amplification was frequent in pediatric (29.3%) and adult (20.9%) tumors. *PDGFR*α amplification was reported to increase with grade and in particular to be associated with a less favorable prognosis in *IDH1* mutant de novo GBMs (Phillips et al, *Brain Pathology*, 2013;23:565-73).

[10] The *PDGFR*α locus in *PDGFR*α-amplified gliomas has been demonstrated to present a *PDGFR*α exon 8,9 intragenic deletion rearrangement. This intragenic deletion was common, being present in 40% of the glioblastoma multiformes (GBMs) presenting with *PDGFR*α amplification. Tumors with this rearrangement displayed histologic features of oligodendroglioma, and the *PDGFR*α exon 8,9 intragenic deletion showed constitutively elevated tyrosine kinase activity (Ozawa et al, *Genes and Development* 2010; 24:2205-18).

[11] The FIP1L1-PDGFRA fusion protein is oncogenic in a subset of patients with hypereosinophilic syndrome (Elling et al, *Blood* 2011;117;2935). *FIP1L1- PDGFR*α fusion has also been identified in eosinophilia-associated acute myeloid leukemia and lymphoblastic T-cell lymphoma (Metzgeroth et al, *Leukemia* 2007;21:1183-88).

[12] In summary, mutations, deletions, rearrangements, and amplification of the *PDGFR*α gene are linked to a number of solid and hematological cancers. Given the complex function of the PDGRFα gene and the potential utility for PDGFRα inhibitors in the treatment of various solid and hematological cancers, there is a need for inhibitors with good therapeutic properties.

Summary

[13] One aspect of the disclosure refers to a use of 1-[4-bromo-5-[1-ethyl-7-(methylamino)-2-oxo-1,2-dihydro-1,6-naphthyridin-3-yl]-2-fluorophenyl]-3-phenylurea, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for treating or preventing a PDGFR kinase-mediated tumor growth or tumor progression. In one example, there is described a method of treating or preventing a PDGFR kinase-mediated tumor growth or tumor progression comprising administering to a patient in need thereof an effective amount of 1-[4-bromo-5-[1-ethyl-7-(methylamino)-2-oxo-1,2-dihydro-1,6-naphthyridin-3-yl]-2-fluorophenyl]-3-phenylurea, or a pharmaceutically acceptable salt thereof.

[14] Another aspect of the disclosure refers to a use of 1-[4-bromo-5-[1-ethyl-7-(methylamino)-2-oxo-1,2-dihydro-1,6-naphthyridin-3-yl]-2-fluorophenyl]-3-phenylurea, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for treating lung adenocarcinoma, squamous cell lung cancer, glioblastoma, pediatric glioma, astrocytomas, sarcomas, gastrointestinal stromal tumors, malignant peripheral nerve sheath sarcoma, intimal sarcomas, hypereosinophilic syndrome, idiopathic hypereosinophilic syndrome, chronic eosinophilic leukemia,

eosinophilia-associated acute myeloid leukemia, or lymphoblastic T-cell lymphoma by inhibiting PDGFR kinase. In one example, there is disclosed a method of inhibiting PDGFR kinase comprising administering to a patient in need thereof an effective amount of 1-[4-bromo-5-[1-ethyl-7-(methylamino)-2-oxo-1,2-dihydro-1,6-naphthyridin-3-yl]-2-fluorophenyl]-3-phenylurea, or a pharmaceutically acceptable salt thereof.

[15] In another example, there is described a method of inhibiting a PDGFR kinase or treating a PDGFR kinase-mediated tumor growth or tumor progression. The method comprises administering to a patient in need thereof 1-[4-bromo-5-[1-ethyl-7-(methylamino)-2-oxo-1,2-dihydro-1,6-naphthyridin-3-yl]-2-fluorophenyl]-3-phenylurea, or a pharmaceutically acceptable salt thereof as a single agent or in combination with other cancer targeted therapeutic agents, cancer-targeted biologicals, immune checkpoint inhibitors, or chemotherapeutic agents.

[16] Yet another aspect of the disclosure refers to a use of 1-[4-bromo-5-[1-ethyl-7-(methylamino)-2-oxo-1,2-dihydro-1,6-naphthyridin-3-yl]-2-fluorophenyl]-3-phenylurea, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for treating glioblastoma. In another example, there is described a method of treating glioblastoma, comprising administering to a patient in need thereof an effective amount of 1-[4-bromo-5-[1-ethyl-7-(methylamino)-2-oxo-1,2-dihydro-1,6-naphthyridin-3-yl]-2-fluorophenyl]-3-phenylurea, or a pharmaceutically acceptable salt thereof.

[17] Another aspect of the disclosure refers to a use of 1-[4-bromo-5-[1-ethyl-7-(methylamino)-2-oxo-1,2-dihydro-1,6-naphthyridin-3-yl]-2-fluorophenyl]-3-phenylurea, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for treating PDGFRα-mediated gastrointestinal stromal tumors. In one example, there is disclosed a method of treating PDGFRα-mediated gastrointestinal stromal tumors, comprising administering to a patient in need thereof an effective amount of 1-[4-bromo-5-[1-ethyl-7-(methylamino)-2-oxo-1,2-dihydro-1,6-naphthyridin-3-yl]-2-fluorophenyl]-3-phenylurea, or a pharmaceutically acceptable salt thereof.

