CLAIMS:

1. An anti-glyco-MUC4 antibody or antigen binding fragment that specifically binds to a MUC4 peptide CTIPSTAMHTR**ST**AAPIPILP (SEQ ID NO:154) that has been glycosylated with GalNAc on the serine and threonine residues shown with bold and underlined text ("the MUC4 glycopeptide").

2. The anti-glyco-MUC4 antibody or antigen binding fragment of claim 1, which specifically binds to COSMC knock-out T3M4 cells.

3. The anti-glyco-MUC4 antibody or antigen-binding fragment of claim 1 or 2, which comprises:

(a) a VH comprising CDR-H1, CDR-H2, and CDR-H3 having the amino sequences of SEQ ID NOs:3-5, respectively, and a VL comprising CDR-L1, CDR-L2, and CDR-L3 having the amino acid sequences of SEQ ID NOs:6-8, respectively;

(b) a VH comprising CDR-H1, CDR-H2, and CDR-H3 having the amino sequences of SEQ ID NOs:9-11, respectively, and a VL comprising CDR-L1, CDR-L2, and CDR-L3 having the amino acid sequences of SEQ ID NOs:12-14, respectively; or

(c) a VH comprising CDR-H1, CDR-H2, and CDR-H3 having the amino sequences of SEQ ID NOs:15-17, respectively, and a VL comprising CDR-L1, CDR-L2, and CDR-L3 having the amino acid sequences of SEQ ID NOs:18-20, respectively.

4. The anti-glyco-MUC4 antibody or antigen-binding fragment of claim 1 or 2, which comprises:

(a) a VH comprising CDR-H1, CDR-H2, and CDR-H3 having the amino sequences of SEQ ID NOs:25-27, respectively, and a VL comprising CDR-L1, CDR-L2, and CDR-L3 having the amino acid sequences of SEQ ID NOs:28-30, respectively;

(b) a VH comprising CDR-H1, CDR-H2, and CDR-H3 having the amino sequences of SEQ ID NOs:31-33, respectively, and a VL comprising CDR-L1, CDR-L2, and CDR-L3 having the amino acid sequences of SEQ ID NOs:34-36, respectively; or

(c) a VH comprising CDR-H1, CDR-H2, and CDR-H3 having the amino sequences of SEQ ID NOs:37-39, respectively, and a VL comprising CDR-L1, CDR-L2, and CDR-L3 having the amino acid sequences of SEQ ID NOs:40-42, respectively.

5. The anti-glyco-MUC4 antibody or antigen-binding fragment of claim 1 or 2, which comprises:

(a) a VH comprising CDR-H1, CDR-H2, and CDR-H3 having the amino sequences of SEQ ID NOs:47-49, respectively, and a VL comprising CDR-L1, CDR-L2, and CDR-L3 having the amino acid sequences of SEQ ID NOs:50-52, respectively;

(b) a VH comprising CDR-H1, CDR-H2, and CDR-H3 having the amino sequences of SEQ ID NOs:53-55, respectively, and a VL comprising CDR-L1, CDR-L2, and CDR-L3 having the amino acid sequences of SEQ ID NOs:56-58, respectively; or

(c) a VH comprising CDR-H1, CDR-H2, and CDR-H3 having the amino sequences of SEQ ID NOs:59-61, respectively, and a VL comprising CDR-L1, CDR-L2, and CDR-L3 having the amino acid sequences of SEQ ID NOs:62-64, respectively.

6. The anti-glyco-MUC4 antibody or antigen-binding fragment of any one of claims 3 to 5, which is a chimeric or humanized antibody or antigen-binding fragment of a chimeric or humanized antibody.

7. The anti-glyco-MUC4 antibody or antigen-binding fragment of any one of claims 3 to 6, which comprises:

(a) a VH comprising an amino acid sequence having at least 95% sequence identity to SEQ ID NO:1 and a VL comprising an amino acid sequence having at least 95% sequence identity to SEQ ID NO:2;

(b) a VH comprising an amino acid sequence having at least 95% sequence identity to SEQ ID NO:23 and a VL comprising an amino acid sequence having at least 95% sequence identity to SEQ ID NO:24.

