

levels of Siglec-9 or that disrupt the interactions between Siglec-9 and one or more of its ligands have been reported.

[0016] Accordingly, there is a need for therapeutic antibodies that specifically bind Siglec-9 and reduce Siglec-9 expression on the cell surface, reduce interactions between Siglec-9 and one or more Siglec-9 ligands, and/or reduce one or more Siglec-9 activities in order to treat one or more diseases, disorders, and conditions associated with undesired Siglec-9 activity.

[0017] All references cited herein, including patents, patent applications and publications, are hereby incorporated by reference in their entirety.

SUMMARY OF THE INVENTION

[0017a] In one aspect, the present invention provides an isolated anti-Siglec-9 antibody, wherein the anti-Siglec-9 antibody decreases cell surface levels of Siglec-9 without inhibiting interaction between Siglec-9 and one or more Siglec-9 ligands.

[0017b] In another aspect, the present invention provides an isolated anti-Siglec-9 antibody, wherein the anti-Siglec-9 antibody binds to one or more amino acids within amino acid residues selected from the group consisting of:

- i. amino acid residues 185-194 of SEQ ID NO: 1, or amino acid residues on a mammalian Siglec-9 protein corresponding to amino acid residues 185-194 of SEQ ID NO: 1;
- ii. amino acid residues 86-96 of SEQ ID NO: 1, or amino acid residues on a mammalian Siglec-9 protein corresponding to amino acid residues 86-96 of SEQ ID NO: 1;
- iii. amino acid residues 86-96 and 105-116 of SEQ ID NO: 1, or amino acid residues on a mammalian Siglec-9 protein corresponding to amino acid residues 86-96 and 105-116 of SEQ ID NO: 1;
- iv. amino acid residues 105-116 of SEQ ID NO: 1, or amino acid residues on a mammalian Siglec-9 protein corresponding to amino acid residues 105-116 of SEQ ID NO: 1; and
- v. amino acid residues 107-115 of SEQ ID NO: 1, or amino acid residues on a mammalian Siglec-9 protein corresponding to amino acid residues 107-115 of SEQ ID NO: 1.

[0017c] In yet another aspect, the present invention provides an isolated anti-Siglec-9 antibody, wherein the anti-Siglec-9 antibody competes with one or more antibodies selected from the group consisting of 2D4, 5B1, 6B2, 6D8, 7H12, and any combination thereof for binding to Siglec-9.

[0017d] In yet another aspect, the present invention provides an isolated anti-Siglec-9 antibody which binds essentially the same Siglec-9 epitope as a monoclonal antibody selected from the group consisting of: 2D4, 5B1, 6B2, 6D8, and 7H12.

[0017e] In yet another aspect, the present invention provides an isolated nucleic acid comprising a nucleic acid sequence encoding the anti-Siglec-9 antibody disclosed herein.

[0017f] In yet another aspect, the present invention provides a vector comprising the nucleic acid disclosed herein.

[0017g] In yet another aspect, the present invention provides an isolated host cell comprising the vector disclosed herein.

[0017h] In yet another aspect, the present invention provides a method of producing an anti-Siglec-9 antibody, comprising culturing the host cell disclosed herein so that the anti-Siglec-9 antibody is produced.

[0017i] In yet another aspect, the present invention provides a pharmaceutical composition comprising the anti-Siglec-9 antibody disclosed herein, and a pharmaceutically acceptable carrier.

[0017j] In yet another aspect, the present invention provides use of a therapeutically effective amount of the anti-Siglec-9 antibody disclosed herein in the manufacture of a medicament for preventing, reducing risk, or treating a disease, disorder, or injury selected from the group consisting of dementia, frontotemporal dementia, Alzheimer's disease, vascular dementia, mixed dementia, tauopathy disease, infections, and cancer.

[0018] The present disclosure is generally directed to Siglec-9 agents, such as anti-Siglec-9 antibodies, and methods of using such Siglec-9 agents. The methods provided herein find use in preventing, reducing risk, or treating an individual having dementia, frontotemporal dementia, Alzheimer's disease, vascular dementia, mixed dementia, Creutzfeldt-Jakob disease, normal pressure hydrocephalus, amyotrophic lateral sclerosis, Huntington's disease, tauopathy disease, Nasu-Hakola disease, stroke, acute trauma, chronic trauma, lupus, acute and chronic colitis, rheumatoid arthritis, wound healing, Crohn's disease, inflammatory bowel disease, ulcerative colitis, obesity, malaria, essential tremor, central nervous system lupus, Behcet's disease, Parkinson's disease, dementia with Lewy bodies, multiple system atrophy, Shy-Drager syndrome, progressive supranuclear palsy, cortical basal ganglionic degeneration, acute disseminated encephalomyelitis, granulomatous disorders, sarcoidosis, diseases of aging, seizures, spinal cord injury, traumatic brain injury, age related macular degeneration, glaucoma, retinitis pigmentosa, retinal degeneration, respiratory tract infection, sepsis, eye infection, systemic infection, lupus, arthritis, multiple sclerosis, low bone density, osteoporosis, osteogenesis, osteopetrotic disease, Paget's disease of bone, solid and blood cancer, bladder cancer, brain cancer, breast cancer, colon cancer, rectal cancer, endometrial cancer, kidney cancer, renal cell cancer, renal pelvis cancer, leukemia, lung cancer, melanoma, non-Hodgkin's lymphoma, pancreatic cancer, prostate cancer, ovarian cancer, fibrosarcoma, acute lymphoblastic leukemia (ALL), acute myeloid leukemia (AML), chronic lymphocytic leukemia (CLL), chronic myeloid leukemia (CML), multiple myeloma, polycythemia vera, essential

thrombocytosis, primary or idiopathic myelofibrosis, primary or idiopathic myelosclerosis, myeloid-derived tumors, tumors that express Siglec-9 and/or Siglec-9 ligands, thyroid cancer, infections, CNS herpes, parasitic infections, Trypanosome infection, Cruzi infection, *Pseudomonas aeruginosa* infection, *Leishmania donovani* infection, group B *Streptococcus* infection, *Campylobacter jejuni* infection, *Neisseria meningitidis* infection, type I HIV, and Haemophilus influenza. The methods provided herein also find use in inducing or promoting the survival, maturation, functionality, migration, or proliferation of one or more immune cells in an individual in need thereof. The

methods provided herein find further use in decreasing the activity, functionality, or survival of regulatory T cells, tumor-imbedded immunosuppressor dendritic cells, tumor-imbedded immunosuppressor macrophages, neutrophils, natural killer (NK) cells, myeloid-derived suppressor cells, tumor-associated macrophages, neutrophils, NK cells, acute myeloid leukemia (AML) cells, chronic lymphocytic leukemia (CLL) cell, or chronic myeloid leukemia (CML) cell in an individual in need thereof. The methods provided herein also find use in decreasing cellular levels of Siglec-9.

[0019] Certain parts of the present disclosure are based, at least in part, on the identification of anti-Siglec-9 antibodies that are capable of decreasing cell surface levels of Siglec-9 on human primary immune cells and Siglec-9-expressing cell lines and/or that are capable of inhibiting the binding of Siglec-9 ligands to Siglec-9 (*see, e.g., Examples 3-5*).

[0020] Accordingly, disclosed is an isolated (e.g., monoclonal) anti-Siglec-9 antibody, wherein the anti-Siglec-9 antibody decreases cellular levels of Siglec-9. In some examples, the anti-Siglec-9 antibody decreases cellular levels of Siglec-9 without inhibiting interaction between Siglec-9 and one or more Siglec-9 ligands. In some examples, the antibody further inhibits interaction between Siglec-9 and one or more Siglec-9 ligands. Also disclosed is an isolated (e.g., monoclonal) anti-Siglec-9 antibody, wherein the anti-Siglec-9 antibody decreases cellular levels of Siglec-9 and inhibits interaction between Siglec-9 and one or more Siglec-9 ligands.

[0021] In some examples that may be combined with any of the preceding examples, the anti-Siglec-9 antibody decreases cell surface levels of Siglec-9, decreases intracellular levels of Siglec-9, decreases total levels of Siglec-9, or any combination thereof. In some examples that may be combined with any of the preceding examples, the anti-Siglec-9 antibody induces Siglec-9 degradation, Siglec-9 cleavage, Siglec-9 internalization, Siglec-9 shedding, downregulation of Siglec-9 expression, or any combination thereof. In some examples that may be combined with any of the preceding examples, the antibody decreases cellular levels of Siglec-9 *in vivo*. In some examples that may be combined with any of the preceding examples, the anti-Siglec-9 antibody inhibits cell surface clustering of Siglec-9. In some examples that may be combined with any of the preceding examples, the anti-Siglec-9 antibody inhibits one or more Siglec-9 activities. In some examples that may be combined with any of the preceding examples, the one or more Siglec-9 activities selected from the group consisting of: (a) Siglec-9 binding to one or more Siglec-9 ligands, optionally wherein the one or more Siglec-9 ligands are selected from the group consisting of sialic acid-containing glycoproteins, sialic acid-containing glycolipids, and any combination thereof; (b) Siglec-9 binding to SHP1 or SHP2; (c) phosphorylation of Tyr-433, Tyr-456, or both, induced by one or more SRC family tyrosine kinases, optionally, wherein the one or more SRC family tyrosine kinases are selected from the group consisting of Syk, LCK, FYM, and

growth rate; (aaa) increasing metastasis; (bbb) increasing rate of tumor recurrence; (ccc) decreasing efficacy of one or more immune-therapies that modulate anti-tumor T cell responses, optionally wherein the one or more immune-therapies are immune-therapies that target one or more target proteins selected from the group consisting of PD1/PDL1, CD40, OX40, ICOS, CD28, CD137/4-1BB, CD27, GITR, PD-L1, CTLA4, PD-L2, PD-1, B7-H3, B7-H4, HVEM, BTLA, KIR, GAL9, TIM3, A2AR, LAG, DR-5, TREM1, TREM2, CSF-1 receptor, and any combination thereof, or of one or more cancer vaccines; (ddd) inhibition of PLC γ /PKC/calcium mobilization; and (eee) inhibition of PI3K/Akt, Ras/MAPK signaling. In some examples that may be combined with any of the preceding examples, the one or more Siglec-9 activities are selected from the group consisting of: (a) enhancing infiltration of one or more of immunosuppressor dendritic cells, immunosuppressor macrophages, myeloid derived suppressor cells, tumor-associated macrophages, immunosuppressor neutrophils, non-tumorigenic CD45⁺CD14⁺ myeloid cells, and regulatory T cells into tumors; (b) increasing number of tumor-promoting myeloid/granulocytic immune-suppressive cells in a tumor, in peripheral blood, or other lymphoid organ; (r) enhancing tumor-promoting activity of non-tumorigenic myeloid-derived suppressor cells and/or non-tumorigenic CD45⁺CD14⁺ myeloid cells; (c) enhancing survival of non-tumorigenic myeloid-derived suppressor cells (MDSC) and/or non-tumorigenic CD45⁺CD14⁺ myeloid cells; (d) decreasing activation of tumor-specific T lymphocytes with tumor killing potential; (e) decreasing activation of CD45⁺CD3⁺ T lymphocytes with tumor killing potential; (f) decreasing infiltration of tumor-specific NK cells with tumor killing potential; (g) decreasing infiltration of tumor-specific B lymphocytes with potential to enhance immune response; (h) decreasing infiltration of tumor-specific T lymphocytes with tumor killing potential; and (i) decreasing infiltration of CD45⁺CD3⁺ T lymphocytes. In some examples that may be combined with any of the preceding examples, the one or more Siglec-9 activities selected from the group consisting of: (a) Siglec-9 binding to one or more Siglec-9 ligands, optionally wherein the one or more Siglec-9 ligands are selected from the group consisting of sialic acid-containing glycoproteins, sialic acid-containing glycolipids, and any combination thereof; (b) decreasing proliferation of one or more cells selected from the group consisting of dendritic cells, bone marrow-derived dendritic cells, macrophages, neutrophils, NK cells, M1 macrophages, M1 neutrophils, M1 NK cells, activated M1 macrophages, activated M1 neutrophils, activated M1 NK cells, M2 macrophages, M2 neutrophils, M2 NK cells, monocytes, osteoclasts, T cells, T helper cells, cytotoxic T cells, granulocytes, neutrophils, microglia, M1 microglia, activated M1 microglia, and M2 microglia; (c) inhibiting migration of one or more cells selected from the group consisting of dendritic cells, bone marrow-derived dendritic cells, macrophages, neutrophils, NK cells, M1 macrophages, M1 neutrophils, M1 NK cells, activated M1 macrophages, activated M1 neutrophils, activated M1 NK cells, M2 macrophages, M2 neutrophils, M2 NK cells, monocytes, osteoclasts, T

macrophages, tumor-associated neutrophils, tumor-associated NK cells, and regulatory T cells; (j) increasing infiltration of one or more of immunosuppressor dendritic cells, immunosuppressor macrophages, immunosuppressor neutrophils, immunosuppressor NK cells, myeloid-derived suppressor cells, tumor-associated macrophages, tumor-associated neutrophils, tumor-associated NK cells, non-tumorigenic CD45⁺CD14⁺ myeloid cells, and regulatory T cells into tumors; (k) increasing the number of tumor-promoting myeloid/granulocytic immune-suppressive cells and/or non-tumorigenic CD45⁺CD14⁺ myeloid cells in a tumor, in peripheral blood, or other lymphoid organ; (l) enhancing tumor-promoting activity of myeloid-derived suppressor cells and/or non-tumorigenic CD45⁺CD14⁺ myeloid cells; (m) enhancing survival of non-tumorigenic myeloid-derived suppressor cells and/or non-tumorigenic CD45⁺CD14⁺ myeloid cells; (n) decreasing activation of tumor-specific T lymphocytes with tumor killing potential; (o) decreasing infiltration of tumor-specific NK cells with tumor killing potential; (p) increasing tumor volume; (q) increasing tumor growth rate; and (r) decreasing efficacy of one or more immune-therapies that modulate anti-tumor T cell responses, optionally wherein the one or more immune-therapies are immune-therapies that target one or more target proteins selected from the group consisting of PD1/PDL1, CD40, OX40, ICOS, CD28, CD137/4-1BB, CD27, GITR, PD-L1, CTLA4, PD-L2, PD-1, B7-H3, B7-H4, HVEM, LIGHT, BTLA, CD30, TIGIT, VISTA, KIR, GAL9, TIM1, TIM3, TIM4, A2AR, LAG3, DR-5, CD2, CD5, TREM1, TREM2, CD39, CD73, CSF-1 receptor, and any combination thereof, or of one or more cancer vaccines. In some examples that may be combined with any of the preceding examples, the anti-Siglec-9 antibody exhibits one or more activities selected from the group consisting of:

