

ANTI-TIGIT ANTIBODIES

CROSS-REFERENCE TO RELATED APPLICATIONS

[0001] This application claims the benefit of priority of US Provisional Application No. 62/722,063, filed August 23, 2018; US Provisional Application No. 62/734,130, filed September 20, 2018; and US Provisional Application No. 62/822,674, filed March 22, 2019; each of which is incorporated by reference herein in its entirety for any purpose.

FIELD

[0002] Provided herein are antibodies that bind to human TIGIT (T-cell immunoreceptor with Ig and ITIM domains), and uses thereof.

BACKGROUND

[0003] TIGIT (“T-cell immunoreceptor with Ig and ITIM domains”) is an immune receptor that is expressed on subsets of T cells, such as activated, memory, and regulatory T cells and natural killer (NK) cells. TIGIT is a member of the CD28 family within the Ig superfamily of proteins, and serves as a co-inhibitory molecule that limits T cell proliferation and activation and NK cell function. TIGIT mediates its immunosuppressive effect by competing with CD226 (also known as DNAX Accessory Molecule-1, or “DNAM-1”) for the same set of ligands: CD155 (also known as poliovirus receptor or “PVR”) and CD112 (also known as poliovirus receptor-related 2 or “PVRL2”). *See*, Levin et al., *Eur. J. Immunol.*, 2011, 41:902-915. Because the affinity of CD155 for TIGIT is higher than its affinity for CD226, in the presence of TIGIT CD226 signaling is inhibited, thereby limiting T cell proliferation and activation.

[0004] In patients with melanoma, TIGIT expression is upregulated on tumor antigen (TA)-specific CD8⁺ T cells and CD8⁺ tumor-infiltrating lymphocytes (TILs). Blockade of TIGIT in the presence of TIGIT ligand (CD155)-expressing cells increased the proliferation, cytokine production, and degranulation of both TA-specific CD8⁺ T cells and CD8⁺ TILs *See*, Chauvin et al., *J Clin Invest.*, 2015, 125:2046-2058. Thus, TIGIT represents a potential therapeutic target for stimulating anti-tumor T cell responses in patients, although there remains a need for improved methods of blocking TIGIT and promoting anti-tumor responses.

BRIEF SUMMARY

[0004a] In one aspect, provided herein is a composition comprising antibodies that bind to human TIGIT (T-cell immunoreceptor with Ig and ITIM domains), wherein at least 90%, at least

Embodiment 12. The composition of embodiment 10 or embodiment 11, wherein amino acid positions 81 and 82 are Phe81 and Lys82.

Embodiment 13. The composition of any one of embodiments 1 to 12, wherein the antibodies bind to an epitope on human TIGIT that comprises one or both of amino acid positions 81 and 82.

Embodiment 14. A composition comprising isolated antibodies that binds to human TIGIT, wherein the antibodies when bound to human TIGIT bind one or both of amino acid positions 81 and 82, and wherein at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% of the antibodies in the composition are afucosylated.

Embodiment 15. The composition of embodiment 14, wherein the antibodies bind both of amino acid positions 81 and 82.

Embodiment 16. The composition of embodiment 14 or embodiment 15, wherein amino acid positions 81 and 82 are Phe81 and Lys82.

Embodiment 17. A composition comprising isolated antibodies that binds to human TIGIT, wherein the antibodies bind to an epitope on human TIGIT that comprises one or both of amino acid positions 81 and 82, and wherein at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% of the antibodies in the composition are afucosylated.

(f) a light chain CDR3 sequence comprising the amino acid sequence of SEQ ID NO:71.

Embodiment 31. The composition of embodiment 29 or embodiment 30, wherein each of the antibodies comprises a heavy chain CDR1, CDR2, and CDR3 and a light chain CDR1, CDR, and CDR3 comprising the sequences of:

- (a) SEQ ID NOs: 4, 6, 8, 13, 15, and 17, respectively; or
- (b) SEQ ID NOs: 22, 24, 26, 31, 33, and 35, respectively; or
- (c) SEQ ID NOs: 40, 42, 44, 49, 51, and 53, respectively; or
- (d) SEQ ID NOs: 58, 60, 62, 67, 69, and 71, respectively; or
- (e) SEQ ID NOs: 283, 285, 62, 287, 288, and 71, respectively; or
- (f) SEQ ID NOs: 284, 60, 286, 67, 69, and 71, respectively; or
- (g) SEQ ID NOs: 76, 78, 80, 85, 87, and 89, respectively; or
- (h) SEQ ID NOs: 94, 96, 98, 103, 105, and 107, respectively; or
- (i) SEQ ID NOs: 112, 114, 116, 121, 123, and 125, respectively; or
- (j) SEQ ID NOs: 130, 132, 134, 139, 141, and 143, respectively; or
- (k) SEQ ID NOs: 148, 150, 152, 157, 159, and 161, respectively; or
- (l) SEQ ID NOs: 166, 168, 170, 175, 177, and 179, respectively; or
- (m) SEQ ID NOs: 184, 186, 188, 193, 195, and 197, respectively; or
- (n) SEQ ID NOs: 202, 204, 206, 211, 213, and 215, respectively; or
- (o) SEQ ID NOs: 221, 222, 223, 13, 15, and 17, respectively; or
- (p) SEQ ID NOs: 224, 225, 62, 67, 69, and 71, respectively; or
- (q) SEQ ID NOs: 293, 297, 62, 287, 288, and 71, respectively; or
- (r) SEQ ID NOs: 294, 225, 286, 67, 69, and 71, respectively; or
- (s) SEQ ID NOs: 226, 227, 228, 67, 69, and 71, respectively; or
- (t) SEQ ID NOs: 289, 291, 228, 287, 288, and 71, respectively; or
- (u) SEQ ID NOs: 290, 227, 292, 67, 69, and 71, respectively; or
- (v) SEQ ID NOs: 224, 229, 230, 67, 69, and 71, respectively; or
- (w) SEQ ID NOs: 293, 295, 230, 287, 288, and 71, respectively; or
- (x) SEQ ID NOs: 294, 229, 296, 67, 69, and 71, respectively; or
- (y) SEQ ID NOs: 224, 227, 230, 67, 69, and 71, respectively; or
- (z) SEQ ID NOs: 293, 291, 230, 287, 288, and 71, respectively; or
- (aa) SEQ ID NOs: 294, 227, 296, 67, 69, and 71, respectively; or
- (bb) SEQ ID NOs: 231, 232, 235, 103, 105, and 107, respectively; or
- (cc) SEQ ID NOs: 233, 234, 236, 103, 105, and 107, respectively; or

Embodiment 63. The composition of any one of embodiments 1 to 62, wherein the antibodies are bispecific antibodies.

Embodiment 64. The composition of any one of embodiments 1 to 63, wherein the antibodies are antibody-drug conjugates.