(c) a VH comprising an amino acid sequence having at least 95% sequence identity to SEQ ID NO:45 and a VL comprising an amino acid sequence having at least 95% sequence identity to SEQ ID NO:46.

8. The anti- glyco-MUC4 antibody or antigen-binding fragment of claim 7, which comprises:

(a) a VH comprising SEQ ID NO:1 and a VL comprising SEQ ID NO:2;

(b) a VH comprising SEQ ID NO:23 and a VL comprising SEQ ID NO:24; or

(c) a VH comprising SEQ ID NO:45 and a VL comprising SEQ ID NO:46.

9. The anti-glyco-MUC4 antibody or antigen-binding fragment of claim 7, which comprises a VH comprising SEQ ID NO:1 and a VL comprising SEQ ID NO:2.

10. An anti-glyco-MUC4 antibody or antigen-binding fragment comprising the heavy chain CDR sequences of any one of SEQ ID NOS:133-144 and the light chain CDR sequences of any one of SEQ ID NOS:145-153.

11. The anti-glyco-MUC4 antibody or antigen-binding fragment of claim 10, which comprises a VH comprising the amino acid sequence of any one of SEQ ID NOS:133-144 and a VL comprising the amino acid sequence of any one of SEQ ID NOS:145-153.

12. The anti-glyco-MUC4 antibody or antigen-binding fragment of claim 10, which comprises a VH comprising the heavy chain CDR sequences of SEQ ID NO:140 and the light chain CDR sequences of SEQ ID NO:145.

13. The anti-glyco-MUC4 antibody or antigen-binding fragment of claim 10, which comprises a VH comprising SEQ ID NO:140 and a VL comprising SEQ ID NO:145.

14. The anti-glyco-MUC4 antibody or antigen-binding fragment of claim 10, which comprises a VH comprising the heavy chain CDR sequences of SEQ ID NO:140 and the light chain CDR sequences of SEQ ID NO:152.

15. The anti-glyco-MUC4 antibody or antigen-binding fragment of claim 10, which comprises a VH comprising SEQ ID NO:140 and a VL comprising SEQ ID NO:152.

16. The anti-glyco-MUC4 antibody or antigen-binding fragment of any one of claims 3 to 15, which preferentially binds to a glyco-MUC4 epitope that is overexpressed on cancer cells as compared to normal cells.

17. The anti-glyco-MUC4 antibody or antigen-binding fragment of any one of claims 3 to 15, which specifically binds to a MUC4 peptide CTIPSTAMHTR**ST**AAPIPILP (SEQ ID NO:154) that has been glycosylated with STn on the serine and threonine residues shown with bold and underlined text.

18. The anti-glyco-MUC4 antibody or antigen-binding fragment of any one of claims 3 to 15, which does not specifically bind to a MUC4 peptide CTIPSTAMHTRSTAAPIPILP (SEQ ID NO:154) that has been glycosylated with STn on the serine and threonine residues shown with bold and underlined text.

19. The anti-glyco-MUC4 antibody or antigen-binding fragment of any of claims 3 to 18, which binds to the MUC4 glycopeptide with a binding affinity (KD) of:

(a) 1 nM to 200 nM as measured by surface plasmon resonance or bio-layer interferometry;

(b) 1 nM to 150 nM as measured by surface plasmon resonance or bio-layer interferometry;

(c) 1 nM to 100 nM as measured by surface plasmon resonance or bio-layer interferometry;

(d) 1 nM to 50 nM as measured by surface plasmon resonance or bio-layer interferometry;

(e) 5 nM to 200 nM as measured by surface plasmon resonance or bio-layer interferometry;

(f) 5 nM to 100 nM as measured by surface plasmon resonance or bio-layer interferometry;

(g) 5 nM to 50 nM as measured by surface plasmon resonance or bio-layer interferometry;

(h) 5 nM to 25 nM as measured by surface plasmon resonance or bio-layer interferometry;

(i) 5 nM to 10 nM as measured by surface plasmon resonance or bio-layer interferometry;

(j) 10 nM to 200 nM as measured by surface plasmon resonance or bio-layer interferometry;

(k) 10 nM to 100 nM as measured by surface plasmon resonance or bio-layer interferometry;