[18] In one example, there is disclosed a method of treating or preventing a PDGFR kinase-mediated tumor growth or tumor progression comprising administering to a patient in need thereof an effective amount of 1-(5-(7-amino-1-ethyl-2-oxo-1,2-dihydro-1,6-naphthyridin-3-yl)-4-bromo-2-fluorophenyl)-3-phenylurea, or a pharmaceutically acceptable salt thereof.

[19] In another example, there is disclosed a method of inhibiting PDGFR kinase, comprising administering to a patient in need thereof an effective amount of 1-(5-(7-amino-1-ethyl-2-oxo-1,2-dihydro-1,6-naphthyridin-3-yl)-4-bromo-2-fluorophenyl)-3-phenylurea, or a pharmaceutically acceptable salt thereof.

[20] In yet another example, there is disclosed a method of inhibiting a PDGFR kinase or treating a PDGFR kinase-mediated tumor growth or tumor progression. The method comprises administering to a patient in need thereof 1-(5-(7-amino-1-ethyl-2-oxo-1,2-dihydro-1,6-naphthyridin-3-yl)-4-bromo-2-fluorophenyl)-3-phenylurea, or a pharmaceutically acceptable salt thereof as a single agent or in combination with other cancer targeted therapeutic agents, cancer-targeted biologicals, immune checkpoint inhibitors, or chemotherapeutic agents.

[21] In a further example, there is disclosed a method of treating glioblastoma, comprising administering to a patient in need thereof an effective amount of 1-(5-(7-amino-1-ethyl-2-oxo-1,2-dihydro-1,6-naphthyridin-3-yl)-4-bromo-2-fluorophenyl)-3-phenylurea, or a pharmaceutically acceptable salt thereof.

[22] In one example, there is disclosed a method of treating PDGFRα-mediated gastrointestinal stromal tumors, comprising administering to a patient in need thereof an effective amount of 1-(5-(7-amino-1-ethyl-2-oxo-1,2-dihydro-1,6-naphthyridin-3-yl)-4-bromo-2-fluorophenyl)-3-phenylurea, or a pharmaceutically acceptable salt thereof.

[23] In one example, there is disclosed the *in vivo* biosynthetic formation of 1-(5-(7-amino-1-ethyl-2-oxo-1,2-dihydro-1,6-naphthyridin-3-yl)-4-bromo-2-fluorophenyl)-3-phenylurea (Compound B) after oral administration of 1-[4-bromo-5-[1-ethyl-7-(methylamino)-2-oxo-1,2-dihydro-1,6-naphthyridin-3-yl]-2-fluorophenyl]-3-phenylurea (Compound A).

[24] The present disclosure further describes methods of inhibiting PDGFR kinases and treating cancers and disorders associated with inhibition of PDGFR kinases including lung adenocarcinoma, squamous cell lung cancer, glioblastoma, pediatric glioma, astrocytomas, sarcomas, gastrointestinal stromal tumors, malignant peripheral nerve sheath sarcoma, intimal sarcomas, hypereosinophilic syndrome, idiopathic hypereosinophilic syndrome, chronic eosinophilic leukemia, eosinophilia-associated acute myeloid leukemia, or lymphoblastic T-cell lymphoma.

[25] The disclosure also describes methods of inhibiting PDGFRα kinase, oncogenic PDGFRα missense mutations, oncogenic deletion PDGFRα mutations, oncogenic *PDGFR*α gene rearrangements leading to PDGFRα fusion proteins, or oncogenic *PDGFRα* gene amplification.

[26] The disclosure also describes methods of use of 1-[4-bromo-5-[1-ethyl-7-(methylamino)-2-oxo-1,2-dihydro-1,6-naphthyridin-3-yl]-2-fluorophenyl]-3-phenylurea or 1-(5-(7-amino-1-ethyl-2-oxo-1,2-dihydro-1,6-naphthyridin-3-yl)-4-bromo-2-fluorophenyl)-3-phenylurea.

Claims:

1. Use of 1-[4-bromo-5-[1-ethyl-7-(methylamino)-2-oxo-1,2-dihydro-1,6-naphthyridin-3-yl]-2-fluorophenyl]-3-phenylurea, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for treating or preventing a PDGFR kinase-mediated tumor growth or tumor progression.

2. The use of claim 1, wherein tumor growth or tumor progression is caused by one or more of PDGFRα kinase overexpression, oncogenic *PDGFR*α missense mutations, oncogenic deletion *PDGFR*α mutations, oncogenic *PDGFR*α gene rearrangements leading to PDGFRα fusion proteins, *PDGFR*α intragenic in-frame deletions, or oncogenic *PDGFR*α gene amplification.

3. The use of claim 1 or 2, wherein tumor growth or tumor progression is caused by PDGFRα kinase overexpression.

4. The use of claim 1 or 2, wherein tumor growth or tumor progression is caused by oncogenic *PDGFR*α missense mutations or oncogenic deletion *PDGFR*α mutations.

5. The use of claim 1 or 2, wherein tumor growth or tumor progression is caused by oncogenic *PDGFR*α gene rearrangements leading to PDGFRα fusion proteins or *PDGFR*α intragenic in-frame deletions.