Embodiment 65. An antibody that binds to human TIGIT (T-cell immunoreceptor with Ig and ITIM domains), wherein the antibody has a binding affinity (K_D) for human TIGIT of less than 5 nM, and wherein the antibody is afucosylated.

Embodiment 66. The antibody of embodiment 65, wherein the antibody has a K_D for human TIGIT of less than 1 nM.

Embodiment 67. The antibody of embodiment 66, wherein antibody has a K_D for human TIGIT of less than 100 pM.

Embodiment 68. The antibody of any one of embodiments 65 to 67, wherein antibody exhibits cross-reactivity with cynomolgus monkey TIGIT and/or mouse TIGIT.

Embodiment 69. The antibody of embodiment 68, wherein the antibody exhibits cross-reactivity with both cynomolgus monkey TIGIT and mouse TIGIT.

Embodiment 70. The antibody of any one of embodiments 65 to 69, wherein the antibody blocks binding of CD155 to TIGIT.

Embodiment 71. The antibody of any one of embodiments 65 to 70, wherein the antibody blocks binding of CD112 to TIGIT.

Embodiment 72. The antibody of any one of embodiments 65 to 71, wherein the antibody blocks binding of both CD155 and CD112 to TIGIT.

Embodiment 73. The antibody of any one of embodiments 65 to 72, wherein the antibody competes for binding to human TIGIT with an antibody comprising a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 55 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 64.

Embodiment 74. The antibody of any one of embodiments 65 to 73, wherein when bound to human TIGIT binds one or both of amino acid positions 81 and 82.

Embodiment 75. The antibody of embodiment 74, wherein the antibody binds both of amino acid positions 81 and 82.

Embodiment 76. The antibody of embodiment 74 or embodiment 75, wherein amino acid positions 81 and 82 are Phe81 and Lys82.

Embodiment 77. The antibody of any one of embodiments 65 to 76, wherein the antibody binds to an epitope on human TIGIT that comprises one or both of amino acid positions 81 and 82.

Embodiment 78. An antibody that binds to human TIGIT, wherein when bound to human TIGIT binds one or both of amino acid positions 81 and 82, and wherein the antibody is afucosylated.

Embodiment 79. The antibody of embodiment 78, wherein the antibody binds both of amino acid positions 81 and 82.

Embodiment 80. The antibody of embodiment 78 or embodiment 79, wherein amino acid positions 81 and 82 are Phe81 and Lys82.

Embodiment 81. An antibody that binds to human TIGIT, wherein the antibody binds to an epitope on human TIGIT that comprises one or both of amino acid positions 81 and 82, and wherein the antibody is afucosylated.

Embodiment 82. The antibody of embodiment 77 or embodiment 81, wherein the epitope comprises Phe at position 81.

Embodiment 83. The antibody of any one of embodiments 77, 81, and 82, wherein the epitope comprises Lys or Ser at position 82.

Embodiment 122. The antibody of any one of embodiments 65 to 121, wherein the antibody is monoclonal.

Embodiment 123. The antibody of any one of embodiments 65 to 122, wherein the antibody is a fully human antibody.

Embodiment 124. The antibody of any one of embodiments 65 to 123, wherein the antibody is a chimeric antibody.

Embodiment 125. The antibody of any one of embodiments 65 to 92 and 109 to 124, wherein the antibody is humanized.

Embodiment 126. The antibody of any one of embodiments 65 to 125, wherein the antibody is an antibody fragment.

Embodiment 127. The antibody of embodiment 126, wherein the antibody fragment is a Fab, a Fab', a F(ab')₂, a scFv, or a diabody.

Embodiment 128. The antibody of any one of embodiments 65 to 127, wherein the antibody is a bispecific antibody.

Embodiment 129. The antibody of any one of embodiments 65 to 128, wherein the antibody is an antibody-drug conjugate.

Embodiment 130. A pharmaceutical formulation comprising the composition of any one of embodiments 1 to 64 or the antibody of any one of embodiments 65 to 129 and a pharmaceutically acceptable carrier.

Embodiment 131. An isolated polynucleotide that encodes (i) the heavy chain of the antibody of any one of embodiments 106 to 108; (ii) the light chain of the antibody of any one of embodiments 106 to 108; or (iii) the heavy chain and the light chain of the antibody of any one of embodiments 106 to 108.

Embodiment 132. The isolated polynucleotide of embodiment 131, wherein the polynucleotide comprises (i) a nucleotide sequence selected from SEQ ID NOs: 259, 261, 263, 265, 267, 269, and 271; or (ii) a nucleotide sequence of SEQ ID NO: 273; or (iii) a nucleotide sequence selected from SEQ ID NOs: 259, 261, 263, 265, 267, 269, and 271, and a nucleotide sequence of SEQ ID NO: 273.

embodiments 1 to 64, the antibody of any one of embodiments 65 to 129, or the pharmaceutical composition of embodiment 130.

Embodiment 170. The method of embodiment 169, wherein the cancer is a cancer that is enriched for expression of CD112 or CD155.

Embodiment 171. The method of embodiment 169 or embodiment 170, wherein the cancer is a cancer that is enriched for T cells or natural killer (NK) cells that express TIGIT.

Embodiment 172. The method of any one of embodiments 169 to 171, wherein the cancer is bladder cancer, breast cancer, uterine cancer, cervical cancer, ovarian cancer, prostate cancer, testicular cancer, esophageal cancer, gastrointestinal cancer, gastric cancer, pancreatic cancer, colorectal cancer, colon cancer, kidney cancer, clear cell renal carcinoma, head and neck cancer, lung cancer, lung adenocarcinoma, stomach cancer, germ cell cancer, bone cancer, liver cancer, thyroid cancer, skin cancer, melanoma, neoplasm of the central nervous system, mesothelioma, lymphoma, leukemia, chronic lymphocytic leukemia, diffuse large B cell lymphoma, follicular lymphoma, Hodgkin lymphoma, myeloma, or sarcoma.

Embodiment 173. The method of embodiment 172, wherein the cancer is lymphoma, leukemia, chronic lymphocytic leukemia, diffuse large B cell lymphoma, follicular lymphoma, or Hodgkin lymphoma.

Embodiment 174. The method of any one of embodiments 169 to 173, further comprising administering to the subject a therapeutically effective amount of an additional therapeutic agent.

Embodiment 175. The method of embodiment 174, wherein the additional therapeutic is an anti-cancer agent.

Embodiment 176. The method of embodiment 174 or embodiment 175, wherein the additional therapeutic agent is an antibody.

erlotinib, gefitinib, imatinib, vemurafenib, or vismodegib), a nucleoside analog or precursor analog (*e.g.*, azacitidine, azathioprine, capecitabine, cytarabine, fluorouracil, gemcitabine, hydroxyurea, mercaptopurine, methotrexate, or thioguanine), a peptide antibiotic (*e.g.*, actinomycin or bleomycin), a platinum-based agent (*e.g.*, cisplatin, oxaloplatin, or carboplatin), or a plant alkaloid (*e.g.*, vincristine, vinblastine, vinorelbine, vindesine, podophyllotoxin, paclitaxel, or docetaxel), galardin, thalidomide, lenalidomide, and pomalidomide.

