Claims

1. Use of a sGC stimulator or activator selected from the group comprising 2-[1-(2-fluorobenzyl)-1H-pyrazolo[3,4-b]pyridine-3-yl]-5-(4-morpholinyl)-4,6-pyrimidine-diamine (1), 2-[1-(2-fluorobenzyl)-1H-pyrazolo[3,4-b]pyridine-3-yl]-5-(4-pyridinyl)-4-pyrimidinamine (2), methyl-4,6-diamino-2-[1-(2-fluorobenzyl)-1H-pyrazolo[3,4-b]pyridine-3-yl]-5-pyrimidinyl(methyl)carbamate (3), methyl-4,6-diamino-2-[1-(2-fluorobenzyl)-1H-pyrazolo[3,4-b]pyridine-3-yl]-5-pyrimidinylcarbamate (4), 3-(4-amino-5-cyclopropylpyrimidine-2-yl)-1-(2-fluorobenzyl)1H-pyrazolo[3,4-b]pyridine (4a), 5-chloro-2-(5-chlorothiophene-2-sulfonylamino-N-(4-(morpholine-4-sulfonyl)-phenyl)-benzamide sodium salt (6), 2-(4-chloro-phenylsulfonylamino)-4,5-dimethoxy-N-(4-(thiomorpholine-4-sulfonyl)-phenyl)-benzamide (7), and/or 4-({(4-carboxybutyl)[2-(2-{[4-(2-phenylethyl) benzyl] oxy}phenyl)ethyl]amino}methyl) benzoic acid (5), 1-{6-[5-chloro-2-({4-trans-4-}trifluoromethyl)cyclohexyl]benzyl}oxy)phenyl] pyridin-2-yl}-5-(trifluoromethyl)-1H-pyrazole-4-carboxylic acid (8), 1-[6-(2-(2-methyl-4-(4-trifluoromethoxyphenyl)benzyloxy)-phenyl)pyridin-2-yl]-5-trifluoromethyl-pyrazole-4-carboxylic acid (9), 1[6-(3,4-dichlorophenyl)-2-pyridinyl-5-(trifluoromethyl)-1H-pyrazole-4-carboxylic acid (10), 1-({2-[3-chloro-5-(trifluoromethyl)phenyl]-5-methyl-1,3-thiazol-4-yl}methyl)-1H-pyrazole-4-carboxylic acid (11), 4-({2-[3-(trifluoromethyl)phenyl]-1,3-thiazol-4-yl}methyl)benzoic acid (12), 1-({2-[2-fluoro-3-(trifluoromethyl)phenyl]-5-methyl-1,3-thiazol-4-yl}methyl)-1H-pyrazole-4-carboxylic acid (13) for the manufacture of a medicament for the treatment of Cystic Fibrosis (CF).

2. Use of a sGC stimulator selected from the group comprising methyl-4,6-diamino-2-[1-(2-fluorobenzyl)-1H-pyrazolo[3,4-b]pyridine-3-yl]-5-pyrimidinyl-(methyl)carbamate (3), methyl-4,6-diamino-2-[1-(2-fluorobenzyl)-1H-pyrazolo[3,4-b]pyridine-3-yl]-5-pyrimidinylcarbamate (4), 3-(4-amino-5-cyclopropylpyrimidine-2-yl)-1-(2-fluorobenzyl)1H-pyrazolo[3,4-b]pyridine (4a) for the manufacture of a medicament for the treatment of Cystic Fibrosis (CF).

3. Use of methyl-4,6-diamino-2-[1-(2-fluorobenzyl)-1H-pyrazolo[3,4-b]pyridine-3-yl]-5-pyrimidinyl(methyl)carbamate (3) for the manufacture of a medicament for the treatment of Cystic Fibrosis (CF).

4. Use of 3-(4-amino-5-cyclopropylpyrimidine-2-yl)-1-(2-fluorobenzyl)1H-pyrazolo[3,4-b]pyridine (4a) for the manufacture of a medicament for the treatment of Cystic Fibrosis (CF).

5. Compounds according to claims 1 to 4 for the use in patients suffering from Cystic Fibrosis (CF).

6. Pharmaceutical formulation comprising at least one compound according to claims 1 to 4 for the use in patients suffering from Cystic Fibrosis (CF).

