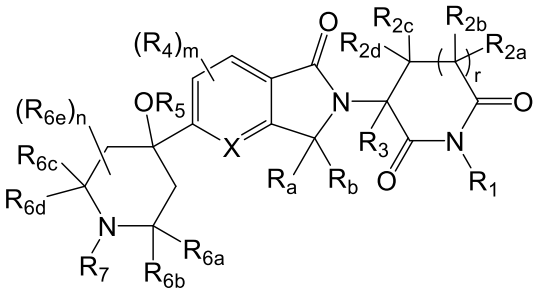
CLAIMS

What is claimed is:

1. A compound of Formula (I):



(I),

or a pharmaceutically acceptable salt, hydrate, solvate, prodrug, stereoisomer, or tautomer thereof, wherein:

X is $C(R_{4'})$;

R_a and R_b are each independently H, D, or $(C_1\text{-}C_6)$alkyl;

R_1 is H, D, $-C(O)R_{11}$, $-CH_2OC(O)R_{11}$, $-CH_2OC(O)NHR_{12}$, $-CH_2OC(O)OR_{12}$, $-P(O)(OR_{12})_2$, $-CH_2OP(O)(OR_{12})_2$, $-CH_2OP(O)(OH)OR_{12}$, $-CH_2OP(O)(R_{12})_2$, $-CH_2OC(O)CH_2NHC(O)CH_2NH_2$, $-CH_2OC(O)CH(R_{12'})NHR_{12'}$, $-CH_2OC(O)(CH_2)_qC(O)OR_{12'}$, or $-CH_2OC(O)$-(5- or 6-membered heteroaryl comprising 1 to 4 heteroatoms selected from O, N, NH, and S);

R_{2a}, R_{2b}, R_{2c}, and R_{2d} are each independently H, D, $(C_1\text{-}C_6)$alkyl, $(C_1\text{-}C_6)$deuteroalkyl, halogen, or -OH, wherein two of R_{2a}, R_{2b}, R_{2c}, and R_{2d} may be taken together with the carbon atom to which they are attached to form a $(C_3\text{-}C_7)$carbocyclyl or $(C_3\text{-}C_7)$spirocarbocyclyl;

R_3 is H, D, $(C_1\text{-}C_6)$alkyl, $(C_1\text{-}C_6)$deuteroalkyl, or halogen, wherein R_3 may be taken together with one of R_{2a}, R_{2b}, R_{2c}, and R_{2d} with the carbon atom to which they are attached to form a $(C_3\text{-}C_7)$carbocyclyl or $(C_3\text{-}C_7)$spirocarbocyclyl;

each R_4 is independently at each occurrence D, $(C_1\text{-}C_6)$alkyl, $(C_1\text{-}C_6)$halohalkyl, or halogen;

each $R_{4'}$ is independently at each occurrence H, D, $(C_1\text{-}C_6)$alkyl, $(C_1\text{-}C_6)$deuteroalkyl, $(C_1\text{-}C_6)$haloalkyl, $(C_1\text{-}C_6)$alkoxy, $(C_1\text{-}C_6)$deuteroalkoxy, $(C_1\text{-}C_6)$haloalkoxy, $(C_3\text{-}C_7)$carbocyclyl, $O(C_3\text{-}C_7)$carbocyclyl, 4- to 7-membered heterocyclyl comprising 1 to 4 heteroatoms selected from O, N, NH, and S; halogen, -OH, -CN, -SH, $-NR_9R_{9'}$, or $-S(O)_pR_{19}$;

R_5 is H, D, $(C_2\text{-}C_6)$alkyl, $(C_1\text{-}C_6)$hydroxyalkyl, $(C_1\text{-}C_6)$halohydroxyalkyl, $(C_1\text{-}C_6)$aminoalkyl, $(C_1\text{-}C_6)$alkyl-O-$(C_1\text{-}C_6)$hydroxyalkyl, $-C(O)R_{12}$, $-CH_2OC(O)R_{12}$, $-CH_2OC(O)N(R_{12})_2$, $-CH_2OC(O)_2R_{12}$, $-P(O)(OR_{12})_2$, $-CH_2OP(O)(OH)OR_{12}$, or $-CH_2OP(O)(R_{12})_2$;

R_{6a}, R_{6b}, R_{6c}, and R_{6d} are each independently H, D, $(C_1\text{-}C_6)$alkyl, $(C_1\text{-}C_6)$deuteroalkyl, $(C_1\text{-}C_6)$hydroxyalkyl, $(C_1\text{-}C_6)$haloalkyl, $(C_1\text{-}C_6)$alkoxy, $(C_1\text{-}C_6)$haloalkoxy, or $(C_3\text{-}C_7)$carbocyclyl; or

two of R_{6a}, R_{6b}, R_{6c}, and R_{6d} together with the atoms to which they are attached form a (C_3-C_7)carbocyclyl, (C_3-C_7)spirocarbocyclyl, 4- to 7-membered spiroheterocyclyl comprising 1 to 4 heteroatoms selected from O, N, NH, and S, or 4- to 7-membered heterocyclyl comprising 1 to 4 heteroatoms selected from O, N, NH, and S, wherein the carbocyclyl, spirocarbocyclyl, heterocyclyl, and spiroheterocyclyl are optionally substituted with one or more R_{10};

each R_{6e} is independently at each occurrence D, (C_1-C_6)alkyl, (C_1-C_6)deuteroalkyl, (C_1-C_6)haloalkyl, (C_1-C_6)alkoxy, (C_1-C_6)haloalkoxy, halogen, (C_1-C_6)hydroxyalkyl, -CN, -OH, -O-(C_1-C_6)hydroxyalkyl, -(C_1-C_6)alkylene-O-(C_1-C_6)alkyl, (C_6-C_{10})aryl, 5- or 6-membered heteroaryl comprising 1 to 4 heteroatoms selected from O, N, NH, and S, (C_3-C_7)carbocyclyl, or 4- to 7-membered heterocyclyl comprising 1 to 4 heteroatoms selected from O, N, NH, and S, wherein the alkyl is optionally substituted with one or more R_{13}, the aryl and heteroaryl are optionally substituted with one or more R_{22}, and the carbocyclyl and heterocyclyl are optionally substituted with one or more R_{23}; or

two R_{6e}, when on the same carbon atom, together with the carbon atom to which they are attached form a (C_3-C_7)carbocyclyl, (C_3-C_7)spirocarbocyclyl, a 4- to 7-membered spiroheterocyclyl comprising 1 to 4 heteroatoms selected from O, N, NH, and S, or 4- to 7-membered heterocyclyl comprising 1 to 4 heteroatoms selected from O, N, NH, and S, wherein the carbocyclyl, spirocarbocyclyl, heterocyclyl, and spiroheterocyclyl are optionally substituted with one or more R_{15}; or

one R_{6e} taken together with any one of R_{6a}, R_{6b}, R_{6c}, and R_{6d} and the atoms to which they are attached form a (C_3-C_7)carbocyclyl or 4- to 7-membered heterocyclyl comprising 1 to 4 heteroatoms selected from O, N, NH, and S, wherein the carbocyclyl and heterocyclyl are optionally substituted with one or more R_{15};

R_7 is (C_1-C_6)alkyl, (C_1-C_6)haloalkyl, (C_1-C_6)hydroxyalkyl, (C_1-C_6)halohydroxyalkyl, or (C_3-C_7)carbocyclyl, wherein alkyl, haloalkyl, hydroxyalkyl, halohydroxyalkyl, and carbocyclyl are optionally substituted with one or more substituents independently selected from R_{21}, D, (C_1-C_6)alkoxy, -SF_5, -SR_{16a}, -$NR_{16}R_{16'}$,-C(O)$NR_{32}R_{33}$, phenyl, 5- or 6-membered heteroaryl comprising 1 to 4 heteroatoms selected from O, N, NH, and S, (C_3-C_7)carbocyclyl, or 4- to 7-membered heterocyclyl comprising 1 to 4 heteroatoms selected from O, N, NH, and S, wherein the phenyl and heteroaryl are optionally substituted with one or more R_{15} and the carbocyclyl and heterocyclyl are optionally substituted with one or more $R_{8'}$;

when $R_{4'}$ is H, m is 1, n is 0 and R_{2a}, R_{2b}, R_{2c}, R_{2d}, R_3, and R_5 are all simultaneously H, then R_7 is (C_1-C_6)haloalkyl, (C_1-C_6)hydroxyalkyl, (C_1-C_6)halohydroxyalkyl, (C_1-C_6)alkyl, or (C_3-C_7)carbocyclyl optionally substituted with one or more substituents independently selected from R_{41}, D, (C_1-C_6)alkoxy, -OR_{16a}, -SF_5, -SR_{16a}, -$NR_{16}R_{16'}$, phenyl, 5- or 6-membered heteroaryl comprising 1 to 4 heteroatoms selected from O, N, NH, and S, (C_3-C_7)carbocyclyl, and 4- to 7-membered heterocyclyl comprising 1 to 4 heteroatoms selected from O, N, NH, and S, wherein the phenyl is substituted with one or more R_8, the

heteroaryl is optionally substituted with one or more R_8, and the carbocyclyl and heterocyclyl are optionally substituted with one or more $R_{8'}$.

