maturation/activation of myeloid DCs, and the induction of tolerogenic DCs by HLA-G was through disrupting the MHC class II presentation pathway (Ristich *et al.* Eur J Immunol. 2005).

An unmet medical need exists for patients that do not respond to T-cell therapy but may benefit from relief of tissue associated-macrophage/ MDSC-mediated tumor tolerance (*e.g.* myeloid “rich” tumors). ILT4 blockade would fill this need and would differentiate from current T-cell-targeted antibodies (*e.g.* anti-PD1, anti-TIGIT) by relieving suppression of tolerogenic myeloid cells in the tumor microenvironment.

Summary

The present disclosure provides antibodies or antigen-binding fragments thereof that bind to human ILT4. In certain examples, the antibody or antigen-binding fragment thereof binds to one or more amino acid residues in a human ILT4 epitope selected from the group consisting of LYREKKSASW (SEQ ID NO:59), TRIRPEL (SEQ ID NO:60), NGQF (SEQ ID NO:61), and HTGRYGCQ (SEQ ID NO:62). In certain examples, the antibody or antigen-binding fragment thereof protects the epitope from deuterium exchange with a deuterium source, such as D_2O. In one aspect, there is provided an antibody or antigen-binding fragment thereof that binds one or more amino acid residues in a human immunoglobulin-like transcript 4 (ILT4) epitope selected from the group consisting of LYREKKSASW (SEQ ID NO:59), TRIRPEL (SEQ ID NO:60), NGQF (SEQ ID NO:61), and HTGRYGCQ (SEQ ID NO:62) and protects the epitope from deuterium exchange in the presence of a deuterium source. In one example, the antibody or antigen-binding fragment thereof binds to one or more amino acid residues in the epitope LYREKKSASW (SEQ ID NO:59). In another example, the antibody or antigen-binding fragment thereof binds to one or more amino acid residues in the epitope TRIRPEL (SEQ ID NO:60). In yet another example, the antibody or antigen-binding fragment thereof binds to one or more amino acid residues in the epitope NGQF (SEQ ID NO:61). In still another example, the antibody or antigen-binding fragment thereof binds to one or more amino acid residues in the epitope HTGRYGCQ (SEQ ID NO:62). In yet still another example, the antibody or antigen-binding fragment thereof binds to one or more amino acid residues in two, three, or four ILT4 epitopes selected from the group consisting of LYREKKSASW (SEQ ID NO:59), TRIRPEL (SEQ ID NO:60), NGQF (SEQ ID NO:61), and HTGRYGCQ (SEQ ID NO:62). In one example, the antibody or antigen-binding fragment thereof binds to one or more amino acid residues in the epitope LYREKKSASW (SEQ ID NO:59) and protects the epitope from deuterium exchange with a deuterium source such as D_2O. In another

example, the antibody or antigen-binding fragment thereof binds to one or more amino acid residues in the epitope TRIRPEL (SEQ ID NO:60) and protects the epitope from deuterium exchange with a deuterium source such as D_2O. In yet another example, the antibody or antigen-binding fragment thereof binds to one or more amino acid residues in the epitope NGQF (SEQ ID NO:61) and protects the epitope from deuterium exchange with a deuterium source such as D_2O. In still another example, the antibody or antigen-

binding fragment thereof binds to one or more amino acid residues in the epitope HTGRYGCQ (SEQ ID NO:62) and protects the epitope from deuterium exchange with a deuterium source such as D_2O. In yet still another example, the antibody or antigen-binding fragment thereof binds to one or more amino acid residues in two, three, or four ILT4 epitopes selected from the group consisting of LYREKKSASW (SEQ ID NO:59), TRIRPEL (SEQ ID NO:60), NGQF (SEQ ID NO:61), and HTGRYGCQ (SEQ ID NO:62) and protects the epitopes from deuterium exchange with a deuterium source such as D_2O.

The present disclosure also provides an antibody or antigen-binding fragment thereof that binds to the same epitope of human ILT4 as any antibody or antigen-binding fragment thereof disclosed herein. In certain examples, the antibody or antigen-binding fragment thereof binds to the same epitope of human ILT4 as an antibody or antigen-binding fragment thereof comprising the heavy chain and light chain amino acid sequences set forth in SEQ ID NOs:1 and 3; 2 and 4; 2 and 5; 2 and 6; 2 and 7; 2 and 3; 8 and 11; 9 and 11; 10 and 11; 12 and 13; 14 and 15; 79 and 3; 80 and 4; 80 and 5; 80 and 6; 80 and 7; 80 and 3; 82 and 11; 83 and 11; 84 and 11; 85 and 13; and 86 and 15; respectively. In some examples, the antibody or antigen-binding fragment thereof binds to the same epitope of human ILT4 as an antibody or antigen-binding fragment thereof comprising the heavy chain variable domain and light chain variable domain amino acid sequences set forth in SEQ ID NOs:63 and 70; 57 and 71; 57 and 72; 57 and 73; 57 and 58; 57 and 70; 64 and 74; 65 and 74; 66 and 74; 67 and 75; 68 and 76; respectively.

In another aspect, there is provided an antibody or antigen-binding fragment thereof that competes with a reference antibody for binding to a human ILT4 epitope selected from the group consisting of LYREKKSASW (SEQ ID NO:59), TRIRPEL (SEQ ID NO:60), NGQF (SEQ ID NO:61), and HTGRYGCQ (SEQ ID NO:62), wherein the reference antibody comprises a heavy chain immunoglobulin comprising the amino acid sequence set forth in SEQ ID NO:2 and a light chain immunoglobulin comprising the amino acid sequence set forth in SEQ ID NO:7.

The present disclosure further provides an antibody or antigen-binding fragment thereof that competes for binding to human ILT4 with an antibody or antigen-binding fragment thereof disclosed herein. In certain examples, the antibody or antigen-binding fragment thereof competes for binding to human ILT4 with an antibody or fragment comprising the heavy chain and light chain amino acid sequences set forth in SEQ ID NOs:1 and 3; 2 and 4; 2 and 5; 2 and 6; 2 and 7; 2 and 3; 8 and 11; 9 and 11; 10 and 11; 12 and 13; 14 and 15; 79 and 3; 80 and 4; 80 and 5; 80 and 6; 80 and 7; 80 and 3; 82 and 11; 83 and 11; 84 and 11; 85 and 13; and 86 and 15; respectively. In some

examples, the antibody or antigen-binding fragment thereof competes for binding to human ILT4 with an antibody or fragment comprising the heavy chain variable domain and light chain variable domain amino acid sequences set forth in SEQ ID NOs:63 and 70; 57 and 71; 57 and 72; 57 and 73; 57 and 58; 57 and 70; 64 and 74; 65 and 74; 66 and 74; 67 and 75; 68 and 76; respectively.

