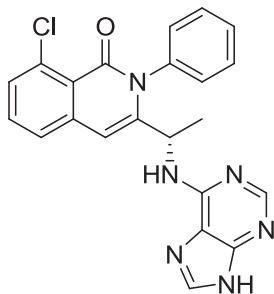


## SUMMARY

**[0009]** In one aspect, the present disclosure refers to the use of a composition comprising a polymorph of a



compound of Formula (I):

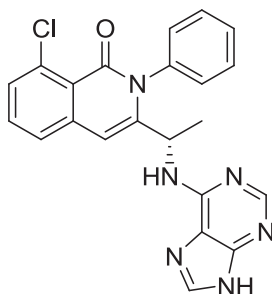
Formula (I),

and a filler or glidant,

in the manufacture of a pharmaceutical composition for combination therapy to treat cancer, an inflammatory disease, or an auto-immune disease,

wherein said polymorph is of polymorph “Form C”, having the following characteristic X-ray Powder Diffraction (XRPD) peaks:  $2\theta = 10.4^\circ (\pm 0.2^\circ)$ ,  $13.3^\circ (\pm 0.2^\circ)$ , and  $24.3^\circ (\pm 0.2^\circ)$ .

**[0009a]** In another aspect, the present disclosure refers to the use of a composition comprising a polymorph of a compound of Formula (I):



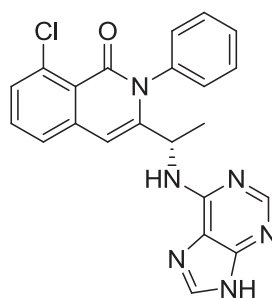
Formula (I),

and a filler or glidant; and

one or more second therapeutic agents in the manufacture of a pharmaceutical composition for combination therapy to treat cancer, an inflammatory disease, or an auto-immune disease,

wherein said polymorph is of polymorph “Form C”, having the following characteristic X-ray Powder Diffraction (XRPD) peaks:  $2\theta = 10.4^\circ (\pm 0.2^\circ)$ ,  $13.3^\circ (\pm 0.2^\circ)$ , and  $24.3^\circ (\pm 0.2^\circ)$ .

**[0009b]** In another aspect, the present disclosure refers to the use of a composition comprising a polymorph of a compound of Formula (I):



Formula (I),

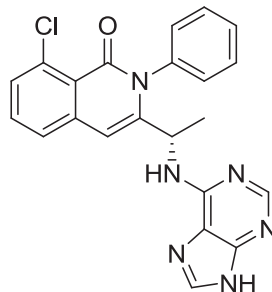
a filler or glidant;

one or more second therapeutic agents; and

a therapeutic antibody in the manufacture of a pharmaceutical composition for combination therapy to treat cancer, an inflammatory disease, or an auto-immune disease,

wherein said polymorph is of polymorph “Form C”, having the following characteristic X-ray Powder Diffraction (XRPD) peaks:  $2\theta = 10.4^\circ (\pm 0.2^\circ)$ ,  $13.3^\circ (\pm 0.2^\circ)$ , and  $24.3^\circ (\pm 0.2^\circ)$ .

**[0009c]** In another aspect, the present disclosure refers to the use of a composition comprising a polymorph of a compound of Formula (I):



Formula (I),

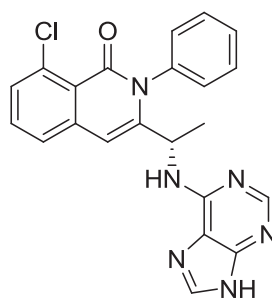
a filler or glidant;

one or more second therapeutic agents; and

a nitrogen mustard in the manufacture of a pharmaceutical composition for combination therapy to treat cancer, an inflammatory disease, or an auto-immune disease,

wherein said polymorph is of polymorph “Form C”, having the following characteristic X-ray Powder Diffraction (XRPD) peaks:  $2\theta = 10.4^\circ (\pm 0.2^\circ)$ ,  $13.3^\circ (\pm 0.2^\circ)$ , and  $24.3^\circ (\pm 0.2^\circ)$ .

**[0009d]** In another aspect, the present disclosure refers to the use of a composition comprising a polymorph of a compound of Formula (I):



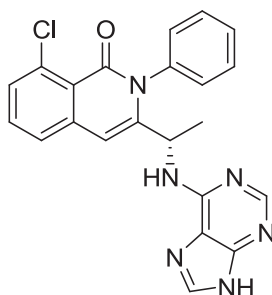
Formula (I),

a filler or glidant;

one or more second therapeutic agents; and

rituximab and bendamustine in the manufacture of a pharmaceutical composition for combination therapy to treat cancer, an inflammatory disease, or an auto-immune disease, wherein said polymorph is of polymorph “Form C”, having the following characteristic X-ray Powder Diffraction (XRPD) peaks:  $2\theta = 10.4^\circ (\pm 0.2^\circ)$ ,  $13.3^\circ (\pm 0.2^\circ)$ , and  $24.3^\circ (\pm 0.2^\circ)$ .

**[0009e]** In another aspect, the present disclosure refers to the use of a composition comprising a polymorph of a compound of Formula (I):



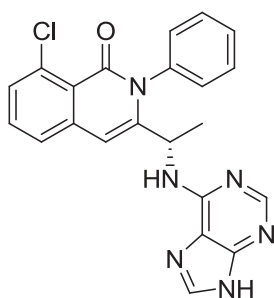
Formula (I),

a filler or glidant;

one or more second therapeutic agent; and

a combination of fludarabine, cyclophosphamide and rituximab in the manufacture of a pharmaceutical composition for combination therapy to treat cancer, an inflammatory disease, or an auto-immune disease, wherein said polymorph is of polymorph “Form C”, having the following characteristic X-ray Powder Diffraction (XRPD) peaks:  $2\theta = 10.4^\circ (\pm 0.2^\circ)$ ,  $13.3^\circ (\pm 0.2^\circ)$ , and  $24.3^\circ (\pm 0.2^\circ)$ .

