

-C(O)OC₁-C₆ alkyl, -C(O)NH₂, -C(O)NH(C₁-C₆ alkyl), -C(O)N(C₁-C₆ alkyl)₂, C₃-C₆ cycloalkyl, or monocyclic 5- to 7-membered heterocycloalkyl;

[0011] R⁵, R⁶ and R⁷ are each independently selected from the group consisting of H, fluoro, chloro, bromo, C₁-C₆ alkyl, -OH, -CN, -OC₁-C₆ alkyl, -NHC₁-C₆ alkyl, -N(C₁-C₆ alkyl)₂, C₃-C₆ cycloalkyl, 3- to 7-membered heterocycloalkyl, -O-(C₃-C₆ cycloalkyl), -O-(3- to 7-membered heterocycloalkyl), 5- to 7-membered heteroaryl, C₆-C₁₀ aryl, and -CF₃; wherein each hydrogen atom in C₁-C₆ alkyl, -OC₁-C₆ alkyl, -NHC₁-C₆ alkyl, -N(C₁-C₆ alkyl)₂, C₃-C₆ cycloalkyl, 3- to 7-membered heterocycloalkyl, -O-(C₃-C₆ cycloalkyl), -O-(3- to 7-membered heterocycloalkyl), 5- to 7-membered heteroaryl and C₆-C₁₀ aryl is independently optionally substituted by fluoro, chloro, bromo, -OH, -CN, -OC₁-C₆ alkyl, -NH₂, -NH(C₁-C₆ alkyl), -N(C₁-C₆ alkyl)₂, C₃-C₇ cycloalkyl, 3- to 7-membered heterocycloalkyl, C₆-C₁₀ aryl, 5- to 7-membered heteroaryl, -CO₂H, -C(O)OC₁-C₆ alkyl, -C(O)NH₂, -C(O)NH(C₁-C₆ alkyl) and -C(O)N(C₁-C₆ alkyl)₂;

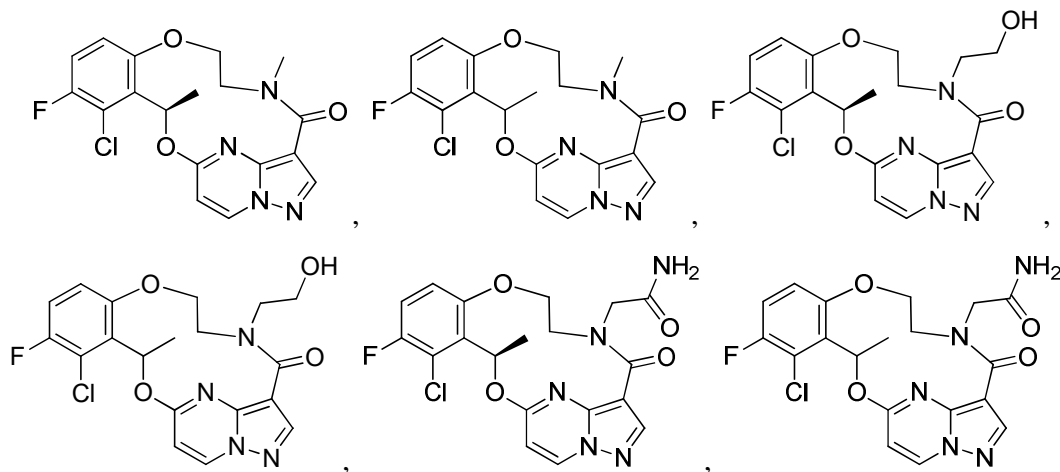
[0012] each R⁸ and R⁹ is independently H, deuterium, C₁-C₆ alkyl, C₂-C₆ alkenyl, C₂-C₆ alkynyl, C₃-C₆ cycloalkyl, 3- to 7-membered heterocycloalkyl, C₆-C₁₀ aryl or heteroaryl;

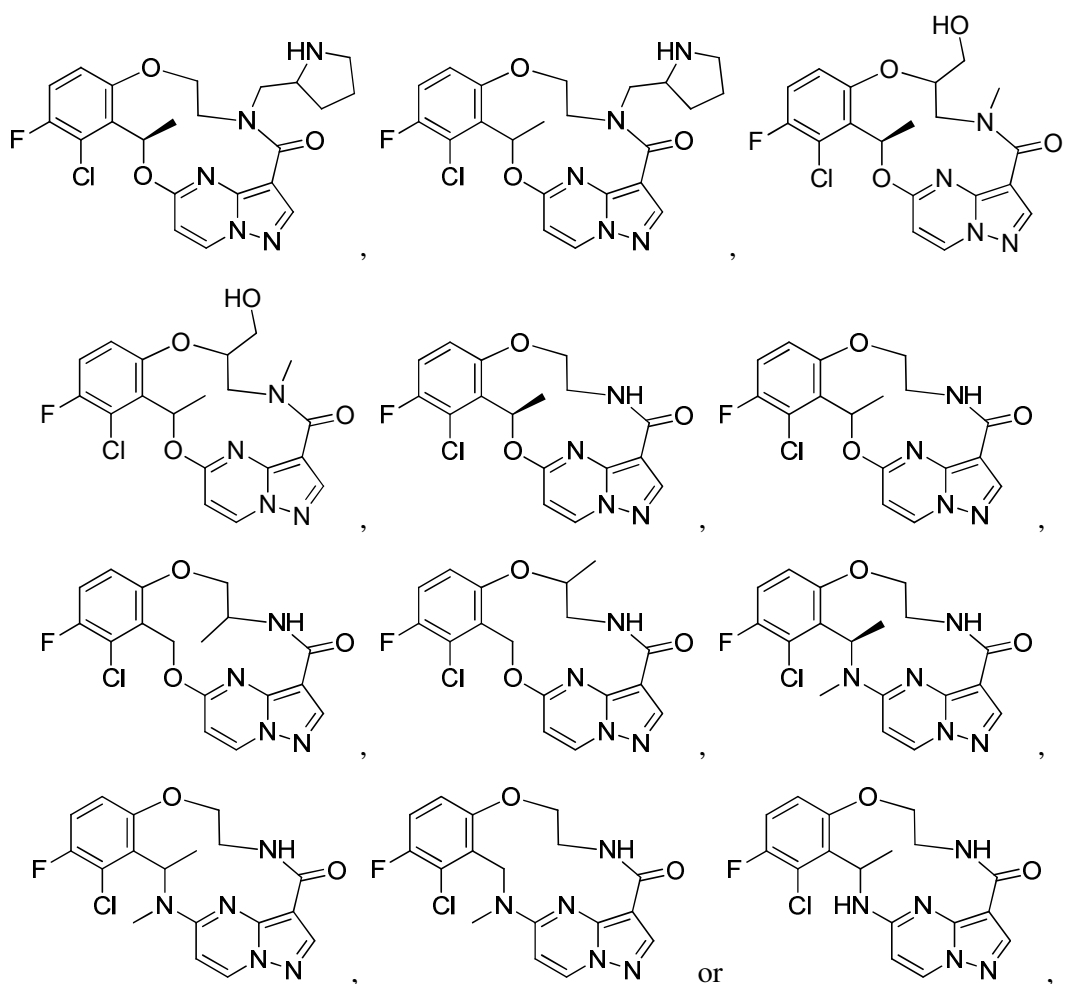
[0013] each R¹⁰ is independently H, deuterium, C₁-C₆ alkyl, C₂-C₆ alkenyl, C₂-C₆ alkynyl, C₃-C₆ cycloalkyl, 3- to 7-membered heterocycloalkyl, C₆-C₁₀ aryl, or mono- or bicyclic heteroaryl; wherein each hydrogen atom in C₁-C₆ alkyl, C₂-C₆ alkenyl, C₂-C₆ alkynyl, C₃-C₆ cycloalkyl, 3- to 7-membered heterocycloalkyl, C₆-C₁₀ aryl, or mono- or bicyclic heteroaryl is independently optionally substituted by deuterium, halogen, C₁-C₆ alkyl, C₁-C₆ haloalkyl or -OR⁸;

[0014] n is 1 or 2; and

[0015] provided that at least one of R⁵ or R⁷ is not H.

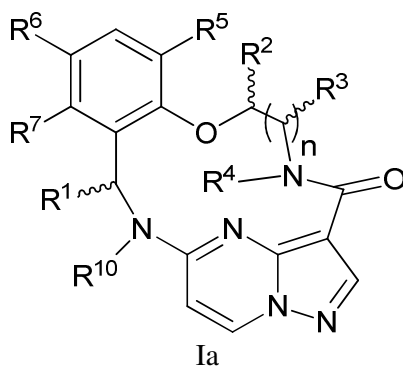
[0016] In some examples, the compound of the formula I is not of the formula





or a pharmaceutically acceptable salt thereof.

[018] In another example, there is provided a compound of the formula Ia



[019] or a pharmaceutically acceptable salt thereof, wherein

[020] R^1 is H, deuterium, C_1 - C_6 alkyl, C_2 - C_6 alkenyl, C_2 - C_6 alkynyl, C_3 - C_6 cycloalkyl, C_6 - C_{10} aryl, $-C(O)OR^8$ or $-C(O)NR^8R^9$; wherein each hydrogen atom in C_1 - C_6 alkyl, C_2 - C_6 alkenyl, C_2 - C_6 alkynyl, C_3 - C_6 cycloalkyl and C_6 - C_{10} aryl is independently optionally substituted by deuterium, halogen, $-OH$, $-CN$, $-OC_1$ - C_6 alkyl, $-NH_2$, $-NH(C_1$ - C_6 alkyl), $-N(C_1$ - C_6 alkyl) $_2$,

-C(O)OC₁-C₆ alkyl, -C(O)NH₂, -C(O)NH(C₁-C₆ alkyl), -C(O)N(C₁-C₆ alkyl)₂, C₃-C₆ cycloalkyl, or monocyclic 5- to 7-membered heterocycloalkyl;

