

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-5 and/or Siglec-5 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-5.

[0013] Certain examples of the present disclosure are based, at least in part, on the identification of anti-Siglec-5 antibodies that are capable of decreasing cell surface levels of Siglec-5 on cells, such as human primary immune cells and Siglec-5-expressing cell lines, that do not inhibit or block the binding of Siglec-5 ligands to Siglec-5, that do not cross-react with Siglec-14, that are capable of inducing reactive oxygen species (ROS) production, that are capable of inducing neutrophil extracellular trap (NET) formation, and/or that increase phagocytosis activity in macrophages.

[0014] Accordingly, certain examples of the present disclosure relate to an isolated monoclonal anti-Siglec-5 antibody, wherein the anti-Siglec-5 antibody decreases cellular levels of Siglec-5. Other examples of the present disclosure relate to an isolated monoclonal anti-Siglec-5 antibody, wherein the anti-Siglec-5 antibody decreases cellular levels of Siglec-5 and does not inhibit interaction between Siglec-5 and one or more Siglec-5 ligands. Other examples of the present disclosure relate to an isolated monoclonal anti-

Siglec-5 antibody, wherein the anti-Siglec-5 antibody decreases cellular levels of Siglec-5 and does not bind Siglec-14. In one aspect, the present disclosure refers to an isolated monoclonal anti-Siglec-5 antibody, wherein the anti-Siglec-5 antibody decreases cellular levels of Siglec-5, and wherein the antibody does not bind Siglec-14.

[0015] In some examples that may be combined with any of the preceding examples, the anti-Siglec-5 antibody decreases cell surface levels of Siglec-5, decreases intracellular levels of Siglec-5, decreases total levels of Siglec-5, or any combination thereof. In some examples that may be combined with any of the preceding examples, the anti-Siglec-5 antibody induces Siglec-5 degradation, Siglec-5 cleavage, Siglec-5 internalization, Siglec-5 shedding, downregulation of Siglec-5 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-5 *in vitro*. In some examples that may be combined with any of the preceding examples, the antibody decreases cellular levels of Siglec-5 *in vivo*. In some examples that may be combined with any of the preceding examples, the anti-Siglec-5 antibody induces reactive oxygen species (ROS) production in neutrophils. In some examples that may be combined with any of the preceding examples, the anti-Siglec-5 antibody induces neutrophil extracellular traps (NET) formation in neutrophils. In some examples that may be combined with any of the preceding examples, the anti-Siglec-5 antibody induces neutrophil activation in neutrophils. In some examples that may be combined with any of the preceding examples, the anti-Siglec-5 antibody increases phagocytosis activity in macrophages.

[0016] In some examples that may be combined with any of the preceding examples, the anti-Siglec-5 antibody increases expression of CD86 in myeloid derived suppressor cells. In some examples, the anti-Siglec-5 antibody increases cell surface levels of CD86 in myeloid derived suppressor cells. In some examples that may be combined with any of the preceding examples, the anti-Siglec-5 antibody increases expression of CCL4 in myeloid derived suppressor cells. In some examples, the anti-Siglec-5 antibody increases cell surface levels of CCL4 in myeloid derived suppressor cells.

[0017] In some examples that may be combined with any of the preceding examples, the anti-Siglec-5 antibody binds a linear Siglec-5 epitope. In some examples that may be combined with any of the preceding examples, the anti-Siglec-5 antibody binds a discontinuous or conformational Siglec-5 epitope. In some examples that may be combined with any of the preceding examples, the anti-Siglec-5 antibody competes with one or more antibodies selected from the group consisting of S5-172, S5-174, S5-175, S5-176, S5-182, S5-183, S5-190, S5-202, S5-G-03, S5-G-07, S5-G-10, S5-172-H1, S5-172-H2, S5-172-H3, S5-172-H4, S5-172-H5, S5-172-H6, S5-174-H1, S5-174-H2, S5-174-H3, S5-174-H4, S5-174-H5, S5-174-H6, S5-174-H7, S5-174-H8, S5-G-03-H1, S5-G-03-H2, S5-G-03-H3, S5-G-03-H4, S5-G-03-H5, S5-G-03-H6, S5-G-03-H7, S5-G-03-H8, and S5-G-03-H9, and any combination thereof for binding to Siglec-5. In some examples that may be combined with any of the preceding examples, the anti-Siglec-5 antibody binds to the same or overlapping epitope as one or

more antibodies selected from the group consisting of S5-172, S5-174, S5-175, S5-176, S5-182, S5-183, S5-190, S5-202, S5-G-03, S5-G-07, S5-G-10, S5-172-H1, S5-172-H2, S5-172-H3, S5-172-H4, S5-172-H5, S5-172-H6, S5-174-H1, S5-174-H2, S5-174-H3, S5-174-H4, S5-174-H5, S5-174-H6, S5-174-H7, S5-174-H8, S5-G-03-H1, S5-G-03-H2, S5-G-03-H3, S5-G-03-H4, S5-G-03-H5, S5-G-03-H6, S5-G-03-H7, S5-G-03-H8, and S5-G-03-H9, and any combination thereof for binding to Siglec-5.

[0018] In some examples that may be combined with any of the preceding examples, the anti-Siglec-5 antibody binds to one or more amino acid residues within amino acid residues 268-278 of SEQ ID NO: 1 or amino acid residues on a Siglec-5 protein corresponding to amino acid residues 268-278 of SEQ ID NO: 1. In some examples that may be combined with any of the preceding examples, the anti-Siglec-5 antibody binds to one or more amino acid residues within the amino acid sequence LSWFQGSPALN (SEQ ID NO:221). In some examples that may be combined with any of the preceding examples, the anti-Siglec-5 antibody binds to one or more amino acid residues within amino acid residues 226-244 of SEQ ID NO: 1 or amino acid residues on a Siglec-5 protein corresponding to amino acid residues 226-244 of SEQ ID NO: 1. In some examples that may be combined with any of the preceding examples, the anti-Siglec-5 antibody binds to one or more amino acid residues within the amino acid sequence QTITIFRNGIALEILQNTS (SEQ ID NO:220). In some examples that may be combined with any of the preceding examples, the anti-Siglec-5 antibody binds to one or more amino acid residues within amino acid residues 228-238 of SEQ ID NO: 1 or amino acid residues corresponding to amino acid residues 228-238 of SEQ ID NO: 1. In some examples that may be combined with any of the preceding examples, the anti-Siglec-5 antibody binds to the amino acid sequence ITIFRNGIALE (SEQ ID NO:219).

[0019] In some examples that may be combined with any of the preceding examples, the anti-Siglec-5 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: S5-172, S5-174, S5-175, S5-176, S5-182, S5-183, S5-190, S5-202, S5-G-03, S5-G-07, S5-G-10, S5-172-H1, S5-172-H2, S5-172-H3, S5-172-H4, S5-172-H5, S5-172-H6, S5-174-H1, S5-174-H2, S5-174-H3, S5-174-H4, S5-174-H5, S5-174-H6, S5-174-H7, S5-174-H8, S5-G-03-H1, S5-G-03-H2, S5-G-03-H3, S5-G-03-H4, S5-G-03-H5, S5-G-03-H6, S5-G-03-H7, S5-G-03-H8, and S5-G-03-H9. 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: 103-115; (b) the HVR-L2 comprises an amino acid sequence selected from the group consisting of SEQ ID NOs: 127-135; (c) the HVR-L3 comprises an amino acid sequence selected from the group consisting of SEQ ID NOs: 153-163; (d) the HVR-H1 comprises an amino acid sequence selected from the group consisting of SEQ ID NOs: 20-28; (e) the HVR-H2 comprises an amino acid sequence selected from the group consisting of SEQ ID NOs: 39-51; or (f) the HVR-H3 comprises

