

CLAIMS

1. An antibody or an antigen-binding fragment thereof, wherein the antibody

(a) immunospecifically binds to a cell recombinantly expressing a first form of MUC16, which first form is glycosylated, and wherein the amino acid sequence of the first form is SEQ ID NO:133;

(b) lacks immunospecific binding to a cell recombinantly expressing a second form of MUC16, which second form is unglycosylated, and wherein the amino acid sequence of the second form is SEQ ID NO:139;

(c) inhibits matrigel invasion in vitro of cells recombinantly expressing said first form of MUC16; and

(d) immunospecifically binds to an epitope comprising N-glycosylated asparagine 1806 of SEQ ID NO:150.

2. The antibody or antigen-binding fragment thereof of claim 1, wherein (i) the cell recombinantly expressing the first form of MUC16 is a SKOV3 cell; (ii) the cell recombinantly expressing the second form of MUC16 is a SKOV3 cell; and (iii) the cells in step (c) are SKOV3 cells.

3. The antibody or antigen-binding fragment thereof of any of claims 1 or 2, wherein the antibody or antigen-binding fragment thereof immunospecifically binds to the amino acid sequence CTRNGTQLQNFTLDRSSV (SEQ ID NO:130), wherein amino acid residue number 4 (N4) and amino acid residue number 10 (N10) of CTRNGTQLQNFTLDRSSV (SEQ ID NO:130) are glycosylated.

4. The antibody or antigen-binding fragment thereof of any of claims 1-3, wherein the antibody or antigen-binding fragment thereof immunospecifically binds to the amino acid sequence CGTQLQNFTLDRSSV (SEQ ID NO:131), wherein amino acid residue number 7 (N7) of CGTQLQNFTLDRSSV (SEQ ID NO:131) is glycosylated.

5. The antibody or antigen-binding fragment thereof of any of claims 3 or 4, wherein the glycosylation consists of an N-linked chitobiose.

6. The antibody or antigen-binding fragment thereof of any of claims 1-5, wherein the antibody inhibits growth of a tumor that expresses a glycosylated form of MUC16.

7. The antibody or antigen-binding fragment thereof of any of claims 1-6, wherein the antibody is a monoclonal antibody.

8. The antibody or antigen-binding fragment thereof of any one of claims 1-7, wherein the antibody lacks immunospecific binding to a cell recombinantly expressing a third form of MUC16, which third form is glycosylated, and wherein the amino acid sequence of the third form is SEQ ID NO: 139.

9. The antibody or antigen-binding fragment thereof of any of claims 1-7, wherein the antibody or antigen-binding fragment thereof comprises a heavy chain variable region (VH), which comprises:

- (I) (a) a VH complementarity determining region (CDR)1 comprising the amino acid sequence TX₁GMGVG (SEQ ID NO:103), wherein X₁ is L or V;
- (b) a VH CDR2 comprising the amino acid sequence HIWWDDX₂DKYYX₃PALKS (SEQ ID NO:104), wherein X₂ is E or absent, and X₃ is Y or N; and
- (c) a VH CDR3 comprising the amino acid sequence IGTAQATDALDY (SEQ ID NO:105); or

- (II) a VH CDR1 comprising the amino acid sequence of SEQ ID NO:83, a VH CDR2 comprising the amino acid sequence of SEQ ID NO:84, and a VH CDR3 comprising the amino acid sequence of SEQ ID NO:85; or
- (III) a VH CDR1 comprising the amino acid sequence of SEQ ID NO:89, a VH CDR2 comprising the amino acid sequence of SEQ ID NO:90, and a VH CDR3 comprising the amino acid sequence of SEQ ID NO:91; or
- (IV) a VH CDR1 comprising the amino acid sequence of SEQ ID NO:95, a VH CDR2 comprising the amino acid sequence of SEQ ID NO:96, and a VH CDR3 comprising the amino acid sequence of SEQ ID NO:97; or
- (V) (a) a VH CDR1 comprising the amino acid sequence GFSLX₈TX₉GM (SEQ ID NO:109), wherein X₈ is N or S, and wherein X₉ is L or V;

 (b) a VH CDR2 comprising the amino acid sequence WDDX₁₀ (SEQ ID NO:110), wherein X₁₀ is E or absent; and

 (c) a VH CDR3 comprising the amino acid sequence GTAQATDALD (SEQ ID NO:111); or
- (VI) (a) a VH CDR1 comprising the amino acid sequence GFSLX₁₅TX₁₆GMG (SEQ ID NO:115), wherein X₁₅ is N or S, and X₁₆ is V or L;

 (b) a VH CDR2 comprising the amino acid sequence IWWDDX₁₇DK (SEQ ID NO:116), wherein X₁₇ is E or absent; and

 (c) a VH CDR3 comprising the amino acid sequence X₁₈RIGTAQATDALDY (SEQ ID NO:117), wherein X₁₈ is T, A, or S; or