6. The use of claim 1 or 2, wherein tumor growth or tumor progression is caused by oncogenic *PDGFR*α gene amplification.

7. The use of any one of claims 1-6, wherein the tumor is lung adenocarcinoma, squamous cell lung cancer, glioblastoma, pediatric glioma, astrocytomas, sarcomas, gastrointestinal stromal tumors, malignant peripheral nerve sheath sarcoma, intimal sarcomas, hypereosinophilic syndrome, idiopathic hypereosinophilic syndrome, chronic eosinophilic leukemia, eosinophilia-associated acute myeloid leukemia, or lymphoblastic T-cell lymphoma.

8. The use of any one of claims 1-7, wherein the tumor is glioblastoma.

9. The use of any one of claims 1-7, wherein the tumor is gastrointestinal stromal tumors.

10. The use of any one of claims 1-9, wherein 1-[4-bromo-5-[1-ethyl-7-(methylamino)-2-oxo-1,2-dihydro-1,6-naphthyridin-3-yl]-2-fluorophenyl]-3-phenylurea, or a pharmaceutically acceptable salt thereof is to be administered as a single agent or in combination with one or more

additional therapeutic agents including cancer-targeted biologicals, immune checkpoint inhibitors, chemotherapeutic agents, or other cancer targeted therapeutic agents.

11. The use of claim 10, wherein the additional therapeutic agent is selected from the group consisting of cytotoxic agent, cisplatin, doxorubicin, etoposide, irinotecan, topotecan, paclitaxel, docetaxel, the epothilones, tamoxifen, 5-fluorouracil, methotrexate, temozolomide, cyclophosphamide, lonafarib, tipifarnib, 4-((5-((4-(3-chlorophenyl)-3-oxopiperazin-1-yl)methyl)-1H-imidazol-1-yl)methyl)benzonitrile hydrochloride, (R)-1-((1H-imidazol-5-yl)methyl)-3-benzyl-4-(thiophen-2-ylsulfonyl)-2,3,4,5-tetrahydro-1H-benzo diazepine-7-carbonitrile, cetuximab, imatinib, interferon alfa-2b, Pegylated interferon alfa-2b, aromatase combinations, gemcitabine, uracil mustard, chlormethine, ifosfamide, melphalan, chlorambucil, pipobroman, triethylenemelamine, triethylenethiophosphoramine, busulfan, carmustine, lomustine, streptozocin, dacarbazine, floxuridine, cytarabine, 6-mercaptopurine, 6-thioguanine, fludarabine phosphate, leucovorin, oxaliplatin, pentostatine, vinblastine, vincristine, vindesine, bleomycin, dactinomycin, daunorubicin, epirubicin, idarubicin, mithramycin, deoxycoformycin, mitomycin -C, L-asparaginase, teniposide 17α-ethinyl estradiol, diethylstilbestrol, testosterone, prednisone, fluoxymesterone, dromostanolone propionate, testolactone, megestrol acetate, methylprednisolone, methyltestosterone, prednisolone, triamcinolone, chlorotrianisene, 17α-hydroxyprogesterone, aminoglutethimide, estramustine, medroxyprogesterone acetate, leuprolide acetate, flutamide, toremifene citrate, goserelin acetate, carboplatin, hydroxyurea, amsacrine, procarbazine, mitotane, mitoxantrone, levamisole, vinorelbine, anastrazole, letrozole, capecitabine, raloxifene, droloxafine, hexamethylmelamine, bevacizumab, trastuzumab, tositumomab, bortezomib, ibritumomab tiuxetan, arsenic trioxide, porfimer sodium, cetuximab, thioTEPA, altretamine, fulvestrant, exemestane, rituximab, alemtuzumab, dexamethasone, bicalutamide, chlorambucil, or valrubicin.

12. The use of claim 10, wherein the immune checkpoint inhibitor is selected from the group consisting of CTLA4 inhibitors ipilimumab and tremelimumab; PD1 inhibitors pembrolizumab, and nivolumab; PDL1 inhibitors atezolizumab (formerly MPDL3280A), durvalumab (MEDI4736), avelumab, and monoclonal antibody PDR001; 4‑1BB ligand inhibitors urelumab and utomilumab PF05082566; OX40 agonist monoclonal antibody MEDI6469; glucocorticoid-induced tumor necrosis factor receptor (GITR) inhibitor monoclonal antibody TRX518; CD27

