

WHAT IS CLAIMED:

1. A binding agent that specifically binds the extracellular domain of leukocyte-associated immunoglobulin-like receptor 1 (LAIR-1), wherein: (i) the binding agent binds to human LAIR-1 and to cynomolgus LAIR-1, (ii) the binding agent binds to human LAIR-1 with a dissociation constant (K_D) of less than 1×10^{-9} M, and/or (iii) the binding agent binds to cynomolgus LAIR-1 with a K_D of less than 1×10^{-8} M; and wherein the binding agent is an antibody or an antigen-binding fragment thereof.
2. A binding agent that specifically binds the extracellular domain of LAIR-1, comprising:
 - (a) a heavy chain variable region (VH) comprising a VH-complementarity determining region (CDR)1, a VH-CDR2 and a VH-CDR3 from SEQ ID NO: 119, and a light chain variable region (VL) comprising a VL-CDR1, a VL-CDR2 and a VL-CDR3 from SEQ ID NO: 120; or
 - (b) a VH comprising a VH-CDR1, a VH-CDR2 and a VH-CDR3 from SEQ ID NO: 117, and a VL comprising a VL-CDR1, a VL-CDR2 and a VL-CDR3 from SEQ ID NO: 118; or
 - (c) a VH comprising a VH-CDR1, a VH-CDR2 and a VH-CDR3 from SEQ ID NO: 115, and a VL comprising a VL-CDR1, a VL-CDR2 and a VL-CDR3 from SEQ ID NO: 116; or
 - (d) a VH comprising a VH-CDR1, a VH-CDR2 and a VH-CDR3 from SEQ ID NO: 121, and a VL comprising a VL-CDR1, a VL-CDR2 and a VL-CDR3 from SEQ ID NO: 122; or
 - (e) a VH comprising a VH-CDR1, a VH-CDR2 and a VH-CDR3 from SEQ ID NO: 123, and a VL comprising a VL-CDR1, a VL-CDR2 and a VL-CDR3 from SEQ ID NO: 124; or
 - (f) a VH comprising a VH-CDR1, a VH-CDR2 and a VH-CDR3 from SEQ ID NO: 125, and a VL comprising a VL-CDR1, a VL-CDR2 and a VL-CDR3 from SEQ ID NO: 126; or
 - (g) a VH comprising a VH-CDR1, a VH-CDR2 and a VH-CDR3 from SEQ ID NO: 127, and a VL comprising a VL-CDR1, a VL-CDR2 and a VL-CDR3 from SEQ ID NO: 128; or
 - (h) a VH comprising a VH-CDR1, a VH-CDR2 and a VH-CDR3 from SEQ ID NO: 129, and a VL comprising a VL-CDR1, a VL-CDR2 and a VL-CDR3 from SEQ ID NO: 130.
3. The binding agent of claim 2, wherein
 - (i) the VH comprising the VH CDR1 comprising the amino acid sequence set forth in SEQ ID NO:25, the VH CDR2 comprising the amino acid sequence set forth in SEQ ID NO:41, the VH CDR3 comprising the amino acid sequence set forth in SEQ ID NO:27; and the VL comprising the VL CDR1 comprising the amino acid sequence set forth in SEQ ID NO:28, the

VL CDR2 comprising the amino acid sequence set forth in SEQ ID NO:42, and the VL CDR3 comprising the amino acid sequence set forth in SEQ ID NO:30; or

(ii) the VH comprising the VH CDR1 comprising the amino acid sequence set forth in SEQ ID NO:31, the VH CDR2 comprising the amino acid sequence set forth in SEQ ID NO:43, the VH CDR3 comprising the amino acid sequence set forth in SEQ ID NO:27; and the VL comprising the VL CDR1 comprising the amino acid sequence set forth in SEQ ID NO:28, the VL CDR2 comprising the amino acid sequence set forth in SEQ ID NO:42, and the VL CDR3 comprising the amino acid sequence set forth in SEQ ID NO:30; or

(iii) the VH comprising the VH CDR1 comprising the amino acid sequence set forth in SEQ ID NO:25, the VH CDR2 comprising the amino acid sequence set forth in SEQ ID NO:44, the VH CDR3 comprising the amino acid sequence set forth in SEQ ID NO:27; and the VL comprising the VL CDR1 comprising the amino acid sequence set forth in SEQ ID NO:28, the VL CDR2 comprising the amino acid sequence set forth in SEQ ID NO:42, and the VL CDR3 comprising the amino acid sequence set forth in SEQ ID NO:30; or

(iv) the VH comprising the VH CDR1 comprising the amino acid sequence set forth in SEQ ID NO:34, the VH CDR2 comprising the amino acid sequence set forth in SEQ ID NO:41, the VH CDR3 comprising the amino acid sequence set forth in SEQ ID NO:27; and the VL comprising the VL CDR1 comprising the amino acid sequence set forth in SEQ ID NO:28, the VL CDR2 comprising the amino acid sequence set forth in SEQ ID NO:42, and the VL CDR3 comprising the amino acid sequence set forth in SEQ ID NO:30; or

(v) the VH comprising the VH CDR1 comprising the amino acid sequence set forth in SEQ ID NO:35, the VH CDR2 comprising the amino acid sequence set forth in SEQ ID NO:45, the VH CDR3 comprising the amino acid sequence set forth in SEQ ID NO:37; and the VL comprising the VL CDR1 comprising the amino acid sequence set forth in SEQ ID NO:38, the VL CDR2 comprising the amino acid sequence set forth in SEQ ID NO:39, and the VL CDR3 comprising the amino acid sequence set forth in SEQ ID NO:40.