(a) increasing the number of tumor infiltrating CD3⁺ T cells; (b) decreasing cellular levels of CD33 in non-tumorigenic CD14⁺ myeloid cells, optionally wherein the non-tumorigenic CD14⁺ myeloid cells are tumor infiltrating cells or optionally wherein the non-tumorigenic CD14⁺ myeloid cells are present in blood; (c) reducing the number of non-tumorigenic CD14⁺ myeloid cells, optionally wherein the non-tumorigenic CD14⁺ myeloid cells are tumor infiltrating cells or optionally wherein the non-tumorigenic CD14⁺ myeloid cells are present in blood; (d) reducing PD-L1 levels in one or more cells, optionally wherein the one or more cells are non-tumorigenic myeloid-derived suppressor cells (MDSC); (e) reducing PD-L2 levels in one or more cells, optionally wherein the one or more cells are non-tumorigenic myeloid-derived suppressor cells (MDSC); (f) reducing B7-H2 levels in one or more cells, optionally wherein the one or more cells are non-tumorigenic myeloid-derived suppressor cells (MDSC); (g) reducing B7-H3 levels in one or more cells, optionally wherein the one or more cells are non-tumorigenic myeloid-derived suppressor cells (MDSC); (h) reducing CD200R levels in one or more cells, optionally wherein the one or more cells are non-tumorigenic myeloid-derived suppressor cells (MDSC); (i) reducing CD163 levels in one or more cells, optionally wherein the one or more cells are non-tumorigenic myeloid-derived suppressor cells (MDSC); (j)

reducing CD206 levels in one or more cells, optionally wherein the one or more cells are non-tumorigenic myeloid-derived suppressor cells (MDSC); (k) decreasing tumor growth rate of solid tumors; (l) reducing tumor volume; (m) increasing efficacy of one or more PD-1 inhibitors; (n) increasing efficacy of one or more checkpoint inhibitor therapies and/or immune-modulating therapies, optionally wherein the one or more checkpoint inhibitor therapies and/or immune-modulating therapies target one or more of CTLA4, the adenosine pathway, PD-L1, PD-L2, OX40, TIM3, LAG3, or any combination thereof; (o) increasing efficacy of one or more chemotherapy agents, optionally wherein the one or more of the chemotherapy agents are gemcitabine, capecitabine, anthracyclines, doxorubicin (Adriamycin[®]), epirubicin (Ellence[®]), taxanes, paclitaxel (Taxol[®]), docetaxel (Taxotere[®]), 5-fluorouracil (5-FU), cyclophosphamide (Cytosan[®]), carboplatin (Paraplatin[®]), and any combination thereof; (p) increasing proliferation of T cells in the presence of non-tumorigenic myeloid-derived suppressor cells (MDSC); (q) inhibiting differentiation, survival, and/or one or more functions of non-tumorigenic myeloid-derived suppressor cells (MDSC); and (r) killing CD33-expressing immunosuppressor non-tumorigenic myeloid cells and/or non-tumorigenic CD14-expressing cells in solid tumors and associated blood vessels when conjugated to a chemical or radioactive toxin. In some examples that may be combined with any of the preceding examples, the one or more Siglec-9 ligands are selected from the group consisting of Siglec-9 ligands expressed on red blood cells, Siglec-9 ligands expressed on bacterial cells, Siglec-9 ligands expressed on apoptotic cells, Siglec-9 ligands expressed on nerve cells, Siglec-9 ligands expressed on glia cells, Siglec-9 ligands expressed on microglia, Siglec-9 ligands expressed on astrocytes, Siglec-9 ligands expressed on tumor cells, Siglec-9 ligands expressed on viruses, Siglec-9 ligands expressed on dendritic cells, Siglec-9 ligands bound to beta amyloid plaques, Siglec-9 ligands bound to Tau tangles, Siglec-9 ligands on disease-causing proteins, Siglec-9 ligands on disease-causing peptides, Siglec-9 ligands expressed on macrophages, Siglec-9 ligands expressed on neutrophils, Siglec-9 ligands expressed on natural killer cells, Siglec-9 ligands expressed on monocytes, Siglec-9 ligands expressed on T cells, Siglec-9 ligands expressed on T helper cells, Siglec-9 ligands expressed on cytotoxic T cells, Siglec-9 ligands expressed on B cells, Siglec-9 ligands expressed on tumor-imbedded immunosuppressor dendritic cells, Siglec-9 ligands expressed on tumor-imbedded immunosuppressor macrophages, Siglec-9 ligands expressed on myeloid-derived suppressor cells, Siglec-9 ligands expressed on regulatory T cells, secreted mucins, sialic acid, sialic acid-containing glycolipids, sialic acid-containing glycoproteins, alpha-2,8-disialyl containing glycolipids, branched alpha-2,6-linked sialic acid-containing glycoproteins, terminal alpha-2,6-linked sialic acid-containing glycolipids, terminal alpha-2,3-linked sialic acid-containing glycoproteins, and disialogangliosides. In some examples that may be combined with any of the preceding examples, the cellular levels of Siglec-9 are measured on primary cells selected from the group consisting of dendritic cells,

bone marrow-derived dendritic cells, monocytes, microglia, macrophages, neutrophils, and NK cells, or on cell lines, and wherein the cellular levels of Siglec-9 are measured utilizing an *in vitro* cell assay. In some examples that may be combined with any of the preceding examples, the anti-Siglec-9 antibody does not reduce TREM2 expression. In some examples that may be combined with any of the preceding examples, the anti-Siglec-9 antibody exhibits one or more activities selected from the group consisting of: (a) increasing the number of tumor infiltrating CD3⁺ T cells; (b) decreasing cellular levels of Siglec-9 in non-tumorigenic CD14⁺ myeloid cells, optionally wherein the non-tumorigenic CD14⁺ myeloid cells are tumor infiltrating cells or optionally wherein the non-tumorigenic CD14⁺ myeloid cells are present in blood; (c) reducing the number of non-tumorigenic CD14⁺ myeloid cells, optionally wherein the non-tumorigenic CD14⁺ myeloid cells are tumor infiltrating cells or optionally wherein the non-tumorigenic CD14⁺ myeloid cells are present in blood; (d) reducing PD-L1 levels in one or more cells, optionally wherein the one or more cells are non-tumorigenic myeloid-derived suppressor cells (MDSC); (e) reducing PD-L2 levels in one or more cells, optionally wherein the one or more cells are non-tumorigenic myeloid-derived suppressor cells (MDSC); (f) reducing B7-H2 levels in one or more cells, optionally wherein the one or more cells are non-tumorigenic myeloid-derived suppressor cells (MDSC); (g) reducing B7-H3 levels in one or more cells, optionally wherein the one or more cells are non-tumorigenic myeloid-derived suppressor cells (MDSC); (h) reducing CD200R levels in one or more cells, optionally wherein the one or more cells are non-tumorigenic myeloid-derived suppressor cells (MDSC); (i) reducing CD163 levels in one or more cells, optionally wherein the one or more cells are non-tumorigenic myeloid-derived suppressor cells (MDSC); (j) reducing CD206 levels in one or more cells, optionally wherein the one or more cells are non-tumorigenic myeloid-derived suppressor cells (MDSC); (k) decreasing tumor growth rate of solid tumors; (l) reducing tumor volume; (m) increasing efficacy of one or more PD-1 inhibitors; (n) increasing efficacy of one or more checkpoint inhibitor therapies and/or immune-modulating therapies, optionally wherein the one or more checkpoint inhibitor therapies and/or immune-modulating therapies target one or more of CTLA4, the adenosine pathway, PD-L1, PD-L2, PD-L1, PD-L2, OX40, TIM3, LAG3, or any combination thereof; (o) increasing efficacy of one or more chemotherapy agents, optionally wherein the one or more of the chemotherapy agents are gemcitabine, capecitabine, anthracyclines, doxorubicin (Adriamycin[®]), epirubicin (Ellence[®]), taxanes, paclitaxel (Taxol[®]), docetaxel (Taxotere[®]), 5-fluorouracil (5-FU), cyclophosphamide (Cytoxan[®]), carboplatin (Paraplatin[®]), and any combination thereof; (p) increasing proliferation of T cells in the presence of non-tumorigenic myeloid-derived suppressor cells (MDSC); (q) inhibiting differentiation, survival, and/or one or more functions of non-tumorigenic myeloid-derived suppressor cells (MDSC); and (r) killing Siglec-9-expressing

immunosuppressor non-tumorigenic myeloid cells and/or non-tumorigenic CD14-expressing cells in solid tumors and associated blood vessels when conjugated to a chemical or radioactive toxin.

[0022] In some examples that may be combined with any of the preceding examples, the anti-Siglec-9 antibody binds a discontinuous Siglec-9 epitope. In some examples that may be combined with any of the preceding examples, the discontinuous Siglec-9 epitope comprises two or more peptides, three or more peptides, four or more peptides, five or more peptides, six or more peptides, seven or more peptides, eight or more peptides, nine or more peptides, or 10 or more peptides. In some examples that may be combined with any of the preceding examples, each of the peptides comprise five or more, six or more, seven or more, eight or more, nine or more, 10 or more, 11 or more, 12 or more, 13 or more, 14 or more, 15 or more, 16 or more, 17 or more, 18 or more, 19 or more, or 20 or more amino acid residues of the amino acid sequence of SEQ ID NO: 1; or five or more, six or more, seven or more, eight or more, nine or more, 10 or more, 11 or more, 12 or more, 13 or more, 14 or more, 15 or more, 16 or more, 17 or more, 18 or more, 19 or more, or 20 or more amino acid residues on a mammalian Siglec-9 protein corresponding to the amino acid sequence of SEQ ID NO: 1. In some examples that may be combined with any of the preceding examples, the anti-Siglec-9 antibody binds to a conformational epitope of Siglec-9. In some examples that may be combined with any of the preceding examples, the anti-Siglec-9 antibody binds to one or more amino acids within amino acid residues 20-347, 20-140, 141-347, 146-347, 146-229, 236-336, or 146-347 of SEQ ID NO: 1; or within amino acid residues on a mammalian Siglec-9 protein corresponding to amino acid residues 20-347, 20-140, 141-347, 146-347, 146-229, 236-336, or 146-347 of SEQ ID NO: 1. In some examples that may be combined with any of the preceding examples, the anti-Siglec-9 antibody binds to one or more amino acids within amino acid residues selected from the group consisting of: i. amino acid residues 62-76 of SEQ ID NO: 1, or amino acid residues on a mammalian Siglec-9 protein corresponding to amino acid residues 62-76 of SEQ ID NO: 1; ii. amino acid residues 62-76 and 86-92 of SEQ ID NO: 1, or amino acid residues on a mammalian Siglec-9 protein corresponding to amino acid residues 62-76 and 86-92 of SEQ ID NO: 1; iii. amino acid residues 86-92 of SEQ ID NO: 1, or amino acid residues on a mammalian Siglec-9 protein corresponding to amino acid residues 86-92 of SEQ ID NO: 1; iv. amino acid residues 86-96 of SEQ ID NO: 1, or amino acid residues on a mammalian Siglec-9 protein corresponding to amino acid residues 86-96 of SEQ ID NO: 1; v. amino acid residues 86-96 and 105-116 of SEQ ID NO: 1, or amino acid residues on a mammalian Siglec-9 protein corresponding to amino acid residues 86-96 and 105-116 of SEQ ID NO: 1; vi. amino acid residues 105-116 of SEQ ID NO: 1, or amino acid residues on a mammalian Siglec-9 protein corresponding to amino acid residues 105-116 of SEQ ID NO: 1; vii. amino acid residues 107-115 of SEQ ID NO: 1, or amino acid residues on a mammalian Siglec-9 protein corresponding to amino acid residues 107-115 of SEQ ID NO: 1; and viii. amino

acid residues 185-194 of SEQ ID NO: 1, or amino acid residues on a mammalian Siglec-9 protein corresponding to amino acid residues 185-194 of SEQ ID NO: 1. In some examples that may be combined with any of the preceding examples, the anti-Siglec-9 antibody binds to one or more amino acids within amino acid residues 62-76 of SEQ ID NO: 1, or amino acid residues on a mammalian Siglec-9 protein corresponding to amino acid residues 62-76 of SEQ ID NO: 1. In some examples that may be combined with any of the preceding examples, the anti-Siglec-9 antibody binds to one or more amino acids within amino acid residues 62-76 and 86-92 of SEQ ID NO: 1, or amino acid residues on a mammalian Siglec-9 protein corresponding to amino acid residues 62-76 and 86-92 of SEQ ID NO: 1. In some examples that may be combined with any of the preceding examples, the anti-Siglec-9 antibody binds to one or more amino acids within amino acid residues 86-92 of SEQ ID NO: 1, or amino acid residues on a mammalian Siglec-9 protein corresponding to amino acid residues 86-92 of SEQ ID NO: 1. In some examples that may be combined with any of the preceding examples, the anti-Siglec-9 antibody binds to one or more amino acids within amino acid residues 86-96 of SEQ ID NO: 1, or amino acid residues on a mammalian Siglec-9 protein corresponding to amino acid residues 86-96 of SEQ ID NO: 1. In some examples that may be combined with any of the preceding examples, the anti-Siglec-9 antibody binds to one or more amino acids within amino acid residues 86-96 and 105-116 of SEQ ID NO: 1, or amino acid residues on a mammalian Siglec-9 protein corresponding to amino acid residues 86-96 and 105-116 of SEQ ID NO: 1. In some examples that may be combined with any of the preceding examples, the anti-Siglec-9 antibody binds to one or more amino acids within amino acid residues 105-116 of SEQ ID NO: 1, or amino acid residues on a mammalian Siglec-9 protein corresponding to amino acid residues 105-116 of SEQ ID NO: 1. In some examples that may be combined with any of the preceding examples, the anti-Siglec-9 antibody binds to one or more amino acids within amino acid residues 107-115 of SEQ ID NO: 1, or amino acid residues on a mammalian Siglec-9 protein corresponding to amino acid residues 107-115 of SEQ ID NO: 1. In some examples that may be combined with any of the preceding examples, the anti-Siglec-9 antibody binds to one or more amino acids within amino acid residues 185-194 of SEQ ID NO: 1, or amino acid residues on a mammalian Siglec-9 protein corresponding to amino acid residues 185-194 of SEQ ID NO: 1. In some examples that may be combined with any of the preceding examples, the anti-Siglec-9 antibody binds to one or more amino acid residues selected from the group consisting of L22, H48, W50, I51, Y52, K123, I126, D189, P190, R194 of SEQ ID NO: 1, or one or more amino acid residues on a mammalian Siglec-7 protein corresponding to an amino acid residue selected from the group consisting of L22, H48, W50, I51, Y52, K123, I126, D189, P190, R194 of SEQ ID NO: 1. In some examples that may be combined with any of the preceding examples, the anti-Siglec-9 antibody competes with one or more antibodies selected from the

group consisting of 2D4, 2D5, 5B1, 6B2, 6D8, 7H12, 5C6, 12B12, 17C2, and any combination thereof for binding to Siglec-9.

[0023] In some examples that may be combined with any of the preceding examples, the anti-Siglec-9 antibody comprises a light chain variable domain and a heavy chain variable domain, wherein the light chain variable domain, the heavy chain variable domain, or both comprise at least one, two, three, four, five, or six HVRs selected from HVR-L1, HVR-L2, HVR-L3, HVR-H1, HVR-H2, and HVR-H3 of a monoclonal antibody selected from the group consisting of: 2D4, 2D5, 5B1, 6B2, 6D8, 7H12, 5C6, 12B12, and 17C2. In some examples that may be combined with any of the preceding examples: (a) the HVR-L1 comprises an amino acid sequence selected from the group consisting of SEQ ID NOs: 6-9, 172, and 173; or (b) the HVR-L2 comprises an amino acid sequence selected from the group consisting of SEQ ID NOs: 10-13, 174, and 175; or (c) the HVR-L3 comprises an amino acid sequence selected from the group consisting of SEQ ID NOs: 14-18, 176, and 177; or (d) the HVR-H1 comprises an amino acid sequence selected from the group consisting of SEQ ID NOs: 19-21, 178, and 179; or (e) the HVR-H2 comprises an amino acid sequence selected from the group consisting of SEQ ID NOs: 22-25, 180, and 181; or (f) the HVR-H3 comprises an amino acid sequence selected from the group consisting of SEQ ID NOs: 26-29, 182, and 183. In some examples that may be combined with any of the preceding examples: (a) the HVR-L1 comprises the amino acid sequence of SEQ ID NO: 6, the HVR-L2 comprises the amino acid sequence of SEQ ID NO: 10, the HVR-L3 comprises the amino acid sequence of SEQ ID NO: 14, the HVR-H1 comprises the amino acid sequence of SEQ ID NO: 19, the HVR-H2 comprises the amino acid sequence of SEQ ID NO: 22, and the HVR-H3 comprises the amino acid sequence of SEQ ID NO: 26; or (b) the HVR-L1 comprises the amino acid sequence of SEQ ID NO: 7, the HVR-L2 comprises the amino acid sequence of SEQ ID NO: 11, the HVR-L3 comprises the amino acid sequence of SEQ ID NO: 15, the HVR-H1 comprises the amino acid sequence of SEQ ID NO: 20, the HVR-H2 comprises the amino acid sequence of SEQ ID NO: 23, and the HVR-H3 comprises the amino acid sequence of SEQ ID NO: 27; or (c) the HVR-L1 comprises the amino acid sequence of SEQ ID NO: 8, the HVR-L2 comprises the amino acid sequence of SEQ ID NO: 12, the HVR-L3 comprises the amino acid sequence of SEQ ID NO: 16, the HVR-H1 comprises the amino acid sequence of SEQ ID NO: 21, the HVR-H2 comprises the amino acid sequence of SEQ ID NO: 24, and the HVR-H3 comprises the amino acid sequence of SEQ ID NO: 28; or (d) the HVR-L1 comprises the amino acid sequence of SEQ ID NO: 9, the HVR-L2 comprises the amino acid sequence of SEQ ID NO: 13, the HVR-L3 comprises the amino acid sequence of SEQ ID NO: 17, the HVR-H1 comprises the amino acid sequence of SEQ ID NO: 21, the HVR-H2 comprises the amino acid sequence of SEQ ID NO: 25, and the HVR-H3 comprises the amino acid sequence of SEQ ID NO: 29; or (e) the HVR-L1 comprises the amino acid sequence of SEQ ID NO: 8, the HVR-L2

