[00198] As used herein, the IC_{50} refers to an amount, concentration or dosage of a particular test compound that achieves a 50% inhibition of a maximal response, such as inhibition of Btk, in an assay that measures such response.

[00199] As used herein, EC_{50} refers to a dosage, concentration or amount of a particular test compound that elicits a dose-dependent response at 50% of maximal expression of a particular response that is induced, provoked or potentiated by the particular test compound.

[00198] As used herein, the IC_{50} refers to an amount, concentration or dosage of a particular test compound that achieves a 50% inhibition of a maximal response, such as inhibition of Btk, in an assay that measures such response.

[00199] As used herein, EC_{50} refers to a dosage, concentration or amount of a particular test compound that elicits a dose-dependent response at 50% of maximal expression of a particular response that is induced, provoked or potentiated by the particular test compound.

BRIEF DESCRIPTION OF THE FIGURES

[00200] **FIG. 1(A)** presents an illustrative table of GI_{50} concentrations of Compound **1** that results in 50% decrease in cell proliferation. A variety of lymphoma cell lines incubated with a range of concentrations of Compound **1**. **(B)** presents an illustrative line graph showing inhibition of tumor growth in DLCL2 xenograft models. **(C)** presents an illustrative line graph showing inhibition of tumor growth in DOHH2 xenograft models. For in vivo lymphoma xenograft studies, 5E6 DOHH2 or DLCL2 cells in 50% matrigel were implanted subcutaneously in SCID mice and dosed orally with Compound **1** beginning when tumor size reached 100 mm2.

[00201] **FIG. 2** presents an illustrative line graph showing inhibition of collagen-induced arthritis in male DBA/1OlaHsd mice. Compound **1**or vehicle was dosed orally once per day starting at day 1. Dexamethasone was included as a positive control. Paw inflammation was scored from 0-5 and averaged across all paws from all animals for each group in the study. Compound **1** at 12.5 mg/kg and 50 mg/kg regressed inflammation through the end of the study (day 11) while 3.125 mg/kg significantly reduced the increase in paw inflammation.

[00202] **FIG. 3** presents an illustrative line graph showing inhibition of disease progression in a mouse MRL/lpr model of lupus. MRL/lpr mice (Jax strain 000485) were dosed orally once per day from 8 weeks of age until 20 weeks of age and urine protein levels were measured weekly. Compound **1** at 3.125 mg/kg, 12.5 mg/kg, and 50 mg/kg significantly reduced proteinuria, indicating amelioration of the progressive autoimmune renal failure seen in this mouse strain.

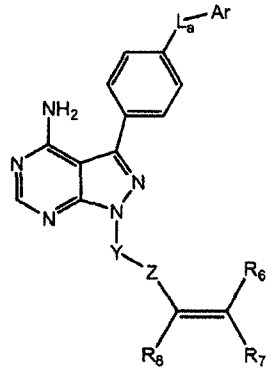
[00203] **FIG. 4** presents an illustrative bar graph showing inhibition of mast cell degranulation in a mouse passive cutaneous anaphylaxis model. 23 hours after mice were sensitized with an intradermal injection of monoclonal anti-DNP-IgE in the back, they received a single oral dose of Compound **1** or vehicle. After one hour, animals were challenged with an intravenous injection of DNP-BSA and Evans Blue dye and the area of extravasation was measured. Increasing doses of Compound **1** significantly decreased the amount of Evans Blue release, indicating decreased mast cell activation and vascular permeabilization.

[00204] **FIG. 5** presents an illustrative line graph showing in vivo plasma concentrations post-dosing of male jugular vein cannulated rats with Compounds 1, 7, 8, and 12. Blood samples were collected at 0.0833 (5 minutes), 0.333 (20 minutes), 1, 3, 6, 9, and 24 hours post-dosing from orally dosed rats. Compound **1** and Compound **12** have a short half-life in vivo. In contrast, Compound **7** and Compound **8** have a significantly longer in vivo half-life. Compounds like **1** and **12** are predicted to have enhanced kinase selectivity in vivo because inhibition will be sustained only for those kinases that are irreversibly inhibited.

[00205] **FIG. 6** presents an illustrative bar graph showing brief exposure to Compound **1** in vitro is sufficient to inhibit B cell activation in normal human B cells. B cells were purified from blood from healthy donors by negative selecting using the RosetteSep Human B cell enrichment cocktail. Cells were plated in growth media and indicated concentrations of Compound **1** were added. After incubation for 1 hour at 37°C,

The present invention also provides any one of the embodiments disclosed below and indicated with the numbers 1 to 100.

1. A compound of Formula (I) having the structure:



Formula (I)

wherein:

L_a is CH_2, O, NH or S;

Ar is a substituted or unsubstituted aryl, or a substituted or unsubstituted heteroaryl; and either

(i) Y is an optionally substituted group selected from among alkylene, heteroalkylene, arylene, heteroarylene, alkylenearylene, alkyleneheteroarylene, alkylenecycloalkylene and alkyleneheterocycloalkylene;

Z is C(=O), NHC(=O), $NR^aC(=O)$, $NR^aS(=O)_x$, where x is 1 or 2, and R^a is H, substituted or unsubstituted alkyl, substituted or unsubstituted cycloalkyl; and either

(a) R_7 and R_8 are H;

R_6 is H, substituted or unsubstituted C_1-C_4alkyl, substituted or unsubstituted C_1-C_4heteroalkyl, C_1-C_8alkylaminoalkyl, C_1-C_8hydroxyalkylaminoalkyl, C_1-C_8alkoxyalkylaminoalkyl, substituted or unsubstituted C_3-C_6cycloalkyl, substituted or unsubstituted C_1-C_8alkylC_3-C_6cycloalkyl, substituted or unsubstituted aryl, substituted or unsubstituted C_2-C_8heterocycloalkyl, substituted or unsubstituted heteroaryl, C_1-C_4alkyl(aryl), C_1-C_4alkyl(heteroaryl), C_1-C_8alkylethers, C_1-C_8alkylamides, or C_1-C_4alkyl(C_2-C_8heterocycloalkyl);

(b) R_6 and R_8 are H;

R_7 is H, substituted or unsubstituted C_1-C_4alkyl, substituted or unsubstituted C_1-C_4heteroalkyl, C_1-C_8alkylaminoalkyl, C_1-C_8hydroxyalkylaminoalkyl, C_1-C_8alkoxyalkylaminoalkyl, substituted or unsubstituted C_3-C_6cycloalkyl, substituted or unsubstituted C_1-C_8alkylC_3-C_6cycloalkyl, substituted or unsubstituted aryl, substituted or unsubstituted C_2-C_8heterocycloalkyl, substituted or unsubstituted heteroaryl, C_1-C_4alkyl(aryl), C_1-C_4alkyl(heteroaryl), C_1-C_8alkylethers, C_1-C_8alkylamides, or C_1-C_4alkyl(C_2-C_8heterocycloalkyl); or

