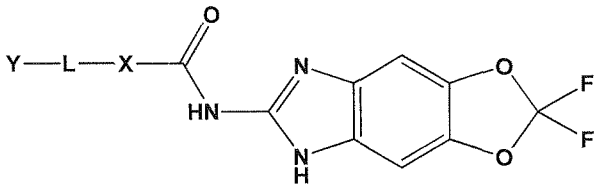
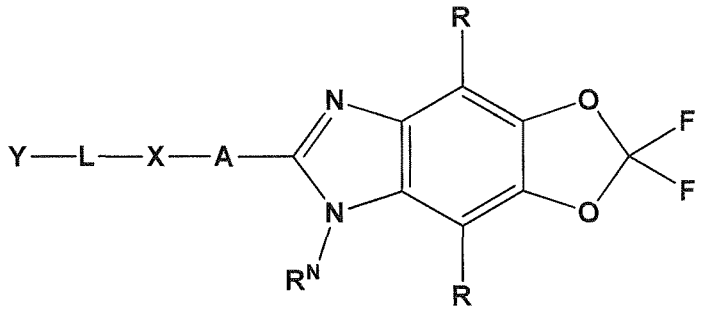


(I)



(Ia)

In one aspect, the present disclosure provides compound of the general formula (I) or a solvate or salt thereof, or a pharmaceutically acceptable derivative thereof, or a salt of said pharmaceutically acceptable derivative, or solvates of said salt and pharmaceutically acceptable derivative, or solvates of salts of said pharmaceutically acceptable derivative, wherein said pharmaceutically acceptable derivative comprises at least one of the following groups being derivatized as specified in the following: A carboxylic acid group is derivatized into an ester, a hydroxyl group is derivatized into an ester, a carboxylic acid is derivatized into an amide, an amine is derivatized into an amide, or a hydroxyl group is derivatized into a phosphate ester,



(I) , wherein

R is independently selected from the group comprising H, halogen, C_{1-4}-alkyl, C_{1-4}-haloalkyl, C_{1-4}-haloalkoxy, C_{1-4}-alkoxy, ~~C_{1-6}-alkyl, C_{1-6}-haloalkyl, C_{1-6}-haloalkoxy,~~ OH, ~~C_{1-6}-alkoxy,~~ ~~-S-R'''~~, -SO-R''', ~~nitro,~~ ~~-N(R''')$_2$~~, -NH(R'''),

-NHCO(R'''), -$CONH_2$, -CONH(R'''), -CO(R'''), -COH, -COO(R'''), -COOH, -SO_2NH_2, -SO_2NH(R'''), -SO_2(R'''), and -NH-SO_2(R'''),

wherein in the cases where said group R is C_{1-4}-alkyl, C_{1-4}-haloalkyl, C_{1-4}-haloalkoxy, C_{1-4}-alkoxy~~C_{1-6}-alkyl, C_{1-6}-haloalkyl, C_{1-6}-haloalkoxy, or C_{1-6}-alkoxy~~, said group R may be substituted with one or more substituents R'' independently selected from the group comprising H, halogen, and OH~~, nitro, NH_2, $N(C_{1-6}$-alkyl$)_2$, $NH(C_{1-6}$-alkyl), $NHCO(C_{1-6}$-alkyl), $CONH_2$, $CONH(C_{1-6}$-alkyl), $CO(C_{1-6}$-alkyl), -COH, $COO(C_{1-6}$-alkyl), -COOH, and -CN~~,

and wherein R''' is independently selected from the group comprising H, C_{1-2}-alkyl and C_{1-2}-haloalkyl~~C_{1-6}-alkyl, C_{1-6}-haloalkyl, aryl, heteroaryl, cycloalkyl and heterocyclyl~~;