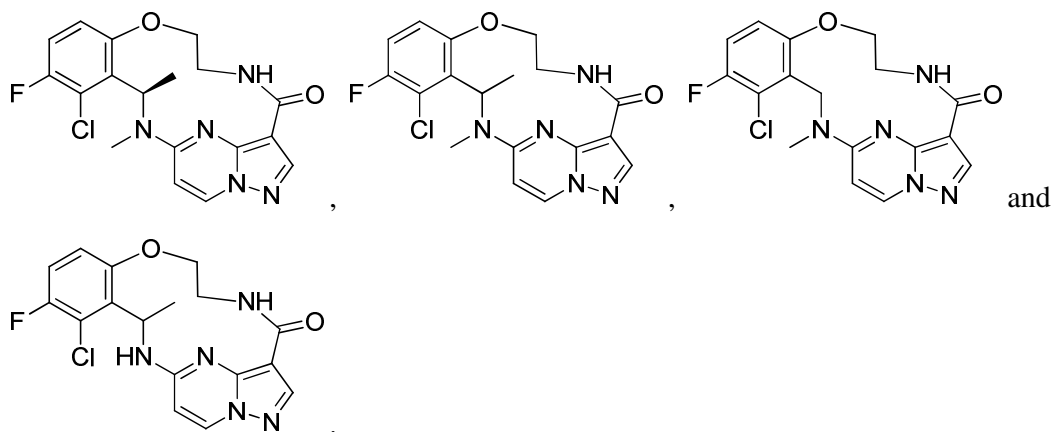
[023] R⁵, R⁶ and R⁷ are each independently selected from the group consisting of H, fluoro, chloro, bromo, C₁-C₆ alkyl, -OH, -CN, -OC₁-C₆ alkyl, -NHC₁-C₆ alkyl, -N(C₁-C₆ alkyl)₂, C₃-C₆ cycloalkyl, 3- to 7-membered heterocycloalkyl, -O-(C₃-C₆ cycloalkyl), -O-(3- to 7-membered heterocycloalkyl), 5- to 7-membered heteroaryl, C₆-C₁₀ aryl, and -CF₃; wherein each hydrogen atom in C₁-C₆ alkyl, -OC₁-C₆ alkyl, -NHC₁-C₆ alkyl, -N(C₁-C₆ alkyl)₂, C₃-C₆ cycloalkyl, 3- to 7-membered heterocycloalkyl, -O-(C₃-C₆ cycloalkyl), -O-(3- to 7-membered heterocycloalkyl), 5- to 7-membered heteroaryl and C₆-C₁₀ aryl is independently optionally substituted by fluoro, chloro, bromo, -OH, -CN, -OC₁-C₆ alkyl, -NH₂, -NH(C₁-C₆ alkyl), -N(C₁-C₆ alkyl)₂, C₃-C₇ cycloalkyl, 3-to 7-membered heterocycloalkyl, C₆-C₁₀ aryl, 5- to 7-membered heteroaryl, -CO₂H, -C(O)OC₁-C₆ alkyl, -C(O)NH₂, -C(O)NH(C₁-C₆ alkyl) and -C(O)N(C₁-C₆ alkyl)₂;

[024] each R⁸ and R⁹ is independently H, deuterium, C₁-C₆ alkyl, C₂-C₆ alkenyl, C₂-C₆ alkynyl, C₃-C₆ cycloalkyl, 3- to 7-membered heterocycloalkyl, C₆-C₁₀ aryl or heteroaryl;

[025] each R¹⁰ is independently H, deuterium, C₁-C₆ alkyl, C₂-C₆ alkenyl, C₂-C₆ alkynyl, C₃-C₆ cycloalkyl, 3- to 7-membered heterocycloalkyl, C₆-C₁₀ aryl, or mono- or bicyclic heteroaryl; wherein each hydrogen atom in C₁-C₆ alkyl, C₂-C₆ alkenyl, C₂-C₆ alkynyl, C₃-C₆ cycloalkyl, 3- to 7-membered heterocycloalkyl, C₆-C₁₀ aryl, or mono- or bicyclic heteroaryl is independently optionally substituted by deuterium, halogen, C₁-C₆ alkyl, C₁-C₆ haloalkyl or -OR⁸;

[026] n is 1 or 2;

[027] provided that at least one of R⁵ or R⁷ is not H; and provided that the compound is not of the formula

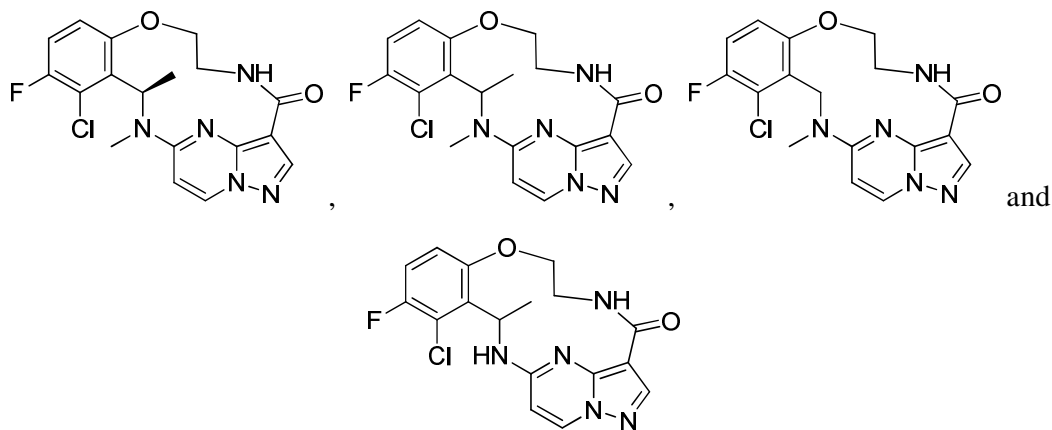


[028] In another example, there is provided a compound of the formula Ib

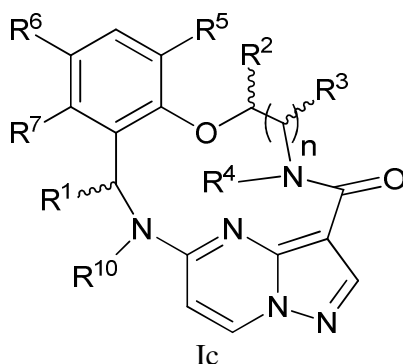
[036] each R¹⁰ is independently H, deuterium, C₁-C₆ alkyl, C₂-C₆ alkenyl, C₂-C₆ alkynyl, C₃-C₆ cycloalkyl, 3- to 7-membered heterocycloalkyl, C₆-C₁₀ aryl, or mono- or bicyclic heteroaryl; wherein each hydrogen atom in C₁-C₆ alkyl, C₂-C₆ alkenyl, C₂-C₆ alkynyl, C₃-C₆ cycloalkyl, 3- to 7-membered heterocycloalkyl, C₆-C₁₀ aryl, or mono- or bicyclic heteroaryl is independently optionally substituted by deuterium, halogen, C₁-C₆ alkyl, C₁-C₆ haloalkyl or -OR⁸;

[037] n is 1 or 2; and

[038] provided that the compound is not of the formula



[039] In another example, there is provided a compound of the formula Ic



[040] or a pharmaceutically acceptable salt thereof, wherein

[041] R¹ is H, deuterium, C₁-C₆ alkyl, C₂-C₆ alkenyl, C₂-C₆ alkynyl, C₃-C₆ cycloalkyl, C₆-C₁₀ aryl, -C(O)OR⁸ or -C(O)NR⁸R⁹; wherein each hydrogen atom in C₁-C₆ alkyl, C₂-C₆ alkenyl, C₂-C₆ alkynyl, C₃-C₆ cycloalkyl and C₆-C₁₀ aryl is independently optionally substituted by deuterium, halogen, -OH, -CN, -OC₁-C₆ alkyl, -NH₂, -NH(C₁-C₆ alkyl), -N(C₁-C₆ alkyl)₂, -NHC(O)C₁-C₆ alkyl, -N(C₁-C₆ alkyl)C(O)C₁-C₆ alkyl, -NHC(O)NH₂, -NHC(O)NHC₁-C₆ alkyl, -N(C₁-C₆ alkyl)C(O)NH₂, -N(C₁-C₆ alkyl)C(O)NHC₁-C₆ alkyl, -NHC(O)N(C₁-C₆ alkyl)₂, -N(C₁-C₆ alkyl)C(O)N(C₁-C₆ alkyl)₂, -NHC(O)OC₁-C₆ alkyl, -N(C₁-C₆ alkyl)C(O)OC₁-C₆ alkyl, -NHS(O)(C₁-C₆ alkyl), -NHS(O)₂(C₁-C₆ alkyl), -N(C₁-C₆ alkyl)S(O)(C₁-C₆ alkyl),

[044] R^5 is selected from the group consisting of fluoro, chloro, bromo, C_1 - C_6 alkyl, -OH, -CN, -OC $_1$ - C_6 alkyl, -NHC $_1$ - C_6 alkyl, -N(C_1 - C_6 alkyl) $_2$, C_3 - C_6 cycloalkyl, 3- to 7-membered heterocycloalkyl, -O-(C_3 - C_6 cycloalkyl), -O-(3- to 7-membered heterocycloalkyl), 5- to 7-membered heteroaryl, C_6 - C_{10} aryl, and -CF $_3$; wherein each hydrogen atom in C_1 - C_6 alkyl, -OC $_1$ - C_6 alkyl, -NHC $_1$ - C_6 alkyl, -N(C_1 - C_6 alkyl) $_2$, C_3 - C_6 cycloalkyl, 3- to 7-membered heterocycloalkyl, -O-(C_3 - C_6 cycloalkyl), -O-(3- to 7-membered heterocycloalkyl), 5- to 7-membered heteroaryl and C_6 - C_{10} aryl is independently optionally substituted by fluoro, chloro, bromo, -OH, -CN, -OC $_1$ - C_6 alkyl, -NH $_2$, -NH(C_1 - C_6 alkyl), -N(C_1 - C_6 alkyl) $_2$, C_3 - C_7 cycloalkyl, 3- to 7-membered heterocycloalkyl, C_6 - C_{10} aryl, 5- to 7-membered heteroaryl, -CO $_2$ H, -C(O)OC $_1$ - C_6 alkyl, -C(O)NH $_2$, -C(O)NH(C_1 - C_6 alkyl) and -C(O)N(C_1 - C_6 alkyl) $_2$;

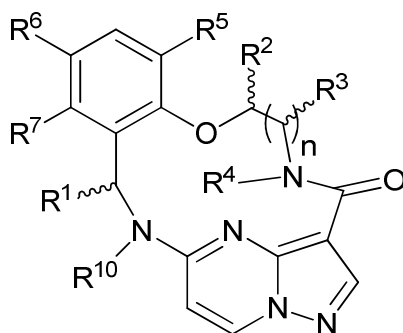
[045] R^6 and R^7 are each independently selected from the group consisting of H, fluoro, chloro, bromo, C_1 - C_6 alkyl, -OH, -CN, -OC $_1$ - C_6 alkyl, -NHC $_1$ - C_6 alkyl, -N(C_1 - C_6 alkyl) $_2$, 5- to 7-membered heteroaryl, C_6 - C_{10} aryl, and -CF $_3$; wherein each hydrogen atom in C_1 - C_6 alkyl, 5- to 7-membered heteroaryl and C_6 - C_{10} aryl is independently optionally substituted by fluoro, chloro, bromo, -OH, -CN, -OC $_1$ - C_6 alkyl, -NH $_2$, -NH(C_1 - C_6 alkyl), -N(C_1 - C_6 alkyl) $_2$, -CO $_2$ H, -C(O)OC $_1$ - C_6 alkyl, -C(O)NH $_2$, -C(O)NH(C_1 - C_6 alkyl) and -C(O)N(C_1 - C_6 alkyl) $_2$;

[046] each R^8 and R^9 is independently H, deuterium, C_1 - C_6 alkyl, C_2 - C_6 alkenyl, C_2 - C_6 alkynyl, C_3 - C_6 cycloalkyl, 3- to 7-membered heterocycloalkyl, C_6 - C_{10} aryl or heteroaryl;

[047] each R^{10} is independently H, deuterium, C_1 - C_6 alkyl, C_2 - C_6 alkenyl, C_2 - C_6 alkynyl, C_3 - C_6 cycloalkyl, 3- to 7-membered heterocycloalkyl, C_6 - C_{10} aryl, or mono- or bicyclic heteroaryl; wherein each hydrogen atom in C_1 - C_6 alkyl, C_2 - C_6 alkenyl, C_2 - C_6 alkynyl, C_3 - C_6 cycloalkyl, 3- to 7-membered heterocycloalkyl, C_6 - C_{10} aryl, or mono- or bicyclic heteroaryl is independently optionally substituted by deuterium, halogen, C_1 - C_6 alkyl, C_1 - C_6 haloalkyl or -OR ^{8} ; and

[048] n is 1 or 2.