- (VII) a VH CDR1 comprising the amino acid sequence of SEQ ID NO:3, a VH CDR2 comprising the amino acid sequence of SEQ ID NO:4, and a VH CDR3 comprising the amino acid sequence of SEQ ID NO:5; or
- (VIII) a VH CDR1 comprising the amino acid sequence of SEQ ID NO:9, a VH CDR2 comprising the amino acid sequence of SEQ ID NO:10, and a VH CDR3 comprising the amino acid sequence of SEQ ID NO:11; or
- (IX) a VH CDR1 comprising the amino acid sequence of SEQ ID NO:15, a VH CDR2 comprising the amino acid sequence of SEQ ID NO:16, and a VH CDR3 comprising the amino acid sequence of SEQ ID NO:17; or
- (X) a VH CDR1 comprising the amino acid sequence of SEQ ID NO:23, a VH CDR2 comprising the amino acid sequence of SEQ ID NO:24, and a VH CDR3 comprising the amino acid sequence of SEQ ID NO:25; or
- (XI) a VH CDR1 comprising the amino acid sequence of SEQ ID NO:29, a VH CDR2 comprising the amino acid sequence of SEQ ID NO:30, and a VH CDR3 comprising the amino acid sequence of SEQ ID NO:31; or
- (XII) a VH CDR1 comprising the amino acid sequence of SEQ ID NO:35, a VH CDR2 comprising the amino acid sequence of SEQ ID NO:36, and a VH CDR3 comprising the amino acid sequence of SEQ ID NO:37; or
- (XIII) a VH CDR1 comprising the amino acid sequence of SEQ ID NO:43, a VH CDR2 comprising the amino acid sequence of SEQ ID NO:44, and a VH CDR3 comprising the amino acid sequence of SEQ ID NO:45; or
- (XIV) a VH CDR1 comprising the amino acid sequence of SEQ ID NO:49, a VH CDR2 comprising the amino acid sequence of SEQ ID NO:50, and a VH CDR3 comprising the amino acid sequence of SEQ ID NO:51; or

(XV) a VH CDR1 comprising the amino acid sequence of SEQ ID NO:55, a VH CDR2 comprising the amino acid sequence of SEQ ID NO:56, and a VH CDR3 comprising the amino acid sequence of SEQ ID NO:57; or

(XVI) a VH CDR1 comprising the amino acid sequence of SEQ ID NO:63, a VH CDR2 comprising the amino acid sequence of SEQ ID NO:64, and a VH CDR3 comprising the amino acid sequence of SEQ ID NO:65; or

(XVII) a VH CDR1 comprising the amino acid sequence of SEQ ID NO:69, a VH CDR2 comprising the amino acid sequence of SEQ ID NO:70, and a VH CDR3 comprising the amino acid sequence of SEQ ID NO:71; or

(XVIII) a VH CDR1 comprising the amino acid sequence of SEQ ID NO:75, a VH CDR2 comprising the amino acid sequence of SEQ ID NO:76, and a VH CDR3 comprising the amino acid sequence of SEQ ID NO:77.

10. The antibody or antigen-binding fragment thereof of any of claims 1-7, wherein the antibody or antigen-binding fragment thereof comprises a VH comprising the amino acid sequence of:

(I) QVX₂₁LKESGPGX₂₂LQPSQTL_{SL}TCSFSGFSLX₂₃TX₂₄GMGVGWX₂₅RQX₂₆SGKGLE WLAHIWWDDX₂₇DKYYX₂₈PALKSRLTISX₂₉X₃₀X₃₁SKNQVFLKIX₃₂NVX₃₃TADX₃₄AT YYCX₃₅RIGTAQATDALDYWGQGTSVTVSS (SEQ ID NO:101), wherein X₂₁ is T or N, X₂₂ is I or K, X₂₃ is N or S, X₂₄ is V or L, X₂₅ is S or I, X₂₆ is P or S, X₂₇ is E or absent, X₂₈ is N or Y, X₂₉ is K or R, X₃₀ is A or D, X₃₁ is T or S, X₃₂ is V or A, X₃₃ is G or D, X₃₄ is T, I, or S, and X₃₅ is T, S, or A; or

(II) SEQ ID NO:81; or

(III) SEQ ID NO:1; or

(IV) SEQ ID NO:21; or

(V) SEQ ID NO:41; or

(VI) SEQ ID NO:61.

11. The antibody or antigen-binding fragment thereof of any of claims 1-7, wherein the antibody or antigen-binding fragment thereof comprises a VL comprising the amino acid sequence of:

(I) DIVMTQAAPSX₃₆X₃₇VTPGESVSISCRSSKSLX₃₈X₃₉SNGNTYLYWFLQRPGQSPQR LIYYMSNLASGVDPDRFSGRSGTDFTLX₄₀ISRVEAX₄₁DVGVYYCMQX₄₂LEX₄₃PLTFG GGTKLEIK (SEQ ID NO:102), wherein X₃₆ is I or V, X₃₇ is P or S, X₃₈ is R or L, X₃₉ is K or H, X₄₀ is R or K, X₄₁ is E or G, X₄₂ is S or G, and X₄₃ is Y or H; or

(II) SEQ ID NO:82; or

(III) SEQ ID NO:22; or

(IV) SEQ ID NO:42; or

(V) SEQ ID NO:2; or

(VI) SEQ ID NO:62.

12. The antibody or antigen-binding fragment thereof of any of claims 1-7, wherein the antibody or antigen-binding fragment thereof comprises:

(a) (i) a VH comprising a VH CDR1 comprising the amino acid sequence TX1GMGVG (SEQ ID NO:103), wherein X1 is L or V; a VH CDR2 comprising the amino acid sequence HIWWDDX2DKYYX3PALKS (SEQ ID NO:104), wherein X2 is E or absent, and X3 is Y or N; and a VH CDR3 comprising the amino acid sequence IGTAQATDALDY (SEQ ID NO:105); and (ii) a VL comprising a VL CDR1 comprising the amino acid sequence

RSSKSLX4X5SNGNTYLY (SEQ ID NO:106), wherein X4 is R or L, and X5 is K or H; a VL CDR2 comprising the amino acid sequence YMSNLAS (SEQ ID NO:107); and a VL CDR3 comprising the amino acid sequence MQX6LEX7PLT (SEQ ID NO:108), wherein X6 is G or S, and X7 is H or Y; or

(b) (i) a VH comprising a VH CDR1 comprising the amino acid sequence GFSLX8TX9GM (SEQ ID NO:109), wherein X8 is N or S, and wherein X9 is L or V; a VH CDR2 comprising the amino acid sequence WDDX10 (SEQ ID NO:110), wherein X10 is E or absent; and a VH CDR3 comprising the amino acid sequence GTAQATDALD (SEQ ID NO:111); and (ii) a VL comprising a VL CDR1 comprising the amino acid sequence SKSLX11X12SNGNTY (SEQ ID NO:112), wherein X11 is L or R, and X12 is H or K; a VL CDR2 comprising the amino acid sequence YMS (SEQ ID NO:113); and a VL CDR3 comprising the amino acid sequence X13LEX14PL (SEQ ID NO:114), wherein X13 is G or S, and X14 is H or Y; or