comprises the amino acid sequence of SEQ ID NO: 12, the HVR-L3 comprises the amino acid sequence of SEQ ID NO: 18, the HVR-H1 comprises the amino acid sequence of SEQ ID NO: 21, the HVR-H2 comprises the amino acid sequence of SEQ ID NO: 24, and the HVR-H3 comprises the amino acid sequence of SEQ ID NO: 28; or (f) the HVR-L1 comprises the amino acid sequence of SEQ ID NO: 172, the HVR-L2 comprises the amino acid sequence of SEQ ID NO: 174, the HVR-L3 comprises the amino acid sequence of SEQ ID NO: 176, the HVR-H1 comprises the amino acid sequence of SEQ ID NO: 178, the HVR-H2 comprises the amino acid sequence of SEQ ID NO: 180, and the HVR-H3 comprises the amino acid sequence of SEQ ID NO: 182; or (g) the HVR-L1 comprises the amino acid sequence of SEQ ID NO: 173, the HVR-L2 comprises the amino acid sequence of SEQ ID NO: 175, the HVR-L3 comprises the amino acid sequence of SEQ ID NO: 177, the HVR-H1 comprises the amino acid sequence of SEQ ID NO: 179, the HVR-H2 comprises the amino acid sequence of SEQ ID NO: 181, and the HVR-H3 comprises the amino acid sequence of SEQ ID NO: 183. In some examples that may be combined with any of the preceding examples, the anti-Siglec-9 antibody comprises a light chain variable domain and a heavy chain variable domain, wherein the light chain variable domain comprises: an HVR-L1 comprising the amino acid sequence of SEQ ID NO: 6, an HVR-L2 comprising the amino acid sequence of SEQ ID NO: 10, and an HVR-L3 comprising the amino acid sequence of SEQ ID NO: 14, and wherein the heavy chain variable region comprises: an HVR-H1 comprising the amino acid sequence of SEQ ID NO: 19, an HVR-H2 comprising the amino acid sequence of SEQ ID NO: 22, and an HVR-H3 comprising the amino acid sequence of SEQ ID NO: 26. In some examples that may be combined with any of the preceding examples, the anti-Siglec-9 antibody comprises a light chain variable domain and a heavy chain variable domain, wherein the light chain variable domain comprises: an HVR-L1 comprising the amino acid sequence of SEQ ID NO: 7, an HVR-L2 comprising the amino acid sequence of SEQ ID NO: 11, and an HVR-L3 comprising the amino acid sequence of SEQ ID NO: 15, and wherein the heavy chain variable region comprises: an HVR-H1 comprising the amino acid sequence of SEQ ID NO: 20, an HVR-H2 comprising the amino acid sequence of SEQ ID NO: 23, and an HVR-H3 comprising the amino acid sequence of SEQ ID NO: 27. In some examples that may be combined with any of the preceding examples, the anti-Siglec-9 antibody comprises a light chain variable domain and a heavy chain variable domain, wherein the light chain variable domain comprises: an HVR-L1 comprising the amino acid sequence of SEQ ID NO: 8, an HVR-L2 comprising the amino acid sequence of SEQ ID NO: 12, and an HVR-L3 comprising the amino acid sequence of SEQ ID NO: 16, and wherein the heavy chain variable region comprises: an HVR-H1 comprising the amino acid sequence of SEQ ID NO: 21, an HVR-H2 comprising the amino acid sequence of SEQ ID NO: 24, and an HVR-H3 comprising the amino acid sequence of SEQ ID NO: 28. In some examples that may be combined with any of the preceding

examples, the anti-Siglec-9 antibody comprises a light chain variable domain and a heavy chain variable domain, wherein the light chain variable domain comprises: an HVR-L1 comprising the amino acid sequence of SEQ ID NO: 9, an HVR-L2 comprising the amino acid sequence of SEQ ID NO: 13, and an HVR-L3 comprising the amino acid sequence of SEQ ID NO: 17, and wherein the heavy chain variable region comprises: an HVR-H1 comprising the amino acid sequence of SEQ ID NO: 21, an HVR-H2 comprising the amino acid sequence of SEQ ID NO: 25, and an HVR-H3 comprising the amino acid sequence of SEQ ID NO: 29. In some examples that may be combined with any of the preceding examples, the anti-Siglec-9 antibody comprises a light chain variable domain and a heavy chain variable domain, wherein the light chain variable domain comprises: an HVR-L1 comprising the amino acid sequence of SEQ ID NO: 8, an HVR-L2 comprising the amino acid sequence of SEQ ID NO: 12, and an HVR-L3 comprising the amino acid sequence of SEQ ID NO: 18, and wherein the heavy chain variable region comprises: an HVR-H1 comprising the amino acid sequence of SEQ ID NO: 21, an HVR-H2 comprising the amino acid sequence of SEQ ID NO: 24, and an HVR-H3 comprising the amino acid sequence of SEQ ID NO: 28. In some examples that may be combined with any of the preceding examples, the anti-Siglec-9 antibody comprises a light chain variable domain and a heavy chain variable domain, wherein the light chain variable domain comprises: an HVR-L1 comprising the amino acid sequence of SEQ ID NO: 172, an HVR-L2 comprising the amino acid sequence of SEQ ID NO: 174, and an HVR-L3 comprising the amino acid sequence of SEQ ID NO: 176, and wherein the heavy chain variable region comprises: an HVR-H1 comprising the amino acid sequence of SEQ ID NO: 178, an HVR-H2 comprising the amino acid sequence of SEQ ID NO: 180, and an HVR-H3 comprising the amino acid sequence of SEQ ID NO: 182. In some examples that may be combined with any of the preceding examples, the anti-Siglec-9 antibody comprises a light chain variable domain and a heavy chain variable domain, wherein the light chain variable domain comprises: an HVR-L1 comprising the amino acid sequence of SEQ ID NO: 173, an HVR-L2 comprising the amino acid sequence of SEQ ID NO: 175, and an HVR-L3 comprising the amino acid sequence of SEQ ID NO: 177, and wherein the heavy chain variable region comprises: an HVR-H1 comprising the amino acid sequence of SEQ ID NO: 179, an HVR-H2 comprising the amino acid sequence of SEQ ID NO: 181, and an HVR-H3 comprising the amino acid sequence of SEQ ID NO: 183. In some examples that may be combined with any of the preceding examples, the anti-Siglec-9 antibody comprises a light chain variable domain and a heavy chain variable domain, wherein the light chain variable domain comprises: (a) an HVR-L1 comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 6-9, 172, and 173, or an amino acid sequence with at least about 90% homology to an amino acid sequence selected from the group consisting of SEQ ID NOs: 6-9, 172, and 173; (b) an HVR-L2 comprising an amino acid sequence selected from the group consisting of

SEQ ID NOs: 10-13, 174, and 175, or an amino acid sequence with at least about 90% homology to an amino acid sequence selected from the group consisting of SEQ ID NOs: 10-13, 174, and 175; and (c) an HVR-L3 comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 14-18, 176, and 177, or an amino acid sequence with at least about 90% homology to an amino acid sequence selected from the group consisting of SEQ ID NOs: 14-18, 176, and 177; and wherein the heavy chain variable domain comprises: (a) an HVR-H1 comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 19-21, 178, and 179, or an amino acid sequence with at least about 90% homology to an amino acid sequence selected from the group consisting of SEQ ID NOs: 19-21, 178, and 179; (b) an HVR-H2 comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 22-25, 180, and 181, or an amino acid sequence with at least about 90% homology to an amino acid sequence selected from the group consisting of SEQ ID NOs: 22-25, 180, and 181; and (c) an HVR-H3 comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 26-29, 182, and 183, or an amino acid sequence with at least about 90% homology to an amino acid sequence selected from the group consisting of SEQ ID NOs: 26-29, 182, and 183. In some examples that may be combined with any of the preceding examples, the anti-Siglec-9 antibody comprises a light chain variable domain comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 61-115 and 197-204; and/or a heavy chain variable domain comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 116-170 and 205-212. In some examples that may be combined with any of the preceding examples, the anti-Siglec-9 antibody comprises a light chain variable domain and a heavy chain variable domain, wherein: (a) the light chain variable domain comprises the amino acid sequence of SEQ ID NO: 61; and the heavy chain variable domain comprises the amino acid sequence of SEQ ID NO: 116; or (b) the light chain variable domain comprises the amino acid sequence of SEQ ID NO: 72; and the heavy chain variable domain comprises the amino acid sequence of SEQ ID NO: 127; or (c) the light chain variable domain comprises the amino acid sequence of SEQ ID NO: 83; and the heavy chain variable domain comprises the amino acid sequence of SEQ ID NO: 138; or (d) the light chain variable domain comprises the amino acid sequence of SEQ ID NO: 94; and the heavy chain variable domain comprises the amino acid sequence of SEQ ID NO: 149; or (e) the light chain variable domain comprises the amino acid sequence of SEQ ID NO: 105; and the heavy chain variable domain comprises the amino acid sequence of SEQ ID NO: 160; or (f) the light chain variable domain comprises the amino acid sequence of SEQ ID NO: 197; and the heavy chain variable domain comprises the amino acid sequence of SEQ ID NO: 205; or (g) the light chain variable domain comprises the amino acid sequence of SEQ ID NO: 201; and the heavy chain variable domain comprises the amino acid sequence of SEQ ID NO: 210. In some examples that may be combined with any of the preceding examples, the anti-Siglec-9 antibody comprises a

light chain variable domain of a monoclonal antibody selected from the group consisting of: 2D4, 2D5, 5B1, 6B2, 6D8, 7H12, 5C6, 12B12, and 17C2; and/or a heavy chain variable domain of a monoclonal antibody selected from the group consisting of: 2D4, 2D5, 5B1, 6B2, 6D8, 7H12, 5C6, 12B12, and 17C2.

[0024] Also disclosed is an isolated (e.g., monoclonal) anti-Siglec-9 antibody, wherein the anti-Siglec-9 antibody binds to one or more amino acids within amino acid residues 20-347, 20-140, 141-347, 146-347, 146-229, 236-336, or 146-347 of SEQ ID NO: 1; or within amino acid residues on a mammalian Siglec-9 protein corresponding to amino acid residues 20-347, 20-140, 141-347, 146-347, 146-229, 236-336, or 146-347 of SEQ ID NO: 1. In some examples, the anti-Siglec-9 antibody binds to one or more amino acids within amino acid residues selected from the group consisting of: i. amino acid residues 62-76 of SEQ ID NO: 1, or amino acid residues on a mammalian Siglec-9 protein corresponding to amino acid residues 62-76 of SEQ ID NO: 1; ii. amino acid residues 62-76 and 86-92 of SEQ ID NO: 1, or amino acid residues on a mammalian Siglec-9 protein corresponding to amino acid residues 62-76 and 86-92 of SEQ ID NO: 1; iii. amino acid residues 86-92 of SEQ ID NO: 1, or amino acid residues on a mammalian Siglec-9 protein corresponding to amino acid residues 86-92 of SEQ ID NO: 1; iv. amino acid residues 86-96 of SEQ ID NO: 1, or amino acid residues on a mammalian Siglec-9 protein corresponding to amino acid residues 86-96 of SEQ ID NO: 1; v. amino acid residues 86-96 and 105-116 of SEQ ID NO: 1, or amino acid residues on a mammalian Siglec-9 protein corresponding to amino acid residues 86-96 and 105-116 of SEQ ID NO: 1; vi. amino acid residues 105-116 of SEQ ID NO: 1, or amino acid residues on a mammalian Siglec-9 protein corresponding to amino acid residues 105-116 of SEQ ID NO: 1; vii. amino acid residues 107-115 of SEQ ID NO: 1, or amino acid residues on a mammalian Siglec-9 protein corresponding to amino acid residues 107-115 of SEQ ID NO: 1; and viii. amino acid residues 185-194 of SEQ ID NO: 1, or amino acid residues on a mammalian Siglec-9 protein corresponding to amino acid residues 185-194 of SEQ ID NO: 1. In some examples, the anti-Siglec-9 antibody binds to one or more amino acids within amino acid residues 62-76 of SEQ ID NO: 1, or amino acid residues on a mammalian Siglec-9 protein corresponding to amino acid residues 62-76 of SEQ ID NO: 1. In some examples, the anti-Siglec-9 antibody binds to one or more amino acids within amino acid residues 62-76 and 86-92 of SEQ ID NO: 1, or amino acid residues on a mammalian Siglec-9 protein corresponding to amino acid residues 62-76 and 86-92 of SEQ ID NO: 1. In some examples, the anti-Siglec-9 antibody binds to one or more amino acids within amino acid residues 86-92 of SEQ ID NO: 1, or amino acid residues on a mammalian Siglec-9 protein corresponding to amino acid residues 86-92 of SEQ ID NO: 1. In some examples, the anti-Siglec-9 antibody binds to one or more amino acids within amino acid residues 86-96 of SEQ ID NO: 1, or amino acid residues on a mammalian Siglec-9 protein corresponding to amino acid residues 86-

96 of SEQ ID NO: 1. In some examples, the anti-Siglec-9 antibody binds to one or more amino acids within amino acid residues 86-96 and 105-116 of SEQ ID NO: 1, or amino acid residues on a mammalian Siglec-9 protein corresponding to amino acid residues 86-96 and 105-116 of SEQ ID NO: 1. In some examples, the anti-Siglec-9 antibody binds to one or more amino acids within amino acid residues 105-116 of SEQ ID NO: 1, or amino acid residues on a mammalian Siglec-9 protein corresponding to amino acid residues 105-116 of SEQ ID NO: 1. In some examples, the anti-Siglec-9 antibody binds to one or more amino acids within amino acid residues 107-115 of SEQ ID NO: 1, or amino acid residues on a mammalian Siglec-9 protein corresponding to amino acid residues 107-115 of SEQ ID NO: 1. In some examples, the anti-Siglec-9 antibody binds to one or more amino acids within amino acid residues 185-194 of SEQ ID NO: 1, or amino acid residues on a mammalian Siglec-9 protein corresponding to amino acid residues 185-194 of SEQ ID NO: 1. Also disclosed is an isolated anti-Siglec-9 antibody, wherein the anti-Siglec-9 antibody binds to one or more amino acid residues selected from the group consisting of L22, H48, W50, I51, Y52, K123, I126, D189, P190, R194 of SEQ ID NO: 1, or one or more amino acid residues on a mammalian Siglec-7 protein corresponding to an amino acid residue selected from the group consisting of L22, H48, W50, I51, Y52, K123, I126, D189, P190, R194 of SEQ ID NO: 1.

[0025] Also disclosed is an isolated anti-Siglec-9 antibody, wherein the anti-Siglec-9 antibody binds to one or more amino acids within amino acid residues 62-76 of SEQ ID NO: 1, or amino acid residues on a mammalian Siglec-9 protein corresponding to amino acid residues 62-76 of SEQ ID NO: 1. Also disclosed is an isolated anti-Siglec-9 antibody, wherein the anti-Siglec-9 antibody binds to one or more amino acids within amino acid residues 62-76 and 86-92 of SEQ ID NO: 1, or amino acid residues on a mammalian Siglec-9 protein corresponding to amino acid residues 62-76 and 86-92 of SEQ ID NO: 1. Also disclosed is an isolated anti-Siglec-9 antibody, wherein the anti-Siglec-9 antibody binds to one or more amino acids within amino acid residues 86-92 of SEQ ID NO: 1, or amino acid residues on a mammalian Siglec-9 protein corresponding to amino acid residues 86-92 of SEQ ID NO: 1. Also disclosed is an isolated anti-Siglec-9 antibody, wherein the anti-Siglec-9 antibody binds to one or more amino acids within amino acid residues 86-96 of SEQ ID NO: 1, or amino acid residues on a mammalian Siglec-9 protein corresponding to amino acid residues 86-96 of SEQ ID NO: 1. Also disclosed is an isolated anti-Siglec-9 antibody, wherein the anti-Siglec-9 antibody binds to one or more amino acids within amino acid residues 86-96 and 105-116 of SEQ ID NO: 1, or amino acid residues on a mammalian Siglec-9 protein corresponding to amino acid residues 86-96 and 105-116 of SEQ ID NO: 1. Also disclosed is an isolated anti-Siglec-9 antibody, wherein the anti-Siglec-9 antibody binds to one or more amino acids within amino acid residues 105-

116 of SEQ ID NO: 1, or amino acid residues on a mammalian Siglec-9 protein corresponding to amino acid residues 105-116 of SEQ ID NO: 1. Also disclosed is an isolated anti-Siglec-9 antibody, wherein the anti-Siglec-9 antibody binds to one or more amino acids within amino acid residues 107-115 of SEQ ID NO: 1, or amino acid residues on a mammalian Siglec-9 protein corresponding to amino acid residues 107-115 of SEQ ID NO: 1. Also disclosed is an isolated anti-Siglec-9 antibody, wherein the anti-Siglec-9 antibody binds to one or more amino acids within amino acid residues 185-194 of SEQ ID NO: 1, or amino acid residues on a mammalian Siglec-9 protein corresponding to amino acid residues 185-194 of SEQ ID NO: 1.

