrile

3-(4-amino-2-oxo-7-(trifluoromethyl)pyrido[2,3-d]pyrimidin-1(2H)-yl)-2-methylbenzonitrile

4-amino-7-cyclopropyl-1-(2,6-difluorophenyl)pyrido[2,3-d]pyrimidin-2(1H)-one

4-amino-7-cyclopropyl-1-(2-fluorophenyl)pyrido[2,3-d]pyrimidin-2(1H)-one

4-amino-7-cyclopropyl-1-(3-fluorophenyl)pyrido[2,3-d]pyrimidin-2(1H)-one

4-amino-7-cyclopropyl-1-[1-(oxetan-3-yl)ethyl]pyrido[2,3-d]pyrimidin-2-one

4-amino-7-(difluoromethoxy)-1-(2-methylphenyl)pyrido[2,3-d]pyrimidin-2-one

4-amino-7-cyclopropyl-1-(1-pyridin-2-ylethyl)pyrido[2,3-d]pyrimidin-2-one

4-amino-1-(2-methyl-3-pyridyl)-7-(2,2,2-trifluoroethyl)quinazolin-2-one hydrochloride

4-amino-7-cyclopropyl-1-(tetrahydro-2H-pyran-4-yl)pyrido[2,3-d]pyrimidin-2(1H)-one

4-amino-1-(2-chloropyridin-3-yl)-7-cyclopropylpyrido[2,3-d]pyrimidin-2(1H)-one

4-amino-2-cyclopentyl-7-(2-methyl-3-pyridyl)pyrazolo[3,4-d]pyrimidin-6-one

4-amino-5-chloro-1-(2-methylpyridin-3-yl)-7-(trifluoromethyl)quinazolin-2(1H)-one

4-amino-1-(3-fluoro-2-methylphenyl)-7-(trifluoromethyl)pyrido[2,3-d]pyrimidin-2(1H)-one

4-amino-7-cyclopropyl-1-(1H-indol-4-yl)pyrido[2,3-d]pyrimidin-2-one

4-amino-7-cyclopropyl-1-[6-(trifluoromethoxy)pyridin-2-yl]pyrido[2,3-d]pyrimidin-2-one

4-amino-1-(2,3-dihydrobenzofuran-4-yl)-7-(trifluoromethyl)pyrido[2,3-d]pyrimidin-2(1H)-one

4-amino-1-(3-chloro-2-fluorophenyl)-7-cyclopropylpyrido[2,3-d]pyrimidin-2-one

4-amino-1-(2,3-dihydro-1-benzofuran-4-yl)-7-(trifluoromethoxy)quinazolin-2-one

4-amino-1-(3-fluoro-2-methylphenyl)-7-(trifluoromethoxy)quinazolin-2-one

3-[4-amino-2-oxo-7-(trifluoromethoxy)quinazolin-1-yl]-2-methylbenzonitrile

4-amino-7-cyclopropyl-1-(2,3-dihydro-1H-indol-4-yl)pyrido[2,3-d]pyrimidin-2-one

4-amino-1-(2-chloro-5-fluorophenyl)-7-cyclopropylpyrido[2,3-d]pyrimidin-2-one

4-amino-1-(2-chloro-4-fluorophenyl)-7-cyclopropylpyrido[2,3-d]pyrimidin-2(1H)-one

4-amino-7-cyclopropyl-1-(2,5-difluorophenyl)pyrido[2,3-d]pyrimidin-2(1H)-one

4-amino-7-(ethylamino)-1-(o-tolyl)quinazolin-2-one

4-amino-1-(3-chlorophenyl)-7-cyclopropylpyrido[2,3-d]pyrimidin-2(1H)-one

3-(4-amino-7-cyclopropyl-2-oxopyrido[2,3-d]pyrimidin-1(2H)-yl)benzonitrile

4-amino-7-(difluoromethoxy)-1-(4-oxaspiro[2.5]octan-8-yl)quinazolin-2(1H)-one

1-amino-4-(2-chlorophenyl)-6-(trifluoromethyl)pyrido[1,2-c]pyrimidin-3-one

4-amino-1-(benzo[d]oxazol-4-yl)-7-cyclopropylpyrido[2,3-d]pyrimidin-2(1H)-one

4-amino-7-cyclopropyl-1-(3,4-difluorophenyl)pyrido[2,3-d]pyrimidin-2(1H)-one

3-(4-amino-7-cyclopropyl-2-oxopyrido[2,3-d]pyrimidin-1(2H)-yl)-2-methylbenzonitrile