an amino acid sequence selected from the group consisting of SEQ ID NOs: 70-79. In some examples that may be combined with any of the preceding examples: (a) 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:39, the HVR-H3 comprises the amino acid sequence of SEQ ID NO:70, the HVR-L1 comprises the amino acid sequence of SEQ ID NO:103, HVR-L2 comprises the amino acid sequence of SEQ ID NO:127, and the HVR-L3 comprises the amino acid sequence of SEQ ID NO:153; (b) 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:40, the HVR-H3 comprises the amino acid sequence of SEQ ID NO:71, the HVR-L1 comprises the amino acid sequence of SEQ ID NO:104, the HVR-L2 comprises the amino acid sequence of SEQ ID NO:128, and the HVR-L3 comprises the amino acid sequence of SEQ ID NO:154; (c) the HVR-H1 comprises the amino acid sequence of SEQ ID NO:22, the HVR-H2 comprises the amino acid sequence of SEQ ID NO:41, the HVR-H3 comprises the amino acid sequence of SEQ ID NO:72, the HVR-L1 comprises the amino acid sequence of SEQ ID NO:105, the HVR-L2 comprises the amino acid sequence of SEQ ID NO:129, and the HVR-L3 comprises the amino acid sequence of SEQ ID NO:155; (d) the HVR-H1 comprises the amino acid sequence of SEQ ID NO:23, the HVR-H2 comprises the amino acid sequence of SEQ ID NO:42, the HVR-H3 comprises the amino acid sequence of SEQ ID NO:73, the HVR-L1 comprises the amino acid sequence of SEQ ID NO:106, the HVR-L2 comprises the amino acid sequence of SEQ ID NO:127, and the HVR-L3 comprises the amino acid sequence of SEQ ID NO:156; (e) the HVR-H1 comprises the amino acid sequence of SEQ ID NO:24, the HVR-H2 comprises the amino acid sequence of SEQ ID NO:43, the HVR-H3 comprises the amino acid sequence of SEQ ID NO:74, the HVR-L1 comprises the amino acid sequence of SEQ ID NO:107, the HVR-L2 comprises the amino acid sequence of SEQ ID NO:130, and the HVR-L3 comprises the amino acid sequence of SEQ ID NO:157; (f) the HVR-H1 comprises the amino acid sequence of SEQ ID NO:25, the HVR-H2 comprises the amino acid sequence of SEQ ID NO:44, the HVR-H3 comprises the amino acid sequence of SEQ ID NO:75, the HVR-L1 comprises the amino acid sequence of SEQ ID NO:108, the HVR-L2 comprises the amino acid sequence of SEQ ID NO:131, and the HVR-L3 comprises the amino acid sequence of SEQ ID NO:158; (g) 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:39, the HVR-H3 comprises the amino acid sequence of SEQ ID NO:70, the HVR-L1 comprises the amino acid sequence of SEQ ID NO:109, the HVR-L2 comprises the amino acid sequence of SEQ ID NO:127, and the HVR-L3 comprises the amino acid sequence of SEQ ID NO:159; (h) the HVR-H1 comprises the amino acid sequence of SEQ ID NO:25, the HVR-H2 comprises the amino acid sequence of SEQ ID NO:45, the HVR-H3 comprises the amino acid sequence of SEQ ID NO:76, the HVR-L1 comprises the amino acid sequence of SEQ ID NO:110, the HVR-L2 comprises the amino acid sequence of SEQ ID NO:132, and the HVR-L3 comprises the amino acid sequence of SEQ ID NO:160; (i) the HVR-H1 comprises the amino acid sequence of SEQ ID NO:26, the HVR-H2 comprises the amino acid sequence of SEQ ID NO:46, the HVR-H3 comprises the amino acid sequence of SEQ ID

NO:77, the HVR-L1 comprises the amino acid sequence of SEQ ID NO:111, the HVR-L2 comprises the amino acid sequence of SEQ ID NO:133, and the HVR-L3 comprises the amino acid sequence of SEQ ID NO:161; (j) the HVR-H1 comprises the amino acid sequence of SEQ ID NO:27, the HVR-H2 comprises the amino acid sequence of SEQ ID NO:47, the HVR-H3 comprises the amino acid sequence of SEQ ID NO:78, the HVR-L1 comprises the amino acid sequence of SEQ ID NO:112, the HVR-L2 comprises the amino acid sequence of SEQ ID NO:134, and the HVR-L3 comprises the amino acid sequence of SEQ ID NO:162; (k) the HVR-H1 comprises the amino acid sequence of SEQ ID NO:28, the HVR-H2 comprises the amino acid sequence of SEQ ID NO:48, the HVR-H3 comprises the amino acid sequence of SEQ ID NO:79, the HVR-L1 comprises the amino acid sequence of SEQ ID NO:113, the HVR-L2 comprises the amino acid sequence of SEQ ID NO:135, and the HVR-L3 comprises the amino acid sequence of SEQ ID NO:163; (l) 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:49, the HVR-H3 comprises the amino acid sequence of SEQ ID NO:70, the HVR-L1 comprises the amino acid sequence of SEQ ID NO:114, the HVR-L2 comprising the amino acid sequence of SEQ ID NO:127, and the HVR-L3 comprises the amino acid sequence of SEQ ID NO:153; (m) 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:50, the HVR-H3 comprises the amino acid sequence of SEQ ID NO:71, the HVR-L1 comprises the amino acid sequence of SEQ ID NO:115, the HVR-L2 comprises the amino acid sequence of SEQ ID NO:128, and the HVR-L3 comprises the amino acid sequence of SEQ ID NO:154; and (n) the HVR-H1 comprises the amino acid sequence of SEQ ID NO:26, the HVR-H2 comprises the amino acid sequence of SEQ ID NO:51, the HVR-H3 comprises the amino acid sequence of SEQ ID NO:77, the HVR-L1 comprises the amino acid sequence of SEQ ID NO:111, the HVR-L2 comprises the amino acid sequence of SEQ ID NO:133, and the HVR-L3 comprises the amino acid sequence of SEQ ID NO:161.

[0020] In some examples that may be combined with any of the preceding examples, the anti-Siglec-5 antibody comprises a light chain variable domain comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 194-211; and/or a heavy chain variable domain comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 174-193. In some examples that may be combined with any of the preceding examples, the anti-Siglec-5 antibody comprises a light chain variable domain of a monoclonal antibody selected from the group consisting of: S5-172, S5-174, S5-175, S5-176, S5-182, S5-183, S5-190, S5-202, S5-G-03, S5-G-07, S5-G-10, S5-172-H1, S5-172-H2, S5-172-H3, S5-172-H4, S5-172-H5, S5-172-H6, S5-174-H1, S5-174-H2, S5-174-H3, S5-174-H4, S5-174-H5, S5-174-H6, S5-174-H7, S5-174-H8, S5-G-03-H1, S5-G-03-H2, S5-G-03-H3, S5-G-03-H4, S5-G-03-H5, S5-G-03-H6, S5-G-03-H7, S5-G-03-H8, and S5-G-03-H9; and/or a heavy chain variable domain of a monoclonal antibody selected from the group consisting of: S5-172, S5-174, S5-175, S5-176, S5-182, S5-183, S5-190, S5-202, S5-G-03, S5-G-07, S5-G-10, S5-172-H1, S5-172-H2, S5-172-H3, S5-172-H4, S5-172-H5, S5-172-H6, S5-174-H1, S5-174-H2, S5-174-H3, S5-174-H4, S5-

174-H5, S5-174-H6, S5-174-H7, S5-174-H8, S5-G-03-H1, S5-G-03-H2, S5-G-03-H3, S5-G-03-H4, S5-G-03-H5, S5-G-03-H6, S5-G-03-H7, S5-G-03-H8, and S5-G-03-H9.

