

We claim:

1. A composition comprising a dendrimer complexed or covalently conjugated with one or more immunomodulatory agents in an amount effective to suppress or inhibit one or more immunosuppressive cells associated with a tumor in a subject in need thereof.
2. The composition of claim 1, wherein the dendrimer is a hydroxyl-terminated dendrimer.
3. The composition of claim 1 or 2, wherein the dendrimer is a generation 4, generation 5, or generation 6 PAMAM dendrimer.
4. The composition of any one of claims 1-3, wherein the immunomodulatory agents are one or more selected from the group consisting of STING agonists, CSF1R inhibitors, PARP inhibitors, VEGFR tyrosine kinase inhibitors, MEK inhibitors, glutaminase inhibitors, TIE II antagonists, CXCR2 inhibitors, CD73 inhibitors, arginase inhibitors, PI3K inhibitors, TLR4 agonists, TLR7 agonists, SHP2 inhibitors, cytotoxic agents, and combinations thereof.
5. The composition of claim 4, wherein the immunomodulatory agent is a STING agonist.
6. The composition of claim 5, wherein the STING agonist is a cyclic dinucleotide GMP-AMP or DMXAA.
7. The composition of claim 4, wherein the immunomodulatory agent is a CSF1R inhibitor.
8. The composition of claim 7, wherein the CSF1R inhibitor is selected from the group consisting of PLX3397, PLX108-01, ARRY-382, PLX7486, BLZ945, JNJ-40346527, and GW 2580.
9. The composition of claim 4, wherein the immunomodulatory agent is a PARP inhibitor.
10. The composition of claim 9, wherein the PARP inhibitor is selected from the group consisting of Olaparib, Veliparib, Niraparib, and Rucaparib.
11. The composition of claim 4, wherein the immunomodulatory agent is a VEGFR tyrosine kinase inhibitor.
12. The composition of claim 11, wherein the VEGFR tyrosine kinase inhibitor is selected from the group consisting of sunitinib, sorafenib,

pazopanib, vandetanib, axitinib, cediranib, vatalanib, dasatinib, nintedanib, and motesanib.

13. The composition of claim 11, wherein the VEGFR tyrosine kinase inhibitor is sunitinib, or a derivative or analog thereof.

14. The composition of claim 4, wherein the immunomodulatory agent is a MEK inhibitor.

15. The composition of claim 14, wherein the MEK inhibitor is selected from the group consisting of Trametinib, Cobimetinib, Binimetinib, Selumetinib, PD325901, PD035901, PD032901, and TAK-733.

16. The composition of claim 4, wherein the immunomodulatory agent is a glutaminase inhibitor.

17. The composition of claim 16, wherein the glutaminase inhibitor is selected from the group consisting of Bis-2-(5-phenylacetimido-1,2,4-thiadiazol-2-yl)ethyl sulfide (BPTES) and 6-diazo-5-oxo-L-norleucine (DON), azaserine, acivicin, and CB-839.

18. The composition of claim 4, wherein the immunomodulatory agent is a TIE II antagonist.

19. The composition of claim 4, wherein the immunomodulatory agent is a CXCR2 inhibitor.

20. The composition of claim 19, wherein the CXCR2 inhibitor is Navarixin, SB225002, or SB332235.

21. The composition of claim 4, wherein the immunomodulatory agent is a CD73 inhibitor.

22. The composition of claim 21, wherein the CD73 inhibitor is APCP, quercetin, or tenofovir, or a derivative, analogue thereof.

23. The composition of claim 4, wherein the immunomodulatory agent is an arginase inhibitor.

24. The composition of claim 23, wherein the arginase inhibitor is a derivative or analogue of 2-(S)-amino-6-boronoheptanoic acid.

25. The composition of claim 4, wherein the immunomodulatory agent is a PI3K inhibitor.

26. The composition of claim 25, wherein the PI3K inhibitor is alpelisib, serabelisib, pilaralisib, WX-037, dactolisib, prexasertib, voxtalisib, PX-866, ZSTK474, buparlisib, pictilisib, copanlisib, or a derivative, analogue thereof.