[0026] Also disclosed is an isolated (e.g., monoclonal) anti-Siglec-9 antibody, wherein the anti-Siglec-9 antibody comprises a light chain variable domain and a heavy chain variable domain, wherein the light chain variable domain, the heavy chain variable domain, or both comprise at least one, two, three, four, five, or six HVRs selected from HVR-L1, HVR-L2, HVR-L3, HVR-H1, HVR-H2, and HVR-H3 of a monoclonal antibody selected from the group consisting of: 2D4, 2D5, 5B1, 6B2, 6D8, 7H12, 5C6, 12B12, and 17C2. In some examples: (a) the HVR-L1 comprises an amino acid sequence selected from the group consisting of SEQ ID NOs: 6-9, 172, and 173; or (b) the HVR-L2 comprises an amino acid sequence selected from the group consisting of SEQ ID NOs: 10-13, 174, and 175; or (c) the HVR-L3 comprises an amino acid sequence selected from the group consisting of SEQ ID NOs: 14-18, 176, and 177; or (d) the HVR-H1 comprises an amino acid sequence selected from the group consisting of SEQ ID NOs: 19-21, 178, and 179; or (e) the HVR-H2 comprises an amino acid sequence selected from the group consisting of SEQ ID NOs: 22-25, 180, and 181; or (f) the HVR-H3 comprises an amino acid sequence selected from the group consisting of SEQ ID NOs: 26-29, 182, and 183. In some examples: (a) the HVR-L1 comprises the amino acid sequence of SEQ ID NO: 6, the HVR-L2 comprises the amino acid sequence of SEQ ID NO: 10, the HVR-L3 comprises the amino acid sequence of SEQ ID NO: 14, the HVR-H1 comprises the amino acid sequence of SEQ ID NO: 19, the HVR-H2 comprises the amino acid sequence of SEQ ID NO: 22, and the HVR-H3 comprises the amino acid sequence of SEQ ID NO: 26; or (b) the HVR-L1 comprises the amino acid sequence of SEQ ID NO: 7, the HVR-L2 comprises the amino acid sequence of SEQ ID NO: 11, the HVR-L3 comprises the amino acid sequence of SEQ ID NO: 15, the HVR-H1 comprises the amino acid sequence of SEQ ID NO: 20, the HVR-H2 comprises the amino acid sequence of SEQ ID NO: 23, and the HVR-H3 comprises the amino acid sequence of SEQ ID NO: 27; or (c) the HVR-L1 comprises the amino acid sequence of SEQ ID NO: 8, the HVR-L2 comprises the amino acid sequence of SEQ ID NO: 12, the HVR-L3 comprises the amino acid sequence of SEQ ID NO: 16, the HVR-H1 comprises the amino acid sequence of SEQ ID NO: 21, the HVR-H2 comprises the amino

acid sequence of SEQ ID NO: 24, and the HVR-H3 comprises the amino acid sequence of SEQ ID NO: 28; or (d) the HVR-L1 comprises the amino acid sequence of SEQ ID NO: 9, the HVR-L2 comprises the amino acid sequence of SEQ ID NO: 13, the HVR-L3 comprises the amino acid sequence of SEQ ID NO: 17, the HVR-H1 comprises the amino acid sequence of SEQ ID NO: 21, the HVR-H2 comprises the amino acid sequence of SEQ ID NO: 25, and the HVR-H3 comprises the amino acid sequence of SEQ ID NO: 29; or (e) the HVR-L1 comprises the amino acid sequence of SEQ ID NO: 8, the HVR-L2 comprises the amino acid sequence of SEQ ID NO: 12, the HVR-L3 comprises the amino acid sequence of SEQ ID NO: 18, the HVR-H1 comprises the amino acid sequence of SEQ ID NO: 21, the HVR-H2 comprises the amino acid sequence of SEQ ID NO: 24, and the HVR-H3 comprises the amino acid sequence of SEQ ID NO: 28; or (f) the HVR-L1 comprises the amino acid sequence of SEQ ID NO: 172, the HVR-L2 comprises the amino acid sequence of SEQ ID NO: 174, the HVR-L3 comprises the amino acid sequence of SEQ ID NO: 176, the HVR-H1 comprises the amino acid sequence of SEQ ID NO: 178, the HVR-H2 comprises the amino acid sequence of SEQ ID NO: 180, and the HVR-H3 comprises the amino acid sequence of SEQ ID NO: 182; or (g) the HVR-L1 comprises the amino acid sequence of SEQ ID NO: 173, the HVR-L2 comprises the amino acid sequence of SEQ ID NO: 175, the HVR-L3 comprises the amino acid sequence of SEQ ID NO: 177, the HVR-H1 comprises the amino acid sequence of SEQ ID NO: 179, the HVR-H2 comprises the amino acid sequence of SEQ ID NO: 181, and the HVR-H3 comprises the amino acid sequence of SEQ ID NO: 183. In some examples, the anti-Siglec-9 antibody comprises a light chain variable domain and a heavy chain variable domain, wherein the light chain variable domain comprises: an HVR-L1 comprising the amino acid sequence of SEQ ID NO: 6, an HVR-L2 comprising the amino acid sequence of SEQ ID NO: 10, and an HVR-L3 comprising the amino acid sequence of SEQ ID NO: 14, and wherein the heavy chain variable domain comprises: an HVR-H1 comprising the amino acid sequence of SEQ ID NO: 19, an HVR-H2 comprising the amino acid sequence of SEQ ID NO: 22, and an HVR-H3 comprising the amino acid sequence of SEQ ID NO: 26. In some examples, the anti-Siglec-9 antibody comprises a light chain variable domain and a heavy chain variable domain, wherein the light chain variable domain comprises: an HVR-L1 comprising the amino acid sequence of SEQ ID NO: 7, an HVR-L2 comprising the amino acid sequence of SEQ ID NO: 11, and an HVR-L3 comprising the amino acid sequence of SEQ ID NO: 15, and wherein the heavy chain variable domain comprises: an HVR-H1 comprising the amino acid sequence of SEQ ID NO: 20, an HVR-H2 comprising the amino acid sequence of SEQ ID NO: 23, and an HVR-H3 comprising the amino acid sequence of SEQ ID NO: 27. In some examples, the anti-Siglec-9 antibody comprises a light chain variable domain and a heavy chain variable domain, wherein the light chain variable domain comprises: an HVR-L1 comprising the amino acid sequence of SEQ ID NO: 8, an HVR-L2 comprising the amino acid

sequence of SEQ ID NO: 12, and an HVR-L3 comprising the amino acid sequence of SEQ ID NO: 16, and wherein the heavy chain variable domain comprises: an HVR-H1 comprising the amino acid sequence of SEQ ID NO: 21, an HVR-H2 comprising the amino acid sequence of SEQ ID NO: 24, and an HVR-H3 comprising the amino acid sequence of SEQ ID NO: 28. In some examples, the anti-Siglec-9 antibody comprises a light chain variable domain and a heavy chain variable domain, wherein the light chain variable domain comprises: an HVR-L1 comprising the amino acid sequence of SEQ ID NO: 9, an HVR-L2 comprising the amino acid sequence of SEQ ID NO: 13, and an HVR-L3 comprising the amino acid sequence of SEQ ID NO: 17, and wherein the heavy chain variable domain comprises: an HVR-H1 comprising the amino acid sequence of SEQ ID NO: 21, an HVR-H2 comprising the amino acid sequence of SEQ ID NO: 25, and an HVR-H3 comprising the amino acid sequence of SEQ ID NO: 29. In some examples, the anti-Siglec-9 antibody comprises a light chain variable domain and a heavy chain variable domain, wherein the light chain variable domain comprises: an HVR-L1 comprising the amino acid sequence of SEQ ID NO: 8, an HVR-L2 comprising the amino acid sequence of SEQ ID NO: 12, and an HVR-L3 comprising the amino acid sequence of SEQ ID NO: 18, and wherein the heavy chain variable domain comprises: an HVR-H1 comprising the amino acid sequence of SEQ ID NO: 21, an HVR-H2 comprising the amino acid sequence of SEQ ID NO: 24, and an HVR-H3 comprising the amino acid sequence of SEQ ID NO: 28. In some examples, the anti-Siglec-9 antibody comprises a light chain variable domain and a heavy chain variable domain, wherein the light chain variable domain comprises: an HVR-L1 comprising the amino acid sequence of SEQ ID NO: 172, an HVR-L2 comprising the amino acid sequence of SEQ ID NO: 174, and an HVR-L3 comprising the amino acid sequence of SEQ ID NO: 176, and wherein the heavy chain variable domain comprises: an HVR-H1 comprising the amino acid sequence of SEQ ID NO: 178, an HVR-H2 comprising the amino acid sequence of SEQ ID NO: 180, and an HVR-H3 comprising the amino acid sequence of SEQ ID NO: 182. In some examples, the anti-Siglec-9 antibody comprises a light chain variable domain and a heavy chain variable domain, wherein the light chain variable domain comprises: an HVR-L1 comprising the amino acid sequence of SEQ ID NO: 173, an HVR-L2 comprising the amino acid sequence of SEQ ID NO: 175, and an HVR-L3 comprising the amino acid sequence of SEQ ID NO: 177, and wherein the heavy chain variable domain comprises: an HVR-H1 comprising the amino acid sequence of SEQ ID NO: 179, an HVR-H2 comprising the amino acid sequence of SEQ ID NO: 181, and an HVR-H3 comprising the amino acid sequence of SEQ ID NO: 183. In some examples, the light chain variable domain comprises: (a) an HVR-L1 comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 6-9, 172, and 173, or an amino acid sequence with at least about 90% homology to an amino acid sequence selected from the group consisting of SEQ ID NOs: 6-9, 172, and 173; (b) an HVR-L2 comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 10-

13, 174, and 175, or an amino acid sequence with at least about 90% homology to an amino acid sequence selected from the group consisting of SEQ ID NOs: 10-13, 174, and 175; and (c) an HVR-L3 comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 14-18, 176, and 177, or an amino acid sequence with at least about 90% homology to an amino acid sequence selected from the group consisting of SEQ ID NOs: 14-18, 176, and 177; and wherein the heavy chain variable domain comprises: (a) an HVR-H1 comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 19-21, 178, and 179, or an amino acid sequence with at least about 90% homology to an amino acid sequence selected from the group consisting of SEQ ID NOs: 19-21, 178, and 179; (b) an HVR-H2 comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 22-25, 180, and 181, or an amino acid sequence with at least about 90% homology to an amino acid sequence selected from the group consisting of SEQ ID NOs: 22-25, 180, and 181; and (c) an HVR-H3 comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 26-29, 182, and 183, or an amino acid sequence with at least about 90% homology to an amino acid sequence selected from the group consisting of SEQ ID NOs: 26-29, 182, and 183.

[0027] Also disclosed is an isolated anti-Siglec-9 antibody, wherein the anti-Siglec-9 antibody comprises a light chain variable domain and a heavy chain variable domain, wherein the light chain variable domain comprises: an HVR-L1 comprising the amino acid sequence of SEQ ID NO: 6, an HVR-L2 comprising the amino acid sequence of SEQ ID NO: 10, and an HVR-L3 comprising the amino acid sequence of SEQ ID NO: 14, and wherein the heavy chain variable domain comprises: an HVR-H1 comprising the amino acid sequence of SEQ ID NO: 19, an HVR-H2 comprising the amino acid sequence of SEQ ID NO: 22, and an HVR-H3 comprising the amino acid sequence of SEQ ID NO: 26. Also disclosed is an isolated anti-Siglec-9 antibody, wherein the anti-Siglec-9 antibody comprises a light chain variable domain and a heavy chain variable domain, wherein the light chain variable domain comprises: an HVR-L1 comprising the amino acid sequence of SEQ ID NO: 7, an HVR-L2 comprising the amino acid sequence of SEQ ID NO: 11, and an HVR-L3 comprising the amino acid sequence of SEQ ID NO: 15, and wherein the heavy chain variable domain comprises: an HVR-H1 comprising the amino acid sequence of SEQ ID NO: 20, an HVR-H2 comprising the amino acid sequence of SEQ ID NO: 23, and an HVR-H3 comprising the amino acid sequence of SEQ ID NO: 27. Also disclosed is an isolated anti-Siglec-9 antibody, wherein the anti-Siglec-9 antibody comprises a light chain variable domain and a heavy chain variable domain, wherein the light chain variable domain comprises: an HVR-L1 comprising the amino acid sequence of SEQ ID NO: 8, an HVR-L2 comprising the amino acid sequence of SEQ ID NO: 12, and an HVR-L3 comprising the amino acid sequence of SEQ ID NO: 16, and wherein the heavy chain variable

domain comprises: an HVR-H1 comprising the amino acid sequence of SEQ ID NO: 21, an HVR-H2 comprising the amino acid sequence of SEQ ID NO: 24, and an HVR-H3 comprising the amino acid sequence of SEQ ID NO: 28. Also disclosed is an isolated anti-Siglec-9 antibody, wherein the anti-Siglec-9 antibody comprises a light chain variable domain and a heavy chain variable domain, wherein the light chain variable domain comprises: an HVR-L1 comprising the amino acid sequence of SEQ ID NO: 9, an HVR-L2 comprising the amino acid sequence of SEQ ID NO: 13, and an HVR-L3 comprising the amino acid sequence of SEQ ID NO: 17, and wherein the heavy chain variable domain comprises: an HVR-H1 comprising the amino acid sequence of SEQ ID NO: 21, an HVR-H2 comprising the amino acid sequence of SEQ ID NO: 25, and an HVR-H3 comprising the amino acid sequence of SEQ ID NO: 29. Also disclosed is an isolated anti-Siglec-9 antibody, wherein the anti-Siglec-9 antibody comprises a light chain variable domain and a heavy chain variable domain, wherein the light chain variable domain comprises: an HVR-L1 comprising the amino acid sequence of SEQ ID NO: 8, an HVR-L2 comprising the amino acid sequence of SEQ ID NO: 12, and an HVR-L3 comprising the amino acid sequence of SEQ ID NO: 18, and wherein the heavy chain variable domain comprises: an HVR-H1 comprising the amino acid sequence of SEQ ID NO: 21, an HVR-H2 comprising the amino acid sequence of SEQ ID NO: 24, and an HVR-H3 comprising the amino acid sequence of SEQ ID NO: 28. Also disclosed is an isolated anti-Siglec-9 antibody, wherein the anti-Siglec-9 antibody comprises a light chain variable domain and a heavy chain variable domain, wherein the light chain variable domain comprises: an HVR-L1 comprising the amino acid sequence of SEQ ID NO: 172, an HVR-L2 comprising the amino acid sequence of SEQ ID NO: 174, and an HVR-L3 comprising the amino acid sequence of SEQ ID NO: 176, and wherein the heavy chain variable domain comprises: an HVR-H1 comprising the amino acid sequence of SEQ ID NO: 178, an HVR-H2 comprising the amino acid sequence of SEQ ID NO: 180, and an HVR-H3 comprising the amino acid sequence of SEQ ID NO: 182. Also disclosed is an isolated anti-Siglec-9 antibody, wherein the anti-Siglec-9 antibody comprises a light chain variable domain and a heavy chain variable domain, wherein the light chain variable domain comprises: an HVR-L1 comprising the amino acid sequence of SEQ ID NO: 173, an HVR-L2 comprising the amino acid sequence of SEQ ID NO: 175, and an HVR-L3 comprising the amino acid sequence of SEQ ID NO: 177, and wherein the heavy chain variable domain comprises: an HVR-H1 comprising the amino acid sequence of SEQ ID NO: 179, an HVR-H2 comprising the amino acid sequence of SEQ ID NO: 181, and an HVR-H3 comprising the amino acid sequence of SEQ ID NO: 183. Also disclosed is an isolated (e.g., monoclonal) anti-Siglec-9 antibody, wherein the anti-Siglec-9 antibody comprises a light chain variable domain comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 61-115 and 197-204 and/or a heavy chain

variable domain comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 116-170 and 205-212. Also disclosed is an isolated (e.g., monoclonal) anti-Siglec-9 antibody, wherein the anti-Siglec-9 antibody comprises a light chain variable domain and a heavy chain variable domain, and wherein: (a) the light chain variable domain comprises the amino acid sequence of SEQ ID NO: 61; and the heavy chain variable domain comprises the amino acid sequence of SEQ ID NO: 116; or (b) the light chain variable domain comprises the amino acid sequence of SEQ ID NO: 72; and the heavy chain variable domain comprises the amino acid sequence of SEQ ID NO: 127; or (c) the light chain variable domain comprises the amino acid sequence of SEQ ID NO: 83; and the heavy chain variable domain comprises the amino acid sequence of SEQ ID NO: 138; or (d) the light chain variable domain comprises the amino acid sequence of SEQ ID NO: 94; and the heavy chain variable domain comprises the amino acid sequence of SEQ ID NO: 149; or (e) the light chain variable domain comprises the amino acid sequence of SEQ ID NO: 105; and the heavy chain variable domain comprises the amino acid sequence of SEQ ID NO: 160; or (f) the light chain variable domain comprises the amino acid sequence of SEQ ID NO: 197; and the heavy chain variable domain comprises the amino acid sequence of SEQ ID NO: 205; or (g) the light chain variable domain comprises the amino acid sequence of SEQ ID NO: 201; and the heavy chain variable domain comprises the amino acid sequence of SEQ ID NO: 210. Also disclosed is an isolated (e.g., monoclonal) anti-Siglec-9 antibody, wherein the anti-Siglec-9 antibody comprises a light chain variable domain of a monoclonal antibody selected from the group consisting of: 2D4, 2D5, 5B1, 6B2, 6D8, 7H12, 5C6, 12B12, and 17C2; and/or a heavy chain variable domain of a monoclonal antibody selected from the group consisting of: 2D4, 2D5, 5B1, 6B2, 6D8, 7H12, 5C6, 12B12, and 17C2. Also disclosed is an isolated (e.g., monoclonal) anti-Siglec-9 antibody, wherein the anti-Siglec-9 antibody competes with one or more antibodies selected from the group consisting of 2D4, 2D5, 5B1, 6B2, 6D8, 7H12, 5C6, 12B12, 17C2, and any combination thereof for binding to Siglec-9. Also disclosed is an isolated (e.g., monoclonal) anti-Siglec-9 antibody which binds essentially the same Siglec-9 epitope as a monoclonal antibody selected from the group consisting of: 2D4, 2D5, 5B1, 6B2, 6D8, 7H12, 5C6, 12B12, and 17C2. Also disclosed is an isolated (e.g., monoclonal) anti-Siglec-9 antibody, wherein the anti-Siglec-9 antibody comprises a light chain variable domain and a heavy chain variable domain, wherein the light chain variable domain comprises: (a) an HVR-L1 comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 6-9, 172, and 173, or an amino acid sequence with at least about 90% homology to an amino acid sequence selected from the group consisting of SEQ ID NOs: 6-9, 172, and 173; (b) an HVR-L2 comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 10-

13, 174, and 175, or an amino acid sequence with at least about 90% homology to an amino acid sequence selected from the group consisting of SEQ ID NOs: 10-13, 174, and 175; and (c) an HVR-L3 comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 14-18, 176, and 177, or an amino acid sequence with at least about 90% homology to an amino acid sequence selected from the group consisting of SEQ ID NOs: 14-18, 176, and 177; and wherein the heavy chain variable domain comprises: (a) an HVR-H1 comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 19-21, 178, and 179, or an amino acid sequence with at least about 90% homology to an amino acid sequence selected from the group consisting of SEQ ID NOs: 19-21, 178, and 179; (b) an HVR-H2 comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 22-25, 180, and 181, or an amino acid sequence with at least about 90% homology to an amino acid sequence selected from the group consisting of SEQ ID NOs: 22-25, 180, and 181; and (c) an HVR-H3 comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 26-29, 182, and 183, or an amino acid sequence with at least about 90% homology to an amino acid sequence selected from the group consisting of SEQ ID NOs: 26-29, 182, and 183.

