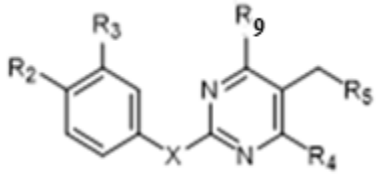
1/PD-L1 inhibitor compounds treating cancer and other diseases or conditions associated with activation of PD-1/PD-L1 would open new opportunities in the realm of cancer treatment.

SUMMARY

[00010] The present disclosure refers to subject matter as defined in the attached set of claims. In an example of the present disclosure, there is disclosed a compound of Formula Ib

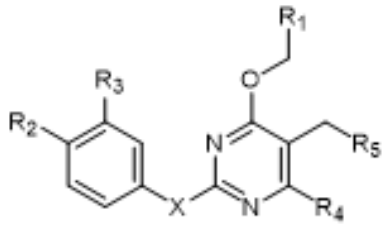


Formula Ib

their polymorphs, stereoisomers, tautomers, prodrugs, solvates, and pharmaceutically acceptable salts thereof, wherein X is selected from -CH_2O-, -OCH_2-, -C(O)NH- or -NHC(O)-; R_2, R_3, R_4, and R_9 are independently selected from hydrogen, cyano, C_{1-10} alkyl, C_{1-10} alkoxy, C_{1-6} haloalkyl, C_{1-6} haloalkoxy, C_{3-6} cycloalkyl, C_{1-6} alkylamino, aminoC_{1-6} alkyl, C_{1-6} alkoxyamino, C_{1-6} acylamino, C_{5-10} aryl, and 5-10 membered monocyclic or bicyclic heteroaryl with 1-5 heteroatoms selected from N, S or O, wherein C_{1-10} alkyl, C_{1-10} alkoxy, C_{5-10} aryl, and 5-10 membered monocyclic or bicyclic heteroaryl, are optionally substituted with one or more of the groups selected from hydrogen, halogen, hydroxyl, cyano, C_{1-6} alkyl, C_{1-6} alkoxy, C_{1-6} haloalkyl, C_{1-6} haloalkoxy, C_{3-6} cycloalkyl, C_{1-6} alkylamino, C_{1-6} alkoxyamino, C_{1-6} acylamino, C_{1-10} heterocyclyl, or -$COOR_a$, wherein C_{1-6} alkyl, C_{1-6} alkoxy, and C_{1-10} heterocyclyl are optionally substituted with one or more of the groups selected from hydroxy, cyano, C_{1-6} alkyl, C_{3-6} cycloalkyl, C_{1-6} heterocyclyl, C_{1-6} alkoxy, or $COOR_a$, wherein C_{1-6} heterocyclyl is optionally substituted with one or more groups selected from hydroxy, halogen, or cyano; and R_a is selected from hydrogen, halogen, cyano, C_{1-6} alkyl, C_{3-8} cycloalkyl, C_{5-6} aryl, C_{5-6} arylalkyl, C_{2-6} heterocyclyl, C_{1-6} heteroaryl, or C_{1-6} heteroarylalkyl; R_5 is -NR_7R_8, wherein R_7 and R_8 are selected from the group consisting of hydrogen, C_{3-10} cycloalkyl, C_{1-6} alkyl, C_{2-6} alkenyl, 5-10 membered monocyclic or bicyclic, saturated or unsaturated heterocyclic ring with 1-3 heteroatoms selected from N, S or O, and combinations thereof, wherein C_{3-10} cycloalkyl, C_{1-6} alkyl, C_{2-6} alkenyl, and the 5-10 membered monocyclic or bicyclic, saturated or unsaturated heterocyclic

ring are optionally substituted with one or more substituents selected from oxo, cyano, halogen, hydroxyl, morpholino, $C(O)NH_2$, $C(O)CH_2CN$, NHR_6, COOH, $COOR_6$, $NHC(O)R_6$, C_{1-6} alkyl, C_{1-6} haloalkyl, C_{3-10} cycloalkyl, C_{5-6} aryl, SR_6, or 5-10 membered monocyclic or bicyclic, saturated or unsaturated heterocyclic ring with 1-3 heteroatoms selected from N, S or O, wherein C_{1-6} alkyl, and the 5-10 membered monocyclic or bicyclic, saturated or unsaturated heterocyclic ring are independently substituted with one or more substituents selected from hydroxyl, and R_6; or R_7 and R_8 can be taken together to form a 4-10 membered monocyclic or bicyclic, saturated or unsaturated heterocyclic ring with 1-3 heteroatoms selected from N, S or O, wherein the 4-10 membered monocyclic or bicyclic, saturated or unsaturated heterocyclic ring is optionally substituted with one or more substituents selected from the group consisting of oxo, hydroxyl, halogen, C_{1-6} alkyl, COOH, $COOR_6$, R_6, NHR_6, $C(O)NHR_6$, $C(O)NHSO_2R_6$, $C(O)(CH_2)_nNHC(O)CH_3$, and combinations thereof, wherein C_{1-6} alkyl is further substituted with groups selected from hydroxyl, COOH, or NHR_6; n is 1-6; and R_6 is selected from the group consisting of hydrogen, C_{1-6} alkyl, $C(O)C_{1-6}$ alkyl, and combinations thereof, wherein C_{1-6} alkyl, and $C(O)C_{1-6}$ alkyl are optionally substituted with substituents selected from the group consisting of hydroxyl, COOH, NHR_6, $NHC(O)NHR_6$, and combinations thereof.

[00011] In another example of the present disclosure there is disclosed a compound of Formula Ia



Formula Ia

their polymorphs, stereoisomers, tautomers, prodrugs, solvates, and pharmaceutically acceptable salts thereof, wherein X is selected from $-CH_2O$, $-OCH_2$, C(O)NH or NHC(O); R_1, R_2, R_3, and R_4 are independently selected from hydrogen, cyano, C_{1-10} alkyl, C_{1-10} alkoxy, C_{1-6} haloalkyl, C_{1-6} haloalkoxy, C_{3-6} cycloalkyl, C_{1-6} alkylamino, aminoC_{1-6} alkyl, C_{1-6} alkoxyamino, C_{1-6} acylamino, C_{5-10} aryl, and 5-10 membered monocyclic or bicyclic heteroaryl with 1-5 heteroatoms selected from N, S or O, wherein C_{1-10} alkyl, C_{5-10} aryl, and 5-10 membered monocyclic or bicyclic heteroaryl,

are optionally substituted with one or more of the groups selected from the group consisting of hydrogen, halogen, hydroxyl, cyano, C_{1-6} alkyl, C_{1-6} alkoxy, C_{1-6} haloalkyl, C_{1-6} haloalkoxy, C_{3-6} cycloalkyl, C_{1-6} alkylamino, C_{1-6} alkoxyamino, C_{1-6} acylamino, C_{1-10} heterocyclyl, $-COOR_a$, wherein C_{1-6} alkyl, C_{1-6} alkoxy, C_{1-10} heterocyclyl are optionally substituted with one or more of the groups selected from C_{1-6} alkyl, C_{3-6} cycloalkyl, C_{1-6} heterocyclyl, C_{1-6} alkoxy, or $COOR_a$, wherein C_{1-6} heterocyclyl is optionally substituted with one or more groups selected from hydroxy, halogen, or cyano, and R_a is selected from hydrogen, C_{1-6} alkyl, C_{3-8} cycloalkyl, C_{5-6} aryl, C_{5-6} arylalkyl, C_{2-6} heterocyclyl, C_{1-6} heteroaryl or C_{1-6} heteroarylalkyl; R_5 is $-NR_7R_8$, wherein R_7, and R_8 are selected from the group consisting of hydrogen, C_{3-10} cycloalkyl, C_{1-6} alkyl, C_{2-6} alkenyl, 5-10 membered monocyclic or bicyclic, saturated or unsaturated heterocyclic ring with 1-3 heteroatoms selected from N, S or O, and combinations thereof, wherein C_{3-10} cycloalkyl, C_{1-6} alkyl, C_{2-6} alkenyl, and the 5-10 membered monocyclic or bicyclic, saturated or unsaturated heterocyclic ring are optionally substituted with one or more substituents selected from oxo, cyano, halogen, hydroxyl, morpholino, $C(O)NH_2$, $C(O)CH_2CN$, NHR_6, COOH, $COOR_6$, $NHC(O)R_6$, C_{1-6} alkyl, C_{1-6} haloalkyl, C_{3-10} cycloalkyl, C_{5-6} aryl, SR_6, or 5-10 membered monocyclic or bicyclic, saturated or unsaturated heterocyclic ring with 1-3 heteroatoms selected from N, S or O, wherein C_{1-6} alkyl, and the 5-10 membered monocyclic or bicyclic, saturated or unsaturated heterocyclic ring are independently substituted with one or more substituents selected from hydroxyl, and R_6; or R_7 and R_8 can be taken together to form a 4-10 membered monocyclic or bicyclic, saturated or unsaturated heterocyclic ring with 1-3 heteroatoms selected from N, S or O, wherein the 4-10 membered monocyclic or bicyclic saturated or unsaturated heterocyclic ring is optionally substituted with substituents selected from the group consisting of oxo, hydroxyl, halogen, C_{1-6} alkyl, COOH, $COOR_6$, R_6, NHR_6, $C(O)NHR_6$, $C(O)NHSO_2R_6$, $C(O)(CH_2)_nNHC(O)CH_3$, and combinations thereof, wherein C_{1-6} alkyl is further substituted with groups selected from hydroxyl, COOH, or NHR_6; n is 1-6; and R_6 is selected from the group consisting of hydrogen, C_{1-6} alkyl, $C(O)C_{1-6}$ alkyl, and combinations thereof, wherein C_{1-6} alkyl, and $C(O)C_{1-6}$ alkyl are optionally substituted with substituents selected from the group consisting of hydroxyl, COOH, NHR_6, $NHC(O)NHR_6$, and combinations thereof.

