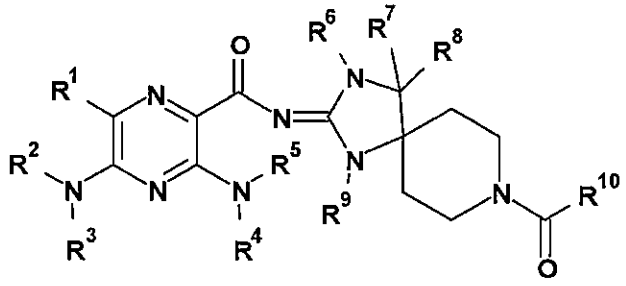
Claims

1. A compound of Formula I:



I

or a pharmaceutically acceptable salt thereof, wherein

R^1 is H, halogen, C_1-C_8-alkyl, C_1-C_8-haloalkyl, C_1-C_8-haloalkoxy, C_3-C_{15}-carbocyclic group, nitro, cyano, a C_6-C_{15}-membered aromatic carbocyclic group, or a C_1-C_8-alkyl substituted by a C_6-C_{15}-membered aromatic carbocyclic group;

R^2, R^3, R^4 and R^5 are each independently selected from H and C_1-C_6 alkyl;

R^6, R^7, R^8 and R^9 are each independently selected from H; SO_2R^{16}; aryl optionally substituted by one or more Z groups; a C_3-C_{10} carbocyclic group optionally substituted by one or more Z groups; C_3-C_{14} heterocyclic group optionally substituted by one or more Z groups; C_1-C_8 alkyl optionally substituted by an aryl group which is optionally substituted by one or more Z groups, a C_3-C_{10} carbocyclic group optionally substituted by one or more Z groups or a C_3-C_{14} heterocyclic group optionally substituted by one or more Z groups;

R^{10} is represented by the formula 2:

$-(C_0$-C_3alkylene$)$-B-X-$(CR^{11a}R^{12a})_m$-$(CR^{11b}R^{12b})_n$-$(CR^{11c}R^{12c})_p$-$C(O)OR^{13}$,

wherein the alkylene groups are optionally substituted by one or more Z groups;

B is aryl optionally substituted by one or more Z groups;

X is selected from a bond, $-NR^{15}(SO_2)$-, $-(SO_2)NR^{15}$-, $-(SO_2)$-, $-NR^{15}C(O)$-, $-C(O)NR^{15}$-, $-NR^{15}C(O)NR^{17}$-, $-NR^{15}C(O)O$-, $-NR^{15}$-, C(O)O, OC(O), C(O), O and S;

R^{11a}, R^{11b}, R^{11c}, R^{12a}, R^{12b} and R^{12c} are each independently selected from H and C_1-C_6 alkyl;or

R^{11a} and R^{12a} together with the carbon atom to which they are attached form a 3- to 8-membered cycloalkyl group; or

R^{11b} and R^{12b} together with the carbon atom to which they are attached form a 3- to 8-membered cycloalkyl group; or

R^{11c} and R^{12c} together with the carbon atom to which they are attached form a 3- to 8-membered cycloalkyl group;

R^{13} is selected from (C_1-C_3 alkyl)-$C(O)NR^{22}R^{23}$; (C_1-C_3 alkyl)-$C(O)OR^{23}$; and (C_1-C_3 alkyl)-$NR^{23}C(O)R^{22}$

R^{15} and R^{17} are each independently selected from H and C_1-C_6 alkyl;

R^{16} is selected from C_1-C_8 alkyl, aryl and a 3- to 14-membered heterocyclic group, the heterocyclic group including one or more heteroatoms selected from N, O and S;

Z is independently selected from -OH, aryl, -O-aryl, C_7-C_{14} aralkyl, -O-C_7-C_{14} aralkyl, C_1-C_6 alkyl, C_1-C_6 alkoxy, $-NR^{19}(SO_2)R^{21}$, $-(SO_2)NR^{19}R^{21}$, $-(SO_2)R^{20}$, $-NR^{19}C(O)R^{20}$, $-C(O)NR^{19}R^{20}$, $-NR^{19}C(O)NR^{20}R^{18}$, $-NR^{19}C(O)OR^{20}$, $-NR^{19}R^{21}$, $C(O)OR^{19}$, $-C(O)R^{19}$, SR^{19}, $-OR^{19}$, oxo, CN, NO_2, and halogen, wherein the alkyl, alkoxy, aralkyl and aryl groups are each optionally substituted by one or more substituents selected from OH, halogen, C_1-C_4 haloalkyl and C_1-C_4 alkoxy;

