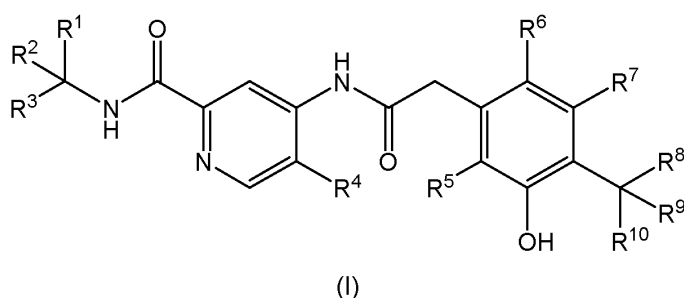


CLAIMS

1. A compound of general formula (I) including all tautomeric forms, all enantiomers, isotopic variants, and salts and solvates thereof:

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wherein:

10 R^1 is selected from methyl, fluoromethyl, difluoromethyl, trifluoromethyl, chlorodifluoromethyl, dichlorofluoromethyl, ethynyl and CN; or

when R^2 and R^3 together with the carbon atom to which they are attached form a 4- to 6-membered carbocyclic ring substituted, in addition to the R^1 group, with OH, halo, methyl or CH_2OH , R^1 may also be H; or

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when R^2 and R^3 together with the carbon atom to which they are attached form a 4- to 6-membered carbocyclic ring, which is unsubstituted apart from the R^1 group; R^1 may also be CH_2OH ;

20 R^2 is selected from methyl and CH_2OH ;

R^3 is selected from H and methyl; or

25 R^2 and R^3 together with the carbon atom to which they are attached form a 3- to 10-membered carbocyclic or oxygen-containing heterocyclic ring system, either of which is optionally substituted, in addition to the R^1 group, with one or more substituents selected from OH, halo, C_{1-4} alkyl, C_{1-4} alkyl substituted with one or more OH substituents, and C_{1-4} haloalkyl; or

30 R^1 , R^2 and R^3 together with the carbon atom to which they are attached combine to form

a 5- to 8-membered bridged carbocyclic or heterocyclic ring system optionally substituted with one or more substituents selected from OH, halo, C₁₋₄ alkyl and C₁₋₄ haloalkyl;

R⁴ is H or halo;

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each of R⁵ and R⁷ is independently selected from H, halo, C₁₋₃ alkyl and C₁₋₃ haloalkyl;

R⁶ is selected from H, halo, CN and C₁₋₄ alkyl optionally substituted with one or more substituents selected from halo and OH;

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R⁸ is methyl or ethyl, either of which is optionally substituted with one or more halogen substituents;

R⁹ is OH, CH₂OH or methyl or ethyl, either of which is optionally substituted with one or more halogen substituents; or

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R⁸ and R⁹ together with the carbon atom to which they are attached form either a 3- to 6-membered cycloalkyl or oxygen-containing heterocyclic ring optionally substituted, in addition to the R¹⁰ group, with one or more substituents selected from OH, F and CH₂OH; or an ethenyl group optionally substituted with one or two halogen substituents;

20

R¹⁰ is selected from H, CN, OH, cycloalkyl optionally substituted with OH, and C₁₋₄ alkyl optionally substituted with one or more substituents selected from halo, OH and a 3- to 6-membered cycloalkyl or heterocyclic group, either of which is optionally substituted with OH; or

25

R⁸, R⁹ and R¹⁰ together with the carbon atom to which they are attached form a 5- to 8-membered fused or bridged carbocyclic ring system optionally substituted with one or more substituents selected from OH, F and CH₂OH;

30

provided that:

i. when R⁵ and R⁷ are H and R⁶ is H or F, R¹, R², R³, R⁸, R⁹ and R¹⁰ are not all methyl; and

ii. when R², R³, R⁸, R⁹ and R¹⁰ are all methyl, R⁵, R⁶ and R⁷ are not all H; and

35 iii. when R¹ is CN and R² and R³ together with the carbon atom to which they are

attached form a 3- to 10-membered oxygen-containing heterocyclic ring, R^8 , R^9 and R^{10} are not all methyl; and

iv. R^9 and R^{10} are not both OH.

5 2. A compound according to claim 1 wherein either:

R^8 and R^9 together with the carbon atom to which they are attached form a 3- to 6-membered cycloalkyl or oxygen-containing heterocyclic ring substituted, in addition to the R^{10} group, with one or more CH_2OH substituents and optionally with one or more further substituents selected from OH and F; or

10

R^8 and R^9 together with the carbon atom to which they are attached form a 3- to 6-membered cycloalkyl or oxygen-containing heterocyclic ring optionally substituted, in addition to the R^{10} group, with one or more substituents selected from OH and F; and R^{10} is CN or C_{1-4} alkyl substituted with one or more substituents selected from OH, a 3- to 6-membered cycloalkyl group optionally substituted with OH and a 3- to 6-membered heterocyclic group optionally substituted with OH; or

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R^8 and R^9 together with the carbon atom to which they are attached form an ethenyl group optionally substituted with one or two halogen substituents; or

20

R^8 , R^9 and R^{10} together with the carbon atom to which they are attached form a 5- to 8-membered fused or bridged carbocyclic ring system substituted with one or more CH_2OH substituents and optionally with one or more further substituents selected from OH and F.