7. Combination of at least one sGC stimulator or activator selected from the group comprising 2-[1-(2-fluorobenzyl)-1H-pyrazolo[3,4-b]pyridine-3-yl]-5-(4-morpholinyl)-4,6-pyrimidinediamine (1), 2-[1-(2-fluorobenzyl)-1H-pyrazolo[3,4-b]pyridine-3-yl]-5-(4-pyridinyl)-4-pyrimidinamine (2), methyl-4,6-diamino-2-[1-(2-fluorobenzyl)-1H-pyrazolo[3,4-b]pyridine-3-yl]-5-pyrimidinyl(methyl)carbamate (3), methyl-4,6-diamino-2-[1-(2-fluorobenzyl)-1H-pyrazolo[3,4-b]pyridine-3-yl]-5-pyrimidinylcarbamate (4), 3-(4-amino-5-cyclopropylpyrimidine-2-yl)-1-(2-fluorobenzyl)1H-pyrazolo[3,4-b]pyridine (4a), 5-chloro-2-(5-chlorothiophene-2-sulfonylamino-N-(4-(morpholine-4-sulfonyl)-phenyl)-benzamide sodium salt (6), 2-(4-chloro-phenylsulfonylamino)-4,5-dimethoxy-N-(4-(thiomorpholine-4-sulfonyl)-phenyl)-benzamide (7), and/or 4-({(4-carboxybutyl)[2-(2-{[4-(2-phenylethyl) benzyl] oxy}phenyl)ethyl]amino}methyl) benzoic acid (5), 1-{6-[5-chloro-2-({4-trans-4-}trifluoromethyl)cyclohexyl]benzyl}oxy)phenyl] pyridin-2-yl}-5-(trifluoromethyl)-1H-pyrazole-4-carboxylic acid (8), 1-[6-(2-(2-methyl-4-(4-trifluoromethoxyphenyl)benzyloxy)-phenyl)pyridin-2-yl]-5-trifluoromethyl-pyrazole-4-carboxylic acid (9), 1[6-(3,4-dichlorophenyl)-2-pyridinyl-5-(trifluoromethyl)-1H-pyrazole-4-carboxylic acid (10), 1-({2-[3-chloro-5-(trifluoromethyl)phenyl]-5-methyl-1,3-thiazol-4-yl}methyl)-1H-pyrazole-4-carboxylic acid (11), 4-({2-[3-(trifluoromethyl)phenyl]-1,3-thiazol-4-yl}methyl)benzoic acid (12), 1-({2-[2-fluoro-3-(trifluoromethyl)phenyl]-5-methyl-1,3-thiazol-4-yl}methyl)-1H-pyrazole-4-carboxylic acid (13) with a PDE5 inhibitor selected form the group comprising Vardenafil, Sildenafil, Tadalafil, Udenafil, Dasantafil, Avanafil, Mirodenafil, Lodenafil, UK 369.003, UK 371.800, SLx2101 and LAS34179 in which the combination comprises 0.01 to 10 mg of the sGC stiumulator or activator and 2.5 to 20 mg of the PDE5 inhibitor.

8. Combination according to claim 7 in which the sGC stimulator is methyl-4,6-diamino-2-[1-(2-fluorobenzyl)-1H-pyrazolo[3,4-b]pyridine-3-yl]-5-pyrimidinyl-(methyl)carbamate (3) or methyl-4,6-diamino-2-[1-(2-fluorobenzyl)-1H-pyrazolo[3,4-b]pyridine-3-yl]-5-pyrimidinylcarbamate (4).

9. Combination according to claims 7 and 8 in which the PDE5 inhibitor is Vardenafil or Sildenafil.

10. Combination according to claims 7 to 9 for the use as a medicament.

11. Use of combination according to claims 7 to 10 for the manufacture of a medicament for the treatment of Cystic Fibrosis (CF).

12. Combination according to claims 7 to 10 for the use in patients suffering from Cystic Fibrosis (CF).

13. Pharmaceutical formulation comprising at least one combination according to claims 7 to 9.

14. Pharmaceutical formulation comprising at least one combination according to claims 7 to 9 for the use in patients suffering from Cystic Fibrosis (CF).

