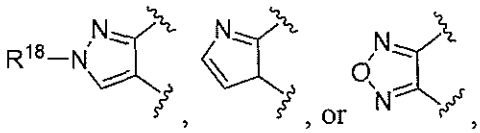
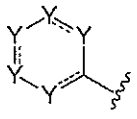
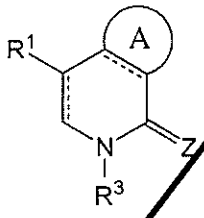
substituted 5 or 6 membered heteroaryl formed by two adjacent R^4 together with the carbon atoms to which they are attached is selected from , one of the bonds represented by a solid and dashed line in  is a single bond.

124. The compound of Claim 80, wherein the compound is selected from the group consisting of **Compounds 163-216, 241-243, 245, 246, 248-252, 254, 255, 258-261, 263, 415-430, 552-561, 566** and **629** of Table 1, or pharmaceutically acceptable salts thereof.

125. A compound having the structure of formula (III):



(III)

or a pharmaceutically acceptable salt thereof, wherein

R^1 is selected from the group consisting of bromo, chloro, fluoro, -CN, $-C(O)R^8$, $-SO_2R^{16}$, C_{1-6} alkyl optionally substituted with one or more R^4, C_{2-6} alkenyl optionally substituted with one or more R^4, C_{2-6} alkynyl optionally substituted with one or more R^4, C_{6-10} aryl optionally substituted with one or more R^4, 5 to 6 membered heteroaryl optionally substituted with one or more R^4, C_{3-10} carbocyclyl optionally substituted with one or more R^4, and 3-10 membered heterocyclyl optionally substituted with one or more R^4;

R^3 is selected from the group consisting of hydrogen, phenyl, $-(CH_2)_n$-(5-10 membered heteroaryl), and 3-10 membered heterocyclyl, each optionally substituted with one or more R^9;

ring A is selected from the group consisting of phenyl, 5-6 membered heteroaryl, C_{3-7} carbocyclyl, and 3-7 membered heterocyclyl, each optionally substituted with one or more R^4;

each R^4 is independently selected from the group consisting of halogen, -CN, -OH, $-C(O)R^8$, $-SO_2R^{16}$, optionally substituted C_{1-6} alkyl, optionally substituted C_{2-6} alkenyl, optionally substituted C_{2-6} alkynyl, optionally substituted C_{1-6} alkoxy, optionally substituted C_{6-10} aryl optionally substituted with one or more R^{11}, C_{7-14}

aralkyl optionally substituted with one or more R^{11}, 5-10 membered heteroaryl optionally substituted with one or more R^{11}, or independently two geminal R^4 together are oxo;

each R^9 is independently selected from the group consisting of hydroxy, halogen, optionally substituted C_{1-6} alkyl, optionally substituted C_{2-6} alkenyl, optionally substituted C_{2-6} alkynyl, optionally substituted C_{1-6} alkylthio, optionally substituted C_{2-8} alkoxyalkyl, optionally substituted C_{3-10} carbocyclyl, optionally substituted C_{6-10} aryl, $-OR^5$, $-NR^{14}R^{15}$, $-C(O)R^8$, $-SO_2R^{16}$, -CN, and $-NO_2$;

R^{14} is selected from the group consisting of hydrogen, optionally substituted C_{1-6} alkyl, optionally substituted C_{6-10} aryl, and $-C(O)R^8$;

R^{15} is selected from the group consisting of hydrogen, optionally substituted C_{1-6} alkyl, optionally substituted C_{6-10} aryl, and $-C(O)R^8$;

each R^8 is independently selected from the group consisting of hydrogen, optionally substituted C_{1-6} alkyl, optionally substituted C_{2-6} alkenyl, optionally substituted C_{2-6} alkynyl, C_{6-10} aryl optionally substituted with one or more R^{11}, C_{7-14} aralkyl optionally substituted with one or more R^{11}, $-NR^{12}R^{13}$, and $-OR^5$;

each R^{12} is independently selected from the group consisting of hydrogen, optionally substituted C_{1-6} alkyl, optionally substituted C_{2-6} alkenyl, optionally substituted C_{2-6} alkynyl, C_{6-10} aryl optionally substituted with one or more R^{11}, and C_{7-14} aralkyl optionally substituted with one or more R^{11};

each R^{13} is independently selected from the group consisting of hydrogen, optionally substituted C_{1-6} alkyl, optionally substituted C_{2-6} alkenyl, optionally substituted C_{2-6} alkynyl, C_{6-10} aryl optionally substituted with one or more R^{11}, and C_{7-14} aralkyl optionally substituted with one or more R^{11};

each R^5 is independently selected from the group consisting of hydrogen, optionally substituted C_{1-6} alkyl, optionally substituted C_{2-6} alkenyl, optionally substituted C_{2-6} alkynyl, optionally substituted C_{2-8} alkoxyalkyl, C_{6-10} aryl optionally substituted with one or more R^{11}, C_{7-14} aralkyl optionally substituted with one or more R^{11}, and $-(CH_2)_n$-(3-10 membered heterocyclyl) optionally substituted with one or more R^{10};

each R^{10} is independently selected from the group consisting of optionally substituted C_{1-6} alkyl, optionally substituted C_{2-6} alkenyl, and optionally substituted C_{2-6} alkynyl, or independently two geminal R^{10} together are oxo;

each R^{11} is independently selected from the group consisting of halogen, -CN, optionally substituted C_{1-6} alkyl, optionally substituted C_{2-6} alkenyl, optionally substituted C_{2-6} alkynyl, and optionally substituted C_{1-6} alkoxy;

each R^{16} is independently selected from the group consisting of optionally substituted C_{1-6} alkyl, optionally substituted C_{2-6} alkenyl, optionally substituted C_{2-6} alkynyl, C_{6-10} aryl optionally substituted with one or more R^{11}, C_{7-14} aralkyl optionally substituted with one or more R^{11}, $-NR^{12}R^{13}$, and $-OR^5$;

Z is selected from oxygen and sulfur;

each n is independently an integer from 0 to 4; and

the bonds represented by a solid and dashed line are independently selected from the group consisting of a single bond and a double bond, provided that

when R^3 is hydrogen, then R^1 is selected from C_{6-10} aryl optionally substituted with one or more R^4, or 5 to 6 membered heteroaryl optionally substituted with one or more R^4;

when R^3 is phenyl optionally substituted with one or more R^9, and Z is O; then ring A cannot be optionally substituted phenyl;

when ring A is selected from cyclopentenyl, optionally substituted pyrrolyl or optionally substituted dihydropyrrolidinyl, R^3 is phenyl optionally substituted with one or more R^9, and Z is O; then R^1 is not bromo, chloro, fluoro, 3-methoxy phenyl or 3,5-dimethoxy phenyl;

when ring A is pyridyl, R^1 is optionally substituted phenyl, and Z is O; then n in R^3 is zero and R^3 is not halogen substituted phenyl;

when ring A is optionally substituted pyrimidyl, R^3 is phenyl or benzyl, and Z is O; then R^1 is not methyl or benzyl;

when ring A is optionally substituted furanyl, R^3 is phenyl optionally substituted with one or more R^9, and Z is O; then R^1 is not fluoro;

when ring A is optionally substituted pyrrolyl, R^3 is phenyl optionally substituted with one or more R^9, and Z is O; then R^1 is not methyl;

when ring A is tetrahydrofuranyl, R^3 is phenyl, and Z is O; then R^1 is not methyl or phenyl; and

when ring A is pyradizinyl, R^3 is 4-NO_2-phenyl, and Z is O; then R^1 is not methyl.

126. The compound of Claim 125, wherein

R^3 is selected from the group consisting of phenyl, $-(CH_2)_n$-(5-10 membered heteroaryl), and 3-10 membered heterocyclyl, each optionally substituted with one or more R^9; and

each R^9 is independently selected from the group consisting of halogen, optionally substituted C_{1-6} alkyl, optionally substituted C_{2-6} alkenyl, optionally

substituted C_{2-6} alkynyl, optionally substituted C_{1-6} alkylthio, optionally substituted C_{2-8} alkoxyalkyl, optionally substituted C_{3-10} carbocyclyl, optionally substituted C_{6-10} aryl, $-OR^5$, $-NR^{14}R^{15}$, $-C(O)R^8$, $-SO_2R^{16}$, and $-NO_2$.

127. The compound of Claim 125, wherein R^1 is selected from bromo, chloro, fluoro, C_{1-6} alkyl optionally substituted with one or more R^4, C_{6-10} aryl optionally substituted with one or more R^4, or 5 to 6 membered heteroaryl optionally substituted with one or more R^4.

128. The compound of Claim 127, wherein R^1 is bromo or fluoro.

129. The compound of Claim 127, wherein R^1 is methyl optionally substituted with one or more R^4.

130. The compound of Claim 127, wherein R^1 is phenyl optionally substituted with one or more R^4.

131. The compound of Claim 127, wherein R^1 is pyridazinyl optionally substituted with one or more R^4.

132. The compound of Claim 127, wherein R^1 is pyrazolyl or 1-methyl pyrazolyl optionally substituted with one or more R^4.

133. The compound of any one of Claims 125 to 132, wherein R^3 is hydrogen.

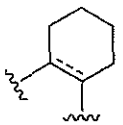
134. The compound of any one of Claims 125 to 132, wherein R^3 is selected from phenyl optionally substituted with one or more R^9.

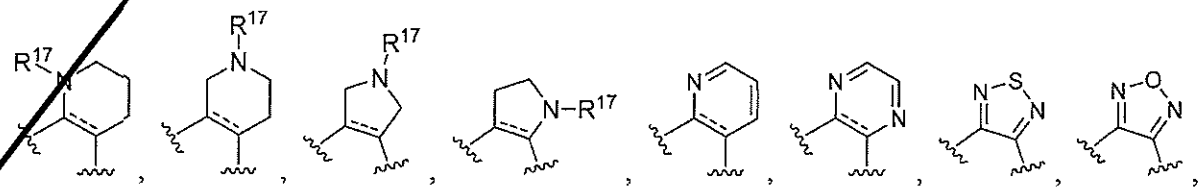
135. The compound of Claim 134, wherein R^3 is unsubstituted.

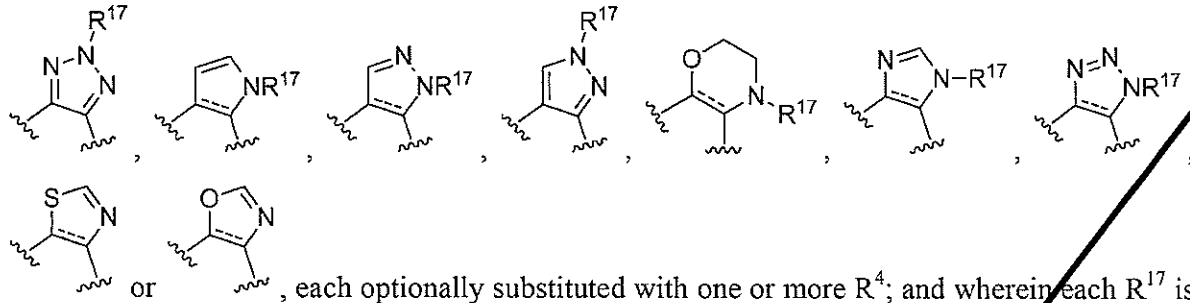
136. The compound of Claim 134, wherein R^9 is selected from cyano, halogen, optionally substituted C_{1-6} alkyl, or optionally substituted C_{1-6} alkoxy.

137. The compound of Claim 136, wherein R^9 is selected from cyano, fluoro, chloro, methyl, ethyl, ethoxy, methoxy, trifluoromethyl, trifluoromethoxy or difluoromethoxy.

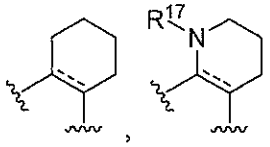
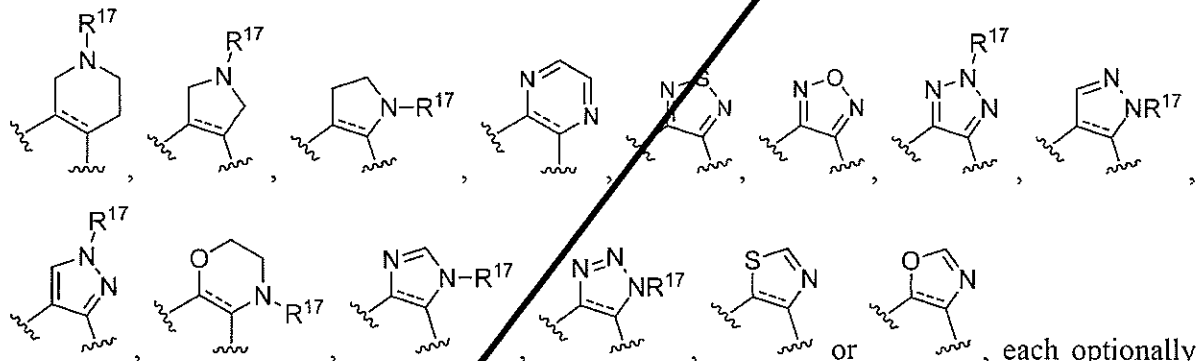
138. The compound of any one of Claims 125 to 137, wherein ring A is selected from C_{3-10} carbocyclyl, 5-membered heteroaryl, 6-membered heteroaryl, 5-membered heterocyclyl or 6-membered heterocyclyl, each optionally substituted with one or more R^4.

139. The compound of Claim 138, wherein ring A is selected from ,

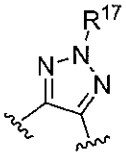
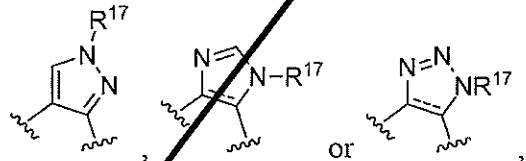




or , each optionally substituted with one or more R^4; and wherein each R^{17} is independently selected from hydrogen, optionally substituted C_{1-6} alkyl, optionally substituted C_{3-6} cycloalkyl, optionally substituted C_{2-8} alkoxyalkyl, optionally substituted C-carboxy, acyl, C_{6-10} aryl optionally substituted with one or more R^{11}, or C_{7-14} aralkyl optionally substituted with one or more R^{11}.

140. The compound of Claim 139, ring A is selected from , 

or , each optionally substituted with one or more R^4.

141. The compound of Claim 139 or 140, wherein ring A is selected from , 

or , each optionally substituted with one or more R^4.

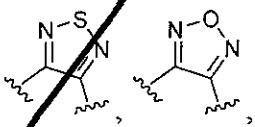
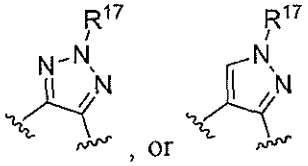
142. The compound of any one of Claims 139 to 141, wherein R^{17} is selected from hydrogen, methyl, ethyl, isopropyl, cyclopropyl, $-(CH_2)_2F$, $-(CH_2)_2OH$, $-(CH_2)_2OCH_3$, $-(CH_2)_2OC_2H_5$, $-(CH_2)_2OC_3H_7$, -C(O)O-*t*-Bu, $-C(O)CH_3$ or benzyl.

143. The compound of any one of Claims 125 to 142, wherein R^4 is selected from halogen, optionally substituted C_{1-6} alkyl, or C_{7-14} aralkyl optionally substituted with one or more R^{11}, or two geminal R^4 together are oxo.

144. The compound of Claim 143, wherein R^4 is selected from fluoro, methyl, trifluoromethyl, $-(CH_2)_2OH$, benzyl, or two geminal R^4 together are oxo.

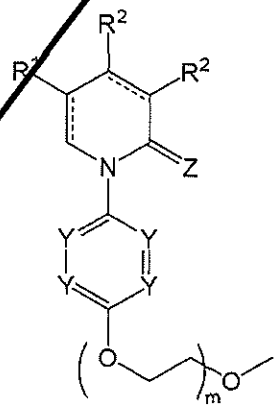
145. The compound of any one of Claim 138 to 142, wherein ring A is unsubstituted.

146. The compound of any one of Claims 125 to 145, wherein Z is oxygen.

147. The compound of any one of Claims 125 to 146, wherein the bonds represented by a solid and dashed line are double bonds, provided that when ring A is , , or , one of the bonds represented by a solid and dashed line is a single bond.

148. The compound of Claim 125, wherein the compound is selected from the group consisting of **Compounds 29-63, 392-400, 568, 569, 571-574, 576-584, 586-608, 611-626, 631, 634-638, 640, 642-655, 657-661, 665**, and **669-695** of Table 1, or pharmaceutically acceptable salts thereof.