[00012] In another example of the present disclosure there is disclosed a compound of Formula I

a 4-10 membered monocyclic or bicyclic, saturated or unsaturated heterocyclic ring with 1-3 heteroatoms selected from N, S or O, wherein the 4-10 membered monocyclic or bicyclic, saturated or unsaturated heterocyclic ring is optionally substituted with one or more substituents selected from the group consisting of oxo, hydroxyl, C_{1-6} alkyl, COOH, $COOR_6$, R_6, NHR_6, $C(O)NHR_6$, $C(O)NHSO_2R_6$, $C(O)(CH_2)_nNHC(O)CH_3$, and combinations thereof, wherein C_{1-6} alkyl is further substituted with groups selected from hydroxyl, COOH, or NHR_6; n is 1-6; and R_6 is selected from the group consisting of hydrogen, C_{1-6} alkyl, $C(O)C_{1-6}$ alkyl, and combinations thereof, wherein C_{1-6} alkyl, and $C(O)C_{1-6}$ alkyl are optionally substituted with substituents selected from the group consisting of hydroxyl, COOH, NHR_6, $NHC(O)NHR_6$, and combinations thereof.

[00013] In an example of the present disclosure there is disclosed a process of preparation of compounds of Formula Ib, Formula Ia, and Formula I or their polymorphs, stereoisomers, tautomers, prodrugs, solvates, and pharmaceutically acceptable salts thereof.

[00014] In an example of the present disclosure there is disclosed a pharmaceutical composition comprising a compound of Formula Ib, Formula Ia, Formula I or a pharmaceutically acceptable salt thereof together with a pharmaceutically acceptable carrier, optionally in combination with one or more other pharmaceutical compositions.

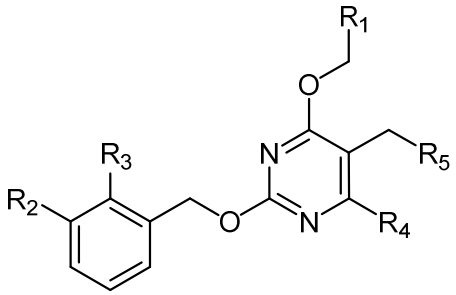
[00015] In an example of the present disclosure there is disclosed a method for the treatment and/or prevention of various diseases, including cancer and infectious diseases, comprising administering to a subject suffering from the proliferative disorder or cancer a therapeutically effective amount of the compound of Formula Ib, Formula Ia, and Formula I or the pharmaceutical composition, with other clinically relevant cytotoxic agents or non-cytotoxic agents to a subject in need thereof.

[00016] In an example of the present disclosure there is disclosed a method of treatment and/or prevention of various diseases, including cancer and infectious diseases, comprising administering to a subject suffering from the viral infectious diseases such as HIV, Influenza, herpes virus, Hepatitis A, Hepatitis B, Hepatitis C, and Hepatitis D, a therapeutically effective amount of the compound of Formula Ib, Formula Ia, and Formula I or the pharmaceutical composition, with other clinically relevant anti-viral drugs to a subject in need thereof.

[00017] In an example of the present disclosure there is disclosed use of the compounds of Formula Ib, Formula Ia, and Formula I or the pharmaceutical composition for the treatment and/or prevention of various diseases including proliferative disorder or cancer; or treatment of cancer together with other clinically relevant cytotoxic agents or non-cytotoxic agents.

I/We claim:

1. A compound of Formula I



Formula I

their stereoisomers and pharmaceutically acceptable salts thereof,

wherein

R_1 is selected from hydrogen, C_{1-10} alkyl, C_{1-6} haloalkyl, C_{5-10} aryl, and 5-10 membered monocyclic or bicyclic heteroaryl with 1-5 heteroatoms selected from N, S or O,

wherein C_{1-10} alkyl, C_{5-10} aryl, and 5-10 membered monocyclic or bicyclic heteroaryl, are optionally substituted with one or more of the groups selected from hydrogen, halogen, hydroxyl, and cyano,

R_2 is selected from hydrogen, C_{1-10} alkyl, C_{1-10} alkoxy, C_{5-10} aryl, and 5-10 membered monocyclic or bicyclic heteroaryl with 1-5 heteroatoms selected from N, S or O,

wherein C_{1-10} alkyl, C_{5-10} aryl, and 5-10 membered monocyclic or bicyclic heteroaryl, are optionally substituted with one or more of the groups selected from hydrogen, halogen, C_{1-6} alkyl, C_{1-6} alkoxy and C_{1-6} heterocyclyl,

wherein C_{1-6} alkyl, C_{1-6} alkoxy, and C_{1-6} heterocyclyl are optionally substituted with one or more of the groups selected from C_{1-6} alkyl or C_{1-6} heterocyclyl,

wherein C_{1-6} heterocyclyl is optionally substituted with halogen;

R_3 and R_4 are independently selected from hydrogen, C_{1-10} alkyl, and C_{1-10} alkoxy,

O is absent or is oxygen;

R_5 is $-NR_7R_8$, wherein R_7 and R_8 are selected from the group consisting of hydrogen, C_{3-10} cycloalkyl, C_{1-6} alkyl, 5-10 membered monocyclic or bicyclic, saturated or unsaturated heterocyclic ring with 1-3 heteroatoms selected from N, S or O, and combinations thereof, wherein C_{3-10} cycloalkyl, C_{1-6} alkyl, and the 5-10 membered monocyclic or bicyclic, saturated or

unsaturated heterocyclic ring are optionally substituted with one or more substituents selected from oxo, cyano, halogen, hydroxyl, morpholino, $C(O)NH_2$, $C(O)CH_2CN$, NHR_6, COOH, $COOR_6$, $NHC(O)R_6$, C_{1-6} alkyl, C_{1-6} haloalkyl, C_{3-10} cycloalkyl, C_{5-6} aryl, SR_6, 5-10 membered monocyclic or bicyclic, saturated or unsaturated heterocyclic ring with 1-3 heteroatoms selected from N, S or O, wherein C_{1-6} alkyl, and the 5-10 membered monocyclic or bicyclic, saturated or unsaturated heterocyclic ring are independently substituted with one or more substituents selected from hydroxyl, and R_6; or R_7 and R_8 can be taken together to form a 4-10 membered monocyclic or bicyclic, saturated or unsaturated heterocyclic ring with 1-3 heteroatoms selected from N, S or O, wherein the 4-10 membered monocyclic or bicyclic, saturated or unsaturated heterocyclic ring is optionally substituted with one or more substituents selected from the group consisting of hydroxyl, halogen, C_{1-6} alkyl, COOH, R_6, NHR_6, $C(O)NHR_6$, $C(O)NHSO_2R_6$, $C(O)(CH_2)_nNHC(O)CH_3$, and combinations thereof, wherein C_{1-6} alkyl is further substituted with groups selected from oxo, hydroxyl, COOH, $COOR_6$, or NHR_6; n is 1-6; and R_6 is selected from the group consisting of hydrogen, C_{1-6} alkyl, $C(O)C_{1-6}$ alkyl, and combinations thereof, wherein C_{1-6} alkyl, and $C(O)C_{1-6}$ alkyl are optionally substituted with substituents selected from the group consisting of hydroxyl, COOH, NHR_6, $NHC(O)NHR_6$, and combinations thereof.

