

BRIEF SUMMARY

[0004] In one example, isolated antibodies or antigen-binding portions thereof that bind to human TIGIT (T-cell immunoreceptor with Ig and ITIM domains) are provided. In some examples, the antibody or antigen-binding portion thereof has a binding affinity (K_D) for human TIGIT of less than 5 nM. In some examples, the antibody or antigen-binding portion thereof has a K_D for human TIGIT of less than 1 nM. In some examples, the antibody or antigen-binding portion thereof has a K_D for human TIGIT of less than 100 pM.

[0004a] In a first aspect, there is provided an isolated antibody, or antigen-binding portion thereof, that binds to human TIGIT (T-cell immunoreceptor with Ig and ITIM domains), wherein the antibody or antigen-binding portion thereof has a binding affinity (K_D) for human TIGIT of less than 5 nM.

[0005] In some examples, the antibody or antigen-binding portion thereof exhibits cross-reactivity with cynomolgus monkey TIGIT and/or mouse TIGIT. In some examples, the antibody or antigen-binding portion thereof exhibits cross-reactivity with both cynomolgus monkey TIGIT and mouse TIGIT.

[0006] In some examples, the antibody or antigen-binding portion thereof blocks binding of CD155 to TIGIT. In some examples, the antibody or antigen-binding portion thereof blocks binding of CD112 to TIGIT. In some examples, the antibody or antigen-binding portion thereof blocks binding of both CD155 and CD112 to TIGIT.

[0007] In some examples, the antibody or antigen-binding portion thereof binds to an epitope on human TIGIT that comprises amino acid positions 81 and 82. In some examples, the epitope comprises Phe at position 81 and/or Lys or Ser at position 82. In some examples, the epitope comprises Phe81 and Lys82.

[0007a] In a second aspect, there is provided an isolated antibody, or antigen-binding portion thereof, that binds to human TIGIT, wherein the antibody or antigen-binding portion thereof binds to an epitope on human TIGIT that comprises amino acid positions 81 and 82.

[0008] In some examples, the epitope is a discontinuous epitope.

[0009] In some examples, the antibody or antigen-binding portion thereof 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. In some examples, 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. In some examples, 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. In some examples, the epitope comprises the amino acid residues Ala52, Gln53, Leu73, Gly74, Trp75, Pro79, Phe81, Lys82, Asp83, Arg84,

Val85, and Ala86. In some examples, the epitope comprises the sequence ICNADLGWHISPSFK (SEQ ID NO:258).

[0010] In some examples, the antibody or antigen-binding portion thereof comprises one or more sequences listed in Table 3 below. In some examples, the antibody or antigen-binding portion thereof comprises one or more of:

(a) a heavy chain CDR1 comprising the 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, or SEQ ID NO:243;

(b) a heavy chain CDR2 comprising the 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, SEQ ID NO:204, SEQ ID NO:222, SEQ ID NO:225, SEQ ID NO:227, SEQ ID NO:229, SEQ ID NO:232, SEQ ID NO:234, SEQ ID NO:238, or SEQ ID NO:240;

(c) a heavy chain CDR3 comprising the sequence of any of SEQ ID NO:8, SEQ ID NO:26, SEQ ID NO:44, SEQ ID NO:62, SEQ ID NO:80, SEQ ID NO:98, SEQ ID NO:116, SEQ ID NO:134, SEQ ID NO:152, SEQ ID NO:170, SEQ ID NO:188, SEQ ID NO:206, SEQ ID NO:223, SEQ ID NO:228, SEQ ID NO:230, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:241, SEQ ID NO:242, or SEQ ID NO:244;

(d) a light chain CDR1 comprising the sequence of any of SEQ ID NO:13, SEQ ID NO:31, SEQ ID NO:49, SEQ ID NO:67, SEQ ID NO:85, SEQ ID NO:103, SEQ ID NO:121, SEQ ID NO:139, SEQ ID NO:157, SEQ ID NO:175, SEQ ID NO:193, or SEQ ID NO:211;

(e) a light chain CDR2 comprising the sequence of any of SEQ ID NO:15, SEQ ID NO:33, SEQ ID NO:51, SEQ ID NO:69, SEQ ID NO:87, SEQ ID NO:105, SEQ ID NO:123, SEQ ID NO:141, SEQ ID NO:159, SEQ ID NO:177, SEQ ID NO:195, or SEQ ID NO:213; or

(f) a light chain CDR3 comprising the sequence of any of SEQ ID NO:17, SEQ ID NO:35, SEQ ID NO:53, SEQ ID NO:71, SEQ ID NO:89, SEQ ID NO:107, SEQ ID NO:125, SEQ ID NO:143, SEQ ID NO:161, SEQ ID NO:179, SEQ ID NO:197, or SEQ ID NO:215.

[0011] In some examples, the antibody or antigen-binding portion thereof comprises a heavy chain CDR1, CDR2, and CDR3 and a light chain CDR1, CDR2, and CDR3 comprising the sequences of:

- (a) SEQ ID NOs: 4, 6, 8, 13, 15, and 17, respectively; or
- 5 (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: 76, 78, 80, 85, 87, and 89, respectively; or
- (f) SEQ ID NOs: 94, 96, 98, 103, 105, and 107, respectively; or
- 10 (g) SEQ ID NOs: 112, 114, 116, 121, 123, and 125, respectively; or
- (h) SEQ ID NOs: 130, 132, 134, 139, 141, and 143, respectively; or
- (i) SEQ ID NOs: 148, 150, 152, 157, 159, and 161, respectively; or
- (j) SEQ ID NOs: 166, 168, 170, 175, 177, and 179, respectively; or
- (k) SEQ ID NOs: 184, 186, 188, 193, 195, and 197, respectively; or
- 15 (l) SEQ ID NOs: 202, 204, 206, 211, 213, and 215, respectively; or
- (m) SEQ ID NOs: 221, 222, 223, 13, 15, and 17, respectively; or
- (n) SEQ ID NOs: 224, 225, 62, 67, 69, and 71, respectively; or
- (o) SEQ ID NOs: 226, 227, 228, 67, 69, and 71, respectively; or
- (p) SEQ ID NOs: 224, 229, 230, 67, 69, and 71, respectively; or
- 20 (q) SEQ ID NOs: 224, 227, 230, 67, 69, and 71, respectively; or
- (r) SEQ ID NOs: 231, 232, 235, 103, 105, and 107, respectively; or
- (s) SEQ ID NOs: 233, 234, 236, 103, 105, and 107, respectively; or
- (t) SEQ ID NOs: 233, 234, 237, 103, 105, and 107, respectively; or
- (u) SEQ ID NOs: 166, 238, 170, 175, 177, and 179, respectively; or
- 25 (v) SEQ ID NOs: 239, 240, 170, 175, 177, and 179, respectively; or
- (w) SEQ ID NOs: 239, 240, 241, 175, 177, and 179, respectively; or
- (x) SEQ ID NOs: 239, 240, 242, 175, 177, and 179, respectively; or
- (y) SEQ ID NOs: 243, 168, 244, 175, 177, and 179, respectively.

