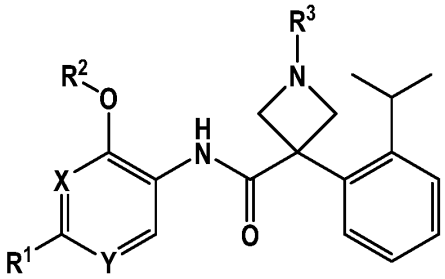
Claims

1. A compound of Formula (I):



Formula (I)

wherein

- **X** is CH; **Y** is N; and **R²** is methyl, ethyl, or isopropyl; or
- **X** is N; **Y** is CH; and **R²** is methyl, ethyl, or isopropyl, or difluoromethyl;

R¹ is fluoro, chloro, bromo, or methyl; and

R³ represents

- $-(CH_2)_{2\text{-}3}-C(CH_3)_2-COOH$;
- $-CO-(CH_2)_{1\text{-}2}-C(CH_3)_2-COOH$; or
- $-SO_2-NH_2$;

or a pharmaceutically acceptable salt thereof;

for combination use in the prevention or treatment of fibrotic diseases;

wherein said compound of formula (I) is to be administered in combination with one or more therapeutically active ingredients acting as anti-fibrotic agent(s); especially

- in combination with pirfenidone, or a pharmaceutically acceptable salt thereof;
- in combination with nintedanib, or a pharmaceutically acceptable salt thereof; or
- in combination with both pirfenidone, or a pharmaceutically acceptable salt thereof, and nintedanib, or a pharmaceutically acceptable salt thereof.

2. The compound of formula (I), or pharmaceutically acceptable salt thereof, for combination use according to claim 1, wherein **X** is CH; **Y** is N; and **R²** is methyl, ethyl, or isopropyl.

3. The compound of formula (I) for combination use according to claim 1 or 2, wherein **R¹** is fluoro, chloro, or bromo.

4. The compound of formula (I), or pharmaceutically acceptable salt thereof, for combination use according to claim 1, wherein **X** is N; **Y** is CH; and **R²** is difluoromethyl.

5. The compound of formula (I), or pharmaceutically acceptable salt thereof, for combination use according to claim 1 or 4, wherein R^1 is methyl.

6. The compound of formula (I), or pharmaceutically acceptable salt thereof, for combination use according to any one of claims 1 to 5, wherein R^3 represents

- $-CH_2-CH_2-C(CH_3)_2-COOH$;
- $-CO-CH_2-C(CH_3)_2-COOH$; or
- $-SO_2-NH_2$.

7. The compound of formula (I), or pharmaceutically acceptable salt thereof, for combination use according to any one of claims 1 to 3, wherein R^3 represents $-SO_2-NH_2$.

8. The compound of formula (I), or pharmaceutically acceptable salt thereof, for combination use according to claim 1, wherein the compound is

4-(3-((2-(difluoromethoxy)-6-methylpyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-2,2-dimethylbutanoic acid;

5-(3-((2-(difluoromethoxy)-6-methylpyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-2,2-dimethylpentanoic acid;

4-(3-((2-(difluoromethoxy)-6-methylpyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-2,2-dimethyl-4-oxobutanoic acid;

5-(3-((2-(difluoromethoxy)-6-methylpyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-2,2-dimethyl-5-oxopentanoic acid;

N-(2-(difluoromethoxy)-6-methylpyridin-3-yl)-3-(2-isopropylphenyl)-1-sulfamoylazetidine-3-carboxamide;

3-(2-isopropylphenyl)-N-(2-methoxy-6-methylpyridin-3-yl)-1-sulfamoylazetidine-3-carboxamide;

N-(2-ethoxy-6-methylpyridin-3-yl)-3-(2-isopropylphenyl)-1-sulfamoylazetidine-3-carboxamide;

N-(2-isopropoxy-6-methylpyridin-3-yl)-3-(2-isopropylphenyl)-1-sulfamoylazetidine-3-carboxamide;

4-(3-((6-chloro-4-methoxypyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-2,2-dimethylbutanoic acid;

4-(3-((6-chloro-4-ethoxypyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-2,2-dimethylbutanoic acid;

4-(3-((6-chloro-4-isopropoxypyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-2,2-dimethylbutanoic acid;

4-(3-((6-bromo-4-methoxypyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-2,2-dimethylbutanoic acid;

5-(3-((6-chloro-4-methoxypyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-2,2-dimethylpentanoic acid;

5-(3-((6-chloro-4-ethoxypyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-2,2-dimethylpentanoic acid;

4-(3-((6-chloro-4-methoxypyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-2,2-dimethyl-4-oxobutanoic acid;

4-(3-((6-bromo-4-methoxypyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-2,2-dimethyl-4-oxobutanoic acid;
4-(3-((6-chloro-4-ethoxypyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-2,2-dimethyl-4-oxobutanoic acid;
N-(6-fluoro-4-methoxypyridin-3-yl)-3-(2-isopropylphenyl)-1-sulfamoylazetidine-3-carboxamide;
N-(6-chloro-4-methoxypyridin-3-yl)-3-(2-isopropylphenyl)-1-sulfamoylazetidine-3-carboxamide;
N-(6-chloro-4-ethoxypyridin-3-yl)-3-(2-isopropylphenyl)-1-sulfamoylazetidine-3-carboxamide;
N-(6-chloro-4-isopropoxypyridin-3-yl)-3-(2-isopropylphenyl)-1-sulfamoylazetidine-3-carboxamide;
N-(6-bromo-4-methoxypyridin-3-yl)-3-(2-isopropylphenyl)-1-sulfamoylazetidine-3-carboxamide; or
3-(2-isopropylphenyl)-N-(4-methoxy-6-methylpyridin-3-yl)-1-sulfamoylazetidine-3-carboxamide;
or a pharmaceutically acceptable salt thereof.