Claims

1. Use of a sGC stimulator or activator selected from the group comprising 2-[1-(2-fluorobenzyl)-1H-pyrazolo[3,4-b]pyridine-3-yl]-5-(4-morpholinyl)-4,6-pyrimidine-diamine (1), 2-[1-(2-fluorobenzyl)-1H-pyrazolo[3,4-b]pyridine-3-yl]-5-(4-pyridinyl)-4-pyrimidinamine (2), methyl-4,6-diamino-2-[1-(2-fluorobenzyl)-1H-pyrazolo[3,4-b]pyridine-3-yl]-5-pyrimidinyl(methyl)carbamate (3), methyl-4,6-diamino-2-[1-(2-fluorobenzyl)-1H-pyrazolo[3,4-b]pyridine-3-yl]-5-pyrimidinylcarbamate (4), 3-(4-amino-5-cyclopropylpyrimidine-2-yl)-1-(2-fluorobenzyl)1H-pyrazolo[3,4-b]pyridine (4a), 5-chloro-2-(5-chlorothiophene-2-sulfonylamino-N-(4-(morpholine-4-sulfonyl)-phenyl)-benzamide sodium salt (6), 2-(4-chloro-phenylsulfonylamino)-4,5-dimethoxy-N-(4-(thiomorpholine-4-sulfonyl)-phenyl)-benzamide (7), and/or 4-({(4-carboxybutyl)[2-(2-{[4-(2-phenylethyl) benzyl] oxy}phenyl)ethyl]amino}methyl) benzoic acid (5), 1-{6-[5-chloro-2-({4-trans-4-}trifluoromethyl)cyclohexyl]benzyl}oxy)phenyl] pyridin-2-yl}-5-(trifluoromethyl)-1H-pyrazole-4-carboxylic acid (8), 1-[6-(2-(2-methyl-4-(4-trifluoromethoxyphenyl)benzyloxy)-phenyl)pyridin-2-yl]-5-trifluoromethyl-pyrazole-4-carboxylic acid (9), 1[6-(3,4-dichlorophenyl)-2-pyridinyl-5-(trifluoromethyl)-1H-pyrazole-4-carboxylic acid (10), 1-({2-[3-chloro-5-(trifluoromethyl)phenyl]-5-methyl-1,3-thiazol-4-yl}methyl)-1H-pyrazole-4-carboxylic acid (11), 4-({2-[3-(trifluoromethyl)phenyl]-1,3-thiazol-4-yl}methyl)benzoic acid (12), 1-({2-[2-fluoro-3-(trifluoromethyl)phenyl]-5-methyl-1,3-thiazol-4-yl}methyl)-1H-pyrazole-4-carboxylic acid (13) for the manufacture of a medicament for the treatment of Cystic Fibrosis (CF).
2. Use according to claim 1 of a sGC stimulator selected from the group comprising methyl-4,6-diamino-2-[1-(2-fluorobenzyl)-1H-pyrazolo[3,4-b]pyridine-3-yl]-5-pyrimidinyl(methyl)carbamate (3), methyl-4,6-diamino-2-[1-(2-fluorobenzyl)-1H-pyrazolo[3,4-b]pyridine-3-yl]-5-pyrimidinylcarbamate (4), 3-(4-amino-5-cyclopropylpyrimidine-2-yl)-1-(2-fluorobenzyl)1H-pyrazolo[3,4-b]pyridine (4a) for the manufacture of a medicament for the treatment of Cystic Fibrosis (CF).
3. Use according to claims 1 and 2 of methyl-4,6-diamino-2-[1-(2-fluorobenzyl)-1H-pyrazolo[3,4-b]pyridine-3-yl]-5-pyrimidinyl(methyl)carbamate (3) for the manufacture of a medicament for the treatment of Cystic Fibrosis (CF).
4. Use according to claims 1 to 2
   of 3-(4-amino-5-cyclopropylpyrimidine-2-yl)-1-(2-fluorobenzyl)1H-pyrazolo[3,4-b]pyridine (4a) for the manufacture of a medicament

for the treatment of Cystic Fibrosis (CF).

