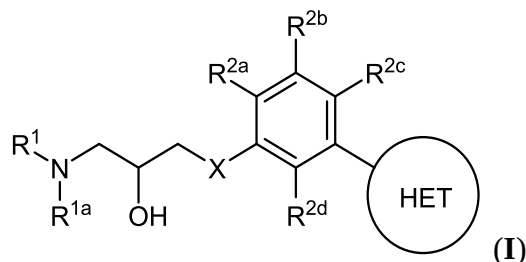


Claims

What is claimed is

1. A compound of Formula (I):



or a pharmaceutically acceptable salt thereof;

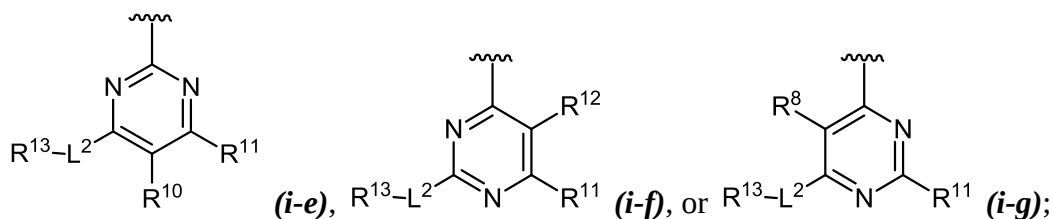
wherein:

X is $-O-$;

R^1 and R^{1a} are each independently hydrogen or C_{1-4} alkyl;

each of R^{2a} , R^{2b} , R^{2c} , and R^{2d} is independently hydrogen, halogen, $-CN$, $-OR^{A2}$, $-SR^{A2}$, $-N(R^{A2})_2$, C_{1-6} haloalkyl, C_{1-6} alkyl, C_{2-6} alkenyl, C_{2-6} alkynyl, carbocyclyl, or heterocyclyl, wherein each instance of R^{A2} is independently hydrogen or C_{1-6} alkyl, or two R^{A2} groups attached to the same nitrogen atom are joined to form a heterocyclyl or heteroaryl ring;

Ring HET is a 6-membered monocyclic heteroaryl ring system of the Formula:



each instance of R^8 , R^{10} , R^{11} , and R^{12} is independently selected from the group consisting of hydrogen, halo, $-CN$, $-NO_2$, $-C(=O)R'$, $-C(=O)OR'$, $-C(=O)N(R')_2$, optionally substituted C_{1-6} alkyl, optionally substituted C_{3-4} cycloalkyl, and $-L^1-R^3$;

each instance of R' is independently hydrogen or C_{1-6} alkyl;

each instance of L^1 and L^2 is independently a bond, $-O-$, $-N(R^L)-$, $-S-$, $-C(O)-$, $-C(O)O-$, $-C(O)N(R^L)-$, $-OC(O)-$, $-OC(O)N(R^L)-$, $-NR^LC(O)-$, $-NR^LC(O)N(R^L)-$, $-NR^LC(O)O-$, or an optionally substituted C_{1-6} saturated or unsaturated hydrocarbon chain, wherein one or more moieties selected from the group consisting of $-O-$, $-N(R^L)-$, $-S-$, $-C(O)-$, $-C(O)O-$, $-C(O)N(R^L)-$, $-OC(O)-$, $-OC(O)N(R^L)-$, $-NR^LC(O)-$, $-NR^LC(O)N(R^L)-$, and $-NR^LC(O)O-$ is

optionally and independently present between two carbon atoms of the hydrocarbon chain, and optionally and independently present at one or both ends of the hydrocarbon chain;

each R^L is independently hydrogen or C_{1-6} alkyl;

R^3 is hydrogen, optionally substituted C_{1-6} alkyl, optionally substituted C_{2-6} alkenyl, optionally substituted C_{2-6} alkynyl, optionally substituted carbocyclyl, optionally substituted heterocyclyl, optionally substituted aryl, or optionally substituted heteroaryl, provided when R^3 is hydrogen, then L^1 is not a bond; and