149. A compound having the structure of formula (IV):



(IV)

or a pharmaceutically acceptable salt thereof, wherein

R^1 is selected from the group consisting of hydrogen, C_{1-6} alkyl optionally substituted with one or more R^4, C_{2-6} alkenyl optionally substituted with one or more R^4, C_{2-6} alkynyl optionally substituted with one or more R^4, C_{6-10} aryl optionally substituted with one or more R^4, 5-10 membered heteroaryl optionally substituted with one or more R^4, C_{3-10} carbocyclyl optionally substituted with one or more R^4, and 3-10 membered heterocyclyl optionally substituted with one or more R^4;

each R^2 is independently selected from the group consisting of hydrogen, halogen, optionally substituted C_{1-6} alkyl, optionally substituted C_{2-6} alkenyl, optionally substituted C_{2-6} alkynyl, -CN, $-OR^5$, $-NR^6R^7$, and $-C(O)R^8$,

or both R^2 together with the carbon atoms to which they are attached form a fused ring selected from the group consisting of phenyl, 5-6 membered heteroaryl, C_{3-7} carbocyclyl, and 3-7 membered heterocyclyl, each optionally substituted with one or more R^4;

each R^4 is independently selected from the group consisting of halogen, -CN, optionally substituted C_{1-6} alkyl, optionally substituted C_{2-6} alkenyl, optionally substituted C_{2-6} alkynyl, and optionally substituted C_{1-6} alkoxy;

each R^5 is independently selected from the group consisting of hydrogen, optionally substituted C_{1-6} alkyl, optionally substituted C_{2-6} alkenyl, optionally substituted C_{2-6} alkynyl, optionally substituted C_{2-8} alkoxyalkyl, C_{6-10} aryl optionally substituted with one or more R^{11}, C_{7-14} aralkyl optionally substituted with one or more R^{11}, $-(CH_2)_n$-(3-10 membered heterocyclyl) optionally substituted with one or more R^{10}, and $-(CH_2)_n$-(C_{6-10} aryl) optionally substituted with one or more R^{11};

R^6 is selected from the group consisting of hydrogen, optionally substituted C_{1-6} alkyl, optionally substituted C_{2-6} alkenyl, optionally substituted C_{2-6} alkynyl, C_{6-10} aryl optionally substituted with one or more R^{11}, C_{7-14} aralkyl optionally substituted with one or more R^{11}, (5-10 membered heteroaryl)alkyl optionally substituted with one or more R^{11}, $-C(O)R^8$, and $-C(O)OR^5$;

R^7 is selected from the group consisting of hydrogen, optionally substituted C_{1-6} alkyl, optionally substituted C_{2-6} alkenyl, optionally substituted C_{2-6} alkynyl, C_{6-10} aryl optionally substituted with one or more R^{11}, C_{7-14} aralkyl optionally substituted with one or more R^{11}, (5-10 membered heteroaryl)alkyl optionally substituted with one or more R^{11}, $-C(O)R^8$, and $-C(O)OR^5$;

or R^6 and R^7 together with the nitrogen to which they are attached form an 3-10 membered heterocyclyl optionally substituted with one or more R^{10};

each R^8 is independently selected from the group consisting of optionally substituted C_{1-6} alkyl, optionally substituted C_{2-6} alkenyl, optionally substituted C_{2-6} alkynyl, $-NR^{12}R^{13}$, and $-OR^5$;

each Y is independently N or CR^9;

each R^9 is independently selected from the group consisting of hydrogen, halogen, optionally substituted C_{1-6} alkyl, optionally substituted C_{2-6} alkenyl, optionally substituted C_{2-6} alkynyl, optionally substituted C_{1-6} alkoxy, and $-NR^{14}R^{15}$,

or independently two adjacent R^9 together with the ring atoms to which they are attached form a fused optionally substituted 3-10 membered heterocyclyl or a fused optionally substituted 5-10 membered heteroaryl;

each R^{10} is independently selected from the group consisting of oxo, optionally substituted C_{1-6} alkyl, optionally substituted C_{2-6} alkenyl, and optionally substituted C_{2-6} alkynyl;

each R^{11} is independently selected from the group consisting of halogen, -CN, optionally substituted C_{1-6} alkyl, optionally substituted C_{2-6} alkenyl, optionally substituted C_{2-6} alkynyl, and optionally substituted C_{1-6} alkoxy;

each R^{12} is independently selected from the group consisting of hydrogen, optionally substituted C_{1-6} alkyl, optionally substituted C_{2-6} alkenyl, optionally substituted C_{2-6} alkynyl, C_{6-10} aryl optionally substituted with one or more R^{11}, and C_{7-14} aralkyl optionally substituted with one or more R^{11};

each R^{13} is independently selected from the group consisting of hydrogen, optionally substituted C_{1-6} alkyl, optionally substituted C_{2-6} alkenyl, optionally substituted C_{2-6} alkynyl, C_{6-10} aryl optionally substituted with one or more R^{11}, and C_{7-14} aralkyl optionally substituted with one or more R^{11};

R^{14} is selected from the group consisting of hydrogen, optionally substituted C_{1-6} alkyl, optionally substituted C_{6-10} aryl, and $-C(O)R^8$;

R^{15} is selected from the group consisting of hydrogen, optionally substituted C_{1-6} alkyl, optionally substituted C_{6-10} aryl, and $-C(O)R^8$;

Z is selected from oxygen and sulfur;

n is an integer from 0 to 4;

m is an integer from 1 to 4; and

the bonds represented by a solid and dashed line are independently selected from the group consisting of a single bond and a double bond.

150. The compound of Claim 149, wherein R^1 is selected from the group consisting of hydrogen, C_{1-6} alkyl optionally substituted with one or more R^4, or 5-membered heteroaryl optionally substituted with one or more R^4.

151. The compound of Claim 150, wherein R^1 is selected from methyl, phenyl, pyrazolyl, or 1-methyl pyrazolyl, each optionally substituted with one or more R^4.

152. The compound of Claim 151, wherein R^1 is unsubstituted.

153. The compound of any one of Claims 149 to 151, wherein R^2 is selected from hydrogen or optionally substituted C_{1-6} alkyl.

154. The compound of any one of Claims 149 to 153, wherein all Y are CR^9.

155. The compound of any one of Claims 149 to 153, wherein at least one Y is N.

156. The compound of any one of Claims 149 to 155, wherein R^4 is selected from halogen, C_{1-6} alkyl or C_{1-6} alkoxy.

157. The compound of Claim 156, wherein R^4 is selected from fluoro or methyl.

158. The compound of any one of Claims 149 to 157, wherein m is 1.

159. The compound of any one of Claims 149 to 157, wherein m is 2.

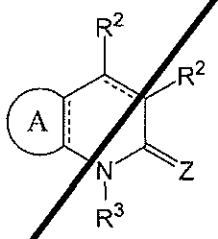
160. The compound of any one of Claims 149 to 157, wherein m is 3.

161. The compound of any one of Claims 149 to 160, wherein Z is oxygen.

162. The compound of any one of Claims 149 to 161, wherein the bonds represented by a solid and dashed line are double bonds.

163. The compound of Claim 149, wherein the compound is selected from the group consisting of **Compounds 21-26** of Table 1, or pharmaceutically acceptable salts thereof.

164. A compound having the structure of formula (V):



(V)

or a pharmaceutically acceptable salt thereof, wherein

A is a C_{5-7} carbocyclyl optionally substituted with one or more R^4;

each R^2 is independently selected from the group consisting of hydrogen, halogen, optionally substituted C_{1-6} alkyl, optionally substituted C_{2-6} alkenyl, optionally substituted C_{2-6} alkynyl, -CN, $-OR^5$, $-NR^6R^7$, and $-C(O)R^8$,

or both R^2 together with the carbon atoms to which they are attached form a fused ring selected from the group consisting of phenyl, 5-6 membered heteroaryl, C_{3-7} carbocyclyl, and 3-7 membered heterocyclyl, each optionally substituted with one or more R^4;

R^3 is selected from the group consisting of phenyl, $-(CH_2)_n$-(5-10 membered heteroaryl), and $-(CH_2)_n$-(3-10 membered heterocyclyl), each optionally substituted with one or more R^9;

each R^4 is independently selected from the group consisting of halogen, -CN, -OH, $-C(O)R^8$, $-SO_2R^{16}$, optionally substituted C_{1-6} alkyl, optionally substituted C_{2-6} alkenyl, optionally substituted C_{2-6} alkynyl, optionally substituted C_{1-6} alkoxy, optionally substituted C_{6-10} aryl optionally substituted with one or more R^{11}, C_{7-14}

aralkyl optionally substituted with one or more R^{11}, 5-10 membered heteroaryl optionally substituted with one or more R^{11}, or independently two geminal R^4 together are oxo;

each R^5 is independently selected from the group consisting of hydrogen, optionally substituted C_{1-6} alkyl, optionally substituted C_{2-6} alkenyl, optionally substituted C_{2-6} alkynyl, optionally substituted C_{2-8} alkoxyalkyl, C_{6-10} aryl optionally substituted with one or more R^{11}, C_{7-14} aralkyl optionally substituted with one or more R^{11}, and $-(CH_2)_n$-(3-10 membered heterocyclyl) optionally substituted with one or more R^{10};

R^6 is selected from the group consisting of hydrogen, optionally substituted C_{1-6} alkyl, optionally substituted C_{2-6} alkenyl, optionally substituted C_{2-6} alkynyl, C_{6-10} aryl optionally substituted with one or more R^{11}, C_{7-14} aralkyl optionally substituted with one or more R^{11}, (5-10 membered heteroaryl)alkyl optionally substituted with one or more R^{11}, $-C(O)R^8$, and $-C(O)OR^5$;

R^7 is selected from the group consisting of hydrogen, optionally substituted C_{1-6} alkyl, optionally substituted C_{2-6} alkenyl, optionally substituted C_{2-6} alkynyl, C_{6-10} aryl optionally substituted with one or more R^{11}, C_{7-14} aralkyl optionally substituted with one or more R^{11}, (5-10 membered heteroaryl)alkyl optionally substituted with one or more R^{11}, $-C(O)R^8$, and $-C(O)OR^5$;

or R^6 and R^7 together with the nitrogen to which they are attached form an 3-10 membered heterocyclyl optionally substituted with one or more R^{10};

each R^8 is independently selected from the group consisting of hydrogen, optionally substituted C_{1-6} alkyl, optionally substituted C_{2-6} alkenyl, optionally substituted C_{2-6} alkynyl, C_{6-10} aryl optionally substituted with one or more R^{11}, C_{7-14} aralkyl optionally substituted with one or more R^{11}, $-NR^{12}R^{13}$, and $-OR^5$;

each R^9 is independently selected from the group consisting of halogen, optionally substituted C_{1-6} alkyl, optionally substituted C_{2-6} alkenyl, optionally substituted C_{2-6} alkynyl, optionally substituted C_{1-6} alkylthio, optionally substituted C_{2-8} alkoxyalkyl, optionally substituted C_{3-10} carbocyclyl, optionally substituted C_{6-10} aryl, $-OR^5$, $-NR^{14}R^{15}$, $-C(O)R^8$, $-SO_2R^{16}$, and $-NO_2$;

each R^{10} is independently selected from the group consisting of optionally substituted C_{1-6} alkyl, optionally substituted C_{2-6} alkenyl, and optionally substituted C_{2-6} alkynyl, or independently two geminal R^{10} together are oxo;

each R^{11} is independently selected from the group consisting of halogen, -CN, optionally substituted C_{1-6} alkyl, optionally substituted C_{2-6} alkenyl, optionally substituted C_{2-6} alkynyl, and optionally substituted C_{1-6} alkoxy;

each R^{12} is independently selected from the group consisting of hydrogen, optionally substituted C_{1-6} alkyl, optionally substituted C_{2-6} alkenyl, optionally substituted C_{2-6} alkynyl, C_{6-10} aryl optionally substituted with one or more R^{11}, and C_{7-14} aralkyl optionally substituted with one or more R^{11};

each R^{13} is independently selected from the group consisting of hydrogen, optionally substituted C_{1-6} alkyl, optionally substituted C_{2-6} alkenyl, optionally substituted C_{2-6} alkynyl, C_{6-10} aryl optionally substituted with one or more R^{11}, and C_{7-14} aralkyl optionally substituted with one or more R^{11};

R^{14} is selected from the group consisting of hydrogen, optionally substituted C_{1-6} alkyl, optionally substituted C_{6-10} aryl, and $-C(O)R^8$;

R^{15} is selected from the group consisting of hydrogen, optionally substituted C_{1-6} alkyl, optionally substituted C_{6-10} aryl, and $-C(O)R^8$;

each R^{16} is independently selected from the group consisting of optionally substituted C_{1-6} alkyl, optionally substituted C_{2-6} alkenyl, optionally substituted C_{2-6} alkynyl, C_{6-10} aryl optionally substituted with one or more R^{11}, C_{7-14} aralkyl optionally substituted with one or more R^{11}, $-NR^{12}R^{13}$, and $-OR^5$;

Z is selected from oxygen and sulfur;

each n is independently an integer from 0 to 4; and

the bonds represented by a solid and dashed line are independently selected from the group consisting of a single bond and a double bond.

165. The compound of Claim 164, wherein each R^2 is independently selected from hydrogen, C_{1-6} alkyl or $-OR^5$.

166. The compound of Claim 165, wherein R^2 is hydrogen.

167. The compound of any one of Claims 164 to 166, wherein R^3 is phenyl, optionally substituted with one or more R^9.

168. The compound of Claim 167, wherein R^9 is selected from halogen, optionally substituted C_{1-6} alkyl, optionally substituted C_{2-8} alkoxyalkyl, $-OR^5$, or $-NR^{14}R^{15}$.

169. The compound of Claim 168, wherein R^9 is selected from fluoro, chloro, methyl, ethyl, methoxy, ethoxy, trifluoromethyl, trifluoromethoxy, $-NHCH_3$, $-NH_2$, or $-NHC(O)CH_3$.

170. The compound of Claim 169, wherein R^9 is trifluoromethoxy.

171. The compound of any one of Claims 164 to 170, wherein ring A is a C_5 carbocyclyl optionally substituted with one or more R^4.

172. The compound of any one of Claims 164 to 170, wherein ring A is a C_6 carbocyclyl optionally substituted with one or more R^4.

173. The compound of any one of Claims 164 to 172, wherein R^4 is selected from halogen, optionally substituted C_{1-6} alkyl, optionally substituted C_{1-6} alkoxy, or independently two geminal R^4 together are oxo.

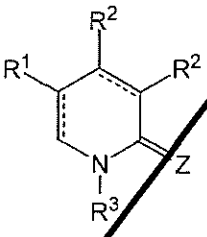
174. The compound of any one of Claims 164, 171 and 172, wherein ring A is unsubstituted.

175. The compound of any one of Claims 164 to 174, wherein Z is oxygen.

176. The compound of any one of Claims 164 to 175, wherein the bonds represented by a solid and dashed line are double bonds.

177. The compound of Claim 164, wherein the compound is selected from the group consisting of **Compounds 27** and **28** of Table 1, or pharmaceutically acceptable salts thereof.

178. A compound having the structure of formula (VIa):



(VIa)

or a pharmaceutically acceptable salt thereof, wherein

R^1 is a C_{4-7} carbocyclyl optionally substituted with one or more R^4;

each R^2 is independently selected from the group consisting of hydrogen, halogen, optionally substituted C_{1-6} alkyl, optionally substituted C_{2-6} alkenyl, optionally substituted C_{2-6} alkynyl, -CN, $-OR^5$, $-NR^6R^7$, and $-C(O)R^8$,

or both R^2 together with the carbon atoms to which they are attached form a fused ring selected from the group consisting of phenyl, 5-6 membered heteroaryl, C_{3-7} carbocyclyl, and 3-7 membered heterocyclyl, each optionally substituted with one or more R^4;

R^3 is selected from the group consisting of $-(CH_2)_n-(C_{6-10}$ aryl), $-(CH_2)_n-(5$-10 membered heteroaryl), $-(CH_2)_n-(C_{3-10}$ carbocyclyl), and $-(CH_2)_n-(3$-10 membered heterocyclyl), each optionally substituted with one or more R^9;

each R^4 is independently selected from the group consisting of halogen, -CN, -OH, $-C(O)R^8$, $-SO_2R^{16}$, optionally substituted C_{1-6} alkyl, optionally substituted C_{2-6} alkenyl, optionally substituted C_{2-6} alkynyl, optionally substituted C_{1-6} alkoxy, optionally substituted C_{6-10} aryl optionally substituted with one or more R^{11}, C_{7-14} aralkyl optionally substituted with one or more R^{11}, 5-10 membered heteroaryl optionally substituted with one or more R^{11}, or independently two geminal R^4 together are oxo;

each R^5 is independently selected from the group consisting of hydrogen, optionally substituted C_{1-6} alkyl, optionally substituted C_{2-6} alkenyl, optionally substituted C_{2-6} alkynyl, optionally substituted C_{2-8} alkoxyalkyl, C_{6-10} aryl optionally substituted with one or more R^{11}, C_{7-14} aralkyl optionally substituted with one or more R^{11}, and $-(CH_2)_n$-(3-10 membered heterocyclyl) optionally substituted with one or more R^{10};

R^6 is selected from the group consisting of hydrogen, optionally substituted C_{1-6} alkyl, optionally substituted C_{2-6} alkenyl, optionally substituted C_{2-6} alkynyl, C_{6-10} aryl optionally substituted with one or more R^{11}, C_{7-14} aralkyl optionally substituted with one or more R^{11}, (5-10 membered heteroaryl)alkyl optionally substituted with one or more R^{11}, $-C(O)R^8$, and $-C(O)OR^5$;

R^7 is selected from the group consisting of hydrogen, optionally substituted C_{1-6} alkyl, optionally substituted C_{2-6} alkenyl, optionally substituted C_{2-6} alkynyl, C_{6-10} aryl optionally substituted with one or more R^{11}, C_{7-14} aralkyl optionally substituted with one or more R^{11}, (5-10 membered heteroaryl)alkyl optionally substituted with one or more R^{11}, $-C(O)R^8$, and $-C(O)OR^5$;

or R^6 and R^7 together with the nitrogen to which they are attached form an 3-10 membered heterocyclyl optionally substituted with one or more R^{10};

each R^8 is independently selected from the group consisting of hydrogen, optionally substituted C_{1-6} alkyl, optionally substituted C_{2-6} alkenyl, optionally substituted C_{2-6} alkynyl, C_{6-10} aryl optionally substituted with one or more R^{11}, C_{7-14} aralkyl optionally substituted with one or more R^{11}, $-NR^{12}R^{13}$, and $-OR^5$;

each R^9 is independently selected from the group consisting of halogen, optionally substituted C_{1-6} alkyl, optionally substituted C_{2-6} alkenyl, optionally substituted C_{2-6} alkynyl, optionally substituted C_{1-6} alkylthio, optionally substituted C_{2-8} alkoxyalkyl, optionally substituted C_{3-10} carbocyclyl, optionally substituted C_{6-10} aryl, $-OR^5$, $-NR^{14}R^{15}$, $-C(O)R^8$, $-SO_2R^{16}$, and $-NO_2$;

each R^{10} is independently selected from the group consisting of optionally substituted C_{1-6} alkyl, optionally substituted C_{2-6} alkenyl, and optionally substituted C_{2-6} alkynyl, or independently two geminal R^{10} together are oxo;

each R^{11} is independently selected from the group consisting of halogen, -CN, optionally substituted C_{1-6} alkyl, optionally substituted C_{2-6} alkenyl, optionally substituted C_{2-6} alkynyl, and optionally substituted C_{1-6} alkoxy;

each R^{12} is independently selected from the group consisting of hydrogen, optionally substituted C_{1-6} alkyl, optionally substituted C_{2-6} alkenyl, optionally

substituted C_{2-6} alkynyl, C_{6-10} aryl optionally substituted with one or more R^{11}, and C_{7-14} aralkyl optionally substituted with one or more R^{11};

each R^{13} is independently selected from the group consisting of hydrogen, optionally substituted C_{1-6} alkyl, optionally substituted C_{2-6} alkenyl, optionally substituted C_{2-6} alkynyl, C_{6-10} aryl optionally substituted with one or more R^{11}, and C_{7-14} aralkyl optionally substituted with one or more R^{11};

R^{14} is selected from the group consisting of hydrogen, optionally substituted C_{1-6} alkyl, optionally substituted C_{6-10} aryl, and $-C(O)R^8$;

R^{15} is selected from the group consisting of hydrogen, optionally substituted C_{1-6} alkyl, optionally substituted C_{6-10} aryl, and $-C(O)R^8$;

each R^{16} is independently selected from the group consisting of optionally substituted C_{1-6} alkyl, optionally substituted C_{2-6} alkenyl, optionally substituted C_{2-6} alkynyl, C_{6-10} aryl optionally substituted with one or more R^{11}, C_{7-14} aralkyl optionally substituted with one or more R^{11}, $-NR^{12}R^{13}$, and $-OR^9$;

Z is selected from oxygen and sulfur;

each n is independently an integer from 0 to 4; and

the bonds represented by a solid and dashed line are independently selected from the group consisting of a single bond and a double bond.