when $R_{4'}$ is H, m is 0, n is 0, and R_{2a}, R_{2b}, R_{2c}, R_{2d}, R_3, and R_5 are not all simultaneously H or when $R_{4'}$ is H, m is 0 or 1, and n is 1, 2, 3, or 4, then R_7 is $(C_1$-$C_6)$haloalkyl, $(C_1$-$C_6)$hydroxyalkyl, $(C_1$-$C_6)$halohydroxyalkyl, $(C_1$-$C_6)$alkyl, or $(C_3$-$C_7)$carbocyclyl optionally substituted with one or more substituents independently selected from R_{41}, D, $(C_1$-$C_6)$alkoxy, $-OR_{16a}$, $-SF_5$, $-SR_{16a}$, $-NR_{16}R_{16'}$, phenyl, 5- or 6-membered heteroaryl comprising 1 to 4 heteroatoms selected from O, N, NH, and S, $(C_3$-$C_7)$carbocyclyl, and 4- to 7-membered heterocyclyl comprising 1 to 4 heteroatoms selected from O, N, NH, and S, wherein the phenyl and heteroaryl are optionally substituted with one or more R_8 and the carbocyclyl and heterocyclyl are optionally substituted with one or more $R_{8'}$;

when $R_{4'}$ is (C_1)alkyl, then R_7 is $(C_1$-$C_6)$haloalkyl, $(C_1$-$C_6)$hydroxyalkyl, $(C_1$-$C_6)$halohydroxyalkyl, or $(C_1$-$C_6)$alkyl optionally substituted with one or more substituents independently selected from D, $(C_1$-$C_6)$alkoxy, $-SF_5$, $-SR_{16a}$, $-NR_{16}R_{16'}$, phenyl, 5- or 6-membered heteroaryl comprising 1 to 4 heteroatoms selected from O, N, NH, and S, $(C_3$-$C_7)$carbocyclyl, and 4- to 7-membered heterocyclyl comprising 1 to 4 heteroatoms selected from O, N, NH, and S, wherein the phenyl is substituted with one or more R_8, the heteroaryl is optionally substituted with one or more R_8, and the carbocyclyl and heterocyclyl are optionally substituted with one or more $R_{8'}$;

when $R_{4'}$ is D, $(C_2$-$C_4)$alkyl, $(C_1$-$C_6)$haloalkyl, $(C_1$-$C_6)$alkoxy, $(C_1$-$C_6)$haloalkoxy, halogen, -OH, -CN, -SH, $-NR_9R_{9'}$, or $-S(O)_pR_{19}$, then R_7 is $(C_1$-$C_6)$haloalkyl, $(C_1$-$C_6)$hydroxyalkyl, $(C_1$-$C_6)$halohydroxyalkyl, $(C_1$-$C_6)$alkyl, or $(C_3$-$C_7)$carbocyclyl optionally substituted with one or more substituents independently selected from R_{41}, D, $(C_1$-$C_6)$alkoxy, $-OR_{16a}$, $-SF_5$, $-SR_{16a}$, $-NR_{16}R_{16'}$, phenyl, 5- or 6-membered heteroaryl comprising 1 to 4 heteroatoms selected from O, N, NH, and S, $(C_3$-$C_7)$carbocyclyl, and 4- to 7-membered heterocyclyl comprising 1 to 4 heteroatoms selected from O, N, NH, and S, wherein the phenyl and heteroaryl are optionally substituted with one or more R_8 and the carbocyclyl and heterocyclyl are optionally substituted with one or more $R_{8'}$;

R_8 and $R_{8'}$ are each independently at each occurrence D, $(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$deuteroalkyl, $(C_1$-$C_6)$haloalkyl, $(C_1$-$C_6)$alkoxy, $(C_1$-$C_6)$haloalkoxy, $(C_1$-$C_6)$hydroxyalkyl, halogen, -OH, $-NR_{30}R_{31}$, $-SF_5$, $-SR_{24}$, -CN, $-C(O)NR_{32}R_{33}$, $-C(O)OR_{32}$, $(C_3$-$C_7)$carbocyclyl, $-O(C_3$-$C_7)$carbocyclyl, phenyl, -O-phenyl, monocyclic or bicyclic 5- to 10-membered heteroaryl comprising 1 to 4 heteroatoms selected from O, N, NH, and S, -O-(monocyclic or bicyclic 5- to 10-membered heteroaryl comprising 1 to 4 heteroatoms selected from O, N, NH, and S), 4- to 7-membered heterocyclyl comprising 1 to 4 heteroatoms selected from O, N, NH, and S or -O-(4- to 7-membered heterocyclyl comprising 1 to 4 heteroatoms selected from O, N, NH, and S), wherein the alkyl, deuteroalkyl, haloalkyl, alkoxy, haloalkoxy, hydroalkyl, phenyl, heteroaryl, carbocyclyl, and heterocyclyl are optionally substituted with one or more substituents selected

from $(C_1$-$C_6)$alkyl, $(C_3$-$C_7)$carbocyclyl, $(C_1$-$C_6)$haloalkyl, $(C_1$-$C_6)$alkoxy, $(C_1$-$C_6)$haloalkoxy, $(C_1$-$C_6)$hydroxyalkyl, halogen, –OH, $-NR_{35}R_{36}$, $-C(O)NR_{37}R_{38}$, $-C(O)R_{37}$, $-C(O)OR_{37}$, $-SF_5$, $-SR_{40}$, and -CN, and R_{13}; or

two R_8, when on adjacent atoms, together with the atoms to which they are attached form a phenyl, 5- or 6-membered heteroaryl comprising 1 to 4 heteroatoms selected from O, N, NH, and S, $(C_3$-$C_7)$carbocyclyl, or 4- to 7-membered heterocyclyl comprising 1 to 4 heteroatoms selected from O, N, NH, and S, wherein the phenyl, heteroaryl, carbocyclyl, and heterocyclyl are optionally substituted with one or more R_{10};

two $R_{8'}$, when on adjacent atoms, together with the atoms to which they are attached form a phenyl or 5- or 6-membered heteroaryl comprising 1 to 4 heteroatoms selected from O, N, NH, and S, wherein the phenyl and heteroaryl are optionally substituted with one or more R_{10}; or

two $R_{8'}$ together with the atoms to which they are attached form a $(C_3$-$C_7)$carbocyclyl or 4- to 7-membered heterocyclyl comprising 1 to 4 heteroatoms selected from O, N, NH, and S, wherein the carbocyclyl and heterocyclyl are optionally substituted with one or more R_{10}; or

two $R_{8'}$ when on the same carbon atom form C=(O);

R_9 and $R_{9'}$ are each independently at each occurrence H or $(C_1$-$C_6)$alkyl;

R_{10} is independently at each occurrence D, $(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$deuteroalkyl, $(C_1$-$C_6)$haloalkyl, $(C_1$-$C_6)$alkoxy, $(C_1$-$C_6)$haloalkoxy, $(C_1$-$C_6)$hydroxyalkyl, halogen, -OH, $-NH_2$, $-SF_5$, $-SR_{25}$, -CN, $C(O)OR_9$, $-C(O)R_9$, and $-C(O)NR_9R_{9'}$;

R_{11} is independently at each occurrence H, $(C_1$-$C_6)$alkoxy, $-NH_2$, $-N(H)(C_1$-$C_6)$alkyl, $-N((C_1$-$C_6)$alkyl$)_2$, $(C_1$-$C_6)$alkyl optionally substituted with one or more substituents independently selected from $(C_6$-$C_{10})$aryl, $(C_1$-$C_6)$alkoxy, $(C_1$-$C_6)$hydroxyalkyl, $(C_1$-$C_6)$haloalkyl, halogen, -OH, $-NH_2$, and -CN, or $(C_6$-$C_{10})$aryl optionally substituted with one or more substituents independently selected from $(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$alkoxy, $(C_1$-$C_6)$hydroxyalkyl, $(C_1$-$C_6)$haloalkyl, halogen, -OH, $-NH_2$, and -CN;

R_{12} is independently at each occurrence H, $(C_1$-$C_6)$alkyl optionally substituted with one or more substituents independently selected from $(C_6$-$C_{10})$aryl, $(C_1$-$C_6)$alkoxy, $(C_1$-$C_6)$hydroxyalkyl, $(C_1$-$C_6)$haloalkyl, halogen, -OH, $-NH_2$, and -CN, or $(C_6$-$C_{10})$aryl optionally substituted with one or more substituents independently selected from $(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$alkoxy, $(C_1$-$C_6)$hydroxyalkyl, $(C_1$-$C_6)$haloalkyl, halogen, -OH, $-NH_2$, and -CN;

$R_{12'}$ is independently at each occurrence H or $(C_1$-$C_6)$alkyl;

each R_{13} is independently at each occurrence $(C_1$-$C_6)$alkoxy, $(C_1$-$C_6)$haloalkoxy, $-NR_{14}R_{14'}$, -CN, $(C_3$-$C_7)$carbocyclyl, 4- to 7-membered heterocyclyl comprising 1 to 4 heteroatoms selected from O, N, NH, and S, $(C_6$-$C_{10})$ aryl, or monocyclic or bicyclic 5- to 10-membered heteroaryl comprising 1 to 4 heteroatoms

selected from O, N, NH, and S, wherein carbocyclyl and heterocyclyl are optionally substituted with one or more R_{20} and the aryl and heteroaryl are optionally substituted with one or more R_{21}; or

two R_{13} when on the same carbon atom may be taken together to form C=(O);

R_{14} and $R_{14'}$ are each independently at each occurrence H or $(C_1$-$C_6)$alkyl;

each R_{15} is independently at each occurrence D, $(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$deuteroalkyl, $(C_1$-$C_6)$haloalkyl, $(C_1$-$C_6)$alkoxy, $(C_1$-$C_6)$haloalkoxy, $(C_1$-$C_6)$hydroxyalkyl, halogen, -C(O)OR_{17}, -C(O)R_{18}, or -C(O)$NR_{17}R_{17}$ optionally substituted with one or more R_{20};

R_{16} and $R_{16'}$ are each independently at each occurrence H or $(C_1$-$C_6)$alkyl;

R_{16a} is H, $(C_1$-$C_6)$alkyl, or $(C_1$-$C_6)$haloalkyl;

R_{17} is independently at each occurrence H, $(C_1$-$C_6)$alkyl, or $(C_1$-$C_6)$haloalkyl;

R_{18} is independently at each occurrence $(C_1$-$C_6)$alkyl, or $(C_1$-$C_6)$haloalkyl;

R_{19} is $(C_1$-$C_6)$alkyl or $(C_1$-$C_6)$haloalkyl;

each R_{20} is independently at each occurrence D, $(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$haloalkyl, $(C_1$-$C_6)$alkoxy, $(C_1$-$C_6)$haloalkoxy, $(C_1$-$C_6)$hydroxyalkyl, halogen, -OH, -NH_2, -SF_5, -SR_{26}, -CN, phenyl, 5- or 6-membered heteroaryl comprising 1 to 4 heteroatoms selected from O, N, NH, and S, $(C_3$-$C_7)$carbocyclyl, or 4- to 7-membered heterocyclyl comprising 1 to 4 heteroatoms selected from O, N, NH, and S; or

two R_{20} together with the atoms to which they are attached form a $(C_3$-$C_7)$carbocyclyl or a 4- to 7-membered heterocyclyl comprising 1 to 4 heteroatoms selected from O, N, NH, and S;

each R_{21} is independently at each occurrence D, $(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$haloalkyl, $(C_1$-$C_6)$alkoxy, $(C_1$-$C_6)$haloalkoxy, $(C_1$-$C_6)$hydroxyalkyl, halogen, -OH, -NH_2, -SF_5, -SR_{27}, -CN, phenyl, 5- or 6-membered heteroaryl comprising 1 to 4 heteroatoms selected from O, N, NH, and S, $(C_3$-$C_7)$carbocyclyl, or 4- to 7-membered heterocyclyl comprising 1 to 4 heteroatoms selected from O, N, NH, and S;

each R_{22} is independently at each occurrence $(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$haloalkyl, $(C_1$-$C_6)$alkoxy, $(C_1$-$C_6)$haloalkoxy, $(C_1$-$C_6)$hydroxyalkyl, halogen, -OH, -NH_2, -SF_5, -SR_{28}, -CN, phenyl, 5- or 6-membered heteroaryl comprising 1 to 4 heteroatoms selected from O, N, NH, and S, $(C_3$-$C_7)$carbocyclyl, or 4- to 7-membered heterocyclyl comprising 1 to 4 heteroatoms selected from O, N, NH, and S; or

two R_{22}, when on adjacent atoms, together with the atoms to which they are attached form a phenyl or 5- or 6-membered heteroaryl comprising 1 to 4 heteroatoms selected from O, N, NH, and S;

each R_{23} is independently at each occurrence $(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$haloalkyl, $(C_1$-$C_6)$alkoxy, $(C_1$-$C_6)$haloalkoxy, $(C_1$-$C_6)$hydroxyalkyl, halogen, -OH, -NH_2, -SF_5, -SR_{29}, -CN, phenyl, 5- or 6-membered heteroaryl comprising 1 to 4 heteroatoms selected from O, N, NH, and S, $(C_3$-$C_7)$carbocyclyl, or 4- to 7-membered heterocyclyl comprising 1 to 4 heteroatoms selected from O, N, NH, and S; or

two R_{23} together with the atoms to which they are attached form a $(C_3$-$C_7)$carbocyclyl or a 4- to 7-membered heterocyclyl comprising 1 to 4 heteroatoms selected from O, N, NH, and S;

