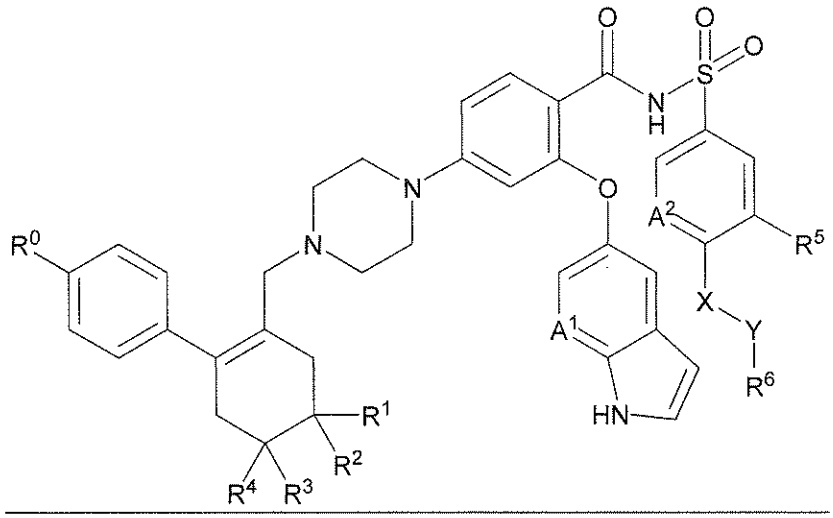
enable combination therapies with other chemotherapeutics.

SUMMARY

[0028a] In one aspect, there is provided a solid dispersion comprising a compound of Formula I



where:

R^0 is chloro;

R^1 and R^2 are H;

R^3 and R^4 are methyl;

A^1 is N and A^2 is CH;

R^5 is nitro;

X is –NH–;

Y is $–(CH_2)_n–$ where n is 1; and

R^6 is is selected from the group consisting of tetrahydropyranyl and 4-hydroxy-4-methylcyclohexyl;

or a pharmaceutically acceptable salt thereof; wherein the compound of Formula I or the pharmaceutically acceptable salt thereof is dispersed in a solid matrix that comprises (a) at least one pharmaceutically acceptable water-soluble polymeric carrier and (b) at least one pharmaceutically acceptable surfactant,

wherein less than 5% of the compound or pharmaceutically acceptable salt thereof is in crystalline form, as observed by X-ray diffraction analysis,

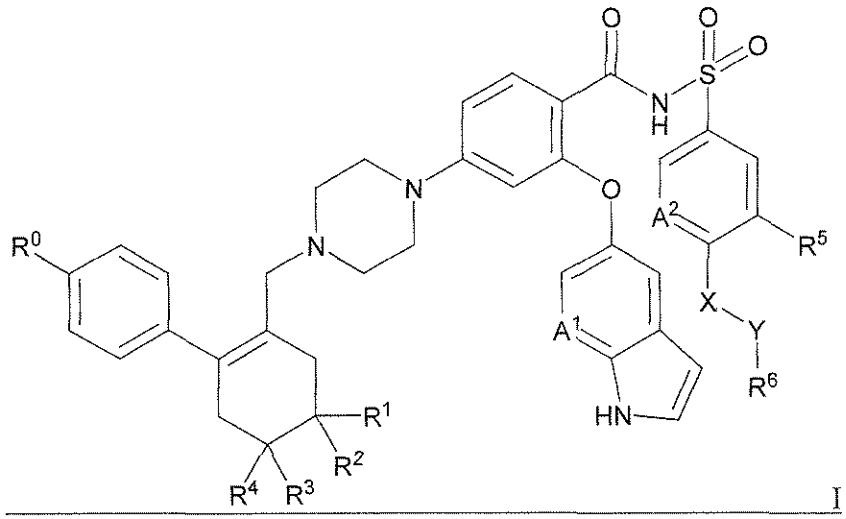
wherein the compound or pharmaceutically acceptable salt thereof is present in a parent-compound-equivalent amount of 5% to 40% by weight, the at least one pharmaceutically acceptable water-soluble polymeric carrier is present in an amount of 40% to 85% by weight, and the at least one pharmaceutically acceptable surfactant is present in an amount of 5% to 20% by weight,

wherein the at least one pharmaceutically acceptable water-soluble polymeric carrier is selected from the group consisting of N-vinyl lactams, cellulose esters, cellulose ethers, high molecular weight polyalkylene oxides, polyacrylates, polymethacrylates, polyacrylamides, vinyl acetate polymers, graft copolymers of polyethylene glycol, polyvinyl caprolactam and polyvinyl acetate, oligo- and polysaccharides and mixtures thereof, and

wherein the at least one pharmaceutically acceptable surfactant is selected from the group consisting of polyoxyethylene glycerides, fatty acid monoesters of sorbitan, polysorbates, α-tocopheryl polyethylene glycol succinate (TPGS) and mixtures thereof.

[0028b] In one aspect, there is provided a process for preparing a solid dispersion, comprising:

(a) subjecting to elevated temperature (i) an active pharmaceutical ingredient (API) that comprises a compound of Formula I



I

where:

R^0 is chloro;

R^1 and R^2 are H;

R^3 and R^4 are methyl;

A^1 is N and A^2 is CH;

R^5 is nitro;

X is –NH–;

Y is $-(CH_2)_n-$ where n is 1 ; and

R^6 is is selected from the group consisting of tetrahydropyranyl and 4-hydroxy-4-methylcyclohexyl;

or a pharmaceutically acceptable salt thereof, (ii) a pharmaceutically acceptable water-soluble polymeric carrier and (iii) a pharmaceutically acceptable surfactant to provide an extrudable semi-solid mixture;

(b) extruding the semi-solid mixture; and

(c) cooling the resulting extrudate to provide a solid matrix comprising the polymeric carrier and the surfactant and having the compound or salt thereof dispersed therein, wherein less 5% of the compound or pharmaceutically acceptable salt thereof is in crystalline form, as observed by X-ray diffraction analysis,

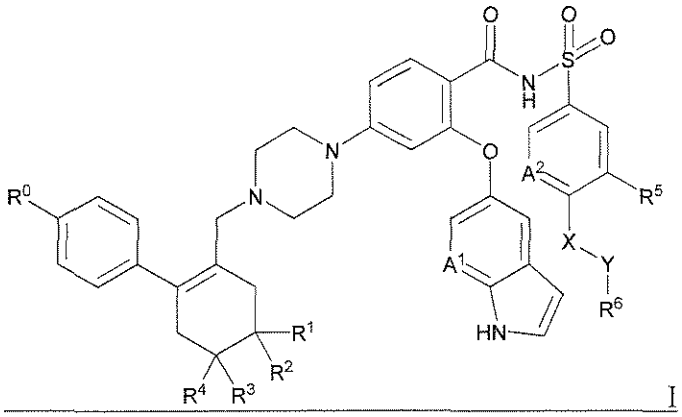
wherein the compound or pharmaceutically acceptable salt thereof is present in a parent-compound-equivalent amount of 5% to 40% by weight, the at least one pharmaceutically acceptable water-soluble polymeric carrier is present in an amount of 40% to 85% by weight, and the at least one pharmaceutically acceptable surfactant is present in an amount of 5% to 20% by weight,

wherein the at least one pharmaceutically acceptable polymeric carrier is selected from the group consisting of N-vinyl lactams, cellulose esters, cellulose ethers, high molecular weight polyalkylene oxides, polyacrylates, polymethacrylates, polyacrylamides, vinyl acetate polymers, graft copolymers of polyethylene glycol, polyvinyl caprolactam and polyvinyl acetate, oligo- and polysaccharides and mixtures thereof, and

wherein the at least one surfactant is selected from the group consisting of polyoxyethylene glycerides, fatty acid monoesters of sorbitan, polysorbates, α-tocopheryl polyethylene glycol succinate (TPGS) and mixtures thereof.

