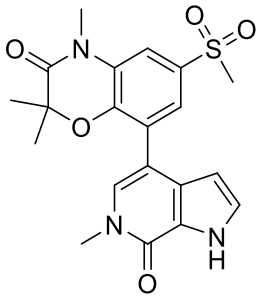
What is claimed is:

1. A solid form of a compound having the formula:



Compound 1

wherein the solid form is crystalline;
and wherein the solid form is selected from Form Ia, Form III, Form IV, Form V, Form Va, Form VI, Form VII, Form VIII, Form IX, Form X, Form XI, Form XII, Form XIII, Form XIV and XV.

~~2. The solid form of claim 1 which is an anhydrate.~~

~~3.~~2.The solid form of claim 1, wherein the solid form has Form Ia ~~having Form I~~.

~~4.~~3. The solid form of claim ~~3~~2, having three or more characteristic XRPD peaks, in terms of 2-theta, selected from about 8.8~~8.7~~, about 10.0~~9.8~~, about 11.7~~11.6~~, about 12.8~~12.7~~, about 13.5~~14.7, about 15.7~~, about 20.0, about 21.5~~21.4~~, about 22.6~~23.3~~, and about 23.3~~27.1~~ degrees.

~~5. The solid form of claim 3 having an XRPD pattern substantially as shown in FIG. 1.~~

~~6. The solid form of any one of claims 3-5 having a DSC thermogram characterized by an endothermic peak at a temperature of about 266 ºC.~~

~~7. The solid form of any one of claims 3-5 having a DSC thermogram substantially as shown in FIG. 2.~~

~~8. The solid form of any one of claims 3-5 having a TGA thermogram substantially as shown in FIG. 3.~~

~~9.~~4. The solid form of claim 1 ~~having Form II~~wherein the solid form has Form III.

~~10.~~5. The solid form of claim ~~4~~9, having three or more characteristic XRPD peaks, in terms of 2-theta, selected from about 7.8~~6.7~~, about 12.4~~9.5~~, about 15.2~~10.5~~, about 15.5~~14.8~~, about 16.9~~16.2~~, about 17.5~~17.0, about 18.8~~, and about 20.3~~19.3~~ degrees.

~~11. The solid form of claim 9 having an XRPD pattern substantially as shown in FIG. 4.~~

~~12. The solid form of any one of claims 9-11 having a DSC thermogram characterized by an endothermic peak at a temperature of about 268 ºC.~~

~~13. The solid form of any one of claims 9-11 having a DSC thermogram substantially as shown in FIG. 5.~~

~~14. The solid form of any one of claims 9-11 having a TGA thermogram substantially as shown in FIG. 6.~~

~~15. A pharmaceutical composition comprising a solid form of any one of claims 1-14 and at least one pharmaceutically acceptable carrier.~~

~~16. A method of inhibiting a BET protein comprising contacting a solid form of any one of claims 1-24 or a pharmaceutical composition of claim 15 with said BET protein.~~

~~17. A method of treating a disease or condition that is associated with a BET protein, comprising administering to a patient in need of such treatment a therapeutically effective amount of a solid form of any one of claims 1-14 or a pharmaceutical composition of claim 15.~~

~~18. A method of treating a proliferative disorder comprising administering to a patient in need of such treatment a therapeutically effective amount of a solid form of any one of claims 1-14 or a pharmaceutical composition of claim 15.~~

~~19. The method of claim 18, wherein the proliferative disorder is cancer.~~

~~20. The method of claim 19, wherein the cancer is a hematological cancer.~~

~~21. The method of claim 19, wherein the cancer is adenocarcinoma, bladder cancer, blastoma, bone cancer, breast cancer, brain cancer, carcinoma, myeloid sarcoma, cervical cancer, colorectal cancer, esophageal cancer, gastrointestinal cancer, glioblastoma~~

multiforme, glioma, gallbladder cancer, gastric cancer, head and neck cancer, Hodgkin's lymphoma, non-Hodgkin's lymphoma, intestinal cancer, kidney cancer, laryngeal cancer, leukemia, lung cancer, lymphoma, liver cancer, small cell lung cancer, non-small cell lung cancer, mesothelioma, multiple myeloma, AML, DLBCL, ocular cancer, optic nerve tumor, oral cancer, ovarian cancer, pituitary tumor, primary central nervous system lymphoma, prostate cancer, pancreatic cancer, pharyngeal cancer, renal cell carcinoma, rectal cancer, sarcoma, skin cancer, spinal tumor, small intestine cancer, stomach cancer, T-cell leukemia, T-cell lymphoma, testicular cancer, thyroid cancer, throat cancer, urogenital cancer, urothelial carcinoma, uterine cancer, vaginal cancer, or Wilms' tumor.