(c) R_7 and R_8 taken together form a bond;

R_6 is H, substituted or unsubstituted C_1-C_4alkyl, substituted or unsubstituted C_1-C_4heteroalkyl, C_1-C_8alkylaminoalkyl, C_1-C_8hydroxyalkylaminoalkyl, C_1-C_8alkoxyalkylaminoalkyl, substituted or unsubstituted C_3-C_6cycloalkyl, substituted or unsubstituted C_1-C_8alkylC_3-C_6cycloalkyl, substituted or unsubstituted aryl, substituted or

unsubstituted C_2-C_8heterocycloalkyl, substituted or unsubstituted heteroaryl, C_1-C_4alkyl(aryl), C_1-C_4alkyl(heteroaryl), C_1-C_8alkylethers, C_1-C_8alkylamides, or C_1-C_4alkyl(C_2-C_8heterocycloalkyl); or

(ii) Y is an optionally substituted group selected from cycloalkylene or heterocycloalkylene;
Z is C(=O), NHC(=O), $NR^aC(=O)$, $NR^aS(=O)_x$, where x is 1 or 2, and R^a is H, substituted or unsubstituted alkyl, substituted or unsubstituted cycloalkyl; and either

(a) R_7 and R_8 are H;
R_6 is substituted or unsubstituted C_1-C_4heteroalkyl, C_1-C_8hydroxyalkylaminoalkyl, C_1-C_8alkoxyalkylaminoalkyl, substituted or unsubstituted C_3-C_6cycloalkyl, substituted or unsubstituted C_1-C_8alkylC_3-C_6cycloalkyl, substituted or unsubstituted aryl, substituted or unsubstituted C_2-C_8heterocycloalkyl, substituted or unsubstituted heteroaryl, C_1-C_4alkyl(aryl), C_1-C_4alkyl(heteroaryl), C_1-C_8alkylethers, C_1-C_8alkylamides, or C_1-C_4alkyl(C_2-C_8heterocycloalkyl);

(b) R_6 and R_8 are H;
R_7 is substituted or unsubstituted C_1-C_4heteroalkyl, C_1-C_8hydroxyalkylaminoalkyl, C_1-C_8alkoxyalkylaminoalkyl, substituted or unsubstituted C_3-C_6cycloalkyl, substituted or unsubstituted C_1-C_8alkylC_3-C_6cycloalkyl, substituted or unsubstituted aryl, substituted or unsubstituted C_2-C_8heterocycloalkyl, substituted or unsubstituted heteroaryl, C_1-C_4alkyl(aryl), C_1-C_4alkyl(heteroaryl), C_1-C_8alkylethers, C_1-C_8alkylamides, or C_1-C_4alkyl(C_2-C_8heterocycloalkyl); or

(c) R_7 and R_8 taken together form a bond;
R_6 is substituted or unsubstituted C_1-C_4alkyl, substituted or unsubstituted C_1-C_4heteroalkyl, C_1-C_8alkylaminoalkyl, C_1-C_8hydroxyalkylaminoalkyl, C_1-C_8alkoxyalkylaminoalkyl, substituted or unsubstituted C_3-C_6cycloalkyl, substituted or unsubstituted C_1-C_8alkylC_3-C_6cycloalkyl, substituted or unsubstituted aryl, substituted or unsubstituted C_2-C_8heterocycloalkyl, substituted or unsubstituted heteroaryl, C_1-C_4alkyl(aryl), C_1-C_4alkyl(heteroaryl), C_1-C_8alkylethers, C_1-C_8alkylamides, or C_1-C_4alkyl(C_2-C_8heterocycloalkyl); and

pharmaceutically active metabolites, or pharmaceutically acceptable solvates, pharmaceutically acceptable salts, or pharmaceutically acceptable prodrugs thereof.

2. The compound of Claim 1, wherein L_a is O.

3. The compound of Claim 2, wherein Ar is phenyl.

4. The compound of Claim 3, wherein:
Z is C(=O), NHC(=O), or $NCH_3C(=O)$.

5. The compound of any of claims 1-4, wherein

Y is an optionally substituted group selected from among alkylene, heteroalkylene, arylene, heteroarylene, alkylenearylene, alkyleneheteroarylene, alkylenecycloalkylene and alkyleneheterocycloalkylene;

Z is C(=O), NHC(=O), $NR^aC(=O)$, $NR^aS(=O)_x$, where x is 1 or 2, and R^a is H, substituted or unsubstituted alkyl, substituted or unsubstituted cycloalkyl; and either

(a) R_7 and R_8 are H;

R_6 is H, substituted or unsubstituted C_1-C_4alkyl, substituted or unsubstituted C_1-C_4heteroalkyl, C_1-C_8alkylaminoalkyl, C_1-C_8hydroxyalkylaminoalkyl, C_1-C_8alkoxyalkylaminoalkyl, substituted or unsubstituted C_3-C_6cycloalkyl, substituted or unsubstituted C_1-C_8alkylC_3-C_6cycloalkyl, substituted or unsubstituted aryl, substituted or unsubstituted C_2-C_8heterocycloalkyl, substituted or unsubstituted heteroaryl, C_1-C_4alkyl(aryl), C_1-C_4alkyl(heteroaryl), C_1-C_8alkylethers, C_1-C_8alkylamides, or C_1-C_4alkyl(C_2-C_8heterocycloalkyl);

(b) R_6 and R_8 are H;

R_7 is H, substituted or unsubstituted C_1-C_4alkyl, substituted or unsubstituted C_1-C_4heteroalkyl, C_1-C_8alkylaminoalkyl, C_1-C_8hydroxyalkylaminoalkyl, C_1-C_8alkoxyalkylaminoalkyl, substituted or unsubstituted C_3-C_6cycloalkyl, substituted or unsubstituted C_1-C_8alkylC_3-C_6cycloalkyl, substituted or unsubstituted aryl, substituted or unsubstituted C_2-C_8heterocycloalkyl, substituted or unsubstituted heteroaryl, C_1-C_4alkyl(aryl), C_1-C_4alkyl(heteroaryl), C_1-C_8alkylethers, C_1-C_8alkylamides, or C_1-C_4alkyl(C_2-C_8heterocycloalkyl); or

(c) R_7 and R_8 taken together form a bond;

R_6 is H, substituted or unsubstituted C_1-C_4alkyl, substituted or unsubstituted C_1-C_4heteroalkyl, C_1-C_8alkylaminoalkyl, C_1-C_8hydroxyalkylaminoalkyl, C_1-C_8alkoxyalkylaminoalkyl, substituted or unsubstituted C_3-C_6cycloalkyl, substituted or unsubstituted C_1-C_8alkylC_3-C_6cycloalkyl, substituted or unsubstituted aryl, substituted or unsubstituted C_2-C_8heterocycloalkyl, substituted or unsubstituted heteroaryl, C_1-C_4alkyl(aryl), C_1-C_4alkyl(heteroaryl), C_1-C_8alkylethers, C_1-C_8alkylamides, or C_1-C_4alkyl(C_2-C_8heterocycloalkyl).

