

What is claimed is:

1. A modified release formulation comprising a therapeutically effective amount of 2-methyl-2-(3-methyl-4-(4-(methylamino)-5-(trifluoromethyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)propanenitrile and at least one release-modifying agent.
2. The modified release formulation of claim 1 comprising pellets containing 2-methyl-2-(3-methyl-4-(4-(methylamino)-5-(trifluoromethyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)propanenitrile and coated with the at least one release-modifying agent.
3. The formulation of claim of any of the preceding claims, wherein release of 2-methyl-2-(3-methyl-4-(4-(methylamino)-5-(trifluoromethyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)propanenitrile is less than 60% at two hours and greater than 60% at 8 hours when tested using USP Type-II Apparatus at 50-75 rpm and 37°C in pH 3 McIlvaine buffer, wherein the formulation is a tablet.
4. The formulation of claim 2, wherein release of 2-methyl-2-(3-methyl-4-(4-(methylamino)-5-(trifluoromethyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)propanenitrile is less than 60% at one hour when tested using USP Type-II Apparatus at 100 rpm and 37°C in pH 3 McIlvaine buffer, wherein the formulation is a capsule containing pellets.
5. The formulation of any one of the preceding claims, wherein the 2-methyl-2-(3-methyl-4-(4-(methylamino)-5-(trifluoromethyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)propanenitrile has a $C_{\max}$ that is decreased relative to an immediate release formulation after administration to a subject.
6. The formulation of claim 5, wherein the $C_{\max}$ is decreased by at least 20%.
7. The formulation of any one of the preceding claims, wherein the modified release formulation comprises 10% to 50% by weight of 2-methyl-2-(3-methyl-4-(4-(methylamino)-5-(trifluoromethyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)propanenitrile.
8. The formulation of any one of the preceding claims, wherein the 2-methyl-2-(3-methyl-4-(4-(methylamino)-5-(trifluoromethyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)propanenitrile is crystalline.
9. The method of claim 8, wherein crystalline 2-methyl-2-(3-methyl-4-(4-(methylamino)-5-(trifluoromethyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)propanenitrile is milled or micronized.
10. The formulation of any one of the preceding claims, wherein the release-modifying agent comprises from 3% to 60% by weight of the formulation.
11. The formulation of any of one of the preceding claims, wherein the release-modifying agent is selected from the group consisting of MCC (Microcrystalline cellulose),

HPC (Hydroxypropyl cellulose), HPMC (Hydroxypropyl methylcellulose), PEG (Polyethylene glycol glycerides), PVA (Polyvinyl alcohol), PVP (Polyvinylpyrrolidone), CAP (Cellulose acetate phthalate), CMC-Na (Carboxymethylcellulosesodium), HPMCAS (Hydroxypropyl methylcellulose acetate succinate), HPMCP (Hydroxypropyl methylcellulose phthalate), Poly(methylacrylate-co-methyl methacrylate-co-methacrylic acid), Poly(methacrylic acid-co-ethyl acrylate), Poly(methacrylic acid-co-methyl methacrylate), CA (Cellulose acetate); CAB (Cellulose acetate butyrate); EC (Ethylcellulose), Poly(ethyl acrylate-co-methyl methacrylate), Poly(ethyl acrylate-co-methyl methacrylate-co-trimethylammonium ethyl methacrylate chloride), PVAc (Polyvinyl acetate), and HPMC/CMC.

12. The formulation of any of one of the preceding claims, wherein the release-modifying agent is selected from the group consisting of Aquacoat®, Walocel®, HP 50/HP 55, Acoat®, EUDRAGIT® FS 30 D, EUDRAGIT® L 30 D-55/L 100-55, EUDRAGIT® L 12,5/EUDRAGIT® L 100, EUDRAGIT® S 12,5/EUDRAGIT® S 100, Carbopol® polymers, Eastman CA, Eastman CAB, Eastman CAB, Ethocel™, Aquacoat® ECD, or Surelease®, or Glyceride GatteCoat™, EUDRAGIT® NE 30 D, EUDRAGIT® NM 30 D, EUDRAGIT® RL 30 D, EUDRAGIT® RL 100/RL PO, EUDRAGIT® RS 30 D, EUDRAGIT® RS 100/RS, Kollicoat® SR 30 D, Walocel® HM-PPA, Kollicoat® MAE 30 DP/100 P, and Eastacryl 30 D.

13. The formulation of any of one of the preceding claims, wherein the release-modifying agent is selected from the group consisting of microcrystalline cellulose, hydroxypropyl methylcellulose, polyethylene glycol, polyvinyl alcohol, polyvinyl acetate, polyvinylpyrrolidone, KOLLICOAT®, CARBOPOL®, and AQUACOAT®.

14. The formulation of any of one of the preceding claims, comprising one or more excipients selected from the group consisting of microcrystalline cellulose, hydroxypropyl methylcellulose, croscarmellose sodium, polyethylene glycol, polyvinyl alcohol, polyvinyl acetate, polyvinylpyrrolidone, purified talc, colloidal silicon dioxide, and magnesium stearate, and a coating.

15. The formulation of any of one of the preceding claims, wherein the formulation is a tablet.

16. The formulation of claim 15, wherein the tablet comprises 10 to 500 mg of 2-methyl-2-(3-methyl-4-(4-(methylamino)-5-(trifluoromethyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)propanenitrile.

17. The formulation of claim 15, wherein the tablet comprises 40 to 120 mg of 2-methyl-2-(3-methyl-4-(4-(methylamino)-5-(trifluoromethyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)propanenitrile.