25 3. A compound according to claim 2 wherein either:

R^8 and R^9 together with the carbon atom to which they are attached form a 3- to 6-membered cycloalkyl or oxygen-containing heterocyclic ring system which is unsubstituted except for the R^{10} group; and R^{10} is selected from CN and CH_2OH ; or

30 R^8 , R^9 and R^{10} together with the carbon atom to which they are attached form a 5- to 8-membered fused or bridged carbocyclic ring system substituted with CH_2OH .

4. A compound according to claim 1 wherein:

R^8 is methyl or ethyl, either of which is optionally substituted with one or more halogen substituents; and

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R⁹ is OH, CH₂OH or methyl or ethyl, either of which is optionally substituted with one or more halogen substituents; or

R⁸ and R⁹ together with the carbon atom to which they are attached form a 3- to 6-membered cycloalkyl or oxygen-containing heterocyclic ring optionally substituted, in addition to the R¹⁰ group, with one or more substituents selected from OH and F, and R¹⁰ is H, OH or C₁₋₄ alkyl optionally substituted with one or more halo substituents; or

R⁸, R⁹ and R¹⁰ together with the carbon atom to which they are attached form a 5- to 8-membered fused or bridged carbocyclic ring system optionally substituted with one or more substituents selected from OH and F.

5. A compound according to claim 4 wherein:

R⁸ is methyl or ethyl, R⁹ is OH or CH₂OH and R¹⁰ is methyl or ethyl;

R⁸ is methyl or ethyl, R⁹ is methyl or ethyl and R¹⁰ is OH or C₁₋₄ alkyl substituted with OH; or

R⁸, R⁹ and R¹⁰ are all methyl.

6. A compound according to any one of claims 1 to 5 wherein R¹ is methyl, difluoromethyl, trifluoromethyl, ethynyl or CN.

7. A compound according to any one of claims 1 to 6 wherein either:

R² is methyl and/or R³ is H or methyl; or

R² and R³ together with the carbon atom to which they are attached form a 3- to 6-membered cycloalkyl or oxygen-containing heterocyclic ring system, optionally substituted, in addition to R¹, with one or more substituents selected from OH, halo, C₁₋₄ alkyl and C₁₋₄ haloalkyl; or

R¹ is H and R² and R³ together with the carbon atom to which they are attached form a 4- to 6-membered carbocyclic ring substituted with OH; or

R¹ is trifluoromethyl; and R² and R³ together with the carbon atom to which they are attached form a cyclopropyl ring which is unsubstituted except for R¹.

8. A compound according to any one of claims 1 to 7 wherein:

R⁴ is H; and/or

each of R⁵ and R⁷ is H; and/or

R⁶ is H, halo, CN, CH₃, CF₃, CHF₂, CH₂F or CH₂OH.

- 5 9. A compound according to any one of claims 1 to 8 wherein R⁸ is methyl or ethyl, especially methyl; and R⁹ is methyl, CH₂OH or OH; or
R⁸ and R⁹ are each independently methyl or ethyl; or

10 R⁸ and R⁹ together with the carbon atom to which they are attached form a 3- to 6-membered cycloalkyl or oxygen-containing heterocyclic ring, wherein the ring is unsubstituted except for the R¹⁰ moiety and is selected from cycloalkyl rings and heterocyclic rings having a single ring oxygen atom.

- 15 10. A compound according to any one of claims 1 or 4 to 9, wherein R¹⁰ is selected from CN, cyclopropyl, cyclobutyl, unsubstituted methyl or methyl substituted with one or more substituents selected from fluoro, OH and a 3- to 6-membered cycloalkyl or heterocyclyl group.

- 20 11. A compound according to any one of claims 1 to 10 wherein R⁸ and R⁹ together with the carbon atom to which they are attached form a cyclopropyl, cyclobutyl, cyclopentyl or oxetanyl ring, which is either unsubstituted except for the R¹⁰ group or has a single CH₂OH substituent in addition to the R¹⁰ group; and R¹⁰ is methyl, CH₂OH, trifluoromethyl or cyano.

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12. A compound according to any one of claims 1 to 11 wherein R⁸, R⁹ and R¹⁰ together with the carbon atom to which they are attached form a bridged ring system such as bicyclo[1.1.1]pentane, bicyclo[2.1.1]hexane or bicyclo[2.2.1]heptane, wherein the ring is unsubstituted or is substituted with a single CH₂OH substituent.

