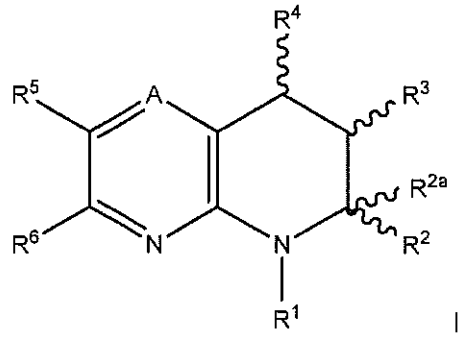
Claims

We Claim:

1. A compound represented by Formula Ia



Ia

or a pharmaceutically acceptable salt thereof, wherein

A is N or CR';

R' is H, C_1-C_8 alkyl optionally substituted by one or more halogen atoms;

R^1 is H, C_1-C_8 alkyl optionally substituted by one or more halogen atoms, C_1-C_4 alkyl, OH, OR', -$NR^{19}R^{21}$, CN or C_3-C_7 cycloalkyl; or

R^1 is -X-Y; or

R^1 is -W-R^7-X-Y; or

R^1 is –$S(O)_2$-W-X-Y; or

R^1 is –$S(O)_2$-W-R^7-X-Y;

R^2 is H, C_1-C_8 alkyl optionally substituted by one or more halogen atoms, C_1-C_4 alkyl, OH, OR', -$NR^{19}R^{21}$, CN or C_3-C_7 cycloalkyl; or

R^2 is -X-Y; or

R^2 is -W-R^7-X-Y; or

R^2 is –$S(O)_2$-W-X-Y;

R^2 is –$S(O)_2$-W-R^7-X-Y;

wherein either R^1 or R^2 is -X-Y, -W-R^7-X-Y, –$S(O)_2$-W-X-Y; or –$S(O)_2$-W-R^7-X-Y;

R^{2a} is hydrogen;

R^2 and R^{2a} together are oxo;

R^3 is H, C_1-C_4 alkoxy, OH, -$NR^{19}R^{21}$, CN, halogen, C_3-C_7 cycloalkyl or C_1-C_8 alkyl optionally substituted by one or more halogen atoms;

R^4 is H, C_1-C_4 alkoxy, OH, -$NR^{19}R^{21}$, CN, halogen, C_3-C_7 cycloalkyl or C_1-C_8 alkyl optionally substituted by one or more halogen atoms;

R^5 is C_1-C_8 alkyl optionally substituted by one or more halogen atoms, C_1-C_4 alkyl, OH, OR', -$NR^{19}R^{21}$, CN or C_3-C_7 cycloalkyl; C_1-C_8 alkoxy optionally substituted by one or more halogen atoms; C_6-C_{14} aryl; -(C_0-C_4 alkyl)-4 to 14 membered heteroaryl, or -(C_0-C_4 alkyl)-3 to 14 membered heterocyclyl wherein the heteroaryl and heterocyclyl contain at least one heteroatom selected from N, O and S, wherein the aryl, heteroaryl and heterocyclyl are each optionally substituted by one or more Z substituents;

R^6 is C_6-C_{14} aryl; -(C_0-C_4 alkyl)-4 to 14 membered heteroaryl, -(C_0-C_4 alkyl)-3 to 14 membered heterocyclyl wherein the heteroaryl and heterocyclyl contain at least one heteroatom selected from N, O and S, wherein the aryl, heteroaryl and heterocyclyl are each optionally substituted by one or more Z substituents;

W is C_1-C_8 alkylene optionally substituted by hydroxy, halogens or C_1-C_4 alkyl;

X is C_1-C_8 alkylene optionally substituted by hydroxy, halogens or C_1-C_4 alkyl;

Y is carboxy, alkoxycarbonyl, tetrazolyl, carbamoyl, monoalkylcarbamoyl, dialkylcarbamoyl, or -CONH-$S(O)_q$-R^x, wherein R^x is -C_1-C_4 alkyl or -$NR^{19}R^{21}$;

q is 0, 1 or 2;