(c) (i) a VH CDR1 comprising the amino acid sequence GFSLX15TX16GMG (SEQ ID NO:115), wherein X15 is N or S, and X16 is V or L; a VH CDR2 comprising the amino acid sequence IWWDDX17DK (SEQ ID NO:116), wherein X17 is E or absent; and a VH CDR3 comprising the amino acid sequence X18RIGTAQATDALDY (SEQ ID NO:117), wherein X18 is T, A, or S; and (ii) a VL comprising a VL CDR1 comprising the amino acid sequence KSLX19X20SNGNTY (SEQ ID NO:118), wherein X19 is V or L, and X20 is H or K; a VL CDR2 comprising the amino acid sequence YMS (SEQ ID NO:119); and a VL CDR3 comprising the amino acid sequence MQSLEYPLT (SEQ ID NO:120); or

(d) (i) a VH comprising a VH CDR1 comprising the amino acid sequence of SEQ ID NO:83, a VH CDR2 comprising the amino acid sequence of SEQ ID NO:84, and a VH CDR3 comprising the amino acid sequence of SEQ ID NO:85; and (ii) a VL comprising a VL CDR1 comprising the amino acid sequence of SEQ ID NO:86, a VL CDR2 comprising the amino acid sequence of SEQ ID NO:87, and a VL CDR3 comprising the amino acid sequence of SEQ ID NO:88; or

(e) (i) a VH comprising a VH CDR1 comprising the amino acid sequence of SEQ ID NO:89, a VH CDR2 comprising the amino acid sequence of SEQ ID NO:90, and a VH CDR3 comprising the amino acid sequence of SEQ ID NO:91; and (ii) a VL comprising a VL CDR1 comprising the amino acid sequence of SEQ ID NO:92, a VL CDR2 comprising the amino acid sequence of SEQ ID NO:93, and a VL CDR3 comprising the amino acid sequence of SEQ ID NO:94; or

(f) (i) a VH comprising a VH CDR1 comprising the amino acid sequence of SEQ ID NO:95, a VH CDR2 comprising the amino acid sequence of SEQ ID NO:96, and a VH CDR3 comprising the amino acid sequence of SEQ ID NO:97 and (ii) a VL comprising a VL CDR1 comprising the amino acid sequence of SEQ ID NO:98, a VL CDR2 comprising the amino acid sequence of SEQ ID NO:99, and a VL CDR3 comprising the amino acid sequence of SEQ ID NO:100; or

(g) (i) a VH comprising a VH CDR1 comprising the amino acid sequence of SEQ ID NO:23, a VH CDR2 comprising the amino acid sequence of SEQ ID NO:24, and a VH CDR3 comprising the amino acid sequence of SEQ ID NO:25; and (ii) a VL comprising a VL CDR1 comprising the amino acid sequence of SEQ ID NO:26, a VL CDR2 comprising the amino acid sequence of SEQ ID NO:27, and a VL CDR3 comprising the amino acid sequence of SEQ ID NO:28; or

(h) (i) a VH comprising a VH CDR1 comprising the amino acid sequence of SEQ ID NO:29, a VH CDR2 comprising the amino acid sequence of SEQ ID NO:30, and a VH CDR3 comprising the amino acid sequence of SEQ ID NO:31; and (ii) a VL comprising a VL CDR1 comprising the amino acid sequence of SEQ ID NO:32, a VL CDR2 comprising the amino acid sequence of SEQ ID NO:33, and a VL CDR3 comprising the amino acid sequence of SEQ ID NO:34; or

(i) (i) a VH comprising a VH CDR1 comprising the amino acid sequence of SEQ ID NO:35, a VH CDR2 comprising the amino acid sequence of SEQ ID NO:36, and a VH CDR3 comprising the amino acid sequence of SEQ ID NO:37; and (ii) a VL comprising a VL CDR1 comprising the amino acid sequence of SEQ ID NO:38, a VL CDR2 comprising the amino acid sequence of SEQ ID NO:39, and a VL CDR3 comprising the amino acid sequence of SEQ ID NO:40; or

(j) (i) a VH comprising a VH CDR1 comprising the amino acid sequence of SEQ ID NO:43, a VH CDR2 comprising the amino acid sequence of SEQ ID NO:44, and a VH CDR3 comprising the amino acid sequence of SEQ ID NO:45; and (ii) a VL comprising a VL CDR1 comprising the amino acid sequence of SEQ ID NO:46, a VL CDR2 comprising the amino acid sequence of SEQ ID NO:47, and a VL CDR3 comprising the amino acid sequence of SEQ ID NO:48; or

(k) (i) a VH comprising a VH CDR1 comprising the amino acid sequence of SEQ ID NO:49, a VH CDR2 comprising the amino acid sequence of SEQ ID NO:50, and a VH CDR3 comprising the amino acid sequence of SEQ ID NO:51; and (ii) a VL comprising a VL CDR1 comprising the amino acid sequence of SEQ ID NO:52, a VL CDR2 comprising the amino acid sequence of SEQ ID NO:53, and a VL CDR3 comprising the amino acid sequence of SEQ ID NO:54; or

(l) (i) a VH comprising a VH CDR1 comprising the amino acid sequence of SEQ ID NO:55, a VH CDR2 comprising the amino acid sequence of SEQ ID NO:56, and a VH CDR3 comprising the amino acid sequence of SEQ ID NO:57; and (ii) a VL comprising a VL CDR1 comprising the amino acid sequence of SEQ ID NO:58, a VL CDR2 comprising the amino acid sequence of SEQ ID NO:59, and a VL CDR3 comprising the amino acid sequence of SEQ ID NO:60; or