R^{13} is optionally substituted carbocyclyl, optionally substituted heterocyclyl, optionally substituted aryl, or optionally substituted heteroaryl,

wherein, and unless otherwise specified,

heterocyclyl or heterocyclic refers to a radical of a 3–10 membered non–aromatic ring system having ring carbon atoms and 1–4 ring heteroatoms, wherein each heteroatom is independently selected from nitrogen, oxygen, and sulfur;

carbocyclyl or carbocyclic refers to a radical of a non–aromatic cyclic hydrocarbon group having from 3 to 10 ring carbon atoms and zero heteroatoms in the non–aromatic ring system;

aryl refers to a radical of a monocyclic or polycyclic $4n+2$ aromatic ring system having 6–14 ring carbon atoms and zero heteroatoms provided in the aromatic ring system; and

heteroaryl refers to a radical of a 5–10 membered monocyclic or bicyclic $4n+2$ aromatic ring system having ring carbon atoms and 1–4 ring heteroatoms provided in the aromatic ring system, wherein each heteroatom is independently selected from nitrogen, oxygen and sulfur;

wherein optional substituents on a carbon atom include halogen, $-CN$, $-OH$, $-OR^{aa}$, $-N(R^{bb})_2$, $-SH$, $-SR^{aa}$, $-C(=O)R^{aa}$, $-CO_2H$, $-CHO$, $-C(OR^{cc})_2$, $-CO_2R^{aa}$, $-OC(=O)R^{aa}$, $-C(=O)N(R^{bb})_2$, $-OC(=O)N(R^{bb})_2$, $-NR^{bb}C(=O)R^{aa}$, $-NR^{bb}CO_2R^{aa}$, $-NR^{bb}C(=O)N(R^{bb})_2$, $-C(=NR^{bb})R^{aa}$, $-SO_2R^{aa}$, C_{1-4} alkyl, C_{1-4} perhaloalkyl, C_{2-4} alkenyl, C_{2-4} alkynyl, C_{3-10} carbocyclyl, 5–8 membered heterocyclyl, C_{6-10} aryl, and 5–10 membered heteroaryl, wherein each alkyl, alkenyl, alkynyl, carbocyclyl, heterocyclyl, aryl, and heteroaryl is independently substituted with 0, 1, 2, 3, 4, or 5 R^{dd} groups; or two geminal hydrogens on a carbon atom are replaced with the group $=O$;

each instance of R^{aa} is, independently, selected from C_{1-4} alkyl, C_{1-4} perhaloalkyl, C_{2-4} alkenyl, C_{2-4} alkynyl, C_{3-6} carbocyclyl, 3–8 membered heterocyclyl, C_{6-10} aryl, and 5–10

membered heteroaryl, wherein each alkyl, alkenyl, alkynyl, carbocyclyl, heterocyclyl, aryl, and heteroaryl is independently substituted with 0, 1, 2, 3, 4, or 5 R^{dd} groups;

each instance of R^{bb} is, independently, selected from hydrogen, -C(=O)R^{aa}, -C(=O)N(R^{cc})₂, -CO₂R^{aa}, -SO₂R^{aa}, C₁₋₄ alkyl, C₁₋₄ perhaloalkyl, C₂₋₄ alkenyl, C₂₋₄ alkynyl, C₃₋₆ carbocyclyl, 5-8 membered heterocyclyl, C₆₋₁₀ aryl, and 5-10 membered heteroaryl, or two R^{bb} groups are joined to form a 3-14 membered heterocyclyl or 5-14 membered heteroaryl ring, wherein each alkyl, alkenyl, alkynyl, carbocyclyl, heterocyclyl, aryl, and heteroaryl is independently substituted with 0, 1, 2, 3, 4, or 5 R^{dd} groups;

each instance of R^{cc} is, independently, selected from hydrogen, C₁₋₄ alkyl, C₁₋₄ perhaloalkyl, C₂₋₄ alkenyl, C₂₋₄ alkynyl, C₃₋₆ carbocyclyl, 3-8 membered heterocyclyl, C₆₋₁₀ aryl, and 5-10 membered heteroaryl, or two R^{cc} groups are joined to form a 3-14 membered heterocyclyl or 5-14 membered heteroaryl ring, wherein each alkyl, alkenyl, alkynyl, carbocyclyl, heterocyclyl, aryl, and heteroaryl is independently substituted with 0, 1, 2, 3, 4, or 5 R^{dd} groups;