In addition, the present disclosure provides an antibody or antigen-binding fragment thereof that binds human ILT4, comprising: (a) the complementarity determining region-L1 (CDR-L1), complementarity determining region-L2 (CDR-L2), and complementarity

determining region-L3 (CDR-L3) of a light chain variable (V_L) domain of an immunoglobulin chain that comprises the amino acid sequence set forth in SEQ ID NO: 3-7, 11, 13, 15, or 45; and/or (b) the complementarity determining region-H1 (CDR-H1), complementarity determining region-H2 (CDR-H2), and complementarity determining region-H3 (CDR-H3) of a heavy chain variable (V_H) domain of an immunoglobulin chain that comprises the amino acid sequence set forth in SEQ ID NO: 1, 2, 8-10, 12, 14, 44, or 79-86.

In an example of the disclosure, the antibody or antigen-binding fragment thereof comprises: (1) a V_H domain comprising: CDR-H1: GYYWS (SEQ ID NO: 16), CDR-H2: EINHXGSTNYNPSLKS wherein X is S or A (SEQ ID NO: 17); and CDR-H3: LPTRWVTTRYFDL (SEQ ID NO: 18); and/or, a V_L domain comprising: CDR-L1: TGSSSNIGAGYDVH (SEQ ID NO: 19), CDR-L2: GX_1X_2NRPS; wherein X_1 is S or A and X_2 is N, Q, E or D (SEQ ID NO: 20); and CDR-L3: QSFDNSLSAYV (SEQ ID NO: 21); (2) a V_H domain comprising: CDR-H1: SYAIS (SEQ ID NO: 22); CDR-H2: GIIPIFGTANYAQKFQG (SEQ ID NO: 23); and CDR-H3: $YFX_1X_2SGWYKGGAFDI$; wherein X_1 is D or S and X_2 is S or A (SEQ ID NO: 24); and/or, a V_L domain comprising: CDR-L1: TLRSGINVDTYRIH (SEQ ID NO: 25); CDR-L2: YKSDSDKHQGS (SEQ ID NO: 26); and CDR-L3: AIWYSSTWV (SEQ ID NO: 27); (3) a V_H domain comprising: CDR-H1: SYAMH (SEQ ID NO: 28); CDR-H2: VISYDGSNKYYADSVKG (SEQ ID NO: 29); and CDR-H3: VGEWIQLWSPFDY (SEQ ID NO: 30); and/or, a V_L domain comprising: CDR-L1: RASQGISSWLA (SEQ ID NO: 31); CDR-L2: AASSLQS (SEQ ID NO: 32); and CDR-L3: QQYNSYPPT (SEQ ID NO: 33); and/or (4) a V_H domain comprising: CDR-H1: ELSMH (SEQ ID NO: 34); CDR-H2: GFDPEDGETIYAQKFQG (SEQ ID NO: 35); and CDR-H3: AGPLYTIFGVVIIPDNWFDP (SEQ ID NO: 36); and/or, a V_L domain comprising: CDR-L1: TGSSSNIGAGYDVH (SEQ ID NO: 37); CDR-L2: GNSNRPS (SEQ ID NO: 38); and CDR-L3: QSYDSSLSGSGVV (SEQ ID NO: 39).

In another aspect, there is provided an antibody or antigen-binding fragment thereof that binds human ILT4, comprising:

(1) a heavy chain variable domain comprising:

CDR-H1: GYYWS (SEQ ID NO: 16),

CDR-H2: EINHXGSTNYNPSLKS wherein X is S or A (SEQ ID NO: 17), and

CDR-H3: LPTRWVTTRYFDL (SEQ ID NO: 18); and,

a light chain variable domain comprising:

CDR-L1: TGSSSNIGAGYDVH (SEQ ID NO: 19),

CDR-L2: GX_1X_2NRPS, wherein X_1 is N, Q, E or D and X_2 is S or A (SEQ ID NO: 20), and

CDR-L3: QSFDNSLSAYV (SEQ ID NO: 21);

(2) a heavy chain variable domain comprising:

CDR-H1: SYAIS (SEQ ID NO: 22),

CDR-H2: GIIPIFGTANYAQKFQG (SEQ ID NO: 23), and

CDR-H3: YFX_1X_2SGWYKGGAFDI, wherein X_1 is D or S and X_2 is S or A (SEQ ID NO: 24); and,

a light chain variable domain comprising:

CDR-L1: TLRSGINVDTYRIH (SEQ ID NO: 25),

CDR-L2: YKSDSDKHQGS (SEQ ID NO: 26), and

CDR-L3: AIWYSSTWV (SEQ ID NO: 27);

(3) a heavy chain variable domain comprising:

CDR-H1: SYAMH (SEQ ID NO: 28),

CDR-H2: VISYDGSNKYYADSVKG (SEQ ID NO: 29), and

CDR-H3: VGEWIQLWSPFDY (SEQ ID NO: 30); and,

a light chain variable domain comprising:

CDR-L1: RASQGISSWLA (SEQ ID NO: 31),

CDR-L2: AASSLQS (SEQ ID NO: 32), and

CDR-L3: QQYNSYPPT (SEQ ID NO: 33); or

(4) a heavy chain variable domain comprising:

CDR-H1: ELSMH (SEQ ID NO: 34),

CDR-H2: GFDPEDGETIYAQKFQG (SEQ ID NO: 35), and

CDR-H3: AGPLYTIFGVVIIPDNWFDP (SEQ ID NO: 36); and,

a light chain variable domain comprising:

CDR-L1: TGSSSNIGAGYDVH (SEQ ID NO: 37),

CDR-L2: GNSNRPS (SEQ ID NO: 38), and

CDR-L3: QSYDSSLSGSGVV (SEQ ID NO: 39).

In one example, the antibody or antigen-binding fragment comprises: a V_H domain comprising: CDR-H1: GYYWS (SEQ ID NO: 16), CDR-H2: EINHSGSTNYNPSLKS (SEQ ID NO: 47), and CDR-H3: LPTRWVTTRYFDL (SEQ ID NO: 18); and/or, a V_L domain comprising: CDR-L1: TGSSSNIGAGYDVH (SEQ ID NO: 19), CDR-L2: GNSNRPS(SEQ ID NO: 49), and CDR-L3: QSFDNSLSAYV (SEQ ID NO: 21).

In another example, the antibody or antigen-binding fragment comprises: a V_H domain comprising: CDR-H1: GYYWS (SEQ ID NO: 16), CDR-H2: EINHSGSTNYNPSLKS (SEQ ID NO: 47), and CDR-H3: LPTRWVTTRYFDL (SEQ ID NO: 18); and/or, a V_L domain comprising: CDR-L1: TGSSSNIGAGYDVH (SEQ ID NO: 19), CDR-L2: GQSNRPS(SEQ ID NO: 50), and CDR-L3: QSFDNSLSAYV (SEQ ID NO: 21).

