

[00013] Slack *et al.* demonstrated the use of PAD4 inhibitors in the treatment of cancers (J. L. Slack et al., Cellular and Molecular Life Sciences, 2011, 68(4), 709-720). Overexpression of PAD4 had already been demonstrated in numerous cancers (X. Chang et al., BMC Cancer, 2009, 9, 40). It is suggested that PAD4 inhibitors have an anti-proliferative role as well. PAD4 deiminases arginine residues in histones at the promoters of p53- target genes such as p21, which are involved in cell cycle arrest and induction of apoptosis (P. Li et al., Molecular & Cell Biology, 2008, 28(15), 4745-4758).

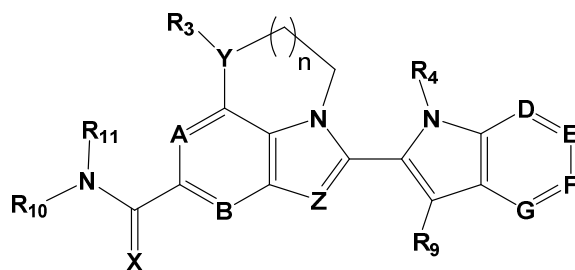
SUMMARY

their polymorphs, stereoisomers, prodrugs, solvates, co-crystals, intermediates, pharmaceutically acceptable salts, and metabolites thereof, wherein

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membered monocyclic or bicyclic heteroaryl are optionally substituted with 1-5 substituents selected from the group consisting of hydroxyl, cyano, halogen, C₁₋₆ alkyl, C₁₋₆ alkoxy, C₃₋₆ cycloalkyl, C₁₋₆ haloalkyl, C₁₋₆ haloalkoxy, C₁₋₆ acylamino, C₁₋₆ alkylamino, C₅₋₆ aryl, C₁₋₆ alkyl-C₅₋₆ aryl, C₂₋₆ alkenyl- C₅₋₆ aryl, C₁₋₆ heterocyclyl, C₁₋₆ alkyl-C₁₋₆ heterocyclyl, C₁₋₆ heteroaryl, and C₁₋₆ alkyl- C₁₋₆ heteroaryl, wherein C₁₋₆ alkyl, C₁₋₆ alkoxy, C₃₋₆ cycloalkyl, C₅₋₆ aryl, C₁₋₆ alkyl-C₅₋₆ aryl, C₁₋₆ heteroaryl, C₁₋₆ alkyl-C₁₋₆ heteroaryl, and C₁₋₆ alkyl-C₁₋₆ heterocyclyl is optionally substituted with one or more of the groups selected from hydrogen, C₁₋₆ alkyl, C₁₋₆ alkoxy, C₃₋₈ cycloalkyl, C₁₋₆ heteroaryl, halogen, hydroxyl, -CH₂OH, -COOH, and cyano; R₁₇ is selected from the group consisting of hydrogen, hydroxyl, cyano, halogen, C₁₋₆ alkyl, C₁₋₆ alkoxy, C₁₋₆ haloalkyl, C₁₋₆ haloalkoxy, C₁₋₆ acylamino, C₁₋₆ alkylamino, C₅₋₆ aryl, and C₁₋₆ heteroaryl, wherein C₁₋₆ alkoxy, and C₁₋₆ haloalkoxy, is optionally substituted with one or more of the groups selected from hydrogen, C₁₋₆ alkyl, C₁₋₆ alkoxy, C₁₋₆ haloalkyl, C₁₋₆ alkylhydroxy, cyano, and hydroxyl; and R₁₈ is independently selected from the group consisting of hydrogen, C₁₋₆ alkyl, and combinations thereof.

[00016] In another aspect, present disclosure also discloses compound of Formula (II)



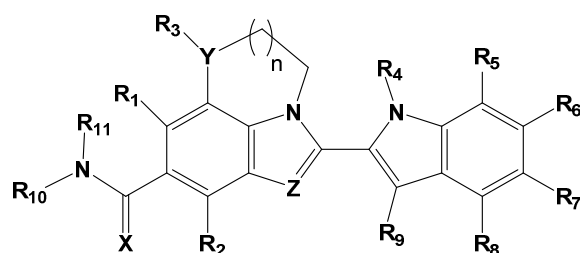
Formula (II)

their polymorphs, stereoisomers, prodrugs, solvates, co-crystals, intermediates, pharmaceutically acceptable salts, and metabolites thereof,

wherein

X is selected from O or S; Y is selected from O, N, S, S(O), SO₂ or C; Z is selected from N or CR₁₇; A is selected from N or CR₁; B is selected from N or CR₂; D is selected from N or CR₅; E is selected from N or CR₆; F is selected from N or CR₇; G is selected from N or CR₈; n is 0-2; R₁, R₂, R₅, R₆, R₇, R₈, and R₉ are independently selected from the group consisting of hydrogen, hydroxyl, cyano, halogen, C₁₋₆ alkyl, C₁₋₆ alkoxy, C₁₋₆ haloalkyl, C₁₋₆ haloalkoxy, C₁₋₆ acylamino, C₁₋₆ alkylamino, C₅₋₆ aryl, and C₁₋₆ heteroaryl,

[00017] In yet another aspect, present disclosure further discloses compound of Formula (III)



Formula (III)

their polymorphs, stereoisomers, prodrugs, solvates, co-crystals, intermediates, pharmaceutically acceptable salts, and metabolites thereof,

wherein

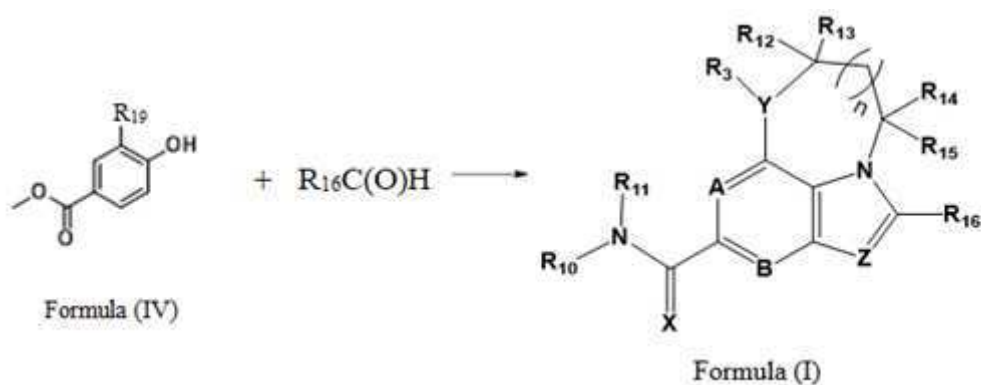
X is selected from O or S; Y is selected from O, N, S, S(O), SO₂ or C; Z is selected from N or CR₁₇; n is 0-2; R₁, R₂, R₅, R₆, R₇, R₈, and R₉ are independently selected from the group consisting of hydrogen, hydroxyl, cyano, halogen, C₁₋₆ alkyl, C₁₋₆ alkoxy, C₁₋₆ haloalkyl, C₁₋₆ haloalkoxy, C₁₋₆ acylamino, C₁₋₆ alkylamino, C₅₋₆ aryl, C₂₋₆ alkenyl-, C₅₋₆ aryl, and C₁₋₆ heteroaryl, wherein C₁₋₆ alkoxy, and C₁₋₆ haloalkoxy, is optionally substituted with one or more of the groups selected from hydrogen, C₁₋₆ alkyl, C₁₋₆ alkoxy, C₁₋₆ haloalkyl, C₁₋₆ alkylhydroxy, cyano, and hydroxyl; R₃ is absent or is selected from the group consisting of hydrogen, C₁₋₆ alkyl, C₃₋₆ cycloalkyl, C₁₋₆ alkylamino, C₁₋₆ haloalkyl, C(O)C₁₋₆ alkyl, C(O)C₁₋₆ haloalkyl, C(O)NR₁₈, C(O)C₁₋₆ alkylamino, SO₂C₁₋₆ alkyl, SO₂C₁₋₆ haloalkyl, SO₂C₃₋₆ cycloalkyl, SO₂NR₁₈, SO₂NC₁₋₆ alkylamino, C₅₋₆ aryl, C₁₋₆ heteroaryl, C(O)C₅₋₆ aryl, C(O)C₁₋₆ heteroaryl, SO₂C₅₋₆ aryl, and SO₂C₁₋₆ heteroaryl, wherein C₁₋₆ alkyl, (CO)C₁₋₆ alkyl, C(O)C₁₋₆ haloalkyl, SO₂C₅₋₆ aryl, and SO₂C₁₋₆ alkyl, is optionally substituted with C₁₋₆ alkoxy, halogen, C₅₋₆ aryl, and C₁₋₆ heteroaryl; R₄ is selected from the group consisting of hydrogen, C₁₋₆ alkyl, C₁₋₆ haloalkyl, C₁₋₆ alkoxy, C₃₋₆ cycloalkyl, C(O)C₁₋₆ alkyl, C(O)C₁₋₆ haloalkyl, C(O)NR₁₈, C(O)C₁₋₆ alkylamino, SO₂C₁₋₆ alkyl, SO₂C₁₋₆ haloalkyl, SO₂NR₁₈, SO₂NC₁₋₆ alkylamino, C₅₋₆ aryl, C₁₋₆ alkyl-C₅₋₆ aryl, C₁₋₆ heterocyclyl, C₁₋₆ alkyl-C₁₋₆ heterocyclyl, C₁₋₆ heteroaryl, C₁₋₆ alkyl-C₁₋₆ heteroaryl, C(O)C₅₋₆ aryl, C(O)C₁₋₆ heteroaryl, SO₂C₅₋₆ aryl, and SO₂C₁₋₆ heteroaryl, wherein C₁₋₆ alkyl, C₁₋₆ alkoxy, C₃₋₆ cycloalkyl, C₅₋₆ aryl, C₁₋₆ alkyl-C₅₋₆ aryl, C₁₋₆ heterocyclyl, C₁₋₆ alkyl-C₁₋₆ heterocyclyl, C₁₋₆ heteroaryl, C₁₋₆ alkyl-C₁₋₆ heteroaryl, (CO)C₁₋₆ alkyl, C(O)C₁₋₆ haloalkyl, and SO₂C₁₋₆ alkyl, is optionally substituted with one or more groups selected from hydrogen, C₁₋₆ alkyl, C₁₋₆ alkoxy, C₃₋₆ cycloalkyl, C₅₋₆ aryl, C₁₋₆ heteroaryl, halogen, hydroxyl, CH₂OH, COOH, and cyano; R₁₀ is hydrogen; R₁₁ is selected from the group consisting of hydrogen, C₁₋₆ alkyl, C₃₋₆ cycloalkyl, C₁₋₆

alkylamino, C₁₋₆ haloalkyl, C(O)C₁₋₆ alkyl, C(O)C₁₋₆ haloalkyl, C(O)NR₁₈, C(O)C₁₋₆ alkylamino, SO₂C₁₋₆ alkyl, SO₂C₁₋₆ haloalkyl, SO₂C₃₋₆ cycloalkyl, SO₂NR₁₈, SO₂NC₁₋₆ alkylamino, C₅₋₆ aryl, C₁₋₆ heteroaryl, C(O)C₅₋₆ aryl, C(O)C₁₋₆ heteroaryl, SO₂C₅₋₆ aryl, and SO₂C₁₋₆ heteroaryl, wherein C₁₋₆ alkyl, (CO)C₁₋₆ alkyl, C(O)C₁₋₆ haloalkyl, SO₂C₅₋₆ aryl, and SO₂C₁₋₆ alkyl, is optionally substituted with C₁₋₆ alkoxy, halogen, C₅₋₆ aryl, and C₁₋₆ heteroaryl; and 5-10 membered monocyclic or bicyclic saturated heterocyclic ring with 1-3 heteroatoms selected from N, S or O, or R₁₀ and R₁₁ can be taken together to form a 5-10 membered monocyclic or bicyclic saturated or unsaturated heterocyclic ring, wherein the 5-10 membered monocyclic or bicyclic saturated or unsaturated heterocyclic ring is optionally substituted with the substituents selected from the group consisting of amino, C₁₋₆ alkylamino, C₁₋₆ acylamino, -NHC(NH)CH₂Cl, -NHC(O)CH=CHCH₂N(CH₃)₂, C₁₋₆ alkyl, halogen, C₁₋₆ alkoxy, and hydroxyl; R₁₇ is selected from the group consisting of hydrogen, hydroxyl, cyano, halogen, C₁₋₆ alkyl, C₁₋₆ alkoxy, C₁₋₆ haloalkyl, C₁₋₆ haloalkoxy, C₁₋₆ acylamino, C₁₋₆ alkylamino, C₅₋₆ aryl, and C₁₋₆ heteroaryl, wherein C₁₋₆ alkoxy, and C₁₋₆ haloalkoxy, is optionally substituted with one or more of the groups selected from hydrogen, C₁₋₆ alkyl, C₁₋₆ alkoxy, C₁₋₆ haloalkyl, C₁₋₆ alkylhydroxy, cyano, and hydroxyl; and R₁₈ is independently selected from the group consisting of hydrogen, C₁₋₆ alkyl, and combinations thereof.

[00018] The present disclosure further describes the process of preparation of compounds of Formula (I), Formula (II), and Formula (III) or its polymorphs, stereoisomers, prodrugs, solvates, co-crystals, intermediates, pharmaceutically acceptable salts, and metabolites thereof.

[00019] The present disclosure further discloses a pharmaceutical composition comprising a compound of Formula (I), Formula (II), and Formula (III) or a pharmaceutically acceptable salt thereof, together with a pharmaceutically acceptable carrier, optionally in combination with one or more other pharmaceutical compositions.

[00019a] In yet another aspect, the present disclosure provides a process of preparation of compounds of Formula (I) provided herein or its polymorphs, stereoisomers, prodrugs, solvates, co-crystals, intermediates, pharmaceutically acceptable salts, and metabolites thereof, the process comprising reacting Formula (IV) and R₁₆C(O)H

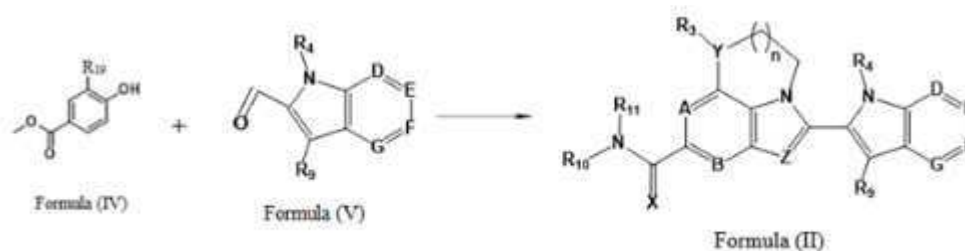


wherein R_{19} of Formula (IV) is selected from nitro, and C_{1-6} alkoxy; R_{16} of $R_{16}C(O)H$ is selected from the group consisting of hydrogen, 5-10 membered monocyclic or bicyclic aryl, and 5-10 membered monocyclic or bicyclic heteroaryl with 1-5 heteroatoms selected from N, S or O, wherein 5-10 membered monocyclic or bicyclic aryl, and 5-10 membered monocyclic or bicyclic heteroaryl are optionally substituted with 1-5 substituents selected from the group consisting of hydroxyl, cyano, halogen, C_{1-6} alkyl, C_{1-6} alkoxy, C_{3-6} cycloalkyl, C_{1-6} haloalkyl, C_{1-6} haloalkoxy, C_{1-6} acylamino, C_{1-6} alkylamino, C_{5-6} aryl, C_{1-6} alkyl- C_{5-6} aryl, C_{2-6} alkenyl- C_{5-6} aryl, C_{1-6} heterocyclyl, C_{1-6} alkyl- C_{1-6} heterocyclyl, C_{1-6} heteroaryl, and C_{1-6} alkyl- C_{1-6} heteroaryl, wherein C_{1-6} alkyl, C_{1-6} alkoxy, C_{3-6} cycloalkyl, C_{5-6} aryl, C_{1-6} alkyl- C_{5-6} aryl, C_{1-6} heteroaryl, C_{1-6} alkyl- C_{1-6} heteroaryl, and C_{1-6} alkyl- C_{1-6} heterocyclyl is optionally substituted with one or more of the groups selected from hydrogen, C_{1-6} alkyl, C_{1-6} alkoxy, C_{3-8} cycloalkyl, C_{1-6} heteroaryl, halogen, hydroxyl, $-CH_2OH$, $-COOH$, and cyano; X of Formula (I) is selected from O or S; Y is selected from O, N, S, $S(O)$, SO_2 or C; Z is selected from N or CR_{17} ; A is selected from N or CR_1 ; B is selected from N or CR_2 ; n is 0-2; R_1 , and R_2 are independently selected from the group consisting of hydrogen, hydroxyl, cyano, halogen, C_{1-6} alkyl, C_{1-6} alkoxy, C_{1-6} haloalkyl, C_{1-6} haloalkoxy, C_{1-6} acylamino, C_{1-6} alkylamino, C_{5-6} aryl, and C_{1-6} heteroaryl, wherein C_{1-6} alkoxy, and C_{1-6} haloalkoxy, is optionally substituted with one or more of the groups selected from hydrogen, C_{1-6} alkyl, C_{1-6} alkoxy, C_{1-6} haloalkyl, C_{1-6} alkylhydroxy, cyano, and hydroxyl; R_3 is absent or is selected from the group consisting of hydrogen, C_{1-6} alkyl, C_{3-6} cycloalkyl, C_{1-6} alkylamino, C_{1-6} haloalkyl, $C(O)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $C(O)NR_{18}$, $C(O)C_{1-6}$ alkylamino, SO_2C_{1-6} alkyl, SO_2C_{3-6} cycloalkyl, SO_2C_{1-6} haloalkyl, SO_2NR_{18} , SO_2NC_{1-6} alkylamino, C_{5-6} aryl, C_{1-6} heteroaryl, $C(O)C_{5-6}$ aryl, $C(O)C_{1-6}$ heteroaryl, SO_2C_{5-6} aryl, and SO_2C_{1-6} heteroaryl, wherein C_{1-6} alkyl, $(CO)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, SO_2C_{5-6} aryl, and SO_2C_{1-6} alkyl,