Embodiment 183. The method of any one of embodiments 174 to 182, wherein the composition, the antibody, or the pharmaceutical composition is administered concurrently with the additional therapeutic agent.

Embodiment 184. The method of any one of embodiments 174 to 183, wherein the composition, the antibody, or the pharmaceutical composition is administered sequentially to the additional therapeutic agent.

BRIEF DESCRIPTION OF THE DRAWINGS

[0005] FIG. 1. Binding of 65 anti-TIGIT antibody clones and an irrelevant isotype control antibody to HEK 293 cells engineered to express human TIGIT (top panel), cynomolgus monkey TIGIT (middle panel), and mouse TIGIT (bottom panel).

[0006] FIG. 2. Binding of 65 anti-TIGIT antibody clones and an irrelevant isotype control antibody to primary human T cells (top panel), cynomolgus monkey T cells (middle panel), and mouse T cells (bottom panel). For the bottom panel, 35 of 65 clones were evaluated. Of the 35 clones evaluated, 5 of the 35 did not bind mTIGIT-Fc protein (clones 20, 27, 55, 56, and 60), as indicated by the light green bars.

[0007] FIG. 3A-3D. (A-C) Binding titration values of eight anti-TIGIT antibody clones (clones 2, 5, 13, 16, 17, 20, 25, and 54) to human (A), mouse (B), and cynomolgus monkey (C) TIGIT expressed on HEK 293 cells. Results are shown for singlicate wells. (D) EC₅₀ values of eight anti-TIGIT antibody clones (clones 2, 5, 13, 16, 17, 20, 25, and 54) to human, mouse, and cynomolgus monkey TIGIT expressed on HEK 293 cells.

[0008] FIG. 4. Binding titration of anti-TIGIT antibody clones 13 and 25 to activated mouse splenic T cells. Results are shown for singlicate wells. Clone 13 had an EC₅₀ of 0.24 µg/mL. Clone 25 had an EC₅₀ of 2.28 µg/mL.

Table E: Clone 13D alternative CDR definitions

CDR definition	Heavy chain (HC) CDR1	SEQ ID NO	HC CDR2	SEQ ID NO	HC CDR3	SEQ ID NO
Composite	GTFLSSAIS	224	SIIPYFGKANYAQKFQG	227	ARGPSEVKGILGYVWFDP	230
IMGT	GGTFLSSA	293	IIPYFGKA	291	ARGPSEVKGILGYVWFDP	230
Kabat	SSAIS	294	SIIPYFGKANYAQKFQG	227	GPSEVKGILGYVWFDP	296
CDR definition	Light chain (LC) CDR1	SEQ ID NO	LC CDR2	SEQ ID NO	LC CDR3	SEQ ID NO
Composite	RSSQSLHSHNGYNYLD	67	LGSNRAS	69	MQARRIPIT	71
IMGT	QSLHSHNGYNY	287	LGS	288	MQARRIPIT	71
Kabat	RSSQSLHSHNGYNYLD	67	LGSNRAS	69	MQARRIPIT	71

[00100] In some embodiments, an anti-TIGIT antibody comprises one or more (e.g., one, two, three, four, five, or six) of:

a heavy chain CDR1 sequence comprising an amino acid sequence selected from SEQ ID NO:58, SEQ ID NO:283, SEQ ID NO:284, SEQ ID NO:224, SEQ ID NO:293, SEQ ID NO:294, SEQ ID NO:226, SEQ ID NO:289, and SEQ ID NO:290;

a heavy chain CDR2 sequence comprising an amino acid sequence selected from SEQ ID NO:60, SEQ ID NO:285, SEQ ID NO:225, SEQ ID NO:297, SEQ ID NO:227, SEQ ID NO:291, SEQ ID NO:229, and SEQ ID NO:295;

a heavy chain CDR3 sequence comprising an amino acid sequence selected from SEQ ID NO:62, SEQ ID NO:286, SEQ ID NO:228, SEQ ID NO:292, SEQ ID NO:230, and SEQ ID NO:296;

a light chain CDR1 sequence comprising an amino acid sequence selected from SEQ ID NO:67 and SEQ ID NO:287;

a light chain CDR2 sequence comprising an amino acid sequence selected from SEQ ID NO:69 and SEQ ID NO:288; and/or

a light chain CDR3 sequence comprising the amino acid sequence of SEQ ID NO:71.

[00101] In some embodiments, an anti-TIGIT antibody comprises a heavy chain CDR1 sequence comprising the amino acid sequence of any of SEQ ID NO:58, SEQ ID NO:283, SEQ ID NO:284, SEQ ID NO:224, SEQ ID NO:293, SEQ ID NO:294, SEQ ID NO:226, SEQ ID NO:289, or SEQ ID NO:290; a heavy chain CDR2 sequence comprising the amino acid sequence of any of SEQ ID NO:60, SEQ ID NO:285, SEQ ID NO:225, SEQ ID NO:297, SEQ ID NO:227, SEQ ID NO:291, SEQ ID NO:229, or SEQ ID NO:295; a heavy chain CDR3 sequence comprising the amino acid sequence of any of SEQ ID NO:62, SEQ ID NO:286, SEQ

[00106] In some embodiments, an anti-TIGIT antibody comprises: (i) a heavy chain CDR1 sequence comprising the amino acid sequence of SEQ ID NO:226, SEQ ID NO:289, or SEQ ID NO:290; (ii) a heavy chain CDR2 sequence comprising the amino acid sequence of SEQ ID NO:227 or SEQ ID NO:291; (iii) a heavy chain CDR3 sequence comprising the amino acid sequence of SEQ ID NO:228 or SEQ ID NO:292; (iv) a light chain CDR1 sequence comprising the amino acid sequence of SEQ ID NO:67 or SEQ ID NO:287; (v) a light chain CDR2 sequence comprising the amino acid sequence of SEQ ID NO:69 or SEQ ID NO:288; and (vi) a light chain CDR3 sequence comprising the amino acid sequence of SEQ ID NO:71.

[00107] In some embodiments, an anti-TIGIT antibody comprises: (i) a heavy chain CDR1 sequence comprising the amino acid sequence of SEQ ID NO:224, SEQ ID NO:293, or SEQ ID NO:294; (ii) a heavy chain CDR2 sequence comprising the amino acid sequence of SEQ ID NO:229 or SEQ ID NO:295; (iii) a heavy chain CDR3 sequence comprising the amino acid sequence of SEQ ID NO:230 or SEQ ID NO:296; (iv) a light chain CDR1 sequence comprising the amino acid sequence of SEQ ID NO:67 or SEQ ID NO:287; (v) a light chain CDR2 sequence comprising the amino acid sequence of SEQ ID NO:69 or SEQ ID NO:288; and (vi) a light chain CDR3 sequence comprising the amino acid sequence of SEQ ID NO:71.

