

H;

C₁₋₄ alkyl; and

C₃₋₇ cycloalkyl; and

each R¹⁰ is independently selected from the group consisting of

C₁₋₆ alkyl; and

phenyl; wherein phenyl is optionally substituted with one or more independently selected R^A groups;

each R¹¹ is independently selected from the group consisting of

4-6 membered monocyclic heterocycle comprising 1 or 2 heteroatoms independently selected from the group consisting of O, S, and N; wherein the monocyclic heterocycle is optionally substituted with one or more independently selected R^A groups;

5-6 membered monocyclic heteroaryl comprising 1, 2, or 3 heteroatoms independently selected from the group consisting of O, S, and N; wherein the monocyclic heteroaryl is optionally substituted with one or more independently selected R^A groups;

C₃₋₇ cycloalkyl; wherein the C₃₋₇ cycloalkyl is optionally substituted with one or more independently selected R^A groups; and

phenyl; wherein phenyl is optionally substituted with one or more independently selected R^A groups; and

each R^A is independently selected from the group consisting of

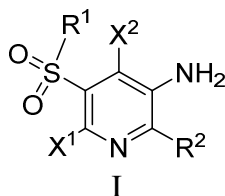
-CN,

halo;

C₁₋₄ alkyl optionally substituted with one or more independently selected halo; and

C₁₋₄ alkoxy optionally substituted with one or more independently selected halo.

[0021a] In another aspect, there is provided a compound of Formula I, or a pharmaceutically acceptable salt thereof,



wherein

X¹ and X² are independently selected

H;

halo;

C₁₋₄ alkyl optionally substituted with one or more independently selected halo;

C₁₋₄ alkoxy optionally substituted with one or more independently selected

-OH;

C₁₋₄ alkoxy; or

-NR^{8A}R^{8B};

-NR^{9A}R^{9B};

cyclopropyl optionally substituted with one or more independently selected R⁵ groups;

phenoxy optionally substituted with one or more independently selected R⁵ groups; or

phenyl optionally substituted with one or more independently selected R⁵ groups;

R¹ is

phenyl optionally substituted with one or more independently selected R⁴ groups; or -NR⁶R⁷;

R² is 5-6 membered monocyclic heteroaryl comprising 1, 2, or 3 heteroatoms independently selected from the group consisting of O, S, and N, wherein the monocyclic heteroaryl is optionally substituted with one or more independently selected R³ groups;

each R³ is independently selected from the group consisting of:

C₁₋₄ alkyl optionally substituted with one or more independently selected

C₃₋₇ cycloalkyl; wherein the C₃₋₇ cycloalkyl is optionally substituted with one or more independently selected R^A groups;

4-6 membered monocyclic heterocycle comprising 1 or 2 heteroatoms independently selected from the group consisting of O, S, and N; wherein the monocyclic heterocycle is optionally substituted with one or more independently selected R^A groups;

phenyl; wherein the phenyl is optionally substituted with one or more independently selected R^A groups;

C₁₋₄ alkoxy optionally substituted with one or more independently selected C₃₋₇ cycloalkyl, halo, or -OCH₃;

-OR¹¹;

-OH;

halo;

-CN;

-OC(O)R¹⁰;

-OS(O)₂OH;

-NHC(=S)R¹¹; or

-OP(O)(OH)(OH);

-C(O)NH₂;

phenyl; wherein the phenyl is optionally substituted with one or more independently selected R^A groups;

5-6 membered monocyclic heteroaryl comprising 1, 2, or 3 heteroatoms independently selected from the group consisting of O, S, and N; wherein the monocyclic heteroaryl is optionally substituted with one or more independently selected R^A groups;

C₃₋₇ cycloalkyl; wherein the C₃₋₇ cycloalkyl is optionally substituted with one or more independently selected R^A groups; and

4-6 membered monocyclic heterocycle comprising 1 or 2 heteroatoms independently selected from the group consisting of O, S, and N; wherein the monocyclic heterocycle is optionally substituted with one or more independently selected R^A groups;

each R⁴ is independently selected from the group consisting of:

halo;

C₁₋₄ alkyl optionally substituted with one or more independently selected halo; and

C₁₋₄ alkoxy optionally substituted with one or more independently selected halo;

each R⁵ is independently selected from the group consisting of:

-OH;

halo;

C₁₋₄ alkyl optionally substituted with one or more independently selected C₁₋₄ alkoxy, halo or -OH; and