179. The compound of Claim 178, wherein R^1 is a C_4 carbocyclyl optionally substituted with one or more R^4.

180. The compound of Claim 178, wherein R^1 is a C_5 carbocyclyl optionally substituted with one or more R^4.

181. The compound of Claim 178, wherein R^1 is a C_6 carbocyclyl optionally substituted with one or more R^4.

182. The compound of any one of Claims 178 to 181, wherein R^4 is selected from halogen, optionally substituted C_{1-6} alkyl, or optionally substituted C_{1-6} alkoxy.

183. The compound of Claim 182, wherein R^4 is selected from fluoro, chloro, methyl, methoxy, ethoxy, trifluoromethyl, or trifluoromethoxy.

184. The compound of Claim 178, wherein R^1 is unsubstituted.

185. The compound of any one of Claims 178 to 184, wherein each R^2 is independently selected from hydrogen, halogen, optionally substituted C_{1-6} alkyl, $-OR^5$ or $-NR^6R^7$.

186. The compound of Claim 185, wherein R^2 is hydrogen.

187. The compound of Claim 185, wherein R^2 is halogen.

188. The compound of Claim 185, wherein R^2 is optionally substituted C_{1-6} alkyl.

189. The compound of Claim 188, wherein R^2 is selected from methyl or trifluoromethyl.

190. The compound of any one of Claims 178 to 189, wherein R^3 is selected from -$(CH_2)_n$-(C_{6-10} aryl), optionally substituted with one or more R^9.

191. The compound of Claim 190, wherein R^3 is phenyl, optionally substituted with one or more R^9.

192. The compound of Claim 191, wherein R^9 is selected from halogen, optionally substituted C_{1-6} alkyl, optionally substituted C_{2-8} alkoxyalkyl, -OR^5, or -$NR^{14}R^{15}$.

193. The compound of Claim 192, wherein R^9 is selected from fluoro, chloro, methyl, ethyl, methoxy, ethoxy, trifluoromethyl, trifluoromethoxy, -$NHCH_3$, -NH_2, or -$NHC(O)CH_3$.

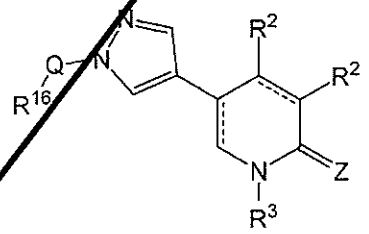
194. The compound of Claim 191, wherein R^3 is unsubstituted phenyl.

195. The compound of any one of Claims 178 to 194, wherein Z is oxygen.

196. The compound of any one of Claims 178 to 195, wherein the bonds represented by a solid and dashed line are double bonds.

197. The compound of Claim 178, wherein the compound is selected from the group consisting of **Compounds 64-66** of Table 1, or pharmaceutically acceptable salts thereof.

198. A compound having the structure of formula (VII):



(VII)

or a pharmaceutically acceptable salt thereof, wherein

each R^2 is independently selected from the group consisting of hydrogen, halogen, optionally substituted C_{1-6} alkyl, optionally substituted C_{2-6} alkenyl, optionally substituted C_{2-6} alkynyl, -CN, -OR^5, -NR^6R^7, and -$C(O)R^8$,

or both R^2 together with the carbon atoms to which they are attached form a fused ring selected from the group consisting of phenyl, 5-6 membered heteroaryl, C_{3-7} carbocyclyl, and 3-7 membered heterocyclyl, each optionally substituted with one or more R^4;

R^3 is selected from the group consisting of -$(CH_2)_n$-(C_{6-10} aryl), -$(CH_2)_n$-(5-10 membered heteroaryl), -$(CH_2)_n$-(C_{3-10} carbocyclyl), and -$(CH_2)_n$-(3-10 membered heterocyclyl), each optionally substituted with one or more R^9;

each R^4 is independently selected from the group consisting of halogen, -CN, -OH, $-C(O)R^8$, $-SO_2R^{16}$, optionally substituted C_{1-6} alkyl, optionally substituted C_{2-6} alkenyl, optionally substituted C_{2-6} alkynyl, optionally substituted C_{1-6} alkoxy, optionally substituted C_{6-10} aryl optionally substituted with one or more R^{11}, C_{7-14} aralkyl optionally substituted with one or more R^{11}, 5-10 membered heteroaryl optionally substituted with one or more R^{11}, or independently two geminal R^4 together are oxo;

each R^5 is independently selected from the group consisting of hydrogen, optionally substituted C_{1-6} alkyl, optionally substituted C_{2-6} alkenyl, optionally substituted C_{2-6} alkynyl, optionally substituted C_{2-8} alkoxyalkyl, C_{6-10} aryl optionally substituted with one or more R^{11}, C_{7-14} aralkyl optionally substituted with one or more R^{11}, and $-(CH_2)_n$-(3-10 membered heterocyclyl) optionally substituted with one or more R^{10};

R^6 is selected from the group consisting of hydrogen, optionally substituted C_{1-6} alkyl, optionally substituted C_{2-6} alkenyl, optionally substituted C_{2-6} alkynyl, C_{6-10} aryl optionally substituted with one or more R^{11}, C_{7-14} aralkyl optionally substituted with one or more R^{11}, (5-10 membered heteroaryl)alkyl optionally substituted with one or more R^{11}, $-C(O)R^8$, and $-C(O)OR^5$;

R^7 is selected from the group consisting of hydrogen, optionally substituted C_{1-6} alkyl, optionally substituted C_{2-6} alkenyl, optionally substituted C_{2-6} alkynyl, C_{6-10} aryl optionally substituted with one or more R^{11}, C_{7-14} aralkyl optionally substituted with one or more R^{11}, (5-10 membered heteroaryl)alkyl optionally substituted with one or more R^{11}, $-C(O)R^8$, and $-C(O)OR^5$;

or R^6 and R^7 together with the nitrogen to which they are attached form an 3-10 membered heterocyclyl optionally substituted with one or more R^{10};

each R^8 is independently selected from the group consisting of hydrogen, optionally substituted C_{1-6} alkyl, optionally substituted C_{2-6} alkenyl, optionally substituted C_{2-6} alkynyl, C_{6-10} aryl optionally substituted with one or more R^{11}, C_{7-14} aralkyl optionally substituted with one or more R^{11}, $-NR^{12}R^{13}$, and $-OR^5$;

each R^9 is independently selected from the group consisting of halogen, optionally substituted C_{1-6} alkyl, optionally substituted C_{2-6} alkenyl, optionally substituted C_{2-6} alkynyl, optionally substituted C_{1-6} alkylthio, optionally substituted C_{2-8} alkoxyalkyl, optionally substituted C_{3-10} carbocyclyl, optionally substituted C_{6-10} aryl, $-OR^5$, $-NR^{14}R^{15}$, $-C(O)R^8$, $-SO_2R^{16}$, and $-NO_2$;

each R^{10} is independently selected from the group consisting of optionally substituted C_{1-6} alkyl, optionally substituted C_{2-6} alkenyl, and optionally substituted C_{2-6} alkynyl, or independently two geminal R^{10} together are oxo;

each R^{11} is independently selected from the group consisting of halogen, -CN, optionally substituted C_{1-6} alkyl, optionally substituted C_{2-6} alkenyl, optionally substituted C_{2-6} alkynyl, and optionally substituted C_{1-6} alkoxy;

each R^{12} is independently selected from the group consisting of hydrogen, optionally substituted C_{1-6} alkyl, optionally substituted C_{2-6} alkenyl, optionally substituted C_{2-6} alkynyl, C_{6-10} aryl optionally substituted with one or more R^{11}, and C_{7-14} aralkyl optionally substituted with one or more R^{11};

each R^{13} is independently selected from the group consisting of hydrogen, optionally substituted C_{1-6} alkyl, optionally substituted C_{2-6} alkenyl, optionally substituted C_{2-6} alkynyl, C_{6-10} aryl optionally substituted with one or more R^{11}, and C_{7-14} aralkyl optionally substituted with one or more R^{11};

R^{14} is selected from the group consisting of hydrogen, optionally substituted C_{1-6} alkyl, optionally substituted C_{6-10} aryl, and $-C(O)R^8$;

R^{15} is selected from the group consisting of hydrogen, optionally substituted C_{1-6} alkyl, optionally substituted C_{6-10} aryl, and $-C(O)R^8$;

Q is selected from C(O) and $S(O)_t$;

each R^{16} is independently selected from the group consisting of optionally substituted C_{1-6} alkyl, optionally substituted C_{2-6} alkenyl, optionally substituted C_{2-6} alkynyl, C_{6-10} aryl optionally substituted with one or more R^{11}, C_{7-14} aralkyl optionally substituted with one or more R^{11}, $-NR^{12}R^{13}$, and $-OR^5$;

Z is selected from oxygen and sulfur;

each n is independently an integer from 0 to 4;

t is 1 or 2; and

the bonds represented by a solid and dashed line are independently selected from the group consisting of a single bond and a double bond.

199. The compound of Claim 198, wherein each R^2 is independently selected from hydrogen, halogen, optionally substituted C_{1-6} alkyl, $-OR^5$ or $-NR^6R^7$.

200. The compound of Claim 199, wherein R^2 is hydrogen.

201. The compound of Claim 199, wherein R^2 is halogen.

202. The compound of Claim 199, wherein R^2 is optionally substituted C_{1-6} alkyl.

203. The compound of Claim 202, wherein R^2 is methyl or trifluoromethyl.

204. The compound of any one of Claims 198 to 203, wherein R^3 is selected from -$(CH_2)_n$-(C_{6-10} aryl), optionally substituted with one or more R^9.

205. The compound of Claim 204, wherein R^3 is phenyl optionally substituted with one or more R^9.

206. The compound of Claim 205, wherein R^9 is selected from halogen, optionally substituted C_{1-6} alkyl, optionally substituted C_{2-8} alkoxyalkyl, -OR^5, or -$NR^{14}R^{15}$.

207. The compound of Claim 206, wherein R^9 is selected from fluoro, chloro, methyl, ethyl, methoxy, ethoxy, trifluoromethyl, trifluoromethoxy, -$NHCH_3$, -NH_2, or -$NHC(O)CH_3$.

208. The compound of Claim 205, wherein R^3 is unsubstituted phenyl.

209. The compound of any one of Claims 198 to 208, wherein Q is C(O).

210. The compound of any one of Claims 198 to 208, wherein Q is $S(O)_t$.

211. The compound of Claim 210, wherein t is 2.

212. The compound of any one of Claims 198 to 211, wherein R^{16} is selected from optionally substituted C_{1-6} alkyl, C_{6-10} aryl optionally substituted with one or more R^{11}, C_{7-14} aralkyl optionally substituted with one or more R^{11}, -$NR^{12}R^{13}$, or -OR^5.

213. The compound of Claim 212, wherein R^{16} is optionally substituted C_{1-6} alkyl.

214. The compound of Claim 213, wherein R^{16} is selected from methyl, ethyl, propyl, isopropyl, or butyl.

215. The compound of Claim 212, wherein R^{16} is phenyl optionally substituted with one or more R^{11}.

216. The compound of Claim 215, wherein R^{16} is unsubstituted phenyl.

217. The compound of Claim 212, wherein R^{16} is benzyl optionally substituted with one or more R^{11}.

218. The compound of Claim 217, wherein R^{16} is unsubstituted benzyl.

219. The compound of Claim 212, wherein R^{16} is -$NR^{12}R^{13}$.

220. The compound of Claim 219, wherein each R^{12} and R^{13} is independently selected from hydrogen or optionally substituted C_{1-6} alkyl.

221. The compound of Claim 212, wherein R^{16} is -OR^5.

222. The compound of Claim 221, wherein R^5 is selected from hydrogen or optionally substituted C_{1-6} alkyl.

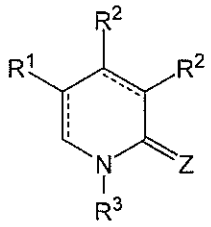
223. The compound of Claim 222, wherein R^5 is selected from methyl, ethyl, propyl, isopropyl, or butyl.

224. The compound of any one of Claims 198 to 223, wherein Z is oxygen.

225. The compound of any one of Claims 198 to 224, wherein the bonds represented by a solid and dashed line are double bonds.

226. The compound of Claim 198, wherein the compound is selected from the group consisting of **Compounds 67-76** of Table 1, or pharmaceutically acceptable salts thereof.

227. A compound having the structure of formula (VIb):



(VIb)

R^1 is selected from the group consisting of bromo, chloro, fluoro, -CN, $-C(O)R^8$, $-SO_2R^{16}$, C_{1-6} alkyl, C_{2-6} alkenyl optionally substituted with one or more R^4, C_{2-6} alkynyl optionally substituted with one or more R^4, C_{6-10} aryl optionally substituted with one or more R^4, 5 to 6 membered heteroaryl optionally substituted with one or more R^4, C_{3-10} carbocyclyl optionally substituted with one or more R^4, and 3-10 membered heterocyclyl optionally substituted with one or more R^4;

each R^2 is independently selected from the group consisting of hydrogen, halogen, optionally substituted C_{1-6} alkyl, optionally substituted C_{2-6} alkenyl, optionally substituted C_{2-6} alkynyl, -CN, $-OR^5$, $-NR^6R^7$, and $-C(O)R^8$,

or both R^2 together with the carbon atoms to which they are attached form a fused ring selected from the group consisting of 5-6 membered heteroaryl, C_{3-7} carbocyclyl, and 3-7 membered heterocyclyl, each optionally substituted with one or more R^4;

R^3 is selected from the group consisting of $-(CH_2)_{1-4}$-(C_{6-10} aryl), $-(CH_2)_{1-4}$-(5-10 membered heteroaryl), $-(CH_2)_{1-4}$-(C_{3-10} carbocyclyl), and $-(CH_2)_{1-4}$-(3-10 membered heterocyclyl), each optionally substituted with one or more R^9;

each R^4 is independently selected from the group consisting of halogen, -CN, -OH, $-C(O)R^8$, $-SO_2R^{16}$, optionally substituted C_{1-6} alkyl, optionally substituted C_{2-6} alkenyl, optionally substituted C_{2-6} alkynyl, optionally substituted C_{1-6} alkoxy, optionally substituted C_{6-10} aryl optionally substituted with one or more R^{11}, C_{7-14} aralkyl optionally substituted with one or more R^{11}, 5-10 membered heteroaryl optionally substituted with one or more R^{11};

each R^5 is independently selected from the group consisting of optionally substituted C_{1-6} alkyl, optionally substituted C_{2-6} alkenyl, optionally substituted C_{2-6} alkynyl, optionally substituted C_{2-8} alkoxyalkyl, C_{6-10} aryl optionally substituted with one or more R^{11}, C_{7-14} aralkyl optionally substituted with one or more R^{11}, and $-(CH_2)_n$-(3-10 membered heterocyclyl) optionally substituted with one or more R^{10};

R^6 is selected from the group consisting of hydrogen, optionally substituted C_{1-6} alkyl, optionally substituted C_{2-6} alkenyl, optionally substituted C_{2-6} alkynyl, C_{6-10} aryl optionally substituted with one or more R^{11}, C_{7-14} aralkyl optionally substituted with one or more R^{11}, (5-10 membered heteroaryl)alkyl optionally substituted with one or more R^{11}, -C(O)R^8, and -C(O)OR^5;

