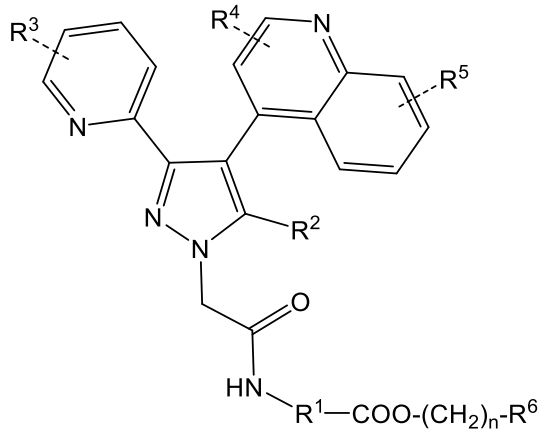
CLAIMS

1. A compound of formula (I):



(I)

wherein:

- R^1 represents a group selected from:

a) phenyl ring unsubstituted or substituted by 1 or 2 groups selected from halogen atom, linear or branched C_1-C_3 haloalkyl, linear or branched C_1-C_3 alkyl, linear or branched C_1-C_3 alkoxy, cyano group and hydroxy group,

b) 5- or 6-membered heteroaryl ring unsubstituted or substituted by 1 or 2 groups selected from halogen atom, linear or branched C_1-C_3 haloalkyl, linear or branched C_1-C_3 alkyl, linear or branched C_1-C_3 alkoxy, cyano group and hydroxy group,

- R^2 is a group selected from:

a) hydrogen atom,

b) linear or branched C_1-C_3 alkyl optionally substituted by 1, 2 or 3 halogen atoms,

- R^3 represents a group selected from:

a) hydrogen atom,

b) linear or branched C_1-C_3 alkyl optionally substituted by 1, 2 or 3 halogen atoms,

c) halogen atom,

- R^4 and R^5 represent independently a group selected from:

a) hydrogen atom,

b) linear or branched C_1-C_3 alkyl optionally substituted by 1, 2 or 3 halogen atoms,

c) halogen atom,

- n is an integer from 0 to 3,

- R^6 represents a group selected from the group consisting of:

a) $-N(R^7)(R^8)$, wherein R^7 and R^8 represent independently a linear or branched C_1-C_6 alkyl group or a hydrogen atom, and

b) saturated 4- to 10-membered, monocyclic or bicyclic, nitrogen-containing heterocyclyl optionally comprising another heteroatom selected from the group consisting of oxygen and nitrogen, said heterocyclyl being optionally substituted by a group selected from C_1-C_3 alkyl group,

and pharmaceutically acceptable salts thereof.

2. A compound according to claim 1 wherein R^2, R^4 and R^5 represent hydrogen atom.

3. A compound according to any one of claims 1 to 2 wherein R^3 represents methyl group.

4. A compound according to any one of claims 1 to 3 wherein R^1 represents a phenyl ring substituted by 1 or 2 halogen atoms.

5. A compound according to any one of claims 1 to 4 wherein n is an integer from 1 to 2 and R^6 represents a $-N(R^7)(R^8)$ group.

6. A compound according to claim 5 wherein R^7 and R^8 represent independently a group selected from linear C_1-C_3 alkyl group and hydrogen atom.

7. A compound according to any one of claims 1 to 4 wherein R^6 represents a saturated 6-membered heterocyclic group containing 1 or 2 nitrogen atoms, optionally substituted by a methyl group.

8. A compound according to claim 7 wherein R^6 represents a group selected from piperazinyl and piperidinyl group.

9. A compound according to claim 1 wherein R^2, R^4 and R^5 represent hydrogen atom, R^3 represents linear C_1-C_3 alkyl, R^1 represents a phenyl ring substituted by 1 or 2 halogen atoms, n is an integer from 0 to 2 and R^6 represents a group selected from the group consisting of:

a) $-N(R^7)(R^8)$, wherein R^7 and R^8 are selected from linear C_1-C_3 alkyl group and hydrogen atom,

b) a saturated 6-membered heterocyclic group containing 1 or 2 nitrogen atoms, optionally substituted by a methyl group, and

c) 1-aza-bicyclo[2.2.2]octanyl.

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

2-(dimethylamino)ethyl 3-fluoro-5-(2-(3-(6-methylpyridin-2-yl)-4-(quinolin-4-yl)-1*H*-pyrazol-1-yl)acetamido)benzoate;

2-(dimethylamino)ethyl 5-(2-(3-(6-methylpyridin-2-yl)-4-(quinolin-4-yl)-1*H*-pyrazol-1-yl)acetamido)nicotinate;

2-(dimethylamino)ethyl 6-(2-(3-(6-methylpyridin-2-yl)-4-(quinolin-4-yl)-1*H*-pyrazol-1-yl)acetamido)nicotinate;

2-morpholinoethyl 3-fluoro-5-(2-(3-(6-methylpyridin-2-yl)-4-(quinolin-4-yl)-1*H*-pyrazol-1-yl)acetamido)benzoate;

