

WHAT IS CLAIMED:

1. A binding agent comprising an antigen-binding domain, wherein the antigen binding domain binds specifically to both human immunoglobulin-like transcript 2 (ILT2) and human immunoglobulin-like transcript 4 (ILT4).

2. The binding agent of claim 1, wherein the antigen-binding domain comprises:
~~a heavy chain variable region a VH comprising a heavy chain variable region CDR1 (VH-CDR1), a heavy chain variable region CDR2 (VH-CDR2), and a heavy chain variable region CDR3 (VH-CDR3) from the amino acid sequence of SEQ ID NO:144; and a light chain variable region VL comprising a light chain variable region CDR1 (VL-CDR1), a light chain variable region CDR2 (VL-CDR2), and a light chain variable region CDR3 (VL-CDR3) from the amino acid sequence of SEQ ID NO:145;~~

~~a heavy chain variable region comprising a heavy chain variable region CDR1 (VH-CDR1), a heavy chain variable region CDR2 (VH-CDR2), and a heavy chain variable region CDR3 (VH-CDR3) from the amino acid sequence of SEQ ID NO:139; and a light chain variable region comprising a light chain variable region CDR1 (VL-CDR1), a light chain variable region CDR2 (VL-CDR2), and a light chain variable region CDR3 (VL-CDR3) from the amino acid sequence of SEQ ID NO:140;~~

~~a heavy chain variable region comprising a heavy chain variable region CDR1 (VH-CDR1), a heavy chain variable region CDR2 (VH-CDR2), and a heavy chain variable region CDR3 (VH-CDR3) from the amino acid sequence of SEQ ID NO:133; and a light chain variable region comprising a light chain variable region CDR1 (VL-CDR1), a light chain variable region CDR2 (VL-CDR2), and a light chain variable region CDR3 (VL-CDR3) from the amino acid sequence of SEQ ID NO:134;~~

~~a heavy chain variable region comprising a heavy chain variable region CDR1 (VH-CDR1), a heavy chain variable region CDR2 (VH-CDR2), and a heavy chain variable region CDR3 (VH-CDR3) from the amino acid sequence of SEQ ID NO:143; and a light chain variable region comprising a light chain variable region CDR1 (VL-CDR1), a light chain variable region CDR2 (VL-CDR2), and a light chain variable region CDR3 (VL-CDR3) from the amino acid sequence of SEQ ID NO:142;~~

~~a heavy chain variable region comprising a heavy chain variable region CDR1 (VH-CDR1), a heavy chain variable region CDR2 (VH-CDR2), and a heavy chain variable region CDR3 (VH-CDR3) from the amino acid sequence of SEQ ID NO:131; and a light chain variable region~~

~~comprising a light chain variable region CDR1 (VL-CDR1), a light chain variable region CDR2 (VL-CDR2), and a light chain variable region CDR3 (VL-CDR3) from the amino acid sequence of SEQ ID NO:132;~~

~~a heavy chain variable region comprising a heavy chain variable region CDR1 (VH-CDR1), a heavy chain variable region CDR2 (VH-CDR2), and a heavy chain variable region CDR3 (VH-CDR3) from the amino acid sequence of SEQ ID NO:137; and a light chain variable region comprising a light chain variable region CDR1 (VL-CDR1), a light chain variable region CDR2 (VL-CDR2), and a light chain variable region CDR3 (VL-CDR3) from the amino acid sequence of SEQ ID NO:138;~~

~~a heavy chain variable region comprising a heavy chain variable region CDR1 (VH-CDR1), a heavy chain variable region CDR2 (VH-CDR2), and a heavy chain variable region CDR3 (VH-CDR3) from the amino acid sequence of SEQ ID NO:135; and a light chain variable region comprising a light chain variable region CDR1 (VL-CDR1), a light chain variable region CDR2 (VL-CDR2), and a light chain variable region CDR3 (VL-CDR3) from the amino acid sequence of SEQ ID NO:136; or~~

~~a heavy chain variable region comprising a heavy chain variable region CDR1 (VH-CDR1), a heavy chain variable region CDR2 (VH-CDR2), and a heavy chain variable region CDR3 (VH-CDR3) from the amino acid sequence of SEQ ID NO:141; and a light chain variable region comprising a light chain variable region CDR1 (VL-CDR1), a light chain variable region CDR2 (VL-CDR2), and a light chain variable region CDR3 (VL-CDR3) from the amino acid sequence of SEQ ID NO:142.~~

3. The binding agent of claim 2, wherein:

(a) ~~the heavy chain variable region comprises the VH-CDR1 having~~
comprises the amino acid sequence of SEQ ID NO:115, the VH-CDR2
~~having~~comprises the amino acid sequence of SEQ ID NO:112, ~~and the VH-~~
CDR3 ~~having~~comprises the amino acid sequence of SEQ ID NO:107; ~~and the~~
~~light chain variable region comprises,~~ the VL-CDR1 ~~having~~comprises the
amino acid sequence of SEQ ID NO:89, the VL-CDR2 ~~having~~comprises the
amino acid sequence of SEQ ID NO:90, and the VL-CDR3 ~~having~~comprises
the amino acid sequence of SEQ ID NO:91;

(b) ~~the heavy chain variable region comprises the VH-CDR1~~
~~having~~comprises the amino acid sequence of SEQ ID NO:111, the VH-CDR2
~~having~~comprises the amino acid sequence of SEQ ID NO:112, ~~and the VH-~~

CDR3 having comprises the amino acid sequence of SEQ ID NO:107;₁ ~~and the light chain variable region comprises~~ the VL-CDR1 having comprises the amino acid sequence of SEQ ID NO:89, the VL-CDR2 having comprises the amino acid sequence of SEQ ID NO:90, and the VL-CDR3 ~~having comprises~~ the amino acid sequence of SEQ ID NO:91;

(c) ~~the heavy chain variable region comprises~~ the VH-CDR1 having comprises the amino acid sequence of SEQ ID NO:76, the VH-CDR2 having comprises the amino acid sequence of SEQ ID NO:113, ~~and the VH-CDR3 having comprises~~ the amino acid sequence of SEQ ID NO:107;₁ ~~and the light chain variable region comprises~~ the VL-CDR1 having comprises the amino acid sequence of SEQ ID NO:89, the VL-CDR2 having comprises the amino acid sequence of SEQ ID NO:90, and the VL-CDR3 having comprises the amino acid sequence of SEQ ID NO:91;

(d) ~~a heavy chain variable region comprises~~ the VH-CDR1 having comprises the amino acid sequence of SEQ ID NO:111, the VH-CDR2 having comprises the amino acid sequence of SEQ ID NO:114, ~~and the VH-CDR3 having comprises~~ the amino acid sequence of SEQ ID NO:107;₁ ~~and the light chain variable region comprises~~ the VL-CDR1 having comprises the amino acid sequence of SEQ ID NO:89, the VL-CDR2 having comprises the amino acid sequence of SEQ ID NO:90, and the VL-CDR3 ~~having comprises~~ the amino acid sequence of SEQ ID NO:91; or

(e) ~~a heavy chain variable region comprises~~ the VH-CDR1 having comprises the amino acid sequence of SEQ ID NO:116, the VH-CDR2 having comprises the amino acid sequence of SEQ ID NO:124, ~~and the VH-CDR3 having comprises~~ the amino acid sequence of SEQ ID NO:110;₁ ~~and the light chain variable region comprises~~ the VL-CDR1 having comprises the amino acid sequence of SEQ ID NO:99, the VL-CDR2 having comprises the amino acid sequence of SEQ ID NO:100, and the VL-CDR3 having comprises the amino acid sequence of SEQ ID NO:101.

4. ~~The binding agent of claim 2, wherein:~~

(1) ~~the heavy chain variable region comprises the VH-CDR1, the VH-CDR2, the VH-CDR3, the VL-CDR1, the VL-CDR2, and the VL-CDR3 comprising~~

- amino acid sequences of any one of the five CDR definitions set forth in Table 6B;
- (2) ~~the heavy chain variable region comprises the VH CDR1, the VH CDR2, the VH CDR3, the VL CDR1, the VL CDR2, and the VL CDR3 comprising amino acid sequences of any one of the five CDR definitions set forth in Table 4B;~~(3) ~~the heavy chain variable region comprises the VH CDR1, the VH CDR2, the VH CDR3, the VL CDR1, the VL CDR2, and the VL CDR3 comprising amino acid sequences of any one of the five CDR definitions set forth in Table 8A;~~
- (4) ~~the heavy chain variable region comprises the VH CDR1, the VH CDR2, the VH CDR3, the VL CDR1, the VL CDR2, and the VL CDR3 comprising amino acid sequences of any one of the five CDR definitions set forth in Table 4A;~~
- (5) ~~the heavy chain variable region comprises the VH CDR1, the VH CDR2, the VH CDR3, the VL CDR1, the VL CDR2, and the VL CDR3 comprising amino acid sequences of any one of the five CDR definitions set forth in Table 6A;~~
- (6) ~~the heavy chain variable region comprises the VH CDR1, the VH CDR2, the VH CDR3, the VL CDR1, the VL CDR2, and the VL CDR3 comprising amino acid sequences of any one of the five CDR definitions set forth in Table 5; or~~
- (7) ~~the heavy chain variable region comprises the VH CDR1, the VH CDR2, the VH CDR3, the VL CDR1, the VL CDR2, and the VL CDR3 comprising amino acid sequences of any one of the five CDR definitions set forth in Table 7.~~

54. The binding agent of claim 2 or 3, wherein:

- (a) ~~the heavy chain variable region comprises an amino acid sequence having the VH has~~ at least 80% sequence identity to the amino acid sequence set forth in of SEQ ID NO:144; and/or
- (b) ~~the light chain variable region comprises an amino acid sequence having VL has~~ at least 80% sequence identity to the sequence set forth in of SEQ ID NO:145; or
- (c) ~~(b) the heavy chain variable region comprises an amino acid sequence having VH~~ comprises the amino acid sequence of at least 80% sequence identity to SEQ ID NO:144, and/or

the light chain variable region comprises an amino acid sequence having at least 80% sequence identity to SEQ ID NO:145.