R^7 is selected from the group consisting of hydrogen, optionally substituted C_{1-6} alkyl, optionally substituted C_{2-6} alkenyl, optionally substituted C_{2-6} alkynyl, C_{6-10} aryl optionally substituted with one or more R^{11}, C_{7-14} aralkyl optionally substituted with one or more R^{11}, (5-10 membered heteroaryl)alkyl optionally substituted with one or more R^{11}, -C(O)R^8, and -C(O)OR^5;

or R^6 and R^7 together with the nitrogen to which they are attached form an 3-10 membered heterocyclyl optionally substituted with one or more R^{10};

each R^8 is independently selected from the group consisting of hydrogen, optionally substituted C_{1-6} alkyl, optionally substituted C_{2-6} alkenyl, optionally substituted C_{2-6} alkynyl, C_{6-10} aryl optionally substituted with one or more R^{11}, C_{7-14} aralkyl optionally substituted with one or more R^{11}, -N$R^{12}R^{13}$, and -OR^5;

each R^9 is independently selected from the group consisting of halogen, optionally substituted C_{1-6} alkyl, optionally substituted C_{2-6} alkenyl, optionally substituted C_{2-6} alkynyl, optionally substituted C_{1-6} alkylthio, optionally substituted C_{2-8} alkoxyalkyl, optionally substituted C_{3-10} carbocyclyl, optionally substituted C_{6-10} aryl, -OR^5, -N$R^{14}R^{15}$, -C(O)R^8, -SO_2R^{16}, and $-NO_2$;

each R^{10} is independently selected from the group consisting of optionally substituted C_{1-6} alkyl, optionally substituted C_{2-6} alkenyl, and optionally substituted C_{2-6} alkynyl, or independently two geminal R^{10} together are oxo;

each R^{11} is independently selected from the group consisting of halogen, -CN, optionally substituted C_{1-6} alkyl, optionally substituted C_{2-6} alkenyl, optionally substituted C_{2-6} alkynyl, and optionally substituted C_{1-6} alkoxy;

each R^{12} is independently selected from the group consisting of hydrogen, optionally substituted C_{1-6} alkyl, optionally substituted C_{2-6} alkenyl, optionally substituted C_{2-6} alkynyl, C_{6-10} aryl optionally substituted with one or more R^{11}, and C_{7-14} aralkyl optionally substituted with one or more R^{11};

each R^{13} is independently selected from the group consisting of hydrogen, optionally substituted C_{1-6} alkyl, optionally substituted C_{2-6} alkenyl, optionally substituted C_{2-6} alkynyl, C_{6-10} aryl optionally substituted with one or more R^{11}, and C_{7-14} aralkyl optionally substituted with one or more R^{11};

R^{14} is selected from the group consisting of hydrogen, optionally substituted C_{1-6} alkyl, optionally substituted C_{6-10} aryl, and $-C(O)R^8$;

R^{15} is selected from the group consisting of hydrogen, optionally substituted C_{1-6} alkyl, optionally substituted C_{6-10} aryl, and $-C(O)R^8$;

each R^{16} is independently selected from the group consisting of optionally substituted C_{1-6} alkyl, optionally substituted C_{2-6} alkenyl, optionally substituted C_{2-6} alkynyl, C_{6-10} aryl optionally substituted with one or more R^{11}, C_{7-14} aralkyl optionally substituted with one or more R^{11}, $-NR^{12}R^{13}$, and $-OR^5$;

Z is selected from oxygen and sulfur;

each n is independently an integer from 0 to 4; and

the bonds represented by a solid and dashed line are independently selected from the group consisting of a single bond and a double bond; provided that

when R^1 is selected from the group consisting of optionally substituted C_{6-10} aryl, optionally substituted 5 to 6 membered heteroaryl, optionally substituted 6 to 10 membered heterocyclyl, optionally substituted hexyl, C_{1-6}alkyl, optionally substituted C_{2-6} alkenyl; each of R^2 is hydrogen or one of R^2 is hydrogen and the other R^2 is methyl; and Z is O; then R^3 is not $-CH_2$-phenyl substituted with one or more halogen atoms; and provided that

R^1 is not 4-methoxy phenyl.

228. The compound of Claim 227, wherein R^1 is selected from C_{1-6} alkyl optionally substituted with one or more R^4, C_{6-10} aryl optionally substituted with one or more R^4, or 5to 6 membered heteroaryl optionally substituted with one or more R^4.

229. The compound of Claim 228, wherein R^1 is selected from C_{1-6} alkyl.

230. The compound of Claim 229, wherein R^1 is selected from methyl, ethyl, propyl, or isopropyl.

231. The compound of Claim 228, wherein R^1 is phenyl optionally substituted with one or more R^4.

232. The compound of Claim 228, wherein R^1 is selected from 5 or 6 membered heteroaryl each optionally substituted with one or more R^4.

233. The compound of Claim 232, wherein R^1 is selected from pyrazolyl or 1-methyl pyrazolyl, each optionally substituted with one or more R^4.

234. The compound of any one of Claims 227 to 233, wherein R^4 is selected from halogen or optionally substituted C_{1-6} alkyl.

235. The compound of Claim 234, wherein R^4 is fluoro.

236. The compound of any one of Claims 227 to 233, wherein R^1 is unsubstituted.

237. The compound of any one of Claims 227 to 236, wherein each R^2 is independently selected from hydrogen, halogen, or optionally substituted C_{1-6} alkyl.

238. The compound of Claim 237, wherein R^2 is hydrogen.

239. The compound of any one of Claims 227 to 238, wherein R^3 is $-(CH_2)_{1-4}$-(C_{6-10} aryl), optionally substituted with one or more R^9.

240. The compound of Claim 239, wherein R^3 is $-(CH_2)_{1-4}$-phenyl, optionally substituted with one or more R^9.

241. The compound of Claim 240, wherein R^3 is $-(CH_2)$-phenyl, optionally substituted with one or more R^9.

242. The compound of Claim 240, wherein R^3 is $-(CH_2)_2$-phenyl, optionally substituted with one or more R^9.

243. The compound of any one of Claims 227 to 242, wherein R^9 is selected from halogen, optionally substituted C_{1-6} alkyl, optionally substituted C_{2-8} alkoxyalkyl, $-OR^5$, $-C(O)R^8$ or $-NR^{14}R^{15}$.

244. The compound of Claim 243, wherein R^9 is selected from fluoro, chloro, methyl, ethyl, methoxy, ethoxy, trifluoromethyl, trifluoromethoxy, $-C(O)CH_3$, $-NHCH_3$, $-NH_2$, or $-NHC(O)CH_3$.

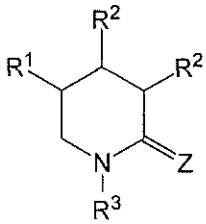
245. The compound of any one of Claims 239 to 242, wherein R^3 is unsubstituted.

246. The compound of any one of Claims 227 to 245, wherein Z is oxygen.

247. The compound of any one of Claims 227 to 246, wherein the bonds represented by a solid and dashed line are double bonds.

248. The compound of Claim 227, wherein the compound is selected from the group consisting of **Compounds 77-80** of Table 1, or pharmaceutically acceptable salts thereof.

249. A compound having the structure of formula (IX):



(IX)

R^1 is selected from the group consisting of hydrogen, halogen, $-CN$, $-C(O)R^8$, $-SO_2R^{16}$, C_{1-6} alkyl optionally substituted with one or more R^4, C_{2-6} alkenyl optionally substituted with one or more R^4, C_{2-6} alkynyl optionally substituted with one or more R^4, C_{6-10} aryl optionally substituted with one or more R^4, 5-10 membered heteroaryl optionally substituted with one or more R^4, C_{3-10} carbocyclyl

optionally substituted with one or more R^4, and 3-10 membered heterocyclyl optionally substituted with one or more R^4;

each R^2 is independently selected from the group consisting of hydrogen, halogen, optionally substituted C_{1-6} alkyl, optionally substituted C_{2-6} alkenyl, optionally substituted C_{2-6} alkynyl, -CN, $-OR^5$, $-NR^6R^7$, and $-C(O)R^8$,

or both R^2 together with the carbon atoms to which they are attached form a fused ring selected from the group consisting of C_{3-7} carbocyclyl and 5-7 membered heterocyclyl, each optionally substituted with one or more R^4;

R^3 is selected from the group consisting of $-(CH_2)_n-(C_{6-10}$ aryl), 5-10 membered heteroaryl, $-(CH_2)_n-(C_{3-10}$ carbocyclyl), and $-(CH_2)_n-$(3-10 membered heterocyclyl), each optionally substituted with one or more R^9;

each R^4 is independently selected from the group consisting of halogen, -CN, -OH, $-C(O)R^8$, $-SO_2R^{16}$, optionally substituted C_{1-6} alkyl, optionally substituted C_{2-6} alkenyl, optionally substituted C_{2-6} alkynyl, optionally substituted C_{1-6} alkoxy, optionally substituted C_{6-10} aryl optionally substituted with one or more R^{11}, C_{7-14} aralkyl optionally substituted with one or more R^{11}, 5-10 membered heteroaryl optionally substituted with one or more R^{11}, or independently two geminal R^4 together are oxo;

each R^5 is independently selected from the group consisting of hydrogen, optionally substituted C_{1-6} alkyl, optionally substituted C_{2-6} alkenyl, optionally substituted C_{2-6} alkynyl, optionally substituted C_{2-8} alkoxyalkyl, C_{6-10} aryl optionally substituted with one or more R^{11}, C_{7-14} aralkyl optionally substituted with one or more R^{11}, and $-(CH_2)_n-$(3-10 membered heterocyclyl) optionally substituted with one or more R^{10};

R^6 is selected from the group consisting of hydrogen, optionally substituted C_{1-6} alkyl, optionally substituted C_{2-6} alkenyl, optionally substituted C_{2-6} alkynyl, C_{6-10} aryl optionally substituted with one or more R^{11}, C_{7-14} aralkyl optionally substituted with one or more R^{11}, (5-10 membered heteroaryl)alkyl optionally substituted with one or more R^{11}, $-C(O)R^8$, and $-C(O)OR^5$;

R^7 is selected from the group consisting of hydrogen, optionally substituted C_{1-6} alkyl, optionally substituted C_{2-6} alkenyl, optionally substituted C_{2-6} alkynyl, C_{6-10} aryl optionally substituted with one or more R^{11}, C_{7-14} aralkyl optionally substituted with one or more R^{11}, (5-10 membered heteroaryl)alkyl optionally substituted with one or more R^{11}, $-C(O)R^8$, and $-C(O)OR^5$;

or R^6 and R^7 together with the nitrogen to which they are attached form an 3-10 membered heterocyclyl optionally substituted with one or more R^{10};

each R^8 is independently selected from the group consisting of hydrogen, optionally substituted C_{1-6} alkyl, optionally substituted C_{2-6} alkenyl, optionally substituted C_{2-6} alkynyl, C_{6-10} aryl optionally substituted with one or more R^{11}, C_{7-14} aralkyl optionally substituted with one or more R^{11}, $-NR^{12}R^{13}$, and $-OR^5$;

each R^9 is independently selected from the group consisting of halogen, optionally substituted C_{1-6} alkyl, optionally substituted C_{2-6} alkenyl, optionally substituted C_{2-6} alkynyl, optionally substituted C_{1-6} alkylthio, optionally substituted C_{2-8} alkoxyalkyl, optionally substituted C_{3-10} carbocyclyl, optionally substituted C_{6-10} aryl, $-OR^5$, $-NR^{14}R^{15}$, $-C(O)R^8$, $-SO_2R^{16}$, and $-NO_2$;

each R^{10} is independently selected from the group consisting of optionally substituted C_{1-6} alkyl, optionally substituted C_{2-6} alkenyl, and optionally substituted C_{2-6} alkynyl, or independently two geminal R^{10} together are oxo;

each R^{11} is independently selected from the group consisting of halogen, -CN, optionally substituted C_{1-6} alkyl, optionally substituted C_{2-6} alkenyl, optionally substituted C_{2-6} alkynyl, and optionally substituted C_{1-6} alkoxy;

each R^{12} is independently selected from the group consisting of hydrogen, optionally substituted C_{1-6} alkyl, optionally substituted C_{2-6} alkenyl, optionally substituted C_{2-6} alkynyl, C_{6-10} aryl optionally substituted with one or more R^{11}, and C_{7-14} aralkyl optionally substituted with one or more R^{11};

each R^{13} is independently selected from the group consisting of hydrogen, optionally substituted C_{1-6} alkyl, optionally substituted C_{2-6} alkenyl, optionally substituted C_{2-6} alkynyl, C_{6-10} aryl optionally substituted with one or more R^{11}, and C_{7-14} aralkyl optionally substituted with one or more R^{11};

R^{14} is selected from the group consisting of hydrogen, optionally substituted C_{1-6} alkyl, optionally substituted C_{6-10} aryl, and $-C(O)R^8$;

R^{15} is selected from the group consisting of hydrogen, optionally substituted C_{1-6} alkyl, optionally substituted C_{6-10} aryl, and $-C(O)R^8$;

each R^{16} is independently selected from the group consisting of optionally substituted C_{1-6} alkyl, optionally substituted C_{2-6} alkenyl, optionally substituted C_{2-6} alkynyl, C_{6-10} aryl optionally substituted with one or more R^{11}, C_{7-14} aralkyl optionally substituted with one or more R^{11}, $-NR^{12}R^{13}$, and $-OR^5$;

Z is selected from oxygen and sulfur; and

each n is independently an integer from 0 to 4.

250. The compound of Claim 249, wherein R^1 is selected from C_{1-6} alkyl optionally substituted with one or more R^4, C_{6-10} aryl optionally substituted with one or more R^4, or 5-10 membered heteroaryl optionally substituted with one or more R^4.

251. The compound of Claim 250, wherein R^1 is C_{1-6} alkyl optionally substituted with one or more R^4.

252. The compound of Claim 250, wherein R^1 is C_{6-10} aryl optionally substituted with one or more R^4.

253. The compound of Claim 252, wherein R^1 is phenyl optionally substituted with one or more R^4.

254. The compound of Claim 250, wherein R^1 is 5 or 6 membered heteroaryl optionally substituted with one or more R^4.

255. The compound of Claim 254, wherein R^1 is pyrazolyl or 1-methyl pyrazolyl optionally substituted with one or more R^4.

256. The compound of any one of Claims 250 to 255, wherein R^4 is selected from halogen, optionally substituted C_{1-6} alkyl or optionally substituted C_{1-6} alkoxy.

257. The compound of any one of Claims 250 to 255, wherein R^1 is unsubstituted.

258. The compound of any one of Claims 249 to 257, wherein each R^2 is independently selected from hydrogen, halogen or optionally substituted C_{1-6} alkyl.

259. The compound of Claim 258, wherein R^2 is hydrogen.

260. The compound of any one of Claims 249 to 259, wherein R^3 is $-(CH_2)_n-(C_{6-10}$ aryl), optionally substituted with one or more R^9.

261. The compound of Claim 260, wherein R^3 is phenyl optionally substituted with one or more R^9.

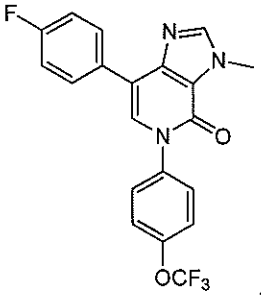
262. The compound of Claim 260 or 261, wherein R^9 is selected from halogen, optionally substituted C_{1-6} alkyl, optionally substituted C_{2-8} alkoxyalkyl, $-OR^5$, $-C(O)R^8$ or $-NR^{14}R^{15}$.

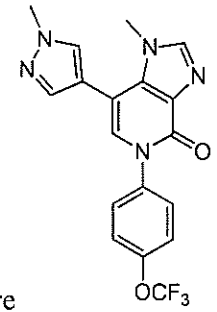
263. The compound of Claim 262, wherein R^9 is selected from fluoro, chloro, methyl, ethyl, methoxy, ethoxy, trifluoromethyl, trifluoromethoxy, $-C(O)CH_3$, $-NHCH_3$, $-NH_2$, or $-NHC(O)CH_3$.

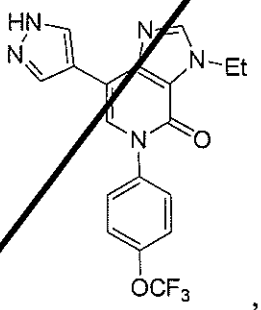
264. The compound of Claim 260 or 261, wherein R^3 is unsubstituted.

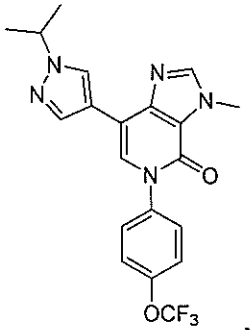
265. The compound of any one of Claims 249 to 264, wherein Z is oxygen.

266. The compound of Claim 249, wherein the compound is selected from the group consisting of **Compounds 83, 84, 520-522** of Table 1, or pharmaceutically acceptable salts thereof.

267. A compound of structure , or a pharmaceutically acceptable salt thereof.

268. A compound of structure , or a pharmaceutically acceptable salt thereof.

269. A compound of structure , or a pharmaceutically acceptable salt thereof.

270. A compound of structure , or a pharmaceutically acceptable salt thereof.

271. A pharmaceutical composition comprising an effective amount of a compound of any one of Claims 1 to 270, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier, diluent, excipient or combination thereof.