[048a] In an aspect, there is provided a use of a compound of the formula Ic



Ic

or a pharmaceutically acceptable salt thereof,

in the preparation of a medicament for the treatment of a disease mediated by a Bruton's tyrosine kinase (BTK), wherein the disease is selected from the group consisting of cancer, pain, neurological disease, autoimmune diseases, or inflammation, wherein

R¹ is H, deuterium, C₁-C₆ alkyl, C₂-C₆ alkenyl, C₂-C₆ alkynyl, C₃-C₆ cycloalkyl, C₆-C₁₀ aryl, -C(O)OR⁸ or -C(O)NR⁸R⁹; wherein each hydrogen atom in C₁-C₆ alkyl, C₂-C₆ alkenyl, C₂-C₆ alkynyl, C₃-C₆ cycloalkyl and C₆-C₁₀ aryl is independently optionally substituted by deuterium, halogen, -OH, -CN, -OC₁-C₆ alkyl, -NH₂, -NH(C₁-C₆ alkyl), -N(C₁-C₆ alkyl)₂, -NHC(O)C₁-C₆ alkyl, -N(C₁-C₆ alkyl)C(O)C₁-C₆ alkyl, -NHC(O)NH₂, -NHC(O)NHC₁-C₆ alkyl, -N(C₁-C₆ alkyl)C(O)NH₂, -N(C₁-C₆ alkyl)C(O)NHC₁-C₆ alkyl, -NHC(O)N(C₁-C₆ alkyl)₂, -N(C₁-C₆ alkyl)C(O)N(C₁-C₆ alkyl)₂, -NHC(O)OC₁-C₆ alkyl, -N(C₁-C₆ alkyl)C(O)OC₁-C₆ alkyl, -NHS(O)(C₁-C₆ alkyl), -NHS(O)₂(C₁-C₆ alkyl), -N(C₁-C₆ alkyl)S(O)(C₁-C₆ alkyl), -N(C₁-C₆ alkyl)S(O)₂(C₁-C₆ alkyl), -NHS(O)NH₂, -NHS(O)₂NH₂, -N(C₁-C₆ alkyl)S(O)NH₂, -N(C₁-C₆ alkyl)S(O)₂NH₂, -NHS(O)NH(C₁-C₆ alkyl), -NHS(O)₂NH(C₁-C₆ alkyl), -NHS(O)N(C₁-C₆ alkyl)₂, -NHS(O)₂N(C₁-C₆ alkyl)₂, -N(C₁-C₆ alkyl)S(O)NH(C₁-C₆ alkyl), -N(C₁-C₆ alkyl)S(O)₂NH(C₁-C₆ alkyl), -N(C₁-C₆ alkyl)S(O)N(C₁-C₆ alkyl)₂, -N(C₁-C₆ alkyl)S(O)₂N(C₁-C₆ alkyl)₂, -CO₂H, -C(O)OC₁-C₆ alkyl, -C(O)NH₂, -C(O)NH(C₁-C₆ alkyl), -C(O)N(C₁-C₆ alkyl)₂, -SC₁-C₆ alkyl, -S(O)C₁-C₆ alkyl, -S(O)₂C₁-C₆ alkyl, -S(O)NH(C₁-C₆ alkyl), -S(O)₂NH(C₁-C₆ alkyl), -S(O)N(C₁-C₆ alkyl)₂, -S(O)₂N(C₁-C₆ alkyl)₂, -P(C₁-C₆ alkyl)₂, -P(O)(C₁-C₆ alkyl)₂, C₃-C₆ cycloalkyl, or 3- to 7-membered heterocycloalkyl; each R² and R³ is independently H, deuterium, C₁-C₆ alkyl, C₂-C₆ alkenyl, C₂-C₆ alkynyl, C₃-C₆ cycloalkyl, C₆-C₁₀ aryl, -C(O)OR⁸ or -C(O)NR⁸R⁹; wherein each hydrogen atom in C₁-C₆ alkyl, C₂-C₆ alkenyl, C₂-C₆ alkynyl, C₃-C₆ cycloalkyl and C₆-C₁₀ aryl is independently optionally substituted by deuterium, halogen, -OH, -CN, -OC₁-C₆ alkyl, -NH₂, -NH(C₁-C₆ alkyl), -N(C₁-C₆ alkyl)₂, -NHC(O)C₁-C₆ alkyl, -N(C₁-C₆ alkyl)C(O)C₁-C₆ alkyl, -NHC(O)NH₂, -NHC(O)NHC₁-C₆ alkyl, -N(C₁-C₆ alkyl)C(O)NH₂, -N(C₁-C₆ alkyl)C(O)NHC₁-C₆ alkyl, -NHC(O)N(C₁-C₆ alkyl)₂, -N(C₁-C₆ alkyl)C(O)N(C₁-C₆ alkyl)₂, -NHC(O)OC₁-C₆ alkyl, -N(C₁-C₆ alkyl)C(O)OC₁-C₆ alkyl, -NHS(O)(C₁-C₆ alkyl), -NHS(O)₂(C₁-C₆ alkyl), -N(C₁-C₆ alkyl)S(O)(C₁-C₆ alkyl), -N(C₁-C₆ alkyl)S(O)₂(C₁-C₆ alkyl), -NHS(O)NH₂, -NHS(O)₂NH₂, -N(C₁-C₆ alkyl)S(O)NH₂, -N(C₁-C₆ alkyl)S(O)₂NH₂, -NHS(O)NH(C₁-C₆ alkyl), -NHS(O)₂NH(C₁-C₆ alkyl), -NHS(O)N(C₁-C₆ alkyl)₂, -NHS(O)₂N(C₁-C₆ alkyl)₂, -N(C₁-C₆ alkyl)S(O)NH(C₁-C₆ alkyl), -N(C₁-C₆ alkyl)S(O)₂NH(C₁-C₆ alkyl), -N(C₁-C₆ alkyl)S(O)N(C₁-C₆ alkyl)₂, -N(C₁-C₆ alkyl)S(O)₂N(C₁-C₆ alkyl)₂, -CO₂H, -C(O)OC₁-C₆ alkyl, -C(O)NH₂, -C(O)NH(C₁-C₆ alkyl), -C(O)N(C₁-C₆ alkyl)₂, -SC₁-C₆ alkyl, -S(O)C₁-C₆ alkyl, -S(O)₂C₁-C₆ alkyl, -S(O)NH(C₁-C₆ alkyl), -S(O)₂NH(C₁-C₆ alkyl), -S(O)N(C₁-C₆ alkyl)₂,

-S(O)₂N(C₁-C₆ alkyl)₂, -P(C₁-C₆ alkyl)₂, -P(O)(C₁-C₆ alkyl)₂, C₃-C₆ cycloalkyl, or 3- to 7-membered heterocycloalkyl; or R² and R³ taken together with the carbon atoms to which they are attached optionally form a C₅-C₇ cycloalkyl or a 5- to 7-membered heterocycloalkyl; or R² and R⁶ taken together with the atoms to which they are attached optionally form a 5- to 7-membered heterocycloalkyl;

[048e] R⁴ is H, C₁-C₆ alkyl or 3- to 7-membered heterocycloalkyl, wherein each hydrogen atom in C₁-C₆ alkyl or 3- to 7-membered heterocycloalkyl is independently optionally substituted by halogen, -OH, -CN, -OC₁-C₆ alkyl, -NH₂, -NH(C₁-C₆ alkyl), -N(C₁-C₆ alkyl)₂, -CO₂H, -C(O)OC₁-C₆ alkyl, -C(O)NH₂, -C(O)NH(C₁-C₆ alkyl), -C(O)N(C₁-C₆ alkyl)₂, C₃-C₆ cycloalkyl, or monocyclic 5- to 7-membered heterocycloalkyl;

R⁵ is selected from the group consisting of fluoro, chloro, bromo, C₁-C₆ alkyl, -OH, -CN, -OC₁-C₆ alkyl, -NHC₁-C₆ alkyl, -N(C₁-C₆ alkyl)₂, C₃-C₆ cycloalkyl, 3- to 7-membered heterocycloalkyl, -O-(C₃-C₆ cycloalkyl), -O-(3- to 7-membered heterocycloalkyl), 5- to 7-membered heteroaryl, C₆-C₁₀ aryl, and -CF₃; wherein each hydrogen atom in C₁-C₆ alkyl, -OC₁-C₆ alkyl, -NHC₁-C₆ alkyl, -N(C₁-C₆ alkyl)₂, C₃-C₆ cycloalkyl, 3- to 7-membered heterocycloalkyl, -O-(C₃-C₆ cycloalkyl), -O-(3- to 7-membered heterocycloalkyl), 5- to 7-membered heteroaryl and C₆-C₁₀ aryl is independently optionally substituted by fluoro, chloro, bromo, -OH, -CN, -OC₁-C₆ alkyl, -NH₂, -NH(C₁-C₆ alkyl), -N(C₁-C₆ alkyl)₂, C₃-C₇ cycloalkyl, 3- to 7-membered heterocycloalkyl, C₆-C₁₀ aryl, 5- to 7-membered heteroaryl, -CO₂H, -C(O)OC₁-C₆ alkyl, -C(O)NH₂, -C(O)NH(C₁-C₆ alkyl) and -C(O)N(C₁-C₆ alkyl)₂;