In yet another example, the antibody or antigen-binding fragment thereof comprises: a V_H domain comprising: CDR-H1: GYYWS (SEQ ID NO: 16), CDR-H2: EINHSGSTNYNPSLKS (SEQ ID NO: 47), and CDR-H3: LPTRWVTTRYFDL (SEQ ID NO: 18); and/or, a V_L domain comprising: CDR-L1: TGSSSNIGAGYDVH (SEQ ID NO: 19), CDR-L2: GESNRPS(SEQ ID NO: 51), and CDR-L3: QSFDNSLSAYV (SEQ ID NO: 21).

In still another example, the antibody or antigen-binding fragment thereof comprises: a V_H domain comprising: CDR-H1: GYYWS (SEQ ID NO: 16), CDR-H2: EINHSGSTNYNPSLKS (SEQ ID NO: 47), and CDR-H3: LPTRWVTTRYFDL (SEQ ID NO: 18); and/or, a V_L domain comprising: CDR-L1: TGSSSNIGAGYDVH (SEQ ID NO: 19), CDR-L2: GDSNRPS(SEQ ID NO: 52), and CDR-L3: QSFDNSLSAYV (SEQ ID NO: 21).

In one example, the antibody or antigen-binding fragment thereof comprises: a V_H domain comprising: CDR-H1: GYYWS (SEQ ID NO: 16), CDR-H2: EINHSGSTNYNPSLKS (SEQ ID NO: 47), and CDR-H3: LPTRWVTTRYFDL (SEQ ID NO: 18); and/or, a V_L domain comprising: CDR-L1: TGSSSNIGAGYDVH (SEQ ID NO: 19), CDR-L2: GNANRPS(SEQ ID NO: 53), and CDR-L3: QSFDNSLSAYV (SEQ ID NO: 21).

In another example, the antibody or antigen-binding fragment thereof comprises: a V_H domain comprising: CDR-H1: GYYWS (SEQ ID NO: 16), CDR-H2: EINHSGSTNYNPSLKS (SEQ ID NO: 47), and CDR-H3: LPTRWVTTRYFDL (SEQ ID NO: 18); and/or, a V_L domain comprising: CDR-L1: TGSSSNIGAGYDVH (SEQ ID NO: 19), CDR-L2: GQANRPS(SEQ ID NO: 54), and CDR-L3: QSFDNSLSAYV (SEQ ID NO: 21).

In yet another example, the antibody or antigen-binding fragment thereof comprises: a V_H domain comprising: CDR-H1: GYYWS (SEQ ID NO: 16), CDR-H2: EINHSGSTNYNPSLKS (SEQ ID NO: 47), and CDR-H3: LPTRWVTTRYFDL (SEQ ID NO: 18); and/or, a V_L domain comprising: CDR-L1: TGSSSNIGAGYDVH (SEQ ID NO: 19), CDR-L2: GEANRPS(SEQ ID NO: 55), and CDR-L3: QSFDNSLSAYV (SEQ ID NO: 21).

In still another example, the antibody or antigen-binding fragment thereof comprises: a V_H domain comprising: CDR-H1: GYYWS (SEQ ID NO: 16), CDR-H2: EINHSGSTNYNPSLKS (SEQ ID NO: 47), and CDR-H3: LPTRWVTTRYFDL (SEQ ID NO: 18); and/or, a V_L domain comprising: CDR-L1: TGSSSNIGAGYDVH (SEQ ID NO: 19), CDR-L2: GDANRPS(SEQ ID NO: 56), and CDR-L3: QSFDNSLSAYV (SEQ ID NO: 21).

In one example, the antibody or antigen-binding fragment thereof comprises: a V_H domain comprising: CDR-H1: GYYWS (SEQ ID NO: 16), CDR-H2: EINHAGSTNYNPSLKS (SEQ ID NO: 48), and CDR-H3: LPTRWVTTRYFDL (SEQ ID NO: 18); and/or, a V_L domain comprising: CDR-L1: TGSSSNIGAGYDVH (SEQ ID NO: 19), CDR-L2: GNSNRPS(SEQ ID NO: 49), and CDR-L3: QSFDNSLSAYV (SEQ ID NO: 21).

In another example, the antibody or antigen-binding fragment thereof comprises: a V_H domain comprising: CDR-H1: GYYWS (SEQ ID NO: 16), CDR-H2: EINHAGSTNYNPSLKS (SEQ ID NO: 48), and CDR-H3: LPTRWVTTRYFDL (SEQ ID NO: 18); and/or, a V_L domain comprising: CDR-L1: TGSSSNIGAGYDVH (SEQ ID NO: 19), CDR-L2: GQSNRPS(SEQ ID NO: 50), and CDR-L3: QSFDNSLSAYV (SEQ ID NO: 21).

In yet another example, the antibody or antigen-binding fragment thereof comprises: a V_H domain comprising:CDR-H1: GYYWS (SEQ ID NO: 16), CDR-H2: EINHAGSTNYNPSLKS (SEQ ID NO: 48), and CDR-H3: LPTRWVTTRYFDL (SEQ ID NO: 18); and/or, a V_L domain comprising: CDR-L1: TGSSSNIGAGYDVH (SEQ ID NO: 19), CDR-L2: GESNRPS(SEQ ID NO: 51), and CDR-L3: QSFDNSLSAYV (SEQ ID NO: 21).

In still another example, the antibody or antigen-binding fragment thereof comprises: a V_H domain comprising: CDR-H1: GYYWS (SEQ ID NO: 16), CDR-H2: EINHAGSTNYNPSLKS (SEQ ID NO: 48), and CDR-H3: LPTRWVTTRYFDL (SEQ ID NO: 18); and/or, a V_L domain comprising: CDR-L1: TGSSSNIGAGYDVH (SEQ ID NO: 19), CDR-L2: GDSNRPS(SEQ ID NO: 52), and CDR-L3: QSFDNSLSAYV (SEQ ID NO: 21).

In one example, the antibody or antigen-binding fragment thereof comprises: a V_H domain comprising: CDR-H1: GYYWS (SEQ ID NO: 16), CDR-H2: EINHAGSTNYNPSLKS (SEQ ID NO: 48), and CDR-H3: LPTRWVTTRYFDL (SEQ ID NO: 18); and/or, a V_L domain comprising: CDR-L1: TGSSSNIGAGYDVH (SEQ ID NO: 19), CDR-L2: GNANRPS(SEQ ID NO: 53), and CDR-L3: QSFDNSLSAYV (SEQ ID NO: 21).

