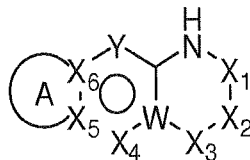


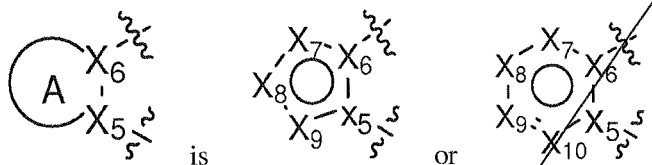
CLAIMS

WHAT IS CLAIMED IS:

1. A compound of Formula I:



or a pharmaceutically acceptable salt or prodrug thereof; wherein:



X₁ is C=O, C=S, SO, SO₂, or PO₂; Y is CR₅; W is N or C;

X₂ is NR₁ or CR₁R₁' and X₃ is a bond, CR₃R₃' or C=O; or X₂-X₃ is R₁₁C=CR₃ or R₁₁C=N or N=CR₃ or NR₁₂-CR₁₁=CR₃;

X₄ is N, CR₄, C=O; X₅ is N or C; X₆ is N or C;

X₇ is O, N, NR₇₂ or CR₇₁; X₈ is O, N, NR₈₂ or CR₈₁;

X₉ is O, N, NR₂₂ or CR₂₁; X₁₀ is O, N, NR₉₂ or CR₉₁;

R₁ is -C₁₋₁₀alkyl, -C₂₋₁₀alkenyl, -C₂₋₁₀alkynyl, -C₁₋₁₀heteroalkyl, -C₃₋₁₀aryl, -C₁₋₁₀hetaryl, -C₃₋₁₀cycloalkyl, -C₁₋₁₀heterocyclyl, -C₁₋₁₀alkyl-C₃₋₁₀aryl, -C₁₋₁₀alkyl-C₁₋₁₀hetaryl, -C₁₋₁₀alkyl-C₃₋₁₀cycloalkyl, -C₁₋₁₀alkyl-C₁₋₁₀heterocyclyl, -C₂₋₁₀alkenyl-C₃₋₁₀aryl, -C₂₋₁₀alkenyl-C₁₋₁₀hetaryl, -C₂₋₁₀alkenyl-C₃₋₁₀cycloalkyl, -C₂₋₁₀alkenyl-C₁₋₁₀heterocyclyl, -C₂₋₁₀alkynyl-C₃₋₁₀aryl, -C₂₋₁₀alkynyl-C₁₋₁₀hetaryl, -C₂₋₁₀alkynyl-C₃₋₁₀cycloalkyl, -C₂₋₁₀alkynyl-C₁₋₁₀heterocyclyl, -C₁₋₁₀alkoxy-C₃₋₁₀aryl, -C₁₋₁₀alkoxy-C₁₋₁₀hetaryl, -C₁₋₁₀alkoxy-C₃₋₁₀cycloalkyl, -C₁₋₁₀alkoxy-C₁₋₁₀heterocyclyl, -C₁₋₁₀heteroalkyl-C₃₋₁₀aryl, -C₁₋₁₀heteroalkyl-C₁₋₁₀hetaryl, -C₁₋₁₀heteroalkyl-C₃₋₁₀cycloalkyl, -C₁₋₁₀heteroalkyl-C₁₋₁₀heterocyclyl, -C₃₋₁₀aryl-C₁₋₁₀alkyl, -C₃₋₁₀aryl-C₂₋₁₀alkenyl, -C₃₋₁₀aryl-C₂₋₁₀alkynyl, -C₃₋₁₀aryl-C₃₋₁₀hetaryl, -C₃₋₁₀aryl-C₃₋₁₀cycloalkyl, -C₃₋₁₀aryl-C₁₋₁₀heterocyclyl, -C₁₋₁₀hetaryl-C₁₋₁₀alkyl, -C₁₋₁₀hetaryl-C₂₋₁₀alkenyl, -C₁₋₁₀hetaryl-C₂₋₁₀alkynyl, -C₃₋₁₀hetaryl-C₃₋₁₀aryl, -C₁₋₁₀hetaryl-C₃₋₁₀cycloalkyl, -C₁₋₁₀hetaryl-C₁₋₁₀heterocyclyl, -C₃₋₁₀cycloalkyl-C₁₋₁₀alkyl, -C₃₋₁₀cycloalkyl-C₂₋₁₀alkenyl, -C₃₋₁₀cycloalkyl-C₂₋₁₀alkynyl, -C₃₋₁₀cycloalkyl-C₃₋₁₀aryl, -C₃₋₁₀cycloalkyl-C₁₋₁₀hetaryl, -C₃₋₁₀cycloalkyl-C₁₋₁₀heterocyclyl, -C₁₋₁₀heterocyclyl-C₁₋₁₀alkyl, -C₁₋₁₀heterocyclyl-C₂₋₁₀alkenyl, -C₁₋₁₀heterocyclyl-C₂₋₁₀alkynyl, -C₁₋₁₀heterocyclyl-C₃₋₁₀aryl, -C₁₋₁₀heterocyclyl-C₁₋₁₀hetaryl, or -C₁₋₁₀heterocyclyl-C₃₋₁₀cycloalkyl, each of which is unsubstituted or substituted by one or more independent R₁₀ or R₁₁ substituents;

R₁' is hydrogen, -C₁₋₁₀alkyl, -C₂₋₁₀alkenyl, -C₂₋₁₀alkynyl, -C₁₋₁₀heteroalkyl, -C₃₋₁₀aryl, -C₁₋₁₀hetaryl, -C₃₋₁₀cycloalkyl, -C₁₋₁₀heterocyclyl, -C₁₋₁₀alkyl-C₃₋₁₀aryl, -C₁₋₁₀alkyl-C₁₋₁₀hetaryl, -C₁₋₁₀alkyl-C₃₋₁₀cycloalkyl, -C₁₋₁₀alkyl-C₁₋₁₀heterocyclyl, -C₂₋₁₀alkenyl-C₃₋₁₀aryl, -C₂₋₁₀alkenyl-C₁₋₁₀hetaryl, -C₂₋₁₀alkenyl-C₃₋₁₀cycloalkyl, -C₂₋₁₀alkenyl-C₁₋₁₀heterocyclyl, -C₂₋₁₀alkynyl-C₃₋₁₀aryl, -C₂₋₁₀alkynyl-C₁₋₁₀hetaryl, -C₂₋₁₀alkynyl-C₃₋₁₀cycloalkyl, -C₂₋₁₀alkynyl-C₁₋₁₀heterocyclyl, -C₁₋₁₀alkoxy-C₃₋₁₀aryl, -C₁₋₁₀alkoxy-C₁₋₁₀hetaryl, -C₁₋₁₀alkoxy-C₃₋₁₀cycloalkyl, -C₁₋₁₀alkoxy-C₁₋₁₀heterocyclyl, -C₁₋₁₀heteroalkyl-C₃₋₁₀aryl, -C₁₋₁₀heteroalkyl-C₁₋₁₀hetaryl, -C₁₋₁₀heteroalkyl-C₃₋₁₀cycloalkyl, -C₁₋₁₀heteroalkyl-C₁₋₁₀heterocyclyl, -C₃₋₁₀aryl-C₁₋₁₀alkyl, -C₃₋₁₀aryl-C₂₋₁₀alkenyl, -C₃₋₁₀aryl-C₂₋₁₀alkynyl, -C₃₋₁₀aryl-C₃₋₁₀hetaryl, -C₃₋₁₀aryl-C₃₋₁₀cycloalkyl, -C₃₋₁₀aryl-C₁₋₁₀heterocyclyl, -C₁₋₁₀hetaryl-C₁₋₁₀alkyl, -C₁₋₁₀hetaryl-C₂₋₁₀alkenyl, -C₁₋₁₀hetaryl-C₂₋₁₀alkynyl, -C₃₋₁₀hetaryl-C₃₋₁₀aryl, -C₁₋₁₀hetaryl-C₃₋₁₀cycloalkyl, -C₁₋₁₀hetaryl-C₁₋₁₀heterocyclyl, -C₃₋₁₀cycloalkyl-C₁₋₁₀alkyl, -C₃₋₁₀cycloalkyl-C₂₋₁₀alkenyl, -C₃₋₁₀cycloalkyl-C₂₋₁₀alkynyl, -C₃₋₁₀cycloalkyl-C₃₋₁₀aryl, -C₃₋₁₀cycloalkyl-C₁₋₁₀hetaryl, -C₃₋₁₀cycloalkyl-C₁₋₁₀heterocyclyl, -C₁₋₁₀heterocyclyl-C₁₋₁₀alkyl, -C₁₋₁₀heterocyclyl-C₂₋₁₀alkenyl, -C₁₋₁₀heterocyclyl-C₂₋₁₀alkynyl, -C₁₋₁₀heterocyclyl-C₃₋₁₀aryl, -C₁₋₁₀heterocyclyl-C₁₋₁₀hetaryl, or -C₁₋₁₀heterocyclyl-C₃₋₁₀cycloalkyl, each of which is unsubstituted or substituted by one or more independent R₁₀ or R₁₁ substituents;