R⁶ is selected from the group consisting of H, fluoro, chloro, bromo, C₁-C₆ alkyl, -OH, -CN, -OC₁-C₆ alkyl, -NHC₁-C₆ alkyl, -N(C₁-C₆ alkyl)₂, 5- to 7-membered heteroaryl, C₆-C₁₀ aryl, and -CF₃; wherein each hydrogen atom in C₁-C₆ alkyl, 5- to 7-membered heteroaryl and C₆-C₁₀ aryl is independently optionally substituted by fluoro, chloro, bromo, -OH, -CN, -OC₁-C₆ alkyl, -NH₂, -NH(C₁-C₆ alkyl), -N(C₁-C₆ alkyl)₂, -CO₂H, -C(O)OC₁-C₆ alkyl, -C(O)NH₂, -C(O)NH(C₁-C₆ alkyl) and -C(O)N(C₁-C₆ alkyl)₂;

R⁷ is H;

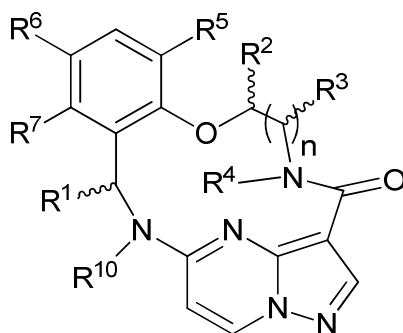
each R⁸ and R⁹ is independently H, deuterium, C₁-C₆ alkyl, C₂-C₆ alkenyl, C₂-C₆ alkynyl, C₃-C₆ cycloalkyl, 3- to 7-membered heterocycloalkyl, C₆-C₁₀ aryl or heteroaryl;

R¹⁰ is independently H, deuterium, C₁-C₆ alkyl, C₂-C₆ alkenyl, C₂-C₆ alkynyl, C₃-C₆ cycloalkyl, 3- to 7-membered heterocycloalkyl, C₆-C₁₀ aryl, or mono- or bicyclic heteroaryl; wherein each hydrogen atom in C₁-C₆ alkyl, C₂-C₆ alkenyl, C₂-C₆ alkynyl, C₃-C₆ cycloalkyl, 3-

to 7-membered heterocycloalkyl, C₆-C₁₀ aryl, or mono- or bicyclic heteroaryl is independently optionally substituted by deuterium, halogen, C₁-C₆ alkyl, C₁-C₆ haloalkyl or -OR⁸; and

n is 1 or 2.

[048b] In another aspect, there is provided a compound or pharmaceutically acceptable salt thereof, for use in treating a disease mediated by a Bruton's tyrosine kinase (BTK) in a patient, wherein the disease is selected from the group consisting of cancer, pain, neurological disease, or an autoimmune disease, wherein the compound has Formula Ic:



Ic

or a pharmaceutically acceptable salt thereof, wherein

R¹ is H, deuterium, C₁-C₆ alkyl, C₂-C₆ alkenyl, C₂-C₆ alkynyl, C₃-C₆ cycloalkyl, C₆-C₁₀ aryl, -C(O)OR⁸ or -C(O)NR⁸R⁹; wherein each hydrogen atom in C₁-C₆ alkyl, C₂-C₆ alkenyl, C₂-C₆ alkynyl, C₃-C₆ cycloalkyl and C₆-C₁₀ aryl is independently optionally substituted by deuterium, halogen, -OH, -CN, -OC₁-C₆ alkyl, -NH₂, -NH(C₁-C₆ alkyl), -N(C₁-C₆ alkyl)₂, -NHC(O)C₁-C₆ alkyl, -N(C₁-C₆ alkyl)C(O)C₁-C₆ alkyl, -NHC(O)NH₂, -NHC(O)NHC₁-C₆ alkyl, -N(C₁-C₆ alkyl)C(O)NH₂, -N(C₁-C₆ alkyl)C(O)NHC₁-C₆ alkyl, -NHC(O)N(C₁-C₆ alkyl)₂, -N(C₁-C₆ alkyl)C(O)N(C₁-C₆ alkyl)₂, -NHC(O)OC₁-C₆ alkyl, -N(C₁-C₆ alkyl)C(O)OC₁-C₆ alkyl, -NHS(O)(C₁-C₆ alkyl), -NHS(O)₂(C₁-C₆ alkyl), -N(C₁-C₆ alkyl)S(O)(C₁-C₆ alkyl), -N(C₁-C₆ alkyl)S(O)₂(C₁-C₆ alkyl), -NHS(O)NH₂, -NHS(O)₂NH₂, -N(C₁-C₆ alkyl)S(O)NH₂, -N(C₁-C₆ alkyl)S(O)₂NH₂, -NHS(O)NH(C₁-C₆ alkyl), -NHS(O)₂NH(C₁-C₆ alkyl), -NHS(O)N(C₁-C₆ alkyl)₂, -NHS(O)₂N(C₁-C₆ alkyl)₂, -N(C₁-C₆ alkyl)S(O)NH(C₁-C₆ alkyl), -N(C₁-C₆ alkyl)S(O)₂NH(C₁-C₆ alkyl), -N(C₁-C₆ alkyl)S(O)N(C₁-C₆ alkyl)₂, -N(C₁-C₆ alkyl)S(O)₂N(C₁-C₆ alkyl)₂, -CO₂H, -C(O)OC₁-C₆ alkyl, -C(O)NH₂, -C(O)NH(C₁-C₆ alkyl), -C(O)N(C₁-C₆ alkyl)₂, -SC₁-C₆ alkyl, -S(O)C₁-C₆ alkyl, -S(O)₂C₁-C₆ alkyl, -S(O)NH(C₁-C₆ alkyl), -S(O)₂NH(C₁-C₆ alkyl), -S(O)N(C₁-C₆ alkyl)₂, -S(O)₂N(C₁-C₆ alkyl)₂, -P(C₁-C₆ alkyl)₂, -P(O)(C₁-C₆ alkyl)₂, C₃-C₆ cycloalkyl, or 3- to 7-membered heterocycloalkyl;

each R² and R³ is independently H, deuterium, C₁-C₆ alkyl, C₂-C₆ alkenyl, C₂-C₆ alkynyl, C₃-C₆ cycloalkyl, C₆-C₁₀ aryl, -C(O)OR⁸ or -C(O)NR⁸R⁹; wherein each hydrogen atom in C₁-C₆ alkyl, C₂-C₆ alkenyl, C₂-C₆ alkynyl, C₃-C₆ cycloalkyl and C₆-C₁₀ aryl is independently

optionally substituted by deuterium, halogen, -OH, -CN, -OC₁-C₆ alkyl, -NH₂, -NH(C₁-C₆ alkyl), -N(C₁-C₆ alkyl)₂, -NHC(O)C₁-C₆ alkyl, -N(C₁-C₆ alkyl)C(O)C₁-C₆ alkyl, -NHC(O)NH₂, -NHC(O)NHC₁-C₆ alkyl, -N(C₁-C₆ alkyl)C(O)NH₂, -N(C₁-C₆ alkyl)C(O)NHC₁-C₆ alkyl, -NHC(O)N(C₁-C₆ alkyl)₂, -N(C₁-C₆ alkyl)C(O)N(C₁-C₆ alkyl)₂, -NHC(O)OC₁-C₆ alkyl, -N(C₁-C₆ alkyl)C(O)OC₁-C₆ alkyl, -NHS(O)(C₁-C₆ alkyl), -NHS(O)₂(C₁-C₆ alkyl), -N(C₁-C₆ alkyl)S(O)(C₁-C₆ alkyl), -N(C₁-C₆ alkyl)S(O)₂(C₁-C₆ alkyl), -NHS(O)NH₂, -NHS(O)₂NH₂, -N(C₁-C₆ alkyl)S(O)NH₂, -N(C₁-C₆ alkyl)S(O)₂NH₂, -NHS(O)NH(C₁-C₆ alkyl), -NHS(O)₂NH(C₁-C₆ alkyl), -NHS(O)N(C₁-C₆ alkyl)₂, -NHS(O)₂N(C₁-C₆ alkyl)₂, -N(C₁-C₆ alkyl)S(O)NH(C₁-C₆ alkyl), -N(C₁-C₆ alkyl)S(O)₂NH(C₁-C₆ alkyl), -N(C₁-C₆ alkyl)S(O)N(C₁-C₆ alkyl)₂, -N(C₁-C₆ alkyl)S(O)₂N(C₁-C₆ alkyl)₂, -CO₂H, -C(O)OC₁-C₆ alkyl, -C(O)NH₂, -C(O)NH(C₁-C₆ alkyl), -C(O)N(C₁-C₆ alkyl)₂, -SC₁-C₆ alkyl, -S(O)C₁-C₆ alkyl, -S(O)₂C₁-C₆ alkyl, -S(O)NH(C₁-C₆ alkyl), -S(O)₂NH(C₁-C₆ alkyl), -S(O)N(C₁-C₆ alkyl)₂, -S(O)₂N(C₁-C₆ alkyl)₂, -P(C₁-C₆ alkyl)₂, -P(O)(C₁-C₆ alkyl)₂, C₃-C₆ cycloalkyl, or 3- to 7-membered heterocycloalkyl; or R² and R³ taken together with the carbon atoms to which they are attached optionally form a C₅-C₇ cycloalkyl or a 5- to 7-membered heterocycloalkyl; or R² and R⁶ taken together with the atoms to which they are attached optionally form a 5- to 7-membered heterocycloalkyl;

R⁴ is H, C₁-C₆ alkyl or 3- to 7-membered heterocycloalkyl, wherein each hydrogen atom in C₁-C₆ alkyl or 3- to 7-membered heterocycloalkyl is independently optionally substituted by halogen, -OH, -CN, -OC₁-C₆ alkyl, -NH₂, -NH(C₁-C₆ alkyl), -N(C₁-C₆ alkyl)₂, -CO₂H, -C(O)OC₁-C₆ alkyl, -C(O)NH₂, -C(O)NH(C₁-C₆ alkyl), -C(O)N(C₁-C₆ alkyl)₂, C₃-C₆ cycloalkyl, or monocyclic 5- to 7-membered heterocycloalkyl;