[0012] In some examples, the antibody or antigen-binding portion thereof comprises:

- 30 (a) a heavy chain variable region comprising an amino acid sequence that has at least 90% sequence identity to SEQ ID NO:1, SEQ ID NO:19, SEQ ID NO:37, SEQ ID NO:55, SEQ ID NO:73, SEQ ID NO:91, SEQ ID NO:109, SEQ ID NO:127, SEQ ID

NO:145, SEQ ID NO:163, SEQ ID NO:181, SEQ ID NO:199, SEQ ID NO:245, SEQ ID NO:246, SEQ ID NO:247, SEQ ID NO:248, SEQ ID NO:249, SEQ ID NO:250, SEQ ID NO:251, SEQ ID NO:252, SEQ ID NO:253, SEQ ID NO:254, SEQ ID NO:255, SEQ ID NO:256, or SEQ ID NO:257; and/or

- 5 (b) a light chain variable region comprising an amino acid sequence that has at least 90% sequence identity to SEQ ID NO:10, SEQ ID NO:28, SEQ ID NO:46, SEQ ID NO:64, SEQ ID NO:82, SEQ ID NO:100, SEQ ID NO:118, SEQ ID NO:136, SEQ ID NO:154, SEQ ID NO:172, SEQ ID NO:190, or SEQ ID NO:208.

[0013] In some examples, the antibody or antigen-binding portion thereof comprises:

- 10 (a) a heavy chain variable region comprising an amino acid sequence that has at least 90% sequence identity to SEQ ID NO:1 or SEQ ID NO:245 and a light chain variable region comprising an amino acid sequence that has at least 90% sequence identity to SEQ ID NO:10; or

- (b) a heavy chain variable region comprising an amino acid sequence that
15 has at least 90% sequence identity to SEQ ID NO:19 and a light chain variable region comprising an amino acid sequence that has at least 90% sequence identity to SEQ ID NO:28; or

- (c) a heavy chain variable region comprising an amino acid sequence that has at least 90% sequence identity to SEQ ID NO:37 and a light chain variable region
20 comprising an amino acid sequence that has at least 90% sequence identity to SEQ ID NO:46; or

- (d) 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
25 that has at least 90% sequence identity to SEQ ID NO:64; or

- (e) a heavy chain variable region comprising an amino acid sequence that has at least 90% sequence identity to SEQ ID NO:73 and a light chain variable region comprising an amino acid sequence that has at least 90% sequence identity to SEQ ID NO:82; or

- (f) a heavy chain variable region comprising an amino acid sequence that
30 has at least 90% sequence identity to any one of SEQ ID NO:91, SEQ ID NO:250, SEQ ID NO:251, or SEQ ID NO:252 and a light chain variable region comprising an amino acid sequence that has at least 90% sequence identity to SEQ ID NO:100; or

(g) a heavy chain variable region comprising an amino acid sequence that has at least 90% sequence identity to SEQ ID NO:109 and a light chain variable region comprising an amino acid sequence that has at least 90% sequence identity to SEQ ID NO:118; or

5 (h) a heavy chain variable region comprising an amino acid sequence that has at least 90% sequence identity to SEQ ID NO:127 and a light chain variable region comprising an amino acid sequence that has at least 90% sequence identity to SEQ ID NO:136; or

10 (i) a heavy chain variable region comprising an amino acid sequence that has at least 90% sequence identity to SEQ ID NO:145 and a light chain variable region comprising an amino acid sequence that has at least 90% sequence identity to SEQ ID NO:154; or

15 (j) a heavy chain variable region comprising an amino acid sequence that has at least 90% sequence identity to any one of SEQ ID NO:163, SEQ ID NO:253, SEQ ID NO:254, SEQ ID NO:255, SEQ ID NO:256, or SEQ ID NO:257 and a light chain variable region comprising an amino acid sequence that has at least 90% sequence identity to SEQ ID NO:172; or

20 (k) a heavy chain variable region comprising an amino acid sequence that has at least 90% sequence identity to SEQ ID NO:181 and a light chain variable region comprising an amino acid sequence that has at least 90% sequence identity to SEQ ID NO:190; or

25 (l) a heavy chain variable region comprising an amino acid sequence that has at least 90% sequence identity to SEQ ID NO:199 and a light chain variable region comprising an amino acid sequence that has at least 90% sequence identity to SEQ ID NO:208.

[0014] In another example, antibodies or antigen-binding portions thereof that bind to human TIGIT are provided, wherein the antibody or antigen-binding portion thereof binds to an epitope on human TIGIT that comprises amino acid positions 81 and 82. In some examples, the epitope comprises Phe at position 81 and/or Lys or Ser at position 82. In some examples, the epitope comprises Phe81 and Lys82.

[0015] In some examples, the epitope is a discontinuous epitope.

[0016] In some examples, the antibody or antigen-binding portion thereof 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. In some examples, 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. In some examples, 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. In some examples, the epitope comprises the amino acid residues Ala52, Gln53, Leu73, Gly74, Trp75, Pro79, Phe81, Lys82, Asp83, Arg84, Val85, and Ala86. In some examples, the epitope comprises the sequence ICNADLGWHISPSFK (SEQ ID NO:258).

[0017] In still another example, antibodies or antigen-binding portions thereof comprising one or more sequences as disclosed herein (e.g., one or more sequences listed in Table 3 below) are provided. In some examples, the antibody or antigen-binding portion thereof comprises one more CDR, heavy chain variable region, light chain variable region, or framework region sequences as disclosed herein (e.g., as listed in Table 3 below). In some examples, the antibody or antigen-binding portion thereof comprises one or more of:

(a) a heavy chain CDR1 comprising the 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, or SEQ ID NO:243;

(b) a heavy chain CDR2 comprising the 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, SEQ ID NO:204, SEQ ID NO:222, SEQ ID NO:225, SEQ ID NO:227, SEQ ID NO:229, SEQ ID NO:232, SEQ ID NO:234, SEQ ID NO:238, or SEQ ID NO:240;

(c) a heavy chain CDR3 comprising the sequence of any of SEQ ID NO:8, SEQ ID NO:26, SEQ ID NO:44, SEQ ID NO:62, SEQ ID NO:80, SEQ ID NO:98, SEQ ID NO:116, SEQ ID NO:134, SEQ ID NO:152, SEQ ID NO:170, SEQ ID NO:188, SEQ ID NO:206, SEQ ID NO:223, SEQ ID NO:228, SEQ ID NO:230, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:241, SEQ ID NO:242, or SEQ ID NO:244;

(d) a light chain CDR1 comprising the sequence of any of SEQ ID NO:13, SEQ ID NO:31, SEQ ID NO:49, SEQ ID NO:67, SEQ ID NO:85, SEQ ID NO:103, SEQ ID NO:121, SEQ ID NO:139, SEQ ID NO:157, SEQ ID NO:175, SEQ ID NO:193, or SEQ ID NO:211;

5 (e) a light chain CDR2 comprising the sequence of any of SEQ ID NO:15, SEQ ID NO:33, SEQ ID NO:51, SEQ ID NO:69, SEQ ID NO:87, SEQ ID NO:105, SEQ ID NO:123, SEQ ID NO:141, SEQ ID NO:159, SEQ ID NO:177, SEQ ID NO:195, or SEQ ID NO:213; or

(f) a light chain CDR3 comprising the sequence of any of SEQ ID NO:17, SEQ ID NO:35, SEQ ID NO:53, SEQ ID NO:71, SEQ ID NO:89, SEQ ID NO:107, SEQ ID NO:125, SEQ ID NO:143, SEQ ID NO:161, SEQ ID NO:179, SEQ ID NO:197, or SEQ ID NO:215.