5. Pharmaceutical formulation comprising at least one compound according to claims 1 to 4 for the use in patients suffering from Cystic Fibrosis (CF).

6. Combination of at least one sGC stimulator or activator selected from the group comprising 2-[1-(2-fluorobenzyl)-1H-pyrazolo[3,4-b]pyridine-3-yl]-5-(4-morpholinyl)-4,6-pyrimidinediamine (1), 2-[1-(2-fluorobenzyl)-1H-pyrazolo[3,4-b]pyridine-3-yl]-5-(4-pyridinyl)-4-pyrimidinamine (2), methyl-4,6-diamino-2-[1-(2-fluorobenzyl)-1H-pyrazolo[3,4-b]pyridine-3-yl]-5-pyrimidinyl(methyl)carbamate (3), methyl-4,6-diamino-2-[1-(2-fluorobenzyl)-1H-pyrazolo[3,4-b]pyridine-3-yl]-5-pyrimidinylcarbamate (4), 3-(4-amino-5-cyclopropylpyrimidine-2-yl)-1-(2-fluorobenzyl)1H-pyrazolo[3,4-b]pyridine (4a), 5-chloro-2-(5-chlorothiophene-2-sulfonylamino-N-(4-(morpholine-4-sulfonyl)-phenyl)-benzamide sodium salt (6), 2-(4-chloro-phenylsulfonylamino)-4,5-dimethoxy-N-(4-(thiomorpholine-4-sulfonyl)-phenyl)-benzamide (7), and/or 4-({(4-carboxybutyl)[2-(2-{[4-(2-phenylethyl) benzyl] oxy}phenyl)ethyl]amino}methyl) benzoic acid (5), 1-{6-[5-chloro-2-({4-trans-4-}trifluoromethyl)cyclohexyl]benzyl}oxy)phenyl] pyridin-2-yl}-5-(trifluoromethyl)-1H-pyrazole-4-carboxylic acid (8), 1-[6-(2-(2-methyl-4-(4-trifluoromethoxyphenyl)benzyloxy)-phenyl)pyridin-2-yl]-5-trifluoromethyl-pyrazole-4-carboxylic acid (9), 1[6-(3,4-dichlorophenyl)-2-pyridinyl-5-(trifluoromethyl)-1H-pyrazole-4-carboxylic acid (10), 1-({2-[3-chloro-5-(trifluoromethyl)phenyl]-5-methyl-1,3-thiazol-4-yl}methyl)-1H-pyrazole-4-carboxylic acid (11), 4-({2-[3-(trifluoromethyl)phenyl]-1,3-thiazol-4-yl}methyl)benzoic acid (12), 1-({2-[2-fluoro-3-(trifluoromethyl)phenyl]-5-methyl-1,3-thiazol-4-yl}methyl)-1H-pyrazole-4-carboxylic acid (13) with a PDE5 inhibitor selected form the group comprising Vardenafil, Sildenafil, Tadalafil, Udenafil, Dasantafil, Avanafil, Mirodenafil, Lodenafil, UK 369.003, UK 371.800, SLx2101 and LAS34179 in which the combination comprises 0.01 to 10 mg of the sGC stimulator or activator and 2.5 to 20 mg of the PDE5 inhibitor.

7. Combination according to claim 6 in which the sGC stimulator is methyl-4,6-diamino-2-[1-(2-fluorobenzyl)-1H-pyrazolo[3,4-b]pyridine-3-yl]-5-pyrimidinyl-(methyl)carbamate (3) or methyl-4,6-diamino-2-[1-(2-fluorobenzyl)-1H-pyrazolo[3,4-b]pyridine-3-yl]-5-pyrimidinylcarbamate (4).

8. Combination according to claims 6 and 7 in which the PDE5 inhibitor is Vardenafil or Sildenafil.

9. Combination according to claims 6 to 8 for the use as a medicament.

10. Use of combination according to claims 6 to 9 for the manufacture of a medicament for the treatment of Cystic Fibrosis (CF).

11. Combination according to claims 6 to 9 for the use in patients suffering from Cystic Fibrosis (CF).

12. Pharmaceutical formulation comprising at least one combination according to claims 6 to 8.