2. The compound of Formula I as claimed in claim 1, their stereoisomers and pharmaceutically acceptable salts thereof, wherein

R_1 is selected from hydrogen, C_{1-6} alkyl, C_{1-4} haloalkyl, C_{5-9} aryl, and 5-10 membered monocyclic or bicyclic heteroaryl with 1-5 heteroatoms selected from N, S or O,

wherein C_{1-6} alkyl, C_{5-9} aryl, and 5-10 membered monocyclic or bicyclic heteroaryl, is optionally substituted with one or more of the groups selected from hydrogen, halogen, hydroxyl, and cyano;

R_2 is selected from hydrogen, C_{1-6} alkyl, C_{1-6} alkoxy, C_{5-9} aryl, and 5-10 membered monocyclic or bicyclic heteroaryl with 1-5 heteroatoms selected from N, S or O,

wherein C_{1-6} alkyl, C_{5-9} aryl, and 5-10 membered monocyclic or bicyclic heteroaryl, is optionally substituted with one or more of the groups selected from hydrogen, halogen, C_{1-4} alkyl, and C_{1-4} alkoxy,

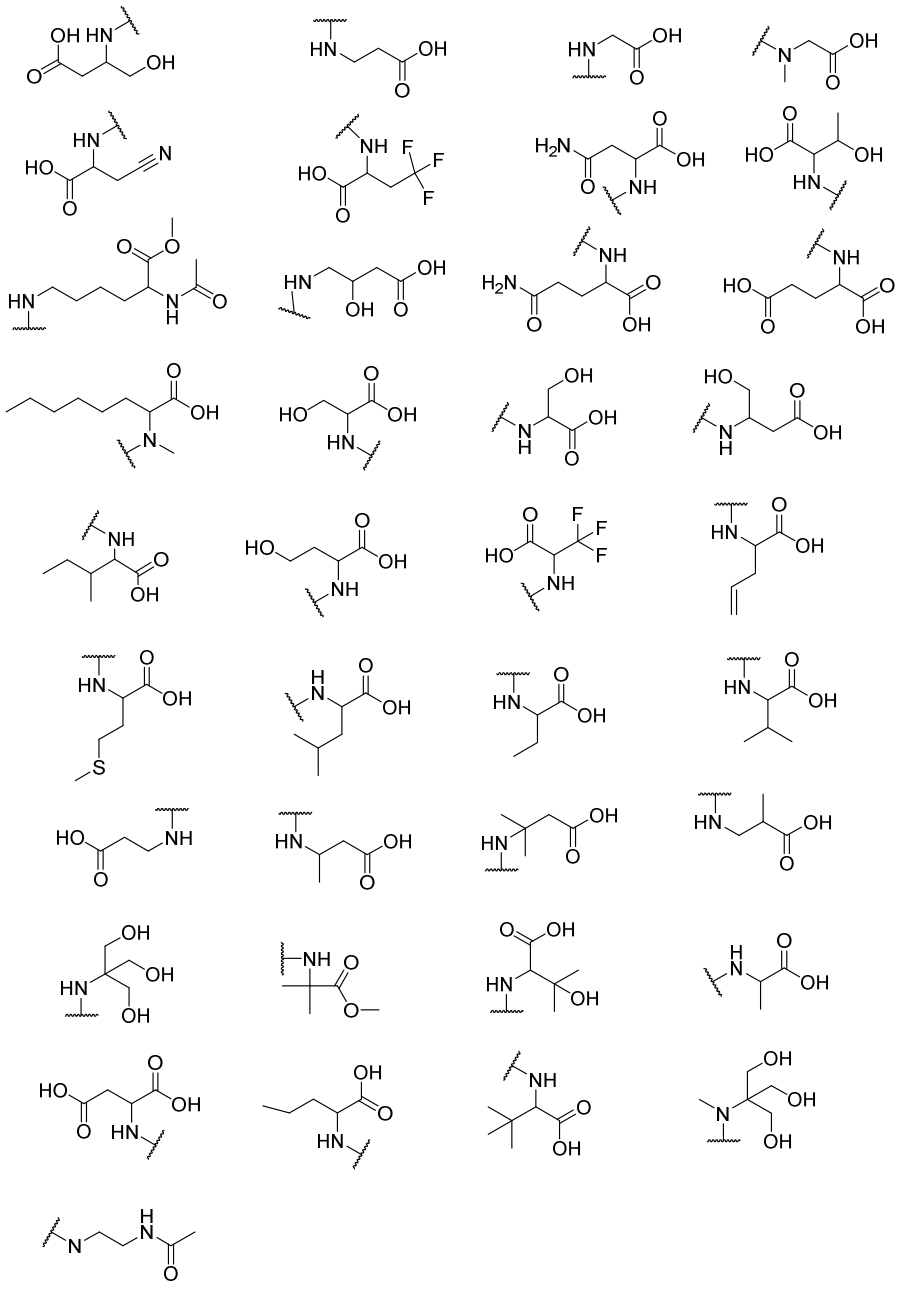
wherein C_{1-4} alkyl, C_{1-4} alkoxy, and C_{1-6} heterocyclyl are optionally substituted with one or more of the groups selected from C_{1-4} alkyl, or C_{1-6} heterocyclyl,

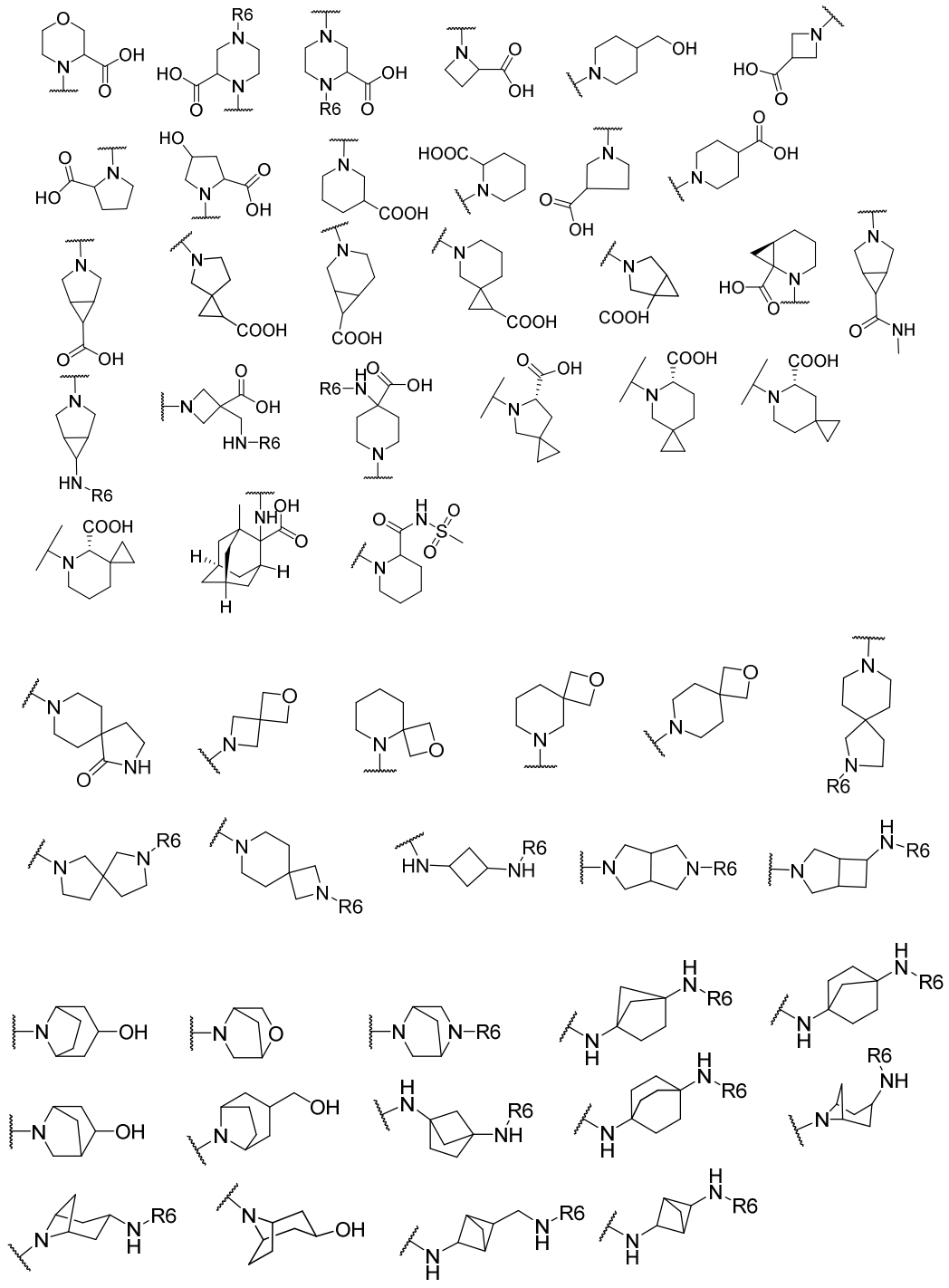
wherein C_{1-6} heterocyclyl is optionally substituted with halogen;