is optionally substituted with C₁₋₆ alkoxy, halogen, C₅₋₆ aryl, and C₁₋₆ heteroaryl; R₁₀ is hydrogen; R₁₁ is selected from the group consisting of hydrogen, C₁₋₆ alkyl, C₃₋₆ cycloalkyl, C₁₋₆ alkylamino, C₁₋₆ haloalkyl, C(O)C₁₋₆ alkyl, C(O)C₁₋₆ haloalkyl, C(O)NR₁₈, C(O)C₁₋₆ alkylamino, SO₂C₁₋₆ alkyl, SO₂C₁₋₆ haloalkyl, SO₂C₃₋₆ cycloalkyl, SO₂NR₁₈, SO₂NC₁₋₆ alkylamino, C₅₋₆ aryl, C₁₋₆ heteroaryl, C(O)C₅₋₆ aryl, C(O)C₁₋₆ heteroaryl, SO₂C₅₋₆ aryl, and SO₂C₁₋₆ heteroaryl, wherein C₁₋₆ alkyl, (CO)C₁₋₆ alkyl, C(O)C₁₋₆ haloalkyl, SO₂C₅₋₆ aryl, and SO₂C₁₋₆ alkyl, is optionally substituted with C₁₋₆ alkoxy, halogen, C₅₋₆ aryl, and C₁₋₆ heteroaryl; and 5-10 membered monocyclic or bicyclic saturated heterocyclic ring with 1-3 heteroatoms selected from N, S or O, or R₁₀ and R₁₁ can be taken together to form a 5-10 membered monocyclic or bicyclic saturated or unsaturated heterocyclic ring, wherein the 5-10 membered monocyclic or bicyclic saturated or unsaturated heterocyclic ring is optionally substituted with the substituents selected from the group consisting of amino, C₁₋₆ alkylamino, C₁₋₆ acylamino, -NHC(NH)CH₂Cl, -NHC(O)CH=CHCH₂N(CH₃)₂, C₁₋₆ alkyl, halogen, C₁₋₆ alkoxy, and hydroxyl; R₁₂, R₁₃, R₁₄, and R₁₅ are independently selected from the group consisting of hydrogen, C₁₋₆ alkyl, C₁₋₆ haloalkyl, C₁₋₆ alkylamino, C₅₋₆ aryl, and C₁₋₆ heteroaryl; or R₁₂ and R₁₃ can be taken together to form =O or =S; or R₁₄ and R₁₅ can be taken together to form =O or =S; R₁₆ is selected from the group consisting of hydrogen, 5-10 membered monocyclic or bicyclic aryl, and 5-10 membered monocyclic or bicyclic heteroaryl with 1-5 heteroatoms selected from N, S or O, wherein 5-10 membered monocyclic or bicyclic aryl, and 5-10 membered monocyclic or bicyclic heteroaryl are optionally substituted with 1-5 substituents selected from the group consisting of hydroxyl, cyano, halogen, C₁₋₆ alkyl, C₁₋₆ alkoxy, C₃₋₆ cycloalkyl, C₁₋₆ haloalkyl, C₁₋₆ haloalkoxy, C₁₋₆ acylamino, C₁₋₆ alkylamino, C₅₋₆ aryl, C₁₋₆ alkyl-C₅₋₆ aryl, C₂₋₆ alkenyl-C₅₋₆ aryl, C₁₋₆ heterocyclyl, C₁₋₆ alkyl-C₁₋₆ heterocyclyl, C₁₋₆ heteroaryl, and C₁₋₆ alkyl-C₁₋₆ heteroaryl, wherein C₁₋₆ alkyl, C₁₋₆ alkoxy, C₃₋₆ cycloalkyl, C₅₋₆ aryl, C₁₋₆ alkyl-C₅₋₆ aryl, C₁₋₆ heteroaryl, C₁₋₆ alkyl-C₁₋₆ heteroaryl, and C₁₋₆ alkyl-C₁₋₆ heterocyclyl is optionally substituted with one or more of the groups selected from hydrogen, C₁₋₆ alkyl, C₁₋₆ alkoxy, C₃₋₈ cycloalkyl, C₁₋₆ heteroaryl, halogen, hydroxyl, -CH₂OH, -COOH, and cyano; R₁₇ is selected from the group consisting of hydrogen, hydroxyl, cyano, halogen, C₁₋₆ alkyl, C₁₋₆ alkoxy, C₁₋₆ haloalkyl, C₁₋₆ haloalkoxy, C₁₋₆ acylamino, C₁₋₆ alkylamino, C₅₋₆ aryl, and C₁₋₆ heteroaryl, wherein C₁₋₆ alkoxy, and C₁₋₆ haloalkoxy, is optionally substituted with one or more of the groups selected from hydrogen, C₁₋₆ alkyl, C₁₋₆ alkoxy, C₁₋₆ haloalkyl,

C₁₋₆ alkylhydroxy, cyano, and hydroxyl; and R₁₈ is independently selected from the group consisting of hydrogen, C₁₋₆ alkyl, and combinations thereof.

[00019b] In yet another aspect, the present disclosure provides a process of preparation of compounds of Formula (II) provided herein or its polymorphs, stereoisomers, prodrugs, solvates, co-crystals, intermediates, pharmaceutically acceptable salts, and metabolites thereof, the process comprising reacting Formula (IV) and Formula (V)

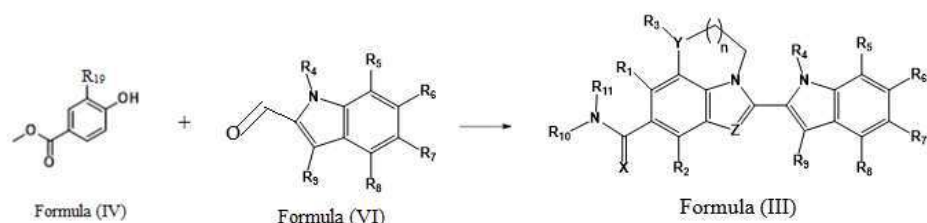


wherein R₁₉ of Formula (IV) is selected from nitro, and C₁₋₆ alkoxy; X of Formula (II) is selected from O or S; Y is selected from O, N, S, S(O), SO₂ or C; Z is selected from N or CR₁₇; A is selected from N or CR₁; B is selected from N or CR₂; D is selected from N or CR₅; E is selected from N or CR₆; F is selected from N or CR₇; G is selected from N or CR₈; n is 0-2; R₁, R₂, R₅, R₆, R₇, R₈, and R₉ are independently selected from the group consisting of hydrogen, hydroxyl, cyano, halogen, C₁₋₆ alkyl, C₁₋₆ alkoxy, C₁₋₆ haloalkyl, C₁₋₆ haloalkoxy, C₁₋₆ acylamino, C₁₋₆ alkylamino, C₅₋₆ aryl, C₂₋₆ alkenyl- C₅₋₆ aryl, and C₁₋₆ heteroaryl, wherein C₁₋₆ alkoxy, and C₁₋₆ haloalkoxy, is optionally substituted with one or more of the groups selected from hydrogen, C₁₋₆ alkyl, C₁₋₆ alkoxy, C₁₋₆ haloalkyl, C₁₋₆ alkylhydroxy, cyano, and hydroxyl; R₃ is absent or is selected from the group consisting of hydrogen, C₁₋₆ alkyl, C₃₋₆ cycloalkyl, C₁₋₆ alkylamino, C₁₋₆ haloalkyl, C(O)C₁₋₆ alkyl, C(O)C₁₋₆ haloalkyl, C(O)NR₁₈, C(O)C₁₋₆ alkylamino, SO₂C₁₋₆ alkyl, SO₂C₁₋₆ haloalkyl, SO₂C₃₋₆ cycloalkyl, SO₂NR₁₈, SO₂NC₁₋₆ alkylamino, C₅₋₆ aryl, C₁₋₆ heteroaryl, C(O)C₅₋₆ aryl, C(O)C₁₋₆ heteroaryl, SO₂C₅₋₆ aryl, and SO₂C₁₋₆ heteroaryl, wherein C₁₋₆ alkyl, (CO)C₁₋₆ alkyl, C(O)C₁₋₆ haloalkyl, SO₂C₅₋₆ aryl, and SO₂C₁₋₆ alkyl, is optionally substituted with C₁₋₆ alkoxy, halogen, C₅₋₆ aryl, and C₁₋₆ heteroaryl; R₄ is selected from the group consisting of hydrogen, C₁₋₆ alkyl, C₁₋₆ haloalkyl, C₁₋₆ alkoxy, C₃₋₆ cycloalkyl, C(O)C₁₋₆ alkyl, C(O)C₁₋₆ haloalkyl, C(O)NR₁₈, C(O)C₁₋₆ alkylamino, SO₂C₁₋₆ alkyl, SO₂C₁₋₆ haloalkyl, SO₂NR₁₈, SO₂NC₁₋₆ alkylamino, C₅₋₆ aryl, C₁₋₆ alkyl-C₅₋₆ aryl, C₁₋₆ heterocyclyl, C₁₋₆ alkyl-C₁₋₆ heterocyclyl, C₁₋₆ heteroaryl, C₁₋₆ alkyl-C₁₋₆ heteroaryl, C(O)C₅₋₆ aryl, C(O)C₁₋₆ heteroaryl, SO₂C₅₋₆ aryl, and SO₂C₁₋₆ heteroaryl, wherein C₁₋₆ alkyl, C₁₋₆ alkoxy, C₃₋₆ cycloalkyl, C₅₋₆ aryl,

C_{1-6} alkyl- C_{5-6} aryl, C_{1-6} heterocyclyl, C_{1-6} alkyl- C_{1-6} heterocyclyl, C_{1-6} heteroaryl, C_{1-6} alkyl- C_{1-6} heteroaryl, $(CO)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, and SO_2C_{1-6} alkyl, is optionally substituted with one or more groups selected from hydrogen, C_{1-6} alkyl, C_{1-6} alkoxy, C_{3-8} cycloalkyl, C_{5-6} aryl, C_{1-6} heteroaryl, halogen, hydroxyl, $-CH_2OH$, $-COOH$, and cyano; R_{10} is hydrogen; R_{11} is selected from the group consisting of hydrogen, C_{1-6} alkyl, C_{3-6} cycloalkyl, C_{1-6} alkylamino, C_{1-6} haloalkyl, $C(O)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $C(O)NR_{18}$, $C(O)C_{1-6}$ alkylamino, SO_2C_{1-6} alkyl, SO_2C_{1-6} haloalkyl, SO_2C_{3-6} cycloalkyl, SO_2NR_{18} , SO_2NC_{1-6} alkylamino, C_{5-6} aryl, C_{1-6} heteroaryl, $C(O)C_{5-6}$ aryl, $C(O)C_{1-6}$ heteroaryl, SO_2C_{5-6} aryl, and SO_2C_{1-6} heteroaryl, wherein C_{1-6} alkyl, $(CO)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, SO_2C_{5-6} aryl, and SO_2C_{1-6} alkyl, is optionally substituted with C_{1-6} alkoxy, halogen, C_{5-6} aryl, and C_{1-6} heteroaryl; and 5-10 membered monocyclic or bicyclic saturated heterocyclic ring with 1-3 heteroatoms selected from N, S or O, or R_{10} and R_{11} can be taken together to form a 5-10 membered monocyclic or bicyclic saturated or unsaturated heterocyclic ring, wherein the 5-10 membered monocyclic or bicyclic saturated or unsaturated heterocyclic ring is optionally substituted with the substituents selected from the group consisting of amino, C_{1-6} alkylamino, C_{1-6} acylamino, $-NHC(NH)CH_2Cl$, $-NHC(O)CH=CHCH_2N(CH_3)_2$, C_{1-6} alkyl, halogen, C_{1-6} alkoxy, and hydroxyl; R_{17} is selected from the group consisting of hydrogen, hydroxyl, cyano, halogen, C_{1-6} alkyl, C_{1-6} alkoxy, C_{1-6} haloalkyl, C_{1-6} haloalkoxy, C_{1-6} acylamino, C_{1-6} alkylamino, C_{5-6} aryl, and C_{1-6} heteroaryl, wherein C_{1-6} alkoxy, and C_{1-6} haloalkoxy, is optionally substituted with one or more of the groups selected from hydrogen, C_{1-6} alkyl, C_{1-6} alkoxy, C_{1-6} haloalkyl, C_{1-6} alkylhydroxy, cyano, and hydroxyl; and R_{18} is independently selected from the group consisting of hydrogen, C_{1-6} alkyl, and combinations thereof; D of Formula (V) is selected from N or CR_5 ; E is selected from N or CR_6 ; F is selected from N or CR_7 ; G is selected from N or CR_8 , R_9 is H; and R_4 is selected from the group consisting of hydrogen, C_{1-6} alkyl, C_{1-6} haloalkyl, C_{1-6} alkoxy, C_{3-6} cycloalkyl, $C(O)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, $C(O)NR_{18}$, $C(O)C_{1-6}$ alkylamino, SO_2C_{1-6} alkyl, SO_2C_{1-6} haloalkyl, SO_2NR_{18} , SO_2NC_{1-6} alkylamino, C_{5-6} aryl, C_{1-6} alkyl- C_{5-6} aryl, C_{1-6} heterocyclyl, C_{1-6} alkyl- C_{1-6} heterocyclyl, C_{1-6} heteroaryl, C_{1-6} alkyl- C_{1-6} heteroaryl, $C(O)C_{5-6}$ aryl, $C(O)C_{1-6}$ heteroaryl, SO_2C_{5-6} aryl, and SO_2C_{1-6} heteroaryl, wherein C_{1-6} alkyl, C_{1-6} alkoxy, C_{3-6} cycloalkyl, C_{5-6} aryl, C_{1-6} alkyl- C_{5-6} aryl, C_{1-6} heterocyclyl, C_{1-6} alkyl- C_{1-6} heterocyclyl, C_{1-6} heteroaryl, C_{1-6} alkyl- C_{1-6} heteroaryl, $(CO)C_{1-6}$ alkyl, $C(O)C_{1-6}$ haloalkyl, and SO_2C_{1-6} alkyl, is optionally substituted with one

or more groups selected from hydrogen, C₁₋₆ alkyl, C₁₋₆ alkoxy, C₃₋₈ cycloalkyl, C₅₋₆ aryl, C₁₋₆ heteroaryl, halogen, hydroxyl, -CH₂OH, -COOH, and cyano

[00019c] In yet another aspect, the present disclosure provides a process of preparation of compounds of Formula (III) provided herein or its polymorphs, stereoisomers, prodrugs, solvates, co-crystals, intermediates, pharmaceutically acceptable salts, and metabolites thereof, the process comprising reacting Formula (IV) and Formula (VI)



wherein R₁₉ of Formula (IV) is selected from nitro, and C₁₋₆ alkoxy; X of Formula (III) is selected from O or S; Y is selected from O, N, S, S(O), SO₂ or C; Z is selected from N or CR₁₇; n is 0-2; R₁, R₂, R₅, R₆, R₇, R₈, and R₉ are independently selected from the group consisting of hydrogen, hydroxyl, cyano, halogen, C₁₋₆ alkyl, C₁₋₆ alkoxy, C₁₋₆ haloalkyl, C₁₋₆ haloalkoxy, C₁₋₆ acylamino, C₁₋₆ alkylamino, C₅₋₆ aryl, C₂₋₆ alkenyl-, C₅₋₆ aryl, and C₁₋₆ heteroaryl, wherein C₁₋₆ alkoxy, and C₁₋₆ haloalkoxy, is optionally substituted with one or more of the groups selected from hydrogen, C₁₋₆ alkyl, C₁₋₆ alkoxy, C₁₋₆ haloalkyl, C₁₋₆ alkylhydroxy, cyano, and hydroxyl; R₃ is absent or is selected from the group consisting of hydrogen, C₁₋₆ alkyl, C₃₋₆ cycloalkyl, C₁₋₆ alkylamino, C₁₋₆ haloalkyl, C(O)C₁₋₆ alkyl, C(O)C₁₋₆ haloalkyl, C(O)NR₁₈, C(O)C₁₋₆ alkylamino, SO₂C₁₋₆ alkyl, SO₂C₁₋₆ haloalkyl, SO₂C₃₋₆ cycloalkyl, SO₂NR₁₈, SO₂NC₁₋₆ alkylamino, C₅₋₆ aryl, C₁₋₆ heteroaryl, C(O)C₅₋₆ aryl, C(O)C₁₋₆ heteroaryl, SO₂C₅₋₆ aryl, and SO₂C₁₋₆ heteroaryl, wherein C₁₋₆ alkyl, (CO)C₁₋₆ alkyl, C(O)C₁₋₆ haloalkyl, SO₂C₅₋₆ aryl, and SO₂C₁₋₆ alkyl, is optionally substituted with C₁₋₆ alkoxy, halogen, C₅₋₆ aryl, and C₁₋₆ heteroaryl; R₄ is selected from the group consisting of hydrogen, C₁₋₆ alkyl, C₁₋₆ haloalkyl, C₁₋₆ alkoxy, C₃₋₆ cycloalkyl, C(O)C₁₋₆ alkyl, C(O)C₁₋₆ haloalkyl, C(O)NR₁₈, C(O)C₁₋₆ alkylamino, SO₂C₁₋₆ alkyl, SO₂C₁₋₆ haloalkyl, SO₂NR₁₈, SO₂NC₁₋₆ alkylamino, C₅₋₆ aryl, C₁₋₆ alkyl-C₅₋₆ aryl, C₁₋₆ heterocyclyl, C₁₋₆ alkyl-C₁₋₆ heterocyclyl, C₁₋₆ heteroaryl, C₁₋₆ alkyl-C₁₋₆ heteroaryl, C(O)C₅₋₆ aryl, C(O)C₁₋₆ heteroaryl, SO₂C₅₋₆ aryl, and SO₂C₁₋₆ heteroaryl, wherein C₁₋₆ alkyl, C₁₋₆ alkoxy, C₃₋₆ cycloalkyl, C₅₋₆ aryl, C₁₋₆ alkyl-C₅₋₆ aryl, C₁₋₆ heterocyclyl, C₁₋₆ alkyl-C₁₋₆ heterocyclyl, C₁₋₆ heteroaryl, C₁₋₆ alkyl-C₁₋₆ heteroaryl, (CO)C₁₋₆ alkyl, C(O)C₁₋₆ haloalkyl, and SO₂C₁₋₆ alkyl, is optionally substituted with one or more groups selected from hydrogen, C₁₋₆ alkyl, C₁₋₆