5. The binding agent of any one of claims 2-4, wherein the antigen-binding domain comprises (a) a heavy chain comprising an amino acid sequence having at least 80% sequence identity to the amino acid sequence of SEQ ID NO:156, and/or a light chain comprising an amino acid sequence having at least 80% sequence identity to the amino acid sequence of SEQ ID NO:157; or (b) a heavy chain comprising the amino acid sequence of SEQ ID NO:156, and/or a light chain comprising the amino acid sequence of SEQ ID NO:157.

6. The binding agent of claim 1, wherein the antigen-binding domain comprises:

(i) a VH comprising a VH-CDR1, a VH-CDR2, and a VH-CDR3 from the amino acid sequence of SEQ ID NO:139; and a VL comprising a VL-CDR1, a VL-CDR2, and a VL-CDR3 from the amino acid sequence of SEQ ID NO:140;

(ii) a VH comprising a VH-CDR1, a VH-CDR2, and a VH-CDR3 from the amino acid sequence of SEQ ID NO:133; and a VL comprising a VL-CDR1, a VL-CDR2, and a VL-CDR3 from the amino acid sequence of SEQ ID NO:134;

(iii) a VH comprising a VH-CDR1, a VH-CDR2, and a VH-CDR3 from the amino acid sequence of SEQ ID NO:143; and a VL comprising a VL-CDR1, a VL-CDR2, and a VL-CDR3 from the amino acid sequence of SEQ ID NO:142;

(iv) a VH comprising a VH-CDR1, a VH-CDR2, and a VH-CDR3 from the amino acid sequence of SEQ ID NO:131; and a VL comprising a VL-CDR1, a VL-CDR2, and a VL-CDR3 from the amino acid sequence of SEQ ID NO:132;

(v) a VH comprising a VH-CDR1, a VH-CDR2, and a VH-CDR3 from the amino acid sequence of SEQ ID NO:137; and a VL comprising a VL-CDR1, a VL-CDR2, and a VL-CDR3 from the amino acid sequence of SEQ ID NO:138;

(vi) a VH comprising a VH-CDR1, a VH-CDR2, and a VH-CDR3 from the amino acid sequence of SEQ ID NO:135; and a VL comprising a VL-CDR1, a VL-CDR2, and a VL-CDR3 from the amino acid sequence of SEQ ID NO:136; or

(vii) a VH comprising a VH-CDR1, a VH-CDR2, and a VH-CDR3 from the amino acid sequence of SEQ ID NO:141; and a VL comprising a VL-CDR1, a VL-CDR2, and a VL-CDR3 from the amino acid sequence of SEQ ID NO:142.

7. The binding agent of claim 6, wherein

(i) the VH comprises the VH-CDR1, the VH-CDR2, and the VH-CDR3 from the amino acid sequence of SEQ ID NO:139; and the VL comprises the VL-CDR1, the VL-CDR2, and the VL-CDR3 from the amino acid sequence of SEQ ID NO:140, and wherein

(a) the VH-CDR1 comprises the amino acid sequence of SEQ ID NO:95, the VH-CDR2 comprises the amino acid sequence of SEQ ID NO:87, the VH-CDR3 comprises the amino acid sequence of SEQ ID NO:102, the VL-CDR1 comprises the amino acid sequence of SEQ ID NO:103, the VL-CDR2 comprises the amino acid sequence of SEQ ID NO:90, and the VL-CDR3 comprises the amino acid sequence of SEQ ID NO:91;

(b) the VH-CDR1 comprises the amino acid sequence of SEQ ID NO:86, the VH-CDR2 comprises the amino acid sequence of SEQ ID NO:87, the VH-CDR3 comprises the amino acid sequence of SEQ ID NO:102, the VL-CDR1 comprises the amino acid sequence of SEQ ID NO:103, the VL-CDR2 comprises the amino acid sequence of SEQ ID NO:90, and the VL-CDR3 comprises the amino acid sequence of SEQ ID NO:91;

(c) the VH-CDR1 comprises the amino acid sequence of SEQ ID NO:92, the VH-CDR2 comprises the amino acid sequence of SEQ ID NO:93, the VH-CDR3 comprises the amino acid sequence of SEQ ID NO:102, the VL-CDR1 comprises the amino acid sequence of SEQ ID NO:103, the VL-CDR2 comprises the amino acid sequence of SEQ ID NO:90, and the VL-CDR3 comprises the amino acid sequence of SEQ ID NO:91;

(d) the VH-CDR1 comprises the amino acid sequence of SEQ ID NO:86, the VH-CDR2 comprises the amino acid sequence of SEQ ID NO:94, the VH-CDR3 comprises the amino acid sequence of SEQ ID NO:102, the VL-CDR1 comprises the amino acid sequence of SEQ ID NO:103, the VL-CDR2 comprises the amino acid sequence of SEQ ID NO:90, and the VL-CDR3 comprises the amino acid sequence of SEQ ID NO:91; or

(e) the VH-CDR1 comprises the amino acid sequence of SEQ ID NO:96, the VH-CDR2 comprises the amino acid sequence of SEQ ID NO:97, the VH-CDR3 comprises the amino acid sequence of SEQ ID NO:123, the VL-CDR1 comprises the amino acid sequence of SEQ ID NO:105, the VL-CDR2 comprises the amino acid sequence of SEQ ID NO:100, and the VL-CDR3 comprises the amino acid sequence of SEQ ID NO:101; or

(ii) the VH comprises the VH-CDR1, the VH-CDR2, and the VH-CDR3 from the amino acid sequence of SEQ ID NO:133; and the VL comprises the VL-CDR1, the VL-CDR2, and the VL-CDR3 from the amino acid sequence of SEQ ID NO:134, and wherein

(a) the VH-CDR1 comprises the amino acid sequence of SEQ ID NO:79, the VH-CDR2 comprises the amino acid sequence of SEQ ID NO:118, the VH-CDR3 comprises the amino acid sequence of SEQ ID NO:72, the VL-CDR1 comprises the amino acid sequence

of SEQ ID NO:73, the VL-CDR2 comprises the amino acid sequence of SEQ ID NO:74, and the VL-CDR3 comprises the amino acid sequence of SEQ ID NO:75;

(b) the VH-CDR1 comprises the amino acid sequence of SEQ ID NO:70, the VH-CDR2 comprises the amino acid sequence of SEQ ID NO:118, the VH-CDR3 comprises the amino acid sequence of SEQ ID NO:72, the VL-CDR1 comprises the amino acid sequence of SEQ ID NO:73, the VL-CDR2 comprises the amino acid sequence of SEQ ID NO:74, and the VL-CDR3 comprises the amino acid sequence of SEQ ID NO:75;

(c) the VH-CDR1 comprises the amino acid sequence of SEQ ID NO:76, the VH-CDR2 comprises the amino acid sequence of SEQ ID NO:119, the VH-CDR3 comprises the amino acid sequence of SEQ ID NO:72, the VL-CDR1 comprises the amino acid sequence of SEQ ID NO:73, the VL-CDR2 comprises the amino acid sequence of SEQ ID NO:74, and the VL-CDR3 comprises the amino acid sequence of SEQ ID NO:75;

(d) the VH-CDR1 comprises the amino acid sequence of SEQ ID NO:70, the VH-CDR2 comprises the amino acid sequence of SEQ ID NO:120, the VH-CDR3 comprises the amino acid sequence of SEQ ID NO:72, the VL-CDR1 comprises the amino acid sequence of SEQ ID NO:73, the VL-CDR2 comprises the amino acid sequence of SEQ ID NO:74, and the VL-CDR3 comprises the amino acid sequence of SEQ ID NO:75; or

(e) the VH-CDR1 comprises the amino acid sequence of SEQ ID NO:80, the VH-CDR2 comprises the amino acid sequence of SEQ ID NO:121, the VH-CDR3 comprises the amino acid sequence of SEQ ID NO:82, the VL-CDR1 comprises the amino acid sequence of SEQ ID NO:83, the VL-CDR2 comprises the amino acid sequence of SEQ ID NO:122, and the VL-CDR3 comprises the amino acid sequence of SEQ ID NO:85; or

