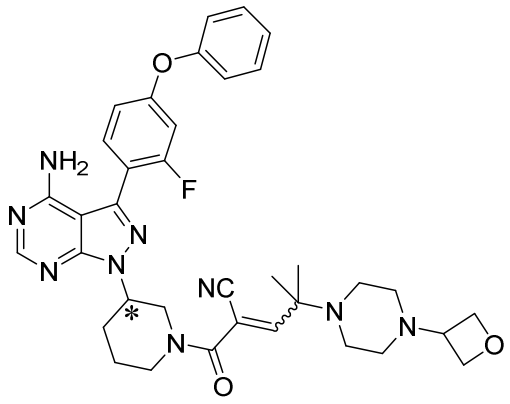
What is claimed is: p

1. A modified release solid oral dosage form comprising:

(a) a core composition comprising the (E) isomer, (Z) isomer, or a mixture of (E) and (Z) isomers of (R)-2-[3-[4-amino-3-(2-fluoro-4-phenoxy-phenyl)pyrazolo[3,4-d]pyrimidin-1-yl]piperidine-1-carbonyl]-4-methyl-4-[4-(oxetan-3-yl)piperazin-1-yl]pent-2-enenitrile, (S)-2-[3-[4-amino-3-(2-fluoro-4-phenoxy-phenyl)pyrazolo[3,4-d]pyrimidin-1-yl]piperidine-1-carbonyl]-4-methyl-4-[4-(oxetan-3-yl)piperazin-1-yl]pent-2-enenitrile, or a mixture of (R) and (S) isomers of 2-[3-[4-amino-3-(2-fluoro-4-phenoxy-phenyl)pyrazolo[3,4-d]pyrimidin-1-yl]piperidine-1-carbonyl]-4-methyl-4-[4-(oxetan-3-yl)piperazin-1-yl]pent-2-enenitrile (Compound (I)) having the structure:



where *C is a stereochemical center, and/or a pharmaceutically acceptable salt thereof, wherein the core composition comprises by weight:

6% to 20% of Compound (I) and/or a pharmaceutically acceptable salt thereof;

34% to 72% of microcrystalline cellulose;

5% to 25% mannitol;

0% to 20% of hydroxypropyl methyl cellulose;

0.5% to 1.5% of crosslinked homopolymer of N-vinyl-2-pyrrolidone; and

0.5% to 1.5% of sodium stearyl fumarate;

(b) a sub-coating layer coating the core composition, the sub-coating layer comprising a polyvinyl alcohol and/or a hydroxypropyl methyl cellulose; and

(c) an enteric coating layer encapsulating the sub-coating layer and the core composition, said enteric coating layer comprising at least one polymer selected from an acrylic/methacrylic/ethacrylic acid homopolymer and copolymers thereof, a cellulose derivative, and a polyvinylpyrrolidone.

2. The modified release solid oral dosage form of claim 1, wherein the sub-coating layer (b) comprises a polyvinyl alcohol.

3. The modified release solid oral dosage form of claim 1 or claim 2, wherein the cellulose derivative is selected from cellulose acetate phthalate, cellulose acetate tritnellitate, methylcellulose, hydroxypropylmethyl cellulose phthalate (HPMCP), hydroxypropylmethyl cellulose succinate (HPMCS), and hydroxypropylmethylcellulose acetate succinate (HPMCAS).

4. The modified release solid oral dosage form of any one of claims 1 to 3, wherein the sub-coating layer (b) comprises a polyvinyl alcohol, and the enteric coating layer (c) comprises a poly (methacrylic acid-co-ethyl acrylate) copolymer.

5. The modified release solid oral dosage form of claim 4, wherein the polyvinyl alcohol is a pigmented polyvinyl alcohol.

6. The modified release solid oral dosage form of any of claims 1-5, wherein:

the modified solid oral dosage form releases less than 10% by weight of Compound (I) and/or a pharmaceutically acceptable salt thereof, in less than two hours at a pH less than or equal to about 2.0;

at least 80% by weight of Compound (I) and/or the pharmaceutically acceptable salt thereof in about 15 minutes to two hours at a pH equal to or more than 6.0; and any

unreleased amount of Compound (I) is released by the end of 7.5 hours at a pH equal to or more than 6.0.

7. The modified release solid oral dosage form of any of claims 1-6, wherein the core composition comprises Compound (I).

8. The modified release solid oral dosage form of any of claims 1-7, wherein:

(a) Compound (I) and/or a pharmaceutically acceptable salt thereof is an (E) and (Z) mixture of a mixture of (R) and (S) isomers of 2-[3-[4-amino-3-(2-fluoro-4-phenoxy-phenyl)-pyrazolo[3,4-d]pyrimidin-1-yl]piperidine-1-carbonyl]-4-methyl-4-[4-(oxetan-3-yl)piperazin-1-yl]pent-2-enenitrile; or

(b) Compound (I) and/or a pharmaceutically acceptable salt thereof is an (E) and (Z) mixture of (R)-2-[3-[4-amino-3-(2-fluoro-4-phenoxy-phenyl)-pyrazolo[3,4-d]pyrimidin-1-yl]piperidine-1-carbonyl]-4-methyl-4-[4-(oxetan-3-yl)piperazin-1-yl]pent-2-enenitrile.