R^7 is a divalent moiety represented by -O-, -NHC(O)-, -CH_2=CH_2-, -C_6-C_{14} aryl-D-; -3 to 14 membered heterocyclyl-D-, wherein the heterocyclyl contains at least one heteroatom selected from N, O and S, wherein D is O, S, NH or not present;

Z is independently OH, aryl, O-aryl, benzyl, O-benzyl, C_1-C_6 alkyl optionally substituted by one or more OH groups or NH_2 groups, C_1-C_6 alkyl optionally substituted by one or more halogen atoms, C_1-C_6 alkoxy optionally substituted by one or more OH groups, C_1-C_6 alkoxy optionally substituted by one or more halogen, C_1-C_6 alkoxy optionally substituted by C_1-C_4 alkoxy, $NR^{18}(SO_2)R^{21}$, $(SO_2)NR^{19}R^{21}$, $(SO_2)R^{21}$, $NR^{18}C(O)R^{21}$, $C(O)NR^{19}R^{21}$, $NR^{18}C(O)NR^{19}R^{21}$, $NR^{18}C(O)OR^{19}$, $NR^{19}R^{21}$, $C(O)OR^{19}$, $C(O)R^{19}$, SR^{19}, OR^{19}, oxo, CN, NO_2, halogen or a 3 to 14 membered heterocyclyl, wherein the heterocyclyl contains at least one heteroatom selected from N, O and S;

R^{18} is independently H or C_1-C_6 alkyl;

R^{19} and R^{21} are each independently H; C_1-C_8 alkyl; C_3-C_8 cycloalkyl; C_1-C_4 alkoxy-C_1-C_4 alkyl; (C_0-C_4 alkyl)-aryl optionally substituted by one or more groups selected from C_1-C_6 alkyl, C_1-C_6 alkoxy and halogen; (C_0-C_4 alkyl)- 3- to 14-membered heterocyclyl, the heterocyclyl including one or more heteroatoms selected from N, O and S, optionally substituted by one or more groups selected from halogen, oxo, C_1-C_6 alkyl and $C(O)C_1$-C_6 alkyl; (C_0-C_4 alkyl)-O-aryl optionally substituted by one or more groups selected from C_1-C_6 alkyl, C_1-C_6 alkoxy and halogen; and (C_0-C_4 alkyl)- O-3- to 14-membered heterocyclyl, the heterocyclyl including one or more heteroatoms selected from N, O and S, optionally substituted by one or more groups selected from halogen, C_1-C_6 alkyl or $C(O)C_1$-C_6 alkyl; wherein the alkyl groups are optionally substituted by one or more halogen atoms, C_1-C_4 alkoxy, $C(O)NH_2$, $C(O)NHC_1$-C_6 alkyl or $C(O)N(C_1$-C_6 alkyl$)_2$; or

R^{19} and R^{21} together with the nitrogen atom to which they attached form a 5- to 10-membered heterocyclyl, the heterocyclyl including one or more further heteroatoms selected from N, O and S, the heterocyclyl being optionally substituted by one or more substituents selected from OH; halogen; aryl; 5- to 10-membered heterocyclyl including one or more heteroatoms selected from N, O and S; $S(O)_2$-aryl; $S(O)_2$-C_1-C_6 alkyl; C_1-C_6 alkyl optionally substituted by one or more halogen atoms; C_1-C_6 alkoxy optionally substituted by one or more OH groups or C_1-C_4 alkoxy; and $C(O)OC_1$-C_6 alkyl, wherein the aryl and heterocyclyl substituent groups are themselves optionally substituted by C_1-C_6 alkyl, C_1-C_6 haloalkyl or C_1-C_6 alkoxy.

2. The compound according to claim 1, wherein

R^1 is X-Y;

R^2 is H, or C_1-C_8 alkyl optionally substituted by one or more halogen atoms;

R^{2a} is hydrogen;

X is C_1-C_6 alkylene optionally substituted by hydroxy, halogens or C_1-C_4 alkyl;

Y is -C(O)OH, -C(O)OR^x or -CONH-$S(O)_q$-R^x, wherein R^x is -C_1-C_4 alkyl;

q is 2;

R^3 is H, C_1-C_4 alkoxy, OH, CN, halogen, C_3-C_7 cycloalkyl or C_1-C_4 alkyl optionally substituted by one or more halogen atoms;

R^4 is H, C_1-C_4 alkoxy, OH, CN, halogen, C_3-C_7 cycloalkyl or C_1-C_4 alkyl optionally substituted by one or more halogen atoms.