(m) (i) a VH comprising a VH CDR1 comprising the amino acid sequence of SEQ ID NO:3, a VH CDR2 comprising the amino acid sequence of SEQ ID NO:4, and a VH CDR3

comprising the amino acid sequence of SEQ ID NO:5; and (ii) a VL comprising a VL CDR1 comprising the amino acid sequence of SEQ ID NO:6, a VL CDR2 comprising the amino acid sequence of SEQ ID NO:7, and a VL CDR3 comprising the amino acid sequence of SEQ ID NO:8; or

(n) (i) a VH comprising a VH CDR1 comprising the amino acid sequence of SEQ ID NO:9, a VH CDR2 comprising the amino acid sequence of SEQ ID NO:10, and a VH CDR3 comprising the amino acid sequence of SEQ ID NO:11; and (ii) a VL comprising a VL CDR1 comprising the amino acid sequence of SEQ ID NO:12, a VL CDR2 comprising the amino acid sequence of SEQ ID NO:13, and a VL CDR3 comprising the amino acid sequence of SEQ ID NO:14; or

(o) (i) a VH comprising a VH CDR1 comprising the amino acid sequence of SEQ ID NO:15, a VH CDR2 comprising the amino acid sequence of SEQ ID NO:16, and a VH CDR3 comprising the amino acid sequence of SEQ ID NO:17; and (ii) a VL comprising a VL CDR1 comprising the amino acid sequence of SEQ ID NO:18, a VL CDR2 comprising the amino acid sequence of SEQ ID NO:19, and a VL CDR3 comprising the amino acid sequence of SEQ ID NO:20; or

(p) (i) a VH comprising a VH CDR1 comprising the amino acid sequence of SEQ ID NO:63, a VH CDR2 comprising the amino acid sequence of SEQ ID NO:64, and a VH CDR3 comprising the amino acid sequence of SEQ ID NO:65; and (ii) a VL comprising a VL CDR1 comprising the amino acid sequence of SEQ ID NO:66, a VL CDR2 comprising the amino acid sequence of SEQ ID NO:67, and a VL CDR3 comprising the amino acid sequence of SEQ ID NO:68; or

(q) (i) a VH comprising a VH CDR1 comprising the amino acid sequence of SEQ ID NO:69, a VH CDR2 comprising the amino acid sequence of SEQ ID NO:70, and a VH CDR3 comprising the amino acid sequence of SEQ ID NO:71; and (ii) a VL comprising a VL CDR1 comprising the amino acid sequence of SEQ ID NO:72, a VL CDR2 comprising the amino

acid sequence of SEQ ID NO:73, and a VL CDR3 comprising the amino acid sequence of SEQ ID NO:74; or

(r) (i) a VH comprising a VH CDR1 comprising the amino acid sequence of SEQ ID NO:75, a VH CDR2 comprising the amino acid sequence of SEQ ID NO:76, and a VH CDR3 comprising the amino acid sequence of SEQ ID NO:77; and (ii) a VL comprising a VL CDR1 comprising the amino acid sequence of SEQ ID NO:78, a VL CDR2 comprising the amino acid sequence of SEQ ID NO:79, and a VL CDR3 comprising the amino acid sequence of SEQ ID NO:80.

13. The antibody or antigen-binding fragment thereof of any of claims 1-7, wherein the antibody or antigen-binding fragment thereof comprises:

(a) (i) a VH comprising the amino acid sequence of QVX21LKESGPGX22LQPSQTLTLTCSFSGFSLX23TX24GMGVGWX25RQX26SGKGL EWLAIHWDDX27DKYYX28PALKSRLTISX29X30X31SKNQVFLKIX32NVX33TAD X34ATYYCX35RIGTAQATDALDYWGQGTSVTVSS (SEQ ID NO:101), wherein X21 is T or N, X22 is I or K, X23 is N or S, X24 is V or L, X25 is S or I, X26 is P or S, X27 is E or absent, X28 is N or Y, X29 is K or R, X30 is A or D, X31 is T or S, X32 is V or A, X33 is G or D, X34 is T, I, or S, and X35 is T, S, or A; and (ii) a VL comprising the amino acid sequence of DIVMTQAAPSX36X37VTPGESVSISCRSSKSLX38X39SNGNTYLYWFLQRPQGQSPQR LIYYMSNLAGVPDRFSGRSGTDFTLX40ISRVEAX41DVG VYYCMQX42LEX43PLT FGGGTKLEIK (SEQ ID NO:102), wherein X36 is I or V, X37 is P or S, X38 is R or L, X39 is K or H, X40 is R or K, X41 is E or G, X42 is S or G, and X43 is Y or H; or

(b) (i) a VH comprising the amino acid sequence of SEQ ID NO:81; and (ii) a VL comprising the amino acid sequence of SEQ ID NO:82; or

(c) (i) a VH comprising the amino acid sequence of SEQ ID NO:1; and (ii) a VL comprising the amino acid sequence of SEQ ID NO:2; or

(d) (i) a VH comprising the amino acid sequence of SEQ ID NO:21; and (ii) a VL comprising the amino acid sequence of SEQ ID NO:22; or

(e) (i) a VH comprising the amino acid sequence of SEQ ID NO:41; and (ii) a VL comprising the amino acid sequence of SEQ ID NO:42; or

(f) (i) a VH comprising the amino acid sequence of SEQ ID NO:61; and (ii) a VL comprising the amino acid sequence of SEQ ID NO:62.