**[0009f]** In another aspect, the present disclosure refers to a formulation comprising a polymorph of a compound of Formula (I):

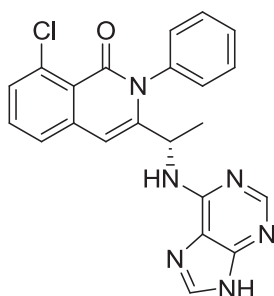


Formula (I),

and a filler or glidant,

wherein the polymorph is of polymorph “Form C”, having the following characteristic X-ray Powder Diffraction (XRPD) peaks:  $2\theta = 10.4^\circ (\pm 0.2^\circ)$ ,  $13.3^\circ (\pm 0.2^\circ)$ , and  $24.3^\circ (\pm 0.2^\circ)$ .

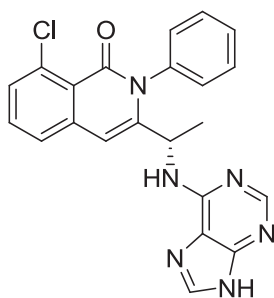
**[0009g]** In one example, provided herein are polymorphic forms of a compound of Formula (I):



(I),

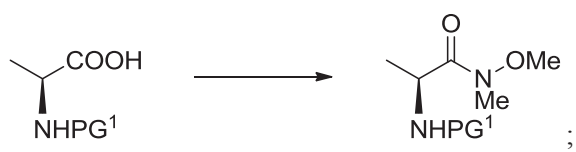
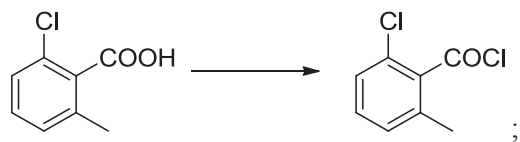
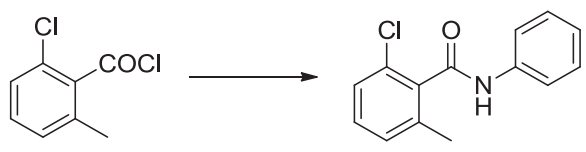
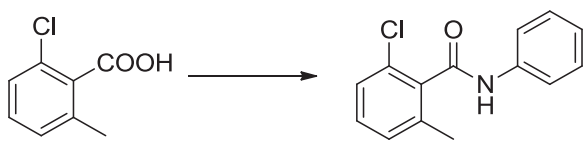
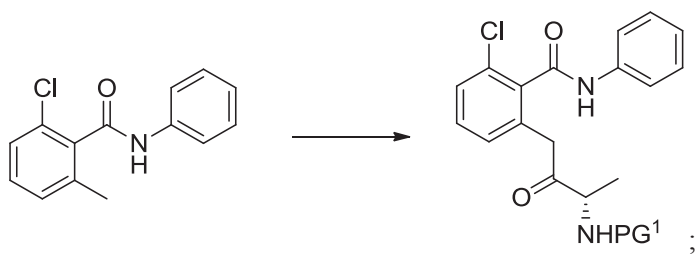
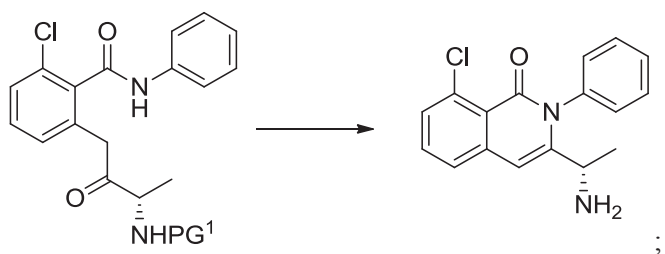
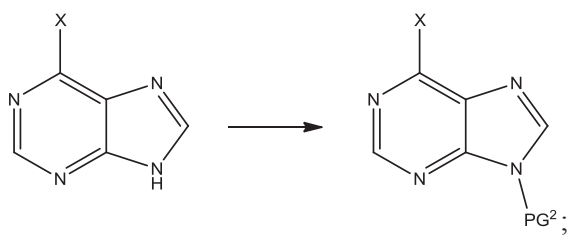
herein referred to as Form A, Form B, Form C, Form D, Form E, Form F, Form G, Form H, Form I, Form J, or an amorphous form of a compound of Formula (I), or a salt, solvate, or hydrate thereof; or a mixture of two or more thereof. In one example, the polymorphic form of a compound of Formula (I) can be a crystalline form, a partially crystalline form, an amorphous form, or a mixture of crystalline form(s) and/or amorphous form(s).