[0018] In some examples, the antibody or antigen-binding portion thereof comprises a heavy chain CDR1, CDR2, and CDR3 and a light chain CDR1, CDR2, and CDR3

15 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
- 20 (e) SEQ ID NOs: 76, 78, 80, 85, 87, and 89, respectively; or
- (f) SEQ ID NOs: 94, 96, 98, 103, 105, and 107, respectively; or
- (g) SEQ ID NOs: 112, 114, 116, 121, 123, and 125, respectively; or
- (h) SEQ ID NOs: 130, 132, 134, 139, 141, and 143, respectively; or
- (i) SEQ ID NOs: 148, 150, 152, 157, 159, and 161, respectively; or
- 25 (j) SEQ ID NOs: 166, 168, 170, 175, 177, and 179, respectively; or
- (k) SEQ ID NOs: 184, 186, 188, 193, 195, and 197, respectively; or
- (l) SEQ ID NOs: 202, 204, 206, 211, 213, and 215, respectively; or
- (m) SEQ ID NOs: 221, 222, 223, 13, 15, and 17, respectively; or
- (n) SEQ ID NOs: 224, 225, 62, 67, 69, and 71, respectively; or
- 30 (o) SEQ ID NOs: 226, 227, 228, 67, 69, and 71, respectively; or
- (p) SEQ ID NOs: 224, 229, 230, 67, 69, and 71, respectively; or
- (q) SEQ ID NOs: 224, 227, 230, 67, 69, and 71, respectively; or
- (r) SEQ ID NOs: 231, 232, 235, 103, 105, and 107, respectively; or

- (s) SEQ ID NOs: 233, 234, 236, 103, 105, and 107, respectively; or
- (t) SEQ ID NOs: 233, 234, 237, 103, 105, and 107, respectively; or
- (u) SEQ ID NOs: 166, 238, 170, 175, 177, and 179, respectively; or
- (v) SEQ ID NOs: 239, 240, 170, 175, 177, and 179, respectively; or
- 5 (w) SEQ ID NOs: 239, 240, 241, 175, 177, and 179, respectively; or
- (x) SEQ ID NOs: 239, 240, 242, 175, 177, and 179, respectively; or
- (y) SEQ ID NOs: 243, 168, 244, 175, 177, and 179, respectively.

[0019] In some examples, the antibody or antigen-binding portion thereof comprises:

- (a) a heavy chain variable region comprising an amino acid sequence that has at
10 least 90% sequence identity to SEQ ID NO:1, SEQ ID NO:19, SEQ ID NO:37, SEQ ID NO:55, SEQ
ID NO:73, SEQ ID NO:91, SEQ ID NO:109, SEQ ID NO:127, SEQ ID NO:145, SEQ ID NO:163,
SEQ ID NO:181, SEQ ID NO:199, SEQ ID NO:245, SEQ ID NO:246, SEQ ID NO:247, SEQ ID
NO:248, SEQ ID NO:249, SEQ ID NO:250, SEQ ID NO:251, SEQ ID NO:252, SEQ ID NO:253,
SEQ ID NO:254, SEQ ID NO:255, SEQ ID NO:256, or SEQ ID NO:257; and/or
- 15 (b) a light chain variable region comprising an amino acid sequence that
has at least 90% sequence identity to SEQ ID NO:10, SEQ ID NO:28, SEQ ID NO:46, SEQ
ID NO:64, SEQ ID NO:82, SEQ ID NO:100, SEQ ID NO:118, SEQ ID NO:136, SEQ ID
NO:154, SEQ ID NO:172, SEQ ID NO:190, or SEQ ID NO:208.

[0020] In some examples, the antibody or antigen-binding portion thereof comprises:

- 20 (a) a heavy chain variable region comprising an amino acid sequence that
has at least 90% sequence identity to SEQ ID NO:1 or SEQ ID NO:245 and a light chain
variable region comprising an amino acid sequence that has at least 90% sequence identity to
SEQ ID NO:10; or
- (b) a heavy chain variable region comprising an amino acid sequence that
25 has at least 90% sequence identity to SEQ ID NO:19 and a light chain variable region
comprising an amino acid sequence that has at least 90% sequence identity to SEQ ID
NO:28; or
- (c) a heavy chain variable region comprising an amino acid sequence that
has at least 90% sequence identity to SEQ ID NO:37 and a light chain variable region
30 comprising an amino acid sequence that has at least 90% sequence identity to SEQ ID
NO:46; or

- (d) 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; or
- 5 (e) a heavy chain variable region comprising an amino acid sequence that has at least 90% sequence identity to SEQ ID NO:73 and a light chain variable region comprising an amino acid sequence that has at least 90% sequence identity to SEQ ID NO:82; or
- 10 (f) a heavy chain variable region comprising an amino acid sequence that has at least 90% sequence identity to any one of SEQ ID NO:91, SEQ ID NO:250, SEQ ID NO:251, or SEQ ID NO:252 and a light chain variable region comprising an amino acid sequence that has at least 90% sequence identity to SEQ ID NO:100; or
- 15 (g) a heavy chain variable region comprising an amino acid sequence that has at least 90% sequence identity to SEQ ID NO:109 and a light chain variable region comprising an amino acid sequence that has at least 90% sequence identity to SEQ ID NO:118; or
- (h) a heavy chain variable region comprising an amino acid sequence that has at least 90% sequence identity to SEQ ID NO:127 and a light chain variable region comprising an amino acid sequence that has at least 90% sequence identity to SEQ ID
- 20 NO:136; or
- (i) a heavy chain variable region comprising an amino acid sequence that has at least 90% sequence identity to SEQ ID NO:145 and a light chain variable region comprising an amino acid sequence that has at least 90% sequence identity to SEQ ID NO:154; or
- 25 (j) a heavy chain variable region comprising an amino acid sequence that has at least 90% sequence identity to any one of SEQ ID NO:163, SEQ ID NO:253, SEQ ID NO:254, SEQ ID NO:255, SEQ ID NO:256, or SEQ ID NO:257 and a light chain variable region comprising an amino acid sequence that has at least 90% sequence identity to SEQ ID NO:172; or
- 30 (k) a heavy chain variable region comprising an amino acid sequence that has at least 90% sequence identity to SEQ ID NO:181 and a light chain variable region comprising an amino acid sequence that has at least 90% sequence identity to SEQ ID NO:190; or

(l) a heavy chain variable region comprising an amino acid sequence that has at least 90% sequence identity to SEQ ID NO:199 and a light chain variable region comprising an amino acid sequence that has at least 90% sequence identity to SEQ ID NO:208.