In another example, the antibody or antigen-binding fragment thereof comprises: a V_H domain comprising: CDR-H1: GYYWS (SEQ ID NO: 16), CDR-H2: EINHAGSTNYNPSLKS (SEQ ID NO: 48), and CDR-H3: LPTRWVTTRYFDL (SEQ ID NO: 18); and/or, a V_L domain comprising: CDR-L1: TGSSSNIGAGYDVH (SEQ ID NO: 19), CDR-L2: GQANRPS(SEQ ID NO: 54), and CDR-L3: QSFDNSLSAYV (SEQ ID NO: 21).

In yet another example, the antibody or antigen-binding fragment thereof comprises: a V_H domain comprising: CDR-H1: GYYWS (SEQ ID NO: 16), CDR-H2: EINHAGSTNYNPSLKS (SEQ ID NO: 48), and CDR-H3: LPTRWVTTRYFDL (SEQ ID NO: 18); and/or, a V_L domain comprising: CDR-L1: TGSSSNIGAGYDVH (SEQ ID NO: 19), CDR-L2: GEANRPS(SEQ ID NO: 55), and CDR-L3: QSFDNSLSAYV (SEQ ID NO: 21).

In still another example, the antibody or antigen-binding fragment thereof comprises: a V_H domain comprising: CDR-H1: GYYWS (SEQ ID NO: 16), CDR-H2: EINHAGSTNYNPSLKS (SEQ ID NO: 48), and CDR-H3: LPTRWVTTRYFDL (SEQ ID NO: 18); and/or, a V_L domain comprising: CDR-L1: TGSSSNIGAGYDVH (SEQ ID NO: 19), CDR-L2: GDANRPS(SEQ ID NO: 56), and CDR-L3: QSFDNSLSAYV (SEQ ID NO: 21).

In certain examples, the antibody or antigen-binding fragment thereof comprises a light chain immunoglobulin, a heavy chain immunoglobulin, or both a light and heavy chain immunoglobulin, wherein the light chain immunoglobulin has at least 90% amino acid sequence identity to the amino acid sequence set forth in SEQ ID NO:3, 4, 5, 6 ,7, 11, 13, 15, or 45, and/or the heavy chain immunoglobulin has at least 90% amino acid sequence identity to the amino acid sequence set forth in SEQ ID NO:1, 2, 8, 9, 10, 12, 14, 44, 79, 80, 81, 82, 83, 84, 85, or 86.

In some examples, the antibody or antigen-binding fragment thereof comprises a light chain immunoglobulin, a heavy chain immunoglobulin, or both a light and heavy chain immunoglobulin, wherein the light chain immunoglobulin comprises a light chain variable domain having at least 90% amino acid sequence identity to the amino acid sequence set forth in SEQ ID NO:70, 71, 72, 73, 58, 74, 75, 76, or 77, and/or the heavy chain immunoglobulin comprises a heavy chain variable domain having at least 90% amino acid sequence identity to the amino acid sequence set forth in SEQ ID NO:63, 57, 64, 65, 66, 67, 68, or 69.

In still other examples, the antibody or antigen-binding fragment thereof comprises a light chain immunoglobulin, a heavy chain immunoglobulin, or both a light and heavy chain immunoglobulin, wherein the light chain immunoglobulin comprises the amino acid sequence set forth in SEQ ID NO:3, 4, 5, 6 ,7, 11, 13, 15, or 45; and/or the heavy chain immunoglobulin comprises the amino acid sequence set forth in SEQ ID NO: 1, 2, 8, 9, 10, 12, 14, 44, 79, 80, 81, 82, 83, 84, 85, or 86.

In yet still other examples, the antibody or antigen-binding fragment thereof comprises a light chain immunoglobulin, a heavy chain immunoglobulin, or both a light and heavy chain immunoglobulin, wherein the light chain variable domain comprises the amino acid sequence set forth in SEQ ID NO:70, 71, 72, 73, 58, 74, 75, 76, or 77, and/or the heavy chain variable domain comprise the amino acid sequence set forth in SEQ ID NO:63, 57, 64, 65, 66, 67, 68, or 69.

Further provided is an antibody or antigen-binding fragment thereof comprising any of the following sets of heavy chain immunoglobulins and light chain immunoglobulins: (1) a heavy chain immunoglobulin comprising the amino acid sequence set forth in SEQ ID NO:1; a light chain immunoglobulin comprising the amino acid sequence set forth in SEQ ID NO:3; (2) a heavy chain immunoglobulin comprising the amino acid sequence set forth in SEQ ID NO:2; a light chain immunoglobulin comprising the amino acid sequence set forth in SEQ ID NO:4; (3) a heavy chain immunoglobulin comprising the amino acid sequence set forth in SEQ ID NO:2;a light chain immunoglobulin comprising the amino acid sequence set forth in SEQ ID NO:5; (4) a heavy chain immunoglobulin comprising the amino acid sequence set

forth in SEQ ID NO:11; (21) a heavy chain immunoglobulin comprising the amino acid sequence set forth in SEQ ID NO:85; a light chain immunoglobulin comprising the amino acid sequence set forth in SEQ ID NO:13; or (22) a heavy chain immunoglobulin comprising the amino acid sequence set forth in SEQ ID NO:86; a light chain immunoglobulin comprising the amino acid sequence set forth in SEQ ID NO:15.

In addition, provided herein is an antibody or antigen-binding fragment thereof comprising any of the following sets of heavy chain variable domain and light chain variable domain: (1) a heavy chain variable domain comprising the amino acid sequence set forth in SEQ ID NO:63; and a light chain variable domain comprising the amino acid sequence set forth in SEQ ID NO:70; (2) a heavy chain variable domain comprising the amino acid sequence set forth in SEQ ID NO:57; and a light chain variable domain comprising the amino acid sequence set forth in SEQ ID NO:71; (3) a heavy chain variable domain comprising the amino acid sequence set forth in SEQ ID NO:57; and a light chain variable domain comprising the amino acid sequence set forth in SEQ ID NO:72; (4) a heavy chain variable domain comprising the amino acid sequence set forth in SEQ ID NO:57; and a light chain variable domain comprising the amino acid sequence set forth in SEQ ID NO:73; (5) a heavy chain variable domain comprising the amino acid sequence set forth in SEQ ID NO:57; and a light chain variable domain comprising the amino acid sequence set forth in SEQ ID NO:58; (6) a heavy chain variable domain comprising the amino acid sequence set forth in SEQ ID NO:57; and a light chain variable domain comprising the amino acid sequence set forth in SEQ ID NO:70; (7) a heavy chain variable domain comprising the amino acid sequence set forth in SEQ ID NO:64; and a light chain variable domain comprising the amino acid sequence set forth in SEQ ID NO:74; (8) a heavy chain variable domain comprising the amino acid sequence set forth in SEQ ID NO:65; and a light chain variable domain comprising the amino acid sequence set forth in SEQ ID NO:74; (9) a heavy chain variable domain comprising the amino acid sequence set forth in SEQ ID NO:66; and a light chain variable domain comprising the amino acid sequence set forth in SEQ ID NO:74; (10) a heavy chain variable domain comprising the amino acid sequence set forth in SEQ ID NO:67; and a light chain variable domain comprising the amino acid sequence set forth in SEQ ID NO:75; or (11) a heavy chain variable domain comprising the amino acid sequence set forth in SEQ ID NO:68; and a light chain variable domain comprising the amino acid sequence set forth in SEQ ID NO:76.