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13. A compound according to claim 1 selected from:

4-[[2-(4-*tert*-Butyl-2-fluoro-5-hydroxy-phenyl)acetyl]amino]-N-(1-methylcyclopropyl)pyridine-2-carboxamide (Compound 1);

- 35 4-[[2-(4-*tert*-Butyl-2-fluoro-5-hydroxy-phenyl)acetyl]amino]-N-(1,1-dimethylprop-2-ynyl)pyridine-2-carboxamide (Compound 1.1);

- 4-[[2-(4-*tert*-Butyl-2-fluoro-5-hydroxy-phenyl)acetyl]amino]-N-(1-ethynylcyclopentyl)pyridine-2-carboxamide (Compound 1.2);
- 4-[[2-(4-*tert*-Butyl-2-fluoro-5-hydroxy-phenyl)acetyl]amino]-N-(1-cyanoethyl)pyridine-2-carboxamide (Compound 1.3);
- 5 4-[[2-(4-*tert*-Butyl-2-fluoro-5-hydroxy-phenyl)acetyl]amino]-N-[(1R)-1-cyanoethyl]pyridine-2-carboxamide (Compound 1.3a/b);
- 4-[[2-(4-*tert*-butyl-2-fluoro-5-hydroxy-phenyl)acetyl]amino]-N-[(1S)-1-cyanoethyl]pyridine-2-carboxamide (Compound 1.3 a/b);
- 4-[[2-(4-*tert*-Butyl-2-fluoro-5-hydroxy-phenyl)acetyl]amino]-N-(1-cyano-1-methyl-ethyl)pyridine-2-carboxamide (Compound 1.4);
- 10 4-[[2-(4-*tert*-Butyl-2-fluoro-5-hydroxy-phenyl)acetyl]amino]-N-(1-cyanocyclopropyl)pyridine-2-carboxamide (Compound 1.5);
- 4-[[2-(4-*tert*-Butyl-2-fluoro-5-hydroxy-phenyl)acetyl]amino]-N-(1-cyano-2-hydroxy-1-methyl-ethyl)pyridine-2-carboxamide (Compound 1.6);
- 15 4-[[2-(4-*tert*-Butyl-2-fluoro-5-hydroxy-phenyl)acetyl]amino]-N-[(1R)-1-cyano-2-hydroxy-1-methyl-ethyl]pyridine-2-carboxamide (Compound 1.6 a/b);
- 4-[[2-(4-*tert*-butyl-2-fluoro-5-hydroxy-phenyl)acetyl]amino]-N-[(1S)-1-cyano-2-hydroxy-1-methyl-ethyl]pyridine-2-carboxamide (Compound 1.6 a/b);
- 4-[[2-(4-*tert*-Butyl-2-fluoro-5-hydroxy-phenyl)acetyl]amino]-N-[1-(trifluoromethyl)cyclopropyl]pyridine-2-carboxamide (Compound 1.7);
- 20 4-[[2-[2-Fluoro-5-hydroxy-4-(1-hydroxy-1-methyl-ethyl)phenyl]acetyl]amino]-N-[1-(trifluoromethyl)cyclopropyl]pyridine-2-carboxamide (Compound 2);
- N-(1-Cyano-1-methyl-ethyl)-4-[[2-[2-fluoro-5-hydroxy-4-(1-hydroxy-1-methyl-ethyl)phenyl]acetyl]amino]pyridine-2-carboxamide (Compound 2.1);
- 25 N-*tert*-Butyl-4-[[2-[4-(1-cyano-1-methyl-ethyl)-2-fluoro-5-hydroxy-phenyl]acetyl]amino]pyridine-2-carboxamide (Compound 2.2);
- 4-[[2-[4-(1-Cyano-1-methyl-ethyl)-2-fluoro-5-hydroxy-phenyl]acetyl]amino]-N-[1-(trifluoromethyl)cyclopropyl]pyridine-2-carboxamide (Compound 2.3);
- N-*tert*-Butyl-4-[[2-[4-(1-cyanocyclopropyl)-2-fluoro-5-hydroxy-phenyl]acetyl]amino]pyridine-2-carboxamide (Compound 2.4);
- 30 N-(1-Cyano-1-methyl-ethyl)-4-[[2-[4-(1,1-dimethyl-2-morpholino-ethyl)-2-fluoro-5-hydroxy-phenyl]acetyl]amino]pyridine-2-carboxamide (Compound 2.5);
- 4-[[2-[2-fluoro-5-hydroxy-4-(2-hydroxy-1,1-dimethyl-ethyl)phenyl]acetyl]amino]-N-[1-(trifluoromethyl)cyclopropyl]pyridine-2-carboxamide (Compound 2.6);
- 35 N-(1-Cyano-1-methyl-ethyl)-4-[[2-[2-fluoro-5-hydroxy-4-(2,2,2-trifluoro-1-hydroxy-1-