27. The composition of claim 4, wherein the immunomodulatory agent is a TLR4 agonist or a TLR7 agonist.
28. The composition of claim 4, wherein the immunomodulatory agent is a SHP2 inhibitor.
29. The composition of claim 4, wherein the immunomodulatory agent is a cytotoxic agent.
30. The composition of claim 29, wherein the cytotoxic agent is Auristatin E or Mertansine.
31. The composition of any one of claims 1-30, wherein the immunomodulatory agent is covalently conjugated to the dendrimer.
32. The composition of any one of claims 1-31, wherein the immunomodulatory agent is covalently conjugated to the dendrimer via a linker or spacer moiety.
33. The composition of claim 32, wherein the linker or spacer moiety is bound to the dendrimer via a linkage selected from the group consisting of an ether, ester, and amide linkage.
34. The composition of claim 32 or 33, wherein the linker or spacer moiety is bound to the dendrimer via an ether linkage.
35. The composition of any one of claims 32-34, wherein the linker or spacer moiety is bound to the immunomodulatory agent via a linkage selected from the group consisting of an ether, ester, and amide linkage.
36. The composition of any one of claims 32-35, wherein the linker or spacer moiety is bound to the immunomodulatory agent via an amide or ether linkage.
37. The composition of any one of claims 1-36, wherein the dendrimer is further complexed or conjugated with one or more chemotherapeutic agents.
38. The composition of claim 37, wherein the one or more chemotherapeutic agents are selected from the group consisting of amsacrine, bleomycin, busulfan, camptothecin, capecitabine, carboplatin, carmustine, chlorambucil, cisplatin, cladribine, clofarabine, crisantaspase, cyclophosphamide, cytarabine, dacarbazine, dactinomycin, daunorubicin, docetaxel, doxorubicin, epipodophyllotoxins, epirubicin, etoposide, etoposide phosphate, fludarabine, fluorouracil, gemcitabine, hydroxycarbamide, idarubicin, ifosfamide, innotecan, leucovorin, liposomal doxorubicin,

liposomal daunorubici , lomustine, mechlorethamine, melphalan, mercaptopurine, mesna, methotrexate, mitomycin, mitoxantrone, oxaliplatin, paclitaxel, pemetrexed, pentostatin, procarbazine, raltitrexed, satraplatin, streptozocin, teniposide, tegafur-uracil, temozolomide, teniposide, thiotepa, tioguanine, topotecan, treosulfan, vinblastine, vincristine, vindesine, vinorelbine, vorinostat, taxol, trichostatin A and derivatives thereof, trastuzumab, cetuximab, rituximab, bevacizumab, and combinations thereof.

39. The composition of any one of claims 1-38, in an amount effective to suppress or inhibit the one or more immunosuppressive cells associated with a tumor in a subject in need thereof.

40. The composition of any one of claims 1-39, wherein the dendrimer is further complexed or conjugated with one or more diagnostic or labelling agents in an amount effective to diagnose or label the one or more immunosuppressive cells associated with a tumor in a subject in need thereof.

41. The composition of any one of claims 1-40, wherein the immunosuppressive cells are myeloid-derived suppressor cells and/or tumor-associated macrophages (M2 macrophages).

42. A pharmaceutical composition comprising an effective amount of the composition of any one of claims 1-41.

43. A method of treating a cancer comprising administering to a subject in need thereof an effective amount of the pharmaceutical composition of claim 42.

44. The method of claim 43, wherein the one or more immunomodulatory agents are selected from the group consisting of STING agonists, CSF1R inhibitors, PARP inhibitors, VEGFR tyrosine kinase inhibitors, MEK inhibitors, glutaminase inhibitors, TIE II antagonists, CXCR2 inhibitors, CD73 inhibitors, arginase inhibitors, PI3K inhibitors, TLR4 agonists, TLR7 agonists, SHP2 inhibitors, cytotoxic agents, and combinations thereof.

45. The method of claim 43 or 44, wherein the cancer is breast cancer, ovarian cancer, uterine cancer, prostate cancer, testicular germ cell tumor, brain cancer, gastric cancer, esophagus cancer, lung cancer, liver cancer, renal cell cancer and colon cancer.