R_{24}, R_{25}, R_{26}, R_{27}, R_{28}, and R_{29} are each independently at each occurrence H, $(C_1\text{-}C_6)$alkyl or $(C_1\text{-}C_6)$haloalkyl;

R_{30} and R_{31} are each independently at each occurrence H, $(C_1\text{-}C_6)$alkyl, $(C_1\text{-}C_6)$haloalkyl, $(C_3\text{-}C_7)$carbocyclyl, $-C(O)R_{34}$, phenyl, or 5- or 6-membered heteroaryl comprising 1 to 4 heteroatoms selected from O, N, NH, and S, wherein the phenyl or heteroaryl can be substituted with one or more R_{17};

R_{32}, R_{33}, and R_{34} are each independently at each occurrence H or $(C_1\text{-}C_6)$alkyl;

R_{35} and R_{36} are each independently at each occurrence H, $(C_1\text{-}C_6)$alkyl, or $-C(O)R_{39}$;

R_{37}, R_{38}, and R_{39} are each independently at each occurrence H or $(C_1\text{-}C_6)$alkyl;

R_{40} is H, $(C_1\text{-}C_6)$alkyl, or $(C_1\text{-}C_6)$haloalkyl;

two R_{41}, when on adjacent atoms, together with the atoms to which they are attached form a phenyl or 5- or 6-membered heteroaryl comprising 1 to 4 heteroatoms selected from O, N, NH, and S, wherein the phenyl and heteroaryl are optionally substituted with one or more R_{10}; or

two R_{41} together with the atoms to which they are attached form a $(C_3\text{-}C_7)$carbocyclyl or 4- to 7-membered heterocyclyl comprising 1 to 4 heteroatoms selected from O, N, NH, and S, wherein the carbocyclyl and heterocyclyl are optionally substituted with one or more R_{10}; or

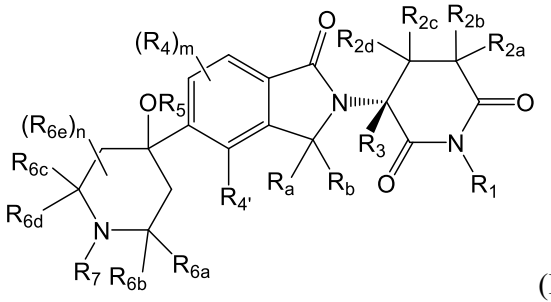
m and p are each independently 0, 1, or 2;

q is 1, 2, or 3;

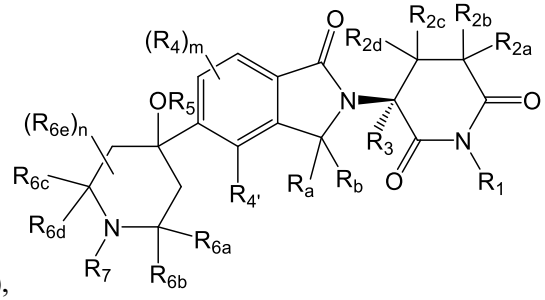
n is 0, 1, 2, 3 or 4; and

r is 0 or 1.

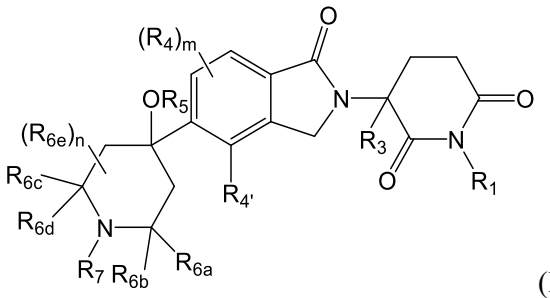
2. The compound according to claim 1, having a Formula (Ia), Formula (Ib), Formula (Ic), Formula (Id), Formula (Ie), or Formula (If):



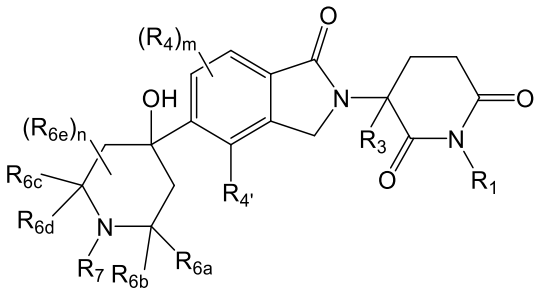
(Ia),



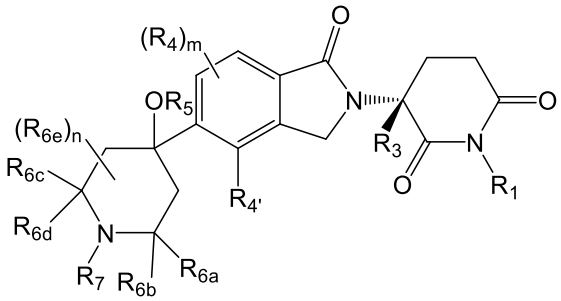
(Ib),



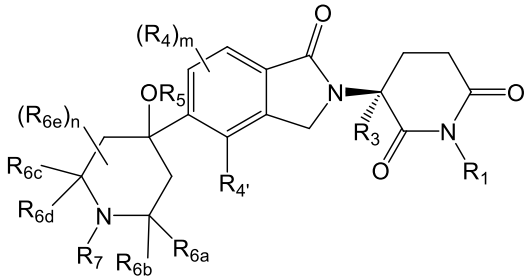
(Ic),



(Id),



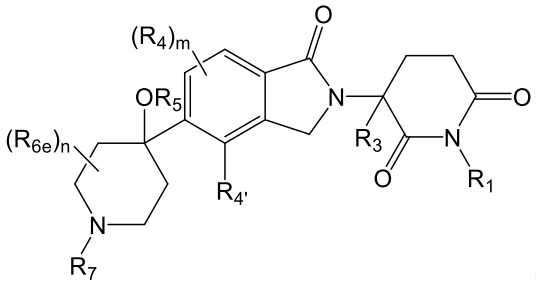
(Ie), or



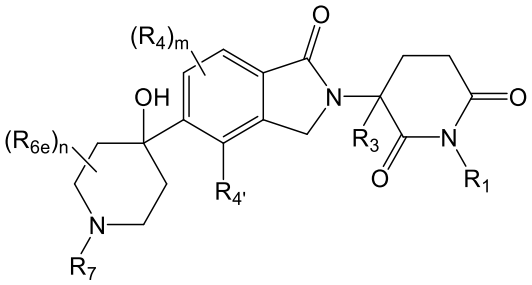
(If),

or a pharmaceutically acceptable salt, hydrate, solvate, prodrug, stereoisomer, or tautomer thereof.

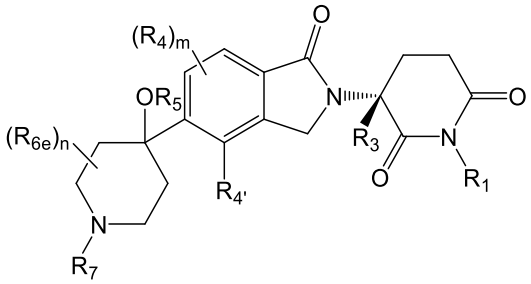
3. The compound according to claim 1, having a Formula (Ig), Formula (Ih), Formula (Ii), Formula (Ij), Formula (Ik), Formula (Il), or Formula (Im):



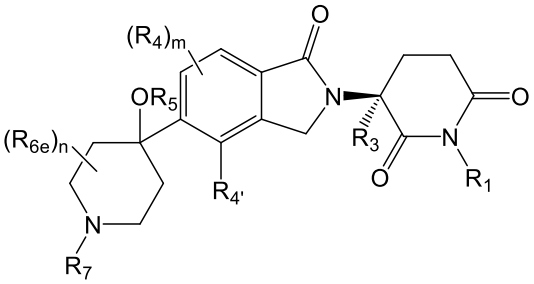
(Ig),



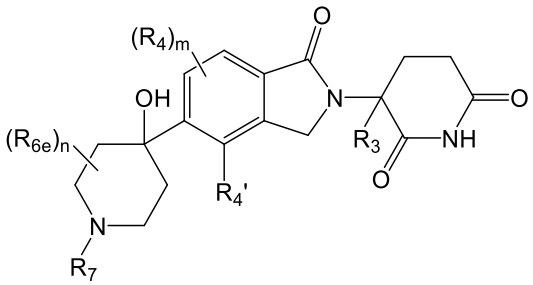
(Ih),



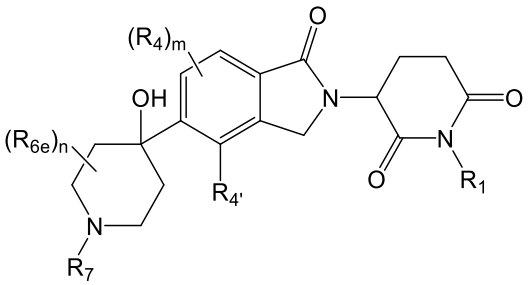
(Ii),



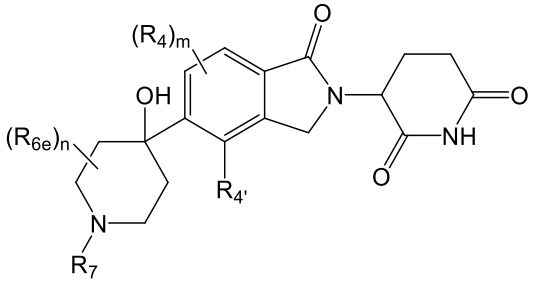
(Ij),



(Ik),



(Il), or



(Im)

or a pharmaceutically acceptable salt, hydrate, solvate, prodrug, stereoisomer, or tautomer thereof.

