

ANTIBODIES TARGETING A COMPLEX COMPRISING NON-CLASSICAL HLA-I AND NEOANTIGEN AND THEIR METHODS OF USE

RELATED APPLICATIONS

5 [0001] The present application claims priority to U.S. Patent Application No. 17/199,258, filed March 11, 2021, now pending, and U.S. Provisional Patent Application No. 63/032,886, filed June 1, 2020; now pending, the entire contents of each of which are hereby incorporated by reference for all purposes.

REFERENCE TO A SEQUENCE LISTING

10 [0001.1] This application contains a Sequence Listing in computer readable form. The computer readable form is incorporated herein by reference. Said ASCII copy, created on September 12, 2022, is named ABX-006WO_SL.txt and is 27,238 bytes in size.

SUMMARY

15 [0002] In one aspect, the present disclosure provides a monoclonal antibody or an antigen-binding fragment thereof, comprising (a) a light chain complementarity determining region (CDR)1 having the amino acid sequence set forth as SEQ ID NO: 1, a light chain CDR2 having the amino acid sequence set forth as SEQ ID NO: 2, and a light chain CDR3 having the amino acid sequence set forth as SEQ ID NO: 3; and (b) a heavy chain CDR1 having the amino acid sequence set forth as SEQ ID NO: 4, a heavy chain CDR2 having the amino acid sequence set forth as SEQ ID NO: 5, and a heavy chain CDR3 having the amino acid sequence set forth as SEQ ID NO: 6. In another aspect,
20 the present disclosure provides a monoclonal antibody or an antigen-binding fragment thereof, comprising: (a) a HC comprising an amino acid sequence at least 95% identical to the amino acid sequence set forth as SEQ ID NO: 21; and (b) a heavy chain CDR1 having the amino acid sequence set forth as SEQ ID NO: 4, a heavy chain CDR2 having the amino acid sequence set forth as SEQ ID NO: 5, and a heavy chain CDR3 having the amino acid sequence set forth as SEQ ID NO: 6. In yet
25 another aspect, the present disclosure provides a monoclonal antibody or an antigen-binding fragment thereof, comprising: (a) a HC comprising an amino acid sequence at least 95% identical to the amino acid sequence set forth as SEQ ID NO: 20; and (b) a heavy chain CDR1 having the amino acid sequence set forth as SEQ ID NO: 4, a heavy chain CDR2 having the amino acid sequence set forth as SEQ ID NO: 5, and a heavy chain CDR3 having the amino acid sequence set forth as SEQ
30 ID NO: 6.

[0002a] In yet another aspect, the present disclosure provides a bispecific T cell engager antibody, comprising (a) a first antigen-binding arm, comprising: (i) a light chain CDR1 having the amino acid sequence set forth as SEQ ID NO: 1, a light chain CDR2 having the amino acid sequence set forth as SEQ ID NO: 2, and a light chain CDR3 having the amino acid sequence set forth as SEQ ID NO: 3; and (ii) a heavy chain CDR1 having the amino acid sequence set forth as SEQ ID NO: 4, a heavy chain CDR2 having the amino acid sequence set forth as SEQ ID NO: 5, and a heavy chain CDR3 having the amino acid sequence set forth as SEQ ID NO: 6; and (b) a second antigen-binding arm that specifically binds to a CD3 protein associated with a T cell receptor (TCR). In yet another aspect, the present disclosure provides a pharmaceutical composition comprising the monoclonal antibody as described herein or an antigen-binding fragment thereof, or the bispecific T cell engager as described herein, and a pharmaceutically acceptable carrier or excipient. In yet another aspect, the present disclosure provides a pharmaceutical composition for use in treating a HLA-E expressing cancer, comprising the monoclonal antibody as described herein or an antigen-binding fragment thereof, or the bispecific T cell engager of any one as described herein, and a pharmaceutically acceptable carrier or excipient. In a further aspect, the present disclosure provides a use of a monoclonal antibody as described herein or an antigen-binding fragment thereof, or a bispecific T cell engager as described herein, in the preparation of a medicament for treating a HLA-E-expressing cancer in an individual in need thereof.

[0002b] Disclosed herein, in certain embodimentexamples, are monoclonal antibodies or an antigen-binding fragments thereof, comprising a light chain variable domain (VL) comprising an amino acid sequence at least 80% identical to an amino acid sequence set forth as SEQ ID NO: 7. Disclosed herein, in certain embodimentexamples, are monoclonal antibodies or antigen-binding fragments thereof, comprising a light chain variable domain (VL) comprising an amino acid sequence at least 90% identical to an amino acid sequence set forth as SEQ ID NO: 7. Disclosed herein, in certain embodimentexamples, are monoclonal antibodies or antigen-binding fragments thereof, comprising a light chain variable domain (VL) comprising an amino acid sequence at least 95% identical to an amino acid sequence set forth as SEQ ID NO: 7. Disclosed herein, in certain embodimentexamples, are monoclonal antibodies or antigen-binding fragments thereof, comprising a light chain variable domain (VL) comprising an amino acid sequence at least 99% identical to an amino acid sequence set forth as SEQ ID NO: 7. Disclosed herein, in certain embodimentexamples, are monoclonal antibodies or antigen-binding fragments thereof, comprising a light chain variable domain (VL) comprising an amino acid sequence 100% identical to an amino acid sequence set forth as SEQ ID NO: 7. In some embodimentexamples, the monoclonal antibodies or antigen-binding fragments thereof comprise a heavy chain variable domain (VH) comprising an amino acid sequence at least 80% identical to an amino acid sequence set forth as SEQ ID NO: 8. In some embodimentexamples, the monoclonal antibodies or antigen-binding fragments thereof

comprise a heavy chain variable domain (VH) comprising an amino acid sequence at least 90% identical to an amino acid sequence set forth as SEQ ID NO: 8. In some embodimentexamples, the monoclonal antibodies or antigen-binding fragments thereof comprise a heavy chain variable domain (VH) comprising an amino acid sequence at least 95% identical to an amino acid sequence set forth as

5 SEQ ID NO: 8. In some embodimentexamples, the monoclonal antibodies

or antigen-binding fragments thereof comprise a heavy chain variable domain (VH) comprising an amino acid sequence at least 99% identical to an amino acid sequence set forth as SEQ ID NO: 8. In some embodimentexamples, the monoclonal antibodies or antigen-binding fragments thereof comprise a heavy chain variable domain (VH) comprising an amino acid sequence 100% identical to an amino acid sequence set forth as SEQ ID NO: 8. In some embodimentexamples, the monoclonal antibodies or antigen-binding fragments thereof selectively bind to a complex comprising an HLA-E and a neoantigen. In some embodimentexamples, the monoclonal antibodies or antigen-binding fragments thereof do not have a binding affinity to the HLA-E alone. In some embodimentexamples, the monoclonal antibodies or antigen-binding fragments thereof do not have a binding affinity to the neoantigen alone. In some embodimentexamples, the neoantigen is expressed by an antigen processing machinery (APM)-proficient cell. In some embodimentexamples, the neoantigen is expressed by a TAP1/2-proficient cell. In some embodimentexamples, the neoantigen comprises, consists essentially of, or consists of a sequence according to SEQ ID NO: 18 (VMAPRTLFL). In some embodimentexamples, the HLA-E is HLA-E*0101 or HLA-E*0103. In some embodimentexamples, the antibodies selectively bind to the complex comprising: (a) the HLA-E*0101 and the neoantigen; (b) the HLA-E*0103 and the neoantigen; or (c) the HLA-E*0101 and the neoantigen, and the HLA-E*0103 and the neoantigen. In some embodimentexamples, the monoclonal antibodies or antigen-binding fragments thereof are murine antibodies, chimeric antibodies, camelid antibodies, humanized antibodies, or human antibodies. In some embodimentexamples, the monoclonal antibodies or antigen-binding fragments thereof are TCR-like antibodies. In some embodimentexamples, the monoclonal antibodies or antigen-binding fragments thereof are multispecific antibodies. In some embodimentexamples, the monoclonal antibodies or antigen-binding fragments thereof are bispecific antibodies. In some embodimentexamples, the monoclonal antibodies or antigen-binding fragments thereof are bispecific T cell engagers (BiTE). In some embodimentexamples, the BiTE binds to a CD3 protein associated with a T cell receptor (TCR). In some embodimentexamples, the BiTE further comprises a light chain variable domain (VL) comprising an amino acid sequence at least 80% identical to an amino acid sequence set forth as SEQ ID NO: 15. In some embodimentexamples, the BiTE further comprises a heavy chain variable domain (VH) comprising an amino acid sequence at least 80% identical to an amino acid sequence set forth as SEQ ID NO: 16. In some embodimentexamples, the monoclonal antibodies or antigen-binding fragments thereof are multifunctional antibodies. In some embodimentexamples, the monoclonal antibodies or antigen-binding fragments thereof antibody further comprise a conjugated therapeutic moiety. In some embodimentexamples, the selective binding of the antibodies to the complex comprising the HLA-E and the neoantigen induces an immune response in

a cell. In some [embodimentexamples](#), the immune response comprises activation of (i) NK cells, (ii) T cells, or (iii) NK cells and T cells. In some [embodimentexamples](#), the T cell is a CD4+ T cell or a CD8+ T cell. In some [embodimentexamples](#), the immune response comprises activation of cytotoxic T cells (CTLs). In some [embodimentexamples](#), the cell is a cancer cell.

5 **[0003]** Disclosed herein, in certain [embodimentexamples](#), are monoclonal antibodies or antigen-binding fragments thereof, comprising a heavy chain variable domain (VH) comprising an amino acid sequence at least 80% identical to an amino acid sequence set forth as SEQ ID NO: 8. Disclosed herein, in certain [embodimentexamples](#), are monoclonal antibodies or antigen-binding fragments thereof, comprising a heavy chain variable domain (VH) comprising an amino acid sequence at least 90% identical to an amino acid sequence set forth as SEQ ID NO: 8. Disclosed herein, in certain [embodimentexamples](#), are monoclonal antibodies or antigen-binding fragments thereof, comprising a heavy chain variable domain (VH) comprising an amino acid sequence at least 95% identical to an amino acid sequence set forth as SEQ ID NO: 8. Disclosed herein, in certain [embodimentexamples](#), are monoclonal antibodies or antigen-binding fragments thereof, comprising a heavy chain variable domain (VH) comprising an amino acid sequence at least 99% identical to an amino acid sequence set forth as SEQ ID NO: 8. Disclosed herein, in certain [embodimentexamples](#), are monoclonal antibodies or antigen-binding fragments thereof, comprising a heavy chain variable domain (VH) comprising an amino acid sequence 100% identical to an amino acid sequence set forth as SEQ ID NO: 8. In some [embodimentexamples](#), the monoclonal antibodies or antigen-binding fragments thereof comprise a light chain variable domain (VL) comprising an amino acid sequence at least 80% identical to an amino acid sequence set forth as SEQ ID NO: 7. In some [embodimentexamples](#), the monoclonal antibodies or antigen-binding fragments thereof comprise a light chain variable domain (VL) comprising an amino acid sequence at least 90% identical to an amino acid sequence set forth as SEQ ID NO: 7. In some [embodimentexamples](#), the monoclonal antibodies or antigen-binding fragments thereof comprise a light chain variable domain (VL) comprising an amino acid sequence at least 95% identical to an amino acid sequence set forth as SEQ ID NO: 7. In some [embodimentexamples](#), the monoclonal antibodies or antigen-binding fragments thereof comprise a light chain variable domain (VL) comprising an amino acid sequence at least 99% identical to an amino acid sequence set forth as SEQ ID NO: 7. In some [embodimentexamples](#), the monoclonal antibodies or antigen-binding fragments thereof comprise a light chain variable domain (VL) comprising an amino acid sequence 100% identical to an amino acid sequence set forth as SEQ ID NO: 7. In some [embodimentexamples](#), the monoclonal antibodies or antigen-binding fragments thereof selectively binds to a complex comprising an HLA-E and a neoantigen. In

some [embodimentexamples](#), the monoclonal antibodies or antigen-binding fragments thereof do not have a binding affinity to the HLA-E alone. In some [embodimentexamples](#), the monoclonal antibodies or antigen-binding fragments thereof do not have a binding affinity to the neoantigen alone. In some [embodimentexamples](#), the neoantigen is expressed by an antigen processing machinery (APM)-proficient cell. In some [embodimentexamples](#), the neoantigen is expressed by a TAP1/2-proficient cell. In some [embodimentexamples](#), the neoantigen comprises, consists essentially of, or consists of a sequence according to SEQ ID NO: 18 (VMAPRTLFL). In some [embodimentexamples](#), the HLA-E is HLA-E*0101 or HLA-E*0103. In some [embodimentexamples](#), the antibodies selectively binds to the complex comprising: (a) the HLA-E*0101 and the neoantigen; (b) the HLA-E*0103 and the neoantigen; or (c) the HLA-E*0101 and the neoantigen, and the HLA-E*0103 and the neoantigen. In some [embodimentexamples](#), the monoclonal antibodies or antigen-binding fragments thereof are murine antibodies, chimeric antibodies, camelid antibodies, humanized antibodies, or human antibodies. In some [embodimentexamples](#), the monoclonal antibodies or antigen-binding fragments thereof are TCR-like antibodies. In some [embodimentexamples](#), the monoclonal antibodies or antigen-binding fragments thereof are multispecific antibodies. In some [embodimentexamples](#), the monoclonal antibodies or antigen-binding fragments thereof are bispecific antibodies. In some [embodimentexamples](#), the monoclonal antibodies or antigen-binding fragments thereof are bispecific T cell engagers (BiTE). In some [embodimentexamples](#), the BiTE binds to a CD3 protein associated with a T cell receptor (TCR). In some [embodimentexamples](#), the BiTE further comprises a light chain variable domain (VL) comprising an amino acid sequence at least 80% identical to an amino acid sequence set forth as SEQ ID NO: 15. In some [embodimentexamples](#), the BiTE further comprises a heavy chain variable domain (VH) comprising an amino acid sequence at least 80% identical to an amino acid sequence set forth as SEQ ID NO: 16. In some [embodimentexamples](#), the monoclonal antibodies or antigen-binding fragments thereof are multifunctional antibodies. In some [embodimentexamples](#), the monoclonal antibodies or antigen-binding fragments thereof antibody further comprise a conjugated therapeutic moiety. In some [embodimentexamples](#), the selective binding of the antibody to the complex comprising the HLA-E and the neoantigen induces an immune response in a cell. In some [embodimentexamples](#), the immune response comprises activation of (i) NK cells, (ii) T cells, or (iii) NK cells and T cells. In some [embodimentexamples](#), the T cell is a CD4+ T cell or a CD8+ T cell. In some [embodimentexamples](#), the immune response comprises activation of cytotoxic T cells (CTLs). In some [embodimentexamples](#), the cell is a cancer cell.

[0004] Disclosed herein, in certain [embodimentexamples](#), are monoclonal antibodies or antigen-binding fragments thereof, comprising a light chain complementarity determining region (CDR) having an

amino acid sequence at least 80% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 1-3. Disclosed herein, in certain embodimentexamples, are monoclonal antibodies or antigen-binding fragments thereof, comprising a light chain complementarity determining region (CDR) having an amino acid sequence at least 90% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 1-3. Disclosed herein, in certain embodimentexamples, are monoclonal antibodies or antigen-binding fragments thereof, comprising a light chain complementarity determining region (CDR) having an amino acid sequence at least 95% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 1-3. Disclosed herein, in certain embodimentexamples, are monoclonal antibodies or antigen-binding fragments thereof, comprising a light chain complementarity determining region (CDR) having an amino acid sequence at least 99% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 1-3. Disclosed herein, in certain embodimentexamples, are monoclonal antibodies or antigen-binding fragments thereof, comprising a light chain complementarity determining region (CDR) having an amino acid sequence 100% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 1-3.

In some embodimentexamples, the monoclonal antibodies or antigen-binding fragments thereof comprise a heavy chain complementarity determining region (CDR) having an amino acid sequence at least 80% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 4-6. In some embodimentexamples, the monoclonal antibodies or antigen-binding fragments thereof comprise a heavy chain complementarity determining region (CDR) having an amino acid sequence at least 90% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 4-6. In some embodimentexamples, the monoclonal antibodies or antigen-binding fragments thereof comprise a heavy chain complementarity determining region (CDR) having an amino acid sequence at least 95% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 4-6. In some embodimentexamples, the monoclonal antibodies or antigen-binding fragments thereof comprise a heavy chain complementarity determining region (CDR) having an amino acid sequence at least 99% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 4-6. In some embodimentexamples, the monoclonal antibodies or antigen-binding fragments thereof comprise a heavy chain complementarity determining region (CDR) having an amino acid sequence 100% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 4-6. In some embodimentexamples, the monoclonal antibodies or antigen-binding fragments thereof comprise a light chain variable domain (VL) comprising an amino acid sequence at least 80% identical to an amino acid sequence set forth as SEQ ID NO: 7. In some embodimentexamples, the monoclonal antibodies or antigen-binding fragments

thereof comprise a heavy chain variable domain (VH) comprising an amino acid sequence at least 80% identical to an amino acid sequence set forth as SEQ ID NO: 8. In some [embodimentexamples](#), the monoclonal antibodies or antigen-binding fragments thereof selectively binds to a complex comprising an HLA-E and a neoantigen. In some [embodimentexamples](#), the monoclonal antibodies or antigen-binding fragments thereof do not have a binding affinity to the HLA-E alone. In some [embodimentexamples](#), the monoclonal antibodies or antigen-binding fragments thereof do not have a binding affinity to the neoantigen alone. In some [embodimentexamples](#), the neoantigen is expressed by an antigen processing machinery (APM)-proficient cell. In some [embodimentexamples](#), the neoantigen is expressed by a TAP1/2-proficient cell. In some [embodimentexamples](#), the neoantigen comprises, consists essentially of, or consists of a sequence according to SEQ ID NO: 18 (VMAPRTLFL). In some [embodimentexamples](#), the HLA-E is HLA-E*0101 or HLA-E*0103. In some [embodimentexamples](#), the antibodies selectively binds to the complex comprising: the HLA-E*0101 and the neoantigen; the HLA-E*0103 and the neoantigen; or the HLA-E*0101 and the neoantigen, and the HLA-E*0103 and the neoantigen. In some [embodimentexamples](#), the monoclonal antibodies or antigen-binding fragments thereof are murine antibodies, chimeric antibodies, camelid antibodies, humanized antibodies, or human antibodies. In some [embodimentexamples](#), the monoclonal antibodies or antigen-binding fragments thereof are TCR-like antibodies. In some [embodimentexamples](#), the monoclonal antibodies or antigen-binding fragments thereof are multispecific antibodies. In some [embodimentexamples](#), the monoclonal antibodies or antigen-binding fragments thereof are bispecific antibodies. In some [embodimentexamples](#), the monoclonal antibodies or antigen-binding fragments thereof are bispecific T cell engagers (BiTE). In some [embodimentexamples](#), the BiTE binds to a CD3 protein associated with a T cell receptor (TCR). In some [embodimentexamples](#), the BiTE further comprises a light chain complementarity determining region (CDR) having an amino acid sequence at least 80% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 9-11. In some [embodimentexamples](#), the BiTE further comprises a heavy chain complementarity determining region (CDR) having an amino acid sequence at least 80% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 12-14. In some [embodimentexamples](#), the BiTE further comprises a light chain variable domain (VL) comprising an amino acid sequence at least 80% identical to an amino acid sequence set forth as SEQ ID NO: 15. In some [embodimentexamples](#), the BiTE further comprises a heavy chain variable domain (VH) comprising an amino acid sequence at least 80% identical to an amino acid sequence set forth as SEQ ID NO: 16. In some [embodimentexamples](#), the monoclonal antibodies or antigen-binding fragments thereof are multifunctional antibodies. In some [embodimentexamples](#), the monoclonal antibodies or antigen-binding fragments thereof antibody further

comprise a conjugated therapeutic moiety. In some [embodimentexamples](#), the selective binding of the antibody to the complex comprising the HLA-E and the neoantigen induces an immune response in a cell. In some [embodimentexamples](#), the immune response comprises activation of (i) NK cells, (ii) T cells, or (iii) NK cells and T cells. In some [embodimentexamples](#), the T cell is a CD4+ T cell or a CD8+ T cell. In some [embodimentexamples](#), the immune response comprises activation of cytotoxic T cells (CTLs). In some [embodimentexamples](#), the cell is a cancer cell.

