Claims

It is claimed:

1. An isolated antibody, or an antigen binding fragment thereof, which specifically binds to trophoblast cell-surface antigen-2 (Trop-2), wherein the antibody comprises

(a) a heavy chain variable (VH) region complementary determining regions comprising (i) a VH complementary determining region one (CDR1) comprising the sequence SYGVH (SEQ ID NO: 30), GGSISSY (SEQ ID NO: 36), or GGSISSYGVH (SEQ ID NO: 37); (ii) a VH CDR2 comprising the sequence VIWTX$_1$GX$_2$TDYNSALMX$_3$, wherein X$_1$ is G or S; X$_2$ is S or V; X$_3$ is S or G (SEQ ID NO: 49), or WTX$_1$GX$_2$, wherein X$_1$ is G or S, X$_2$ is S or V (SEQ ID NO: 50); and iii) a VH CDR3 comprising the sequence DYDRYTX$_1$DY, wherein X$_1$ is E or M (SEQ ID NO: 82); and/or

(b) a light chain variable region (VL) region complementary determining regions comprising (i) a VL CDR1 comprising the sequence RASKSVSTSX$_1$YSYMH, wherein X$_1$ is G, L, or N (SEQ ID NO: 63); (ii) a VL CDR2 comprising the sequence LASNLES (SEQ ID NO: 55); and (iii) a VL CDR3 comprising the sequence QHSRELPYT (SEQ ID NO: 56);

2. An isolated antibody, or an antigen binding fragment thereof, which specifically binds to Trop-2, wherein the antibody comprises:

a VH region comprising a VH CDR1, VH CDR2, and VH CDR3 of the VH sequence shown in SEQ ID NO: 5 or 85; and/or

a VL region comprising VL CDR1, VL CDR2, and VL CDR3 of the VL sequence shown in SEQ ID NO:3 or 6.

3. The antibody or the antigen binding fragment of claim 2, wherein the VH region comprises (i) a VH CDR1 comprising the sequence SYGVH (SEQ ID NO: 30), GGSISSY (SEQ ID NO: 36), or GGSISSYGVH (SEQ ID NO: 37); (ii) a VH CDR2 comprising the sequence VIWTSGVTDYNSALMG (SEQ ID NO: 38) or WTSGV (SEQ

ID NO: 39); and (iii) a VH CDR3 comprising the sequence DGDYDRYTMDY (SEQ ID NO: 35), DYDRYTMDY (SEQ ID NO: 99), or DYDRYTEDY (SEQ ID NO: 100).

4. The antibody or antigen binding fragment of claim 3, wherein the VL region comprises (i) a VL CDR1 comprising the sequence RASKSVSTSGYSYMH (SEQ ID NO: 54) or RASKSVSTSLYSYMH (SEQ ID NO: 57) ; (ii) a VL CDR2 comprising the sequence LASNLES (SEQ ID NO: 55); and (iii) a VL CDR3 comprising the sequence QHSRELPYT (SEQ ID NO: 56).

5. The antibody or the antigen binding fragment of claim 4, wherein the VH region comprises the sequence shown in SEQ ID NO: 5, 85 or a variant with one or several conservative amino acid substitutions in residues that are not within a CDR and/or the VL region comprises the amino acid sequence shown in SEQ ID NO: 3, 6 or a variant thereof with one or several amino acid substitutions in amino acids that are not within a CDR.

6. The antibody or the antigen binding fragment of claim 5, wherein the antibody comprises a light chain comprising the sequence shown in SEQ ID NO: 66 and a heavy chain comprising the sequence shown in SEQ ID NO: 65 or 102 .

7. The antibody or the antigen binding fragment of claim 3, wherein the antibody comprises a VH region produced by the expression vector with ATCC Accession No. PTA-12872.

8. The antibody or the antigen binding fragment of claim 4, wherein the antibody comprises a VL region produced by the expression vector with ATCC Accession No. PTA-12871.

9. An isolated antibody, or an antigen binding fragment thereof, which specifically binds to domain 3 and domain 4 of human Trop-2 (SEQ ID NO:27) with a monovalent antibody binding affinity (K_D) of about 6.5 nM or less as measured by surface plasmon resonance.