3-(4-amino-7-cyclopropyl-2-oxopyrido[2,3-d]pyrimidin-1(2H)-yl)-2-methylbenzonitrile

4-amino-7-(difluoromethoxy)-1-(o-tolyl)quinazolin-2(1H)-one

3-(4-amino-7-cyclopropyl-2-oxopyrido[2,3-d]pyrimidin-1(2H)-yl)-2-chlorobenzonitrile

4-amino-7-cyclopropyl-1-[(8S)-4-oxaspiro[2.5]octan-8-yl]pyrido[2,3-d]pyrimidin-2-one

4-amino-7-cyclopropyl-1-[(8R)-4-oxaspiro[2.5]octan-8-yl]pyrido[2,3-d]pyrimidin-2-one

4-amino-1-(1H-benzo[d]imidazol-4-yl)-7-cyclopropylpyrido[2,3-d]pyrimidin-2(1H)-one

4-amino-7-cyclopropyl-1-(1H-indazol-4-yl)pyrido[2,3-d]pyrimidin-2(1H)-one

4-amino-7-cyclopropyl-1-(2,3-dimethylphenyl)pyrido[2,3-d]pyrimidin-2(1H)-one
4-amino-1-(2-chloropyridin-3-yl)-7-(difluoromethoxy)quinazolin-2(1H)-one
4-amino-1-(2-chloropyridin-3-yl)-7-cyclopropylpyrido[2,3-d]pyrimidin-2(1H)-one
4-amino-1-(2-chloropyridin-3-yl)-7-cyclopropylpyrido[2,3-d]pyrimidin-2(1H)-one
4-amino-7-(difluoromethoxy)-1-(m-tolyl)quinazolin-2(1H)-one
4-amino-7-(difluoromethoxy)-1-(2-fluoro-3-methylphenyl)quinazolin-2(1H)-one
4-amino-7-cyclopropyl-1-(2-(trifluoromethyl)phenyl)pyrido[2,3-d]pyrimidin-2(1H)-one
4-amino-7-cyclopropyl-1-(3-(fluoromethyl)-2-methylphenyl)pyrido[2,3-d]pyrimidin-2(1H)-one
4-amino-1-(2-chloro-3-methylphenyl)-7-cyclopropylpyrido[2,3-d]pyrimidin-2-one
4-amino-1-(3-chloro-2-methylphenyl)-7-cyclopropylpyrido[2,3-d]pyrimidin-2-one
4-amino-7-cyclopropyl-1-(2,3-dichlorophenyl)pyrido[2,3-d]pyrimidin-2(1H)-one
4-amino-7-cyclopropyl-1-(2-fluoro-3-methylphenyl)pyrido[2,3-d]pyrimidin-2(1H)-one
3-(4-amino-7-cyclopropyl-2-oxopyrido[2,3-d]pyrimidin-1(2H)-yl)-2-fluorobenzonitrile
(S)-4-amino-7-cyclopropyl-1-(oxepan-3-yl)pyrido[2,3-d]pyrimidin-2(1H)-one
(R)-4-amino-7-cyclopropyl-1-(oxepan-3-yl)pyrido[2,3-d]pyrimidin-2(1H)-one
4-amino-7-cyclopropyl-1-(3-hydroxy-2-methylphenyl)pyrido[2,3-d]pyrimidin-2(1H)-one
4-amino-7-(difluoromethoxy)-1-(3-fluoro-2-methylphenyl)quinazolin-2(1H)-one
4-amino-7-cyclopropyl-1-[rac-(2S,3S)-2-methyltetrahydropyran-3-yl]pyrido[2,3-d]pyrimidin-2-one
4-amino-1-(benzo[d]thiazol-7-yl)-7-cyclopropylpyrido[2,3-d]pyrimidin-2(1H)-one
4-amino-7-cyclopropyl-1-((2S,3R)-2-methyltetrahydro-2H-pyran-3-yl)pyrido[2,3-d]pyrimidin-2(1H)-one
4-amino-7-cyclopropyl-1-((2R,3S)-2-methyltetrahydro-2H-pyran-3-yl)pyrido[2,3-d]pyrimidin-2(1H)-one
(-)-4-amino-1-(2-chloro-3-fluorophenyl)-7-cyclopropylpyrido[2,3-d]pyrimidin-2(1H)-one
(+)-4-amino-1-(2-chloro-3-fluorophenyl)-7-cyclopropylpyrido[2,3-d]pyrimidin-2(1H)-one
(-)-4-amino-1-(2-chlorophenyl)-7-cyclopropylpyrido[2,3-d]pyrimidin-2(1H)-one
(+)-4-amino-1-(2-chlorophenyl)-7-cyclopropylpyrido[2,3-d]pyrimidin-2(1H)-one
4-amino-7-cyclopropyl-6-(difluoromethoxy)-1-(o-tolyl)pyrido[2,3-d]pyrimidin-2-one
4-amino-7-cyclopropyl-1-(6,7-dihydro-5H-pyrrolo[1,2-c]imidazol-7-yl)pyrido[2,3-d]pyrimidin-2-one;formic acid
4-(2-chlorophenyl)-6-cyclopropyl-1-imino-pyrido[1,2-c]pyrimidin-3-one;formic acid
4-amino-7-cyclopropyl-1-[2-(trifluoromethoxy)phenyl]pyrido[2,3-d]pyrimidin-2-one
4-amino-1-(2-chloro-3-pyridyl)-7-(trifluoromethoxy)quinazolin-2-one
4-amino-7-cyclopropyl-1-(6-(difluoromethoxy)pyridin-2-yl)pyrido[2,3-d]pyrimidin-2(1H)-one
4-amino-7-cyclopropyl-1-(1,4-dioxepan-6-yl)pyrido[2,3-d]pyrimidin-2-one
4-amino-7-cyclopropyl-1-(3-fluoro-2-methylphenyl)quinazolin-2-one