- methyl-ethyl)phenyl]acetyl]amino]pyridine-2-carboxamide (Compound 2.7);
- 4-[[2-[4-(1-Cyclopropyl-1-hydroxy-ethyl)-2-fluoro-5-hydroxy-phenyl]acetyl] amino]-N-[1-(trifluoromethyl)cyclopropyl]pyridine-2-carboxamide (Compound 2.8);
- 4-[[2-[4-(4-Cyanotetrahydropyran-4-yl)-2-fluoro-5-hydroxy-phenyl]acetyl] amino]-N-[1-(trifluoromethyl)cyclopropyl]pyridine-2-carboxamide (Compound 2.9);
- 5 4-[[2-[2-Fluoro-5-hydroxy-4-[2-(trifluoromethyl)oxetan-2-yl]phenyl] acetyl]amino]-N-[1-(trifluoromethyl)cyclopropyl]pyridine-2-carboxamide (Compound 2.10);
- 4-[[2-[2-Fluoro-5-hydroxy-4-(1-hydroxy-1-methyl-propyl)phenyl] acetyl]amino]-N-[1-(trifluoromethyl)cyclopropyl]pyridine-2-carboxamide (Compound 2.11);
- 10 4-[[2-[2-Fluoro-5-hydroxy-4-[(1S)-1-hydroxy-1-methyl-propyl]phenyl]acetyl] amino]-N-[1-(trifluoromethyl)cyclopropyl]pyridine-2-carboxamide (Compound 2.11 a/b);
- 4-[[2-[2-fluoro-5-hydroxy-4-[(1R)-1-hydroxy-1-methyl-propyl]phenyl]acetyl]amino]-N-[1-(trifluoromethyl)cyclopropyl] pyridine-2-carboxamide (Compound 2.11 a/b);
- 4-[[2-[5-Hydroxy-4-(1-hydroxy-1-methyl-ethyl)-2-methyl-phenyl]acetyl]amino]-N-[1-(trifluoromethyl)cyclopropyl]pyridine-2-carboxamide (Compound 2.12);
- 15 4-[[2-[2-Fluoro-5-hydroxy-4-[1-(hydroxymethyl)cyclobutyl]phenyl]acetyl]amino]-N-[1-(trifluoromethyl)cyclopropyl]pyridine-2-carboxamide (Compound 2.13);
- N-(1-Cyano-1-methyl-ethyl)-4-[[2-[2-fluoro-5-hydroxy-4-[2-(trifluoromethyl)oxetan-2-yl]phenyl]acetyl]amino]pyridine-2-carboxamide (Compound 2.14);
- 20 4-[[2-[2-Fluoro-5-hydroxy-4-[4-(hydroxymethyl)tetrahydropyran-4-yl]phenyl]acetyl] amino]-N-[1-(trifluoromethyl)cyclopropyl]pyridine-2-carboxamide (Compound 2.15);
- 4-[[2-[2-Fluoro-5-hydroxy-4-[1-(hydroxymethyl)cyclopropyl]phenyl]acetyl]amino]-N-[1-(trifluoromethyl)cyclopropyl]pyridine-2-carboxamide (Compound 2.16);
- 4-[[2-(4-*tert*-Butyl-2-fluoro-5-hydroxy-phenyl)acetyl]amino]-N-(1-cyano-1-methyl-ethyl)-5-fluoro-pyridine-2-carboxamide (Compound 3);
- 25 N-(1-Cyanocyclopropyl)-4-[[2-[2-deuterio-6-fluoro-3-hydroxy-4-[2,2,2-trideuterio-1,1-bis(trideuteriomethyl)ethyl]phenyl]acetyl]amino]pyridine-2-carboxamide (Compound 4);
- N-(1-Cyano-1-methyl-ethyl)-4-[[2-[2-fluoro-5-hydroxy-4-(1-methylcyclobutyl)phenyl]acetyl]amino]pyridine-2-carboxamide (Compound 5);
- 30 N-*tert*-Butyl-4-[[2-(4-*tert*-butyl-5-hydroxy-2-isopropyl-phenyl)acetyl]amino] pyridine-2-carboxamide (Compound 6);
- N-*tert*-Butyl-4-[[2-[2-fluoro-5-hydroxy-4-(1-hydroxy-1-methyl-ethyl)phenyl] acetyl]amino]pyridine-2-carboxamide (Compound 7);
- 4-[[2-(2-Fluoro-5-hydroxy-4-isopropenyl-phenyl)acetyl]amino]-N-[1-(trifluoromethyl)cyclopropyl]pyridine-2-carboxamide (Compound 7.1);
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- N-*tert*-Butyl-4-[[2-[2-fluoro-5-hydroxy-4-(1-methylcyclopropyl)phenyl]acetyl]amino]pyridine-2-carboxamide (Compound 8);
- N-(1-Cyanocyclopropyl)-4-[[2-[2-fluoro-5-hydroxy-4-[1-(trifluoromethyl)cyclopropyl]phenyl]acetyl]amino]pyridine-2-carboxamide (Compound 9);
- 5 4-[[2-(4-*tert*-Butyl-2-chloro-5-hydroxy-phenyl)acetyl]amino]-N-(1-cyano-1-methyl-ethyl)pyridine-2-carboxamide (Compound 10);
- 4-[[2-(4-*tert*-Butyl-2-chloro-5-hydroxy-phenyl)acetyl]amino]-N-[1-(trifluoromethyl)cyclopropyl]pyridine-2-carboxamide (Compound 10.1);
- 4-[[2-(4-*tert*-Butyl-2-chloro-5-hydroxy-phenyl)acetyl]amino]-N-(1-cyanocyclopropyl)pyridine-2-carboxamide (Compound 10.2);
- 10 4-[[2-[2-Fluoro-5-hydroxy-4-(3-hydroxy-1,1-dimethyl-propyl)phenyl]acetyl]amino]-N-[1-(trifluoromethyl)cyclopropyl]pyridine-2-carboxamide (Compound 11);
- N-(4-Cyanotetrahydropyran-4-yl)-4-[[2-[2-fluoro-5-hydroxy-4-(2-hydroxy-1,1-dimethyl-ethyl)phenyl]acetyl]amino]pyridine-2-carboxamide (Compound 12);
- 15 4-[[2-[2-Fluoro-5-hydroxy-4-(2-hydroxy-1,1-dimethyl-ethyl)phenyl]acetyl]amino]-N-[3-(trifluoromethyl)oxetan-3-yl]pyridine-2-carboxamide (Compound 12.1);
- 4-[[2-[2-Fluoro-5-hydroxy-4-(2-hydroxy-1,1-dimethyl-ethyl)phenyl]acetyl]amino]-N-[(1S,2S)-2-hydroxycyclopentyl]pyridine-2-carboxamide (Compound 12.2);
- 4-[[2-[2-Fluoro-5-hydroxy-4-(2-hydroxy-1,1-dimethyl-ethyl)phenyl]acetyl]amino]-N-(2-hydroxy-1,1-dimethyl-ethyl)pyridine-2-carboxamide (Compound 12.3);
- 20 4-[[2-[2-Fluoro-5-hydroxy-4-(2-hydroxy-1,1-dimethyl-ethyl)phenyl]acetyl]amino]-N-[1-(hydroxymethyl)cyclobutyl]pyridine-2-carboxamide (Compound 12.4);
- 4-[[2-[2-Fluoro-5-hydroxy-4-(4-hydroxytetrahydropyran-4-yl)phenyl]acetyl]amino]-N-[1-(trifluoromethyl)cyclopropyl]pyridine-2-carboxamide (Compound 13);
- 25 4-[[2-[2-Chloro-5-hydroxy-4-(2-hydroxy-1,1-dimethyl-ethyl)phenyl]acetyl]amino]-N-[1-(trifluoromethyl)cyclopropyl]pyridine-2-carboxamide (Compound 14);
- 4-[[2-[5-Hydroxy-4-(2-hydroxy-1,1-dimethyl-ethyl)-2-methyl-phenyl]acetyl]amino]-N-[1-(trifluoromethyl)cyclopropyl]pyridine-2-carboxamide (Compound 14.1);
- N-(3,3-Difluoro-1-methyl-cyclobutyl)-4-[[2-[2-fluoro-5-hydroxy-4-(2-hydroxy-1,1-dimethyl-ethyl)phenyl]acetyl]amino]pyridine-2-carboxamide (Compound 15);
- 30 4-[[2-[2-Chloro-5-hydroxy-4-(2-hydroxy-1,1-dimethyl-ethyl)phenyl]acetyl]amino]-N-(1,1-dimethylprop-2-ynyl)pyridine-2-carboxamide (Compound 15.1);
- 4-[[2-[2-Chloro-5-hydroxy-4-(2-hydroxy-1,1-dimethyl-ethyl)phenyl]acetyl]amino]-N-(3,3-difluoro-1-methyl-cyclobutyl)pyridine-2-carboxamide (Compound 15.2);
- 35 4-[[2-[2-Chloro-5-hydroxy-4-(2-hydroxy-1,1-dimethyl-ethyl)phenyl]acetyl]amino]-N-[1-