alkoxy, C₃₋₈ cycloalkyl, C₅₋₆ aryl, C₁₋₆ heteroaryl, halogen, hydroxyl, -CH₂OH, COOH, and cyano; R₁₀ is hydrogen; R₁₁ is selected from the group consisting of hydrogen, C₁₋₆ alkyl, C₃₋₆ cycloalkyl, C₁₋₆ alkylamino, C₁₋₆ haloalkyl, C(O)C₁₋₆ alkyl, C(O)C₁₋₆ haloalkyl, C(O)NR₁₈, C(O)C₁₋₆ alkylamino, SO₂C₁₋₆ alkyl, SO₂C₁₋₆ haloalkyl, SO₂C₃₋₆ cycloalkyl, SO₂NR₁₈, SO₂NC₁₋₆ alkylamino, C₅₋₆ aryl, C₁₋₆ heteroaryl, C(O)C₅₋₆ aryl, C(O)C₁₋₆ heteroaryl, SO₂C₅₋₆ aryl, and SO₂C₁₋₆ heteroaryl, wherein C₁₋₆ alkyl, (CO)C₁₋₆ alkyl, C(O)C₁₋₆ haloalkyl, SO₂C₅₋₆ aryl, and SO₂C₁₋₆ alkyl, is optionally substituted with C₁₋₆ alkoxy, halogen, C₅₋₆ aryl, and C₁₋₆ heteroaryl; and 5-10 membered monocyclic or bicyclic saturated heterocyclic ring with 1-3 heteroatoms selected from N, S or O, or R₁₀ and R₁₁ can be taken together to form a 5-10 membered monocyclic or bicyclic saturated or unsaturated heterocyclic ring, wherein the 5-10 membered monocyclic or bicyclic saturated or unsaturated heterocyclic ring is optionally substituted with the substituents selected from the group consisting of amino, C₁₋₆ alkylamino, C₁₋₆ acylamino, -NHC(NH)CH₂Cl, -NHC(O)CH=CHCH₂N(CH₃)₂, C₁₋₆ alkyl, halogen, C₁₋₆ alkoxy, and hydroxyl; R₁₇ is selected from the group consisting of hydrogen, hydroxyl, cyano, halogen, C₁₋₆ alkyl, C₁₋₆ alkoxy, C₁₋₆ haloalkyl, C₁₋₆ haloalkoxy, C₁₋₆ acylamino, C₁₋₆ alkylamino, C₅₋₆ aryl, and C₁₋₆ heteroaryl, wherein C₁₋₆ alkoxy, and C₁₋₆ haloalkoxy, is optionally substituted with one or more of the groups selected from hydrogen, C₁₋₆ alkyl, C₁₋₆ alkoxy, C₁₋₆ haloalkyl, C₁₋₆ alkylhydroxy, cyano, and hydroxyl; and R₁₈ is independently selected from the group consisting of hydrogen, C₁₋₆ alkyl, and combinations thereof; and R₅, R₆, R₇, R₈, and R₉ are independently selected from the group consisting of hydrogen, hydroxyl, cyano, halogen, C₁₋₆ alkyl, C₁₋₆ alkoxy, C₁₋₆ haloalkyl, C₁₋₆ haloalkoxy, C₁₋₆ acylamino, C₁₋₆ alkylamino, C₅₋₆ aryl, C₂₋₆ alkenyl-, C₅₋₆ aryl, and C₁₋₆ heteroaryl, wherein C₁₋₆ alkoxy, and C₁₋₆ haloalkoxy, is optionally substituted with one or more of the groups selected from hydrogen, C₁₋₆ alkyl, C₁₋₆ alkoxy, C₁₋₆ haloalkyl, C₁₋₆ alkylhydroxy, cyano, and hydroxyl; R₄ is selected from the group consisting of hydrogen, C₁₋₆ alkyl, C₁₋₆ haloalkyl, C₁₋₆ alkoxy, C₃₋₆ cycloalkyl, C(O)C₁₋₆ alkyl, C(O)C₁₋₆ haloalkyl, C(O)NR₁₈, C(O)C₁₋₆ alkylamino, SO₂C₁₋₆ alkyl, SO₂C₁₋₆ haloalkyl, SO₂NR₁₈, SO₂NC₁₋₆ alkylamino, C₅₋₆ aryl, C₁₋₆ alkyl-C₅₋₆ aryl, C₁₋₆ heterocyclyl, C₁₋₆ alkyl-C₁₋₆ heterocyclyl, C₁₋₆ heteroaryl, C₁₋₆ alkyl-C₁₋₆ heteroaryl, C(O)C₅₋₆ aryl, C(O)C₁₋₆ heteroaryl, SO₂C₅₋₆ aryl, and SO₂C₁₋₆ heteroaryl, wherein C₁₋₆ alkyl, C₁₋₆ alkoxy, C₃₋₆ cycloalkyl, C₅₋₆ aryl, C₁₋₆ alkyl-C₅₋₆ aryl, C₁₋₆ heterocyclyl, C₁₋₆ alkyl-C₁₋₆ heterocyclyl, C₁₋₆ heteroaryl, C₁₋₆ alkyl-C₁₋₆ heteroaryl, (CO)C₁₋₆ alkyl, C(O)C₁₋₆ haloalkyl, and SO₂C₁₋₆ alkyl, is optionally substituted with one or more groups

selected from hydrogen, C₁₋₆ alkyl, C₁₋₆ alkoxy, C₃₋₈ cycloalkyl, C₅₋₆ aryl, C₁₋₆ heteroaryl, halogen, hydroxyl, -CH₂OH, COOH, and cyano; and R₁₈ is independently selected from the group consisting of hydrogen, C₁₋₆ alkyl, and combinations thereof.

[00019d] In yet another aspect, the present disclosure provides a pharmaceutical composition comprising a compound of Formula (I), Formula (II), and Formula (III) or a pharmaceutically acceptable salt thereof as provided herein with a pharmaceutically acceptable carrier, optionally in combination with one or more other pharmaceutical compositions.

[00019e] In yet another aspect, the present disclosure provides use of the compounds provided herein or a pharmaceutically acceptable salt thereof in the manufacture of a medicament for inhibiting one or more PADs in a cell.

[00020] In yet another aspect, the present disclosure further discloses a method for inhibiting one or more PAD family in a cell with an effective amount of the compound of the present disclosure.

[00021] The present disclosure further discloses a method of treating a condition mediated by one or more PAD's, the method comprising administering to a subject suffering from a condition mediated by one or more PAD family, a therapeutically effective amount of the compound of Formula (I), Formula (II), and Formula (III) or the pharmaceutical composition of the present disclosure with other clinically relevant agents or biological agents to a subject in need thereof.

[00021a] In yet another aspect, the present disclosure provides use of a therapeutically effective amount of the compound provided herein or the pharmaceutical composition provided herein in the manufacture of a medicament for treating a condition mediated by one or more PAD's, wherein the compound or the pharmaceutical composition is to be administered to a subject suffering from a condition mediated by one or more PAD family.

[00021b] In yet another aspect, the present disclosure provides use of the compound of Formula (I), Formula (II), and Formula (III) as provided herein in the manufacture of a medicament for the treatment of rheumatoid arthritis, vasculitis, systemic lupus erythematosus, ulcerative colitis, cancer, cystic fibrosis, asthma, cutaneous lupus erythematosus, and psoriasis.

[00022] In yet another aspect, the present disclosure further discloses a compound of Formula (I), Formula (II) and Formula (III) used for the treatment of rheumatoid arthritis, vasculitis, systemic lupus erythematosus, ulcerative colitis, cancer, cystic fibrosis, asthma, cutaneous lupus erythematosus, and psoriasis.

[00022a] In yet another aspect, the present disclosure provides use of the compound provided herein or the pharmaceutical composition provided herein together with other clinically relevant agents or biological agents in the manufacture of a medicament for the treatment of a condition mediated by one or more PAD family; or the treatment and/or prevention of treatment of rheumatoid arthritis, vasculitis, systemic lupus erythematosus, ulcerative colitis, cancer, cystic fibrosis, asthma, cutaneous lupus erythematosus, and psoriasis.

[00022b] In yet another aspect, the present disclosure provides use of the compound provided herein or the pharmaceutical composition provided herein together with other clinically relevant agents or biological agents in the manufacture of a medicament for the treatment of a condition mediated by one or more PAD family; or the treatment and/or prevention of acid-induced lung injury, respiratory distress syndrome, allergen induced asthma, allergic bronchopulmonary, chronic lung disease of prematurity, chronic obstructive pulmonary disease, colitis, cystic fibrosis, gouty arthritis, inflammatory bowel disease, inflammatory lung disease, inflammatory pain, juvenile rheumatoid arthritis, kidney disease, kidney injury caused by parasitic infections, kidney transplant rejection prophylaxis, lung injury, lupus, lupus nephritis, multiple sclerosis, muscular dystrophy, non-allergen induced asthma, osteoarthritis, periodontitis, peritoneal endometriosis, psoriasis, pulmonary disease, pulmonary fibrosis, pyogenic sterile arthritis, renal disease, rheumatic disease, rheumatoid arthritis, sepsis, severe pain and ulcerative colitis.

[00022c] In yet another aspect, the present disclosure provides use of a therapeutically effective amount of the compound provided herein or the pharmaceutical composition provided herein in the manufacture of a medicament for the treatment and/or prevention of a condition mediated by one or more PAD family disorder, wherein the compound or the pharmaceutical composition is to be administered to a subject suffering from the condition mediated by one or more PAD family.

[00022d] In yet another aspect, the present disclosure provides use of a combination of the compounds provided herein or the pharmaceutical composition provided herein with

other clinically relevant agents or biological agents in the manufacture of a medicament for the treatment of rheumatoid arthritis.

[00022e] In yet another aspect, the present disclosure provides use of a combination of the compounds provided herein or the pharmaceutical composition provided herein with other clinically relevant immune modulators agents in the manufacture of a medicament for the treatment of cancer.

[00023] These and other features, aspects, and advantages of the present subject matter will become better understood with reference to the following description. This summary is provided to introduce a selection of concepts in a simplified form. This summary is not intended to identify key features or essential features of the disclosure, nor is it intended to be used to limit the scope of the subject matter.

DETAILED DESCRIPTION

[00024] Those skilled in the art will be aware that the present disclosure is subject to variations and modifications other than those specifically described. It is to be understood that the present disclosure includes all such variations and modifications. The disclosure also includes all such steps, features, compositions and compounds referred to or indicated in this specification, individually or collectively, and any and all combinations of any or more of such steps or features.

Definitions

[00025] For convenience, before further description of the present disclosure, certain terms employed in the specification, and examples are collected here. These definitions should be read in the light of the remainder of the disclosure and understood as by a person of skill in the art. The terms used herein have the meanings recognized and known to those of skill in the art, however, for convenience and completeness, particular terms and their meanings are set forth below.

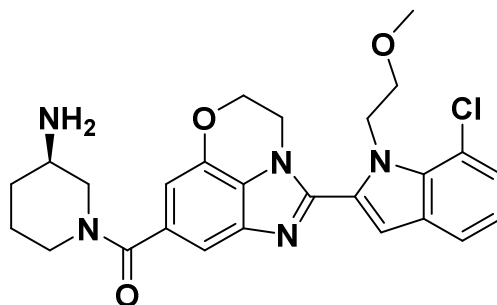
[00026] The articles “a”, “an” and “the” are used to refer to one or to more than one (i.e., to at least one) of the grammatical object of the article.

[00027] Throughout the description and the claims which follow, unless the context requires otherwise, the word “comprise”, and variations such as “comprises” and “comprising”, will be understood to imply the inclusion of a stated integer or step or group of integers but not to the exclusion of any other integer or step or group of integers or steps.

[00028] The term “including” is used to mean “including but not limited to”. “Including” and “including but not limited to” are used interchangeably.

- 73)** (R)-(3-aminopiperidin-1-yl)(2-(1-(cyclopropylmethyl)-6-methoxy-1H-indol-2-yl)-5,6-dihydro-4H-imidazo[1,5,4-de]quinoxalin-8-yl)methanone
- 74)** (R)-(3-aminopiperidin-1-yl)(2-(1-(cyclopropylmethyl)-6-methoxy-1H-indol-2-yl)-6-methyl-5,6-dihydro-4H-imidazo[1,5,4-de]quinoxalin-8-yl)methanone,
- 75)** (R)-(3-aminopiperidin-1-yl)(2-(1-(cyclopropylmethyl)-5-fluoro-1H-indol-2-yl)-6-methyl-5,6-dihydro-4H-imidazo[1,5,4-de]quinoxalin-8-yl)methanone,
- 76)** (R)-(3-aminopiperidin-1-yl)(2-(1-(cyclopropylmethyl)-1H-indol-2-yl)-6-(methylsulfonyl)-5,6-dihydro-4H-imidazo[1,5,4-de]quinoxalin-8-yl)methanone,
- 77)** (R)-(3-aminopiperidin-1-yl)(2-(1-(cyclopropylmethyl)-5,6-difluoro-1H-indol-2-yl)-5,6-dihydro-4H-imidazo[1,5,4-de]quinoxalin-8-yl)methanone,
- 78)** (R)-(3-aminopiperidin-1-yl)(6-cyclopropyl-2-(1-(cyclopropylmethyl)-1H-indol-2-yl)-5,6-dihydro-4H-imidazo[1,5,4-de]quinoxalin-8-yl)methanone,
- 79)** (R)-(3-aminopiperidin-1-yl)(2-(1-(cyclopropylmethyl)-1H-indol-2-yl)-6-(phenethylsulfonyl)-5,6-dihydro-4H-imidazo[1,5,4-de]quinoxalin-8-yl)methanone,
- 80)** (R)-(3-aminopiperidin-1-yl)(2-(1-(cyclopropylmethyl)-4-fluoro-1H-indol-2-yl)-5,6-dihydro-4H-imidazo[1,5,4-de]quinoxalin-8-yl)methanone,
- 81)** (R)-(3-aminopiperidin-1-yl)(6-((4-chlorophenyl)sulfonyl)-2-(1-(cyclopropylmethyl)-1H-indol-2-yl)-5,6-dihydro-4H-imidazo[1,5,4-de]quinoxalin-8-yl)methanone,
- 82)** (R)-(3-aminopiperidin-1-yl)(2-(1-(cyclopropylmethyl)-1H-indol-2-yl)-6-(cyclopropylsulfonyl)-5,6-dihydro-4H-imidazo[1,5,4-de]quinoxalin-8-yl)methanone,
- 83)** (R)-(3-aminopiperidin-1-yl)(2-(1-(cyclopropylmethyl)-1H-indol-2-yl)-6-((2-ethoxyethyl)sulfonyl)-5,6-dihydro-4H-imidazo[1,5,4-de]quinoxalin-8-yl)methanone,
- 84)** (R)-(3-aminopiperidin-1-yl)(2-(1-(cyclopropylmethyl)-7-methyl-1H-indol-2-yl)-5,6-dihydro-4H-imidazo[1,5,4-de]quinoxalin-8-yl)methanone,
- 85)** (R)-1-(8-(3-aminopiperidine-1-carbonyl)-2-(1-(cyclopropylmethyl)-1H-indol-2-yl)-4,5-dihydro-6H-imidazo[1,5,4-de]quinoxalin-6-yl)ethan-1-one,
- 86)** (R)-(3-aminopiperidin-1-yl)(2-(1-(cyclopropylmethyl)-1H-indol-2-yl)-5,6-dihydro-4H-imidazo[1,5,4-de]quinoxalin-8-yl)methanethione.
- 87)** (R)-(3-aminopiperidin-1-yl)(2-(7-chloro-1-(cyclopropylmethyl)-6-fluoro-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone, and
- 88)** (R)-(3-aminopiperidin-1-yl)(2-(7-chloro-1-(pyrimidin-5-ylmethyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone

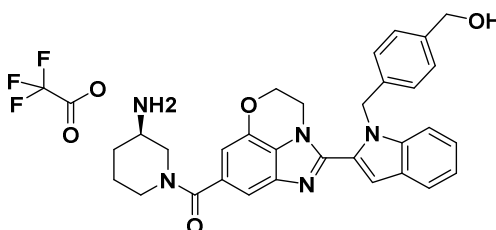
(R)-(3-aminopiperidin-1-yl)(2-(7-chloro-1-(2-methoxyethyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone



[000194] ^1H NMR (400 MHz, DMSO- d_6) δ (ppm): 7.68 (d, J = 7.8 Hz, 1H), 7.34 (d, J = 7.9 Hz, 1H), 7.31 (s, 1H), 7.22 (s, 1H), 7.15 (t, J = 7.7 Hz, 1H), 6.77 (s, 1H), 5.23 (t, J = 5.4 Hz, 2H), 4.57 (s, 4H), 3.58 (t, J = 5.48 Hz, 2H), 2.97 (s, 3H), 2.92 (bs, 2H), 2.66 (m, 2H), 1.85 (d, J = 10.2 Hz, 2H), 1.66 (bs, 2H), 1.43 (m, 1H), 1.23-1.15 (m, 2H). MS (ESI): mass calcd. for $\text{C}_{26}\text{H}_{28}\text{ClN}_5\text{O}_3$ 493.1; found m/z 494.5 $[\text{M}+\text{H}]^+$.

Example-37:

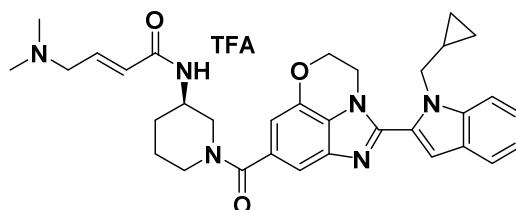
(R)-(3-aminopiperidin-1-yl)(2-(1-(4-(hydroxymethyl)benzyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone trifluoroacetic acid salt



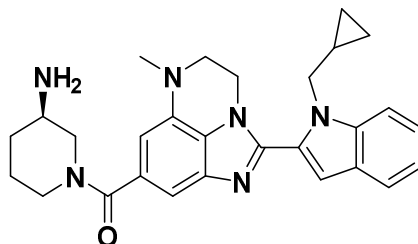
[000195] ^1H NMR (400 MHz, DMSO- d_6) δ (ppm): 7.71 (d, J = 7.7 Hz, 1H), 7.47 (d, J = 8.3 Hz, 1H), 7.27 (s, 2H), 7.23 (t, J = 7.5 Hz, 1H), 7.15-7.11 (m, 3H), 7.02 (d, J = 8.0 Hz, 2H), 6.75 (s, 1H), 6.10 (s, 2H), 5.04 (bs, 1H), 4.69 (s, 2H), 4.56 (s, 2H), 4.36 (s, 2H), 2.91 (bs, 2H), 2.69 (m, 2H), 1.90-1.83 (m, 2H), 1.64 (m, 2H), 1.39 (m, 1H), 1.25-1.23 (m, 2H). MS (ESI): mass calcd. for $\text{C}_{31}\text{H}_{31}\text{N}_5\text{O}_3$ 521.2; found m/z 522.2 $[\text{M}+\text{H}]^+$.