C₁₋₄ alkoxy optionally substituted with one or more independently selected halo;

R⁶ is H, C₁₋₄ alkyl, or C₃₋₇ cycloalkyl wherein the C₃₋₇ cycloalkyl is optionally substituted with one or more independently selected R⁵ groups;

R⁷ is

C₁₋₄ alkyl optionally substituted with one or more independently selected halo;

phenyl optionally substituted with one or more independently selected halo;

C₁₋₄ alkyl optionally substituted with one or more independently selected halo; or

C₁₋₄ alkoxy optionally substituted with one or more independently selected halo;
 C₁₋₄ alkoxy optionally substituted with one or more independently selected halo; or
 4-6 membered monocyclic heterocycle comprising 1 or 2 heteroatoms independently
 selected from the group consisting of O, S, and N; wherein the monocyclic
 heterocycle is optionally substituted with one or more independently selected R⁵
 groups;

each R^{8a} and R^{8b} is independently selected from the group consisting of
 H; and
 C₁₋₄ alkyl;

R^{9a} and R^{9b} are independently selected from the group consisting of
 H;
 C₁₋₄ alkyl; and
 C₃₋₇ cycloalkyl; and

each R¹⁰ is independently selected from the group consisting of
 C₁₋₆ alkyl; and
 phenyl; wherein phenyl is optionally substituted with one or more independently selected R^A
 groups;

each R¹¹ is independently selected from the group consisting of
 4-6 membered monocyclic heterocycle comprising 1 or 2 heteroatoms independently selected
 from the group consisting of O, S, and N; wherein the monocyclic heterocycle is
 optionally substituted with one or more independently selected R^A groups;
 5-6 membered monocyclic heteroaryl comprising 1, 2, or 3 heteroatoms independently
 selected from the group consisting of O, S, and N; wherein the monocyclic heteroaryl
 is optionally substituted with one or more independently selected R^A groups;
 C₃₋₇ cycloalkyl; wherein the C₃₋₇ cycloalkyl is optionally substituted with one or more
 independently selected R^A groups; and
 phenyl; wherein phenyl is optionally substituted with one or more independently selected R^A
 groups; and

each R^A is independently selected from the group consisting of
 -CN,
 halo;

C₁₋₄ alkyl optionally substituted with one or more independently selected halo; and

[0022] C₁₋₄ alkoxy optionally substituted with one or more independently selected halo. Another example of the disclosure relates to pharmaceutical compositions comprising a compound of the disclosure, and a pharmaceutical carrier. In one aspect, there is provided a pharmaceutical composition comprising a therapeutically effective amount of a compound disclosed herein, or a pharmaceutically acceptable salt thereof, in combination with a pharmaceutically acceptable carrier. Such compositions can be administered in accordance with a method of the disclosure, typically as part of a therapeutic regimen for treatment or prevention of conditions and disorders related to Cystic Fibrosis Transmembrane Conductance Regulator activity. In a particular example, the pharmaceutical compositions may additionally comprise further therapeutically active ingredients suitable for use in combination with the compounds of the disclosure. In a more particular example, the further therapeutically active ingredient is an agent for the treatment of cystic fibrosis.

[0023] Moreover, the compounds of the disclosure, useful in the pharmaceutical compositions and treatment methods disclosed herein, are pharmaceutically acceptable as prepared and used. In another aspect, there is provided a pharmaceutical composition comprising a compound described herein, or a pharmaceutically acceptable salt thereof, and one or more correctors. In another aspect, there is provided a pharmaceutical composition comprising a compound described herein, or a pharmaceutically acceptable salt thereof, and one or more additional therapeutic agents.

[0024] Yet another example of the disclosure relates to a method for treating, or preventing conditions and disorders related to Cystic Fibrosis Transmembrane Conductance Regulator activity in mammals. More particularly, the method is useful for treating or preventing conditions and disorders related to cystic fibrosis, Sjögren's syndrome, pancreatic insufficiency, chronic obstructive lung disease, or chronic obstructive airway disease. Accordingly, the compounds and compositions of the disclosure are useful as a medicament for treating or preventing Cystic Fibrosis Transmembrane Conductance Regulator modulated disease. In another aspect, there is provided use of a therapeutically effective amount of a compound disclosed herein, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for the treatment of cystic fibrosis in a subject in need thereof. In another aspect, there is provided use of a compound described herein, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for the treatment of cystic fibrosis in a subject in need thereof, wherein the medicament is to be administered with one or more correctors. In another aspect, there is provided use of a compound disclosed herein, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for the treatment of cystic fibrosis in a subject in need thereof, wherein the medicament is to be administered with one or more additional therapeutic agents.