[0028c] In one aspect, there is provided a process for preparing a solid dispersion, comprising:

(a) subjecting to elevated temperature (i) an active pharmaceutical ingredient (API) that comprises a compound of Formula I



I

where:

R^0 is chloro;

R^1 and R^2 are H;

R^3 and R^4 are methyl;

A^1 is N and A^2 is CH;

R^5 is nitro;

X is –NH–;

Y is $-(CH_2)_n-$ where n is 1; and

R^6 is is selected from the group consisting of tetrahydropyranyl and 4-hydroxy-4-methylcyclohexyl;

or a pharmaceutically acceptable salt thereof, (ii) a pharmaceutically acceptable water-soluble polymeric carrier and (iii) a pharmaceutically acceptable surfactant to provide an extrudable semi-solid mixture;

(b) extruding and calendering the semi-solid mixture; and

(c) cooling the resulting extrudate to provide a solid matrix comprising the polymeric carrier and the surfactant and having the compound or salt thereof dispersed

therein, wherein less 5% of the compound or pharmaceutically acceptable salt thereof is in crystalline form, as observed by X-ray diffraction analysis,

wherein the compound or pharmaceutically acceptable salt thereof is present in a parent-compound-equivalent amount of 5% to 40% by weight, the at least one pharmaceutically acceptable water-soluble polymeric carrier is present in an amount of 40% to 85% by weight, and the at least one pharmaceutically acceptable surfactant is present in an amount of 5% to 20% by weight,

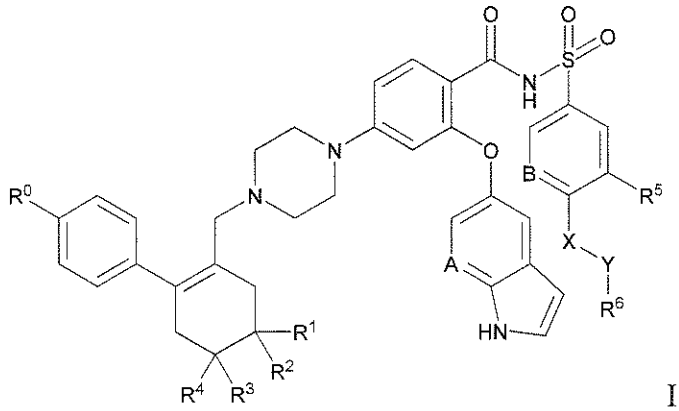
wherein the at least one pharmaceutically acceptable polymeric carrier is selected from the group consisting of N-vinyl lactams, cellulose esters, cellulose ethers, high molecular weight polyalkylene oxides, polyacrylates, polymethacrylates, polyacrylamides, vinyl acetate polymers, graft copolymers of polyethylene glycol, polyvinyl caprolactam and polyvinyl acetate, oligo- and polysaccharides and mixtures thereof, and

wherein the at least one surfactant is selected from the group consisting of polyoxyethylene glycerides, fatty acid monoesters of sorbitan, polysorbates, α-tocopheryl polyethylene glycol succinate (TPGS) and mixtures thereof.

[0028d] In one aspect, there is provided an orally deliverable pharmaceutical dosage form comprising the solid dispersion as disclosed herein.

[0028e] In one aspect, there is provided the use of the solid dispersion as disclosed herein in the manufacture of a medicament for treating a neoplastic, immune or autoimmune disease, said use comprising orally administering to a subject having the disease a therapeutically effective amount of the medicament.

[0029] There is now provided a solid dispersion comprising, in essentially non-crystalline, for example amorphous, form, a compound of Formula I:



I

where:

R^0 is halo;

R^1 and R^2 are H or are independently methyl or methoxy;

R^3 and R^4 are independently methyl or methoxy if R^1 and R^2 are H, or are H if R^1 and R^2 are independently methyl or methoxy;

A and B are each independently CH or N;

R^5 is C_{1-4} alkyl or haloalkyl, C_{1-4} alkylsulfonyl or haloalkylsulfonyl, halo, nitro or cyano;

X is –O– or –NH–;

Y is $–(CH_2)_n–$ where n is 0, 1, 2 or 3; and

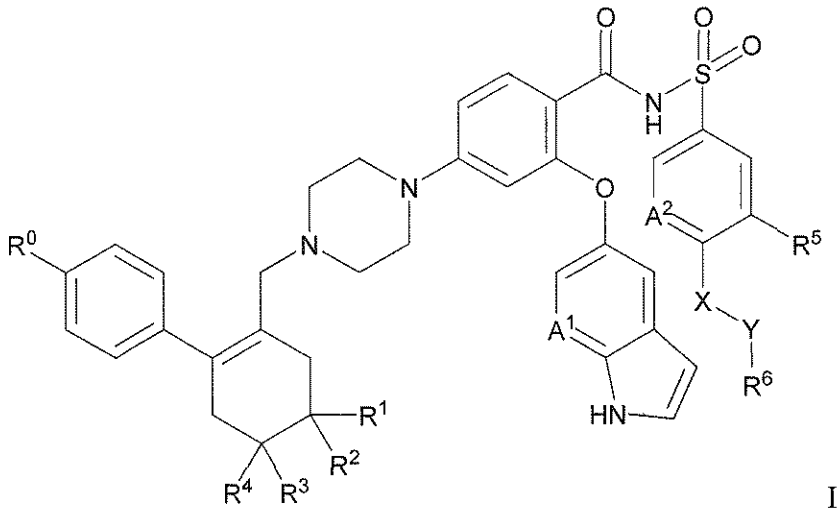
R^6 is an unsubstituted or substituted 3- to 7-membered carbocyclic or heterocyclic ring as defined herein, or is NR^7R^8;

wherein, if R^6 is NR^7R^8, R^7 and R^8 are each independently H or $R^9–(CH_2)_m–$ groups, no more than one of R^7 and R^8 being H, where each R^9 is independently a 3- to 7-membered carbocyclic or heterocyclic ring, optionally substituted with no more than two Z^1 groups as defined below, and each m is independently 0 or 1; and

wherein, if R^6 is a substituted carbocyclic or heterocyclic ring, substituents thereon are no more than two Z^1 groups and/or no more than one Z^2 group, Z^1 groups

CLAIMS

1. A solid dispersion comprising a compound of Formula I



I

where:

R^0 is chloro;

R^1 and R^2 are H;

R^3 and R^4 are methyl;

A^1 is N and A^2 is CH;

R^5 is nitro;

X is –NH–;

Y is $–(CH_2)_n–$ where n is 1; and

R^6 is is selected from the group consisting of tetrahydropyranyl and 4-hydroxy-4-methylcyclohexyl;

or a pharmaceutically acceptable salt thereof; wherein the compound of Formula I or the pharmaceutically acceptable salt thereof is dispersed in a solid matrix that comprises (a) at least one pharmaceutically acceptable water-soluble polymeric carrier and (b) at least one

pharmaceutically acceptable surfactant,

wherein less than 5% of the compound or pharmaceutically acceptable salt thereof is in crystalline form, as observed by X-ray diffraction analysis,

wherein the compound or pharmaceutically acceptable salt thereof is present in a parent-compound-equivalent amount of 5% to 40% by weight, the at least one pharmaceutically acceptable water-soluble polymeric carrier is present in an amount of 40% to 85% by weight, and the at least one pharmaceutically acceptable surfactant is present in an amount of 5% to 20% by weight,

wherein the at least one pharmaceutically acceptable water-soluble polymeric carrier is selected from the group consisting of N-vinyl lactams, cellulose esters, cellulose ethers, high molecular weight polyalkylene oxides, polyacrylates, polymethacrylates, polyacrylamides, vinyl acetate polymers, graft copolymers of polyethylene glycol, polyvinyl caprolactam and polyvinyl acetate, oligo- and polysaccharides and mixtures thereof, and

wherein the at least one pharmaceutically acceptable surfactant is selected from the group consisting of polyoxyethylene glycerides, fatty acid monoesters of sorbitan, polysorbates, α-tocopheryl polyethylene glycol succinate (TPGS) and mixtures thereof.