10. An isolated antibody, or an antigen binding fragment thereof, which specifically binds to Trop-2, wherein the antibody comprises

(a) a heavy chain variable (VH) region complementary determining regions comprising (i) a VH complementary determining region one (CDR1) comprising the sequence SYWIN (SEQ ID NO: 40), GYTFTSY (SEQ ID NO: 41), or GYTFTSYWIN (SEQ ID NO: 42); (ii) a VH CDR2 comprising the sequence $NIX_1PSDSYSNYNX_2KFKD$ wherein X_1 is Y or F; X_2 is Q or K, or X_1PSDSY wherein X_1 is Y or F (SEQ ID NO: 52); and iii) a VH CDR3 comprising the sequence GSX_1FDY wherein X_1 is S or G (SEQ ID NO: 53); and/or

(b) a light chain variable region (VL) region complementary determining regions comprising (i) a VL CDR1 comprising the sequence RASQTIGTSIH (SEQ ID NO: 59); (ii) a VL CDR2 comprising the sequence YASESIS (SEQ ID NO: 60); and (iii) a VL CDR3 comprising the sequence X_1QSX_2SWPFT wherein X_1 is Q or S; X_2 is N or F (SEQ ID NO:64).

11. An isolated antibody, or an antigen binding fragment thereof, which specifically binds to Trop-2, wherein the antibody comprises:

a VH region comprising a VH CDR1, VH CDR2, and VH CDR3 of the VH sequence shown in SEQ ID NO: 13; and/or

a VL region comprising VL CDR1, VL CDR2, and VL CDR3 of the VL sequence shown in SEQ ID NO: 12.

12. The antibody or the antigen binding fragment of claim 11, wherein the VH region comprises (i) a VH CDR1 comprising the sequence SYWIN (SEQ ID NO: 40), GYTFTSY (SEQ ID NO: 41), or GYTFTSYWIN (SEQ ID NO: 42); (ii) a VH CDR2 comprising the sequence NIFPSDSYSNYNKKFKD (SEQ ID NO: 46) or FPSDSY (SEQ ID NO: 47); and (iii) a VH CDR3 comprising the sequence GSGFDY (SEQ ID NO: 48).

13. The antibody or antigen binding fragment of claim 12, wherein the VL region comprises (i) a VL CDR1 comprising the sequence RASQTIGTSIH (SEQ ID NO: 59); (ii) a VL CDR2 comprising the sequence YASESIS (SEQ ID NO: 60); and (iii) a VL CDR3 comprising the sequence SQSFSWPFT (SEQ ID NO: 62).

14. The antibody or the antigen binding fragment of claim 13, wherein the VH region comprises the sequence shown in SEQ ID NO: 13 or a variant with one or several conservative amino acid substitutions in residues that are not within a CDR and/or the VL region comprises the amino acid sequence shown in SEQ ID NO: 12 or a variant thereof with one or several amino acid substitutions in amino acids that are not within a CDR.

15. The antibody or the antigen binding fragment of claim 14, wherein the antibody comprises a light chain comprising the sequence shown in SEQ ID NO: 68 and a heavy chain comprising the sequence shown in SEQ ID NO: 67.

16. An isolated antibody which specifically binds to Trop-2 and competes with the antibody of claim 2 or 4.

17. The antibody of claim 16, wherein the antibody has a monovalent antibody binding affinity (K_D) of about 6.5 nM or less as measured by surface plasmon resonance.

18. The antibody of any one of claims 1-15, wherein the antibody comprises an acyl donor glutamine-containing tag engineered at a specific site.

19. The antibody of claim 18, wherein the tag comprises an amino acid sequence GGLLQGG (SEQ ID NO: 78), LLQGA (SEQ ID NO:79), or LLQ.

20. The antibody of claim 19, wherein the antibody further comprises an amino acid modification at position 222, 340, or 370.

21. The antibody of claim 20, wherein the amino acid modification is a substitution from lysine to arginine.

22. A conjugate of the antibody or the antigen binding fragment of any one of claims 1-15 and 18-21, wherein the antibody or the antigen binding fragment is conjugated to an agent, wherein the agent is selected from the group consisting of a cytotoxic agent, an immunomodulating agent, an imaging agent, a therapeutic protein, a biopolymer, and an oligonucleotide.