[0025] The compounds, compositions comprising the compounds, methods for making the compounds, and methods for treating or preventing conditions and disorders by administering the compounds are further described herein.

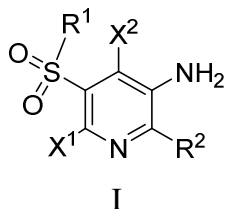
[0026] In a particular example, the compounds of the disclosure are provided for use in the treatment of cystic fibrosis. In a particular example, the compounds of the disclosure are provided for use in the treatment of cystic fibrosis caused by class I, II, III, IV, V, and/or VI mutations.

[0027] The present disclosure also provides pharmaceutical compositions comprising a compound of the disclosure, and a suitable pharmaceutical carrier for use in medicine. In another aspect, there is provided a compound disclosed herein, or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition disclosed herein, for use in medicine. In a particular example, the pharmaceutical composition is for use in the treatment of cystic fibrosis. In another aspect, there is provided a compound disclosed herein, or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition disclosed herein, for use in the treatment of cystic fibrosis. In another aspect, there is provided (5-{3-amino-5-[4-(trifluoromethoxy)benzene-1-sulfonyl]pyridin-2-yl}-1,3,4-oxadiazol-2-yl)methanol, or a pharmaceutically acceptable salt thereof. In another aspect, there is provided (5-{3-amino-5-[4-(trifluoromethoxy)benzene-1-sulfonyl]pyridin-2-yl}-1,3,4-oxadiazol-2-yl)methanol.

[0028] These and other objects of the disclosure are described in the following paragraphs. These objects should not be deemed to narrow the scope of the disclosure.

DETAILED DESCRIPTION OF THE INVENTION

[0029] Described herein are compounds of Formula I,

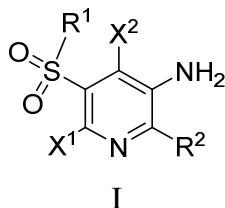


wherein X^1 , X^2 , R^1 , and R^2 are defined above in the Summary and below in the Detailed Description. Further, compositions comprising such compounds and methods for treating conditions and disorders using such compounds and compositions are also included.

[0030] Compounds included herein may contain one or more variable(s) that occur more than one time in any substituent or in the formulae herein. Definition of a variable on each

WHAT IS CLAIMED IS:

1. A compound of Formula I, or a pharmaceutically acceptable salt thereof,



wherein

X^1 and X^2 are independently selected

H;

halo;

C_{1-4} alkyl optionally substituted with one or more independently selected halo;

C_{1-4} alkoxy optionally substituted with one or more independently selected

-OH;

C_{1-4} alkoxy; or

$-NR^{8A}R^{8B}$;

$-NR^{9A}R^{9B}$;

cyclopropyl optionally substituted with one or more independently selected R^5 groups;

phenoxy optionally substituted with one or more independently selected R^5 groups; or

phenyl optionally substituted with one or more independently selected R^5 groups;

R^1 is

phenyl optionally substituted with one or more independently selected R^4 groups; or $-NR^6R^7$;

R^2 is 5-6 membered monocyclic heteroaryl comprising 1, 2, or 3 heteroatoms independently selected from the group consisting of O, S, and N, wherein the monocyclic heteroaryl is optionally substituted with one or more independently selected R^3 groups;

each R^3 is independently selected from the group consisting of:

C_{1-4} alkyl optionally substituted with one or more independently selected

C_{3-7} cycloalkyl; wherein the C_{3-7} cycloalkyl is optionally substituted with one or more independently selected R^A groups;

4-6 membered monocyclic heterocycle comprising 1 or 2 heteroatoms independently selected from the group consisting of O, S, and N; wherein the monocyclic heterocycle is optionally substituted with one or more independently selected R^A groups;

phenyl; wherein the phenyl is optionally substituted with one or more independently selected R^A groups;

C₁₋₄ alkoxy optionally substituted with one or more independently selected C₃₋₇ cycloalkyl, halo, or -OCH₃;

-OR¹¹;

-OH;

halo;

-CN;

-OC(O)R¹⁰;

-OS(O)₂OH;

-NHC(=S)R¹¹; or

-OP(O)(OH)(OH);