4. The compound according to claim 1, wherein:

(i) one of R_{2a}, R_{2b}, R_{2c}, R_{2d}, R_3, and R_5 is not H;

(ii) R_{2a} is H, R_{2b} is H, R_{2c} is H, R_{2d} is H, and R_7 is $(C_1$-$C_6)$alkyl optionally substituted with one to three phenyl, 5- or 6-membered heteroaryl comprising 1 to 4 heteroatoms selected from O, N, NH, and S, $(C_3$-$C_7)$carbocyclyl, or 4- to 7-membered heterocyclyl comprising 1 to 4 heteroatoms selected from O, N, NH, and S, wherein the phenyl is substituted with one to three R_8, the heteroaryl is optionally substituted with one to three R_8, and the carbocyclyl and heterocyclyl are optionally substituted with one to three $R_{8'}$;

(iii) R_3 is H;

(iv) $R_{4'}$ is (C_1)alkyl and R_7 is $(C_1$-$C_6)$alkyl optionally substituted with one to three phenyl, 5- or 6-membered heteroaryl comprising 1 to 4 heteroatoms selected from O, N, NH, and S, $(C_3$-$C_7)$carbocyclyl, or 4- to 7-membered heterocyclyl comprising 1 to 4 heteroatoms selected from O, N, NH, and S, wherein the phenyl and heteroaryl are optionally substituted with one to three R_8 and the carbocyclyl and heterocyclyl are optionally substituted with one to three $R_{8'}$;

(v) $R_{4'}$ is $(C_2$-$C_6)$alkyl, $(C_1$-$C_6)$haloalkyl, $(C_1$-$C_6)$alkoxy, $(C_1$-$C_6)$haloalkoxy, halogen, -OH, -CN, -SH, $-NR_9R_{9'}$, or $-S(O)_pR_{19}$ and R_7 is $(C_1$-$C_6)$alkyl optionally substituted with one to three phenyl, 5- or 6-membered heteroaryl comprising 1 to 4 heteroatoms selected from O, N, NH, and S, $(C_3$-$C_7)$carbocyclyl, or 4- to 7-membered heterocyclyl comprising 1 to 4 heteroatoms selected from O, N, NH, and S, wherein the phenyl and heteroaryl are optionally substituted with one to three R_8 and the carbocyclyl and heterocyclyl are optionally substituted with one to three $R_{8'}$;

(vi) $R_{4'}$ is H;

(vii) m is 0;

(viii) m is 1;

(ix) n is 0;

(x) n is 1;

(xi) n is 2;

(xii) m is 0, and n is 0;

(xiii) m is 0 or 1, and n is 1, 2, or 3;

(xiv) m is 1, and n is 0;

(xv) R_5 is H;

(xvi) R_{6a} is H;

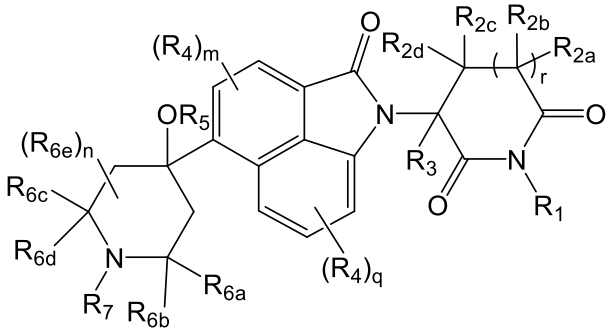
(xvii) R_{6b} is H;

(xviii) R_{6c} is H;

(xiii) R_{6d} is H; or

(xix) R_7 is (C_1-C_6)alkyl optionally substituted with one to three phenyl, 5- or 6-membered heteroaryl comprising 1 to 4 heteroatoms selected from O, N, NH, and S, (C_3-C_7)carbocyclyl, or 4- to 7-membered heterocyclyl comprising 1 to 4 heteroatoms selected from O, N, NH, and S, wherein the phenyl and heteroaryl are optionally substituted with one to three R_8 and the carbocyclyl and heterocyclyl are optionally substituted with one to three $R_{8'}$.

5. A compound of Formula (II):



(II),

or a pharmaceutically acceptable salt, hydrate, solvate, prodrug, stereoisomer, or tautomer thereof, wherein:

R_1 is H, D, -C(O)R_{11}, -CH_2OC(O)R_{11}, -CH_2OC(O)NHR_{12}, -CH_2OC(O)OR_{12}, -P(O)(OR_{12})$_2$, -CH_2OP(O)(OR_{12})$_2$, -CH_2OP(O)(OH)OR_{12}, -CH_2OP(O)(R_{12})$_2$, -CH_2OC(O)CH_2NHC(O)CH_2NH_2, -CH_2OC(O)CH($R_{12'}$)N$HR_{12'}$, -CH_2OC(O)(CH_2)$_q$C(O)O$R_{12'}$, or -CH_2OC(O)-(5- or 6-membered heteroaryl comprising 1 to 4 heteroatoms selected from O, N, NH, and S);

R_{2a}, R_{2b}, R_{2c}, and R_{2d} are each independently H, D, (C_1-C_6)alkyl, (C_1-C_6)deuteroalkyl, halogen, or -OH, wherein two of R_{2a}, R_{2b}, R_{2c}, and R_{2d} may be taken together with the carbon atom to which they are attached to form a (C_3-C_7)carbocyclyl or (C_3-C_7)spirocarbocyclyl;

R_3 is H, D, (C_1-C_6)alkyl, (C_1-C_6)deuteroalkyl, or halogen, wherein R_3 may be taken together with one of R_{2a}, R_{2b}, R_{2c}, and R_{2d} with the carbon atom to which they are attached to form a (C_3-C_7)carbocyclyl or (C_3-C_7)spirocarbocyclyl;

each R_4 is independently at each occurrence D, (C_1-C_6)alkyl, (C_1-C_6)halohalkyl, or halogen;

R_5 is H, D, (C_2-C_6)alkyl, (C_1-C_6)hydroxyalkyl, (C_1-C_6)halohydroxyalkyl, (C_1-C_6)aminoalkyl, (C_1-C_6)alkyl-O-(C_1-C_6)hydroxyalkyl, -C(O)R_{12}, -CH_2OC(O)R_{12}, -CH_2OC(O)N(R_{12})$_2$, -CH_2OC(O)$_2R_{12}$, -P(O)(OR_{12})$_2$, -CH_2OP(O)(OH)OR_{12}, or -CH_2OP(O)(R_{12})$_2$;

R_{6a}, R_{6b}, R_{6c}, and R_{6d} are each independently H, D, (C_1-C_6)alkyl, (C_1-C_6)deuteroalkyl, (C_1-C_6)hydroxyalkyl, (C_1-C_6)haloalkyl, (C_1-C_6)alkoxy, (C_1-C_6)haloalkoxy, or (C_3-C_7)carbocyclyl; or

two of R_{6a}, R_{6b}, R_{6c}, and R_{6d} together with the atoms to which they are attached form a (C_3-C_7)carbocyclyl, (C_3-C_7)spirocarbocyclyl, 4- to 7-membered spiroheterocyclyl comprising 1 to 4 heteroatoms selected from O, N, NH, and S, or 4- to 7-membered heterocyclyl comprising 1 to 4 heteroatoms selected from O, N, NH, and S, wherein the carbocyclyl, spirocarbocyclyl, heterocyclyl, and spiroheterocyclyl are optionally substituted with one or more R_{10};

each R_{6e} is independently at each occurrence D, (C_1-C_6)alkyl, (C_1-C_6)deuteroalkyl, (C_1-C_6)haloalkyl, (C_1-C_6)alkoxy, (C_1-C_6)haloalkoxy, halogen, (C_1-C_6)hydroxyalkyl, -CN, -OH, -O-(C_1-C_6)hydroxyalkyl, -(C_1-C_6)alkylene-O-(C_1-C_6)alkyl, (C_6-C_{10})aryl, 5- or 6-membered heteroaryl comprising 1 to 4 heteroatoms selected from O, N, NH, and S, (C_3-C_7)carbocyclyl, or 4- to 7-membered heterocyclyl comprising 1 to 4 heteroatoms selected from O, N, NH, and S, wherein the alkyl is optionally substituted with one or more R_{13}, the aryl and heteroaryl are optionally substituted with one or more R_{22}, and the carbocyclyl and heterocyclyl are optionally substituted with one or more R_{23}; or

two R_{6e}, when on the same carbon atom, together with the carbon atom to which they are attached form a (C_3-C_7)carbocyclyl, (C_3-C_7)spirocarbocyclyl, a 4- to 7-membered spiroheterocyclyl comprising 1 to 4 heteroatoms selected from O, N, NH, and S, or 4- to 7-membered heterocyclyl comprising 1 to 4 heteroatoms selected from O, N, NH, and S, wherein the carbocyclyl, spirocarbocyclyl, heterocyclyl, and spiroheterocyclyl are optionally substituted with one or more R_{15}; or

one R_{6e} taken together with any one of R_{6a}, R_{6b}, R_{6c}, and R_{6d} and the atoms to which they are attached form a (C_3-C_7)carbocyclyl or 4- to 7-membered heterocyclyl comprising 1 to 4 heteroatoms selected from O, N, NH, and S, wherein the carbocyclyl and heterocyclyl are optionally substituted with one or more R_{15};

R_7 is (C_1-C_6)alkyl, (C_1-C_6)haloalkyl, (C_1-C_6)hydroxyalkyl, (C_1-C_6)halohydroxyalkyl, or (C_3-C_7)carbocyclyl, wherein alkyl, haloalkyl, hydroxyalkyl, halohydroxyalkyl, and carbocyclyl are optionally substituted with one or more substituents independently selected from R_{21}, D, (C_1-C_6)alkoxy, -SF_5, -SR_{16a}, -$NR_{16}R_{16'}$,-C(O)$NR_{32}R_{33}$, phenyl, 5- or 6-membered heteroaryl comprising 1 to 4 heteroatoms selected from

O, N, NH, and S, (C_3-C_7)carbocyclyl, or 4- to 7-membered heterocyclyl comprising 1 to 4 heteroatoms selected from O, N, NH, and S, wherein the phenyl and heteroaryl are optionally substituted with one or more R_{15} and the carbocyclyl and heterocyclyl are optionally substituted with one or more $R_{8'}$;