[0021] Other examples of the present disclosure relate to an isolated monoclonal anti-Siglec-5 antibody, wherein the anti-Siglec-5 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: S5-172, S5-174, S5-175, S5-176, S5-182, S5-183, S5-190, S5-202, S5-G-03, S5-G-07, S5-G-10, S5-172-H1, S5-172-H2, S5-172-H3, S5-172-H4, S5-172-H5, S5-172-H6, S5-174-H1, S5-174-H2, S5-174-H3, S5-174-H4, S5-174-H5, S5-174-H6, S5-174-H7, S5-174-H8, S5-G-03-H1, S5-G-03-H2, S5-G-03-H3, S5-G-03-H4, S5-G-03-H5, S5-G-03-H6, S5-G-03-H7, S5-G-03-H8, and S5-G-03-H9. In some examples: (a) the HVR-L1 comprises an amino acid sequence selected from the group consisting of SEQ ID NOs: 103-115; (b) the HVR-L2 comprises an amino acid sequence selected from the group consisting of SEQ ID NOs: 127-135; (c) the HVR-L3 comprises an amino acid sequence selected from the group consisting of SEQ ID NOs: 153-163; (d) the HVR-H1 comprises an amino acid sequence selected from the group consisting of SEQ ID NOs: 20-28; (e) the HVR-H2 comprises an amino acid sequence selected from the group consisting of SEQ ID NOs: 39-51; or (f) the HVR-H3 comprises an amino acid sequence selected from the group consisting of SEQ ID NOs: 70-79. In some examples: wherein (a) 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:39, the HVR-H3 comprises the amino acid sequence of SEQ ID NO:70, the HVR-L1 comprises the amino acid sequence of SEQ ID NO:103, HVR-L2 comprises the amino acid sequence of SEQ ID NO:127, and the HVR-L3 comprises the amino acid sequence of SEQ ID NO:153; (b) 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:40, the HVR-H3 comprises the amino acid sequence of SEQ ID NO:71, the HVR-L1 comprises the amino acid sequence of SEQ ID NO:104, the HVR-L2 comprises the amino acid sequence of SEQ ID NO:128, and the HVR-L3 comprises the amino acid sequence of SEQ ID NO:154; (c) the HVR-H1 comprises the amino acid sequence of SEQ ID NO:22, the HVR-H2 comprises the amino acid sequence of SEQ ID NO:41, the HVR-H3 comprises the amino acid sequence of SEQ ID NO:72, the HVR-L1 comprises the amino acid sequence of SEQ ID NO:105, the HVR-L2 comprises the amino acid sequence of SEQ ID NO:129, and the HVR-L3 comprises the amino acid sequence of SEQ ID NO:155; (d) the HVR-H1 comprises the amino acid sequence of SEQ ID NO:23, the HVR-H2 comprises the amino acid sequence of SEQ ID NO:42, the HVR-H3 comprises the amino acid sequence of SEQ ID NO:73, the HVR-L1 comprises the amino acid sequence of SEQ ID NO:106, the HVR-L2 comprises the amino acid sequence of SEQ ID NO:127, and the HVR-L3 comprises the amino acid sequence of SEQ ID NO:156; (e) the HVR-H1 comprises the amino acid sequence of SEQ ID NO:24, the HVR-H2 comprises the amino acid sequence of SEQ ID NO:43, the HVR-H3 comprises the amino acid sequence of SEQ ID

of SEQ ID NO:77, the HVR-L1 comprises the amino acid sequence of SEQ ID NO:111, the HVR-L2 comprises the amino acid sequence of SEQ ID NO:133, and the HVR-L3 comprises the amino acid sequence of SEQ ID NO:161.

[0022] Other examples of the present disclosure relate to an isolated monoclonal anti-Siglec-5 antibody, wherein the anti-Siglec-5 antibody comprises a light chain variable domain comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 194-211 and/or a heavy chain variable domain comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 174-193. Other examples of the present disclosure relate to an isolated monoclonal anti-Siglec-5 antibody, wherein the anti-Siglec-5 antibody comprises a light chain variable domain of a monoclonal antibody selected from the group consisting of: S5-172, S5-174, S5-175, S5-176, S5-182, S5-183, S5-190, S5-202, S5-G-03, S5-G-07, S5-G-10, S5-172-H1, S5-172-H2, S5-172-H3, S5-172-H4, S5-172-H5, S5-172-H6, S5-174-H1, S5-174-H2, S5-174-H3, S5-174-H4, S5-174-H5, S5-174-H6, S5-174-H7, S5-174-H8, S5-G-03-H1, S5-G-03-H2, S5-G-03-H3, S5-G-03-H4, S5-G-03-H5, S5-G-03-H6, S5-G-03-H7, S5-G-03-H8, and S5-G-03-H9; and/or a heavy chain variable domain of a monoclonal antibody selected from the group consisting of: S5-172, S5-174, S5-175, S5-176, S5-182, S5-183, S5-190, S5-202, S5-G-03, S5-G-07, S5-G-10, S5-172-H1, S5-172-H2, S5-172-H3, S5-172-H4, S5-172-H5, S5-172-H6, S5-174-H1, S5-174-H2, S5-174-H3, S5-174-H4, S5-174-H5, S5-174-H6, S5-174-H7, S5-174-H8, S5-G-03-H1, S5-G-03-H2, S5-G-03-H3, S5-G-03-H4, S5-G-03-H5, S5-G-03-H6, S5-G-03-H7, S5-G-03-H8, and S5-G-03-H9. In another aspect, the present disclosure relates to an isolated monoclonal anti-Siglec-5 antibody, wherein the anti-Siglec-5 antibody competes with one or more antibodies selected from the group consisting of S5-172, S5-174, S5-175, S5-176, S5-182, S5-183, S5-190, S5-202, S5-G-03, S5-G-07, S5-G-10, S5-172-H1, S5-172-H2, S5-172-H3, S5-172-H4, S5-172-H5, S5-172-H6, S5-174-H1, S5-174-H2, S5-174-H3, S5-174-H4, S5-174-H5, S5-174-H6, S5-174-H7, S5-174-H8, S5-G-03-H1, S5-G-03-H2, S5-G-03-H3, S5-G-03-H4, S5-G-03-H5, S5-G-03-H6, S5-G-03-H7, S5-G-03-H8, and S5-G-03-H9, and any combination thereof for binding to Siglec-5. In another aspect, the present disclosure relates to an isolated monoclonal anti-Siglec-5 antibody which binds essentially the same Siglec-5 epitope as a monoclonal antibody selected from the group consisting of: S5-172, S5-174, S5-175, S5-176, S5-182, S5-183, S5-190, S5-202, S5-G-03, S5-G-07, S5-G-10, S5-172-H1, S5-172-H2, S5-172-H3, S5-172-H4, S5-172-H5, S5-172-H6, S5-174-H1, S5-174-H2, S5-174-H3, S5-174-H4, S5-174-H5, S5-174-H6, S5-174-H7, S5-174-H8, S5-G-03-H1, S5-G-03-H2, S5-G-03-H3, S5-G-03-H4, S5-G-03-H5, S5-G-03-H6, S5-G-03-H7, S5-G-03-H8, and S5-G-03-H9.

[0023] Other examples of the present disclosure relate to an isolated monoclonal anti-Siglec-5 antibody which binds one or more amino acid residues within amino acid residues selected from the group consisting of: amino acid residues 268-278 of SEQ ID NO: 1 or amino acid residues on a Siglec-5 protein that correspond to amino acid residues 268-278 of SEQ ID NO: 1, amino acid residues 226-244 of SEQ ID NO: 1 or amino acid residues on a Siglec-5 protein that correspond to amino acid residues 226-244 of

SEQ ID NO: 1, and amino acid residues 228-238 of SEQ ID NO: 1 or amino acid residues on a Siglec-5 protein that correspond to amino acid residues 228-238 of SEQ ID NO: 1. Other examples of the present disclosure relate to an isolated monoclonal anti-Siglec-5 antibody which binds to one or more amino acid residues within amino acid sequences selected from the group consisting of: the amino acid sequence LSWFQGSPALN (SEQ ID NO:221), the amino acid sequence QTITIFRNGIALEILQNTS (SEQ ID NO:220), and the amino acid sequence ITIFRNGIALE (SEQ ID NO:219).

[0024] 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-5 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-5 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, E430G, V263L, V266L, V273C, V273E, V273F, V273L, V273M, V273S, V273Y, V305K, V305W, 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-5 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 YTCNVDPHKPS NTKVDKTVRKCCVECPPCP (SEQ ID NO: 218), 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-5 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, C127S, E430G, and any combination thereof, wherein the numbering of the residues is according to EU numbering; (d) the anti-Siglec-5 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-5 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-5 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 numbering; (b) the anti-Siglec-5 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, C127S, E430G, and any combination thereof, wherein the numbering of the residues is according to EU numbering; or (c) the anti-Siglec-5 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 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 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 numbering; or (c) the Fc region further comprises a S228P amino acid substitution according to EU numbering. In some examples that may be combined with any of the preceding examples, the antibody has an IgG4 isotype. In some examples that may be combined with any of the preceding examples, the anti-Siglec-5 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 numbering.