22. The method of claim 19, wherein the cancer is multiple myeloma, AML, or DLBCL.

23. The method of claim 18, wherein the proliferative disorder is a non-cancerous proliferative disorder.

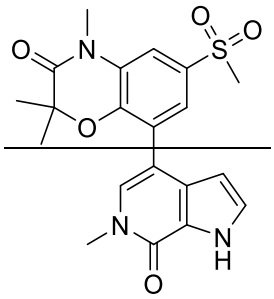
24. A method of treating an autoimmune or inflammatory disease comprising administering to a patient in need of such treatment a therapeutically effective amount of a solid form of any one of claims 1-14 or a pharmaceutical composition of claim 15.

25. The method of claim 24, wherein the autoimmune or inflammatory disease is selected from allergy, allergic rhinitis, arthritis, asthma, chronic obstructive pulmonary disease, degenerative joint disease, dermatitis, organ rejection, eczema, hepatitis, inflammatory bowel disease, multiple sclerosis, myasthenia gravis, psoriasis, sepsis, sepsis syndrome, septic shock, systemic lupus erythematosus, tissue graft rejection, and type I diabetes.

26. A method of treating a viral infection comprising administering to a patient in need of such treatment a therapeutically effective amount of a solid form of any one of claims 1-14 or a pharmaceutical composition of claim 15.

27. The method of claim 26, wherein the viral infection is infection with adenovirus, Epstein-Barr virus, hepatitis B virus, hepatitis C virus, a herpes virus, human immunodeficiency virus, human papilloma virus or a pox virus.

28. A process of preparing Form I of Compound 1:



~~Compound 1~~

~~comprising precipitating Form I from a solution comprising Compound 1 and a solvent.~~

~~29. The process of claim 28, wherein the solvent comprises methanol, acetone, n-heptane, or a mixture thereof.~~

~~30. The process of claim 28, wherein the precipitating is carried out by (1) reducing the temperature of the solution of Compound 1, (2) concentrating the solution of Compound 1, (3) adding an anti-solvent to the solution of Compound 1, or (4) any combination thereof.~~

~~31. The process of claim 28, wherein the preparation of Form I comprises:~~

~~(ia) heating the solution of Compound 1 to a temperature of about 50 ºC to about 60 ºC;~~

~~(iia) reducing the volume of the solution of Compound 1 at the temperature of about 50 ºC to about 60 ºC to form a reduced-volume solution of Compound 1;~~

~~(iiia) adding an anti-solvent to the reduced-volume solution of Compound 1 while maintaining the temperature at about 55 ºC to about 65 ºC to form a warm solution of Compound 1; and~~

~~(iva) cooling the warm solution of Compound 1 to a temperature of about 15 ºC to about 30 ºC to precipitate Form I.~~

~~32. The process of any one of claims 28-31, wherein the preparation of Form I comprises:~~

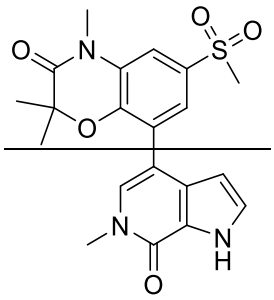
~~(ib) heating the solution of Compound 1, wherein the solution comprises methanol and acetone as solvent, to a temperature of about 50 ºC to about 60 ºC;~~

~~(iib) reducing the volume of the solution of Compound 1 at the temperature of about 50 ºC to about 60 ºC to form a reduced-volume solution of Compound 1;~~

~~(iiib) adding n-heptane to the reduced-volume solution of Compound 1 while maintaining the temperature at about 55 ºC to about 65 ºC to form a warm solution of Compound 1; and~~

~~(ivb) cooling the warm solution of Compound 1 to a temperature of about 15 ºC to about 30 ºC to precipitate Form I.~~

~~33. A process of preparing Form II of Compound 1:~~



~~Compound 1~~

~~comprising precipitating Form II from a solution comprising Compound I and a solvent.~~

~~34. The process of claim 33, wherein the solvent comprises tetrahydrofuran (THF), acetone, n-heptane, or a mixture thereof.~~