(iii) the VH comprises the VH-CDR1, the VH-CDR2, and the VH-CDR3 from the amino acid sequence of SEQ ID NO:143; and the VL comprises the VL-CDR1, the VL-CDR2, and the VL-CDR3 from the amino acid sequence of SEQ ID NO:142, and wherein

(a) the VH-CDR1 comprises the amino acid sequence of SEQ ID NO:115, the VH-CDR2 comprises the amino acid sequence of SEQ ID NO:112, the VH-CDR3 comprises the amino acid sequence of SEQ ID NO:107, the VL-CDR1 comprises the amino acid sequence of SEQ ID NO:89, the VL-CDR2 comprises the amino acid sequence of SEQ ID NO:90, and the VL-CDR3 comprises the amino acid sequence of SEQ ID NO:91;

(b) the VH-CDR1 comprises the amino acid sequence of SEQ ID NO:111, the VH-CDR2 comprises the amino acid sequence of SEQ ID NO:112, the VH-CDR3 comprises the amino acid sequence of SEQ ID NO:107, the VL-CDR1 comprises the amino acid sequence

of SEQ ID NO:89, the VL-CDR2 comprises the amino acid sequence of SEQ ID NO:90, and the VL-CDR3 comprises the amino acid sequence of SEQ ID NO:91;

(c) the VH-CDR1 comprises the amino acid sequence of SEQ ID NO:76, the VH-CDR2 comprises the amino acid sequence of SEQ ID NO:113, the VH-CDR3 comprises the amino acid sequence of SEQ ID NO:107, the VL-CDR1 comprises the amino acid sequence of SEQ ID NO:89, the VL-CDR2 comprises the amino acid sequence of SEQ ID NO:90, and the VL-CDR3 comprises the amino acid sequence of SEQ ID NO:91;

(d) the VH-CDR1 comprises the amino acid sequence of SEQ ID NO:111, the VH-CDR2 comprises the amino acid sequence of SEQ ID NO:114, the VH-CDR3 comprises the amino acid sequence of SEQ ID NO:107, the VL-CDR1 comprises the amino acid sequence of SEQ ID NO:89, the VL-CDR2 comprises the amino acid sequence of SEQ ID NO:90, and the VL-CDR3 comprises the amino acid sequence of SEQ ID NO:91; or

(e) the VH-CDR1 comprises the amino acid sequence of SEQ ID NO:116, the VH-CDR2 comprises the amino acid sequence of SEQ ID NO:117, the VH-CDR3 comprises the amino acid sequence of SEQ ID NO:110, the VL-CDR1 comprises the amino acid sequence of SEQ ID NO:99, the VL-CDR2 comprises the amino acid sequence of SEQ ID NO:100, and the VL-CDR3 comprises the amino acid sequence of SEQ ID NO:101; or

(iv) the VH comprises the VH-CDR1, the VH-CDR2, and the VH-CDR3 from the amino acid sequence of SEQ ID NO:131; and the VL comprises the VL-CDR1, the VL-CDR2, and the VL-CDR3 from the amino acid sequence of SEQ ID NO:132, and wherein

(a) the VH-CDR1 comprises the amino acid sequence of SEQ ID NO:79, the VH-CDR2 comprises the amino acid sequence of SEQ ID NO:71, the VH-CDR3 comprises the amino acid sequence of SEQ ID NO:72, the VL-CDR1 comprises the amino acid sequence of SEQ ID NO:73, the VL-CDR2 comprises the amino acid sequence of SEQ ID NO:74, and the VL-CDR3 comprises the amino acid sequence of SEQ ID NO:75;

(b) the VH-CDR1 comprises the amino acid sequence of SEQ ID NO:70, the VH-CDR2 comprises the amino acid sequence of SEQ ID NO:71, the VH-CDR3 comprises the amino acid sequence of SEQ ID NO:72, the VL-CDR1 comprises the amino acid sequence of SEQ ID NO:73, the VL-CDR2 comprises the amino acid sequence of SEQ ID NO:74, and the VL-CDR3 comprises the amino acid sequence of SEQ ID NO:75;

(c) the VH-CDR1 comprises the amino acid sequence of SEQ ID NO:76, the VH-CDR2 comprises the amino acid sequence of SEQ ID NO:77, the VH-CDR3 comprises the amino acid sequence of SEQ ID NO:72, the VL-CDR1 comprises the amino acid sequence

of SEQ ID NO:73, the VL-CDR2 comprises the amino acid sequence of SEQ ID NO:74, and the VL-CDR3 comprises the amino acid sequence of SEQ ID NO:75;

(d) the VH-CDR1 comprises the amino acid sequence of SEQ ID NO:70, the VH-CDR2 comprises the amino acid sequence of SEQ ID NO:78, the VH-CDR3 comprises the amino acid sequence of SEQ ID NO:72, the VL-CDR1 comprises the amino acid sequence of SEQ ID NO:73, the VL-CDR2 comprises the amino acid sequence of SEQ ID NO:74, and the VL-CDR3 comprises the amino acid sequence of SEQ ID NO:75; or

(e) the VH-CDR1 comprises the amino acid sequence of SEQ ID NO:80, the VH-CDR2 comprises the amino acid sequence of SEQ ID NO:81, the VH-CDR3 comprises the amino acid sequence of SEQ ID NO:82, the VL-CDR1 comprises the amino acid sequence of SEQ ID NO:83, the VL-CDR2 comprises the amino acid sequence of SEQ ID NO:84, and the VL-CDR3 comprises the amino acid sequence of SEQ ID NO:85; or

(v) the VH comprises the VH-CDR1, the VH-CDR2, and the VH-CDR3 from the amino acid sequence of SEQ ID NO:137; and the VL comprises the VL-CDR1, the VL-CDR2, and the VL-CDR3 from the amino acid sequence of SEQ ID NO:138, and wherein

(a) the VH-CDR1 comprises the amino acid sequence of SEQ ID NO:95, the VH-CDR2 comprises the amino acid sequence of SEQ ID NO:87, the VH-CDR3 comprises the amino acid sequence of SEQ ID NO:102, the VL-CDR1 comprises the amino acid sequence of SEQ ID NO:103, the VL-CDR2 comprises the amino acid sequence of SEQ ID NO:90, and the VL-CDR3 comprises the amino acid sequence of SEQ ID NO:91;

(b) the VH-CDR1 comprises the amino acid sequence of SEQ ID NO:86, the VH-CDR2 comprises the amino acid sequence of SEQ ID NO:87, the VH-CDR3 comprises the amino acid sequence of SEQ ID NO:102, the VL-CDR1 comprises the amino acid sequence of SEQ ID NO:103, the VL-CDR2 comprises the amino acid sequence of SEQ ID NO:90, and the VL-CDR3 comprises the amino acid sequence of SEQ ID NO:91;

(c) the VH-CDR1 comprises the amino acid sequence of SEQ ID NO:92, the VH-CDR2 comprises the amino acid sequence of SEQ ID NO:93, the VH-CDR3 comprises the amino acid sequence of SEQ ID NO:102, the VL-CDR1 comprises the amino acid sequence of SEQ ID NO:103, the VL-CDR2 comprises the amino acid sequence of SEQ ID NO:90, and the VL-CDR3 comprises the amino acid sequence of SEQ ID NO:91;

(d) the VH-CDR1 comprises the amino acid sequence of SEQ ID NO:86, the VH-CDR2 comprises the amino acid sequence of SEQ ID NO:94, the VH-CDR3 comprises the amino acid sequence of SEQ ID NO:102, the VL-CDR1 comprises the amino acid sequence

of SEQ ID NO:103, the VL-CDR2 comprises the amino acid sequence of SEQ ID NO:90, and the VL-CDR3 comprises the amino acid sequence of SEQ ID NO:91; or

(e) the VH-CDR1 comprises the amino acid sequence of SEQ ID NO:96, the VH-CDR2 comprises the amino acid sequence of SEQ ID NO:97, the VH-CDR3 comprises the amino acid sequence of SEQ ID NO:104, the VL-CDR1 comprises the amino acid sequence of SEQ ID NO:105, the VL-CDR2 comprises the amino acid sequence of SEQ ID NO:100, and the VL-CDR3 comprises the amino acid sequence of SEQ ID NO:101; or

(vi) the VH comprises the VH-CDR1, the VH-CDR2, and the VH-CDR3 from the amino acid sequence of SEQ ID NO:135; and the VL comprises the VL-CDR1, the VL-CDR2, and the VL-CDR3 from the amino acid sequence of SEQ ID NO:136, and wherein

(a) the VH-CDR1 comprises the amino acid sequence of SEQ ID NO:95, the VH-CDR2 comprises the amino acid sequence of SEQ ID NO:87, the VH-CDR3 comprises the amino acid sequence of SEQ ID NO:88, the VL-CDR1 comprises the amino acid sequence of SEQ ID NO:89, the VL-CDR2 comprises the amino acid sequence of SEQ ID NO:90, and the VL-CDR3 comprises the amino acid sequence of SEQ ID NO:91;