2. The solid dispersion of Claim 1, wherein, in the compound of Formula I, R^6 is tetrahydropyran.

3. The solid dispersion of Claim 2, wherein the compound is 4-(4-{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl}piperazin-1-yl)-N-({3-nitro-4-[(tetrahydro-2H-pyran-4-ylmethyl)amino]phenyl}sulfonyl)-2-(1H-pyrrolo[2,3-b]pyridin-5-yloxy)benzamide or a pharmaceutically acceptable salt thereof.

4. The solid dispersion of Claim 1, comprising 4-(4-{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl}piperazin-1-yl)-N-[(4-{[(trans-4-hydroxy-4-methylcyclohexyl)methyl]amino}-3-nitrophenyl)sulfonyl]-2-(1H-pyrrolo[2,3-b]pyridin-5-yloxy)benzamide or a pharmaceutically acceptable salt thereof.

5. The solid dispersion of Claim 1, comprising 4-(4-{[2-(4-chlorophenyl)-4,4-

dimethylcyclohex-1-en-1-yl]methyl}piperazin-1-yl)-N-[(4-{[(cis-4-hydroxy-4-methylcyclohexyl)methyl]amino}-3-nitrophenyl)sulfonyl]-2-(1H-pyrrolo[2,3-b]pyridin-5-yloxy)benzamide or a pharmaceutically acceptable salt thereof.

6. The solid dispersion of Claim 1, wherein the at least one polymeric carrier is selected from the group consisting of povidones, copovidones, HPMCs, polyethylene glycol/polyvinyl caprolactam/polyvinyl acetate graft copolymers and mixtures thereof.

7. The solid dispersion of Claim 1, further comprising at least one glidant.

8. The solid dispersion of Claim 7, wherein the at least one glidant comprises colloidal silicon dioxide.

9. The solid dispersion of Claim 1, wherein the compound or salt is present in a parent-compound-equivalent amount of about 5% to about 15% by weight, the at least one polymeric carrier is present in an amount of about 70% to about 85% by weight and the at least one surfactant is present in an amount of about 5% to about 15% by weight.

10. The solid dispersion of Claim 9, wherein the compound is 4-(4-{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl}piperazin-1-yl)-N-({3-nitro-4-[(tetrahydro-2H-pyran-4-ylmethyl)amino]phenyl}sulfonyl)-2-(1H-pyrrolo[2,3-b]pyridin-5-yloxy)benzamide or a pharmaceutically acceptable salt thereof.

11. The solid dispersion of Claim 9, comprising 4-(4-{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl}piperazin-1-yl)-N-[(4-{[(trans-4-hydroxy-4-methylcyclohexyl)methyl]amino}-3-nitrophenyl)sulfonyl]-2-(1H-pyrrolo[2,3-b]pyridin-5-yloxy)benzamide or a pharmaceutically acceptable salt thereof.

12. The solid dispersion of Claim 9, comprising 4-(4-{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl}piperazin-1-yl)-N-[(4-{[(cis-4-hydroxy-4-methylcyclohexyl)methyl]amino}-3-nitrophenyl)sulfonyl]-2-(1H-pyrrolo[2,3-b]pyridin-5-yloxy)benzamide or a pharmaceutically acceptable salt thereof.

13. The solid dispersion of Claim 10, wherein the at least one polymeric carrier is a copovidone.

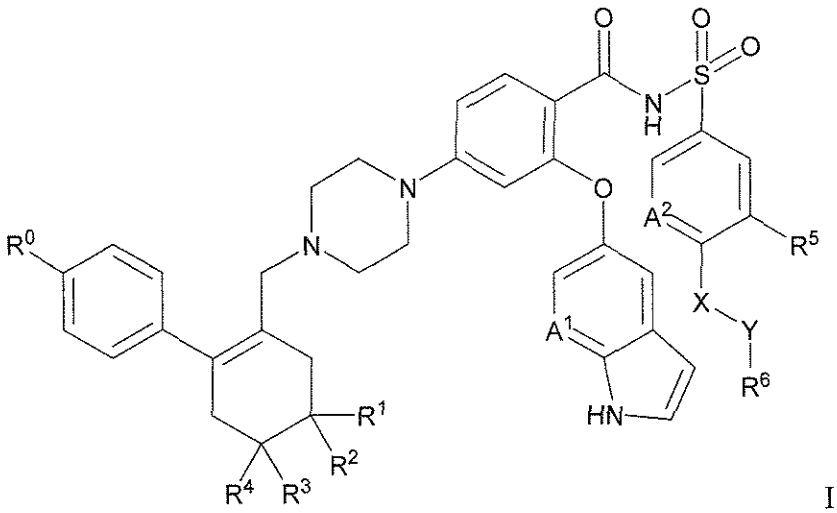
14. The solid dispersion of Claim 13, wherein the at least one surfactant is a polysorbate.

15. The solid dispersion of Claim 14, further comprising at least one glidant.

16. The solid dispersion of Claim 15, wherein the at least one glidant comprises colloidal silicon dioxide.

17. A process for preparing a solid dispersion, comprising:

(a) subjecting to elevated temperature (i) an active pharmaceutical ingredient (API) that comprises a compound of Formula I



I

where:

R^0 is chloro;

R^1 and R^2 are H;

R^3 and R^4 are methyl;

A^1 is N and A^2 is CH;

R^5 is nitro;

X is –NH–;

Y is $-(CH_2)_n-$ where n is 1 ; and

R^6 is is selected from the group consisting of tetrahydropyranyl and 4-hydroxy-4-methylcyclohexyl;

or a pharmaceutically acceptable salt thereof, (ii) a pharmaceutically acceptable water-soluble polymeric carrier and (iii) a pharmaceutically acceptable surfactant to provide an extrudable semi-solid mixture;

(b) extruding the semi-solid mixture; and

(c) cooling the resulting extrudate to provide a solid matrix comprising the polymeric carrier and the surfactant and having the compound or salt thereof dispersed therein, wherein less 5% of the compound or pharmaceutically acceptable salt thereof is in crystalline form, as observed by X-ray diffraction analysis,

wherein the compound or pharmaceutically acceptable salt thereof is present in a parent-compound-equivalent amount of 5% to 40% by weight, the at least one pharmaceutically acceptable water-soluble polymeric carrier is present in an amount of 40% to 85% by weight, and the at least one pharmaceutically acceptable surfactant is present in an amount of 5% to 20% by weight,

wherein the at least one pharmaceutically acceptable polymeric carrier is selected from the group consisting of N-vinyl lactams, cellulose esters, cellulose ethers, high molecular weight polyalkylene oxides, polyacrylates, polymethacrylates, polyacrylamides, vinyl acetate polymers, graft copolymers of polyethylene glycol, polyvinyl caprolactam and polyvinyl acetate, oligo- and polysaccharides and mixtures thereof, and

wherein the at least one surfactant is selected from the group consisting of polyoxyethylene glycerides, fatty acid monoesters of sorbitan, polysorbates, α-tocopheryl polyethylene glycol succinate (TPGS) and mixtures thereof.

18. The process of Claim 17, wherein the API, polymeric carrier and surfactant are mixed together before said subjecting to elevated temperature.

19. The process of Claim 17, wherein the API, polymeric carrier and surfactant are mixed together while subjecting to elevated temperature.

20. The process of Claim 17, wherein said elevated temperature is about 70°C to about 250°C.

21. The process of Claim 17, wherein said elevated temperature is about 90°C to about 160°C.

22. The process of Claim 17, further comprising calendering the extrudate before or while cooling.

23. The process of Claim 17, wherein API is 4-(4-{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl}piperazin-1-yl)-N-({3-nitro-4-[(tetrahydro-2H-pyran-4-ylmethyl)amino]phenyl}sulfonyl)-2-(1H-pyrrolo[2,3-b]pyridin-5-yloxy)benzamide or a pharmaceutically acceptable salt thereof.