~~35. The process of claim 33, wherein the precipitating is carried out by (1) reducing the temperature of the solution of Compound 1, (2) concentrating the solution of Compound 1, (3) adding an anti-solvent to the solution of Compound 1, or (4) any combination thereof.~~

~~36. The process of any claim 33, wherein the preparation of Form II comprises:~~

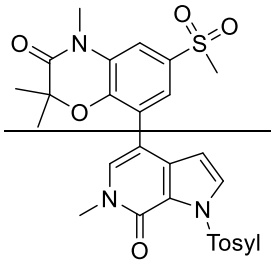
~~(ic) heating the solution of Compound 1 to a temperature of about 50 ºC to about 60 ºC;~~

~~(iic) reducing the volume of the solution of Compound 1 at the temperature of about 50 ºC to about 60 ºC to form a reduced-volume solution of Compound 1;~~

~~(iiic) adding an anti-solvent to the reduced-volume solution of Compound 1 while maintaining the temperature at about 55 ºC to about 65 ºC to form a warm solution of Compound 1; and~~

~~(ivc) cooling the warm solution of Compound 1 to a temperature of about 15 ºC to about 30 ºC to precipitate Form II.~~

~~37. The process of any one of claims 28-36 further comprising preparing Compound 1, or a salt thereof, by a process comprising reacting Compound 8:~~



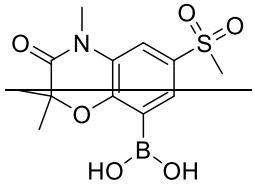
~~Compound 8~~

~~with B1, wherein B1 is a base.~~

~~38. The process of claim 37, wherein B1 is an alkali metal hydroxide base.~~

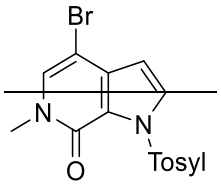
~~39. The process of any one of claims 37-38, wherein the reacting of Compound 8 with B1 is carried out in a first solvent.~~

~~40. The process of any one of claims 37-39 further comprising preparing Compound 8 by a process comprising reacting Compound 7:~~



~~Compound 7~~

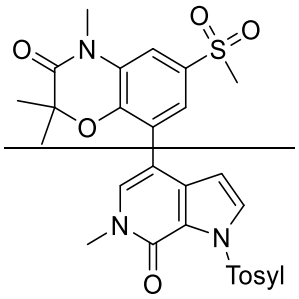
~~with Compound 9:~~



~~Compound 9~~

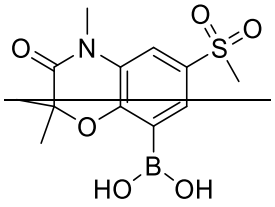
~~in the presence of P2 and B2, wherein P2 is a transition metal catalyst and B2 is a base.~~

~~41. A process of preparing Compound 8:~~



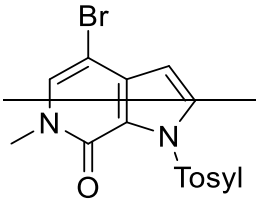
~~Compound 8~~

~~comprising reacting Compound 7:~~



~~Compound 7~~

~~with Compound 9:~~



~~Compound 9~~

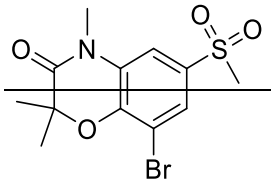
~~in the presence of P2 and B2, wherein P2 is a transition metal catalyst and B2 is a base.~~

~~42. The process of claim 40 or 41, wherein P2 is a palladium catalyst.~~

~~43. The process of any one of claims 40-42, wherein B2 is an alkali metal bicarbonate base.~~

~~44. The process of any one of claims 40-43, wherein the reacting of Compound 7 with Compound 9 is carried out in a second solvent.~~

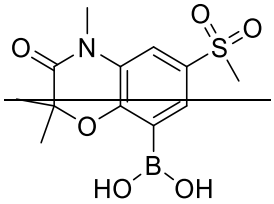
~~45. The process of any one of claims 40-44 further comprising preparing Compound 7 by a process comprising reacting Compound 6:~~



~~Compound 6~~

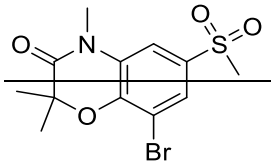
~~with 4,4,4',4',5,5,5',5'-octamethyl-2,2'-bi(1,3,2-dioxaborolane) in the presence of P3 and B3, wherein P3 is a transition metal catalyst and B3 is a base.~~