6. The compound of claim 5, wherein

R_7 and R_8 are H; and

R_6 is H, substituted or unsubstituted C_1-C_4alkyl, substituted or unsubstituted C_1-C_4heteroalkyl, C_1-C_8alkylaminoalkyl, C_1-C_8hydroxyalkylaminoalkyl, C_1-C_8alkoxyalkylaminoalkyl, substituted or unsubstituted C_3-C_6cycloalkyl, substituted or unsubstituted C_1-C_8alkylC_3-C_6cycloalkyl, substituted or unsubstituted aryl, substituted or unsubstituted C_2-C_8heterocycloalkyl, substituted or unsubstituted heteroaryl, C_1-C_4alkyl(aryl), C_1-C_4alkyl(heteroaryl), C_1-C_8alkylethers, C_1-C_8alkylamides, or C_1-C_4alkyl(C_2-C_8heterocycloalkyl).

7. The compound of claim 6, wherein Y is alkyleneheterocycloalkylene.

8. The compound of claim 6, wherein:

R_6 is H, substituted or unsubstituted C_1-C_4alkyl, C_1-C_8alkylaminoalkyl, substituted or unsubstituted C_1-C_8alkylC_3-C_6cycloalkyl, or C_1-C_4alkyl(C_2-C_8heterocycloalkyl)

9. The compound of claim 5, wherein

R_6 and R_8 are H; and

R_7 is H, substituted or unsubstituted C_1-C_4alkyl, substituted or unsubstituted C_1-C_4heteroalkyl, C_1-C_8alkylaminoalkyl, C_1-C_8hydroxyalkylaminoalkyl, C_1-C_8alkoxyalkylaminoalkyl, substituted or unsubstituted C_3-C_6cycloalkyl, substituted or unsubstituted C_1-C_8alkylC_3-C_6cycloalkyl, substituted or unsubstituted aryl, substituted or unsubstituted C_2-C_8heterocycloalkyl, substituted or unsubstituted heteroaryl, C_1-C_4alkyl(aryl), C_1-C_4alkyl(heteroaryl), C_1-C_8alkylethers, C_1-C_8alkylamides, or C_1-C_4alkyl(C_2-C_8heterocycloalkyl).

10. The compound of claim 9, wherein Y is alkyleneheterocycloalkylene.

11. The compound of claim 9, wherein:

R_7 is H, substituted or unsubstituted C_1-C_4alkyl, C_1-C_8alkylaminoalkyl, substituted or unsubstituted C_1-C_8alkylC_3-C_6cycloalkyl, or C_1-C_4alkyl(C_2-C_8heterocycloalkyl)

12. The compound of claim 5, wherein

R_7 and R_8 taken together form a bond; and

R_6 is H, substituted or unsubstituted C_1-C_4alkyl, substituted or unsubstituted C_1-C_4heteroalkyl, C_1-C_8alkylaminoalkyl, C_1-C_8hydroxyalkylaminoalkyl, C_1-C_8alkoxyalkylaminoalkyl, substituted or unsubstituted C_3-C_6cycloalkyl, substituted or unsubstituted C_1-C_8alkylC_3-C_6cycloalkyl, substituted or unsubstituted aryl, substituted or unsubstituted C_2-C_8heterocycloalkyl, substituted or unsubstituted heteroaryl, C_1-C_4alkyl(aryl), C_1-C_4alkyl(heteroaryl), C_1-C_8alkylethers, C_1-C_8alkylamides, or C_1-C_4alkyl(C_2-C_8heterocycloalkyl).

13. The compound of claim 12, wherein Y is alkyleneheterocycloalkylene.

14. The compound of claim 12, wherein:

R_6 is H, substituted or unsubstituted C_1-C_4alkyl, C_1-C_8alkylaminoalkyl, substituted or unsubstituted C_1-C_8alkylC_3-C_6cycloalkyl, or C_1-C_4alkyl(C_2-C_8heterocycloalkyl)

15. The compound of any of claims 1-4, wherein

Y is an optionally substituted group selected from cycloalkylene or heterocycloalkylene;

Z is C(=O), NHC(=O), $NR^aC(=O)$, $NR^aS(=O)_x$, where x is 1 or 2, and R^a is H, substituted or unsubstituted alkyl, substituted or unsubstituted cycloalkyl; and either

(a) R_7 and R_8 are H;

R_6 is substituted or unsubstituted C_1-C_4heteroalkyl, C_1-C_8hydroxyalkylaminoalkyl, C_1-C_8alkoxyalkylaminoalkyl, substituted or unsubstituted C_3-C_6cycloalkyl, substituted or unsubstituted C_1-C_8alkylC_3-C_6cycloalkyl, substituted or unsubstituted aryl, substituted or unsubstituted C_2-C_8heterocycloalkyl, substituted or unsubstituted heteroaryl, C_1-C_4alkyl(aryl), C_1-C_4alkyl(heteroaryl), C_1-C_8alkylethers, C_1-C_8alkylamides, or C_1-C_4alkyl(C_2-C_8heterocycloalkyl);

(b) R_6 and R_8 are H;

R_7 is substituted or unsubstituted C_1-C_4heteroalkyl, C_1-C_8hydroxyalkylaminoalkyl, C_1-C_8alkoxyalkylaminoalkyl, substituted or unsubstituted C_3-C_6cycloalkyl, substituted or unsubstituted C_1-C_8alkylC_3-C_6cycloalkyl, substituted or unsubstituted aryl, substituted or unsubstituted C_2-C_8heterocycloalkyl, substituted or unsubstituted heteroaryl, C_1-C_4alkyl(aryl), C_1-C_4alkyl(heteroaryl), C_1-C_8alkylethers, C_1-C_8alkylamides, or C_1-C_4alkyl(C_2-C_8heterocycloalkyl); or

(c) R_7 and R_8 taken together form a bond;

R_6 is substituted or unsubstituted C_1-C_4alkyl, substituted or unsubstituted C_1-C_4heteroalkyl, C_1-C_8alkylaminoalkyl, C_1-C_8hydroxyalkylaminoalkyl, C_1-C_8alkoxyalkylaminoalkyl, substituted or unsubstituted C_3-C_6cycloalkyl, substituted or unsubstituted C_1-C_8alkylC_3-C_6cycloalkyl, substituted or unsubstituted aryl, substituted or unsubstituted C_2-C_8heterocycloalkyl, substituted or unsubstituted heteroaryl, C_1-C_4alkyl(aryl), C_1-C_4alkyl(heteroaryl), C_1-C_8alkylethers, C_1-C_8alkylamides, or C_1-C_4alkyl(C_2-C_8heterocycloalkyl).