[00108] In some embodiments, an anti-TIGIT antibody comprises: (i) a heavy chain CDR1 sequence comprising the amino acid sequence of SEQ ID NO:224, SEQ ID NO:293, or SEQ ID NO:294; (ii) a heavy chain CDR2 sequence comprising the amino acid sequence of SEQ ID NO:227 or SEQ ID NO:291; (iii) a heavy chain CDR3 sequence comprising the amino acid sequence of SEQ ID NO:230 or SEQ ID NO:296; (iv) a light chain CDR1 sequence comprising the amino acid sequence of SEQ ID NO:67 or SEQ ID NO:287; (v) a light chain CDR2 sequence comprising the amino acid sequence of SEQ ID NO:69 or SEQ ID NO:288; and (vi) a light chain CDR3 sequence comprising the amino acid sequence of SEQ ID NO:71.

[00109] In some embodiments, an anti-TIGIT antibody comprises one or more (e.g., one, two, three, four, five, or six) of:

a heavy chain CDR1 sequence comprising the amino acid sequence of any of SEQ ID NO:4, SEQ ID NO:22, SEQ ID NO:40, SEQ ID NO:58, SEQ ID NO:76, SEQ ID NO:94, SEQ ID NO:112, SEQ ID NO:130, SEQ ID NO:148, SEQ ID NO:166, SEQ ID NO:184, SEQ ID NO:202, SEQ ID NO:221, SEQ ID NO:224, SEQ ID NO:226, SEQ ID NO:231, SEQ ID NO:233, SEQ ID NO:239, SEQ ID NO:243, SEQ ID NO:283, SEQ ID NO:284, SEQ ID NO:293, SEQ ID NO:294, SEQ ID NO:289, or SEQ ID NO:290;

a heavy chain CDR2 sequence comprising the amino acid sequence of any of SEQ ID NO:6, SEQ ID NO:24, SEQ ID NO:42, SEQ ID NO:60, SEQ ID NO:78, SEQ ID NO:96, SEQ ID NO:114, SEQ ID NO:132, SEQ ID NO:150, SEQ ID NO:168, SEQ ID NO:186,

CLAIMS

1. A composition comprising antibodies that bind to human TIGIT (T-cell immunoreceptor with Ig and ITIM domains), wherein at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% of the antibodies in the composition are afucosylated, wherein each of the antibodies comprises a heavy chain CDR1, CDR2, and CDR3 and a light chain CDR1, CDR, and CDR3 comprising the sequences of:

- (a) SEQ ID NOs: 58, 60, 62, 67, 69, and 71, respectively; or
- (b) SEQ ID NOs: 283, 285, 62, 287, 288, and 71, respectively; or
- (c) SEQ ID NOs: 284, 60, 286, 67, 69, and 71, respectively; or
- (d) SEQ ID NOs: 224, 225, 62, 67, 69, and 71, respectively; or
- (e) SEQ ID NOs: 293, 297, 62, 287, 288, and 71, respectively; or
- (f) SEQ ID NOs: 294, 225, 286, 67, 69, and 71, respectively; or
- (g) SEQ ID NOs: 226, 227, 228, 67, 69, and 71, respectively; or
- (h) SEQ ID NOs: 289, 291, 228, 287, 288, and 71, respectively; or
- (i) SEQ ID NOs: 290, 227, 292, 67, 69, and 71, respectively; or
- (j) SEQ ID NOs: 224, 229, 230, 67, 69, and 71, respectively; or
- (k) SEQ ID NOs: 293, 295, 230, 287, 288, and 71, respectively; or
- (l) SEQ ID NOs: 294, 229, 296, 67, 69, and 71, respectively; or
- (m) SEQ ID NOs: 224, 227, 230, 67, 69, and 71, respectively; or
- (n) SEQ ID NOs: 293, 291, 230, 287, 288, and 71, respectively; or
- (o) SEQ ID NOs: 294, 227, 296, 67, 69, and 71, respectively.

2. An antibody that binds to human TIGIT (T-cell immunoreceptor with Ig and ITIM domains), wherein the antibody is afucosylated, and wherein the antibody comprises a heavy chain CDR1, CDR2, and CDR3 and a light chain CDR1, CDR, and CDR3 comprising the sequences of:

- (a) SEQ ID NOs: 58, 60, 62, 67, 69, and 71, respectively; or
- (b) SEQ ID NOs: 283, 285, 62, 287, 288, and 71, respectively; or
- (c) SEQ ID NOs: 284, 60, 286, 67, 69, and 71, respectively; or
- (d) SEQ ID NOs: 224, 225, 62, 67, 69, and 71, respectively; or
- (e) SEQ ID NOs: 293, 297, 62, 287, 288, and 71, respectively; or
- (f) SEQ ID NOs: 294, 225, 286, 67, 69, and 71, respectively; or
- (g) SEQ ID NOs: 226, 227, 228, 67, 69, and 71, respectively; or
- (h) SEQ ID NOs: 289, 291, 228, 287, 288, and 71, respectively; or

- (i) SEQ ID NOs: 290, 227, 292, 67, 69, and 71, respectively; or
- (j) SEQ ID NOs: 224, 229, 230, 67, 69, and 71, respectively; or
- (k) SEQ ID NOs: 293, 295, 230, 287, 288, and 71, respectively; or
- (l) SEQ ID NOs: 294, 229, 296, 67, 69, and 71, respectively; or
- (m) SEQ ID NOs: 224, 227, 230, 67, 69, and 71, respectively; or
- (n) SEQ ID NOs: 293, 291, 230, 287, 288, and 71, respectively; or
- (o) SEQ ID NOs: 294, 227, 296, 67, 69, and 71, respectively.

3. The composition of claim 1 or the antibody of claim 2, wherein each of the antibodies or the antibody has a K_D for human TIGIT of less than 5 nM, or less than 1 nM.

4. The composition or antibody of any one of claims 1 to 3, wherein each of the antibodies or the antibody has a K_D for human TIGIT of less than 100 pM.

5. The composition or antibody of any one of claims 1 to 4, wherein each of the antibodies or the antibody exhibits cross-reactivity with cynomolgus monkey TIGIT and/or mouse TIGIT.

6. The composition or antibody of claim 5, wherein each of the antibodies or the antibody exhibits cross-reactivity with both cynomolgus monkey TIGIT and mouse TIGIT.

7. The composition or antibody of any one of claims 1 to 6, wherein each of the antibodies or the antibody blocks binding of CD155 to TIGIT.

8. The composition or antibody of any one of claims 1 to 7, wherein each of the antibodies or the antibody blocks binding of CD112 to TIGIT.

9. The composition or antibody of any one of claims 1 to 8, wherein each of the antibodies or the antibody blocks binding of both CD155 and CD112 to TIGIT.