23. The conjugate of claim 22, wherein the agent is a cytotoxic agent.

24. The conjugate of claim 23, wherein the cytotoxic agent is MMAD (Monomethyl Auristatin D) or 0101 (2-methylalanyl-*N*-[(3*R*,4*S*,5*S*)-3-methoxy-1-{(2*S*)-2-[(1*R*,2*R*)-1-methoxy-2-methyl-3-oxo-3-{[(1*S*)-2-phenyl-1-(1,3-thiazol-2-yl)ethyl]amino}propyl]pyrrolidin-1-yl}-5-methyl-1-oxoheptan-4-yl]-*N*-methyl-L-valinamide).

25. The conjugate of claim 24, wherein the conjugate comprises the formula: antibody-(acyl donor glutamine-containing tag)-(linker)-(cytotoxic agent).

26. The conjugate of claim 25, wherein the acyl donor glutamine-containing tag comprises an amino acid sequence GGLLQGG (SEQ ID NO: 78), LLQGA (SEQ NO: 79), LLQ, or $LLQX_1X_2X_3X_4X_5$, wherein X_1 is G or P, wherein X_2 is A, G, P, or absent, wherein X_3 is A, G, K, P, or absent, wherein X_4 is G, K, or absent, and wherein X_5 is K or absent (SEQ ID NO: 88), and wherein the linker comprises acetyl-lysine-valine-citrulline-*p*-aminobenzyloxycarbonyl or amino-PEG6-propionyl.

27. The conjugate of claim 26, wherein the conjugate is selected from the group consisting of 1) antibody-LLQGA (SEQ ID NO: 79)- (acetyl-lysine-valine-citrulline-*p*-aminobenzyloxycarbonyl (AcLys-VC-PABC))-0101; 2) antibody-LLQGA (SEQ ID NO: 79)-(AcLys-VC-PABC)-MMAD; 3) antibody-$LLQX_1X_2X_3X_4X_5$ (SEQ ID NO: 88)-(AcLys-VC-PABC)-0101; 4) antibody-$LLQX_1X_2X_3X_4X_5$ (SEQ ID NO: 88)-(AcLys-VC-PABC)-MMAD; 5) antibody –GGLLQGG (SEQ ID NO: 78)- (AcLys-VC-PABC)-0101; and 6) antibody–GGLLQGG (SEQ ID NO: 78)-(AcLys-VC-PABC)-MMAD.

28. The conjugate of claim 27, wherein the conjugate 1) antibody –GGLLQGG (SEQ ID NO: 78)-(AcLys-VC-PABC)-0101; 2) antibody–GGLLQGG (SEQ ID NO: 78)-(AcLys-VC-PABC)-MMAD; 3) antibody-$LLQX_1X_2X_3X_4X_5$ (SEQ ID NO: 88)-(AcLys-VC-PABC)-0101; 4) antibody-$LLQX_1X_2X_3X_4X_5$ (SEQ ID NO: 88)-(AcLys-VC-PABC)-MMAD; 5) antibody-LLQGA (SEQ ID NO: 79)-(AcLys-VC-PABC)-0101; or 6) antibody-LLQGA (SEQ ID NO: 79)- AcLys-VC-PABC-MMAD comprises an amino acid substitution from lysine to arginine at position 222.

29. The conjugate of claim 27, wherein the conjugate 1) antibody-LLQGA (SEQ ID NO: 79)-(AcLys-VC-PABC)-0101; 2) antibody-LLQGA (SEQ ID NO: 79)-

AcLys-VC-PABC-MMAD; 3) antibody-LLQX$_1$X$_2$X$_3$X$_4$X$_5$ (SEQ ID NO: 88)-(AcLys-VC-PABC)-0101; or 4) antibody-LLQX$_1$X$_2$X$_3$X$_4$X$_5$ (SEQ ID NO: 88)-(AcLys-VC-PABC)-MMAD, wherein the amino acid lysine at the C-terminus of heavy chain of the antibody is deleted.

30. The conjugate of claim 24, wherein the conjugate comprises amino acid substitutions at position N297Q and K222R, a linker comprising amino-PEG6-propionyl, and a cytotoxic agent comprising MMAD.