R^N is independently selected from the group comprising H, C_{1-4}-alkyl, C_{1-4}-haloalkyl, ~~alkyl, haloalkyl, OH, aryl, heteroaryl, cycloalkyl, heterocyclyl, SO-R''', $N(R''')_2$,~~ -NH_2, ~~-N(R''')$_2$,~~ -NH(R'''), ~~-NHCO(R'''),~~ -$CONH_2$, -CONH(R'''), -CO(R'''), -COH, -COO(R'''), ~~-COOH,~~ -SO_2NH_2, -SO_2NH(R'''), -SO_2(R'''), and -NH-SO_2(R'''), wherein R''' is as defined above,

~~wherein in the cases where said group R^N is alkyl, haloalkyl, aryl, heteroaryl, cycloalkyl, or heterocyclyl, said group R^N may be substituted with one or more substituents R''' as defined above;~~

A is independently selected from *-N(R^a)CO-, *-CON(R^a)-, *-SO_2N(R^a)-, and *-N(R^a)-SO_2-,

wherein R^a is selected from H and C_{1-4}-alkyl,

and wherein * specifies the point of attachment to X;

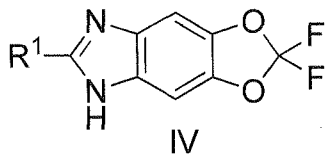
X is independently selected from the group comprising aryl, cycloalkyl, aralkyl, heterocyclyl and heteroaryl, wherein said group X may be substituted with one or more R^X independently selected from the group comprising halogen, C_{1-6}-alkyl, C_{1-6}-haloalkyl, C_{1-6}-haloalkoxy, OH, C_{1-6}-alkoxy, aryl, heteroaryl, cycloalkyl, heterocyclyl,

-S-C_{1-6}-alkyl, -S-C_{1-6}-haloalkyl, nitro, -NH_2, -N(C_{1-6}-alkyl)$_2$, -NH(C_{1-6}-alkyl), -NHCO(C_{1-6}-alkyl), -$CONH_2$, -CONH(C_{1-6}-alkyl), -CO(C_{1-6}-alkyl), -COH, -COO(C_{1-6}-alkyl), -COOH, -SO_2NH_2, -SO_2NH(C_{1-6}-alkyl), -SO_2(C_{1-6}-alkyl), -NH-SO_2(C_{1-6}-alkyl), C_{3-6}-cycloalkyl, and -CN;

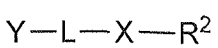
L is independently a bond or a linker group selected from the group comprising *-NHCO-, *-CONH-, *-NH-, *-N(C_{1-4}-alkyl)-, *-C=N(C_{1-4}-alkyl)-, *-NH-C_{1-4}-alkyl-, *-C_{1-4}-alkyl-NH-, *-NHCONH-, *-CO-, *-SO_2-, C_{1-4}-alkyl, *-C_{1-2}-alkyl-O-C_{1-2}-alkyl-, *-NHCO-CH=CH-, *-CH=CH-CONH-, * -SO_2NH-, * -$NHSO_2$-, and pyridinyl, wherein * specifies the point of attachment to X; and

Y is independently selected from the group comprising H, alkyl, aryl, aralkyl, cycloalkyl, heterocyclyl and heteroaryl, wherein said group Y may optionally be substituted with one or more R^Y independently selected from the group comprising halogen, C_{1-6}-alkyl, C_{1-6}-haloalkyl, C_{1-6}-haloalkoxy, OH, C_{1-6}-alkoxy, aryl, heteroaryl, cycloalkyl, heterocyclyl, -S-C_{1-6}-alkyl, -S-C_{1-6}-haloalkyl, nitro, -NH_2, -N(C_{1-6}-alkyl)$_2$, -NH(C_{1-6}-alkyl), -NHCO(C_{1-6}-alkyl), -$CONH_2$, -CONH(C_{1-6}-alkyl), -CO(C_{1-6}-alkyl), -COH, -COO(C_{1-6}-alkyl), -COOH, -SO_2NH_2, -SO_2NH(C_{1-6}-alkyl), -SO_2(C_{1-6}-alkyl), -NH-SO_2(C_{1-6}-alkyl), C_{1-6}-alkyl-heterocyclyl, cycloalkyl and -CN.