24. The process of Claim 17, wherein the API is 4-(4-{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl}piperazin-1-yl)-N-[(4-{[(trans-4-hydroxy-4-methylcyclohexyl)methyl]amino}-3-nitrophenyl)sulfonyl]-2-(1H-pyrrolo[2,3-b]pyridin-5-yloxy)benzamide.

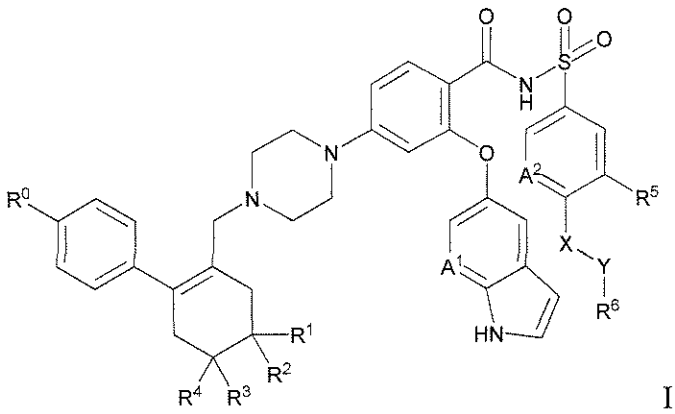
25. The process of Claim 17, wherein the API is 4-(4-{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl}piperazin-1-yl)-N-[(4-{[(cis-4-hydroxy-4-methylcyclohexyl)methyl]amino}-3-nitrophenyl)sulfonyl]-2-(1H-pyrrolo[2,3-b]pyridin-5-yloxy)benzamide.

26. The process of claim 23, wherein the polymeric carrier is a copovidone.

27. The process of Claim 26, wherein the surfactant is a polysorbate.

28. A process for preparing a solid dispersion, comprising:

(a) subjecting to elevated temperature (i) an active pharmaceutical ingredient (API) that comprises a compound of Formula I



I

where:

R^0 is chloro;

R^1 and R^2 are H;

R^3 and R^4 are methyl;

A^1 is N and A^2 is CH;

R^5 is nitro;

X is –NH–;

Y is $-(CH_2)_n-$ where n is 1; and

R^6 is is selected from the group consisting of tetrahydropyranyl and 4-hydroxy-4-methylcyclohexyl;

or a pharmaceutically acceptable salt thereof, (ii) a pharmaceutically acceptable water-soluble polymeric carrier and (iii) a pharmaceutically acceptable surfactant to provide an extrudable semi-solid mixture;

(b) extruding and calendering the semi-solid mixture; and

(c) cooling the resulting extrudate to provide a solid matrix comprising the polymeric carrier and the surfactant and having the compound or salt thereof dispersed therein, wherein less

5% of the compound or pharmaceutically acceptable salt thereof is in crystalline form, as observed by X-ray diffraction analysis,

wherein the compound or pharmaceutically acceptable salt thereof is present in a parent-compound-equivalent amount of 5% to 40% by weight, the at least one pharmaceutically acceptable water-soluble polymeric carrier is present in an amount of 40% to 85% by weight, and the at least one pharmaceutically acceptable surfactant is present in an amount of 5% to 20% by weight,

wherein the at least one pharmaceutically acceptable polymeric carrier is selected from the group consisting of N-vinyl lactams, cellulose esters, cellulose ethers, high molecular weight polyalkylene oxides, polyacrylates, polymethacrylates, polyacrylamides, vinyl acetate polymers, graft copolymers of polyethylene glycol, polyvinyl caprolactam and polyvinyl acetate, oligo- and polysaccharides and mixtures thereof, and

wherein the at least one surfactant is selected from the group consisting of polyoxyethylene glycerides, fatty acid monoesters of sorbitan, polysorbates, α-tocopheryl polyethylene glycol succinate (TPGS) and mixtures thereof.

29. The process of Claim 28, wherein API is 4-(4-{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl}piperazin-1-yl)-N-({3-nitro-4-[(tetrahydro-2H-pyran-4-ylmethyl)amino]phenyl}sulfonyl)-2-(1H-pyrrolo[2,3-b]pyridin-5-yloxy)benzamide or a pharmaceutically acceptable salt thereof.

30. The process of Claim 28, wherein the API is 4-(4-{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl}piperazin-1-yl)-N-[(4-{[(trans-4-hydroxy-4-methylcyclohexyl)methyl]amino}-3-nitrophenyl)sulfonyl]-2-(1H-pyrrolo[2,3-b]pyridin-5-yloxy)benzamide.

31. The process of Claim 28, wherein the API is 4-(4-{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl}piperazin-1-yl)-N-[(4-{[(cis-4-hydroxy-4-methylcyclohexyl)methyl]amino}-3-nitrophenyl)sulfonyl]-2-(1H-pyrrolo[2,3-b]pyridin-5-yloxy)benzamide.

32. The process of claim 29, wherein the polymeric carrier is a copovidone.

33. The process of Claim 32, wherein the surfactant is a polysorbate.

34. An orally deliverable pharmaceutical dosage form comprising the solid dispersion of Claim 1.

35. Use of the solid dispersion of claim 1 in the manufacture of a medicament for treating a neoplastic, immune or autoimmune disease, said use comprising orally administering to a subject having the disease a therapeutically effective amount of the medicament.

36. The use of Claim 35, wherein the disease is a neoplastic disease.

37. The use of Claim 36, wherein the neoplastic disease is selected from the group consisting of cancer, mesothelioma, bladder cancer, pancreatic cancer, skin cancer, cancer of the head or neck, cutaneous or intraocular melanoma, ovarian cancer, breast cancer, uterine cancer, carcinoma of the fallopian tubes, carcinoma of the endometrium, carcinoma of the cervix, carcinoma of the vagina, carcinoma of the vulva, bone cancer, colon cancer, rectal cancer, cancer of the anal region, stomach cancer, gastrointestinal (gastric, colorectal and/or duodenal) cancer, chronic lymphocytic leukemia, acute lymphocytic leukemia, esophageal cancer, cancer of the small intestine, cancer of the endocrine system, cancer of the thyroid gland, cancer of the parathyroid gland, cancer of the adrenal gland, sarcoma of soft tissue, cancer of the urethra, cancer of the penis, testicular cancer, hepatocellular (hepatic and/or biliary duct) cancer, primary or secondary central nervous system tumor, primary or secondary brain tumor, Hodgkin's disease, chronic or acute leukemia, chronic myeloid leukemia, lymphocytic lymphoma, lymphoblastic leukemia, follicular lymphoma, lymphoid malignancies of T-cell or B-cell origin, melanoma, multiple myeloma, oral cancer, non-small-cell lung cancer, prostate cancer, small-cell lung cancer, cancer of the kidney and/or ureter, renal cell carcinoma, carcinoma of the renal pelvis, neoplasms of the central nervous system, primary central nervous system lymphoma, non-Hodgkin's lymphoma, spinal axis tumors, brain stem glioma, pituitary adenoma, adrenocortical cancer, gall bladder cancer, cancer of the spleen, cholangiocarcinoma, fibrosarcoma, neuroblastoma, retinoblastoma and combinations thereof.

38. The use of Claim 36, wherein the neoplastic disease is a lymphoid malignancy.

39. The use of Claim 38, wherein the lymphoid malignancy is non-Hodgkin's lymphoma.

40. The use of Claim 36, wherein the neoplastic disease is chronic lymphocytic leukemia or acute lymphocytic leukemia.

41. The use of Claim 35, wherein the disease is an immune or autoimmune disease.

42. The use of Claim 35, wherein the solid dispersion is administered in a parent-compound-equivalent dose of about 50 to about 500 mg per day of the compound of Formula I or salt thereof at an average treatment interval of about 3 hours to about 7 days.

43. The use of Claim 35, wherein the solid dispersion is administered once daily in a parent-compound-equivalent dose of about 50 to about 500 mg per day of the compound of Formula I or salt thereof.