2-(dimethylamino)ethyl 5-(2-(3-(6-methylpyridin-2-yl)-4-(quinolin-4-yl)-1*H*-pyrazol-1-yl)acetamido)picolinate;

2-(4-methylpiperazin-1-yl)ethyl 3-fluoro-5-(2-(3-(6-methylpyridin-2-yl)-4-(quinolin-4-yl)-1*H*-pyrazol-1-yl)acetamido)benzoate;

2-(diethylamino)ethyl 3-fluoro-5-(2-(3-(6-methylpyridin-2-yl)-4-(quinolin-4-yl)-1*H*-pyrazol-1-yl)acetamido)benzoate;

1-methylpiperidin-4-yl 3-fluoro-5-(2-(3-(6-methylpyridin-2-yl)-4-(quinolin-4-yl)-1*H*-pyrazol-1-yl)acetamido)benzoate;

(1-methylpiperidin-4-yl)methyl 3-fluoro-5-(2-(3-(6-methylpyridin-2-yl)-4-(quinolin-4-yl)-1*H*-pyrazol-1-yl)acetamido)benzoate;

(*R*)-quinuclidin-3-yl 3-fluoro-5-(2-(3-(6-methylpyridin-2-yl)-4-(quinolin-4-yl)-1*H*-pyrazol-1-yl)acetamido)benzoate;

(*S*)-quinuclidin-3-yl 3-fluoro-5-(2-(3-(6-methylpyridin-2-yl)-4-(quinolin-4-yl)-1*H*-pyrazol-1-yl)acetamido)benzoate;

quinuclidin-4-yl 3-fluoro-5-(2-(3-(6-methylpyridin-2-yl)-4-(quinolin-4-yl)-1*H*-pyrazol-1-yl)acetamido)benzoate;

2-(azetidin-1-yl)ethyl 3-fluoro-5-(2-(3-(6-methylpyridin-2-yl)-4-(quinolin-4-yl)-1*H*-pyrazol-1-yl)acetamido)benzoate;

2-(aziridin-1-yl)ethyl 3-fluoro-5-(2-(3-(6-methylpyridin-2-yl)-4-(quinolin-4-yl)-1*H*-pyrazol-1-yl)acetamido)benzoate;

2-(methylamino)ethyl 3-fluoro-5-(2-(3-(6-methylpyridin-2-yl)-4-(quinolin-4-yl)-1*H*-pyrazol-1-yl)acetamido)benzoate;

2-aminoethyl 3-fluoro-5-(2-(3-(6-methylpyridin-2-yl)-4-(quinolin-4-yl)-1*H*-pyrazol-1-yl)acetamido)benzoate;

2-(ethylamino)ethyl 3-fluoro-5-(2-(3-(6-methylpyridin-2-yl)-4-(quinolin-4-yl)-1*H*-pyrazol-1-yl)acetamido)benzoate;

2-(isopropylamino)ethyl 3-fluoro-5-(2-(3-(6-methylpyridin-2-yl)-4-(quinolin-4-yl)-1*H*-pyrazol-1-yl)acetamido)benzoate;

2-(piperazin-1-yl)ethyl 3-fluoro-5-(2-(3-(6-methylpyridin-2-yl)-4-(quinolin-4-yl)-1*H*-pyrazol-1-yl)acetamido)benzoate;

piperidin-4-ylmethyl 3-fluoro-5-(2-(3-(6-methylpyridin-2-yl)-4-(quinolin-4-yl)-1*H*-pyrazol-1-yl)acetamido)benzoate; and

piperidin-4-yl 3-fluoro-5-(2-(3-(6-methylpyridin-2-yl)-4-(quinolin-4-yl)-1*H*-pyrazol-1-yl)acetamido)benzoate;

or a pharmaceutically acceptable salt thereof.

11. Use of compound according to any one of claims 1 to 10 in the manufacture of a medicament for the treatment of a disease or pathological condition that can be ameliorated by inhibition of transforming growth factor-β receptor I (TGFβRI)/ALK5, such as respiratory diseases such as pulmonary fibrosis, asthma, chronic obstructive pulmonary disease, adult respiratory distress syndrome, interstitial pulmonary fibrosis, pulmonary arterial hypertension and lung cancer; fibrotic skin diseases, such as scleroderma, nephrogenic fibrosing dermopathy, mixed connective tissue disease, scleromyxedema, scleroderma, and eosinophilic fasciitis; fibrotic eye diseases such as dry eyes, age-related macular degeneration, scarring in the cornea and conjunctiva, post-cataract fibrosis, proliferative vitreoretinopathy and proliferative diabetic retinopathy.

12. Use of compound according to any one of claims 1 to 10 in the manufacture of a medicament for administration to a mammal in the treatment of a respiratory disease selected from lung cancer, adult respiratory distress syndrome, idiopathic pulmonary fibrosis, interstitial pulmonary fibrosis, asthma, chronic obstructive pulmonary disease (COPD), and pulmonary arterial hypertension, wherein the administration is oral.