16. The compound of claim 15, wherein:

R_7 and R_8 are H; and

R_6 is substituted or unsubstituted C_1-C_4heteroalkyl, C_1-C_8hydroxyalkylaminoalkyl, C_1-C_8alkoxyalkylaminoalkyl, substituted or unsubstituted C_3-C_6cycloalkyl, substituted or unsubstituted C_1-C_8alkylC_3-C_6cycloalkyl, substituted or unsubstituted aryl, substituted or unsubstituted C_2-C_8heterocycloalkyl, substituted or unsubstituted heteroaryl, C_1-C_4alkyl(aryl), C_1-C_4alkyl(heteroaryl), C_1-C_8alkylethers, C_1-C_8alkylamides, or C_1-C_4alkyl(C_2-C_8heterocycloalkyl).

17. The compound of claim 16, wherein:

R_6 is substituted or unsubstituted C_1-C_8alkylC_3-C_6cycloalkyl, or C_1-C_4alkyl(C_2-C_8heterocycloalkyl).

18. The compound of claim 15, wherein:

R_6 and R_8 are H; and

R_7 is substituted or unsubstituted C_1-C_4heteroalkyl, C_1-C_8hydroxyalkylaminoalkyl, C_1-C_8alkoxyalkylaminoalkyl, substituted or unsubstituted C_3-C_6cycloalkyl, substituted or unsubstituted C_1-C_8alkylC_3-C_6cycloalkyl, substituted or unsubstituted aryl, substituted or unsubstituted C_2-C_8heterocycloalkyl, substituted or unsubstituted heteroaryl, C_1-C_4alkyl(aryl), C_1-C_4alkyl(heteroaryl), C_1-C_8alkylethers, C_1-C_8alkylamides, or C_1-C_4alkyl(C_2-C_8heterocycloalkyl).

19. The compound of claim 18, wherein:

R_7 is substituted or unsubstituted C_1-C_8alkylC_3-C_6cycloalkyl, or C_1-C_4alkyl(C_2-C_8heterocycloalkyl).

20. The compound of claim 15, wherein:

R_7 and R_8 taken together form a bond; and

R_6 is substituted or unsubstituted C_1-C_4alkyl, substituted or unsubstituted C_1-C_4heteroalkyl, C_1-C_8alkylaminoalkyl, C_1-C_8hydroxyalkylaminoalkyl, C_1-C_8alkoxyalkylaminoalkyl, substituted or unsubstituted C_3-C_6cycloalkyl, substituted or unsubstituted C_1-C_8alkylC_3-C_6cycloalkyl, substituted or unsubstituted aryl, substituted or unsubstituted C_2-C_8heterocycloalkyl, substituted or unsubstituted heteroaryl, C_1-C_4alkyl(aryl), C_1-C_4alkyl(heteroaryl), C_1-C_8alkylethers, C_1-C_8alkylamides, or C_1-C_4alkyl(C_2-C_8heterocycloalkyl).

21. The compound of claim 16, wherein:

R_6 is substituted or unsubstituted C_1-C_4alkyl, C_1-C_8alkylaminoalkyl, substituted or unsubstituted C_1-C_8alkylC_3-C_6cycloalkyl, or C_1-C_4alkyl(C_2-C_8heterocycloalkyl).

22. A compound selected from among:

(E)-4-(N-(2-hydroxyethyl)-N-methylamino)-1-(3-(4-phenoxyphenyl)-1H-pyrazolo[3,4-*d*]pyrimidin-1-yl)piperidin-1-yl)but-2-en-1-one (Compound **3**); (E)-1-(3-(4-amino-3-(4-phenoxyphenyl)-1*H*-pyrazolo[3,4-*d*-]pyrimidin-1-yl)-3-(1*H*-imidazol-4-yl)prop-2-en-1-one (Compound **4**); (E)-1-(3-(4-amino-3-(4-phenoxyphenyl)-1*H*-pyrazolo[3,4-*d*]pyrimidin-1-yl)piperidin-1-yl)-4-morpholinobut-2-en-1-one (Compound **5**); (E)-1-(4-(4-amino-3-(4-phenoxyphenyl)-1*H*-pyrazolo[3,4-*d*]pyrimidin-1-yl)piperidin-1-yl)-4-(dimethylamino)but-2-en-1-one (Compound **7**); (E)-*N*-((1*s*,4*s*)-4-(4-amino-3-(4-phenoxyphenyl)-1*H*-pyrazolo[3,4-*d*]pyrimidin-1-yl)cyclohexyl)-4-(dimethylamino)but-2-enamide (Compound **8**); *N*-((1*r*,4*r*)-4-(4-amino-3-(4-phenoxyphenyl)-1*H*-pyrazolo[3,4-*d*]pyrimidin-1-yl)cyclohexyl)acrylamide (Compound **10**); (*E*)-1-((*R*)-2-((4-amino-3-(4-phenoxyphenyl)-1*H*-pyrazolo[3,4-*d*]pyrimidin-1-yl)methyl)pyrolidin-1-yl)-4-(dimethylamino)but-2-en-1-one (Compound **11**); (*E*)-1-((*S*)-2-((4-amino-3-(4-phenoxyphenyl)-1*H*-pyrazolo[3,4-*d*]pyrimidin-1-yl)methyl)pyrolidin-1-yl)-4-(dimethylamino)but-2-en-1-one (Compound **12**); 1-((*R*)-2-((4-amino-3-(4-phenoxyphenyl)-1*H*-pyrazolo[3,4-*d*]pyrimidin-1-yl)methyl)pyrrolidin-1-yl)prop-2-en-1-one (Compound **13**); 1-((*S*)-2-((4-amino-3-(4-phenoxyphenyl)-1*H*-pyrazolo[3,4-*d*]pyrimidin-1-yl)methyl)pyrrolidin-1-yl)prop-2-en-1-one (Compound **14**); 1((*R*)-2-((4-amino-3-(4-phenoxyphenyl)-1*H*-pyrazolo[3,4-*d*]pyrimidin-1-yl)methyl)pyrrolidin-1-yl)but-2-yn-1-one (Compound **15**); 1-((*S*)-2-((4-amino-3-(4-phenoxyphenyl)-1*H*-pyrazolo[3,4-*d*]pyrimidin-1-yl)methyl)pyrrolidin-1-yl)but-2-yn-1-one (Compound **16**); 1-((*R*)-3-(4-amino-3-(4-phenoxyphenyl)-1*H*-pyrazolo[3,4-*d*]pyrimidin-1-yl)piperidin-1-yl)but-2-yn-1-one (Compound **17**); (*E*)-*N*-((1,*r*,4*r*)-4-(4-amino-3-(4-phenoxyphenyl)-1*H*-pyrazolo[3,4-*d*]pyrimidin-1-yl)cyclohexyl-4-(dimethylamino)but-2-enamide (Compound **18**); *N*-(2-(4-amino-3-(4-phenoxyphenyl)-1*H*-pyrazolo[3,4-*d*]pyrimidin-1-yl)ethyl)-*N*-methylacrylamide (Compound **19**); (*E*)-1-(4-(4-amino-3-(4-phenoxyphenyl)-1*H*-pyrazolo[3,4-*d*]pyrimidin-1-yl)-4-morpholinobut-2-en-1-one (Compound **20**); (*E*)-1-((*S*_-2-((4-amino-3-(4-phenoxyphenyl)-1*H*-pyrazolo[3,4-*d*]pyrimidin-1-yl)methyl)pyrrolidin-1-yl)-4-morpholinobut-2-en-1-one (Compound **21**); *N*-((1*s*,4*s*)-4-(4-amino-3-(4-phenoxyphenyl)-1*H*-pyrazolo[3,4-*d*]pyrimidin-1-yl)cyclohexyl)but-2-ynamide (Compound **22**); *N*-(2-(4-amino-3-(4-phenoxyphenyl)-1*H*-pyrazolo[3,4-*d*]pyrimidin-1-yl)ethyl)acrylamide (Compound **23**); (*E*)-1-((*R*)-3-(4-amino-3-(4-phenoxyphenyl)-1*H*-pyrazolo[3,4-*d*]pyrimidin-1-yl)piperidin-1-yl)-4-morpholinobut-2-en-1-one (Compound **24**); (*E*)-*N*-((1*s*,4*s*)-4-(4-amino-3-(4-phenoxyphenyl)-1*H*-pyrazolo[3,4-*d*]pyrimidin-1-yl)cyclohexyl)-4-morpholinobut-2-enamide (Compound **25**).