31. A pharmaceutical composition comprising a therapeutically effective amount of the antibody of any one of claims 1-15 or the conjugate of any one of claims 22-30 and a pharmaceutically acceptable carrier.

32. An isolated polynucleotide comprising a nucleotide sequence encoding the antibody of any one of claims 1-15.

33. A vector comprising the polynucleotide of claim 32.

34. An isolated host cell that recombinantly produces the antibody of any one of claims 1-15.

35. A method of producing an antibody, comprising culturing the host cell of claim 34 under conditions that result in production of the antibody, and isolating the antibody from the host cell or culture.

36. A method of treating a condition associated with Trop-2 expression in a subject comprising administering to a subject in need thereof an effective amount of the pharmaceutical composition of claim 31.

37. The method of claim 36, wherein the condition is a cancer.

38. The method of claim 37, wherein the cancer is selected from the group consisting of bladder, breast, cervical, choriocarcinoma, colon, esophageal, gastric, glioblastoma, head and neck, kidney, lung, oral, ovarian, pancreatic, prostate, and skin cancer

39. A method of inhibiting tumor growth or progression in a subject who has a Trop-2 expressing tumor, comprising administering to the subject in need thereof an effective amount of the pharmaceutical composition of claim 31 to the subject.

40. A method of inhibiting metastasis of Trop-2 expressing cancer cells in a subject, comprising administering to the subject in need thereof an effective amount of the pharmaceutical composition of claim 31 to the subject.

41. A method of induce tumor regression in a subject who has a Trop-2 expressing tumor, comprising administering to the subject in need thereof an effective amount of the pharmaceutical composition of claim 31 to the subject.

Claims

1. An isolated antibody, or an antigen binding fragment thereof, which specifically binds to trophoblast cell-surface antigen-2 (Trop-2), wherein the antibody comprises

(a) a heavy chain variable (VH) region complementary determining regions comprising (i) a VH complementary determining region one (CDR1) comprising the sequence SYGVH (SEQ ID NO: 30), GGSISSY (SEQ ID NO: 36), or GGSISSYGVH (SEQ ID NO: 37); (ii) a VH CDR2 comprising the sequence VIWTX$_1$GX$_2$TDYNSALMX$_3$, wherein X$_1$ is G or S; X$_2$ is S or V; X$_3$ is S or G (SEQ ID NO: 49), or WTX$_1$GX$_2$, wherein X$_1$ is G or S, X$_2$ is S or V (SEQ ID NO: 50); and iii) a VH CDR3 comprising the sequence DYDRYTX$_1$DY, wherein X$_1$ is E or M (SEQ ID NO: 82); and/or

(b) a light chain variable region (VL) region complementary determining regions comprising (i) a VL CDR1 comprising the sequence RASKSVSTSX$_1$YSYMH, wherein X$_1$ is G, L, or N (SEQ ID NO: 63); (ii) a VL CDR2 comprising the sequence LASNLES (SEQ ID NO: 55); and (iii) a VL CDR3 comprising the sequence QHSRELPYT (SEQ ID NO: 56).

2. An isolated antibody, or an antigen binding fragment thereof, which specifically binds to Trop-2, wherein the antibody comprises:

a VH region comprising a VH CDR1, VH CDR2, and VH CDR3 of the VH sequence shown in SEQ ID NO: 5 or 85; and/or

a VL region comprising VL CDR1, VL CDR2, and VL CDR3 of the VL sequence shown in SEQ ID NO:3 or 6.

3. The antibody or the antigen binding fragment of claim 2, wherein the VH region comprises (i) a VH CDR1 comprising the sequence SYGVH (SEQ ID NO: 30), GGSISSY (SEQ ID NO: 36), or GGSISSYGVH (SEQ ID NO: 37); (ii) a VH CDR2 comprising the sequence VIWTSGVTDYNSALMG (SEQ ID NO: 38) or WTSGV (SEQ

ID NO: 39); and (iii) a VH CDR3 comprising the sequence DGDYDRYTMDY (SEQ ID NO: 35), DYDRYTMDY (SEQ ID NO: 99), or DYDRYTEDY (SEQ ID NO: 100).