-C(O)NH₂;

phenyl; wherein the phenyl is optionally substituted with one or more independently selected R^A groups;

5-6 membered monocyclic heteroaryl comprising 1, 2, or 3 heteroatoms independently selected from the group consisting of O, S, and N; wherein the monocyclic heteroaryl is optionally substituted with one or more independently selected R^A groups;

C₃₋₇ cycloalkyl; wherein the C₃₋₇ cycloalkyl is optionally substituted with one or more independently selected R^A groups; and

4-6 membered monocyclic heterocycle comprising 1 or 2 heteroatoms independently selected from the group consisting of O, S, and N; wherein the monocyclic heterocycle is optionally substituted with one or more independently selected R^A groups;

each R⁴ is independently selected from the group consisting of:

halo;

C₁₋₄ alkyl optionally substituted with one or more independently selected halo; and

C₁₋₄ alkoxy optionally substituted with one or more independently selected halo;

each R⁵ is independently selected from the group consisting of:

-OH;

halo;

C₁₋₄ alkyl optionally substituted with one or more independently selected C₁₋₄ alkoxy, halo or -OH; and

C₁₋₄ alkoxy optionally substituted with one or more independently selected halo;

R⁶ is H, C₁₋₄ alkyl, or C₃₋₇ cycloalkyl wherein the C₃₋₇ cycloalkyl is optionally substituted with one or more independently selected R⁵ groups;

R⁷ is

C₁₋₄ alkyl optionally substituted with one or more independently selected halo;

phenyl optionally substituted with one or more independently selected halo;

C₁₋₄ alkyl optionally substituted with one or more independently selected halo; or

C₁₋₄ alkoxy optionally substituted with one or more independently selected halo;

C₁₋₄ alkoxy optionally substituted with one or more independently selected halo; or

4-6 membered monocyclic heterocycle comprising 1 or 2 heteroatoms independently selected from the group consisting of O, S, and N; wherein the monocyclic heterocycle is optionally substituted with one or more independently selected R⁵ groups;

each R^{8a} and R^{8b} is independently selected from the group consisting of

H; and

C₁₋₄ alkyl;

R^{9a} and R^{9b} are independently selected from the group consisting of

H;

C₁₋₄ alkyl; and

C₃₋₇ cycloalkyl; and

each R¹⁰ is independently selected from the group consisting of

C₁₋₆ alkyl; and

phenyl; wherein phenyl is optionally substituted with one or more independently selected R^A groups;

each R¹¹ is independently selected from the group consisting of

4-6 membered monocyclic heterocycle comprising 1 or 2 heteroatoms independently selected from the group consisting of O, S, and N; wherein the monocyclic heterocycle is optionally substituted with one or more independently selected R^A groups;

5-6 membered monocyclic heteroaryl comprising 1, 2, or 3 heteroatoms independently selected from the group consisting of O, S, and N; wherein the monocyclic heteroaryl is optionally substituted with one or more independently selected R^A groups;

C₃₋₇ cycloalkyl; wherein the C₃₋₇ cycloalkyl is optionally substituted with one or more independently selected R^A groups; and

phenyl; wherein phenyl is optionally substituted with one or more independently selected R^A groups; and

each R^A is independently selected from the group consisting of

-CN,

halo;

C₁₋₄ alkyl optionally substituted with one or more independently selected halo; and

C₁₋₄ alkoxy optionally substituted with one or more independently selected halo.

2. The compound of claim 1, or a pharmaceutically acceptable salt thereof, wherein R¹ is phenyl optionally substituted with one independently selected R⁴ group.
3. The compound of claim 1, or a pharmaceutically acceptable salt thereof, wherein R¹ is phenyl substituted with one -OCF₃.
4. The compound of claim 1, or a pharmaceutically acceptable salt thereof, wherein X¹ and X² are each H.
5. The compound of claim 1, or a pharmaceutically acceptable salt thereof, wherein R² is 5-6 membered monocyclic heteroaryl comprising 1, 2, or 3 heteroatoms independently selected from the group consisting of O, S, and N, wherein the monocyclic heteroaryl is optionally substituted with one R³ group.

6. The compound of claim 1, or a pharmaceutically acceptable salt thereof, wherein R^2 is 1,3,4-oxadiazolyl, 1,2,4-oxadiazolyl, 1,3,4-thiadiazolyl, or thiazolyl wherein the 1,3,4-oxadiazolyl, 1,2,4-oxadiazolyl, 1,3,4-thiadiazolyl, and thiazolyl are substituted with one independently selected R^3 .