R^{18}, R^{20} and R^{22} are each independently selected from H and C_1-C_6 alkyl;

R^{19} , R^{21} and R^{23} are each independently selected from 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 heterocyclic group, the heterocyclic group 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 heterocyclic group, the heterocyclic group 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 and $-C(O)C_1$-C_6 alkyl; wherein the alkyl groups are

optionally substituted by one or more halogen atoms, hydroxyl, 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^{20} together with the nitrogen atom to which they are attached form a 5- to 10-membered heterocyclic group, the heterocyclic group including one or more further heteroatoms selected from N, O and S, the heterocyclic group being optionally substituted by one or more substituents selected from OH; halogen; aryl; 5- to 10-membered heterocyclic group 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 heterocyclic substituent groups are themselves optionally substituted by C_1-C_6 alkyl, C_1-C_6 haloalkyl or C_1-C_6 alkoxy; or

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

R^{18} and R^{20} together with the nitrogen atom to which they are attached form a 5- to 10-membered heterocyclic group, the heterocyclic group including one or more further heteroatoms selected from N, O and S, the heterocyclic group being optionally substituted by one or more substituents selected from OH; halogen; aryl; 5- to 10-membered heterocyclic group 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 heterocyclic substituent groups are themselves optionally substituted by C_1-C_6 alkyl, C_1-C_6 haloalkyl or C_1-C_6 alkoxy; or

R^{22} and R^{23} together with the atom(s) to which they are attached form a 5- to 10-membered heterocyclic group, the heterocyclic group including one or more further heteroatoms selected from N, O and S, the heterocyclic group being optionally substituted by one or more Z groups;

m is 0, 1 , 2 or 3;
n is 0, 1 , 2 or 3;
p is 0, 1 , 2 or 3;
wherein at least one of m, n or p is not 0.

2. A compound according to claim 1, wherein
R^1 is halogen;
R^2, R^3, R^4 and R^5 are H; and
R^6, R^7, R^8 and R^9 are H.

3. A compound according to claim 1 or 2 wherein B is phenyl optionally substituted by halogen.

4. A compound according to any preceding claim wherein X is selected from -$(SO_2)NR^{15}$-, -$NR^{15}C(O)NR^{17}$-, and O.

5. A compound according to any preceding claim wherein R^{11a}, R^{11b}, R^{11c}, R^{12a}, R^{12b} and R^{12c} are each independently selected from H and C_1-C_3 alkyl;or
R^{11a} and R^{12a} together with the carbon atom to which they are attached form a 3, 4- or 5-membered cycloalkyl group; or
R^{11b} and R^{12b} together with the carbon atom to which they are attached form a 3, 4- or 5-membered cycloalkyl group; or
R^{11c} and R^{12c} together with the carbon atom to which they are attached form a 3, 4- or 5-membered cycloalkyl group.

6. A compound according to any preceding claim wherein the sum of m, n and p is is 1, 2, or, 3.

7. A compound according to any preceding claim wherein R^{13} is selected from (C_1-C_3 alkyl)-$C(O)NR^{22}R^{23}$ and (C_1-C_3 alkyl)-$C(O)OR^{23}$; and wherein

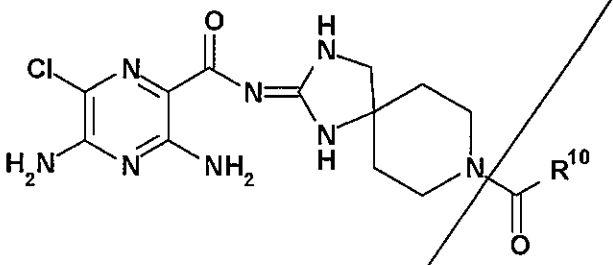
R^{22} is selected from H and C_1-C_3 alkyl;

R^{23} is selected from 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 heterocyclic group, the

heterocyclic group 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 heterocyclic group, the heterocyclic group 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 and C(O)C_1-C_6 alkyl; wherein the alkyl groups are optionally substituted by one or more halogen atoms, hydroxyl 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^{22} and R^{23} together with the nitrogen to which they are attached form a 5- to 7-membered heterocycloalkyl group, the heterocycloalkyl group including one or more further heteroatoms selected from N, O and S, the heterocycloalkyl group being optionally substituted by one or more Z groups.