[0005] Disclosed herein, in certain [embodimentexamples](#), are monoclonal antibodies or antigen-binding fragments thereof, comprising a heavy chain complementarity determining region (CDR) having an amino acid sequence at least 80% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 4-6. Disclosed herein, in certain [embodimentexamples](#), are monoclonal antibodies or antigen-binding fragments thereof, comprising a heavy chain complementarity determining region (CDR) having an amino acid sequence at least 90% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 4-6. Disclosed herein, in certain [embodimentexamples](#), are monoclonal antibodies or antigen-binding fragments thereof, comprising a heavy chain complementarity determining region (CDR) having an amino acid sequence at least 95% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 4-6. Disclosed herein, in certain [embodimentexamples](#), are monoclonal antibodies or antigen-binding fragments thereof, comprising a heavy chain complementarity determining region (CDR) having an amino acid sequence at least 99% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 4-6. Disclosed herein, in certain [embodimentexamples](#), are monoclonal antibodies or antigen-binding fragments thereof, comprising a heavy chain complementarity determining region (CDR) having an amino acid sequence 100% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 4-6. In some [embodimentexamples](#), the monoclonal antibody or antigen-binding fragment comprises a light chain complementarity determining region (CDR) having an amino acid sequence at least 80% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 1-3. In some [embodimentexamples](#), the monoclonal antibody or antigen-binding fragment comprises a light chain complementarity determining region (CDR) having an amino acid sequence at least 90% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 1-3. In some [embodimentexamples](#), the monoclonal antibody or antigen-binding fragment comprises a light chain complementarity determining region (CDR) having an amino acid sequence at least 95% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 1-3. In some [embodimentexamples](#), the monoclonal antibody or antigen-binding fragment comprises a light chain complementarity determining region (CDR) having an amino acid

sequence at least 99% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 1-3.

In some embodimentexamples, the monoclonal antibody or antigen-binding fragment comprises a light chain complementarity determining region (CDR) having an amino acid sequence 100% identical to at

least one of the amino acid sequences set forth as SEQ ID NOS: 1-3. In some embodimentexamples, the

monoclonal antibodies or antigen-binding fragments thereof comprise a heavy chain variable domain (VH) comprising an amino acid sequence at least 80% identical to an amino acid sequence set forth as

SEQ ID NO: 8. In some embodimentexamples, the monoclonal antibodies or antigen-binding fragments thereof comprise a light chain variable domain (VL) comprising an amino acid sequence at least 80%

identical to an amino acid sequence set forth as SEQ ID NO: 7. In some embodimentexamples, the

monoclonal antibodies or antigen-binding fragments thereof selectively binds to a complex comprising an HLA-E and a neoantigen. In some embodimentexamples, the monoclonal antibodies or antigen-

binding fragments thereof do not have a binding affinity to the HLA-E alone. In some

embodimentexamples, the monoclonal antibodies or antigen-binding fragments thereof do not have a binding affinity to the neoantigen alone. In some embodimentexamples, the neoantigen is expressed by

an antigen processing machinery (APM)-proficient cell. In some embodimentexamples, the neoantigen is expressed by a TAP1/2-proficient cell. In some embodimentexamples, the neoantigen comprises,

consists essentially of, or consists of a sequence according to SEQ ID NO: 18 (VMAPRTLFL). In some

embodimentexamples, the HLA-E is HLA-E*0101 or HLA-E*0103. In some embodimentexamples, the antibodies selectively bind to the complex comprising: (a) the HLA-E*0101 and the neoantigen; (b) the

HLA-E*0103 and the neoantigen; or (c) the HLA-E*0101 and the neoantigen, and the HLA-E*0103 and the neoantigen. In some embodimentexamples, the monoclonal antibodies or antigen-binding fragments

thereof are murine antibodies, chimeric antibodies, camelid antibodies, humanized antibodies, or human antibodies. In some embodimentexamples, the monoclonal antibodies or antigen-binding fragments

thereof are TCR-like antibodies. In some embodimentexamples, the monoclonal antibodies or antigen-

binding fragments thereof are multispecific antibodies. In some embodimentexamples, the monoclonal

antibodies or antigen-binding fragments thereof are bispecific antibodies. In some embodimentexamples,

the monoclonal antibodies or antigen-binding fragments thereof are bispecific T cell engagers (BiTE). In

some embodimentexamples, the BiTE binds to a CD3 protein associated with a T cell receptor (TCR). In

some embodimentexamples, the BiTE further comprises a light chain complementarity determining

region (CDR) having an amino acid sequence at least 80% identical to at least one of the amino acid

sequences set forth as SEQ ID NOS: 9-11. In some embodimentexamples, the BiTE further comprises a

heavy chain complementarity determining region (CDR) having an amino acid sequence at least 80% identical to at least one of

the amino acid sequences set forth as SEQ ID NOS: 12-14. In some embodimentexamples, the BiTE further comprises a light chain variable domain (VL) comprising an amino acid sequence at least 80% identical to an amino acid sequence set forth as SEQ ID NO: 15. In some embodimentexamples, the BiTE further comprises a heavy chain variable domain (VH) comprising an amino acid sequence at least 80% identical to an amino acid sequence set forth as SEQ ID NO: 16. In some embodimentexamples, the monoclonal antibodies or antigen-binding fragments thereof are multifunctional antibodies. In some embodimentexamples, the monoclonal antibodies or antigen-binding fragments thereof antibody further comprise a conjugated therapeutic moiety. In some embodimentexamples, the selective binding of the antibody to the complex comprising the HLA-E and the neoantigen induces an immune response in a cell. In some embodimentexamples, the immune response comprises activation of (i) NK cells, (ii) T cells, or (iii) NK cells and T cells. In some embodimentexamples, the cell is a CD4⁺ T cell or a CD8⁺ T cell. In some embodimentexamples, the immune response comprises activation of cytotoxic T cells (CTLs). In some embodimentexamples, the cell is a cancer cell.

[0006] Disclosed herein, in certain embodimentexamples, are bispecific antibodies or an antigen-binding fragment thereof, comprising: a light chain complementarity determining region (CDR) having an amino acid sequence at least 80% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 1-3; or a heavy chain complementarity determining region (CDR) having an amino acid sequence at least 80% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 4-6; and a light chain complementarity determining region (CDR) having an amino acid sequence at least 80% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 9-11; or a heavy chain complementarity determining region (CDR) having an amino acid sequence at least 80% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 12-14. In some embodimentexamples, the bispecific antibodies comprise: (a) a light chain variable domain (VL) comprising an amino acid sequence at least 80% identical to an amino acid sequence set forth as SEQ ID NO: 7; or a heavy chain variable domain (VH) comprising an amino acid sequence at least 80% identical to an amino acid sequence set forth as SEQ ID NO: 8; and (b) a light chain variable domain (VL) comprising an amino acid sequence at least 80% identical to an amino acid sequence set forth as SEQ ID NO: 15; or a heavy chain variable domain (VH) comprising an amino acid sequence at least 80% identical to an amino acid sequence set forth as SEQ ID NO: 16. Disclosed herein, in certain embodimentexamples, are bispecific antibodies or an antigen-binding fragment thereof, comprising: a light chain complementarity determining region (CDR) having an amino acid sequence at least 80% identical to at least one of the amino acid sequences set forth as SEQ ID NOS:

1-3; and a heavy chain complementarity determining region (CDR) having an amino acid sequence at least 80% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 4-6; and a light chain complementarity determining region (CDR) having an amino acid sequence at least 80% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 9-11; and a heavy chain complementarity determining region (CDR) having an amino acid sequence at least 80% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 12-14. In some

embodimentexamples, the bispecific antibodies comprise: (a) a light chain variable domain (VL) comprising an amino acid sequence at least 80% identical to an amino acid sequence set forth as SEQ ID NO: 7; and a heavy chain variable domain (VH) comprising an amino acid sequence at least 80% identical to an amino acid sequence set forth as SEQ ID NO: 8; and (b) a light chain variable domain (VL) comprising an amino acid sequence at least 80% identical to an amino acid sequence set forth as SEQ ID NO: 15; and a heavy chain variable domain (VH) comprising an amino acid sequence at least 80% identical to an amino acid sequence set forth as SEQ ID NO: 16. In some embodimentexamples, the bispecific antibodies selectively bind to a complex comprising an HLA-E and a neoantigen. In some embodimentexamples, the bispecific antibodies do not have a binding affinity to the HLA-E alone. In some embodimentexamples, the bispecific antibodies do not have a binding affinity to the neoantigen alone. In some embodimentexamples, the neoantigen is expressed by an antigen processing machinery (APM)-proficient cell. In some embodimentexamples, the neoantigen is expressed by a TAP1/2-proficient cell. In some embodimentexamples, the neoantigen comprises, consists essentially of, or consists of a sequence according to SEQ ID NO: 18 (VMAPRTLFL). In some embodimentexamples, the HLA-E is HLA-E*0101 or HLA-E*0103. In some embodimentexamples, the antibodies selectively binds to the complex comprising: the HLA-E*0101 and the neoantigen; the HLA-E*0103 and the neoantigen; or the HLA-E*0101 and the neoantigen, and the HLA-E*0103 and the neoantigen. In some embodimentexamples, the monoclonal antibodies or antigen-binding fragments thereof are murine antibodies, chimeric antibodies, camelid antibodies, humanized antibodies, or human antibodies. In some embodimentexamples, the monoclonal antibodies or antigen-binding fragments thereof are bispecific T cell engagers (BiTE). In some embodimentexamples, the BiTE binds to a CD3 protein associated with a T cell receptor (TCR). In some embodimentexamples, the monoclonal antibodies or antigen-binding fragments thereof are multifunctional antibodies. In some embodimentexamples, the monoclonal antibodies or antigen-binding fragments thereof antibody further comprise a conjugated therapeutic moiety. In some embodimentexamples, the selective binding of the antibody to the complex comprising the HLA-E and the neoantigen induces an immune response in a cell. In some embodimentexamples, the immune response comprises activation of (i)

NK cells, (ii) T cells, or (iii) NK cells and T cells. In some embodimentexamples, the T cell is a CD4+ T cell or a CD8+ T cell. In some embodimentexamples, the immune response comprises activation of cytotoxic T cells (CTLs). In some embodimentexamples, the cell is a cancer cell.

[0007] Disclosed herein, in certain embodimentexamples, are pharmaceutical compositions

5 comprising: (a) a monoclonal antibody or an antigen-binding fragment thereof disclosed herein or a bispecific antibody or an antigen-binding fragment thereof disclosed herein; and (b) a pharmaceutically acceptable carrier or excipient.

[0008] Disclosed herein, in certain embodimentexamples, are methods of treating cancer in an individual in need thereof, comprising administering to the individual an effective amount of a

10 monoclonal antibody or an antigen-binding fragment thereof comprising a light chain complementarity determining region (CDR) having an amino acid sequence at least 80% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 1-3. Disclosed herein, in certain

embodimentexamples, are methods of treating cancer in an individual in need thereof, comprising administering to the individual an effective amount of a monoclonal antibody or an antigen-binding

15 fragment thereof comprising a heavy chain complementarity determining region (CDR) having an amino acid sequence at least 80% identical to at least one of the amino acid sequences set forth as

SEQ ID NOS: 4-6. In some embodimentexamples, the monoclonal antibodies or antigen-binding fragments thereof comprise (a) a light chain complementarity determining region (CDR) having an

20 amino acid sequence at least 80% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 1-3; and (b) a heavy chain complementarity determining region (CDR) having an

amino acid sequence at least 80% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 4-6. In some embodimentexamples, the monoclonal antibodies or antigen-binding

fragments thereof comprise (a) a light chain complementarity determining region (CDR) having an amino acid sequence at least 90% identical to at least one of the amino acid sequences set forth as

25 SEQ ID NOS: 1-3; and (b) a heavy chain complementarity determining region (CDR) having an amino acid sequence at least 90% identical to at least one of the amino acid sequences set forth as

SEQ ID NOS: 4-6. In some embodimentexamples, the monoclonal antibodies or antigen-binding fragments thereof comprise (a) a light chain complementarity determining region (CDR) having an

30 amino acid sequence at least 95% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 1-3; and (b) a heavy chain complementarity determining region (CDR) having an

amino acid sequence at least 95% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 4-6. In some embodimentexamples, the monoclonal antibodies or antigen-binding

fragments thereof

comprise (a) a light chain complementarity determining region (CDR) having an amino acid sequence at least 99% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 1-3; and (b) a heavy chain complementarity determining region (CDR) having an amino acid sequence at least 99% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 4-6. In some

5 embodimentexamples, the monoclonal antibodies or antigen-binding fragments thereof comprise (a) a light chain complementarity determining region (CDR) having an amino acid sequence 100% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 1-3; and (b) a heavy chain complementarity determining region (CDR) having an amino acid sequence 100% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 4-6. In some embodimentexamples, the

10 monoclonal antibodies or antigen-binding fragments thereof comprise a light chain variable domain (VL) comprising an amino acid sequence at least 80% identical to an amino acid sequence set forth as SEQ ID NO: 7. In some embodimentexamples, the monoclonal antibodies or antigen-binding fragments thereof comprise a heavy chain variable domain (VH) comprising an amino acid sequence at least 80% identical to an amino acid sequence set forth as SEQ ID NO: 8. In some embodimentexamples, the monoclonal

15 antibodies or antigen-binding fragments thereof selectively binds to a complex comprising an HLA-E and a neoantigen. In some embodimentexamples, the monoclonal antibodies or antigen-binding fragments thereof do not have a binding affinity to the HLA-E alone. In some embodimentexamples, the monoclonal antibodies or antigen-binding fragments thereof do not have a binding affinity to the neoantigen alone. In some embodimentexamples, the neoantigen is expressed by an antigen processing

20 machinery (APM)-proficient cell. In some embodimentexample, the neoantigen is expressed by a TAP1/2-proficient cell. In some embodimentexamples, the neoantigen comprises, consists essentially of, or consists of a sequence according to SEQ ID NO: 18 (VMAPRTLFL). In some embodimentexamples, the HLA-E is HLA-E*0101 or HLA-E*0103. In some embodimentexamples, the antibodies selectively binds to the complex comprising: the HLA-E*0101 and the neoantigen; the HLA-E*0103 and the

25 neoantigen; or the HLA-E*0101 and the neoantigen, and the HLA-E*0103 and the neoantigen. In some embodimentexamples, the monoclonal antibodies or antigen-binding fragments thereof are murine antibodies, chimeric antibodies, camelid antibodies, humanized antibodies, or human antibodies. In some embodimentexamples, the monoclonal antibodies or antigen-binding fragments thereof are TCR-like antibodies. In some embodimentexamples, the monoclonal antibodies or antigen-binding fragments

30 thereof are multispecific antibodies. In some embodimentexamples, the monoclonal antibodies or antigen-binding fragments thereof are bispecific antibodies. In some embodimentexamples, the monoclonal antibodies or antigen-binding fragments thereof are bispecific T cell engagers (BiTE). In some

embodimentexamples, the BiTE binds to a CD3 protein associated with a T cell receptor (TCR). In some embodimentexamples, the BiTE further comprises a light chain complementarity determining region (CDR) having an amino acid sequence at least 80% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 9-11. In some embodimentexamples, the BiTE further comprises a heavy chain complementarity determining region (CDR) having an amino acid sequence at least 80% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 12-14. In some embodimentexamples, the BiTE further comprises a light chain variable domain (VL) comprising an amino acid sequence at least 80% identical to an amino acid sequence set forth as SEQ ID NO: 15. In some embodimentexamples, the BiTE further comprises a heavy chain variable domain (VH) comprising an amino acid sequence at least 80% identical to an amino acid sequence set forth as SEQ ID NO: 16. In some embodimentexamples, the monoclonal antibodies or antigen-binding fragments thereof are multifunctional antibodies. In some embodimentexamples, the monoclonal antibodies or antigen-binding fragments thereof antibody further comprise a conjugated therapeutic moiety. In some embodimentexamples, the selective binding of the antibody to the complex comprising the HLA-E and the neoantigen induces an immune response in a cell. In some embodimentexamples, the immune response comprises activation of (i) NK cells, (ii) T cells, or (iii) NK cells and T cells. In some embodimentexamples, the T cell is a CD4+ T cell or a CD8+ T cell. In some embodimentexamples, the immune response comprises activation of cytotoxic T cells (CTLs). In some embodimentexamples, the cancer is breast cancer, kidney cancer, lung cancer, ovarian cancer, colorectal cancer, pancreatic cancer, choriocarcinoma, non-small cell lung carcinoma (NSCLC), gastric cancer, cervical cancer, or head and neck cancer. In some embodimentexamples, the cancer is a myeloma, leukemia or lymphoma. In some embodimentexamples, the cancer is acute myeloid leukemia (AML), multiple myeloma, or a myelodysplastic syndrome. In some embodimentexamples, the cancer is a B cell malignancy. In some embodimentexamples, the cancer is mantle cell lymphoma.