7. The compound of claim 5, or a pharmaceutically acceptable salt thereof, wherein R^3 is C_{1-4} alkyl optionally substituted with one or more independently selected

-OH;

halo; or

-OP(O)(OH)(OH).

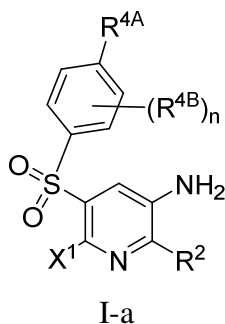
8. The compound of claim 6, or a pharmaceutically acceptable salt thereof, wherein R^3 is C_{1-4} alkyl optionally substituted with one or more independently selected

-OH;

halo; or

-OP(O)(OH)(OH).

9. The compound of claim 1 of Formula I-a, or a pharmaceutically acceptable salt thereof,



wherein

n is 0, 1, or 2;

R^{4A} is H, F, $-CH_3$, $-CH(CH_3)_2$, $t\text{-Bu}$, CF_3 , $-OCH_3$, $-OCH(CH_3)_2$, or $-OCF_3$;

each R^{4B} is independently F or $-OCF_3$; and

X^1 and R^2 are as set forth in claim 1.

10. The compound of claim 9, or a pharmaceutically acceptable salt thereof, wherein X^1 is H.

11. The compound of claim 9, or a pharmaceutically acceptable salt thereof, wherein

n is 0; and

R^{4A} is -OCF₃.

12. The compound of claim 9, or a pharmaceutically acceptable salt thereof, wherein

X¹ is H;

n is 0;

R^{4A} is -OCF₃;

R² is 1,3,4-oxadiazolyl or thiazolyl substituted with one R³; and

R³ is C₁₋₄ alkyl optionally substituted with one or more independently selected

-OH;

halo; or

-OP(O)(OH)(OH).

13. The compound of claim 1, or a pharmaceutically acceptable salt thereof, wherein the compound is selected from the group consisting of:

(5-{3-amino-5-[4-(trifluoromethoxy)benzene-1-sulfonyl]pyridin-2-yl}-1,3,4-oxadiazol-2-yl)methanol;

(5-{3-amino-5-[4-(trifluoromethoxy)benzene-1-sulfonyl]pyridin-2-yl}-1,3,4-oxadiazol-2-yl)methyldihydrogenphosphate;

2-(5-{3-amino-5-[4-(trifluoromethoxy)benzene-1-sulfonyl]pyridin-2-yl}-1,3,4-oxadiazol-2-yl)-1,1,1-trifluoropropan-2-ol;

1-(5-{3-amino-5-[4-(trifluoromethoxy)benzene-1-sulfonyl]pyridin-2-yl}-1,3,4-oxadiazol-2-yl)-2,2,2-trifluoroethan-1-ol;

(2-{3-amino-5-[4-(trifluoromethoxy)benzene-1-sulfonyl]pyridin-2-yl}-1,3-thiazol-5-yl)methanol;

2-(1,3,4-oxadiazol-2-yl)-5-[4-(trifluoromethoxy)benzene-1-sulfonyl]pyridin-3-amine;

(5-{3-amino-5-[4-(trifluoromethyl)benzene-1-sulfonyl]pyridin-2-yl}-1,3,4-oxadiazol-2-yl)methanol;

5-{3-amino-5-[4-(trifluoromethoxy)benzene-1-sulfonyl]pyridin-2-yl}-1,3,4-oxadiazole-2-carboxamide;

{5-[3-amino-5-(4-fluorobenzene-1-sulfonyl)pyridin-2-yl]-1,3,4-oxadiazol-2-yl}methanol;

2-(5-cyclohexyl-1,3,4-oxadiazol-2-yl)-5-[4-(trifluoromethoxy)benzene-1-sulfonyl]pyridin-3-amine;

2-{5-[(*S*)-methoxy(phenyl)methyl]-1,3,4-oxadiazol-2-yl}-5-[4-(trifluoromethoxy)benzene-1-sulfonyl]pyridin-3-amine;

2-{5-[(cyclopropylmethoxy)methyl]-1,3,4-oxadiazol-2-yl}-5-[4-(trifluoromethoxy)benzene-1-sulfonyl]pyridin-3-amine;

2-[5-(phenoxymethyl)-1,3,4-oxadiazol-2-yl]-5-[4-(trifluoromethoxy)benzene-1-sulfonyl]pyridin-3-amine;