[0025] In some examples that may be combined with any of the preceding examples, the Siglec-5 protein is a mammalian protein or a human protein. In some examples that may be combined with any of the preceding examples, the Siglec-5 protein is a wild-type protein. In some examples that may be combined with any of the preceding examples, the Siglec-5 protein is a naturally occurring variant. In some examples that may be combined with any of the preceding examples, the Siglec-5 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 B cells, human T cells, human T helper cell, human cytotoxic T cells, human granulocytes, and human microglia. In some examples that may be combined with any of the preceding examples, the anti-Siglec-5 antibody binds specifically to human Siglec-5 protein. In some examples that may be combined with any of the preceding examples, the anti-Siglec-5 antibody is an antibody fragment that binds to an epitope comprising amino acid residues on human Siglec-5. In some examples that may be combined with any of the preceding examples, the anti-Siglec-5 antibody is an antibody fragment that binds to one or more human proteins selected from the group consisting of human Siglec-5, a naturally occurring variant of human Siglec-5, and a disease variant of human Siglec-5. In some examples that 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-5, a naturally occurring variant of human Siglec-5, and a disease variant of human Siglec-5. In some examples that 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 examples that may be combined with any of the preceding examples, the anti-Siglec-5 antibody is a murine antibody. In some examples that may be combined with any of the preceding examples, the anti-Siglec-5 antibody is a humanized antibody, a bispecific 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-5 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-5 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) (SEQ ID NO: 225) 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, 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; (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-5 antibody is a conjugated antibody. In some examples that may be combined with any of the preceding examples, the anti-Siglec-5 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-5 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-5 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-6, Siglec-7, Siglec-9, Siglec-10, Siglec-11, phosphatidylserine, disease-causing nucleic acids, antisense GGCCCC (G2C4) (SEQ ID NO: 225) repeat-expansion RNA, and any combination thereof. In some examples that may be combined with any of the preceding examples, the anti-Siglec-5 antibody has dissociation constant (K_D) for human Siglec-5 that ranges from about 0.42 nM to about 79 nM, from about 79 nM to about 61 nM, from about 15 nM to

about 5.3 nM, or from about 1.7 nM to about 0.42 nM, wherein the K_D is determined at a temperature of approximately 25°C.

[0026] In another aspect, the present disclosure relates to an isolated nucleic acid comprising a nucleic acid sequence encoding the anti-Siglec-5 antibody as disclosed herein. In another aspect, the present disclosure relates to a vector comprising the nucleic acid as disclosed herein. In another aspect, the present disclosure relates to an isolated host cell comprising the vector as disclosed herein. In another aspect, the present disclosure relates to a method of producing an anti-Siglec-5 antibody, comprising culturing the host cell as disclosed herein so that the anti-Siglec-5 antibody is produced. In some examples, the method further comprises recovering the anti-Siglec-5 antibody produced by the host cell. In another aspect, the present disclosure relates to an isolated anti-Siglec-5 antibody produced by the method as disclosed herein. In another aspect, the present disclosure relates to a pharmaceutical composition comprising the anti-Siglec-5 antibody as disclosed herein, and a pharmaceutically acceptable carrier.

[0027] Other examples of the present disclosure relate to 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-5, tumors that express one or more Siglec-5 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 anti-

Siglec-5 antibody that decreases cellular levels of Siglec-5. Other examples of the present disclosure relate to an anti-Siglec-5 antibody that decreases cellular levels of Siglec-5 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-5, tumors that express one or more Siglec-5 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. Other examples of the present disclosure relate to use of an anti-Siglec-5 antibody that decreases cellular levels of Siglec-5 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-5, tumors that express one or more Siglec-5 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. Other examples of the present disclosure relate to 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-5. Other examples of the present disclosure relate to an anti-Siglec-5 antibody that decreases cellular levels of Siglec-5 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. Other examples of the present disclosure relate to use of an anti-Siglec-5 antibody that decreases cellular levels of Siglec-5 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 anti-Siglec-5 antibody is the anti-Siglec-5 antibody of any of the preceding examples. In another aspect, the present disclosure refers to the use of the anti-Siglec-5 antibody as 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, taupathy disease, infections, and cancer, in an individual in need thereof.

[0027a] In another aspect, the present disclosure relates to the use of the anti-Siglec-5 antibody as disclosed herein 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.

[0027b] In another aspect, the present disclosure relates to the use of the anti-Siglec-5 antibody as disclosed herein 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.

[0028] Other examples of the present disclosure relate to a method of decreasing cellular levels of Siglec-5 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-5 antibody. Other examples of the present disclosure relate to an isolated anti-Siglec-5 antibody for use in decreasing cellular levels of Siglec-5 on one or more cells in an individual in need thereof. Other examples of the present disclosure relate to use of an isolated anti-Siglec-5 antibody in the manufacture of a medicament for decreasing cellular levels of Siglec-5 on one or more cells in an individual in need thereof. In some examples, the anti-Siglec-5 antibody is the anti-Siglec-5 antibody of any of the preceding examples. In another aspect, the present disclosure relates to the use of the anti-Siglec-5 antibody as disclosed herein in the manufacture of a medicament for decreasing cellular levels of Siglec-5 on one or more cells, in an individual in need thereof.

[0029] Other examples of the present disclosure relate to a method of inducing reactive oxygen species (ROS) production in one or more neutrophils in an individual in need thereof, comprising administering to the individual a therapeutically effective amount of an isolated anti-Siglec-5 antibody. Other examples of the present disclosure relate to an isolated anti-Siglec-5 antibody for use in inducing reactive oxygen species (ROS) production in one or more neutrophils in an individual in need thereof. Other examples of

the present disclosure relate to use of an isolated anti-Siglec-5 antibody in the manufacture of a medicament for inducing reactive oxygen species (ROS) production in one or more neutrophils in an individual in need thereof. In some examples, the anti-Siglec-5 antibody is the anti-Siglec-5 antibody of any of the preceding examples. In another aspect, the present disclosure relates to the use of the anti-Siglec-5 antibody as disclosed herein in the manufacture of a medicament for inducing reactive oxygen species (ROS) production in one or more neutrophils, in an individual in need thereof.

[0030] Other examples of the present disclosure relate to a method of inducing neutrophil extracellular trap (NET) formation in one or more neutrophils in an individual in need thereof, comprising administering to the individual a therapeutically effective amount of an isolated anti-Siglec-5 antibody. Other examples of the present disclosure relate to an isolated anti-Siglec-5 antibody for use in inducing neutrophil extracellular trap (NET) formation in one or more neutrophils in an individual in need thereof. Other examples of the present disclosure relate to use of an isolated anti-Siglec-5 antibody in the manufacture of a medicament for inducing neutrophil extracellular trap (NET) formation in one or more neutrophils in an individual in need thereof. In some examples, the anti-Siglec-5 antibody is the anti-Siglec-5 antibody of any of the preceding examples. In another aspect, the present disclosure relates to the use of the anti-Siglec-5 antibody as disclosed herein in the manufacture of a medicament for inducing neutrophil extracellular trap (NET) formation in one or more neutrophils in an individual in need thereof.

[0031] Other examples of the present disclosure relate to a method of inducing neutrophil activation in one or more neutrophils in an individual in need thereof, comprising administering to the individual a therapeutically effective amount of an isolated anti-Siglec-5 antibody. Other examples of the present disclosure relate to an isolated anti-Siglec-5 antibody for use in inducing neutrophil activation in one or more neutrophils in an individual in need thereof. Other examples of the present disclosure relate to use of an isolated anti-Siglec-5 antibody in the manufacture of a medicament for inducing neutrophil activation in one or more neutrophils in an individual in need thereof. In some examples, the anti-Siglec-5 antibody is the anti-Siglec-5 antibody of any of the preceding examples. In another aspect, the present disclosure refers to the use of the anti-Siglec-5 antibody as disclosed herein in the manufacture of a medicament for inducing neutrophil activation in one or more neutrophils, in an individual in need thereof.

[0032] Other examples of the present disclosure relate to a method of relieving one or more immunosuppressed neutrophils in an individual in need thereof, comprising administering to the individual a therapeutically effective amount of an isolated anti-Siglec-5 antibody. Other examples of the present disclosure relate to an isolated anti-Siglec-5 antibody for use in relieving one or more immunosuppressed neutrophils in an individual in need thereof. Other examples of the present disclosure relate to use of an isolated anti-Siglec-5 antibody in the manufacture of a medicament for relieving one or more immunosuppressed neutrophils in an individual in need thereof. In some examples, the anti-Siglec-5 antibody is the anti-Siglec-5 antibody of any of the preceding examples. In another aspect, the present disclosure refers to the use of the anti-Siglec-5 antibody as disclosed herein in the manufacture of a medicament for relieving one or more immunosuppressed neutrophils, in an individual in need thereof.

[0033] Other examples of the present disclosure relate to a method of increase phagocytosis activity in macrophages in an individual in need thereof, comprising administering to the individual a therapeutically effective amount of an isolated anti-Siglec-5 antibody. In another aspect, the present disclosure refers to the use of the anti-Siglec-5 antibody as disclosed herein in the manufacture of a medicament for increasing phagocytosis activity in macrophages, in an individual in need thereof.