$_{10}$ hetaryl, $-C_{2-10}$ alkynyl- C_{3-10} cycloalkyl, $-C_{2-10}$ alkynyl- C_{1-10} heterocyclyl, $-C_{1-10}$ alkoxy- C_{3-10} aryl, $-C_{1-10}$ alkoxy- C_{1-10} hetaryl, $-C_{1-10}$ alkoxy- C_{3-10} cycloalkyl, $-C_{1-10}$ alkoxy- C_{1-10} heterocyclyl, $-C_{1-10}$ heteroalkyl- C_{3-10} aryl, $-C_{1-10}$ heteroalkyl- C_{1-10} hetaryl, $-C_{1-10}$ heteroalkyl- C_{3-10} cycloalkyl, $-C_{1-10}$ heteroalkyl- C_{1-10} heterocyclyl, $-C_{3-10}$ aryl- C_{1-10} alkyl, $-C_{3-10}$ aryl- C_{2-10} alkenyl, $-C_{3-10}$ aryl- C_{2-10} alkynyl, $-C_{3-10}$ aryl- C_{3-10} hetaryl, $-C_{3-10}$ aryl- C_{3-10} cycloalkyl, $-C_{3-10}$ aryl- C_{1-10} heterocyclyl, $-C_{1-10}$ hetaryl- C_{1-10} alkyl, $-C_{1-10}$ hetaryl- C_{2-10} alkenyl, $-C_{1-10}$ hetaryl- C_{2-10} alkynyl, $-C_{3-10}$ hetaryl- C_{3-10} aryl, $-C_{1-10}$ hetaryl- C_{3-10} cycloalkyl, $-C_{1-10}$ hetaryl- C_{1-10} heterocyclyl, $-C_{3-10}$ cycloalkyl- C_{1-10} alkyl, $-C_{3-10}$ cycloalkyl- C_{2-10} alkenyl, $-C_{3-10}$ cycloalkyl- C_{2-10} alkynyl, $-C_{3-10}$ cycloalkyl- C_{3-10} aryl, $-C_{3-10}$ cycloalkyl- C_{1-10} hetaryl, $-C_{3-10}$ cycloalkyl- C_{1-10} heterocyclyl, $-C_{1-10}$ heterocyclyl- C_{1-10} alkyl, $-C_{1-10}$ heterocyclyl- C_{2-10} alkenyl, $-C_{1-10}$ heterocyclyl- C_{2-10} alkynyl, $-C_{1-10}$ heterocyclyl- C_{3-10} aryl, $-C_{1-10}$ heterocyclyl- C_{1-10} hetaryl, or $-C_{1-10}$ heterocyclyl- C_{3-10} cycloalkyl, each of which is unsubstituted or substituted by one or more independent R_{10} or R_{11} substituents;

R_{21} is hydrogen, halogen, $-OH$, $-CF_3$, $-OCF_3$, $-OR^{31}$, $-NR^{31}R^{32}$, $-C(O)R^{31}$, $-CO_2R^{31}$, $-C(=O)NR^{31}$, $-NO_2$, $-CN$, $-S(O)_{0-2}R^{31}$, $-SO_2NR^{31}R^{32}$, $-NR^{31}C(=O)R^{32}$, $-NR^{31}C(=O)OR^{32}$, $-NR^{31}C(=O)NR^{32}R^{33}$, $-NR^{31}S(O)_{0-2}R^{32}$, $-C(=S)OR^{31}$, $-C(=O)SR^{31}$, $-NR^{31}C(=NR^{32})NR^{32}R^{33}$, $-NR^{31}C(=NR^{32})OR^{33}$, $-NR^{31}C(=NR^{32})SR^{33}$, $-OC(=O)OR^{33}$, $-OC(=O)NR^{31}R^{32}$, $-OC(=O)SR^{31}$, $-SC(=O)SR^{31}$, $-P(O)OR^{31}OR^{32}$, $-SC(=O)NR^{31}R^{32}$, $-L-C_{1-10}$ alkyl, $-L-C_{2-10}$ alkenyl, $-L-C_{2-10}$ alkynyl, $-L-C_{1-10}$ heteroalkyl, $-L-C_{3-10}$ aryl, $-L-C_{1-10}$ hetaryl, $-L-C_{3-10}$ cycloalkyl, $-L-C_{1-10}$ heterocyclyl, $-L-C_{1-10}$ alkyl- C_{3-10} aryl, $-L-C_{1-10}$ alkyl- C_{1-10} hetaryl, $-L-C_{1-10}$ alkyl- C_{3-10} cycloalkyl, $-L-C_{1-10}$ alkyl- C_{1-10} heterocyclyl, $-L-C_{2-10}$ alkenyl- C_{3-10} aryl, $-L-C_{2-10}$ alkenyl- C_{1-10} hetaryl, $-L-C_{2-10}$ alkenyl- C_{3-10} cycloalkyl, $-L-C_{2-10}$ alkenyl- C_{1-10} heterocyclyl, $-L-C_{2-10}$ alkynyl- C_{3-10} aryl, $-L-C_{2-10}$ alkynyl- C_{1-10} hetaryl, $-L-C_{2-10}$ alkynyl- C_{3-10} cycloalkyl, $-L-C_{2-10}$ alkynyl- C_{1-10} heterocyclyl, $-L-C_{1-10}$ alkoxy- C_{3-10} aryl, $-L-C_{1-10}$ alkoxy- C_{1-10} hetaryl, $-L-C_{1-10}$ alkoxy- C_{3-10} cycloalkyl, $-L-C_{1-10}$ alkoxy- C_{1-10} heterocyclyl, $-L-C_{1-10}$ heteroalkyl- C_{3-10} aryl, $-L-C_{1-10}$ heteroalkyl- C_{1-10} hetaryl, $-L-C_{1-10}$ heteroalkyl- C_{3-10} cycloalkyl, $-L-C_{1-10}$ heteroalkyl- C_{1-10} heterocyclyl, $-L-C_{3-10}$ aryl- C_{1-10} alkyl, $-L-C_{3-10}$ aryl- C_{2-10} alkenyl, $-L-C_{3-10}$ aryl- C_{2-10} alkynyl, $-L-C_{3-10}$ aryl- C_{1-10} hetaryl, $-L-C_{3-10}$ aryl- C_{3-10} cycloalkyl, $-L-C_{3-10}$ aryl- C_{1-10} heterocyclyl, $-L-C_{1-10}$ hetaryl- C_{1-10} alkyl, $-L-C_{1-10}$ hetaryl- C_{2-10} alkenyl, $-L-C_{1-10}$ hetaryl- C_{2-10} alkynyl, $-L-C_{1-10}$ hetaryl- C_{3-10} aryl, $-L-C_{1-10}$ hetaryl- C_{3-10} cycloalkyl, $-L-C_{1-10}$ hetaryl- C_{1-10} heterocyclyl, $-L-C_{3-10}$ cycloalkyl- C_{1-10} alkyl, $-L-C_{3-10}$ cycloalkyl- C_{2-10} alkenyl, $-L-C_{3-10}$ cycloalkyl- C_{2-10} alkynyl, $-L-C_{3-10}$ cycloalkyl- C_{3-10} aryl, $-L-C_{3-10}$ cycloalkyl- C_{1-10} hetaryl, $-L-C_{3-10}$ cycloalkyl- C_{1-10} heterocyclyl, $-L-C_{1-10}$ heterocyclyl- C_{1-10} alkyl, $-L-C_{1-10}$ heterocyclyl- C_{2-10} alkenyl, $-L-C_{1-10}$ heterocyclyl- C_{2-10} alkynyl, $-L-C_{1-10}$ heterocyclyl- C_{3-10} aryl, $-L-C_{1-10}$ heterocyclyl- C_{1-10} hetaryl, or $-L-C_{1-10}$ heterocyclyl- C_{3-10} cycloalkyl, each of which is unsubstituted or substituted by one or more independent R_{12} substituents;