2-{5-[(cyclopentyloxy)methyl]-1,3,4-oxadiazol-2-yl}-5-[4-(trifluoromethoxy)benzene-1-sulfonyl]pyridin-3-amine;

5-[4-(trifluoromethoxy)benzene-1-sulfonyl]-2-{5-[(trifluoromethoxy)methyl]-1,3,4-oxadiazol-2-yl}pyridin-3-amine;

2-(5-{[(oxolan-3-yl)oxy]methyl}-1,3,4-oxadiazol-2-yl)-5-[4-(trifluoromethoxy)benzene-1-sulfonyl]pyridin-3-amine;

2-{5-[(2-methoxyethoxy)methyl]-1,3,4-thiadiazol-2-yl}-5-[4-(trifluoromethoxy)benzene-1-sulfonyl]pyridin-3-amine;

N-[(5-{3-amino-5-[4-(trifluoromethoxy)benzene-1-sulfonyl]pyridin-2-yl}-1,3,4-thiadiazol-2-yl)methyl]cyclopropanecarbothioamide;

2-{5-[(*S*)-methoxy(phenyl)methyl]-1,3,4-thiadiazol-2-yl}-5-[4-(trifluoromethoxy)benzene-1-sulfonyl]pyridin-3-amine;

(2*S*)-2-(5-{3-amino-5-[4-(trifluoromethoxy)benzene-1-sulfonyl]pyridin-2-yl}-1,3,4-thiadiazol-2-yl)-1,1,1-trifluoropropan-2-ol;

2-{5-[(1*R*)-1-methoxyethyl]-1,3,4-thiadiazol-2-yl}-5-[4-(trifluoromethoxy)benzene-1-sulfonyl]pyridin-3-amine;

2-[5-(1-methoxyethyl)-1,3,4-thiadiazol-2-yl]-5-[4-(trifluoromethoxy)benzene-1-sulfonyl]pyridin-3-amine;

2-{5-[(1*S*)-1-methoxyethyl]-1,3,4-thiadiazol-2-yl}-5-[4-(trifluoromethoxy)benzene-1-sulfonyl]pyridin-3-amine;

2-{5-[(cyclopropylmethoxy)methyl]-1,3,4-thiadiazol-2-yl}-5-[4-(trifluoromethoxy)benzene-1-sulfonyl]pyridin-3-amine;

2-[5-(ethoxymethyl)-1,3,4-thiadiazol-2-yl]-5-[4-(trifluoromethoxy)benzene-1-sulfonyl]pyridin-3-amine;

2-[5-(methoxymethyl)-1,3,4-thiadiazol-2-yl]-5-[4-(trifluoromethoxy)benzene-1-sulfonyl]pyridin-3-amine;

2-(5-{[(pyridin-3-yl)oxy]methyl}-1,3,4-thiadiazol-2-yl)-5-[4-(trifluoromethoxy)benzene-1-sulfonyl]pyridin-3-amine;

5-[4-(trifluoromethoxy)benzene-1-sulfonyl]-2-{5-[(trifluoromethoxy)methyl]-1,3,4-thiadiazol-2-yl}pyridin-3-amine;

2-(5-{[(oxolan-3-yl)oxy]methyl}-1,3,4-thiadiazol-2-yl)-5-[4-(trifluoromethoxy)benzene-1-sulfonyl]pyridin-3-amine;

2-{5-[(difluoromethoxy)methyl]-1,3,4-thiadiazol-2-yl}-5-[4-(trifluoromethoxy)benzene-1-sulfonyl]pyridin-3-amine;

2-(5-{[(2*S*)-oxolan-2-yl]methyl}-1,3,4-thiadiazol-2-yl)-5-[4-(trifluoromethoxy)benzene-1-sulfonyl]pyridin-3-amine;

2-(5-{[(2*R*)-oxolan-2-yl]methyl}-1,3,4-thiadiazol-2-yl)-5-[4-(trifluoromethoxy)benzene-1-sulfonyl]pyridin-3-amine;

2-{5-[(2-methoxyethoxy)methyl]-1,3,4-oxadiazol-2-yl}-5-[4-(trifluoromethoxy)benzene-1-sulfonyl]pyridin-3-amine;

2-{5-[(1*R*)-1-methoxyethyl]-1,3,4-oxadiazol-2-yl}-5-[4-(trifluoromethoxy)benzene-1-sulfonyl]pyridin-3-amine;