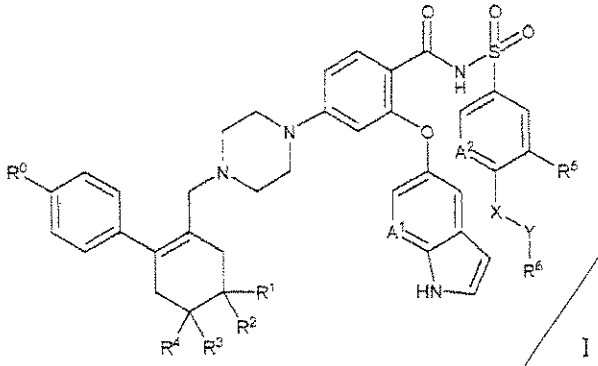
44. The use of Claim 35, wherein the compound is 4-(4-{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl}piperazin-1-yl)-N-({3-nitro-4-[(tetrahydro-2H-pyran-4-ylmethyl)amino]phenyl}sulfonyl)-2-(1H-pyrrolo[2,3-b]pyridin-5-yloxy)benzamide or a pharmaceutically acceptable salt thereof.

45. The use of claim 35, wherein the compound is 4-(4-{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl}piperazin-1-yl)-N-[(4-{[(trans-4-hydroxy-4-methylcyclohexyl)methyl]amino}-3-nitrophenyl)sulfonyl]-2-(1H-pyrrolo[2,3-b]pyridin-5-yloxy)benzamide.

46. The use of claim 35, wherein the compound is 4-(4-{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl}piperazin-1-yl)-N-[(4-{[(cis-4-hydroxy-4-methylcyclohexyl)methyl]amino}-3-nitrophenyl)sulfonyl]-2-(1H-pyrrolo[2,3-b]pyridin-5-yloxy)benzamide.

WHAT IS CLAIMED IS:

1. A solid dispersion comprising, in essentially non-crystalline form, a compound of Formula I



I

where:

R^0 is halo;

R^1 and R^2 are H or are independently methyl or methoxy;

R^3 and R^4 are independently methyl or methoxy if R^1 and R^2 are H, or are H if R^1 and R^2 are independently methyl or methoxy;

A^1 and A^2 are each independently CH or N;

R^5 is C_{1-4} alkyl or haloalkyl, C_{1-4} alkylsulfonyl or haloalkylsulfonyl, halo, nitro or cyano;

X is –O– or –NH–;

Y is $-(CH_2)_n-$ where n is 0, 1, 2 or 3; and

R^6 is an unsubstituted or substituted 3- to 7-membered carbocyclic or heterocyclic ring as defined herein, or is NR^7R^8;

wherein, if R^6 is NR^7R^8, R^7 and R^8 are each independently H or $R^9-(CH_2)_m-$ groups, no more than one of R^7 and R^8 being H, where each R^9 is independently a 3- to 7-membered carbocyclic or heterocyclic ring, optionally substituted with no more than two Z^1 groups as defined below, and each m is independently 0 or 1; and

wherein, if R^6 is a substituted carbocyclic or heterocyclic ring, substituents thereon are no more than two Z^1 groups and/or no more than one Z^2 group, Z^1 groups being independently selected from (a) C_{1-4} alkyl, C_{2-4} alkenyl, C_{1-4} alkoxy,

C_{1-4} alkylthio, C_{1-4} alkylamino, C_{1-4} alkylsulfonyl, C_{1-4} alkylsulfonylamino, C_{1-4} alkylcarbonyl, C_{1-4} alkylcarbonylamino and C_{1-4} alkylcarboxy, each optionally substituted with one or more substituents independently selected from halo, hydroxy, C_{1-4} alkoxy, amino, C_{1-4} alkylamino, di-(C_{1-4} alkyl)amino and cyano, (b) halo, (e) hydroxy, (f) amino and (g) oxo groups, and Z^2 being (i) a further 3- to 6-membered carbocyclic or heterocyclic ring, optionally substituted with no more than two Z^1 groups as defined above, or (ii) NR^7R^8 where R^7 and R^8 are as defined above;

or a pharmaceutically acceptable salt thereof; dispersed in a solid matrix that comprises (a) at least one pharmaceutically acceptable water-soluble polymeric carrier and (b) at least one pharmaceutically acceptable surfactant.

2. The solid dispersion of Claim 1, wherein, in the compound of Formula I, R^0 is chloro.

3. The solid disperson of Claim 2, wherein, in the compound of Formula I, R^3 and R^4 are each methyl.

4. The solid disperson of Claim 3, wherein, in the compound of Formula I, R^1 and R^2 are each hydrogen.

5. The solid disperson of Claim 4, wherein, in the compound of Formula I, A^1 is N and A^2 is CH.

6. The solid disperson of Claim 5, wherein, in the compound of Formula I, R^5 is nitro.

7. The solid disperson of Claim 6, wherein, in the compound of Formula I, X is –NH–.

8. The solid disperson of Claim 7, wherein, in the compound of Formula I, Y is $-(CH_2)_n-$ where n is 1.

9. The solid disperson of Claim 8, wherein, in the compound of Formula I, R^6 is tetrahydropyran.

10. The solid dispersion of Claim 9, wherein the compound is 4-(4-{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl}piperazin-1-yl)-N-({3-nitro-4-[(tetrahydro-2H-pyran-4-ylmethyl)amino]phenyl}sulfonyl)-2-(1H-pyrrolo[2,3-b]pyridin-5-yloxy)benzamide.

11. The solid dispersion of Claim 1, wherein, in the compound of Formula I, R^1 is methyl or methoxy, R^2 is methyl, and R^3 and R^4 are each H.

12. The solid dispersion of Claim 1, wherein, in the compound of Formula I, if A^2 is –CH– then R^5 is nitro; and if A^2 is –N– then R^5 is bromo.

13. The solid dispersion of Claim 1, wherein, in the compound of Formula I, R^6 is a 3- to 7-membered carbocyclic or heterocyclic ring, unsubstituted or substituted with no more than two Z^1 groups and/or no more than one Z^2 group.

14. The solid dispersion of Claim 13, wherein, in the compound of Formula I, said carbocyclic or heterocyclic ring is a saturated ring.

15. The solid dispersion of Claim 14, wherein, in the compound of Formula I, said saturated ring is selected from the group consisting of cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, azetidinyl, oxetanyl, thietanyl, pyrrolidinyl, imazolidinyl, pyrazolidinyl, tetrahydrofuranyl, oxazolidinyl, isoxazolidinyl, thiophanyl, thiazolidinyl, isothiazolidinyl, piperidinyl, piperazinyl, tetrahydropyranyl, 1,4-dioxanyl, morpholinyl and tetrahydrothiopyranyl rings.

16. The solid dispersion of Claim 1, wherein the compound is selected from the group consisting of

4-(4-{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl}piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-({3-nitro-4-[(1-tetrahydro-2H-pyran-4-ylpiperidin-4-yl)amino]phenyl}sulfonyl)benzamide;

4-(4-{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl}piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-({4-[(4-methylpiperazin-1-yl)amino]-3-nitrophenyl}sulfonyl)benzamide;

4-(4-{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl}piperazin-1-yl)-N-({3-nitro-4-[(tetrahydro-2H-pyran-4-ylmethyl)amino]phenyl}sulfonyl)-2-(1*H*-pyrrolo[2,3-b]pyridin-5-yloxy)benzamide;

trans-4-(4-{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl}piperazin-1-yl)-N-({4-[(4-morpholin-4-ylcyclohexyl)amino]-3-nitrophenyl}sulfonyl)-2-(1H-pyrrolo[2,3-b]pyridin-5-yloxy)benzamide;

cis-4-(4-{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl}piperazin-1-yl)-N-[(4-{[(4-methoxycyclohexyl)methyl]amino}-3-nitrophenyl)sulfonyl]-2-(1H-pyrrolo[2,3-b]pyridin-5-yloxy)benzamide;

trans-4-(4-{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl}piperazin-1-yl)-N-[(4-{[(4-methoxycyclohexyl)methyl]amino}-3-nitrophenyl)sulfonyl]-2-(1H-pyrrolo[2,3-b]pyridin-5-yloxy)benzamide;