14. An antibody or antigen-binding fragment thereof of claim 1 that immunospecifically binds to MUC16, wherein the antibody or antigen-binding fragment thereof comprises a VH, which VH comprises:

(a) a VH CDR1 comprising the amino acid sequence TX1GMGVG (SEQ ID NO:103), wherein X1 is L or V; a VH CDR2 comprising the amino acid sequence HIWWDDX2DKYYX3PALKS (SEQ ID NO:104), wherein X2 is E or absent, and X3 is Y or N; and a VH CDR3 comprising the amino acid sequence IGTAQATDLDY (SEQ ID NO:105); or

(b) a VH CDR1 comprising the amino acid sequence GFSLX8TX9GM (SEQ ID NO:109), wherein X8 is N or S, and wherein X9 is L or V; a VH CDR2 comprising the amino acid sequence WDDX10 (SEQ ID NO:110), wherein X10 is E or absent; and a VH CDR3 comprising the amino acid sequence GTAQATDALD (SEQ ID NO:111); or

(c) a VH CDR1 comprising the amino acid sequence GFSLX15TX16GMG (SEQ ID NO:115), wherein X15 is N or S, and X16 is V or L; a VH CDR2 comprising the amino acid sequence IWWDDX17DK (SEQ ID NO:116), wherein X17 is E or absent; and a VH CDR3 comprising the amino acid sequence X18RIGTAQATDALDY (SEQ ID NO:117), wherein X18 is T, A, or S; or

(d) a VH CDR1 comprising the amino acid sequence of SEQ ID NO:83, a VH CDR2 comprising the amino acid sequence of SEQ ID NO:84, and a VH CDR3 comprising the amino acid sequence of SEQ ID NO:85; or

(e) a VH CDR1 comprising the amino acid sequence of SEQ ID NO:89, a VH CDR2 comprising the amino acid sequence of SEQ ID NO:90, and a VH CDR3 comprising the amino acid sequence of SEQ ID NO:91; or

(f) a VH CDR1 comprising the amino acid sequence of SEQ ID NO:95, a VH CDR2 comprising the amino acid sequence of SEQ ID NO:96, and a VH CDR3 comprising the amino acid sequence of SEQ ID NO:97; or

(g) a VH CDR1 comprising the amino acid sequence of SEQ ID NO:3, a VH CDR2 comprising the amino acid sequence of SEQ ID NO:4, and a VH CDR3 comprising the amino acid sequence of SEQ ID NO:5; or

(h) a VH CDR1 comprising the amino acid sequence of SEQ ID NO:9, a VH CDR2 comprising the amino acid sequence of SEQ ID NO:10, and a VH CDR3 comprising the amino acid sequence of SEQ ID NO:11; or

(i) a VH CDR1 comprising the amino acid sequence of SEQ ID NO:15, a VH CDR2 comprising the amino acid sequence of SEQ ID NO:16, and a VH CDR3 comprising the amino acid sequence of SEQ ID NO:17; or

(j) a VH CDR1 comprising the amino acid sequence of SEQ ID NO:23, a VH CDR2 comprising the amino acid sequence of SEQ ID NO:24, and a VH CDR3 comprising the amino acid sequence of SEQ ID NO:25; or

(k) a VH CDR1 comprising the amino acid sequence of SEQ ID NO:29, a VH CDR2 comprising the amino acid sequence of SEQ ID NO:30, and a VH CDR3 comprising the amino acid sequence of SEQ ID NO:31; or

(l) a VH CDR1 comprising the amino acid sequence of SEQ ID NO:35, a VH CDR2 comprising the amino acid sequence of SEQ ID NO:36, and a VH CDR3 comprising the amino acid sequence of SEQ ID NO:37; or

(m) a VH CDR1 comprising the amino acid sequence of SEQ ID NO:43, a VH CDR2 comprising the amino acid sequence of SEQ ID NO:44, and a VH CDR3 comprising the amino acid sequence of SEQ ID NO:45; or

(n) a VH CDR1 comprising the amino acid sequence of SEQ ID NO:49, a VH CDR2 comprising the amino acid sequence of SEQ ID NO:50, and a VH CDR3 comprising the amino acid sequence of SEQ ID NO:51; or

(o) a VH CDR1 comprising the amino acid sequence of SEQ ID NO:55, a VH CDR2 comprising the amino acid sequence of SEQ ID NO:56, and a VH CDR3 comprising the amino acid sequence of SEQ ID NO:57; or

(p) a VH CDR1 comprising the amino acid sequence of SEQ ID NO:63, a VH CDR2 comprising the amino acid sequence of SEQ ID NO:64, and a VH CDR3 comprising the amino acid sequence of SEQ ID NO:65; or

(q) a VH CDR1 comprising the amino acid sequence of SEQ ID NO:69, a VH CDR2 comprising the amino acid sequence of SEQ ID NO:70, and a VH CDR3 comprising the amino acid sequence of SEQ ID NO:71; or

(r) a VH CDR1 comprising the amino acid sequence of SEQ ID NO:75, a VH CDR2 comprising the amino acid sequence of SEQ ID NO:76, and a VH CDR3 comprising the amino acid sequence of SEQ ID NO:77.

15. An antibody or antigen-binding fragment thereof that immunospecifically binds to MUC16, wherein the antibody or antigen-binding fragment thereof comprises:

(a) (i) a VH comprising: a VH CDR1 comprising the amino acid sequence TX1GMGVG (SEQ ID NO:103), wherein X1 is L or V; a VH CDR2 comprising the amino acid sequence HIWWDDX2DKYYX3PALKS (SEQ ID NO:104), wherein X2 is E or absent, and X3 is Y or N; and a VH CDR3 comprising the amino acid sequence IGTAQATDALDY (SEQ ID NO:105); and (ii) a VL comprising: a VL CDR1 comprising the amino acid sequence RSSKSLX4X5SNGNTYLY (SEQ ID NO:106), wherein X4 is R or L, and X5 is K or H; a VL CDR2 comprising the amino acid sequence YMSNLAS (SEQ ID NO:107); and a VL CDR3 comprising the amino acid sequence MQX6LEX7PLT (SEQ ID NO:108), wherein X6 is G or S, and X7 is H or Y; or