[0009] Disclosed herein, in certain embodimentexamples, are methods of treating cancer in an individual in need thereof, comprising administering to the individual an effective amount of a bispecific antibody or an antigen-binding fragment thereof, comprising: a light chain complementarity determining region (CDR) having an amino acid sequence at least 80% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 1-3; or a heavy chain complementarity determining region (CDR) having an amino acid sequence at least 80% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 4-6; and a light chain complementarity determining region (CDR) having an amino acid sequence at least 80% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 9-11; or a heavy chain complementarity determining region

(CDR) having an amino acid sequence at least 80% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 12-14. In some embodimentexamples, the bispecific antibodies comprise: a light chain variable domain (VL) comprising an amino acid sequence at least 80% identical to an amino acid sequence set forth as SEQ ID NO: 7; or a heavy chain variable domain (VH) comprising an amino acid sequence at least 80% identical to an amino acid sequence set forth as SEQ ID NO: 8; and a light chain variable domain (VL) comprising an amino acid sequence at least 80% identical to an amino acid sequence set forth as SEQ ID NO: 15; or a heavy chain variable domain (VH) comprising an amino acid sequence at least 80% identical to an amino acid sequence set forth as SEQ ID NO: 16. Disclosed herein, in certain embodimentexamples, are methods of treating cancer in an individual in need thereof, comprising administering to the individual an effective amount of a bispecific antibody or an antigen-binding fragment thereof, comprising: a light chain complementarity determining region (CDR) having an amino acid sequence at least 80% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 1-3; and a heavy chain complementarity determining region (CDR) having an amino acid sequence at least 80% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 4-6; and a light chain complementarity determining region (CDR) having an amino acid sequence at least 80% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 9-11; and a heavy chain complementarity determining region (CDR) having an amino acid sequence at least 80% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 12-14. In some embodimentexamples, the bispecific antibodies comprise: a light chain variable domain (VL) comprising an amino acid sequence at least 80% identical to an amino acid sequence set forth as SEQ ID NO: 7; and a heavy chain variable domain (VH) comprising an amino acid sequence at least 80% identical to an amino acid sequence set forth as SEQ ID NO: 8; and a light chain variable domain (VL) comprising an amino acid sequence at least 80% identical to an amino acid sequence set forth as SEQ ID NO: 15; and a heavy chain variable domain (VH) comprising an amino acid sequence at least 80% identical to an amino acid sequence set forth as SEQ ID NO: 16. In some embodimentexample, the bispecific antibody or antigen-binding fragment thereof selectively binds to a complex comprising an HLA-E and a neoantigen. In some embodimentexamples, the bispecific antibody or antigen-binding fragment thereof does not have a binding affinity to the HLA-E alone. In some embodimentexamples, the bispecific antibody or antigen-binding fragment thereof does not have a binding affinity to the neoantigen alone. In some embodimentexamples, the neoantigen is expressed by an antigen processing machinery (APM)-proficient cell. In some embodimentexample, the neoantigen is expressed by a TAP1/2-proficient cell. In

some embodimentexamples, the neoantigen comprises, consists essentially of, or consists of a sequence according to SEQ ID NO: 18 (VMAPRTLFL). In some embodimentexamples, the HLA-E is HLA-E*0101 or HLA-E*0103. In some embodimentexamples, the bispecific antibodies selectively bind to the complex comprising: the HLA-E*0101 and the neoantigen; the HLA-E*0103 and the neoantigen; or the HLA-E*0101 and the neoantigen, and the HLA-E*0103 and the neoantigen. In some embodimentexamples, the bispecific antibody or antigen-binding fragment thereof is a murine antibody, a chimeric antibody, a camelid antibody, a humanized antibody, or a human antibody. In some embodimentexamples, the bispecific antibody or antigen-binding fragment thereof is a TCR-like antibody. In some embodimentexamples, the bispecific antibody or antigen-binding fragment thereof is a bispecific T cell engager (BiTE). In some embodimentexamples, the BiTE binds to a CD3 protein associated with a T cell receptor (TCR). In some embodimentexamples, the bispecific antibody or antigen-binding fragment thereof is a multifunctional antibody. In some embodimentexamples, the bispecific antibody or antigen-binding fragment thereof antibody further comprise a conjugated therapeutic moiety. In some embodimentexamples, the selective binding of the antibody to the complex comprising the HLA-E and the neoantigen induces an immune response in a cell. In some embodimentexamples, the immune response comprises activation of (i) NK cells, (ii) T cells, or (iii) NK cells and T cells. In some embodimentexamples, the T cell is a CD4⁺ T cell or a CD8⁺ T cell. In some embodimentexamples, the immune response comprises activation of cytotoxic T cells (CTLs). In some embodimentexamples, the bispecific antibody is administered at a therapeutically effective amount. In some embodimentexamples, the cancer is breast cancer, kidney cancer, lung cancer, ovarian cancer, colorectal cancer, pancreatic cancer, choriocarcinoma, non-small cell lung carcinoma (NSCLC), gastric cancer, cervical cancer, or head and neck cancer. In some embodimentexamples, the cancer is a myeloima, leukemia or lymphoma. In some embodimentexamples, the cancer is acute myeloid leukemia (AML), multiple myeloma, or a myelodysplastic syndrome. In some embodimentexamples, the cancer is a B cell malignancy. In some embodimentexamples, the cancer is mantel cell lymphoma.

[0010] Disclosed herein, in certain embodimentexamples, are monoclonal antibodies or an antigen-binding fragments thereof, comprising a light chain (LC) comprising an amino acid sequence at least 80% identical to an amino acid sequence set forth as SEQ ID NO: 19. Disclosed herein, in certain embodimentexamples, are monoclonal antibodies or antigen-binding fragments thereof, comprising a light chain (LC) comprising an amino acid sequence at least 90% identical to an amino acid sequence set forth as SEQ ID NO: 19. Disclosed herein, in certain embodimentexamples, are monoclonal antibodies or antigen-binding fragments thereof, comprising a light chain (LC) comprising an amino acid

sequence at least 95% identical to an amino acid sequence set forth as SEQ ID NO: 19. Disclosed herein, in certain embodimentexamples, are monoclonal antibodies or antigen-binding fragments thereof, comprising a light chain (LC) comprising an amino acid sequence at least 99% identical to an amino acid sequence set forth as SEQ ID NO: 19. Disclosed herein, in certain

5 embodimentexamples, are monoclonal antibodies or antigen-binding fragments thereof, comprising a light chain (LC) comprising an amino acid sequence 100% identical to an amino acid sequence set forth as SEQ ID NO: 19. In some embodimentexamples, the monoclonal antibodies or antigen-binding fragments thereof comprise a heavy chain (HC) comprising an amino acid sequence at least 80% identical to an amino acid sequence set forth as SEQ ID NO: 20. In some

10 embodimentexample, the monoclonal antibodies or antigen-binding fragments thereof comprise a heavy chain (HC) comprising an amino acid sequence at least 90% identical to an amino acid sequence set forth as SEQ ID NO: 20. In some embodimentexamples, the monoclonal antibodies or antigen-binding fragments thereof comprise a heavy chain (HC) comprising an amino acid sequence at least 95% identical to an amino acid sequence set forth as SEQ ID NO: 20. In some

15 embodimentexample, the monoclonal antibodies or antigen-binding fragments thereof comprise a heavy chain (HC) comprising an amino acid sequence at least 99% identical to an amino acid sequence set forth as SEQ ID NO: 20. In some embodimentexamples, the monoclonal antibodies or antigen-binding fragments thereof comprise a heavy chain (HC) comprising an amino acid sequence 100% identical to an amino acid sequence set forth as SEQ ID NO: 20.

20 **[0011]** In some embodimentexamples, the monoclonal antibodies or antigen-binding fragments thereof comprise a heavy chain (HC) comprising an amino acid sequence at least 80% identical to an amino acid sequence set forth as SEQ ID NO: 21. In some embodimentexamples, the monoclonal antibodies or antigen-binding fragments thereof comprise a heavy chain (HC) comprising an amino acid sequence at least 90% identical to an amino acid sequence set forth as SEQ ID NO: 21. In some

25 embodimentexamples, the monoclonal antibodies or antigen-binding fragments thereof comprise a heavy chain (HC) comprising an amino acid sequence at least 95% identical to an amino acid sequence set forth as SEQ ID NO: 21. In some embodimentexamples, the monoclonal antibodies or antigen-binding fragments thereof comprise a heavy chain (HC) comprising an amino acid sequence at least 99% identical to an amino acid sequence set forth as SEQ ID NO: 21. In some

30 embodimentexample, the monoclonal antibodies or antigen-binding fragments thereof comprise a heavy chain (HC) comprising an amino acid sequence 100% identical to an amino acid sequence set forth as SEQ ID NO: 21.

[0012] Disclosed herein, in certain embodimentexamples, are monoclonal antibodies or an antigen-binding fragments thereof, comprising a light chain (LC) comprising an amino acid sequence at least 80% identical to an amino acid sequence set forth as SEQ ID NO: 22. Disclosed herein, in certain embodimentexamples, are monoclonal antibodies or antigen-binding fragments thereof, comprising a light chain (LC) comprising an amino acid sequence at least 90% identical to an amino acid sequence set forth as SEQ ID NO: 22. Disclosed herein, in certain embodimentexamples, are monoclonal antibodies or antigen-binding fragments thereof, comprising a light chain (LC) comprising an amino acid sequence at least 95% identical to an amino acid sequence set forth as SEQ ID NO: 22. Disclosed herein, in certain embodimentexamples, are monoclonal antibodies or antigen-binding fragments thereof, comprising a light chain (LC) comprising an amino acid sequence at least 99% identical to an amino acid sequence set forth as SEQ ID NO: 22. Disclosed herein, in certain embodimentexamples, are monoclonal antibodies or antigen-binding fragments thereof, comprising a light chain (LC) comprising an amino acid sequence 100% identical to an amino acid sequence set forth as SEQ ID NO: 22. In some embodimentexamples, the monoclonal antibodies or antigen-binding fragments thereof comprise a heavy chain (HC) comprising an amino acid sequence at least 80% identical to an amino acid sequence set forth as SEQ ID NO: 23. In some embodimentexamples, the monoclonal antibodies or antigen-binding fragments thereof comprise a heavy chain (HC) comprising an amino acid sequence at least 90% identical to an amino acid sequence set forth as SEQ ID NO: 23. In some embodimentexamples, the monoclonal antibodies or antigen-binding fragments thereof comprise a heavy chain (HC) comprising an amino acid sequence at least 95% identical to an amino acid sequence set forth as SEQ ID NO: 23. In some embodimentexamples, the monoclonal antibodies or antigen-binding fragments thereof comprise a heavy chain (HC) comprising an amino acid sequence at least 99% identical to an amino acid sequence set forth as SEQ ID NO: 23. In some embodimentexamples, the monoclonal antibodies or antigen-binding fragments thereof comprise a heavy chain (HC) comprising an amino acid sequence 100% identical to an amino acid sequence set forth as SEQ ID NO: 23.

[0013] Disclosed herein, in certain embodimentexamples, are monoclonal antibodies or antigen-binding fragments thereof, comprising a heavy chain (HC) comprising an amino acid sequence at least 80% identical to an amino acid sequence set forth as SEQ ID NO: 20. Disclosed herein, in certain embodimentexamples, are monoclonal antibodies or antigen-binding fragments thereof, comprising a heavy chain (HC) comprising an amino acid sequence at least 90% identical to an amino acid sequence set forth as SEQ ID NO: 20. Disclosed herein, in certain embodimentexamples, are monoclonal antibodies or antigen-binding fragments thereof, comprising a heavy chain (HC) comprising an amino acid sequence at

least 95% identical to an amino acid sequence set forth as SEQ ID NO: 20. Disclosed herein, in certain embodimentexamples, are monoclonal antibodies or antigen-binding fragments thereof, comprising a heavy chain (HC) comprising an amino acid sequence at least 99% identical to an amino acid sequence set forth as SEQ ID NO: 20. Disclosed herein, in certain embodimentexamples, are monoclonal antibodies or antigen-binding fragments thereof, comprising a heavy chain (HC) comprising an amino acid sequence 100% identical to an amino acid sequence set forth as SEQ ID NO: 20. Disclosed herein, in certain embodimentexamples, are monoclonal antibodies or antigen-binding fragments thereof, comprising a heavy chain (HC) comprising an amino acid sequence at least 80% identical to an amino acid sequence set forth as SEQ ID NO: 21. Disclosed herein, in certain embodimentexamples, are monoclonal antibodies or antigen-binding fragments thereof, comprising a heavy chain (HC) comprising an amino acid sequence at least 90% identical to an amino acid sequence set forth as SEQ ID NO: 21. Disclosed herein, in certain embodimentexamples, are monoclonal antibodies or antigen-binding fragments thereof, comprising a heavy chain (HC) comprising an amino acid sequence at least 95% identical to an amino acid sequence set forth as SEQ ID NO: 21. Disclosed herein, in certain embodimentexamples, are monoclonal antibodies or antigen-binding fragments thereof, comprising a heavy chain (HC) comprising an amino acid sequence 100% identical to an amino acid sequence set forth as SEQ ID NO: 21. In some embodimentexamples, the monoclonal antibodies or antigen-binding fragments thereof comprise a light chain (LC) comprising an amino acid sequence at least 80% identical to an amino acid sequence set forth as SEQ ID NO: 19. In some embodimentexamples, the monoclonal antibodies or antigen-binding fragments thereof comprise a light chain (LC) comprising an amino acid sequence at least 90% identical to an amino acid sequence set forth as SEQ ID NO: 19. In some embodimentexamples, the monoclonal antibodies or antigen-binding fragments thereof comprise a light chain (LC) comprising an amino acid sequence at least 95% identical to an amino acid sequence set forth as SEQ ID NO: 19. In some embodimentexamples, the monoclonal antibodies or antigen-binding fragments thereof comprise a light chain (LC) comprising an amino acid sequence at least 99% identical to an amino acid sequence set forth as SEQ ID NO: 19. In some embodimentexamples, the monoclonal antibodies or antigen-binding fragments thereof comprise a light chain (LC) comprising an amino acid sequence 100% identical to an amino acid sequence set forth as SEQ ID NO: 19.

[0014] Disclosed herein, in certain embodimentexamples, are monoclonal antibodies or antigen-binding fragments thereof, comprising a heavy chain (HC) comprising an amino acid sequence at least 80% identical to an amino acid sequence set forth as SEQ ID NO: 23. Disclosed herein, in certain embodimentexamples, are monoclonal antibodies or antigen-binding fragments thereof, comprising a heavy chain (HC) comprising an amino acid sequence at least 90% identical to an amino acid sequence set forth as SEQ ID NO: 23. Disclosed herein, in certain embodimentexamples, are monoclonal antibodies or antigen-binding fragments thereof, comprising a heavy chain (HC) comprising an amino acid sequence at least 95% identical to an amino acid sequence set forth as SEQ ID NO: 23. Disclosed herein, in certain embodimentexamples, are monoclonal antibodies or antigen-binding fragments thereof, comprising a heavy chain (HC) comprising an amino acid sequence at least 99% identical to an amino acid sequence set forth as SEQ ID NO: 23. Disclosed herein, in certain embodimentexamples, are monoclonal antibodies or antigen-binding fragments thereof, comprising a heavy chain (HC) comprising an amino acid sequence 100% identical to an amino acid sequence set forth as SEQ ID NO: 23. In some embodimentexamples, the monoclonal antibodies or antigen-binding fragments thereof comprise a light chain (LC) comprising an amino acid sequence at least 80% identical to an amino acid sequence set forth as SEQ ID NO: 22. In some embodimentexamples, the monoclonal antibodies or antigen-binding fragments thereof comprise a light chain (LC) comprising an amino acid sequence at least 90% identical to an amino acid sequence set forth as SEQ ID NO: 22. In some embodimentexamples, the monoclonal antibodies or antigen-binding fragments thereof comprise a light chain (LC) comprising an amino acid sequence at least 95% identical to an amino acid sequence set forth as SEQ ID NO: 22. In some embodimentexamples, the monoclonal antibodies or antigen-binding fragments thereof comprise a light chain (LC) comprising an amino acid sequence at least 99% identical to an amino acid sequence set forth as SEQ ID NO: 22. In some embodimentexamples, the monoclonal antibodies or antigen-binding fragments thereof comprise a light chain (LC) comprising an amino acid sequence 100% identical to an amino acid sequence set forth as SEQ ID NO: 22. . In some embodimentexamples, the monoclonal antibodies or antigen-binding fragments thereof selectively bind to a complex comprising an HLA-E and a neoantigen. In some embodimentexamples, the monoclonal antibodies or antigen-binding fragments thereof do not have a binding affinity to the HLA-E alone. In some embodimentexamples, the monoclonal antibodies or antigen-binding fragments thereof do not have a binding affinity to the neoantigen alone. In some embodimentexamples, the neoantigen is expressed by an antigen processing machinery (APM)-proficient cell. In some embodimentexamples, the neoantigen is expressed by a TAP1/2-proficient cell. In some embodimentexamples, the neoantigen comprises, consists essentially of, or

consists of a sequence according to SEQ ID NO: 18 (VMAPRTLFL). In some embodimentexamples, the HLA-E is HLA-E*0101 or HLA-E*0103. In some embodimentexamples, the antibodies selectively bind to the complex comprising: (a) the HLA-E*0101 and the neoantigen; (b) the HLA-E*0103 and the neoantigen; or (c) the HLA-E*0101 and the neoantigen, and the HLA-E*0103 and the neoantigen. In some embodimentexamples, the monoclonal antibodies or antigen-binding fragments thereof are murine antibodies, chimeric antibodies, camelid antibodies, humanized antibodies, or human antibodies. In some embodimentexamples, the monoclonal antibodies or antigen-binding fragments thereof are TCR-like antibodies. In some embodimentexamples, the monoclonal antibodies or antigen-binding fragments thereof are multispecific antibodies. In some embodimentexamples, the monoclonal antibodies or antigen-binding fragments thereof are bispecific antibodies. In some embodimentexamples, the monoclonal antibodies or antigen-binding fragments thereof are bispecific T cell engagers (BiTE). In some embodimentexamples, the BiTE binds to a CD3 protein associated with a T cell receptor (TCR). In some embodimentexamples, the BiTE further comprises a light chain variable domain (VL) comprising an amino acid sequence at least 80% identical to an amino acid sequence set forth as SEQ ID NO: 15. In some embodimentexamples, the BiTE further comprises a heavy chain variable domain (VH) comprising an amino acid sequence at least 80% identical to an amino acid sequence set forth as SEQ ID NO: 16. In some embodimentexamples, the monoclonal antibodies or antigen-binding fragments thereof are multifunctional antibodies. In some embodimentexamples, the monoclonal antibodies or antigen-binding fragments thereof antibody further comprise a conjugated therapeutic moiety. In some embodimentexamples, the selective binding of the antibodies to the complex comprising the HLA-E and the neoantigen induces an immune response in a cell. In some embodimentexamples, the immune response comprises activation of (i) NK cells, (ii) T cells, or (iii) NK cells and T cells. In some embodimentexamples, the T cell is a CD4+ T cell or a CD8+ T cell. In some embodimentexamples, the immune response comprises activation of cytotoxic T cells (CTLs). In some embodimentexamples, the cell is a cancer cell.

BRIEF DESCRIPTION OF THE DRAWINGS

[0015] The novel features of the invention are set forth with particularity in the appended claims. A better understanding of the features and advantages of the present invention will be obtained by reference to the following detailed description that sets forth illustrative embodiments, in which the principles of the invention are utilized, and the accompanying drawings of which:

target V-0025 used at 0.25 µg/mL while ABX0011 and HLA-E were titrated from 2 µg/mL down to 3.8 pg/mL (3.8×10^{-6} µg/mL). Thermostability of ABX0011 (**Fig. 9F**) was assessed by ELISA.

ABX0011 binding to HLA-E/VMAPRTLFL ([SEQ ID NO: 18](#)) was evaluated after antibody was incubated in mouse serum at 37°C for 7 to 14 days. Selectivity of binding (**Fig. 9G**) of clone 3D12 and ABX0011 to unpulsed and peptide-pulsed K562.E cells. K562.E cells were pulsed with 20mM of peptide for 2hrs followed by staining with antibody at 1 µg/mL. Further assessment of ABX0011 binding selectivity was performed using ABX0012 (ABX0011 with mouse IgG1) with related and unrelated peptides. HLA-E (**FIG. 9H**) and ABX0012 (**Fig. 9I**) staining on peptide-pulsed and unpulsed K562.E cells. The limit of detection for ABX0011 was determined with target V-0025 peptide pulsed K562.E (**Fig. 9J**). Controls were unpulsed K562.E cells and parent K562 (lack HLA-E expression) and K562.E cells pulsed with irrelevant peptides (V-0034, V-0044, V-0046 and P-0550). Epitope mapping for ABX0011 was carried out using K562.E cells pulsed with alanine substituted V-0025 peptides (**Fig. 9K**).

[0025] Fig. 10A-Fig. 10C exemplify ABX0011 binding specificity to a cell line that expresses HLA-E and HLA-G (**Fig. 10A**) and no binding was observed to human peripheral blood mononuclear cells (huPBMC) and primary human umbilical vascular endothelial cells (huVEC) lacking HLA-G (**Fig. 10B and Fig. 10C**). Antibody binding studies were performed at 1 µg/mL. (**Fig. 10A**) Binding to IFNγ-stimulated JEG3 wild type (WT, top panel), E^{ko} (middle panel) and Tap-1^{ko} (bottom panel). (**Fig. 10B**) Binding to huPBMC and (**Fig. 10C**) to huVEC.