[0034] In some examples that may be combined with any of the preceding examples, the method further comprises 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 examples that 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-5 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 checkpoint molecule is selected from the group consisting of 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-6 antibody, an anti-Siglec-7 antibody, an anti-Siglec-9 antibody, an anti-Siglec-10 antibody, an anti-Siglec-11 antibody, an antagonistic anti-TREM1 antibody, an antagonistic anti-TREM2 antibody, and any combination thereof. In some examples that 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 examples that may be combined with any of the preceding examples, the method further comprises administering to the individual at least one antibody that specifically binds to an inhibitory cytokine. 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 administered in combination with the anti-Siglec-5 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 comprises 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-5 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-BTLA antibody, an agonist HVEM antibody, an agonist anti-CD30 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 comprises 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-5 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- γ , IFN- α , IL-1 β , TNF- α , IL-6, IL-8, CRP, IL-20 family members, LIF, IFN-gamma, 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.

BRIEF DESCRIPTION OF THE DRAWINGS

[0035] **FIG. 1A** shows an amino acid sequence alignment between human Siglec-5 (SEQ ID NO: 1) and cynomolgus monkey Siglec-5 (SEQ ID NO: 2). 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** shows an amino acid alignment between human Siglec-5 (SEQ ID NO:1) and human Siglec-14 (SEQ ID NO:3). 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.

[0036] **FIG. 2A** shows results of FACS analysis of anti-Siglec-5 antibodies binding to CHO cells expressing recombinant human Siglec-5 or recombinant human Siglec-14. **FIG. 2B** shows results of FACS analysis of anti-Siglec-5-specific antibodies binding to primary human neutrophils, compared to isotype controls. In **FIG. 2A** and in **FIG. 2B**, antibody 1A5 recognizes both human Siglec-5 and human Siglec-14.

[0037] **FIG. 3** shows results demonstrating that anti-Siglec-5 antibodies of the present disclosure do not block the interaction between immobilized Siglec-5-Fc protein and Siglec-5 ligands on red blood cells.

[0038] **FIG. 4A** shows anti-Siglec-5 antibody-dependent downregulation of cell surface Siglec-5 receptor on CHO-S5 transfectant cells. **FIG. 4B** shows Siglec-5 antibody- dependent downregulation of cell surface Siglec- 5 receptor on human primary B cells from Siglec-14 null donors. **FIG. 4C** shows the downregulation of Siglec-5 in differentiated human macrophages M0, M1 and M2a in the presence of anti-Siglec-5 specific antibodies.

[0039] **FIG. 5** shows induction of reactive oxygen species (ROS) production in human primary neutrophils in the presence of anti-Siglec-5 antibodies.

CLAIMS

What is claimed is:

1. An isolated monoclonal anti-Siglec-5 antibody, wherein the anti-Siglec-5 antibody decreases cellular levels of Siglec-5, and wherein the antibody does not bind Siglec-14.
2. The anti-Siglec-5 antibody of claim 1, wherein the anti-Siglec-5 antibody does not inhibit the interaction between Siglec-5 and one or more Siglec-5 ligands.
3. The anti-Siglec-5 antibody of any one of claims 1-**Error! Reference source not found.**, wherein the anti-Siglec-5 antibody decreases cell surface levels of Siglec-5, decreases intracellular levels of Siglec-5, decreases total levels of Siglec-5, or any combination thereof.
4. The anti-Siglec-5 antibody of any one of claims 1-3, wherein the anti-Siglec-5 antibody induces Siglec-5 degradation, Siglec-5 cleavage, Siglec-5 internalization, Siglec-5 shedding, downregulation of Siglec-5 expression, or any combination thereof.
5. The anti-Siglec-5 antibody of any one of claims 1-4, wherein the antibody decreases cellular levels of Siglec-5 *in vivo*.
6. The anti-Siglec-5 antibody of any one of claims 1-5, wherein the anti-Siglec-5 antibody:
 - (a) induces reactive oxygen species (ROS) production in neutrophils;
 - (b) induces neutrophil extracellular traps (NET) formation in neutrophils;
 - (c) increases phagocytosis activity in macrophages;
 - (d) increases expression of CD86 in myeloid derived suppressor cells; and/or
 - (e) increases expression of CCL4 in myeloid derived suppressor cells.
7. The anti-Siglec-5 antibody of any one of claims 1-6, wherein the anti-Siglec-5 antibody inhibits one or more Siglec-5 activities.
8. The anti-Siglec-5 antibody of any one of claims 1-7, wherein the cellular levels of Siglec-5 are measured on primary cells selected from the group consisting of dendritic cells, bone marrow-derived dendritic cells, monocytes, microglia, macrophages, neutrophils, B cells, and NK cells, or on cell lines, and wherein the cellular levels of Siglec-5 are measured utilizing an *in vitro* cell assay.
9. The anti-Siglec-5 antibody of any one of claims 1-8, wherein the anti-Siglec-5 antibody competes with one or more antibodies selected from the group consisting of S5-172, S5-174, S5-175, S5-176, S5-182, S5-183, S5-190, S5-202, S5-G-03, S5-G-07, S5-G-10, S5-172-H1, S5-172-H2, S5-172-H3, S5-172-H4, S5-172-H5, S5-172-H6, S5-174-H1, S5-174-H2, S5-174-H3, S5-174-H4, S5-174-H5, S5-174-H6, S5-174-H7, S5-174-H8, S5-G-03-H1, S5-G-03-H2, S5-G-03-H3, S5-G-03-H4, S5-G-03-H5, S5-G-03-H6, S5-G-03-H7, S5-G-03-H8, and S5-G-03-H9, and any combination thereof for binding to Siglec-5.

10. The anti-Siglec-5 antibody of any one of claims 1-9, wherein the anti-Siglec-5 antibody binds to one or more amino acid residues within amino acid residues selected from the group consisting of: amino acid residues 268-278 of SEQ ID NO: 1 or amino acid residues on a Siglec-5 protein that correspond to amino acid residues 268-278 of SEQ ID NO: 1, amino acid residues 226-244 of SEQ ID NO: 1 or amino acid residues on a Siglec-5 protein that correspond to amino acid residues 226-244 of SEQ ID NO: 1, and amino acid residues 228-238 of SEQ ID NO: 1 or amino acid residues on a Siglec-5 protein that correspond to amino acid residues 228-238 of SEQ ID NO: 1.

11. The anti-Siglec-5 antibody of any one of claims 1-10, wherein the anti-Siglec-5 antibody binds to one or more amino acid residues within amino acid sequences selected from the group consisting of: the amino acid sequence LSWFQGSPALN (SEQ ID NO:221), the amino acid sequence QTITIFRNGIALEILQNTS (SEQ ID NO:220), and the amino acid sequence ITIFRNGIALE (SEQ ID NO:219).

12. The anti-Siglec-5 antibody of any one of claims 1-11, wherein the anti-Siglec-5 antibody comprises a light chain variable domain and a heavy chain variable domain, wherein the light chain variable domain comprises an HVR-L1, an HVR-L2, and an HVR-L3, and the heavy chain variable domain comprises an HVR-H1, an HVR-H2, and an HVR-H3, wherein:

- (a) the HVR-L1 comprises the amino acid sequence of SEQ ID NO: 103 or an amino acid sequence with at least about 90% homology to the amino acid sequence of SEQ ID NO: 103, the HVR-L2 comprises the amino acid sequence of SEQ ID NO: 127 or an amino acid sequence with at least about 90% homology to the amino acid sequence of SEQ ID NO: 127, the HVR-L3 comprises the amino acid sequence of SEQ ID NO: 153 or an amino acid sequence with at least about 90% homology to the amino acid sequence of SEQ ID NO: 153, the HVR-H1 comprises the amino acid sequence of SEQ ID NO: 20 or an amino acid sequence with at least about 90% homology to the amino acid sequence of SEQ ID NO: 20, the HVR-H2 comprises the amino acid sequence of SEQ ID NO: 39 or an amino acid sequence with at least about 90% homology to the amino acid sequence of SEQ ID NO: 39, and the HVR-H3 comprises the amino acid sequence of SEQ ID NO: 70 or an amino acid sequence with at least about 90% homology to the amino acid sequence of SEQ ID NO: 70;
- (b) the HVR-L1 comprises the amino acid sequence of SEQ ID NO: 104 or an amino acid sequence with at least about 90% homology to the amino acid sequence of SEQ ID NO: 104, the HVR-L2 comprises the amino acid sequence of SEQ ID NO: 128 or an amino acid sequence with at least about 90% homology to the amino acid sequence of SEQ ID NO: 128, the HVR-L3 comprises the amino acid sequence of SEQ ID NO: 154 or an amino acid sequence with at least about 90% homology to the amino acid sequence

of SEQ ID NO: 154, the HVR-H1 comprises the amino acid sequence of SEQ ID NO: 21 or an amino acid sequence with at least about 90% homology to the amino acid sequence of SEQ ID NO: 21, the HVR-H2 comprises the amino acid sequence of SEQ ID NO: 40 or an amino acid sequence with at least about 90% homology to the amino acid sequence of SEQ ID NO: 40, and the HVR-H3 comprises the amino acid sequence of SEQ ID NO: 71 or an amino acid sequence with at least about 90% homology to the amino acid sequence of SEQ ID NO: 71;