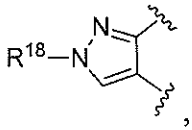
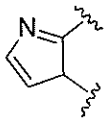
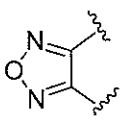
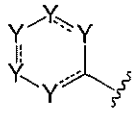
272. A therapeutically effective amount of a compound of any one of Claims 1 to 270, a pharmaceutically acceptable salt thereof, or a pharmaceutical composition of Claim 271 for use in the treatment of a fibrotic condition.

273. The compound for use of Claim 272, wherein the fibrotic condition is selected from pulmonary fibrosis, dermal fibrosis, pancreatic fibrosis, liver fibrosis, and renal fibrosis.

274. The compound for use of Claim 273, wherein the fibrotic condition is idiopathic pulmonary fibrosis.

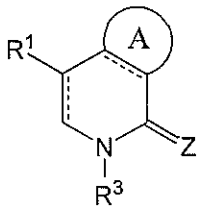
275. The compound for use of any one of Claims 272 to 274, wherein the compound, the pharmaceutical acceptable salt thereof, or the pharmaceutical composition is for use by inhalation.

276. Use of a therapeutically effective amount of a compound of any one of Claims 1 to 270, a pharmaceutically acceptable salt thereof, or a pharmaceutical composition of Claim 271 in the preparation of a medicament for treating a fibrotic condition.

substituted 5 or 6 membered heteroaryl formed by two adjacent R^4 together with the carbon atoms to which they are attached is selected from , , or , one of the bonds represented by a solid and dashed line in  is a single bond.

124. The compound of Claim 80, wherein the compound is selected from the group consisting of **Compounds 163-216, 241-243, 245, 246, 248-252, 254, 255, 258-261, 263, 415-430, 552-561, 566** and **629** of Table 1, or pharmaceutically acceptable salts thereof.

125. A compound having the structure of formula (III):



(III)

or a pharmaceutically acceptable salt thereof, wherein

R^1 is selected from the group consisting of bromo, chloro, fluoro, -CN, $-SO_2R^{16}$, C_{1-6} alkyl optionally substituted with one or more R^4, C_{2-6} alkenyl optionally substituted with one or more R^4, C_{2-6} alkynyl optionally substituted with one or more R^4, C_{6-10} aryl optionally substituted with one or more R^4, 5 to 6 membered heteroaryl optionally substituted with one or more R^4, C_{3-10} carbocyclyl optionally substituted with one or more R^4, and 3-10 membered heterocyclyl optionally substituted with one or more R^4;

R^3 is selected from the group consisting of phenyl, $-(CH_2)_n$-(5-10 membered heteroaryl), and 3-10 membered heterocyclyl, each optionally substituted with one or more R^9;

ring A is selected from the group consisting of 5-6 membered heteroaryl, C_{6-7} carbocyclyl, and 3-7 membered heterocyclyl, each optionally substituted with one or more R^4;

each R^4 is independently selected from the group consisting of halogen, -CN, -OH, $-C(O)R^8$, $-SO_2R^{16}$, optionally substituted C_{1-6} alkyl, optionally substituted C_{2-6} alkenyl, optionally substituted C_{2-6} alkynyl, optionally substituted C_{1-6} alkoxy, optionally substituted C_{6-10} aryl optionally substituted with one or more R^{11}, C_{7-14} aralkyl optionally substituted with one or more R^{11}, 5-10 membered heteroaryl optionally substituted with one or more R^{11}, or independently two geminal R^4 together are oxo;

each R^9 is independently selected from the group consisting of hydroxy, halogen, optionally substituted C_{1-6} alkyl, optionally substituted C_{2-6} alkenyl, optionally substituted C_{2-6} alkynyl, optionally substituted C_{1-6} alkylthio, optionally substituted C_{2-8} alkoxyalkyl, optionally substituted C_{3-10} carbocyclyl, optionally substituted C_{6-10} aryl, $-OR^5$, $-NR^{14}R^{15}$, $-C(O)R^8$, $-SO_2R^{16}$, -CN, and $-NO_2$;

R^{14} is selected from the group consisting of hydrogen, optionally substituted C_{1-6} alkyl, optionally substituted C_{6-10} aryl, and $-C(O)R^8$;

R^{15} is selected from the group consisting of hydrogen, optionally substituted C_{1-6} alkyl, optionally substituted C_{6-10} aryl, and $-C(O)R^8$;

each R^8 is independently selected from the group consisting of hydrogen, optionally substituted C_{1-6} alkyl, optionally substituted C_{2-6} alkenyl, optionally substituted C_{2-6} alkynyl, C_{6-10} aryl optionally substituted with one or more R^{11}, C_{7-14} aralkyl optionally substituted with one or more R^{11}, $-NR^{12}R^{13}$, and $-OR^5$;

each R^{12} is independently selected from the group consisting of hydrogen, optionally substituted C_{1-6} alkyl, optionally substituted C_{2-6} alkenyl, optionally substituted C_{2-6} alkynyl, C_{6-10} aryl optionally substituted with one or more R^{11}, and C_{7-14} aralkyl optionally substituted with one or more R^{11};

each R^{13} is independently selected from the group consisting of hydrogen, optionally substituted C_{1-6} alkyl, optionally substituted C_{2-6} alkenyl, optionally substituted C_{2-6} alkynyl, C_{6-10} aryl optionally substituted with one or more R^{11}, and C_{7-14} aralkyl optionally substituted with one or more R^{11};

each R^5 is independently selected from the group consisting of hydrogen, optionally substituted C_{1-6} alkyl, optionally substituted C_{2-6} alkenyl, optionally substituted C_{2-6} alkynyl, optionally substituted C_{2-8} alkoxyalkyl, C_{6-10} aryl optionally substituted with one or more R^{11}, C_{7-14} aralkyl optionally substituted with one or more R^{11}, and $-(CH_2)_n$-(3-10 membered heterocyclyl) optionally substituted with one or more R^{10};

each R^{10} is independently selected from the group consisting of optionally substituted C_{1-6} alkyl, optionally substituted C_{2-6} alkenyl, and optionally substituted C_{2-6} alkynyl, or independently two geminal R^{10} together are oxo;

each R^{11} is independently selected from the group consisting of halogen, -CN, optionally substituted C_{1-6} alkyl, optionally substituted C_{2-6} alkenyl, optionally substituted C_{2-6} alkynyl, and optionally substituted C_{1-6} alkoxy;

each R^{16} is independently selected from the group consisting of optionally substituted C_{1-6} alkyl, optionally substituted C_{2-6} alkenyl, optionally substituted C_{2-6}

alkynyl, C_{6-10} aryl optionally substituted with one or more R^{11}, C_{7-14} aralkyl optionally substituted with one or more R^{11}, $-NR^{12}R^{13}$, and $-OR^5$;

Z is selected from oxygen and sulfur;

each n is independently an integer from 0 to 4; and

the bonds represented by a solid and dashed line are independently selected from the group consisting of a single bond and a double bond, provided that

when ring A is selected from optionally substituted pyrrolyl or optionally substituted dihydropyrrolidinyl, R^3 is phenyl optionally substituted with one or more R^9, and Z is O; then R^1 is not bromo, chloro, fluoro, 3-methoxy phenyl or 3,5-dimethoxy phenyl;

when ring A is pyridyl, R^1 is optionally substituted phenyl, and Z is O; then n in R^3 is zero and R^3 is not halogen substituted phenyl;

when ring A is optionally substituted pyrimidyl, R^3 is phenyl or benzyl, and Z is O; then R^1 is not methyl or benzyl;

when ring A is optionally substituted furanyl, R^3 is phenyl optionally substituted with one or more R^9, and Z is O; then R^1 is not fluoro;

when ring A is optionally substituted pyrrolyl, R^3 is phenyl optionally substituted with one or more R^9, and Z is O; then R^1 is not methyl;

when ring A is tetrahydrofuranyl, R^3 is phenyl, and Z is O; then R^1 is not methyl or phenyl; and

when ring A is pyradizinyl, R^3 is 4-NO_2-phenyl, and Z is O; then R^1 is not methyl.

126. The compound of Claim 125, wherein

R^3 is selected from the group consisting of phenyl, $-(CH_2)_n$-(5-10 membered heteroaryl), and 3-10 membered heterocyclyl, each optionally substituted with one or more R^9; and

each R^9 is independently selected from the group consisting of halogen, optionally substituted C_{1-6} alkyl, optionally substituted C_{2-6} alkenyl, optionally substituted C_{2-6} alkynyl, optionally substituted C_{1-6} alkylthio, optionally substituted C_{2-8} alkoxyalkyl, optionally substituted C_{3-10} carbocyclyl, optionally substituted C_{6-10} aryl, $-OR^5$, $-NR^{14}R^{15}$, $-C(O)R^8$, $-SO_2R^{16}$, and $-NO_2$.

127. The compound of Claim 125, wherein R^1 is selected from bromo, chloro, fluoro, C_{1-6} alkyl optionally substituted with one or more R^4, C_{6-10} aryl optionally substituted with one or more R^4, or 5 to 6 membered heteroaryl optionally substituted with one or more R^4.

128. The compound of Claim 127, wherein R^1 is bromo or fluoro.

129. The compound of Claim 127, wherein R^1 is methyl optionally substituted with one or more R^4.

130. The compound of Claim 127, wherein R^1 is phenyl optionally substituted with one or more R^4.

131. The compound of Claim 127, wherein R^1 is pyridazinyl optionally substituted with one or more R^4.

132. The compound of Claim 127, wherein R^1 is pyrazolyl or 1-methyl pyrazolyl optionally substituted with one or more R^4.

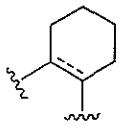
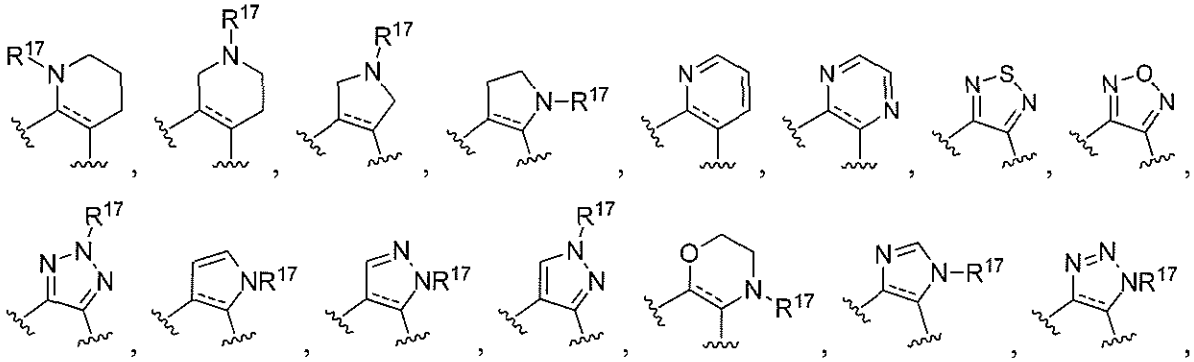
133. The compound of any one of Claims 125 to 132, wherein R^3 is selected from phenyl optionally substituted with one or more R^9.

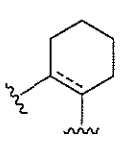
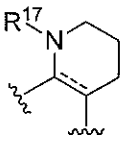
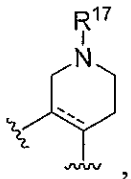
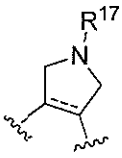
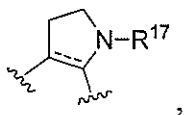
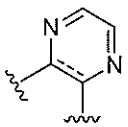
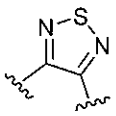
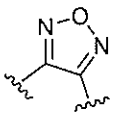
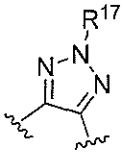
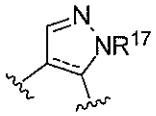
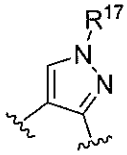
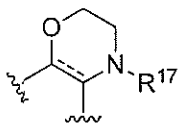
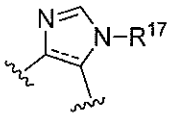
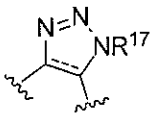
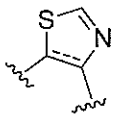
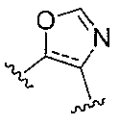
134. The compound of Claim 133, wherein R^3 is unsubstituted.

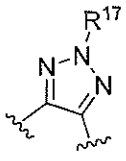
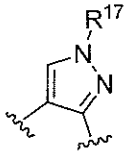
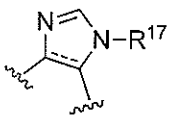
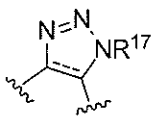
135. The compound of Claim 133, wherein R^9 is selected from cyano, halogen, optionally substituted C_{1-6} alkyl, or optionally substituted C_{1-6} alkoxy.

136. The compound of Claim 135, wherein R^9 is selected from cyano, fluoro, chloro, methyl, ethyl, ethoxy, methoxy, trifluoromethyl, trifluoromethoxy or difluoromethoxy.

137. The compound of any one of Claims 125 to 136, wherein ring A is selected from C_{6-7} carbocyclyl, 5-membered heteroaryl, 6-membered heteroaryl, 5-membered heterocyclyl or 6-membered heterocyclyl, each optionally substituted with one or more R^4.

138. The compound of Claim 137, wherein ring A is selected from , , each optionally substituted with one or more R^4; and wherein each R^{17} is independently selected from hydrogen, optionally substituted C_{1-6} alkyl, optionally substituted C_{3-6} cycloalkyl, optionally substituted C_{2-8} alkoxyalkyl, optionally substituted C-carboxy, acyl, C_{6-10} aryl optionally substituted with one or more R^{11}, or C_{7-14} aralkyl optionally substituted with one or more R^{11}.

139. The compound of Claim 138, ring A is selected from  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  ,  or  , each optionally substituted with one or more R^4.

140. The compound of Claim 138 or 139, wherein ring A is selected from  ,  ,  or  , each optionally substituted with one or more R^4.

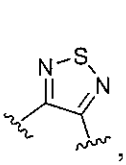
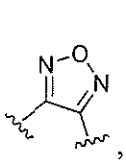
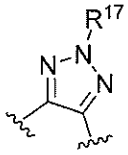
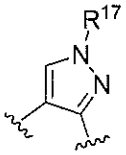
141. The compound of any one of Claims 138 to 140, wherein R^{17} is selected from hydrogen, methyl, ethyl, isopropyl, cyclopropyl, $-(CH_2)_2F$, $-(CH_2)_2OH$, $-(CH_2)_2OCH_3$, $-(CH_2)_2OC_2H_5$, $-(CH_2)_2OC_3H_7$, -C(O)O-*t*-Bu, $-C(O)CH_3$ or benzyl.

142. The compound of any one of Claims 125 to 141, wherein R^4 is selected from halogen, optionally substituted C_{1-6} alkyl, or C_{7-14} aralkyl optionally substituted with one or more R^{11}, or two geminal R^4 together are oxo.

143. The compound of Claim 142, wherein R^4 is selected from fluoro, methyl, trifluoromethyl, $-(CH_2)_2OH$, benzyl, or two geminal R^4 together are oxo.

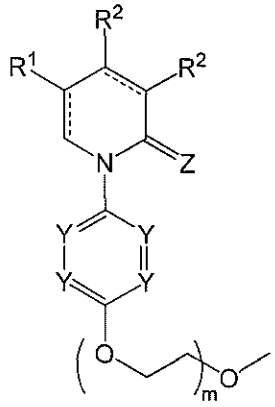
144. The compound of any one of Claim 137 to 141, wherein ring A is unsubstituted.

145. The compound of any one of Claims 125 to 144, wherein Z is oxygen.

146. The compound of any one of Claims 125 to 145, wherein the bonds represented by a solid and dashed line in formula (III) are double bonds, provided that when ring A is  ,  ,  , or  , one of the bonds represented by a solid and dashed line is a single bond.

147. The compound of Claim 125, wherein the compound is selected from the group consisting of **Compounds 29-63, 392-400, 568, 569, 571-574, 577, 579-584, 586-589, 591-594, 596-608, 614, 615, 617, 619, 620, 624-626, 631, 634-636, 640, 642-655, 657-661, 665,** and **669-695** of Table 1, or pharmaceutically acceptable salts thereof.