23. A pharmaceutical formulation comprising a therapeutically effective amount of a compound of any of Claims 1-22, and a pharmaceutically acceptable excipient.

24. The pharmaceutical formulation of claim 23 that is formulated for a route of administration selected from oral administration, parenteral administration, buccal administration, nasal administration, topical administration, or rectal administration.

25. A method for treating an autoimmune disease or condition comprising administering to a patient in need the pharmaceutical formulation of claim 23.

26. The method of Claim 25, wherein the autoimmune disease is selected from rheumatoid arthritis or lupus.

27. A method for treating a heteroimmune disease or condition comprising administering to a patient in need the pharmaceutical formulation of claim 23.

28. A method for treating a cancer comprising administering to a patient in need the pharmaceutical formulation of claim 23.

29. The method of claim 28, wherein the cancer is a B-cell proliferative disorder.

30. The method of claim 29, wherein the B-cell proliferative disorder is diffuse large B cell lymphoma, follicular lymphoma or chronic lymphocytic leukemia.

31. A method for treating mastocytosis comprising administering to a patient in need the pharmaceutical formulation of claim 23.

32. A method for treating osteoporosis or bone resorption disorders comprising administering to a patient in need the pharmaceutical formulation of claim 23.

33. A method for treating an inflammatory disease or condition comprising administering to a patient in need the pharmaceutical formulation of claim 23.

34. A method for treating lupus comprising administering to a subject in need thereof a composition containing a therapeutically effective amount of a compound that forms a covalent bond with a cysteine sidechain of a Bruton's tyrosine kinase or a Bruton's tyrosine kinase homolog.

35. A method for treating a heteroimmune disease or condition comprising administering to a subject in need thereof a composition containing a therapeutically effective amount of a compound that forms a covalent bond with a cysteine sidechain of a Bruton's tyrosine kinase or a Bruton's tyrosine kinase homolog.

36. A method for treating diffuse large B cell lymphoma, follicular lymphoma or chronic lymphocytic leukemia comprising administering to a subject in need thereof a composition containing a therapeutically effective amount of a compound that forms a covalent bond with a cysteine sidechain of a Bruton's tyrosine kinase or a Bruton's tyrosine kinase homolog.

37. A method for treating mastocytosis, comprising administering to a subject in need thereof a composition containing a therapeutically effective amount of a compound that forms a covalent bond with a cysteine sidechain of a Bruton's tyrosine kinase or a Bruton's tyrosine kinase homolog.

38. A method for treating osteoporosis or bone resorption disorders comprising administering to a subject in need thereof a composition containing a therapeutically effective amount of a compound that forms a covalent bond with a cysteine sidechain of a Bruton's tyrosine kinase or a Bruton's tyrosine kinase homolog.

39. A method for treating an inflammatory disease or condition comprising administering to a subject in need thereof a composition containing a therapeutically effective amount of a compound that forms a covalent bond with a cysteine sidechain of a Bruton's tyrosine kinase or a Bruton's tyrosine kinase homolog.

40. A kinase inhibitor that selectively and irreversibly binds to a protein tyrosine kinase selected from Btk, a Btk homolog, and a Btk kinase cysteine homolog, in which the kinase inhibitor reversibly and non-selectively binds to a multiplicity of protein tyrosine kinases, and further in which the plasma half life of the kinase inhibitor is less than about 4 hours.

41. The kinase inhibitor of claim 40 that selectively and irreversibly binds to at least one of Btk, Jak3, Blk, Bmx, Tec, and Itk.

42. The kinase inhibitor of claim 41 that selectively and irreversibly binds to Btk.

43. The kinase inhibitor of claim 41 that selectively and irreversibly binds to Jak3.

44. The kinase inhibitor of claim 41 that selectively and irreversibly binds to Tec.

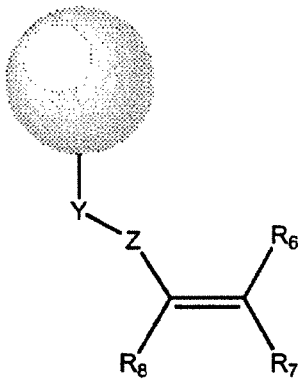
45. The kinase inhibitor of claim 41 that selectively and irreversibly binds to Btk and Tec.

46. The kinase inhibitor of claim 41 that selectively and irreversibly binds to Blk.

47. The kinase inhibitor of claim 40 that reversibly and non-selectively binds to a multiplicity of src-family protein kinase inhibitors.

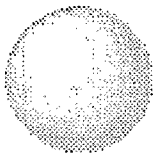
48. The kinase inhibitor of claim 40, in which the plasma half life of the kinase inhibitor is less than about 3 hours.