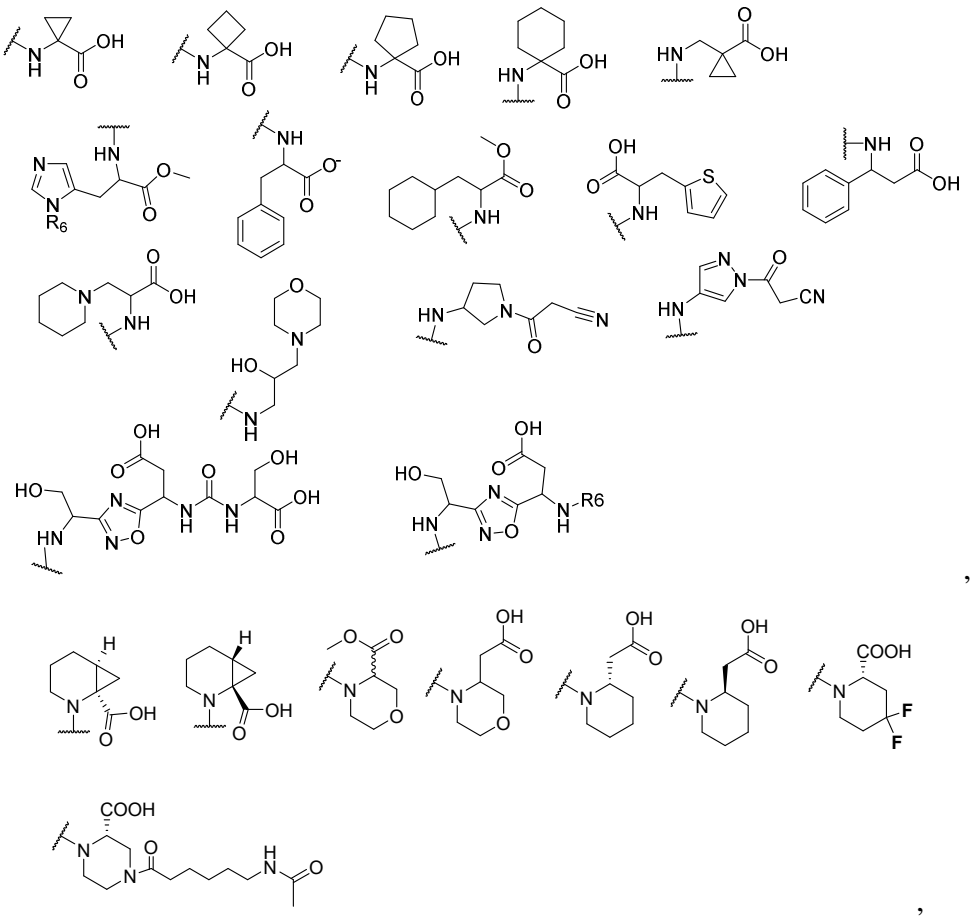
R_3 and R_4 are independently selected from hydrogen, C_{1-6} alkyl, and C_{1-6} alkoxy,

O is absent or is oxygen; and

R_5 is selected from







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wherein R_6 is selected from the group consisting of hydrogen, C_{1-6} alkyl, $C(O)C_{1-6}$ alkyl, and combinations thereof, wherein C_{1-6} alkyl, and $C(O)C_{1-6}$ alkyl are optionally substituted with substituents selected from the group consisting of hydroxyl, COOH, NHR_6, $NHC(O)NHR_6$, and combinations thereof.

3. The compound of Formula I as claimed in claim 1, their stereoisomers and pharmaceutically acceptable salts thereof, wherein

R_1 is selected from hydrogen, C_{1-4} alkyl, C_{5-6} aryl, and 5-9 membered monocyclic or bicyclic heteroaryl with 1-5 heteroatoms selected from N, S or O, wherein C_{1-4} alkyl, C_{5-6} aryl, and 5-9 membered monocyclic or bicyclic heteroaryl, are optionally substituted with one or more groups selected from hydrogen, halogen, hydroxyl, and cyano;

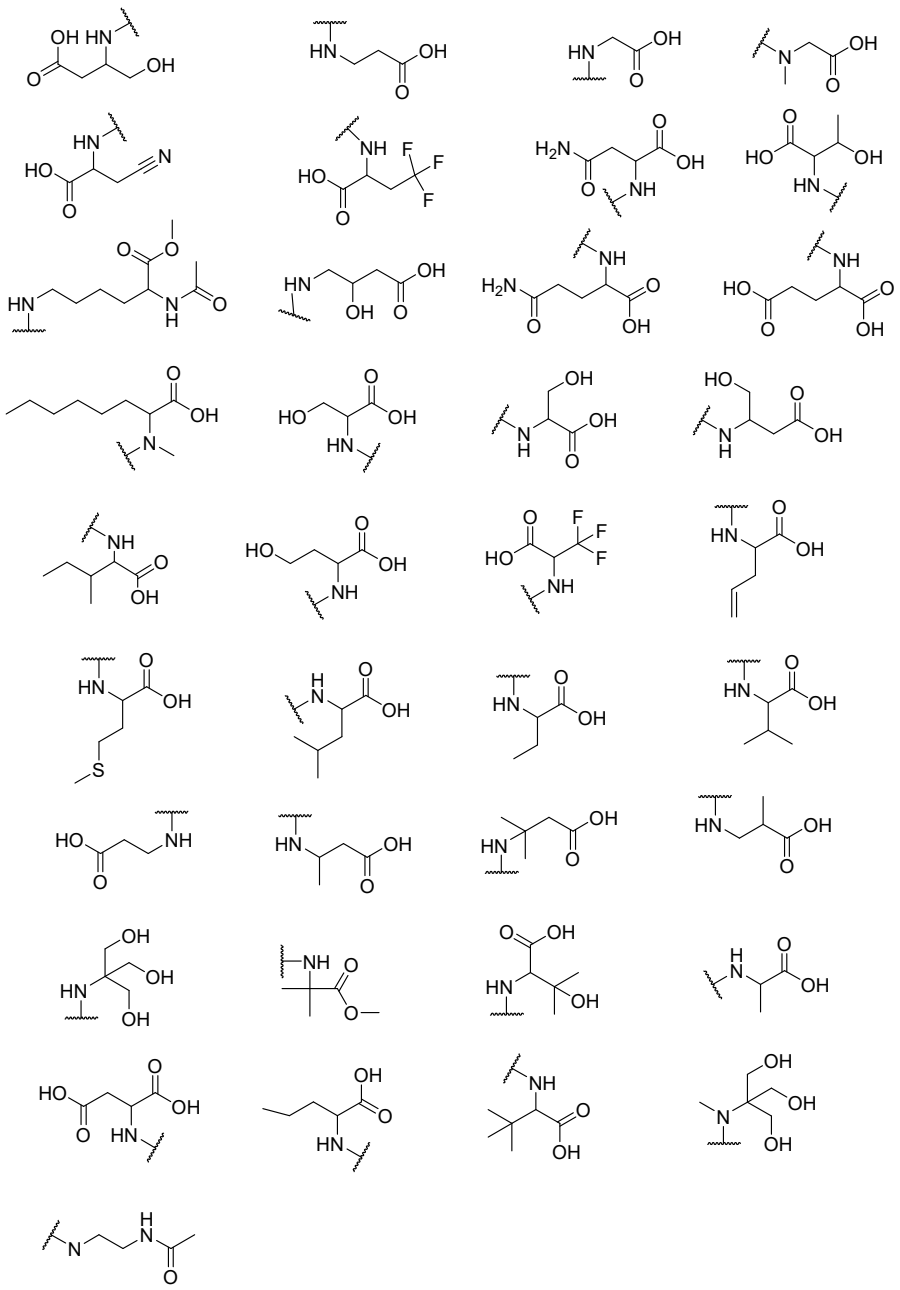
R_2 is selected from hydrogen, C_{5-6} aryl, and 5-10 membered monocyclic or bicyclic heteroaryl with 1-5 heteroatoms selected from N, S or O, wherein C_{5-6} aryl, and 5-10 membered monocyclic or bicyclic heteroaryl, is optionally substituted with one or more groups selected from hydrogen, fluoro, chloro, bromo, iodo, C_{1-4} alkyl, and C_{1-4} alkoxy,