inhibitor varlilumab; TNFRSF25–TL1A inhibitors; CD40 agonist monoclonal antibody CP 870893; HVEM–LIGHT–LTA and HVEM–BTLA–CD160 inhibitors; LAG3 inhibitors monoclonal antibody BMS 986016; TIM3 inhibitors; Siglecs inhibitors; ICOS ligand agonists; B7‑H3 inhibitor enoblituzumab MGA271; B7‑H4 inhibitors; VISTA inhibitors; HHLA2–TMIGD2 inhibitors; inhibitors of butyrophilins; BTNL2 inhibitors; CD244–CD48 inhibitors; inhibitors of TIGIT and PVR family members; KIRs inhibitor lirilumab; inhibitors of ILTs and LIRs; NKG2D and NKG2A inhibitor monalizumab IPH2201; inhibitors of MICA and MICB; CD244 inhibitors; CSF1R inhibitors emactuzumab, cabiralizumab, pexidartinib, ARRY382, and BLZ945; IDO inhibitor (3E)-3-[(3-bromo-4-fluoroanilino)-nitrosomethylidene]-4-[2-(sulfamoylamino)ethylamino]-1,2,5-oxadiazole INCB024360; TGFβ inhibitor galunisertib; Adenosine–CD39–CD73 inhibitors; CXCR4–CXCL12 inhibitors ulocuplumab and (3S,6S,9S,12R,17R,20S,23S,26S,29S,34aS)-N-((S)-1-amino-5-guanidino-1-oxopentan-2-yl)-26,29-bis(4-aminobutyl)-17-((S)-2-((S)-2-((S)-2-(4-fluorobenzamido)-5-guanidinopentanamido)-5-guanidinopentanamido)-3-(naphthalen-2-yl)propanamido)-6-(3-guanidinopropyl)-3,20-bis(4-hydroxybenzyl)-1,4,7,10,18,21,24,27,30-nonaoxo-9,23-bis(3-ureidopropyl)triacontahydro-1H,16H-pyrrolo[2,1-p][1,2]dithia[5,8,11,14,17,20,23,26,29]nonaazacyclodotriacontine-12-carboxamide BKT140; Phosphatidylserine inhibitors bavituximab; SIRPA–CD47 inhibitor monoclonal antibody CC 90002; VEGF inhibitor bevacizumab; and or Neuropilin inhibitor monoclonal antibody MNRP1685A.

13. The use of claim 11, wherein the additional therapeutic agent is temozolomide.

14. The use of claim 1, further comprising ionizing radiation to be administered.

15. The use of claim 1, further comprising temozolomide and ionizing radiation to be administered.

16. The use of claim 10, wherein the additional therapeutic agent is selected from the group consisting of AKT inhibitor, alkylating agent, all-trans retinoic acid, antiandrogen, azacitidine, BCL2 inhibitor, BCL-XL inhibitor, BCR-ABL inhibitor, BTK inhibitor, BTK/LCK/LYN inhibitor, CDK1/2/4/6/7/9 inhibitor, CDK4/6 inhibitor, CDK9 inhibitor, CBP/p300 inhibitor, EGFR inhibitor, endothelin receptor antagonist, ERK inhibitor, farnesyltransferase inhibitor, FLT3 inhibitor, glucocorticoid receptor agonist, HDM2 inhibitor, histone deacetylase inhibitor, IKKβ inhibitor, immunomodulatory drug (IMiD), ingenol, ionizing radiation, ITK inhibitor,

JAK1/JAK2/JAK3/TYK2 inhibitor, MEK inhibitor, midostaurin, MTOR inhibitor, PI3 kinase inhibitor, dual PI3 kinase/MTOR inhibitor, proteasome inhibitor, protein kinase C agonist, SUV39H1 inhibitor, TRAIL, VEGFR2 inhibitor, Wnt/β-catenin signaling inhibitor, decitabine, and anti-CD20 monoclonal antibody.

17. Use of 1-[4-bromo-5-[1-ethyl-7-(methylamino)-2-oxo-1,2-dihydro-1,6-naphthyridin-3-yl]-2-fluorophenyl]-3-phenylurea, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for treating lung adenocarcinoma, squamous cell lung cancer, glioblastoma, pediatric glioma, astrocytomas, sarcomas, gastrointestinal stromal tumors, malignant peripheral nerve sheath sarcoma, intimal sarcomas, hypereosinophilic syndrome, idiopathic hypereosinophilic syndrome, chronic eosinophilic leukemia, eosinophilia-associated acute myeloid leukemia, or lymphoblastic T-cell lymphoma by inhibiting PDGFR kinase.

18. The use of claim 17, wherein the PDGFR kinase is *PDGFR*α or *PDGFR*β.

19. The use of claim 17, further comprising one or more additional therapeutic agents including a cancer-targeted biological, immune checkpoint inhibitor, chemotherapeutic agent, or other cancer targeted therapeutic agent to be administered.

20. The use of claim 19, wherein the additional therapeutic agent is selected from the group consisting of cytotoxic agent, cisplatin, doxorubicin, etoposide, irinotecan, topotecan, paclitaxel, docetaxel, the epothilones, tamoxifen, 5-fluorouracil, methotrexate, temozolomide, cyclophosphamide, lonafarib, tipifarnib, 4-((5-((4-(3-chlorophenyl)-3-oxopiperazin-1-yl)methyl)-1H-imidazol-1-yl)methyl)benzonitrile hydrochloride, (R)-1-((1H-imidazol-5-yl)methyl)-3-benzyl-4-(thiophen-2-ylsulfonyl)-2,3,4,5-tetrahydro-1H-benzo diazepine-7-carbonitrile, cetuximab, imatinib, interferon alfa-2b, Pegylated interferon alfa-2b, aromatase combinations, gemcitabine, uracil mustard, chlormethine, ifosfamide, melphalan, chlorambucil, pipobroman, triethylenemelamine, triethylenethiophosphoramine, busulfan, carmustine, lomustine, streptozocin, dacarbazine, floxuridine, cytarabine, 6-mercaptopurine, 6-thioguanine, fludarabine phosphate, leucovorin, oxaliplatin, pentostatine, vinblastine, vincristine, vindesine, bleomycin, dactinomycin, daunorubicin, epirubicin, idarubicin, mithramycin, deoxycoformycin, mitomycin -C, L-asparaginase, teniposide 17α-ethinyl estradiol, diethylstilbestrol, testosterone, prednisone, fluoxymesterone, dromostanolone propionate, testolactone, megestrol acetate, methylprednisolone, methyltestosterone, prednisolone, triamcinolone, chlorotrianisene, 17α-

