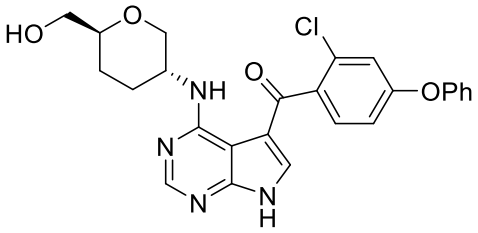
cells. For example, impaired IgE-mediated mast cell activation and reduced TNF-alpha production by activated monocytes has been associated with BTK deficiency in mice and humans. Thus, BTK inhibition can be useful for the treatment of allergic disorders and/or autoimmune and/or inflammatory diseases such as: SLE, rheumatoid arthritis, multiple vasculitides, idiopathic thrombocytopenic purpura (ITP), myasthenia gravis, allergic rhinitis, and asthma (DiPaolo et. al., *Nature Chem. Biol.* **2011**, 7(*1*):41-50; Liu et. al., *Jour. Pharmacol. and Exp. Ther.* **2011**, 338(1):154-163).

**[0004]** Moreover, BTK's role in apoptosis demonstrates the utility of inhibition of BTK activity for the treatment of cancers, B-cell lymphoma, leukemia, and other hematological malignancies. In addition, given the role of BTK in osteoclast function, inhibition of BTK activity can be useful for the treatment of bone disorders such as osteoporosis.

**[0005]** Inhibition of BTK with small molecule inhibitors therefore has the potential to be a treatment for immune disorders, cancer, cardiovascular diseases, viral infections, inflammation, metabolism/endocrine function disorders, and neurological disorders. Thus, there remains a considerable need for potent small molecule inhibitors of BTK.

## Summary

**[0006]** The application relates to a compound of Formula (I):




(I),

or pharmaceutically acceptable salts thereof, tautomers, prodrugs, solvates, metabolites, polymorphs, analogs or derivatives thereof. As used herein, the expressions "compound of Formula (I)" and "Compound (I)," refer to the same compound and can be used interchangeably.

**[0007]** The application relates to a pharmaceutical composition comprising the compound of Formula (I) or a pharmaceutically acceptable salt, tautomer, prodrug, solvate, metabolite, polymorph, analog or derivative thereof, and a pharmaceutically acceptable diluent, excipient or carrier.

**[0008]** The application relates to a method of treating a BTK-mediated disorder. The method comprises administering to a patient in need of a treatment for diseases or disorders associated with modulation of BTK kinase a therapeutically effective amount of the compound of Formula (I), or a pharmaceutically acceptable salt, tautomer, prodrug, solvate, metabolite, polymorph, analog or derivative thereof.

**[0009]** The application relates to a method of treating a BTK-mediated disorder. The method comprises administering to a patient in need of a treatment for diseases or disorders associated with modulation of BTK kinase a therapeutically effective amount of a pharmaceutical composition comprising the compound of Formula (I) or a pharmaceutically acceptable salt, tautomer, prodrug, solvate, metabolite, polymorph, analog or derivative thereof, and a pharmaceutically acceptable diluent, excipient or carrier.

**[0010]** The application relates to a method of treating a cell proliferative disorder. The method comprises administering to a patient in need thereof a therapeutically effective amount of the compound of Formula (I), or a pharmaceutically acceptable salt, tautomer, prodrug, solvate, metabolite, polymorph, analog or derivative thereof.

**[0011]** The application relates to a method of treating a cell proliferative disorder. The method comprises administering to a patient in need thereof a therapeutically effective amount of a pharmaceutical composition comprising the compound of Formula (I) or a pharmaceutically acceptable salt, tautomer, prodrug, solvate, metabolite, polymorph, analog or derivative thereof, and a pharmaceutically acceptable diluent, excipient or carrier.

**[0012]** The application relates to a method of treating cancer. The method comprises administering to a patient in need thereof a therapeutically effective amount of the compound of Formula (I), or a pharmaceutically acceptable salt, tautomer, prodrug, solvate, metabolite, polymorph, analog or derivative thereof.

**[0013]** The application relates to a method of treating cancer. The method comprises administering to a patient in need thereof a therapeutically effective amount of a pharmaceutical composition comprising the compound of Formula (I) or a pharmaceutically acceptable salt, tautomer, prodrug, solvate, metabolite, polymorph, analog or derivative thereof, and a pharmaceutically acceptable diluent, excipient or carrier.

