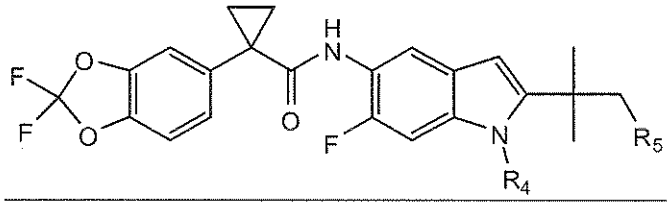
[0028] SUMMARY ~~OF THE INVENTION~~

[0028a] In a first aspect of the present disclosure, there is provided a compound of formula IIa:



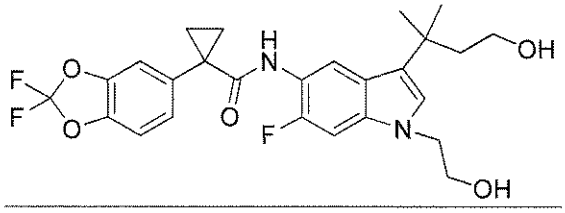
IIa

or a pharmaceutically acceptable salt thereof, wherein independently for each occurrence:

R_4 is $-CH_2CH(OH)CH_2OH$, $-CH_2CH_2N^+(CH_3)_3$, or $-CH_2CH_2OH$; and

R_5 is OH, $-CH_2OCH_2CH(OH)CH_2OH$, $-CH_2OH$, or R_4 and R_5 taken together form a fused pyrrolidine ring;

provided that the compound is not

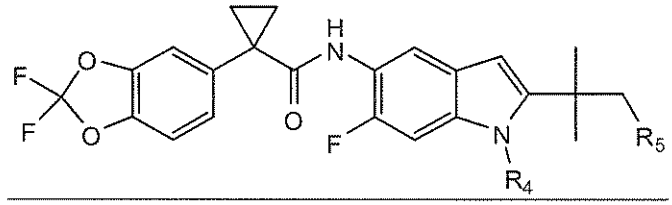


[0028b] In a second aspect of the present disclosure, there is provided a pharmaceutical composition comprising

(i) a disclosed compound; and

(ii) a pharmaceutically acceptable carrier.

[0028c] In a third aspect of the present disclosure, there is provided an in vitro use of the compound of formula IIa to increase the number of functional ABC transporters in a membrane of a cell, comprising the step of contacting said cell with a compound of formula IIa:



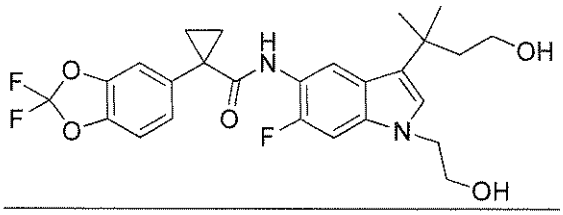
IIa

or a pharmaceutically acceptable salt thereof, wherein independently for each occurrence:

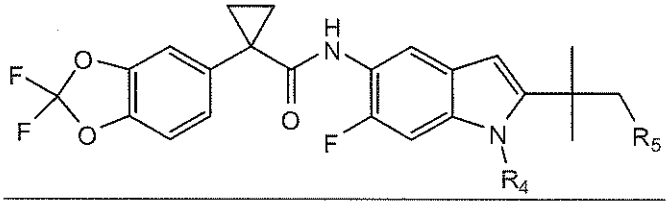
R_4 is H, $-CH_2CH(OH)CH_2OH$, $-CH_2CH_2N^+(CH_3)_3$, or $-CH_2CH_2OH$; and

R_5 is OH, $-CH_2OCH_2CH(OH)CH_2OH$, $-CH_2OH$, or R_4 and R_5 taken together form a fused pyrrolidine ring;

provided that the compound is not



[0028d] In a fourth aspect of the present disclosure, there is provided a compound having formula IIa:



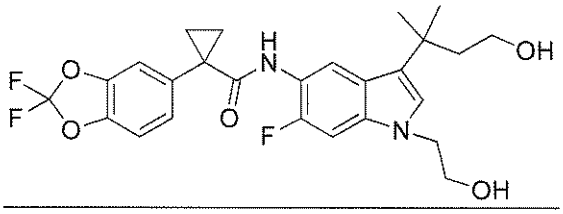
IIa

or a pharmaceutically acceptable salt thereof, wherein independently for each occurrence:

R_4 is H, $-CH_2CH(OH)CH_2OH$, $-CH_2CH_2N^+(CH_3)_3$, or $-CH_2CH_2OH$; and

R_5 is OH, $-CH_2OCH_2CH(OH)CH_2OH$, $-CH_2OH$, or R_4 and R_5 taken together form a fused pyrrolidine ring;

provided that the compound is not

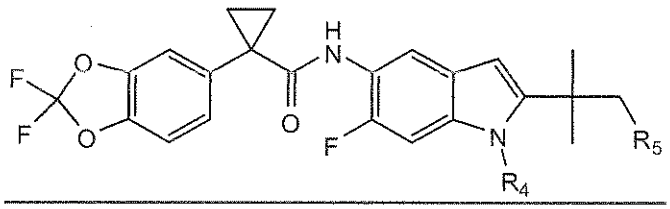


for use in treating a condition, disease, or disorder selected from cystic fibrosis, hereditary emphysema, hereditary hemochromatosis, coagulation-fibrinolysis deficiencies, such as protein C deficiency, Type 1 hereditary angioedema, lipid processing deficiencies, such as familial hypercholesterolemia, Type 1 chylomicronemia, abetalipoproteinemia, lysosomal storage

diseases, such as I-cell disease/pseudo-Hurler, mucopolysaccharidoses, Sandhof/Tay-Sachs, Crigler-Najjar type II, polyendocrinopathy/hyperinsulinemia, diabetes mellitus, laron dwarfism, myeloperoxidase deficiency, primary hypoparathyroidism, melanoma, glycanosis CDG type 1, hereditary emphysema, congenital hyperthyroidism, osteogenesis imperfecta, hereditary hypofibrinogenemia, ACT deficiency, diabetes insipidus (DI), neurohypophyseal DI, nephrogenic DI, Charcot-Marie Tooth syndrome, Pelizaeus-Merzbacher disease, neurodegenerative diseases such as Alzheimer's disease, Parkinson's disease, amyotrophic lateral sclerosis, progressive supranuclear plasy, Pick's disease, several polyglutamine neurological disorders such as Huntington, spinocerebellar ataxia type I, spinal and bulbar muscular atrophy, dentatorubral pallidoluysian atrophy, and myotonic dystrophy, as well as spongiform encephalopathies, such as hereditary Creutzfeldt-Jakob disease, Fabry disease, Gerstmann-Sträussler-Scheinker syndrome, COPD, dry-eye disease and Sjögren's disease, male infertility and pancreatic insufficiency.

[0028e] In a fifth aspect of the present disclosure, there is provided a kit for use in measuring the activity of a ABC transporter or a fragment thereof in a biological sample *in vitro* or *in vivo*, comprising:

(i) a first composition comprising a compound of formula IIa:



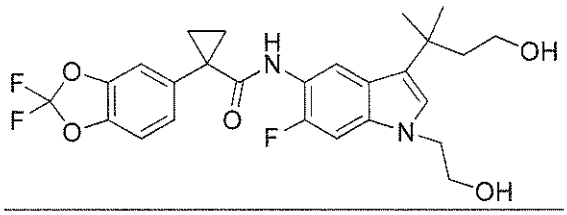
IIa

or a pharmaceutically acceptable salt thereof, wherein independently for each occurrence:

R_4 is (H), $-CH_2CH(OH)CH_2OH$, $-CH_2CH_2N^+(CH_3)_3$, or $-CH_2CH_2OH$; and

R_5 is OH, $-CH_2OCH_2CH(OH)CH_2OH$, $-CH_2OH$, or R_4 and R_5 taken together form a fused pyrrolidine ring;

provided that the compound is not

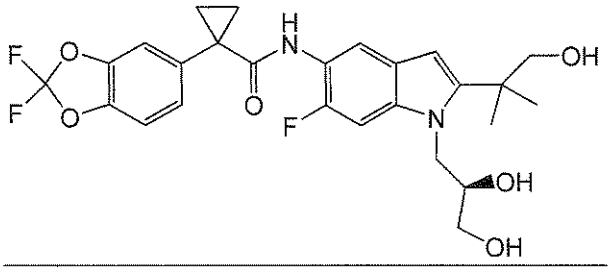


(ii) instructions for:

a) contacting the composition with the biological sample;

b) measuring activity of said ABC transporter or a fragment thereof.