(b) the VH-CDR1 comprises the amino acid sequence of SEQ ID NO:86, the VH-CDR2 comprises the amino acid sequence of SEQ ID NO:87, the VH-CDR3 comprises the amino acid sequence of SEQ ID NO:88, the VL-CDR1 comprises the amino acid sequence of SEQ ID NO:89, the VL-CDR2 comprises the amino acid sequence of SEQ ID NO:90, and the VL-CDR3 comprises the amino acid sequence of SEQ ID NO:91;

(c) the VH-CDR1 comprises the amino acid sequence of SEQ ID NO:92, the VH-CDR2 comprises the amino acid sequence of SEQ ID NO:93, the VH-CDR3 comprises the amino acid sequence of SEQ ID NO:88, the VL-CDR1 comprises the amino acid sequence of SEQ ID NO:89, the VL-CDR2 comprises the amino acid sequence of SEQ ID NO:90, and the VL-CDR3 comprises the amino acid sequence of SEQ ID NO:91;

(d) the VH-CDR1 comprises the amino acid sequence of SEQ ID NO:86, the VH-CDR2 comprises the amino acid sequence of SEQ ID NO:94, the VH-CDR3 comprises the amino acid sequence of SEQ ID NO:88, the VL-CDR1 comprises the amino acid sequence of SEQ ID NO:89, the VL-CDR2 comprises the amino acid sequence of SEQ ID NO:90, and the VL-CDR3 comprises the amino acid sequence of SEQ ID NO:91; or

(e) the VH-CDR1 comprises the amino acid sequence of SEQ ID NO:96, the VH-CDR2 comprises the amino acid sequence of SEQ ID NO:97, the VH-CDR3 comprises the amino acid sequence of SEQ ID NO:98, the VL-CDR1 comprises the amino acid sequence

of SEQ ID NO:99, the VL-CDR2 comprises the amino acid sequence of SEQ ID NO:100, and the VL-CDR3 comprises the amino acid sequence of SEQ ID NO:101; or

(vii) the VH comprises the VH-CDR1, the VH-CDR2, and the VH-CDR3 from the amino acid sequence of SEQ ID NO:141; and the VL comprises the VL-CDR1, the VL-CDR2, and the VL-CDR3 from the amino acid sequence of SEQ ID NO:142, and wherein

(a) the VH-CDR1 comprises the amino acid sequence of SEQ ID NO:79, the VH-CDR2 comprises the amino acid sequence of SEQ ID NO:106, the VH-CDR3 comprises the amino acid sequence of SEQ ID NO:107, the VL-CDR1 comprises the amino acid sequence of SEQ ID NO:89, the VL-CDR2 comprises the amino acid sequence of SEQ ID NO:90, and the VL-CDR3 comprises the amino acid sequence of SEQ ID NO:91;

(b) the VH-CDR1 comprises the amino acid sequence of SEQ ID NO:70, the VH-CDR2 comprises the amino acid sequence of SEQ ID NO:106, the VH-CDR3 comprises the amino acid sequence of SEQ ID NO:107, the VL-CDR1 comprises the amino acid sequence of SEQ ID NO:89, the VL-CDR2 comprises the amino acid sequence of SEQ ID NO:90, and the VL-CDR3 comprises the amino acid sequence of SEQ ID NO:91;

(c) the VH-CDR1 comprises the amino acid sequence of SEQ ID NO:76, the VH-CDR2 comprises the amino acid sequence of SEQ ID NO:77, the VH-CDR3 comprises the amino acid sequence of SEQ ID NO:107, the VL-CDR1 comprises the amino acid sequence of SEQ ID NO:89, the VL-CDR2 comprises the amino acid sequence of SEQ ID NO:90, and the VL-CDR3 comprises the amino acid sequence of SEQ ID NO:91;

(d) the VH-CDR1 comprises the amino acid sequence of SEQ ID NO:70, the VH-CDR2 comprises the amino acid sequence of SEQ ID NO:108, the VH-CDR3 comprises the amino acid sequence of SEQ ID NO:107, the VL-CDR1 comprises the amino acid sequence of SEQ ID NO:89, the VL-CDR2 comprises the amino acid sequence of SEQ ID NO:90, and the VL-CDR3 comprises the amino acid sequence of SEQ ID NO:91; or

(e) the VH-CDR1 comprises the amino acid sequence of SEQ ID NO:80, the VH-CDR2 comprises the amino acid sequence of SEQ ID NO:109, the VH-CDR3 comprises the amino acid sequence of SEQ ID NO:110, the VL-CDR1 comprises the amino acid sequence of SEQ ID NO:99, the VL-CDR2 comprises the amino acid sequence of SEQ ID NO:100, and the VL-CDR3 comprises the amino acid sequence of SEQ ID NO:101.

~~6. The binding agent of claim 5, wherein the heavy chain variable region comprises the amino acid sequence of SEQ ID NO:144.~~

7. ~~The binding agent of claim 5 or claim 6, wherein the light chain variable region comprises the amino acid sequence of SEQ ID NO:145.~~

8. The binding agent of claim ~~46~~ or 7, wherein:

- (a) ~~the heavy chain variable region comprises~~ VH has at least 80% sequence identity to an ~~the amino acid sequence of SEQ ID NO.: 139, and/or having at~~ the VL has at least 80% sequence identity to the amino acid sequence of SEQ ID NO.: 140; or the VH comprises the amino acid sequence of SEQ ID NO.:139, and/or any one of the sequences set forth in SEQ ID NOs:139, 133, 143, 131, 137, 135, or 141;
- (b) ~~the light chain variable region comprises an amino acid sequence having at least 80% sequence identity to any one of the sequences set forth in the VL comprises the amino acid sequence of SEQ ID NOs:140, 134, 142, 132, 138, 136, or 142;~~
~~or~~
- (c) ~~the variable region comprises any one of the following amino acid sequences:~~
 - ~~(i) the heavy chain variable region comprises an amino acid sequence having at least 80% sequence identity to the sequence of SEQ ID NO:139 and the light chain variable region comprises an amino acid sequence having at least 80% sequence identity to the sequence of SEQ ID NO:140;~~
 - ~~(ii) the heavy chain variable region comprises the VH has at least 80% sequence identity to an~~ the amino acid sequence having at least 80% sequence identity to the sequence of SEQ ID NO:133, and/or and the light chain variable region comprises an amino acid sequence having at the VL has at least 80% sequence identity to the amino acid sequence of SEQ ID NO:134; or the VH comprises the amino acid sequence of SEQ ID NO:133, and/or the VL comprises the amino acid sequence of SEQ ID NO:134,
 - ~~(iii) the heavy chain variable region comprises~~ VH has at least 80% sequence identity to an ~~the amino acid sequence having at least 80% sequence identity to the sequence of SEQ ID NO:143, and/or and the light chain variable region comprises the VL has at least an amino acid sequence having at least 80% sequence identity to the amino acid sequence of SEQ ID NO: 142; or the VH comprises the amino acid sequence of SEQ ID NO.: 143, and/or the VL comprises the amino acid sequence of~~ to the sequence of SEQ ID NO:142;
 - ~~(iv) the heavy chain variable region comprises an amino acid sequence having~~ VH has at least 80% sequence identity to the amino acid sequence of SEQ ID NO:131, and/or and

~~the light chain variable region comprises the VL has at least 80% sequence identity to the amino acid sequence of SEQ ID NO: 132; or the VH comprises an~~the amino acid sequence having at least 80% sequence identity to the sequence of SEQ ID NO:132; or the VH comprises the amino acid sequence of SEQ ID NO:131, and/or the VL comprises the amino acid sequence of SEQ ID NO:132,

~~——(ve) the heavy chain variable region comprises an amino acid sequence having VH has at least 80% sequence identity to the amino acid sequence of SEQ ID NO:137, and/or and the light chain variable region comprises an amino acid sequence having VL has at least 80% sequence identity to the amino acid sequence of SEQ ID NO:138; or the VH comprises the amino acid sequence of SEQ ID NO:137, and/or the VL comprises the amino acid sequence of SEQ ID NO:138,~~

~~——(vif) the heavy chain variable region comprises an amino acid sequence having VH has at least 80% sequence identity to the amino acid sequence of SEQ ID NO:135, and/or the light chain variable region comprises VL has at least an amino acid sequence having at least 80% sequence identity to the amino acid sequence of SEQ ID NO:136; or the VH comprises the amino acid sequence of SEQ ID NO:135, and/or the VL comprises the amino acid sequence of SEQ ID NO:136, or~~

~~——(viig) the heavy chain variable region comprises VH has an amino acid sequence having at least 80% sequence identity to the amino acid sequence of SEQ ID NO:141, and/or the light chain variable region comprises an amino acid sequence having VL has at least 80% sequence identity to the amino acid sequence of SEQ ID NO:142.; or the VH comprises the amino acid sequence of SEQ ID NO:141, and/or the VL comprises the amino acid sequence of SEQ ID NO:142.~~

9. ~~The binding agent of claim 8, wherein the heavy chain variable region comprises the amino acid sequence of any one of SEQ ID NOs:139, 133, 143, 131, 137, 135, or 141.~~

10. ~~The binding agent of claim 8, wherein the light chain variable region comprises the amino acid sequence of any one of SEQ ID NOs:140, 134, 142, 132, 138, 136, or 142.~~