49. The kinase inhibitor of claim 40, having the structure of Formula (VII):



Formula (VII)

wherein:



is a moiety that binds to the active site of a kinase, including a tyrosine kinase, further including a Btk kinase cysteine homolog;

Y is an optionally substituted group selected from among alkylene, heteroalkylene, arylene, heteroarylene, heterocycloalkylene, cycloalkylene, alkylenearylene, alkyleneheteroarylene, alkylenecycloalkylene, and alkyleneheterocycloalkylene;

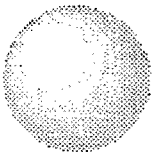
Z is C(=O), OC(=O), NHC(=O), $NCH_3C(=O)$, C(=S), $S(=O)_x$, $OS(=O)_x$, $NHS(=O)_x$, where x is 1 or 2;

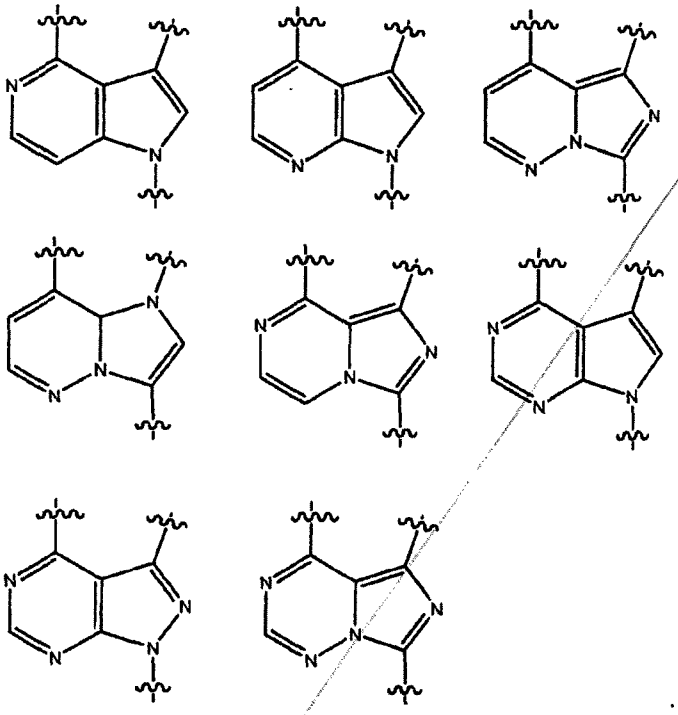
R_7 and R_8 are independently selected from among H, unsubstituted C_1-C_4 alkyl, substituted C_1-C_4alkyl, unsubstituted C_1-C_4heteroalkyl, substituted C_1-C_4heteroalkyl, unsubstituted C_3-C_6cycloalkyl, substituted C_3-C_6cycloalkyl, unsubstituted C_2-C_6heterocycloalkyl, and substituted C_2-C_6heterocycloalkyl; or

R_7 and R_8 taken together form a bond;

R_6 is H, substituted or unsubstituted C_1-C_4alkyl, substituted or unsubstituted C_1-C_4heteroalkyl, C_1-C_6alkoxyalkyl, C_1-C_8alkylaminoalkyl, C_1-C_8hydroxyalkylaminoalkyl, substituted or unsubstituted C_3-C_6cycloalkyl, substituted or unsubstituted aryl, substituted or unsubstituted C_2-C_8heterocycloalkyl, substituted or unsubstituted heteroaryl, C_1-C_4alkyl(aryl), C_1-C_4alkyl(heteroaryl), C_1-C_4alkyl(C_3-C_8cycloalkyl), or C_1-C_4alkyl(C_2-C_8heterocycloalkyl); and

pharmaceutically active metabolites, or pharmaceutically acceptable solvates, pharmaceutically acceptable salts, or pharmaceutically acceptable prodrugs thereof.

50. The kinase inhibitor of Claim 49, wherein  is a substituted fused biaryl moiety selected from



51. The kinase inhibitor of Claim 49, wherein:

Z is C(=O), NHC(=O), $NCH_3C(=O)$, or $S(=O)_2$.

52. The kinase inhibitor of Claim 49, wherein:

each of R_7 and R_8 is H; or

R_7 and R_8 taken together form a bond.

53. The kinase inhibitor of Claim 49, wherein:

R_6 is H, substituted or unsubstituted C_1-C_4alkyl, substituted or unsubstituted C_1-C_4heteroalkyl, C_1-C_6alkoxyalkyl, C_1-C_8alkylaminoalkyl, C_1-C_8hydroxyalkylaminoalkyl, C_1-C_8alkoxyalkylaminoalkyl, C_1-C_4alkyl(aryl), C_1-C_4alkyl(heteroaryl), C_1-C_4alkyl(C_3-C_8cycloalkyl), or C_1-C_4alkyl(C_2-C_8heterocycloalkyl).

54. The kinase inhibitor of Claim 49, wherein:

Y is a 4-, 5-, 6-, or 7-membered cycloalkylene ring; or

Y is a 4-, 5-, 6-, or 7-membered heterocycloalkylene ring; or

Y is a C_1-C_4 alkylene, or 4-, 5-, 6-, or 7-membered heterocycloalkylene ring.

55. A pharmaceutical formulation comprising the kinase inhibitor of any of claims 40-54 and a pharmaceutically acceptable excipient.

56. The pharmaceutical formulation of claim 55 that is formulated for a route of administration selected from oral administration, parenteral administration, buccal administration, nasal administration, topical administration, or rectal administration.

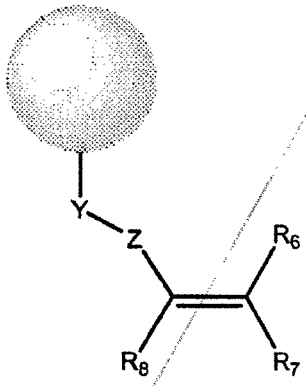
57. The pharmaceutical formulation of claim 56 that is formulated for oral administration.

58. A method for treating rheumatoid arthritis comprising administering to a subject the kinase inhibitor of claim 41 that selectively and irreversibly binds to Btk and Tec.

59. A method for increasing the selectivity of a test protein tyrosine kinase inhibitor that irreversibly and selectively binds to at least one protein kinase inhibitor selected from Btk, a Btk homolog, or a Btk kinase cysteine homolog, in which the test protein tyrosine kinase inhibitor is chemically modified to decrease the plasma half life to less than about 4 hours.

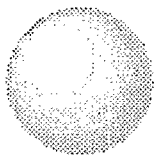
60. The method of claim 59, in which the test protein tyrosine kinase inhibitor is chemically modified to decrease the plasma half life to less than about 3 hours.