148. A compound having the structure of formula (IV):



(IV)

or a pharmaceutically acceptable salt thereof, wherein

R^1 is selected from the group consisting of hydrogen, C_{1-6} alkyl optionally substituted with one or more R^4, C_{2-6} alkenyl optionally substituted with one or more R^4, C_{2-6} alkynyl optionally substituted with one or more R^4, C_{6-10} aryl optionally substituted with one or more R^4, 5-10 membered heteroaryl optionally substituted with one or more R^4, C_{3-10} carbocyclyl optionally substituted with one or more R^4, and 3-10 membered heterocyclyl optionally substituted with one or more R^4;

each R^2 is independently selected from the group consisting of hydrogen, halogen, optionally substituted C_{1-6} alkyl, optionally substituted C_{2-6} alkenyl, optionally substituted C_{2-6} alkynyl, -CN, $-OR^5$, $-NR^6R^7$, and $-C(O)R^8$,

or both R^2 together with the carbon atoms to which they are attached form a fused ring selected from the group consisting of phenyl, 5-6 membered heteroaryl, C_{3-7} carbocyclyl, and 3-7 membered heterocyclyl, each optionally substituted with one or more R^4;

each R^4 is independently selected from the group consisting of halogen, -CN, optionally substituted C_{1-6} alkyl, optionally substituted C_{2-6} alkenyl, optionally substituted C_{2-6} alkynyl, and optionally substituted C_{1-6} alkoxy;

each R^5 is independently selected from the group consisting of hydrogen, optionally substituted C_{1-6} alkyl, optionally substituted C_{2-6} alkenyl, optionally substituted C_{2-6} alkynyl, optionally substituted C_{2-8} alkoxyalkyl, C_{6-10} aryl optionally substituted with one or more R^{11}, C_{7-14} aralkyl optionally substituted with one or more

R^{11}, -$(CH_2)_n$-(3-10 membered heterocyclyl) optionally substituted with one or more R^{10}, and -$(CH_2)_n$-(C_{6-10} aryl) optionally substituted with one or more R^{11};

R^6 is selected from the group consisting of hydrogen, optionally substituted C_{1-6} alkyl, optionally substituted C_{2-6} alkenyl, optionally substituted C_{2-6} alkynyl, C_{6-10} aryl optionally substituted with one or more R^{11}, C_{7-14} aralkyl optionally substituted with one or more R^{11}, (5-10 membered heteroaryl)alkyl optionally substituted with one or more R^{11}, -C(O)R^8, and -C(O)OR^5;

R^7 is selected from the group consisting of hydrogen, optionally substituted C_{1-6} alkyl, optionally substituted C_{2-6} alkenyl, optionally substituted C_{2-6} alkynyl, C_{6-10} aryl optionally substituted with one or more R^{11}, C_{7-14} aralkyl optionally substituted with one or more R^{11}, (5-10 membered heteroaryl)alkyl optionally substituted with one or more R^{11}, -C(O)R^8, and -C(O)OR^5;

or R^6 and R^7 together with the nitrogen to which they are attached form an 3-10 membered heterocyclyl optionally substituted with one or more R^{10};

each R^8 is independently selected from the group consisting of optionally substituted C_{1-6} alkyl, optionally substituted C_{2-6} alkenyl, optionally substituted C_{2-6} alkynyl, -$NR^{12}R^{13}$, and -OR^5;

each Y is independently N or CR^9;

each R^9 is independently selected from the group consisting of hydrogen, halogen, optionally substituted C_{1-6} alkyl, optionally substituted C_{2-6} alkenyl, optionally substituted C_{2-6} alkynyl, optionally substituted C_{1-6} alkoxy, and -$NR^{14}R^{15}$,

or independently two adjacent R^9 together with the ring atoms to which they are attached form a fused optionally substituted 3-10 membered heterocyclyl or a fused optionally substituted 5-10 membered heteroaryl;

each R^{10} is independently selected from the group consisting of oxo, optionally substituted C_{1-6} alkyl, optionally substituted C_{2-6} alkenyl, and optionally substituted C_{2-6} alkynyl;

each R^{11} is independently selected from the group consisting of halogen, -CN, optionally substituted C_{1-6} alkyl, optionally substituted C_{2-6} alkenyl, optionally substituted C_{2-6} alkynyl, and optionally substituted C_{1-6} alkoxy;

each R^{12} is independently selected from the group consisting of hydrogen, optionally substituted C_{1-6} alkyl, optionally substituted C_{2-6} alkenyl, optionally substituted C_{2-6} alkynyl, C_{6-10} aryl optionally substituted with one or more R^{11}, and C_{7-14} aralkyl optionally substituted with one or more R^{11};

each R^{13} is independently selected from the group consisting of hydrogen, optionally substituted C_{1-6} alkyl, optionally substituted C_{2-6} alkenyl, optionally substituted C_{2-6} alkynyl, C_{6-10} aryl optionally substituted with one or more R^{11}, and C_{7-14} aralkyl optionally substituted with one or more R^{11};

R^{14} is selected from the group consisting of hydrogen, optionally substituted C_{1-6} alkyl, optionally substituted C_{6-10} aryl, and $-C(O)R^8$;

R^{15} is selected from the group consisting of hydrogen, optionally substituted C_{1-6} alkyl, optionally substituted C_{6-10} aryl, and $-C(O)R^8$;

Z is selected from oxygen and sulfur;

n is an integer from 0 to 4;

m is an integer from 1 to 4; and

the bonds represented by a solid and dashed line are independently selected from the group consisting of a single bond and a double bond.

149. The compound of Claim 148, wherein R^1 is selected from the group consisting of hydrogen, C_{1-6} alkyl optionally substituted with one or more R^4, or 5-membered heteroaryl optionally substituted with one or more R^4.

150. The compound of Claim 149, wherein R^1 is selected from methyl, phenyl, pyrazolyl, or 1-methyl pyrazolyl, each optionally substituted with one or more R^4.

151. The compound of Claim 150, wherein R^1 is unsubstituted.

152. The compound of any one of Claims 148 to 150, wherein R^2 is selected from hydrogen or optionally substituted C_{1-6} alkyl.

153. The compound of any one of Claims 148 to 152, wherein all Y are CR^9.

154. The compound of any one of Claims 148 to 152, wherein at least one Y is N.

155. The compound of any one of Claims 148 to 154, wherein R^4 is selected from halogen, C_{1-6} alkyl or C_{1-6} alkoxy.

156. The compound of Claim 155, wherein R^4 is selected from fluoro or methyl.

157. The compound of any one of Claims 148 to 156, wherein m is 1.

158. The compound of any one of Claims 148 to 156, wherein m is 2.

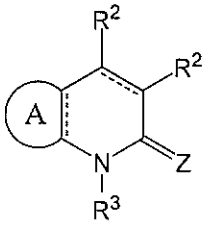
159. The compound of any one of Claims 148 to 156, wherein m is 3.

160. The compound of any one of Claims 148 to 159, wherein Z is oxygen.

161. The compound of any one of Claims 148 to 160, wherein the bonds represented by a solid and dashed line are double bonds.

162. The compound of Claim 148, wherein the compound is selected from the group consisting of **Compounds 21-26** of Table 1, or pharmaceutically acceptable salts thereof.

163. A compound having the structure of formula (V):



(V)

or a pharmaceutically acceptable salt thereof, wherein

A is a C_{5-7} carbocyclyl optionally substituted with one or more R^4;

each R^2 is independently selected from the group consisting of hydrogen, halogen, optionally substituted C_{1-6} alkyl, optionally substituted C_{2-6} alkenyl, optionally substituted C_{2-6} alkynyl, -CN, $-OR^5$, $-NR^6R^7$, and $-C(O)R^8$,

or both R^2 together with the carbon atoms to which they are attached form a fused ring selected from the group consisting of phenyl, 5-6 membered heteroaryl, C_{3-7} carbocyclyl, and 3-7 membered heterocyclyl, each optionally substituted with one or more R^4;

R^3 is selected from the group consisting of phenyl, $-(CH_2)_n$-(5-10 membered heteroaryl), and $-(CH_2)_n$-(3-10 membered heterocyclyl), each optionally substituted with one or more R^9;

each R^4 is independently selected from the group consisting of halogen, -CN, -OH, $-C(O)R^8$, $-SO_2R^{16}$, optionally substituted C_{1-6} alkyl, optionally substituted C_{2-6} alkenyl, optionally substituted C_{2-6} alkynyl, optionally substituted C_{1-6} alkoxy, optionally substituted C_{6-10} aryl optionally substituted with one or more R^{11}, C_{7-14} aralkyl optionally substituted with one or more R^{11}, 5-10 membered heteroaryl optionally substituted with one or more R^{11}, or independently two geminal R^4 together are oxo;

each R^5 is independently selected from the group consisting of hydrogen, optionally substituted C_{1-6} alkyl, optionally substituted C_{2-6} alkenyl, optionally substituted C_{2-6} alkynyl, optionally substituted C_{2-8} alkoxyalkyl, C_{6-10} aryl optionally substituted with one or more R^{11}, C_{7-14} aralkyl optionally substituted with one or more R^{11}, and $-(CH_2)_n$-(3-10 membered heterocyclyl) optionally substituted with one or more R^{10};

R^6 is selected from the group consisting of hydrogen, optionally substituted C_{1-6} alkyl, optionally substituted C_{2-6} alkenyl, optionally substituted C_{2-6} alkynyl, C_{6-10} aryl optionally substituted with one or more R^{11}, C_{7-14} aralkyl optionally substituted with one or more R^{11}, (5-10 membered heteroaryl)alkyl optionally substituted with one or more R^{11}, $-C(O)R^8$, and $-C(O)OR^5$;

R^7 is selected from the group consisting of hydrogen, optionally substituted C_{1-6} alkyl, optionally substituted C_{2-6} alkenyl, optionally substituted C_{2-6} alkynyl, C_{6-10} aryl optionally substituted with one or more R^{11}, C_{7-14} aralkyl optionally substituted with one or more R^{11}, (5-10 membered heteroaryl)alkyl optionally substituted with one or more R^{11}, -C(O)R^8, and -C(O)OR^5;

or R^6 and R^7 together with the nitrogen to which they are attached form an 3-10 membered heterocyclyl optionally substituted with one or more R^{10};

each R^8 is independently selected from the group consisting of hydrogen, optionally substituted C_{1-6} alkyl, optionally substituted C_{2-6} alkenyl, optionally substituted C_{2-6} alkynyl, C_{6-10} aryl optionally substituted with one or more R^{11}, C_{7-14} aralkyl optionally substituted with one or more R^{11}, -N$R^{12}R^{13}$, and -OR^5;

each R^9 is independently selected from the group consisting of halogen, optionally substituted C_{1-6} alkyl, optionally substituted C_{2-6} alkenyl, optionally substituted C_{2-6} alkynyl, optionally substituted C_{1-6} alkylthio, optionally substituted C_{2-8} alkoxyalkyl, optionally substituted C_{3-10} carbocyclyl, optionally substituted C_{6-10} aryl, -OR^5, -N$R^{14}R^{15}$, -C(O)R^8, -SO_2R^{16}, and –NO_2;

each R^{10} is independently selected from the group consisting of optionally substituted C_{1-6} alkyl, optionally substituted C_{2-6} alkenyl, and optionally substituted C_{2-6} alkynyl, or independently two geminal R^{10} together are oxo;

each R^{11} is independently selected from the group consisting of halogen, -CN, optionally substituted C_{1-6} alkyl, optionally substituted C_{2-6} alkenyl, optionally substituted C_{2-6} alkynyl, and optionally substituted C_{1-6} alkoxy;

each R^{12} is independently selected from the group consisting of hydrogen, optionally substituted C_{1-6} alkyl, optionally substituted C_{2-6} alkenyl, optionally substituted C_{2-6} alkynyl, C_{6-10} aryl optionally substituted with one or more R^{11}, and C_{7-14} aralkyl optionally substituted with one or more R^{11};

each R^{13} is independently selected from the group consisting of hydrogen, optionally substituted C_{1-6} alkyl, optionally substituted C_{2-6} alkenyl, optionally substituted C_{2-6} alkynyl, C_{6-10} aryl optionally substituted with one or more R^{11}, and C_{7-14} aralkyl optionally substituted with one or more R^{11};

R^{14} is selected from the group consisting of hydrogen, optionally substituted C_{1-6} alkyl, optionally substituted C_{6-10} aryl, and -C(O)R^8;

R^{15} is selected from the group consisting of hydrogen, optionally substituted C_{1-6} alkyl, optionally substituted C_{6-10} aryl, and -C(O)R^8;

each R^{16} is independently selected from the group consisting of optionally substituted C_{1-6} alkyl, optionally substituted C_{2-6} alkenyl, optionally substituted C_{2-6} alkynyl, C_{6-10} aryl optionally substituted with one or more R^{11}, C_{7-14} aralkyl optionally substituted with one or more R^{11}, $-NR^{12}R^{13}$, and $-OR^5$;

Z is selected from oxygen and sulfur;

each n is independently an integer from 0 to 4; and

the bonds represented by a solid and dashed line are independently selected from the group consisting of a single bond and a double bond.

164. The compound of Claim 163, wherein each R^2 is independently selected from hydrogen, C_{1-6} alkyl or $-OR^5$.

165. The compound of Claim 164, wherein R^2 is hydrogen.

166. The compound of any one of Claims 163 to 165, wherein R^3 is phenyl, optionally substituted with one or more R^9.

167. The compound of Claim 166, wherein R^9 is selected from halogen, optionally substituted C_{1-6} alkyl, optionally substituted C_{2-8} alkoxyalkyl, $-OR^5$, or $-NR^{14}R^{15}$.

168. The compound of Claim 167, wherein R^9 is selected from fluoro, chloro, methyl, ethyl, methoxy, ethoxy, trifluoromethyl, trifluoromethoxy, $-NHCH_3$, $-NH_2$, or $-NHC(O)CH_3$.

169. The compound of Claim 168, wherein R^9 is trifluoromethoxy.

170. The compound of any one of Claims 163 to 169, wherein ring A is a C_5 carbocyclyl optionally substituted with one or more R^4.

171. The compound of any one of Claims 163 to 169, wherein ring A is a C_6 carbocyclyl optionally substituted with one or more R^4.

172. The compound of any one of Claims 163 to 171, wherein R^4 is selected from halogen, optionally substituted C_{1-6} alkyl, optionally substituted C_{1-6} alkoxy, or independently two geminal R^4 together are oxo.

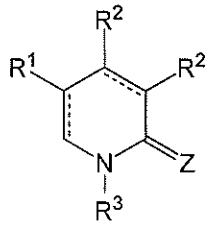
173. The compound of any one of Claims 163, 170 and 171, wherein ring A is unsubstituted.

174. The compound of any one of Claims 163 to 173, wherein Z is oxygen.

175. The compound of any one of Claims 163 to 174, wherein the bonds represented by a solid and dashed line are double bonds.

176. The compound of Claim 163, wherein the compound is selected from the group consisting of **Compounds 27** and **28** of Table 1, or pharmaceutically acceptable salts thereof.

177. A compound having the structure of formula (VIa):



(VIa)

or a pharmaceutically acceptable salt thereof, wherein

R^1 is a C_{4-7} carbocyclyl optionally substituted with one or more R^4;

each R^2 is independently selected from the group consisting of hydrogen, halogen, optionally substituted C_{1-6} alkyl, optionally substituted C_{2-6} alkenyl, optionally substituted C_{2-6} alkynyl, -CN, $-OR^5$, $-NR^6R^7$, and $-C(O)R^8$,

or both R^2 together with the carbon atoms to which they are attached form a fused ring selected from the group consisting of phenyl, 5-6 membered heteroaryl, C_{3-7} carbocyclyl, and 3-7 membered heterocyclyl, each optionally substituted with one or more R^4;

R^3 is selected from the group consisting of $-(CH_2)_n-(C_{6-10}$ aryl), $-(CH_2)_n-(5$-10 membered heteroaryl), $-(CH_2)_n-(C_{3-10}$ carbocyclyl), and $-(CH_2)_n-(3$-10 membered heterocyclyl), each optionally substituted with one or more R^9;

each R^4 is independently selected from the group consisting of halogen, -CN, -OH, $-C(O)R^8$, $-SO_2R^{16}$, optionally substituted C_{1-6} alkyl, optionally substituted C_{2-6} alkenyl, optionally substituted C_{2-6} alkynyl, optionally substituted C_{1-6} alkoxy, optionally substituted C_{6-10} aryl optionally substituted with one or more R^{11}, C_{7-14} aralkyl optionally substituted with one or more R^{11}, 5-10 membered heteroaryl optionally substituted with one or more R^{11}, or independently two geminal R^4 together are oxo;

each R^5 is independently selected from the group consisting of hydrogen, optionally substituted C_{1-6} alkyl, optionally substituted C_{2-6} alkenyl, optionally substituted C_{2-6} alkynyl, optionally substituted C_{2-8} alkoxyalkyl, C_{6-10} aryl optionally substituted with one or more R^{11}, C_{7-14} aralkyl optionally substituted with one or more R^{11}, and $-(CH_2)_n-(3$-10 membered heterocyclyl) optionally substituted with one or more R^{10};

R^6 is selected from the group consisting of hydrogen, optionally substituted C_{1-6} alkyl, optionally substituted C_{2-6} alkenyl, optionally substituted C_{2-6} alkynyl, C_{6-10} aryl optionally substituted with one or more R^{11}, C_{7-14} aralkyl optionally substituted with one or more R^{11}, (5-10 membered heteroaryl)alkyl optionally substituted with one or more R^{11}, $-C(O)R^8$, and $-C(O)OR^5$;

R^7 is selected from the group consisting of hydrogen, optionally substituted C_{1-6} alkyl, optionally substituted C_{2-6} alkenyl, optionally substituted C_{2-6} alkynyl, C_{6-10} aryl optionally substituted with one or more R^{11}, C_{7-14} aralkyl optionally substituted with one or more R^{11}, (5-10 membered heteroaryl)alkyl optionally substituted with one or more R^{11}, -C(O)R^8, and -C(O)OR^5;

or R^6 and R^7 together with the nitrogen to which they are attached form an 3-10 membered heterocyclyl optionally substituted with one or more R^{10};

each R^8 is independently selected from the group consisting of hydrogen, optionally substituted C_{1-6} alkyl, optionally substituted C_{2-6} alkenyl, optionally substituted C_{2-6} alkynyl, C_{6-10} aryl optionally substituted with one or more R^{11}, C_{7-14} aralkyl optionally substituted with one or more R^{11}, -N$R^{12}R^{13}$, and -OR^5;

each R^9 is independently selected from the group consisting of halogen, optionally substituted C_{1-6} alkyl, optionally substituted C_{2-6} alkenyl, optionally substituted C_{2-6} alkynyl, optionally substituted C_{1-6} alkylthio, optionally substituted C_{2-8} alkoxyalkyl, optionally substituted C_{3-10} carbocyclyl, optionally substituted C_{6-10} aryl, -OR^5, -N$R^{14}R^{15}$, -C(O)R^8, -SO_2R^{16}, and –NO_2;

each R^{10} is independently selected from the group consisting of optionally substituted C_{1-6} alkyl, optionally substituted C_{2-6} alkenyl, and optionally substituted C_{2-6} alkynyl, or independently two geminal R^{10} together are oxo;

each R^{11} is independently selected from the group consisting of halogen, -CN, optionally substituted C_{1-6} alkyl, optionally substituted C_{2-6} alkenyl, optionally substituted C_{2-6} alkynyl, and optionally substituted C_{1-6} alkoxy;

each R^{12} is independently selected from the group consisting of hydrogen, optionally substituted C_{1-6} alkyl, optionally substituted C_{2-6} alkenyl, optionally substituted C_{2-6} alkynyl, C_{6-10} aryl optionally substituted with one or more R^{11}, and C_{7-14} aralkyl optionally substituted with one or more R^{11};

each R^{13} is independently selected from the group consisting of hydrogen, optionally substituted C_{1-6} alkyl, optionally substituted C_{2-6} alkenyl, optionally substituted C_{2-6} alkynyl, C_{6-10} aryl optionally substituted with one or more R^{11}, and C_{7-14} aralkyl optionally substituted with one or more R^{11};

R^{14} is selected from the group consisting of hydrogen, optionally substituted C_{1-6} alkyl, optionally substituted C_{6-10} aryl, and -C(O)R^8;

R^{15} is selected from the group consisting of hydrogen, optionally substituted C_{1-6} alkyl, optionally substituted C_{6-10} aryl, and -C(O)R^8;

each R^{16} is independently selected from the group consisting of optionally substituted C_{1-6} alkyl, optionally substituted C_{2-6} alkenyl, optionally substituted C_{2-6} alkynyl, C_{6-10} aryl optionally substituted with one or more R^{11}, C_{7-14} aralkyl optionally substituted with one or more R^{11}, $-NR^{12}R^{13}$, and $-OR^5$;

Z is selected from oxygen and sulfur;

each n is independently an integer from 0 to 4; and

the bonds represented by a solid and dashed line are independently selected from the group consisting of a single bond and a double bond.