In one preferred example, the antibody or antigen-binding fragment thereof comprises a V_H domain comprising the amino acid sequence set forth in SEQ ID NO:57; and a V_L domain comprising the amino acid sequence set forth in SEQ ID NO:58.

In another preferred example, the antibody or antigen-binding fragment thereof comprises: a heavy chain immunoglobulin comprising the amino acid sequence set forth in SEQ ID NO:2; and a light chain immunoglobulin comprising the amino acid sequence set forth in SEQ ID NO:7.

In yet another preferred example, the antibody or antigen-binding fragment thereof comprises: a heavy chain immunoglobulin comprising the amino acid sequence set forth in SEQ ID NO:80; and a light chain immunoglobulin comprising the amino acid sequence set forth in SEQ ID NO:7.

In one example, the antibody consists of two heavy chains and two light chains, wherein each light chain comprises the amino acid sequence set forth in SEQ ID NO:58 and each heavy chain comprises the amino acid sequence set forth in SEQ ID NO:57.

In another example, the antibody consists of two heavy chains and two light chains, wherein each light chain comprises the amino acid sequence set forth in SEQ ID NO:58 and each heavy chain comprises the amino acid sequence set forth in SEQ ID NO:57, wherein the light chain further comprises the amino acid sequence set forth in SEQ ID NO:90.

In yet another example, the antibody consists of two heavy chains and two light chains, wherein each light chain comprises the amino acid sequence set forth in SEQ ID NO:58 and each heavy chain comprises the amino acid sequence set forth in SEQ ID NO:57, wherein the heavy chain further comprises the amino acid sequence set forth in SEQ ID NO:89.

In still another example, the antibody consists of two heavy chains and two light chains, wherein each light chain comprises the amino acid sequence set forth in SEQ ID NO:58 and each heavy chain comprises the amino acid sequence set forth in SEQ ID NO:57, wherein the light chain further comprises the amino acid sequence set forth in SEQ ID NO:90 and the heavy chain further comprises the amino acid sequence set forth in SEQ ID NO:89.

In one example, the antibody consists of two heavy chains and two light chains, wherein each light chain comprises the amino acid sequence set forth in SEQ ID NO:7 and each heavy chain comprises the amino acid sequence set forth in SEQ ID NO:2.

In another example, the antibody consists of two heavy chains and two light chains, wherein each light chain consists of the amino acid sequence set forth in SEQ ID NO:7 and each heavy chain consists of the amino acid sequence set forth in SEQ ID NO:2.

In an example of the disclosure, the antibody or antigen-binding fragment thereof is glycosylated, *e.g.*, with engineered yeast N-linked glycans or Chinese hamster ovary

(CHO) cell N-linked glycans. In an example of the disclosure, the antibody or antigen-binding fragment thereof is an antibody.

In another aspect, the present disclosure provides a pharmaceutical composition comprising an antibody or antigen-binding fragment thereof disclosed herein. In certain examples, the composition further comprises a therapeutic agent (*e.g.*, pembrolizumab). In some examples, the composition further comprises a pharmaceutically acceptable carrier. In other examples, the composition further comprises a therapeutic agent (*e.g.*, pembrolizumab) and a pharmaceutically acceptable carrier.

In one example, the pharmaceutical composition comprises: (i) an antibody that consists of two heavy chains and two light chains, wherein each light chain consists of the amino acid sequence set forth in SEQ ID NO:7 and each heavy chain consists of the amino acid sequence set forth in SEQ ID NO:2, and (ii) pembrolizumab.

The present disclosure further provides a polypeptide (*e.g.*, an isolated polypeptide) which includes the immunoglobulin light chain and/or immunoglobulin heavy chain or a variable domain thereof of any antibody or antigen-binding fragment thereof disclosed herein. For example, in an example of the disclosure, the polypeptide comprises an amino acid sequence selected from the group consisting of SEQ ID NOs: 1-39, 44, 45, 47-58, 63-77, and 79-86. Also provided by the present disclosure is any polynucleotide (*e.g.*, DNA or RNA) that encodes any polypeptide disclosed herein. In another aspect, there is provided a polynucleotide comprising nucleotide sequence encoding a VH, a VL, both a VH and a VL, a heavy chain immunoglobulin, a light chain immunoglobulin, or both a heavy chain and a light chain immunoglobulin of the antibody or antigen-binding fragment disclosed herein. In another aspect, provided is a vector comprising the polynucleotide disclosed herein. In another aspect, the present disclosure also provides a host cell (*e.g.*, a CHO cell) comprising the polynucleotide or the vector disclosed herein.

The present disclosure provides a method for blocking binding of ILT4 to HLA-G, HLA-A, HLA-B, and/or HLA-F, *e.g.*, *in vitro* or *in vivo*, for example, in the body of a subject (*e.g.*, a human subject) in need thereof, comprising administering to the subject an effective amount of the antibody or antigen-binding fragment thereof disclosed herein. In certain examples, the method for blocking binding of ILT4 to HLA-G, HLA-A, HLA-B, and/or HLA-F further comprises performing a therapeutic procedure (*e.g.*, anti-cancer radiation therapy or surgical tumorectomy) to the subject. In some examples, the method for blocking binding of ILT4 to HLA-G, HLA-A, HLA-B, and/or HLA-F further comprises administering a therapeutic agent (*e.g.*, pembrolizumab) to

the subject. In other examples, the method for blocking binding of ILT4 to HLA-G, HLA-A, HLA-B, and/or HLA-F further comprises performing a therapeutic procedure (*e.g.*, anti-cancer radiation therapy or surgical tumorectomy) and administering a therapeutic agent (*e.g.*, pembrolizumab) to the subject.

In another aspect, there is provided an antibody or antigen-binding fragment thereof disclosed herein, for use in blocking the binding of ILT4 to HLA-G, HLA-A, HLA-B and/or HLA-F in a human subject.

The present disclosure also provides a method of treating a cancer in a subject (*e.g.*, a human subject), comprising administering to the subject an effective amount of the antibody or antigen-binding fragment thereof disclosed herein. In certain examples, the method of treating a cancer further comprises performing a therapeutic procedure (*e.g.*, anti-cancer radiation therapy or surgical tumorectomy) to the subject. In some examples, the method of treating a cancer further comprises administering a therapeutic agent (*e.g.*, pembrolizumab) to the subject. In other examples, the method of treating a cancer further comprises performing a therapeutic procedure (*e.g.*, anti-cancer radiation therapy or surgical tumorectomy) and administering a therapeutic agent (*e.g.*, pembrolizumab) to the subject.