(l) 10 nM to 150 nM as measured by surface plasmon resonance or bio-layer interferometry;

(m) 10 nM to 100 nM as measured by surface plasmon resonance or bio-layer interferometry;

(n) 10 nM to 50 nM as measured by surface plasmon resonance or bio-layer interferometry;

(o) 10 nM to 25 nM as measured by surface plasmon resonance or bio-layer interferometry;

(p) 50 nM to 200 nM as measured by surface plasmon resonance or bio-layer interferometry;

(q) 50 nM to 150 nM as measured by surface plasmon resonance or bio-layer interferometry;

(r) 50 nM to 100 nM as measured by surface plasmon resonance or bio-layer interferometry;

(s) 100 nM to 200 nM as measured by surface plasmon resonance or bio-layer interferometry; or

(t) 100 nM to 150 nM as measured by surface plasmon resonance or bio-layer interferometry.

20. The anti-glyco-MUC4 antibody or antigen-binding fragment of any of claims 3 to 19, which does not specifically bind to the unglycosylated MUC4 peptide CTIPSTAMHTRSTAAPIPILP (SEQ ID NO:155) (the “unglycosylated MUC4 peptide”).

21. The anti-glyco-MUC4 antibody or antigen-binding fragment of any of claims 3 to 20, which does not specifically bind to the MUC1 tandem repeat $(VTSAPDTRPAPGSTAPPAHG)_3$ (SEQ ID NO:201) that has been glycosylated in vitro using purified recombinant human glycosyltransferases GalNAc-T1, GalNAc-T2, and GalNAc-T4 (“the first MUC1 glycopeptide”).

22. The anti-glyco-MUC4 antibody or antigen-binding fragment of any of claims 3 to 21, which does not specifically bind to the MUC1 peptide TAPPAHGV**TS**APD**T**RPAPG**ST**APPAHGVT (SEQ ID NO:202) that has been glycosylated in vitro with GalNAc on the serine and threonine residues shown with bold and underlined text (the “second MUC1 glycopeptide”).

23. The anti-glyco-MUC4 antibody or antigen-binding fragment of any of claims 3 to 22, which does not specifically bind to the CD44v6 peptide GYRQ**T**PKEDSH**S**TTGTAAA (SEQ ID NO:218) that has been glycosylated in vitro with GalNAc on the threonine and serine residues shown with bold and underlined text (the “CD44v6 glycopeptide”).

24. The anti-glyco-MUC4 antibody or antigen-binding fragment of any of claims 3 to 23, which does not specifically bind to the LAMP1 peptide CEQDRP**S**P**TT**APPAPPSPSP (SEQ ID NO:219) that has been glycosylated in vitro with GalNAc on the serine and threonine residues shown with bold and underlined text (the “LAMP1 glycopeptide”).

25. The anti-glyco-MUC4 antibody or antigen-binding fragment of any of claims 3 to 24, which does not specifically bind to the cMET peptide PTKSFISGG**ST**ITGVGKNLN (SEQ ID NO:220) that has been glycosylated in vitro with GalNAc on the serine and threonine residues shown with bold and underlined text (the “cMET glycopeptide”).

26. The anti-glyco-MUC4 antibody or antigen-binding fragment of any of claims 3 to 25, which is multivalent.

27. The anti-glyco-MUC4 antibody or antigen-binding fragment of any of claims 3 to 26, which is an antigen-binding fragment.

28. The anti-glyco-MUC4 antibody or antigen-binding fragment of claim 27, wherein the antigen-binding fragment is in the form of a single-chain variable fragment (scFv).

29. The anti-glyco-MUC4 antibody or antigen-binding fragment of any of claims 3 to 26, which is in the form of a multispecific antibody.

30. The anti-glyco-MUC4 antibody or antigen-binding fragment of claim 29, wherein the multispecific antibody is a bispecific antibody that binds to a second epitope that is different from the first epitope.

31. The anti-glyco-MUC4 antibody or antigen-binding fragment of claim 30, wherein the bispecific antibody is a bottle opener, mAb-Fv, mAb-scFv, central-scFv, one-armed central-scFv, or dual scFv format bispecific antibody.