8. A compound according to any preceding claim which is a compound of Formula Ia



Ia

or a pharmaceutically acceptable salt or solvate thereof wherein R^{10} is as defined in any preceding claim.

9. A compound according to claim 1 selected from:

3-(3-{2-[(E)-3,5-Diamino-6-chloro-pyrazine-2-carbonylimino]-1,3,8-triaza-spiro[4.5]decane-8-carbonyl}-benzenesulfonylamino)-propionic acid dipropylcarbamoylmethyl ester;

[4-(3-{2-[(Z)-3,5-Diamino-6-chloro-pyrazine-2-carbonylimino]-1,3,8-triaza-spiro[4.5]dec-8-yl}-3-oxo-propyl)-phenoxy]-acetic acid [(2-hydroxy-ethyl)-methyl-carbamoyl]-methyl ester;

[4-(3-{2-[(E)-3,5-Diamino-6-chloro-pyrazine-2-carbonylimino]-1,3,8-triaza-spiro[4.5]dec-8-yl}-3-oxo-propyl)-phenoxy]-acetic acid cyclohexyl oxycarbonylmethyl ester;

3-(3-{2-[(E)-3,5-Diamino-6-chloro-pyrazine-2-carbonylimino]-1,3,8-triaza-spiro[4.5]decane-8-carbonyl}-benzene sulfonylamino)-propionic acid cyclohexyloxy carbonylmethyl ester;

[4-(3-{2-[(E)-3,5-Diamino-6-chloro-pyrazine-2-carbonylimino]-1,3,8-triaza-spiro[4.5]dec-8-yl}-3-oxo-propyl)-phenoxy]-acetic acid dimethylcarbamoylmethyl ester;

[4-(3-{2-[(E)-3,5-Diamino-6-chloro-pyrazine-2-carbonylimino]-1,3,8-triaza-spiro[4.5]dec-8-yl}-3-oxo-propyl)-phenoxy]-acetic acid dipropylcarbamoylmethyl ester;

[4-(3-{2-[(E)-3,5-Diamino-6-chloro-pyrazine-2-carbonylimino]-1,3,8-triaza-spiro[4.5]dec-8-yl}-3-oxo-propyl)-phenoxy]-acetic acid tert-butoxycarbonylmethyl ester;

[4-(3-{2-[(E)-3,5-Diamino-6-chloro-pyrazine-2-carbonyl imino]-1,3,8-triaza-spiro[4.5]dec-8-yl}-3-oxo-propyl)-phenoxy]-acetic acid benzyloxycarbonylmethyl ester;

[4-(3-{2-[(E)-3,5-Diamino-6-chloro-pyrazine-2-carbonylimino]-1,3,8-triaza-spiro[4.5]dec-8-yl}-3-oxo-propyl)-phenoxy]-acetic acid diethylcarbamoylmethyl ester;

[4-(3-{2-[(E)-3,5-Diamino-6-chloro-pyrazine-2-carbonylimino]-1,3,8-triaza-spiro[4.5]dec-8-yl}-3-oxo-propyl)-phenoxy]-acetic acid 2-oxo-2-piperidin-1-yl-ethyl ester;

[2-Chloro-4-(3-{2-[(E)-3,5-diamino-6-chloro-pyrazine-2-carbonylimino]-1,3,8-triaza-spiro[4.5]dec-8-yl}-3-oxo-propyl)-phenoxy]-acetic acid dipropylcarbamoylmethyl ester;

3-(3-{2-[(E)-3,5-Diamino-6-chloro-pyrazine-2-carbonylimino]-1,3,8-triaza-spiro[4.5]decane-8-carbonyl}-benzenesulfonylamino)-propionic acid 2-oxo-2-(2-trifluoromethyl-pyrrolidin-1-yl)-ethyl ester;

[2-Chloro-4-(3-{2-[(E)-3,5-diamino-6-chloro-pyrazine-2-carbonylimino]-1,3,8-triaza-spiro[4.5]dec-8-yl}-3-oxo-propyl)-phenoxy]-acetic acid 2-(2-oxo-piperidin-1-yl)-ethyl ester;

[4-(3-{2-[(E)-3,5-Diamino-6-chloro-pyrazine-2-carbonylimino]-1,3,8-triaza-spiro[4.5]dec-8-yl}-3-oxo-propyl)-phenoxy]-acetic acid 2-morpholin-4-yl-2-oxo-ethyl ester;