18. The formulation of claim 15, wherein the tablet comprises 30 to 80 mg of 2-

methyl-2-(3-methyl-4-(4-(methylamino)-5-(trifluoromethyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)propanenitrile.

19. The formulation of claim 15, wherein the release-modifying agent is HPMC.
20. The formulation of claim 15, wherein the release-modifying agent is a PARTECK® polymer.
21. The formulation of claims 19 or 20 wherein the release-modifying agent comprises 20-30% w/w of the formulation.
22. The formulation of any of one of the preceding claims, wherein the formulation is a capsule containing pellets.
23. The formulation of claim 22, wherein the capsule is a multi-unit particulate combination of immediate release pellets and modified release pellets contained in the capsule.
24. The formulation of claims 22-23, wherein the pellets comprise a release-modifying agent selected from KOLLICOAT®, CARBOPOL®, and AQUACOAT®.
25. The formulation of claims 22-24, wherein the formulation is a multi-unit particulate combination of immediate release pellets and delayed release pellets contained in a capsule.
26. The formulation of claims 22-25, wherein the modified release formulation is selected from a delayed-release pellet formulation, a controlled-release pellet formulation, an extended-release pellet formulation, and a pulsatile-release pellet formulation.
27. The formulation of claim 22-26, wherein the formulation comprises a coating agent, wherein the coating agent is EUDRAGIT®.
28. The formulation of claim 27, wherein the coating agent comprises from 3% to 60% of EUDRAGIT® by weight of the formulation.
29. The formulation of claim 28, wherein the coating agent comprises EUDRAGIT® RS 30 D of up to 20% w/w.
30. The formulation of claim 29, wherein the coating agent comprises EUDRAGIT® NM 30 D of up to 60% w/w.
31. The formulation of claim 22-26, wherein the formulation comprises a coating agent, wherein the coating agent is KOLLICOAT® SR 30D.
32. The formulation of claim 31 wherein the KOLLICOAT® SR 30D provides about a 5% weight gain.
33. The formulation of claim 31 wherein the KOLLICOAT® SR 30D provides about a 7% weight gain.
34. The formulation of claim 31 wherein the KOLLICOAT® SR 30D provides about a 8% weight gain.

35. The formulation of claim 31 wherein the KOLLICOAT® SR 30D provides a 5-9% weight gain.
36. A method of preparing a modified release formulation comprising:
- (a) coating an inert core selected from the group consisting of sugar, MCC and tartaric acid, with 2-methyl-2-(3-methyl-4-(4-(methylamino)-5-(trifluoromethyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)propanenitrile to form an API-core pellet;
 - (b) coating the API-core pellet with a cosmetic, non-functional seal coating to form a seal-coated pellet; and
 - (c) coating the seal-coated pellet with a release-modifying agent to form the modified release formulation.
37. The method of claim 36 wherein the inert core is selected from a sugar, microcrystalline cellulose (MCC), tartaric acid, polyols, carnauba wax, silicon dioxide, and combinations thereof.
38. The method of claim 36 wherein the cosmetic, non-functional seal coating is selected from hydroxypropyl methylcellulose (HPMC), and a mixture of hypromellose and ethylcellulose.
39. The method of claim 38 wherein the release-modifying agent is selected from the group consisting of KOLLICOAT®, EUDRAGIT®, hydroxypropyl methylcellulose (HPMC), and a mixture of hypromellose and ethylcellulose.
40. A method of preparing a modified release formulation comprising:
- (a) roller compaction of 2-methyl-2-(3-methyl-4-(4-(methylamino)-5-(trifluoromethyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)propanenitrile and one or more excipients selected from the group consisting of microcrystalline cellulose, hydroxypropyl methylcellulose, croscarmellose sodium, polyethylene glycol, polyvinyl alcohol, polyvinyl acetate, polyvinylpyrrolidone, purified talc, colloidal silicon dioxide, and magnesium stearate, whereby a pellet is formed; and
 - (b) polymer coating the pellet with a dispersion of a coating agent selected from KOLLICOAT®, CARBOPOL®, AQUACOAT®, and OPADRY® White.
41. The method of claim 40 further comprising one or more steps selected from extrusion, spheronization, and compression.
42. The method of claim 40 further comprising filling a soft or hard capsule shell with the coated pellets.
43. A method of preparing a modified release formulation tablet comprising:

- (a) blending a dry mixture of 2-methyl-2-(3-methyl-4-(4-(methylamino)-5-(trifluoromethyl)pyrimidin-2-ylamino)-1H-pyrazol-1-yl)propanenitrile, povidone, croscarmellose sodium, silicon dioxide, talc, microcrystalline cellulose, and magnesium stearate;
- (b) preparing a dry-granulation of the dry mixture by roller compaction as granules;
- (c) milling the granules;
- (d) adding croscarmellose sodium, silicon dioxide, talc, and magnesium stearate to the milled granules to form an extra-granular mixture;
- (e) compressing the extra-granular mixture into tablets; and
- (f) coating the tablets with a coating agent selected from KOLLICOAT®, CARBOPOL®, AQUACOAT®, and EUDRAGIT®.

44. A method of treating a LRRK2 mediated disease comprising administering to a subject in need thereof a formulation of any one of the preceding claims.

45. The method of claim 44 wherein one or more of the formulations are administered to the subject once per day, twice per day, or three times per day.

46. The method of claim 45 wherein the formulations are administered to the subject twice per day.

47. The method of claim 46 wherein the LRRK2 mediated disease is a neurodegenerative disease.

48. The method of claim 47 wherein the LRRK2 mediated disease is Parkinson's disease.