hydroxyprogesterone, aminoglutethimide, estramustine, medroxyprogesterone acetate, leuprolide acetate, flutamide, toremifene citrate, goserelin acetate, carboplatin, hydroxyurea, amsacrine, procarbazine, mitotane, mitoxantrone, levamisole, vinorelbine, anastrazole, letrozole, capecitabine, raloxifene, droloxafine, hexamethylmelamine, bevacizumab, trastuzumab, tositumomab, bortezomib, ibritumomab tiuxetan, arsenic trioxide, porfimer sodium, cetuximab, thioTEPA, altretamine, fulvestrant, exemestane, rituximab, alemtuzumab, dexamethasone, bicalutamide, chlorambucil, or valrubicin.

21. The use of claim 19, wherein the immune checkpoint inhibitor is selected from the group consisting of CTLA4 inhibitors ipilimumab and tremelimumab; PD1 inhibitors pembrolizumab, and nivolumab; PDL1 inhibitors atezolizumab (formerly MPDL3280A), durvalumab (formerly MEDI4736), avelumab, and monoclonal antibody PDR001; 4‑1BB ligand inhibitors urelumab and utomilumab (PF05082566); OX40 ligand agonist monoclonal antibody MEDI6469; glucocorticoid-induced tumor necrosis factor receptor (GITR) inhibitor monoclonal antibody TRX518; CD27 inhibitor varlilumab; TNFRSF25–TL1A inhibitors; CD40 ligand agonist monoclonal antibody CP 870893; HVEM–LIGHT–LTA and HVEM–BTLA–CD160 inhibitors; LAG3 inhibitors monoclonal antibody BMS 986016; TIM3 inhibitors; Siglecs inhibitors; ICOS ligand agonists; B7‑H3 inhibitor EnoblituzumabMGA271; B7‑H4 inhibitors; VISTA inhibitors; HHLA2–TMIGD2 inhibitors; inhibitors of butyrophilins; BTNL2 inhibitors; CD244–CD48 inhibitors; inhibitors of TIGIT and PVR family members; KIRs inhibitor lirilumab; inhibitors of ILTs and LIRs; NKG2D and NKG2A inhibitor monalizumab IPH2201; inhibitors of MICA and MICB; CD244 inhibitors; CSF1R inhibitors, emactuzumab, cabiralizumab, pexidartinib, ARRY382, and BLZ945; IDO inhibitor (3E)-3-[(3-bromo-4-fluoroanilino)-nitrosomethylidene]-4-[2-(sulfamoylamino)ethylamino]-1,2,5-oxadiazole INCB024360; TGFβ inhibitor galunisertib; Adenosine–CD39–CD73 inhibitors; CXCR4–CXCL12 inhibitors ulocuplumab and (3S,6S,9S,12R,17R,20S,23S,26S,29S,34aS)-N-((S)-1-amino-5-guanidino-1-oxopentan-2-yl)-26,29-bis(4-aminobutyl)-17-((S)-2-((S)-2-((S)-2-(4-fluorobenzamido)-5-guanidinopentanamido)-5-guanidinopentanamido)-3-(naphthalen-2-yl)propanamido)-6-(3-guanidinopropyl)-3,20-bis(4-hydroxybenzyl)-1,4,7,10,18,21,24,27,30-nonaoxo-9,23-bis(3-ureidopropyl)triacontahydro-1H,16H-pyrrolo[2,1-p][1,2]dithia[5,8,11,14,17,20,23,26,29]nonaazacyclodotriacontine-12-

carboxamide BKT140; Phosphatidylserine inhibitors bavituximab; SIRPA–CD47 inhibitor monoclonal antibody CC 90002; VEGF inhibitors bevacizumab; and or neuropilin inhibitor monoclonal antibody MNRP1685A.

22. The use of claim 19, wherein the additional therapeutic agent is temozolomide.

23. The use of claim 17, further comprising ionizing radiation to be administered.

24. The use of claim 17, further comprising temozolomide and ionizing radiation to be administered.

25. The use of claim 19, wherein the additional therapeutic agent is selected from the group consisting of AKT inhibitor, alkylating agent, all-trans retinoic acid, antiandrogen, azacitidine, BCL2 inhibitor, BCL-XL inhibitor, BCR-ABL inhibitor, BTK inhibitor, BTK/LCK/LYN inhibitor, CDK1/2/4/6/7/9 inhibitor, CDK4/6 inhibitor, CDK9 inhibitor, CBP/p300 inhibitor, EGFR inhibitor, endothelin receptor antagonist, ERK inhibitor, farnesyltransferase inhibitor, FLT3 inhibitor, glucocorticoid receptor agonist, HDM2 inhibitor, histone deacetylase inhibitor, IKKβ inhibitor, immunomodulatory drug (IMiD), ingenol, ionizing radiation, ITK inhibitor, JAK1/JAK2/JAK3/TYK2 inhibitor, MEK inhibitor, midostaurin, MTOR inhibitor, PI3 kinase inhibitor, dual PI3 kinase/MTOR inhibitor, proteasome inhibitor, protein kinase C agonist, SUV39H1 inhibitor, TRAIL, VEGFR2 inhibitor, Wnt/β-catenin signaling inhibitor, decitabine, and anti-CD20 monoclonal antibody.