- (c) the HVR-L1 comprises the amino acid sequence of SEQ ID NO: 105 or an amino acid sequence with at least about 90% homology to the amino acid sequence of SEQ ID NO: 105, the HVR-L2 comprises the amino acid sequence of SEQ ID NO: 129 or an amino acid sequence with at least about 90% homology to the amino acid sequence of SEQ ID NO: 129, the HVR-L3 comprises the amino acid sequence of SEQ ID NO: 155 or an amino acid sequence with at least about 90% homology to the amino acid sequence of SEQ ID NO: 155, the HVR-H1 comprises the amino acid sequence of SEQ ID NO: 22 or an amino acid sequence with at least about 90% homology to the amino acid sequence of SEQ ID NO: 22, the HVR-H2 comprises the amino acid sequence of SEQ ID NO: 41 or an amino acid sequence with at least about 90% homology to the amino acid sequence of SEQ ID NO: 41, and the HVR-H3 comprises the amino acid sequence of SEQ ID NO: 72 or an amino acid sequence with at least about 90% homology to the amino acid sequence of SEQ ID NO: 72;
- (d) the HVR-L1 comprises the amino acid sequence of SEQ ID NO: 106 or an amino acid sequence with at least about 90% homology to the amino acid sequence of SEQ ID NO: 106, the HVR-L2 comprises the amino acid sequence of SEQ ID NO: 127 or an amino acid sequence with at least about 90% homology to the amino acid sequence of SEQ ID NO: 127, the HVR-L3 comprises the amino acid sequence of SEQ ID NO: 156 or an amino acid sequence with at least about 90% homology to the amino acid sequence of SEQ ID NO: 156, the HVR-H1 comprises the amino acid sequence of SEQ ID NO: 23 or an amino acid sequence with at least about 90% homology to the amino acid sequence of SEQ ID NO: 23, the HVR-H2 comprises the amino acid sequence of SEQ ID NO: 342 or an amino acid sequence with at least about 90% homology to the amino acid sequence of SEQ ID NO: 342, and the HVR-H3 comprises the amino acid sequence of SEQ ID NO: 73 or an amino acid sequence with at least about 90% homology to the amino acid sequence of SEQ ID NO: 73;
- (e) the HVR-L1 comprises the amino acid sequence of SEQ ID NO: 107 or an amino acid sequence with at least about 90% homology to the amino acid sequence of SEQ ID NO: 107, the HVR-L2 comprises the amino acid sequence of SEQ ID NO: 130 or an amino

acid sequence with at least about 90% homology to the amino acid sequence of SEQ ID NO: 130, the HVR-L3 comprises the amino acid sequence of SEQ ID NO: 157 or an amino acid sequence with at least about 90% homology to the amino acid sequence of SEQ ID NO: 157, the HVR-H1 comprises the amino acid sequence of SEQ ID NO: 24 or an amino acid sequence with at least about 90% homology to the amino acid sequence of SEQ ID NO: 24, the HVR-H2 comprises the amino acid sequence of SEQ ID NO: 43 or an amino acid sequence with at least about 90% homology to the amino acid sequence of SEQ ID NO: 43, and the HVR-H3 comprises the amino acid sequence of SEQ ID NO: 74 or an amino acid sequence with at least about 90% homology to the amino acid sequence of SEQ ID NO: 74;

- (f) the HVR-L1 comprises the amino acid sequence of SEQ ID NO: 108 or an amino acid sequence with at least about 90% homology to the amino acid sequence of SEQ ID NO: 108, the HVR-L2 comprises the amino acid sequence of SEQ ID NO: 131 or an amino acid sequence with at least about 90% homology to the amino acid sequence of SEQ ID NO: 131, the HVR-L3 comprises the amino acid sequence of SEQ ID NO: 158 or an amino acid sequence with at least about 90% homology to the amino acid sequence of SEQ ID NO: 158, the HVR-H1 comprises the amino acid sequence of SEQ ID NO: 25 or an amino acid sequence with at least about 90% homology to the amino acid sequence of SEQ ID NO: 25, the HVR-H2 comprises the amino acid sequence of SEQ ID NO: 44 or an amino acid sequence with at least about 90% homology to the amino acid sequence of SEQ ID NO: 44, and the HVR-H3 comprises the amino acid sequence of SEQ ID NO: 75 or an amino acid sequence with at least about 90% homology to the amino acid sequence of SEQ ID NO: 75;
- (g) the HVR-L1 comprises the amino acid sequence of SEQ ID NO: 109 or an amino acid sequence with at least about 90% homology to the amino acid sequence of SEQ ID NO: 109, the HVR-L2 comprises the amino acid sequence of SEQ ID NO: 127 or an amino acid sequence with at least about 90% homology to the amino acid sequence of SEQ ID NO: 127, the HVR-L3 comprises the amino acid sequence of SEQ ID NO: 159 or an amino acid sequence with at least about 90% homology to the amino acid sequence of SEQ ID NO: 159, the HVR-H1 comprises the amino acid sequence of SEQ ID NO: 20 or an amino acid sequence with at least about 90% homology to the amino acid sequence of SEQ ID NO: 20, the HVR-H2 comprises the amino acid sequence of SEQ ID NO: 39 or an amino acid sequence with at least about 90% homology to the amino acid sequence of SEQ ID NO: 39, and the HVR-H3 comprises the amino acid sequence of SEQ ID NO: 70 or an amino acid sequence with at least about 90% homology to the amino acid sequence of SEQ ID NO: 70;

- (h) the HVR-L1 comprises the amino acid sequence of SEQ ID NO: 110 or an amino acid sequence with at least about 90% homology to the amino acid sequence of SEQ ID NO: 110, the HVR-L2 comprises the amino acid sequence of SEQ ID NO: 132 or an amino acid sequence with at least about 90% homology to the amino acid sequence of SEQ ID NO: 132, the HVR-L3 comprises the amino acid sequence of SEQ ID NO: 160 or an amino acid sequence with at least about 90% homology to the amino acid sequence of SEQ ID NO: 160, the HVR-H1 comprises the amino acid sequence of SEQ ID NO: 25 or an amino acid sequence with at least about 90% homology to the amino acid sequence of SEQ ID NO: 25, the HVR-H2 comprises the amino acid sequence of SEQ ID NO: 45 or an amino acid sequence with at least about 90% homology to the amino acid sequence of SEQ ID NO: 45, and the HVR-H3 comprises the amino acid sequence of SEQ ID NO: 76 or an amino acid sequence with at least about 90% homology to the amino acid sequence of SEQ ID NO: 76;
- (i) the HVR-L1 comprises the amino acid sequence of SEQ ID NO: 111 or an amino acid sequence with at least about 90% homology to the amino acid sequence of SEQ ID NO: 111, the HVR-L2 comprises the amino acid sequence of SEQ ID NO: 133 or an amino acid sequence with at least about 90% homology to the amino acid sequence of SEQ ID NO: 133, the HVR-L3 comprises the amino acid sequence of SEQ ID NO: 161 or an amino acid sequence with at least about 90% homology to the amino acid sequence of SEQ ID NO: 161, the HVR-H1 comprises the amino acid sequence of SEQ ID NO: 26 or an amino acid sequence with at least about 90% homology to the amino acid sequence of SEQ ID NO: 26, the HVR-H2 comprises the amino acid sequence of SEQ ID NO: 46 or an amino acid sequence with at least about 90% homology to the amino acid sequence of SEQ ID NO: 46, and the HVR-H3 comprises the amino acid sequence of SEQ ID NO: 77 or an amino acid sequence with at least about 90% homology to the amino acid sequence of SEQ ID NO: 77;
- (j) the HVR-L1 comprises the amino acid sequence of SEQ ID NO: 112 or an amino acid sequence with at least about 90% homology to the amino acid sequence of SEQ ID NO: 112, the HVR-L2 comprises the amino acid sequence of SEQ ID NO: 134 or an amino acid sequence with at least about 90% homology to the amino acid sequence of SEQ ID NO: 134, the HVR-L3 comprises the amino acid sequence of SEQ ID NO: 162 or an amino acid sequence with at least about 90% homology to the amino acid sequence of SEQ ID NO: 162, the HVR-H1 comprises the amino acid sequence of SEQ ID NO: 27 or an amino acid sequence with at least about 90% homology to the amino acid sequence of SEQ ID NO: 27, the HVR-H2 comprises the amino acid sequence of SEQ ID NO: 47 or an amino acid sequence with at least about 90% homology to the amino acid sequence of