1-[(3-{2-[(E)-3,5-Diamino-6-chloro-pyrazine-2-carbonylimino]-1,3,8-triaza-spiro[4.5]decane-8-carbonyl}-benzenesulfonylamino)-methyl]-cyclobutanecarboxylic acid dipropylcarbamoylmethyl ester;

3-[3-(3-{2-[(E)-3,5-Diamino-6-chloro-pyrazine-2-carbonylimino]-1,3,8-triaza-spiro[4.5]decane-8-carbonyl}-phenyl)-ureido]-propionic acid dipropylcarbamoylmethyl ester; and

1-[(3-{2-[(E)-3,5-Diamino-6-chloro-pyrazine-2-carbonylimino]-1,3,8-triaza-spiro[4.5]decane-8-carbonyl}-benzenesulfonylamino)-methyl]-cyclobutanecarboxylic acid 2-oxo-2-(2-trifluoromethyl-pyrrolidin-1-yl)-ethyl ester;

or a pharmaceutically acceptable salt or solvate thereof.

10. A pharmaceutical composition including a compound according to any of claims 1 to 9 and one or more pharmaceutically acceptable excipients, diluents and/or carriers.

11. A pharmaceutical composition according to claim 10 in combination with one or more other therapeutic agents.

12. A compound according to any of claims 1 to 9 for use as a pharmaceutical.

13. A compound according to any of claims 1 to 9 for use in treating or preventing a disease or condition mediated by blockade of the epithelial sodium channel.

14. Use of a compound according to any of claims 1 to 9 in the manufacture of a medicament for the prevention or treatment of a disease or condition mediated by blockade of the epithelial sodium channel

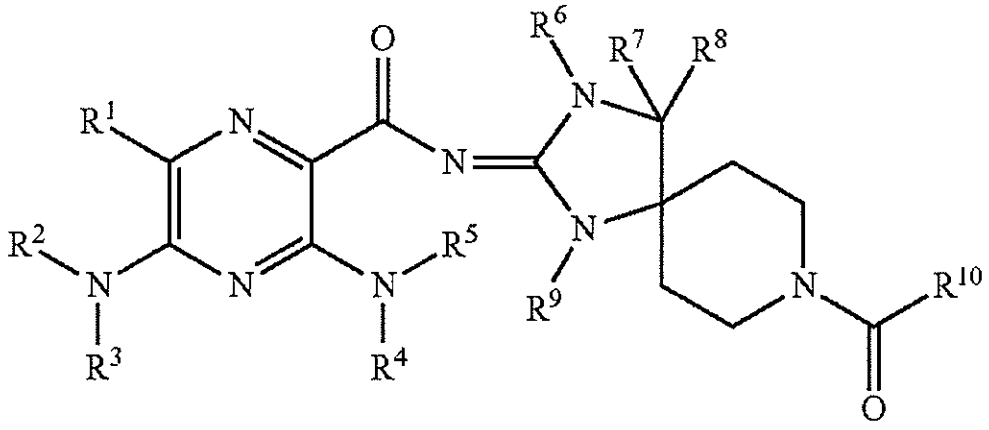
15. A method for preventing or treating a disease or condition mediated by blockade of the epithelial sodium channel, comprising:

adiminstering an effective amount of a compound according to any of claims 1 to 9 is administered to a patient in need of such treatment.

The invention claimed is:

1. A compound of Formula I:

I



or a pharmaceutically acceptable salt thereof, wherein
R^1 is H, halogen, C_1-C_8-alkyl, C_1-C_8-haloalkyl, C_1-C_8-haloalkoxy, C_3-C_{15}-carbocyclic group, nitro, cyano, a C_6-C_{15}-membered aromatic carbocyclic group, or a C_1-C_8-alkyl substituted by a C_6-C_{15}-membered aromatic carbocyclic group;
R^2, R^3, R^4 and R^5 are each independently selected from H and C_1-C_6 alkyl;
R^6, R^7, R^8 and R^9 are each independently selected from H; SO_2R^{16}; aryl optionally substituted by one or more Z groups; a C_3-C_{10} carbocyclic group optionally substituted by one or more Z groups; C_3-C_{14} heterocyclic group optionally substituted by one or more Z groups; C_1-C_8 alkyl optionally substituted by an aryl group which is optionally substituted by one or more Z groups;
R^{10} is represented by the formula 2:
—(C_0-C_3alkylene)-B—X—$(CR^{11a}R^{12a})_m$—$(CR^{11b}R^{12b})_n$—$(CR^{11c}R^{12c})_p$—C(O)OR^{13},
wherein the alkylene groups are optionally substituted by one or more Z groups;
B is aryl optionally substituted by one or more Z groups;