61. The method of claim 59 or claim 60, in which the test protein tyrosine kinase inhibitor has the structure of Formula (VII):



Formula (VII)

wherein:



is a moiety that binds to the active site of a kinase, including a tyrosine kinase, further including a Btk kinase cysteine homolog;

Y is an optionally substituted group selected from among alkylene, heteroalkylene, arylene, heteroarylene, heterocycloalkylene, cycloalkylene, alkylenearylene, alkyleneheteroarylene, alkylenecycloalkylene, and alkyleneheterocycloalkylene;

Z is C(=O), OC(=O), NHC(=O), $NCH_3C(=O)$, C(=S), $S(=O)_x$, $OS(=O)_x$, $NHS(=O)_x$, where x is 1 or 2;

R_7 and R_8 are independently selected from among H, unsubstituted C_1-C_4 alkyl, substituted C_1-C_4alkyl, unsubstituted C_1-C_4heteroalkyl, substituted C_1-C_4heteroalkyl, unsubstituted C_3-C_6cycloalkyl, substituted C_3-C_6cycloalkyl, unsubstituted C_2-C_6heterocycloalkyl, and substituted C_2-C_6heterocycloalkyl; or

R_7 and R_8 taken together form a bond; and

R_6 is H, substituted or unsubstituted C_1-C_4alkyl, substituted or unsubstituted C_1-C_4heteroalkyl, C_1-C_6alkoxyalkyl, C_1-C_8alkylaminoalkyl, C_1-C_8hydroxyalkylaminoalkyl, C_1-C_8alkoxyalkylaminoalkyl, substituted or unsubstituted C_3-C_6cycloalkyl, substituted or unsubstituted aryl, substituted or unsubstituted C_2-C_8heterocycloalkyl, substituted or unsubstituted heteroaryl, C_1-C_4alkyl(aryl), C_1-C_4alkyl(heteroaryl), C_1-C_4alkyl(C_3-C_8cycloalkyl), or C_1-C_4alkyl(C_2-C_8heterocycloalkyl).

62. The method of claim 59, in which the test protein tyrosine kinase inhibitor non-selectively and reversibly binds to a multiplicity of src-family protein tyrosine kinases.

63. A method for treating a B-cell proliferative disorder or a mast cell proliferative disorder comprising administering to a patient in need the pharmaceutical composition of claim 55.

64. A method for treating a rheumatoid arthritis or condition comprising administering to a patient in need the pharmaceutical composition of claim 55.

65. A method for treating a disease characterized by hyperactive B cells comprising administering to a patient in need the pharmaceutical composition of claim 55.

66. A method for treating a disease characterized by hyperactive mast cells comprising administering to a patient in need the pharmaceutical composition of claim 55.

67. A method for treating a disease characterized by both hyperactive B cells and hyperactive mast cells comprising administering to a patient in need the pharmaceutical composition of claim 55.

68. The methods of any of claims 63 to 67, in which the pharmaceutical composition is administered once a day.

69. A method of identifying an irreversible inhibitor of a kinase selected from Btk, a Btk homolog, or a Btk kinase cysteine homolog comprising:

(1) contacting a multiplicity of kinases selected from Btk, a Btk homolog, or a Btk kinase cysteine homolog with a compound that comprises a Michael acceptor moiety;

(2) contacting at least one non-kinase molecule having at least one accessible SH group with the compound that comprises a Michael acceptor moiety; and

(3) determining the covalent binding of the compound that comprises a Michael acceptor with the multiplicity of kinases and the at least one non-kinase molecule; and

repeating steps (1), (2), and (3) for at least one other compound that comprises a Michael acceptor moiety.

70. The method of claim 69, further comprising

(4) comparing the covalent binding of the compound that comprises a Michael acceptor with the multiplicity of kinases and the at least one non-kinase molecule; and

repeating steps (1), (2), (3) and (4) for at least one other compound that comprises a Michael acceptor moiety.

71. The method of claim 69, wherein the at least one non-kinase molecule having at least one accessible SH group includes glutathione and/or hemoglobin.

72. The method of claim 71, wherein a desired irreversible inhibitor is selective for a particular kinase relative to other kinases, glutathione and hemoglobin.

73. The method of claim 69, further comprising contacting each kinase with an Activity Probe.

74. The method of claim 69, wherein steps (1) and (2) are conducted in vivo and step (3) is conducted in part using an Activity Probe.

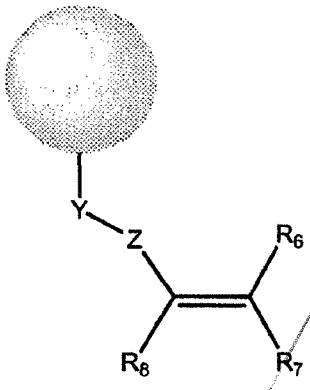
75. The method of claim 69, wherein the determining step uses mass spectrometry.

76. The method of claim 69, wherein the determining step uses fluorescence.

77. The method of claim 70, wherein the compound further comprises an active site binding moiety.

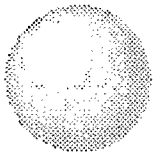
78. The method of claim 77, wherein the compound further comprises a linker moiety that links the Michael acceptor moiety to the active site binding moiety.

79. The method of claim 69, wherein the at least one compound has the structure of Formula (VII):



Formula (VII)

wherein:



is a moiety that binds to the active site of a kinase, including a tyrosine kinase, further including a Btk kinase cysteine homolog;

Y is an optionally substituted group selected from among alkylene, heteroalkylene, arylene, heteroarylene, heterocycloalkylene, cycloalkylene, alkylenearylene, alkyleneheteroarylene, alkylenecycloalkylene, and alkyleneheterocycloalkylene;

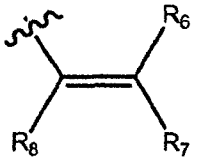
Z is C(=O), OC(=O), NHC(=O), $NCH_3C(=O)$, C(=S), $S(=O)_x$, $OS(=O)_x$, $NHS(=O)_x$, where x is 1 or 2;

R_7 and R_8 are independently selected from among H, unsubstituted C_1-C_4 alkyl, substituted C_1-C_4alkyl, unsubstituted C_1-C_4heteroalkyl, substituted C_1-C_4heteroalkyl, unsubstituted C_3-C_6cycloalkyl, substituted C_3-C_6cycloalkyl, unsubstituted C_2-C_6heterocycloalkyl, and substituted C_2-C_6heterocycloalkyl; or

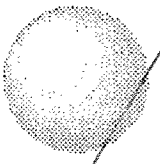
R_7 and R_8 taken together form a bond; and

R_6 is H, substituted or unsubstituted C_1-C_4alkyl, substituted or unsubstituted C_1-C_4heteroalkyl, C_1-C_6alkoxyalkyl, C_1-C_8alkylaminoalkyl, C_1-C_8hydroxyalkylaminoalkyl, C_1-C_8alkoxyalkylaminoalkyl, substituted or unsubstituted C_3-C_6cycloalkyl, substituted or unsubstituted aryl, substituted or unsubstituted C_2-C_8heterocycloalkyl, substituted or unsubstituted heteroaryl, C_1-C_4alkyl(aryl), C_1-C_4alkyl(heteroaryl), C_1-C_4alkyl(C_3-C_8cycloalkyl), or C_1-C_4alkyl(C_2-C_8heterocycloalkyl).

80. The method of claim 78, further comprising analyzing the structure-function activity relationship between the structure of the linker moiety and/or the Michael acceptor moiety of each compound, and the binding and/or selectivity of each compound to at least one kinase.

81. The method of claim 79, further comprising analyzing the structure-function activity relationship between the structure of Y-Z and/or  of each compound, and the binding and/or selectivity of each compound to at least one kinase.