10. The composition or antibody of any one of claims 1 to 9, wherein each of the antibodies or the antibody competes for binding to human TIGIT with an antibody comprising a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 55 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 64.

11. The composition or antibody of any one of claims 1 to 10, wherein each of the antibodies or the antibody when bound to human TIGIT binds one or both of amino acid positions 81 and 82 of human TIGIT comprising the amino acid sequence of SEQ ID NO: 218.

12. The composition or antibody of claim 11, wherein each of the antibodies or the antibody binds both of amino acid positions 81 and 82 of human TIGIT comprising the amino acid sequence of SEQ ID NO: 218.

13. The composition or antibody of claim 11 or claim 12, wherein amino acid positions 81 and 82 are Phe81 and Lys82 of human TIGIT comprising the amino acid sequence of SEQ ID NO: 218.

14. The composition or antibody of any one of claims 1 to 13, wherein each of the antibodies or the antibody binds to an epitope on human TIGIT that comprises one or both of amino acid positions 81 and 82 of human TIGIT comprising the amino acid sequence of SEQ ID NO: 218.

15. The composition or antibody of claim 14, wherein the epitope comprises Phe at position 81 of human TIGIT comprising the amino acid sequence of SEQ ID NO: 218.

16. The composition or antibody of claim 14 or claim 15, wherein the epitope comprises Lys or Ser at position 82 of human TIGIT comprising the amino acid sequence of SEQ ID NO: 218.

17. The composition or antibody of any one of claims 14 to 16, wherein the epitope comprises Phe at position 81 and Lys or Ser at position 82 of human TIGIT comprising the amino acid sequence of SEQ ID NO: 218.

18. The composition or antibody of claim 17, wherein the epitope comprises Phe81 and Lys82 of human TIGIT comprising the amino acid sequence of SEQ ID NO: 218.

19. The composition or antibody of any one of claims 14 to 18, wherein the epitope is a discontinuous epitope.

20. The composition or antibody of any one of claims 14 to 19, wherein each of the antibodies or the antibody binds to an epitope on human TIGIT that further comprises one or more of amino acid positions 51, 52, 53, 54, 55, 73, 74, 75, 76, 77, 79, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, or 93 of human TIGIT comprising the amino acid sequence of SEQ ID NO: 218.

21. The composition or antibody of claim 20, wherein the epitope further comprises one or more amino acid residues selected from the group consisting of Thr51, Ala52, Gln53, Val54, Thr55, Leu73, Gly74, Trp75, His76, Ile77, Pro79, Asp83, Arg84, Val85, Ala86, Pro87,

Gly88, Pro89, Gly90, Leu91, Gly92, and Leu93 of human TIGIT comprising the amino acid sequence of SEQ ID NO: 218.

22. The composition or antibody of claim 21, wherein the epitope comprises the amino acid residues Thr51, Ala52, Gln53, Val54, Thr55, Gly74, Trp75, His76, Ile77, Phe81, Lys82, Pro87, Gly88, Pro89, Gly90, Leu91, Gly92, and Leu93 of human TIGIT comprising the amino acid sequence of SEQ ID NO: 218.

23. The composition or antibody of claim 21, wherein the epitope comprises the amino acid residues Ala52, Gln53, Leu73, Gly74, Trp75, Pro79, Phe81, Lys82, Asp83, Arg84, Val85, and Ala86 of human TIGIT comprising the amino acid sequence of SEQ ID NO: 218.

24. The composition or antibody of any one of claims 14 to 23, wherein the epitope comprises the sequence ICNADLGWHISPSFK (SEQ ID NO: 258).

25. The composition or antibody of any one of claims 1 to 24, wherein each of the antibodies or the antibody comprises a heavy chain CDR1, CDR2, and CDR3 and a light chain CDR1, CDR, and CDR3 comprising the sequences of:

- (a) SEQ ID NOs: 58, 60, 62, 67, 69, and 71, respectively; or
- (b) SEQ ID NOs: 283, 285, 62, 287, 288, and 71, respectively; or
- (c) SEQ ID NOs: 284, 60, 286, 67, 69, and 71, respectively.

26. The composition or antibody of any one of claims 1 to 25, wherein each of the antibodies or the antibody comprises:

a heavy chain variable region comprising an amino acid sequence that has at least 90% sequence identity to any one of SEQ ID NO:55, SEQ ID NO:246, SEQ ID NO:247, SEQ ID NO:248, or SEQ ID NO:249 and a light chain variable region comprising an amino acid sequence that has at least 90% sequence identity to SEQ ID NO:64.

27. The composition or antibody of claim 26, wherein each of the antibodies or the antibody comprises:

a heavy chain variable region comprising the amino acid sequence of any one of SEQ ID NO:55, SEQ ID NO:246, SEQ ID NO:247, SEQ ID NO:248, or SEQ ID NO:249 and a light chain variable region comprising the amino acid sequence of SEQ ID NO:64.

28. The composition or antibody of any one of claims 1 to 27, wherein each of the antibodies or the antibody comprises a heavy chain variable region comprising the amino acid

sequence of SEQ ID NO:55, and a light chain variable region comprising the amino acid sequence of SEQ ID NO:64.

29. The composition or antibody of any one of claims 1 to 28, wherein each of the antibodies or the antibody is an IgG antibody.

30. The composition or antibody of claim 29, wherein each of the antibodies or the antibody is an IgG1 antibody or IgG3 antibody.

31. The composition or antibody of any one of claims 1 to 30, wherein each of the antibodies or the antibody comprises a heavy chain comprising an amino acid sequence selected from SEQ ID NOs: 260, 262, 264, 266, 268, 270, and 272; and a light chain comprising the amino acid sequence of SEQ ID NO: 274.

32. The composition or antibody of claim 31, wherein each of the antibodies or the antibody comprises a heavy chain comprising the amino acid sequence of SEQ ID NO: 260; and a light chain comprising the amino acid sequence of SEQ ID NO: 274.

33. The composition or antibody of claim 31, wherein each of the antibodies or the antibody comprises a heavy chain consisting of the amino acid sequence of SEQ ID NO: 260; and a light chain consisting of the amino acid sequence of SEQ ID NO: 274.

34. A composition comprising antibodies that bind to human TIGIT, wherein at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% of the antibodies in the composition are afucosylated, and wherein each of the antibodies comprises a heavy chain comprising the amino acid sequence of SEQ ID NO: 260; and a light chain comprising the amino acid sequence of SEQ ID NO: 274.

35. A composition comprising antibodies that bind to human TIGIT, wherein at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% of the antibodies in the composition are afucosylated, and wherein each of the antibodies comprises a heavy chain consisting of the amino acid sequence of SEQ ID NO: 260; and a light chain consisting of the amino acid sequence of SEQ ID NO: 274.

36. The composition or antibody of any one of claims 1 to 35, wherein each of the antibodies or the antibody exhibit synergy with an anti-PD-1 antibody or an anti-PD-L1 antibody.