R_{22} is hydrogen, $-OH$, $-CF_3$, $-C(O)R^{31}$, $-CO_2R^{31}$, $-C(=O)NR^{31}$, $-S(O)_{0-2}R^{31}$, $-C(=S)OR^{31}$, $-C(=O)SR^{31}$, $-L-C_{1-10}$ alkyl, $-L-C_{2-10}$ alkenyl, $-L-C_{2-10}$ alkynyl, $-L-C_{1-10}$ heteroalkyl, $-L-C_{3-10}$ aryl, $-L-C_{1-10}$ hetaryl, $-L-C_{3-10}$ cycloalkyl, $-L-C_{1-10}$ heterocyclyl, $-L-C_{1-10}$ alkyl- C_{3-10} aryl, $-L-C_{1-10}$ alkyl- C_{1-10} hetaryl, $-L-C_{1-10}$ alkyl- C_{3-10} cycloalkyl, $-L-C_{1-10}$ alkyl- C_{1-10} heterocyclyl, $-L-C_{2-10}$ alkenyl- C_{3-10} aryl, $-L-C_{2-10}$ alkenyl- C_{1-10} hetaryl, $-L-C_{2-10}$ alkenyl- C_{3-10} cycloalkyl, $-L-C_{2-10}$ alkenyl- C_{1-10} heterocyclyl, $-L-C_{2-10}$ alkynyl- C_{3-10} aryl, $-L-C_{2-10}$ alkynyl- C_{1-10} hetaryl, $-L-C_{2-10}$ alkynyl- C_{3-10} cycloalkyl, $-L-C_{2-10}$ alkynyl- C_{1-10} heterocyclyl, $-L-C_{1-10}$ alkoxy- C_{3-10} aryl, $-L-C_{1-10}$ alkoxy- C_{1-10} hetaryl, $-L-C_{1-10}$ alkoxy- C_{3-10} cycloalkyl, $-L-C_{1-10}$ alkoxy- C_{1-10} heterocyclyl, $-L-C_{1-10}$ heteroalkyl- C_{3-10} aryl, $-L-C_{1-10}$ heteroalkyl- C_{1-10} hetaryl, $-L-C_{1-10}$ heteroalkyl- C_{3-10} cycloalkyl, $-L-C_{1-10}$ heteroalkyl- C_{1-10} heterocyclyl, $-L-C_{3-10}$ aryl- C_{1-10} alkyl, $-L-C_{3-10}$ aryl- C_{2-10} alkenyl, $-L-C_{3-10}$ aryl- C_{2-10} alkynyl, $-L-C_{3-10}$ aryl- C_{1-10} hetaryl, $-L-C_{3-10}$ aryl- C_{3-10} cycloalkyl, $-L-C_{3-10}$ aryl- C_{1-10} heterocyclyl, $-L-C_{1-10}$ hetaryl- C_{1-10} alkyl, $-L-C_{1-10}$ hetaryl- C_{2-10} alkenyl, $-L-C_{1-10}$ hetaryl- C_{2-10} alkynyl, $-L-C_{1-10}$ hetaryl- C_{3-10} aryl, $-L-C_{1-10}$ hetaryl- C_{3-10} cycloalkyl, $-L-C_{1-10}$ hetaryl- C_{1-10} heterocyclyl, $-L-C_{3-10}$ cycloalkyl- C_{1-10} alkyl, $-L-C_{3-10}$ cycloalkyl- C_{2-10} alkenyl, $-L-C_{3-10}$ cycloalkyl- C_{2-10} alkynyl, $-L-C_{3-10}$ cycloalkyl- C_{3-10} aryl, $-L-C_{3-10}$ cycloalkyl- C_{1-10} hetaryl, $-L-C_{3-10}$ cycloalkyl- C_{1-10} heterocyclyl, $-L-C_{1-10}$ heterocyclyl- C_{1-10} alkyl, $-L-C_{1-10}$ heterocyclyl- C_{2-10} alkenyl, $-L-C_{1-10}$ heterocyclyl- C_{2-10} alkynyl, $-L-C_{1-10}$ heterocyclyl- C_{3-10} aryl, $-L-C_{1-10}$ heterocyclyl- C_{1-10} hetaryl, or $-L-C_{1-10}$ heterocyclyl- C_{3-10} cycloalkyl, each of which is unsubstituted or substituted by one or more independent R_{12} substituents;

$L-C_{1-10}alkoxy-C_{3-10}aryl$, $-L-C_{1-10}alkoxy-C_{1-10}hetaryl$, $-L-C_{1-10}alkoxy-C_{3-10}cycloalkyl$, $-L-C_{1-10}alkoxy-C_{1-10}heterocyclyl$, $-L-C_{1-10}heteroalkyl-C_{3-10}aryl$, $-L-C_{1-10}heteroalkyl-C_{1-10}hetaryl$, $-L-C_{1-10}heteroalkyl-C_{3-10}cycloalkyl$, $-L-C_{1-10}heteroalkyl-C_{1-10}heterocyclyl$, $-L-C_{3-10}aryl-C_{1-10}alkyl$, $-L-C_{3-10}aryl-C_{2-10}alkenyl$, $-L-C_{3-10}aryl-C_{2-10}alkynyl$, $-L-C_{3-10}aryl-C_{1-10}hetaryl$, $-L-C_{3-10}aryl-C_{3-10}cycloalkyl$, $-L-C_{3-10}aryl-C_{1-10}heterocyclyl$, $-L-C_{1-10}hetaryl-C_{1-10}alkyl$, $-L-C_{1-10}hetaryl-C_{2-10}alkenyl$, $-L-C_{1-10}hetaryl-C_{2-10}alkynyl$, $-L-C_{1-10}hetaryl-C_{3-10}aryl$, $-L-C_{1-10}hetaryl-C_{3-10}cycloalkyl$, $-L-C_{1-10}hetaryl-C_{1-10}heterocyclyl$, $-L-C_{3-10}cycloalkyl-C_{1-10}alkyl$, $-L-C_{3-10}cycloalkyl-C_{2-10}alkenyl$, $-L-C_{3-10}cycloalkyl-C_{2-10}alkynyl$, $-L-C_{3-10}cycloalkyl-C_{3-10}aryl$, $-L-C_{3-10}cycloalkyl-C_{1-10}hetaryl$, $-L-C_{3-10}cycloalkyl-C_{1-10}heterocyclyl$, $-L-C_{1-10}heterocyclyl-C_{1-10}alkyl$, $-L-C_{1-10}heterocyclyl-C_{2-10}alkenyl$, $-L-C_{1-10}heterocyclyl-C_{2-10}alkynyl$, $-L-C_{1-10}heterocyclyl-C_{3-10}aryl$, $-L-C_{1-10}heterocyclyl-C_{1-10}hetaryl$, or $-L-C_{1-10}heterocyclyl-C_{3-10}cycloalkyl$, each of which is unsubstituted or substituted by one or more independent R_{12} substituents;