82. The method of claim 80, wherein the structure of the active site binding moiety of each compound is not varied.

83. The method of claim 79, wherein the structure of  of each compound is not varied.

84. An assay comprising the method of any of claims 70 to 83.

85. A system comprising the assay of claim 80 or any method of claims 70 to 63.

86. An irreversible inhibitor of a kinase selected from Btk, a Btk homolog, and a Btk kinase cysteine homolog, wherein the inhibitor is identified using any method of claims 70 to 83, the assay of claim 84, or the system of claim 85.

87. The irreversible inhibitor of claim 86, wherein the inhibitor is selective for one kinase selected from Btk, a Btk homolog, and a Btk kinase cysteine homolog over at least one other kinase selected from Btk, a Btk homolog, and a Btk kinase cysteine homolog.

88. The irreversible inhibitor of claim 87, wherein the inhibitor is at least 5 times more selective for one kinase selected from Btk, a Btk homolog, and a Btk kinase cysteine homolog over at least one other kinase selected from Btk, a Btk homolog, and a Btk kinase cysteine homolog.

89. The irreversible inhibitor of claim 88, wherein the inhibitor is at least 50 times more selective for one kinase selected from Btk, a Btk homolog, and a Btk kinase cysteine homolog over at least one other kinase selected from Btk, a Btk homolog, and a Btk kinase cysteine homolog.

90. The irreversible inhibitor of claim 86, wherein the inhibitor is selective for at least one kinase selected from Btk, a Btk homolog, and a Btk kinase cysteine homolog over at least one other non-kinase molecule having an accessible SH group.

91. A pharmaceutical composition comprising the compound of any of claim 86, 87, or 88.

92. A method for improving the kinase selectivity of an inhibitor comprising use of the methods of claims 70 to 83.

93. A method for treating an autoimmune disease or condition comprising administering to a patient in need a composition containing a therapeutically effective amount of a compound that forms a covalent bond with a cysteine sidechain of a Blk or a Blk homolog.

94. The method of Claim 91, wherein the autoimmune disease is selected from rheumatoid arthritis or lupus.

95. A method for treating a B-cell proliferative disorder comprising administering to a patient in need a composition containing a therapeutically effective amount of a compound that forms a covalent bond with a cysteine sidechain of a Blk or a Blk homolog.

96. The method of claim 93, wherein the B-cell proliferative disorder is diffuse large B cell lymphoma, follicular lymphoma or chronic lymphocytic leukemia.

97. A method for treating an inflammatory disease or condition comprising administering to a patient in need a composition containing a therapeutically effective amount of a compound that forms a covalent bond with a cysteine sidechain of a Blk or a Blk homolog.

98. A method for identifying biomarkers suitable for determining patient response to a compound of Formula (I) comprising administering to a test subject a composition containing an amount of compound of Formula (I) sufficient to inhibit B cell receptor signaling and correlating B cell receptor signaling with apoptosis.

99. A method for selecting a patient for treatment for lymphoma with a compound of Formula (I) comprising measuring pErk levels or Erk transcriptional target levels in a patient sample, correlating a high level of pERK or ERK transcriptional target levels with a positive response to the treatment, and selecting or excluding the patient for treatment based on the pErk level or Erk transcriptional target levels.

100. A method for measuring a patient's response to treatment comprising administering to the patient a compound of Formula (I), measuring pErk levels or Erk transcriptional target levels in a patient sample, correlating a reduced level of pERK or Erk transcriptional targets with a positive response to the administration of the compound of Formula (I), and continuing or stopping treatment of the patient with the compound based on the pErk levels or the Erk transcriptional target levels.

BRIEF DESCRIPTION OF THE FIGURES

[00200] **FIG. 1(A)** presents an illustrative table of GI_{50} concentrations of Compound **1** that results in 50% decrease in cell proliferation. A variety of lymphoma cell lines incubated with a range of concentrations of Compound **1**. **(B)** presents an illustrative line graph showing inhibition of tumor growth in DLCL2 xenograft models. **(C)** presents an illustrative line graph showing inhibition of tumor growth in DOHH2 xenograft models. For in vivo lymphoma xenograft studies, 5E6 DOHH2 or DLCL2 cells in 50% matrigel were implanted subcutaneously in SCID mice and dosed orally with Compound **1** beginning when tumor size reached 100 mm2.

[00201] **FIG. 2** presents an illustrative line graph showing inhibition of collagen-induced arthritis in male DBA/1OlaHsd mice. Compound 1or vehicle was dosed orally once per day starting at day 1. Dexamethasone was included as a positive control. Paw inflammation was scored from 0-5 and averaged across all paws from all animals for each group in the study. Compound **1** at 12.5 mg/kg and 50 mg/kg regressed inflammation through the end of the study (day 11) while 3.125 mg/kg significantly reduced the increase in paw inflammation.

[00202] **FIG. 3** presents an illustrative line graph showing inhibition of disease progression in a mouse MRL/lpr model of lupus. MRL/lpr mice (Jax strain 000485) were dosed orally once per day from 8 weeks of age until 20 weeks of age and urine protein levels were measured weekly. Compound **1** at 3.125 mg/kg, 12.5 mg/kg, and 50 mg/kg significantly reduced proteinuria, indicating amelioration of the progressive autoimmune renal failure seen in this mouse strain.

[00203] **FIG. 4** presents an illustrative bar graph showing inhibition of mast cell degranulation in a mouse passive cutaneous anaphylaxis model. 23 hours after mice were sensitized with an intradermal injection of monoclonal anti-DNP-IgE in the back, they received a single oral dose of Compound **1** or vehicle. After one hour, animals were challenged with an intravenous injection of DNP-BSA and Evans Blue dye and the area of extravasation was measured. Increasing doses of Compound **1** significantly decreased the amount of Evans Blue release, indicating decreased mast cell activation and vascular permeabilization.

[00204] **FIG. 5** presents an illustrative line graph showing in vivo plasma concentrations post-dosing of male jugular vein cannulated rats with Compounds 1, 7, 8, and 12. Blood samples were collected at 0.0833 (5 minutes), 0.333 (20 minutes), 1, 3, 6, 9, and 24 hours post-dosing from orally dosed rats. Compound **1** and Compound **12** have a short half-life in vivo. In contrast, Compound **7** and Compound **8** have a significantly longer in vivo half-life. Compounds like **1** and **12** are predicted to have enhanced kinase selectivity in vivo because inhibition will be sustained only for those kinases that are irreversibly inhibited.

[00205] **FIG. 6** presents an illustrative bar graph showing brief exposure to Compound **1** in vitro is sufficient to inhibit B cell activation in normal human B cells. B cells were purified from blood from healthy donors by negative selecting using the RosetteSep Human B cell enrichment cocktail. Cells were plated in growth media and indicated concentrations of Compound **1** were added. After incubation for 1 hour at 37°C,