R_8 and $R_{8'}$ are each independently at each occurrence D, (C_1-C_6)alkyl, (C_1-C_6)deuteroalkyl, (C_1-C_6)haloalkyl, (C_1-C_6)alkoxy, (C_1-C_6)haloalkoxy, (C_1-C_6)hydroxyalkyl, halogen, -OH, -$NR_{30}R_{31}$, -SF_5, -SR_{24}, -CN, -$C(O)NR_{32}R_{33}$, -$C(O)OR_{32}$, (C_3-C_7)carbocyclyl, -O(C_3-C_7)carbocyclyl, phenyl, -O-phenyl, monocyclic or bicyclic 5- to 10-membered heteroaryl comprising 1 to 4 heteroatoms selected from O, N, NH, and S, -O-(monocyclic or bicyclic 5- to 10-membered heteroaryl comprising 1 to 4 heteroatoms selected from O, N, NH, and S), 4- to 7-membered heterocyclyl comprising 1 to 4 heteroatoms selected from O, N, NH, and S or -O-(4- to 7-membered heterocyclyl comprising 1 to 4 heteroatoms selected from O, N, NH, and S), wherein the alkyl, deuteroalkyl, haloalkyl, alkoxy, haloalkoxy, hydroalkyl, phenyl, heteroaryl, carbocyclyl, and heterocyclyl are optionally substituted with one or more substituents selected from (C_1-C_6)alkyl, (C_3-C_7)carbocyclyl, (C_1-C_6)haloalkyl, (C_1-C_6)alkoxy, (C_1-C_6)haloalkoxy, (C_1-C_6)hydroxyalkyl, halogen, –OH, -$NR_{35}R_{36}$, -$C(O)NR_{37}R_{38}$, -$C(O)R_{37}$, -$C(O)OR_{37}$, -SF_5, -SR_{40}, and -CN, and R_{13}; or

two R_8, when on adjacent atoms, together with the atoms to which they are attached form a phenyl, 5- or 6-membered heteroaryl comprising 1 to 4 heteroatoms selected from O, N, NH, and S, (C_3-C_7)carbocyclyl, or 4- to 7-membered heterocyclyl comprising 1 to 4 heteroatoms selected from O, N, NH, and S, wherein the phenyl, heteroaryl, carbocyclyl, and heterocyclyl are optionally substituted with one or more R_{10};

two $R_{8'}$, when on adjacent atoms, together with the atoms to which they are attached form a phenyl or 5- or 6-membered heteroaryl comprising 1 to 4 heteroatoms selected from O, N, NH, and S, wherein the phenyl and heteroaryl are optionally substituted with one or more R_{10}; or

two $R_{8'}$ together with the atoms to which they are attached form a (C_3-C_7)carbocyclyl or 4- to 7-membered heterocyclyl comprising 1 to 4 heteroatoms selected from O, NH, N, and S, wherein the carbocyclyl and heterocyclyl are optionally substituted with one or more R_{10}; or

two $R_{8'}$ when on the same carbon atom form C=(O);

R_9 and $R_{9'}$ are each independently at each occurrence (C_1-C_6)alkoxy, (C_1-C_6)haloalkoxy, -$NR_{13}R_{13'}$, -CN,

(C_3-C_7)carbocyclyl, 4- to 7-membered heterocyclyl comprising 1 to 4 heteroatoms selected from O, N, NH, and S, (C_6-C_{10}) aryl, or monocyclic or bicyclic 5- to 10-membered heteroaryl comprising 1 to 4 heteroatoms selected from O, N, NH, and S, wherein carbocyclyl and heterocyclyl are optionally substituted with one or more R_{20} and the aryl and heteroaryl are optionally substituted with one or more R_{21};

R_{10} is independently at each occurrence D, $(C_1\text{-}C_6)$alkyl, $(C_1\text{-}C_6)$deuteroalkyl, $(C_1\text{-}C_6)$haloalkyl, $(C_1\text{-}C_6)$alkoxy, $(C_1\text{-}C_6)$haloalkoxy, $(C_1\text{-}C_6)$hydroxyalkyl, halogen, -OH, - OH, $-NH_2$, $-SF_5$, $-SR_{25}$, -CN, $C(O)OR_9$, $-C(O)R_9$, and $-C(O)NR_9R_9$;

R_{11} is independently at each occurrence H, $(C_1\text{-}C_6)$alkoxy, $-NH_2$, $-N(H)(C_1\text{-}C_6)$alkyl, $-N((C_1\text{-}C_6)\text{alkyl})_2$, $(C_1\text{-}C_6)$alkyl optionally substituted with one or more substituents independently selected from $(C_6\text{-}C_{10})$aryl, $(C_1\text{-}C_6)$alkoxy, $(C_1\text{-}C_6)$hydroxyalkyl, $(C_1\text{-}C_6)$haloalkyl, halogen, -OH, $-NH_2$, and -CN, or $(C_6\text{-}C_{10})$aryl optionally substituted with one or more substituents independently selected from $(C_1\text{-}C_6)$alkyl, $(C_1\text{-}C_6)$alkoxy, $(C_1\text{-}C_6)$hydroxyalkyl, $(C_1\text{-}C_6)$haloalkyl, halogen, -OH, $-NH_2$, and -CN;

R_{12} is independently at each occurrence H, $(C_1\text{-}C_6)$alkyl optionally substituted with one or more substituents independently selected from $(C_6\text{-}C_{10})$aryl, $(C_1\text{-}C_6)$alkoxy, $(C_1\text{-}C_6)$hydroxyalkyl, $(C_1\text{-}C_6)$haloalkyl, halogen, -OH, $-NH_2$, and -CN, or $(C_6\text{-}C_{10})$aryl optionally substituted with one or more substituents independently selected from $(C_1\text{-}C_6)$alkyl, $(C_1\text{-}C_6)$alkoxy, $(C_1\text{-}C_6)$hydroxyalkyl, $(C_1\text{-}C_6)$haloalkyl, halogen, -OH, $-NH_2$, and -CN;

$R_{12'}$ is independently at each occurrence H or $(C_1\text{-}C_6)$alkyl;

R_{13} and $R_{13'}$ are each independently at each occurrence H or $(C_1\text{-}C_6)$alkyl;

each R_{14} is independently at each occurrence D, $(C_1\text{-}C_6)$alkyl, $(C_1\text{-}C_6)$deuteroalkyl, $(C_1\text{-}C_6)$haloalkyl, $(C_1\text{-}C_6)$alkoxy, $(C_1\text{-}C_6)$haloalkoxy, $(C_1\text{-}C_6)$hydroxyalkyl, halogen, $-C(O)OR_{17}$, $-C(O)R_{18}$, or $-C(O)NR_{17}R_{17}$;

R_{15} and $R_{15'}$ are each independently at each occurrence H or $(C_1\text{-}C_6)$alkyl;

R_{15a} is H, $(C_1\text{-}C_6)$alkyl, or $(C_1\text{-}C_6)$haloalkyl;

each R_{16} is independently at each occurrence $(C_1\text{-}C_6)$alkyl, $(C_1\text{-}C_6)$haloalkyl, $(C_1\text{-}C_6)$alkoxy, $(C_1\text{-}C_6)$haloalkoxy, $(C_1\text{-}C_6)$hydroxyalkyl, halogen, -OH, $-NH_2$, $-SF_5$, $-SR_{24}$, -CN, phenyl, 5- or 6-membered heteroaryl comprising 1 to 4 heteroatoms selected from O, N, NH, and S, $(C_3\text{-}C_7)$carbocyclyl, or 4- to 7-membered heterocyclyl comprising 1 to 4 heteroatoms selected from O, N, NH, and S; or

two R_{16}, when on adjacent atoms, together with the atoms to which they are attached form a phenyl or 5- or 6-membered heteroaryl comprising 1 to 4 heteroatoms selected from O, N, NH, and S;

R_{17} is independently at each occurrence H, $(C_1\text{-}C_6)$alkyl, or $(C_1\text{-}C_6)$haloalkyl;

R_{18} is independently at each occurrence $(C_1\text{-}C_6)$alkyl or $(C_1\text{-}C_6)$haloalkyl;

each R_{19} is independently at each occurrence $(C_1\text{-}C_6)$alkyl, $(C_1\text{-}C_6)$haloalkyl, $(C_1\text{-}C_6)$alkoxy, $(C_1\text{-}C_6)$haloalkoxy, $(C_1\text{-}C_6)$hydroxyalkyl, halogen, -OH, $-NH_2$, $-SF_5$, $-SR_{25}$, -CN, phenyl, 5- or 6-membered heteroaryl comprising 1 to 4 heteroatoms selected from O, N, NH, and S, $(C_3\text{-}C_7)$carbocyclyl, or 4- to 7-membered heterocyclyl comprising 1 to 4 heteroatoms selected from O, N, NH, and S; or

two R_{19} together with the atoms to which they are attached form a $(C_3\text{-}C_7)$carbocyclyl or a 4- to 7-membered heterocyclyl comprising 1 to 4 heteroatoms selected from O, N, NH, and S;

each R_{20} is independently at each occurrence D, $(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$haloalkyl, $(C_1$-$C_6)$alkoxy, $(C_1$-$C_6)$haloalkoxy, $(C_1$-$C_6)$hydroxyalkyl, halogen, -OH, $-NH_2$, $-SF_5$, $-SR_{26}$, -CN, phenyl, 5- or 6-membered heteroaryl comprising 1 to 4 heteroatoms selected from O, N, NH, and S, $(C_3$-$C_7)$carbocyclyl, or 4- to 7-membered heterocyclyl comprising 1 to 4 heteroatoms selected from O, N, NH, and S; or

two R_{20} together with the atoms to which they are attached form a $(C_3$-$C_7)$carbocyclyl or a 4- to 7-membered heterocyclyl comprising 1 to 4 heteroatoms selected from O, N, NH, and S;

each R_{21} is independently at each occurrence D, $(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$haloalkyl, $(C_1$-$C_6)$alkoxy, $(C_1$-$C_6)$haloalkoxy, $(C_1$-$C_6)$hydroxyalkyl, halogen, -OH, $-NH_2$, $-SF_5$, $-SR_{27}$, -CN, phenyl, 5- or 6-membered heteroaryl comprising 1 to 4 heteroatoms selected from O, N, NH, and S, $(C_3$-$C_7)$carbocyclyl, or 4- to 7-membered heterocyclyl comprising 1 to 4 heteroatoms selected from O, N, NH, and S;

R_{22}, R_{23}, R_{24}, R_{25}, R_{26}, and R_{27} are each independently at each occurrence H, $(C_1$-$C_6)$alkyl, or $(C_1$-$C_6)$haloalkyl;

R_{30} and R_{31} are each independently at each occurrence H, $(C_1$-$C_6)$alkyl, $(C_1$-$C_6)$haloalkyl, $(C_3$-$C_7)$carbocyclyl, $-C(O)R_{32}$, phenyl, or 5- or 6-membered heteroaryl comprising 1 to 4 heteroatoms selected from O, N, NH, and S, wherein the phenyl or heteroaryl can be substituted with one or more R_{17};

R_{30}, R_{31}, and R_{32} are each independently at each occurrence H or $(C_1$-$C_6)$alkyl;

R_{33} and R_{34} are each independently at each occurrence H, $(C_1$-$C_6)$alkyl, or $-C(O)R_{37}$;

R_{35}, R_{36}, and R_{37} are each independently at each occurrence H or $(C_1$-$C_6)$alkyl;

R_{38} is H, $(C_1$-$C_6)$alkyl, or $(C_1$-$C_6)$haloalkyl;

m is 0, 1, or 2;

q is 1, 2, or 3;

n is 0, 1, 2, 3, or 4; and

r is 0 or 1.

