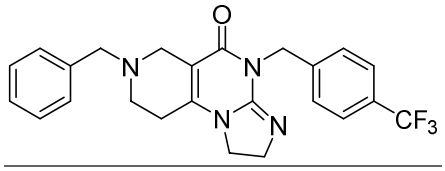
CLAIMS

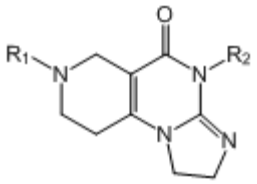
What is claimed is:

1. A compound



or a pharmaceutically acceptable salt thereof.

~~A compound having formula (**10**)~~



(10)

~~or a pharmaceutically acceptable salt thereof; wherein R_1 and R_2 are independently selected from the group consisting of H, C_{1-4}alkyl, C_{1-4}alkylphenyl, C_{1-4}alkylphenylketone, C_{1-4}benzyl-piperazine, C_{1-4}alkylthienyl, C_{1-4}alkylpyridinyl, C_{1-4}alkylisoxazolidinyl, C_{1-4}alkylmorpholinyl, C_{1-4}alkylthiazolyl, and C_{1-4}alkylpyrazinyl wherein C_{1-4}alkyl, C_{1-4}alkylphenyl, C_{1-4}alkylphenylketone, C_{1-4}benzyl-piperazine, C_{1-4}alkylthienyl, C_{1-4}alkylpyridinyl, C_{1-4}alkylisoxazolidinyl, C_{1-4}alkylmorpholinyl, C_{1-4}alkylthiazolyl, and C_{1-4}alkylpyrazinyl are optionally substituted with C_{1-4}alkyl, C_{1-4}alkoxyl, hydroxyl, perhalogenated C_{1-4}alkyl, or halogen, and wherein when R_1 represents CH_2Ph, R_2 does not represent CH_2-((2-CH_3)-Ph.~~

~~2. The compound of claim **1**, wherein R_1 and/or R_2 is a benzyl optionally substituted with one or more of the following substituents on the benzyl ring: X, $-CH_3$, $-NO_2$, $-OCH_3$, -CN, $-CXH_2$, $-CX_2H$, C_2-C_4 alkyl, $-CX_3$, $-CH_2(CX_3)$, $-CH(CX_3)_2$, $-C(CX_3)_3$, $-C_pX_{2p+1}$, $-OCX_3$, $-OC_pH_{2p+1}$, $-OC_pX_{2p+1}$, OR^m, SR^m, NR^mR^n, $NR^mC(O)R^n$, SOR^m, SO_2R^m, $C(O)R^m$, and $C(O)OR^m$;~~

~~where R^m and R^n are independently selected from hydrogen or a C_1-C_4 alkyl;~~

~~where p is an integer from 2 to 20; and~~

~~X represents a halogen.~~

3. The compound of claim **1**, wherein R_1 is a hydrogen or an unsubstitued benzyl.

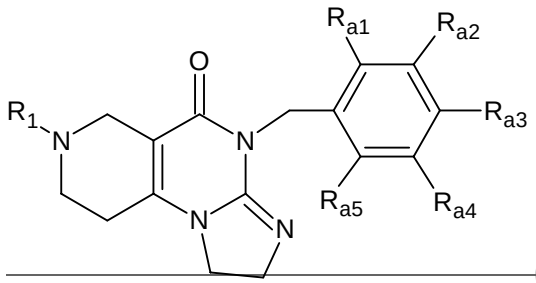
4. The compound of claim **1**, wherein R_2 is a substituted or an unsubstituted, heterocycloalkylalkyl.

5. The compound of claim **4**, wherein the substituted heterocycloalkylalkyl is a morpholinoalkyl or piperazinylalkyl group.

6. The compound of claim **1**, wherein R_2 is a substituted or an unsubstituted heteroarylalkyl.

7. The compound of claim **5**, wherein the substituted heteroarylalkyl is a pyridylalkyl or isoxazolidinylalkyl or group.

8. The compound of claim **1**, wherein the compound is represented by formula (**40**)



(**40**)

or a pharmaceutically acceptable salt thereof; wherein

wherein R_{a1}, R_{a2}, R_{a3}, R_{a4}, and R_{a5} are each independently selected from the group consisting of hydrogen, X, $-CH_3$, $-NO_2$, $-OCH_3$, $-CN$, $-CXH_2$, $-CX_2H$, C_2-C_4 alkyl, $-CX_3$, $-CH_2(CX_3)$, $-CH(CX_3)_2$, $-C(CX_3)_3$, $-C_pX_{2p+1}$, $-OCX_3$, $-OC_pH_{2p+1}$, $-OC_pX_{2p+1}$, OR^m, SR^m, NR^mR^n, $NR^mC(O)R^n$, SOR^m, SO_2R^m, $C(O)R^m$, and $C(O)OR^m$;

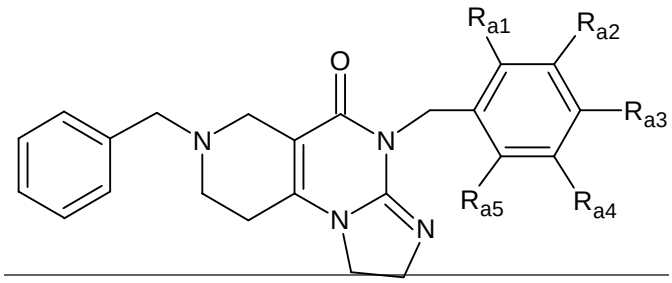
where R^m and R^n are independently selected from hydrogen or a C_1-C_4 alkyl;

p is an integer from 2 to 20; and

X represents a halogen.

9. The compound of claim **8**, wherein R_1 is a hydrogen.

10. The compound of claim **8**, wherein the compound is represented by formula (**45**)



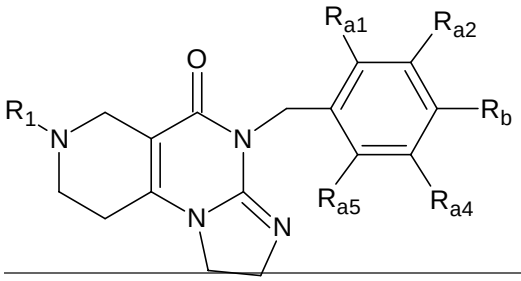
(**45**)

or a pharmaceutically acceptable salt thereof.

11. The compound of claim **8**, wherein R_{a3} is fluorine.

12. The compound of claim **8**, wherein R_{a2} and R_{a4} are fluorine.

13. The compound of claim **1** having formula (**50**)



(**50**)

or a pharmaceutically acceptable salt thereof; wherein

R_b is selected from the group consisting of X, $-CH_3$, $-NO_2$, $-OCH_3$, $-CN$, $-CXH_2$, $-CX_2H$, C_2-C_4 alkyl, $-CX_3$, $-CH_2(CX_3)$, $-CH(CX_3)_2$, $-C(CX_3)_3$, $-C_pX_{2p+1}$, $-OCX_3$, $-OC_pH_{2p+1}$, $-OC_pX_{2p+1}$, OR^m, SR^m, NR^mR^n, $NR^mC(O)R^n$, SOR^m, SO_2R^m, $C(O)R^m$, and $C(O)OR^m$;

R_{a1}, R_{a2}, R_{a4}, and R_{a5} are each independently selected from the group consisting of hydrogen, X, $-CH_3$, $-NO_2$, $-OCH_3$, $-CN$, $-CXH_2$, $-CX_2H$, C_2-C_4 alkyl, $-CX_3$, $-CH_2(CX_3)$, $-CH(CX_3)_2$, $-C(CX_3)_3$, $-C_pX_{2p+1}$, $-OCX_3$, $-OC_pH_{2p+1}$, $-OC_pX_{2p+1}$, OR^m, SR^m, NR^mR^n, $NR^mC(O)R^n$, SOR^m, SO_2R^m, $C(O)R^m$, and $C(O)OR^m$;

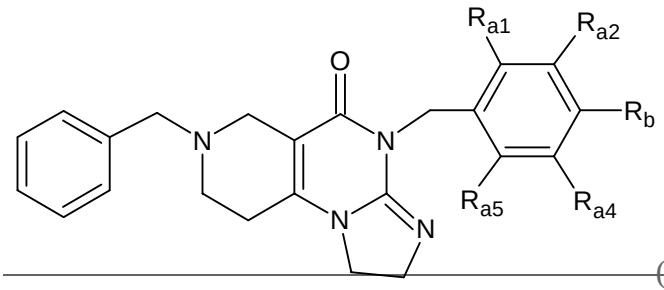
where R^m and R^n are independently selected from hydrogen or a C_1-C_4 alkyl;

p is an integer from 2 to 20;

and X represents a halogen.

14. The compound of claim **13**, wherein R_1 is a hydrogen.

15. The compound of claim **13** , wherein the compound is represented by formula (**55**)



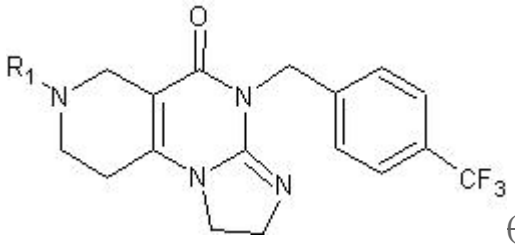
(55)

or a pharmaceutically acceptable salt thereof.

16. The compound of claim **13**, wherein R_b is a fluorine and R_{a1} is a methyl.

17. The compound of claim **13**, wherein R_b and R_{a2} are each selected from fluorine or chlorine.

18. The compound of claim **13** having formula (**60**)



(**60**)

or a pharmaceutically acceptable salt thereof.

19. The compound of claim **13**, wherein R_b is a CH_3 or a OCH_3 substituent.

20. The compound of claim **13**, wherein R_b is Cl, and R_{a1} is Cl.

212. A pharmaceutically acceptable composition comprising a salt of a the compound of claim 1 any one of claims **1** – **20**.

223. The pharmaceutically acceptable salt composition according to claim **212**, wherein the salt comprises a counterion selected from the group consisting of: hydrochloride, hydrobromide, hydrogensulphate, sulfate, phosphate, fumarats, succinate, oxalates and lactates, bisulfate, hydroxyl, tartrate, nitrate, citrate, bitartrate, carbonate, malate, maleate, fumarate sulfonate, methylsulfonate, formate, acetate, and carboxylate, p-toluene-sulfonate, benzenesulfonate, methanesulfonate, oxalate, succinate, tartrate, citrate, fumarate, glucuronate, ascorbate and maleate, ammonium, sodium, potassium, calcium, magnesium, zinc, lithium, methylamino, dimethylamino, diethylamino and triethylamino.

~~23~~4. The pharmaceutically acceptable salt ~~composition~~ according to claim ~~21~~2, wherein the salt is a di-salt.

~~24~~5. The pharmaceutically acceptable salt ~~composition~~ according to claim ~~23~~4, wherein the di-salt is a hydrochloride di-salt.

~~25~~6. The pharmaceutically acceptable salt ~~composition~~ according to claim ~~23~~4, wherein the di-salt is a hydrobromide di-salt.

~~26~~7. A pharmaceutical composition comprising a compound according to claim 1 ~~any one of claims **1 – 20**~~ or a pharmaceutically acceptable salt thereof and a pharmaceutically acceptable carrier.

~~27. A method of treatment, comprising administering to a subject in need of such treatment a pharmaceutically acceptable amount of a compound according to any one of claims **1 – 20** or a pharmaceutically acceptable salt thereof.~~

~~28. The method of claim **27**, wherein the treatment is for a Non-Hodgkin's lymphoma or an acute leukemia.~~

~~29. The method of claim **27**, wherein the treatment is a salvage therapy.~~

~~30. The method of claim **27**, wherein the pharmaceutically acceptable amount of the compound is administered according to an infrequent dosing regimen.~~

~~31. The method of claim **27**, wherein the pharmaceutically acceptable amount of the compound or the pharmaceutically acceptable salt thereof is a dose ranging from about 100 mg to about 200 mg.~~

~~32. A method of treating a condition in a subject, comprising:~~

~~(i) administering to the subject the first therapeutic agent including a compound according to any one of claims **1 – 20** or a pharmaceutically acceptable salt thereof; and~~

~~(ii) monitoring level of the compound or a pharmaceutically acceptable salt thereof or a metabolite thereof in the subject using pharmacokinetic profiling~~

~~33. The method of claim **32**, wherein dosing of the compound or a pharmaceutically acceptable salt thereof is selected to maintain a maximum concentration of the compound or~~

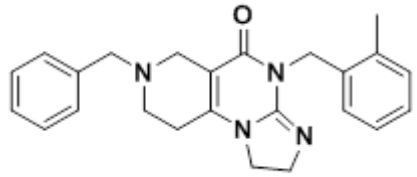
a pharmaceutically acceptable salt thereof in blood (whole blood, plasma, or serum) of the subject between about 85 ng/mL and 1500 ng/mL for a therapeutic time period.

34. The method of claim **32**, wherein dosing of the compound or a pharmaceutically acceptable salt thereof is selected to maintain an exposure of the compound or a pharmaceutically acceptable salt thereof over time as measured in blood (whole blood, plasma, or serum) of the subject between about 150 ng hr/mL and about 8000 ng hr/mL for a therapeutic time period.

35. The method according to claim **32**, further comprising administering the second therapeutic agent conditional on the level of the first therapeutic agent in the subject.

36. A method of treatment, comprising administering to a subject in need of such treatment:
(i) a first therapeutic agent including a compound according to any one of claims **1** – **20** or a pharmaceutically acceptable salt thereof in combination with (ii) a second therapeutic agent, wherein the first therapeutic agent and the second therapeutic agent are administered either simultaneously or sequentially.

37. A method of treating a condition in a subject, comprising:
(i) over a first time interval, administering a plurality of doses of a therapeutic agent including compound (**1**):



Compound (**1**)

, an analog thereof, or a pharmaceutically acceptable salt of compound (**1**) or an analog thereof, wherein the plurality of doses is administered over a second time interval within the first time interval; and
(ii) repeating step (i) one or more additional times.

38. The method of claim **37**, wherein the condition is cancer.

39. The method of claim **37**, wherein the subject is a human.

~~40. The method of claim **37**, wherein the subject is a domesticated pet.~~

~~41. The method of claim **37**, wherein the therapeutic agent is compound (**1**) or a pharmaceutically acceptable salt thereof.~~

~~42. The method of claim **37**, wherein the therapeutic agent is an analog of compound (**1**) or a pharmaceutically acceptable salt thereof.~~

~~43. The method of claim **42**, wherein the analog of compound (**1**) has the structure of compound (**10**).~~

~~44. The method of claim **43**, wherein the analog is a compound according to any one of claims **1 – 20** or a pharmaceutically acceptable salt thereof.~~

~~45. The method of claim **37**, further comprising the step of waiting for a predetermined waiting time between one or more repetitions of step (i).~~

~~46. The method of claim **45,** wherein the predetermined waiting time is the same length as the first time interval.~~

~~47. The method of claim **46**, wherein the pharmaceutically acceptable salt is a di-salt.~~

~~48. The method of claim **47**, wherein the di-salt is a hydrochloride di-salt.~~

~~49. The method of claim **37**, wherein the therapeutic agent is administered orally.~~

~~50. The method of claim **49**, wherein each oral dose ranges from about 1 mg to about 1000 mg.~~

~~51. The method of claim **37**, wherein the therapeutic agent is administered intravenously.~~

~~52. The method of claim **37**, wherein the therapeutic agent is administered topically.~~

~~53. The method of claim **37**, wherein the subject has received at least one prior therapy.~~

~~54. The method of claim **37**, wherein the first time interval is 7 days.~~

~~55. The method of claim **54**, wherein the second time interval is from two to five consecutive days.~~

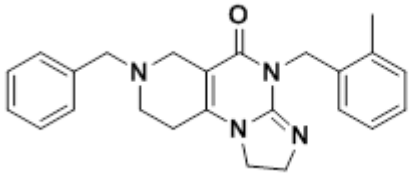
56. The method of claim **55**, wherein the second time interval is two consecutive days.

57. The method of claim **55**, wherein the second time interval is three consecutive days.

58. The method of claim **54**, wherein the therapeutic agent is administered once daily within the second time interval.

59. The method of claim **54**, wherein the therapeutic agent is administered twice daily within the second time interval.

60. A method of treating or preventing a disease or condition comprising: administering to a human or animal subject in need of such treatment a pharmaceutical composition comprising a therapeutically effective amount of compound (**1**):



Compound (**1**)

or a pharmaceutically acceptable salt thereof.

61. The method of claim **60**, wherein the disease is a B-cell cancer.

62. The method of claim **61**, wherein the B-cell cancer is a multiple myeloma, B-cell lymphoma or a B-cell leukemia.

63. The method of claim **60**, wherein the disease is a pediatric cancer.

64. The method of claim **63**, wherein the subject is younger than 18, wherein is younger than 13 years old, or is younger than 5 years old.

65. The method of claim **60**, wherein the pediatric cancer is selected from the group consisting of pediatric solid tumors, pediatric sarcomas, pediatric Ewing's sarcomas, pediatric gliomas, pediatric central nervous system cancers, pediatric leukemia and pediatric lymphoma.

66. The method of claim **60**, where the disease or condition prevented or treated is metastases.

67. The method of claim **60**, wherein the condition is pain.

68. The method of claim **60**, wherein the condition is edema.

69. The method of claim **60**, wherein the condition is hemiplegia.

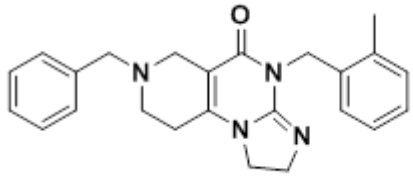
70. The method of claim **60**, wherein the disease is a lymphadenopathy.

71. The method of claim **60**, wherein the disease is a cancer and the treatment does not cause severe or serious adverse events.

72. The method of claim **60**, wherein the disease is a cancer and the treatment does not cause peripheral neuropathy.

73. The method of claim **60**, wherein the disease is a cancer and the treatment does not cause cardiotoxicity.

74. A method of treating or preventing a disease or condition comprising: administering to a human or animal subject in need of such treatment a pharmaceutical composition comprising an effective amount of compound (**1**):



Compound (**1**)

or a pharmaceutically acceptable salt thereof, wherein the effective amount of compound (**1**) or the pharmaceutically acceptable salt thereof is a dose ranging from about 125 mg to about 625 mg.

75. The method of claim **74**, wherein the dose of compound (**1**) or the pharmaceutically acceptable salt thereof ranges from about 250 mg to about 625 mg.

76. The method of claim **75**, wherein the dose of compound (**1**) or the pharmaceutically acceptable salt thereof ranges from about 375 mg to about 625 mg.

77. The method of claim **76**, wherein the dose of compound (**1**) or the pharmaceutically acceptable salt thereof ranges from about 500 mg to about 625 mg

78. The method of claim **77**, wherein the dose of compound (**1**) or the pharmaceutically acceptable salt thereof is about 625 mg.

79. The method of claim **74**, where the dosage is based on compound (**1**) in its free base form.

80. The method of claim **74**, wherein the pharmaceutical composition is administered twice a day.

81. The method of claim **74**, wherein the pharmaceutical composition is administered daily, continuously or without intermittent periods of withholding drug administration.

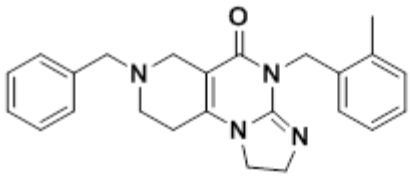
82. The method of claim **74**, wherein the pharmaceutical composition is administered twice per week or once per week.

83. The method of claim **74**, wherein the pharmaceutical composition is administered once every two weeks, once every three weeks, or once every four weeks.

84. The method according to any one of claims **74**-**83**, further comprising the step of administering a second therapeutic agent, wherein compound (**1**) or the pharmaceutically acceptable salt thereof is administered before, simultaneously, or after the second therapeutic agent.

85. A method of treating a disease or condition in a human or animal subject in need of such treatment, the method comprising:

(i) administering to the subject a pharmaceutical composition comprising a therapeutically effective amount of compound (**1**):



Compound (**1**)

or a pharmaceutically acceptable salt thereof; and

(ii) monitoring levels of compound (**1**), the pharmaceutically acceptable salt thereof, or a metabolite thereof in the subject using pharmacokinetic profiling, wherein dosing of compound (**1**) or a pharmaceutically acceptable salt thereof is selected to maintain a concentration of compound (**1**), the pharmaceutically acceptable salt thereof, or the metabolite thereof in whole blood, plasma, serum, or cerebrospinal fluid of the subject is at least about 400 ng/mL for a therapeutic time period within 4 hours post-treatment.

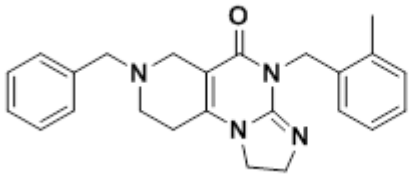
86. The method of claim **85**, wherein the concentration is at least about 1,500 ng/mL.

87. The method of claim **85**, wherein the concentration is between about 400 to 8,000 ng/mL

88. The method of claim **85**, wherein the concentration is between about 1,500 to 8,000 ng/mL.

89. A method of treating a disease or condition in a human or animal subject in need of such treatment, the method comprising:

(i) administering to the subject a pharmaceutical composition comprising a therapeutically effective amount of compound (**1**):



Compound (**1**)

or a pharmaceutically acceptable salt thereof; and

(ii) monitoring levels of compound (**1**), the pharmaceutically acceptable salt thereof, or a metabolite thereof in the subject using pharmacokinetic profiling, wherein dosing of compound (**1**) or a pharmaceutically acceptable salt thereof is selected to obtain an AUC of compound (**1**), the pharmaceutically acceptable salt thereof, or the metabolite thereof in whole blood, plasma, serum, or cerebrospinal fluid of the subject is at least about 3,500 hr-ng/mL with a time period of 24 or 48 hours post-treatment or extrapolated to infinity.

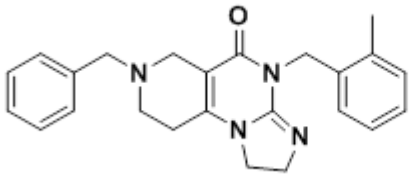
90. The method of claim **89**, wherein the AUC is at least about 15,000 hr-ng/mL.

91. The method of claim **89**, wherein the AUC is between about 3,500 and 65,000 hr-ng/mL.

92. The method of claim **89**, wherein the AUC is between about 15,000 and 65,000 hr-ng/mL.

93. A method of treating a disease or condition in a human or animal subject in need of such treatment, the method comprising:

(i) administering to the subject a pharmaceutical composition comprising a therapeutically effective amount of compound (**1**):



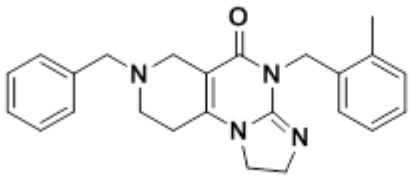
Compound (**1**)

, or a pharmaceutically acceptable salt thereof; and

(ii) monitoring levels of compound (**1**), the pharmaceutically acceptable salt thereof, or a metabolite thereof in the subject using pharmacokinetic profiling, wherein dosing of compound (**1**) or a pharmaceutically acceptable salt thereof is selected to result in undetectable concentrations of compound (**1**), the pharmaceutically acceptable salt thereof, or the metabolite thereof in whole blood, plasma, serum, or cerebrospinal fluid of the subject at 3 days, 4 days, 5 days, 6 days, or 7 days post-treatment.

94. The method according to any one of claims **85**-**93**, wherein the metabolite is selected from monohydroxylated or dihydroxylated compound (**1**).

95. A method of treating or preventing a disease, disorder, or condition comprising: administering to a human or animal subject in need of such treatment a pharmaceutical composition comprising a therapeutically effective amount of



Compound (**1**)

compound (**1**): or a pharmaceutically acceptable salt thereof.

96. The method of claim **95**, wherein the disease is prostate cancer or endometrial cancer.

97. The method of claim **95**, wherein the disorder is psychosis.

98. The method of claim **95**, wherein the disorder is a CNS disorder.

99. The method of claim **95**, wherein the disorder or disease is associated with dysregulated dopamine signaling.

100. The method of claim **95**, wherein the disorder Tourette syndrome.

101. The method of claim **100**, wherein the subject suffers from nausea or emesis.

102. The method of claim **95**, wherein the disorder is schizophrenia or bipolar disorder.

103. The method of claim **95**, wherein the disorder is anxiety.

104. The method of claim **95**, wherein the disorder is hypotension.

105. The method of claim **95**, wherein the disease is a virus.

106. The method of claim **105**, wherein the virus is an RNA virus, DNA virus, or retroviruses.

107. The method of claim **105**, wherein the virus is selected from the group consisting of influenza A virus including subtype H1N1, influenza B virus, influenza C virus, rotavirus A, rotavirus B, rotavirus C, rotavirus D, rotavirus E, SARS coronavirus, human adenovirus types (HAdV-1 to 55), human papillomavirus (HPV) Types 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, parvovirus B19, molluscum contagiosum virus, JC virus (JCV), BK virus, Merkel cell polyomavirus, coxsackie A virus, norovirus, Rubella virus, lymphocytic choriomeningitis virus (LCMV), yellow fever virus, measles virus, mumps virus, respiratory syncytial virus, rinderpest virus, California encephalitis virus, hantavirus, rabies virus, ebola virus, marburg virus, herpes simplex virus-1 (HSV-1), herpes simplex virus-2 (HSV-2), varicella zoster virus (VZV), Epstein-Barr virus (EBV), cytomegalovirus (CMV), herpes lymphotropic virus, roseolovirus, Kaposi's sarcoma-associated herpesvirus, hepatitis A (HAV), hepatitis B (HBV), hepatitis C (HCV), hepatitis D (HDV), hepatitis E (HEV), humanimmunodeficiency virus (HIV), The Human T-lymphotropic virus Type I (HTLV-1), Friend spleen focus-forming virus (SFFV) or Xenotropic MuLV-Related Virus (XMRV).

108. The method according to any one of claims **95-107**, further comprising the step of administering a second therapeutic agent, wherein compound (**1**) or salt thereof is administered before, simultaneously, or after the second therapeutic agent.

109. The method of claim **108**, wherein the administration of compound (**1**) or salt thereof and the administration of the second therapeutic agent are separated by a time interval of at least one day, at least two days, or at least three days.

110. The method according to any one of claims **95-107**, further comprising assaying cleaved cytokeratin-18 in a sample obtained from the subject.

111. The method of claim **110**, wherein the cleaved cytokeratin-18 is measured from blood from the subject using a M30 ELISA assay.

112. The method of either claim 48 or claim 49, determining whether cleaved cytokeratin-18 has increased upon treatment with compound (**1**) or salt thereof.

113. The method according to any one of claims **95-107**, further comprising assaying total cytokeratin-18 in a sample obtained from the subject.

114. The method of claim **113**, wherein the cleaved cytokeratin-18 is measured from blood from the subject using a M65 ELISA assay.

115. The method according to any one of claims **95-107**, comprising assaying both cleaved and total cytokeratin-18 in the sample obtained from the subject.

116. The method of claim **115**, where is the sample is obtained on days 1-21, 2-21, 7-21, 14-21, or 21 after administering compound (**1**) or salt thereof.

117. The method of claim **115**, continuing the treatment of the subject with compound (**1**) or salt thereof, if there is a disproportionate increase in the amount of cleaved cytokeratin 18 relative to total cytokeratin 18.

118. A method of identifying whether a subject having cancer is likely to be responsive to administration of compound (**1**), comprising:

(i) obtaining a biological sample from the subject;

(ii) measuring expression, post-translational modifications, or activity levels of or mutations in eIF2-alpha, ATF4, CHOP, or DR5 in the sample;

(iii) comparing the levels measured and/or the mutations found in the sample to those for a pre-determined standard; and

(iv) determining whether the subject is likely to be responsive to administration of compound (**1**), based on the levels measured and/or mutations found in the sample to those for the pre-determined standard.

119. A method of assessing the effectiveness of or monitoring a subject having cancer and undergoing administration of compound (**1**), comprising:

(i) obtaining a biological sample from the subject;

(ii) measuring expression, post-translational modifications, or activity levels of or mutations in eIF2-alpha, ATF4, CHOP, DR5, or cleaved or total cytokeratin 18 in the sample;

(iii) comparing the levels measured and/or the mutations found in the sample to those for a pre-determined standard; and

(iv) determining whether the subject is responsive to administration of compound (**1**), based on the levels measured and/or mutations found in the sample to those for the pre-determined standard.

120. A method of identifying whether a subject having cancer is likely to be responsive to administration of compound (**1**), comprising:

(i) obtaining a biological sample from the subject;

(ii) measuring expression, post-translational modifications, or activity levels of or mutations in at least one dopamine receptor in the sample;

(iii) comparing the levels measured and/or the mutations found in the sample to those for a pre-determined standard; and

(iv) determining whether the subject is likely to be responsive to administration of compound (**1**), based on the levels measured and/or mutations found in the sample to those for the pre-determined standard.

121. The method of claim **120**, wherein the dopamine receptor is selected from DRD2, DRD2S, DRD2L, and DRD3.

122. The method of claim **120**, wherein the dopamine receptor is from the D2-like family of dopamine receptors.

123. The method of of claim **120**, further comprising the step of administering an effective amount of compound (**1**) to the subject.

124. A method of assessing the effectiveness of or monitoring a subject having cancer and undergoing administration of compound (**1**), comprising:

(i) obtaining a biological sample from the subject;

(ii) measuring expression, post-translational modifications, or activity levels of or mutations in at least one dopamine receptor in the sample;

(iii) comparing the levels measured and/or the mutations found in the sample to those for a pre-determined standard; and

(iv) determining whether the subject is responsive to administration of compound (**1**), based on the levels measured and/or mutations found in the sample to those for the pre-determined standard.

125. The method of claim **124**, wherein the dopamine receptor is selected from DRD2, DRD2S, DRD2L, and DRD3.

126. The method of claim **124**, wherein the dopamine receptor is from the D2-like family of dopamine receptors.

127. A method for screening a potential cancer therapeutic, comprising:

(i) contacting at least one G protein–coupled receptor (GPCR) with a test compound suspected of being a cancer therapeutic;

(ii) measuring the binding affinity, interaction or GPCR signalling of the test compound to the GPCR; and

(iii) comparing the binding affinity or interaction of test compound to a pre-determined threshold, wherein GPCR antagonism or GPCR signaling antagonism of the test compound comparable to or greater than the threshold is indicative of a cancer therapeutic.

128. A method for screening a potential cancer therapeutic, comprising:

(i) contacting at least one dopamine receptor with a test compound suspected of being a cancer therapeutic;

(ii) measuring the binding affinity or interaction of the test compound to the at least one dopamine receptor; and

(iii) comparing the binding affinity or interaction of the test compound to a pre-determined threshold, wherein inhibition of the at least one dopamine receptor by the test compound comparable to or greater than the threshold is indicative of a cancer therapeutic.

129. The method of claim **128**, wherein the dopamine receptor is selected from DRD2, DRD2S, DRD2L, and DRD3.

130. The method of claim **128**, wherein inhibition of the D2-like family of dopamine receptors is indicative of a cancer therapeutic.

131. The method of claim **128**, wherein inhibition of both DRD2 and DRD3 dopamine receptors is indicative of a cancer therapeutic.

132. The method according to any one of claims **128**-**131**, wherein the pre-determined threshold is the inhibition of the at least one dopamine receptor by compound (**1**).

133. A method for screening a potential cancer therapeutic using a processor, comprising:

(i) using a computational docking method to model binding or interaction, if any, of one or more 3-dimensional structures of a test molecule suspected of being a cancer therapeutic to a 3-dimensional structure or model of at least one dopamine receptor;

(ii) using the computational method to estimate the binding affinity or interaction of the test molecule structure to the structure of the at least one dopamine receptor; and

(iii) using the computational method to compare the binding affinity or interaction of the test molecule to a pre-determined threshold, wherein inhibition of the at least one dopamine receptor by the test compound comparable to or greater than the threshold is indicative of a cancer therapeutic.

134. The method of claim **133**, wherein the dopamine receptor is selected from DRD2, DRD2S, DRD2L, and DRD3.

135. The method of claim **133**, wherein inhibition of the D2-like family of dopamine receptors is indicative of a cancer therapeutic.

~~136. The method of claim **133**, wherein inhibition of both DRD2 and DRD3 dopamine receptors is indicative of a cancer therapeutic.~~

~~137. The method according to any one of claims **133-136**, wherein the pre-determined threshold is the inhibition of the at least one dopamine receptor by compound (**1**).~~

~~138. A method of identifying whether a subject having cancer is likely to be responsive to administration of compound (**1**), comprising:~~

~~(i) obtaining a biological sample from the subject;~~

~~(ii) measuring prolactin levels;~~

~~(iii) determining whether the subject is likely to be responsive to administration of compound (**1**), based on the levels measured relative to those for a pre-determined standard.~~

~~139. A method of assessing the effectiveness of or monitoring a subject having cancer and undergoing administration of compound (**1**), comprising:~~

~~(i) obtaining a biological sample from the subject;~~

~~(ii) measuring prolactin levels;~~

~~(iii) determining whether the subject is likely to be responsive to administration of compound (**1**), based on the levels measured relative to those for a pre-determined standard.~~

~~140. A method for screening a potential cancer therapeutic that induces prolactin in pituitary cells or causes prolactin secretion into the peripheral blood.~~

~~141. A method of treatment comprising administering a compound that induces prolactin in pituitary cells or causes prolactin secretion into the peripheral blood.~~

8. The pharmaceutical composition of claim 7, wherein the composition is formulated for oral administration.

9. The compound of claim 1, or the pharmaceutically acceptable salt of any one of claims 2-6, or the pharmaceutical composition of any one of claims 7-8, for use in the treatment of cancer.

10. The pharmaceutically acceptable salt according to claim 9, wherein the salt comprises a counterion selected from the group consisting of: hydrochloride, hydrobromide,

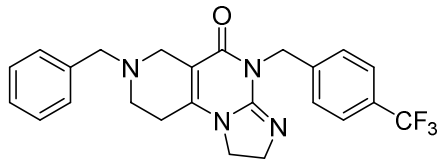
hydrogensulphate, sulfate, phosphate, fumarats, succinate, oxalates and lactates, bisulfate, hydroxyl, tartrate, nitrate, citrate, bitartrate, carbonate, malate, maleate, fumarate sulfonate, methylsulfonate, formate, acetate, and carboxylate, p-toluene-sulfonate, benzenesulfonate, methanesulfonate, oxalate, succinate, tartrate, citrate, fumarate, glucuronate, ascorbate and maleate, ammonium, sodium, potassium, calcium, magnesium, zinc, lithium, methylamino, dimethylamino, diethylamino and triethylamino.

11. The pharmaceutically acceptable salt according to claim 9, wherein the salt is a di-salt.

12. The pharmaceutically acceptable salt according to claim 11, wherein the di-salt is a hydrochloride di-salt.

13. The pharmaceutically acceptable salt according to claim 11, wherein the di-salt is a hydrobromide di-salt.

14. Use of a compound



or a pharmaceutically acceptable salt thereof in the manufacture of a pharmaceutical composition for the treatment of cancer.

15. The use according to claim 14, wherein the pharmaceutically acceptable salt comprises a counterion selected from the group consisting of: hydrochloride, hydrobromide, hydrogensulphate, sulfate, phosphate, fumarats, succinate, oxalates and lactates, bisulfate, hydroxyl, tartrate, nitrate, citrate, bitartrate, carbonate, malate, maleate, fumarate sulfonate, methylsulfonate, formate, acetate, and carboxylate, p-toluene-sulfonate, benzenesulfonate, methanesulfonate, oxalate, succinate, tartrate, citrate, fumarate, glucuronate, ascorbate and maleate, ammonium, sodium, potassium, calcium, magnesium, zinc, lithium, methylamino, dimethylamino, diethylamino and triethylamino.

16. The use according to claim 14, wherein the pharmaceutically acceptable salt is a di-salt.

17. The use according to claim 16, wherein the di-salt is a hydrochloride di-salt.

18. The use according to claim 16, wherein the di-salt is a hydrobromide di-salt.