4. The antibody or antigen binding fragment of claim 3, wherein the VL region comprises (i) a VL CDR1 comprising the sequence RASKSVSTSGYSYMH (SEQ ID NO: 54) or RASKSVSTSLYSYMH (SEQ ID NO: 57) ; (ii) a VL CDR2 comprising the sequence LASNLES (SEQ ID NO: 55); and (iii) a VL CDR3 comprising the sequence QHSRELPYT (SEQ ID NO: 56).

5. The antibody or the antigen binding fragment of claim 4, wherein the VH region comprises the sequence shown in SEQ ID NO: 5, 85 or a variant with one or several conservative amino acid substitutions in residues that are not within a CDR and/or the VL region comprises the amino acid sequence shown in SEQ ID NO: 3, 6 or a variant thereof with one or several amino acid substitutions in amino acids that are not within a CDR.

6. The antibody or the antigen binding fragment of claim 5, wherein the antibody comprises a light chain comprising the sequence shown in SEQ ID NO: 66 and a heavy chain comprising the sequence shown in SEQ ID NO: 65 or 102 .

7. The antibody or the antigen binding fragment of claim 3, wherein the antibody comprises a VH region produced by the expression vector with ATCC Accession No. PTA-12872.

8. The antibody or the antigen binding fragment of claim 4, wherein the antibody comprises a VL region produced by the expression vector with ATCC Accession No. PTA-12871.

9. An isolated antibody, or an antigen binding fragment thereof, which specifically binds to domain 3 and domain 4 of human Trop-2 (SEQ ID NO:27) with a monovalent antibody binding affinity (K_D) of about 6.5 nM or less as measured by surface plasmon resonance.

10. An isolated antibody, or an antigen binding fragment thereof, which specifically binds to Trop-2, wherein the antibody comprises

(a) a heavy chain variable (VH) region complementary determining regions comprising (i) a VH complementary determining region one (CDR1) comprising the sequence SYWIN (SEQ ID NO: 40), GYTFTSY (SEQ ID NO: 41), or GYTFTSYWIN (SEQ ID NO: 42); (ii) a VH CDR2 comprising the sequence $NIX_1PSDSYSNYNX_2KFKD$ wherein X_1 is Y or F; X_2 is Q or K, or X_1PSDSY wherein X_1 is Y or F (SEQ ID NO: 52); and iii) a VH CDR3 comprising the sequence GSX_1FDY wherein X_1 is S or G (SEQ ID NO: 53); and/or

(b) a light chain variable region (VL) region complementary determining regions comprising (i) a VL CDR1 comprising the sequence RASQTIGTSIH (SEQ ID NO: 59); (ii) a VL CDR2 comprising the sequence YASESIS (SEQ ID NO: 60); and (iii) a VL CDR3 comprising the sequence X_1QSX_2SWPFT wherein X_1 is Q or S; X_2 is N or F (SEQ ID NO:64).

11. An isolated antibody, or an antigen binding fragment thereof, which specifically binds to Trop-2, wherein the antibody comprises:

a VH region comprising a VH CDR1, VH CDR2, and VH CDR3 of the VH sequence shown in SEQ ID NO: 13; and/or

a VL region comprising VL CDR1, VL CDR2, and VL CDR3 of the VL sequence shown in SEQ ID NO: 12.

12. The antibody or the antigen binding fragment of claim 11, wherein the VH region comprises (i) a VH CDR1 comprising the sequence SYWIN (SEQ ID NO: 40), GYTFTSY (SEQ ID NO: 41), or GYTFTSYWIN (SEQ ID NO: 42); (ii) a VH CDR2 comprising the sequence NIFPSDSYSNYNKKFKD (SEQ ID NO: 46) or FPSDSY (SEQ ID NO: 47); and (iii) a VH CDR3 comprising the sequence GSGFDY (SEQ ID NO: 48).

13. The antibody or antigen binding fragment of claim 12, wherein the VL region comprises (i) a VL CDR1 comprising the sequence RASQTIGTSIH (SEQ ID NO:

59); (ii) a VL CDR2 comprising the sequence YASESIS (SEQ ID NO: 60); and (iii) a VL CDR3 comprising the sequence SQSFSWPFT (SEQ ID NO: 62).