[0026] Fig. 11A-Fig. 11B exemplify binding to AML cell lines that express both HLA-E and HLA-G (THP-1 and OCI-AML3) or only express HLA-E (KG-1). AML cells stained at 1 µg/ml of antibody using 3D12 (HLA-E), MEM-G/09 (HLA-G) and W632 (pan HLA I) (**Fig. 11A**). ABX0012 (ABX0011 with mouse IgG1) was titrated (10 to 0.004 mg/ml) and binding to target positive AML cell lines was observed (**Fig. 11B**).

[0027] Fig. 12A-Fig. 12D exemplify ABX0011 mediated NK cytotoxicity against tumor cell lines expressing target. NK cells were co-cultured with V-0025 peptide-pulsed K562.E cells or with THP-1 cells with an isotype control (hlgG1). The frequency of CD107a-positive NK cells and CD107a-positive NKG2A+ NK cells are shown (**Fig. 12 A and Fig. 12B**). The frequency of dead target cells (K562.E) and THP-1 cells is shown in **Fig. 12C and Fig. 12D**, respectively.

[0028] Fig. 13A-Fig. 13B exemplify QC data for the production of ABX0030, a bispecific T cell engager that contains the V_L and V_H domains of ABX0011 linked covalently to an anti-CD3 scFv fragment.

K562 and K562.HLA-E + V-0025 (VMAPRTLFL) peptide ([SEQ ID NO: 18](#)) pulsed cells were pelleted, treated with OCI compound and flash frozen to prepare frozen cell blocks for immunohistochemistry. ABX-0012 antibody (1.95 ug/ml) was used to stain K562.E + V-0025 and K562 cells. Upper panel shows positive ABX-0012 staining while control cells (lower panel) are not stained. These findings confirm the method for using ABX-0012 to stain frozen tissue sections.

[0043] Fig. 28 exemplifies that positive ABX-0012 staining of human placenta tissue and specifically trophoblast cells.

[0044] Fig. 29A and Fig. 29B exemplify frozen section samples of Head and Neck tumor and normal adjacent tissue (NAT). **Fig. 29A** shows (left) staining with anti-HLA-E antibody (2.25ug/ml) and (right) with ABX0012 antibody (1.95ug/ml). **Fig. 29B** shows (left) NAT staining with anti-HLA-E antibody but not with ABX-0012 antibody (right).

[0045] Fig. 30 exemplifies frozen section samples of colon adenocarcinoma and NAT. the Panel on the left shows staining with anti-HLA-E antibody (2.25ug/ml) and panel on the right with ABX0012 antibody (1.95ug/ml).

[0046] Fig. 31A- Fig. 31B exemplify frozen section samples of lung squamous cell carcinoma and NAT. **Fig. 31A** shows (left panel) staining with anti-HLA-E antibody (2.25ug/ml) and (right panel) with ABX0012 antibody (1.95ug/ml). **Fig. 31B** does not show ABX-0012 staining of normal adjacent lung tissue.

DETAILED DESCRIPTION

[0047] Disclosed herein, in certain embodiments, are antibodies comprising at least one heavy chain comprising a heavy chain variable domain (VH) and at least one light chain comprising a light chain variable domain (VL). Each VH and VL comprises three complementarity determining regions (CDR). In some embodiments, the antibodies are bispecific antibodies. In some embodiments, the bispecific antibodies are bispecific T cell engagers (BiTEs). In some embodiments, the bispecific antibodies bind to a CD3 protein associated with a T cell receptor (TCR). Further disclosed herein, in certain embodiments, are methods of treating a cancer by administering an antibody that selectively binds to a complex comprising a non-classical HLA-I (e.g. HLA-E) and a neoantigen. In some embodiments, the antibodies that selectively bind to a complex comprising a non-classical HLA-I (e.g. HLA-E) and a neoantigen modulate immune response against cancer cells, thereby treating cancer. In some embodiments, the antibodies are bispecific antibodies.

EXAMPLES

[00225] The following examples are given for the purpose of illustrating various embodiments of the invention and are not meant to limit the present invention in any fashion. The present examples, along with the methods described herein are presently representative of preferred
5 embodiments, are exemplary, and are not intended as limitations on the scope of the invention. Changes therein and other uses which are encompassed within the spirit of the invention as defined by the scope of the claims will occur to those skilled in the art.

Example 1. Generation of antibodies

[00226] R4 clone 1 (R4c1) was first isolated from a semi-synthetic human antibody phage library. In brief, this was performed as follows. A human scFv antibody phage display library (1.42×10^9 clones) constructed by Creative Biolabs (HuScL-2 phage library) was used to screen against
10 HLA-G signal peptide/HLA-E*0103 complex (ABI-V-0025; VMAPRTLFL ([SEQ ID NO: 18](#))). Briefly, 30 µg of a mix of five internal peptide/HLA-A2*0201 complexes (ABI-AV-007-Biot, ABI-
15 AV-0010-Biot, ABI-AV-0014-Biot, ABI-AV-0019 and ABI-AB-0030-Biot) were used for depletion and pre-blocking, followed by enrichment with 50 µg of ABI-V-0025. The enrichment factor of the phage library was 2.73×10^6 (phage input: 5×10^{11} , phage output: 1.83×10^5). This process was repeated for the second round of biopanning, with an enrichment factor of 4.03×10^2 . This process was repeated for the third round of biopanning, but using 20 µg of the complex mix for depletion
20 (enrichment factor 2.31×10^2). For the fourth round of biopanning, 50 µg of ABI-V-0018 was used for depletion and pre-blocking, followed by enrichment with 50 µg of ABI-V-0025 (enrichment factor 44). From the phage output of the fourth round of biopanning, 40 clones were picked and sequenced, revealing one unique sequence. This clone was designated as R4 clone 1 (R4c1) (**Fig. 1A-Fig. 1B**). To determine affinity of the R4c1 antibody it was diluted in 0.1% BSA, 0.1%
25 Tween20, PBS dilution/wash buffer and immobilized on the ForteBio Octet Protein A biosensor tip at 20 ug/ml for 50 seconds. Tips were subsequently washed in dilution/wash buffer for 50 seconds. Antibody binding association was measured using six concentrations (serial dilutions starting at 100 ug/ml in dilution/wash buffer) of canonical 0025-E 01:03 monomer complex over the course of 150 seconds immediately followed by dissociation (dilution/wash buffer) for 150 seconds (**Fig. 1C**). The
30 equilibrium dissociation constant (KD) for clone R4 (clone 1) was determined to be 411 nM (**Fig. 1D**).

[00227] *Affinity maturation of R4c1: Cycle 2:* To increase the binding affinity of clone R4c1 to V-0025, the R4c1 scFv construct was cloned into a yeast vector to create a library of R4c1 mutants by changing two amino acid in the CDRH3 region. In brief, the yeast display library generated used EBY100 yeast competent cells that were prepared for transformation by incubation in 100 mM lithium acetate (LiAc, Sigma) plus 10 mM Dithiothreitol (DTT, Sigma). Electroporation was achieved using a GenePulser (BioRad) with 60 OD prepared yeast per 2 mm cuvette (BioRad) in 10 mM LiAc, with 1 µg of scFv clones and 100 ng of pYES3 (ThermoFisher) altered to include Aga2 after the GAL1 promoter and a Flag (DYKDDDDK) epitope tag (SEQ ID NO: 38) after the scFv. To determine the number of transformants, 100 µL of 1/10, 1/100 and 1/1000 dilutions of transformed yeast were spread on glucose plates minus tryptophan and uracil (D-UT, Teknova). Transformation efficiency was calculated after incubation at 30°C for 2 days. Random clones were then picked for insertion diversity by PCR. Yeast were grown at 30°C with shaking at 200 rpm in CM broth with glucose minus tryptophan and uracil (D-UT, Teknova). scFv surface induction was achieved by growing yeast for at least 20 hrs in CM broth with galactose minus tryptophan and uracil (G-UT, Teknova) supplemented with 0.1% raffinose (Sigma) (GR-UT).

[00228] Yeast were stained after first blocking with 2% BSA in PBS 0.05% tween (blocking buffer) for 30 minutes to 1 hour at room temperature with rotation. Yeast were then incubated with biotinylated peptide/HLA complex monomers on ice for 30 minutes to 90 minutes, depending on monomer concentration. Secondary labeling was achieved with Streptavidin PE (ThermoFisher) and DYKDDDDK epitope tag (SEQ ID NO: 38) Alexa Fluor 488 (R&D Systems) on ice for 30 minutes. Samples were acquired using a LSR II flow cytometer (BD Biosciences) or a CytoFLEX S (Beckman Coulter). Data was prepared using Flowjo Software version 10 or FACSDiva (BD Biosciences).

[00229] Screening was achieved by either magnetic-activated cell sorting (MACS) or fluorescence-activated cell sorting (FACS), using at least ten-fold coverage of the library size. For MACS screening, yeast were first blocked with 2% BSA in PBS 0.05% tween (blocking buffer) for 30 minutes to 1 hour at room temperature with rotation. Biotinylated peptide/HLA complex monomers were then incubated on ice for 30 minutes at 1 µM. Secondary labeling was achieved using streptavidin microbeads (Miltenyi Biotec). Labeled yeast were poured over a MACS Column on a MACS Separator (Miltenyi Biotec). Yeast bound to the column were harvested and considered as an enriched population. For FACS screening, yeast were prepared as described in the flow cytometry section. Samples were sorted using a FACS Aria II (BD Bioscience). Sorted yeast were considered an enriched population.

Example 5. Creating a bispecific antibody capable of retargeting T-cells to lyse tumor target cells

[00246] ABX0030 was constructed as a bispecific antibody to be able to activate CD3+ T-cells to kill tumor cells. ABX0030 was made as an Fab-Fc-scFv construct containing ABX0011 (Fab) coupled to a single-chain (scFv) of clone SP34 (mouse anti-human CD3e) on a non-glycosylated (N297D mutation) human IgG1 scaffold. A 20 amino acid linker (GKPGSGKPGSGKPGSGKPGS ([SEQ ID NO: 24](#))) was used to covalently join the ABX0011 Fab with the SP34 scFv. ABX0030 was produced in a transiently transfected CHO cell and purified on a Protein-A affinity column. ABX0030 was run on a reducing SDS-PAGE gel and shows the expected two bands at the anticipated MW (25kD for the ABX0011 light chain and ~55kD for ABX0030 without light chain) (**Fig. 13A**). Greater than 91% of ABX0030 migrates as a single peak on an analytical SEC-HPLC column (**Fig. 13B**).

[00247] The binding affinity of ABX0030 was determined using a label-free assay (ResoSens instrument, Resonant Sensors, Inc). Briefly, V-0025 HLA-E 01:03 monomer complex (diluted in 0.1% BSA, 0.1% Tween20, PBS buffer) was immobilized on neutravidin coated Bionetic label-free microarray plate at 5 µg/ml until binding reached equilibration. Plate was subsequently washed in dilution/wash buffer 3X. The ABX0030 (serial dilutions starting at 10 µg/ml in dilution/wash buffer) binding association was evaluated for approximately 20 minutes and immediately followed by dissociation (dilution/wash buffer) for approximately 15 minutes. Binding affinity calculated using Tracedrawer kinetic analysis software. The findings revealed a dissociation equilibrium constant of 8.97 nM (**Fig. 14**).

[00248] *Binding properties of ABX0030:* ABX0030 binding to target tumor cells was first confirmed. As shown in **Fig. 15**, ABX0030 binds to V-0025 peptide pulsed K562 cells expressing HLA-E similarly to the parent clone (ABX0011). This binding is HLA-E restricted, as HLA-E negative parent K562 cells do not exhibit binding to ABX0030 (**Fig. 15**). Binding to T cells in peripheral blood mononuclear cells (PBMCs) was used to confirm the anti-CD3 arm (**Fig. 16**). The K562 cell line was acquired from ATCC. K562 cells expressing HLA-E cells were acquired from (Dr. Thorbald van Hall, Leiden University Medical Center, Netherlands). Cells were cultured per the supplier's recommendation. For cell binding, cells were blocked with anti-human CD16 (clone KD1), anti-human CD32 (clone AT10), and anti-human CD64 (clone 10.1) (Bio-Rad) or with Human TruStain FcX (BioLegend) at room temperature for 5-10 min before surface staining with unlabeled antibody at 1µg/mL or with AF647-labeled antibody, and with HLA-E/PE-Cy7 (clone

Table 4. List of peptide/HLA complexes

Peptide family	Peptide ID	Sequence	<u>SEQ ID NO:</u>	HLA complex	Gene Origin
Classical HLA	V-0021	VMAPRTLIL	<u>25</u>	HLA-E	HLA-C HLA-Cw*01, -Cw*03, -Cw*04, -Cw*05, -Cw*06, -Cw*08, -Cw*12, -Cw*14, -Cw*16 and -Cw*17:02
	V-0034	VMAPRTLVL	<u>26</u>	HLA-E	HLA-A*02, -A*23, -A*24, -A*25, -A*26, -A*34:02, -A*34:06, -A*43, -A*66 and -A*69
	V-0035	VTAPRTLIL	<u>27</u>	HLA-E	HLA-B*13, -B*18, -B*27, -B*37, -B*40, -B*44, -B*47, -B*54, B*55 - B*56, -B*59, -B*82 and B*83
	V-0037	IMAPRTLVL	<u>28</u>	HLA-E	HLA-A*34:01
	V-0040	VMAPQALLL	<u>29</u>	HLA-E	HLA-Cw*17:01, Cw*17:03 and -Cw*17:05
	V-0041	VMAPRALLL	<u>30</u>	HLA-E	HLA-Cw*06:17, -Cw*07 and -Cw*18
	V-0042	VMAPRTLIL	<u>31</u>	HLA-E	HLA-A*01, -A*03, -A*11, -A*29, -A*30, A*31, -A*32, -A*33, -A*36, and A*74, HLA-Cw02 and Cw*15
	V-0043	VMAPRTLTL	<u>32</u>	HLA-E	HLA-Cw*08:09
	V-0044	VMAPRTVLL	<u>33</u>	HLA-E	HLA-B*07, -B*08, -B*14, -B*38, -B*39, -B*42, -B*48, -B*67, -B*73 and -B*81
	V-0045	VMPRTLIL	<u>34</u>	HLA-E	HLA-A*80
	V-0046	VTAPRTVLL	<u>35</u>	HLA-E	HLA-B*15, -B35, -B*40, -B*41, -B*44:18, -B*45, -B*46 -B*49, -B*50, -B*51, -B*52, -B*53, -B*57, -B*58 and -B*78
Non-classical HLA	V-0025	VMAPRTLFL	<u>18</u>	HLA-E	HLA-G
Additional	V-0038	QMRPVSRVL	<u>36</u>	HLA-E	Hsp60
	P-0550	RAARLPPLL	<u>37</u>	HLA-E	PODXL2

Example 6 ABX0012 does not bind to immune cells in the periphery

[00252] In order to test binding of ABX0012 to immune cells, immune cells were purified, cultured, stained, and assessed by Flow Cytometry as described below.

Human primary cells

[00253] Blood from healthy volunteers was acquired from Carter BloodCare. PBMCs were isolated by density-gradient centrifugation using Ficoll-Paque PLUS (GE Healthcare) or Lymphoprep (StemCell Technologies). Total T cells were purified using EasySep human T cell isolation kit (StemCell Technologies). Natural Killer (NK) cells were purified using EasySep human NK cell enrichment kit (StemCell Technologies). Neutrophils were purified using EasySep direct human neutrophil isolation kit (StemCell Technologies). Eosinophils were purified using EasySep direct human eosinophil isolation kit (StemCell Technologies). Dendritic cells (DCs) were purified using EasySep human pan-DC pre-enrichment kit (StemCell Technologies). Monocytes (MO) were purified using either EasySep human monocyte

antibody (anti-HLA-E (MEM-E/02, AbCam), mouse IgG1 isotype control, or AB0012) for 60 min. Slides were rinsed 3x with Ventana Reaction buffer and incubated with FineFix working solution (Milestone, Kalamazoo, MI, Cat. #70147WG) for 4 min (post-fixation step) and rinsed 3x. Discovery anti-mouse HQ (Ventana, Cat. #760-4814) was applied to slides for 24 min, rinsed 3x using Ventana Reaction buffer. One drop of DISC anti-HQ HRP (Ventana, Cat.#760-4820) was applied to slides, incubated for 24 min and rinsed 3x with Ventana Reaction buffer. Next, one drop of Discovery ChromoMap DAB kit (Ventana, Cat.#760-159) and one drop of CM H2O2 (Ventana) was applied to slides, incubated for 8 min followed by rinsing 3x with Ventana Reaction buffer. Then one drop of copper CM (Ventana) was applied to slides, incubated for 4 min followed by rinsing 3x with Ventana Reaction buffer before applying one drop of Hematoxylin (counterstain) to slide for 12 min. Following rinsing (2x) with Ventana Reaction buffer one drop of Bluing Reagent (post counterstain) was applied and after 8 min slides were rinsed 2x with Ventana Reaction buffer. Slides were then removed from Ventana XT, washed with dishwash detergent and treated with alcohol and xylene for dehydration. A coverslip was added to slides and slides were read on Discovery Ultra instrument.

[00264] ABX0012 was used at 1.95ug/ml, anti-HLA-E (MEM-E/02) antibody and mouse IgG1 isotype control antibody was used at 2.25 ug/ml to stain cell blocks of K562 cells or K562 cells transfected with HLA-E (K562.E) pulsed for 2 hr with 20ug/ml of V-0025 (VM Δ PRTLFL) peptide ([SEQ ID NO: 18](#)) (**FIG. 27**). Images show that ABX0012 stains strong (3+++ out of 3) to K562.E + V-0025 peptide pulsed cells and not to K562 cells (-). These data show ABX0012 is binding selectively to cells presenting HLA-E/V-0025 and validates the immunohistochemistry (IHC) staining protocol.

Example 10 Staining positive control tissue

[00265] Fresh frozen human placenta tissue was used as a positive control for ABX0012. It is well known that trophoblast cells express HLA-E and HLA-G and therefore staining with ABX0012 was anticipated in placental tissue. In **FIG. 28**, ABX0012 shows strong (2++ to 3+++) staining of trophoblast cells in placenta tissue and demonstrates that the HLA-E + canonical leader sequence peptides are present on the surface of trophoblastic cells.

Example 11 ABX0012 stains Head and Neck tumor tissue

[00266] **FIG. 29** is a representative image of ABX0012 staining frozen tumor tissue collected from a head and neck patient. **FIG. 29A** left panel shows strong tumor cell staining with anti-HLA-

E antibody (clone MEM-E/02). Same panel shows staining of stroma area with MEM-E/02 antibody. Right panel shows ABX0012 antibody staining of tumor tissue. Tumor stroma shows strong staining (3+++) while tumor cells show weak to moderate staining. Images indicate that target, HLA-E + leader sequence non-classical HLA-G (VMAPRTLFL ([SEQ ID NO: 18](#))) is present in tumor tissue of head and neck cancer patients. **FIG. 29B** shows image of normal adjacent tissue (NAT) stained with MEM-E/02 (panel left) and ABX0012 (right). Note that NAT epithelium is positive for HLA-E expression (panel left), however absence of ABX0012 staining indicates lack of HLA-E/VMAPRTLFL peptide ([SEQ ID NO: 18](#)) complex in NAT epithelium (panel right).