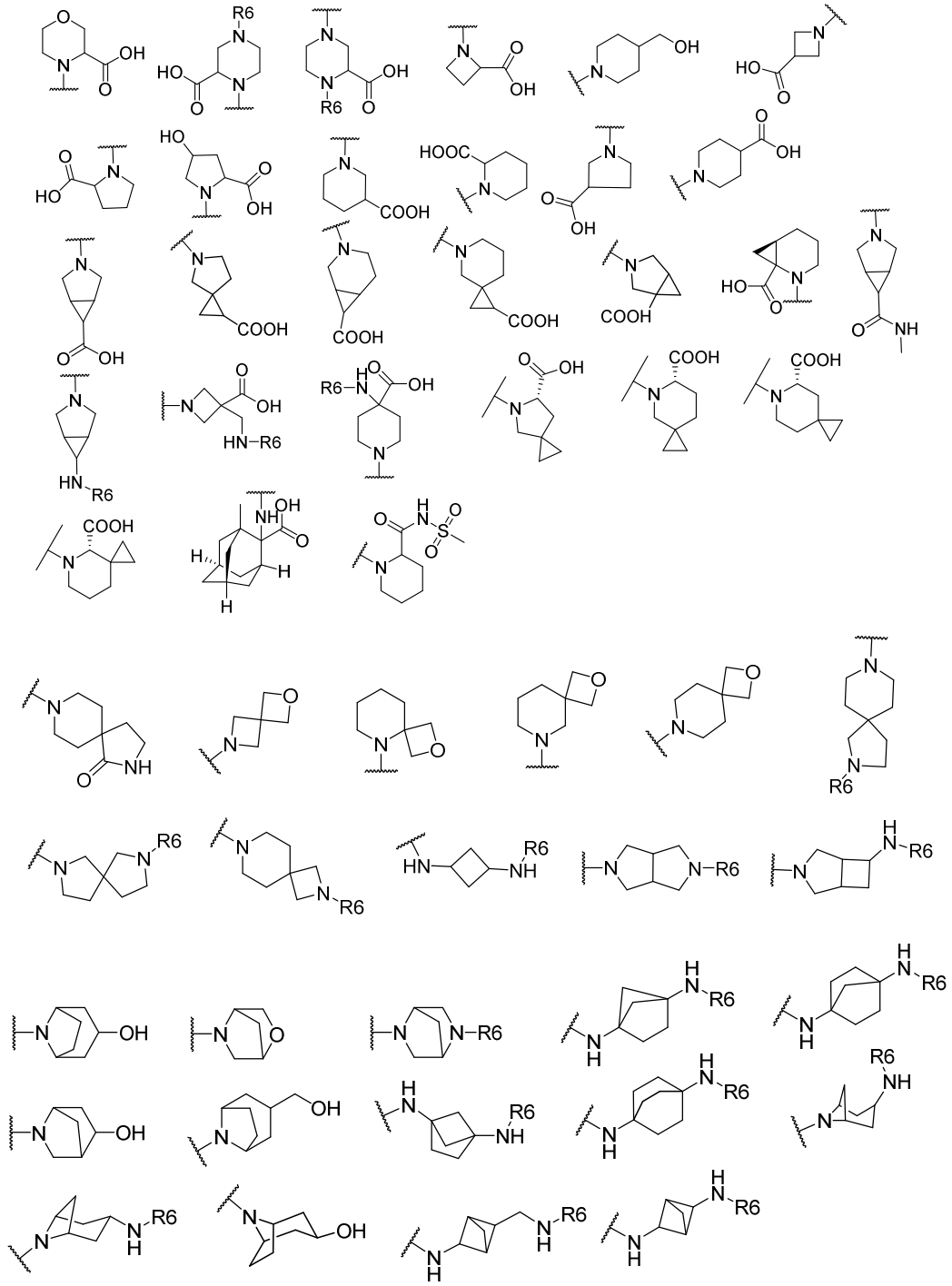
wherein C_{1-4} alkyl, C_{1-4} alkoxy, and C_{1-6} heterocyclyl is optionally substituted with one or more of the groups selected from C_{1-4} alkyl, or C_{1-6} heterocyclyl,

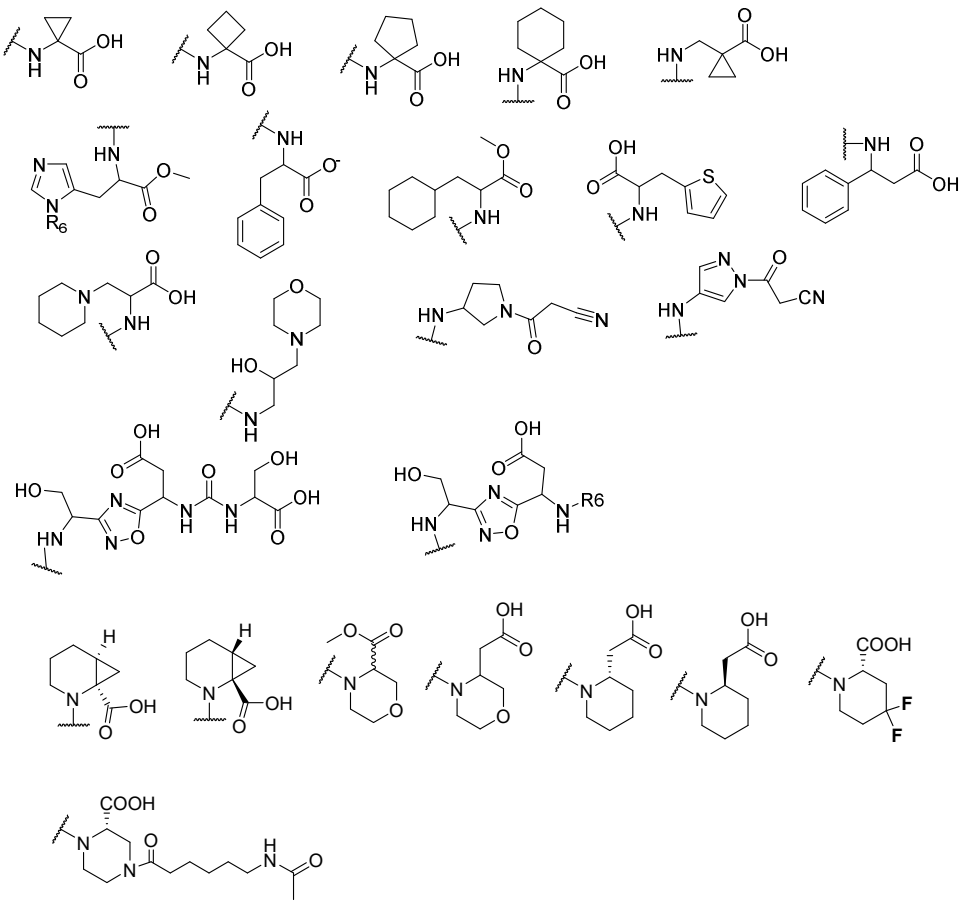
wherein C_{1-6} heterocyclyl is optionally substituted with halogen;

R_3 and R_4 are independently selected from hydrogen, C_{1-4} alkyl, and C_{1-4} alkoxy;

O is absent or is oxygen; and R_5 is selected from







, wherein R_6 is selected from the group consisting of hydrogen, C_{1-6} alkyl, $C(O)C_{1-6}$ alkyl, and combinations thereof, wherein C_{1-6} alkyl, and $C(O)C_{1-6}$ alkyl are optionally substituted with substituents selected from the group consisting of hydroxyl, COOH, NHR_6, $NHC(O)NHR_6$, and combinations thereof.

