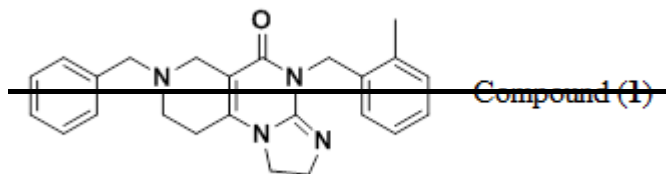


CLAIMS

1. ~~A method of treatment, comprising administering to a subject in need of such treatment:~~

~~(i) a first therapeutic agent including compound (1):~~



~~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.~~

2. ~~The method of treatment according to claim 1, wherein the second therapeutic agent includes one or more of the following compounds or classes of compounds: hormone analogues and antihormones, aromatase inhibitors, LHRH agonists and antagonists, inhibitors of growth factors, growth factor antibodies, growth factor receptor antibodies, tyrosine kinase inhibitors; antimetabolites; antitumour antibiotics; platinum derivatives; alkylation agents; antimitotic agents; tubuline inhibitors; PARP inhibitors, topoisomerase inhibitors, serine/threonine kinase inhibitors, tyrosine kinase inhibitors, protein protein interaction inhibitors, MEK inhibitors, ERK inhibitors, IGF-1R inhibitors, ErbB receptor inhibitors, rapamycin analogs, amifostin, anagrelid, clodronat, filgrastin, interferon, interferon alpha, leucovorin, rituximab, procarbazine, levamisole, mesna, mitotane, pamidronate and porfimer, 2-chlorodesoxyadenosine, 2-fluorodesoxy-cytidine, 2-methoxyoestradiol, 2C4,3-aletine, 131-I-TM-601, 3CPA, 7-ethyl-10-hydroxycamptothecin, 16-aza-epothilone B, A-105972, A-204197, abiraterone, aldesleukin, alitretinoin, allovectin-7, altretamine, alvocidib, amonafide, anthracycline, AG-2037, AP-5280, apaziquone, apomine, aranose, arglabin, arzoxifene, atamestane, atrasentan, auristatin PE, AVL-B, AZ-10992, ABX-EGF, AMG-479 (ganitumab), ARRY-162, ARRY-438162, ARRY-300, ARRY-142886/AZD-6244 (selumetinib), ARRY-704/AZD-8330, AR-12, AR-42, AS-703988, AXL-1717, AZD-8055, AZD-5363, AZD-6244, ARQ-736, ARQ-680, AS-703026 (primasertib), avastin, AZD-2014, azacytidine, azaepothilone B, azonafide, BAY-43-9006, BAY-80-6946, BBR-3464, BBR-3576, bevacizumab, BEZ-235, biricodar dicitrate, BCX-1777, BKM-120, bleocin, BLP-25,~~

~~BMS-184476, BMS-247550, BMS-188797, BMS-275291, BMS-663513, BMS-754807, BNP-1350, BNP-7787, BIBW-2992 (afatinib, tomtovok), BIBF-1120 (vargatef), BI-836845, BI-2536, BI-6727, BI-836845, BI-847325, BI-853520, BUB-022, bleomycinic acid, bleomycin A, bleomycin B, brivanib, bryostatin-1, bortezomib, brostallicin, busulphan, BYL-719, CA-4 prodrug, CA-4, CapCell, calcitriol, canertinib, canfosfamide, capecitabine, carboxyphthalatoplatin, CCI-779, CC-115, CC-223, CEP-701, CEP-751, CBT-1 cefixime, ceftalonin, ceftriaxone, celecoxib, celmoleukin, cemadotin, CH4987655/RO-4987655, chlorotrianisene, cilengitide, ciclosporin, CDA-II, CDC-394, CKD-602, CKI-27, elofarabin, colchicin, combretastatin A4, COT inhibitors, CHS-828, CH-5132799, CLL-Thera, CMT-3 cryptophycin 52, CTP-37, CTLA-4 monoclonal antibodies, CP-461, CV-247, cyanomorpholinedoxorubicin, cytarabine, D-24851, decitabine, doxorubicin, doxyrubicin, deoxycoformycin, depsipeptide, desoxyepothilone B, dexamethasone, dexrazoxane, diethylstilbestrol, diflomotecan, didox, DMDC, dolastatin 10, doranidazole, DS-7423, E7010, E-6201, edatrexat, edotreotide, efaproxiral, eflornithine, EGFR inhibitors, EKB-569, EKB-509, enzastaurin, enzalutamide, elsamitrucin, epothilone B, epratuzumab, ER-86526, erlotinib, ET-18-OCH₃, ethynyletydine, ethynyloestradiol, exatecan, exatecan mesylate, exemestane, exisulind, fenretinide, figitumumab, floxuridine, folie acid, FOLFOX, FOLFOX4, FOLFIRI, formestane, fotemustine, galarubicin, gallium maltolate, gefinitib, gemtuzumab, gimatecan, glufosfamide, GCS-100, GDC-0623, GDC-0941 (pictrelisib), GDC-0980, GDC-0032, GDC-0068, GDC-0349, GDC-0879, G17DT immunogen, GMK, GPX-100, gp100-peptide vaccines, GSK-5126766, GSK-690693, GSK-1120212 (trametinib), GSK-2118436 (dabrafenib), GSK-2126458, GSK-2132231A, GSK-2334470, GSK-2110183, GSK-2141795, GW2016, granisetron, herceptine, hexamethylmelamine, histamine, homoharringtonine, hyaluronic acid, hydroxyurea, hydroxyprogesterone caproate, ibandronate, ibritumomab, idatrexate, idenestrol, IDN-5109, IGF-1R inhibitors, IMC-1C11, IMC-A12 (cixutumumab), immunol, indisulam, interferon alpha-2a, interferon alpha-2b, pegylated interferon alpha-2b, interleukin-2, INK-1117, INK-128, INSM-18, ionafarnib, ipilimumab, iproplatin, irofulven, isohomohalichondrin B, isoflavone, isotretinoin, ixabepilone, JRX-2, JSF-154, J-107088, conjugated oestrogens, kahalid F, ketoconazole, KW-2170, KW-2450, lobaplatin, leflunomide, lenograstim, leuprolide, leuporelin, lexitronam, LGD-1550, linezolid, lutetium texaphyrin, lometrexol, losoxantrone, LU-223651, lurtotecan, LY-S6AKT1, LY-2780301, mafosfamide, marimastat, mechloroethamine, MEK inhibitors, MEK-162, methyltestosterone, methylprednisolone, MEDI-573, MEN-10755, MDX-H210,~~

MDX-447, MDX-1379, MG-V, midostaurin, minodronic acid, mitomycin, mivobulin, MK-2206, MK-0646 (dalotuzumab), MLN518, motexafin gadolinium, MS-209, MS-275, MX-6, neridronate, neratinib, Nexavar, neovastat, nilotinib, nimesulide, nitroglycerin, nolatrexed, norelin, N-acetylcysteine, O6-benzylguanine, oblimersen, omeprazole, oncoVEXGM-CSF, ormaplatin, ortataxel, OX44 antibodies, OSI-027, OSI-906 (linsitinib), 4-1BB antibodies, oxantrazole, oestrogen, panitumumab, patupilone, pegfilgrastim, PCK-3145, pegfilgrastim, PBI-1402, PBI-05204, PDO325901, PD-1 antibodies, PEG-paclitaxel, albumin-stabilized paclitaxel, PEP-005, PF-05197281, PF-05212384, PF-04691502, PHT-427, P-04, PKC412, P54, PI-88, pelitinib, pemetrexed, pentrix, perfosine, perillyl alcohol, pertuzumab, PI3K-inhibitors, PI3K/mTOR-inhibitors, PG-TXL, PG2, PLX-4032/RO-5185426 (vemurafenib), PLX-3603/RO-5212054, PT-100, PWT-33597, PX-866, picoplatin, pivaloyloxymethylbutyrate, pixantrone, phenoxodiol-O, PKI166, plevitrexed, plicamycin, polyprenic acid, porfiromycin, prednisone, prednisolone, quinamed, quinupristin, R115777, RAF-265, ramosetron, ranpirinase, RDEA-119/BAY-869766, RDEA-436, rebeccamycin analogues, receptor tyrosine kinase (RTK)-inhibitors, revimid, RG-7167, RG-7304, RG-7421, RG-7321, RG-7440, rhizoxin, rhu-MAb, rinfabate, risedronate, rituximab, robatumumab, rofecoxib, RO-31-7453, RO-5126766, RO-5068760, RPR-109881A, rubidazole, rubitecan, R-flurbiprofen, RX-0201, S-9788, sabarubicin, SAHA, sargramostim, satraplatin, SB-408075, Se-015/Ve-015, SU5416, SU6668, SDX-101, semustin, seocalcitol, SM-11355, SN-38, SN-4071, SR-27897, SR-31747, SR-13668, SRL-172, sorafenib, spiroplatin, squalamine, suberanilohydroxamic acid, sutent, T-900607, T-138067, TAK-733, TAS-103, tacedinaline, talaporfin, Tareeva, tariquitar, tasisulam, taxotere, taxoprexin, tazarotene, tegafur, temozolamide, tesmilifene, testosterone, testosterone propionate, tesmilifene, tetraplatin, tetrodotoxin, tezacitabine, thalidomide, theralux, therarubicin, thymalfasin, thymectacin, tiazofurin, tipifarnib, tirapazamine, tocladesine, tomudex, toremofin, trabectedin, TransMID-107, transretinoic acid, traszutumab, tremelimumab, tretinoin, triacetyluridine, triapine, tricirbine, trimetrexate, TLK-286TXD 258, tykerb/tyverb, urocidin, valrubicin, vatalanib, vincristine, vinflunine, virulizin, WX-UK1, WX-554, vectibix, xeloda, XELOX, XL-147, XL-228, XL-281, XL-518/R-7420/GDC-0973, XL-765, YM-511, YM-598, ZD-4190, ZD-6474, ZD-4054, ZD-0473, ZD-6126, ZD-9331, ZD1839, ZSTK-474, zoledronat, zosuquidar, and combinations thereof.

3. — The method of treatment according to claim 2, wherein the second therapeutic agent is one or more of: 2-chlorodesoxyadenosine, 2-fluorodesoxy-cytidine, 2-methoxyoestradiol, 2C4,3-alethine, 131-1-TM-601, 3CPA, 7-ethyl-10-hydroxycamptothecin, 16-aza-epothilone B, A-105972, A-204197, abiraterone, aldesleukin, alitretinoin, allovectin-7, altretamine, alvociclib, amonafide, anthracycline, AP-2037, AP-5280, apaziquone, apomine, araneson, arglabin, arzoxifene, atamestane, atrasentan, auristatin PE, AVL-B, AZ-10992, ABX-EGF, AMG-479 (ganitumab), ARRY-162, ARRY-438162, ARRY-300, ARRY-142886/AZD-6244 (selumetinib), ARRY-704/AZD-8330, AR-12, AR-42, AS-703988, AXL-1717, AZD-8055, AZD-5363, AZD-6244, ARQ-736, ARQ-680, AS-703026 (primasertib), avastin, AZD-2014, aza-cytidine, azaepothilone B, azonafide, BAY-43-9006, BAY-80-6946, BBR-3464, BBR-3576, bevacizumab, BEZ-235, biricodar dicitrate, BCX-1777, BKM-120, bleocin, BLP-25, BMS-184476, BMS-247550, BMS-188797, BMS-275291, BMS-663513, BMS-754807, BNP-1350, BNP-7787, BIBW-2992 (afatinib, tomtovok), BIBF-1120 (vargatef), BI-836845, BI-2536, BI-6727, BI-836845, BI-847325, BI-853520, BUB-022, bleomycinic acid, bleomycin A, bleomycin B, brivanib, bryostatins, bortezomib, brostallicin, busulfan, BYL-719, CA-4 prodrug, CA-4, CapCell, calcitriol, canertinib, canfosfamide, capecitabine, carboxyphthalatoplatin, CCI-779, CC-115, CC-223, CEP-701, CEP-751, CBT-1, cefixime, ceftazidime, ceftriaxone, celecoxib, celmoleukin, cemadotin, CH-4987655/RO-4987655, chlorotrianisene, cilengitide, ciclosporin, CDA-II, CDC-394, CKD-602, CKI-27, clofarabine, colchicine, combretastatin A4, COT-inhibitors, CHS-828, CH-5132799, CLL-Thera, CMT-3-cryptophycin 52, CTP-37, CTLA-4 monoclonal antibodies, CP-461, CV-247, cyanomorpholinodoxorubicin, cytarabine, D-24851, decitabine, doxorubicin, doxorubicin, deoxycoformycin, desisipeptide, desoxyepothilone B, dexamethasone, dexrazoxane, diethylstilbestrol, diflomotecan, didox, DMDC, dolastatin 10, doranidazole, DS-7423, E7010, E-6201, edatrexat, edotreotide, efaproxiral, eflornithine, EGFR-inhibitors, EKB-569, EKB-509, enzastaurin, enzalutamide, elsamitucin, epothilone B, epratuzumab, ER-86526, erlotinib, ET-18-0CH3, ethynyletydine, ethynylestradiol, exatecan, exatecan mesylate, exemestane, exisulind, fenretinide, figitumumab, floxuridine, folic acid, FOLFOLX, FOLFOLX4, FOLFIRI, formestane, fotemustine, galarubicin, gallium maltolate, gefitinib, gemtuzumab, gimatecan, glufosfamide, GCS-100, GDC-0623, GDC-0941 (pictrelisib), GDC-0980, GDC-0032, GDC-0068, GDC-0349, GDC-0879, G17DT immunogen, GMK, GPX-100, gp100-peptide vaccines, GSK-5126766, GSK-690693, GSK-1120212 (trametinib), GSK-2118436 (dabrafenib), GSK-2126458, GSK-2132231A,

GSK-2334470, GSK-2110183, GSK-2141795, GW2016, granisetron, herceptine, hexamethylmelamine, histamine, homoharringtonine, hyaluronic acid, hydroxyurea, hydroxyprogesterone caproate, ibandronate, ibritumomab, idatrexate, idenestrol, IDN-5109, IGF-1R inhibitors, IMC-1C11, IMC-A12 (eixutumumab), immunol, indisulam, interferon alpha-2a, interferon alpha-2b, pegylated interferon alpha-2b, interleukin-2, INK-1117, INK-128, INSM-18, ionafarnib, ipilimumab, iproplatin, irofulven, isohomohalichondrin-B, isoflavone, isotretinoin, ixabepilone, JRX-2, JSF-154, J-107088, conjugated oestrogens, kahalid F, ketoconazole, KW-2170, KW-2450, lobaplatin, leflunomide, lenograstim, leuprolide, leuporelin, lexicidronam, LGD-1550, linezolid, lutetium texaphyrin, lometrexol, losoxantrone, LU-223651, lurtotecan, LY-S6AKT1, LY-2780301, mafosfamide, marimastat, mechloroethamine, MEK inhibitors, MEK-162, methyltestosterone, methylprednisolone, MEDI-573, MEN-10755, MDX-H210, MDX-447, MDX-1379, MGV, midostaurin, minodronic acid, mitomycin, mivobulin, MK-2206, MK-0646 (dalotuzumab), MLN518, motexafin gadolinium, MS-209, MS-275, MX6, neridronate, neratinib, Nexavar, neovastat, nilotinib, nimesulide, nitroglycerin, nolatrexed, norelin, N-acetylcysteine, 06-benzylguanine, oblimersen, omeprazole, oncopage, oncoVEXGM-CSF, ormiplatin, ortataxel, OX44 antibodies, OSI-027, OSI-906 (linsitinib), 4-1BB antibodies, oxantrazole, oestrogen, panitumumab, patupilone, pegfilgrastim, PCK-3145, pegfilgrastim, PBI-1402, PBI-05204, PDO325901, PD-1 antibodies, PEG-paclitaxel, albumin-stabilized paclitaxel, PEP-005, PF-05197281, PF-05212384, PF-04691502, PHT-427, P-04, PKC412, P54, PI-88, pelitinib, pemetrexed, pentrix, perifosine, perillyl alcohol, pertuzumab, PI3K inhibitors, PI3K/mTOR inhibitors, PG-TXL, PG2, PLX-4032/RO-5185426 (vemurafenib), PLX-3603/RO-5212054, PT-100, PWT-33597, PX-866, picoplatin, pivaloyloxymethylbutyrate, pixantrone, phenoxodiol O, PKI166, plevitrexed, plicamycin, polyprenic acid, porfiromycin, prednisone, prednisolone, quinamed, quinupristin, R115777, RAF-265, ramosetron, ranpirnase, RDEA-119/BAY-869766, RDEA-436, rebeccamycin analogues, receptor tyrosine kinase (RTK) inhibitors, revimid, RG-7167, RG-7304, RG-7421, RG-7321, RG-7440, rhizoxin, rhu-MAb, rinfabate, risedronate, rituximab, robatumumab, rofecoxib, RO-31-7453, RO-5126766, RO-5068760, RPR-109881A, rubidazole, rubitecan, R-flurbiprofen, RX-0201, S-9788, sabarubicin, SAHA, sargramostim, satraplatin, SB-408075, Se-015/Ve-015, SU5416, SU6668, SDX-101, semustin, seocalcitol, SM-11355, SN-38, SN-4071, SR-27897, SR-31747, SR-13668, SRL-172, sorafenib, spiroplatin, squalamine, suberanilohydroxamic acid, sutent, T-900607, T-138067, TAK-733, TAS-103, tacedinaline, talaporfin, Tarceva, tariquitar,

~~tasisulam, taxotere, taxoprexin, tazarotene, tegafur, temozolamide, tesmilifene, testosterone, testosterone propionate, tesmilifene, tetraplatin, tetrodotoxin, tezacitabine, thalidomide, theralux, therarubicin, thymalfasin, thymectacin, tiazofurin, tipifarnib, tirapazamine, tocladesine, tomudex, toremofin, trabectedin, TransMID-107, transretinic acid, traszutumab, tremelimumab, tretinoin, triacetylluridine, triapine, triceribine, trimetrexate, TLK-286TXD 258, tykerb/tyverb, urocidin, valrubicin, vatalanib, vincristine, vinflunine, virulizin, WX-UK1, WX-554, vectibix, xeloda, XELOX, XL-147, XL-228, XL-281, XL-518/R-7420/GDC-0973, XL-765, YM-511, YM-598, ZD-4190, ZD-6474, ZD-4054, ZD-0473, ZD-6126, ZD-9331, ZD1839, ZSTK-474, zoledronat, zosuquidar, and combinations thereof.~~

4. ~~—The method of treatment according to claim 2, for treating a cancer selected from the group consisting of acute leukemia, Acute Lymphoblastic Leukemia, Acute Myeloid Leukemia, Adrenocortical Carcinoma, AIDS-Related Cancers, AIDS-Related Lymphoma, Anal or Rectal Cancer, Appendix Cancer, Astrocytomas, and Atypical Teratoid/Rhabdoid Tumor.~~

5. ~~—The method of treatment according to claim 2, for treating a cancer selected from the group consisting of Basal Cell Carcinoma, Basal Cell Nevus Syndrome, Gorlin Nevus Syndrome, Bile Duct Cancer, Bladder Cancer, Bone Cancer, Osteosarcoma and Malignant Fibrous Histiocytoma, Brain Tumor, Breast Cance, Bronchial Tumors, Burkitt Lymphoma, and Spinal Cord Tumors.~~

6. ~~—The method of treatment according to claim 2, for treating a cancer selected from the group consisting of Carcinoid Tumor, Carcinoma of Unknown Primary, Central Nervous System Atypical Teratoid/Rhabdoid Tumor, Central Nervous System Embryonal Tumors, Central Nervous System Lymphoma, Cervical Cancer, Chordoma, Chronic Lymphocytic Leukemia, Chronic Myelogenous Leukemia, Chronic Myeloproliferative Disorders, Colon Cancer, Colorectal Cancer, Craniopharyngioma, Cutaneous T-Cell Lymphoma, Sezary Syndrome, and Mycosis fungoides.~~

7. ~~—The method of treatment according to claim 2, for treating a cancer selected from the group consisting of Embryonal Tumors of Central Nervous System, Endometrial Cancer, Ependymblastoma, Ependymoma, Esophageal Cancer, Ewing Sarcoma Family of Tumors,~~

Extracranial Germ Cell Tumor, Extragonadal Germ Cell Tumor, Extrahepatic Bile Duct Cancer, and Eye Cancer.

8. — The method of treatment according to claim 2, for treating a cancer selected from the group consisting of Gallbladder Cancer, Gastric (Stomach) Cancer, Gastrointestinal Carcinoid Tumor, Gastrointestinal Stromal Tumor (GIST), Germ Cell Tumor, Gestational Trophoblastic Tumor, and Glioma.

9. — The method of treatment according to claim 2, for treating a cancer selected from the group consisting of Hairy Cell Leukemia, , Head and Neck Cancer, Hepatocellular (Liver) Cancer, Histiocytosis, Hodgkin Lymphoma, and Hypopharyngeal Cancer.

10. — The method of treatment according to claim 2, for treating a cancer selected from the group consisting of Kaposi Sarcoma, and Kidney (Renal Cell) Cancer.

11. — The method of treatment according to claim 2, for treating a cancer selected from the group consisting of Langerhans Cell Histiocytosis, Laryngeal Cancer, Lip and Oral Cavity Cancer, Liver Cancer, Lung Cancer, Non-Hodgkin Lymphoma, and Primary Central Nervous System Lymphoma.

12. — The method of treatment according to claim 2, for a treating cancer selected from the group consisting of Waldenström's macroglobulinemia (lymphoplasmacytic lymphoma), Malignant Fibrous Histiocytoma of Bone and Osteosarcoma, Medulloblastoma, Medulloepithelioma, Melanoma, , Merkel Cell Carcinoma, Mesothelioma, Metastatic Squamous Neck Cancer with Occult Primary, Multiple Endocrine Neoplasia Syndrome, Mouth Cancer, Multiple Myeloma/Plasma Cell Neoplasm, Mycosis Fungoides, Myelodysplastic Syndromes, Myelodysplastic/Myeloproliferative Neoplasms, Multiple Myeloma, and Myeloproliferative Disorders.

13. — The method of treatment according to claim 2, for treating a cancer selected from the group consisting of Nasal Cavity and Paranasal Sinus Cancer, Nasopharyngeal Cancer, Neuroblastoma, and Non-Hodgkin's lymphoma.

14. —The method of treatment according to claim 2, for treating a cancer selected from the group consisting of Oral Cancer, Lip and Oral Cavity Cancer, Oropharyngeal Cancer, Osteosarcoma and Malignant Fibrous Histiocytoma of Bone, Ovarian Cancer, Ovarian Germ Cell Tumor, Ovarian Epithelial Cancer, and Ovarian Low Malignant Potential Tumor.

15. —The method of treatment according to claim 2, for treating a cancer selected from the group consisting of Pancreatic Cancer, Papillomatosis, Paranasal Sinus and Nasal Cavity Cancer, Parathyroid Cancer, Penile Cancer, Pharyngeal Cancer, Pineal Parenchymal Tumors of Intermediate Differentiation, Pineoblastoma and Supratentorial Primitive Neuroectodermal Tumors, Pituitary Tumor, Pleuropulmonary Blastoma, Pregnancy and Breast Cancer, Primary Central Nervous System Lymphoma, and Prostate Cancer.

16. —The method of treatment according to claim 2, for treating a cancer selected from the group consisting of Rectal Cancer, Renal Cell (Kidney) Cancer, Renal Pelvis and Ureter, Respiratory Tract Carcinoma Involving the NUT Gene on Chromosome 15, Retinoblastoma, and Rhabdomyosarcoma.

17. The method according to claim 1, for the treatment of a Non-Hodgkin's lymphoma.

18. The method according to claim 17, wherein the Non-Hodgkin's lymphoma is selected from the group consisting of mantle cell lymphoma, diffuse large B-cell lymphoma, follicular lymphoma, marginal zone lymphoma, small lymphocytic lymphoma, lymphoplasmacytic Non-Hodgkin's lymphoma, Waldenstrom's macroglobulinaemia, and skin lymphoma.

19. The method according to claim 1, for the treatment of an acute leukemia.

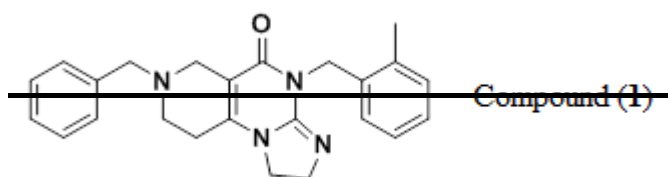
20. The method according to claim 19, wherein the acute leukemia is selected from the group consisting of acute lymphocyte leukemia, acute myeloid leukemia, chronic lymphoblastic leukemia, chronic myeloid leukemia, myelodysplastic syndrome, and myeloproliferative disease.

21. The method according to claim 1, for the treatment of a solid tumor.

22. The method according to claim 1, for the treatment of a liquid tumor.

- ~~23. The method according to claim 1, wherein the subject is over the age of 50 years.~~
- ~~24. The method according to claim 1, wherein the subject is under the age of 65 years.~~
- ~~25. The method according to claim 1, wherein the subject has received at least one prior therapy.~~
- ~~26. The method according to claim 1 for treating a cancer, wherein the cancer no longer responds to treatment with ibrutinib, bortezomib, carfilzomib, temozolomide, bevacizumab, cyclophosphamide, hydroxydaunorubicin, vincristine, prednisone, cytarabine, cisplatin, rituximab, 5-fluorouracil, oxaliplatin, leucovorin, lenalidomide, radiation, surgery, or a combination thereof.~~
- ~~27. The method according to claim 1, for the treatment of an autoimmune disease.~~
- ~~28. The method according to claim 1, for the treatment of an acute allograft rejection.~~
- ~~29. The method according to claim 1, for the treatment of lupus nephritis.~~
- ~~30. The method according to claim 1, for the treatment of ischemic stroke.~~
- ~~31. The method according to claim 1, for the treatment of an inflammatory disease selected from the group consisting of arthritis, psoriasis, asthma, and colitis.~~
- ~~32. The method according to claim 1, further comprising assaying the expression of an endoplasmic reticulum stress response gene signature in a biological sample.~~
- ~~33. The method according to claim 32, wherein the endoplasmic reticulum stress response gene is selected from C/EBP Homologous Protein and Activating Transcription Factor 3.~~
- ~~34. The method according to claim 32, further comprising adjusting a dose of compound (1) to achieve induction of 50% or more of the endoplasmic reticulum stress response gene.~~

35. ~~The method according to claim 1, further comprising assaying the expression of one or more proteasomal activities in a biological sample.~~
36. ~~The method according to claim 35, wherein the proteasomal activity is chymotrypsin-like activity, trypsin-like activity, caspase-like activity or a combination thereof.~~
37. ~~The method according to claim 35, further comprising adjusting a dose of compound (1) to achieve inhibition of at least 30% of one or more of the proteasomal activities.~~
38. ~~A method of treatment, comprising administering to a subject in need of such treatment a therapeutic agent comprising compound (1):~~



~~or a pharmaceutically acceptable salt thereof, wherein the treatment is for a condition selected from the group consisting of Acute Lymphoblastic Leukemia, Acute Myeloid Leukemia, Adrenocortical Carcinoma, AIDS-Related Cancers, AIDS-Related Lymphoma, Anal or Rectal Cancer, Appendix Cancer, Astrocytomas, Atypical Teratoid/Rhabdoid Tumor, Basal Cell Carcinoma, Basal Cell Nevus Syndrome, Gorlin-Nevus Syndrome, Bile Duct Cancer, Bladder Cancer, Bone Cancer, Osteosarcoma and Malignant Fibrous Histiocytoma, Bronchial Tumors, Burkitt Lymphoma, and Spinal Cord Tumors, Carcinoid Tumor, Carcinoma of Unknown Primary, Central Nervous System Atypical Teratoid/Rhabdoid Tumor, Central Nervous System Embryonal Tumors, Central Nervous System Lymphoma, Cervical Cancer, Chordoma, Chronic Lymphocytic Leukemia, Chronic Myelogenous Leukemia, Chronic Myeloproliferative Disorders, Craniopharyngioma, and Cutaneous T-Cell Lymphoma, Sezary Syndrome, Mycosis fungoides, Embryonal Tumors of Central Nervous System, Endometrial Cancer, Ependymoblastoma, Ependymoma, Esophageal Cancer, Ewing Sarcoma Family of Tumors, Extracranial Germ Cell Tumor, Extragonadal Germ Cell Tumor, Extrahepatic Bile Duct Cancer, and Eye Cancer, Gallbladder Cancer, Gastric (Stomach) Cancer, Gastrointestinal Carcinoid Tumor, Gastrointestinal Stromal Tumor (GIST), Germ Cell Tumor, Gestational Trophoblastic Tumor, Glioma, Hairy Cell Leukemia, , Head and Neck Cancer, Hepatocellular (Liver) Cancer, Histiocytosis, Hodgkin Lymphoma, Hypopharyngeal Cancer, Kaposi~~

~~Sarcoma, Kidney (Renal Cell) Cancer, Langerhans Cell Histiocytosis, Laryngeal Cancer, Lip and Oral Cavity Cancer, Liver Cancer, Non-Hodgkin Lymphoma, Primary Central Nervous System Lymphoma, Waldenström's macroglobulinemia (lymphoplasmaeytic lymphoma), Malignant Fibrous Histiocytoma of Bone and Osteosarcoma, Medulloblastoma, Medulloepithelioma, Melanoma, Merkel Cell Carcinoma, Mesothelioma, Metastatic Squamous Neck Cancer with Occult Primary, Multiple Endocrine Neoplasia Syndrome, Mouth Cancer, Multiple Myeloma/Plasma Cell Neoplasm, Mycosis Fungoides, Myelodysplastic Syndromes, Myelodysplastic/Myeloproliferative Neoplasms, Multiple Myeloma, Myeloproliferative Disorders, Nasal Cavity and Paranasal Sinus Cancer, Nasopharyngeal Cancer, Neuroblastoma, Oral Cancer, Lip and Oral Cavity Cancer, Oropharyngeal Cancer, Osteosarcoma and Malignant Fibrous Histiocytoma of Bone, Ovarian Cancer, Ovarian Germ Cell Tumor, Ovarian Epithelial Cancer, Ovarian Low Malignant Potential Tumor, Pancreatic Cancer, Papillomatosis, Paranasal Sinus and Nasal Cavity Cancer, Parathyroid Cancer, Penile Cancer, Pharyngeal Cancer, Pineal Parenchymal Tumors of Intermediate Differentiation, Pineoblastoma and Supratentorial Primitive Neuroectodermal Tumors, Pituitary Tumor, Pleuropulmonary Blastoma, Pregnancy and Breast Cancer, Primary Central Nervous System Lymphoma, Prostate Cancer, Rectal Cancer, Renal Cell (Kidney) Cancer, Renal Pelvis and Ureter, Respiratory Tract Carcinoma Involving the NUT Gene on Chromosome 15, Retinoblastoma, Rhabdomyosarcoma, an autoimmune disease, an acute allograft rejection, lupus nephritis, ischemic stroke, and an inflammatory disease.~~

~~39. The method according to claim 38, wherein the subject is under the age of 65 years.~~

~~40. The method accordign to claim 38, wherein the subject has received at least one prior therapy.~~

~~41. The method according to claim 38, wherein the condition no longer responds to treatment with ibrutinib, bortezomib, carfilzomib, temozolomide, bevacizumab, cyclophosphamide, hydroxydaunorubicin, vincristine, prednisone, cytarabine, cisplatin, rituximab, 5-fluorouracil, oxaliplatin, leucovorin, lenalidomide, radiation, surgery, or a combination thereof.~~

~~42. The method according to claim 38, further comprising assaying the expression of an endoplasmic reticulum stress response gene signature in a biological sample.~~

~~43. The method according to claim 42, wherein the endoplasmic reticulum stress response gene is selected from C/EBP-Homologous Protein and Activating Transcription Factor 3.~~

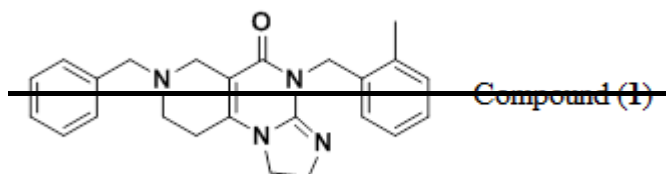
~~44. The method according to claim 42, further comprising adjusting a dose of compound (1) to achieve induction of 50% or more of the endoplasmic reticulum stress response gene.~~

~~45. The method according to claim 38, further comprising assaying the expression of proteasomal activity in a biological sample.~~

~~46. The method according to claim 45, wherein the proteasomal activity is chymotrypsin-like activity, trypsin-like activity, caspase-like activity or a combination thereof.~~

~~47. The method according to claim 45, further comprising adjusting a dose of compound (1) to achieve inhibition of at least 30% of one or more of the proteasomal activities.~~

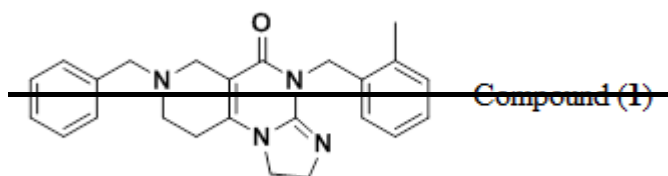
~~48. A method of treatment, comprising administering to a subject in need of such treatment a first therapeutic agent comprising compound (1):~~



~~or a pharmaceutically acceptable salt thereof, wherein the treatment is for a Non Hodgkin's lymphoma.~~

~~49. The method of treatment according to claim 48, wherein the Non Hodgkin's lymphoma is selected from the group consisting of mantle cell lymphoma, diffuse large B-cell lymphoma, follicular lymphoma, marginal zone lymphoma, small lymphocytic lymphoma, lymphoplasmacytic Non Hodgkin's lymphoma, Waldenstrom's macroglobulinaemia, and skin lymphoma.~~

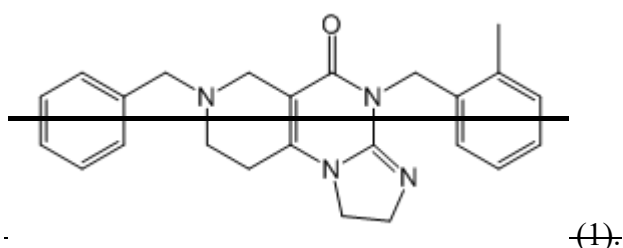
~~50. A method of treatment, comprising administering to a subject in need of such treatment a first therapeutic agent comprising compound (1):~~



or a pharmaceutically acceptable salt thereof, wherein the treatment is for an acute leukemia.

51. The method of treatment according to claim 50, wherein the acute leukemia is selected from the group consisting of acute lymphocyte leukemia, acute myeloid leukemia, chronic lymphoblastic leukemia, chronic myeloid leukemia, myelodysplastic syndrome, and myeloproliferative disease.

52. A composition comprising a salt of compound (1):



53. The composition according to claim 52, wherein the salt of compound (1) comprises a counterion selected from the group consisting of: hydrochloride, hydrobromide, hydrogensulphate, sulfate, phosphate, fumarate, succinate, oxalate and lactate, 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.

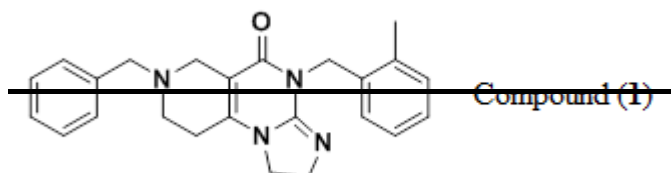
54. The composition according to claim 52, wherein the salt of compound (1) is a di-salt.

55. The composition according to claim 54, wherein the di-salt is a hydrochloride di-salt.

56. The composition according to claim 54, wherein the di-salt is a hydrobromide di-salt.

57. — A method of treatment, which comprises administering to a subject in need of such treatment a combination of a first therapeutic agent and a second therapeutic agent, the method comprising:

—— (i) administering to the subject the first therapeutic agent including compound (1):



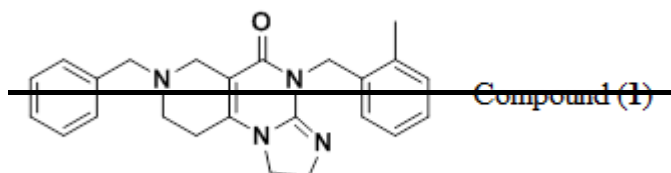
· , or a pharmaceutically acceptable salt thereof; and

—— (ii) monitoring level of compound (1) or a 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 such that maximum concentration of compound (1) or a pharmaceutically acceptable salt thereof in blood (whole blood, plasma, or serum) is maintained at a value less than 1500 ng/ml for a therapeutic time period.

58. The method of treatment according to claim 57, further comprising administering the second therapeutic agent conditional on the level of the first therapeutic agent in the subject.

59. — A method of treatment, which comprises administering to a subject in need of such treatment a combination of a first therapeutic agent and a second therapeutic agent, the method comprising:

(i) administering to the subject the first therapeutic agent including compound (1):



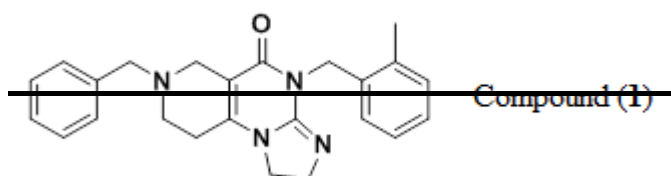
· , or a pharmaceutically acceptable salt thereof; and

—— (ii) monitoring level of compound (1) or a 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 maximum concentration of compound (1) 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.

60. The method according to claim 58, further comprising administering the second therapeutic agent conditional on the level of the first therapeutic agent in the subject.

61. — A composition for use in a treatment, the composition comprising, separately or together, — (i) a first therapeutic agent including compound (1):

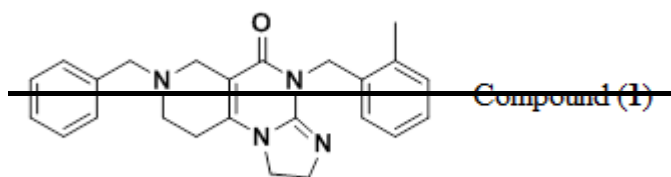


— or a pharmaceutically acceptable salt thereof; and

— (ii) at least one second therapeutic agent, for simultaneous, sequential or separate administration to a subject in need of such treatment.

62. — A method of treating a condition in a subject, comprising:

— (i) administering to the subject the first therapeutic agent including compound (1):



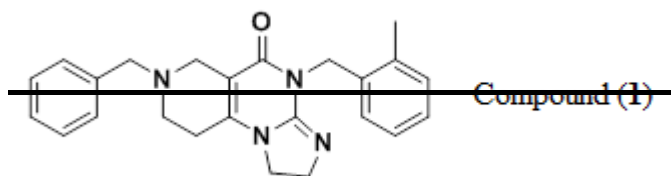
— or a pharmaceutically acceptable salt thereof; and

— (ii) monitoring level of compound (1) or a 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 such that exposure of compound (1) or a pharmaceutically acceptable salt thereof in blood (whole blood, plasma, or serum) is maintained at a value less than or equal to about 8000 ng hr/ml for a therapeutic time period.

63. — The method according to claim 62, further comprising administering the second therapeutic agent conditional on the level of the first therapeutic agent in the subject.

64. A method of treating a condition in a subject comprising:

(i) administering to the subject the first therapeutic agent including compound (1):



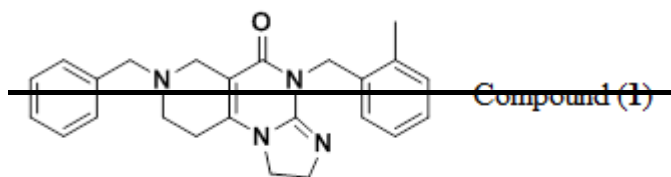
, or a pharmaceutically acceptable salt

thereof;

—— (ii) monitoring level of compound (1) or a 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 an exposure of compound (1) 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.

65. — The method according to claim 64, further administering the second therapeutic agent conditional on the level of the first therapeutic agent in the subject.

66. — A composition for use in a treatment, the composition comprising, separately or together, (i) a first therapeutic agent including compound (1):

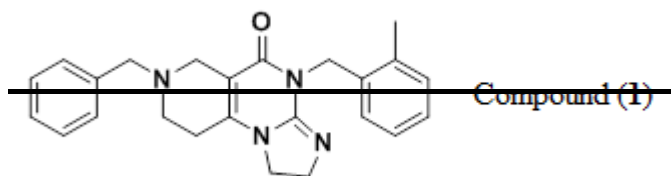


, or a pharmaceutically acceptable salt

thereof; and

—— (ii) at least one second therapeutic agent,
for simultaneous, sequential or separate administration to a subject in need of such treatment.

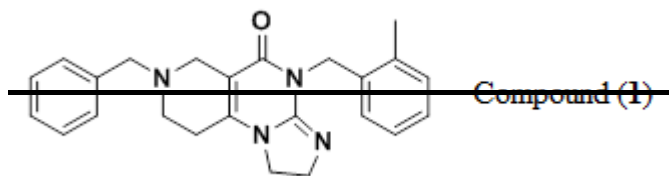
67. — A composition for use in a treatment, the composition comprising, separately or together, (i) a first therapeutic agent including compound (1):



or a pharmaceutically acceptable salt thereof; and

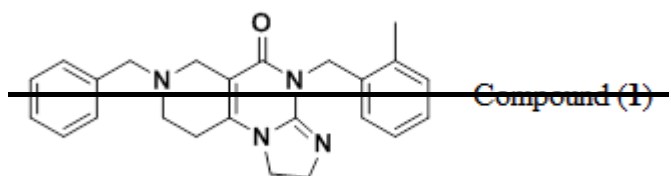
— (ii) at least one second therapeutic agent, for sequential administration to a subject in need of such treatment, wherein administration of the second therapeutic agent is conditioned on the level of the first therapeutic agent in the subject.

68. A method of treatment comprising administering to a subject in need of such treatment a pharmaceutically acceptable amount of compound (1):



or a pharmaceutically acceptable salt thereof, wherein the pharmaceutically acceptable amount of compound (1) is administered as a salvage therapy.

69. A method of treatment comprising administering to a subject in need of such treatment a pharmaceutically acceptable amount of compound (1):



or a pharmaceutically acceptable salt thereof, wherein the pharmaceutically acceptable amount of compound (1) is administered according to an infrequent dosing regimen.

70. The method according to claim 69, wherein the pharmaceutical composition is administered once per week.

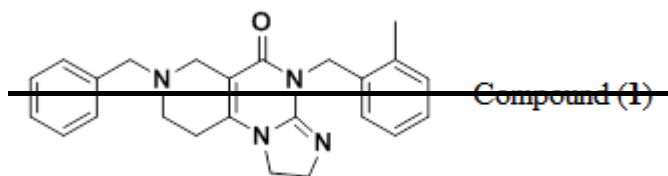
71. The method according to claim 69, wherein the pharmaceutical composition is administered once every two weeks.

~~72. The method according to claim 69, wherein the pharmaceutical composition is administered once every three weeks.~~

~~73. The method according to claim 69, wherein the pharmaceutical composition is administered once every four weeks.~~

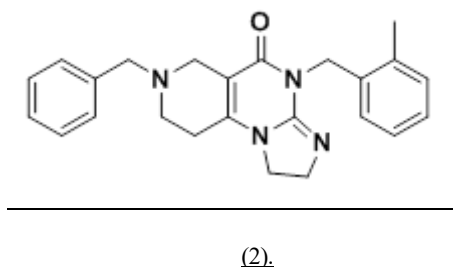
~~74. The method according to claim 69, wherein the pharmaceutical composition is administered in a repeated cycle of once weekly, once every two weeks, once every three weeks, once every four weeks or combinations thereof.~~

~~75. A method of treatment comprising administering to a subject in need of such treatment a pharmaceutically acceptable amount of compound (1):~~



~~or a pharmaceutically acceptable salt thereof, wherein the pharmaceutically acceptable amount of compound (1) or the pharmaceutically acceptable salt thereof is a dose ranging from about 100 mg to about 200 mg.~~

1. Compound (2), having the chemical structure



2. A pharmaceutical composition comprising compound (2) of claim 1, and a pharmaceutically acceptable carrier.

3. The pharmaceutical composition of claim 2, further comprising an additional anticancer agent.

4. Compound (2) of claim 1, or the pharmaceutical composition of claim 2 or 3, for use as a medicament.

5. Compound (2) of claim 1, or the pharmaceutical composition of claim 2 or 3, for use in the treatment of cancer.

6. Use of compound (2) of claim 1 in the manufacture of a medicament for the treatment of cancer.