The present disclosure also provides a method of producing the antibody or antigen-binding fragment thereof of the present disclosure or an immunoglobulin chain thereof (*e.g.*, a V_H and/or V_L thereof), comprising culturing a host cell (*e.g.*, a CHO cell) comprising a polynucleotide (*e.g.*, wherein the polynucleotide is in a vector and/or is integrated into one or more chromosomes of the host cell) encoding the antibody or antigen-binding fragment thereof or an immunoglobulin chain thereof to express the antibody or antigen-binding fragment thereof or an immunoglobulin chain thereof.

In another aspect, there is provided a method of producing the antibody or antigen-binding fragment thereof disclosed herein, comprising culturing the host cell disclosed herein to express the antibody or antigen-binding fragment thereof.

Also provided is a method of producing the antibody or antigen-binding fragment thereof of the present disclosure or an immunoglobulin chain thereof (*e.g.*, a V_H and/or V_L thereof), comprising: expressing a polynucleotide encoding the antibody or antigen-binding fragment thereof or an immunoglobulin chain thereof.

In another aspect, there is provided a method of producing the antibody or antigen-binding fragment thereof disclosed herein, comprising expressing the polynucleotide disclosed herein.

An antibody or antigen-binding fragment thereof that binds human ILT4 or an immunoglobulin chain thereof which is a product of said method is also part of the present disclosure. In another aspect, there is provided an antibody or antigen-binding fragment thereof that binds to human ILT4 which is a product of the method disclosed herein.

A method for detecting the presence of an ILT4 peptide or a fragment thereof in a sample also forms part of the present disclosure. The method comprises contacting the sample with an antibody or antigen-binding fragment of the present disclosure and detecting the presence of a complex between the antibody or

antigen-binding fragment and the ILT4 peptide or fragment thereof, wherein detection of the complex indicates the presence of the ILT4 peptide or fragment thereof. In another aspect, there is provided a method for detecting an ILT4 peptide or fragment thereof in a sample, comprising contacting the sample with the antibody or antigen-binding fragment thereof disclosed herein and detecting the presence of a complex between the antibody or antigen-binding fragment thereof and the ILT4 peptide or fragment thereof; wherein detection of the complex indicates the presence of the ILT4 peptide or fragment thereof. In an example of the disclosure, the method is performed *in vitro, e.g.*, in a biological sample, *e.g.*, surgical section or blood sample, of a subject. In another example, the method is performed *in vivo*, *e.g*., in the body of a subject. In yet another example, the subject is a human being.

In another aspect, there is provided use of the antibody or antigen-binding fragment thereof disclosed herein in the manufacture of a medicament for the treatment of cancer.

In another aspect, there is provided an antibody or antigen-binding fragment thereof disclosed herein for use in treating cancer.

In another aspect, there is provided an antibody that consists of two heavy chains and two light chains, wherein each light chain comprises the amino acid sequence set forth in SEQ ID NO:58 and each heavy chain comprises the amino acid sequence set forth in SEQ ID NO:57.

In another aspect, there is provided an antibody that consists of two heavy chains and two light chains, wherein each light chain comprises the amino acid sequence set forth in SEQ ID NO:7 and each heavy chain comprises the amino acid sequence set forth in SEQ ID NO:2.

In another aspect, there is provided an antibody that consists of two heavy chains and two light chains, wherein each light chain consists of the amino acid sequence set forth in SEQ ID NO:7 and each heavy chain consists of the amino acid sequence set forth in SEQ ID NO:2.

In another aspect, there is provided a pharmaceutical composition comprising: (i) an antibody that consists of two heavy chains and two light chains, wherein each light chain consists of the amino acid sequence set forth in SEQ ID NO:7 and each heavy chain consists of the amino acid sequence set forth in SEQ ID NO:2, and (ii) pembrolizumab.

Brief Description of the Figures

Figure 1. Deuterium labeling Heatmap of p1E1(G1) binding to ILT4-His.

We claim:

1. An antibody or antigen-binding fragment thereof that binds one or more amino acid residues in a human immunoglobulin-like transcript 4 (ILT4) epitope selected from the group consisting of LYREKKSASW (SEQ ID NO:59), TRIRPEL (SEQ ID NO:60), NGQF (SEQ ID NO:61), and HTGRYGCQ (SEQ ID NO:62) and protects the epitope from deuterium exchange in the presence of a deuterium source.

2. The antibody or antigen-binding fragment thereof of claim 1, wherein the ILT4 epitope is LYREKKSASW (SEQ ID NO:59).

3. The antibody or antigen-binding fragment thereof of claim 1, wherein the ILT4 epitope is TRIRPEL (SEQ ID NO:60).

4. The antibody or antigen-binding fragment thereof of claim 1, wherein the ILT4 epitope is NGQF (SEQ ID NO:61).

5. The antibody or antigen-binding fragment thereof of claim 1, wherein the ILT4 epitope is HTGRYGCQ (SEQ ID NO:62).

6. An antibody or antigen-binding fragment thereof that competes with a reference antibody for binding to a human ILT4 epitope selected from the group consisting of LYREKKSASW (SEQ ID NO:59), TRIRPEL (SEQ ID NO:60), NGQF (SEQ ID NO:61), and HTGRYGCQ (SEQ ID NO:62), wherein the reference antibody comprises a heavy chain immunoglobulin comprising the amino acid sequence set forth in SEQ ID NO:2 and a light chain immunoglobulin comprising the amino acid sequence set forth in SEQ ID NO:7.