Example 12 ABX0012 stain colon adenocarcinoma tumor tissue

[00267] A representative image showing fresh frozen human colon adenocarcinoma tissue stained with anti-HLA-E (left; 10x magnification) or ABX-0012 (right; 10x magnification). **FIG. 30** shows HLA-E expression in both tumor and stroma areas (top (1.4x magnification & bottom 14.4x, left) and HLA-E/VMAPRTLFL peptide ([SEQ ID NO: 18](#)) complexes detectable by ABX0012 in both tumor (2++) and stroma (3+++) areas (top 1.4x magnification and bottom 14.4x, right).

Example 13 ABX0012 stains lung squamous carcinoma tissue

[00268] A representative image shows fresh frozen lung squamous carcinoma tissue stained with anti-HLA-E (left, top 10x magnification) or ABX0012 (right; 10x magnification). **FIG. 31A** shows tumor and stroma staining with both anti-HLA-E antibody (2++) or ABX0012 (1+ to 2++) indicating HLA-E and HLA-E/VMAPRTLFL peptide ([SEQ ID NO: 18](#)) complex expression in lung cancer, respectively. **FIG. 31B** shows that ABX0012 does not stain normal adjacent lung tissue indicating the HLA-E loaded with VMAPRTLFL peptide ([SEQ ID NO: 18](#)) from is not present in normal lung tissue.

[00269] While preferred embodiments of the present invention have been shown and described herein, it will be obvious to those skilled in the art that such embodiments are provided by way of example only. Numerous variations, changes, and substitutions will now occur to those skilled in the art without departing from the invention. It should be understood that various alternatives to the embodiments described herein may be employed. It is intended that the following claims define the scope of the invention and that methods and structures within the scope of these claims and their equivalents be covered thereby.

CLAIMS

WHAT IS CLAIMED IS:

1.—A monoclonal antibody or an antigen-binding fragment thereof, comprising a light chain variable domain (VL) comprising an amino acid sequence at least 80% identical to an amino acid sequence set forth as SEQ ID NO: 7.

2.—A monoclonal antibody or an antigen-binding fragment thereof, comprising a light chain variable domain (VL) comprising an amino acid sequence at least 90% identical to an amino acid sequence set forth as SEQ ID NO: 7.

3.—A monoclonal antibody or an antigen-binding fragment thereof, comprising a light chain variable domain (VL) comprising an amino acid sequence at least 95% identical to an amino acid sequence set forth as SEQ ID NO: 7.

4.—A monoclonal antibody or an antigen-binding fragment thereof, comprising a light chain variable domain (VL) comprising an amino acid sequence at least 99% identical to an amino acid sequence set forth as SEQ ID NO: 7.

5.—A monoclonal antibody or an antigen-binding fragment thereof, comprising a light chain variable domain (VL) comprising an amino acid sequence 100% identical to an amino acid sequence set forth as SEQ ID NO: 7.

6.—The monoclonal antibody of any one of claims 1-5, wherein the monoclonal antibody or antigen-binding fragment thereof comprises a heavy chain variable domain (VH) comprising an amino acid sequence at least 80% identical to an amino acid sequence set forth as SEQ ID NO: 8.

7.—The monoclonal antibody of any one of claims 1-5, wherein the monoclonal antibody or antigen-binding fragment thereof comprises a heavy chain variable domain (VH) comprising an amino acid sequence at least 90% identical to an amino acid sequence set forth as SEQ ID NO: 8.

8.—The monoclonal antibody of any one of claims 1-5, wherein the monoclonal antibody or antigen-binding fragment thereof comprises a heavy chain variable domain (VH) comprising an amino acid sequence at least 95% identical to an amino acid sequence set forth as SEQ ID NO: 8.

9.—The monoclonal antibody of any one of claims 1-5, wherein the monoclonal antibody or antigen-binding fragment thereof comprises a heavy chain variable domain (VH) comprising an amino acid sequence at least 99% identical to an amino acid sequence set forth as SEQ ID NO: 8.

10. The monoclonal antibody of any one of claims 1-5, wherein the monoclonal antibody or antigen-binding fragment thereof comprises a heavy chain variable domain (VH) comprising an amino acid sequence 100% identical to an amino acid sequence set forth as SEQ ID NO: 8.

11. The monoclonal antibody of any one of claims 1-10, wherein the monoclonal antibody or antigen-binding fragment thereof selectively binds to a complex comprising an HLA-E and a neoantigen.

12. The monoclonal antibody of any one of claims 1-11, wherein the monoclonal antibody or antigen-binding fragment thereof does not have a binding affinity to the HLA-E alone.

13. The monoclonal antibody of any one of claims 1-12, wherein the monoclonal antibody or antigen-binding fragment thereof does not have a binding affinity to the neoantigen alone.

14. The monoclonal antibody of any one of claims 1-13, wherein the neoantigen is expressed by an antigen processing machinery (APM)-proficient cell.

15. The monoclonal antibody of claim 14, wherein the neoantigen is expressed by a TAP1/2-proficient cell.

16. The monoclonal antibody of any one of claims 1-15, wherein the neoantigen comprises, consists essentially of, or consists of a sequence according to SEQ ID NO: 18 (VMAPRTLFL).

17. The monoclonal antibody of any one of claims 1-16, wherein the HLA-E is HLA-E*0101 or HLA-E*0103.

18. The monoclonal antibody of claim 17, wherein the antibody selectively binds to the complex comprising:

———(a) the HLA-E*0101 and the neoantigen;

———(b) the HLA-E*0103 and the neoantigen; or

———(c) the HLA-E*0101 and the neoantigen, and the HLA-E*0103 and the neoantigen.

19. The monoclonal antibody of any one of claims 1-18, wherein the monoclonal antibody or antigen-binding fragment thereof is a murine antibody, a chimeric antibody, a camelid antibody, a humanized antibody, or a human antibody.

20. The monoclonal antibody of any one of claims 1-19, wherein the monoclonal antibody or antigen-binding fragment thereof is a TCR-like antibody.

21. The monoclonal antibody of any one of claims 1-20, wherein the monoclonal antibody or antigen-binding fragment thereof is a multispecific antibody.

22. The monoclonal antibody of any one of claims 1-21, wherein the monoclonal antibody or antigen-binding fragment thereof is a bispecific antibody.

5 23. The monoclonal antibody of any one of claims 1-22, wherein the monoclonal antibody or antigen-binding fragment thereof is a bispecific T-cell engager (BiTE).

24. The monoclonal antibody of claim 23, wherein the BiTE binds to a CD3 protein associated with a T-cell receptor (TCR).

10 25. The monoclonal antibody of any one of claims 23-24, wherein the BiTE further comprises a light chain variable domain (VL) comprising an amino acid sequence at least 80% identical to an amino acid sequence set forth as SEQ ID NO: 15.

26. The monoclonal antibody of any one of claims 23-25, wherein the BiTE further comprises a heavy chain variable domain (VH) comprising an amino acid sequence at least 80% identical to an amino acid sequence set forth as SEQ ID NO: 16.

15 27. The monoclonal antibody of any one of claims 1-26, wherein the monoclonal antibody or antigen-binding fragment thereof is a multifunctional antibody.

28. The monoclonal antibody of any one of claims 1-27, wherein the monoclonal antibody or antigen-binding fragment thereof antibody further comprises a conjugated therapeutic moiety.

20 29. The monoclonal antibody of any one of claims 1-28, wherein the selective binding of the antibody to the complex comprising the HLA-E and the neoantigen induces an immune response in a cell.

30. The monoclonal antibody of claim 29, wherein the immune response comprises activation of (i) NK cells, (ii) T cells, or (iii) NK cells and T cells.

25 31. The monoclonal antibody of claim 30, wherein the T cell is a CD4⁺ T cell or a CD8⁺ T cell.

32. The monoclonal antibody of claim 30, wherein the immune response comprises activation of cytotoxic T cells (CTLs).

33. The monoclonal antibody of claim 29, wherein the cell is a cancer cell.

34. ~~A monoclonal antibody or an antigen-binding fragment thereof, comprising a heavy chain variable domain (VH) comprising an amino acid sequence at least 80% identical to an amino acid sequence set forth as SEQ ID NO: 8.~~

5 35. ~~A monoclonal antibody or an antigen-binding fragment thereof, comprising a heavy chain variable domain (VH) comprising an amino acid sequence at least 90% identical to an amino acid sequence set forth as SEQ ID NO: 8.~~

36. ~~A monoclonal antibody or an antigen-binding fragment thereof, comprising a heavy chain variable domain (VH) comprising an amino acid sequence at least 95% identical to an amino acid sequence set forth as SEQ ID NO: 8.~~

10 37. ~~A monoclonal antibody or an antigen-binding fragment thereof, comprising a heavy chain variable domain (VH) comprising an amino acid sequence at least 99% identical to an amino acid sequence set forth as SEQ ID NO: 8.~~

15 38. ~~A monoclonal antibody or an antigen-binding fragment thereof, comprising a heavy chain variable domain (VH) comprising an amino acid sequence 100% identical to an amino acid sequence set forth as SEQ ID NO: 8.~~

39. ~~The monoclonal antibody of any one of claims 34-38, wherein the monoclonal antibody or antigen-binding fragment thereof comprises a light chain variable domain (VL) comprising an amino acid sequence at least 80% identical to an amino acid sequence set forth as SEQ ID NO: 7.~~

20 40. ~~The monoclonal antibody of any one of claims 34-38, wherein the monoclonal antibody or antigen-binding fragment thereof comprises a light chain variable domain (VL) comprising an amino acid sequence at least 90% identical to an amino acid sequence set forth as SEQ ID NO: 7.~~

41. ~~The monoclonal antibody of any one of claims 34-38, wherein the monoclonal antibody or antigen-binding fragment thereof comprises a light chain variable domain (VL) comprising an amino acid sequence at least 95% identical to an amino acid sequence set forth as SEQ ID NO: 7.~~

25 42. ~~The monoclonal antibody of any one of claims 34-38, wherein the monoclonal antibody or antigen-binding fragment thereof comprises a light chain variable domain (VL) comprising an amino acid sequence at least 99% identical to an amino acid sequence set forth as SEQ ID NO: 7.~~

~~43. The monoclonal antibody of any one of claims 34-38, wherein the monoclonal antibody or antigen-binding fragment thereof comprises a light chain variable domain (VL) comprising an amino acid sequence 100% identical to an amino acid sequence set forth as SEQ ID NO: 7.~~

~~44. The monoclonal antibody of any one of claims 34-43, wherein the monoclonal antibody or antigen-binding fragment thereof selectively binds to a complex comprising an HLA-E and a neoantigen.~~

~~45. The monoclonal antibody of any one of claims 34-44, wherein the monoclonal antibody or antigen-binding fragment thereof does not have a binding affinity to the HLA-E alone.~~

~~46. The monoclonal antibody of any one of claims 34-45, wherein the monoclonal antibody or antigen-binding fragment thereof does not have a binding affinity to the neoantigen alone.~~

~~47. The monoclonal antibody of any one of claims 34-46, wherein the neoantigen is expressed by an antigen-processing machinery (APM)-proficient cell.~~

~~48. The monoclonal antibody of claim 47, wherein the neoantigen is expressed by a TAP1/2-proficient cell.~~

~~49. The monoclonal antibody of any one of claims 34-48, wherein the neoantigen comprises, consists essentially of, or consists of a sequence according to SEQ ID NO: 18 (VMAPRTLFL).~~

~~50. The monoclonal antibody of any one of claims 34-49, wherein the HLA-E is HLA-E*0101 or HLA-E*0103.~~

~~51. The monoclonal antibody of claim 50, wherein the antibody selectively binds to the complex comprising:~~

~~——(a) the HLA-E*0101 and the neoantigen;~~

~~——(b) the HLA-E*0103 and the neoantigen; or~~

~~——(c) the HLA-E*0101 and the neoantigen, and the HLA-E*0103 and the neoantigen.~~

~~52. The monoclonal antibody of any one of claims 34-51, wherein the monoclonal antibody or antigen-binding fragment thereof is a murine antibody, a chimeric antibody, a camelid antibody, a humanized antibody, or a human antibody.~~

~~53. The monoclonal antibody of any one of claims 34-52, wherein the monoclonal antibody or antigen-binding fragment thereof is a TCR-like antibody.~~

~~54. The monoclonal antibody of any one of claims 34-53, wherein the monoclonal antibody or antigen-binding fragment thereof is a multispecific antibody.~~

~~55. The monoclonal antibody of any one of claims 34-54, wherein the monoclonal antibody or antigen-binding fragment thereof is a bispecific antibody.~~

5 ~~56. The monoclonal antibody of any one of claims 34-55, wherein the monoclonal antibody or antigen-binding fragment thereof is a bispecific T cell engager (BiTE).~~

~~57. The monoclonal antibody of claim 56, wherein the BiTE binds to a CD3 protein associated with a T cell receptor (TCR).~~

10 ~~58. The monoclonal antibody of any one of claims 56-57, wherein the BiTE further comprises a light chain variable domain (VL) comprising an amino acid sequence at least 80% identical to an amino acid sequence set forth as SEQ ID NO: 15.~~

~~59. The monoclonal antibody of any one of claims 56-58, wherein the BiTE further comprises a heavy chain variable domain (VH) comprising an amino acid sequence at least 80% identical to an amino acid sequence set forth as SEQ ID NO: 16.~~

15 ~~60. The monoclonal antibody of any one of claims 34-59, wherein the monoclonal antibody or antigen-binding fragment thereof is a multifunctional antibody.~~

~~61. The monoclonal antibody of any one of claims 34-60, wherein the monoclonal antibody or antigen-binding fragment thereof antibody further comprises a conjugated therapeutic moiety.~~

20 ~~62. The monoclonal antibody of any one of claims 34-61, wherein the selective binding of the antibody to the complex comprising the HLA-E and the neoantigen induces an immune response in a cell.~~

~~63. The monoclonal antibody of claim 62, wherein the immune response comprises activation of (i) NK cells, (ii) T cells, or (iii) NK cells and T cells.~~

25 ~~64. The monoclonal antibody of claim 63, wherein the T cell is a CD4⁺ T cell or a CD8⁺ T cell.~~

~~65. The monoclonal antibody of claim 62, wherein the immune response comprises activation of cytotoxic T cells (CTLs).~~

~~66. The monoclonal antibody of claim 62, wherein the cell is a cancer cell.~~

67.1. A monoclonal antibody or an antigen-binding fragment thereof, comprising

(a) a light chain complementarity determining region (CDR)1 having ~~an~~the amino acid sequence ~~at least 80% identical to at least one of the amino acid sequences~~ set forth as SEQ ID NOS: ~~1-3~~1;

68. ~~A monoclonal antibody or an antigen-binding fragment thereof, comprising a light chain complementarity determining region (CDR~~2~~) having an~~the amino acid sequence ~~at least 90% identical to at least one of the amino acid sequences~~ set forth as SEQ ID NOS: ~~1-32~~1, and;

69. ~~A monoclonal antibody or an antigen-binding fragment thereof, comprising a light chain complementarity determining region (CDR~~3~~) having an~~the amino acid sequence ~~at least 95% identical to at least one of the amino acid sequences~~ set forth as SEQ ID NOS: ~~1-3~~1; and

70. ~~A monoclonal antibody or an antigen-binding fragment thereof, comprising a light chain complementarity determining region (CDR) having an amino acid sequence at least 99% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 1-3.~~

71. ~~A monoclonal antibody or an antigen-binding fragment thereof, comprising a light chain complementarity determining region (CDR) having an amino acid sequence 100% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 1-3.~~

72. ~~The monoclonal antibody of any one of claims 67-71, wherein the monoclonal antibody or antigen-binding fragment thereof comprises (b) a heavy chain complementarity determining region (CDR~~1~~) having an~~the amino acid sequence ~~at least 80% identical to at least one of the amino acid sequences~~ set forth as SEQ ID NOS: ~~4-6~~1.

73. ~~The monoclonal antibody of any one of claims 67-71, wherein the monoclonal antibody or antigen-binding fragment thereof comprises a heavy chain complementarity determining region (CDR~~2~~) having an~~the amino acid sequence ~~at least 90% identical to at least one of the amino acid sequences~~ set forth as SEQ ID NOS: ~~4-6~~5, and;

74. ~~The monoclonal antibody of any one of claims 67-71, wherein the monoclonal antibody or antigen-binding fragment thereof comprises a heavy chain complementarity determining region (CDR~~3~~) having an~~the amino acid sequence ~~at least 95% identical to at least one of the amino acid sequences~~ set forth as SEQ ID NOS: ~~4-6~~6.

2. The monoclonal antibody of claim 1 or an antigen-binding fragment thereof, comprising:
 (a) a light chain variable domain (VL) comprising an amino acid sequence at least 95% identical to the amino acid sequence set forth as SEQ ID NO: 7; and
 (b) a heavy chain variable domain (VH) comprising an amino acid sequence at least 95% identical to the amino acid sequence set forth as SEQ ID NO: 8.
3. The monoclonal antibody of claim 1 or 2 or an antigen-binding fragment thereof, comprising:
 (a) a VL comprising an amino acid sequence at least 99% identical to the amino acid sequence set forth as SEQ ID NO: 7; and
 (b) a VH comprising an amino acid sequence at least 99% identical to the amino acid sequence set forth as SEQ ID NO: 8.
4. The monoclonal antibody of any one of claims 1-3 or an antigen-binding fragment thereof, comprising:
 (a) a VL comprising an amino acid sequence set forth as SEQ ID NO: 7; and
 (b) a VH comprising an amino acid sequence set forth as SEQ ID NO: 8.
5. The monoclonal antibody of any one of claims 1-4 or an antigen-binding fragment thereof, comprising:
 (a) a heavy chain (HC) comprising an amino acid sequence at least 95% identical to the amino acid sequence set forth as SEQ ID NO: 21; and
 (b) a light chain (LC) comprising an amino acid sequence at least 95% identical to the amino acid sequence set forth as SEQ ID NO: 19.
6. The monoclonal antibody of any one of claims 1-5 or an antigen-binding fragment thereof, comprising:
 (a) a HC comprising an amino acid sequence at least 99% identical to the amino acid sequence set forth as SEQ ID NO: 21; and
 (b) a LC comprising an amino acid sequence at least 99% identical to the amino acid sequence set forth as SEQ ID NO: 19.

7. The monoclonal antibody of any one of claims 1-6 or an antigen-binding fragment thereof, comprising:

(a) a HC comprising an amino acid sequence set forth as SEQ ID NO: 21; and

(b) a LC comprising an amino acid sequence set forth as SEQ ID NO: 19.

8. The monoclonal antibody of any one of claims 1-4 or an antigen-binding fragment thereof, comprising:

(a) a HC comprising an amino acid sequence at least 95% identical to the amino acid sequence set forth as SEQ ID NO: 20; and

(b) a LC comprising an amino acid sequence at least 95% identical to the amino acid sequence set forth as SEQ ID NO: 19.

9. The monoclonal antibody of any one of claims 1-4 or 8 or an antigen-binding fragment thereof, comprising:

(a) a HC comprising an amino acid sequence at least 99% identical to the amino acid sequence set forth as SEQ ID NO: 20; and

(b) a LC comprising an amino acid sequence at least 99% identical to the amino acid sequence set forth as SEQ ID NO: 19.

10. The monoclonal antibody of any one of claims 1-4, 8, or 9 or an antigen-binding fragment thereof, comprising:

(a) a HC comprising an amino acid sequence set forth as SEQ ID NO: 20; and

(b) a LC comprising an amino acid sequence set forth as SEQ ID NO: 19.

11. A monoclonal antibody or an antigen-binding fragment thereof, comprising:

(a) a HC comprising an amino acid sequence at least 95% identical to the amino acid sequence set forth as SEQ ID NO: 21; and

(b) a heavy chain CDR1 having the amino acid sequence set forth as SEQ ID NO: 4, a heavy chain CDR2 having the amino acid sequence set forth as SEQ ID NO: 5, and a heavy chain CDR3 having the amino acid sequence set forth as SEQ ID NO: 6.

