

WHAT IS CLAIMED IS:

1. A pharmaceutical composition, comprising a T-cell activator and/or proliferator, one or more immune checkpoint inhibitor, and a FPPS inhibitor.
2. The composition of claim 1, wherein the T-cell activator and/or proliferator is a tubulin binding agent.
3. The composition of claim 2, wherein the tubulin binding agent is selected from a group consisting of vinblastine, vincristine, vinorelbine, vinflunine, cryptophycin 52, halichondrins, dolastatins, hemicasterlins, colchicine, combretastatins, 2-methoxyestradiol, E7010, paclitaxel, docetaxel, epothilone, discodermolide, and plinabulin.
4. The composition of claim 2 or 3, wherein the tubulin binding agent is plinabulin.
5. The composition of claim 1, wherein the FPPS inhibitor is a nitrogen-containing bisphosphonate compound.
6. The composition of claim 1, wherein the FPPS inhibitor is quinolone derivative compound or an allosteric non-bisphosphonate compound.
7. The composition of claim 1 or 5, wherein the FPPS inhibitor is selected from pamidronate, alendronate, risedronate, zoledronate, and ibandronate, or an acid or salt thereof.
8. The composition of claim 1, wherein the immune checkpoint inhibitor is an inhibitor of PD-1, PD-L1, PD-L2, PD-L3, PD-L4, CTLA-4, LAG3, B7-H3, B7-H4, KIR or TIM3.
9. The composition of claim 1 or 8, wherein the immune checkpoint inhibitor is a PD-1 antibody, a PD-L1 antibody, a PD-L2 antibody, a CTLA-4 antibody, or a combination thereof.
10. The composition of claim 9, wherein the a PD-1 antibody, a PD-L1 antibody, a PD-L2 antibody, a CTLA-4 antibody is selected from α -CD3-APC, α -CD3-APC-H7, α -

CD4-ECD, α -CD4-PB, α -CD8-PE-Cy7, α -CD-8-PerCP-Cy5.5, α -CD11c-APC, α -CD11b-PE-Cy7, α -CD11b-AF700, α -CD14-FITC, α -CD16-PB, α -CD19-AF780, α -CD19-AF700, α -CD20-PO, α -CD25-PE-Cy7, α -CD40-APC, α -CD45-Biotin, Streptavidin-BV605, α -CD62L-ECD, α -CD69-APC-Cy7, α -CD80-FITC, α -CD83-Biotin, Streptavidin-PE-Cy7, α -CD86-PE-Cy7, α -CD86-PE, α -CD123-PE, α -CD154-PE, α -CD161-PE, α -CTLA4-PE-Cy7, α -FoxP3-AF488 (clone 259D), IgG1-isotype-AF488, α -ICOS (CD278)-PE, α -HLA-A2-PE, α -HLA-DR-PB, α -HLA-DR-PerCPCy5.5, α -PD1-APC, VISTA, co-stimulatory molecule OX40, and CD137.

11. The composition of any one of claims 1 to 10, further comprising one or more pharmaceutically acceptable excipients.

12. The composition of any one of claims 1 or 9, wherein the immune checkpoint inhibitor is nivolumab, pembrolizumab, pidilizumab, ipilimumab, BMS 936559, atezolizumab, durvalimumab, or any combinations thereof.

13. The composition of claim 1, further comprising one or more additional chemotherapeutic agent.

14. A method for treating or ameliorating cancer in a subject, comprising administering a T-cell activator, one or more immune checkpoint inhibitor, and a FPPS inhibitor to a subject in need thereof.

15. The method of claim 14, wherein the T-cell activator is a tubulin binding agent.

16. The method of claim 15, wherein the tubulin binding agent is selected from a group consisting of vinblastine, vincristine, vinorelbine, vinflunine, crytophyecin 52, halichondrins, dolastatins, hemicasterlins, colchicine, combretastatins, 2-methoxyestradiol, E7010, paclitaxel, docetaxel, epothilone, discodermolide, and plinabulin.