11. ~~The binding agent of claim 8, wherein:~~

~~——(i) the heavy chain variable region comprises the amino acid sequence of SEQ ID NO:139 and the light chain variable region comprises the amino acid sequence of SEQ ID NO:140;~~

- ~~—— (ii) the heavy chain variable region comprises the amino acid sequence of SEQ ID NO:133 and the light chain variable region comprises the amino acid sequence of SEQ ID NO:134;~~
- ~~—— (iii) the heavy chain variable region comprises the amino acid sequence of SEQ ID NO:143 and the light chain variable region comprises the amino acid sequence of SEQ ID NO:142;~~
- ~~—— (iv) the heavy chain variable region comprises the amino acid sequence of SEQ ID NO:131 and the light chain variable region comprises the amino acid sequence of SEQ ID NO:132;~~
- ~~—— (v) the heavy chain variable region comprises the amino acid sequence of SEQ ID NO:137 and the light chain variable region comprises the amino acid sequence of SEQ ID NO:138;~~
- ~~—— (vi) the heavy chain variable region comprises the amino acid sequence of SEQ ID NO:135 and the light chain variable region comprises the amino acid sequence of SEQ ID NO:136; or~~
- ~~—— (vii) the heavy chain variable region comprises the amino acid sequence of SEQ ID NO:141 and the light chain variable region comprises the amino acid sequence of SEQ ID NO:142.~~

9. The binding agent of any one of claims 6-8, wherein the antigen-binding domain comprises:

—— (a) a heavy chain comprising an amino acid sequence having at least 80% sequence identity to the amino acid sequence of SEQ ID NO:148, and/or a light chain comprising an amino acid sequence having at least 80% sequence identity to the amino acid sequence of SEQ ID NO:149;

—— (b) a heavy chain comprising an amino acid sequence having at least 80% sequence identity to the amino acid sequence of SEQ ID NO:152, and/or a light chain comprising an amino acid sequence having at least 80% sequence identity to the amino acid sequence of SEQ ID NO:153;

—— (c) a heavy chain comprising the amino acid sequence of SEQ ID NO:148, and/or a light chain comprising the amino acid sequence of SEQ ID NO:149; or

—— (d) a heavy chain comprising the amino acid sequence of SEQ ID NO:152, and/or a light chain comprising the amino acid sequence of SEQ ID NO:153.

~~1210.~~ A binding agent that specifically binds human ILT2 comprising ~~an antigen-binding domain comprising a heavy chain variable region comprising a VH comprising a VH-CDR1, a VH-CDR2, and a VH-CDR3 from the amino acid sequence of SEQ ID NO:125; and a light chain variable region VL comprising a VL-CDR1, a VL-CDR2, and a VL-CDR3 from the amino acid sequence of SEQ ID NO:126.~~

~~1311.~~ The binding agent of claim ~~1210~~, wherein:

- ~~(4i)~~ the ~~heavy chain variable region comprises the~~ VH-CDR1 havingcomprises the amino acid sequence of SEQ ID NO:31, the VH-CDR2 havingcomprises the amino acid sequence of SEQ ID NO:23, ~~and the VH-CDR3 havingcomprises the amino acid sequence of SEQ ID NO:24; and the light chain variable region comprises the~~ VL-CDR1 havingcomprises the amino acid sequence of SEQ ID NO:25, the VL-CDR2 havingcomprises the amino acid sequence of SEQ ID NO:26, and the VL-CDR3 havingcomprises the amino acid sequence of SEQ ID NO:27;
- ~~(2ii)~~ the ~~heavy chain variable region comprises the~~ VH-CDR1 havingcomprises the amino acid sequence of SEQ ID NO:22, the VH-CDR2 havingcomprises the amino acid sequence of SEQ ID NO:23, ~~and the VH-CDR3 havingcomprises the amino acid sequence of SEQ ID NO:24; and the light chain variable region comprises the~~ VL-CDR1 havingcomprises the amino acid sequence of SEQ ID NO:25, the VL-CDR2 havingcomprises the amino acid sequence of SEQ ID NO:26, and the VL-CDR3 havingcomprises the amino acid sequence of SEQ ID NO:27;
- ~~(3iii)~~ the ~~heavy chain variable region comprises the~~ VH-CDR1 havingcomprises the amino acid sequence of SEQ ID NO:28, the VH-CDR2 havingcomprises the amino acid sequence of SEQ ID NO:29, ~~and the VH-CDR3 havingcomprises the amino acid sequence of SEQ ID NO:24; and the light chain variable region comprises the~~ VL-CDR1 havingcomprises the amino acid sequence of SEQ ID NO:25, the VL-CDR2 havingcomprises the amino acid sequence of SEQ ID NO:26, and the VL-CDR3 havingcomprises the amino acid sequence of SEQ ID NO:27;
- ~~(4iv)~~ the ~~heavy chain variable region comprises the~~ VH-CDR1 havingcomprises the amino acid sequence of SEQ ID NO:22, the VH-CDR2 havingcomprises the amino acid sequence of SEQ ID NO:30, ~~and the VH-CDR3 havingcomprises~~

the amino acid sequence of SEQ ID NO:24; ~~and the light chain variable region comprises the VL-CDR1 having~~comprises the amino acid sequence of SEQ ID NO:25, the VL-CDR2 ~~having~~comprises the amino acid sequence of SEQ ID NO:26, and the VL-CDR3 ~~having~~comprises the amino acid sequence of SEQ ID NO:27; or

- (5v) ~~the heavy chain variable region comprises the VH-CDR1 having~~comprises the amino acid sequence of SEQ ID NO:32, the VH-CDR2 ~~having~~ comprises the amino acid sequence of SEQ ID NO:33, ~~and the VH-CDR3 having~~comprises the amino acid sequence of SEQ ID NO:34; ~~and the light chain variable region comprises the VL-CDR1 having~~comprises the amino acid sequence of SEQ ID NO:35, the VL-CDR2 ~~having~~comprises the amino acid sequence of SEQ ID NO:36, and the VL-CDR3 ~~having~~comprises the amino acid sequence of SEQ ID NO:37.

~~1412.~~ The binding agent of claim ~~12~~10 or 11, wherein:

- (a) ~~the heavy chain variable region comprises an amino acid sequence having~~ VH has at least 80% sequence identity to the sequence set forth in amino acid sequence of SEQ ID NO:125, and/or the VL has at least 80% sequence identity to the amino acid sequence of SEQ ID NO:126; or
- (b) ~~the light chain variable region comprises an amino acid sequence having at least 80% sequence identity to the sequence set forth in SEQ ID NO:126; or~~
- (c) ~~the heavy chain variable region comprises an amino acid sequence having at least 80% sequence identity to the sequence set forth in SEQ ID NO:125 and /or the light chain variable region comprises an amino acid sequence having at least 80% sequence identity to the sequence set forth in SEQ ID NO:126.~~
- (b) the VH comprises the amino acid sequence of SEQ ID NO:125, and/or the VL comprises the amino acid sequence of SEQ ID NO:126.

~~15.~~ The binding agent of claim 12, wherein:

- (a) ~~the heavy chain variable region comprises the amino acid sequence set forth in SEQ ID NO:125;~~
- (b) ~~the light chain variable region comprises the amino acid sequence set forth in SEQ ID NO:126; or~~

(c) ~~the heavy chain variable region comprises the amino acid sequence set forth in SEQ ID NO:125 and /or the light chain variable region comprises the amino acid sequence set forth in SEQ ID NO:126.~~

~~1613.~~ A binding agent that specifically binds human ILT4 comprising ~~an antigen-binding domain comprising:~~

(a) ~~a heavy chain variable region~~ VH comprising a VH-CDR1, a VH-CDR2, and a VH-CDR3 from the amino acid sequence of SEQ ID NO:129; and ~~a light chain variable region~~ VL comprising a VL-CDR1, a VL-CDR2, and a VL-CDR3 from the amino acid sequence of SEQ ID NO:130; or

(b) ~~a heavy chain variable region~~ VH comprising a VH-CDR1, a VH-CDR2, and a VH-CDR3 from the amino acid sequence of SEQ ID NO:127; and ~~a light chain variable region~~ VL comprising a VL-CDR1, a VL-CDR2, and a VL-CDR3 from the amino acid sequence of SEQ ID NO:128.