6. The compound according to claim 5, wherein;

(i) R_{2a} is H;

(ii) R_{2b} is H;

(iii) R_{2c} is H;

(iv) R_{2d} is H;

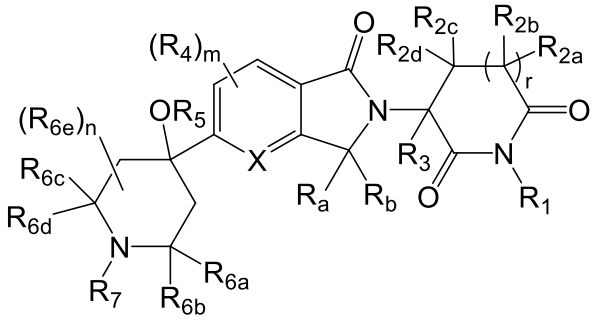
(v) R_3 is H;

(vi) R_5 is H; or

(vii) R_7 is $(C_1$-$C_6)$alkyl, wherein the alkyl is optionally substituted with one to three phenyl, 5- or 6-membered heteroaryl comprising 1 to 4 heteroatoms selected from O, N, NH, and S, $(C_3$-$C_7)$carbocyclyl, or 4- to 7-membered heterocyclyl comprising 1 to 4 heteroatoms selected from O, N, NH, and S, wherein

the phenyl and heteroaryl are optionally substituted with one to three R_8 and the carbocyclyl and heterocyclyl are optionally substituted with one to three $R_{8'}$.

7. A compound of Formula (III):



(III),

or a pharmaceutically acceptable salt, hydrate, solvate, prodrug, stereoisomer, or tautomer thereof, wherein:

X is N or N(O);

R_a and R_b are each independently H, D, or (C_1-C_6)alkyl;

R_1 is H, D, -C(O)R_{11}, -CH_2OC(O)R_{11}, -CH_2OC(O)NHR_{12}, -CH_2OC(O)OR_{12}, -P(O)(OR_{12})$_2$, -CH_2OP(O)(OR_{12})$_2$, -CH_2OP(O)(OH)OR_{12}, -CH_2OP(O)(R_{12})$_2$, -CH_2OC(O)CH_2NHC(O)CH_2NH_2, -CH_2OC(O)CH($R_{12'}$)N$HR_{12'}$, -CH_2OC(O)(CH_2)$_q$C(O)$OR_{12'}$, or -CH_2OC(O)-(5- or 6-membered heteroaryl comprising 1 to 4 heteroatoms selected from O, N, NH, and S);

R_{2a}, R_{2b}, R_{2c}, and R_{2d} are each independently H, D, (C_1-C_6)alkyl, (C_1-C_6)deuteroalkyl, halogen, or -OH, wherein two of R_{2a}, R_{2b}, R_{2c}, and R_{2d} may be taken together with the carbon atom to which they are attached to form a (C_3-C_7)carbocyclyl or (C_3-C_7)spirocarbocyclyl;

R_3 is H, D, (C_1-C_6)alkyl, (C_1-C_6)deuteroalkyl, or halogen, wherein R_3 may be taken together with one of R_{2a}, R_{2b}, R_{2c}, and R_{2d} with the carbon atom to which they are attached to form a (C_3-C_7)carbocyclyl or (C_3-C_7)spirocarbocyclyl;

each R_4 is independently at each occurrence D, (C_1-C_6)alkyl, (C_1-C_6)haloalkyl, or halogen;

R_5 is H, D, (C_2-C_6)alkyl, (C_1-C_6)hydroxyalkyl, (C_1-C_6)halohydroxyalkyl, (C_1-C_6)aminoalkyl, (C_1-C_6)alkyl-O-(C_1-C_6)hydroxyalkyl, -C(O)R_{12}, -CH_2OC(O)R_{12}, -CH_2OC(O)N(R_{12})$_2$, -CH_2OC(O)$_2R_{12}$, -P(O)(OR_{12})$_2$, -CH_2OP(O)(OH)OR_{12}, or -CH_2OP(O)(R_{12})$_2$;

R_{6a}, R_{6b}, R_{6c}, and R_{6d} are each independently H, D, (C_1-C_6)alkyl, (C_1-C_6)deuteroalkyl, (C_1-C_6)hydroxyalkyl, (C_1-C_6)haloalkyl, (C_1-C_6)alkoxy, (C_1-C_6)haloalkoxy,, or (C_3-C_7)carbocyclyl; or

two of R_{6a}, R_{6b}, R_{6c}, and R_{6d} together with the atoms to which they are attached form a (C_3-C_7)carbocyclyl, (C_3-C_7)spirocarbocyclyl, 4- to 7-membered spiroheterocyclyl comprising 1 to 4 heteroatoms selected from O, N, NH, and S, or 4- to 7-membered heterocyclyl comprising 1 to 4

heteroatoms selected from O, N, NH, and S, wherein the carbocyclyl, spirocarbocyclyl, heterocyclyl, and spiroheterocyclyl are optionally substituted with one or more R_{10};

each R_{6e} is independently at each occurrence D, (C_1-C_6)alkyl, (C_1-C_6)deuteroalkyl, (C_1-C_6)haloalkyl, (C_1-C_6)alkoxy, (C_1-C_6)haloalkoxy, halogen, (C_1-C_6)hydroxyalkyl, -CN, -OH, -O-(C_1-C_6)hydroxyalkyl, -(C_1-C_6)alkylene-O-(C_1-C_6)alkyl, (C_6-C_{10})aryl, 5- or 6-membered heteroaryl comprising 1 to 4 heteroatoms selected from O, N, NH, and S, (C_3-C_7)carbocyclyl, or 4- to 7-membered heterocyclyl comprising 1 to 4 heteroatoms selected from O, N, NH, and S, wherein the alkyl is optionally substituted with one or more R_{13}, the aryl and heteroaryl are optionally substituted with one or more R_{22}, and the carbocyclyl and heterocyclyl are optionally substituted with one or more R_{23}; or

two R_{6e}, when on the same carbon atom, together with the carbon atom to which they are attached form a (C_3-C_7)carbocyclyl, (C_3-C_7)spirocarbocyclyl, a 4- to 7-membered spiroheterocyclyl comprising 1 to 4 heteroatoms selected from O, N, NH, and S, or 4- to 7-membered heterocyclyl comprising 1 to 4 heteroatoms selected from O, N, NH, and S, wherein the carbocyclyl, spirocarbocyclyl, heterocyclyl, and spiroheterocyclyl are optionally substituted with one or more R_{15}; or

one R_{6e} taken together with any one of R_{6a}, R_{6b}, R_{6c}, and R_{6d} and the atoms to which they are attached form a (C_3-C_7)carbocyclyl or 4- to 7-membered heterocyclyl comprising 1 to 4 heteroatoms selected from O, N, NH, and S, wherein the carbocyclyl and heterocyclyl are optionally substituted with one or more R_{15};

R_7 is (C_1-C_6)alkyl, (C_1-C_6)haloalkyl, (C_1-C_6)hydroxyalkyl, (C_1-C_6)halohydroxyalkyl, or (C_3-C_7)carbocyclyl, wherein alkyl, haloalkyl, hydroxyalkyl, halohydroxyalkyl, and carbocyclyl are optionally substituted with one or more substituents independently selected from R_{21}, D, (C_1-C_6)alkoxy, -SF_5, -SR_{14a}, -$NR_{14}R_{14'}$,-C(O)$NR_{29}R_{30}$, phenyl, 5- or 6-membered heteroaryl comprising 1 to 4 heteroatoms selected from O, N, NH, and S, (C_3-C_7)carbocyclyl, or 4- to 7-membered heterocyclyl comprising 1 to 4 heteroatoms selected from O, N, NH, and S, wherein the phenyl and heteroaryl are optionally substituted with one or more R_{15} and the carbocyclyl and heterocyclyl are optionally substituted with one or more $R_{8'}$;

R_8 and $R_{8'}$ are each independently at each occurrence D, (C_1-C_6)alkyl, (C_1-C_6)deuteroalkyl, (C_1-C_6)haloalkyl, (C_1-C_6)alkoxy, (C_1-C_6)haloalkoxy, (C_1-C_6)hydroxyalkyl, halogen, -OH, -$NR_{27}R_{28}$, -SF_5, -SR_9, -CN, -C(O)$NR_{29}R_{30}$, -C(O)OR_{29}, (C_3-C_7)carbocyclyl, -O(C_3-C_7)carbocyclyl, phenyl, -O-phenyl, monocyclic or bicyclic 5- to 10-membered heteroaryl comprising 1 to 4 heteroatoms selected from O, N, NH, and S, -O-(monocyclic or bicyclic 5- to 10-membered heteroaryl comprising 1 to 4 heteroatoms selected from O, N, NH, and S), 4- to 7-membered heterocyclyl comprising 1 to 4 heteroatoms selected from O, N, NH, and S or -O-(4- to 7-membered heterocyclyl comprising 1 to 4 heteroatoms selected from O, N, NH, and S), wherein the phenyl, heteroaryl, carbocyclyl, and heterocyclyl are optionally substituted

with one or more substituents selected from (C_1-C_6)alkyl, (C_3-C_7)carbocyclyl, (C_1-C_6)haloalkyl, (C_1-C_6)alkoxy,
(C_1-C_6)haloalkoxy, (C_1-C_6)hydroxyalkyl, halogen, –OH, -$NR_{32}R_{33}$, -$C(O)NR_{34}R_{35}$, -$C(O)R_{34}$, -$C(O)OR_{34}$, -SF_5, -SR_{37}, and -CN; or

two R_8, when on adjacent atoms, together with the atoms to which they are attached form a phenyl, 5- or 6-membered heteroaryl comprising 1 to 4 heteroatoms selected from O, N, NH, and S,
(C_3-C_7)carbocyclyl, or 4- to 7-membered heterocyclyl comprising 1 to 4 heteroatoms selected from O, N, NH, and S, wherein the phenyl, heteroaryl, carbocyclyl, and heterocyclyl are optionally substituted with one or more R_{10};

two $R_{8'}$, when on adjacent atoms, together with the atoms to which they are attached form a phenyl or 5- or 6-membered heteroaryl comprising 1 to 4 heteroatoms selected from O, N, NH, and S, wherein the phenyl and heteroaryl are optionally substituted with one or more R_{10}; or

two $R_{8'}$ together with the atoms to which they are attached form a (C_3-C_7)carbocyclyl or 4- to 7-membered heterocyclyl comprising 1 to 4 heteroatoms selected from O, N, NH, and S, wherein the carbocyclyl and heterocyclyl are optionally substituted with one or more R_{10}; or

two $R_{8'}$ when on the same carbon atom form C=(O);