~~46. A process of preparing Compound 7:~~



~~Compound 7~~

~~comprising reacting Compound 6:~~



~~Compound 6~~

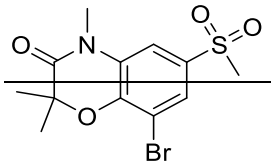
~~with 4,4,4',4',5,5,5',5'-octamethyl-2,2'-bi(1,3,2-dioxaborolane) in the presence of P3 and B3, wherein P3 is a transition metal catalyst and B3 is a base.~~

~~47. The process of any one of claims 45-46, wherein B3 is an alkali metal acetate base.~~

~~48. The process of any one of claims 45-47, wherein the reacting of Compound 6 with 4,4,4',4',5,5,5',5'-octamethyl-2,2'-bi(1,3,2-dioxaborolane) is carried out in a third solvent.~~

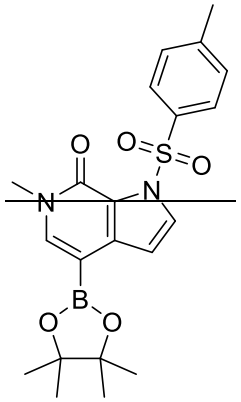
~~49. The process of any one of claims 45-48, wherein the reacting of Compound 6 with 4,4,4',4',5,5,5',5'-octamethyl-2,2'-bi(1,3,2-dioxaborolane) is carried out at a temperature of about 70 ºC to about 90 ºC.~~

~~50. The process of any one of claims 37-39 further comprising preparing Compound 8 by a process comprising reacting Compound 6:~~



~~Compound 6~~

~~with Compound 15:~~



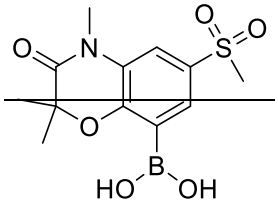
~~Compound 15~~

~~in the presence of P4 and B4, wherein P4 is transition metal catalyst and B4 is a base.~~

~~51. The process of claim 50, wherein P4 is a palladium catalyst.~~

~~52. The process of any one of claims 50-51, wherein the reacting of Compound 6 with Compound 15 is carried out in a fourth solvent.~~

~~53. A compound which is~~



~~Compound 7~~

~~or a salt thereof.~~

6. The solid form of claim 1, wherein the solid form has Form IV.

7. The solid form of claim 6, having one or more characteristic XRPD peaks, in terms of 2-theta, selected from about 11.2, about 16.3, about 18.7, and about 22.1 degrees.

8. The solid form of claim 1, wherein the solid form has Form V.

9. The solid form of claim 8, having one or more characteristic XRPD peaks, in terms of 2-theta, selected from 8.2, about 8.5, about 14.1, about 16.3, about 17.1, about 18.9, about 19.8, about 21.8, and about 22.7 degrees.

10. The solid form of claim 1, wherein the solid form has Form Va.

11. The solid form of claim 10, having one or more characteristic XRPD peaks, in terms of 2-theta, selected from about 8.7, about 16.5, about 17.3, about 19.9, and about 21.6 degrees.

12. The solid form of claim 1, wherein the solid form has Form VI.

13. The solid form of claim 12, having one or more characteristic XRPD peaks, in terms of 2-theta, selected from about 8.5, about 9.6, about 11.4, about 12.1, about 13.5, about 14.5, about 15.2, about 17.1, about 17.7, about 18.1, about 19.2, and about 20.7 degrees.

14. The solid form of claim 1, wherein the solid form has Form VII.

15. The solid form of claim 14, having one or more characteristic XRPD peaks, in terms of 2-theta, selected from about 9.9, about 12.2, about 14.8, about 15.7, about 17.0, about 17.5, and about 18.8 degrees.

16. The solid form of claim 1, wherein the solid form has Form VIII.

17. The solid form of claim 16, having one or more characteristic XRPD peaks, in terms of 2-theta, selected from about 8.1, about 8.5, about 16.2, about 16.6, about 17.0, about 17.5, about 18.0, about 18.9, about 19.6, and about 20.1 degrees.

18. The solid form of claim 1, wherein the solid form has Form IX.

19. The solid form of claim 18, having one or more characteristic XRPD peaks, in terms of 2-theta, selected from about 8.6, about 9.1, about 11.4, about 13.4, about 15.2, about 18.2, about 22.1, about 22.8, and about 23.9 degrees.