2-{5-[(1*S*)-1-methoxyethyl]-1,3,4-oxadiazol-2-yl}-5-[4-(trifluoromethoxy)benzene-1-sulfonyl]pyridin-3-amine;

2-[5-(ethoxymethyl)-1,3,4-oxadiazol-2-yl]-5-[4-(trifluoromethoxy)benzene-1-sulfonyl]pyridin-3-amine;

2-[5-(methoxymethyl)-1,3,4-oxadiazol-2-yl]-5-[4-(trifluoromethoxy)benzene-1-sulfonyl]pyridin-3-amine;

2-(5-[(pyridin-3-yl)oxy]methyl)-1,3,4-oxadiazol-2-yl)-5-[4-(trifluoromethoxy)benzene-1-sulfonyl]pyridin-3-amine;

2-{5-[(difluoromethoxy)methyl]-1,3,4-oxadiazol-2-yl}-5-[4-(trifluoromethoxy)benzene-1-sulfonyl]pyridin-3-amine;

2-(5-[(2*S*)-oxolan-2-yl]methyl)-1,3,4-oxadiazol-2-yl)-5-[4-(trifluoromethoxy)benzene-1-sulfonyl]pyridin-3-amine;

2-(5-[(2*R*)-oxolan-2-yl]methyl)-1,3,4-oxadiazol-2-yl)-5-[4-(trifluoromethoxy)benzene-1-sulfonyl]pyridin-3-amine;

1-(5-{3-amino-5-[4-(trifluoromethoxy)benzene-1-sulfonyl]pyridin-2-yl}-1,3,4-oxadiazol-2-yl)ethan-1-ol;

2-(5-{3-amino-5-[4-(trifluoromethoxy)benzene-1-sulfonyl]pyridin-2-yl}-1,3,4-oxadiazol-2-yl)propan-2-ol;

(1*S*)-1-(5-{3-amino-5-[4-(trifluoromethoxy)benzene-1-sulfonyl]pyridin-2-yl}-1,3,4-oxadiazol-2-yl)-2-phenylethan-1-ol;

(*S*)-(5-{3-amino-5-[4-(trifluoromethoxy)benzene-1-sulfonyl]pyridin-2-yl}-1,3,4-oxadiazol-2-yl)(phenyl)methanol;

2-[3-(2-methoxypropan-2-yl)-1,2,4-oxadiazol-5-yl]-5-[4-(trifluoromethoxy)benzene-1-sulfonyl]pyridin-3-amine;

2-[3-(1-methoxyethyl)-1,2,4-oxadiazol-5-yl]-5-[4-(trifluoromethoxy)benzene-1-sulfonyl]pyridin-3-amine;

2-[3-(oxan-4-yl)-1,2,4-oxadiazol-5-yl]-5-[4-(trifluoromethoxy)benzene-1-sulfonyl]pyridin-3-amine;

2-{3-[(4-fluorophenoxy)methyl]-1,2,4-oxadiazol-5-yl}-5-[4-(trifluoromethoxy)benzene-1-sulfonyl]pyridin-3-amine;

2-[3-(cyclopropylmethyl)-1,2,4-oxadiazol-5-yl]-5-[4-(trifluoromethoxy)benzene-1-sulfonyl]pyridin-3-amine;

2-{3-[(oxolan-2-yl)methyl]-1,2,4-oxadiazol-5-yl}-5-[4-(trifluoromethoxy)benzene-1-sulfonyl]pyridin-3-amine;

2-(3-cyclopropyl-1,2,4-oxadiazol-5-yl)-5-[4-(trifluoromethoxy)benzene-1-sulfonyl]pyridin-3-amine;

2-[3-(oxolan-3-yl)-1,2,4-oxadiazol-5-yl]-5-[4-(trifluoromethoxy)benzene-1-sulfonyl]pyridin-3-amine;

2-(3-*tert*-butyl-1,2,4-oxadiazol-5-yl)-5-[4-(trifluoromethoxy)benzene-1-sulfonyl]pyridin-3-amine;

2-[3-(2-methoxyethyl)-1,2,4-oxadiazol-5-yl]-5-[4-(trifluoromethoxy)benzene-1-sulfonyl]pyridin-3-amine;

2-[3-(methoxymethyl)-1,2,4-oxadiazol-5-yl]-5-[4-(trifluoromethoxy)benzene-1-sulfonyl]pyridin-3-amine;