X is selected from a bond, —$NR^{15}(SO_2)$—, —$(SO_2)NR^{15}$—, —(SO_2)—, —$NR^{15}C(O)$—, —$C(O)NR^{15}$—, —$NR^{15}C(O)NR^{17}$—, —$NR^{15}C(O)O$—, —NR^{15}—, C(O)O, OC(O), C(O), O and S; R^{11a}, R^{11b}, R^{11c}, R^{12a}, R^{12c} are each independently selected from H and C_1-C_6 alkyl; or

R^{11a} and R^{12a} together with the carbon atom to which they are attached form a 3- to 8-membered cycloalkyl group; or

R^{11b} and R^{12b} together with the carbon atom to which they are attached form a 3- to 8-membered cycloalkyl group; or

R^{11c} and R^{12c} together with the carbon atom to which they are attached form a 3- to 8-membered cycloalkyl group;

R^{13} is selected from (C_1-C_3 alkyl)-$C(O)NR^{22}R^{23}$; (C_1-C_3 alkyl)-$C(O)OR^{23}$; and (C_1-C_3 alkyl)-$NR^{23}C(O)R^{22}$

R^{15} and R^{17} are each independently selected from H and C_1-C_6 alkyl;

R^{16} is selected from C_1-C_8 alkyl, aryl and a 3- to 14-membered heterocyclic group, the heterocyclic group including one or more heteroatoms selected from N, O and S;

Z is independently selected from —OH, aryl, —O-aryl, C_7-C_{14} aralkyl, —O—C_7-C_{14} aralkyl, C_1-C_6 alkyl, C_1-C_6 alkoxy, —$NR^{19}(SO_2)R^{21}$, —$(SO_2)NR^{19}R^{21}$, —$(SO_2)R^{20}$, —$NR^{19}C(O)R^{20}$, —$C(O)NR^{19}R^{20}$, —$NR^{19}C(O)NR^{20}R^{18}$, —$NR^{19}C(O)OR^{20}$, —$NR^{19}R^{21}$, $C(O)OR^{19}$, —$C(O)R^{19}$, SR^{19}, —OR^{19}, oxo, CN, NO_2, and halogen, wherein the alkyl, alkoxy, aralkyl and aryl groups are each optionally substituted by one or more substituents selected from OH, halogen, C_1-C_4 haloalkyl and C_1-C_4 alkoxy;

R^{18}, R^{20} and R^{22} are each independently selected from H and C_1-C_6 alkyl;

R^{19}, R^{21} and R^{23} are each independently selected from H; C_1-C_8 alkyl; C_3-C_8 cycloalkyl; C_1-C_4 alkoxy-C_1-C_4 alkyl; (C_0-C_a 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 heterocyclic group, the heterocyclic group 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_a alkyl)-O-3- to 14-membered heterocyclic group, the heterocyclic group 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 and —C(O)C_1-C_6 alkyl; wherein the alkyl groups are optionally substituted by one or more halogen atoms, hydroxyl, 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^{20} together with the nitrogen atom to which they are attached form a 5- to 10-membered heterocyclic group, the heterocyclic group including one or more further heteroatoms selected from N, O and S, the heterocyclic group being optionally substituted by one or more substituents selected from OH; halogen; aryl; 5- to 10-membered heterocyclic group 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 heterocyclic substituent groups are themselves optionally substituted by C_1-C_6 alkyl, C_1-C_6 haloalkyl or C_1-C_6 alkoxy; or

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

R^{18} and R^{20} together with the nitrogen atom to which they are attached form a 5- to 10-membered heterocyclic group, the heterocyclic group including one or more further heteroatoms selected from N, O and S, the heterocyclic group being optionally substituted by one or more substituents selected from OH; halogen; aryl; 5- to 10-membered heterocyclic group 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 heterocyclic substituent groups are themselves optionally substituted by C_1-C_6 alkyl, C_1-C_6 haloalkyl or C_1-C_6 alkoxy; or

R^{22} and R^{23} together with the atom(s) to which they are attached form a 5- to 10-membered heterocyclic group, the

heterocyclic group including one or more further heteroatoms selected from N, O and S, the heterocyclic group being optionally substituted by one or more Z groups;
m is 0, 1, 2 or 3;
n is 0, 1, 2 or 3;
p is 0, 1, 2 or 3;
wherein at least one of m, n or p is not 0.