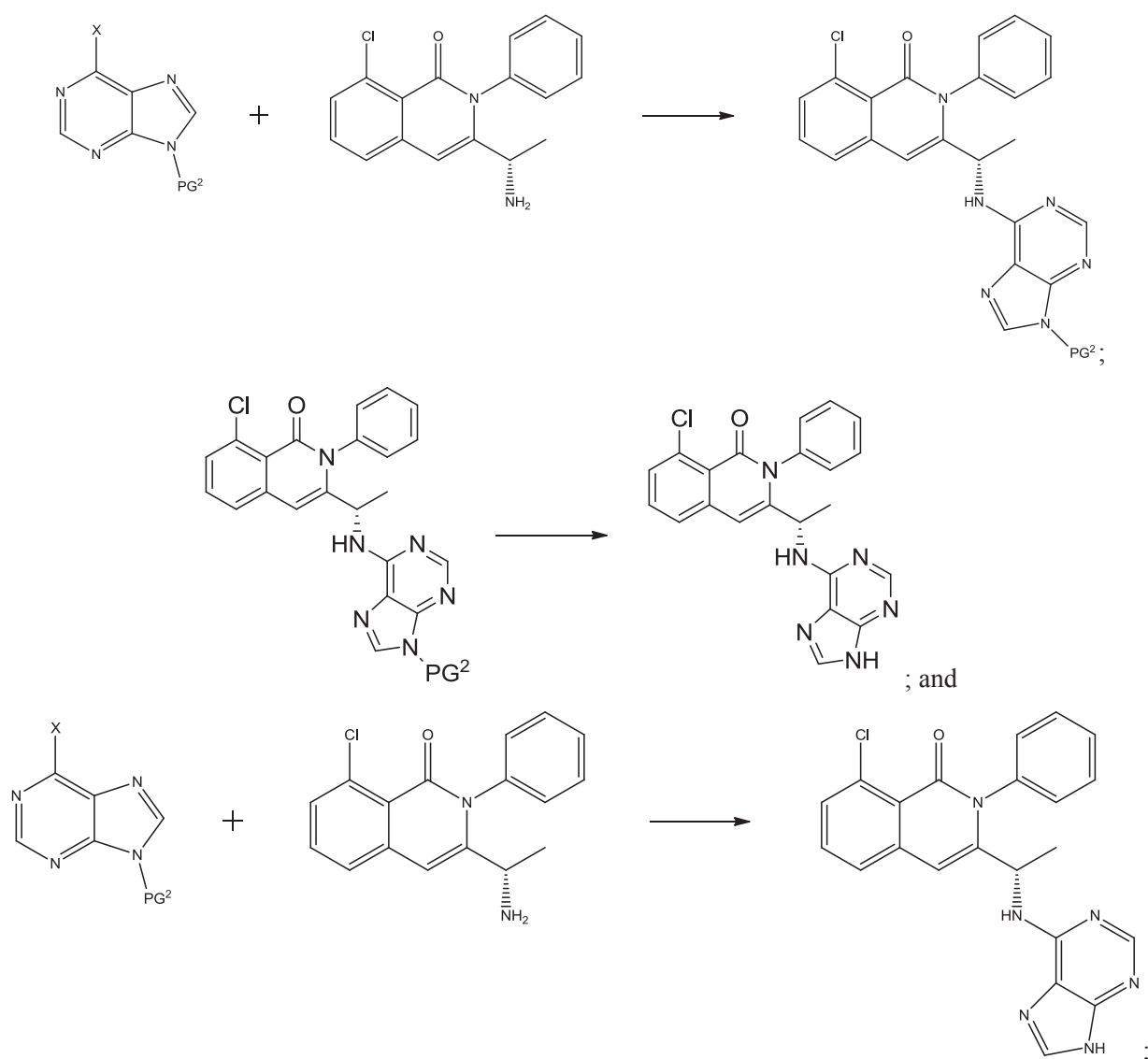
**[0010]** In one example, provided herein is a method of preparing a compound of Formula (I):



(I),

or a pharmaceutically acceptable salt, solvate, or hydrate thereof. In one example, the method comprises any one, two, three, four, five, six, seven, or eight, or more of the following steps:





wherein:

X is selected from fluoro, chloro, bromo, iodo, -O-SO<sub>2</sub>-4-methylphenyl, and -O-SO<sub>2</sub>-methyl;

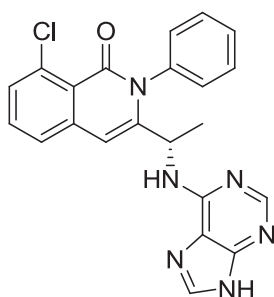
PG<sup>1</sup> is selected from benzyl, substituted benzyl, methoxycarbonyl, ethoxycarbonyl, substituted ethoxycarbonyl, 9-fluorenyloxycarbonyl, substituted 9-fluorenyloxycarbonyl, 2,2,2,-trichloroethoxycarbonyl, 2-trimethylsilylethoxycarbonyl, (2-phenyl-2-trimethylsilyl)ethoxycarbonyl, 2-phenylethoxycarbonyl, 1,1-dimethyl-2,2-dibromoethoxycarbonyl, 1,1-dimethyl-2,2,2-trichloroethoxycarbonyl, t-butoxycarbonyl, 1-adamantyloxycarbonyl, 2-adamantyloxycarbonyl, triisopropylsiloxycarbonyl, vinyloxycarbonyl, 1-isopropoxycarbonyl, 8-quinolyloxycarbonyl, 2,4-dimethylpent-3-yloxycarbonyl, benzyloxycarbonyl, and substituted benzyloxycarbonyl;

PG<sup>2</sup> is selected from methylsulfonyl, substituted methylsulfonyl, benzenesulfonyl, substituted benzenesulfonyl, benzyloxycarbonyl, substituted benzyloxycarbonyl, 2,2,2,-trichloroethoxycarbonyl, 2-trimethylsilylethoxycarbonyl, t-butoxycarbonyl, 1-adamantyloxycarbonyl, 2-

adamantyloxycarbonyl, alkyl, substituted alkyl, t-butyldimethylsilyl, triisopropylsilyl, allyl, benzyl, substituted benzyl, hydroxymethyl, methoxymethyl, diethoxymethyl, (2-chloroethoxy)methyl, t-butoxymethyl, t-butyldimethylsiloxymethyl, pivaloyloxymethyl, benzyloxymethyl, dimethylaminomethyl, 2-tetrahydropyranyl, substituted alkoxymethyl and substituted aryloxymethyl; and

where substituents are selected from alkyl, heteroalkyl, alkenyl, alkynyl, cycloalkyl, heterocyclyl, aryl, arylalkyl, heteroaryl, heteroarylalkyl, alkoxy, cycloalkoxy, heterocycloxy, aryloxy, heteroaryloxy, amido, amino, acyl, acyloxy, alkoxycarbonyl, ester, ether, thio, sulfinyl, sulfonyl, sulfonamido, halo, cyano, hydroxyl, nitro, phosphate, urea, carbamate, and carbonate.

**[0011]** In one example, provided herein is a method of preparing a polymorph Form C of a compound of Formula (I):



(I),

wherein the method comprises:

(i) exposing a composition comprising at least one non-Form C polymorph of a compound of Formula (I), or a salt, solvate, or hydrate thereof, to a non-anhydrous condition for a period of time sufficient to convert at least about 50% of the total amount of non-Form C polymorph(s) into Form C of a compound of Formula (I); and

(ii) recovering said polymorph Form C.