R⁵ is selected from the group consisting of fluoro, chloro, bromo, C₁-C₆ alkyl, -OH, -CN, -OC₁-C₆ alkyl, -NHC₁-C₆ alkyl, -N(C₁-C₆ alkyl)₂, C₃-C₆ cycloalkyl, 3- to 7-membered heterocycloalkyl, -O-(C₃-C₆ cycloalkyl), -O-(3- to 7-membered heterocycloalkyl), 5- to 7-membered heteroaryl, C₆-C₁₀ aryl, and -CF₃; wherein each hydrogen atom in C₁-C₆ alkyl, -OC₁-C₆ alkyl, -NHC₁-C₆ alkyl, -N(C₁-C₆ alkyl)₂, C₃-C₆ cycloalkyl, 3- to 7-membered heterocycloalkyl, -O-(C₃-C₆ cycloalkyl), -O-(3- to 7-membered heterocycloalkyl), 5- to 7-membered heteroaryl and C₆-C₁₀ aryl is independently optionally substituted by fluoro, chloro, bromo, -OH, -CN, -OC₁-C₆ alkyl, -NH₂, -NH(C₁-C₆ alkyl), -N(C₁-C₆ alkyl)₂, C₃-C₇ cycloalkyl, 3- to 7-membered heterocycloalkyl, C₆-C₁₀ aryl, 5- to 7-membered heteroaryl, -CO₂H, -C(O)OC₁-C₆ alkyl, -C(O)NH₂, -C(O)NH(C₁-C₆ alkyl) and -C(O)N(C₁-C₆ alkyl)₂;

R⁶ is selected from the group consisting of H, fluoro, chloro, bromo, C₁-C₆ alkyl, -OH, -CN, -OC₁-C₆ alkyl, -NHC₁-C₆ alkyl, -N(C₁-C₆ alkyl)₂, 5- to 7-membered heteroaryl, C₆-C₁₀ aryl, and -CF₃; wherein each hydrogen atom in C₁-C₆ alkyl, 5- to 7-membered heteroaryl and C₆-C₁₀ aryl is independently optionally substituted by fluoro, chloro, bromo, -OH, -CN, -OC₁-C₆ alkyl, -NH₂, -NH(C₁-C₆ alkyl), -N(C₁-C₆ alkyl)₂, -CO₂H, -C(O)OC₁-C₆ alkyl, -C(O)NH₂, -C(O)NH(C₁-C₆ alkyl) and -C(O)N(C₁-C₆ alkyl)₂;

R⁷ is H;

each R⁸ and R⁹ is independently H, deuterium, C₁-C₆ alkyl, C₂-C₆ alkenyl, C₂-C₆ alkynyl, C₃-C₆ cycloalkyl, 3- to 7-membered heterocycloalkyl, C₆-C₁₀ aryl or heteroaryl;

R¹⁰ is independently H, deuterium, C₁-C₆ alkyl, C₂-C₆ alkenyl, C₂-C₆ alkynyl, C₃-C₆ cycloalkyl, 3- to 7-membered heterocycloalkyl, C₆-C₁₀ aryl, or mono- or bicyclic heteroaryl; wherein each hydrogen atom in C₁-C₆ alkyl, C₂-C₆ alkenyl, C₂-C₆ alkynyl, C₃-C₆ cycloalkyl, 3- to 7-membered heterocycloalkyl, C₆-C₁₀ aryl, or mono- or bicyclic heteroaryl is independently optionally substituted by deuterium, halogen, C₁-C₆ alkyl, C₁-C₆ haloalkyl or -OR⁸; and

n is 1 or 2.

[049] In another example, there is provided a pharmaceutical composition comprising a compound of the formula I, Ia, Ib or Ic, or a pharmaceutically acceptable salt thereof, and optionally at least one diluent, carrier or excipient.

[050] The disclosure is directed to a method of treating cancer, pain, neurological diseases, autoimmune diseases, or inflammation comprising administering to a subject in need of such treatment an effective amount of at least one compound of formula I, Ia, Ib or Ic, or a pharmaceutically acceptable salt thereof. cancer, pain, neurological diseases, autoimmune diseases, or inflammation.

[051] In another example, there is provided use of a compound of formula I, Ia, Ib or Ic, or a pharmaceutically acceptable salt thereof, in the preparation of a medicament for the treatment of cancer, pain, neurological diseases, autoimmune diseases, or inflammation. In some embodiments, the disease is a cancer. In some examples, the disease is an autoimmune disease. In some examples, the disease is inflammation.

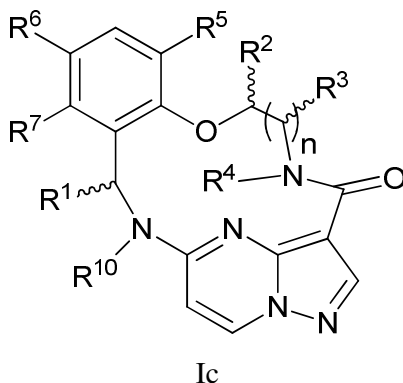
[052] The disclosure is directed to use of a compound of formula I, Ia, Ib or Ic, or a pharmaceutically acceptable salt thereof, for treating cancer, pain, neurological diseases, autoimmune diseases, or inflammation. In some examples, the disease is a cancer. In some examples, the disease is an autoimmune disease. In some embodiments, the disease is inflammation.

[053] The disclosure is directed to use of a compound of formula I, Ia, Ib or Ic, or a pharmaceutically acceptable salt thereof, in the preparation of a medicament for the treatment of cancer, pain, neurological diseases, autoimmune diseases, or inflammation, and the use of such compounds and salts for treatment of cancer, pain, neurological diseases, autoimmune diseases, or inflammation. In some examples, the disease is a cancer. In some examples, the disease is an autoimmune disease. In some embodiments, the disease is inflammation.

[054] The disclosure relates to a method of inhibiting non-receptor tyrosine kinases, including one or more of JAK2 or BTK, comprising contacting a cell comprising one or more of such kinases with an effective amount of at least one compound of formula I, Ia, Ib or Ic, or a pharmaceutically acceptable salt thereof, and/or with at least one pharmaceutical composition of the disclosure, wherein the contacting is *in vitro*, *ex vivo*, or *in vivo*.

WHAT IS CLAIMED IS:

1. Use of a compound of the formula Ic



or a pharmaceutically acceptable salt thereof,

in the preparation of a medicament for the treatment of a disease mediated by a Bruton's tyrosine kinase (BTK), wherein the disease is selected from the group consisting of cancer, pain, neurological disease, autoimmune diseases, or inflammation,

wherein

R¹ is H, deuterium, C₁-C₆ alkyl, C₂-C₆ alkenyl, C₂-C₆ alkynyl, C₃-C₆ cycloalkyl, C₆-C₁₀ aryl, -C(O)OR⁸ or -C(O)NR⁸R⁹; wherein each hydrogen atom in C₁-C₆ alkyl, C₂-C₆ alkenyl, C₂-C₆ alkynyl, C₃-C₆ cycloalkyl and C₆-C₁₀ aryl is independently optionally substituted by deuterium, halogen, -OH, -CN, -OC₁-C₆ alkyl, -NH₂, -NH(C₁-C₆ alkyl), -N(C₁-C₆ alkyl)₂, -NHC(O)C₁-C₆ alkyl, -N(C₁-C₆ alkyl)C(O)C₁-C₆ alkyl, -NHC(O)NH₂, -NHC(O)NHC₁-C₆ alkyl, -N(C₁-C₆ alkyl)C(O)NH₂, -N(C₁-C₆ alkyl)C(O)NHC₁-C₆ alkyl, -NHC(O)N(C₁-C₆ alkyl)₂, -N(C₁-C₆ alkyl)C(O)N(C₁-C₆ alkyl)₂, -NHC(O)OC₁-C₆ alkyl, -N(C₁-C₆ alkyl)C(O)OC₁-C₆ alkyl, -NHS(O)(C₁-C₆ alkyl), -NHS(O)₂(C₁-C₆ alkyl), -N(C₁-C₆ alkyl)S(O)(C₁-C₆ alkyl), -N(C₁-C₆ alkyl)S(O)₂(C₁-C₆ alkyl), -NHS(O)NH₂, -NHS(O)₂NH₂, -N(C₁-C₆ alkyl)S(O)NH₂, -N(C₁-C₆ alkyl)S(O)₂NH₂, -NHS(O)NH(C₁-C₆ alkyl), -NHS(O)₂NH(C₁-C₆ alkyl), -NHS(O)N(C₁-C₆ alkyl)₂, -NHS(O)₂N(C₁-C₆ alkyl)₂, -N(C₁-C₆ alkyl)S(O)NH(C₁-C₆ alkyl), -N(C₁-C₆ alkyl)S(O)₂NH(C₁-C₆ alkyl), -N(C₁-C₆ alkyl)S(O)N(C₁-C₆ alkyl)₂, -N(C₁-C₆ alkyl)S(O)₂N(C₁-C₆ alkyl)₂, -CO₂H, -C(O)OC₁-C₆ alkyl, -C(O)NH₂, -C(O)NH(C₁-C₆ alkyl), -C(O)N(C₁-C₆ alkyl)₂, -SC₁-C₆ alkyl, -S(O)C₁-C₆ alkyl, -S(O)₂C₁-C₆ alkyl, -S(O)NH(C₁-C₆ alkyl), -S(O)₂NH(C₁-C₆ alkyl), -S(O)N(C₁-C₆ alkyl)₂, -S(O)₂N(C₁-C₆ alkyl)₂, -P(C₁-C₆ alkyl)₂, -P(O)(C₁-C₆ alkyl)₂, C₃-C₆ cycloalkyl, or 3- to 7-membered heterocycloalkyl;

each R² and R³ is independently H, deuterium, C₁-C₆ alkyl, C₂-C₆ alkenyl, C₂-C₆ alkynyl, C₃-C₆ cycloalkyl, C₆-C₁₀ aryl, -C(O)OR⁸ or -C(O)NR⁸R⁹; wherein each hydrogen atom in C₁-C₆ alkyl, C₂-C₆ alkenyl, C₂-C₆ alkynyl, C₃-C₆ cycloalkyl and C₆-C₁₀ aryl is independently