4. The compound of Formula I as claimed in any one of the claims 1-3 or its stereoisomers and pharmaceutically acceptable salts thereof, which is selected from a group consisting of:

N-(2-(((2-((4'-fluoro-2-methyl-[1,1'-biphenyl]-3-yl)methoxy)-4-methoxypyrimidin-5-yl)methyl)amino) ethyl)acetamide (Compound -1),

N-((4-ethoxy-2-((2-methyl-[1,1'-biphenyl]-3-yl)methoxy)pyrimidin-5-yl)methyl)-N-methyl glycine (Compound -2),

N-((4-ethoxy-2-((2-methyl-[1,1'-biphenyl]-3-yl)methoxy)pyrimidin-5-yl)methyl)-N-methyl glycine (Compound -3),

(1R,6R)-2-((4,6-dimethoxy-2-((2-methyl-[1,1'-biphenyl]-3-yl)methoxy)pyrimidin-5-yl)methyl)-2-azabicyclo[4.1.0]heptane-1-carboxylic acid (Compound-4),

(1S,6R)-2-((4,6-dimethoxy-2-((2-methyl-[1,1'-biphenyl]-3-yl)methoxy)pyrimidin-5-yl)methyl)-2-azabicyclo[4.1.0]heptane-1-carboxylic acid (Compound-5),
N-(2-(((4,6-diethoxy-2-((2-methyl-[1,1'-biphenyl]-3-yl)methoxy) pyrimidin-5-yl) methyl)amino)ethyl) acetamide (Compound-6),
(*S*)-1-((4-methoxy-2-((2-methyl-[1,1'-biphenyl]-3-yl) methoxy) pyrimidin-5-yl)methyl)piperidine-2-carboxylic acid (Compound-7),
S)-1-((4-((3-cyano-4-fluorobenzyl)oxy)-2-((2-methyl-[1,1'-biphenyl]-3-yl)methoxy)pyrimidin-5-yl)methyl)piperidine-2-carboxylic acid (Compound-8),
(*S*)-1-((2-((2-methyl-[1,1'-biphenyl]-3-yl)methoxy)-4-(2,2,2-trifluoroethoxy)pyrimidin-5-yl)methyl)piperidine-2-carboxylic acid (Compound-9),
(S)-1-((4-(4-hydroxybutoxy)-2-((2-methyl-[1,1'-biphenyl]-3-yl)methoxy)pyrimidin-5-yl)methyl)piperidine-2-carboxylic acid (Compound-10),
(2S,4R)-1-((2-((3-(2,3-dihydrobenzo[b][1,4]dioxin-6-yl)-2-methylbenzyl)oxy)-4,6-dimethoxypyrimidin-5-yl)methyl)-4-hydroxypyrrolidine-2-carboxylic acid (Compound-11),
(*S*)-1-((4-((5-cyanopyridin-3-yl)methoxy)-2-((2-methyl-[1,1'-biphenyl]-3-yl)methoxy)pyrimidin-5-yl)methyl)piperidine-2-carboxylic acid (Compound-12),
(S)-1-((2-((3'-(3-(3,3-difluoropyrrolidin-1-yl)propoxy)-2,2'-dimethyl-[1,1'-biphenyl]-3-yl)methoxy)-4-methoxypyrimidin-5-yl)methyl)piperidine-2-carboxylic acid (Compound-13),
N-(2-(((4-methoxy-2-((2-methyl-[1,1'-biphenyl]-3-yl)methoxy)pyrimidin-5-yl)methyl)amino) ethyl)acetamide (Compound-14),
(R)-1-((4-methoxy-2-((2-methyl-[1,1'-biphenyl]-3-yl)methoxy)pyrimidin-5-yl)methyl)piperidine-2-carboxylic acid (Compound 15),
(S)-1-((2-((4'-fluoro-2-methyl-[1,1'-biphenyl]-3-yl)methoxy)-4-methoxypyrimidin-5-yl) methyl)piperidine-2-carboxylic acid (Compound-16),
(S)-1-((2-((3'-fluoro-2-methyl-[1,1'-biphenyl]-3-yl)methoxy)-4-methoxypyrimidin-5-yl)methyl)piperidine-2-carboxylic acid (Compound 17),
N-(2-(((2-((3'-fluoro-2-methyl-[1,1'-biphenyl]-3-yl)methoxy)-4-methoxypyrimidin-5-yl)methyl)amino)ethyl)acetamide (Compound-18),
(S)-1-((2-((2'-fluoro-2-methyl-[1,1'-biphenyl]-3-yl)methoxy)-4-methoxypyrimidin-5-yl)methyl)piperidine-2-carboxylic acid (Compound 19),

N-(2-(((2-((2'-fluoro-2-methyl-[1,1'-biphenyl]-3-yl)methoxy)-4-methoxypyrimidin-5-yl)methyl)amino)ethyl)acetamide (Compound 20),
N-(2-(((4-ethoxy-2-((2-methyl-[1,1'-biphenyl]-3-yl)methoxy)pyrimidin-5-yl)methyl) amino)ethyl)acetamide (Compound 21),
(S)-1-((4-ethoxy-2-((2-methyl-[1,1'-biphenyl]-3-yl)methoxy)pyrimidin-5-yl)methyl) piperidine-2-carboxylic acid (Compound 22),
1-(((4-ethoxy-2-((2-methyl-[1,1'-biphenyl]-3-yl)methoxy)pyrimidin-5-yl)methyl) amino)cyclopropane-1-carboxylic acid (Compound 23),
(3-(((4-ethoxy-2-((2-methyl-[1,1'-biphenyl]-3-yl)methoxy)pyrimidin-5-yl)methyl) amino)propanoic acid (Compound 24),
2-(((4-ethoxy-2-((2-methyl-[1,1'-biphenyl]-3-yl)methoxy)pyrimidin-5-yl)methyl) amino)-2-(hydroxymethyl)propane-1,3-diol (Compound 25),
(2-(((4-ethoxy-2-((2-methyl-[1,1'-biphenyl]-3-yl)methoxy)pyrimidin-5-yl)methyl) (methyl)amino)-2-(hydroxymethyl)propane-1,3-diol (Compound 26),
(S)-3-(((4-ethoxy-2-((2-methyl-[1,1'-biphenyl]-3-yl)methoxy)pyrimidin-5-yl)methyl)amino)butanoic acid (Compound 27),
((4-ethoxy-2-((2-methyl-[1,1'-biphenyl]-3-yl)methoxy)pyrimidin-5-yl)methyl)-D-alanine (Compound 28),
((4-ethoxy-2-((2-methyl-[1,1'-biphenyl]-3-yl)methoxy)pyrimidin-5-yl)methyl)asparagine (Compound 29),
(2R,4R)-1-((4-ethoxy-2-((2-methyl-[1,1'-biphenyl]-3-yl)methoxy)pyrimidin-5-yl)methyl)-4-hydroxypyrrolidine-2-carboxylic acid (Compound 30),
1-((4-ethoxy-2-((2-methyl-[1,1'-biphenyl]-3-yl)methoxy)pyrimidin-5-yl)methyl)azetidine-2-carboxylic acid (Compound 31),
N-(2-(((4-(benzyloxy)-2-((2-methyl-[1,1'-biphenyl]-3-yl)methoxy)pyrimidin-5-yl)methyl)amino)ethyl)acetamide (Compound 32),
1-((4-(benzyloxy)-2-((2-methyl-[1,1'-biphenyl]-3-yl)methoxy)pyrimidin-5-yl)methyl)piperidine-2-carboxylic acid (Compound 33),
(2S,4R)-1-((4,6-dimethoxy-2-((2-methyl-[1,1'-biphenyl]-3-yl)methoxy)pyrimidin-5-yl)methyl)-4-hydroxypyrrolidine-2-carboxylic acid (Compound 34),