4. The binding agent of claim 3, wherein

(i) the VH has at least 80% sequence identity to the amino acid sequence of SEQ ID NO:119, and/or the VL has at least 80% sequence identity to the amino acid sequence of SEQ ID NO:120; and/or

(ii) the VH has at least 90% sequence identity to the amino acid sequence of SEQ ID

NO:119, and/or the VL has at least 90% sequence identity to the amino acid sequence of SEQ ID NO:120; and/or

(iii) the VH comprises the amino acid sequence of SEQ ID NO:119, and/or the VL comprises the amino acid sequence of SEQ ID NO:120.

5. The binding agent of claim 3 or claim 4, comprising

(i) a heavy chain having at least 90% sequence identity to the amino acid sequence of SEQ ID NO:134 and/or a light chain having at least 90% sequence identity to the amino acid sequence of SEQ ID NO:136; and/or

(ii) a heavy chain comprising the amino acid sequence of SEQ ID NO:134 and/or a light chain comprising the amino acid sequence of SEQ ID NO:136.

6. The binding agent of claim 2, wherein

(a) (i) the VH comprising the VH CDR1 comprising the amino acid sequence set forth in SEQ ID NO:25, the VH CDR2 comprising the amino acid sequence set forth in SEQ ID NO:26, the VH CDR3 comprising the amino acid sequence set forth in SEQ ID NO:27; and the VL comprising the VL CDR1 comprising the amino acid sequence set forth in SEQ ID NO:28, the VL CDR2 comprising the amino acid sequence set forth in SEQ ID NO:29, and the VL CDR3 comprising the amino acid sequence set forth in SEQ ID NO:30; or

(ii) the VH comprising the VH CDR1 comprising the amino acid sequence set forth in SEQ ID NO:31, the VH CDR2 comprising the amino acid sequence set forth in SEQ ID NO:32, the VH CDR3 comprising the amino acid sequence set forth in SEQ ID NO:27; and the VL comprising the VL CDR1 comprising the amino acid sequence set forth in SEQ ID NO:28, the VL CDR2 comprising the amino acid sequence set forth in SEQ ID NO:29, and the VL CDR3 comprising the amino acid sequence set forth in SEQ ID NO:30; or

(iii) the VH comprising the VH CDR1 comprising the amino acid sequence set forth in SEQ ID NO:25, the VH CDR2 comprising the amino acid sequence set forth in SEQ ID NO:33, the VH CDR3 comprising the amino acid sequence set forth in SEQ ID NO:27; and the VL comprising the VL CDR1 comprising the amino acid sequence set forth in SEQ ID NO:28, the VL CDR2 comprising the amino acid sequence set forth in SEQ ID NO:29, and the VL CDR3 comprising the amino acid sequence set forth in SEQ ID NO:30; or

(iv) the VH comprising the VH CDR1 comprising the amino acid sequence set

forth in SEQ ID NO:34, the VH CDR2 comprising the amino acid sequence set forth in SEQ ID NO:26, the VH CDR3 comprising the amino acid sequence set forth in SEQ ID NO:27; and the VL comprising the VL CDR1 comprising the amino acid sequence set forth in SEQ ID NO:28, the VL CDR2 comprising the amino acid sequence set forth in SEQ ID NO:29, and the VL CDR3 comprising the amino acid sequence set forth in SEQ ID NO:30; or

(v) the VH comprising the VH CDR1 comprising the amino acid sequence set forth in SEQ ID NO:35, the VH CDR2 comprising the amino acid sequence set forth in SEQ ID NO:36, the VH CDR3 comprising the amino acid sequence set forth in SEQ ID NO:37; and the VL comprising the VL CDR1 comprising the amino acid sequence set forth in SEQ ID NO:38, the VL CDR2 comprising the amino acid sequence set forth in SEQ ID NO:39, and the VL CDR3 comprising the amino acid sequence set forth in SEQ ID NO:40; or

(b) (i) the VH comprising the VH CDR1 comprising the amino acid sequence set forth in SEQ ID NO:9, the VH CDR2 comprising the amino acid sequence set forth in SEQ ID NO:10, the VH CDR3 comprising the amino acid sequence set forth in SEQ ID NO:11; and the VL comprising the VL CDR1 comprising the amino acid sequence set forth in SEQ ID NO:12, the VL CDR2 comprising the amino acid sequence set forth in SEQ ID NO:13, and the VL CDR3 comprising the amino acid sequence set forth in SEQ ID NO:14; or

(ii) the VH comprising the VH CDR1 comprising the amino acid sequence set forth in SEQ ID NO:15, the VH CDR2 comprising the amino acid sequence set forth in SEQ ID NO:16, the VH CDR3 comprising the amino acid sequence set forth in SEQ ID NO:11; and the VL comprising the VL CDR1 comprising the amino acid sequence set forth in SEQ ID NO:12, the VL CDR2 comprising the amino acid sequence set forth in SEQ ID NO:13, and the VL CDR3 comprising the amino acid sequence set forth in SEQ ID NO:14; or

(iii) the VH comprising the VH CDR1 comprising the amino acid sequence set forth in SEQ ID NO:9, the VH CDR2 comprising the amino acid sequence set forth in SEQ ID NO:17, the VH CDR3 comprising the amino acid sequence set forth in SEQ ID NO:11; and the VL comprising the VL CDR1 comprising the amino acid sequence set forth in SEQ ID NO:12, the VL CDR2 comprising the amino acid sequence set forth in SEQ ID NO:13, and the VL CDR3 comprising the amino acid sequence set forth in SEQ ID NO:14; or

(iv) the VH comprising the VH CDR1 comprising the amino acid sequence set forth in SEQ ID NO:18, the VH CDR2 comprising the amino acid sequence set forth in SEQ ID