optionally substituted by deuterium, halogen, -OH, -CN, -OC₁₋₆ alkyl, -NH₂, -NH(C₁₋₆ alkyl), -N(C₁₋₆ alkyl)₂, -NHC(O)C₁₋₆ alkyl, -N(C₁₋₆ alkyl)C(O)C₁₋₆ alkyl, -NHC(O)NH₂, -NHC(O)NHC₁₋₆ alkyl, -N(C₁₋₆ alkyl)C(O)NH₂, -N(C₁₋₆ alkyl)C(O)NHC₁₋₆ alkyl, -NHC(O)N(C₁₋₆ alkyl)₂, -N(C₁₋₆ alkyl)C(O)N(C₁₋₆ alkyl)₂, -NHC(O)OC₁₋₆ alkyl, -N(C₁₋₆ alkyl)C(O)OC₁₋₆ alkyl, -NHS(O)(C₁₋₆ alkyl), -NHS(O)₂(C₁₋₆ alkyl), -N(C₁₋₆ alkyl)S(O)(C₁₋₆ alkyl), -N(C₁₋₆ alkyl)S(O)₂(C₁₋₆ alkyl), -NHS(O)NH₂, -NHS(O)₂NH₂, -N(C₁₋₆ alkyl)S(O)NH₂, -N(C₁₋₆ alkyl)S(O)₂NH₂, -NHS(O)NH(C₁₋₆ alkyl), -NHS(O)₂NH(C₁₋₆ alkyl), -NHS(O)N(C₁₋₆ alkyl)₂, -NHS(O)₂N(C₁₋₆ alkyl)₂, -N(C₁₋₆ alkyl)S(O)NH(C₁₋₆ alkyl), -N(C₁₋₆ alkyl)S(O)₂NH(C₁₋₆ alkyl), -N(C₁₋₆ alkyl)S(O)N(C₁₋₆ alkyl)₂, -N(C₁₋₆ alkyl)S(O)₂N(C₁₋₆ alkyl)₂, -CO₂H, -C(O)OC₁₋₆ alkyl, -C(O)NH₂, -C(O)NH(C₁₋₆ alkyl), -C(O)N(C₁₋₆ alkyl)₂, -SC₁₋₆ alkyl, -S(O)C₁₋₆ alkyl, -S(O)₂C₁₋₆ alkyl, -S(O)NH(C₁₋₆ alkyl), -S(O)₂NH(C₁₋₆ alkyl), -S(O)N(C₁₋₆ alkyl)₂, -S(O)₂N(C₁₋₆ alkyl)₂, -P(C₁₋₆ alkyl)₂, -P(O)(C₁₋₆ alkyl)₂, C₃₋₆ cycloalkyl, or 3- to 7-membered heterocycloalkyl; or R² and R³ taken together with the carbon atoms to which they are attached optionally form a C₅₋₇ cycloalkyl or a 5- to 7-membered heterocycloalkyl; or R² and R⁶ taken together with the atoms to which they are attached optionally form a 5- to 7-membered heterocycloalkyl;

R⁴ is H, C₁₋₆ alkyl or 3- to 7-membered heterocycloalkyl, wherein each hydrogen atom in C₁₋₆ alkyl or 3- to 7-membered heterocycloalkyl is independently optionally substituted by halogen, -OH, -CN, -OC₁₋₆ alkyl, -NH₂, -NH(C₁₋₆ alkyl), -N(C₁₋₆ alkyl)₂, -CO₂H, -C(O)OC₁₋₆ alkyl, -C(O)NH₂, -C(O)NH(C₁₋₆ alkyl), -C(O)N(C₁₋₆ alkyl)₂, C₃₋₆ cycloalkyl, or monocyclic 5- to 7-membered heterocycloalkyl;

R⁵ is selected from the group consisting of fluoro, chloro, bromo, C₁₋₆ alkyl, -OH, -CN, -OC₁₋₆ alkyl, -NHC₁₋₆ alkyl, -N(C₁₋₆ alkyl)₂, C₃₋₆ cycloalkyl, 3- to 7-membered heterocycloalkyl, -O-(C₃₋₆ cycloalkyl), -O-(3- to 7-membered heterocycloalkyl), 5- to 7-membered heteroaryl, C₆₋₁₀ aryl, and -CF₃; wherein each hydrogen atom in C₁₋₆ alkyl, -OC₁₋₆ alkyl, -NHC₁₋₆ alkyl, -N(C₁₋₆ alkyl)₂, C₃₋₆ cycloalkyl, 3- to 7-membered heterocycloalkyl, -O-(C₃₋₆ cycloalkyl), -O-(3- to 7-membered heterocycloalkyl), 5- to 7-membered heteroaryl and C₆₋₁₀ aryl is independently optionally substituted by fluoro, chloro, bromo, -OH, -CN, -OC₁₋₆ alkyl, -NH₂, -NH(C₁₋₆ alkyl), -N(C₁₋₆ alkyl)₂, C₃₋₇ cycloalkyl, 3- to 7-membered heterocycloalkyl, C₆₋₁₀ aryl, 5- to 7-membered heteroaryl, -CO₂H, -C(O)OC₁₋₆ alkyl, -C(O)NH₂, -C(O)NH(C₁₋₆ alkyl) and -C(O)N(C₁₋₆ alkyl)₂;

R⁶ is selected from the group consisting of H, fluoro, chloro, bromo, C₁-C₆ alkyl, -OH, -CN, -OC₁-C₆ alkyl, -NHC₁-C₆ alkyl, -N(C₁-C₆ alkyl)₂, 5- to 7-membered heteroaryl, C₆-C₁₀ aryl, and -CF₃; wherein each hydrogen atom in C₁-C₆ alkyl, 5- to 7-membered heteroaryl and C₆-C₁₀ aryl is independently optionally substituted by fluoro, chloro, bromo, -OH, -CN, -OC₁-C₆ alkyl, -NH₂, -NH(C₁-C₆ alkyl), -N(C₁-C₆ alkyl)₂, -CO₂H, -C(O)OC₁-C₆ alkyl, -C(O)NH₂, -C(O)NH(C₁-C₆ alkyl) and -C(O)N(C₁-C₆ alkyl)₂;

R⁷ is H;

each R⁸ and R⁹ is independently H, deuterium, C₁-C₆ alkyl, C₂-C₆ alkenyl, C₂-C₆ alkynyl, C₃-C₆ cycloalkyl, 3- to 7-membered heterocycloalkyl, C₆-C₁₀ aryl or heteroaryl;

R¹⁰ is independently H, deuterium, C₁-C₆ alkyl, C₂-C₆ alkenyl, C₂-C₆ alkynyl, C₃-C₆ cycloalkyl, 3- to 7-membered heterocycloalkyl, C₆-C₁₀ aryl, or mono- or bicyclic heteroaryl; wherein each hydrogen atom in C₁-C₆ alkyl, C₂-C₆ alkenyl, C₂-C₆ alkynyl, C₃-C₆ cycloalkyl, 3- to 7-membered heterocycloalkyl, C₆-C₁₀ aryl, or mono- or bicyclic heteroaryl is independently optionally substituted by deuterium, halogen, C₁-C₆ alkyl, C₁-C₆ haloalkyl or -OR⁸; and

n is 1 or 2.

2. The use of claim 1, wherein in the compound, or a pharmaceutically acceptable salt thereof, R⁵ is selected from the group consisting of fluoro, chloro, bromo, C₁-C₆ alkyl, -OH, -CN, -OC₁-C₆ alkyl, C₃-C₆ cycloalkyl, 3- to 7-membered heterocycloalkyl, -O-(C₃-C₆ cycloalkyl), -O-(3- to 7-membered heterocycloalkyl), 5- to 7-membered heteroaryl, C₆-C₁₀ aryl and -CF₃, wherein each hydrogen atom in C₁-C₆ alkyl, -OC₁-C₆ alkyl, C₃-C₆ cycloalkyl, 3- to 7-membered heterocycloalkyl, -O-(C₃-C₆ cycloalkyl), -O-(3- to 7-membered heterocycloalkyl), 5- to 7-membered heteroaryl and C₆-C₁₀ aryl is independently optionally substituted by fluoro, chloro, bromo, -OH, -CN, -OC₁-C₆ alkyl, -NH₂, -NH(C₁-C₆ alkyl), -N(C₁-C₆ alkyl)₂, C₃-C₇ cycloalkyl, 3- to 7-membered heterocycloalkyl, C₆-C₁₀ aryl, 5- to 7-membered heteroaryl, -CO₂H, -C(O)OC₁-C₆ alkyl, -C(O)NH₂, -C(O)NH(C₁-C₆ alkyl) and -C(O)N(C₁-C₆ alkyl)₂.

3. The use of claim 1, wherein in the compound, or a pharmaceutically acceptable salt thereof, R⁵ is fluoro, chloro, bromo, -OH, -CN, -CF₃, methoxy, ethoxy, iso-propoxy, or n-propoxy.

4. The use of claim 1, wherein in the compound, or a pharmaceutically acceptable salt thereof, R⁵ is 5- to 7-membered heteroaryl; wherein each hydrogen atom in 5- to 7-membered heteroaryl is independently optionally substituted by fluoro, chloro, bromo, -OH, -CN, -OC₁-C₆

alkyl, -NH₂, -NH(C₁-C₆ alkyl), -N(C₁-C₆ alkyl)₂, -CO₂H, -C(O)OC₁-C₆ alkyl, -C(O)NH₂, -C(O)NH(C₁-C₆ alkyl) and -C(O)N(C₁-C₆ alkyl)₂.

5. The use of claim 4, wherein in the compound, or a pharmaceutically acceptable salt thereof, the 5- to 7-membered heteroaryl is pyrazolyl substituted with one or more substituents selected from the group consisting of fluoro, chloro, bromo, -OH, -CN, -OC₁-C₆ alkyl, -NH₂, -NH(C₁-C₆ alkyl), -N(C₁-C₆ alkyl)₂, -CO₂H, -C(O)OC₁-C₆ alkyl, -C(O)NH₂, -C(O)NH(C₁-C₆ alkyl) and -C(O)N(C₁-C₆ alkyl)₂.

6. The use of claim 1, wherein in the compound, or a pharmaceutically acceptable salt thereof, R⁵ is C₆-C₁₀ aryl, wherein each hydrogen atom in C₆-C₁₀ aryl is independently optionally substituted by fluoro, chloro, bromo, -OH, -CN, -OC₁-C₆ alkyl, -NH₂, -NH(C₁-C₆ alkyl), -N(C₁-C₆ alkyl)₂, -CO₂H, -C(O)OC₁-C₆ alkyl, -C(O)NH₂, -C(O)NH(C₁-C₆ alkyl) and -C(O)N(C₁-C₆ alkyl)₂.

7. The use of any one of the preceding claims, wherein in the compound, or a pharmaceutically acceptable salt thereof, R¹⁰ is H or C₁-C₆ alkyl.

8. The use of claim 7, wherein in the compound, or a pharmaceutically acceptable salt thereof, R¹⁰ is methyl, ethyl or isopropyl.