2. A compound according to claim **1**, or a pharmaceutically acceptable salt thereof, wherein

R^1 is halogen;

R^2, R^3, R^4 and R^5 are H; and

R^6, R^7, R^8 and R^9 are H.

3. A compound according to claim **1**, or a pharmaceutically acceptable salt thereof, wherein B is phenyl optionally substituted by halogen.

4. A compound according to claim **1**, or a pharmaceutically acceptable salt thereof, wherein X is selected from —(SO_2) NR^{15}—, —$NR^{15}C(O)NR^{17}$—, and O.

5. A compound according to claim **1**, or a pharmaceutically acceptable salt thereof, wherein R^{11a}, R^{11b}, R^{11c}, R^{12a}, R^{12b} and R^{12c} are each independently selected from H and C_1-C_3 alkyl; or

R^{11a} and R^{12a} together with the carbon atom to which they are attached form a 3,4- or 5-membered cycloalkyl group; or

R^{11b} and R^{12b} together with the carbon atom to which they are attached form a 3,4- or 5-membered cycloalkyl group; or

R^{11c} and R^{12c} together with the carbon atom to which they are attached form a 3,4- or 5-membered cycloalkyl group.

6. A compound according to claim **1**, or a pharmaceutically acceptable salt thereof, wherein the sum of m, n and p is 1, 2, or, 3.

7. A compound according to claim **1**, or a pharmaceutically acceptable salt thereof, wherein R^{13} is selected from (C_1-C_3 alkyl)-C(O)$NR^{22}R^{23}$ and (C_1-C_3 alkyl)-C(O)OR^{23}; and wherein

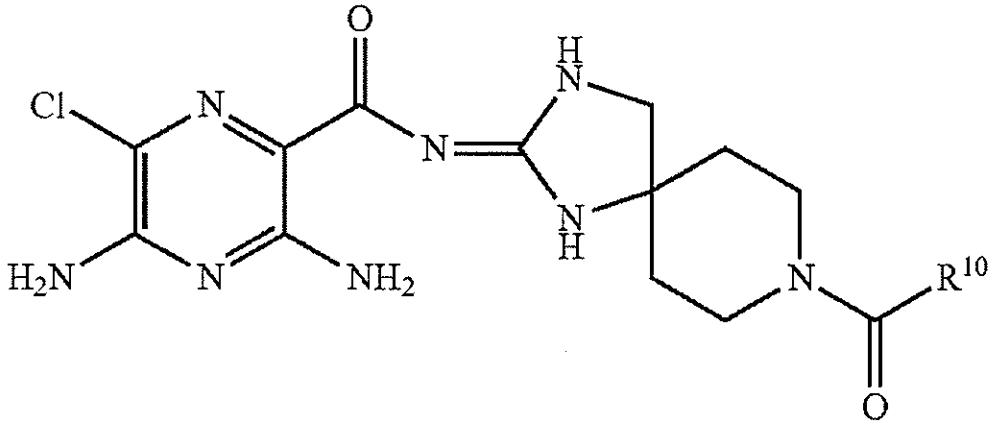
R^{22} is selected from H and C_1-C_3 alkyl;

R^{23} is selected from 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 heterocyclic group, the heterocyclic group 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_a 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 heterocyclic group, the heterocyclic group 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 and C(O)C_1-C_6 alkyl; wherein the alkyl groups are optionally substituted by one or more halogen atoms, hydroxyl 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^{22} and R^{23} together with the nitrogen to which they are attached form a 5- to 7-membered heterocycloalkyl group, the heterocycloalkyl group including one or more further heteroatoms selected from N, O and S, the heterocycloalkyl group being optionally substituted by one or more Z groups.

8. A compound according to claim **1**, which is a compound of Formula Ia

Ia



or a pharmaceutically acceptable salt thereof.

9. A compound according to claim **1** selected from the group consisting of:

3-(3-{2-[(E)-3,5-Diamino-6-chloro-pyrazine-2-carbonylimino]-1,3,8-triaza-spiro[4.5]decane-8-carbonyly}-benzenesulfonylamino)-propionic acid dipropylcarbamoylmethyl ester;

[4-(3-{2-[(Z)-3,5-Diamino-6-chloro-pyrazine-2-carbonylimino]-1,3,8-triaza-spiro[4.5]dec-8-yl}-3-oxo-propyl)-phenoxy]acetic acid [(2-hydroxy-ethyl)-methyl-carbamoyl]-methyl ester;