(5-{3-amino-4-chloro-5-[4-(trifluoromethoxy)benzene-1-sulfonyl]pyridin-2-yl}-1,3,4-oxadiazol-2-yl)methanol;

(5-{3-amino-5-[3-(trifluoromethoxy)benzene-1-sulfonyl]pyridin-2-yl}-1,3,4-oxadiazol-2-yl)methanol;

(5-{3-amino-5-[2-(trifluoromethoxy)benzene-1-sulfonyl]pyridin-2-yl}-1,3,4-oxadiazol-2-yl)methanol;

5-amino-*N*-benzyl-6-[5-(hydroxymethyl)-1,3,4-oxadiazol-2-yl]-*N*-methylpyridine-3-sulfonamide;

{5-[3-amino-5-(benzenesulfonyl)pyridin-2-yl]-1,3,4-oxadiazol-2-yl}methanol;

(5-{3-amino-5-[4-(trifluoromethyl)benzene-1-sulfonyl]pyridin-2-yl}-1,3,4-thiadiazol-2-yl)methanol;

(5-{3-amino-6-bromo-5-[4-(trifluoromethoxy)benzene-1-sulfonyl]pyridin-2-yl}-1,3,4-oxadiazol-2-yl)methanol;

(5-{3-amino-6-chloro-5-[4-(trifluoromethoxy)benzene-1-sulfonyl]pyridin-2-yl}-1,3,4-oxadiazol-2-yl)methanol;

(5-{3-amino-5-[2-(propan-2-yl)benzene-1-sulfonyl]pyridin-2-yl}-1,3,4-oxadiazol-2-yl)methanol;

(5-{3-amino-4-bromo-5-[4-(trifluoromethoxy)benzene-1-sulfonyl]pyridin-2-yl}-1,3,4-oxadiazol-2-yl)methanol; and

2-(5-{3-amino-5-[4-(trifluoromethoxy)benzene-1-sulfonyl]pyridin-2-yl}-1,2,4-oxadiazol-3-yl)ethan-1-ol.

14. A pharmaceutical composition comprising a therapeutically effective amount of a compound of claim 1, or a pharmaceutically acceptable salt thereof, in combination with a pharmaceutically acceptable carrier.
15. A compound of claim 1, or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition of claim 14, for use in medicine.
16. A compound of claim 1, or a pharmaceutically acceptable salt thereof, or a pharmaceutical composition of claim 14, for use in the treatment of cystic fibrosis.
17. Use of a therapeutically effective amount of a compound of claim 1, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for the treatment of cystic fibrosis in a subject in need thereof.
18. A pharmaceutical composition comprising a compound of claim 1, or a pharmaceutically acceptable salt thereof, and one or more correctors.
19. Use of a compound of claim 1, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for the treatment of cystic fibrosis in a subject in need thereof, wherein the medicament is to administered with one or more correctors.
20. A pharmaceutical composition comprising a compound of claim 1, or a pharmaceutically acceptable salt thereof, and one or more additional therapeutic agents.
21. The pharmaceutical composition of claim 20 wherein the additional therapeutic agents are selected from the group consisting of CFTR modulators and CFTR amplifiers.
22. The pharmaceutical composition of claim 20 wherein the additional therapeutic agents are CFTR modulators.

23. Use of a compound of claim 1, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for the treatment of cystic fibrosis in a subject in need thereof, wherein the medicament is to be administered with one or more additional therapeutic agents.
24. The use of claim 23 wherein the additional therapeutic agents are selected from the group consisting of CFTR modulators and CFTR amplifiers.
25. The use of claim 23 wherein the additional therapeutic agents are CFTR modulators.
26. The use of claim 23, wherein the additional therapeutic agents are CFTR correctors.
27. The use of claim 23, wherein the compound of claim 1, or a pharmaceutically acceptable salt thereof, is administered with one CFTR corrector.
28. The use of claim 23, wherein the compound of claim 1, or a pharmaceutically acceptable salt thereof, is administered with two CFTR correctors.
29. (5-{3-amino-5-[4-(trifluoromethoxy)benzene-1-sulfonyl]pyridin-2-yl}-1,3,4-oxadiazol-2-yl)methanol, or a pharmaceutically acceptable salt thereof.
30. (5-{3-amino-5-[4-(trifluoromethoxy)benzene-1-sulfonyl]pyridin-2-yl}-1,3,4-oxadiazol-2-yl)methanol.