178. The compound of Claim 177, wherein R^1 is a C_4 carbocyclyl optionally substituted with one or more R^4.

179. The compound of Claim 177, wherein R^1 is a C_5 carbocyclyl optionally substituted with one or more R^4.

180. The compound of Claim 177, wherein R^1 is a C_6 carbocyclyl optionally substituted with one or more R^4.

181. The compound of any one of Claims 177 to 180, wherein R^4 is selected from halogen, optionally substituted C_{1-6} alkyl, or optionally substituted C_{1-6} alkoxy.

182. The compound of Claim 181, wherein R^4 is selected from fluoro, chloro, methyl, methoxy, ethoxy, trifluoromethyl, or trifluoromethoxy.

183. The compound of Claim 177, wherein R^1 is unsubstituted.

184. The compound of any one of Claims 177 to 183, wherein each R^2 is independently selected from hydrogen, halogen, optionally substituted C_{1-6} alkyl, $-OR^5$ or $-NR^6R^7$.

185. The compound of Claim 184, wherein R^2 is hydrogen.

186. The compound of Claim 184, wherein R^2 is halogen.

187. The compound of Claim 184, wherein R^2 is optionally substituted C_{1-6} alkyl.

188. The compound of Claim 187, wherein R^2 is selected from methyl or trifluoromethyl.

189. The compound of any one of Claims 177 to 188, wherein R^3 is selected from $-(CH_2)_n-(C_{6-10}$ aryl), optionally substituted with one or more R^9.

190. The compound of Claim 189, wherein R^3 is phenyl, optionally substituted with one or more R^9.

191. The compound of Claim 190, wherein R^9 is selected from halogen, optionally substituted C_{1-6} alkyl, optionally substituted C_{2-8} alkoxyalkyl, $-OR^5$, or $-NR^{14}R^{15}$.

192. The compound of Claim 191, wherein R^9 is selected from fluoro, chloro, methyl, ethyl, methoxy, ethoxy, trifluoromethyl, trifluoromethoxy, $-NHCH_3$, $-NH_2$, or $-NHC(O)CH_3$.

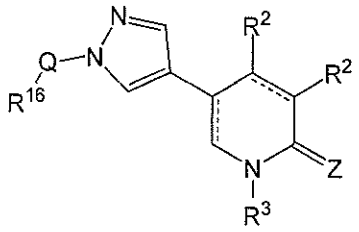
193. The compound of Claim 190, wherein R^3 is unsubstituted phenyl.

194. The compound of any one of Claims 177 to 193, wherein Z is oxygen.

195. The compound of any one of Claims 177 to 194, wherein the bonds represented by a solid and dashed line are double bonds.

196. The compound of Claim 177, wherein the compound is selected from the group consisting of **Compounds 64-66** of Table 1, or pharmaceutically acceptable salts thereof.

197. A compound having the structure of formula (VII):



(VII)

or a pharmaceutically acceptable salt thereof, wherein

each R^2 is independently selected from the group consisting of hydrogen, halogen, optionally substituted C_{1-6} alkyl, optionally substituted C_{2-6} alkenyl, optionally substituted C_{2-6} alkynyl, -CN, $-OR^5$, $-NR^6R^7$, and $-C(O)R^8$,

or both R^2 together with the carbon atoms to which they are attached form a fused ring selected from the group consisting of phenyl, 5-6 membered heteroaryl, C_{3-7} carbocyclyl, and 3-7 membered heterocyclyl, each optionally substituted with one or more R^4;

R^3 is selected from the group consisting of $-(CH_2)_n-(C_{6-10}$ aryl), $-(CH_2)_n-(5$-10 membered heteroaryl), $-(CH_2)_n-(C_{3-10}$ carbocyclyl), and $-(CH_2)_n-(3$-10 membered heterocyclyl), each optionally substituted with one or more R^9;

each R^4 is independently selected from the group consisting of halogen, -CN, -OH, $-C(O)R^8$, $-SO_2R^{16}$, optionally substituted C_{1-6} alkyl, optionally substituted C_{2-6} alkenyl, optionally substituted C_{2-6} alkynyl, optionally substituted C_{1-6} alkoxy, optionally substituted C_{6-10} aryl optionally substituted with one or more R^{11}, C_{7-14} aralkyl optionally substituted with one or more R^{11}, 5-10 membered heteroaryl optionally substituted with one or more R^{11}, or independently two geminal R^4 together are oxo;

each R^5 is independently selected from the group consisting of hydrogen, optionally substituted C_{1-6} alkyl, optionally substituted C_{2-6} alkenyl, optionally substituted C_{2-6} alkynyl, optionally substituted C_{2-8} alkoxyalkyl, C_{6-10} aryl optionally substituted with one or more R^{11}, C_{7-14} aralkyl optionally substituted with one or more

R^{11}, and -$(CH_2)_n$-(3-10 membered heterocyclyl) optionally substituted with one or more R^{10};

R^6 is selected from the group consisting of hydrogen, optionally substituted C_{1-6} alkyl, optionally substituted C_{2-6} alkenyl, optionally substituted C_{2-6} alkynyl, C_{6-10} aryl optionally substituted with one or more R^{11}, C_{7-14} aralkyl optionally substituted with one or more R^{11}, (5-10 membered heteroaryl)alkyl optionally substituted with one or more R^{11}, -C(O)R^8, and -C(O)OR^5;

R^7 is selected from the group consisting of hydrogen, optionally substituted C_{1-6} alkyl, optionally substituted C_{2-6} alkenyl, optionally substituted C_{2-6} alkynyl, C_{6-10} aryl optionally substituted with one or more R^{11}, C_{7-14} aralkyl optionally substituted with one or more R^{11}, (5-10 membered heteroaryl)alkyl optionally substituted with one or more R^{11}, -C(O)R^8, and -C(O)OR^5;

or R^6 and R^7 together with the nitrogen to which they are attached form an 3-10 membered heterocyclyl optionally substituted with one or more R^{10};

each R^8 is independently selected from the group consisting of hydrogen, optionally substituted C_{1-6} alkyl, optionally substituted C_{2-6} alkenyl, optionally substituted C_{2-6} alkynyl, C_{6-10} aryl optionally substituted with one or more R^{11}, C_{7-14} aralkyl optionally substituted with one or more R^{11}, -N$R^{12}R^{13}$, and -OR^5;

each R^9 is independently selected from the group consisting of halogen, optionally substituted C_{1-6} alkyl, optionally substituted C_{2-6} alkenyl, optionally substituted C_{2-6} alkynyl, optionally substituted C_{1-6} alkylthio, optionally substituted C_{2-8} alkoxyalkyl, optionally substituted C_{3-10} carbocyclyl, optionally substituted C_{6-10} aryl, -OR^5, -N$R^{14}R^{15}$, -C(O)R^8, -SO_2R^{16}, and –NO_2;

each R^{10} is independently selected from the group consisting of optionally substituted C_{1-6} alkyl, optionally substituted C_{2-6} alkenyl, and optionally substituted C_{2-6} alkynyl, or independently two geminal R^{10} together are oxo;

each R^{11} is independently selected from the group consisting of halogen, -CN, optionally substituted C_{1-6} alkyl, optionally substituted C_{2-6} alkenyl, optionally substituted C_{2-6} alkynyl, and optionally substituted C_{1-6} alkoxy;

each R^{12} is independently selected from the group consisting of hydrogen, optionally substituted C_{1-6} alkyl, optionally substituted C_{2-6} alkenyl, optionally substituted C_{2-6} alkynyl, C_{6-10} aryl optionally substituted with one or more R^{11}, and C_{7-14} aralkyl optionally substituted with one or more R^{11};

each R^{13} is independently selected from the group consisting of hydrogen, optionally substituted C_{1-6} alkyl, optionally substituted C_{2-6} alkenyl, optionally

substituted C_{2-6} alkynyl, C_{6-10} aryl optionally substituted with one or more R^{11}, and C_{7-14} aralkyl optionally substituted with one or more R^{11};

R^{14} is selected from the group consisting of hydrogen, optionally substituted C_{1-6} alkyl, optionally substituted C_{6-10} aryl, and $-C(O)R^8$;

R^{15} is selected from the group consisting of hydrogen, optionally substituted C_{1-6} alkyl, optionally substituted C_{6-10} aryl, and $-C(O)R^8$;

Q is selected from C(O) and $S(O)_t$;

each R^{16} is independently selected from the group consisting of optionally substituted C_{1-6} alkyl, optionally substituted C_{2-6} alkenyl, optionally substituted C_{2-6} alkynyl, C_{6-10} aryl optionally substituted with one or more R^{11}, C_{7-14} aralkyl optionally substituted with one or more R^{11}, $-NR^{12}R^{13}$, and $-OR^5$;

Z is selected from oxygen and sulfur;

each n is independently an integer from 0 to 4;

t is 1 or 2; and

the bonds represented by a solid and dashed line are independently selected from the group consisting of a single bond and a double bond.

198. The compound of Claim 197, wherein each R^2 is independently selected from hydrogen, halogen, optionally substituted C_{1-6} alkyl, $-OR^5$ or $-NR^6R^7$.

199. The compound of Claim 198, wherein R^2 is hydrogen.

200. The compound of Claim 198, wherein R^2 is halogen.

201. The compound of Claim 198, wherein R^2 is optionally substituted C_{1-6} alkyl.

202. The compound of Claim 201, wherein R^2 is methyl or trifluoromethyl.

203. The compound of any one of Claims 197 to 202, wherein R^3 is selected from $-(CH_2)_n-(C_{6-10}$ aryl), optionally substituted with one or more R^9.

204. The compound of Claim 203, wherein R^3 is phenyl optionally substituted with one or more R^9.

205. The compound of Claim 204, wherein R^9 is selected from halogen, optionally substituted C_{1-6} alkyl, optionally substituted C_{2-8} alkoxyalkyl, $-OR^5$, or $-NR^{14}R^{15}$.

206. The compound of Claim 205, wherein R^9 is selected from fluoro, chloro, methyl, ethyl, methoxy, ethoxy, trifluoromethyl, trifluoromethoxy, $-NHCH_3$, $-NH_2$, or $-NHC(O)CH_3$.

207. The compound of Claim 204, wherein R^3 is unsubstituted phenyl.

208. The compound of any one of Claims 197 to 207, wherein Q is C(O).

209. The compound of any one of Claims 197 to 207, wherein Q is $S(O)_t$.

210. The compound of Claim 209, wherein t is 2.

211. The compound of any one of Claims 197 to 210, wherein R^{16} is selected from optionally substituted C_{1-6} alkyl, C_{6-10} aryl optionally substituted with one or more R^{11}, C_{7-14} aralkyl optionally substituted with one or more R^{11}, $-NR^{12}R^{13}$, or $-OR^5$.

212. The compound of Claim 211, wherein R^{16} is optionally substituted C_{1-6} alkyl.

213. The compound of Claim 212, wherein R^{16} is selected from methyl, ethyl, propyl, isopropyl, or butyl.

214. The compound of Claim 211, wherein R^{16} is phenyl optionally substituted with one or more R^{11}.

215. The compound of Claim 214, wherein R^{16} is unsubstituted phenyl.

216. The compound of Claim 211, wherein R^{16} is benzyl optionally substituted with one or more R^{11}.

217. The compound of Claim 216, wherein R^{16} is unsubstituted benzyl.

218. The compound of Claim 211, wherein R^{16} is $-NR^{12}R^{13}$.

219. The compound of Claim 218, wherein each R^{12} and R^{13} is independently selected from hydrogen or optionally substituted C_{1-6} alkyl.

220. The compound of Claim 211, wherein R^{16} is $-OR^5$.

221. The compound of Claim 220, wherein R^5 is selected from hydrogen or optionally substituted C_{1-6} alkyl.

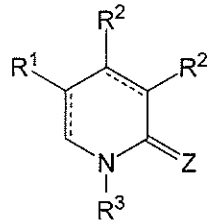
222. The compound of Claim 221, wherein R^5 is selected from methyl, ethyl, propyl, isopropyl, or butyl.

223. The compound of any one of Claims 197 to 222, wherein Z is oxygen.

224. The compound of any one of Claims 197 to 223, wherein the bonds represented by a solid and dashed line are double bonds.

225. The compound of Claim 197, wherein the compound is selected from the group consisting of **Compounds 67-76** of Table 1, or pharmaceutically acceptable salts thereof.

226. A compound having the structure of formula (VIb):



(VIb)

R^1 is selected from the group consisting of bromo, chloro, fluoro, -CN, $-C(O)R^8$, $-SO_2R^{16}$, C_{1-6} alkyl, C_{2-6} alkenyl optionally substituted with one or more R^4, C_{2-6} alkynyl optionally substituted with one or more R^4, C_{6-10} aryl optionally

substituted with one or more R^4, 5 to 6 membered heteroaryl optionally substituted with one or more R^4, C_{3-10} carbocyclyl optionally substituted with one or more R^4, and 3-10 membered heterocyclyl optionally substituted with one or more R^4;

each R^2 is independently selected from the group consisting of hydrogen, halogen, optionally substituted C_{1-6} alkyl, optionally substituted C_{2-6} alkenyl, optionally substituted C_{2-6} alkynyl, -CN, $-OR^5$, $-NR^6R^7$, and $-C(O)R^8$,

or both R^2 together with the carbon atoms to which they are attached form a fused ring selected from the group consisting of 5-6 membered heteroaryl, C_{3-7} carbocyclyl, and 3-7 membered heterocyclyl, each optionally substituted with one or more R^4;

R^3 is selected from the group consisting of $-(CH_2)_{1-4}$-(C_{6-10} aryl), $-(CH_2)_{1-4}$-(5-10 membered heteroaryl), $-(CH_2)_{1-4}$-(C_{3-10} carbocyclyl), and $-(CH_2)_{1-4}$-(3-10 membered heterocyclyl), each optionally substituted with one or more R^9;

each R^4 is independently selected from the group consisting of halogen, -CN, -OH, $-C(O)R^8$, $-SO_2R^{16}$, optionally substituted C_{1-6} alkyl, optionally substituted C_{2-6} alkenyl, optionally substituted C_{2-6} alkynyl, optionally substituted C_{1-6} alkoxy, optionally substituted C_{6-10} aryl optionally substituted with one or more R^{11}, C_{7-14} aralkyl optionally substituted with one or more R^{11}, 5-10 membered heteroaryl optionally substituted with one or more R^{11};

each R^5 is independently selected from the group consisting of optionally substituted C_{1-6} alkyl, optionally substituted C_{2-6} alkenyl, optionally substituted C_{2-6} alkynyl, optionally substituted C_{2-8} alkoxyalkyl, C_{6-10} aryl optionally substituted with one or more R^{11}, C_{7-14} aralkyl optionally substituted with one or more R^{11}, and $-(CH_2)_n$-(3-10 membered heterocyclyl) optionally substituted with one or more R^{10};

R^6 is selected from the group consisting of hydrogen, optionally substituted C_{1-6} alkyl, optionally substituted C_{2-6} alkenyl, optionally substituted C_{2-6} alkynyl, C_{6-10} aryl optionally substituted with one or more R^{11}, C_{7-14} aralkyl optionally substituted with one or more R^{11}, (5-10 membered heteroaryl)alkyl optionally substituted with one or more R^{11}, $-C(O)R^8$, and $-C(O)OR^5$;

