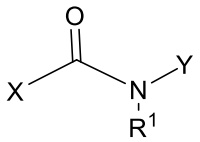
[0020a] In an aspect, there is provided a compound or a pharmaceutically acceptable salt thereof, wherein the compound is *trans*-4-[(2*R*,4*R*)-4-{[(7*R*)-2,2-difluoro-7-methyl-6,7-dihydro-2*H*-furo[2,3-*f*][1,3]benzodioxole-7-carbonyl]amino}-7-methoxy-3,4-dihydro-2*H*-1-benzopyran-2-yl]cyclohexane-1-carboxylic acid.

[0020b] In another aspect, there is provided a pharmaceutical composition comprising a therapeutically effective amount of a compound as defined above, or a pharmaceutically acceptable salt thereof, in combination with a pharmaceutically acceptable carrier.

[0021] In one example the present disclosure provides for compounds of formula (I)

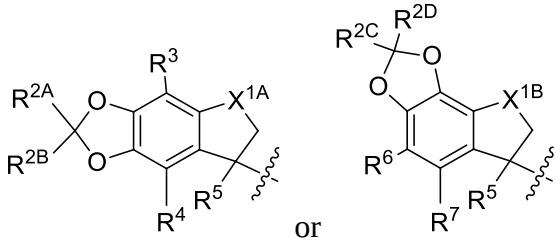


(I)

or a pharmaceutically acceptable salt thereof, wherein

R^1 is H or C_1-C_3 alkyl;

X is formula (a) or formula (b)



(a) or (b)

wherein

R^{2A}, R^{2B}, R^{2C}, and R^{2D}, are each independently hydrogen or halogen;

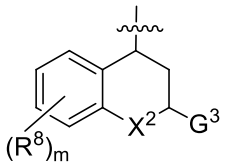
R^3, R^4, R^6, and R^7, are each independently hydrogen, C_1-C_3 alkyl, or halogen;

R^5, at each occurrence, is independently hydrogen, C_1-C_3 alkyl, C_2-C_4 alkenyl, or C_1-C_3 haloalkyl;

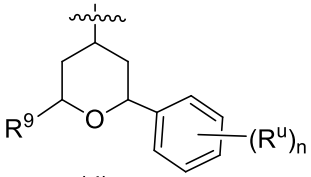
X^{1A} is O or CH_2;

X^{1B} is O or CH_2;

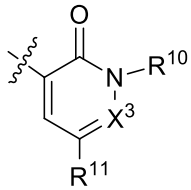
Y is -G^1, or Y is formula (c), (d), (e), (f), or (g);


X2
G3
(R8)m

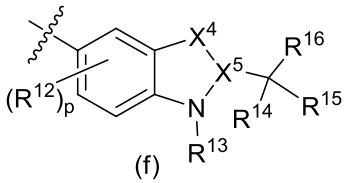
(c) ,


R9
O
(Ru)n

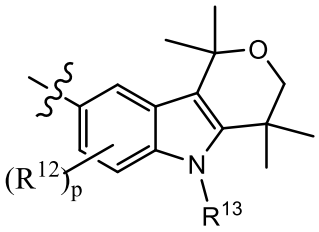
(d) ,


O
N
R10
X3
R11

(e) ,


X4
X5
R16
(R12)p
N
R14
R15
R13

(f) , or


O
(R12)p
N
R13

G^{3B}, at each occurrence, is independently a phenyl, a 4-7 membered monocyclic heterocycle, or a 3-10 memebered cycloalkyl, each of which is optionally substituted with 1, 2, 3, or 4 independently selected R^c groups;

R^c, R^u, R^v, R^w, and R^z, at each occurrence, are each independently C_2-C_6 alkenyl, C_2-C_6 alkynyl, halogen, C_1-C_6 haloalkyl, -CN, oxo, NO_2, $-OR^j$, $-OC(O)R^k$, $-OC(O)N(R^j)_2$, $-SR^j$, $-S(O)_2R^j$, $-S(O)_2N(R^j)_2$, $-C(O)R^j$, $-C(O)OR^j$, $-C(O)N(R^j)_2$, $-C(O)N(R^j)S(O)_2R^k$, $-N(R^j)_2$, $-N(R^j)C(O)R^k$, $-N(R^j)S(O)_2R^k$, $-N(R^j)C(O)O(R^k)$, $-N(R^j)C(O)N(R^j)_2$, or C_1-C_6 alkyl which is optionally substituted with 1 or 2 substituents independently selected from the group consisting of -CN, NO_2, $-OR^j$, $-OC(O)R^k$, $-OC(O)N(R^j)_2$, $-SR^j$, $-S(O)_2R^j$, $-S(O)_2N(R^j)_2$, $-C(O)R^j$, $-C(O)OR^j$, $-C(O)N(R^j)_2$, $-C(O)N(R^j)S(O)_2R^k$, $-N(R^j)_2$, $-N(R^j)C(O)R^k$, $-N(R^j)S(O)_2R^k$, $-N(R^j)C(O)O(R^k)$, and $-N(R^j)C(O)N(R^j)_2$;

R^j, at each occurrence, is independently hydrogen, C_1-C_6 alkyl, or C_1-C_6 haloalkyl; and

R^k, at each occurrence, is independently C_1-C_6 alkyl or C_1-C_6 haloalkyl.

[0022] Another example of the disclosure relates to pharmaceutical compositions comprising a compound of the disclosure, and a pharmaceutical 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 disclsoure, useful in the pharmaceutical compositions and treatment methods disclosed herein, are pharmaceutically acceptable as prepared and used.

[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.

[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.

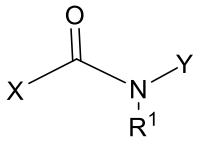
[0026] In a particular example, the compounds of the disclosure are provided for use in the treatment of cystic fibrosis. In a particular example, the compounds of the disclosure are provided for use in the treatment of cystic fibrosis caused by class I, II, III, IV, V, and/or VI mutations.

[0027] The present disclosure also provides pharmaceutical compositions comprising a compound of the disclosure, and a suitable pharmaceutical carrier for use in medicine. In a particular example, the pharmaceutical composition is for use in the treatment of cystic fibrosis.

[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)



(I)

wherein R^1, X, and Y are defined above in the Summary of the Invention 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 described.

[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 occurrence is independent of its definition at another occurrence. Further, combinations of substituents are permissible only if such combinations result in stable compounds. Stable compounds are compounds, which can be isolated from a reaction mixture.

Definitions

[0031] It is noted that, as used in this specification and the intended claims, the singular form "a," "an," and "the" include plural referents unless the context clearly dictates otherwise. Thus,

for example, reference to “a compound” includes a single compound as well as one or more of the same or different compounds, reference to “a pharmaceutically acceptable carrier” means a

We claim:

1. A compound or a pharmaceutically acceptable salt thereof, wherein the compound is *trans*-4-[(2*R*,4*R*)-4-{[(7*R*)-2,2-difluoro-7-methyl-6,7-dihydro-2*H*-furo[2,3-*f*][1,3]benzodioxole-7-carbonyl]amino}-7-methoxy-3,4-dihydro-2*H*-1-benzopyran-2-yl]cyclohexane-1-carboxylic acid.

2. The compound of claim 1, which is *trans*-4-[(2*R*,4*R*)-4-{[(7*R*)-2,2-difluoro-7-methyl-6,7-dihydro-2*H*-furo[2,3-*f*][1,3]benzodioxole-7-carbonyl]amino}-7-methoxy-3,4-dihydro-2*H*-1-benzopyran-2-yl]cyclohexane-1-carboxylic acid.

3. 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.