9. The use of any one of the preceding claims, wherein in the compound, or a pharmaceutically acceptable salt thereof, R² is H or C₁-C₆ alkyl; wherein each hydrogen atom in C₁-C₆ alkyl is independently optionally substituted by deuterium, halogen, -OH, -CN, -OC₁-C₆ alkyl, -NH₂, -NH(C₁-C₆ alkyl), -N(C₁-C₆ alkyl)₂, -NHC(O)C₁-C₆ alkyl, -N(C₁-C₆ alkyl)C(O)C₁-C₆ alkyl, -NHC(O)NH₂, -NHC(O)NHC₁-C₆ alkyl, -N(C₁-C₆ alkyl)C(O)NH₂, -N(C₁-C₆ alkyl)C(O)NHC₁-C₆ alkyl, -NHC(O)N(C₁-C₆ alkyl)₂, -N(C₁-C₆ alkyl)C(O)N(C₁-C₆ alkyl)₂, -NHC(O)OC₁-C₆ alkyl, -N(C₁-C₆ alkyl)C(O)OC₁-C₆ alkyl, -NHS(O)(C₁-C₆ alkyl), -NHS(O)₂(C₁-C₆ alkyl), -N(C₁-C₆ alkyl)S(O)(C₁-C₆ alkyl), -N(C₁-C₆ alkyl)S(O)₂(C₁-C₆ alkyl), -NHS(O)NH₂, -NHS(O)₂NH₂, -N(C₁-C₆ alkyl)S(O)NH₂, -N(C₁-C₆ alkyl)S(O)₂NH₂, -NHS(O)NH(C₁-C₆ alkyl), -NHS(O)₂NH(C₁-C₆ alkyl), -NHS(O)N(C₁-C₆ alkyl)₂, -NHS(O)₂N(C₁-C₆ alkyl)₂, -N(C₁-C₆ alkyl)S(O)NH(C₁-C₆ alkyl), -N(C₁-C₆ alkyl)S(O)₂NH(C₁-C₆ alkyl), -N(C₁-C₆ alkyl)S(O)N(C₁-C₆ alkyl)₂, -N(C₁-C₆ alkyl)S(O)₂N(C₁-C₆ alkyl)₂, -CO₂H, -C(O)OC₁-C₆ alkyl, -C(O)NH₂, -C(O)NH(C₁-C₆ alkyl),

-C(O)N(C₁-C₆ alkyl)₂, -SC₁-C₆ alkyl, -S(O)C₁-C₆ alkyl, -S(O)₂C₁-C₆ alkyl, -S(O)NH(C₁-C₆ alkyl), -S(O)₂NH(C₁-C₆ alkyl), -S(O)N(C₁-C₆ alkyl)₂, -S(O)₂N(C₁-C₆ alkyl)₂, -P(C₁-C₆ alkyl)₂, -P(O)(C₁-C₆ alkyl)₂, C₃-C₆ cycloalkyl, or 3- to 7-membered heterocycloalkyl.

10. The use of any one of the preceding claims, wherein in the compound, or a pharmaceutically acceptable salt thereof, R² is C₁-C₆ alkyl, wherein one hydrogen atom in C₁-C₆ alkyl substituted by -OH.

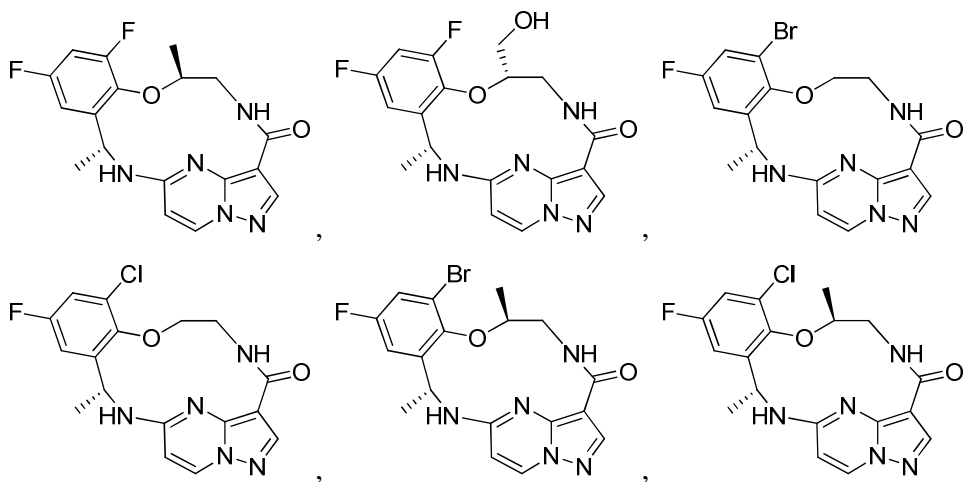
11. The use of any one of the preceding claims, wherein in the compound, or a pharmaceutically acceptable salt thereof, R² is -CH₂OH.

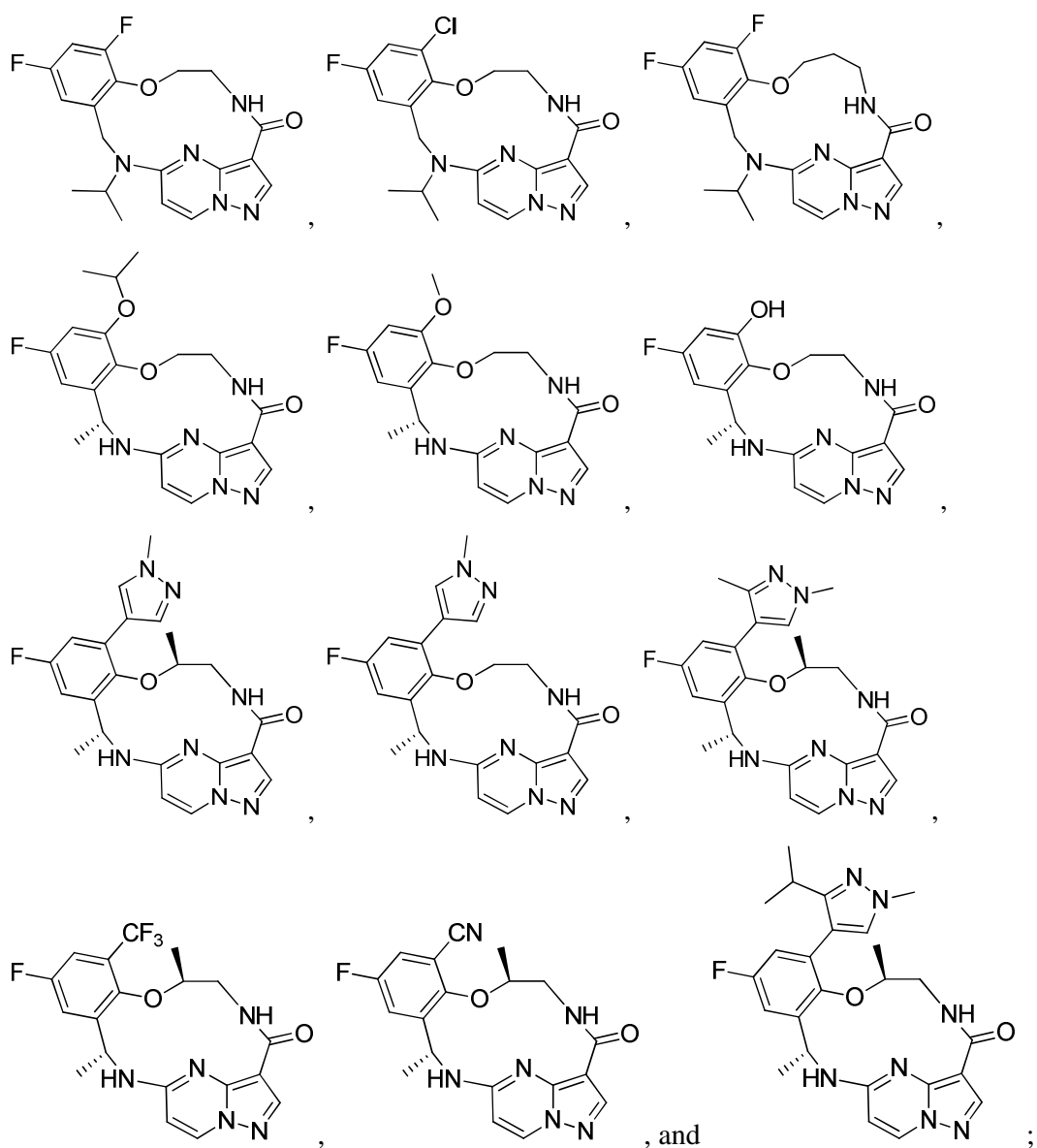
12. The use of any one of the preceding claims, wherein in the compound, or a pharmaceutically acceptable salt thereof, each R³ is H.

13. The use of any one of the preceding claims, wherein in the compound, or a pharmaceutically acceptable salt thereof, R⁴ is H.

14. The use of any one of the preceding claims, wherein in the compound, or a pharmaceutically acceptable salt thereof, R⁶ is fluoro.

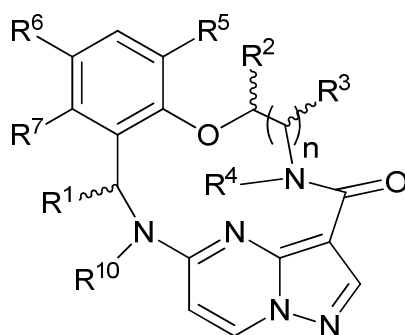
15. The use of claim 1, wherein the compound is selected from the group consisting of





or a pharmaceutically acceptable salt thereof.

16. A compound or pharmaceutically acceptable salt thereof, for use in treating a disease mediated by a Bruton's tyrosine kinase (BTK) in a patient, wherein the disease is selected from the group consisting of cancer, pain, neurological disease, or an autoimmune disease, wherein the compound has Formula Ic:



Ic

or a pharmaceutically acceptable salt thereof,

wherein

R^1 is H, deuterium, C_1 - C_6 alkyl, C_2 - C_6 alkenyl, C_2 - C_6 alkynyl, C_3 - C_6 cycloalkyl, C_6 - C_{10} aryl, $-C(O)OR^8$ or $-C(O)NR^8R^9$; wherein each hydrogen atom in C_1 - C_6 alkyl, C_2 - C_6 alkenyl, C_2 - C_6 alkynyl, C_3 - C_6 cycloalkyl and C_6 - C_{10} aryl is independently optionally substituted by deuterium, halogen, $-OH$, $-CN$, $-OC_1$ - C_6 alkyl, $-NH_2$, $-NH(C_1$ - C_6 alkyl), $-N(C_1$ - C_6 alkyl) $_2$, $-NHC(O)C_1$ - C_6 alkyl, $-N(C_1$ - C_6 alkyl) $C(O)C_1$ - C_6 alkyl, $-NHC(O)NH_2$, $-NHC(O)NHC_1$ - C_6 alkyl, $-N(C_1$ - C_6 alkyl) $C(O)NH_2$, $-N(C_1$ - C_6 alkyl) $C(O)NHC_1$ - C_6 alkyl, $-NHC(O)N(C_1$ - C_6 alkyl) $_2$, $-N(C_1$ - C_6 alkyl) $C(O)N(C_1$ - C_6 alkyl) $_2$, $-NHC(O)OC_1$ - C_6 alkyl, $-N(C_1$ - C_6 alkyl) $C(O)OC_1$ - C_6 alkyl, $-NHS(O)(C_1$ - C_6 alkyl), $-NHS(O)_2(C_1$ - C_6 alkyl), $-N(C_1$ - C_6 alkyl) $S(O)(C_1$ - C_6 alkyl), $-N(C_1$ - C_6 alkyl) $S(O)_2(C_1$ - C_6 alkyl), $-NHS(O)NH_2$, $-NHS(O)_2NH_2$, $-N(C_1$ - C_6 alkyl) $S(O)NH_2$, $-N(C_1$ - C_6 alkyl) $S(O)_2NH_2$, $-NHS(O)NH(C_1$ - C_6 alkyl), $-NHS(O)_2NH(C_1$ - C_6 alkyl), $-NHS(O)N(C_1$ - C_6 alkyl) $_2$, $-NHS(O)_2N(C_1$ - C_6 alkyl) $_2$, $-N(C_1$ - C_6 alkyl) $S(O)NH(C_1$ - C_6 alkyl), $-N(C_1$ - C_6 alkyl) $S(O)_2NH(C_1$ - C_6 alkyl), $-N(C_1$ - C_6 alkyl) $S(O)N(C_1$ - C_6 alkyl) $_2$, $-N(C_1$ - C_6 alkyl) $S(O)_2N(C_1$ - C_6 alkyl) $_2$, $-CO_2H$, $-C(O)OC_1$ - C_6 alkyl, $-C(O)NH_2$, $-C(O)NH(C_1$ - C_6 alkyl), $-C(O)N(C_1$ - C_6 alkyl) $_2$, $-SC_1$ - C_6 alkyl, $-S(O)C_1$ - C_6 alkyl, $-S(O)_2C_1$ - C_6 alkyl, $-S(O)NH(C_1$ - C_6 alkyl), $-S(O)_2NH(C_1$ - C_6 alkyl), $-S(O)N(C_1$ - C_6 alkyl) $_2$, $-S(O)_2N(C_1$ - C_6 alkyl) $_2$, $-P(C_1$ - C_6 alkyl) $_2$, $-P(O)(C_1$ - C_6 alkyl) $_2$, C_3 - C_6 cycloalkyl, or 3- to 7-membered heterocycloalkyl;

each R^2 and R^3 is independently H, deuterium, C_1 - C_6 alkyl, C_2 - C_6 alkenyl, C_2 - C_6 alkynyl, C_3 - C_6 cycloalkyl, C_6 - C_{10} aryl, $-C(O)OR^8$ or $-C(O)NR^8R^9$; wherein each hydrogen atom in C_1 - C_6 alkyl, C_2 - C_6 alkenyl, C_2 - C_6 alkynyl, C_3 - C_6 cycloalkyl and C_6 - C_{10} aryl is independently optionally substituted by deuterium, halogen, $-OH$, $-CN$, $-OC_1$ - C_6 alkyl, $-NH_2$, $-NH(C_1$ - C_6 alkyl), $-N(C_1$ - C_6 alkyl) $_2$, $-NHC(O)C_1$ - C_6 alkyl, $-N(C_1$ - C_6 alkyl) $C(O)C_1$ - C_6 alkyl, $-NHC(O)NH_2$, $-NHC(O)NHC_1$ - C_6 alkyl, $-N(C_1$ - C_6 alkyl) $C(O)NH_2$, $-N(C_1$ - C_6 alkyl) $C(O)NHC_1$ - C_6 alkyl, $-NHC(O)N(C_1$ - C_6 alkyl) $_2$, $-N(C_1$ - C_6 alkyl) $C(O)N(C_1$ - C_6 alkyl) $_2$, $-NHC(O)OC_1$ - C_6 alkyl, $-N(C_1$ - C_6 alkyl) $C(O)OC_1$ - C_6 alkyl, $-NHS(O)(C_1$ - C_6 alkyl), $-NHS(O)_2(C_1$ - C_6 alkyl), $-N(C_1$ - C_6 alkyl) $S(O)(C_1$ - C_6 alkyl), $-N(C_1$ - C_6 alkyl) $S(O)_2(C_1$ - C_6 alkyl), $-NHS(O)NH_2$, $-NHS(O)_2NH_2$,

-N(C₁-C₆ alkyl)S(O)NH₂, -N(C₁-C₆ alkyl)S(O)₂NH₂, -NHS(O)NH(C₁-C₆ alkyl), -NHS(O)₂NH(C₁-C₆ alkyl), -NHS(O)N(C₁-C₆ alkyl)₂, -NHS(O)₂N(C₁-C₆ alkyl)₂, -N(C₁-C₆ alkyl)S(O)NH(C₁-C₆ alkyl), -N(C₁-C₆ alkyl)S(O)₂NH(C₁-C₆ alkyl), -N(C₁-C₆ alkyl)S(O)N(C₁-C₆ alkyl)₂, -N(C₁-C₆ alkyl)S(O)₂N(C₁-C₆ alkyl)₂, -CO₂H, -C(O)OC₁-C₆ alkyl, -C(O)NH₂, -C(O)NH(C₁-C₆ alkyl), -C(O)N(C₁-C₆ alkyl)₂, -SC₁-C₆ alkyl, -S(O)C₁-C₆ alkyl, -S(O)₂C₁-C₆ alkyl, -S(O)NH(C₁-C₆ alkyl), -S(O)₂NH(C₁-C₆ alkyl), -S(O)N(C₁-C₆ alkyl)₂, -S(O)₂N(C₁-C₆ alkyl)₂, -P(C₁-C₆ alkyl)₂, -P(O)(C₁-C₆ alkyl)₂, C₃-C₆ cycloalkyl, or 3- to 7-membered heterocycloalkyl; or R² and R³ taken together with the carbon atoms to which they are attached optionally form a C₅-C₇ cycloalkyl or a 5- to 7-membered heterocycloalkyl; or R² and R⁶ taken together with the atoms to which they are attached optionally form a 5- to 7-membered heterocycloalkyl;

R⁴ is H, C₁-C₆ alkyl or 3- to 7-membered heterocycloalkyl, wherein each hydrogen atom in C₁-C₆ alkyl or 3- to 7-membered heterocycloalkyl is independently optionally substituted by halogen, -OH, -CN, -OC₁-C₆ alkyl, -NH₂, -NH(C₁-C₆ alkyl), -N(C₁-C₆ alkyl)₂, -CO₂H, -C(O)OC₁-C₆ alkyl, -C(O)NH₂, -C(O)NH(C₁-C₆ alkyl), -C(O)N(C₁-C₆ alkyl)₂, C₃-C₆ cycloalkyl, or monocyclic 5- to 7-membered heterocycloalkyl;

R⁵ is selected from the group consisting of fluoro, chloro, bromo, C₁-C₆ alkyl, -OH, -CN, -OC₁-C₆ alkyl, -NHC₁-C₆ alkyl, -N(C₁-C₆ alkyl)₂, C₃-C₆ cycloalkyl, 3- to 7-membered heterocycloalkyl, -O-(C₃-C₆ cycloalkyl), -O-(3- to 7-membered heterocycloalkyl), 5- to 7-membered heteroaryl, C₆-C₁₀ aryl, and -CF₃; wherein each hydrogen atom in C₁-C₆ alkyl, -OC₁-C₆ alkyl, -NHC₁-C₆ alkyl, -N(C₁-C₆ alkyl)₂, C₃-C₆ cycloalkyl, 3- to 7-membered heterocycloalkyl, -O-(C₃-C₆ cycloalkyl), -O-(3- to 7-membered heterocycloalkyl), 5- to 7-membered heteroaryl and C₆-C₁₀ aryl is independently optionally substituted by fluoro, chloro, bromo, -OH, -CN, -OC₁-C₆ alkyl, -NH₂, -NH(C₁-C₆ alkyl), -N(C₁-C₆ alkyl)₂, C₃-C₇ cycloalkyl, 3- to 7-membered heterocycloalkyl, C₆-C₁₀ aryl, 5- to 7-membered heteroaryl, -CO₂H, -C(O)OC₁-C₆ alkyl, -C(O)NH₂, -C(O)NH(C₁-C₆ alkyl) and -C(O)N(C₁-C₆ alkyl)₂;

R⁶ is selected from the group consisting of H, fluoro, chloro, bromo, C₁-C₆ alkyl, -OH, -CN, -OC₁-C₆ alkyl, -NHC₁-C₆ alkyl, -N(C₁-C₆ alkyl)₂, 5- to 7-membered heteroaryl, C₆-C₁₀ aryl, and -CF₃; wherein each hydrogen atom in C₁-C₆ alkyl, 5- to 7-membered heteroaryl and C₆-C₁₀ aryl is independently optionally substituted by fluoro, chloro, bromo, -OH, -CN, -OC₁-C₆ alkyl, -NH₂, -NH(C₁-C₆ alkyl), -N(C₁-C₆ alkyl)₂, -CO₂H, -C(O)OC₁-C₆ alkyl, -C(O)NH₂, -C(O)NH(C₁-C₆ alkyl) and -C(O)N(C₁-C₆ alkyl)₂;

R⁷ is H;

each R⁸ and R⁹ is independently H, deuterium, C₁-C₆ alkyl, C₂-C₆ alkenyl, C₂-C₆ alkynyl, C₃-C₆ cycloalkyl, 3- to 7-membered heterocycloalkyl, C₆-C₁₀ aryl or heteroaryl;

R¹⁰ is independently H, deuterium, C₁-C₆ alkyl, C₂-C₆ alkenyl, C₂-C₆ alkynyl, C₃-C₆ cycloalkyl, 3- to 7-membered heterocycloalkyl, C₆-C₁₀ aryl, or mono- or bicyclic heteroaryl; wherein each hydrogen atom in C₁-C₆ alkyl, C₂-C₆ alkenyl, C₂-C₆ alkynyl, C₃-C₆ cycloalkyl, 3- to 7-membered heterocycloalkyl, C₆-C₁₀ aryl, or mono- or bicyclic heteroaryl is independently optionally substituted by deuterium, halogen, C₁-C₆ alkyl, C₁-C₆ haloalkyl or -OR⁸; and

n is 1 or 2.

17. The use of claim 1 or compound for use of claim 16, wherein the cancer is mediated by a genetically altered BTK.

18. The use or compound for use of claim 17, wherein the genetically altered BTK comprises at least one resistance mutation.

19. The use or compound for use of claim 18, wherein the at least one resistance mutation is C481S.

20. The use of claim 1 or compound for use of claim 16, wherein the cancer is selected from the group consisting of NSCLC, triple negative breast cancer, leukemia, myeloproliferative neoplasms, chronic lymphocytic leukemia, mantle cell leukemia and pancreas adenocarcinoma.

21. The use of claim 1 or compound for use of claim 16, wherein the cancer is NSCLC.