9. The compound of formula (I) for combination use according to claim 1, wherein the compound is
4-(3-((2-(difluoromethoxy)-6-methylpyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-2,2-dimethylbutanoic acid;
4-(3-((2-(difluoromethoxy)-6-methylpyridin-3-yl)carbamoyl)-3-(2-isopropylphenyl)azetidin-1-yl)-2,2-dimethyl-4-oxobutanoic acid; or
N-(6-chloro-4-methoxypyridin-3-yl)-3-(2-isopropylphenyl)-1-sulfamoylazetidine-3-carboxamide;
or a pharmaceutically acceptable salt thereof.

10. The compound of formula (I), or a pharmaceutically acceptable salt thereof, for combination use according to any one of claims 1 to 9, wherein said compound of formula (I) is administered in combination with pirfenidone, or a pharmaceutically acceptable salt thereof.

11. The compound of formula (I), or a pharmaceutically acceptable salt thereof, for combination use according to claim 10, wherein pirfenidone, or a pharmaceutically acceptable salt thereof, is administered in a pharmaceutical unit dosage form suitable for the oral administration of a total of about 2403 mg per day or below.

12. The compound of formula (I), or a pharmaceutically acceptable salt thereof, for combination use according to any one of claims 1 to 11; wherein said combination use is for the prevention or treatment of

- pulmonary fibrosis; wherein notably said pulmonary fibrosis is selected from idiopathic pulmonary fibrosis, pulmonary fibrosis secondary to systemic inflammatory disease, pulmonary fibrosis secondary to sarcoidosis, iatrogenic pulmonary fibrosis, silicosis-induced pulmonary fibrosis, asbestos-induced pulmonary fibrosis, pleural fibrosis, and pulmonary fibrosis associated with COVID-19;
- renal fibrosis; wherein notably said renal fibrosis is selected from renal fibrosis associated with CKD, chronic renal failure, tubulointerstitial nephritis, and chronic nephropathies selected from primary glomerulonephritis and glomerulonephritis secondary to a systemic inflammatory disease, diabetes, focal segmental glomerular sclerosis, IgA nephropathy, hypertension, renal allograft, and Alport syndrome; or

- liver fibrosis; wherein notably said liver fibrosis is selected from cirrhosis, alcohol-induced liver fibrosis, nonalcoholic steatohepatitis, biliary duct injury, primary biliary cirrhosis, infection- or viral-induced liver fibrosis, and autoimmune hepatitis.

13. The compound of formula (I), or a pharmaceutically acceptable salt thereof, for combination use according to any one of claims 1 to 11; wherein said combination use is for the prevention or treatment of

- idiopathic pulmonary fibrosis;
- pulmonary fibrosis secondary to systemic inflammatory disease;
- pulmonary fibrosis secondary to sarcoidosis;
- radiation-induced fibrosis;
- silicosis-induced pulmonary fibrosis;
- asbestos-induced pulmonary fibrosis; or
- pulmonary fibrosis associated with COVID-19.

14. A pharmaceutical composition comprising, as active principles, a compound of formula (I) as defined in any one of claims 1 to 11, or a pharmaceutically acceptable salt thereof; in combination with one or more therapeutically active ingredients acting as anti-fibrotic agent(s); wherein said anti-fibrotic agent(s) is/are pirfenidone and/or nintedanib; or a pharmaceutically acceptable salt thereof; as well as at least one pharmaceutically acceptable excipient.

15. A method for the prophylaxis or treatment of

- pulmonary fibrosis; wherein notably said pulmonary fibrosis is selected from idiopathic pulmonary fibrosis; pulmonary fibrosis secondary to systemic inflammatory disease; pulmonary fibrosis secondary to sarcoidosis; iatrogenic pulmonary fibrosis; silicosis-induced pulmonary fibrosis; asbestos-induced pulmonary fibrosis; pleural fibrosis; and pulmonary fibrosis associated with COVID-19;
- renal fibrosis; wherein notably said renal fibrosis is selected from renal fibrosis associated with CKD, chronic renal failure, tubulointerstitial nephritis, and chronic nephropathies selected from primary glomerulonephritis and glomerulonephritis secondary to a systemic inflammatory disease, diabetes, focal segmental glomerular sclerosis, IgA nephropathy, hypertension, renal allograft, or Alport syndrome; or
- liver fibrosis; wherein notably said liver fibrosis is selected from cirrhosis, alcohol-induced liver fibrosis, nonalcoholic steatohepatitis, biliary duct injury, primary biliary cirrhosis, infection or viral-induced liver fibrosis, and autoimmune hepatitis;

said method comprising the administration of a pharmaceutically effective amount of a compound of formula (I) as defined in any one of claims 1 to 11, or of a pharmaceutically acceptable salt thereof; in combination with one or more therapeutically active ingredients acting as anti-fibrotic agent(s); wherein said anti-fibrotic agent(s) especially is/are pirfenidone and/or nintedanib; or a pharmaceutically acceptable salt thereof.