- (difluoromethyl)cyclopropyl]pyridine-2-carboxamide (Compound 15.3);
 N-[1-(Difluoromethyl)cyclopropyl]-4-[[2-[2-fluoro-5-hydroxy-4-(2-hydroxy-1,1-dimethyl-ethyl)phenyl]acetyl]amino]pyridine-2-carboxamide (Compound 15.4);
 N-(1,1-Dimethylprop-2-ynyl)-4-[[2-[2-fluoro-5-hydroxy-4-(2-hydroxy-1,1-dimethyl-ethyl)phenyl]acetyl]amino]pyridine-2-carboxamide (Compound 16);
 4-[[2-[2-Fluoro-5-hydroxy-4-(2-hydroxy-1,1-dimethyl-ethyl)phenyl]acetyl]amino]-N-(4-methyltetrahydropyran-4-yl)pyridine-2-carboxamide (Compound 16.1);
 N-(1-Cyano-1-methyl-ethyl)-4-[[2-[2-fluoro-5-hydroxy-4-(2-hydroxy-1,1-dimethyl-ethyl)phenyl]acetyl]amino]pyridine-2-carboxamide (Compound 16.2);
 4-[[2-[2-Fluoro-5-hydroxy-4-(2-hydroxy-1-methyl-ethyl)phenyl]acetyl]amino]-N-(4-methyltetrahydropyran-4-yl)pyridine-2-carboxamide (Compound 16.3);
 4-[[2-[2,6-Difluoro-3-hydroxy-4-(2-hydroxy-1,1-dimethyl-ethyl)phenyl]acetyl]amino]-N-[1-(trifluoromethyl)cyclopropyl]pyridine-2-carboxamide (Compound 16.4);
 4-[[2-[2-Fluoro-5-hydroxy-4-[2,2,2-trifluoro-1-(hydroxymethyl)ethyl]phenyl]acetyl] amino]-N-[1-(trifluoromethyl)cyclopropyl]pyridine-2-carboxamide (Compound 17);
 4-[[2-[2-Chloro-6-fluoro-3-hydroxy-4-(1-hydroxy-1-methyl-ethyl)phenyl]acetyl]amino]-N-[1-(trifluoromethyl)cyclopropyl]pyridine-2-carboxamide (Compound 18);
 4-[[2-[2-Chloro-5-hydroxy-4-(1-hydroxy-1-methyl-ethyl)phenyl]acetyl]amino]-N-[1-(trifluoromethyl)cyclopropyl]pyridine-2-carboxamide (Compound 19);
 4-[[2-[2-Fluoro-5-hydroxy-4-(2-hydroxy-1-methyl-ethyl)phenyl]acetyl]amino]-N-[1-(trifluoromethyl)cyclopropyl]pyridine-2-carboxamide (Compound 20);
 4-[[2-[2-Fluoro-5-hydroxy-4-[(1S)-2-hydroxy-1-methyl-ethyl]phenyl]acetyl] amino]-N-[1-(trifluoromethyl)cyclopropyl]pyridine-2-carboxamide (Compound 20a/b);
 4-[[2-[2-fluoro-5-hydroxy-4-[(1R)-2-hydroxy-1-methyl-ethyl]phenyl]acetyl]amino]-N-[1-(trifluoromethyl)cyclopropyl] pyridine-2-carboxamide (Compound 20a/b);
 and salts and solvates of the above.