[0028] In some examples that may be combined with any of the preceding examples, the antibody is of the IgG class the IgM class, or the IgA class. In some examples that may be combined with any of the preceding examples, the anti-Siglec-9 antibody has an IgG1, IgG2, IgG3, or IgG4 isotype. In some examples that may be combined with any of the preceding examples, the antibody binds an inhibitory Fc receptor. In some examples that may be combined with any of the preceding examples, the inhibitory Fc receptor is inhibitory Fc-gamma receptor IIB (FcγIIB). In some examples that may be combined with any of the preceding examples: (a) the anti-Siglec-9 antibody has a human or mouse IgG1 isotype and comprises one or more amino acid substitutions in the Fc region at a residue position selected from the group consisting of: N297A, D265A, D270A, L234A, L235A, G237A, P238D, L328E, E233D, G237D, H268D, P271G, A330R, C226S, C229S, E233P, L234V, L234F, L235E, P331S, S267E, L328F, A330L, M252Y, S254T, T256E, N297Q, P238S, P238A, A327Q, A327G, P329A, K322A, T394D, and any combination thereof, wherein the numbering of the residues is according to EU or Kabat numbering, or comprises an amino acid deletion in the Fc region at a position corresponding to glycine 236; (b) the anti-Siglec-9 antibody has an IgG1 isotype and comprises an IgG2 isotype heavy chain constant domain 1(CH1) and hinge region, optionally wherein the IgG2 isotype CH1 and hinge region comprises the amino acid sequence of ASTKGPSVFP LAPCSRSTSE STAALGCLVK DYFPEPVTVS WNSGALTSGVHTFPAVLQSS GLYSLSSVVT VPSSNFGTQT YTCNVDPKPS NTKVDKTVKRCCECP (SEQ ID NO: 171), and optionally wherein the antibody Fc region comprises a S267E amino acid substitution, a L328F amino acid substitution, or both, and/or a

N297A or N297Q amino acid substitution, wherein the numbering of the residues is according to EU numbering; (c) the anti-Siglec-9 antibody has an IgG2 isotype and comprises one or more amino acid substitutions in the Fc region at a residue position selected from the group consisting of: P238S, V234A, G237A, H268A, H268Q, V309L, A330S, P331S, C214S, C232S, C233S, S267E, L328F, M252Y, S254T, T256E, H268E, N297A, N297Q, A330L, and any combination thereof, wherein the numbering of the residues is according to EU or Kabat numbering; (d) the anti-Siglec-9 antibody has a human or mouse IgG4 isotype and comprises one or more amino acid substitutions in the Fc region at a residue position selected from the group consisting of: L235A, G237A, S228P, L236E, S267E, E318A, L328F, M252Y, S254T, T256E, E233P, F234V, L234A/F234A, S228P, S241P, L248E, T394D, N297A, N297Q, L235E, and any combination thereof, wherein the numbering of the residues is according to EU or Kabat numbering; or (e) the anti-Siglec-9 antibody has a hybrid IgG2/4 isotype, and optionally wherein the antibody comprises an amino acid sequence comprising amino acids 118 to 260 of human IgG2 and amino acids 261 to 447 of human IgG4, wherein the numbering of the residues is according to EU or Kabat numbering. In some examples that may be combined with any of the preceding examples: (a) the anti-Siglec-9 antibody has a human or mouse IgG1 isotype and comprises one or more amino acid substitutions in the Fc region at a residue position selected from the group consisting of: N297A, N297Q, D270A, D265A, L234A, L235A, C226S, C229S, P238S, E233P, L234V, P238A, A327Q, A327G, P329A, K322A, L234F, L235E, P331S, T394D, A330L, M252Y, S254T, T256E, and any combination thereof, wherein the numbering of the residues is according to EU or Kabat numbering; (b) the anti-Siglec-9 antibody has an IgG2 isotype and comprises one or more amino acid substitutions in the Fc region at a residue position selected from the group consisting of: P238S, V234A, G237A, H268A, H268Q, H268E, V309L, N297A, N297Q, A330S, P331S, C232S, C233S, M252Y, S254T, T256E, and any combination thereof, wherein the numbering of the residues is according to EU or Kabat numbering; or (c) the anti-Siglec-9 antibody has an IgG4 isotype and comprises one or more amino acid substitutions in the Fc region at a residue position selected from the group consisting of: E233P, F234V, L234A/F234A, L235A, G237A, E318A, S228P, L236E, S241P, L248E, T394D, M252Y, S254T, T256E, N297A, N297Q, and any combination thereof, wherein the numbering of the residues is according to EU or Kabat numbering. In some examples that may be combined with any of the preceding examples: (a) the Fc region further comprises one or more additional amino acid substitutions at a position selected from the group consisting of A330L, L234F, L235E, P331S, and any combination thereof, wherein the numbering of the residues is according to EU or Kabat numbering; (b) the Fc region further comprises one or more additional amino acid substitutions at a position selected from the group consisting of M252Y, S254T, T256E, and any combination thereof, wherein the numbering of the residues is according to EU or Kabat numbering; or (c) the Fc region further comprises a S228P

amino acid substitution according to EU or Kabat numbering. In some examplesthat may be combined with any of the preceding examples, the antibody has an IgG4 isotype. In some examplesthat may be combined with any of the preceding examples, the anti-Siglec-9 antibody comprises an S228P amino acid substitution at residue position 228, an F234A amino acid substitution at residue position 234, and an L235A amino acid substitution at residue position 235, wherein the numbering of the residue position is according to EU or Kabat numbering. In some examplesthat may be combined with any of the preceding examples, the Siglec-9 protein is a mammalian protein or a human protein. In some examplesthat may be combined with any of the preceding examples, the Siglec-9 protein is a wild-type protein. In some examplesthat may be combined with any of the preceding examples, the Siglec-9 protein is a naturally occurring variant. In some examplesthat may be combined with any of the preceding examples, the Siglec-9 protein is expressed on one or more cells selected from the group consisting of human dendritic cells, human macrophages, human neutrophils, human NK cells, human monocytes, human osteoclasts, human T cells, human T helper cell, human cytotoxic T cells, human granulocytes, and human microglia. In some examplesthat may be combined with any of the preceding examples, the anti-Siglec-9 antibody binds specifically to a mammalian Siglec-9 protein, human Siglec-9 protein, or both. In some examplesthat may be combined with any of the preceding examples, the anti-Siglec-9 antibody binds Siglec-9 in a pH dependent manner. In some examplesthat may be combined with any of the preceding examples, the anti-Siglec-9 antibody binds Siglec-9 at a pH that ranges from 5.5 to 8.0. In some examplesthat may be combined with any of the preceding examples, the anti-Siglec-9 antibody dissociates from Siglec-9 at a pH of less than 5.0. In some examplesthat may be combined with any of the preceding examples, the anti-Siglec-9 antibody is an antibody fragment that binds to an epitope comprising amino acid residues on human Siglec-9 or a mammalian Siglec-9 protein. In some examplesthat may be combined with any of the preceding examples, the anti-Siglec-9 antibody is an antibody fragment that binds to one or more human proteins selected from the group consisting of human Siglec-9, a naturally occurring variant of human Siglec-9, and a disease variant of human Siglec-9. In some examplesthat may be combined with any of the preceding examples, the antibody fragment is cross-linked to a second antibody fragment that binds to one or more human proteins selected from the group consisting of human Siglec-9, a naturally occurring variant of human Siglec-9, and a disease variant of human Siglec-9. In some examplesthat may be combined with any of the preceding examples, the fragment is an Fab, Fab', Fab'-SH, F(ab')₂, Fv, or scFv fragment. In some examplesthat may be combined with any of the preceding examples, the anti-Siglec-9 antibody is a murine antibody. In some examplesthat may be combined with any of the preceding examples, the anti-Siglec-9 antibody is a humanized antibody, a bispecific antibody, a

monoclonal antibody, a multivalent antibody, a conjugated antibody, or a chimeric antibody. In some examples that may be combined with any of the preceding examples, the anti-Siglec-9 antibody is a bispecific antibody recognizing a first antigen and a second antigen. In some examples that may be combined with any of the preceding examples, the first antigen is Siglec-9 and the second antigen is: (a) an antigen facilitating transport across the blood-brain-barrier; (b) an antigen facilitating transport across the blood-brain-barrier selected from the group consisting of transferrin receptor (TR), insulin receptor (HIR), insulin-like growth factor receptor (IGFR), low-density lipoprotein receptor related proteins 1 and 2 (LPR-1 and 2), diphtheria toxin receptor, CRM197, a llama single domain antibody, TMEM 30(A), a protein transduction domain, TAT, Syn-B, penetratin, a poly-arginine peptide, an angiopep peptide, and ANG1005; (c) a disease-causing agent selected from the group consisting of disease-causing peptides or proteins or, disease-causing nucleic acids, wherein the disease-causing nucleic acids are antisense GGCCCC (G2C4) repeat-expansion RNA, the disease-causing proteins are selected from the group consisting of amyloid beta, oligomeric amyloid beta, amyloid beta plaques, amyloid precursor protein or fragments thereof, Tau, IAPP, alpha-synuclein, TDP-43, FUS protein, C9orf72 (chromosome 9 open reading frame 72), c9RAN protein, prion protein, PrPSc, huntingtin, calcitonin, superoxide dismutase, ataxin, ataxin 1, ataxin 2, ataxin 3, ataxin 7, ataxin 8, ataxin 10, Lewy body, atrial natriuretic factor, islet amyloid polypeptide, insulin, apolipoprotein AI, serum amyloid A, medin, prolactin, transthyretin, lysozyme, beta 2 microglobulin, gelsolin, keratopithelin, cystatin, immunoglobulin light chain AL, S-IBM protein, Repeat-associated non-ATG (RAN) translation products, DiPeptide repeat (DPR) peptides, glycine-alanine (GA) repeat peptides, glycine-proline (GP) repeat peptides, glycine-arginine (GR) repeat peptides, proline-alanine (PA) repeat peptides, ubiquitin, and proline-arginine (PR) repeat peptides; (d) ligands and/or proteins expressed on immune cells, wherein the ligands and/or proteins selected from the group consisting of PD1/PDL1, CD40, OX40, ICOS, CD28, CD137/4-1BB, CD27, GITR, PD-L1, CTLA4, PD-L2, PD-1, B7-H3, B7-H4, HVEM, LIGHT, BTLA, CD30, TIGIT, VISTA, KIR, GAL9, TIM1, TIM3, TIM4, A2AR, LAG3, DR-5, CD2, CD5, CD39, CD73, and phosphatidylserine; and (e) a protein, lipid, polysaccharide, or glycolipid expressed on one or more tumor cells. In some examples that may be combined with any of the preceding examples, the anti-Siglec-9 antibody is a conjugated antibody. In some examples that may be combined with any of the preceding examples, the anti-Siglec-9 antibody is conjugated to a detectable marker, a toxin, or a therapeutic agent. In some examples that may be combined with any of the preceding examples, the anti-Siglec-9 antibody is conjugated to a toxin selected from the group consisting of ricin, ricin A-chain, doxorubicin, daunorubicin, a maytansinoid, taxol, ethidium bromide, mitomycin, etoposide, tenoposide, vincristine, vinblastine, colchicine, dihydroxy anthracin dione, actinomycin, diphtheria toxin, *Pseudomonas* exotoxin (PE) A, PE40, abrin, abrin A chain,

modeccin A chain, alpha-sarcin, gelonin, mitogellin, retstrictocin, phenomycin, enomycin, curicin, crotin, calicheamicin, *Saponaria officinalis* inhibitor, glucocorticoid, auristatin, auromycin, yttrium, bismuth, combrestatin, duocarmycins, dolastatin, cc1065, and a cisplatin. In some examples that may be combined with any of the preceding examples, the anti-Siglec-9 antibody is used in combination with one or more antibodies that specifically bind a disease-causing protein selected from the group consisting of amyloid beta, oligomeric amyloid beta, amyloid beta plaques, amyloid precursor protein or fragments thereof, Tau, IAPP, alpha-synuclein, TDP-43, FUS protein, C9orf72 (chromosome 9 open reading frame 72), prion protein, PrPSc, huntingtin, calcitonin, superoxide dismutase, ataxin, ataxin 1, ataxin 2, ataxin 3, ataxin 7, ataxin 8, ataxin 10, Lewy body, atrial natriuretic factor, islet amyloid polypeptide, insulin, apolipoprotein AI, serum amyloid A, medin, prolactin, transthyretin, lysozyme, beta 2 microglobulin, gelsolin, keratoepithelin, cystatin, immunoglobulin light chain AL, S-IBM protein, Repeat-associated non-ATG (RAN) translation products, DiPeptide repeat (DPR) peptides, glycine-alanine (GA) repeat peptides, glycine-proline (GP) repeat peptides, glycine-arginine (GR) repeat peptides, proline-alanine (PA) repeat peptides, ubiquitin, and proline-arginine (PR) repeat peptides, and any combination thereof; or with one or more antibodies that bind an immunomodulatory protein selected from the group consisting of: PD1/PDL1, CD40, OX40, ICOS, CD28, CD137/4-1BB, CD27, GITR, PD-L1, CTLA4, PD-L2, PD-1, B7-H3, B7-H4, HVEM, LIGHT, BTLA, CD30, TIGIT, VISTA, KIR, GAL9, TIM1, TIM3, TIM4, A2AR, LAG3, DR-5, CD2, CD5, CD39, CD73, TREM1, TREM2, CD33, Siglec-5, Siglec-7, Siglec-11, phosphatidylserine, disease-causing nucleic acids, antisense GGCCCC (G2C4) repeat-expansion RNA, and any combination thereof. In some examples that may be combined with any of the preceding examples, the anti-Siglec-9 antibody has dissociation constant (K_D) for human Siglec-9 and mammalian Siglec-9 that ranges from about 10 nM to about 10 pM, or less than 10 pM, wherein the K_D is determined at a temperature of approximately 25°C. In some examples that may be combined with any of the preceding examples, the anti-Siglec-9 antibody has dissociation constant (K_D) for human Siglec-9 that ranges from about 9 nM to about 300 pM, or less than 300 pM, wherein the K_D is determined at a temperature of approximately 25°C. In some examples that may be combined with any of the preceding examples, the anti-Siglec-9 antibody has dissociation constant (K_D) for human Siglec-9 that ranges from about 9 nM to about 230 pM, or less than 230 pM, wherein the K_D is determined at a temperature of approximately 25°C.

[0029] Also disclosed is an isolated nucleic acid comprising a nucleic acid sequence encoding the anti-Siglec-9 antibody of any of the preceding examples. Also disclosed is a vector comprising the nucleic acid of any of the preceding examples. Other aspects of the present disclosure relate to an isolated host cell comprising the vector of any of the preceding examples. Also disclosed is

a method of producing an anti-Siglec-9 antibody, comprising culturing the host cell of any of the preceding examples so that the anti-Siglec-9 antibody is produced. In some examples, the method further comprises recovering the anti-Siglec-9 antibody produced by the host cell. Also disclosed is an isolated anti-Siglec-9 antibody produced by the method of any of the preceding examples. Also disclosed is a pharmaceutical composition comprising the anti-Siglec-9 antibody of any of the preceding examples, and a pharmaceutically acceptable carrier.