3. The compound according to any of the preceding claims, wherein

R^1 is X-Y, wherein X-Y is -$(CH_2)_m$-C(O)OR", or -$(CH_2)_m$-R^7-$(CH_2)_n$- C(O)OR";

R^2 is H, C_1-C_4 alkyl optionally substituted by one or more halogen atoms;

R^{2a} is hydrogen;

R^3 is H, C_1-C_4 alkoxy, OH, CN, halogen, C_3-C_7 cycloalkyl or C_1-C_4 alkyl optionally substituted by one or more halogen atoms;

R^4 is H, C_1-C_4 alkoxy, OH, CN, halogen, C_3-C_7 cycloalkyl or C_1-C_4 alkyl optionally substituted by one or more halogen atoms;

R" is H or C_1-C_4 alkyl optionally substituted by one or more halogen atoms;

m is 1, 2, 3, 4, 5, 6, 7 or 8;

n is 0, 1, 2 or 3.

4. The compound according to any of the preceding claims, wherein

R^1 is X-Y, wherein X-Y is -$(CH_2)_m$-C(O)OR";

R^2 is H or C_1-C_4 alkyl optionally substituted by one or more halogen atoms;

R^{2a} is hydrogen;

R^3 is H, C_1-C_4 alkoxy, OH, CN, halogen, cyclopropyl or C_1-C_4 alkyl optionally substituted by one or more halogen atoms;

R^4 is H, C_1-C_4 alkoxy, OH, CN, halogen, cyclopropyl or C_1-C_4 alkyl optionally substituted by one or more halogen atoms; and

R" is H.

5. The compound according to any of the preceding claims, wherein

R^2 is H;

R^{2a} is hydrogen;

R'' is H;

R^3 is H, methyl, methoxy, OH, CN, fluorine or cyclopropyl;

R^4 is H, methyl, methoxy, OH, CN, fluorine or cyclopropyl; and

m is 4, 5 or 6.

6. The compound according to any of the preceding claims wherein

R^5 is phenyl optionally substituted by C_1-C_4 alkoxy, halogen or C_1-C_4 alkyl optionally substituted by one or more halogen atoms; and

R^6 is phenyl optionally substituted by C_1-C_4 alkoxy, halogen or C_1-C_4 alkyl optionally substituted by one or more halogen atoms.

7. The compound according to any of the preceding claims, wherein A is N.

8. A pharmaceutical composition, comprising:

a therapeutically effective amount of the compound according to any one of claims 1 to 7, or a pharmaceutically acceptable salt thereof, and

one or more pharmaceutically acceptable carriers.

9. A pharmaceutical combination, comprising:

a therapeutically effective amount of the compound according to any one of claims 1 to 7, or a pharmaceutically acceptable salt thereof, and

a second active agent.

10. A method of treating pulmonary arterial hypertension in a patient in need thereof, comprising:

administering to the subject in need thereof a therapeutically effective amount of the compound according to any one of claims 1 to 7, or a pharmaceutically acceptable salt thereof.

11. The compound according to any one of claims 1 to 7, or a pharmaceutically acceptable salt thereof, for use as a medicament.

12. Use of a compound according to any one of claims 1 to 7, or a pharmaceutically acceptable salt thereof in the manufacture of a medicament for the treatment of a disorder or disease in a subject mediated by activating IP receptor.

13. Use of a compound according to any one of claims 1 to 7, or a pharmaceutically acceptable salt thereof for the treatment of a disorder or disease in a subject by activating the IP receptor.