L is a bond, $-O-$, $-N(R^{31})-$, $-S(O)_{0-2}-$, $-C(=O)-$, $-C(=O)O-$, $-OC(=O)-$, $-C(=O)N(R^{31})-$, $-N(R^{31})C(=O)-$, $-NR^{31}C(=O)O-$, $-NR^{31}C(=O)NR^{32}-$, $-NR^{31}S(O)_{0-2}-$, $-S(O)_{0-2}N(R^{31})-$, $-C(=S)O-$, $-C(=O)S-$, $-NR^{31}C(=NR^{32})NR^{32}-$, $-NR^{31}C(=NR^{32})O-$, $-NR^{31}C(=NR^{32})S-$, $-OC(=O)O-$, $-OC(=O)NR^{31}-$, $-OC(=O)S-$, $-SC(=O)S-$, $-P(O)OR^{31}O-$, $-SC(=O)NR^{31}-$;

each of R_3 , R_3' and R_4 is independently hydrogen, halogen, $-OH$, $-CF_3$, $-OCF_3$, $-OR^{31}$, $-NR^{31}R^{32}$, $-C(O)R^{31}$, $-CO_2R^{31}$, $-C(=O)NR^{31}$, $-NO_2$, $-CN$, $-S(O)_{0-2}R^{31}$, $-SO_2NR^{31}R^{32}$, $-NR^{31}C(=O)R^{32}$, $-NR^{31}C(=O)OR^{32}$, $-NR^{31}C(=O)NR^{32}R^{33}$, $-NR^{31}S(O)_{0-2}R^{32}$, $-C(=S)OR^{31}$, $-C(=O)SR^{31}$, $-NR^{31}C(=NR^{32})NR^{32}R^{33}$, $-NR^{31}C(=NR^{32})OR^{33}$, $-NR^{31}C(=NR^{32})SR^{33}$, $-OC(=O)OR^{33}$, $-OC(=O)NR^{31}R^{32}$, $-OC(=O)SR^{31}$, $-SC(=O)SR^{31}$, $-P(O)OR^{31}OR^{32}$, $-SC(=O)NR^{31}R^{32}$, $-C_{1-10}alkyl$, $-C_{2-10}alkenyl$, $-C_{2-10}alkynyl$, $-C_{1-10}heteroalkyl$, $-C_{3-10}aryl$, $-C_{1-10}hetaryl$, $-C_{3-10}cycloalkyl$, $-C_{1-10}heterocyclyl$, $-C_{1-10}alkyl-C_{3-10}aryl$, $-C_{1-10}alkyl-C_{1-10}hetaryl$, $-C_{1-10}alkyl-C_{3-10}cycloalkyl$, $-C_{1-10}alkyl-C_{1-10}heterocyclyl$, $-C_{2-10}alkenyl-C_{3-10}aryl$, $-C_{2-10}alkenyl-C_{1-10}hetaryl$, $-C_{2-10}alkenyl-C_{3-10}cycloalkyl$, $-C_{2-10}alkenyl-C_{1-10}heterocyclyl$, $-C_{2-10}alkynyl-C_{3-10}aryl$, $-C_{2-10}alkynyl-C_{1-10}hetaryl$, $-C_{2-10}alkynyl-C_{3-10}cycloalkyl$, $-C_{2-10}alkynyl-C_{1-10}heterocyclyl$, $-C_{1-10}alkoxy-C_{3-10}aryl$, $-C_{1-10}alkoxy-C_{1-10}hetaryl$, $-C_{1-10}alkoxy-C_{3-10}cycloalkyl$, $-C_{1-10}alkoxy-C_{1-10}heterocyclyl$, $-C_{1-10}heteroalkyl-C_{3-10}aryl$, $-C_{1-10}heteroalkyl-C_{1-10}hetaryl$, $-C_{1-10}heteroalkyl-C_{3-10}cycloalkyl$, $-C_{1-10}heteroalkyl-C_{1-10}heterocyclyl$, $-C_{3-10}aryl-C_{1-10}alkyl$, $-C_{3-10}aryl-C_{2-10}alkenyl$, $-C_{3-10}aryl-C_{2-10}alkynyl$, $-C_{3-10}aryl-C_{3-10}hetaryl$, $-C_{3-10}aryl-C_{3-10}cycloalkyl$, $-C_{3-10}aryl-C_{1-10}heterocyclyl$, $-C_{1-10}hetaryl-C_{1-10}alkyl$, $-C_{1-10}hetaryl-C_{2-10}alkenyl$, $-C_{1-10}hetaryl-C_{2-10}alkynyl$, $-C_{3-10}hetaryl-C_{3-10}aryl$, $-C_{1-10}hetaryl-C_{3-10}cycloalkyl$, $-C_{1-10}hetaryl-C_{1-10}heterocyclyl$, $-C_{3-10}cycloalkyl-C_{1-10}alkyl$, $-C_{3-10}cycloalkyl-C_{2-10}alkenyl$, $-C_{3-10}cycloalkyl-C_{2-10}alkynyl$, $-C_{3-10}cycloalkyl-C_{3-10}aryl$, $-C_{3-10}cycloalkyl-C_{1-10}hetaryl$, $-C_{3-10}cycloalkyl-C_{1-10}heterocyclyl$, $-C_{1-10}heterocyclyl-C_{1-10}alkyl$, $-C_{1-10}heterocyclyl-C_{2-10}alkenyl$, $-C_{1-10}heterocyclyl-C_{2-10}alkynyl$, $-C_{1-10}heterocyclyl-C_{3-10}aryl$, $-C_{1-10}heterocyclyl-C_{1-10}hetaryl$, or $-C_{1-10}heterocyclyl-C_{3-10}cycloalkyl$, each of which is unsubstituted or substituted by one or more independent R_{13} substituents; or R_3' is $-OR^6$, $-NR^6R^{34}$, $-S(O)_{0-2}R^6$, $-C(=O)R^6$, $-C(=O)OR^6$, $-OC(=O)R^6$, $-C(=O)N(R^{34})R^6$, or $-N(R^{34})C(=O)R^6$, wherein R^6 together with R^{34} can optionally form a heterocyclic ring;

each of R_5 , R_{71} , R_{81} and R_{91} is independently hydrogen, halogen, $-C_{1-10}$ alkyl, $-C_{2-10}$ alkenyl, $-C_{2-10}$ alkynyl, $-C_{1-10}$ heteroalkyl, $-C_{3-10}$ aryl, $-C_{1-10}$ hetaryl, $-C_{3-10}$ cycloalkyl, $-C_{1-10}$ heterocyclyl, $-OH$, $-CF_3$, $-OCF_3$, $-OR^{31}$, $-NR^{31}R^{32}$, $-C(O)R^{31}$, $-CO_2R^{31}$, $-C(=O)NR^{31}$, $-NO_2$, $-CN$, $-S(O)_{0-2}R^{31}$, $-SO_2NR^{31}R^{32}$, $-NR^{31}C(=O)R^{32}$, $-NR^{31}C(=O)OR^{32}$, $-NR^{31}C(=O)NR^{32}R^{33}$, $-NR^{31}S(O)_{0-2}R^{32}$, $-C(=S)OR^{31}$, $-C(=O)SR^{31}$, $-NR^{31}C(=NR^{32})NR^{32}R^{33}$, $-NR^{31}C(=NR^{32})OR^{33}$, $-NR^{31}C(=NR^{32})SR^{33}$, $-OC(=O)OR^{33}$, $-OC(=O)NR^{31}R^{32}$, $-OC(=O)SR^{31}$, $-SC(=O)SR^{31}$, $-P(O)OR^{31}OR^{32}$, or $-SC(=O)NR^{31}NR^{32}$;