~~1714.~~ The binding agent of claim ~~1613~~, wherein ~~for (a):~~

(a) the VH comprises the VH-CDR1, the VH-CDR2, and the VH-CDR3 from the amino acid sequence of SEQ ID NO:129; and the VL comprises the VL-CDR1, the VL-CDR2, and the VL-CDR3 from the amino acid sequence of SEQ ID NO:130, and wherein

(4i) ~~the heavy chain variable region comprises the~~ VH-CDR1 havingcomprises the amino acid sequence of SEQ ID NO:63, ~~the VH-CDR2 comprises the~~ VH-CDR2 havingcomprises the amino acid sequence of SEQ ID NO:55, ~~and the VH-CDR3 comprises the~~ VH-CDR3 havingcomprises the amino acid sequence of SEQ ID NO:56; ~~and the light chain variable region comprises, the~~ VL-CDR1 havingcomprises the amino acid sequence of SEQ ID NO:57, ~~the VL-CDR2 comprises the~~ VL-CDR2 havingcomprises the amino acid sequence of SEQ ID NO:58, and ~~the VL-CDR3 comprises the~~ VL-CDR3 havingcomprises the amino acid sequence of SEQ ID NO:59;

(2ii) ~~the heavy chain variable region comprises~~ VH-CDR1 havingcomprises the amino acid sequence of SEQ ID NO:54, ~~the VH-CDR2 comprises the~~ VH-CDR2 havingcomprises the amino acid sequence of SEQ ID NO:55, ~~and the VH-CDR3 comprises the~~ VH-CDR3 havingcomprises the amino acid sequence of SEQ ID NO:56; ~~and the light chain variable region comprises the~~ the VL-CDR1 havingcomprises the amino acid sequence of SEQ ID NO:57, ~~the VL-CDR2 comprises the~~ VL-CDR2 havingcomprises the amino acid sequence of SEQ ID NO:58, and ~~the VL-CDR3 comprises the~~ VL-CDR3 havingcomprises the amino acid sequence of SEQ ID NO:59;

~~(3iii) the heavy chain variable region comprises the~~ VH comprises VH-CDR1 havingcomprises the amino acid sequence of SEQ ID NO:60, the VH-CDR2 havingcomprises the amino acid sequence of SEQ ID NO:61, ~~and the VH-CDR3~~ having comprises the amino acid sequence of SEQ ID NO:56; ~~and the light chain variable region comprises the~~ VL-CDR1 havingcomprises the amino acid sequence of SEQ ID NO:57, the VL-CDR2 havingcomprises the amino acid sequence of SEQ ID NO:58, and the VL-CDR3 havingcomprises the amino acid sequence of SEQ ID NO:59;

~~(4iv) the heavy chain variable region comprises the~~ VH-CDR1 havingcomprises the amino acid sequence of SEQ ID NO:54, the VH-CDR2 havingcomprises the amino acid sequence of SEQ ID NO:62, ~~and the VH-CDR3~~ havingcomprises the amino acid sequence of SEQ ID NO:56; ~~and the light chain variable region comprises the~~ VL-CDR1 havingcomprises the amino acid sequence of SEQ ID NO:57, the VL-CDR2 havingcomprises the amino acid sequence of SEQ ID NO:58, and the VL-CDR3 havingcomprises the amino acid sequence of SEQ ID NO:59; or

~~(5v) the heavy chain variable region comprises the~~ VH-CDR1 havingcomprises the amino acid sequence of SEQ ID NO:64, the VH-CDR2 havingcomprises the amino acid sequence of SEQ ID NO:65, and the VH-CDR3 havingcomprises the amino acid sequence of SEQ ID NO:66; ~~and the light chain variable region comprises the~~ VL-CDR1 havingcomprises the amino acid sequence of SEQ ID NO:67, the VL-CDR2 having comprises the amino acid sequence of SEQ ID NO:68, and the VL-CDR3 having comprises the amino acid sequence of SEQ ID NO:69; or

~~wherein for (b):~~ (b) the VH comprises the VH-CDR1, the VH-CDR2, and the VH-CDR3 from the amino acid sequence of SEQ ID NO:127; and the VL comprises the VL-CDR1, the VL-CDR2, and the VL-CDR3 from the amino acid sequence of SEQ ID NO:128, and
wherein

~~(4i) the heavy chain variable region comprises the~~ VH-CDR1 havingcomprises the amino acid sequence of SEQ ID NO:47, the VH-CDR2 havingcomprises the amino acid sequence of SEQ ID NO:39, ~~and the VH-CDR3~~ havingcomprises the amino acid sequence of SEQ ID NO:40; ~~and the light chain variable region comprises the~~ VL-CDR1 havingcomprises the amino acid sequence of SEQ ID NO:41, the VL-CDR2 havingcomprises the amino acid sequence of SEQ ID NO:42, and the VL-CDR3 havingcomprises the amino acid sequence of SEQ ID NO:43;

~~(2ii) the heavy chain variable region comprises the~~ VH-CDR1 havingcomprises the amino acid sequence of SEQ ID NO:38, the VH-CDR2 havingcomprises the amino

acid sequence of SEQ ID NO:39, ~~and the VH-CDR3~~ having comprises the amino acid sequence of SEQ ID NO:40; ~~and the light chain variable region comprises the VL-CDR1~~ having comprises the amino acid sequence of SEQ ID NO:41, the VL-CDR2 ~~having comprises~~ the amino acid sequence of SEQ ID NO:42, and the VL-CDR3 having comprises the amino acid sequence of SEQ ID NO:43;

(3iii) ~~the heavy chain variable region comprises the VH-CDR1~~ having comprises the amino acid sequence of SEQ ID NO:44, the VH-CDR2 having comprises the amino acid sequence of SEQ ID NO:45, ~~and the VH-CDR3~~ having comprises the amino acid sequence of SEQ ID NO:40; ~~and the light chain variable region comprises the VL-CDR1~~ having the amino acid sequence of SEQ ID NO:41, the VL-CDR2 having comprises the amino acid sequence of SEQ ID NO:42, and the VL-CDR3 having comprises the amino acid sequence of SEQ ID NO:43;

(4iv) ~~the heavy chain variable region comprises the VH-CDR1~~ having comprises the amino acid sequence of SEQ ID NO:38, the VH-CDR2 having comprising the amino acid sequence of SEQ ID NO:46, ~~and the VH-CDR3~~ having comprises the amino acid sequence of SEQ ID NO:40; ~~and the light chain variable region comprises the VL-CDR1~~ having comprises the amino acid sequence of SEQ ID NO:41, the VL-CDR2 having comprises the amino acid sequence of SEQ ID NO:42, and the VL-CDR3 having comprises the amino acid sequence of SEQ ID NO:43; or

(5v) ~~the heavy chain variable region comprises the VH-CDR1~~ having comprises the amino acid sequence of SEQ ID NO:48, the VH-CDR2 having comprises the amino acid sequence of SEQ ID NO:49, ~~and the VH-CDR3~~ having comprises the amino acid sequence of SEQ ID NO:50; ~~and the light chain variable region comprises the VL-CDR1~~ having comprises the amino acid sequence of SEQ ID NO:51, the VL-CDR2 having comprises the amino acid sequence of SEQ ID NO:52, and the VL-CDR3 having comprises an amino acid sequence of SEQ ID NO:53.

1815. The binding agent of claim ~~16~~ 13 or 14, wherein:

(a) ~~the heavy chain variable region comprises an amino acid sequence having VH~~ has at least 80% sequence identity to the amino acid sequence set forth in of SEQ ID NO:129, and/or the VL has at least 80% sequence identity to the amino acid sequence of SEQ ID NO:130;

(b) ~~the light chain variable region comprises VH~~ an amino acid sequence having has at least 80% sequence identity to the amino acid sequence of SEQ ID NO: 127,

and/or the VL has at least 80% sequence identity to the amino acid sequence of SEQ ID NO:128; set forth in SEQ ID NO:130; or

(c) the heavy chain variable region ~~VH~~ comprises ~~an~~ the amino acid sequence having at least 80% sequence identity to the sequence set forth in ~~of~~ SEQ ID NO:129 and /or the light chain variable region comprises an amino acid sequence having at least 80% sequence identity to the sequence set forth in ~~VL~~ comprises the amino acid sequence of SEQ ID NO:130; or

(d) the VH comprises the amino acid sequence of SEQ ID NO:127, and/or the VL comprises the amino acid sequence of SEQ ID NO:128.

19. — The binding agent of claim 16, wherein:

~~(a) — the heavy chain variable region comprises the amino acid sequence set forth in SEQ ID NO:129; (b) the light chain variable region comprises the amino acid sequence set forth in SEQ ID NO:130; or (c) the heavy chain variable region comprises the amino acid sequence set forth in SEQ ID NO:129 and /or the light chain variable region comprises the amino acid sequence set forth in SEQ ID NO:130.~~

20. — The binding agent of claim 16, wherein:

~~(a) — the heavy chain variable region comprises an amino acid sequence having at least 80% sequence identity to the sequence set forth in SEQ ID NO:127;~~
~~(b) — the light chain variable region comprises an amino acid sequence having at least 80% sequence identity to the sequence set forth in SEQ ID NO:128; or~~
~~(c) — the heavy chain variable region comprises an amino acid sequence having at least 80% sequence identity to the sequence set forth in SEQ ID NO:127 and /or the light chain variable region comprises an amino acid sequence having at least 80% sequence identity to the sequence set forth in SEQ ID NO:128.~~

21. — The binding agent of claim 16, wherein:

~~(a) — the heavy chain variable region comprises the amino acid sequence set forth in SEQ ID NO:127;~~
~~(b) — the light chain variable region comprises the amino acid sequence set forth in SEQ ID NO:128; or~~

(c) ~~the heavy chain variable region comprises the amino acid sequence set forth in SEQ ID NO:127 and /or the light chain variable region comprises the amino acid sequence set forth in SEQ ID NO:128.~~

~~2216.~~ The binding agent of any one of claims 1-~~21~~15, wherein the binding agent is which is
(a) an antibody;

(b) an antibody fragment comprising at least one antigen-binding site;

~~23.~~ The binding agent of any one of claims 1-22, which is a recombinant antibody.