In another embodiment, the present disclosure provides methods for preparation of compounds of Formulae (I) or (Ia), physiologically functional derivatives or salts thereof, as detailed further herein below. In another aspect, the present disclosure provides a process for the preparation of a compound as disclosed herein, wherein A is an -CONH- or -NHCO-, the process comprising the step of coupling a compound of below Formula IV with a compound of below formula II;



IV



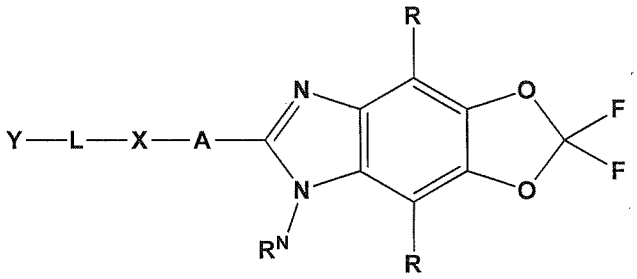
II ,

wherein Y, L and X are as defined above, and

wherein either R^1 is NH_2 and R^2 is COOH or COOCl, or wherein R^2 is NH_2 and R^1 is COOH or COOCl.

CLAIMS

1. A compound of the general formula (I) or a solvate or salt thereof, or a pharmaceutically acceptable derivative thereof, or a salt of said pharmaceutically acceptable derivative, or solvates of said salt and pharmaceutically acceptable derivative, or solvates of salts of said pharmaceutically acceptable derivative, wherein said pharmaceutically acceptable derivative comprises at least one of the following groups being derivatized as specified in the following: A carboxylic acid group is derivatized into an ester, a hydroxyl group is derivatized into an ester, a carboxylic acid is derivatized into an amide, an amine is derivatized into an amide, or a hydroxyl group is derivatized into a phosphate ester,



(I) , wherein

R is independently selected from the group comprising H, halogen, C_{1-4}-alkyl, C_{1-4}-haloalkyl, C_{1-4}-haloalkoxy, C_{1-4}-alkoxy, ~~C_{1-6}-alkyl, C_{1-6}-haloalkyl, C_{1-6}-haloalkoxy,~~ OH, ~~C_{1-6}-alkoxy,~~ -S-R''', -SO-R''', ~~nitro,~~ -N(R''')$_2$, -NH(R'''), -NHCO(R'''), -$CONH_2$, -CONH(R'''), -CO(R'''), -COH, -COO(R'''), -COOH, -SO_2NH_2, -SO_2NH(R'''), -SO_2(R'''), and -NH-SO_2(R'''),

wherein in the cases where said group R is C_{1-4}-alkyl, C_{1-4}-haloalkyl, C_{1-4}-haloalkoxy, C_{1-4}-alkoxy,~~C_{1-6}-alkyl, C_{1-6}-haloalkyl, C_{1-6}-haloalkoxy, or C_{1-6}-alkoxy,~~ said group R may be substituted with one or more substituents R'' independently selected from the group comprising H, halogen, and OH, ~~nitro, $-NH_2$, $-N(C_{1-6}$-alkyl$)_2$, $-NH(C_{1-6}$-alkyl), $-NHCO(C_{1-6}$-alkyl), $-CONH_2$, $-CONH(C_{1-6}$-alkyl), $-CO(C_{1-6}$-alkyl), -COH, $-COO(C_{1-6}$-alkyl), -COOH, and -CN,~~

and wherein R''' is independently selected from the group comprising H, C_{1-2}-alkyl and C_{1-2}-haloalkyl; ~~C_{1-6}-alkyl, C_{1-6}-haloalkyl, aryl, heteroaryl, cycloalkyl and heterocyclyl;~~