Example-38:

(R,E)-N-(1-(2-(1-(cyclopropylmethyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylene-7-carbonyl)piperidin-3-yl)-4-(dimethylamino)but-2-enamide trifluoroacetic acid salt



R-(3-aminopiperidin-1-yl)(2-(1-(cyclopropylmethyl)-1H-indol-2-yl)-6-methyl-5,6-dihydro-4H-imidazo[1,5,4-de]quinoxalin-8-yl)methanone (Example-72)

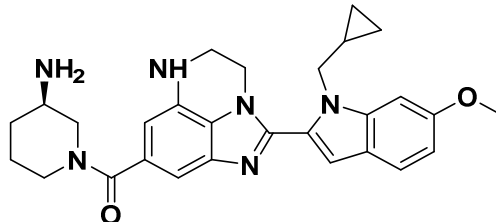


[000258] ^1H NMR (400 MHz, DMSO- d_6) δ (ppm): 7.67 (t, J = 8 Hz, 2H), 7.28 (t, J = 8 Hz, 1H), 7.13-7.05 (m, 3H), 6.45 (s, 1H), 4.65 (d, J = 8 Hz, 2H), 4.47 (m, 2H), 4.12 (m, 2H), 3.46 (m, 2H), 2.96 (s, 4H), 2.80 (m, 2H), 1.99 (m, 2H), 1.66 (m, 1H), 1.46-1.44 (m, 1H), 1.33-1.18 (m, 3H), 0.31-1.33 (m, 4H). MS (ESI): mass calcd. for $\text{C}_{28}\text{H}_{32}\text{N}_6\text{O}$, 468.61; m/z found, 469.3 $[\text{M}+\text{H}]^+$.

[000259] Following compounds (**Examples 73, 77 and 80**) were synthesized using the procedure as exemplified for **Example-63**.

Example-73

(R)-(3-aminopiperidin-1-yl)(2-(1-(cyclopropylmethyl)-6-methoxy-1H-indol-2-yl)-5,6-dihydro-4H-imidazo[1,5,4-de]quinoxalin-8-yl)methanone



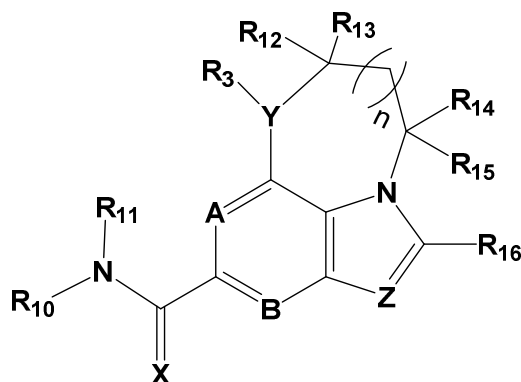
[000260] ^1H NMR (400 MHz, DMSO- d_6) δ (ppm): 7.60 (m, 1H), 7.14 (bs, 1H), 6.98 (s, 1H), 6.91 (m, 1H), 6.74 (m, 1H), 6.38 (m, 2H), 4.65 (d, J = 8 Hz, 2H), 4.45 (m, 2H), 3.83 (bs, 4H), 2.91 (bs, 1H), 2.53 (m, 3H), 1.88 (m, 2H), 1.64 (m, 2H), 1.41 (m, 2H), 1.22-1.17 (m, 3H), 0.21-0.20 (m, 2H), 0.01 (m, 2H). MS (ESI): mass calcd. for $\text{C}_{28}\text{H}_{32}\text{N}_6\text{O}_2$, 484.26; m/z found, 485.3 $[\text{M}+\text{H}]^+$.

Example-74

(R)-(3-aminopiperidin-1-yl)(2-(1-(cyclopropylmethyl)-6-methoxy-1H-indol-2-yl)-6-methyl-5,6-dihydro-4H-imidazo[1,5,4-de]quinoxalin-8-yl)methanone

I/We claim:

1. A compound of Formula (I)



Formula (I)

their polymorphs, stereoisomers, prodrugs, solvates, co-crystals, intermediates, pharmaceutically acceptable salts, and metabolites thereof,

wherein

X is selected from O or S;

Y is selected from O, N, S, S(O), SO₂ or C;

Z is selected from N or CR₁₇;

A is selected from N or CR₁;

B is selected from N or CR₂;

n is 0-2;

R₁, and R₂ are independently selected from the group consisting of hydrogen, hydroxyl, cyano, halogen, C₁₋₆ alkyl, C₁₋₆ alkoxy, C₁₋₆ haloalkyl, C₁₋₆ haloalkoxy, C₁₋₆ acylamino, C₁₋₆ alkylamino, C₅₋₆ aryl, and C₁₋₆ heteroaryl, wherein

C₁₋₆ alkoxy, and C₁₋₆ haloalkoxy, is optionally substituted with one or more of the groups selected from hydrogen, C₁₋₆ alkyl, C₁₋₆ alkoxy, C₁₋₆ haloalkyl, C₁₋₆ alkylhydroxy, cyano, and hydroxyl;

R₃ is absent or is selected from the group consisting of hydrogen, C₁₋₆ alkyl, C₃₋₆ cycloalkyl, C₁₋₆ alkylamino, C₁₋₆ haloalkyl, C(O)C₁₋₆ alkyl, C(O)C₁₋₆ haloalkyl, C(O)NR₁₈, C(O)C₁₋₆ alkylamino, SO₂C₁₋₆ alkyl, SO₂C₃₋₆ cycloalkyl, SO₂C₁₋₆ haloalkyl, SO₂NR₁₈, SO₂NC₁₋₆ alkylamino, C₅₋₆ aryl, C₁₋₆ heteroaryl, C(O)C₅₋₆ aryl, C(O)C₁₋₆ heteroaryl, SO₂C₅₋₆ aryl, and SO₂C₁₋₆ heteroaryl, wherein

C₁₋₆ alkyl, (CO)C₁₋₆ alkyl, C(O)C₁₋₆ haloalkyl, SO₂C₅₋₆ aryl, and SO₂C₁₋₆ alkyl, is optionally substituted with C₁₋₆ alkoxy, halogen, C₅₋₆ aryl, and C₁₋₆ heteroaryl;

R₁₀ is hydrogen;

R₁₁ is selected from the group consisting of hydrogen, C₁₋₆ alkyl, C₃₋₆ cycloalkyl, C₁₋₆ alkylamino, C₁₋₆ haloalkyl, C(O)C₁₋₆ alkyl, C(O)C₁₋₆ haloalkyl, C(O)NR₁₈, C(O)C₁₋₆ alkylamino, SO₂C₁₋₆ alkyl, SO₂C₁₋₆ haloalkyl, SO₂C₃₋₆ cycloalkyl, SO₂NR₁₈, SO₂NC₁₋₆ alkylamino, C₅₋₆ aryl, C₁₋₆ heteroaryl, C(O)C₅₋₆ aryl, C(O)C₁₋₆ heteroaryl, SO₂C₅₋₆ aryl, and SO₂C₁₋₆ heteroaryl, wherein

C₁₋₆ alkyl, (CO)C₁₋₆ alkyl, C(O)C₁₋₆ haloalkyl, SO₂C₅₋₆ aryl, and SO₂C₁₋₆ alkyl, is optionally substituted with C₁₋₆ alkoxy, halogen, C₅₋₆ aryl, and C₁₋₆ heteroaryl; and 5-10 membered monocyclic or bicyclic saturated heterocyclic ring with 1-3 heteroatoms selected from N, S or O, or

R₁₀ and R₁₁ can be taken together to form a 5-10 membered monocyclic or bicyclic saturated or unsaturated heterocyclic ring, wherein

the 5-10 membered monocyclic or bicyclic saturated or unsaturated heterocyclic ring is optionally substituted with the substituents selected from the group consisting of amino, C₁₋₆ alkylamino, C₁₋₆ acylamino, -NHC(NH)CH₂Cl, -NHC(O)CH=CHCH₂N(CH₃)₂, C₁₋₆ alkyl, halogen, C₁₋₆ alkoxy, and hydroxyl;

R₁₂, R₁₃, R₁₄, and R₁₅ are independently selected from the group consisting of hydrogen, C₁₋₆ alkyl, C₁₋₆ haloalkyl, C₁₋₆ alkylamino, C₅₋₆ aryl, and C₁₋₆ heteroaryl; or

R₁₂ and R₁₃ can be taken together to form =O or =S; or

R₁₄ and R₁₅ can be taken together to form =O or =S;

R₁₆ is selected from the group consisting of hydrogen, 5-10 membered monocyclic or bicyclic aryl, and 5-10 membered monocyclic or bicyclic heteroaryl with 1-5 heteroatoms selected from N, S or O, wherein

5-10 membered monocyclic or bicyclic aryl, and 5-10 membered monocyclic or bicyclic heteroaryl are optionally substituted with 1-5 substituents selected from the group consisting of hydroxyl, cyano, halogen, C₁₋₆ alkyl, C₁₋₆ alkoxy, C₃₋₆ cycloalkyl, C₁₋₆ haloalkyl, C₁₋₆ haloalkoxy, C₁₋₆ acylamino, C₁₋₆ alkylamino, C₅₋₆ aryl, C₁₋₆ alkyl-C₅₋₆ aryl, C₂₋₆ alkenyl-C₅₋₆ aryl, C₁₋₆ heterocyclyl, C₁₋₆ alkyl-C₁₋₆ heterocyclyl, C₁₋₆ heteroaryl, and C₁₋₆ alkyl-C₁₋₆ heteroaryl, wherein C₁₋₆ alkyl, C₁₋₆ alkoxy, C₃₋₆ cycloalkyl, C₅₋₆ aryl, C₁₋₆ alkyl-C₅₋₆ aryl, C₁₋₆ heteroaryl, C₁₋₆ alkyl-C₁₋₆ heteroaryl, and C₁₋₆ alkyl-C₁₋₆ heterocyclyl is optionally substituted with one or more of the groups

selected from hydrogen, C₁₋₆ alkyl, C₁₋₆ alkoxy, C₃₋₈ cycloalkyl, C₁₋₆ heteroaryl, halogen, hydroxyl, -CH₂OH, -COOH, and cyano;

R₁₇ is selected from the group consisting of hydrogen, hydroxyl, cyano, halogen, C₁₋₆ alkyl, C₁₋₆ alkoxy, C₁₋₆ haloalkyl, C₁₋₆ haloalkoxy, C₁₋₆ acylamino, C₁₋₆ alkylamino, C₅₋₆ aryl, and C₁₋₆ heteroaryl, wherein

C₁₋₆ alkoxy, and C₁₋₆ haloalkoxy, is optionally substituted with one or more of the groups selected from hydrogen, C₁₋₆ alkyl, C₁₋₆ alkoxy, C₁₋₆ haloalkyl, C₁₋₆ alkylhydroxy, cyano, and hydroxyl; and

R₁₈ is independently selected from the group consisting of hydrogen, C₁₋₆ alkyl, and combinations thereof.

2. The compound of Formula (I) as claimed in claim 1, their polymorphs, stereoisomers, prodrugs, solvates, co-crystals, intermediates, pharmaceutically acceptable salts, and metabolites thereof, wherein

X is selected from O or S;

Y is selected from O, N, S, S(O), SO₂ or C;

Z is selected from N or CR₁₇;

A is selected from N or CR₁;

B is selected from N or CR₂;

n is 0-1;

R₁, and R₂ are independently selected from the group consisting of hydrogen, hydroxyl, C₁₋₆ alkyl, C₁₋₆ alkoxy, C₁₋₆ haloalkyl, and C₁₋₆ haloalkoxy, wherein

C₁₋₆ alkoxy, and C₁₋₆ haloalkoxy, is optionally substituted with one or more of the groups selected from hydrogen, C₁₋₆ alkyl, C₁₋₆ alkoxy, C₁₋₆ haloalkyl, C₁₋₆ alkylhydroxy, cyano, and hydroxyl;

R₃ is absent or is selected from the group consisting of hydrogen, C₁₋₆ alkyl, C₃₋₆ cycloalkyl, C₁₋₆ alkylamino, C₁₋₆ haloalkyl, C(O)C₁₋₆ alkyl, C(O)C₁₋₆ haloalkyl, C(O)NR₁₈, C(O)C₁₋₆ alkylamino, SO₂C₁₋₆ alkyl, SO₂C₁₋₆ haloalkyl, SO₂C₃₋₆ cycloalkyl, SO₂NR₁₈, SO₂NC₁₋₆ alkylamino, C₅₋₆ aryl, C₁₋₆ heteroaryl, C(O)C₅₋₆ aryl, C(O)C₁₋₆ heteroaryl, SO₂C₅₋₆ aryl, and SO₂C₁₋₆ heteroaryl, wherein C₁₋₆ alkyl, (CO)C₁₋₆ alkyl, C(O)C₁₋₆ haloalkyl, SO₂C₅₋₆ aryl, and SO₂C₁₋₆ alkyl, is optionally substituted with C₁₋₆ alkoxy, halogen, C₅₋₆ aryl, and C₁₋₆ heteroaryl;

R₁₀ is hydrogen;

R₁₁ is selected from the group consisting of hydrogen, C₁₋₆ alkyl, C₃₋₆ cycloalkyl, C₁₋₆ alkylamino, C₁₋₆ haloalkyl, C(O)C₁₋₆ alkyl, C(O)C₁₋₆ haloalkyl, C(O)NR₁₈, C(O)C₁₋₆

alkylamino, SO₂C₁₋₆ alkyl, SO₂C₁₋₆ haloalkyl, SO₂C₃₋₆ cycloalkyl, SO₂NR₁₈, SO₂NC₁₋₆ alkylamino, C₅₋₆ aryl, C₁₋₆ heteroaryl, C(O)C₅₋₆ aryl, C(O)C₁₋₆ heteroaryl, SO₂C₅₋₆ aryl, and SO₂C₁₋₆ heteroaryl, wherein

C₁₋₆ alkyl, (CO)C₁₋₆ alkyl, C(O)C₁₋₆ haloalkyl, SO₂C₅₋₆ aryl, and SO₂C₁₋₆ alkyl, is optionally substituted with C₁₋₆ alkoxy, halogen, C₅₋₆ aryl, and C₁₋₆ heteroaryl; and 5-10 membered monocyclic or bicyclic saturated heterocyclic ring with 1-3 heteroatoms selected from N, S or O, or

R₁₀ and R₁₁ can be taken together to form a 5-10 membered monocyclic or bicyclic saturated or unsaturated heterocyclic ring, wherein

the 5-10 membered monocyclic or bicyclic saturated or unsaturated heterocyclic ring is optionally substituted with the substituents selected from the group consisting of amino, C₁₋₆ alkylamino, C₁₋₆ acylamino, -NHC(NH)CH₂Cl, -NHC(O)CH=CHCH₂N(CH₃)₂, C₁₋₆ alkyl, halogen, C₁₋₆ alkoxy, and hydroxyl;

R₁₂, R₁₃, R₁₄, and R₁₅ are independently selected from the group consisting of hydrogen, C₁₋₆ alkyl, C₁₋₆ haloalkyl, C₁₋₆ alkylamino, C₅₋₆ aryl, and C₁₋₆ heteroaryl; or

R₁₂ and R₁₃ can be taken together to form =O or =S; or

R₁₄ and R₁₅ can be taken together to form =O or =S;

R₁₆ is selected from the group consisting of hydrogen, 5-10 membered monocyclic or bicyclic aryl, and 5-10 membered monocyclic or bicyclic heteroaryl with 1-5 heteroatoms selected from N, S or O, wherein

5-10 membered monocyclic or bicyclic aryl, and 5-10 membered monocyclic or bicyclic heteroaryl are optionally substituted with 1-5 substituents selected from the group consisting of hydroxyl, cyano, halogen, C₁₋₆ alkyl, C₁₋₆ alkoxy, C₃₋₆ cycloalkyl, C₁₋₆ haloalkyl, C₁₋₆ haloalkoxy, C₁₋₆ acylamino, C₁₋₆ alkylamino, C₅₋₆ aryl, C₁₋₆ alkyl-C₅₋₆ aryl, C₂₋₆ alkenyl-C₅₋₆ aryl, C₁₋₆ heterocyclyl, C₁₋₆ alkyl-C₁₋₆ heterocyclyl, C₁₋₆ heteroaryl, and C₁₋₆ alkyl-C₁₋₆ heteroaryl, wherein C₁₋₆ alkyl, C₁₋₆ alkoxy, C₃₋₆ cycloalkyl, C₅₋₆ aryl, C₁₋₆ alkyl-C₅₋₆ aryl, C₁₋₆ heteroaryl, C₁₋₆ alkyl-C₁₋₆ heteroaryl, and C₁₋₆ alkyl-C₁₋₆ heterocyclyl is optionally substituted with one or more of the groups selected from hydrogen, C₁₋₆ alkyl, C₁₋₆ alkoxy, C₃₋₈ cycloalkyl, C₁₋₆ heteroaryl, halogen, hydroxyl, -CH₂OH, -COOH, and cyano;

R₁₇ is selected from the group consisting of hydrogen, hydroxyl, cyano, halogen, C₁₋₆ alkyl, C₁₋₆ alkoxy, C₁₋₆ haloalkyl, C₁₋₆ haloalkoxy, C₁₋₆ acylamino, C₁₋₆ alkylamino, C₅₋₆ aryl, and C₁₋₆ heteroaryl, wherein

C₁₋₆ alkoxy, and C₁₋₆ haloalkoxy, is optionally substituted with one or more of the groups selected from hydrogen, C₁₋₆ alkyl, C₁₋₆ alkoxy, C₁₋₆ haloalkyl, C₁₋₆ alkylhydroxy, cyano, and hydroxyl; and

R₁₈ is independently selected from the group consisting of hydrogen, C₁₋₆ alkyl, and combinations thereof.