R^7 is selected from the group consisting of hydrogen, optionally substituted C_{1-6} alkyl, optionally substituted C_{2-6} alkenyl, optionally substituted C_{2-6} alkynyl, C_{6-10} aryl optionally substituted with one or more R^{11}, C_{7-14} aralkyl optionally substituted with one or more R^{11}, (5-10 membered heteroaryl)alkyl optionally substituted with one or more R^{11}, $-C(O)R^8$, and $-C(O)OR^5$;

or R^6 and R^7 together with the nitrogen to which they are attached form an 3-10 membered heterocyclyl optionally substituted with one or more R^{10};

each R^8 is independently selected from the group consisting of hydrogen, optionally substituted C_{1-6} alkyl, optionally substituted C_{2-6} alkenyl, optionally substituted C_{2-6} alkynyl, C_{6-10} aryl optionally substituted with one or more R^{11}, C_{7-14} aralkyl optionally substituted with one or more R^{11}, $-NR^{12}R^{13}$, and $-OR^5$;

each R^9 is independently selected from the group consisting of halogen, optionally substituted C_{1-6} alkyl, optionally substituted C_{2-6} alkenyl, optionally substituted C_{2-6} alkynyl, optionally substituted C_{1-6} alkylthio, optionally substituted C_{2-8} alkoxyalkyl, optionally substituted C_{3-10} carbocyclyl, optionally substituted C_{6-10} aryl, $-OR^5$, $-NR^{14}R^{15}$, $-C(O)R^8$, $-SO_2R^{16}$, and $-NO_2$;

each R^{10} is independently selected from the group consisting of optionally substituted C_{1-6} alkyl, optionally substituted C_{2-6} alkenyl, and optionally substituted C_{2-6} alkynyl, or independently two geminal R^{10} together are oxo;

each R^{11} is independently selected from the group consisting of halogen, -CN, optionally substituted C_{1-6} alkyl, optionally substituted C_{2-6} alkenyl, optionally substituted C_{2-6} alkynyl, and optionally substituted C_{1-6} alkoxy;

each R^{12} is independently selected from the group consisting of hydrogen, optionally substituted C_{1-6} alkyl, optionally substituted C_{2-6} alkenyl, optionally substituted C_{2-6} alkynyl, C_{6-10} aryl optionally substituted with one or more R^{11}, and C_{7-14} aralkyl optionally substituted with one or more R^{11};

each R^{13} is independently selected from the group consisting of hydrogen, optionally substituted C_{1-6} alkyl, optionally substituted C_{2-6} alkenyl, optionally substituted C_{2-6} alkynyl, C_{6-10} aryl optionally substituted with one or more R^{11}, and C_{7-14} aralkyl optionally substituted with one or more R^{11};

R^{14} is selected from the group consisting of hydrogen, optionally substituted C_{1-6} alkyl, optionally substituted C_{6-10} aryl, and $-C(O)R^8$;

R^{15} is selected from the group consisting of hydrogen, optionally substituted C_{1-6} alkyl, optionally substituted C_{6-10} aryl, and $-C(O)R^8$;

each R^{16} is independently selected from the group consisting of optionally substituted C_{1-6} alkyl, optionally substituted C_{2-6} alkenyl, optionally substituted C_{2-6} alkynyl, C_{6-10} aryl optionally substituted with one or more R^{11}, C_{7-14} aralkyl optionally substituted with one or more R^{11}, $-NR^{12}R^{13}$, and $-OR^5$;

Z is selected from oxygen and sulfur;

each n is independently an integer from 0 to 4; and

the bonds represented by a solid and dashed line are independently selected from the group consisting of a single bond and a double bond; provided that

when R^1 is selected from the group consisting of optionally substituted C_{6-10} aryl, optionally substituted 5 to 6 membered heteroaryl, optionally substituted 6 to 10 membered heterocyclyl, optionally substituted hexyl, C_{1-6}alkyl, optionally substituted C_{2-6} alkenyl; each of R^2 is hydrogen or one of R^2 is hydrogen and the other R^2 is methyl; and Z is O; then R^3 is not -CH_2-phenyl substituted with one or more halogen atoms; and provided that

R^1 is not 4-methoxy phenyl.

227. The compound of Claim 226, wherein R^1 is selected from C_{1-6} alkyl optionally substituted with one or more R^4, C_{6-10} aryl optionally substituted with one or more R^4, or 5to 6 membered heteroaryl optionally substituted with one or more R^4.

228. The compound of Claim 227, wherein R^1 is selected from C_{1-6} alkyl.

229. The compound of Claim 228, wherein R^1 is selected from methyl, ethyl, propyl, or isopropyl.

230. The compound of Claim 227, wherein R^1 is phenyl optionally substituted with one or more R^4.

231. The compound of Claim 227, wherein R^1 is selected from 5 or 6 membered heteroaryl, each optionally substituted with one or more R^4.

232. The compound of Claim 231, wherein R^1 is selected from pyrazolyl or 1-methyl pyrazolyl, each optionally substituted with one or more R^4.

233. The compound of any one of Claims 226 to 232, wherein R^4 is selected from halogen or optionally substituted C_{1-6} alkyl.

234. The compound of Claim 233, wherein R^4 is fluoro.

235. The compound of any one of Claims 226 to 232, wherein R^1 is unsubstituted.

236. The compound of any one of Claims 226 to 235, wherein each R^2 is independently selected from hydrogen, halogen, or optionally substituted C_{1-6} alkyl.

237. The compound of Claim 236, wherein R^2 is hydrogen.

238. The compound of any one of Claims 226 to 237, wherein R^3 is -$(CH_2)_{1-4}$-(C_{6-10} aryl), optionally substituted with one or more R^9.

239. The compound of Claim 238, wherein R^3 is -$(CH_2)_{1-4}$-phenyl, optionally substituted with one or more R^9.

240. The compound of Claim 239, wherein R^3 is -(CH_2)-phenyl, optionally substituted with one or more R^9.

241. The compound of Claim 239, wherein R^3 is -$(CH_2)_2$-phenyl, optionally substituted with one or more R^9.

242. The compound of any one of Claims 226 to 241, wherein R^9 is selected from halogen, optionally substituted C_{1-6} alkyl, optionally substituted C_{2-8} alkoxyalkyl, $-OR^5$, $-C(O)R^8$ or $-NR^{14}R^{15}$.

243. The compound of Claim 242, wherein R^9 is selected from fluoro, chloro, methyl, ethyl, methoxy, ethoxy, trifluoromethyl, trifluoromethoxy, $-C(O)CH_3$, $-NHCH_3$, $-NH_2$, or $-NHC(O)CH_3$.

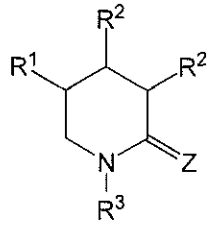
244. The compound of any one of Claims 238 to 241, wherein R^3 is unsubstituted.

245. The compound of any one of Claims 226 to 244, wherein Z is oxygen.

246. The compound of any one of Claims 226 to 245, wherein the bonds represented by a solid and dashed line are double bonds.

247. The compound of Claim 226, wherein the compound is selected from the group consisting of **Compounds 77-80** of Table 1, or pharmaceutically acceptable salts thereof.

248. A compound having the structure of formula (IX):



(IX)

R^1 is selected from the group consisting of hydrogen, halogen, -CN, $-C(O)R^8$, $-SO_2R^{16}$, C_{1-6} alkyl optionally substituted with one or more R^4, C_{2-6} alkenyl optionally substituted with one or more R^4, C_{2-6} alkynyl optionally substituted with one or more R^4, C_{6-10} aryl optionally substituted with one or more R^4, 5-10 membered heteroaryl optionally substituted with one or more R^4, C_{3-10} carbocyclyl optionally substituted with one or more R^4, and 3-10 membered heterocyclyl optionally substituted with one or more R^4;

each R^2 is independently selected from the group consisting of hydrogen, halogen, optionally substituted C_{1-6} alkyl, optionally substituted C_{2-6} alkenyl, optionally substituted C_{2-6} alkynyl, -CN, $-OR^5$, $-NR^6R^7$, and $-C(O)R^8$,

or both R^2 together with the carbon atoms to which they are attached form a fused ring selected from the group consisting of C_{3-7} carbocyclyl and 3-7 membered heterocyclyl, each optionally substituted with one or more R^4;

R^3 is selected from the group consisting of $-(CH_2)_n$-(C_{6-10} aryl), 5-10 membered heteroaryl, $-(CH_2)_n$-(C_{3-10} carbocyclyl), and $-(CH_2)_n$-(3-10 membered heterocyclyl), each optionally substituted with one or more R^9;

each R^4 is independently selected from the group consisting of halogen, -CN, -OH, $-C(O)R^8$, $-SO_2R^{16}$, optionally substituted C_{1-6} alkyl, optionally substituted C_{2-6} alkenyl, optionally substituted C_{2-6} alkynyl, optionally substituted C_{1-6} alkoxy, optionally substituted C_{6-10} aryl optionally substituted with one or more R^{11}, C_{7-14} aralkyl optionally substituted with one or more R^{11}, 5-10 membered heteroaryl optionally substituted with one or more R^{11}, or independently two geminal R^4 together are oxo;

each R^5 is independently selected from the group consisting of hydrogen, optionally substituted C_{1-6} alkyl, optionally substituted C_{2-6} alkenyl, optionally substituted C_{2-6} alkynyl, optionally substituted C_{2-8} alkoxyalkyl, C_{6-10} aryl optionally substituted with one or more R^{11}, C_{7-14} aralkyl optionally substituted with one or more R^{11}, and $-(CH_2)_n$-(3-10 membered heterocyclyl) optionally substituted with one or more R^{10};

R^6 is selected from the group consisting of hydrogen, optionally substituted C_{1-6} alkyl, optionally substituted C_{2-6} alkenyl, optionally substituted C_{2-6} alkynyl, C_{6-10} aryl optionally substituted with one or more R^{11}, C_{7-14} aralkyl optionally substituted with one or more R^{11}, (5-10 membered heteroaryl)alkyl optionally substituted with one or more R^{11}, $-C(O)R^8$, and $-C(O)OR^5$;

R^7 is selected from the group consisting of hydrogen, optionally substituted C_{1-6} alkyl, optionally substituted C_{2-6} alkenyl, optionally substituted C_{2-6} alkynyl, C_{6-10} aryl optionally substituted with one or more R^{11}, C_{7-14} aralkyl optionally substituted with one or more R^{11}, (5-10 membered heteroaryl)alkyl optionally substituted with one or more R^{11}, $-C(O)R^8$, and $-C(O)OR^5$;

or R^6 and R^7 together with the nitrogen to which they are attached form an 3-10 membered heterocyclyl optionally substituted with one or more R^{10};

each R^8 is independently selected from the group consisting of hydrogen, optionally substituted C_{1-6} alkyl, optionally substituted C_{2-6} alkenyl, optionally substituted C_{2-6} alkynyl, C_{6-10} aryl optionally substituted with one or more R^{11}, C_{7-14} aralkyl optionally substituted with one or more R^{11}, $-NR^{12}R^{13}$, and $-OR^5$;

each R^9 is independently selected from the group consisting of halogen, optionally substituted C_{1-6} alkyl, optionally substituted C_{2-6} alkenyl, optionally substituted C_{2-6} alkynyl, optionally substituted C_{1-6} alkylthio, optionally substituted C_{2-8} alkoxyalkyl, optionally substituted C_{3-10} carbocyclyl, optionally substituted C_{6-10} aryl, $-OR^5$, $-NR^{14}R^{15}$, $-C(O)R^8$, $-SO_2R^{16}$, and $-NO_2$;

each R^{10} is independently selected from the group consisting of optionally substituted C_{1-6} alkyl, optionally substituted C_{2-6} alkenyl, and optionally substituted C_{2-6} alkynyl, or independently two geminal R^{10} together are oxo;

each R^{11} is independently selected from the group consisting of halogen, -CN, optionally substituted C_{1-6} alkyl, optionally substituted C_{2-6} alkenyl, optionally substituted C_{2-6} alkynyl, and optionally substituted C_{1-6} alkoxy;

each R^{12} is independently selected from the group consisting of hydrogen, optionally substituted C_{1-6} alkyl, optionally substituted C_{2-6} alkenyl, optionally substituted C_{2-6} alkynyl, C_{6-10} aryl optionally substituted with one or more R^{11}, and C_{7-14} aralkyl optionally substituted with one or more R^{11};

each R^{13} is independently selected from the group consisting of hydrogen, optionally substituted C_{1-6} alkyl, optionally substituted C_{2-6} alkenyl, optionally substituted C_{2-6} alkynyl, C_{6-10} aryl optionally substituted with one or more R^{11}, and C_{7-14} aralkyl optionally substituted with one or more R^{11};

R^{14} is selected from the group consisting of hydrogen, optionally substituted C_{1-6} alkyl, optionally substituted C_{6-10} aryl, and $-C(O)R^8$;

R^{15} is selected from the group consisting of hydrogen, optionally substituted C_{1-6} alkyl, optionally substituted C_{6-10} aryl, and $-C(O)R^8$;

each R^{16} is independently selected from the group consisting of optionally substituted C_{1-6} alkyl, optionally substituted C_{2-6} alkenyl, optionally substituted C_{2-6} alkynyl, C_{6-10} aryl optionally substituted with one or more R^{11}, C_{7-14} aralkyl optionally substituted with one or more R^{11}, $-NR^{12}R^{13}$, and $-OR^5$;

Z is selected from oxygen and sulfur; and

each n is independently an integer from 0 to 4.

249. The compound of Claim 248, wherein R^1 is selected from C_{1-6} alkyl optionally substituted with one or more R^4, C_{6-10} aryl optionally substituted with one or more R^4, or 5-10 membered heteroaryl optionally substituted with one or more R^4.

250. The compound of Claim 249, wherein R^1 is C_{1-6} alkyl optionally substituted with one or more R^4.

251. The compound of Claim 249, wherein R^1 is C_{6-10} aryl optionally substituted with one or more R^4.

252. The compound of Claim 251, wherein R^1 is phenyl optionally substituted with one or more R^4.

253. The compound of Claim 249, wherein R^1 is 5 or 6 membered heteroaryl optionally substituted with one or more R^4.

254. The compound of Claim 253, wherein R^1 is pyrazolyl or 1-methyl pyrazolyl optionally substituted with one or more R^4.

255. The compound of any one of Claims 249 to 254, wherein R^4 is selected from halogen, optionally substituted C_{1-6} alkyl or optionally substituted C_{1-6} alkoxy.

256. The compound of any one of Claims 249 to 254, wherein R^1 is unsubstituted.

257. The compound of any one of Claims 248 to 256, wherein each R^2 is independently selected from hydrogen, halogen or optionally substituted C_{1-6} alkyl.

258. The compound of Claim 257, wherein R^2 is hydrogen.

259. The compound of any one of Claims 248 to 258, wherein R^3 is $-(CH_2)_n-(C_{6-10}$ aryl), optionally substituted with one or more R^9.

260. The compound of Claim 259, wherein R^3 is phenyl optionally substituted with one or more R^9.

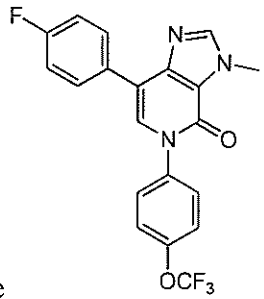
261. The compound of Claim 259 or 260, wherein R^9 is selected from halogen, optionally substituted C_{1-6} alkyl, optionally substituted C_{2-8} alkoxyalkyl, $-OR^5$, $-C(O)R^8$ or $-NR^{14}R^{15}$.

262. The compound of Claim 261, wherein R^9 is selected from fluoro, chloro, methyl, ethyl, methoxy, ethoxy, trifluoromethyl, trifluoromethoxy, $-C(O)CH_3$, $-NHCH_3$, $-NH_2$, or $-NHC(O)CH_3$.

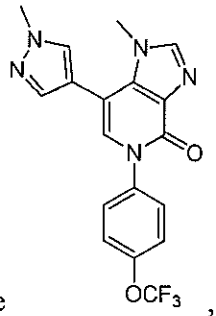
263. The compound of Claim 259 or 260, wherein R^3 is unsubstituted.

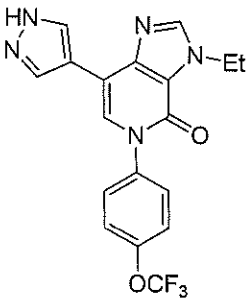
264. The compound of any one of Claims 248 to 263, wherein Z is oxygen.

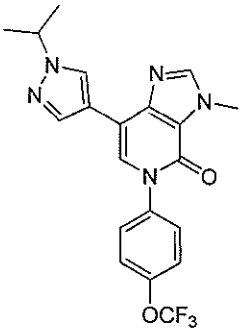
265. The compound of Claim 248, wherein the compound is selected from the group consisting of **Compounds 83**, **84**, **520-522** of Table 1, or pharmaceutically acceptable salts thereof.

266. A compound of structure 

, or a pharmaceutically acceptable salt thereof.

267. A compound of structure  , or a pharmaceutically acceptable salt thereof.

268. A compound of structure  , or a pharmaceutically acceptable salt thereof.

269. A compound of structure  , or a pharmaceutically acceptable salt thereof.

270. A pharmaceutical composition comprising an effective amount of a compound of any one of Claims 1 to 269, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier, diluent, excipient or combination thereof.

271. A therapeutically effective amount of a compound of any one of Claims 1 to 269, a pharmaceutically acceptable salt thereof, or a pharmaceutical composition of Claim 270 for use in the treatment of a fibrotic condition.

272. The compound for use of Claim 271, wherein the fibrotic condition is selected from pulmonary fibrosis, dermal fibrosis, pancreatic fibrosis, liver fibrosis, and renal fibrosis.

273. The compound for use of Claim 272, wherein the fibrotic condition is idiopathic pulmonary fibrosis.

274. The compound for use of any one of Claims 271 to 273, wherein the compound, the pharmaceutical acceptable salt thereof, or the pharmaceutical composition is for use by inhalation.

275. Use of a therapeutically effective amount of a compound of any one of Claims 1 to 269, a pharmaceutically acceptable salt thereof, or a pharmaceutical composition of Claim 270 in the preparation of a medicament for treating a fibrotic condition.