[4-(3-{2-[(E)-3,5-Diamino-6-chloro-pyrazine-2-carbonylimino]-1,3,8-triaza-spiro[4.5]dec-8-yl}-3-oxo-propyl)-phenoxy]-acetic acid cyclohexyl oxycarbonylmethyl ester;

3-(3-{2-[(E)-3,5-Diamino-6-chloro-pyrazine-2-carbonylimino]-1,3,8-triaza-spiro[4.5]decane-8-carbonyly}-benzene sulfonylamino)-propionic acid cyclohexyloxy carbonylmethyl ester;

[4-(3-{2-[(E)-3,5-Diamino-6-chloro-pyrazine-2-carbonylimino]-1,3,8-triaza-spiro[4.5]dec-8-yl}-3-oxo-propyl)-phenoxy]-acetic acid dimethylcarbamoylmethyl ester;
[4-(3-{2-[(E)-3,5-Diamino-6-chloro-pyrazine-2-carbonylimino]-1,3,8-triaza-spiro[4.5]dec-8-yl}-3-oxo-propyl)-phenoxy]-acetic acid tert-butoxycarbonylmethyl ester;
[4-(3-{2-[(E)-3,5-Diamino-6-chloro-pyrazine-2-carbonyl imino]-1,3,8-triaza-spiro[4.5]dec-8-yl}-3-oxo-propyl)-phenoxy]-acetic acid benzyloxycarbonylmethyl ester;
[4-(3-{2-[(E)-3,5-Diamino-6-chloro-pyrazine-2-carbonylimino]-1,3,8-triaza-spiro[4.5]dec-8-yl}-3-oxo-propyl)-phenoxy]-acetic acid diethylcarbamoylmethyl ester;
[4-(3-{2-[(E)-3,5-Diamino-6-chloro-pyrazine-2-carbonylimino]-1,3,8-triaza-spiro[4.5]dec-8-yl}-3-oxo-propyl)-phenoxy]-acetic acid 2-oxo-2-piperidin-1-yl-ethyl ester;
3-(3-{2-[(E)-3,5-Diamino-6-chloro-pyrazine-2-carbonylimino]-1,3,8-triaza-spiro[4.5]decane-8-carbonyl}-benzenesulfonylamino)-propionic acid 2-oxo-2-(2-trifluoromethyl-pyrrolidin-1-yl)-ethyl ester;
[2-Chloro-4-(3-{2-[(E)-3,5-diamino-6-chloro-pyrazine-2-carbonylimino}-1,3,8-triaza-spiro[4.5]dec-8-yl]-3-oxo-propyl)-phenoxy]-acetic acid 2-(2-oxo-piperidin-1-yl)-ethyl ester;
[4-(3-{2-[(E)-3,5-Diamino-6-chloro-pyrazine-2-carbonylimino]-1,3,8-triaza-spiro[4.5]dec-8-yl}-3-oxo-propyl)-phenoxy]-acetic acid 2-morpholin-4-yl-2-oxo-ethyl ester;
1-[(3-{2-[(E)-3,5-Diamino-6-chloro-pyrazine-2-carbonylimino]-1,3,8-triaza-spiro[4.5]decane-8-carbonyl}-benzenesulfonylamino)-methylycyclobutanecarboxylic acid dipropylcarbamoylmethyl ester;

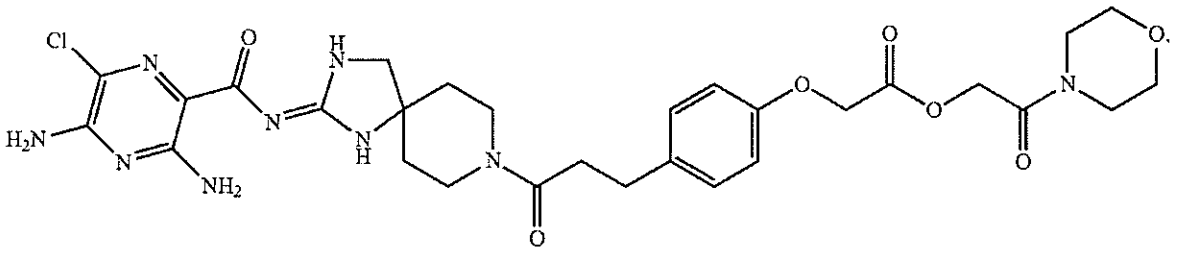
3-[3-(3-{2-[(E)-3,5-Diamino-6-chloro-pyrazine-2-carbonylimino]-1,3,8-triaza-spiro[4.5]decane-8-carbonyl}-phenyl)-ureidoypropionic acid dipropylcarbamoylmethyl ester;
and
1-[(3-{2-[(E)-3,5-Diamino-6-chloro-pyrazine-2-carbonylimino]-1,3,8-triaza-spiro[4.5]decane-8-carbonyl}-benzenesulfonylamino)-methyly]-cyclobutanecarboxylic acid 2-oxo-2-(2-trifluoromethyl-pyrrolidin-1-yl)-ethyl ester;
or a pharmaceutically acceptable salt thereof.