3. The compound of Formula (I) as claimed in claim 1, their polymorphs, stereoisomers, prodrugs, solvates, co-crystals, intermediates, pharmaceutically acceptable salts, and metabolites thereof, wherein

X is selected from O or S;

Y is selected from O, N, S, S(O), SO₂ or C;

Z is selected from N or CR₁₇;

A is selected from N or CR₁;

B is selected from N or CR₂;

n is 0-2;

R₁, and R₂ are independently selected from the group consisting of hydrogen, hydroxyl, cyano, halogen, C₁₋₆ alkyl, C₁₋₆ alkoxy, C₁₋₆ haloalkyl, C₁₋₆ haloalkoxy, C₁₋₆ acylamino, C₁₋₆ alkylamino, C₅₋₆ aryl, and C₁₋₆ heteroaryl, wherein

C₁₋₆ alkoxy, and C₁₋₆ haloalkoxy, is optionally substituted with one or more of the groups selected from hydrogen, C₁₋₆ alkyl, C₁₋₆ alkoxy, C₁₋₆ haloalkyl, C₁₋₆ alkylhydroxy, cyano, and hydroxyl;

R₃ is absent or is selected from the group consisting of hydrogen, C₁₋₆ alkyl, C₃₋₆ cycloalkyl, C₁₋₆ alkylamino, C(O)C₁₋₆ alkyl, C(O)NR₁₈, C(O)C₁₋₆ alkylamino, SO₂C₁₋₆ alkyl, SO₂C₃₋₆ cycloalkyl, SO₂NR₁₈, SO₂NC₁₋₆ alkylamino, C₅₋₆ aryl, C₁₋₆ heteroaryl, C(O)C₅₋₆ aryl, C(O)C₁₋₆ heteroaryl, SO₂C₅₋₆ aryl, and SO₂C₁₋₆ heteroaryl, wherein C₁₋₆ alkyl, (CO)C₁₋₆ alkyl, SO₂C₅₋₆ aryl, and SO₂C₁₋₆ alkyl, is optionally substituted with C₁₋₆ alkoxy, halogen, C₅₋₆ aryl, and C₁₋₆ heteroaryl;

R₁₀ and R₁₁ is taken together to form a 5-10 membered monocyclic or bicyclic saturated or unsaturated heterocyclic ring, wherein

the 5-10 membered monocyclic or bicyclic saturated or unsaturated heterocyclic ring is optionally substituted with the substituents selected from the group consisting of amino, C₂₋₄ alkylamino, C₂₋₄ acylamino, -NHC(NH)CH₂Cl, -NHC(O)CH=CHCH₂N(CH₃)₂, C₂₋₄ alkyl, halogen, C₂₋₄ alkoxy, and hydroxyl;

R₁₂, R₁₃, R₁₄, and R₁₅ are independently selected from the group consisting of hydrogen, C₁₋₆ alkyl, C₁₋₆ haloalkyl, C₁₋₆ alkylamino, C₅₋₆ aryl, and C₁₋₆ heteroaryl; or

R₁₂ and R₁₃ can be taken together to form =O or =S; or

R₁₄ and R₁₅ can be taken together to form =O or =S;

R₁₆ is selected from the group consisting of hydrogen, 5-10 membered monocyclic or bicyclic aryl, and 5-10 membered monocyclic or bicyclic heteroaryl with 1-5 heteroatoms selected from N, S or O, wherein

5-10 membered monocyclic or bicyclic aryl, and 5-10 membered monocyclic or bicyclic heteroaryl are optionally substituted with 1-5 substituents selected from the group consisting of hydroxyl, cyano, halogen, C₁₋₆ alkyl, C₁₋₆ alkoxy, C₃₋₆ cycloalkyl, C₁₋₆ haloalkyl, C₁₋₆ haloalkoxy, C₁₋₆ acylamino, C₁₋₆ alkylamino, C₅₋₆ aryl, C₁₋₆ alkyl-C₅₋₆ aryl, C₂₋₆ alkenyl-C₅₋₆ aryl, C₁₋₆ heterocyclyl, C₁₋₆ alkyl-C₁₋₆ heterocyclyl, C₁₋₆ heteroaryl, and C₁₋₆ alkyl-C₁₋₆ heteroaryl, wherein C₁₋₆ alkyl, C₁₋₆ alkoxy, C₃₋₆ cycloalkyl, C₅₋₆ aryl, C₁₋₆ alkyl-C₅₋₆ aryl, C₁₋₆ heteroaryl, C₁₋₆ alkyl-C₁₋₆ heteroaryl, and C₁₋₆ alkyl-C₁₋₆ heterocyclyl is optionally substituted with one or more of the groups selected from hydrogen, C₁₋₆ alkyl, C₁₋₆ alkoxy, C₃₋₈ cycloalkyl, C₁₋₆ heteroaryl, halogen, hydroxyl, -CH₂OH, -COOH, and cyano;

R₁₇ is selected from the group consisting of hydrogen, hydroxyl, cyano, halogen, C₁₋₆ alkyl, C₁₋₆ alkoxy, C₁₋₆ haloalkyl, C₁₋₆ haloalkoxy, C₁₋₆ acylamino, C₁₋₆ alkylamino, C₅₋₆ aryl, and C₁₋₆ heteroaryl, wherein

C₁₋₆ alkoxy, and C₁₋₆ haloalkoxy, is optionally substituted with one or more of the groups selected from hydrogen, C₁₋₆ alkyl, C₁₋₆ alkoxy, C₁₋₆ haloalkyl, C₁₋₆ alkylhydroxy, cyano, and hydroxyl; and

R₁₈ is independently selected from the group consisting of hydrogen, C₁₋₆ alkyl, and combinations thereof.

4. The compound of Formula (I) as claimed in claim 1, their polymorphs, stereoisomers, prodrugs, solvates, co-crystals, intermediates, pharmaceutically acceptable salts, and metabolites thereof, wherein

X is selected from O or S;

Y is selected from O, N, S, S(O), SO₂ or C;

Z is selected from N or CR₁₇;

A is selected from N or CR₁;

B is selected from N or CR₂;

n is 0-1;

R₁, and R₂ are independently selected from the group consisting of hydrogen, hydroxyl, C₁₋₆ alkyl, C₁₋₆ alkoxy, C₁₋₆ haloalkyl, and C₁₋₆ haloalkoxy, wherein

C₁₋₆ alkoxy, and C₁₋₆ haloalkoxy, is optionally substituted with one or more of the groups selected from hydrogen, C₁₋₆ alkyl, C₁₋₆ alkoxy, C₁₋₆ haloalkyl, C₁₋₆ alkylhydroxy, cyano, and hydroxyl;

R₃ is absent or is selected from the group consisting of hydrogen, C₁₋₆ alkyl, C₃₋₆ cycloalkyl, C₁₋₆ alkylamino, C₁₋₆ haloalkyl, C(O)C₁₋₆ alkyl, C(O)C₁₋₆ haloalkyl, C(O)NR₁₈, C(O)C₁₋₆ alkylamino, SO₂C₁₋₆ alkyl, SO₂C₁₋₆ haloalkyl, SO₂C₃₋₆ cycloalkyl, SO₂NR₁₈, SO₂NC₁₋₆ alkylamino, C₅₋₆ aryl, C₁₋₆ heteroaryl, C(O)C₅₋₆ aryl, C(O)C₁₋₆ heteroaryl, SO₂C₅₋₆ aryl, and SO₂C₁₋₆ heteroaryl wherein C₁₋₆ alkyl, (CO)C₁₋₆ alkyl, C(O)C₁₋₆ haloalkyl, SO₂C₅₋₆ aryl, and SO₂C₁₋₆ alkyl, is optionally substituted with C₁₋₆ alkoxy, halogen, C₅₋₆ aryl, and C₁₋₆ heteroaryl;

R₁₀ and R₁₁ are taken together to form a 5-10 membered monocyclic or bicyclic saturated or unsaturated heterocyclic ring, wherein

the 5-10 membered monocyclic or bicyclic saturated or unsaturated heterocyclic ring is optionally substituted with the substituents selected from the group consisting of amino, C₂₋₄ alkylamino, C₂₋₄ acylamino, -NHC(NH)CH₂Cl, -NHC(O)CH=CHCH₂N(CH₃)₂, C₂₋₄ alkyl, halogen, C₂₋₄ alkoxy, and hydroxyl;

R₁₂ and R₁₃ can be taken together to form =O or =S; or

R₁₄ and R₁₅ can be taken together to form =O or =S;

R₁₆ is selected from the group consisting of hydrogen, 5-10 membered monocyclic or bicyclic aryl, and 5-10 membered monocyclic or bicyclic heteroaryl with 1-5 heteroatoms selected from N, S or O, wherein

5-10 membered monocyclic or bicyclic aryl, and 5-10 membered monocyclic or bicyclic heteroaryl are optionally substituted with 1-5 substituents selected from the group consisting of hydroxyl, cyano, halogen, C₁₋₆ alkyl, C₁₋₆ alkoxy, C₃₋₆ cycloalkyl, C₁₋₆ haloalkyl, C₁₋₆ haloalkoxy, C₁₋₆ acylamino, C₁₋₆ alkylamino, C₅₋₆ aryl, C₁₋₆ alkyl-C₅₋₆ aryl, C₂₋₆ alkenyl-C₅₋₆ aryl, C₁₋₆ heterocyclyl, C₁₋₆ alkyl-C₁₋₆ heterocyclyl, C₁₋₆ heteroaryl, and C₁₋₆ alkyl-C₁₋₆ heteroaryl, wherein C₁₋₆ alkyl, C₁₋₆ alkoxy, C₃₋₆ cycloalkyl, C₅₋₆ aryl, C₁₋₆ alkyl-C₅₋₆ aryl, C₁₋₆ heteroaryl, C₁₋₆ alkyl-C₁₋₆ heteroaryl, and C₁₋₆ alkyl-C₁₋₆ heterocyclyl is optionally substituted with one or more of the groups selected from hydrogen, C₁₋₆ alkyl, C₁₋₆ alkoxy, C₃₋₈ cycloalkyl, C₁₋₆ heteroaryl, halogen, hydroxyl, -CH₂OH, -COOH, and cyano;

R₁₇ is selected from the group consisting of hydrogen, hydroxyl, cyano, halogen, C₁₋₆ alkyl, C₁₋₆ alkoxy, C₁₋₆ haloalkyl, C₁₋₆ haloalkoxy, C₁₋₆ acylamino, C₁₋₆ alkylamino, C₅₋₆ aryl, and C₁₋₆ heteroaryl, wherein

C₁₋₆ alkoxy, and C₁₋₆ haloalkoxy, is optionally substituted with one or more of the groups selected from hydrogen, C₁₋₆ alkyl, C₁₋₆ alkoxy, C₁₋₆ haloalkyl, C₁₋₆ alkylhydroxy, cyano, and hydroxyl; and

R₁₈ is independently selected from the group consisting of hydrogen, C₁₋₆ alkyl, and combinations thereof.

5. The compound of Formula (I) as claimed in claim 1, their polymorphs, stereoisomers, prodrugs, solvates, co-crystals, intermediates, pharmaceutically acceptable salts, and metabolites thereof, wherein

X is O or S;

Y is selected from O, N, S, S(O), SO₂ or C;

Z is selected from N or CR₁₇;

A is CR₁;

B is CR₂;

n is 0-1;

R₁, and R₂ are independently selected from hydrogen;

R₃ is absent or is selected from hydrogen, C₁₋₆ alkyl, C₃₋₆ cycloalkyl, C(O)C₁₋₆ alkyl, SO₂C₃₋₆ cycloalkyl, SO₂C₅₋₆ aryl, and SO₂C₁₋₆ alkyl, wherein SO₂C₁₋₆ alkyl, SO₂C₅₋₆ aryl is optionally substituted with C₁₋₆ alkoxy, halogen, C₅₋₆ aryl, and C₁₋₆ heteroaryl;

R₁₀ and R₁₁ are taken together to form a 5-6 membered monocyclic saturated heterocyclic ring, wherein

the 5-6 membered monocyclic saturated heterocyclic ring is optionally substituted with the substituents selected from amino, -NHC(O)CH=CHCH₂N(CH₃)₂, or C₁₋₆ alkylamino;

R₁₂, R₁₃, R₁₄, and R₁₅ are independently selected from hydrogen or C₁₋₆ alkyl; or;

R₁₂ and R₁₃ can be taken together to form =O or =S; or

R₁₄ and R₁₅ can be taken together to form =O or =S;

R₁₆ is selected from the group consisting of hydrogen, 5-10 membered bicyclic aryl, and 5-10 membered bicyclic heteroaryl with 1-2 heteroatoms selected from N or S, wherein

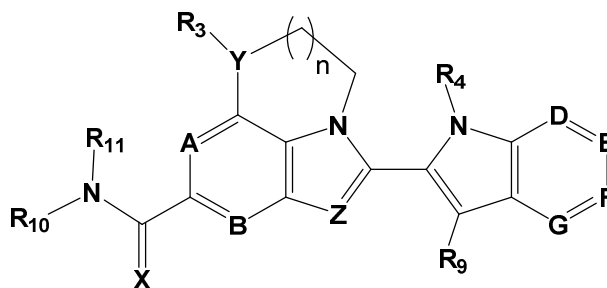
5-10 membered bicyclic aryl, and 5-10 membered bicyclic heteroaryl are optionally substituted with 1-3 substituents selected from the group consisting of halogen, C₁₋₆ alkyl, C₁₋₆ alkoxy, C₁₋₆ haloalkyl, C₅₋₆ aryl, C₁₋₆ alkyl-C₅₋₆ aryl, C₂₋₆ alkenyl-C₅₋₆ aryl, C₁₋₆ heterocyclyl, C₁₋₆ alkyl-C₁₋₆ heterocyclyl, C₁₋₆ heteroaryl, and C₁₋₆ alkyl-C₁₋₆ heteroaryl, wherein C₁₋₆ alkyl, C₁₋₆ alkoxy, C₅₋₆ aryl, C₁₋₆ alkyl-C₅₋₆ aryl, C₁₋₆ heteroaryl,

C₁₋₆ alkyl-C₁₋₆ heteroaryl, and C₁₋₆ alkyl-C₁₋₆ heterocyclyl is optionally substituted with one or more of the groups selected from hydrogen, C₁₋₆ alkyl, C₁₋₆ alkoxy, C₃₋₈ cycloalkyl, C₁₋₆ heteroaryl, halogen, hydroxyl, -CH₂OH, -COOH, and cyano;

R₁₇ is selected from hydrogen, or C₁₋₆ alkyl; and

R₁₈ is independently selected from the group consisting of hydrogen, C₁₋₆ alkyl, and combinations thereof.

6. A compound of Formula (II)



Formula (II)

their polymorphs, stereoisomers, prodrugs, solvates, co-crystals, intermediates, pharmaceutically acceptable salts, and metabolites thereof,

wherein

X is selected from O or S;

Y is selected from O, N, S, S(O), SO₂ or C;

Z is selected from N or CR₁₇;

A is selected from N or CR₁;

B is selected from N or CR₂;

D is selected from N or CR₅;

E is selected from N or CR₆;

F is selected from N or CR₇;

G is selected from N or CR₈;

n is 0-2;

R₁, R₂, R₅, R₆, R₇, R₈, and R₉ are independently selected from the group consisting of hydrogen, hydroxyl, cyano, halogen, C₁₋₆ alkyl, C₁₋₆ alkoxy, C₁₋₆ haloalkyl, C₁₋₆ haloalkoxy, C₁₋₆ acylamino, C₁₋₆ alkylamino, C₅₋₆ aryl, C₂₋₆ alkenyl- C₅₋₆ aryl, and C₁₋₆ heteroaryl, wherein

C₁₋₆ alkoxy, and C₁₋₆ haloalkoxy, is optionally substituted with one or more of the groups selected from hydrogen, C₁₋₆ alkyl, C₁₋₆ alkoxy, C₁₋₆ haloalkyl, C₁₋₆ alkylhydroxy, cyano, and hydroxyl;

R₃ is absent or is selected from the group consisting of hydrogen, C₁₋₆ alkyl, C₃₋₆ cycloalkyl, C₁₋₆ alkylamino, C₁₋₆ haloalkyl, C(O)C₁₋₆ alkyl, C(O)C₁₋₆ haloalkyl, C(O)NR₁₈, C(O)C₁₋₆ alkylamino, SO₂C₁₋₆ alkyl, SO₂C₁₋₆ haloalkyl, SO₂C₃₋₆ cycloalkyl, SO₂NR₁₈, SO₂NC₁₋₆ alkylamino, C₅₋₆ aryl, C₁₋₆ heteroaryl, C(O)C₅₋₆ aryl, C(O)C₁₋₆ heteroaryl, SO₂C₅₋₆ aryl, and SO₂C₁₋₆ heteroaryl, wherein C₁₋₆ alkyl, (CO)C₁₋₆ alkyl, C(O)C₁₋₆ haloalkyl, SO₂C₅₋₆ aryl, and SO₂C₁₋₆ alkyl, is optionally substituted with C₁₋₆ alkoxy, halogen, C₅₋₆ aryl, and C₁₋₆ heteroaryl;

R₄ is selected from the group consisting of hydrogen, C₁₋₆ alkyl, C₁₋₆ haloalkyl, C₁₋₆ alkoxy, C₃₋₆ cycloalkyl, C(O)C₁₋₆ alkyl, C(O)C₁₋₆ haloalkyl, C(O)NR₁₈, C(O)C₁₋₆ alkylamino, SO₂C₁₋₆ alkyl, SO₂C₁₋₆ haloalkyl, SO₂NR₁₈, SO₂NC₁₋₆ alkylamino, C₅₋₆ aryl, C₁₋₆ alkyl-C₅₋₆ aryl, C₁₋₆ heterocyclyl, C₁₋₆ alkyl-C₁₋₆ heterocyclyl, C₁₋₆ heteroaryl, C₁₋₆ alkyl-C₁₋₆ heteroaryl, C(O)C₅₋₆ aryl, C(O)C₁₋₆ heteroaryl, SO₂C₅₋₆ aryl, and SO₂C₁₋₆ heteroaryl, wherein C₁₋₆ alkyl, C₁₋₆ alkoxy, C₃₋₆ cycloalkyl, C₅₋₆ aryl, C₁₋₆ alkyl-C₅₋₆ aryl, C₁₋₆ heterocyclyl, C₁₋₆ alkyl-C₁₋₆ heterocyclyl, C₁₋₆ heteroaryl, C₁₋₆ alkyl-C₁₋₆ heteroaryl, (CO)C₁₋₆ alkyl, C(O)C₁₋₆ haloalkyl, and SO₂C₁₋₆ alkyl, is optionally substituted with one or more groups selected from hydrogen, C₁₋₆ alkyl, C₁₋₆ alkoxy, C₃₋₈ cycloalkyl, C₅₋₆ aryl, C₁₋₆ heteroaryl, halogen, hydroxyl, -CH₂OH, -COOH, and cyano;

R₁₀ is hydrogen;