R_9 is H, (C_1-C_6)alkyl, or (C_1-C_6)haloalkyl;

R_{10} is independently at each occurrence D, (C_1-C_6)alkyl, (C_1-C_6)deuteroalkyl, (C_1-C_6)haloalkyl, (C_1-C_6)alkoxy, (C_1-C_6)haloalkoxy, (C_1-C_6)hydroxyalkyl, halogen, -OH, -NH_2, -SF_5, -SR_{26}, or -CN;

R_{11} is independently at each occurrence H, (C_1-C_6)alkoxy, -NH_2, -N(H)(C_1-C_6)alkyl, -N((C_1-C_6)alkyl)$_2$, (C_1-C_6)alkyl optionally substituted with one or more substituents independently selected from (C_6-C_{10})aryl, (C_1-C_6)alkoxy, (C_1-C_6)hydroxyalkyl, (C_1-C_6)haloalkyl, halogen, -OH, -NH_2, and -CN, or (C_6-C_{10})aryl optionally substituted with one or more substituents independently selected from (C_1-C_6)alkyl, (C_1-C_6)alkoxy, (C_1-C_6)hydroxyalkyl, (C_1-C_6)haloalkyl, halogen, -OH, -NH_2, and -CN;

R_{12} is independently at each occurrence H, (C_1-C_6)alkyl optionally substituted with one or more substituents independently selected from (C_6-C_{10})aryl, (C_1-C_6)alkoxy, (C_1-C_6)hydroxyalkyl, (C_1-C_6)haloalkyl, halogen, -OH, -NH_2, and -CN, or (C_6-C_{10})aryl optionally substituted with one or more substituents independently selected from (C_1-C_6)alkyl, (C_1-C_6)alkoxy, (C_1-C_6)hydroxyalkyl, (C_1-C_6)haloalkyl, halogen, -OH, -NH_2, and -CN;

$R_{12'}$ is independently at each occurrence H or (C_1-C_6)alkyl;

each R_{13} is independently at each occurrence D, (C_1-C_6)alkyl, (C_1-C_6)deuteroalkyl, (C_1-C_6)haloalkyl, (C_1-C_6)alkoxy, (C_1-C_6)haloalkoxy, (C_1-C_6)hydroxyalkyl, halogen, -$C(O)OR_{15'}$, -$C(O)R_{15}$, or -$C(O)NR_{15'}R_{15'}$;

R_{14} and $R_{14'}$ are each independently at each occurrence H or (C_1-C_6)alkyl;

R_{14a} is H, (C_1-C_6)alkyl, or (C_1-C_6)haloalkyl;

R_{15} is independently at each occurrence (C_1-C_6)alkyl, or (C_1-C_6)haloalkyl;

$R_{15'}$ is independently at each occurrence H, (C_1-C_6)alkyl, or (C_1-C_6)haloalkyl;

each R_{16} is independently at each occurrence (C_1-C_6)alkoxy, (C_1-C_6)haloalkoxy, -$NR_{17}R_{17'}$, -CN, (C_3-C_7)carbocyclyl, 4- to 7-membered heterocyclyl comprising 1 to 4 heteroatoms selected from O, N, NH, and S, (C_6-C_{10}) aryl, or monocyclic or bicyclic 5- to 10-membered heteroaryl comprising 1 to 4 heteroatoms selected from O, N, NH, and S, wherein carbocyclyl and heterocyclyl are optionally substituted with one or more R_{22} and the aryl and heteroaryl are optionally substituted with one or more R_{23};

R_{17} and $R_{17'}$ are each independently at each occurrence H or (C_1-C_6)alkyl;

each R_{18} is independently at each occurrence (C_1-C_6)alkyl, (C_1-C_6)haloalkyl, (C_1-C_6)alkoxy, (C_1-C_6)haloalkoxy, (C_1-C_6)hydroxyalkyl, halogen, -OH, -NH_2, -SF_5, -SR_{20}, -CN, phenyl, 5- or 6-membered heteroaryl comprising 1 to 4 heteroatoms selected from O, N, NH, and S, (C_3-C_7)carbocyclyl, or 4- to 7-membered heterocyclyl comprising 1 to 4 heteroatoms selected from O, N, NH, and S; or

two R_{18}, when on adjacent atoms, together with the atoms to which they are attached form a phenyl or 5- or 6-membered heteroaryl comprising 1 to 4 heteroatoms selected from O, N, NH, and S;

each R_{19} is independently at each occurrence (C_1-C_6)alkyl, (C_1-C_6)haloalkyl, (C_1-C_6)alkoxy, (C_1-C_6)haloalkoxy, (C_1-C_6)hydroxyalkyl, halogen, -OH, -NH_2, -SF_5, -SR_{21}, -CN, phenyl, 5- or 6-membered heteroaryl comprising 1 to 4 heteroatoms selected from O, N, NH, and S, (C_3-C_7)carbocyclyl, or 4- to 7-membered heterocyclyl comprising 1 to 4 heteroatoms selected from O, N, NH, and S; or

two R_{19} together with the atoms to which they are attached form a (C_3-C_7)carbocyclyl or a 4- to 7-membered heterocyclyl comprising 1 to 4 heteroatoms selected from O, N, NH, and S;

R_{20} and R_{21} are each independently at each occurrence H, (C_1-C_6)alkyl, or (C_1-C_6)haloalkyl;

each R_{22} is independently at each occurrence D, (C_1-C_6)alkyl, (C_1-C_6)haloalkyl, (C_1-C_6)alkoxy, (C_1-C_6)haloalkoxy, (C_1-C_6)hydroxyalkyl, halogen, -OH, -NH_2, -SF_5, -SR_{24}, -CN, phenyl, 5- or 6-membered heteroaryl comprising 1 to 4 heteroatoms selected from O, N, NH, and S, (C_3-C_7)carbocyclyl, or 4- to 7-membered heterocyclyl comprising 1 to 4 heteroatoms selected from O, N, NH, and S; or

two R_{22} together with the atoms to which they are attached form a (C_3-C_7)carbocyclyl or a 4- to 7-membered heterocyclyl comprising 1 to 4 heteroatoms selected from O, N, NH, and S;

each R_{23} is independently at each occurrence D, (C_1-C_6)alkyl, (C_1-C_6)haloalkyl, (C_1-C_6)alkoxy,

(C_1-C_6)haloalkoxy, (C_1-C_6)hydroxyalkyl, halogen, -OH, -NH_2, -SF_5, -SR_{25}, -CN, phenyl, 5- or 6-membered heteroaryl comprising 1 to 4 heteroatoms selected from O, N, NH, and S, (C_3-C_7)carbocyclyl, or 4- to 7-membered heterocyclyl comprising 1 to 4 heteroatoms selected from O, N, NH, and S;

R_{24}, R_{25} and R_{26} are each independently at each occurrence H, (C_1-C_6)alkyl, or (C_1-C_6)haloalkyl;

R_{27} and R_{28} are each independently at each occurrence H, (C_1-C_6)alkyl, (C_1-C_6)haloalkyl, (C_3-C_7)carbocyclyl, -C(O)R_{31}, phenyl, or 5- or 6-membered heteroaryl comprising 1 to 4 heteroatoms selected from O, N, NH, and S, wherein the phenyl or heteroaryl can be substituted with one or more R_{17};

R_{29}, R_{30}, and R_{31} are each independently at each occurrence H or (C_1-C_6)alkyl;

R_{32} and R_{33} are each independently at each occurrence H, (C_1-C_6)alkyl, or -C(O)R_{36};

R_{34}, R_{35}, and R_{36} are each independently at each occurrence H or (C_1-C_6)alkyl;

R_{37} is H, (C_1-C_6)alkyl or (C_1-C_6)haloalkyl;

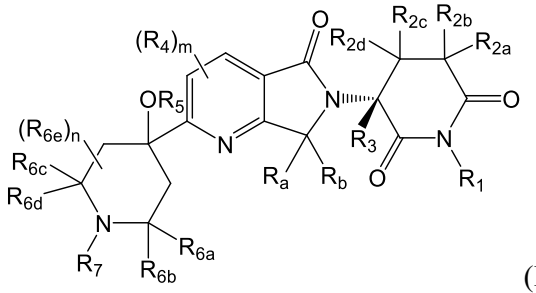
q is 1, 2, or 3;

m is 0, 1 or 2;

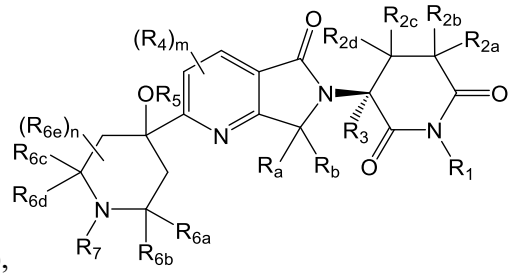
n is 0, 1, 2, 3 or 4; and

r is 0 or 1.