26. Use of 1-[4-bromo-5-[1-ethyl-7-(methylamino)-2-oxo-1,2-dihydro-1,6-naphthyridin-3-yl]-2-fluorophenyl]-3-phenylurea, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for treating glioblastoma.

27. The use of claim 26, further comprising one or more additional therapeutic agent including a cancer-targeted biological, immune checkpoint inhibitor, chemotherapeutic agent, or other cancer targed therapeutic agend to be administered.

28. The use of claim 27, wherein the additional therapeutic agent is selected from the group consisting of cytotoxic agent, cisplatin, doxorubicin, etoposide, irinotecan, topotecan, paclitaxel, docetaxel, the epothilones, tamoxifen, 5-fluorouracil, methotrexate, temozolomide, cyclophosphamide, lonafarib, tipifarnib, 4-((5-((4-(3-chlorophenyl)-3-oxopiperazin-1-yl)methyl)-1H-imidazol-1-yl)methyl)benzonitrile hydrochloride, (R)-1-((1H-imidazol-5-yl)methyl)-3-benzyl-4-(thiophen-2-ylsulfonyl)-2,3,4,5-tetrahydro-1H-benzo diazepine-7-

carbonitrile, cetuximab, imatinib, interferon alfa-2b, Pegylated interferon alfa-2b, aromatase combinations, gemcitabine, uracil mustard, chlormethine, ifosfamide, melphalan, chlorambucil, pipobroman, triethylenemelamine, triethylenethiophosphoramine, busulfan, carmustine, lomustine, streptozocin, dacarbazine, floxuridine, cytarabine, 6-mercaptopurine, 6-thioguanine, fludarabine phosphate, leucovorin, oxaliplatin, pentostatine, vinblastine, vincristine, vindesine, bleomycin, dactinomycin, daunorubicin, epirubicin, idarubicin, mithramycin, deoxycoformycin, mitomycin -C, L-asparaginase, teniposide 17α-ethinyl estradiol, diethylstilbestrol, testosterone, prednisone, fluoxymesterone, dromostanolone propionate, testolactone, megestrol acetate, methylprednisolone, methyltestosterone, prednisolone, triamcinolone, chlorotrianisene, 17α-hydroxyprogesterone, aminoglutethimide, estramustine, medroxyprogesterone acetate, leuprolide acetate, flutamide, toremifene citrate, goserelin acetate, carboplatin, hydroxyurea, amsacrine, procarbazine, mitotane, mitoxantrone, levamisole, vinorelbine, anastrazole, letrozole, capecitabine, raloxifene, droloxafine, hexamethylmelamine, bevacizumab, trastuzumab, tositumomab, bortezomib, ibritumomab tiuxetan, arsenic trioxide, porfimer sodium, cetuximab, thioTEPA, altretamine, fulvestrant, exemestane, rituximab, alemtuzumab, dexamethasone, bicalutamide, chlorambucil, or valrubicin.

29. The use of claim 27, wherein the immune checkpoint inhibitor is selected from the group consisting of CTLA4 inhibitors ipilimumab and tremelimumab; PD1 inhibitors pembrolizumab, and nivolumab; PDL1 inhibitors atezolizumab (formerly MPDL3280A), durvalumab (formerly MEDI4736), avelumab, and monoclonal antibody PDR001; 4‑1BB ligand inhibitors urelumab and utomilumab PF 05082566; OX40 ligand agonist monoclonal antibody MEDI6469; glucocorticoid-induced tumor necrosis factor receptor (GITR) inhibitor monoclonal antibody TRX518; CD27 inhibitor varlilumab; TNFRSF25–TL1A inhibitors; CD40 ligand agonist monoclonal antibody CP 870893; HVEM–LIGHT–LTA and HVEM–BTLA–CD160 inhibitors; LAG3 inhibitors monoclonal antibody BMS 986016; TIM3 inhibitors; Siglecs inhibitors; ICOS ligand agonists; B7‑H3 inhibitor EnoblituzumabMGA271; B7‑H4 inhibitors; VISTA inhibitors; HHLA2–TMIGD2 inhibitors; inhibitors of butyrophilins; BTNL2 inhibitors; CD244–CD48 inhibitors; inhibitors of TIGIT and PVR family members; KIRs inhibitor lirilumab; inhibitors of ILTs and LIRs; NKG2D and NKG2A inhibitor monalizumab IPH2201; inhibitors of MICA and