9. The modified release solid oral dosage form of any of claims 1-8, wherein Compound (I) and/or a pharrmaceutically acceptable salt thereof is an (E) and (Z) mixture of (R)-2-[3-[4-amino-3-(2-fluoro-4-phenoxy-phenyl)-pyrazolo[3,4-d]pyrimidin-1-yl]piperidine-1-carbonyl]-4-methyl-4-[4-(oxetan-3-yl)piperazin-1-yl]pent-2-enenitrile.

10. The modified release solid oral dosage form of any of claims 1-9, wherein at least 85% by weight of Compound (I) and/or a pharmaceutically acceptable salt thereof is the (E) isomer.

11. The modified release solid oral dosage form of claim 10, wherein at least 90% by weight of Compound (I) and/or a pharmaceutically acceptable salt thereof is the (E) isomer.

12. The modified release solid oral dosage form of any of claims 1-11, wherein Compound (I) and/or a pharmaceutically acceptable salt thereof is a substantially pure amorphous form.

13. The modified release solid oral dosage form of any of claims 1-12, wherein the core composition comprises 30 mg to 100 mg of Compound (I) and/or a pharmaceutically acceptable salt thereof.

14. The modified release solid oral dosage form of any of claims 1-13, wherein:

(a) the core composition weighs from 80% to 91% of the total weight of the solid oral dosage form;

(b) the sub-coating layer weighs 2% to 4% by weight of the modified release solid oral dosage form;

(c) the enteric coating layer further comprises a solubilizer and a plasticizer/anti-tacking agent;

(d) the enteric coating layer weighs 6% to 20% of the total weight of the modified release solid oral dosage form; and/or

(e) the enteric coating layer comprises by total weight of the modified release solid oral dosage form:

5% to 16% of EUDRAGIT® L 30 D-55 or EUDRAGIT® L 100-55;

1% to 3% of PlasACRYL™ T20; and

0.3% to 0.8% of Polysorbate 80.

15. The modified release solid oral dosage form of claim 14, wherein the core composition weighs from 83% to 91% of the total weight of the solid oral dosage form.

16. Use of a modified release solid oral dosage form according to any one of claims 1-15, in the manufacture of a medicament for inhibiting Bruton's tyrosine kinase (BTK) in a mammal in need thereof.

17. Use of a modified release solid oral dosage form according to any one of claims 1-15, in the manufacture of a medicament for treating a disease mediated by Bruton's tyrosine kinase (BTK) in a mammal in need thereof.

18. The use of claim 17, wherein the disease is an autoimmune disease, an inflammatory disease, or a cancer.

19. The use of claim 17, wherein the disease is acute necrotizing hemorrhagic leukoencephalitis, acute disseminated encephalomyelitis, autoimmune inner ear disease (AIED), autoimmune retinopathy, axonal & neuronal neuropathies, chronic inflammatory demyelinating polyneuropathy (CIDP), demyelinating neuropathies, Devic's disease (neuromyelitis optica), experimental allergic encephalomyelitis, giant cell arteritis (temporal arteritis), Guillain-Barre syndrome, Lambert-Eaton syndrome, chronic Meniere's disease, myasthenia gravis, neuromyotonia, opsoclonus-myoclonus syndrome, optic neuritis, paraneoplastic cerebellar degeneration, peripheral neuropathy, perivenous encephalomyelitis, restless legs syndrome, stiff person syndrome, sympathetic ophthalmia, Takayasu's arteritis, temporal arteritis/Giant cell arteritis, transverse myelitis, multiple sclerosis, dysautonomia, age-related macular degeneration (wet and dry), corneal transplantation, encephalitis, meningitis, vasculitis, systemic lupus erythematosus (SLE), rheumatoid arthritis, psoriatic arthritis, lupus, uveitis, myasthenia gravis, warm autoimmune hemolytic anemia, Wegener's granulomatosis, Sjogren's disease, Sjogren's dry eye, non-Sjogren's dry eye disease, psoriasis, pemphigus, urticaria, asthma, diffuse large B cell lymphoma, follicular lymphoma, chronic lymphocytic lymphoma, chronic lymphocytic leukemia, B-cell prolymphocytic leukemia, small lymphocytic lymphoma (SLL), multiple myeloma, B-cell non-Hodgkin lymphoma, lymphoplamascytic lymphoma/Waldenstrom macroglobulinemia, splenic marginal zone lymphoma, plasma cell myeloma, plasmacytoma, extranodal marginal zone B cell lymphoma, nodal marginal zone B cell lymphoma, mantle cell lymphoma, mediastinal

(thymic) large B cell lymphoma, intravascular large B cell lymphoma, primary effusion lymphoma, Burkitt lymphoma/leukemia, or lymphomatoid granulomatosis.

20. The use of claim 17, wherein Compound (I) and/or a pharmaceutically acceptable salt thereof is to be administered in combination with one or more anti-cancer or anti-inflammatory agents.