17. The method of claim 15 or 16, wherein the tubulin binding agent is plinabulin.

18. The method of claim 14, wherein the FPPS inhibitor is a nitrogen-containing bisphosphonate compound.

19. The method of claim 14, wherein the FPPS inhibitor is quinolone derivative compound or an allosteric non-bisphosphonate compound.

20. The method of claim 14 or 15, wherein the FPPS inhibitor is selected from pamidronate, alendronate, risedronate, zoledronate, and ibandronate, or an acid or salt thereof.

21. The method of claim 14, wherein the cancer comprises cells expressing farnesyl pyrophosphate synthetase.

22. The method of claim 14, wherein the cancer is a low-grade immunogenic cancer

23. The method of claim 14, wherein the cancer is rhabdoid tumor, Ewing sarcoma, thyroid cancer, acute myeloid leukemia (AML), medulloblastoma cancer, carcinoid cancer, neuroblastoma, prostate cancer, chronic lymphocytic leukemia (CLL), low-grade glioma, breast cancer, pancreas, multiple myeloma, kidney papillary cell, ovarian cancer, glioblastoma multiforme, cervical, diffuse large B-cell lymphoma (DLBCL), head and neck, colorectal, esophageal adenocarcinoma, bladder cancer, lung adenocarcinoma, lung squamous cell carcinoma, or melanoma.

24. The method of claim 14, wherein the cancer is selected from breast cancer, colon cancer, rectal cancer, lung cancer, prostate cancer, melanoma, leukemia, ovarian cancer, gastric cancer, renal cell carcinoma, liver cancer, pancreatic cancer, lymphomas and myeloma.

25. The method of any one of claims 14 to 22, wherein the cancer is glioblastoma multiforme.

26. The method of any one of claims 14 to 25, wherein the immune checkpoint inhibitor is an inhibitor of PD-1, PD-L1, PD-L2, PD-L3, PD-L4, CTLA-4, LAG3, B7-H3, B7-H4, KIR or TIM3.

27. The method of claim 14, further comprising co-administering one or more additional chemotherapeutic agent.

28. The method of claim any one of claims 13 to 27, comprising co-administering a first immune checkpoint inhibitor and a second immune checkpoint inhibitor, wherein the first immune checkpoint inhibitor is different from the second immune checkpoint inhibitor.

29. The method of claim 28, wherein the first and the second immune checkpoint inhibitor is independently an inhibitor of PD-1, PD-L1, PD-L2, PD-L3, PD-L4, CTLA-4, LAG3, B7-H3, B7-H4, KIR or TIM3.

30. The method of claim 29, wherein the first immune checkpoint inhibitor is a PD-1 inhibitor, and the second immune checkpoint inhibitor is a CTLA-4 inhibitor.

31. The method of any one of claims 13 to 30, wherein the immune checkpoint inhibitor is an antibody.

32. The method of claim 31, wherein the immune checkpoint inhibitor is a PD-1 antibody, a PD-L1 antibody, a PD-L2 antibody, or a CTLA-4 antibody.

33. The method of claim 32, wherein the antibody is selected from α -CD3-APC, α -CD3-APC-H7, α -CD4-ECD, α -CD4-PB, α -CD8-PE-Cy7, α -CD-8-PerCP-Cy5.5, α -CD11c-APC, α -CD11b-PE-Cy7, α -CD11b-AF700, α -CD14-FITC, α -CD16-PB, α -CD19-AF780, α -CD19-AF700, α -CD20-PO, α -CD25-PE-Cy7, α -CD40-APC, α -CD45-Biotin, Streptavidin-BV605, α -CD62L-ECD, α -CD69-APC-Cy7, α -CD80-FITC, α -CD83-Biotin, Streptavidin-PE-Cy7, α -CD86-PE-Cy7, α -CD86-PE, α -CD123-PE, α -CD154-PE, α -CD161-PE, α -CTLA4-PE-Cy7, α -FoxP3-AF488 (clone 259D), IgG1-isotype-AF488, α -ICOS (CD278)-PE, α -HLA-A2-PE, α -HLA-DR-PB, α -HLA-DR-PerCPCy5.5, α -PD1-APC, VISTA, co-stimulatory molecule OX40, and CD137.