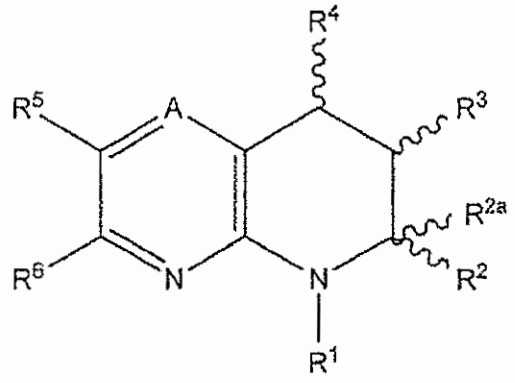
14. Use of a compound according to any one of claims 1 to 7, or a pharmaceutically acceptable salt thereof for the treatment of pulmonary arterial hypertension by activating the IP receptor.

15. A method for the prevention or treatment of a condition affected by activation of the IP receptor, comprising:

administering an effective amount to activate the IP receptor of at least one compound according to any of claims 1 to 7 to a subject in need of such treatment.

CLAIMS

1. A compound represented by Formula Ia



Ia

or a pharmaceutically acceptable salt thereof, wherein

A is N or CR';

R' is H, C_1-C_8 alkyl optionally substituted by one or more halogen atoms;

R^1 is H, C_1-C_8 alkyl optionally substituted by one or more halogen atoms, C_1-C_4 alkyl, OH, OR', -$NR^{19}R^{21}$, CN or C_3-C_7 cycloalkyl; or

R^1 is -X-Y; or

R^1 is -W-R^7-X-Y; or

R^1 is –$S(O)_2$-W-X-Y; or

R^1 is –$S(O)_2$-W-R^7-X-Y;

R^2 is H, C_1-C_8 alkyl optionally substituted by one or more halogen atoms, C_1-C_4 alkyl, OH, OR', -$NR^{19}R^{21}$, CN or C_3-C_7 cycloalkyl; or

R^2 is -X-Y; or

R^2 is -W-R^7-X-Y; or

R^2 is –$S(O)_2$-W-X-Y; *or*

R^2 is –$S(O)_2$-W-R^7-X-Y;

wherein either R^1 or R^2 is -X-Y, -W-R^7-X-Y, –$S(O)_2$-W-X-Y; or –$S(O)_2$-W-R^7-X-Y;

R^{2a} is hydrogen; *or*

R^2 and R^{2a} taken together are oxo;

R^3 is H, C_1-C_4 alkoxy, OH, -$NR^{19}R^{21}$, CN, halogen, C_3-C_7 cycloalkyl or C_1-C_8 alkyl optionally substituted by one or more halogen atoms,;

R^4 is H, C_1-C_4 alkoxy, OH, -$NR^{19}R^{21}$, CN, halogen, C_3-C_7 cycloalkyl or C_1-C_8 alkyl optionally substituted by one or more halogen atoms;

R^5 is C_1-C_8 alkyl optionally substituted by one or more halogen atoms, C_1-C_4 alkyl, OH, OR', -$NR^{19}R^{21}$, CN or C_3-C_7 cycloalkyl; C_1-C_8 alkoxy optionally substituted by one or more halogen atoms; C_6-C_{14} aryl; -(C_0-C_4 alkyl)-4 to 14 membered heteroaryl, or -(C_0-C_4 alkyl)-3 to 14 membered heterocyclyl wherein the heteroaryl and heterocyclyl contain at least one heteroatom selected from N, O and S, wherein the aryl, heteroaryl and heterocyclyl are each optionally substituted by one or more Z substituents;

R^6 is C_6-C_{14} aryl; -(C_0-C_4 alkyl)-4 to 14 membered heteroaryl, or -(C_0-C_4 alkyl)-3 to 14 membered heterocyclyl wherein the heteroaryl and heterocyclyl contain at least one heteroatom selected from N, O and S, wherein the aryl, heteroaryl and heterocyclyl are each optionally substituted by one or more Z substituents;

W is C_1-C_8 alkylene optionally substituted by hydroxy, halogens or C_1-C_4 alkyl;

X is C_1-C_8 alkylene optionally substituted by hydroxy, halogens or C_1-C_4 alkyl;

Y is carboxy, alkoxycarbonyl, tetrazolyl, carbamoyl, monoalkylcarbamoyl, dialkylcarbamoyl, or -CONH-$S(O)_q$-R^x, where R^x is -C_1-C_4 alkyl or -$NR^{19}R^{21}$;

q is 0, 1 or 2;