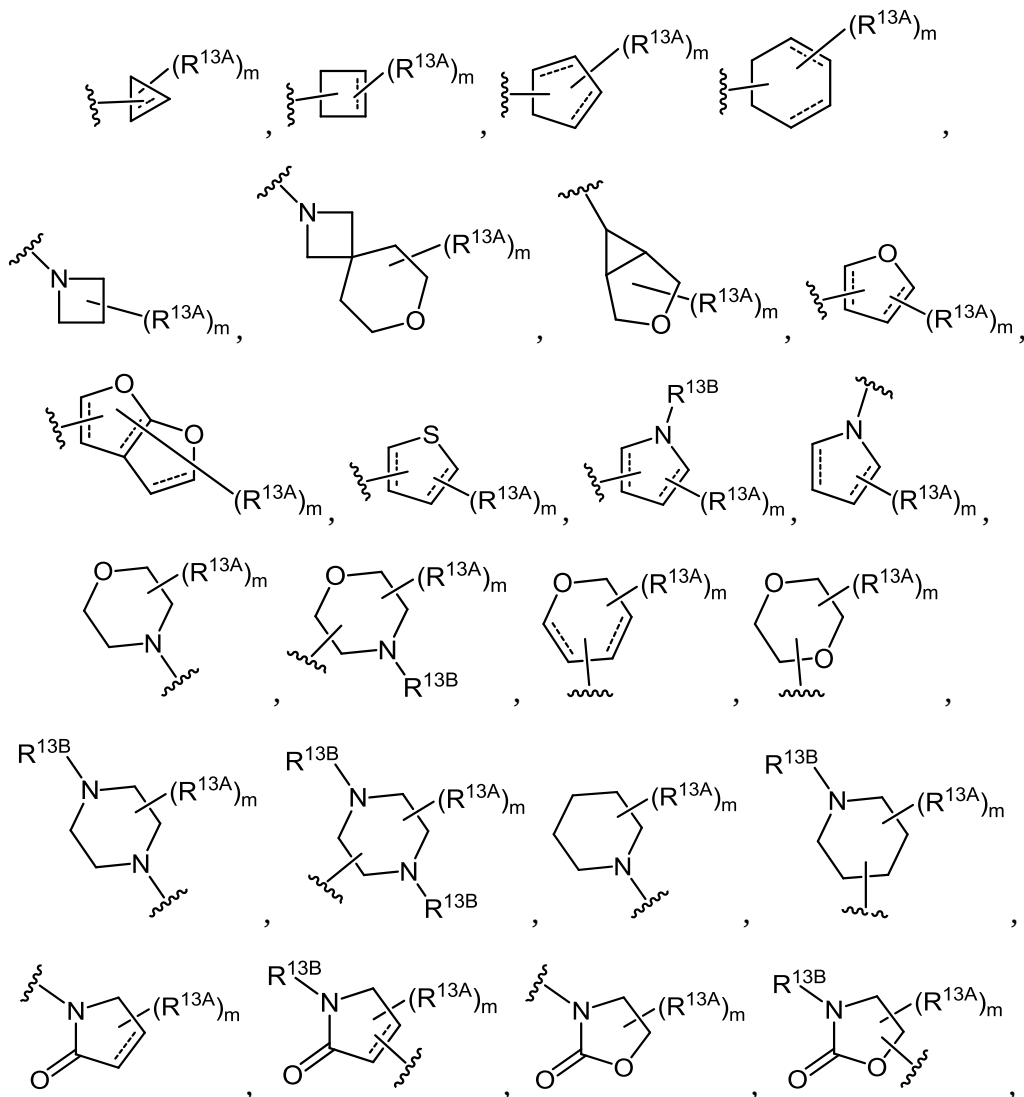
each instance of R^{dd} is, independently, selected from halogen, -CN, -OH, -OR^{ee}, -N(R^{ff})₂, -C(=O)R^{ee}, -CO₂H, -CO₂R^{ee}, -OC(=O)R^{ee}, -C(=O)N(R^{ff})₂, -OC(=O)N(R^{ff})₂, -NR^{ff}C(=O)R^{ee}, -NR^{ff}CO₂R^{ee}, -NR^{ff}C(=O)N(R^{ff})₂, -SO₂R^{ee}, C₁₋₄ alkyl, C₁₋₄ perhaloalkyl, C₂₋₄ alkenyl, or C₂₋₄ alkynyl; or two geminal R^{dd} substituents can be joined to form =O;