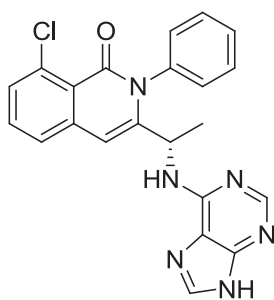
**[0012]** In one example, a non-anhydrous condition includes water, such as, in a form of water vapor and/or liquid water. In one example, a non-anhydrous condition includes a solvent system comprising a non-water solvent and liquid water. In one example, the non-water solvent is a water-miscible solvent. For example, liquid water can be present in an amount of about 1%, about 2%, about 3%, about 4%, about 5%, about 6%, about 7%, about 8%, about 9%, about 10%, about 15%, about 20%, about 25%, about 30%, about 35%, about 40%, about 45%, about 50% , about 55%, about 60%, about 65%, about 70%, about 75%, about 80%, about 85%, about 90%, about 95%, about 96%, about 97%, about 98%, about 99%, or about 100% by volume of the solvent system. In one example, liquid water is present in an amount of between about 10% and about 50% by volume of the solvent system.

**[0013]** In one example, a non-anhydrous condition includes a solvent system comprising water (*e.g.*, about 90% v/v) and isopropyl alcohol (*e.g.*, about 10% v/v). In one example, a non-anhydrous condition includes a solvent system comprising water and ethanol. In one example, a non-anhydrous condition includes a solvent

system comprising water and a water-miscible solvent, such as, *e.g.*, C<sub>1</sub>–C<sub>4</sub> alcohol, acetone, acetonitrile, among others. In one example, a water-miscible solvent is an alcohol, such as, *e.g.*, methanol, ethanol, 1-propanol, 2-propanol, 1-butanol, 2-butanol, t-butanol, ethylene glycol, among others. In one example, the ratio of water and water-miscible solvent in a solvent system provided herein is about 50:1, about 40:1, about 30:1, about 20:1, about 10:1, about 9:1, about 8:1, about 7:1, about 6:1, about 5:1, about 4:1, about 3:1, about 2:1, about 1:1, about 1:2, about 1:3, about 1:4, about 1:5, about 1:6, about 1:7, about 1:8, about 1:9, about 1:10, about 1:20, about 1:30, about 1:40, or about 1:50 v/v. In one example, the ratio of water and water-miscible solvent in a solvent system provided herein is from about 50:1 to about 1:1, from about 40:1 to about 1:1, from about 30:1 to about 1:1, from about 20:1 to about 1:1, from about 10:1 to about 1:1, from about 9:1 to about 1:1, from about 8:1 to about 1:1, from about 7:1 to about 1:1, from about 6:1 to about 1:1, from about 5:1 to about 1:1, from about 4:1 to about 1:1, from about 3:1 to about 3:1, from about 2:1 to about 1:2, from about 1:1 to about 1:4, from about 1:1 to about 1:5, from about 1:1 to about 1:6, from about 1:1 to about 1:7, from about 1:1 to about 1:8, from about 1:1 to about 1:9, from about 1:1 to about 1:10, from about 1:1 to about 1:20, from about 1:1 to about 1:30, from about 1:1 to about 1:40, or from about 1:1 to about 1:50 v/v.

**[0014]** In one example, a non-Form C polymorph is a solid form of a compound of Formula (I), or a salt, solvate, or hydrate thereof (*e.g.*, a crystalline form, an amorphous form, or a mixture of crystalline form(s) and/or amorphous form(s)), which is not polymorph Form C of a compound of Formula (I). In one example, a non-Form C polymorph is Form A, Form B, Form D, Form E, Form F, Form G, Form H, Form I, Form J, or an amorphous form of a compound of Formula (I), or a salt, solvate, or hydrate thereof; or a mixture of two or more thereof. In one example, a non-Form C polymorph can comprise at least about 50% by weight polymorph Form A of a compound of Formula (I). In one example, a non-Form C polymorph (*e.g.*, Form A or Form B) can be obtained from a composition comprising Form C.

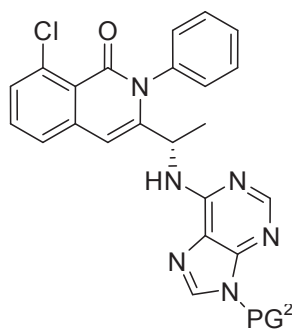
**[0015]** In one example, provided herein is a method of preparing polymorph Form C of a compound of Formula (I):



(I),

wherein the method comprises:

- (i) combining a compound of Formula (Ia):



(Ia),

wherein

PG<sup>2</sup> is a protecting group selected from methylsulfonyl, substituted methylsulfonyl, benzenesulfonyl, substituted benzenesulfonyl, benzyloxycarbonyl, substituted benzyloxycarbonyl, 2,2,2-trichloroethoxycarbonyl, 2-trimethylsilylethoxycarbonyl, t-butoxycarbonyl, 1-adamantyloxycarbonyl, 2-adamantyloxycarbonyl, alkyl, substituted alkyl, t-butyldimethylsilyl, triisopropylsilyl, allyl, benzyl, substituted benzyl, hydroxymethyl, methoxymethyl, diethoxymethyl, (2-chloroethoxy)methyl, t-butoxymethyl, t-butyldimethylsiloxymethyl, pivaloyloxymethyl, benzyloxymethyl, dimethylaminomethyl, 2-tetrahydropyranyl, substituted alkoxymethyl and substituted aryloxymethyl, and

where substituents are selected from alkyl, heteroalkyl, alkenyl, alkynyl, cycloalkyl, heterocyclyl, aryl, arylalkyl, heteroaryl, heteroarylalkyl, alkoxy, cycloalkoxy, heterocycloxy, aryloxy, heteroaryloxy, amido, amino, acyl, acyloxy, alkoxycarbonyl, ester, ether, thio, sulfinyl, sulfonyl, sulfonamido, halo, cyano, hydroxyl, nitro, phosphate, urea, carbamate, and carbonate;

with one or more reagents to remove the protecting group PG<sup>2</sup> to form the compound of Formula (I); and

(ii) recovering polymorph Form C of the compound of Formula (I);

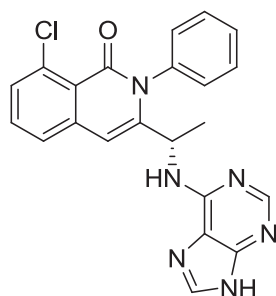
wherein at least one of steps (i) and (ii) occurs in a non-anhydrous condition.