**[0014]** The application relates to a method of modulating (*e.g.*, inhibiting) BTK. The method comprises administering to a patient in need thereof a therapeutically

effective amount of the compound of Formula (I), or a pharmaceutically acceptable salt, tautomer, prodrug, solvate, metabolite, polymorph, analog or derivative thereof.

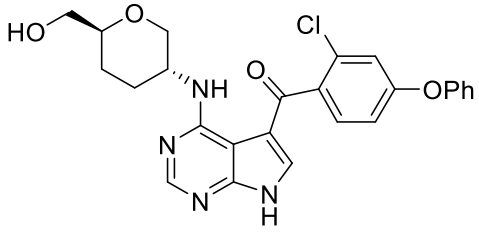
**[0015]** The application relates to a method of modulating (*e.g.*, inhibiting) BTK. The method comprises administering to a patient in need thereof a therapeutically effective amount of a pharmaceutical composition comprising the compound of Formula (I) or a pharmaceutically acceptable salt, tautomer, prodrug, solvate, metabolite, polymorph, analog or derivative thereof, and a pharmaceutically acceptable diluent, excipient or carrier.

**[0016]** The application relates to the compound of Formula (I) or a pharmaceutically acceptable salt, tautomer, prodrug, solvate, metabolite, polymorph, analog or derivative thereof, for use in a method of treating a BTK-mediated disorder, a cell proliferative disorder, or cancer, or of modulating (*e.g.*, inhibiting) BTK. The compound of Formula (I), or a pharmaceutically acceptable salt, tautomer, prodrug, solvate, metabolite, polymorph, analog or derivative thereof is administered in a therapeutically effective amount to a patient in need thereof.

**[0017]** The application relates to a pharmaceutical composition comprising the compound of Formula (I) or a pharmaceutically acceptable salt, tautomer, prodrug, solvate, metabolite, polymorph, analog or derivative thereof, and a pharmaceutically acceptable diluent, excipient or carrier for use in a method of treating a BTK-mediated disorder, a cell proliferative disorder, or cancer, or of modulating (*e.g.*, inhibiting) BTK. The composition is administered in a therapeutically effective amount to a patient in need thereof.

**[0018]** The application relates to the use of the compound of Formula (I) or a pharmaceutically acceptable salt, tautomer, prodrug, solvate, metabolite, polymorph, analog or derivative thereof, in the manufacture of a medicament for treating a BTK-mediated disorder, a cell proliferative disorder, or cancer, or for modulating (*e.g.*, inhibiting) BTK. The compound of Formula (I), or a pharmaceutically acceptable salt, tautomer, prodrug, solvate, metabolite, polymorph, analog or derivative thereof is administered in a therapeutically effective amount to a patient in need thereof.

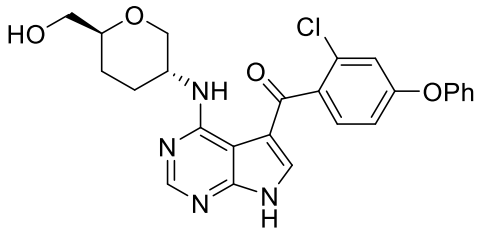
**[0018a]** A first aspect of the application relates to use of a compound of Formula (I):




(I),

or pharmaceutically acceptable salt, tautomer, prodrug, solvate, metabolite, polymorph, analog or derivative thereof, in the manufacture of a medicament for treating cancer in a subject, wherein a mutant BTK has been detected in a sample from the subject.

**[0018b]** Another aspect of the application relates to a compound of Formula (I):




(I),

or pharmaceutically acceptable salt, tautomer, prodrug, solvate, metabolite, polymorph, analog or derivative thereof, for treating cancer in a subject, wherein a mutant BTK has been detected in a sample from the subject.

**[0019]** The application relates to the use of a pharmaceutical composition comprising the compound of Formula (I) or a pharmaceutically acceptable salt, tautomer, prodrug, solvate, metabolite, polymorph, analog or derivative thereof, and a pharmaceutically acceptable diluent, excipient or carrier in the manufacture of a medicament for treating a BTK-