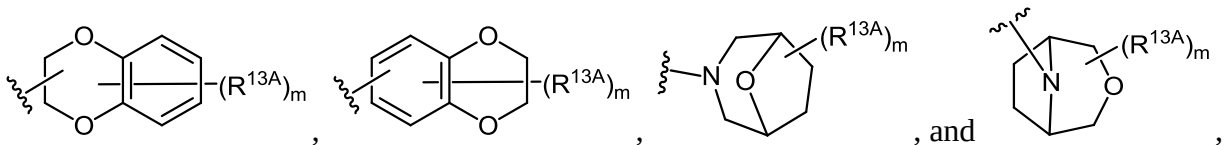
each instance of R^{ee} is, independently, selected from C₁₋₄ alkyl, C₁₋₄ perhaloalkyl, C₂₋₄ alkenyl, or C₂₋₄ alkynyl; and

each instance of R^{ff} is, independently, selected from hydrogen, C₁₋₄ alkyl, C₁₋₄ perhaloalkyl, C₂₋₄ alkenyl, or C₂₋₄ alkynyl;

wherein optional substituents when on a nitrogen atom include hydrogen, -CN, -C(=O)R^{aa}, -C(=O)N(R^{cc})₂, -CO₂R^{aa}, -C(=NR^{bb})R^{aa}, -C(=NR^{cc})OR^{aa}, -C(=NR^{cc})N(R^{cc})₂, C₁₋₄ alkyl, C₁₋₄ perhaloalkyl, C₂₋₄ alkenyl, C₂₋₄ alkynyl, C₃₋₁₀ carbocyclyl, 5-8 membered heterocyclyl, C₆₋₁₀ aryl, and 5-10 membered heteroaryl, or two R^{cc} groups attached to a nitrogen atom are joined to form a 5-8 membered heterocyclyl or 5-10 membered heteroaryl ring, wherein each alkyl, alkenyl, alkynyl, carbocyclyl, heterocyclyl, aryl, and heteroaryl is independently substituted with 0, 1, 2, 3, 4, or 5 R^{dd} groups, and wherein R^{aa}, R^{bb}, R^{cc} and R^{dd} are as defined above.

9. The compound of any one of claims 1-7, wherein at least one of R^{2a} , R^{2b} , R^{2c} , and R^{2d} is halogen.
10. The compound of any one of claims 1-9, wherein L^2 is a bond, $-N(R^L)-$, $-NR^LC(O)O-$, $-NR^LC(O)N(R^L)-$, $-NR^L-(CH_2)_x-C(O)O-$, $-NR^L-(CH_2)_x-O-$, $-NR^L-(CH_2)_x-$, $-(CH_2)_x-NR^L-$, $-NR^LC(O)O(CH_2)_x-$, $-NR^LC(O)NR^L(CH_2)_x-$, or $-NR^L(CH_2)_xNR^LC(O)-$, wherein x is 1, 2, 3, or 4.
11. The compound of any one of claims 1-10, wherein R^{13} is selected from the group consisting of:





wherein:

each instance of ----- independently represents a single or double bond;

m is 0, 1, 2, or 3;