(b) (i) a VH comprising: a VH CDR1 comprising the amino acid sequence GFSLX8TX9GM (SEQ ID NO:109), wherein X8 is N or S, and wherein X9 is L or V; a VH CDR2 comprising the amino acid sequence WDDX10 (SEQ ID NO:110), wherein X10 is E or absent; and a VH

CDR3 comprising the amino acid sequence GTAQATDALD (SEQ ID NO:111); and (ii) a VL comprising: a VL CDR1 comprising the amino acid sequence SKSLX11X12SNGNTY (SEQ ID NO:112), wherein X11 is L or R, and X12 is H or K; a VL CDR2 comprising the amino acid sequence YMS (SEQ ID NO:113); and a VL CDR3 comprising the amino acid sequence X13LEX14PL (SEQ ID NO:114), wherein X13 is G or S, and X14 is H or Y; or

(c) (i) a VH comprising: a VH CDR1 comprising the amino acid sequence GFSLX15TX16GMG (SEQ ID NO:115), wherein X15 is N or S, and X16 is V or L; a VH CDR2 comprising the amino acid sequence IWWDDX17DK (SEQ ID NO:116), wherein X17 is E or absent; and a VH CDR3 comprising the amino acid sequence X18RIGTAQATDALDY (SEQ ID NO:117), wherein X18 is T, A, or S; and (ii) a VL comprising: a VL CDR1 comprising the amino acid sequence KSLX19X20SNGNTY (SEQ ID NO:118), wherein X19 is V or L, and X20 is H or K; a VL CDR2 comprising the amino acid sequence YMS (SEQ ID NO:119); and a VL CDR3 comprising the amino acid sequence MQSLEYPLT (SEQ ID NO:120).

16. An antibody or antigen-binding fragment thereof that immunospecifically binds to MUC16, wherein the antibody or antigen-binding fragment thereof comprises:

(a) (i) a VH comprising a VH CDR1 comprising the amino acid sequence of SEQ ID NO:83, a VH CDR2 comprising the amino acid sequence of SEQ ID NO:84, and a VH CDR3 comprising the amino acid sequence of SEQ ID NO:85; and (ii) a VL comprising a VL CDR1 comprising the amino acid sequence of SEQ ID NO:86, a VL CDR2 comprising the amino acid sequence of SEQ ID NO:87, and a VL CDR3 comprising the amino acid sequence of SEQ ID NO:88; or

(b) (i) a VH comprising a VH CDR1 comprising the amino acid sequence of SEQ ID NO:89, a VH CDR2 comprising the amino acid sequence of SEQ ID NO:90, and a VH CDR3 comprising the amino acid sequence of SEQ ID NO:91; and (ii) a VL comprising a VL CDR1

comprising the amino acid sequence of SEQ ID NO:92, a VL CDR2 comprising the amino acid sequence of SEQ ID NO:93, and a VL CDR3 comprising the amino acid sequence of SEQ ID NO:94; or

(c) (i) a VH comprising a VH CDR1 comprising the amino acid sequence of SEQ ID NO:95, a VH CDR2 comprising the amino acid sequence of SEQ ID NO:96, and a VH CDR3 comprising the amino acid sequence of SEQ ID NO:97; and (ii) a VL comprising a VL CDR1 comprising the amino acid sequence of SEQ ID NO:98, a VL CDR2 comprising the amino acid sequence of SEQ ID NO:99, and a VL CDR3 comprising the amino acid sequence of SEQ ID NO:100.

17. An antibody or antigen-binding fragment thereof that immunospecifically binds to MUC16, wherein the antibody or antigen-binding fragment thereof comprises:

(a) (i) a VH comprising a VH CDR1 comprising the amino acid sequence of SEQ ID NO:23, a VH CDR2 comprising the amino acid sequence of SEQ ID NO:24, and a VH CDR3 comprising the amino acid sequence of SEQ ID NO:25; and (ii) a VL comprising a VL CDR1 comprising the amino acid sequence of SEQ ID NO:26, a VL CDR2 comprising the amino acid sequence of SEQ ID NO:27, and a VL CDR3 comprising the amino acid sequence of SEQ ID NO:28; or

(b) (i) a VH comprising a VH CDR1 comprising the amino acid sequence of SEQ ID NO:29, a VH CDR2 comprising the amino acid sequence of SEQ ID NO:30, and a VH CDR3 comprising the amino acid sequence of SEQ ID NO:31; and (ii) a VL comprising a VL CDR1 comprising the amino acid sequence of SEQ ID NO:32, a VL CDR2 comprising the amino acid sequence of SEQ ID NO:33, and a VL CDR3 comprising the amino acid sequence of SEQ ID NO:34; or

(c) (i) a VH comprising a VH CDR1 comprising the amino acid sequence of SEQ ID NO:35, a VH CDR2 comprising the amino acid sequence of SEQ ID NO:36, and a VH CDR3 comprising the amino acid sequence of SEQ ID NO:37; and (ii) a VL comprising a VL CDR1 comprising the amino acid sequence of SEQ ID NO:38, a VL CDR2 comprising the amino acid sequence of SEQ ID NO:39, and a VL CDR3 comprising the amino acid sequence of SEQ ID NO:40.