5 [0021] In some examples, an antibody or antigen-binding portion thereof as disclosed herein exhibits synergy with an anti-PD1 antibody or an anti-PD-L1 antibody.

[0022] In some examples, an antibody or antigen-binding portion thereof as disclosed herein is a monoclonal antibody. In some examples, the antibody is a humanized antibody. In some examples, the antibody is a fully human antibody. In some examples, the antibody is a
10 chimeric antibody. In some examples, the antigen-binding fragment is a Fab, a F(ab')₂, a scFv, or a bivalent scFv.

[0023] In another example, pharmaceutical compositions comprising an isolated antibody or antigen-binding portion thereof as described herein and a pharmaceutically acceptable carrier are provided.

15 [0023a] In a third aspect, there is provided a pharmaceutical composition comprising the isolated antibody of the first or second aspect and a pharmaceutically acceptable carrier.

[0024] In yet another example, bispecific antibodies comprising an isolated antibody or antigen-binding portion thereof as described herein are provided.

[0024a] In a fourth aspect, there is provided a bispecific antibody comprising the antibody of
20 the first or second aspect.

[0025] In yet another example, antibody-drug conjugates comprising an isolated antibody or antigen-binding portion thereof as described herein are provided.

[0025a] In a fifth aspect, there is provided an antibody-drug conjugate comprising the antibody of the first or second aspect.

25 [0026] In still another example, isolated polynucleotides are provided. In some examples, the polynucleotide comprises one or more nucleotide sequences encoding an antibody or antigen-binding portion thereof as described herein. In some examples, the polynucleotide comprises one or more nucleotide sequences encoding a polypeptide disclosed in Table 3 below. In some examples, the

polynucleotide comprises one or more nucleotide sequences encoding an antibody, or an antigen-binding portion thereof, that binds to human TIGIT, wherein the isolated polynucleotide comprises:

5 (a) the nucleotide sequence of SEQ ID NO:2, SEQ ID NO:20, SEQ ID NO:38, SEQ ID NO:56, SEQ ID NO:74, SEQ ID NO:92, SEQ ID NO:110, SEQ ID NO:128, SEQ ID NO:146, SEQ ID NO:164, SEQ ID NO:182, or SEQ ID NO:200; and/or

(b) the nucleotide sequence of SEQ ID NO:11, SEQ ID NO:29, SEQ ID NO:47, SEQ ID NO:65, SEQ ID NO:83, SEQ ID NO:101, SEQ ID NO:119, SEQ ID NO:137, SEQ ID NO:155, SEQ ID NO:173, SEQ ID NO:191, or SEQ ID NO:209.

10 **[0026a]** In a sixth aspect, there is provided an isolated polynucleotide comprising a nucleotide sequence encoding the antibody of the first or second aspect.

[0026b] In a seventh aspect, there is provided an isolated polynucleotide comprising a nucleotide sequence encoding an antibody, or an antigen-binding portion thereof, that binds to human TIGIT, wherein the isolated polynucleotide comprises:

15 (a) the nucleotide sequence of SEQ ID NO:2, SEQ ID NO:20, SEQ ID NO:38, SEQ ID NO:56, SEQ ID NO:74, SEQ ID NO:92, SEQ ID NO:110, SEQ ID NO:128, SEQ ID NO:146, SEQ ID NO:164, SEQ ID NO:182, or SEQ ID NO:200; and/or

(b) the nucleotide sequence of SEQ ID NO:11, SEQ ID NO:29, SEQ ID NO:47, SEQ ID NO:65, SEQ ID NO:83, SEQ ID NO:101, SEQ ID NO:119, SEQ ID NO:137, SEQ ID
20 NO:155, SEQ ID NO:173, SEQ ID NO:191, or SEQ ID NO:209.

[0027] In yet another example, vectors and host cells comprising a polynucleotide as described herein are provided. In another example, methods of producing an antibody comprising culturing a host cell as described herein under conditions suitable for producing the antibody are provided.

5 **[0027a]** In an eighth aspect, there is provided a vector comprising the polynucleotide of the sixth or seventh aspect.

[0027b] In a ninth aspect, there is provided a host cell comprising the polynucleotide of the sixth or seventh aspect or the vector of the eighth aspect.

10 **[0027c]** In a tenth aspect, there is provided a method of producing an antibody, comprising culturing the host cell of the ninth aspect under conditions suitable for producing the antibody.

[0028] In another example, kits (e.g., for use in a therapeutic method as described herein) are provided. In some examples, the kit comprises an isolated anti-TIGIT antibody or antigen-binding portion thereof as described herein, or a pharmaceutical composition
15 comprising an anti-TIGIT antibody or antigen-binding portion thereof as described herein; and further comprises an immuno-oncology agent. In some examples, the immuno-oncology agent is a PD-1 pathway inhibitor. In some examples, the PD-1 pathway inhibitor is an anti-PD1 antibody or an anti-PD-L1 antibody. In some examples, the PD-1 pathway inhibitor is an antagonist or inhibitor of a T cell coinhibitor. In some examples, the immuno-oncology agent
20 is an agonist of a T cell coactivator. In some examples, the immuno-oncology agent is an immune stimulatory cytokine.

[0028a] In an eleventh aspect, there is provided a kit comprising: the isolated antibody of the first or second aspect, the pharmaceutical composition of the third aspect; and an immune-oncology agent.

25 **[0029]** In another example, methods of treating a cancer in a subject are provided. In some examples, the method comprises administering to the subject a therapeutic amount of an isolated antibody or antigen-binding portion thereof as described herein, or a pharmaceutical composition as described herein, a bispecific antibody as described herein, or an antibody-drug conjugate as described herein.

30 **[0029a]** In a twelfth aspect, there is provided use of the isolated antibody of the first or second aspect, the pharmaceutical composition of the third aspect, the bispecific antibody of

the fourth aspect, or the antibody-drug conjugate of the fifth aspect in the manufacture of a medicament for treating a cancer in a subject.

[0030] In some examples, the cancer is a cancer that is enriched for expression of CD112 or CD115. In some examples, the cancer is a cancer that is enriched for T cells or natural killer (NK) cells that express TIGIT. In some examples, the cancer is bladder cancer, breast cancer, uterine cancer, cervical cancer, ovarian cancer, prostate cancer, testicular cancer, esophageal cancer, gastrointestinal cancer, pancreatic cancer, colorectal cancer, colon cancer, kidney cancer, head and neck cancer, lung cancer, stomach cancer, germ cell cancer, bone cancer, liver cancer, thyroid cancer, skin cancer, neoplasm of the central nervous system, lymphoma, leukemia, myeloma, or sarcoma. In some examples, the cancer is a lymphoma or a leukemia.