13. Use of compound according to claim 12 wherein oral administration is inhaled administration.

14. Compound of formula (I) as defined in any one of claims 1 to 10 for use as a medicament.

15. Compound of formula (I) as defined in any one of claims 1 to 10 for use in the treatment of a disease or pathological condition that can be ameliorated by inhibition of transforming growth factor-β receptor I (TGFβRI)/ALK5, such as respiratory diseases such as pulmonary fibrosis, asthma, chronic obstructive pulmonary disease, adult

respiratory distress syndrome, interstitial pulmonary fibrosis, pulmonary arterial hypertension and lung cancer; fibrotic skin diseases, such as scleroderma, nephrogenic fibrosing dermopathy, mixed connective tissue disease, scleromyxedema, scleroderma, and eosinophilic fasciitis; fibrotic eye diseases such as dry eyes, age-related macular degeneration, scarring in the cornea and conjunctiva, post-cataract fibrosis, proliferative vitreoretinopathy and proliferative diabetic retinopathy.

16. Compound for use according to claim 15 wherein the disease is selected from the group consisting of a respiratory disease selected from lung cancer, adult respiratory distress syndrome, idiopathic pulmonary fibrosis, interstitial pulmonary fibrosis, asthma, chronic obstructive pulmonary disease (COPD), and pulmonary arterial hypertension and wherein the administration is oral.

17. Compound for use according to claim 16 wherein oral administration is inhaled administration.

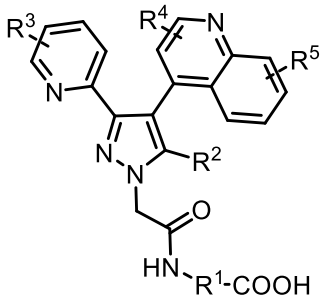
18. A pharmaceutical composition comprising a compound as defined in any one of claims 1 to 10 and a pharmaceutically acceptable diluent or carrier.

19. A pharmaceutical composition according to claim 16 further comprising a therapeutically effective amount of a therapeutic agent selected from agent useful for the treatment of disease or pathological condition that can be ameliorated by inhibition of transforming growth factor-β receptor I (TGFβRI)/ALK5, such as respiratory diseases such as pulmonary fibrosis, asthma, chronic obstructive pulmonary disease, adult respiratory distress syndrome, interstitial pulmonary fibrosis, pulmonary arterial hypertension and lung cancer; fibrotic skin diseases, such as scleroderma, nephrogenic fibrosing dermopathy, mixed connective tissue disease, scleromyxedema, scleroderma, and eosinophilic fasciitis; fibrotic eye diseases such as dry eyes, age-related macular degeneration, scarring in the cornea and conjunctiva, post-cataract fibrosis, proliferative vitreoretinopathy and proliferative diabetic retinopathy.

20. A combination product comprising a compound according to any one of claims 1 to 10 and at least a therapeutic agent selected from an agent useful for the treatment of disease or pathological condition that can be ameliorated by inhibition of transforming growth factor-β receptor I (TGFβRI)/ALK5, such as respiratory diseases such as pulmonary fibrosis, asthma, chronic obstructive pulmonary disease, adult respiratory distress syndrome, interstitial pulmonary fibrosis, pulmonary arterial hypertension and lung cancer; fibrotic skin diseases, such as scleroderma, nephrogenic fibrosing dermopathy, mixed connective tissue disease, scleromyxedema, scleroderma, and eosinophilic fasciitis; fibrotic eye diseases such as dry eyes, age-related macular

degeneration, scarring in the cornea and conjunctiva, post-cataract fibrosis, proliferative vitreoretinopathy and proliferative diabetic retinopathy.

21. A compound of formula (II):



(II)

or a salt thereof;

wherein R^1, R^2, R^3, R^4 and R^5 are as defined in any one of claims 1 to 10.

22. The compound according to claim 21 selected from the group consisting of:

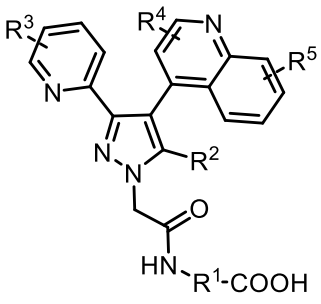
3-(2-(3-(6-methylpyridin-2-yl)-4-(quinolin-4-yl)-1H-pyrazol-1-yl)acetamido)-5-fluorobenzoic acid;

5-(2-(3-(6-methylpyridin-2-yl)-4-(quinolin-4-yl)-1H-pyrazol-1-yl)acetamido)picolinic acid; and

6-(2-(3-(6-methylpyridin-2-yl)-4-(quinolin-4-yl)-1H-pyrazol-1-yl)acetamido)pyridine-3-carboxylic acid;

or a salt thereof.

23. A process for the preparation of the compound of formula (I) or pharmaceutically acceptable salts thereof according to any one of claims 1 to 10 which comprises reacting a compound of formula (II):



(II)

or a salt thereof;

with a compound of formula (III):

$$OH\text{-}(CH_2)_n\text{-}R^6$$

(III)

or a salt thereof;

wherein n, R^1, R^2, R^3, R^4, R^5 and R^6 are as defined in any one of claims 1 to 10.