18. An antibody or antigen-binding fragment thereof that immunospecifically binds to MUC16, wherein the antibody or antigen-binding fragment thereof comprises:

(a) (i) a VH comprising a VH CDR1 comprising the amino acid sequence of SEQ ID NO:43, a VH CDR2 comprising the amino acid sequence of SEQ ID NO:44, and a VH CDR3 comprising the amino acid sequence of SEQ ID NO:45; and (ii) a VL comprising a VL CDR1 comprising the amino acid sequence of SEQ ID NO:46, a VL CDR2 comprising the amino acid sequence of SEQ ID NO:47, and a VL CDR3 comprising the amino acid sequence of SEQ ID NO:48; or

(b) (i) a VH comprising a VH CDR1 comprising the amino acid sequence of SEQ ID NO:49, a VH CDR2 comprising the amino acid sequence of SEQ ID NO:50, and a VH CDR3 comprising the amino acid sequence of SEQ ID NO:51; and (ii) a VL comprising a VL CDR1 comprising the amino acid sequence of SEQ ID NO:52, a VL CDR2 comprising the amino acid sequence of SEQ ID NO:53, and a VL CDR3 comprising the amino acid sequence of SEQ ID NO:54; or

(c) (i) a VH comprising a VH CDR1 comprising the amino acid sequence of SEQ ID NO:55, a VH CDR2 comprising the amino acid sequence of SEQ ID NO:56, and a VH CDR3 comprising the amino acid sequence of SEQ ID NO:57; and (ii) a VL comprising a VL CDR1 comprising the amino acid sequence of SEQ ID NO:58, a VL CDR2 comprising the amino acid sequence of SEQ ID NO:59, and a VL CDR3 comprising the amino acid sequence of SEQ ID NO:60.

19. An antibody or antigen-binding fragment thereof that immunospecifically binds to MUC16, wherein the antibody or antigen-binding fragment thereof comprises:

(a) (i) a VH comprising a VH CDR1 comprising the amino acid sequence of SEQ ID NO:3, a VH CDR2 comprising the amino acid sequence of SEQ ID NO:4, and a VH CDR3 comprising the amino acid sequence of SEQ ID NO:5; and (ii) a VL comprising a VL CDR1 comprising the amino acid sequence of SEQ ID NO:6, a VL CDR2 comprising the amino acid sequence of SEQ ID NO:7, and a VL CDR3 comprising the amino acid sequence of SEQ ID NO:8; or

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

(c) (i) a VH comprising a VH CDR1 comprising the amino acid sequence of SEQ ID NO:15, a VH CDR2 comprising the amino acid sequence of SEQ ID NO:16, and a VH CDR3 comprising the amino acid sequence of SEQ ID NO:17; and (ii) a VL comprising a VL CDR1 comprising the amino acid sequence of SEQ ID NO:18, a VL CDR2 comprising the amino acid sequence of SEQ ID NO:19, and a VL CDR3 comprising the amino acid sequence of SEQ ID NO:20.

20. An antibody or antigen-binding fragment thereof that immunospecifically binds to MUC16, wherein the antibody or antigen-binding fragment thereof comprises:

(a) (i) a VH comprising a VH CDR1 comprising the amino acid sequence of SEQ ID NO:63, a VH CDR2 comprising the amino acid sequence of SEQ ID NO:64, and a VH CDR3 comprising the amino acid sequence of SEQ ID NO:65; and (ii) a VL comprising a VL CDR1

comprising the amino acid sequence of SEQ ID NO:66, a VL CDR2 comprising the amino acid sequence of SEQ ID NO:67, and a VL CDR3 comprising the amino acid sequence of SEQ ID NO:68; or

(b) (i) a VH comprising a VH CDR1 comprising the amino acid sequence of SEQ ID NO:69, a VH CDR2 comprising the amino acid sequence of SEQ ID NO:70, and a VH CDR3 comprising the amino acid sequence of SEQ ID NO:71; and (ii) a VL comprising a VL CDR1 comprising the amino acid sequence of SEQ ID NO:72, a VL CDR2 comprising the amino acid sequence of SEQ ID NO:73, and a VL CDR3 comprising the amino acid sequence of SEQ ID NO:74; or

(c) (i) a VH comprising a VH CDR1 comprising the amino acid sequence of SEQ ID NO:75, a VH CDR2 comprising the amino acid sequence of SEQ ID NO:76, and a VH CDR3 comprising the amino acid sequence of SEQ ID NO:77; and (ii) a VL comprising a VL CDR1 comprising the amino acid sequence of SEQ ID NO:78, a VL CDR2 comprising the amino acid sequence of SEQ ID NO:79, and a VL CDR3 comprising the amino acid sequence of SEQ ID NO:80.

21. An antibody or antigen-binding fragment thereof that immunospecifically binds to MUC16, wherein the antibody or antigen-binding fragment thereof comprises:

(a) (i) a VH comprising the amino acid sequence of QVX₂₁LKESGPGX₂₂LQPSQTLSTCSFSGFSLX₂₃TX₂₄GMGVGWX₂₅RQX₂₆SGKGLEWL AHIWWDDX₂₇DKYYX₂₈PALKSRLTISX₂₉X₃₀X₃₁SKNQVFLKIX₃₂NVX₃₃TADX₃₄ATYY CX₃₅RIGTAQATDALDYWGQGTSVTVSS (SEQ ID NO:101), wherein X₂₁ is T or N, X₂₂ is I or K, X₂₃ is N or S, X₂₄ is V or L, X₂₅ is S or I, X₂₆ is P or S, X₂₇ is E or absent, X₂₈ is N or Y, X₂₉ is K or R, X₃₀ is A or D, X₃₁ is T or S, X₃₂ is V or A, X₃₃ is G or D, X₃₄ is T, I, or S, and X₃₅ is T, S, or A; and (ii) a VL comprising the amino acid sequence of DIVMTQAAPSX₃₆X₃₇VTPGESVSISCRSSKSLX₃₈X₃₉SNGNTYLYWFLQRPQGSPQRLIY YMSNLASGVPDRFSGRSGTDFTLX₄₀ISRVEAX₄₁DVG VYYCMQX₄₂LEX₄₃PLTFGGG

TKLEIK (SEQ ID NO:102), wherein X₃₆ is I or V, X₃₇ is P or S, X₃₈ is R or L, X₃₉ is K or H, X₄₀ is R or K, X₄₁ is E or G, X₄₂ is S or G, and X₄₃ is Y or H; or