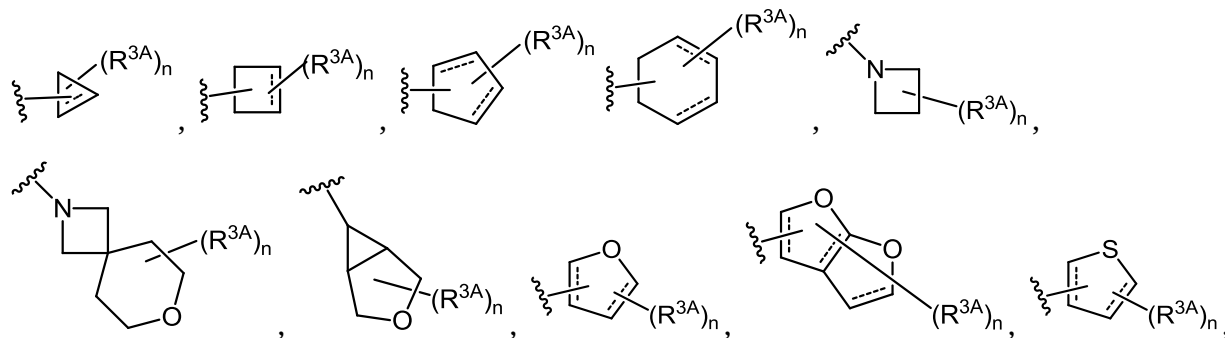
each instance of R^{13A} is independently halogen, $-\text{CN}$, $-\text{OH}$, $-\text{OR}^{aa}$, $-\text{N}(\text{R}^{bb})_2$, $-\text{SH}$, $-\text{SR}^{aa}$, $-\text{C}(=\text{O})\text{R}^{aa}$, $-\text{CO}_2\text{H}$, $-\text{CHO}$, $-\text{C}(\text{OR}^{cc})_2$, $-\text{CO}_2\text{R}^{aa}$, $-\text{OC}(=\text{O})\text{R}^{aa}$, $-\text{C}(=\text{O})\text{N}(\text{R}^{bb})_2$, $-\text{OC}(=\text{O})\text{N}(\text{R}^{bb})_2$, $-\text{NR}^{bb}\text{C}(=\text{O})\text{R}^{aa}$, $-\text{NR}^{bb}\text{CO}_2\text{R}^{aa}$, $-\text{NR}^{bb}\text{C}(=\text{O})\text{N}(\text{R}^{bb})_2$, $-\text{C}(=\text{NR}^{bb})\text{R}^{aa}$, $-\text{SO}_2\text{R}^{aa}$, or C_{1-4} alkyl, or two R^{13A} groups are joined to form a carbocyclic, heterocyclic, aryl, or heteroaryl ring, or R^{13A} and R^{13B} group are joined to form a carbocyclic, heterocyclic, aryl, or heteroaryl ring, wherein each alkyl, carbocyclyl, heterocyclyl, aryl, and heteroaryl is independently substituted with 0, 1, 2, 3, 4, or 5 R^{dd} groups; or two geminal hydrogens on a carbon atom are replaced with the group $=\text{O}$; and

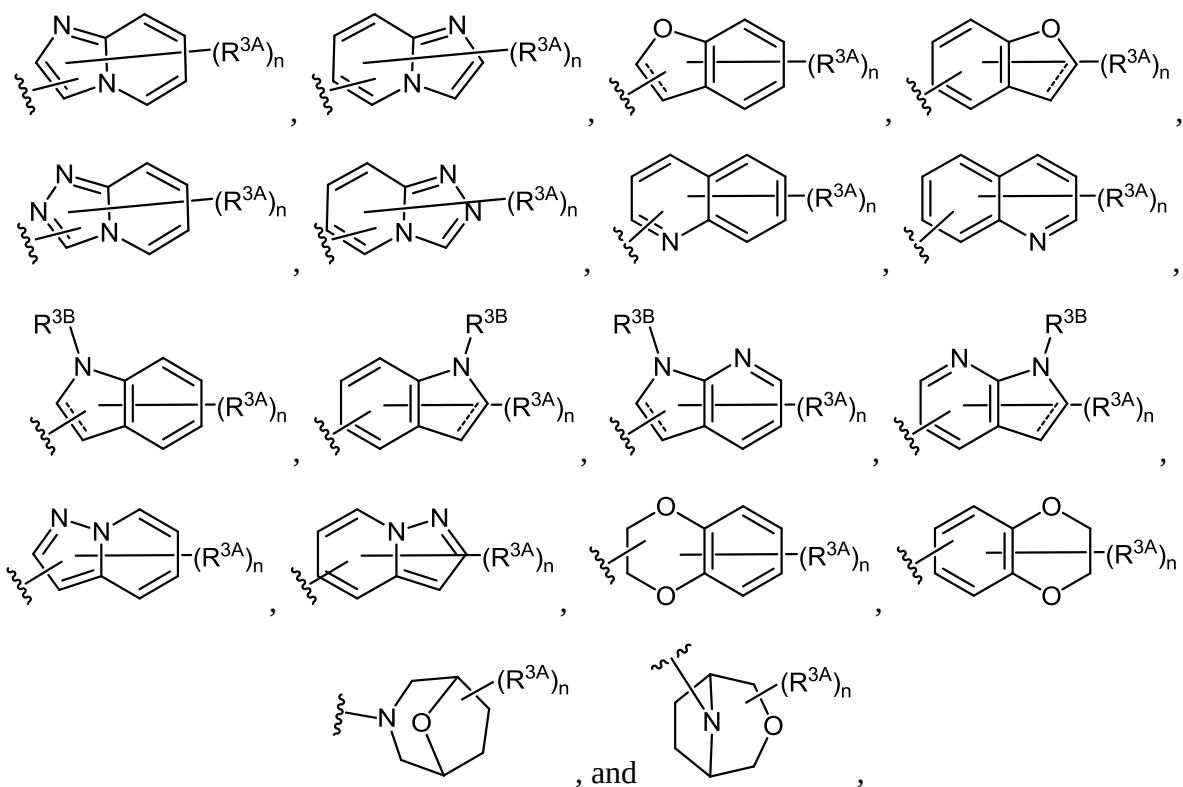
R^{3B} and R^{13B} are independently hydrogen, C_{1-6} alkyl, or C_{1-6} haloalkyl.