~~24.~~ The binding agent of any one of claims 1-23, which is (c) a chimeric antibody;

~~25.~~ The binding agent of any one of claims 1-23, which is (d) a humanized antibody;

~~26.~~ The binding agent of any one of claims 1-25, which is (e) a bispecific antibody or a multispecific antibody; or

(f) attached to a half-life extending moiety.

~~27.~~ The binding agent of any one of claims 22-26, wherein the antibody is an antibody fragment comprising at least one antigen-binding site.

~~28.~~ The binding agent of claim 27, wherein the antibody fragment is a Fab, Fab', F(ab')₂, Fv, scFv, (scFv)₂, single chain antibody, dual variable region antibody, diabody, or nanobody.

~~29~~17. The binding agent of ~~any one of claims 1-25~~ claim 16, wherein the binding agent is which is an IgG1 antibody, an IgG2 antibody, or an IgG4 antibody, optionally wherein the binding agent is a human IgG1 antibody, a human IgG2 antibody, or a human IgG4 antibody; ~~and further optionally a human IgG1 antibody having~~has reduced or no effector function.

~~30.~~ The binding agent of any one of claims 1-25, which is an IgG2 antibody, optionally a human IgG2 antibody.

~~31. The binding agent of any one of claims 1-25, which is an IgG4 antibody, optionally a human IgG4 antibody.~~

~~3218. The binding agent of any one of claims 1-25 or 29-31 claim 16 or 17, which comprises comprising a kappa light chain or a lambda light chain, constant region, optionally wherein the antibody comprises a human kappa light chain constant region or a human lambda light chain.~~

~~33. The binding agent of any one of claims 1-25 or 29-31, which comprises a lambda light chain constant region, optionally a human lambda light chain constant region.~~

~~19. The binding agent of claim 16, wherein the antibody fragment is a Fab, a Fab', a F(ab')₂, a Fv, a scFv, a (scFv)₂, a single chain antibody, a dual variable region antibody, a diabody, or a nanobody.~~

~~34. The binding agent of any one of claims 1-11, comprising:~~

- ~~—(a) a heavy chain comprising an amino acid sequence with 80% identity to the sequence of SEQ ID NO:148 and a light chain comprising an amino acid sequence with 80% identity to the sequence of SEQ ID NO:149;~~
- ~~(b) a heavy chain comprising an amino acid sequence with 80% identity to the sequence of SEQ ID NO:152 and a light chain comprising an amino acid sequence with 80% identity to the sequence of SEQ ID NO:153; or~~
- ~~(c) a heavy chain comprising an amino acid sequence with 80% identity to the sequence of SEQ ID NO:156 and a light chain comprising an amino acid sequence with 80% identity to the sequence of SEQ ID NO:157.~~

~~35. An antibody that specifically binds human ILT2 and ILT4, which comprises:~~

- ~~(a) a heavy chain comprising the amino acid sequence of SEQ ID NO:148 and a light chain comprising the amino acid sequence of SEQ ID NO:149;~~
- ~~(b) a heavy chain comprising the amino acid sequence of SEQ ID NO:152 and a light chain comprising the amino acid sequence of SEQ ID NO:153; or~~
- ~~(c) a heavy chain comprising the amino acid sequence of SEQ ID NO:156 and a light chain comprising the amino acid sequence of SEQ ID NO:157.~~

~~3620.~~ The binding agent ~~or antibody of any one of claims 1-35~~ of any one of claims 1-19, wherein the binding agent ~~which~~ has one or more of the following properties:

- (1) ~~binds~~binding rhesus ILT2;
- (2) ~~binds~~binding cyno ILT2;
- (3) ~~does not bind~~not binding ILT3, ILT5, and LILRB5;
- (4) ~~does not bind~~not binding LILRA2, LILRA4, LILRA5, and LILRA6;
- (5) ~~is~~being an ILT2 antagonist;
- (6) ~~is~~being an ILT4 antagonist;
- (7) ~~inhibits~~inhibiting ILT2 activity;
- (8) ~~inhibits~~inhibiting ILT4 activity;
- (9) ~~inhibits~~inhibiting ILT2 signaling in cells that express ILT2;
- (10) ~~inhibits~~inhibiting ILT4 signaling in cells that express ILT4;
- (11) ~~inhibits~~inhibiting binding of ILT2 to MHC I molecules;
- (12) ~~inhibits~~inhibiting binding of ILT4 to MHC I molecules;
- (13) ~~inhibits~~inhibiting ILT2-induced suppression of myeloid cells;
- (14) ~~inhibits~~inhibiting ILT4-induced suppression of myeloid cells;
- (15) ~~inhibits~~inhibiting ILT2-induced suppression of myeloid cell activity;
- (16) ~~inhibits~~inhibiting ILT4-induced suppression of myeloid cell activity;
- (17) ~~restores~~restoring FcR activation in myeloid cells;
- (18) ~~enhances~~enhancing NK cell activity;
- (19) ~~enhances~~enhancing CTL activity;
- (20) ~~enhances~~enhancing macrophage phagocytosis; and
- (21) ~~inhibits~~inhibiting MDSC mediated suppression of immune cells.

~~37.~~ The binding agent or antibody of any one of claims 1-36, wherein the binding agent or antibody is attached to a half-life extending moiety.

~~3821.~~ ~~An antibody~~ A binding agent -that competes with the binding agent ~~or antibody~~ of any one of claims 1-~~36~~20 for binding to human ILT2 and/or human ILT4.

~~3922.~~ A pharmaceutical composition that comprises the binding agent ~~or antibody~~ of any one of claims 1-~~38~~21 and a pharmaceutically acceptable carrier.

~~4023.~~ An isolated polynucleotide or polynucleotides encoding the binding agent ~~or antibody~~ of any one of claims 1-~~39~~21.

~~4124.~~ A vector or vectors comprising the polynucleotide or polynucleotides of claim ~~4023~~.

~~4225.~~ An isolated cell comprising the polynucleotide or polynucleotides of claim ~~4023~~.

~~43.~~ ~~An isolated cell comprising~~ or the vector or vectors of claim ~~4124~~.

~~44.~~ ~~An isolated cell for producing the binding agent or antibody of any one of claims 1-~~
~~36~~21.

~~45.~~ ~~A method of disrupting, inhibiting, or blocking the binding of ILT2 and/or ILT4 to a MHC I molecule in a mixture of cells, the method comprising contacting the cells with the binding agent or antibody of any one of claims 1-38 or the pharmaceutical composition of claim 39.~~

~~46.~~ ~~A method of disrupting, inhibiting, or blocking MHC I induced ILT2 and/or ILT4 activity in a mixture of cells, the method comprising contacting the cells with the binding agent or antibody of any one of claims 1-38 or the pharmaceutical composition of claim 39.~~

~~47.~~ ~~The method of claim 45 or 46, wherein the MHC I molecule is HLA-A, HLA-B, HLA-C, HLA-E, and/or HLA-G.~~

26. A method of making the binding agent of any one of claims 1-21, the method comprising:

(a) culturing the cell of claim 25 under conditions that result in the expression of the binding agent, and

(b) isolating the binding agent.

~~4827.~~ A method of

(a) disrupting, inhibiting, or blocking ILT2- and ILT4-induced suppression of myeloid cells; ~~the method comprising contacting the myeloid cells with the binding agent or antibody of any one of claims 1-15 and 22-38.~~

49. ~~A method of disrupting, inhibiting, or blocking ILT4 induced suppression of myeloid cells, comprising contacting cells the myeloid cells with the binding agent or antibody of any one of claims 1-11 and 16-38.~~

50. ~~A method of disrupting, inhibiting, or blocking ILT2 and/or ILT4 induced suppression of myeloid cells, comprising contacting cells the myeloid cells with the binding agent or antibody of any one of claims 1-38.~~

51. ~~A method of (b) inhibiting or decreasing myeloid-derived suppressor cell (MDSC) activity, the method comprising contacting the MDSCs with the binding agent or antibody of any one of claims 1-38;~~

52. ~~A method of (c) enhancing or increasing natural killer (NK) cell activity; or, the method comprising contacting the NK cells with the binding agent or antibody of any one of claims 1-38.~~

53. ~~A method of (d) enhancing or increasing cytolytic T lymphocyte (CTL) activity;~~
~~the method comprising contacting CTLs with the binding agent or antibody of any one of claims 1-38;~~ the method comprising contacting respectively the myeloid cells of (a); the MDSCs of (b); the NK cells of (c); or the CTLs of (d) with the binding agent of any one of claims 1-21.

28. A method of disrupting, inhibiting, or blocking in a mixture of cells at least one of the following:

(a) the binding of ILT2 and/or ILT4 to an MHC I molecule, and
(b) MHC I-induced ILT2 and/or ILT4 activity;
the method comprising contacting the cells with the binding agent of any one of claims 1-21 or the pharmaceutical composition of claim 22; optionally wherein the MHC I molecule is HLA-A, HLA-B, HLA-C, HLA-E, and/or HLA-G.