37. The composition or antibody of claim 44, wherein synergy is determined using an assay that comprises contacting a co-culture comprising (i) Jurkat effector cells that express PD-1, TIGIT and CD226, wherein the Jurkat effector cells comprise a luciferase reporter gene driven by the IL-2 promoter; and (ii) CHO-K1 artificial antigen presenting cells (aAPCs) expressing a TCR activator, PD-L1 and CD155; with the composition and an anti-PD-1 antibody or an anti-PD-L1 antibody.

38. The composition or antibody of any one of claims 1 to 37, wherein regulatory T (Treg) cells are depleted from human PBMCs contacted with the composition or antibody.

39. The composition or antibody of any one of claims 1 to 38, expression of MCP1, IL-8, and MIP1 α is increased in human PBMCs contacted with the composition or antibody.

40. The composition or antibody of any one of claims 1 to 39, wherein monocyte/macrophages are activated when contacted with the composition or antibody.

41. The composition or antibody of any one of claims 1 to 40, wherein CD86 and MHCII are upregulated when CD14+ monocyte/macrophages are contacted with the composition or antibody.

42. The composition or antibody of any one of claims 1 to 41, wherein CD14+ monocyte/macrophages contacted with the composition or antibody mature into antigen presenting cells.

43. The composition or antibody of any one of claims 1 to 42, wherein memory T cells contacted with the composition or antibody show increased IFN γ production in response to antigen.

44. The composition or antibody of any one of claims 1 to 43, wherein memory T cells contacted with the composition or antibody demonstrate enhanced response to antigen.

45. The composition or antibody of any one of claims 1 to 44, wherein effector memory CD8+ T cells and/or effector memory CD4+ T cells are increased in tumors contacted with the composition or antibody.

46. The composition or antibody of any one of claims 1 to 45, wherein the composition enhances a Th1 response in an animal administered the composition or antibody.

47. The composition or antibody of any one of claims 1 to 46, wherein each of the antibodies that is afucosylated or the antibody has lower binding affinity for FcγRIIa and/or FcγRIIb compared to the corresponding anti-TIGIT antibody with the same sequence that is not afucosylated; and/or wherein each of the antibodies that is afucosylated or the antibody is an IgG1 antibody, and wherein each of the antibodies that is afucosylated or the antibody binds with increased affinity to FcγRIIIa and binds with decreased affinity to FcγRIIa and FcγRIIb, compared to the corresponding anti-TIGIT antibody with the same sequence that is not afucosylated.

48. The composition or antibody of any one of claims 1 to 47, wherein the composition or antibody mediates antibody-dependent cellular phagocytosis (ADCP) of cells that express TIGIT in the presence of monocyte macrophages.

49. The composition or antibody of any one of claims 1 to 48, wherein each of the antibodies or the antibody is monoclonal.

50. The composition or antibody of any one of claims 1 to 49, wherein each of the antibodies or the antibody is a fully human antibody.

51. The composition or antibody of any one of claims 1 to 50, wherein each of the antibodies or the antibody is a chimeric antibody.

52. The composition or antibody of any one of claims 1 to 51, wherein each of the antibodies or the antibody is humanized.

53. The composition or antibody of any one of claims 1 to 52, wherein each of the antibodies or the antibody is an antibody fragment.

54. The composition or antibody of claim 53, wherein the antibody fragment is a Fab, Fab', F(ab')₂, scFv, or diabody.

55. The composition or antibody of any one of claims 1 to 54, wherein each of the antibodies or the antibody is a bispecific antibody.

56. The composition or antibody of any one of claims 1 to 55, wherein each of the antibodies or the antibody is comprised in an antibody-drug conjugate.

57. An antibody that binds to human TIGIT, wherein the antibody comprises a heavy chain comprising an amino acid sequence selected from SEQ ID NOs: 260, 262, 264, 266, 268, 270, and 272; and a light chain comprising the amino acid sequence of SEQ ID NO: 274.

58. An antibody that binds to human TIGIT, wherein the antibody comprises a heavy chain comprising the amino acid sequence of SEQ ID NO: 260; and a light chain comprising the amino acid sequence of SEQ ID NO: 274.

59. An antibody that binds to human TIGIT, wherein the antibody comprises a heavy chain consisting of the amino acid sequence of SEQ ID NO: 260; and a light chain consisting of the amino acid sequence of SEQ ID NO: 274.

60. A pharmaceutical formulation comprising the composition or antibody of any one of claims 1 to 59 and a pharmaceutically acceptable carrier.

61. An isolated polynucleotide that encodes (i) the heavy chain of the antibody of any one of claims 57 to 59; (ii) the light chain of the antibody of any one of claims 57 to 59; or (iii) the heavy chain and the light chain of the antibody of any one of claims 57 to 59.

62. The isolated polynucleotide of claim 61, wherein the polynucleotide comprises (i) a nucleotide sequence selected from SEQ ID NOs: 259, 261, 263, 265, 267, 269, and 271; or (ii) a nucleotide sequence of SEQ ID NO: 273; or (iii) a nucleotide sequence selected from SEQ ID NOs: 259, 261, 263, 265, 267, 269, and 271, and a nucleotide sequence of SEQ ID NO: 273.

63. A vector comprising the polynucleotide of claim 61 or claim 62.

64. An isolated host cell comprising the isolated polynucleotide of claim 61 or claim 62, or the vector of claim 63.

65. An isolated host cell that expresses the antibody of any one of claims 57 to 59.

66. The host cell of claim 64 or claim 65, which is engineered to produce afucosylated antibodies.

67. A method of producing an antibody that binds to human TIGIT, comprising incubating the host cell of any one of claims 64 to 66 under conditions suitable for producing the antibody.

68. The method of claim 67, wherein the host cell is engineered to produce afucosylated antibodies.

69. The method of claim 67, wherein the host cell is cultured in the presence of a fucose analogue under conditions suitable for producing afucosylated antibodies.

70. The method of any one of claims 67 to 69, further comprising isolating the antibodies.

71. A composition of antibodies that bind to human TIGIT, wherein at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% of the antibodies in the composition are afucosylated, wherein the antibodies are produced by the method of any one of claims 68 to 70.

72. A composition of antibodies that bind to human TIGIT, wherein at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% of the antibodies in the composition are afucosylated, wherein the antibodies are produced by the method comprising incubating the host cell of claim 64 or claim 65 under conditions suitable for producing afucosylated antibodies, and isolating the antibodies to form the composition of antibodies.

73. The composition of claim 72, wherein the host cell is engineered to produce afucosylated antibodies.

74. The composition of claim 72, wherein the host cell is cultured in the presence of a fucose analogue under conditions suitable for producing afucosylated antibodies.

75. A host cell comprising a polynucleotide comprising a nucleotide sequence encoding the (i) antibodies of the composition of any one of claims 1 and 3 to 56, or (ii) the antibody of any one of claims 2 to 33 and 36 to 59, wherein the host cell is engineered to produce afucosylated antibodies.