49. The compound according to any one of claims 1 to 47, selected from the group consisting of:

4-amino-7-cyclopropyl-1-(o-tolyl)pyrido[2,3-d]pyrimidin-2(1H)-one
4-amino-7-cyclopropyl-1-(2-methylpyridin-3-yl)pyrido[2,3-d]pyrimidin-2(1H)-one

3-(4-amino-7-cyclopropyl-2-oxopyrido[2,3-d]pyrimidin-1(2H)-yl)-2-methylbenzonitrile
4-amino-7-cyclopropyl-1-(2,3-dihydrobenzofuran-4-yl)pyrido[2,3-d]pyrimidin-2(1H)-one
4-amino-7-cyclopropyl-1-(3-fluoro-2-methylphenyl)pyrido[2,3-d]pyrimidin-2(1H)-one
4-amino-7-cyclopropyl-1-(oxan-3-yl)pyrido[2,3-d]pyrimidin-2-one
4-amino-7-(difluoromethoxy)-1-(2-methylpyridin-3-yl)quinazolin-2(1H)-one
4-amino-1-(2-methylpyridin-3-yl)-7-(trifluoromethoxy)quinazolin-2(1H)-one
4-amino-7-cyclopropyl-1-(2,3-dihydrobenzofuran-4-yl)quinazolin-2(1H)-one
4-amino-7-cyclopropyl-1-(2,3-dihydrobenzofuran-7-yl)pyrido[2,3-d]pyrimidin-2(1H)-one
4-amino-1-(2-chlorophenyl)-7-cyclopropylpyrido[2,3-d]pyrimidin-2-one
4-amino-7-cyclopropyl-1-(4-oxaspiro[2.5]octan-8-yl)pyrido[2,3-d]pyrimidin-2(1H)-one
4-amino-1-(2-chloropyridin-3-yl)-7-cyclopropylpyrido[2,3-d]pyrimidin-2(1H)-one
4-amino-7-(difluoromethoxy)-1-(2-methylphenyl)pyrido[2,3-d]pyrimidin-2-one
3-(4-amino-2-oxo-7-(trifluoromethyl)pyrido[2,3-d]pyrimidin-1(2H)-yl)-2-methylbenzonitrile
4-amino-7-cyclopropyl-1-(m-tolyl)pyrido[2,3-d]pyrimidin-2(1H)-one
4-amino-7-cyclopropyl-1-[(8S)-4-oxaspiro[2.5]octan-8-yl]pyrido[2,3-d]pyrimidin-2-one
4-amino-7-cyclopropyl-1-[(8R)-4-oxaspiro[2.5]octan-8-yl]pyrido[2,3-d]pyrimidin-2-one
(R)-4-amino-7-cyclopropyl-1-(oxepan-3-yl)pyrido[2,3-d]pyrimidin-2(1H)-one
4-amino-7-cyclopropyl-1-((2S,3R)-2-methyltetrahydro-2H-pyran-3-yl)pyrido[2,3-d]pyrimidin-2(1H)-one