46. The method of any of claims 43-45, wherein the effective amount is effective to reduce tumor size.
47. A method of reducing or inhibiting one or more immunosuppressive cells at a site of tumor comprising administering to a subject identified as having cancer an effective amount of the pharmaceutical composition of claim 42.
48. The method of claim 47, wherein the immunosuppressive cells are myeloid-derived suppressor cells and/or tumor-associated macrophages (M2 macrophages).
49. A method for enhancing tumor-specific cytotoxic T cell responses in a subject identified as having cancer, comprising administering to the subject an effective amount of the pharmaceutical composition of claim 42.
50. The method of any one of claims 43-49 further comprising administering to the subject one or more immune checkpoint modulators selected from the group consisting of PD-1 antagonists, PD-1 ligand antagonists, and CTLA4 antagonists.
51. The method of any one of claims 43-50 further comprising administering to the subject one or more additional active agents selected from the group consisting of a chemotherapeutic agent, an anti-infective agent, and combinations thereof.
52. The method of any one of claims 43-51 further comprising administering to the subject adoptive T cell therapy, and/or a cancer vaccine.
53. The method of any one of claims 43-52 further comprising administering to the subject surgery or radiation therapy.
54. A composition comprising a dendrimer complexed or conjugated with one or more immunomodulatory agents in an amount effective to suppress or inhibit one or more pro-inflammatory cells associated with an inflammatory disease in a subject in need thereof.
55. The composition of claim 54, wherein the dendrimer is a hydroxyl-terminated dendrimer.
56. The composition of claim 54 or 55, wherein the dendrimer is a generation 4, generation 5, or generation 6 PAMAM dendrimer.
57. The composition of any one of claims 54-56, wherein the immunomodulatory agents are one or more selected from the group

consisting of STING antagonists, JAK1 inhibitors, anti-inflammatory agents, and combinations thereof.

58. The composition of claim 57, wherein the immunomodulatory agent is a STING antagonist.

59. The composition of claim 58, wherein the STING antagonist is C-178, C-176, C18, Astin C, No₂-cLA, H-151, and alpha-mangostin.

60. The composition of claim 57, wherein the immunomodulatory agent is a JAK1 inhibitor.

61. The composition of claim 60, wherein the JAK1 inhibitor is selected from the group consisting of tofacitinib, ruxolitinib, baricitinib, peficitinib, decernotiniba, filgotinib, solcitinibb, itacitinib, SHR0302, upadacitinib, PF-04965842, Target-007, and Target-006, or combinations thereof.

62. The composition of any one of claims 54-61, wherein the immunomodulatory agent is covalently conjugated to the dendrimer.

63. The composition of any one of claims 54-62, wherein the dendrimer is further complexed or conjugated with one or more diagnostic or labelling agents in an amount effective to diagnose or label one or more pro-inflammatory cells associated with an autoimmune disease in a subject in need thereof.

64. The composition of any one of claims 54-63, wherein the pro-inflammatory cells are pro-inflammatory macrophages (M1 macrophages).

65. A pharmaceutical composition comprising an effective amount of the composition of any one of claims 54-64.

66. A method of treating an inflammatory disease comprising administering to a subject in need thereof an effective amount of the pharmaceutical composition of claim 65.

67. The method of claim 66, wherein the inflammatory disease is an autoimmune disease.

68. The method of claim 67, wherein the autoimmune diseases is selected from the group consisting of rheumatoid arthritis, psoriasis, psoriatic arthritis, systemic lupus erythematosus (SLE), type 1 diabetes, inflammatory bowel disease, and thyroid diseases.

69. The method of claim 66, wherein the inflammatory diseases is an inflammatory joint disease.

70. The method of claim 69, wherein the inflammatory joint disease is selected from the group consisting of osteoarthritis, rheumatoid arthritis, psoriatic arthritis, and juvenile arthritis.

71. A composition for treating a disease or disorder of the bone, comprising hydroxyl-terminated dendrimers complexed or conjugated with one or more therapeutic agents in an amount effective for treating one or more disorders of the bone, wherein the dendrimers are further covalently conjugated with alendronate.

72. The composition of claim 71, wherein the one or more therapeutic agents is covalently conjugated to the dendrimer via one or more covalent linkers.

73. A method for treating a disease or disorder of the bone in a subject in need thereof, comprising administering to the subject in need thereof a composition comprising hydroxyl-terminated dendrimers complexed or conjugated with one or more therapeutic agents in an amount effective for treating the one or more disorders of the bone, wherein the dendrimers are further covalently conjugated with alendronate.