[0030] Also disclosed is a method of preventing, reducing risk, or treating a disease, disorder, or injury selected from the group consisting of dementia, frontotemporal dementia, Alzheimer's disease, vascular dementia, mixed dementia, Creutzfeldt-Jakob disease, normal pressure hydrocephalus, amyotrophic lateral sclerosis, Huntington's disease, taupathy disease, Nasu-Hakola disease, stroke, acute trauma, chronic trauma, lupus, acute and chronic colitis, rheumatoid arthritis, wound healing, Crohn's disease, inflammatory bowel disease, ulcerative colitis, obesity, malaria, essential tremor, central nervous system lupus, Behcet's disease, Parkinson's disease, dementia with Lewy bodies, multiple system atrophy, Shy-Drager syndrome, progressive supranuclear palsy, cortical basal ganglionic degeneration, acute disseminated encephalomyelitis, granulomatous disorders, sarcoidosis, diseases of aging, seizures, spinal cord injury, traumatic brain injury, age related macular degeneration, glaucoma, retinitis pigmentosa, retinal degeneration, respiratory tract infection, sepsis, eye infection, systemic infection, lupus, arthritis, multiple sclerosis, low bone density, osteoporosis, osteogenesis, osteopetrotic disease, Paget's disease of bone, and cancer, bladder cancer, brain cancer, breast cancer, colon cancer, rectal cancer, endometrial cancer, kidney cancer, renal cell cancer, renal pelvis cancer, leukemia, lung cancer, melanoma, non-Hodgkin's lymphoma, pancreatic cancer, prostate cancer, ovarian cancer, fibrosarcoma, acute lymphoblastic leukemia (ALL), acute myeloid leukemia (AML), chronic lymphocytic leukemia (CLL), chronic myeloid leukemia (CML), multiple myeloma, polycythemia vera, essential thrombocytosis, primary or idiopathic myelofibrosis, primary or idiopathic myelosclerosis, myeloid-derived tumors, tumors that express Siglec-9, tumors that express one or more Siglec-9 ligands, thyroid cancer, infections, CNS herpes, parasitic infections, Trypanosome infection, Cruzi infection, *Pseudomonas aeruginosa* infection, *Leishmania donovani* infection, group B *Streptococcus* infection, *Campylobacter jejuni* infection, *Neisseria meningitidis* infection, type I HIV, and Haemophilus influenza, comprising administering to an individual in need thereof a therapeutically effective amount of an agent that decreases cellular levels of Siglec-9, inhibits interaction between Siglec-9 and one or more Siglec-9 ligands, or both. Also disclosed is an agent that decreases cellular levels of Siglec-9, inhibits interaction between Siglec-9 and one or more Siglec-9 ligands, or both for use in preventing, reducing risk, or treating a disease, disorder, or injury

selected from the group consisting of dementia, frontotemporal dementia, Alzheimer's disease, vascular dementia, mixed dementia, Creutzfeldt-Jakob disease, normal pressure hydrocephalus, amyotrophic lateral sclerosis, Huntington's disease, taupathy disease, Nasu-Hakola disease, stroke, acute trauma, chronic trauma, lupus, acute and chronic colitis, rheumatoid arthritis, wound healing, Crohn's disease, inflammatory bowel disease, ulcerative colitis, obesity, malaria, essential tremor, central nervous system lupus, Behcet's disease, Parkinson's disease, dementia with Lewy bodies, multiple system atrophy, Shy-Drager syndrome, progressive supranuclear palsy, cortical basal ganglionic degeneration, acute disseminated encephalomyelitis, granulomatous disorders, sarcoidosis, diseases of aging, seizures, spinal cord injury, traumatic brain injury, age related macular degeneration, glaucoma, retinitis pigmentosa, retinal degeneration, respiratory tract infection, sepsis, eye infection, systemic infection, lupus, arthritis, multiple sclerosis, low bone density, osteoporosis, osteogenesis, osteopetrotic disease, Paget's disease of bone, and cancer, bladder cancer, brain cancer, breast cancer, colon cancer, rectal cancer, endometrial cancer, kidney cancer, renal cell cancer, renal pelvis cancer, leukemia, lung cancer, melanoma, non-Hodgkin's lymphoma, pancreatic cancer, prostate cancer, ovarian cancer, fibrosarcoma, acute lymphoblastic leukemia (ALL), acute myeloid leukemia (AML), chronic lymphocytic leukemia (CLL), chronic myeloid leukemia (CML), multiple myeloma, polycythemia vera, essential thrombocytosis, primary or idiopathic myelofibrosis, primary or idiopathic myelosclerosis, myeloid-derived tumors, tumors that express Siglec-9, tumors that express one or more Siglec-9 ligands, thyroid cancer, infections, CNS herpes, parasitic infections, Trypanosome infection, Cruzi infection, *Pseudomonas aeruginosa* infection, *Leishmania donovani* infection, group B *Streptococcus* infection, *Campylobacter jejuni* infection, *Neisseria meningitidis* infection, type I HIV, and Haemophilus influenza. Also disclosed is use of an agent that decreases cellular levels of Siglec-9, inhibits interaction between Siglec-9 and one or more Siglec-9 ligands, or both in the manufacture of a medicament for preventing, reducing risk, or treating a disease, disorder, or injury selected from the group consisting of dementia, frontotemporal dementia, Alzheimer's disease, vascular dementia, mixed dementia, Creutzfeldt-Jakob disease, normal pressure hydrocephalus, amyotrophic lateral sclerosis, Huntington's disease, taupathy disease, Nasu-Hakola disease, stroke, acute trauma, chronic trauma, lupus, acute and chronic colitis, rheumatoid arthritis, wound healing, Crohn's disease, inflammatory bowel disease, ulcerative colitis, obesity, malaria, essential tremor, central nervous system lupus, Behcet's disease, Parkinson's disease, dementia with Lewy bodies, multiple system atrophy, Shy-Drager syndrome, progressive supranuclear palsy, cortical basal ganglionic degeneration, acute disseminated encephalomyelitis, granulomatous disorders, sarcoidosis, diseases of aging, seizures, spinal cord injury, traumatic brain injury, age related macular degeneration, glaucoma, retinitis pigmentosa, retinal degeneration, respiratory tract infection, sepsis, eye infection, systemic infection, lupus, arthritis, multiple sclerosis,

low bone density, osteoporosis, osteogenesis, osteopetrotic disease, Paget's disease of bone, and cancer, bladder cancer, brain cancer, breast cancer, colon cancer, rectal cancer, endometrial cancer, kidney cancer, renal cell cancer, renal pelvis cancer, leukemia, lung cancer, melanoma, non-Hodgkin's lymphoma, pancreatic cancer, prostate cancer, ovarian cancer, fibrosarcoma, acute lymphoblastic leukemia (ALL), acute myeloid leukemia (AML), chronic lymphocytic leukemia (CLL), chronic myeloid leukemia (CML), multiple myeloma, polycythemia vera, essential thrombocytosis, primary or idiopathic myelofibrosis, primary or idiopathic myelosclerosis, myeloid-derived tumors, tumors that express Siglec-9, tumors that express one or more Siglec-9 ligands, thyroid cancer, infections, CNS herpes, parasitic infections, Trypanosome infection, Cruzi infection, *Pseudomonas aeruginosa* infection, *Leishmania donovani* infection, group B *Streptococcus* infection, *Campylobacter jejuni* infection, *Neisseria meningitidis* infection, type I HIV, and Haemophilus influenza. Also disclosed is a method of preventing, reducing risk, or treating a disease, disorder, or injury selected from the group consisting of dementia, frontotemporal dementia, Alzheimer's disease, vascular dementia, mixed dementia, taupathy disease, infections, and cancer, comprising administering to an individual in need thereof a therapeutically effective amount of an agent that decreases cellular levels of Siglec-9, inhibits interaction between Siglec-9 and one or more Siglec-9 ligands, or both. Also disclosed is an agent that decreases cellular levels of Siglec-9, inhibits interaction between Siglec-9 and one or more Siglec-9 ligands, or both for use in preventing, reducing risk, or treating a disease, disorder, or injury selected from the group consisting of dementia, frontotemporal dementia, Alzheimer's disease, vascular dementia, mixed dementia, taupathy disease, infections, and cancer. Also disclosed is use of an agent that decreases cellular levels of Siglec-9, inhibits interaction between Siglec-9 and one or more Siglec-9 ligands, or both in the manufacture of a medicament for preventing, reducing risk, or treating a disease, disorder, or injury selected from the group consisting of dementia, frontotemporal dementia, Alzheimer's disease, vascular dementia, mixed dementia, taupathy disease, infections, and cancer. In some examples the disease, disorder, or injury is cancer, and wherein the agent inhibits one or more Siglec-9 activities selected from the group consisting of: (a) promoting proliferation, maturation, migration, differentiation, and/or functionality of one or more of immunosuppressor dendritic cells, immunosuppressor macrophages, immunosuppressor neutrophils, immunosuppressor NK cells, myeloid derived suppressor cells, tumor-associated macrophages, tumor-associated suppressor neutrophils, tumor-associated suppressor NK cells, and regulatory T cells; (b) enhancing infiltration of one or more of immunosuppressor dendritic cells, immunosuppressor macrophages, immunosuppressor neutrophils, immunosuppressor NK cells, myeloid derived suppressor cells, tumor-associated macrophages, tumor-associated suppressor neutrophils, tumor-associated suppressor NK cells, and regulatory T cells into tumors; (c)

increasing number of tumor-promoting myeloid/granulocytic immune-suppressive cells in a tumor, in peripheral blood, or other lymphoid organ; (d) enhancing tumor-promoting activity of myeloid-derived suppressor cells (MDSC); (e) increasing expression of tumor-promoting cytokines in a tumor or in peripheral blood, optionally wherein the tumor-promoting cytokines are TGF-beta or IL-10; (f) increasing tumor infiltration of tumor-promoting FoxP3⁺ regulatory T lymphocytes; (g) decreasing activation of tumor-specific T lymphocytes with tumor killing potential; (h) decreasing infiltration of tumor-specific T lymphocytes with tumor killing potential; (i) increasing infiltration of one or more of immunosuppressor dendritic cells, immunosuppressor macrophages, immunosuppressor neutrophils, immunosuppressor NK cells, myeloid-derived suppressor cells, tumor-associated macrophages, tumor-associated neutrophils, tumor-associated NK cells, non-tumorigenic CD45⁺CD14⁺ myeloid cells, and regulatory T cells into tumors; (j) increasing the number of tumor-promoting myeloid/granulocytic immune-suppressive cells and/or non-tumorigenic CD45⁺CD14⁺ myeloid cells in a tumor, in peripheral blood, or other lymphoid organ; (k) enhancing tumor-promoting activity of myeloid-derived suppressor cells and/or non-tumorigenic CD45⁺CD14⁺ myeloid cells; (l) enhancing survival of non-tumorigenic myeloid-derived suppressor cells and/or non-tumorigenic CD45⁺CD14⁺ myeloid cells; (m) decreasing activation of tumor-specific T lymphocytes with tumor killing potential; (n) decreasing infiltration of tumor-specific NK cells with tumor killing potential; (o) increasing tumor volume; (p) increasing tumor growth rate; (q) increasing metastasis; (r) increasing rate of tumor recurrence; (s) decreasing efficacy of one or more immune-therapies that modulate anti-tumor T cell responses, optionally wherein the one or more immune-therapies are immune-therapies that target one or more target proteins selected from the group consisting of PD1/PDL1, CD40, OX40, ICOS, CD28, CD137/4-1BB, CD27, GITR, PD-L1, CTLA4, PD-L2, PD-1, B7-H3, B7-H4, HVEM, LIGHT, BTLA, CD30, TIGIT, VISTA, KIR, GAL9, TIM1, TIM3, TIM4, A2AR, LAG3, DR-5, CD2, CD5, CD39, CD73, and any combination thereof, or one or more cancer vaccines; (t) inhibition of PLCγ/PKC/calcium mobilization; and (u) inhibition of PI3K/Akt, Ras/MAPK signaling. In some examples, the cancer expresses Siglec-9 or one or more Siglec-9 ligands. In some examples that may be combined with any of the preceding examples, the disease, disorder, or injury is cancer, and the agent inhibits one or more Siglec-9 activities selected from the group consisting of: (a) promoting proliferation, maturation, migration, differentiation, and/or functionality of one or more of immunosuppressor dendritic cells, immunosuppressor macrophages, immunosuppressor neutrophils, non-tumorigenic myeloid derived suppressor cells, tumor-associated macrophages, , non-tumorigenic CD14⁺ myeloid cells, and regulatory T cells; (b) enhancing infiltration of one or more of immunosuppressor dendritic cells, immunosuppressor macrophages, immunosuppressor neutrophils, non-tumorigenic myeloid derived suppressor cells, tumor-associated macrophages, and regulatory T cells into tumors; (c) increasing

number of tumor-promoting myeloid/granulocytic immune-suppressive cells and/or non-tumorigenic CD14⁺ myeloid cells in a tumor, in peripheral blood, or other lymphoid organ; (d) enhancing tumor-promoting activity of non-tumorigenic myeloid-derived suppressor cells and/or non-tumorigenic CD14⁺ myeloid cells; (e) increasing expression of tumor-promoting cytokines in a tumor or in peripheral blood, optionally wherein the tumor-promoting cytokines are TGF-beta or IL-10; (f) increasing tumor infiltration of tumor-promoting FoxP3⁺ regulatory T lymphocytes; (g) decreasing activation of tumor-specific T lymphocytes with tumor killing potential; (h) decreasing infiltration of tumor-specific T lymphocytes with tumor killing potential; (i) decreasing infiltration of tumor-specific NK cells with tumor killing potential; (j) decreasing tumor killing potential of NK cells; (k) decreasing infiltration of tumor-specific B lymphocytes with potential to enhance immune response; (l) increasing tumor volume; (m) increasing tumor growth rate; (n) increasing metastasis; (o) increasing rate of tumor recurrence; (p) increasing expression of one or more PD-1 ligands; (q) decreasing efficacy of one or more immune-therapies that modulate anti-tumor T cell responses, optionally wherein the one or more immune-therapies are immune-therapies that target one or more proteins selected from the group consisting of CD40, OX40, ICOS, CD28, CD137/4-1BB, CD27, GITR, PD-L1, CTLA4, PD-L2, PD-1, B7-H3, B7-H4, HVEM, BTLA, KIR, GAL9, TIM3, A2AR, LAG, DR-5, TREM1, TREM2, CSF-1 receptor, and any combination thereof, or of one or more cancer vaccines; (r) inhibition of PLCγ/PKC/calcium mobilization; (s) inhibition of PI3K/Akt, Ras/MAPK signaling; and (t) decreasing efficacy of one or more chemotherapy agents, optionally wherein the one or more of the chemotherapy agents are gemcitabine, capecitabine, anthracyclines, doxorubicin (Adriamycin[®]), epirubicin (Ellence[®]), taxanes, paclitaxel (Taxol[®]), docetaxel (Taxotere[®]), 5-fluorouracil (5-FU), cyclophosphamide (Cytosan[®]), carboplatin (Paraplatin[®]), and any combination thereof. In some examples that may be combined with any of the preceding examples, the disease, disorder, or injury is cancer, and the agent exhibits one or more activities selected from the group consisting of: (a) increasing the number of tumor infiltrating CD3⁺ T cells; (b) decreasing cellular levels of Siglec-9 in non-tumorigenic CD14⁺ myeloid cells, optionally wherein the non-tumorigenic CD14⁺ myeloid cells are tumor infiltrating cells or optionally wherein the non-tumorigenic CD14⁺ myeloid cells are present in blood; (c) reducing the number of non-tumorigenic CD14⁺ myeloid cells, optionally wherein the non-tumorigenic CD14⁺ myeloid cells are tumor infiltrating cells or optionally wherein the non-tumorigenic CD14⁺ myeloid cells are present in blood; (d) reducing PD-L1 levels in one or more cells, optionally wherein the one or more cells are non-tumorigenic myeloid-derived suppressor cells (MDSC); (e) reducing PD-L2 levels in one or more cells, optionally wherein the one or more cells are non-tumorigenic myeloid-derived suppressor cells (MDSC); (f) reducing B7-H2 levels in one or more cells, optionally wherein the one or more cells are non-tumorigenic myeloid-derived suppressor cells (MDSC); (g) reducing B7-H3