R^7 is a divalent moiety represented by -O-, -NHC(O)-, -CH_2=CH_2-, -C_6-C_{14} aryl-D-; -3 to 14 membered heterocyclyl-D-, wherein the heterocyclyl contains at least one heteroatom selected from N, O and S, wherein D is O, S, NH or not present;

Z is independently OH, aryl, O-aryl, benzyl, O-benzyl, C_1-C_6 alkyl optionally substituted by one or more OH groups or NH_2 groups, C_1-C_6 alkyl optionally substituted by one or more halogen atoms, C_1-C_6 alkoxy optionally substituted by one or more OH groups, C_1-C_6 alkoxy optionally substituted by one or more halogen, C_1-C_6 alkoxy optionally substituted by C_1-C_4 alkoxy, $NR^{18}(SO_2)R^{21}$, $(SO_2)NR^{19}R^{21}$, $(SO_2)R^{21}$, $NR^{18}C(O)R^{21}$, $C(O)NR^{19}R^{21}$, $NR^{18}C(O)NR^{19}R^{21}$, $NR^{18}C(O)OR^{19}$, $NR^{19}R^{21}$, $C(O)OR^{19}$, $C(O)R^{19}$, SR^{19}, OR^{19}, oxo, CN, NO_2, halogen or a 3 to 14 membered heterocyclyl, wherein the heterocyclyl contains at least one heteroatom selected from N, O and S;

R^{18} is independently H or C_1-C_6 alkyl;

R^{19} and R^{21} are each independently H; C_1-C_8 alkyl; C_3-C_8 cycloalkyl; C_1-C_4 alkoxy-C_1-C_4 alkyl; (C_0-C_4 alkyl)-aryl optionally substituted by one or more groups selected from C_1-C_6 alkyl, C_1-C_6 alkoxy and halogen; (C_0-C_4 alkyl)- 3- to 14-membered heterocyclyl, the heterocyclyl including one or more heteroatoms selected from N, O and S, optionally substituted by one or more groups selected from halogen, oxo, C_1-C_6 alkyl and C(O)C_1-C_6 alkyl; (C_0-C_4 alkyl)-O-aryl optionally substituted by one or more groups selected from C_1-C_6 alkyl, C_1-C_6 alkoxy and halogen; and (C_0-C_4 alkyl)- O-3- to 14-membered heterocyclyl, the heterocyclyl including one or more heteroatoms selected from N, O and S, optionally substituted by one or more groups selected from halogen, C_1-C_8 alkyl or C(O)C_1-C_6 alkyl; wherein the alkyl groups are optionally substituted by one or more halogen atoms, C_1-C_4 alkoxy, C(O)NH_2, C(O)NHC_1-C_6 alkyl or C(O)N(C_1-C_6 alkyl)$_2$; or

R^{19} and R^{21} together with the nitrogen atom to which they attached form a 5- to 10-membered heterocyclyl, the heterocyclyl including one or more further heteroatoms selected from N, O and S, the heterocyclyl being optionally substituted by one or more substituents selected from OH; halogen; aryl; 5- to 10-membered heterocyclyl including one or more heteroatoms selected from N, O and S; $S(O)_2$-aryl; $S(O)_2$-C_1-C_6 alkyl; C_1-C_6 alkyl optionally substituted by one or more halogen atoms; C_1-C_6 alkoxy optionally substituted by one or more OH groups or C_1-C_4 alkoxy; and C(O)OC_1-C_6 alkyl, wherein the aryl and heterocyclyl substituent groups are themselves optionally substituted by C_1-C_6 alkyl, C_1-C_6 haloalkyl or C_1-C_6 alkoxy.