R_6 is hydrogen, $-C_{1-10}$ alkyl, $-C_{2-10}$ alkenyl, $-C_{2-10}$ alkynyl, $-C_{1-10}$ heteroalkyl, $-C_{3-10}$ aryl, $-C_{1-10}$ hetaryl, $-C_{3-10}$ cycloalkyl, $-C_{1-10}$ heterocyclyl, $-C_{1-10}$ alkyl- C_{3-10} aryl, $-C_{1-10}$ alkyl- C_{1-10} hetaryl, $-C_{1-10}$ alkyl- C_{3-10} cycloalkyl, $-C_{1-10}$ alkyl- C_{1-10} heterocyclyl, $-C_{2-10}$ alkenyl- C_{3-10} aryl, $-C_{2-10}$ alkenyl- C_{1-10} hetaryl, $-C_{2-10}$ alkenyl- C_{3-10} cycloalkyl, $-C_{2-10}$ alkenyl- C_{1-10} heterocyclyl, $-C_{2-10}$ alkynyl- C_{3-10} aryl, $-C_{2-10}$ alkynyl- C_{1-10} hetaryl, $-C_{2-10}$ alkynyl- C_{3-10} cycloalkyl, $-C_{2-10}$ alkynyl- C_{1-10} heterocyclyl, $-C_{1-10}$ alkoxy- C_{3-10} aryl, $-C_{1-10}$ alkoxy- C_{1-10} hetaryl, $-C_{1-10}$ alkoxy- C_{3-10} cycloalkyl, $-C_{1-10}$ alkoxy- C_{1-10} heterocyclyl, $-C_{1-10}$ heteroalkyl- C_{3-10} aryl, $-C_{1-10}$ heteroalkyl- C_{1-10} hetaryl, $-C_{1-10}$ heteroalkyl- C_{3-10} cycloalkyl, $-C_{1-10}$ heteroalkyl- C_{1-10} heterocyclyl, $-C_{3-10}$ aryl- C_{1-10} alkyl, $-C_{3-10}$ aryl- C_{2-10} alkenyl, $-C_{3-10}$ aryl- C_{2-10} alkynyl, $-C_{3-10}$ aryl- C_{3-10} cycloalkyl, $-C_{3-10}$ aryl- C_{1-10} heterocyclyl, $-C_{1-10}$ hetaryl- C_{1-10} alkyl, $-C_{1-10}$ hetaryl- C_{2-10} alkenyl, $-C_{1-10}$ hetaryl- C_{2-10} alkynyl, $-C_{3-10}$ hetaryl- C_{3-10} aryl, $-C_{1-10}$ hetaryl- C_{3-10} cycloalkyl, $-C_{1-10}$ hetaryl- C_{1-10} heterocyclyl, $-C_{3-10}$ cycloalkyl- C_{1-10} alkyl, $-C_{3-10}$ cycloalkyl- C_{2-10} alkenyl, $-C_{3-10}$ cycloalkyl- C_{2-10} alkynyl, $-C_{3-10}$ cycloalkyl- C_{3-10} aryl, $-C_{3-10}$ cycloalkyl- C_{1-10} hetaryl, $-C_{3-10}$ cycloalkyl- C_{1-10} heterocyclyl, $-C_{1-10}$ heterocyclyl- C_{1-10} alkyl, $-C_{1-10}$ heterocyclyl- C_{2-10} alkenyl, $-C_{1-10}$ heterocyclyl- C_{2-10} alkynyl, $-C_{1-10}$ heterocyclyl- C_{3-10} aryl, $-C_{1-10}$ heterocyclyl- C_{1-10} hetaryl, or $-C_{1-10}$ heterocyclyl- C_{3-10} cycloalkyl, each of which is unsubstituted or substituted by one or more independent R_{14} or R_{15} substituents;

each of R_{72} , R_{82} and R_{92} is independently hydrogen, $-C_{1-10}$ alkyl, $-C_{2-10}$ alkenyl, $-C_{2-10}$ alkynyl, $-C_{1-10}$ heteroalkyl, $-C_{3-10}$ aryl, $-C_{1-10}$ hetaryl, $-C_{3-10}$ cycloalkyl, $-C_{1-10}$ heterocyclyl, $-OH$, $-CF_3$, $-C(O)R^{31}$, $-CO_2R^{31}$, $-C(=O)NR^{31}$, $-S(O)_{0-2}R^{31}$, $-C(=S)OR^{31}$, $-C(=O)SR^{31}$;

each of R_{10} and R_{14} is $-C_{1-10}$ alkyl, $-C_{2-10}$ alkenyl, $-C_{2-10}$ alkynyl, $-C_{1-10}$ heteroalkyl, $-C_{3-10}$ aryl, $-C_{1-10}$ hetaryl, $-C_{3-10}$ cycloalkyl, $-C_{1-10}$ heterocyclyl, optionally substituted by one or more independent R_{11} substituents;

each of R_{11} , R_{12} , R_{13} and R_{15} is independently hydrogen, halogen, $-C_{1-10}$ alkyl, $-C_{2-10}$ alkenyl, $-C_{2-10}$ alkynyl, $-C_{1-10}$ heteroalkyl, $-C_{3-10}$ aryl, $-C_{1-10}$ hetaryl, $-C_{3-10}$ cycloalkyl, $-C_{1-10}$ heterocyclyl, $-OH$, $-CF_3$, $-OCF_3$, $-OR^{31}$, $-NR^{31}R^{32}$, $-C(O)R^{31}$, $-CO_2R^{31}$, $-C(=O)NR^{31}$, $-NO_2$, $-CN$, $-S(O)_{0-2}R^{31}$, $-SO_2NR^{31}R^{32}$, $-NR^{31}C(=O)R^{32}$, $-NR^{31}C(=O)OR^{32}$, $-NR^{31}C(=O)NR^{32}R^{33}$, $-NR^{31}S(O)_{0-2}R^{32}$, $-C(=S)OR^{31}$, $-C(=O)SR^{31}$, $-NR^{31}C(=NR^{32})NR^{32}R^{33}$, $-NR^{31}C(=NR^{32})OR^{33}$, $-NR^{31}C(=NR^{32})SR^{33}$, $-OC(=O)OR^{33}$, $-OC(=O)NR^{31}R^{32}$, $-OC(=O)SR^{31}$, $-SC(=O)SR^{31}$, $-P(O)OR^{31}OR^{32}$, or $-SC(=O)NR^{31}NR^{32}$;

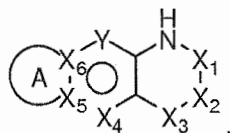
each of R^{31} , R^{32} , R^{33} and R^{34} is independently hydrogen, halogen, $-C_{1-10}$ alkyl, $-C_{2-10}$ alkenyl, $-C_{2-10}$ alkynyl, $-C_{1-10}$ heteroalkyl, $-C_{3-10}$ aryl, $-C_{1-10}$ hetaryl, $-C_{3-10}$ cycloalkyl, $-C_{1-10}$ heterocyclyl, or wherein R^{31} together with R^{32} form a heterocyclic ring;

wherein ring A comprises one or more heteroatoms selected from N, O, or S; and

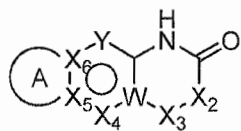
wherein if X_7 is O or X_2-X_3 is $R_1C=CR_3$, ring A comprises at least two heteroatoms selected from N, O, or S; and

wherein if X_3 is O or N, or X_2-X_3 is $R_1C=N$, at least one of X_7 or X_9 is not N.

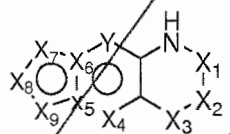
2. The compound, pharmaceutically acceptable salt, or prodrug of claim 1, wherein the compound is of Formula I-A:



3. The compound, pharmaceutically acceptable salt, or prodrug of claim 1, wherein the compound is of Formula I-B:



4. The compound, pharmaceutically acceptable salt, or prodrug of claim 1, wherein the compound is of Formula II:



5. The compound, pharmaceutically acceptable salt, or prodrug of claim 4, wherein X_1 is $C=O$.

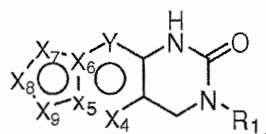
6. The compound, pharmaceutically acceptable salt, or prodrug of claim 4, wherein X_2 is NR_1 .

7. The compound, pharmaceutically acceptable salt, or prodrug of claim 4, wherein X_5 is N and X_6 is C.

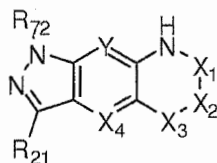
8. The compound, pharmaceutically acceptable salt, or prodrug of claim 4, wherein X_5 is C and X_6 is C.