[0031] In some examples, the method further comprises administering to the subject a therapeutic amount of an immuno-oncology agent. In some examples, the immuno-oncology agent is a PD-1 pathway inhibitor. In some examples, the PD-1 pathway inhibitor is an anti-PD1 antibody or an anti-PD-L1 antibody. In some examples, the PD-1

pathway inhibitor is an antagonist or inhibitor of a T cell coinhibitor. In some examples, the immuno-oncology agent is an agonist of a T cell coactivator. In some examples, the immuno-oncology agent is an immune stimulatory cytokine. In some examples, the isolated antibody, the pharmaceutical composition, the bispecific antibody, or the antibody-drug conjugate is administered concurrently with the immuno-oncology agent. In some examples, the isolated antibody, the pharmaceutical composition, the bispecific antibody, or the antibody-drug conjugate is administered sequentially to the immuno-oncology agent.

BRIEF DESCRIPTION OF THE DRAWINGS

[0032] 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).

[0033] 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.

[0034] 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.

[0035] 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.

[0036] FIG. 5A-5B. Anti-TIGIT antibodies blocked CD155 interaction with TIGIT expressed on HEK 293 cells, for both human CD155 binding to HEK 293 cells expressing human TIGIT (A) and mouse CD155 binding to HEK 293 cells expressing mouse TIGIT (B). Results are shown for singlicate wells.

[0037] FIG. 6. Anti-TIGIT antibodies blocked human CD112 interaction with human TIGIT expressed on HEK 293 cells. Results are shown for singlicate wells.

WHAT IS CLAIMED IS:

1. An isolated antibody, or antigen-binding portion thereof, that binds to human TIGIT (T-cell immunoreceptor with Ig and ITIM domains), wherein the antibody or antigen-binding portion thereof has a binding affinity (K_D) for human TIGIT of less than 5 nM.
2. The isolated antibody of claim 1, wherein the antibody or antigen-binding portion thereof has a K_D for human TIGIT of less than 1 nM.
3. The isolated antibody of claim 1, wherein the antibody or antigen-binding portion thereof has a K_D for human TIGIT of less than 100 pM.
4. The isolated antibody of any of claims 1 to 3, wherein the antibody or antigen-binding portion thereof exhibits cross-reactivity with cynomolgus monkey TIGIT and/or mouse TIGIT.
5. The isolated antibody of claim 4, wherein the antibody or antigen-binding portion thereof exhibits cross-reactivity with both cynomolgus monkey TIGIT and mouse TIGIT.
6. The isolated antibody of any of claims 1 to 5, wherein the antibody or antigen-binding portion thereof blocks binding of CD155 to TIGIT.
7. The isolated antibody of any of claims 1 to 5, wherein the antibody or antigen-binding portion thereof blocks binding of CD112 to TIGIT.
8. The isolated antibody of any of claims 1 to 5, wherein the antibody or antigen-binding portion thereof blocks binding of both CD155 and CD112 to TIGIT.
9. The isolated antibody of any of claims 1 to 8, wherein the antibody or antigen-binding portion thereof binds to an epitope on human TIGIT that comprises one or both of amino acid positions 81 and 82.
10. The isolated antibody of claim 9, wherein the epitope comprises Phe at position 81.

11. The isolated antibody of claim 8, wherein the epitope comprises Lys or Ser at position 82.

12. The isolated antibody of any of claims 9 to 11, wherein the epitope comprises Phe at position 81 and Lys or Ser at position 82.

13. The isolated antibody of claim 12, wherein the epitope comprises Phe81 and Lys82.

14. The isolated antibody of any of claims 9 to 13, wherein the epitope is a discontinuous epitope.

15. The isolated antibody of any of claims 9 to 14, wherein the antibody or antigen-binding portion thereof 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.

16. The isolated antibody of claim 15, 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.

17. The isolated antibody of claim 16, 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.

18. The isolated antibody of claim 16, wherein the epitope comprises the amino acid residues Ala52, Gln53, Leu73, Gly74, Trp75, Pro79, Phe81, Lys82, Asp83, Arg84, Val85, and Ala86.

19. The isolated antibody of any of claims 9 to 18, wherein the epitope comprises the sequence ICNADLGWHISPSFK.

20. The isolated antibody of any of claims 1 to 19, wherein the antibody or antigen-binding portion thereof comprises one or more of:

(a) a heavy chain CDR1 comprising the 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, or SEQ ID NO:243;

(b) a heavy chain CDR2 comprising the 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, SEQ ID NO:204, SEQ ID NO:222, SEQ ID NO:225, SEQ ID NO:227, SEQ ID NO:229, SEQ ID NO:232, SEQ ID NO:234, SEQ ID NO:238, or SEQ ID NO:240;

(c) a heavy chain CDR3 comprising the sequence of any of SEQ ID NO:8, SEQ ID NO:26, SEQ ID NO:44, SEQ ID NO:62, SEQ ID NO:80, SEQ ID NO:98, SEQ ID NO:116, SEQ ID NO:134, SEQ ID NO:152, SEQ ID NO:170, SEQ ID NO:188, SEQ ID NO:206, SEQ ID NO:223, SEQ ID NO:228, SEQ ID NO:230, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:241, SEQ ID NO:242, or SEQ ID NO:244;

(d) a light chain CDR1 comprising the sequence of any of SEQ ID NO:13, SEQ ID NO:31, SEQ ID NO:49, SEQ ID NO:67, SEQ ID NO:85, SEQ ID NO:103, SEQ ID NO:121, SEQ ID NO:139, SEQ ID NO:157, SEQ ID NO:175, SEQ ID NO:193, or SEQ ID NO:211;

(e) a light chain CDR2 comprising the sequence of any of SEQ ID NO:15, SEQ ID NO:33, SEQ ID NO:51, SEQ ID NO:69, SEQ ID NO:87, SEQ ID NO:105, SEQ ID NO:123, SEQ ID NO:141, SEQ ID NO:159, SEQ ID NO:177, SEQ ID NO:195, or SEQ ID NO:213; or

(f) a light chain CDR3 comprising the sequence of any of SEQ ID NO:17, SEQ ID NO:35, SEQ ID NO:53, SEQ ID NO:71, SEQ ID NO:89, SEQ ID NO:107, SEQ ID NO:125, SEQ ID NO:143, SEQ ID NO:161, SEQ ID NO:179, SEQ ID NO:197, or SEQ ID NO:215.