**[0016]** In some examples, one or more reagents to remove the protecting group PG<sup>2</sup> includes, but is not limited to, acids such as HCl, HBr and TFA; carbonate bases, such as Na<sub>2</sub>CO<sub>3</sub> and K<sub>2</sub>CO<sub>3</sub>; hydroxide bases, such as NaOH and KOH; lithium bases, such as methyl lithium, ethyl lithium, propyl lithium, n-butyl lithium, n-pentyl lithium, and n-hexyl lithium; oxidants such as ceric ammonium nitrate; hydrogenation conditions, such as cyclohexadiene/Pd black, and H<sub>2</sub>/Pd on carbon; TBAF, and BF<sub>3</sub>·Et<sub>2</sub>O. In one example, a non-anhydrous condition includes water, such as in a form of water vapor and/or liquid water. In one example, a non-anhydrous condition includes a solvent system comprising a non-water solvent and liquid water, as described herein elsewhere.

**[0017]** In certain examples, a polymorph provided herein is polymorph Form C of a compound of Formula (I). In certain examples, provided herein is a solid form of a compound of Formula (I) comprising Form C of

a compound of Formula (I). In certain examples, provided herein is a solid form of a compound of Formula (I) comprising Form C of a compound of Formula (I), which is substantially pure. In one example, Form C can be characterized by having X-ray powder diffraction (XRPD) peaks at about 10.4, about 13.3, and about 24.3 degrees 2 $\theta$ . In certain examples, Form C is characterized by having differential scanning calorimetry (DSC) comprising an endotherm at about 208 °C. In other examples, Form C is characterized by having differential scanning calorimetry (DSC) comprising an endotherm at about 208 °C, and exotherm at about 222 °C, and an endotherm at about 280 °C. In certain examples, Form C can be characterized by thermogravimetric analysis where the %weight loss observed is about 1.7% at about 80 °C and about 0.2% at about 190 °C.

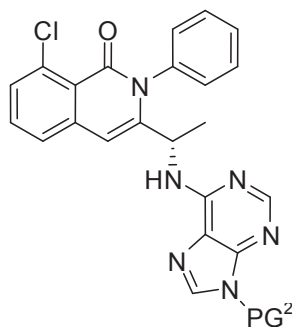
**[0018]** In one example, provided herein is a method of preparing polymorph Form A of a compound of Formula (I):



(I),

wherein the method comprises:

(i) combining a compound of Formula (Ia):



(Ia),

wherein

PG<sup>2</sup> is a protecting group selected from methylsulfonyl, substituted methylsulfonyl, benzenesulfonyl, substituted benzenesulfonyl, benzyloxycarbonyl, substituted benzyloxycarbonyl, 2,2,2,-trichloroethoxycarbonyl, 2-trimethylsilylethoxycarbonyl, t-butoxycarbonyl, 1-adamantyloxycarbonyl, 2-adamantyloxycarbonyl, alkyl, substituted alkyl, t-butyldimethylsilyl, triisopropylsilyl, allyl, benzyl, substituted benzyl, hydroxymethyl, methoxymethyl, diethoxymethyl, (2-chloroethoxy)methyl, t-

butoxymethyl, t-butyldimethylsiloxymethyl, pivaloyloxymethyl, benzyloxymethyl, dimethylaminomethyl, 2-tetrahydropyranyl, substituted alkoxymethyl and substituted aryloxymethyl, and

where substituents are selected from alkyl, heteroalkyl, alkenyl, alkynyl, cycloalkyl, heterocyclyl, aryl, arylalkyl, heteroaryl, heteroarylalkyl, alkoxy, cycloalkoxy, heterocyclyloxy, aryloxy, heteroaryloxy, amido, amino, acyl, acyloxy, alkoxycarbonyl, ester, ether, thio, sulfinyl, sulfonyl, sulfonamido, halo, cyano, hydroxyl, nitro, phosphate, urea, carbamate, and carbonate;

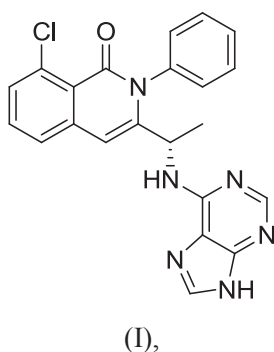
with one or more reagents to remove the protecting group PG<sup>2</sup> to form a compound of Formula (I); and

(ii) recovering polymorph Form A of the compound of Formula (I).

**[0019]** In some examples, step (ii) can include recrystallization of a compound of Formula (I), or a salt, solvate, or hydrate thereof, from a mono-solvent system, or from a multi-solvent system that does not contain both ethyl acetate and hexane. In certain examples, the method further comprises a step of dissolving a compound of Formula (I), or a salt, solvate, or hydrate thereof, in a mono-solvent system or a multi-solvent system, removing residual solid matter to yield a liquid solution, cooling said liquid solution at a rate to effect crystallization of Form A, and recovering Form A from the liquid solution.

**[0020]** In some examples, one or more reagents to remove the protecting group PG<sup>2</sup> includes, but is not limited to, acids such as HCl, HBr and TFA; carbonate bases, such as Na<sub>2</sub>CO<sub>3</sub> and K<sub>2</sub>CO<sub>3</sub>; hydroxide bases, such as NaOH and KOH; lithium bases, such as methyl lithium, ethyl lithium, propyl lithium, n-butyl lithium, n-pentyl lithium, and n-hexyl lithium; oxidants such as ceric ammonium nitrate; hydrogenation conditions, such as cyclohexadiene/Pd black, and H<sub>2</sub>/Pd on carbon; TBAF, and BF<sub>3</sub>·Et<sub>2</sub>O.