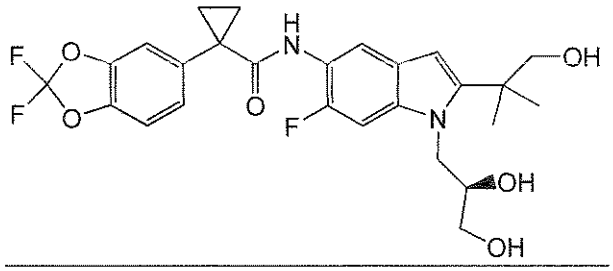
[0028f] In a sixth aspect of the present disclosure, there is provided a compound which is:



or a pharmaceutically acceptable salt thereof.

[0028g] In a seventh aspect of the present disclosure, there is provided a pharmaceutical composition comprising

(i) a compound which is:



(ii) a pharmaceutically acceptable carrier.

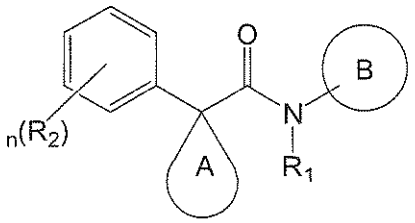
[0028h] In an eighth aspect of the present disclosure, there is provided a use of a disclosed compound in the manufacture of a medicament for the treatment of a disease or disorder selected from male infertility and pancreatic insufficiency.

[0028i] In a ninth aspect of the present disclosure, there is provided a use of a disclosed compound in the manufacture of a medicament for the treatment of cystic fibrosis.

[0028j] In a tenth aspect of the present disclosure, there is provided a use of a disclosed compound in the manufacture of a medicament for the treatment of a disease or disorder selected

from hereditary emphysema, COPD, and dry-eye disease.

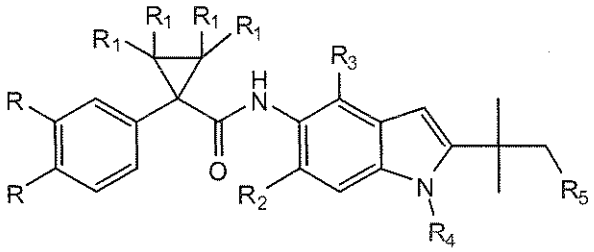
[0029] It has now been found that compounds of the present disclosure~~this invention~~, and pharmaceutically acceptable compositions thereof, are useful as modulators of ABC transporter activity, particularly CTFR activity. These compounds have the general formula I:



I

or a pharmaceutically acceptable salt thereof, wherein R_1, R_2, ring A, ring B, and n are defined below.

It has also now been found that compounds of the present disclosure~~this invention~~, and pharmaceutically acceptable compositions thereof, are useful as modulators of ABC transporter activity. These compounds have the general formula **II:**



II

or a pharmaceutically acceptable salt thereof, wherein R, R_1, R_2, R_3, R_4, and R_5 are defined below.

[0030] These compounds and pharmaceutically acceptable compositions are useful for treating or lessening the severity of a variety of diseases, disorders, or conditions, including, but not limited to, cystic fibrosis, hereditary emphysema, hereditary hemochromatosis, coagulation-fibrinolysis deficiencies, such as protein C deficiency, Type 1 hereditary angioedema, lipid processing deficiencies, such as familial hypercholesterolemia, Type 1 chylomicronemia, abetalipoproteinemia, lysosomal storage diseases, such as I-cell disease/pseudo-Hurler, mucopolysaccharidoses, Sandhof/Tay-Sachs, Crigler-Najjar type II, polyendocrinopathy/hyperinsulemia, diabetes mellitus, laron dwarfism, myeloperoxidase deficiency, primary hypoparathyroidism, melanoma, glycanosis CDG type 1, hereditary