NO:10, the VH CDR3 comprising the amino acid sequence set forth in SEQ ID NO:11; and the VL comprising the VL CDR1 comprising the amino acid sequence set forth in SEQ ID NO:12, the VL CDR2 comprising the amino acid sequence set forth in SEQ ID NO:13, and the VL CDR3 comprising the amino acid sequence set forth in SEQ ID NO:14; or

(v) the VH comprising the VH CDR1 comprising the amino acid sequence set forth in SEQ ID NO:19, the VH CDR2 comprising the amino acid sequence set forth in SEQ ID NO:20, the VH CDR3 comprising the amino acid sequence set forth in SEQ ID NO:21; and the VL comprising the VL CDR1 comprising the amino acid sequence set forth in SEQ ID NO:22, the VL CDR2 comprising the amino acid sequence set forth in SEQ ID NO:23, and the VL CDR3 comprising the amino acid sequence set forth in SEQ ID NO:24; or

(c) (i) the VH comprising the VH CDR1 comprising the amino acid sequence set forth in SEQ ID NO:46, the VH CDR2 comprising the amino acid sequence set forth in SEQ ID NO:47, the VH CDR3 comprising the amino acid sequence set forth in SEQ ID NO:48; and the VL comprising the VL CDR1 comprising the amino acid sequence set forth in SEQ ID NO:49, the VL CDR2 comprising the amino acid sequence set forth in SEQ ID NO:50, and the VL CDR3 comprising the amino acid sequence set forth in SEQ ID NO:51; or

(ii) the VH comprising the VH CDR1 comprising the amino acid sequence set forth in SEQ ID NO:52, the VH CDR2 comprising the amino acid sequence set forth in SEQ ID NO:53, the VH CDR3 comprising the amino acid sequence set forth in SEQ ID NO:48; and the VL comprising the VL CDR1 comprising the amino acid sequence set forth in SEQ ID NO:49, the VL CDR2 comprising the amino acid sequence set forth in SEQ ID NO:50, and the VL CDR3 comprising the amino acid sequence set forth in SEQ ID NO:51; or

(iii) the VH comprising the VH CDR1 comprising the amino acid sequence set forth in SEQ ID NO:46, the VH CDR2 comprising the amino acid sequence set forth in SEQ ID NO:54, the VH CDR3 comprising the amino acid sequence set forth in SEQ ID NO:48; and the VL comprising the VL CDR1 comprising the amino acid sequence set forth in SEQ ID NO:49, the VL CDR2 comprising the amino acid sequence set forth in SEQ ID NO:50, and the VL CDR3 comprising the amino acid sequence set forth in SEQ ID NO:51; or

(iv) the VH comprising the VH CDR1 comprising the amino acid sequence set forth in SEQ ID NO:55, the VH CDR2 comprising the amino acid sequence set forth in SEQ ID NO:47, the VH CDR3 comprising the amino acid sequence set forth in SEQ ID NO:48; and the

(v) the VH comprising the VH CDR1 comprising the amino acid sequence set forth in SEQ ID NO:56, the VH CDR2 comprising the amino acid sequence set forth in SEQ ID NO:57, the VH CDR3 comprising the amino acid sequence set forth in SEQ ID NO:58; and the VL comprising the VL CDR1 comprising the amino acid sequence set forth in SEQ ID NO:59, the VL CDR2 comprising the amino acid sequence set forth in SEQ ID NO:60, and the VL CDR3 comprising the amino acid sequence set forth in SEQ ID NO:61; or

(ii) the VH comprising the VH CDR1 comprising the amino acid sequence set forth in SEQ ID NO:68, the VH CDR2 comprising the amino acid sequence set forth in SEQ ID NO:69, the VH CDR3 comprising the amino acid sequence set forth in SEQ ID NO:64; and the VL comprising the VL CDR1 comprising the amino acid sequence set forth in SEQ ID NO:65, the VL CDR2 comprising the amino acid sequence set forth in SEQ ID NO:66, and the VL CDR3 comprising the amino acid sequence set forth in SEQ ID NO:67; or

(iv) the VH comprising the VH CDR1 comprising the amino acid sequence set forth in SEQ ID NO:71, the VH CDR2 comprising the amino acid sequence set forth in SEQ ID NO:63, the VH CDR3 comprising the amino acid sequence set forth in SEQ ID NO:64; and the VL comprising the VL CDR1 comprising the amino acid sequence set forth in SEQ ID NO:65,

the VL CDR2 comprising the amino acid sequence set forth in SEQ ID NO:66, and the VL CDR3 comprising the amino acid sequence set forth in SEQ ID NO:67; or

(v) the VH comprising the VH CDR1 comprising the amino acid sequence set forth in SEQ ID NO:72, the VH CDR2 comprising the amino acid sequence set forth in SEQ ID NO:73, the VH CDR3 comprising the amino acid sequence set forth in SEQ ID NO:74; and the VL comprising the VL CDR1 comprising the amino acid sequence set forth in SEQ ID NO:75, the VL CDR2 comprising the amino acid sequence set forth in SEQ ID NO:76, and the VL CDR3 comprising the amino acid sequence set forth in SEQ ID NO:77; or

(e) (i) the VH comprising the VH CDR1 comprising the amino acid sequence set forth in SEQ ID NO:25, the VH CDR2 comprising the amino acid sequence set forth in SEQ ID NO:78, the VH CDR3 comprising the amino acid sequence set forth in SEQ ID NO:79; and the VL comprising the VL CDR1 comprising the amino acid sequence set forth in SEQ ID NO:80, the VL CDR2 comprising the amino acid sequence set forth in SEQ ID NO:29, and the VL CDR3 comprising the amino acid sequence set forth in SEQ ID NO:81; or

(ii) the VH comprising the VH CDR1 comprising the amino acid sequence set forth in SEQ ID NO:31, the VH CDR2 comprising the amino acid sequence set forth in SEQ ID NO:82, the VH CDR3 comprising the amino acid sequence set forth in SEQ ID NO:79; and the VL comprising the VL CDR1 comprising the amino acid sequence set forth in SEQ ID NO:80, the VL CDR2 comprising the amino acid sequence set forth in SEQ ID NO:29, and the VL CDR3 comprising the amino acid sequence set forth in SEQ ID NO:81; or

(iii) the VH comprising the VH CDR1 comprising the amino acid sequence set forth in SEQ ID NO:25, the VH CDR2 comprising the amino acid sequence set forth in SEQ ID NO:83, the VH CDR3 comprising the amino acid sequence set forth in SEQ ID NO:79; and the VL comprising the VL CDR1 comprising the amino acid sequence set forth in SEQ ID NO:80, the VL CDR2 comprising the amino acid sequence set forth in SEQ ID NO:29, and the VL CDR3 comprising the amino acid sequence set forth in SEQ ID NO:81; or

(iv) the VH comprising the VH CDR1 comprising the amino acid sequence set forth in SEQ ID NO:34, the VH CDR2 comprising the amino acid sequence set forth in SEQ ID NO:78, the VH CDR3 comprising the amino acid sequence set forth in SEQ ID NO:79; and the VL comprising the VL CDR1 comprising the amino acid sequence set forth in SEQ ID NO:80, the VL CDR2 comprising the amino acid sequence set forth in SEQ ID NO:29, and the VL

CDR3 comprising the amino acid sequence set forth in SEQ ID NO:81; or

(v) the VH comprising the VH CDR1 comprising the amino acid sequence set forth in SEQ ID NO:35, the VH CDR2 comprising the amino acid sequence set forth in SEQ ID NO:84, the VH CDR3 comprising the amino acid sequence set forth in SEQ ID NO:85; and the VL comprising the VL CDR1 comprising the amino acid sequence set forth in SEQ ID NO:86, the VL CDR2 comprising the amino acid sequence set forth in SEQ ID NO:39, and the VL CDR3 comprising the amino acid sequence set forth in SEQ ID NO:8; or

(f) (i) the VH comprising the VH CDR1 comprising the amino acid sequence set forth in SEQ ID NO:25, the VH CDR2 comprising the amino acid sequence set forth in SEQ ID NO:88, the VH CDR3 comprising the amino acid sequence set forth in SEQ ID NO:89; and the VL comprising the VL CDR1 comprising the amino acid sequence set forth in SEQ ID NO:90, the VL CDR2 comprising the amino acid sequence set forth in SEQ ID NO:91, and the VL CDR3 comprising the amino acid sequence set forth in SEQ ID NO:92; or

(ii) the VH comprising the VH CDR1 comprising the amino acid sequence set forth in SEQ ID NO:31, the VH CDR2 comprising the amino acid sequence set forth in SEQ ID NO:32, the VH CDR3 comprising the amino acid sequence set forth in SEQ ID NO:89; and the VL comprising the VL CDR1 comprising the amino acid sequence set forth in SEQ ID NO:90, the VL CDR2 comprising the amino acid sequence set forth in SEQ ID NO:91, and the VL CDR3 comprising the amino acid sequence set forth in SEQ ID NO:92; or

(iii) the VH comprising the VH CDR1 comprising the amino acid sequence set forth in SEQ ID NO:25, the VH CDR2 comprising the amino acid sequence set forth in SEQ ID NO:93, the VH CDR3 comprising the amino acid sequence set forth in SEQ ID NO:89; and the VL comprising the VL CDR1 comprising the amino acid sequence set forth in SEQ ID NO:90, the VL CDR2 comprising the amino acid sequence set forth in SEQ ID NO:91, and the VL CDR3 comprising the amino acid sequence set forth in SEQ ID NO:92; or

(iv) the VH comprising the VH CDR1 comprising the amino acid sequence set forth in SEQ ID NO:34, the VH CDR2 comprising the amino acid sequence set forth in SEQ ID NO:88, the VH CDR3 comprising the amino acid sequence set forth in SEQ ID NO:89; and the VL comprising the VL CDR1 comprising the amino acid sequence set forth in SEQ ID NO:90, the VL CDR2 comprising the amino acid sequence set forth in SEQ ID NO:91, and the VL CDR3 comprising the amino acid sequence set forth in SEQ ID NO:92; or

(v) the VH comprising the VH CDR1 comprising the amino acid sequence set forth in SEQ ID NO:35, the VH CDR2 comprising the amino acid sequence set forth in SEQ ID NO:94, the VH CDR3 comprising the amino acid sequence set forth in SEQ ID NO:95; and the VL comprising the VL CDR1 comprising the amino acid sequence set forth in SEQ ID NO:96, the VL CDR2 comprising the amino acid sequence set forth in SEQ ID NO:97, and the VL CDR3 comprising the amino acid sequence set forth in SEQ ID NO:98.

7. The binding agent of claim 6, wherein

(a) (i) the VH has at least 80% sequence identity to the amino acid sequence of SEQ ID NO:117, and/or the VL has at least 80% sequence identity to the amino acid sequence of SEQ ID NO:118; or

(ii) the VH has at least 80% sequence identity to the amino acid sequence of SEQ ID NO:115, and/or the VL has at least 80% sequence identity to the amino acid sequence of SEQ ID NO:116; or

(iii) the VH has at least 80% sequence identity to the amino acid sequence of SEQ ID NO:121, and/or the VL has at least 80% sequence identity to the amino acid sequence of SEQ ID NO:122; or

(iv) the VH has at least 80% sequence identity to the amino acid sequence of SEQ ID NO:123, and/or the VL has at least 80% sequence identity to the amino acid sequence of SEQ ID NO:124; or

(v) the VH has at least 80% sequence identity to the 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

(vi) the VH 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; or

(vii) the VH has at least 80% sequence identity to the amino acid sequence of SEQ ID NO:129, and/or the light chain variable region has at least 80% sequence identity to the amino acid sequence of SEQ ID NO:130; and/or

(b) (i) the VH comprises the amino acid sequence of SEQ ID NO:117, and/or the VL comprises the amino acid sequence of SEQ ID NO:118; or

(ii) the VH comprises the amino acid sequence of SEQ ID NO:115, and/or the VL

comprises the amino acid sequence of SEQ ID NO:116; or

(iii) the VH comprises the amino acid sequence of SEQ ID NO:121, and/or the VL comprises the amino acid sequence of SEQ ID NO:122; or

(iv) the VH comprises the amino acid sequence of SEQ ID NO:123, and/or the VL comprises the amino acid sequence of SEQ ID NO:124; or

(v) 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; or

(vi) 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; or

(vii) the VH comprises the amino acid sequence of SEQ ID NO:129, and/or the VL comprises the amino acid sequence of SEQ ID NO:130.

8. The binding agent of claim 6 or claim 7, comprising

(i) a heavy chain having at least 90% sequence identity to the amino acid sequence of SEQ ID NO:138 and/or a light chain having at least 90% sequence identity to the amino acid sequence of SEQ ID NO:140; and/or

(ii) a heavy chain comprising the amino acid sequence of SEQ ID NO:138 and/or a light chain comprising the amino acid sequence of SEQ ID NO:140.

9. The binding agent of any one of claims 0-8, wherein the binding agent has at least one of the following properties:

- (i) binds human LAIR-1;
- (ii) binds cyno LAIR-1;
- (iii) does not bind mouse LAIR-1;
- (iv) does not bind human LAIR-2;
- (v) is a LAIR-1 antagonist;
- (vi) inhibits LAIR-1 activity;
- (vii) inhibits LAIR-1 signaling in cells that express LAIR-1;
- (viii) inhibits binding of LAIR-1 to collagen;
- (ix) inhibits binding of LAIR-1 to MARCO;
- (x) inhibits binding of LAIR-1 to COLEC12;
- (xi) inhibits LAIR-1-induced suppression of myeloid cells;

- (xii) inhibits LAIR-1-induced suppression of myeloid cell activity;
- (xiii) restores FcR activation in myeloid cells;
- (xiv) restores cytokine and/or chemokine production in myeloid cells;
- (xv) inhibits LAIR-1-induced suppression of NK cells;
- (xvi) inhibits LAIR-1-induced suppression of NK activity;
- (xvii) inhibits LAIR-1-induced suppression of T-cell activity; and
- (xviii) inhibits MDSC activity,

optionally wherein the one or more LAIR ligands is selected from the group consisting of collagen, MARCO, COLEC12, MBL, SPD, and C1 complex.

10. A binding agent that specifically binds the extracellular domain of mouse LAIR-1, wherein the binding agent comprises 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 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: 132.

11. The binding agent of claim 10, comprising

(i) the VH comprising the VH CDR1 comprising the amino acid sequence set forth in SEQ ID NO:99, the VH CDR2 comprising the amino acid sequence set forth in SEQ ID NO:100, the VH CDR3 comprising the amino acid sequence set forth in SEQ ID NO:101; and the VL comprising the VL CDR1 comprising the amino acid sequence set forth in SEQ ID NO:102, the VL CDR2 comprising the amino acid sequence set forth in SEQ ID NO:103, and the VL CDR3 comprising the amino acid sequence set forth in SEQ ID NO:104; or

(ii) the VH comprising the VH CDR1 comprising the amino acid sequence set forth in SEQ ID NO:105, the VH CDR2 comprising the amino acid sequence set forth in SEQ ID NO:106, the VH CDR3 comprising the amino acid sequence set forth in SEQ ID NO:101; and the VL comprising the VL CDR1 comprising the amino acid sequence set forth in SEQ ID NO:102, the VL CDR2 comprising the amino acid sequence set forth in SEQ ID NO:103, and the VL CDR3 comprising the amino acid sequence set forth in SEQ ID NO:104; or

(iii) the VH comprising the VH CDR1 comprising the amino acid sequence set forth in SEQ ID NO:99, the VH CDR2 comprising the amino acid sequence set forth in SEQ ID NO:107, the VH CDR3 comprising the amino acid sequence set forth in SEQ ID NO:101; and the VL

comprising the VL CDR1 comprising the amino acid sequence set forth in SEQ ID NO:102, the VL CDR2 comprising the amino acid sequence set forth in SEQ ID NO:103, and the VL CDR3 comprising the amino acid sequence set forth in SEQ ID NO:104; or

(iv) the VH comprising the VH CDR1 comprising the amino acid sequence set forth in SEQ ID NO:108, the VH CDR2 comprising the amino acid sequence set forth in SEQ ID NO:100, the VH CDR3 comprising the amino acid sequence set forth in SEQ ID NO:101; and the VL comprising the VL CDR1 comprising the amino acid sequence set forth in SEQ ID NO:102, the VL CDR2 comprising the amino acid sequence set forth in SEQ ID NO:103, and the VL CDR3 comprising the amino acid sequence set forth in SEQ ID NO:104; or

(v) the VH comprising the VH CDR1 comprising the amino acid sequence set forth in SEQ ID NO:109, the VH CDR2 comprising the amino acid sequence set forth in SEQ ID NO:110, the VH CDR3 comprising the amino acid sequence set forth in SEQ ID NO:111; and the VL comprising the VL CDR1 comprising the amino acid sequence set forth in SEQ ID NO:112, the VL CDR2 comprising the amino acid sequence set forth in SEQ ID NO:113, and the VL CDR3 comprising the amino acid sequence set forth in SEQ ID NO:114.

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

(i) the VH has at least 80% sequence identity to the amino acid sequence of SEQ ID NO:131, and/or the light chain variable region has at least 80% sequence identity to the amino acid sequence of SEQ ID NO:132; and/or

(ii) 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.

13. A binding agent that specifically binds the extracellular domain of MARCO, comprising:

(a) a VH comprising a VH-CDR1, a VH-CDR2 and a VH-CDR3 from the amino acid sequence of SEQ ID NO: 160, 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: 161; or

(b) a VH comprising a VH-CDR1, a VH-CDR2 and a VH-CDR3 from the amino acid sequence of SEQ ID NO: 162, 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: 163; or

(c) a VH comprising a VH-CDR1, a VH-CDR2 and a VH-CDR3 from the amino acid

sequence of SEQ ID NO: 164, 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: 165.

14. The binding agent of claim 13, comprising

(a) (i) the VH comprising the VH CDR1 comprising the amino acid sequence of SEQ ID NO:178, the VH CDR2 comprising the amino acid sequence of SEQ ID NO:179, and the VH CDR3 comprising the amino acid sequence of SEQ ID NO:180; and the VL comprising the VL CDR1 comprising the amino acid sequence of SEQ ID NO:181, the VL CDR2 comprising the amino acid sequence of SEQ ID NO:182, and the VL CDR3 comprising the amino acid sequence of SEQ ID NO:183; or

(ii) the VH comprising the VH CDR1 comprising the amino acid sequence of SEQ ID NO:184, the VH CDR2 comprising the amino acid sequence of SEQ ID NO:185, and the VH CDR3 comprising the amino acid sequence of SEQ ID NO:180; and the VL comprising the VL CDR1 comprising the amino acid sequence of SEQ ID NO:181, the VL CDR2 comprising the amino acid sequence of SEQ ID NO:182, and the VL CDR3 comprising the amino acid sequence of SEQ ID NO:183; or

(iii) the VH comprising the VH CDR1 comprising the amino acid sequence of SEQ ID NO:178, the VH CDR2 comprising the amino acid sequence of SEQ ID NO:186, the VH CDR3 comprising the amino acid sequence of SEQ ID NO:180; and the VL comprising the VL CDR1 comprising the amino acid sequence of SEQ ID NO:181, the VL CDR2 comprising the amino acid sequence of SEQ ID NO:182, and the VL CDR3 comprising the amino acid sequence of SEQ ID NO:183; or

(iv) the VH comprising the VH CDR1 comprising the amino acid sequence of SEQ ID NO:187, the VH CDR2 comprising the amino acid sequence of SEQ ID NO:179, the VH CDR3 comprising the amino acid sequence of SEQ ID NO:180; and the VL comprising the VL CDR1 comprising the amino acid sequence of SEQ ID NO:181, the VL CDR2 comprising the amino acid sequence of SEQ ID NO:182, and the VL CDR3 comprising the amino acid sequence of SEQ ID NO:183; or

(v) the VH comprising the VH CDR1 comprising the amino acid sequence of SEQ ID NO:188, the VH CDR2 comprising the amino acid sequence of SEQ ID NO:189, the VH CDR3 comprising the amino acid sequence of SEQ ID NO:190; and the VL comprising the VL CDR1 comprising the amino acid sequence of SEQ ID NO:191, the VL CDR2 comprising

the amino acid sequence of SEQ ID NO:192, and the VL CDR3 comprising the amino acid sequence of SEQ ID NO:193; or

(b) (i) the VH comprising the VH CDR1 comprising the amino acid sequence of SEQ ID NO:194, the VH CDR2 comprising the amino acid sequence of SEQ ID NO:195, the VH CDR3 comprising the amino acid sequence of SEQ ID NO:196; and the VL comprising the VL CDR1 comprising the amino acid sequence of SEQ ID NO:197, the VL CDR2 comprising the amino acid sequence of SEQ ID NO:198, and the VL CDR3 comprising the amino acid sequence of SEQ ID NO:199; or

(ii) the VH comprising the VH CDR1 comprising the amino acid sequence of SEQ ID NO:200, the VH CDR2 comprising the amino acid sequence of SEQ ID NO:185, the VH CDR3 comprising the amino acid sequence of SEQ ID NO:196; and the VL comprising the VL CDR1 comprising the amino acid sequence of SEQ ID NO:197, the VL CDR2 comprising the amino acid sequence of SEQ ID NO:198, and the VL CDR3 comprising the amino acid sequence of SEQ ID NO:199; or

(iii) the VH comprising the VH CDR1 comprising the amino acid sequence of SEQ ID NO:194, the VH CDR2 comprising the amino acid sequence of SEQ ID NO:201, the VH CDR3 comprising the amino acid sequence of SEQ ID NO:196; and the VL comprising the VL CDR1 comprising the amino acid sequence of SEQ ID NO:197, the VL CDR2 comprising the amino acid sequence of SEQ ID NO:198, and the VL CDR3 comprising the amino acid sequence of SEQ ID NO:199; or

(iv) the VH comprising the VH CDR1 comprising the amino acid sequence of SEQ ID NO:202, the VH CDR2 comprising the amino acid sequence of SEQ ID NO:195, the VH CDR3 comprising the amino acid sequence of SEQ ID NO:196; and the VL comprising the VL CDR1 comprising the amino acid sequence of SEQ ID NO:197, the VL CDR2 comprising the amino acid sequence of SEQ ID NO:198, and the VL CDR3 comprising the amino acid sequence of SEQ ID NO:199; or

(v) the VH comprising the VH CDR1 comprising the amino acid sequence of SEQ ID NO:203, the VH CDR2 comprising the amino acid sequence of SEQ ID NO:204, the VH CDR3 comprising the amino acid sequence of SEQ ID NO:205; and the VL comprising the VL CDR1 comprising the amino acid sequence of SEQ ID NO:206, the VL CDR2 comprising the amino acid sequence of SEQ ID NO:207, and the VL CDR3 comprising the amino acid

sequence of SEQ ID NO:208; or

(b) (i) the VH comprising the VH CDR1 comprising the amino acid sequence of SEQ ID NO:209, the VH CDR2 comprising the amino acid sequence of SEQ ID NO:210, the VH CDR3 comprising the amino acid sequence of SEQ ID NO:211; and the VL comprising the VL CDR1 comprising the amino acid sequence of SEQ ID NO:212, the VL CDR2 comprising the amino acid sequence of SEQ ID NO:213, and the VL CDR3 comprising the amino acid sequence of SEQ ID NO:214; or

(ii) the VH comprising the VH CDR1 comprising the amino acid sequence of SEQ ID NO:215, the VH CDR2 comprising the amino acid sequence of SEQ ID NO:216, the VH CDR3 comprising the amino acid sequence of SEQ ID NO:211; and the VL comprising the VL CDR1 comprising the amino acid sequence of SEQ ID NO:212, the VL CDR2 comprising the amino acid sequence of SEQ ID NO:213, and the VL CDR3 comprising the amino acid sequence of SEQ ID NO:214; or

(iii) the VH comprising the VH CDR1 comprising the amino acid sequence of SEQ ID NO:209, the VH CDR2 comprising the amino acid sequence of SEQ ID NO:217, the VH CDR3 comprising the amino acid sequence of SEQ ID NO:211; and the VL comprising the VL CDR1 comprising the amino acid sequence of SEQ ID NO:212, the VL CDR2 comprising the amino acid sequence of SEQ ID NO:213, and the VL CDR3 comprising the amino acid sequence of SEQ ID NO:214; or

(iv) the VH comprising the VH CDR1 comprising the amino acid sequence of SEQ ID NO:218, the VH CDR2 comprising the amino acid sequence of SEQ ID NO:210, the VH CDR3 comprising the amino acid sequence of SEQ ID NO:211; and the VL comprising the VL CDR1 comprising the amino acid sequence of SEQ ID NO:212, the VL CDR2 comprising the amino acid sequence of SEQ ID NO:213, and the VL CDR3 comprising the amino acid sequence of SEQ ID NO:213; or

(v) the VH comprising the VH CDR1 comprising the amino acid sequence of SEQ ID NO:219, the VH CDR2 comprising the amino acid sequence of SEQ ID NO:220, the VH CDR3 comprising the amino acid sequence of SEQ ID NO:221; and the VL comprising the VL CDR1 comprising the amino acid sequence of SEQ ID NO:222, the VL CDR2 comprising the amino acid sequence of SEQ ID NO:223, and the VL CDR3 comprising the amino acid sequence of SEQ ID NO:224.

15. The binding agent of claim 13 or 14, wherein:
- (a) (i) the VH has at least 80% sequence identity to the amino acid sequence of SEQ ID NO:160 and/or the VL has at least 80% sequence identity to the amino acid sequence of SEQ ID NO:161; or
 - (ii) the VH has at least 80% sequence identity to the amino acid sequence of SEQ ID NO:162 and/or the VL has at least 80% sequence identity to the amino acid sequence of SEQ ID NO:163; or
 - (iii) the VH has at least 80% sequence identity to the amino acid sequence of SEQ ID NO:164 and/or the VL has at least 80% sequence identity to the amino acid sequence of SEQ ID NO:165; and/or
- (b) (i) the VH comprises the amino acid sequence of SEQ ID NO:160 and/or the VL comprises the amino acid sequence of SEQ ID NO:161; or
- (ii) the VH comprises the amino acid sequence of SEQ ID NO:162 and/or the VL comprises the amino acid sequence of SEQ ID NO:163; or
- (iii) the VH comprises the amino acid sequence of SEQ ID NO:164 and/or the VL comprises the amino acid sequence of SEQ ID NO:165.
16. The binding agent of any one of claims 13-15, which comprises a detectable moiety, optionally wherein the detectable moiety is a fluorescent label, a bioluminescent label, a chemiluminescent label, an enzyme, a small molecule, a radioisotope, or colloidal gold.
17. The binding agent of any one of claims 0-16, which is
- (a) an antibody;
 - (b) an antibody fragment comprising at least one antigen-binding site;
 - (c) a chimeric antibody;
 - (d) a humanized antibody;
 - (e) a bispecific or multispecific antibody; or
 - (f) attached to a half-life extending moiety.
18. The binding agent of claim 17, which is an IgG1 antibody, an IgG2 antibody, or an IgG4 antibody; optionally wherein the antibody is a human IgG1 antibody, a human IgG2 antibody, or a human IgG4 antibody.

19. The binding agent of claim 17 or 18, comprising a kappa light chain or a lambda light chain, optionally wherein the antibody comprises a human kappa light chain or a human lambda light chain.
20. The binding agent of claim 17, 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.
21. A pharmaceutical composition that comprises the binding agent of any one of claims 0-20 and a pharmaceutically acceptable carrier.
22. An isolated polynucleotide or polynucleotides encoding the binding agent of any one of claims 0-20.
23. A vector or vectors comprising the polynucleotide or polynucleotides of claim 22.
24. An isolated cell comprising the polynucleotide or polynucleotides of claim 22 or the vector or vectors of claim 23.
25. An isolated cell producing the binding agent of any one of claims 0-20.
26. A method of making the binding a binding agent, comprising:
 - (a) culturing the cell of claim 24 or 25, and
 - (b) isolating the binding agent or antibody.
27. A method of detecting MARCO in a biological sample comprising:
 - (a) contacting the biological sample with the binding agent of any one of claims 13-20; and
 - (b) detecting the binding between the binding agent and MARCO in the sample, optionally wherein the detecting comprises using flow cytometry, immunohistochemistry (IHC), western blot analysis, ELISA, or mass spectrometry.
28. A method of disrupting, inhibiting, or blocking
 - (i) the binding of LAIR-1 to collagen, MARCO, and/or COLEC12 in a cell mixture;
 - (ii) collagen-induced LAIR-1 activity in a cell;

(iii) LAIR-1-induced suppression of a myeloid cell or myeloid cell activity, optionally wherein the myeloid cell is a monocyte, a macrophage, a dendritic cell, or an APC;

(iv) LAIR-1-induced suppression of a natural killer cell or natural killer cell activity;

(v) LAIR-1-induced suppression of a T-cell or T-cell activity, optionally wherein the T-cell is a cytotoxic T-cell (CTL);

(vi) the activity of a myeloid-derived suppressor cell (MDSC); and/or

(vii) the activity of a regulatory T-cell (Treg);

wherein the method comprises contacting the cell mixture, the cell, the myeloid cell, the natural killer cell, the T-cell, the MDSC, and/or the Treg with the binding agent of any one of claims 0-12 and 17-20.

29. Use of the binding agent of any one of claims 0-12 and 17-20 in the manufacture of a medicament for disrupting, inhibiting, or blocking, in a subject,

(i) the binding of LAIR-1 to collagen, MARCO, and/or COLEC12;

(ii) collagen-induced LAIR-1 activity;

(iii) LAIR-1-induced suppression of a myeloid cell or myeloid cell activity, optionally wherein the myeloid cell is a monocyte, a macrophage, a dendritic cell, or an APC;

(iv) LAIR-1-induced suppression of a natural killer cell or natural killer cell activity;

(v) LAIR-1-induced suppression of a T-cell or T-cell activity, optionally wherein the T-cell is a cytotoxic T-cell (CTL);

(vi) the activity of a myeloid-derived suppressor cell (MDSC); and/or

(vii) the activity of a regulatory T-cell (Treg),

wherein a therapeutically effective amount of the binding agent or the pharmaceutical composition is to be administered to the subject.

30. Use of the binding agent of any one of claims 0-12 and 17-20 in the manufacture of a medicament for,

(i) treating cancer in a subject;

(ii) inhibiting tumor growth in a subject;

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

(iv) activating or enhancing a persistent or long-term immune response to a tumor or tumor cells in a subject;

- (v) inhibiting tumor relapse or tumor regrowth in a subject;
- (vi) inducing a persistent or long-term immunity that inhibits tumor relapse or tumor regrowth in a subject;
- (vii) activating myeloid cells in the tumor microenvironment in a subject having a tumor, optionally wherein the myeloid cells are dendritic cells, monocytes, or macrophages; and/or
- (viii) activating T cells in the tumor microenvironment in a subject having a tumor, optionally wherein the T-cells are cytotoxic T-cells (CTLs),

wherein a therapeutically effective amount of the binding agent or the pharmaceutical composition is to be administered to the subject,

optionally wherein the cancer or tumor is a pancreatic cancer, breast cancer, mesothelioma, gastric, NSCLC, cervical and endocervical, biliary duct, SCCHN, bladder urothelial, CRC, esophageal cancer, ovarian, RCC, prostate or melanoma.

31. The use of claim 29 or 30, wherein the binding agent is to be administered as part of a combination therapy, optionally wherein the combination therapy comprises at least one additional therapeutic agent, further optionally wherein the at least one additional therapeutic agent is a PD-1 inhibitor.

32. An antibody that binds human LAIR-1 and inhibits binding of LAIR-1 to one or more LAIR ligands and optionally which has at least one of the following properties:

- (i) binds cyno LAIR-1;
- (ii) does not bind mouse LAIR-1;
- (iii) does not bind human LAIR-2;
- (iv) is a LAIR-1 antagonist;
- (v) inhibits LAIR-1 activity;
- (vi) inhibits LAIR-1 signaling in cells that express LAIR-1;
- (vii) inhibits LAIR-1-induced suppression of myeloid cells;
- (viii) inhibits LAIR-1-induced suppression of myeloid cell activity;
- (ix) restores FcR activation in myeloid cells;
- (x) restores cytokine and/or chemokine production in myeloid cells;
- (xi) inhibits LAIR-1-induced suppression of NK cells;
- (xii) inhibits LAIR-1-induced suppression of NK activity;

(xiii) inhibits LAIR-1-induced suppression of T-cell activity; and

(xiv) inhibits MDSC activity,

optionally wherein the one or more LAIR ligands is selected from the group consisting of collagen, MARCO, COLEC12, MBL, SPD, and C1 complex.

33. A pharmaceutical composition comprising the antibody of claim 32, and a pharmaceutically acceptable carrier.

34. A pharmaceutical composition comprising:

(a) a means for inhibiting the interaction between LAIR1 and a LAIR-1 ligand, optionally wherein the LAIR-1 ligand is collagen, MBL, SPD, C1 complex, MARCO, or COLEC12, further optionally the collagen is Collagen 1, Collagen 4, a Tumor Cell Collagen, or a Polymerized Collagen Matrix; and

(b) a pharmaceutically acceptable carrier,.

35. The pharmaceutical composition of claim 34, wherein the means for inhibiting the interaction between LAIR1 and a LAIR-1 ligand is anti-LAIR-1 antibody, optionally wherein the anti-LAIR-1 antibody comprises a heavy chain variable region comprising VH CDR1, VH CDR2, and VH CDR3, and a light chain variable region comprising VL CDR1, VL CDR2, and VL CDR3 of any one of Hz47H1.v4, Hz62G10.v1, or 57D12.