32. The anti-glyco-MUC4 antibody or antigen-binding fragment of claim 30, wherein the bispecific antibody is a bispecific domain-exchanged antibody (e.g., a CrossMab), a Fab-arm exchange antibody, a bispecific T-cell engager (BiTE), or a dual-affinity retargeting molecule (DART).

33. The anti-glyco-MUC4 antibody or antigen-binding fragment of any one of claims 30 to 32, wherein the second epitope is a MUC4 epitope.

34. The anti-glyco-MUC4 antibody of antigen-binding fragment of any one of claims 30 to 32, wherein the second epitope is a MUC4 epitope that is overexpressed on cancer cells as compared to normal cells.

35. The anti-glyco-MUC4 antibody or antigen-binding fragment of any one of claims 30 to 32, wherein the second epitope is a T-cell epitope.

36. The anti-glyco-MUC4 antibody or antigen-binding fragment of claim 35, wherein the T-cell epitope comprises a CD3 epitope, a CD8 epitope, a CD16 epitope, a CD25 epitope, a CD28 epitope, or an NKG2D epitope.

37. A fusion protein comprising the amino acid sequence of the anti-glyco-MUC4 antibody or antigen-binding fragment of any of claims 3 to 36 operably linked to at least a second amino acid sequence.

38. A chimeric antigen receptor (CAR) comprising one or more antigen-binding fragments according to claim 27 or claim 28.

39. An antibody-drug conjugate comprising the anti-glyco-MUC4 antibody or antigen-binding fragment of any of claims 3 to 36 or the fusion protein of claim 37 conjugated to a cytotoxic agent.

40. A chimeric T cell receptor (TCR) comprising:

(a) an antigen-binding fragment according to claim 27 or claim 28;

(b) a first polypeptide chain comprising a transmembrane domain from a TCR α chain, TCR β chain, TCR γ chain, or TCR δ chain; and

(c) a second polypeptide chain comprising a transmembrane domain from a TCR α chain, TCR β chain, TCR γ chain, or TCR δ chain.

41. A nucleic acid comprising a coding region for an anti-glyco-MUC4 antibody or antigen-binding fragment of any of claims 1 to 36, the fusion protein of claim 37, the CAR of claim 38, or the chimeric TCR of claim 40.

42. A vector comprising the nucleic acid of claim 41.

43. A host cell engineered to express the nucleic acid of claim 41 or comprising the vector of claim 43.

44. A pharmaceutical composition comprising (a) the anti-glyco-MUC4 antibody or antigen binding fragment of any of claims 1 to 36, the fusion protein of claim 38, the CAR of claim 38, the antibody-drug conjugate of claim 39, the chimeric TCR of claim 40, the nucleic acid of claim 41, the vector of claim 42, or the host cell of claim 43, and (b) a physiologically suitable buffer, adjuvant, diluent, or combination thereof.

45. Use of the anti-glyco-MUC4 antibody or antigen binding fragment of any of claims 3 to 36, the fusion protein of claim 37, the CAR of claim 38, the antibody-drug conjugate of claim 39, the chimeric TCR of claim 40, the nucleic acid of claim 41, the vector of claim 42, the host cell of claim 43, or the pharmaceutical composition of claim 44 in the manufacture of a medicament for treating cancer.

46. The use of claim 45, wherein the cancer is pancreatic cancer, lung cancer, breast cancer, cancer of the gall bladder, salivary gland cancer, prostate cancer, biliary tract cancer,

esophageal cancer, papillary thyroid carcinoma, low-grade fibromyxoid sarcoma, or ovarian cancer.

47. A method of detecting cancer in a biological sample, comprising contacting a sample (e.g., a sample comprising or suspected of comprising cancer cells and/or cancer-derived extracellular vesicles) with an anti-glyco-MUC4 antibody or antigen-binding fragment according to any one of claims 3 to 36 and detecting binding of the anti-glyco-MUC4 antibody or antigen-binding fragment.

48. The method of claim 47, wherein the cancer is pancreatic cancer, lung cancer, breast cancer, cancer of the gall bladder, salivary gland cancer, prostate cancer, biliary tract cancer, esophageal cancer, papillary thyroid carcinoma, low-grade fibromyxoid sarcoma, or ovarian cancer.