76. The host cell of claim 75, wherein the polynucleotide is a vector.

77. A host cell that expresses (i) the antibodies of the composition of any one of claims 1 and 3 to 56, or (ii) the antibody of any one of claims 2 to 33 and 36 to 59, wherein the host cell is engineered to produce afucosylated antibodies.

78. The host cell of any one of claims 75 to 77, wherein the host cell comprises:
(a) the nucleotide sequence of SEQ ID NO:259, SEQ ID NO:265, SEQ ID NO:267, SEQ ID NO:269, SEQ ID NO:271, or SEQ ID NO:56; and/or
(b) the nucleotide sequence of SEQ ID NO:273 or SEQ ID NO:65.

79. A method of producing afucosylated antibodies that bind TIGIT, comprising culturing the host cell of any one of claims 75 to 78 under conditions suitable for producing the afucosylated antibodies.

80. A method of producing afucosylated antibodies that bind TIGIT, comprising culturing a host cell in the presence of a fucose analogue under conditions suitable for producing afucosylated antibodies, wherein the host cell comprises a polynucleotide comprising a nucleotide sequence encoding the (i) antibodies of the composition of any one of claims 1 and 3 to 56, or (ii) the antibody of any one of claims 2 to 33 and 36 to 59.

81. The method of claim 80, wherein the polynucleotide is a vector.

82. A method of producing afucosylated antibodies that bind TIGIT, comprising culturing a host cell in the presence of a fucose analogue under conditions suitable for producing afucosylated antibodies, wherein the host cell expresses (i) the antibodies of the composition of any one of claims 1 and 3 to 56, or (ii) the antibody of any one of claims 2 to 33 and 36 to 59.

83. The method of any one of claims 80 to 82, wherein the host cell comprises:

- (a) the nucleotide sequence of SEQ ID NO:259, SEQ ID NO:265, SEQ ID NO:267, SEQ ID NO:269, SEQ ID NO:271, or SEQ ID NO:56; and/or
- (b) the nucleotide sequence of SEQ ID NO:273 or SEQ ID NO:65.

84. The method of any one of claims 80 to 83, wherein the fucose analogue is 2-fluorofucose.

85. The method of any one of claims 79 to 84, further comprising isolating the afucosylated antibodies.

86. A composition of antibodies that bind to human TIGIT, wherein at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% of the antibodies in the composition are afucosylated, wherein the antibodies are produced by the method of any one of claims 79 to 85.

87. A composition of antibodies that bind to human TIGIT, wherein at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% of the antibodies in the composition are afucosylated, wherein the antibodies are produced by a method comprising incubating the host cell of any one of claims 75

to 77 under conditions suitable for producing afucosylated antibodies, and isolating the antibodies to form the composition of antibodies.

88. A composition of antibodies that bind to human TIGIT, wherein at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% of the antibodies in the composition are afucosylated, wherein the antibodies are produced by a method comprising culturing a host cell in the presence of a fucose analogue under conditions suitable for producing afucosylated antibodies, wherein the host cell comprises a polynucleotide comprising a nucleotide sequence encoding the (i) antibodies of the composition of any one of claims 1 and 3 to 56, or (ii) the antibody of any one of claims 2 to 33 and 36 to 59.

89. A composition of antibodies that bind to human TIGIT, wherein at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% of the antibodies in the composition are afucosylated, wherein the antibodies are produced by a method comprising culturing a host cell in the presence of a fucose analogue under conditions suitable for producing afucosylated antibodies, wherein the host cell expresses (i) the antibodies of the composition of any one of claims 1 and 3 to 56, or (ii) the antibody of any one of claims 2 to 33 and 36 to 59.

90. A kit comprising:
the composition of any one of claims 1 and 3 to 56, the antibody of any one of claims 2 to 33 and 36 to 59, or the pharmaceutical composition of claim 60; and
an additional therapeutic agent.

91. The kit of claim 90, wherein the additional therapeutic is an anti-cancer agent.

92. The kit of claim 90 or claim 91, wherein the additional therapeutic agent is an antibody.

93. The kit of any one of claims 90 to 92, wherein the additional therapeutic agent is an immune stimulatory cytokine or SGN-2FF.

94. The kit of any one of claims 90 to 92, wherein the additional therapeutic agent binds a protein selected from CD25, PD-1, PD-L1, Tim3, Lag3, CTLA4, 41BB, OX40, CD3, CD40, CD47M, GM-CSF, CSF1R, TLR, STING, RIGI, TAM receptor kinase, NKG2A, NKG2D, GD2, HER2, EGFR, PDGFR α , SLAMF7, VEGF, CTLA-4, CD20, cCLB8, KIR, and CD52.

95. The kit of claim any one of claims 90 to 92, wherein the additional therapeutic agent is selected from an anti-CD25 antibody, anti-PD-1 antibody, anti-PD-L1 antibody, anti-Tim3 antibody, anti-Lag3 antibody, anti-CTLA4 antibody, anti-41BB antibody, anti-OX40 antibody, anti-CD3 antibody, anti-CD40 antibody, anti-CD47M antibody, anti-CSF1R antibody, anti-TLR antibody, anti-STING antibody, anti-RIGI antibody, anti-TAM receptor kinase antibody, anti-NKG2A antibody, an anti-NKG2D antibody, an anti-GD2 antibody, an anti-HER2 antibody, an anti-EGFR antibody, an anti-PDGFR- α -antibody, an anti-SLAMF7 antibody, an anti-VEGF antibody, an anti-CTLA-4 antibody, an anti-CD20 antibody, an anti-cCLB8 antibody, an anti-KIR antibody, and an anti-CD52 antibody.

96. The kit of any one of claims 90 to 92, wherein the additional therapeutic agent comprises a cytokine selected from IL-15, IL-21, IL-2, GM-CSF, M-CSF, G-CSF, IL-1, IL-3, IL-12, and IFN γ .

97. The kit of any one of claims 90 to 92, wherein the additional therapeutic agent is selected from SEA-CD40, avelumab, durvalumab, nivolumab, pembrolizumab, pidilizumab, atezolizumab, Hu1.18K322A, Hu3F8, dinituximab, trastuzumab, cetuximab, olaratumab, necitumumab, elotuzumab, ramucirumab, pertuzumab, ipilimumab, bevacizumab, rituximab, obinutuzumab, siltuximab, ofatumumab, lirilumab, and alemtuzumab.