7. The antibody or antigen-binding fragment thereof of claim 6, wherein the ILT4 epitope is LYREKKSASW (SEQ ID NO:59).

8. The antibody or antigen-binding fragment thereof of claim 6, wherein the ILT4 epitope is TRIRPEL (SEQ ID NO:60).

9. The antibody or antigen-binding fragment thereof of claim 6, wherein the ILT4 epitope is NGQF (SEQ ID NO:61).

10. The antibody or antigen-binding fragment thereof of claim 6, wherein the ILT4 epitope is HTGRYGCQ (SEQ ID NO:62).

11. An antibody or antigen-binding fragment thereof that binds human ILT4, comprising:
(1) a heavy chain variable domain comprising:
CDR-H1: GYYWS (SEQ ID NO: 16),
CDR-H2: EINHXGSTNYNPSLKS wherein X is S or A (SEQ ID NO: 17), and
CDR-H3: LPTRWVTTRYFDL (SEQ ID NO: 18); and,
a light chain variable domain comprising:
CDR-L1: TGSSSNIGAGYDVH (SEQ ID NO: 19),
CDR-L2: GX_1X_2NRPS, wherein X_1 is N, Q, E or D and X_2 is S or A (SEQ ID NO: 20), and
CDR-L3: QSFDNSLSAYV (SEQ ID NO: 21);
(2) a heavy chain variable domain comprising:
CDR-H1: SYAIS (SEQ ID NO: 22),
CDR-H2: GIIPIFGTANYAQKFQG (SEQ ID NO: 23), and
CDR-H3: $YFX_1X_2SGWYKGGAFDI$, wherein X_1 is D or S and X_2 is S or A (SEQ ID NO: 24); and,
a light chain variable domain comprising:
CDR-L1: TLRSGINVDTYRIH (SEQ ID NO: 25),
CDR-L2: YKSDSDKHQGS (SEQ ID NO: 26), and
CDR-L3: AIWYSSTWV (SEQ ID NO: 27);
(3) a heavy chain variable domain comprising:
CDR-H1: SYAMH (SEQ ID NO: 28),
CDR-H2: VISYDGSNKYYADSVKG (SEQ ID NO: 29), and
CDR-H3: VGEWIQLWSPFDY (SEQ ID NO: 30); and,
a light chain variable domain comprising:
CDR-L1: RASQGISSWLA (SEQ ID NO: 31),
CDR-L2: AASSLQS (SEQ ID NO: 32), and
CDR-L3: QQYNSYPPT (SEQ ID NO: 33); or
(4) a heavy chain variable domain comprising:
CDR-H1: ELSMH (SEQ ID NO: 34),
CDR-H2: GFDPEDGETIYAQKFQG (SEQ ID NO: 35), and
CDR-H3: AGPLYTIFGVVIIPDNWFDP (SEQ ID NO: 36); and,
a light chain variable domain comprising:

CDR-L1: TGSSSNIGAGYDVH (SEQ ID NO: 37),
CDR-L2: GNSNRPS (SEQ ID NO: 38), and
CDR-L3: QSYDSSLSGSGVV (SEQ ID NO: 39).

12. The antibody or antigen-binding fragment thereof of claim 11, comprising:
a heavy chain variable domain comprising:
CDR-H1: GYYWS (SEQ ID NO: 16),
CDR-H2: EINHAGSTNYNPSLKS (SEQ ID NO: 48), and
CDR-H3: LPTRWVTTRYFDL (SEQ ID NO: 18); and,
a light chain variable domain comprising:
CDR-L1: TGSSSNIGAGYDVH (SEQ ID NO: 19),
CDR-L2: GDSNRPS(SEQ ID NO: 52), and
CDR-L3: QSFDNSLSAYV (SEQ ID NO: 21).

13. The antibody or antigen-binding fragment thereof of claim 11, comprising:
a light chain immunoglobulin having at least 90% amino acid sequence identity to the amino acid sequence set forth in SEQ ID NO:3, 4, 5, 6 ,7, 11, 13, 15, or 45, and/or
a heavy chain immunoglobulin having at least 90% amino acid sequence identity to the amino acid sequence set forth in SEQ ID NO:1, 2, 8, 9, 10, 12, 14, 44, 79, 80, 81, 82, 83, 84, 85, or 86.

14. The antibody or antigen-binding fragment thereof of claim 11, comprising:
a light chain immunoglobulin comprising a light chain variable domain having at least 90% amino acid sequence identity to the amino acid sequence set forth in SEQ ID NO:70, 71, 72, 73, 58, 74, 75, 76, or 77, and/or
a heavy chain immunoglobulin comprising a heavy chain variable domain having at least 90% amino acid sequence identity to the amino acid sequence set forth in SEQ ID NO:63, 57, 64, 65, 66, 67, 68, or 69.

15. The antibody or antigen-binding fragment thereof of claim 11, comprising:
a light chain immunoglobulin comprising the amino acid sequence set forth in SEQ ID NO:3, 4, 5, 6 ,7, 11, 13, 15, or 45; and/or
a heavy chain immunoglobulin comprising the amino acid sequence set forth in SEQ ID NO: 1, 2, 8, 9, 10, 12, 14, 44, 79, 80, 81, 82, 83, 84, 85, or 86.

16. The antibody or antigen-binding fragment thereof of claim 11, comprising:

a light chain variable domain comprising the amino acid sequence set forth in SEQ ID NO:70, 71, 72, 73, 58, 74, 75, 76, or 77, and/or

a heavy chain variable domain comprising the amino acid sequence set forth in SEQ ID NO:63, 57, 64, 65, 66, 67, 68, or 69.

17. The antibody or antigen-binding fragment thereof of claim 11, comprising:

(1)

a heavy chain immunoglobulin comprising the amino acid sequence set forth in SEQ ID NO: 1 or 79; and

a light chain immunoglobulin comprising the amino acid sequence set forth in SEQ ID NO: 3;

(2)

a heavy chain immunoglobulin comprising the amino acid sequence set forth in SEQ ID NO: 2 or 80; and

a light chain immunoglobulin comprising the amino acid sequence set forth in SEQ ID NO: 4;

(3)

a heavy chain immunoglobulin comprising the amino acid sequence set forth in SEQ ID NO: 2 or 80; and

a light chain immunoglobulin comprising the amino acid sequence set forth in SEQ ID NO: 5;

(4)

a heavy chain immunoglobulin comprising the amino acid sequence set forth in SEQ ID NO: 2 or 80; and

a light chain immunoglobulin comprising the amino acid sequence set forth in SEQ ID NO: 6;

(5)

a heavy chain immunoglobulin comprising the amino acid sequence set forth in SEQ ID NO: 2 or 80; and

a light chain immunoglobulin comprising the amino acid sequence set forth in SEQ ID NO: 7;

(6)

a heavy chain immunoglobulin comprising the amino acid sequence set forth in SEQ ID NO: 2 or 80; and

a light chain immunoglobulin comprising the amino acid sequence set forth in SEQ ID NO: 3;

(7)
a heavy chain immunoglobulin comprising the amino acid sequence set forth in SEQ ID NO: 8 or 82; and
a light chain immunoglobulin comprising the amino acid sequence set forth in SEQ ID NO: 11;
(8)
a heavy chain immunoglobulin comprising the amino acid sequence set forth in SEQ ID NO: 9 or 83; and
a light chain immunoglobulin comprising the amino acid sequence set forth in SEQ ID NO: 11;
(9)
a heavy chain immunoglobulin comprising the amino acid sequence set forth in SEQ ID NO: 10 or 84; and
a light chain immunoglobulin comprising the amino acid sequence set forth in SEQ ID NO: 11;
(10)
a heavy chain immunoglobulin comprising the amino acid sequence set forth in SEQ ID NO: 12 or 85; and
a light chain immunoglobulin comprising the amino acid sequence set forth in SEQ ID NO: 13; or
(11)
a heavy chain immunoglobulin comprising the amino acid sequence set forth in SEQ ID NO: 14 or 86; and
a light chain immunoglobulin comprising the amino acid sequence set forth in SEQ ID NO: 15.