2. The compound according to claim 1, wherein

R^1 is -X-Y; or -W-R^7-X-Y;

R^2 is H, C_1-C_8 alkyl optionally substituted by one or more halogen atoms, C_1-C_4 alkyl, OH, or OR';

R^3 is H, C_1-C_4 alkoxy, OH, -$NR^{19}R^{21}$, CN, halogen, C_3-C_7 cycloalkyl or C_1-C_4 alkyl optionally substituted by one or more halogen atoms;

R^4 is H, C_1-C_4 alkoxy, OH, -$NR^{19}R^{21}$, CN, halogen, C_3-C_7 cycloalkyl or C_1-C_4 alkyl optionally substituted by one or more halogen atoms;

W is C_1-C_6 alkylene optionally substituted by hydroxy, halogens or C_1-C_4 alkyl;

X is C_1-C_5 alkylene optionally substituted by hydroxy, halogens or C_1-C_4 alkyl;

Y is -C(O)OH, -C(O)OR^X, tetrazolyl, carbamoyl, monoalkylcarbamoyl, dialkylcarbamoyl, or -CONH-$S(O)_q$-R^x, wherein R^x is -C_1-C_4 alkyl or -$NR^{19}R^{21}$;

q is 2;

R' is H, C_1-C_4 alkyl optionally substituted by one or more halogen atoms;

R^7 is a divalent moiety represented by -C_6-C_{14} aryl-D-; -3 to 14 membered heterocyclyl-D-, wherein the heterocyclyl contains at least one heteroatom selected from N, O and S, wherein D is O; and

R^{19} and R^{21} are each independently H; C_1-C_8 alkyl.

3. The compound according to claim 1 or 2, wherein

R^1 is -$(CH_2)_m$-C(O)OR", or -$(CH_2)_m$-R^7-$(CH_2)_n$- C(O)OR";

R^2 is H, C_1-C_4 alkyl optionally substituted by one or more halogen atoms;

R^3 is H, C_1-C_4 alkoxy, OH, -$NR^{19}R^{21}$, CN, halogen, C_3-C_7 cycloalkyl or C_1-C_4 alkyl optionally substituted by one or more halogen atoms,

R^4 is H, C_1-C_4 alkoxy, OH, -$NR^{19}R^{21}$, CN, halogen, C_3-C_7 cycloalkyl or C_1-C_4 alkyl optionally substituted by one or more halogen atoms;

m is 1, 2, 3, 4, 5 or 6,

n is 0, 1, 2 or 3;

R" is H or C_1-C_4 alkyl; and

R^7 is a divalent moiety represented by -C_6-C_{14} aryl-D-; -3 to 14 membered heterocyclyl-D-, wherein the heterocyclyl contains at least one heteroatom selected from N, O and S, wherein D is O.

4. The compound according to any one of claims 1 to 3, wherein

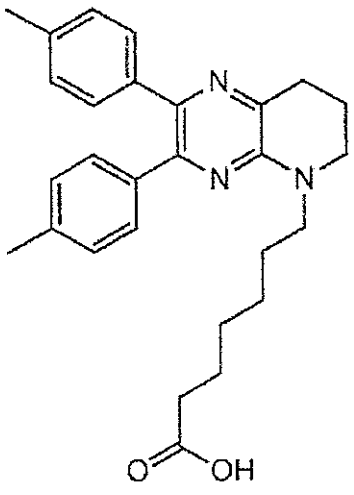
R^5 is phenyl optionally substitued by OH, C_1-C_4 alkyl optionally substituted by one or more OH groups or NH_2 groups; C_1-C_4 alkyl optionally substituted by one or more halogen atoms; C_1-C_4 alkoxy optionally substituted by one or more OH groups or C_1-C_4 alkoxy; $NR^{19}R^{21}$; $C(O)OR^{19}$; $C(O)R^{19}$; SR^{19}; OR^{19}; CN; NO_2; or halogen; and

R^6 is phenyl optionally substituted by OH, C_1-C_4 alkyl optionally substituted by one or more OH groups or NH_2 groups; C_1-C_4 alkyl optionally substituted by one or more halogen atoms; C_1-C_4 alkoxy optionally substituted by one or more OH groups or C_1-C_4 alkoxy; $NR^{15}R^{21}$, $C(O)OR^{19}$, $C(O)R^{19}$, SR^{19}, OR^{19}, CN, NO_2, or halogen.