12. The monoclonal antibody of claim 11 or an antigen-binding fragment thereof, comprising a HC comprising an amino acid sequence at least 99% identical to the amino acid sequence set forth as SEQ ID NO: 21.

13. The monoclonal antibody of claim 11 or 12 or an antigen-binding fragment thereof, comprising a HC comprising the amino acid sequence set forth as SEQ ID NO: 21.

14. The monoclonal antibody of any one of claims 11-13 or an antigen-binding fragment thereof, comprising:

(a) a LC comprising an amino acid sequence at least 95% identical to the amino acid sequence set forth as SEQ ID NO: 19; and

(b) a light chain CDR1 having the amino acid sequence set forth as SEQ ID NO: 1, a light chain CDR2 having the amino acid sequence set forth as SEQ ID NO: 2, and a light chain CDR3 having the amino acid sequence set forth as SEQ ID NO: 3.

15. The monoclonal antibody of any one of claims 11-14 or an antigen-binding fragment thereof, comprising:

(a) a LC comprising an amino acid sequence at least 99% identical to the amino acid sequence set forth as SEQ ID NO: 19; and

(b) a light chain CDR1 having the amino acid sequence set forth as SEQ ID NO: 1, a light chain CDR2 having the amino acid sequence set forth as SEQ ID NO: 2, and a light chain CDR3 having the amino acid sequence set forth as SEQ ID NO: 3.

16. The monoclonal antibody of any one of claims 11-15 or an antigen-binding fragment thereof, comprising:

(a) a LC comprising an amino acid sequence set forth as SEQ ID NO: 19; and

(b) a light chain CDR1 having the amino acid sequence set forth as SEQ ID NO: 1, a light chain CDR2 having the amino acid sequence set forth as SEQ ID NO: 2, and a light chain CDR3 having the amino acid sequence set forth as SEQ ID NO: 3.

17. The monoclonal antibody of any one of claims 11-16 or an antigen-binding fragment thereof, comprising:

(a) a VL comprising an amino acid sequence at least 95% identical to the amino acid sequence set forth as SEQ ID NO: 7; and

(b) a VH comprising an amino acid sequence at least 95% identical to the amino acid sequence set forth as SEQ ID NO: 8.

5
18. The monoclonal antibody of any one of claims 11-17 or an antigen-binding fragment thereof, comprising:

(a) a VL comprising an amino acid sequence at least 99% identical to the amino acid sequence set forth as SEQ ID NO: 7; and

10
(b) a VH comprising an amino acid sequence at least 99% identical to the amino acid sequence set forth as SEQ ID NO: 8.

19. The monoclonal antibody of any one of claims 11-18 or an antigen-binding fragment thereof, comprising:

15
(a) a VL comprising an amino acid sequence set forth as SEQ ID NO: 7; and

(b) a VH comprising an amino acid sequence set forth as SEQ ID NO: 8.

20. A monoclonal antibody or an antigen-binding fragment thereof, comprising:

20
(a) a HC comprising an amino acid sequence at least 95% identical to the amino acid sequence set forth as SEQ ID NO: 20; and

(b) a heavy chain CDR1 having the amino acid sequence set forth as SEQ ID NO: 4, a heavy chain CDR2 having the amino acid sequence set forth as SEQ ID NO: 5, and a heavy chain CDR3 having the amino acid sequence set forth as SEQ ID NO: 6.

25
21. The monoclonal antibody of claim 20 or an antigen-binding fragment thereof, comprising a HC comprising an amino acid sequence at least 99% identical to the amino acid sequence set forth as SEQ ID NO: 20.

30
22. The monoclonal antibody of claim 20 or 21 or an antigen-binding fragment thereof, comprising a HC comprising the amino acid sequence set forth as SEQ ID NO: 20.

23. The monoclonal antibody of any one of claims 20-22 or an antigen-binding fragment thereof, comprising:

(a) a LC comprising an amino acid sequence at least 95% identical to the amino acid sequence set forth as SEQ ID NO: 19; and

(b) a light chain CDR1 having the amino acid sequence set forth as SEQ ID NO: 1, a light chain CDR2 having the amino acid sequence set forth as SEQ ID NO: 2, and a light chain CDR3 having the amino acid sequence set forth as SEQ ID NO: 3.

24. The monoclonal antibody of any one of claims 20-23 or an antigen-binding fragment thereof, comprising:

(a) a LC comprising an amino acid sequence at least 99% identical to the amino acid sequence set forth as SEQ ID NO: 19; and

(b) a light chain CDR1 having the amino acid sequence set forth as SEQ ID NO: 1, a light chain CDR2 having the amino acid sequence set forth as SEQ ID NO: 2, and a light chain CDR3 having the amino acid sequence set forth as SEQ ID NO: 3.

25. The monoclonal antibody of any one of claims 20-24 or an antigen-binding fragment thereof, comprising:

(a) a LC comprising an amino acid sequence set forth as SEQ ID NO: 19; and

(b) a light chain CDR1 having the amino acid sequence set forth as SEQ ID NO: 1, a light chain CDR2 having the amino acid sequence set forth as SEQ ID NO: 2, and a light chain CDR3 having the amino acid sequence set forth as SEQ ID NO: 3.

26. The monoclonal antibody of any one of claims 20-25 or an antigen-binding fragment thereof, comprising:

(a) a VL comprising an amino acid sequence at least 95% identical to the amino acid sequence set forth as SEQ ID NO: 7; and

(b) a VH comprising an amino acid sequence at least 95% identical to the amino acid sequence set forth as SEQ ID NO: 8.

27. The monoclonal antibody of any one of claims 20-26 or an antigen-binding fragment thereof, comprising:

(a) a VL comprising an amino acid sequence at least 99% identical to the amino acid sequence set forth as SEQ ID NO: 7; and

(b) a VH comprising an amino acid sequence at least 99% identical to the amino acid sequence set forth as SEQ ID NO: 8.

5 28. The monoclonal antibody of any one of claims 20-27 or an antigen-binding fragment thereof, comprising:

(a) a VL comprising an amino acid sequence set forth as SEQ ID NO: 7; and

(b) a VH comprising an amino acid sequence set forth as SEQ ID NO: 8.

10 29. The monoclonal antibody of any one of claims 1-28 or antigen-binding fragment thereof, wherein the monoclonal antibody or antigen binding thereof selectively binds to a complex comprising a HLA-E and a neoantigen comprising the amino acid sequence set forth as SEQ ID NO: 18 (VMAPRTLFL).

15 30. A bispecific T cell engager antibody, comprising:

(a) a first antigen-binding arm, comprising:

(i) a light chain CDR1 having the amino acid sequence set forth as SEQ ID NO: 1, a light chain CDR2 having the amino acid sequence set forth as SEQ ID NO: 2, and a light chain CDR3 having the amino acid sequence set forth as SEQ ID NO: 3; and

20 (ii) a heavy chain CDR1 having the amino acid sequence set forth as SEQ ID NO: 4, a heavy chain CDR2 having the amino acid sequence set forth as SEQ ID NO: 5, and a heavy chain CDR3 having the amino acid sequence set forth as SEQ ID NO: 6; and

25 (b) a second antigen-binding arm that specifically binds to a CD3 protein associated with a T cell receptor (TCR).

31. The bispecific T cell engager of claim 30, comprising a second antigen-binding arm comprising:

30 (a) a light chain CDR1 having the amino acid sequence set forth as SEQ ID NO: 9, a light chain CDR2 having the amino acid sequence set forth as SEQ ID NO: 10, and a light chain CDR3 having the amino acid sequence set forth as SEQ ID NO: 11; and

(b) a heavy chain CDR1 having the amino acid sequence set forth as SEQ ID NO: 12, a heavy chain CDR2 having the amino acid sequence set forth as SEQ ID NO: 13, and a heavy chain CDR3 having the amino acid sequence set forth as SEQ ID NO: 14.

5 32. The bispecific T cell engager of claim 30 or 31, comprising a first antigen-binding arm comprising:

(a) a VL comprising an amino acid sequence at least 95% identical to the amino acid sequence set forth as SEQ ID NO: 7; and

10 (b) a VH comprising an amino acid sequence at least 95% identical to the amino acid sequence set forth as SEQ ID NO: 8.

33. The bispecific T cell engager of any one of claims 30-32, comprising a first antigen-binding arm comprising:

15 (a) a VL comprising an amino acid sequence at least 99% identical to the amino acid sequence set forth as SEQ ID NO: 7; and

(b) a VH comprising an amino acid sequence at least 99% identical to the amino acid sequence set forth as SEQ ID NO: 8.

20 34. The bispecific T cell engager of any one of claims 30-33, comprising a first antigen-binding arm comprising:

(a) a VL comprising an amino acid sequence set forth as SEQ ID NO: 7; and

(b) a VH comprising an amino acid sequence set forth as SEQ ID NO: 8.

25 35. The bispecific T cell engager of any one of claims 30-34, comprising a first antigen-binding arm comprising:

(a) a HC comprising an amino acid sequence at least 95% identical to the amino acid sequence set forth as SEQ ID NO: 21; and

30 (b) a LC comprising an amino acid sequence at least 95% identical to the amino acid sequence set forth as SEQ ID NO: 19.

36. The bispecific T cell engager of any one of claims 30-35, comprising a first antigen-binding arm comprising:

(a) a HC comprising an amino acid sequence at least 99% identical to the amino acid sequence set forth as SEQ ID NO: 21; and

(b) a LC comprising an amino acid sequence at least 99% identical to the amino acid sequence set forth as SEQ ID NO: 19.

5
37. The bispecific T cell engager of any one of claims 30-36, comprising a first antigen-binding arm comprising:

(a) a HC comprising an amino acid sequence set forth as SEQ ID NO: 21; and

(b) a LC comprising an amino acid sequence set forth as SEQ ID NO: 19.

10
38. The bispecific T cell engager of any one of claims 30-34, comprising a first antigen-binding arm comprising:

(a) a HC comprising an amino acid sequence at least 95% identical to the amino acid sequence set forth as SEQ ID NO: 20; and

15
(b) a LC comprising an amino acid sequence at least 95% identical to the amino acid sequence set forth as SEQ ID NO: 19.

39. The bispecific T cell engager of any one of claims 30-34 or 38, comprising a first antigen-binding arm comprising:

20
(a) a HC comprising an amino acid sequence at least 99% identical to the amino acid sequence set forth as SEQ ID NO: 20; and

(b) a LC comprising an amino acid sequence at least 99% identical to the amino acid sequence set forth as SEQ ID NO: 19.

25
40. The bispecific T cell engager of any one of claims 30-34, 38, or 39, comprising a first antigen-binding arm comprising:

(a) a HC comprising an amino acid sequence set forth as SEQ ID NO: 20; and

(b) a LC comprising an amino acid sequence set forth as SEQ ID NO: 19.

30
41. The bispecific T cell engager of any one of claims 30-40, comprising a second antigen-binding arm comprising:

(a) a VL comprising an amino acid sequence set forth as SEQ ID NO: 15; and

(b) a VH comprising an amino acid sequence set forth as SEQ ID NO: 16.

42. The bispecific T cell engager of any one of claims 30-41, wherein the monoclonal antibody or antigen binding thereof selectively binds to a complex comprising a HLA-E and a neoantigen comprising the amino acid sequence set forth as SEQ ID NO: 18 (VMAPRTLFL).

5

43. A pharmaceutical composition comprising the monoclonal antibody of any one of claims 1-29 or an antigen-binding fragment thereof, or the bispecific T cell engager of any one of claims 30-42, and a pharmaceutically acceptable carrier or excipient.

10 44. A pharmaceutical composition for use in treating a HLA-E expressing cancer, comprising the monoclonal antibody of any one of claims 1-29 or an antigen-binding fragment thereof, or the bispecific T cell engager of any one of claims 30-42, and a pharmaceutically acceptable carrier or excipient.

15 45. The pharmaceutical composition according to claim 44, wherein the HLA-E-expressing cancer is breast cancer, kidney cancer, lung cancer, ovarian cancer, colorectal cancer, pancreatic cancer, choriocarcinoma, non-small cell lung carcinoma (NSCLC), gastric cancer, cervical cancer, head and neck cancer, leukemia, lymphoma, myeloma, multiple myeloma (MM), acute myeloid leukemia (AML), myelodysplastic syndrome, a B-cell malignancy, and mantel cell lymphoma.

20 46. Use of a monoclonal antibody of any one of claims 1-29 or an antigen-binding fragment thereof, or a bispecific T cell engager of any one of claims 30-42, in the preparation of a medicament for treating a HLA-E-expressing cancer in an individual in need thereof.

25 47. The use according to claim 46, wherein the HLA-E-expressing cancer is breast cancer, kidney cancer, lung cancer, ovarian cancer, colorectal cancer, pancreatic cancer, choriocarcinoma, non-small cell lung carcinoma (NSCLC), gastric cancer, cervical cancer, head and neck cancer, leukemia, lymphoma, myeloma, multiple myeloma (MM), acute myeloid leukemia (AML), myelodysplastic syndrome, a B-cell malignancy, and mantel cell lymphoma.

30 75. ~~The monoclonal antibody of any one of claims 67-71, wherein the monoclonal antibody or antigen-binding fragment thereof comprises a heavy chain complementarity determining region (CDR) having an amino acid sequence at least 99% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 4-6.~~

76. —The monoclonal antibody of any one of claims 67-71, wherein the monoclonal antibody or antigen-binding fragment thereof comprises a heavy chain complementarity determining region (CDR) having an amino acid sequence 100% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 4-6.

77. —The monoclonal antibody of any one of claims 67-76, wherein the monoclonal antibody or antigen-binding fragment thereof comprises a light chain variable domain (VL) comprising an amino acid sequence at least 80% identical to an amino acid sequence set forth as SEQ ID NO: 7.

78. —The monoclonal antibody of any one of claims 67-77, wherein the monoclonal antibody or antigen-binding fragment thereof comprises a heavy chain variable domain (VH) comprising an amino acid sequence at least 80% identical to an amino acid sequence set forth as SEQ ID NO: 8.

79. —The monoclonal antibody of any one of claims 67-78, wherein the monoclonal antibody or antigen-binding fragment thereof selectively binds to a complex comprising an HLA-E and a neoantigen.

80. —The monoclonal antibody of any one of claims 67-79, wherein the monoclonal antibody or antigen-binding fragment thereof does not have a binding affinity to the HLA-E alone.

81. —The monoclonal antibody of any one of claims 67-80, wherein the monoclonal antibody or antigen-binding fragment thereof does not have a binding affinity to the neoantigen alone.

82. —The monoclonal antibody of any one of claims 67-81, wherein the neoantigen is expressed by an antigen processing machinery (APM)-proficient cell.

83. —The monoclonal antibody of claim 82, wherein the neoantigen is expressed by a TAP1/2-proficient cell.

84. —The monoclonal antibody of any one of claims 67-83, wherein the neoantigen comprises, consists essentially of, or consists of a sequence according to SEQ ID NO: 18 (VMAPRTLFL).

85. The monoclonal antibody of any one of claims 67-84, wherein the HLA-E is HLA-E*0101 or HLA-E*0103.

86. The monoclonal antibody of claim 85, wherein the antibody selectively binds to the complex comprising:

—(a) the HLA-E*0101 and the neoantigen;

—(b) the HLA-E*0103 and the neoantigen; or

—(c) the HLA-E*0101 and the neoantigen, and the HLA-E*0103 and the neoantigen.

87. The monoclonal antibody of any one of claims 67-86, wherein the monoclonal antibody or antigen-binding fragment thereof is a murine antibody, a chimeric antibody, a camelid antibody, a humanized antibody, or a human antibody.

88. The monoclonal antibody of any one of claims 67-87, wherein the monoclonal antibody or antigen-binding fragment thereof is a TCR-like antibody.

89. The monoclonal antibody of any one of claims 67-88, wherein the monoclonal antibody or antigen-binding fragment thereof is a multispecific antibody.

90. The monoclonal antibody of any one of claims 67-89, wherein the monoclonal antibody or antigen-binding fragment thereof is a bispecific antibody.

91. The monoclonal antibody of any one of claims 67-90, wherein the monoclonal antibody or antigen-binding fragment thereof is a bispecific T cell engager (BiTE).

92. The monoclonal antibody of claim 91, wherein the BiTE binds to a CD3 protein associated with a T cell receptor (TCR).

93. The monoclonal antibody of any one of claims 91-92, wherein the BiTE further comprises a light chain complementarity determining region (CDR) having an amino acid sequence at least 80% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 9-11.

94. The monoclonal antibody of any one of claims 91-93, wherein the BiTE further comprises a heavy chain complementarity determining region (CDR) having an amino acid sequence at least 80% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 12-14.

95. The monoclonal antibody of any one of claims 91-94, wherein the BiTE further comprises a light chain variable domain (VL) comprising an amino acid sequence at least 80% identical to an amino acid sequence set forth as SEQ ID NO: 15.

96. The monoclonal antibody of any one of claims 91-95, wherein the BiTE further comprises a heavy chain variable domain (VH) comprising an amino acid sequence at least 80% identical to an amino acid sequence set forth as SEQ ID NO: 16.

97. The monoclonal antibody of any one of claims 67-96, wherein the monoclonal antibody or antigen-binding fragment thereof is a multifunctional antibody.

98. The monoclonal antibody of any one of claims 67-97, wherein the monoclonal antibody or antigen-binding fragment thereof antibody further comprises a conjugated therapeutic moiety.