21. The isolated antibody of claim 20, wherein the antibody or antigen-binding portion thereof 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: 76, 78, 80, 85, 87, and 89, respectively; or

- (f) SEQ ID NOs: 94, 96, 98, 103, 105, and 107, respectively; or
- (g) SEQ ID NOs: 112, 114, 116, 121, 123, and 125, respectively; or
- (h) SEQ ID NOs: 130, 132, 134, 139, 141, and 143, respectively; or
- (i) SEQ ID NOs: 148, 150, 152, 157, 159, and 161, respectively; or
- (j) SEQ ID NOs: 166, 168, 170, 175, 177, and 179, respectively; or
- (k) SEQ ID NOs: 184, 186, 188, 193, 195, and 197, respectively; or
- (l) SEQ ID NOs: 202, 204, 206, 211, 213, and 215, respectively; or
- (m) SEQ ID NOs: 221, 222, 223, 13, 15, and 17, respectively; or
- (n) SEQ ID NOs: 224, 225, 62, 67, 69, and 71, respectively; or
- (o) SEQ ID NOs: 226, 227, 228, 67, 69, and 71, respectively; or
- (p) SEQ ID NOs: 224, 229, 230, 67, 69, and 71, respectively; or
- (q) SEQ ID NOs: 224, 227, 230, 67, 69, and 71, respectively; or
- (r) SEQ ID NOs: 231, 232, 235, 103, 105, and 107, respectively; or
- (s) SEQ ID NOs: 233, 234, 236, 103, 105, and 107, respectively; or
- (t) SEQ ID NOs: 233, 234, 237, 103, 105, and 107, respectively; or
- (u) SEQ ID NOs: 166, 238, 170, 175, 177, and 179, respectively; or
- (v) SEQ ID NOs: 239, 240, 170, 175, 177, and 179, respectively; or
- (w) SEQ ID NOs: 239, 240, 241, 175, 177, and 179, respectively; or
- (x) SEQ ID NOs: 239, 240, 242, 175, 177, and 179, respectively; or
- (y) SEQ ID NOs: 243, 168, 244, 175, 177, and 179, respectively.

22. The isolated antibody of any of claims 1 to 21, wherein the antibody or antigen-binding portion thereof comprises:

(a) a heavy chain variable region comprising an amino acid sequence that has at least 90% sequence identity to SEQ ID NO:1, SEQ ID NO:19, SEQ ID NO:37, SEQ ID NO:55, SEQ ID NO:73, SEQ ID NO:91, SEQ ID NO:109, SEQ ID NO:127, SEQ ID NO:145, SEQ ID NO:163, SEQ ID NO:181, SEQ ID NO:199, SEQ ID NO:245, SEQ ID NO:246, SEQ ID NO:247, SEQ ID NO:248, SEQ ID NO:249, SEQ ID NO:250, SEQ ID NO:251, SEQ ID NO:252, SEQ ID NO:253, SEQ ID NO:254, SEQ ID NO:255, SEQ ID NO:256, or SEQ ID NO:257; and/or

(b) a light chain variable region comprising an amino acid sequence that has at least 90% sequence identity to SEQ ID NO:10, SEQ ID NO:28, SEQ ID NO:46, SEQ ID NO:64, SEQ ID NO:82, SEQ ID NO:100, SEQ ID NO:118, SEQ ID NO:136, SEQ ID NO:154, SEQ ID NO:172, SEQ ID NO:190, or SEQ ID NO:208.

23. The isolated antibody of claim 22, wherein the antibody or antigen-binding portion thereof comprises:

(a) a heavy chain variable region comprising an amino acid sequence that has at least 90% sequence identity to SEQ ID NO:1 or SEQ ID NO:245 and a light chain variable region comprising an amino acid sequence that has at least 90% sequence identity to SEQ ID NO:10; or

(b) a heavy chain variable region comprising an amino acid sequence that has at least 90% sequence identity to SEQ ID NO:19 and a light chain variable region comprising an amino acid sequence that has at least 90% sequence identity to SEQ ID NO:28; or

(c) a heavy chain variable region comprising an amino acid sequence that has at least 90% sequence identity to SEQ ID NO:37 and a light chain variable region comprising an amino acid sequence that has at least 90% sequence identity to SEQ ID NO:46; or

(d) 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; or

(e) a heavy chain variable region comprising an amino acid sequence that has at least 90% sequence identity to SEQ ID NO:73 and a light chain variable region comprising an amino acid sequence that has at least 90% sequence identity to SEQ ID NO:82; or

(f) a heavy chain variable region comprising an amino acid sequence that has at least 90% sequence identity to any one of SEQ ID NO:91, SEQ ID NO:250, SEQ ID NO:251, or SEQ ID NO:252 and a light chain variable region comprising an amino acid sequence that has at least 90% sequence identity to SEQ ID NO:100; or

(g) a heavy chain variable region comprising an amino acid sequence that has at least 90% sequence identity to SEQ ID NO:109 and a light chain variable region comprising an amino acid sequence that has at least 90% sequence identity to SEQ ID NO:118; or

(h) a heavy chain variable region comprising an amino acid sequence that has at least 90% sequence identity to SEQ ID NO:127 and a light chain variable region

comprising an amino acid sequence that has at least 90% sequence identity to SEQ ID NO:136; or

(i) a heavy chain variable region comprising an amino acid sequence that has at least 90% sequence identity to SEQ ID NO:145 and a light chain variable region comprising an amino acid sequence that has at least 90% sequence identity to SEQ ID NO:154; or

(j) a heavy chain variable region comprising an amino acid sequence that has at least 90% sequence identity to any one of SEQ ID NO:163, SEQ ID NO:253, SEQ ID NO:254, SEQ ID NO:255, SEQ ID NO:256, or SEQ ID NO:257 and a light chain variable region comprising an amino acid sequence that has at least 90% sequence identity to SEQ ID NO:172; or

(k) a heavy chain variable region comprising an amino acid sequence that has at least 90% sequence identity to SEQ ID NO:181 and a light chain variable region comprising an amino acid sequence that has at least 90% sequence identity to SEQ ID NO:190; or

(l) a heavy chain variable region comprising an amino acid sequence that has at least 90% sequence identity to SEQ ID NO:199 and a light chain variable region comprising an amino acid sequence that has at least 90% sequence identity to SEQ ID NO:208.

24. The isolated antibody of any of claims 1 to 23, wherein the antibody or antigen-binding portion thereof exhibits synergy with an anti-PD1 antibody or an anti-PD-L1 antibody.

25. An isolated antibody, or antigen-binding portion thereof, that binds to human TIGIT, wherein the antibody or antigen-binding portion thereof binds to an epitope on human TIGIT that comprises amino acid positions 81 and 82.

26. The isolated antibody of claim 25, wherein the epitope comprises Phe at position 81 and/or Lys or Ser at position 82.

27. The isolated antibody of claim 26, wherein the epitope comprises Phe81 and Lys82.

28. The isolated antibody of any of claims 25 to 27, wherein the epitope is a discontinuous epitope.

29. The isolated antibody of any of claims 25 to 28, wherein the antibody or antigen-binding portion thereof 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.