50. A compound according to any one of claims 1 to 49 for use as a therapeutically active substance.
51. Pharmaceutical compositions comprising compounds of formula I or II according to any one of claims 1 to 49 or their pharmaceutically acceptable salts and one or more pharmaceutically acceptable excipients.
52. Compounds of formula I or II according to any one of claims 1 to 49 or their pharmaceutically acceptable salts above for use as therapeutically active substances.
53. Compounds of formula I or II according to any one of claims 1 to 49 or their pharmaceutically acceptable salts for the use in the treatment, prevention and/or delay of progression of Lung Aenocarcinoma, Melanoma, Pancreatic Adenocarcinoma, Head and Neck Squamous Cell Carcinoma, Lung Squamous Cell Carcinoma, Esophageal Carcinoma, Glioblastmoa Multiforme, and Mesothelioma.
54. Compounds for the use according to claim 53, ~~for the use~~ in the treatment, prevention and/or delay of progression of Lung Adenocarcinoma, Lung Squamous Carcinoma, Pancreatic Adenocarcinoma, Glioblastoma Multiforme, and Head and Neck Squamous Carcinoma.

~~55. A method for the treatment or prevention of Lung Aenocarcinoma, Melanoma, Pancreatic Adenocarcinoma, Head and Neck Squamous Cell Carcinoma, Lung Squamous Cell Carcinoma, Esophageal Carcinoma, Glioblastmoa Multiforme, and Mesothelioma, which method comprises administering compounds of formula I according to any one of claims 1 to 49 or their pharmaceutically acceptable salts as defined above to a subject.~~

~~56. A method according to claim 55 for the treatment or prevention of Lung Adenocarcinoma, Lung Squamous Carcinoma, Pancreatic Adenocarcinoma, Glioblastoma Multiforme, and Head and Neck Squamous Carcinoma.~~

~~57. The use of compounds of formula I according to any one of claims 1 to 49 or their pharmaceutically acceptable salts for the treatment, prevention and/or delay of progression of Lung Aenocarcinoma, Melanoma, Pancreatic Adenocarcinoma, Head and Neck Squamous Cell Carcinoma, Lung Squamous Cell Carcinoma, Esophageal Carcinoma, Glioblastmoa Multiforme, and Mesothelioma.~~

~~58. The use of compounds according to claim 57, for the treatment, prevention and/or delay of progression of Lung Adenocarcinoma, Lung Squamous Carcinoma, Pancreatic Adenocarcinoma, Glioblastoma Multiforme, and Head and Neck Squamous Carcinoma.~~

~~59.~~55. ~~The use~~Use of compounds of formula I according to any one of claims 1 to 49 or their pharmaceutically acceptable salts ~~for~~ in the preparation of ~~medicaments~~ a medicament for the treatment or prevention of Lung Aenocarcinoma, Melanoma, Pancreatic Adenocarcinoma, Head and Neck Squamous Cell Carcinoma, Lung Squamous Cell Carcinoma, Esophageal Carcinoma, Glioblastmoa Multiforme, and Mesothelioma.

~~60.~~56. The use of compounds according to claim ~~59~~ 55, wherein the medicament is for the treatment, prevention and/or delay of progression of Lung Adenocarcinoma, Lung Squamous Carcinoma, Pancreatic Adenocarcinoma, Glioblastoma Multiforme, and Head and Neck Squamous Carcinoma.