MICB; CD244 inhibitors; CSF1R inhibitors emactuzumab, cabiralizumab, pexidartinib, ARRY382, and BLZ945; IDO inhibitor (3E)-3-[(3-bromo-4-fluoroanilino)-nitrosomethylidene]-4-[2-(sulfamoylamino)ethylamino]-1,2,5-oxadiazoleINCB024360; TGFβ inhibitor galunisertib; Adenosine–CD39–CD73 inhibitors; CXCR4–CXCL12 inhibitors ulocuplumab and (3S,6S,9S,12R,17R,20S,23S,26S,29S,34aS)-N-((S)-1-amino-5-guanidino-1-oxopentan-2-yl)-26,29-bis(4-aminobutyl)-17-((S)-2-((S)-2-((S)-2-(4-fluorobenzamido)-5-guanidinopentanamido)-5-guanidinopentanamido)-3-(naphthalen-2-yl)propanamido)-6-(3-guanidinopropyl)-3,20-bis(4-hydroxybenzyl)-1,4,7,10,18,21,24,27,30-nonaoxo-9,23-bis(3-ureidopropyl)triacontahydro-1H,16H-pyrrolo[2,1-p][1,2]dithia[5,8,11,14,17,20,23,26,29]nonaazacyclodotriacontine-12-carboxamide BKT140; Phosphatidylserine inhibitors bavituximab; SIRPA–CD47 inhibitor monoclonal antibody CC 90002; VEGF inhibitors bevacizumab; and or neuropilin inhibitor monoclonal antibody MNRP1685A.

30. The use of claim 28, wherein the additional therapeutic agent is temozolomide.

31. The use of claim 26, further comprising ionizing radiation to be administered.

32. The use of claim 26, further comprising temozolomide and ionizing radiation to be administered.

33. The use of claim 27, wherein the additional therapeutic agent is selected from the group consisting of AKT inhibitor, alkylating agent, all-trans retinoic acid, antiandrogen, azacitidine, BCL2 inhibitor, BCL-XL inhibitor, BCR-ABL inhibitor, BTK inhibitor, BTK/LCK/LYN inhibitor, CDK1/2/4/6/7/9 inhibitor, CDK4/6 inhibitor, CDK9 inhibitor, CBP/p300 inhibitor, EGFR inhibitor, endothelin receptor antagonist, ERK inhibitor, farnesyltransferase inhibitor, FLT3 inhibitor, glucocorticoid receptor agonist, HDM2 inhibitor, histone deacetylase inhibitor, IKKβ inhibitor, immunomodulatory drug (IMiD), ingenol, ionizing radiation, ITK inhibitor, JAK1/JAK2/JAK3/TYK2 inhibitor, MEK inhibitor, midostaurin, MTOR inhibitor, PI3 kinase inhibitor, dual PI3 kinase/MTOR inhibitor, proteasome inhibitor, protein kinase C agonist, SUV39H1 inhibitor, TRAIL, VEGFR2 inhibitor, Wnt/β-catenin signaling inhibitor, decitabine, and anti-CD20 monoclonal antibody.

34. Use of 1-[4-bromo-5-[1-ethyl-7-(methylamino)-2-oxo-1,2-dihydro-1,6-naphthyridin-3-yl]-2-fluorophenyl]-3-phenylurea, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for treating PDGFRα-mediated gastrointestinal stromal tumors.

35. The use of claim 34, further comprising one or more additional therapeutic agent including a cancer-targeted biological, immune checkpoint inhibitor, chemotherapeutic agent, or other cancer targed therapeutic agent to be administered.

36. The use of claim 35, wherein the additional therapeutic agent is selected from the group consisting of cytotoxic agent, cisplatin, doxorubicin, etoposide, irinotecan, topotecan, paclitaxel, docetaxel, the epothilones, tamoxifen, 5-fluorouracil, methotrexate, temozolomide, cyclophosphamide, lonafarib, tipifarnib, 4-((5-((4-(3-chlorophenyl)-3-oxopiperazin-1-yl)methyl)-1H-imidazol-1-yl)methyl)benzonitrile hydrochloride, (R)-1-((1H-imidazol-5-yl)methyl)-3-benzyl-4-(thiophen-2-ylsulfonyl)-2,3,4,5-tetrahydro-1H-benzo diazepine-7-carbonitrile, cetuximab, imatinib, interferon alfa-2b, Pegylated interferon alfa-2b, aromatase combinations, gemcitabine, uracil mustard, chlormethine, ifosfamide, melphalan, chlorambucil, pipobroman, triethylenemelamine, triethylenethiophosphoramine, busulfan, carmustine, lomustine, streptozocin, dacarbazine, floxuridine, cytarabine, 6-mercaptopurine, 6-thioguanine, fludarabine phosphate, leucovorin, oxaliplatin, pentostatine, vinblastine, vincristine, vindesine, bleomycin, dactinomycin, daunorubicin, epirubicin, idarubicin, mithramycin, deoxycoformycin, mitomycin -C, L-asparaginase, teniposide 17α-ethinyl estradiol, diethylstilbestrol, testosterone, prednisone, fluoxymesterone, dromostanolone propionate, testolactone, megestrol acetate, methylprednisolone, methyltestosterone, prednisolone, triamcinolone, chlorotrianisene, 17α-hydroxyprogesterone, aminoglutethimide, estramustine, medroxyprogesterone acetate, leuprolide acetate, flutamide, toremifene citrate, goserelin acetate, carboplatin, hydroxyurea, amsacrine, procarbazine, mitotane, mitoxantrone, levamisole, vinorelbine, anastrazole, letrozole, capecitabine, raloxifene, droloxafine, hexamethylmelamine, bevacizumab, trastuzumab, tositumomab, bortezomib, ibritumomab tiuxetan, arsenic trioxide, porfimer sodium, cetuximab, thioTEPA, altretamine, fulvestrant, exemestane, rituximab, alemtuzumab, dexamethasone, bicalutamide, chlorambucil, or valrubicin.