54. ~~A method of disrupting, inhibiting, or blocking the binding of ILT2 or ILT4 to a MHC I molecule in a subject, the method comprising administering to the subject an effective amount~~

of the binding agent or antibody of any one of claims 1-38 or the pharmaceutical composition of claim 39.

55. — A method of disrupting, inhibiting, or blocking MHC I induced ILT2 and/or ILT4 activity in a subject, the method comprising administering to the subject an effective amount of the binding agent or antibody of any one of claims 1-38 or the pharmaceutical composition of claim 39.

56. — The method of claim 49 or claim 50, wherein the MHC I molecule is HLA-A, HLA-B, HLA-C, HLA-E, and/or HLA-G.

57. — A method of disrupting, inhibiting, or blocking ILT2 or ILT4 induced suppression of myeloid cells in a subject, the method comprising administering to the subject an effective amount of the binding agent or antibody of any one of claims 1-38 or the pharmaceutical composition of claim 39.

58. — A method of inhibiting or decreasing MDSC activity in a subject, the method comprising administering to the subject an effective amount of the binding agent or antibody of any one of claims 1-38 or the pharmaceutical composition of claim 39.

59. — A method of enhancing or increasing NK cell activity in a subject, the method comprising administering to the subject an effective amount of the binding agent or antibody of any one of claims 1-38 or the pharmaceutical composition of claim 39.

60. — A method of enhancing or increasing CTL activity in a subject, the method comprising administering to the subject an effective amount of the binding agent or antibody of any one of claims 1-38 or the pharmaceutical composition of claim 39.

61. — A method of treating cancer in a subject, the method comprising administering to the subject a therapeutically effective amount of the binding agent or antibody of any one of claims 1-38 or the pharmaceutical composition of claim 39.

62. — The method of claim 61, wherein the cancer is mesothelioma, glioblastoma, renal cell carcinoma, non-small cell lung cancer, melanoma, pancreatic ductal adenocarcinoma, gastric

~~cancer, squamous cell carcinoma of the head and neck, biliary duct cancer, breast cancer, ovarian cancer, cervical cancer, endocervical cancer, colorectal cancer, or esophageal cancer.~~

~~63.—A method of inhibiting tumor growth in a subject, the method comprising administering to the subject a therapeutically effective amount of the binding agent or antibody of any one of claims 1-38 or the pharmaceutical composition of claim 39.~~

~~64.—A method of increasing or enhancing an immune response to a tumor or tumor cells in a subject, the method comprising administering to the subject a therapeutically effective amount of the binding agent or antibody of any one of claims 1-38 or the pharmaceutical composition of claim 39.~~

~~65.—A method of activating or enhancing a persistent or long-term immune response to a tumor or tumor cells in a subject, the method comprising administering to the subject a therapeutically effective amount of the binding agent or antibody of any one of claims 1-38 or the pharmaceutical composition of claim 39.~~

~~66.—A method of inhibiting tumor relapse or tumor regrowth in a subject, the method comprising administering to the subject a therapeutically effective amount of the binding agent or antibody of any one of claims 1-38 or the pharmaceutical composition of claim 39.~~

~~67.—A method of inducing a persistent or long-term immunity that inhibits tumor relapse or tumor regrowth in a subject, the method comprising administering to the subject a therapeutically effective amount of the binding agent or antibody of any one of claims 1-38 or the pharmaceutical composition of claim 39.~~

~~68.—The method of any one of claims 63-67, wherein the tumor is a pancreatic tumor, a breast tumor, a lung tumor, a non-small cell lung tumor, a head and neck tumor, a colorectal tumor, a prostate tumor, a skin tumor, a melanoma, a gastric tumor, a colorectal tumor, an ovarian tumor, a cervical tumor, a uterine tumor, an endometrial tumor, an endocervical tumor, a bladder tumor, a brain tumor, an esophageal tumor, a liver tumor, a kidney tumor, a renal tumor, mesothelioma, glioblastoma, a biliary duct tumor, or a testicular tumor.~~

~~69. — A method of activating myeloid cells in the tumor microenvironment in a subject with a tumor, the method comprising administering to the subject a therapeutically effective amount of the binding agent or antibody of any one of claims 1-38 or the pharmaceutical composition of claim 39.~~

29. Use of the binding agent of any one of claims 1-21 or the pharmaceutical composition of claim 22 in the manufacture of a medicament for

(a) disrupting, inhibiting, or blocking the binding of ILT2 and/or ILT4 to an MHC I molecule in a subject;

(b) disrupting, inhibiting, or blocking MHC I-induced ILT2 and/or ILT4 activity in a subject;

(c) disrupting, inhibiting, or blocking ILT2 or ILT4-induced suppression of myeloid cells in a subject;

(d) inhibiting or decreasing MDSC activity in a subject;

(e) enhancing or increasing NK cell activity in a subject;

(f) enhancing or increasing CTL activity in a subject;

(g) treating cancer in a subject;

(h) inhibiting tumor growth in a subject;

(i) increasing or enhancing an immune response to a tumor or tumor cells in a subject;

(j) inhibiting tumor relapse or tumor regrowth in a subject; or

(k) activating myeloid cells in the tumor microenvironment in a subject with a tumor;

wherein the binding agent of any one of claims 1-21 or the pharmaceutical composition of claim 22 is to be administered to the subject; optionally wherein the MHC I molecule is HLA-A, HLA-B, HLA-C, HLA-E, and/or HLA-G.

30. The use of claim 29, wherein the cancer is mesothelioma, glioblastoma, renal cell carcinoma, non-small cell lung cancer, melanoma, pancreatic ductal adenocarcinoma, gastric cancer, squamous cell carcinoma of the head and neck, biliary duct cancer, breast cancer, ovarian cancer, cervical cancer, endocervical cancer, colorectal cancer, or esophageal cancer.

31. The use of claim 29, wherein the tumor is a pancreatic tumor, a breast tumor, a lung tumor, a non-small cell lung tumor, a head and neck tumor, a colorectal tumor, a prostate tumor, a skin tumor, a melanoma, a gastric tumor, a colorectal tumor, an ovarian tumor, a cervical tumor, a uterine tumor, an endometrial tumor, an endocervical tumor, a bladder tumor, a brain

tumor, an esophageal tumor, a liver tumor, a kidney tumor, a renal tumor, mesothelioma, glioblastoma, a biliary duct tumor, or a testicular tumor.

~~7032. The method of any one of claims 36, 48-51, 57, and 69~~ use of claim 29, wherein the myeloid cells are dendritic cells.

~~71. The method of any one of claims 36, 48-51, 57, and 69, wherein the myeloid cells are,~~
monocytes or macrophages.

~~7233. The method of any one of claims 54-71~~ use of any one of claims 28-32, wherein the binding agent or antibody is to be administered as part of a combination therapy comprising ~~and~~ at least one additional therapeutic agent.

~~7334. The method~~ use of claim 7233, wherein ~~the combination therapy comprises the~~
additional therapeutic agent is a PD-1 antagonist, an anti-PD-1 antibody or anti-PD-L1
antibody.

35. The use of claim 34, wherein PD-1 antagonist is pembrolizumab, pidilizumab, nivolumab, durvalumab, cemiplimab, tislelizumab, spartalizumab, or STI-A1110.

~~74. The method of claim 73, wherein the combination therapy comprises at least one~~
additional therapeutic agent.

~~75. The method of any one of claims 54-74, wherein the subject is a human.~~

~~76. Use of the binding agent or antibody of any one of claims 1-39 for treatment of cancer.~~

~~77. Use of the binding agent or antibody of any one of claims 1-39 in the manufacture of a~~
medicament for treatment of cancer.

~~7836.~~ A pharmaceutical composition, comprising:

- (a) a means for inhibiting the interaction between ILT2 and/or ILT4 and MHC Class I (e.g., on tumor cells); and
- (b) a pharmaceutically acceptable carrier.

7937. The pharmaceutical composition of claim 7838, wherein the means for inhibiting the interaction between ILT2 and/or ILT4 and MHC Class I comprises an antibody comprising a heavy chain variable region comprising VH-CDR1, VH-CDR-2, and VH-CDR-3 and a light chain variable region comprising VL-CDR1, VL-CDR2, and VL-CDR3 from any one of 27F9, 47C8, 48A5, 47H6, Hz47H6.v2, 51A1, 64A12, Hz64A12, 73C4, 73D1, and Hz73D1.v1.

8038. A combination comprising a means for inhibiting the interaction between ILT2 and/or ILT4 and MHC Class I (e.g., on tumor cells), and a modulator of PD-1 or PD-L1 activity.

~~81. The method of claim 73, wherein the anti-PD-1 antibody is Pembrolizumab (MK-3475; KEYTRUDA), Pidilizumab (CT-011), Nivolumab (OPDIVO), Durvalumab (MEDI0680), Cemiplimab (REGN2810), Tislelizumab (BGB-A317), Spartalizumab (PDR-001), or STI-A1110.~~