levels in one or more cells, optionally wherein the one or more cells are non-tumorigenic myeloid-derived suppressor cells (MDSC); (h) reducing CD200R levels in one or more cells, optionally wherein the one or more cells are non-tumorigenic myeloid-derived suppressor cells (MDSC); (i) reducing CD163 levels in one or more cells, optionally wherein the one or more cells are non-tumorigenic myeloid-derived suppressor cells (MDSC); (j) reducing CD206 levels in one or more cells, optionally wherein the one or more cells are non-tumorigenic myeloid-derived suppressor cells (MDSC); (k) decreasing tumor growth rate of solid tumors; (l) reducing tumor volume; (m) increasing efficacy of one or more PD-1 inhibitors; (n) increasing efficacy of one or more checkpoint inhibitor therapies and/or immune-modulating therapies, optionally wherein the one or more checkpoint inhibitor therapies and/or immune-modulating therapies target one or more of CTLA4, the adenosine pathway, PD-L1, PD-L2, OX40, TIM3, LAG3, or any combination thereof; (o) increasing efficacy of one or more chemotherapy agents, optionally wherein the one or more of the chemotherapy agents are gemcitabine, capecitabine, anthracyclines, doxorubicin (Adriamycin[®]), epirubicin (Ellence[®]), taxanes, paclitaxel (Taxol[®]), docetaxel (Taxotere[®]), 5-fluorouracil (5-FU), cyclophosphamide (Cytosan[®]), carboplatin (Paraplatin[®]), and any combination thereof; (p) increasing proliferation of T cells in the presence of non-tumorigenic myeloid-derived suppressor cells (MDSC); and (q) inhibiting differentiation, survival, and/or one or more functions of non-tumorigenic myeloid-derived suppressor cells (MDSC); and (r) killing Siglec-9-expressing immunosuppressor myeloid cells and/or CD14-expressing cells in solid tumors and associated blood vessels when conjugated to a chemical or radioactive toxin. In some examples that may be combined with any of the preceding examples, the agent exhibits one or more activities selected from the group consisting of: (a) increasing the number of tumor infiltrating CD3⁺ T cells; (b) decreasing cellular levels of CD33 in non-tumorigenic CD14⁺ myeloid cells, optionally wherein the non-tumorigenic CD14⁺ myeloid cells are tumor infiltrating cells or optionally wherein the non-tumorigenic CD14⁺ myeloid cells are present in blood; (c) reducing the number of non-tumorigenic CD14⁺ myeloid cells, optionally wherein the non-tumorigenic CD14⁺ myeloid cells are tumor infiltrating cells or optionally wherein the non-tumorigenic CD14⁺ myeloid cells are present in blood; (d) reducing PD-L1 levels in one or more cells, optionally wherein the one or more cells are non-tumorigenic myeloid-derived suppressor cells (MDSC); (e) reducing PD-L2 levels in one or more cells, optionally wherein the one or more cells are non-tumorigenic myeloid-derived suppressor cells (MDSC); (f) reducing B7-H2 levels in one or more cells, optionally wherein the one or more cells are non-tumorigenic myeloid-derived suppressor cells (MDSC); (g) reducing B7-H3 levels in one or more cells, optionally wherein the one or more cells are non-tumorigenic myeloid-derived suppressor cells (MDSC); (h) reducing CD200R levels in one or more cells, optionally wherein the one or more cells are non-tumorigenic myeloid-derived suppressor cells (MDSC); (i) reducing CD163 levels in one or more cells, optionally

wherein the one or more cells are non-tumorigenic myeloid-derived suppressor cells (MDSC); (j) reducing CD206 levels in one or more cells, optionally wherein the one or more cells are non-tumorigenic myeloid-derived suppressor cells (MDSC); (k) decreasing tumor growth rate of solid tumors; (l) reducing tumor volume; (m) increasing efficacy of one or more PD-1 inhibitors; (n) increasing efficacy of one or more checkpoint inhibitor therapies and/or immune-modulating therapies, optionally wherein the one or more checkpoint inhibitor therapies and/or immune-modulating therapies target one or more of CTLA4, the adenosine pathway, PD-L1, PD-L2, OX40, TIM3, LAG3, or any combination thereof; (o) increasing efficacy of one or more chemotherapy agents, optionally wherein the one or more of the chemotherapy agents are gemcitabine, capecitabine, anthracyclines, doxorubicin (Adriamycin[®]), epirubicin (Ellence[®]), taxanes, paclitaxel (Taxol[®]), docetaxel (Taxotere[®]), 5-fluorouracil (5-FU), cyclophosphamide (Cytosan[®]), carboplatin (Paraplatin[®]), and any combination thereof; (p) increasing proliferation of T cells in the presence of non-tumorigenic myeloid-derived suppressor cells (MDSC); and (q) inhibiting differentiation, survival, and/or one or more functions of non-tumorigenic myeloid-derived suppressor cells (MDSC); and (r) killing CD33-expressing immunosuppressor myeloid cells and/or CD14-expressing cells in solid tumors and associated blood vessels when conjugated to a chemical or radioactive toxin. In some examples, the cancer is selected from the group consisting of bladder cancer, brain cancer, breast cancer, colon cancer, rectal cancer, endometrial cancer, kidney cancer, renal cell cancer, renal pelvis cancer, leukemia, lung cancer, melanoma, non-Hodgkin's lymphoma, pancreatic cancer, prostate cancer, ovarian cancer, fibrosarcoma, acute lymphoblastic leukemia (ALL), acute myeloid leukemia (AML), chronic lymphocytic leukemia (CLL), chronic myeloid leukemia (CML), and multiple myeloma. In some examples, the agent is selected from the group consisting of an antibody, a soluble Siglec-9 receptor, a Siglec-9-Fc fusion protein, a Siglec-9 immunoadhesin, an antisense molecule, an siRNA, a small molecule inhibitor, a protein, and a peptide. In some examples, the agent is an isolated anti-Siglec-9 antibody. In some examples, the anti-Siglec-9 antibody is the anti-Siglec-9 antibody of any of the preceding examples. In some examples, the one or more immune cells are selected from the group consisting of dendritic cells, macrophages, neutrophils, NK cells, microglia, T cells, T helper cells, cytotoxic T cells, and any combination thereof.

[0031] Also disclosed is a method of inducing or promoting the survival, maturation, functionality, migration, or proliferation of one or more immune cells in an individual in need thereof, comprising administering to the individual a therapeutically effective amount of an agent that decreases cellular levels of Siglec-9, inhibits interaction between Siglec-9 and one or more Siglec-9 ligands, or both. Also disclosed is an agent that decreases cellular levels of Siglec-9, inhibits interaction between Siglec-9 and one or more

Siglec-9 ligands, or both for use in inducing or promoting the survival, maturation, functionality, migration, or proliferation of one or more immune cells in an individual in need thereof. Also disclosed is use of an agent that decreases cellular levels of Siglec-9, inhibits interaction between Siglec-9 and one or more Siglec-9 ligands, or both in the manufacture of a medicament for inducing or promoting the survival, maturation, functionality, migration, or proliferation of one or more immune cells in an individual in need thereof. In some examples the one or more immune cells are selected from the group consisting of dendritic cells, macrophages, neutrophils, NK cells, microglia, T cells, T helper cells, cytotoxic T cells, and any combination thereof. In some examples, the agent is selected from the group consisting of an antibody, a soluble Siglec-9 receptor, a Siglec-9-Fc fusion protein, a Siglec-9 immunoadhesin, an antisense molecule, an siRNA, a small molecule inhibitor, a protein, and a peptide. In some examples, the agent is an isolated anti-Siglec-9 antibody. In some examples, the anti-Siglec-9 antibody is the anti-Siglec-9 antibody of any of the preceding examples. In some examples, the one or more immune cells are selected from the group consisting of dendritic cells, macrophages, neutrophils, NK cells, microglia, T cells, T helper cells, cytotoxic T cells, and any combination thereof.

[0032] Also disclosed is a method of decreasing the activity, functionality, or survival of regulatory T cells, tumor-imbedded immunosuppressor dendritic cells, tumor-imbedded immunosuppressor macrophages, myeloid-derived suppressor cells, tumor-associated macrophages, acute myeloid leukemia (AML) cells, chronic lymphocytic leukemia (CLL) cell, or chronic myeloid leukemia (CML) cells in an individual in need thereof, comprising administering to the individual a therapeutically effective amount of an agent that binds or interacts with Siglec-9. Also disclosed is use of an agent that binds or interacts with Siglec-9 for use in decreasing the activity, functionality, or survival of regulatory T cells, tumor-imbedded immunosuppressor dendritic cells, tumor-imbedded immunosuppressor macrophages, myeloid-derived suppressor cells, tumor-associated macrophages, acute myeloid leukemia (AML) cells, chronic lymphocytic leukemia (CLL) cell, or chronic myeloid leukemia (CML) cells in an individual in need thereof. Also disclosed is use of an agent that binds or interacts with Siglec-9 in the manufacture of a medicament for decreasing the activity, functionality, or survival of regulatory T cells, tumor-imbedded immunosuppressor dendritic cells, tumor-imbedded immunosuppressor macrophages, myeloid-derived suppressor cells, tumor-associated macrophages, acute myeloid leukemia (AML) cells, chronic lymphocytic leukemia (CLL) cell, or chronic myeloid leukemia (CML) cells in an individual in need thereof. In some examples, the agent is an isolated anti-Siglec-9 antibody or anti-Siglec-9 antibody conjugate. In some examples, the anti-Siglec-9 antibody is the anti-Siglec-9 antibody of any of the preceding examples.

[0033] Also disclosed is relate a method of decreasing cellular levels of Siglec-9 on one or more cells in an individual in need thereof, comprising administering to the individual a therapeutically effective amount of an isolated anti-Siglec-9 antibody. Also disclosed is use of an isolated anti-Siglec-9 antibody for use in decreasing cellular levels of Siglec-9 on one or more cells in an individual in need thereof. Also disclosed is use of an isolated anti-Siglec-9 antibody in the manufacture of a medicament for decreasing cellular levels of Siglec-9 on one or more cells in an individual in need thereof. In some examples, the anti-Siglec-9 antibody decreases cellular levels of Siglec-9 *in vivo*. In some examples, the anti-Siglec-9 antibody is the anti-Siglec-9 antibody of any of the preceding examples.

[0034] In some examplesthat may be combined with any of the preceding examples, the method further comprising administering to the individual at least one antibody that specifically binds to an inhibitory checkpoint molecule, and/or one or more standard or investigational anti-cancer therapies. In some examplesthat may be combined with any of the preceding examples, the at least one antibody that specifically binds to an inhibitory checkpoint molecule is administered in combination with the anti-Siglec-9 antibody. In some examplesthat may be combined with any of the preceding examples, the at least one antibody that specifically binds to an inhibitory checkpoint molecule is selected from the group consisting of an anti-PD-L1 antibody, an anti-CTLA4 antibody, an anti-PD-L2 antibody, an anti-PD-1 antibody, an anti-B7-H3 antibody, an anti-B7-H4 antibody, and anti-HVEM antibody, an anti- B- and T-lymphocyte attenuator (BTLA) antibody, an anti-Killer inhibitory receptor (KIR) antibody, an anti-GAL9 antibody, an anti-TIM-1 antibody, an anti-TIM3 antibody, an anti-TIM-4 antibody, an anti-A2AR antibody, an anti-CD39 antibody, an anti-CD73 antibody, an anti-LAG-3 antibody, an anti-phosphatidylserine antibody, an anti-CD27 antibody, an anti-CD30 antibody, an anti-TNF α antibody, an anti-CD33 antibody, an anti-Siglec-5 antibody, an anti-Siglec-7 antibody, an anti-Siglec-11 antibody, an antagonistic anti-TREM1 antibody, an antagonistic anti-TREM2 antibody, an anti-TIGIT antibody, an anti-VISTA antibody, an anti-CD2 antibody, an anti-CD5 antibody, and any combination thereof. In some examplesthat may be combined with any of the preceding examples, the one or more standard or investigational anti-cancer therapies are selected from the group consisting of radiotherapy, cytotoxic chemotherapy, targeted therapy, imatinib therapy, trastuzumab therapy, etanercept therapy, adoptive cell transfer (ACT) therapy, chimeric antigen receptor T cell transfer (CAR-T) therapy, vaccine therapy, and cytokine therapy. In some examplesthat may be combined with any of the preceding examples, the method further comprising administering to the individual at least one antibody that specifically binds to an inhibitory cytokine. In some examplesthat may be combined with any of the preceding examples, the at least one antibody that specifically binds to an inhibitory

cytokine is administered in combination with the anti-Siglec-9 antibody. In some examples that may be combined with any of the preceding examples, the at least one antibody that specifically binds to an inhibitory cytokine is selected from the group consisting of an anti-CCL2 antibody, an anti-CSF-1 antibody, an anti-IL-2 antibody, and any combination thereof. In some examples that may be combined with any of the preceding examples, the method further comprising administering to the individual at least one agonistic antibody that specifically binds to a stimulatory checkpoint protein. In some examples that may be combined with any of the preceding examples, the at least one agonistic antibody that specifically binds to a stimulatory checkpoint protein is administered in combination with the anti-Siglec-9 antibody. In some examples that may be combined with any of the preceding examples, the at least one agonistic antibody that specifically binds to a stimulatory checkpoint protein is selected from the group consisting of an agonist anti-CD40 antibody, an agonist anti-OX40 antibody, an agonist anti-ICOS antibody, an agonist anti-CD28 antibody, an agonistic anti-TREM1 antibody, an agonistic anti-TREM2 antibody, an agonist anti-CD137/4-1BB antibody, an agonist anti-CD27 antibody, an agonist anti-glucocorticoid-induced TNFR-related protein GITR antibody, an agonist anti-CD30 antibody, an agonist anti-BTLA antibody, an agonist anti-HVEM antibody, an agonist anti-CD2 antibody, an agonist anti-CD5 antibody, and any combination thereof. In some examples that may be combined with any of the preceding examples, the method further comprising administering to the individual at least one stimulatory cytokine. In some examples that may be combined with any of the preceding examples, the at least one stimulatory cytokine is administered in combination with the anti-Siglec-9 antibody. In some examples that may be combined with any of the preceding examples, the at least one stimulatory cytokine is selected from the group consisting of IFN- α 4, IFN- β , IL-1 β , TNF- α , IL-6, IL-8, CRP, IL-20 family members, LIF, IFN- γ , OSM, CNTF, GM-CSF, IL-11, IL-12, IL-17, IL-18, IL-23, CXCL10, IL-33, MCP-1, MIP-1-beta, and any combination thereof.

[0035] Also disclosed is a method of assessing responsiveness of a subject in need thereof to an agent that binds or interacts with Siglec-9, the method comprising: a. measuring the expression levels of CD45⁺ and CD14⁺ on non-tumorigenic myeloid cells in a blood sample obtained from the subject prior to administering to the subject an anti-Siglec-9 antibody; b. administering to the subject a therapeutically effective amount of the agent; and c. measuring the expression levels of CD45⁺ and CD14⁺ on non-tumorigenic myeloid cells in a blood sample obtained from the subject after administration of the anti-Siglec-9 antibody, wherein a reduction in the levels of CD45⁺ CD14⁺ on non-tumorigenic myeloid cells after administration of the anti-Siglec-9 antibody indicates the subject is responsive to the agent. In some examples, the method of assessing responsiveness further comprises administering one or more additional therapeutically effective

amounts of the agent. In some examples that may be combined with any of the preceding examples, the agent is selected from the group consisting of an antibody, a soluble Siglec-9 receptor, a Siglec-9-Fc fusion protein, a Siglec-9 immunoadhesin, a soluble Siglec receptor, a Siglec-Fc fusion protein, a Siglec immunoadhesin, an antisense molecule, an siRNA, a small molecule inhibitor, a protein, and a peptide. In some examples that may be combined with any of the preceding examples, the agent is an isolated anti-Siglec-9 antibody or anti-Siglec-9 antibody conjugate. In some examples that may be combined with any of the preceding examples, the anti-Siglec-9 antibody is the anti-Siglec-9 antibody of any of the preceding examples.

BRIEF DESCRIPTION OF THE DRAWINGS

[0036] **FIG. 1A** depicts an amino acid sequence alignment between human Siglec-9 (SEQ ID NO: 1), chimpanzee Siglec-9 (SEQ ID NO: 2), green monkey Siglec-9 (SEQ ID NO: 3), rhesus macaque Siglec-9 (SEQ ID NO: 4), and mouse Siglec-9 (SEQ ID NO: 5). An asterisk ("*") indicates positions which have a single, fully conserved residue; A colon (":") indicates conservation between groups of strongly similar properties - scoring > 0.5 in the Gonnet PAM 250 matrix; and a period (".") indicates conservation between groups of weakly similar properties - scoring ≤ 0.5 in the Gonnet PAM 250 matrix. **FIG. 1B** depicts binding reactivity in percentage to wild-type Siglec-9 (% WT) of antibodies of the present disclosure to the indicated Siglec-9 mutants. **FIG. 1C** depicts a Phyre2-derived model of Siglec-9 (based on the crystal structure of Siglec-5; PDB ID 2ZG2) indicating amino acid residues involved in binding of anti-Siglec-9 antibody 2D4. Critical residues for binding are indicated with red spheres. **FIG. 1D** depicts a Phyre2-derived model of Siglec-9 (based on the crystal structure of Siglec-5; PDB ID 2ZG2) indicating amino acid residues involved in binding of anti-Siglec-9 antibody 5C6. Critical residues for binding are indicated with red spheres. **FIG. 1E** depicts a Phyre2-derived model of Siglec-9 (based on the crystal structure of Siglec-5; PDB ID 2ZG2) indicating amino acid residues involved in binding of anti-Siglec-9 antibody 12B12. Critical residues for binding are indicated with red spheres.