20. The solid form of claim 1, wherein the solid form has Form X.

21. The solid form of claim 20, having one or more characteristic XRPD peaks, in terms of 2-theta, selected from about 14.9, about 15.3, about 15.8, about 17.0, about 17.7, about 18.3, and about 19.7 degrees.

22. The solid form of claim 1, wherein the solid form has Form XI.

23. The solid form of claim 22, having one or more characteristic XRPD peaks, in terms of 2-theta, selected from about 8.9, about 12.8, about 18.0 about 21.5, about 22.6, and about 23.3 degrees.

24. The solid form of claim 1, wherein the solid form has Form XII.

25. The solid form of claim 24, having one or more characteristic XRPD peaks, in terms of 2-theta, selected from about 5.6, about 11.7, about 13.8, about 14.5, about 16.9, about 17.7, about 18.7, about 23.5, about 24.6, about 34.3, about 44.2, and 44.6 degrees.

26. The solid form of claim 1, wherein the solid form has Form XIII.

27. The solid form of claim 26, having one or more characteristic XRPD peaks, in terms of 2-theta, selected from about 5.7, about 8.6, about 9.8, about 11.8, about 12.6, about 13.4, about 14.1, about 14.8, about 16.6, and about 19.1 degrees.

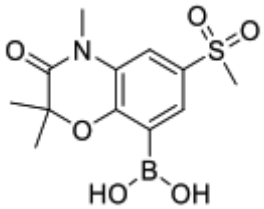
28. The solid form of claim 1, wherein the solid form has Form XIV.

29. The solid form of claim 28, having one or more characteristic XRPD peaks, in terms of 2-theta, selected from about 5.7, about 8.6, about 9.8, about 11.8, about 12.6, about 13.4, about 14.1, about 14.8, about 16.6, and about 19.1 degrees.

30. The solid form of claim 1, wherein the solid form has Form XV.

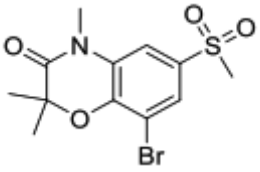
31. The solid form of claim 30, having one or more characteristic XRPD peaks, in terms of 2-theta, selected from about 7.4, about 9.6, about 12.4, about 13.4, about 15.5, about 16.9, about 17.7, about 19.0, about 19.5, about 20.6, and about 22.5 degrees.

32. A process of preparing Compound 7:



Compound 7

comprising reacting Compound 6:



Compound 6

with 4,4,4',4',5,5,5',5'-octamethyl-2,2'-bi(1,3,2-dioxaborolane) in the presence of P3 and B3, wherein P3 is a transition metal catalyst and B3 is a base.

33. The process of claim 32, wherein P3 is a palladium catalyst.

34. The process of claim 33, wherein the palladium catalyst is [1,1′-bis(diphenylphosphino)ferrocene]dichloropalladium(II).

35. The process of claim 33, wherein the palladium catalyst is selected from [1,1′-bis(diphenylphosphino)ferrocene]dichloropalladium(II), dichloro(bis{di-tert-butyl[4-(dimethylamino)phenyl]-phosphoranyl})palladium (Pd-132), Pd(PPh3)4, and tetrakis(tri(o-tolyl)phosphine)palladium(0).

36. The process of claim 32, wherein B3 is an alkali metal acetate base.

37. The process of claim 36, wherein the alkali metal acetate base is potassium acetate.

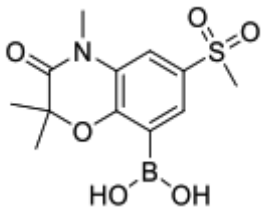
38. The process of claim 32, wherein the reacting of Compound 6 with 4,4,4',4',5,5,5',5'-octamethyl-2,2'-bi(1,3,2-dioxaborolane) is carried out in a third solvent.

39. The process of claim 32, wherein the reacting of Compound 6 with 4,4,4',4',5,5,5',5'-octamethyl-2,2'-bi(1,3,2-dioxaborolane) is carried out at a temperature of about 70 ºC to about 90 ºC.

40. The process of claim 32, wherein about 0.01 to about 0.05 equivalent of P3 is used based on 1 equivalent of Compound 6.

41. The process of claim 32, wherein about 3 to about 3.5 equivalent of B3 are used based on 1 equivalent of Compound 6.

42. A compound which is



Compound 7

or a salt thereof.

43. The compound of claim 42, wherein Compound 7 is a salt thereof.