14. The antibody or the antigen binding fragment of claim 13, wherein the VH region comprises the sequence shown in SEQ ID NO: 13 or a variant with one or several conservative amino acid substitutions in residues that are not within a CDR and/or the VL region comprises the amino acid sequence shown in SEQ ID NO: 12 or a variant thereof with one or several amino acid substitutions in amino acids that are not within a CDR.

15. The antibody or the antigen binding fragment of claim 14, wherein the antibody comprises a light chain comprising the sequence shown in SEQ ID NO: 68 and a heavy chain comprising the sequence shown in SEQ ID NO: 67.

16. An isolated antibody which specifically binds to Trop-2 and competes with the antibody of claim 2 or 4.

17. The antibody of claim 16, wherein the antibody has a monovalent antibody binding affinity (K_D) of about 6.5 nM or less as measured by surface plasmon resonance.

18. The antibody of any one of claims 1-15, wherein the antibody comprises an acyl donor glutamine-containing tag engineered at a specific site.

19. The antibody of claim 18, wherein the tag comprises an amino acid sequence GGLLQGG (SEQ ID NO: 78), LLQGA (SEQ ID NO:79), or LLQ.

20. The antibody of claim 19, wherein the antibody further comprises an amino acid modification at position 222, 340, or 370.

21. The antibody of claim 20, wherein the amino acid modification is a substitution from lysine to arginine.

22. A conjugate of the antibody or the antigen binding fragment of any one of claims 1-15 and 18-21, wherein the antibody or the antigen binding fragment is

conjugated to an agent, wherein the agent is selected from the group consisting of a cytotoxic agent, an immunomodulating agent, an imaging agent, a therapeutic protein, a biopolymer, and an oligonucleotide.

23. The conjugate of claim 22, wherein the agent is a cytotoxic agent.

24. The conjugate of claim 23, wherein the cytotoxic agent is MMAD (Monomethyl Auristatin D) or 0101 (2-methylalanyl-*N*-[(3*R*,4*S*,5*S*)-3-methoxy-1-{(2*S*)-2-[(1*R*,2*R*)-1-methoxy-2-methyl-3-oxo-3-{[(1*S*)-2-phenyl-1-(1,3-thiazol-2-yl)ethyl]amino}propyl]pyrrolidin-1-yl}-5-methyl-1-oxoheptan-4-yl]-*N*-methyl-L-valinamide).

25. The conjugate of claim 24, wherein the conjugate comprises the formula: antibody-(acyl donor glutamine-containing tag)-(linker)-(cytotoxic agent).

26. The conjugate of claim 25, wherein the acyl donor glutamine-containing tag comprises an amino acid sequence GGLLQGG (SEQ ID NO: 78), LLQGA (SEQ NO: 79), LLQ, or $LLQX_1X_2X_3X_4X_5$, wherein X_1 is G or P, wherein X_2 is A, G, P, or absent, wherein X_3 is A, G, K, P, or absent, wherein X_4 is G, K, or absent, and wherein X_5 is K or absent (SEQ ID NO: 88), and wherein the linker comprises acetyl-lysine-valine-citrulline-*p*-aminobenzyloxycarbonyl or amino-PEG6-propionyl.

27. The conjugate of claim 26, wherein the conjugate is selected from the group consisting of 1) antibody-LLQGA (SEQ ID NO: 79)- (acetyl-lysine-valine-citrulline-*p*-aminobenzyloxycarbonyl (AcLys-VC-PABC))-0101; 2) antibody-LLQGA (SEQ ID NO: 79)-(AcLys-VC-PABC)-MMAD; 3) antibody-$LLQX_1X_2X_3X_4X_5$ (SEQ ID NO: 88)-(AcLys-VC-PABC)-0101; 4) antibody-$LLQX_1X_2X_3X_4X_5$ (SEQ ID NO: 88)-(AcLys-VC-PABC)-MMAD; 5) antibody –GGLLQGG (SEQ ID NO: 78)- (AcLys-VC-PABC)-0101; and 6) antibody–GGLLQGG (SEQ ID NO: 78)-(AcLys-VC-PABC)-MMAD.