R₁₁ is selected from the group consisting of hydrogen, C₁₋₆ alkyl, C₃₋₆ cycloalkyl, C₁₋₆ alkylamino, C₁₋₆ haloalkyl, C(O)C₁₋₆ alkyl, C(O)C₁₋₆ haloalkyl, C(O)NR₁₈, C(O)C₁₋₆ alkylamino, SO₂C₁₋₆ alkyl, SO₂C₁₋₆ haloalkyl, SO₂C₃₋₆ cycloalkyl, SO₂NR₁₈, SO₂NC₁₋₆ alkylamino, C₅₋₆ aryl, C₁₋₆ heteroaryl, C(O)C₅₋₆ aryl, C(O)C₁₋₆ heteroaryl, SO₂C₅₋₆ aryl, and SO₂C₁₋₆ heteroaryl, wherein

C₁₋₆ alkyl, (CO)C₁₋₆ alkyl, C(O)C₁₋₆ haloalkyl, SO₂C₅₋₆ aryl, and SO₂C₁₋₆ alkyl, is optionally substituted with C₁₋₆ alkoxy, halogen, C₅₋₆ aryl, and C₁₋₆ heteroaryl; and 5-10 membered monocyclic or bicyclic saturated heterocyclic ring with 1-3 heteroatoms selected from N, S or O, or

R₁₀ and R₁₁ can be taken together to form a 5-10 membered monocyclic or bicyclic saturated or unsaturated heterocyclic ring, wherein

the 5-10 membered monocyclic or bicyclic saturated or unsaturated heterocyclic ring is optionally substituted with the substituents selected from the group consisting of amino,

C₁₋₆ alkylamino, C₁₋₆ acylamino, -NHC(NH)CH₂Cl, -NHC(O)CH=CHCH₂N(CH₃)₂,

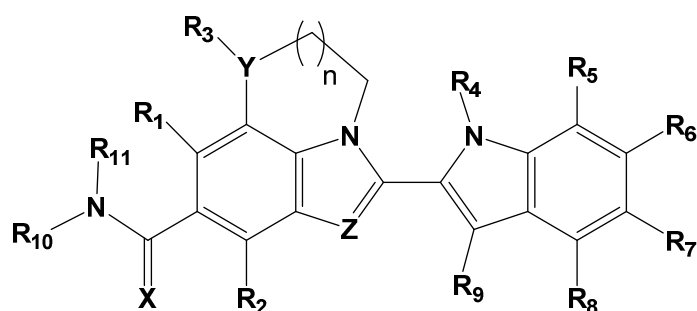
C₁₋₆ alkyl, halogen, C₁₋₆ alkoxy, and hydroxyl;

R₁₇ is selected from the group consisting of hydrogen, hydroxyl, cyano, halogen, C₁₋₆ alkyl, C₁₋₆ alkoxy, C₁₋₆ haloalkyl, C₁₋₆ haloalkoxy, C₁₋₆ acylamino, C₁₋₆ alkylamino, C₅₋₆ aryl, and C₁₋₆ heteroaryl, wherein

C₁₋₆ alkoxy, and C₁₋₆ haloalkoxy, is optionally substituted with one or more of the groups selected from hydrogen, C₁₋₆ alkyl, C₁₋₆ alkoxy, C₁₋₆ haloalkyl, C₁₋₆ alkylhydroxy, cyano, and hydroxyl; and

R₁₈ is independently selected from the group consisting of hydrogen, C₁₋₆ alkyl, and combinations thereof.

7. A compound of Formula (III)



Formula (III)

their polymorphs, stereoisomers, prodrugs, solvates, co-crystals, intermediates, pharmaceutically acceptable salts, and metabolites thereof,

wherein

X is selected from O or S;

Y is selected from O, N, S, S(O), SO₂ or C;

Z is selected from N or CR₁₇;

n is 0-2;

R₁, R₂, R₅, R₆, R₇, R₈, and R₉ are independently selected from the group consisting of hydrogen, hydroxyl, cyano, halogen, C₁₋₆ alkyl, C₁₋₆ alkoxy, C₁₋₆ haloalkyl, C₁₋₆ haloalkoxy, C₁₋₆ acylamino, C₁₋₆ alkylamino, C₅₋₆ aryl, C₂₋₆ alkenyl- C₅₋₆ aryl, and C₁₋₆ heteroaryl, wherein

C₁₋₆ alkoxy, and C₁₋₆ haloalkoxy, is optionally substituted with one or more of the groups selected from hydrogen, C₁₋₆ alkyl, C₁₋₆ alkoxy, C₁₋₆ haloalkyl, C₁₋₆ alkylhydroxy, cyano, and hydroxyl;

R₃ is absent or is selected from the group consisting of hydrogen, C₁₋₆ alkyl, C₃₋₆ cycloalkyl, C₁₋₆ alkylamino, C₁₋₆ haloalkyl, C(O)C₁₋₆ alkyl, C(O)C₁₋₆ haloalkyl, C(O)NR₁₈, C(O)C₁₋₆ alkylamino, SO₂C₁₋₆ alkyl, SO₂C₁₋₆ haloalkyl, SO₂C₃₋₆ cycloalkyl, SO₂NR₁₈, SO₂NC₁₋₆ alkylamino, C₅₋₆ aryl, C₁₋₆ heteroaryl, C(O)C₅₋₆ aryl, C(O)C₁₋₆

heteroaryl, SO₂C₅₋₆ aryl, and SO₂C₁₋₆ heteroaryl, wherein C₁₋₆ alkyl, (CO)C₁₋₆ alkyl, C(O)C₁₋₆ haloalkyl, SO₂C₅₋₆ aryl, and SO₂C₁₋₆ alkyl, is optionally substituted with C₁₋₆ alkoxy, halogen, C₅₋₆ aryl, and C₁₋₆ heteroaryl;

R₄ is selected from the group consisting of hydrogen, C₁₋₆ alkyl, C₁₋₆ haloalkyl, C₁₋₆ alkoxy, C₃₋₆ cycloalkyl, C(O)C₁₋₆ alkyl, C(O)C₁₋₆ haloalkyl, C(O)NR₁₈, C(O)C₁₋₆ alkylamino, SO₂C₁₋₆ alkyl, SO₂C₁₋₆ haloalkyl, SO₂NR₁₈, SO₂NC₁₋₆ alkylamino, C₅₋₆ aryl, C₁₋₆ alkyl-C₅₋₆ aryl, C₁₋₆ heterocyclyl, C₁₋₆ alkyl-C₁₋₆ heterocyclyl, C₁₋₆ heteroaryl, C₁₋₆ alkyl-C₁₋₆ heteroaryl, C(O)C₅₋₆ aryl, C(O)C₁₋₆ heteroaryl, SO₂C₅₋₆ aryl, and SO₂C₁₋₆ heteroaryl, wherein C₁₋₆ alkyl, C₁₋₆ alkoxy, C₃₋₆ cycloalkyl, C₅₋₆ aryl, C₁₋₆ alkyl-C₅₋₆ aryl, C₁₋₆ heterocyclyl, C₁₋₆ alkyl-C₁₋₆ heterocyclyl, C₁₋₆ heteroaryl, C₁₋₆ alkyl-C₁₋₆ heteroaryl, (CO)C₁₋₆ alkyl, C(O)C₁₋₆ haloalkyl, and SO₂C₁₋₆ alkyl, is optionally substituted with one or more groups selected from hydrogen, C₁₋₆ alkyl, C₁₋₆ alkoxy, C₃₋₈ cycloalkyl, C₅₋₆ aryl, C₁₋₆ heteroaryl, halogen, hydroxyl, -CH₂OH, -COOH, and cyano; R₁₀ is hydrogen;

R₁₁ is selected from the group consisting of hydrogen, C₁₋₆ alkyl, C₃₋₆ cycloalkyl, C₁₋₆ alkylamino, C₁₋₆ haloalkyl, C(O)C₁₋₆ alkyl, C(O)C₁₋₆ haloalkyl, C(O)NR₁₈, C(O)C₁₋₆ alkylamino, SO₂C₁₋₆ alkyl, SO₂C₁₋₆ haloalkyl, SO₂C₃₋₆ cycloalkyl, SO₂NR₁₈, SO₂NC₁₋₆ alkylamino, C₅₋₆ aryl, C₁₋₆ heteroaryl, C(O)C₅₋₆ aryl, C(O)C₁₋₆ heteroaryl, SO₂C₅₋₆ aryl, and SO₂C₁₋₆ heteroaryl, wherein

C₁₋₆ alkyl, (CO)C₁₋₆ alkyl, C(O)C₁₋₆ haloalkyl, SO₂C₅₋₆ aryl, and SO₂C₁₋₆ alkyl, is optionally substituted with C₁₋₆ alkoxy, halogen, C₅₋₆ aryl, and C₁₋₆ heteroaryl; and 5-10 membered monocyclic or bicyclic saturated heterocyclic ring with 1-3 heteroatoms selected from N, S or O, or

R₁₀ and R₁₁ can be taken together to form a 5-10 membered monocyclic or bicyclic saturated or unsaturated heterocyclic ring, wherein

the 5-10 membered monocyclic or bicyclic saturated or unsaturated heterocyclic ring is optionally substituted with the substituents selected from the group consisting of amino, C₁₋₆ alkylamino, C₁₋₆ acylamino, -NHC(NH)CH₂Cl, -NHC(O)CH=CHCH₂N(CH₃)₂, C₁₋₆ alkyl, halogen, C₁₋₆ alkoxy, and hydroxyl;

R₁₇ is selected from the group consisting of hydrogen, hydroxyl, cyano, halogen, C₁₋₆ alkyl, C₁₋₆ alkoxy, C₁₋₆ haloalkyl, C₁₋₆ haloalkoxy, C₁₋₆ acylamino, C₁₋₆ alkylamino, C₅₋₆ aryl, and C₁₋₆ heteroaryl, wherein

C₁₋₆ alkoxy, and C₁₋₆ haloalkoxy, is optionally substituted with one or more of the groups selected from hydrogen, C₁₋₆ alkyl, C₁₋₆ alkoxy, C₁₋₆ haloalkyl, C₁₋₆ alkylhydroxy, cyano, and hydroxyl; and

R₁₈ is independently selected from the group consisting of hydrogen, C₁₋₆ alkyl, and combinations thereof.

8. The compound of Formula (I) as claimed in claim 1 or its polymorphs, stereoisomers, prodrugs, solvates, co-crystals, intermediates, pharmaceutically acceptable salts, and metabolites thereof, which is selected from a group consisting of:

(R)-(3-aminopiperidin-1-yl)(2-(1-(cyclopropylmethyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone **(1)**,

(R)-(3-aminopyrrolidin-1-yl)(2-(1-(cyclopropylmethyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone **(2)**,

(R)-(3-aminopiperidin-1-yl)(2-(1-ethyl-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone **(3)**,

(2-(aminomethyl)piperidin-1-yl)(2-(1-(cyclopropylmethyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone **(4)**,

(R)-(3-aminopiperidin-1-yl)(2-(1-ethyl-1H-pyrrolo[2,3-b]pyridin-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone **(5)**, (R)-(3-aminopiperidin-1-yl)(1-(1-(cyclopropylmethyl)-1H-indol-2-yl)-8,9-dihydro-7H-6-oxa-2,9a-diazabenzocd]azulen-4-yl)methanone **(6)**,

(R)-(3-aminopyrrolidin-1-yl)(1-(1-(cyclopropylmethyl)-1H-indol-2-yl)-8,9-dihydro-7H-6-oxa-2,9a-diazabenzocd]azulen-4-yl)methanone **(7)**,

(R)-(3-aminopiperidin-1-yl)(2-(1-(cyclopropylmethyl)-7-methyl-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone **(8)**,

(R)-(3-aminopiperidin-1-yl)(2-(1-(cyclopropylmethyl)-5-fluoro-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone **(9)**,

(R)-(3-aminopiperidin-1-yl)(2-(1-(pyridin-4-ylmethyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone **(10)**,

(R)-(3-aminopiperidin-1-yl)(2-(1-(pyridin-2-ylmethyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone **(11)**,

(R)-(3-aminopiperidin-1-yl)(2-(3-ethylbenzo[b]thiophen-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone **(12)**,

(R)-(3-aminopiperidin-1-yl)(2-(1-(4-chlorobenzyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone **(13)**,

(R)-(3-aminopiperidin-1-yl)(2-(1-(2-fluorobenzyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone **(14)**,

(R)-(3-aminopiperidin-1-yl)(2-(1-(4-fluorobenzyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone **(15)**,

(R)-(3-aminopiperidin-1-yl)(2-(1-(pyridin-3-ylmethyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone **(16)**,

(R)-(3-aminopiperidin-1-yl)(2-(1-(cyclopropylmethyl)-5,6-dimethoxy-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone **(17)**,

(R)-(3-aminopiperidin-1-yl)(2-(1-benzyl-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone **(18)**,

(R)-(3-aminopiperidin-1-yl)(2-(1-(4-methoxybenzyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone **(19)**,

(R)-(3-aminopiperidin-1-yl)(2-(1-(2-methoxyethyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone **(20)**,

(R)-(3-aminopiperidin-1-yl)(2-(6-methoxy-1-(2-methoxyethyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone **(21)**,

(R)-(3-aminopiperidin-1-yl)(2-(1-(2-hydroxyethyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone **(22)**,

(R)-(3-aminopiperidin-1-yl)(2-(1-(cyclopropylmethyl)-6-methoxy-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone **(23)**,

(R)-(3-aminopiperidin-1-yl)(2-(1-((3-fluoropyridin-4-yl)methyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone **(24)**,

(R)-(3-aminopiperidin-1-yl)(2-(1-(pyrazin-2-ylmethyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone **(25)**,

(R)-(3-aminopiperidin-1-yl)(2-(1-((3-fluoropyridin-2-yl)methyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone **(26)**,

(R)-(3-aminopiperidin-1-yl)(2-(1-(pyrimidin-2-ylmethyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone **(27)**,

(R)-(3-aminopiperidin-1-yl)(2-(1-(cyclopropylmethyl)-6-fluoro-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone **(28)**,

(R)-(3-aminopiperidin-1-yl)(2-(1-(pyrimidin-5-ylmethyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone **(29)**,

(R)-(3-aminopiperidin-1-yl)(2-(1-(pyridazin-3-ylmethyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone **(30)**,

(R)-(3-aminopiperidin-1-yl)(2-(1-isobutyl-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone **(31)**,

(R)-(3-aminopiperidin-1-yl)(2-(1-(cyclopropylmethyl)-5,6-difluoro-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone **(32)**,

(R)-(3-aminopiperidin-1-yl)(2-(1-((3-fluoropyridin-2-yl)methyl)-6-methoxy-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone **(33)**,

(R)-(3-aminopiperidin-1-yl)(2-(7-chloro-1-((3-fluoropyridin-2-yl)methyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone **(34)**,

(R)-(3-aminopiperidin-1-yl)(2-(6-fluoro-1-((3-fluoropyridin-2-yl)methyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone **(35)**,

(R)-(3-aminopiperidin-1-yl)(2-(7-chloro-1-(2-methoxyethyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone **(36)**,

(R)-(3-aminopiperidin-1-yl)(2-(1-(4-(hydroxymethyl)benzyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone trifluoroacetic acid salt **(37)**,

(R,E)-N-(1-(2-(1-(cyclopropylmethyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylene-7-carbonyl)piperidin-3-yl)-4-(dimethylamino)but-2-enamide trifluoroacetic acid salt **(38)**,

(R)-(3-aminopiperidin-1-yl)(2-(7-chloro-1-(4-methoxybenzyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone **(39)**,

(R)-(3-aminopiperidin-1-yl)(2-(1-((tetrahydro-2H-pyran-4-yl)methyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone **(40)**,

(R)-(3-aminopiperidin-1-yl)(2-(1-(cyclobutylmethyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone **(41)**,

(R)-2-(2-(7-(3-aminopiperidine-1-carbonyl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-2-yl)-1H-indol-1-yl)acetic acid **(42)**,

(R)-(3-aminopiperidin-1-yl)(2-(1-(piperidin-4-ylmethyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone **(43)**,

(R)-(3-aminopiperidin-1-yl)(2-(1-(oxetan-3-ylmethyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone **(44)**,

(R)-(3-aminopiperidin-1-yl)(2-(1-((1-methylpiperidin-4-yl)methyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone **(45)**,

(R)-(3-aminopiperidin-1-yl)(2-(5-fluoro-1-(4-methoxybenzyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone **(46)**,

(R)-(3-aminopiperidin-1-yl)(2-(1-(2,2-difluoroethyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone **(47)**,

(R)-(3-aminopiperidin-1-yl)(2-(5-fluoro-1-(2-methoxyethyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone **(48)**,

(R)-(3-aminopiperidin-1-yl)(2-(6-fluoro-1-(4-fluorobenzyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone **(49)**,

(R)-(3-aminopiperidin-1-yl)(2-(6-fluoro-1-(4-methoxybenzyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone **(50)**,

(R)-(3-aminopiperidin-1-yl)(2-(1-(4-fluorobenzyl)-6-methoxy-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone **(51)**,

3-aminopiperidin-1-yl)(2-(6-fluoro-1-(2-methoxyethyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone **(52)**,

(R)-(3-aminopiperidin-1-yl)(2-(7-chloro-1-(cyclobutylmethyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone **(53)**,

(R)-(3-aminopiperidin-1-yl)(2-(5,6-difluoro-1-(2-methoxyethyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone **(54)**,

(R)-(3-aminopiperidin-1-yl)(2-(7-chloro-1-isobutyl-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone **(55)**,

(R)-(3-aminopiperidin-1-yl)(2-(7-chloro-1-(2,2-difluoroethyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone **(56)**,

(R)-(3-aminopiperidin-1-yl)(2-(7-chloro-1-(cyclopropylmethyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone **(57)**,

(R,E)-(3-aminopiperidin-1-yl)(2-(1-(cyclopropylmethyl)-5-styryl-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone **(58)**,

(R)-(3-aminopiperidin-1-yl)(2-(1-((4-methylthiazol-2-yl)methyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone **(59)**,

(R)-(3-aminopiperidin-1-yl)(2-(1-(cyclopropylmethyl)-5-methoxy-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone **(60)**,

(R)-(3-aminopiperidin-1-yl)(2-(1-(cyclopropylmethyl)-6-(hydroxymethyl)-1H-indol-2-yl)-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone **(61)**,

(R)-(3-aminopiperidin-1-yl)(2-(1-(cyclopropylmethyl)-1H-indol-2-yl)-3,3-dimethyl-3,4-dihydro-5-oxa-1,2a-diazaacenaphthylen-7-yl)methanone **(62)**,