9. The compound, pharmaceutically acceptable salt, or prodrug of claim 4, wherein X_9 is CR_{21} .

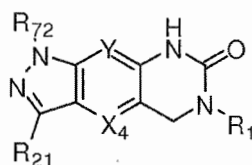
10. The compound, pharmaceutically acceptable salt, or prodrug of claim 4, wherein the compound is of Formula II-A:



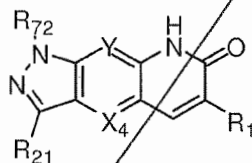
11. The compound, pharmaceutically acceptable salt, or prodrug of claim 4, wherein the compound is of Formula II-B:



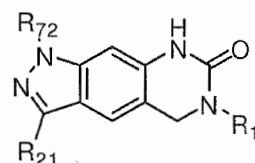
12. The compound, pharmaceutically acceptable salt, or prodrug of claim 4, wherein the compound is of Formula II-C:



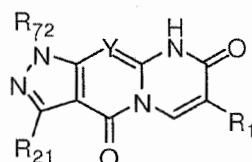
13. The compound, pharmaceutically acceptable salt, or prodrug of claim 4, wherein the compound is of Formula II-D:



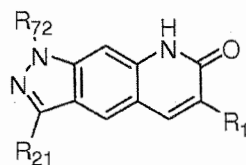
14. The compound, pharmaceutically acceptable salt, or prodrug of claim 4, wherein the compound is of Formula II-E:



15. The compound, pharmaceutically acceptable salt, or prodrug of claim 4, wherein the compound is of Formula II-F:



16. The compound, pharmaceutically acceptable salt, or prodrug of claim 13, wherein the compound is of Formula II-G:



17. The compound, pharmaceutically acceptable salt, or prodrug of any one of claims 14-16, wherein R_{21} is selected from the group consisting of $-L-C_{1-10}$ heteroalkyl, $-L-C_{3-10}$ aryl, $-L-C_{1-10}$ hetaryl, $-L-C_{3-10}$ cycloalkyl, and $-L-C_{1-10}$ heterocyclyl, each of which is unsubstituted or substituted by one or more independent R_{12} substituents; and L is bond.

18. The compound, pharmaceutically acceptable salt, or prodrug of claim 17, wherein R_{21} is $-L-C_{1-10}$ hetaryl unsubstituted or substituted by one or more independent R_{12} substituents; and L is bond.

19. The compound, pharmaceutically acceptable salt, or prodrug of claim 18, wherein the C_{1-10} hetaryl of R_{21} comprises one or more nitrogen atoms.

20. The compound, pharmaceutically acceptable salt, or prodrug of claim 19, wherein the C_{1-10} hetaryl of R_{21} is selected from the group consisting of pyrazolyl, pyridinyl, pyrazinyl, pyrimidinyl, and pyridazinyl.

21. The compound, pharmaceutically acceptable salt, or prodrug of claim 20, wherein the C_{1-10} hetaryl of R_{21} is unsubstituted.

22. The compound, pharmaceutically acceptable salt, or prodrug of claim 20, wherein the C_{1-10} hetaryl or R_{21} is substituted with one, two, or three independent R_{12} substituents.

23. The compound, pharmaceutically acceptable salt, or prodrug of any one of claims 17-20 or 22, wherein each R_{12} substituent is independently selected from the group consisting of $-C_{1-10}$ alkyl, $-C_{2-10}$ alkenyl, $-C_{2-10}$ alkynyl, $-C_{1-10}$ heteroalkyl, $-C_{3-10}$ aryl, $-C_{1-10}$ hetaryl, $-C_{3-10}$ cycloalkyl, $-C_{1-10}$ heterocyclyl, $-OH$, $-CF_3$, $-OCF_3$, $-OR^{31}$, wherein each R_{31} is independently hydrogen or $-C_{1-10}$ alkyl.

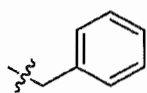
24. The compound, pharmaceutically acceptable salt, or prodrug of claim 23, wherein each R_{12} substituent is independently selected from the group consisting $-Me$, $-Et$, $-i-Pr$, $-n-Pr$, OH , $-OMe$, $-OEt$, $-OPr$.

25. The compound, pharmaceutically acceptable salt, or prodrug of any one of claims 14-24, wherein R_1 is $-C_{1-10}$ alkyl, $-C_{1-10}$ heterocyclyl, $-C_{1-10}$ alkyl- C_{3-10} heterocyclyl, $-C_{1-10}$ alkyl- C_{3-10} aryl, $-C_{1-10}$ alkyl- $-C_{1-10}$ hetaryl, $-C_{1-10}$ heterocyclyl- C_{1-10} alkyl, or $-C_{1-10}$ heterocyclyl- C_{3-10} aryl, unsubstituted or substituted by one or more independent R_{10} or R_{11} substituents.

26. The compound, pharmaceutically acceptable salt, or prodrug of claim 25, wherein R_1 is $-C_{1-10}$ alkyl- C_{3-10} aryl, $-C_{1-10}$ alkyl- $-C_{1-10}$ hetaryl, $-C_{1-10}$ heterocyclyl- C_{1-10} alkyl, or $-C_{1-10}$ heterocyclyl- C_{3-10} aryl, unsubstituted or substituted by one or more independent R_{10} or R_{11} substituents.

27. The compound, pharmaceutically acceptable salt, or prodrug of claim 26, wherein R_1 is $-C_{1-10}$ alkyl- C_{3-10} aryl or $-C_{1-10}$ heterocyclyl- C_{3-10} aryl, unsubstituted or substituted by one or more independent R_{10} or R_{11} substituents.

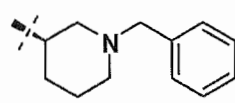
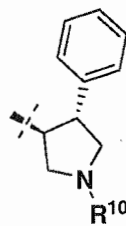
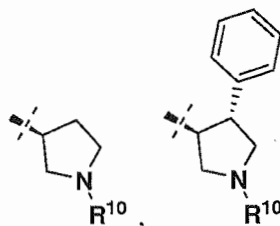
28. The compound, pharmaceutically acceptable salt, or prodrug of claim 26, wherein R_1 is



, unsubstituted or substituted by one or more independent R_{10} or R_{11} substituents.

29. The compound, pharmaceutically acceptable salt, or prodrug of claim 25, wherein R_1 is $-C_{1-10}$ heterocyclyl, $-C_{1-10}$ heterocyclyl- C_{1-10} alkyl, or $-C_{1-10}$ heterocyclyl- C_{3-10} aryl, unsubstituted or substituted by one or more independent R_{10} or R_{11} substituents.

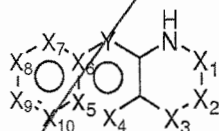
30. The compound, pharmaceutically acceptable salt, or prodrug of claim 29, wherein R_1 is



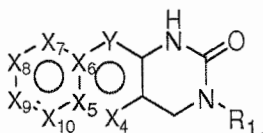
, unsubstituted or substituted by one or more independent R_{10} or R_{11} substituents.

31. The compound, pharmaceutically acceptable salt, or prodrug of any preceding claim, wherein R_{72} is H.

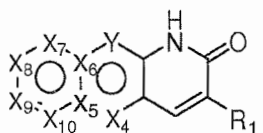
32. The compound, pharmaceutically acceptable salt, or prodrug of claim 1, wherein the compound is of Formula III:



33. The compound, pharmaceutically acceptable salt, or prodrug of claim 32, wherein X_1 is $C=O$.
34. The compound, pharmaceutically acceptable salt, or prodrug of claim 32, wherein X_2 is NR_1 .
35. The compound, pharmaceutically acceptable salt, or prodrug of claim 32, wherein X_5 is N and X_6 is C.
36. The compound, pharmaceutically acceptable salt, or prodrug of claim 32, wherein X_5 is C and X_6 is C.
37. The compound, pharmaceutically acceptable salt, or prodrug of claim 32, wherein X_8 is N and X_{10} is N.
38. The compound, pharmaceutically acceptable salt, or prodrug of claim 32, wherein X_9 is CR_{21} .
39. The compound, pharmaceutically acceptable salt, or prodrug of claim 32, wherein the compound is of Formula III-A:



40. The compound, pharmaceutically acceptable salt, or prodrug of claim 32, wherein the compound is of Formula III-B:



41. The compound, pharmaceutically acceptable salt, or prodrug of any of the preceding claims, wherein R₅ is hydrogen.

42. The compound, pharmaceutically acceptable salt, or prodrug of any of the preceding claims, wherein X₄ is CR₄.

43. The compound, pharmaceutically acceptable salt, or prodrug of claim 42, wherein R₄ is hydrogen.

44. The compound, pharmaceutically acceptable salt, or prodrug of any of the preceding claims, wherein X₄ is N.

45. The compound, pharmaceutically acceptable salt, or prodrug of any of the preceding claims, wherein X₉ is CR₂₁ or NR₂₂, wherein R₂₁ or R₂₂ is halogen, -CN, -L-C₃₋₁₀aryl, -L-C₁₋₁₀hetaryl, -L-C₃₋₁₀cycloalkyl, or -L-C₁₋₁₀heterocyclyl, unsubstituted or substituted by one or more independent R₁₂ substituents.

46. The compound, pharmaceutically acceptable salt, or prodrug of claim 45, wherein X₉ is CR₂₁ and R₂₁ is halogen or -CN.