R^N is independently selected from the group comprising H, C_{1-4}-alkyl, C_{1-4}-haloalkyl, ~~alkyl, haloalkyl, OH, aryl, heteroaryl, cycloalkyl, heterocyclyl, SO-R''', $-NH_2$, $-N(R''')_2$,~~ -NH(R'''), ~~-NHCO(R'''),~~ -$CONH_2$, -CONH(R'''), -CO(R'''), -COH, -COO(R'''), ~~-COOH,~~ -SO_2NH_2, -SO_2NH(R'''), -SO_2(R'''), and -NH-SO_2(R'''), wherein R''' is as defined above,

~~wherein in the cases where said group R^N is alkyl, haloalkyl, aryl, heteroaryl, cycloalkyl, or heterocyclyl, said group R^N may be substituted with one or more substituents R''' as defined above;~~

A is independently selected from *-N(R^a)CO-, *-CON(R^a)-, *-SO_2N(R^a)-, and *-N(R^a)-SO_2-,

wherein R^a is selected from H and C_{1-4}-alkyl,

and wherein * specifies the point of attachment to X;

X is independently selected from the group comprising aryl, cycloalkyl, aralkyl, heterocyclyl and heteroaryl, wherein said group X may be substituted with one or more R^X independently selected from the group comprising halogen, C_{1-6}-alkyl, C_{1-6}-haloalkyl, C_{1-6}-haloalkoxy, OH, C_{1-6}-alkoxy, aryl, heteroaryl, cycloalkyl, heterocyclyl, -S-C_{1-6}-alkyl, -S-C_{1-6}-haloalkyl, nitro, -NH_2, -N(C_{1-6}-alkyl)$_2$, -NH(C_{1-6}-alkyl), -NHCO(C_{1-6}-alkyl), -$CONH_2$, -CONH(C_{1-6}-alkyl), -CO(C_{1-6}-alkyl), -COH, -COO(C_{1-6}-alkyl), -COOH, -SO_2NH_2, -SO_2NH(C_{1-6}-alkyl), -SO_2(C_{1-6}-alkyl), -NH-SO_2(C_{1-6}-alkyl), C_{3-6}-cycloalkyl, and -CN;

L is independently a bond or a linker group selected from the group comprising *-NHCO-, *-CONH-, *-NH-, *-N(C_{1-4}-alkyl)-, *-C=N(C_{1-4}-alkyl)-, *-NH-C_{1-4}-alkyl-, *-C_{1-4}-alkyl-NH-, *-NHCONH-, *-CO-, *-SO_2-, C_{1-4}-alkyl, *-C_{1-2}-alkyl-O-C_{1-2}-alkyl-, *-NHCO-CH=CH-, *-CH=CH-CONH-, * -SO_2NH-, * -$NHSO_2$-, and pyridinyl, wherein * specifies the point of attachment to X; and

Y is independently selected from the group comprising H, alkyl, aryl, aralkyl, cycloalkyl, heterocyclyl and heteroaryl, wherein said group Y may optionally be substituted with one or more R^Y independently selected from the group comprising halogen, C_{1-6}-alkyl, C_{1-6}-haloalkyl, C_{1-6}-haloalkoxy, OH, C_{1-6}-alkoxy, aryl, heteroaryl, cycloalkyl, heterocyclyl, -S-C_{1-6}-alkyl, -S-C_{1-6}-haloalkyl, nitro, -NH_2, -N(C_{1-6}-alkyl)$_2$, -NH(C_{1-6}-alkyl), -NHCO(C_{1-6}-alkyl), -$CONH_2$, -CONH(C_{1-6}-alkyl), -CO(C_{1-6}-alkyl), -COH, -COO(C_{1-6}-alkyl), -COOH, -SO_2NH_2, -SO_2NH(C_{1-6}-alkyl), -SO_2(C_{1-6}-alkyl), -NH-SO_2(C_{1-6}-alkyl), C_{1-6}-alkyl-heterocyclyl, cycloalkyl and -CN.