4-(4-{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl}piperazin-1-yl)-N-({4-[(4-fluorotetrahydro-2H-pyran-4-yl)methoxy]-3-nitrophenyl}sulfonyl)-2-(1H-pyrrolo[2,3-b]pyridin-5-yloxy)benzamide;

N-[(5-chloro-6-{[4-fluoro-1-(oxetan-3-yl)piperidin-4-yl]methoxy}pyridin-3-yl)-sulfonyl]-4-(4-{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl}-piperazin-1-yl)-2-(1H-pyrrolo[2,3-b]pyridin-5-yloxy)benzamide;

N-({5-bromo-6-[(1-tetrahydro-2H-pyran-4-ylpiperidin-4-yl)amino]pyridin-3-yl}-sulfonyl)-4-(4-{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl}-piperazin-1-yl)-2-(1H-pyrrolo[2,3-b]pyridin-5-yloxy)benzamide;

4-(4-{[2-(4-chlorophenyl)-5-methoxy-5-methylcyclohex-1-en-1-yl]methyl}piperazin-1-yl)-N-({3-nitro-4-[(tetrahydro-2H-pyran-4-ylmethyl)amino]phenyl}-sulfonyl)-2-(1H-pyrrolo[2,3-b]pyridin-5-yloxy)benzamide;

4-(4-{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl}piperazin-1-yl)-N-[(4-{[(3R)-1-(methylsulfonyl)pyrrolidin-3-yl]amino}-3-nitrophenyl)-sulfonyl]-2-(1H-pyrrolo[2,3-b]pyridin-5-yloxy)benzamide;

4-(4-{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl}piperazin-1-yl)-N-[(4-{[(*trans*-4-hydroxy-4-methylcyclohexyl)methyl]amino}-3-nitrophenyl)-sulfonyl]-2-(1H-pyrrolo[2,3-b]pyridin-5-yloxy)benzamide;

4-(4-{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl}piperazin-1-yl)-N-[(4-{[(*cis*-4-hydroxy-4-methylcyclohexyl)methyl]amino}-3-nitrophenyl)-sulfonyl]-2-(1H-pyrrolo[2,3-b]pyridin-5-yloxy)benzamide;

4-(4-{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl}piperazin-1-yl)-N-{[4-({3-[cyclopropyl(oxetan-3-yl)amino]propyl}amino)-3-nitrophenyl]-sulfonyl}-2-(1H-pyrrolo[2,3-b]pyridin-5-yloxy)benzamide;

4-(4-{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl}piperazin-1-yl)-

N-{[3-nitro-4-({[(3R)-1-tetrahydro-2H-pyran-4-ylpyrrolidin-3-yl]methyl}-amino)phenyl]sulfonyl}-2-(1H-pyrrolo[2,3-b]pyridin-5-yloxy)benzamide;

4-(4-{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl}piperazin-1-yl)-N-[(4-{[(4-methylmorpholin-2-yl)methyl]amino}-3-nitrophenyl)sulfonyl]-2-(1H-pyrrolo[2,3-b]pyridin-5-yloxy)benzamide;

N-[(5-chloro-6-{[1-(cyanomethyl)piperidin-4-yl]methoxy}pyridin-3-yl)sulfonyl]-4-(4-{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl}piperazin-1-yl)-2-(1H-pyrrolo[2,3-b]pyridin-5-yloxy)benzamide;

N-[(4-{[(4-aminotetrahydro-2H-pyran-4-yl)methyl]amino}-3-nitrophenyl)sulfonyl]-4-(4-{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl}piperazin-1-yl)-2-(1H-pyrrolo[2,3-b]pyridin-5-yloxy)benzamide;

4-(4-{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl}piperazin-1-yl)-N-({4-[(4-methoxytetrahydro-2H-pyran-4-yl)methoxy]-3-nitrophenyl}sulfonyl)-2-(1H-pyrrolo[2,3-b]pyridin-5-yloxy)benzamide;

and pharmaceutically acceptable salts thereof.

17. The solid dispersion of Claim 1, wherein the compound or salt is present in a parent-compound-equivalent amount of about 5% to about 40% by weight.

18. The solid dispersion of Claim 1, wherein the at least one polymeric carrier is present in an amount of about 40% to about 85% by weight and the at least one surfactant is present in an amount of about 5% to about 20% by weight.

19. The solid dispersion of Claim 1, wherein the at least one polymeric carrier is selected from the group consisting of homopolymers and copolymers of N-vinyl lactams, cellulose esters, cellulose ethers, high molecular weight polyalkylene oxides, polyacrylates, polymethacrylates, polyacrylamides, vinyl acetate polymers, graft copolymers of polyethylene glycol, polyvinyl caprolactam and polyvinyl acetate, oligo- and polysaccharides and mixtures thereof.

20. The solid dispersion of Claim 1, wherein the at least one polymeric carrier is selected from the group consisting of povidones, copovidones, HPMCs, polyethylene glycol/polyvinyl caprolactam/polyvinyl acetate graft copolymers and mixtures thereof.

21. The solid dispersion of Claim 1, wherein the at least one surfactant is non-ionic.

22. The solid dispersion of Claim 1, wherein the at least one surfactant is selected from the group consisting of polyoxyethylene glycerides, fatty acid monoesters of sorbitan, polysorbates, α-tocopheryl polyethylene glycol succinate (TPGS) and mixtures thereof.

23. The solid dispersion of Claim 1, further comprising at least one glidant.

24. The solid dispersion of Claim 23, wherein the at least one glidant comprises colloidal silicon dioxide.

25. The solid dispersion of Claim 1, wherein the compound or salt is present in a parent-compound-equivalent amount of about 5% to about 40% by weight, the at least one polymeric carrier is present in an amount of about 40% to about 85% by weight and the at least one surfactant is present in an amount of about 5% to about 20% by weight.

26. The solid dispersion of Claim 25, wherein the compound or salt is present in a parent-compound-equivalent amount of about 5% to about 15% by weight, the at least one polymeric carrier is present in an amount of about 70% to about 85% by weight and the at least one surfactant is present in an amount of about 5% to about 15% by weight.

27. The solid dispersion of Claim 26, wherein the compound is 4-(4-{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl}piperazin-1-yl)-N-({3-nitro-4-[(tetrahydro-2H-pyran-4-ylmethyl)amino]phenyl}sulfonyl)-2-(1H-pyrrolo[2,3-b]pyridin-5-yloxy)benzamide.

28. The solid dispersion of Claim 27, wherein the at least one polymeric carrier is a copovidone.

29. The solid dispersion of Claim 28, wherein the at least one surfactant is a polysorbate.

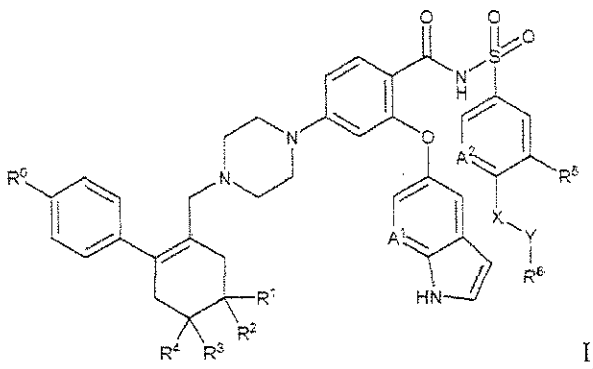
30. The solid dispersion of Claim 30, further comprising at least one glidant.