5. The compound according to any one of claims 1 to 4, wherein A is N.

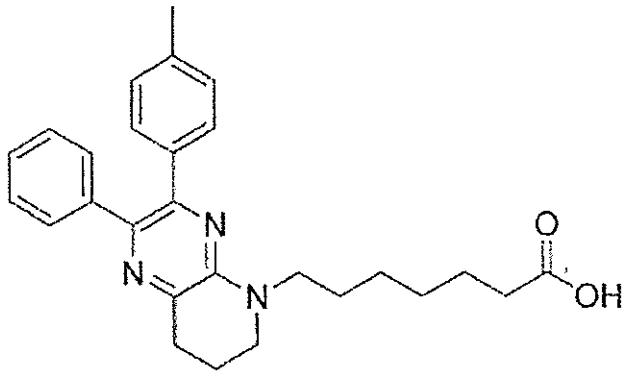
6. The compound according to claim 1 selected from the group consisting of
7-(2-phenyl-3-p-tolyl-7,8-dihydropyrido[2,3-b]pyrazin-5(6H)-yl)heptanoic acid;
7-(8-hydroxy-2,3-dip-tolyl-7,8-dihydropyrido[2,3-b]pyrazin-5(6H)-yl)heptanoic acid;
7-(7-hydroxy-6-oxo-2,3-dip-tolyl-7,8-dihydropyrido[2,3-b]pyrazin-5(6H)-yl)heptanoic acid;
7-(2,3-di-p-tolyl-7,8-dihydropyrido[2,3-b]pyrazin-5(6H)-yl)heptanoic acid;
2-(3-((2,3-diphenyl-7,8-dihydropyrido[3,2-b]pyrazin-5(6H)-yl)methyl)phenoxy)acetic acid; and
7-(3-phenyl-2-p-tolyl-7,8-dihydropyrido[2,3-b]pyrazin-5(6H)-yl)heptanoic acid; or a pharmaceutically acceptable salt thereof.

7. The compound according to claim 1, which is
7-(2,3-di-p-tolyl-7,8-dihydropyrido[2,3-b]pyrazin-5(6H)-yl)heptanoic acid of formula



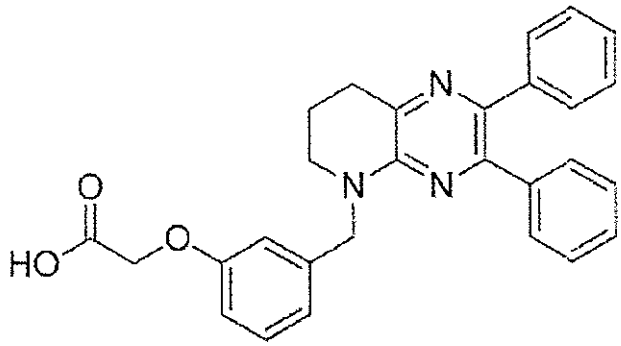
or a pharmaceutically acceptable salt thereof.

8. The compound according to claim 1, which is
7-(2-phenyl-3-p-tolyl-7,8-dihydropyrido[2,3-b]pyrazin-5(6H)-yl)heptanoic acid of formula



or a pharmaceutically acceptable salt thereof.

9. The compound according to claim 1, which is
2-(3-((2,3-diphenyl-7,8-dihydropyrido [3,2-b] pyrazin -5 (6H)-yl) methyl) phenoxy) acetic acid of formula



or a pharmaceutically acceptable salt thereof.

10. The compound according to any one of claims 6 to 9, wherein the compound is in free form.

11. A pharmaceutical composition, comprising:
a therapeutically effective amount of the compound according to any one of claims 1 to 10, or a pharmaceutically acceptable salt thereof, and
one or more pharmaceutically acceptable carriers.

12. A pharmaceutical combination, comprising:
a therapeutically effective amount of the compound according to any one of claims 1 to 10, or a pharmaceutically acceptable salt thereof, and a second active agent.

13. The compound according to any one of claims 1 to 10, or a pharmaceutically acceptable salt thereof, for use as a medicament.

14. The compound according to claim 13, or a pharmaceutically acceptable salt thereof, for use in the treatment of PAH, disorders in need of antiplatlet therapy, atherosclerosis, asthma, COPD, hyperglycemia, inflammatory disease, or fibrotic diseases.

15. The compound according to claim 13, or a pharmaceutically acceptable salt thereof, for use in the treatment of PAH, asthma, COPD, or cystic fibrosis.