99. ~~The monoclonal antibody of any one of claims 67-98, wherein the selective binding of the antibody to the complex comprising the HLA-E and the neoantigen induces an immune response in a cell.~~

100. ~~—The monoclonal antibody of claim 99, wherein the immune response comprises activation of (i) NK cells, (ii) T cells, or (iii) NK cells and T cells.~~

101. ~~—The monoclonal antibody of claim 100, wherein the T cell is a CD4+ T cell or a CD8+ T cell.~~

102. ~~—The monoclonal antibody of claim 99, wherein the immune response comprises activation of cytotoxic T cells (CTLs).~~

103. ~~—The monoclonal antibody of claim 99, wherein the cell is a cancer cell.~~

104. ~~—A monoclonal antibody or an antigen-binding fragment thereof, comprising a heavy chain complementarity determining region (CDR) having an amino acid sequence at least 80% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 4-6.~~

105. ~~—A monoclonal antibody or an antigen-binding fragment thereof, comprising a heavy chain complementarity determining region (CDR) having an amino acid sequence at least 90% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 4-6.~~

106. ~~—A monoclonal antibody or an antigen-binding fragment thereof, comprising a heavy chain complementarity determining region (CDR) having an amino acid sequence at least 95% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 4-6.~~

107. ~~—A monoclonal antibody or an antigen-binding fragment thereof, comprising a heavy chain complementarity determining region (CDR) having an amino acid sequence at least 99% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 4-6.~~

108. ~~—A monoclonal antibody or an antigen-binding fragment thereof, comprising a heavy chain complementarity determining region (CDR) having an amino acid sequence 100% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 4-6.~~

109. ~~—The monoclonal antibody of any one of claims 104-108, wherein the monoclonal antibody or antigen-binding fragment comprises a light chain complementarity determining region (CDR) having an amino acid sequence at least 80% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 1-3.~~

110.—~~The monoclonal antibody of any one of claims 104-108, wherein the monoclonal antibody or antigen-binding fragment comprises a light chain complementarity-determining region (CDR) having an amino acid sequence at least 90% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 1-3.~~

5 111.—~~The monoclonal antibody of any one of claims 104-108, wherein the monoclonal antibody or antigen-binding fragment comprises a light chain complementarity-determining region (CDR) having an amino acid sequence at least 95% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 1-3.~~

10 112.—~~The monoclonal antibody of any one of claims 104-108, wherein the monoclonal antibody or antigen-binding fragment comprises a light chain complementarity-determining region (CDR) having an amino acid sequence at least 99% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 1-3.~~

15 113.—~~The monoclonal antibody of any one of claims 104-108, wherein the monoclonal antibody or antigen-binding fragment comprises a light chain complementarity-determining region (CDR) having an amino acid sequence 100% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 1-3.~~

20 114.—~~The monoclonal antibody of any one of claims 104-113, wherein the monoclonal antibody or antigen-binding fragment thereof comprises a heavy chain variable domain (VH) comprising an amino acid sequence at least 80% identical to an amino acid sequence set forth as SEQ ID NO: 8.~~

25 115.—~~The monoclonal antibody of any one of claims 104-114, wherein the monoclonal antibody or antigen-binding fragment thereof comprises a light chain variable domain (VL) comprising an amino acid sequence at least 80% identical to an amino acid sequence set forth as SEQ ID NO: 7.~~

30 116.—~~The monoclonal antibody of any one of claims 104-115, wherein the monoclonal antibody or antigen-binding fragment thereof selectively binds to a complex comprising an HLA-E and a neoantigen.~~

35 117.—~~The monoclonal antibody of any one of claims 104-116, wherein the monoclonal antibody or antigen-binding fragment thereof does not have a binding affinity to the HLA-E alone.~~

118.—~~The monoclonal antibody of any one of claims 104-117, wherein the monoclonal antibody or antigen-binding fragment thereof does not have a binding affinity to the neoantigen alone.~~

119.—~~The monoclonal antibody of any one of claims 104-118, wherein the neoantigen is expressed by an antigen-processing machinery (APM)-proficient cell.~~

120.—~~The monoclonal antibody of claim 119, wherein the neoantigen is expressed by a TAP1/2-proficient cell.~~

121.—~~The monoclonal antibody of any one of claims 104-120, wherein the neoantigen comprises, consists essentially of, or consists of a sequence according to SEQ ID NO: 18 (VMAPRTLFL).~~

122.—~~The monoclonal antibody of any one of claims 104-121, wherein the HLA-E is HLA-E*0101 or HLA-E*0103.~~

123.—~~The monoclonal antibody of claim 122, wherein the antibody selectively binds to the complex comprising:~~

—~~(a) the HLA-E*0101 and the neoantigen;~~

—~~(b) the HLA-E*0103 and the neoantigen; or~~

—~~(c) the HLA-E*0101 and the neoantigen, and the HLA-E*0103 and the neoantigen.~~

124.—~~The monoclonal antibody of any one of claims 104-123, wherein the monoclonal antibody or antigen-binding fragment thereof is a murine antibody, a chimeric antibody, a camelid antibody, a humanized antibody, or a human antibody.~~

125.—~~The monoclonal antibody of any one of claims 104-124, wherein the monoclonal antibody or antigen-binding fragment thereof is a TCR-like antibody.~~

126.—~~The monoclonal antibody of any one of claims 104-125, wherein the monoclonal antibody or antigen-binding fragment thereof is a multispecific antibody.~~

127.—~~The monoclonal antibody of any one of claims 104-126, wherein the monoclonal antibody or antigen-binding fragment thereof is a bispecific antibody.~~

128.—~~The monoclonal antibody of any one of claims 104-127, wherein the monoclonal antibody or antigen-binding fragment thereof is a bispecific T-cell engager (BiTE).~~

129.—The monoclonal antibody of claim 128, wherein the BiTE binds to a CD3 protein associated with a T cell receptor (TCR).

130.—The monoclonal antibody of any one of claims 128-129, wherein the BiTE further comprises a light chain complementarity determining region (CDR) having an amino acid sequence at least 80% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 9-11.

131.—The monoclonal antibody of any one of claims 128-130, wherein the BiTE further comprises a heavy chain complementarity determining region (CDR) having an amino acid sequence at least 80% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 12-14.

132.—The monoclonal antibody of any one of claims 128-131, wherein the BiTE further comprises a light chain variable domain (VL) comprising an amino acid sequence at least 80% identical to an amino acid sequence set forth as SEQ ID NO: 15.

133.—The monoclonal antibody of any one of claims 128-132, wherein the BiTE further comprises a heavy chain variable domain (VH) comprising an amino acid sequence at least 80% identical to an amino acid sequence set forth as SEQ ID NO: 16.

134.—The monoclonal antibody of any one of claims 104-133, wherein the monoclonal antibody or antigen-binding fragment thereof is a multifunctional antibody.

135.—The monoclonal antibody of any one of claims 104-134, wherein the monoclonal antibody or antigen-binding fragment thereof antibody further comprises a conjugated therapeutic moiety.

136.—The monoclonal antibody of any one of claims 104-135, wherein the selective binding of the antibody to the complex comprising the HLA-E and the neoantigen induces an immune response in a cell.

137.—The monoclonal antibody of claim 136, wherein the immune response comprises activation of (i) NK cells, (ii) T cells, or (iii) NK cells and T cells.

138.—The monoclonal antibody of claim 137, wherein the T cell is a CD4⁺ T cell or a CD8⁺ T cell.

139-48. The monoclonal antibody of claim 136, wherein the immune response comprises activation of cytotoxic T cells (CTLs).

140.—The monoclonal antibody of claim 136, wherein the cell is a cancer cell.

141. — A bispecific antibody or an antigen-binding fragment thereof, comprising:
—— (a) a light chain complementarity determining region (CDR) having an amino acid sequence at least 80% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 1-3; or a heavy chain complementarity determining region (CDR) having an amino acid sequence at least 80% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 4-6; and

(b) a light chain complementarity determining region (CDR) having an amino acid sequence at least 80% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 9-11; or a heavy chain complementarity determining region (CDR) having an amino acid sequence at least 80% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 12-14.

142. — The bispecific antibody of claim 141, wherein the bispecific antibody comprises:—

—— (a) a light chain variable domain (VL) comprising an amino acid sequence at least 80% identical to an amino acid sequence set forth as SEQ ID NO: 7; or a heavy chain variable domain (VH) comprising an amino acid sequence at least 80% identical to an amino acid sequence set forth as SEQ ID NO: 8; and

(b) a light chain variable domain (VL) comprising an amino acid sequence at least 80% identical to an amino acid sequence set forth as SEQ ID NO: 15; or a heavy chain variable domain (VH) comprising an amino acid sequence at least 80% identical to an amino acid sequence set forth as SEQ ID NO: 16.

143. — A bispecific antibody or an antigen-binding fragment thereof, comprising:

—— (a) a light chain complementarity determining region (CDR) having an amino acid sequence at least 80% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 1-3; and a heavy chain complementarity determining region (CDR) having an amino acid sequence at least 80% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 4-6; and

(b) a light chain complementarity determining region (CDR) having an amino acid sequence at least 80% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 9-11; and a heavy chain complementarity determining region (CDR) having an amino acid sequence at least 80% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 12-14.

~~144.—The bispecific antibody of claim 143, wherein the bispecific antibody comprises:—
——(a) a light chain variable domain (VL) comprising an amino acid sequence at least
80% identical to an amino acid sequence set forth as SEQ ID NO: 7; and a heavy chain
variable domain (VH) comprising an amino acid sequence at least 80% identical to an amino
acid sequence set forth as SEQ ID NO: 8; and~~

~~(b) a light chain variable domain (VL) comprising an amino acid sequence at least
80% identical to an amino acid sequence set forth as SEQ ID NO: 15; and a heavy chain
variable domain (VH) comprising an amino acid sequence at least 80% identical to an amino
acid sequence set forth as SEQ ID NO: 16.~~

~~145.—The bispecific antibody of any one of claims 141-144, wherein the bispecific
antibody selectively binds to a complex comprising an HLA-E and a neoantigen.~~

~~146.—The bispecific antibody of any one of claims 141-145, wherein the bispecific
antibody does not have a binding affinity to the HLA-E alone.~~

~~147.—The bispecific antibody of any one of claims 141-146, wherein the bispecific
antibody does not have a binding affinity to the neoantigen alone.~~

~~148.—The bispecific antibody of any one of claims 141-147, wherein the neoantigen is
expressed by an antigen processing machinery (APM)-proficient cell.~~

~~149.—The bispecific antibody of claim 148, wherein the neoantigen is expressed by a
TAP1/2-proficient cell.~~

~~150.—The bispecific antibody of any one of claims 141-149, wherein the neoantigen
comprises, consists essentially of, or consists of a sequence according to SEQ ID NO: 18
(VMAPRTLFL).~~

~~151.—The bispecific antibody of any one of claims 141-150, wherein the HLA-E is HLA-
E*0101 or HLA-E*0103.~~

~~152.—The bispecific antibody of claim 151, wherein the antibody selectively binds to the
complex comprising:~~

~~——(a) the HLA-E*0101 and the neoantigen;~~

~~——(b) the HLA-E*0103 and the neoantigen; or~~

~~——(c) the HLA-E*0101 and the neoantigen, and the HLA-E*0103 and the neoantigen.~~

153.—~~The bispecific antibody of any one of claims 141-152, wherein the monoclonal antibody or antigen-binding fragment thereof is a murine antibody, a chimeric antibody, a camelid antibody, a humanized antibody, or a human antibody.~~

154.—~~The bispecific antibody of any one of claims 104-153, wherein the monoclonal antibody or antigen-binding fragment thereof is a bispecific T cell engager (BiTE).~~

155.—~~The bispecific antibody of claim 154, wherein the BiTE binds to a CD3 protein associated with a T cell receptor (TCR).~~

156.—~~The bispecific antibody of any one of claims 141-155, wherein the monoclonal antibody or antigen-binding fragment thereof is a multifunctional antibody.~~

157.—~~The bispecific antibody of any one of claims 141-156, wherein the monoclonal antibody or antigen-binding fragment thereof antibody further comprises a conjugated therapeutic moiety.~~

158.—~~The bispecific antibody of any one of claims 141-157, wherein the selective binding of the antibody to the complex comprising the HLA-E and the neoantigen induces an immune response in a cell.~~

159.—~~The bispecific antibody of claim 158, wherein the immune response comprises activation of (i) NK cells, (ii) T cells, or (iii) NK cells and T cells.~~

160.—~~The bispecific antibody of claim 159, wherein the T cell is a CD4+ T cell or a CD8+ T cell.~~

161.—~~The bispecific antibody of claim 158, wherein the immune response comprises activation of cytotoxic T cells (CTLs).~~

162.—~~The bispecific antibody of claim 158, wherein the cell is a cancer cell.~~

163.—~~A pharmaceutical composition comprising: (a) a monoclonal antibody or an antigen-binding fragment thereof according to any one of claims 1-140, or a bispecific antibody or an antigen-binding fragment thereof according to any one of claims 141-162; and (b) a pharmaceutically acceptable carrier or excipient.~~

164.—~~A method of treating cancer in an individual in need thereof, comprising administering to the individual an effective amount of a monoclonal antibody or an antigen-binding fragment thereof comprising a light chain complementarity determining region (CDR) having an~~

amino acid sequence at least 80% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 1-3.

165.—A method of treating cancer in an individual in need thereof, comprising administering to the individual an effective amount of a monoclonal antibody or an antigen-binding fragment thereof comprising a heavy chain complementarity determining region (CDR) having an amino acid sequence at least 80% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 4-6.

166.—The method of claim 164 or claim 165, wherein the monoclonal antibody or antigen-binding fragment thereof comprises (a) a light chain complementarity determining region (CDR) having an amino acid sequence at least 80% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 1-3; and (b) a heavy chain complementarity determining region (CDR) having an amino acid sequence at least 80% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 4-6.

167.—The method of any one of claims 164-166, wherein the monoclonal antibody or antigen-binding fragment thereof comprises (a) a light chain complementarity determining region (CDR) having an amino acid sequence at least 90% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 1-3; and (b) a heavy chain complementarity determining region (CDR) having an amino acid sequence at least 90% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 4-6.

168.—The method of any one of claims 164-167, wherein the monoclonal antibody or antigen-binding fragment thereof comprises (a) a light chain complementarity determining region (CDR) having an amino acid sequence at least 95% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 1-3; and (b) a heavy chain complementarity determining region (CDR) having an amino acid sequence at least 95% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 4-6.

169.—The method of any one of claims 164-168, wherein the monoclonal antibody or antigen-binding fragment thereof comprises (a) a light chain complementarity determining region (CDR) having an amino acid sequence at least 99% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 1-3; and (b) a heavy chain complementarity determining region (CDR) having an amino acid sequence at least 99% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 4-6.

170.—The method of any one of claims 164-169, wherein the monoclonal antibody or antigen-binding fragment thereof comprises (a) a light chain complementarity determining region (CDR) having an amino acid sequence 100% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 1-3; and (b) a heavy chain complementarity determining region (CDR) having an amino acid sequence 100% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 4-6.

171.—The method of any one of claims 164-170, wherein the monoclonal antibody or antigen-binding fragment thereof comprises a light chain variable domain (VL) comprising an amino acid sequence at least 80% identical to an amino acid sequence set forth as SEQ ID NO: 7.

172.—The method of any one of claims 164-171, wherein the monoclonal antibody or antigen-binding fragment thereof comprises a heavy chain variable domain (VH) comprising an amino acid sequence at least 80% identical to an amino acid sequence set forth as SEQ ID NO: 8.

173.—The method of any one of claims 164-172, wherein the monoclonal antibody or antigen-binding fragment thereof selectively binds to a complex comprising an HLA-E and a neoantigen.

174.—The method of any one of claims 164-173, wherein the monoclonal antibody or antigen-binding fragment thereof does not have a binding affinity to the HLA-E alone.

175.—The method of any one of claims 164-174, wherein the monoclonal antibody or antigen-binding fragment thereof does not have a binding affinity to the neoantigen alone.

176.—The method of any one of claims 164-175, wherein the neoantigen is expressed by an antigen-processing machinery (APM)-proficient cell.

177.—The method of claim 176, wherein the neoantigen is expressed by a TAP1/2-proficient cell.

178.—The method of any one of claims 164-177, wherein the neoantigen comprises, consists essentially of, or consists of a sequence according to SEQ ID NO: 18 (VMAPRTLFL).

179.—The method of any one of claims 164-178, wherein the HLA-E is HLA-E*0101 or HLA-E*0103.

180.—The method of claim 179, wherein the antibody selectively binds to the complex comprising:

—(a) the HLA-E*0101 and the neoantigen;

~~——(b) the HLA-E*0103 and the neoantigen; or~~

~~——(c) the HLA-E*0101 and the neoantigen, and the HLA-E*0103 and the neoantigen.~~

181. ~~The method of any one of claims 164-180, wherein the monoclonal antibody or antigen-binding fragment thereof is a murine antibody, a chimeric antibody, a camelid antibody, a humanized antibody, or a human antibody.~~

182. ~~The method of any one of claims 164-181, wherein the monoclonal antibody or antigen-binding fragment thereof is a TCR-like antibody.~~

183. ~~The method of any one of claims 164-182, wherein the monoclonal antibody or antigen-binding fragment thereof is a multispecific antibody.~~

184. ~~The method of any one of claims 164-183, wherein the monoclonal antibody or antigen-binding fragment thereof is a bispecific antibody.~~

185. ~~The method of any one of claims 164-184, wherein the monoclonal antibody or antigen-binding fragment thereof is a bispecific T-cell engager (BiTE).~~

186. ~~The method of claim 185, wherein the BiTE binds to a CD3 protein associated with a T-cell receptor (TCR).~~

187. ~~The method of any one of claims 185-186, wherein the BiTE further comprises a light chain complementarity-determining region (CDR) having an amino acid sequence at least 80% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 9-11.~~

188. ~~The method of any one of claims 185-187, wherein the BiTE further comprises a heavy chain complementarity-determining region (CDR) having an amino acid sequence at least 80% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 12-14.~~

189. ~~The method of any one of claims 185-188, wherein the BiTE further comprises a light chain variable domain (VL) comprising an amino acid sequence at least 80% identical to an amino acid sequence set forth as SEQ ID NO: 15.~~

190. ~~The method of any one of claims 185-189, wherein the BiTE further comprises a heavy chain variable domain (VH) comprising an amino acid sequence at least 80% identical to an amino acid sequence set forth as SEQ ID NO: 16.~~

191. ~~The method of any one of claims 164-190, wherein the monoclonal antibody or antigen-binding fragment thereof is a multifunctional antibody.~~

192.—The method of any one of claims 164-191, wherein the monoclonal antibody or antigen-binding fragment thereof antibody further comprises a conjugated therapeutic moiety.

193.—The method of any one of claims 164-192, wherein the selective binding of the antibody to the complex comprising the HLA-E and the neoantigen induces an immune response in a cell.

194.—The method of claim 193, wherein the immune response comprises activation of (i) NK cells, (ii) T cells, or (iii) NK cells and T cells.

195.—The method of claim 194, wherein the T cell is a CD4⁺ T cell or a CD8⁺ T cell.

196.—The method of claim 193, wherein the immune response comprises activation of cytotoxic T cells (CTLs).

197.—The method of any one of claims 164-196, wherein the cancer is breast cancer, kidney cancer, lung cancer, ovarian cancer, colorectal cancer, pancreatic cancer, choriocarcinoma, non-small cell lung carcinoma (NSCLC), gastric cancer, cervical cancer, or head and neck cancer.

198.—The method of any one of claims 164-196, wherein the cancer is a myeloma, leukemia or lymphoma.

199.—The method of any of claims 164-196, wherein the cancer is acute myeloid leukemia (AML), multiple myeloma, or a myelodysplastic syndrome.

200.—The method any of claims 164-196, wherein the cancer is a B-cell malignancy.

201.—The method any of claims 164-196, wherein the cancer is mantle cell lymphoma.

202.—A method of treating cancer in an individual in need thereof, comprising administering to the individual an effective amount of a bispecific antibody or an antigen-binding fragment thereof, comprising:

—(a) a light chain complementarity determining region (CDR) having an amino acid sequence at least 80% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 1-3; or a heavy chain complementarity determining region (CDR) having an amino acid sequence at least 80% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 4-6; and

(b) a light chain complementarity determining region (CDR) having an amino acid sequence at least 80% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 9-11; or a heavy chain complementarity determining region (CDR) having an

amino acid sequence at least 80% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 12-14.

203. — The method of claim 199, wherein the bispecific antibody comprises: —

— (a) a light chain variable domain (VL) comprising an amino acid sequence at least 80% identical to an amino acid sequence set forth as SEQ ID NO: 7; or a heavy chain variable domain (VH) comprising an amino acid sequence at least 80% identical to an amino acid sequence set forth as SEQ ID NO: 8; and

(b) a light chain variable domain (VL) comprising an amino acid sequence at least 80% identical to an amino acid sequence set forth as SEQ ID NO: 15; or a heavy chain variable domain (VH) comprising an amino acid sequence at least 80% identical to an amino acid sequence set forth as SEQ ID NO: 16.

204. — A method of treating cancer in an individual in need thereof, comprising administering to the individual an effective amount of a bispecific antibody or an antigen binding fragment thereof, comprising:

— (a) a light chain complementarity determining region (CDR) having an amino acid sequence at least 80% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 1-3; and a heavy chain complementarity determining region (CDR) having an amino acid sequence at least 80% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 4-6; and

(b) a light chain complementarity determining region (CDR) having an amino acid sequence at least 80% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 9-11; and a heavy chain complementarity determining region (CDR) having an amino acid sequence at least 80% identical to at least one of the amino acid sequences set forth as SEQ ID NOS: 12-14.