14. A compound according to any one of claims 1 to 13 for use in medicine.
15. A compound according to any one of claims 1 to 13 for use in the treatment or prophylaxis of diseases and conditions affected by modulation of TMEM16A.
16. The use of a compound according to any one of claims 1 to 13 in the manufacture of a medicament for the treatment or prophylaxis of diseases and conditions affected by modulation of TMEM16A.

17. A method for the treatment or prophylaxis of diseases and conditions affected by modulation of TMEM16A, the method comprising administering to a patient in need of such treatment an effective amount of a compound according to any one of claims 1 to 13.

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18. A compound for use, a use or a method according to any one of claims 14 to 17, wherein the diseases and conditions affected by modulation of TMEM16A are selected from respiratory diseases and conditions, dry mouth (xerostomia), intestinal hypermobility, cholestasis and ocular conditions.

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19. A compound for use, a use or a method according to claim 18, wherein: the respiratory disease and conditions are selected from cystic fibrosis, chronic obstructive pulmonary disease (COPD), chronic bronchitis, emphysema, bronchiectasis, including non-cystic fibrosis bronchiectasis, asthma and primary ciliary dyskinesia; and/or

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the dry mouth (xerostomia) results from Sjorgens syndrome, radiotherapy treatment or xerogenic drugs; and/or

the intestinal hypermobility is associated with gastric dyspepsia, gastroparesis, chronic constipation or irritable bowel syndrome; and/or

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the ocular disease is dry eye disease.

20. A pharmaceutical composition comprising a compound according to any one of claims 1 to 13 and a pharmaceutically acceptable excipient.

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21. A pharmaceutical composition according to claim 20, further comprising an additional active agent useful in the treatment or prevention of respiratory conditions as a combined preparation for simultaneous, sequential or separate use in the treatment of a disease or condition affected by modulation of TMEM16A.

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22. A product comprising a compound according to any one of claims 1 to 13 and an additional agent useful in the treatment or prevention of respiratory conditions as a combined preparation for simultaneous, sequential or separate use in the treatment of a disease or condition affected by modulation of TMEM16A.