31. The solid dispersion of Claim 30, wherein the at least one glidant comprises colloidal silicon dioxide.

32. A process for preparing a solid dispersion, comprising:

(a) subjecting to elevated temperature (i) an active pharmaceutical ingredient (API)

that comprises a compound of Formula I



I

where:

R^0 is halo;

R^1 and R^2 are H or are independently methyl or methoxy;

R^3 and R^4 are independently methyl or methoxy if R^1 and R^2 are H, or are H if R^1 and R^2 are independently methyl or methoxy;

A^1 and A^2 are each independently CH or N;

R^5 is C_{1-4} alkyl or haloalkyl, C_{1-4} alkylsulfonyl or haloalkylsulfonyl, halo, nitro or cyano;

X is –O– or –NH–;

Y is $-(CH_2)_n-$ where n is 0, 1, 2 or 3; and

R^6 is an unsubstituted or substituted 3- to 7-membered carbocyclic or heterocyclic ring as defined herein, or is NR^7R^8;

wherein, if R^6 is NR^7R^8, R^7 and R^8 are each independently H or $R^9-(CH_2)_m-$ groups, no more than one of R^7 and R^8 being H, where each R^9 is independently a 3- to 7-membered carbocyclic or heterocyclic ring, optionally substituted with no more than two Z^1 groups as defined below, and each m is independently 0 or 1; and

wherein, if R^6 is a substituted carbocyclic or heterocyclic ring, substituents thereon are no more than two Z^1 groups and/or no more than one Z^2 group, Z^1 groups being independently selected from (a) C_{1-4} alkyl, C_{2-4} alkenyl, C_{1-4} alkoxy, C_{1-4} alkylthio, C_{1-4} alkylamino, C_{1-4} alkylsulfonyl, C_{1-4} alkylsulfonylamino, C_{1-4} alkylcarbonyl, C_{1-4} alkylcarbonylamino and C_{1-4} alkylcarboxy, each

optionally substituted with one or more substituents independently selected from halo, hydroxy, C_{1-4} alkoxy, amino, C_{1-4} alkylamino, di-(C_{1-4} alkyl)amino and cyano, (b) halo, (e) hydroxy, (f) amino and (g) oxo groups, and Z^2 being (i) a further 3- to 6-membered carbocyclic or heterocyclic ring, optionally substituted with no more than two Z^1 groups as defined above, or (ii) NR^7R^8 where R^7 and R^8 are as defined above;

or a pharmaceutically acceptable salt thereof, (ii) a pharmaceutically acceptable water-soluble polymeric carrier and (iii) a pharmaceutically acceptable surfactant to provide an extrudable semi-solid mixture;

(b) extruding the semi-solid mixture; and

(c) cooling the resulting extrudate to provide a solid matrix comprising the polymeric carrier and the surfactant and having the compound or salt thereof dispersed in an essentially non-crystalline form therein.

33. The process of Claim 32, wherein the API, polymeric carrier and surfactant are mixed together before said subjecting to elevated temperature.

34. The process of Claim 32, wherein the API, polymeric carrier and surfactant are mixed together while subjecting to elevated temperature.

35. The process of Claim 32, wherein said elevated temperature is about 70°C to about 250°C.

36. The process of Claim 32, wherein said elevated temperature is about 90°C to about 160°C.

37. The process of Claim 32, further comprising calendering the extrudate before or while cooling.

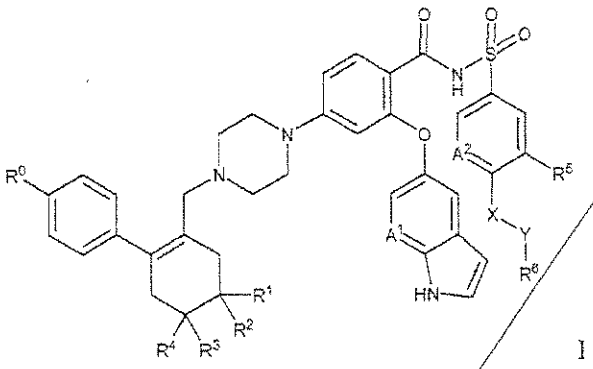
38. The process of Claim 32, wherein API is 4-(4-{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl}piperazin-1-yl)-N-({3-nitro-4-[(tetrahydro-2H-pyran-4-ylmethyl)amino]phenyl}sulfonyl)-2-(1H-pyrrolo[2,3-b]pyridin-5-yloxy)benzamide.

39. The process of claim 38, wherein the polymeric carrier is a copovidone.

40. The process of Claim 39, wherein the surfactant is a polysorbate.

41. A process for preparing a solid dispersion, comprising:

(a) subjecting to elevated temperature (i) an active pharmaceutical ingredient (API) that comprises a compound of Formula I



I

where:

R^6 is halo;

R^1 and R^2 are H or are independently methyl or methoxy;

R^3 and R^4 are independently methyl or methoxy if R^1 and R^2 are H, or are H if R^1 and R^2 are independently methyl or methoxy;

A^1 and A^2 are each independently CH or N;

R^5 is C_{1-4} alkyl or haloalkyl, C_{1-4} alkylsulfonyl or haloalkylsulfonyl, halo, nitro or cyano;

X is –O– or –NH–;

Y is $-(CH_2)_n-$ where n is 0, 1, 2 or 3; and

R^6 is an unsubstituted or substituted 3- to 7-membered carbocyclic or heterocyclic ring as defined herein, or is NR^7R^8;

wherein, if R^6 is NR^7R^8, R^7 and R^8 are each independently H or $R^9-(CH_2)_m-$ groups, no more than one of R^7 and R^8 being H, where each R^9 is independently a 3- to 7-membered carbocyclic or heterocyclic ring, optionally substituted with no more than two Z^1 groups as defined below, and each m is independently 0 or 1; and

wherein, if R^6 is a substituted carbocyclic or heterocyclic ring, substituents thereon

are no more than two Z^1 groups and/or no more than one Z^2 group, Z^1 groups being independently selected from (a) C_{1-4} alkyl, C_{2-4} alkenyl, C_{1-4} alkoxy, C_{1-4} alkylthio, C_{1-4} alkylamino, C_{1-4} alkylsulfonyl, C_{1-4} alkylsulfonylamino, C_{1-4} alkylcarbonyl, C_{1-4} alkylcarbonylamino and C_{1-4} alkylcarboxy, each optionally substituted with one or more substituents independently selected from halo, hydroxy, C_{1-4} alkoxy, amino, C_{1-4} alkylamino, di-(C_{1-4} alkyl)amino and cyano, (b) halo, (e) hydroxy, (f) amino and (g) oxo groups, and Z^2 being (i) a further 3- to 6-membered carbocyclic or heterocyclic ring, optionally substituted with no more than two Z^1 groups as defined above, or (ii) NR^7R^8 where R^7 and R^8 are as defined above:

or a pharmaceutically acceptable salt thereof, (ii) a pharmaceutically acceptable water-soluble polymeric carrier and (iii) a pharmaceutically acceptable surfactant to provide an extrudable semi-solid mixture;

(b) extruding and calendering the semi-solid mixture; and

(c) cooling the resulting extrudate to provide a solid matrix comprising the polymeric carrier and the surfactant and having the compound or salt thereof dispersed in an essentially non-crystalline form therein.

42. The process of Claim 41, wherein API is 4-(4-{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl}piperazin-1-yl)-N-({3-nitro-4-[(tetrahydro-2H-pyran-4-ylmethyl)amino]phenyl}sulfonyl)-2-(1H-pyrrolo[2,3-b]pyridin-5-yloxy)benzamide.

43. The process of claim 42, wherein the polymeric carrier is a copovidone.

44. The process of Claim 43, wherein the surfactant is a polysorbate.

45. An orally deliverable pharmaceutical dosage form comprising the solid dispersion of Claim 1.

46. A method for treating a neoplastic, immune or autoimmune disease, comprising orally administering to a subject having the disease a therapeutically effective amount of the solid dispersion of Claim 1.