98. The kit of claim 90 or claim 91, wherein the additional therapeutic agent is selected from an alkylating agent (*e.g.*, cyclophosphamide, ifosfamide, chlorambucil, busulfan, melphalan, mechlorethamine, uramustine, thiotepe, nitrosoureas, or temozolomide), an anthracycline (*e.g.*, doxorubicin, adriamycin, daunorubicin, epirubicin, or mitoxantrone), a cytoskeletal disruptor (*e.g.*, paclitaxel or docetaxel), a histone deacetylase inhibitor (*e.g.*, vorinostat or romidepsin), an inhibitor of topoisomerase (*e.g.*, irinotecan, topotecan, amsacrine, etoposide, or teniposide), a kinase inhibitor (*e.g.*, bortezomib, erlotinib, gefitinib, imatinib, vemurafenib, or vismodegib), a nucleoside analog or precursor analog (*e.g.*, azacitidine, azathioprine, capecitabine, cytarabine, fluorouracil, gemcitabine, hydroxyurea, mercaptopurine, methotrexate, or thioguanine), a peptide antibiotic (*e.g.*, actinomycin or bleomycin), a platinum-based agent (*e.g.*, cisplatin, oxaloplatin, or carboplatin), or a plant alkaloid (*e.g.*, vincristine, vinblastine, vinorelbine, vindesine, podophyllotoxin, paclitaxel, or docetaxel), galardin, thalidomide, lenalidomide, and pomalidomide.

99. Use of a therapeutically effective amount of the composition of any one of claims 1 and 3 to 56, the antibody of any one of claims 2 to 33 and 36 to 59, or the pharmaceutical

composition of claim 60 in the manufacture of a medicament for treating a cancer in a subject, wherein the medicament is to be administered to the subject.

100. The use of claim 99, wherein the cancer is a cancer that is enriched for expression of CD112 or CD155.

101. The use of claim 99 or claim 100, wherein the cancer is a cancer that is enriched for T cells or natural killer (NK) cells that express TIGIT.

102. The use of any one of claims 99 to 101, wherein the cancer is bladder cancer, breast cancer, uterine cancer, cervical cancer, ovarian cancer, prostate cancer, testicular cancer, esophageal cancer, gastrointestinal cancer, gastric cancer, pancreatic cancer, colorectal cancer, colon cancer, kidney cancer, clear cell renal carcinoma, head and neck cancer, lung cancer, lung adenocarcinoma, stomach cancer, germ cell cancer, bone cancer, liver cancer, thyroid cancer, skin cancer, melanoma, neoplasm of the central nervous system, mesothelioma, lymphoma, leukemia, chronic lymphocytic leukemia, diffuse large B cell lymphoma, follicular lymphoma, Hodgkin lymphoma, myeloma, or sarcoma.

103. The use of claim 102, wherein the cancer is lymphoma, leukemia, chronic lymphocytic leukemia, diffuse large B cell lymphoma, follicular lymphoma, or Hodgkin lymphoma.

104. The use of any one of claims 99 to 103, wherein a therapeutically effective amount of an additional therapeutic agent is to be further administered to the subject.

105. The use of claim 104, wherein the additional therapeutic is an anti-cancer agent.

106. The use of claim 104 or claim 105, wherein the additional therapeutic agent is an antibody.

107. The use of any one of claims 104 to 106, wherein the additional therapeutic agent is an immune stimulatory cytokine or SGN-2FF.

108. The use of any one of claims 104 to 106, wherein the additional therapeutic agent binds a protein selected from CD25, PD-1, PD-L1, Tim3, Lag3, CTLA4, 41BB, OX40, CD3, CD40, CD47M, GM-CSF, CSF1R, TLR, STING, RIGI, TAM receptor kinase, NKG2A, NKG2D, GD2, HER2, EGFR, PDGFR α , SLAMF7, VEGF, CTLA-4, CD20, cCLB8, KIR, and CD52.

109. The use of claim 108, wherein the additional therapeutic agent is selected from an anti-CD25 antibody, anti-PD-1 antibody, anti-PD-L1 antibody, anti-Tim3 antibody, anti-Lag3 antibody, anti-CTLA4 antibody, anti-41BB antibody, anti-OX40 antibody, anti-CD3 antibody, anti-CD40 antibody, anti-CD47M antibody, anti-CSF1R antibody, anti-TLR antibody, anti-STING antibody, anti-RIGI antibody, anti-TAM receptor kinase antibody, anti-NKG2A antibody, an anti-NKG2D antibody, an anti-GD2 antibody, an anti-HER2 antibody, an anti-EGFR antibody, an anti-PDGFR- α -antibody, an anti-SLAMF7 antibody, an anti-VEGF antibody, an anti-CTLA-4 antibody, an anti-CD20 antibody, an anti-cCLB8 antibody, an anti-KIR antibody, and an anti-CD52 antibody.

110. The use of claim 104 or claim 105, wherein the additional therapeutic agent comprises a cytokine selected from IL-15, IL-21, IL-2, GM-CSF, M-CSF, G-CSF, IL-1, IL-3, IL-12, and IFN γ .

111. The use of any one of claims 104 to 106, wherein the additional therapeutic agent is selected from SEA-CD40, avelumab, durvalumab, nivolumab, pembrolizumab, pidilizumab, atezolizumab, Hu4.18K322A, Hu3F8, dinituximab, trastuzumab, cetuximab, olaratumab, necitumumab, elotuzumab, ramucirumab, pertuzumab, ipilimumab, bevacizumab, rituximab, obinutuzumab, siltuximab, ofatumumab, lirilumab, and alemtuzumab.

112. The use of claim 104 or claim 105, wherein the additional therapeutic agent is selected from an alkylating agent (*e.g.*, cyclophosphamide, ifosfamide, chlorambucil, busulfan, melphalan, mechlorethamine, uramustine, thiotepe, nitrosoureas, or temozolomide), an anthracycline (*e.g.*, doxorubicin, adriamycin, daunorubicin, epirubicin, or mitoxantrone), a cytoskeletal disruptor (*e.g.*, paclitaxel or docetaxel), a histone deacetylase inhibitor (*e.g.*, vorinostat or romidepsin), an inhibitor of topoisomerase (*e.g.*, irinotecan, topotecan, amsacrine, etoposide, or teniposide), a kinase inhibitor (*e.g.*, bortezomib, erlotinib, gefitinib, imatinib, vemurafenib, or vismodegib), a nucleoside analog or precursor analog (*e.g.*, azacitidine, azathioprine, capecitabine, cytarabine, fluorouracil, gemcitabine, hydroxyurea, mercaptopurine, methotrexate, or thioguanine), a peptide antibiotic (*e.g.*, actinomycin or bleomycin), a platinum-based agent (*e.g.*, cisplatin, oxaloplatin, or carboplatin), or a plant alkaloid (*e.g.*, vincristine, vinblastine, vinorelbine, vindesine, podophyllotoxin, paclitaxel, or docetaxel), galardin, thalidomide, lenalidomide, and pomalidomide.

113. The use of any one of claims 104 to 112, wherein the medicament is to be administered concurrently with the additional therapeutic agent.

114. The use of any one of claims 104 to 113, wherein the medicament is to be administered sequentially to the additional therapeutic agent.

115. The composition of any one of claims 1 and 3 to 56, the antibody of any one of claims 2 to 33 and 36 to 59, or the pharmaceutical composition of claim 60 for use in therapy.