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23. A pharmaceutical composition according to claim 21 or a product according to claim 22, wherein the additional active agent is selected from:
- β 2 adrenoreceptor agonists such as metaproterenol, isoproterenol, isoprenaline, albuterol, salbutamol, formoterol, salmeterol, indacaterol, terbutaline, orciprenaline, bitolterol mesylate, pirbuterol, olodaterol, vilanterol and abediterol;
- antihistamines, for example histamine H₁ receptor antagonists such as loratadine, cetirizine, desloratadine, levocetirizine, fexofenadine, astemizole, azelastine and chlorpheniramine or H₄ receptor antagonists;
- dornase alpha;
- corticosteroids such as prednisone, prednisolone, flunisolide, triamcinolone acetonide, beclomethasone dipropionate, budesonide, fluticasone propionate mometasone furoate and fluticasone furoate;
- Leukotriene antagonists such as montelukast and zafirlukast;
- anticholinergic compounds, particularly muscarinic antagonists such as ipratropium, tiotropium, glycopyrrolate, aclidinium and umeclidinium;
- CFTR repair therapies (e.g. CFTR potentiators, correctors or amplifiers) such as Ivacaftor, QBW251, Bamacaftor (VX659), Elexacaftor (VX445), VX561/CPT-656, VX152, VX440, GLP2737, GLP2222, GLP2451, PTI438, PTI801, PTI808, FDL-169 and FDL-176 and CFTR correctors such as Lumacaftor and Tezacaftor or combinations thereof (for example a combination of Ivacaftor, Tezacaftor and Elexacaftor);
- ENaC modulators, particularly ENaC inhibitors such as amiloride, VX-371, AZD5634, QBW276, SPX-101, BI443651, BI1265162, ETD001 and compounds having a cation selected from:
- 2-[(3-amino-5*H*-pyrrolo[2,3-*b*]pyrazin-2-yl)formamido) ethyl]-6-(4-{bis[(2*S*,3*R*,4*R*,5*R*)-2,3,4,5,6-pentahydroxyhexyl]amino}piperidine-1-carbonyl)-1,3-diethyl-1*H*-1,3-benzodiazol-3-ium;
- 2-[(3-amino-5*H*-pyrrolo[2,3-*b*]pyrazin-2-yl)formamido) methyl]-6-[[2-(4-{bis[(2*S*,3*R*,4*R*,5*R*)-2,3,4,5,6-pentahydroxyhexyl]amino}piperidin-1-yl)ethyl]carbamoyl]-1,3-diethyl-1*H*-1,3-benzodiazol-3-ium;
- 2-[(3-amino-5*H*-pyrrolo[2,3-*b*]pyrazin-2-yl)formamido)methyl]-5-[4-({bis[(2*S*,3*R*,4*R*,5*R*)-2,3,4,5,6-pentahydroxyhexyl]amino)methyl]piperidine-1-carbonyl)-1,3-diethyl-1*H*-1,3-benzodiazol-3-ium;
- 2-[(3-amino-5*H*-pyrrolo[2,3-*b*]pyrazin-2-yl)formamido)methyl]-6-[(3*R*)-3-{bis[(2*S*,3*R*,4*R*,5*R*)-2,3,4,5,6-pentahydroxyhexyl]amino}pyrrolidine-1-carbonyl]-1,3-

diethyl-1*H*-1,3-benzodiazol-3-ium;

2-[(3-amino-5*H*-pyrrolo[2,3-*b*]pyrazin-2-yl)formamido)methyl]-6-[(3*S*)-3-{bis[(2*S*,3*R*,4*R*,5*R*)-2,3,4,5,6-pentahydroxyhexyl]amino}pyrrolidine-1-carbonyl]-1,3-diethyl-1*H*-1,3-benzodiazol-3-ium;

5 2-[(3-amino-5*H*-pyrrolo[2,3-*b*]pyrazin-2-yl)formamido)methyl]-1,3-diethyl-6-[(1*r*,4*r*)-4-{bis[(2*S*,3*R*,4*R*,5*R*)-2,3,4,5,6-pentahydroxyhexyl]amino}cyclohexyl]carbamoyl]-1*H*-1,3-benzodiazol-3-ium;

2-[(3-amino-5*H*-pyrrolo[2,3-*b*]pyrazin-2-yl)formamido)methyl]-1,3-diethyl-6-[(1*s*,4*s*)-4-{bis[(2*S*,3*R*,4*R*,5*R*)-2,3,4,5,6-pentahydroxyhexyl]amino}cyclohexyl]carbamoyl]-1*H*-1,3-benzodiazol-3-ium;

and a suitable anion, for example halide, sulfate, nitrate, phosphate, formate, acetate, trifluoroacetate, fumarate, citrate, tartrate, oxalate, succinate, mandelate, methane sulfonate or *p*-toluene sulfonate;

Antibiotics;

15 Antivirals such as ribavirin and neuraminidase inhibitors such as zanamivir;

Antifungals such as PUR1900;

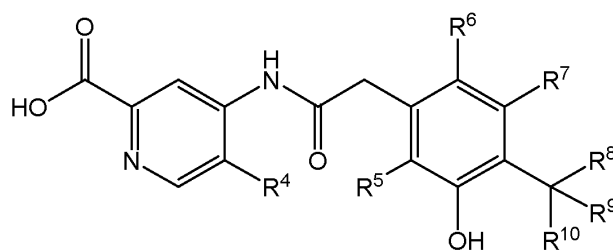
Airway hydrating agents (osmoloytes) such as hypertonic saline and mannitol (Bronchitol®); and

Mucolytic agents such as. N-acetyl cysteine.