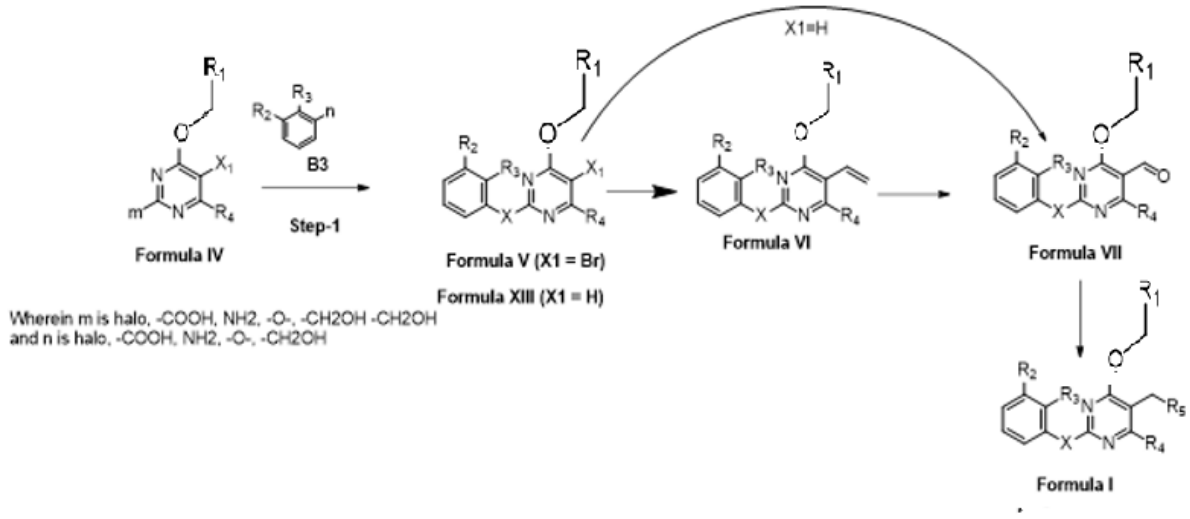
2-(((4,6-dimethoxy-2-((2-methyl-[1,1'-biphenyl]-3-yl)methoxy)pyrimidin-5-yl)methyl)amino)-2-(hydroxymethyl)propane-1,3-diol (Compound 35),
((4,6-dimethoxy-2-((2-methyl-[1,1'-biphenyl]-3-yl)methoxy)pyrimidin-5-yl)methyl)-L-proline (Compound 36),
Methyl 4-((4,6-dimethoxy-2-((2-methyl-[1,1'-biphenyl]-3-yl)methoxy) pyrimidin-5-yl)methyl) morpholine-3-carboxylate (Compound 37),
4-((4,6-dimethoxy-2-((2-methyl-[1,1'-biphenyl]-3-yl)methoxy)pyrimidin-5-yl)methyl)morpholine-3-carboxylic acid (Compound 38),
(2S,4R)-1-((4,6-diethoxy-2-((2-methyl-[1,1'-biphenyl]-3-yl)methoxy)pyrimidin-5-yl)methyl)-4-hydroxypyrrolidine-2-carboxylic acid (Compound 39),
((S)-1-((4,6-diethoxy-2-((2-methyl-[1,1'-biphenyl]-3-yl)methoxy)pyrimidin-5-yl)methyl)piperidine-2-carboxylic acid (Compound 40),
2-(((4,6-diethoxy-2-((2-methyl-[1,1'-biphenyl]-3-yl)methoxy)pyrimidin-5-yl)methyl)amino)-2-(hydroxymethyl)propane-1,3-diol (Compound 41),
2-(((4,6-dimethoxy-2-((2-methyl-[1,1'-biphenyl]-3-yl)methoxy)pyrimidin-5-yl)methyl)amino)-2-(hydroxymethyl)propane-1,3-diol (Compound 42),
(*S*)-4-((4,6-dimethoxy-2-((2-methyl-[1,1'-biphenyl]-3-yl)methoxy)pyrimidin-5-yl)methyl)morpholine-3-carboxylic acid (Compound 43),
2-(4-((4,6-dimethoxy-2-((2-methyl-[1,1'-biphenyl]-3-yl)methoxy)pyrimidin-5-yl)methyl)morpholin-3-yl)acetic acid (Compound 44),
(*S*)-1-((4,6-dimethoxy-2-((2-methyl-[1,1'-biphenyl]-3-yl)methoxy)pyrimidin-5-yl)methyl)piperidine-2-carboxylic acid (Compound 45),
(*S*)-5-((4,6-dimethoxy-2-((2-methyl-[1,1'-biphenyl]-3-yl)methoxy)pyrimidin-5-yl)methyl)-5-azaspiro[2.4]heptane-6-carboxylic acid (Compound 46),
7-((4,6-dimethoxy-2-((2-methyl-[1,1'-biphenyl]-3-yl)methoxy)pyrimidin-5-yl) methyl) -2,7-diazaspiro[4.5]decan-1-one (Compound 47),
rac-(1*R*,6*S*)-2-((4,6-dimethoxy-2-((2-methyl-[1,1'-biphenyl]-3-yl)methoxy) pyrimidin-5-yl)methyl)-2-azabicyclo[4.1.0]heptane-1-carboxylic acid (Compound 48),
(*S*)-4-acetyl-1-((4-methoxy-2-((2-methyl-[1,1'-biphenyl]-3-yl)methoxy)pyrimidin-5-yl)methyl)piperazine-2-carboxylic acid (Compound 49),

(*S*)-1-((4-methoxy-2-((2-methyl-[1,1'-biphenyl]-3-yl)methoxy)pyrimidin-5-yl)methyl)piperazine-2-carboxylic acid (Compound 50),
(S)-5-((4-methoxy-2-((2-methyl-[1,1'-biphenyl]-3-yl)methoxy)pyrimidin-5-yl)methyl)-5-azaspiro[2.4]heptane-6-carboxylic acid (Compound 51),
7-((4-methoxy-2-((2-methyl-[1,1'-biphenyl]-3-yl)methoxy)pyrimidin-5-yl)methyl)-2,7-diazaspiro[4.5]decan-1-one (Compound 52),
N-(2-(((4-((3-cyano-4-fluorobenzyl)oxy)-2-((2-methyl-[1,1'-biphenyl]-3-yl)methoxy)pyrimidin-5-yl)methyl)amino)ethyl)acetamide (Compound 53),
(2*S*,4*R*)-1-((4-((3-cyano-4-fluorobenzyl)oxy)-2-((2-methyl-[1,1'-biphenyl]-3-yl)methoxy)pyrimidin-5-yl)methyl)-4-hydroxypyrrolidine-2-carboxylicacid (Compound 54),
(S)-1-((2-((3-(2,3-dihydrobenzo[b][1,4]dioxin-6-yl)-2-methylbenzyl)oxy)-4,6-dimethoxypyrimidin-5-yl)methyl)piperidine-2-carboxylic acid (Compound 55),
N-(2-(((2-((3-(2,3-dihydrobenzo[b][1,4]dioxin-6-yl)-2-methylbenzyl)oxy)-4,6-dimethoxypyrimidin-5-yl)methyl)amino)ethyl)acetamide (Compound 56),
N-(2-(((2-((3',4'-dimethoxy-2-methyl-[1,1'-biphenyl]-3-yl)methoxy)-4,6-dimethoxypyrimidin-5-yl)methyl)amino)ethyl)acetamide (Compound 57),
((2S,4R)-1-((2-((3',4'-dimethoxy-2-methyl-[1,1'-biphenyl]-3-yl)methoxy)-4,6-dimethoxypyrimidin-5-yl)methyl)-4-hydroxypyrrolidine-2-carboxylic acid (Compound 58),
(2S,4R)-1-((4-((5-cyanopyridin-3-yl)methoxy)-2-((2-methyl-[1,1'-biphenyl]-3-yl)methoxy)pyrimidin-5-yl)methyl)-4-hydroxypyrrolidine-2-carboxylic acid (Compound 59),
(S)-2-(1-((4-methoxy-2-((2-methyl-[1,1'-biphenyl]-3-yl)methoxy)pyrimidin-5-yl)methyl)piperidin-2-yl) acetic acid (Compound 60),
(R)-2-(1-((4-methoxy-2-((2-methyl-[1,1'-biphenyl]-3-yl)methoxy)pyrimidin-5-yl)methyl)piperidin-2-yl) acetic acid (Compound 61),
(S)-4-(6-acetamidohexanoyl)-1-((4-methoxy-2-((2-methyl-[1,1'-biphenyl]-3-yl)methoxy)pyrimidin-5-yl)methyl)piperazine-2-carboxylic acid (Compound 62),
(S)-4,4-difluoro-1-((4-methoxy-2-((2-methyl-[1,1'-biphenyl]-3-yl)methoxy)pyrimidin-5-yl)methyl)piperidine-2-carboxylic acid (Compound 63),
(*S*)-1-((4-methyl-2-((2-methyl-[1,1'-biphenyl]-3-yl)methoxy)pyrimidin-5-yl)methyl)piperidine-2-carboxylic acid (Compound 64), and

N-(2-(((4-methyl-2-((2-methyl-[1,1'-biphenyl]-3-yl)methoxy)pyrimidin-5-yl)methyl)amino)ethyl)acetamide (Compound 65).

5. A process of preparation of compounds of Formula I as claimed in any one of claims 1 – 4 or its stereoisomers and pharmaceutically acceptable salts thereof.