**[0021]** In one example, provided herein is a composition comprising a compound of Formula (I):



or a pharmaceutically acceptable salt, solvate, or hydrate thereof, and one or more pharmaceutically acceptable excipients.

**[0022]** In one example, the composition comprises polymorph Form C. In one example, the composition comprises a mixture of polymorph Form C and at least one non-Form C polymorph of a compound of Formula (I), or a pharmaceutically acceptable salt, solvate, or hydrate thereof. For example, in certain examples, the composition can comprise polymorph Form C and polymorph Form A. In other examples, the composition can comprise polymorph Form C and polymorph Form B. In other examples, the composition

can comprise polymorph Form C and polymorph Form D. In other examples, the composition can comprise polymorph Form C and polymorph Form E. In other examples, the composition can comprise polymorph Form C and polymorph Form F. In other examples, the composition can comprise polymorph Form C and polymorph Form G. In other examples, the composition can comprise polymorph Form C and polymorph Form H. In other examples, the composition can comprise polymorph Form C and polymorph Form I. In other examples, the composition can comprise polymorph Form C and polymorph Form J. In other examples, the composition can comprise polymorph Form C and an amorphous form of a compound of Formula (I), or a pharmaceutically acceptable salt, solvate, or hydrate thereof. In one example, the ratio of polymorph Form C to the total amount of non-Form C polymorph(s) is greater than about 1:1, greater than about 2:1, greater than about 3:1, greater than about 4:1, greater than about 5:1, greater than about 6:1, greater than about 7:1, greater than about 8:1, or greater than about 9:1. In one example, the composition comprising Form C is a pharmaceutical composition. In one example, the composition is at least about 98% by weight of a compound of Formula (I), or a pharmaceutically acceptable salt, solvate, or hydrate thereof.

**[0023]** In one example, the composition comprises a mixture of polymorph Form A and at least one non-Form A polymorph of a compound of Formula (I), or a pharmaceutically acceptable salt, solvate, or hydrate thereof. For example, in certain examples, the composition can comprise polymorph Form A and polymorph Form B. In other examples, the composition can comprise polymorph Form A and polymorph Form C. In other examples, the composition can comprise polymorph Form A and polymorph Form D. In other examples, the composition can comprise polymorph Form A and polymorph Form E. In other examples, the composition can comprise polymorph Form A and polymorph Form F. In other examples, the composition can comprise polymorph Form A and polymorph Form G. In other examples, the composition can comprise polymorph Form A and polymorph Form H. In other examples, the composition can comprise polymorph Form A and polymorph Form I. In other examples, the composition can comprise polymorph Form A and polymorph Form J. In other examples, the composition can comprise polymorph Form A and an amorphous form of a compound of Formula (I), or a pharmaceutically acceptable salt, solvate, or hydrate thereof. In one example, the ratio of polymorph Form A to the total amount of non-Form A polymorph(s) is greater than about 1:1, greater than about 2:1, greater than about 3:1, greater than about 4:1, greater than about 5:1, greater than about 6:1, greater than about 7:1, greater than about 8:1, or greater than about 9:1. In one example, the ratio of polymorph Form A to the total amount of non-Form A polymorph(s) is less than about 1:1, less than about 2:1, less than about 3:1, less than about 4:1, less than about 5:1, less than about 6:1, less than about 7:1, less than about 8:1, or less than about 9:1. In one example, the composition comprising Form A is a pharmaceutical composition. In one example, the composition is at least about 98% by weight of a compound of Formula (I), or a pharmaceutically acceptable salt, solvate, or hydrate thereof.

**[0024]** In one example, the composition provided herein is a solid dosage form comprising a polymorph of a compound of Formula (I), or a pharmaceutically acceptable salt, solvate, or hydrate thereof and one or more

pharmaceutically acceptable excipients. In one example, the composition provided herein is a single unit dosage form comprising a polymorph of a compound of Formula (I), or a pharmaceutically acceptable salt, solvate, or hydrate thereof. In one example, the composition provided herein is a tablet or a capsule. In one example, the composition provided herein is a capsule.

**[0025]** In one example, the composition provided herein comprises a therapeutically effective amount of a polymorph of a compound of Formula (I), or a pharmaceutically acceptable salt, solvate, or hydrate thereof. In some examples, the therapeutically effective amount is about 0.5, about 1, about 2, about 3, about 4, about 5, about 10, about 15, about 20, about 25, about 30, about 35, about 40, about 45, about 50, about 55, about 60, about 65, about 70, about 75, about 80, about 85, about 90, about 95, about 100, about 110, about 120, about 130, about 140, about 150, about 160, about 170, about 180, about 190, about 200, about 210, about 220, about 230, about 240, about 250, about 260, about 270, about 280, about 290, about 300, about 325, about 350, about 375, about 400, about 425, about 450, about 475, about 500, about 600, about 700, about 800, about 900, or about 1000 mg, or more. In one example, the composition provided herein comprises at least one pharmaceutically acceptable carrier or excipient. In some examples, the composition provided herein comprises one or more pharmaceutically acceptable carrier(s) or excipient(s), including, *e.g.*, microcrystalline cellulose, crospovidone, and/or magnesium stearate. In one example, the composition provided herein is an immediate-release dosage form. In some examples, the composition provided herein is a hard gelatin capsule. In some examples, the composition provided herein is a soft gelatin capsule. In some examples, the composition provided herein comprises Form C of a compound of Formula (I). In some examples, the composition provided herein comprises Form A of a compound of Formula (I). In some examples, the composition provided herein comprises an amorphous form of a compound of Formula (I). In some examples, the composition provided herein comprises a mixture of two or more polymorphs of a compound of Formula (I), or a pharmaceutically acceptable salt, solvate, or hydrate thereof, *e.g.*, polymorphs A, B, C, D, E, F, G, H, I, and J as described herein.