[0037] **FIG. 2** shows glycan-binding specificities of human Siglec proteins, such as Siglec-9. This figure shows a summary of the most commonly reported specificities for the most commonly studied sialylated glycans. Relative binding within studies of each Siglec is indicated as ++, strong binding; +, detectable binding; and –, very weak or undetectable binding. Not shown is the recently reported strong-binding preference of hSiglec-8 and mSiglec-F for 6'-sulfated-sialyl-Lewis x (sLex) and of hSiglec-9 for 6-sulfated-sLex. With a few exceptions (CD22 and MAG), results of binding specificity studies of human Siglecs by different investigators using different assays have varied significantly. In addition to assay formats and glycan linker issues, the density and arrangement of the ligands studied could be responsible for this variation (Varki et al., (2006) *Glycobiol.* 16:1R-27R).

CLAIMS

What is claimed is:

1. An isolated anti-Siglec-9 antibody, wherein the anti-Siglec-9 antibody decreases cell surface levels of Siglec-9 without inhibiting interaction between Siglec-9 and one or more Siglec-9 ligands.
2. The anti-Siglec-9 antibody of claim 1, wherein the antibody decreases cell surface levels of Siglec-9 *in vivo*.
3. The anti-Siglec-9 antibody of any one of claims 1-2, wherein the anti-Siglec-9 antibody inhibits one or more Siglec-9 activities.
4. The anti-Siglec-9 antibody of any one of claims 1-3, wherein the one or more Siglec-9 ligands are selected from the group consisting of Siglec-9 ligands expressed on red blood cells, Siglec-9 ligands expressed on bacterial cells, Siglec-9 ligands expressed on apoptotic cells, Siglec-9 ligands expressed on nerve cells, Siglec-9 ligands expressed on glia cells, Siglec-9 ligands expressed on microglia, Siglec-9 ligands expressed on astrocytes, Siglec-9 ligands expressed on tumor cells, Siglec-9 ligands expressed on viruses, Siglec-9 ligands expressed on dendritic cells, Siglec-9 ligands bound to beta amyloid plaques, Siglec-9 ligands bound to Tau tangles, Siglec-9 ligands on disease-causing proteins, Siglec-9 ligands on disease-causing peptides, Siglec-9 ligands expressed on macrophages, Siglec-9 ligands expressed on neutrophils, Siglec-9 ligands expressed on natural killer cells, Siglec-9 ligands expressed on monocytes, Siglec-9 ligands expressed on T cells, Siglec-9 ligands expressed on T helper cells, Siglec-9 ligands expressed on cytotoxic T cells, Siglec-9 ligands expressed on B cells, Siglec-9 ligands expressed on tumor-imbedded immunosuppressor dendritic cells, Siglec-9 ligands expressed on tumor-imbedded immunosuppressor macrophages, Siglec-9 ligands expressed on myeloid-derived suppressor cells, Siglec-9 ligands expressed on regulatory T cells, secreted mucins, sialic acid, sialic acid-containing glycolipids, sialic acid-containing glycoproteins, alpha-2,8-disialyl containing glycolipids, branched alpha-2,6-linked sialic acid-containing glycoproteins, terminal alpha-2,6-linked sialic acid-containing glycolipids, terminal alpha-2,3-linked sialic acid-containing glycoproteins, and disialogangliosides.
5. The anti-Siglec-9 antibody of any one of claims 1-4, wherein the cell surface levels of Siglec-9 are measured on primary cells selected from the group consisting of dendritic cells, bone marrow-derived dendritic cells, monocytes, microglia, macrophages, neutrophils, and NK cells, or on cell lines, and wherein the cell surface levels of Siglec-9 are measured utilizing an *in vitro* cell assay.
6. The anti-Siglec-9 antibody of any one of claims 1-5, wherein the anti-Siglec-9 antibody does not reduce TREM2 expression.

7. The anti-Siglec-9 antibody of any one of claims 1-6, wherein the anti-Siglec-9 antibody binds to one or more amino acids within amino acid residues selected from the group consisting of:
- amino acid residues 185-194 of SEQ ID NO: 1, or amino acid residues on a mammalian Siglec-9 protein corresponding to amino acid residues 185-194 of SEQ ID NO: 1;
 - amino acid residues 86-96 of SEQ ID NO: 1, or amino acid residues on a mammalian Siglec-9 protein corresponding to amino acid residues 86-96 of SEQ ID NO: 1;
 - amino acid residues 86-96 and 105-116 of SEQ ID NO: 1, or amino acid residues on a mammalian Siglec-9 protein corresponding to amino acid residues 86-96 and 105-116 of SEQ ID NO: 1;
 - amino acid residues 105-116 of SEQ ID NO: 1, or amino acid residues on a mammalian Siglec-9 protein corresponding to amino acid residues 105-116 of SEQ ID NO: 1; and
 - amino acid residues 107-115 of SEQ ID NO: 1, or amino acid residues on a mammalian Siglec-9 protein corresponding to amino acid residues 107-115 of SEQ ID NO: 1.
8. The anti-Siglec-9 antibody of any one of claims 1-6, wherein the anti-Siglec-9 antibody binds to one or more amino acid residues selected from the group consisting of D189, P190, and R194 of SEQ ID NO: 1, or one or more amino acid residues on a mammalian Siglec-7 protein corresponding to an amino acid residue selected from the group consisting of D189, P190, and R194 of SEQ ID NO: 1.
9. The anti-Siglec-9 antibody of any one of claims 1-8, wherein the anti-Siglec-9 antibody competes with one or more antibodies selected from the group consisting of 2D4, 5B1, 6B2, 6D8, 7H12, and any combination thereof for binding to Siglec-9.
10. The anti-Siglec-9 antibody of any one of claims 1-9, wherein the anti-Siglec-9 antibody comprises a light chain variable domain and a heavy chain variable domain, wherein:
- the light chain variable domain comprises an HVR-L1 comprising the amino acid sequence of SEQ ID NO: 6 or an amino acid sequence with at least 90% homology to SEQ ID NO: 6, an HVR-L2 comprising the amino acid sequence of SEQ ID NO: 10 or an amino acid sequence with at least 90% homology to SEQ ID NO: 10, and an HVR-L3 comprising the amino acid sequence of SEQ ID NO: 14 or an amino acid sequence with at least 90% homology to SEQ ID NO: 14, and the heavy chain variable domain comprises an HVR-H1 comprising the amino acid sequence of SEQ ID NO: 19 or an amino acid sequence with at least 90% homology to SEQ ID NO: 19, an HVR-H2 comprising the amino acid sequence of SEQ ID NO: 22 or an amino

- acid sequence with at least 90% homology to SEQ ID NO: 22, and an HVR-H3 comprising the amino acid sequence of SEQ ID NO: 26 or an amino acid sequence with at least 90% homology to SEQ ID NO: 26; or
- (b) the light chain variable domain comprises an HVR-L1 comprising the amino acid sequence of SEQ ID NO: 8 or an amino acid sequence with at least 90% homology to SEQ ID NO: 8, an HVR-L2 comprising the amino acid sequence of SEQ ID NO: 12 or an amino acid sequence with at least 90% homology to SEQ ID NO: 12, and an HVR-L3 comprising the amino acid sequence of SEQ ID NO: 16 or an amino acid sequence with at least 90% homology to SEQ ID NO: 16, and the heavy chain variable domain comprises an HVR-H1 comprising the amino acid sequence of SEQ ID NO: 21 or an amino acid sequence with at least 90% homology to SEQ ID NO: 21, an HVR-H2 comprising the amino acid sequence of SEQ ID NO: 24 or an amino acid sequence with at least 90% homology to SEQ ID NO: 24, and an HVR-H3 comprising the amino acid sequence of SEQ ID NO: 28 or an amino acid sequence with at least 90% homology to SEQ ID NO: 28; or
- (c) the light chain variable domain comprises an HVR-L1 comprising the amino acid sequence of SEQ ID NO: 9 or an amino acid sequence with at least 90% homology to SEQ ID NO: 9, an HVR-L2 comprising the amino acid sequence of SEQ ID NO: 13 or an amino acid sequence with at least 90% homology to SEQ ID NO: 13, and an HVR-L3 comprising the amino acid sequence of SEQ ID NO: 17 or an amino acid sequence with at least 90% homology to SEQ ID NO: 17, and the heavy chain variable domain comprises, an HVR-H1 comprising the amino acid sequence of SEQ ID NO: 21 or an amino acid sequence with at least 90% homology to SEQ ID NO: 21, an HVR-H2 comprising the amino acid sequence of SEQ ID NO: 25 or an amino acid sequence with at least 90% homology to SEQ ID NO: 25, and an HVR-H3 comprising the amino acid sequence of SEQ ID NO: 29 or an amino acid sequence with at least 90% homology to SEQ ID NO: 29; or
- (d) the light chain variable region comprises an HVR-L1 comprising the amino acid sequence of SEQ ID NO: 8 or an amino acid sequence with at least 90% homology to SEQ ID NO: 8, an HVR-L2 comprising the amino acid sequence of SEQ ID NO: 12 or an amino acid sequence with at least 90% homology to SEQ ID NO: 12, and an HVR-L3 comprising the amino acid sequence of SEQ ID NO: 18 or an amino acid sequence with at least 90% homology to SEQ ID NO: 18, and the heavy chain variable domain comprises an HVR-H1 comprising the amino acid sequence of SEQ ID NO: 21 or an amino acid sequence with at least 90% homology to SEQ ID NO:

21, an HVR-H2 comprising the amino acid sequence of SEQ ID NO: 24 or an amino acid sequence with at least 90% homology to SEQ ID NO: 24, and an HVR-H3 comprising the amino acid sequence of SEQ ID NO: 28 or an amino acid sequence with at least 90% homology to SEQ ID NO: 28.

11. An isolated anti-Siglec-9 antibody, wherein the anti-Siglec-9 antibody binds to one or more amino acids within amino acid residues selected from the group consisting of:

- i. amino acid residues 185-194 of SEQ ID NO: 1, or amino acid residues on a mammalian Siglec-9 protein corresponding to amino acid residues 185-194 of SEQ ID NO: 1;
- ii. amino acid residues 86-96 of SEQ ID NO: 1, or amino acid residues on a mammalian Siglec-9 protein corresponding to amino acid residues 86-96 of SEQ ID NO: 1;
- iii. amino acid residues 86-96 and 105-116 of SEQ ID NO: 1, or amino acid residues on a mammalian Siglec-9 protein corresponding to amino acid residues 86-96 and 105-116 of SEQ ID NO: 1;
- iv. amino acid residues 105-116 of SEQ ID NO: 1, or amino acid residues on a mammalian Siglec-9 protein corresponding to amino acid residues 105-116 of SEQ ID NO: 1; and
- v. amino acid residues 107-115 of SEQ ID NO: 1, or amino acid residues on a mammalian Siglec-9 protein corresponding to amino acid residues 107-115 of SEQ ID NO: 1.

12. An isolated anti-Siglec-9 antibody, wherein the anti-Siglec-9 antibody competes with one or more antibodies selected from the group consisting of 2D4, 5B1, 6B2, 6D8, 7H12, and any combination thereof for binding to Siglec-9.

13. An isolated anti-Siglec-9 antibody which binds essentially the same Siglec-9 epitope as a monoclonal antibody selected from the group consisting of: 2D4, 5B1, 6B2, 6D8, and 7H12.

14. The anti-Siglec-9 antibody of any one of claims 1-13, wherein the antibody is of the IgG class, the IgM class, or the IgA class.

15. The anti-Siglec-9 antibody of claim 14, wherein the anti-Siglec-9 antibody has an IgG1, IgG2, IgG3, or IgG4 isotype.

16. The anti-Siglec-9 antibody of claim 15, wherein:

- (a) the anti-Siglec-9 antibody has a human or mouse IgG1 isotype and comprises one or more amino acid substitutions in the Fc region at a residue position selected from the group consisting of: N297A, D265A, D270A, L234A, L235A, G237A, P238D, L328E, E233D, G237D, H268D, P271G, A330R, C226S, C229S, E233P, L234V,

L234F, L235E, P331S, S267E, L328F, A330L, M252Y, S254T, T256E, N297Q, P238S, P238A, A327Q, A327G, P329A, K322A, T394D, and any combination thereof, wherein the numbering of the residues is according to EU numbering, or comprises an amino acid deletion in the Fc region at a position corresponding to glycine 236;

- (b) the anti-Siglec-9 antibody has an IgG1 isotype and comprises an IgG2 isotype heavy chain constant domain 1(CH1) and hinge region, optionally wherein the IgG2 isotype CH1 and hinge region comprises the amino acid sequence of ASTKGPSVFP LAPCSRSTSE STAALGCLVK DYFPEPVTVS WNSGALTSGVHTFPAVLQSS GLYSLSSVVT VPSSNFGTQT YTCNVDHKPS NTKVDKTVERKCCVECPCP (SEQ ID NO: 171), and optionally wherein the antibody Fc region comprises a S267E amino acid substitution, a L328F amino acid substitution, or both, and/or a N297A or N297Q amino acid substitution, wherein the numbering of the residues is according to EU numbering;
- (c) the anti-Siglec-9 antibody has an IgG2 isotype and comprises one or more amino acid substitutions in the Fc region at a residue position selected from the group consisting of: P238S, V234A, G237A, H268A, H268Q, V309L, A330S, P331S, C214S, C232S, C233S, S267E, L328F, M252Y, S254T, T256E, H268E, N297A, N297Q, A330L, and any combination thereof, wherein the numbering of the residues is according to EU numbering;
- (d) the anti-Siglec-9 antibody has a human or mouse IgG4 isotype and comprises one or more amino acid substitutions in the Fc region at a residue position selected from the group consisting of: L235A, G237A, S228P, L236E, S267E, E318A, L328F, M252Y, S254T, T256E, E233P, F234V, L234A/F234A, S228P, S241P, L248E, T394D, N297A, N297Q, L235E, and any combination thereof, wherein the numbering of the residues is according to EU numbering; or
- (e) the anti-Siglec-9 antibody has a hybrid IgG2/4 isotype, and optionally wherein the antibody comprises an amino acid sequence comprising amino acids 118 to 260 of human IgG2 and amino acids 261 to 447 of human IgG4, wherein the numbering of the residues is according to EU numbering.

17. The anti-Siglec-9 antibody of any one of claims 1-16, wherein the Siglec-9 protein is a mammalian protein or a human protein.

18. The anti-Siglec-9 antibody of any one of claims 1-17, wherein the anti-Siglec-9 antibody binds Siglec-9 in a pH dependent manner.

19. The anti-Siglec-9 antibody of any one of claims 1-18, wherein the anti-Siglec-9 antibody is an antibody fragment that binds to an epitope comprising amino acid residues on human Siglec-9 or a mammalian Siglec-9 protein.
20. The anti-Siglec-9 antibody of claim 19, wherein the fragment is an Fab, Fab', Fab'-SH, F(ab')₂, Fv, or scFv fragment.
21. The anti-Siglec-9 antibody of any one of claims 1-20, wherein the anti-Siglec-9 antibody is a murine antibody, a humanized antibody, a bispecific antibody, a monoclonal antibody, a multivalent antibody, a conjugated antibody, or a chimeric antibody.
22. The anti-Siglec-9 antibody of any one of the preceding claims, wherein the anti-Siglec-9 antibody has dissociation constant (K_D) for human Siglec-9 and mammalian Siglec-9 that ranges from about 10 nM to about 10 pM, or less than 10 pM, wherein the K_D is determined at a temperature of approximately 25°C.
23. The anti-Siglec-9 antibody of any one of the preceding claims, wherein the anti-Siglec-9 antibody has dissociation constant (K_D) for human Siglec-9 that ranges from about 9 nM to about 230 pM, or less than 230 pM, wherein the K_D is determined at a temperature of approximately 25°C.
24. An isolated nucleic acid comprising a nucleic acid sequence encoding the anti-Siglec-9 antibody of any one of the preceding claims.
25. A vector comprising the nucleic acid of claim 24.
26. An isolated host cell comprising the vector of claim 25.
27. A method of producing an anti-Siglec-9 antibody, comprising culturing the host cell of claim 26 so that the anti-Siglec-9 antibody is produced.
28. A pharmaceutical composition comprising the anti-Siglec-9 antibody of any one of claims 1-23, and a pharmaceutically acceptable carrier.
29. Use of a therapeutically effective amount of the anti-Siglec-9 antibody of any one of claims 1-23 in the manufacture of a medicament for preventing, reducing risk, or treating a disease, disorder, or injury selected from the group consisting of dementia, frontotemporal dementia, Alzheimer's disease, vascular dementia, mixed dementia, tauopathy disease, infections, and cancer.