(b) (i) a VH comprising the amino acid sequence of SEQ ID NO:81; and (ii) a VL comprising the amino acid sequence of SEQ ID NO:82; or

(c) (i) a VH comprising the amino acid sequence of SEQ ID NO:1; and (ii) a VL comprising the amino acid sequence of SEQ ID NO:2;

(d) (i) a VH comprising the amino acid sequence of SEQ ID NO:21; and (ii) a VL comprising the amino acid sequence of SEQ ID NO:22; or

(e) (i) a VH comprising the amino acid sequence of SEQ ID NO:41; and (ii) a VL comprising the amino acid sequence of SEQ ID NO:42; or

(f) (i) a VH comprising the amino acid sequence of SEQ ID NO:61; and (ii) a VL comprising the amino acid sequence of SEQ ID NO:62.

22. The antibody or antigen-binding fragment thereof of any of claims 1-7, wherein the antibody or antigen-binding fragment thereof comprises:

(a) (i) a VH comprising a VH CDR1 comprising the amino acid sequence of SEQ ID NO:83, a VH CDR2 comprising the amino acid sequence of SEQ ID NO:84, and a VH CDR3 comprising the amino acid sequence of SEQ ID NO:85; and (ii) a VL comprising a VL CDR1 comprising the amino acid sequence of SEQ ID NO:86, a VL CDR2 comprising the amino acid sequence of SEQ ID NO:87, and a VL CDR3 comprising the amino acid sequence of SEQ ID NO:88; or

(b) (i) a VH comprising a VH CDR1 comprising the amino acid sequence of SEQ ID NO:89, a VH CDR2 comprising the amino acid sequence of SEQ ID NO:90, and a VH CDR3 comprising the amino acid sequence of SEQ ID NO:91; and (ii) a VL comprising a VL CDR1

comprising the amino acid sequence of SEQ ID NO:92, a VL CDR2 comprising the amino acid sequence of SEQ ID NO:93, and a VL CDR3 comprising the amino acid sequence of SEQ ID NO:94; or

(c) (i) a VH comprising a VH CDR1 comprising the amino acid sequence of SEQ ID NO:95, a VH CDR2 comprising the amino acid sequence of SEQ ID NO:96, and a VH CDR3 comprising the amino acid sequence of SEQ ID NO:97 and (ii) a VL comprising a VL CDR1 comprising the amino acid sequence of SEQ ID NO:98, a VL CDR2 comprising the amino acid sequence of SEQ ID NO:99, and a VL CDR3 comprising the amino acid sequence of SEQ ID NO:100.

23. An antibody or antigen-binding fragment thereof that immunospecifically binds to MUC16, wherein the antibody or antigen-binding fragment thereof comprises: (i) a VH comprising the amino acid sequence of SEQ ID NO:81; and (ii) a VL comprising the amino acid sequence of SEQ ID NO:82.

24. The antibody or antigen-binding fragment thereof of any of claims 1-9, 12, 14-20, and 22, wherein the antibody or antigen-binding fragment thereof is humanized.

25. The antibody or antigen-binding fragment thereof of any one of claims 1-24, wherein the antibody is a monoclonal antibody.

26. An antibody conjugate comprising the antibody or antigen-binding fragment thereof of any of claims 1-25 conjugated to an agent.

27. The antibody or antigen-binding fragment thereof of any of claims 1-25, wherein the antibody or antigen-binding fragment thereof is a bispecific antibody.

28. The bispecific antibody of claim 27, wherein the bispecific antibody comprises an immunoglobulin that immunospecifically binds MUC16, wherein the light chain of the

immunoglobulin is conjugated via a peptide linker to a single chain variable fragment (scFv) that immunospecifically binds to CD3.

29. A bispecific antibody conjugate comprising the bispecific antibody of claim 27 or 28 conjugated to an agent.

30. The antibody or antigen-binding fragment thereof of any of claims 1-25, wherein the antigen-binding fragment thereof is a scFv.

31. A scFv conjugate comprising the scFv of claim 30 conjugated to an agent.

32. A chimeric antigen receptor (CAR) comprising: the scFv of claim 30 or the scFv conjugate of claim 31.

33. A CAR comprising the antigen-binding fragment of any of claims 1-25.

34. A T cell which recombinantly expresses the CAR of claim 32 or 33.

35. A polynucleotide comprising nucleic acid sequences encoding: (i) the scFv of claim 30, (ii) the scFv conjugate of claim 31, or (iii) the CAR of claim 32 or 33.

36. An *ex vivo* cell comprising one or more polynucleotides encoding the antibody or antigen-binding fragment thereof of any of claims 1-25 operably linked to a promoter.

37. A pharmaceutical composition comprising: a therapeutically effective amount of the antibody or antigen-binding fragment thereof of any of claims 1-25, the antibody conjugate of claim 26, the bispecific antibody of claim 27 or 28, the bispecific antibody conjugate of claim 29, the scFv of claim 30, the scFv conjugate of claim 31, or the CAR of claim 32.

38. A pharmaceutical composition comprising a therapeutically effective amount of the CAR of claim 33 and a pharmaceutically acceptable carrier.

39. The pharmaceutical composition of claim 37 for use in the treatment of cancer in a patient in need thereof.

40. The pharmaceutical composition of claim 38 for use in the treatment of cancer in a patient in need thereof.

41. The pharmaceutical composition of claim 39 or 40, wherein said cancer is a cancer of the lung, pancreas, breast, uterine, fallopian tube, primary peritoneum, or ovary.

42. The pharmaceutical composition of any of claims 39-41, wherein said patient is a human patient.

43. The pharmaceutical composition of any of claims 39-42, wherein the pharmaceutical composition is to be administered to the patient in combination with a therapeutically effective amount of an additional therapeutic agent.