**[0026]** In other examples, the composition provided herein is a suspension comprising carboxymethyl cellulose and water. In one example, the composition provided herein can further comprise one or more excipients, such as, *e.g.*, polysorbate, polyethyleneglycol, cyclodextrin, dextrose, n-methylpyrrolidone, pH buffers, dilute hydrochloric acid, polyoxyethylene esters of 12-hydroxystearic acid, or a mixture of two or more thereof. Other excipients that can be used in exemplary formulations include, but are not limited to, fillers such as lactose, mannitol, starch, sorbitol, sucrose, dicalcium phosphate, and microcrystalline cellulose; disintegrants such as croscarmellose sodium and sodium starch glycolate; glidants such as colloidal silicon dioxide, silicon dioxide, magnesium silicate, and talc; lubricants such as sodium stearyl fumarate and stearic acid; and surfactants such as sodium lauryl sulphate, sodium dodecyl sulphate, Tween® 80, and Lutrol®.

**[0027]** In one example, the composition provided herein is used for the treatment of a PI3K-associated disorder (*e.g.*, a disease or disorder described herein elsewhere or known in the art). In one example, the

composition provided herein is used for inhibiting PI3K kinase activity. The efficacy of the compound of Formula (I) in these methods and others as disclosed herein has been described in, for example, US 2009/0312319.

**[0028]** In one example, provided herein is a method of treating a PI3K-associated disorder (*e.g.*, a disorder or disease described herein elsewhere or known in the art), wherein the method comprises administering a polymorph of a compound of Formula (I), or a pharmaceutically acceptable salt, solvate, or hydrate thereof, to a subject in need thereof. In one example, provided herein is a method of treating a PI3K-associated disorder, wherein the method comprises administering a polymorph of a compound of Formula (I), or a pharmaceutically acceptable salt, solvate, or hydrate thereof, to a subject in need thereof. In one example, provided herein is a method of treating a PI3K-associated disorder, wherein the method comprises administering a composition provided herein, to a subject in need thereof. In one example, the method comprises administering a polymorph of a compound of Formula (I), or a pharmaceutically acceptable salt, solvate, or hydrate thereof, or a composition thereof, to a subject in need thereof, orally, parenterally, or topically. In one example, the method comprises co-administering one or more additional therapeutic agent(s) or treating the subject with one or more additional therapy(ies) (*e.g.*, radiation therapy or surgery).

#### DESCRIPTION OF THE DRAWINGS

**[0029]** FIG. 1 shows an X-ray powder diffraction (XRPD) for Polymorph Form A.

**[0030]** FIG. 2 shows an XRPD for Polymorph Form B.

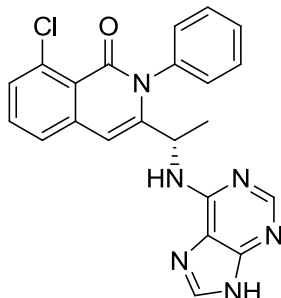
**[0031]** FIG. 3 shows an XRPD for Polymorph Form C.

**[0032]** FIG. 4 shows an XRPD for Polymorph Form D.

## CLAIMS

WHAT IS CLAIMED IS:

1. Use of a composition comprising a polymorph of a compound of Formula (I):



Formula (I),

and a filler or glidant,

in the manufacture of a pharmaceutical composition for combination therapy to treat cancer, an inflammatory disease, or an auto-immune disease,

wherein said polymorph is of polymorph “Form C”, having the following characteristic X-ray Powder Diffraction (XRPD) peaks:  $2\theta = 10.4^\circ (\pm 0.2^\circ)$ ,  $13.3^\circ (\pm 0.2^\circ)$ , and  $24.3^\circ (\pm 0.2^\circ)$ .

2. The use of claim 1, which is for the treatment of cancer; wherein the cancer is leukemia or lymphoma;

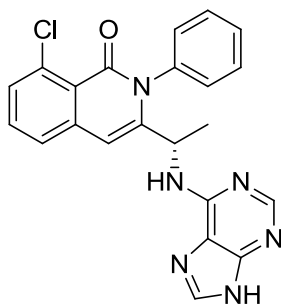
thymus, brain, lung, squamous cell, skin, eye, retinoblastoma, intraocular melanoma, oral cavity and oropharyngeal, bladder, gastric, stomach, pancreatic, bladder, breast, cervical, head, neck, renal, kidney, liver, ovarian, prostate, colorectal, esophageal, testicular, gynecological, thyroid, CNS, PNS, AIDS-related cancer, Kaposi's Sarcoma, mastocytosis or viral-induced cancer;

acute myelogenous leukemia (AML), acute lymphocytic leukemia, T-cell acute lymphocytic leukemia, chronic lymphocytic leukemia (CLL), hairy cell leukemia, myelodysplasia, myeloproliferative disorders, chronic myelogenous leukemia (CML), multiple myeloma (MM), myelodysplastic syndrome (MDS), B-cell acute lymphocytic leukemia or mast cell disorder;

diffuse large B-cell lymphoma, B-cell immunoblastic lymphoma, small non-cleaved cell lymphoma, human lymphotropic virus-type 1 (HTLV-1) leukemia/lymphoma, adult T-cell lymphoma, mantle cell lymphoma (MCL), Hodgkin disease, non-Hodgkin lymphoma, indolent non-Hodgkin lymphoma (iNHL), AIDS-related lymphoma, peripheral T-cell lymphoma, cutaneous T-cell lymphoma, follicular lymphoma or Waldenström Macroglobulinemia;

or post-transplantational lymphoproliferative disorder (PLD).

3. The use of claim 1, which is for the treatment of cancer; wherein the cancer is chronic lymphocytic leukemia (CLL).
4. The use of claim 1, which is for the treatment of cancer; wherein the cancer is non-Hodgkin lymphoma.
5. Use of a composition comprising a polymorph of a compound of Formula (I):

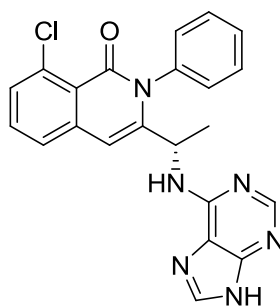


Formula (I),

and a filler or glidant; and

one or more second therapeutic agents in the manufacture of a pharmaceutical composition for combination therapy to treat cancer, an inflammatory disease, or an auto-immune disease, wherein said polymorph is of polymorph “Form C”, having the following characteristic X-ray Powder Diffraction (XRPD) peaks:  $2\theta = 10.4^\circ (\pm 0.2^\circ)$ ,  $13.3^\circ (\pm 0.2^\circ)$ , and  $24.3^\circ (\pm 0.2^\circ)$ .