- SEQ ID NO: 47, and the HVR-H3 comprises the amino acid sequence of SEQ ID NO: 78 or an amino acid sequence with at least about 90% homology to the amino acid sequence of SEQ ID NO: 78;
- (k) the HVR-L1 comprises the amino acid sequence of SEQ ID NO: 113 or an amino acid sequence with at least about 90% homology to the amino acid sequence of SEQ ID NO: 113, the HVR-L2 comprises the amino acid sequence of SEQ ID NO: 135 or an amino acid sequence with at least about 90% homology to the amino acid sequence of SEQ ID NO: 135, the HVR-L3 comprises the amino acid sequence of SEQ ID NO: 163 or an amino acid sequence with at least about 90% homology to the amino acid sequence of SEQ ID NO: 163, the HVR-H1 comprises the amino acid sequence of SEQ ID NO: 28 or an amino acid sequence with at least about 90% homology to the amino acid sequence of SEQ ID NO: 28, the HVR-H2 comprises the amino acid sequence of SEQ ID NO: 48 or an amino acid sequence with at least about 90% homology to the amino acid sequence of SEQ ID NO: 48, and the HVR-H3 comprises the amino acid sequence of SEQ ID NO: 79 or an amino acid sequence with at least about 90% homology to the amino acid sequence of SEQ ID NO: 79;
- (l) the HVR-L1 comprises the amino acid sequence of SEQ ID NO: 114 or an amino acid sequence with at least about 90% homology to the amino acid sequence of SEQ ID NO: 114, the HVR-L2 comprises the amino acid sequence of SEQ ID NO: 127 or an amino acid sequence with at least about 90% homology to the amino acid sequence of SEQ ID NO: 127, the HVR-L3 comprises the amino acid sequence of SEQ ID NO: 153 or an amino acid sequence with at least about 90% homology to the amino acid sequence of SEQ ID NO: 153, the HVR-H1 comprises the amino acid sequence of SEQ ID NO: 20 or an amino acid sequence with at least about 90% homology to the amino acid sequence of SEQ ID NO: 20, the HVR-H2 comprises the amino acid sequence of SEQ ID NO: 49 or an amino acid sequence with at least about 90% homology to the amino acid sequence of SEQ ID NO: 49, and the HVR-H3 comprises the amino acid sequence of SEQ ID NO: 70 or an amino acid sequence with at least about 90% homology to the amino acid sequence of SEQ ID NO: 70;
- (m) the HVR-L1 comprises the amino acid sequence of SEQ ID NO: 115 or an amino acid sequence with at least about 90% homology to the amino acid sequence of SEQ ID NO: 115, the HVR-L2 comprises the amino acid sequence of SEQ ID NO: 128 or an amino acid sequence with at least about 90% homology to the amino acid sequence of SEQ ID NO: 128, the HVR-L3 comprises the amino acid sequence of SEQ ID NO: 154 or an amino acid sequence with at least about 90% homology to the amino acid sequence of SEQ ID NO: 154, the HVR-H1 comprises the amino acid sequence of SEQ ID NO: 21 or

an amino acid sequence with at least about 90% homology to the amino acid sequence of SEQ ID NO: 21, the HVR-H2 comprises the amino acid sequence of SEQ ID NO: 50 or an amino acid sequence with at least about 90% homology to the amino acid sequence of SEQ ID NO: 50, and the HVR-H3 comprises the amino acid sequence of SEQ ID NO: 71 or an amino acid sequence with at least about 90% homology to the amino acid sequence of SEQ ID NO: 71; or

- (n) the HVR-L1 comprises the amino acid sequence of SEQ ID NO: 111 or an amino acid sequence with at least about 90% homology to the amino acid sequence of SEQ ID NO: 111, the HVR-L2 comprises the amino acid sequence of SEQ ID NO: 133 or an amino acid sequence with at least about 90% homology to the amino acid sequence of SEQ ID NO: 133, the HVR-L3 comprises the amino acid sequence of SEQ ID NO: 161 or an amino acid sequence with at least about 90% homology to the amino acid sequence of SEQ ID NO: 161, the HVR-H1 comprises the amino acid sequence of SEQ ID NO: 26 or an amino acid sequence with at least about 90% homology to the amino acid sequence of SEQ ID NO: 26, the HVR-H2 comprises the amino acid sequence of SEQ ID NO: 51 or an amino acid sequence with at least about 90% homology to the amino acid sequence of SEQ ID NO: 51, and the HVR-H3 comprises the amino acid sequence of SEQ ID NO: 77 or an amino acid sequence with at least about 90% homology to the amino acid sequence of SEQ ID NO: 77.

13. The anti-Siglec-5 antibody of any one of claims 1-11, wherein the anti-Siglec-5 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: 194, and the heavy chain variable domain comprises the amino acid sequence of SEQ ID NO: 174;
- (b) the light chain variable domain comprises the amino acid sequence of SEQ ID NO: 195, and the heavy chain variable domain comprises the amino acid sequence of SEQ ID NO: 175;
- (c) the light chain variable domain comprises the amino acid sequence of SEQ ID NO: 196, and the heavy chain variable domain comprises the amino acid sequence of SEQ ID NO: 176;
- (d) 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: 177;
- (e) the light chain variable domain comprises the amino acid sequence of SEQ ID NO: 198, and the heavy chain variable domain comprises the amino acid sequence of SEQ ID NO: 178;
- (f) the light chain variable domain comprises the amino acid sequence of SEQ ID NO: 199, and the heavy chain variable domain comprises the amino acid sequence of SEQ ID NO: 179;
- (g) the light chain variable domain comprises the amino acid sequence of SEQ ID NO: 200, and the heavy chain variable domain comprises the amino acid sequence of SEQ ID NO: 174;
- (h) the light chain variable domain comprises the amino acid sequence of SEQ ID NO: 201, and the heavy

(z) the light chain variable domain comprises the amino acid sequence of SEQ ID NO: 209, and the heavy

chain variable domain comprises the amino acid sequence of SEQ ID NO: 191;

(aa) the light chain variable domain comprises the amino acid sequence of SEQ ID NO: 210 , and the heavy chain variable domain comprises the amino acid sequence of SEQ ID NO: 191;

(bb) the light chain variable domain comprises the amino acid sequence of SEQ ID NO: 211, and the heavy chain variable domain comprises the amino acid sequence of SEQ ID NO: 191;

(cc) the light chain variable domain comprises the amino acid sequence of SEQ ID NO: 209, and the heavy chain variable domain comprises the amino acid sequence of SEQ ID NO: 192;

(dd) the light chain variable domain comprises the amino acid sequence of SEQ ID NO: 210, and the heavy chain variable domain comprises the amino acid sequence of SEQ ID NO: 192;

(ee) the light chain variable domain comprises the amino acid sequence of SEQ ID NO: 211, and the heavy chain variable domain comprises the amino acid sequence of SEQ ID NO: 192;

(ff) the light chain variable domain comprises the amino acid sequence of SEQ ID NO: 209, and the heavy chain variable domain comprises the amino acid sequence of SEQ ID NO: 193;

(gg) the light chain variable domain comprises the amino acid sequence of SEQ ID NO: 210, and the heavy chain variable domain comprises the amino acid sequence of SEQ ID NO: 193; or

(hh) the light chain variable domain comprises the amino acid sequence of SEQ ID NO: 211, and the heavy chain variable domain comprises the amino acid sequence of SEQ ID NO: 193.