12. The compound of any one of claims 1-11, wherein Ring HET comprises a group $-\text{L}^1-\text{R}^3$ attached thereto.

13. The compound of claim 12, wherein L^1 is a bond, $-\text{N}(\text{R}^L)-$, $-\text{NR}^L\text{C}(\text{O})\text{O}-$, $-\text{NR}^L\text{C}(\text{O})\text{N}(\text{R}^L)-$, $-\text{NR}^L-(\text{CH}_2)_x-\text{C}(\text{O})\text{O}-$, $-\text{NR}^L-(\text{CH}_2)_x-\text{O}-$, $-\text{NR}^L-(\text{CH}_2)_x-$, $-(\text{CH}_2)_x-\text{NR}^L-$, $-\text{NR}^L\text{C}(\text{O})\text{O}(\text{CH}_2)_x-$, $-\text{NR}^L\text{C}(\text{O})\text{NR}^L(\text{CH}_2)_x-$, or $-\text{NR}^L(\text{CH}_2)_x\text{NR}^L\text{C}(\text{O})-$, wherein x is 1, 2, 3, or 4.

14. The compound of claim 12 or 13, wherein R^3 is selected from the group consisting of:





wherein:

each instance of ----- independently represents a single or double bond;

n is 0, 1, 2, or 3;

each instance of R^{3A} is independently halogen, $-\text{CN}$, $-\text{OH}$, $-\text{OR}^{aa}$, $-\text{N}(\text{R}^{bb})_2$, $-\text{SH}$, $-\text{SR}^{aa}$, $-\text{C}(=\text{O})\text{R}^{aa}$, $-\text{CO}_2\text{H}$, $-\text{CHO}$, $-\text{C}(\text{OR}^{cc})_2$, $-\text{CO}_2\text{R}^{aa}$, $-\text{OC}(=\text{O})\text{R}^{aa}$, $-\text{C}(=\text{O})\text{N}(\text{R}^{bb})_2$, $-\text{OC}(=\text{O})\text{N}(\text{R}^{bb})_2$, $-\text{NR}^{bb}\text{C}(=\text{O})\text{R}^{aa}$, $-\text{NR}^{bb}\text{CO}_2\text{R}^{aa}$, $-\text{NR}^{bb}\text{C}(=\text{O})\text{N}(\text{R}^{bb})_2$, $-\text{C}(=\text{NR}^{bb})\text{R}^{aa}$, $-\text{SO}_2\text{R}^{aa}$, or C_{1-4} alkyl, or two R^{3A} groups are joined to form a carbocyclic, heterocyclic, aryl, or heteroaryl ring, or R^{3A} and R^{3B} groups are joined to form a carbocyclic, heterocyclic, aryl, or heteroaryl ring, wherein each alkyl, carbocyclyl, heterocyclyl, aryl, and heteroaryl is independently substituted with 0, 1, 2, 3, 4, or 5 R^{dd} groups; or two geminal hydrogens on a carbon atom are replaced with the group $=\text{O}$; and

R^{3B} is hydrogen, C_{1-6} alkyl, or C_{1-6} haloalkyl.

15. The compound of any one of claims 1-3 or 7-14, wherein Ring HET is a 6-membered monocyclic heteroaryl ring system of the Formula: