[0009] CD8+ T cells express CD8, which is a type I transmembrane glycoprotein found on the cell surface as a CD8 alpha (CD8α, CD8a) homodimer and CD8 alpha-CD8 beta (CD8β, CD8b) heterodimer. CD8 dimers interact with the MHC class I molecules on target cells and this interaction keeps the TCR closely engaged with MHC during CD8+ T cell activation. The cytoplasmic tail of CD8α contains binding sites for a T cell kinase (Lck) that initiates signal transduction downstream of the TCR during T cell activation, while the role of CD8β is thought to be in increasing the avidity of CD8 binding to MHC class I and influencing specificity of the CD8/MHC/TCR interaction (Bosselut et al, Immunity. 2000 Apr;12(4):409-18). TCR alpha beta-expressing CD8+ T cells typically express both CD8ab and CD8aa dimers, however high levels of CD8aa but not CD8ab dimers can be found on some innate lymphocytes such as NK cells, mucosal-associated invariant T (MAIT) cells, and gamma delta T cells.

[0010] Accordingly, there is a need for antibodies that selectively bind to CD8ab heterodimers over CD8aa homodimers. These antibodies can be used, *e.g.*, for targeting certain immunomodulatory polypeptides, such as IL-2, to CD8ab+ T cells, and limiting their activity on CD8- immune cells and CD8aa+ immune cells such as NK cells.

[0011] All references cited herein, including patent applications, patent publications, and UniProtKB/Swiss-Prot Accession numbers are herein incorporated by reference in their entirety, as if each individual reference were specifically and individually indicated to be incorporated by reference.

SUMMARY

[0012] The present disclosure describes, *inter alia*, human or humanized antibodies, antigen binding fragments, and fusion proteins that bind human CD8b. In some examples, the human or humanized antibodies, antigen binding fragments, and fusion proteins bind human CD8b or a human CD8ab heterodimer preferentially over binding to a human CD8aa homodimer In some examples, the human or humanized antibodies, antigen binding fragments, and fusion proteins bind CD8b, CD8ab, or both.

[0013] Certain examples of the present disclosure relate to human or humanized antibodies or antigen binding fragments thereof. In some examples, the antibody or fragment specifically binds human CD8b and/or human CD8ab with at least 10-fold higher affinity than its binding to human CD8a and/or human CD8aa. In some examples, the antibody or fragment specifically

binds the extracellular domain(s) of human CD8b and/or human CD8ab with at least 10-fold higher affinity than its binding to the extracellular domain(s) of human CD8a and/or human CD8aa. In some examples, the antibody or fragment binds to a cell expressing a human CD8ab heterodimer on its surface with an EC50 that is less than 1000nM. In some examples, the antibody or fragment binds human CD8+ T cells. In some examples, the antibody or fragment specifically binds human CD8b and/or human CD8ab with at least 10-fold higher affinity than its binding to human CD8a and/or human CD8aa expressed on the surface of an natural killer (NK) cell. In some examples, the antibody or fragment specifically binds a cell expressing human CD8b and/or human CD8ab on its surface (*e.g.*, a T cell) with at least 10-fold higher affinity than its binding to a cell expressing human CD8a and/or human CD8aa on its surface (*e.g.,* an NK cell).

[0013a] In one aspect, the present disclosure refers to a human or humanized antibody or antigen-binding fragment thereof, wherein the antibody or fragment specifically binds human CD8b and/or human CD8ab with at least 10-fold higher affinity than its binding to human CD8a and/or human CD8aa.

[0014] In some examples, the antibody or fragment comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain; wherein the VH domain comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:13, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:14, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:15; and wherein the VL domain comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:16, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:17, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:18. In some examples, the antibody or fragment comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain; wherein the VH domain comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:51, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:52, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:15; and wherein the VL domain comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:16, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:17, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:18. In some examples, the VH domain comprises an amino acid sequence that is at least 90%, at least 95%, at least 99%, or 100% identical to the sequence of SEQ ID NO:62, and wherein the VL domain comprises an amino acid sequence that is at least 90%, at least 95%, at least 99%, or 100% identical to the sequence of SEQ ID NO:63. In some examples, the antibody or fragment comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain; wherein the VH domain comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:19, a CDR-H2 comprising the amino acid sequence of SEQ

ID NO:20, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:21; and wherein the VL domain comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:22, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:23, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:24. In some examples, the antibody or fragment comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain; wherein the VH domain comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:53, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:52, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:21; and wherein the VL domain comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:22, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:23, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:24. In some examples, the VH domain comprises an amino acid sequence that is at least 90%, at least 95%, at least 99%, or 100% identical to the sequence of SEQ ID NO:64, and wherein the VL domain comprises an amino acid sequence that is at least 90%, at least 95%, at least 99%, or 100% identical to the sequence of SEQ ID NO:65. In some examples, the antibody or fragment comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain; wherein the VH domain comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:25, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:26, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:27; and wherein the VL domain comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:28, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:29, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:30. In some examples, the antibody or fragment comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain; wherein the VH domain comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:49, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:52, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:27; and wherein the VL domain comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:28, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:29, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:30. In some examples, the VH domain comprises an amino acid sequence that is at least 90%, at least 95%, at least 99%, or 100% identical to the sequence of SEQ ID NO:66, and wherein the VL domain comprises an amino acid sequence that is at least 90%, at least 95%, at least 99%, or 100% identical to the sequence of SEQ ID NO:67. In some examples, the antibody or

fragment comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain; wherein the VH domain comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:31, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:32, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:33; and wherein the VL domain comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:34, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:35, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:36. In some examples, the antibody or fragment comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain; wherein the VH domain comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:54, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:52, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:33; and wherein the VL domain comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:34, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:35, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:36. In some examples, the VH domain comprises an amino acid sequence that is at least 90%, at least 95%, at least 99%, or 100% identical to the sequence of SEQ ID NO:68, and wherein the VL domain comprises an amino acid sequence that is at least 90%, at least 95%, at least 99%, or 100% identical to the sequence of SEQ ID NO:69. In some examples, the antibody or fragment comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain; wherein the VH domain comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:37, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:38, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:39; and wherein the VL domain comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:40, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:41, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:42. In some examples, the antibody or fragment comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain; wherein the VH domain comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:55, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:56, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:39; and wherein the VL domain comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:40, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:41, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:42. In some examples, the VH domain comprises an amino acid sequence that is at least 90%, at least

95%, at least 99%, or 100% identical to the sequence of SEQ ID NO:70, and wherein the VL domain comprises an amino acid sequence that is at least 90%, at least 95%, at least 99%, or 100% identical to the sequence of SEQ ID NO:71. In some examples, the antibody or fragment comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain; wherein the VH domain comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:43, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:44, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:45; and wherein the VL domain comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:46, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:47, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:48. In some examples, the antibody or fragment comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain; wherein the VH domain comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:55, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:57, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:45; and wherein the VL domain comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:46, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:47, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:48. In some examples, the VH domain comprises an amino acid sequence that is at least 90%, at least 95%, at least 99%, or 100% identical to the sequence of SEQ ID NO:72, and wherein the VL domain comprises an amino acid sequence that is at least 90%, at least 95%, at least 99%, or 100% identical to the sequence of SEQ ID NO:73. In some examples, the antibody or fragment comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain; wherein the VH domain comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:1, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:2, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:3; and wherein the VL domain comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:4, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:5, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:6. In some examples, the antibody or fragment comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain; wherein the VH domain comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:49, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:50, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:3; and wherein the VL domain comprises a CDR-L1 comprising the amino acid sequence of

SEQ ID NO:4, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:5, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:6. In some examples, the antibody or fragment comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain; wherein the VH domain comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:177, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:178, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:179; and wherein the VL domain comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:180, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:181, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:182. In some examples, the antibody or fragment comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain; wherein the VH domain comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:183, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:184, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:179; and wherein the VL domain comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:180, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:181, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:182. In some examples, the VH domain comprises an amino acid sequence that is at least 90%, at least 95%, at least 99%, or 100% identical to the sequence of SEQ ID NO:185, and wherein the VL domain comprises an amino acid sequence that is at least 90%, at least 95%, at least 99%, or 100% identical to the sequence of SEQ ID NO:186.

[0014a] In one aspect, the present disclosure refers to a humanized antibody or antigen-binding fragment thereof that specifically binds CD8b and/or CD8ab, wherein the antibody or fragment comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain; wherein the VH domain comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:13, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:14, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:15; and wherein the VL domain comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:16, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:17, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:18.

[0014b] In one aspect, the present disclosure refers to a humanized antibody or antigen-binding fragment thereof that specifically binds CD8b and/or CD8ab, wherein the antibody or fragment comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain; wherein the VH domain comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:51, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:52, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:15; and wherein the VL domain comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:16, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:17, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:18.

[0014c] In one aspect, the present disclosure refers to a humanized antibody or antigen-binding fragment thereof that specifically binds CD8b and/or CD8ab, wherein the antibody or fragment comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain; wherein the VH domain comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:19, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:20, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:21; and wherein the VL domain comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:22, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:23, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:24.

[0014d] In one aspect, the present disclosure refers to a humanized antibody or antigen-binding fragment thereof that specifically binds CD8b and/or CD8ab, wherein the antibody or fragment comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain; wherein the VH domain comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:53, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:52, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:21; and wherein the VL domain comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:22, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:23, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:24.

[0014e] In one aspect, the present disclosure refers to a humanized antibody or antigen-binding fragment thereof that specifically binds CD8b and/or CD8ab, wherein the antibody or fragment comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain; wherein the VH domain comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:25, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:26, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:27; and wherein the VL domain comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:28, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:29, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:30.

[0014f] In one aspect, the present disclosure refers to a humanized antibody or antigen-binding fragment thereof that specifically binds CD8b and/or CD8ab, wherein the antibody or fragment comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain; wherein the VH domain comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:49, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:52, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:27; and wherein the VL domain comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:28, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:29, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:30.

[0014g] In one aspect, the present disclosure refers to a humanized antibody or antigen-binding fragment thereof that specifically binds CD8b and/or CD8ab, wherein the antibody or fragment comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain; wherein the VH domain comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:31, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:32, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:33; and wherein the VL domain comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:34, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:35, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:36.

[0014h] In one aspect, the present disclosure refers to a humanized antibody or antigen-binding fragment thereof that specifically binds CD8b and/or CD8ab, wherein the antibody or fragment comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain; wherein the VH domain comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:54, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:52, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:33; and wherein the VL domain comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:34, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:35, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:36.

[0014i] In one aspect, the present disclosure refers to a human antibody or antigen-binding fragment thereof that specifically binds CD8b and/or CD8ab, wherein the antibody or fragment comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain; wherein the VH domain comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:37, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:38, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:39; and wherein the VL domain comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:40, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:41, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:42.

[0014j] In one aspect, the present disclosure refers to a human antibody or antigen-binding fragment thereof that specifically binds CD8b and/or CD8ab, wherein the antibody or fragment comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain; wherein the VH domain comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:55, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:56, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:39; and wherein the VL domain comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:40, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:41, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:42.

[0014k] In one aspect, the present disclosure refers to a human antibody or antigen-binding fragment thereof that specifically binds CD8b and/or CD8ab, wherein the antibody or fragment comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain; wherein the VH domain comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:43, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:44, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:45; and wherein the VL

domain comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:46, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:47, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:48.

[0014l] In one aspect, the present disclosure refers to a human antibody or antigen-binding fragment thereof that specifically binds CD8b and/or CD8ab, wherein the antibody or fragment comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain; wherein the VH domain comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:55, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:57, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:45; and wherein the VL domain comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:46, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:47, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:48.

[0014m] In one aspect, the present disclosure refers to a humanized antibody or antigen-binding fragment thereof that specifically binds CD8b and/or CD8ab, wherein the antibody or fragment comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain; wherein the VH domain comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:1, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:2, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:3; and wherein the VL domain comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:4, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:5, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:6.

[0014n] In one aspect, the present disclosure refers to a humanized antibody or antigen-binding fragment thereof that specifically binds CD8b and/or CD8ab, wherein the antibody or fragment comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain; wherein the VH domain comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:49, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:50, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:3; and wherein the VL domain comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:4, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:5, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:6.

[0014o] In one aspect, the present disclosure refers to a humanized antibody or antigen-binding fragment thereof that specifically binds CD8b and/or CD8ab, wherein the antibody or fragment comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain; wherein the VH domain comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:177, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:178, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:179; and wherein the VL domain comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:180, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:181, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:182.

[0014p] In one aspect, the present disclosure refers to a humanized antibody or antigen-binding fragment thereof that specifically binds CD8b and/or CD8ab, wherein the antibody or fragment comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain; wherein the VH domain comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:183, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:184, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:179; and wherein the VL domain comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:180, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:181, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:182.

[0015] In some examples, the antibody or fragment comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain; wherein the VH domain comprises a CDR-H1 comprising the amino acid sequence of X_1X_2AIS, wherein X_1 is S, K, G, N, R, D, T, or G, and wherein X_2 is Y, L, H, or F (SEQ ID NO:259), a CDR-H2 comprising the amino acid sequence of $X_1X_2X_3PX_4X_5X_6X_7X_8X_9YX_{10}QKFX_{11}G$, wherein X_1 is G or H, X_2 is I or F, X_3 is I, N, or M, X_4 is G, N, H, S, R, I, or A, X_5 is A, N, H, S, T, F, or Y, X_6 is A, D, or G, X_7 is T, E, K, V, Q, or A, X_8 is A or T, X_9 is N or K, X_{10} is A or N, and X_{11} is Q or T (SEQ ID NO:260), and a CDR-H3 comprising the amino acid sequence of $X_1X_2X_3GX_4X_5LFX_6X_7$, wherein X_1 is D or A, X_2 is A, G, E, R, Y, K, N, Q, L, or F, X_3 is A, L, P, or Y, X_4 is I or L, X_5 is R, A, Q, or S, X_6 is A or D, and X_7 is D, E, A, or S (SEQ ID NO:261); and wherein the VL domain comprises a CDR-L1 comprising the amino acid sequence of $X_1X_2SX_3X_4IX_5GX_6LN$, wherein X_1 is R or G, X_2 is A or T, X_3 is Q or E, X_4 is E, N, T, S, A, K, D, G, R, or Q, X_5 is Y or S, and X_6 is A or V (SEQ ID

NO:262), a CDR-L2 comprising the amino acid sequence of $GX_1X_2X_3LX_4X_5$, wherein X_1 is A or S, X_2 is T, S, E, Q, or D, X_3 is N, R, A, E, or H, X_4 is Q or A, and X_5 is S or D (SEQ ID NO:263), and a CDR-L3 comprising the amino acid sequence of $QX_1X_2X_3X_4X_5PWT$, wherein X_1 is S, N, D, Q, A, or E, X_2 is T, I, or S, X_3 is Y, L, or F, X_4 is D, G, T, E, Q, A, or Y, and X_5 is A, T, R, S, K, or Y (SEQ ID NO:264). In some examples, the antibody or fragment comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain; wherein the VH domain comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:225, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:226, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:227; and wherein the VL domain comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:16, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:17, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:228. In some examples, the VH domain comprises an amino acid sequence that is at least 90%, at least 95%, at least 99%, or 100% identical to the sequence of SEQ ID NO:245, and wherein the VL domain comprises an amino acid sequence that is at least 90%, at least 95%, at least 99%, or 100% identical to the sequence of SEQ ID NO:246. In some examples, the antibody or fragment comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain; wherein the VH domain comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:225, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:232, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:233; and wherein the VL domain comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:234, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:235, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:236. In some examples, the VH domain comprises an amino acid sequence that is at least 90%, at least 95%, at least 99%, or 100% identical to the sequence of SEQ ID NO:251, and wherein the VL domain comprises an amino acid sequence that is at least 90%, at least 95%, at least 99%, or 100% identical to the sequence of SEQ ID NO:252. In some examples, the VH domain comprises the amino acid sequence of SEQ ID NO:251; and the VL domain comprises the amino acid sequence of SEQ ID NO:252. In some examples, the antibody or fragment comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain; wherein the VH domain comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:225, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:232, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:233; and

wherein the VL domain comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:16, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:17, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:228. In some examples, the VH domain comprises an amino acid sequence that is at least 90%, at least 95%, at least 99%, or 100% identical to the sequence of SEQ ID NO:253, and wherein the VL domain comprises an amino acid sequence that is at least 90%, at least 95%, at least 99%, or 100% identical to the sequence of SEQ ID NO:254. In some examples, the VH domain further comprises a FW-1 comprising the sequence QVQLVQSGAEVKKPGSSVKVSCKASGGTFS (SEQ ID NO:274), a FW-2 comprising the sequence WVRQAPGQGLEWMG (SEQ ID NO:275), a FW-3 comprising the sequence RVTITADESTSTAYMELSSLRSEDTAVYYCAR (SEQ ID NO:276), and/or a FW-4 comprising the sequence WGQGTLVTVSS (SEQ ID NO:277). In some examples, the VL domain further comprises a FW-1 comprising the sequence DIQMTQSPSSLSASVGDRVTITC (SEQ ID NO:289), a FW-2 comprising the sequence WYQQKPGKAPKLLIY (SEQ ID NO:290), a FW-3 comprising the sequence GVPSRFSGSGSGTDFTLTISSLQPEDFATYYC (SEQ ID NO:291), and/or a FW-4 comprising the sequence FGGGTKVEIK (SEQ ID NO:292).

[0015a] In one aspect, the present disclosure refers to a humanized antibody or antigen-binding fragment thereof that specifically binds CD8b and/or CD8ab, wherein the antibody or fragment comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain; wherein the VH domain comprises: a CDR-H1 comprising the amino acid sequence of X_1X_2AIS, wherein X_1 is S, K, G, N, R, D, T, or G, and wherein X_2 is Y, L, H, or F (SEQ ID NO:259), a CDR-H2 comprising the amino acid sequence of $X_1X_2X_3PX_4X_5X_6X_7X_8X_9YX_{10}QKFX_{11}G$, wherein X_1 is G or H, X_2 is I or F, X_3 is I, N, or M, X_4 is G, N, H, S, R, I, or A, X_5 is A, N, H, S, T, F, or Y, X_6 is A, D, or G, X_7 is T, E, K, V, Q, or A, X_8 is A or T, X_9 is N or K, X_{10} is A or N, and X_{11} is Q or T (SEQ ID NO:260), and a CDR-H3 comprising the amino acid sequence of $X_1X_2X_3GX_4X_5LFX_6X_7$, wherein X_1 is D or A, X_2 is A, G, E, R, Y, K, N, Q, L, or F, X_3 is A, L, P, or Y, X_4 is I or L, X_5 is R, A, Q, or S, X_6 is A or D, and X_7 is D, E, A, or S (SEQ ID NO:261); and wherein the VL domain comprises: a CDR-L1 comprising the amino acid sequence of $X_1X_2SX_3X_4IX_5GX_6LN$, wherein X_1 is R or G, X_2 is A or T, X_3 is Q or E, X_4 is E, N, T, S, A, K, D, G, R, or Q, X_5 is Y or S, and X_6 is A or V (SEQ ID NO:262), a CDR-L2 comprising the amino acid sequence of $GX_1X_2X_3LX_4X_5$, wherein X_1 is A or S, X_2 is T, S, E, Q, or D, X_3 is N, R, A, E, or H, X_4 is Q or A, and X_5 is S or D (SEQ ID NO:263), and a CDR-L3 comprising the amino acid sequence of $QX_1X_2X_3X_4X_5PWT$, wherein X_1 is S, N, D, Q, A, or E, X_2 is T, I, or S, X_3 is Y, L, or F, X_4 is D, G, T, E, Q, A, or Y, and X_5 is A, T, R, S, K, or Y (SEQ ID NO:264).

[0016] In some examples, the antibody or fragment comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain; wherein the VH domain comprises a CDR-H1 comprising the amino acid sequence of $GX_1X_2FX_3X_4X_5$, wherein X_1 is G, Y, S, or A, X_2 is T, S, G, R, N, or H, X_3 is S, T, R, H, Y, G, or P, X_4 is S, K, G, N, R, D, T, or G, and X_5 is Y, L, H, or F (SEQ ID NO:265), a CDR-H2 comprising the amino acid sequence of $X_1PX_2X_3X_4X_5$, wherein X_1 is I, N, or M, X_2 is G, N, H, S, R, I, or A, X_3 is A, N, H, S, T, F, or Y, X_4 is A, D, or G, and X_5 is T, E, K, V, Q, or A (SEQ ID NO:266), and a CDR-H3 comprising the amino acid sequence of $X_1X_2X_3GX_4X_5LFX_6X_7$, wherein X_1 is D or A, X_2 is A, G, E, R, Y, K, N, Q, L, or F, X_3 is A, L, P, or Y, X_4 is I or L, X_5 is R, A, Q, or S, X_6 is A or D, and X_7 is D, E, A, or S (SEQ ID NO:267); and wherein the VL domain comprises a CDR-L1 comprising the amino acid sequence of $X_1X_2SX_3X_4IX_5GX_6LN$, wherein X_1 is R or G, X_2 is A or T, X_3 is Q or E, X_4 is E, N, T, S, A, K, D, G, R, or Q, X_5 is Y or S, and X_6 is A or V (SEQ ID NO:262), a CDR-L2 comprising the amino acid sequence of $GX_1X_2X_3LX_4X_5$, wherein X_1 is A or S, X_2 is T, S, E, Q, or D, X_3 is N, R, A, E, or H, X_4 is Q or A, and X_5 is S or D (SEQ ID NO:263), and a CDR-L3 comprising the amino acid sequence of $QX_1X_2X_3X_4X_5PWT$, wherein X_1 is S, N, D, Q, A, or E,

X_2 is T, I, or S, X_3 is Y, L, or F, X_4 is D, G, T, E, Q, A, or Y, and X_5 is A, T, R, S, K, or Y (SEQ ID NO:264). In some examples, the VH domain comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:238, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:239, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:233; and the VL domain comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:16, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:17, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:228. In some examples, the VH domain comprises an amino acid sequence that is at least 90%, at least 95%, at least 99%, or 100% identical to the sequence of SEQ ID NO:245; and wherein the VL domain comprises an amino acid sequence that is at least 90%, at least 95%, at least 99%, or 100% identical to the sequence of SEQ ID NO:246. In some examples, the VH domain comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:238, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:243, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:233; and the VL domain comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:234, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:235, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:236. In some examples, the VH domain comprises an amino acid sequence that is at least 90%, at least 95%, at least 99%, or 100% identical to the sequence of SEQ ID NO:251; and wherein the VL domain comprises an amino acid sequence that is at least 90%, at least 95%, at least 99%, or 100% identical to the sequence of SEQ ID NO:252. In some examples, the VH domain comprises the amino acid sequence of SEQ ID NO:251; and the VL domain comprises the amino acid sequence of SEQ ID NO:252. In some examples, the VH domain comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:238, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:243, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:233; and the VL domain comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:16, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:17, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:228. In some examples, the VH domain comprises an amino acid sequence that is at least 90%, at least 95%, at least 99%, or 100% identical to the sequence of SEQ ID NO:253; and wherein the VL domain comprises an amino acid sequence that is at least 90%, at least 95%, at least 99%, or 100% identical to the sequence of SEQ ID NO:254. In some examples, the VH domain further comprises a FW-1 comprising the sequence QVQLVQSGAEVKKPGSSVKVSCKAS

(SEQ ID NO:278), a FW-2 comprising the sequence AISWVRQAPGQGLEWMGGI (SEQ ID NO:279), a FW-3 comprising the sequence ANYAQKFQGRVTITADESTSTAYMELSSLRSEDTAVYYCAR (SEQ ID NO:280), and/or a FW-4 comprising the sequence WGQGTLVTVSS (SEQ ID NO:277). In some examples, the VL domain further comprises a FW-1 comprising the sequence DIQMTQSPSSLSASVGDRVTITC (SEQ ID NO:289), a FW-2 comprising the sequence WYQQKPGKAPKLLIY (SEQ ID NO:290), a FW-3 comprising the sequence GVPSRFSGSGSGTDFTLTISSLQPEDFATYYC (SEQ ID NO:291), and/or a FW-4 comprising the sequence FGGGTKVEIK (SEQ ID NO:292).

[0016a] In one aspect, the present disclosure refers to a humanized antibody or antigen-binding fragment thereof that specifically binds CD8b and/or CD8ab, wherein the antibody or fragment comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain; wherein the VH domain comprises: a CDR-H1 comprising the amino acid sequence of $GX_1X_2FX_3X_4X_5$, wherein X_1 is G, Y, S, or A, X_2 is T, S, G, R, N, or H, X_3 is S, T, R, H, Y, G, or P, X_4 is S, K, G, N, R, D, T, or G, and X_5 is Y, L, H, or F (SEQ ID NO:265), a CDR-H2 comprising the amino acid sequence of $X_1PX_2X_3X_4X_5$, wherein X_1 is I, N, or M, X_2 is G, N, H, S, R, I, or A, X_3 is A, N, H, S, T, F, or Y, X_4 is A, D, or G, and X_5 is T, E, K, V, Q, or A (SEQ ID NO:266), and a CDR-H3 comprising the amino acid sequence of $X_1X_2X_3GX_4X_5LFX_6X_7$, wherein X_1 is D or A, X_2 is A, G, E, R, Y, K, N, Q, L, or F, X_3 is A, L, P, or Y, X_4 is I or L, X_5 is R, A, Q, or S, X_6 is A or D, and X_7 is D, E, A, or S (SEQ ID NO:267); and wherein the VL domain comprises: a CDR-L1 comprising the amino acid sequence of $X_1X_2SX_3X_4IX_5GX_6LN$, wherein X_1 is R or G, X_2 is A or T, X_3 is Q or E, X_4 is E, N, T, S, A, K, D, G, R, or Q, X_5 is Y or S, and X_6 is A or V (SEQ ID NO:262), a CDR-L2 comprising the amino acid sequence of $GX_1X_2X_3LX_4X_5$, wherein X_1 is A or S, X_2 is T, S, E, Q, or D, X_3 is N, R, A, E, or H, X_4 is Q or A, and X_5 is S or D (SEQ ID NO:263), and a CDR-L3 comprising the amino acid sequence of $QX_1X_2X_3X_4X_5PWT$, wherein X_1 is S, N, D, Q, A, or E, X_2 is T, I, or S, X_3 is Y, L, or F, X_4 is D, G, T, E, Q, A, or Y, and X_5 is A, T, R, S, K, or Y (SEQ ID NO:264).

[0017] In some examples, the antibody or fragment comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain; wherein the VH domain comprises a CDR-H1 comprising the amino acid sequence of X_1YX_2MS, wherein X_1 is S, D, E, A, or Q and X_2 is A, G, or T (SEQ ID NO:268), a CDR-H2 comprising the amino acid sequence of $DIX_1X_2X_3GX_4X_5TX_6YADSVKG$, wherein X_1 is T, N, S, Q, E, H, R, or A, X_2 is Y, W, F, or H, X_3 is A, S, Q, E, or T, X_4 is G or E, X_5 is S or I, and X_6 is A or G (SEQ ID NO:269), and a CDR-H3 comprising the amino acid sequence of $X_1X_2X_3YX_4WX_5X_6AX_7DX_8$, wherein X_1 is S or A, X_2 is N, H, A, D, L, Q, Y, or R, X_3 is A, N, S, or G, X_4 is A, V, R, E, or S, X_5 is D or S, X_6 is D, N, Q, E, S, T, or L, X_7 is L, F, or M, and X_8 is I, Y, or V (SEQ ID NO:270) and a VL domain comprising a CDR-L1 comprising the amino acid sequence of RASQSVSSNLA (SEQ ID NO:40), a CDR-L2 comprising the amino acid sequence of GASSRAT (SEQ ID NO:41), and a CDR-L3 comprising the amino acid sequence of QQYGSSPPVT (SEQ ID NO:42). In some examples, the antibody or fragment comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain; wherein the VH domain comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:229, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:230, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:231; and wherein the VL domain comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:40, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:41, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:42. In some examples, the VH domain comprises an amino acid sequence that is at least 90%, at least 95%, at least 99%, or 100% identical to the sequence of SEQ ID NO:247, and wherein the VL domain comprises an amino acid sequence that is at least 90%, at least 95%, at least 99%, or 100% identical to the sequence

of SEQ ID NO:248. In some examples, the VH domain comprises an amino acid sequence that is at least 90%, at least 95%, at least 99%, or 100% identical to the sequence of SEQ ID NO:249, and wherein the VL domain comprises an amino acid sequence that is at least 90%, at least 95%, at least 99%, or 100% identical to the sequence of SEQ ID NO:250. In some examples, the VH domain comprises the amino acid sequence of SEQ ID NO:249, and wherein the VL domain comprises the amino acid sequence of SEQ ID NO:250. In some examples, the antibody or fragment comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain; wherein the VH domain comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:229, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:237, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:231; and wherein the VL domain comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:40, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:41, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:42. In some examples, the VH domain comprises an amino acid sequence that is at least 90%, at least 95%, at least 99%, or 100% identical to the sequence of SEQ ID NO:255, and wherein the VL domain comprises an amino acid sequence that is at least 90%, at least 95%, at least 99%, or 100% identical to the sequence of SEQ ID NO:256. In some examples, the VH domain comprises an amino acid sequence that is at least 90%, at least 95%, at least 99%, or 100% identical to the sequence of SEQ ID NO:257, and wherein the VL domain comprises an amino acid sequence that is at least 90%, at least 95%, at least 99%, or 100% identical to the sequence of SEQ ID NO:258. In some examples, the VH domain further comprises a FW-1 comprising the sequence EVQLVESGGGLVQPGGSLRLSCAASGFTFS (SEQ ID NO:281), a FW-2 comprising the sequence WVRQAPGKGLEWVS (SEQ ID NO:282), a FW-3 comprising the sequence RFTISRDNAKNSLYLQMNSLRAEDTAVYYCAR (SEQ ID NO:283), and/or a FW-4 comprising the sequence WGQGTMVTVSS (SEQ ID NO:284) or WGQGTLVTVSS (SEQ ID NO:285). In some examples, the VL domain further comprises a FW-1 comprising the sequence EIVLTQSPGTLSLSPGERATLSC (SEQ ID NO:293), a FW-2 comprising the sequence WYQQKPGQAPRLLIY (SEQ ID NO:294), a FW-3 comprising the sequence GIPDRFSGSGSGTDFTLTISRLEPEDFAVYYC (SEQ ID NO:295), and/or a FW-4 comprising the sequence FGQGTKVEIK (SEQ ID NO:296).

[0017a] In one aspect, the present disclosure refers to a humanized antibody or antigen-binding fragment thereof that specifically binds CD8b and/or CD8ab, wherein the antibody or fragment comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain; wherein the VH domain comprises: a CDR-H1 comprising the amino acid sequence of X_1YX_2MS, wherein X_1 is S, D, E, A, or Q and X_2 is A, G, or T (SEQ ID NO:268), a CDR-H2 comprising the amino acid sequence of $DIX_1X_2X_3GX_4X_5TX_6YADSVKG$, wherein X_1 is T, N, S, Q, E, H, R, or A, X_2 is Y, W, F, or H, X_3 is A, S, Q, E, or T, X_4 is G or E, X_5 is S or I, and X_6 is A or G (SEQ ID NO:269), and a CDR-H3 comprising the amino acid sequence of $X_1X_2X_3YX_4WX_5X_6AX_7DX_8$, wherein X_1 is S or A, X_2 is N, H, A, D, L, Q, Y, or R, X_3 is A, N, S, or G, X_4 is A, V, R, E, or S, X_5 is D or S, X_6 is D, N, Q, E, S, T, or L, X_7 is L, F, or M, and X_8 is I, Y, or V (SEQ ID NO:270); and wherein the VL domain comprises: a CDR-L1 comprising the amino acid sequence of RASQSVSSNLA (SEQ ID NO:40), a CDR-L2 comprising the amino acid sequence of GASSRAT (SEQ ID NO:41), and a CDR-L3 comprising the amino acid sequence of QQYGSSPPVT (SEQ ID NO:42).

[0018] In some examples, the antibody or fragment comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain; wherein the VH domain comprises a CDR-H1 comprising the amino acid sequence of $GFTFX_1X_2Y$, wherein X_1 is S, D, E, Q, S, or A and X_2 is S, D, E, A, or Q (SEQ ID NO:271), a CDR-H2 comprising the amino acid sequence of $X_1X_2X_3GX_4X_5$, wherein X_1 is T, N, S, Q, E, H, R or A, X_2 is Y, W, F, or H, X_3 is A, S, Q, E, or T, X_4 is G or E, and X_5 is S or I (SEQ ID NO:272), and a CDR-H3 comprising the amino acid sequence of $X_1X_2X_3YX_4WX_5X_6AX_7DX_8$, wherein X_1 is S or A, X_2 is N, H, A, D, L, Q, Y, or R, X_3 is A, N, S, or G, X_4 is A, V, R, E, or S, X_5 is D or S, X_6 is D, N, Q, E, S, T, or L, X_7 is L, F, or M, and X_8 is I, Y, or V (SEQ ID NO:273); and wherein the VL domain comprises a CDR-L1 comprising the amino acid sequence of RASQSVSSNLA (SEQ ID NO:40), a CDR-L2 comprising the amino acid sequence of GASSRAT (SEQ ID NO:41), and a CDR-L3 comprising the amino acid sequence of QQYGSSPPVT (SEQ ID NO:42). In some examples, the VH domain comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:240, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:241, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:242; and wherein the VL domain comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:40, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:41, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:42. In some examples, the VH domain comprises an amino acid sequence that is at least 90%, at least 95%, at least 99%, or 100% identical to the sequence of SEQ ID NO:247; and wherein the VL domain comprises an amino acid sequence that is at least 90%, at least 95%, at least 99%, or 100% identical to the sequence of SEQ ID NO:248. In some examples, the VH domain comprises an amino acid sequence that is at least 90%, at least 95%, at least 99%, or 100% identical to the sequence of SEQ ID NO:249; and wherein the VL domain comprises an amino acid sequence that is at least 90%, at least 95%, at least 99%, or 100% identical to the sequence of SEQ ID NO:250. In some examples, the VH domain comprises the amino acid sequence of SEQ ID NO:249, and wherein the VL domain comprises the amino acid sequence of SEQ ID NO:250. In some examples, the VH domain comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:240, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:244, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:242; and wherein the VL domain comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:40, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:41, and a CDR-L3

comprising the amino acid sequence of SEQ ID NO:42. In some examples, the VH domain comprises an amino acid sequence that is at least 90%, at least 95%, at least 99%, or 100% identical to the sequence of SEQ ID NO:255; and wherein the VL domain comprises an amino acid sequence that is at least 90%, at least 95%, at least 99%, or 100% identical to the sequence of SEQ ID NO:256. In some examples, the VH domain comprises an amino acid sequence that is at least 90%, at least 95%, at least 99%, or 100% identical to the sequence of SEQ ID NO:257; and wherein the VL domain comprises an amino acid sequence that is at least 90%, at least 95%, at least 99%, or 100% identical to the sequence of SEQ ID NO:258. In some examples, the VH domain further comprises a FW-1 comprising the sequence EVQLVESGGGLVQPGGSLRLSCAAS (SEQ ID NO:286), a FW-2 comprising the sequence AMSWVRQAPGKGLEWVSDI (SEQ ID NO:287), a FW-3 comprising the sequence TAYADSVKGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCAR (SEQ ID NO:288), and/or a FW-4 comprising the sequence WGQGTMVTVSS (SEQ ID NO:284) or WGQGTLVTVSS (SEQ ID NO:285). In some examples, the VL domain further comprises a FW-1 comprising the sequence EIVLTQSPGTLSLSPGERATLSC (SEQ ID NO:293), a FW-2 comprising the sequence WYQQKPGQAPRLLIY (SEQ ID NO:294), a FW-3 comprising the sequence GIPDRFSGSGSGTDFTLTISRLEPEDFAVYYC (SEQ ID NO:295), and a FW-4 comprising the sequence FGQGTKVEIK (SEQ ID NO:296).

[0018a] In one aspect, the present disclosure refers to a humanized antibody or antigen-binding fragment thereof that specifically binds CD8b and/or CD8ab, wherein the antibody or fragment comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain; wherein the VH domain comprises: a CDR-H1 comprising the amino acid sequence of $GFTFX_1X_2Y$, wherein X_1 is S, D, E, Q, S, or A and X_2 is S, D, E, A, or Q (SEQ ID NO:271), a CDR-H2 comprising the amino acid sequence of $X_1X_2X_3GX_4X_5$, wherein X_1 is T, N, S, Q, E, H, R or A, X_2 is Y, W, F, or H, X_3 is A, S, Q, E, or T, X_4 is G or E, and X_5 is S or I (SEQ ID NO:272), and a CDR-H3 comprising the amino acid sequence of $X_1X_2X_3YX_4WX_5X_6AX_7DX_8$, wherein X_1 is S or A, X_2 is N, H, A, D, L, Q, Y, or R, X_3 is A, N, S, or G, X_4 is A, V, R, E, or S, X_5 is D or S, X_6 is D, N, Q, E, S, T, or L, X_7 is L, F, or M, and X_8 is I, Y, or V (SEQ ID NO:273); and wherein the VL domain comprises: a CDR-L1 comprising the amino acid sequence of RASQSVSSNLA (SEQ ID NO:40), a CDR-L2 comprising the amino acid sequence of GASSRAT (SEQ ID NO:41), and a CDR-L3 comprising the amino acid sequence of QQYGSSPPVT (SEQ ID NO:42).

[0019] In some examples according to any of the examples described herein, the antibody is a multispecific antibody (*e.g.*, a bispecific antibody).

[0020] Further provided herein are fusion proteins comprising a first moiety comprising the antibody or fragment of any one of the above examples and a second moiety comprising a cytokine, chemokine, or growth factor. In some examples, the first moiety is fused to the second moiety directly or via a linker. In some examples, the first moiety comprises a human or humanized antibody or antigen-binding fragment thereof that specifically binds CD8b and/or CD8ab, wherein the antibody or fragment comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain, wherein: the VH domain comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:13, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:14, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:15; and wherein the VL domain comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:16, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:17, and a

comprising the amino acid sequence of QQYGSSPPVT (SEQ ID NO:42). In some examples, the first moiety comprises a human or humanized antibody or antigen-binding fragment thereof that specifically binds CD8b and/or CD8ab, wherein the antibody or fragment comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain, wherein: the VH domain comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:51, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:52, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:15, and wherein the VL domain comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:16, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:17, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:18; the VH domain comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:53, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:52, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:21, and wherein the VL domain comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:22, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:23, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:24; the VH domain comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:49, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:52, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:27, and wherein the VL domain comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:28, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:29, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:30; the VH domain comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:54, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:52, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:33, and wherein the VL domain comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:34, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:35, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:36; the VH domain comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:55, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:56, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:39, and wherein the VL domain comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:40, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:41, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:42; the VH domain comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:55, a CDR-H2 comprising the amino acid sequence of SEQ

the amino acid sequence of SEQ ID NO:233, and wherein the VL domain comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:16, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:17, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:228; or the VH domain comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:240, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:244, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:242, and wherein the VL domain comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:40, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:41, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:42.

[0020a] In one aspect, the present disclosure refers to a fusion protein, comprising: (a) a first moiety comprising the antibody or fragment disclosed herein; and (b) a second moiety comprising a cytokine, chemokine, or growth factor; wherein the first moiety is fused to the second moiety directly or via a linker.

[0020b] In one aspect, the present disclosure refers to a fusion protein, comprising: (a) a first moiety comprising a human or humanized antibody or antigen-binding fragment thereof that specifically binds CD8b and/or CD8ab, wherein the antibody or fragment comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain, wherein: the VH domain comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:13, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:14, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:15; and wherein the VL domain comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:16, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:17, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:18; the VH domain comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:19, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:20, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:21; and wherein the VL domain comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:22, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:23, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:24; the VH domain comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:25, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:26, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:27; and wherein the VL domain comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:28, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:29, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:30; the VH domain comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:31, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:32, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:33; and wherein the VL domain comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:34, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:35, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:36; the VH domain comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:37, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:38, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:39; and wherein the VL domain comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:40, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:41, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:42; the VH domain comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:43, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:44, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:45; and wherein the VL domain comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:46, a CDR-L2 comprising the amino acid sequence of

SEQ ID NO:47, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:48; the VH domain comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:1, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:2, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:3; and wherein the VL domain comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:4, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:5, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:6; the VH domain comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:177, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:178, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:179; and wherein the VL domain comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:180, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:181, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:182; the VH domain comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:225, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:226, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:227; and wherein the VL domain comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:16, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:17, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:228; the VH domain comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:229, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:230, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:231; and wherein the VL domain comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:40, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:41, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:42; the VH domain comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:225, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:232, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:233; and wherein the VL domain comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:234, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:235, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:236; the VH domain comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:225, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:232, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:233; and wherein the VL domain comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:16, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:17, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:228; or the VH domain comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:229, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:237, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:231; and wherein the VL domain comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:40, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:41, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:42; and (b) a second moiety comprising a cytokine, chemokine, or growth factor; wherein the first moiety is fused to the second moiety directly or via a linker.

[0020c] In one aspect, the present disclosure refers to a fusion protein, comprising: (a) a first moiety comprising a human or humanized antibody or antigen-binding fragment thereof that specifically binds CD8b and/or CD8ab, wherein the antibody or fragment comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain, wherein: the VH domain comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:51, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:52, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:15; and wherein the VL domain comprises a CDR-L1 comprising

the amino acid sequence of SEQ ID NO:16, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:17, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:18; the VH domain comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:53, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:52, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:21; and wherein the VL domain comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:22, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:23, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:24; the VH domain comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:49, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:52, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:27; and wherein the VL domain comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:28, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:29, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:30; the VH domain comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:54, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:52, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:33; and wherein the VL domain comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:34, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:35, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:36; the VH domain comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:55, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:56, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:39; and wherein the VL domain comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:40, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:41, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:42; the VH domain comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:55, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:57, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:45; and wherein the VL domain comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:46, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:47, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:48; the VH domain comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:49, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:50, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:3; and wherein the VL domain comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:4, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:5, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:6; the VH domain comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:183, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:184, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:179; and wherein the VL domain comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:180, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:181, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:182; the VH domain comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:238, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:239, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:233; and wherein the VL domain comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:16, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:17, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:228; the VH domain comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:240, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:241, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:242; and wherein the VL domain comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:40, a CDR-L2

comprising the amino acid sequence of SEQ ID NO:41, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:42; the VH domain comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:238, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:243, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:233; and wherein the VL domain comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:234, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:235, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:236; the VH domain comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:238, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:243, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:233; and wherein the VL domain comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:16, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:17, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:228; or the VH domain comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:240, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:244, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:242; and wherein the VL domain comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:40, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:41, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:42; and (b) a second moiety comprising a cytokine, chemokine, or growth factor; wherein the first moiety is fused to the second moiety directly or via a linker.

[0021] In some examples according to any of the examples described herein (*e.g.*, a fusion protein of the present disclosure), the second moiety induces activation of CD8+ T cells. In some examples, the fusion protein induces activation of cells expressing a human CD8ab heterodimer with at least 10-fold higher potency than activation of cells expressing a human CD8aa homodimer. In some examples, the fusion protein induces activation of CD8+ T cells with at least 10-fold higher potency than activation of NK cells. In some examples, potency of activation is measured by EC50, as assessed by cell proliferation. In some examples, the first moiety comprises two antibody heavy chain polypeptides comprising a structure according to formula [I], from N-terminus to C-terminus:

VH-CH1-hinge-CH2-CH3 [I]

and two antibody light chain polypeptides comprising a structure according to formula [II], from N-terminus to C-terminus:

VL-CL [II]

wherein VH is an antibody heavy chain variable (VH) domain, wherein CH1 is an antibody CH1 domain, wherein hinge is an antibody hinge domain, wherein CH2-CH3 is an antibody Fc domain, wherein VL is an antibody light chain variable (VL) domain, and wherein CL is an antibody constant light chain domain; and wherein the N-terminus of the second moiety is fused to the C-terminus of one of the two CH3 domains (*e.g.,* via a linker of the present disclosure). In some examples, the first moiety comprises a first antibody heavy chain polypeptide comprising a structure according to formula [I], from N-terminus to C-terminus:

VH-CH1-hinge-CH2-CH3 [I],

an antibody light chain polypeptide comprising a structure according to formula [II], from N-terminus to C-terminus:

VL-CL [II],

and a second antibody heavy chain polypeptide comprising a structure according to formula [III], from N-terminus to C-terminus:

hinge-CH2-CH3 [III],

wherein VH is an antibody heavy chain variable (VH) domain, wherein CH1 is an antibody CH1 domain, wherein hinge is an antibody hinge domain, wherein CH2-CH3 is an antibody Fc domain, wherein VL is an antibody light chain variable (VL) domain, and wherein CL is an antibody constant light chain domain; and wherein the N-terminus of the second moiety is fused to the C-terminus of the CH3 domain of the second antibody heavy chain polypeptide (*e.g.,* via a linker of the present disclosure). In some examples, the N-terminus of the second moiety is fused to the C-terminus of the CH3 domain of the first antibody heavy chain polypeptide (*e.g.,* via a linker of the present disclosure).In some examples, the first moiety comprises a first antibody heavy chain polypeptide comprising a structure according to formula [I], from N-terminus to C-terminus:

VH-CH1-hinge-CH2-CH3 [I],

an antibody light chain polypeptide comprising a structure according to formula [II], from N-terminus to C-terminus:

VL-CL [II],

and a second antibody heavy chain polypeptide comprising a structure according to formula [III], from N-terminus to C-terminus:

hinge-CH2-CH3 [III],

wherein VH is an antibody heavy chain variable (VH) domain, wherein CH1 is an antibody CH1 domain, wherein hinge is an antibody hinge domain, wherein CH2-CH3 is an antibody Fc domain, wherein VL is an antibody light chain variable (VL) domain, and wherein CL is an antibody constant light chain domain; and wherein the C-terminus of the second moiety is fused to the N-terminus of the hinge domain of the second antibody heavy chain polypeptide (*e.g.,* via a linker of the present disclosure). In some examples, the first moiety comprises one or two antibody heavy chain polypeptides and one or two antibody light chain polypeptides. In some examples, the first moiety comprises a single chain antibody or single chain variable

fragment (scFv). In some examples, the first moiety comprises a VHH antibody. In some examples according to any of the examples described herein (*e.g.*, the fusion proteins described above), VH and VL form an antigen binding site (*e.g.*, that specifically binds CD8b and/or CD8ab). In some examples, the first moiety comprises a first antibody heavy chain polypeptide comprising a structure according to formula [I], from N-terminus to C-terminus:

VH-CH1-hinge-CH2-CH3 [I],

an antibody light chain polypeptide comprising a structure according to formula [II], from N-terminus to C-terminus:

VL-CL [II],

and a second antibody heavy chain polypeptide comprising a structure according to formula [III], from N-terminus to C-terminus:

hinge-CH2-CH3 [III],

wherein VH is the VH domain, wherein CH1 is an antibody CH1 domain, wherein hinge is an antibody hinge domain, wherein CH2-CH3 is an antibody Fc domain, wherein VL is the VL domain, and wherein CL is an antibody constant light chain domain; and wherein the N-terminus of the second moiety is fused to the C-terminus of the CH3 domain of the first antibody heavy chain polypeptide. In some examples, the VH domain of both antibody heavy chain polypeptides comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:13, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:14, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:15, and wherein the VL domain of both antibody light chain polypeptides comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:16, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:17, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:18; the VH domain of both antibody heavy chain polypeptides comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:19, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:20, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:21, and wherein the VL domain of both antibody light chain polypeptides comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:22, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:23, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:24; the VH domain of both antibody heavy chain polypeptides comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:25, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:26, and a CDR-H3 comprising the

amino acid sequence of SEQ ID NO:40, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:41, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:42. In some examples, the VH domain of both antibody heavy chain polypeptides comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:51, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:52, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:15, and wherein the VL domain of both antibody light chain polypeptides comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:16, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:17, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:18; the VH domain of both antibody heavy chain polypeptides comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:53, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:52, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:21, and wherein the VL domain of both antibody light chain polypeptides comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:22, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:23, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:24; the VH domain of both antibody heavy chain polypeptides comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:49, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:52, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:27, and wherein the VL domain of both antibody light chain polypeptides comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:28, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:29, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:30; the VH domain of both antibody heavy chain polypeptides comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:54, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:52, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:33, and wherein the VL domain of both antibody light chain polypeptides comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:34, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:35, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:36; the VH domain of both antibody heavy chain polypeptides comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:55, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:56, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:39, and wherein the VL domain of both antibody light chain polypeptides comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:40, a CDR-L2 comprising the amino acid

SEQ ID NO:42; the VH domain of both antibody heavy chain polypeptides comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:238, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:243, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:233, and wherein the VL domain of both antibody light chain polypeptides comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:234, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:235, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:236; the VH domain of both antibody heavy chain polypeptides comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:238, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:243, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:233, and wherein the VL domain of both antibody light chain polypeptides comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:16, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:17, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:228; or the VH domain of both antibody heavy chain polypeptides comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:240, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:244, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:242, and wherein the VL domain of both antibody light chain polypeptides comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:40, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:41, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:42. In some examples, the VH domain comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:13, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:14, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:15, and wherein the VL domain comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:16, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:17, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:18; the VH domain comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:19, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:20, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:21, and wherein the VL domain comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:22, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:23, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:24; the VH domain comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:25, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:26, and a CDR-H3 comprising the amino

comprising the amino acid sequence of SEQ ID NO:16, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:17, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:228; the VH domain comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:229, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:230, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:231, and wherein the VL domain comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:40, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:41, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:42; the VH domain comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:225, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:232, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:233, and wherein the VL domain comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:234, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:235, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:236; the VH domain comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:225, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:232, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:233, and wherein the VL domain comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:16, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:17, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:228; or the VH domain comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:229, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:237, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:231, and wherein the VL domain comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:40, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:41, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:42. In some examples, the VH domain comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:51, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:52, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:15, and wherein the VL domain comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:16, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:17, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:18; the VH domain comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:53, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:52, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:21, and wherein the VL domain comprises a CDR-L1 comprising

sequence of SEQ ID NO:181, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:182; the VH domain comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:238, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:239, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:233, and wherein the VL domain comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:16, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:17, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:228; the VH domain comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:240, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:241, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:242, and wherein the VL domain comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:40, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:41, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:42; the VH domain comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:238, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:243, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:233, and wherein the VL domain comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:234, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:235, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:236; the VH domain comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:238, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:243, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:233, and wherein the VL domain comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:16, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:17, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:228; or the VH domain comprises a CDR-H1 comprising the amino acid sequence of SEQ ID NO:240, a CDR-H2 comprising the amino acid sequence of SEQ ID NO:244, and a CDR-H3 comprising the amino acid sequence of SEQ ID NO:242, and wherein the VL domain comprises a CDR-L1 comprising the amino acid sequence of SEQ ID NO:40, a CDR-L2 comprising the amino acid sequence of SEQ ID NO:41, and a CDR-L3 comprising the amino acid sequence of SEQ ID NO:42. In some examples, the VH domain of both antibody heavy chain polypeptides comprises an amino acid sequence that is at least 90%, at least 95%, at least 99%, or 100% identical to the sequence of SEQ ID NO:62, and wherein the VL domain of both antibody light chain polypeptides comprises an amino acid sequence that is at least 90%, at least 95%, at least 99%, or 100% identical to the

that is at least 90%, at least 95%, at least 99%, or 100% identical to the sequence of SEQ ID NO:251, and wherein the VL domain of both antibody light chain polypeptides comprises an amino acid sequence that is at least 90%, at least 95%, at least 99%, or 100% identical to the sequence of SEQ ID NO:252; the VH domain comprises the amino acid sequence of SEQ ID NO:251, and wherein the VL domain comprises the amino acid sequence of SEQ ID NO:252; the VH domain of both antibody heavy chain polypeptides comprises an amino acid sequence that is at least 90%, at least 95%, at least 99%, or 100% identical to the sequence of SEQ ID NO:253, and wherein the VL domain of both antibody light chain polypeptides comprises an amino acid sequence that is at least 90%, at least 95%, at least 99%, or 100% identical to the sequence of SEQ ID NO:254; the VH domain of both antibody heavy chain polypeptides comprises an amino acid sequence that is at least 90%, at least 95%, at least 99%, or 100% identical to the sequence of SEQ ID NO:247, and wherein the VL domain of both antibody light chain polypeptides comprises an amino acid sequence that is at least 90%, at least 95%, at least 99%, or 100% identical to the sequence of SEQ ID NO:248; the VH domain of both antibody heavy chain polypeptides comprises an amino acid sequence that is at least 90%, at least 95%, at least 99%, or 100% identical to the sequence of SEQ ID NO:249, and wherein the VL domain of both antibody light chain polypeptides comprises an amino acid sequence that is at least 90%, at least 95%, at least 99%, or 100% identical to the sequence of SEQ ID NO:250; the VH domain comprises the amino acid sequence of SEQ ID NO:249, and wherein the VL domain comprises the amino acid sequence of SEQ ID NO:250; the VH domain of both antibody heavy chain polypeptides comprises an amino acid sequence that is at least 90%, at least 95%, at least 99%, or 100% identical to the sequence of SEQ ID NO:255, and wherein the VL domain of both antibody light chain polypeptides comprises an amino acid sequence that is at least 90%, at least 95%, at least 99%, or 100% identical to the sequence of SEQ ID NO:256; or the VH domain of both antibody heavy chain polypeptides comprises an amino acid sequence that is at least 90%, at least 95%, at least 99%, or 100% identical to the sequence of SEQ ID NO:257, and wherein the VL domain of both antibody light chain polypeptides comprises an amino acid sequence that is at least 90%, at least 95%, at least 99%, or 100% identical to the sequence of SEQ ID NO:258. In some examples, the VH domain comprises an amino acid sequence that is at least 90%, at least 95%, at least 99%, or 100% identical to the sequence of SEQ ID NO:62, and wherein the VL domain comprises an amino acid sequence that is at least 90%, at least 95%, at least 99%, or

domain comprises an amino acid sequence that is at least 90%, at least 95%, at least 99%, or 100% identical to the sequence of SEQ ID NO:254; the VH domain comprises an amino acid sequence that is at least 90%, at least 95%, at least 99%, or 100% identical to the sequence of SEQ ID NO:247, and wherein the VL domain comprises an amino acid sequence that is at least 90%, at least 95%, at least 99%, or 100% identical to the sequence of SEQ ID NO:248; the VH domain comprises an amino acid sequence that is at least 90%, at least 95%, at least 99%, or 100% identical to the sequence of SEQ ID NO:249, and wherein the VL domain comprises an amino acid sequence that is at least 90%, at least 95%, at least 99%, or 100% identical to the sequence of SEQ ID NO:250; the VH domain comprises the amino acid sequence of SEQ ID NO:249, and wherein the VL domain comprises the amino acid sequence of SEQ ID NO:250; the VH domain comprises an amino acid sequence that is at least 90%, at least 95%, at least 99%, or 100% identical to the sequence of SEQ ID NO:255, and wherein the VL domain comprises an amino acid sequence that is at least 90%, at least 95%, at least 99%, or 100% identical to the sequence of SEQ ID NO:256; or the VH domain comprises an amino acid sequence that is at least 90%, at least 95%, at least 99%, or 100% identical to the sequence of SEQ ID NO:257, and wherein the VL domain comprises an amino acid sequence that is at least 90%, at least 95%, at least 99%, or 100% identical to the sequence of SEQ ID NO:258. In some examples, one or both of the antibody heavy chain polypeptides comprise(s) the following amino acid substitutions: L234A, L235A, and G237A, numbering according to EU index. In some examples, a first of the antibody heavy chain polypeptides comprises amino acid substitutions Y349C and T366W, and a second of the antibody heavy chain polypeptides comprises amino acid substitutions S354C, T366S, L368A and Y407V, numbering according to EU index.

[0022] In some examples according to any of the examples described herein, the second moiety comprises an IL-2 polypeptide. In some examples, the IL-2 polypeptide is a mutant IL-2 polypeptide comprising one or more mutations relative to a human IL-2 polypeptide comprising the sequence of APTSSSTKKTQLQLEHLLLDLQMILNGINNYKNPKLTRMLTFKFYMPKKATELKHLQCL EEELKPLEEVLNLAQSKNFHLRPRDLISNINVIVLELKGSETTFMCEYADETATIVEFLNR WITFCQSIISTLT (SEQ ID NO:81). In some examples, the mutant IL-2 polypeptide has a binding affinity to IL-2Rα that is reduced by 50% or more, compared to binding affinity of a

wild-type IL-2 polypeptide comprising the sequence of SEQ ID: 81 for IL-2Rα. In some examples, the mutant IL-2 polypeptide has a binding affinity to IL-2Rβ that is reduced by 50% or more, compared to binding affinity of a wild-type IL-2 polypeptide comprising the sequence of SEQ ID: 81 for IL-2Rβ; and/or the mutant IL-2 polypeptide has a binding affinity to IL-2Rγ that is reduced by 50% or more, compared to binding affinity of a wild-type IL-2 polypeptide comprising the sequence of SEQ ID: 81 for IL-2Rγ. In some examples, the IL-2 polypeptide comprises the sequence of SEQ ID NO:81 with one, two, three, four, or five amino acid substitutions relative to SEQ ID NO:81, and wherein the one, two, three, four, or five substitution(s) comprise substitution(s) at positions of SEQ ID NO:81 selected from the group consisting of: Q11, H16, L18, L19, D20, Q22, R38, F42, K43, Y45, E62, P65, E68, V69, L72, D84, S87, N88, V91, I92, T123, Q126, S127, I129, and S130. In some examples, the IL-2 polypeptide comprises the sequence of SEQ ID NO:81 with one of the following sets of amino acid substitutions (relative to the sequence of SEQ ID NO:81): R38E and F42A; R38D and F42A; F42A and E62Q; R38A and F42K; R38E, F42A, and N88S; R38E, F42A, and N88A; R38E, F42A, and N88G; R38E, F42A, and N88R; R38E, F42A, and N88T; R38E, F42A, and N88D; R38E, F42A, and V91E; R38E, F42A, and D84H; R38E, F42A, and D84K; R38E, F42A, and D84R; H16D, R38E and F42A; H16E, R38E and F42A; R38E, F42A and Q126S; R38D, F42A and N88S; R38D, F42A and N88A; R38D, F42A and N88G; R38D, F42A and N88R; R38D, F42A and N88T; R38D, F42A and N88D; R38D, F42A and V91E; R38D, F42A, and D84H; R38D, F42A, and D84K; R38D, F42A, and D84R; H16D, R38D and F42A; H16E, R38D and F42A; R38D, F42A and Q126S; R38A, F42K, and N88S; R38A, F42K, and N88A; R38A, F42K, and N88G; R38A, F42K, and N88R; R38A, F42K, and N88T; R38A, F42K, and N88D; R38A, F42K, and V91E; R38A, F42K, and D84H; R38A, F42K, and D84K; R38A, F42K, and D84R; H16D, R38A, and F42K; H16E, R38A, and F42K; R38A, F42K, and Q126S; F42A, E62Q, and N88S; F42A, E62Q, and N88A; F42A, E62Q, and N88G; F42A, E62Q, and N88R; F42A, E62Q, and N88T; F42A, E62Q, and N88D; F42A, E62Q, and V91E; F42A, E62Q, and D84H; F42A, E62Q, and D84K; F42A, E62Q, and D84R; H16D, F42A, and E62Q; H16E, F42A, and E62Q; F42A, E62Q, and Q126S. In some examples, the IL-2 polypeptide comprises the sequence of SEQ ID NO:81 with a further amino acid substitution relative to SEQ ID NO:81 at position C125. In some examples, the IL-2 polypeptide comprises the sequence of SEQ ID NO:81 with one of the following sets of amino acid substitutions (relative to the

sequence of SEQ ID NO:81): R38E, F42A, and C125A; R38D, F42A , and C125A; F42A, E62Q, and C125A; R38A, F42K, and C125A; R38E, F42A, N88S, and C125A; R38E, F42A, N88A, and C125A; R38E, F42A, N88G, and C125A; R38E, F42A, N88R, and C125A; R38E, F42A, N88T, and C125A; R38E, F42A, N88D, and C125A; R38E, F42A, V91E, and C125A; R38E, F42A, D84H, and C125A; R38E, F42A, D84K, and C125A; R38E, F42A, D84R, and C125A; H16D, R38E, F42A, and C125A; H16E, R38E, F42A, and C125A; R38E, F42A, C125A and Q126S; R38D, F42A, N88S, and C125A; R38D, F42A, N88A, and C125A; R38D, F42A, N88G, and C125A; R38D, F42A, N88R, and C125A; R38D, F42A, N88T, and C125A; R38D, F42A, N88D, and C125A;R38D, F42A, V91E, and C125A; R38D, F42A, D84H, and C125A; R38D, F42A, D84K, and C125A; R38D, F42A, D84R, and C125A; H16D, R38D, F42A, and C125A; H16E, R38D, F42A, and C125A; R38D, F42A , C125A, and Q126S; R38A, F42K, N88S, and C125A; R38A, F42K, N88G, and C125A; R38A, F42K, N88R, and C125A; R38A, F42K, N88T, and C125A; R38A, F42K, N88D, and C125A; R38A, F42K, N88A, and C125A; R38A, F42K, V91E, and C125A; R38A, F42K, D84H, and C125A; R38A, F42K, D84K, and C125A; R38A, F42K, D84R, and C125A; H16D, R38A, F42K, and C125A; H16E, R38A, F42K, and C125A; R38A, F42K, C125A and Q126S; F42A, E62Q, N88S, and C125A; F42A, E62Q, N88A, and C125A; F42A, E62Q, N88G, and C125A; F42A, E62Q, N88R, and C125A; F42A, E62Q, N88T, and C125A; F42A, E62Q, N88D, and C125A; F42A, E62Q, V91E, and C125A; F42A, E62Q, and D84H, and C125A; F42A, E62Q, and D84K, and C125A; F42A, E62Q, and D84R, and C125A; H16D, F42A, and E62Q, and C125A; H16E, F42A, E62Q, and C125A; F42A, E62Q, C125A and Q126S; F42A, N88S, and C125A; F42A, N88A, and C125A; F42A, N88G, and C125A; F42A, N88R, and C125A; F42A, N88T, and C125A; F42A, N88D, and C125A; F42A, V91E, and C125A; F42A, D84H, and C125A; F42A, D84K, and C125A; F42A, D84R, and C125A; H16D, F42A, and C125A; H16E, F42A, and C125A; and F42A, C125A and Q126S. In some examples, the IL-2 polypeptide comprises the sequence APTSSSTKKTQLQLEHLLLDLQMILNGINNYKNPKLTEMLTAKFYMPKKATELKHLQCL EEELKPLEEVLNLAQSKNFHLRPRDLISAINVIVLELKGSETTFMCEYADETATIVEFLNR WITFAQSIISTLT (SEQ ID NO:80). In some examples, the IL-2 polypeptide comprises the sequence
APTSSSTKKTQLQLEELLLDLQMILNGINNYKNPKLTEMLTAKFYMPKKATELKHLQCL EEELKPLEEVLNLAQSKNFHLRPRDLISNINVIVLELKGSETTFMCEYADETATIVEFLNR

WITFAQSIISTLT (SEQ ID NO:297). In some examples, the IL-2 polypeptide comprises a sequence selected from the group consisting of SEQ ID Nos: 85-155 and 190-216. In some examples, the IL-2 polypeptide comprises a sequence selected from the group consisting of SEQ ID Nos: 80, 85-155, 190-216, 297, and 354-383. In some examples, the second moiety comprises a polypeptide that induces signaling via IL2Rβγ. In some examples, the second moiety comprises an IL-21 polypeptide.

[0023] In some examples according to any of the examples described herein (*e.g.*, a fusion protein of the present disclosure), one or both of the antibody Fc domains comprise(s) human IgG1 Fc domains with the following amino acid substitutions: L234A, L235A, G237A, and K322A, numbering according to EU index. In some examples, one or both of the antibody Fc domains do not have a C-terminal lysine. In some examples, one or both of the antibody Fc domains comprise(s) human IgG1 Fc domains with the following amino acid substitutions: L234A, L235A, and G237A, numbering according to EU index. In some examples, one or both of the antibody Fc domains do not have a C-terminal lysine. In some examples, a first of the two Fc domains comprises a human IgG1 Fc domain with amino acid substitutions Y349C and T366W, and a second of the two Fc domain comprises a human IgG1 Fc domain with amino acid substitutions S354C, T366S, L368A and Y407V, numbering according to EU index. In some examples, one or both of the antibody Fc domains do not have a C-terminal lysine. In some examples (*e.g.*, a fusion protein of the present disclosure), the linker comprises the sequence (GGGS)xGn (SEQ ID NO:74), (GGGGS)xGn (SEQ ID NO:75), or (GGGGGS)xGn (SEQ ID NO:76), S(GGGS)xGn (SEQ ID NO:386), S(GGGGS)xGn (SEQ ID NO:387), or S(GGGGGS)xGn (SEQ ID NO:388), wherein x=1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, or 12, and wherein n=0, 1, 2 or 3. In some examples, the linker comprises the sequence GGGGSGGGGSGGGGS (SEQ ID NO:79) or SGGGGSGGGGSGGGGS (SEQ ID NO:389). In some examples (*e.g.*, in a fusion protein of the present disclosure), the linker connects a first moiety of the present disclosure (*e.g.*, a human or humanized antibody or antigen-binding fragment thereof that specifically binds CD8b and/or CD8ab) and a second moiety of the present disclosure (*e.g.*, an IL-2 polypeptide of the present disclosure, IL-21 polypeptide of the present disclosure, or a polypeptide that induces signaling via IL2Rβγ of the present disclosure).

[0024] In some examples, a fusion protein of the present disclosure comprises one or two light chains comprising the amino acid sequence of SEQ ID NO:156, a heavy chain comprising the amino acid sequence of SEQ ID NO:157, and a heavy chain comprising the amino acid sequence of SEQ ID NO:158. In some examples, a fusion protein of the present disclosure comprises one or two light chains comprising the amino acid sequence of SEQ ID NO:156, a heavy chain comprising the amino acid sequence of SEQ ID NO:157, and a heavy chain comprising the amino acid sequence of SEQ ID NO:217. In some examples, a fusion protein of the present disclosure comprises one or two light chains comprising the amino acid sequence of SEQ ID NO:159, a heavy chain comprising the amino acid sequence of SEQ ID NO:160, and a heavy chain comprising the amino acid sequence of SEQ ID NO:161. In some examples, a fusion protein of the present disclosure comprises one or two light chains comprising the amino acid sequence of SEQ ID NO:159, a heavy chain comprising the amino acid sequence of SEQ ID NO:160, and a heavy chain comprising the amino acid sequence of SEQ ID NO:218. In some examples, a fusion protein of the present disclosure comprises one or two light chains comprising the amino acid sequence of SEQ ID NO:162, a heavy chain comprising the amino acid sequence of SEQ ID NO:163, and a heavy chain comprising the amino acid sequence of SEQ ID NO:164. In some examples, a fusion protein of the present disclosure comprises one or two light chains comprising the amino acid sequence of SEQ ID NO:162, a heavy chain comprising the amino acid sequence of SEQ ID NO:163, and a heavy chain comprising the amino acid sequence of SEQ ID NO:219. In some examples, a fusion protein of the present disclosure comprises one or two light chains comprising the amino acid sequence of SEQ ID NO:165, a heavy chain comprising the amino acid sequence of SEQ ID NO:166, and a heavy chain comprising the amino acid sequence of SEQ ID NO:167. In some examples, a fusion protein of the present disclosure comprises one or two light chains comprising the amino acid sequence of SEQ ID NO:165, a heavy chain comprising the amino acid sequence of SEQ ID NO:166, and a heavy chain comprising the amino acid sequence of SEQ ID NO:220. In some examples, a fusion protein of the present disclosure comprises one or two light chains comprising the amino acid sequence of SEQ ID NO:168, a heavy chain comprising the amino acid sequence of SEQ ID NO:169, and a heavy chain comprising the amino acid sequence of SEQ ID NO:170. In some examples, a fusion protein of the present disclosure comprises one or two light chains comprising the amino acid sequence of SEQ ID NO:168, a heavy chain

comprising the amino acid sequence of SEQ ID NO:169, and a heavy chain comprising the amino acid sequence of SEQ ID NO:221. In some examples, a fusion protein of the present disclosure comprises one or two light chains comprising the amino acid sequence of SEQ ID NO:171, a heavy chain comprising the amino acid sequence of SEQ ID NO:172, and a heavy chain comprising the amino acid sequence of SEQ ID NO:173. In some examples, a fusion protein of the present disclosure comprises one or two light chains comprising the amino acid sequence of SEQ ID NO:171, a heavy chain comprising the amino acid sequence of SEQ ID NO:172, and a heavy chain comprising the amino acid sequence of SEQ ID NO:222. In some examples, a fusion protein of the present disclosure comprises one or two light chains comprising the amino acid sequence of SEQ ID NO:174, a heavy chain comprising the amino acid sequence of SEQ ID NO:175, and a heavy chain comprising the amino acid sequence of SEQ ID NO:176. In some examples, a fusion protein of the present disclosure comprises one or two light chains comprising the amino acid sequence of SEQ ID NO:174, a heavy chain comprising the amino acid sequence of SEQ ID NO:175, and a heavy chain comprising the amino acid sequence of SEQ ID NO:223. In some examples, a fusion protein of the present disclosure comprises one or two light chains comprising the amino acid sequence of SEQ ID NO:187, a heavy chain comprising the amino acid sequence of SEQ ID NO:188, and a heavy chain comprising the amino acid sequence of SEQ ID NO:189. In some examples, a fusion protein of the present disclosure comprises one or two light chains comprising the amino acid sequence of SEQ ID NO:187, a heavy chain comprising the amino acid sequence of SEQ ID NO:188, and a heavy chain comprising the amino acid sequence of SEQ ID NO:224. In some examples, a fusion protein of the present disclosure comprises one or two light chains comprising the amino acid sequence of SEQ ID NO:298, a heavy chain comprising the amino acid sequence of SEQ ID NO:299, and a heavy chain comprising the amino acid sequence of SEQ ID NO:300. In some examples, a fusion protein of the present disclosure comprises one or two light chains comprising the amino acid sequence of SEQ ID NO:298, a heavy chain comprising the amino acid sequence of SEQ ID NO:299, and a heavy chain comprising the amino acid sequence of SEQ ID NO:301. In some examples, a fusion protein of the present disclosure comprises one or two light chains comprising the amino acid sequence of SEQ ID NO:302, a heavy chain comprising the amino acid sequence of SEQ ID NO:303, and a heavy chain comprising the amino acid sequence of SEQ ID NO:304. In some examples, a fusion

protein of the present disclosure comprises one or two light chains comprising the amino acid sequence of SEQ ID NO:302, a heavy chain comprising the amino acid sequence of SEQ ID NO:303, and a heavy chain comprising the amino acid sequence of SEQ ID NO:305. In some examples, a fusion protein of the present disclosure comprises one or two light chains comprising the amino acid sequence of SEQ ID NO:306, a heavy chain comprising the amino acid sequence of SEQ ID NO:307, and a heavy chain comprising the amino acid sequence of SEQ ID NO:308. In some examples, a fusion protein of the present disclosure comprises one or two light chains comprising the amino acid sequence of SEQ ID NO:306, a heavy chain comprising the amino acid sequence of SEQ ID NO:307, and a heavy chain comprising the amino acid sequence of SEQ ID NO:309. In some examples, a fusion protein of the present disclosure comprises one or two light chains comprising the amino acid sequence of SEQ ID NO:310, a heavy chain comprising the amino acid sequence of SEQ ID NO:311, and a heavy chain comprising the amino acid sequence of SEQ ID NO:312. In some examples, a fusion protein of the present disclosure comprises one or two light chains comprising the amino acid sequence of SEQ ID NO:310, a heavy chain comprising the amino acid sequence of SEQ ID NO:311, and a heavy chain comprising the amino acid sequence of SEQ ID NO:313. In some examples, a fusion protein of the present disclosure comprises one or two light chains comprising the amino acid sequence of SEQ ID NO:314, a heavy chain comprising the amino acid sequence of SEQ ID NO:315, and a heavy chain comprising the amino acid sequence of SEQ ID NO:316. In some examples, a fusion protein of the present disclosure comprises one or two light chains comprising the amino acid sequence of SEQ ID NO:314, a heavy chain comprising the amino acid sequence of SEQ ID NO:315, and a heavy chain comprising the amino acid sequence of SEQ ID NO:317. In some examples, a fusion protein of the present disclosure comprises one or two light chains comprising the amino acid sequence of SEQ ID NO:318, a heavy chain comprising the amino acid sequence of SEQ ID NO:319, and a heavy chain comprising the amino acid sequence of SEQ ID NO:320. In some examples, a fusion protein of the present disclosure comprises one or two light chains comprising the amino acid sequence of SEQ ID NO:318, a heavy chain comprising the amino acid sequence of SEQ ID NO:319, and a heavy chain comprising the amino acid sequence of SEQ ID NO:321. In some examples, a fusion protein of the present disclosure comprises one or two light chains comprising the amino acid sequence of SEQ ID NO:322, a heavy chain comprising the amino

acid sequence of SEQ ID NO:323, and a heavy chain comprising the amino acid sequence of SEQ ID NO:324. In some examples, a fusion protein of the present disclosure comprises one or two light chains comprising the amino acid sequence of SEQ ID NO:322, a heavy chain comprising the amino acid sequence of SEQ ID NO:323, and a heavy chain comprising the amino acid sequence of SEQ ID NO:325. In some examples, a fusion protein of the present disclosure comprises one or two light chains comprising the amino acid sequence of SEQ ID NO:326, a heavy chain comprising the amino acid sequence of SEQ ID NO:327, and a heavy chain comprising the amino acid sequence of SEQ ID NO:328. In some examples, a fusion protein of the present disclosure comprises one or two light chains comprising the amino acid sequence of SEQ ID NO:326, a heavy chain comprising the amino acid sequence of SEQ ID NO:327, and a heavy chain comprising the amino acid sequence of SEQ ID NO:329. In some examples, a fusion protein of the present disclosure comprises one or two light chains comprising the amino acid sequence of SEQ ID NO:330, a heavy chain comprising the amino acid sequence of SEQ ID NO:331, and a heavy chain comprising the amino acid sequence of SEQ ID NO:332. In some examples, a fusion protein of the present disclosure comprises one or two light chains comprising the amino acid sequence of SEQ ID NO:330, a heavy chain comprising the amino acid sequence of SEQ ID NO:331, and a heavy chain comprising the amino acid sequence of SEQ ID NO:333. In some examples, a fusion protein of the present disclosure comprises one or two light chains comprising the amino acid sequence of SEQ ID NO:334, a heavy chain comprising the amino acid sequence of SEQ ID NO:335, and a heavy chain comprising the amino acid sequence of SEQ ID NO:336. In some examples, a fusion protein of the present disclosure comprises one or two light chains comprising the amino acid sequence of SEQ ID NO:334, a heavy chain comprising the amino acid sequence of SEQ ID NO:335, and a heavy chain comprising the amino acid sequence of SEQ ID NO:337. In some examples, a fusion protein of the present disclosure comprises one or two light chains comprising the amino acid sequence of SEQ ID NO:338, a heavy chain comprising the amino acid sequence of SEQ ID NO:339, and a heavy chain comprising the amino acid sequence of SEQ ID NO:340. In some examples, a fusion protein of the present disclosure comprises one or two light chains comprising the amino acid sequence of SEQ ID NO:338, a heavy chain comprising the amino acid sequence of SEQ ID NO:339, and a heavy chain comprising the amino acid sequence of SEQ ID NO:341. In some examples, a fusion protein of the present

disclosure comprises one or two light chains comprising the amino acid sequence of SEQ ID NO:342, a heavy chain comprising the amino acid sequence of SEQ ID NO:343, and a heavy chain comprising the amino acid sequence of SEQ ID NO:344. In some examples, a fusion protein of the present disclosure comprises one or two light chains comprising the amino acid sequence of SEQ ID NO:342, a heavy chain comprising the amino acid sequence of SEQ ID NO:343, and a heavy chain comprising the amino acid sequence of SEQ ID NO:345. In some examples, a fusion protein of the present disclosure comprises one or two light chains comprising the amino acid sequence of SEQ ID NO:346, a heavy chain comprising the amino acid sequence of SEQ ID NO:347, and a heavy chain comprising the amino acid sequence of SEQ ID NO:348. In some examples, a fusion protein of the present disclosure comprises one or two light chains comprising the amino acid sequence of SEQ ID NO:346, a heavy chain comprising the amino acid sequence of SEQ ID NO:347, and a heavy chain comprising the amino acid sequence of SEQ ID NO:349. In some examples, a fusion protein of the present disclosure comprises one or two light chains comprising the amino acid sequence of SEQ ID NO:350, a heavy chain comprising the amino acid sequence of SEQ ID NO:351, and a heavy chain comprising the amino acid sequence of SEQ ID NO:352. In some examples, a fusion protein of the present disclosure comprises one or two light chains one or two light chains comprising the amino acid sequence of SEQ ID NO:156, a heavy chain comprising the amino acid sequence of SEQ ID NO:157, and a heavy chain comprising the amino acid sequence of SEQ ID NO:217. In some examples, a fusion protein of the present disclosure comprises one or two light chains one or two light chains comprising the amino acid sequence of SEQ ID NO:159, a heavy chain comprising the amino acid sequence of SEQ ID NO:160, and a heavy chain comprising the amino acid sequence of SEQ ID NO:218. In some examples, a fusion protein of the present disclosure comprises one or two light chains one or two light chains comprising the amino acid sequence of SEQ ID NO:162, a heavy chain comprising the amino acid sequence of SEQ ID NO:163, and a heavy chain comprising the amino acid sequence of SEQ ID NO:219. In some examples, a fusion protein of the present disclosure comprises one or two light chains one or two light chains comprising the amino acid sequence of SEQ ID NO:165, a heavy chain comprising the amino acid sequence of SEQ ID NO:166, and a heavy chain comprising the amino acid sequence of SEQ ID NO:220. In some examples, a fusion protein of the present disclosure comprises one or two light chains one or two light chains

comprising the amino acid sequence of SEQ ID NO:168, a heavy chain comprising the amino acid sequence of SEQ ID NO:169, and a heavy chain comprising the amino acid sequence of SEQ ID NO:221. In some examples, a fusion protein of the present disclosure comprises one or two light chains one or two light chains comprising the amino acid sequence of SEQ ID NO:171, a heavy chain comprising the amino acid sequence of SEQ ID NO:172, and a heavy chain comprising the amino acid sequence of SEQ ID NO:222. In some examples, a fusion protein of the present disclosure comprises one or two light chains one or two light chains comprising the amino acid sequence of SEQ ID NO:174, a heavy chain comprising the amino acid sequence of SEQ ID NO:175, and a heavy chain comprising the amino acid sequence of SEQ ID NO:223. In some examples, a fusion protein of the present disclosure comprises one or two light chains one or two light chains comprising the amino acid sequence of SEQ ID NO:187, a heavy chain comprising the amino acid sequence of SEQ ID NO:188, and a heavy chain comprising the amino acid sequence of SEQ ID NO:224. In some examples, a fusion protein of the present disclosure comprises one or two light chains one or two light chains comprising the amino acid sequence of SEQ ID NO:298, a heavy chain comprising the amino acid sequence of SEQ ID NO:299, and a heavy chain comprising the amino acid sequence of SEQ ID NO:301. In some examples, a fusion protein of the present disclosure comprises one or two light chains one or two light chains comprising the amino acid sequence of SEQ ID NO:302, a heavy chain comprising the amino acid sequence of SEQ ID NO:303, and a heavy chain comprising the amino acid sequence of SEQ ID NO:305. In some examples, a fusion protein of the present disclosure comprises one or two light chains one or two light chains comprising the amino acid sequence of SEQ ID NO:306, a heavy chain comprising the amino acid sequence of SEQ ID NO:307, and a heavy chain comprising the amino acid sequence of SEQ ID NO:309. In some examples, a fusion protein of the present disclosure comprises one or two light chains one or two light chains comprising the amino acid sequence of SEQ ID NO:310, a heavy chain comprising the amino acid sequence of SEQ ID NO:311, and a heavy chain comprising the amino acid sequence of SEQ ID NO:313. In some examples, a fusion protein of the present disclosure comprises one or two light chains one or two light chains comprising the amino acid sequence of SEQ ID NO:314, a heavy chain comprising the amino acid sequence of SEQ ID NO:315, and a heavy chain comprising the amino acid sequence of SEQ ID NO:317. In some examples, a fusion protein of the present disclosure comprises

one or two light chains one or two light chains comprising the amino acid sequence of SEQ ID NO:318, a heavy chain comprising the amino acid sequence of SEQ ID NO:319, and a heavy chain comprising the amino acid sequence of SEQ ID NO:321. In some examples, a fusion protein of the present disclosure comprises one or two light chains one or two light chains comprising the amino acid sequence of SEQ ID NO:322, a heavy chain comprising the amino acid sequence of SEQ ID NO:323, and a heavy chain comprising the amino acid sequence of SEQ ID NO:325. In some examples, a fusion protein of the present disclosure comprises one or two light chains one or two light chains comprising the amino acid sequence of SEQ ID NO:326, a heavy chain comprising the amino acid sequence of SEQ ID NO:327, and a heavy chain comprising the amino acid sequence of SEQ ID NO:329. In some examples, a fusion protein of the present disclosure comprises one or two light chains one or two light chains comprising the amino acid sequence of SEQ ID NO:330, a heavy chain comprising the amino acid sequence of SEQ ID NO:331, and a heavy chain comprising the amino acid sequence of SEQ ID NO:333. In some examples, a fusion protein of the present disclosure comprises one or two light chains one or two light chains comprising the amino acid sequence of SEQ ID NO:334, a heavy chain comprising the amino acid sequence of SEQ ID NO:335, and a heavy chain comprising the amino acid sequence of SEQ ID NO:337. In some examples, a fusion protein of the present disclosure comprises one or two light chains one or two light chains comprising the amino acid sequence of SEQ ID NO:338, a heavy chain comprising the amino acid sequence of SEQ ID NO:339, and a heavy chain comprising the amino acid sequence of SEQ ID NO:341. In some examples, a fusion protein of the present disclosure comprises one or two light chains one or two light chains comprising the amino acid sequence of SEQ ID NO:342, a heavy chain comprising the amino acid sequence of SEQ ID NO:343, and a heavy chain comprising the amino acid sequence of SEQ ID NO:345. In some examples, a fusion protein of the present disclosure comprises one or two light chains one or two light chains comprising the amino acid sequence of SEQ ID NO:346, a heavy chain comprising the amino acid sequence of SEQ ID NO:347, and a heavy chain comprising the amino acid sequence of SEQ ID NO:349. In some examples, a fusion protein of the present disclosure comprises one or two light chains one or two light chains comprising the amino acid sequence of SEQ ID NO:350, a heavy chain comprising the amino acid sequence of SEQ ID NO:351, and a heavy chain comprising the amino acid sequence of SEQ ID NO:353. In some examples, the

fusion protein comprises one or two antigen binding sites, each antigen binding site comprising a VL domain from one of the light chain(s) and a VH domain from one of the heavy chains (*e.g.*, the fusion protein comprises two antigen binding sites: one comprising a VL domain from one of the two light chains and a VH domain from one of the heavy chains, and another comprising a VL domain from the other light chain and a VH domain from the other heavy chain).

[0024a] In one aspect, the present disclosure refers to a fusion protein comprising a first moiety that binds to a human CD8b and a second moiety comprising an IL2 polypeptide, wherein the fusion protein comprises four polypeptide chains, wherein: the first polypeptide chain comprises the amino acid sequence of SEQ ID NO:334, the second polypeptide chain comprises the amino acid sequence of SEQ ID NO:335, the third polypeptide chain comprises the amino acid sequence of SEQ ID NO:336, and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO:334; the first polypeptide chain comprises the amino acid sequence of SEQ ID NO:334, the second polypeptide chain comprises the amino acid sequence of SEQ ID NO:335, the third polypeptide chain comprises the amino acid sequence of SEQ ID NO:337, and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO:334; the first polypeptide chain comprises the amino acid sequence of SEQ ID NO:338, the second polypeptide chain comprises the amino acid sequence of SEQ ID NO:339, the third polypeptide chain comprises the amino acid sequence of SEQ ID NO:340, and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO:338; or the first polypeptide chain comprises the amino acid sequence of SEQ ID NO:338, the second polypeptide chain comprises the amino acid sequence of SEQ ID NO:339, the third polypeptide chain comprises the amino acid sequence of SEQ ID NO:341, and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO:338.

[0025] In some examples, a fusion protein of the present disclosure comprises one or two polypeptides comprising the amino acid sequence of SEQ ID NO:156, a polypeptide comprising the amino acid sequence of SEQ ID NO:157, and a polypeptide comprising the amino acid sequence of SEQ ID NO:158. In some examples, a fusion protein of the present disclosure comprises one or two polypeptides comprising the amino acid sequence of SEQ ID NO:156, a polypeptide comprising the amino acid sequence of SEQ ID NO:157, and a polypeptide comprising the amino acid sequence of SEQ ID NO:217. In some examples, a fusion protein of the present disclosure comprises one or two polypeptides comprising the amino acid sequence of SEQ ID NO:159, a polypeptide comprising the amino acid sequence of SEQ ID NO:160, and a polypeptide comprising the amino acid sequence of SEQ ID NO:161. In some examples, a fusion protein of the present disclosure comprises one or two polypeptides comprising the amino acid sequence of SEQ ID NO:159, a polypeptide comprising the amino acid sequence of SEQ ID NO:160, and a polypeptide comprising the amino acid sequence of SEQ ID NO:218. In some examples, a fusion protein of the present disclosure comprises one or two polypeptides comprising the amino acid sequence of SEQ ID NO:162, a polypeptide comprising the amino acid sequence of SEQ ID NO:163, and a polypeptide comprising the amino acid sequence of SEQ ID NO:164. In some examples, a fusion protein of the present disclosure comprises one or two polypeptides comprising the amino acid sequence of SEQ ID NO:162, a polypeptide comprising the amino acid sequence of SEQ ID NO:163, and a polypeptide comprising the amino acid sequence of SEQ ID NO:219. In some examples, a fusion protein of the present disclosure comprises one or two polypeptides comprising the amino acid sequence of SEQ ID NO:165, a polypeptide comprising the amino acid sequence of SEQ ID NO:166, and a polypeptide comprising the amino acid sequence of SEQ ID NO:167. In some examples, a fusion protein of the present disclosure comprises one or two polypeptides comprising the amino acid sequence of SEQ ID NO:165, a polypeptide comprising the amino acid sequence of SEQ ID NO:166, and a polypeptide comprising the amino acid sequence of SEQ ID NO:220. In some

examples, a fusion protein of the present disclosure comprises one or two polypeptides comprising the amino acid sequence of SEQ ID NO:168, a polypeptide comprising the amino acid sequence of SEQ ID NO:169, and a polypeptide comprising the amino acid sequence of SEQ ID NO:170. In some examples, a fusion protein of the present disclosure comprises one or two polypeptides comprising the amino acid sequence of SEQ ID NO:168, a polypeptide comprising the amino acid sequence of SEQ ID NO:169, and a polypeptide comprising the amino acid sequence of SEQ ID NO:221. In some examples, a fusion protein of the present disclosure comprises one or two polypeptides comprising the amino acid sequence of SEQ ID NO:171, a polypeptide comprising the amino acid sequence of SEQ ID NO:172, and a polypeptide comprising the amino acid sequence of SEQ ID NO:173. In some examples, a fusion protein of the present disclosure comprises one or two polypeptides comprising the amino acid sequence of SEQ ID NO:171, a polypeptide comprising the amino acid sequence of SEQ ID NO:172, and a polypeptide comprising the amino acid sequence of SEQ ID NO:222. In some examples, a fusion protein of the present disclosure comprises one or two polypeptides comprising the amino acid sequence of SEQ ID NO:174, a polypeptide comprising the amino acid sequence of SEQ ID NO:175, and a polypeptide comprising the amino acid sequence of SEQ ID NO:176. In some examples, a fusion protein of the present disclosure comprises one or two polypeptides comprising the amino acid sequence of SEQ ID NO:174, a polypeptide comprising the amino acid sequence of SEQ ID NO:175, and a polypeptide comprising the amino acid sequence of SEQ ID NO:223. In some examples, a fusion protein of the present disclosure comprises one or two polypeptides comprising the amino acid sequence of SEQ ID NO:187, a polypeptide comprising the amino acid sequence of SEQ ID NO:188, and a polypeptide comprising the amino acid sequence of SEQ ID NO:189. In some examples, a fusion protein of the present disclosure comprises one or two polypeptides comprising the amino acid sequence of SEQ ID NO:187, a polypeptide comprising the amino acid sequence of SEQ ID NO:188, and a polypeptide comprising the amino acid sequence of SEQ ID NO:224. In some examples, a fusion protein of the present disclosure comprises one or two polypeptides comprising the amino acid sequence of SEQ ID NO:298, a polypeptide comprising the amino acid sequence of SEQ ID NO:299, and a polypeptide comprising the amino acid sequence of SEQ ID NO:300. In some examples, a fusion protein of the present disclosure comprises one or two polypeptides comprising the amino acid sequence of SEQ ID NO:298, a polypeptide

comprising the amino acid sequence of SEQ ID NO:299, and a polypeptide comprising the amino acid sequence of SEQ ID NO:301. In some examples, a fusion protein of the present disclosure comprises one or two polypeptides comprising the amino acid sequence of SEQ ID NO:302, a polypeptide comprising the amino acid sequence of SEQ ID NO:303, and a polypeptide comprising the amino acid sequence of SEQ ID NO:304. In some examples, a fusion protein of the present disclosure comprises one or two polypeptides comprising the amino acid sequence of SEQ ID NO:302, a polypeptide comprising the amino acid sequence of SEQ ID NO:303, and a polypeptide comprising the amino acid sequence of SEQ ID NO:305. In some examples, a fusion protein of the present disclosure comprises one or two polypeptides comprising the amino acid sequence of SEQ ID NO:306, a polypeptide comprising the amino acid sequence of SEQ ID NO:307, and a polypeptide comprising the amino acid sequence of SEQ ID NO:308. In some examples, a fusion protein of the present disclosure comprises one or two polypeptides comprising the amino acid sequence of SEQ ID NO:306, a polypeptide comprising the amino acid sequence of SEQ ID NO:307, and a polypeptide comprising the amino acid sequence of SEQ ID NO:309. In some examples, a fusion protein of the present disclosure comprises one or two polypeptides comprising the amino acid sequence of SEQ ID NO:310, a polypeptide comprising the amino acid sequence of SEQ ID NO:311, and a polypeptide comprising the amino acid sequence of SEQ ID NO:312. In some examples, a fusion protein of the present disclosure comprises one or two polypeptides comprising the amino acid sequence of SEQ ID NO:310, a polypeptide comprising the amino acid sequence of SEQ ID NO:311, and a polypeptide comprising the amino acid sequence of SEQ ID NO:313. In some examples, a fusion protein of the present disclosure comprises one or two polypeptides comprising the amino acid sequence of SEQ ID NO:314, a polypeptide comprising the amino acid sequence of SEQ ID NO:315, and a polypeptide comprising the amino acid sequence of SEQ ID NO:316. In some examples, a fusion protein of the present disclosure comprises one or two polypeptides comprising the amino acid sequence of SEQ ID NO:314, a polypeptide comprising the amino acid sequence of SEQ ID NO:315, and a polypeptide comprising the amino acid sequence of SEQ ID NO:317. In some examples, a fusion protein of the present disclosure comprises one or two polypeptides comprising the amino acid sequence of SEQ ID NO:318, a polypeptide comprising the amino acid sequence of SEQ ID NO:319, and a polypeptide comprising the amino acid sequence of SEQ ID NO:320. In some examples, a

fusion protein of the present disclosure comprises one or two polypeptides comprising the amino acid sequence of SEQ ID NO:318, a polypeptide comprising the amino acid sequence of SEQ ID NO:319, and a polypeptide comprising the amino acid sequence of SEQ ID NO:321. In some examples, a fusion protein of the present disclosure comprises one or two polypeptides comprising the amino acid sequence of SEQ ID NO:322, a polypeptide comprising the amino acid sequence of SEQ ID NO:323, and a polypeptide comprising the amino acid sequence of SEQ ID NO:324. In some examples, a fusion protein of the present disclosure comprises one or two polypeptides comprising the amino acid sequence of SEQ ID NO:322, a polypeptide comprising the amino acid sequence of SEQ ID NO:323, and a polypeptide comprising the amino acid sequence of SEQ ID NO:325. In some examples, a fusion protein of the present disclosure comprises one or two polypeptides comprising the amino acid sequence of SEQ ID NO:326, a polypeptide comprising the amino acid sequence of SEQ ID NO:327, and a polypeptide comprising the amino acid sequence of SEQ ID NO:328. In some examples, a fusion protein of the present disclosure comprises one or two polypeptides comprising the amino acid sequence of SEQ ID NO:326, a polypeptide comprising the amino acid sequence of SEQ ID NO:327, and a polypeptide comprising the amino acid sequence of SEQ ID NO:329. In some examples, a fusion protein of the present disclosure comprises one or two polypeptides comprising the amino acid sequence of SEQ ID NO:330, a polypeptide comprising the amino acid sequence of SEQ ID NO:331, and a polypeptide comprising the amino acid sequence of SEQ ID NO:332. In some examples, a fusion protein of the present disclosure comprises one or two polypeptides comprising the amino acid sequence of SEQ ID NO:330, a polypeptide comprising the amino acid sequence of SEQ ID NO:331, and a polypeptide comprising the amino acid sequence of SEQ ID NO:333. In some examples, a fusion protein of the present disclosure comprises one or two polypeptides comprising the amino acid sequence of SEQ ID NO:334, a polypeptide comprising the amino acid sequence of SEQ ID NO:335, and a polypeptide comprising the amino acid sequence of SEQ ID NO:336. In some examples, a fusion protein of the present disclosure comprises one or two polypeptides comprising the amino acid sequence of SEQ ID NO:334, a polypeptide comprising the amino acid sequence of SEQ ID NO:335, and a polypeptide comprising the amino acid sequence of SEQ ID NO:337. In some examples, a fusion protein of the present disclosure comprises one or two polypeptides comprising the amino acid sequence of SEQ ID NO:338, a polypeptide comprising the amino

acid sequence of SEQ ID NO:339, and a polypeptide comprising the amino acid sequence of SEQ ID NO:340. In some examples, a fusion protein of the present disclosure comprises one or two polypeptides comprising the amino acid sequence of SEQ ID NO:338, a polypeptide comprising the amino acid sequence of SEQ ID NO:339, and a polypeptide comprising the amino acid sequence of SEQ ID NO:341. In some examples, a fusion protein of the present disclosure comprises one or two polypeptides comprising the amino acid sequence of SEQ ID NO:342, a polypeptide comprising the amino acid sequence of SEQ ID NO:343, and a polypeptide comprising the amino acid sequence of SEQ ID NO:344. In some examples, a fusion protein of the present disclosure comprises one or two polypeptides comprising the amino acid sequence of SEQ ID NO:342, a polypeptide comprising the amino acid sequence of SEQ ID NO:343, and a polypeptide comprising the amino acid sequence of SEQ ID NO:345. In some examples, a fusion protein of the present disclosure comprises one or two polypeptides comprising the amino acid sequence of SEQ ID NO:346, a polypeptide comprising the amino acid sequence of SEQ ID NO:347, and a polypeptide comprising the amino acid sequence of SEQ ID NO:348. In some examples, a fusion protein of the present disclosure comprises one or two polypeptides comprising the amino acid sequence of SEQ ID NO:346, a polypeptide comprising the amino acid sequence of SEQ ID NO:347, and a polypeptide comprising the amino acid sequence of SEQ ID NO:349. In some examples, a fusion protein of the present disclosure comprises one or two polypeptides comprising the amino acid sequence of SEQ ID NO:350, a polypeptide comprising the amino acid sequence of SEQ ID NO:351, and a polypeptide comprising the amino acid sequence of SEQ ID NO:352. In some examples, a fusion protein of the present disclosure comprises one or two polypeptides comprising the amino acid sequence of SEQ ID NO:350, a polypeptide comprising the amino acid sequence of SEQ ID NO:351, and a polypeptide comprising the amino acid sequence of SEQ ID NO:353.

[0026] Further provided herein are fusion proteins, comprising a first moiety that binds to a human CD8b and a second moiety comprising an IL2 polypeptide, wherein the fusion protein comprises four polypeptide chains, wherein: (1) the first polypeptide chain comprises the amino acid sequence of SEQ ID NO:334, the second polypeptide chain comprises the amino acid sequence of SEQ ID NO:335, the third polypeptide chain comprises the amino acid sequence of SEQ ID NO:336, and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO:334; (2) the first polypeptide chain comprises the amino acid sequence of SEQ ID

NO:334, the second polypeptide chain comprises the amino acid sequence of SEQ ID NO:335, the third polypeptide chain comprises the amino acid sequence of SEQ ID NO:337, and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO:334; (3) the first polypeptide chain comprises the amino acid sequence of SEQ ID NO:338, the second polypeptide chain comprises the amino acid sequence of SEQ ID NO:339, the third polypeptide chain comprises the amino acid sequence of SEQ ID NO:340, and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO:338; or (4) the first polypeptide chain comprises the amino acid sequence of SEQ ID NO:338, the second polypeptide chain comprises the amino acid sequence of SEQ ID NO:339, the third polypeptide chain comprises the amino acid sequence of SEQ ID NO:341, and the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO:338.

[0027] Further provided herein are polynucleotides (*e.g.,* isolated polynucleotides) encoding the antibody or fusion protein according to any one of the above examples. Further provided herein are vectors (*e.g.*, expression vectors) comprising the polynucleotide(s) according to any one of the above examples. Further provided herein are host cells (*e.g.*, isolated host cells or cell lines) comprising the polynucleotide(s) or vector(s) according to any one of the above examples. Further provided herein are methods of producing an antibody or fusion protein, comprising culturing the host cell according to any one of the above examples under conditions suitable for production of the antibody or fusion protein. In some examples, the methods further comprise recovering the antibody or fusion protein from the host cell.

[0027a] In one aspect, the present disclosure refers to one or more polynucleotides encoding the antibody or fusion protein disclosed herein.

[0027b] In one aspect, the present disclosure refers to one or more vectors comprising the one or more polynucleotides disclosed herein.

[0027c] In one aspect, the present disclosure refers to an isolated host cell comprising the one or more polynucleotides or vectors disclosed herein.

[0027d] In one aspect, the present disclosure refers to a method of producing an antibody or fusion protein, comprising culturing the host cell disclosed herein under conditions suitable for production of the antibody or fusion protein.

[0028] Further provided herein are pharmaceutical compositions comprising the antibody or fusion protein according to any one of the above examples and a pharmaceutically acceptable carrier.

[0028a] In one aspect, the present disclosure refers to a pharmaceutical composition comprising the antibody or fusion protein disclosed herein and a pharmaceutically acceptable carrier.

[0029] Further provided herein is the use of the antibody, fusion protein, or composition according to any one of the above examples as a medicament. Further provided herein is the use of the antibody, fusion protein, or composition according to any one of the above examples in a method for treating cancer or infection (*e.g.*, chronic infection). Further provided herein is the use of the antibody, fusion protein, or composition according to any one of the above examples for the manufacture of a medicament for treating cancer or infection (*e.g.*, chronic infection). Further provided herein are methods of treating cancer comprising

administering to an individual with cancer an effective amount of the antibody, fusion protein, or composition according to any one of the above examples. In some examples, the methods further comprise administering to the individual a T cell therapy, cancer vaccine, chemotherapeutic agent, or immune checkpoint inhibitor (ICI). Further provided herein are methods of treating infection (*e.g.*, chronic infection) comprising administering to an individual with infection an effective amount of the antibody, fusion protein, or composition according to any one of the above examples. Further provided herein are methods of expanding T cells (*e.g.*, *ex vivo*) comprising contacting one or more T cells (*e.g.*, tumor infiltrating lymphocytes) *ex vivo* (*e.g.*, *ex vivo*) with an effective amount of the antibody, fusion protein, or composition according to any one of the above examples.

[0029a] In one aspect, the present disclosure refers to the antibody or fusion protein disclosed herein for use as a medicament.

[0029b] In one aspect, the present disclosure refers to a method of treating cancer comprising administering to an individual with cancer an effective amount of the antibody or fusion protein disclosed herein or the composition disclosed herein.

[0029c] In one aspect, the present disclosure refers to the antibody or fusion protein disclosed herein for use in a method of treating cancer, said method comprising administering to an individual with cancer an effective amount of the antibody or fusion protein.

[0029d] In one aspect, the present disclosure refers to a method of treating infection comprising administering to an individual in need thereof an effective amount of the antibody or fusion protein disclosed herein or the composition disclosed herein.

[0029e] In one aspect, the present disclosure refers to use of the antibody or fusion protein disclosed herein for the manufacture of a medicament for treating cancer or chronic infection.

[0029f] In one aspect, the present disclosure refers to a method of expanding T cells *ex vivo* comprising contacting one or more T cells *ex vivo* with an effective amount of the antibody or fusion protein disclosed herein or the composition disclosed herein.

[0030] It is to be understood that one, some, or all of the properties of the various examples described herein may be combined to form other examples of the present disclosure. These and other examples of the disclosure will become apparent to one of skill in the art. These and other examples of the disclosure are further described by the detailed description that follows.

BRIEF DESCRIPTION OF THE DRAWINGS

[0031] **FIGS. 1A-1C** depict the three types of CD8ab antibodies that could be identified according to their binding preference for CD8a, CD8b and CD8ab heterodimer. Antibodies binding CD8a epitopes are shown in **FIG. 1A**, antibodies binding epitopes that span both CD8a and CD8b are shown in **FIG. 1B**, and antibodies binding to CD8b epitopes are shown in **FIG. 1C**. Binding preference for CD8a, CD8b and CD8ab heterodimer by each antibody type is also depicted.

[0032] **FIGS. 2A-2C** show the results of an ELISA assay used to distinguish the three types of CD8ab antibodies depicted in **FIGS. 1A-1C**. Binding to recombinant CD8a (filled square), CD8b (filled triangle), CD8ab heterodimer (filled circle) and an irrelevant antigen, ovalbumin (open triangles) was measured. xhCD8a1 (clone OKT8) and xhCD8a2 antibodies (clone SK1) were previously described.

[0033] **FIGS. 3A-3C** depict the binding preferences on various CD8+ immune cell types by the three types of anti-CD8ab antibodies depicted in **FIGS. 2A-2C**. Antibodies with CD8a epitopes depicted in **FIG. 1A** bind to both CD8ab+ T cells and CD8aa+ NK cells as depicted in