6. The process of preparation of compounds of Formula I as claimed in claim 5, comprising (a) reacting compounds of Formula IV and Formula B3 in presence of a base, a solvent, and optionally a coupling reagent to obtain compounds of Formula V or Formula XIII; (b) processing the compounds of Formula V and Formula XIII to obtain compounds of Formula VII; and (c) reacting compounds of Formula VII with substituted amines in presence of a reducing agent and a third solvent to obtain compounds of Formula I



wherein X of Formula V, Formula VI, and Formula VII is selected from -CH_2O-, -OCH_2-, -C(O)NH- or -NHC(O)-; R_2, R_3, and R_4 of Formula IV, Formula V, Formula VI, Formula VII, and Formula XIII are independently selected from hydrogen, C_{1-10} alkyl, C_{1-10} alkoxy, C_{5-10} aryl, and 5-10 membered monocyclic or bicyclic heteroaryl with 1-5 heteroatoms selected from N, S or O, wherein C_{1-10} alkyl, C_{1-10} alkoxy, C_{5-10} aryl, and 5-10 membered monocyclic or bicyclic heteroaryl, are optionally substituted with one or more of the groups selected from hydrogen, halogen, C_{1-6} alkyl, and C_{1-6} alkoxy, wherein C_{1-6} alkyl, C_{1-6} alkoxy, and C_{1-10} heterocyclyl are optionally substituted with one or more of the groups selected from C_{1-6} alkyl, and C_{1-6} heterocyclyl, wherein C_{1-6} heterocyclyl is optionally substituted with halogen; X of Formula V, Formula VI, Formula

VII, and Formula XIII is selected from -CH_2O-, -OCH_2-, -C(O)NH- or -NHC(O)-; R_5 of Formula Ib is -NR_7R_8, wherein R_7 and R_8 are independently selected from the group consisting of hydrogen, C_{3-10} cycloalkyl, C_{1-6} alkyl, C_{2-6} alkenyl, 5-10 membered monocyclic or bicyclic, saturated or unsaturated heterocyclic ring with 1-3 heteroatoms selected from N, S or O, and combinations thereof, wherein C_{3-10} cycloalkyl, C_{1-6} alkyl, C_{2-6} alkenyl, and the 5-10 membered monocyclic or bicyclic, saturated or unsaturated heterocyclic ring are optionally substituted with one or more substituents selected from oxo, cyano, halogen, hydroxyl, morpholino, $C(O)NH_2$, $C(O)CH_2CN$, NHR_6, COOH, $COOR_6$, $NHC(O)R_6$, C_{1-6} alkyl, C_{1-6} haloalkyl, C_{3-10} cycloalkyl, C_{5-6} aryl, SR_6, or 5-10 membered monocyclic or bicyclic, saturated or unsaturated heterocyclic ring with 1-3 heteroatoms selected from N, S or O, wherein C_{1-6} alkyl, and the 5-10 membered monocyclic or bicyclic, saturated or unsaturated heterocyclic ring are independently substituted with one or more substituents selected from hydroxyl, and R_6; or R_7 and R_8 can be taken together to form a 4-10 membered monocyclic or bicyclic, saturated or unsaturated heterocyclic ring with 1-3 heteroatoms selected from N, S or O, wherein the 4-10 membered monocyclic or bicyclic, saturated or unsaturated heterocyclic ring is optionally substituted with one or more substituents selected from the group consisting of hydroxyl, halogen, C_{1-6} alkyl, COOH, R_6, NHR_6, $C(O)NHR_6$, $C(O)NHSO_2R_6$, $C(O)(CH_2)_nNHC(O)CH_3$, and combinations thereof, wherein C_{1-6} alkyl is further substituted with groups selected from hydroxyl, COOH, or NHR_6; n is 1-6; and R_6 is selected from the group consisting of hydrogen, C_{1-6} alkyl, $C(O)C_{1-6}$ alkyl, and combinations thereof, wherein C_{1-6} alkyl, and $C(O)C_{1-6}$ alkyl are optionally substituted with substituents selected from the group consisting of hydroxyl, COOH, NHR_6, $NHC(O)NHR_6$, and combinations thereof.

7. The process as claimed in claim 6, wherein processing the compounds of Formula V to obtain compounds of Formula VII comprises: (a) alkenylation of compounds of Formula V in presence of a second base and a second solvent to obtain compounds of Formula VI; and (b) oxidation of compounds of Formula VI to obtain compounds of Formula VII.

8. The process as claimed in claim 6, wherein processing the compounds of Formula XIII to obtain compounds of Formula VII comprises formylation of compounds of Formula XIII to obtain compounds of Formula VII.

9. The process as claimed in any one of the claims 5-8, wherein the coupling reagent is selected from 1-[bis(dimethylamino)methylene]-1*H*-1,2,3-triazolo[4,5-*b*]pyridinium 3-oxid hexafluorophosphate (HATU), N, N'-Dicyclohexylcarbodiimide (DCC), or propylphosphonic

anhydride; the solvent is selected from the group consisting of methanol, ethanol, isopropyl alcohol, *t*-butyl alcohol, dichloromethane, ethyl acetate, dioxane, ether, N,N-dimethylformamide, dimethyl sulfoxide, and combinations thereof; the base is selected from the group consisting of sodium hydride, butyllithium, lithium diisopropylamide, potassium carbonate, cesium carbonate, triethylamine, diisopropylethylamine, 4-dimethylaminopyridine, pyridine, and combinations thereof; the second base is selected from the group consisting of butyl lithium, sodium hydride, lithium diisopropylamide, potassium carbonate, cesium carbonate, triethylamine, diisopropylethylamine, 4-dimethylaminopyridine, pyridine, and combinations thereof, the second solvent is selected from the group consisting of N,N-dimethylformamide, dichloromethane, ethyl acetate, dioxane, isopropyl alcohol, ether, *t*-butyl alcohol, N,N-dimethylformamide, dimethyl sulfoxide, and combinations thereof, the third solvent is selected from the group consisting of acetic acid, methanol, N,N-dimethylformamide, and combinations thereof, and the reducing agent is selected from the group consisting of sodium cyanoborohydride, sodium borohydride, lithiumaluminium hydride, diisobutylaluminium hydride, and combinations thereof.

10. A pharmaceutical composition comprising a compound of Formula I or a pharmaceutically acceptable salt thereof as claimed in any of claims 1-4 together with a pharmaceutically acceptable carrier, optionally in combination with one or more other pharmaceutical compositions.

11. The pharmaceutical composition as claimed in claim 10, wherein the composition is in the form selected from the group consisting of a tablet, capsule, powder, syrup, solution, aerosol and suspension.

12. Use of a therapeutically effective amount of the compound according to any one of claims 1–4 or the pharmaceutical composition as claimed in claim 10, or 11, in the manufacture of a medicament for treating or preventing various diseases in a subject, wherein the medicament is to be administered with other clinically relevant cytotoxic agents or non-cytotoxic agents to a subject in need thereof, wherein the subject is suffering from a proliferative disorder or cancer selected from breast cancer, prostate cancer, pancreatic cancer, gastric cancer, lung cancer, colon cancer, rectal cancer, esophagus cancer, duodenal cancer, tongue cancer, pharyngeal cancer, brain tumor, neurinoma, non-small cell lung cancer, small cell lung cancer, liver cancer, kidney cancer, bile duct cancer, uterine body cancer, cervical cancer, ovarian cancer, urinary bladder, skin cancer, hemangioma, malignant lymphoma, malignant melanoma, thyroid cancer, bone tumor, vascular fibroma, retinoblastoma, penile cancer, pediatric solid cancer, lymphoma, myeloma, leukemia,

acute myelogenous leukemia (AML), chronic myelogenous leukemia (CML), chronic neutrophilic leukemia, chronic eosinophilic leukemia, chronic lymphocytic leukemia (CLL), acute lymphoblastic leukemia (ALL) or hairy cell leukemia.

13. Use of the compounds as claimed in any one of claims 1–4 or the pharmaceutical composition as claimed in claim 10, or 11 for the treatment and/or prevention of various diseases including proliferative disorder or cancer; or treatment of cancer together with other clinically relevant cytotoxic agents or non-cytotoxic agents.

14. Use of the compounds as claimed in any of claims 1–4 or the pharmaceutical composition as claimed in claim 10, in the manufacture of a medicament for treating cancer, wherein the medicament is to be administered in combination with other clinically relevant cytotoxic agents or non-cytotoxic agents to a subject in need thereof.

15. Use of the compounds as claimed in any of claims 1–4 or the pharmaceutical composition as claimed in claim 10, in the manufacture of a medicament for treating cancer, wherein the medicament is to be administered in combination with other clinically relevant immune modulators agents to a subject in need of thereof.

16. Use of the compound according to any one of claims 1–4 or the pharmaceutical composition as claimed in claim 10, or 11, in the manufacture of a medicament for treating or preventing cancer and infectious diseases, wherein the medicament is to be administered with other clinically relevant anti-viral drugs to a subject in need thereof, wherein the subject is suffering from the infectious diseases selected from HIV, Influenza, herpes virus, Hepatitis A, Hepatitis B, Hepatitis C, and Hepatitis D.