47. The compound, pharmaceutically acceptable salt, or prodrug of claim 45, wherein X₉ is CR₂₁ and R₂₁ is -L-C₃₋₁₀aryl, -L-C₁₋₁₀hetaryl, -L-C₃₋₁₀cycloalkyl, or -L-C₃₋₁₀heterocyclyl, unsubstituted or substituted by one or more independent R₁₂ substituents.

48. The compound, pharmaceutically acceptable salt, or prodrug of claim 47, wherein X₉ is CR₂₁ and R₂₁ is -L-C₁₋₁₀hetaryl or -L-C₃₋₁₀heterocyclyl, unsubstituted or substituted by one or more independent R₁₂ substituents.

49. A method of inhibiting activity of a protein kinase present in a cell, comprising contacting said cell with an effective amount of a compound, pharmaceutically acceptable salt, or prodrug of any of the preceding claims.

50. The method of claim 49, wherein the protein kinase is ERK.

51. The method of claim 49, wherein the compound, pharmaceutically acceptable salt, or prodrug inhibits ERK at an IC₅₀ value of less than about 1000 nM.

52. The method of claim 49, wherein the compound, pharmaceutically acceptable salt, or prodrug inhibits ERK at an IC₅₀ value of less than about 100 nM.

53. The method of claim 49, wherein the compound, pharmaceutically acceptable salt, or prodrug inhibits ERK at an IC₅₀ value of less than about 10 nM.

54. The method of claim 49, wherein the contacting step takes place *in vitro*.

55. The method of claim 49, wherein the contacting step takes place *in vivo*.

56. A method of ameliorating a disorder comprising administering to a subject in need thereof an effective amount of a compound, pharmaceutically acceptable salt, or prodrug of a compound of any of the preceding claims, wherein the disorder is selected from the group consisting of cancer, bone disorder, inflammatory disease, immune disease, nervous system disease, metabolic disease, respiratory disease, and cardiac disease.

57. The method of claim 56, wherein the disorder is cancer selected from the group consisting of breast cancer, pancreatic cancer, non-small cell lung cancer (NSCLC), thyroid cancer, seminomas, melanoma, bladder cancer, liver cancer, kidney cancer, myelodysplastic syndrome (MDS), acute myelogenous leukemia (AML), and colorectal cancer.

58. The method of claim 57, wherein the cancer is melanoma or colorectal cancer

59. The method of claim 56, wherein the disorder is mediated by ERK 1 and/or ERK2.

60. The method of claim 56, further comprising administering another anti-cancer agent.

61. A pharmaceutical composition comprising the compound, pharmaceutically acceptable salt, or prodrug of any of the preceding claims and a pharmaceutically acceptable excipient.

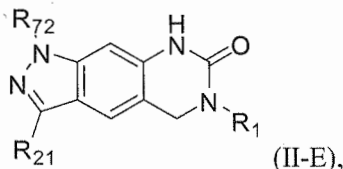
62. The pharmaceutical composition of claim 61, wherein the compound, pharmaceutically acceptable salt, or prodrug is present in a therapeutically effective amount.

63. The pharmaceutical composition of claim 61, wherein said composition is formulated in an oral dosage.

64. The pharmaceutical composition of claim 61, wherein said composition is formulated as a tablet or a capsule.

CLAIMS

1. A compound of Formula II-E:



or a pharmaceutically acceptable salt or prodrug thereof; wherein:

R₁ is -C₁₋₁₀heterocyclyl, -C₁₋₁₀heterocyclyl-C₁₋₁₀alkyl, or -C₁₋₁₀heterocyclyl-C₃₋₁₀aryl, each of which is unsubstituted or substituted by one or more independent R₁₀ or R₁₁ substituents;

R₂₁ is hydrogen, halogen, -OH, -CF₃, -OCF₃, -OR³¹, -NR³¹R³², -C(O)R³¹, -CO₂R³¹, -C(=O)NR³¹, -NO₂, -CN, -S(O)₀₋₂R³¹, -SO₂NR³¹R³², -NR³¹C(=O)R³², -NR³¹C(=O)OR³², -NR³¹C(=O)NR³²R³³, -NR³¹S(O)₀₋₂R³², -C(=S)OR³¹, -C(=O)SR³¹, -NR³¹C(=NR³²)NR³²R³³, -NR³¹C(=NR³²)OR³³, -NR³¹C(=NR³²)SR³³, -OC(=O)OR³³, -OC(=O)NR³¹R³², -OC(=O)SR³¹, -SC(=O)SR³¹, -P(O)OR³¹OR³², -SC(=O)NR³¹R³², -L-C₁₋₁₀alkyl, -L-C₂₋₁₀alkenyl, -L-C₂₋₁₀alkynyl, -L-C₁₋₁₀heteroalkyl, -L-C₃₋₁₀aryl, -L-C₁₋₁₀hetaryl, -L-C₃₋₁₀cycloalkyl, -L-C₁₋₁₀heterocyclyl, -L-C₁₋₁₀alkyl-C₃₋₁₀aryl, -L-C₁₋₁₀alkyl-C₁₋₁₀hetaryl, -L-C₁₋₁₀alkyl-C₃₋₁₀cycloalkyl, -L-C₁₋₁₀alkyl-C₁₋₁₀heterocyclyl, -L-C₂₋₁₀alkenyl-C₃₋₁₀aryl, -L-C₂₋₁₀alkenyl-C₁₋₁₀hetaryl, -L-C₂₋₁₀alkenyl-C₃₋₁₀cycloalkyl, -L-C₂₋₁₀alkenyl-C₁₋₁₀heterocyclyl, -L-C₂₋₁₀alkynyl-C₃₋₁₀aryl, -L-C₂₋₁₀alkynyl-C₁₋₁₀hetaryl, -L-C₂₋₁₀alkynyl-C₃₋₁₀cycloalkyl, -L-C₂₋₁₀alkynyl-C₁₋₁₀heterocyclyl, -L-C₁₋₁₀alkoxy-C₃₋₁₀aryl, -L-C₁₋₁₀alkoxy-C₁₋₁₀hetaryl, -L-C₁₋₁₀alkoxy-C₃₋₁₀cycloalkyl, -L-C₁₋₁₀alkoxy-C₁₋₁₀heterocyclyl, -L-C₁₋₁₀heteroalkyl-C₃₋₁₀aryl, -L-C₁₋₁₀heteroalkyl-C₁₋₁₀hetaryl, -L-C₁₋₁₀heteroalkyl-C₃₋₁₀cycloalkyl, -L-C₁₋₁₀heteroalkyl-C₁₋₁₀heterocyclyl, -L-C₃₋₁₀aryl-C₁₋₁₀alkyl, -L-C₃₋₁₀aryl-C₂₋₁₀alkenyl, -L-C₃₋₁₀aryl-C₂₋₁₀alkynyl, -L-C₃₋₁₀aryl-C₁₋₁₀hetaryl, -L-C₃₋₁₀aryl-C₃₋₁₀cycloalkyl, -L-C₃₋₁₀aryl-C₁₋₁₀heterocyclyl, -L-C₁₋₁₀hetaryl-C₁₋₁₀alkyl, -L-C₁₋₁₀hetaryl-C₂₋₁₀alkenyl, -L-C₁₋₁₀hetaryl-C₂₋₁₀alkynyl, -L-C₁₋₁₀hetaryl-C₃₋₁₀aryl, -L-C₁₋₁₀hetaryl-C₃₋₁₀cycloalkyl, -L-C₁₋₁₀hetaryl-C₁₋₁₀heterocyclyl, -L-C₃₋₁₀cycloalkyl-C₁₋₁₀alkyl, -L-C₃₋₁₀cycloalkyl-C₂₋₁₀alkenyl, -L-C₃₋₁₀cycloalkyl-C₂₋₁₀alkynyl, -L-C₃₋₁₀cycloalkyl-C₃₋₁₀aryl, -L-C₃₋₁₀cycloalkyl-C₁₋₁₀hetaryl, -L-C₃₋₁₀cycloalkyl-C₁₋₁₀heterocyclyl, -L-C₁₋₁₀heterocyclyl-C₁₋₁₀alkyl, -L-C₁₋₁₀heterocyclyl-C₂₋₁₀alkenyl, -L-C₁₋₁₀heterocyclyl-C₂₋₁₀alkynyl, -L-C₁₋₁₀heterocyclyl-C₃₋₁₀aryl, -L-C₁₋₁₀heterocyclyl-C₁₋₁₀hetaryl, or -L-C₁₋₁₀heterocyclyl-C₃₋₁₀cycloalkyl, each of which is unsubstituted or substituted by one or more independent R₁₂ substituents;