37. The use of claim 35, wherein the immune checkpoint inhibitor is selected from the group consisting of CTLA4 inhibitors ipilimumab and tremelimumab; PD1 inhibitors pembrolizumab, and nivolumab; PDL1 inhibitors atezolizumab (formerly MPDL3280A), durvalumab MEDI4736, avelumab, and monoclonal antibody PDR001; 4‑1BB ligand inhibitors urelumab and utomilumab PF05082566; OX40 ligand agonist monoclonal antibody MEDI6469;

glucocorticoid-induced tumor necrosis factor receptor (GITR) inhibitor monoclonal antibody TRX518; CD27 inhibitor varlilumab; TNFRSF25–TL1A inhibitors; CD40 ligand agonist monoclonal antibody CP870893; HVEM–LIGHT–LTA and HVEM–BTLA–CD160 inhibitors; LAG3 inhibitors monoclonal antibody BMS 986016; TIM3 inhibitors; Siglecs inhibitors; ICOS ligand agonists; B7‑H3 inhibitor enoblituzumab MGA271; B7‑H4 inhibitors; VISTA inhibitors; HHLA2–TMIGD2 inhibitors; inhibitors of butyrophilins; BTNL2 inhibitors; CD244–CD48 inhibitors; inhibitors of TIGIT and PVR family members; KIRs inhibitor lirilumab; inhibitors of ILTs and LIRs; NKG2D and NKG2A inhibitor monalizumab IPH2201; inhibitors of MICA and MICB; CD244 inhibitors; CSF1R inhibitor emactuzumab, cabiralizumab, pexidartinib, AMG382, and BLZ945; IDO inhibitor (3E)-3-[(3-bromo-4-fluoroanilino)-nitrosomethylidene]-4-[2-(sulfamoylamino)ethylamino]-1,2,5-oxadiazoleINCB024360; TGFβ inhibitor galunisertib; Adenosine–CD39–CD73 inhibitors; CXCR4–CXCL12 inhibitors ulocuplumab and (3S,6S,9S,12R,17R,20S,23S,26S,29S,34aS)-N-((S)-1-amino-5-guanidino-1-oxopentan-2-yl)-26,29-bis(4-aminobutyl)-17-((S)-2-((S)-2-((S)-2-(4-fluorobenzamido)-5-guanidinopentanamido)-5-guanidinopentanamido)-3-(naphthalen-2-yl)propanamido)-6-(3-guanidinopropyl)-3,20-bis(4-hydroxybenzyl)-1,4,7,10,18,21,24,27,30-nonaoxo-9,23-bis(3-ureidopropyl)triacontahydro-1H,16H-pyrrolo[2,1-p][1,2]dithia[5,8,11,14,17,20,23,26,29]nonaazacyclodotriacontine-12-carboxamide BKT140; Phosphatidylserine inhibitors bavituximab; SIRPA–CD47 inhibitor monoclonal antibody CC 90002; VEGF inhibitor bevacizumab; and or neuropilin inhibitor monoclonal antibody MNRP1685A.

38. The use of claim 36, wherein the additional therapeutic agent is temozolomide.

39. The use of claim 34, further comprising ionizing radiation to be administered.

40. The use of claim 34, further comprising temozolomide and ionizing radiation to be administered.

41. The use of claim 35, wherein the additional therapeutic agent is selected from the group consisting of AKT inhibitor, alkylating agent, all-trans retinoic acid, antiandrogen, azacitidine, BCL2 inhibitor, BCL-XL inhibitor, BCR-ABL inhibitor, BTK inhibitor, BTK/LCK/LYN inhibitor, CDK1/2/4/6/7/9 inhibitor, CDK4/6 inhibitor, CDK9 inhibitor, CBP/p300 inhibitor, EGFR inhibitor, endothelin receptor antagonist, ERK inhibitor, farnesyltransferase inhibitor, FLT3 inhibitor, glucocorticoid receptor agonist, HDM2 inhibitor, histone deacetylase inhibitor,

IKKβ inhibitor, immunomodulatory drug (IMiD), ingenol, ionizing radiation, ITK inhibitor, JAK1/JAK2/JAK3/TYK2 inhibitor, MEK inhibitor, midostaurin, MTOR inhibitor, PI3 kinase inhibitor, dual PI3 kinase/MTOR inhibitor, proteasome inhibitor, protein kinase C agonist, SUV39H1 inhibitor, TRAIL, VEGFR2 inhibitor, Wnt/β-catenin signaling inhibitor, decitabine, and anti-CD20 monoclonal antibody.