(R)-(3-aminopiperidin-1-yl)(2-(1-(cyclopropylmethyl)-1H-indol-2-yl)-5,6-dihydro-4H-imidazo[1,5,4-de]quinoxalin-8-yl)methanone **(63)**,

(R)-(3-aminopiperidin-1-yl)(2-(1-(cyclopropylmethyl)-5-fluoro-1H-indol-2-yl)-5,6-dihydro-4H-imidazo[1,5,4-de]quinoxalin-8-yl)methanone **(64)**,

(R)-(3-aminopiperidin-1-yl)(2-(1-(cyclopropylmethyl)-6-fluoro-1H-indol-2-yl)-5,6-dihydro-4H-imidazo[1,5,4-de]quinoxalin-8-yl)methanone **(65)**,

(R)-(3-aminopiperidin-1-yl)(2-(1-(pyridin-3-ylmethyl)-1H-indol-2-yl)-5,6-dihydro-4H-imidazo[1,5,4-de]quinoxalin-8-yl)methanone **(66)**,

(R)-(3-aminopiperidin-1-yl)(2-(5-bromo-1-(cyclopropylmethyl)-1H-indol-2-yl)-5,6-dihydro-4H-imidazo[1,5,4-de]quinoxalin-8-yl)methanone **(67)**,

(R)-(3-aminopiperidin-1-yl)(2-(1-(cyclopropylmethyl)-5-(pyridin-3-yl)-1H-indol-2-yl)-5,6-dihydro-4H-imidazo[1,5,4-de]quinoxalin-8-yl)methanone **(68)**,

(R)-(3-aminopiperidin-1-yl)(2-(1-(pyridin-2-ylmethyl)-1H-indol-2-yl)-5,6-dihydro-4H-imidazo[1,5,4-de]quinoxalin-8-yl)methanone **(69)**,

(R)-(3-aminopiperidin-1-yl)(2-(1-(2-fluorobenzyl)-1H-indol-2-yl)-5,6-dihydro-4H-imidazo[1,5,4-de]quinoxalin-8-yl)methanone **(70)**,

(R)-(3-aminopiperidin-1-yl)(2-(1-(pyridin-4-ylmethyl)-1H-indol-2-yl)-5,6-dihydro-4H-imidazo[1,5,4-de]quinoxalin-8-yl)methanone **(71)**,

(R)-(3-aminopiperidin-1-yl)(2-(1-(cyclopropylmethyl)-1H-indol-2-yl)-6-methyl-5,6-dihydro-4H-imidazo[1,5,4-de]quinoxalin-8-yl)methanone **(72)**,

(R)-(3-aminopiperidin-1-yl)(2-(1-(cyclopropylmethyl)-6-methoxy-1H-indol-2-yl)-5,6-dihydro-4H-imidazo[1,5,4-de]quinoxalin-8-yl)methanone **(73)**,

(R)-(3-aminopiperidin-1-yl)(2-(1-(cyclopropylmethyl)-6-methoxy-1H-indol-2-yl)-6-methyl-5,6-dihydro-4H-imidazo[1,5,4-de]quinoxalin-8-yl)methanone **(74)**,

(R)-(3-aminopiperidin-1-yl)(2-(1-(cyclopropylmethyl)-5-fluoro-1H-indol-2-yl)-6-methyl-5,6-dihydro-4H-imidazo[1,5,4-de]quinoxalin-8-yl)methanone **(75)**,

(R)-(3-aminopiperidin-1-yl)(2-(1-(cyclopropylmethyl)-1H-indol-2-yl)-6-(methylsulfonyl)-5,6-dihydro-4H-imidazo[1,5,4-de]quinoxalin-8-yl)methanone **(76)**,

(R)-(3-aminopiperidin-1-yl)(2-(1-(cyclopropylmethyl)-5,6-difluoro-1H-indol-2-yl)-5,6-dihydro-4H-imidazo[1,5,4-de]quinoxalin-8-yl)methanone **(77)**,

(R)-(3-aminopiperidin-1-yl)(6-cyclopropyl-2-(1-(cyclopropylmethyl)-1H-indol-2-yl)-5,6-dihydro-4H-imidazo[1,5,4-de]quinoxalin-8-yl)methanone **(78)**,

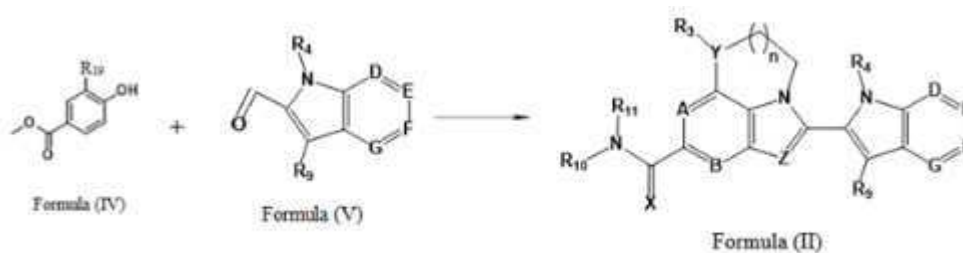
(R)-(3-aminopiperidin-1-yl)(2-(1-(cyclopropylmethyl)-1H-indol-2-yl)-6-(phenethylsulfonyl)-5,6-dihydro-4H-imidazo[1,5,4-de]quinoxalin-8-yl)methanone **(79)**,

(R)-(3-aminopiperidin-1-yl)(2-(1-(cyclopropylmethyl)-4-fluoro-1H-indol-2-yl)-5,6-dihydro-4H-imidazo[1,5,4-de]quinoxalin-8-yl)methanone **(80)**,

membered monocyclic or bicyclic heteroaryl are optionally substituted with 1-5 substituents selected from the group consisting of hydroxyl, cyano, halogen, C₁₋₆ alkyl, C₁₋₆ alkoxy, C₃₋₆ cycloalkyl, C₁₋₆ haloalkyl, C₁₋₆ haloalkoxy, C₁₋₆ acylamino, C₁₋₆ alkylamino, C₅₋₆ aryl, C₁₋₆ alkyl-C₅₋₆ aryl, C₂₋₆ alkenyl-C₅₋₆ aryl, C₁₋₆ heterocyclyl, C₁₋₆ alkyl-C₁₋₆ heterocyclyl, C₁₋₆ heteroaryl, and C₁₋₆ alkyl-C₁₋₆ heteroaryl, wherein C₁₋₆ alkyl, C₁₋₆ alkoxy, C₃₋₆ cycloalkyl, C₅₋₆ aryl, C₁₋₆ alkyl-C₅₋₆ aryl, C₁₋₆ heteroaryl, C₁₋₆ alkyl-C₁₋₆ heteroaryl, and C₁₋₆ alkyl-C₁₋₆ heterocyclyl is optionally substituted with one or more of the groups selected from hydrogen, C₁₋₆ alkyl, C₁₋₆ alkoxy, C₃₋₈ cycloalkyl, C₁₋₆ heteroaryl, halogen, hydroxyl, -CH₂OH, -COOH, and cyano; X of Formula (I) is selected from O or S; Y is selected from O, N, S, S(O), SO₂ or C; Z is selected from N or CR₁₇; A is selected from N or CR₁; B is selected from N or CR₂; n is 0-2; R₁, and R₂ are independently selected from the group consisting of hydrogen, hydroxyl, cyano, halogen, C₁₋₆ alkyl, C₁₋₆ alkoxy, C₁₋₆ haloalkyl, C₁₋₆ haloalkoxy, C₁₋₆ acylamino, C₁₋₆ alkylamino, C₅₋₆ aryl, and C₁₋₆ heteroaryl, wherein C₁₋₆ alkoxy, and C₁₋₆ haloalkoxy, is optionally substituted with one or more of the groups selected from hydrogen, C₁₋₆ alkyl, C₁₋₆ alkoxy, C₁₋₆ haloalkyl, C₁₋₆ alkylhydroxy, cyano, and hydroxyl; R₃ is absent or is selected from the group consisting of hydrogen, C₁₋₆ alkyl, C₃₋₆ cycloalkyl, C₁₋₆ alkylamino, C₁₋₆ haloalkyl, C(O)C₁₋₆ alkyl, C(O)C₁₋₆ haloalkyl, C(O)NR₁₈, C(O)C₁₋₆ alkylamino, SO₂C₁₋₆ alkyl, SO₂C₃₋₆ cycloalkyl, SO₂C₁₋₆ haloalkyl, SO₂NR₁₈, SO₂NC₁₋₆ alkylamino, C₅₋₆ aryl, C₁₋₆ heteroaryl, C(O)C₅₋₆ aryl, C(O)C₁₋₆ heteroaryl, SO₂C₅₋₆ aryl, and SO₂C₁₋₆ heteroaryl, wherein C₁₋₆ alkyl, (CO)C₁₋₆ alkyl, C(O)C₁₋₆ haloalkyl, SO₂C₅₋₆ aryl, and SO₂C₁₋₆ alkyl, is optionally substituted with C₁₋₆ alkoxy, halogen, C₅₋₆ aryl, and C₁₋₆ heteroaryl; R₁₀ is hydrogen; R₁₁ is selected from the group consisting of hydrogen, C₁₋₆ alkyl, C₃₋₆ cycloalkyl, C₁₋₆ alkylamino, C₁₋₆ haloalkyl, C(O)C₁₋₆ alkyl, C(O)C₁₋₆ haloalkyl, C(O)NR₁₈, C(O)C₁₋₆ alkylamino, SO₂C₁₋₆ alkyl, SO₂C₁₋₆ haloalkyl, SO₂C₃₋₆ cycloalkyl, SO₂NR₁₈, SO₂NC₁₋₆ alkylamino, C₅₋₆ aryl, C₁₋₆ heteroaryl, C(O)C₅₋₆ aryl, C(O)C₁₋₆ heteroaryl, SO₂C₅₋₆ aryl, and SO₂C₁₋₆ heteroaryl, wherein C₁₋₆ alkyl, (CO)C₁₋₆ alkyl, C(O)C₁₋₆ haloalkyl, SO₂C₅₋₆ aryl, and SO₂C₁₋₆ alkyl, is optionally substituted with C₁₋₆ alkoxy, halogen, C₅₋₆ aryl, and C₁₋₆ heteroaryl; and 5-10 membered monocyclic or bicyclic saturated heterocyclic ring with 1-3 heteroatoms selected from N, S or O, or R₁₀ and R₁₁ can be taken together to form a 5-10 membered monocyclic or bicyclic saturated or unsaturated heterocyclic ring, wherein the 5-10 membered monocyclic or bicyclic saturated or unsaturated heterocyclic ring is optionally substituted with the substituents selected from the group consisting of amino, C₁₋₆

alkylamino, C₁₋₆ acylamino, -NHC(NH)CH₂Cl, -NHC(O)CH=CHCH₂N(CH₃)₂, C₁₋₆ alkyl, halogen, C₁₋₆ alkoxy, and hydroxyl; R₁₂, R₁₃, R₁₄, and R₁₅ are independently selected from the group consisting of hydrogen, C₁₋₆ alkyl, C₁₋₆ haloalkyl, C₁₋₆ alkylamino, C₅₋₆ aryl, and C₁₋₆ heteroaryl; or R₁₂ and R₁₃ can be taken together to form =O or =S; or R₁₄ and R₁₅ can be taken together to form =O or =S; R₁₆ is selected from the group consisting of hydrogen, 5-10 membered monocyclic or bicyclic aryl, and 5-10 membered monocyclic or bicyclic heteroaryl with 1-5 heteroatoms selected from N, S or O, wherein 5-10 membered monocyclic or bicyclic aryl, and 5-10 membered monocyclic or bicyclic heteroaryl are optionally substituted with 1-5 substituents selected from the group consisting of hydroxyl, cyano, halogen, C₁₋₆ alkyl, C₁₋₆ alkoxy, C₃₋₆ cycloalkyl, C₁₋₆ haloalkyl, C₁₋₆ haloalkoxy, C₁₋₆ acylamino, C₁₋₆ alkylamino, C₅₋₆ aryl, C₁₋₆ alkyl-C₅₋₆ aryl, C₂₋₆ alkenyl-C₅₋₆ aryl, C₁₋₆ heterocyclyl, C₁₋₆ alkyl-C₁₋₆ heterocyclyl, C₁₋₆ heteroaryl, and C₁₋₆ alkyl-C₁₋₆ heteroaryl, wherein C₁₋₆ alkyl, C₁₋₆ alkoxy, C₃₋₆ cycloalkyl, C₅₋₆ aryl, C₁₋₆ alkyl-C₅₋₆ aryl, C₁₋₆ heteroaryl, C₁₋₆ alkyl-C₁₋₆ heteroaryl, and C₁₋₆ alkyl-C₁₋₆ heterocyclyl is optionally substituted with one or more of the groups selected from hydrogen, C₁₋₆ alkyl, C₁₋₆ alkoxy, C₃₋₈ cycloalkyl, C₁₋₆ heteroaryl, halogen, hydroxyl, -CH₂OH, -COOH, and cyano; R₁₇ is selected from the group consisting of hydrogen, hydroxyl, cyano, halogen, C₁₋₆ alkyl, C₁₋₆ alkoxy, C₁₋₆ haloalkyl, C₁₋₆ haloalkoxy, C₁₋₆ acylamino, C₁₋₆ alkylamino, C₅₋₆ aryl, and C₁₋₆ heteroaryl, wherein C₁₋₆ alkoxy, and C₁₋₆ haloalkoxy, is optionally substituted with one or more of the groups selected from hydrogen, C₁₋₆ alkyl, C₁₋₆ alkoxy, C₁₋₆ haloalkyl, C₁₋₆ alkylhydroxy, cyano, and hydroxyl; and R₁₈ is independently selected from the group consisting of hydrogen, C₁₋₆ alkyl, and combinations thereof.

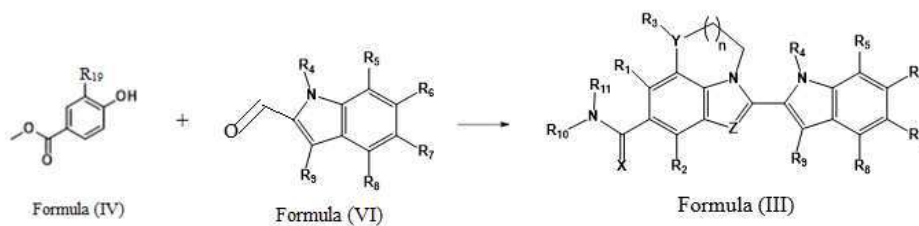
10. A process of preparation of compounds of Formula (II) as claimed in any of claims 1-8 or its polymorphs, stereoisomers, prodrugs, solvates, co-crystals, intermediates, pharmaceutically acceptable salts, and metabolites thereof, the process comprising reacting Formula (IV) and Formula (V)



wherein R₁₉ of Formula (IV) is selected from nitro, and C₁₋₆ alkoxy; X of Formula (II) is selected from O or S; Y is selected from O, N, S, S(O), SO₂ or C; Z is selected from N or CR₁₇; A is selected from N or CR₁; B is selected from N or CR₂; D is selected from N or CR₅; E is selected from N or CR₆; F is selected from N or CR₇; G is selected from N or CR₈; n is 0-2; R₁, R₂, R₅, R₆, R₇, R₈, and R₉ are independently selected from the group consisting of hydrogen, hydroxyl, cyano, halogen, C₁₋₆ alkyl, C₁₋₆ alkoxy, C₁₋₆ haloalkyl, C₁₋₆ haloalkoxy, C₁₋₆ acylamino, C₁₋₆ alkylamino, C₅₋₆ aryl, C₂₋₆ alkenyl- C₅₋₆ aryl, and C₁₋₆ heteroaryl, wherein C₁₋₆ alkoxy, and C₁₋₆ haloalkoxy, is optionally substituted with one or more of the groups selected from hydrogen, C₁₋₆ alkyl, C₁₋₆ alkoxy, C₁₋₆ haloalkyl, C₁₋₆ alkylhydroxy, cyano, and hydroxyl; R₃ is absent or is selected from the group consisting of hydrogen, C₁₋₆ alkyl, C₃₋₆ cycloalkyl, C₁₋₆ alkylamino, C₁₋₆ haloalkyl, C(O)C₁₋₆ alkyl, C(O)C₁₋₆ haloalkyl, C(O)NR₁₈, C(O)C₁₋₆ alkylamino, SO₂C₁₋₆ alkyl, SO₂C₁₋₆ haloalkyl, SO₂C₃₋₆ cycloalkyl, SO₂NR₁₈, SO₂NC₁₋₆ alkylamino, C₅₋₆ aryl, C₁₋₆ heteroaryl, C(O)C₅₋₆ aryl, C(O)C₁₋₆ heteroaryl, SO₂C₅₋₆ aryl, and SO₂C₁₋₆ heteroaryl, wherein C₁₋₆ alkyl, C(O)C₁₋₆ alkyl, C(O)C₁₋₆ haloalkyl, SO₂C₅₋₆ aryl, and SO₂C₁₋₆ alkyl, is optionally substituted with C₁₋₆ alkoxy, halogen, C₅₋₆ aryl, and C₁₋₆ heteroaryl; R₄ is selected from the group consisting of hydrogen, C₁₋₆ alkyl, C₁₋₆ haloalkyl, C₁₋₆ alkoxy, C₃₋₆ cycloalkyl, C(O)C₁₋₆ alkyl, C(O)C₁₋₆ haloalkyl, C(O)NR₁₈, C(O)C₁₋₆ alkylamino, SO₂C₁₋₆ alkyl, SO₂C₁₋₆ haloalkyl, SO₂NR₁₈, SO₂NC₁₋₆ alkylamino, C₅₋₆ aryl, C₁₋₆ alkyl-C₅₋₆ aryl, C₁₋₆ heterocyclyl, C₁₋₆ alkyl-C₁₋₆ heterocyclyl, C₁₋₆ heteroaryl, C₁₋₆ alkyl-C₁₋₆ heteroaryl, C(O)C₅₋₆ aryl, C(O)C₁₋₆ heteroaryl, SO₂C₅₋₆ aryl, and SO₂C₁₋₆ heteroaryl, wherein C₁₋₆ alkyl, C₁₋₆ alkoxy, C₃₋₆ cycloalkyl, C₅₋₆ aryl, C₁₋₆ alkyl-C₅₋₆ aryl, C₁₋₆ heterocyclyl, C₁₋₆ alkyl-C₁₋₆ heterocyclyl, C₁₋₆ heteroaryl, C₁₋₆ alkyl-C₁₋₆ heteroaryl, C(O)C₁₋₆ alkyl, C(O)C₁₋₆ haloalkyl, and SO₂C₁₋₆ alkyl, is optionally substituted with one or more groups selected from hydrogen, C₁₋₆ alkyl, C₁₋₆ alkoxy, C₃₋₈ cycloalkyl, C₅₋₆ aryl, C₁₋₆ heteroaryl, halogen, hydroxyl, -CH₂OH, -COOH, and cyano; R₁₀ is hydrogen; R₁₁ is selected from the group consisting of hydrogen, C₁₋₆ alkyl, C₃₋₆ cycloalkyl, C₁₋₆ alkylamino, C₁₋₆ haloalkyl, C(O)C₁₋₆ alkyl, C(O)C₁₋₆ haloalkyl, C(O)NR₁₈, C(O)C₁₋₆ alkylamino, SO₂C₁₋₆ alkyl, SO₂C₁₋₆ haloalkyl, SO₂C₃₋₆ cycloalkyl, SO₂NR₁₈, SO₂NC₁₋₆ alkylamino, C₅₋₆ aryl, C₁₋₆ heteroaryl, C(O)C₅₋₆ aryl, C(O)C₁₋₆ heteroaryl, SO₂C₅₋₆ aryl, and SO₂C₁₋₆ heteroaryl, wherein C₁₋₆ alkyl, C(O)C₁₋₆ alkyl, C(O)C₁₋₆ haloalkyl, SO₂C₅₋₆ aryl, and SO₂C₁₋₆ alkyl, is optionally substituted with C₁₋₆ alkoxy, halogen, C₅₋₆ aryl, and C₁₋₆ heteroaryl; and 5-10 membered monocyclic or bicyclic saturated heterocyclic ring with 1-3 heteroatoms selected from N, S or O, or