30. The isolated antibody of claim 29, 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.

31. The isolated antibody of claim 30, 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.

32. The isolated antibody of claim 30, wherein the epitope comprises the amino acid residues Ala52, Gln53, Leu73, Gly74, Trp75, Pro79, Phe81, Lys82, Asp83, Arg84, Val85, and Ala86.

33. The isolated antibody of any of claims 25 to 32, wherein the epitope comprises the sequence ICNADLGWHISPSFK.

34. The isolated antibody of any of claims 25 to 32, wherein the antibody or antigen-binding portion thereof comprises one or more of:

(a) a heavy chain CDR1 comprising the 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, or SEQ ID NO:243;

(b) a heavy chain CDR2 comprising the 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, SEQ ID NO:204, SEQ ID NO:222, SEQ ID NO:225, SEQ ID NO:227, SEQ ID NO:229, SEQ ID NO:232, SEQ ID NO:234, SEQ ID NO:238, or SEQ ID NO:240;

(c) a heavy chain CDR3 comprising the sequence of any of SEQ ID NO:8, SEQ ID NO:26, SEQ ID NO:44, SEQ ID NO:62, SEQ ID NO:80, SEQ ID NO:98, SEQ ID

NO:116, SEQ ID NO:134, SEQ ID NO:152, SEQ ID NO:170, SEQ ID NO:188, SEQ ID NO:206, SEQ ID NO:223, SEQ ID NO:228, SEQ ID NO:230, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:241, SEQ ID NO:242, or SEQ ID NO:244;

(d) a light chain CDR1 comprising the sequence of any of SEQ ID NO:13, SEQ ID NO:31, SEQ ID NO:49, SEQ ID NO:67, SEQ ID NO:85, SEQ ID NO:103, SEQ ID NO:121, SEQ ID NO:139, SEQ ID NO:157, SEQ ID NO:175, SEQ ID NO:193, or SEQ ID NO:211;

(e) a light chain CDR2 comprising the sequence of any of SEQ ID NO:15, SEQ ID NO:33, SEQ ID NO:51, SEQ ID NO:69, SEQ ID NO:87, SEQ ID NO:105, SEQ ID NO:123, SEQ ID NO:141, SEQ ID NO:159, SEQ ID NO:177, SEQ ID NO:195, or SEQ ID NO:213; or

(f) a light chain CDR3 comprising the sequence of any of SEQ ID NO:17, SEQ ID NO:35, SEQ ID NO:53, SEQ ID NO:71, SEQ ID NO:89, SEQ ID NO:107, SEQ ID NO:125, SEQ ID NO:143, SEQ ID NO:161, SEQ ID NO:179, SEQ ID NO:197, or SEQ ID NO:215.

35. The isolated antibody of claim 34, wherein the antibody or antigen-binding portion thereof 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: 76, 78, 80, 85, 87, and 89, respectively; or
- (f) SEQ ID NOs: 94, 96, 98, 103, 105, and 107, respectively; or
- (g) SEQ ID NOs: 112, 114, 116, 121, 123, and 125, respectively; or
- (h) SEQ ID NOs: 130, 132, 134, 139, 141, and 143, respectively; or
- (i) SEQ ID NOs: 148, 150, 152, 157, 159, and 161, respectively; or
- (j) SEQ ID NOs: 166, 168, 170, 175, 177, and 179, respectively; or
- (k) SEQ ID NOs: 184, 186, 188, 193, 195, and 197, respectively; or
- (l) SEQ ID NOs: 202, 204, 206, 211, 213, and 215, respectively; or
- (m) SEQ ID NOs: 221, 222, 223, 13, 15, and 17, respectively; or
- (n) SEQ ID NOs: 224, 225, 62, 67, 69, and 71, respectively; or
- (o) SEQ ID NOs: 226, 227, 228, 67, 69, and 71, respectively; or

- (p) SEQ ID NOs: 224, 229, 230, 67, 69, and 71, respectively; or
- (q) SEQ ID NOs: 224, 227, 230, 67, 69, and 71, respectively; or
- (r) SEQ ID NOs: 231, 232, 235, 103, 105, and 107, respectively; or
- (s) SEQ ID NOs: 233, 234, 236, 103, 105, and 107, respectively; or
- (t) SEQ ID NOs: 233, 234, 237, 103, 105, and 107, respectively; or
- (u) SEQ ID NOs: 166, 238, 170, 175, 177, and 179, respectively; or
- (v) SEQ ID NOs: 239, 240, 170, 175, 177, and 179, respectively; or
- (w) SEQ ID NOs: 239, 240, 241, 175, 177, and 179, respectively; or
- (x) SEQ ID NOs: 239, 240, 242, 175, 177, and 179, respectively; or
- (y) SEQ ID NOs: 243, 168, 244, 175, 177, and 179, respectively.

36. The isolated antibody of claim 34, wherein the antibody or antigen-binding portion thereof comprises:

- (a) a heavy chain variable region comprising an amino acid sequence that has at least 90% sequence identity to SEQ ID NO:1, SEQ ID NO:19, SEQ ID NO:37, SEQ ID NO:55, SEQ ID NO:73, SEQ ID NO:91, SEQ ID NO:109, SEQ ID NO:127, SEQ ID NO:145, SEQ ID NO:163, SEQ ID NO:181, SEQ ID NO:199, SEQ ID NO:245, SEQ ID NO:246, SEQ ID NO:247, SEQ ID NO:248, SEQ ID NO:249, SEQ ID NO:250, SEQ ID NO:251, SEQ ID NO:252, SEQ ID NO:253, SEQ ID NO:254, SEQ ID NO:255, SEQ ID NO:256, or SEQ ID NO:257; and/or
- (b) a light chain variable region comprising an amino acid sequence that has at least 90% sequence identity to SEQ ID NO:10, SEQ ID NO:28, SEQ ID NO:46, SEQ ID NO:64, SEQ ID NO:82, SEQ ID NO:100, SEQ ID NO:118, SEQ ID NO:136, SEQ ID NO:154, SEQ ID NO:172, SEQ ID NO:190, or SEQ ID NO:208.