28. The conjugate of claim 27, wherein the conjugate 1) antibody –GGLLQGG (SEQ ID NO: 78)-(AcLys-VC-PABC)-0101; 2) antibody–GGLLQGG (SEQ ID NO: 78)-(AcLys-VC-PABC)-MMAD; 3) antibody-$LLQX_1X_2X_3X_4X_5$ (SEQ ID NO: 88)-(AcLys-VC-PABC)-0101; 4) antibody-$LLQX_1X_2X_3X_4X_5$ (SEQ ID NO: 88)-(AcLys-VC-PABC)-MMAD;

5) antibody-LLQGA (SEQ ID NO: 79)-(AcLys-VC-PABC)-0101; or 6) antibody-LLQGA (SEQ ID NO: 79)- AcLys-VC-PABC-MMAD comprises an amino acid substitution from lysine to arginine at position 222.

29. The conjugate of claim 27, wherein the conjugate 1) antibody-LLQGA (SEQ ID NO: 79)-(AcLys-VC-PABC)-0101; 2) antibody-LLQGA (SEQ ID NO: 79)-AcLys-VC-PABC-MMAD; 3) antibody-LLQ$X_1X_2X_3X_4X_5$ (SEQ ID NO: 88)-(AcLys-VC-PABC)-0101; or 4) antibody-LLQ$X_1X_2X_3X_4X_5$ (SEQ ID NO: 88)-(AcLys-VC-PABC)-MMAD, wherein the amino acid lysine at the C-terminus of heavy chain of the antibody is deleted.

30. The conjugate of claim 24, wherein the conjugate comprises amino acid substitutions at position N297Q and K222R, a linker comprising amino-PEG6-propionyl, and a cytotoxic agent comprising MMAD.

31. A pharmaceutical composition comprising a therapeutically effective amount of the antibody of any one of claims 1-15 or the conjugate of any one of claims 22-30 and a pharmaceutically acceptable carrier.

32. An isolated polynucleotide comprising a nucleotide sequence encoding the antibody of any one of claims 1-15.

33. A vector comprising the polynucleotide of claim 32.

34. An isolated host cell that recombinantly produces the antibody of any one of claims 1-15.

35. A method of producing an antibody, comprising culturing the host cell of claim 34 under conditions that result in production of the antibody, and isolating the antibody from the host cell or culture.

36. The pharmaceutical composition of claim 31 for use in the treatment of a condition associated with Trop-2 expression in a subject in need thereof.

37. The composition of claim 36, wherein the condition is a cancer.

38. The composition of claim 37, wherein the cancer is selected from the group consisting of bladder, breast, cervical, choriocarcinoma, colon, esophageal, gastric, glioblastoma, head and neck, kidney, lung, oral, ovarian, pancreatic, prostate, and skin cancer.

39. The pharmaceutical composition of claim 31 for use in the treatment of inhibiting tumor growth or progression in a subject who has a Trop-2 expressing tumor.

40. The pharmaceutical composition of claim 31 for use in the treatment of inhibiting metastasis of Trop-2 expressing cancer cells in a subject need thereof.

41. The pharmaceutical composition of claim 31 for use in the treatment of inducing regression in a subject who has a Trop-2 expressing tumor.

42. Use of the pharmaceutical composition of claim 31 in the manufacture of a medicament for the therapeutic and/or prophylactic treatment of a condition associated with Trop-2 expression in a subject in need thereof.

43. The use of claim 42, wherein the condition is a cancer.

44. The use of claim 43, wherein the cancer is selected from the group consisting of bladder, breast, cervical, choriocarcinoma, colon, esophageal, gastric, glioblastoma, head and neck, kidney, lung, oral, ovarian, pancreatic, prostate, and skin cancer.

45. Use of the pharmaceutical composition of claim 31 in the manufacture of a medicament for the therapeutic and/or prophylactic treatment of inhibiting tumor growth or progression in a subject who has a Trop-2 expressing tumor.

46. Use of the pharmaceutical composition of claim 31 in the manufacture of a medicament for the therapeutic and/or prophylactic treatment of inhibiting metastasis of Trop-2 expressing cancer cells in a subject need thereof.

47. Use of the pharmaceutical composition of claim 31 in the manufacture of a medicament for the therapeutic and/or prophylactic treatment of inducing regression in a subject who has a Trop-2 expressing tumor.