L is a bond, -O-, -N(R³¹)-, -S(O)₀₋₂-, -C(=O)-, -C(=O)O-, -OC(=O)-, -C(=O)N(R³¹)-, -N(R³¹)C(=O)-, -NR³¹C(=O)O-, -NR³¹C(=O)NR³²-, -NR³¹S(O)₀₋₂-, -S(O)₀₋₂N(R³¹)-, -C(=S)O-, -C(=O)S-, -NR³¹C(=NR³²)NR³²-, -NR³¹C(=NR³²)O-, -NR³¹C(=NR³²)S-, -OC(=O)O-, -OC(=O)NR³¹-, -OC(=O)S-, -SC(=O)S-, -P(O)OR³¹O-, or -SC(=O)NR³¹-;

R₇₂ is hydrogen, -C₁₋₁₀ alkyl, -C₂₋₁₀ alkenyl, -C₂₋₁₀ alkynyl, -C₁₋₁₀ heteroalkyl, -C₃₋₁₀ aryl, -C₁₋₁₀ hetaryl, -C₃₋₁₀ cycloalkyl, -C₁₋₁₀ heterocyclyl, -OH, -CF₃, -C(O)R³¹, -CO₂R³¹, -C(=O)NR³¹, -S(O)₀₋₂R³¹, -C(=S)OR³¹, or -C(=O)SR³¹;

R₁₀ is -C₁₋₁₀ alkyl, -C₂₋₁₀ alkenyl, -C₂₋₁₀ alkynyl, -C₁₋₁₀ heteroalkyl, -C₃₋₁₀ aryl, -C₁₋₁₀ hetaryl, -C₃₋₁₀ cycloalkyl, or -C₁₋₁₀ heterocyclyl, each of which is unsubstituted or substituted by one or more independent R₁₁ substituents;

R₁₁ and R₁₂ are independently hydrogen, halogen, -C₁₋₁₀ alkyl, -C₂₋₁₀ alkenyl, -C₂₋₁₀ alkynyl, -C₁₋₁₀ heteroalkyl, -C₃₋₁₀ aryl, -C₁₋₁₀ hetaryl, -C₃₋₁₀ cycloalkyl, -C₁₋₁₀ heterocyclyl, -OH, -CF₃, -OCF₃, -OR³¹, -NR³¹R³², -C(O)R³¹, -CO₂R³¹, -C(=O)NR³¹, -NO₂, -CN, -S(O)₀₋₂R³¹, -SO₂NR³¹R³², -NR³¹C(=O)R³², -NR³¹C(=O)OR³², -NR³¹C(=O)NR³²R³³, -NR³¹S(O)₀₋₂R³², -C(=S)OR³¹, -C(=O)SR³¹, -NR³¹C(=NR³²)NR³²R³³, -NR³¹C(=NR³²)OR³³, -NR³¹C(=NR³²)SR³³, -OC(=O)OR³³, -OC(=O)NR³¹R³², -OC(=O)SR³¹, -SC(=O)SR³¹, -P(O)OR³¹OR³², or -SC(=O)NR³¹R³²;

each of R³¹, R³², and R³³ is independently hydrogen, halogen, -C₁₋₁₀ alkyl, -C₂₋₁₀ alkenyl, -C₂₋₁₀ alkynyl, -C₁₋₁₀ heteroalkyl, -C₃₋₁₀ aryl, -C₁₋₁₀ hetaryl, -C₃₋₁₀ cycloalkyl, or -C₁₋₁₀ heterocyclyl, or R³¹ together with R³² form a heterocyclic ring.

2. The compound of claim 1, wherein R₂₁ is selected from the group consisting of -L-C₁₋₁₀ heteroalkyl, -L-C₃₋₁₀ aryl, -L-C₁₋₁₀ hetaryl, -L-C₃₋₁₀ cycloalkyl, and -L-C₁₋₁₀ heterocyclyl, each of which is unsubstituted or substituted by one or more independent R₁₂ substituents; and wherein L is a bond.

3. The compound of claim 2, wherein R₂₁ is -L-C₁₋₁₀ hetaryl unsubstituted or substituted by one or more independent R₁₂ substituents; and wherein L is a bond.

4. The compound of claim 3, wherein the C₁₋₁₀ hetaryl of R₂₁ comprises one or more nitrogen atoms.

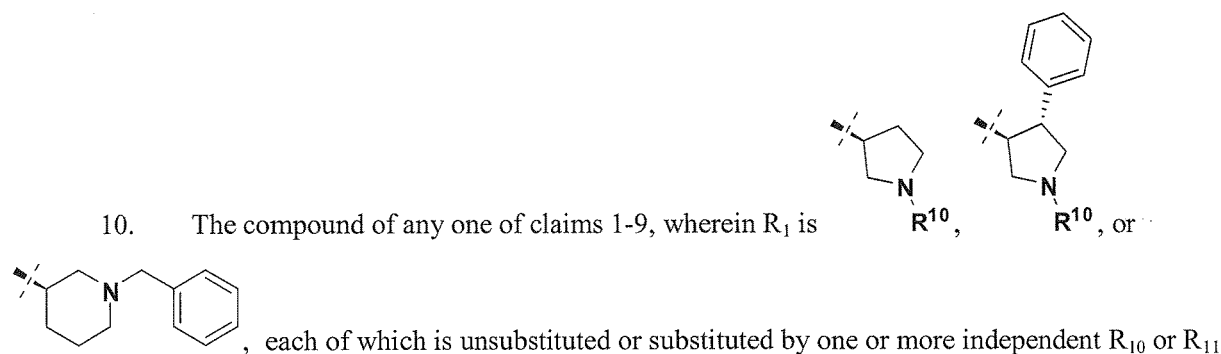
5. The compound of claim 4, wherein the C₁₋₁₀ hetaryl of R₂₁ is selected from the group consisting of pyrazolyl, pyridinyl, pyrazinyl, pyrimidinyl, and pyridazinyl.

6. The compound of claim 5, wherein the C₁₋₁₀ hetaryl of R₂₁ is unsubstituted.

7. The compound of claim 5, wherein the C₁₋₁₀ hetaryl or R₂₁ is substituted with one, two, or three independent R₁₂ substituents.

8. The compound of any one of claims 2-5 or 7, wherein each R₁₂ substituent is independently selected from the group consisting of -C₁₋₁₀ alkyl, -C₂₋₁₀ alkenyl, -C₂₋₁₀ alkynyl, -C₁₋₁₀ heteroalkyl, -C₃₋₁₀ aryl, -C₁₋₁₀ hetaryl, -C₃₋₁₀ cycloalkyl, -C₁₋₁₀ heterocyclyl, -OH, -CF₃, -OCF₃, and -OR³¹; wherein each R³¹ is independently hydrogen or -C₁₋₁₀ alkyl.

9. The compound of claim 8, wherein each R₁₂ substituent is independently selected from the group consisting -Me, -Et, -*i*-Pr, -*n*-Pr, -OH, -OMe, -OEt, and -OPr.



11. The compound of any one of claims 1-10, wherein R_{72} is H.
12. A method of inhibiting activity of a protein kinase present in a cell, comprising contacting said cell with an effective amount of the compound of any one of claims 1-11.
13. The method of claim 12, wherein the protein kinase is ERK.
14. Use of the compound of any one of claims 1-11 for the manufacture of a medicament for treatment of cancer, optionally wherein the cancer is selected from the group consisting of breast cancer, pancreatic cancer, non-small cell lung cancer (NSCLC), thyroid cancer, seminomas, melanoma, bladder cancer, liver cancer, kidney cancer, myelodysplastic syndrome (MDS), acute myelogenous leukemia (AML), and colorectal cancer.
15. A pharmaceutical composition comprising the compound of any one of claims 1-11 and a pharmaceutically acceptable excipient, optionally wherein the composition is formulated in an oral dosage.