47. The method of Claim 46, wherein the disease is a neoplastic disease.

48. The method of Claim 47, wherein the neoplastic disease is selected from the group consisting of cancer, mesothelioma, bladder cancer, pancreatic cancer, skin cancer, cancer of the head or neck, cutaneous or intraocular melanoma, ovarian cancer, breast cancer, uterine cancer, carcinoma of the fallopian tubes, carcinoma of the endometrium, carcinoma of the cervix, carcinoma of the vagina, carcinoma of the vulva, bone cancer, colon cancer, rectal cancer, cancer of the anal region, stomach cancer, gastrointestinal (gastric, colorectal and/or duodenal) cancer, chronic lymphocytic leukemia, acute lymphocytic leukemia, esophageal cancer, cancer of the small intestine, cancer of the endocrine system, cancer of the thyroid gland, cancer of the parathyroid gland, cancer of the adrenal gland, sarcoma of soft tissue, cancer of the urethra, cancer of the penis, testicular cancer, hepatocellular (hepatic and/or biliary duct) cancer, primary or secondary central nervous system tumor, primary or secondary brain tumor, Hodgkin's disease, chronic or acute leukemia, chronic myeloid leukemia, lymphocytic lymphoma, lymphoblastic leukemia, follicular lymphoma, lymphoid malignancies of T-cell or B-cell origin, melanoma, multiple myeloma, oral cancer, non-small-cell lung cancer, prostate cancer, small-cell lung cancer, cancer of the kidney and/or ureter, renal cell carcinoma, carcinoma of the renal pelvis, neoplasms of the central nervous system, primary central nervous system lymphoma, non-Hodgkin's lymphoma, spinal axis tumors, brain stem glioma, pituitary adenoma, adrenocortical cancer, gall bladder cancer, cancer of the spleen, cholangiocarcinoma, fibrosarcoma, neuroblastoma, retinoblastoma and combinations thereof.

49. The method of Claim 47, wherein the neoplastic disease is a lymphoid malignancy.

50. The method of Claim 49, wherein the lymphoid malignancy is non-Hodgkin's lymphoma.

51. The method of Claim 47, wherein the neoplastic disease is chronic lymphocytic leukemia or acute lymphocytic leukemia.

52. The method of Claim 46, wherein the disease is an immune or autoimmune disease.

53. The method of Claim 46, wherein the solid dispersion is administered in a parent-compound-equivalent dose of about 50 to about 500 mg per day of the compound of

Formula I or salt thereof at an average treatment interval of about 3 hours to about 7 days.

54. The method of Claim 46, wherein the solid dispersion is administered once daily in a parent-compound-equivalent dose of about 50 to about 500 mg per day of the compound of Formula I or salt thereof.

55. The method of Claim 46, wherein the compound is selected from the group consisting of

4-(4-{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl}piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-({3-nitro-4-[(1-tetrahydro-2H-pyran-4-ylpiperidin-4-yl)amino]phenyl}sulfonyl)benzamide;

4-(4-{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl}piperazin-1-yl)-2-(1H-indol-5-yloxy)-N-({4-[(4-methylpiperazin-1-yl)amino]-3-nitrophenyl}sulfonyl)benzamide;

4-(4-{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl}piperazin-1-yl)-N-({3-nitro-4-[(tetrahydro-2H-pyran-4-ylmethyl)amino]phenyl}sulfonyl)-2-(1H-pyrrolo[2,3-b]pyridin-5-yloxy)benzamide;

trans-4-(4-{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl}piperazin-1-yl)-N-({4-[(4-morpholin-4-ylcyclohexyl)amino]-3-nitrophenyl}sulfonyl)-2-(1H-pyrrolo[2,3-b]pyridin-5-yloxy)benzamide;

cis-4-(4-{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl}piperazin-1-yl)-N-[(4-{[(4-methoxycyclohexyl)methyl]amino}-3-nitrophenyl)sulfonyl]-2-(1H-pyrrolo[2,3-b]pyridin-5-yloxy)benzamide;

trans-4-(4-{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl}piperazin-1-yl)-N-[(4-{[(4-methoxycyclohexyl)methyl]amino}-3-nitrophenyl)sulfonyl]-2-(1H-pyrrolo[2,3-b]pyridin-5-yloxy)benzamide;

4-(4-{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl}piperazin-1-yl)-N-({4-[(4-fluorotetrahydro-2H-pyran-4-yl)methoxy]-3-nitrophenyl}sulfonyl)-2-(1H-pyrrolo[2,3-b]pyridin-5-yloxy)benzamide;

N-[(5-chloro-6-{[4-fluoro-1-(oxetan-3-yl)piperidin-4-yl]methoxy}pyridin-3-yl)-sulfonyl]-4-(4-{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl}-piperazin-1-yl)-2-(1H-pyrrolo[2,3-b]pyridin-5-yloxy)benzamide:

N-({5-bromo-6-[(1-tetrahydro-2H-pyran-4-ylpiperidin-4-yl)amino]pyridin-3-yl}-sulfonyl)-4-(4-{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl}-piperazin-1-yl)-2-(1H-pyrrolo[2,3-b]pyridin-5-yloxy)benzamide;

4-(4-{[2-(4-chlorophenyl)-5-methoxy-5-methylcyclohex-1-en-1-yl]methyl}piperazin-1-yl)-N-({3-nitro-4-[(tetrahydro-2H-pyran-4-ylmethyl)amino]phenyl}-sulfonyl)-2-(1H-pyrrolo[2,3-b]pyridin-5-yloxy)benzamide;

4-(4-{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl}piperazin-1-yl)-N-[(4-{[(3R)-1-(methylsulfonyl)pyrrolidin-3-yl]amino}-3-nitrophenyl)-sulfonyl]-2-(1H-pyrrolo[2,3-b]pyridin-5-yloxy)benzamide;

4-(4-{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl}piperazin-1-yl)-N-[(4-{[(*trans*-4-hydroxy-4-methylcyclohexyl)methyl]amino}-3-nitrophenyl)-sulfonyl]-2-(1H-pyrrolo[2,3-b]pyridin-5-yloxy)benzamide;

4-(4-{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl}piperazin-1-yl)-N-[(4-{[(*cis*-4-hydroxy-4-methylcyclohexyl)methyl]amino}-3-nitrophenyl)-sulfonyl]-2-(1H-pyrrolo[2,3-b]pyridin-5-yloxy)benzamide;

4-(4-{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl}piperazin-1-yl)-N-{[4-({3-[cyclopropyl(oxetan-3-yl)amino]propyl}amino)-3-nitrophenyl]-sulfonyl}-2-(1H-pyrrolo[2,3-b]pyridin-5-yloxy)benzamide;

4-(4-{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl}piperazin-1-yl)-N-{[3-nitro-4-({[(3R)-1-tetrahydro-2H-pyran-4-ylpyrrolidin-3-yl]methyl}-amino)phenyl]sulfonyl}-2-(1H-pyrrolo[2,3-b]pyridin-5-yloxy)benzamide;

4-(4-{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl}piperazin-1-yl)-N-[(4-{[(4-methylmorpholin-2-yl)methyl]amino}-3-nitrophenyl)sulfonyl]-2-(1H-pyrrolo[2,3-b]pyridin-5-yloxy)benzamide;

N-[(5-chloro-6-{[1-(cyanomethyl)piperidin-4-yl]methoxy}pyridin-3-yl)sulfonyl]-4-(4-{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl}piperazin-1-yl)-2-(1H-pyrrolo[2,3-b]pyridin-5-yloxy)benzamide;

N-[(4-{[(4-aminotetrahydro-2H-pyran-4-yl)methyl]amino}-3-nitrophenyl)sulfonyl]-4-(4-{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl}piperazin-1-yl)-2-(1H-pyrrolo[2,3-b]pyridin-5-yloxy)benzamide;

4-(4-{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl}piperazin-1-yl)-

N-({4-[(4-methoxytetrahydro-2H-pyran-4-yl)methoxy]-3-nitrophenyl}sulfonyl)-2-(1H-pyrrolo[2,3-b]pyridin-5-yloxy)benzamide;

and pharmaceutically acceptable salts thereof.

56. The method of Claim 46, wherein the compound is 4-(4-{[2-(4-chlorophenyl)-4,4-dimethylcyclohex-1-en-1-yl]methyl}piperazin-1-yl)-N-({3-nitro-4-[(tetrahydro-2H-pyran-4-ylmethyl)amino]phenyl}sulfonyl)-2-(1H-pyrrolo[2,3-b]pyridin-5-yloxy)benzamide.