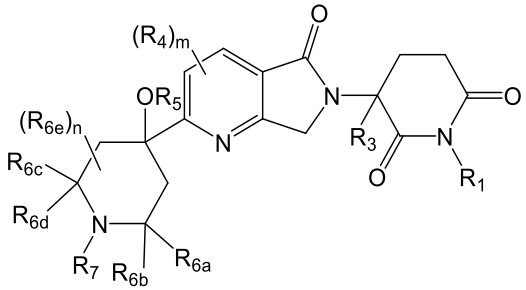
8. The compound according to claim 7, having a Formula (IIIa), Formula (IIIb), Formula (IIIc), Formula (IIId), Formula (IIIe), Formula (IIIf), or Formula (IIIg):



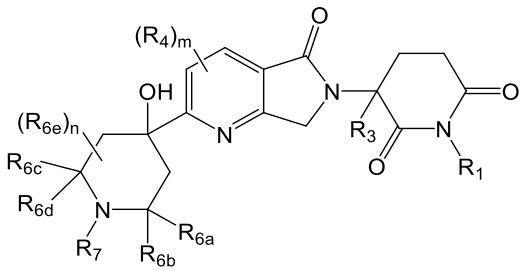
(IIIa),



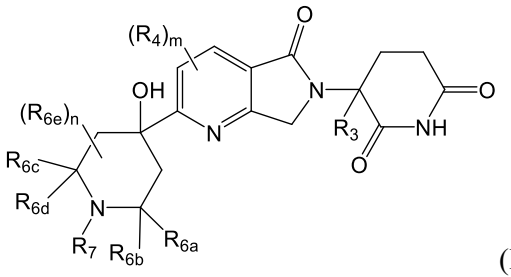
(IIIb),



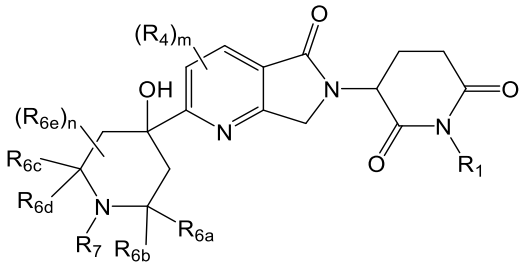
(IIIc),



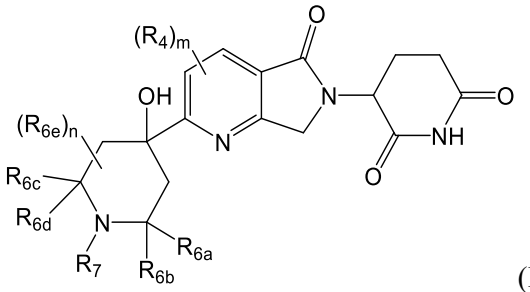
(IIId),



(IIIe),



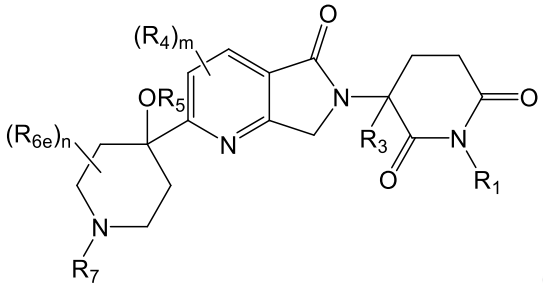
(IIIf), or



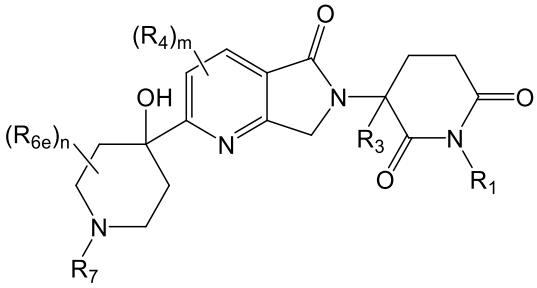
(IIIg),

or a pharmaceutically acceptable salt, hydrate, solvate, prodrug, stereoisomer, or tautomer thereof.

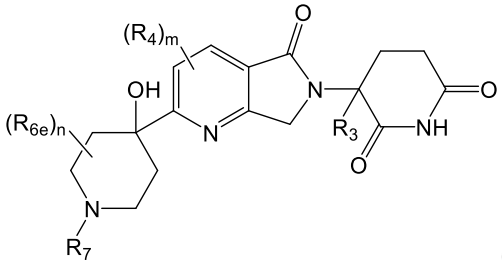
9. The compound according to claim 7, having a Formula (IIIh), Formula (IIIi), Formula (IIIj), Formula (IIIk), or Formula (IIIl):



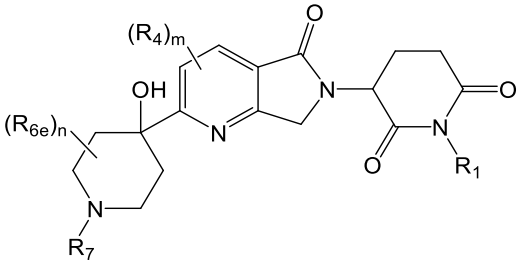
(IIIh),



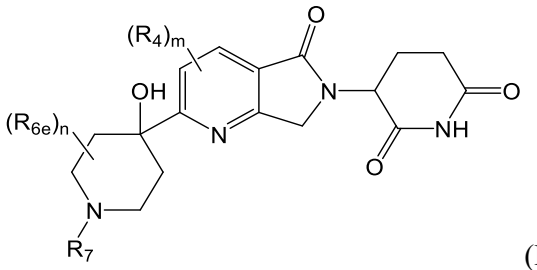
(IIIi),



(IIIj),



(IIIk), or



(IIIl),

or a pharmaceutically acceptable salt, hydrate, solvate, prodrug, stereoisomer, or tautomer thereof.

10. The compound according to claim 7, wherein;

(i) R_1 is H;

(ii) R_{2a}, R_{2b}, R_{2c}, and R_{2d} are each H;

(iii) R_3 is H, D, or methyl;

(iv) R_a and R_b are both H;

(v) m is 0;

(vi) R_5 is H;

(vii) R_{6a}, R_{6b}, R_{6c}, and R_{6d} are each independently H or (C_1-C_6)alkyl;

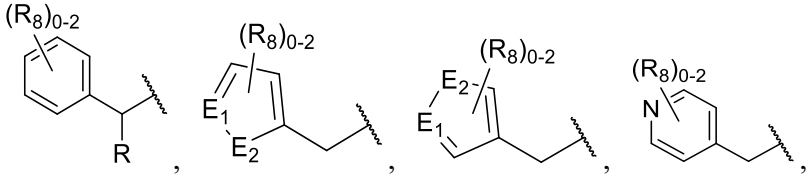
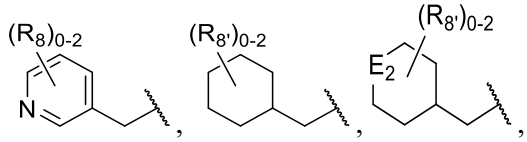
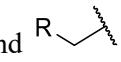
(viii) each R_{6e} is independently at each occurrence (C_1-C_6)alkyl, (C_1-C_6)deuteroalkyl, -(C_1-C_6)alkylene-O-(C_1-C_6)alkyl, wherein the alkyl is optionally substituted with one or more R_{13}, the aryl is optionally substituted with one or more R_{22}; or

two R_{6e}, when on the same carbon atom, together with the carbon atom to which they are attached form a (C_3-C_7)spirocarbocyclyl or a 4- to 7-membered spiroheterocyclyl comprising 1 to 4 heteroatoms selected from O, N, NH, and S, wherein the spirocarbocyclyl and spiroheterocyclyl are optionally substituted with one or more R_{15};

(ix) n is 0;

(x) n is 1;

(xi) n is 2; or

(xii) R_7 is selected from , , and , wherein

R is selected from H and (C_1-C_3)alkyl; E_1 is selected from CH and N; E_2 is selected from O, NH, NR_8, and S; and R_8 and $R_{8'}$ are defined according to the above claim 7.

11. The compound according to any one of claims 1, 5 and 7 , wherein the compound is provided in Table 1 or Table 2.

12. A pharmaceutical composition according to any one of claims 1-11, or a pharmaceutically acceptable salt, hydrate, solvate, prodrug, stereoisomer, or tautomer thereof.

13. The pharmaceutical composition according to claim 12, further comprising a pharmaceutically acceptable additive or excipient.

14. The pharmaceutical composition according to claim 12, for use in the treatment of a disease or disorder that is affected by the reduction of HIF-1β levels.

15. A compound according to claim 1, 5, or 7, or a pharmaceutically acceptable salt, hydrate, solvate, prodrug, stereoisomer, or tautomer thereof, for use in degrading HIF-1β or modulating HIF-1β levels.

16. A compound according to claim 1, 5, or 7, or a pharmaceutically acceptable salt, hydrate, solvate, prodrug, stereoisomer, or tautomer thereof, for use in treating a disease or disorder that is affected by the modulation of HIF-1β levels.

17. The compound for use according to claim 16, wherein the disease or disorder is selected from cancer, von Hippel-Lindau (VHL) disease, iron overload disorders, cardiovascular diseases, pulmonary diseases, autoimmune and inflammatory-related diseases and conditions, neurodegenerative diseases, viral diseases, metabolic diseases, neovascular diseases, retinal vascular diseases, fibrosis, endometriosis, preeclampsia, and allergic and genetic diseases.

18. The compound for use according to claim 17, wherein the disease or disorder is selected from renal cell carcinoma (RCC), von Hippel-Lindau disease (VHL), advanced pheochromocytoma/paraganglioma (PPGL), pancreatic neuroendocrine tumor (pNET), pulmonary arterial hypertension (PAH), glioblastoma, colitis, Crohn's disease, ulcerative colitis, T cell leukemia or T cell lymphoma, Hodgkin's lymphoma or non-Hodgkin's lymphoma, non-small cell lung cancer (NSCLC), melanoma, triple-negative breast cancer (TNBC), nasopharyngeal cancer (NPC), microsatellite stable colorectal cancer (mssCRC), thymoma, carcinoid, gastrointestinal stromal tumor (GIST), myeloid leukemia, and coronary heart disease.

19. A compound according to claim 1, 5, or 7, or a pharmaceutically acceptable salt, hydrate, solvate, prodrug, stereoisomer, or tautomer thereof, for use in treating a disease or disorder selected from cancer, von Hippel-Lindau (VHL) disease, iron overload disorders, cardiovascular diseases, pulmonary arterial hypertension (PAH), autoimmune and inflammatory-related diseases and conditions, neurodegenerative diseases, viral diseases, metabolic diseases, and allergic and genetic diseases.

20 The compound for use according to claim 19, wherein disease or disorder is selected from cancer or von Hippel-Lindau (VHL) disease.

21. The compound for use according to claim 19, wherein the cancer is selected from renal cell carcinoma (RCC), glioblastoma, T cell leukemia or T cell lymphoma, Hodgkin's lymphoma or non-Hodgkin's lymphoma, non-small cell lung cancer (NSCLC), melanoma, triple-negative breast cancer (TNBC), nasopharyngeal cancer (NPC), microsatellite stable colorectal cancer (mssCRC), thymoma, carcinoid, gastrointestinal stromal tumor (GIST), and myeloid leukemia.

22. The compound for use of claim 19, wherein the disease or disorder is renal cell carcinoma (RCC).

23. The compound for use of claim 22, wherein the renal cell carcinoma is clear cell renal cell carcinoma (ccRCC).

24. The compound for use according to claim 16 or 19, wherein the administration is oral, parenteral, subcutaneous, by injection, or by infusion.