10. A pharmaceutical composition, comprising a compound according to claim **1**, or a pharmaceutically acceptable salt thereof, and one or more pharmaceutically acceptable excipients, diluents and/or carriers.

11. The compound according to claim **1**, wherein the compound is 3-(3-{2-[(E)-3,5-Diamino-6-chloro-pyrazine-2-carbonylimino]-1,3,8-triaza-spiro[4.5]decane-8-carbonyl}-benzenesulfonylamino)-propionic acid dipropylcarbamoylmethyl ester, or a pharmaceutically acceptable salt thereof.

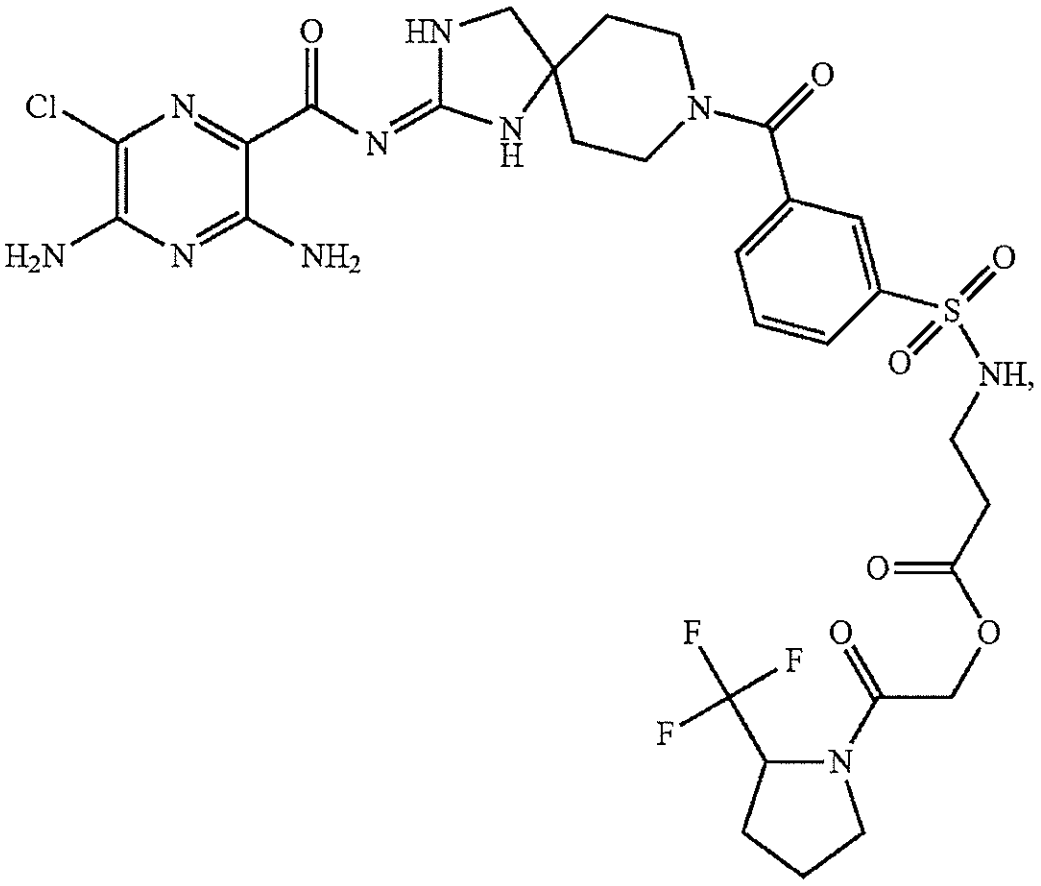
12. The compound according to claim **11**, wherein the compound is a succinate salt.

13. The compound according to claim **1**, wherein the compound is:



or a pharmaceutically acceptable salt thereof.

14. The compound according to claim **1**, wherein the compound is:



or a pharmaceutically acceptable salt thereof.