18. The antibody or antigen-binding fragment thereof of claim 11, comprising:
(1)
a heavy chain variable domain comprising the amino acid sequence set forth in SEQ ID NO:63; and
a light chain variable domain comprising the amino acid sequence set forth in SEQ ID NO:70;
(2)
a heavy chain variable domain comprising the amino acid sequence set forth in SEQ ID NO:57; and

a light chain variable domain comprising the amino acid sequence set forth in SEQ ID NO:71;

(3)

a heavy chain variable domain comprising the amino acid sequence set forth in SEQ ID NO:57; and

a light chain variable domain comprising the amino acid sequence set forth in SEQ ID NO:72;

(4)

a heavy chain variable domain comprising the amino acid sequence set forth in SEQ ID NO:57; and

a light chain variable domain comprising the amino acid sequence set forth in SEQ ID NO:73;

(5)

a heavy chain variable domain comprising the amino acid sequence set forth in SEQ ID NO:57; and

a light chain variable domain comprising the amino acid sequence set forth in SEQ ID NO:58;

(6)

a heavy chain variable domain comprising the amino acid sequence set forth in SEQ ID NO:57; and

a light chain variable domain comprising the amino acid sequence set forth in SEQ ID NO:70;

(7)

a heavy chain variable domain comprising the amino acid sequence set forth in SEQ ID NO:64; and

a light chain variable domain comprising the amino acid sequence set forth in SEQ ID NO:74;

(8)

a heavy chain variable domain comprising the amino acid sequence set forth in SEQ ID NO:65; and

a light chain variable domain comprising the amino acid sequence set forth in SEQ ID NO:74;

(9)

a heavy chain variable domain comprising the amino acid sequence set forth in SEQ ID NO:66; and

a light chain variable domain comprising the amino acid sequence set forth in SEQ ID NO:74;

(10)

a heavy chain variable domain comprising the amino acid sequence set forth in SEQ ID NO:67; and

a light chain variable domain comprising the amino acid sequence set forth in SEQ ID NO:75; or

(11)

a heavy chain variable domain comprising the amino acid sequence set forth in SEQ ID NO:68; and

a light chain variable domain comprising the amino acid sequence set forth in SEQ ID NO:76.

19. The antibody or antigen-binding fragment thereof of claim 11, comprising:

a heavy chain variable domain comprising the amino acid sequence set forth in SEQ ID NO:57; and

a light chain variable domain comprising the amino acid sequence set forth in SEQ ID NO:58.

20. The antibody or antigen-binding fragment thereof of claim 11, comprising:

a heavy chain immunoglobulin comprising the amino acid sequence set forth in SEQ ID NO:2; and

a light chain immunoglobulin comprising the amino acid sequence set forth in SEQ ID NO:7.

21. The antibody or antigen-binding fragment thereof of claim 11, comprising:

a heavy chain immunoglobulin comprising the amino acid sequence set forth in SEQ ID NO:80; and

a light chain immunoglobulin comprising the amino acid sequence set forth in SEQ ID NO:7.

22. The antibody or antigen-binding fragment thereof of any one of claims 1-21, wherein the antibody or antigen-binding fragment thereof is glycosylated with engineered yeast N-linked glycans or CHO N-linked glycans.

23. A pharmaceutical composition comprising the antibody or antigen-binding fragment thereof of any of claims 1-22.

24. The pharmaceutical composition of claim 23, further comprises a therapeutic agent.

25. The pharmaceutical composition of claim 23 or 24, further comprises a pharmaceutically acceptable carrier.

26. A polynucleotide comprising nucleotide sequence encoding a VH, a VL, both a VH and a VL, a heavy chain immunoglobulin, a light chain immunoglobulin, or both a heavy chain and a light chain immunoglobulin of the antibody or antigen-binding fragment according to any one of the claims 1-21.

27. A vector comprising the polynucleotide of claim 26.

28. A host cell comprising the polynucleotide of claim 26 or the vector of claim 27.

29. An antibody or antigen-binding fragment thereof of any one of claims 1-22, for use in blocking the binding of ILT4 to HLA-G, HLA-A, HLA-B and/or HLA-F in a human subject.

30. The antibody or antigen-binding fragment thereof of any one of claims 1-22 for use according to claim 29, further comprising a therapeutic procedure to be performed and/or a therapeutic agent to be administered to the human subject.

31. A method of producing the antibody or antigen-binding fragment thereof of any one of claims 1-22, comprising culturing the host cell of claim 28 to express the antibody or antigen-binding fragment thereof.

32. A method of producing the antibody or antigen-binding fragment thereof of any one of claims 1-22, comprising expressing the polynucleotide of claim 26.

33. An antibody or antigen-binding fragment thereof that binds to human ILT4 which is a product of the method of claim 31 or 32.

34. A method for detecting an ILT4 peptide or fragment thereof in a sample, comprising contacting the sample with the antibody or antigen-binding fragment thereof of any one

of claims 1-22 and detecting the presence of a complex between the antibody or antigen-binding fragment thereof and the ILT4 peptide or fragment thereof; wherein detection of the complex indicates the presence of the ILT4 peptide or fragment thereof.

35. Use of the antibody or antigen-binding fragment thereof of any one of claims 1-22 in the manufacture of a medicament for the treatment of cancer.

36. An antibody or antigen-binding fragment thereof of any one of claims 1-22 for use in treating cancer.

37. An antibody that consists of two heavy chains and two light chains, wherein each light chain comprises the amino acid sequence set forth in SEQ ID NO:58 and each heavy chain comprises the amino acid sequence set forth in SEQ ID NO:57.

38. The antibody of claim 37, wherein the light chain further comprises the amino acid sequence set forth in SEQ ID NO:90 and/or the heavy chain further comprises the amino acid sequence set forth in SEQ ID NO:89.

39. An antibody that consists of two heavy chains and two light chains, wherein each light chain comprises the amino acid sequence set forth in SEQ ID NO:7 and each heavy chain comprises the amino acid sequence set forth in SEQ ID NO:2.

40. An antibody that consists of two heavy chains and two light chains, wherein each light chain consists of the amino acid sequence set forth in SEQ ID NO:7 and each heavy chain consists of the amino acid sequence set forth in SEQ ID NO:2.

41. A pharmaceutical composition comprising: (i) an antibody that consists of two heavy chains and two light chains, wherein each light chain consists of the amino acid sequence set forth in SEQ ID NO:7 and each heavy chain consists of the amino acid sequence set forth in SEQ ID NO:2, and (ii) pembrolizumab.