20

24. A process for the preparation of a compound according to any one of claims 1 to 13 comprising:

A. reacting a compound of general formula (II):



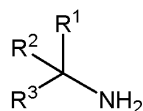
25

(II)

wherein R^4 , R^5 , R^6 , R^7 , R^8 , R^9 and R^{10} are as in claim 1;

with a compound of general formula (III):

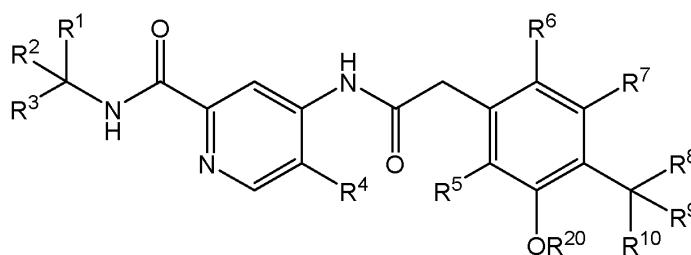
243



(III)

wherein R^1 , R^2 and R^3 are as defined in claim 1; or

- 5 B. deprotecting a compound of general formula (XXI):



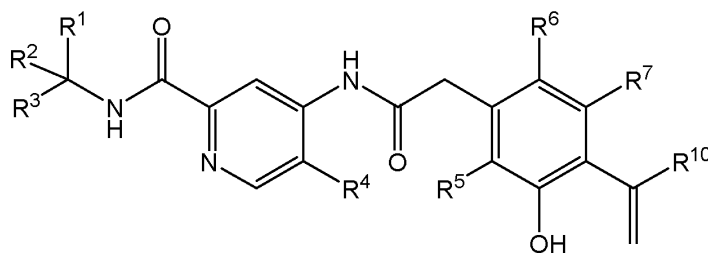
(XXI)

wherein R^1 , R^2 , R^3 , R^4 , R^5 , R^6 , R^7 , R^8 , R^9 and R^{10} are as defined in claim 1; and R^{20} is benzyl; or

10

- C. for a compound of general formula (I) in which R^9 is OH and R^{10} is methyl optionally substituted with halo:

reacting a compound of general formula (L):



(L)

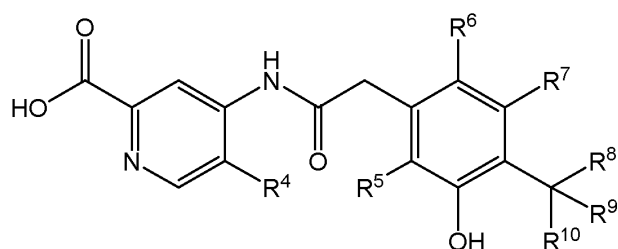
wherein R^1 , R^2 , R^3 , R^4 , R^5 , R^6 and R^7 are as defined in claim 1; and R^{10} is methyl optionally substituted with halo;

with an acid of a leaving group, for example methane sulfonic acid or toluene sulfonic acid;

20 or

- D. converting a compound of general formula (I) to another compound of general formula (I).

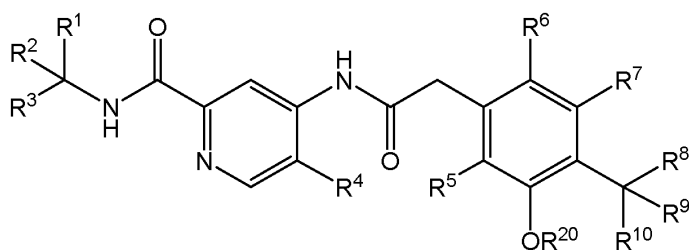
25. A compound of general formula (II):



(II)

wherein R^4 , R^5 , R^6 and R^7 are as defined in claim 1 and R^8 , R^9 and R^{10} are as defined in claim 2; or a salt thereof.

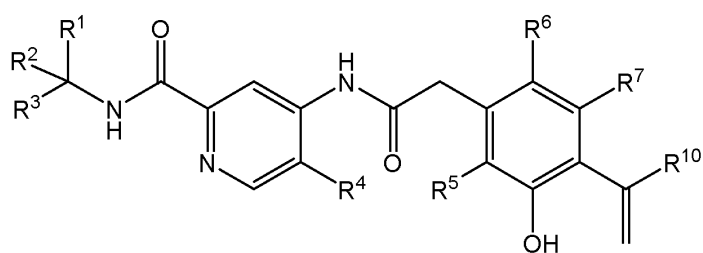
26. A compound of general formula (XXI):



(XXI)

wherein R^1 , R^2 , R^3 , R^4 , R^5 and R^6 are as defined in claim 1, R^7 , R^8 , R^9 and R^{10} are as defined in claim 2 and R^{20} is benzyl; or a salt thereof.

27. A compound of general formula (L):



(L)

wherein R^1 , R^2 , R^3 , R^4 , R^5 , R^6 and R^7 are as defined in claim 1 and R^{10} is methyl optionally substituted with halo; or a salt thereof.