R₁₀ and R₁₁ can be taken together to form a 5-10 membered monocyclic or bicyclic saturated or unsaturated heterocyclic ring, wherein the 5-10 membered monocyclic or bicyclic saturated or unsaturated heterocyclic ring is optionally substituted with the substituents selected from the group consisting of amino, C₁₋₆ alkylamino, C₁₋₆ acylamino, -NHC(NH)CH₂Cl, -NHC(O)CH=CHCH₂N(CH₃)₂, C₁₋₆ alkyl, halogen, C₁₋₆ alkoxy, and hydroxyl; R₁₇ is selected from the group consisting of hydrogen, hydroxyl, cyano, halogen, C₁₋₆ alkyl, C₁₋₆ alkoxy, C₁₋₆ haloalkyl, C₁₋₆ haloalkoxy, C₁₋₆ acylamino, C₁₋₆ alkylamino, C₅₋₆ aryl, and C₁₋₆ heteroaryl, wherein C₁₋₆ alkoxy, and C₁₋₆ haloalkoxy, is optionally substituted with one or more of the groups selected from hydrogen, C₁₋₆ alkyl, C₁₋₆ alkoxy, C₁₋₆ haloalkyl, C₁₋₆ alkylhydroxy, cyano, and hydroxyl; and R₁₈ is independently selected from the group consisting of hydrogen, C₁₋₆ alkyl, and combinations thereof; D of Formula (V) is selected from N or CR₅; E is selected from N or CR₆; F is selected from N or CR₇; G is selected from N or CR₈, R₉ is H; and R₄ is selected from the group consisting of hydrogen, C₁₋₆ alkyl, C₁₋₆ haloalkyl, C₁₋₆ alkoxy, C₃₋₆ cycloalkyl, C(O)C₁₋₆ alkyl, C(O)C₁₋₆ haloalkyl, C(O)NR₁₈, C(O)C₁₋₆ alkylamino, SO₂C₁₋₆ alkyl, SO₂C₁₋₆ haloalkyl, SO₂NR₁₈, SO₂NC₁₋₆ alkylamino, C₅₋₆ aryl, C₁₋₆ alkyl-C₅₋₆ aryl, C₁₋₆ heterocyclyl, C₁₋₆ alkyl-C₁₋₆ heterocyclyl, C₁₋₆ heteroaryl, C₁₋₆ alkyl-C₁₋₆ heteroaryl, C(O)C₅₋₆ aryl, C(O)C₁₋₆ heteroaryl, SO₂C₅₋₆ aryl, and SO₂C₁₋₆ heteroaryl, wherein C₁₋₆ alkyl, C₁₋₆ alkoxy, C₃₋₆ cycloalkyl, C₅₋₆ aryl, C₁₋₆ alkyl-C₅₋₆ aryl, C₁₋₆ heterocyclyl, C₁₋₆ alkyl-C₁₋₆ heterocyclyl, C₁₋₆ heteroaryl, C₁₋₆ alkyl-C₁₋₆ heteroaryl, (CO)C₁₋₆ alkyl, C(O)C₁₋₆ haloalkyl, and SO₂C₁₋₆ alkyl, is optionally substituted with one or more groups selected from hydrogen, C₁₋₆ alkyl, C₁₋₆ alkoxy, C₃₋₈ cycloalkyl, C₅₋₆ aryl, C₁₋₆ heteroaryl, halogen, hydroxyl, -CH₂OH, -COOH, and cyano.

11. A process of preparation of compounds of Formula (III) as claimed in any of claims 1-8 or its polymorphs, stereoisomers, prodrugs, solvates, co-crystals, intermediates, pharmaceutically acceptable salts, and metabolites thereof, the process comprising reacting Formula (IV) and Formula (VI)



wherein R₁₉ of Formula (IV) is selected from nitro, and C₁₋₆ alkoxy; X of Formula (III) is selected from O or S; Y is selected from O, N, S, S(O), SO₂ or C; Z is selected from

N or CR₁₇; n is 0-2; R₁, R₂, R₅, R₆, R₇, R₈, and R₉ are independently selected from the group consisting of hydrogen, hydroxyl, cyano, halogen, C₁₋₆ alkyl, C₁₋₆ alkoxy, C₁₋₆ haloalkyl, C₁₋₆ haloalkoxy, C₁₋₆ acylamino, C₁₋₆ alkylamino, C₅₋₆ aryl, C₂₋₆ alkenyl- C₅₋₆ aryl, and C₁₋₆ heteroaryl, wherein C₁₋₆ alkoxy, and C₁₋₆ haloalkoxy, is optionally substituted with one or more of the groups selected from hydrogen, C₁₋₆ alkyl, C₁₋₆ alkoxy, C₁₋₆ haloalkyl, C₁₋₆ alkylhydroxy, cyano, and hydroxyl; R₃ is absent or is selected from the group consisting of hydrogen, C₁₋₆ alkyl, C₃₋₆ cycloalkyl, C₁₋₆ alkylamino, C₁₋₆ haloalkyl, C(O)C₁₋₆ alkyl, C(O)C₁₋₆ haloalkyl, C(O)NR₁₈, C(O)C₁₋₆ alkylamino, SO₂C₁₋₆ alkyl, SO₂C₁₋₆ haloalkyl, SO₂C₃₋₆ cycloalkyl, SO₂NR₁₈, SO₂NC₁₋₆ alkylamino, C₅₋₆ aryl, C₁₋₆ heteroaryl, C(O)C₅₋₆ aryl, C(O)C₁₋₆ heteroaryl, SO₂C₅₋₆ aryl, and SO₂C₁₋₆ heteroaryl, wherein C₁₋₆ alkyl, C(O)C₁₋₆ alkyl, C(O)C₁₋₆ haloalkyl, SO₂C₅₋₆ aryl, and SO₂C₁₋₆ alkyl, is optionally substituted with C₁₋₆ alkoxy, halogen, C₅₋₆ aryl, and C₁₋₆ heteroaryl; R₄ is selected from the group consisting of hydrogen, C₁₋₆ alkyl, C₁₋₆ haloalkyl, C₁₋₆ alkoxy, C₃₋₆ cycloalkyl, C(O)C₁₋₆ alkyl, C(O)C₁₋₆ haloalkyl, C(O)NR₁₈, C(O)C₁₋₆ alkylamino, SO₂C₁₋₆ alkyl, SO₂C₁₋₆ haloalkyl, SO₂NR₁₈, SO₂NC₁₋₆ alkylamino, C₅₋₆ aryl, C₁₋₆ alkyl-C₅₋₆ aryl, C₁₋₆ heterocyclyl, C₁₋₆ alkyl-C₁₋₆ heterocyclyl, C₁₋₆ heteroaryl, C₁₋₆ alkyl-C₁₋₆ heteroaryl, C(O)C₅₋₆ aryl, C(O)C₁₋₆ heteroaryl, SO₂C₅₋₆ aryl, and SO₂C₁₋₆ heteroaryl, wherein C₁₋₆ alkyl, C₁₋₆ alkoxy, C₃₋₆ cycloalkyl, C₅₋₆ aryl, C₁₋₆ alkyl-C₅₋₆ aryl, C₁₋₆ heterocyclyl, C₁₋₆ alkyl-C₁₋₆ heterocyclyl, C₁₋₆ heteroaryl, C₁₋₆ alkyl-C₁₋₆ heteroaryl, (CO)C₁₋₆ alkyl, C(O)C₁₋₆ haloalkyl, and SO₂C₁₋₆ alkyl, is optionally substituted with one or more groups selected from hydrogen, C₁₋₆ alkyl, C₁₋₆ alkoxy, C₃₋₈ cycloalkyl, C₅₋₆ aryl, C₁₋₆ heteroaryl, halogen, hydroxyl, -CH₂OH, COOH, and cyano; R₁₀ is hydrogen; R₁₁ is selected from the group consisting of hydrogen, C₁₋₆ alkyl, C₃₋₆ cycloalkyl, C₁₋₆ alkylamino, C₁₋₆ haloalkyl, C(O)C₁₋₆ alkyl, C(O)C₁₋₆ haloalkyl, C(O)NR₁₈, C(O)C₁₋₆ alkylamino, SO₂C₁₋₆ alkyl, SO₂C₁₋₆ haloalkyl, SO₂C₃₋₆ cycloalkyl, SO₂NR₁₈, SO₂NC₁₋₆ alkylamino, C₅₋₆ aryl, C₁₋₆ heteroaryl, C(O)C₅₋₆ aryl, C(O)C₁₋₆ heteroaryl, SO₂C₅₋₆ aryl, and SO₂C₁₋₆ heteroaryl, wherein C₁₋₆ alkyl, (CO)C₁₋₆ alkyl, C(O)C₁₋₆ haloalkyl, SO₂C₅₋₆ aryl, and SO₂C₁₋₆ alkyl, is optionally substituted with C₁₋₆ alkoxy, halogen, C₅₋₆ aryl, and C₁₋₆ heteroaryl; and 5-10 membered monocyclic or bicyclic saturated heterocyclic ring with 1-3 heteroatoms selected from N, S or O, or R₁₀ and R₁₁ can be taken together to form a 5-10 membered monocyclic or bicyclic saturated or unsaturated heterocyclic ring, wherein the 5-10 membered monocyclic or bicyclic saturated or unsaturated heterocyclic ring is optionally substituted with the substituents selected from the group consisting of amino, C₁₋₆ alkylamino, C₁₋₆

acylamino, $\text{-NHC(NH)CH}_2\text{Cl}$, $\text{-NHC(O)CH=CHCH}_2\text{N(CH}_3)_2$, C_{1-6} alkyl, halogen, C_{1-6} alkoxy, and hydroxyl; R_{17} is selected from the group consisting of hydrogen, hydroxyl, cyano, halogen, C_{1-6} alkyl, C_{1-6} alkoxy, C_{1-6} haloalkyl, C_{1-6} haloalkoxy, C_{1-6} acylamino, C_{1-6} alkylamino, C_{5-6} aryl, and C_{1-6} heteroaryl, wherein C_{1-6} alkoxy, and C_{1-6} haloalkoxy, is optionally substituted with one or more of the groups selected from hydrogen, C_{1-6} alkyl, C_{1-6} alkoxy, C_{1-6} haloalkyl, C_{1-6} alkylhydroxy, cyano, and hydroxyl; and R_{18} is independently selected from the group consisting of hydrogen, C_{1-6} alkyl, and combinations thereof; and R_5 , R_6 , R_7 , R_8 , and R_9 are independently selected from the group consisting of hydrogen, hydroxyl, cyano, halogen, C_{1-6} alkyl, C_{1-6} alkoxy, C_{1-6} haloalkyl, C_{1-6} haloalkoxy, C_{1-6} acylamino, C_{1-6} alkylamino, C_{5-6} aryl, C_{2-6} alkenyl- C_{5-6} aryl, and C_{1-6} heteroaryl, wherein C_{1-6} alkoxy, and C_{1-6} haloalkoxy, is optionally substituted with one or more of the groups selected from hydrogen, C_{1-6} alkyl, C_{1-6} alkoxy, C_{1-6} haloalkyl, C_{1-6} alkylhydroxy, cyano, and hydroxyl; R_4 is selected from the group consisting of hydrogen, C_{1-6} alkyl, C_{1-6} haloalkyl, C_{1-6} alkoxy, C_{3-6} cycloalkyl, C(O)C_{1-6} alkyl, C(O)C_{1-6} haloalkyl, C(O)NR_{18} , C(O)C_{1-6} alkylamino, $\text{SO}_2\text{C}_{1-6}$ alkyl, $\text{SO}_2\text{C}_{1-6}$ haloalkyl, $\text{SO}_2\text{NR}_{18}$, $\text{SO}_2\text{NC}_{1-6}$ alkylamino, C_{5-6} aryl, C_{1-6} alkyl- C_{5-6} aryl, C_{1-6} heterocyclyl, C_{1-6} alkyl- C_{1-6} heterocyclyl, C_{1-6} heteroaryl, C_{1-6} alkyl- C_{1-6} heteroaryl, C(O)C_{5-6} aryl, C(O)C_{1-6} heteroaryl, $\text{SO}_2\text{C}_{5-6}$ aryl, and $\text{SO}_2\text{C}_{1-6}$ heteroaryl, wherein C_{1-6} alkyl, C_{1-6} alkoxy, C_{3-6} cycloalkyl, C_{5-6} aryl, C_{1-6} alkyl- C_{5-6} aryl, C_{1-6} heterocyclyl, C_{1-6} alkyl- C_{1-6} heterocyclyl, C_{1-6} heteroaryl, C_{1-6} alkyl- C_{1-6} heteroaryl, (CO)C_{1-6} alkyl, C(O)C_{1-6} haloalkyl, and $\text{SO}_2\text{C}_{1-6}$ alkyl, is optionally substituted with one or more groups selected from hydrogen, C_{1-6} alkyl, C_{1-6} alkoxy, C_{3-8} cycloalkyl, C_{5-6} aryl, C_{1-6} heteroaryl, halogen, hydroxyl, $\text{-CH}_2\text{OH}$, COOH , and cyano; and R_{18} is independently selected from the group consisting of hydrogen, C_{1-6} alkyl, and combinations thereof.

12. A pharmaceutical composition comprising a compound of Formula (I), Formula (II), and Formula (III) or a pharmaceutically acceptable salt thereof as claimed in any of claims 1-8 together with a pharmaceutically acceptable carrier, optionally in combination with one or more other pharmaceutical compositions.

13. The pharmaceutical composition as claimed in claim 12, wherein the composition is in the form selected from the group consisting of a tablet, capsule, powder, syrup, solution, aerosol, and suspension.

14. Use of the compounds as claimed in any of the claims 1-8 or a pharmaceutically acceptable salt thereof in the manufacture of a medicament for inhibiting one or more PADs in a cell.

- 15.** A method for inhibiting one or more PAD family in a cell with an effective amount of the compound as claimed in any of the claims 1-8.
- 16.** Use of a therapeutically effective amount of the compound as claimed in any one of claims 1-8 or the pharmaceutical composition as claimed in any one of the claim 12 or 13 in the manufacture of a medicament for treating a condition mediated by one or more PAD's, wherein the compound or the pharmaceutical composition is to be administered to a subject suffering from a condition mediated by one or more PAD family.
- 17.** Use of the compound of Formula (I), Formula (II), and Formula (III) as claimed in any one of claims 1-8 in the manufacture of a medicament for the treatment of rheumatoid arthritis, vasculitis, systemic lupus erythematosus, ulcerative colitis, cancer, cystic fibrosis, asthma, cutaneous lupus erythematosus, and psoriasis.
- 18.** Use of the compound as claimed in any one of claims 1-8 or the pharmaceutical composition as claimed in claim 12, or 13 together with other clinically relevant agents or biological agents in the manufacture of a medicament for the treatment of a condition mediated by one or more PAD family; or the treatment and/or prevention of treatment of rheumatoid arthritis, vasculitis, systemic lupus erythematosus, ulcerative colitis, cancer, cystic fibrosis, asthma, cutaneous lupus erythematosus, and psoriasis.
- 19.** Use of the compound as claimed in any one of claims 1-8 or the pharmaceutical composition as claimed in claim 12, or 13 together with other clinically relevant agents or biological agents in the manufacture of a medicament for the treatment of a condition mediated by one or more PAD family; or the treatment and/or prevention of acid-induced lung injury, respiratory distress syndrome, allergen induced asthma, allergic bronchopulmonary, chronic lung disease of prematurity, chronic obstructive pulmonary disease, colitis, cystic fibrosis, gouty arthritis, inflammatory bowel disease, inflammatory lung disease, inflammatory pain, juvenile rheumatoid arthritis, kidney disease, kidney injury caused by parasitic infections, kidney transplant rejection prophylaxis, lung injury, lupus, lupus nephritis, multiple sclerosis, muscular dystrophy, non-allergen induced asthma, osterarthritis, periodontitis, peritoneal endometriosis, psoriasis, pulmonary disease, pulmonary fibrosis, pyogenic sterile arthritis, renal disease, rheumatic disease, rheumatoid arthritis, sepsis, severe pain and ulcerative colitis.
- 20.** Use of a therapeutically effective amount of the compound as claimed in any one of the claims 1-8, or the pharmaceutical composition as claimed in claim 12 or 13

in the manufacture of a medicament for the treatment and/or prevention of a condition mediated by one or more PAD family disorder, wherein the compound or the pharmaceutical composition is to be administered to a subject suffering from the condition mediated by one or more PAD family.

21. Use of a combination of the compounds as claimed in any of claims 1-20 or the pharmaceutical composition as claimed in claim 12 or 13, with other clinically relevant agents or biological agents in the manufacture of a medicament for the treatment of rheumatoid arthritis.

22. Use of a combination of the compounds as claimed in any of claims 1-8 or the pharmaceutical composition as claimed in claim 12 or 13, with other clinically relevant immune modulators agents in the manufacture of a medicament for the treatment of cancer.