37. The isolated antibody of claim 36, wherein the antibody or antigen-binding portion thereof comprises:

- (a) a heavy chain variable region comprising an amino acid sequence that has at least 90% sequence identity to SEQ ID NO:1 or SEQ ID NO:245 and a light chain variable region comprising an amino acid sequence that has at least 90% sequence identity to SEQ ID NO:10; or
- (b) a heavy chain variable region comprising an amino acid sequence that has at least 90% sequence identity to SEQ ID NO:19 and a light chain variable region

comprising an amino acid sequence that has at least 90% sequence identity to SEQ ID NO:28; or

(c) a heavy chain variable region comprising an amino acid sequence that has at least 90% sequence identity to SEQ ID NO:37 and a light chain variable region comprising an amino acid sequence that has at least 90% sequence identity to SEQ ID NO:46; or

(d) 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; or

(e) a heavy chain variable region comprising an amino acid sequence that has at least 90% sequence identity to SEQ ID NO:73 and a light chain variable region comprising an amino acid sequence that has at least 90% sequence identity to SEQ ID NO:82; or

(f) a heavy chain variable region comprising an amino acid sequence that has at least 90% sequence identity to any one of SEQ ID NO:91, SEQ ID NO:250, SEQ ID NO:251, or SEQ ID NO:252 and a light chain variable region comprising an amino acid sequence that has at least 90% sequence identity to SEQ ID NO:100; or

(g) a heavy chain variable region comprising an amino acid sequence that has at least 90% sequence identity to SEQ ID NO:109 and a light chain variable region comprising an amino acid sequence that has at least 90% sequence identity to SEQ ID NO:118; or

(h) a heavy chain variable region comprising an amino acid sequence that has at least 90% sequence identity to SEQ ID NO:127 and a light chain variable region comprising an amino acid sequence that has at least 90% sequence identity to SEQ ID NO:136; or

(i) a heavy chain variable region comprising an amino acid sequence that has at least 90% sequence identity to SEQ ID NO:145 and a light chain variable region comprising an amino acid sequence that has at least 90% sequence identity to SEQ ID NO:154; or

(j) a heavy chain variable region comprising an amino acid sequence that has at least 90% sequence identity to any one of SEQ ID NO:163, SEQ ID NO:253, SEQ ID NO:254, SEQ ID NO:255, SEQ ID NO:256, or SEQ ID NO:257 and a light chain variable

region comprising an amino acid sequence that has at least 90% sequence identity to SEQ ID NO:172; or

(k) a heavy chain variable region comprising an amino acid sequence that has at least 90% sequence identity to SEQ ID NO:181 and a light chain variable region comprising an amino acid sequence that has at least 90% sequence identity to SEQ ID NO:190; or

(l) a heavy chain variable region comprising an amino acid sequence that has at least 90% sequence identity to SEQ ID NO:199 and a light chain variable region comprising an amino acid sequence that has at least 90% sequence identity to SEQ ID NO:208.

38. The isolated antibody of any of claims 1 to 37, wherein the antibody is a monoclonal antibody.

39. The isolated antibody of any of claims 1 to 38, wherein the antibody is a humanized antibody.

40. The isolated antibody of any of claims 1 to 38, wherein the antibody is a fully human antibody.

41. The isolated antibody of any of claims 1 to 38, wherein the antibody is a chimeric antibody.

42. The isolated antibody of any of claims 1 to 38, wherein the antigen-binding fragment is a Fab, a F(ab')₂, a scFv, or a bivalent scFv.

43. A pharmaceutical composition comprising the isolated antibody of any of claims 1 to 42 and a pharmaceutically acceptable carrier.

44. A bispecific antibody comprising the antibody of any of claims 1 to 42.

45. An antibody-drug conjugate comprising the antibody of any of claims 1 to 42.

46. An isolated polynucleotide comprising a nucleotide sequence encoding the antibody of any of claims 1 to 42.

47. An isolated polynucleotide comprising a nucleotide sequence encoding an antibody, or an antigen-binding portion thereof, that binds to human TIGIT, wherein the isolated polynucleotide comprises:

(a) the nucleotide sequence of SEQ ID NO:2, SEQ ID NO:20, SEQ ID NO:38, SEQ ID NO:56, SEQ ID NO:74, SEQ ID NO:92, SEQ ID NO:110, SEQ ID NO:128, SEQ ID NO:146, SEQ ID NO:164, SEQ ID NO:182, or SEQ ID NO:200; and/or

(b) the nucleotide sequence of SEQ ID NO:11, SEQ ID NO:29, SEQ ID NO:47, SEQ ID NO:65, SEQ ID NO:83, SEQ ID NO:101, SEQ ID NO:119, SEQ ID NO:137, SEQ ID NO:155, SEQ ID NO:173, SEQ ID NO:191, or SEQ ID NO:209.

48. A vector comprising the polynucleotide of claim 46 or claim 47.

49. A host cell comprising the polynucleotide of claim 46 or claim 47 or the vector of claim 48.

50. A method of producing an antibody, comprising culturing the host cell of claim 49 under conditions suitable for producing the antibody.

51. A kit comprising:
the isolated antibody of any of claims 1 to 42, the pharmaceutical composition of claim 43; and
an immuno-oncology agent.

52. The kit of claim 51, wherein the immuno-oncology agent is a PD-1 pathway inhibitor.

53. The kit of claim 52, wherein the PD-1 pathway inhibitor is an anti-PD1 antibody or an anti-PD-L1 antibody.

54. The kit of claim 51, wherein the immuno-oncology agent is an antagonist or an inhibitor of a T cell coinhibitor.

55. The kit of claim 51, wherein the immuno-oncology agent is an agonist of a T cell coactivator.

56. The kit of claim 51, wherein the immuno-oncology agent is an immune stimulatory cytokine.

57. Use of the isolated antibody of any of claims 1 to 42, the pharmaceutical composition of claim 43, the bispecific antibody of claim 44, or the antibody-drug conjugate of claim 45 in the manufacture of a medicament for treating a cancer in a subject.

58. The use of claim 57, wherein the cancer is a cancer that is enriched for expression of CD112 or CD155.

59. The use of claim 57, wherein the cancer is a cancer that is enriched for T cells or natural killer (NK) cells that express TIGIT.

60. The use of any of claims 57 to 59, wherein the cancer is bladder cancer, breast cancer, uterine cancer, cervical cancer, ovarian cancer, prostate cancer, testicular cancer, esophageal cancer, gastrointestinal cancer, pancreatic cancer, colorectal cancer, colon cancer, kidney cancer, head and neck cancer, lung cancer, stomach cancer, germ cell cancer, bone cancer, liver cancer, thyroid cancer, skin cancer, neoplasm of the central nervous system, lymphoma, leukemia, myeloma, or sarcoma.

61. The use of claim 60, wherein the cancer is a lymphoma or a leukemia.

62. The use of any of claims 57 to 61, wherein the medicament is to be administered in combination with a therapeutic amount of an immuno-oncology agent.

63. The use of claim 62, wherein the immuno-oncology agent is a PD-1 pathway inhibitor.

64. The use of claim 63, wherein the PD-1 pathway inhibitor is an anti-PD1 antibody or an anti-PD-L1 antibody.

65. The use of claim 62, wherein the immuno-oncology agent is an antagonist or an inhibitor of a T cell coinhibitor.

66. The use of claim 62, wherein the immuno-oncology agent is an agonist of a T cell coactivator.

67. The use of claim 62, wherein the immuno-oncology agent is an immune stimulatory cytokine.

68. The use of any of claims 62 to 67, wherein the isolated antibody, the pharmaceutical composition, the bispecific antibody, or the antibody-drug conjugate is to be administered concurrently with the immuno-oncology agent.

69. The use of any of claims 62 to 67, wherein the isolated antibody, the pharmaceutical composition, the bispecific antibody, or the antibody-drug conjugate is to be administered sequentially to the immuno-oncology agent.