6. Use of a composition comprising a polymorph of a compound of Formula (I):



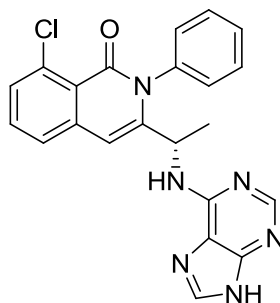
Formula (I),

a filler or glidant;

one or more second therapeutic agents; and

a therapeutic antibody in the manufacture of a pharmaceutical composition for combination therapy to treat cancer, an inflammatory disease, or an auto-immune disease, wherein said polymorph is of polymorph “Form C”, having the following characteristic X-ray Powder Diffraction (XRPD) peaks:  $2\theta = 10.4^\circ (\pm 0.2^\circ)$ ,  $13.3^\circ (\pm 0.2^\circ)$ , and  $24.3^\circ (\pm 0.2^\circ)$ .

7. The use of claim 6, wherein the therapeutic antibody is an anti-CD20 antibody.
8. The use of claim 7, wherein the therapeutic antibody is rituximab, cetuximab, panitumumab, trastuzumab, tositumomab, alemtuzumab, bevacizumab or gemtuzumab.
9. The use of claim 5, wherein the one or more second therapeutic agents are selected from everolimus, chlorambucil, chlornaphazine, estramustine, ifosfamide, mechlorethamine, mechlorethamine oxide hydrochloride, melphalan, novembichin, phenesterine, prednimustine, trofosfamide, uracil mustard, fludarabine, cyclophosphamide, bortezomib, gemcitabine, a corticosteroid or dexamethasone.
10. Use of a composition comprising a polymorph of a compound of Formula (I):



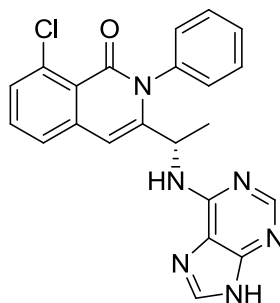
Formula (I),

a filler or glidant;

one or more second therapeutic agents; and

a nitrogen mustard in the manufacture of a pharmaceutical composition for combination therapy to treat cancer, an inflammatory disease, or an auto-immune disease, wherein said polymorph is of polymorph “Form C”, having the following characteristic X-ray Powder Diffraction (XRPD) peaks:  $2\theta = 10.4^\circ (\pm 0.2^\circ)$ ,  $13.3^\circ (\pm 0.2^\circ)$ , and  $24.3^\circ (\pm 0.2^\circ)$ .

11. The use of claim 10, wherein the nitrogen mustard is bendamustine.
12. Use of a composition comprising a polymorph of a compound of Formula (I):



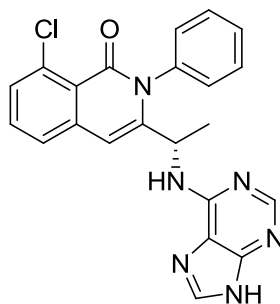
Formula (I),

a filler or glidant;

one or more second therapeutic agents; and

rituximab and bendamustine in the manufacture of a pharmaceutical composition for combination therapy to treat cancer, an inflammatory disease, or an auto-immune disease, wherein said polymorph is of polymorph “Form C”, having the following characteristic X-ray Powder Diffraction (XRPD) peaks:  $2\theta = 10.4^\circ (\pm 0.2^\circ)$ ,  $13.3^\circ (\pm 0.2^\circ)$ , and  $24.3^\circ (\pm 0.2^\circ)$ .

13. Use of a composition comprising a polymorph of a compound of Formula (I):



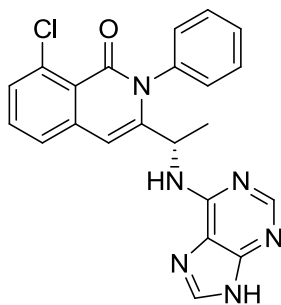
Formula (I),

a filler or glidant;

one or more second therapeutic agent; and

a combination of fludarabine, cyclophosphamide and rituximab in the manufacture of a pharmaceutical composition for combination therapy to treat cancer, an inflammatory disease, or an auto-immune disease, wherein said polymorph is of polymorph “Form C”, having the following characteristic X-ray Powder Diffraction (XRPD) peaks:  $2\theta = 10.4^\circ (\pm 0.2^\circ)$ ,  $13.3^\circ (\pm 0.2^\circ)$ , and  $24.3^\circ (\pm 0.2^\circ)$ .

14. A formulation comprising a polymorph of a compound of Formula (I):



Formula (I),

and a filler or glidant,

wherein the polymorph is of polymorph “Form C”, having the following characteristic X-ray Powder Diffraction (XRPD) peaks:  $2\theta = 10.4^\circ (\pm 0.2^\circ)$ ,  $13.3^\circ (\pm 0.2^\circ)$ , and  $24.3^\circ (\pm 0.2^\circ)$ .

15. The formulation of claim 14, comprising about 1% to about 30% w/w of the polymorph.
16. The formulation of claim 14 or claim 15, comprising about 70% to about 99% w/w of the filler or glidant.
17. The formulation of any one of claims 14–16, wherein the filler or glidant is silicified microcrystalline cellulose.
18. A formulation of any one of claims 14–17, further comprising a disintegrant and a lubricant.
19. The formulation of claim 18, comprising up to about 7% w/w of the disintegrant.
20. The formulation of claim 18 or claim 19, wherein the disintegrant is croscopovidone.
21. The formulation of any one of claims 18–20, comprising up to about 2% w/w of the lubricant.
22. The formulation of any one of claims 18–21, wherein the lubricant is magnesium stearate.
23. The formulation of any one of claims 14–22, wherein the formulation is a capsule.