14. An isolated monoclonal anti-Siglec-5 antibody, wherein the anti-Siglec-5 antibody competes with one or more antibodies selected from the group consisting of S5-172, S5-174, S5-175, S5-176, S5-182, S5-183, S5-190, S5-202, S5-G-03, S5-G-07, S5-G-10, S5-172-H1, S5-172-H2, S5-172-H3, S5-172-H4, S5-172-H5, S5-172-H6, S5-174-H1, S5-174-H2, S5-174-H3, S5-174-H4, S5-174-H5, S5-174-H6, S5-174-H7, S5-174-H8, S5-G-03-H1, S5-G-03-H2, S5-G-03-H3, S5-G-03-H4, S5-G-03-H5, S5-G-03-H6, S5-G-03-H7, S5-G-03-H8, and S5-G-03-H9, and any combination thereof for binding to Siglec-5.

15. An isolated monoclonal anti-Siglec-5 antibody which binds essentially the same Siglec-5 epitope as a monoclonal antibody selected from the group consisting of: S5-172, S5-174, S5-175, S5-176, S5-182, S5-183, S5-190, S5-202, S5-G-03, S5-G-07, S5-G-10, S5-172-H1, S5-172-H2, S5-172-H3, S5-172-H4, S5-172-H5, S5-172-H6, S5-174-H1, S5-174-H2, S5-174-H3, S5-174-H4, S5-174-H5, S5-174-H6, S5-174-H7, S5-174-H8, S5-G-03-H1, S5-G-03-H2, S5-G-03-H3, S5-G-03-H4, S5-G-03-H5, S5-G-03-H6, S5-G-03-H7, S5-G-03-H8, and S5-G-03-H9.

16. The anti-Siglec-5 antibody of any one of claims 1-15, wherein the antibody is of the IgG class, the IgM class, or the IgA class.

17. The anti-Siglec-5 antibody of claim 16, wherein the anti-Siglec-5 antibody has an IgG1, IgG2, IgG3, or IgG4 isotype.

18. The anti-Siglec-5 antibody of claim 17, wherein the antibody binds an inhibitory Fc receptor.

19. The anti-Siglec-5 antibody of claim 18, wherein the inhibitory Fc receptor is inhibitory Fc-gamma receptor IIB (FcγIIB).
20. The anti-Siglec-5 antibody of claim 19, wherein:
 - (a) the anti-Siglec-5 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, E430G, V263L, V266L, V273C, V273E, V273F, V273L, V273M, V273S, V273Y, V305K, V305W, 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-5 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 NTKVDKTVERKCCVECPPCP (SEQ ID NO: 218), 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-5 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, C127S, E430G, and any combination thereof, wherein the numbering of the residues is according to EU numbering;
 - (d) the anti-Siglec-5 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-5 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.

21. The anti-Siglec-5 antibody of claim 20, wherein:

- (a) the anti-Siglec-5 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 numbering;
- (b) the anti-Siglec-5 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, C127S, E430G, and any combination thereof, wherein the numbering of the residues is according to EU numbering; or
- (c) the anti-Siglec-5 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 numbering.

22. The anti-Siglec-5 antibody of claim 21, wherein:

- (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 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 numbering; or
- (c) the Fc region further comprises a S228P amino acid substitution according to EU numbering.

23. The anti-Siglec-5 antibody of any one of claims 1-17, wherein the antibody has an IgG4 isotype.

24. The anti-Siglec-5 antibody of claim 23, wherein the anti-Siglec-5 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 numbering.

25. The anti-Siglec-5 antibody of any one of claims 1-24, wherein the Siglec-5 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.

26. The anti-Siglec-5 antibody of any one of claims 1- 25, wherein the anti-Siglec-5 antibody binds specifically to a human Siglec-5 protein.

27. The anti-Siglec-5 antibody of any one of claims 1-26, wherein the anti-Siglec-5 antibody is an antibody fragment that binds to one or more human proteins selected from the group consisting of human Siglec-5, a naturally occurring variant of human Siglec-5, a wild-type protein, and a disease variant of human Siglec-5.

28. The anti-Siglec-5 antibody of claim 27, wherein the antibody fragment is an Fab, Fab', Fab'-SH, F(ab')₂, Fv, or scFv fragment.

29. The anti-Siglec-5 antibody of any one of claims 1-28, wherein the anti-Siglec-5 antibody is a murine antibody.

30. The anti-Siglec-5 antibody of any one of claims 1-28, wherein the anti-Siglec-5 antibody is a humanized antibody, a bispecific antibody, a multivalent antibody, a conjugated antibody, or a chimeric antibody.

31. The anti-Siglec-5 antibody of any one of claims 1-28, wherein the anti-Siglec-5 antibody is a bispecific antibody recognizing a first antigen and a second antigen.

32. The anti-Siglec-5 antibody of claim 31, wherein the first antigen is Siglec-5 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) (SEQ ID NO: 225) 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, 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;

(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.

33. The anti-Siglec-5 antibody of any one of claims 1-30, wherein the anti-Siglec-5 antibody is a conjugated antibody.

34. The anti-Siglec-5 antibody of claim 33, wherein the anti-Siglec-5 antibody is conjugated to a detectable marker, a toxin, or a therapeutic agent.

35. The anti-Siglec-5 antibody of claim 34, wherein the anti-Siglec-5 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.

36. The anti-Siglec-5 antibody of any one of claims 1-35, wherein the anti-Siglec-5 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-6, Siglec-7, Siglec-9, Siglec-10, Siglec-11, phosphatidylserine, disease-causing nucleic acids, antisense GGCCCC (G2C4) (SEQ ID NO: 225) repeat-expansion RNA, and any combination thereof.

37. The anti-Siglec-5 antibody of any one of the preceding claims, wherein the anti-Siglec-5 antibody has dissociation constant (K_D) for human Siglec-5 and mammalian Siglec-5 that ranges from about 0.42 nM to about 79 nM, wherein the K_D is determined at a temperature of approximately 25°C.

38. The anti-Siglec-5 antibody of any one of the preceding claims, wherein the anti-Siglec-5 antibody has dissociation constant (K_D) for human Siglec-5 that ranges from about 79 nM to about 61 nM, from about 15 nM to about 5.3 nM, or from about 1.7 nM to about 0.42 nM, wherein the K_D is determined at a temperature of approximately 25°C.

39. An isolated nucleic acid comprising a nucleic acid sequence encoding the anti-Siglec-5 antibody of any one of the preceding claims.

40. A vector comprising the nucleic acid of claim 39.

41. An isolated host cell comprising the vector of claim 40.

42. A method of producing an anti-Siglec-5 antibody, comprising culturing the host cell of claim 41 so that the anti-Siglec-5 antibody is produced.

43. The method of claim 42, further comprising recovering the anti-Siglec-5 antibody produced by the host cell.

44. An isolated anti-Siglec-5 antibody produced by the method of claim 42 or claim 43.

45. A pharmaceutical composition comprising the anti-Siglec-5 antibody of any one of claims 1-38, and a pharmaceutically acceptable carrier.

46. The use of the anti-Siglec-5 antibody of any one of claims 1-38 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, in an individual in need thereof.

47. The use of the anti-Siglec-5 antibody of any one of claims 1-38 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.
48. The use of the anti-Siglec-5 antibody of any one of claims 1-38 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.
49. The use of the anti-Siglec-5 antibody of any one of claims 1-38 in the manufacture of a medicament for decreasing cellular levels of Siglec-5 on one or more cells, in an individual in need thereof.
50. The use of the anti-Siglec-5 antibody of any one of claims 1-38 in the manufacture of a medicament for inducing reactive oxygen species (ROS) production in one or more neutrophils, in an individual in need thereof.
51. The use of the anti-Siglec-5 antibody of any one of claims 1-38 in the manufacture of a medicament for inducing neutrophil extracellular trap (NET) formation in one or more neutrophils in an individual in need thereof.
52. The use of the anti-Siglec-5 antibody of any one of claims 1-38 in the manufacture of a medicament for inducing neutrophil activation in one or more neutrophils, in an individual in need thereof.
53. The use of the anti-Siglec-5 antibody of any one of claims 1-38 in the manufacture of a medicament for relieving one or more immunosuppressed neutrophils, in an individual in need thereof.
54. The use of the anti-Siglec-5 antibody of any one of claims 1-38 in the manufacture of a medicament for increasing phagocytosis activity in macrophages, in an individual in need thereof.