205. — The method of claim 204, wherein the bispecific antibody comprises: —

— (a) a light chain variable domain (VL) comprising an amino acid sequence at least 80% identical to an amino acid sequence set forth as SEQ ID NO: 7; and a heavy chain variable domain (VH) comprising an amino acid sequence at least 80% identical to an amino acid sequence set forth as SEQ ID NO: 8; and

(b) a light chain variable domain (VL) comprising an amino acid sequence at least 80% identical to an amino acid sequence set forth as SEQ ID NO: 15; and a heavy chain

variable domain (VH) comprising an amino acid sequence at least 80% identical to an amino acid sequence set forth as SEQ ID NO: 16.

5 206.—The method of any one of claims 202-205, wherein the bispecific antibody or antigen-binding fragment thereof selectively binds to a complex comprising an HLA-E and a neoantigen.

207.—The method of any one of claims 202-206, wherein the bispecific antibody or antigen-binding fragment thereof does not have a binding affinity to the HLA-E alone.

208.—The method of any one of claims 202-207, wherein the bispecific antibody or antigen-binding fragment thereof does not have a binding affinity to the neoantigen alone.

10 209.—The method of any one of claims 202-208, wherein the neoantigen is expressed by an antigen processing machinery (APM)-proficient cell.

210.—The method of claim 209, wherein the neoantigen is expressed by a TAP1/2-proficient cell.

15 211.—The method of any one of claims 202-210, wherein the neoantigen comprises, consists essentially of, or consists of a sequence according to SEQ ID NO: 18 (VMAPRTLFL).

212.—The method of any one of claims 202-211, wherein the HLA-E is HLA-E*0101 or HLA-E*0103.

20 213.—The method of claim 212, wherein the bispecific antibody selectively binds to the complex comprising:

———(a) the HLA-E*0101 and the neoantigen;

———(b) the HLA-E*0103 and the neoantigen; or

———(c) the HLA-E*0101 and the neoantigen, and the HLA-E*0103 and the neoantigen.

214.—~~The method of any one of claims 202-213, wherein the bispecific antibody or antigen-binding fragment thereof is a murine antibody, a chimeric antibody, a camelid antibody, a humanized antibody, or a human antibody.~~

215.—~~The method of any one of claims 202-214, wherein the bispecific antibody or antigen-binding fragment thereof is a TCR-like antibody.~~

216.—~~The method of any one of claims 202-215, wherein the bispecific antibody or antigen-binding fragment thereof is a bispecific T cell engager (BiTE).~~

217.—~~The method of claim 216, wherein the BiTE binds to a CD3 protein associated with a T cell receptor (TCR).~~

218.—~~The method of any one of claims 202-217, wherein the bispecific antibody or antigen-binding fragment thereof is a multifunctional antibody.~~

219.—~~The method of any one of claims 202-218, wherein the bispecific antibody or antigen-binding fragment thereof antibody further comprises a conjugated therapeutic moiety.~~

220.—~~The method of any one of claims 202-219, wherein the selective binding of the antibody to the complex comprising the HLA-E and the neoantigen induces an immune response in a cell.~~

221.—~~The method of claim 220, wherein the immune response comprises activation of (i) NK cells, (ii) T cells, or (iii) NK cells and T cells.~~

222.—~~The method of claim 221, wherein the T cell is a CD4⁺ T cell or a CD8⁺ T cell.~~

223.—~~The method of claim 221, wherein the immune response comprises activation of cytotoxic T cells (CTLs).~~

224.—~~The method of any one of claims 202-223, wherein the bispecific antibody is administered at a therapeutically effective amount.~~

225.—~~The method of any one of claims 202-224, wherein the cancer is breast cancer, kidney cancer, lung cancer, ovarian cancer, colorectal cancer, pancreatic cancer,~~

choriocarcinoma, non-small cell lung carcinoma (NSCLC), gastric cancer, cervical cancer, or head and neck cancer..

226.—The method of any one of claims 202-224, wherein the cancer is a myeloma, leukemia or lymphoma.

227.—The method of any of claims 202-224, wherein the cancer is acute myeloid leukemia (AML), multiple myeloma, or a myelodysplastic syndrome.

228.—The method any of claims 202-224, wherein the cancer is a B-cell malignancy.

229.—The method any of claims 202-224, wherein the cancer is mantle cell lymphoma.

230.—A monoclonal antibody or an antigen-binding fragment thereof, comprising a light chain (LC) comprising an amino acid sequence at least 80% identical to an amino acid sequence set forth as SEQ ID NO: 19.

231.—A monoclonal antibody or an antigen-binding fragment thereof comprising a light chain (LC) comprising an amino acid sequence at least 90% identical to an amino acid sequence set forth as SEQ ID NO: 19.

232.—A monoclonal antibody or an antigen-binding fragment thereof, comprising a light chain (LC) comprising an amino acid sequence at least 95% identical to an amino acid sequence set forth as SEQ ID NO: 19.

233.—A monoclonal antibody or an antigen-binding fragment thereof, comprising a light chain (LC) comprising an amino acid sequence at least 99% identical to an amino acid sequence set forth as SEQ ID NO: 19.

234.—A monoclonal antibody or an antigen-binding fragment thereof, comprising a light chain (LC) comprising an amino acid sequence 100% identical to an amino acid sequence set forth as SEQ ID NO: 19.

235.—The monoclonal antibody of any one of claims 230-234, wherein the monoclonal antibody or antigen-binding fragment thereof comprises a heavy chain (HC)

comprising an amino acid sequence at least 80% identical to an amino acid sequence set forth as SEQ ID NO: 20.

236.—The monoclonal antibody of any one of claims 230-234 wherein the monoclonal antibody or antigen-binding fragment thereof comprises a heavy chain (HC) comprising an amino acid sequence at least 90% identical to an amino acid sequence set forth as SEQ ID NO: 20.

237.—The monoclonal antibody of any one of claims 230-234, wherein the monoclonal antibody or antigen-binding fragment thereof comprises a heavy chain (HC) comprising an amino acid sequence at least 95% identical to an amino acid sequence set forth as SEQ ID NO: 20.

238.—The monoclonal antibody of any one of claims 230-234, wherein the monoclonal antibody or antigen-binding fragment thereof comprises a heavy chain (HC) comprising an amino acid sequence at least 99% identical to an amino acid sequence set forth as SEQ ID NO: 20.

239.—The monoclonal antibody of any one of claims 230-234, wherein the monoclonal antibody or antigen-binding fragment thereof comprises a heavy chain (HC) comprising an amino acid sequence 100% identical to an amino acid sequence set forth as SEQ ID NO: 20.

240.—The monoclonal antibody of any one of claims 230-234, wherein the monoclonal antibody or antigen-binding fragment thereof comprises a heavy chain (HC) comprising an amino acid sequence at least 80% identical to an amino acid sequence set forth as SEQ ID NO: 21.

241.—The monoclonal antibody of any one of claims 230-234, wherein the monoclonal antibody or antigen-binding fragment thereof comprises a heavy chain (HC) comprising an amino acid sequence at least 90% identical to an amino acid sequence set forth as SEQ ID NO: 21.

242.—The monoclonal antibody of any one of claims 230-234, wherein the monoclonal antibody or antigen-binding fragment thereof comprises a heavy chain (HC)

comprising an amino acid sequence at least 95% identical to an amino acid sequence set forth as SEQ ID NO: 21.

243.—The monoclonal antibody of any one of claims 230-234, wherein the monoclonal antibody or antigen-binding fragment thereof comprises a heavy chain (HC) comprising an amino acid sequence at least 99% identical to an amino acid sequence set forth as SEQ ID NO: 21.

244.—The monoclonal antibody of any one of claims 230-234, wherein the monoclonal antibody or antigen-binding fragment thereof comprises a heavy chain (HC) comprising an amino acid sequence 100% identical to an amino acid sequence set forth as SEQ ID NO: 21.

245.—A monoclonal antibody or an antigen-binding fragment thereof, comprising a light chain (LC) comprising an amino acid sequence at least 80% identical to an amino acid sequence set forth as SEQ ID NO: 22.

246.—A monoclonal antibody or an antigen-binding fragment thereof comprising a light chain (LC) comprising an amino acid sequence at least 90% identical to an amino acid sequence set forth as SEQ ID NO: 22.

247.—A monoclonal antibody or an antigen-binding fragment thereof, comprising a light chain (LC) comprising an amino acid sequence at least 95% identical to an amino acid sequence set forth as SEQ ID NO: 22.

248.—A monoclonal antibody or an antigen-binding fragment thereof, comprising a light chain (LC) comprising an amino acid sequence at least 99% identical to an amino acid sequence set forth as SEQ ID NO: 22.

249.—A monoclonal antibody or an antigen-binding fragment thereof, comprising a light chain (LC) comprising an amino acid sequence 100% identical to an amino acid sequence set forth as SEQ ID NO: 22.

250.—The monoclonal antibody of any one of claims 245-249, wherein the monoclonal antibody or antigen-binding fragment thereof comprises a heavy chain (HC)

comprising an amino acid sequence at least 80% identical to an amino acid sequence set forth as SEQ ID NO: 23.

251.—The monoclonal antibody of any one of claims 245-249, wherein the monoclonal antibody or antigen-binding fragment thereof comprises a heavy chain (HC) comprising an amino acid sequence at least 90% identical to an amino acid sequence set forth as SEQ ID NO: 23.

252.—The monoclonal antibody of any one of claims 245-249, wherein the monoclonal antibody or antigen-binding fragment thereof comprises a heavy chain (HC) comprising an amino acid sequence at least 95% identical to an amino acid sequence set forth as SEQ ID NO: 23.

253.—The monoclonal antibody of any one of claims 245-249, wherein the monoclonal antibody or antigen-binding fragment thereof comprises a heavy chain (HC) comprising an amino acid sequence at least 99% identical to an amino acid sequence set forth as SEQ ID NO: 23.

254.—The monoclonal antibody of any one of claims 245-249, wherein the monoclonal antibody or antigen-binding fragment thereof comprises a heavy chain (HC) comprising an amino acid sequence 100% identical to an amino acid sequence set forth as SEQ ID NO: 23.

255.—A monoclonal antibody or an antigen-binding fragment thereof, comprising a heavy chain (HC) comprising an amino acid sequence at least 80% identical to an amino acid sequence set forth as SEQ ID NO: 20.

256.—A monoclonal antibody or an antigen-binding fragment thereof, comprising a heavy chain (HC) comprising an amino acid sequence at least 90% identical to an amino acid sequence set forth as SEQ ID NO: 20.

257.—A monoclonal antibody or an antigen-binding fragment thereof, comprising a heavy chain (HC) comprising an amino acid sequence at least 95% identical to an amino acid sequence set forth as SEQ ID NO: 20.

258.—~~A monoclonal antibody or an antigen-binding fragment thereof, comprising a heavy chain (HC) comprising an amino acid sequence at least 99% identical to an amino acid sequence set forth as SEQ ID NO: 20.~~

259.—~~A monoclonal antibody or an antigen-binding fragment thereof, comprising a heavy chain (HC) comprising an amino acid sequence 100% identical to an amino acid sequence set forth as SEQ ID NO: 20.~~

260.—~~A monoclonal antibody or an antigen-binding fragment thereof, comprising a heavy chain (HC) comprising an amino acid sequence at least 80% identical to an amino acid sequence set forth as SEQ ID NO: 21.~~

261.—~~A monoclonal antibody or an antigen-binding fragment thereof, comprising a heavy chain (HC) comprising an amino acid sequence at least 90% identical to an amino acid sequence set forth as SEQ ID NO: 21.~~

262.—~~A monoclonal antibody or an antigen-binding fragment thereof, comprising a heavy chain (HC) comprising an amino acid sequence at least 95% identical to an amino acid sequence set forth as SEQ ID NO: 21.~~

263.—~~A monoclonal antibody or an antigen-binding fragment thereof, comprising a heavy chain (HC) comprising an amino acid sequence at least 99% identical to an amino acid sequence set forth as SEQ ID NO: 21.~~

264.—~~A monoclonal antibody or an antigen-binding fragment thereof, comprising a heavy chain (HC) comprising an amino acid sequence 100% identical to an amino acid sequence set forth as SEQ ID NO: 21.~~

265.—~~The monoclonal antibody of any one of claims 255-264, wherein the monoclonal antibody or antigen-binding fragment thereof comprises a light chain (LC) comprising an amino acid sequence at least 80% identical to an amino acid sequence set forth as SEQ ID NO: 19.~~

266.—~~The monoclonal antibody of any one of claims 255-264, wherein the monoclonal antibody or antigen-binding fragment thereof comprises a light chain (LC)~~

comprising an amino acid sequence at least 90% identical to an amino acid sequence set forth as SEQ ID NO: 19.

267.—The monoclonal antibody of any one of claims 255-264, wherein the monoclonal antibody or antigen-binding fragment thereof comprises a light chain (LC) comprising an amino acid sequence at least 95% identical to an amino acid sequence set forth as SEQ ID NO: 19.

268.—The monoclonal antibody of any one of claims 255-264, wherein the monoclonal antibody or antigen-binding fragment thereof comprises a light chain (LC) comprising an amino acid sequence at least 99% identical to an amino acid sequence set forth as SEQ ID NO: 19.

269.—The monoclonal antibody of any one of claims 255-264, wherein the monoclonal antibody or antigen-binding fragment thereof comprises a light chain (LC) comprising an amino acid sequence 100% identical to an amino acid sequence set forth as SEQ ID NO: 19.

270.—A monoclonal antibody or an antigen-binding fragment thereof, comprising a heavy chain (HC) comprising an amino acid sequence at least 80% identical to an amino acid sequence set forth as SEQ ID NO: 23.

271.—A monoclonal antibody or an antigen-binding fragment thereof, comprising a heavy chain (HC) comprising an amino acid sequence at least 90% identical to an amino acid sequence set forth as SEQ ID NO: 23.

272.—A monoclonal antibody or an antigen-binding fragment thereof, comprising a heavy chain (HC) comprising an amino acid sequence at least 95% identical to an amino acid sequence set forth as SEQ ID NO: 23.

273.—A monoclonal antibody or an antigen-binding fragment thereof, comprising a heavy chain (HC) comprising an amino acid sequence at least 99% identical to an amino acid sequence set forth as SEQ ID NO: 23.

274.—~~A monoclonal antibody or an antigen-binding fragment thereof, comprising a heavy chain (HC) comprising an amino acid sequence 100% identical to an amino acid sequence set forth as SEQ ID NO: 23.~~

275.—~~The monoclonal antibody of any one of claims 270-274, wherein the monoclonal antibody or antigen-binding fragment thereof comprises a light chain (LC) comprising an amino acid sequence at least 80% identical to an amino acid sequence set forth as SEQ ID NO: 22.~~

276.—~~The monoclonal antibody of any one of claims 270-274, wherein the monoclonal antibody or antigen-binding fragment thereof comprises a light chain (LC) comprising an amino acid sequence at least 90% identical to an amino acid sequence set forth as SEQ ID NO: 22.~~

277.—~~The monoclonal antibody of any one of claims 270-274, wherein the monoclonal antibody or antigen-binding fragment thereof comprises a light chain (LC) comprising an amino acid sequence at least 95% identical to an amino acid sequence set forth as SEQ ID NO: 22.~~

278.—~~The monoclonal antibody of any one of claims 270-274, wherein the monoclonal antibody or antigen-binding fragment thereof comprises a light chain (LC) comprising an amino acid sequence at least 99% identical to an amino acid sequence set forth as SEQ ID NO: 22.~~

279.—~~The monoclonal antibody of any one of claims 270-274, wherein the monoclonal antibody or antigen-binding fragment thereof comprises a light chain (LC) comprising an amino acid sequence 100% identical to an amino acid sequence set forth as SEQ ID NO: 22.~~

280.—~~The monoclonal antibody of any one of claims 230-279, wherein the monoclonal antibody or antigen-binding fragment thereof selectively binds to a complex comprising an HLA-E and a neoantigen.~~

281.—~~The monoclonal antibody of any one of claims 230-280, wherein the monoclonal antibody or antigen-binding fragment thereof does not have a binding affinity to the HLA-E alone.~~

282.—~~The monoclonal antibody of any one of claims 230-281, wherein the monoclonal antibody or antigen-binding fragment thereof does not have a binding affinity to the neoantigen alone.~~

283.—~~The monoclonal antibody of any one of claims 230-282, wherein the neoantigen is expressed by an antigen-processing machinery (APM)-proficient cell.~~

284.—~~The monoclonal antibody of claim 283, wherein the neoantigen is expressed by a TAP1/2-proficient cell.~~

285.—~~The monoclonal antibody of any one of claims 230-284, wherein the neoantigen comprises, consists essentially of, or consists of a sequence according to SEQ ID NO: 18 (VMAPRTLFL).~~

286.—~~The monoclonal antibody of any one of claims 230-284, wherein the HLA-E is HLA-E*0101 or HLA-E*0103.~~

287.—~~The monoclonal antibody of claim 286, wherein the antibody selectively binds to the complex comprising:~~

—~~(a) the HLA-E*0101 and the neoantigen;~~

—~~(b) the HLA-E*0103 and the neoantigen; or~~

—~~(c) the HLA-E*0101 and the neoantigen, and the HLA-E*0103 and the neoantigen.~~

288.—~~The monoclonal antibody of any one of claims 230-287, wherein the monoclonal antibody or antigen-binding fragment thereof is a murine antibody, a chimeric antibody, a camelid antibody, a humanized antibody, or a human antibody.~~

289.—~~The monoclonal antibody of any one of claims 230-289, wherein the monoclonal antibody or antigen-binding fragment thereof is a TCR-like antibody.~~

290.—~~The monoclonal antibody of any one of claims 230-289, wherein the monoclonal antibody or antigen-binding fragment thereof is a multispecific antibody.~~

291.—~~The monoclonal antibody of any one of claims 230-290, wherein the monoclonal antibody or antigen-binding fragment thereof is a bispecific antibody.~~

292.—~~The monoclonal antibody of any one of claims 230-291, wherein the monoclonal antibody or antigen-binding fragment thereof is a bispecific T cell engager (BiTE).~~

293.—~~The monoclonal antibody of claim 292, wherein the BiTE binds to a CD3 protein associated with a T cell receptor (TCR).~~

294.—~~The monoclonal antibody of any one of claims 292-293, wherein the BiTE further comprises a light chain variable domain (VL) comprising an amino acid sequence at least 80% identical to an amino acid sequence set forth as SEQ ID NO: 15.~~

295.—~~The monoclonal antibody of any one of claims 292-293, wherein the BiTE further comprises a heavy chain variable domain (VH) comprising an amino acid sequence at least 80% identical to an amino acid sequence set forth as SEQ ID NO: 16.~~

296.—~~The monoclonal antibody of any one of claims 280-295, wherein the monoclonal antibody or antigen-binding fragment thereof is a multifunctional antibody.~~

297.—~~The monoclonal antibody of any one of claims 280-296, wherein the monoclonal antibody or antigen-binding fragment thereof antibody further comprises a conjugated therapeutic moiety.~~

298.—~~The monoclonal antibody of any one of claims 280-297, wherein the selective binding of the antibody to the complex comprising the HLA-E and the neoantigen induces an immune response in a cell.~~

299.—~~The monoclonal antibody of claim 298, wherein the immune response comprises activation of (i) NK cells, (ii) T cells, or (iii) NK cells and T cells.~~

300.—~~The monoclonal antibody of claim 299, wherein the T cell is a CD4⁺ T cell or a CD8⁺ T cell.~~

301.—~~The monoclonal antibody of claim 300, wherein the immune response comprises activation of cytotoxic T cells (CTLs).~~

302. ~~The monoclonal antibody of claim 298 wherein the cell is a cancer cell.~~